Identification of driver nodes in biological networks

Résumé du projet de recherche (Langue 1)

Complex networks are widely present in natural and man-made systems, highlighting the dominant role played by interconnections in forming and shaping the collective behavior of a system made by interacting units [1]. The traditional way to study complex systems is given by the reductionist approach, in which each component is analyzed separately [5]. The more recent theory of complex networks, a holistic approach, added to the picture the critical role of interactions. The idea to apply mathematical theory of control to complex networks is quite recent and different frameworks have been studied to this end, structural [2] and exact [3] controllability are the two main examples. The problem of network controllability is of critical importance from both a computational and a functional perspective, it enables a better understanding of complex systems and how to influence them to promote specific desired states (e.g., brain activity or gene expression). Two distinct teams of the Institut du Cerveau et de la Moelle Épinière (ICM) will collaborate in this project: "ARAMIS - algorithms, models and methods for images and signals of the human brain", which focuses mainly on the computational and mathematical aspects; and "Cellular and molecular approaches for myelin repair", whose central concern is the biological perspective. This project intends to develop methodologies from networks and control theory to study the controllability of both brain and molecular networks. In particular, will be of interest to analyze the case of systems in which it is not possible to suppose a linear temporal dynamics (e.g., for network built from the gene expressions of multiple individuals), to explore admissible target states and to study the structure of the input signal on the control nodes. The developed techniques will then be applied to data regarding both brain and molecular networks available from the ICM teams and from public large databases (e.g. Allen Institute [4]). The final goal is to characterize multimodal biological networks in both healthy and diseased (e.g., multiple sclerosis and Alzheimer's disease) subjects, identify statistically significant differences and develop predictive biomarkers. The broader impact of this project relies on the fact that it achieves a better understanding of both brain and genetic/molecular networks, developing computational models of activation or inhibition of network nodes that will help identifying potential disease-specific biomarkers or specific targets for therapeutic intervention.

Résumé du projet de recherche (Langue 2)

1) Development of analytical tools to identify driver nodes in complex networks: Control theory applied to complex systems is a quite new branch in network theory and it is not yet fully explored; the project intends to develop some theoretical aspects which remain poorly understood. In particular, the usual frame for these studies assumes that the system follows a linear temporal dynamics. This is a very restrictive hypothesis, for example, when the network is built from the gene expressions of multiple individuals. Another objective of the study is the target state: what configurations are admissible for the system and which structure should posses the input signal on the control nodes are interesting open questions. This project intends to develop methodologies from networks and control theory to characterize both brain and molecular networks with the ultimate objective of integrating the available knowledge and identify predictive biomarkers. 2) Application to biological networks, obtained from genetic and neuroimaging data in healthy and diseased subjects: Once validated, the developed tools will be applied to brain and molecular networks derived from neuroimaging and genetic data available at the ICM and from public large databases (e.g. Allen Institute [4]). In particular, this project will focus on raw data collected from healthy and diseased subjects (i.e., MS and AD). To build genetic networks, methods based on crosscorrelation can will be used for data of coexpression of genes [6]. Brain networks will be constructed by using structural and functional connectivity estimates from neuroimaging data such as Diffusion Tensor Imaging and fMRI [7]. 3) Statistical analysis of results and integration of the information from brain and molecular networks to evaluate the clinical potential: The project aims to collect statistics on driver nodes in healthy and diseased (i.e., multiple sclerosis MS and Alzheimers disease AD) subjects and integrate them statistically to obtain more robust biomarkers of MS and AD. Differently from gene expressions collected post-mortem from the brain (e.g., the Allen Institute for Brain Science database [4]), this project will access genetic expression from samples of blood, thus making it possible to examine both healthy and diseased subjects. The project expects to identify sets of biologically and functionally defined markers (predictive biomarkers) that will be further validated for clinical purposes (diagnostics). The information obtained will then be analyzed from a statistical perspective in order to rank importance among driver nodes across different configurations. The importance of this project relies on the fact that it achieves a better understanding of both brain and neural networks, developing computational models of activation or inhibition of network nodes that will help identifying...
The PhD project will be realized in the Inria ARAMIS team “Algorithms, models and methods for images and signals of the human brain” at the Institut du Cerveau et de la Moelle (ICM) in Paris. Key interactions with other national and international teams working on complex networks are envisaged in the course of the PhD project.

Informations complémentaires (Langue 2)