# Nanoparticle-Cell Interactions: Liver Transportation Model

Chenghao Li

School of Mathematics & Statistics

## Introduction

The unique capabilities of nanoparticles can greatly aid medical applications, for example, in vitro/vivo detection and diagnosis, multimodal imaging, chemotherapy and phototherapy. However, to safely and effectively make use of the nanoparticle technology, we have to fully understand its interaction with in-vivo cells (for example, to prevent unwanted nanoparticles remaining in the body after the therapy is finished).
Faria et al. (2019)'s Cell Carrying Capacity(CCC) Model [1] established a solid mathematical foundation of symbolising cell-particle interactions. Inspired by the model of Faria et al. (2019), we developed a detailed mathematical for the analysis of nanoparticle transport through the liver. We present numerical solutions to the model and reveal the impact of immune cells in the liver.

## General Liver-Particle Transportation Structure

The graph below helps illustrate how nanoparticles transport through the liver to the bile duct and finally excrete the human body.

- A **Kupffer Cells:** localized in the blood vessel of the liver, take in particles by endocytosis.
- B **Fenestrae:** Windows between each endothelial cell, particles can easily travel through if they are larger than the fenestrae.
- C **Endothelial Cells:** As a single-layer barrier of the vessel, they control fluid and particles into and out of a tissue/blood.
- D **Hepatocyte Cells:** Main cells in the liver, take up particles in liver tissue, then deliver them to the bile duct.

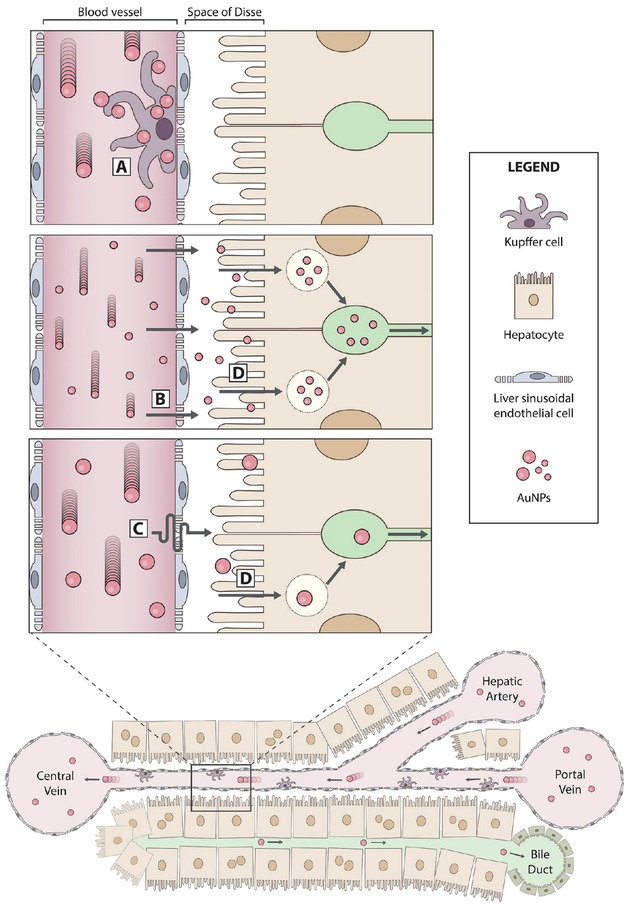


Figure 1. Liver structure for particle's transportation (Wilson Poon, et al., 2019)[2]

## Cell&Fluid-Particle Association Model

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

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

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

Where $f_{XtoY}$ representing rate of particles moving from X compartment to Y. $C_{xxx}(t)$ is the concentration of that compartment at time t. $SC_{cell}$ is the surface coverage of the cell in vivo $r_{in}$ and $r_{out}$ are rates of particles association/disassociation with that part. For example, when representing particles moving from the blood to the space of disse, $f_{FluidToFluid}$ can be utilised. The change of particle concentration in the blood or the space of disse is related to each fluid's specific rate of association with the particles ($r_A$ and $r_B$), size of the particles $Size_{Particle}$, the fenestrae size $Size_{fenestrae}$ and the input particle concentration $C_{FluidA}$.
Specifically, $f_{FluidtoCell}$ is a unique cell-particle association function inspired by the CCC model by Faria et al. (2019). Their research successfully takes our understanding of cell-particle association from a quantitative level to a next level that enable us for quantitative analysis.

## Liver Transportation Mathematical Model

The follow diagram shows the connections between different components of the liver and body. For the purpose of this model, the particles are injected into the blood and finally excrete the body through bile duct.

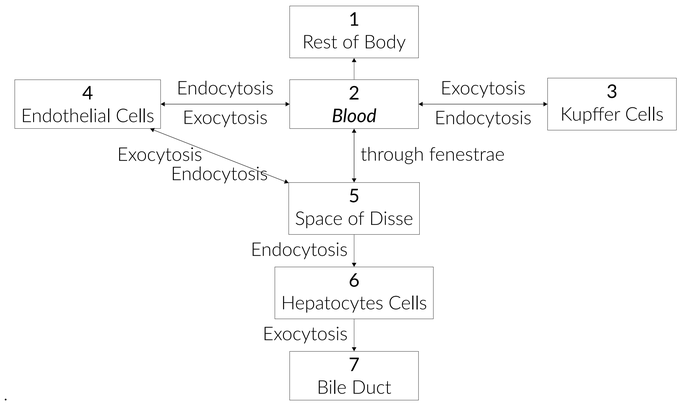


Figure 2. Liver Transportation Model Diagram

### Mathematical Ordinary Differential Equations

After drawing the connection diagram we can construct a mathematical model based on the cell&fluid-particle association model. Each equation represents the change of particle concentration in each body part. For example, the change of particle concentration in **Kupffer Cells** consists of the rate that particles enter the Kupffer cells minus the rate of them exit the Kupffer cells and return back to the blood.

$$\begin{aligned}\frac{\mathrm{d}C_{Blood}}{\mathrm{d}t} = &-r_{RestOfBody} * c_{Blood}(t) + f_{CelltoFluid}(Kupffer, Blood) - f_{FluidtoCell}(Blood, Kupffer) \\ &+ f_{CelltoFluid}(Endothelial, Blood) - f_{FluidtoCell}(Blood, Endothelial) \\ &+ f_{FluidtoFluid}(Space, Blood) - f_{FluidtoFluid}(Blood, Space)\end{aligned} \quad (4)$$

$$\frac{\mathrm{d}c_{Kupffer}}{\mathrm{d}t} = f_{FluidtoCell}(Blood, Kupffer) - f_{CelltoFluid}(Kupffer, Blood) \quad (5)$$

## Full Model and Simulation Scenarios

Only two of seven ODE equations and a single simulated scenario has been shown due to the limited space. For the full model, please click here

## Results

By setting up some initial values, I coded a python program using advanced Euler method iteratively, the full model is now solved. To analyse the impact of Kupffer cells been kept or removed, some diagnostic plots have been drawn.

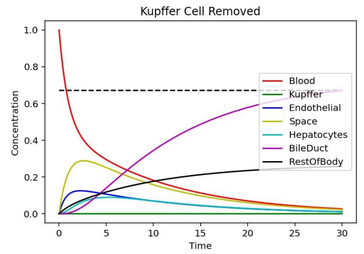


Figure 3. Kupffer Cell Removed

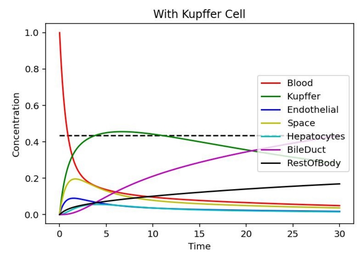


Figure 4. Kupffer Cell Kept

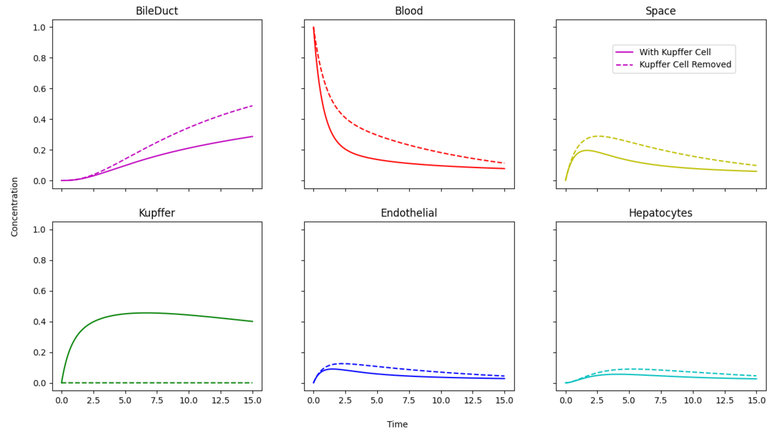


Figure 5. Liver structure for particle's transportation

From Figure 5, it is interesting that particles in the blood may get to the BileDuct more effectively if the Kupffer Cells, the "devourers", are removed by making $SC_{KupfferCells}$ equals zero. However, although Kupffer cells may retain particles to slow down the particle excretion process, they could lead to less particle outflow to the rest of the body as most particles are been kept in Kupffer Cells in Blood.

## Conclusions

A quantitative mathematical model of nanoparticles transportation through the liver has been developed. It would be fascinating if experimental data can be obtained for model fitting. A more detailed model could lead to further biomedical research towards nanoparticle applications.

## Acknowledgements

My profound gratitude goes to my wonderful supervisor, Stuart Johnston, for his invaluable support, patience, time and guidance in seeing me to the completion of this research project. Also, my gratitude goes to our School of Mathematics & Statistics, especially Roy Ridgway and Thomas Quella who foster me a great opportunity for this research project.

## References

[1] Qiong Dai Mattias Björnmalm Stuart T. Johnston Kristian Kempe Frank Caruso Edmund J. Crampina Matthew Faria, Ka Fung Noi. Revisiting cell–particle association in vitro: A quantitative method to compare particle performance. *Journal of Controlled Release*, 307:355–367, 2019.

[2] Ben Ouyang Benjamin R. Kingston Jamie L. Y. Wu Stefan Wilhelm Warren C. W. Chan Wilson Poon, Yi-Nan Zhang. Elimination pathways of nanoparticles. *ACS Nano*, 13:5785–5798, 2019.