Enabling Chip Characterization & Providing Chip Information

Characterizing fluid flow in a microphysiological system using PIV-experiments, Lattice-Boltzmann and COMSOL Multiphysics simulations and creating a tool to provide this information to users with a scenario-based rapid-prototyping co-creation process.

Joris Kaal

377

UNIVERSITY OF TWENTE.

TISSUSE
Emulating Human Biology

Enabling Chip Characterization & Providing Chip Information

Characterizing fluid flow in a microphysiological system using PIV-experiments, Lattice-Boltzmann and COMSOL Multiphysics simulations and creating a tool to provide this information to users with a scenario-based rapid-prototyping co-creation process

Master thesis by

Joris Kaal
August 4, 2021

Chair of Engineering Fluid Dynamics
Department of Mechanical Engineering

and

Chair of Biomechanical Engineering
Department of Industrial Design Engineering

Faculty of Engineering Technology
University of Twente, Enschede

Exam committee:
Prof. dr. ir. C.H. Venner
Dr. K. Jain
Ir. E.E.G. Hekman
Felix Rambo MSc.

Summary

Newly developed microfluidic microphysiological systems form a great opportunity for drug development, disease modelling and toxicological analyses. They are chips with the size of a credit card with microchannels and compartments for fluidics inside of them. These channels and compartments are housing and connecting different organ models. Such systems are a leap forward in terms of replicating the complicated, interconnected and interdependent human physiology compared to current animal or in-vitro models. Berlin-based company TissUse GmbH is one of the pioneers in this field.

Different cells, such as donor cells and induced pluripotent stem cells, are the building blocks of the organs in a microphysiological system. These cells are developed into the desired configuration and are highly sensitive to their environment. They are put into the chips as single cells. The environment and flow in the system then causes them to self-organize into a specific structure such as a blood vessel or a spheroid. To increase cell-survival, controllability and reproducibility of experiments, users would like to know the fluidic circumstances in the chip.

To this end, this study combines µPIV experiments, Lattice-Boltzmann simulations and simulations using COMSOL Multiphysics to find a way to characterize the flow in TissUse's multi-organ microphysiological systems. Consequently, the data that this generates should be presented properly to the users of these systems. To this end a tool is developed that can do precisely that. The adapted design process can be described as a scenario-based rapid-prototyping co-creation process. It combines the user's needs and wishes with company philosophy and an elaborate study of UI design and information visualization. End users participated in every step and tested the final prototype.

Three methods to characterize the microphysiological systems were applied to TissUse's HUMIMIC Chip2 96-Well. Their results are compared. This leads to the conclusion that although COMSOL performed slightly better, neither LBM nor COMSOL Multiphysics were – with the current simulation setup – able to adequately represent the flow in a real chip. The flow out of the chip's pump is properly transferred to simulations though.

Furthermore, the prototype for the flow characteristics tool was perceived as clear, good-looking and functioning properly. Using the feedback from the user tests, it can be even further improved. Once this tool will actually be programmed, it is confidently expected that it will indeed deliver the desired information most conveniently and suitably to end users.

Recommendations for the continuation of this project include; TissUse should expand its µPIV activities on their chips as it currently is the best way to understand the microfluidic flow. To make simulation a competitive method as well, it is recommended to focus on COMSOL Multiphysics. Here, mesh generation and air-liquid interface need some attention. The tool that would represent flow characteristics is expected to be ready for development after one final improvement round. Specific improvements are incorporated in this work.

Daily supervisor from TissUse's side is Felix Rambo MSc. His supervision is complemented by ir. Edsko Hekman (University of Twente, Industrial Design Engineering) and Dr. Kartik Jain (University of Twente, Mechanical Engineering). Final supervisor from the University of Twente is Prof.dr.ir. Kees Venner.

Acknowledgements

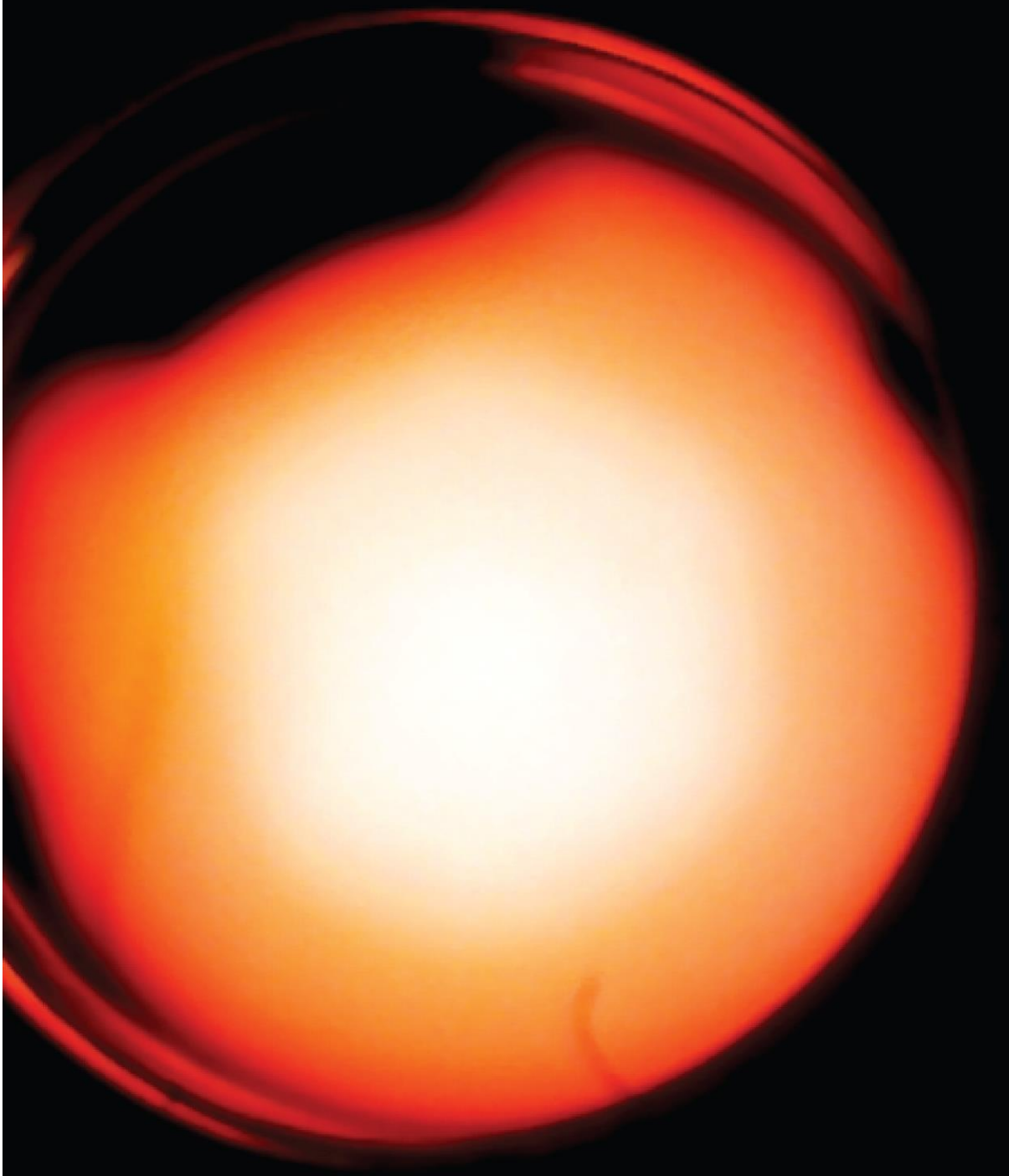
First and foremost, I would like to thank my daily supervisor at TissUse, Felix Rambo. I am very thankful that you have been my supervisor during this project. Your expertise and kindness have helped and guided me a lot within the project and outside of it.

Secondly, I owe a word of gratitude to my academic supervisors dr. Kartik Jain and ir. Edsko Hekman. Thank you both for your guidance and support.

Finally, I would like to deeply thank my friend and study-buddy Lisanne Grevinga for being there almost every day for the past year. A rough estimate puts us on 944 Skype-working-hours together. I am thankful for every minute of it. Without your online presence it would have been a rough year.

Table of contents

1.
Introduction



1. Introduction

1.1. TissUse and its organs

There is a myth surrounding the first emperor of China, Qin Shihuang. The man that ordered the creation of the famous terra cotta army and unified large portions of what is now known as the Great Wall of China (Encyclopaedia Britannica, 2021), supposedly died after consuming mercury pills. The pills were developed specifically to make him immortal (Wright, 2000).

Nowadays luckily, drug development and toxicological studies have improved a lot, so if there were any emperors around today, they would not have to worry about mercury pills anymore. However, modern pharmaceutical industry is not flawless yet. A significant problem they have is that current methods of testing drugs still leads to worrying failure rates in their clinical studies (FDA, 2004).

Before a drug goes up for approval by the EMA or FDA it goes through several development phases (FDA, 2018). In the first phase thousands of compounds can be tested to see if any of them have some effect against a certain disease. Then a small number of those continues into the second phase, the pre-clinical trials, which is when the lab testing and animal testing take place. Once a compound survived this phase it can continue to the third phase. Here drugs are tested on people. These are the clinical studies. Once a drug makes it through this phase, a request for approval will be delivered at the authorities.

According to a study in 2016 across over 1100 companies with FDA-approval enabling programs, the chance of a compound to make it through all the phases of drug development was rather low (Thomas et al., 2016, p. 8). Figure 1-1 goes to show the likelihood that a compound in the first phase will eventually make it to an approved drug. This likelihood of approval is different for different medicinal categories that the study distinguished. Similar numbers are projected by several other studies (Mikulic, 2021; Retzios, 2009). Overall, about half of the drugs that already made it all the way to the clinical trials will eventually make it to approval and become available to use by the public (Thomas et al., 2016, p. 9).

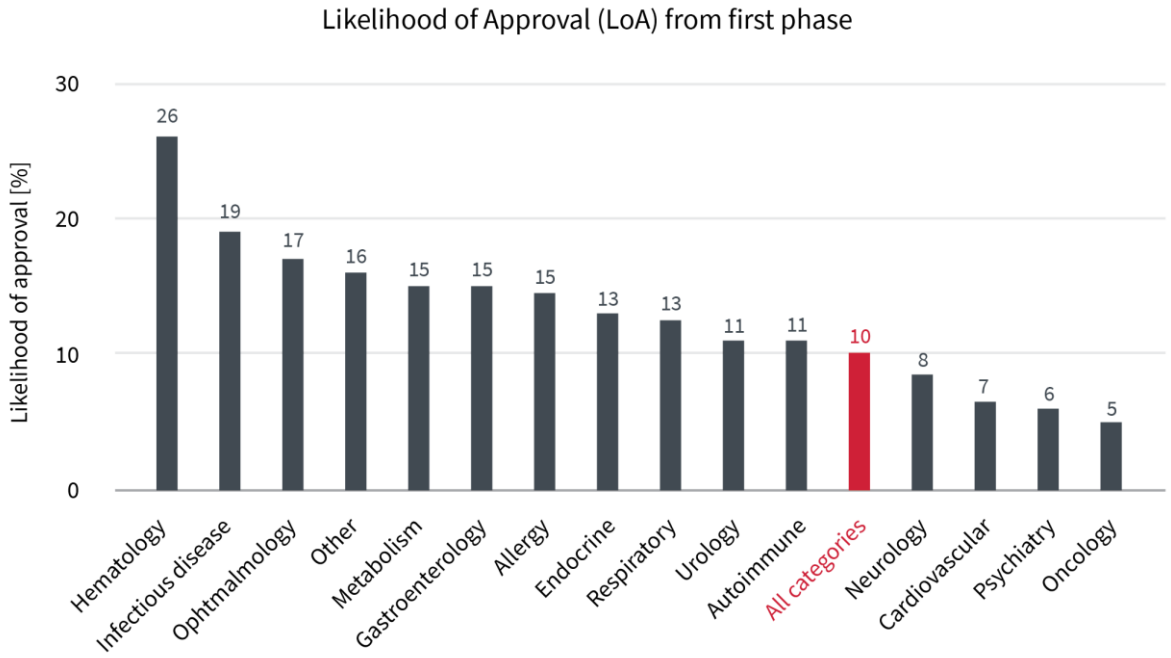


Figure 1-1 – Selection of the success rates of compounds in the first phase to approval and release to the public. Image redrawn based on (Thomas et al., 2016, p.8)

An important contributor to these low success rates is the methods with which drugs are nowadays developed. The clinical trials are the first point at which a compound comes into contact with a living human. Until then it has only been tested either in-vitro with cell cultures and on animals. Both these methods have serious drawbacks. The cell cultures are made of human cells as opposed to animals. This way the model would be representative of a human. However, human tissue is scarce, it degenerates relatively quickly and the cell cultures are mostly 2D models. It does hence not incorporate a correct physical microstructure. Hence, pharmaceutical companies have to opt for animal testing. Animal testing is more readily available, has a microstructure and the cells do not decay as much. However, the translation of pathologies and cell-behaviour from animals to humans is rather poor. This is because animal physiology is not representative of human physiology. Besides, the on-going ethical debate surrounding animal testing is a disadvantage.

On top of the marginal success rates in the drug-development process, the FDA expressed worries about the soaring costs of drug development already two decades ago (FDA, 2004). As Figure 1-2 shows, the trend in spending of pharmaceutical companies, which is considered a good indication of the cost of drug development, has continued in recent years.

This increase in budget has sadly not returned in number of effective treatments (Congressional Budget Office, 2021, p. 7). This is hampered by the low success rates of the development process. An example that neatly portrays this obstacle is the following: It just so happens that the discipline where investments increased the most is oncology (Congressional Budget Office, 2021, p. 8). At the same time this is the discipline that has the lowest developmental success rate in Figure 1-1.

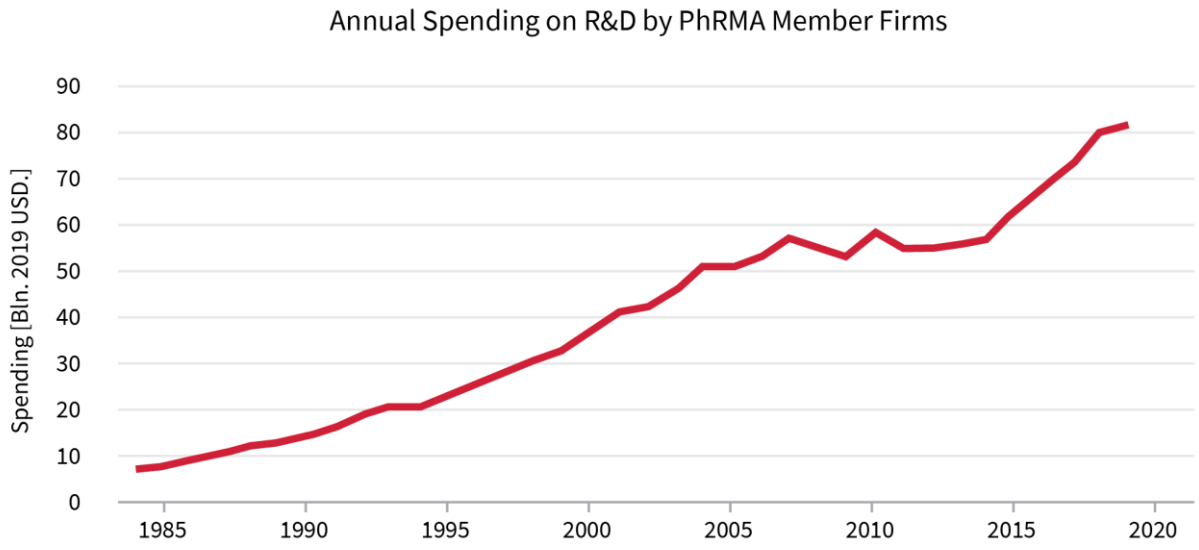


Figure 1-2 - Increasing trend in the R&D spending of pharmaceutical companies that are member of PhRMA over time Image redrawn based on (Congressional Budget Office, 2021, p. 7).

The recent development of microfluidic microphysiological systems might be a solution the problems of the pharmaceutical industry. These systems are also known under the name Organ-on-a-Chip. They are called so, because they comprise of “chips” with human organ models inside. Have a look at Figure 1-3 for an idea of what that means. The chips are not electronic chips, but microfluidic chips. They come in different shapes and sizes, but the ones used in this study are about the size of a credit card and several millimetres thick. Commonly made of Polycarbonate, PDMS or glass, they have channels and compartments inside of them. The channels have a cross-section usually smaller than a millimetre and are filled with liquid. Hence these Organs-on-a-Chip are referred to as microfluidic systems. It is the compartments that house the organ models: small models that replicate the physiological

microstructure of organs in a human. The channels aim to replicate blood or lymph circulation. Say for example you have a lung model and a liver model, both in their own compartment. You could expose the lung model to smoke, this would get absorbed in the systems blood circulation and can get carried towards the liver model. Then you could see what the influence of inhaled smoke is on the liver model. This is what gives Organs-on-a-Chip the classification of microphysiological systems. They aim to mimic a physiological system at a microscale.

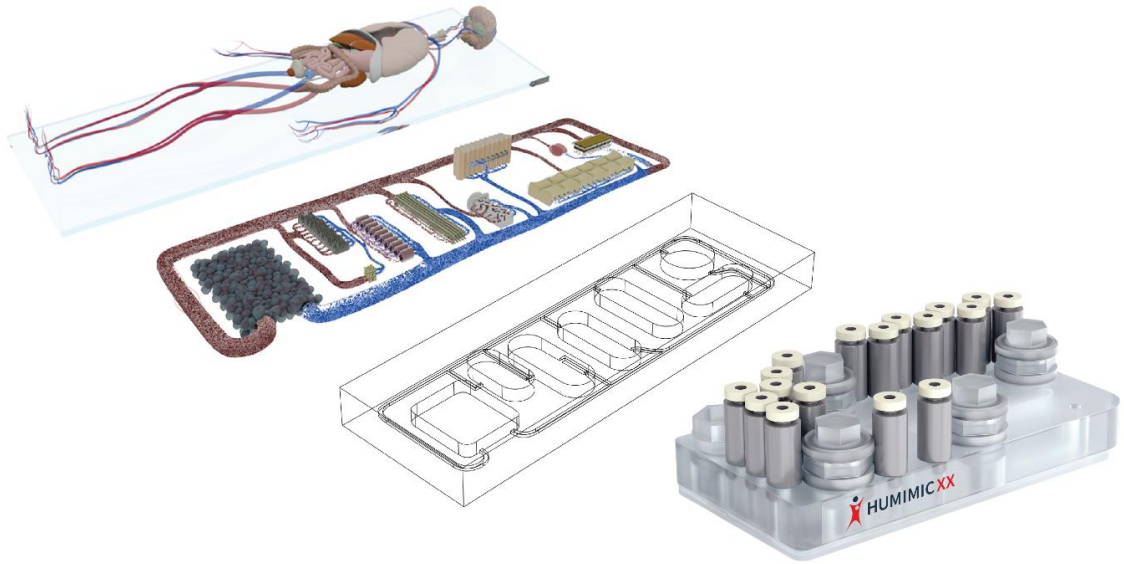


Figure 1-3 - A microphysiological system consists of models of organs that are interconnected through microchannels inside a chip. One starts with a real human at the top left. Next is a schematic visual of the organ models. Then a rather simplified schematic of the microfluidic structure. At the bottom right is an example of an actual microphysiological system. Combined images from TissUse GmbH.

Researchers use several different types of cells as building blocks of the organ models in a microphysiological system. Examples include donor cells, cell lines and induced pluripotent stem cells. Stem cells are cells that have not yet been differentiated into a specific type of cell, such as a lung- or a liver-cell. This means they could potentially still differentiate to any kind of cell, which makes them pluripotent (multi-capable). In the human body they are somewhat rare and hard to obtain. Several years ago Shinya Yamanaka and John Gurdon won a Nobel-prize for their discovery that normal differentiated cells from a human body could be treated such that they would become these pluripotent stem cells again (Nobel Prize Outreach AB, 2021). So, microphysiological systems do not use just pluripotent stem cells, but induced pluripotent stem cells.

As one might imagine, these cells do not magically turn into a lung-cell or lung-model when they are put in the compartment that is labelled “lung-model”. They are inserted into a system as single cells. Under influence of the flow and circumstances inside a system they self-organize into structures, such as a blood vessel or a liver spheroid. A series of detailed steps makes sure that the environment in the chips is exactly right for the specific organ model. For their survival and proper development, the cells are highly sensitive to their environment.

A small linguistic difference between an Organ-on-a-chip and a microphysiological system, is that an Organ-on-a-Chip consists of one organ model. A microphysiological system is a broader term that includes systems connecting several organ models together. All Organs-on-a-Chip could be categorized as a microphysiological system, but a microphysiological system can consist of several Organs-on-a-Chip.

One of the pioneers in the field of microphysiological systems is the German company TissUse GmbH. A start-up/scale-up with around thirty employees and a number of master students located in Berlin. In 2010 Dr. Uwe Marx, together with a number of cofounders, started the company. Their goal was to establish a paradigm shift in drug development. They intended to achieve this with the creation of what they called “Chippatienten”; miniature in-vitro models of a patient cultured out of donated human tissue. They can accurately represent the physiology and pathology of a patient without consciousness or the ability to feel pain. They avoid the opposing disadvantages of current in-vitro and animal testing and only combine their advantages, see .

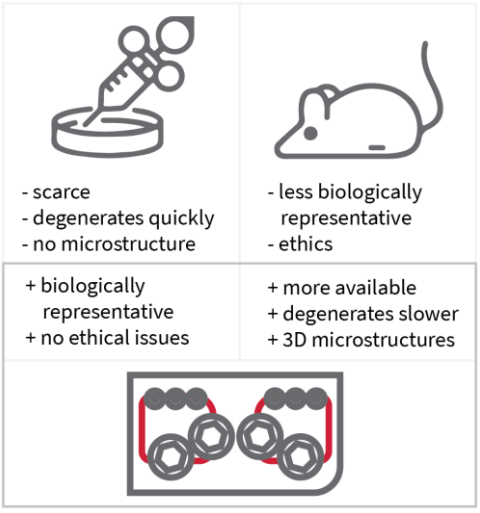


Figure 1-4 - Advantages and disadvantages of in-vitro and animal testing. Showing Organs-on-a-Chip, or microphysiological systems combining only the advantages of both methods.

With these advantages TissUse expects these Patients-on-a-Chip, or microphysiological systems, to be able to largely replace animal testing and testing on healthy humans. This might lead to a paradigm shift which they themselves visualize as in Figure 1-5.

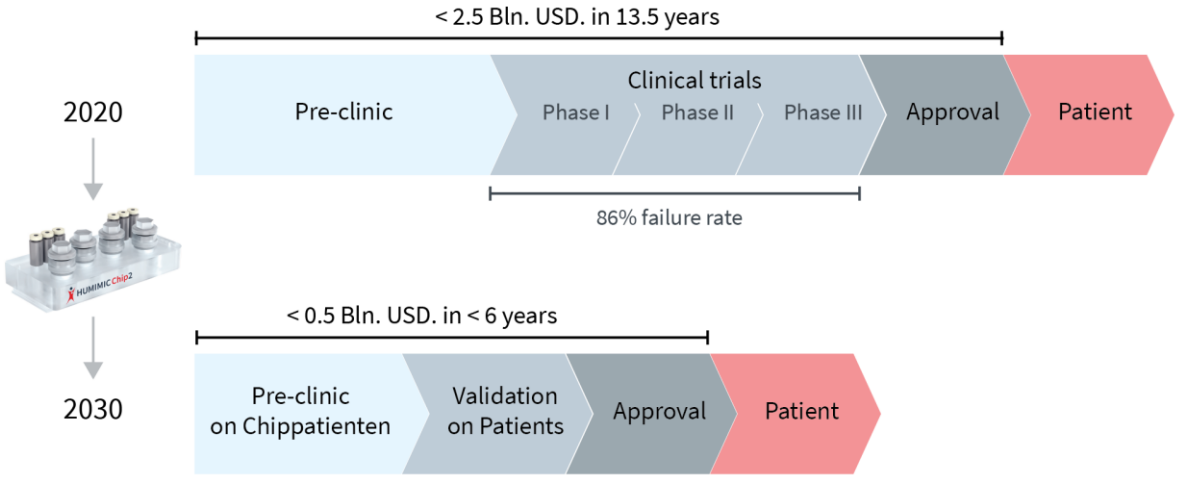


Figure 1-5 - Intended paradigm switch in drug development that microphysiological systems could initiate. Image taken from the Firmenhandbuch of TissUse GmbH.

The changes in Figure 1-5 neatly collide with the problems that the pharmaceutical industry currently faces. Microphysiological systems like those from TissUse might solve the problems of increasing costs and low success rates.

The concept of microphysiological chip patients has now been shaped into products that TissUse develops and markets. TissUse put in a lot of labour to create good organ-models and is currently able to emulate more than fifteen different organs. Together with stem cells, protocols and assistance they can provide clients with their microphysiological systems, called chips from now on, and their necessary accessories. If a researcher wants to do a specific study – also called assay – TissUse is nowadays so comfortable with their technology that they can help create custom chip designs and organ models.

Like said before, one can combine multiple organs into a microphysiological system. The number of organs that researchers want to combine depends on the application. The most extensive one is ChipXX/XY which can house around ten organ models. It is the one shown in Figure 1-3. More common are chips with for example three or four organ models. These are appropriately called Chip3 and Chip4. The most commonly used chip is Chip2 96-Well. Figure 1-6 shows a few of TissUse's chips.

Figure 1-6 - A selection of TissUse's microphysiological systems. From left to right, HUMIMIC Chip4, HUMIMIC Chip3 and the most commonly used HUMIMIC Chip2 96-Well. Images from TissUse GmbH.

Chip2 96-Well is a chip with two compartments, that can each house one organ model. Have a look at Figure 1-7 for reference. These compartments are connected by means of microchannels (500 x 100 µm) which creates a circuit. In this circuit, fluid circulates with nutrients for culturing the cells, called culture-medium or medium. This circulation is controlled by a peristaltic pump. A peristaltic pump functions similarly to how people milk a cow or how or intestines push digested food forwards. One progressively squeezes or closes the channel in one direction.

The pump in Chip2 96-Well (and the other TissUse chips for that matter) is integrated in the chip's circuit and consists of three cavities with membranes above them. The membranes are thin (500 µm) and made of PDMS, which is a flexible plastic. This allows them to deflect up and down. The membranes are pneumatically actuated by a TissUse Control Unit, shown in Figure 1-8. Via the TCU the user can set the frequency and pressure with which the pump in the chip is actuated.

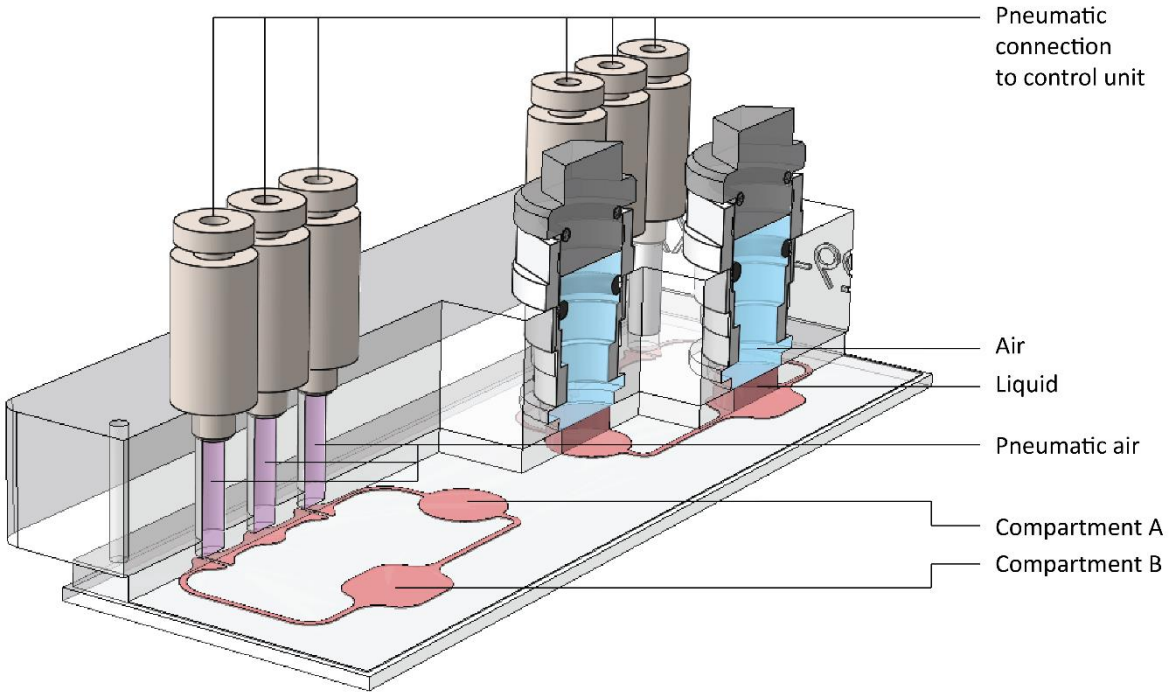


Figure 1-7 - An overview of the microfluidics inside Chip2 96-well.

Figure 1-8 - TissUse Control Unit (TCU) connected to a Chip2 96-Well. The TCU actuates the pumps in the chip pneumatically via the tubes.

A membrane is pushed down when an overpressure is applied to it from the TCU. This way it closes the channel and empties its cavity of liquid. A membrane goes up when the control unit applies a vacuum. This way the cavity opens up again and liquid is naturally pulled towards it. The pump and control unit have four strokes. Let's assume that the circuit is filled with medium, the channels and the pump are full. One pump cycle, as shown in Figure 1-9, can then be described as:

1. The left membrane closes.
2. The left membrane is still closed. The middle (main and largest) membrane closes.
3. The left membrane opens. The right membrane also closes simultaneously. The main membrane remains closed.
4. The main membrane opens again. The right membrane stays closed.
5. The left membrane closes again (the right membrane opens simultaneously)

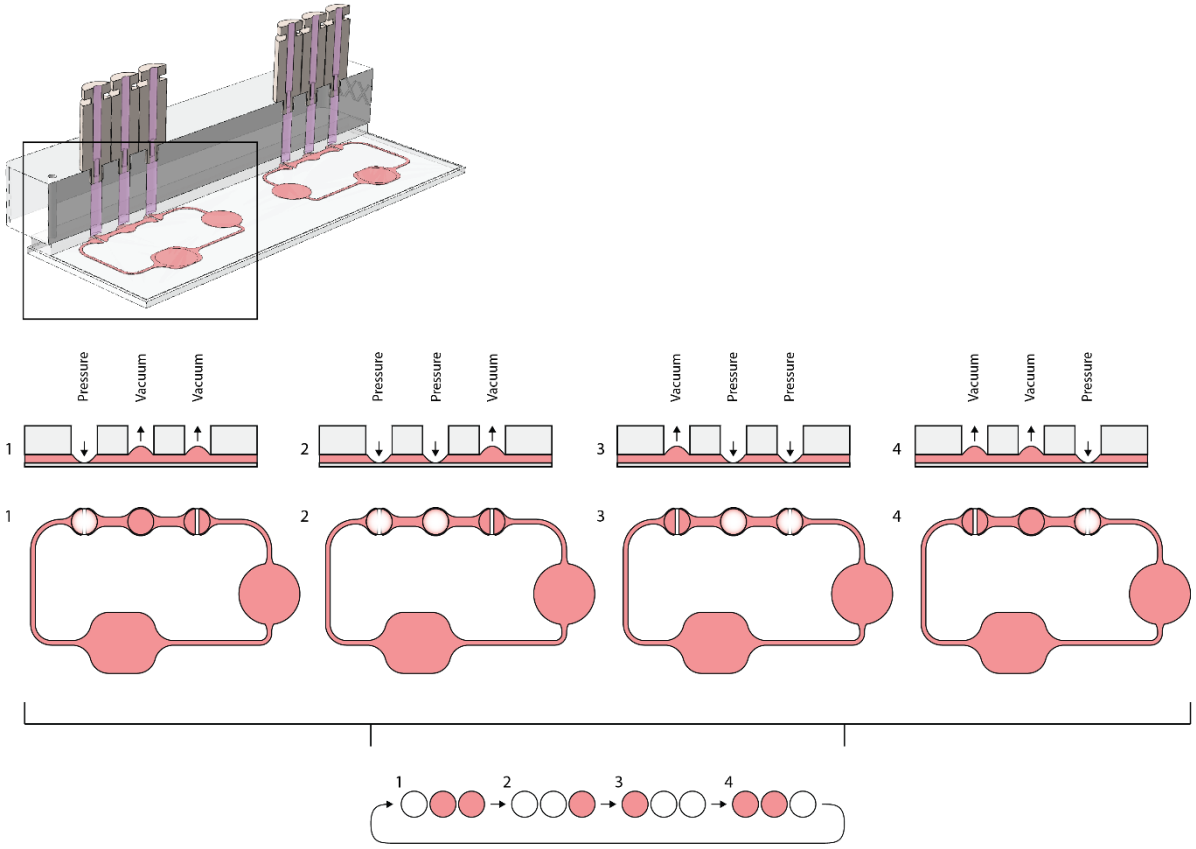


Figure 1-9 - Visualization of how the pump cycle in a TissUse chip looks. Membranes move up and down due to pneumatic air from the Control Unit creating a pulsatile pump.

1.2. Goal

The context surrounding this thesis has now been set. This context yields two subsequent goals for this thesis, which will be established now.

1.2.1. Enabling chip characterization

Ten years ago, TissUse started as a multi-organ-chip developer. This means they create chips that cultivate several organ models simultaneously. Each organ model has its own compartment. These compartments are all connected by microchannels to form a closed microfluidic circulatory system. A peristaltic pump creates a pulsatile flow through this system. The pump and the microfluidics have a strong influence on the behaviour of the flow. The flow in its turn heavily affects the behaviour of the organ models. Currently, TissUse aims to have a more thorough understanding of the flow in their chips and the interaction of the flow with different geometrical, physical and biological parameters.

Once TissUse obtains this understanding, they will be able to provide clients with vital information regarding shear stresses and flow velocities in the chips. With such knowledge TissUse themselves will be able to perform better assays as well. Apart from improved application of the chips, the development of chips can become more effective and efficient. Especially for this latter aspect it would be convenient not to need a physical prototype of any microfluidic chip.

The goal is to create a validated method to characterize and simulate the flow in any possible chip design without the need of a physical prototype.

1.2.2. Providing chip information

The product and service portfolio of TissUse unites under the HUMIMIC brand. This includes the multi-organ chips (e.g. HUMIMIC Chip2 96-Well), pump units (e.g. the HUMIMIC Starter), cell models (e.g. HUMIMIC iPSCs or HUMIMIC Hepatocytes), matching software, accessories and services. With the HUMIMIC brand, TissUse provides everything users need to run pharmacological assays on the multi-organ chips from start to finish.

As 1.2.1 suggested, TissUse can use data from the characterization of the chips to strengthen its customer support. They can provide their clients and own in-house researchers with knowledge of the fluid flow in the microchannels. This can help them improve their studies in many ways. The desired form of this information is dependent on the situation at hand.

Delivering the desired information about the physical circumstances in a chip in the most convenient and suitable way is very valuable. Hence, the goal of this thesis is to develop such a service and incorporating it in the HUMIMIC product portfolio.

1.3. Outline

This report has the intention to be able to function as a reference work for anyone continuing with the project. If/when TissUse continues with this project, anyone new to any of the relevant topics will hopefully have a good starting point at hand here.

The work can be divided into three parts: The background theory, the actual report and the appendices. Figure 1-10 is an attempt to visualize the description of the structure that follows now.

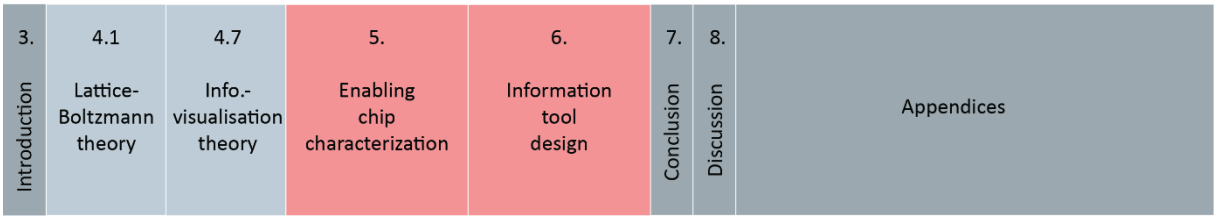


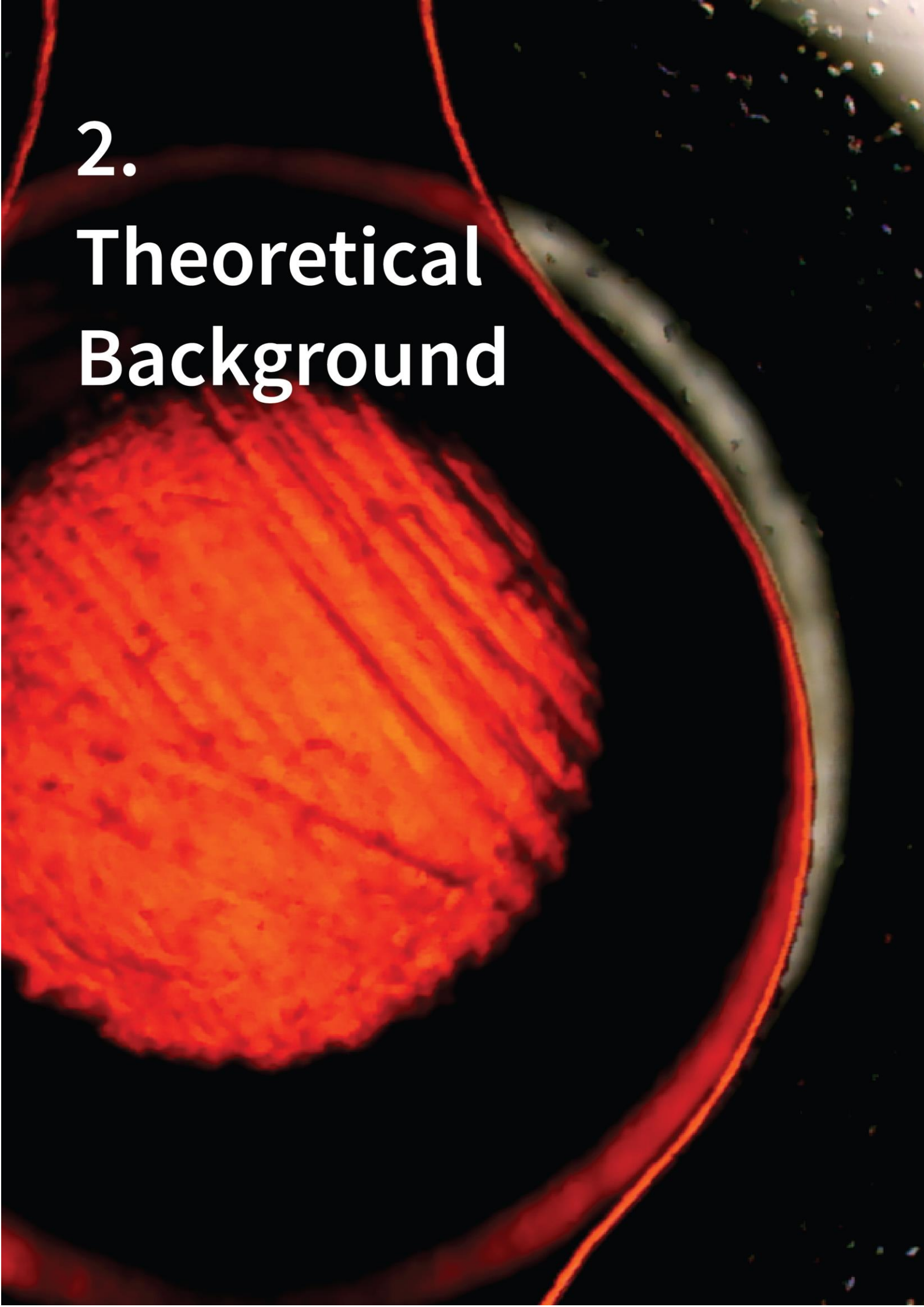
Figure 1-10 - The global structure of this report.

Chapter 2 contains the theoretical background. Its first half discusses topics considering the flow characterization. Starting with the basics of fluid dynamics in 2.1 it builds up to an explanation of the lattice Boltzmann method (2.4) the simulation software (2.5) and µPIV (2.6). The second half of the background theory delves into information visualization (2.7) and user interface design (2.8).

After the theoretical background is established, Chapter 3 and 4 report on the processes, results and conclusions of enabling the characterization of the flow in the chip (Chapter 3) and the design of tool to present that information (Chapter 4). Chapter 5 then draws the main conclusions and Chapter 6 discusses recommendations and room for improvement.

The largest part of this work consists of the appendices. These are reference for further research and continuation of the project. For a complete list of the appendices have a look at the Table of contents.

If you are interested in the characterization of the flow and not familiar with the lattice Boltzmann method I would recommend reading the theory in 2.3 – 2.6 and then continue to Chapter 3. If you are interested in the development of the tool to visualize and provide information, start reading the background theory from 2.7 onwards. If you are already familiar with information visualization or User Interface design, you could continue directly to the report in Chapter 4. Anyone unfamiliar with TissUse GmbH or microphysiological systems in general and who has not already done so might benefit from reading the introduction that precedes this paragraph.



2. Theoretical Background

2. Theoretical background

2.1. Basics of fluid dynamics

Although widely applicable, the lattice Boltzmann method is mainly used for fluid mechanical purposes. The intended use in this thesis will be on microfluidic calculations. Hence, it is useful to regard some basic fluid mechanical concepts. The knowledge in this paragraph is based on (Krüger et al., 2017). In this book they state that five equations are needed to describe the entire state of a fluid. These are: the continuity equation, the Navier-Stokes equations and an equation of state. Each of these will be shortly explained.

2.1.1. Continuity equation

The continuity equation prescribes the conservation of mass. Let's assume a volume of fluid. The mass in this fluid element can only change due to the flow of molecules into or out of this element. Mathematically, for a fluid element with volume V and surface area A this comes down to:

$$\frac{d}{dt}\int_V \rho \, dV = -\oint_A \rho \boldsymbol{u} \, dA \qquad 2\text{-}1$$

Here, ρ is the density of the fluid element is, $\boldsymbol{u}$ is the fluid velocity and the outward normal is used at the surface of the fluid element. Via the divergence theorem this turns into the continuity equation:

$$\frac{d\rho}{dt} + \boldsymbol{\nabla} \cdot (\rho \boldsymbol{u}) = 0 \qquad 2\text{-}2$$

2.1.2. Navier-Stokes equation

Besides regarding the mass in a fluid element one can regard the momentum in a fluid element as well. Analogously to the density, one can establish due to which factors the momentum in a fluid element could change. The momentum in a fluid element changes due to:

1. Flow of momentum into the fluid element
2. Pressure fluctuations
3. External body forces

Mathematically, for a fluid element of volume V with surface area A this comes down to the following terms respectively:

$$\frac{d}{dt}\int_V \rho \boldsymbol{u} \, dV = -\oint_A \rho \boldsymbol{u}\boldsymbol{u} \, dA - \oint_A p \, dA + \int_V \boldsymbol{F} \, dV \qquad 2\text{-}3$$

Where ρ is the density of the fluid element, $\boldsymbol{u}$ is the fluid velocity, p is the pressure on the fluid element and $\boldsymbol{F}$ denotes the vector of external body forces. The outward normal is used at the surface of the fluid element. Also, this equation can be altered and via the divergence theorem this turns into the Euler equation of an ideal fluid:

$$\frac{d(\rho \boldsymbol{u})}{dt} = -\boldsymbol{\nabla}\rho \boldsymbol{u}\boldsymbol{u} - \boldsymbol{\nabla} p + \boldsymbol{F} \qquad 2\text{-}4$$

Through a series of mathematical steps this equation eventually translates to the Navier-Stokes equations. If one makes the assumptions of constant viscosity and constant density with the incompressible Navier-Stokes equations:

$$\rho \frac{D\boldsymbol{u}}{Dt} = -\boldsymbol{\nabla} p + \eta \Delta \boldsymbol{u} + \boldsymbol{F} \qquad 2\text{-}5$$

Where Δ is the Laplace operator. Appendix A contains a different and extensive approach for the derivation of the Navier-Stokes equations. The interested reader is referred there.

2.1.3. Equations of state

Now there are four equations to describe the behaviour of a fluid element: one continuity equation and three Navier-Stokes equations. To describe the entire behaviour of a fluid there are however five unknowns (density, pressure, and three velocity components). Hence, the system of equations cannot be solved without fixing one of those variables.

Luckily there is the state principle of equilibrium of thermodynamics. This says that any state variable (for example pressure, temperature and entropy) describing the thermodynamic state of a fluid can be expressed by any combination of two other state variables. Equations of state do exactly that. They link one state variable to two others. The most well-known of these equations of state is the ideal gas law, which links the pressure to the density and temperature of a fluid. For completeness:

$$P = \frac{nRT}{V} \qquad 2\text{-}6$$

Adapted from (Khan Academy, 2021). Here P is the pressure of the gas, V is the volume it occupies, n is the number of moles of the gas, R is the gas constant and T is the gas' absolute temperature.

Equations of state mostly introduce an extra unknown variable (because it expresses one variable in two others). 2-6 introduces the temperature for example. Hence, this equation alone does not close the system of equations. There are three ways in which the equation of state can close the system of equations.

The first option: One can find an equation describing the behaviour of this extra introduced variable. This can be done from the energy equation, but leads to a rather cumbersome system of equations.

The second option follows from the fact that equations of state allow better application of approximations. For example, assuming that the system is nearly isentropic allows for the use of the isentropic equation of state, (Krüger et al., 2017, p. 7):

$$p = p_0 \left(\frac{\rho}{\rho_0}\right)^{\gamma} \qquad 2\text{-}7$$

Another option is if the system is close to isothermal around a certain temperature T_0. Then the equation of state can be simplified to the following form, which then actually does close the system, (Krüger et al., 2017, p. 7):

$$p = \rho R T_0 \qquad 2\text{-}8$$

As can be seen in 2-7 and 2-8 these simplified forms of the equations of state based on assumed approximations do not introduce an extra variable anymore. Hence they can close the system of equations that describes the full behaviour of the fluid.

A third and final option, for small deviations, one can linearize the non-linear equations of state, for example using the total derivative. This way closing the system of equations as well.

2.2. Basics of microfluidics

The protagonist of this thesis is a microfluidic chip. This means that the scale at which physics plays out is in the order of micrometres. At this level fluid starts to behave differently than people are used to in daily life. In the following paragraphs the vocabulary of relevant length scales is stated. After that the step from normal fluidics to microfluidics is taken, guided by the work of (Squires & Quake, 2005).

2.2.1. Relevant scales

Different sizes of systems ask for different types of simulations. Figure 2-1 (taken from (Krüger et al., 2017, p. 9) shows an order of different length scales. With them come different time relevant scales, shown in Table 1.

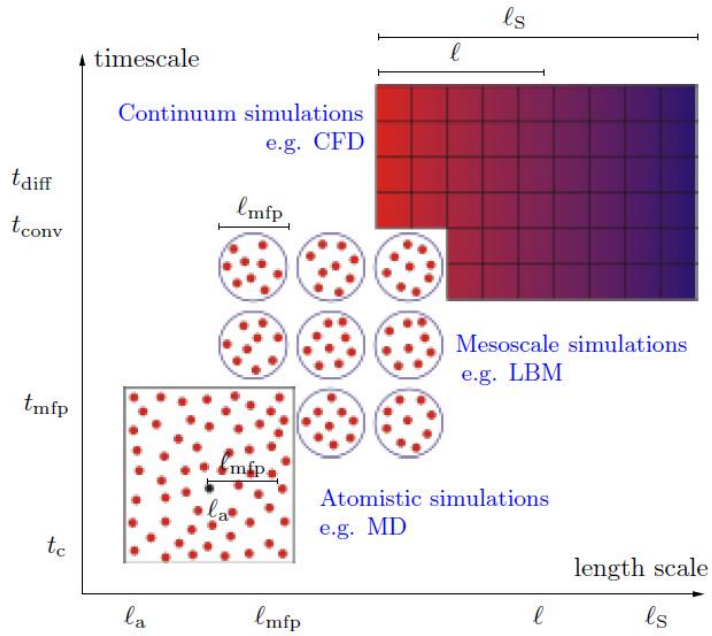


Figure 2-1 - Different time and length scales for fluidic systems. Showing also their appropriate simulation methods. Image from (Krüger et al., 2017, p. 9).

Characteristic length scale	Time scale
Atomic length	Collision time
Mean free path	Mean free flight time
Gradient length	-
System size	Convective and diffusive time scale Acoustic time scale

Table 1 - Different characteristic length scales and their relevant time scales in fluidic systems.

With microfluidic systems, the system size comes in the order of magnitude of the mean free path. As conveniently suggests this is where LBM is a preferred choice as it will consider physics on a similar scale. It considers populations of particles and their relaxation time. This will all be further explained later in 2.3 and 2.4.

2.2.2. From macro- to microfluidics

Just like the integrated circuit board revolutionized the way we computed things, microfluidics is expected to change the way we study biology, chemistry and medicine. A fundamental difference between the two revolutions is however, that integrated circuitry has only just reached a scale at which the physical laws commonly used do not apply anymore. At the scale of mean free paths and microfluidics common physical fluidic laws already start to break down.

For example: in a micro physiological system inertial effects are generally negligible and viscous effects determine the behaviour of the fluid. These inertial effects would normally cause nonlinearities and turbulence. This statement makes sense from a Reynolds number point of view as well. When the characteristic length becomes very small, the viscous term becomes relatively more important.

The example above showed that dimensionless number are well capable of explaining the different physics at macro and micro level. (Squires & Quake, 2005, p. 979) put it beautifully as: *'The essential fluid physics of a system is dictated by a competition between various phenomena, which is captured by a series of dimensionless numbers expressing their relative importance'*. Here below the different relevant dimensionless numbers will explain the differences between everyday fluid mechanics and microfluidics. Some directly incorporate a characteristic length, so their relevance is trivial. Others do not, but are still of importance. The complete list is shown in Figure 2-2 (taken from (Squires & Quake, 2005, p. 980)). It is recommended to keep referring to this list while reading the description of the dimensionless numbers. For all dimensionless numbers explained below (Squires & Quake, 2005) have elaborated as well. Any additional sources are mentioned for numbers that were less common in the eyes of the author.

Re	Reynolds	$\frac{\rho U_0 L_0}{\eta}$	inertial/viscous
Pe	Péclet	$\frac{U_0 L_0}{D}$	convection/diffusion
Ca	capillary	$\frac{\eta U_0}{\gamma}$	viscous/interfacial
Wi	Weissenberg	$\tau_p \dot{\gamma}$	polymer relaxation time/shear rate time
De	Deborah	$\frac{\tau_p}{\tau_{\text{flow}}}$	polymer relaxation time/flow time
El	elasticity	$\frac{\tau_p \eta}{\rho h^2}$	elastic effects/inertial effects
Gr	Grashof	$\frac{\rho U_b L_0}{\eta}$	Re for buoyant flow
Ra	Rayleigh	$\frac{U_b L_0}{D}$	Pe for buoyant flow
Kn	Knudsen	$\frac{\beta}{L_0}$	slip length/macroscopic length

Figure 2-2 - The relevant dimensionless numbers that will be discussed to describe the difference between macroscale fluidics and microfluidics. Image from (Squires & Quake, 2005, p. 980).

The Reynolds number

The first dimensionless number is the Reynolds number. As the inertial forces and the characteristic lengths at microscale usually are very small, the Reynolds numbers are very small as well (order of 10^{-6} to 10). Hence, turbulence due to inertial forces usually does not exist. Also, balancing the unsteady inertial force density with the viscous force density allows us to determine the time it takes to establish a steady flow: $\tau_i = \frac{\rho L_0^2}{\eta}$ (Squires & Quake, 2005, p. 982). Which you could interpret as the time it takes for vorticity to diffuse distance L_0 with diffusivity $\nu = \frac{\rho}{\eta}$. This time is usually a few microseconds.

The Péclet number

In case there is no more vorticity and you have a laminar flow, the mixing of substances is only driven by diffusion. This means that mixing can take a few minutes, which for industry and applications is quite long. Say we put two substances together in a channel. Using the diffusion time and the flow velocity it is possible to estimate how much distance the flow has covered before two substances are mixed purely due to diffusion. This leads to the Péclet number: the number of channel widths needed to mix two substances due to diffusion alone.

The capillary number

This is a measure for the ratio between capillary/interfacial stresses and viscous stresses. Because the surface to area ratio in microfluidic devices usually is quite big, the capillary forces can be large enough to cause surface deformations or bulk fluid motion. An important consequence is that capillary forces draw fluid into a microchannel where the liquid-solid interface energy is lower for the specific circuit than the solid-gas interface energy (bulk fluid motion). The front of the flow has this famous meniscus shape (surface deformations).

The Deborah number

It relates the relaxation time of the polymers (speculating maybe also proteins) in your fluid to the characteristic time length of the environment they are in. It is named after the prophetess Deborah who said '…the mountains flow before the Lord…' The mountains flow on geological timescales, they are rigid to human time scales. (Ruzicka, 2008, p. 843) has a particularly clear explanation of the Deborah number.

The elasticity number

The elasticity number describes the ratio between the elastic and the inertial effects and is defined as the Deborah number divided by the Reynolds number, see Figure 2-2. As the flow speed increases, elasticity effects become more important and the Deborah number increases as well. The small dimensions of microfluidic devices allow for a more elastic flow to develop more easily. Not sure, if this also applies to flows without polymers in them, such as just pure water. Cool fun fact: the finite polymer relaxation time gives a memory to the fluid, making its properties dependent on more than just the boundary conditions like a regular Newtonian fluid.

The Rayleigh number

When one puts two fluids together of which one is heavier than the other, buoyancy starts playing a role. The buoyancy forces cause the fluid to have a certain velocity (for example: bubbles of water moving up through oil, two liquids moving over and under each other from an equilibrium vertical interface). The Rayleigh number relates the convective flux (by buoyancy) to the diffusive flux. If the buoyancy velocity is low, diffusion will determine the interaction. If the buoyancy velocity is higher, then a gravity current of the fluids will penetrate each other. If the flow gets even faster, the fluid will start splashing as inertial forces start playing a part. The Rayleigh number describes in which region of diffusion; buoyancy or inertia you are. Have a look at (Connor, 2019) for an elaboration on the Rayleigh number.

The Grashof number

Before inertial forces can play a role, they must be of significant proportion. Something that is described by the Grashof number. This is basically a Reynolds number where the velocity is the buoyancy velocity. The difference between the two lays in that for the Grashof number the part with the velocity is the tracer itself. (Hoy & Roos, 2005) elaborates further on what the Grashof number actually is.

The Knudsen number

The Knudsen number is usually used to see if the continuum assumption holds up. It compares the mean free path of a fluid to the characteristic length of the system. Roughly speaking, molecules that are more than the mean free path away from a wall, do not notice the wall. Hence, if the distance between your walls comes close to the mean free path, it will start influencing the behaviour of your entire fluid. There are three regimes generally for a Knudsen number.

- $Kn \ll 1$ when the fluid behaves like a non-slip fluid and can be regarded as a continuum,
- $Kn \sim 1$ where the fluid behaves as a continuum but starts to slip at the boundaries,
- $Kn \gg 1$ where the continuum assumption does not hold anymore.

More specifics on the Knudsen number can be found in (Barber & Emerson, 2002, p. 209) and (Krüger et al., 2017, p. 11).

2.3. Kinetic theory

The following paragraph about kinetic theory is based on (Krüger et al., 2017, Ch. 1.3). Kinetic theory is a mesoscopic theory regarding the distribution of particles in a gas. In Figure 2-1 it fits in the middle with the mesoscopic simulations like the lattice Boltzmann method, to which we will come later. By understanding kinetic theory, one understands the basic physical concepts that form the fundaments for the lattice Boltzmann method later on.

Kinetic theory is based on the assumption that most particles do not spend a lot of their time colliding with other particles. That is why it works well for dilute gases, but is not very well applicable to denser gases and liquids. The behaviour of denser gases and liquids is also possible with kinetic theory, but it is more complex.

When looking at dilute gases on a microscopic level, one can distinguish between monoatomic and polyatomic gases. When particles of a monatomic gas collide, they collide elastically (i.e. total energy only contains translational energy and is conserved). Molecules existing of multiple atoms can contain vibrational and rotational energy as well. Thus, in polyatomic gases collisions can additionally be inelastic (i.e. translational energy becomes vibrational or rotational) and superelastic (i.e. vibrational or rotational energy becomes translational energy), all while conserving the particles' total energy. As the particles spend very little time colliding, the macroscopic behaviour of the gases is largely similar.

Bohr's correspondence principle also applies to kinetic theory. If the system is large enough its quantum behaviour will reduce to classical behaviour. Kinetic theory is a statistical description of a large number of particles. This confirms the mesoscopic nature of the theory. It describes the distribution of particles. However, as Bohr's correspondence principle suggests: if the system is large enough the quantum (microscopic) behaviour will reduce to classical (macroscopic) behaviour.

2.3.1. The distribution function

In kinetic theory, one formula is key to all macroscopic variables. This is the distribution function $f(\boldsymbol{x}, \boldsymbol{\xi}, t)$. All macroscopic variables can be determined, when the distribution function is known. It is an extension of the commonly used mass density. One could say it is a particle density in some way. It extends from the density of mass in three-dimensional physical space and includes the density of mass in three-dimensional velocity space.

Two illustrative examples were given by (Krüger et al., 2017, Ch. 1.3.1) to understand the concept of this distribution function and its extension upon the density. The first is that of the unit of the distribution function. Since the distribution function describes the mass density in both physical and velocity space over all three dimensions, the units look as follows:

$$[f] = kg \times \frac{1}{m^3} \times \frac{1}{\left(\frac{m}{s}\right)^3} = \frac{kgs^3}{m^6} \qquad 2\text{-}9$$

Here the first two units are those of the density and the ones from velocity space are clearly added.

The second example is more practical in nature. Imagine a box with volume $V = L_x \times L_y \times L_z$ that is filled with a certain gas. If one wants to know the total mass of the gas in this volume, one would trivially integrate the density over the entire volume:

$$\int_V \rho \, d^3x \qquad 2\text{-}10$$

Say you only want to know the mass of the gas in the left half of the box, one could change the boundaries of the integral:

$$\int_{x=0}^{x=\frac{L_x}{2}} \rho \, d^3x \qquad 2\text{-}11$$

One could calculate the same thing with the distribution function. When considering all possible particle velocities in the velocity space and the same boundaries within physical space:

$$\int_{x=0}^{x=\frac{L_x}{2}} \int_{-\infty}^{\infty} f \, d^3\xi \, d^3x \qquad 2\text{-}12$$

Finally, one can get even more specific with the distribution function. It is for example also possible to determine the total mass of right-moving particles in the left half of the box:

$$\int_{x=0}^{x=\frac{L_x}{2}} \int_{\xi_x>0} f \, d^3\xi \, d^3x \qquad 2\text{-}13$$

Moments of the distribution function

As already said when introducing this distribution function, it allows for the determination of macroscopic quantities. One can calculate these quantities, such as the density, the momentum and the internal energy, with the moments of the distribution function. These moments are integrals over the entire velocity space of the distribution function weighted with some function of $\boldsymbol{\xi}$.

The most trivial one is the mass density, which can be calculated by integrating the distribution function over all velocities without any additional multiplications:

$$\rho(\boldsymbol{x},t) = \int f(\boldsymbol{x},\boldsymbol{\xi},t)\, d^3\xi \qquad 2\text{-}14$$

The first extension or alteration is the momentum density, which is calculated by multiplying the distribution function with the velocity before integration:

$$\rho(\boldsymbol{x},t)\, \boldsymbol{u}(\boldsymbol{x},t) = \int \boldsymbol{\xi}\, f(\boldsymbol{x},\boldsymbol{\xi},t)\, d^3\xi \qquad 2\text{-}15$$

A similar approach leads to the total energy density. This includes both the kinetic energy due to bulk motion of the fluid as well as the internal energy due to random particle motion:

$$\rho(\boldsymbol{x},t)\, E(\boldsymbol{x},t) = \frac{1}{2}\int |\boldsymbol{\xi}|^2\, f(\boldsymbol{x},\boldsymbol{\xi},t)\, d^3\xi \qquad 2\text{-}16$$

If one is only interested in the internal energy, it makes sense to define a relative velocity $\boldsymbol{v}$ of the particles with respect to the bulk velocity $\boldsymbol{u}$: $\boldsymbol{v} = \boldsymbol{\xi} - \boldsymbol{u}$. This can be used to calculate the internal energy density:

$$\rho(\boldsymbol{x},t)\, e(\boldsymbol{x},t) = \frac{1}{2}\int |\boldsymbol{v}|^2\, f(\boldsymbol{x},\boldsymbol{\xi},t)\, d^3\xi \qquad 2\text{-}17$$

2.3.2. The equilibrium distribution function

Given the nature of collision, namely highly sensitive to small variations in initial relative positions, the distribution of particle velocities tends to even out around a certain mean velocity. This results over time, when a gas or liquid is left alone, in an equilibrium distribution $f^{eq}(\boldsymbol{x},\boldsymbol{\xi},t)$ as well. In a reference frame that moves with the same velocity as the bulk velocity of the gas, the equilibrium distribution can be expressed as $f^{eq}(\boldsymbol{x},|\boldsymbol{v}|,t)$ which is: an equilibrium distribution of the particles in a fluid dependent on the position, absolute particle velocity and time.

Assuming that this equilibrium distribution function is separable for each velocity direction in velocity space, and assuming that it is constant, leads to the conclusion that each individual 1D equilibrium function must be of the form: $f_{1D}^{eq}(v_x^2) = a + bv_x^2$ where a and b are generic constants. Hence, the three-dimensional equilibrium distribution function has the form:

$$f^{eq}(|\boldsymbol{v}|) = e^{3a}e^{b|v^2|} \qquad 2\text{-}18$$

2.3.3. The Boltzmann equation

Now that the concept of the distribution function is explained, it is time to look at its evolution over time. The distribution function is dependent of position, particle velocity and time: $f(\boldsymbol{x},\boldsymbol{\xi},t)$. Hence its total derivative to time should be:

$$\frac{df}{dt} = \left(\frac{\partial f}{\partial t}\right)\frac{dt}{dt} + \left(\frac{\partial f}{\partial x_i}\right)\frac{dx_i}{dt} + \left(\frac{\partial f}{\partial \xi_i}\right)\frac{d\xi_i}{dt} \qquad 2\text{-}19$$

This describes the evolution of the distribution function over time. In this description several terms can be interpreted and rewritten. Firstly, $\frac{dt}{dt} = 1$. Secondly, the particle velocity is present: $\frac{dx_i}{dt} = \xi_i$. Thirdly, Newton's second law changes the final term to the specific body force: $\frac{d\xi_i}{dt} = \frac{F_i}{\rho}$. Finally, the

time derivative term on the left side is commonly rewritten: $\frac{df}{dt} = \Omega(f)$. All these changes together turn the total time derivative of the distribution function into the Boltzmann equation:

$$\frac{\partial f}{\partial t} + \xi_i \frac{\partial f}{\partial x_i} + \frac{F_i}{\rho} \frac{\partial f}{\partial \xi_i} = \Omega(f) \qquad 2\text{-}20$$

The Boltzmann equation has a form similar to an advection equation. The first two terms describe the actual advection of the distribution function with particle velocity $\boldsymbol{\xi}$. The third term describes forces affecting this advection. The term on the right hand side is a source term.

The source term describes a local redistribution of the distribution function. When a gas moves or is excited, collisions between particles take place. These collisions lead to a local redistribution of the distribution function. Because the redistribution that the source term describes is a consequence of these collisions, the source term is also called the collision operator $\Omega(f)$.

Any collision should still conserve mass and momentum and translational energy in a monatomic gas. Just as the moments of the distribution function could be used to describe the mass and momentum of the entire gas, the moments of the collision operator be used to describe the conservation of these properties. As an example: to describe mass conservation one can integrate the source term over all possible velocity space. There should be no new particles, so this integral should be zero. Applying the same reasoning to the other quantities leads to:

Mass conservation:

$$\int \Omega(f)\, d^3\xi = 0 \qquad 2\text{-}21$$

Momentum conservation:

$$\int \boldsymbol{\xi}\, \Omega(f)\, d^3\xi = 0 \qquad 2\text{-}22$$

Total energy conservation:

$$\int |\boldsymbol{\xi}|^2\, \Omega(f)\, d^3\xi = 0 \qquad 2\text{-}23$$

Internal energy conservation:

$$\int |\mathbf{v}|^2\, \Omega(f)\, d^3\xi = 0 \qquad 2\text{-}24$$

After Boltzmann found the equation, he defined a collision operator as well. This is a rather complex double integral over velocity space considering all possible outcomes of a two-particle collision. This integral is a significant difficulty in solving the Lattice-Boltzmann equation (Mohamad et al., 2010, p. 106). As the exact solution of the outcome of one collision is not likely to influence the macroscopic behaviour of the entire fluid, it is possible to approximate the integral without introducing significant errors. These approximated collision operators used in the Lattice-Boltzmann method generally are much simpler. The most common one is the Bhatnagar-Gross-Krook (BGK) collision operator (Mohamad et al., 2010, p. 28):

$$\Omega(f) = -\frac{1}{\tau}(f - f^{eq}) \qquad 2\text{-}25$$

Which describes the relaxation of the distribution function to its equilibrium distribution. One could interpret it as: "how much is the distribution influenced by the particles' tendency towards the equilibrium distribution?". It is inversely proportional to the relaxation time τ. Which is directly related to macroscopic transport coefficients such as the viscosity or the thermal conductivity. The BGK collision operator neatly ensures evolution of the distribution function to its equilibrium and adheres to the conservation laws described above. It is however still slightly less accurate than Boltzmann's original collision operator.

The BGK collision operator is sometimes referred to as the single-relaxation-time scheme (SRT). Other approximations of Boltzmann's collision integral are possibly more stable or accurate. Common ones are the multi-relaxation-time scheme (MRT) or the two-relaxation-time scheme (TRT), which are more thoroughly explained in (Mohamad et al., 2010, Ch. 10) and (Krüger et al., 2017, p. 83 and Ch. 10).

2.3.4. From Boltzmann equation to macroscopic conservation

If the macroscopic quantities can all be derived from the distribution function, it would make sense that the macroscopic conservation equations can all be derived directly from the Boltzmann equation as well. How to do that is shown here below. Again, the trick of taking the moments of the equation is applied.

Mass conservation

When integrating the Boltzmann equation (2-20) over velocity space, the following equation comes up:

$$\frac{\partial}{\partial t}\int f\, d^3\xi + \frac{\partial}{\partial x_i}\int \xi_i f\, d^3\xi + \frac{F_i}{\rho}\int \frac{\partial f}{\partial \xi_i}\, d^3\xi = \int \Omega(f)\, d^3\xi \qquad 2\text{-}26$$

In the first term one can recognize the time derivative of the density from 2-14. In the second term one can see the spatial derivative of the momentum density from 2-15. The integral in the third term is zero. The integral of the collision operator was determined to be zero previously in 2-21, because of mass conservation. Hence, this allows for the equation to be rewritten to:

$$\frac{\partial \rho}{\partial t} + \frac{\partial(\rho u_i)}{\partial x_i} = 0 \qquad 2\text{-}27$$

Which is the continuity equation.

Momentum conservation

When first multiplying the Boltzmann equation with the particle velocity ξ_i and then integrating it over velocity space, one gets:

$$\frac{\partial}{\partial t}\int \xi_i f\, d^3\xi + \frac{\partial}{\partial x_i}\int \xi_i\xi_i\, f\, d^3\xi + \frac{F_i}{\rho}\int \xi_i \frac{\partial f}{\partial \xi_i}\, d^3\xi = \int \xi_i \Omega(f)\, d^3\xi \qquad 2\text{-}28$$

Where the first term shows the time derivative of the momentum density from 2-15. The second term is the spatial derivative of the moment flux tensor $\rho u_i u_j - \sigma_{ij}$. The third term comes down to F_i. And the term with the collision parameter is again zero according to 2-22. Leading to the Cauchy momentum equation:

$$\frac{\partial(\rho u_j)}{\partial t} + \frac{\partial(\rho u_j u_i)}{\partial x_i} = \frac{\partial \sigma_{ij}}{\partial x_i} + F_j \qquad 2\text{-}29$$

Energy conservation

The energy conservation equation can be derived from the Boltzmann equation via the trace of its second moment. Which means, that it is multiplied twice with the particle velocity and then integrated over velocity space.

$$\frac{\partial}{\partial t}\int \xi_i\xi_i f\, d^3\xi + \frac{\partial}{\partial x_i}\int \xi_i\xi_i\xi_i\, f\, d^3\xi + \frac{F_i}{\rho}\int \xi_i\xi_i \frac{\partial f}{\partial \xi_i}\, d^3\xi = \int \xi_i\xi_i\Omega(f)\, d^3\xi \qquad 2\text{-}30$$

The first term turns into the time derivative of the energy density from 2-16. The second term can be split, just like with the momentum conservation equation. The third term turns into $F_i u_i$ and the term with the collision operator is still zero according to 2-23. This allows for the notation of the total energy equation:

$$\frac{\partial(\rho E)}{\partial t} + \frac{\partial(\rho u_i E)}{\partial x_i} = \frac{\partial\left(u_j\sigma_{ij}\right)}{\partial x_i} + F_i u_i - \frac{\partial q_i}{\partial x_i} \qquad 2\text{-}31$$

Boltzmann's $\mathcal{H}$-theorem

In addition to the conservation equations, Boltzmann has defined a certain quantity $\mathcal{H}$. He defined that quantity as follows:

$$\mathcal{H} = \int f\ln(f)\ d^3\xi \qquad 2\text{-}32$$

With this quantity he derived a theorem. This theorem showed that on top of the conservation laws, the natural behaviour of entropy is also properly represented in the Boltzmann equation.

For any value of the distribution function $\mathcal{H}$ is larger than it is at the equilibrium distribution function. Behaviour equal to that of entropy. In a nutshell the derivation of the theorem looks like this: If one multiplies the Boltzmann equation with $(1+\ln(f))$, applies the chain rule and takes the zeroth moment of the resulting equation, one gets a formula which is a balance equation for $\mathcal{H}$:

$$\frac{\partial}{\partial t}\int f\ln(f)\ d^3\xi + \frac{\partial}{\partial x_i}\int \xi_i\, f\ln(f)\ d^3\xi = \int \ln(f)\ \Omega(f)\, d^3\xi \qquad 2\text{-}33$$

Where the left hand side shows the time change of the quantity and the flux of the quantity. The right hand side can be shown to be non-positive for the BGK collision operator. This goes for the original Boltzmann collision operator and for any functional collision operator in kinetic theory for that matter. Hence, together with the definition of $\mathcal{H}$ in 2-32 this leads to the following equation:

$$\frac{\partial\mathcal{H}}{\partial t} + \frac{\partial\mathcal{H}_i}{\partial x_i} \leq 0 \qquad 2\text{-}34$$

For ideal gases, $\mathcal{H}$ turns out to be proportional to the entropy density ρs according to:

$$\rho s = -R\mathcal{H} \qquad 2\text{-}35$$

This goes to show, that apart from the conservation laws the behaviour of entropy can be derived from the Boltzmann equation.

2.4. The lattice Boltzmann method

The Boltzmann equation describes the time evolution of the distribution function. From this all macroscopic behaviour can be deduced. Now that the Boltzmann equation is explained, it is time to

take a look at the simulation method that uses it. This is the lattice Boltzmann method. It is very suitable for simulating incompressible, viscous flows in complex geometries (Filippova & Hänel, 2000, p. 407). Especially when these simulations are performed in parallel (Krüger et al., 2017, p. 45) (Mohamad et al., 2010, p. ix).

Like most simulation methods it is discrete and requires a certain grid, or lattice, which is explained in 2.4.1. Once this lattice is established, the discretization of the Boltzmann equation will be elaborated on in 2.4.2. When reaching this point, everything is available to understand the algorithm (2.4.3). For this algorithm to work, there are certain requirements to a few parameters, which will be explained in 2.4.4. Finally, 2.4.5 pays attention to what boundaries are suitable for a proper simulation.

2.4.1. The lattice

Lattice Boltzmann reduces the possible spatial coordinates and momentum states to those on a lattice. This simplifies Boltzmann's statistical mechanical concept significantly. Historically, people used hexagonal grids. They have the advantage that all velocity vectors can have a same maximum magnitude and weight (Krüger et al., 2017, p. 73). Nowadays rectangular grids are used.

These grids are described by how many dimensions they span and the number of velocities they use for the discretization. A lattice model widely in use is D2Q9, shown in Figure 2-3. It spans two dimensions and discretizes a particle's velocity into nine velocity bins. These nine bins are eight velocities and one stationary bin. Each bin's value is defined by c_i (i indicating which bin) and weighted by a weight factor w_i. Together, these form the velocity set of the lattice point. A rectangular grid has the advantage that elements of the vectors c_i can conveniently only be ±1 or 0. Each particle on the grid has a unit mass.

In 3D the concept is the same. A cubical grid of size $2\Delta x$ is used to discretize space and velocities. The number of bins that is used is optional. Common are fifteen bins (D3Q15), nineteen (D3Q19) and twenty-seven (D3Q27), see Figure 2-4. For completeness the velocity set of D3Q19 is given in Table 2.

Naturally, the computational efficiency of D3Q15 is higher than that of D3Q19. The latter in turn needs about 40% less memory and computing power than D3Q27. It turns out that D3Q27 has certain characteristics that make it an especially suitable grid for turbulence modelling. However, since the Reynolds numbers in microfluidics are extremely low, this does not add much value. For solving fluidic motion D3Q19 is recommended (Mohamad et al., 2010, p. 34).

Now that the lattice is established, we need a single-particle distribution function. Instead of a continuous function that would be used in continuum mechanics, it is now a one-particle discrete distribution function.

To go from the Boltzmann equations (2-20) to the lattice Boltzmann equation, one first calculates the discrete velocity distribution function $f_i(\boldsymbol{x}, t)$. It is similar to the distribution function used to derive the Boltzmann equation, however all parameters are now discrete. It describes the distribution of particles over a discrete velocity space on a specific point in physical space at a specific point in time. The velocity space is a small discrete set of velocities, c_i. The index of f_i and c_i refer to the same velocity. f_i is only defined on certain grid-positions $\boldsymbol{x}$ with a spacing size Δx and on certain times $\boldsymbol{t}$ with time step δ_t.

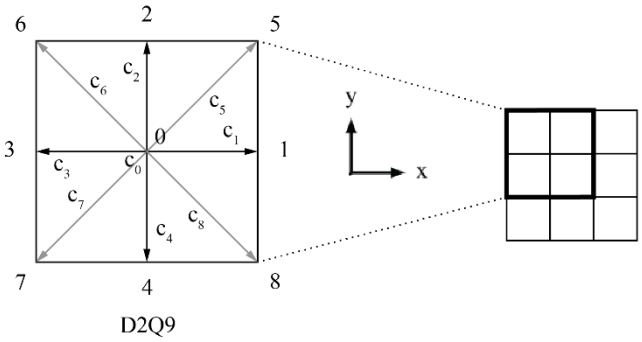


Figure 2-3 - The D2Q9 lattice model spanning two dimensions and splitting the particles velocity into nine discrete velocity bins

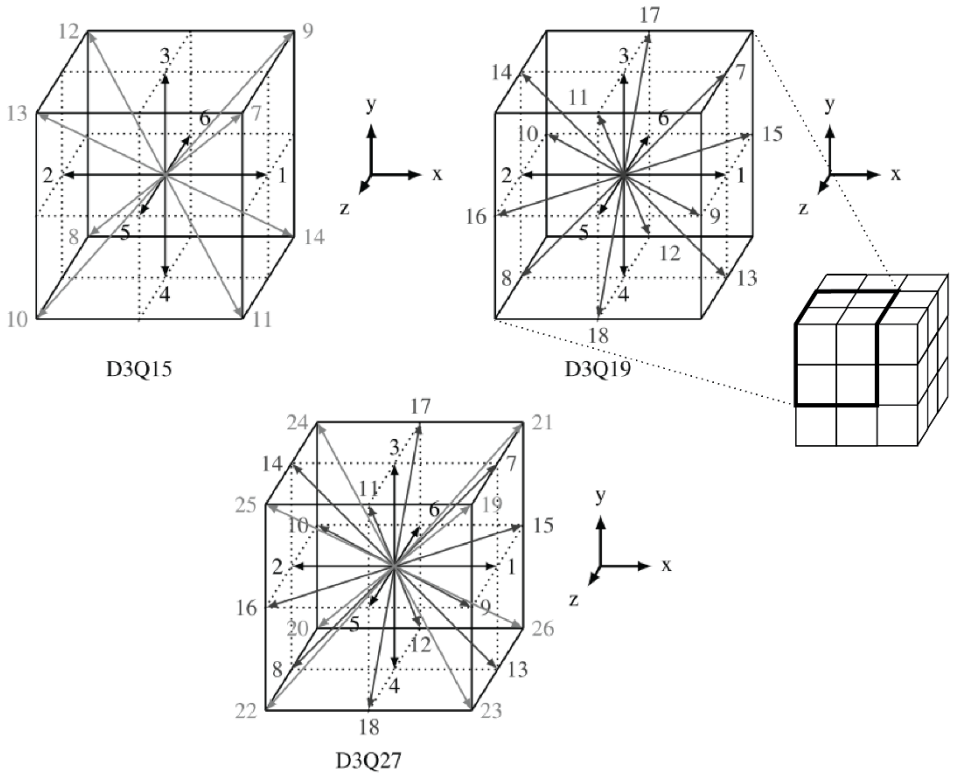


Figure 2-4 - The three most popular three dimensional lattice models. Each grid spanning three dimensions (D3) with either 15, 19 or 27 velocity bins. Image is from (Krüger et al., 2017, *p. 72*).

i	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
w_i	$\frac{1}{3}$	$\frac{1}{18}$	$\frac{1}{18}$	$\frac{1}{18}$	$\frac{1}{18}$	$\frac{1}{18}$	$\frac{1}{18}$	$\frac{1}{36}$	$\frac{1}{36}$	$\frac{1}{36}$	$\frac{1}{36}$	$\frac{1}{36}$	$\frac{1}{36}$	$\frac{1}{36}$	$\frac{1}{36}$	$\frac{1}{36}$	$\frac{1}{36}$	$\frac{1}{36}$	$\frac{1}{36}$
c_{ix}	0	+1	-1	0	0	0	0	+1	-1	+1	-1	0	0	+1	-1	+1	-1	0	0
c_{iy}	0	0	0	+1	-1	0	0	+1	-1	0	0	+1	-1	-1	+1	0	0	+1	-1
c_{iz}	0	0	0	0	0	+1	-1	0	0	+1	-1	+1	-1	0	0	-1	+1	-1	+1

Table 2 - The set of velocity bins c_i and their weight w_i for the D3Q19 lattice. Table reinterpreted from (Krüger et al., 2017, p. 72)

Just like with the continuous distribution function it is possible to determine mass density ρ and momentum density $\rho \boldsymbol{u}$ at a point where the discrete velocity distribution function is defined. These are the discrete equivalents of the moments of f_i and stated in (Krüger et al., 2017, p. 47).

$$\rho(\boldsymbol{x}, t) = \sum_i f_i(\boldsymbol{x}, t) \qquad 2\text{-}36$$

$$\rho \boldsymbol{u}_i(\boldsymbol{x}, t) = \sum_i \boldsymbol{c} f_i(\boldsymbol{x}, t) \qquad 2\text{-}37$$

2.4.2. The lattice Boltzmann equation

It is possible to make a discrete distribution function. It is then also possible to create a discrete Boltzmann equation. This equation is what results, when the Boltzmann equation is discretized in velocity space, physical space and time:

$$f_i(\boldsymbol{x} + \boldsymbol{c}_i \Delta t, t + \Delta t) = f_i(\boldsymbol{x}, t) + \Omega_i(\boldsymbol{x}, t) \qquad 2\text{-}38$$

It shows that the particles at gridpoint $\boldsymbol{x}$ move to the neighbouring gridpoint $\boldsymbol{x} + \boldsymbol{c}_i$ over one time step δ_t. The collision operator influences this movement or streaming of particles from one gridpoint to another. Boltzmann himself suggested a collision operator, but the most common is the Bhatnagar-Gross-Krook collision operator, described in 2.3.3. (Krüger et al., 2017, p. 48) state the discrete form of this operator as:

$$\Omega_i(f) = -\frac{f_i - f_i^{eq}}{\tau} \delta_t \qquad 2\text{-}39$$

This collision operator relaxes the particles towards an equilibrium distribution over relaxation time τ. This equilibrium distribution is given by (Krüger et al., 2017) on p. 48 as:

$$f_i^{eq}(\boldsymbol{x}, t) = w_i \rho \left(1 + \frac{\boldsymbol{u}\boldsymbol{c}_i}{c_s^2} + \frac{(\boldsymbol{u}\boldsymbol{c}_i)^2}{2c_s^4} - \frac{\boldsymbol{u}\boldsymbol{u}}{2c_s^2}\right) \qquad 2\text{-}40$$

Where w_i refers to the weight of the weighing factors and $\boldsymbol{c}_i$ the velocity bins described in Table 2. $\boldsymbol{u}$ and ρ are local macroscopic values for fluid velocity and density. Finally, c_s is the lattice speed of sound.

2.4.3. The algorithm

Calculating a single time step in an LB model is done in two parts which succeed each other: a collision step and a streaming step. If one takes the lattice Boltzmann equation 2-38 and inserts the discrete BGK collision operator 2-39, one gets the following equation:

$$f_i(\boldsymbol{x} + \boldsymbol{c}_i \delta_t, t + \delta_t) = f_i(\boldsymbol{x}, t) - \frac{\delta_t}{\tau}\left(f_i(\boldsymbol{x}, t) - f_i^{eq}(\boldsymbol{x}, t)\right) \qquad 2\text{-}41$$

This equation shows the two steps. On the right hand side one sees the collision influencing the distribution function. (Krüger et al., 2017) define the distribution function after collision as:

$$f_i^*(\boldsymbol{x}, t) = f_i(\boldsymbol{x}, t) - \frac{\delta_t}{\tau}\left(f_i(\boldsymbol{x}, t) - f_i^{eq}(\boldsymbol{x}, t)\right) \qquad 2\text{-}42$$

This calculates how the distribution function looks after the particles have collided. It is calculated locally per grid point. If the collision operator would not have been there, the entire particle population

of point $\boldsymbol{x}$ would have been able to move to the next gridpoint. The collision operator influences the particle population that is available for the second step.

Once the collisions have been calculated, the second part takes place, the streaming. One calculates the distribution functions on the grid for the next time step by:

$$f_i(\boldsymbol{x} + \boldsymbol{c}_i\delta_t, t + \delta_t) = f_i^*(\boldsymbol{x}, t) \qquad 2\text{-}43$$

Now that the distribution functions for the next time step have been calculated, this time step is completed. Each next time step repeats this two-part process. This way the progression and evolution of the fluid quantities is simulated.

2.4.4. Parameter selection

As is now clear, LBM uses a lattice to represent a physical system. On this lattice the aforementioned algorithm (see 2.4.3) solves the lattice Boltzmann equation (see 2.4.2). Two requirements influence the definition of the "lattice variables", the simulated quantities. The quantities on the lattice have to represent the macroscopic quantities of the physical system. Besides the lattice must be tuned such that the simulation's solution on the lattice is sufficiently accurate.

$$\text{Physical system (P)} \quad \overset{\text{Re},l_0,t_0}{\longleftrightarrow} \quad \text{Dimensionless system (D)} \quad \overset{\text{Re},\delta_x,\delta_t}{\longleftrightarrow} \quad \text{Discrete system (LB)}$$

Figure 2-5 - translation from the physical system to the dimensionless system and the discrete lattice system as described by (Latt, 2008, p. 1)

To translate the macroscopic physical quantities to the microscopic lattice quantities one can use a two-step approach (Latt, 2008). Firstly, the physical system of variables is translated into a dimensionless system. This is a common procedure in fluid mechanics. Secondly, this dimensionless system is converted into the discrete lattice system. Figure 2-5 is a graphical representation of the relation between these systems. It shows that certain variables are used for the conversion. For the first transition, the non-dimensionalisation, a characteristic length l_0 and timescale t_0 are chosen. For the step to the discrete system the discrete space step δ_x and the simulation's time step δ_t are defined. These four variables must lead to an identical Reynold's number in both the physical as the discrete system. Otherwise, the discrete system will not correspond with the physical system (Jain, 2020).

According to (Latt, 2008, p. 4) the LBM is a quasi-compressible model. This means, that some small compressibility effects might occur when solving the necessary equations. These effects naturally affect the numerical accuracy of the simulation. Compressibility effects scale with the square of the Mach number. Hence, if one wants to limit the influence of compressibility, one must keep the Mach number low. The Mach number on the lattice is simply the lattice velocity u_{lb} over the speed of sound in the lattice (c_{lb}): $Ma = u_{lb}/c_{lb}$. As the error caused by compressibility effects is in the order of $\varepsilon_c \sim Ma^2$ it is proportional to the lattice velocity squared. Hence the compressibility error is in the order of $\varepsilon_c \sim \delta_t^2/\delta_x^2$.

The LBM is a second order method. Hence the numerical error scales with $\varepsilon_n \sim \delta_x^2$. If one were to refine the grid used in a simulation to reduce this numerical error, one must keep in mind that the compressibility effects error should stay in the same order of magnitude. Otherwise the numerical error might reduce, but the compressibility error takes over. To make sure that $\varepsilon_c \sim \delta_x^2$ as well, the following restriction for δ_t follows:

$$\delta_t \sim \delta_x^2 \qquad 2\text{-}44$$

A proper way to ensure this, is by applying diffusive scaling. This is a set of relations that ensures the relation in 2-44. More on what this practically means for the simulation can be found in setup of the LBM simulations in 3.3.1 and in (Jain, 2020, p. 1820). Another important restriction to keep in mind when setting the parameters of a simulation is given by (Jain, 2020, p. 1820). It states that the collision operator (see 2.4.2) can have a maximum value of 2 to ensure stability:

$$\Omega \leq 2 \qquad 2\text{-}45$$

On top of that the lattice velocity must not exceed the speed of sound on the lattice, because the LBM is not suitable for supersonic flow. For a D3Q19 lattice this gives the following parameter restriction (Jain, 2020, p. 1820):

$$u_{lb} \leq 0.15 \qquad 2\text{-}46$$

If one wants to tune this lattice velocity, one can firstly adapt the aforementioned collision operator. Beyond the limits of the collision operator, one must refine the grid to lower the lattice velocity. So, δ_t is not only dependent on δ_x, but also influenced by the limits of the collision operator and the lattice velocity.

2.4.5. Boundary conditions

The simulations naturally need boundary conditions. Three different kinds of boundaries will be used. These boundary conditions come from (University of Siegen, 2020b).

Firstly, most trivially, some boundaries will be set as a “wall”. As the name suggests, this means that the fluid cannot penetrate this boundary. Just like in the chip this boundary assumes a no-slip condition. It is possible to set a friction factor for a wall in Musubi. In some simulations a factor of 1 will be used. This represents a full-slip wall.

The other two boundaries concern the inlet and the outlet of the geometry. The inlet uses a popularly used “velocity_bounceback” boundary condition (Lai et al., 2001, p. 40). Based on the set velocity, the densities of the boundary elements will be set to the equilibrium distribution. The bounceback means that when a particle reaches the boundary it will bounce back with the same angle as it came with. See (University of Siegen, 2020g) for extra information.

The outlet has a “pressure_expol” boundary condition. This means that the variables in the domain are extrapolated during the simulation in order to simulate the boundary behaviour. It should be analogous to an open outlet. One can still set a pressure such that certain numerical reflection phenomena do not occur. In this case a pressure of 1 bar is used. See (University of Siegen, 2020e) for additional information.

2.4.6. Accuracy

Just like any numerical method, the LBM has a certain accuracy. (Krüger et al., 2017, Ch. 4.5) describes three general groups of errors in computational fluid dynamics simulations.

Firstly, there are the round-off errors. Inherent to any kind of computation, but they start to play a bigger role when time steps and element sizes become smaller. Besides there are the iterative errors. That describe a form of steady state error.

On top of these two is the discretization error. Which is the leading factor in numerical errors. For direct approximations the discretization error and truncation error are directly relatable. However, unlike in standard CFD procedures, LBM does not directly discretize the continuous Navier-Stokes equations. They are rather reproduced by a relaxation of the discrete Boltzmann equation. This has for

a consequence, that in LBM a solution is not only dependent on the non-dimensional parameters. On top of that the solution of the LBM is dependent on the relaxation parameters, such as the collision operator. In the case of the BGK collision operator (shown in 2-39) this means that the solution becomes dependent of the relaxation time τ.

Taken all this into account, LBM is considered second order accurate in space and time. When discretizing the Boltzmann equation 2-20 in space and time either with a first or second order approximation, in turns out both lead to the same form of formula 2-38. Hence both approximations are second order. When filling in the actual discrete BGK collision operator 2-39 then into 2-38 one can again find the same form, confirming that also with the BGK collision operator LBM is second order accurate in space and time.

Important detail: keeping the compressibility error of the same order of magnitude as the discretization error (as described in 2.4.4 by 2-44), makes the LBM effectively first order accurate in time.

2.5. APES

The above described algorithm and boundary conditions are all incorporated in a lattice Boltzmann solver called Musubi. It is developed by the University of Siegen and part of the APES suite. The APES suite is developed for flexible, presumably parallel, calculation of mesh-based simulations (University of Siegen, 2020a). Three of the tools in the APES suite are of importance.

Firstly, the mesh will be generated with Seeder (University of Siegen, 2020f) based on a configuration file and a specified geometry, in this case an STL file of the chip's microfluidics. Seeder uses recursive bisection to generate a mesh. The configuration file is especially written for this particular simulation in Lua (LabLua PUC-Rio, 2020). Once the mesh files are generated, they can be used by Musubi (the actual lattice Boltzmann solver, (University of Siegen, 2020d)) to run the simulation. How this simulation is run is again determined by a configuration file. See (University of Siegen, 2020c) for more explanation on how to configure Musubi. Finally, the results can be post-processed by Harvester. In this case Musubi Harvester for the results of the simulation and Seeder Harvester for checking the mesh.

A machinefile, or hostfile, can be used to determine how the computational load will be distributed over the cluster tfe2 of the University of Twente, for more information on how to do that, see (Sun Microsystems Inc., 2008). Part of the calculations were done on Cartesius, the Dutch national supercomputer (SURFsara, n.d.). This uses Slurm as a workload manager. This means that a run file is used to put in an order for computational power on Cartesius (SchedMD, 2020).

2.6. Particle Image Velocimetry

Micro Particle Image Velocimetry (µPIV) plays a significant role in this project. µPIV can determine the average flow velocity at different locations in the chip. TissUse has gained experience with µPIV in a former version of their Chip2. They used it to determine the flow speed at three different sites in that chip (Hasenberg, 2017, p. 4). In this project the same locations will be analysed. The measurements will be used to determine boundary conditions for the simulation and to validate the simulations. More on that in 3.1.

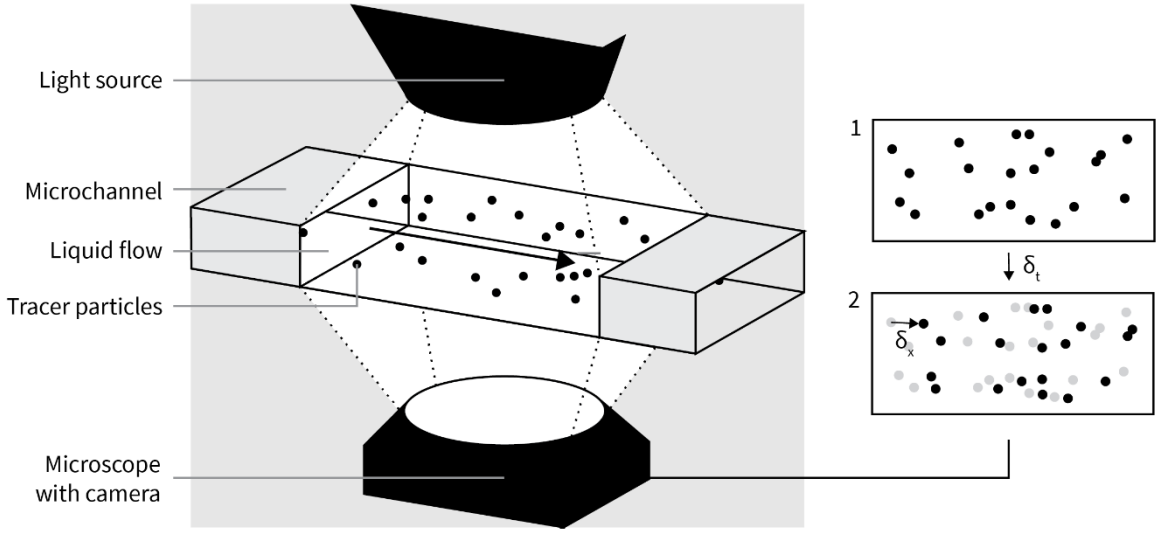


Figure 2-6 - The concept of µPIV. Tracer particles in a microchannel are captured with a high-speed camera. Change in position and time combined lead to an estimate of the flow velocity.

µPIV is µPIV applied to microfluidic flows. µPIV is a way to determine the velocity in a flow. It works by inserting tracer particles into the flow, see Figure 2-6. These particles must have a density similar to that of the fluid, such that they follow (trace) and do not influence the flow (Thielicke, 2014, p. 29). The flow is then illuminated such that the particles become visible. Once you have an illuminated flow you can take images of the flow at a specified relatively high framerate. In each of these images the particles are visible. Based on the location of a particle in each of the frames and the time between two frames, one can determine the local velocity of the particle. Hence one can determine the local velocity of the flow. For another explanation of µPIV please refer to (Doda, 2008). For an extensive discussion of µPIV take a look at the practical guide by (Raffel et al., 2007).

Usually lasers are used to illuminate the flow. Pulsating lasers can be used quite conveniently to create thin and high intensity sheets of light (Raffel et al., 2007). However, at TissUse the channel is illuminated with a microscope LED from the opposite side of the where the camera is. More on that in 3.2.1.

Several aspects influence the choice of particles for µPIV. A selection of three will be highlighted here below. For a more extensive explanation of particle selection, please have a look at (Hasenberg, 2017, p. 8).

1. Firstly, TissUse does not use a laser, but the standard lighting system of a ZEISS Axio Vert.A1 microscope (Carl Zeiss Microscopy GmbH, n.d.). Normally one would want reflective particles to reflect the laser light into the camera. Now however, that feature is not important anymore. Wat is important is that the particles block the light, thus creating a black image against the white background.
2. Secondly, the particles need to have a density similar to that of the fluid. If they do, they will have a similar inertia and buoyancy. Then they will not influence the flow.
3. It is important that the particles have a low enough inertia to follow rapid movement of the flow. Especially for the pulsatile pump that is in TissUse's chips it is important that the particles follow the pulses of the flow.

2.7. Information Visualization

Until this point the theory behind the characterization of flow in the chips was discussed. This knowledge will help to figure out how the fluid behaves and how that can be properly determined. Once there is data about the flow, the next step is to provide this data to the user. Researches, biologists, chip developers all want to know about the fluid flow in the chips.

It is the goal of this thesis to provide that information to them in the most convenient way. Doing this requires some background knowledge on how to visualize information.

2.7.1. Good information visualization

Most of the knowledge below is based on (Tufte, 1998). Edward R. Tufte, a renowned information design professor at Yale University. It describes general design principles that cause certain visual effects or consequences. These principles might be used to make choices that lead to a better visualization of information.

Here, "better" can be defined as having a high expressiveness and effectiveness (Heer, 2017, p. 2) (Mahoney, 2019,):

- Expressiveness: a visualization should express all the facts in the dataset and only the facts in the dataset.
- Effectiveness: a visualization is more effective when its information is more readily perceived than in another visualization.

This definition echoes from other areas of expertise such as cognitive load theory (Schwabisch, 2017). Which describes that good information visualization reduces extraneous cognitive load. Which is the cognitive power necessity caused by the method of explanation or the way of visualization of certain information. This reduction goes in favor of cognitive power available for understanding the subject matter itself. A similar perception of good information visualization also resonates in Tufte's words throughout his book.

2.7.2. Data density

According to (Tufte, 1998), having a visually dense data representation is complementary to human capabilities. Practically, this means that the more data is visible within one eye span the better we can grasp it. It prevents us from having to rely on visual memory, which is a much weaker human skill. It is the difference between searching with your finger through a large table or having to flip the page and remembering.
On top of that, dense data representation allows viewers to narrate, select, personalize and recast data. The viewer gains control over the information.

(Tufte, 1998, p. 37) mentions a way to increase data density: micro/macro readings. It suggests that, if one adds a lot of details and structures these details in hierarchical layers, one can add a lot of data without creating an unperceivable mess. A good example is that of the Isometric Map of Midtown Manhattan by Constantine Anderson, Figure 2-7. The map is so detailed that it shows individual windows, building names and trees. And one could very closely read out all these details. From afar, however, they all blend into each other creating a different layer of information.

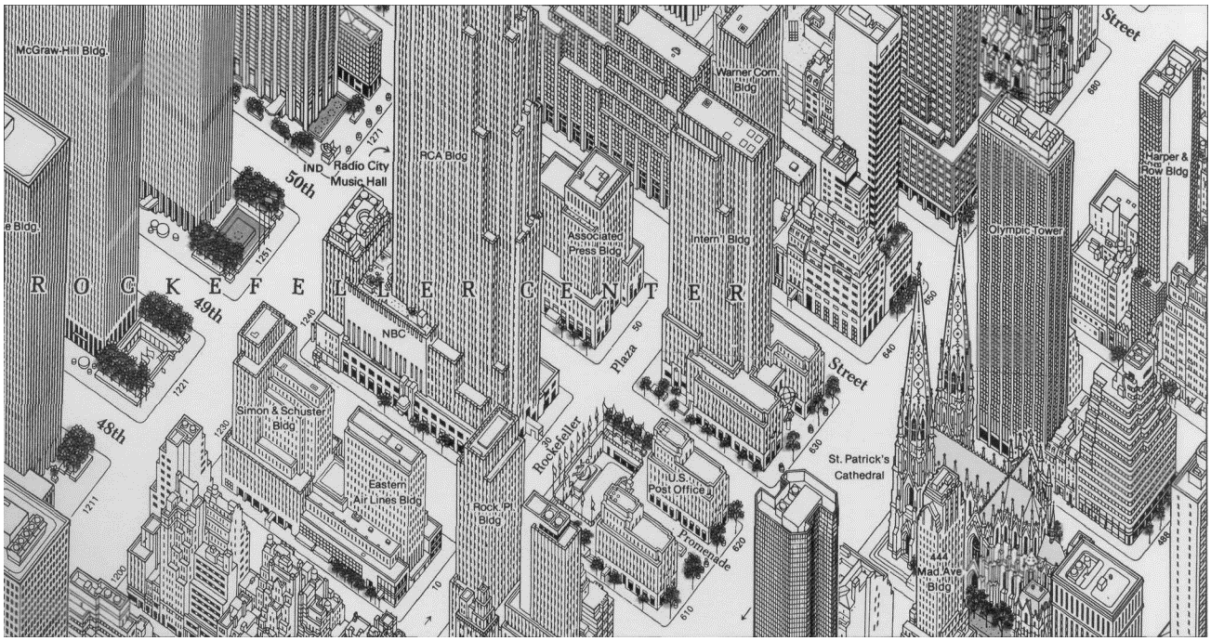


Figure 2-7 - The Isometric Map of Midtown Manhattan by Constantine Anderson. A good example of how different hierarchical layers of information can provide a visually dense data representation. © 1989 The Manhattan Map Company, all rights reserved. Taken from (Tufte, 1998, p. 37).

2.7.3. Proportion and harmony

So, layers can help increase data density. Here the relationship between the layers is important. Proportion and harmony are the concepts that influence this relation. These concepts apply on all visual elements, not only layering. In graphic design it is common knowledge that visual objects with similar characteristics, rhythm and proportion are in harmony with each other (see the Gestalt page on (Yablonski, 2021c), (Rutledge, 2009) or (Mads Soegaard & Interaction Design Foundation, 2020)). Therefore, the viewer perceives them as relating to each other. In the analogous but opposite way objects that are not in harmony with each other become more separate.

Intended harmony or disharmony play a major role in where the attention of the viewer goes. Whether it goes to a specific site or whether it might not know where to go at all. According to (Tufte, 1998, p. 53-58) and (Mahoney, 2019) there are five characteristics to a visual object which control whether it is in harmony with others. The list below states them in order of perception speed:

1. Position: people in the Western world inherently expect that values further away from the bottom left of a graph are higher. (Mahoney, 2019)
2. Size: people in general perceive the area of an object as an ordered characteristic.
3. Colour: what colour an object has (hue) is non-ordered in human perception. Hence it can be used to distinguish between equal categories. Gradients can introduce order in color.
4. Value: how intense a colour is (chroma) or how bright (luminescence) are ordered in human perception.
5. Shape: is non-ordered so can be used to categorize. It is not recommended to use too many different shapes. (Mahoney, 2019) suggests to use a maximum of three to four different shapes.

An ordered characteristic is inherently perceived as having an order in its different values. Position, size, and value are ordered. Meaning that an object which has a darker tone than another might be intrinsically perceived as having more of a certain quantity. Shape is non-order, just like colour without a gradient. A datapoint represented by a rectangle is not necessarily perceived as having more or less

of anything than a circle. For an example of each of these five visual characteristics and their perception see Appendix B.

Specifically regarding the use of colour, (Tufte, 1998, Ch. 5) states a couple of rules regarding its use:

1. Bright colours are unpleasant to the eye when used in large areas and next to each other.
2. However, using bright colours sparingly against muted background can create illustrative patterns which enhance information reading.
3. Background colours should be quiet. Usually mixed tones of grey can help.
4. A palette of natural colours is most soothing to the eye in general.
5. If the picture is composed of two or more large, enclosed areas of colour it will fall apart. Unity can be restored by having small details in the opposite areas accentuated with the colour of the other area. Take note that small colour differences may complicate the reading of information.
6. When choosing a colour palette keep in mind that about eight percent of the population has some form of colour-blindness. (Oogvereniging, 2021)

2.7.4. Comparing data

To summarize until now: in order to get a good information visualization – that is an expressive and effective information visualization – make use of a high visual data density within one eye span and intentionally create harmony and disharmony.

It will become clear during this project that comparing data is an important task for the users. (Tufte, 1998, Ch. 4) says that using small multiples is a reliable option to enable comparison. Once the viewer understands the structure, the consistency in design allows for focus on the change of information, instead of a change in composition. This way the designer can let the viewer's subconscious do the heavy lifting. Which speeds up perception (Mahoney, 2019).

Tables are a common example of small multiples. They are a compact means of providing vast amounts of data. On top of that you can show averages and variances around averages, which are of interest for this project particularly. Alignment within a grid can be insinuated subtly by intentionally creating the proper visual harmony.

2.7.5. Remove Chartjunk

A final remark of Tufte's is to remove chartjunk. Focus should lay on the data itself. It should not lay on the apparatus that displays it or any unnecessary ornaments. Besides chartjunk can disturb the harmony in a design. Which, especially for large datasets, is undesirable. *Clutter and confusion are failures of design, not attributes of information* (Tufte, 1998, p. 51). On top of that, chartjunk can reduce credibility and could come across as patronizing to a well-informed viewer. Simpicity and clarity make for a good information representation.

2.8. User Interface Design

Now that there are clear guidelines for visualizing information, it is time to look at the artefact in which this information visualization will be housed. In this case, for reasons explained in 4.3, it will be a digital tool. Chip users can use this tool to look up their desired information about the flow characteristics.

When designing a digital tool, it mostly comes down to the two widely used terms: User Experience (UX) and User Interface (UI). The user interface entails all points of interaction between the program and the human. A mouse and keyboard are part of the interface. However, most focus lays on the visual representation of the program on screen. Which is called the graphical user interface (GUI). When using the term UI reference is made to this visual on screen user interface.

The purpose of the UI is to create an optimal UX. The user should have an optimal experience in performing the task they want to do. An optimal experience in this case is defined as finding the right information as quickly and conveniently as possible.

A good UI is the basis of a good UX. The following pages contain background theory on how to create a good interface. This section is almost entirely based on the book by (McKay, 2013).

2.8.1. UI is a conversation

The main point of McKay's book is: *A user interface (UI) is essentially a conversation between users and a product to perform tasks that achieve users' goals* (McKay, 2013, p. 11). The term conversation can be taken quite literally here. McKay suggests that the only way UI communication differs from a real conversation is the language. A real conversation uses natural language. A UI conversation uses the visual language and elements of UI. Other than that it is the same kind of communication.

Since UI is the same as natural conversation, the same standards apply to this human-computer interaction as to human-human interaction. A UI should be polite, respectful and intelligent. It should communicate clearly and concisely as anyone would when talking a to a real human. After all, your UI is in fact talking to a real human. A human that has feelings, emotions, tries their best and makes mistakes.

Every element in a UI can be evaluated on what it communicates and how well it communicates that. This might sound familiar from the information visualization, where effectiveness was one of the aspects of evaluation. Having an effective communication is considered the best way to create an intuitive UI.

Intuitive UI

Creating an "intuitive UI" is the holy grail of interface designers. To have a clear idea of what it means to have an intuitive interface McKay proposes the following definition: *A UI is intuitive when target users understand its behaviour and effect without use of reason, memorization, experimentation, assistance or training* (McKay, 2013, p. 22).

This definition is still a bit vague to work with in a design discussion. You cannot really use it when trying to make design decisions. The following list of more quantifiable characteristics gives aims to give a more concrete definition of intuitive. A good or intuitive UI will have the right combination of the following aspects (McKay, 2013, p. 25):

- Discoverability: users can easily find the starting point of what they want to do. It is clear that it does what they want it to do.
- Understandability: since many task steps come down to making decisions, it is important that users can make confident and quick decisions without needing assistance or explanation.
- Affordance: it is clear from its visual appearance how an interaction should be performed. A button should look like something you can click on. a checkbox should look like something that can be checked.
- Predictability: interaction with the UI should deliver the results that the users expect. Users should not have to experiment to find out what a button will do for example. Neither should they stand for any surprises when clicking something.
- Efficiency: the interface enables users to achieve their goals with a minimum amount of effort. Cumbersome interaction will feel unintuitive.

- Responsive feedback: The UI is clear about what action is happening currently. At the end of an action it should be concise and specific about whether the action was successful or especially unsuccessful.
- Forgiveness: if users make a mistake – which they will, because they are human – the UI should allow them to correct it easily. It could also do the right thing anyways when the UI notices something is not right.
- Explorability: users can explore the interface confidently. They should not be afraid to do something wrong or getting lost.

In a design discussion it will be much more efficient to say that there is a lack of forgiveness in a certain interaction than to say that an interaction is unintuitive. When evaluating a design iteration, it is possible to evaluate a design's explorability, but quite hard to evaluate its intuitiveness (McKay, 2013, p. 26).

Inductive UI

The characteristics described above apply to individual elements of a UI. However, they do not apply on a higher level. At a higher level it is important that an entire task feels intuitive as well. To achieve this, McKay suggests to create what he calls an inductive UI (McKay, 2013, p. 36). An inductive UI prevents any need for deduction. Inductive UIs are self-explanatory. There is no need for the user to experiment and deduce how the UI works.

Several aspects make a UI inductive. First of all, it must be easy to understand. Multistep tasks should be divided in smaller steps that are easy to grasp. Secondly, in each of these tasks the user's first and most prominent questions needs to answered: "What am I supposed to do here?". A prominent and concise instruction line can do this quickly. Thirdly, to prevent any need for deduction by the user, make each page reflect what the user is supposed to do. In 2.8.2 an overview of what interaction elements can be used to properly represent a task. 2.8.2 dives into how to visually design a page such that it represents what it should represent.

2.8.2. Interaction design

This paragraph is largely based on (McKay, 2013, Ch. 2). It is established now that a UI communicates by means of its own language. The following paragraphs will begin to define that language. The language of UI consists of several elements. There are controls; which are the words of expression. Commands are the verbs of a UI. They perform commands. Labels and instructions form the textual elements of a UI. They can be used, for example, to provide feedback. This feedback can be about a command that is being performed or whether a command was successful. All these controls and their feedback enable tasks. Tasks could be considered the paragraphs of a UI. When you write a book, you split it up in paragraphs. Similarly, one splits their UI up in different tasks. Finally, just like in a real conversation, sometimes something might happen that requires attention and the conversation is interrupted. These interruptions entail errors, warning, confirmation and notifications.

All the elements above form the language of UI. Which element you use, why and how is important in creating an intuitive UI. Each group will be elaborated on. The list of elements in each group is reduced to only explain the applied concepts in the end result. For a complete and extensive list, please have a look at (McKay, 2013, Ch. 2).

Before discussing different part of the language of UI. There is an interesting rule that applies in general. McKay suggests a slightly altered version of Jakob's law (Yablonski, 2021b): *Users spend most*

of their time using software other than yours (McKay, 2013, p. 27). So, whether picking controls, labels or forms of feedback, it is wise to make sure it is coherent with other software that the user knows.

Controls

When you talk, there is what words you say and there is how you say them. The same is true for controls in UI. They can in fact have a body language. This is a selection of common examples of body language of controls (McKay, 2013, p. 69):

- Size of expected input: the size of a textbox suggests how much input text is expected.
- Screen space required: the more space, the more prominent or important the control appears.
- Immediate or delayed effect: Command buttons and sliders might have an immediate effect, but drop-down lists and checkboxes will have a delayed effect.
- Default values: a default value can be a nudge in a certain direction. It can introduce a bias.
- Required input: it is asked/demanded that the user gives input.
- Encourage change: easily changeable control encourage change. Sliders, for example, stimulate users to try different values.
- Level of commitment: can an action be undone? A button with "Next" does not imply too much commitment, but a button with "Purchase" does.
- Forgiveness: when user mistakes take place are they easy to correct? This gives a control a different feeling.

The choice for a control is usually driven by its purpose. Its body language is less important. However, when designing controls, it is possible to tweak them using this body language.

The list of common controls in (McKay, 2013, p. 69) is rather extensive. To keep this background theory relevant and perceivable only a selection of controls applied in the final design will be discussed. Each control is suitable for a specific purpose. Like discussed just now, they can all have body language as well. Both will be shortly explained for each control:

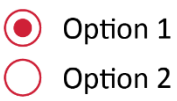
- Numeric textboxes

  purpose: input unconstrained numeric values
  body language: its width suggests input size.
- Sliders

  purpose: select a value from a range where the desired valued is not known exactly
  body language: needs immediate effect to enable and encourage change and experimentation.
- Radio buttons

  purpose: select an exclusive choice from a small number of choices
  body language: takes up quite some screen space

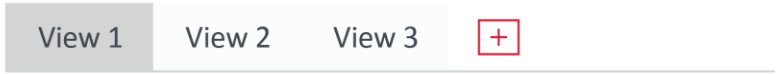
- Checkboxes

  purpose: enable or disable a small number of options
  body language: takes up quite some screen space
- Drop-down lists

  purpose: select and exclusive choice from a larger number of choices
  body language: if presented with a default value it can discourage change. If presented with a “select an option” it encourages change.
- Tabs

  purpose: display different views of the same information (and possibly compare)
  body language: takes up a lot of screen space per tab
- Command buttons

  purpose: initiate an action
  body language: high discoverability makes them suitable for primary commands. They usually have immediate effect. Unless they have three dots behind their label, that suggests delayed effect.
- Links

  purpose: initiate an action or navigate to another window
  body language: their lower discoverability makes them more suitable for less important commands. Usually they still have immediate effect with the exception of having three dots in their label.

Commands

The controls are defined now. These represent all the words in the vocabulary of the UI elements. The commands are the verbs. There are several ways to group and display commands. Each has its own characteristics. A relevant selection out of (McKay, 2013, p. 78):

- In-place commands
  are commands that are directly visible in the UI. They are direct, simple and very discoverable. They become unpleasant quickly when there are many commands.
- Menu bars
  if there is a larger number of commands, menu bars are a great way to summarize them. Users will expect them to be at the top of the screen. They are a bit less direct, because the labels are often in text and the user has to click to see all the commands before selecting anything. It is common to combine them with toolbars. The toolbars would have the frequently used commands in icons and the menu bar would have the less common commands in text.

- Pop-up menus
  are menus that slide out or pop up by clicking a button. They can display clearly related commands.

Labels and instructions

All different types of words (the controls) and the verbs (the commands) are established. Now it is time to look at the actual text that helps represent these controls and commands. That text are the labels and the instructions.

Labels are the text and icons that are directly on a control. An instruction is additional text that explains what is going on(McKay, 2013, p. 87). Each page in a UI usually has a main instruction. Which is a line at the top of a page that describes the purpose of the page. Below a main instruction you could specify even more with regular instructions. This should only be done when the user really needs additional information.

It can be useful to realize that users treat labels differently from instructions. It is rare that a user uses a control without reading its label first. However, more often than not do they skip over instruction without reading them. A clear example of this is shown in Figure 2-8.

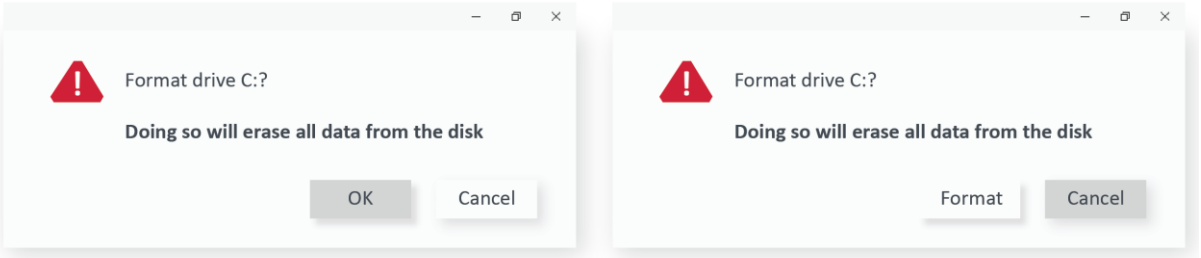


Figure 2-8 - A clear example of how people do read the labels, but usually skip the instruction. Image reinterpreted from (McKay, 2013, *p. 88*).

Labelling commands can be divided into three groups:

1. Text-only: self-explanatory, but difficult to scan quickly
2. Text and icon: bot self-explanatory and scannable, but costs more space
3. Icon-only: not self-explanatory which can be problematic for non-standard commands

When drafting the text of labels and instructions, keep in mind that UI is communication. So ask yourself what you would say to the user in person. You probably want to give them useful information that they need right now. You want it to be easy to understand so you speak clearly and naturally. On one hand you do not want to omit any necessary information. On the other hand, you want to let them get back to work quickly and not confuse them with unnecessary details. It sounds like a lot to take into account. However, you can rely on your human skills in interpersonal interaction.

Task steps

It is now possible to use labels and text to convey the functions and purpose of commands and controls. Imagine the task the user wants to do is complex. It might need several inputs to provide an output. Then the paragraphs of the UI language come into play: the task steps (McKay, 2013, p. 100).

When users are engaging in a series of task steps, it is important that they stay confident. They know where they are and they know where they want to go. Along the way the UI must at least give some sense of where they are, such that the user remains confident to go to the next step.

There are certain UI elements that can help to give this sense of location. Just like on a map one can add a figurative “you are here” sign. This can be combined with a rough indication of how the task is going to progress from here. On top of that a tracker of what parts of the progress have been finished already can help. These things combined provide a sense of awareness.

Once the sense of awareness is established, give the user a clear opportunity to go to the next step and to go to the previous step. Also, provide them with a means to go back to start. Make sure that that button is forgiving though. No-one wants to start all over by accident.

Usually in each step the user has to do something, make a decision of give input. Make sure that the user has enough information to confidently make an informed decision. It can be assistive to give a default value for certain common settings or recommendations.

Feedback

So, currently controls and commands have been established. Their labels are regulated, and it is shortly explained how to use all this to enable complex tasks. When doing a task, the user will expect feedback. After a command is given, it takes about 200ms before the user will start wondering if something is happening (McKay, 2013, p. 93).

Feedback will indicate that a certain command is performed. When a command is finished, it says so with feedback. When it fails it must especially give feedback. Two forms of feedback will be relevant for the UI design of this project. For a somewhat more extensive list, reference is made to (McKay, 2013, Ch. 2).

Progress feedback is especially suitable for processes that take longer than a few seconds. It differs from an activity indicator (such as the loading indicator on Windows or Youtube) in that it indicates how far the process actually is.

Most feedback and task steps will be displayed with dialog boxes. They are quite heavy and obtrusive. Due to these character, they demand the user’s attention. However, they maintain context, which can be beneficial. If there is feedback with which the user has to interact they become a preferred choice.

Interruptions

Sometimes when you are performing a task in a UI with controls, labels and natural feedback something might happen that requires attention. This is when the UI should interrupt. McKay differentiates four different forms of interruptions (McKay, 2013, p. 109).

Firstly, there are warnings. These alert a user when the UI thinks something undesirable for the user is about to happen. Secondly, there are confirmations. They make sure that the user is certain they want to continue. Thirdly, a notification. Which simply provides a timely dose of relevant and useful information. The information in a notification is however not critical. Finally, an error can occur. This when a problem has already occurred.

For each of these interruptions the general guideline is that they should appear rarely. Like the name say, they interrupt the flow of the user. Hence, they can be perceived as annoying quite quickly. On top of that there are some guidelines for each interruption on its own.

Warnings should state a specific condition which might cause problems in the future. They should state specifically what is wrong, what problems it might cause and how the user can prevent that. A good rule of thumb is to only give a warning when you expect the user to change something. When the user is unlikely to change anything, the warning loses its purpose.

Confirmations should be used to alert the user that some unintended consequences might happen. Like with the warnings, only ask for confirmation, when there is a chance that the user might not want to proceed. An interesting trick to have a user read the confirmation, is to use self-explanatory labels instead of trivial labels such as OK or Cancel. Users tend to read those. However, it is not uncommon that users click OK without reading what they are saying OK to.

Notifications are much less critical than the other three interruptions. Use these when wanting to update the user of relevant and timely information. It should not be necessary for a user to see a notification. Notifications are suitable for information that the user does not have to interact with.

Errors are similar to warnings. Do not give them unless the user is likely to do something differently and be specific in the description of the problem. Also, make sure that you suggest a solution, so that the users know what they can do. When something would go wrong in person you would also say “try this and this, that might help”. Under no circumstances blame the user and try not to use an aggressive tone. Words like Fatal, Failure and Abort come across technical. Keep in mind there is a human on the other end of the UI. Instead, you could say there is a serious problem, and some process has stopped.

Dynamic aspects

An entire process or task can now be properly prepared in terms of UI. With the right interactions, the necessary feedback and correct use of interruptions. In between all the controls, commands and tasks there might be some things appearing, changing or resizing. These are dynamic elements, meaning they are not static on the page.

Dynamic elements allow to keep a UI simple but at the same time incorporate a lot of options (McKay, 2013, p. 114). Most dynamic elements initially are not visible. You have to hover over something to make them appear for example. This means that their discoverability and affordance (see 2.8.1) are lower. Hence it is advisable to only use dynamic elements for commands or controls that are used infrequently or a bit redundant.

Just like other elements, one can categorize dynamic elements (McKay, 2013, p. 114). First up is progressive disclosure. A widely applied concept, which shows the most common controls, but more can be shown on demand. It can be used to make a UI customizable. Users can choose what they want to see. The discoverability and affordance of the disclosure controls are quite clear.

Similar to progressive disclosure are dynamic secondary commands. The user has to hover or click for example to show certain commands. Difference between dynamic secondary commands and progressive disclosure is that with the former the user does not perform an action specifically to see the extra controls. The appearing controls are a side effect of what they are actually doing. This approach works especially well when it is inevitable for users to discover these secondary commands when they use the UI normally.

Finally, elements of the UI can resize dynamically. Usually, the controls are always discoverable or directly visible. When a control is then clicked, it will grow at the cost of other controls. This provides an efficient design.

2.8.3. Visual design

2.8.2 described guidelines for interactive elements of the UI. Another layer of UI design is its visual appearance. This paragraph will elaborate on how to create a visual design that communicates as is intended. To keep this background theory perceivable and relevant, basics such as font size or animations will not be discussed. This paragraph is largely based on (McKay, 2013, Ch. 3). For a complete and extensive overview of visual design elements, it is recommended to have a look at that.

The looks of a UI are part of what and how the interface communicates with the user. Each visual element can be reviewed on the effectiveness of its communication. If it does not communicate anything, it might be superfluous. If it does not communicate what it should communicate, it might need revision.

The significance of a good visual design lays in two aspects. Firstly, there is something called the aesthetic-usability effect (Yablonski, 2021a). It suggests that a product that looks better is perceived as functioning better as well. In the opposite way, if a product does not look well-designed, the user will assume that the rest of the product will be of a similar low quality. Secondly, apart from superficial prejudice, the product will actually function better with a good visual design. It comes down to good communication again. The user needs to know where to look, what different elements are, what the affordance of an element is. Text needs to be legible and pages need to be scannable.

Scannable pages

(Krug, 2000) introduced a now commonly known concept in UI design: Users do not read your pages, they scan them. This means that the user will take a quick overall look at the page to find out what is there. According to the Gutenberg Diagram (Lidwell et al., 2010, p. 118), shown in Figure 2-9, users tend to start in the top left corner – appropriately called the primary optical area. With an arch that slightly tends to the top right, they move towards the bottom right corner – the terminal optical area. The other two corners are covered much less, see Figure 2-9. The top right corner is slightly more likely to get a visit from the user's gaze and is therefore called the strong fallow area.

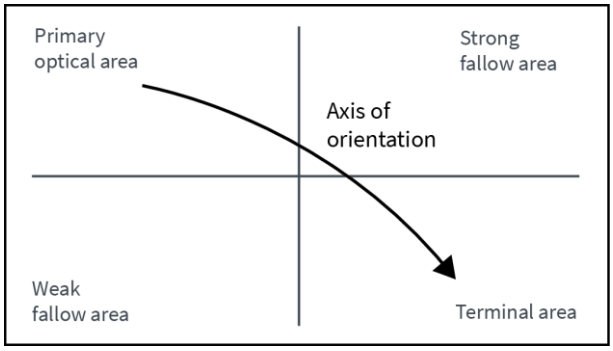


Figure 2-9 - Gutenberg diagram showing the rough trajectory of a user scanning a page. It starts wih the primary optical area and ends in the terminal optical area. Both fallow areas are much less visited. The upper right corner slightly pulls on the trajectory making it the strong fallow area. Left image from (Lidwell et al., 2010, p. 118)

When people scan a page they want to quickly find things. Therefore, a page that is properly designed for scanning makes sure that the most important elements of a page attract the user's attention. These elements should be understandable just by quickly seeing them. Based on the elements it should be clear to the user what they can do on the page. As said in 2.8.1 the primary question users have upon arrival on a page is "What am I supposed to be doing here?". A scannable page provides a quickly perceivable answer.

Naturally, users don't always exactly adhere to the Gutenberg diagram. Along the way they tend to look at things that attract their attention. Interactive controls for example, the more prominent, the stronger the diversion. On the other hand, users tend to disregard elements that repulse their attention. An interesting example is anything that looks like an advertisement. Banner blindness is the ironic effect that people think a banner contains an ad so they disregard it, despite the fact that banners are intended to attract attention. Apart from these two pulling and pushing forces there is another effect in play. Also introduced by (Krug, 2000): users don't optimize, they satisfice. This means that the moment a user thinks they know what to do, or have the right option, they stop scanning. They do not look for better options anymore. Figure 2-10 shows a summary of these effects.

Keeping all the above in mind leads to some guidelines for scannable page design. Following the Gutenberg diagram, place the elements that initiate a task in the top left and elements that complete tasks in the bottom right. It is recommended to put primary UI elements prominently along the scanning line. The strong fallow area is suitable for general tasks. (McKay, 2013, p. 147) recommends to put controls for interaction with a page in the weak fallow area. Large blocks of text or banners are unadvisable for crucial elements, as they repulse the user's attention. Figure 2-10 shows a generally good layout for a scannable page.

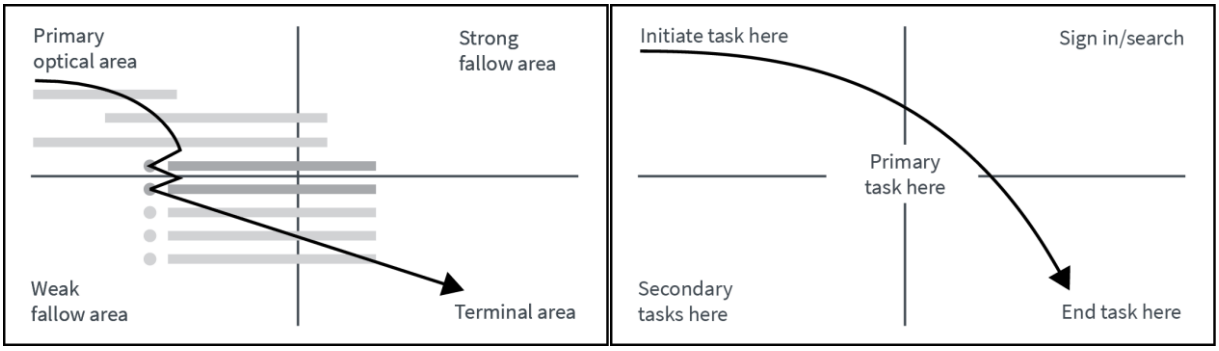


Figure 2-10 - Scannable page design. Left: a realistic path of the user's scope over a page. Right: the resulting sensible layout of tasks over the page. Images from (McKay, 2013, *p. 149 and p. 150*).

Affordance

From 2.8.1 the definition of affordance is the visual properties that indicate how to interact with a control. A dropdown shows that it can be folded out, a button shows that it can be clicked on and regular text should not look like you can do something with it. Affordances must be consistent throughout the entire UI. Affordances are hence an aspect where visual design plays a crucial role in the guidance of the user.

The downside of adding affordance to controls is that they add visual clutter. Hence, when designing affordances, try to find a balance between how visually crowded your pages become and the clarity of the affordances.

Demanding attention

It is now clear how to properly design a page and some of the elements on it. This is all with the goal make everything go as smoothly as possible for the user. Sometimes it might be necessary to interrupt though. 2.8.2 discussed when an interruption is a proper way of interacting. Here the proper way to interrupt is established.

There are different techniques to demand the user's attention. They all come in a different visual form. Here are a number of examples of ways to make sure a user pays attention:

Firstly, one can use labels of controls. When discussing labels in 2.8.2 it was stated that users are very unlikely to click on a button without reading its label. By using critical information as a label you make sure the user will read it.

Secondly, one can use obvious visual clues such as colour, size and layout to make a control look critical.

Thirdly, dialog boxes are an option. They force the user to respond before allowing them to continue their work. A dialog box is an effective interrupter, but should be used with care for that same reason.

Less forceful ways to demand attention include warning icons, animations, notifications and flashing. Whilst they can be interruptive, they do not force the user to interact directly. Flashing, and on top of that alarms or beeping, are not always as effective as expected. It happens that the user wants the obtrusive sound or light to disappear. Once they got rid of that they do not necessarily proceed to fix the issue that the alarm was asking attention for.

All modes of demanding attention are susceptible to this kind of behaviour. Using a form of interruption too often or without good reason, might cause user to start filtering them out. They get used to the notification and just skip it, thinking nothing serious is happening.

To prevent this, it is recommendable to think of what you would do in person. This is again an example of where normal human interaction is a good example of how a UI should interact. You would probably only interrupt someone for something serious. How would you then interrupt? Would you make them stop what they are doing? Or just put the right text on a button? In general, the least obtrusive interruption is best. A good way to go about demanding attention is by progressive escalation. As an issue gets more prominent change the attention-demanding element according to its importance.

2.8.4. Personality design

The concept of a UI being communication has been established now. It has been elaborated with guidelines on how proper interaction can be designed and what visual elements might be suitable in which situation. The final thing that is relevant when designing an interface between a human and a machine is personality. This paragraph is based on (McKay, 2013, Ch. 4).

A user interface inevitably has a personality. How the text is written conveys a certain tone. What colours are used create a certain atmosphere. Whether it is possible to make mistakes that force you to start all over shows a certain attitude of a program. It is therefore important to think about what kind of personality the UI should have.

Consciously creating a good personality in a UI has benefits. People want software that does not just mechanically enable the task at hand. (McKay, 2013, p. 197) suggests that people connect with software that has a nice personality and therefore they want to use it. On the other hand, if a product does not have a good tone or give the best assistance to the user, you have a strong competitive disadvantage. The upcoming paragraphs contain three traits that are commonly overlooked in UI development: forgivingness, trustworthiness and intelligence. A lack of any of these three can – just like with real people – cause annoyance.

Forgivingness

Forgivingness was already discussed throughout this chapter. Hence, here are only a few examples of how a UI can be forgiving (McKay, 2013, p. 213):

Firstly, a good option is to prevent the mistake. The size of controls can prevent missing a click. Also it can limit the input to a valid value for example. Besides, if the program knows the user's intent, it could

be courageous and do the right thing despite the user's mistake. The Google "Showing results for" search results are a good example of this one. Lastly, make sure that problems are easy to correct. When discussing interruptions in 2.8.2 a rule was that you should only interrupt if you offered an actionable solution. So if there is a mistake, make sure there is an easy solution and provide the user with this solution.

Trustworthiness

A UI can earn a user's trust by the same traits a person gains someone's trust (McKay, 2013, p. 221). First of all, one needs to be competent. Provide value to the user and do so proficiently. Proficiently also entails that the user should not come to stand for any unwanted surprises. If there is anything wrong, be specific about what is wrong and again, show how to fix it. Finally, a user will notice the difference between a program working for them and a program working for the company that made it. Just like with people that have a double agenda, someone is much less likely to trust it.

These few traits can gain a user's trust. It can be of importance to realize that it is also necessary for a UI to earn the user's trust. Similar to meeting a new person, real trust takes some time to develop. Finally, also similar to reality, once trust is broken, it is hard to earn it back.

Intelligence

It is tempting to make a program intelligent or smart nowadays. A basic level of intelligence can be achieved without the need of a complete artificial neural network. Understanding the user and their goals is key in this. One can think ahead of what their goals might be, using scenario-based design for example. Also during the usage of the program, the program can keep track of all the input from the user. The program can remember the user's preferences. Naturally, always pay attention to the context in which something is happening. It can eliminate certain options for example, sparing the user some unnecessary work (McKay, 2013, p. 227).

3.
Enabling Chip Characterization

3. Enabling chip characterization

The goal is to create a validated method to characterize and simulate the flow in any possible chip design without the need of a physical prototype. This chapter will describe the work towards that goal.

3.1. Approach

There are four ways known to TissUse of characterizing flow in a chip currently. Two of those are simulations. The other two are empirical.

Until now, TissUse used micro-Particle Image Velocimetry (µPIV). This is an experimental method where one inserts tracer particles into a flow and, using a backlight, creates images of these particles. A high-speed camera takes images of the flow with particles. Based on the change in position of the particles between different images a velocity can be estimated. The other experimental method functions similarly. However, it uses a different algorithm called Optical Flow (OF) to determine the velocity based on these pictures. The application of both these methods requires a physical chip.

Simulations do not need an actual chip. TissUse has therefore started looking into COMSOL Multiphysics, a commercial computational fluid dynamics analysis software package. In order to validate these simulations critically, this master thesis adds the Lattice-Boltzmann simulation method (LBM). This method is especially suitable for parallel calculation of fluids flowing through complex geometries. The University of Siegen developed a code, which will allow a more fundamental understanding of the simulation than a graphical interface.

Because of practical reasons, only three of the four methods will be considered in this thesis. µPIV, COMSOL and LBM will be studied. This is the first phase of the project. Its result is shown in the theoretical background. Once they were all understood, a set of simulations and experiments followed. The results will be compared to each other. This allows for a suggestion on how TissUse would be able to characterize the flow in any chip design without the need of a physical model. The first chip subject to characterization is the two-organ chip in TissUse's product-line called HUMIMIC Chip2 96-Well. Afterwards, documentation of the method follows to ensure this knowledge stays available.

Three different methods of characterizing the flow in a chip will be used. All three play a different role and their results will be compared to each other. 3.2 describes the µPIV measurements. These are used to define boundary conditions for the other two methods and to validate their results. 3.3 dives into the lattice Boltzmann simulations. Thirdly, 3.4 will describe the simulations done with COMSOL Multiphysics. 3.5 then discusses the comparison between the results of the three methods.

3.2. PIV measurements

The goal of the first set of µPIV measurements is to create a time-dependent function of the fluid flow at the inlet of the pump. This function can be used as a boundary condition in the simulations with LBM and COMSOL Multiphysics later. The simulations can be compared to each other if they use the same boundary conditions. On top of that, if these boundary conditions are realistic, the results of the simulations can be verified against the real chip.

PIV measurements are done in three places in the chip, called windows. The windows are labelled A. B and C. From now on they will be referred to as WinA, WinB and WinC. Figure 3-1 shows the windows. The flow circulates in clockwise direction. Hence, WinA can be used to determine the inlet flow, WinB and WinC could be used for verification.

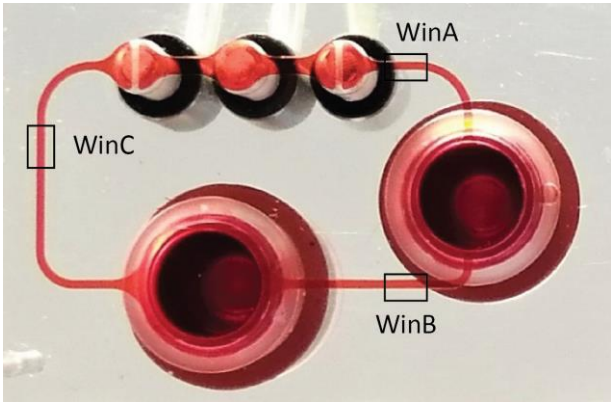


Figure 3-1 - Windows of view of the µPIV experiments. Labelled WinA, WinB and WinC with the clockwise flow direction.

3.2.1. PIV setup

To do µPIV measurements and work all the way through to a time-dependent boundary function, some hardware and software is necessary.

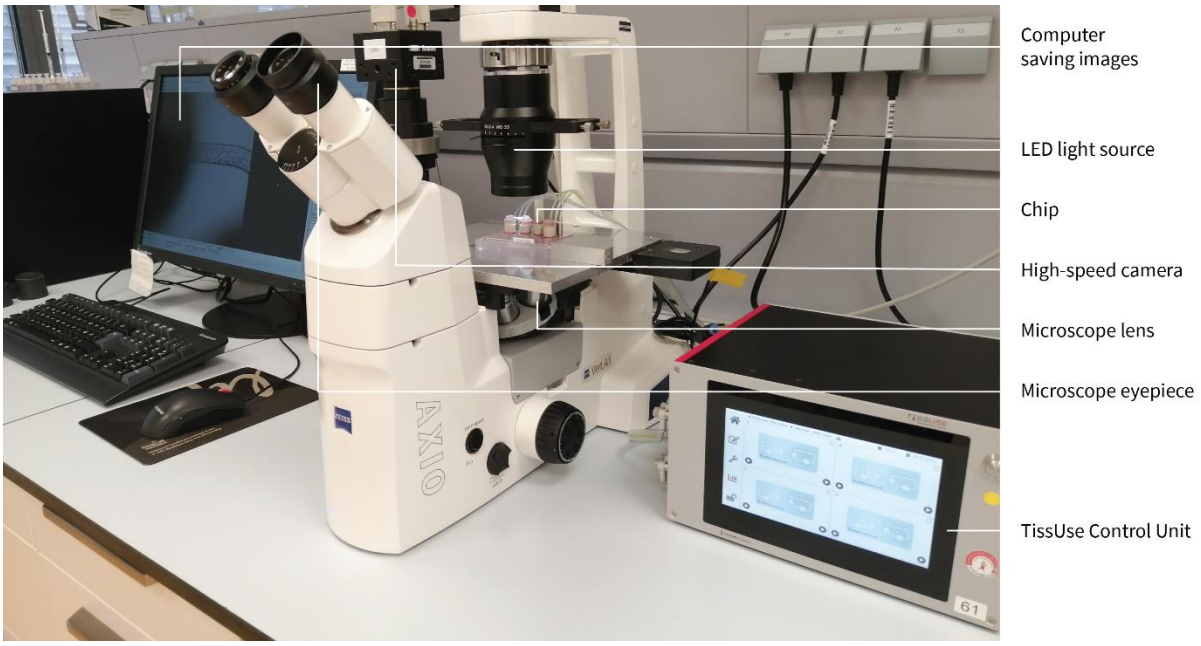


Figure 3-2 - Experimental setup for µPIV experiments in the TissUse laboratory.

Camera setup

The complete setup used for the µPIV experiments is shown in Figure 3-2. In the TissUse laboratory, a ZEISS Axio Vert.A1 microscope can be equipped with a camera (Carl Zeiss Microscopy GmbH, n.d.). This camera is a Baumer HXC40 (Baumer GmbH, 2021a). It can take monochrome images with a maximum resolution of 2048x2048 pixels. The frequency with which it takes these images is 180 fps for the full image, but increases when the image gets smaller. Based on experience, there are two ways to do this. Both will be explained, but only the latter – cropping – is applied in this work.

Firstly, one can use subsampling. It tells the camera to use only every second pixel in its sensor. This reduces the maximum resolution to 1024x1024 pixels. This doubles the possible framerate. Another way to increase the framerate is by cropping the image. The framerate is dependent on the

number of rows of pixels that are in the image. By cropping the view of the camera to the flow area of interest only, the framerate increases. For a view of 216x480 pixels (so 216 rows) the framerate reaches 1585 fps. Some additional tests were necessary to find the exact framerate as the software indicated values which fluctuated a lot. A detailed description of this check is given in Appendix C. For a quick estimation of the framerate of the Baumer HXC40 camera, see (Baumer GmbH, 2021b). For the settings suggested by Baumer's customer support see Appendix D.

Both alterations mentioned above can be done using the software that connects the Baumer HXC40 camera to a computer. This is CameraLink software and works together with Baumer Camerafinder.

A Zeiss 2.5x magnification objective is used to get a clear image of the entire channel.

Measurements

To do an actual measurement, a HUMIMIC Chip2-96 well is connected to a TCU (TissUse Control Unit) and run in clockwise direction at a frequency of 30 bpm (0.5 Hz) with pressure and vacuum values of 500 and -500 mbar respectively. These are common pump settings for real assays.

Within the chip are 5 µm opaque nylon beads (Thermo Fisher Scientific Inc., 2021)diluted to a 0.4% w/v solution with a 0.1% w/v Triton-X-100 PBS solution without Ca^{2+} and Mg^{2+}. These are the tracer particles with which the PIVlab software will be able to do the µPIV calculations later. PIVlab is a tool in Matlab which is able to do µPIV-calculations when it is given a set of images (Thielicke, 2021). It recognizes particles in the images and then determines their velocity based on the difference between images and the framerate.

Once the chip is running, it is placed under the microscope to check if it functions properly. The check includes among other things: looking for contaminations, anything obstructing the flow and air bubbles.

When the chips are filled with the particle solution, checked and up and running, it is time to perform the µPIV measurements. Each window in the chip (Figure 3-1) will be measured three times. Each measurement has an image size of 216x48 pixels and consequently a framerate of 1585 fps (see Appendix C and Appendix D for more elaboration on different framerates with different image sizes). Each measurement takes 10.000 frames. The resulting data includes for each of the three windows three sets of 10.000 images.

PIVlab analysis

The calculations on one set of 10.000 images took about 1500 seconds. Because there were nine sets of images, the PIVlab code was altered slightly. Instead of having the user browse to a folder with images, the folders were coded into the program such that it would automatically open them and make the necessary calculations sequentially. For more information on PIVlab, have a look at (Thielicke, 2021).

Determine pixel size

Previous µPIV measurements at TissUse used subsampling to increase the framerate. Which means that it only uses every second pixel in the camera's sensor. It changes the size of the physical area that one pixel in the image represents. The current µPIV measurements do not use subsampling, because it makes the images vaguer.

The pixels in the sensor of the Baumer HXC40 are 5.5x5.5 µm (Baumer GmbH, 2021a). The magnification of the objective is 2.5x. Since the standard Zeiss camera tube is used, there is no extra

magnification factor due to the camera tube. The size of the physical length represented by one pixel is hence:

$$\frac{5.5}{2.5} = 2.2\ \mu m \qquad 3\text{-}1$$

This calculation confirms what comes out of the Thorlabs magnification and field-of-view calculator, which takes a similar approach (Thorlabs Inc., 1999).

3.2.2. Results

Figure 3-3 and Figure 3-4 show the resulting flow profiles of each window in the Chip2 96-well. These profiles show one pump cycle which repeats continuously. The profiles that are shown are the result of careful selection of non-erroneous sequences, synchronization, and scaling to the correct framerate as described Appendix C. Full processing of the resulting data from the PIVlab calculations is described in Appendix E.

The results of the µPIV neatly show the stages of the peristaltic pump. The peaks are at different points in time between WinA and WinC and they are clearly dampened between the compartments. Have a look at Figure 3-35 for the relation between the peaks and the pump stages. Useful to know is that the flow is considered to be positive when it goes in clockwise direction (as the pump is set). It is considered negative when it goes in counter clockwise direction. From stage 4 to stage 1 of the pump cycle in Figure 1-9 it happens that the flow is negative.

Interpretation of the µPIV results will take place in 3.5. Discussion of the net volume flows not being the same in all three windows can be found there as well.

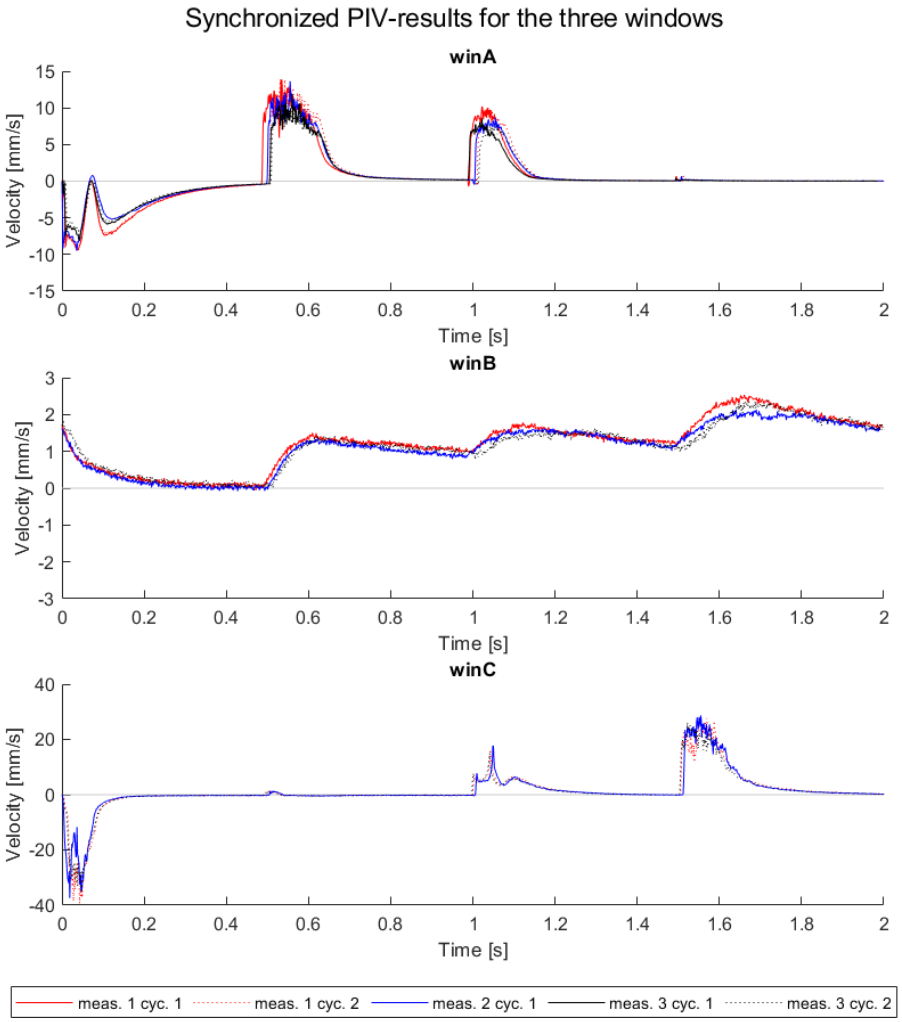


Figure 3-3 - Average flow velocities measured during the µPIV experiments on Chip2 96-well. Positive flow goes clockwise; negative flow goes counterclockwise.

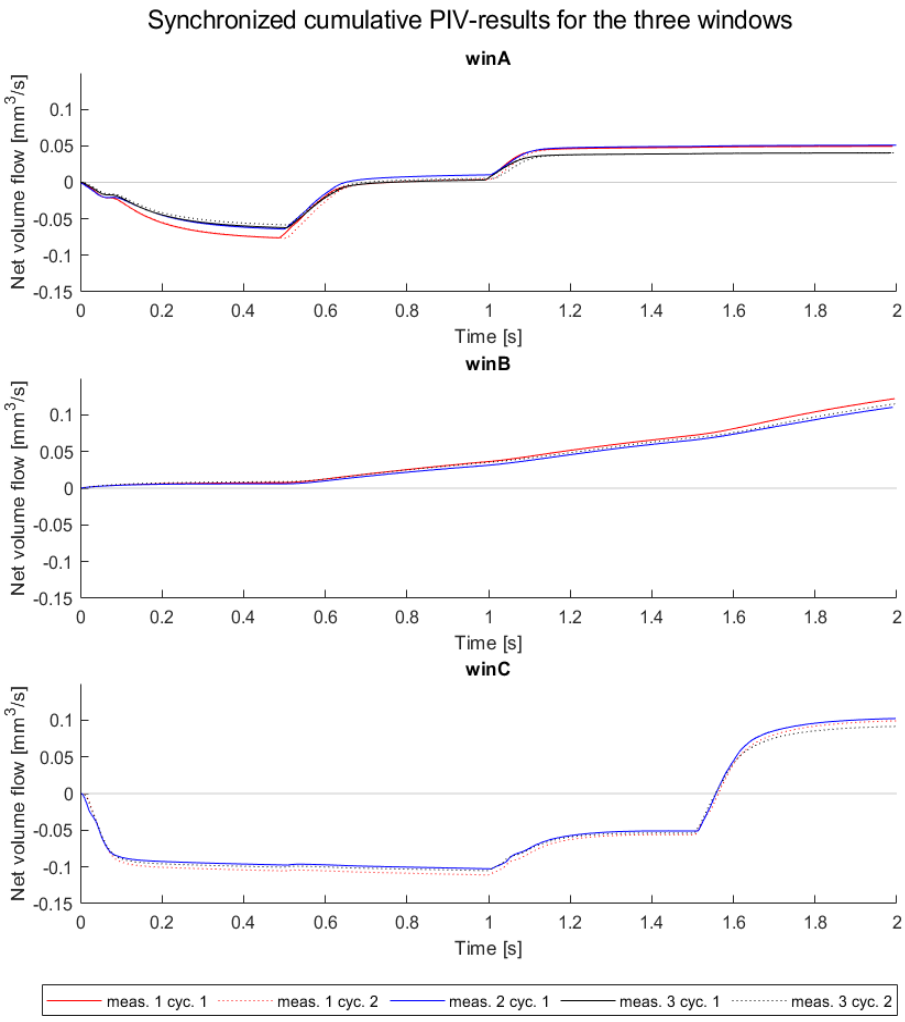


Figure 3-4 - Calculated net volume flow in the µPIV experiments on Chip2 96-well. Positive flow goes clockwise; negative flow goes counterclockwise.

3.2.3. Determining time-dependent boundary condition

It is eventually intended to compare the flow in a real chip with simulation. To do that the flow in the simulations needs to be the same as in a real chip. Now that the flow profiles have been determined in a real chip, it is time to figure out how to get that same profile as an inlet boundary condition in the LBM and COMSOL Multiphysics simulations. Both with Musubi (the LBM solver) and with COMSOL Multiphysics there are two ways to define time-dependent boundary conditions. One can define a time-dependent variable or use a data-file.

The first cycle of the second µPIV measurement of WinA will be analysed (measurement 2, cycle 1 in Figure 3-3). This one was selected as it appeared quite averaged. The differences between cycles were small enough that any other would have functioned as well. The µPIV results had quite some noise on the peaks of the flow velocity. This was undesirable for the simulation. For the inlet boundary condition it would be nice to have smooth function or data file.

First attempts to transform the velocity profile of WinA to a function dependent on time tried a Fourier transformation (Sormann et al., n.d.) and several types of polynomial fits. This did not lead to the desired results. For future reference they are shown in Figure 3-5. It shows that the Fourier series and splines include all the noise at the peaks and the polynomials fail to approximate the straight parts.

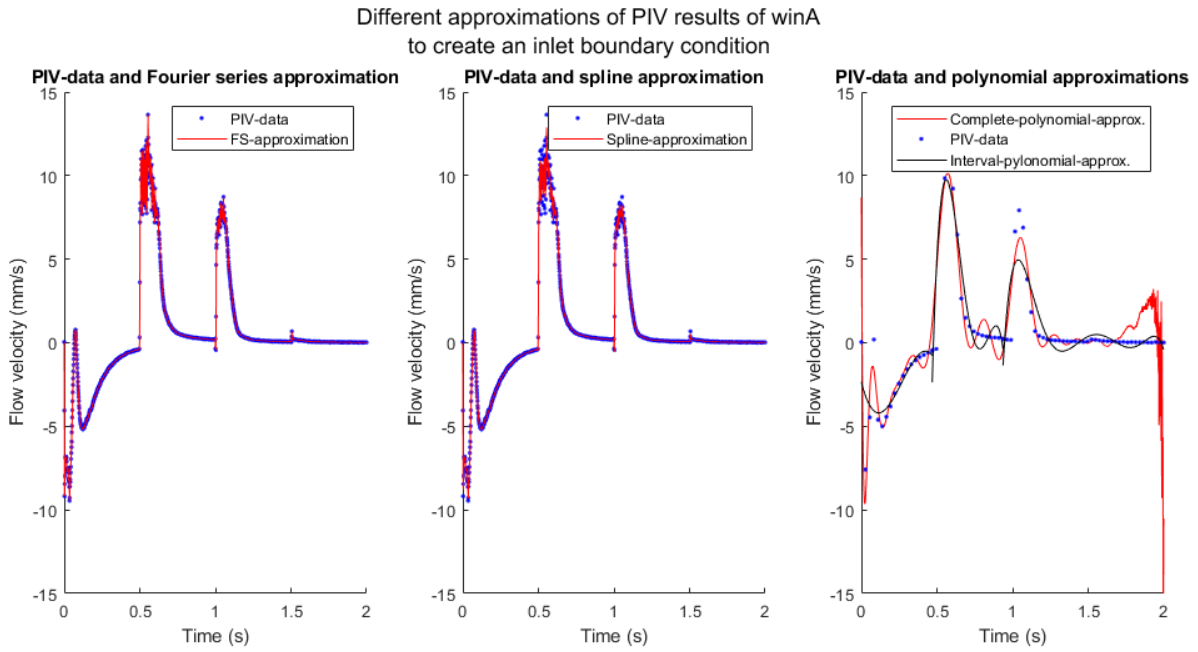


Figure 3-5 - Different methods attempting to create a good inlet boundary condition. Left to right: Fourier series, a spline approximation and polynomial approximations. The polynomial approximation was done of the complete dataset at once and of separated intervals of the dataset. Both had undesirable results.

Since finding a proper time-dependent function did not work, it was more convenient to use a data file for the inlet velocity. To still get rid of the noise, the data was smoothened. Splitting the data in intervals improved smoothening. Figure 3-6 shows the intervals. On each of these intervals Gaussian smoothening was applied. This lead to the smooth dataset in Figure 3-6. Matlab exported this dataset together with its timestamps to a .dat-file. This file now gives the inlet velocity for one complete pump cycle in the simulations to follow.

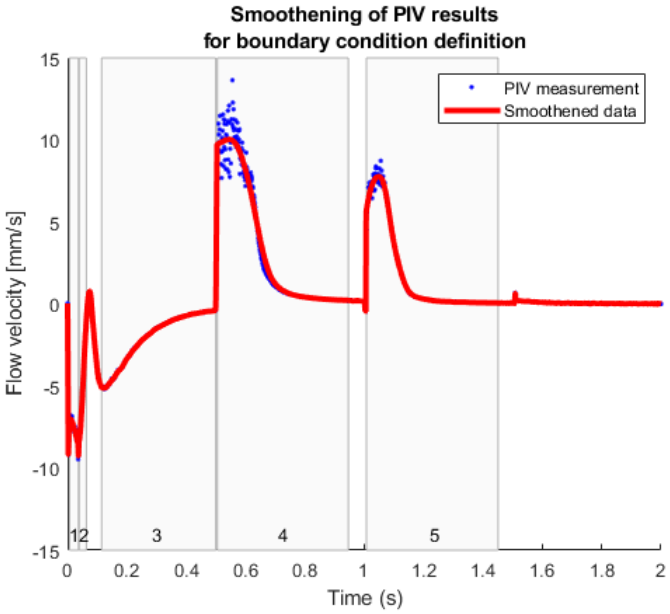


Figure 3-6 - Smoothened data used as inlet velocity boundary condition for the LBM and COMSOL Multiphysics simulations. The µPIV conditions were smoothened on five different intervals, whose numbering is shown at the bottom of the figure.

3.3. LBM simulation

The µPIV experiments have been analysed and resulted in a smooth inlet velocity profile. Next up are the LBM simulations. 3.3.1 describes how the simulations were set up, how the simulations were defined and what variables were tracked during the simulations. Before any proper simulations can be done a mesh independence study is required. This is discussed in 3.3.2. Paragraph 3.3.3 then presents the results of the LBM.

3.3.1. Simulation setup

The first thing to do when setting up a simulation, is to define the geometry. This geometry is taken from a Chip2 96-Well. TissUse has a 3D model of the chip and its microfluidics.

Geometry

The microfluidics of the chip consist of channels and two compartments. Where the channels are completely submerged, the liquid does not reach all the way to the top of the compartments (see Figure 3-7). When the compartments are closed during operation, there is some air trapped in them. For the simulation only the liquid is considered. The geometry only goes till the interface between air and liquid and ignores the air trapped in the compartments.

The pump is too complex to simulate. Hence, it will be replaced by the PIV-based inlet boundary condition. It is thus not incorporated in the mesh.

Since the boundary conditions are determined in the channels, the outer parts of the pump will be cut off as well such as in Figure 3-8. This way the boundary condition that is determined using µPIV in 3.2.3 can be used as the inlet velocity in the channel. This leads to the microfluidics in Figure 3-9, which is the geometry that is meshed for the simulations.

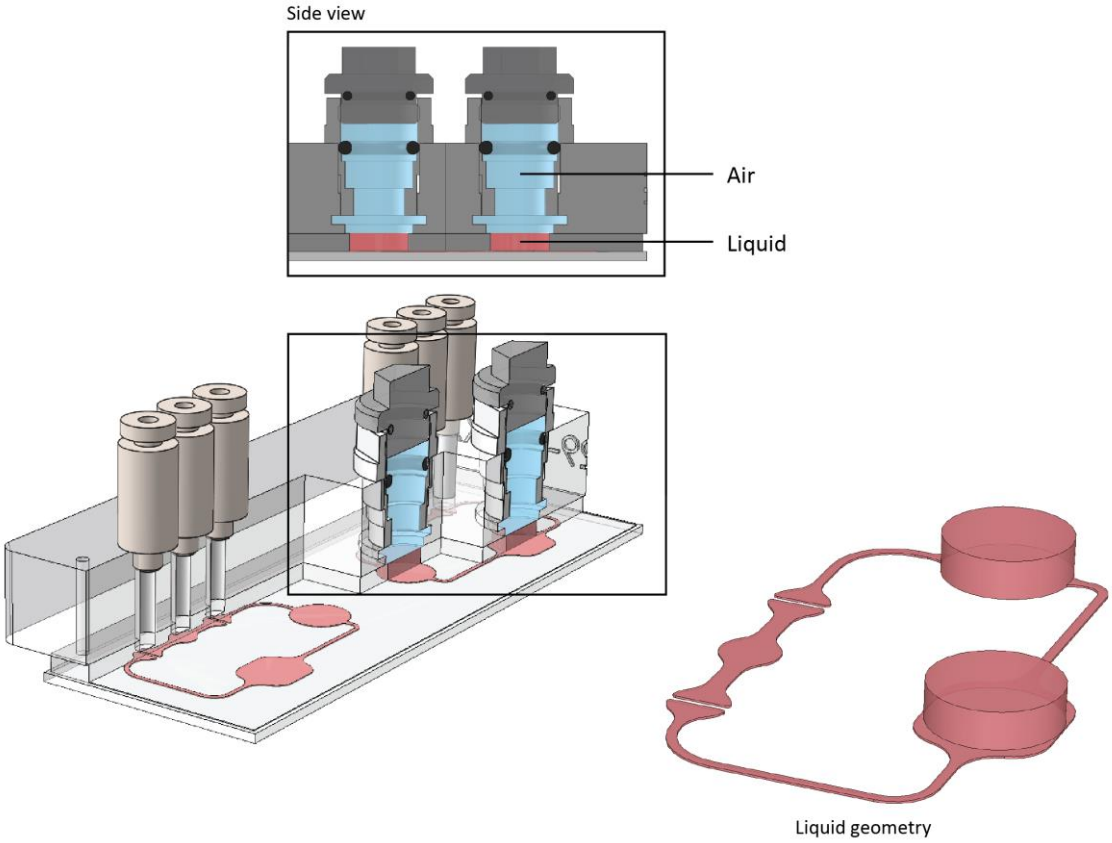


Figure 3-7 - Liquid inside the channels, compartments and pump. This is the geometry that is extracted from the chip's CAD model and converted into an STL. Excluding the pump.

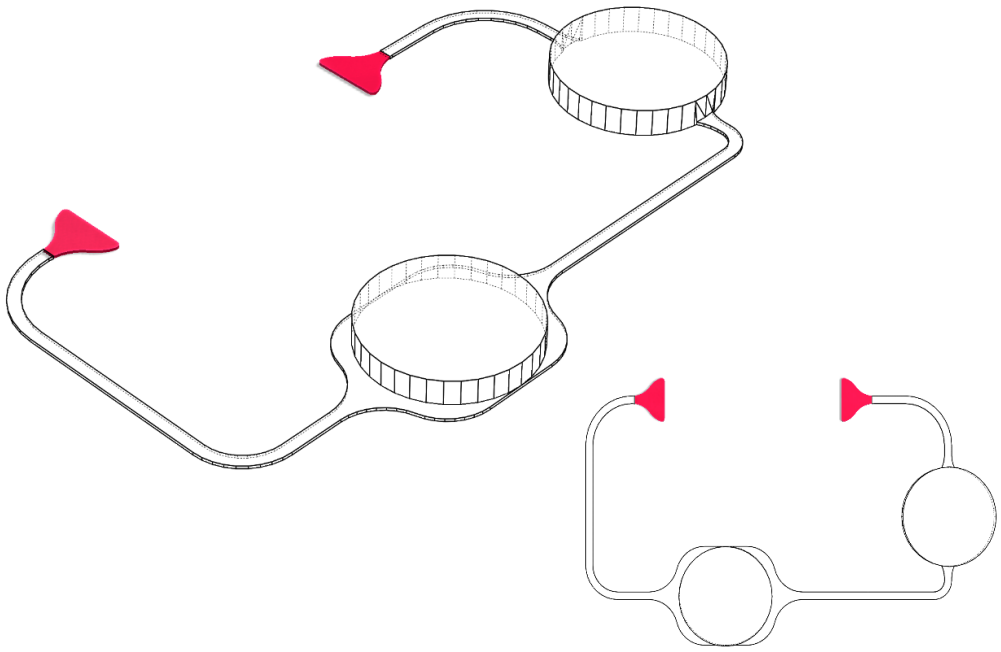


Figure 3-8 - Picture of the inlet and outlet of the pump being cut off.

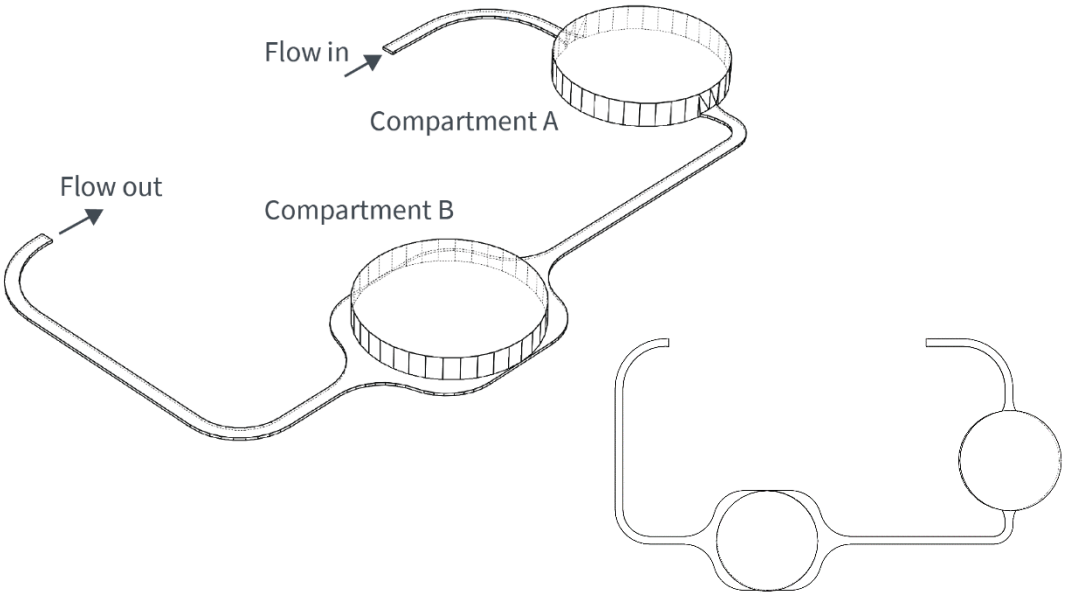


Figure 3-9 - Geometry of the microfluidics that is used for the simulations.

Fluid

The liquid in the simulation is set as water at a standard temperature 18 $°C$. Hence, the fluid is simulated as being incompressible. Table 3 gives the variables used in the simulations:

Quantity	Symbol	Value
Density	ρ	$998 \cdot 10^{-9}\ kg/mm^3$
Dynamic viscosity	μ	$1.05 \cdot 10^{-6}\ kg/mms$
Pressure	p	$1\ bar = 100\ kg/mms^2$

Table 3 - Physical properties of the liquid used in the LBM simulations. The values are for water at $18°C$. Density is from (Engineering Toolbox, 2003d) and the dynamic viscosity comes from (Engineering Toolbox, 2004). Pressure is approximately atmospheric pressure.

Simulations

Three simulations were performed.

1. First of all, there is a simulation with a constant inflow of 4 mm/s. Here a total time of 1 s was simulated. This first simulation will be referred to as “the constant simulation”.
2. The inflow in the second simulation follows the data file determined in 3.2.3. Consequently, one full pump cycle was simulated, which in real life lasts 2 s. From now on this is called “the transient simulation”.
3. Besides these two simulations an additional simulation was done. This simulation is the same as the transient simulation, however it simulates the top of the compartments as being open. This will be explained further on when the boundary conditions are discussed. Also, this simulation was done on a grid with an element size of 0.016 mm.

The time step in these simulations is determined using diffusive scaling. It does not have much to do with physical diffusion. The shape of the relation that defines the time step is merely similar to the diffusion equation (Krüger et al., 2017, p. 244). See the parameter selection in 2.4.4 for further explanation. With diffusive scaling the time step is defined as:

$$\delta_t = \frac{\nu_{lat}}{\nu_{phy}} \cdot \delta_x^2 \qquad 3\text{-}2$$

Here δ_t is the simulations time step and δ_x its grid size. ν_{phy} is the physical kinematic viscosity and ν_{lat} is it counterpart on the lattice of the simulation. See 2.4.4 for explanation of the relation between the two. For diffusive scaling it goes that:

$$\nu_{lat} = \frac{1}{3}\left(\frac{1}{\Omega} - \frac{1}{2}\right) \qquad 3\text{-}3$$

Table 4 shows the value of collision operator Ω and what parameters resulted from this scaling. The grid size given here is the result of the mesh independence study which will be discussed in the next section 3.3.2.

Quantity	Symbol	Value
Grid size	δ_x	$0.01\ mm$
Time step	δ_t	$4.06 \cdot 10^{-7} s$
Collision operator	Ω	1.95

Table 4 - Parameters regarding diffusive scaling in the LBM simulation

Boundary conditions

The geometry, the fluid and the intended simulation are defined. Now the boundary conditions are needed. Initially, all velocities inside the geometry are zero and the pressure is 1 bar.

- The entire geometry is defined as a no-slip rigid wall.
- The inlet is defined by a flow velocity. This flow velocity is either constant at 4 mm/s (constant simulation) or follows the PIV-based boundary condition (transient simulation).
- At the outlet a pressure is defined. The pressure is set to an approximately atmospheric pressure such that it resembles a simple open exit.

The additional simulation is the same as the transient simulation. The only way it differs is that the roofs of the compartments are also defined by a pressure instead of as a rigid wall. This means that in this simulation the liquid can also flow out the geometry there, see Figure 3-10. More on the types of boundary conditions is described in the background theory in 2.4.5.

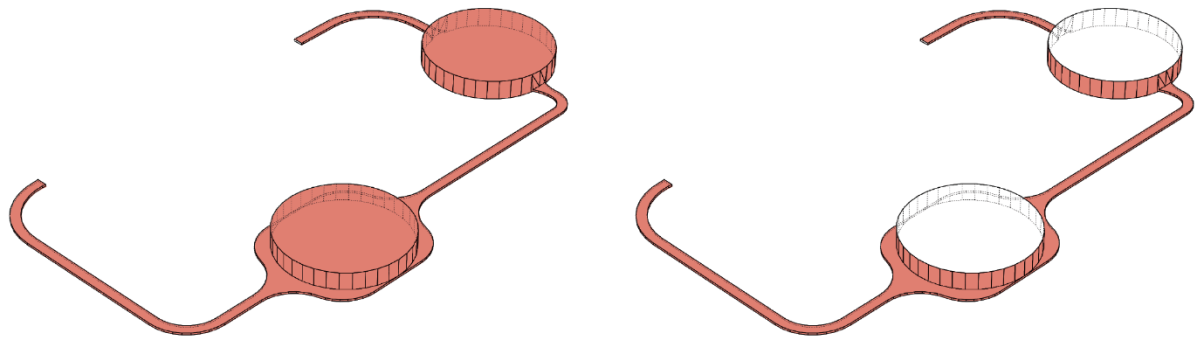


Figure 3-10 - Boundary conditions of the simulations. Red is no-slip wall. Left is the boundary conditions in the constant and transient simulation. The image on the right shows the top of the compartment being open outlets. This is how the additional simulation works.

Flow quantity trackers

In order to get results from the simulation, the simulation program Musubi needs flow quantity trackers. These are points, planes or cuboids that keep track of flow quantities during the simulation and save them so they are available for study. In the simulations there were four different flow quantity trackers, which were defined as follows:

1. **The full-slice-tracker**: a plane exactly on the middle of the height of the channels. It spans the entire chip, see Figure 3-11.

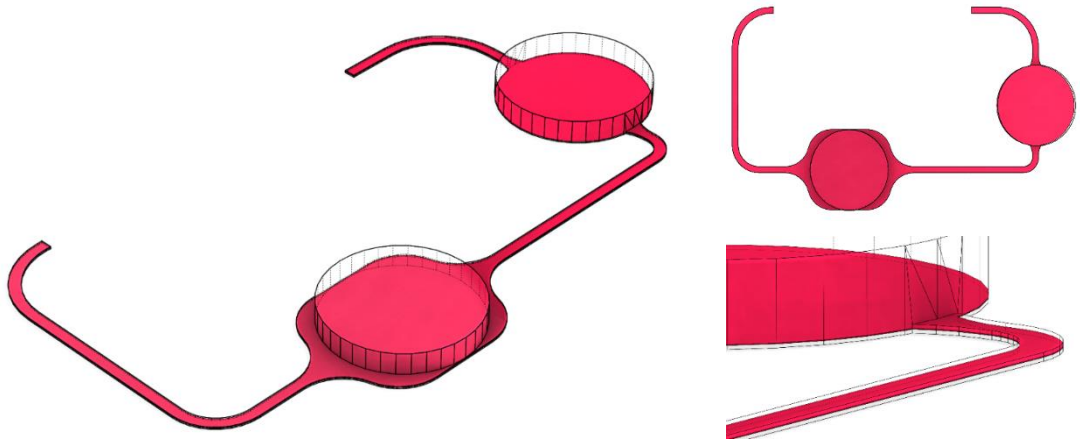


Figure 3-11 – Full-slice-tracker spanning the entire chip. As can be seen at the bottom right, it is exactly in the middle of the height of the channel.

2. **The compartment-slice-trackers**: To see how the liquid behaves in the compartments they are cut through the middle in flow direction. They go into the channels pre- and succeeding the compartments a little bit as well, see Figure 3-12.

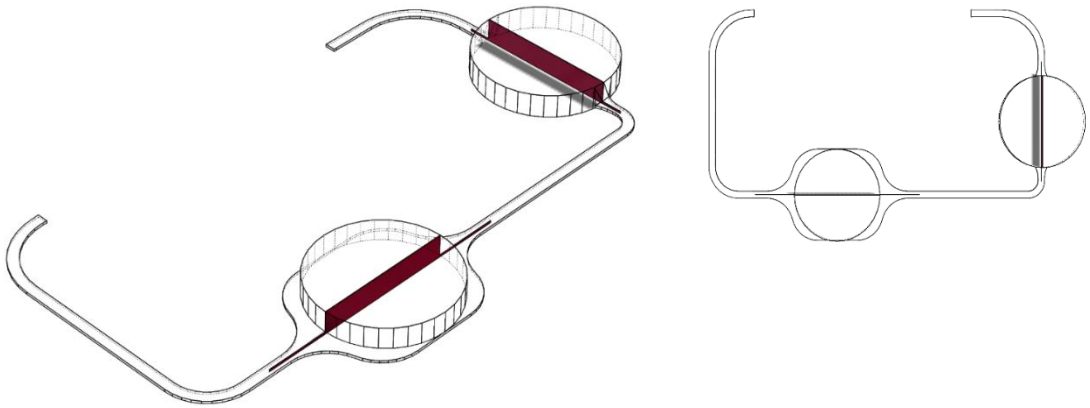


Figure 3-12 - Compartment trackers exactly in the centre of both compartments in flow direction.

3. **The PIV-window-trackers**: These trackers are 3D and span exactly the same volume as the fields of view in the PIV-experiments. Tracking these windows will allow the LBM to be compared directly to the PIV-experiments. See Figure 3-13 for the three windows.

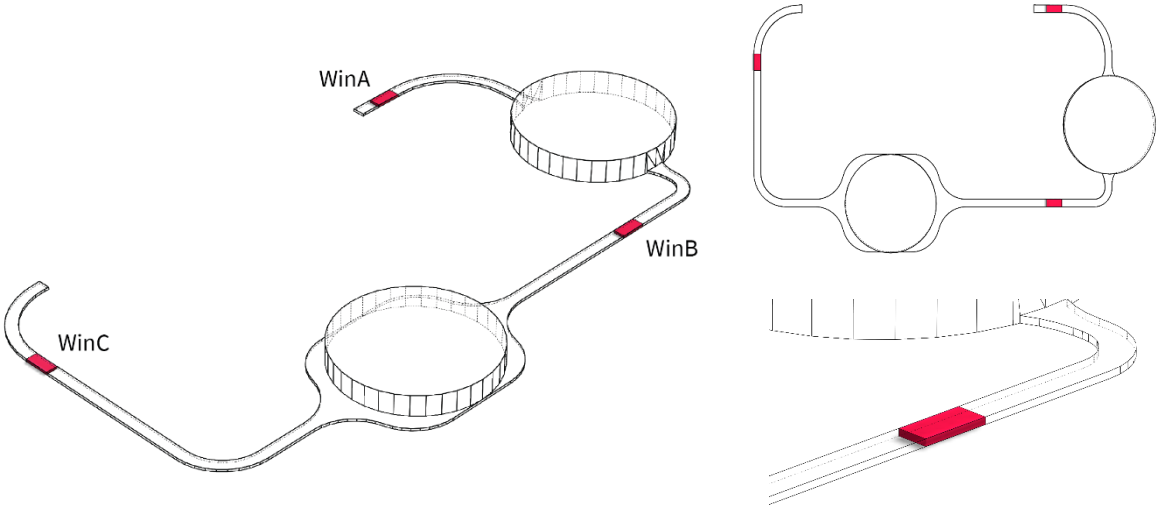


Figure 3-13 - Three trackers. One for each of the windows of the µPIV experiments, WinA, WinB and WinC

4. **The point-trackers**: These are seven points, shown in Figure 3-14. Three of them are in the centre of the PIV-windows. Consequently, they are in the centre of their respective channels. The other four are at the entrances and exits of the compartments. They are at the same height as the full-slice-tracker and the three points in the centre of the PIV-windows. The point-trackers in Compartment A are central 1 mm from the entrance and exit. Those in Compartment B are 1.5 mm from the start of the curvature in the channel.

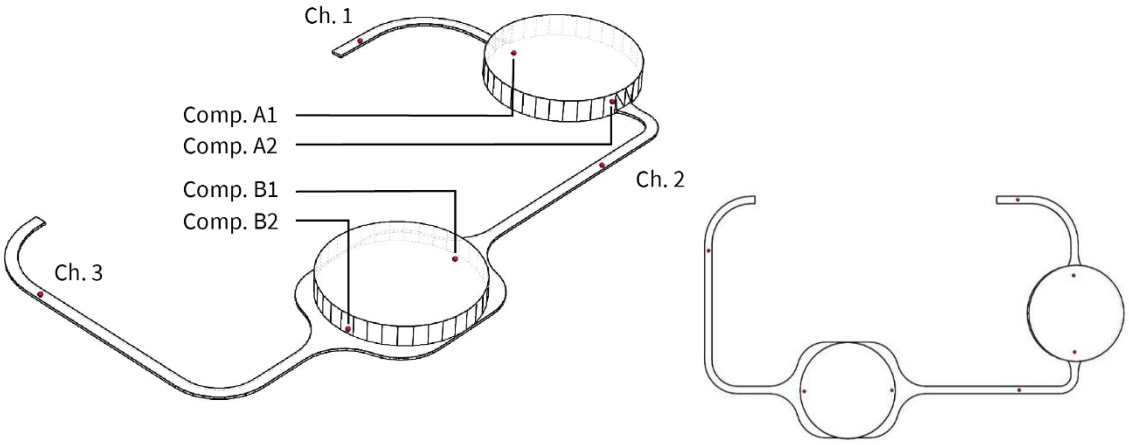


Figure 3-14 - The seven point trackers in the centre of the flow.

3.3.2. Mesh independence study

Before any proper simulations will be performed, a mesh independence study will be done. The study used four different grid sizes. Simulations with a constant inflow velocity as described in 3.3.1 were performed. The simulations started with an element size of $\delta_x = 0.020\ mm$. This yields 5 elements in the height direction of the channels as a starting point. From there it is important to figure out what element size is appropriate.

The point-trackers in channel 1, 2 and 3 (so at the centre of µPIV WinA, WinB and WinC respectively) provided the data for this mesh independence study. These trackers are defined in 3.3.1. They tracked the velocity in their location. The resulting velocities for each tracker in each simulation are gathered in Table 5. Figure 3-15 is a visual representation of this data.

Grid size δ_x [mm]	Ch. 1 (WinA) [mm/s]	Ch. 2 (WinB) [mm/s]	Ch. 3 (WinC) [mm/s]
0.020	6.08	1.44	1.47
0.016	5.06	1.87	2.48
0.012	6.09	4.54	4.94
0.010	6.55	6.22	6.29

Table 5 - Velocities at the centre of WinA, WinB and WinC resulting from simulations with a constant inflow of 4 mm/s at different grid sizes

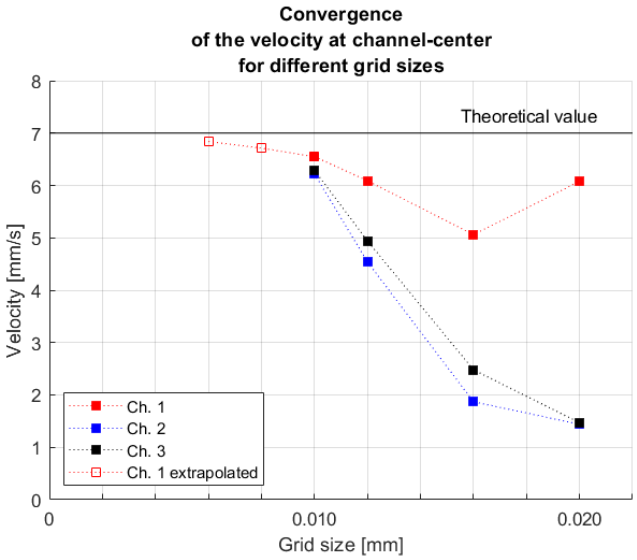


Figure 3-15 - Convergence of the velocities in the centre of WinA, WinB and WinC on different grids. Filled square markers are simulated, outlined square markers are estimated with Richardson extrapolation.

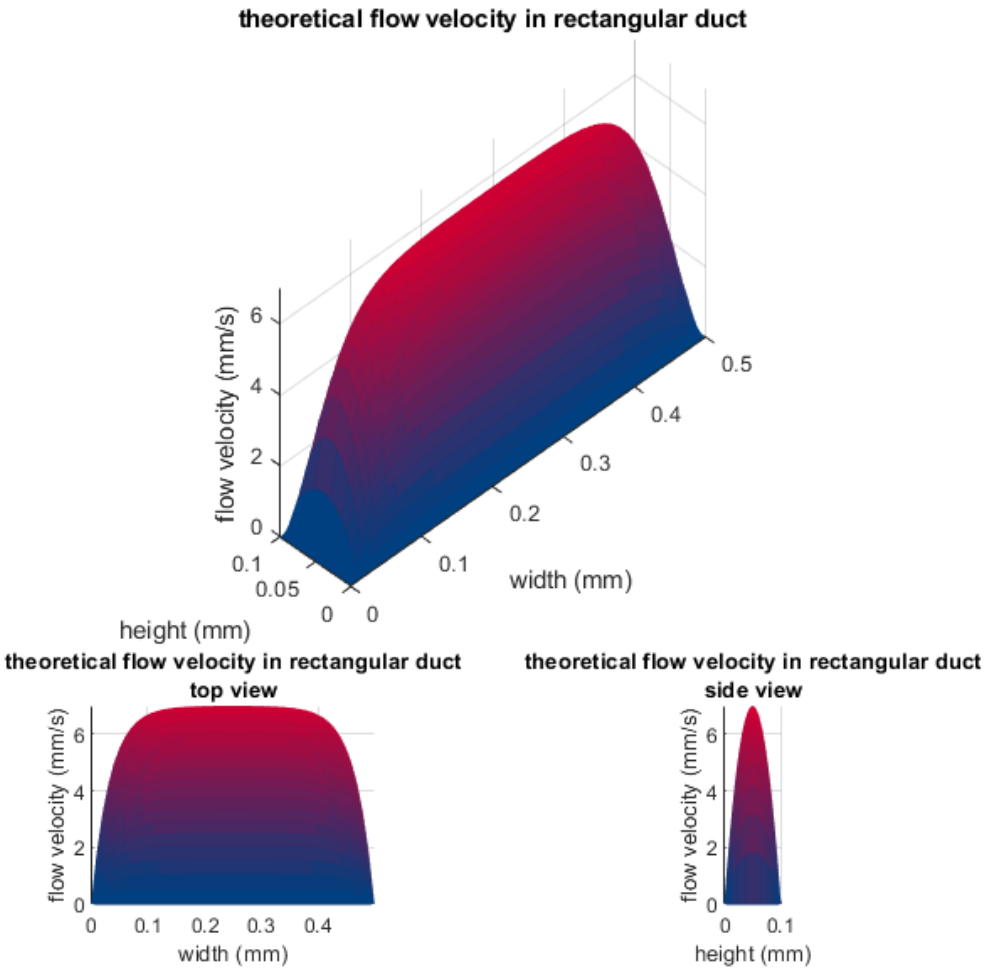


Figure 3-16 - Theoretical fully developed flow profile in the channels of a Chip2 96-well.

The flow in the chips was determined theoretically. This way there would be a theoretical solution to compare with the simulations and estimate the errors of each simulation. For completeness it must be noted that the LBM's continuum solution might not comply with theoretical solution. Appendix F elaborately explains how the theoretical flow profile was determined. Some critical study of existing literature was required. The explanation in Appendix F uses the volume flow rate, entrance length and a Fourier series approximation of the Navier-Stokes equations to find the theoretical fully developed flow profile in the chip's channel. Figure 3-16 shows the resulting flow profile. The theoretical fully developed flow profile has a maximum velocity at its center of 7.0018 mm/s.

With the theoretically correct flow velocity at all the channel centres known, it is possible to calculate the relative errors of all the grids. This is done with the following formula:

$$\epsilon = \frac{7.0018 - u}{7.0018} \cdot 100 \qquad 3\text{-}4$$

Here, ϵ is the relative error and u the size of the velocity vector.

Table 6 shows these relative errors of each grid in percentages. Figure 3-17 is a visual representation of that data. It shows that from a grid size of 0.016 mm the simulations start to properly converge. The velocity distributions of the full-slice-tracker in Figure 3-18 to Figure 3-21 depict this behavior neatly too. From that grid size the flow gradually becomes more similar throughout the chip and goes towards the theoretical value.

Grid size [mm]	Ch. 1 (WinA) [%]	Ch. 2 (WinB) [%]	Ch. 3 (WinC) [%]
0.020	13.1	79.4	79.0
0.016	27.7	73.3	64.6
0.012	13.0	35.1	29.4
0.010	6.43	11.1	10.1

Table 6 - Relative errors of the velocities at the centre of WinA, WinB and WinC from simulations with a constant inflow of 4 mm/s at different grid sizes.

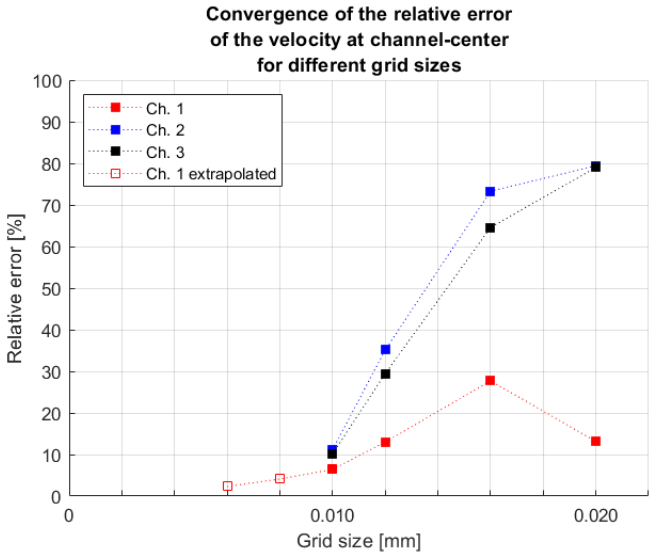


Figure 3-17 - Relative errors of the velocities in the centres of WinA, WinB and WinC for different grids. The filled square markers indicate simulation results. The two red outlined square markers are extrapolations.

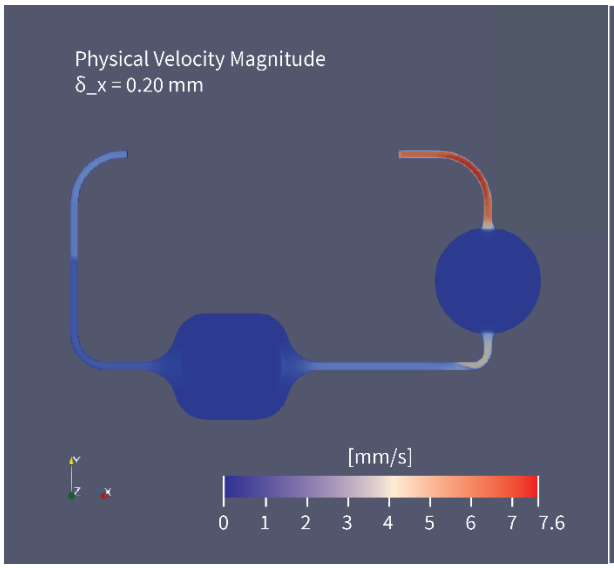


Figure 3-18 - Velocity distribution on a grid of 0.020 mm

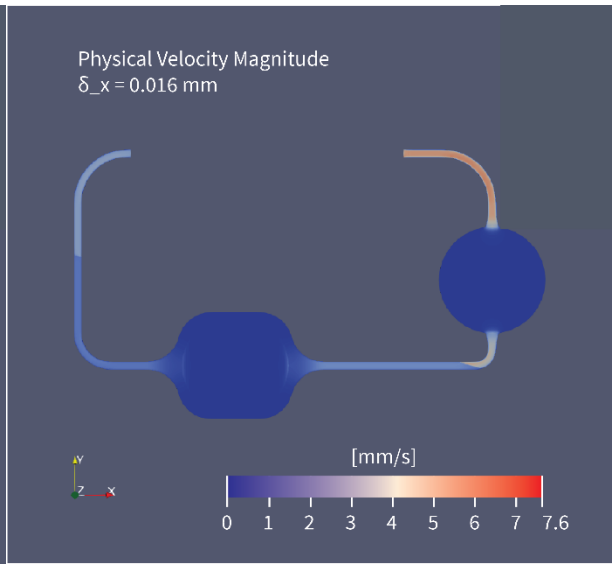


Figure 3-19 - Velocity distribution on a grid of 0.016 mm

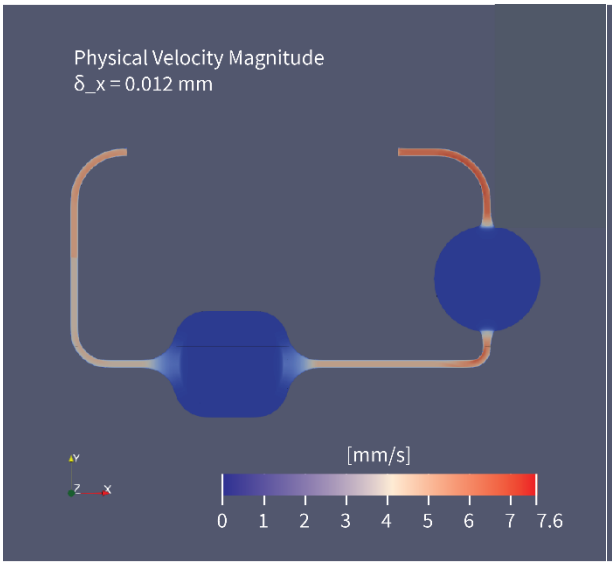


Figure 3-20 - Velocity distribution on a grid of 0.012 mm

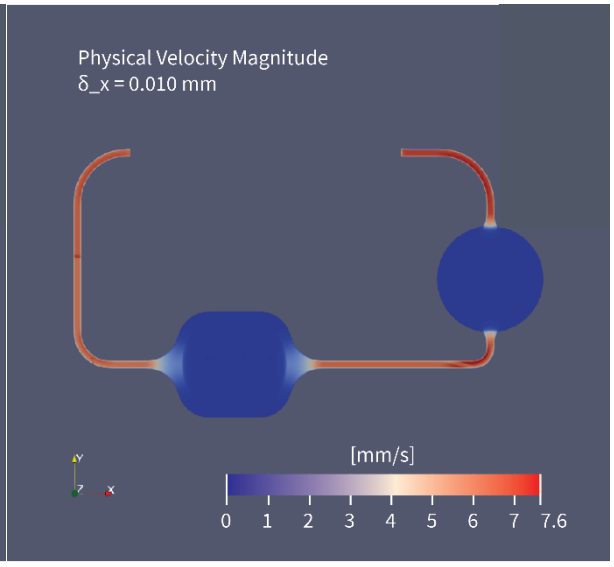


Figure 3-21 - Velocity distribution on a grid of 0.010 mm

Richardson extrapolation

The grid convergence and mesh independence is established. Before the final simulations are performed, it is interesting to know how much better the solutions might get with even finer grids. Combining this with the expected calculation time of finer grids helps with picking a suitable grid size.

To this end, take the standard formula for Richardson extrapolation (J.W. Slater, 2021):

$$f_{\delta_x=0} = f_1 + \frac{f_1 - f_2}{r^p - 1} \qquad 3\text{-}5$$

Here f_1 is the solution on a finer grid. f_2 is the solution on the coarser grid. $f_{\delta_x=0}$ is the numerical solution in the limit of the grid size going infinitesimally small, so the limit to the continuum solution. r is the ratio between the coarser and the finer grid: $r = \delta_{x_2}/\delta_{x_1}$. Finally, p is the theoretical order of convergence for LBM, which is 2, as was established in 2.4.6.

3-5 uses two solutions to give a higher order indication of the continuum solution. Since the continuum solution is already theoretically defined (in Figure 3-16 and Appendix F), this formula is not needed anymore. It is interesting at this point to estimate what the solution would be at finer grids. Hence 3-5 is rewritten to:

$$f_1 = \frac{f_{\delta_x=0} + \frac{f_2}{r^p - 1}}{1 + \frac{1}{r^p - 1}} \qquad 3\text{-}6$$

Now, 3-6 is an estimation of the solution on a finer grid based on the order of convergence, a coarser solution and the continuum solution. This formula is now used to estimate the expected errors on a grid of 0.008 and 0.006 mm. Among other things Table 7 shows these errors. Table 7 contains more characteristics of the different grids. Right next to the errors is the calculation time witnessed during the study's simulations. Data shown in black is empirical, those in red are estimates.

The characteristics of the simulation with a grid of 0.010 mm looked most feasible. The calculation time was still reasonable with 19 hours. The error reduction expected by going to 0.008 mm did not justify an expected calculation time of 58 hours. Hence the simulation will be done with a grid of 0.010 mm, outlined with black in Table 7.

	Mesh			Simulation					
Grid	N° elems.	Size	Calctime	Simtime	N° procs	Calctime	Error [%]		
[mm]	[-]	[MB]	[s]	[s]	[-]	[s]	WinA	WinB	WinC
0.020	8.346.433	255	179	0.8	128 (t)	24.020	13.1	79.4	79.0
0.016	16.267.599	451	290	0.8	224 (t)	200.638	27.7	73.3	64.6
		451	129	2.0	2400 (c)	6600			
0.012	39.395.892	995	328	0.8	2400 (c)	12.592	13.0	35.1	29.4
				2.0	2400 (c)	31.480			
0.010	68.046.743	1587	378	0.8	2400 (c)	26.781	6.43	11.1	10.1
				1.0	2400 (c)	33.671			
				2.0	2400 (c)	67.861			
0.008				2.0	2400 (c)	204.321	4.11	7.13	6.49
0.006	317.171.532	6399	2399	2.0	2400 (c)	861.006	2.31	4.01	3.65

Data in black	Empirical
Data in red	Estimated
Data with black outline	Selected grid for LBM simulations

Table 7 - Simulation characteristics for different grid sizes. Right most columns show the (expected) calculation times and relative errors. Data in black is empirical, data in read is estimated. Data shown from left to right: Grid size, Number of elements in the mesh, size of the mesh, calculation time to create the mesh, physical time simulated, number of processors used for the simulation, calculation time needed for the simulation and error compared to theoretical velocity in channel centres. Choice for the final simulation is marked in black outline. Processor numbers with (t) are on a cluster tfe2. Those with a (c) are on supercomputer Cartesius.

3.3.3. Results

So, it was concluded that a grid with size $\delta_x = 0.010\,mm$ should be a proper grid. The PIV-based boundary condition for the inlet of the simulations has been determined in 3.2.3. The setup of the three simulations was discussed in 3.3.1. The results of these simulations are gathered in this paragraph.

Firstly, Figure 3-22 depicts the flow velocities measured by the point-trackers during the constant simulation. Interesting detail here is that there appears to be a delay in the flow. The flow in Channel 2 and 3 needs a bit of time to reach the right velocity compared to Channel 1. Zoomed-in figures of Compartment A are incorporated, because in those areas the flow was relatively minimal.

Next, Figure 3-23 shows the flow velocity from the point trackers in the transient simulation. Here again enlarged graphs of Compartment A are added.

Thirdly, Figure 3-24 shows the flow velocities in the same point-trackers for the additional transient simulation that simulated the tops of the compartments as being open. All graphs could use a zoom in. Only compartment A1 and Channel 2 have one. The other graphs were similar to those.

Finally, Figure 3-25 and Figure 3-26 show the results that were tracked by the PIV-window-trackers during the transient simulation. Figure 3-25 depicts the average of the actually tracked flow velocity over each window's region. Figure 3-26 shows the calculated cumulative net volume flow per window. These results can be compared directly with the µPIV results in Figure 3-3 and Figure 3-4. This comparison, together with the results from the COMSOL simulations will take place in 3.5. For now, it appears that the static simulation is quite right, but the transient and additional simulation leave something to be desired.

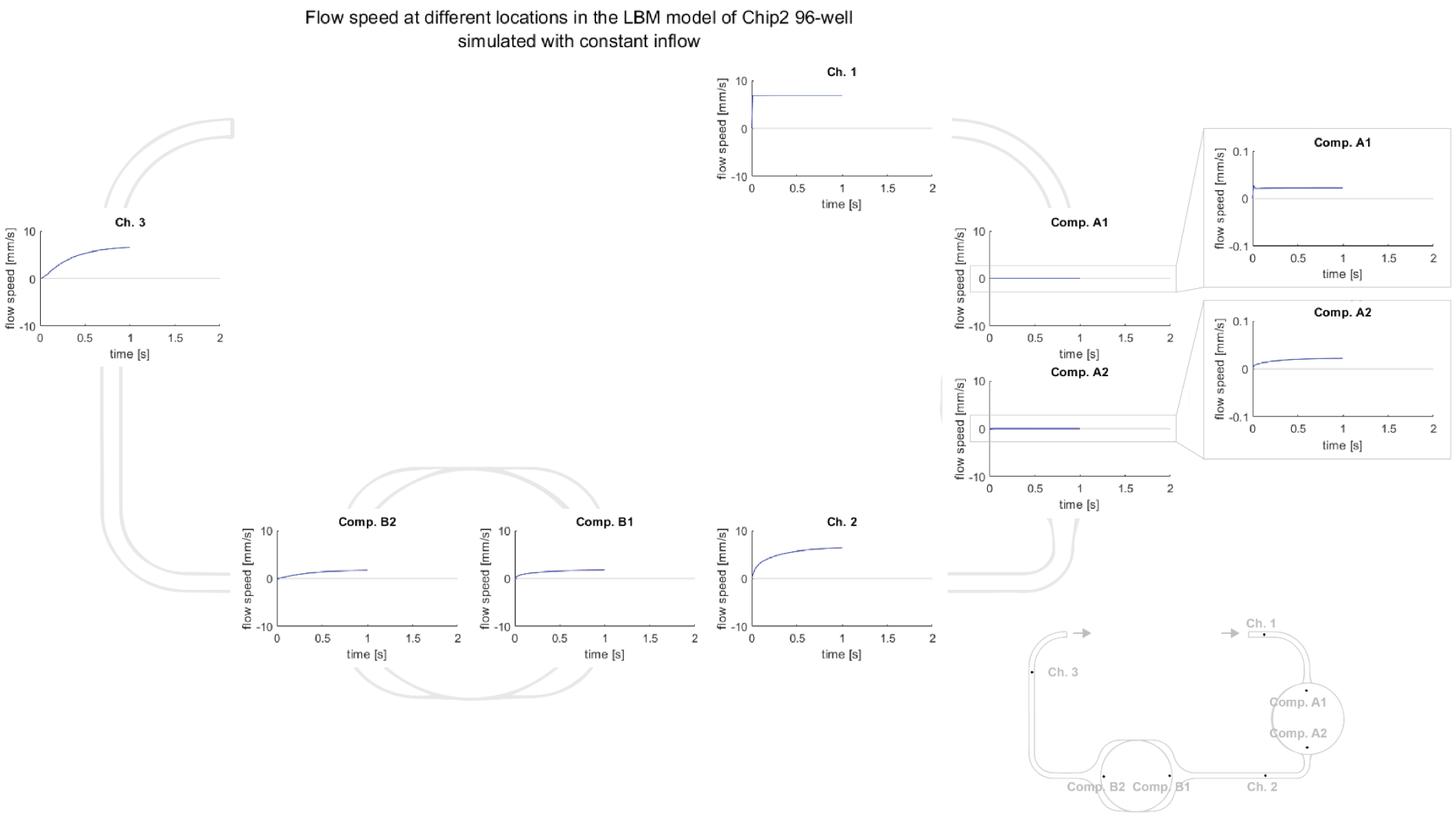


Figure 3-22 - Results of point trackers of the constant simulation with LBM. Showing a close-up of the flow in Compartment A. As this simulation was with constant inlet flow, the lines were horizontal or asymptotic. It contains no pump profile.

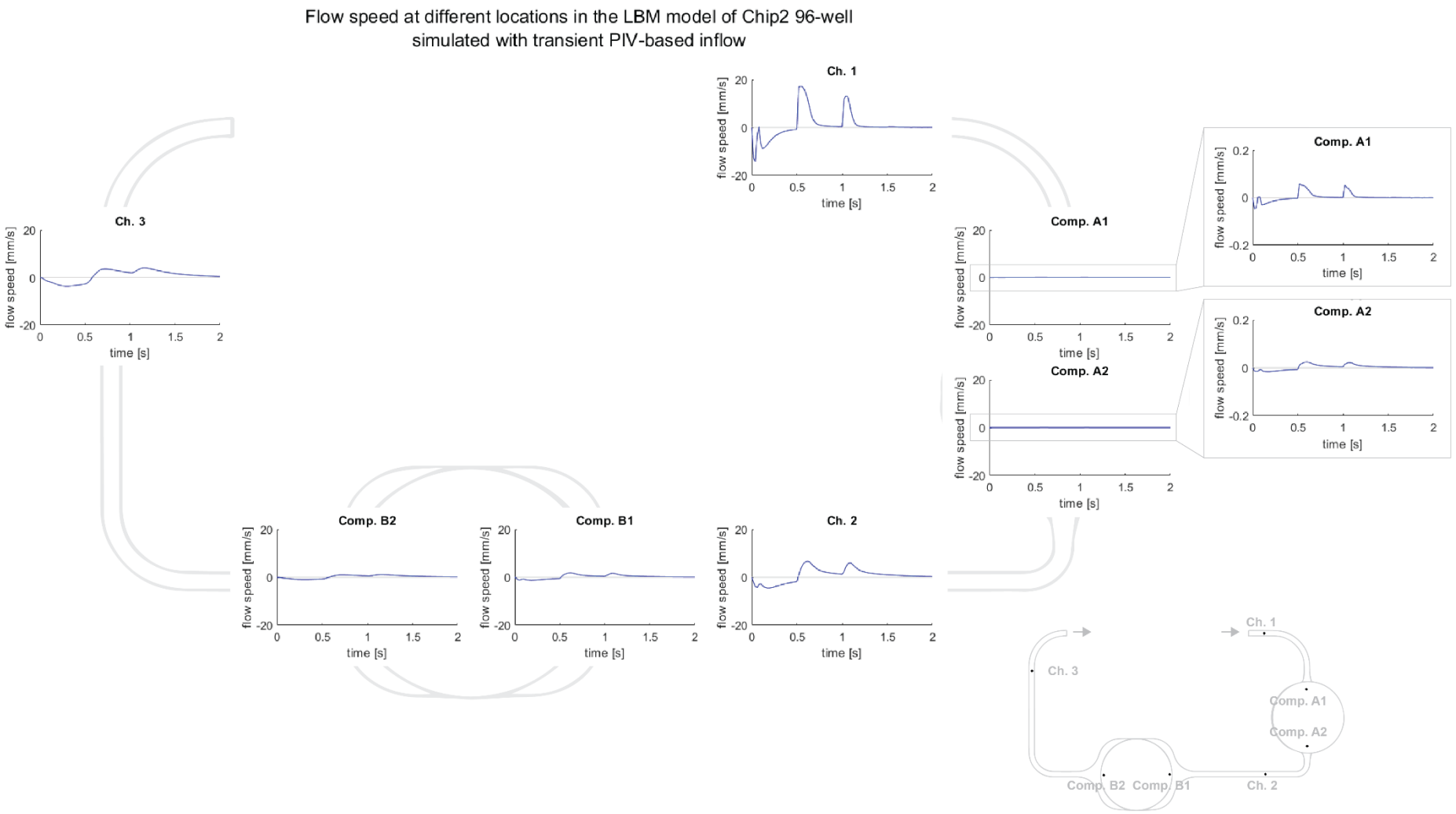


Figure 3-23 - Results of the point trackers of the transient simulation with LBM. Showing exactly one full pump cycle of 2 seconds. Enlargement of the results in Compartment A are included.

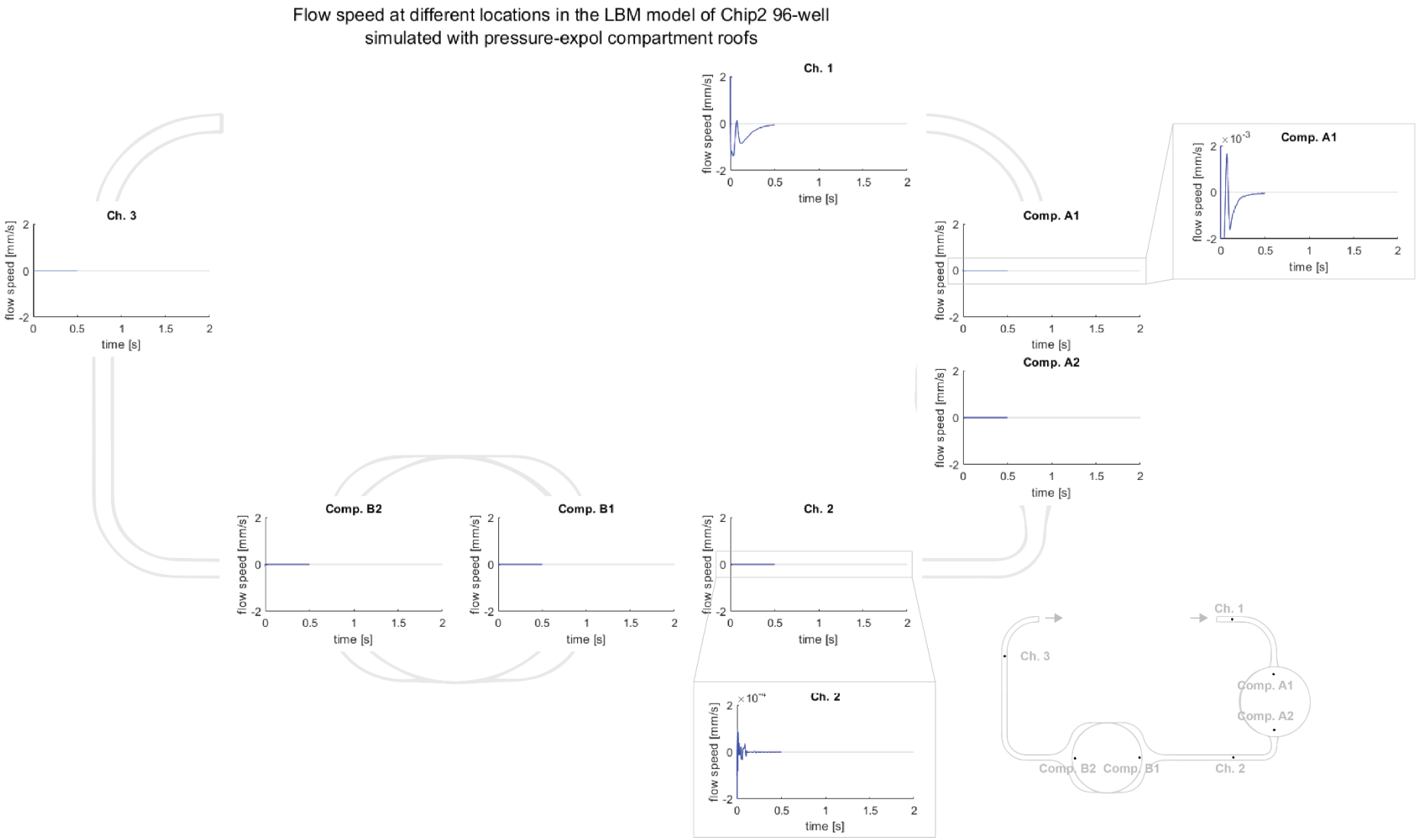


Figure 3-24 - Results of the additional transient simulation with LBM. Additional zoomed-in graphs of Compartment A1 and Channel 2 are shown. Only the first half second of the pump cycle was simulated.

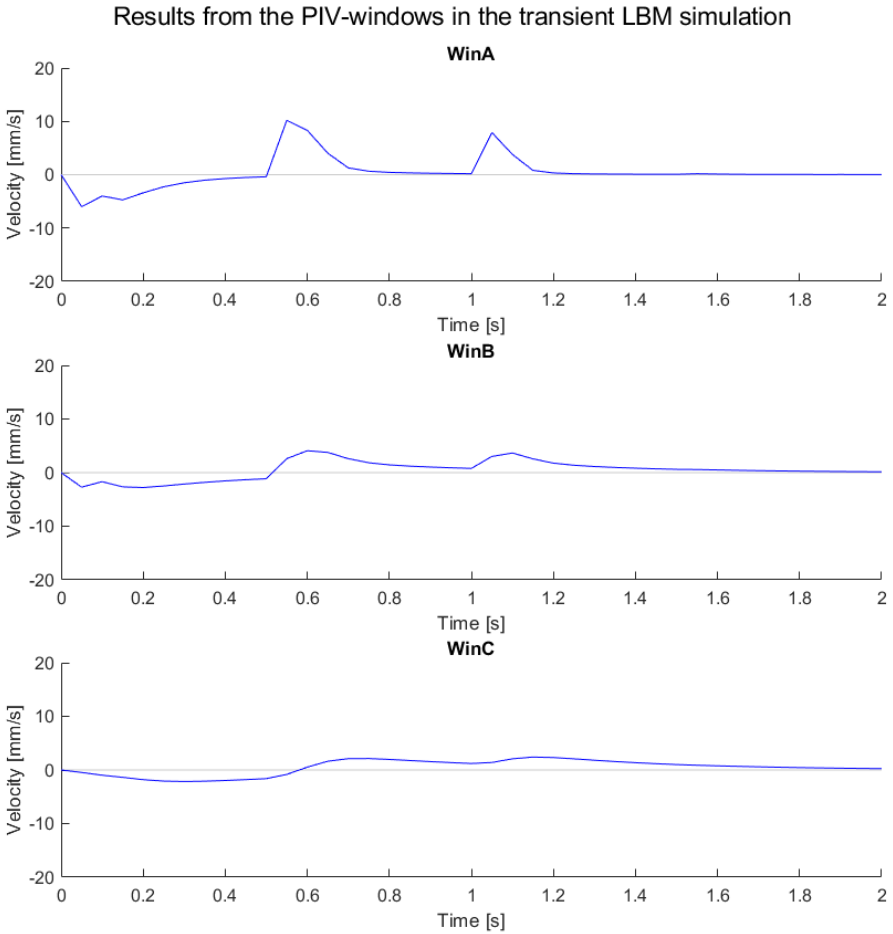


Figure 3-25 - Average velocities measured in the µPIV window trackers of the LBM simulation. Positive flow goes clockwise; negative flow goes counter clockwise.

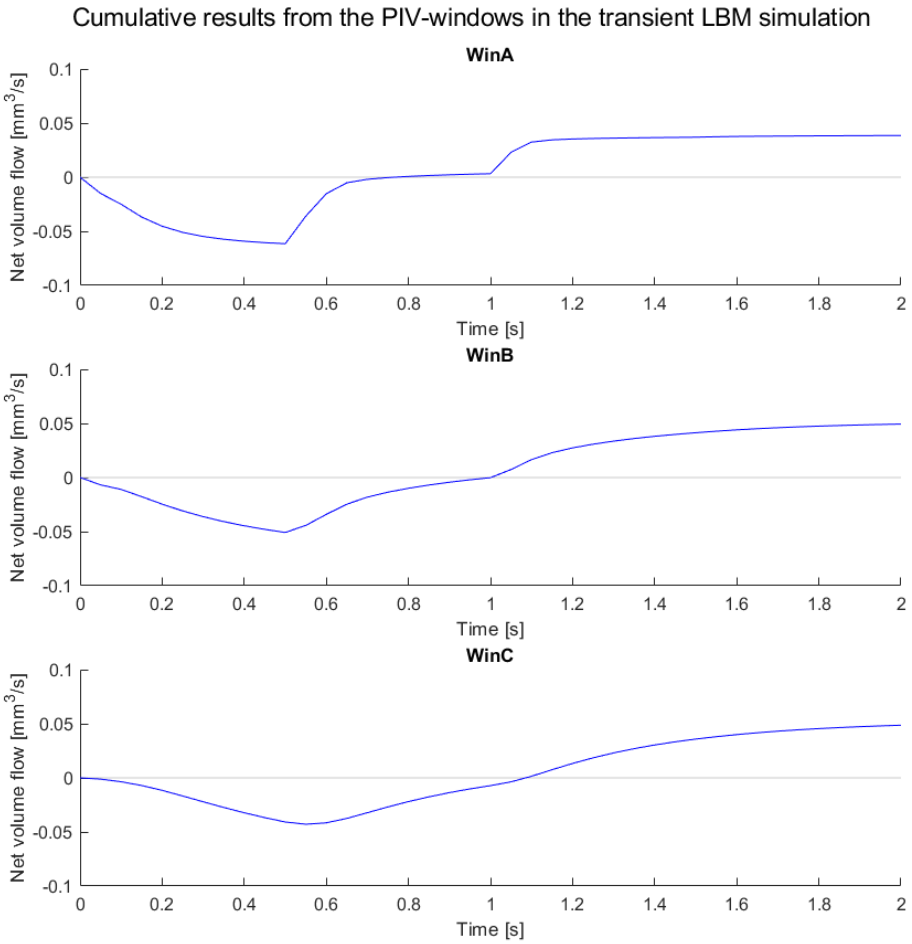


Figure 3-26 - Net volume flow in the µPIV window trackers of the LBM simulation. Positive flow goes clockwise; negative flow goes counter clockwise.

3.4. COMSOL Multiphysics simulations

Chip2 96-well has now been subject to µPIV experiments, and LBM simulations have attempted to mimic that behaviour. It is now time for the third method to characterize the flow in the chip: simulation with COMSOL Multiphysics.

Just like with the chapter regarding LBM, the setup of the simulations will be discussed first in 3.4.1. Then a mesh independence study follows (3.4.2) before considering the results in 3.4.3.

3.4.1. Simulation setup

The setup of the simulations in COMSOL Multiphysics is rather similar to those with LBM.

Geometry

The geometry is identical as that used for LBM and shown in Figure 3-9.

Fluid

The only place where the COMSOL Multiphysics simulations differ from the LBM simulations is in the liquid. Both methods use incompressible fluid. However, with COMSOL the water was at a slightly higher temperature. LBM used a room temperature of 18 °C. COMSOL assumed the chip runs inside an cell-culture incubator at 37 °C. Table 8 shows the resulting physical properties.

Quantity	Symbol	Value
Density	ρ	$994 \cdot 10^{-9}\ kg/mm^3$
Dynamic viscosity	μ	$0.69 \cdot 10^{-6}\ kg/mms$
Pressure	p	$1\ bar = 100\ kg/mms^2$

Table 8 - Physical properties of the water used in the COMSOL Multiphysics simulations. Density and dynamic viscosity came from the COMSOL Multiphysics database automatically when setting the temperature and the material.

Simulations

COMSOL performed the same simulations as LBM. Here repeated for convenience:

1. A constant simulation with inflow velocity of 4 mm/s.
2. A transient simulation. Just like the transient LBM simulation it had an inlet velocity profile that was based on the µPIV experiments as determined in Figure 3-6. This time-dependent inlet boundary condition represents one complete pump-cycle, which lasts 2 s. The simulation will hence simulate 2 s.
3. An additional transient simulation with the compartment roofs being simulated as outlets.

Boundary conditions

Initially, all velocities inside the geometry are zero and the pressure is 1 bar. Regarding the boundary conditions:

- The inlet is defined the same as with LBM. It is set to have a certain inlet velocity. Which again is either 4 mm/s (for the mesh independence study) or the PIV-based inflow boundary condition.
- Also the outlet is set to the same approximately atmospheric pressure of 1 bar.
- The rest of the exterior of the geometry is defined as a no-slip wall as shown on the left side of Figure 3-10.

Trackers

Trackers function differently in COMSOL Multiphysics than in the LBM solver Musubi. Most of the results have to be extracted from the complete set of results after a simulation is complete. Data equivalent from LBM's PIV-window-trackers (which were defined in Figure 3-13) and the point-trackers (which were defined in Figure 3-14) will be gathered in this report.

3.4.2. Mesh independence study

Just like with LBM it is good to get to know whether the solutions COMSOL will give are close to reality. Despite being a commercial program, a mesh independence study is still in place. To this end three simulations with constant inflow were performed. They all had an inlet velocity of 4 mm/s.

COMSOL Multiphysics does not necessarily work by defining element sizes. Default for COMSOL is to generate a physics-controlled mesh. The user can then choose how coarse or fine they want the mesh to be. There are nine levels, starting from normal they go to coarse, coarser, extra coarse and extremely coarse. The same range goes in the normal-fine-finer direction. The mesh independence study started with a normal grid, then a coarse one and a finer one. On top of that, a user-defined grid was used. This set the general element size to coarse, and around corners and the boundary layer areas it was set to finer. To get an idea of how these relate to each other, Table 9 shows the number of elements on each mesh. Figure 3-27 shows a close up of the exit of Compartment B for the different grids.

Grid level	Nº elements	Constant sim. Calc. time [min, s]
Finer	1.619.038	12:53
Normal	230.305	3:31
Coarse	112.057	1:46
Custom	137.746	0:38

Table 9 - Number of elements of the different grids in the mesh independence study with COMSOL Multiphysics. The calculation time for a simulation of the constant simulation and for one complete pump-cycle of 2 seconds is also included, if available.

Each simulation will develop its flow. The theoretically fully developed flow profile is already known from the mesh independence study with LBM. See Figure 3-16 for this theoretical fully developed flow profile. Appendix F again describes how this theoretical profile was defined. Important to know now is that the maximum velocity at the centre of this profile is 7.0018 mm/s.

It is this velocity at the centre of the channels that was extracted from the three simulations. The point-trackers in channel 1, 2 and 3 (so at the centre of PIV's WinA, WinB and WinC respectively) were used for this. So, for each grid the flow velocities at the centres of all three PIV-window-trackers were collected. They are gathered in Table 10 graphically depicted in Figure 3-28.

Grid level	Ch. 1 (WinA) [mm/s]	Ch. 2 (WinB) [mm/s]	Ch. 3 (WinC) [mm/s]
Finer	6.80	6.89	6.64
Normal	6.62	6.58	6.52
Coarse	6.45	6.29	6.49
Custom	8.63	7.09	7.39

Table 10 - Flow velocities at the centre of channel 1, 2 and 3 for different grid sizes simulated with COMSOL Multiphysics.

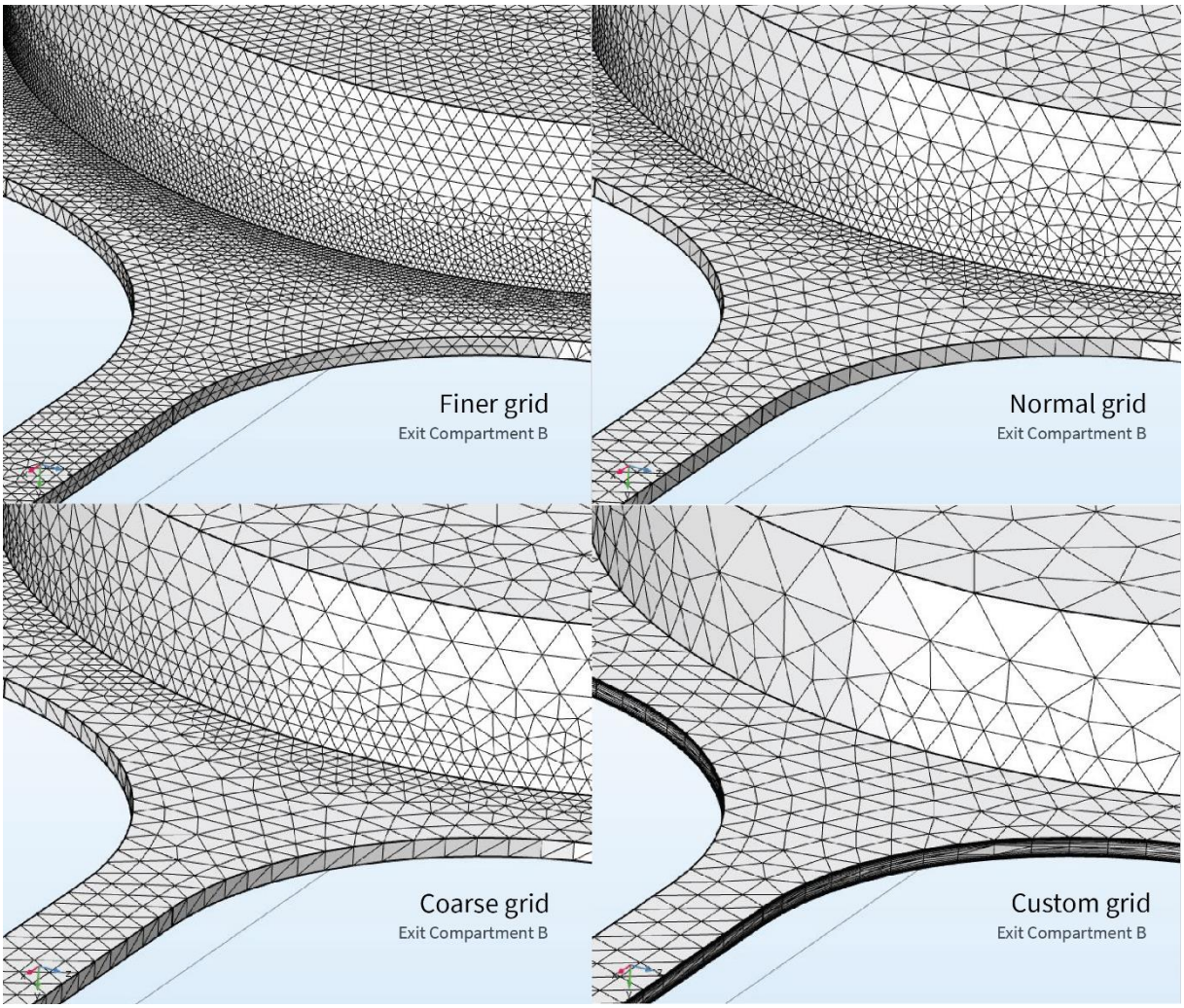


Figure 3-27 - Indication of the grid at the exit of Compartment B on three different standard settings of COMSOL Multiphysics. One grid is made of custom user settings.

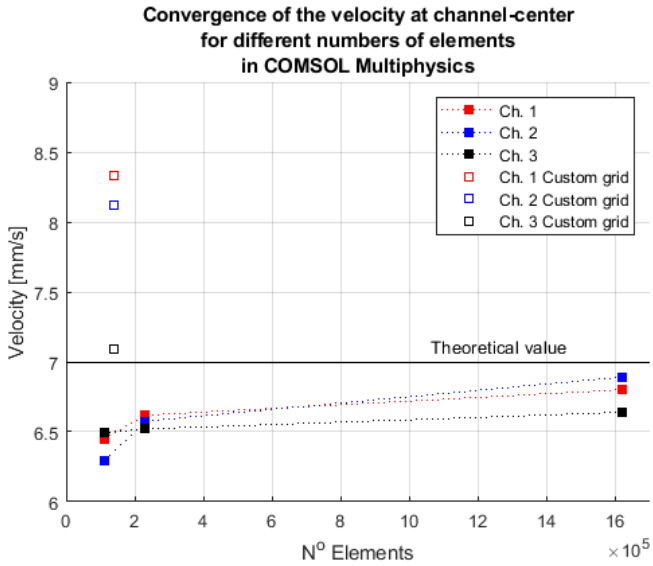


Figure 3-28 - The resulting flow velocities from the three simulations with different grids simulated in COMSOL Multiphysics with a constant inlet velocity of 4 mm/s.

Comparing Figure 3-28 to the results from the LBM mesh independence study in Figure 3-15 quickly leads to the conclusion, that even the results on the coarse grid here are comparable to those of an LBM simulation with an element size of 0.010 mm. Normally one would combine this knowledge with the calculation times in Table 9. However, unfortunately, COMSOL was unable to calculate the transient simulation with the PIV-based inlet boundary condition on any of the standard COMSOL grids. Only the custom grid functioned. Hence the custom grid will be used for the transient and the additional simulation. The constant simulation will still be done with the normal grid.

3.4.3. Results

The simulations have been prepared and the custom grid was selected. This paragraph gathers the results from the simulations with COMSOL Multiphysics.

First, Table 11 shows the results from the point-trackers in the constant simulation. Due to how constant simulations work in COMSOL, it only gives values and not a graph such as the LBM constant simulation results. Because this simulation did function on all grids, only for these results the normal grid was used instead of the custom grid.

Figure 3-29 shows the flow velocities tracked by the point-trackers during the transient simulation.

Next, Figure 3-30 shows the flow velocities tracked by the point-trackers during the additional transient simulation that simulated the tops of the compartments as being open. Similar to the LBM results, these results are close to zero for almost the entire chip.

Finally, Figure 3-32 and Figure 3-31 show results from the PIV-window-trackers. Again the average velocity is determined over each window as well as their cumulative net volume flow. Comparison of these PIV-window-tracker results takes place in 3.5.

Flow Quantity tracker	Flow velocity [mm/s]
Ch. 1	6.62
Comp. A1	0.028
Comp. A2	0.036
Ch. 2	6.58
Comp. B1	1.22
Comp. B2	1.54
Ch. 3	6.52

Table 11 - Results from the point-trackers in the constant simulation with COMSOL Multiphysics calculated on the normal grid.

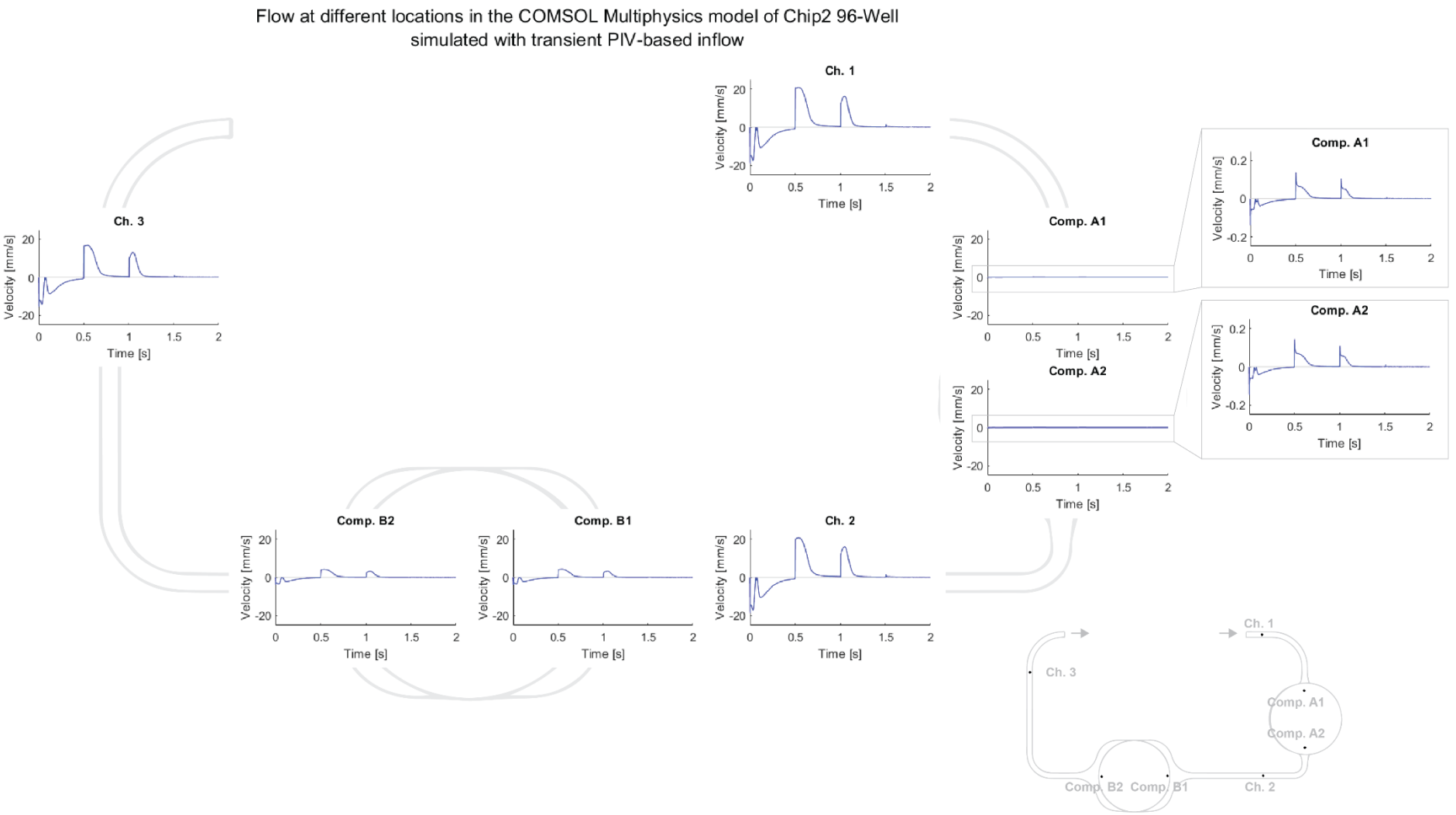


Figure 3-29 - Flow velocities tracked by the point-trackers in the transient COMSOL Multiphysics simulation with PIV-based inlet boundary condition. Showing Compartment A2 with a close-up.

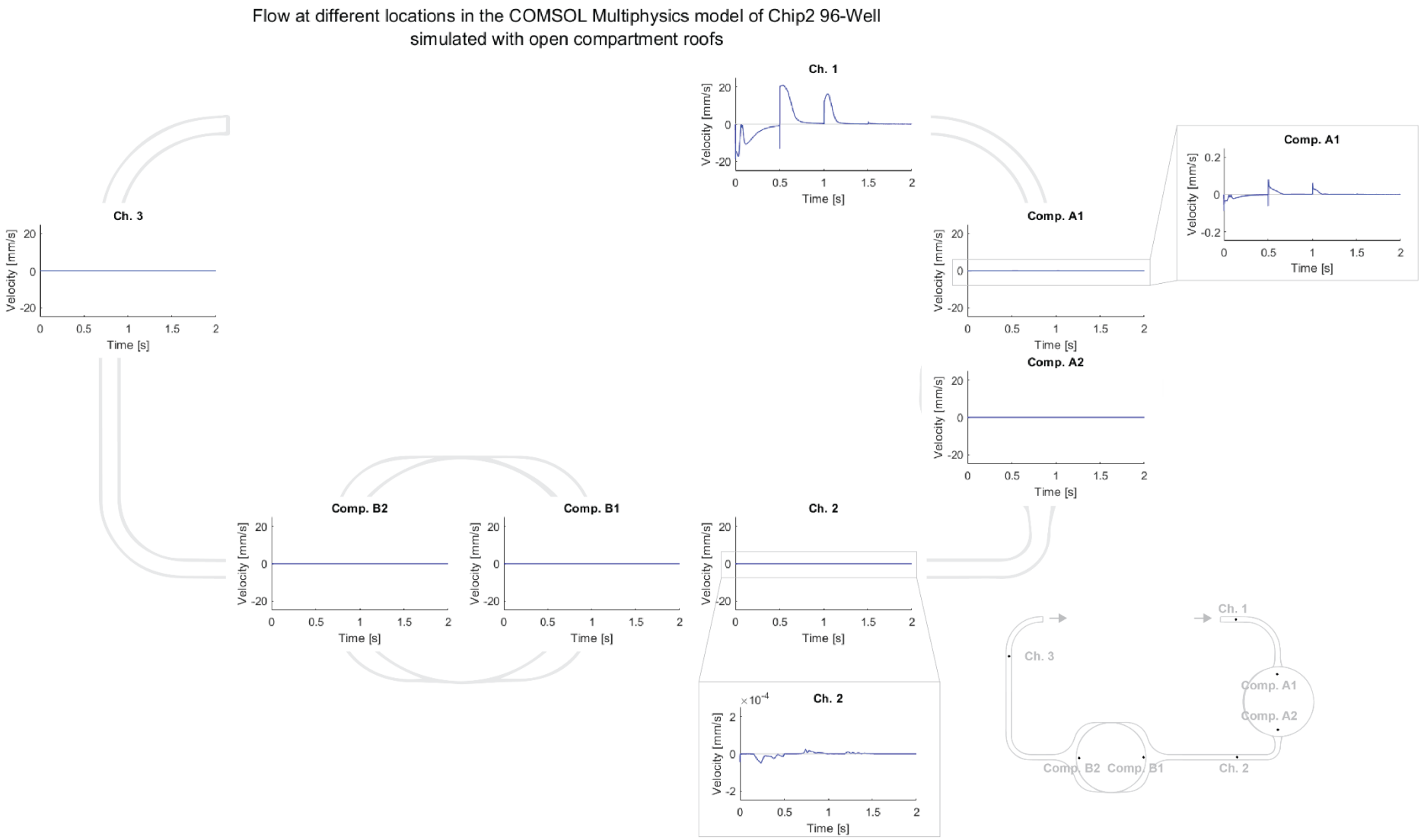


Figure 3-30 - Results of the additional transient simulation with COMSOL Multiphysics. Additional zoomed-in graphs of Compartment A1 and Channel 2 are shown.

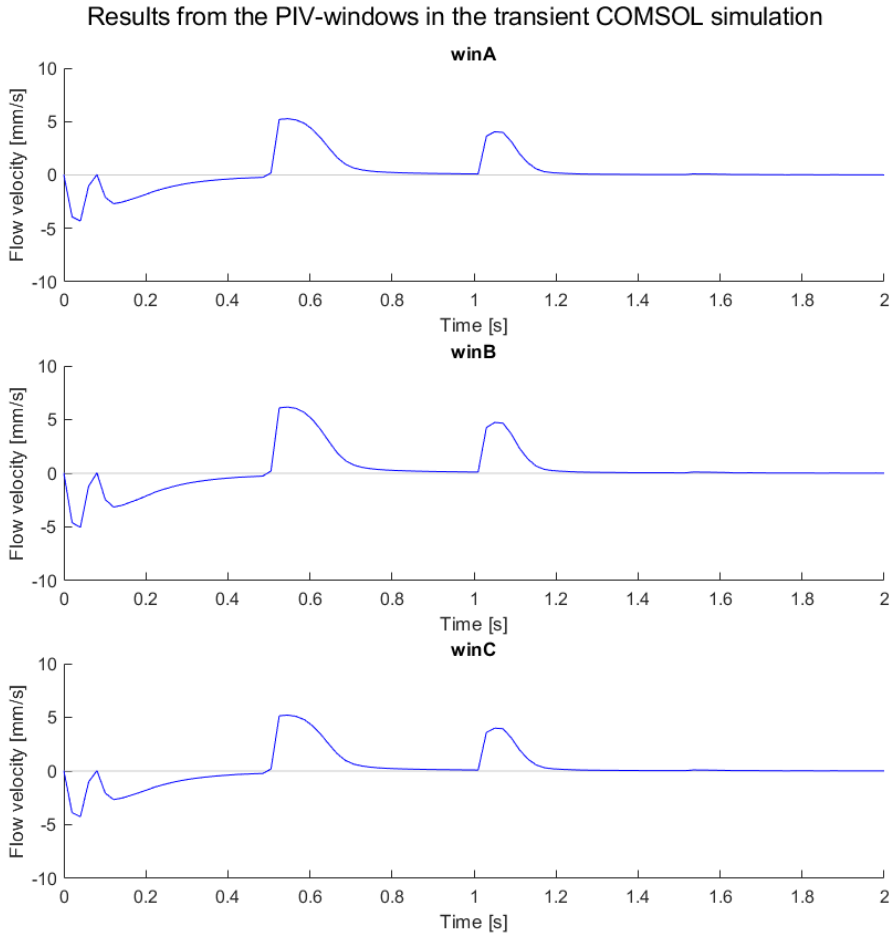


Figure 3-32 - Average velocities measured in the PIV-window-trackers of the COMSOL Multiphysics simulation. Positive flow goes clockwise; negative flow goes counter clockwise.

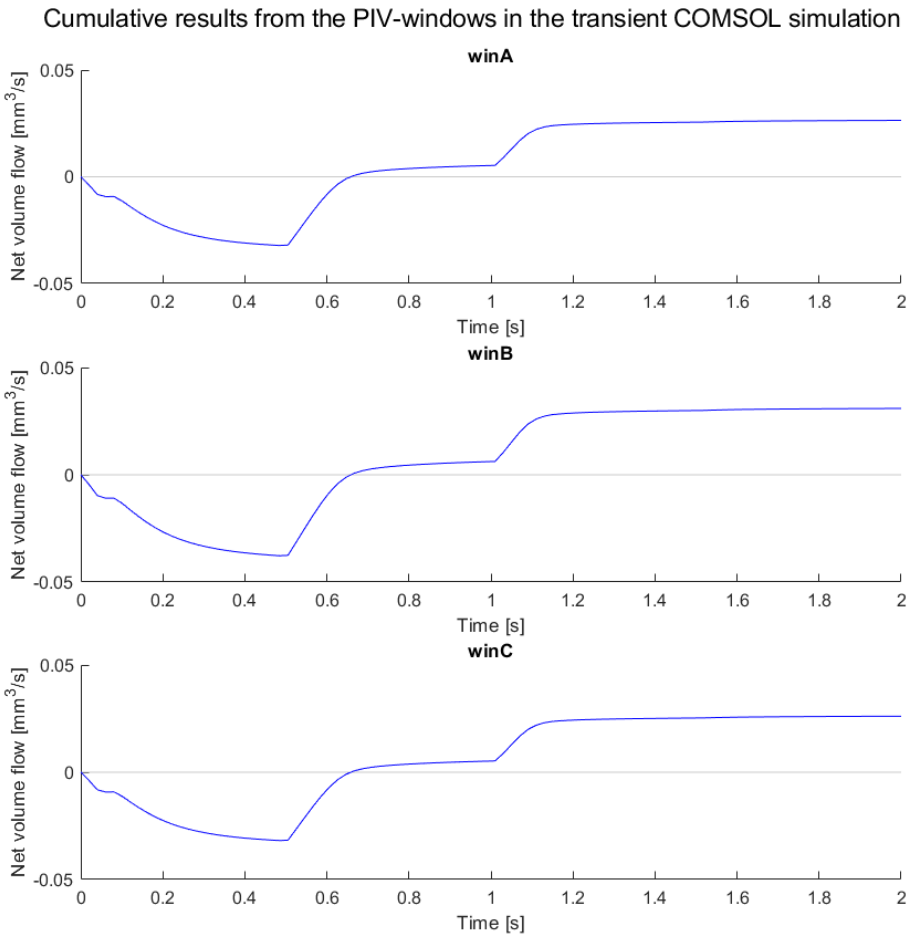


Figure 3-31 - Calculated net volume flow in the PIV-window-trackers of the COMSOL Multiphysics simulations. Positive flow goes clockwise; negative flow goes counterclockwise.

3.5. Discussion

An interpretation of the results, comparison of the different methods and discussion of some limitations in this study will be discussed here. It is structured as follows: 3.5.1 takes a look at the results from the constant simulations with LBM and COMSOL Multiphysics. 3.5.2 then continues to compare the transient simulations of both methods. 3.5.3 shortly discusses the additional simulations. 3.5.4 is where the µPIV results are compared to the µPIV equivalent flow quantity trackers in LBM and COMSOL Multiphysics.

3.5.1. Constant LBM vs. COMSOL

For convenience Figure 3-22 with the results from the constant LBM simulation is expanded with the values from the constant COMSOL Multiphysics simulation in Table 11. This leads to Figure 3-33, which will be used to make a comparison between the two methods.

Please note: the constant simulation is the only simulation where COMSOL Multiphysics used its normal grid. This grid was properly converged. The other simulations used the custom grid. See 3.4.2 for further explanation.

At first sight the results appear quite similar. The figures of the mesh independence studies of both methods showed that LBM (Figure 3-15) and COMSOL Multiphysics (Figure 3-28) both converged to the same theoretical value. Both methods used a grid on which the solution was deemed reasonably mesh-independent. Hence it is expected that the results of a constant simulation on these grids are similar.

What is clear though, is that it takes LBM some time to approach the correct constant flow. This suggests that it is necessary to simulate about 1 physical second with LBM in order to fully develop to a steady state. (Krüger et al., 2017, p. 121) mentions that LBM inherently needs some time to converge to a steady-state solution because it is time-explicit. It references several sources that made attempts at increasing the steady-state convergence of LBM (Filippova & Hänel, 2000; Guo et al., 2004; Izquierdo & Fueyo, 2009). (Guo et al., 2004, p. 1) and (Lai et al., 2001, p. 40) state that LBM is known to converge rather slowly to a steady state. Both the amount of work on the topic and more explicitly (Izquierdo & Fueyo, 2009, p. 6494) suggest that this is an important aspect of LBM. None of them explicitly mention how long it generally takes to reach a steady-state solution, but they suggest it could be sped up by using an MRT collision operator and a slightly altered LBM. This increase could be as much as an order of magnitude (Guo et al., 2004, p. 1) and (Izquierdo & Fueyo, 2009, p. 6494).

Simulation time for the simulation with COMSOL Multiphysics was 211 seconds (Table 9). LBM needed 33.671 seconds (Table 7) for its simulation. Which is 160 times longer. This is a strong advantage of COMSOL Multiphysics over LBM when it comes to constant simulations.

There is a slight difference visible in Compartment A between COMSOL and LBM. The simulations simulate the same physics, so they should have the same value. The difference in Figure 3-33 might be because the tracker in COMSOL Multiphysics simulation was at a slightly different location than in the LBM. Theoretically all trackers are put on exactly the same spot. However, LBM uses a homogeneous rectangular grid made with recursive bisection. COMSOL Multiphysics uses different forms (tetrahedral, cubic, etc.) and sizes of elements throughout its mesh Hence, the exact spot might differ in the order of one tenth of a millimetre. As the flow velocity is quite low and is somewhat prominent around the trackers in the compartments, a slightly different tracker-location could explain the difference.

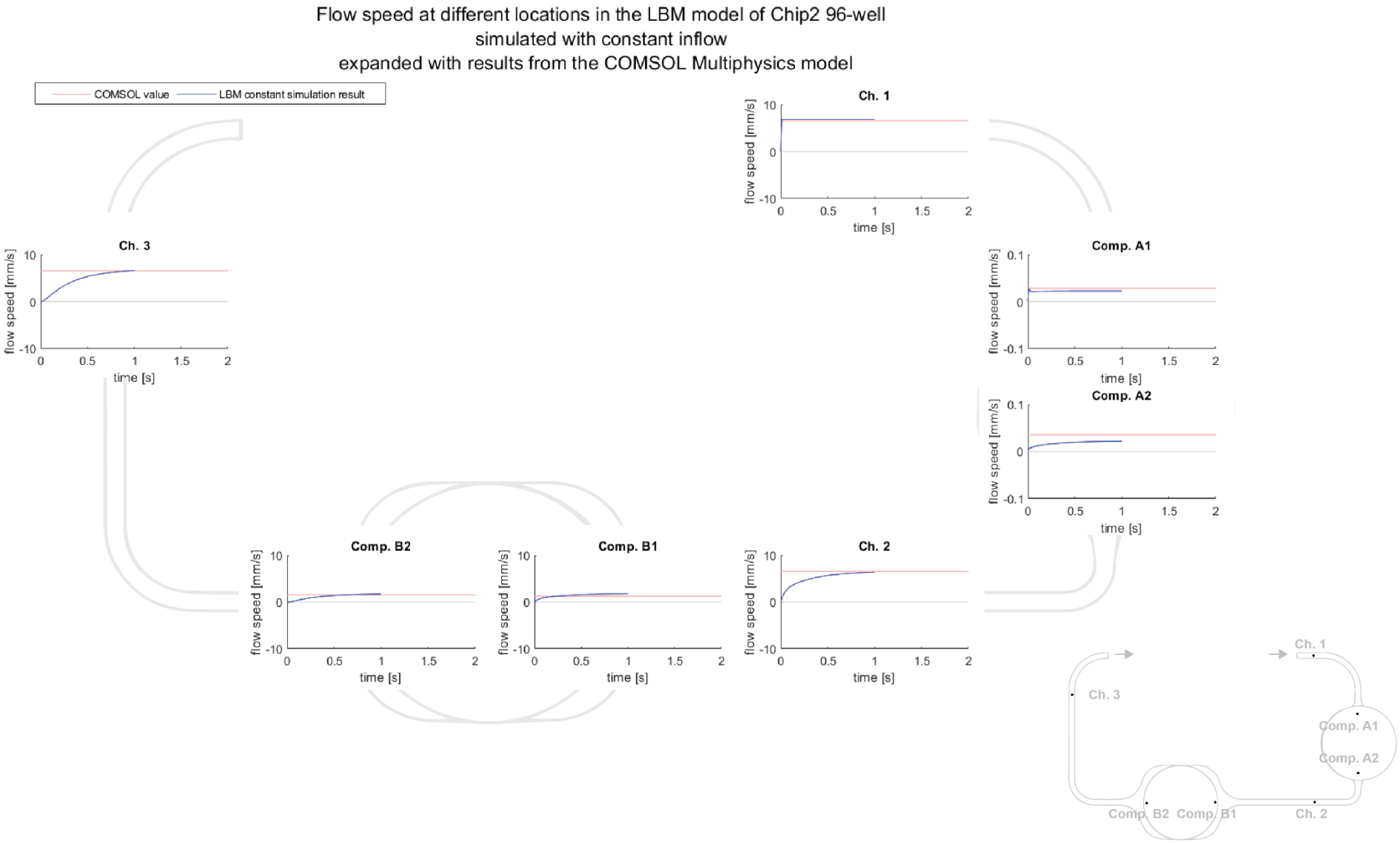


Figure 3-33 - Combining the results from the constant LBM simulation and the constant COMSOL Multiphysics simulation.

3.5.2. Transient LBM vs. COMSOL

Figure 3-34 combines Figure 3-23 with Figure 3-29. It shows the flow velocities recorded by the point trackers in both the LBM and COMSOL Multiphysics model. Please note, that the velocity-axes in the compartments are different from the original figures to better enable comparison.

The first thing that might strike is that the shapes of the velocity profiles of both methods in Ch. 1 of Figure 3-34 are very similar to each other. The results from COMSOL come out a bit higher than those of the LBM. This is in accordance with what the mesh independence studies of both methods would suggest. The custom grid that was used in COMSOL overshoots the theoretical value by about 15% (see Figure 3-28 for COMSOL convergence). LBM with its grid of element size $\delta_x = 0.010\ mm$ is neatly converged and only about 8% below the theoretical value (see Figure 3-17 for LBM's convergence).

Apart from their small differences both shapes look very similar to the input velocity profile that was established based on the µPIV experiments (shown in Figure 3-6). When the same logic that was used to determine the theoretical developed flow profile in 3.2.3 is applied to the PIV-based inlet boundary condition. One would expect the first negative and positive peaks in Ch. 1 in Figure 3-34 to have a size around 17.5 mm/s. Both peaks meet this expectation. This suggests that the PIV-based inflow boundary condition is successfully transferred to both simulation models.

Overall, the order of magnitude of both LBM's and COMSOL's results seem sensible. The flow slows down in the compartments. Here Compartment A has lower values than Compartment B due to the placement of the flow quantity trackers. In Compartment A, the trackers are really in the compartment. Compartment B puts them more on the edge of the compartment, where it is still smaller.

Throughout the chip, the flow in the LBM model appears to become dampened. This is somewhat strange, since the LBM was set to be an incompressible simulation in a geometry with rigid walls. Hence, it might have something to do with a numerical error. LBM's inherent compressibility error – as discussed in 2.4.4 – should not play a role because the simulations used diffusive scaling. On top of that the grid size appeared to sufficiently small in the mesh independence study.

There is one mention in (Krüger et al., 2017, p. 236) of LBM becoming strongly collision-operator-dependent. The case mentioned in (Krüger et al., 2017, p. 236) speaks of a channel size in the order of a few elements, using a simple-bounce-back wall and the BGK collision operator. The channels in the transient LBM simulations are ten elements high. They use a standard "wall" boundary condition from Musubi. The solver uses a BGK collision operator. The transient LBM simulation is thus somewhat similar to the case mentioned in (Krüger et al., 2017, p. 236). During preliminary simulations for this study it was found that for this simulation the influence of the collision operator was also very significant. Increasing the collision operator drastically improved the homogeneity of the flow throughout the chip.

In case this is what causes the flow profile to become dampened, here follow two possible solutions. Firstly, (Krüger et al., 2017, p. 236) suggests to use the MRT collision operator instead of the BGK collision operator. This would lead to significant improvements. Secondly, the collision operator influences the lattice viscosity. When using diffusive scaling, as this simulation does, the lattice viscosity is dependent on the collision operator according to 3-7 (Jain, 2020, p. 1820):

$$\nu_{lat} = \frac{1}{3}\left(\frac{1}{\Omega} - \frac{1}{2}\right) \qquad 3\text{-}7$$

The collision operator is now set at 1.95 (see the simulation setup in Table 4). Its limit due to stability is at 2 (see the parameter selection in 2.4.4). Increasing it to 1.99 would mean a reduction of the lattice

viscosity by a factor of around 4. A lower viscosity might mean less dampening throughout the chip and a higher central velocity in the rectangular channels throughout the chip. This second solution does lead to a reduction of the time step by factor of approximately 5 and an equal increase in calculation time.

Something else that might play a role in the slight difference between LBM and COMSOL is that they used water at different temperatures. For density this does not matter much, but the dynamic viscosity is about thirty percent lower in the COMSOL simulations. For the future, as chips probably run mostly in incubators around $37°C$, the COMSOL values might be more realistic.

COMSOL Multiphysics's flows throughout the chip are much more consistent than LBM's. The peaks lower a little from Channel 1 to 2 and 3. The results from COMSOL look more like what you would expect in an incompressible simulation. The velocities distribute directly through the entire chip. The simulation by COMSOL Multiphysics is not collision-operator dependent, because it is not a relaxation-based Navier-Stokes approximation. Given the size of the dampening and its apparent slowly increasing nature throughout the chip, it is expected to be due to numeric error. As stated before in Figure 3-28, this was somewhat significant on the custom grid.

The reason the numeric error is quite significant on the custom grid, might be its element aspect ratio. The ratio between an elements shortest and longest edges. The custom grid was created with the intention to make it denser where the gradients are bigger and economize on elements where the gradients are smaller. This did lead however to some elements having a higher aspect ratio (for example in the channels, see Figure 3-27). This is commonly known to influence numerical accuracy. When generating the mesh, COMSOL Multiphysics in fact gave a warning that there might be elements with a narrow edge that is smaller than the minimum element size. This warning only come up with elements with an aspect ratio higher than 100 (Gothäll, 2017). Looking at the element quality histogram shows a large peak in lower quality elements as well. Literature generally suggests to keep aspect ratios low. Solidworks for example recommends not exceeding a ratio of 5 (Dassault Systèmes, 2021). Ansys on the other hand says that anything below 1000 generally does not influence analysis accuracy (Ansys, 2004).

Finally, in the COMSOL Multiphysics results there are spikes in Compartment A. this only appears in Compartment A, where the flow velocities are very low, this might be a numeric error having an influence on the solution. However, if it were, this would be expected to continue in the rest of the chip, which it does not.

3.5.3. Additional LBM vs. COMSOL

As the inflow of the additional LBM simulation was done with an inflow one tenth the size of the additional COMSOL simulation, they are not merged in a new figure.

The simulation with LBM was done with a scaled inlet boundary condition and a grid with element size $\delta_x = 0.016\ mm$. Despite the difference in boundary condition and grid, both the point-trackers in the LBM simulation (Figure 3-24) and those in the COMSOL Multiphysics simulation (Figure 3-29) pointed in the same direction. The flow becomes insignificantly small either in or directly after it enters the first compartment. Naturally, the velocity decreases there, but it does not pick up speed again in the subsequent channel.

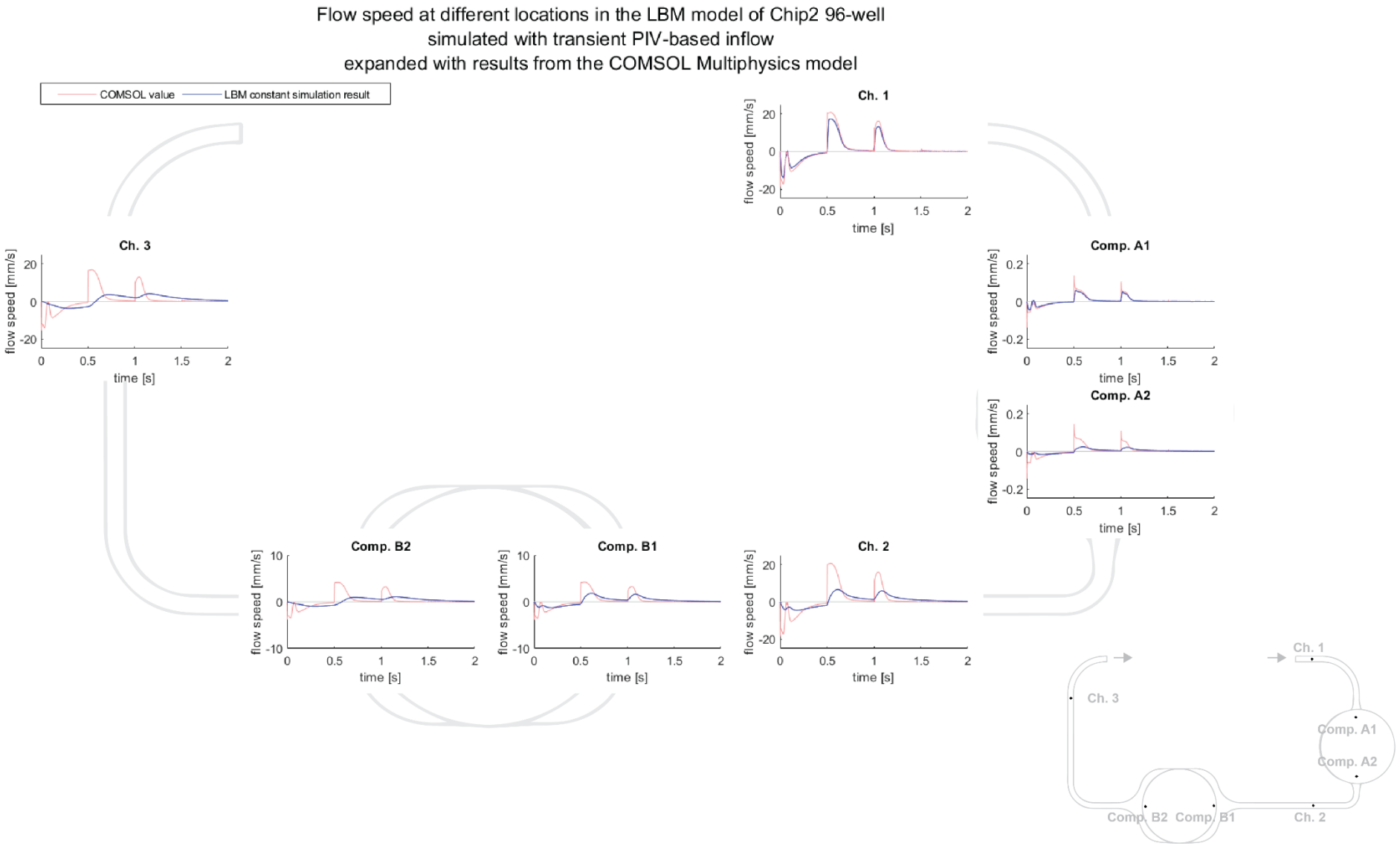


Figure 3-34 - Combining the results from the point-trackers in the transient LBM simulation and the transient COMSOL Multiphysics simulation.

3.5.4. PIV vs. LBM vs. COMSOL

Three methods have now characterized the flow in a Chip2 96-Well from TissUse GmbH. PIV-experiments on a real chip, an LBM simulation and a COMSOL Multiphysics simulation were performed. All these three methods generated results in a common location, namely the original PIV-windows. The fields of view from the µPIV experiments were tracked in both simulation methods. Those results are now gathered to enable comparison.

Figure 3-36 shows the resulting flow velocities for each window (WinA, WinB and WinC) ordered by method. Figure 3-37 goes one step further by showing the calculated net volume flow through each window, also ordered by method.

The µPIV results neatly represent the known stages of the pump. When aligning the three windows each with the know pump stages, one ends up with Figure 3-35. Take WinA as an example. From stage 1 to 2 the largest peak occurs, as the middle main cavity of the pump closes. Next (from 2 to 3) is the right compartment creating a similar peak. From 3 to 4 nothing much happens, because from WinA's perspective the middle cavity all the way at the other end of the circuit opens. This is all damped out by the compartments. Finally, from 4 back to 1, the left and right cavity close and open simultaneously causing a somewhat chaotic sequence of liquid being pulled back and forth. It mainly goes back in WinA because of the opening of the right cavity of the pump.

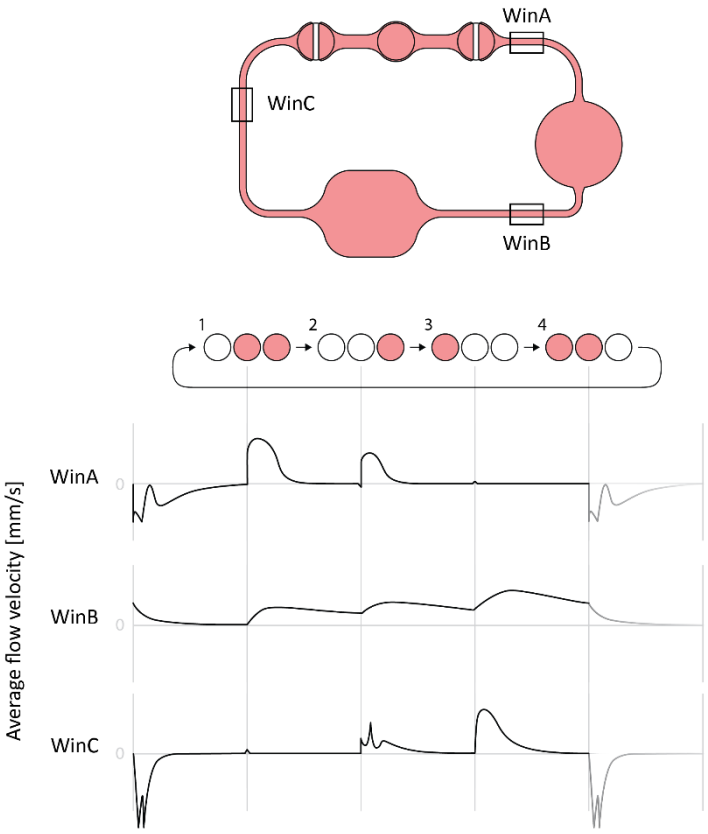


Figure 3-35 - Flow velocity µPIV results aligned with the know pump cycles of a TCU. The flow profiles are smoothened and the scale of WinB is off to keep the shape of the profile recognisable.

All in all, the resemblance between µPIV and the simulations is not too strong. There is one prominent explanation for that. When setting up the simulations, it was assumed that the water in the chip was incompressible, which it is. However, as Figure 1-7 already showed, in reality there is air trapped inside the compartments during operation of the chip. This air is compressible in a real chip.

It is this compressibility of the air in the compartments that is believed to cause the delay of the pump excitation through the chip seen in the µPIV experiments. The compartments function as two large dampeners on the flow. Just like dampeners would in a dynamic system, they cause a decrease in excitation and a difference in phase. The flow velocities close to the pump (WinA and WinC) have sharp excitations. WinB between the compartments has a much lower maximum but never gets below zero.

The influence of this air in the compartments is quite significant. It renders the fluid inside the chip (air and water together) effectively compressible. Since the LBM model and the COMSOL Multiphysics model are simulating incompressible fluid, they fail to represent these effects of the air in the compartments.

3.5.2 already discussed the dampened flow profiles through the LBM model. This is seen again in the velocities of LBM in Figure 3-36. However, the net volume flows in Figure 3-37 are consistent over all windows. This would suggest that the incompressibility is properly maintained in LBM. Also, it might point again towards the flaw laying in the viscosity dependence of LBM.

Regarding the net volume flow; problem occurred with the µPIV experiments. As can be seen in Figure 3-37, the net volume flow in WinA is about half that in WinB and WinC. When connecting a chip to a TissUse Control Unit (TCU), it is advised to let it run for some time. This way the flow gets some time to develop especially in the compartments. Some liquid might otherwise accumulate in the compartments. At first it was thought that the µPIV experiments were performed to shortly after hooking the chips up to the TCU. However, when interpreting where the net volume flow is lower (WinA right after the pump) and higher (WinB and WinC) this would mean that liquid would accumulate inside the pump, which is not possible. Thus it was thought that something had gone wrong with setting the pixel sizes in the PIVlab calculations. The pixel size determined in 3.2.1 was exactly half as big as in µPIV experiments from predecessors. As the volume flow was also differing by a factor two, this was worth a check. Checks and re-calculated PIVlab calculations kept giving the same results. Hence, identifying the cause and solution to this issue is kept for further research.

The flow profile of WinA was still used to determine a boundary condition for the simulations. Have a look at WinA in of all three methods in both Figure 3-36 and Figure 3-37. As the transient simulation's analysis in 3.5.2 already suggested, both simulation methods neatly simulated the inlet boundary condition and had a similar behaviour as the physical chip with a real pump up till this point.

On both the velocity profile as the net volume flow in WinA LBM slightly outperforms COMSOL Multiphysics when it comes to similarity. This is probably due to the lower quality custom grid in COMSOL (see mesh independence study in Figure 3-17) compared to LBM's better performing grid (mesh independence study in Figure 3-28). COMSOL's better consistency through the chip is again probably due to its independence of any collision operator.

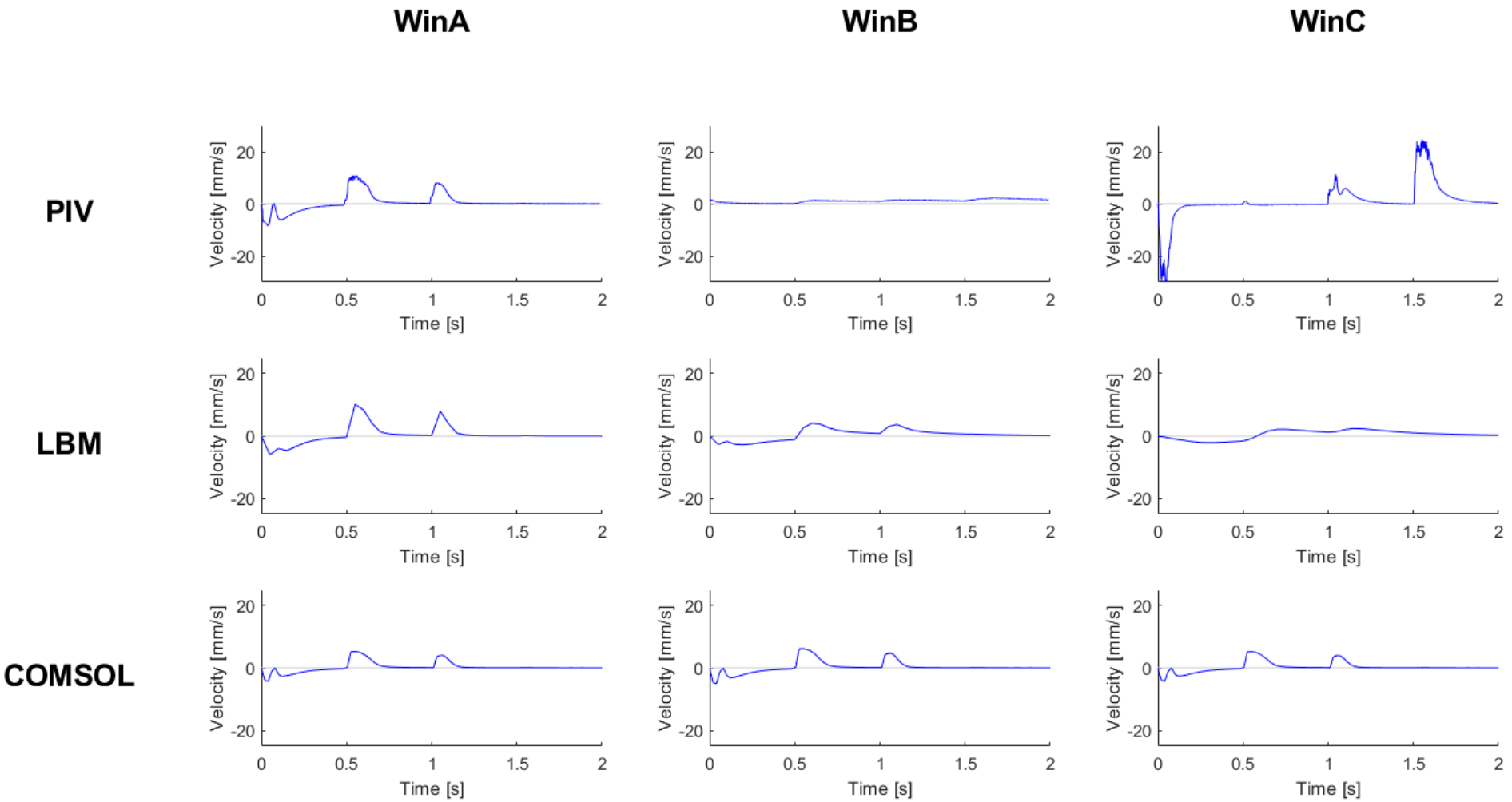


Figure 3-36 - Comparative view of the average flow velocities measured in the three PIV-window(s)-(trackers) sorted by each of the three methods of characterization

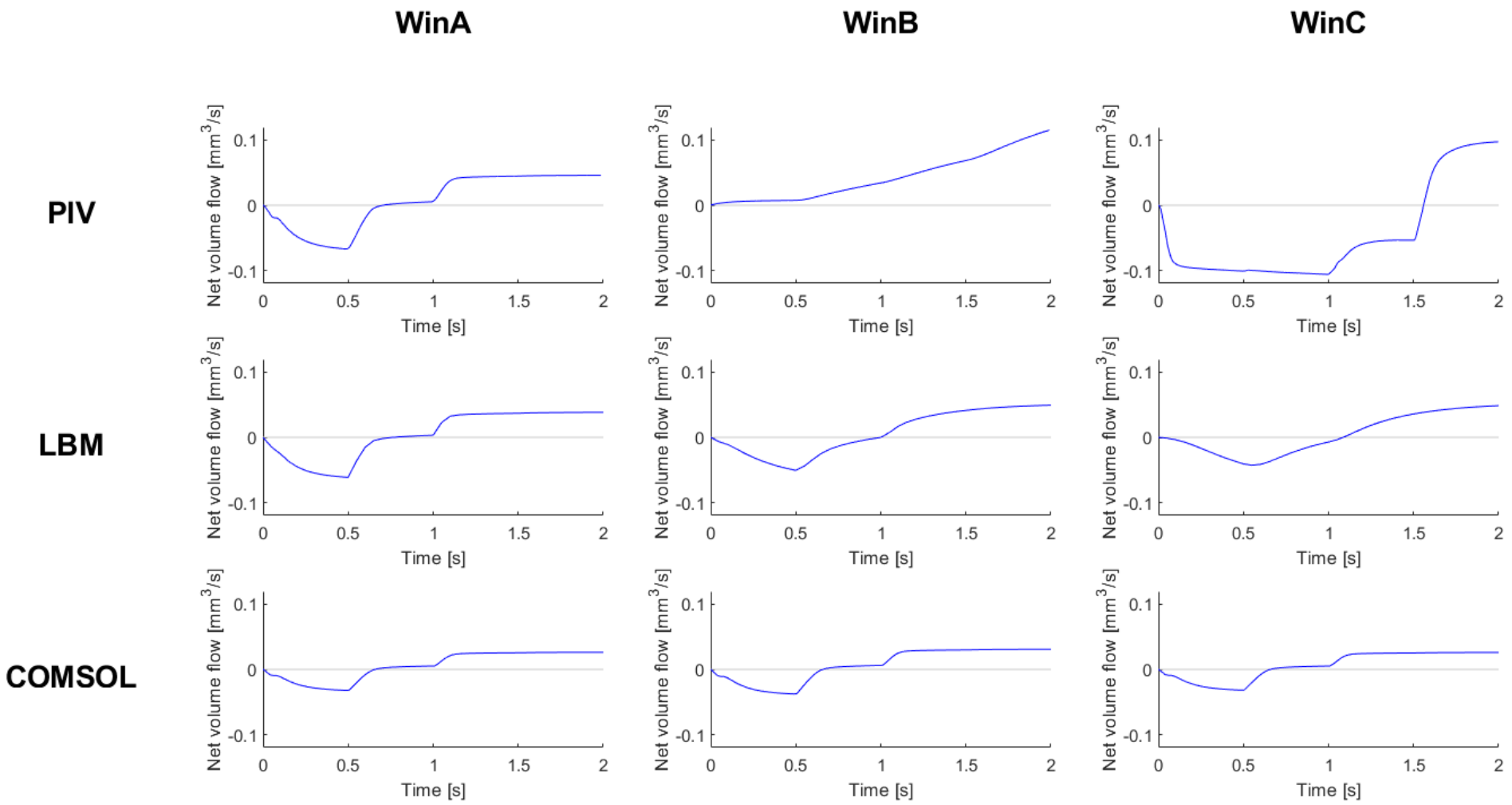


Figure 3-37 - Comparative view of the cumulative net volume flows calculated for the PIV-window(s)-(trackers) sorted by each of three methods of characterization

3.6. Sub-conclusion

The goal of this thesis was to create a validated method to characterize and simulate the flow in any possible chip design without the need of a physical prototype.

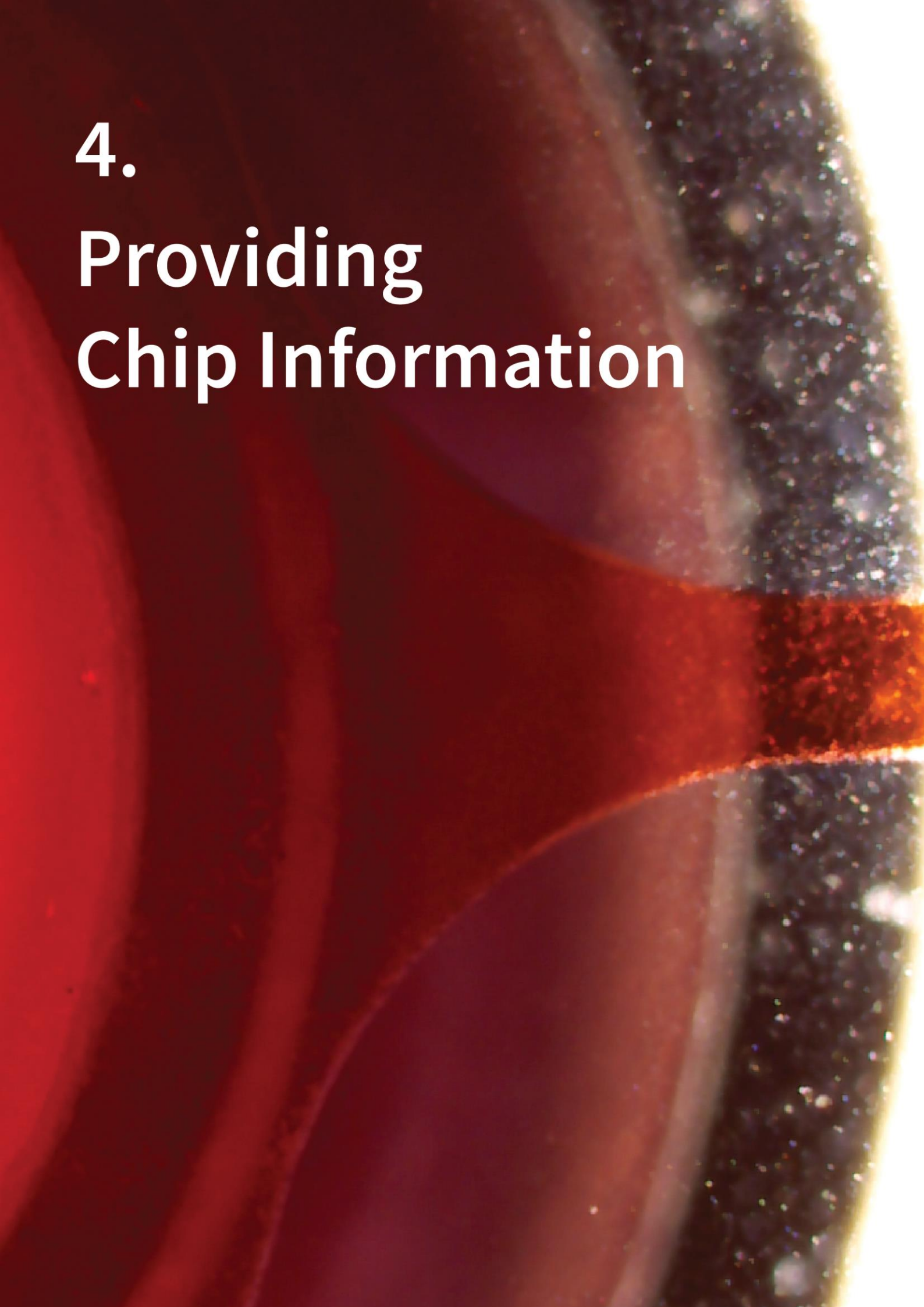
PIV-experiments were done on a HUMIMIC Chip2 96-Well. After mesh independence studies, these experiments served as a reference and to create a boundary condition for simulations with LBM and COMSOL Multiphysics. It appears that transferring the fluid behaviour directly after the pump from experiments to simulations was successful.

Comparison of the µPIV results with their equivalent flow quantity trackers in the simulations leads to the following remark: neither LBM nor COMSOL Multiphysics were able to properly emulate the flow throughout the chip using the current simulation setup. In the real chips there is air in the compartments which render the liquid inside the circuit practically compressible. These cannot be properly represented by an incompressible simulation with rigid no-slip walls. Adaptation of the simulations with open compartment roofs did not improve the simulation's results.

Suggestions for how simulation setups might be improved to make simulations a viable option and eliminate the need for a physical prototype follow in the Recommendations for future research in Chapter 6.

COMSOL Multiphysics appears to outperform LBM both when it comes to physical correctness of the results and calculation times. LBM needs longer to converge to a steady state and might be heavily dependent on its collision operator. A possible solution to both these issues might lay in the application of the MRT collision operator instead of the BGK collision operator.

The best way to characterize the flow in a chip thus remains PIV-experiments. The experiments were able to accurately determine the flow at three locations in the chip. This method requires a physical chip and a thorough check of the pixel size settings is recommended.



4. Providing Chip Information

4. Providing chip information

The analysis of the flow in the chip provides a lot of data. This data can be valuable for researchers and business developers alike. To make sure that they can access the data in such a way that it becomes valuable to them, something needs to visualize it. This part of the thesis is about the development of a digital tool that visualizes the chip characteristics. The goal is to make this tool as convenient and suitable as possible.

4.1. Approach

The work starts with finding TissUse's values (4.2) by interviewing its employees and studying company representative documents and handbooks. The other puzzle piece, the user requirements, are defined also by interviewing employees. They represent the end users. The requirements are described in 4.3. The next step involves writing several scenarios that represent how different user groups intend to use the tool (4.4). Literature suggested that scenario-based design is specifically suitable for the development of a user interface (McKay, 2013). These scenarios are validated by users again.

At this point the groundwork has been laid and ideation can start (4.5). Soon this went from ideation to prototyping (4.6). Prototyping took about two weeks. During these two weeks, meetings were planned almost daily with a different employee. Each time the employee evaluated the prototype in its then current state. A week's worth of micro iterations was the result. These iterations helped improve the final result, which is discussed in 4.7. The final result is a prototype ready for user testing. These tests were used to distinguish points of improvement in the prototype. The recommendations in 4.8 show those points of improvement.

Employees of TissUse are involved in the entire process. They represent both the company and the different kinds of user groups. They are business developers, engineers and researchers. This brings the approach close to complete co-creation as defined by (Jansen & Pieters, 2019).

4.2. TissUse's philosophy

One can regard the optimal product as a puzzle piece. If one wants to develop a piece that fits, one needs to know what the pieces around it look like. In this project two surrounding puzzle pieces will be considered.

1. The company's values/philosophy/capabilities
2. The users' requirements/needs/wishes

This paragraph looks at TissUse's values and philosophy. There are multiple ways and places to find this out. The first step will be to study the way the company presents itself. There are company presentations, a firm handbook (Firmenhandbuch), an internal employee study by the business development department, social media accounts and a website. From these it is possible to get an idea of what reputation TissUse wants to have and how they want to come across.

Secondly, the values manifest themselves daily by the decisions and behaviour of TissUse employees (Kapferer, 2008). Different people will have different interaction with the values of the company. Hence interviews are conducted with people from all different departments within TissUse. These include researchers, biologist, business developers and engineers.

The abovementioned interviews have the goal to find or deduce the values of TissUse as a company. Further down the road in the project it is important to take the employees into account as a stakeholder. This might come in handy when making prototypes, presenting the product or integrating it in the workflow once it is done. Hence the reason for people to work at TissUse might come in handy.

The interviews and studying of documentation resulted in knowledge on the following four topics:

1. What are important values to TissUse?
2. Why do people work at TissUse?
3. Where do ideas come from?
4. How are customers included in the development process?

Notes of the interviews about values and philosophy of TissUse are gathered in Appendix G.

What is striking about the results, is that they appear to be very coherent. All different sources appear to point in a similar direction. As the analysis will show for example: things that are written in the Firmenhandbuch come back in the answers of the employee study. What the employees say in the interviews is underlined by the content of the Firmenhandbuch and the way it is written. Finally, the different employees, appear to independently agree on a lot of things. The way the bachelor student describes his experience appears to be his perspective on the same family feeling that the business developer and the chip development department leader are so thankful for and proud of.

This consistency is a blessing; its intertwined representation makes it more of a curse to extract them. In the following paragraphs an attempt is made to structure the results without describing every nitty detail, but retaining a strong foundation.

4.2.1. What are important values to TissUse?

The company presentation of 2021 describes TissUse's goal as:

Improve predictability
of substance safety and efficacy
by Multi-organ-chip testing

Reliable and competent

One of the first things you see when opening the HUMIMIC company presentation is that TissUse's products are reliable. This is not just marketing talk on a company presentation. An internal study posed the question to employees "How do you want customers to view TissUse?". Employees answered with "powerful", "competent" and "reliable". To ensure this, the company has all the basics in place. It is ISO-9001-qualified and has an ethics code. Besides it has a Firmenhandbuch and a quality coordinator to guide the continuous improvement of the processes in the company.

Three examples to show that TissUse is acting on this promise to be reliable:

1. According to their company presentation TissUse has 41 publications and over 140 patents. This is mentioned to show that they have a solid knowledge of organ chips and know how to protect that knowledge.
2. The Firmenhandbuch says how to behave with customers: "Customer communication should be friendly, serious and competent." - TissUse Firmenhandbuch p. 22
3. When considering the idea to develop a Human-on-a-Chip, with ten significant organs on it, the validity of this idea was checked with other scientists in the sector. Showing that their idea is a valid one before starting on it. - TissUse Firmenhandbuch p. 9

This drive to reliability is inherent in the employees, but also a necessity for the company. In the interview with the development department leader (Appendix C) he stated, that TissUse's clients are heavily regulated and hence somewhat conservative. The 41 publications that TissUse has done over

the past ten years largely have the purpose to have the chips approved by regulators such as the FDA and EMA.

He added that loyalty is important in a finite customer pool of pharmaceutical companies. TissUse wants to build long-term customer relations by building a reliable relationship of trust. Projects in the pharmaceutical industry can last in the order of a decade. TissUse needs to develop and provide their products reliably to be an eligible partner.

Business developer 1, Appendix C, said in the interview that she thinks that words such as these in company presentations can be empty. However, just as the internal study suggested, she thinks, here at TissUse they are not. In that same interview she said "we really take the time for our customers". A statement which you would expect from someone that is crafting a long-term relationship. This brings us to the next aspect of TissUse's way of providing service.

Complete solution

A subtle difference between the company presentation of 2019 and 2020, is that the title changed from "Simplify substance profiling with Human-on-Chip" to "Simplify substance profiling with Human-on-Chip solutions". TissUse wants to be able to provide a complete solution and, as business developer 1 said, takes the time to do so. They go from creating a tailored Multi-Organ-Chip for a specific assay, to transferring the technology, to finally helping with education and process support. Even publication is often done cooperatively (read Researcher 3 in Appendix C).

Highly innovative

The slogan of TissUse already implies it: "Redefining research", the employee study shows its importance as well. "hochinnovativ" (highly innovative) and "Spitzenforschung ermöglichend" (enabling top research) came forth as answers to how employees want TissUse to be perceived. TissUse has an ambitious goal. They are working on highly innovative technology and want to enable their customers to perform highly innovative research. This is what they want to portray as well.

Flexible

This is an aspect that came back in the internal study as well. Employees want TissUse to come across as flexible to the clients. In practice this translates to several different variants of the most common HUMIMIC Chip2. The bloody chip and the bone marrow insert are both examples of where the standard microfluidics are redesigned to meet the needs of a customer-specific assay.

This has a root in the company's survival as well. The Organ-on-a-Chip market is not saturated yet. Hence it is important to have loyal customers and bind them to you early. The development department leader stated "We have no lower-limit for the contract size so we can just try stuff". Also: "Every customer has different requirements. Hence a modular system for your chip development makes you flexible and capable to adapt to a lot of applications." TissUse wants to be flexible and is willing to cooperate early with clients. This fits the goal of the long lasting relationship again.

A factor in this flexibility is that you do need to take care of yourself. Engineer 1 confirms what the development department leader said about early cooperation by saying that sometimes TissUse takes on projects for less profit. He adds to it, that in these cases it can be useful to look at ways to make the project useful for TissUse in other areas. Business developer 2 confirms this by saying: "You need to watch out as a startup not too lose sight of your own long term goals. You get this risk when you listen to clients too much. Uwe [founder of TissUse] is very good at keeping this long term view in mind." So there are limits to this flexibility.

4.2.2. Why do people work at TissUse?

The greater goal

The goal of TissUse to improve the way pharmacological studies are done lives among the employees as well. This bigger goal that is described in the Firmenhandbuch and is captured by the slogan of the company is what attracts every single employee of TissUse as far as the interviews go. Especially among students the question "Why do you work at TissUse" was answered with "to find an alternative to animal testing" – Master student 3, "working on something that is bigger than what I can imagine" – Master student 2 and "improve the technology to show that it has potential and can be used instead of animal testing" – Master student 1. All these answers are noted in Appendix C.

Learning bio and tech

When asked what specifically they like about the work, two things come forth. The employees are eager. This drive to improve does not only apply to the technology, but apparently also to themselves. The multidisciplinary work among biologist and engineers is mentioned by several employees (the software development employee, the manufacturing employee and Master student 3) and confirmed by the Bachelor student. The bachelor student mentioned that he could chose a broad variety of projects, does different kinds of tasks and sees several aspects of the engineering process. This sounds like the bachelor thesis equivalent of what the employees describe. What demonstrates the eagerness to learn is that the absence of learning leads to a decreased motivation: "the work is a bit monotone currently, due to circumstances. I look forward to being more creative and working on the development again" – manufacturing employee.

The family feeling

All these people co-working towards a greater goal leads to TissUse most prominent feature. It says in the Firmenhandbuch: "TissUse sees its employees as its greatest capital and wants to create a comfortable, equal and stimulating environment for them.". The first thing that comes up in the employee study when employees describe their company is "supercool". Practically every interview stated the family feeling was what they cherished the most about the company. Own experience shows that this sentiment is indeed very strong in everyday work.

Interfering overload

When asked about the core values of TissUse, business developer 1 said: "Two things that both combat and complement each other. One: an open and friendly climate. Two: expecting a lot of effort. It is only with a good team that you can achieve a lot" This shows the importance and sincerity of the TissUse family. It also brings out the aspect that members of the TissUse family experience as negative. The workload is so high, that it interferes with the flawlessness of the work. Several employees have mentioned "it would be cool to have more money/employees to be able to focus more on development" – manufacturing employee (Appendix C). There is simply not enough time to do everything. Especially documentation becomes an extra in this way. This trend might in the long term become troublesome.

4.2.3. Where do ideas come from?

Sparks can be initiated from several places. Naturally ideas can be randomly triggered, but there appear to be some commonly occurring sources for product development ideas.

Customer enquiries

There are customer enquiries. These come from two different customer groups. Firstly, the existing customers come with questions. TissUse has a close cooperation usually with these clients. Weekly, biweekly of monthly meetings enable the exchange of knowledge and ideas.

The other group are the new customers. Usually they contact TissUse by email, possibly after being in touch at a conference. They ask whether a certain specific development is possible. This may lead to new ideas.

Government tenders

Apart from these two groups, there are third-party funds. Usually driven by the German government. They put out a tender for certain developments and TissUse participates in those. These are incentives for product development.

In-house researchers

An important customer or user pool for TissUse product development ideas are the in-house researchers. The direct contact, weekly seminars, or status meetings all lead to interaction between the scientist and the engineers.

Engineers' own initiative

The engineers themselves naturally have a sense of initiative as well. They might conclude certain basic components or aspects might need some improvement. Also, sometimes the company itself needs certain developments. These own initiatives usually consider the more basic necessities.

An interesting sort of extra layer of new developments is that new developments might spark new ideas. Certain aspects of a failed project can be used to improve another project.

Since a lot of the ideas come from customer questions, it might be good to know, that nowadays those become more and more in the nature of TissUse providing certain technology. According to business developer 1, TissUse is able to sell more instead of being a Contracted-Research-Organisation. TissUse has developed multiple protocols and perform a large amount of research. They still do, but they have reached a point where they are able to provide customers with the technological results of their previous research too. When the question is "we want to combine an intestine and a liver", there is a model available already nowadays.

4.2.4. How are customers included in the development process?

From the interviews so far, it appears there are two prominent ways of customer or user participation in any developments at TissUse.

Colleagues are users

The first is clearly summarized by Engineer 2: "my colleagues were my first "customers" and their comments my first "market analysis"". This approach will be present in this thesis as well. It was found in other TissUse development projects too. TissUse has their own clients basically in-house in the form of their own scientist team. They are a source for product requirements and execute the first tests. The software development employee, who used a similar way of working on the robot development

stated the following: “The importance of certain requirements I estimated myself and then got it confirmed by the biologists. Actually I did it more together with the biologists. Both me and the biologists have to confirm the requirements are correct.” Then regarding the testing, he said: “The biologists understand the processes best. Hence it should be the biologist who estimates whether the UX is in order and if the requirements are met.”

Contract development

The second way customers/users are included is in the contract development. The existing customers usually take on a close relationship with TissUse to develop certain organ models or technologies together. These relationships last in the order of several months or years. The customers and TissUse simultaneously develop parts, and they have monthly or biweekly meetings to exchange ideas and discuss the developments. This way the client has a lot of influence on the development and TissUse gains a lot of valuable feedback.

4.3. User requirements

From one side, the company and its philosophy form a puzzle piece. On the other hand, the users with their wishes and needs form a puzzle piece. This paragraph discusses the latter.

To find the requirements interviews with employees were conducted again. This time not as employees, but as potential end-users. The goal was to find out:

1. What they want to be able to find in the tool
2. How they want it to be presented
3. Why they need it

The first two – what and how – lead to concrete requirements. The third is useful for the creation of scenarios. Notes of all the interviews, spanning all different departments of TissUse again, can be found in Appendix H.

Requirements can be structured based on importance. Systems such as Critical-to-Quality (Mind Tools Content Team, 2021) can be used to structure the requirements. The five product levels of Kotler (Expert Program Management, 2017) come in handy for prioritization. This leads to an ordered list of requirements where one can directly see which ones are must-haves and which are less vital. Table 12 shows the resulting list of requirements. They form the demands on the flow characteristics data visualization tool. The structure, prioritization and completeness of Table 12 were again validated with end users.

Category	Requirement
What flow characteristics should be shown?	Flow speed [mm/s]
	Net flow rate/volume flow [µl/s]
	Shearstress/-force [dyn/mm^2]
	Distribution times of substances (turnover time, travel time, mixing time)
	Blood pressure
	Substance concentration distribution
	pH-value distribution
	Temperature distribution
What values of these characteristics should be shown?	Peak and average
	Flow profile during one pump cycle
On which measuring locations should they be shown?	Channel and compartment
	Distribution inside compartments (entrance, middle, exit or entirely)
	Multiple spots
	Entire chip
What parameters should be changeable?	The pump's pressure and frequency
	Chip variant (Chip2 96-well, Chip2 24-well, ...)
	Obstacles (Transwell, Ceramic in the compartments, …)
	Pump direction ((counter-)clockwise)
	Endothelialized (yes or no)
	Different cell-culturing media
	Throttling
What are the demands on the way of presentation?	Readily available everywhere anytime
	Understandable for clients with a different background or little experience with our chips
	Expandable to future versions of chips
	Reliable and showing accuracy
	Aesthetically pleasing/interactive
	Able to generate tables/numbers
	Able to generate images/graphs
	Providable to clients (who should not be able to change or distribute data)

Required: generic product	
Expected: expected product	
Desired: augmented product	
Would be nice: potential products	

Table 12 - Structured and prioritized requirements list for the data visualization. This table is based on and validated by end-user interviews.

The end-users were asked what they would need the information for. In what circumstances and for what purpose would they go looking for flow characteristics? Below is a list of the most prevalent answers. Flow characteristics were needed…

- To consciously steer the physical circumstances in the chip (person-specific or general)
    - As physiological as possible
    - Disease-models
- To make experiments better comparable
- During customer acquisition
- During chip redesign
- During assay planning
- For acceptance by regulatory authorities such as the EMA or FDA.
- For exclusion of physical factors while drawing conclusions

4.4. Scenarios

The two puzzle pieces are defined now. The philosophy of the company and the requirements of the users are both clear. As the list above shows, there is a multitude of situations that require knowledge of the flow behaviour in the microchannels. For example, when scientists develop a new assay and they need a certain shear stress for a period of time in order to induce a specific phenotype from the cells in the chip. A study can prescribe certain nourishment concentrations, which depend on mass flow rates. Another example is that once results of a study will be published it is valuable to state the flow circumstances during the study in the method description of the article. All these different scenarios might require a different form of presentation of data gained from a chip's characterization.

Appendix I includes the most common scenarios (McKay, 2013, p. 253) in which employees of TissUse or users of organ-chips want to know information of the flow in the organ chips. Only the first scenario is written out here to keep things manageable. The other scenarios are kept in Appendix I. The following scenarios can be found in Appendix I:

1. **Scenario 1 Business Development:** How to answer all kinds of general questions from customers as clearly and quickly as possible?
2. **Scenario 2 Assay planning:** What pump settings do I need to get certain physiological circumstances?
3. **Scenario 3 Contract Development:** What is the difference in flow between a standard Chip2 and a custom Chip2?
4. **Scenario 4 Paper publishing:** How to get a proper and clear image in my paper?
5. **Scenario 5 Chip development:** How to add newly characterized chip data?

They are based on the interviews with employees thus far, questions from webinars and competitors. The scenarios are specific, but intentionally left unspecific with respect to certain details to keep different options for solutions open for the final tool (Anggreeni & van der Voort, 2007, p. 6). These scenarios will serve as a starting point for the information visualization and UI design (McKay, 2013, p. 253-255).

Once the scenarios have been written and verified, it is clear what the tool will be used for and how. To come up with a good task flow and eventually a good UI, the conversation that the user will have with the tool is added to each scenario. This approach is suggested by (McKay, 2013, p. 262). The intended goal or the question the user has, is the starting point for each conversation.

All scenarios were validated. Besides the scenarios and the UI conversations, Appendix I also contains the feedback from the end-users. It shows for example that Business developer 2 strongly recognized herself in the scenario. Researcher 1 and 3 corrected some things in their scenario and sketched an ideal situation. The feedback was used to improve the scenarios and kept in mind during the following stages of the project.

To understand the scenarios more thoroughly, they were sketched out as well. This opened up several questions and details which helped in the development of the UI. The graphic representation of scenarios regarding business development, contract development and paper publishing can be found in Appendix J. The visualization of the first scenario, business development is also attached here in Figure 4-1.

Scenario 1: Business Development

Business developer 2 gets questions from customers such as:

- Are all cells subject to the same shear stress?
- What is the influence of medium change and shear stress on cell development?
- Did you evaluate the impact of flux on the different culture types?
- Is the use of hydrogel relevant?
- What are the flow speeds in the chip?

She might get these questions during a meeting. As she expected these kinds of questions, she has already opened the tool in the background on her laptop. To provide an answer she shows the potential client the information about the chip characteristics.

Later she gets another question while she is on the road. This time she opens the tool, identifies herself and copies an image of the information. She attaches it in the email or LinkedIn message that she just got.

The client is happy to see that TissUse can provide this information and gets a reliable feeling from it.

UI conversation

How do I show this potential client that we understand the flow in the chips?

1. Go to the home screen (if not already there)
2. Choose whatever chip you want to show (probably Chip2, for the example it does not really matter)
3. You can show them that the flow is different at different spots in the chip. Also, what the values are in the entire chip. That it depends on the pump settings can be demonstrated. Even the use of different media or inserts can be shown. This allows for answering questions more generally such as about using hydrogel.
4. If you want, you can copy an image and paste it in whatever communications app you or the client likes.

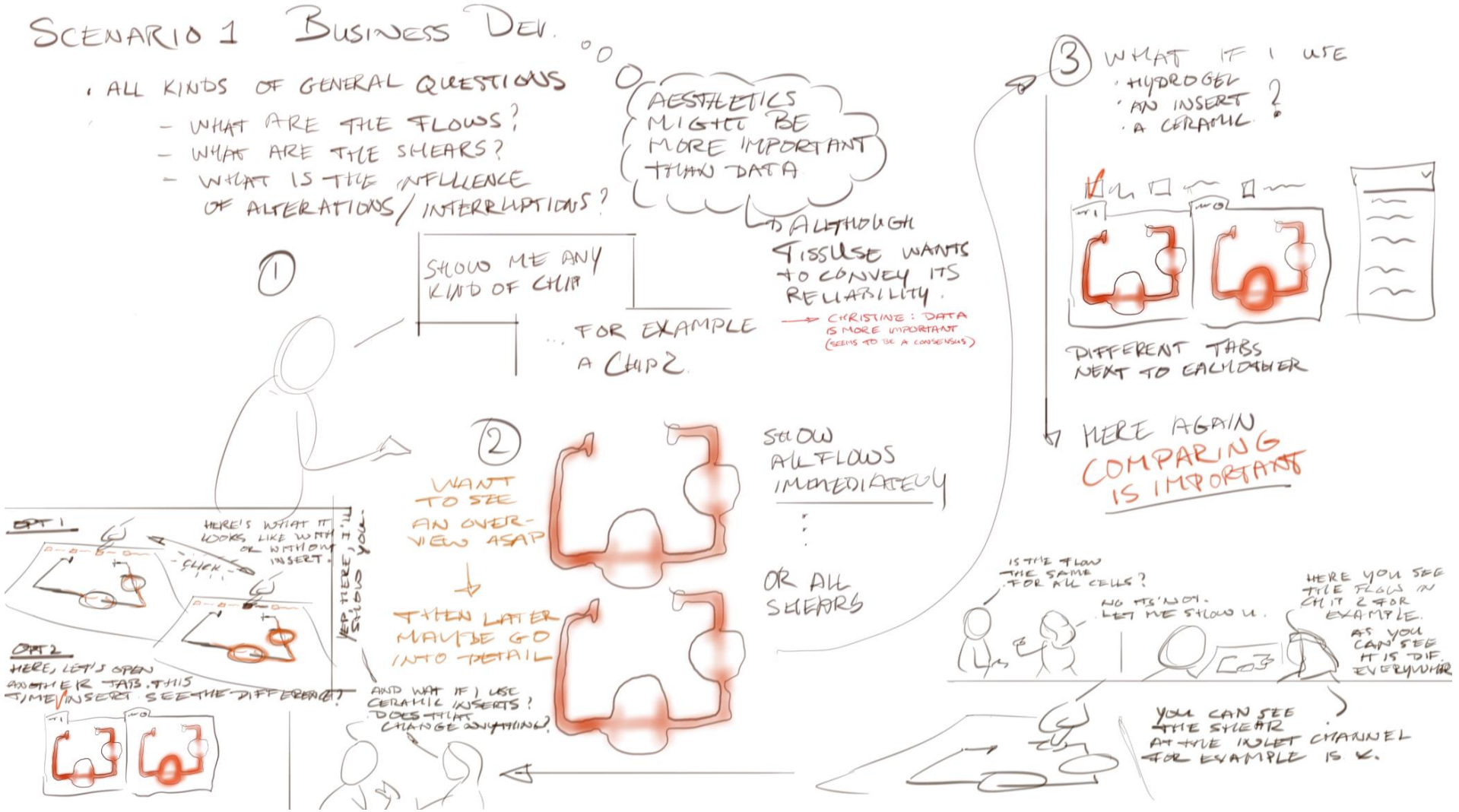


Figure 4-1 - Sketch of the business development scenario with considerations and annotations.

4.5. Ideation

The user requirements, company's philosophy and user scenarios are all established. It is thus time to start ideating. This involves developing a lot of divergent ideas that might meet the fit the problem space that is defined so far. This was done by the form of sketching. An example of this is shown in Figure 4-2. Additional sketches are gathered in Appendix K. The scenarios were partly converted into task flows. For each specific task several UI options could be thought up.

During the ideation process it was nice to see all different studies coming together. The knowledge of UI, the scenarios and the knowledge about the company helped in making objective design choices. On the first two pages of Appendix K a few examples of the direct application of this knowledge were marked with blue pen.

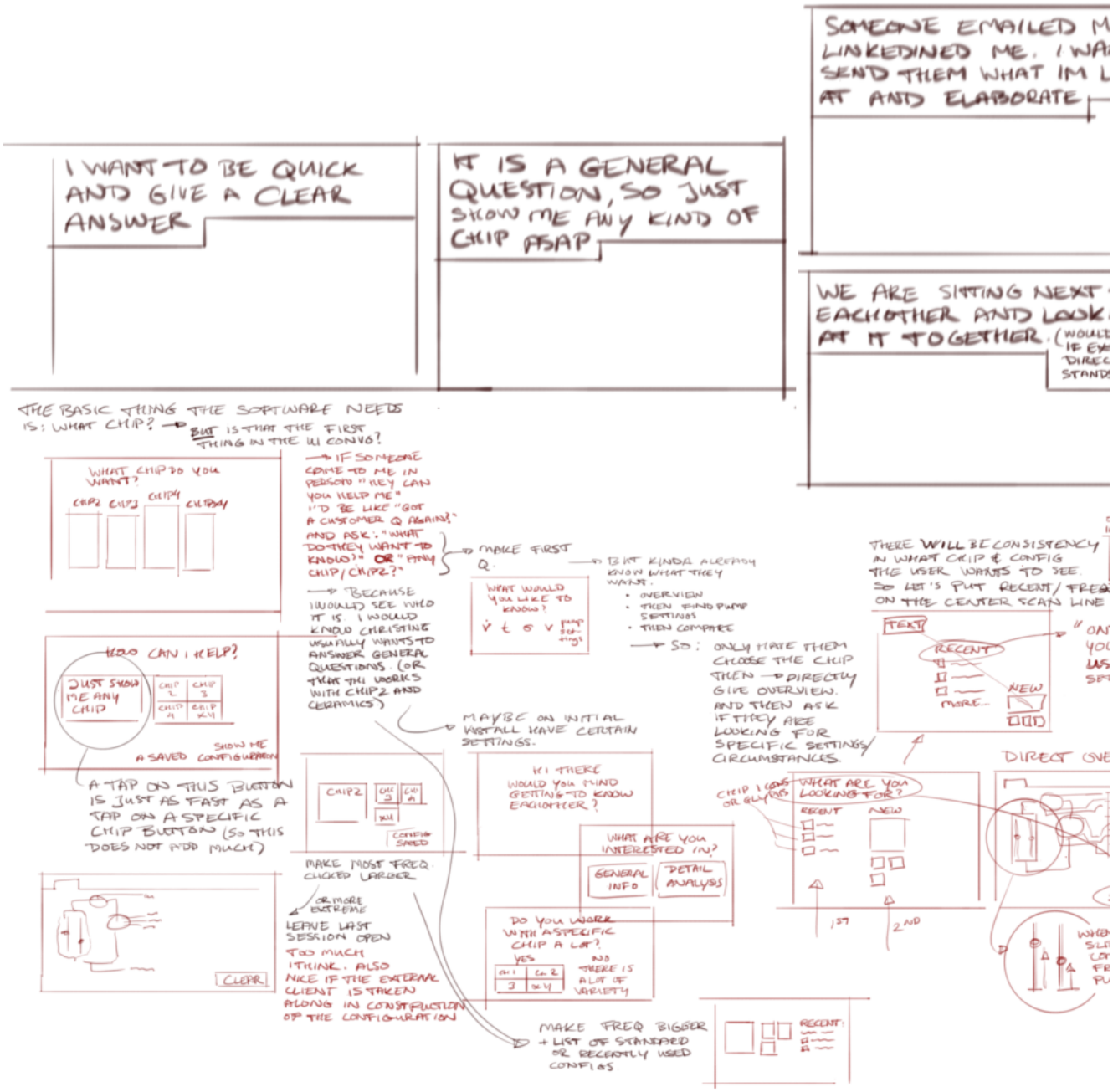
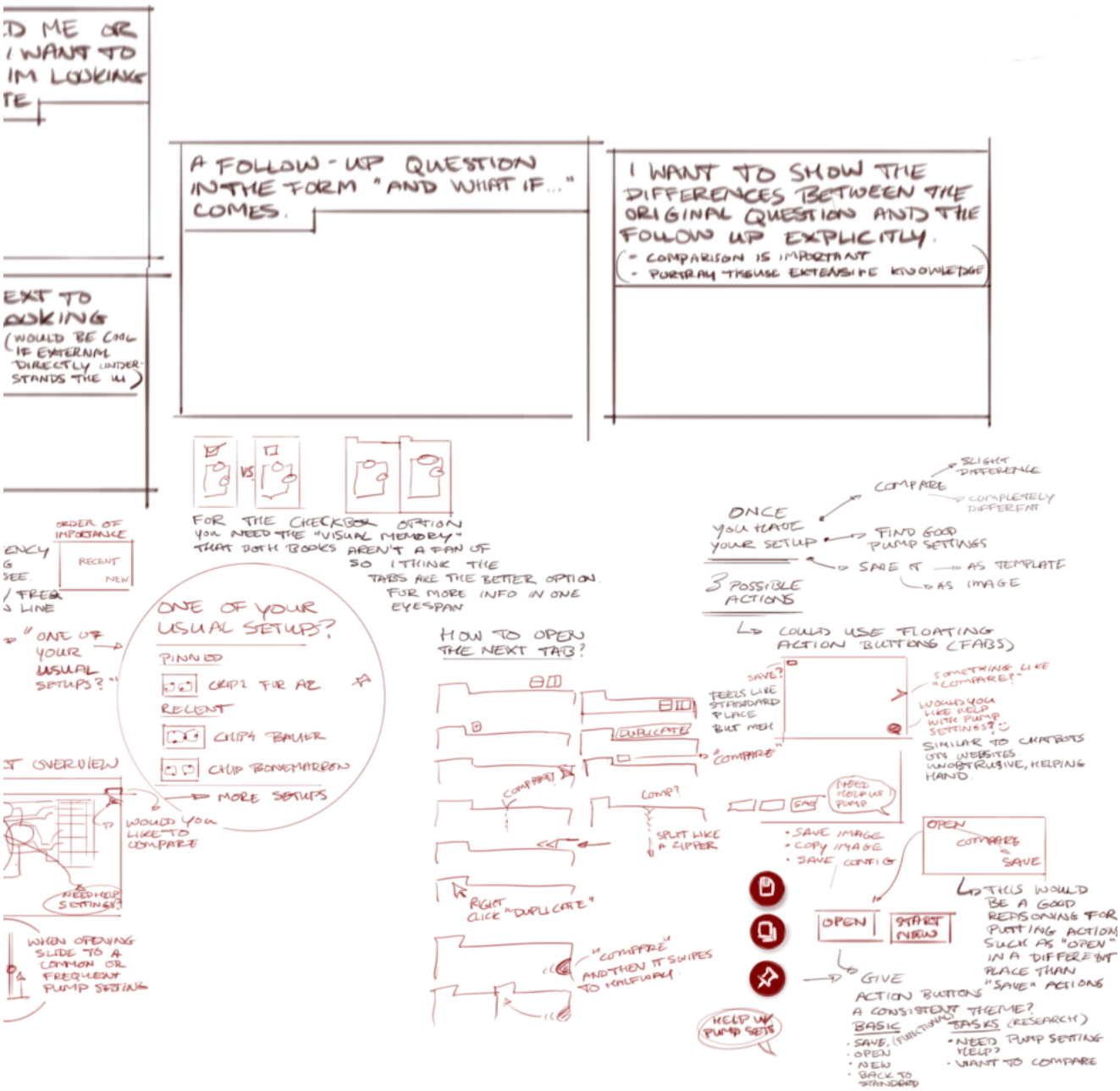


Figure 4-2 - Example of an ideation sketch. the sketch uses the tasks in the taskflow to find appropriate UI designs and elements.


A FOLLOW-UP QUESTION IN THE FORM "AND WHAT IF..." COMES.
I WANT TO SHOW THE DIFFERENCES BETWEEN THE ORIGINAL QUESTION AND THE FOLLOW UP EXPLICITLY.
- COMPARISON IS IMPORTANT
- PORTRAY THE USE EXTENSIVE KNOWLEDGE
ONCE YOU HAVE YOUR SETUP
COMPARE
SLIGHT DIFFERENCE
COMPLETELY DIFFERENT
FIND GOOD PUMP SETTINGS
SAVE IT
AS TEMPLATE
AS IMAGE
3 POSSIBLE ACTIONS
COULD USE FLOATING ACTION BUTTONS (FABS)
FOR THE CHECKBOX OPTION YOU NEED THE "VISUAL MEMORY" THAT BOTH BOOKS AREN'T A FAN OF SO I THINK THE TABS ARE THE BETTER OPTION. FOR MORE INFO IN ONE EYESPAN
ONE OF YOUR USUAL SETUPS?
PINNED
RECENT
MORE SETUPS
HOW TO OPEN THE NEXT TAB?
DUPLICATE
COMPARE
SAVE?
FEELS LIKE STEREOTYPICAL PLACE BUT MEH
SOMETHING LIKE "COMPARE?"
WOULD YOU LIKE HELP WITH PUMP SETTINGS?
SIMILAR TO CHATBOTS OR WEBSITES UNOBTRUSIVE, HELPING HAND.
NEED HELP W/ PUMP
SAVE IMAGE
COPY IMAGE
SAVE CONFIG
OPEN
COMPARE
SAVE
THIS WOULD BE A GOOD RESPONSIBLE FOR PUTTING ACTIONS SUCH AS "OPEN" IN A DIFFERENT PLACE THAN "SAVE" ACTIONS
OPEN
START NEW
GIVE ACTION BUTTONS A CONSISTENT THEME?
BASIC
SAVE
OPEN
NEW
BACK TO STANDARD
TASKS (RESEARCH)
NEED PUMP SETTING HELP?
WANT TO COMPARE
HELP W/ PUMP SETS
RIGHT CLICK "DUPLICATE"
"COMPARE" AND THEN IT SWIPES TO HALFWAY
SPLIT LIKE A CLIPPER
WOULD YOU LIKE TO COMPARE
NEED HELP SETTINGS?
WHEN OPENING SLIDE TO A COMMON OR FREQUENT PUMP SETTING
ORDER OF IMPORTANCE
RECENT
NEW

4.6. Prototyping

Plain ideation soon grew into rapid prototyping. Adobe XD was used to create a prototype of a UI. For little over a week, the prototype was improved and elaborated. At the end of each day, there would be a meeting with a potential end-user. This potential end user evaluated the prototype in its current state. This lead to several – sometimes recurring – points of improvement. This approach can be considered the rapid prototype version of a UI development process. Each day a micro iteration would take place. Figure 4-3 shows an example of how the landing page and the dashboard of the tool gradually developed.

A total of six micro iterations preceded a meeting where the prototype was shown to all biologists of the company. During this “Bereichsmeeting” of the Contract Development department, the prototype was demonstrated and all kinds of questions and feedback were discussed. For completeness, notes of these micro iterations and the Bereichsmeeting are included in Appendix L.

Based on the micro iterations and the feedback from the Bereichsmeeting a final prototype was made ready for user testing. Of the upcoming two paragraphs, 4.7 will firstly describe the final prototype. 4.8 explains the tests of this final prototype. 4.9 then continues to describe recommendations regarding the prototype. It discusses where there is still room for improvement.

Figure 4-3 - Example of how the prototype developed during the micro iterations and rapid prototyping. On the left hand: development of the landing page. On the right hand: development of the dashboard.

4.7. Results

The result of the ideation and iterations was a UI prototype. It was functional enough to use for testing. However, all data was thought up. No real database is behind it. It is merely used to test the design, interactions and functionalities. A video showing a walkthrough of the entire prototype is delivered with this report. The figures that follow now are intended to give an overview of the main screens in the UI.

The entire UI was naturally designed based on the knowledge described in the background theory. To ensure a cohesive and recognisable layout style guidelines were drafted. These were based on the background theory combined with the TissUse Corporate Identity Design Basics. The design guidelines structuring the design of this prototype are shown in Appendix M. One example of the guideline is shown for the tab titles in Figure 4-4.

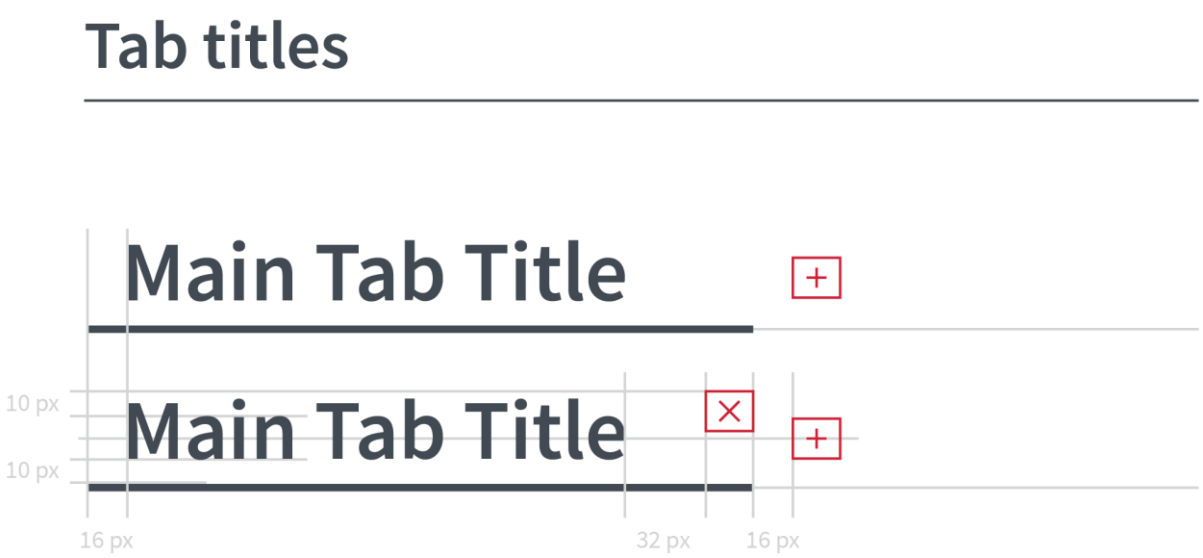


Figure 4-4 - Design guideline for the main tab titles in the UI prototype.

The following images are included below:

1. The landing page — Figure 4-5
2. The new setup page — Figure 4-6
3. The setup dashboard — Figure 4-7
4. Adding a feature — Figure 4-8
5. Pump Setting Assistant step 1 — Figure 4-9
6. Pump Setting Assistant step 2 — Figure 4-10
7. Pump Setting Assistant step 3 — Figure 4-11
8. Pump Setting Assistant step 4 — Figure 4-12
9. Searching pump settings in tables — Figure 4-13
10. Comparing similar setups — Figure 4-14

Each figure has a description shortly explaining important aspects of the screen.

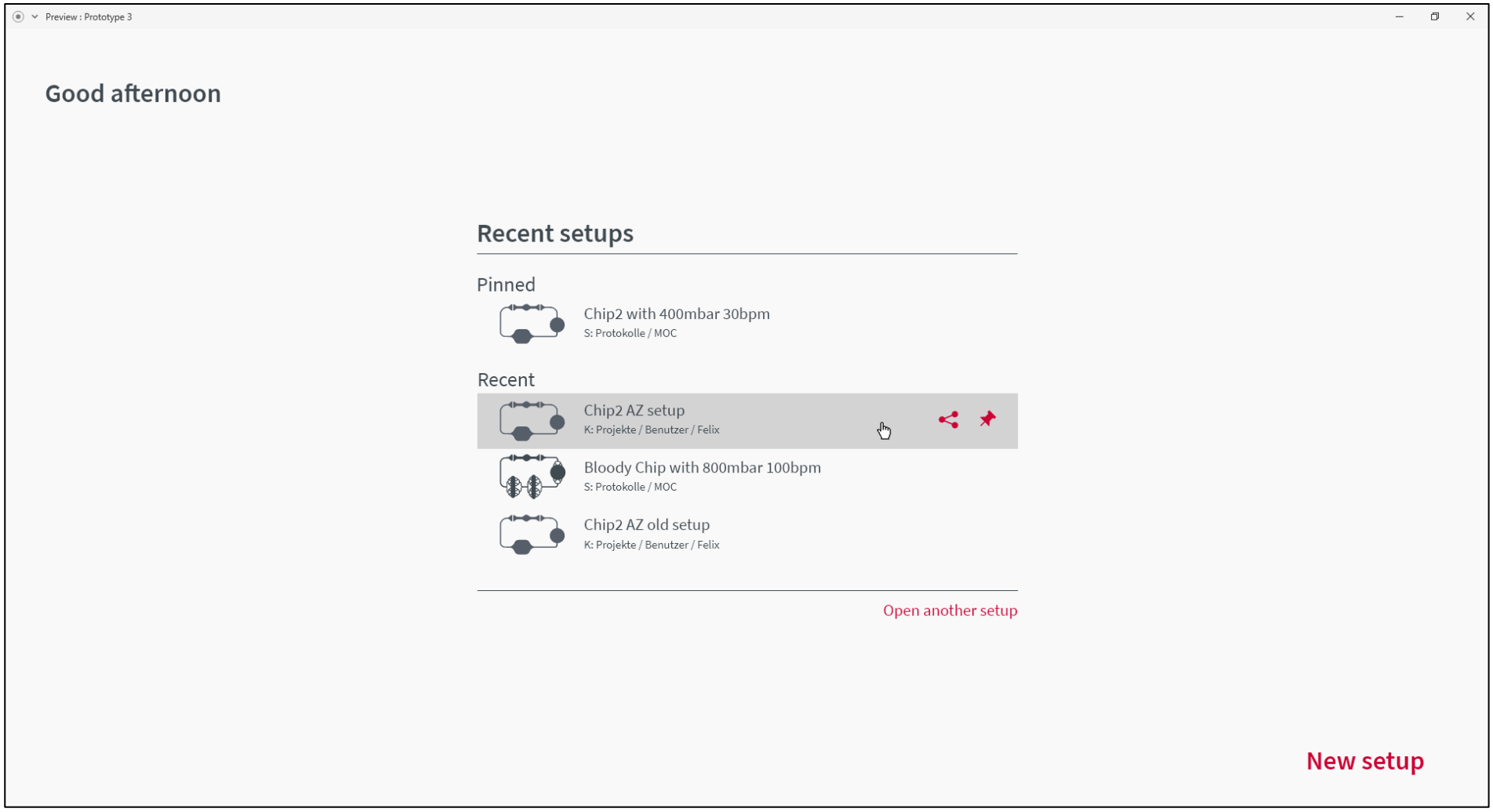


Figure 4-5 - This is the landing screen. It is where the user lands when starting the application. A strong visual focus draws the eye to the recent setups. Favourites can be pinned. The scanning line goes from top left "Good afternoon" to "Recent setups" and ends at "New setup" at the bottom right.

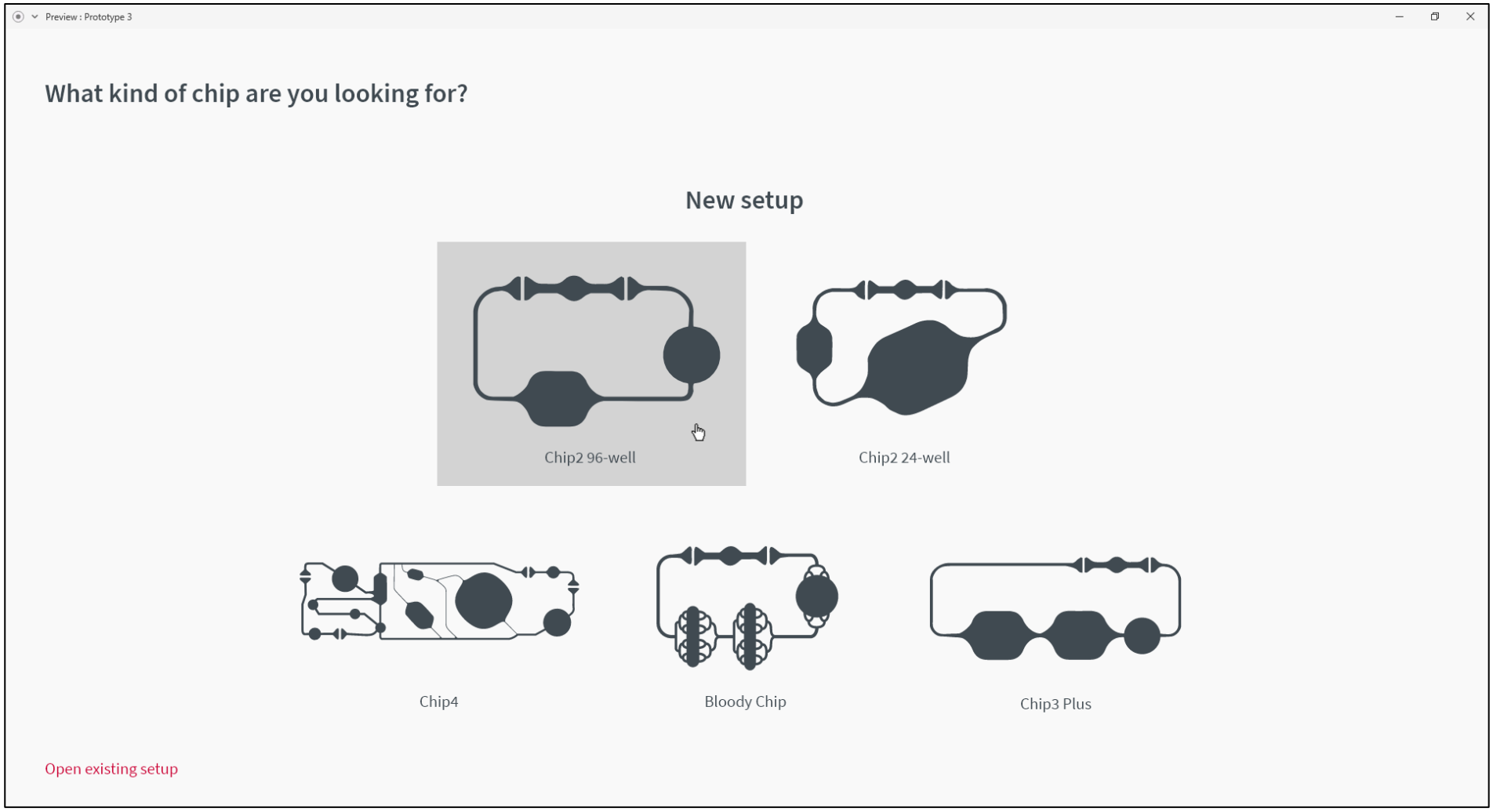


Figure 4-6 - This is where the user arrives when clicking "New setup". The scanning line is taken into consideration again. A prominent place is given to the two most common chips.

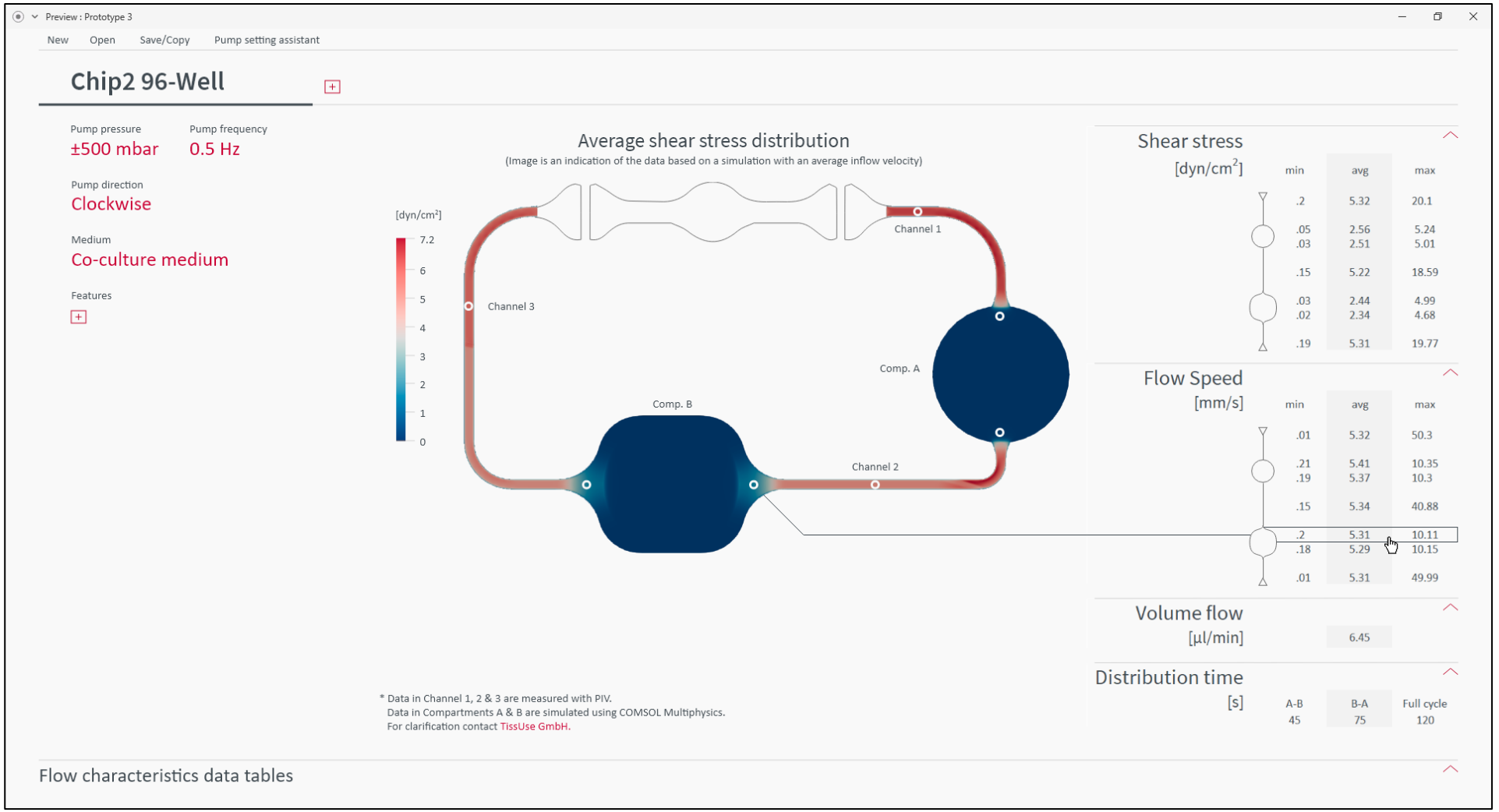


Figure 4-7 - Once a chip is selected, this is the screen that the user goes to. An image in the middle rapidly shows the global distribution of average shear stress. The flow again goes from left to right. An educated guess is taken in the settings and starts at 500 mbar with 0.5 Hz. Visualization is then in the middle and data can be read on the right.

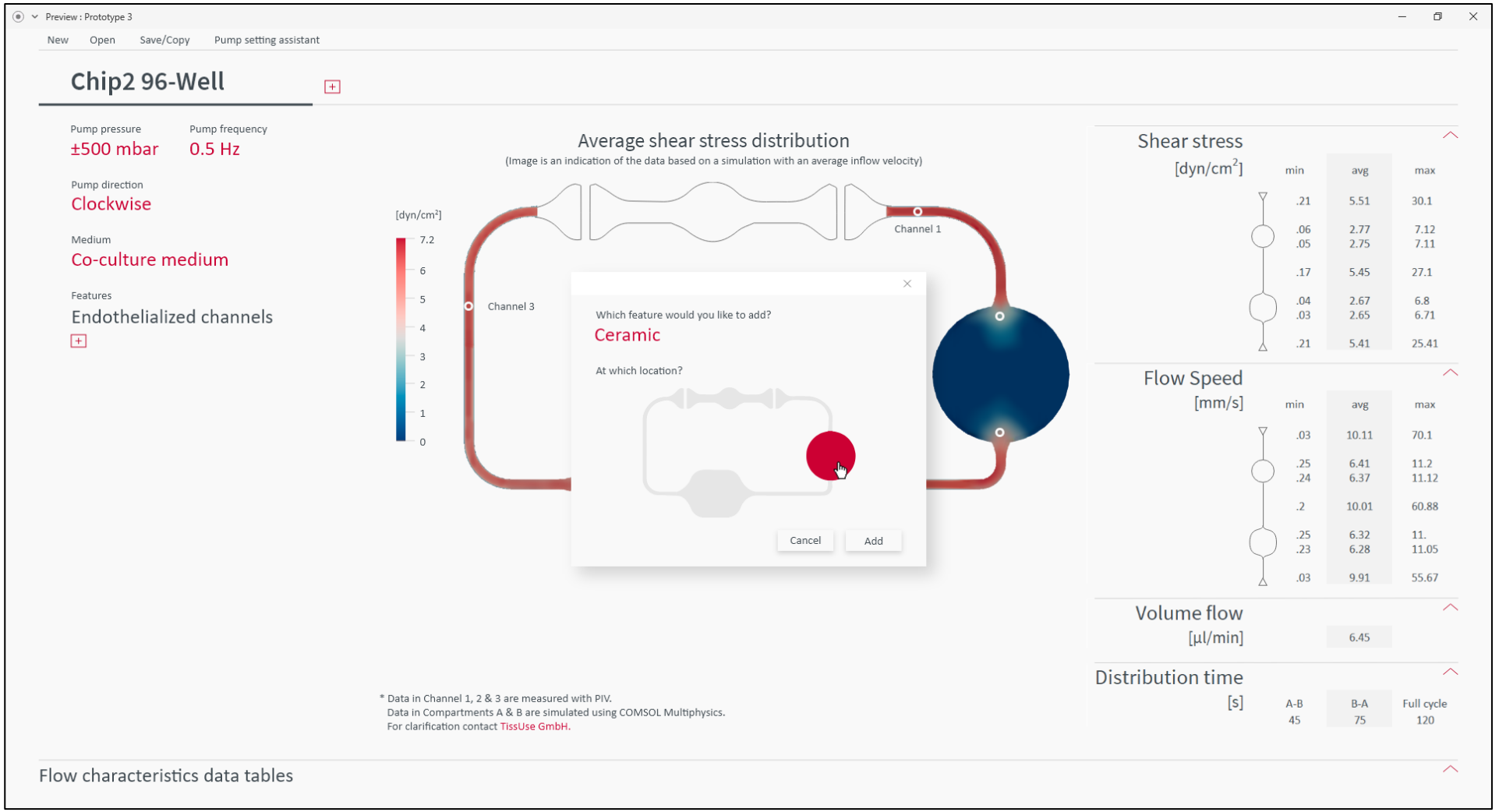


Figure 4-8 - Among other things, it is possible to add features to the basic setup. Chips can be endotheliazed (adding an endothelial cell layer to the channels), or a ceramic can be insert in a compartment for example. These feature influence the flow. The user can add them in the settings area on the left via this screen.

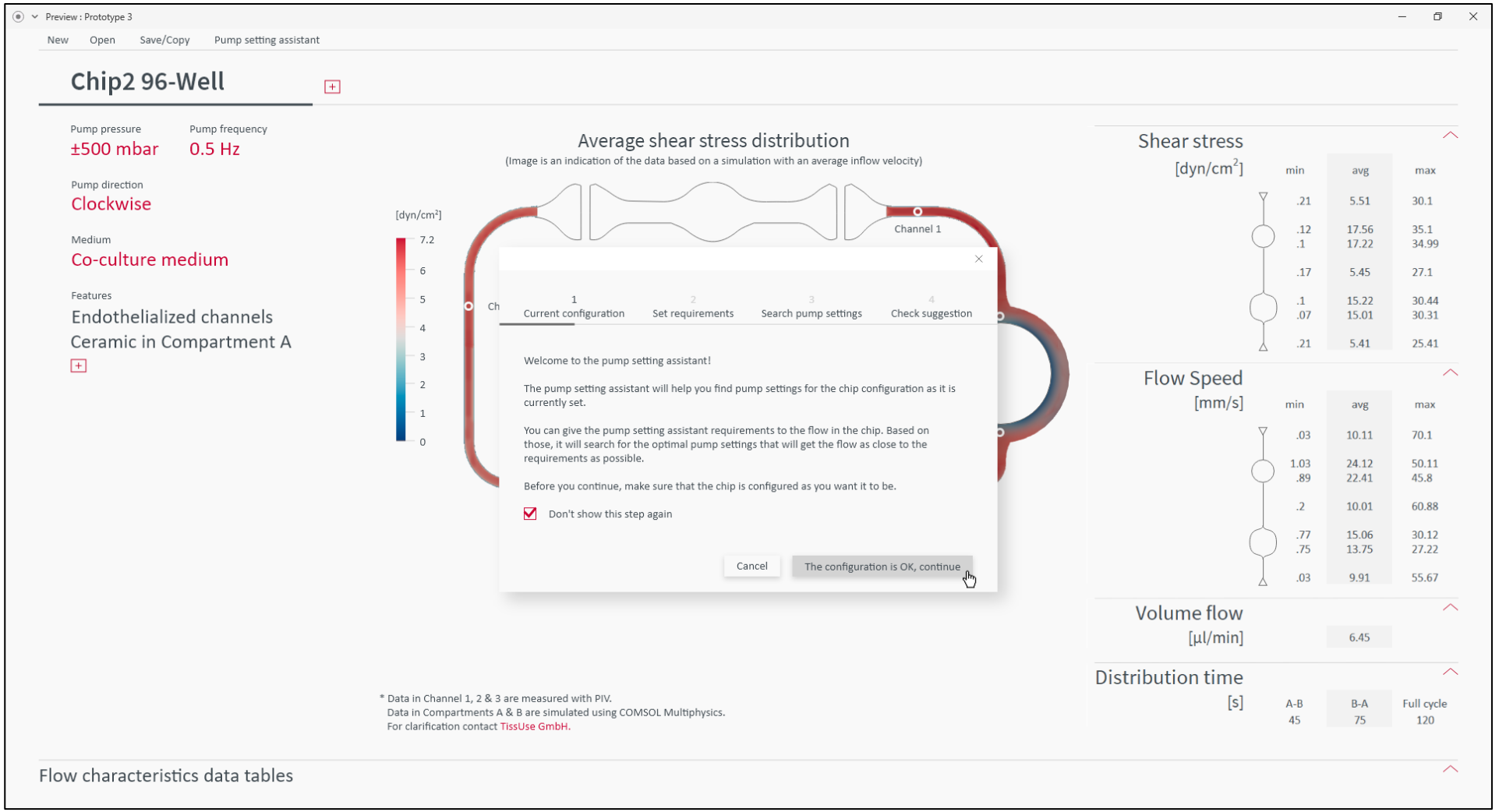


Figure 4-9 - This is the first screen of the Pump Setting Assistant. When users want to know what pump settings are optimal to get certain flow circumstances, the assistant can help. Based on the micro iterations it was clear that this step is needed. It explains that the assistant will use the chip with the features as they are set now.

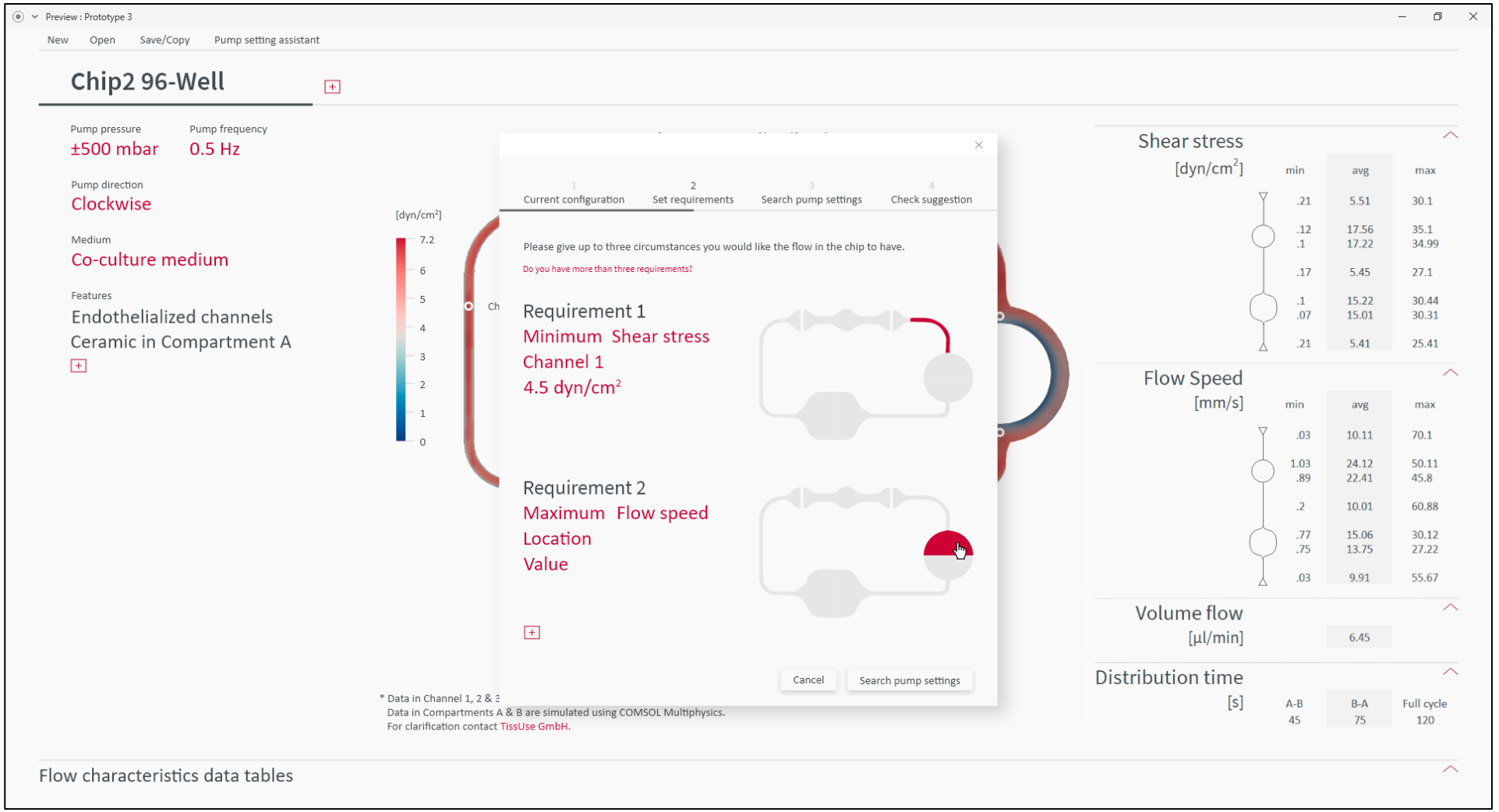


Figure 4-10 - This is the second screen of the Pump Setting Assistant. Here the user can give the requirements they have on the flow. Order of input was intended to follow normal human sentence structure.

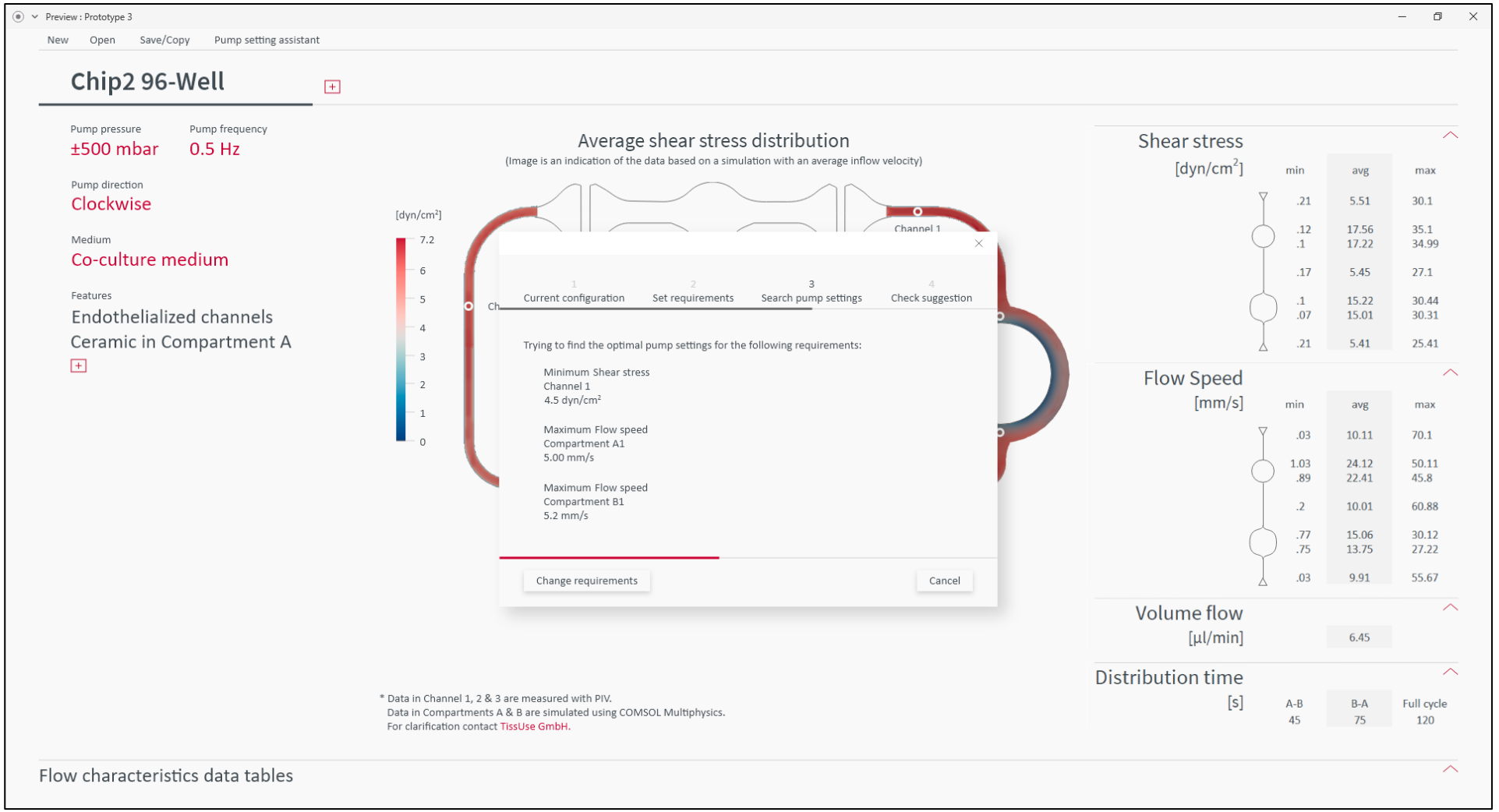


Figure 4-11 - The third screen of the Pump Setting Assistant shows the progress of the search for pump settings. The requirements are still shown and users can go back if they notice something is wrong with the requirements.

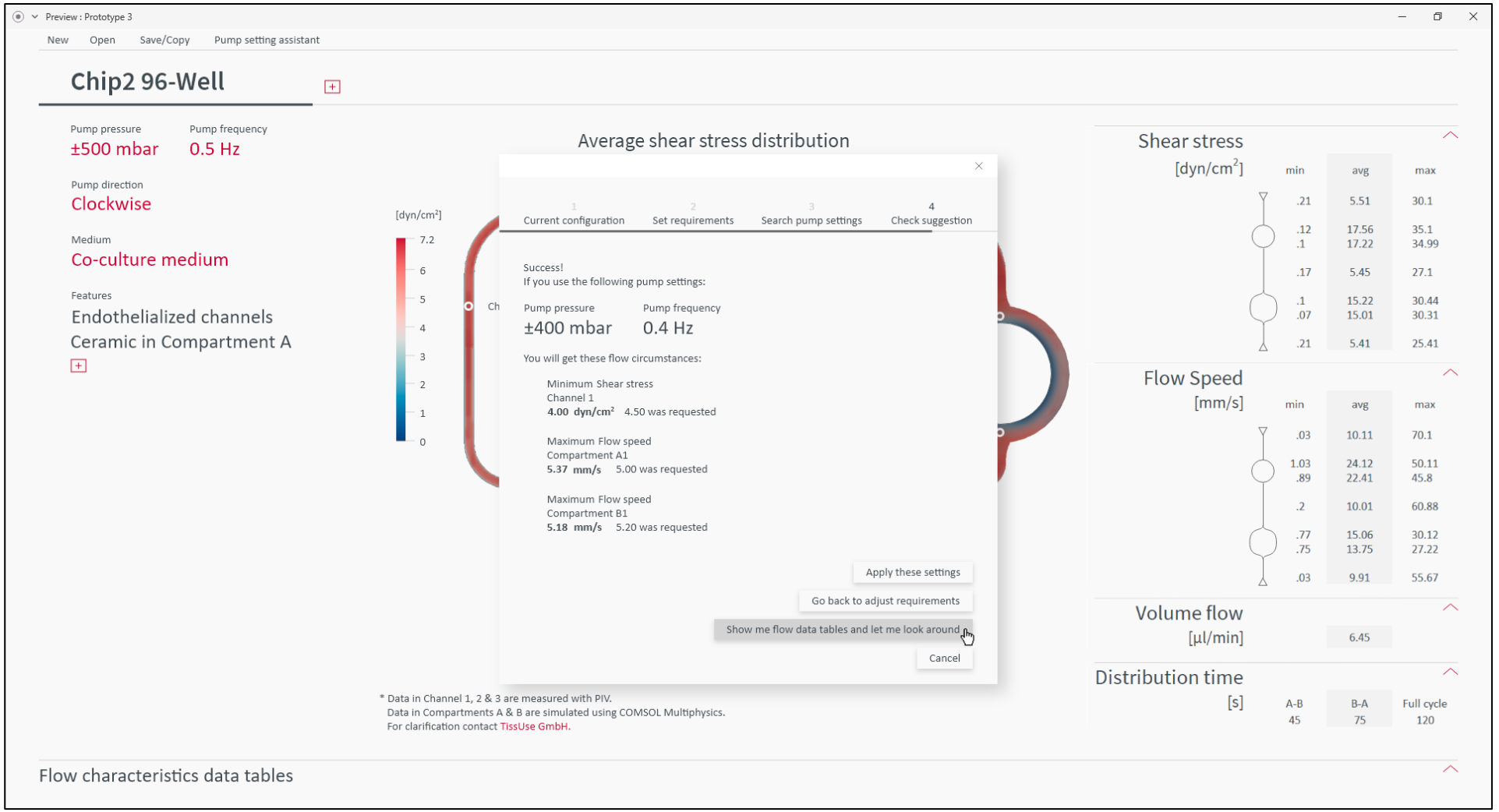


Figure 4-12 - The final screen of the Pump Setting Assistant suggests a pump setting. Graphically the pump settings are prominent and grouped. The resulting flow characteristics are also grouped. Four different options for what the user can do with the suggestion are given.

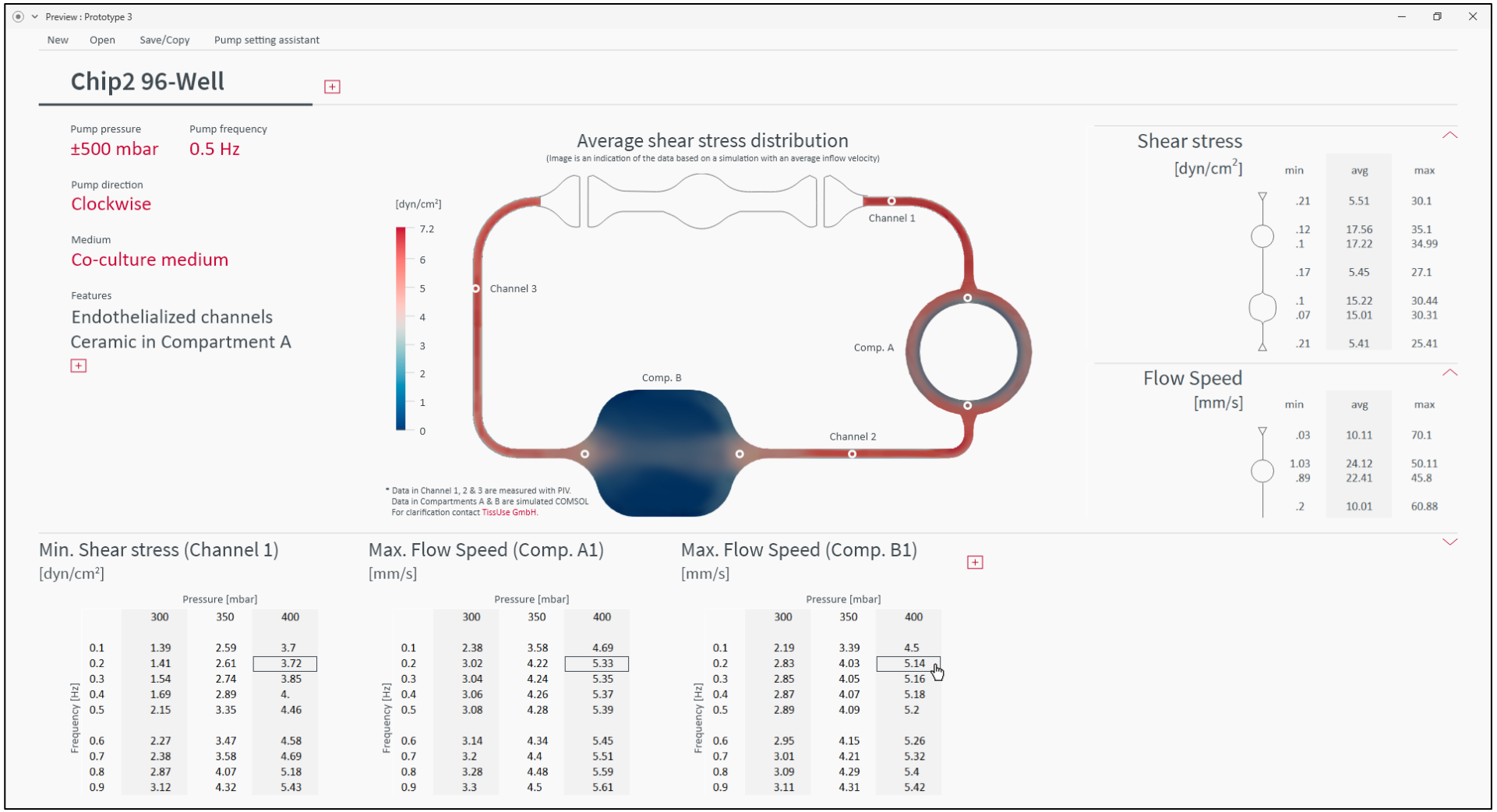


Figure 4-13 - If the user thinks "Well these results are alright, but let me look around and see if I can find something a bit better still." They can tap that button in screen four of the Pump Setting Assistant. This will show the tables of the three requirements that the user set in the Pump Setting Assistant. Hovering over cells highlights them in all tables simultaneously.

Figure 4-14 - Finally, a different scenario is where the user wants to compare two similar setups. When the user taps the plus sign next to the "Chip2 96-Well" main tab, a copy of the current setup is opened. The user can then for example remove a feature and compare the flow data of both setups.

4.8. Testing

Now that the prototype is ready, it is time for the final user testing. This was done with three people per test (Thomé, 2020). Figure 4-15 shows their roles.

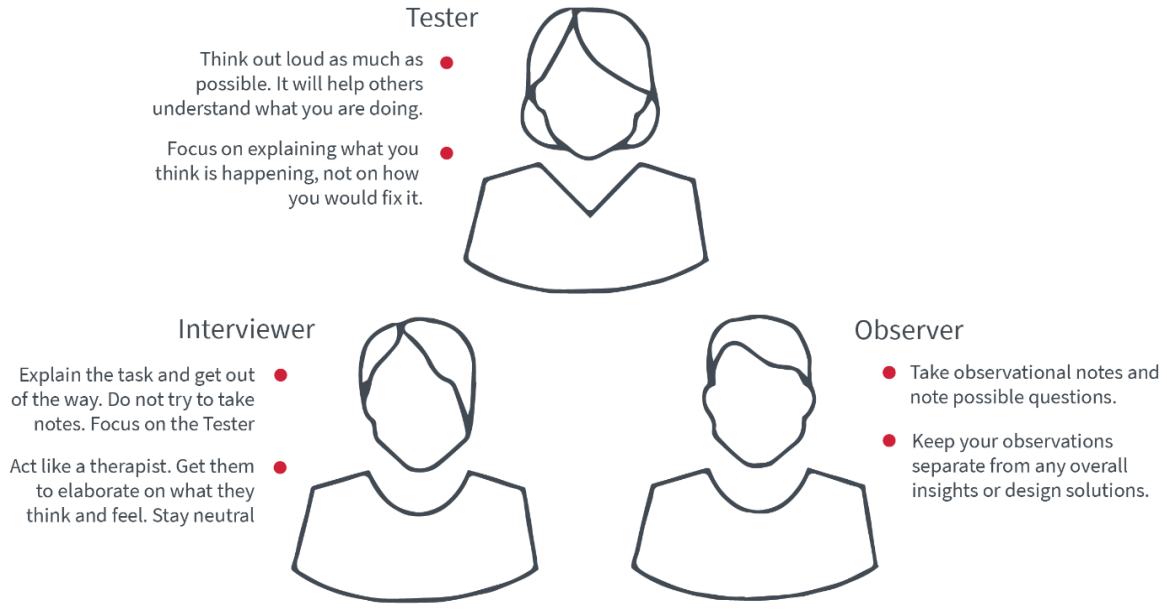


Figure 4-15 - Three different roles during a UI testing session: Interviewer, tester and observer. Image redrawn based on (Thomé, 2020).

The interviewer in Figure 4-15 explains the task that the tester has to perform. Four different functionalities of the tool were of interest. These four tasks were thus included in the test. All tests followed the same script, which is the following:

1. **Open a new setup:** Could you open a new setup of Chip2 96-Well?

- Could you describe what you are seeing right now?

2. **Add a feature:** Could you tell me the minimum shear stress in Channel 1 in a setup that has two specific features? The features being:
    a. Firstly, endotheliazed channels throughout the chip
    b. Secondly, a ceramic in Compartment A
    c. Minimum shear stress in Channel 1 should be: 0.21 dyn/cm^2
3. **Use the pump setting assistant:** Could you use the Pump Setting Assistant to find the optimal pump settings? You have a few specific requirements to the flow inside the chip. The requirements being:
    a. The minimum shear stress in Channel 1 should be at least 4.5 dyn/cm2
    b. The maximum flow speed at the entrance of Compartment A should be 5 mm/s
    c. The maximum flow speed at the entrance of Compartment B should be 5.2 mm/s

- Click “show me tables and let me look around”
- Set pump pressure to 400 mbar
- Click “pump pressure” to actually set the pressure to 400 mbar
- Minimize tables

4. **Compare two setups:** Could you compare the time that it takes a substance to travel from Compartment A to Compartment B in this setup with and without a ceramic in Compartment A?
    a. Difference in distribution time is none.

This testing script was also validated with a few try-out tests to make sure it worked properly. The outcomes of the user tests are used to craft the recommendations in 4.8.

4.9. Discussion

In general, the prototype was perceived as clear, good-looking and functioning properly. Even though some testers had a little trouble finding the button to open a new setup on the home screen, all of them then directly recognised the shape of a Chip2 96-well. Which lead them to the dashboard. Here they all distinguished three parts of the screen – as was intended. They noted those parts in the following order: the image, then the settings on the left and the data on the right. A few even mentioned that this distribution with the settings on the left and the data on the right felt natural to them. It was reassuring to see that the theory on visual harmony and scanning lines in fact lead to something which users then called “intuitive”.

From the dashboard the first task was to add a feature. This button was found instantly by all testers without explanation. Inside the dialog that then opened there was significant confusion, which will be elaborated on in the recommendations further down in this paragraph. The Pump Setting Assistant created the opposite experience. Several testers were not able to find the button to initiate the dialog, but once inside, they walked through the steps rather smoothly. The testers especially neatly understood the dialog’s final screen, which had a heavy visually harmony and disharmony to structure its somewhat dense information.

Two interesting details are that the users considered the additional information at the bottom of the image clear. Secondly, the linear representation of the chip in the data table on the right took all users some time to recognize or even notice. However, once they did, they considered it quite helpful.

Improvements on the current prototype

Notes of the prototype tests generated a list of possible points of improvement. There was still significant room for improvement. Some things were mentioned by several users. Others only appeared once. The most prominent ones will be explained here. This list can be expanded by the flaws mentioned in Appendix O.

In the following text, the testers that mentioned the flaw are referred to with a P. This is analogous to the numbering of the testers in the test notes in Appendix N. For each point of improvement, a suggestion is made on how this could be improved.

It is unclear that the word Feature in the Features dialog, shown in Figure 4-16, is a dropdown (P1 – P6). It now commonly gets recognised as a title, which is not the intention. Two suggestions to solve this are the following: Further down it became clear that some users prefer to first set the location and then choose what feature they want to add. If the location is put on top in the dialog and then the Feature button at the bottom, it is more difficult to interpret it as a title. Another option is to make the affordance of the dropdown menu more prominent. A little arrow could be added besides the word for example. Given that the dropdown menus more often don’t get recognised, this might be the better solution.

It is unclear which compartment carries which name in the Features dialog (P1, P2, P5, P6). Several testers did not know which compartment was A or B in the dialog shown in Figure 4-16. In the prototype the dialog was fixed, because of limits Adobe XD. In an eventual functioning program, it would not be. Just like any other dialog on a PC you would be able to move it aside. This way the user could have a look at the labels in the image behind. Most users tried this, but could not, because of the fixed dialog. To save the user this trouble it would be possible to label the graph in the dialog as

well. However, given that it would only take the user once to know which compartment is which and the additional clutter on the dialog, it would be recommended to refrain from this.

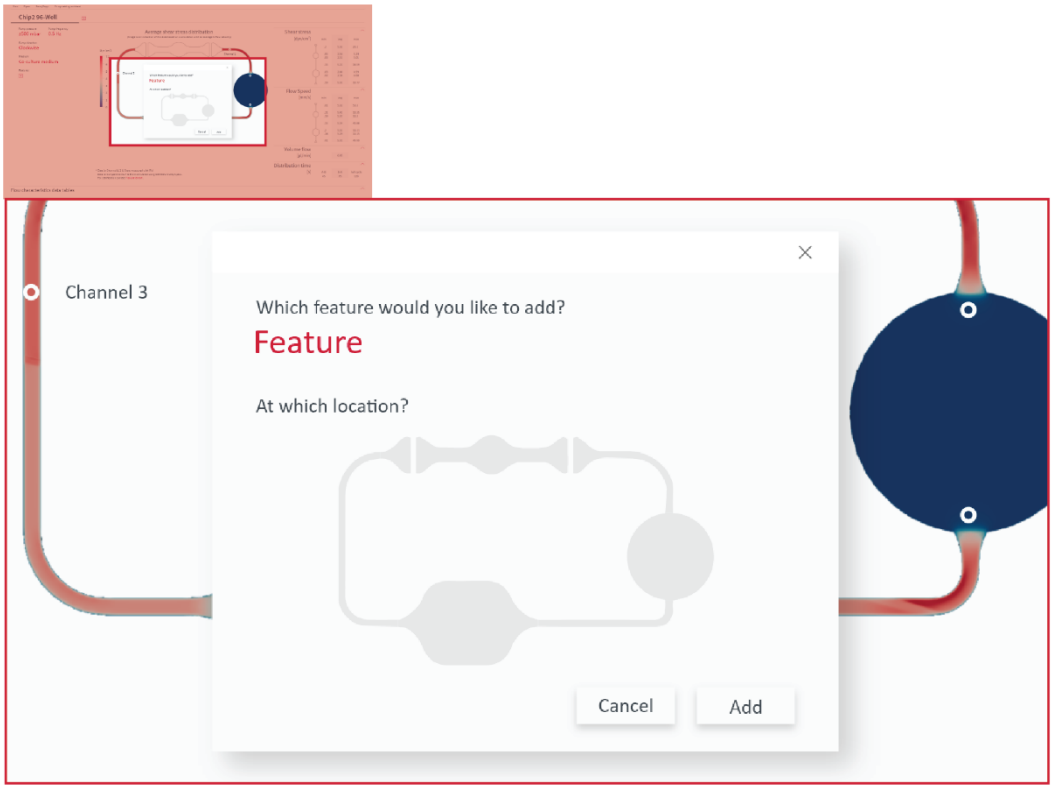


Figure 4-16 - Close-up of the Feature dialog.

It is unclear that the Pump Setting Assistant exists (P1 – P6). When the user comes into the program, they are not in any way made aware of the existence of this function. This is only a program for beginning users. Hence, it might be interesting to little pop up for the first time opening the program. This pop-up could point out and quickly explain the Pump Setting Assistant. It is important to keep the disturbance of the pop-up minimal and add an option for the user to say they do not need the pop-up anymore in the future.

It is unclear where the Pump Setting Assistant can be found (P1, P2, P3, P4). During the tests, the testers were explained that the Pump Setting Assistant exists. They were then asked to use it. Most of them could then not find the button shown in Figure 4-17. Again the solution could be twofold. First of all, the just-mentioned pop-up could make a big difference here already. Secondly, the affordance of the button does not fit the type of action that it performs. A floating action button might be more suitable than what it is now. Also, it is now in harmony with standard functions such as Save or Open. Since it has more to do with the settings or the data, it would be better to make a button for the Pump Setting Assistant visually harmonize with these groups.

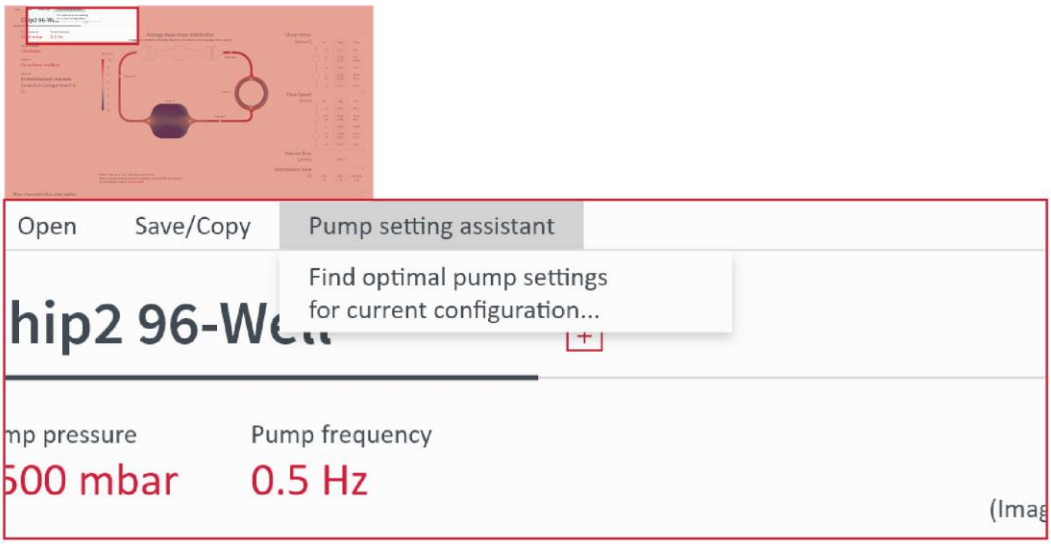


Figure 4-17 - Close-up of the Pump Setting Assistant button.

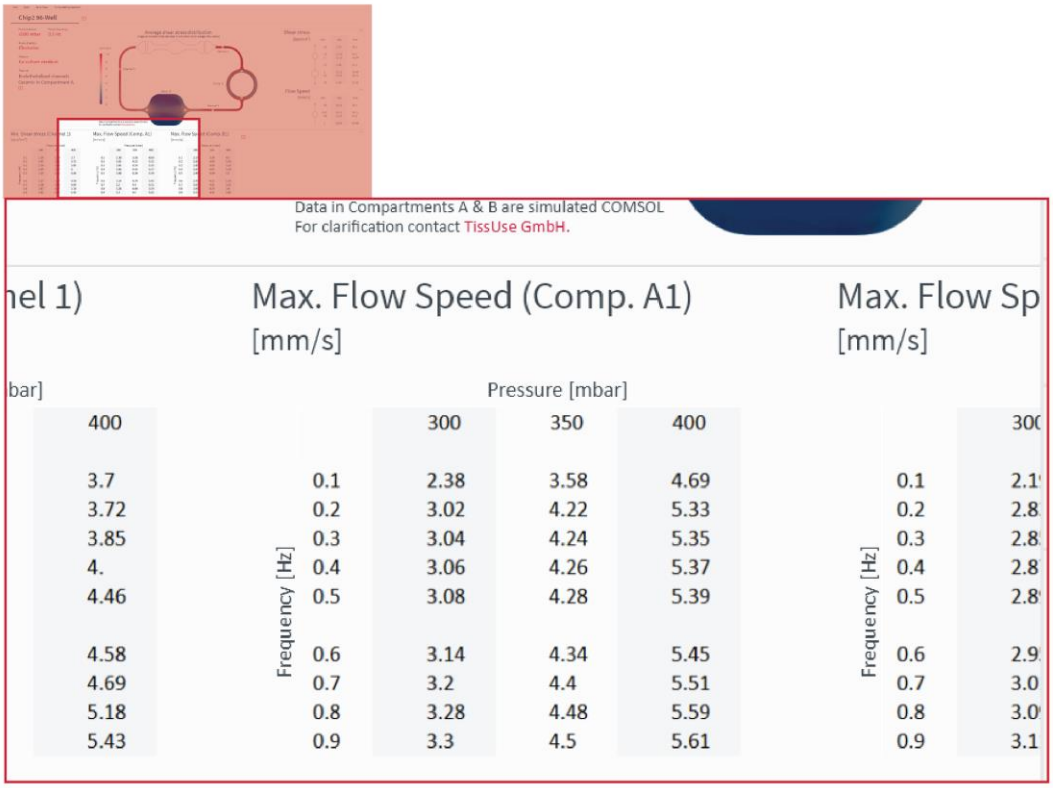


Figure 4-18 - Close-up of the Flow Characteristics Table.

It is unclear that the Data Characteristics Tables can be moved around to show more pressures and frequencies (P1, P2, P5). The Data Characteristics Tables, shown in Figure 4-18, contain data ranging between 300 – 850 mbar and 0.1 – 2.0 Hz. However, only a small part can be shown at once. From Figure 4-18 it can be seen that there is no affordance that the user can move around in the table. This was noted by the testers too. Hence it would be recommended to add some form of affordance. Either subtle with a gradient on the movable edges or more direct with button or sliders.

Write the zero before the decimal points, such as 0.2 instead of .2 which it is now (P1, P2, P3). Figure 4-19 shows that currently the data tables in the UI do not show a 0 before the decimal points. This is because the tables were made in MS Excel. To align the data on the decimal points, MS Excel forced to remove the zeros before them. When this tool is eventually programmed, the data will not have to be shown using MS Excel. Hence, this problem is expected to solve by itself.

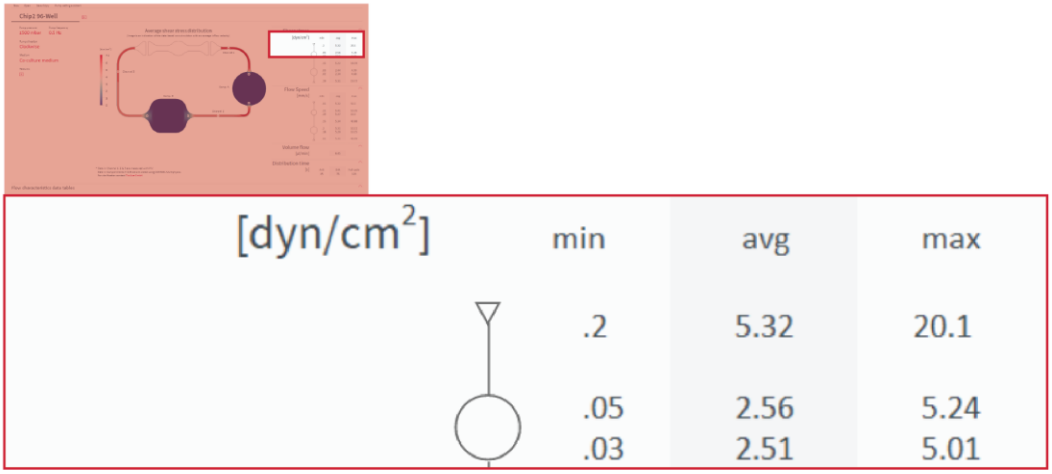


Figure 4-19 - Close-up of data with a decimal point but without a zero in advance.

It is unclear where the button for a new setup is in the landing page (P4, P5, P6). Even though the theory of the scanning line was applied to the landing page. Half of the testers found it hard to find the new setup button at the bottom right, Figure 4-20. However, they eventually did find it. Once they know where it is, everything works smoothly. If it is decided to change the design of the New Setup button, please make sure that it stays consistent with the design guidelines in Appendix M.

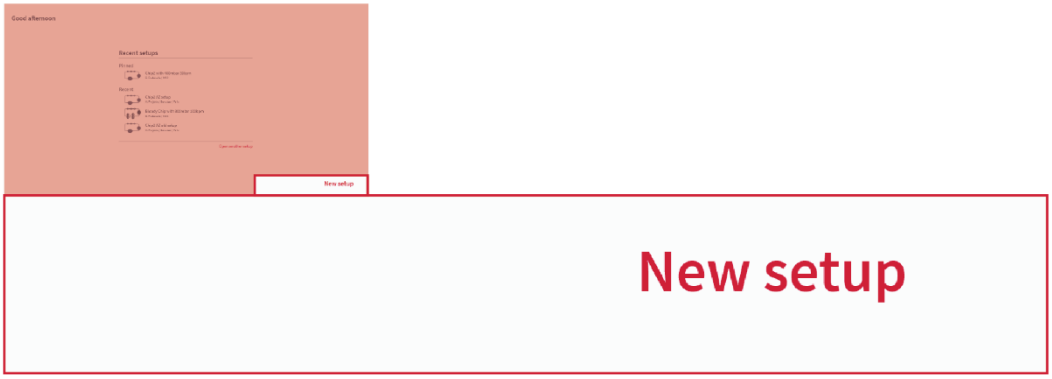


Figure 4-20 - Close-up of the New Setup button.

It is unclear that “Compartment A1” indicates the entrance of Compartment A in the requirements screen of the Pump Setting Assistant (P1, P4, P5). In the dropdown in Figure 4-21 it is not clear what Compartment A1 through Compartment B2 mean. What might be a better description is to call it “Compartment A pump side” and “Compartment A circuit side”. Both compartments have a side that goes directly to the pump, and a side that connects to the circuit.

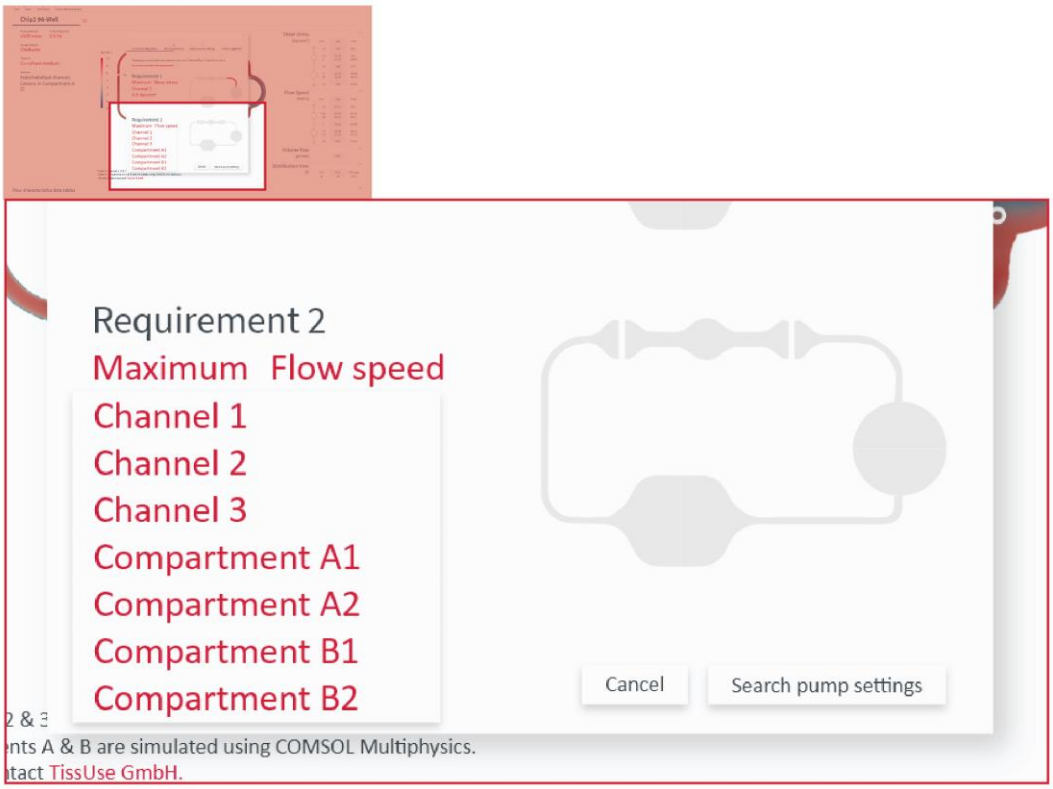


Figure 4-21 - Close-up of the location dropdown menu in the requirements screen of the Pump Setting Assistant.

The visual image of the chip circuit is too large (P1, P4). Especially on the screen with the Data Characteristics Tables, shown in Figure 4-22, it was noted that the image was too big for how useful it is. P4 mentioned that at this point the data in the tables is important. One would not read data from the image. Right now the space that the image takes up goes at the cost of the data tables.

The table on the right should not be cropped when the Data Characteristics Tables come up (P1, P2). This connects to previous point. The conclusion can be: make the image smaller and do not compromise on the space for the tables.

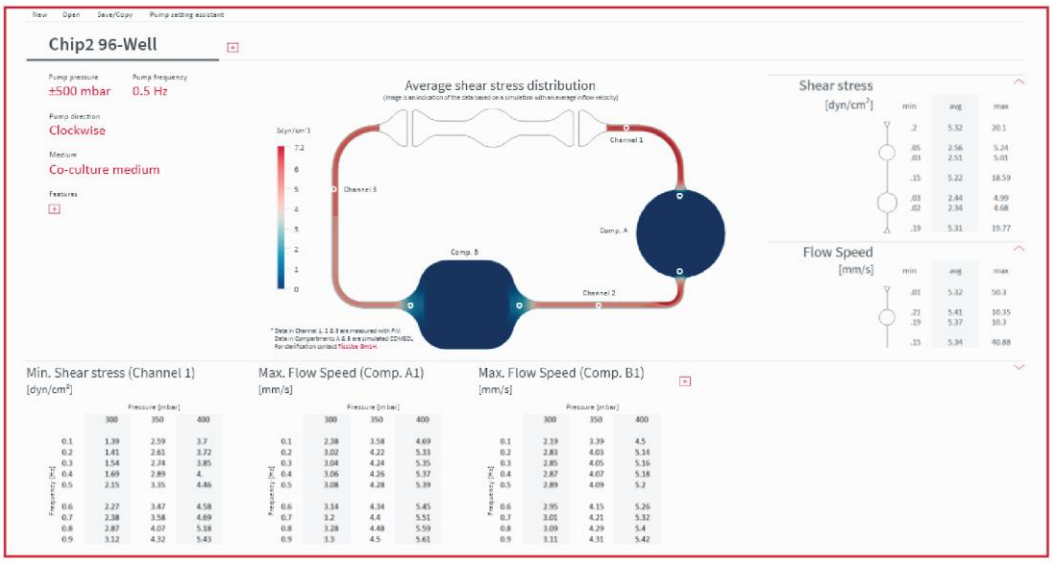


Figure 4-22 - Screen showing the image and cropped data table on the right.

It is unclear where the button to open a comparative view is and what it does (P2, P3). The plus button in Figure 4-23 is the button to open an identical dashboard on the right for comparison. It took the testers quite some time to find it and some did not find it. A similar solution to that of the Pump Setting Assistant might be suitable here. Firstly, make it clearer what it does. For example, let it say “Open a comparative view” instead of just a plus sign. Also, a small pop-up with the first time opening the program saying “if you want to compare two similar setups, click here” could be useful. Again, make sure it is not too intrusive and the user can say they do not want to see it in the future anymore.

Figure 4-23 - Close-up of the button to open a comparative view.

It is unclear that the words such as “Min/avg/max” and “Quantity” in the requirements screen of the Pump Setting Assistant are dropdowns (P1, P3). Figure 4-24 shows a close-up of the requirement screen. The problem is similar to that of the Feature dialog. A clearer affordance with a little arrow on the side of the buttons would probably solve the issue. A little arrow makes it clear that there are dropdown menus behind these words.

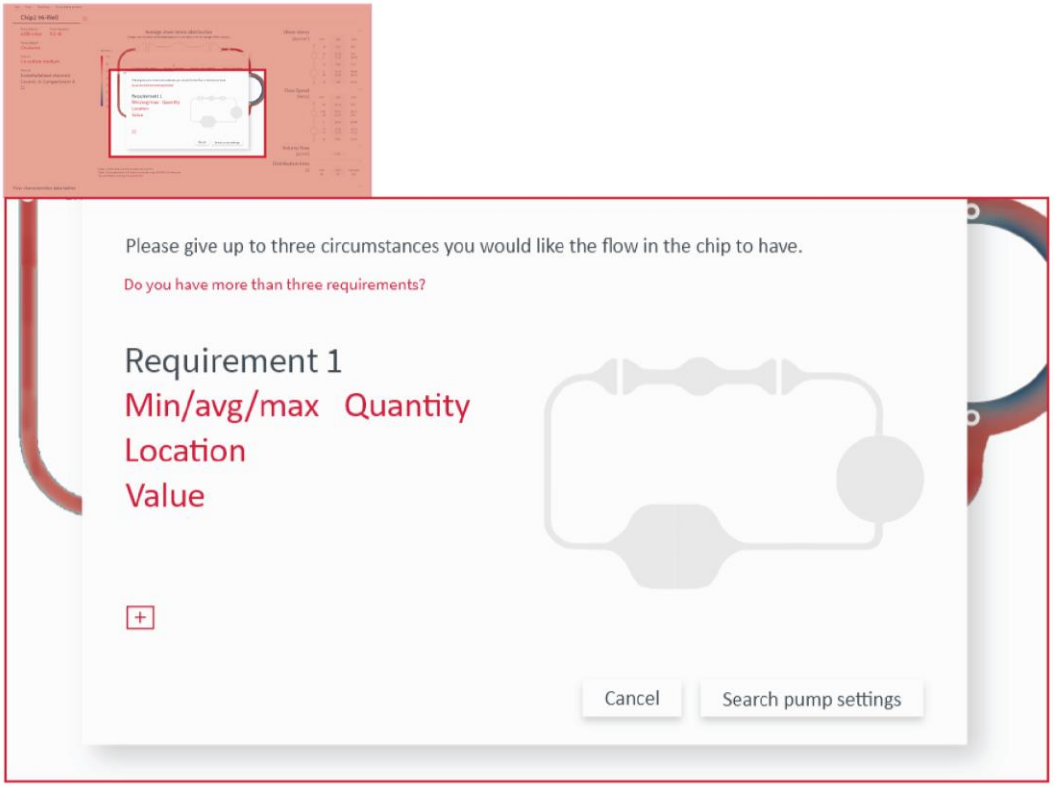


Figure 4-24 - Close-up of the min/avg/max-, quantity-, and location buttons in the requirement screen of the Pump Setting Assistant.

One final note; what was reassuring, is that if users did not understand something the first time, they did on their second try. The users fluently went through the Feature dialog on their second attempt. Even though it had confused all of them on their first try. This does not justify the conclusion that it does not need improvement. However, it could be comforting to know that even for some of the most confusing parts of this UI, it only requires one attempt to quickly understand it.

4.10. Sub-conclusion

The goal of this thesis was to develop a service that delivers the desired information about the physical circumstances in a chip in the most convenient and suitable way. This product should be incorporated in the HUMIMIC-product portfolio.

An elaborate study of the philosophy of TissUse, the user requirements and scenarios lead to a prototype for this service. The end-users contributed significantly throughout the entire process. This prototype was sculpted using knowledge from UI design and information visualization. In general, the prototype was perceived as clear, good-looking and functioning properly. The space for improvement was defined with user tests. Using this feedback, it can be even further improved. Once this tool will actually be programmed, it is confidently expected that it will indeed deliver the desired information most conveniently and suitably to end users.

5. Conclusion

5. Conclusion

The goal of this thesis was to create a validated method to characterize and simulate the flow in any possible chip design without the need of a physical prototype. Using the resulting data from this method, the second goal was to create a service that delivers the desired information about the physical circumstances in a chip in the most convenient and suitable way.

PIV-experiments were performed to characterize the flow in a Chip2 96-Well. These have yielded an inlet boundary condition for simulations using the lattice Boltzmann-method and COMSOL Multiphysics. This boundary condition successfully recreates the inlet flow caused by the pump in the chip.

After thoroughly studying LBM, creating LBM and COMSOL Multiphysics models and performing mesh independence studies, simulations were setup and performed. Although COMSOL performed slightly better, neither LBM nor COMSOL Multiphysics were – with the current simulation setup – able to adequately represent the flow in a real chip. Suggestions for how to improve are incorporated in Chapter 6.

For now, µPIV thus remains the most reliable method for TissUse to characterize the flow in their microphysiological systems.

Simultaneous to the simulation process, an elaborate study of the philosophy, values and user requirements on a flow visualization tool was conducted. These insights were combined with knowledge of user interface design and information visualization. A process of rapid-prototyping and close co-creation with end users has yielded a clear, good-looking and properly functioning prototype for the UI of the tool. User tests have laid bare what can still be improved on this prototype. Implementing those improvements is confidently expected to lead to a tool that will deliver the desired information most conveniently and suitable to end users. Suggestions on how to continue towards a real product can be found in Chapter 6.

6. Recommendation for Future projects

6. Recommendations for future projects

6.1. Recommendations regarding characterization of chips

If TissUse wants to know more about the flow in its chips, it is recommended to dedicate more time to PIV. The method is now properly understood and it is the only method that reliably characterizes the flow in the chips at the moment.

Since the µPIV experiments yielded a successful boundary condition for the simulations, it would be good to do µPIV experiments on Chip2 96-Well with different pump settings. It is the most commonly used chip. Having this data would be valuable to a large part of researchers that use TissUse's chips already. Later, once a proper simulation setup is found it can be used to create the inlet boundary conditions.

When performing more µPIV experiments, do not only try different pump settings. It is highly recommended to check the consistency of µPIV results of different specimens of the same chip type. In this study the same chip was used for all µPIV experiments. Preliminary results for another study within TissUse suggested, that there might be a significant difference between specimens of the same chip. It is wise to identify this (in)consistency so researchers can be provided with an estimation of the reliability of the flow characteristics data.

Lastly, make sure to properly document the knowledge on how to perform µPIV experiments within TissUse. It is expected that µPIV will play an important role in discovering the flow of the fluid in the chips. It might be very valuable to secure this knowledge for the future.

6.2. Recommendation regarding future simulations

In general, the use of COMSOL Multiphysics over LBM is recommended for TissUse. The COMSOL Multiphysics models used in this study simulate reality better and faster than their LBM counterparts. Other disadvantages from LBM compared to COMSOL are the need for a parallel-computation cluster of supercomputer and knowledge of LBM itself.

If TissUse wants to unlock simulations as a viable tool to characterize flow in a chip, it would be good to try to incorporate the dampening of the compartments in the real chip in the simulations. Some suggestions on how to try that:

- Since the liquid in a real chip is practically compressible due to its consistency of water and compressible air, it might make more sense to do a simulation with a compressible liquid. Using the ratio of air volume and water volume in the closed chips, it might be possible to define an effective compressibility factor.
- In COMSOL Multiphysics it might be possible to include the actual air in a simulation. Creating a water-air interface. This would be the most realistic simulation option, but is dependent on COMSOL's capabilities. This option is deemed worth looking into.
- Preliminary results that were not included in this report of simulations simulating the roofs of the compartments as no-slip walls, were not promising. It is unlikely that this will create the desired behaviour in the simulation's fluid.
- No need to try compartments with open roofs anymore. These were unsuccessful in creating a realistic flow.

Naturally, it is recommended to study mesh generation in COMSOL Multiphysics more. Something has caused the standard meshes to be unable to simulate a transient simulation. Probably some kind of

setting is wrong. It seems unlikely that COMSOL would not be able to perform transient simulations on meshes it generates itself. Another option is to try to improve the custom grid.

A small note; Since the chips during research will most likely run inside an incubator at a constant temperature of $37°C$, it would be recommended to use the characteristics of water at that temperature. It might also be worth looking into if it matters much for the fluids behaviour.

6.3. Recommendations regarding development of the flow data visualization tool

The tool to visualize flow data is ready for a final iteration. Given the recommendations in 4.9 and Appendix O, the current prototype can be even further improved. There is confidence that this will lead to a successful design of the tool.

An aspect which was a bit underrepresented in the development is the developers. It is of course cool to go all out on the design of the tool and ignore its functionality. However, to create a successful product it must function properly and people should be able to develop it. Hence, it is recommended that for the next iteration either the in-house developers or an external program developer is involved.

Once this prototype is ready for testing, test it. If it gets confirmed, that the prototype is indeed even better, it might be ready to develop the actual tool.

With the risk of trotting territory that the author is not too familiar with, a suggestion for how the tool could incorporate data. It might be easy to create .csv-files or per pump setting. The tool could then read those out of a folder and simply visualize data from the .csv-file of the pump setting that is selected in the tool. This would make it very easy for the chip engineers to add newly characterized pump settings and chips. Also, it could keep the tool itself computationally lightweight.

Some final notes on the way the current prototype came to be and what might be improved. 4.2 said that two puzzle pieces defined the solution space for this tool. TissUse's philosophy and capabilities on one hand, the user requirements on the other. There are naturally more aspects that could be taken into account, such as market trends, competition, programmability. It might be wise to study those aspects for any future iterations

7. References

Anggreeni, I., & van der Voort, M. (2007). *Tracking the Scenarios in Scenario-Based Product Design*. https://research.utwente.nl/en/publications/tracing-the-scenarios-in-scenario-based-product-design-a-study-to

Ansys, I. (2004). *Theory reference* (P. Kohnke (ed.); Release 9.). Ansys, Inc. https://cloudflare-ipfs.com/ipfs/bafykbzacecivehztxrdgq55dnep3rtkqoilx4fub3ntikmysqugtbikmv36xy?filename=SAS - ANSYS%2C Inc. Theory Reference_ ANSYS Release 9.0 %282004%29.pdf

Barber, R. W., & Emerson, D. R. (2002). The influence of Knudsen number on the hydrodynamic development length within parallel plate micro-channels. *Advances in Fluid Mechanics IV*, 207–216. https://www.witpress.com/Secure/elibrary/papers/AFM02/AFM02019FU.pdf

Baumer GmbH. (2021a). *Baumer HXC40*. https://www.baumer.com/se/en/product-overview/industrial-cameras-image-processing/industrial-cameras/long-term-availability/hx-series/camera-link-interface/hxc40/p/23850

Baumer GmbH. (2021b). *Frame Rate Calculator*. https://www.baumer.com/de/de/frame-rate-calculator/a/frame-rate

Carl Zeiss Microscopy GmbH. (n.d.). *ZEISS Axio Vert.A1; Inverted Microscop for Advanced Routine*. Retrieved March 24, 2021, from https://www.zeiss.com/microscopy/int/products/light-microscopes/axio-vert-a1-for-biology.html

Congressional Budget Office. (2021). *Research and Development in the Pharmaceutical Industry*. https://www.cbo.gov/system/files/2021-04/57025-Rx-RnD.pdf

Connor, N. (2019). *What is Rayleigh number - Definition*. https://www.thermal-engineering.org/what-is-rayleigh-number-definition/

Dassault Systèmes. (2021). *Mesh Quality Checks*. Solidworks Online Help. http://help.solidworks.com/2021/english/solidworks/cworks/c_mesh_quality_checks.htm

Demyanko, K. V., & Nechepurenko, Y. M. (2013). Linear stability analysis of Poiseuille flow in a rectangular duct. *Russian Journal of Numerical Analysis and Mathematical Modelling*, *28*(2), 125–148. https://doi.org/10.1515/rnam-2013-0008

Doda, B. (2008). *Micro PIV*. https://velocimetry.net/micropiv_principles.htm

Encyclopaedia Britannica. (2021). Great Wall of China. In *Encyclopaedia Britannica*. https://www.britannica.com/topic/Great-Wall-of-China

Engineering Toolbox. (2003a). *Entrance lenght and Developed flow*. https://www.engineeringtoolbox.com/entrance-length-flow-d_615.html

Engineering Toolbox. (2003b). *Hydraulic diameter*. https://www.engineeringtoolbox.com/hydraulic-equivalent-diameter-d_458.html

Engineering Toolbox. (2003c). *Reynolds number*. https://www.engineeringtoolbox.com/reynolds-number-d_237.html

Engineering Toolbox. (2003d). *Water - Density, Specific Weight and Thermal Expansion Coefficient*. https://www.engineeringtoolbox.com/water-density-specific-weight-d_595.html

Engineering Toolbox. (2004). *Water - Dynamic and Kinematic viscosity*. https://www.engineeringtoolbox.com/water-dynamic-kinematic-viscosity-d_596.html

Expert Program Management. (2017). *Five Product Levels (Kotler)*. https://expertprogrammanagement.com/2017/10/five-product-levels/

FDA. (2004). *Innovation or Stagnation: Challenge and Opportunity on the Critical Parth to New Medical Products*. http://wayback.archive-it.org/7993/20180125035500/https://www.fda.gov/downloads/ScienceResearch/SpecialTopics/CriticalPathInitiative/CriticalPathOpportunitiesReports/UCM113411.pdf

FDA. (2018). *The Drug Development Process*. https://www.fda.gov/patients/learn-about-drug-and-device-approvals/drug-development-process

Filippova, O., & Hänel, D. (2000). Acceleration of Lattice-BGK Schemes with Grid Refinement. *Journal of Computational Physics*, *165*(2), 407–427. https://www-sciencedirect-com.ezproxy2.utwente.nl/science/article/pii/S0021999100966178

Gothäll, H. (2017). How to inspect your mesh in COMSOL Multiphysics? *Comsol Blog*. https://www.comsol.com/blogs/how-to-inspect-your-mesh-in-comsol-multiphysics/

Guo, Z., Zhao, T. S., & Shi, Y. (2004). Preconditioned lattice-Boltzmann method for steady flows. *Physical Review E*, *70*, 066706. https://journals-aps-org.ezproxy2.utwente.nl/pre/pdf/10.1103/PhysRevE.70.066706

Hasenberg, T. (2017). *Emulating the Human Vasculature in a Multi-Organ-Chip Platform Rheology and Vasculogenesis*.

Heer, J. (2017). *CSE 442 - Data visualization: Visual Encoding Design*. https://courses.cs.washington.edu/courses/cse442/17au/lectures/CSE442-VisualEncoding.pdf

Hoagland, L. C. (1960). *Fully Developed Turbulent Flow in Straight Rectangular Ducts*. 168.

Hoy, W., & Roos, T. (2005). *What is the Grashof number?* http://www.owlnet.rice.edu/~ceng402/proj05/hoy/hoyroos/background/background.html

Izquierdo, S., & Fueyo, N. (2009). Optimal preconditioning of lattice Boltzmann methods. *Journal of Computational Physics*, *228*, 6479–6495.

J.W. Slater. (2021). *Examining Spatial (Grid) Convergence*. https://www.grc.nasa.gov/www/wind/valid/tutorial/spatconv.html

Jain, K. (2020). Efficacy of the FDA nozzle benchmark and the lattice Boltzmann method for the analysis of biomedical flows in transitional regime. *ArXiv*, 1817–1830.

Jansen, S., & Pieters, M. (2019). *CoCreatie Revolutie* (1st ed.). Van Duuren Management.

Kapferer, J. N. (2008). The New Strategic Brand Management. In *Marketing Management*. Kogan Page. https://doi.org/10.1007/978-0-230-36367-0_7

Khan Academy. (2021). *What is the ideal gas law?* https://www.khanacademy.org/science/physics/thermodynamics/temp-kinetic-theory-ideal-gas-law/a/what-is-the-ideal-gas-law

Krug, S. (2000). *Don't make me think* (K. Witehouse & L. Brazieal (eds.); 1st ed.). New Riders Publishing.

Krüger, T., Kusumaatmaja, H., Kuzmin, A., Shardt, O., Silva, G., & Viggen, E. M. (2017). The Lattice Boltzmann Method - Principles and Practice. In *Graduate Text in Physics*. Springer International Publishing. https://doi.org/10.1007/978-3-319-44649-3

LabLua PUC-Rio. (2020). *About Lua*. http://www.lua.org/about.html

Lai, Y. G., Lin, C.-L., & Huang, J. (2001). Accuracy and Efficiency Study of Lattice Boltzmann Method for Steady-State Flow Simulations. *Numerical Heat Transfer, Part B.*, *39*(1), 21–43. https://www-tandfonline-com.ezproxy2.utwente.nl/doi/pdf/10.1080/104077901460669?needAccess=true

Latt, J. (2008). Choice of units in lattice Boltzmann simulations. *Lattice Boltzmann Howtos*, *April*, 1–6. http://wiki.palabos.org/_media/howtos:lbunits.pdf

LearnMechE. (2017). *Description and Derivation of Navier-Stokes equations*. https://www.youtube.com/watch?v=NjoMoH51UZc

Lidwell, W., Holden, K., & Butler, J. (2010). *Universal Principles of Design* (Revised an). Rockport Publishers, Inc.

Mads Soegaard, & Interaction Design Foundation. (2020). *Laws of Proximity, Uniform Connectedness, and Continuation – Gestalt Principles (2)*. https://www.interaction-design.org/literature/article/laws-of-proximity-uniform-connectedness-and-continuation-gestalt-principles-2

Mahoney, M. (2019). *The Art and Science of Data Visualization*. https://towardsdatascience.com/the-art-and-science-of-data-visualization-6f9d706d673e

McKay, E. N. (2013). *UI is Communication* (M. Dunkerley (ed.); first). Elsevier Inc. https://doi.org/https://doi.org/10.1016/C2011-0-07788-8

Mikulic, M. (2021). *Clinical trial success rates by therapeutic area as of 2020*. https://www.statista.com/statistics/1201162/clinical-trial-success-rates-by-therapeutic-area/

Mind Tools Content Team. (2021). *Critical to Quality (CTQ) Trees*. https://www.mindtools.com/pages/article/ctq-trees.htm

Mohamad, A. A., Succi, S., Sbragaglia, M., & Ubertini, S. (2010). Lattice Boltzmann Method. In *Scholarpedia* (second, Vol. 5, Issue 5). Springer International Publishing. https://doi.org/10.4249/scholarpedia.9507

Nobel Prize Outreach AB. (2021). *Shinya Yamanaka*. https://www.nobelprize.org/prizes/medicine/2012/yamanaka/lecture/

Oogvereniging. (2021). *Kleurenblindheid*. https://www.oogvereniging.nl/oogaandoeningen/oogaandoeningen-overzicht/kleurenblindheid/

Raffel, M., Willert, C. E., Wereley, S. T., & Kompenhans, J. (2007). Particle Image Velocimetry: A Practical Guide, 2nd Edition. *Springer*.

Retzios, A. D. (2009). *Why Do So Many Phase 3 Clinical Trials Fail?* http://www.adrclinresearch.com/Issues_in_Clinical_Research_links/Why Pivotal Clinical Trials Fail - Part 1_v12L_a.pdf

Rieschel, E., & Brandt, L. (2016). *A Study on the Flow of Viscous Fluids in a Square Duct*. 1–30.

Rutledge, A. (2009). *Gestalt Principles of Perception - 3: Proximity, Uniform Connectedness, and Good Continuation*. http://www.andyrutledge.com/gestalt-principles-3.html

Ruzicka, M. C. (2008). On dimensionless numbers. *Chemical Engineering Research and Design*, *86*(8), 835–868. https://doi.org/10.1016/j.cherd.2008.03.007

SchedMD. (2020). *Overview*. https://slurm.schedmd.com/overview.html

Schwabisch, J. (2017). *Applying Cognitive Load Theory to Presentation Delivery*.

https://policyviz.com/2017/01/05/applying-cognitive-load-theory-to-presentation-delivery/

Sormann, H., Boeri, L., Pilz, J., Hadley, P., & Maislinger, F. (n.d.). *Numerical Methods: Fourier analysis of real datasets*. Retrieved March 24, 2021, from http://lampx.tugraz.at/~hadley/num/ch3/3.3a.php?

Spiegel, C. (2019). *Transport Phenomena in Micro and MEMS Fuel Cells*. https://www.fuelcellstore.com/blog-section/transport-phenomena-in-micro-and-mems-fuel-cells

Spiga, M., & Morino, G. L. (1994). A symmetric solution for velocity profile in laminar flow through rectangular ducts. *International Communications in Heat and Mass Transfer*, *21*(4), 469–475. https://doi.org/10.1016/0735-1933(94)90046-9

Squires, T. M., & Quake, S. R. (2005). Microfluidics: Fluid physics at the nanoliter scSquires, T. M., & Quake, S. R. (2005). Microfluidics: Fluid physics at the nanoliter scale. Reviews of Modern Physics, 77(3), 977–1026.ale. *Reviews of Modern Physics*, *77*(3), 977–1026.

Sun Microsystems Inc. (2008). *Running programs with the mpirun command;* https://docs.oracle.com/cd/E19356-01/820-3176-10/ExecutingPrograms.html

SURFsara. (n.d.). *Cartesius*. Retrieved June 20, 2021, from https://userinfo.surfsara.nl/systems/cartesius

The Mathworks, I. (2021). surfc. In *Matlab Documentation*. https://de.mathworks.com/help/matlab/ref/surfc.html?s_tid=doc_ta

Thermo Fisher Scientific Inc. (2021). *Aldehyde/Sulfate Latex Beads, 4% w/v, 5 µm*. https://www.thermofisher.com/order/catalog/product/A37306#/A37306

Thielicke, W. (2014). *The Flapping Flight of Birds Analysis and Application*.

Thielicke, W. (2021). *PIVlab - particle image velocimetry (PIV) tool with GUI*. https://de.mathworks.com/matlabcentral/fileexchange/27659-pivlab-particle-image-velocimetry-piv-tool-with-gui

Thomas, D. W., Burns, J., Audette, J., Carroll, A., Dow-Hygelund, C., & Hay, M. (2016). *Clinical Development Success Rate*. https://www.bio.org/sites/default/files/legacy/bioorg/docs/Clinical Development Success Rates 2006-2015 - BIO, Biomedtracker, Amplion 2016.pdf

Thomé, A. (2020). *UX Design: How to set up a user testing session*. https://medium.com/nyc-design/ux-design-how-to-set-up-a-user-testing-session-d14b74ca803

Thorlabs Inc. (1999). *Magnification and Sample Area Calculations*. https://www.thorlabs.com/newgrouppage9.cfm?objectgroup_ID=8564&tabname=Magnification %26 FOV#tabTitles

Tufte, E. R. (1998). *Envisioning Information* (sixth). Graphics Press. http://okhaos.com/tufte.pdf

University of Siegen. (2020a). *APES Overview*. https://geb.sts.nt.uni-siegen.de/doxy/ateles/page/apes_overview.html

University of Siegen. (2020b). *Boundary Conditions*. https://geb.sts.nt.uni-siegen.de/doxy/musubi/page/examples/tutorials/tut_04_boundaries.html

University of Siegen. (2020c). *Musubi; Configuration*. https://geb.sts.nt.uni-siegen.de/doxy/musubi/page/examples/tutorials/tut_01_mus_config.html

University of Siegen. (2020d). *Musubi; Introduction to Musubi*. https://geb.sts.nt.uni-siegen.de/doxy/musubi/index.html

University of Siegen. (2020e). *pressure_expol Subroutine*. https://geb.sts.nt.uni-siegen.de/doxy/musubi/proc/pressure_expol.html

University of Siegen. (2020f). *Seeder; Seeder Mesh Generator*. https://geb.sts.nt.uni-siegen.de/doxy/seeder/index.html

University of Siegen. (2020g). *velocity_bounceback Subroutine*. https://geb.sts.nt.uni-siegen.de/doxy/musubi/proc/velocity_bounceback.html

University of Sydney. (2005). *Entrance Length*. http://www-mdp.eng.cam.ac.uk/web/library/enginfo/aerothermal_dvd_only/aero/fprops/pipeflow/node9.html

Wright, D. C. (2000). *The History of China*. Greenwood Press. https://archive.org/details/historyofchina00wrig/page/48/mode/2up

Yablonski, J. (2021a). *Aesthetic-usability effect*. https://lawsofux.com/aesthetic-usability-effect/

Yablonski, J. (2021b). *Jakob's Law*. https://lawsofux.com/jakobs-law/

Yablonski, J. (2021c). *Laws of UX*. https://lawsofux.com/

Appendices

Appendix A Derivation of the Navier-Stokes equations

The following derivation of the Navier-Stokes equations is written along the video of (LearnMechE, 2017), which was a webcast of the College of Engineering and Applied Sciences of the University of Colorado Boulder.

In essence the Navier-Stokes equations are analogous to Newton's second law applied to an infinitesimally small blob of fluid. The forces on this element of fluid are due to gravity, differences in pressure and the forces due to viscosity. The Navier-Stokes equations are in fact these forces written down per unit volume in a balance equation, just like Newton's second law.

Let's start with Newton's second law for one direction. The same mathematics apply to all directions:

$$\sum F_x = ma_x \tag{7-1}$$

As stated, the Navier-Stokes equations describe this force balance per unit volume. One could say that there is a force density and mass density. In order to get this, Newton's second law will be divided by the volume of the infinitesimal element V:

$$\frac{\sum F_x}{V} = \frac{ma_x}{V} \tag{7-2}$$

It is trivial that this yields the mass density on the right side.

What is less trivial is the elaboration on the acceleration in x-direction. When regarding the x-velocity of the fluid element, u, one can say that this velocity is dependent of the position of the blob and the time, so $u(x, y, z, t)$. Newton's second law uses the acceleration. The chain rule can be applied to differentiate the velocity:

$$a_x = \frac{du}{dt} = \frac{\partial u}{\partial t} + \frac{\partial u}{\partial x}\frac{dx}{dt} + \frac{\partial u}{\partial y}\frac{dy}{dt} + \frac{\partial u}{\partial z}\frac{dz}{dt} \tag{7-3}$$

Conventionally saying $\frac{dx}{dt} = u, \frac{dy}{dt} = v, \frac{dz}{dt} = w$ and substituting this in Newton's second law yields:

$$\frac{\sum F_x}{V} = \rho\left(\frac{\partial u}{\partial t} + u\frac{\partial u}{\partial x} + v\frac{\partial u}{\partial y} + w\frac{\partial u}{\partial z}\right) \tag{7-4}$$

Now let's take a look at the forces on the differential element of fluid. The first force is the gravitational force. Assuming that some component of gravity might point in the x-direction we are considering, one can say:

$$F_g = \rho g_x dxdydz \tag{7-5}$$

One can consider forces in x-direction due to stresses on the block of fluid as well. Each plane of the block will have a stress translated into a force by its surface area.

$$\begin{aligned} F_\sigma &= \sigma_{xx}(x + dx)dydz - \sigma_{xx}(x)dydz \\ &+ \tau_{yx}(y + dy)dxdz - \tau_{yx}(y)dxdz \\ &+ \tau_{zx}(z + dz)dxdy - \tau_{zx}(z)dxdy\mathcal{H} = \int f \ln(f)\ d^3\xi \end{aligned} \tag{7-6}$$

If one divides these two forces by the volume of the blob of fluid $V = dxdydz$ and puts them together in the force balance, this yields:

$$\begin{aligned}&\frac{\rho g_x dxdydz}{dxdydz}\\&+\frac{\sigma_{xx}(x+dx)dydz-\sigma_{xx}(x)dydz}{dxdydz}\\&+\frac{\tau_{yx}(y+dy)dxdz-\tau_{yx}(y)dxdz}{dxdydz}\\&+\frac{\tau_{zx}(z+dz)dxdy-\tau_{zx}(z)dxdy}{dxdydz}=\rho a_x\end{aligned}\qquad 7\text{-}7$$

Which can be simplified to:

$$\begin{aligned}&\rho g_x\\&+\frac{\sigma_{xx}(x+dx)-\sigma_{xx}(x)}{dx}\\&+\frac{\tau_{yx}(y+dy)-\tau_{yx}(y)}{dy}\\&+\frac{\tau_{zx}(z+dz)-\tau_{zx}(z)}{dz}=\rho a_x\end{aligned}\qquad 7\text{-}8$$

Which, when taking into account that the volume is infinitesimally small, can be interpreted as the differentials of the stresses:

$$\rho g_x+\frac{\partial\sigma_{xx}}{\partial x}+\frac{\partial\tau_{yx}}{\partial y}+\frac{\partial\tau_{zx}}{\partial z}=\rho a_x \qquad 7\text{-}9$$

Where one can expand the right hand side again, into:

$$\rho g_x+\frac{\partial\sigma_{xx}}{\partial x}+\frac{\partial\tau_{yx}}{\partial y}+\frac{\partial\tau_{zx}}{\partial z}=\rho\left(\frac{\partial u}{\partial t}+u\frac{\partial u}{\partial x}+v\frac{\partial u}{\partial y}+w\frac{\partial u}{\partial z}\right) \qquad 7\text{-}10$$

The terms containing stresses can be split into a pressure component and a viscosity term. For this the constituent equations are necessary. To arrive at the Navier-Stokes equations the constituent equations of a Newtonian fluid are used. Via a number of algebraic steps this leads to the x-component of the Navier-Stokes equations:

$$\rho g_x-\frac{\partial P}{\partial x}+\mu\left(\frac{\partial^2 u}{\partial x^2}+\frac{\partial^2 u}{\partial y^2}+\frac{\partial^2 u}{\partial z^2}\right)=\rho\left(\frac{\partial u}{\partial t}+u\frac{\partial u}{\partial x}+v\frac{\partial u}{\partial y}+w\frac{\partial u}{\partial z}\right) \qquad 7\text{-}11$$

Doing the same procedure for the y- and z-direction will complete the set of Navier-Stokes equations:

$$\rho g_y-\frac{\partial P}{\partial y}+\mu\left(\frac{\partial^2 v}{\partial x^2}+\frac{\partial^2 v}{\partial y^2}+\frac{\partial^2 v}{\partial z^2}\right)=\rho\left(\frac{\partial v}{\partial t}+u\frac{\partial v}{\partial x}+v\frac{\partial v}{\partial y}+w\frac{\partial v}{\partial z}\right) \qquad 7\text{-}12$$

$$\rho g_z-\frac{\partial P}{\partial z}+\mu\left(\frac{\partial^2 w}{\partial x^2}+\frac{\partial^2 w}{\partial y^2}+\frac{\partial^2 w}{\partial z^2}\right)=\rho\left(\frac{\partial w}{\partial t}+u\frac{\partial w}{\partial x}+v\frac{\partial w}{\partial y}+w\frac{\partial w}{\partial z}\right) \qquad 7\text{-}13$$

To sum up, what these equations in practice represent, one can say: the fluid equivalent of the sum of the forces equals the mass times acceleration, expressed per unit volume. The left-hand side represents the force densities. The first is due to gravity, the second because of any pressure differences, the third is due to viscosity. The right-hand side represents the mass and the local and convective elements of the fluids acceleration.

Appendix B Perception of visual characteristics

The following five images are examples of how the five visual characteristics of visual objects can be used to created intentional harmony or disharmony. In this case it is applied to data set, but the principles work in general.

The five characteristics are – in order of perception speed:

1. Position
2. Size
3. Color
4. Value
5. Shape

Position

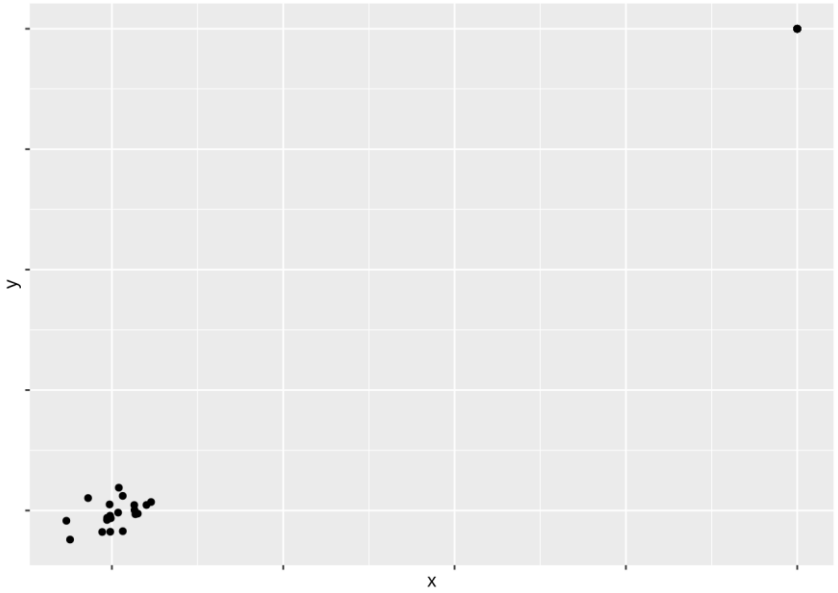


Figure 7-1 - Example of position being inherently interpreted as an ordered characteristic. Most people from Western cultures will perceive the dot in the top right as being of a higher value than those in the bottom left. Taken from (Mahoney, 2019).

Size

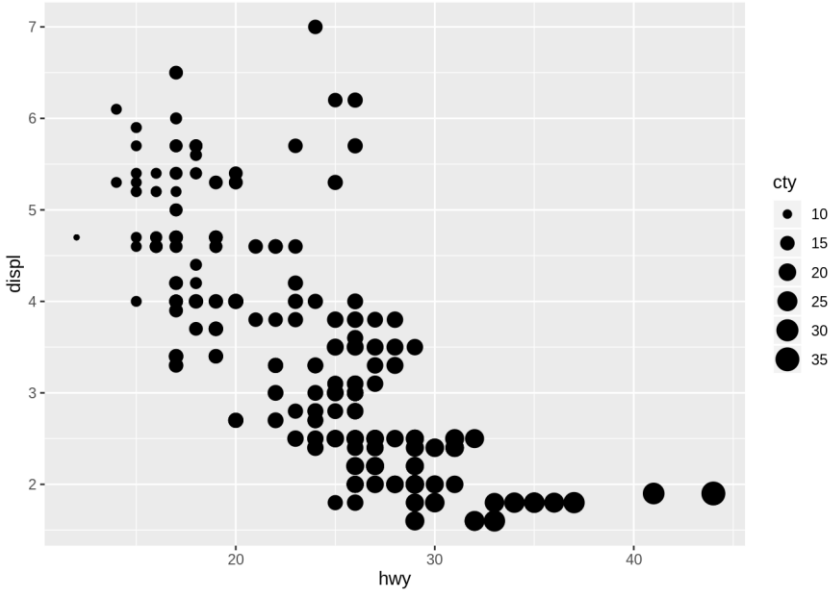


Figure 7-2 - Example of area of dots playing a role in how fast information is perceived. Looking at the size of the dots is much faster than reading the axes. Taken from (Mahoney, 2019).

Color

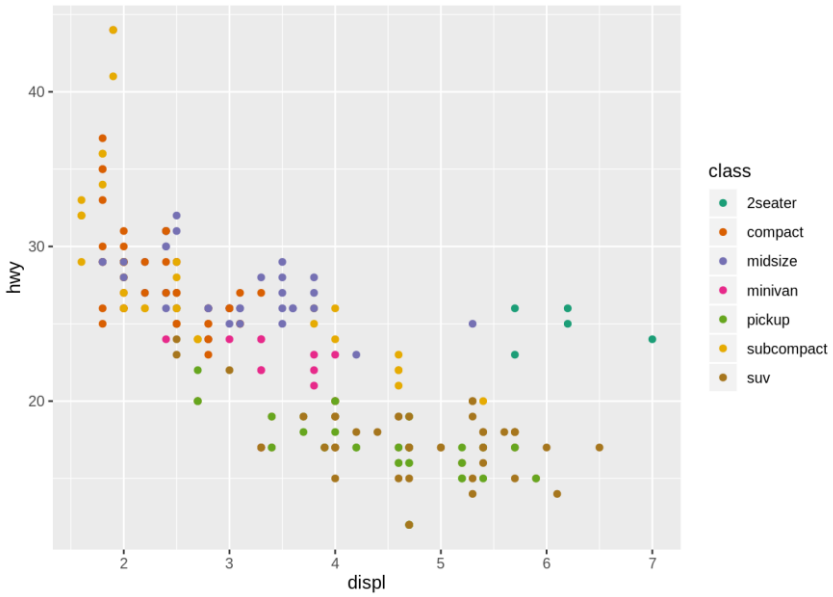


Figure 7-3 - Example of how colour can be used to categorize data without order. The different colours do not insinuate certain relationships or order between the different groups. Taken from (Mahoney, 2019).

Value

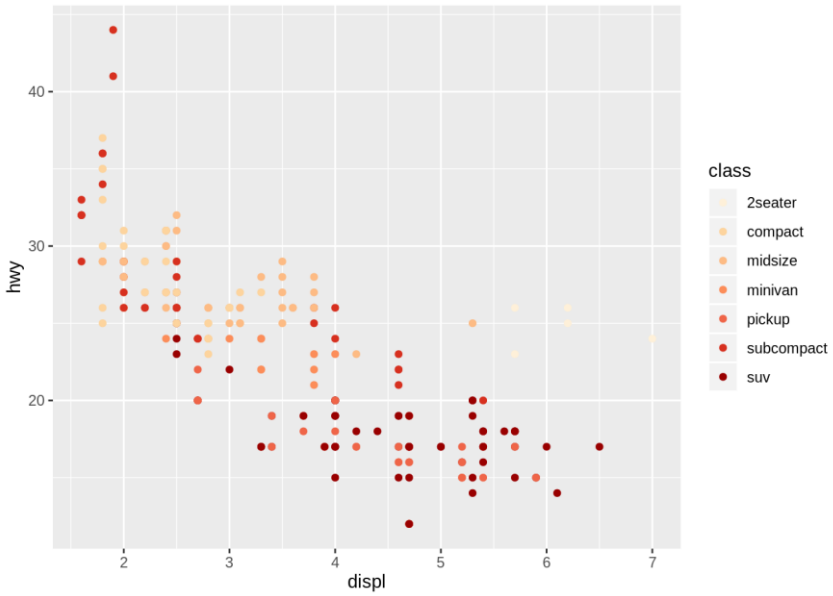


Figure 7-4 - Example of how the value, chroma or luminescence, can create an order in data. The closer the saturation of a dot the more similar the groups are. Value is therefore an ordered characteristic. Taken from (Mahoney, 2019).

Shape

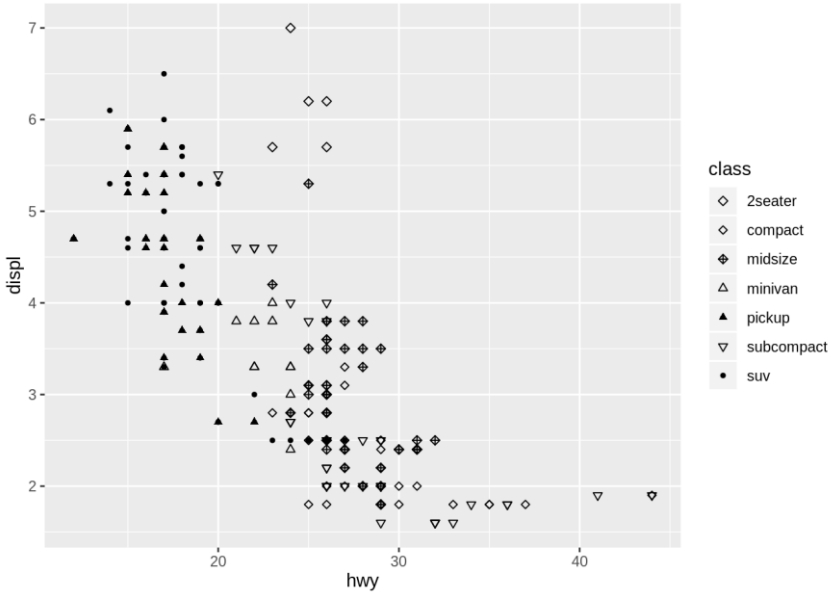


Figure 7-5 - Example of how the non-ordered characteristic shape can be used to group certain data together. Interesting detail is that this representation suggests a stronger relation between the first three groups and singles out SUVs. This way creating an extra layer of information. Taken from (Mahoney, 2019).

Appendix C Framerate and pump-sequence consistency

After seeing the inconsistencies in the duration of a pump sequence in the µPIV measurements, it seemed wise to check the framerate of the camera. According to Baumer's customer service the framerate is only dependent on the number of rows of pixels that are captured and should be very consistent. The framerate taken from the CameraLink software, however, appeared to change strongly and constantly. This lead to the conclusion, that it is necessary to check the consistency of the framerate and the consistency of the pump-sequence. This appendix explains how this consistency was checked.

The setup

The setup shown in Figure 7-6 checks two things:

1. The consistency of the framerate of the camera
2. The consistency of the pumping sequence of the control unit

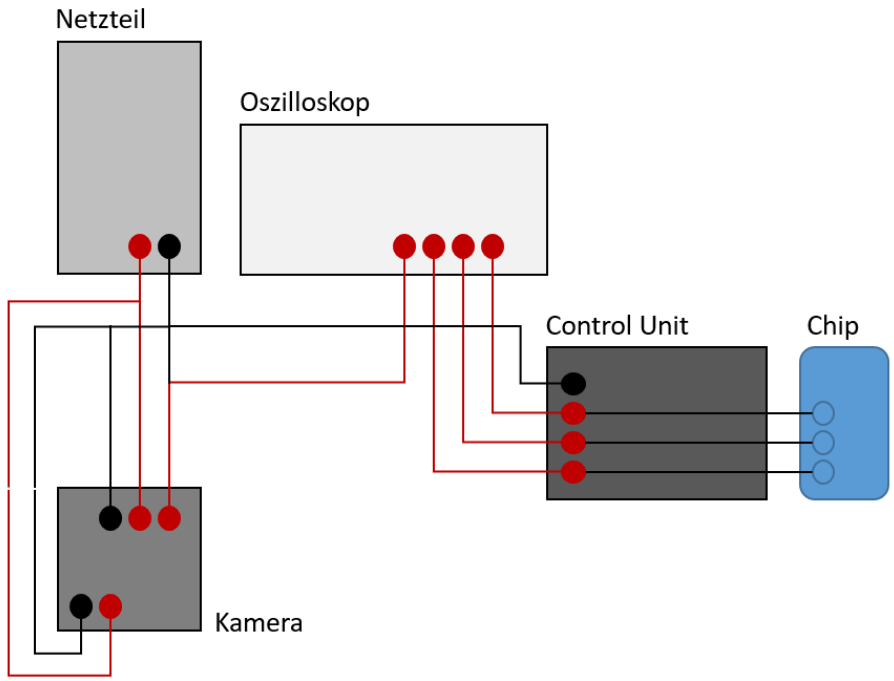


Figure 7-6 - Setup for checking the consistency of the framerate of the camera and the pumping sequence. Red lines carry voltage. Black lines represent ground wires. From the control unit to the chip the lines represent the entire control unit, which goes from electrical signal to air-pressure on the membranes in the chip.

The Netzteil provides a 12V input to the camera (Baumer HXC40), which only goes through to the oscilloscope (Peaktech® 1300 200 MHz / 4 CH, 2 GS/s Touchscreen Oscilloscope), when the camera is exposed and grabs a frame. This way the oscilloscope receives a signal with the exact frequency with which the camera is grabbing frames.

The oscilloscope also connects to the control unit (BCU 62). Here it is connected to the PCB at four spots. The first is the ground wire. The other three are the spots where voltage arises for each of the three pneumatic pumps for the membranes in the chip. This way the oscilloscope receives a signal of the activity of each of the pumps on a microfluidic circuit.

During the µPIV measurements, all images had a size of 216x480 pixels. This means that they had 216 rows of pixels. It is hence desirable to know what the framerate of the camera actually is when

grabbing images of that size. When reading out this value from the oscilloscope, its stability will show the consistency of the framerate.

The control units were set at 0.5 Hz during the µPIV measurements. Hence, the consistency of the frequency at this setting will be checked.

All signals were on the screen of the oscilloscope for about ten minutes, making sure to see a large number of sequences for both the camera and the pumping signals.

Results

Table 13 shows the frequencies stated by the oscilloscope for the signal that came from the camera.

Nº rows of pixels	Framerate [Hz]
2048	180.2
218	1569
216	1585
215	1590
214	1596

Table 13 - Framerate of the Baumer HXC40 with different image sizes. As the framerate is only dependent on the number of rows of pixels in the image, only this variable was changed.

During the entire measurement, the frequency of the frame grabbing stated by the oscilloscope did not change for a given number of rows of pixels in the frame.

The frequency of all signals from the control unit was a constant 0.500 Hz and did again not change during the measured period. This had to be measured manually with the oscilloscope.

Conclusion

The results show that the camera has a highly consistent 1585 Hz framerate when taking frames of 216x480 pixels. This suggests that the µPIV measurements had the same very constant framerate.

In the µPIV measurements and their calculation, Matlab uses the framerate to calculate the velocity of the particles. It finds the difference in position and divides it by the difference in time between the two frames. Hence, all velocities calculated by Matlab so far need to be rescaled to have framerate of 1585 fps.

Discussion

When measuring the frequency of the pump cycle this looked highly consistent. The 0.500 Hz had to be set/measured manually in the oscilloscope though.

In the µPIV measurements some sequences had a number of frames different from 1585. For example, the sequences in WinA had: 1575, 1595, 1578, 1582, 1588 frames. It is expected that these measurements all still had a framerate of 1585, but the pump cycle can differ slightly in frequency. 10 frames less on 1585 frames per second means a deviation of 6.3µs. This could probably not have been noticed by hand in the oscilloscope. The framerate was however measured automatically and stayed the same exact value throughout the measurements.

Note: the number of frames in WinA is actually the number of calculation steps between frames. So there are twice as many frames, leading to this number of calculation points?

Appendix D Settings of Baumer HXC40 Framerate calculator

In order to determine the framerate of the Baumer HXC40 camera Baumer provides a framerate calculator on their website. Since the exact type HXC40 was not available, Baumer customer support suggested the following settings to get to the right calculation.

Note that what came out of this calculator is slightly different (1597 fps) from what the measurements described in Appendix C (1585 fps). As it says all the way at the bottom of the calculator: actual framerate depends on system setup.

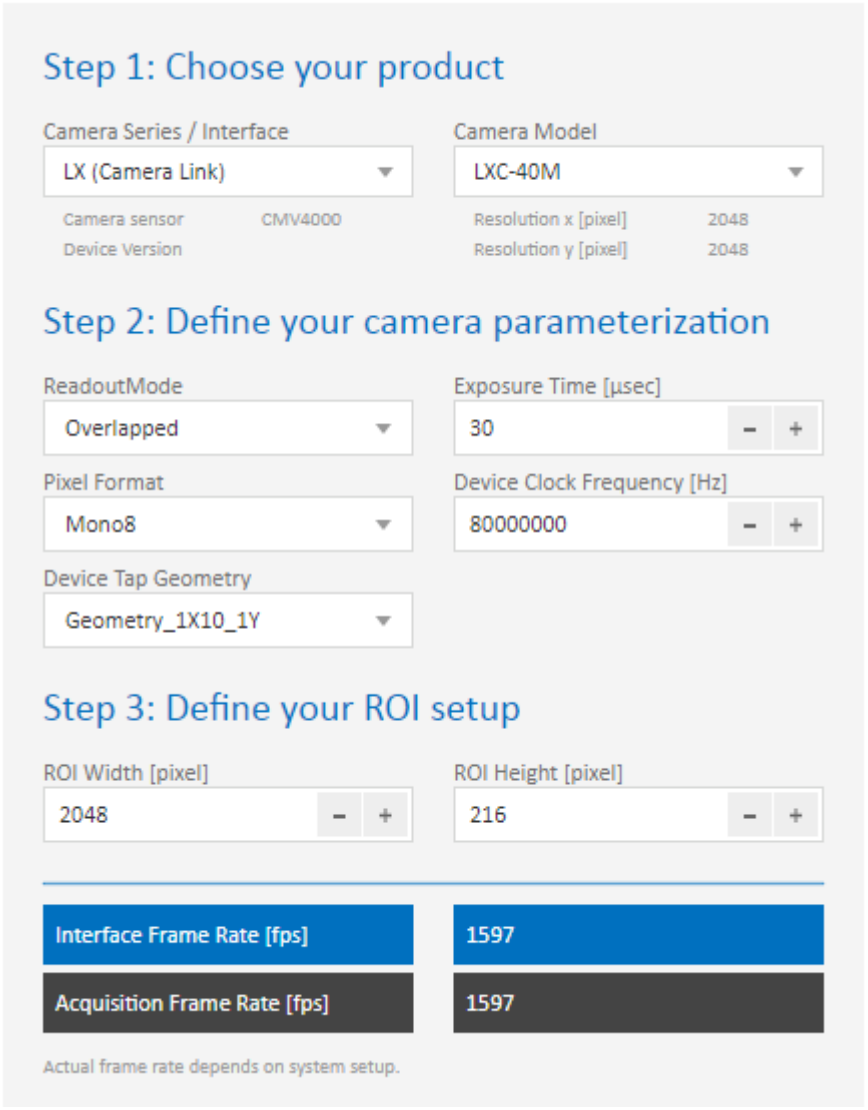


Figure 7-7 - Settings of the Baumer Framerate calculator to get the framerate of the Baumer HXC40. These settings were suggested by Baumer customer support

Appendix E Analysis µPIV results

Before any boundary conditions can be created with the µPIV results, some work needs to be done. First of all, the raw results from PIVlab are shown. Three measurements of 10.000 frames were done for WinA, WinB and WinC each. Secondly, the separate pump cycles need to be isolated from these results. Then some faulty cycles will be excluded. Discussing time alignment is the final step. Then the data is ready to use for a boundary condition.

WinA

Figure 7-8, Figure 7-9 and Figure 7-10 show the profiles of window A based on the first, second and third measurement.

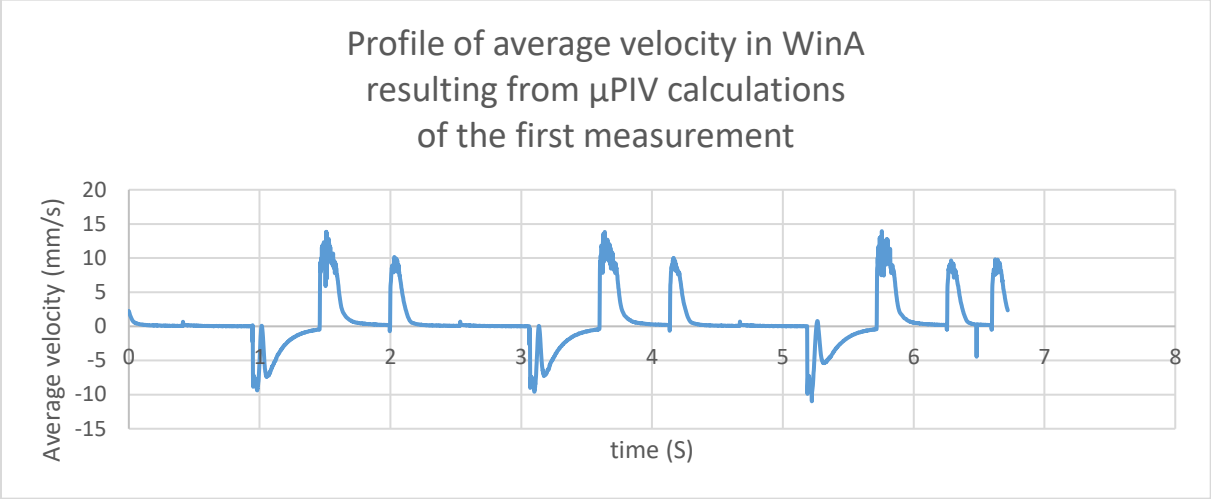


Figure 7-8 - Velocity data directly out of the PIVlab calculations of measurement 1 of WinA.

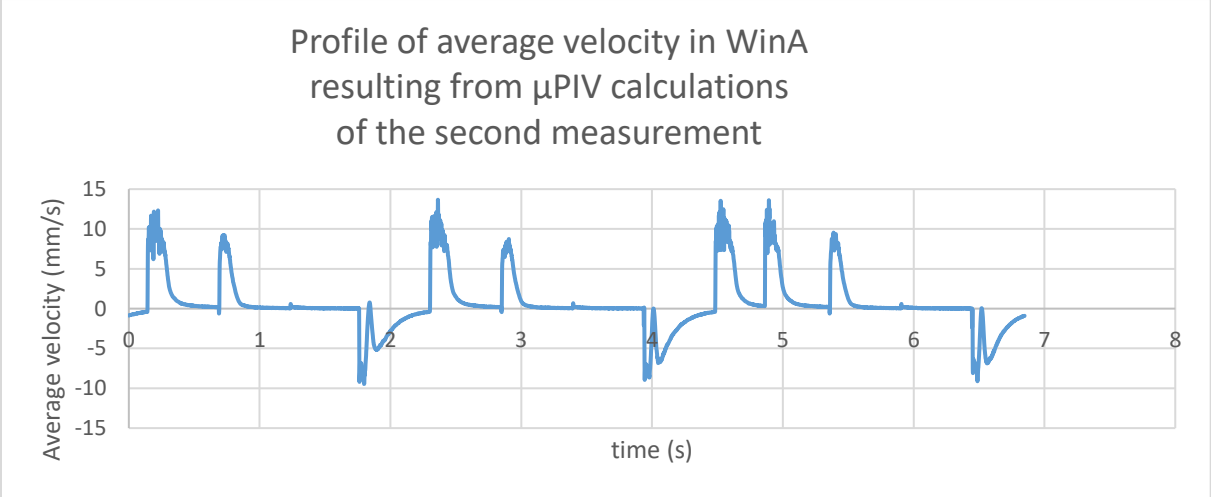


Figure 7-9 - Velocity data directly out of the PIVlab calculations of measurement 2 of WinA.

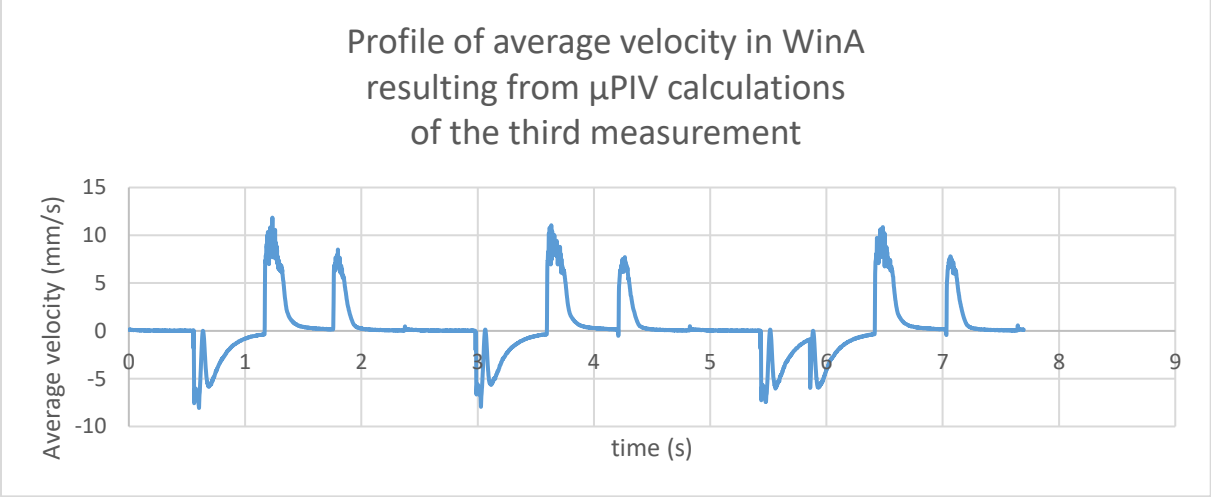


Figure 7-10 - Velocity data directly out of the PIVlab calculations of measurement 3 of WinA.

WinB

Figure 7-11, Figure 7-12 and Figure 7-13 show the average velocities calculated based of the first, second and third measurements in WinB.

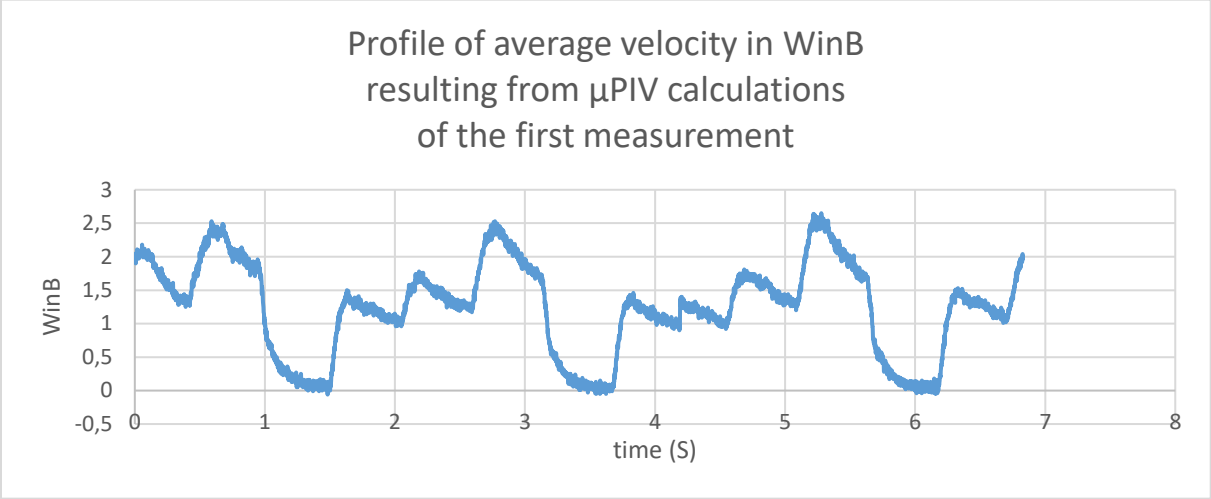


Figure 7-11 - Velocity data directly out of the PIVlab calculations of measurement 1 of WinB.

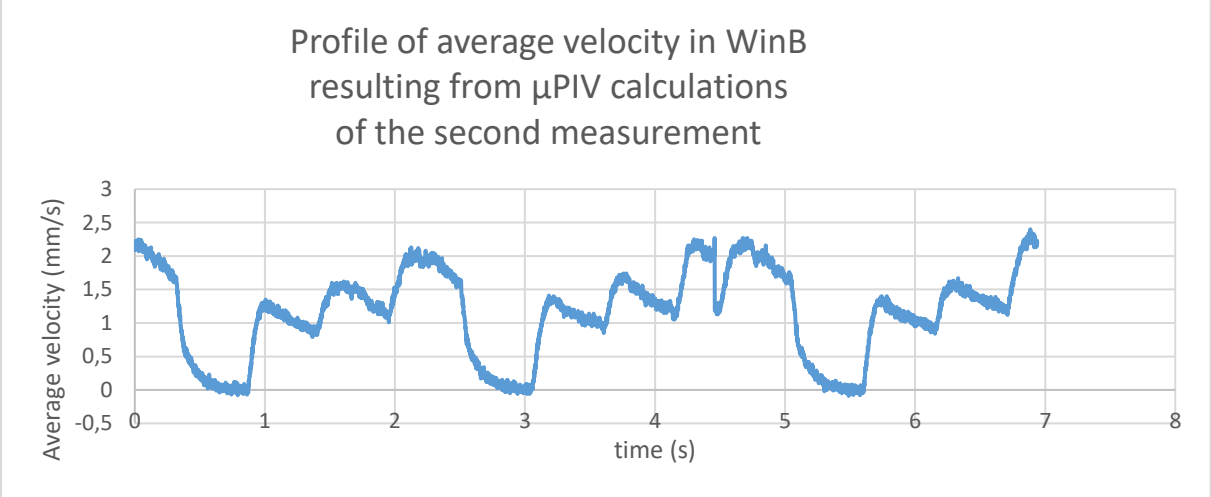


Figure 7-12 - Velocity data directly out of the PIVlab calculations of measurement 2 of WinB.

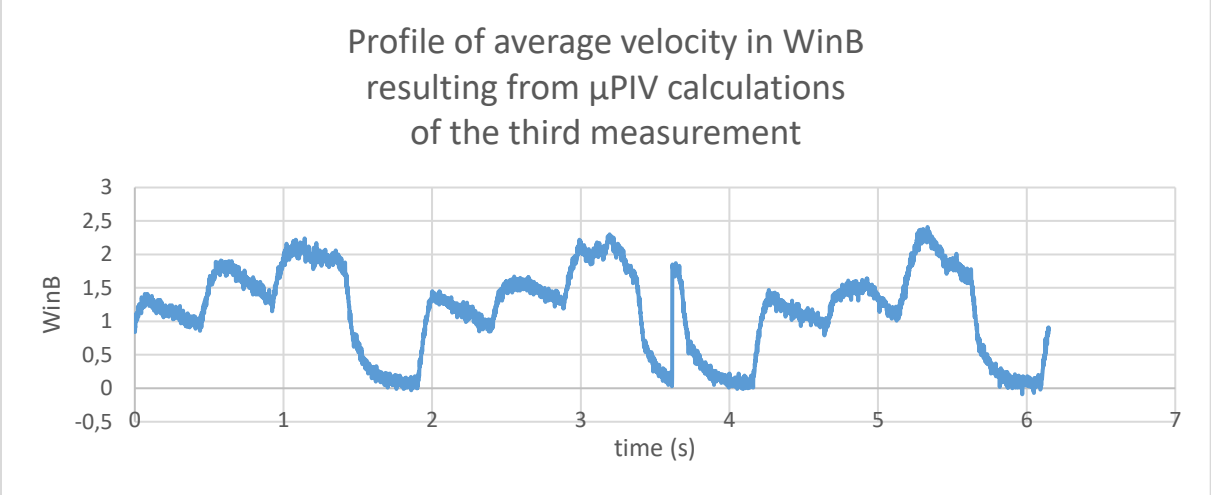


Figure 7-13 - Velocity data directly out of the PIVlab calculations of measurement 3 of WinB.

WinC

Figure 7-14, Figure 7-15 and Figure 7-16 show the average velocities calculated based of the first, second and third measurements in WinC.

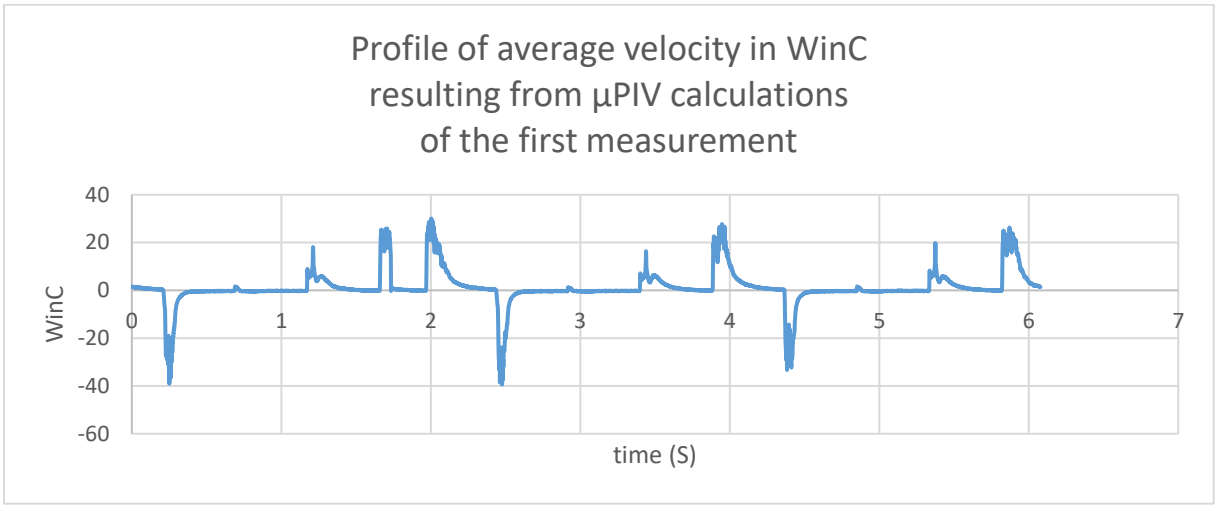


Figure 7-14 - Velocity data directly out of the PIVlab calculations of measurement 1 of WinC.

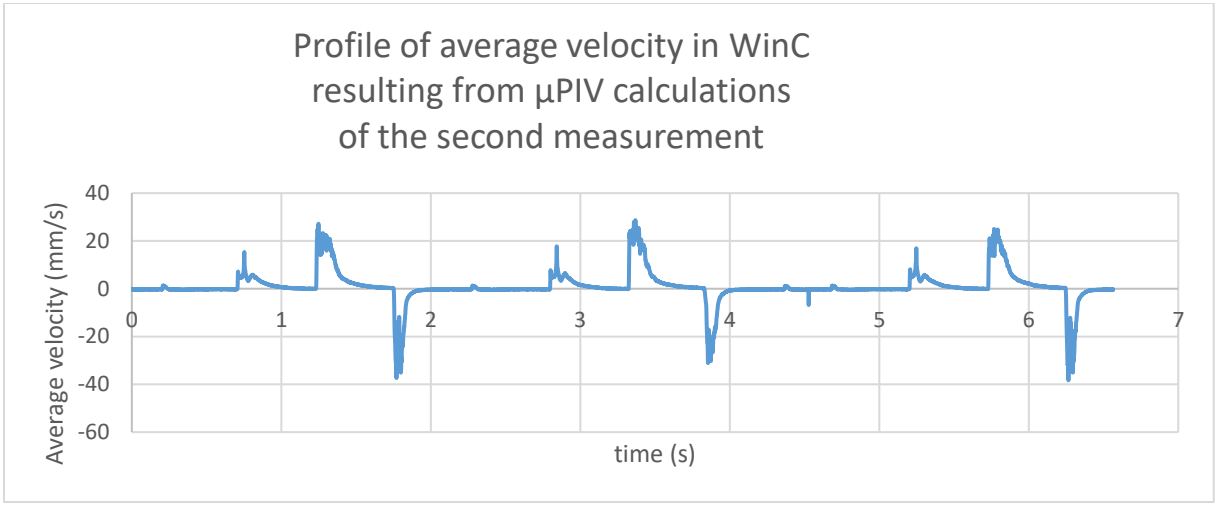


Figure 7-15 - Velocity data directly out of the PIVlab calculations of measurement 2 of WinC.

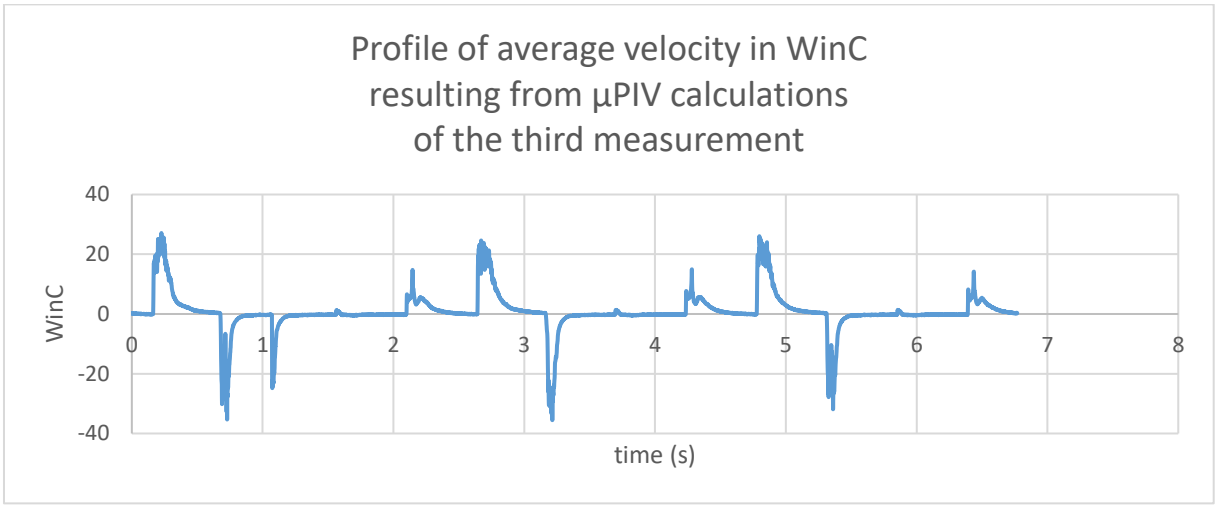


Figure 7-16 - Velocity data directly out of the PIVlab calculations of measurement 3 of WinC.

Determination of cycle shapes

The TCUs are four stroke pumping units. This means there are four stages to each cycle. Some analysis leads to the conclusion that the pump cycles are aligned as in Figure 7-17.

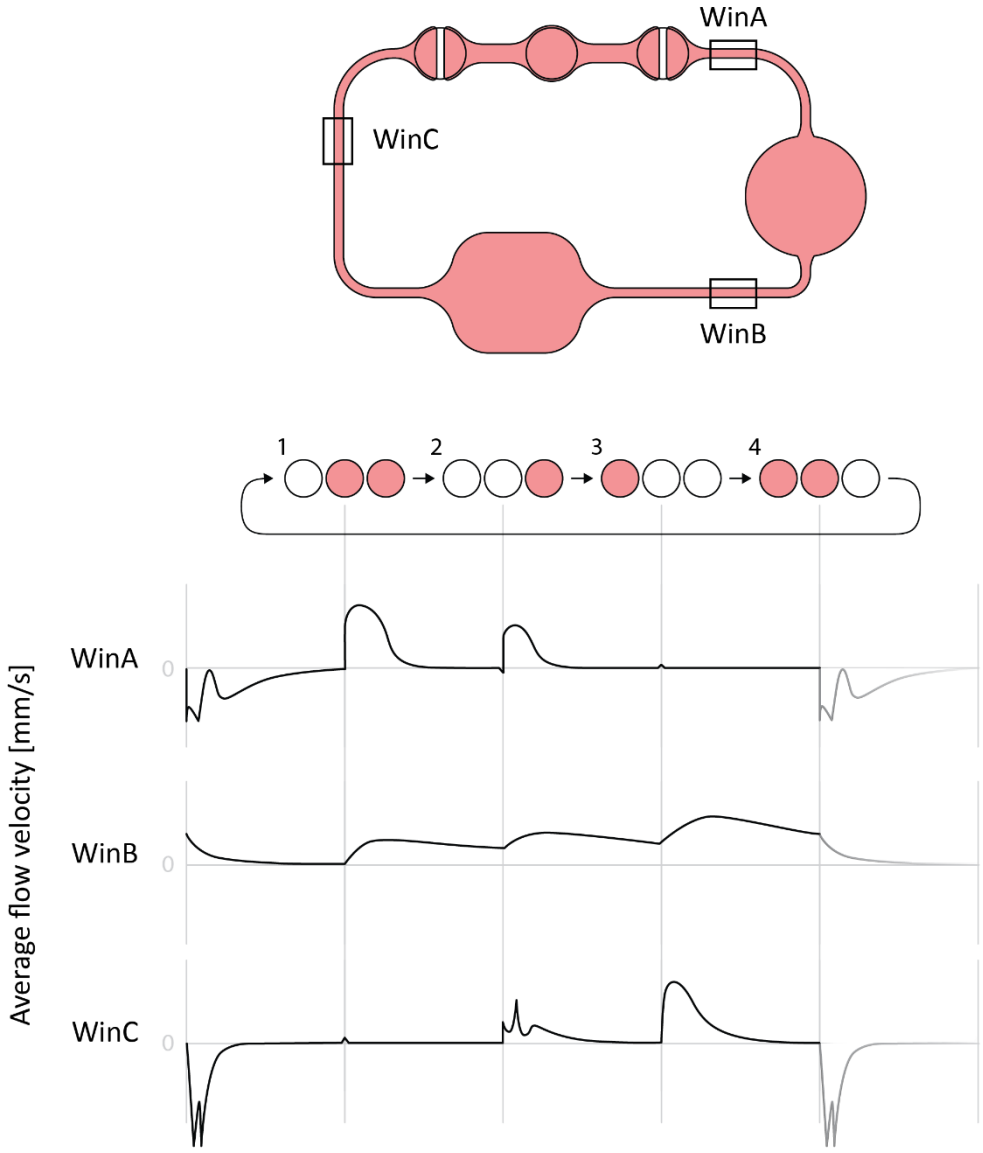


Figure 7-17 - Pump cycle stages in the different windows of a HUMIMIC Chip2 96-well. The velocity profiles are slightly simplified and WinB is comparatively larger than it should be. This is so its shape remains clear.

Selection of intervals

Each measurement had two complete cycles in its data set.

The cycles in WinA are expected to start with a stark downward peak. This can be easily found in the datapoints. The average velocity is about zero and rather suddenly jumps to a negative value. This is how the cycles beginning and end were determined.

The cycles in WinB were selected with the eye, picking the point closest to where the big slide down starts from the diagram and selecting that in the dataset of the results.

The cycles in WinC were selected in the same way as the ones in WinA by finding the first negative datapoint of the sharp peak downward.

Erroneous intervals

According to the developers of the BCU, the control unit gets triggered when something is out of the ordinary. For example, when connecting a new chip to the control unit, it gets triggered. When the control unit gets triggered, it restarts with the cycle. This might cause the extra peaks that sometimes occur.

The extra peaks occur in:

1. The last cycles noticed in all the measurements of WinA
2. Each second cycle of the measurements in WinB
3. The first cycle of the first and third measurement of WinC

The faulty cycles are not considered.

Figure 7-18, Figure 7-19 and Figure 7-20 show the isolated intervals that were good.

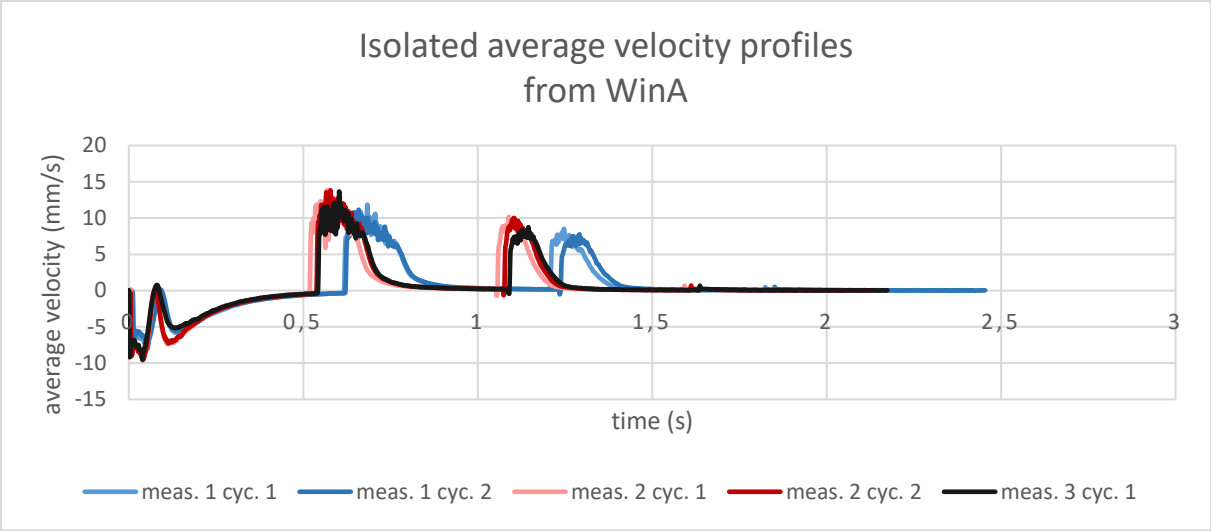


Figure 7-18 - Isolated pump cycles in WinA out of the direct data of PIVlab.

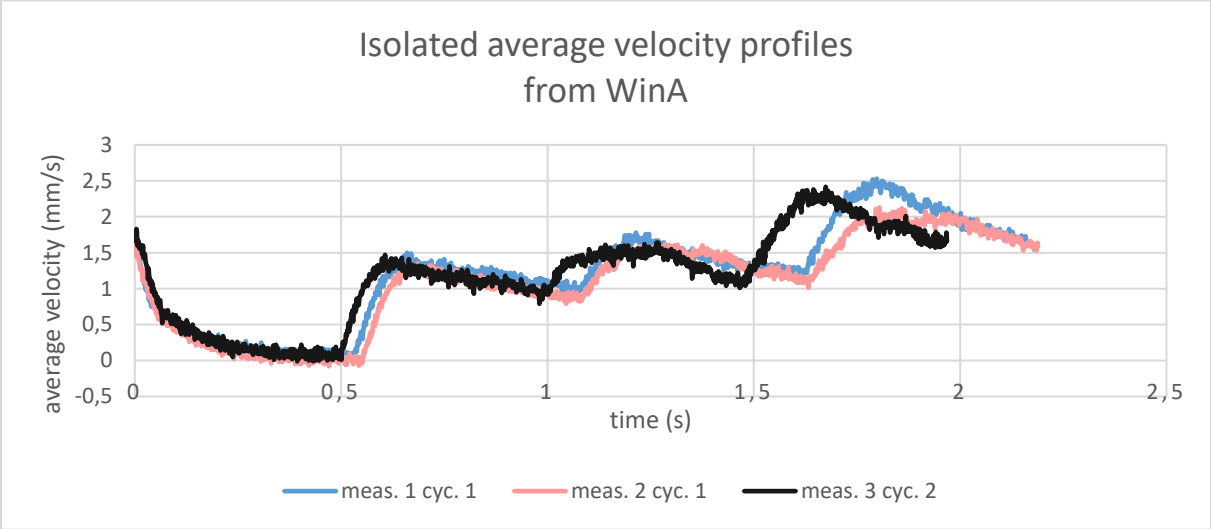


Figure 7-19 - Isolated pump cycles in WinB out of the direct data of PIVlab.

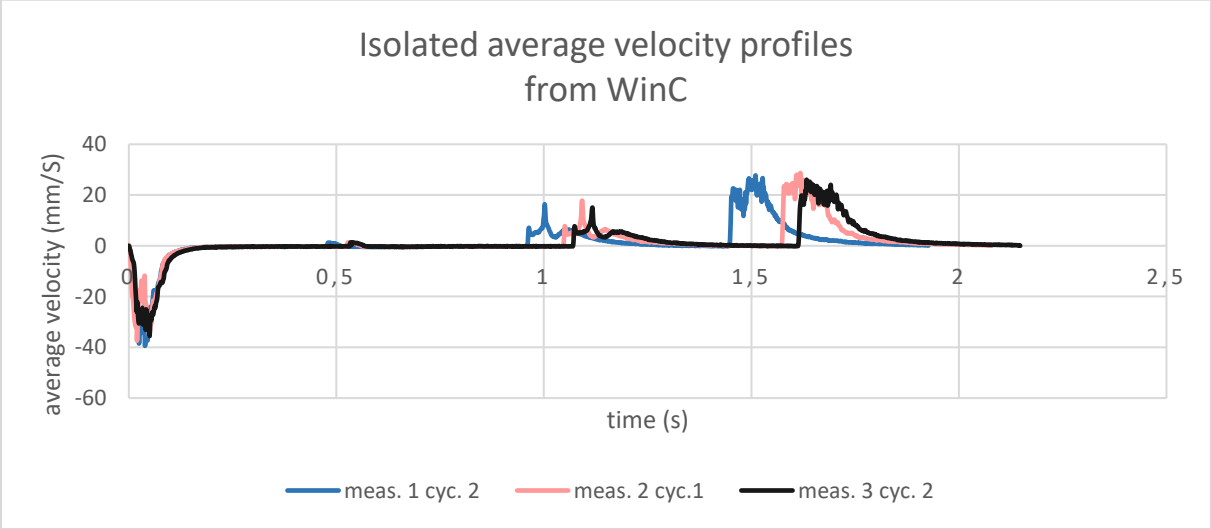


Figure 7-20 - Isolated pump cycles in WinC out of the direct data of PIVlab.

Time alignment

As can be seen in the isolated cycles there appears to be quite a difference in length of the cycles. This came as a surprise and needed a closer look.

First of all, a basic check was done with the BCUs. A timer was taken and using the ticking sound that comes from the BCU when they run, the duration of each cycle was estimated. The deviation from the rhythm was very small. A few hundredths of a second on a cycle time of two seconds.

On top of that a study from a company that has done quality control of the BCU showed that the cycle time is rather consistent and definitely does not vary to the extent witnessed in the isolated intervals.

When looking at the differences in the profiles it appeared proportional to the total length of the entire cycle. This sparked the suspicion that the framerate might be the cause of the problem. The framerate is simply taken from the CameraLink software. It is not constant during the frame-grabbing however. It could be that the value that is taken from CameraLink at the end of the frame-grabbing might be different from the actual framerate.

Figure 7-21, Figure 7-22 and Figure 7-23 show the results adapted to the 1585 fps that the frame-grabber actually used.

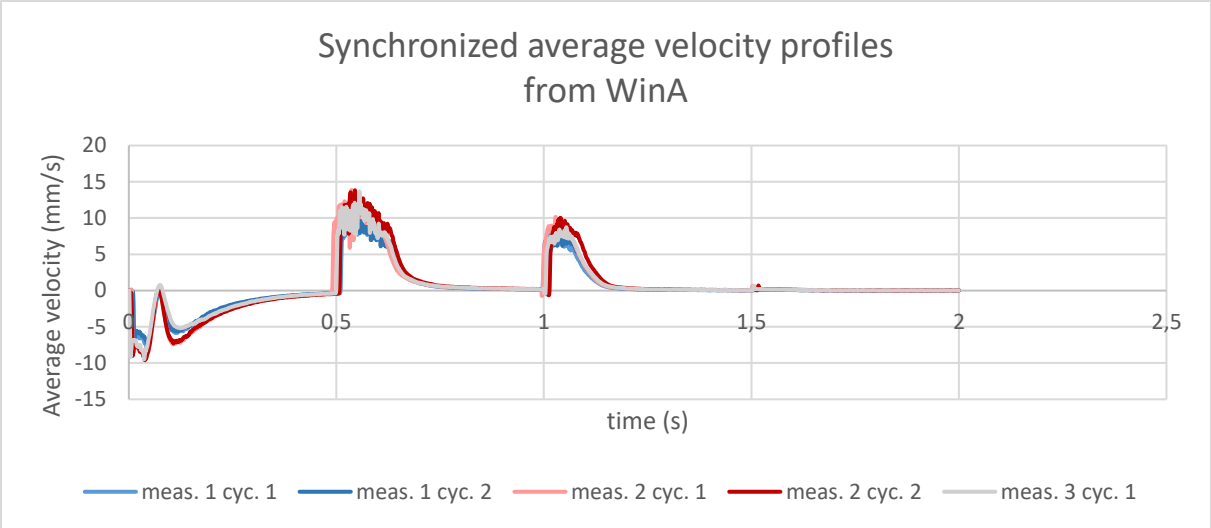


Figure 7-21 - Synchronized pump cycles in WinA scaled to the correct framerate of 1585 fps.

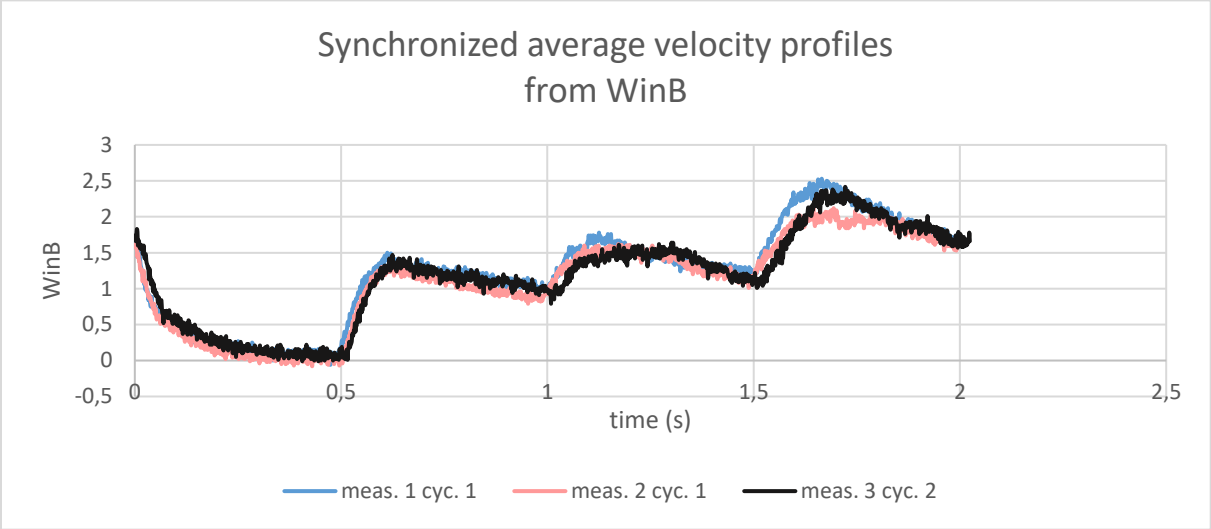


Figure 7-22 - Synchronized pump cycles in WinB scaled to the correct framerate of 1585 fps.

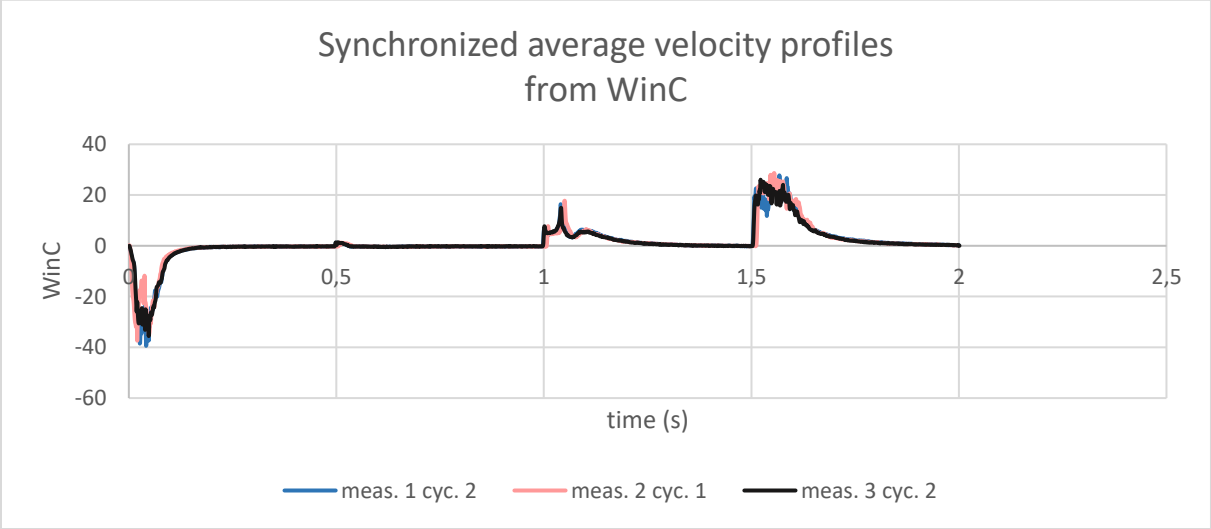


Figure 7-23 - Synchronized pump cycles in WinC scaled to the correct framerate of 1585 fps.

Appendix F Theoretical flow profile in Chip2 96-Well

It would be convenient to know an analytical solution of the flow in the chip. That would enable a good estimate of the error in the simulation. To this end this paragraph determines the analytical flow profile in a rectangular duct. This duct is representative of the channels in the chip.

Assume this duct looks like Figure 7-24. Variables of the channel are:

$$a = 0.5\ mm$$
$$b = 0.1\ mm$$

The x- and y-coordinate are non-dimensionalized as follows (Spiga & Morino, 1994, p. 470):

$\bar{x} = \frac{\xi}{a}$, with $0 \leq \bar{x} \leq 1$

$\bar{y} = \frac{\eta}{a}$, with $0 \leq \bar{y} \leq \beta$

These formulas use the following ratio (Spiga & Morino, 1994, p. 470):

$$\beta = \frac{b}{a}$$

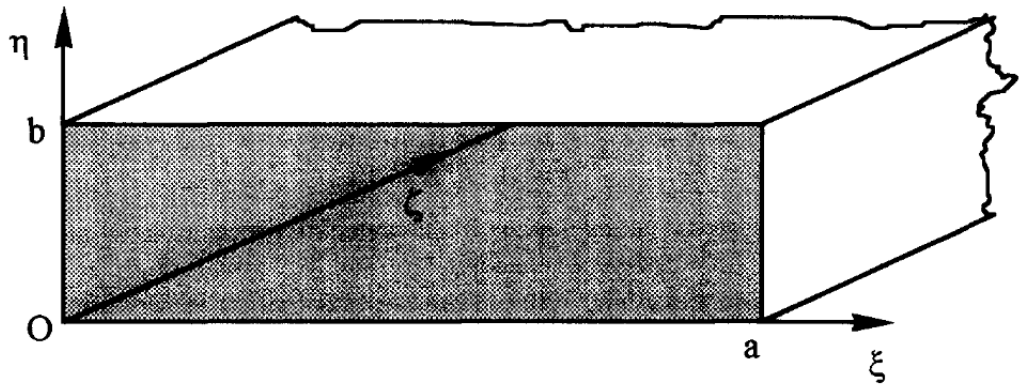


Figure 7-24 - model of the rectangular duct. Image from (Spiga & Morino, 1994, *p. 470*).

The flow in a rectangular duct is axisymmetric around both middle planes of the channel. The flow profile can be derived as a Fourier series (Spiga & Morino, 1994, p. 471):

$$\bar{v}(\bar{x},\bar{y}) = \frac{16\beta^2}{\pi^4} \sum_{n\ odd}^{\infty} \sum_{m\ odd}^{\infty} \frac{\sin\left(n\pi\frac{\xi}{a}\right)\sin\left(m\pi\frac{\eta}{b}\right)}{nm(\beta^2 n^2 + m^2)} \qquad 7\text{-}1$$

This describes the dimensionless velocity profile in a rectangular duct. It can be plotted using MATLAB. An example code was taken from (Rieschel & Brandt, 2016, p. 26).

Based on the description of the flow by (Spiga & Morino, 1994, p. 472), the images in (Hoagland, 1960, p. 137-139), (Demyanko & Nechepurenko, 2013, p.143), and the discussion of the input arguments x and y in (The Mathworks, 2021), it was concluded that there was that the indices county and countx on line 31 of the example code in (Rieschel & Brandt, 2016, p. 26) needed to switch places. This way they properly represent the flow in a rectangular duct.

Running the corrected code leads to the dimensionless velocity profile in a rectangular duct of size 0.5 x 0.1 mm, shown in Figure 7-25.

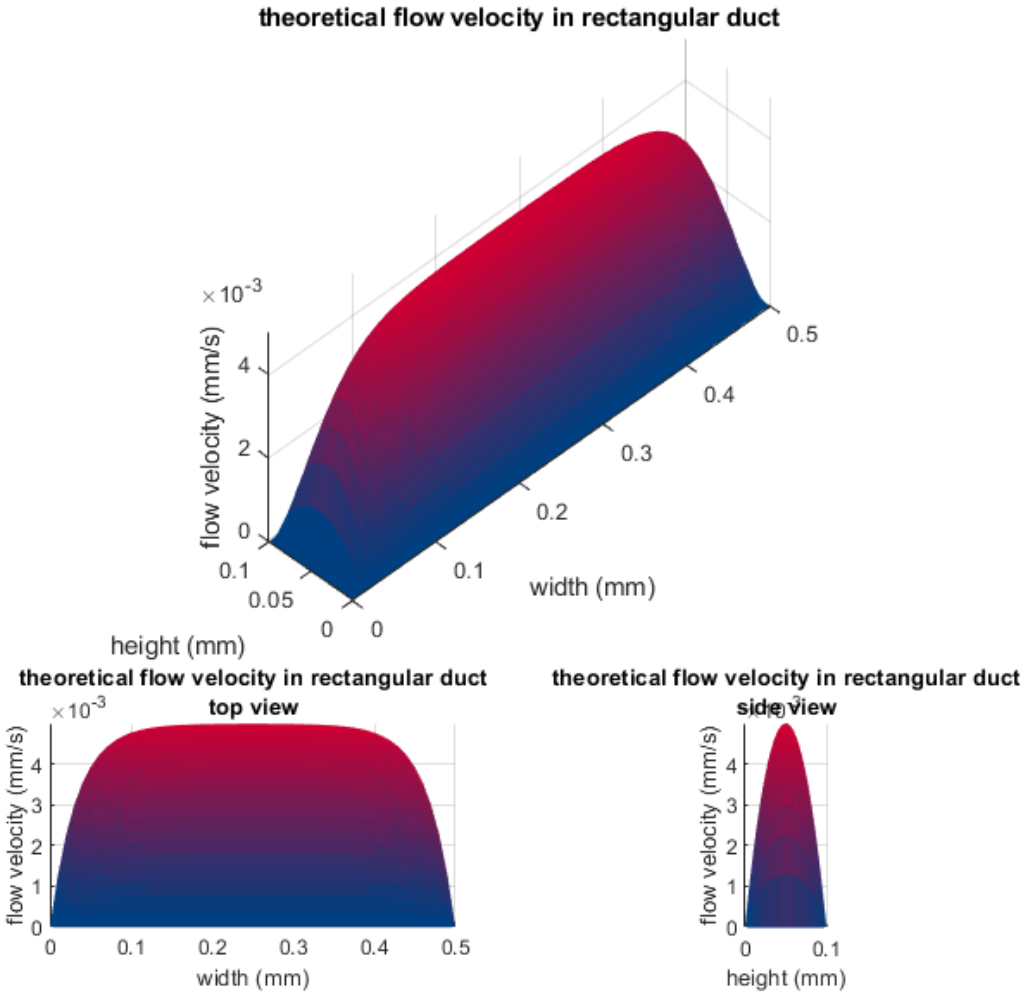


Figure 7-25 - Theoretical dimensionless velocity profile of a fully developed flow in a channel of size 0.5x0.1mm.

Determine volume flow rate

The calculation thus far describes a dimensionless velocity. Normally a factor is used to convert this back to a dimensional velocity. This factor looks as follows (Spiga & Morino, 1994, p. 470):

$$factor = \frac{a^2}{\mu}\left(-\frac{\partial p}{\partial \zeta} + \rho g_\zeta\right) \qquad 7\text{-}2$$

In 7-2 μ is the dynamic viscosity of the fluid, ζ is the third dimension in direction of the flow. p the pressure, ρ the density and g_ζ describes any body forces in ζ-direction. There is no estimate for the pressure gradient in 7-2.

Instead the factor needed to multiply the dimensionless flow profile with was found using the volume flow rate.

The simulation used a constant inlet velocity of 4 mm/s. Using the size of the lumen of the channel, this means that at this inlet velocity the volume flow rate through the channel is 0.2 mm^3/s. The velocity profile in Figure 7-25 has a certain volume flow rate as well. It turns out, that multiplying the

dimensionless velocity profile by a factor of 1401.5 leads to a volume flow rate of 0.1959 mm^3/s. Hence, the dimensionless velocity profile multiplied by 1401.5 represent the velocity profile that is present in the channel of this chip with a constant inlet velocity of 4 mm/s. Figure 7-26 shows the resulting velocity profile. The maximum flow speed in the centre of the channel is 7.0018 mm/s.

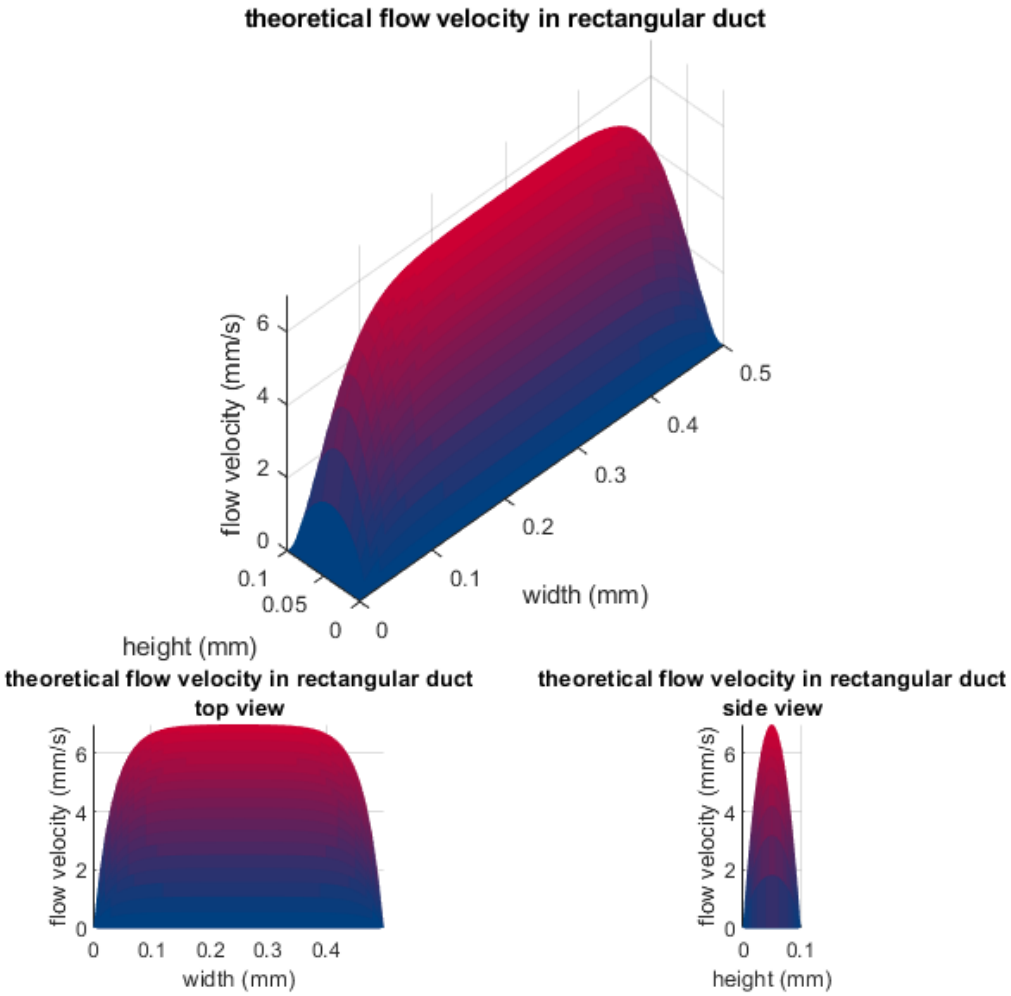


Figure 7-26 - Theoretical fully developed velocity profile in a Chip2 96-Well channel with constant inlet velocity of 4 mm/s

Determining entrance length

Thus far a fully developed flow was considered. It takes some time for the flow to develop. The distance that the flow travels during that time is called the entrance length. To determine the entrance length for the Chip2 96-Well used in the simulations and experiment, the Reynolds number is required. The Reynolds number in a rectangular duct is defined as (Engineering Toolbox, 2003c):

$$Re = \frac{\rho u d_h}{\mu} \qquad 7\text{-}3$$

Where the maximum velocity u with the pulsating entrance velocity is about 15 mm/s. ρ is taken from water at 18 $°C$ and is 998e-9 kg/mm^3 (Engineering Toolbox, 2003d). μ is the dynamic viscosity. Also taken from water at 18 °C it is 1.05e-6 kg/mms (Engineering Toolbox, 2004). Presumably, we need to use the hydraulic diameter of the duct d_h (Engineering Toolbox, 2003b):

$$h = 0.1\ mm$$

$$d = 0.5\,mm$$

$$d_h = \frac{4\,hd}{2(h+d)} = 0.16\,mm$$

Filling all variables into 7-3 yields a Reynolds number of:

$$Re = \frac{998 \cdot 10^{-9} \cdot 15 \cdot 0.16}{1.05 \cdot 10^{-6}}$$

$$Re = 2.28$$

There are two ways to determine the entrance length now. Firstly, there is a formula specifically for microfluidic systems (Spiegel, 2019). This suggests that the entrance length for the chip will be:

$$L_{FD} = \left(\frac{0.6}{1 + 0.035 \cdot Re} + 0.056 \cdot Re\right) d_h$$

$$L_{FD} = \left(\frac{0.6}{1 + 0.035 \cdot 2.28} + 0.056 \cdot 2.28\right) 0.16$$

$$L_{FD} = 0.11\,mm$$

Another more common method is suggested by the Engineering Toolbox (Engineering Toolbox, 2003a) (University of Sydney, 2005). This suggests that the hydrodynamic entrance length for a laminar flow in the chip is:

$$L_{FD} = 0.06 \cdot Re \cdot d_h = 0.06 \cdot 2.28 \cdot 0.16 = 0.02\,mm$$

The suggested entrance lengths differ. However, it should be safe to assume that 1 mm from the entrance should be sufficient to see a fully developed flow according to both methods.

Appendix G TissUse philosophy interviews

Of particular interest for analysis

Software development employee
Phone
14-1-2021 17:00

Short sidenote: Ich bin der Entwickler, nicht der Benutzer

1. **Why did you choose to go work at TissUse?**

Es hat ein innovativer Ansatz der interdisziplinär ist und Biologie mit Technologie verbindet. Ich muss die Biologie verstehen bei der Entwicklung des Roboters. Bio ist für mich komplett neu und dass hat mir gereizt. Alle Prozesse die im Körper losgehen muss ich verstehen.

AR Brille für Tech Training und Anleitungen wäre mega-cool.

2. **What do you like/dislike about the work and the company?**

Immer wieder neues lernen auf anwenderorientierte Weise. – Ich lerne was ich wissen muss um etwas anwenden zu können. Bisher hauptsächlich für den Roboter, jetzt auch User Interface.

Am Ende letzten Jahres troffen wir uns mehrmals mit Biologen und Maschinenbauern. Welche Features wollen wir und wie weit sind wir mit diesen Features. Das machen wir mit Biologen (was wollen wir und brauchen wir etc.). Bisher fast immer Biologen von TissUse. Auch schon AZ und andere. In diesen Gesprächen bekommt man sehr praktische Feedback. Es gibt aber keine Schleife bei AZ weil die einfach bei uns waren. Also wir zeigen die unsere Produkte, dann sind die interessiert, aber gehen dann wieder zurück um zu überlegen. Daher gibt es also nicht so viel Feedback.

Dokumentation ist schlechtgemacht, weil wir zu beschäftigt sind. Das könnt eine Gefahr für „being reliable“ werden vielleicht in die Zukunft.

3. **What is your favourite thing to do at work?**

Probleme lösen. Z.B. Gegenteil davon ist Dokumentation. Dokumentation hat erst später Effekt, ein gelöstes Problem mach dir sofort froh. Interdisziplinäre Probleme sind echt cool.

4. **In the products that you develop, how do you find requirements, which the products should meet?**

Wir bilden Prozesse nach, die es schon gibt bei den Biologen. Wir gucken an wie das manuelle Prozess aussieht und das ahmen wir dann nach. Kontrolle mit den Biologen: ist das alles in Ordnung? Mediumwechsel ist am wichtigsten, danach Pipettieren, dann Analyse, Auswertung. Diese Reihenfolge habe ich selbst eingeschätzt und dann bestätigen lassen, ging eigentlich zusammen mit den Biologen. Bestätigung ist wichtig: Bevor etwas gemacht wird, müssen sowohl ich als den Biologen sagen, dass es in Ordnung ist. Ich muss erstmal verstehen wie ich rechne bevor ich mit der Mathematik anfange.

5. **Who are the users of your products?**

Zweck: Pharma- Kosmetikforschung. Da gibt es verschiedene Ebene:

- Pharmafirmen (die Chefs)
- die Biologen, Biotechnologen und Laborassistenten

Erstens interessant bei den Chefs der Pharmafirmen, dann schicken die ein Biologe und die sagen dann tatsächlich ob es interessant ist.

Würdest du mal ein anderes Produkt entwickeln für Chefs und Biologen? Nein, aber Chef sage ich: beste Ergebnisse in Pharmaforschung. Biologe sage ich: weniger Zeit im Labor. Bewerbung ist anders, Produkt ist das gleiche.

6. **Do you incorporate users in the product development process?**

Ja

   a. **If so how?**

Sprint Meetings (alle Stakeholders, auch interne Kunden) Neue Tests werden von den Biologen gemacht (meistens intern, weil es noch nicht so viele Externen gibt)

   b. **And why?**

Sprint Meetings: Ich muss verstehen wie der Kunde denkt um es ihm so bequem wie möglich zu machen.
Tests: Der Biologe versteht die Prozesse am besten, deswegen sollte es auch der Biologe sein, der/die einschätzt ob die UX in Ordnung ist und die Anforderungen erfüllt.

Ergänzung: wir machen gerne etwas was gegen Tierversuche, also Nachhaltigkeit ist wichtig.

Business developer 1
Phone
14-1-2021 18:30

1. **In short, how does a usual partnership get developed?**

E-Mail-Kontakt (kommen nach uns), Konferenz, hin und her über Email, Präsentationen zeigen, per Webex ist bequemer.

Feasibility study. Halbes jahr/Jahr.

1. Wir sind CRO. (Bayer)
2. Einfach Produkte liefern.

was ist Organ-on-a-Chip ist noch nicht immer deutlich. Wie wir es machen müssen wir es erklären. Betriebe mit Chefs überlegen. Forschungsinstitute Anträge Drittmittelprojekte.

2. **As what kind of company do you portray TissUse?**

Besondere an uns: zirkulierendes System

Wir machen auch ein Training, wenn man es kauft. Wir nehmen die Zeit für die Kunden. Was kann man mit unserem System, erklären wir sie auch. Fragen was wäre für die Kunde gewünscht. Hochwertig sein.

- Hochinnovativ: Leute sagten, dass ich verrückt war, dass ich Organs-on-a-Chip machen würde.
- Zuverlässig: bei uns ja.
- Firmenklima: ist auch besonderes.

Wörter können leer sein, hier nicht.

3. **What would you say are the core values of TissUse?**

zwei Sachen die sich miteinander streiten und kombinieren:

eins: offenes und freundliches Klima

zwei: es wird viel Leistung verlangt

Nur mit einem guten Team kannst du richtig starke Leistung liefern. was für eine Person wäre TissUse: Starke Persönlichkeit, die viel Abliefern kann. Im Gegensatz zu Emulate, die haben 40 mal so viel Geld wie wir, aber die haben ein viel größerer Durchfluss. Bei uns bleibt man. Starke freundliche Person der viel leisten kann.

4. **There are two slogans: redefining research and emulating human biology. How do these two relate to each other.**

Ask Reyk.

5. **In the company's presentation the title changed from: "Human on chip" to "Human on chip solutions"**

wir wollten mehr nach Microphysiological System statt human on a Chip. Wir wollen nicht, dass Leute denken, dass es Menschen auf einem Chip gibt. (Researcher 5 mal fragen?)

6. **Who are our customers?**

Industrie und Akademie

Industrie: Pharma (Roche, AZ, Bayer), Cosmetic (Cosmetics Europe, Beiersdorf), Biotech (food/animal food additives)

Akademie: Forschungsinstitute (Charité bonemarrow, TUBerlin, VUMC), Flagship project of Horizon2020 Eutoxrisk (Business developer 3) Darm, Niere, Neuro und Leber. PBPK Modellierung.

7. **What would be their biggest problems?**

Wir haben ein dynamisches System wo man mehrere Organe kombinieren kann. Haut und Leber mit Cosmetics Europe. Man kann auch ohne, aber es würde die Biologen ganz stark helfen, wenn wir wissen was passiert. Dynamik ist Kern von Vorteile HUMIMIC Chips.

8. **How do they partake in the product development of TissUse?**

sie äußern Wünschen. Meistens über Telefon oder über dem direkten Kontakt. Mit bestehend Kunden haben wir engen Kontakt.

Heutzutage können wir mehr und mehr verkaufen. Wir waren vor allem Forscher. Wir entwickeln die Protokolle und wir machten die tatsächliche Forschung. Wenn man jetzt Darm und Leber kombinieren will, dann können wir es bei ihnen installieren. Techtransfer, Installierung, heißt, dass die es benutzen dürfen, aber nicht weiterverkaufen. Es ist auf Lizenzbasis.

Engineer 1
Phone
15-1-2021 11:00

1. **How does a common development process start?**

Drittmittel - Bundesamt bedenkt etwas und fragt Wettbewerbe dabei helfen kann. Von verschiedene Anfragen von Kunden bekommen wir bestimmte Ideen. Abhängig von was Kunden wollen bekommen wir oft Ideen. Es ist wichtig dabei unsere eigenen Wünsche auch mitzunehmen. Was ist möglich was wollen wir was wollen die Kunden und wie könne wir es so machen, dass es für allen passt.

Wenn es einen Kunden zu uns kommt, sagen die meistens wir wollen das und das Machen. Wenn es unendlich viel Geld gibt, können wir natürlich ganz viel. Wenn es nicht so viel Geld gibt denken wir ob wir es kombinieren konnten mit einem anderen Projekt was wir schon hatten. Manchmal Machen wir auch Projekten für wenig gewinn.

Das hatten wir viel dieses Jahr. Wegen dass den Hype von Organs-on-a-Chip schon gewesen ist, ist es jetzt ein bisschen schwieriger.

Dann gibt es noch grundlegende Sachen wovon wir finden, dass wir es sowieso haben müssen. So wie Membrane. HOC ist zu auch einen Startpunkt für weitere Entwicklung von andere Chips gewesen. Wenn wir Problemen sehen können wir auch Sachen neu anschauen.

Es gibt auch Projekten die gar nicht von Kunden abhängig sind. zu diese HOC produktionstechnology machte es viel billiger, alles spritzgiesfertig Machen wäre auch so ein Project. Wenn ich nur Verbesserungen Machen wollen wurde. Kunden Hilfen auch dabei eine Richtung zu geben. Wenn die voll enthusiastisch sind wissen wir, dass wir dort weiterarbeiten können und die sind dann auch bereit Projekte dafür auszuschreiben.

2. **What role does the end-user play in this process?**

Anforderung, Feedback, Es gibt monatliche Meetings, Forschungsergebnisse, habt ihr Fragen oder hinweisen? Es gibt sehr viel Interaktion in diese Monatliche Meetings.

Manufacturing employee
Phone
19-1-2021 16:00

1. **Why do you work at TissUse?**

Direct nach Studium angefangen als Studentin. War ein bisschen gluck. Thema war interessant bio plus tech.

2. **What do you like and dislike about the work?**

Bio und tech. lerne viel

Mag nicht: Routine Arbeit in Produktion. Momentan zu viel Routine wegen zu wenig Personal. Möchte gerne mehr koordinieren. Damit auch kreativer und Mit Entwicklung.

3. **What do you like and dislike about the company?**

Ziel der Firme, farma verbessern, Tierversuche ersetzen. nicht nur Inhalt, aber auch wegen der Leute. Wäre cool das wir mehr Zeit hätten für Neuentwicklung. Mehr Geld und Personal.

4. **What is your favourite thing to do at work?**

Neue Produkte zu entwickeln oder wenn wir etwas verbessern wollen.

Wenn kreative arbeit de reinkommt wird es echt cool. Plan überlegen versuchen und Ergebnisse beim Chip2 Generation.

Master student 1
Whatsapp
18-1-2021
Master student biochemist

1. **Why do you work at TissUse?**

I love the idea! It's this outside of a box thinking which I like, and the good cause. Another motivation is of course to be a part of the development and to improve the technology to show that it has potential and can be used instead of animal testing

2. **What do you like about the company?**

I like that it is like a „family ". Everyone is helping you and is interested in your projects. But to be honest: I haven't worked in another company so far, so I cannot compare it that well

3. **What do you like about the work?**

my project

Bachelor student
Whatsapp
18-1-2021
Bachelor student mechanical engineering

1. **Why do you work at TissUse?**

Good choice of different projects for my bachelor thesis, in general very interesting projects and good flexibility for the student to modify his project goals if wants.

2. **What do you like about the company?**

The atmosphere and the people. The laid-back way that everybody is allowed to work how it fits them the best.

3. **What do you like about the work?**

It is really good for a young student to participate in completely different aspects of the engineering process (e.g. construction, montage, testing, programming, etc.).

Also, since the engineering team is very small in comparison, you have to do multiple different kinds of tasks all the time, which provides lots of variety at work.

Master student 2
Whatsapp
20-1-2021

1. **Why do you work at TissUse?**

Before coming here, I didn't know the company, but after talking with my professor and after some research in their website I was really enthusiastic to come here for my internship and master thesis. It was a new experience, first time abroad, and the thought to do it in a company like this, that is working on the future of science, full of young minds that work together to find the best solution made me really interested in their world.

2. **What do you like about the company?**

About the company I like exactly this, the environment, the air that you can feel around the rooms, the people that try their best to make you feel home, the that everyone is working on its own project, but is always ready to help someone else. And I also like the fact that the students have a lot of responsibility, and they trust them in their work.

3. **What do you like about the work?**

About my work I like the fact that is something new, not usual, that one day will be useful for something bigger than what I can imagine, and that it's really into my topic, really into what I studied.

Master student 3
Mattermost
18-1-2021

1. **Why do you work at TissUse?**

Ich arbeite bei TissUse, weil mir der Themenbereich sehr gut gefällt und wichtig ist. Für mich persönlich vor allem eine Alternative zu Tierversuchen zu finden.

2. **What (de)motivates you during work?**

Was mich motiviert ist das junge und aufgeschlossene Team. Man versteht sich hier wirklich mit jedem und kann jeden alles immer fragen :slightly_smiling_face:

Demotivierend finde ich eigentlich kaum etwas. Vielleicht könnte man öfters mal ein (gutes) Feedback bekommen.

Engineer 2
Mattermost
14-1-2021

1. **Would there be any documentation on the development of ActSense?**

Not really. Just the PCB, GUI and Case design files

2. **How is the development going?**

The design of the electronics, GUI and mechanical case has been finished. The electronics needs to be tested. overall we are at a 2nd iteration of design

3. **How do you figure out which data the researchers and customers? So how do you determine what data to put in ActSense and what to show?**

When we decide to produce a device, we keep this in mind: 1- We want to have products that offer better performance than our competitors 2- Based on scientific discoveries or technological advents, we want to offer products with new feature that are not on the market 3- We want to combine existing technology (e.g., coming from different field) to create a product that provide more flexibility for the user

4. **The three things you mention to keep in mind when developing a new device are interesting. Do the end users play a role in selecting what products you make? If so, how? If not, why not?**

I would say so. For example, if we (meaning the business development unit) decide to target Academics (meaning research labs), likely we would propose a device that is not too expensive, probably with a very specific set of features (e.g. HUMIMIC Starter). If we target industry, we would rather provide a device that is more expensive, but equipped with everything you need now and in the future (e.g. Roboter). In the case of the HUMIMIC ActSense, since there are many competitors providing solution for TEER (Transepithelial electrical resistance) measurement (which was our initial goal), we decided to "boost up" the features of the device, providing not only TEER (1 single frequency), but also Impedance spectroscopy (10-100kHz), together with stimulation and eeg/ecg recording. The idea is

that a customer would spend a bit more compared to standard TEER devices, but on the other hand the application possibilities are limitless. This should appeal to both academic and industrial customers

5. **Alright, interesting. I see a split in two groups of customers, academic and industrial. Where does the idea to add spectroscopy specifically come from? I am trying to find out how you find out, what the wishes of a target group are, hence this question.**

well, it was my decision. I come from electrical engineering background and impedance spectroscopy is something quite standard. But in organ-on-chip is almost never done, mostly because people working in this field have different background. So when I saw that my colleagues were using a TEER device as a standard tool to characterize the TissUse quality and they had many complain about it (measurements were often unreliable and noisy etc.), I decided to add some degree of complexity to get rid of the uncertainty coming from the fact that the measurement is performed at a single frequency. With a spectrum it is possible to interpolate the measurement and extrapolate not only the resistance of the TissUse, but also other parameters like the membrane capacitance etc.

I will send you a couple of slides so that it is clearer

so to answer your question, my colleague were my first "customers" and their comment my first "market analysis" :wink:

6. **Aha! that sounds familiar, that the colleagues are the first "customers". How is your contact with them now, with regards to the development of ActSense?**

when we will have a prototype, we´ll do measurements using the ActSense and a standard TEER device. and then compare the results

that depends on the projects/experiments/availability of people

7. **the second slide show was clear indeed. Do I understand correctly, that with impedance spectroscopy you get more reliable or consistent results? and then if you want to know the cell growth over time you need to do several spectroscopic measurements at different time points?**

Exactly. we can decide to do a very slow (many averaged points) impedance spectrum, or just pick one frequency and monitor it over time, or do something in between in which we monitor the "impedance signature" of the TissUse over time

8. **in this sentence, the "we" that does the measurements, who is that? is the purpose of the measurements just to verify the results, or is to check the usability as well?**

"we" --> a biotechnologist that performs routinely TEER in their project + me (or a student if I´ll have a Master´s project proposal)

The purpose is

1- to check if the device works

2- to check that the TissUse is not damaged by the device

3- to compare the performance of the ActSense vs commercially available device

4- to note down improvements (if necessary) in the usability of the device

Business developer 2
Phone
18-1-2021

Kunden:

Bestandskunden/nicht Bestandskunden (ist es ein Problem, wenn es einfach offenbar ist?)

Bestandskunden:

1. Manche interessieren sich

2. Manche nicht

Bestimmte Kunden benutzen unsere Chips schon in Routine. Diese sind die Leute die am detaillierten interessiert sind in wie die Strömung aussieht.

Man muss Leute keine Daten liefern, wenn die das nicht wollen.

Zur Verfügung stellen ohne dass sie es weiterteilen können. Mitgliederbereich wo man nichts runterladen kann.

Für uns: je mehr du umsetzen kannst, je besser. (aber ich muss zwei Arbeiten schreiben, also man braucht auch Zeit für die Produktentwicklung)

Business developer 2 war Wissenschaftlerin, jetzt bizdev, wissen was die Kunden normalerweise fragen.

Pass auf als Startup: verliere nicht Weitblick, wenn du zu viel nach Kunden hörst. Uwe ist gut drin um diese Weitblick zu behalten.

Was wollen Kunden:

Pharma:

1. Effektivität Medikamenten testen
2. Toxizität
3. Target validation (low throughput after target identification)

Akademia:

1. Eigenes Modell reinsetzen und rumforschen

Akademia

1. Wie verteilen Teilchen sich? Small particles or antibodies for example. Do they for example get into the bone marrow insert or not?
2. Was ist die Strömung
3. Sind alle Zellen exposed?
4. Wie sind die supplied mit Oxygen und Ernährung, und Strömung.

Sources of information:

Lieferdruck kann entstehen, wenn wir sagen das wir daran arbeiten diese Daten herzustellen. kann aber mit Strategische Wörterwahl umgehen werden.

also zuerst Fragebogen, dann schauen was die Response ist, dann vielleicht Gespräch. Gespräch ist nutzloser wenn die noch gar nicht wissen worum es geht.

Wichtig zu erfragen wie viel ich wissen darf.

Wie vergrößern wir Reichweite ohne Konferenzen: Social Media. Könnten wir eventuell auch noch benutzen für einen Fragebogen.

Längere Kontrakten sind besser für ehrlicheres Feedback.

Researcher 8 Folie bei Statusmeeting: Contract development Partner von alle Projekte, die kannst du als erste frageliste schicken mit bizdev und TissUse Forscher in CC.

Von intern viel Feedback womit ich sowieso arbeiten kann.

Vielleicht kann ich mitkommen in einem wöchentlichen Meeting.

Bio Papers Uber Charakterisierung. Mal schauen was die Konkurrenten wissen wollten.

Bei BD machen die auch Marktanalyse. Business developer 2 denkt die wird so innerhalb eine Monat fertig sein.

Development department leader
Phone
20-1-2021

1. **How does a typical product development process look?**

Quellen: von Mitarbeiter, von interne Anwendern, von extern, von Drittmittel (auch extern). Forschende Entwicklung und industrielle Entwicklung forschende Entwicklung: so schnell wie möglich prototype, chaotisch. industrielle Entwicklung: Weiterentwicklung bis verkauf klar, mehr vorgegeben, iterativ.
große Unterschied ist Technology Readiness Level.

Bei industrielle Entwickelung macht man auch Lieferanten Qualifikation (oberflächlich) Für CE Kennzeichnung braucht man auch Dokumentation.

Forschende Entwicklung: HOC verrückte Idee. Proof of Concept machen. Weil wir noch nicht wissen ob und wie es funktioniert muss man einfach ein bisschen rumprobieren. Endergebnis ist Proof of Concept. Nur so weit Charakterisierung als notwendig für Proof of Concept.

Industrielle Entwicklung: von Proof of Concept zu CE, Lieferantenquali und verkaufbares/lieferbares Produkt.
ich nehme fertige Chips, und zeige was die Chips können und die werden dann auch nicht weiterentwickelt, also ich bin mehr im Bereich industrielle Entwicklung beschäftigt.

2. **There are several groups of users. Let's say internal and external. What is the role of both of these in the product development process?**

Anforderungen kommen von beiden. Je nach wie wichtig es ist wird es priorisiert. Intern und Extern gleiche Qualität.

Industrielle Entwicklung: am Anfang: intern Nutzer fragen was die wollen als Funktion. Die bringen dann auch ein was die Kunden haben. Intern Nutzer sind eigentlich die Leute die es testen.

Ein Projekt zusammen mit Kunde von Forschung bis zum Verkauf. PMI von Engineer 1.

3. **What do you think are the things TissUse finds most important?**

Qualität muss hoch sein und Kundenzufriedenheit. Wir haben ja regulierte und konservative Kunden.

Es muss dann auch über längere Zeit verfügbar sein. Wenn die Kunden investieren dann wollen die nicht wechseln. Deshalb konstante Qualität und Verfügbarkeit. Mindestens fünf Jahren (neue Generation), wegen Ersatzteilen die man liefern können (10-20 Jahren)

4. **What kind of reputation does TissUse want to have?**

Hochinnovativ, Zuverlässig, Hochtechnologisch.

Person: immer freundlich, reisefreudig, Kunde ist König – wir haben keine Untergrenze für die Große der Verträge um Sachen auch einfach mal versuchen zu können. Wir sind noch nicht im Markt verankert sein und der Markt ist noch nicht gesättigt, deshalb Kunden so früh wie möglich binden.

5. **TissUse wants to develop long term relationships with their customers. Why?**

Kunden früh binden, bessere Feedback. Entwicklungszeit von Wirkstoffe dauert so zehn Jahre, wenn du das ganze Projekt mitlaufen willst, dauert das einfach zehn Jahren.

Die Kundenmärkte sind nicht unendlich groß, deshalb ist Loyalität wichtig.

Kundenanforderung sind alle anders – Baukastensystem macht dir flexibel um dir an vielen Applikationen anzupassen. > Methode kann deshalb cooler sein als eine Charakterisierung, standard Kombination is aber interessant.

6. **Two slogans: redefining research and emulating human biology. What is their relation?**

Emulating ist von der Firma > kann nur raten: wir entwickeln meds für Menschen, keine Tiere mehr, und per Mensch unterschiedlich

Redefining ist von HUMIMIC > wir streben nach einem großen Ziel.

7. **Company presentation title went from human-on-chip to human-on-chip solutions. Why?**

Nowadays it is Universal Physiological Template: UPT: Produktkatalog. Ist geändert wegen Dokumentation/Interviews/Podcast Leute denken sofort an kleine Menschen auf einem Chip. Wir wollen nicht das diese Verwirrung da ist. Gab ein Workshop wo alle sich geeinigt haben. Vor allem für Presse, wir wollen später auch in klinische Markt reintreten. Dann müssen nicht fachkundigen auch verstehen was passiert und die Microphysiological Systems verstehen.

Appendix H User requirement interviews

Business developer 2
1-2-2021

Kleines Feedback am Rand: Ein Kunde interessiert sich besonders für Flow-Speed. Anwendung des Chips: PKPD modelling, PET Scan

Another question from a client: Did you evaluate the impact of flux in your system on the different culture type? Is the use of hydrogel relevant (the medium flux is not in direct contact with cells)?

Master student 1
1-2-2021

ich wüsste allerdings gerne wie genau sich das Medium im Kompartiment verteilt, da ich meine Leber Sphäroide in einem Transwell habe und gerne wissen würde wie gut der Medium Austausch wirklich ist.

Ich meine damit die Strömung, wenn das Medium durch den Kanal in dem Kompartiment gelangt, fließt es dann eher nach oben oder diffundiert es nur nach oben.

Engineer 1
5-2-2021
Chip development

1. **Anforderungsliste**

Engineer 1 seine Anforderungen an irgendeinem Darstellungstool von Chipdaten:

- Gute Darstellung der Daten damit die Biologen wissen was los geht in den Chips.
- Flussgeschwindigkeiten
    - Peak und Durchschnitt
    - So ein bisschen wie Engineer 3 es in seinem Excel Tabelle hingesetzt hat.
- Scherstress
- Schön wäre, wenn man schnell Diagramme und Grafiken bauen könnte. Das vermisse ich momentan in der Tabelle von Engineer 3.
- Kennzeichnung zwischen Werten. Wenn du etwas extra- oder interpolierst, sag dann das dann dazu. Biologen wollen wohl wissen, wenn die eine gemessene Wert benutzen und wenn eine Schätzung. Man könnte auch sagen, das hier ist eine Schätzung auf Basis dieser zwei Werte. (Anschluss bei the development department leader „zeig Genauigkeit/Zuverlässigkeit der Daten“ und Evas „nicht alle Werte in triplo messen“)
- Es soll pflegearm sein, also weiter erweiterbar, man muss die Datenset ausbreiten können.
    - Z.B. im PIVlab Programm ist es schwierig um im Code Fehler zu finden momentan. Ich will kein C# lernen müssen, nur um neue Daten einfügen zu können. µPIV Programm
    - Wir haben auch viel Sonderchips, und wir werden immer mehr haben. Sowie Researcher 3 sagte: wir haben genug Benutzer von den anderen Chips um einen guten Grund zu haben die auch Charakterisieren zu wollen.
    - Wäre ganz cool, wenn wir am Ende deiner Masterarbeit etwas hätten was ganz ausgedacht wäre. Nur dass wir noch jemand brauchen, die einfach messt wie ein Blöder um die Daten noch zu generieren und einzufügen.

Researcher 1
27-1-2021
Contract development

UCB project: Proof of concept to make a blood-brain-barrier in the HUMIMIC Chip2 24-well chip. The chip has blood-brain-barrier-specific endothelial cells in a standing insert in this chip. The cells appear to be differentiated before insertion into the chip.

Keimblätter are further developed parts of the embryo. They are so to say partially differentiated groups of cells. When the differentiation is like a tree, the Keimblätter are the first split in four different branches. You can go back after this splitting. So cells from one branch can't be altered to cells from another branch/Keimblatt.

1. **What would you like to know about the flow in the chip? (When was the last time you thought: "I wish I knew this or that about the chips – so I could do XYZ ")**

Wichtigsten: Scherkräfte und Flussraten (diese sind verbunden)

Wenn wir aus Druck und Frequenz Einstellungen die Flussrate finden könnten und daraus dann die Kraft auf den Zellen, wäre ganz hilfreich.

Die Frage die wir damit eigentlich immer beantworten wollen ist: Haben wir überhaupt körperliche Bedingungen? Z.B. in Große Arterien ist es anders als in kleine Kapillare. Je weiter man vom Herz ist, oder je weiter man in einem Organ geht, desto schwächer wird die Strömung. Wenn man so etwas nachahmen kann, ist das interessant für die Entwicklung komplexeren Organmodelle.

Geht auch um Mengen von Nährstoffe und Sauerstoff. Blutdruck, Flussrate, Flussstarke und Menge des Volumens sind alle Sachen die man so physiologisch wie möglich haben will. Für Mengen von Substanzen ist es aber schwierig, dass es viele Faktoren gibt die Einfluss haben. Das PDMS, die Zellen selbst in entweder den Kompartimenten oder in den Kanälen.

Ideal wäre: Simulationsbild und pünktlich sehen was der Flussrate ist, wo man dann höhere Frequenz oder höhere druck sozusagen wählen könnte und dass das Bild sich dann ändert.
Es gibt Zellen in den Kanälen und in den Kompartimenten, also beide sind interessant um die Flussrate zu wissen.

2. **Why? (With what purpose? What would you like to do with it?)**

Wir wollen die Kräfte auf Zellen wissen, weil das das Phänotyp von den Endothelzellen beeinflusst. Man will kontrollieren können wie die Bedingungen für die Zellen sind.

Wenn man diese Standardeinstellung oder diesen Standardentwurf gemacht hat wo es physiologisch Standardfluss gibt, kann man noch weitergehen. Person-spezifische Blutdrucke kann man noch immer emulieren z.B. Also es gibt dir mehr Spielraum um Einflussfaktoren zu bringen, wenn du mehr weißt über die Strömung bei verschiedenen Pumpeinstellungen außer den Standardeinstellungen. Wir können dann besser das Herz nachahmen.

Versuchen können auch besser vergleichbar werden. Wenn wir sagen können was unsere Bedingungen waren.

3. **Under what circumstances do these needs come up? (in what situation?)**

Drei Situationen gefunden:

- Beim Design oder Redesign vom Chip ist es wichtig zu wissen wie der Fluss sich ändert.

- Anpassung von Differenzierung: Manche Zellen brauchen Scherkräfte um sich gut zu differenzieren oder aufzuwachsen.
- Anpassung eines Assay: wenn man sieht, dass die Strömung nicht ist was sie sein sollte, dann könnte man die Pumpeinstellungen sofort ändern.

Für die Anpassung eines Assay wäre es ganz cool, wenn du die Regelung auf „Flussgeschwindigkeit“ statt Frequenz einstellen könntest.

Training ist beim Kunde im Büro. Wenn die schon wissen was die machen wollen, gibt es mal Fragen wie: Wie lange dauert es bis alles durchmischt ist, oder wie lange dauert es von A nach B zu kommen? Was sind die Kräfte? Kommt aber nicht so häufig vor, weil die meisten noch nicht so genau wissen was die machen wollen/können. Leute haben die Komplexität noch nicht erreicht. Erstens macht man nur ein Organ, dann zwei, und erst dann gibt es auch ein Fluss. Erstens „wie bleiben meine Zellen leben“. Dann kommt erst später „bin ich im physiologische Bereich“.

4. **What would your clients like to know about the flow in the chip?**

Für UCB wollen wir Chip2-24 neudesignen. Wir wollen nach ein PDMS-freier Chip. Dann gibt es also eine neue Pumpe und ein neuer Chip. Wäre ganz praktisch wenn den Chip dann neudesignen könnten damit wir die gleichen Pumpeinstellungen benutzen können. Statt der gleichen Mikrofluidik im Chip und andere Pumpeinstellungen. (von Ingenieursseite, würde ich damit nicht sofort einverstanden sein)

Wir haben auch BBB Zellen an einem Insert in den Kompartimenten. Fragen wie: Wie ist der Fluss da? Ist die stark genug für gute Entwicklung der Zellen?

5. **Why?**
6. **Under what circumstances do these needs come up?**

Einfach Daten zeigen.

schönes Bild.

kann sein für ein PowerPoint, Report oder Paper

Zulassungsbehörde muss genehmigen. Also etwas womit wir den zeigen könnten, dass unsere Bedingungen physiologisch sind, ist dabei wertvoll. (Beim ersten klinischen Studie sind die Patienten meistens männlich, 20-30 und gesund, also nicht repräsentativ für die Welt Bevölkerung, deshalb sind unsere Chips auch interessant. Unsere Chips können repräsentativer sein.)

Um in eine klinische Studie oder überhaupt irgendwann eine Extrapolierung machen zu können, brauchen wir auch diese Daten über die Strömung. Wenn es ein perfekt designter Chip gibt: Faktor 1:100.000 und braucht man Daten. Wenn imperfekter Chip: vielleicht andere Faktor aber dann kann man mit den Flussdaten vielleicht noch immer extrapolieren.

7. **How would you like to have this data presented?**

Schönes Bild. Was Engineer 1 rumgeschickt hast ist schon ganz cool. Jedes Punkt wo man klicken könnte wäre mega-gut.

Ich mache Experimente mit Endothelzellen im Kanal drin. Stell dir mal vor du macht eine Substanz dazu der die Zellen leuchten lässt. Dann siehst du zum Beispiel „O, oben ist es heller als unten“. Dann wäre es cool, wenn man sehen könnte ob der Scherkraft oder der Flussrate oben anders ist als unten, oder nicht. Damit man Aussagen machen kann. Man kann herausfinden oder ausschließen, dass der Fluss Einfluss hat oder nicht. Damit kann man wissenschaftliche Aussagen machen.

Development department leader
1-2-2021
Chip development department leader

Airliquide project: check the influence of gaseous substances on a liver model. These gases used to flow around the chip and through the PDMS in what appears to be a custom made gasification device. Nowadays it is flowing through an open cap especially made for Airliquide. From the development department leader, it is interesting to get this engineer's and customer view.

1. **What would you like to know about the flow in the chip? (When was the last time you thought: "I wish I knew this or that about the chips – so I could do XYZ ")**

Generell:

1. Absolute Strömungsgeschwindigkeit: z.B. Endothelzellen richten sich aus an Hand von den Peaks und die absolut Wert. Der Puls ist wichtig für die Ausrichtung von anderen Zellen von größeren Blutgefäßen.
2. Net Volumenstrom: ist die Versorgung/Ernährung in Ordnung?
3. Strömungsverteilung: Wird alles in den Kompartimenten gleichmäßig umspült? Sind verschiedene Leberspheroiden (am Boden oder oben am Rand z.B.) alle gleich versorgt? Wenn nicht, wie stark ist dann der Unterschied?
   Manche Zellen brauchen wenig Sauerstoff, andere brauchen viel. Die Gase gehen momentan vom Gas durch das PDMS, in Fluss rein und dann kommen die bei den Organen. Man kann da Design alterations machen, um die richte Sauerstoffmenge auf verschiedene Stellen zu bekommen. Kommt es momentan überhaupt genug Sauerstoff darüber?

Für Airliquide spezifisch gibt es momentan keine anderen Fragen.

2. **Why? (with what purpose? What would you like to do with it?)**

Grundsätzlich wollen wir die Bedingungen im Chip gezielt einstellen können. Das heißt meistens wollen wir sicherstellen, dass es alles so physiologisch wie möglich ist. Wenn wir aber Krankheitsmodelle entwickeln, muss es aber nicht immer physiologisch sein. So könnte man ein Herzinfarkt nachahmen durch die Strömung für dreißig Sekunden zu stoppen.

Wenn wir wissen, dass die Bedingungen im Chip gut eingestellt sind, kann man z.B. auch ausschließen, dass die Umgebungsfaktoren ein Einfluss hatten. Wenn man ein Medikament testet und sieht, dass die Zellen sterben, ist es wichtig ausschließen zu können, dass die Zellen zu wenig Sauerstoff bekamen oder etwas Anderes. Je besser die Umgebungsbedingungen (bekannt) sind, desto genauer die Aussagen über der Funktion der Medikamente.

Die Kundenanfragen haben diese obere zwei Ziele auch als Hintergrund.

Man kann die Charakterisierungsdaten benutzen für:

- Technisch design für richtige Bedingungen.
- Assay planen kann man Zellzahl planen oder Mediumwechsel planen.
- Versuchsauswertung kann besser mit guter Charakterisierung.

Schöne bunte Bilder müssen hilfreich sein und Aussagekraft haben. Wenn die das sind und haben ist es ganz cool wenn die Bilder dann auch noch bunt und schön sind.

Die meisten Publikationen sind von Kunden und TissUse zusammen. Es ist dann abhängig von den Kunden wie cool/schön/bunt es alles aussehen muss.

3. **Under what circumstances do these needs come up? (in what situation?)**

Es gibt so drei Vorbilder:

- Kundenanfrage (kommen meistens per Email)
- Kundenakquise (so etwas hat Researcher 4 auch beschrieben als Projektanbahnung glaube ich. Fragen als „wie gut funktioniert es?“ kommen dann vorbei. Du willst dann eigentlich ein PowerPoint mit die richtige Antworte mitgenommen haben.)
- Während des Projektes einfach irgendwann (Planung, Charakterisierung und Auswertung wohl im Büro)

Wahrscheinlich ist diese Liste nicht vollständig.

4. **How would you like to have this data presented?**

Das ist Anwendung abhängig:

Bei Kunden: ein PowerPoint?

Noch besser: etwas Interaktives.

Wäre gut, wenn wir das mitnehmen oder an der Hand geben könnten.

Zuverlässigkeit und Genauigkeit sind wichtig. Reihenfolge: Genauigkeit/Zuverlässigkeit und dann schön. Genauso wie bei den Bildern. (vielleicht auch eine Linie mit warum Researcher 4 sagt, dass sie zuerst feste Daten haben wollen würde für die Behörden und danach die schönen Bilder für den Kunden).

Researcher 2
1-2-2021
Biotechnologist

RESHAPE/bloody organ project: Developing a vascularized chip model that should eventually allow vascularization of the organ models as well. Required chip adaptation with several prototypes, endothelialization and a specific co-culture medium (Isi's modified co-culture medium IMCC).

Das Ziel ist Zelltherapie testen. Es gibt Immunzellen die anwachsen lassen kann und dann zurücksetzen im Körper um Organabstoßung zu verhindern. Vaskularisierung ist dabei notwendig, denn Immunzellen müssen an genauen stellen im Organ kommen.

1. **What would you like to know about the flow in the chip? (When was the last time you thought: "I wish I knew this or that about the chips – so I could do XYZ ")**

Fließgeschwindigkeit und Scherkraft – Es sind Prototypen von Chip2 angefertigt für mich die extra geeignet sind für Vaskularisierung. Die Chips haben mehrere Kanäle mit verschiedene Größen. Weil ich verschiedene Zelltypen habe (Erythrozyten und Immunzellen) möchte ich auch unterschiedliche Geschwindigkeiten haben.

Für die Endothelzellen brauche ich bestimmte Scherkräfte in den Kanälen. Für die Erythrozyten muss die Geschwindigkeit nicht zu hoch sein, sonst platzen die. Die Geschwindigkeit muss auch nicht zu niedrig sein, weil dann das Blut festigen könnte.

Für die Immunzellen will ich vor allem in den Kapillaren niedrige Geschwindigkeit haben, damit das anheften von Immunzellen ermöglicht wird.

Eigentlich wird also überall im Chip die Fließgeschwindigkeit gefragt. Also in den großen Kanälen, den kleinen Kanälen und den Kompartimenten.

Wie ist die oberflache behaftet? Ich muss es mit Proteine bearbeiten, sonst haften meine Endothelzellen weniger gut. Wie die oberflache beschichtet ist wäre interessant zu wissen.

Wenn wir die Nährstoffkonzentration/-verteilung wussten konnte man die Vaskularisierung vielleicht auch kontrollieren. Chemotaxis sorgt dafür, dass die Blutgefäße sich formen an Stellen wo es mehr Sauerstoff gibt z.B.

Also interessant zu wissen wäre eventuell auch noch: Sauerstoffkonzentration im ganzen Chip. Stickstoffkonzentration, CO2-konzentration oder pH-Wert.

2. **Why? (with what purpose? What would you like to do with it?)**

Fließgeschwindigkeit:

- Das Verhalten von Immunzellen einschätzen zu können (Tabelle mit Immunzellverhalten bei verschiedenen Pumpeinstellungen. Für Planung eines Assay zum Beispiel, wenn ich Zellen gut wachsen lassen wollte.)
- Das Verhalten von Endothelzellen einschätzen zu können
- Für einfach überleben der Zellen
- Nicht akkumulieren von Erythrozyten oder verstopfen von Blutgefäßen.

Volumenstrom:

- Angiogenese kann man durch Nährstoff und Sauerstoff induzieren (Chemotaxis).

Für Publikation ist es cool zeigen zu können, dass es physiologisch ist.

Ich war nicht da bei der Planung dieses Experiment. Ist aber orientiert an der HUMIMIC XX/XY. Da drauf hatten wir die verschiede Kanalstrukturen basiert. The development department leader war daran beteiligt.

3. **Under what circumstances do these needs come up? (in what situation?)**

Während der Planung. Wäre cool wenn es auf dem Server steht. Dann kann man es im Labor auch einfach sehen. Laminiertes A4 Blatt wäre auch ganz in Ordnung. Neben den HUMIMIC Starter z.B. Das gibt es schon für das an- und ausschalten der Geräte und für Zellkonzentrationen. Es wäre vielleicht auch mit Fließgeschwindigkeiten interessant.

Wenn es chipspezifisch ist (und alle abhängig von allen anderen Faktoren) werden es aber viele Zettel.

Jeder Zelltyp hat sein eigens medium wenn du es monokultiviert. Wenn du die aber kombinierst braucht man Co-Kultur-Medium. Es gibt unendliche viele Medien. Viele Nährstoffe, pH Indikatoren, Proteinen/Aminosäure, Salze etc. Die letzte zwei wechseln ein bisschen pro Organ. Die sind aber alle wässrig und ziemlich ähnlich. Es sollte chemisch ähnlich sein an Blut.

Übersicht für den Kunden konnte auch ein bisschen weniger vollständig sein. Wir sollten die nur Daten geben von den wir sicher sind, dass sie stimmen. Wir sollen die nicht überfordern mit der Komplexität. Es ist jetzt ein neues Produkt, die lernen noch damit zu arbeiten. Deshalb lass es möglichst übersichtlich und simpel für die Kunden.

4. **How would you like to have this data presented?**

Bilder von Chiptypen woran die Kanalstruktur ausgezeigt wird. Pro Pumpeinstellung die und die Fließgeschwindigkeit im Chip. Wie sich das ändern würde, wenn ich Immunzellen da drin setze, wenn es endothelialisiert ist, wenn es Blut statt Medium drin gibt.

3D Modell + Pumpeinstellung: wenn ich dann die Pumpeinstellung ändere, ändert sich das ganze Bild auch im 3d Datei.

Researcher 3
1-2-2021
Biotechnologist

RESHAPE/bloody organ project: Developing a vascularized chip model, that should eventually allow vascularization of the organ models as well. Required chip adaptation with several prototypes, endothelialization and a specific co-culture medium (Isi's modified co-culture medium IMCC).

1. **What would you like to know about the flow in the chip? (When was the last time you thought: "I wish I knew this or that about the chips – so I could do XYZ ")**

Alles was wir wissen wollen ist eigentlich:

- Wie hoch ist die Flussgeschwindigkeit?
- Wie hoch ist der Scherstress?

Für Publikation braucht man eigentlich nur ein Wert. Eine Tabelle mit diese Werte wäre eigentlich schon genug. In verschiedene Publikationen bis jetzt gibt es Grafiken mit Druck vs. Frequenz und dann die Flussgeschwindigkeit oder Scherkraft. Vorbilder von Publikationen mit Grafiken:

- Researcher 6 hat eine Publikation über den Flow rate mit Sphäroiden (Seite 2 letzte Absatz, Seite 3 steht Grafik)
- Researcher 7 hat auch gute Diagrammen als Vorbilder in ihre Publikation (Seite 6). Da gibt es ein Plot mit dem Geschwindigkeitsprofil, mit dem Herzschlagartige Form. Da kann man sehen das es nicht konstant ist. Daneben gibt es ein Plot mit Druck vs. Frequenz. Das zeigt mehr den Mittelwert. Dieses ist was Modellierer in ihren Modellen einspeichern wollen. In so einem Modell geht es nämlich mehr um wie viel nach 24 oder 2 Stunden rundgegangen ist. Dann ist das Geschwindigkeitsprofil weniger interessant und der Mittelwert hilfreicher.
- Business developer 1 hat eine Publikation über das erste Chip4 Design (Seite 2 wieder ein Diagramm)
- Engineer 3 hat alle diese Daten erstellt.
  Daneben hat Engineer 3 ein Excel Sheet von Chip2 gemacht, wo man Druck und Frequenz auslesen kann, und dann diese Charakterisierungsdaten finden kann. Diese ist superschön. Weiß aber nicht ob es auch stimmt. Alle die hier oben genannten Dateien stehen in: „O:\Protokolle\02_MOC\02_Flow Models"

Die Modellierer womit wir zusammenarbeiten brauchen einfach eine Zahl. Diese Zahlen sind basiert auf unsere Experimentdaten. Also die Pumpeinstellungen stehen dann schon fest. Wenn die Fragen um diese Zähle, geben wir immer Antwort mit Engineer 3's alten Daten. Da müssen wir aber immer dazu sagen, dass es nicht die gleiche Steuerung und Chip sind. Wir sehen, dass diese Daten auch nicht eins zu eins übertragbar sind. (Researcher 9 hat vielleicht ein Paper mit Daten?).

Eigentlich ist die Flussgeschwindigkeit in den Kompartimenten wichtig für die Kunden. CFD Davon wäre dann interessant zeigen zu können.

Andere Kunden die erst jetzt anfangen fragen meistens welche Pumpeinstellung sie brauchen für welche Fluss. Wie schnell verteilt sich ein Stoff durch den Chip? Das ist die turn-over Zeit: wie lange bis ein Stoff rundgegangen ist.

Der Widerstand ändert sich auch wenn wir ein Transwell oder Knochenmark drin setzen. Darüber können wir momentan nicht so viel sagen. Wäre auch interessant. Fluss am Blutgefäßzellen unten am Transwell ist z.B. interessant. Was passiert überhaupt mit dem Fluss? Die meisten Kunden haben irgendwelche Sphäroide in den Kompartimenten.

Aktuelle Daten wären schon ganz cool. Momentan µPIV zu aufwendig. Ich finde, dass es ein bisschen höhere Priorität haben sollte, aber ja, ich habe dann einfach auch andere Prioritäten und andere Sachen die einfach auch wichtig sind.

Daten in zwei Windows wären auch schon interessant. Wenn die Schwankung zwischen verschiedenen Stellen im Chip nicht zu groß sind. In Publikation benutzen wir nur eine Stelle.

In Chip4 gibt es mehr verschiedene Stellen, weil die Strömung sich splittet. Bei jeder Abspaltung wäre der Flussrate interessant. Können wir das mit µPIV überprüfen?

Tabelle wie ändert sich die Strömung an irgendeine stelle mit Pumpeinstellung.

2. **Why? (with what purpose? What would you like to do with it?)**
3. **Under what circumstances do these needs come up? (in what situation?)**
4. **How would you like to have this data presented?**

Tabelle wo ich eintragen kann:

- Welcher Chip
- Welche Barriere (bzw. Transwell/Lebersphäroide)

dann kommt raus

- Flussgeschwindigkeit
- mittlere Flussgeschwindigkeit
- Scherstress unter dem Transwell und an den Lebersphäroiden

Ich arbeite nicht mit Endothelzellen. Dann wären die Scherkräfte in den Kanälen auch interessant.

Ich denke vielen wollen der mittlere Wert wissen von der Geschwindigkeit und Scherstress. Mittlere und Maximum wären interessant. Mit dem Geschwindigkeitsprofil kann man dann einschätzen wie lange es auf dem Maximum ist. Mittlere Scherspannung ist wohl wichtiger für Differenzierung – denke ich. Was wird es in der Literatur angegeben? Wir vergleichen unsere Daten mit den körperlichen Bedingungen die in die Literatur stehen. Also, wenn die Literatur redet von maximale Scherspannung, dann ist es klug um bei uns auch die maximale Scherspannung zu nennen.

Researcher 5 und Researcher 7 haben die meiste Erfahrung, und brauchen µPIV viel. Beiden sind wichtige Ansprechpartnerinnen in Sachen PIV. Researcher 5 hat Forschungsüberblick und Draht zu Kerstin.

Researcher 4
2-2-2021
Biochemist

1. **What would you like to know about the flow in the chip? (When was the last time you thought: "I wish I knew this or that about the chips – so I could do XYZ ")**

Wo ist die Strömung am schnellsten? Wie ist der Strom im Kanal in Vergleich zu Kompartiment? Wie verändert sich der Strom, wenn man die Pumpeinstellung ändert. Engineer 3's Matrix ist dabei auch hilfreich. Diese dabei zu haben mit aktualisierten Daten.

Es gibt zwei verschiedene Größen die man ableiten kann von der Flussgeschwindigkeit: Volumenflow: Verteilung von Stoffen ist auch interessant. Wie schnell verteilt ein Stoff sich bei bestimmte Strömungsgeschwindigkeit?

Scherkräfte: Zellentwicklung.

Die Stellen wo wir diese Größen zu mindestens wissen möchten sind:

- Im Kanal (dabei sind die Große Kanäle vielleicht interessanter als zwischen den Kompartimenten, aber nicht sicher)
- Im Kompartiment
    - Eingang
    - Mitte
    - Ausgang

Momentan sind die verschiedenen Medien die wir benutzen nicht so anders. Wenn es Vollblut gibt, wird es anders. Momentan ist alles halt wässerig. Eher interessant die anderen Chips zu charakterisieren. Viskoses medium wird wahrscheinlich eben dauern.

2. **Why? (with what purpose? What would you like to do with it?)**

Wir wollen unsere Systeme so physiologisch wie möglich haben natürlich. Wir sagen, dass unseren Chip naher an der biologischen Situation sind als statische Kultur. Wir brauchen dann auch Details die tatsächlich zeigen, dass das auch echt so ist. Deshalb wollen wir so viel wie möglich charakterisiert haben vom Chip.

Wir arbeiten großenteils mit Chip2. Da gibt es also immer Kombinationen von Organmodellen. Jedes Organ braucht aber eine andere Scherkraft oder Stromvolum. Endothelzellen brauchen starke Scherkräfte, Leberzellen genau niedrige Strömungsgeschwindigkeiten. Für jedes Modell bräuchte man also andere Pumpeinstellungen, die man wählen kann, wenn man weiß bei welche Einstellungen welche Strömung entsteht.

Fragen die wir haben können:

Leber-Haut-Assay: wir applizieren Substanz, wie lange dauert es bis die in anderem Kompartiment ist? Oder gleich verteilt (Péclet Nummer?)? Substanz auf die Haut, wie lange dauert es bis es durch die Haut ist? Wie lange bleibt es dann darunter? Wie lange bis es bei der Leber ist? Das sind Sachen die müssen wir experimentell ermitteln. Wurde helfen bei der Planung zu wissen wie lange es dauert, damit wir einschätzen können, wenn wir messen müssen/können. Man kann Zeitrahmen besser einengen wo etwas Interessantes passieren wird. Momentan mache ich acht Stunden proben jeder Stunde. Aber manchmal sehe ich dann, dass es eine schnelle Metaboliser war, und nur die erste zwei Stunden interessant waren. Oder dass der Substanz erst nach zwei Stunden beim Leber ankam oder so.

Je besser charakterisiert, je besser deine Publikation ist. AZ zum Beispiel sind heiß drauf um mehr Charakterisierungsdaten zu bekommen für die Publikation.

3. **Under what circumstances do these needs come up? (in what situation?)**

Vor allem bei mir im Büro, wenn ich das Experiment plane. Auswerten ist auch im Büro. Könnte auch interessant sein im Labor, aber nicht ganz überzeugt.

Ganz oft, bei ersten Gesprächen mit den Kunden, was ist alles möglich. Bei der Projektanbahnung, in Gespräch, fragt man oft was passiert da genau im Chip?

4. **How would you like to have this data presented?**

Anforderungsliste:

- Verständlich: auch für Leute mit einem anderen Hintergrund soll es verständlich sein. Oder Leute die noch nie mit unseren Chips gearbeitet haben. Das sind ja viele unserer Kunden. Die müssen auch denken: „Ah, das und das kann ich ändern, diese und diese Parameter kann ich einstellen und dann passiert etwas“
- Bilder für eine Publikation generieren können: sind dann vielleicht mehr die Grafiken und Tabellen
- Einfach visualisieren können während Gespräche oder in eine Publikation oder beim Projektanbahnung: Manchen verstehen es dann besser.
- Wir müssen es intern benutzen können.
- Einfach ausbreitbar für neue Chips: ein Template oder Plattform wäre gut. Wir haben genug Kunden die anderen Chiparten benutzen, also wir haben auch Gründe um die Charakterisierung nach anderen Chips auszubreiten.
- Version die nach den Kunden kann die sie benutzen können aber nicht bearbeiten.

Ideale Form wäre eine visualisierte, bildliche Darstellung. Vielleicht eine bewegende oder Video Darstellung. Ähnlich wie Researcher 1 es beschrieben hat hört sich gut an. Wäre ganz nett, wenn ich sehen kann: Der Fluss verändert sich so, wenn ich diese Keramik einstellen.

Was würdest du mal als erste charakterisiert haben wollen? Davon ausgehende, dass ich Chip2 schon für eine Pumpeinstellung charakterisiert habe, wird die Liste mit nächsten Schritten priorisiert:

1. Frequenz und Druck (Für Chip2 verschiedene Pumpeinstellungen)
2. Obstakeln (was passiert, wenn ich ein Transwell, Gel, Keramik, Leberspheroiden drin stelle)
3. Chip Variant (Dann das gleiche für andere Chips)
4. Endothelialisiert (diese ist vielleicht für andere Leute, so wie Isi wichtiger)
5. Medium (ist momentan noch nicht so wichtig, erst viel später wenn wir Vollblut benutzen werden)

Für Charakterisierung und Validierung braucht man für die Behörden richtig Zahlen und Daten und nicht nur ein schönes Bild.

- Feste Daten sind gut für Behörden und Publikation.
- Schone Bilder besser für Kunden.

Momentan wurde ich, denke ich, für die Daten wählen. Weil es am Ende uns am weitesten bringt, wenn wir unsere Systeme validieren werden können. Wenn es einmal validiert/akzeptiert ist von offiziellen Behörden, kommen die Kunden von selbst.

Researcher 5
5-2-2021
Program head Human-on-Chip

1. **How did Engineer 3 generate so much data?**

Er hat einfach sehr viel µPIV gemacht. Er war der erste der µPIV bei uns etabliert hat. Wir waren damals ziemlich unerfahren. Er hat es, glaube ich auch mit Partikeln und Blut gemacht. Er hat nachgedacht welche Parameter alle wichtig sein könnten. Danach hat er sich beraten lassen von einem Statistiklehrer an der Uni über Design of Experiments (DoE). Mit DoE hat er geschaut welche Parameter tatsächlich bestimmte Einfluss hatten und welche nicht. Daraus hat er also gefunden, dass der Druck und Frequenz wichtig sind und Schlauchlänge z.B. nicht. Deshalb hat er eine Tabelle gemacht mit Druck und Frequenz und dafür Versuchen gemacht.

Für seine Versuche hat er nicht alle Parameterkombinationen in triplo gemacht. Wenn du bzw. Die Geschwindigkeit wissen willst für 300, 400 und 500 mbar. Dann kannst du den mit 400 mbar dreimal machen, um den Fehler einzuschätzen. Die von 300 und 500 kann man dann mit nur einmal messen.

2. **Why did you decide to ask help from Kerstin?**

Sie hat der Blutfluss wie im Blutgefäßen modelliert. Damit war sie beteiligt bei der Entwicklung vom HOC, Chip4 und der neuen Pumpe. Dabei wird die ganze Strömung natürlich komplexer und anders als beim Chip2. Du hast ja gesehen wie stark die Pumpe ist. Auch hat es weniger Rückfluss. Sie hat da auch versucht die Charakterisierung von der Pumpe aus Moskau zu benutzen. Leider war die aber schwierig. Es waren nur Simulationen oder nur Messungen, also hat nicht so geklappt. Kerstin war damit auch nicht so zufrieden. Sie ist momentan in England. Wegen Zeit und Resource-Grunden nicht weitergearbeitet.

Nach jeder Studie hat sie ein Bericht geschrieben mit darin Anforderungen, Randbedingungen, wie sie es gelöst hat, wie es dann aussah, welche Fragen offengeblieben sind. Solche sollte es auch irgendwo noch geben vom HOC und Chip4.

3. **What would you like to know about the flow in the chip? (When was the last time you thought: "I wish I knew this or that about the chips – so I could do XYZ ")**

Was ich bräuchte:

- Mittlere Flussgeschwindigkeit: um zu schauen wie etwas über die Zeit von A nach B transportiert wird. Wie lange dauert es rund zu gehen oder vom einen Kompartiment zum anderen.
- Maximale Wandshubspannung ganz wichtig für Endothelzellen. Ein zu hohes Maximum kann schlecht sein für Endothelzellen. Mittlere ist auch interessant.

Also letztendlich können fast alle Variablen interessant werden. Zum Beispiel die Wandschubspannung in entgegengesetzte Richtung hat auch ein Peak. Da der Peak der mit der Richtung der generellen Strömung mitgeht großer ist, ist der entgegengesetzte nicht so wichtig.

In Chip4 wird es komplexer, weil es dort parallele Kompartimente gibt. Dafür würde man sowieso mehrere Punkte brauchen.

Sowie Researcher 3 schon sagte: Mach erstmal Chip2 mit verschiedenen Drücken und Geschwindigkeiten. Danach könntest du noch Throttling anschauen, aber wird wohl nicht geändert von den Forschern. Pumprichtung könnte man auch noch ändern. Was interessant wäre, ist wie es aussehen würde mit einem Transwell Halter oder eine Keramik drin. Andere Medien und Chips sind

für später. Wir wollten vielleicht irgendwann diesem Jahr mit Blut arbeiten, aber dann noch nicht so viskös anders als was wir jetzt haben. Also, ist echt für später erst.

4. **Why? (with what purpose? What would you like to do with it?)**

Es gibt ziemlich viele Parameter. Pro Assay ist es unterschiedlich welche am wichtigsten sind. Es ist also nicht deutlich welche Parameter wir genau wie physiologisch haben möchten. Das ist unterschiedlich pro Versuch. Also, „so physiologisch wie möglich" kann auf Grund verschiedene Variablen sein. Deshalb ist es gut so viel wie möglich über den Chip zu wissen.

Die Zellen müssen zuerst lebend bleiben. Dafür denken wir, dass physiologische Parameterwerte am besten sind. Wir wissen momentan ziemlich gut wie wir den Zellen lebend halten können. Deshalb werden wir diese Werte wohl nicht zu viel ändern. (auch nicht, wenn die gar nicht physiologisch scheinen zu sein vielleicht). Wir wollen aber gut wissen was dann tatsächlich in den Chips passiert. Das stimmt mit der Idee von besser vergleichbare Versuchen die von Researcher 1 (?) genannt wurde.

Die Liste von „Warum"-wir diese Kenntnisse brauchen, oder was wir damit machen wollen, ist ziemlich korrekt. Sachen wie besser vergleichbare Versuchen sind wichtig für uns, wie gesagt. Wenn man zeigen kann, dass man viel weiß über die Bedingungen im Chip, ist das auch ein gutes Verkaufsargument. Beim Design von der neuen Pumpe, wie Engineer 1 jetzt macht, ist es wichtig.

Bei der Assay Planung werden z.B. Metaboliten benutzt wovon man gerne wissen würde wie schnell die rundkommen im Chip. Beim NanoINHALT-Chip gibt es ein eigen Medium Reservoir und eine eigene Pumpe. Damit sollte der Chip mindestens fünf Stunden/Tage(?) selbständig überleben können. Dafür ist es spannend den Volumenstrom zu wissen. Wie viel frisches Medium geht in eine halbe Stunde rein z.B.

5. **Under what circumstances do these needs come up? (in what situation?)**
6. **How would you like to have this data presented?**

Wie ich es gerne sehen würde:

- Sowieso online auf meinem Rechner. Ich will es einfach überall angreifen können.
- Eine interaktive Tabelle wäre ganz nett. Mit Parameters auf einer Axis oder so. Wie verändert sich dann meine Wandschubspannung oder Strömung, wenn ich Parameter ändere.
- Windows A, B, C wären wichtig, aber gerade bei der mittleren Strömung kann man es auf dem ganzen Chip nehmen. Scherkraftspitzen wird es aber Unterschiede geben.

Wir haben Kunden die Chips kaufen. Die wollen dann z.B. wissen welche Einstellungen die brauchen um innerhalb von einer Stunde eine bestimmte Menge Substanz vom ersten Kompartiment zum zweiten zu kriegen.
Also vielleicht sollte so eine Tabelle dann noch einfacher werden als die Volumenstromdaten. Wenn wir Volumenstromen angeben, müssen die Kunden noch immer selbst rechnen. Man könnte auch Datenblätter machen die so eine Frage beantworten, statt trockene Volumenstromwerte geben. Also ein Schritt weiter als nur die Werte vielleicht. (man könnte auch Speech-activated machen)

Wenn die Kaffeemaschine kaputt ist, möchte ich gerne auch ohne Gehirn funktionieren – Researcher 5 2021.

Appendix I Scenarios

The following scenarios are included in this appendix:

Scenario 1: Business Development
Scenario 2: Assay planning
Scenario 3: Contract Development
Scenario 4: Paper publishing
Scenario 5: Chip development

Scenario 1: Business Development

Comments Business developer 2

Ich war direkt sehr angetan, weil es meine Situation gut beschreibt. "In einem Meeting" ist auch allgemein genug formuliert - es umfasst also das Auftreten auf einem Kongress (und dort angesprochen werden) oder ein virtuelles Verkaufsgespräch mit einer Präsentation. Ich habe aktuell nichts hinzuzufügen.

Business developer 2 gets questions from customers such as:

- Are all cells subject to the same shear stress?
- What is the influence of medium change and shear stress on cell development?
- Did you evaluate the impact of flux on the different culture types?
- Is the use of hydrogel relevant?
- What are the flow speeds in the chip?

She might get these questions during a meeting. As she expected these kinds of questions, she has already opened the tool in the background on her laptop. To provide an answer she shows the potential client the information about the chip characteristics.

Later she gets another question while she is on the road. This time she opens the tool, identifies herself and copies an image of the information. She attaches it in the email or LinkedIn message that she just got.

The client is happy to see that TissUse can provide this information and gets a reliable feeling from it.

UI conversation

How do I show this potential client that we understand the flow in the chips?

5. Go to the home screen (if not already there)
6. Choose whatever chip you want to show (probably Chip2, for the example it does not really matter)
7. You can show them that the flow is different at different spots in the chip. Also, what the values are in the entire chip. That it depends on the pump settings can be demonstrated. Even the use of different media or inserts can be shown. This allows for answering questions more generally such as about using hydrogel.
8. If you want, you can copy an image and paste it in whatever communications app you or the client likes.

Back to main text

Scenario 2: Assay planning

Comments Researcher 1
Comments Researcher 3

Researcher 3 is planning an experiment for in the organ chip. She wants a certain shear stress at a specific location in the chip she will be using. This is important if she wants the cells to survive and do what she wants them to do.

She is sitting in the office behind her desk. After grabbing the tool, she searches which pump settings she needs to get the desired circumstances at the specific point in the chip.

On top of that Researcher 3 wants to know how much food the cells are going to get. She checks what the average volume flow rate is for the chosen pump settings. This is a specific case for feeding the Chip4 only via the intestine compartment. I think in most cases we are interested, in how fast factors that are secreted by one organ reach the other organ.

Unfortunately, the nutrition rate is not high enough. However, the shear stresses are. Researcher 3 wants to figure out if there are better pump settings to get the right over-all nutrition rate and the right shear stress at the specific site.

UI conversation

How do I figure out the right pump settings for my cells preferred circumstances?

1. Go to the home screen (if not already there)
2. Tell me which chip you are using (probably Chip2) and if it has any alterations compared to the standard chip configuration. I would say it's more likely to be a new Chip design like Chip3 or Chip4 as the settings for the Chip2 are described by Engineer 3's data already and we have standard settings for the Chip2 assays.
3. At what spot in the chip do you want to know the circumstances? (assumption: in the channel for endothelialized and in the compartment)
4. Which peak or average shear stress would you like at this spot? Have a look around and see what pump setting belongs to that.
5. Write down the pump frequency and pressure that you need.

How do I figure out the right pump settings for my cells' nutritional needs? See above. It is more about distribution of secreted factors.

1. Since you already gave me the chip type and configuration, I know what chip we are talking about. Also, you have just chosen a pump frequency and pressure. This is the average volume flow rate in your chip: X µl/min.

I would like to know how much glucose my cells get per hour. How do I find that out?

1. If you tell me what type of medium you are using, I can tell you in detail. (water, PBS, blood with concentrations). Otherwise, you can multiply the concentration of any substance with the volume flow rate, and you have an approximate answer. As I said, this might be too complex and it would need to include models of glucose consumption for each organ model. The only interesting thing would be; how fast glucose distributes if given to only once compartment.

If my cells start excreting a substance, how long would it take to get from one compartment to the other?

1. For your given chip type, chip configuration and pump settings the approximate turnover time from compartment A to compartment B is X, from Compartment B to compartment A is then Y and for a full circle it takes approximately X+Y.

What if one of these parameters is not as I want it to be? How can I optimize my pump settings to find a good compromise?

1. Which parameter is not as you would want it to be?
2. I can give you a scale for this parameter. You can move it around a bit around the value that you chose. Say you want it to be X. Then you would need pump pressure Y and frequency F. Then this would be the shear stresses and the volume flow rate. Would that work for the cells?
3. If yes, great, then work with these pump settings
4. If no, I am not sure if there will be a pump setting that complies to both your requirements on the volume flow, the shear stresses and the turnover times. Maybe try a different concentration medium if you want to change your nutrients. If something more thorough is needed, contact TissUse's scientists or engineers.

Questions:

- Are there recipes for the different types of medium that you use for assays? Yes, there are recipes, but each project/co-culture setup has its own formulation.
- Is there a standard medium? No
- Is there common knowledge on how much nutrition certain cells consume per hour? No, different for each organ model/medium formulation.
- Do you want to know the shear stresses in the channels, in the compartments, everywhere simultaneously? Ideally ;)
- I imagine you come in with a question "I want an endothelialized channel, so I need a certain shear stress at point A, B and C. Also, I want a gut model in compartment 1 and a liver model in compartment 2. They need sufficient amounts of food. So, I want the total volume flow rate to be X. What pump settings do I need for that?" What do you think of this question? Yes, that would be good ☺ Das wäre der Idealfall. Wenn du Anforderungen hast an die Kanäle und im Kompartiments wirst du wohl limitiert sein.
    - Über wie viel Einsicht ich haben woll. Engineer 3's Tabelle wusste ich nicht was ich damit anfangen sollte. Ich will es so einfach wie möglich. Vielleicht wäre es interessant so eine Art Expertenmodus. Ich will die Kunden nicht zeigen was für Modelle da hinter stecken. Expertenmodus vielleicht interessanter bei Assay Entwicklung. Wenn wir ein festen Assay haben, dann muss man sich auch daranhalten.
    - wieder mal: die Möglichkeit zum Ausschließen, dass der Flow einen Grund der irgendwelchen Problemen ist, ist ganz interessant.
    - Über Eingabe von Flowanforderungen: Ich würde überall alles eingeben. Vor allem Shearstresses Maxima und Minima. Daneben kann ich mich vorstellen, dass verschiedene Leute etwas anderes Bevorzugen. Also, manchen möchten vielleicht gerne selbst rumspielen mit den Pumpeinstellungen um zu schauen was rauskommt.
- Does it ever happen that you are not exactly sure what flow circumstances you want? If so, what do you want to know to have everything clear for yourself? I think most of the time; we want the fastest distribution/fastest flow rate at a shear stress that is still accepted/nor harmful to the organ models in the organ compartment. If there are

endothelial cells, we would probably also consider, if the shear stress in the channels is sufficient, but as I am not working with endothelial cells, it would be good, if Researcher 4/Researcher 5/Researcher 7/Researcher 8 would give their input.

- Do circulation time and volume flow always come after the shear stress in importance? No, for me the circulation time is more important, however, I always need to test if this leads to a shear stress which is not harmful to my organ models.
- Are the medium change moments in a rhythm or does that vary during the assay? Sometimes they are in a rhythm, sometimes they vary (like every 2-3 days)
- In Engineer 3's table it is possible to see several pump settings in one eye-span and compare them. Is that interesting, or do you simply want to see which pump settings you need for the circumstances that you want? I think it would be good to also have the option to see, how a change in pressure/frequency would influence the shear stress or circulation time.
- Does the above scenario cover all scenarios that you see yourselves in? Or are there other scenarios in which you want to know chip flow data? I think we should have asked this to everybody, so that we do not miss a scenario. Especially the transfer of one setup in the Chip2 to another Chip design/Chip setup (including Transwells, Dynarrays, Hydrogels) is definitely something that would be interesting for several projects. But this is covered by the next paragraph. Btw, the assay planning it also part of the contract development and the transfer of assay settings to different configurations is not solely a thing that is done in contract development. I would therefore not call the next paragraph contract development, but rather 'Comparison between different setups'.

Back to main text

Scenario 3: Contract Development

Immer zeigen wo der Flow wie ist. Ein Contract developer will auch schon am Anfang wissen wie der Flow wo ist. Also ist nicht ganz anderes als normale generelle Assay Planung.

Wir machen versuchen und da raus kommt ein Assay. Erst wenn es ein Protokoll gibt kannst du es ein Assay nennen. Man kann z.B. Stoffe A B oder C alles auf einem gleichen Assay testen.

Researcher 4 works with a big company. Together they are developing a new organ model. It involves an alteration to the standard chip configuration (endothelialized/ceramic/Transwell). For the model development it is important to know what the difference in flow characteristics is between the standard chip and the altered configuration.

Hence Researcher 4 wants to see both the flow characteristics for the standard chip and the chip with an altered configuration. This way she can compare them.

As the altered configuration is only characterized for a Chip2 and Researcher 4 uses a Chip4, she would like to extrapolate the difference between standard and altered configuration to the chip she uses.

UI conversation

How can I compare two different configurations of a chip?

1. Go to the home screen (if not already there)

2. Which chips would you like to compare? (probably standard Chip2 configuration and Chip2 with bone marrow insert or Transwell)
3. This is what they both look like with standard pump settings (0.5Hz and +-500mbar)
4. If you want, you can have a look at different pump settings (currently I do not know if the difference between the chips changes with different pump settings)
5. I would like to show you the difference between the two explicitly. Are you interested in that?
6. You can copy or save both images if you want. So that you can share them with the company during a biweekly meeting for example. Just use your right mouse button on the images, or the explicit save or copy button.

Back to main text

Scenario 4: Paper publishing

Researcher 3 has finished her experiment. She wants to publish the results. In her methods section she wants to show what circumstances she used in the chip. This is important to make her results more meaningful and reproducible.

Sitting behind her desk, typing her paper, she opens the tool and finds the chip and pump settings that she used. After exporting an image, she can copy it into her manuscript and can continue working.

UI conversation

How do I get a good image for my publication? I want to show what circumstances my cells were under.

1. Go to the home screen (if not already there) (Maybe open a saved chip configuration?)
2. What chip are you using (probably Chip2) and are there any inserts or other alterations?
3. Tell me what you would like to know. I assume you want to show
   - the peak and average shear stress (in the channel and in the compartments)
   - the mean volume flow rate and nutrients profile
   - maybe the pump profiles
   - the travel time from each compartment to the next
4. I can provide all these in an image, or in a table. You can copy them, or save them, by clicking the right mouse button. You can also use the copy or save buttons for each image or table.
5. Do the images have to be grayscale or full color?

Back to main text

Scenario 5: Chip development

Comments Engineer 1

ich finde deine Szenarien super! Wirken wirklich gut recherchiert, weshalb ich das ein gutes Gefühl habe, dass du an alles gedacht hast. Außerdem ist es gut strukturiert und mir fällt es schon direkt leicht, daraus klare Anforderungen an das Tool zu definieren, obwohl ich mich damit ja lange nicht so genau befasst habe wie du. Gute Arbeit!

Engineer 1 has just characterized a new chip design. He wants to add it to the database of the tool. He opens the tool on his desktop and identifies himself. Then he defines a new chip design and the available data about it. Once he is done, he checks it and then closes the tool again.

The characteristics of the new chip design are now available for everyone that has the tool.

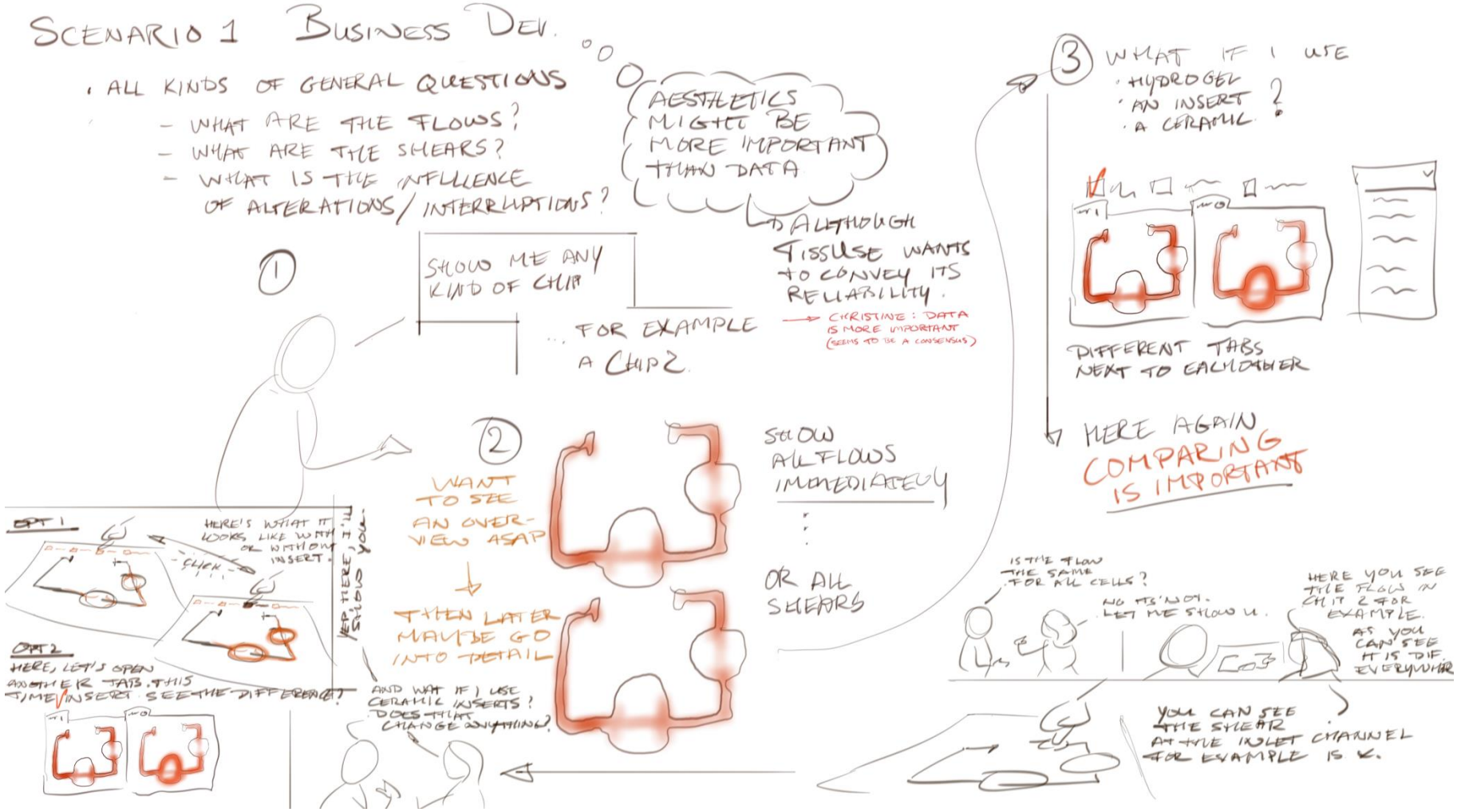
UI conversation

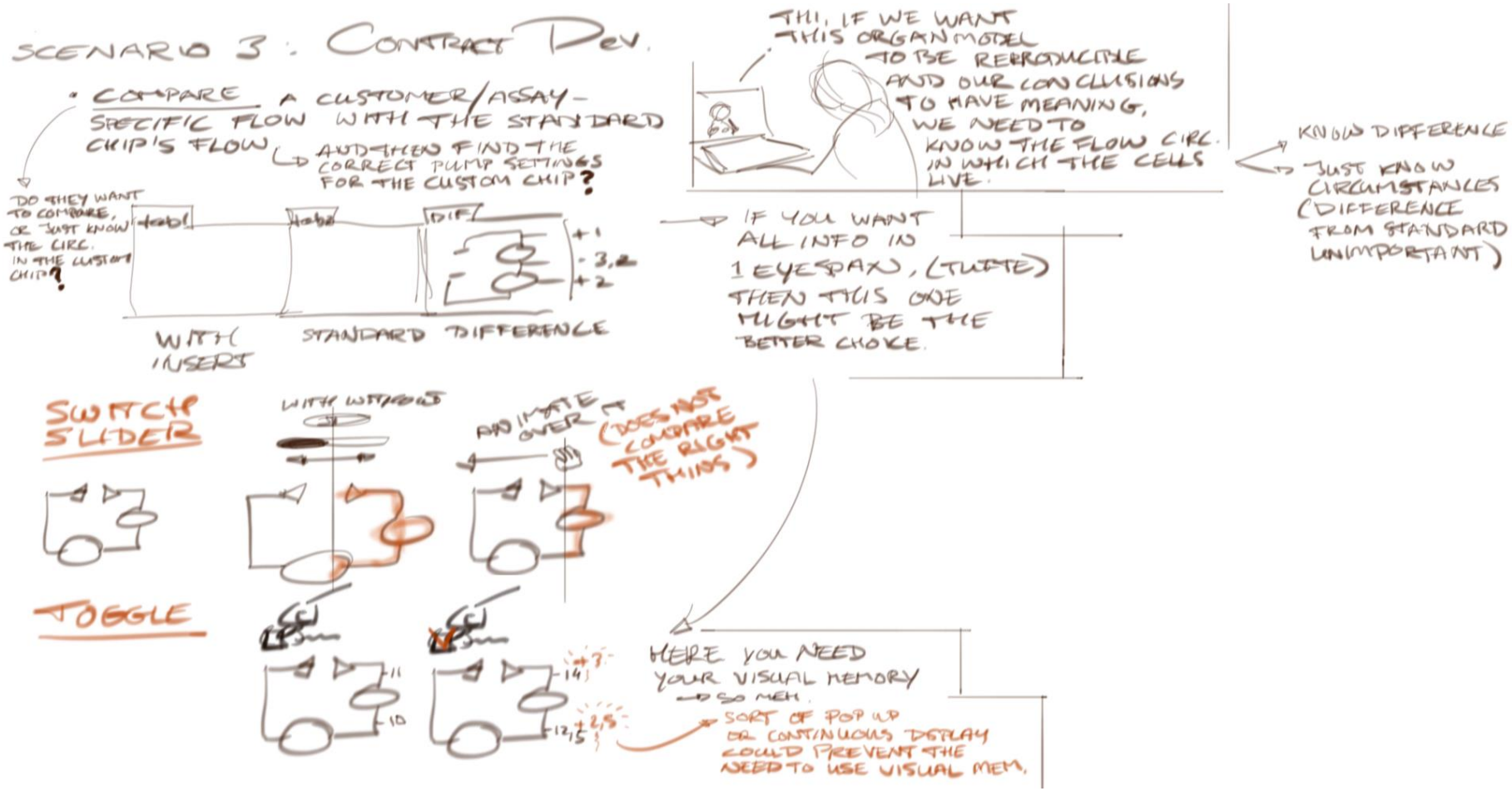
How can I add data about a new chip in the flow information tool?

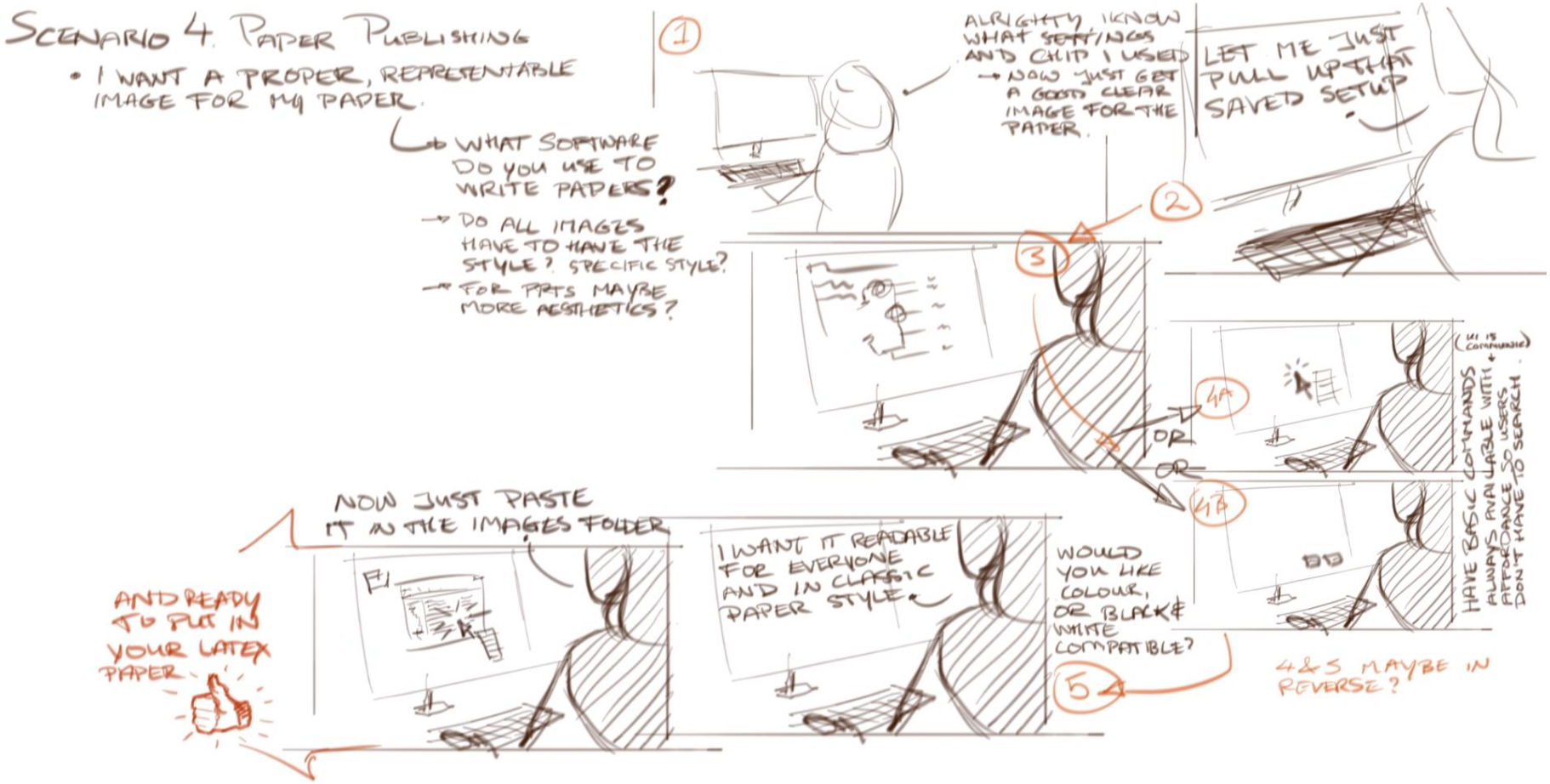
1. Go to the home screen (if not already there)
2. Say you want to add new chip characteristics
3. Not everyone should touch this, so please identify yourself.
4. Would you like to add new characteristics to a chip, or are we talking about a completely new chip design? (or a new medium recipe maybe? Or a new pump design maybe?)
5. Add a new characteristic to a chip:
    a. Open up the database of flow velocities and insert new values that have been verified.
6. Add an entirely new chip:
    a. Upload COMSOL simulation results. You simulated one cycle for one pump setting (combo of pressure and frequency) with a certain medium.
    b. The software can take everything it needs from this.
    c. Just specify some points where you want the scientist to be able to see specific numbers. These are in general the channels and the compartments (entire compartment, entrance, wall, exit, center above and below Transwell/insert)
    d. The software will determine the average values and they will be readable.
7. Added everything you know? Is everything in order?
8. Logout and everything is in order
9. If you want, you can have a look at the new characteristic.

Back to main text

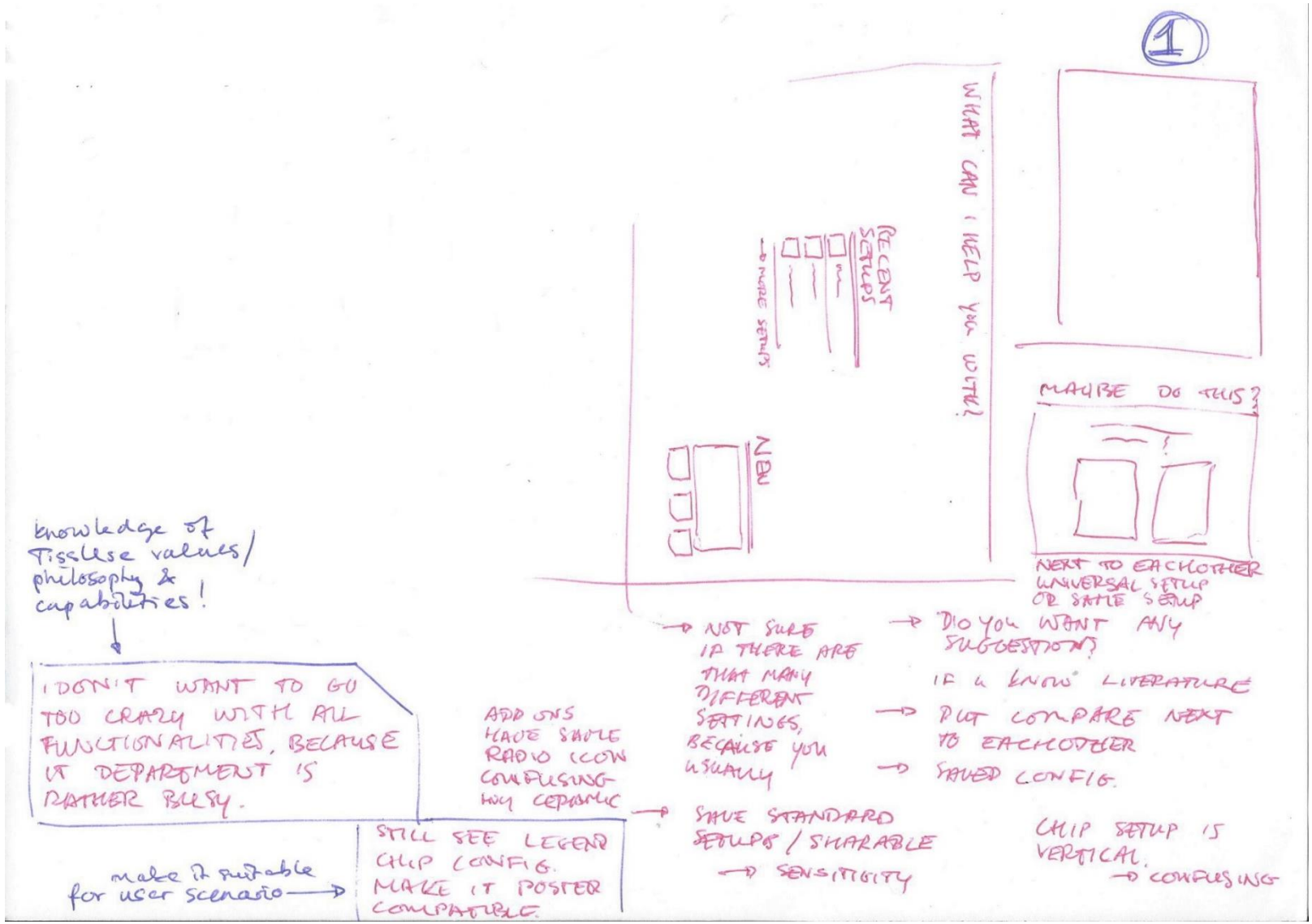
Appendix J Graphical scenarios

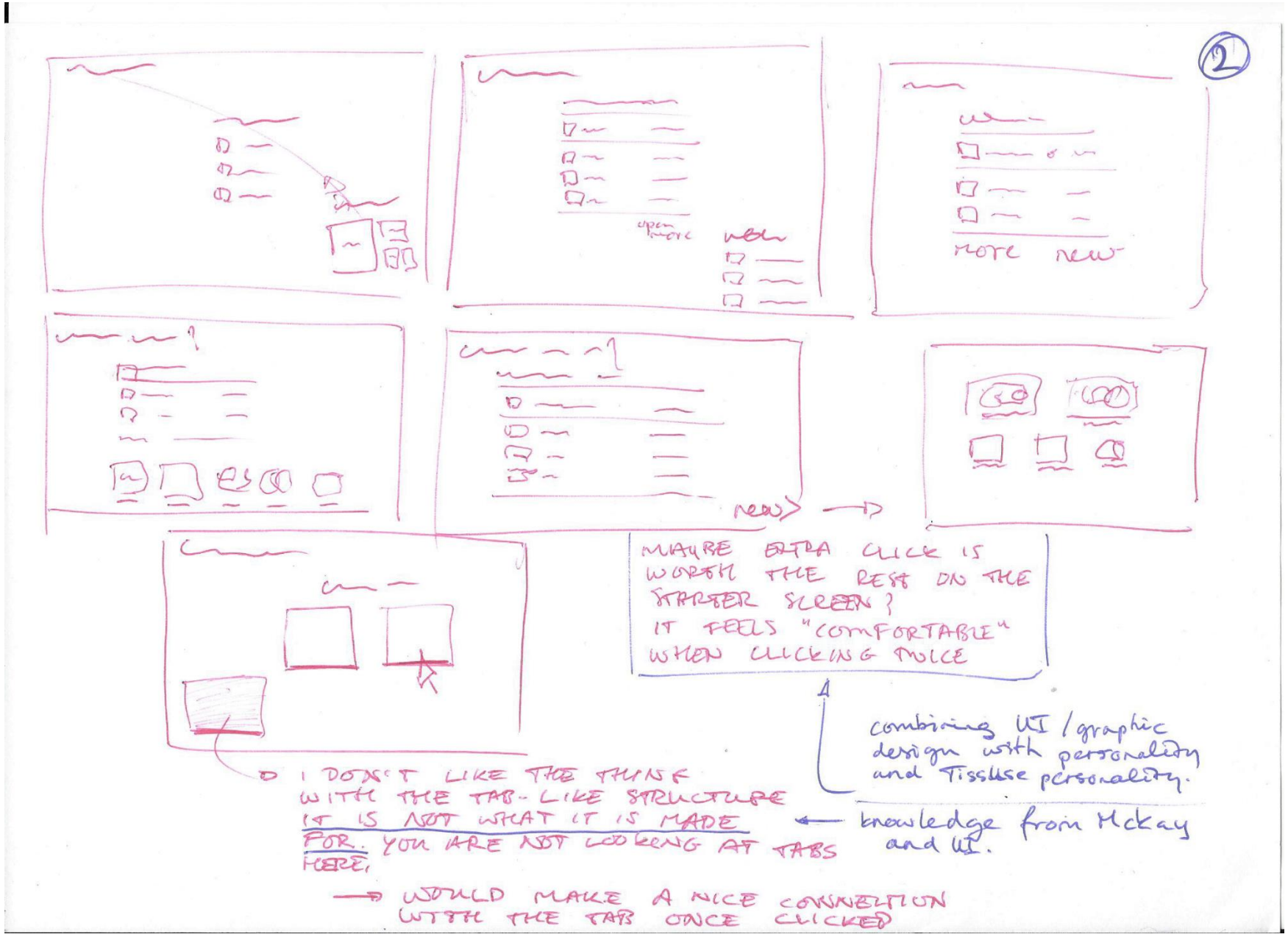


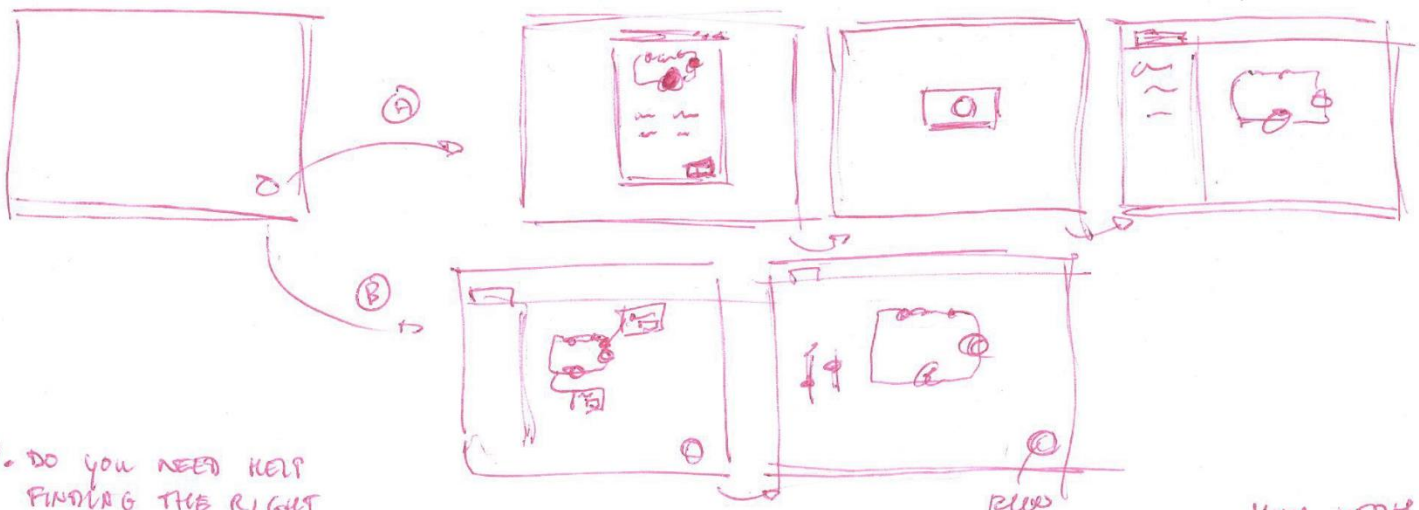

SCENARIO 3: CONTRACT DEV.
• COMPARE A CUSTOMER/ASSAY-SPECIFIC FLOW WITH THE STANDARD CHIP'S FLOW
↳ AND THEN FIND THE CORRECT PUMP SETTINGS FOR THE CUSTOM CHIP?
DO THEY WANT TO COMPARE, OR JUST KNOW THE CIRC. IN THE CUSTOM CHIP?
DIF
+1
-3,2
+2
WITH INSERT
STANDARD DIFFERENCE
THI, IF WE WANT THIS ORGAN MODEL TO BE REPRODUCIBLE AND OUR CONCLUSIONS TO HAVE MEANING, WE NEED TO KNOW THE FLOW CIRC. IN WHICH THE CELLS LIVE.
KNOW DIFFERENCE
JUST KNOW CIRCUMSTANCES (DIFFERENCE FROM STANDARD UNIMPORTANT)
IF YOU WANT ALL INFO IN 1 EYESPAN, (TWEAK) THEN THIS ONE MIGHT BE THE BETTER CHOICE.
SWITCH SLIDER
TOGGLE
WITH WITHOUT
ANIMATE OVER
(DOES NOT COMPARE THE RIGHT THING)
11
10
+7
14
12,5
+2,5
HERE YOU NEED YOUR VISUAL MEMORY
SO MEM.
SORT OF POP UP OR CONTINUOUS DISPLAY COULD PREVENT THE NEED TO USE VISUAL MEM.


SCENARIO 4. PAPER PUBLISHING
• I WANT A PROPER, REPRESENTABLE IMAGE FOR MY PAPER.
WHAT SOFTWARE DO YOU USE TO WRITE PAPERS?
→ DO ALL IMAGES HAVE TO HAVE THE STYLE? SPECIFIC STYLE?
→ FOR PPTS MAYBE MORE AESTHETICS?
1
ALRIGHTY I KNOW WHAT SETTINGS AND CLIP I USED
→ NOW JUST GET A GOOD CLEAR IMAGE FOR THE PAPER.
LET ME JUST PULL UP THAT SAVED SETUP
2
3
4A
OR
OR
4B
HAVE BASIC COMMANDS ALWAYS AVAILABLE WITH + PERFORMANCE SO USERS DON'T HAVE TO SEARCH
(UI is communism)
NOW JUST PASTE IT IN THE IMAGES FOLDER
I WANT IT READABLE FOR EVERYONE AND IN CLASSIC PAPER STYLE.
WOULD YOU LIKE COLOUR, OR BLACK & WHITE COMPATIBLE?
5
4&5 MAYBE IN REVERSE?
AND READY TO PLUG IN YOUR LATEX PAPER

Appendix K Ideation sketches




2
open more
MORE
NEW
NEW
MAYBE EXTRA CLICK IS WORTH THE REST ON THE STARTER SCREEN?
IT FEELS "COMFORTABLE" WHEN CLICKING MOUSE
combining UI / graphic design with personality and Tissluse personality.
knowledge from Mckay and UI.
I DON'T LIKE THE THING WITH THE TAB-LIKE STRUCTURE IT IS NOT WHAT IT IS MADE FOR. YOU ARE NOT LOOKING AT TABS HERE.
WOULD MAKE A NICE CONNECTION WITH THE TAB ONCE CLICKED



3

1. DO YOU NEED HELP FINDING THE RIGHT PUMP SETTINGS?

YES PLEASE

2. WHAT REQUIREMENTS DO YOU HAVE?

- IN THE CHANNELS
- I WANT THE MAX SHEAR
- TO BE X
- AND THE MIN SHEAR
- TO BE Y
- ALSO I NEED A VOLUME FLOW
- TO BE Z

3. ALRIGHTY, LET ME THINK

OK

4. WHAT ABOUT THIS? IF WE TAKE PUMP SETTINGS P & F YOU'LL GET
- MAX SHEAR $x+\Delta x$
- MIN SHEAR $y+\Delta y$
- VOLUME FLOW $z+\Delta z$.

HMM YEAH THATS OK, BUT I NEED THE VOLUME FLOW TO BE CLOSER TO Z

5. HMM WELL THEN MAYBE DO THIS ONE, YOU'LL GET

$x+\Delta x$
$y+\Delta y$
$z-\Delta z$

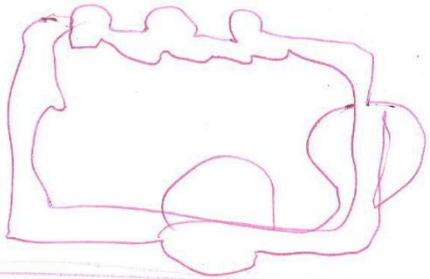
HMM, YEAH THAT IS STILL NOT IT. CAN I LOOK AROUND MYSELF?

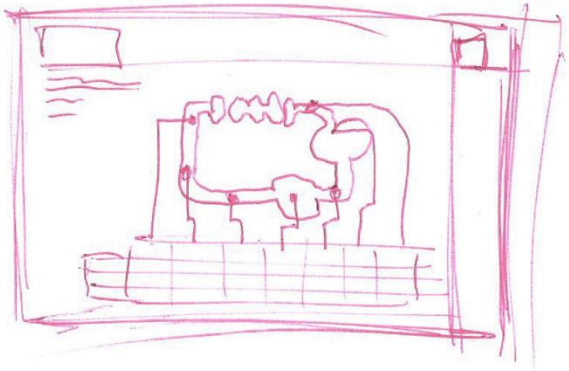
6. YEAH SURE. HERE YOU CAN SEE THE BEHAVIOUR OF THOSE THREE VARIABLES FOR DIFFERENT P & F.

ALRIGHT, I SEE I NEED THIS P & F FOR THE CORRECT VOLUME FLOW. AND THEN MY X AND Y SHEARS ARE THIS. THAT SHOULD BE OK

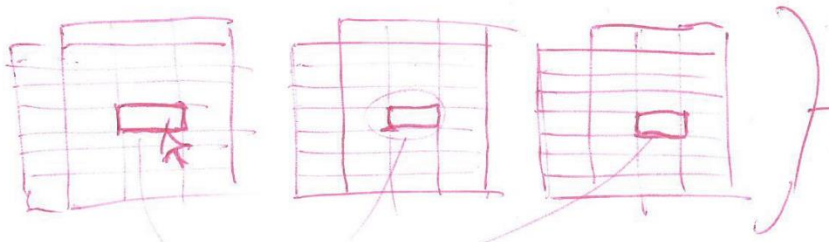
Chip 2
pressure -- :
frequency :

Chip 2
ceramic comp A
transwell with B
PBS filled
pressure x
frequency y





4



→ THESE TABLES ARE WHAT WE CHARACTERIZE. THEY FORM THE INFORMATION BASIS OF THIS TOOL.

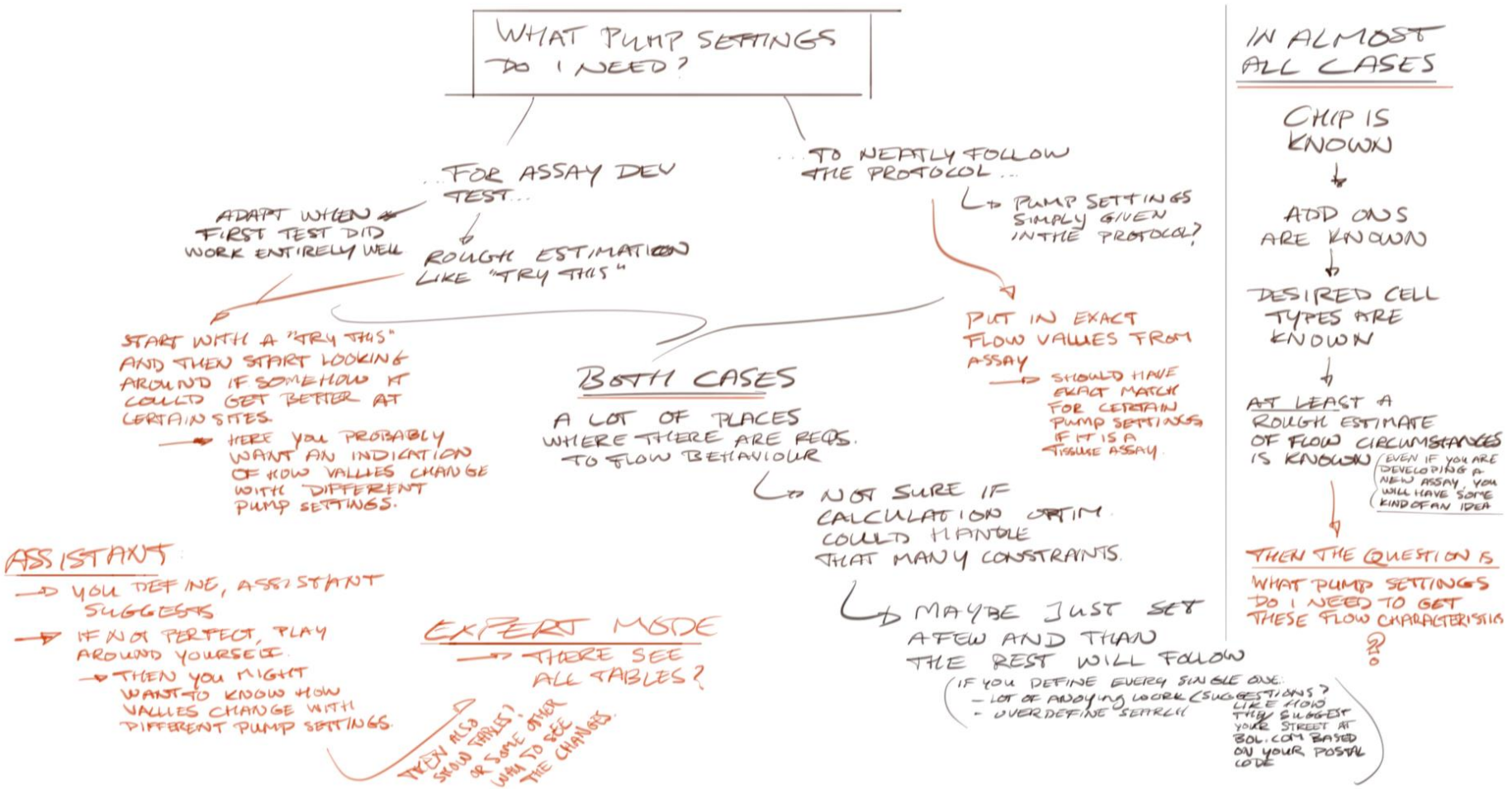
~~BE~~MOVES WITH HOVER
STAYS WITH CLICK/TAP

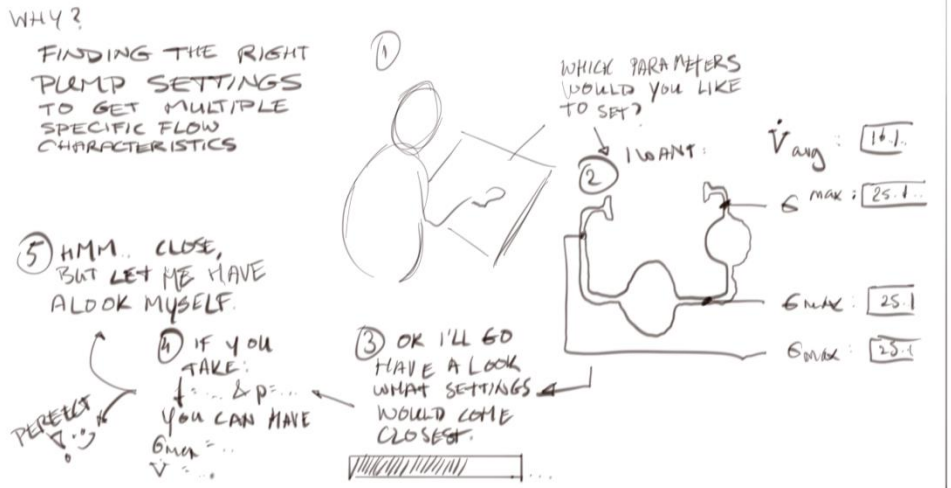
PLEASE GIVE THE FLOW CIRCUMSTANCES THAT YOU WANT IN THE CHIP.

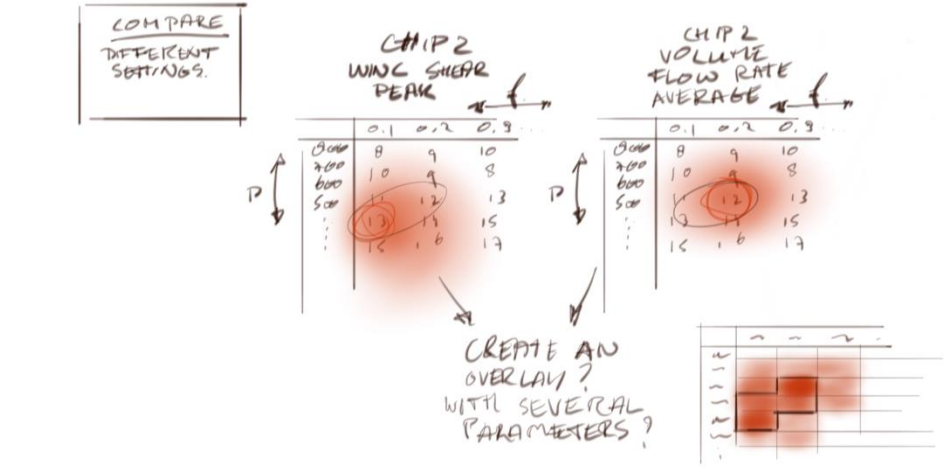
YOU CAN GIVE AT MOST 3 (OTHERWISE IT GETS TOO HARD TO COMPUTE)

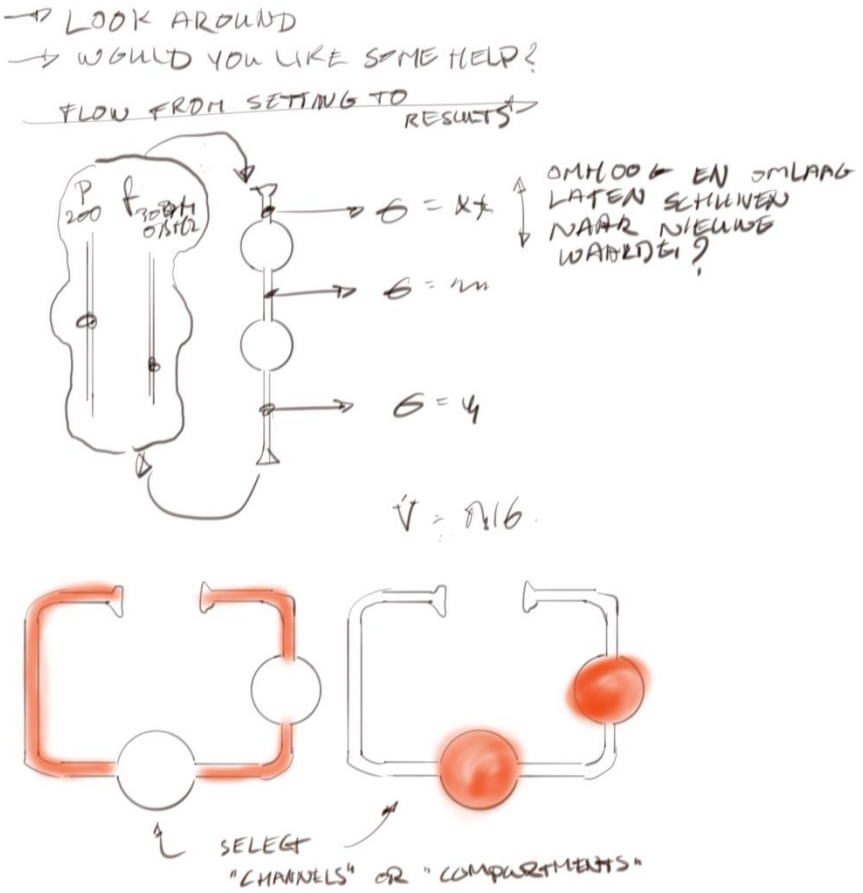
HAVE MORE? → TRY SELECTING THE THREE MOST IMPORTANT ONES PROBABLY THE REST WILL FOLLOW AUTOMATICALLY TO THE RIGHT VALUES

REQUIREMENT:
min Shear
at Channel:
Gr. dyn/cm²


WHAT PUMP SETTINGS DO I NEED?
FOR ASSAY DEV TEST...
ADAPT WHEN FIRST TEST DID WORK ENTIRELY WELL
ROUGH ESTIMATION LIKE "TRY THIS"
START WITH A "TRY THIS" AND THEN START LOOKING AROUND IF SOMEHOW IT COULD GET BETTER AT CERTAIN SITES.
HERE YOU PROBABLY WANT AN INDICATION OF HOW VALUES CHANGE WITH DIFFERENT PUMP SETTINGS.
...TO NEATLY FOLLOW THE PROTOCOL...
PUMP SETTINGS SIMPLY GIVEN IN THE PROTOCOL?
PUT IN EXACT FLOW VALUES FROM ASSAY
SHOULD HAVE EXACT MATCH FOR CERTAIN PUMP SETTINGS IF IT IS A TISSUE ASSAY.
BOTH CASES
A LOT OF PLACES WHERE THERE ARE REQS. TO FLOW BEHAVIOUR
NOT SURE IF CALCULATION OPTIM. COULD HANDLE THAT MANY CONSTRAINTS.
MAYBE JUST SET A FEW AND THAN THE REST WILL FOLLOW
(IF YOU DEFINE EVERY SINGLE ONE:
- LOT OF ANNOYING WORK (SUGGESTIONS? LIKE HOW THEY SUGGEST YOUR STREET AT BOL.COM BASED ON YOUR POSTAL CODE
- OVERDEFINE SEARCH)
ASSISTANT
YOU DEFINE, ASSISTANT SUGGESTS
IF NOT PERFECT, PLAY AROUND YOURSELF.
THEN YOU MIGHT WANT TO KNOW HOW VALUES CHANGE WITH DIFFERENT PUMP SETTINGS.
EXPERT MODE
THERE SEE ALL TABLES?
THEN ALSO SHOW TABLES? OR SOME OTHER WAY TO SEE THE CHANGES.
IN ALMOST ALL CASES
CHIP IS KNOWN
ADD ONS ARE KNOWN
DESIRED CELL TYPES ARE KNOWN
AT LEAST A ROUGH ESTIMATE OF FLOW CIRCUMSTANCES IS KNOWN
(EVEN IF YOU ARE DEVELOPING A NEW ASSAY, YOU WILL HAVE SOME KIND OF AN IDEA
THEN THE QUESTION IS
WHAT PUMP SETTINGS DO I NEED TO GET THESE FLOW CHARACTERISTICS
?!


WHY?
FINDING THE RIGHT PUMP SETTINGS TO GET MULTIPLE SPECIFIC FLOW CHARACTERISTICS
1
WHICH PARAMETERS WOULD YOU LIKE TO SET?
2
I WANT:
$\dot{V}_{avg}$: 10.1
σ_{max} : 25.1
σ_{MAX} : 25.1
σ_{max} : 25.1
3 OK I'LL GO HAVE A LOOK WHAT SETTINGS WOULD COME CLOSEST.
4 IF YOU TAKE: f: ... & p: ... YOU CAN HAVE σ_{max} = ... $\dot{V}$ = ...
PERFECT
5 HMM.. CLOSE, BUT LET ME HAVE A LOOK MYSELF.


WHY WOULD PEOPLE WANT A TABLE?
COMPARE DIFFERENT SETTINGS.
CHIP 2
WALL SHEAR PEAK
f
p
0.1 0.2 0.9
8000 8 9 10
4000 10 9 8
2000 11 12 13
1000 12 11 15
500 14 16 17
CHIP 2
VOLUME FLOW RATE AVERAGE
f
p
0.1 0.2 0.9
8000 8 9 10
4000 10 9 8
2000 11 12 13
1000 12 11 15
500 14 16 17
CREATE AN OVERLAY? WITH SEVERAL PARAMETERS?


LOOK AROUND
WOULD YOU LIKE SOME HELP?
FLOW FROM SETTING TO RESULTS
P 200
f 3000 1500 1000 500
σ = 14
σ = 11
σ = 4
OMHOOG EN OMLAAG LATEN SCHUIVEN NAAR NIEUWE WAARDE?
$\dot{V}$ = 8.16
SELECT "CHANNELS" OR "COMPARTMENTS"

Appendix L Micro iteration notes

Feedback Business developer 2
Business development
Adobe XD prototype
11-5-2021

I think about 80 percent of what I do will be a standard chip configuration. 20 percent will be specific configurations of which half, so 10 percent, actually incorporates inserts. So 80 percent of the time I will click on one of the favourites.

Chip2 ist der simpelste. Anhand davon erklärt sie den Aufbau des Chips

PDF ist vertrauenswürdiger. Deshalb schickt sie meistens PDFs nach Kunden oder anderen mit Fragen. -> an Option to export a PDF directly might hence be a good idea.

Es wäre ganz cool, wenn man so ein Tool auch mitnehmen kann auf einem Tablet nach Messen oder so. Damit man sofort erklären kann was passiert im Chip and Passanten.

As a knowledgeable person I have to explain to the customer/user what is good/bad/physiological. I can't see that in the table right now. It would be cool to have some kind of comparing mechanism.

Variablen apart

Geschwindigkeit auch interessant. Auch wenn Shear schon definiert ist, ist die Flussgeschwindigkeit manchmal noch immer interessant. Also, würde die bestimmt doch zeigen.

Heatmap ist so viel besser Daten in Tabelle ist ja keine schnelle Visualisierung. Wenn ich „schnell und klar" zeigen will was passiert, ist ein Heatmap ja viel besser. Was macht so eine Tabelle dann? Dann muss ich alle diese Werte lesen und selbst ein Bild formen. Wenn du das Bild ja sowieso machst mit der Simulation, kannst du es ja hier auch einfügen, oder?

Ich will doch immer auch die Tabelle. Weil ich die tatsächlichen Daten manchmal auch brauchen werde.

Ich will wissen was im Chip passiert, wenn es ein biologisches Modell im Chip befindet. Das ist das Ziel.

Feedback Engineer 1
Chip development
Adobe XD prototype
11-5-2021

Wenn man die Volumina auslesen könnte wäre ganz interessant. Dann kann man das alles zusammen setzen in einem Tool. Ich denke, dass es viele Sachen in diesem Tool passen letztendlich, aber das erste Ziel, wie Business developer 3 es oben auch beschrieben hat „zu wissen was im Chip passiert, wenn es ein biologisches Modell drin ist" sollte momentan noch am wichtigsten bleiben.

Wäre ganz cool, wenn es so eine Blau, pink, Neon Green Taste gäbe mit Bewerbungsdaten.

Feedback Researcher 1
Biologist
Adobe XD prototype
12-5-2021

Frage Business developer 4 mal um die richtigen Bilder von Flow Circuits. Die hat sie glaube ich.

Welche Punkte sind die Daten in die Tabelle? Ich verstehe diese Verteilung nicht so genau, warum es manchmal eine Wert gibt und manchmal zwei näher an einander. -> Mach deutlicher was welche Messpunkte sind.

Es verwirrt auch, dass die Werte gleich sind in verschiedene Zeilen und die max. Wert kleiner ist als die Minimum Wert.

Legende fehlt im Farbenbild.

Was mit A-B und B-A gemeint wird bei Flow time ist mir nicht ganz deutlich. Es gibt hier auch kein Link mit dem Bild und bei Features wird innere and äußere Kompartiment genutzt statt A und B. Deshalb ist es nicht klar.

Konsistenz und Identifikation sind wichtig.

Sprechensweise ist es im

- Chip2: inner und outer

- Chip2 24: small and big

- Chip4: Darm-, Nier-, Neuro-... Kompartiment. In Chip4 wird meistens ein ADME (application, difussion, metabolation, excretion) Modell gemacht, deshalb sind die Organmodelle fester mit den Kompartimenten verbunden. Kann aber noch immer wechseln. Wenn es wechselt und du nennst es noch immer das Darmkompartiment, aber es ist ein anderes Organ drin, wird es recht verwirrend.

Wenn das Tool nur intern benutzt wird, würde ich vorschlagen um die in Praxis benutzte Wörter zu benutzen. Wenn es nach Kunden geht wirkt das eh verwirrend, also nutze etwas Konsistentes.

Mach es deutlicher, dass es echt nichts drin ist beim Pumpe. Mach die Farbe noch blasser, oder nur die Outline oder so.

Mach deutlicher, dass Volume Flow ein Mittelwert ist. Die Begründung von warum du nur der Mittelwert zeigst ist aber korrekt. Das wäre nur echt interessant für die Nutrition, also ein Mittelwert ist dann genug.

Für Deutlichkeit: Wenn du hoverst über die Messpunkte im Bild, lass dann die gleiche Werte auch in der Tabelle leuchten. Das kann in beide Richtungen. Also, wenn du in der Tabelle hoverst, kannst du die Messpunkte im Bild auch leuchten lassen. Dann versteht man besser welche Daten von welchem Punkt sind.

Ich mochte alles im Bild haben. Also wenn ich das Bild exportiere/kopiere, möchte ich wissen welche Einstellungen benutzt sind, wie es aussieht und was die Daten sind.

Wenn du zwei Anforderungen hast du total quatsch sind, was passiert dann?

Wenn es einen Vorschlag macht ist es danach eine gute Idee zu fragen: Willst du es akzeptieren oder willst du es noch ändern? (dann kommen wir bei die „schau selbst Tabelle an“ Geschichte) Wurde es

gut finden, wenn ich selbst rumgucken kann in den Tabellen. Das wäre besser als wenn ich das Tool die ganze Zeit neu einstellen sollte.

Ich denke, dass es eine gute Idee ist um konsistent zu sein: Alles was rot ist, kann ich klicken.

Nicht deutlich, dass die Konfiguration die jetzt im Tool ist benutzt wird von der Pump Setting Finder.

Auch nicht deutlich was den Unterschied ist zwischen Pump Setting Finder und das Standard Schirm was ich momentan anschaue.

Lass es nicht anfangen mit einer Vorbildanforderung. Einfach eine leere Anforderung wo ich selbst klicken kann.

Beides bpm und Hz. Weil die Hälfte der Leute wird sagen ich will bpm und die andere Hälfte in Hz.

Schreib mal ein Mail nach alle LabUser mit ansagen, dass du präsentieren wirst und dass es cool wäre wenn so viel wie möglich Leute kommen.

Feedback Development department leader
Chip development
Adobe XD prototype
17-5-2021

Make an option to say whether the pump is going clockwise or counter-clockwise

Grafischen Darstellung von flow und shear im Bild. Beiden sollten ja möglich sein, weil manche Leute woll interessierten sein werden in Shear und anderen in Flow Speed. -> Was stellt mein eigentlich genau dar im Bild? Weiß ich eigentlich nicht. Habe jetzt einfach ein Shot vom Simulation genommen, aber die Tabellen zeigen etwas andere eigentlich.

Das Tool ist erstens hauptsächlich für uns selber, aber definitiv für uns und Kunden beides.

Mach mal klar welche Punkte gemessen und welche simulierte Dateien sind. Ist für einen Wissenschaftler auch wichtig zu wissen das es Unterschied gibt.

Feedback Professor 1
Industrial design University of Twente
Adobe XD prototype
18-5-2021

I don’t like the word help in your opening line. It feels a bit condescending towards the user.

I think the lines between the location indicators in the circuit and the table on the right is quite clarifying. -> However when you put them all together it will get quite packed with lines and you lose the ability to distinguish them from each other which is the whole point of the lines.

Feedback Bereichsmeeting
Adobe XD prototype
18-5-2021

Es bedient viele Frage die wir haben.

Sehr cooles Programm! Was mir aufgefallen ist: Bei den Chip Grafiken fehlt der Chip3. Die Grafik, die du für den Chip3 aufgeführt hast ist der Chip3plus.

Pumprichtung fehlt noch? Flow time = turnover time? Oder Flow time = distribution time? Zuordnung Compartment A und B in Grafik wäre wichtig.

Diagramm welche Geschwindigkeit o.ä. hinter den verschiedenen Farben im Bild stehen (du bräuchst eine Legende)

Vakuum fehlt. Bzw. ein Hinweis das Vakuum nicht den Fluss beeinflusst. Es gibt Situationen wo Vakuum und Druck nicht die gleiche Wert haben.

Which programming language is this? Engineer 1: Momentan ist es in Adobe XD aber es visualisiert nur. Später kann es in irgendeine Sprache gemacht werden.

Ist das Bild eine Schematik oder wird das eine richtige Flowsimulation darstellen? Also, wird sich das Bild/die Simulation ändern, wenn man eine Keramik/Transwell einfügt?

Die Bilder müssten aus Simulationen kommen die wir vorher gemacht haben. Also, das Programm selbst mach keine Simulationen, sondern stellt Daten dar, die wir erhoben haben.

Beim Pump Setting Finder: Kann man den Requirements Prioritäten zuordnen? Oder wonach geht das Programm. Software development employee: wenn du die Requirements Prioritäten gibt wird es ja recht eine andere Mathematik die viel komplexer sein wird.

Wie groß ist (oder wird) denn die Datenbasis sein die dem Zugrunde liegt? Ich denke dabei an die Randbereiche wo die Pumpe eventuell an ihr funktionelles Limit kommt (also z.B. hohe Frequenz bei geringerem Druck). Also ich stelle bspw. ein 2 Hz bei ±300 mbar, rechnet das Programm dann einfach hoch von seinen Daten die vielleicht bei 0.5 Hz erhoben wurden oder „weiß“ das Programm, dass bei diesen Settings die Pumpe nicht mehr richtig funktioniert?

Wird der Pump Setting Finder die Chip Features die man eingesetzt hat beachten (Keramik/Transwell)? Bzw. könnte er auch vorschlagen, dass man einen Widerstrand einsetzt um die Flussgeschwindigkeit zu erhöhen?

Bei Prototyp 2 sind die Einheiten in den Tabellen auf der rechten Seite in runden Klammern nicht eckige wie in den Tabellen unten

Soll das Programm auch für Kunden nutzbar sein, also in irgendeiner Form veröffentlicht?

I will definitely use this database of simulations for the PBPK. I will have student working on that starting in the next weeks.

Man müsste nochmal Engineer 4 fragen, aber die Limitationen der Steuerungen hängen ja glaub ich auf von den verwendeten Steuerungen ab.

Man könnte für das fehlende Setting gleich ein Anfragetool einrichten mit dem sammelt man dann Wunschsettings. Wenn es zu einem Setting viele Anfragen gibt erhöht dies die Priorität, dass die Daten ermittelt werden.

Appendix M Design guidelines

This appendix contains the design guidelines by which the UI prototype was designed. They are established based on insights from (Tufte, 1998) and (McKay, 2013) combined with the Design Guidelines from TissUse GmbH.

Color palette

Main elements
TissUse GREY

CMYK: 40 / 25 / 20 / 70
RGB: 65 / 74 / 81
HEXA: #404a51

Interactive elements/Legend maximum
TissUse RED

CMYK: 0 / 100 / 85 / 20
RGB: 204 / 0 / 51
HEXA: #cc0033

Legend minimum
CMYK: 100 / 80 / 20 / 20
RGB: 0 / 64 / 128
HEXA: #004080

Buttons on hover

CMYK: 16 / 12 / 13 / 0
RGB: 211 / 211 / 211
HEXA: #d3d3d3

Filled areas

CMYK: 8 / 6 / 7 / 0
RGB: 230 / 230 / 230
HEXA: #e6e6e6

Table emphasis

CMYK: 4 / 2 / 2 / 0
RGB: 242 / 242 / 242
HEXA: #F2F2F2

Background

CMYK: 1 / 1 / 1 / 0
RGB: 249 / 249 / 249
HEXA: #f9f9f9

Typography

Main Tab Title

Source Sans Pro (semibold)
TissUse GREY
34 pt

Table/Dialog title

Source Sans Pro (regular)
TissUse GREY
26 pt

Table subtitle

Source Sans Pro (regular)
TissUse GREY
21 pt

Body (table headers, buttons)
Calibri (regular)
TissUse GRAY
15 pt

Variable

Calibri (regular)
TissUse GRAY
26 pt

Clickable variable

Calibri (regular)
TissUse RED
26 pt

Caption
Calibri (regular)
TissUse GRAY
12 pt

Clickable caption
Calibri (regular)
TissUse RED
12 pt

Buttons

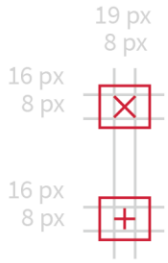
Dividers

Regular divider
#d3d3d3
1 px

Tab divider
TissUse GREY
3 px

Progress indicator
TissUse RED
3 px

Elements



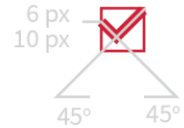
Close
Line thickness: 1 px

Add
Line thickness: 1 px

Fold close
Line thickness: 1 px

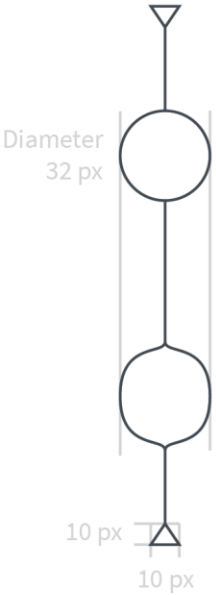
Fold open
Line thickness: 1 px

Checkbox unchecked
Line thickness: 1 px

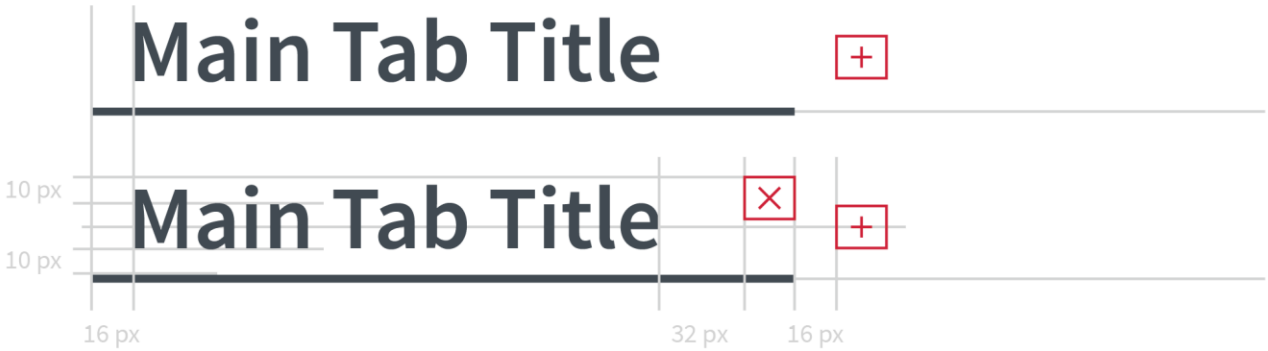


Checkbox checked
Line thickness: 1 px
Check: 3 px

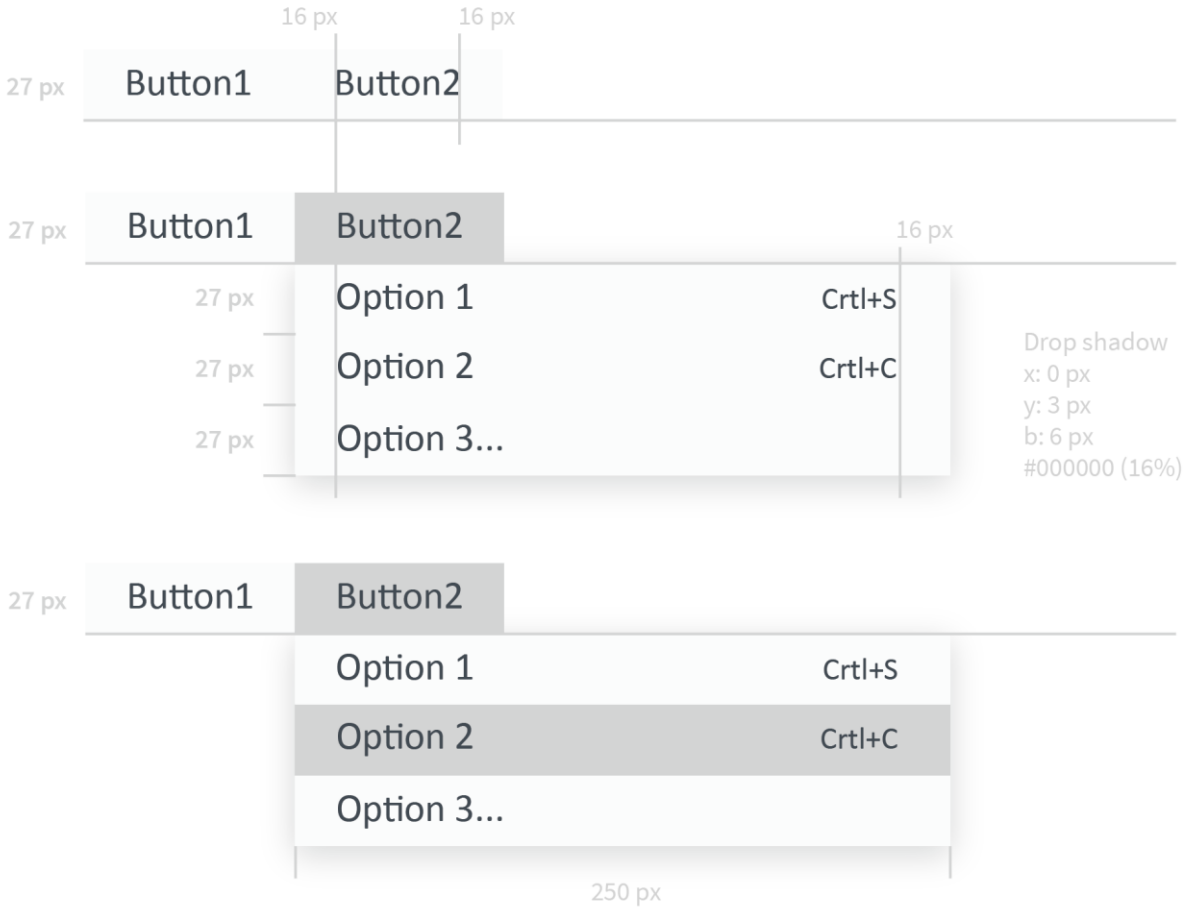
Microfluidic circuit indicator
Data Table aligned
TissUse GREY
1 px



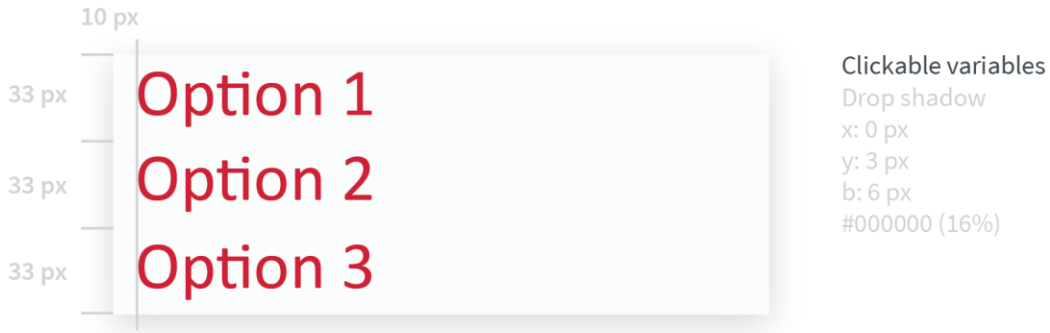
Tab titles

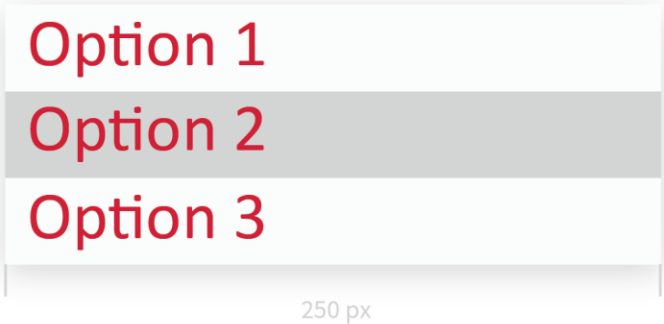


Dropdowns

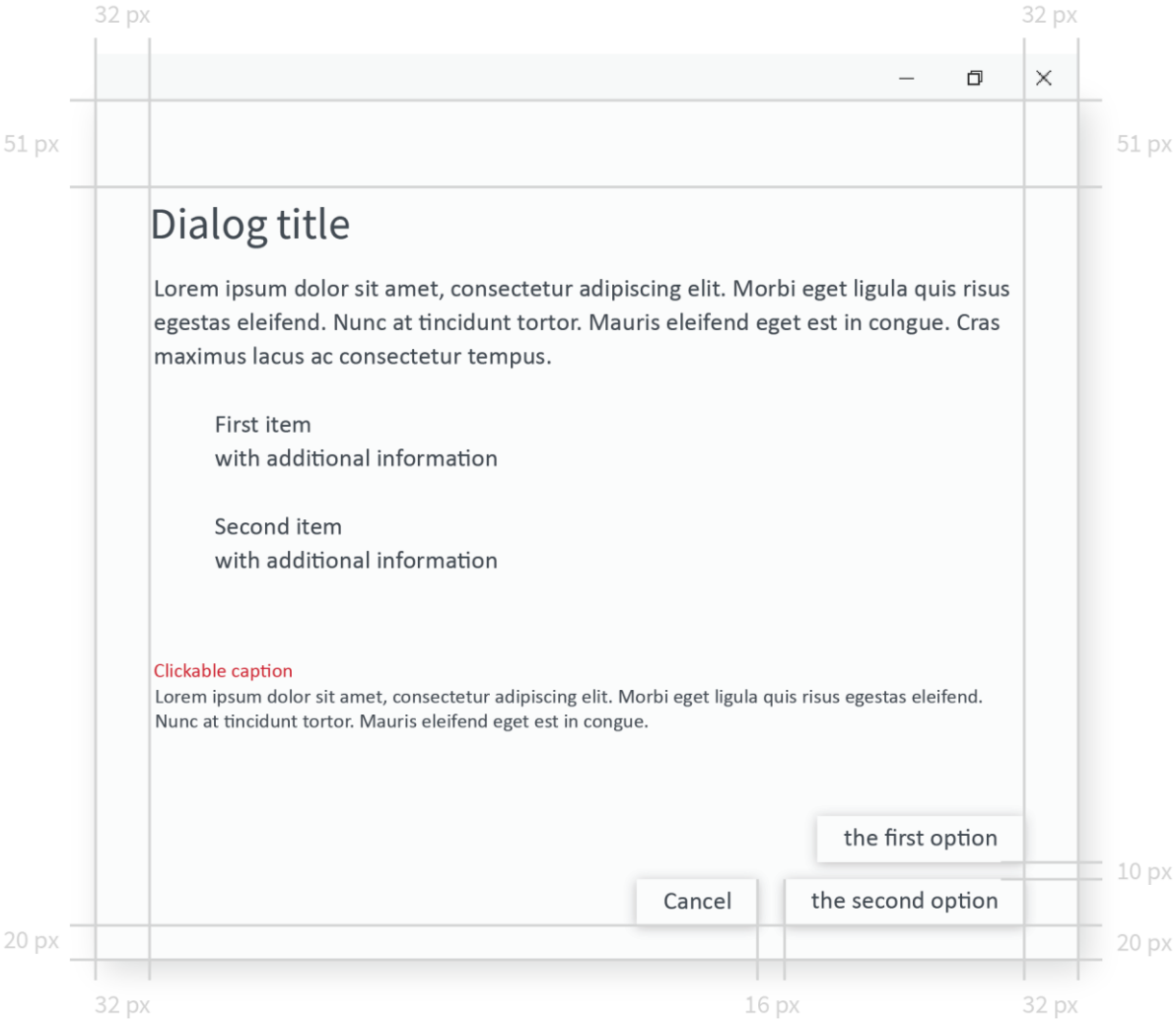

16 px
16 px
27 px
Button1
Button2
27 px
Button1
Button2
16 px
27 px
Option 1
Crtl+S
27 px
Option 2
Crtl+C
27 px
Option 3...
Drop shadow
x: 0 px
y: 3 px
b: 6 px
#000000 (16%)

27 px
Button1
Button2
Option 1
Crtl+S
Option 2
Crtl+C
Option 3...
250 px


10 px
33 px
Option 1
33 px
Option 2
33 px
Option 3
Clickable variables
Drop shadow
x: 0 px
y: 3 px
b: 6 px
#000000 (16%)


Option 1
Option 2
Option 3
250 px

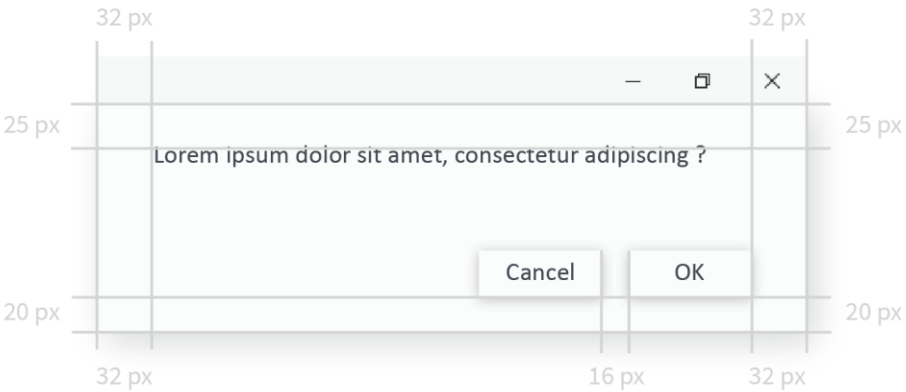
Dialogs



Interactive dialog Width: 640 px

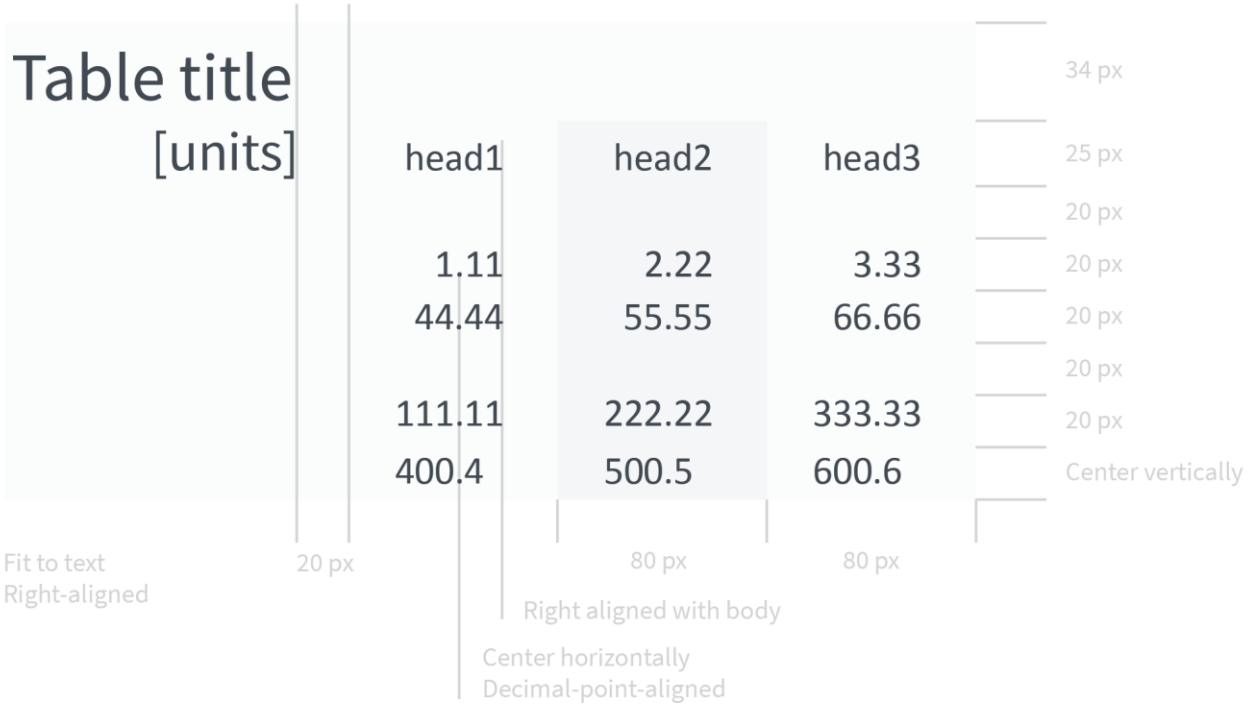
Drop shadow
x: 10 px
y: 10 px
b: 20 px
#000000 (16%)

Minimal dialog Width: 460 px

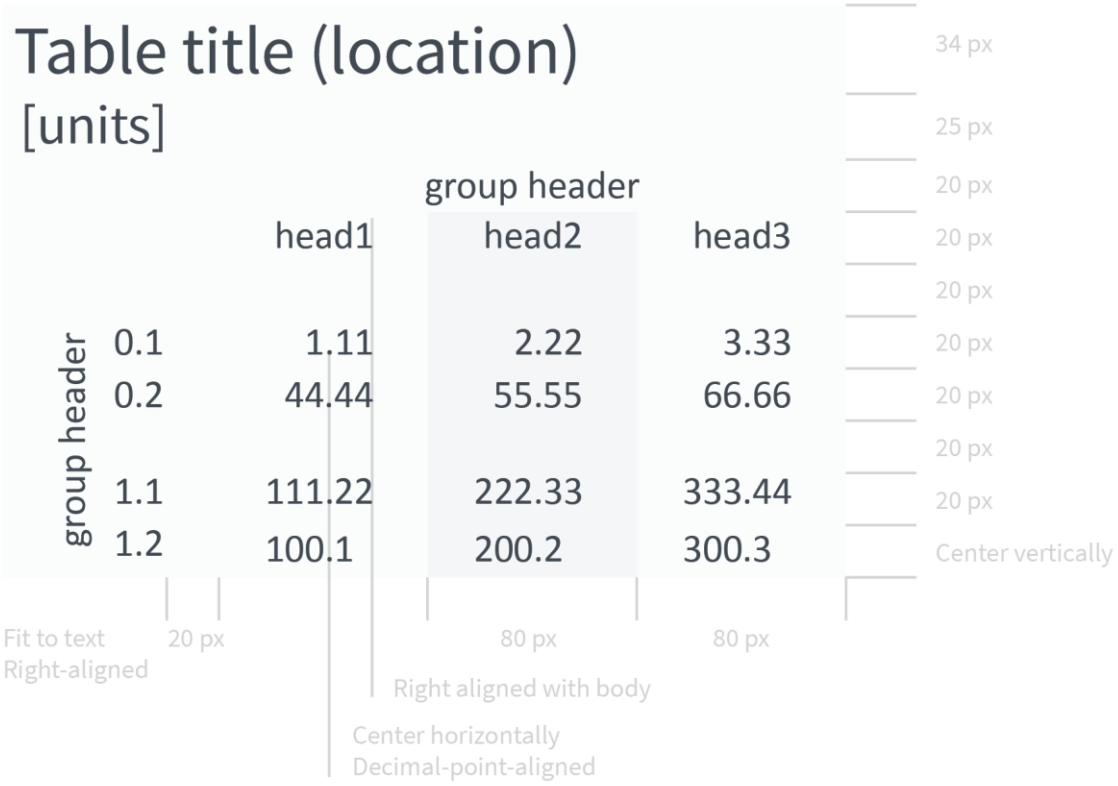


Tables

Data Table



Flow Characteristics Data Table



Tables

Flow Characteristics Data Table
Hovered or clicked
TissUse GREY
1 px

		group header		
		head1	head2	head3
group header	0.1	1.11	2.22	3.33
	0.2	44.44	55.55	66.66
	1.1	111.22	222.33	333.44
	1.2	100.1	200.2	300.3

Flow Characteristics Data Table
Scrollable direction
x: 0 px
y: -10 px
b: 20 px
#000000 (16%)

		group header		
		head1	head2	head3
group header	0.1	1.11	2.22	3.33
	0.2	44.44	55.55	66.66
	1.1	111.22	222.33	333.44
	1.2	100.1	200.2	300.3

Appendix N User test notes

This appendix contains the notes taken during the testing of the UI prototype. There were six testers spanning three different departments of TissUse:

Chip engineering: P1
Business development: P6
Biologist/researchers: P2 – P5

All text marked green is a concrete suggestion or possibility for improvement.

Testperson 1: (P1)

Task 1: Erfüllt

Klickt New Setup: „… weil hier ein neues Setup erstellt wird“. Wählt dann Chip2 96well.

Q: Kannst du bitte beschreiben, was du siehst?

Sieht zuerst den Kreislauf: „Farben haben wahrscheinlich was mit den Flussgeschwindigkeiten zu tun“. Beschreibt dann rechts Schärstress (average, max, min). Kann diesen in Verbindung zur mittleren Abbildung setzen. Darunter entdeckt er Flow Speed, Volume Flow, Distribution time. Wendet sich dann der linken Seite zu: „Hier werden Einstellungen getroffen: … . Aktuell sind anscheinend keine Features gewählt.“ Schaut sich das Sternchen an, Erklärung ist verständlich. Bild vom Kanal scheint ihm ein bisschen groß.

Task 2: Erfüllt

Will Features hinzufügen, klickt auf Features. Klickt zuerst auf Channel 1, erkennt zunächst Dropdown nicht „Sieht aus wie eine Überschrift. Ich würde mir hier z.B. ein Dropdown mit ‚Please select feature‘ wünschen.“ Wählt Endothelialized Channels und Ceramic. Würde gerne direkt im Fenster sehen, welches Compartment es ist. Liest dann erfolgreich Minimal Schärstress ab.

Task 3: mit Hilfestellung

Fällt jetzt die Darstellung in linearer Form auf der rechten Seite auf.

A: Es gibt einen Pump Setting Assistant.

Findet Pump Setting Assistant nicht. Klickt auf Pump pressure und sucht dort.

A: Der Assistent ist ganz oben.

Liest Pump Setting Assistant Text, findet er gut. Wählt Minimum. Versucht dann im Bild zu klicken [geht noch nicht, Prototyp]. Wählt Shear stress. Klickt dann Value. Äußert den Wunsch, dass auch hier wieder ein Dropdown verfügbar sein sollte. Klickt auf das Plus. Wählt Maximum Flow Speed. Kurzes Überlegen „Eingang von Compartment A?“, klickt dann A1. Trifft weitere Einstellungen ohne Probleme. Liest Ergebnisse des Assistenten. Scheinen ihm gut verständlich, Werte sind leicht unter und über den Werten. Optionen (Go Back, …) sind ebenfalls verständlich. Betrachtet dann die Tabelle: „Hier kann ich gut vergleichen. Schade, dass ich hier die 500 nicht angegeben hab. Hier kann ich die Werte auswählen.“ Es ist nicht klar, dass man die Tabelle bewegen kann. Findet das Bild der Channels jetzt

wirklich viel zu groß: „Das könnte alles kleiner werden. Tabelle rechts sollte besser nicht abgeschnitten werden. Tabelle unten sollte richtig fett sein“

Task 4: Erfüllt

Zwischenschritte

Stellt Druck auf 4. Minimalisiert Tabelle: „Pfeil hatte ich vorhin schon gesehen.“

Beginn der Aufgabe

Nimmt Feature (Endotheliasierung) raus [dadurch kurze Probleme mit dem Prototyp]. Fügt neuen Chip hinzu: „Cool, ist hier daneben, und der sieht ja sogar gleich aus.“ Sieht, dass die Keramik in den Channels abgebildet ist „Jetzt hab ich gecheckt, dass das die Keramik sein soll. Würde ich eher knochenmäßig aussehen lassen.“ Fragt sich, ob man die Endothealisierung auch sieht. Vergleicht erfolgreich die beiden Werte.

Sonstiges

Alles was er zunächst nicht wusste, ist ihm dann schnell klargeworden. Design insgesamt ist gut, schön übersichtlich. Schriften gefallen sehr gut, außer Beschriftungen am Channel. Schriftgröße passt nicht. Irgendwie unübersichtlich. Schlägt vor, die Channel auch mit Ch. abzukürzen. Hoher TissUse Wiedererkennungswert, fühlt sich an wie zu Hause!

Q: Wo sollte der Pump Setting Assistant verortet werden? Vielleicht größerer Button rechts oben oder links unten.

Schieberegler für Pump pressure ist schön.

Q: Wie findest du den Hovereffekt bei der Überschrift? Sollte permanent sichtbar sein. Hovereffekte bei Einstellungen könnten auch immer sichtbar sein, weil das Design noch nicht zu überladen ist.

Testperson 2: (P2)

Task 1: Erfüllt

Klickt auf New setup, öffnet Chip2 96well.

Q: Kannst du bitte beschreiben, was du siehst?

Beschreibt die mittlere Abbildung: „In der Mitte ist der Chip2 Modell 96well, mit 2 Compartments, Abbildung mit verschiedenen Farben und Skalierung. Zeigt mir Schärstress an verschiedenen Stellen.“ Beschreibt dann die linke Seite mit den Einstellungen: Pump pressure, Pump frequency, Pump direction, Medium. Schätzt, dass es sich bei den Features z.B. um das Keramikmodell handelt. Rechte Seite: „Rechts habe ich die Angaben von Shearstress, Flow Speed, Volume Flow und Distributionszeit. Wahrscheinlich Werte im Uhrzeigersinn angeordnet. Hier sehe ich also die Werte an unterschiedlichen Stellen. Weiß gerade nicht was A oder B ist [wird vom Fenster verdeckt].“ Sieht den Sternchentext, dabei handele es sich um eine kleine Erklärung. Beschreibt die Optionsleiste oben: „Speichern usw., Standardsettings.“ Sieht Überschrift von Tabelle, will aber gerne nach unten scrollen. Fragt sich, wo die Tabelle ist.

Task 2: Mit Hilfestellung

Will erst die Channels auswählen

A: Du musst noch Endothelialisierung auswählen. Du kannst auf das Wort Feature klicken.

„Für mich sah es so aus als würde ich erst auswählen wo ich das Feature auswählen soll." Wählt dann Endothelialisierung. Sagt, dass auf dem Bild nicht ersichtlich ist, wo das Compartment A ist. Wählt Ceramic. Liest dann erfolgreich den Wert ab. Merkt an, dass die Striche angezeigt werden sollten, wenn man bei dem Punkt ist oder bei der Zahl, nicht einfach zwischendrin [Problem im Prototyp].

Task 3: Erfüllt

Klickt auf Pump Setting Assistant. Sofort gefunden, „aber ist sehr klein geschrieben". Sollte lieber in die Gruppe von den Einstellungen ansiedeln. (Benutzt bei seiner Beschreibung den Begriff Wizard, dieser sei aber gleichwertig zu Assistant). Liest Text. Findet „Konfigurieren" missverständlich – klingt, als sollten die Pumpeinstellungen schon vorher feststehen.

Erste Anforderung: Wählt Minimum. Wählt Schärstress. Wählt Channel 1. Wählt 4.5 dyn/mm²

Zweite Anforderung: Vermutet, dass er zum Hinzufügen einer neuen Anforderung auf das Plus klicken muss.

Merkt an, dass alles was rot ist, klickbar ist. Deshalb würde er denken, dass er auf „Do you have more than three requirements?" auch klicken kann [ist auch so gedacht, nur im Prototypen nicht möglich]. Fragt sich, wie das bei einer Rot-Grün-Schwäche ist. Vielleicht würde man dann die Links nicht sehen. Vielleicht sollte eine andere Farbe gewählt werden.

Fragt sich, warum Flow Speed „Quantity" genannt wird. Quantity ist für ihn eher Anzahl, findet er etwas verwirrend. Überlegt, ob es einen anderen Begriff gibt.

Dritte Anforderung: Wählt alle Einstellungen ohne Probleme.

Q: Würdest du eher das Bild oder das Dropdown für die Auswahl der Location nutzen? Würde das Bild vielleicht nicht unbedingt nutzen.

Klickt jetzt auf „Do you have more than three requirements", liest Text. Klickt weiter, liest Text. Findet es sei sehr viel Text im Button „Show me flow data tables and let me have a look around" und überlegt, ob das vielleicht irgendwie kürzer sein könnte.

Q: Hätte "Show me flow data tables" gleiche Bedeutung? Ja. Will es Lieber kurz und prägnant.

Klickt weiter und sieht die Datentabelle. Gut wäre, wenn man den idealen Wert (also 400) in der Mitte hat und dieser dick gedruckt wäre, damit man sieht welche Einstellungen man getroffen hat. Fragt sich, was man macht, wenn man doch etwas ändern will. „Da würde ich jetzt hier drauf klicken (klickt in der Tabelle). Das wäre schon gut, dass ich das dann ändern kann, indem ich draufklicke."

Entdeckt Bewegung der Tabelle erst nach Hinweis darauf. Drag & Drop seit zu viel Arbeit, lieber Pfeile nach rechts und links oder oben und unten. Findet die Werte rechts sollten nicht verdeckt sein, sind wichtig.

Q: Soll die Tabelle gleichzeitig mit den anderen Werten sichtbar sein? Wäre schon gut, da man ja wissen will was es verändert, wenn man einen Wert (in der Tabelle) anklickt.

Fragt sich, ob die Zahlen so genau sein müssen. Würde als Zahlenformat: statt .21 besser 0.21 schreiben.

Task 4: Erfüllt

Zwischenschritte

Stellt Pump pressure ein. Fragt sich, ob man später Zwischenwerte einstellen kann. Minimalisiert Tabelle.

Beginn der Aufgabe

Klickt auf Plus. Fragt sich wie intuitiv das ist mit dem Plus und ob vielleicht lieber Compare dort stehen sollte: „Mit einem Plus fügt man ja etwas hinzu … ja vielleicht kann man auch das Plus lassen." Nimmt die Ceramic raus und vergleicht erfolgreich die Werte.

Sonstiges

Fragt sich, was man macht, wenn man unterschiedlichen Pressure und Vacuum hat? Testet Einstellung aus. Merkt an, dass oben +500 mbar stehen sollte, wenn unten -250 mbar steht.

Findet den oberen Teil der Abbildung (Pumpen in weiß) verwirrend. Er weiß zwar, dass wir das nicht messen können, aber das müsse dem Anwender klargemacht werden, warum das leer ist.

Testperson 3: (P3)

Task 1: Erfüllt

Klickt auf New Setup, wählt Chip2 96well.

Q: Kannst du bitte beschreiben, was du siehst?

Sieht als erstes den Kreislauf, Chip2 96well Format. Entdeckt die Überschrift, Abbildung zeige demnach den Schärstress an verschiedenen Stellen im Kreislauf. Interpretiert die Farben in den Compartments und den Kanälen. Beschreibt Beschriftungen der Compartments und Channels. Beschreibt die linke Seite, dort sieht man Basic Informationen … oder Einstellungen: Pump pressure, Pump frequency, Pump direction, Medium. Bei dem Plus könne man wahrscheinlich weitere Features hinzufügen. Rechts: „Hier kann ich die detaillierten Informationen ablesen. Erkennt, dass der Channel dort nochmal in der Länge dargestellt ist.

Task 2: Mit Hilfestellung

Klickt auf Features. Will dann Compartment A auswählen [geht nicht, Prototyp]. Fragt, ob die Reihenfolge wichtig ist. Wählt alle Kanäle aus. Wählt dann auch die Compartments. Will dann auf „Add" klicken, was nicht funktioniert.

A: Du musst noch eingeben, dass es endothelialisiert ist.

Findet dann durch Suche mit der Maus den Feature-Button. Wählt dann ohne Probleme Endothelialization und Location aus, fügt dann die Keramik hinzu. Liest dann den Schärstress ab.

Fände es gut, wenn man erst die Location auswählt und danach das Feature. Würde eine 0 vor .21 stellen.

Task 3: Mit kleiner Hilfestellung

Findet nach kurzem Suchen den Assistant. Findet den Button etwas klein. Liest sich den Text durch. „Das bedeutet, dass ich alle Features schon eingegeben habe, bevor es weitergeht.“. Klickt auf Weiter. „Ich kann jetzt hier die Anforderungen angeben“.

Erste Anforderung: Klickt Kanal 1 [geht nicht im Prototyp], Klickt Minimum.

A: Es ist nicht klar, dass man die anderen Sachen klicken kann, oder?

Klickt dann Quantity, Location und Value. Hat gedacht, dass sie die Location in der Grafik auswählen muss [Prototyp]. Findet es verwirrend, dass die Schrift gleich groß und sehr groß ist. Sinnvoller wäre es, wenn Requirement 1 größer wäre und die anderen Sachen kleiner. Außerdem vielleicht mit einem Pfeil, der zeigt, dass man es runterklappen kann. Es wirke etwas random angeordnet, Zugehörigkeiten sind nicht klar.

Zweite Anforderung: Klickt Plus, Wählt Maximum, wählt Flow Speed, Klickt im Bild auf A1. Wählt den Wert.

Dritte Anforderung: Wählt alles ohne Probleme. Merkt an, dass vielleicht Location, Quantity usw. weiter stehen bleiben sollte, mit einem Doppelpunkt und den Auswahlmöglichkeiten dahinter (so wie es bei den Einstellungen auf der Hauptseite ist).

Findet Button „Search Pump settings“ auch etwas zu klein. Liest Text „Hier wird mir eine Anforderung vorgeschlagen“. Sieht dann den Menüpunkt „Apply“ und erklärt, dass sie hier die Einstellungen anwenden könnte. Klickt „Show data table … „

Sieht die Tabelle: „Das sind die verschiedenen … ah ne das sind die drei Locations, bei denen ich die Anforderungen eingegeben hab. Und dann kann ich hier bei verschiedenen Frequenzen den Druck sehen.“

Task 4: Mit Hilfestellung

Zwischenschritte

Wählt pump pressure 400mbar. Minimalisiert die Tabelle.

Beginn der Aufgabe

Sucht nach einer Möglichkeit, das Setup abzuspeichern. Nach einiger Zeit klickt sie dann auf das Plus. Löscht Ceramic. Überlegt dann, wie sie die Werte vergleichen kann. Würde gerne Tabelle rechts Scrollen, das bereitet aber Schwierigkeiten.

A: Du kannst mit dem Maus Scrollen, wenn du über der Tabelle bist

Vergleicht dann die Werte. Würde oben lieber „Compare setups“ statt dem Plus-Zeichen haben. Ein Button wäre toll, mit dem man die Unterschiede zwischen zwei Setups hervorheben könnte.

Sonstiges

Vielleicht könnten die Tabellen rechts zunächst zugeklappt sein, sonst ist es ein bisschen zu viel Informationen.

Testperson 4: (P4)

Task 1: Erfüllt

Entdeckt Pinned Setup Chip2 96 well, dieser hat aber andere Einstellungen. Klickt „Open another setup“. Entdeckt erst dann „New Setup“.

Q: Kannst du bitte beschreiben, was du siehst?

Sieht das PMS Chipdesign von Chip2, es liegt schon ein Modell vom Shearstress über der Geometrie. Beschreibt dann die rechte Seite, dort werden die Punkte angezeigt. Sieht dann links die Einstellungen. Probiert Pump frequency Setup. Würde dort einen Apply-Button erwarten. Fände es schön, wenn man auch eine Keramik einsetzen könnte. Findet Pfeile sehr schön. Sagt, dass sie erst jetzt die Grafik rechts in der Tabelle versteht. Findet, dass diese eine Erleichterung darstellt.

Task 2: mit Hilfestellung

Klickt auf das Plus. Wählt dann Channel 1. Will Apply klicken.

A: Du kannst das Wort Feature klicken.

Fügt Endothelialisierung und Keramik ohne weitere Probleme hinzu. Will dann Pumpeinstellung ändern, um den minimalen Shear Stress abzulesen.

A: Versuche dir die Shear Stress Tabelle nochmal anzuschauen.

Entdeckt minimal, average und maximum.

A: Da steht dann der minimale Shear Stress.

Dachte, dass sie die Pumpeinstellungen herausfinden soll, die den minimalen Shear Stress erzeugt [lag also am Verständnis der Aufgabenstellung]. Dass man das Wort Feature anklicken muss, versteht man ab dem zweiten Mal gut.

Task 3: mit Hilfestellung

Sieht den Pump Setting Assistant nicht. Sucht beim Pump pressure. Entdeckt die Funktion, pressure und vacuum einzeln einzustellen, findet die Funktion gut.

A: Der Pump Setting Assistant ist ganz links oben.

Öffnet Assistant, liest den Text. Klickt weiter.

Erste Anforderung: Stellt diese erfolgreich ein.

Zweite Anforderung: Wählt Maximum Flow Speed. A1 sei wahrscheinlich Eingang von Compartment A. Wählt dieses aus.

Dritte Anforderung: Stellt alles erfolgreich ein.

Liest den Text, findet Zusammenfassung gut. Hätte gerne eine Möglichkeit um zu schauen wie es z.B. bei 450mbar ist. Wünscht sich eine Datentabelle. Klickt Button „Show data table …“ und betrachtet die Tabelle. Scrollt in der Tabelle! Würde erwarten, dass wenn sie in der ersten Tabelle etwas anklickt, das

rechts gehighlighted wird. Diese Funktion ist bereits beinhaltet, findet sie gut. Entdeckt die Möglichkeit, einen zweiten Chip hinzuzufügen (siehe Task 4).

Task 4: mit kleiner Hilfestellung

Zwischenschritte

Wählt 400mbar. Minimalisiert die Tabelle.

Beginn der Aufgabe

Sucht Distribution time. Würde die Überschriften (min, avg, max, A-B, B-A, …) dicker machen. Merkt sich den Wert und will dann die Keramik entfernen [wird vom Tester gestoppt]. Fügt dann einen zweiten Chip hinzu und vergleicht die Distribution time.

Überlegt ob Distr. time A-B vom Ausgang A bis Eingang B oder von der Mitte der Compartments berechnet wird. Überlegt, ob die Punkte (z.B. Eingang und Ausgang eines Compartments) noch genauer benannt werden könnten.

Sonstiges

Findet Input und Output gut. Grafik nimmt sehr großen Bereich ein, dafür, dass man daran recht wenig machen kann. Man arbeitet ja eher mit dem Input und Output. Beschriftung der Grafik könnte größer sein. Man würde eher auf die Zahlen rechts als auf die Farben in den Kanälen schauen. In sich homogenes Design, sieht gut aus, Gewichtung könnte aber etwas anders sein. Findet verlinkte E-Mail auch gut. Fragt sich, was man mit den Pfeilen rechts machen kann, ob man damit die Tabellen zuklappen kann. Button „New Setup“ könnte ein bisschen zentraler sein.

Testperson 5: (P5)

Task 1: Erfüllt

Klickt „Open another setup“. Sieht nach einer Weile den Button. Klickt Chip2 96well Setup.

Q: Kannst du bitte beschreiben, was du siehst?

Sieht Übersicht vom Chip mit dem Schärstress in den Compartments und den Kanälen. Links sieht sie die Einstellungen. Rechts verschiedene Parameter, wie der durchschnittliche und maximale Schärstress und die Flussgeschwindigkeit ist.

Task 2: mit Hilfestellung

Klickt auf Plus, wählt alle Kanäle und will dann Apply klicken.

A: Du kannst auf das Wort Feature klicken.

Fügt Endothelialisierung hinzu. Beim zweiten Feature weiß sie nicht sofort, welches Compartment A ist.

A: Compartment A ist das erste.

Wählt es aus. Bemerkt, dass in der Tabelle rechts die Werte zu unterschiedlichen Punkten passen. und liest dann den minimalen Schärstress ab. Bei der Auswahl des Features wäre es schön, wenn es eindeutig ist, dass es ein Dropdown ist.

Task 3: Erfüllt

Findet Pump Setting Assistant sehr schnell (hatte sie vorher schon entdeckt). Liest Text. Klickt weiter.

Erste Anforderung: Wählt erfolgreich aus.

Zweite Anforderung: Klickt Plus. Wählt Maximum Flow Speed. Fragt sich, welches der Eingang von Compartment A ist, weil das ja je nach Pumprichtung unterschiedlich ist.

Dritte Anforderung: Wählt erfolgreich aus.

Liest den Text. Ergebnisse liegen leicht unter und über den Anforderungen, ist aber evtl. „Close enough“. Erkennt, dass es scheinbar keine perfekte Einstellung gibt. Findet daher irreführend, dass oben „Success“ steht. Findet ansonsten die Einstellung sehr intuitiv.

Schaut Tabelle an, fragt, weshalb die Zellen so markiert werden [Fehler im Prototyp]. Dass man die Tabelle nicht bewegen kann, war ihr nicht klar. Merkt an, dass niemand mit einer so hohen Hertzzahl pumpt.

Task 4: Erfüllt

Zwischenschritte

Stellt Pump pressure ein. Minimalisiert Tabelle.

Beginn der Aufgabe

Klickt Plus, entfernt Keramik. Liest Distribution Time ab, stellt fest, dass es keinen Unterschied macht.

Sonstiges

Generell sehr eindeutig. Der Klick auf Pump pressure zum Bestätigen findet sie nicht so intuitiv [Prototyp].

Q: Was denkst du über die Zeichnung in der Tabelle?

War bisher nicht aufgefallen. Erkennt dann die Compartments.

Testperson 6: (P6)

Task 1: Erfüllt

Klickt erst „Open another setup“. Entdeckt dann „New Setup“. Wählt Chip2 96welll.

Q: Kannst du bitte beschreiben, was du siehst?

Sieht die Shear Stress Distribution in den Channels und Compartments. In den Pumpen sieht man aus irgendeinem Grund nichts. Erklärt, dass sie Pump pressure, Pump frequency, Pump direction. Entdeckt, dass man Features hinzufügen kann.

Task 2: mit Hilfestellung

Befindet sich schon im Features-Menü. Wählt alle Channels und Compartments und möchte dann Apply klicken.

A: Du kannst auf das Wort Feature klicken.

Wählt Endothelialization. Öffnet dann Features-Menü erneut. Fragt sich, welches das Compartment A ist. Fenster sollte beweglich sein oder an der Seite. Fügt Keramik hinzu. Liest erfolgreich minimum Shear Stress ab.

Merkt an, dass die Compartments auch manchmal leer gelassen werden, nur mit endothelialisierten Zellen. Manchmal wird nur Gel hinzugefügt. Dies sollte auch als Feature zur Verfügung stehen.

Mag die Pfeile zwischen Grafik und Tabelle, sind selbsterklärend.

Task 3: mit kleineren Hilfestellungen

[Kurze Absprache zu den Requirements]. Findet schnell den Pump Setting Assistant und öffnet diesen. Liest den Text. Klickt weiter.

Erste Anforderung: Versucht im Bild zu klicken [geht nicht, wegen dem Prototyp]. Klickt nach einigem Suchen auf Minimum. Fragt sich, was die Quantity ist. Klickt dann darauf und wählt Shear stress. Wählt Location und Wert erfolgreich.

Zweite Anforderung: Wählt alles erfolgreich.

Dritte Anforderung: Wählt alles erfolgreich.

Klickt weiter. Liest die Zusammenfassung. Stellt fest, dass die Werte ein bisschen anders sind als die Vorgaben. Sagt, dass sie das Tool wirklich gerne hätte! Fragt sich, ob das Tool dann auch in Verbindung mit dem Roboter oder dem Starter steht. Eine Benutzung via App wäre toll.

Sieht den Button „Show data tables …" und möchte das gerne sehen. Klickt darauf. Erklärt die Tabelle, ist für sie verständlich. Würde gerne in der Tabelle klicken können, um die Einstellungen anzupassen.

In der Menüleiste braucht es aus ihrer Sicht beim Pump Setting Assistant kein Dropdown, weil es keine zweite Option gibt. Ansonsten funktioniert aus ihrer Sicht der Assistant sehr gut.

Task 4: mit Hilfestellung

Zwischenschritte

Wählt 400 mbar. Sucht kurz nach der Möglichkeit, die Tabelle zu minimalisieren.

Beginn der Aufgabe

Klickt auf das Plus. Sucht kurz nach der Möglichkeit, das Feature zu entfernen. Entfernt das Feature. Vergleicht die Distribution time und stellt fest, dass sich nichts geändert hat. Merkt dann aber an, dass sie nur den Full Circle sieht, aber nicht die Zeit von A zu B.

A: Schau nochmal die Header in der Tabelle an.

Sieht dann, dass dort auch A-B steht. Findet aber, dass es eigentlich klar ist. Vielleicht könnte A-B, B-A und Full Circle hervorgehoben werden, bspw. fett. Sah aus wie eine Zahl.

Sonstiges

-

Appendix O Possible improvements on UI

This appendix contains a list of improvements that could be considered in addition to those described in 4.8. For each flaw that was found the testers that mentioned it are referred. For the full conversations with the testers, please have a look at Appendix N.

The improvements are grouped per screen.

Dashboard

- It is unclear why there is no data inside the pump (P2, P5)
- It is unclear that the headers in the tables are headers. At a quick glance they just appear to be values like the rest of the table (P4, P6)
- It is unclear how the features are visually represented in the image (P1)
- The text labels in the image are chaotic (P1)
- The hover effects are not as inevitably discoverable as they should be (P1)
- It is unclear that the tables need to be opened and are not something you can scroll down to (P2)
- The lines between the table on the right and the image should only appear when hovering over the table or the points in the image, not in between (P2)
- When using two different pump settings for pressure and vacuum, put a plus sign in front of the pressure, just like there is a minus sign in front of the vacuum. So +500 mbar instead of 500 mbar (P2)
- It is unclear with which points the distribution time is calculated. Is it from the centre of a compartment to the other, of from exit to entrance? (P4)

Features

- I would expect to first give in the location of a feature and then the feature itself (P2, P3)
- Gel should be added as an option to the Feature dropdown in the Feature dialog (P6)

Pump Setting Assistant

- The word “quantity” is unclear in the requirements screen of the Pump Setting Assistant. Quantity feels more like an amount instead of a physical quantity (P2, P6)
- The word “configuration” is unclear in the first screen of the Pump Setting Assistant. It could be interpreted as though the pump setting should already be set, which is exactly not the point (P2)
- The text on the “Show me tables and let me look around” button in the final screen of the Pump Setting Assistant is too long (P2)
- The word “success” on the final screen of the Pump Setting Assistant is confusing when it does not give a perfect match with the requirements (P5)
- The colour-blindness-compatibility should be checked (P2)

Data Characteristics Tables

- It would be nice to be able to apply a pump setting directly from the Data Characteristics Tables somehow (P2, P6)
- The Data Characteristics Tables should be bigger (P1)
- It would be nice to have the result from the Pump Setting Assistant in the middle and highlighted when opening the Data Characteristics Tables from the Pump Setting Assistant (P2)