Molecular Communications and Networking

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I. INTRODUCTION

Molecular communication (MC) is an emerging paradigm in communication theory and systems engineering where information is encoded into properties of substances at the molecular level and then transmitted, propagated, received, and decoded by means of chemical reactions and molecule transport processes.

The MC paradigm draws direct inspiration from biology, where the exchange of chemically encoded information is an essential aspect of life at different layers, from single cells interacting with their environment, to multiple cells organized into microbial communities or tissues and systems in multicellular organisms.

In the past decade, communication theorists have abstracted, modeled, and characterized the essential elements that define an MC link, and multiple of these links organized into MC networks, building the theoretical foundations essential to understand the peculiarities of this paradigm compared to previously

This Special Issue covers the most relevant theoretical foundations of molecular communications and networking and provides insight into emerging applications in this ever evolving area.

studied communication systems, such as electromagnetic, optical, or acoustic. Although envisioned applications of systems based on MC lie in multiple engineering grand challenges, such as biomedicine, health informatics, environment monitoring and control, the definition of technologies to support them is still very limited.

This Special Issue (SI) on Molecular Communications and Networking aims at capturing the most relevant theoretical foundations of MC established so far while giving a timely perspective on some emerging technological directions for engineering practical MC applications. We believe that this SI can serve as an essential but complete

handbook to approach MC as a research topic, as well as to start contributing to its timely and much needed technological evolution from theoretical exploration to practical implementation.

II. OVERVIEW OF THIS SPECIAL ISSUE

Since the birth of MC as a communication theory research field in the mid-2000s, the community has witnessed a number of novel theoretical models geared toward abstracting the peculiarities of information transmission through molecules. Considering free diffusion as the most basic molecule transport process, channel models and their characterization in terms of noise sources and achievable transmission rates have resulted into foundational theories that are still at the basis of MC as a discipline. By following a natural approach in communication systems engineering, these theories have been applied to design conceptual architectures for information modulation, coding, and detection, which will help in the development of MC-enabled transmitter and receivers. A theoretical view of a complete MC link has been another necessary step to

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understand the peculiarities of future MC-based networking scenarios. In this SI, we reflect this evolution of MC research into the selection of articles and their authors and provide a framework to interpret the essential characteristics of an MC system in light of the fundamental mathematical tool of statistical mechanics. which underlies the propagation of information in any molecular system.

This SI will also lay the groundwork for the future evolution of MC as a research field in the short run and as a practical technology in the long run. This is realized through articles that bridge to other domains and fields, particularly toward biochemistry and molecular biology. Synthetic biology, i.e., the (re-)programming of cell behavior through genetic engineering, is currently one of the most promising tools to practically engineer MC systems based on a biological substrate. In particular, biomolecular circuits, made of networks of interacting genetic code parts with defined functions, have attracted interest among computer engineers given their conceptual similarities with their electrical counterparts. This SI includes a foray in this direction with two contributions by worldwide renown synthetic biology teams.

Although the engineering of MC functionalities on board of biological cells is a necessary step to realize MC systems, another essential challenge stands in the development of interfaces with legacy technologies. In particular, both optical and electrochemical modalities have been studied as feasible solutions. The former is realized by engineering the cell sensitivity to light through genetic engineering, while the latter exploits natural biochemical processes where electrons are propagated through molecular reactions. Two articles of this SI are devoted to introduce these solutions.

Finally, one essential aspect to advance MC as a disruptive technology is to connect its technological advances to future applications, especially in healthcare, where MC systems are set to enable the sensing

and control of health information as it propagates in vivo through the biochemistry underpinning human body, its cells, and their molecular content. In this direction, two of the explored application directions for MC are in the domain of brain-machine interfaces and drug design and delivery system engineering, among others, covered, respectively, by two articles that conclude the SI and offer a glimpse of the future evolution of this emerging technology.

III. ARTICLES IN THIS SPECIAL ISSUE

As part of this SI, we have collected ten contributions from well-known experts in MC theory, as well as other domains currently contributing to MC and networking research, organized according to the overview detailed in Section II.

A. Four Contributions Cover the **Foundations of Molecular Communication Theory**

In "An information theoretic framework to analyze molecular communication systems based on statistical mechanics," a mathematical framework is proposed to define the main functional blocks of MC theory, supported by general models from chemical kinetics and statistical mechanics. In this framework, the Langevin equation is utilized as a unifying modeling tool for molecule propagation in MC systems, and as the core of a methodology to characterize their communication performance.

"Channel modeling for diffusive molecular communication—A tutorial review" focuses on the main research results achieved so far in the mathematical channel modeling for an end-to-end MC channel, including the effects of molecules release mechanisms, the MC environment, as well as the reception mechanism, and how each of these impact on the information transfer performance. The tutorial covers the underlying biological, chemical, and physical phenomena encompassing fixed as well as moving transmitters and receivers.

"Transmitter and receiver In architectures for molecular communications: A survey on physical design with modulation, coding, detection techniques," authors focus on the design of transmitters and receivers for MC. The survey reviews existing literature on transmitter and receiver architectures for realizing MC, including both nanomaterial-based nanomachines and/or biological entities. A complete overview of modulation, coding, and detection techniques employed for MC is also included.

"Capacity bounds on point-to-point communication using molecules" introduces a mathematical framework to infer analytical channel capacity bounds where the discrete nature of molecules is put into perspective in the processes of assemblage, release, and capture of matter in an MC system. This framework focuses on the particular case where a very small number of (or single) molecules are utilized for propagating information between a single transmitter and receiver pair.

B. Two Contributions Focus on Synthetic Biology as an **Enabling Tool**

In "Design of asynchronous genetic circuits," an automated workflow for the design of asynchronous sequential genetic circuits is presented by stemming from the assumption that, while most electronic circuits utilize a timing reference, biological substrates are, in general, lacking a similar reliable high-frequency clock signal. This workflow builds upon existing tools for asynchronous logic design and is based on a new compiler that can translate to/from Verilog to other standard design tool formats.

In "The effect of loads in molecular communications," the design of MC functionalities in biological cells through synthetic biomolecular circuits is discussed in light of their apparent lack of modularity, in contrast to their electrical counterpart. To solve this problem, the concept of the retroactivity to abstract and capture loading problems in these circuits is, here, reviewed as a potential solution to the development of MC systems on biological substrates.

C. Two Contributions Address **Interfaces With Legacy Technologies**

The use of the optical nanobio interface to connect biological networks to electronic computing system is discussed in "Optogenomic interfaces: Bridging biological networks with the electronic digital world." The article reviews the state of the art and future directions in light-mediated control of genomes and consequent control of cell development. This can result in transformative applications for MC

research, such as reconstructive medicine, as well as cancer therapy.

In "Redox is a global biodevice information processing modality," the authors review recent research findings in the study of reduction/oxidation (redox) reactions as an MC modality that propagates both electrical and biological signals. In particular, the authors provide details on the processed underlying redox systems, describe electrochemical measurements, and provide four examples demonstrating that redox enables a viable interface between MC and legacy electronics.

D. Two Contributions Focus on **Enabling Applications**

In "Synaptic communication engineering for future cognitive brainmachine interfaces," the authors outline brain diseases that promote dysfunction in the synaptic communication system, and how these could be addressed through brain implants technology that stem from MC research. In addition, the authors envision future directions for the design and fabrication of cognitive brain-machine interfaces.

The article "Methods and applications of mobile molecular communication" presents an application-driven model to support the development of MC links and networks where the nodes have dynamic behavior while communicating. In this contribution, applications of this model are also detailed in the context of cooperative drug delivery systems.

ABOUT THE GUEST EDITORS

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