Preliminary Implementation of Entropy-driven Tumor Detection within a Blood Vessel Network

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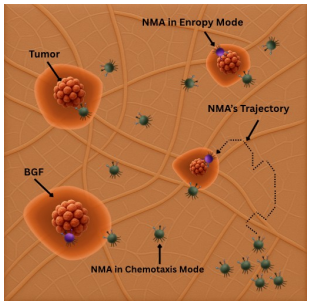
***Abstract*—Targeted Drug Delivery (TDD) is a promising approach to improve cancer treatment. However, TDD suffers from a lack of spatial selectivity and suboptimal outcomes. In this paper, we explore the idea of applying the hybrid entropy-driven transport mechanism for a nanoscale medical agent (NMA) within a bio-realistic tumor microenvironment model. By generating structured and realistic Biological Gradient Fields (BGFs) around a tumor, we aim to address a TDD approximation in real-time. Ensemble simulations performed for both vascular and avascular Tumor Micro Environments (TME) demonstrate that within the vascular TME, the NMA exhibits greater efficacy and efficiency. Though preliminary, this strategy of emulating a biologically feasible multiphysics platform with a readily integrable transport algorithm is promising for developing biologically realistic testbeds.**

***Index Terms*—Entropy, Biological Gradient Fields, Targeted Drug Delivery, Agent-Based Modeling, Bio-realistic Modeling**

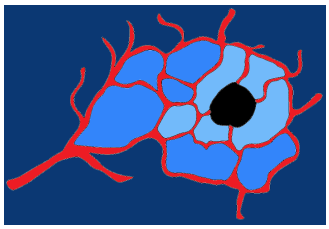
I. Introduction

Cancer remains a major global health problem, and current treatments like chemotherapy suffer from lack of spatial selectivity, causing systemic toxicity and suboptimal outcomes. Targeted Drug Delivery (TDD) seeks to overcome these limitations by directing therapeutic agents specifically to diseased tissue, thereby increasing local drug concentration while reducing side effects and enabling the use of potent drugs [1]. Inspired by efficient natural processes, bioinspired strategies are being developed to improve navigation, sensing, and coordination of therapeutic agents [2]. Advances in nanotechnology and synthetic biology now allow the creation of nanocarriers and engineered bacteria that can encapsulate drugs, cross biological barriers, and release payloads in a controlled manner [1], [3], [4]. Information-theoretic and machine learning frameworks further highlight a broader trend toward integrating computation, communication theory, and AI with biological information processing [5].

The work of B. Hedayati, K. R. Gorla, and M. Magarini was supported by the Institute of Information & communications Technology Planning & Evaluation (IITP) grant funded by the Korea government (MSIT)(No.RS-202400508465).



(a) Transportation Model



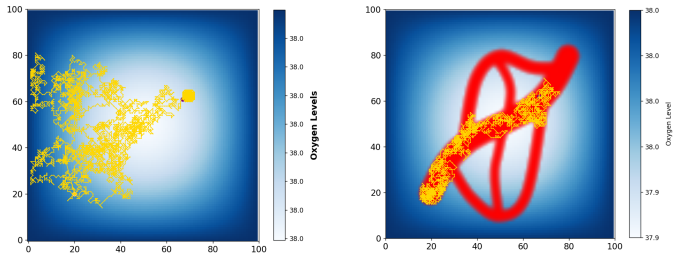
(b) Blood Vessel Model

Fig. 1: (a) Transportation model that envisions a TDD system using NMAs to treat cancer and (b) Bio-realistic blood vessel network model in COMSOL depicting the tumor (black) and the surrounding oxygen concentration levels (blue gradient).

In this paper, we explore the idea of applying the hybrid transport mechanism, introduced in [6], within a bio-realistic tumor environment model studied in [7]. The rest of the paper is structured as follows: Sec. II describes the system overview, then we present the simulation framework in Sec. III, and provide a conclusion and future direction in Sec. IV

II. System Model

Figure 1 presents an overview of the implementation of the system model. The transportation model shown in Fig. 1a, is based on the algorithm proposed in [6] to determine the trajectory of the nanoscale medical agent (NMA) according to the Biological Gradient Fields (BGFs). In Fig. 1b, a bio-realistic vascular model is depicted, which is used to generate more structured and realistic BGFs around a tumor; these fields then serve as input to the transportation model. Through this



(a) Avascular TME (b) Vascular TME

Fig. 2: Comparison of the NMA's tumor detection within the avascular and vascular TMEs.

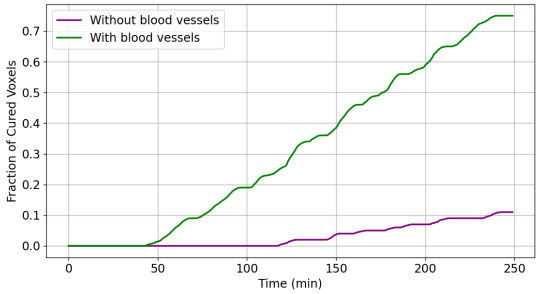


Fig. 3: Mean fraction of cancerous voxels over time compared in avascular (without blood vessels) and vascular (with blood vessels) TMEs.

integration, we obtain a more realistically informed system that can guide NMAs efficiently toward tumor regions, and thereby improve cancer treatment.

III. Simulation and Results

With integration as the main goal, our initial step was to examine the NMA's behaviour under the hybrid navigation mechanism (combining chemotaxis and entropy) while confining it to a simplified vascular network which functions as a geometric mask over the TME framework introduced in [6], consisting of a 100×100 voxel lattice with each voxel being a square of side $100\,\mu\mathrm{m}$. All other simulation parameters and modelling assumptions remained unchanged. The NMA is positioned randomly in the vicinity of the bottom-left region (around coordinates (20, 20)), while a tumour of approximately 30 voxels in size is located near the top-right region (around coordinates (70, 70)). These initial placements of the NMA and tumour are identical for simulations with and without the vascular network. Both the original and modified frameworks were then simulated for a total of 250 minutes of model time.

Figure 2 depicts the trajectory followed by an NMA in a representative simulation for both avascular and vascular TMEs. As time progresses, the elevated oxygen consumption rate of cancerous voxels generates oxygen gradients, which the NMA can sense depending on its distance from the tumor. In the avascular TME, the NMA can move freely, making it likely to wander far from the tumor. In contrast, within the vascular TME, the NMA operates more effectively and efficiently because its movement options are constrained by the vessel walls and the vessels themselves guide it toward the tumor region. Fig. 2b shows the path taken by the NMA inside the vessel as it successfully reaches the tumor.

In addition, we conducted ensemble simulations of the same duration to evaluate the effectiveness and efficiency of the NMA's drug delivery performance over 100 iterations in both the TMEs. In each simulation, the NMA's initial position is chosen randomly, but constrained to the beginning region, i.e., the lower-left corner of the blood vessel shown in Fig. 2b. When comparing the NMA's behavior in the two TMEs, we find that in the vascular TME the NMA not only functions effectively, but also operates substantially more efficient than in the avascular TME. This observation is further supported by Fig. 3, which presents the averaged fraction of cured voxels over time and demonstrates higher effectiveness, particularly at longer time horizons. Overall, these results indicate that the NMA identifies and treats a larger number of cancerous voxels, and does so earlier, when it functions within a vascular blood network.

IV. Future Work

Regarding future work in this collaboration, the initial phase will involve fully integrating the COMSOL model together with the Python-based transport algorithm at each time step. This approach will render the multiphysics framework as biologically realistic as possible, while allowing the transport algorithm to be easily superimposed on it. In the second phase, we plan to expand our simulation engine to account for blood flow within vessels and to incorporate additional tumor biomarkers, including pH, glucose, and others. Subsequent efforts will also evaluate the performance of an NMA swarm as it enters the cardiovascular system, with the goal of detecting and treating multiple tumors throughout the network and its downstream endpoints.

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