



10th Workshop on Molecular Communications

MolCom 2026

Koç University, Istanbul, Turkey

April 15–17, 2026

Workshop Proceedings

molecularcommunications.org



Endorsement & Support

MolCom'26 is endorsed by the Technical Committee on Molecular, Biological and Multi-Scale Communications of the IEEE Communications Society, and supported by TÜBİTAK (The Scientific and Technological Research Council of Türkiye) under the 2223-B Scientific Event Organization Support Program.

Call for Papers

The Workshop Technical Program Committee invited the submission of Abstracts (up to 2 pages) and Letters (up to 5 pages). Letter submissions are intended for presenting original theoretical and/or experimental work, rigorously reviewed for publication in a Special Issue of IEEE Transactions on Molecular, Biological, and Multi-Scale Communications (T-MBMC). Abstract submissions are intended for summarizing work-in-progress or recently published research.

Thematic Areas

Theme 1 — Fundamental Molecular Communication

Leveraging communication theory to model the behavior of living systems or to design and analyze artificial molecular communication systems.

Theme 2 — Applications of Molecular Communication

Applications in biomedical, biological, environmental, and industrial engineering, including natural signaling, health monitoring, and drug delivery.

Theme 3 — Molecular Communication Testbeds

Simulation tools and techniques and experimental methods.

Important Dates

Letter Submission:	January 30, 2026
Abstract Submission:	January 30, 2026
Notification of Acceptance:	February 27, 2026
Abstract Camera Ready:	March 13, 2026
Workshop:	April 15-17, 2026
Revised Letter to T-MBMC for Special Issue:	May 15, 2026

The Microsoft CMT service was used for managing the peer-reviewing process for this workshop. This service was provided for free by Microsoft and they bore all expenses, including costs for Azure cloud services as well as for software development and support.

Preface

The 10th Workshop on Molecular Communications (MolCom 2026) marks a significant milestone in the evolution of a research field that has, over the past decade, grown from a bold interdisciplinary vision into a vibrant and rapidly maturing scientific community. As General Co-Chairs of this anniversary edition, hosted at Koç University in Istanbul, Turkey, we are proud to present this collection of 28 contributions—16 extended abstracts and 12 letters—that together offer a compelling panorama of the state of the art in molecular communications.

Since its inception, the field of molecular communications has drawn inspiration from a fundamental observation: nature has long relied on chemical signaling as its primary medium of information exchange. From intracellular protein cascades and intercellular calcium waves to organism-level pheromone signaling and plant volatile emissions, biological systems demonstrate that molecular-scale communication can be remarkably efficient, adaptive, and robust. The research community has embraced this insight, developing theoretical frameworks, computational models, and experimental platforms that translate biological principles into engineered communication systems.

The contributions presented at MolCom 2026 vividly illustrate the breadth and depth of this endeavor. On the experimental front, several groups have advanced macro-scale and micro-scale testbeds for molecular communication, including superparamagnetic iron oxide nanoparticle (SPION)-based systems with magnetic and optical sensing, graphene Hall-effect receivers for droplet-based signaling, and color-based microfluidic platforms employing quadrature amplitude modulation. These testbeds are crucial for closing the gap between theoretical predictions and physical reality—a recurring theme throughout the workshop. Complementing these efforts, contributions on channel modeling address time-varying dispersive systems with pulsatile flow, permeable channels with diffusive leakage, airborne molecular communication in realistic indoor environments, and odor-based communication channels, each pushing the boundaries of analytical tractability and experimental validation.

The biomedical and therapeutic dimensions of molecular communications remain a central pillar of the field. This year's program features work on targeted drug delivery systems informed by semantic information theory, entropy-driven tumor detection within vascular networks, and therapeutic nanonetworks for brain tumors using cell-based nanobiodevice interfaces. The concept of bio-robots powered by T-cell mechanics and molecular signaling exemplifies the growing convergence between molecular communications, synthetic biology, and bioengineering. In a similar vein, contributions on hybrid artificial-living cell collectives for wetware computing highlight the potential of molecular communication principles to underpin entirely new computational paradigms.

Equally exciting are the emerging applications beyond biomedicine. Researchers are now modeling plant-to-plant communication via volatile organic compounds, exploring plant-based indoor air quality systems, and analyzing multi-trophic signaling networks for sustainable agriculture. These contributions underscore the environmental and agricultural relevance of molecular communication theory and open pathways toward green smart technologies.

At the theoretical frontier, the workshop features advances in MIMO particle communication under random advection, ratio-shift keying modulation for mobile molecular communication, neural-inspired multi-agent architectures for collective intelligence, and information-theoretic modeling of interspecies communication. Machine learning methods for source localization in

endocrine-inspired settings further demonstrate the field's embrace of modern data-driven approaches.

As we reflect on the trajectory of molecular communications—from the early conceptual papers to the sophisticated experimental demonstrations and analytical frameworks presented here—we are encouraged by the community's sustained creativity and rigor. The diversity of topics at MolCom 2026, spanning fundamental channel theory, novel modulation schemes, biomedical nanonetworks, environmental sensing, and bio-inspired computing, confirms that molecular communications has firmly established itself as a multidisciplinary field with both deep scientific foundations and broad societal relevance.

We extend our sincere gratitude to the Technical Program Committee, the Steering Committee, the Organizing Committee, the student volunteers from the CALICO Lab, the keynote and tutorial speakers, and all the authors and participants whose contributions make this workshop a uniquely stimulating forum. We look forward to the discussions that will shape the next decade of molecular communications research.

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PART I — Extended Abstracts

Magnetic SPION Retention in Asymmetric Vascular Bifurcation Models

pp. 13–14

Daniel Fleischhauer, Samuel Schlicht, Dietmar Drummer

Superparamagnetic iron oxide nanoparticles (SPIONs) represent an emerging platform in various fields of nanomedicine. In particular, nanoparticle-based drug delivery techniques that exploit the magnetic properties of SPIONs for targeted transport and accumulation in tumor tissue show considerable promise for cancer therapy. The development of such approaches requires a detailed understanding of how hydrodynamic particle transport, magnetically induced forces, and vascular geometry interact. In this work, we investigate the transient, geometry-induced distribution of SPIONs in generalized vascular structures under magnetic steering. Using statistical scaling laws and empirical data, asymmetric vascular geometries were derived, exhibiting characteristic asymmetry-related vessel diameters. These generalized vascular structures were fabricated via digital light processing (DLP) additive manufacturing and were subsequently tested under varying flow rates and magnetic steering conditions. Optical in situ measurements based on the extinction of transmitted light demonstrated a significant influence of flow rate and daughter-vessel diameter on transient particle distribution. Since magnetic forces depend on both the underlying flow field and local SPION concentration, these findings suggest an artery-size-dependent boundary for effective magnetic steering under given magnetic conditions.

Network Signal Analysis for Engineering Multitrophic Plant Health Communication Systems

pp. 15–16

Islam Ahmed Abdelalim Darwish, David Ryan, Thomais Kakouli-Duarte, and Daniel P. Martins

Sustainable agriculture is increasingly dependent on the soil microbiota to reduce synthetic chemical inputs. Entomopathogenic nematodes (EPN) and plant growth-promoting rhizobacteria (PGPR) are promising agents for pest control and plant health enhancement, yet their co-culture poses design challenges. This work models an EPN-PGPR co-culture as a multitrophic network and applies graph signal processing to analyse interaction dynamics. The results reveal storage-induced structural fragilities and provide a principled basis for optimising experimental design, supporting robust development toward scalable, sustainable plant health applications.

Channel Modeling for Time-Varying Dispersive Closed-Loop MC Systems with Pulsatile Flow

pp. 17–18

Theofilos Symeonidis, Fardad Vakilipoor, Robert Schober, Nunzio Tuccitto, Maximilian Schäfer

Molecular communication (MC) is a communication paradigm in which information is conveyed through the controlled release and propagation of molecules. Especially in in-body application environments, the channel topology is closedloop, and particle propagation is determined by the joint influence of diffusion and pulsatile flow induced by the heartbeat. However, most existing analytical models for dispersive closedloop MC channels assume a constant flow velocity, whereas flows in biological environments are inherently pulsatile. Therefore, in this paper, we present a time-varying one-dimensional (1D) channel model for closed-loop MC systems under pulsatile flow, operating in the dispersive regime. An analytical expression for the channel impulse response (CIR) is derived, resulting in a wrapped Normal distribution with time-variant mean and variance. The proposed model is validated by comparison to three-dimensional (3D) particle-based simulation (PBS) results.

Propagation Characteristics of Permeable MC Channels

pp. 19–20

Michael Gattringer, Martin Frauenlob, Florian Selinger, Stefan Angerbauer, Medina Hamidović, Andreas Springer, Werner Haselmayr

In this work, we investigate the diffusive leakage from capillary channels into the surrounding environment. We propose an approach to estimate the state of the surrounding environment during communication by exploiting this leakage. Furthermore, we introduce a novel design of a macro-scale testbed to experimentally investigate this phenomenon.

Towards T-cell based Bio-Robots: Synergy between Molecular Communications and Bio-Mechanics

pp. 21–22

Stefan Angerbauer, Michael Gattringer, Andreas Springer, Werner Haselmayr

In this paper, we report on our ongoing work in the field of bio-inspired micro robotics. We discuss, how different scientific disciplines, including molecular communications, have to be combined to realize systems capable of tasks like tumor clearance and pathogen elimination.

Graphene Hall Sensor-Based Receiver for Magnetic Droplet-Based Communications

pp. 23–24

Maryam Kahvazi Zadeh, Eren Akyol, Aysa Azmoudeh, Mustafa Uzun, Ali Abdali, and Murat Kuscü

We present the first graphene Hall-effect receiver for magnetic droplet-based communications. By integrating a graphene Hall cross beneath a PDMS microfluidic channel, the device detects passing ferrofluid droplets and distinguishes their sizes through pulse width measurements of Hall voltage changes. The sensor demonstrates linear response across a wide magnetic field range and reliably differentiates droplets generated at varying pressures, validating its potential as a scalable receiver for magnetic droplet-based communication systems.

Semantic Information in Molecular Communication-Based Drug Delivery Systems

pp. 25–26

Milica Lekić, Lukas Brand, Mohammed Zoofaghari, Ilangko Balasingham, and Mladen Veletić

We are employing semantic information theory to quantify how much information about treatment parameters is functionally relevant for achieving a desired therapeutic outcome in a drug delivery system. The framework is evaluated through a simulation study of a focused ultrasound (FUS)-mediated drug delivery system.

Performance of Ratio-Shift Keying Modulation for Diffusive Molecular Communication Scenarios

pp. 27–28

Muskan Ahuja, Abhishek K. Gupta, and Reshma Rastogi

Molecular communication (MC) is a promising communication paradigm that utilizes molecules as information carriers, mimicking natural biological processes. Out of various modulations to encode information onto signaling molecules, on-off keying (OOK) modulation has gained popularity due to its simplicity and efficiency. However, when the channel is unknown, for example, in cases where nodes are mobile, the OOK modulation-based MC systems suffer from a high bit error probability. In this paper, we investigate dynamic MC system with mobile transmit and receiver devices. We consider a variant of ratio-shift-keying (RSK) where the information is encoded in the ratio of the concentration of two different types of signaling molecules with the same propagation characteristics. We derive the optimal maximum likelihood (ML) decoder for OOK and RSK-based MC system. We also present a simpler representation of the optimal decoder under the Poisson assumption and show that the ML decoder for RSK modulation doesn't require channel information, in contrast with the ML decoder for OOK-based MC systems. We further investigate the bit error rate for the considered system. We show that RSK performs better than OOK in a dynamic MC system where the channel varies with time. This is because the ratio of the concentrations of the two types of information molecules is preserved at the receiver, offering improved robustness to variations in channel conditions. Therefore, RSK comes to the rescue in case of unknown or difficult to estimate channel environments. Via numerical investigations, we present various design insights, including optimal symbol design, and the gain of RSK over OOK as a function of node mobility.

Spatiotemporal Modeling of Chemotactic cAMP Signaling by Secretion and Degradation

pp. 29–30

Johannes Konrad, Fardad Vakiliipoor, Maximilian Schäfer

Chemotactic signaling in Dictyostelium cells (Dictys) relies on secretion, diffusion, and degradation of cyclic adenosine monophosphate (cAMP) molecules to enable collective cell responses. This process involves coupled intracellular signaling and extracellular regulation through enzymatic degradation of cAMP by secreted phosphodiesterase (PDE). To capture these interactions, we propose an agent-based modelling (ABM) approach consisting of an environment and agents. The environment takes into account the spatial stochastic dynamics such as diffusion and reaction for intercellular molecular communication (MC). The cells are modeled as autonomous agents governed by chemical reaction networks for cAMP synthesis and PDE production. Both types of molecules are secreted into the environment, where they are affected by diffusion and enzymatic degradation. A transmitter-receiver scenario involving two cells is investigated. Upon binding of extracellular cAMP secreted by the transmitter cell to receptors on the receiver cell, the receiver initiates cAMP synthesis and secretion, thereby elevating the extracellular cAMP level. The coupled amplification of cAMP by the receiver and its enzymatic degradation by PDE regulates signal persistence in the environment, enabling reliable detection of cAMP signal without uncontrolled accumulation of it. From an MC perspective, extracellular cAMP degradation by PDE functions analogously to a natural mechanism for limiting channel memory, thereby mitigating inter-symbol interference arising from residual signaling molecules.

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

pp. 31–32

Bahram Hedayati, Karthik Reddy Gorla, Yue Sun, Yifan Chen, Maurizio Magarini

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 tumor 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.

On the Feasibility of a Plant-based Air Quality System Modeled via Molecular Communication for Green Smart Homes

pp. 33–34

Karthik Reddy Gorla, Silvia Mura, Maurizio Magarini

Indoor air quality in urban homes is influenced by multiple airborne pollutants, including volatile organic compounds (VOCs), carbon dioxide (CO₂), and fine particulate matter (PM) originating from indoor activities and outdoor sources such as vehicular traffic. Although mechanical air filtration systems are effective, they are energy-intensive and offer limited spatial awareness of pollutant dynamics. In this paper, we explore the feasibility of a plant-based indoor-outdoor air quality system modeled through the lens of molecular communication (MC). Pollutants are abstracted as information-carrying molecular species, plants as spatially distributed receivers with absorption and sensing capabilities, and residential spaces as bounded diffusion-dominated channels. This abstraction enables the reuse of MC models to reason about pollutant propagation, assess the feasibility of plant placement, and explore early-stage design trade-offs. Unlike large-scale urban or industrial environments, residential settings operate in confined geometries where diffusion-driven modeling is more applicable, making them well-suited for MC-inspired analysis. Rather than optimizing plant species or placement, this work positions MC as a unifying framework to evaluate feasibility and identify open challenges toward greener, bio-integrated smart home environments.

Modeling Electric-Field Induced Modulation of Ligand-Receptor Binding Kinetics Towards Adaptive MC Receivers

pp. 35–36

Berke Sevindik, Eren Akyol, Maryam Kahvazi Zadeh, and Murat Kuscü

We present a first-principles model for electric-field-controlled DNA hybridization on biosensor surfaces based on Scheutjens-Fleer self-consistent field (SF-SCF) theory. The model derives voltage-dependent probe layer structure by solving the Edwards diffusion equation coupled with Poisson-Boltzmann electrostatics iteratively until self-consistency. Hybridization kinetics are computed via the Halperin-Buhot-Zhulina framework augmented with electrophoretic contributions. We introduce a mechanistic asymmetry wherein association is treated as nucleation-limited, while dissociation is governed by the field-dependent stability of the full duplex. The model predicts sharp transitions between hybridizing and non-hybridizing regimes, offering a theoretical foundation for adaptive MC receivers.

Intrinsic MIMO Particle Communication Channel with Random Advection

pp. 37–38

Fatih Merdan, Ozgur B. Akan

Molecular communication (MC) has emerged as a promising paradigm for information exchange in environments where conventional electromagnetic communication is infeasible, such as biological systems and microfluidic platforms. Early studies in MC predominantly focused on diffusion-driven channels, where molecular propagation is isotropic and inherently slow. Advection has been mostly discussed as a means of increasing the speed of propagation and reducing the channel memory, and as a constant property of the channel. However, random advection with a strong mean direction can preserve pulse ordering, making advection-dominated MC particularly attractive for pulse-based modulation schemes, where information is conveyed through the timing, shape, or orthogonality of released molecular pulses. It is demonstrated that under directed advection, the spatial dispersion induced by random transverse flow results in multiple distinct receiver observations of the same transmitted pulse. This perspective motivates an interpretation of MC as an intrinsically MIMO system, where diversity arises naturally from spatial sampling of the particle cloud rather than from multiple transmitters or molecule types. The purpose of this study is to provide a structured framework for understanding how receiver diversity can be exploited in pulse-based molecular communication under random advection. Several receiver combining strategies are evaluated, and their impact on symbol error rate (SER) is studied through Monte Carlo simulations. Results demonstrate that multi-receiver diversity can improve detection performance, especially in low-to-moderate signal-to-noise ratio (SNR) regimes, even when individual receiver observations are highly noisy.

Therapeutic Nanonetworks for Brain Tumors Enabled by Cell-Based Nanobiodevice Interfaces

pp. 39–40

Andreani Odysseos, Kyriacos Agathangelou, Asif Bilal, Stavros Iezekiel, Theodoulakis Christofi, Costas Pitris

The evolution of Glioblastoma Multiforme (GBM) is defined by the dynamics of distinct cell sub-populations growing bionanomachine networks in an interplay between “senders” or “transceivers” and “receivers”. Central to this process are the inter-communications between sub-cellular bionanomachines secreted by GBM cells in the form of exosomes. Herein we present a dynamic therapeutic nanonetwork of genetically engineered and radiofrequency-responsive active bionanomachines where neural stem cells and exosome cargo therapeutic nucleic acids serve as externally controllable transducer bionanomachines. Interfaces derived from the intercoupling of optically active bionanomachines in co-cultures of tumor cells and therapeutic exosomes exposed to rationally designed RF generators provided a pioneering inmessaging interface for external control of molecular nanonetworks.

Neural-Inspired Multi-Agent Molecular Communication Networks for Collective Intelligence

pp. 41–42

Boran A. Kilic, Ozgur B. Akan

Molecular Communication (MC) is a pivotal enabler for the Internet of Bio-Nano Things (IoBNT). However, current research often relies on highly capable individual agents with complex transceiver architectures that defy the energy and processing constraints of realistic nanomachines. This paper proposes a paradigm shift towards collective intelligence, inspired by the cortical networks of the biological brain. We introduce a decentralized network architecture where simple nanomachines interact via a diffusive medium using a threshold-based firing mechanism modeled by Greenberg-Hastings (GH) cellular automata. We derive fixed-point equations for steady-state populations via mean-field analysis and validate them against stochastic simulations. We demonstrate that tuning the activation threshold allows the network to exhibit critical transition-like behavior, maximizing susceptibility across the swarm.

Toward Clinically-Inspired Validation of ML-Driven Source Localization in Molecular Communication

pp. 43–44

Saswati Pal, Regine Wendt, Cyrus Khandanpour, Malte Sieren, Stefan Fischer, and Falko Dressler

Accurate localization of tumor sources in the human circulatory system is essential for precision oncology. In prior work, we developed a machine learning (ML) framework to localize anomaly sources using temporal biomarker profiles measured at receiver sites. However, the dataset was generated in a generic source-receiver setting, limiting physiological realism. This work-in-progress paper extends the framework by validating the ML model on a clinically-inspired dataset that emulates endocrine signaling in a controlled synthetic environment. The model is retrained and evaluated using a stratified held-out split with 25% reserved for testing. Preliminary results show an accuracy of ~90%, indicating the potential of ML-driven approaches for tumor source localization in clinically relevant molecular communication settings.

PART II — Letters

Density Matters: The Effect of SPION Sedimentation on Molecular Communication

K. Xiao, L.C.P. Wille, D. Fleischhauer, S. Lotter, S. Lyer, D. Drummer, G. Fischer, J. Kirchner

Superparamagnetic iron-oxide nanoparticles (SPIONs) have emerged as promising information carriers in the field of molecular communication (MC). However, a critical discrepancy exists between theoretical models and experimental realities: while theoretical frameworks typically assume neutral buoyancy and neglect gravitational forces, practical implementations suffer from significant gravity-induced sedimentation. This oversight leads to substantial prediction errors and system unreliability. To address this, we developed an experimental testbed featuring a vertically oriented bifurcated channel, specifically designed to isolate and quantify the impact of gravity on signal propagation. Our experimental results empirically demonstrate that sedimentation causes significant deviations in channel signal impulses, contradicting the ideal assumptions found in existing literature. Furthermore, we provide a theoretical explanation based on hydrodynamic instability to clarify the mechanisms driving this settling behaviour. This work highlights the necessity of incorporating gravitational effects into system modelling to ensure accurate performance assessment in realistic MC environments.

The Potential of Spatially Detecting SPIONs Using Multiple Sensor Coils

P. Wolff, L.C.P. Wille, S. Lyer, J. Kirchner

Detecting magnetic nanoparticles with inductive sensor coils is a proven, feasible and cost-efficient method. Recently, molecular communication in fluids, primarily vascular system models, has been investigated. The one-sensor approach is useful for determining the presence of superparamagnetic iron-oxide nanoparticles in the vicinity of the sensor. However, distinguishing between a small number of particles close to the sensor and a greater number further away remains problematic. To solve this, spatial detection using multiple sensors is investigated. This opens up the possibility of utilizing spatial information in a communication context, as well as enabling imaging options that display the particle distribution over the cross-sectional area of the channel. In consequence, the concentration can be determined with greater precision. The stability of the sensors is investigated, proving the reliability of reference scales for the shift to concentration relation. Nonetheless, the presented approach is subject to several limitations and factors that must be considered in future work. To conclude the presented work, it can be said that advances could be achieved in the position and concentration determination of SPIONs, as well as a structured investigation on sensor stability.

Multispectral Optical Sensor Architecture for SPION Detection in Fluidic Testbeds

L. Kroll, A. Hemmis, J. Thiem, S. Lyer, J. Kirchner

In this work a compact multispectral optical sensor architecture for the real-time detection of superparamagnetic iron oxide nanoparticles (SPIONs) in fluidic testbeds is presented. The system is based on a 14-channel AS7343 spectral sensor and integrates transmissive and reflective illumination for inline measurements in tubular flow channels. A calibration procedure is introduced to optimize illumination, gain, and exposure parameters with respect to detection sensitivity and sampling rate. Static measurements demonstrate high signal-to-noise ratios for visible wavelength bands between 515 nm and 640 nm across a wide range of exposure times. Dynamic injection experiments with varying SPION volumes show robust detection performance with consistently high peak-to-noise ratios and only minor degradation of dynamic range for decreased injection volumes. These results indicate that the proposed sensor is well suited for time-resolved SPION monitoring and provides a reliable basis for future concentration estimation and closed-loop magnetic drug targeting testbeds.

A Quadrature Amplitude Modulation for a Color-Based Molecular Communication Testbed

P. Zhou, P. Hofmann, M.F.S. Anoy, R. Zheng, M. Schottlender, F. Rani, J.A. Cabrera, F.H.P. Fitzek

This paper presents a color-based microfluidic molecular communication (MC) testbed that experimentally demonstrates quadrature amplitude modulation (QAM) transmission using dual-dye signaling. Two distinct food dyes with different absorption characteristics are injected through independently controlled syringe pumps, and their concentrations are reconstructed from red, green, blue (RGB) measurements captured by a commercial-off-the-shelf camera. An absorbance-based estimation model is developed to obtain the dye concentrations, and the experimentally measured channel impulse responses (CIRs) reveal strong inter-symbol interference (ISI) and cross-dye coupling. We designed a two-dimensional molecular constellation in which each symbol is represented by a pair of dye concentrations, enabling 4-QAM and 16-QAM transmission within a microfluidic environment. Detection is performed using the minimum Euclidean distance (MED) and maximum likelihood sequence estimation (MLSE). Experimental results demonstrate the feasibility of applying QAM to MC within a microfluidic environment. The measured dye-concentration constellations exhibit systematic distortions and non-uniform spacing compared to conventional electromagnetic QAM, highlighting the unique physical characteristics of molecular transport. Using these experimentally obtained constellations, MED and MLSE detectors are evaluated, and MLSE is shown to reduce symbol error ratio (SER) by leveraging the channel memory introduced by microfluidic ISI.

Physical Limits of Proximal Tumor Detection via MAGE-A Extracellular Vesicles

A.S. Okcu, M.E. Bas, O.B. Akan

Early cancer detection relies on invasive tissue biopsies or liquid biopsies limited by biomarker dilution. In contrast, tumour-derived extracellular vesicles (EVs) carrying biomarkers like melanoma-associated antigen-A (MAGE-A) are highly concentrated in the peri-tumoral interstitial space, offering a promising near-field target. However, at micrometre scales, EV transport is governed by stochastic diffusion in a low-copy-number regime, increasing the risk of false negatives. We theoretically assess the feasibility of a smart-needle sensor detecting MAGE-A-positive microvesicles near a tumour. We use a hybrid framework combining particle-based Brownian dynamics (Smoldyn) to quantify stochastic arrival and false-negative probabilities, and a reaction-diffusion PDE for mean concentration profiles. Formulating detection as a threshold-based binary hypothesis test, we find a maximum feasible detection radius of $\approx 275 \mu\text{m}$ for a 6000 s sensing window. These results outline the physical limits of proximal EV-based detection and inform the design of minimally invasive peri-tumoral sensors.

Joint Detection and Correlation Analysis in Diffusion-Based Molecular Communication

K.K. Pandey, N.V. Sabu, A.K. Gupta

In this paper, we model the single transmitter bionanomachine (TBN) and multiple passive receiver bionanomachines (RBNs), spatially distributed throughout the medium. The TBN emits the signaling molecules (SMs) initially which reaches the RBNs via diffusion. The signal is detected when the concentration of SMs inside the RBN reaches a certain threshold. We derive the detection probability (DP), which measures the probability that the concentration inside a RBN exceeds a threshold at a given time. The results show that the spatial distribution of SMs at a given time strongly influence the DP. These results guide the design of more efficient MC networks for synthetic biology, targeted drug delivery, and nanosensing.

Topology-Dependent Communication and Computing in Bioengineered Neuronal Networks

J. Mullett, A. Mohr, R. Scherer, M. Barros

Bioengineered neuronal systems are increasingly explored as living computational substrates, yet their communication properties remain poorly characterized beyond global activity statistics. We develop a mechanosensitivity model of neuronal networks and a MIMO communication system under noisy channel with the aim to quantify trade-offs between communications and computing in bioengineered neuronal systems. Using a mechanosensitive Izhikevich network model with time-varying substrate stiffness, we compare random, clustered, and disintegrated topologies under matched stimulation. Communication is quantified using transfer entropy, achievable mutual information rate from binned spike observations, and information redundancy. Computing is measured as the receiver-level separability metric posed as a transmitter-identification task. Across noise levels, clustered networks more consistently maintain higher achievable rates and exhibit more concentrated separability than random and disintegrated substrates. Our results demonstrate that our method to quantify the communication and computing trade-offs are informative metrics for bioengineered intelligence performance and optimization.

Hybrid Artificial-Living Cell Collectives for Wetware Computing

C. Savas, M. Javed, M. Kuscu

Living systems continuously sense, integrate, and act on chemical information using multiscale biochemical networks whose dynamics are inherently nonlinear, adaptive, and energy-efficient. Yet, most attempts to harness such “wetware” for external computational tasks have centered on neural tissue and electrical interfaces, leaving the information-processing potential of non-neural collectives comparatively underexplored. In this letter, we study a hybrid artificial-living cell network in which programmable artificial cells write time-varying inputs into a biochemical microenvironment, while a living bacterial collective provides the nonlinear spatiotemporal dynamics required for temporal information processing. Specifically, artificial cells transduce an external input sequence into the controlled secretion of attractant and repellent molecules, thereby modulating the “local biochemical context” that bacteria naturally sense and respond to. The resulting collective bacterial dynamics, together with the evolving molecular fields, form a high-dimensional reservoir state that is sampled coarsely (voxel-wise) and mapped to outputs through a trained linear readout within a physical reservoir computing framework. Using an agent-based *in silico* model, we evaluate the proposed hybrid reservoir on the Mackey–Glass chaotic time-series prediction benchmark. The system achieves normalized root mean square error (NRMSE) values of approximately 0.33–0.40 for prediction horizons $H = 1$ to 5, and exhibits measurable short-term memory as encoded in the distributed spatiotemporal patterns of bacteria and biochemicals. These results motivate the future exploration of non-neural hybrid cell networks for *in situ* temporal signal processing towards novel biomedical applications.

Experimental Characterization of Impact of Paint-Like Solvent Backgrounds on Indoor Airborne Molecular Communication

K. Zhu, S. Carkit-Yilmaz, B. Heinlein, Y.L. Pham, V. Jamali, R. Schober, H. Loos, A. Buettner

Airborne molecular communication (AMC) systems are often subjected to persistent interfering volatile organic compounds (VOCs) originating from paints and coated surfaces in indoor environments. These background chemicals affect metal oxide (MOX) sensor outputs together with the actively released signaling molecules, because of cross-sensitivity, creating drifting sensor-output baselines, and memory-dependent effects that standard AMC models do not address. This study experimentally investigates how a common paint solvent (n-butyl acetate) and alcohol signaling pulses (ethanol) jointly affect an AMC system with MOX sensors. Using a static chamber and a controlled-airflow setup, we examine ethanol pulses in clean air, solvent backgrounds, superimposed signal-background conditions, and different exposure sequences. The measurements show that paint-related VOCs cause slowly varying baseline shifts that reduce ethanol pulse contrast, slow down recovery, and introduce exposure sequence dependent responses. This letter provides an experimental characterization of solvent-background interference and memory effects in MOX sensors-based AMC receivers.

Channel Modeling and Experimental Validation of Odor-Based Molecular Communication Systems

A.B. Kilic, F.E. Bilgen, O.B. Akan

Odor-based Molecular Communication (OMC) employs odor molecules to convey information, contributing to the realization of the Internet of Everything (IoE) vision. Despite this, the practical deployment of OMC systems is currently limited by the lack of comprehensive channel models that accurately characterize particle propagation in diverse environments. While existing literature explores various aspects of molecular transport, a holistic approach that integrates theoretical modeling with experimental validation for bounded channels remains underdeveloped. In this paper, we address this gap by proposing mathematical frameworks for both bounded and unbounded OMC channels. To verify the accuracy of the proposed models, we develop a novel experimental testbed and conduct an extensive performance analysis. Our results demonstrate a strong correlation between the theoretical derivations and experimental data, providing a robust foundation for the design and analysis of future end-to-end OMC systems.

End-to-End Modeling of Plant-to-Plant Communication via Biogenic Volatile Organic Compounds

M. Genoni, G. Lecce, S. Kuriry, K.R. Gorla, M. Magarini, S. Mura

Abstract not provided.

Information Theoretic Modeling of Interspecies Molecular Communication

B. Maitra, M. Kuscü, O.B. Akan

Plants and insects communicate using chemical signals like volatile organic compounds (VOCs). A plant encodes information using different blends of VOCs, which propagate through the air to represent different symbolic information. This communication occurs in a noisy environment, characterized by wind, distance, and complex biological reactions. At the receiver, cross-reactive olfactory receptors produce stochastic binding events whose discretized durations form the receiver observation. In this paper, an information-theoretic framework is developed to model interspecies molecular communication (MC), where receptor responses are modeled probabilistically using a multinomial distribution. Numerical results show that the communication depends on environmental parameters such as wind speed, distance, and the number of released molecules. The proposed framework provides fundamental insights into the VOC-based interspecies communication under realistic biological and environmental conditions.

Magnetic SPION Retention in Asymmetric Vascular Bifurcation Models

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Abstract— Superparamagnetic iron oxide nanoparticles (SPIONs) represent an emerging platform in various fields of nanomedicine. In particular, nanoparticle-based drug delivery techniques that exploit the magnetic properties of SPIONs for targeted transport and accumulation in tumor tissue show considerable promise for cancer therapy. The development of such approaches requires a detailed understanding of how hydrodynamic particle transport, magnetically induced forces, and vascular geometry interact. In this work, we investigate the transient, geometry-induced distribution of SPIONs in generalized vascular structures under magnetic field application. Using statistical scaling laws and empirical data, asymmetric vascular geometries were derived, exhibiting characteristic asymmetry-related vessel diameters. These generalized vascular structures were fabricated via digital light processing (DLP) additive manufacturing and were subsequently tested under magnetic field on and magnetic field off conditions. Optical *in situ* measurements based on the extinction of transmitted light demonstrated a significant influence of geometry and daughter-vessel diameter on transient particle distribution. Since magnetic forces depend on both the underlying flow field and local SPION concentration, these findings suggest an artery-size-dependent boundary for effective magnetic retention under low wash-out conditions.

Keywords—magnetic drug targeting, test bench, particle propagation, nanoparticles

I. INTRODUCTION

Conventional chemotherapy is often limited by systemic toxicity and insufficient drug accumulation at tumor sites. Magnetic drug targeting offers a promising alternative by enabling localized drug accumulation while reducing systemic side effects. Superparamagnetic iron oxide nanoparticles (SPIONs) are particularly suitable carriers due to their surface functionalizability and non-invasive manipulation via external magnetic fields [1]. However, efficient magnetic field dependent SPION retention within the vasculature remains challenging. Nanoparticle transport is governed by competing hydrodynamic, gravitational, and magnetic forces, whose interaction strongly depends on vascular geometry [2,3]. At bifurcations, local flow velocities and shear forces determine particle distribution and emerging flow regimes. While these effects have been studied theoretically and computationally, experimental validation under controlled, physiologically relevant conditions is still limited [4]. To address this gap, we present a generalized, geometrically biosimilar test environment that enables systematic investigation of SPION transport in asymmetric vascular structures. Using optically accessible models fabricated by additive manufacturing, we analyze the

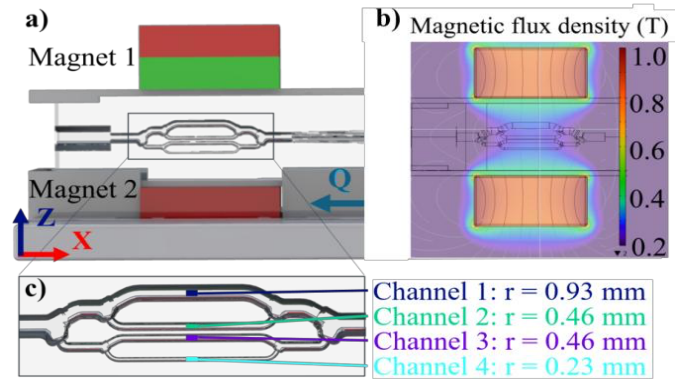


Fig 1: a) Representation of the specimen and magnetic setup according to case 1 as viewed by the camera. b) Representation of the applied magnetic field. c) Illustration of the evaluation positions within the channels and respective channel radii.

transient branch-wise distribution of SPIONs under varying magnetic field conditions.

II. METHODS

A. Specimen Design and Manufacturing

Generalized asymmetric branching structures were derived based on self-similar scaling laws of vascular structures described in the literature. This enables a cross-scale description of the model geometry based on the initial conditions of a few key geometric parameters. According to Murray's law, the relationship between parent- (r_0) and daughter vessel (r_1, r_2) radii is described as follows [5]:

$$r_0^\alpha = r_1^\alpha + r_2^\alpha \quad (1)$$

Depending on tissue type, exponent values between 2 and 3 have been found, with 2.7 ($\approx e$) reported as optimal for elastic-muscular arteries [6]. The vessel segment radius is linked to the segment length l by a similar proportionality law corresponding to physiological geometries [7]. For asymmetric branching, branching angles change according to daughter vessel size ratios, with angles dependent on parent and daughter vessel radii according to [8]. Branching angles were calculated based on an asymmetry ratio of 0.5 between daughter vessels. Boundary conditions were chosen based on imaging data for breast tumor vascular feeding systems: an entering diameter of 2.5 mm and initial segment length of 12.5 mm. Using these values and relationships, branching models were calculated accordingly.

Such vascular models were manufactured on a digital light processing 3D printer using a transparent standard resin according to the protocol described in [9].

B. Testbench Setup

Experiments were done in an optically accessible flow setup with upstream peristaltic pumping and imaging-based extinction analysis reported in [9]. Blood flow was simulated by distilled water at a flow rate of 5 mL min^{-1} . Before the sample, 0.1 mL of colloidal suspension (10 mg mL^{-1}) was injected. Specimens were positioned with the branching plane aligned to the x-z-plane (Fig. 1). The two NdFeB magnets positioned above and below the specimen at 25 mm distance, yielded a flux density of 350 mT at the geometric center of the specimens. Camera recordings were evaluated for particle propagation by analyzing the transient pixel extinction at defined points in the second-order branches. Relative extinction was calculated with respect to the pre-injection baseline intensity of the water-filled channel at the same ROI. Peak extinction denotes the local maximum of the transient relative extinction signal. Two configurations were tested, which included specimens with the higher-diameter branch positioned uppermost (case 1) as well as positioned with the lower-diameter branch uppermost (case 2), both with and without magnetic field application.

III. RESULTS AND DISCUSSION

A. Particle propagation

After injection, particles sediment rapidly to the channel bottom until reaching the first bifurcation. In case 1, despite bottom accumulation, strong extinction signals occur in the upper channels, indicating that higher flow and lower resistance in the upper branch favors particle transport and offsets sedimentation. Upper branches show slightly faster onset compared to channel 3, which exhibits a broader peak due to slower flow velocities. Channel 4 shows significantly delayed, slow onset with a broad peak, indicating slow flow, high resistance, and preference for channel 3 in the lower branch, highlighting the influence of flow distribution and local flow velocities on the particle distribution and signal duration. For Case 2 one pronounced peak occurs in the lowest channel while channel 3 shows only a delayed, weak signal, indicating stratified particles take the high-flow branch. Few particles entering channel 3 suggest disturbances at the branching without significantly offsetting sedimentation.

B. Magnetic field influence

Differences between both cases also show with magnetic field application. Case 2 shows no differences in particle distribution; the large lower channel remains preferred and no particle trapping occurs as extinction decays to initial levels. For case 1, channel 1 exhibits a pronounced particle signal with slower decay compared to the magnet-free condition. Channels 3 and 4 show pronounced signals with faster onset in channel 4 relative to the situation without magnet. While channel 1 flushes out over time, signals in channels 3 and 4 reach a plateau. This persistent deviation from the pre-injection level indicates a macroscopically represented degree of magnetic retention. Particle retention in weak magnetic fields suggests magnetic volume effects exploitable in low-flow vessels. These results indicate a relationship between geometry-induced flow distribution, resulting flow velocities, and magnetic retention capabilities. In particular magnetic

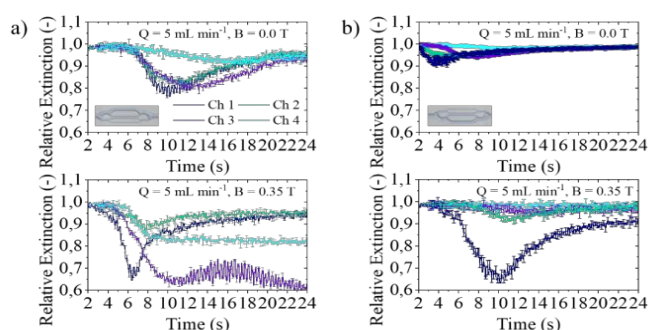


Fig 2: a) Representation of the extinction curves of case 1 without (top) and with (bottom) magnetic setup. b) Representation of the extinction curves of case 2 without (top) and with (bottom) magnetic setup.

retention becomes observable only when local washout is sufficiently weak and residence times are long enough for magnetic forces to act over a relevant duration.

IV. CONCLUSION AND OUTLOOK

The present work shows the influence of locally varying, geometry-induced flow conditions on the duration and shape of the particle signal. Based on the mathematical description of the channel geometry, coupling with simulative data on the flow distribution within the sample will allow for the prediction of signal shape and duration and comparison with the experimental data. Thus allowing for the calculation of a fitting function to correlate the signal shape and magnetic field influence to applied geometric parameters.

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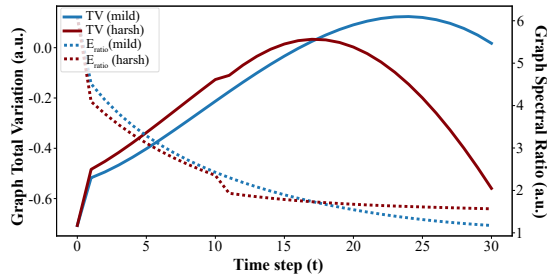


Fig. 2: GSP metrics considered on the analysis of the proposed multitrophic network model of an EPN-PGPR co-culture. In the legend, TV refers to the graph total variation and E_{ratio} refers to the graph spectral ratio.

enable a real-valued spectral decomposition, a symmetrised graph shift operator that preserves the magnitude of pairwise interactions is defined while discarding directionality for the purposes of spectral analysis. The graph shift operator W_s is defined as $W_s \triangleq \frac{1}{2}(W + W^T)$. From W_s , the combinatorial graph Laplacian $L \triangleq D - W_s$ is constructed, where $D = \text{diag}(W_s \mathbf{1})$ is the degree matrix, and $\mathbf{1}$ is a unitary matrix. The Laplacian is used to quantify the smoothness of the evolving biological signal over the multitrophic network. Specifically, the graph total variation (TV) of $\mathbf{x}(t)$ is defined as [4]

$$\text{TV}(\mathbf{x}(t)) \triangleq \mathbf{x}(t)^T L \mathbf{x}(t). \quad (1)$$

Low values of $\text{TV}(\mathbf{x}(t))$ indicate a coherent and spatially smooth behaviour in the multitrophic network, whereas larger values reflect localised heterogeneity and uneven degradation patterns.

To characterise how storage-induced disturbances propagate through the multitrophic network, W_s is initially decomposed into eigenvectors as $W_s = U\Lambda U^T$, where $U = [\mathbf{u}_1, \dots, \mathbf{u}_N]$ is an orthonormal basis of graph Fourier modes and $\Lambda = \text{diag}(\lambda_1, \dots, \lambda_N)$ contains the associated graph frequencies. After performing a graph Fourier transform (GFT) of the network's state, given by $\hat{\mathbf{x}}(t) = U^T \mathbf{x}(t)$, decomposing the GFT coefficients into low- and high-frequency components. Let $\mathcal{I}_\ell$ and $\mathcal{I}_h$ denote the index sets corresponding to the lower and upper halves of the spectrum, respectively, associated spectral energies are then defined as [4]

$$E_\ell(t) \triangleq \sum_{i \in \mathcal{I}_\ell} \hat{x}_i^2(t), \quad E_h(t) \triangleq \sum_{i \in \mathcal{I}_h} \hat{x}_i^2(t). \quad (2)$$

The graph energy ratio $E_{ratio} = E_h(t)/E_\ell(t)$ serves as an indicator of spectral redistribution from global smooth modes to localised network modes.

The simulation of the multitrophic network model also requires the inputs of the storage conditions scenarios (mild and harsh) incorporated through a latent storage index that aggregates multiple normalised environmental variables into a single bounded graph signal. Specifically, storage-related covariates such as temperature, humidity, light exposure, and oxygen availability are normalised to $[0, 1]$ and combined via a weighted sum, followed by a logistic mapping to ensure

boundedness. The resulting index captures the relative severity of storage conditions, with larger values indicating harsher environments. The weighting coefficients encode the relative sensitivity of the system to each variable, while a bias and gain parameter set the nominal operating point and transition steepness. This formulation provides a continuous, differentiable representation of storage effects suitable for spectral and graph-based analysis.

III. PRELIMINARY RESULTS

The behaviour of the multitrophic network model was evaluated by observing the temporal evolutions of $\text{TV}(\mathbf{x}(t))$ and E_{ratio} considering mild and harsh storage scenarios (Figure 2). This analysis reveals how exogenous variables that affect storage conditions modulate the spatial coherence and spectral composition of survival-related signals, allowing the identification of structurally localised vulnerabilities in the encapsulated system. In Figure 2 it can be seen that TV under mild storage conditions took longer to reduce compared to the harsh storage scenario, denoting that storage stress propagates through specific biological pathways rather than uniformly affecting all components. It can also be seen that E_{ratio} in the mild storage scenario leads to a continuous decrease over the observed time period, while in the harsh storage scenario, the network state vector has more high-frequency components resulting in a bumpy decrease of E_{ratio} , hitting a floor after $t = 10$.

The results obtained indicate that encapsulation design variables play a critical role in constraining storage-induced stress to low-frequency, globally coherent modes. The observed shift toward high-frequency activation under harsh storage conditions highlights design-mediated fragilities, implying the need to improve our experimental protocol for the EPN-PGPR culture.

IV. CONCLUSIONS

In this work, graph signal processing metrics were utilised to investigate the experimental design of an encapsulated EPN-PGPR culture intended for the development of a plant health agent. The graph spectral analysis suggests a direct analogy between robust network design in communications and experimental design in wet-lab biological systems, which will be helpful to optimise the design, duration and effectiveness of the plant health agent.

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Channel Modeling for Time-Varying Dispersive Closed-Loop MC Systems with Pulsatile Flow

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Abstract—Molecular communication (MC) is a communication paradigm in which information is conveyed through the controlled release and propagation of molecules. Especially in in-body application environments, the channel topology is closed-loop, and particle propagation is determined by the joint influence of diffusion and pulsatile flow induced by the heartbeat. However, most existing analytical models for dispersive closed-loop MC channels assume a constant flow velocity, whereas flows in biological environments are in many cases pulsatile. Therefore, in this paper, we present a time-varying one-dimensional (1D) channel model for closed-loop MC systems under pulsatile flow, operating in the dispersive regime. An analytical expression for the channel impulse response (CIR) is derived, resulting in a wrapped Normal distribution with time-variant mean and variance. The proposed model is validated by comparison to three-dimensional (3D) particle-based simulation (PBS) results.

I. INTRODUCTION

Molecular communication (MC) enables information transfer in biological environments, and targets various biomedical and healthcare applications. In vascular and circulatory systems, transport takes place in highly branched closed-loop channels and is governed by diffusion and flow [1]. The closed-loop nature of such channels motivates the development of models that account for the periodicity of transport. However, most existing models assume constant flow velocity [2], [3], although physiological flows can exhibit pulsatile behavior due to the periodic pumping of the heart.

Recent advances in transport modeling have shown that, in the dispersive regime [4], diffusion and pulsatile flow with a Womersley velocity profile [5] can be approximated by a one-dimensional (1D) advection–diffusion equation with time-varying flow velocity [6], similar to the Aris–Taylor approximation for time-invariant scenarios. To this end, this work addresses the modeling of dispersive closed-loop MC channels under pulsatile flow.

The main contributions of this work are as follows. First, we extend an existing closed-loop MC channel model to account for pulsatile flow by introducing a time-varying flow velocity expression. Second, we derive an analytical expression for the channel impulse response (CIR) with time-variant mean and variance. Finally, we validate the proposed analytical 1D model through three-dimensional (3D) particle-based simulations (PBSs) of the underlying transport processes.

II. CHANNEL MODEL

This section adopts the reduced 1D transport model for pulsatile flow proposed in [6] and derives an analytical expression for the corresponding CIR in a closed-loop MC system.

Particle transport in a cylindrical MC channel is governed by advection and diffusion in three dimensions. For sufficiently long and slender channels, transverse diffusion is much faster than axial transport, leading to an approximately uniform particle distribution over the cross section. Under these conditions,

the underlying transport processes can be approximated by an equivalent 1D description along the axial direction [4]. The resulting 1D axial transport is described by the following advection–diffusion equation [6, Eq. (41)]

$$\partial_t p(x, t) + u(t) \partial_x p(x, t) = D_{1D}(t) \partial_{xx} p(x, t), \quad (1)$$

where ∂_x and ∂_t denote the first derivatives with respect to space and time, respectively, and ∂_{xx} denotes the second derivative with respect to space. Moreover, $p(x, t)$, $u(t)$, and $D_{1D}(t)$ are the particle concentration, the cross-sectionally averaged, time-variant axial flow velocity, and the corresponding time-variant effective diffusion coefficient. As we consider a closed-loop system of total length L , (1) will be solved for periodic boundary conditions and an impulsive release of particles at $t = 0$, see [1, Sec. III-C].

The axial flow velocity $u(t)$ in (1) is time-varying and periodic, and can be modelled by a finite Fourier series as follows [6, Eq. (48)],

$$u(t) = \bar{u} \left(1 + \sum_{n=1}^N M_n \cos(n\omega t + \phi_n) \right), \quad (2)$$

where $\bar{u}$ denotes the temporal mean velocity over one pulsation period, $\omega = 2\pi f$ is the fundamental angular frequency, f is the pulsation frequency, M_n are dimensionless amplitude coefficients, ϕ_n are phase shifts, and N is the number of harmonics used to approximate the pulsatile velocity waveform. An example waveform is shown in Fig. 1. The representation in (2) allows flexible modeling of physiologically realistic pulsatile waveforms and is consistent with the 3D velocity model in [6, Eq. (31)] used in PBSs.

Similar to the derivation of the effective diffusion coefficient for time-invariant systems [4], the time-varying effective diffusion coefficient in (1) is determined by the pulsatile velocity in (2). A key dimensionless parameter characterizing pulsatile flows is the Womersley number, $Wo = R\sqrt{\omega/\nu}$, which measures how fast the flow velocity changes in time compared to how fast viscosity can adjust the velocity profile across the channel cross section [5]. Here, R denotes the channel radius, and ν the kinematic viscosity.

For the parameter ranges considered in this paper, the Womersley number Wo is within the range for which the diffusion coefficient approximation derived in [6, Eq. (43)] can be directly applied, i.e., $D_{1D}(t) = D + \frac{\bar{u}^2 R^2}{48D} \left(\frac{u(t)}{\bar{u}} \right)^2$, where D is the corresponding 3D molecular diffusion coefficient of the signaling particles.

To obtain $p(x, t)$ from (1), we apply a sequence of variable transformations. First, a moving spatial coordinate is introduced as $\xi = x - \Xi(t)$, where $\Xi(t) = \int_0^t u(s) ds$, and follows the instantaneous mean flow velocity. Using the chain rule, (1) reduces to

$$\partial_t p(\xi, t) = D_{1D}(t) \partial_{\xi\xi} p(\xi, t). \quad (3)$$

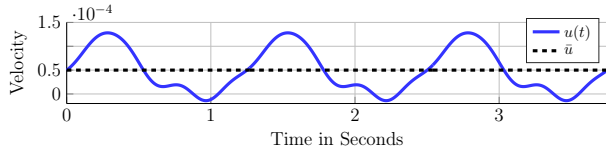


Fig. 1. **Time-varying axial flow velocity** $u(t)$ under pulsatile flow conditions in (2).

Next, a rescaled time variable is defined as $\tau(t) = \int_0^t D_{1D}(s) ds$, which absorbs the time dependence of the diffusion coefficient. Under this transformation, (3) turns into a diffusion equation with constant coefficients

$$\partial_\tau h(\xi, \tau) = \partial_{\xi\xi} h(\xi, \tau), \quad (4)$$

where $h(\xi, \tau) = p(\xi, t(\tau))$.

Solving (4) for periodic boundary conditions and an impulsive release of particles at $t = 0$, and then returning to the original variables by inverting the coordinate transformations, the particle concentration $p(x, t)$, which defines the CIR, in a dispersive closed-loop MC system with diffusion and time-variant flow ends up in a wrapped normal distribution as follows

$$p(x, t) = \sum_{k=-\infty}^{\infty} \frac{1}{\sqrt{2\pi\sigma^2(t)}} \exp\left(-\frac{[x - \Xi(t) + kL]^2}{2\sigma^2(t)}\right), \quad (5)$$

with time-variant mean $\Xi(t) = \int_0^t u(s) ds$ and variance $\sigma^2(t) = 2 \int_0^t D_{1D}(s) ds$. We note that the expressions for $\Xi(t)$ and $\sigma^2(t)$ can be obtained in closed form, but are omitted here for brevity due to the space limitations.

III. SIMULATION RESULTS

In the following, the analytical model in (5) is validated by comparison to the results from 3D PBS. The PBS is implemented for a straight cylinder with reflecting boundaries at the channel walls and the closed-loop characteristic is realized by imposing periodic boundary conditions. Moreover, we compare the model in (5) to the time-invariant solution proposed in [1]. We consider a receiver of length Δx_{det} , located at $x = x_{\text{det}}$. Therefore, the particle concentration inside the receiver follows as

$$p_{\text{det}}(t) = \int_{x_{\text{det}} - \Delta x_{\text{det}}/2}^{x_{\text{det}} + \Delta x_{\text{det}}/2} p(x, t) dx. \quad (6)$$

The parameters were chosen according to [1], [4] such that the system operates in the dispersive regime. Unless stated otherwise, the parameters are fixed to $D = 5 \cdot 10^{-9} \text{ m}^2 \text{ s}^{-1}$, $R = 0.1 \text{ mm}$, $L = 1 \text{ mm}$, and $\Delta x_{\text{det}} = 0.1 \text{ mm}$.

We employ the pulsatile velocity waveform $u(t)$ shown in Fig. 1, generated from (2) using $f = 0.8 \text{ Hz}$ and $N = 4$ harmonics with amplitudes $M_1 = 1.26$, $M_2 = 0.27$, $M_3 = 0.18$, and $M_4 = 0.09$, and phases $\phi_1 = -1.4$, $\phi_2 = -2.6$, $\phi_3 = 1.0$, and $\phi_4 = 2.8$. Unless stated otherwise, the temporal mean velocity is $\bar{u} = 0.5 \cdot 10^{-4} \text{ m s}^{-1}$. For the results in which $\bar{u}$ is varied, the same pulsatile waveform is used, and only the value of $\bar{u}$ is changed. For better comparability, all results are normalized by the equilibrium value $p_\infty = \Delta x_{\text{det}}/L$, obtained from $\lim_{t \rightarrow \infty} p(x, t) = 1/L$.

Figure 2 shows the results from the proposed model in (5) (blue), from PBS (circle markers), and from the time-invariant

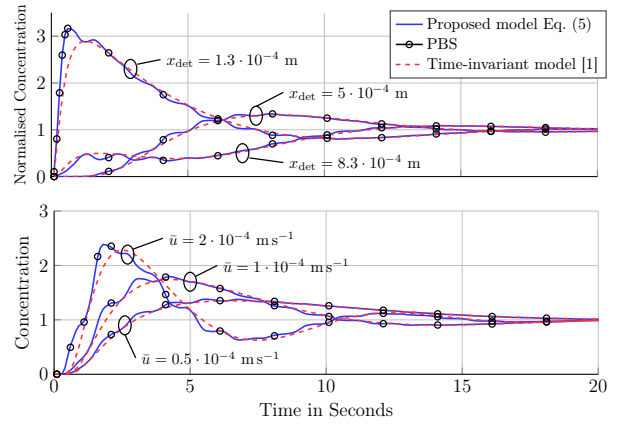


Fig. 2. **Received Signals** for varying receiver distance x_{det} (top) and mean flow velocity $\bar{u}$ (bottom).

model in [1] (red), for different receiver positions x_{det} with fixed mean flow velocity $\bar{u} = 0.5 \cdot 10^{-4} \text{ m s}^{-1}$ (top) and for different mean flow velocities $\bar{u}$ for a fixed receiver position $x_{\text{det}} = 0.3 \text{ mm}$ (bottom). First, we can observe that the proposed model is in excellent agreement with the results from PBS in all considered scenarios. Moreover, we can observe that the time-invariant model from [1] is not able to capture the pulsations, while it is still capable of approximating the overall shape of the received signal. However, it can also be observed that the influence of the pulsatile background flow becomes less pronounced for increasing receiver distance, decreasing mean flow velocities, and over time. This behavior is expected, as for all these variations, the influence of the advective transport gets less important compared to diffusion yielding more dispersive system dynamics [4].

IV. CONCLUSION

In this work, we proposed a channel model for time-varying closed-loop MC systems under pulsatile flow. An analytical expression for the CIR was derived, yielding a wrapped Normal distribution form with time-variant mean and variance. The model extends our previous closed-loop channel model [1] by incorporating pulsatile flow and was validated through comparison with 3D PBSs. The results build the basis for our future work, including the in-depth investigation of the influence of pulsatile flow on the received signal.

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Propagation Characteristics of Permeable MC Channels

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Abstract—In this work, we investigate the diffusive leakage from capillary channels into the surrounding environment. We propose an approach to estimate the state of the surrounding environment during communication by exploiting this leakage. Furthermore, we introduce a novel design of a macro-scale testbed to experimentally investigate this phenomenon.

Index Terms—Molecular Communication, Testbed, Capillary

I. INTRODUCTION

Molecular communications (MC) is an emerging research field that uses molecules as information carriers. It introduces a novel communication paradigm in environments in which conventional wireless communication is challenging, such as health monitoring or targeted drug delivery [1].

In the context of medical applications within the human body, the cardiovascular system represents a promising communication environment as it connects the entire organism [2], [3]. The type of vessel plays a decisive role in terms of modeling, system design and the respective application. In general, blood vessels can be divided into three main categories [2]: *i)* Arteries are thick vessels (~ 10 mm) transporting blood away from the heart; *ii)* Veins are vessels of varying size ($\sim 8 - 100 \mu\text{m}$) transporting blood back to the heart; *iii)* capillaries permeate the biological tissue and supply it with oxygen as well as nutrients. In contrast to arteries and veins, capillaries are very thin ($\sim 10 \mu\text{m}$) and have permeable walls which allows the exchange of nutrients. In contrast to arteries, flow inside capillaries is laminar with constant blood pressure. While larger molecules such as nutrients require active transport mechanisms to enter the surrounding environment, smaller molecules like oxygen diffuse freely into the surrounding environment [4].

The diffusive flow through the walls of capillaries is considered in [5]. In particular, the release of oxygen by red blood-cells as well as the diffusion into the surrounding medium was considered. In [6], diffusion in regions with different diffusion coefficients are investigated. In addition to theoretical works, several experimental works exist on MC in blood vessels [7]–[9]. However, they predominantly consider vessels with non-permeable walls, restricting propagation of molecules solely within the vessel. The testbed in [10] is based on a closed-loop system of capillaries within a fertilized egg. However, the focus lies in the overall system behavior of an entire vessel complex instead of the outflow of a single vessel. Non of the mentioned testbeds explicitly focuses on the diffusive outflow through the wall of a capillary. Also, the diffusive outflow of capillaries is poorly investigated from a communications engineering perspective.

For the design of reliable MC systems, it is essential to account for the state of the surrounding biological environment as it directly affects the reliability of the communication

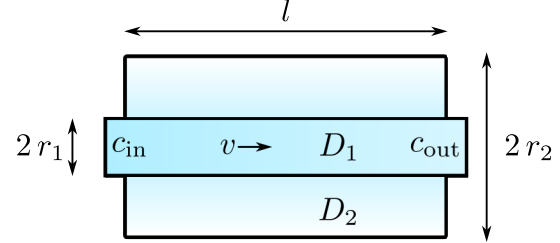


Fig. 1. Cross-section of the channel. Capillary ($r \leq r_1$) with diffusion coefficient D_1 and flow v ; surrounding biological environment ($r_1 < r \leq r_2$) with diffusion coefficient D_2 and no directed flow.

channel. In the case of capillaries, the outflow into the surrounding environment can provide valuable insights regarding the channel integrity as well as health-related physiological parameters.

In this work, we propose a novel approach to estimate the state of the surrounding environment based on the outflow of a capillary. Moreover, we propose the design of a macro-scale testbed for MC in capillaries, which, in contrast to existing testbeds, focuses on the diffusive leakage into the surrounding environment.

II. SYSTEM MODEL

A schematic sketch of the channel is depicted in Fig. 1. The channel consists of a single capillary modeled as a cylinder of length l and radius r_1 . The surrounding biological environment is modeled by a hollow cylinder with inner radius r_1 and outer radius r_2 . The concentration of a certain substance X can be modeled using the advection-diffusion equation [11]

$$\frac{\partial c}{\partial t} = D \Delta c - v \nabla c, \quad (1)$$

with the Laplace operator Δ , the Nabla operator ∇ and flow velocity v . Due to symmetry, the concentration c depends on the position in cylindrical coordinates r and z as well as the time t , i.e., $c(r, z, t)$, which is omitted for the sake of readability. We denote the diffusion coefficient within the inner and outer cylinder with D_1 and D_2 , respectively. Furthermore, we assume a parabolic flow profile within the inner cylinder [3]. Thus, we define

$$D := \begin{cases} D_1, & r \leq r_1, \\ D_2, & r > r_1, \end{cases} \quad v := \begin{cases} \bar{v}(1 - (\frac{r}{r_1})^2) e_z, & r \leq r_1, \\ 0, & r > r_1, \end{cases} \quad (2)$$

with the unit vector e_z pointing in axial direction of the cylinder and the maximum velocity $\bar{v}$. We incorporate the input concentrations $c_{in}(t)$ of X as a boundary condition of (1)

$$c|_{z=0, r \leq r_1} = c_{in}(t), \quad (3)$$

and define the output concentration $c_{out}(t) := c(0, l, t)$. Furthermore, we assume

$$c|_{r=r_2} = 0. \quad (4)$$

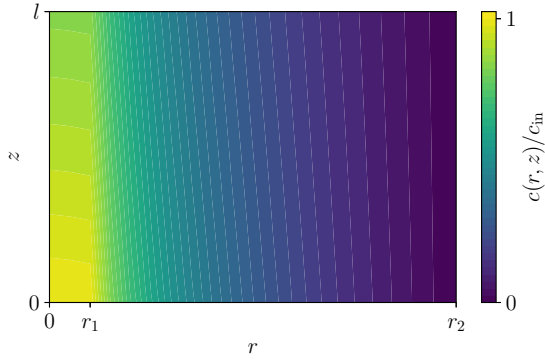


Fig. 2. Simulation results of the FEM of the channel with $D_2 = D_1/10$.

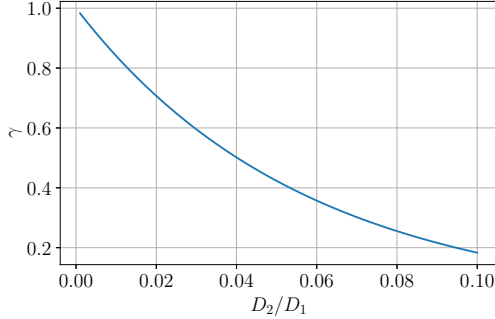


Fig. 3. Function $c_{\text{out}}^{\text{mean}}/c_{\text{in}}^{\text{mean}} = \gamma(D_2)$.

III. ESTIMATION OF SURROUNDING ENVIRONMENT STATE

The objective is to estimate the diffusion coefficient D_2 of the surrounding environment based on the knowledge of $c_{\text{in}}(t)$ and $c_{\text{out}}(t)$. Therefore, we use the temporal mean values $c_{\text{in}}^{\text{mean}}$ and $c_{\text{out}}^{\text{mean}}$. Based on the linearity of the channel, we obtain

$$c_{\text{out}}^{\text{mean}} = c_{\text{in}}^{\text{mean}} \int_{\mathbb{R}} g(\tau) d\tau := c_{\text{in}}^{\text{mean}} \gamma, \quad (5)$$

with the channel impulse response (CIR) $g(t)$. To the best of the authors' knowledge, there does not exist an analytical solution for the partial differential equation (PDE) given in (1) with the boundary conditions (3) and (4). Hence, we solve the PDE of the system numerically for the stationary case of (1), i.e., $\partial c / \partial t = 0$ using a finite element method (FEM). An exemplary result is shown in Fig. 2.¹ It can be seen that the inner tube ($r \leq r_1$) contains the highest amount of concentration. For increasing values of z , the concentration decreases as the molecules leak into the surrounding environment ($r > r_1$). Please note that the values for $c_{\text{in}}^{\text{mean}}$ and $c_{\text{out}}^{\text{mean}}$ correspond to the concentration at $(r, z) = (0, 0)$ and $(r, z) = (0, l)$, respectively. Fig. 3 shows the function $\gamma(D_2)$:

It is obtained by applying the FEM for different values of D_2 and calculating the ratio $\gamma = c_{\text{out}}^{\text{mean}}/c_{\text{in}}^{\text{mean}}$. We observe that for bigger values of D_2 , more molecules diffuse out of the capillary decreasing the value of γ . With $D_2 \rightarrow 0$, no molecules can leave the vessel leading to $c_{\text{in}}^{\text{mean}} \rightarrow c_{\text{out}}^{\text{mean}} \Rightarrow \gamma \rightarrow 1$. Please note, that the diffusion coefficient D_2 can be evaluated according $D_2 = \gamma^{-1}(c_{\text{out}}^{\text{mean}}/c_{\text{in}}^{\text{mean}})$ from Fig. 3.

¹The following simulation parameters were used: $r_1 = 10 \mu\text{m}$ [2], $r_2 = 10 r_1$, $l = 100 r_1$, $D_1 = 10^{-9} \text{m}^2/\text{s}$, $D_2 = D_1/10$, $\bar{v} = 10^{-3} \text{m/s}$ [12].

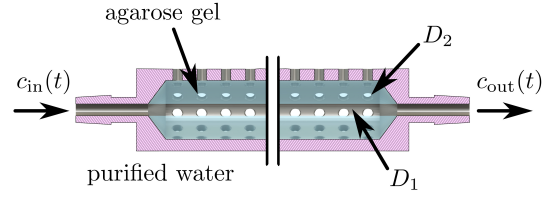


Fig. 4. Sketch of the assembly of the channel.

IV. FIRST SKETCH OF A TESTBED

In order to validate the previously discussed approach experimentally, we propose a first sketch of a macro-scale testbed mimicking the communication behavior within a capillary. The channel is positioned inside a 3D-printed cylinder shown in Fig. 4. On the left- and right-hand side, it is connected with tubes to the transmitter and receiver. Agarose gel [13] mimics the environment surrounding the vessel. Furthermore, the cylinder is placed inside purified water and holes on the exterior of the cylinder (see Fig. 4) connect the Agarose gel with the purified water.

V. OUTLOOK

In future works, we will focus on the implementation of the proposed testbed and validate the used model by comparing theoretical with experimental results while scaling up biological complexity from Agarose gel as tissue mimic to the addition of living cells.

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Towards T-cell based Bio-Robots: Synergy between Molecular Communications and Bio-Mechanics

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Abstract—In this paper, we report on our ongoing work in the field of bio-inspired micro robotics. We discuss, how different scientific disciplines, including molecular communications, have to be combined to realize systems capable of tasks like tumor clearance and pathogen elimination.

I. INTRODUCTION

Molecular communications (MC) is a bio-inspired communication paradigm utilizing molecules as carriers of information. It has been proposed as one of the key communication paradigms for the bio and micro/nano domain. Since MC originated historically from communications engineering, it has been developed in a similar way, i.e., viewing the communication system as an isolated engineering system¹. In bio-micro robotics however, this approach might not be appropriate as the communication system is an integral part of the overall system and cannot be clearly separated from it. Moreover, a common opinion in bio-micro robotics is, that respective systems should not be engineered from scratch, but by modifying pre-existing biological organisms accordingly [1]. As a consequence, it is crucial to understand, model and analyze these organisms to predict and optimize the effect of modifications. In this work, we follow this approach: Inspired partly by the well-known CART-therapy, we propose to use cytotoxic T-cells as bio-micro robots. We sketch a computational modeling framework to simulate the interplay between biological signaling, communications and mechanics ultimately enabling cell locomotion. In future works, we will implement and refine the preliminary framework presented in this abstract.

II. BIOLOGICAL SYSTEM AND COMPUTATIONAL MODEL

A. Considered Scenario

In the following, we consider the simple scenario depicted in Fig. 1: We assume a T-cell crawling on a flat surface. On its membrane surface it exhibits G-protein coupled receptors (GPCRs) used for sensing the environment. Specifically, it uses these sensing units to determine the local concentration of chemo-attractants, i.e., molecules emitted by a source towards which the T-cell aims to crawl. This scenario arises, when other immune cells (e.g., macrophages) encounter pathogens or tumor cells and emit chemokines to attract cytotoxic T-cells. In our simplified scenario, we assume that the source is located at the coordinate origin and that the T-cells surface elements are described by a vector $\mathbf{r} = [\mathbf{r}_1, \mathbf{r}_2, \dots, \mathbf{r}_I]^T$. The vectors $\mathbf{r}_i$, $i \in \{1, 2, \dots, I\}$, are three dimensional vectors indicating the spatial location of a GPCRs on the cells membrane as a function of time.

B. Molecular Communications and Signaling Perspective

From an MC perspective, the molecule source is the transmitter (TX). However, in contrast to classical digital communications, in this scenario the TX continuously releases molecules. The released molecules diffuse across the medium

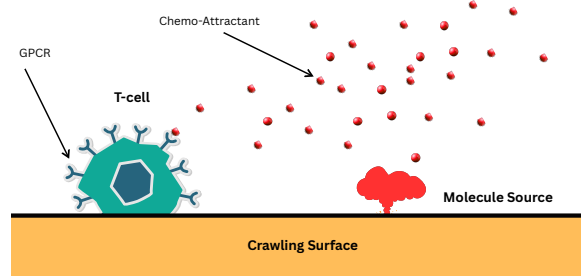


Fig. 1: Considered Scenario: A molecule source emits chemoattractive molecules. A T-cell senses these molecules using GPCRs and uses this information to crawl towards the source.

(i.e., the channel) until they eventually reach the T-cell (i.e., the receiver (RX)). At the RX the chemo-attractant molecules are sensed and converted into intracellular signals, which control the movement of the T-cell towards the source. Using the standard MC-TX models (e.g., point source) and assuming that the release rate Q from the TX is either constant or at least varies much slower than the time scale of molecule transport process (e.g., diffusion) the concentration $C(\mathbf{r}_i)$ at any location $\mathbf{r}_i$ can be computed according to

$$C(\mathbf{r}) = Q(t)g(\mathbf{r}) \quad (1)$$

Thereby, $g()$ describes the static space dependent transfer characteristic. The equation (1) can be used to compute the local concentration on the surface of the T-cell. Next, we discuss how the T-cell translates this information to an intracellular signal. We interpret this as part of the RX, i.e., we interpret the RX as a system which samples the channel at different locations $\mathbf{r}$ and translates it into signals $\mathbf{a} = [a_1, a_2, \dots, a_I]^T$ and $\mathbf{m} = [m_1, m_2, \dots, m_I]^T$ which control the movement of the cell (see II-C). The conversion between extracellular chemo-attractant concentration and signaling molecules inside the T-cell is achieved using GPCRs, which can be modeled as shown in our previous work [2]. As the key intracellular signaling molecule downstream of the GPCR we consider the GTPase Rac, to which we attribute the following functions [3], [4]:

- 1) It promotes actin polymerization
- 2) It inhibits another GTPase called Rho, responsible for myosin contraction

These two functions link the molecular signaling to the biomechanics and, hence, the locomotion of the T-cell. Specifically, actin polymerization tends to expand the cell locally, while myosin activation tends to contract locally. As a consequence, areas with high local Rac concentration tend to expand, while those with low local Rac concentration tend to contract. Moreover, the probability of adhesion to the nearby surfaces is also higher in high Rac regions. A simplified schematic of Rac-induced local and global morphological and biophysical effects is shown in Fig. 2. Crawling emerges by a combination of protrusion formation and attachment in the front and

¹In classical engineering this reductionistic approach is often well justified, because the electrical communication systems are typically much faster than the processes generating the transmitted information, e.g., sensors, actuators, etc..

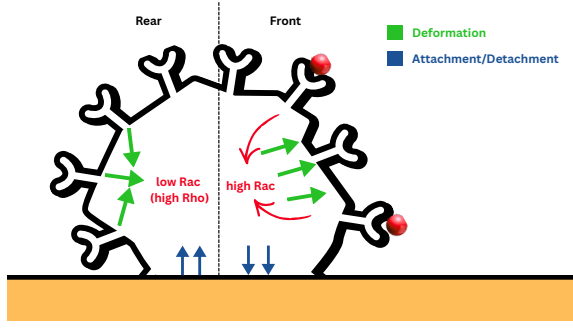


Fig. 2: Simplified crawling model based on Rac signaling: Front and rear can be determined by concentrations of external chemo-attractant molecules (red spheres), which translates (red arrow) to local Rac concentrations. In regions of high Rac, actin polymerization (not shown) leads to outward deformation. Lack of Rac (via missing inhibition on Rho) leads to inward deformation via myosin (not shown) contraction. Cells adhere more strongly to nearby surfaces at high local Rac.

contraction and detachment at the rear. Since Rac is degraded strongly inside cells we assume, that its concentration is elevated predominantly near the respective receptors and hence in the proximity of the surface. It is therefore justified, to associate always one Rac signal a_i with one $\mathbf{r}_i$. As a starting point we choose

$$a_i = [\text{Rac}]_i = \frac{S(C(\mathbf{r}_i))}{\sum_i S(C(\mathbf{r}_i))}, \quad (2)$$

where $S(\cdot)$ is the receptor saturation curve (e.g., $S(x) = \frac{x}{K+x}$ with half saturation constant K). The scaling $\frac{1}{\sum_i S(C(\mathbf{r}_i))}$ models the adaptation of local receptor signaling strength to overall signal strength (see App. III), a well established conceptual mechanism responsible for the polarization of eukaryotic cells [5].

The concentration of Rho can be modeled based on the Rac concentration according to

$$m_i = [\text{Rho}]_i = \frac{K_h}{K_h + [\text{Rac}]_i}, \quad (3)$$

with K_h the half saturation constant.

C. Link to Bio-Mechanics

In the following, we will discuss, how molecular signals can be mapped to forces on the cell. To model the mechanics, we consider a simplified model of the T-cell, which focuses on the cortex, i.e., the active outer shell of the cell. This model will be derived based on the energy approach discussed in [6]. Therefore, the cells cortex is separated into elements obtained by triangular meshing. Each triangle i corresponds to a receptor patch $\mathbf{r}_i$ and therefore has associated signals a_i and m_i . Edges of the triangles are represented by spring with resting length l_0 and spring constant k . Additional springs accounting for bending angle between triangles, normal forces on the crawling surface, etc., will be incorporated successively. The signals a_i and m_i interact with the springs by increasing and decreasing resting lengths, respectively. Under the common assumption of overdamped dynamics, the ODE describing the system dynamics can be written in the general form [6]:

$$\mathbf{R}(\mathbf{r})\dot{\mathbf{r}} = \mathbf{F}(\mathbf{r}, \mathbf{a}, \mathbf{m}), \quad (4)$$

where $\mathbf{R}(\mathbf{r})$ is the dissipation matrix (accounting especially for friction with the crawling surface) and $\mathbf{F}(\mathbf{r})$ the acting forces. These forces can be computed as gradients of a global energy function [6], which allows great flexibility for incorporating various biomechanical properties (e.g., incompressibility of the cell interior).

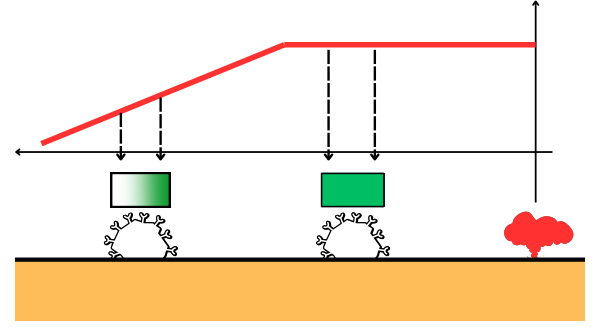


Fig. 3: Challenge of static gain in T-cell gradient sensing

III. CONCLUSION AND OUTLOOK

In this work, we presented a simplified mathematical abstraction of T-cell locomotion, focusing on signaling and its connection to biomechanics. In future works, this model will be implemented in software and is expected to provide novel insights into the challenges and opportunities of MC in the context of bio-micro robotics and engineering in general. Moreover, the model can be used to test and optimize modifications of T-cells for various tasks.

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APPENDIX 1: MOTIVATION FOR ADAPTATION OF LOCAL RECEPTOR GAIN TO GLOBAL SIGNALING STRENGTH

We motivate the need for a local adaptation of signaling strength to global signaling intensity by contradiction: Assume, there were no global adaptation of local signaling intensity. Moreover, assume that $Q(t)$ from (1) can be arbitrary positive. Since the GPCR has some saturation dynamics, it would always be possible to create a scenario as depicted in Fig. 3. The graph depicted in red represents the local Rac concentration as a function of distance², which becomes increasingly flat as we approach the source. While the T-cell on the left operates in a region where a clear concentration difference can be sensed between front and rear, this is not possible for the T-cell on the right, due to receptor saturation. Hence, a model with static gain cannot approach an arbitrary source arbitrarily close. This contradiction can be resolved by acknowledging that, while Rac-signaling itself is highly localized, GPCRs might in parallel transfer information from one receptor patch to another, enabling cell-wide signal adaptation through MC.

²It would also be possible to plot over the chemo-attractant concentration; the conversion is achieved by (1)

Graphene Hall Sensor-Based Receiver for Magnetic Droplet-Based Communications

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Abstract—We present the first graphene Hall-effect receiver for magnetic droplet-based communications. By integrating a graphene Hall cross beneath a PDMS microfluidic channel, the device detects passing ferrofluid droplets and distinguishes their sizes through pulse width measurements of Hall voltage changes. The sensor demonstrates linear response across a wide magnetic field range and reliably differentiates droplets generated at varying pressures, validating its potential as a scalable receiver for magnetic droplet-based communication systems.

Index Terms—Graphene Hall Sensor, Molecular Communication

I. INTRODUCTION

The Internet of Bio-Nano Things (IoBNT) envisions networks of nanoscale devices operating in physiological environments where conventional electromagnetic links are often impractical [1]. Molecular communication (MC) has emerged as an alternative paradigm, encoding information in the controlled release, transport, and detection of chemical or particulate carriers. Within this paradigm, droplet-based communication uses discrete emulsions as compartmentalized information carriers, inspired by biological signaling mechanisms such as extracellular vesicles, and can offer deterministic transport and higher throughput than purely diffusion-based schemes [2].

In this work, we focus on droplet-based communication implemented with ferrofluid droplets containing magnetic nanoparticles (MNPs), which are promising carriers due to their biocompatibility and detectable magnetic signatures in biological media [3]. Given the negligible magnetic background in physiological environments [4], magnetic detection offers a distinct advantage over optical methods for implantable systems. However, existing magnetic receivers for MNP-based MC, such as susceptometers and inductive coils [5], [6], are bulky and unsuitable for on-chip integration, motivating miniaturized magnetic receivers.

Hall-effect sensors provide a chip-scale alternative by converting magnetic flux into voltage via the Lorentz force [7]. Unlike inductive coils, they can be fabricated as planar

structures beneath microfluidic channels [8]. Graphene Hall sensors further enhance sensitivity through atomic thickness and high carrier mobility [9], yet their application in droplet-based communications remains unexplored.

In this work, we introduce a graphene Hall-effect receiver for magnetic droplet-based communications. A graphene Hall cross integrated beneath a PDMS microfluidic channel enables detection of ferrofluid droplets and distinguishing their sizes through Hall voltage variations under controlled magnetic field conditions.

II. METHODOLOGY

A. Device Fabrication

Fabrication of the receiver began with patterning Ti/Au (5/50 nm) contacts on an n-type Si/SiO₂ substrate (525 μ m Si, 90 nm thermal oxide) by photolithography and electron-beam evaporation, followed by lift-off. CVD-grown graphene was then wet-transferred onto the pre-patterned electrodes and defined into Hall-cross geometries (100 μ m $\times$ 15 μ m) using photolithography and O₂ plasma etching. The active region was encapsulated with 20 nm Al₂O₃ deposited by ALD, and contact-pad windows were opened by selective wet etching. Finally, a PDMS microfluidic channel fabricated by soft lithography was plasma-bonded to the chip. The fabrication workflow and assembled device architecture are summarized in Fig. 1(a) and Fig. 1(b), respectively.

B. Experimental Setup

To characterize the system, a measurement setup was assembled comprising a source measurement unit (Keysight B2902B) and an electromagnet generating perpendicular magnetic fields up to 40 mT (Fig. 1 (c)). Water-based ferrofluid (EMG-705, Ferrotec) droplets in silicone oil (100-cSt) containing Fe₃O₄ nanoparticles were generated in a T-junction geometry.

III. PRELIMINARY RESULTS

A. Device Characterization

The device characterization was carried out using scanning electron microscopy (SEM), confirming the intended Hall cross geometry and the integrity of the metal contacts (Fig. 1

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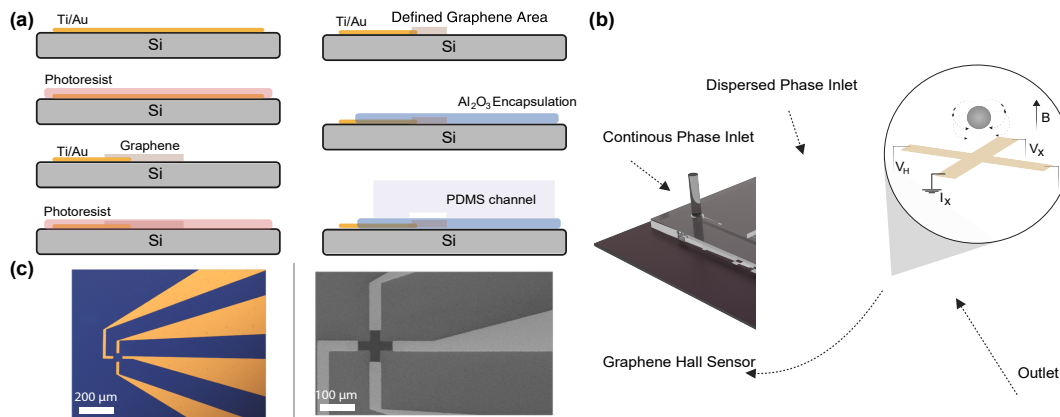


Fig. 1: (a) Fabrication process flow. (b) Schematic of the assembled device with integrated T-junction microfluidic channel. (c) Optical and SEM images of the fabricated device.

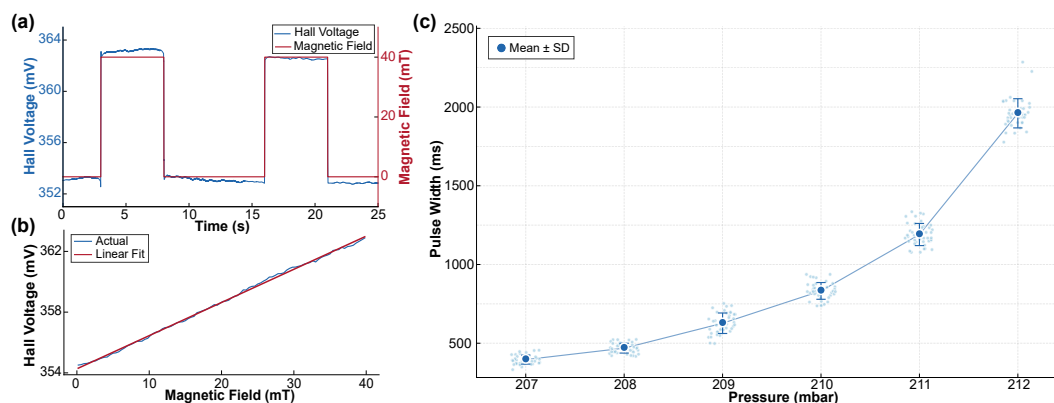


Fig. 2: (a) Hall voltage response at $B = 0$ and $B = 40$ mT. (b) Hall voltage as a function of applied magnetic field. (c) Average pulse width ($n=40$) as a function of pressure and corresponding distributions at each pressure.

(c)). Electrical characterization was then performed by evaluating the graphene Hall sensor sensitivity under controlled out-of-plane magnetic fields. The Hall voltage at representative field levels is shown in Fig. 2(a), and the corresponding V_H versus B calibration obtained from a linear field sweep is presented in Fig. 2(b), where the sensitivity was extracted as 218.5 mV.

Next, we evaluated receiver performance by varying the dispersed phase pressure from 207 to 212 mbar while keeping the continuous phase at 220 mbar, generating droplets of different sizes. As shown in Fig. 2(c), the average pulse width increases monotonically with pressure from 396 to 1960 ms with distinguishable distributions, confirming the sensor's ability to detect droplets of varying sizes. These results validate the graphene Hall sensor as a viable candidate for droplet-based communication receivers. Future work will investigate magnetic field strength effects and implement modulation schemes such as on-off keying (OOK) and pulse width modulation (PWM).

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Semantic Information in Molecular Communication–Based Drug Delivery Systems

Milica Lekić, Lukas Brand, Mohammed Zoofaghari, Ilanko Balasingham, and Mladen Veletić

Abstract—We are employing semantic information theory to quantify how much information about treatment parameters is functionally relevant for achieving a desired therapeutic outcome in a drug delivery system. The framework is evaluated through a simulation study of a focused ultrasound (FUS)–mediated drug delivery system.

Index Terms—Semantic information theory, Molecular Communications, Drug Delivery Systems, Focused Ultrasound

I. INTRODUCTION

Drug delivery systems (DDSs) can be viewed as molecular communication processes [1], in which therapeutic particles convey matter of interest through complex biological environments. In this perspective, particles act as messages and therapeutic outcomes define their meaning, in the sense of their contribution to achieving a specified treatment goal. This abstraction enables the parallelisation of particle transport and data transmission at the modelling level, which then provides an information and communication theoretic-based framework for analysing and optimising DDSs.

We view DDSs as goal-oriented molecular communication processes and adopt semantic information theory [2] to move beyond conventional statistical modelling. Semantic information theory distinguishes between syntactic information, which is the statistical correlation between variables, and semantic information, which quantifies how much of that information contributes to achieving and maintaining a specified goal. The framework has been applied to synthetic molecular communication systems, where engineered cells process the minimal amount of information required to trigger therapeutic responses [3], [4]. Specifically here, a DDS is interpreted as a goal-oriented communication process, in which the treatment setup (parameter configuration) affects a transport process (drug particle propagation and interaction), which ultimately produces a treatment outcome (therapeutic performance). Within this analogy, the treatment parameters constitute the message, and the achieved treatment

outcome defines the meaning of treatment parameters. From this standpoint, semantic information theory is employed to determine how much each treatment parameter contributes to the treatment outcome and what level of control precision is minimally required to achieve it.

To demonstrate the framework’s generality and practical relevance, we evaluate it through a simulation study of a focused ultrasound (FUS)–mediated DDS for brain tumours [5]. FUS-DDS offers a controlled and well-characterised platform for studying the effect of semantic relevance of parameters because it allows modulation of the blood-brain barrier and enables enhanced delivery of therapeutic agents that otherwise cannot reach the brain. The technique is inherently *multiparametric*, with multiple ultrasound parameters collectively determining the extent and duration of BBB opening. We introduce stochasticity to the deterministic model which couples FUS parameters with drug pharmacodynamics across the disrupted BBB and tumour microenvironment [5]. Variations in these parameters directly affect the transvascular transport rate k_{tv} , which governs drug delivery and uptake, further linking FUS control to treatment outcome. The stochastic model allows us to capture biological variability and apply information-theoretic measures that characterise how parameter uncertainty influences treatment outcomes. By embedding this FUS-DDS model into the proposed semantic information framework, we determine each FUS parameter’s contribution to treatment outcome and evaluate how loss of resolution (implemented through coarse-graining procedures) degrades performance.

Understanding how each treatment parameter contributes to the treatment outcome and how robust treatment performance remains under informational uncertainty of treatment parameters is of direct significance for both clinical optimisation and treatment device design. The main contributions of this work are thus as follows:

- We develop a (general) semantic information framework for analysing the information bounds of treatment parameters in DDSs.
- We validate the proposed framework through a simulation study of the FUS-DDS characterising the impact of FUS parameters.
- We demonstrate that the semantic information framework quantifies the meaningful contribution of each parameter, distinguishing refinements that are therapeutically relevant from those that are redundant.

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II. METHODOLOGY

Five steps are required to operationalise semantic information in the context of DDS.

1) *System partitioning*: The system dynamics can be deterministic, stochastic, or a combination of the two, and continuous or discrete. This requires partitioning the system into two components: the agent and the environment. In our formulation, we designate the treatment outcome measure as the state of agent X , and the set of treatment parameters constitutes the environment Y .

2) *Viability*: The viability function relies on the key characteristics of the agent that contribute to its continued existence. The change in information granularity should be reflected in the viability of the agent state X . Each treatment setup corresponds to a particular set of parameters that yields a unique probability density function (PDF) representing the distribution of treatment outcomes. The ensemble of all possible treatment setups thus forms a space of possible treatment outcomes, which can itself be described by a composite PDF. When a restriction (e.g. coarse-graining) is applied to the set of treatment setups, such as reducing parameter variability or merging similar configurations, this restriction alters the corresponding PDF of possible treatment outcomes. In other words, each distinct level of parameter granularity produces a distinct distribution of outcomes, and hence a distinct PDF. To quantify how such changes in treatment information granularity affect the outcome space, we define a viability function based on the difference between the PDFs that characterize successive coarse-graining stages. This viability reflects how robust the agent's behaviour (or state X) remains as the treatment information is compressed. Several possible measures exist to quantify differences between probability distributions, including the Kullback–Leibler (KL) divergence, Hellinger distance, and total variation distance.

3) *Syntactic Information Measure*: We next consider the correlations between the agent and its environment, which can be extracted from the joint distribution $p_{X_t Y_t}$. Correlations between the agent and the environment prevent a factorisation of the joint distribution such that $p_{X_t Y_t} \neq p_{X_t} p_{Y_t}$. These correlations reflect the fact that the process of drug transport in the communication channel is shaped by the treatment parameters Y , also responsible for the treatment outcome X . To quantify this correlation at time t , we use the *mutual information* between the agent X_t and the environment Y_t .

4) *Counter-factual Interventions*: Mutual information reaches its minimum value of 0 if and only if X_t and Y_t are statistically independent under p_{XY} , i.e., when $p_{X_t, Y_t} = p_{X_t} p_{Y_t}$ [2]. This case corresponds to a full intervention that erases all correlations. To identify the meaningful portion of mutual information, we apply partial interventions that allow us to vary the amount of syntactic information preserved under different interventions, and then measure the resulting agent viability. While there are other ways to scramble the channel between the agent and environment, here we adopt a *coarse-graining* procedure

from the information-theoretic perspective and apply it to the communication channel input.

5) *Semantic Information Measure*: The goal of the semantic information framework is to determine how the correlations identified in the previous steps contribute to the viability to distinguish which correlations are functionally relevant to the agent. This is achieved by applying a scrambling protocol that perturbs correlations and observing the resulting change in viability. The point at which the scrambled viability deviates from the actual viability defines the semantic threshold. This relationship can be represented through the information/viability curve as the achievable viability $D_{\text{stored}}(R)$ under any intervention from the set of all possible coarse-graining functions Φ , that preserves a specified amount of mutual information R as:

$$D_{\text{stored}}(R) := V(\hat{p}_X^\phi) \text{ s.t. } I_{\hat{p}^\phi}(X_{\text{tend}} Y) = R. \quad (1)$$

Finally, the (stored) semantic information S_{stored} is then the minimal amount of mutual information necessary to achieve the same viability as the actual distribution:

$$S_{\text{stored}} := \min_{\hat{p}^\phi: \phi \in \Phi} I_{\hat{p}^\phi}(X_{\text{tend}}; Y) \text{ s.t. } V(\hat{p}_X^\phi) = V(p_X). \quad (2)$$

III. A CASE STUDY: FOCUSED ULTRASOUND-MEDIATED DRUG DELIVERY

FUS treatment for central nervous system (CNS) diseases relies on FUS exposure to transiently open the BBB and to enhance the pharmacokinetics and pharmacodynamics (PK/PD) of the administered drug. Key factors in modelling BBB opening include the propagation of the ultrasound signal through the skull and brain tissue, as well as the timing and dosage of microbubble (MB) injection. BBB opening typically occurs within minutes of sonication and is followed by a closure phase that can last several hours. The dynamics of opening and closure are strongly influenced by FUS signal characteristics, the target location in the brain, and MB kinetics [5]. FUS provides a good platform for semantic analysis because it enables precise, controllable, and localised modulation of the BBB using controllable ultrasound signal parameters, such as pulse repetition frequency (PRF), pulse duration (PD), and mechanical index (MI), for treatment performance and robustness.

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Performance of Ratio-Shift Keying Modulation for Diffusive Molecular Communication Scenarios

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Abstract—Molecular communication (MC) is a promising communication paradigm that utilizes molecules as information carriers, mimicking natural biological processes. Out of various modulations to encode information onto signaling molecules, on-off keying (OOK) modulation has gained popularity due to its simplicity and efficiency. However, when the channel is unknown, for example, in cases where nodes are mobile, the OOK modulation-based MC systems suffer from a high bit error probability. In this paper, we investigate dynamic MC system with mobile transmit and receiver devices. We consider a variant of ratio-shift-keying (RSK) where the information is encoded in the ratio of the concentration of two different types of signaling molecules with the same propagation characteristics. We derive the optimal maximum likelihood (ML) decoder for OOK and RSK-based MC system. We also present a simpler representation of the optimal decoder under the Poisson assumption and show that the ML decoder for RSK modulation doesn't require channel information, in contrast with the ML decoder for OOK-based MC systems. We further investigate the bit error rate for the considered system. We show that RSK performs better than OOK in a dynamic MC system where the channel varies with time. This is because the ratio of the concentrations of the two types of information molecules is preserved at the receiver, offering improved robustness to variations in channel conditions. Therefore, RSK comes to the rescue in case of unknown or difficult to estimate channel environments. Via numerical investigations, we present various design insights, including optimal symbol design, and the gain of RSK over OOK as a function of node mobility.

Index Terms—Molecular communication, on-off keying, ratio-shift keying, maximum likelihood detection, time-varying channel.

I. INTRODUCTION

Molecular communication (MC) is a bio-inspired communication paradigm that uses molecules as information carriers, mimicking how biological systems communicate in nature. Among various modulation techniques, on-off keying (OOK) has gained popularity due to its simplicity and efficiency. However, in realistic scenarios where the transmitter (TX) and/or receiver (RX) are mobile, the channel impulse response varies with time and exact channel knowledge may not be available, leading to high bit error probability for OOK-based MC systems. We aim to spark discussion on whether MC decoding can be made invariant to channel conditions even in the presence of noise.

In search of a modulation scheme that preserves symbols in dynamic MC scenarios, ratio-shift keying (RSK) modulation was proposed in [1], [2]. RSK encodes information in the ratio of the concentrations of two types of signaling molecules, often implemented using molecular isomers that have identical prop-

agation characteristics due to their similar physical properties. While [2] provided a brief introduction of RSK modulation without detailed system analysis, [3] considered a static model and noise-free reception and did not enforce fair molecular budget normalization. The authors in [1] studied the capacity and bit error rate performance of RSK using a ligand-receptor receiver that decodes symbols based on receptor bound-time duration measurements.

The comparison between OOK and RSK in [1] is not strictly fair, since OOK employs a simple threshold or count-based detector, whereas RSK relies on bound and unbound time duration measurements, which introduce additional receiver complexity and practical challenges. This motivates the investigation of RSK performance under a decoding mechanism with comparable complexity to OOK, particularly in dynamic MC systems. Accordingly, this paper focuses on evaluating the gain of RSK with a low-complexity decoder over OOK in time-varying channel conditions. We further demonstrate higher-order RSK constellations, including 4-RSK, which preserve channel-independent decoding while enabling higher data rates in noisy environment. Overall, the proposed scheme provides a systematic and scalable modulation framework for reliable MC in noisy dynamic environments.

II. RATIO SHIFT KEYING MODULATION

We consider a MC system in an unbounded three-dimensional fluid environment, where molecules propagate via diffusion without drift. In the dynamic MC scenario, the transmitter (TX) is modeled as a transparent mobile point source undergoing Brownian motion with diffusion coefficient D_{TX} , assumed constant under ideal diffusion conditions. The TX releases two types of information molecules, Type A and Type B. The receiver (RX), synchronized with the TX, is a mobile passive unit consisting of two co-located receiver ports, each specific to one molecular type. Although two RX ports are required, the receiver complexity remains comparable to existing RSK models. The RX mobility is characterized by diffusion coefficient D_{RX} , with $D_{RX} = D_{TX} = D_{TR}$. Information molecules diffuse with coefficient D_{inf} , and all entities follow Brownian motion. In this paper, we consider RSK modulation for encoding information at the TX. The intended information is encoded in a parameter $\rho \in [0, 1]$, defined as the ratio of the concentration of the two types of molecules at the TX. In particular, the bits 0 and 1 are encoded using ratios ρ_0 and ρ_1 , respectively. We term this binary RSK

TABLE I
TRANSMIT SYMBOL FOR EACH BIT IN BRSK MODULATION SCHEME

bit b	Type 1 molecules a_{1b}	Type 2 molecules a_{2b}
0	$\rho_0 c$	$(1 - \rho_0) c$
1	$\rho_1 c$	$(1 - \rho_1) c$

(BRSK). The allocation of different types of molecules for each bit is provided in Table I for better clarity.

A. Optimal ML Decoder for RSK

Each receiver port (RXP) observes the number of molecules present in it after time τ_s from transmission. Hence, i^{th} RXP counts the number of received molecules of type i , given as $m_i = s_i + n_i$. We consider the Poisson approximation for s and n distribution. Therefore, we can write $s_i \sim \text{Poisson}(a_{ib}h)$; $n_i \sim \text{Poisson}(\lambda_N)$, which implies $m \sim \text{Poisson}(a_{ib}h + \lambda_N)$, where a_{ib} is the number of molecules received at RXP i for transmit bit b and h denotes the probability that molecule is detected at the passive receiver. The joint ML decoding region $D(1)$ for bit 1 under Poisson approximation is written as

$$D(1) = \left\{ m_1, m_2 : P(m_1, m_2 | b = 1) \geq P(m_1, m_2 | b = 0) \right\}. \quad (1)$$

The decoding region for bit 1 can be further solved as

$$m_1 \ln \frac{\mu_{11}}{\mu_{10}} + m_2 \ln \frac{\mu_{21}}{\mu_{20}} \geq 0 \implies \sum_{i=1}^2 m_i \ln \left(\frac{\mu_{i1}}{\mu_{i0}} \right) \geq 0, \quad (2)$$

where $\mu_{ib} = a_{ib}h + \lambda_N$ is the mean number of molecules received at the RXP. (2) shows that the optimal ML decoder for RSK-based MC system under Poisson reception is a weighted combiner with weights dependent on the mean received signal strength at both RXPs. Please note that if we consider a symmetric case, i.e., $\rho_0 + \rho_1 = 1$, then decoding becomes independent of the channel conditions. Putting this constraint in (2), the decoding region for bit 1 in the symmetric case is further simplified to a threshold decoder given as $D(1) = \{m_1, m_2 : m_1 \geq m_2\}$. Consequently, we can note that while OOK decoder depends on h , RSK decoding remains independent of channel conditions in the noisy mobile MC scenario.

B. OOK ML Decoder

For the OOK modulation, the optimal decoding region for bit 1 is given as

$$D(1) = \left\{ m : m > \frac{N_a h(t, \tau_s)}{\ln \frac{N_a h(t, \tau_s) + \lambda_N}{\lambda_N}} \right\}, \quad (3)$$

which depends on channel h . Since h is time-varying in mobile MC environment, the optimal threshold requires the exact knowledge of h . In scenarios where exact channel is unknown, we can utilize partial channel information.

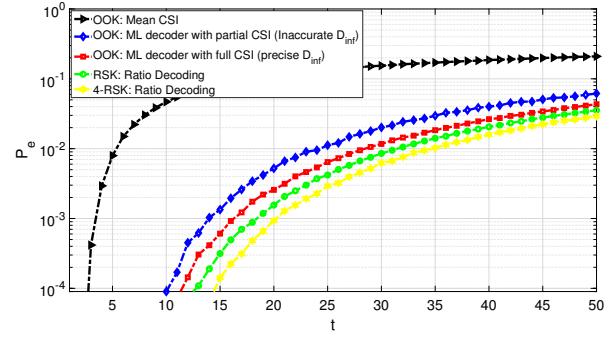


Fig. 1. The variation of the probability of error with time for a dynamic MC system employing OOK, symmetric BRSK, 4-RSK, using a passive Rx. System parameters follow those in [4], with $\rho_0 = 0$, $\rho_1 = 1$, $c = 2 \times 10^5$, $\lambda = 90$, $D_{TR} = 5 \times 10^{-12} \text{m}^2/\text{s}$, $D_{inf} = 5 \times 10^{-9} \text{m}^2/\text{s}$, and inaccurate $D_{inf} = 9 \times 10^{-8} \text{m}^2/\text{s}$.

III. NUMERICAL RESULTS

We conduct particle-based simulations under diffusion model in the noisy mobile MC setting. The performance of symmetric BRSK is compared against OOK under equal molecular budget and bit duration constraints. The results in Fig. 1 demonstrate that in the presence of noise, symmetric BRSK outperforms OOK when only partial (mean of channel) or full statistical channel information (probability distribution of channel) is available, whereas OOK suffers severe degradation. This highlights the inherent robustness of ratio-based encoding in the noisy dynamic MC environments. The higher-order RSK constellation, i.e., 4-RSK, demonstrates better performance than symmetric BRSK while maintaining channel-independent decoding and scalability.

IV. CONCLUSION

We presented the error performance analysis of the RSK modulation technique for noisy mobile MC scenario. It has been demonstrated that when using Poisson approximation, the ML decoder for symmetric RSK modulation becomes a ratio decoder which is independent of channel. The numerical findings show that RSK performs better than the conventional OOK scheme for dynamic MC scenarios when partial or complete statistical information of channel is known for OOK. Moreover, our results confirm that RSK especially in higher-dimensional forms like 4-RSK outperforms traditional methods such as OOK in both robustness and scalability. This positions the proposed scheme as a strong candidate for future MC systems operating under uncertainty.

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Spatiotemporal Modeling of Chemotactic cAMP Signaling by Secretion and Degradation

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Abstract—Chemotactic signaling between *Dictyostelium* cells (*Dictys*) relies on secretion, diffusion, and degradation of cyclic adenosine monophosphat (cAMP) molecules to enable collective cell responses. This process involves coupled intracellular signaling and extracellular regulation through enzymatic degradation of cAMP by secreted phosphodiesterase (PDE). To capture these interactions, we propose an agent-based modelling (ABM) approach consisting of an environment and agents. The environment takes into account the spatial stochastic dynamics such as diffusion and reaction for intercellular molecular communication (MC). The cells are modeled as autonomous agents governed by chemical reaction networks for cAMP synthesis and PDE production. Both types of molecules are secreted into the environment, where they are affected by diffusion and enzymatic degradation. A transmitter–receiver scenario involving two cells is investigated. Upon binding of extracellular cAMP secreted by the transmitter cell to receptors on the receiver cell, the receiver initiates cAMP synthesis and secretion, thereby elevating the extracellular cAMP level. The coupled amplification of cAMP by the receiver and its enzymatic degradation by PDE regulates signal persistence in the environment, enabling reliable detection of cAMP signal without uncontrolled accumulation of it. From an MC perspective, extracellular cAMP degradation by PDE functions analogously to a natural mechanism for limiting channel memory, thereby mitigating inter-symbol interference arising from residual signaling molecules.

I. INTRODUCTION

Chemotaxis is the directed movement of cells or organisms along chemical gradients and underlies many biological processes. In mammalian physiology, leukocytes rely on chemotactic signaling to detect and migrate toward pathogens, enabling rapid, immune responses [1]. In cell biology, the soil amoeba *Dictyostelium* cell (*Dicty*) serves as a prominent model organism for investigating chemotactic processes. *Dicty* shares key sensing and locomotion pathways with human immune cells that have been preserved through evolution, making it a valuable model for studying eukaryotic motility [2]. Importantly, *Dicty* exhibits social behavior and self-organization. Under nutrient deprivation, individual *Dictys* transition from solitary behavior to a collective state, coordinating chemotaxis to aggregate into multicellular structures.

Understanding how *Dicty* achieves collective coordination requires models that explicitly capture the underlying molecular mechanisms of extracellular communication, including cyclic adenosine monophosphat (cAMP) synthesis, secretion, diffusion, sensing, and regulated degradation. cAMP is a chemoattractant secreted by *Dictys* that serves as the extracellular signaling molecule through which cells influence each other's behavior. Once secreted, cAMP diffuses into the extracellular medium, forming chemical gradients that can be sensed by neighboring cells. In [3] intracellular cAMP synthesis and extracellular cAMP is represented by chemical reaction networks and it is shown that stochastic noise is

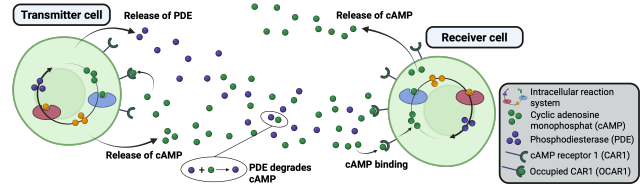


Fig. 1: Schematic illustration of two *Dicty* cells in chemotaxis.

important for robust simulation models. In [4], it was shown that extracellular cAMP concentration dynamics cannot be explained by cAMP production and diffusion alone. Considering extracellular cAMP degradation by phosphodiesterase (PDE) is important to reproduce observed signaling behavior. The authors incorporated experimentally observed cAMP-dependent PDE production regulatory mechanism in their model. This degradation reaction prevents accumulation of signaling molecules in the channel and receptor saturation. From an molecular communication (MC) perspective this observation can be interpreted as natural solution to limit channel memory and consequently reducing inter-symbol interference.

In this paper, we employ an agent-based modelling (ABM) approach to incorporate cellular interactions as agents located in a physical environment. Individual cells are modeled as agents where we combine the stochastic intracellular model, formulated in term of chemical reactions, with additional reaction pathways for cAMP-dependent PDE synthesis. Using the operator splitting method [5], we extend the model to a spatial domain in order to simulate extracellular molecules propagation in the environment.

II. SYSTEM MODEL

In this section, we introduce the proposed model to describe chemotaxis of *Dictys*. The proposed model combines stochastic intracellular reaction networks, segregation of chemical species, e.g., cAMP and PDE, extracellular diffusion, and enzymatic degradation processes in the environment. The model serves as a representation of chemotactic signaling and enables the investigation of signal transmission and amplification mechanisms in cellular systems. In this model, we assume a homogeneous spatial environment in which cells are represented as agents and located at specified positions. Each cell contains a localized intracellular reaction system that governs chemotactic signaling, including the detection of extracellular cAMP and the intracellular synthesis of cAMP based on the reaction network introduced in [3]. This intracellular reaction network is extended to include the production of PDE by translating the corresponding differential equations [4, Eqs. (3)-(4)] into chemical reactions. Both cAMP and PDE are subsequently secreted into the extracellular space and are hereafter referred to as extracellular cAMP and PDE,

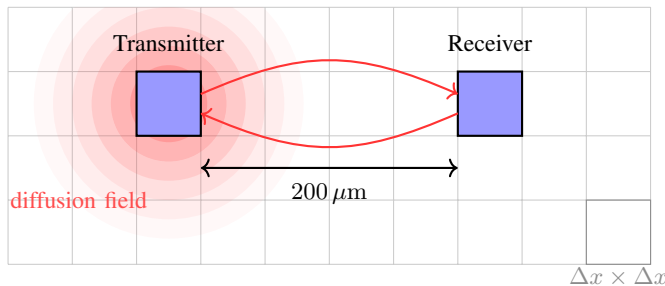


Fig. 2: Schematic illustration of the simulation setup. The two-dimensional domain is discretized into voxels of size Δx . Two cells occupy individual voxels and communicate via diffusible chemical signals (cAMP and PDE) in the extracellular space.

respectively. The extracellular cAMP and PDE diffuse in the environment, creating a chemical concentration field. The extracellular cAMP is degenerated by extracellular PDE with an enzymatic reaction (see Fig. 1).

III. SIMULATION

In this section, we give details about the simulation method, then specify the simulation scenario, and discuss the simulation results. To compute the temporal evolution the space is discretized and the coupled reaction–diffusion system is computed using an operator splitting scheme [5]. In this scheme, the simulation steps are decomposed into two sub-steps, both evaluated over the same fixed time interval Δt . First, the stochastic transfer of molecules between neighboring voxels is modeled as a multimodal binomial process [5]. Second, reactions within the agents and the environment are updated independently in each voxel using a stochastic simulation algorithm.

We consider a minimal multicellular signaling space consisting of two spatially separated cells embedded in a shared extracellular medium. The cells are positioned at a center-to-center distance of $200\ \mu\text{m}$ and the system is simulated for 4000 s. The simulation setup is shown in Fig. 2. In this scenario, one cell acts as a *transmitter*, while the other functions as a *receiver*. In the voxel containing the transmitter cell, an initial amount of extracellular cAMP is present. The initial values of the species in each agent are taken from [3]. Figure 3 (top) shows the number of species (i.e., extracellular cAMP and PDE, and occupied cAMP receptor 1 (OCAR1)) in the voxel corresponding to the transmitter. Due to diffusion and degradation of cAMP by PDE, the extracellular cAMP concentration initially slightly decreases. The high number of initial OCAR1 arises from the initial values from [3] and the sharp drop of OCAR1 in the beginning is due to system dynamic in terms of rate of freeing occupied receptors. However, after the immediate drop we observe a slow upward transition of OCAR1 which demonstrates the existing feedforward mechanism of the cell. In particular, upon availability of the external cAMP around the cell the number of OCAR1 increases. Figure 3 (bottom) shows the number of species in the voxel corresponding to the receiver. The initial values of the intracellular species in the receiver cell are chosen such that no cAMP is synthesized in the absence of extracellular cAMP. An increase of both

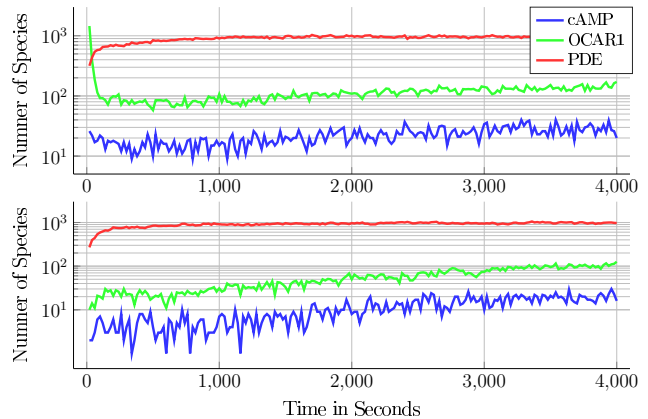


Fig. 3: Number of extracellular cAMP and PDE, and OCAR1 in voxels associated with the transmitter (top) and receiver (bottom) cells.

cAMP and OCAR1 can be observed over time. This behavior indicates that extracellular cAMP released by the transmitter cell reaches the receiver cell via diffusion and subsequently triggers intracellular cAMP synthesis. In both cells, PDE is continuously synthesized but exhibits comparatively slow dynamics compared to cAMP. Consequently, its concentration remains approximately constant over most of the simulation time, apart from an initial transient phase before a stable steady state is established.

IV. CONCLUSION

In this work, we present an agent-based cellular model that couples stochastic intracellular reaction networks to a spatially extracellular signaling field using ABM and the operator splitting method. By extending existing reaction based models to include the PDE as an explicit extracellular enzymatic reaction with cAMP, we obtain a more realistic representation of external cAMP signal regulation. Within this model, we demonstrate that a cell is able to detect and respond to a cAMP wave emitted by another cell. Future research will build upon this model by adjusting reaction rates to enable signal oscillation as a back and forth exchange of cAMP between the two cells and investigating the impact of PDE on inter-symbol interference. Furthermore, we will investigate the impact of PDE through the lens of information theory, i.e., how the channel capacity is affected by the presence of the PDE.

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

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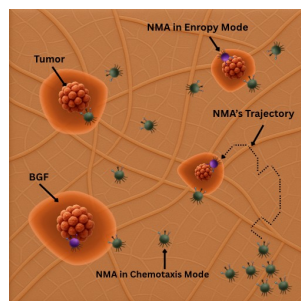
Abstract—Targeted Drug Delivery (TDD) is a promising approach to improve cancer treatment. However, TDD suffers from a lack of spatial selectivity and suboptimal outcomes. In this paper, we explore the idea of applying the hybrid entropy-driven transport mechanism for a nanoscale medical agent (NMA) 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

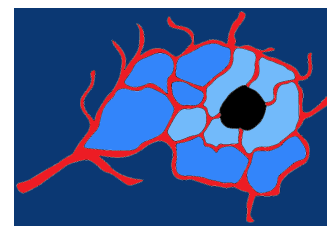
I. INTRODUCTION

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

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(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).

learning frameworks further highlight a broader trend toward integrating computation, communication theory, and AI with biological information processing [5].

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

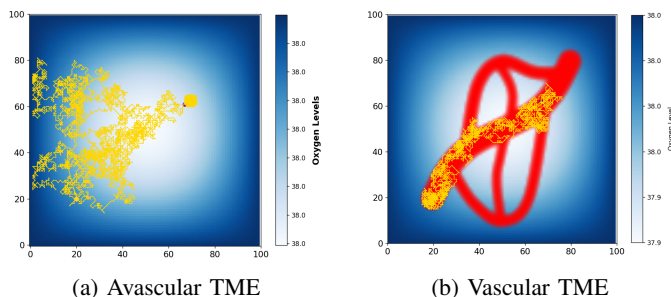


Fig. 2: Comparison of the NMA's tumor detection within the avascular and vascular TMEs.

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 $100 \mu\text{m}$. 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

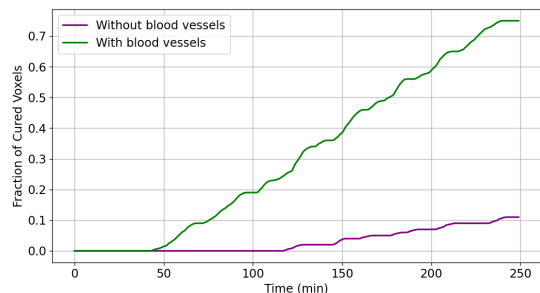


Fig. 3: Mean fraction of cancerous voxels over time compared in avascular (without blood vessels) and vascular (with blood vessels) TMEs.

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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On the Feasibility of a Plant-based Air Quality System Modeled via Molecular Communication for Green Smart Homes

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Abstract—Indoor air quality in urban homes is influenced by multiple airborne pollutants, including volatile organic compounds (VOCs), carbon dioxide (CO₂), and fine particulate matter (PM) originating from indoor activities and outdoor sources such as vehicular traffic. Although mechanical air filtration systems are effective, they are energy-intensive and offer limited spatial awareness of pollutant dynamics. In this paper, we explore the feasibility of a plant-based indoor-outdoor air quality system modeled through the lens of molecular communication (MC). Pollutants are abstracted as information-carrying molecular species, plants as spatially distributed receivers with absorption and sensing capabilities, and residential spaces as bounded diffusion-dominated channels. This abstraction enables the reuse of MC models to reason about pollutant propagation, assess the feasibility of plant placement, and explore early-stage design trade-offs. Unlike large-scale urban or industrial environments, residential settings operate in confined geometries where diffusion-driven modeling is more applicable, making them well-suited for MC-inspired analysis. Rather than optimizing plant species or placement, this work positions MC as a unifying framework to evaluate feasibility and identify open challenges toward greener, bio-integrated smart home environments.

Index Terms—Molecular Communication, Plant Network, Air filtering, Urban Pollution, Ideation

I. INTRODUCTION

Air pollution has become a persistent reality in major cities worldwide, with urban residents routinely exposed to elevated levels of particulate matter, volatile organic compounds (VOCs), and carbon dioxide (CO₂) both outside and inside their homes. In addition, indoor air quality is increasingly affected by everyday human activities, such as cooking, cleaning, and respiration. Although mechanical ventilation and filtration systems can mitigate these effects, they are energy-intensive and provide limited spatial awareness of pollutant distribution within residential spaces [1]. In recent times, increasing emphasis on sustainable and energy-efficient living has renewed interest in bio-integrated solutions for environmental monitoring and mitigation. Indoor and balcony plants are known to passively absorb airborne pollutants, contribute to thermal regulation, and improve indoor comfort [2]. Beyond filtration, plants have the potential to act as environmental

biosensors. However, the use of plants for air quality management remains largely heuristic, with limited frameworks to assess feasibility or guide spatial deployment [2].

Molecular communication (MC) provides a natural abstraction for modeling biological systems [3]. In MC, information is conveyed through molecules propagating within a medium, a paradigm that maps directly to indoor air quality scenarios where pollutants act as molecular species carrying information, residential spaces form bounded diffusion channels, and plants behave as distributed receivers with absorption and sensing capabilities [4]. Residential environments are characterized by confined geometries and limited spatial extents, making diffusion-based modeling assumptions particularly suitable.

In this paper, we assess the feasibility of a plant-based indoor air quality system using MC as our analytical lens. Instead of delivering an optimized design, we present MC as a unified modeling framework to analyze pollutant dynamics, plant deployment, design trade-offs, and to highlight open challenges on the path to greener smart homes.

II. MC-BASED SYSTEM MODEL AND CONSIDERATIONS

We model the residential environment as a bounded indoor space in which airborne pollutants propagate over short spatial scales characterized by a mixed diffusion–advection mechanism: diffusion dominates in most regions and enclosed rooms, while weak advection arises from ventilation, thermal gradients, and human activity. Within an MC abstraction, pollutant emissions are treated as molecular signals released by multiple transmitters, the indoor space forms the communication channel, and plants act as spatially distributed receivers as seen in Fig. 1. Plants absorb and respond to these molecules according to species specific biological properties, which can be mapped to receiver parameters such as absorption efficiency, saturation behavior, and operational lifetime. Plant survivability and response to pollutants can be partially characterized through indices such as the Air Pollution Tolerance Index (APTI) [5].

Beyond pollutant-to-plant interactions, the framework also accommodates plant-to-plant MC. Plants are known to exchange chemical signals through airborne volatiles and other

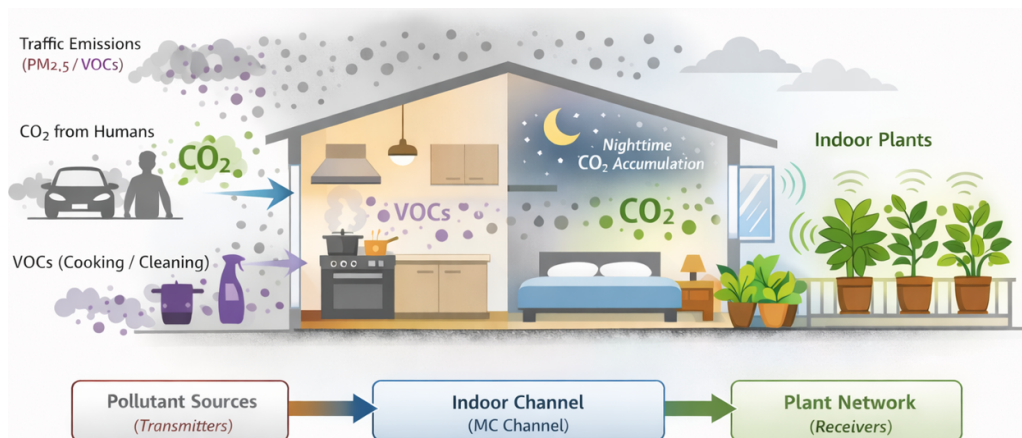


Fig. 1. Overview of a plant-based indoor air quality system modeled as a MC framework.

mechanisms, particularly under stress conditions. In an MC context, this interaction can be interpreted as secondary molecular signaling between receivers, enabling indirect information exchange across the plant network. Such interactions introduce cooperative and interference effects, where the response of one plant may influence neighboring plants, effectively forming a distributed sensing and signaling network.

From a network perspective, the system naturally maps to multi-input multi-output (MIMO) MC scenarios, with multiple pollutant sources interacting with a heterogeneous plant network and with inter-receiver signaling. Established MC models can be used to analyze how receiver density, spatial placement, and inter-plant coupling affect system behavior. Furthermore, information theoretic metrics commonly used in MC, such as received molecule count or mutual information, can be repurposed to evaluate placement strategies in terms of coverage, sensitivity, and robustness.

In terms of methodology, we plan to implement a hybrid COMSOL–Python workflow. COMSOL Multiphysics is used to model the indoor environment as a bounded transport domain with diffusion–advection dynamics for the concentration of particles. The resulting concentration time series will be transferred to Python, where each plant will be modeled as a heterogeneous transceiver with species-specific parameters derived from descriptors such as leaf area and APTI. Python will also be used to represent plant-to-plant signaling, evaluate cumulative stress and purification performance, and compute network-level metrics such as coverage, detection reliability, and mutual information for preliminary placement analysis.

This approach demonstrates that MC provides a coherent framework not only to model pollutant propagation but also to analyze cooperative behavior within plant networks, thus supporting early-stage feasibility assessment and guiding future optimization efforts.

III. OPEN CHALLENGES AND RESEARCH DIRECTION

Although the proposed framework demonstrates the feasibility of modeling plant-based indoor air quality systems using MC, there remain open challenges that motivate future research.

- Plant modeling and biological variability: Indices such as the APTI provide a useful abstraction, but long-term effects including saturation, adaptation, and others require detailed bio-physical models and experimental validation.
- Transport regime transitions: Use of hybrid diffusion–advection models and stochastic airflow effects to improve realism while maintaining analytical tractability.
- Plant-to-plant MC: While the framework allows for inter-plant signaling, the strength, range, and reliability of airborne plant-to-plant communication in indoor environments remain largely unexplored. Characterizing these interactions is essential for understanding network behavior.
- Network-level optimization: Optimizing device placement in realistic homes involves balancing multiple objectives, including pollutant removal, sensing performance, durability, and others. Information theoretic measures from MC can provide a principled basis for capturing these trade-offs tailored to each scenario.
- Experimental validation and hybrid systems: Future work should prioritize validating MC-based models in controlled indoor testbeds and investigating systems that integrate plant signals with low cost sensors. These improve reliability and speed up the adoption of MC inspired design principles in real-world smart home applications.

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Modeling Electric-Field Induced Modulation of Ligand-Receptor Binding Kinetics Towards Adaptive MC Receivers

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Abstract—We present a first-principles model for electric-field-controlled DNA hybridization on biosensor surfaces based on Scheutjens-Fleer self-consistent field (SF-SCF) theory. The model derives voltage-dependent probe layer structure by solving the Edwards diffusion equation coupled with Poisson-Boltzmann electrostatics iteratively until self-consistency. Hybridization kinetics are computed via the Halperin-Buhot-Zhulina framework augmented with electrophoretic contributions. We introduce a mechanistic asymmetry wherein association is treated as nucleation-limited, while dissociation is governed by the field-dependent stability of the full duplex. The model predicts sharp transitions between hybridizing and non-hybridizing regimes, offering a theoretical foundation for adaptive MC receivers.

Index Terms—DNA hybridization, self-consistent field theory, polyelectrolyte brushes, biosensors, molecular communications

I. INTRODUCTION

Molecular communication (MC) systems encode information in signaling molecules, but a fundamental challenge lies in the fixed kinetic parameters of ligand-receptor interactions at the receiver [1]. Unlike electronic receivers with tunable gain, passive MC receivers cannot dynamically adjust their binding characteristics. This limitation manifests critically as inter-symbol interference (ISI), where molecules from previous transmissions persist at the receiver, preventing subsequent symbol detection.

Adaptive receivers with dynamically reconfigurable binding kinetics offer a solution to ISI [2], with modulation mechanisms including thermal [3], photoresponsive [4], magnetic [5], and electric field approaches. Electric field modulation is particularly suited to MC: it offers fast switching, requires no reagents, and integrates with microelectronic fabrication. Experiments confirm that applied fields modulate hybridization rates by orders of magnitude, with high-density probes exhibiting sharp transitions between hybridizing and non-hybridizing regimes [6], [7]. However, existing treatments address equilibrium thermodynamics and electrostatic barriers without deriving brush conformation self-consistently with applied voltage.

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We present the first theoretical framework that couples voltage-dependent brush structure with hybridization kinetics, integrating the SF-SCF theory [8] with the Halperin-Buhot-Zhulina framework [9] and electrophoretic contributions [7] for adaptive MC receiver design.

II. MODEL FORMULATION

A. SF-SCF Theory for Polyelectrolyte Brushes

We consider ssDNA probes of N nucleotides at areal density σ_P on an electrode. Following [8], polymer volume fraction $\phi(z)$ and reduced potential $\psi(z) \equiv e\Phi/(k_B T)$ are solved self-consistently on a lattice with spacing $a \approx 0.43$ nm. The brush height H is derived as the first moment of $\phi(z)$ (computed from Edwards diffusion equation), which is coupled to the $\psi(z)$ through the Poisson-Boltzmann equation:

$$\frac{d^2\psi}{dz^2} = \kappa^2 \sinh \psi + 4\pi\ell_B\alpha\phi(z)/a^3, \quad (1)$$

where $\kappa = \sqrt{8\pi\ell_B c_s}$ is the inverse Debye length, c_s the bulk salt concentration, $\ell_B \approx 0.7$ nm the Bjerrum length, $k_B T$ the thermal energy, and α the ionization fraction (negative for DNA). The mean field is:

$$u(z)/k_B T = \chi_{PS}\phi(z) + \frac{1}{2}\phi^2(z) - \alpha\psi(z), \quad (2)$$

with Flory-Huggins parameter $\chi_{PS} = 0$ for good solvent. The dimensionless surface charge ratio

$$\gamma = \sigma_{\text{surface}}/(\alpha N \sigma_P), \quad (3)$$

represents electrode charge relative to brush charge. For anionic DNA ($\alpha < 0$), $\gamma < 0$ corresponds to an attractive (collapsing) field and $\gamma > 0$ to a repulsive (stretching) field.

B. Hybridization Kinetics

The kinetic landscape is governed by two competing energy contributions [7], [9]: the electrophoretic work ΔG_{ep} , which becomes favorable as the surface potential $\psi(0)$ increases, and the electrostatic brush penalty, which scales inversely with H [9], with $r_D = \kappa^{-1}$ the Debye screening length:

$$\Gamma = 8\pi N \sigma_P \ell_B r_D^2 / H. \quad (4)$$

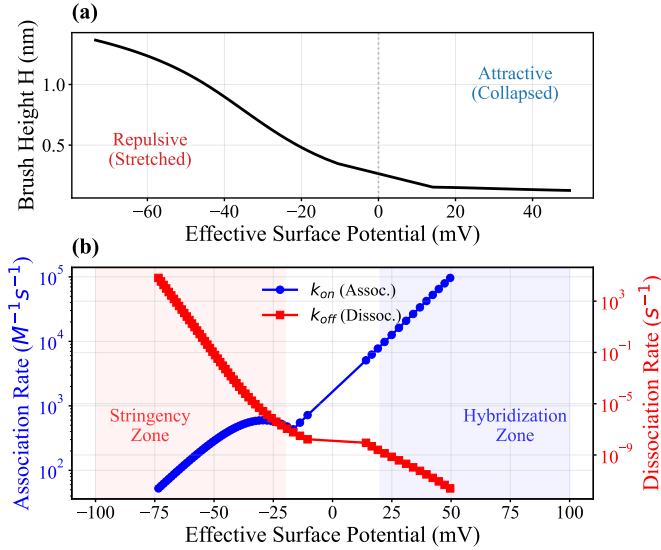


Fig. 1. (a) Brush height vs. surface potential showing conformational change. (b) Voltage-controlled k_{on} and k_{off} ; the single crossover separates the Hybridization and Stringency regimes.

This creates a contradiction: attractive bias lowers ΔG_{ep} but simultaneously collapses the brush, sharply increasing Γ . The total brush penalty also includes a steric contribution:

$$\Delta G_{\text{steric}}/k_B T = N_t \left[\left(\frac{1}{2} - \chi_{PS} \right) \bar{\phi}^2 + \frac{1}{3} \bar{\phi}^3 \right], \quad (5)$$

where N_t is the target strand length and $\bar{\phi} = N \sigma_P a^3 / H$ the average volume fraction.

We model association as a *nucleation-limited* process [10], requiring only a seed of $N_{\text{nuc}} \approx 4$ monomers to penetrate the brush. The effective association rate thus becomes:

$$k_{\text{on}} = k_{\text{react}} \exp \left[-\frac{N_{\text{nuc}}}{N} (\Gamma + \Delta G_{\text{steric}} + \Delta G_{\text{ep}}) / k_B T \right], \quad (6)$$

with an intrinsic rate $k_{\text{react}} \sim 10^5 \text{ M}^{-1} \text{ s}^{-1}$.

Dissociation is governed by the stability of the full helix under load. We apply the Bell–Evans model [11] using the effective charge of the entire target strand (N_t) driven by the local field $E = -d\psi/dz$ [7], such that the off-rate is given by $k_{\text{off}} = k_0 \exp(Fx_\beta/k_B T)$, where $k_0 \sim 4 \times 10^{-4} \text{ s}^{-1}$ represents the thermal breathing of the duplex, and $x_\beta \approx 0.7 \text{ nm}$ is the transition-state distance.

III. RESULTS AND DISCUSSION

Figure 1 shows results for 20-mer ssDNA at $I \approx 0.1 \text{ M}$ and $\sigma_P = 3 \times 10^{12} \text{ cm}^{-2}$. Panel (a) demonstrates conformational response: the brush extends to $\sim 1.4 \text{ nm}$ under repulsive bias ($\psi(0) < 0$) and collapses below 0.2 nm under attractive bias. The gap between -12 mV and $+20 \text{ mV}$ corresponds to a first-order-like phase transition where stretched and collapsed conformations coexist as two free energy minima of comparable depth, preventing the self-consistent solver from settling on either state. Below $H \approx 0.43 \text{ nm}$ (monomer size), the continuum model breaks down, indicating a pancake regime where DNA lies flat on the electrode.

Panel (b) shows the crossover of the k_{on} and k_{off} curves, outlining two distinct operating regimes. In the *Hybridization Zone*, k_{on} approaches the diffusion limit ($\sim 10^5 \text{ M}^{-1} \text{ s}^{-1}$) while dissociation is negligible ($< 10^{-10} \text{ s}^{-1}$). In the *Stringency Zone*, the dissociation rate increases to $\sim 10^5 \text{ s}^{-1}$, enabling rapid clearing of bound targets.

This dual-regime kinetic landscape enables adaptive MC receiver operation. The orders-of-magnitude separation between k_{on} and k_{off} in each regime ensures high contrast between capture and reset states, allowing the receiver to switch between them via applied voltage. This directly targets the key performance bottlenecks in MC systems: reducing ISI and bit error rate (BER), preventing receptor saturation, and improving signal-to-interference-plus-noise ratio (SINR) relative to passive receivers with fixed binding kinetics.

IV. CONCLUSION

We presented an SF-SCF framework for voltage-controlled DNA hybridization that predicts sharp kinetic transitions consistent with experimental observations at high grafting density. The resulting dual-regime kinetic landscape provides a theoretical basis for adaptive MC receivers that mitigate ISI by alternating between capture and reset modes under time-varying channel conditions, such as varying flow rates, bit rates, or background interference. Future work will integrate this model with MC channel models for end-to-end BER analysis and validate the brush response through particle-based simulations and experimental characterization.

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Intrinsic MIMO Particle Communication Channel with Random Advection

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I. INTRODUCTION

MOLECULAR communication (MC) has emerged as a promising paradigm for information exchange in environments where conventional electromagnetic communication is infeasible, such as biological systems and microfluidic platforms. Early studies in MC predominantly focused on diffusion-driven channels, where molecular propagation is isotropic and inherently slow. Advection has been mostly discussed as a means of increasing the speed of propagation and reducing the channel memory [1], and as a constant property of the channel [2], [3]. However, random advection with a strong mean direction can preserve pulse ordering, making advection-dominated MC particularly attractive for pulse-based modulation schemes, where information is conveyed through the timing, shape, or orthogonality of released molecular pulses [4]. It is demonstrated that under directed advection, the spatial dispersion induced by random transverse flow results in multiple distinct receiver observations of the same transmitted pulse. This perspective motivates an interpretation of MC as an intrinsically MIMO system, where diversity arises naturally from spatial sampling of the particle cloud rather than from multiple transmitters or molecule types. The purpose of this study is to provide a structured framework for understanding how receiver diversity can be exploited in pulse-based molecular communication under random advection. Several receiver combining strategies are evaluated, and their impact on symbol error rate (SER) is studied through Monte Carlo simulations. Results demonstrate that multi-receiver diversity can improve detection performance, especially in low-to-moderate signal-to-noise ratio (SNR) regimes, even when individual receiver observations are highly noisy.

II. SYSTEM MODEL

The molecules released from one transmitter can correspond to many different channels if there are properly located receivers. Unlike the conventional communication topologies, in MC, signals are always nonnegative, and there are no phase-coherence problems. This means that every molecule can correspond to a different channel when there is a receiver to read it. This naturally leads to the interpretation of molecular communication as an *intrinsically MIMO* system.

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Complex modulation schemes can be implemented using orthogonal pulses in flows dominated by advection to transform the incoming bit sequence into a symbol sequence [4]. For this purpose, the symbol duration is partitioned into N non-overlapping subintervals, each associated with one rectangular pulse that is active only within its assigned subinterval. These pulses are mutually orthogonal in time and span an N -dimensional signal space. Information is conveyed by selecting one of M discrete amplitude levels independently along each dimension, resulting in a constellation of M^N possible symbols. With this setup, high cardinality modulations can be studied to observe the benefits of the multi-receiver system easily. In [4], an analytical solution is provided for the channel impulse response for a particle-based communication under time-varying advection. The same model is used in this article. Multiple receivers are placed at the same x position with Δy separation in their y positions as shown in Fig. 1. The stochastic behaviour of the x component of the flow velocity can cause consecutive pulses to mix with each other, resulting in severe intersymbol interference (ISI). On the other hand, random characteristics of the y component of the flow velocity reduce the signal power a receiver can get without causing any ISI. However, it can still change the shape of the pulses and distort the structure of the constellation, causing errors. Rx_1 in Fig. 1 is labeled the main receiver since the mean flow carries molecules to this receiver. The receivers are assumed to be fully time-synchronized, and the clock of the main receiver is used. Each receiver works as explained in [4]. After each receiver applies sampling with the symbol period, the results are sent to the combiner, where diversity combining techniques are applied. The output of the combiner goes to the estimation-detection block. Here, receivers use automatic gain control (AGC) for correct scaling, and then decisions are made. Different diversity combining techniques are implemented. Selection Combining (SC): Corresponds to directly choosing the main receiver. This is included for comparison purposes. Equal Gain Combining (EGC): Each receiver output is added together using the same normalized weights. Distribution Gain Combining (DGC): Using the y coordinate of each receiver, The distribution value of the y component of the flow velocity is calculated. These are normalized and used as weights. Pilot Energy Gain Combining (PGC): Pilot energies for each receiver are calculated and normalized and used as weights in the weighted sum.

III. SIMULATION RESULTS

The simulations were performed in MATLAB R2023b. The symbol duration is set to $T_{\text{sym}} = 2$ s. The diffusion–advection

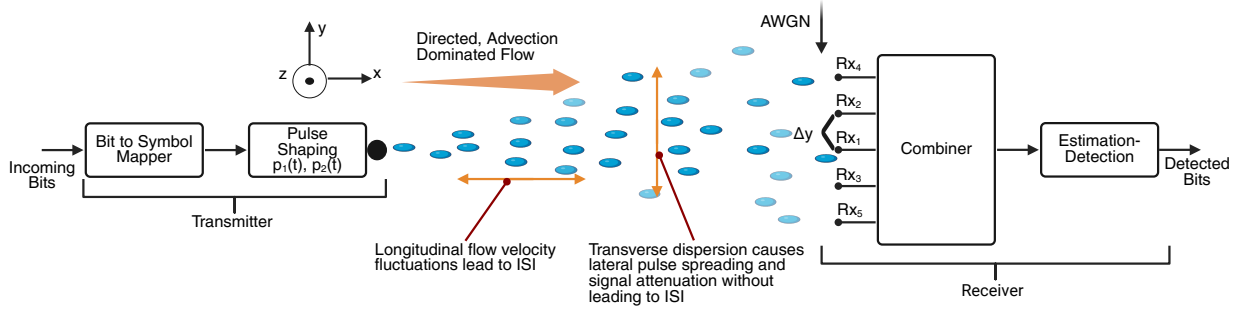


Fig. 1: Block diagram of the proposed end-to-end molecular communication framework under directed advection, illustrating symbol generation and pulse emission at the transmitter, particle transport, and multi-receiver combining and detection at the receiver side. [5].

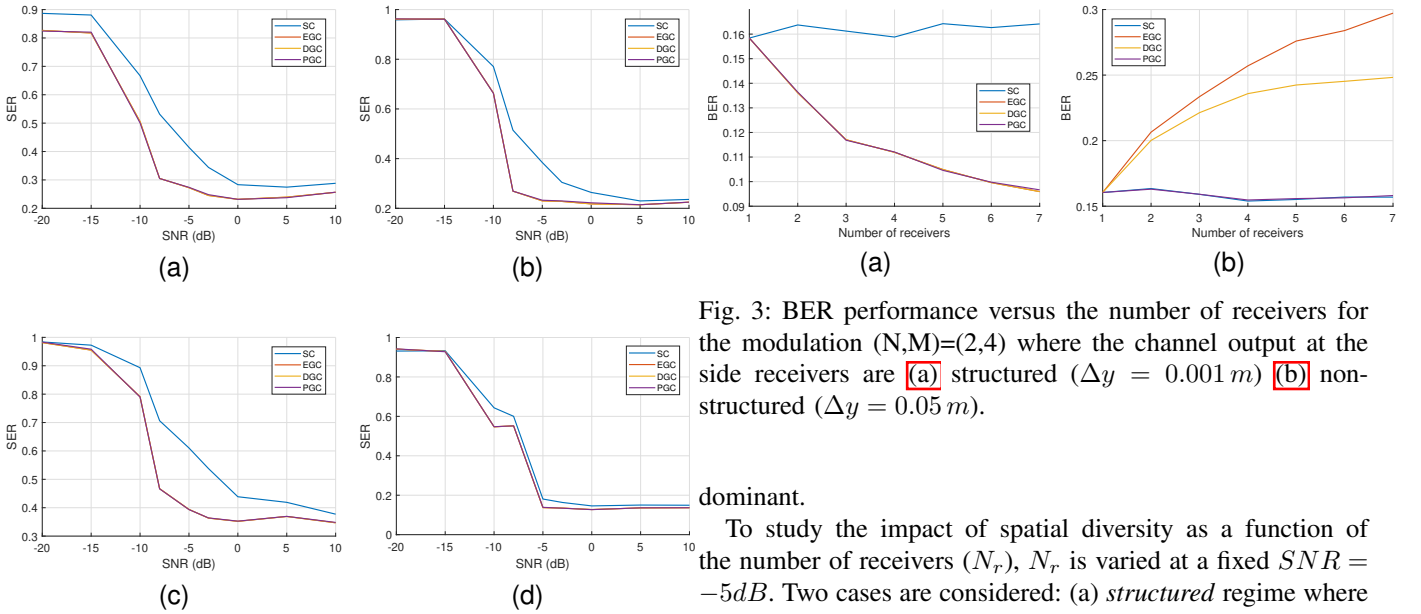


Fig. 2: SER performance versus SNR of the considered combining schemes for modulations (a) $(N,M)=(2,4)$, (b) $(N,M)=(3,3)$, (c) $(N,M)=(3,4)$ and (d) $(N,M)=(4,2)$.

channel is simulated with a sampling rate of $f_{sim} = 1000$ Hz, while the receiver processes the signal at a rate of $f_{rx} = 100$ Hz. The physical channel is characterized by a diffusion coefficient $D = 6.7698 \times 10^{-6} \text{ m}^2/\text{s}$. Advection in the longitudinal direction follows a Gaussian model with mean velocity $\mu_{v_x} = 0.5 \text{ m/s}$ and standard deviation $\sigma_{v_x} = 10^{-3} \text{ m/s}$, while the transverse component has mean $\mu_{v_y} = 0$ and standard deviation $\sigma_{v_y} = 0.1 \text{ m/s}$. The transmitter is positioned at $(0, 0, 1) \text{ m}$ and the main receiver is located at $(1, 0, 1) \text{ m}$. 4 side receivers are positioned at $y = \pm 0.001 \text{ m}, \pm 0.002 \text{ m}$. Diversity combining methods are applied to different modulation schemes for different SNR regimes, and SER is calculated. The resulting plot is given in Fig. 2. In general, SC exhibits the highest error rates across the entire SNR range. In contrast, multi-receiver combining significantly improves performance, particularly in the low-to-moderate SNR regime. The gains diminish at higher SNR values, where noise becomes less

Fig. 3: BER performance versus the number of receivers for the modulation $(N,M)=(2,4)$ where the channel output at the side receivers are (a) structured ($\Delta y = 0.001 \text{ m}$) (b) non-structured ($\Delta y = 0.05 \text{ m}$).

dominant.

To study the impact of spatial diversity as a function of the number of receivers (N_r), N_r is varied at a fixed $SNR = -5 \text{ dB}$. Two cases are considered: (a) *structured* regime where all receivers observe structured signals, and (b) *non-structured* regime where some receivers observe severely attenuated or truncated signals. As shown in Fig. 3(a), increasing N_r in the structured regime yields a clear BER improvement, confirming the presence of diversity gain. In contrast, Fig. 3(b) shows that in the non-structured regime, adding receivers can degrade performance, since unstructured observations contribute noise without useful signal energy. However, PGC can overcome this problem by assigning small weights to them.

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Therapeutic Nanonetworks for Brain Tumors Enabled by Cell-Based Nanobiodevice Interfaces

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Abstract— The evolution of Glioblastoma Multiforme (GBM) is defined by the dynamics of distinct cell sub-populations growing bionanomachine networks in an interplay between “senders” or “transceivers” and “receivers”. Central to this process are the inter-communications between sub-cellular bionanomachines secreted by GBM cells in the form of exosomes. Herein we present a dynamic therapeutic nanonetwork of genetically engineered and radiofrequency-responsive active bionanomachines where neural stem cells and exosome cargo therapeutic nucleic acids serve as externally controllable transducer bionanomachines. Interfaces derived from the intercoupling of optically active bionanomachines in co-cultures of tumor cells and therapeutic exosomes exposed to rationally designed RF generators provided a pioneering *inmessaging* interface for external control of molecular nanonetworks.

Keywords— Molecular Communication, bionanomachine interfaces, external control, Glioblastoma Multiforme, radiofrequency-sensitive genes

I. INTRODUCTION

Molecular Communications (MC) has emerged as a radically new communication paradigm, where *sender* and *receiver* bionanomachines comprised of healthy and diseased cells, genetically engineered cells, exosomes or extracellular vesicles and their macromolecular cargos, communicate propagating chemical signals or molecules, serve to delineate complex diseases by deciphering underlying cellular and sub-cellular processes enabling diagnostic and therapeutic interventions controlled externally [1]. The basic idea of externally controllable MC (ECMC) is to introduce external interfaces into MC in order to interconnect the MC environment (e.g., inside the human body) and the environment external to the MC environment. External interfaces allow conventional devices, such as radiofrequency (RF) sources, serving as *actuators* in the external environment intercoupled to bioinspired bionanodevices, such as implantable biosensors and modular constructs of genetically engineered cells serving as *transducers* to monitor and control MC processes. In this context, ECMC can be engineered to have two types of interfaces: bionanomachine to bionanomachine (BNIs), *inmessaging* (IMIs) and *outmessaging* (OMIs) interfaces, driven by external actuators and implantable biosensors, respectively.

Glioblastoma Multiforme (GBM), the most malignant human tumor, is evolving as a system of cellular bionanomachine networks within an interplay between mutually exclusive cell phenotypes [2]. In the conceptual framework of MC, dynamic processes underlying GBM evolution, progression and recurrence define distinct, albeit interactive prototype networks [3]. Consequently, these processes define the dynamics of growing bionanomachine networks [2] in an interplay between “senders” or “transceivers” and “receivers”, giving rise to recurrent tumor or foci of invasion. Central to this process are the inter-communications and inter-dependencies between subcellular bionanomachines secreted by either cell population in the form of nanosized nano-sized (30–200 nm) vesicles, collectively described as exosomes [1]. Exosome propagation across tissues tissue-mimicking models are supporting promising significant advancements in the MC field and channel models in particular. Herein we present evidence supporting that GBM models intercoupled to simulate RF systems serve as prototype dynamic live test-beds of ECMC. Rationally engineered and tumor-homing neural stem cells (NSCs) release tumor reprogramming EX with therapeutic microRNA (miRNA) cargoes, in response to radiofrequency signals

II. ELECTROMECHANICAL ACTUATORS AND GENETICALLY ENGINEERED TRANSDUCERS IN THE GLIOBLASTOMA MULTIFORME LANDSCAPE

A. RF-Responsive Nucleic Acids as Externally Controllable Transducer Bionanomachines

In the light of the flurry of therapeutic miRNAs against GBM and their high promise to serve as genetic therapy delivered by exosomes, miRNA34a, shown to exhibit potent multifaceted anti-tumor mechanisms [4] has been employed for efficient reprogramming. The miRNA34a gene plasmid has been intercoupled to mKate2, a fluorescent protein that forms effective pairs of Fluorescence Resonance Energy Transfer (FRET) with both eGFP and tdTomato, two extensively studied fluorescent proteins, through the promoter of Egr-1, an RF-responsive gene induced by the modulated RF radiation field of 900 MHz, at an average SAR value of 1W/ kg [5]. The miRNA34a-Erg1-mKate2 gene

system was delivered to induced neural stem cells (iNSCs) by electroporation. For comprehensive RF stimulation under tissue culture conditions a set up achieving multiple optimized Specific Absorption Rate (SAR) was developed (Fig.1A). SAR value distribution was simulated for a 12-well plate and adjusted for the indicated culture media. Such a set up avoids any resonating modes by using RF absorbers placed around the antenna and the well-plates, enabling a wide range of frequencies.

To assess the specificity of the RF-mediated effect compared to heat induction by electromagnetic waves, miRNA34a-ERG-1-mKate2 - NSC cultures were subjected to RF induction (900MHz, 30min, 10W). Brightfield and fluorescence imaging was performed and temperature was recorded at 8h and subsequently at 12h intervals. mKate2 fluorescence under either RF or heat exposure was differentially quantified in a cell growth independent manner. Fluorescent images were processed with MATLAB and thresholded fluorescence intensity was contrasted to the cell covered area disclosing (i) significant increase of fluorescence at 32hrs for both heat and RF exposure, (ii) faster significant increase (20 hrs) after heat treatment that subsequently declined and (iii) a more sustained increase in fluorescence (20 to 56 hrs) with RF exposure (Fig.1B). To assess the effect of fractionated RF exposure on efficacy, cell cultures were grown and imaged to measure the amplitude and duration of the therapeutic “output” as a function of RF frequency, intensity, duration and repetition period. Data analysis yielded: (i) Decreased fluorescence per cell area for control and significantly increased for the irradiated cells. (ii) No statistically significant difference between 1 exposure (30 mins at 0 hrs) and 3 exposures (30 mins at 0, 12, 24 hours), documenting a sustainable RF-sensitive gene activation, further supported by a notable increase at 20h and 56h independent of cell proliferation.

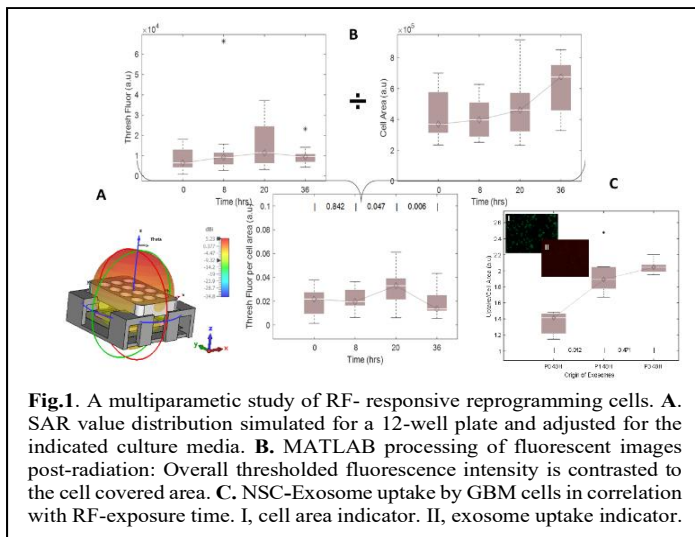


Fig.1. A multiparametric study of RF- responsive reprogramming cells. **A.** SAR value distribution simulated for a 12-well plate and adjusted for the indicated culture media. **B.** MATLAB processing of fluorescent images post-radiation: Overall thresholded fluorescence intensity is contrasted to the cell covered area. **C.** NSC-Exosome uptake by GBM cells in correlation with RF-exposure time. I, cell area indicator. II, exosome uptake indicator.

B. Bionanomachine Interfaces in Cell and Exosome Therapeutic Nanonetworks

The required communication paradigm defined by the interaction between NSC-derived reprogramming EX and target U87-MG GBM cells via dynamic transfer of energies of excited state fluorescent bionanomachine in resonance has

been demonstrated [6]. This was supported by the rational design and implementation of active bionanomachine-to-bionanomachine interfaces. Two- and three-dimensional co-culture set-ups further enabled molecular and mechanistic analysis of the therapeutic effectiveness of exosomes with miRNA cargoes, coupled to RF systems realizing *inmessaging* interfaces. The response of tumor reprogramming-NSCs to RF and release of exosomes under multiparametric exposures has been assessed with quantification of (i) the therapeutic efficacy of RF-mediated miRNA34a exosomes released in conditioned culture media of the U87-MG GBM cells, and, (ii) the uptake of NSC-released exosomes by U87-MG cell-area in correlation with RF-exposure time (Fig.1C). Statistically significant anti-proliferative effect was disclosed in a standard colorimetric assay and exosome uptake per cell area correlated significantly with the RF exposure time. The impact of RF on reprogramming was further documented by coupling co-cultures of reprogramming iNSC organoids and cancer constructs with customized RF sources. Collectively, these data introduce pioneering *inmessaging* interface systems for regulated external control of molecular nanonetworks.

III. CONCLUSIONS

The versatility, multipotency and high specificity of miRNA therapy has been intercoupled with the safety, robustness, transmigration and tumor-homing potential of iNSCs, combined in a system for both localized and systemic delivery, integrating distinct communication channels. The correlation between intensity and duration of radiofrequency *inmessaging* signals in (hyper)fractionated pulses with the viability of tumor cells was verified as well as the correlation of tumor cell viability with the ensuing optical signals of the released exosomes, comprising the *outmessaging* signals. Both findings introduce an *in vitro Proof-of-Concept* for an Externally Controllable Molecular Nano-Communication system with high clinical relevance for GBM management.

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Neural-Inspired Multi-Agent Molecular Communication Networks for Collective Intelligence

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Abstract—Molecular Communication (MC) is a pivotal enabler for the Internet of Bio-Nano Things (IoBNT). However, current research often relies on highly capable individual agents with complex transceiver architectures that defy the energy and processing constraints of realistic nanomachines. This paper proposes a paradigm shift towards collective intelligence, inspired by the cortical networks of the biological brain. We introduce a decentralized network architecture where simple nanomachines interact via a diffusive medium using a threshold-based firing mechanism modeled by Greenberg-Hastings (GH) cellular automata. We derive fixed-point equations for steady-state populations via mean-field analysis and validate them against stochastic simulations. We demonstrate that tuning the activation threshold allows the network to exhibit critical transition-like behavior, maximizing susceptibility across the swarm.

Index Terms—Molecular Communication, Internet of Bio-Nano Things, Cellular Automata, Mean-Field Analysis.

I. INTRODUCTION

Molecular Communication (MC) has established itself as a promising paradigm for information exchange in nanonetworks, particularly within the Internet of Bio-Nano Things (IoBNT) domain [1], [3]. While the fundamental limits of point-to-point diffusion channels have been extensively studied, the field is currently shifting towards understanding large-scale, complex collective interactions. Recent works have begun exploring these complex MC topologies using new methodologies, such as analyzing semi-autonomous in vivo computations for nanomachine swarms [6] and investigating the emergence of communication protocols among artificial agents via Graph Neural Networks (GNNs) [2].

Despite these advances, a significant disconnect remains between theoretical models and practical realizability. Existing works frequently investigate structured, deterministic topologies that are unrepresentative of real-life biological environments, where nanomachines are often distributed randomly. Furthermore, current theoretical frameworks frequently rely on idealized assumptions regarding the capabilities of individual agents, such as perfect temporal synchronization, highly complex transceiver designs, and high-precision molecule counting [7]. Current and near-future nanotechnology limits us to the production of simple, resource-constrained agents incapable of such complex individual tasks.

To bridge this gap, we propose a paradigm shift from highly capable individual agents to a network of simple, numerous

agents. This approach draws direct inspiration from the cortical networks of the brain, where complex information processing emerges not from a single unit but from collective dynamics. Similar collective intelligence paradigms have recently driven innovations in biological reservoir computing and organoid intelligence [4], [5]. We introduce a decentralized architecture where simple agents operate on a threshold-based firing mechanism: if the concentration of molecules absorbed exceeds a threshold, the agent releases molecules. While continuous-variable neuroscience models possess mean-field theorems, we adopt the discrete Greenberg-Hastings (GH) cellular automaton model, which is computationally advantageous for simulating massive, discrete molecular swarms.

II. SYSTEM MODEL

We consider a 3D unbounded medium containing N spherical transceiver agents of radius a_{rx} distributed according to a Poisson point process within a sphere of R . The motion of messenger molecules is governed by free diffusion. We assume an isotropic, homogeneous diffusion coefficient D . Time is slotted into discrete intervals of duration T_s . We employ fully absorbing receivers and assume the agent distribution is sufficiently sparse (i.e., total agent volume is negligible compared to the medium volume) such that no agent significantly obstructs molecule transmission.

The cumulative probability that a molecule emitted by the j -th agent is absorbed by the i -th agent by time t is given by the canonical hitting-time formulation:

$$g_{ij}(t) = \frac{a_{rx}}{d_{ij}} \operatorname{erfc} \left(\frac{d_{ij} - a_{rx}}{\sqrt{4Dt}} \right) \quad (1)$$

where $d_{ij} = |r_i - r_j|$ is the distance between the transceivers. The probability of absorption in the k -th interval is $P_{ij}[k] = g_{ij}(kT_s) - g_{ij}((k-1)T_s)$.

According to the GH model, an agent transitions between three states: quiescent (Q), excited (E), and refractory (R). The state updates are: $Q \rightarrow E$ if the received molecules $N^{(R)} > T_{th}$, where T_{th} is the activation threshold; $E \rightarrow R$ with probability 1; and $R \rightarrow Q$ with probability $\tilde{r}_2$.

Assuming Gaussian arrivals, the number of molecules absorbed by the i -th agent conditioned on the past L states of all agents is $N_i^{(R)}[k] \sim \mathcal{N}(\mu_i[k], \sigma_i^2[k])$, with:

$$\mu[k] = N_0 \sum_{l=1}^L P[l]x[k-l] \quad (2)$$

$$\sigma^2[k] = N_0 \sum_{l=1}^L (P[l] \odot (\mathbf{1} - P[l])) \cdot x[k-l] \quad (3)$$

where N_0 is the emission count, $P[k]$ is the connectivity matrix, $x[k] \in \{0, 1\}$ is the state vector, and $\odot$ denotes element-wise multiplication. By taking the unconditional mean and applying the law of total variance, we derive the steady-state mean-field fixed-point problem:

$$\mathbf{e}^* = \frac{\Gamma(\mathbf{e}^*)}{1 + \Gamma(\mathbf{e}^*)(1 + 1/\tilde{r}_2)}, \quad \Gamma(\mathbf{e}^*) = 1 - \Phi\left(\frac{T - \mu^*}{\sigma^*}\right) \quad (4)$$

$$\mu^* = N_0 \left(\sum_{\ell=1}^L \mathbf{P}[\ell] \right) \cdot \mathbf{e}^* \quad (5)$$

$$\sigma^{*2} = N_0 \left(\sum_{\ell=1}^L \mathbf{P}[\ell] \odot (\mathbf{1} - \mathbf{P}[\ell]) \right) \cdot \mathbf{e}^* \quad (6)$$

$$+ N_0^2 \left(\sum_{\ell=1}^L \mathbf{P}^2[\ell] \right) \cdot \mathbf{e}^* \cdot (\mathbf{1} - \mathbf{e}^*) \quad (7)$$

III. RESULTS

We simulate the stochastic dynamics in MATLAB. Agents initialized as 10% excited and the rest quiescent. We calculate the mean and standard deviation of activity across various thresholds.

TABLE I
SIMULATION PARAMETERS

Parameter	Value	Parameter	Value
Agents (N)	100	Radius (a_{rx})	$4\mu m$
Medium Radius (R)	$20\mu m$	Diff. Coeff (D)	$79.4\mu m^2/s$
Emission (N_0)	100	Memory (L)	5
Time Step (T_s)	1 s	$\tilde{r}_2$	0.5

As shown in Fig. 1, increasing the threshold decreases mean activity. The standard deviation of activity, which measures network susceptibility, peaks during this rapid drop, indicating a phase transition-like behavior. This categorizes the network into a sub-critical saturated phase, a super-critical silent phase, and a critical transitional regime that maximizes the dynamic range of the swarm and should be the ideal operating point.

To validate the mean-field analysis, we compare theoretical excitation probabilities to simulation runs. For this specific validation in Fig. 2, we set $\tilde{r}_2 = 1$ to isolate the excitation dynamics by removing the prolonged refractory period and we use fixed point iteration method to solve Eq. 4.

As seen in Fig. 2, the theoretical estimate strongly aligns with the simulation. The minor divergence at the exact transition point confirms that the mean-field assumption of

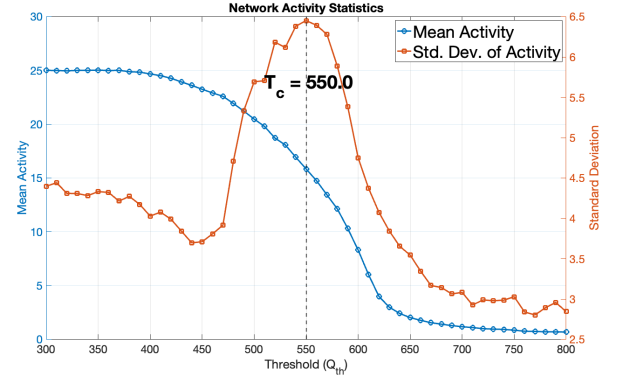


Fig. 1. Mean and standard deviation of activity across varying thresholds.

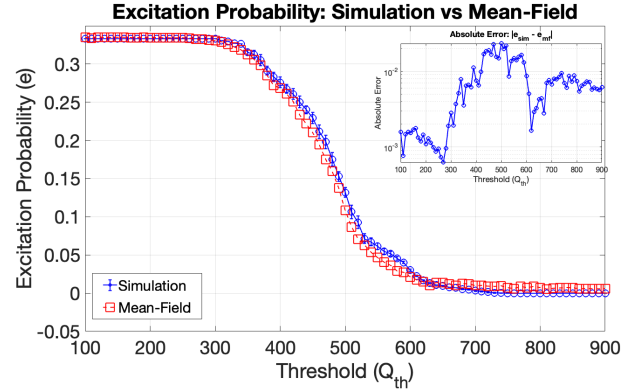


Fig. 2. Theoretical and simulated excitation probabilities (e)

node independence naturally weakens when the system exhibits high correlation during the critical transition.

IV. CONCLUSION

This paper demonstrates that modeling decentralized nanomachines through GH models allows a molecular network to achieve stable, collective operation. By tuning activation thresholds, the network reaches a transitional regime that optimizes signal propagation without requiring complex individual processing capabilities. Future efforts are planned to explore different network geometries, perturbation analysis, and provide further theoretical and simulation-based proof of the system's operation within critical regimes.

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Toward Clinically-Inspired Validation of ML-Driven Source Localization in Molecular Communication

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Abstract—Accurate localization of tumor sources in the human circulatory system is essential for precision oncology. In prior work, we developed a machine learning (ML) framework to localize anomaly sources using temporal biomarker profiles measured at receiver sites. However, the dataset was generated in a generic source-receiver setting, limiting physiological realism. This work-in-progress paper extends the framework by validating the ML model on a clinically-inspired dataset that emulates endocrine signaling in a controlled synthetic environment. The model is retrained and evaluated using a stratified held-out split with 25 % reserved for testing. Preliminary results show an accuracy of $\sim 90\%$, indicating the potential of ML-driven approaches for tumor source localization in clinically relevant molecular communication settings.

Index Terms—Molecular communication, localization, machine learning, tumor, endocrine signaling, human circulatory system

I. INTRODUCTION

Localizing tumor sources within the human body is a fundamental yet challenging problem for diagnosis and treatment [1]. During disease progression, tumor sites release biochemical signals, or biomarkers, into the human circulatory system (HCS) [2]. As these biomarkers propagate through biological fluids such as blood, their concentration profiles are altered by advection, diffusion, degradation, and dilution. Consequently, wearable receiver sites observe distorted, time-varying signals rather than direct signatures of the tumor origin. Understanding molecular communication (MC) in realistic biological fluids is therefore an important step toward clinically relevant in-body modeling [3]. Within this framework, tumor source localization becomes a challenging inverse problem in which the tumor origin is inferred from stochastic molecular signals measured at the receiver.

Machine learning (ML)-based models offer a data-driven approach to this inverse problem by learning spatiotemporal patterns in receiver-side biomarker time-series signals and inferring source locations from the observed molecular dynamics. This approach is especially relevant from a clinical perspective, where biomarker measurements are typically sparse in both space and time due to limited blood draws or infrequent sampling. Building on this motivation, in our prior work [4], we proposed an ML-based framework for localizing infection sources in the HCS using simulated biomarker time-series data.

However, the previous framework relied on a generic source-receiver setup and lacked physiological realism. This work-in-

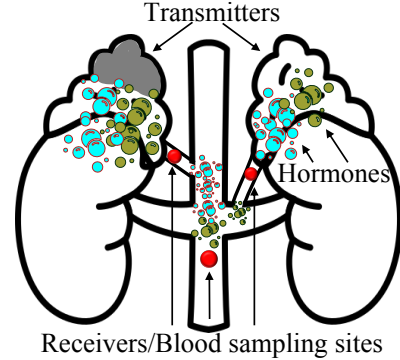


Fig. 1: MC-inspired endocrine signaling model.

progress paper explores validating the prior ML framework in a clinically-inspired endocrine signaling scenario involving aldosterone and cortisol secretion by the adrenal glands. To emulate clinically relevant molecular dynamics, we use the MEHLISSA simulator [5] and generate physiology-aware dataset based on adrenal venous sampling (AVS) settings.

II. SYSTEM MODEL

Following our previous framework [4], we adopt a biologically grounded model of endocrine signaling, as shown in Fig. 1. The adrenal glands are modeled as hormone-secreting transmitters, the HCS acts as the communication channel, and venous blood sampling sites serve as receivers analogous to clinical AVS. Specifically, the right adrenal vein, left adrenal vein, and inferior vena cava (IVC) are represented as passive receivers that measure hormone concentrations. We implement this setup using the MEHLISSA simulation framework [5], [6], which models the human vascular system as a directed 3D network of blood vessels. The framework is extended with separate left and right adrenal glands and veins to enable continuous secretion of aldosterone and cortisol into the vascular network. The hormones propagate through the vessels via diffusion and advection governed by vessel-specific blood flow and are passively observed at the receivers. At each receiver, hormone arrival times and concentrations are recorded, producing time-series signals that serve as input features for the ML-based localization model.

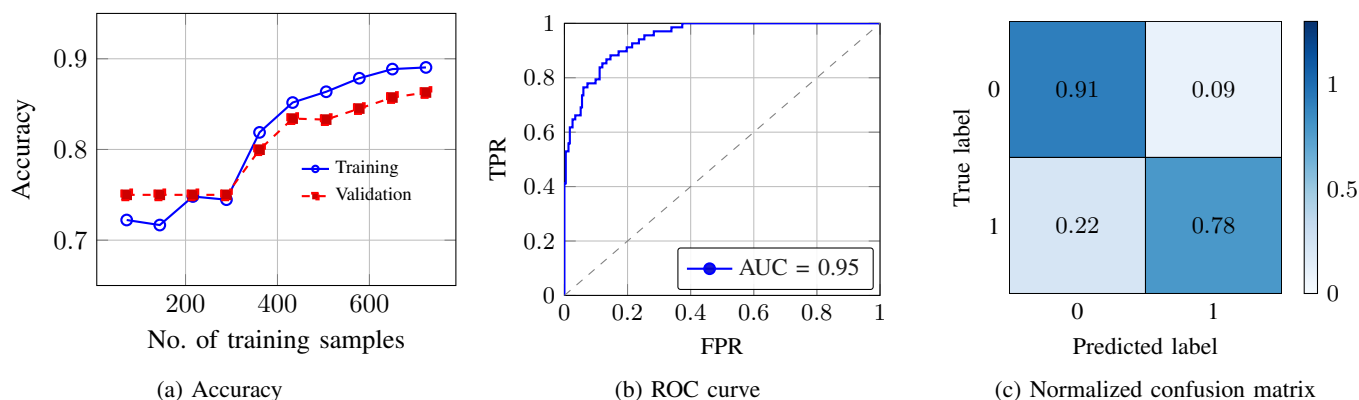


Fig. 2: Performance of the ML model on the held-out test set.

III. CLINICALLY-INSPIRED DATASET AND VALIDATION

In the AVS-derived clinical measurement, the highest hormone concentration is observed at the right adrenal vein, followed by the IVC and the left adrenal vein. We calibrate the simulator to reproduce key AVS-derived metrics, including the selectivity index and lateralization index [7]. The simulated values closely match the clinical reference measurements, with deviations ranging from $\sim 2\%$ to $\sim 7\%$.

Using this configuration, we generate a dataset from 1205 simulations, each with duration 100 s. Hormone concentrations and arrival times are recorded at three receiver sites. From the resulting time-series data, statistical and temporal features such as peak concentration, time-to-peak, and arrival delay are extracted. Since the clinical measurements served only as calibration references, pseudo-labels were assigned by thresholding the mean concentration per sample at the 75th percentile, labeling samples as elevated or normal concentration. To evaluate the adaptability of the prior ensemble model [4], we retrain it on the MEHLISSA-generated dataset. The data are split using an 80/20 stratified train-test split to preserve class balance, and performance is evaluated using standard classification metrics on the held-out test set.

Preliminary results shown in Fig. 2a indicate that the model achieves $\sim 90\%$ accuracy on the held-out test set. The receiver operating characteristic (ROC) curve in Fig. 2b shows an area under the curve (AUC) of about 0.95, demonstrating strong discriminative performance. The confusion matrix in Fig. 2c further depicts reliable separation between normal and elevated hormone secretion patterns. All associated data and code are publicly available in [8] under CC BY and MIT licenses. These early results suggest the feasibility of ML-based localization in clinically inspired MC scenarios. However, the evaluation is limited to synthetic simulations and a simplified endocrine signaling setup and should therefore be interpreted as a methodological proof-of-concept.

IV. CONCLUSION

In this work-in-progress paper, we validate our prior ML-based source localization framework using a clinically-inspired endocrine signaling dataset generated with the MEHLISSA

simulator. The model achieves around 90% classification accuracy and generalizes well, supporting the potential of ML-driven source localization in clinically relevant settings. In practice, however, background molecular signals, patient-specific variability, and time-varying secretion rates may influence the observed signals and thereby affect localization performance. Future work will extend the framework to incorporate these factors.

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