Subject

Name	11010 - Systems Biology
Credits	0.75 in-class (18.75 hours) 2.25 distance (56.25 hours) 3 total (75 hours).
Group	Group 1, 2S
Period	Second semester
Language	English

Lecturers

Lecturers	Office hours for students					
	Starting time	**Finishing time**	**Day**	**Start date**	**End date**	**Office**
Manuel Alberto Matias Muriel	You need to book a date with the professor in order to attend a tutorial.					

Context

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

Recommended

A working knowledge at the level of the courses "Dynamical Systems and Chaos" and "Complex Networks" of this Master is 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., on the other hand, 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 systems that make an efficient use of their resources, namely from the point of view of cost vs. benefit. All these general features 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. In the end, the goal is not just to understand the logic of function in cellular systems, but also to understand how to change the behavior of these systems and to engineer them, in the sense of Synthetic Biology.

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
   Cost, benefit and fitness functions of biological circuits.
9. Demand Rules for Gene Regulation

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

Teaching methodology

Workload

The novelty of the material for students with a Physics background implies a number of theory classes where the main new biological concepts will be explained. On the other hand, students with a more biological background should have no problem with this course after having passed Dynamical Systems and Complex Networks in the first semester. The course is structured such that, while fundamental concepts are given in each chapter (motifs, robust behavior, proofreading, optimality of biological systems, etc.), the concepts are illustrated with a broad number of biological examples that will allow to increase the biological knowledge of the class, with examples like sensory and developmental transcription networks, signal transduction networks, bacterial motility, including chemotaxis, morphogenpatterning, RNA translation, etc.

The goal is that the student is able to work sucessfully with these concepts and this will be accomplished through the assignment of a small number of exercises and mainly with a small individual project, chosen between the instructor and the student. This project will be related to recent research topics and will involve the use of the ideas and methods developped during the course.

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.	1.25
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.	12.25

Modality	Name	Description	Hours
Individual self-study	Realization of the assignment	The student must solve the individual assignment, prepare a report and organize an oral presentation.	30
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 participation in class, homework (assigned exercises) and of the "small project" on a subject related to a recent topic already mentioned.

Oral presentation

Modality	Assessment
Technique	Oral tests **(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 **(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: 40%

Realization of the assignment

Modality	Individual self-study
Technique	Papers and projects **(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: 40%

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 available the pioneering book that will be used as basic bibliography of the course. A new edition is announced for the following months, and will be also used if available when the course starts. This will be complemented by the frequently updated MBOC that is a corpus rather than a book, now in its 6th edition), and is recommended as a reference for particular biological and molecular details of systems studied in particular examples and the project, not for systematic study.
Other resources are seminal contributions in the approach to Systems Biology followed during the course. And this will be complemented with specific bibliography for the project to be carried out by the students.

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. J.E. Ferrell, *Self-perpetuating states in signal transduction: positive feedback, double-negative feedback and bistability*, Curr. Opin. Cell. Biol. **14**, 140-148 (2002)
3. W. Ma, A. Trusina, H. El-Samad, W.A. Lim, and C. Tang, *Defining Network Topologies that Can Achieve Biochemical Adaptation,* Cell **138**, 760-773 (2009).
4. N. Barkai and B.Z. Shilo, *Variability and Robustness in Biomolecular Systems*, Mol. Cell **28**, 755-760 (2007).
5. 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).
6. U. Alon, *Network motifs: theory and experimental approaches,* Nat. Rev. Genet. **8**, 450-461 (2007)

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