A top-down computational approach for unraveling complex dynamical system properties – biological implications

Complex dynamical systems comprise numerous components that interact in a non-trivial topology and non-linear form, giving rise to diverse array of states and rich system properties, spanning from robustness to evolvability. Unveiling such properties is of great importance, enabling better prediction and control of complex systems. However, this endeavor remains challenging due to the incomplete knowledge in many systems. Here, we developed a novel computational top-down approach designed to estimate global features of the complex system from a collection of data samples, without inferring its entire map of interactions. We demonstrate the effectiveness of this approach in two distinct biological cases, by applying it to single-cell RNA sequencing data, inferring different characteristics of the complex machinery of the cell, its gene regulatory network (GRN). First, we found a decrease in the gene-to-gene transcriptional coordination among aging cells, suggesting a general, potentially universal, stochastic attribute of transcriptional dysregulation in aging, implying that the gene regulatory network is progressively losing its consistency across cells as organisms age. In the latter, we leveraged this approach to infer the interaction intensity of GRNs across various cell types. Our findings reveal a pronounced complexity-stability tradeoff, suggesting that a GRN could be stable up to a critical level of complexity, a product of the diversity of gene expression and the intensity of the GRN interactions. This insight suggests that GRNs were shaped by stability constraints, which in turn impose limits on the extent of gene expression diversity within cells.

Bio sketch

Orr Levy graduated B.Sc. in Electrical and computers engineering in 2008 at Ben-Gurion university, and M.Sc. in Bio-Medical engineering in 2013 at the Technion. He then received a Ph.D. from Bar Ilan university (BIU) in 2018 studying the structural and functional properties of complex networks in Shlomo Havlin's lab. During his Ph.D., Orr developed computational approaches based on network science and statistical mechanics to improve our understanding of real networks, spanning from cognitive, traffic, physiological and biological networks. Afterwards, Orr was a postdoctoral fellow at Bar Ilan university working with Dr. Amir Bashan (BIU) and Prof. Yang-Yu Liu from Harvard Medical school and developed a novel data science approach to address a fundamental question in aging tissues and revealed a new universal attribute of aging. Currently, and for the past two years, Orr has been an associate research scientist in Yale school of medicine and Howard Hughes Medical Institute under the mentorship of Prof. Ruslan Medzhitov (Yale) and Prof. Yang-Yu Liu (Harvard). In his research, Orr uses a combination of mathematical models, network theory approaches, computational data analysis and non-linear dynamics to uncover the underlying principles that govern the cells in a tissue in health and disease. Along to his scientific career, Orr has over 10 years of experience in the Israeli air force in multiple roles in the system engineering department and Ofek 324 unit. His roles spanned from hands-on roles in software and embedded systems, to an executive role, as a lieutenant colonel as the Head of Data engineering and systems architecture branch. Orr aspires to advance our understanding of biology and physiology to pave the way for innovative medical implications.

Education

	Associate Research Scientist • under the Supervision of Prof. Ruslan Medzhitov and Prof. Yang-Yu Liu *Yale University, New Haven, USA (2022-current)* Theoretical biology - uncover the underlying principles that govern cells
	Postdoc • under the Supervision of Dr. Amir Bashan and Prof. Yang-Yu Liu *Bar-Ilan University, Bar Ilan, Israel (2018-2022)* Developing Data Science approaches studying aging tissues
	PhD in Physics • under the Supervision of Prof. Shlomo Havlin *Bar-Ilan University, Bar Ilan, Israel (2018)* Structural and functional properties of complex networks
	M.Sc. in Biomedical Engineering *Technion – Israel Institute of Technology, Haifa, Israel (2013)* Specialized in Statistics, Simulations and Biomedical Signal Processing
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