Spheroidal Receiver with Non-Uniform Porosity

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***Abstract*—Spheroids are 3-D cell aggregates with many thousands of cells and are commonly used in biomedical experiments. Molecular communication (MC) can be applied to model propagation within spheroids, e.g., for targeted drug delivery, but more realistic receiver models are needed. In this abstract, the Non-Uniform Porosity Spheroid (NUPS) model with different layers of varying porosity values is considered as an MC receiver in an unbounded fluid environment. The boundary conditions and effective diffusion coefficients of each layer are characterized. It is revealed that the NUPS model demonstrates more complex diffusion behavior than the homogeneous spheroid model.**

I. Introduction

Molecular communication (MC) is a bio-inspired mechanism that is envisioned to realize micro- and nano-scale communication systems using molecules as information carriers. The spheroid, which is a 3D cell aggregate in a spherical shape and commonly used in Organ-on-Chip (OoC) systems, is one realistic transceiver for MC. Potential applications that can be modeled with spheroids include nutrient transport in an OoC system or drug reception by a cancerous tumor site.

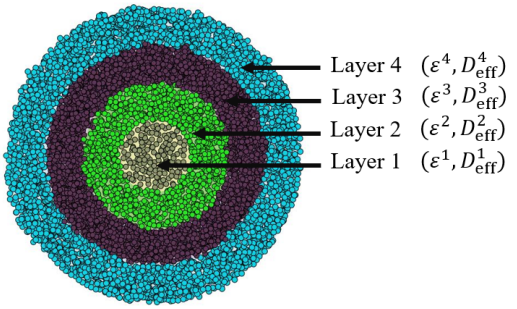
In our previous study [1], we modeled a spheroidal receiver as a homogeneous porous media for diffusive signaling molecules, and then its boundary conditions and effective diffusion coefficients were characterized. We considered uniform spheroid porosity with a dense arrangement of live cells and low porosity everywhere. However, in larger spheroids, this assumption is less valid because there are distinct layers with varying cell density; cells in the outer layer are loosely attached whereas the intermediate layer has tighter cell packing and a denser extracellular matrix. Hence, the diffusion of molecules such as oxygen to the core becomes restricted, leading to cell death and the formation of a necrotic center [2]. Therefore, it is insightful to investigate the impact of non-uniform porosity on propagation within a spheroid.

In this abstract, we consider a diffusive MC system with a spheroidal receiver and a point source transmitter. We analyze the Non-Uniform Porosity Spheroid (NUPS) model for the receiver. For this purpose, we assume a spheroid composed of layers with distinct porosities. We compare this NUPS model with the Uniform Porosity Spheroid (UPS) model, which is uniformly porous.

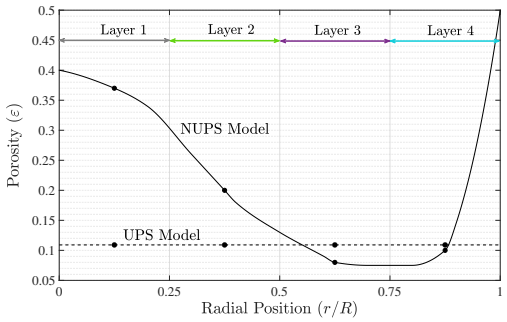
II. System Model

An end-to-end diffusive MC system is considered with a point source transmitter and a spheroidal receiver with radius γ_{s}. Fig. 1a illustrates the cross-section of the spheroidal receiver with N_L layers, indexed from the inside out. The *porosity parameter* of each layer, ε^i, serves as the ratio of the extracellular space of the corresponding layer to its overall volume, i.e., $\varepsilon^i = 1 - \frac{N_{\mathrm{c}}^i V_{\mathrm{c}}}{V_{\mathrm{L}}^i}$, where N_{c}^i, V_{c}, and V_{L}^i are the number of cells within layer i, volume of each cell, and volume of layer i. We assume that the spheroid is immersed in an unbounded fluid medium with zero flow rate (extendable to a system with convection) that fills its extracellular space. The effective diffusion within the whole spheroid volume is reduced compared to the free fluid diffusion outside [1]. Each layer has its own effective diffusion coefficient D_{eff}^i for signaling A molecules, according to its porosity parameter ε^i. D_{eff}^i can be determined from the A molecule free fluid diffusion coefficient D, i.e., $D_{\mathrm{eff}}^i = \frac{\varepsilon^i}{\tau^i} D$, where τ^i is the tortuosity of layer i and it refers to the degree of path irregularity or curvature experienced by a molecule while it traverses through the extracellular space of each layer of the spheroid [3]. τ^i is a function of porosity, i.e., $\tau^i = \frac{1}{(\varepsilon^i)^{0.5}}$.

To describe the environment geometry, we use the spherical coordinate system where $\bar{r} = (r, \theta, \varphi)$ denote radial, elevation, and azimuth coordinates, respectively. At the interface between



(a)



(b)

Fig. 1: (a) NUPS model cross-section with four layers. (b) Porosity variation across radial positions (0=center, 1=outer edge) in NUPS and UPS Models. Markers represent discretized porosity values at the center of each layer.

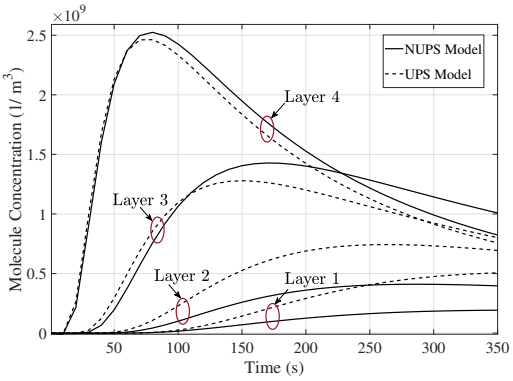


Fig. 2: Molecule concentration in different locations within NUPS and UPS models.

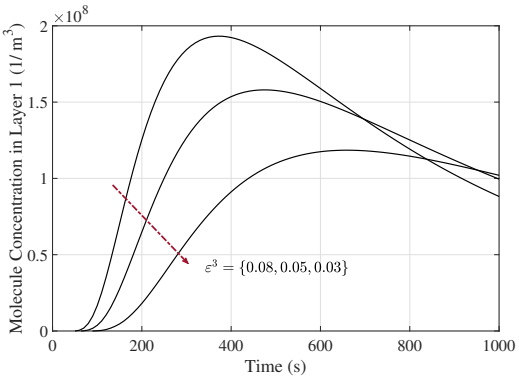


Fig. 3: Impact of porosity of outer layers (e.g., layer 3) on molecule concentration in inner layers (e.g., layer 1) in the NUPS model.

two diffusive environments that have different diffusion coefficients, a continuity condition for flow must be satisfied, which is expressed as

$$D^i_{\text{eff}} \frac{\partial c^i_{\text{s}}(\bar{r},t)}{\partial r} = D \frac{\partial c_{\text{o}}(\bar{r},t)}{\partial r}, \qquad i = N_{\text{L}} \tag{1}$$

$$D^i_{\text{eff}} \frac{\partial c^i_{\text{s}}(\bar{r},t)}{\partial r} = D^{i+1}_{\text{eff}} \frac{\partial c^{i+1}_{\text{s}}(\bar{r},t)}{\partial r}, \quad i \in \{1 : N_{\text{L}} - 1\} \tag{2}$$

and another boundary condition that is generally modeled as [4, Ch. 3]

$$c^i_{\text{s}}(\bar{r},t) = \kappa^i c_{\text{o}}(\bar{r},t), \qquad i = N_{\text{L}} \tag{3}$$

$$c^i_{\text{s}}(\bar{r},t) = \kappa^i c^{i+1}_{\text{s}}(\bar{r},t), \qquad i \in \{1 : N_{\text{L}} - 1\} \tag{4}$$

where $\bar{r} \in \partial\Omega$, $\partial\Omega$ denotes the spheroid boundary region, Ω is the spheroid region, and c^i_{s} and c_{o} denote the concentration function inside layer i and outside the spheroid, respectively. The constant κ^i is determined as $\sqrt{\frac{D}{D^i_{\text{eff}}}}$, for $i = N_{\text{L}}$ and $\sqrt{\frac{D^{i+1}_{\text{eff}}}{D^i_{\text{eff}}}}$, for $i \in \{1 : N_{\text{L}} - 1\}$ [1]. Thus, for $\kappa^i \neq 1$, a concentration discontinuity (i.e., jump) occurs at the boundary.

III. Results

In this abstract, we consider a spheroid with radius $275\,\mu\text{m}$. The volume of each cell is $3.14 \times 10^{-15}\,\text{m}^3$. Due to limited nutrient availability at the spheroid's center, cells without enough nutrients die, which causes increased porosity in the central and surrounding layers. Additionally, the looser packing of cells in the outer layer contributes to slightly higher porosity. Thus, we adopted radially-dependent porosity values from [5], as depicted in Fig. 1.

In Fig. 2, we compare molecule concentration in different locations obtained analytically from the NUPS model with distinct porosity across four layers (solid line in Fig. 1b) and the UPS model with consistent porosity throughout (dashed line in Fig. 1b while maintaining equal cell number. We also assume a zero degradation rate. From Fig. 1b, we observe that the porosity in the third and fourth layers of the NUPS model is lower than that of the UPS model. This lowered porosity in the NUPS model acts as a diffusion barrier and slows down molecule movement, resulting in a delayed increase in concentration. Also, the densely packed structure of outer layers in the NUPS model traps molecules, resulting in stronger signals than in the UPS model. Conversely, the NUPS model's first and second layers have higher porosity than the UPS model, facilitating a faster movement of molecules and, thus, a quicker rise in the signal. However, this increased porosity also decreases signal amplification compared to the amplification in the UPS model. The higher porosity of these inner layers in the NUPS model also enables easier penetration and diffusion of molecules but with a lesser degree of retention, thereby reducing the overall strength of the signal.

Fig. 3 shows the impact of reduced porosity in the outer layers of the NUPS model on molecular diffusion within the inner layers. The lower outer layer's porosity (e.g., layer 3) leads to delayed signals, lower peaks, and increased dispersion in the inner layers (e.g., layer 1). This is mainly because of the intensified difficulty for molecules to traverse the less porous outer layers, which results in delayed and decreased peak signals in the inner layers. Additionally, if molecules enter, escaping becomes harder, which leads to signal dispersion.

In conclusion, we explored molecule propagation in a spheroid with varying porosity. This study will form a robust groundwork for the future development of targeted drug delivery using MC.

References

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