UNIVERSITÀ
DEGLI STUDI DI MILANO-BICOCCA

COURSE SYLLABUS

Analysis, Control and Optimization of Biological Systems

2223-1-F0802Q079

Aims

The course aims to train students in the analysis of biological systems in their most generic and broad sense (networks of biochemical reactions, metabolic and transcription networks, single cells or populations dynamics), to give them the basis for their control and the methods of parametric identification.

Knowledge and understanding.
At the end of the course, students will be able to obtain quantitative and qualitative information on the behavior of biological systems through qualitative analysis and simulations of the mathematical models that describe them. The tools for the numerical simulation in MATLAB of the studied biological systems will also be given.

Ability to apply knowledge and understanding.
At the end of the course, students will be able to apply the acquired methodologies to complex biological systems of various kinds, not necessarily covered in class

Autonomy of judgment.
Students will be able to re-elaborate and apply the most appropriate analysis methodologies learned, according to the biological contexts investigated.

Communication skills.
At the end of the course, students will be able to express themselves appropriately in the description of the topics addressed with properties of language and confidence in exposure.

Learning ability.
At the end of the course, students will be able to analyze, apply, integrate and connect the knowledge acquired - and subsequently matured with the consultation of the literature - with what they have learned in related courses, in order to solve scientific problems in Biological Sciences and Biotechnologies.

Contents

This course provides methodologies for the analysis, identification and control of specific computational models of biological systems. The methodologies can be divided into 3 main categories: (i) qualitative analysis (what are the emergent properties of a system?); (ii) quantitative analysis (how can I simulate the computational model of a biological system?); (iii) control (what control mechanisms are apparent in nature? What kind of specifications can I meet in a control system for biological systems?)
The examples of the course will deal with different biological contexts, including transcription networks, metabolic networks, cell cycle and growth models, epidemic spreading models. Most topics will be analyzed through multidisciplinary analysis of specific case studies. One or more of the case studies will also be anlyzed in the course Systems Biochemistry with a complementary biological, biochemical and molecular perspective

Detailed program

- System definition. Input/output relationships: a biological system is characterized by the richness of laboratory experiments. State/inputs/outputs of a system. Discrete-time and continuous-time systems. Deterministic and stochastic systems. Stationary systems. Discrete and continuous systems. Linear systems. Implicit and explicit models. Free and forced evolution. Regime and transient response.
- Analysis of the qualitative behavior of a system. Equilibrium points, stability and multi-stability. Exponential growth. Bifurcations, oscillations and limit cycles. Chaotic behaviors. Examples on models of transcription networks, enzymatic reactions, cell growth, spread of epidemics.
- Systems identification. Estimating model parameters. Least squares and recursive least squares approaches. Mean and covariance of the estimation error. Minimum variance and maximum likelihood estimates. Akaike index. Case study: integration of kinetic, metabolic and proteomic data for the identification of a metabolic network.
- Simulation of models of biological systems. Deterministic systems and stochastic fluctuations: probability distributions, and first/second order moments for Chemical Master Equations. Examples on transcription networks and enzymatic reactions. Double time scale. Constrained-based models. All simulations will be carried out in MATLAB environment.
- Control of biological systems. Feedback control mechanisms existing in nature (negative self-regulation in transcription networks, optimal expression of genes, glucose-insulin regulation system, metabolic engineering). Feedback regulation schemes: applications to biochemical reactors. Data integration in constrained-based models to identify checkpoints in a metabolic network.

Prerequisites

No specific knowledge of mathematics other than those already acquired in the basic courses of a three-year degree in Biological Sciences or Biotechnology is required.

Teaching form

Frontal lectures and exercises in the classroom
Hands-on sessions on pc for the interactive case studies

Textbook and teaching resource

The slides and MATLAB codes developed at lessons will be available on the e-learning page of the course. Further review articles and book chapters will be recommended in class and uploaded to the e-learning platform of the course

The following texts are recommended for appropriate further information:

- U. Alon, An introduction to systems biology: design principles of biological circuits, Chapman & Hall/CRC, Taylor & Francis Group, 2019
- E. Klipp, W. Liebermeister, C. Wierling, A. Kowald, Systems Biology – A textbook. 2nd Ed. Wiley, 2016

Semester

Second semester

Assessment method

Students will discuss a scientific paper, previously given. Besides, oral questions on the programme

Office hours

Students are invited to contact the teacher by email to agree upon a date (also on WebEx)

Sustainable Development Goals

GOOD HEALTH AND WELL-BEING