Institute for Digital Communications

Prof. Dr.-Ing. Robert Schober
University of Erlangen-Nürnberg

Bachelor Thesis/Research Project/Master Thesis

Molecular Communications Channel Modeling in Capillaries

Background: In molecular communications (MC), information is conveyed between biochemical communication nodes using *signaling molecules*. Within the human body, *natural* MC facilitates essential biological processes such as cellular signaling and neuronal communication. *Synthetic* MC builds upon these natural mechanisms by employing engineered MC systems, e.g., for medical applications, including early cancer detection [1], targeted drug delivery [2], and health monitoring [3].

Channel Modeling in Large vs. Small Blood Vessels: For the design of most envisioned MC applications in the cardiovascular system (CVS), a quantitative understanding of signaling molecule transport in blood vessels is necessary. Mathematical models for molecule distribution in blood vessels can provide such insights. In the context of MC, these models are referred to as *channel models*, because they capture the effects of the communication channel [4]. Up until now, channel models for MC in the CVS are focused on single large/medium-sized arteries (vessel diameters of roughly $\geq 0.1\,\mathrm{mm}$), networks of such arteries, and closed-loop systems [4, 5]. At these larger scales, i.e., in the *macrovasculature*, blood behaves as a Newtonian fluid [6], allowing simplified analytical models that accurately capture molecule transport in blood under transport mechanisms like advection, molecular and turbulent diffusion, ad-/desorption and absorption at the vessel walls, and signaling molecule degradation [2, 4, 5, 7, 8].

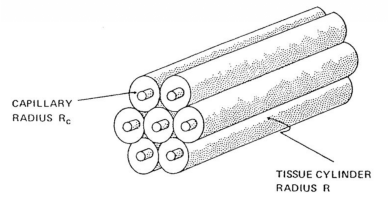
While molecule distribution in macrovasculature is important for MC over long distances (on the order of (centi)meters) in the human body, many envisioned applications, including early cancer detection and targeted drug delivery, ultimately take place in the *microvasculature* in the tumor environment. Here, in networks of capillaries (vessel diameters of roughly $3-7\,\mu\mathrm{m}$), blood flow is slow (flow velocities of around $0.8\,\mathrm{mm\,s^{-1}}$) and non-pulsatile, and vessel walls are highly permeable [9]. This enables the exchange of vital molecules like oxygen and nutrients through the vessel walls into surrounding tissue [10]. Since red blood cells (RBCs) typically have a slightly greater diameter (roughly $6-8\,\mu\mathrm{m}$) than capillary vessels, blood does not behave like a Newtonian fluid in these conditions [6]. Rather, RBCs line up single-file with blood plasma[1] between them, see Fig. 1c, and move through the capillaries at a constant velocity [10, 6]. Signaling molecules distribute between the RBCs and in a small cell-free layer, called the plasma skimming layer (PSL), close to the vessel walls [10], see Fig. 1b. Occasionally, larger plasma-filled gaps between two RBCs occur [9, 11].

Overall Project Aim: While molecule transport modeling in capillaries has been an ongoing topic in medicine for over a century, so far, **no such model has been introduced to the MC community**. This is partly due to the high complexity of the models from medical literature, which limits the insights from and applicability of the models. For this reason, in this project, a simplified (reduced-order) channel model for MC in a single capillary shall be derived from existing models and validated. We will focus on healthy capillary tissue and leave the modeling of tumorous tissue for future work.

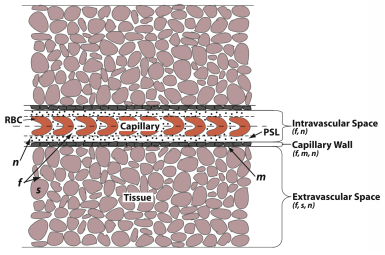
Existing Models for Molecule Transport in Capillaries: Signaling molecule transport[2] in capillaries is typically modeled using computational and mathematical techniques that capture

[1] Whole blood is comprised of plasma (55%), RBCs (erythrocytes, 44%), and white blood cells and platelets (leukocytes and thrombocytes, 1%). Plasma itself consists of 90% water, proteins (like albumin, antibodies, and clotting factors), glucose, ions, hormones, and other substances.

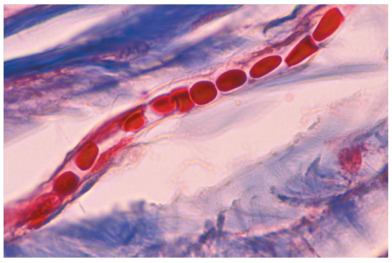
[2] Here, it is assumed that the signaling molecules are much smaller than RBCs.



(a) The Krogh tissue-cylinder model is the most fundamental approach to modeling molecule transport in capillaries and surrounding tissue [12, 13, 14].



(b) Schematic of capillary and surrounding tissue, divided into three regions: the intravascular space, vessel wall, and the extravascular space. The intravascular space consists of a core region containing the RBCs and the PSL. f, n, m, and s denote the fluid phase, signaling molecule, endothelial cells, and tissue cells, respectively [10].



(c) Microscopy image of RBCs lined up in a capillary. Since RBCs have greater diameters than capillaries, the cells have to deform in order to squeeze through the vessel. Image taken from `https://shorturl.at/xq681`.

Figure 1: Blood flow and molecule transport in capillaries.

complex transport mechanisms within vessels, across vessel walls, and in tissue spaces. The most fundamental approach is the *Krogh tissue-cylinder model*, see Fig. 1a, which considers an elementary microvascular unit with a cylindrical blood vessel surrounded by tissue volume [12, 13]. More advanced methods, like mixture theory models, additionally model the PSL and the vessel wall as individual regions, each with a characteristic mixture of constituents (fluid, solids like endothelial cells, membrane, and extracellular matrix, and solute like signaling molecules, nutrients, and proteins) [10], see Fig. 1b. Beyond the modeling of individual capillaries, more advanced models also include the arterioles preceding the capillaries and the venules succeeding the capillaries [10, 14].

Project Objectives: The main objectives of this thesis can be summarized as follows:

- Review literature on existing mathematical models for blood flow and molecule transport in capillaries and surrounding tissue.
- Implement a simple model for a single capillary from literature as a baseline.
- Derive a new simplified model for molecule transport in a single capillary and surrounding tissue, suitable for MC.
- Compare the predictions of the derived model to predictions from existing models and optionally clinical data.

Prerequisites: The following qualifications are required in order to pursue this project:

- Affinity for mathematical modeling
- Basic understanding of partial differential equations
- Basic programming skills in Python

SUPERVISORS Timo Jakumeit, timo.jakumeit@fau.de, Room 04.034
Maximilian Schäfer, max.schaefer@fau.de, Room 04.034

Start date: TBD
End date: TBD

Prof. Dr.-Ing. Robert Schober

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