

Graph Theory and Networks in Biology



Oliver Mason and Mark Verwoerd

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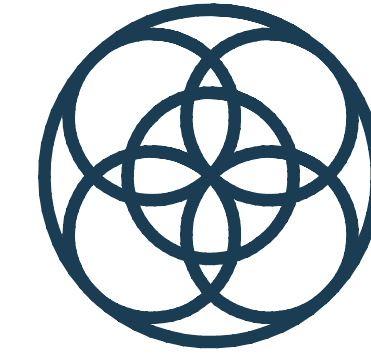
National University of Ireland, Maynooth

{oliver.mason,mark.verwoerd}@nuim.ie

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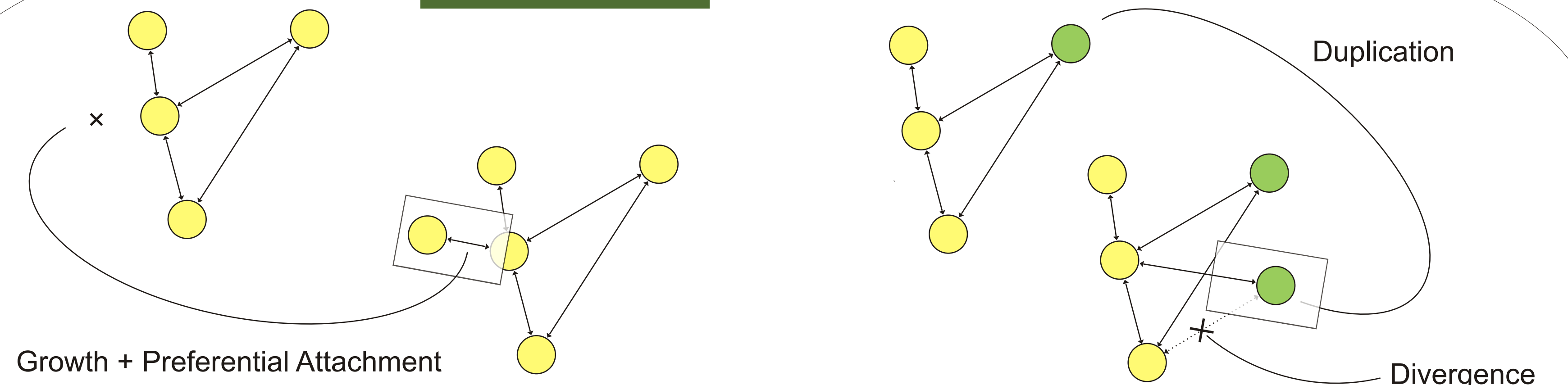
Introduction

There has been great interest recently in applying graph theoretical methods to the study of biological networks. At the level of bio-molecular interactions, metabolic, protein-protein interaction, and transcriptional regulatory networks have attracted the most attention. The large amount of data now available on such networks has led, on the one hand, to a need for systematic tools for their analysis. On the other hand, it has become clear that new models are needed to account for some of the novel properties observed in these networks. The general area of networked dynamical systems is of considerable relevance to several biological questions, with the phenomenon of synchronization and the mechanisms of disease spread being of particular importance.

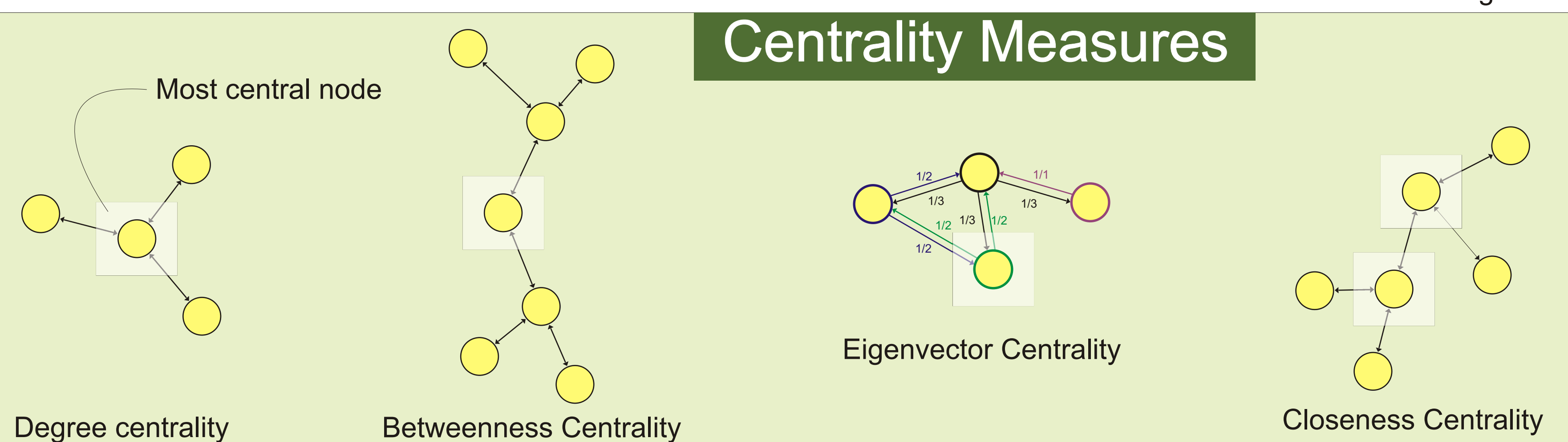
In this work, our aim was to survey the current state of the art in biological network analysis, summarising the key themes that have emerged and highlighting important directions for future research. In particular, we have focussed on the following broad areas:

- Identifying the structure of biological networks with appropriate graph theoretical measures and generating mathematical models to account for their observed properties;
- The use of centrality measures and other systematic techniques for predicting biological importance or essentiality;
- Determining the key building blocks or motifs in biological networks and investigating the modular structure of such networks;
- The role of network structure in synchronization;
- The impact of network structure on disease evolution.

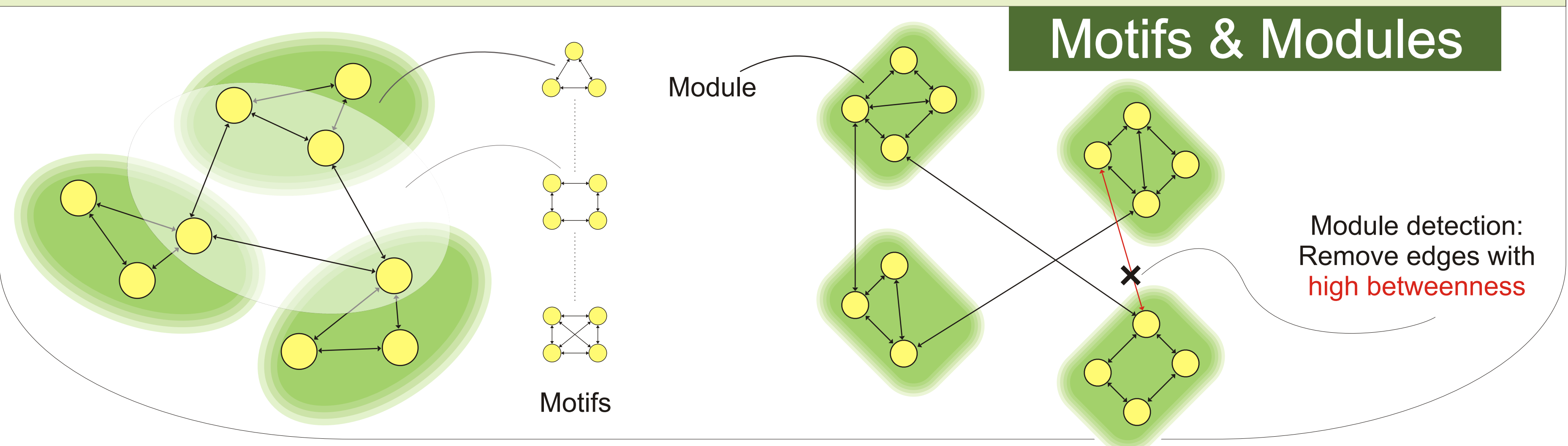
Models



Centrality Measures

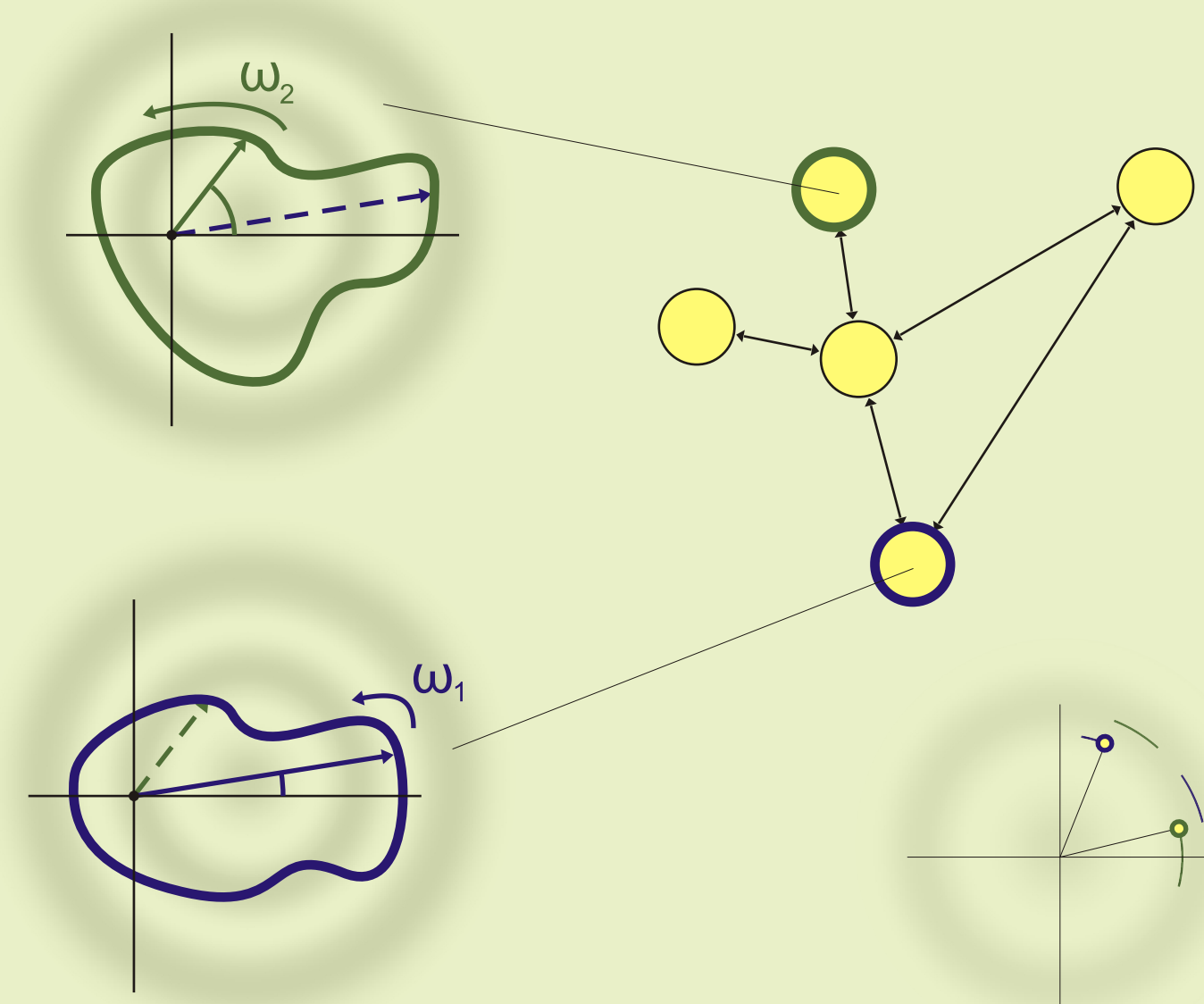


Motifs & Modules

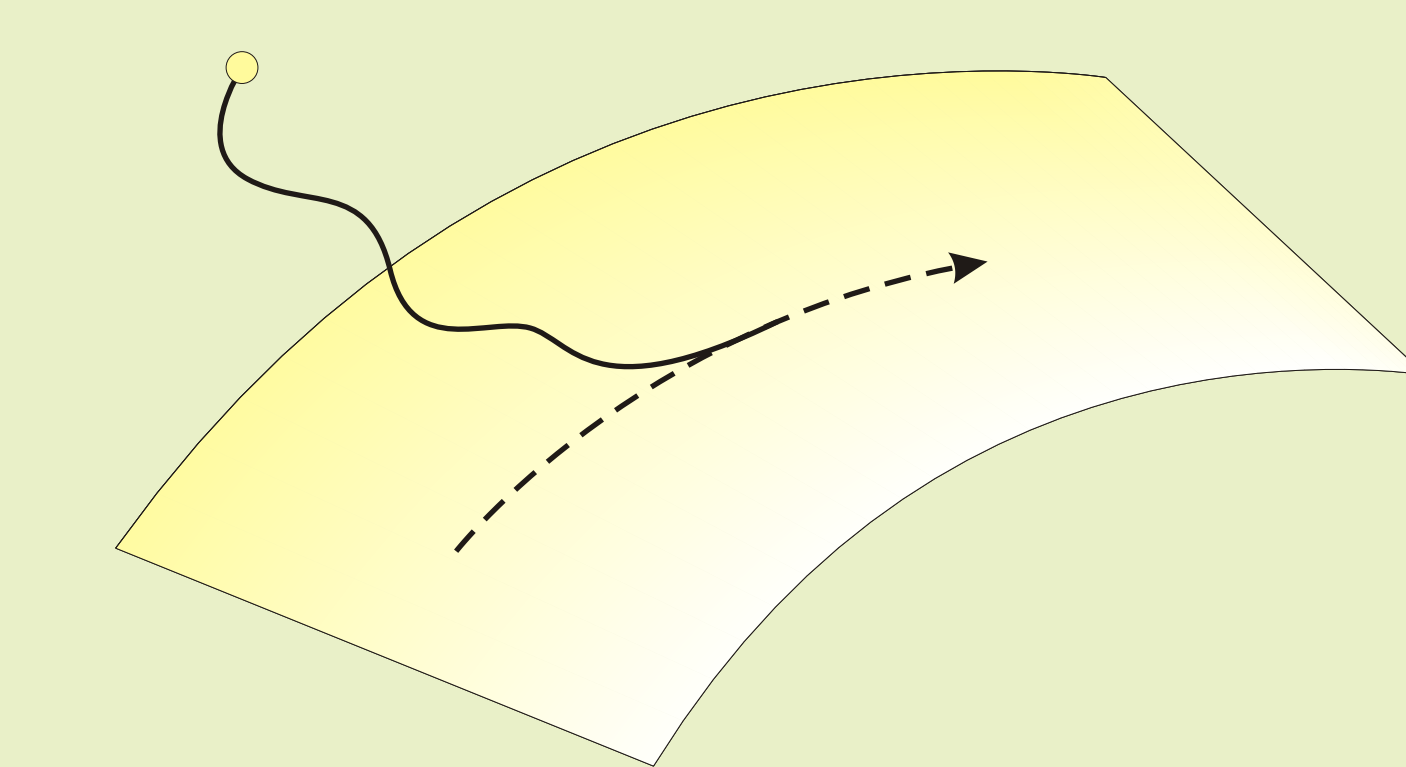


Full paper available at www.arXiv.org

Synchronization

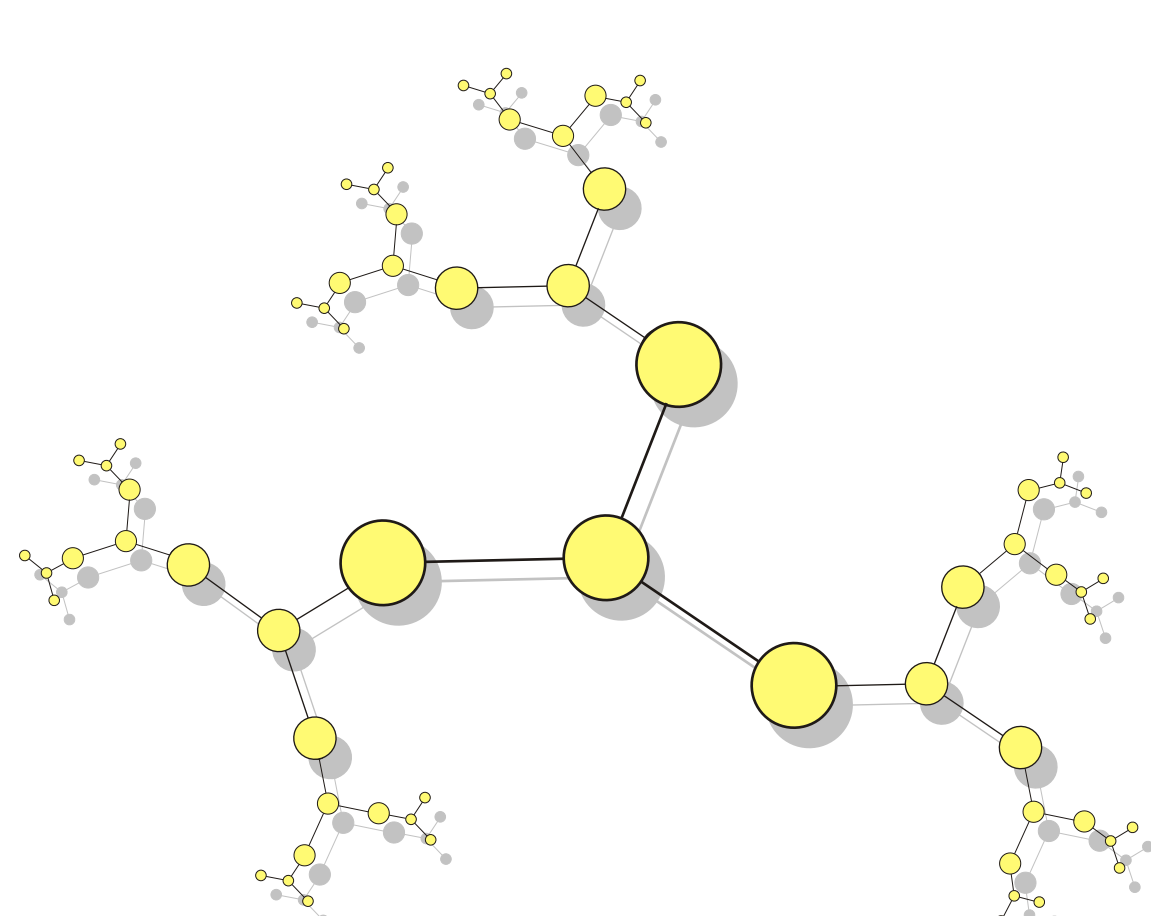


Kuramoto: synchronization of limit-cycle oscillators



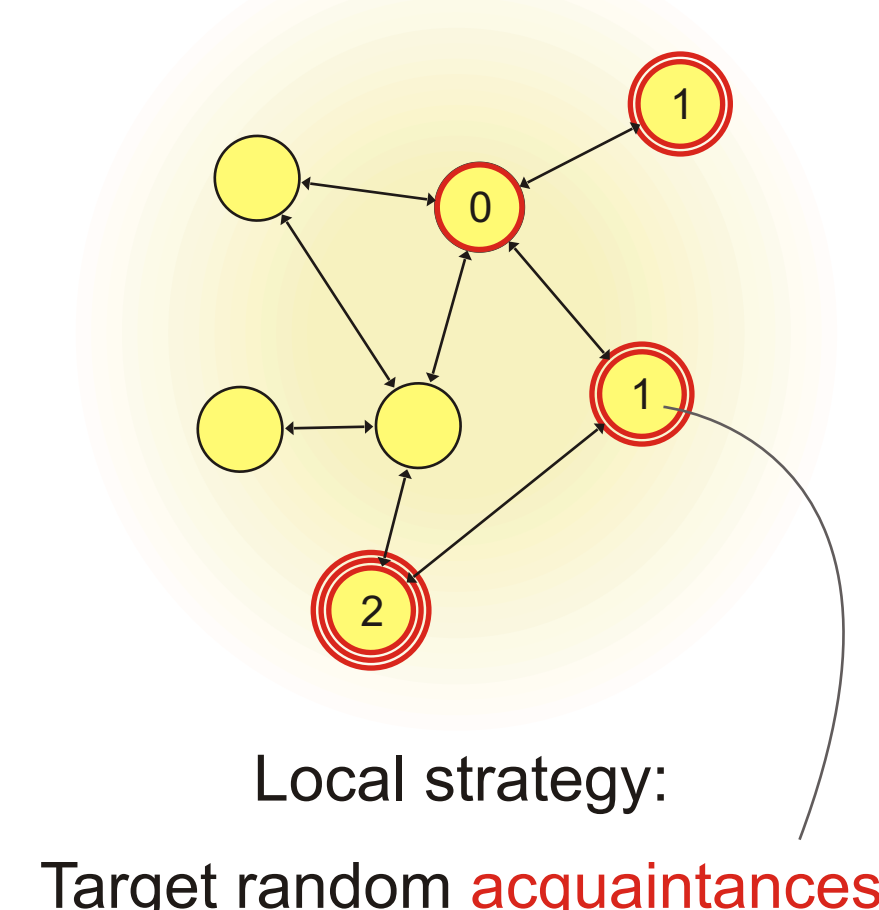
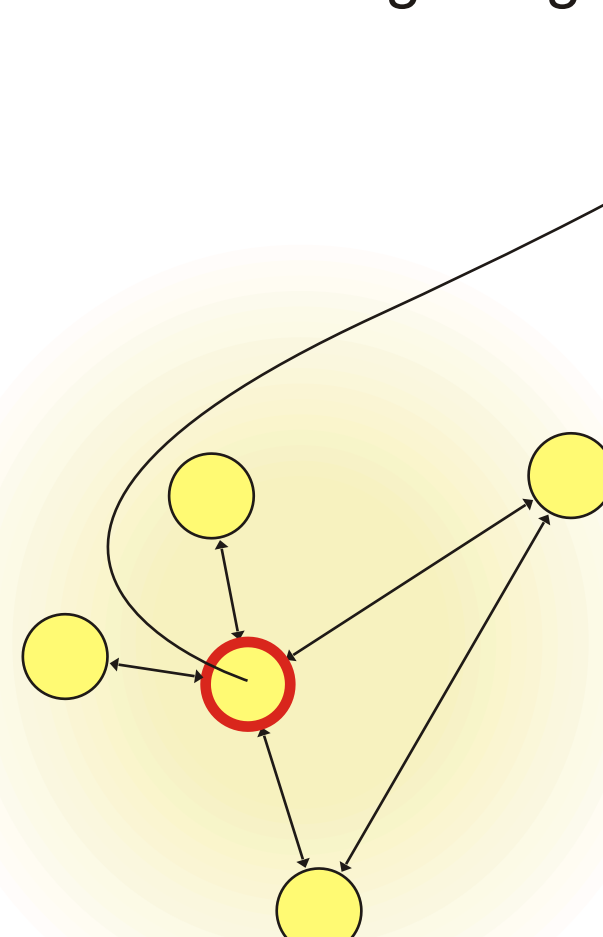
Master Stability Function:
When is the synchronization manifold stable?

Disease Spread



No Threshold for Epidemic Spread
in infinite scale-free networks

Global strategy:
Target nodes with high degree (hubs)



Local strategy:
Target random acquaintances

Conclusion

Biological network analysis is a fundamental aspect of the system-driven integrative approach to Biology. While the area is still at an early stage of development, several promising biological applications of graph theory have already emerged.

- Mathematical models of biological networks can be used to test the performance of algorithms in silico, give insights into the evolution of current networks and be used to design effective strategies for determining the interaction networks of higher organisms.
- The structure of interaction networks can be used to systematically predict the importance and possible function of proteins or genes.
- Identifying the motifs and modular structure of complex networks helps to simplify their analysis and provides insights into the structural and functional organisation of interaction networks.

Several key issues remain outstanding however, including:

- Improved experimental and statistical methods for the generation of network data are required. Much of the current data is still unreliable. Graph theoretical ideas can be used to design strategies for the construction of more reliable network maps.
- The impact of inaccurate and incomplete data on the identification and modelling of biological networks as well as on the various methods to draw biological conclusion from network data needs to be more fully understood.
- The extension of existing techniques for predicting protein function or essentiality to take into account dynamical and biological information (such as in Flux Balance Analysis) is desirable.