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Epistasis on Networks: Genetic Interactions and Network Reliability

Abstract of oral presentation

The biochemical and molecular mechanisms underlying epistatic phenomena observed in various living organisms are poorly understood. *Epistasis*, or *genetic interactions*, refers to functional relationships between genes. It describes the phenotypic effect of perturbing (e.g., knocking down or knocking out) two genes separately versus jointly relative to the unperturbed system. Thus, epistasis is a property of the underlying network of biochemical interactions in the cell. Interacting biological or biochemical entities are often represented as networks (or graphs), where vertices correspond to components (e.g., genes, proteins, or metabolites) and edges correspond to pairwise interactions (e.g., activation, molecular binding, or chemical reaction). This abstract representation provides the conceptual basis for network biology, which aims at understanding the cell's functional organization and the complex behavior of living systems through biological network analysis.

In this work, we introduce a mathematical framework linking epistatic gene interactions to the redundancy of biological networks. Our approach is based on *network reliability*, an engineering concept that allows for computing the probability of functional network operation under different network perturbations, such as the failure of specific components, which, in a genetic system, correspond to the knock-out or knock-down of specific genes. Using this framework, we provide a formal definition of epistasis in terms of network reliability and we show how this concept can be used to infer functional constraints in biological networks from observed genetic interactions.

In this talk, we will introduce the concept of epistasis on networks within the framework of probabilistic graphs. Furthermore, we will present some basic mathematical properties relating redundancy of the network under consideration and epistasis.

Moreover, we will demonstrate, using a concrete experimental data set ([2]), how our methodology can be used to infer functional and topological constraints in biological networks from observed genetic interactions.

Our formalism might help increase our understanding of the systemic properties of the cell that give rise to observed epistatic patterns.

References

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