



## Editorial

### Topical Collection on Emergent Dynamics of Biological Networks

This special issue ‘*Emergent properties of biological networks*’ celebrates the growing and vibrant international community of researchers working on questions in the area of cellular and tissue-level biological physics. Networks are a common way to represent biological systems ranging from sub-cellular protein signaling to the entire ecosystem, elucidating the crosstalk among different interacting entities. Recent advances in high-throughput cellular measurement technologies, cost-effective next-generation sequencing, and development of new computational methods (including algorithmic, statistical, graph theoretical concepts, machine learning, and many artificial intelligence-based techniques) have truly revolutionized the investigation of biological networks by uncovering and predicting emergent phenomena that have great implications in both biology and medicine. There have been notable efforts in an interdisciplinary direction that necessitate intricate collaboration between physicists, chemists, biologists, clinical scientists, and mathematicians. We must acknowledge the contribution of those who pioneered such crosstalk between disciplines, conceiving new thoughts, and shaping theoretical biology – an important branch of modern biological sciences. At an international level, 2023 also marks the 50th anniversary of the foundation of the Society for Mathematical Biology (SMB) – a vibrant academic community promoting research and education in mathematical biology. Through this special issue, we also acknowledge the enormous contribution of Professor Somdatta Sinha, who has not only been actively engaged with SMB and has tirelessly nurtured this interdisciplinary branch of biological sciences in India for close to 50 years, but also inspired many young scientists like us toward this challenging area of research. We take pride in guest editing this special issue of *Journal of Biosciences* in honor of her pivotal contribution to Biological Sciences. Special thanks are due to Professor B.J. Rao (Vice Chancellor, University of Hyderabad, Telangana) and Dr. Prakash Kulkarni (Research Professor and Director, Translational Research, Department of Medical Oncology & Therapeutics, City of Hope, California), who inspired us to collect articles that address problems at the frontiers of biology and would cater to an enlightened biology audience. Through this special issue, we have aimed to collate a comprehensive collection of research and review articles, including perspective articles that curate novel advances in the development and application of network modeling.

Twenty-four articles (14 review articles, 9 research articles, and 1 perspective) were received from a wide community of biology researchers from India and abroad. The topics include, but are not limited to: (i) novel advances in the development of network modeling, (ii) application of network modeling to solving longstanding challenges in biological systems, and (iii) analysis of emergent properties of biological phenomena to yield mechanistic insights. **Srivastava and coauthors** present network formalism to understand biological systems covering single to multilayer networks. They highlight recent advances in studying the structure and dynamics of such multilayered networks, followed by challenges and prospects. In the context of generative modeling, **Achuthan, Kulkarni, and coauthors** describe how several neural network architectures, including recurrent neural networks (RNNs), variational autoencoders (VAEs), and generative adversarial networks (GANs) can help in creating new synthetic data. They emphasize the importance of generating such synthetic data in healthcare and biomedical research. Along the same lines, **Bagler and coauthors**, in their review, illuminate a fascinating area of research – computational gastronomy. By conducting data-driven research, they explore traditional recipes, flavor composition, and health associations. **Barah and coauthors** describe how integrative network-based approaches identify systems-level molecular signatures associated with gallbladder cancer pathogenesis from gallstone disease. **Jalan and coauthors** review how mapping co-mutation patterns in nucleotide networks can reveal genetic

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This article is part of the Topical Collection: Emergent dynamics of biological networks.

signatures of adaptation in extreme environments. **Ray and coauthors** describe universality in bio-rhythms and show that notwithstanding the diverse nature of the underlying biochemical and biophysical processes, the associated kinetic equations can be mapped into the universal form of the Liénard equation, which admits of mono-rhythmic and bi-rhythmic solutions. **Sherman and coauthors** review studies on pancreatic islets of Langerhans, which are home to beta cells that secrete insulin. Their review articulates the current understanding of the mechanisms of bursting oscillations of highly heterogeneous cells and describes the existence of small worldness where democracy rather than oligarchy remains the most likely organizing principle of the islets. **Dutta and coauthors** elucidate how an in-depth study of the underlying molecular mechanisms may provide dynamic network biomarkers that can forecast potential critical transitions in complex diseases. They also discuss the need for such advanced research in developing early warning signals in the field of medicine and healthcare. **Roy, Bagchi, and coauthor** briefly review the effects of immunosuppressants on T-cell dynamics and described how developing simple coarse-grained immune network models helps to understand non-classical immunomodulatory responses induced by various immunosuppressive steroid and secosteroid drugs. **Biswas and Ghosh** study toggle switch networks including transcription factors (TFs) and microRNAs (miRs) to understand the implications of TF–TF and TF–miR circuits in the dynamics of cell fate decisions. **Das and coauthors** investigate the effects of length-dependent positive feedback on length distributions of microtubules undergoing hydrolysis. Their simulations show that regulation of biophysical parameters (e.g., hydrolysis rate and feedback strength) may lead to length diversity in an ensemble of multiple microtubules. **Rao, Sastri, Srivastava, and coauthor** describe how a representation of a protein as an amorphous solid, allows the setting up of a genotype–phenotype map, which helps the amorphous material to evolve and select for fitness. Their analysis provides insight into the architectural demands on a protein that enable a prescribed function and confer stability to mutations. **Jolly and coauthors** discuss how a systems-level approach integrating mathematical modeling and *in vitro/in vivo* experiments can identify therapeutic vulnerabilities of a clonal cancer cell population. Using data from the human protein–protein interaction network, **Sinha and coauthors** demonstrate how genes that are ‘global hubs’ in such networks are significantly more likely to be related to cancer progression than the non-‘global hubs’. **Sarkar and coauthors** have reviewed many approaches from a graph theoretical perspective to understand molecular interaction landscapes and how machine-learning strategies are now being integrated into existing frameworks to overcome challenges in mapping molecular networks in biomedical sciences. Thus, this special issue spans the advancements made in identifying the structure and dynamics of interaction networks under homeostatic and perturbed scenarios.

This special issue also features an important message regarding mathematical modeling in ecology and evolution from **Joshi**. In his perspective, he suggests that the researchers doing modeling in ecology and evolution but trained in the mathematical or physical sciences need to comprehend their systems more acutely and to capture in their modeling of biological systems the fundamental difference from classical physics-based modeling approaches. In ecological systems, elucidating how local interactions can enable complex collective behavior has been an active research area. **De and Chakraborty** discuss several such examples, highlighting the role of self-propelled particle models that have been instrumental in deciphering such collective dynamics. Other investigations in ecological systems led by **Sinha and coauthors** are how Allee effects impact the prevalence of extreme events in a coupled three-species system. Similarly how multilayer network analysis, by integrating behavioral information from many social situations, can be helpful in identifying the potential queen in presence of the previous queen in the Indian paper wasp *Ropalidia marginata*, is discussed by **Gadagkar and coauthors**. Investigating molecular patterns in ecosystems is another emerging area of interest. **Krishna and coauthors** used population dynamics models for open and closed phage–bacteria ecosystems to understand the emergence of patterns in restriction-modification systems (bacterial defense systems against bacteriophages) depending on the selection pressure applicable. These articles highlight how computational modeling approaches can help decode ecological dynamics.

Finally, a set of articles highlight the design principles aspects of biological systems. For instance, **Martin, Samal and coauthors** demonstrate that among a wide range of possible Boolean functions, link operator functions are capable of driving biological network dynamics toward criticality. Similarly, **Tangirala, Raman, and coauthors** review how three different approaches – computational efforts, rule-based methods, and systems theoretic methods – have helped understand oscillation, state switching, and adaptation in biological networks. Graph-theoretic approaches can also explain how molecular constraints could restrict the structure of vesicle

transport graph, as exemplified by **Thattai and coauthors** who show that edge connectivity can serve as a key determinant in segregating the allowed transport graph topologies from the disallowed ones. Finally, taking several examples ranging from stochastic gene expression to biofilms, **Bose** showcases how some transitions in biological systems are reminiscent of critical point phenomena.

Overall, this special issue contains contributions from research groups across disciplines – physics, chemistry, mathematics, chemical engineering, cell/molecular biology, ecology and evolution, thus celebrating diversity in the topics covered, biological systems investigated, and the approaches used to dissect their emergent properties. This special issue also marks the fast-growing community of systems/computational/theoretical biology colleagues in India whose interests span a spectrum of fundamental and applied research ideas. We believe that this collection will provide a roadmap to students and young researchers who wish to venture into this frontier interdisciplinary area of biology. We thank the Editor-in-Chief of the *Journal of Biosciences*, Professor Renee Borges (Indian Institute of Science, Bengaluru) and the staff of the *Journal of Biosciences*, Jai Benjamin, Sushila Rajagopal, and Vinutha Suresh for their support for the timely completion of this special issue. We are grateful to all the authors and coauthors for their contributions to this special issue. We also acknowledge all the reviewers for their valuable comments on the manuscripts.

*Editors*

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