UNIVERSITÀ
DEGLI STUDI DI MILANO-BICOCCA

COURSE SYLLABUS

Computational Systems Biology

2324-1-F0802Q068

Aims

The course will present the main modeling frameworks and computational methodologies in the field of Systems Biology, and provide the necessary theoretical basis to integrate the biological knowledge with mathematical and informatics methods, including artificial intelligence algorithms. The main goal of the course consists in developing the critical capability of the student to understand the application of multidisciplinary approaches in Biology. Several examples taken from the literature will be presented for the investigation of intracellular processes (e.g., gene regulatory networks, metabolic networks, signal transduction pathways, etc.), multicellular systems, onset and progression of multifactorial diseases.

*Knowledge and understanding
The student will gain knowledge about the critical and logical capability to choose the proper modeling approach for any kind of complex biological system under investigation, and to critically discuss the limits and advantages of each modeling approach and computational method.

*Applying knowledge and understanding
The student will be able to apply the knowledge previously listed for the analysis of complex biological systems.

*Making judgements
The student will be able to process the acquired knowledge and choose the proper modeling/computational methods for the analysis of complex biological systems.

*Communication skills
Use of an appropriate scientific vocabulary and ability in oral/written reports.

*Learning skills
Skills in literature reading and understanding, as well as in the elaboration, analysis, and application of the acquired knowledge in other courses related to the study of complex biological systems.

Contents

Introduction to modeling, simulation, and analysis of complex biological systems.
Introduction to artificial intelligence and machine learning.
Interaction-based models.
Logic-based models.
Constraint-based models.
Mechanism-based models.
Computational methods for the simulation and analysis of mechanism-based models.
The concept of robustness of biological systems.

Detailed program

Introduction to modeling, simulation, and analysis of complex biological systems. The notion of complex system. Temporal and spatial complexity scales for the analysis of biological systems. General guidelines for the selection of the modeling approach. The iterative cycle of data-driven model definition, simulation, and analysis in Systems Biology. Basic notions for model definition: system structure, level of abstraction, the goal of modeling. Dichotomies in Systems Biology. Overview of modeling approaches: critical discussion about limits and strengths of each modeling framework. Introduction to the main modeling approaches in Systems Biology: interaction-based models, logic-based models, constraint-based models, mechanism-based models.

Artificial intelligence and machine learning.
Disambiguation: is there any difference between artificial intelligence and machine learning? The concepts of feature, training, validation, test, metrics, overfitting, interpretability. Comparison among supervised, unsupervised and reinforcement learning methods. Applications in biomedical research.

Interaction-based models. Basic notions of graph theory. Graph-based computational methods for the analysis of large-scale biological networks: the concepts of degree distribution, clustering coefficient, hub. Topological features of biological networks: differences among random, scale-free and hierarchical networks. The concepts of preferential attachment and modularity in the development of biological networks. Topological robustness of biological networks. Discussion about published interaction-based models (gene regulatory networks, protein-protein interaction networks, etc.).

Logic-based models. Basic notions of Boolean and fuzzy logic. Main features and analysis methods of logic-based models (attractors, cycles, system dynamics). Discussion about published logic-based models (gene regulatory networks, cell death models, etc.).

Constraint-based models. Basic notions of linear algebra and linear programming for the definition of constraint-based models (metabolic networks, from “toy/core” models to “genome-wide” models). Computational methods for the analysis of constraint-based models: flux balance analysis. Discussion about published constraint-based models.

Mechanism-based models. The notion of dynamical systems. Definition and differences between deterministic, stochastic and hybrid approaches. Reaction-based models. Deterministic approach: systems of ordinary differential equations. Simulation methods for deterministic models: Eulero and Runge-Kutta numerical integrators. Stiff systems and adaptive algorithms. Stochastic approach: physical background, fundamental hypothesis, Chemical Master Equation. The concept of biological noise: intrinsic and extrinsic noise. Effects of biological noise: switching and bistability. Simulation methods for stochastic models: Gillespie’s stochastic simulation algorithm. Hybrid and spatial models. Discussion about published mechanism-based models (signal transduction pathways, cell cycle, etc.).

Computational methods for the simulation and analysis of mechanism-based models. Definition and

importance of model parameters. Computational problems related to data measurements. The notion of optimization problem. Introduction to evolutionary computation methods for the solution of optimization problems related to biological systems. Computational methods for parameter sweep analysis, parameter estimation, sensitivity analysis.

The concept of robustness of biological systems. Relationships between robustness and parameters.
Principles of robust systems: control mechanism, fail-safe mechanism, modularity. Robustness and evolution: the concept of bow-tie architecture. An example of a robust complex biological system (cancer) and discussion about the computational challenges in the study of cancer.

Prerequisites

Background. No particular background in mathematics or computer science is required to attend the course: all preliminary concepts will be explained to understand the topics presented in each lecture.
A strong curiosity and open-mindedness in learning and studying Biology from an innovative perspective are essential, as well as the willingness to actively participate during lectures and to critically discuss the course topics with both the professor and classmates.

Prerequisites. None.

Teaching form

Classroom lectures (35 hours, 5 ECTS) supported by slides.
Classroom teamwork on modeling of biological systems and hands-on sessions on pc for the use of Systems Biology software (10 hours, 1 ECTS).
Tutorials on specific topics (6 hours).

Teaching language: English, upon request by at least 10% of attending students.

Textbook and teaching resource

Slides. All educational material will be available at the e-learning platform of the course.

Textbooks.

- E. Klipp, W. Liebermeister, C. Wierling, A. Kowald. Systems Biology: A Textbook. 2nd Ed. Wiley, 2016.
- E.O. Voit. A first course in Systems Biology. Garland Science, 2017.
- Z. Szallasi, J. Stelling, V. Periwal. System modeling in cellular biology. The MIT Press, 2006.

Semester

First semester.

Assessment method

Written examination (3 hours): 3 open questions concerning any topic of the program.
Non-mandatory oral examination (around 30 minutes): seminar (slide presentation + critical discussion) about a published research paper in Computational Systems Biology.

No mid-terms exams will be scheduled.

Office hours

Contact: on demand by email request to the lecturer.

Sustainable Development Goals

GOOD HEALTH AND WELL-BEING | QUALITY EDUCATION | INDUSTRY, INNOVATION AND INFRASTRUCTURE