Universitat de les Illes Balears

Teaching guide

Subject identification

Subject	11010 - Systems Biology
Credits	0.76 de presencials (19 hours) 2.24 de no presencials (56 hours) 3 de totals (75 hours).
Group	Group 1, 2S
Teaching period	Second semester
Teaching language	English

Professors

Lecturers	Horari d'atenció als alumnes					
	Starting time	Finishing time	Day	Start date	Finish date	Office
Manuel Alberto Matias Muriel	You need to book a date with the professor in order to attend a tutorial.					

Contextualisation

INSTRUCTOR

Manuel Matias holds PhDs in Chemistry (1990) and Physics (1997) and has five 6-year terms ("sexenios") recognized by ANEP. Although his recent research is in Nonlinear Dynamics (Bifurcation Theory, Synchronization, ...), in the last years he has become interested in the quantitative description of some collective phenomena in Cell Biology from the viewpoint of Systems Biology.

COURSE

This is an optional course of the Structural Module of the master of Physics of Complex Systems. The goal of the course is to look at a few general principles of Molecular and Cellular Biology from the viewpoints of Physics and Engineering in order to provide a quantitative framework to these systems and how their constituent elements interact.

Molecular Biology has made Biology advance at an exhilarating pace in the last 50 years. The knowledge acquired has led to a very large amount of data, particularly from genome sequencing and high-throughput measurements, that allow to gain information on the role performed by the relevant molecules, genes and proteins. This may lead to the point that one cannot see the forest for the trees, and, so, a Systems approach is more necessary than ever before. System-level understanding requires a shift in what to see, from the intervening molecules to the understanding of system's structure and dynamics. It is important to realize, that as a system cannot be fully understood merely by drawing diagrams of its interconnections, a biological system is not just an assembly of genes and proteins, that is like listing all the parts of an airplane.

A system-level understanding of a biological system needs insight at different levels:

1) System structures, that include the network of gene interactions and biochemical pathways.

2) System dynamics, how a system behaves over time under various conditions, that includes the analysis from the point of view of dynamical systems (phase space, bifurcations, ...)

3) The control method, mechanisms that systematically control the state of the cell.

4) The design method, strategies to modify and construct biological systems having desired properties can be devised based on definite design principles and simulations, instead of blind trial-and-error.

Once the network structure and its functional properties are understood for a large number of regulatory circuits, studies on classifications and comparison of circuits will provide further insights into the richness of design patterns used and how regulatory circuits have been modified or conserved through evolution.

The system perspective leads to the appreciation of more general features, like robustness (that is an essential property of biological systems) related to adaptativity (ability to cope with environment changes), parameter insensitivity (and thus resilience) and also the fact that they exhibit a graceful degradation (that reflects the characteristic slow degradation of systems function under damage, rather than catastrophic failure). They also appear to maximize the balance between cost and benefit (that can be understood as a fitness optimized by evolution),
These general properties cannot be grasped from the understanding of particular features at the molecular level, as they involve system wide properties.

In essence, from a Physics perspective, Systems Biology amounts to the macro description of a system in which a micro description can be worked out using the powerful tools of Molecular Biology. The process is not a a mere aggregation and averaging of the micro level, but the description of the new (emergent) laws and properties characteristic of the macro scales (as is the emergence of robustness). Here the micro level corresponds to the detailed kinetic description of the intervening molecules (genes, mRNA, proteins, etc.), while the macro level may be a whole cell, but also a tissue, etc., and where one could always define a meso level (organelles inside a cell, cells when describing a tissue, etc.)

Requirements

Recommendable

A working knowledge at the level of the course "Dynamical Systems and Chaos" and a basic knowledge of the course "Complex Networks" of this Master are highly recommended.

Skills

This course develops both specific and generic competences.

Specific

* E8: To know to characterize generic behavior of dynamical systems and their instabilities..
* E11: To know how to apply dynamical systems techniques to physical, chemical, biological and social systems..
* E15: To understand the main concepts and techniques of complex networks..

Generic

* TG1: To be able to describe, both mathematically and physically, complex systems in different situations.
* TG2: To acquire the capacity to develop a complete research plan covering from the bibliographic research and strategy to the conclusions..
* TG3: To be able to write in a clear, precise and rigorous way the different steps of the research process and to present the results to an expert audience..

Basic

* You may consult the basic competencies students will have to achieve by the end of the Master's degree at the following address: http://estudis.uib.cat/master/comp_basiques/

Content

The goal of this course is to offer an introduction to the emerging field of Systems Biology. Systems Biology is a young highly interdisciplinary field among Biology, Biochemistry, Physics, Engineering, etc. that aims to bridge between areas disconnected in the past like Molecular Biology and Genetics on the one hand and Cell and Tissue Biology, Embryology, etc. by integrating detailed microscopic information at the level of genes, proteins, etc. into macroscopic level descriptions of cells, tissues, and organisms. One organizing idea is that of biological networks, that reflect how biological elements interact. Interestingly, these networks are highly modular, with a few elements that are used to build up the network. Biological systems are robust, exhibiting a high tolerance in their operational ranges, what excludes non-robust designs. They are also efficient systems from the point of view of cost vs. benefit.
All these general feature will be addressed with the goal of devising quantitative approaches, but, at the same time, of forecasting the overall qualitative behavior using key approximations in terms of logical operations.

Theme content

1. Introduction
   Introduction of the scope and approach of the course. Some basic biological concepts: DNA transcription and translation.

2. Transcription Networks
   Basic concepts: activators and repressors. Michaelis-Menten kinetics and Hill input functions. Elements of Transcription Networks. Dynamics of simple gene regulation.

3. Network Motifs I
   Autoregulation: negative and positive.

4. Network Motifs II
   Feed-forward loop gene circuits: coherent and incoherent. Single Input Modules. The Multi-Output Feed-forward Loop.

5. Network Motifs at work
   Developmental transcription networks. Signal transduction networks. Motifs for information processing: multi-layer perceptrons. Negative feedback and oscillator motifs.

6. Robustness of biological circuits
   An example: bacterial chemotaxis. Response and exact adaptation. Robust patterning and precision in Development.

7. Kinetic Proofreading
   Kinetic proofreading of the genetic code. Recognizing self and non-self by the immune system.

8. Optimal Gene Circuit Design
   Costs, benefits and fitness functions of biological circuits.

9. Demand Rules for Gene Regulation

Evidence of demand rules. The selection pressure for optimal regulation.

Teaching methodology

In-class work activities

Modality	Name	Typ. Grp.	Description	Hours
Theory classes	Theory classes	Large group (G)	Lectures explaining the theoretical concepts given by the professor.	17
Practical classes	Practical sessions	Large group (G)	Resolution of examples, problems, and questions.	1.5
Assessment	Oral presentation	Large group (G)	Each student will be given an individualized assignment that covers several of the topics of the course. Besides a written report, the student has to give an oral presentation to the whole class.	0.5

At the beginning of the semester a schedule of the subject will be made available to students through the UIBdigital platform. The schedule shall at least include the dates when the continuing assessment tests will be conducted and the hand-in dates for the assignments. In addition, the lecturer shall inform students as to whether the subject work plan will be carried out through the schedule or through another way included in the Campus Extens platform.

Distance education work activities

Modality	Name	Description	Hours
Individual self-study	Exercises	The student has to solve exercises assigned and present the solutions in written form.	10
Individual self-study	Realization of the assignment	The student must solve the individual assignment, prepare a report and organize an oral presentation.	32
Individual self-study	Study and understanding theoretical concepts	This activity aims at the understanding of the theoretical concepts and techniques explained in the lectures	14

Specific risks and protective measures

The learning activities of this course do not entail specific health or safety risks for the students and therefore no special protective measures are needed.

Student learning assessment

The evaluation will be based on the homework (assigned exercises) and of the "small project" on a subject related to a recent topic already mentioned. The evaluation of the work carried out for the project will represent 75% of the final grade.

Oral presentation

Modality	Assessment
Technique	Oral tests **(non-retrievable)**
Description	Each student will be given an individualized assignment that covers several of the topics of the course. Besides a written report, the student has to give an oral presentation to the whole class.
Assessment criteria	Accuracy and quality of the work as well as the clarity in the oral exposition.

Final grade percentage: 20%

Exercises

Modality	Individual self-study
Technique	Papers and projects **(non-retrievable)**
Description	The student has to solve exercises assigned and present the solutions in written form.
Assessment criteria	Accuracy of the answers. Clarity and quality of the explanations.

Final grade percentage: 50%

Realization of the assignment

Modality	Individual self-study
Technique	Papers and projects **(non-retrievable)**
Description	The student must solve the individual assignment, prepare a report and organize an oral presentation.
Assessment criteria	Suitability of the introduction and motivation. Accuracy of the work. Clarity of the ideas and explanations. Relevance of the conclusions. Quality of the written report.

Final grade percentage: 30%

Resources, bibliography and additional documentation

Research on the topic taught in this course with this quantitative approach is quite recent (mostly from the present century). Still, we are fortunate in having the pioneering book that represents the basic bibliography of the course (that, hopefully, will see a new, updated edition soon). This will be complemented by the frequently updated book in the complementary bibliography (now in its 6th edition), that contains a whole corpus with many biological and molecular details of interest for the study of particular examples. This will be complemented with review research papers, and more specific bibliography for the projects.

Basic bibliography

Uri Alon, An introduction to Systems Biology: Design Principles of Biological Circuits, (Chapman & Hall/ CRC, Boca Raton, FL, 2007).

Complementary bibliography

Bruce Alberts et al., Molecular Biology of the Cell, (Garland Science, New York, 2014) (6th Edition)

Other resources

1. J.J. Tyson, K.C. Chen, and B. Novak, *Sniffers, buzzers, toggles and blinkers: dynamics of regulatory and signaling pathways in the cell*, Curr. Opin. Cell Biol. **15**, 221-231 (2003).
2. R. Milo, S. Shen-Orr, S. Itzkovitz, N. Kashtan, D. Chklovskii, and U. Alon, *Network Motifs: Simple Building Blocks of Complex Networks* Science, **298**, 824-827 (2002).
3. U. Alon, *Network motifs: theory and experimental approaches* Nat. Rev. Genet. **8**, 450-461 (2007)