Synthetic Biocommunication Dynamics Through Time-harmonic Electromagnetic Fields

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I. Background and Introduction

Extracellular vesicle (EV) transport in the extracellular space (ECS) is a crucial factor in both molecular communication and drug delivery. Cell-derived EVs are particularly promising for targeted drug delivery (TDD) due to their high biocompatibility. Previous research has successfully addressed the controlled release of EVs [1]; however, this study aims to investigate controlling their behavior post-release from the transmitter cell. Simulating the influence of electromagnetic (EM) fields on EV transport in neuronal communication can provide valuable insights into particle dynamics within the ECS. If these fields significantly affect EVs behavior, their impact could have important implications for TDD.

The interaction of time-harmonic EM fields can manifest in several ways: the Lorentz force acting on charged nanoparticles, dielectrophoresis influencing neutral particles with a dielectric response in a non-uniform electric field, and time-varying magnetic fields affecting magnetic nanoparticles [2]. This interaction can be modeled as a time-varying sinusoidal drift, where the drift amplitude depends on the field strength, particle charge and mass, and the damping mechanisms within the medium.

EVs can contain proteins, mRNA, or other biomolecules. These EVs travel through the ECS and are absorbed by receiver cells as shown in Fig. 1. While diffusion is a primary mechanism governing EV movement, other factors have been shown to influence their trajectories. A study done on the release of EVs [3] suggests that electromagnetic fields can impact the release and composition of EVs, which may have significant implications for fundamental biology and medical applications. Also, the authors in [4] show that directionally-specific pulsed electromagnetic fields stimulate EV release which have scientific, medical, and commercial values. Previous research addressing the post-release of EVs in the ECS has primarily focused on diffusion, often modeled using three-dimensional advection-diffusion equations [5]. Key factors such as tortuosity, volume fraction, and fluid dynamics have been extensively studied. EVs can be loaded with magnetic nanoparticles, such as iron oxide, as well as ions like calcium ions, allowing them to be influenced by external EM fields for TDD applications [6].

This study investigates the impact of EM fields generated by the transmitter cell, along with those from other particles in the ECS, on the probability of EV arrival at the receiver cell.

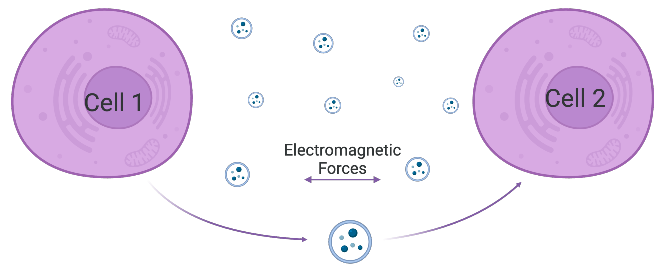

Fig. 1. An EV diffusing from a sender cell (Cell 1) to a receiver cell (Cell 2), through the ECS in the presence of EM field.

This is accomplished by computing the probability distribution of EV positions after their release from the transmitter cell. To achieve this, we will solve the Fokker-Planck equation (FPE), incorporating sinusoidal drift as a simplified model to represent various transport mechanisms.

II. Theory

To model the biophysical theory underlying the EV propagation in ECS in the presence of EM field, we use the FPE with time-harmonic drift given by

$$\frac{\partial P(x,t)}{\partial t} = -\frac{\partial}{\partial x}[v(t)P(x,t)] + D\frac{\partial^2 P(x,t)}{\partial x^2}, \qquad (1)$$

where $P(x,t)$ is the probability density function, $v(t)$ is the drift term with a time-harmonic form:

$$v(t) = v_0 \cos(\omega t + \phi), \qquad (2)$$

and D is the diffusion coefficient. Drift function is characterized by the amplitude, v_0, frequency, ω and phase, ϕ. We seek to derive the Green's function $G(x,t)$ that satisfies (1) with the initial condition,

$$G(x, t_0) = \delta(x). \qquad (3)$$

To simplify the drift term, we introduce coordinate transformation:

$$\zeta(t,x) = x - \frac{v_0}{\omega}\sin(\omega t + \phi). \qquad (4)$$

This transformation removes the time-dependence from the drift term and FPE simplifies to

$$\frac{\partial P(\zeta,t)}{\partial t} = D\frac{\partial^2 P(\zeta,t)}{\partial \zeta^2}. \tag{5}$$

The Green's function $G(\zeta,t)$ for this diffusion equation is

$$G(\zeta,t) = \frac{1}{\sqrt{4\pi D(t)}} \exp\left(-\frac{(\zeta)^2}{4D(t)}\right), \tag{6}$$

and in the original coordinates x and t is given by

$$G(x,t) = \frac{1}{\sqrt{4\pi D(t)}} \exp\left(-\frac{\left(x - \frac{v_0}{\omega}\sin(\omega t + \phi)\right)^2}{4D(t)}\right). \tag{7}$$

The release of EVs from the source can be modeled as gaussian function, described by

$$S(x,t) = e^{-\frac{|x-x_L|^2}{2\sigma_x^2}}, \tag{8}$$

where σ_x is the spatial width of the particles source, and x_L is the source position. Finally, the convolution integral of the source function $S(x,t)$ with the chosen system's Green's function $G(x,t)$ is computed to model the time-space evolution of the probability density function as

$$P(x,t) = G(x,t) * S(x,t). \tag{9}$$

III. Initial Results

For the initial results we run numerical simulations in MATLAB using $D = 1\times10^{-12} m^2/s, v_0 = 2\times10^{-6} m/s, \omega = 2\pi, 20\pi rad/s, x_L = 0m$. The results indicate that the lower time harmonic frequency leads to a higher drift of particles, as deduced from (7). This demonstrates the intriguing effect of the frequency and phase of EM field in controlling the drift of particles.

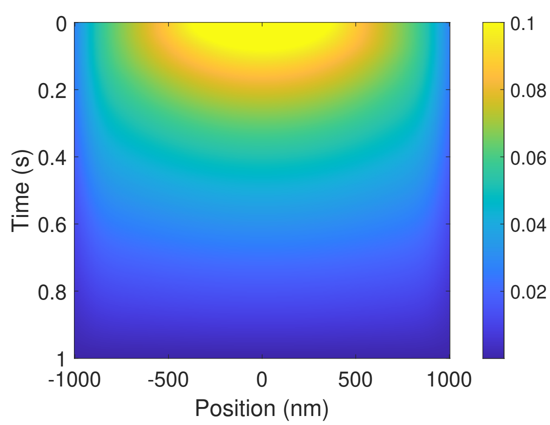

Fig. 2. Probability density function for time-harmonic drift with $\omega = 20\pi rad/s$.

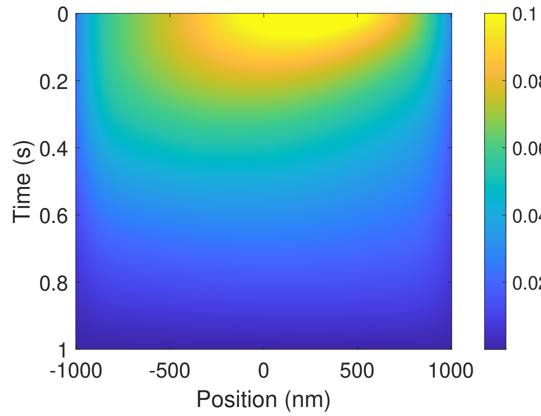

Fig. 3. Probability density function for time-harmonic drift with $\omega = 2\pi rad/s$.

IV. Conclusion

This study underscores the impact of electromagnetic fields on EV transport within the ECS. The model demonstrates that incorporating time-varying electromagnetic fields, with various mechanisms, can influence the drift of EVs, thereby improving their targeting properties. Time-harmonic EM fields offer exceptional capabilities for phase and frequency-based control of particles, which could be leveraged for phase and frequency modulation in molecular communication systems. Future work will extend this model to multiple spatial dimensions for a more comprehensive analysis. Additionally, incorporating polarized electromagnetic fields will provide an extra mechanism for steering particles in multi-dimensional scenarios.

References

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