

SCS 2021

CONFERENCE
ON
COMPLEX
SYSTEMS

25-29 OCT. 2021

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BOOK OF ABSTRACTS



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Preface

Serving as Program Committee Co-Chairs has been an honour that humbled us with strong responsibility, especially during these unsettling times. We are grateful to the General Chairs for the trust and the support they gave us throughout the journey. We were positively struck by the enthusiasm of all the contributors, despite the evident uncertainties, disruptions and challenges related to the current pandemic. The selection process was not significantly different from the usual ones before the COVID-19 pandemic. What was different, and indeed inspiring, was seeing the dedication and care of authors, on the one hand, and members of the Program Committee, despite the challenging external conditions. From this perspective, a special thanks go to all members of the Program Committee. Our profound gratitude goes to them for their generosity in donating their time and knowledge to go through up to 10-15 contributions each. Thanks to them and all the authors, this Book of Abstracts is extraordinarily rich in high-level scientific contributions, and we hope you will all appreciate the contents presented and the conference itself, both remotely and in Lyon. As always, the latitude of contributions is vast, spanning all areas of Complexity Science, from basic foundations to innovative applications. One of the distinctive features of our community has always been the inclusiveness, this unique capacity to welcome contributions from different communities, still sharing the same technical tools and the same aim for excellence. This conference does not make an exception, and you will find the same openness in all the contributions. We hope you will enjoy it! We wish you a pleasant and productive conference, and thanks again for helping us shape the Complex Systems community.

Kristina Lerman and Vittorio Loreto
Program Chairs of CCS 2021 Lyon



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The distance backbone of complex networks

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Redundancy needs more precise characterization as it is a major factor in the evolution and robustness of networks of multivariate interactions. We investigate the complexity of such interactions by inferring a connection transitivity that includes all possible measures of path length for weighted graphs. The result, without breaking the graph into smaller components, is a distance backbone subgraph sufficient to compute all shortest paths. This is important for understanding the dynamics of spread and communication phenomena in real-world networks. The general methodology we formally derive yields a principled graph reduction technique and provides a finer characterization of the triangular geometry of all edges---those that contribute to shortest paths and those that do not but are involved in other network phenomena. We demonstrate that the distance backbone is very small in large networks across domains ranging from air traffic to the human brain connectome, revealing that network robustness to attacks and failures seems to stem from surprisingly vast amounts of redundancy [1].

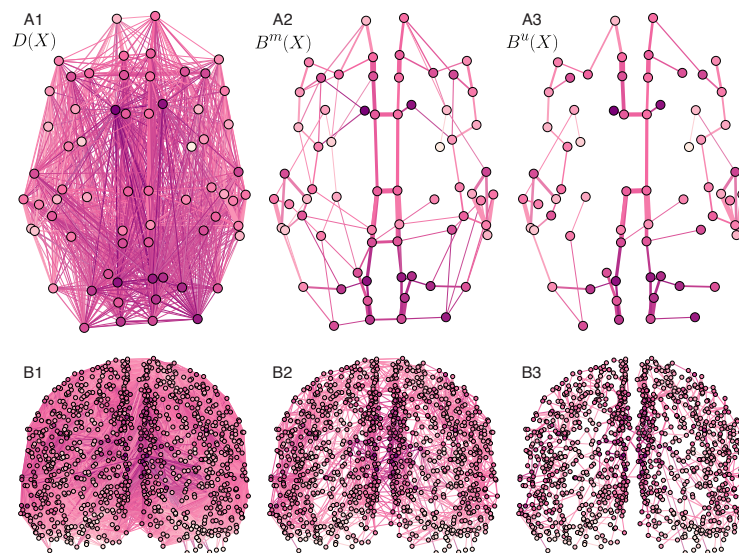


Figure 1: Human Connectome Network (HCN) and Backbones. **(A1-3):** HCN-Coarse. **(B1-3):** HCN-Fine. **(A1,B1):** Original distance Networks [2], whose distance weights are inversely proportional to the volume of cortico-cortical axonal pathways between brain regions (nodes), obtained via diffusion spectrum imaging. **(A2,B2).** Metric backbone with only 9.23% and 17.57% of original edges HCN-Coarse and HCN-Fine, respectively. **(A3,B3).** Ultrametric backbone with only 5.66% and 5.53% of original edges for HCN-Coarse and HCN-Fine, respectively.

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5 Biological and (Bio)Medical Complexity

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The effective graph reveals redundancy, canalization, and control pathways in biochemical regulation and signaling

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The ability to map causal interactions underlying genetic control and cellular signaling has led to increasingly accurate models of the complex biochemical networks that regulate cellular function. These network models provide deep insights into the organization, dynamics, and function of biochemical systems: for example, by revealing genetic control pathways involved in disease. However, the traditional representation of biochemical networks as binary interaction graphs fails to accurately represent an important dynamical feature of these multivariate systems: some pathways propagate control signals much more effectively than do others. Such heterogeneity of interactions reflects canalization—the system is robust to dynamical interventions in redundant pathways but responsive to interventions in effective pathways. Here, we introduce the effective graph, a weighted graph that captures the nonlinear logical redundancy present in biochemical network regulation, signaling, and control. Using 78 experimentally validated models derived from systems biology, we demonstrate that 1) redundant pathways are prevalent in biological models of biochemical regulation, 2) the effective graph provides a probabilistic but precise characterization of multivariate dynamics in a causal graph form, and 3) the effective graph provides an accurate explanation of how dynamical perturbation and control signals, such as those induced by cancer drug therapies, propagate in biochemical pathways. Overall, our results indicate that the effective graph provides an enriched description of the structure and dynamics of networked multivariate causal interactions. We demonstrate that it improves explainability, prediction, and control of complex dynamical systems in general and biochemical regulation in particular.

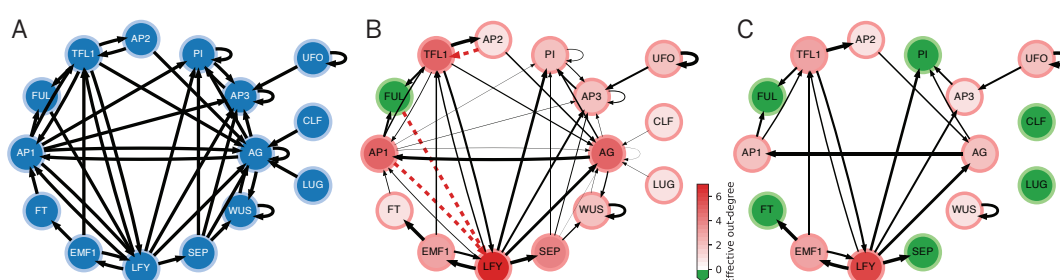


Figure 1: Study of the *A. thaliana* Boolean network model. (A) The interaction graph. (B)

The effective graph. Edge thickness denotes effectiveness; dashed red indicates fully redundant edges; node color intensity denotes effective out-degree; and green nodes denote cases of null effective out-degree. (C) A threshold effective graph showing only edges with effective weight ≥ 0.4 to enhance visibility of the largest connected component that allows

LFY to function as a master regulator and reveals that WUS functions simply as an autoregulator; green nodes denote cases of null effective out-degree at this threshold level.

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Multi population analysis of electronic health records reveal biases in the administration of known drug-drug interactions

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The occurrence of drug-drug-interactions (DDI) from multiple drug dispensation is a serious problem, for patients' health and health-care systems alike, and previously highlighted by our own work [1]. Here we present preliminary results of a multi-population expanded analysis of the DDI phenomena. We characterize the age- and gender-associated biases in drug dispensation patterns from distinct health care systems, both public and private. We analyzed drug dispensations from population-wide electronic health records (EHR) in Blumenau (Brazil; pop. 330K), Catalonia (Spain; pop. 7.5M), and Indianapolis (USA; pop. 864K) with a temporal scale ranging from 1.5 to 10 years' worth of data. We investigate the role of polypharmacy in the observed DDI rates by building a statistical null model that shuffled drug labels while accounting for cohort specific drug availability. In total, 149 shared DDI were found in the three populations. The risk of such DDI as patient age was also characteristically similar in all three populations. We confirmed that in general women are at an increased risk of DDI—with the exception of males over 50 years-old in Indianapolis. Importantly, we found that the increased risk of DDI cannot be solely explained by polypharmacy or increased co-administration rates in the elderly. Finally, we simulated alternative drug regimens for patients dispensed DDI involving Omeprazole, a proton pump inhibitor with substitutes having less known DDI, to characterize the population effect of avoiding overly prescribed interactions. We found that alternatives to Omeprazole can reduce the number of patients affected by DDIs by up to 21% in Blumenau and Catalonia. Interestingly, Omeprazole is less used in Indianapolis, therefore the same simulation reduces only 2% of affected patients, which demonstrates social and/or economic factors at play in the global DDI phenomena.

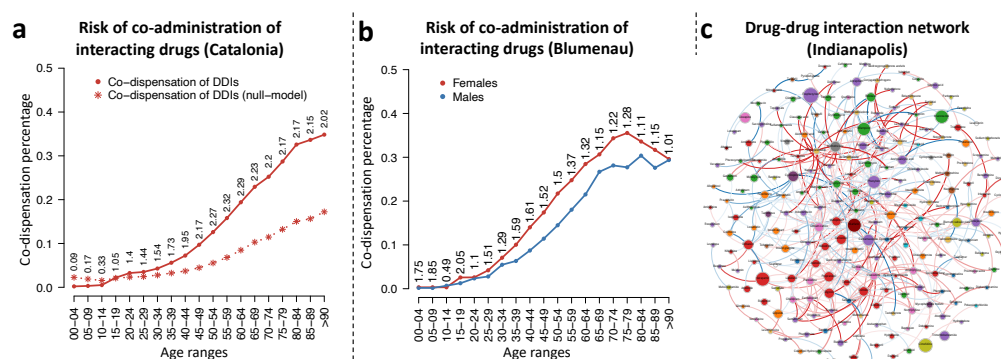


Figure 1: (A) Risk of DDI dispensation (circles) and the associated null model (stars) stratified by age in Catalonia. (B) Risk of DDI dispensation stratified by age and gender in Blumenau, where women (men) are shown in red (blue). (C). A network visualization of the DDI found in Indianapolis; nodes are drugs (size denote the probability of interaction; color their class); edges weights represent the DDI association strength; edge color the gender associated risk.

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