

Molecular Communications and Networking

Ian F. Akyildiz, *Fellow, IEEE*,
Guest Editor

Massimiliano Pierobon, *Member, IEEE*,
Guest Editor

Sasitharan Balasubramaniam, *Senior Member, IEEE*
Guest Editor

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 last 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 studied communication systems, such as electromag-

netic, optical, or acoustic. While 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 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 THE 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 towards 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 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

This work was supported by the U.S. National Science Foundation under Grants CISE CNS-1763969 and CCF-1816969, Science Foundation Ireland through the SFI VistaMilk (16/RC/3835) and CONNECT (13/RC/2077) research centres, and Academy of Finland Research Fellow grant (no. 284531).

Ian F. Akyildiz is with the Broadband Wireless Networking Laboratory, School of Electrical and Computer Engineering, Georgia Institute of Technology, Atlanta, GA 30332, USA (email: ian@ece.gatech.edu).

Massimiliano Pierobon is with the Molecular and Biochemical Telecommunications Laboratory, Department of Computer Science & Engineering, University of Nebraska-Lincoln, Lincoln, NE 68588, USA (email: pierobon@cse.unl.edu).

Sasitharan Balasubramaniam is with the Telecommunication Software and Systems Group, Waterford Institute of Technology, Carriganore, Waterford, X91 P20H, Ireland, and Faculty of Information Technology and Communication Sciences, Tampere University, Finland. (email: sasitharan.balasubramaniam@tuni.fi, sasib@tssg.org).

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, in particular towards 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.

While 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 electro-chemical 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 hu-

man 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, amongst 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 THE SPECIAL ISSUE

As part of this SI, we have collected 10 contributions from well-known experts in MC theory, as well as other domains currently contributing to MC systems and networking research, organized according to the overview detailed in Sec. 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.

In “Transmitter and Receiver Architectures for Molecular Communications: A Survey on Physical Design With Modulation, Coding and Detection Techniques” the 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 optical nano-bio 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 Brain-machine 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.



Massimiliano Pierobon Massimiliano Pierobon (S’05-M’13) received his Ph.D. degree in Electrical and Computer Engineering from the Georgia Institute of Technology, Atlanta,

GA, USA, in 2013. Since August 2013, he is an Assistant Professor with the Department of Computer Science and Engineering, University of Nebraska-Lincoln (UNL), NE, USA, where he also holds a courtesy appointment at the Department of Biochemistry. He is the co-Editor in Chief of Nano Communication Networks (Elsevier) since July 2017, and an Associate Editor of the IEEE Transactions on Communications since 2013. Selected honors: 2017 IEEE INFOCOM Best Paper Runner-up Award, IEEE GLOBECOM 2017 Best Paper Award. Dr. Pierobon is currently the PI of multiple NSF projects in the field of molecular communication applied to biological systems. His research interests are in molecular communication theory, nanonetworks, intra-body networks, communication engineering applied to synthetic biology, and the Internet of Bio-Nano Things. He is a faculty mentor for the UNL iGEM team since 2016.



Ian F. Akyildiz received his M.S., and Ph.D. degrees in computer engineering from the University of Erlangen-Nuremberg, Erlangen, Germany, in 1978, 1981, and 1984, respectively. He

is currently the Ken Byers Chair Professor in Telecommunications in the School of Electrical and Computer Engineering, Georgia Institute of Technology, Atlanta, GA, USA, the Director of the Broadband Wireless Networking Laboratory, and the Chair of the Telecommunication Group at Georgia Tech. His current research interests are in Terahertz Communications, Nanonetworks, Internet of NanoThings, Internet of BioNanothings, 5G/6G Wireless Systems, Internet of Space Things/CUBESATs, and Wireless Sensor Networks in Challenged Environments, where he has published over 400 articles in prestigious journals and conferences. He is a Fellow of the IEEE (1996) and ACM (1997). He received numerous awards from IEEE and ACM. According to Google Scholar, his H-index is 117 and the total number of citations to his papers is 107+K as of June 2019.



Sasitharan Balasubramaniam (SM'14) received the B.E. in electrical and electronic engineering, and PhD degree both from the University of Queensland, in 1998 and 2005, respectively, and the M.E. in computer and communication engineering from the Queensland University of Technology, in 1999. He is currently an Academy

of Finland Research Fellow with the Tampere University, Finland, and he is also the Director of Research with the Telecommunication Software and Systems Group, Waterford Institute of Technology, Ireland. His current research interests include bio-inspired communication networks, as well as molecular communications. He has published over 100 articles in various journals and conferences, and actively participates in a number of technical programme committee for various conferences. He is currently on the steering

board committee of ACM NANOCOM, which he co-founded, and was the TPC co-chair in 2014, as well as the General Chair in 2015. He is currently an Associate Editor for the IEEE Letters of the Computer Society, Elsevier Nano Communication Networks, and Elsevier Digital Communication and Networks. He was a past Associate Editor for IEEE Internet of Things Journal. In 2018 he was the IEEE Nanotechnology Council Distinguished Lecturer. He is a senior member of the IEEE.