UNIVERSITAT POLITÈCNICA DE CATALUNYA BARCELONATECH

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230481 - COMBIO - Computational Biophysics

Coordinating unit: 230 - ETSETB - Barcelona School of Telecommunications Engineering
Teaching unit: 748 - FIS - Department of Physics
Academic year: 2019
Degree: BACHELOR'S DEGREE IN ENGINEERING PHYSICS (Syllabus 2011). (Teaching unit Optional)
ECTS credits: 6 Teaching languages: English

Teaching staff

Coordinator: Alvarez Lacalle, Enrique

Others: Pons Rivero, Antonio Javier
Pastor Satorras, Romualdo
Alonso Muñoz, Sergio

Opening hours

Timetable: Students will be informed using atenea's webpage

Prior skills

- Basic knowledge of the human body obtained in ESO and Biophysics1.
- Knowledge of matlab or any other programming language (seen in MNC1)
- Knowledge of the main step/multistep algorithm to resolve ordinary differential equations, specially Runge-Kutta methods. (seen in MNC2)
- Knowledge and familiarity with the main concepts of ordinary differential equations and partial differential equations. (seen in MM2)
- Knowledge and familiarity with the basic concepts of bacteria, cell and the central dogma of biology (seen in BIOF2)
- Familiarity with the concepts of analytical mechanics related with phase space and dynamical attractors. (seen in MECF)

Requirements

Numerical and Computational Methods 2
Mecànica
Mètodes matemàtics 2
Biophysics 2

Degree competences to which the subject contributes

Specific:

INF1. Understanding and mastery of computer programming, use of operative systems and computational tools (scientific software). Skills to implement numerical algorithms in languages of low (C, F90) and high (Matlab) level.
BIOC1. Ability to describe in general the structure of living things, from cellular to systemic level. Ability to analyze the constraints imposed by the physics laws to the development of biological systems, and the biological solutions to engineering problems.
BIOC2. Ability to analyze biological systems as complex systems.

INF2. Ability to solve problems in physics and engineering using fundamental numerical methods: experimental data processing, interpolation, roots of nonlinear equations, numerical linear algebra and optimization, quadrature and integration of differential equations, properly weighting their different aspects (accuracy, stability and efficiency or cost).

Generical:

3. ABILITY TO IDENTIFY, FORMULATE, AND SOLVE PHYSICAL ENGINEERING PROBLEMS. Planning and solving physical engineering problems with initiative, making decisions and with creativity. Developing methods of analysis and problem solving in a systematic and creative way.

Transversal:

1. THIRD LANGUAGE. Learning a third language, preferably English, to a degree of oral and written fluency that fits in with the future needs of the graduates of each course.
2. SELF-DIRECTED LEARNING - Level 3. Applying the knowledge gained in completing a task according to its relevance and importance. Deciding how to carry out a task, the amount of time to be devoted to it and the most suitable information sources.

Teaching methodology

The course will be centered in code-implementation classes and its theoretical and biological interpretation. Besides the normal classes, a few seminars showing examples of different types of modeling in biology will be given. During the course there will be basically two types of classes

-Theoretical classes will review and address definitions and frameworks in the area of computational sciences, math and biophysics. The basic structure of the class will be to expose the different concepts using blackboard, videos, and interactive resources.

-Practical classes will include time for the student to write and develop small codes. These codes will be useful both as a numerical examples and as toy models of biophysical problems.
One single class can be divided in theoretical and practical time if the topic at hand requires it.

Besides regular classes two different methodologies will be used:
-During the first week a special training program to code in python will be developed using the previous knowledge the students have in matlab.
-Seminar series will be arranged during the course. Professors will give seminars overviewing topics of computational biophysics which aren't addressed in the program so that students can overview more complex numerical methods and analysis.

All the resources will be published in the ATENEA website.

Learning objectives of the subject

Once the student has finished the course he/she must be able to:

-Describe the four main methods of addressing spatio-temporal dynamics in extended systems used in physics: Compartmental models, iterative models, spatio-temporal models and network methods. This includes discerning which one is optimal for addressing the problem.

-Implement a random number generator in any given numerical simulation and know the Gillespie algorithm to code stochastic variables in time propagators. Implement extended nonlinear simulations with diffusion processes and different boundary conditions. Understand the concept of biological network, how to implement it numerically on a computer and how to obtain useful topological information of it. Learn how to implement realistic dynamical processes on top of networks.

-Define the basic dynamical interaction in a typical metabolic process and the kinetic reaction and network theory used to describe it. It must also be able to code a typical oscillatory genetic network and a typical signaling process. It must be able to describe briefly the general gene-protein network structure of the cell. It must be able to analyze the possible stochastic elements in a given biological system and implement it dynamics.

-Make linear stability analysis of pattern forming systems. Be able to solve linear and nonlinear initial value and boundary value problems using different numerical implementations analyzing its stability and accuracy. Understanding the dynamical features of reaction-diffusion-advection systems and to give different examples of pattern forming systems in Biology.

-Understand simple models of population dynamics and its relation to ecology, learning the different factors that can affect the growth and development of a population: spatio-temporal effects, effects of generational delays. At the same time, learn how to control possible chaotic effects in non-linear ecological models.

-Define the basic aspects of epidemiology and the relevant models that display the main features of realistic diseases. Understand the effects of a complex pattern of physical contacts in the spread of a biological disease.

Regarding the seminar series, students must be able to summarize any seminar presentation and be able to explain briefly three areas where biophysics approaches are presently top-edge.

Finally, students must perform a project where they develop a code to show expertise in one particular biophysics problem. At the end of this project , students must be able to show that they can understand the physiology or structure of a given biophysical problem in order to properly simulate it. They must be able to structure a code and clarify its different subroutines checking that the code works correctly and, if possible, perform simulations to draw conclusions about the problem or about future improvements of the code.

Study load

Total learning time: 150h	Hours large group:	65h	43.33%
	Self study:	85h	56.67%

Content

Introduction	Learning time: 45h Theory classes: 5h Self study : 40h

Description:
-System biology. Introduction and general approach.
General structure of the research program. Scales and orders of magnitude. General framework for computation and simulations. Dealing with data: physiological and structural information. Specific computational frameworks: Compartmental methods, iterative methods, extended systems and networks.

-Introduction to python language: basic commands.
Basic commands and data types in Python. Organization of Python code. Higher order structures: hash tables and sets. Modules in Python: Numpy.

-Basic data processing in python.
Managing of data sets to obtain relevant statistical descriptions. Reading and writing numerical data. Analysis, linear and non-linear regression of empirical data. Efficient graphical representation.

Related activities:
Presentación AV1

Non-extended dynamical systems. Genetic networks.	Learning time: 36h Theory classes: 14h Practical classes: 6h Self study : 16h

Description:
-Introduction to ODE's. Fixed points and nullclines.
High order differential equations and ODE's. Fixed points in one-dimensional systems. Generalization. Oscillation and periodicity in two-dimensional system. Nullclines in two-dimensional systems.

-Slaving and freezing conditions. Applications to cell reactions.
Simulation of diffeent time scales. Long time scales and freezing variables. Fast time scales and slaving. Optimal time steps in Euler methods.

-Stability and bifurcations. Decisions in cell genetic networks.
Linear stability analysis. Pitchfork and saddle-node bifurcation. Transcritical bifurcation. Simple gene regulation and expression.

-Limit cycles. Delays and nonlinearities. Application to cell metabolism.
Non-linear oscillations. Hopf bifurcation. Nullcline interpretations. Characteristic times and delays in oscillations. Generation of clocks in genetic networks

-Stochastic modeling: Random number generator. Application to cell signaling.
Systems with small number of particles. Basic algortihms for random number generators. Stochastic states versus stocahstic dynamics. Euler method for stochastic systems. Models for membrane signalling and network control.

Spatially extended systems. Pattern formation in biology	Learning time: 36h Theory classes: 14h Practical classes: 6h Self study : 16h

Description:
-Introduction to Pattern formation
Description. Linear Stability analysis. Amplitude Equations.

-Reaction-diffusion systems.
Morphogenesis and the Turing Mechanism. Finite Difference Methods. Stability and Accuracy.

-Reaction-diffusion-advection systems.
Bioconvection examples. Numerical iterative methods. Modeling of the Inner Ear.

-Pseudo-Spectral methods in biophysics.
General description. Implementation. The Swift-Hohenberg Equation.

-Patterns in the Brain.
Neural fields. Patterns not derived from conservation equations. Derivation and biological interpretation.

Modeling processes in networks. Ecology and epidemiology.	Learning time: 28h Theory classes: 10h Practical classes: 5h Self study : 13h

Description:
-Introduction to networks and their implementation.
Definition of a network. Efficient numerical implementation on the computer using higher order data structures. Topological observables and description of efficient algorithms to compute them.

-Logistic map. Presence of chaos and its control.
Introduction to simple models of population evolution in discrete time. Numerical analysis of non-linear recurrence equations. Development of chaos. The chimaera effect.

-Population dynamics and delays. Predator-prey models. Application to ecology.
Effects of generational effects of populations: recurrence equations with delays. Study of more sophisticated population equations in continuous time: The Lotka-Volterra equation. Integration of coupled non-linear differential equations: The Runge-Kutta method.

-Contact and birth-death process. Gillespie method.
Realistic models of population dynamics. Spatio-temporal stochastic population models: The contact process. Numerical simulation of stochastic processes: The Gillespie method.

-SIS models in networks. Application to epidemiology.
Introduction to epidemiology. Relevant factors in the propagation of a disease. Simple epidemiological models. Analytical approaches. Numerical simulations with the Gillespie method. Epidemics in heterogeneous networks.

Seminar series	Learning time: 5h Practical classes: 5h

Description:
Modeling spatial population genetics.
Modeling self-organization in biology.
Modeling infectious diseases.

Planning of activities

AV1: Main project: Numerical simulation of a biophysical system.	Hours: 43h Guided activities: 3h Self study: 40h

Description:
This project consists on developing a simulation of a relatively complex biophysical system. Students will work in pairs (not necessarily) and learn the fundamentals of the biophysical system, will decide how to address a simulation of the system and will use the numerical algorithms learnt in class (or in autonomous learning) to implement it. The code written by the students will have one of two aims: simulate numerically a full biophysical system or understand via simulations a particular feature of the same. The student will have to test the code modularly. Once the code is up and running, they will comment and comment it and proceed to use it to attain the desired goal. The project will end with a short report of the work done according to given guidelines.

Support materials:
The general structure of the project will be given to the student together with bibliographic support and notes if necessary. The main structure of the code will be developed with the support of a tutor if necessary.

Descriptions of the assignments due and their relation to the assessment:
Commented and documented code (up to 500 lines of code +100 in comments with one page documentation).
Standard brief report with abstract, introduction, implemented model, code tests and results with conclusion (maximum 4 pages).
Evaluation 40% of the total grade

Specific objectives:
Students should develop a project with the aim of applying the different numerical techniques and theoretical knowledge explained during the course. When necessary, students may need to study a new numerical technique specifically useful for the project. All this means the student must learn autonomously, plan and focus in order to reach a clear goal. This would allow the students to consolidate the knowledge of the course, develop the ability to solve new problems and communicate this knowledge clearly and efficiently.

Qualification system

The students' evaluation will consist on grading the work done in class and at home through handed-in homework (HE), and the formal evaluation of the project (PE). There will not be a mid-term exam nor a final exam. The final mark will be given by:
0.6*HE+0.4*PE

Regulations for carrying out activities

All activities are compulsory. Any report or project which is not delivered or presented will have a grade of zero.

Bibliography

Basic:

Gries, P.; Campbell, J.; Montojo, J. Practical programming : an introduction to computer science using Python 3. 2nd ed. The Pragmatic Bookshelf, 2013. ISBN 9781937785451.

DiStefano, J. Dynamic system biology modeling and simulation. Elsevier, 2013. ISBN 9780124104112.

Ingalls, B.P. Mathematical Modeling in Systems Biology [on line]. Cambridge, MA: MIT, 2013 [Consultation: 03/10/2014]. Available on: <http://site.ebrary.com/lib/upcatalunya/docDetail.action?docID=10734711>. ISBN 9780262018883.

Barrat, A.; Barthelemy, M.; Vespignani, A. Dynamical processes on complex networks. Cambridge: Cambridge University Press, 2008. ISBN 9780521879507.

Complementary:

Murray, J.D. Mathematical biology, vol. 1 [on line]. 3rd. ed. Springer, 2002 [Consultation: 09/07/2014]. Available on: <http://link.springer.com/book/10.1007/b98868>. ISBN 9780387952239.

Kriete, A.; Elis. R. Computational Systems biology: from molecular mechanism to diseases [on line]. 2nd. ed. Amsterdam: Elsevier, 2014 [Consultation: 03/10/2014]. Available on: <http://site.ebrary.com/lib/upcatalunya/docDetail.action?docID=10815678>. ISBN 9780124059269.

Brauer, F.; Castillo-Chavez, C. Mathematical models in population biology and epidemiology [on line]. 2nd. ed. New York: Springer, 2012 [Consultation: 03/10/2014]. Available on: <http://site.ebrary.com/lib/upcatalunya/docDetail.action?docID=10652711>. ISBN 9781461416869.

Murray, J.D. Mathematical biology, vol. 2 [on line]. 3rd. ed. Springer, 2003 [Consultation: 09/07/2014]. Available on: <http://link.springer.com/book/10.1007/b98869>. ISBN 9780387952284.

Others resources:

Hyperlink

The virtual heart

http://thevirtualheart.org/

Human Brain Project

https://www.humanbrainproject.eu/es/discover/the-project/overview

Computer material

Curs a atenea.

Web resources in atenea