Liver Nanoparticle Transportation Model Equation Sheet

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23/1/2022

Contents

1 Introduction

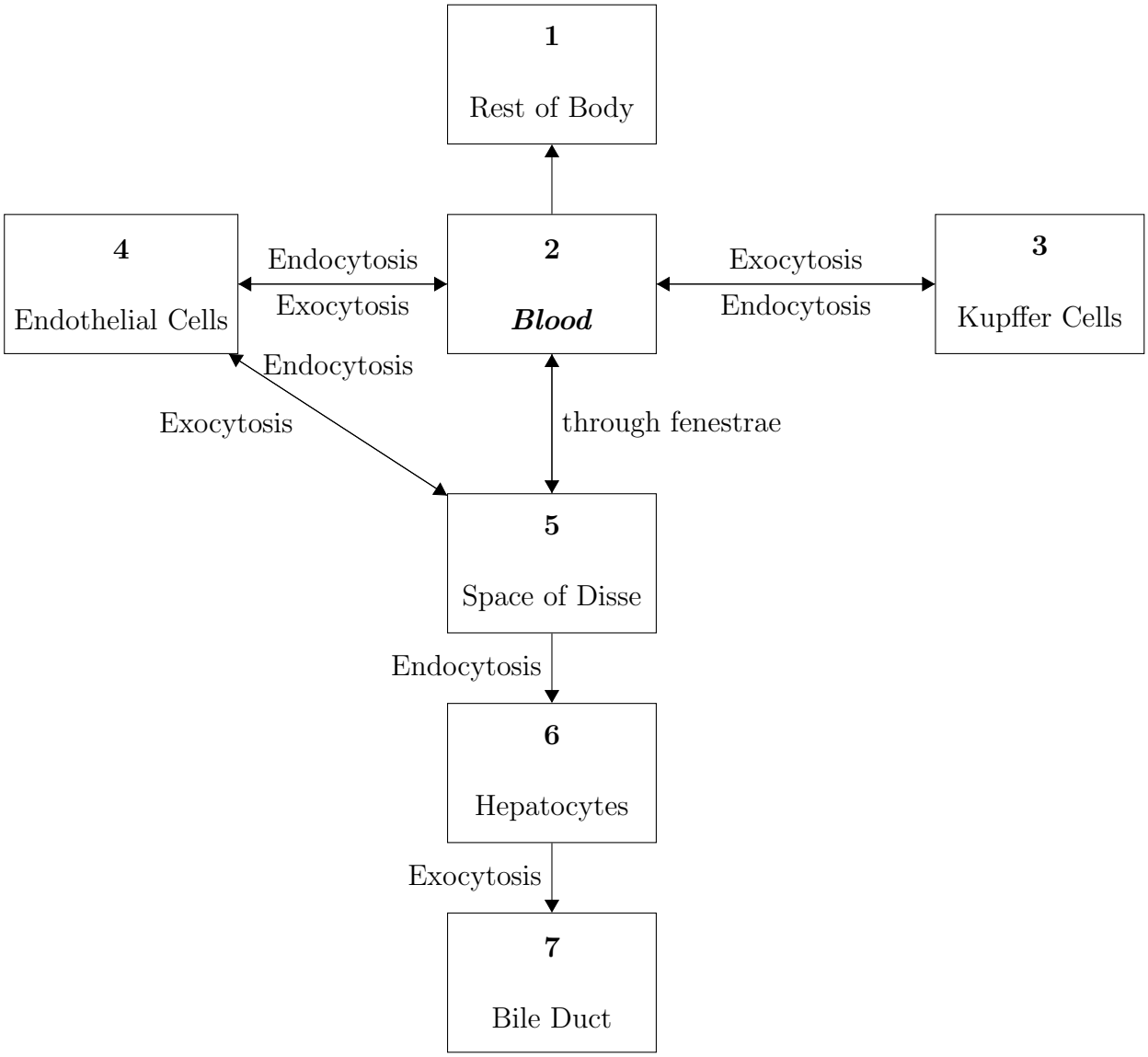
This document is a supplementary material for project "Nanoparticle-Cell Interactions: Liver Transportation Model".

The document contains full model used in the project and scenario analysis after coded the model.

For coding detail, please navigate to GitHub Page.
For a brief overview of the project, please navigate to Poster Link.

2 Illustration Diagram

Assumptions: Continuous Mixing so Dosimetry effect can be neglected.



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Endocytosis = Eat, Exocytosis = spit out
Endocytosis + Exocytosis = Transcytosis

3 Full Model Equations

3.1 Kinetic Models

$$f_{FluidtoCell}(Fluid, Cell) = SC_{cell} \cdot r_{cell} \cdot \frac{P_{cell\_capacity} - C_{Cell}(t)}{P_{cell\_capacity}} \cdot C_{Fluid}(t) \tag{1}$$

$$f_{CelltoFluid}(Cell, Fluid) = SC_{cell} \cdot r_{cell\_out} \cdot C_{Cell}(t) \tag{2}$$

$$f_{FluidtoFluid}(FluidA, FluidB) = r_A \cdot r_B \cdot \frac{Size_{fenestrae}}{Size_{Particle}} \cdot C_{FluidA}(t) \tag{3}$$

$f_{toCell}(Fluid, Cell)$: the cell kinetic model of particles moving from fluid to cell.
SC: surface coverage of the cells in current Fluid.
r_{cell}: rate of cell association.
u: particle concentration.
$P_{capacity}$: carrying capacity of cells for particles
$Cell(t)$: current number of associated particles in cell.
$Fluid(t)$: current number of particles in fluid
$r_{exchange}$: default exchange rate.

3.2 Liver Transportation Model

$$\frac{\mathrm{d}RestOfBody}{\mathrm{d}t} = r_{RestOfBody} * C_{Blood}(t) \tag{4}$$

$$\begin{aligned}\frac{\mathrm{d}C_{Blood}}{\mathrm{d}t} = --r_{OutofBody} * C_{Blood}(t) + f_{CelltoFluid}(Kupffer, Blood) - f_{FluidtoCell}(Blood, Kupffer) \\ + f_{CelltoFluid}(Endothelial, Blood) - f_{FluidtoCell}(Blood, Endothelial) \\ + f_{FluidtoFluid}(Space, Blood) - f_{FluidtoFluid}(Blood, Space)\end{aligned} \tag{5}$$

$$\frac{\mathrm{d}C_{Kupffer}}{\mathrm{d}t} = f_{FluidtoCell}(Blood, Kupffer) - f_{CelltoFluid}(Kupffer, Blood) \tag{6}$$

$$\begin{aligned}\frac{\mathrm{d}C_{Endothelial}}{\mathrm{d}t} = f_{FluidtoCell}(Blood, Endothelial) - f_{CelltoFluid}(Endothelial, Blood) \\ + f_{FluidtoCell}(Space, Endothelial) - f_{CelltoFluid}(Endothelial, Space)\end{aligned} \tag{7}$$

$$\frac{\mathrm{d}C_{Space}}{\mathrm{d}t} = f_{FluidtoFluid}(Blood, Space) - f_{FluidtoFluid}(Space, Blood) + f_{CelltoFluid}(Endothelial, Space) - f_{FluidtoCell}(Space, Endothelial) - f_{FluidtoCell}(Hepatocytes, Space) \quad (8)$$

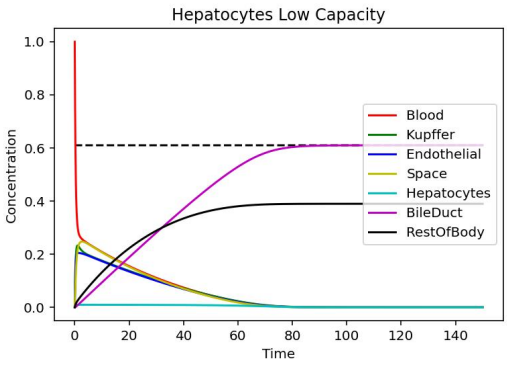
$$\frac{\mathrm{d}C_{Hepatocytes}}{\mathrm{d}t} = f_{FluidtoCell}(Space, Hepatocytes) - f_{CelltoFluid}(Hepatocytes, BileDuct) \quad (9)$$

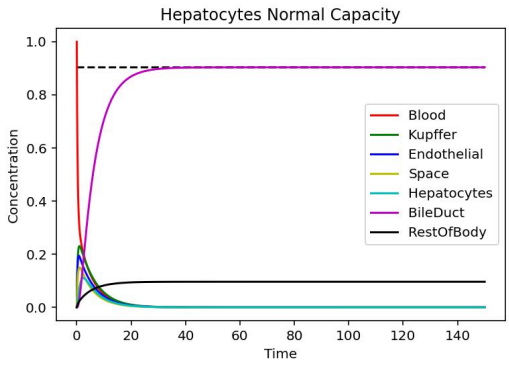
$$\frac{\mathrm{d}C_{BileDuct}}{\mathrm{d}t} = f_{CelltoFluid}(Hepatocytes, BileDuct) \quad (10)$$

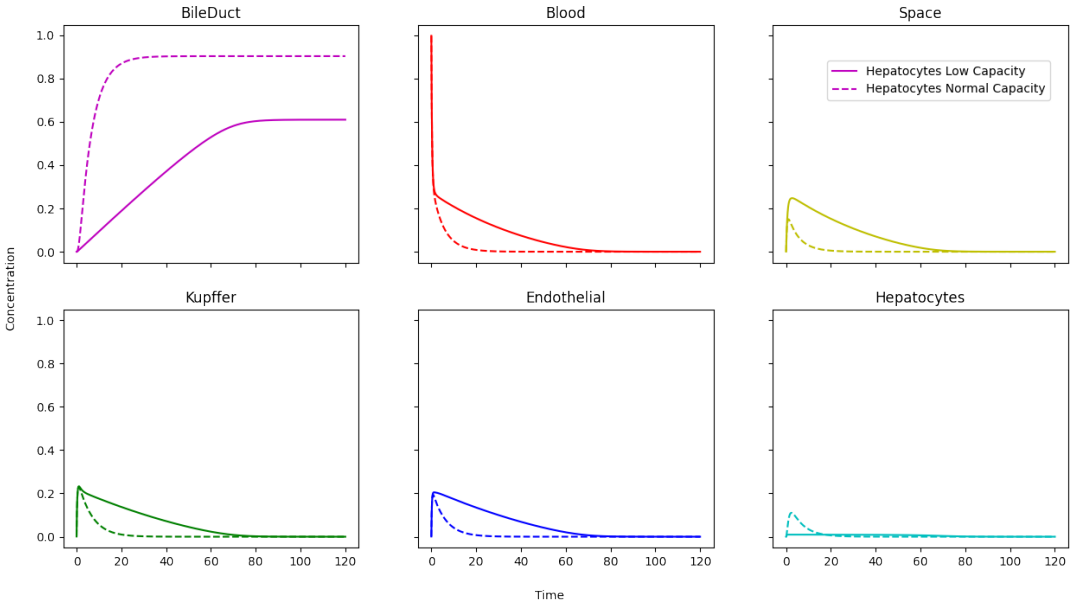
4 Scenarios Analysis

Exploring different Scenarios with program.

4.1 Hepatocytes Reach Max Capacity







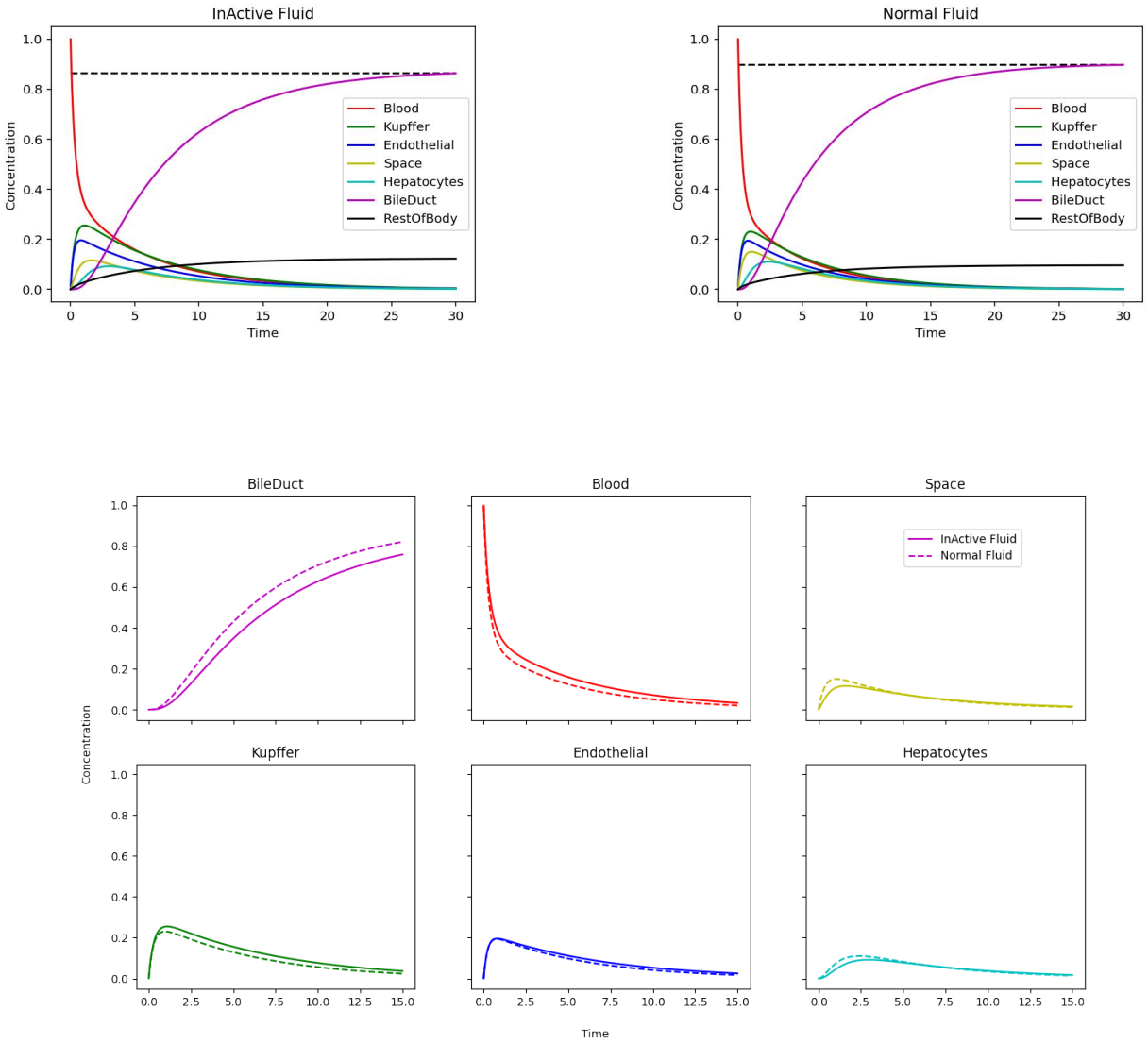
If we model the Hepatocytes with its capacity removed(it never stores any particles). The result is very interesting.

As the graph suggests, the particle concentration in the bile duct indicating a linear increase. It is believed that the rate of that in BileDuct is the same as the rate going out of Hepatocytes.

It also indicates that the actual rate of liver-particle association through different parts are varying across the board. Generally except for the blood and the bile duct, the particles rushes into each part of the liver, making them populated. After the concentration of particles in Blood decrease around a certain amount of value, the process reverse: each liver part's concentration goes down and they are functioning like balloon to become less saturated.

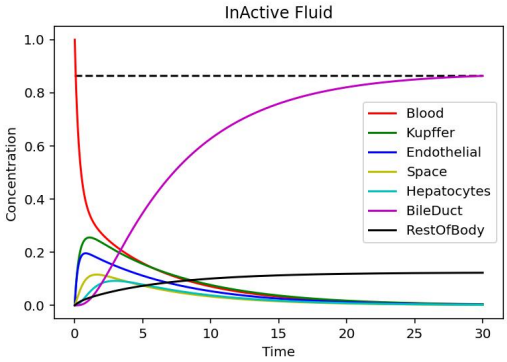
4.2 Between Fluid Transportation

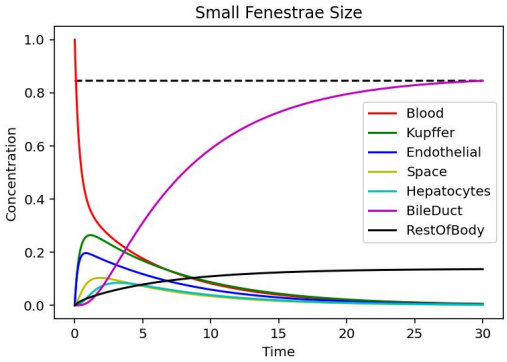
4.2.1 InActive Fluid VS Normal Fluid

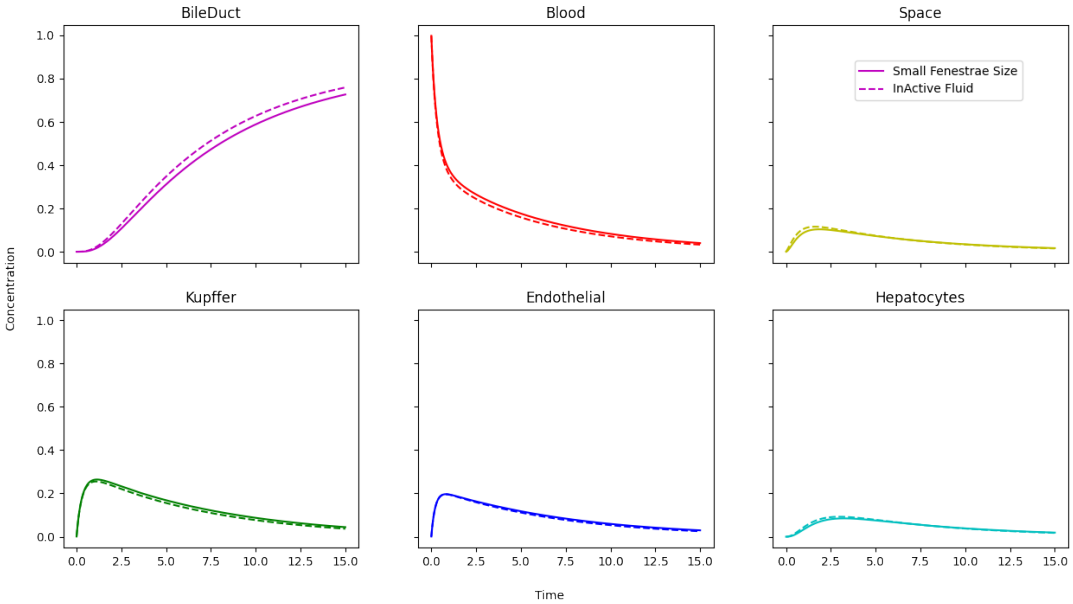


When making body fluid less active (with less particle association rate), it appears to directly affect the particle transportation through the fenestrae since between fluid transportation mainly rely on fenestrae. As the graph suggested, fenestrae transmission takes an important role in particle association as there's significant change of concentration in the bile duct.

4.2.2 InActive Fluid VS Fenestrae Size

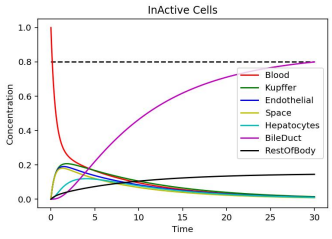


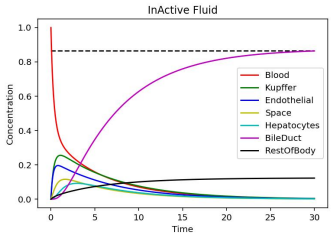


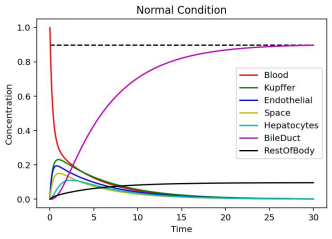


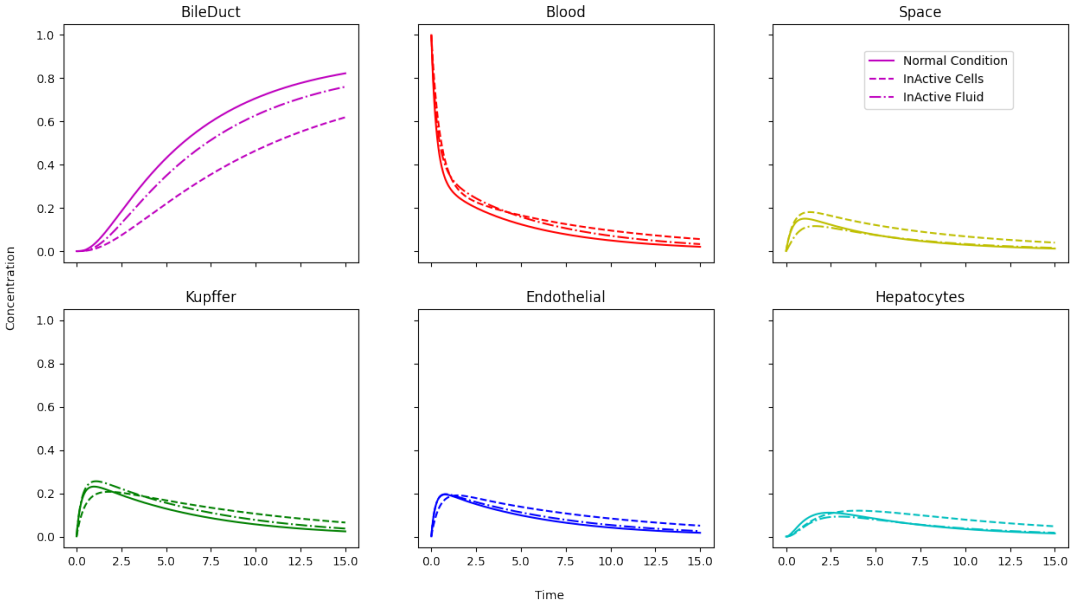
[Be aware that the fenestrae size changes may lead to change in Surface Coverage SC parameter] Discussed Above: - Assume Surface_Coverage is not affected by Fenestrae_Size Since the impact of fenestrae size depends on particle size as well, it needs further experiment data to analyse. However, the analysis above does suggest fenestrae size and the rate of association of fluids do have impact of the transportation process between fluid.

4.2.3 InActive Fluid VS InActive Cells



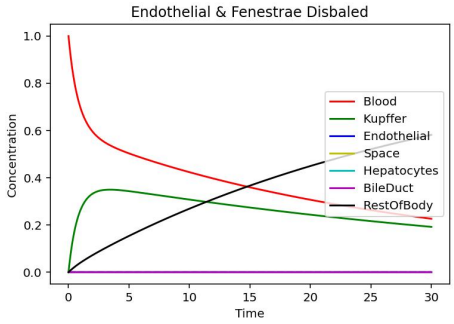


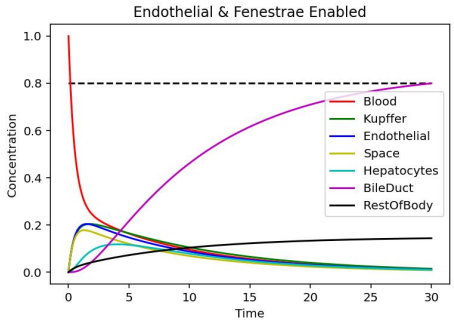


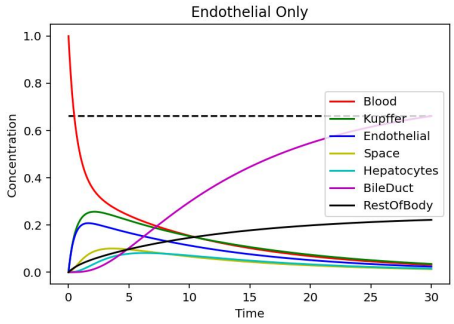


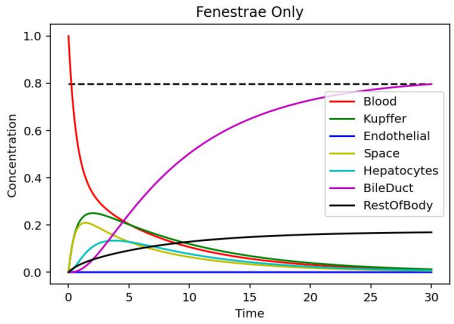
If Cells are more likely inactive, which means they have lower rate_in and rate_out, most likely the whole process is been slowed down. It can be seen that more particles will remain in cells if the fluid is inactive or the Cells are inactive. Therefore, there are significantly more particles in Space of Disse in "inactive Cell Model" as the fenestrae transmission is not affected. Generally, the cells' performance may have large impact on the transportation than fluid's.

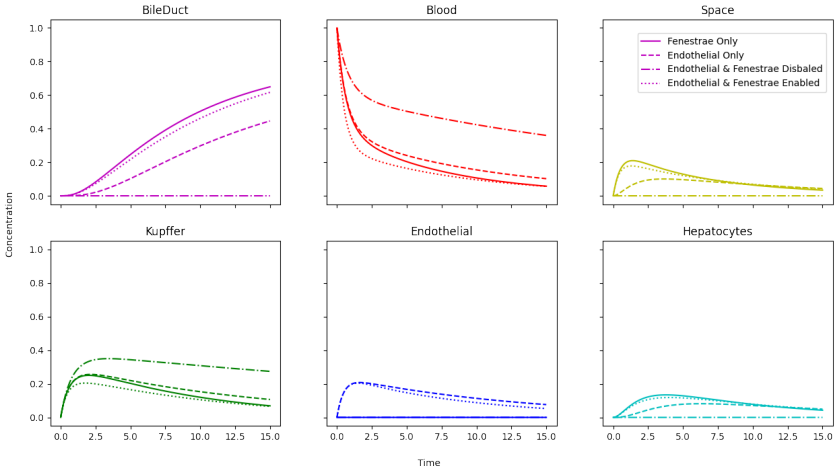
4.2.4 Endothelial VS Fenestrae Size





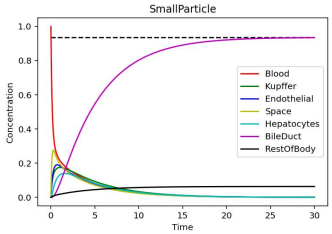


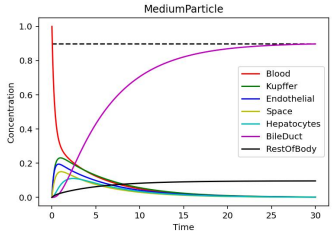


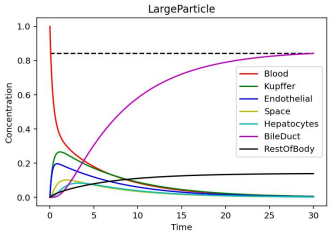


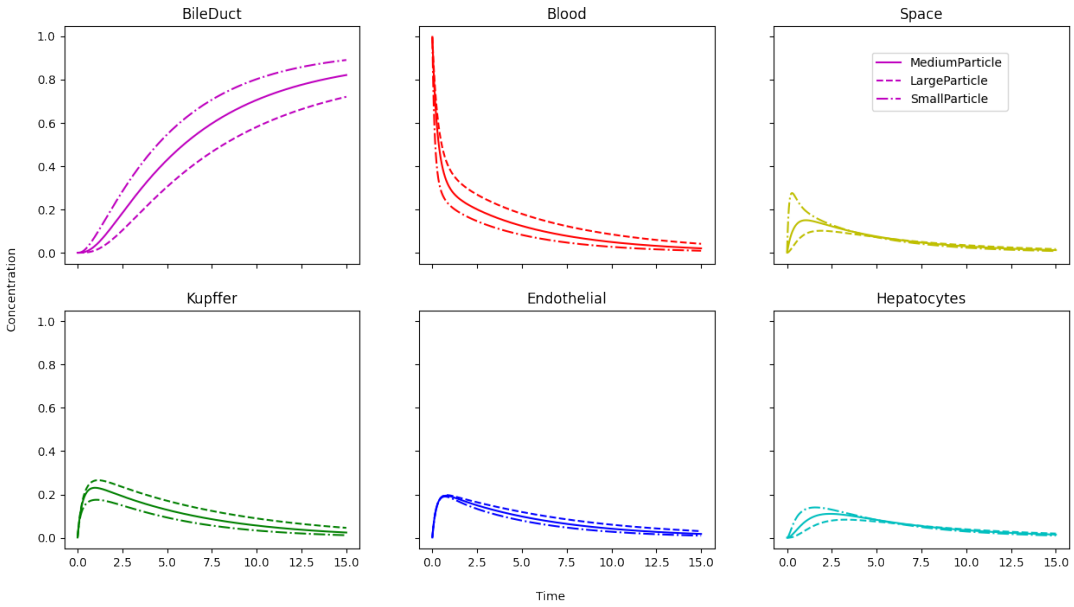
In this part, I tried to explore one of the factor's effect — Endothelial
By making Endothelial Cell incapacitated (r_in=r_out=0), with the help of Fenestrae only, our particles can easily going to the bile duct with a little less effectiveness.
However, when trying to make Endothelial cell function only (with fenestrae size = 0), by only making rate_in and rate_out high enough, can we compensate the loss of the help from the fenestrae, which means by making endothelial cell more effective, we can totally replace the effect of fenestrae transportation.
Moreover, by making r_in and r_out high enough, it is shown that the Endothelial cell may not the threshold of particle's transportation anymore. Further adjustment to rate won't take affect to our model. This generally implies that when treating multi factor models like this, by improving single part of the model (improve single cell/fluid's performance) won't improve the effectiveness overall, it will always reach a threshold limited by other factors.

4.3 Particle Size Small VS Medium VS Large



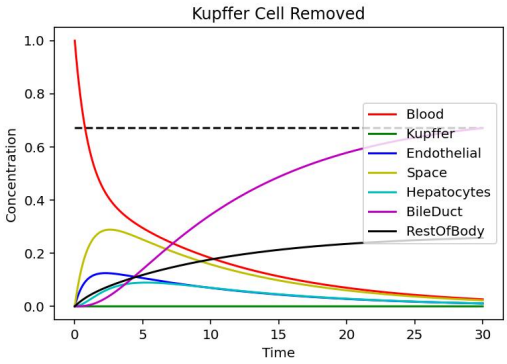


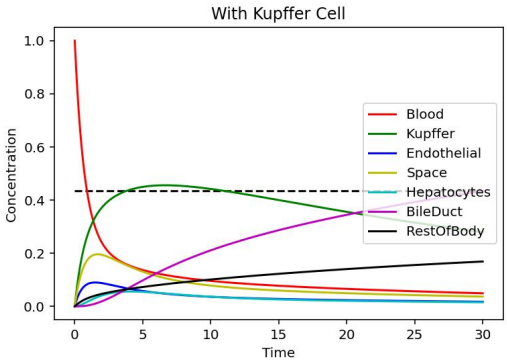


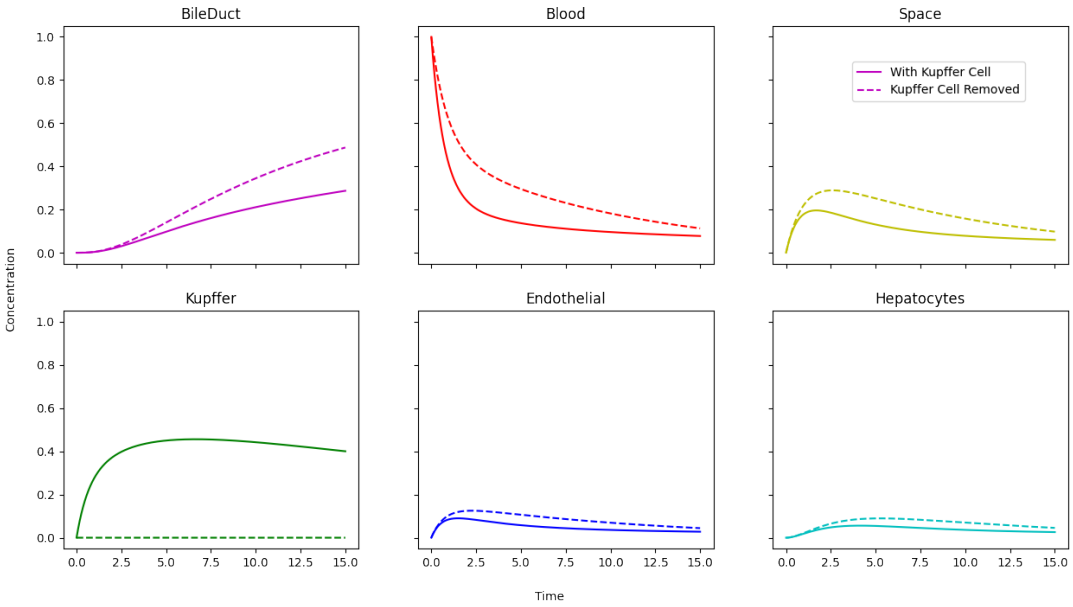


Smaller Particles make the whole process faster. As the particles move faster through fenestrae within the blood and the space of disse. As a result, hepatocytes cells would been fully operating as the concentration in Space of Disse is higher.
With Larger Particles, they go through the fenestrae much more slowly and even been been blocked out. Therefore the particles in the blood can only get to the space of disse by trancytosis across endothelial cells or finally overflow to the rest of the body.

4.4 Remove Kupffer Cells







By making Kupffer Cells surface coverage to 0, we removed the Kupffer Cells' effect. Showing by graph, It is clear that removing Kupffer Cell may increase the overall association rate and more particles swarms into cells.
when Kupffer cell only takes particles, those particles will stuck in the Kupffer cells and it impeded the process of particle intake. While making Kupffer cells have even just a minor outflow rate (r_out), it increases the efficiency of transportation A LOT!
It also suggests the maximum capacity of each cell (max_capacity = 1) may not reach.