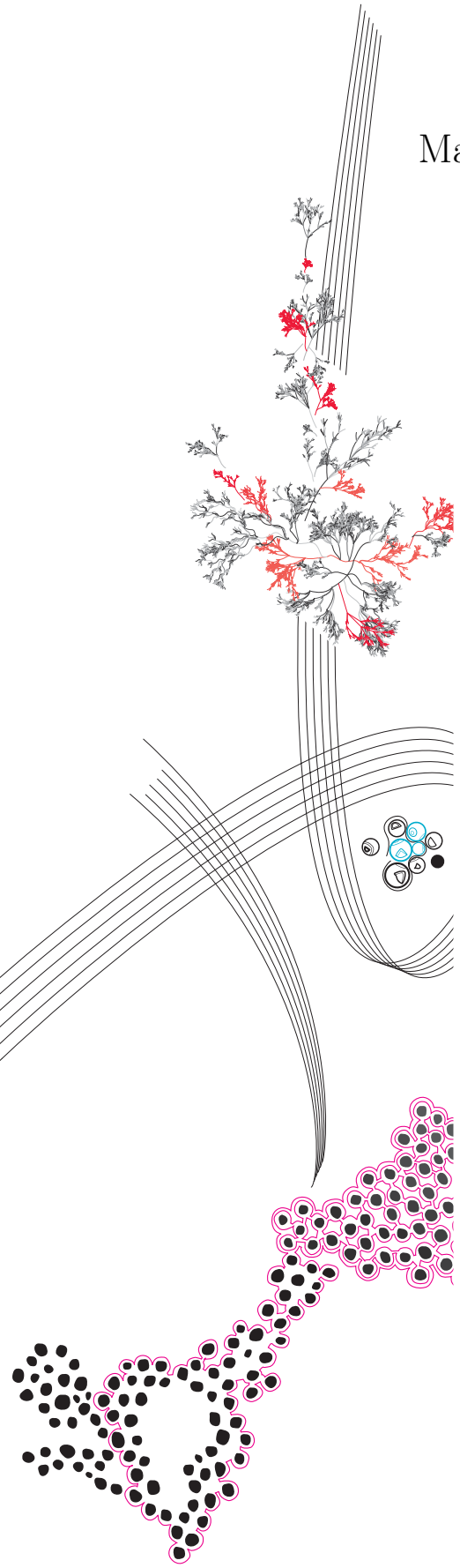

Mathematical modeling of aerosols at air-mucus interface

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1 Introduction

When humans breath they do not only inhale air but also trillions of aerosols. Aerosols are tiny solids or liquids suspended in gasses. Examples of these are pollen, smoke, fumes or mist. We breath in a lot of aerosols but not all will reach the alveoli.

The motion of the aerosols is determined by a number of mechanisms, effective in different size ranges [14]. Most aerosols greater than $5\mu m$ will not be able to follow the airflow and will bounce into the walls of the body, this is called inertial impaction. Then there is also gravitational sedimentation, which as the name suggest is caused by the gravity pulling down the particles. This mainly effects particles from 1-8μm. For smaller particles there is also Brownian diffusion. Deposition by Brownian diffusion results from the random motions of the particles caused by their collisions with gas molecules and is most effective in the alveolar region of the lung where air velocities are low. Only micro and nano sized aerosols reach this area. The lung is a very complex organ in our body. It consists out of 480 million alveoli [15] which each contributes to the respiratory system of our body.

In our research it is of interest to investigate the air and the mucus media. This is chosen because the mucus layer is the first layer that aerosols have to pass by diffusion or sedimentation in the alveoli. There has been little research for the influence of the size of aerosols for diffusion through the mucus layer [1,3]. We have investigated what the influence is and how researchers can apply this information for therapeutic aerosols.

In this report we analyse these aerosols and make a one dimensional mathematical model of the transport rate of the concentration of certain particles by forces of diffusion and sedimentation through various media such as an air layer and through a mucus layer. This will be done using Matlab tools, our general knowledge of PDE's and other papers.

2 Methods

2.1 Description of the model and the aerosols

To investigate aerosol motion we will make use of the In-vitro Sedimentation, Diffusion and Dosimetry model (ISDD) [1]. This model is constructed out of two main parts: an equation for the diffusion coefficient and an equation for the sedimentation coefficient. Both are used in a single differential equation which describes the change of the rate of the concentration of particles in a viscous medium in a 1D dimension by the force of gravity and diffusion.

The particles will flow parallel to the gravity in the vertical direction. We want to analyse how different drug particles pass this barrier and how their transport rates compare against one another. An assumption we make is that there is an absence of any agglomerates forming during the experiment and that the particles are mono-disperse.

The aerosols that are being analysed will be two therapeutic aerosols with different physico-chemical properties: (i) the inhaled bronchodilator Salbutamol sulfate, which, according to the oral Biopharmaceutics Classification System, is a high solubility but low permeability drug; (ii) the non-steroidal anti-inflammatory drug (NSAID) indomethacin which is, in contrast, a low solubility/high permeability molecule. These are both drugs that are commonly used against chronic respiratory diseases. [11]

2.2 Equations

The model before mentioned that we will be using is an ISDD model [1,3]. This is constructed by two major parts. The first being the equation for sedimentation:

$$V = \frac{g(\rho_p - \rho_f)d^2}{18\mu}. \tag{1}$$

This equation is called Stokes' law. Stokes' law defines the gravitationally driven sedimentation rate ($V, m/s$) of particles in solution from the viscosity ($\mu, Pa*s$) of the media, the relative densities (kg/m^3) of the particle (ρ_p) and fluid (ρ_f), the diameter of the particle (d, m) and the acceleration due to gravity ($g, m/s^2$). The second equation we will be using is the Stokes-Einstein equation.

The Stokes-Einstein equation describes the relation between the particle diameter and the diffusion rate ($D, m^2/s$) as a function of viscosity and temperature (T, K):

$$D = \frac{kT}{6\pi\mu d} \tag{2}$$

where k is Boltzmann constant. When a particle moves through a fluid it can cause some motion of the fluid. To describe this flow we will use Reynolds number which is a dimensionless ratio from laminar to turbulent forces. If the Reynolds number is below one then equation 1 and 2 are the only terms necessary for the Mason-Weaver laminar convection-diffusion equation which describes the sedimentation and diffusion of solutes under a uniform force. The Reynolds number is under one for particles smaller than $100\mu m$ [1]. This holds for the particles that we will use so we can use this equation to derive the change of particles per time unit. This equation is a partial differential equation (PDE), given by:

$$\frac{\partial n}{\partial t} = D\frac{\partial^2 n}{\partial x^2} - V\frac{\partial n}{\partial x} \tag{3}$$

where n is the concentration of particles, t is the time (s) and x is the distance (m) in the vertical direction.

2.3 Boundary and initial values

At the start of the experiment we assume that the distribution of particles is uniform (4a). The actual value of n_0 will not influence the results as can be seen at the next section with the nondimensionalization. Furthermore we assume that at $x = L$, where L is the height of the media, there is no flow of particles (4b), and that at the bottom of the media there is no concentration of particles (4c). This means that they do not bundle together at the boundary and as soon as they reach it they do not influence the particle concentration.

$$(a) \quad n_0 = c \,\forall\, x, \quad \text{where c is constant} \quad (b) \quad \frac{\partial n}{\partial x} = 0 \text{ for } x = L \quad (c) \quad n = 0 \text{ for } x = 0 \tag{4}$$

2.4 Nondimensionalization

To analyse what is happening in the model we made the PDE dimensionless. The current dimensions are defined as follows: n can be given in any concentration like g/ml or number of particles per ml, x is the distance in m, V is the sedimentation rate in m/s and D is the diffusion rate in m^2/s. We made the model dimensionless by introducing new variables N, τ and χ that are defined as follows:

$$(a) \quad N = \frac{n}{n_0}, \quad (b) \quad \tau = \frac{t}{t_0}, \quad (c) \quad \chi = \frac{x}{x_0} \tag{5}$$

With this the PDE would boil down to

$$\frac{\partial N}{\partial \tau} = \frac{Dt_0}{x_0^2}\frac{\partial^2 N}{\partial \chi^2} - \frac{Vt_0}{x_0}\frac{\partial N}{\partial \chi} \tag{6}$$

We chose t_0 to be the maximum time over which we measure called T_{max}, we chose x_0 to be the medium length L and we chose n_0 to simply be the initial concentration. These are chosen such that the new variables will run from 0 to 1. Furthermore we will implement two dimensionless parameters alpha and beta where

$$\alpha = \frac{DT_{max}}{L^2}, \beta = \frac{VT_{max}}{L} \tag{7}$$

Now the PDE looks like

$$\frac{\partial N}{\partial \tau} = \alpha\frac{\partial^2 N}{\partial \chi^2} - \beta\frac{\partial N}{\partial \chi} \tag{8}$$

Alpha uses the diffusion coefficient and beta uses the sedimentation coefficient. We will research values of alpha ranging from 1 until 400 and values of beta ranging from -0.01 until 0.4. This

represents transport processes which are dominated by diffusion. The boundary equations and the initial condition would become:

$$(a) \quad N_0 = 1 \,\forall\, \chi, \quad (b) \quad \frac{\partial N}{\partial \chi} = 0 \text{ for } \quad \chi = 1, \quad (c) \quad \text{N} = 0 \text{ for } \quad \chi = 0 \tag{9}$$

This is the main model which is used for explaining results and comparing the different transport rates of the aerosols.

2.5 pdepe

The way we are going to solve the PDE is by using a solver called pdepe from MATLAB. pdepe solves initial-boundary value problems for systems of parabolic and elliptic PDEs in the one space variable x and time t. It solves PDEs of the form

$$c\left(x,t,u,\frac{\partial u}{\partial x}\right)\frac{\partial u}{\partial t} = x^{-m}\frac{\partial}{\partial x}\left(x^m f\left(x,t,u,\frac{\partial u}{\partial x}\right)\right) + s\left(x,t,u,\frac{\partial u}{\partial x}\right) \tag{10}$$

Here x is the independent spatial variable. t is the independent time variable. u, which is in our case n, is the dependent variable being differentiated with respect to x and t. c, f and s are coefficients that could include variables like x, t, u and $\frac{\partial u}{\partial x}$. m is the symmetry constant with values 0, 1 or 2 corresponding to slab, cylindrical, or spherical symmetry, respectively.

This solver has some conditions and properties. The PDE that is solved exists in the space of $t_0 \leq t \leq t_{max}$ and $a \leq x \leq b$. The spatial interval of x: $[a, b]$ must be finite. The coefficient $f\left(x,t,u,\frac{\partial u}{\partial x}\right)$ is called the 'flux' term which must depend on the partial derivative $\frac{\partial u}{\partial x}$ and the coefficient $s\left(x,t,u,\frac{\partial u}{\partial x}\right)$ is called the 'source' term.

The solver function is sol = pdepe(m,pdefun,icfun,bcfun,xmesh,tspan). This consists out of m, three functions and the x and t variable spans. The first function, pdefun, is the function which establishes the c, f and s coefficient as in equation 10. The icfun is the function which states the initial condition. The last function, which makes the boundary conditions, is a bit more complicated since it uses inputs of the form $p(x,t,u)+q(x,t)f\left(x,t,u,\frac{\partial u}{\partial x}\right) = 0$ at $x = a$ and $x = b$. They use the same f as in pdefun and then for the left boundary case and the right boundary case one would have to express the conditions in that formula.

"The MATLAB PDE solver pdepe solves systems of 1-D parabolic and elliptic PDEs of the form of equation 10" [16]. This is the default version for the pdepe solver. To alter the error control and the step size or to add an event logging one has to add an 'options' variable.

3 Results

3.1 Parameters

For the research we had to establish some parameters to reflect the most realistic version of this model. Some of the values in table 1 were constants like the Boltzmann constant and the gravitational constant. Another predetermined value was the symmetry constant since it followed directly from equation 3.

In the human lungs most of the mucus is made form MUC5AC so we decided to use these properties for the model [6]. The density we got for the mucus was around $1390 kg/m^3$ [9] and the viscosity was around $1e-2 Pa*s$ [4]. For the density of air we assume it to be dry air at atmospheric pressure at a temperature of $35°C$ [5], using the ideal gas law we calculated the density. We used the same conditions for the viscosity of air. The density's of both drugs are constant and a given [7-8].

The diameters of the drugs can be varied for many different sizes. We decided to investigate the influence of the diameters where the deposition fraction is higher in the alveolar region than 0.2 [10], starting from $5nm$ going up until $0.1\mu m$.

Description	Name	Value	Dimension
Density of mucus	ρ_{mucus}	998	kg/m^3
Density of air	ρ_{air}	1.1460	kg/m^3
Density of Salbutamol Sulfate	ρ_s	1200	kg/m^3
Density of Indomethacin	ρ_i	1300	kg/m^3
Diameter of Salbutamol Sulfate	d_s	[5e-9, 1e-7]	m
Diameter of Indomethacin	d_i	[5e-9, 1e-7]	m
Viscosity of air	μ_{air}	18.84e-6	$Pa*s$
Viscosity of mucus	μ_{mucus}	1.0016e-2	$Pa*s$
Boltzmann constant	k	1.38064852e-23	$m^2 kg s^{-2} K^{-1}$
Gravitational Constant	g	9.80665	m/s^2
Body temperature in alveolar region	T	305	K
Symmetry constant	m	0	

TABLE 1: Table of parameters with values and dimensions.

3.2 Validation

Before the results can be presented we must make sure that the current discretization is sufficient enough to deliver said results. There will be two cases, one with a dominant diffusion coefficient and one with a dominant sedimentation coefficient. The model will be run with the standard hundred time steps and fifty spatial steps, which will be labeled as normal, and with one million time steps and five thousand spatial steps, which will be labeled as large. More steps could be plotted for higher accuracy but the tools were not available to efficiently handle those plots.

In figure 1 we notice that for both discretizations the curve overlaps. This would suggest that the normal discretization is sufficient enough for alpha dominated cases to deliver results which can be analysed.

A problem arises however when investigating sedimentation dominated cases. As can be noted in figure 2 the curve for normal discretization fluctuates heavily and heading into the negative which should not be physically possible. However when increasing the amount of steps the solver significantly increases in accuracy and almost shapes like a step function. This would indicate that pdepe is valid to use with the current discretization but for sedimentation dominated cases one would need stronger hardware to get sufficient results in an appropriate time.

3.3 Results

These plots were plotted with the parameters as in table 1. Four values of the diameter were taken to investigate. These values were $100nm$, $50nm$, $10nm$ and $5nm$. For the media length of the air

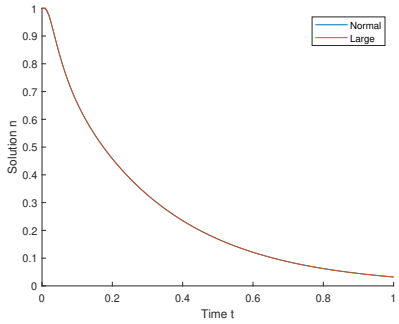

FIGURE 1: **Diffusion dominated case.** Here the concentration n (particles per ml) is given as a function of time (s) for a normal discretization (50 spatial steps, 100 time steps) and for a large discretization(5000 spatial steps, 1e6 time steps)

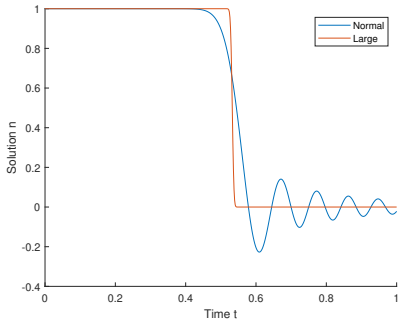

FIGURE 2: **Sedimentation dominated case.** Here the concentration n (particles per ml) is given as a function of time (s) for a normal discretization (50 spatial steps, 100 time steps) and for a large discretization(5000 spatial steps, 1e6 time steps)

layer we chose a length of $1e-4m$ which is half the diameter of an alveoli sack. For the mucus layer the length is $1e-6m$ [6]. In table 2 the alpha, beta, diffusion and sedimentation parameters have been calculated.

Drug	**Media**	**Diameter**	**Alpha**	**Beta**	**Diffusion** (m^2/s)	**Sedimentation** (m/s)
I	Air	1e-7 m	1.1858	0.3756	1.1858e-10	3.7560e-07
I	Air	5e-8 m	2.3715	0.0939	2.3715e-10	9.3900e-08
I	Air	1e-8 m	11.8577	0.0038	1.1858e-09	3.7560e-09
I	Air	1e-9 m	23.7154	0.0009	2.3715e-09	9.3900e-10
I	Mucus	1e-7 m	22.3042	-0.0049	2.2304e-13	1.6427e-10
I	Mucus	5e-8 m	44.6085	-0.0012	4.4608e-13	4.1068e-11
I	Mucus	1e-8 m	223.0425	-4.8955e-4	2.2304e-12	1.6427e-12
I	Mucus	5e-9 m	446.0849	-1.2239e-4	4.4608e-12	4.1068e-13
S	Air	1e-7 m	1.1858	0.3466	1.1858e-10	3.4668e-07
S	Air	5e-8 m	2.3715	0.0867	2.3715e-10	8.6671e-08
S	Air	1e-8 m	11.8577	0.0035	1.1858e-09	3.4668e-09
S	Air	1e-9 m	23.7154	8.667e-3	2.3715e-09	8.6671e-10
S	Mucus	1e-7 m	22.3042	-0.0103	2.2304e-13	1.0988e-10
S	Mucus	5e-8 m	44.6085	-0.0025	4.4608e-13	2.7469e-11
S	Mucus	1e-8 m	223.0425	-1.033e-3	2.2304e-12	1.0988e-12
S	Mucus	5e-9 m	446.0849	-2.583e-4	4.4608e-12	2.7469e-13

TABLE 2: Table of parameters alpha and beta with the according diffusion and sedimentation values

The figures 3 and 4 show the decline of the concentration of particles from Indomethacin and the figures 5 and 6 show the same but now for Salbutamol Sulfate. The time in the plots for the air media is 100 seconds and the time in the plots for the mucus media is 5 seconds. Every concentration starts at $1e16$ particles per ml to make it as realistic as possible. The difference in time is explained by the fact that the length of the mucus media is a factor 100 smaller than the air media.

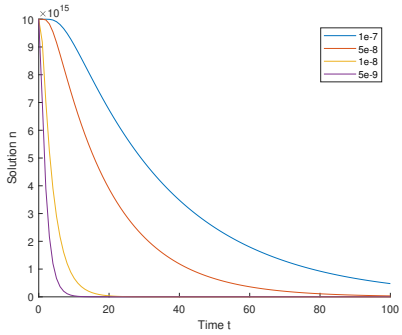

FIGURE 3: **Plot of concentration of Indomethacin in air.** Here the concentration is in particles per ml, the time is in seconds and the diameters are in meters.

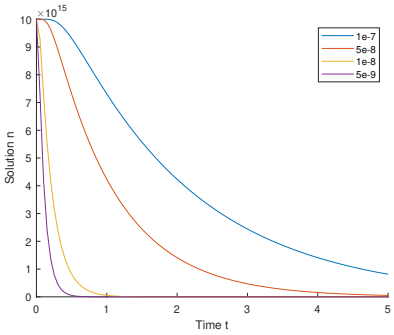

FIGURE 4: **Plot of concentration of Indomethacin in mucus.** Here the concentration is in particles per ml, the time is in seconds and the diameters are in meters.

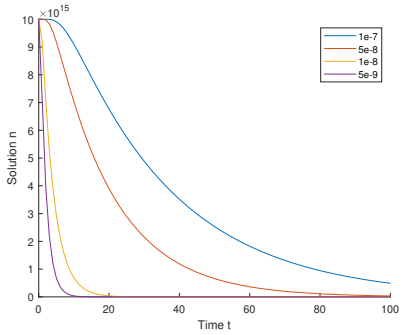

FIGURE 5: **Plot of concentration of Salbutamol Sulfate in air.** Here the concentration is in particles per ml, the time is in seconds and the diameters are in meters.

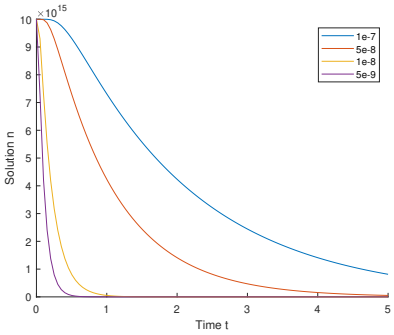

FIGURE 6: **Plot of concentration of Salbutamol Sulfate in mucus.** Here the concentration is in particles per ml, the time is in seconds and the diameters are in meters.

The plots show a faster decline of concentration of particles for smaller particles as can be expected from equation 2. There is no significant difference in transport rates between the two drugs. This can be explained by the fact that the densities are almost alike and that there are no other attribute besides the diameter, which is chosen to be the same, which are being used in equation 1 and 2.

As mentioned before we will analyse the half life of the concentration of the particles. In table 3 the values for the half life where the concentration reaches 5e-15 particles per ml are presented.

Table 3 shows negligible differences for the half life between the two drugs. We notice that for this range of aerosols the half life time value is the fastest for the smallest particles with a linear relation between the time and the diameter.

Drug	Diameter (m)	Half life time value in air (s)	Half life time value in mucus (s)
Indomethacin	1e-7	29.08	1.697
Indomethacin	5e-8	15.82	0.8509
Indomethacin	1e-8	3.203	0.1702
Indomethacin	5e-9	1.602	0.0851
Salbutamol Sulfate	1e-7	29.33	1.702
Salbutamol Sulfate	5e-8	15.82	0.8509
Salbutamol Sulfate	1e-8	3.203	0.1702
Salbutamol Sulfate	5e-9	1.602	0.0851

TABLE 3: Half life time value for each diameter per particle

4 Conclusion

We have shown with the use of the ISDD model that for the two therapeutic drugs the smaller aerosols diffuse faster through the air and mucus layer than the larger aerosols. This holds for aerosols between 5 and 100 nano-meters. The ISDD model simulates in-vitro cases however the ISDD model has been shown [1] to represent experimental data with a small error. Therefore it is acceptable to assume the same results would hold with a small error when done with experiments.

Researchers could use this information when making drugs that are being applied via inhalation to patients. The time for the half life is meant to represent the time for a drug to take effect in a body. The faster it diffuses the faster the drug would be present in the bloodstream and thus help the patient.

For the analysis of the differences between the two drugs we can say that it is negligible. As can be noticed in table 2 the diffusion rate is the same for both but there are small differences in the sedimentation rate. Since we only investigated the diffusion dominated cases it is clear that there will not be any major difference.

5 Discussion

In this report we analysed the transport rate of diffusion dominated cases. Since the diffusion coefficient is only effected by the size of the particle it would be interesting to further research transport rates dominated by the force of sedimentation.

This report shows a relative simple model of the diffusion and sedimentation of particles compared to the complexity of the lungs. However one could spend time and resources to make it more advanced. Then maybe more differences and discoveries would come to light. One could for example simulate agglomerate forming since we assumed it to be absent. This is of course not the case in real life. Another point which is interesting for further research is the interface of the air and mucus layer and how it would react to one another. From there one could even add more layers like the epithelial layer.

In the previous section we conclude that the smaller a particle is the faster it will diffuse. This however is not always possible to apply in real life [12-13]. It has always been a challenge to deliver drugs of micron and nano sized particles. Depending one the need of fast absorption of a drug one would need to think of a suiting particle size along with it.

6 References

[1] *Hinderliter et al., ISDD: A computational model of particle sedimentation, diffusion and target cell dosimetry for in vitro toxicity studies. Particle and Fibre Toxicology 2010 7:36.*
[2] *Ghislaine Lacroix et al., Air–Liquid Interface In Vitro Models for Respiratory Toxicology Research: Consensus Workshop and Recommendations. Applied in vitro toxicology. 2018, 92-103*
[3] *Yen CuW. Mark Saltzman, Mathematical modeling of molecular diffusion through mucus, Advanced Drug Delivery Reviews 61 (2009) 101–114*
[4] *Lai SK, Wang YY, Wirtz D, Hanes J. Micro- and macrorheology of mucus. Adv Drug Deliv Rev. 2009;61(2):86-100. doi:10.1016/j.addr.2008.09.012*
[5] *McFadden ER Jr, Pichurko BM, Bowman HF, Ingenito E, Burns S, Dowling N, Solway J. Thermal mapping of the airways in humans. J Appl Physiol (1985). 1985 Feb;58(2):564-70. doi: 10.1152/jappl.1985.58.2.564. PMID: 3980358.*
[6] *Fahy JV, Dickey BF. Airway mucus function and dysfunction. N Engl J Med. 2010;363(23):2233-2247. doi:10.1056/NEJMra0910061*
[7] *Salbutamol, ACD/Labs, http://www.chemspider.com/Chemical-Structure.1999.html*
[8] *Indomethacin, ACD/Labs, http://www.chemspider.com/Chemical-Structure.3584.html*
[9] *Sheehan JK, Brazeau C, Kutay S, Pigeon H, Kirkham S, Howard M, Thornton DJ. Physical characterization of the MUC5AC mucin: a highly oligomeric glycoprotein whether isolated from cell culture or in vivo from respiratory mucous secretions. Biochem J. 2000 Apr 1;347 Pt 1(Pt 1):37-44. PMID: 10727399; PMCID: PMC1220928.*
[10] *Tsuda A, Henry FS, Butler JP. Particle transport and deposition: basic physics of particle kinetics. Compr Physiol. 2013 Oct;3(4):1437-71. doi: 10.1002/cphy.c100085. PMID: 24265235; PMCID: PMC4398662.*
[11] *Cingolani et al (2019). In vitro Investigation on the Impact of Airway Mucus on Drug Dissolution and Absorption at the Air-Epithelium Interface in the Lungs. European Journal of Pharmaceutics and Biopharmaceutics. 141. 10.1016/j.ejpb.2019.05.022.*
[12] *Vivek Verma, Kevin M. Ryan, Luis Padrela, Production and isolation of pharmaceutical drug nanoparticles, International Journal of Pharmaceutics, Volume 603, 2021, 120708, ISSN 0378-5173, https://doi.org/10.1016/j.ijpharm.2021.120708.*
[13] *Xiangchun Meng, Zeyu Zhang, Linlin Li, Micro/nano needles for advanced drug delivery, Progress in Natural Science: Materials International, Volume 30, Issue 5, 2020, Pages 589-596, ISSN 1002-0071, https://doi.org/10.1016/j.pnsc.2020.09.016.*
[14] *Darquenne C. Aerosol deposition in health and disease. J Aerosol Med Pulm Drug Deliv. 2012;25(3):140-147. doi:10.1089/jamp.2011.0916*
[15] *Ochs M, Nyengaard JR, Jung A, Knudsen L, Voigt M, Wahlers T, Richter J, Gundersen HJ. The number of alveoli in the human lung. Am J Respir Crit Care Med. 2004 Jan 1;169(1):120-4. doi: 10.1164/rccm.200308-1107OC. Epub 2003 Sep 25. PMID: 14512270.*
[16] *1994-2022 The MathWorks, Inc.*
https://ch.mathworks.com/help/matlab/math/partial-differential-equations.html

7 Appendix

A code

```
clear all

%% Constants
g = 9.80665;
rho_f = 1.1460; %density of air
rho_p_s = 1200; %density of salbutamol sulfate in kg/m3
rho_p_i = 1300; %density of indomethacin in kg/m3
d_s = 5e-9; % diameter of salbutamol sulfate in m
d_i = 5e-9; % diameter of indomethacin in m
mu = 18.84e-6; %viscocity of air in Pa*s
```

```
k = 1.38064852e-23; %boltzmann constant m2 kg s-2 K-1
T = 305; %average body temperature in degrees Kelvin
m = 0; %Symmetry constant
L = 100e-6; %Length of air medium
Tmax = 100;
xdim = linspace(0,L,50);
tdim = linspace(0,Tmax,100);

%% Equations
%Ds = (k*T)/(6*pi*mu*d_s); %Diffusion coefficient of salbutamol sulfate
Di = (k*T)/(6*pi*mu*d_i); %Diffusion coefficient of indomethacin
%Vs = (g*(rho_p_s-rho_f)*d_s^2)/(18*mu); %Sedimentation coefficient of salbutamol sulf
Vi = (g*(rho_p_i-rho_f)*d_i^2)/(18*mu); %Sedimentation coefficient of indomethacin

%% Dimensionless convertion
t = tdim/Tmax;
x = xdim/L;


%% Writing down the solution function
%first make a C matrix such that we can use the constants in the functions
C.Di = Di;
C.Vi = Vi;
C.Tmax = Tmax;
C.L = L;
%Here the functions are called and the solution calculated
%options = odeset('RelTol',3e-4,'AbsTol',1e-5,'InitialStep',);
eqn = @(x,t,u,dudx) pdefun(x,t,u,dudx,C);
ic = @(x) icfun(x);
bc = @(xL,uL,xR,uR,t) bcfun(xL,uL,xR,uR,t,C);
sol = pdepe(m,eqn,ic,bc,x,t);

%% Alpha and Beta
Alpha = Di*Tmax/L^2;
Beta = Vi*Tmax/L;

%% Plots
up = sol(:,50,1);
figure
plot(t,up)
xlabel('Time t')
ylabel('Solution n')

%% Function defining
%Here the function is formulated in the form of c*dudt = f * dudx + s
function [c,f,s] = pdefun(x,t,u,dudx,C)
Di = C.Di;
Vi = C.Vi;
L = C.L;
Tmax = C.Tmax;

c = 1;
f = ((Di*Tmax)/L^2)*dudx;
s = -((Vi*Tmax)/L)*dudx;
end
```

```
%Initial condition
function u0 = icfun(x)
u0 = 1;
end

%boundary conditions
%These are put in the form of p + q*f = 0 on the left boundary and the
%right boundary. In my case the lower and upper boundary.
function [pL,qL,pR,qR] = bcfun(xL,uL,xR,uR,t,C)
% Di = C.Di;
% Vi = C.Vi;

pL = uL;
qL = 0;
pR = 0;
qR = 1;
end
```