MSc in Bioinformatics for Health Sciences

CSB. Computational Systems Biology

Syllabus Information

Academic Course: 2018/19

Academic Center: 804 - Official Postgraduate Programme in Biomedicine

Study: 8045 – Bioinformatics for Health Sciences - MSc

Subject: 30180 – CSB. Computational Systems Biology

Credits: 5.0

Course: 1st

Teaching languages: English

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Teaching Period: 3rd term

Presentation

The living body is composed of numerous subsystems, large and small, by which the flows of energy, material and information are controlled. During embryogenesis a multicellular organism emerges from a single cell which divides a finite number of times, in a spatially and temporally ordered way, to generate an ensemble of different cells. -What are the elements that define the different type of cells? -Where do the instructions for the processes lie? -What is the language of those instructions? The sequence of the genome contains some of the information to build an organism but this information is very limited. Genes encode proteins and carry information that determines when and where these proteins are made. However, genes do not contain the information that determines how the proteins will assemble, or when, or where and how they will be active. These pieces of information lie in the proteins themselves, which assemble into functional and regulatory networks. This is a hierarchical system involving subsystems such as metabolism, transcriptional control, signal transduction, cell cycle, and apoptosis at the cell level, though all of these in turn are implemented as subsystems of interacting molecules. At a higher level, populations of cells are the subsystems of various physiological and pathological systems, organ systems, up to the body level.

Traditional study of biological systems requires reductive methods and has generated huge quantities of data in the last decades. In parallel with the data-driven research approach that focuses on speedy handling and analyzing of the huge amount of data, a new approach called ‘model driven research’ is gradually gaining power. Model-driven

research takes the approach that sets up a biological model by combining the knowledge of the system with related data and simulates the behaviour of the system in order to understand the biological mechanism of the system. It is simply called, "Systems Biology". Systems Biology aims to model and simulate the various subsystems and their interactions with one another, for the better understanding of life mechanisms. Biology (including molecular biology) has relied on qualitative and verbal modes of reasoning and explanation, but the human brain cannot be relied upon to model such complex systems intuitively.

Computational Systems Biology demands that all premises in the explanation are made explicit, modes of interaction of components are given a functional form, and the evolution of the system behaviour simulated on this basis. Computational systems biology, defined in Wikipedia as the algorithm and application development arm of systems biology, is also directly associated with bioinformatics and computational biology and aims to develop and use algorithms, databases and communication tools to facilitate the integration of large quantities of biological data with the goal of modelling dynamic characteristics of the biological systems. Computational systems biology projects are going on in different laboratories around the world and models can include for example steady-state metabolic flux or the time-dependent response of signalling networks. Algorithmic methods used in these projects require basic concepts on topics such as optimization, network analysis, graph theory, linear programming, grid computing, flux balance analysis, sensitivity analysis, dynamic modelling, and others that will be presented in the different lectures in this course.

Many important software projects in computational systems biology are developing two important markup languages for systems biology, which are the Systems Computational Systems Markup Language (SBML) and CellML.

In previous subjects of this Master several simulation techniques have been already introduced. In this Computational Systems Biology course knowledge on simulation techniques will be expanded and applied to the modelling of biological systems.

This subject is centered in the understanding of the translation of a biological problem into a mathematical frame to construct models of i.e. metabolic or signalling networks that permit to answer relevant biological and biomedical questions. Modelling of networks of cellular processes will permit to understand its regulation and to design new therapeutic strategies in multifactorial complex diseases such as cancer.

As this is a completely incremental subject, the student is advised of the need of strong interaction with the lecturers and the need of keeping the class material up to date.

Associated skills

General competences

Elements of biology and biochemistry: basic concepts on biochemical network, basic concepts on enzyme kinetics and main metabolic pathways, basic concepts on signalling cascades, basic concepts of gene regulation and expression

Basic concepts on enzyme kinetics

Knowledge of software for modelling biochemical networks

Ability to implement simple dynamical models in a computer program

Concepts of gene regulation

Concepts of network biology

Interpersonal:

1. Ability to solve by yourself a given problem

Systemic:

1. Analysis and synthesis abilities
2. Ability to search for information

Specific competences

1. The system's concept. To understand the concept of biological networks. Levels of organization and description of networks.
2. To know different modes of gene regulation.
3. To understand and implement the concept of positive and negative interaction between genes and understand the concept of gene regulatory networks.
4. To understand the different types of dynamical behavior exhibited by biological networks.
5. To get basic user knowledge of some of the systems biology software tools.
6. To know the basic concepts on enzyme and enzyme kinetics (Michaelis Menten equation).
7. To know basic concepts on metabolism and main metabolic.
8. To understand basic concepts of metabolic network regulation and control.
9. To know how to integrate omics data into genome scale metabolic models.

Contents

Contents section 1: Basics in modelling and kinetics

1.1. Introduction to systems biology and modelling

1.2. Introduction to enzyme kinetics

1.3. Tools to define reaction rates expressions

1.4. Introduction to modelling of simple biological networks

Contents section 2: Computational Systems Biology approach to modelling metabolic networks

2.1. Introduction to metabolic control analysis (MCA)

2.2. Modelling of biological networks using Copasi

2.3. Analysis of control in biological networks using MCA and Copasi

2.4. Introduction to constraint-based modelling using Flux Balance Analysis (FBA)

2.5. Introduction to analysis on genome-scale metabolic networks

Contents section 3: Computational Systems Biology approach to modelling gene regulatory networks

3.1. Principles of gene regulatory networks (GRN)

3.2. Concepts on dynamical behaviour of gene circuits

3.3. Switches, multistability, feedback regulation, sensitivity to kinetic parameters, robustness

Contents section 4: Network biology

4.1. The network abstraction. Basic definitions and issues in converting empirical data into networks (thresholding, time windows, etc.).

4.2. Basic statistical properties of networks (average path length, clustering, degree distribution) and elementary models of them (Erdos-Renyi, Watts-Strogatz and Barabasi-Albert networks).

4.3. Robustness of networks. Understanding robustness. Comparison of scale-free and exponential random networks. Robust networks from optimisation.

4.4. Dynamic processes on networks (cf. cascades on networks). Basic models and lessons from them.

4.5. Dynamic networks. Processes that result in networks. The consequences of link-maintenance costs. Advanced network concepts.

Teaching methods

Approach and general organization of the subject

All sessions of this course, except for the one about the introduction to systems biology and the one about metabolic control analysis, are “hands-on” using a computer. The subject is organized into the four blocks described above, divided in different days.

Training activities

The students are expected to follow the mathematical and computational approaches described in each block of the subject, solving exercises, some of them together in class and others by themselves outside the classroom, that are intertwined throughout the slides. Some exercises will be delivered at the end of each block that will be used to evaluate if the student has consolidated the concepts illustrated during the subject.

Evaluation

Assessment system:

- Attendance to classes (minimum 80% of attendance is mandatory to be evaluated).

- Interest and participation in class.

- Class and home work/exercises.

Grading system:

Evaluation of the understanding of enzyme kinetics (25% of the total grade)

Evaluation of the understanding of control and regulation of metabolic networks (25% of the total grade)

Evaluation of principles of gene regulatory networks (20% of the total grade)

Evaluation of the understanding of topological features in biological networks (20% of the total grade)

Work performed in the hands on session, capacity in answer questions done for teachers and lecturers during the theoretical and hands on session, degree of participation in the classes asking questions and participating in scientific discussions and capacity to solve the exercises proposed. (10% of the total grade)