General Information	MASTER DEGREE IN BIOTECHNOLOGIES
Title of the subject	Modelling of biological systems
Degree Course (class)	Industrial and Environmental Biotechnology (LM-8)
ECTS credits	6
Compulsory attendance	Yes
Language	Italian or English
Academic year	2020-2021

Subject Teacher	
Name and Surname	Fabio Mavelli
email address	fabio.mavelli@uniba.it
Place and time of reception	➢ In presence: Office - room 132 – 1st floor – Chemistry Department – University Campus. ➢ Online: Microsoft Teams Web Site By appointment fixed by email From Monday to Friday 9.00-13.00 and 16.00-19.00

ECTS credits details	Discipline sector (SSD)	Area
	CHIM/02	---

Study plan schedule	Year of study plan	Semester
	1	2

Time management	Lessons	Laboratory	Exercises	Total
CFU	4	2		6
Total hours	100	50		150
In-class study hours	32	24		56
Out-of-class study hours	68	26		94

Syllabus	
Prerequisites / Requirements	Basic knowledge of mathematics, Course of Mathematical Analysis: ordinary and partial differential equations, integral calculus, matrix algebra. Notions of chemical thermodynamics
Expected learning outcomes (according to Dublin descriptors)	
Knowledge and understanding	The course aims to provide knowledge and skills to use modeling as a tool for the study of a metabolic network and for the analysis and development of an industrial process.
Applying knowledge	Address the problems associated with the development of models that allow (a) a better understanding of the complex metabolic network of a cell / organism and (b) predictions related to the change of the network itself, obtained by recombinant DNA techniques or due to changing conditions operational.
Making informed judgments and choices	The students of this course will acquire the ability to independently evaluate the most appropriate approach and techniques to model a

	biological system in terms of costs and results, in relation to an objective of specific interest.
Communicating knowledge	The students of the course will acquire a technical language and the skills to discuss the more suitable modeling approach with experts in the sector also from other disciplinary areas such as mathematicians and / or computer scientists.
Capacities to continue learning	Students will develop learning and in-depth skills and will be able to orient themselves in specific literature. They will be able to critically assess the objectives, costs, technical difficulties, applicability and scope of validity of models in the biological field
Study Program	
Content	Introduction to the modeling of biological systems: holistic and reductionist approach. Chemical Kinetics Reaction mechanism, Reaction rate, stoichiometric equation, Mass action law, Kinetic systems of ordinary and partial differential equations, Autonomous systems, Arrenhius' Law - Formal Kinetic Analysis Construction of the ODE set from the reaction mechanism, Direct Integration, Matrix Method for first-order systems, Approximate Methods, Numerical Methods. - Empirical Kinetic Analysis Kinetic equation, Direct integration method, Differential method, Fractionation time method, Isolation method, Initial velocity method - Study of the Equilibrium Points of ODE systems General notation for the representation of kinetic ODE systems, stoichiometric matrices, velocity vector, points of equilibrium and linear stability analysis, oscillating systems. - Stationary states of biochemical networks. Metabolic maps: pathways and networks, the cell: an open and compartmentalized reacting chemical system - Flux Balance Analysis (FBA) Stoichiometric analysis of metabolic networks and conservation relationships. Stoichiometric matrix. Degrees of freedom of the system. Underdetermined and overdetermined systems. Constraints on flows. Optimization of functions: linear programming. - Metabolic Control Analysis (MCA). Basic definitions: coeff. control, elasticity, coeff. response. Sum (proof) and connectivity theorem. Application of MCA to linear and branched reaction chains. - Stochastic Models Introduction to Stochastic Kinetics. Review of probability theory: Markov processes. Probability of Reaction and Master Equation. Monte Carlo simulation methods: the Gillespie method. The role of stochastic fluctuations: exponential decay, the Lotka-Volterra oscillating system. - Review of Mathematics Hints of matrix algebra, differential and integral calculus, series expansion of functions - Matlab Computing Laboratory Introduction to the Matlab environment, matrix calculation, graphical representation of functions, hints of programming.

	Numerical integration of ODE systems, implementation of programs: for the solution of first-order ODE systems with the method of matrices, and of any ODE system with a method of numerical integration. Empirical analysis of simulated data for the determination of an unknown reaction mechanism. Construction of a cellular model of a simplified metabolic pathway, FBA analysis of the model, calculation of control coefficients and verification of the sum theorem
Bibliography and textbooks	System Biology. E. Klipp, W. Liebermeister, C. Wierling, A. Kowald, H. Lehrach. Wiley-Backwell Understanding the control of the metabolism. D. Fell, Protland Press. Lecture notes
Notes to textbooks	The handouts are exhaustive on the course contents, while the proposed textbooks can be used for in-depth analysis regarding specific topics together with scientific articles and web contents as indicated by the teacher.
Teaching methods	Lessons will be conducted with the aid of projection of lecture notes in multimedia format. For each lesson, there is a computational laboratory activity to put into practice the principles and techniques of calculation presented during the frontal explanation. At the end of the course, each student will have developed computational tools for modeling complex reagent systems. The didactic material discussed in class can be downloaded by the students from the teacher page on the website http://puccini.chimica.uniba.it/~mavelli/Didattica/BioTec/
Assessment methods (oral, written, ongoing assessment)	Oral exam, with ongoing tests at the request of the students
Evaluation criteria (describe criteria for each of the above expected outcomes)	Through the scheduled oral interview, the student is expected to be able to critically tackle with technical language a modeling problem of a chemical / biological system from the point of view of its temporal evolution or in a condition of stationarity / homeostasis. In particular, for a chemical system the student must show that he is able to: - translate a kinetic mechanism into a system of differential equations (ODE set); - test or solve the ODE system analytically, making plausible approximations or propose a suitable numerical integration method. - know how to study the system in stationary conditions; - discuss the difference between a deterministic or stochastic descriptive approach. Regarding a biological system, it must be able to: - build a detailed dynamic model in terms of an ODE system starting from the metabolic map; - convert the metabolic map into the stoichiometric matrix and study the system in stationary conditions according to the principles of Flux balance Analysis (FBA), obtaining the degrees of freedom of the system.
Further information	