ANX-PR/CL/001-01

LEARNING GUIDE

SUBJECT

203000034 - Programmable Biology: Dna Computation And Biocircuits Engineering

DEGREE PROGRAMME

20BC - Master Universitario En Biologia Computacional

ACADEMIC YEAR & SEMESTER

2021/22 - Semester 1

Index

Learning guide

1. Description

1.1. Subject details

Name of the subject	203000034 - Programmable Biology: Dna Computation And Biocircuits Engineering
No of credits	3 ECTS
Type	Optional
Academic year ot the programme	First year
Semester of tuition	Semester 1
Tuition period	September-January
Tuition languages	English
Degree programme	20BC - Master Universitario en Biologia Computacional
Centre	20 - E.T.S. De Ingenieria Agronomica, Alimentaria Y De Biosistemas
Academic year	2021-22

2. Faculty

2.1. Faculty members with subject teaching role

Name and surname	Office/Room	Email	Tutoring hours *
Alfonso Vicente Rodriguez-Paton Aradas (Subject coordinator)	2106	alfonso.rodriguez-paton@upm.es	M - 17:00 - 19:00

* The tutoring schedule is indicative and subject to possible changes. Please check tutoring times with the faculty member in charge.

2.2. Research assistants

Name and surname	Email	Faculty member in charge
Nuñez Berrueco, Elena	elena.nunez@upm.es	Rodriguez-Paton Aradas, Alfonso Vicente

3. Skills and learning outcomes *

3.1. Skills to be learned

CE02 - Utilizar sistemas operativos, programas y herramientas de uso común en biología computacional, así como, manejar plataformas de cómputo de altas prestaciones, lenguajes de programación y análisis bioinformáticos

CE03 - Analizar e interpretar bioinformáticamente los datos que se derivan de las tecnologías ómicas, y proponer soluciones bioinformáticas en relación a dichos datos.

CE05 - Utilizar herramientas de biología computacional para el análisis genómico, incluida la genómica comparativa y biología evolutiva.

CE10 - Conocimiento de las técnicas de representación del conocimiento reutilizables y modelos de razonamiento en entornos centralizados y distribuidos a utilizar en la resolución de problemas que impliquen conducta inteligente.

CG01 - Poseer los conocimientos que constituyen la base científica y tecnológica de la Biología computacional, lo que permitirá el desarrollo de ideas originales en este campo, en un contexto de investigación o desarrollo.

CG03 - Que los estudiantes sepan aplicar los conocimientos adquiridos y su capacidad de resolución de problemas en entornos nuevos o poco conocidos dentro de contextos más amplios (o multidisciplinares) relacionados con el area de la Biología Computacional.

CT02 - Capacidad para aplicar el método científico para la resolución de problemas de forma efectiva y creativa.

3.2. Learning outcomes

RA39 - Abordar los aspectos formales del proyecto inicial de una investigación

RA40 - Valorar la importancia de las fuentes documentales y seleccionar aquéllas que sean más interesantes para publicar sus trabajos

RA41 - Establecer un debate fundamentado sobre el conocimiento científico y las bases de la investigación.

* The Learning Guides should reflect the Skills and Learning Outcomes in the same way as indicated in the Degree Verification Memory. For this reason, they have not been translated into English and appear in Spanish.

4. Brief description of the subject and syllabus

4.1. Brief description of the subject

In this course we will study the basic concepts and topics of Biomolecular Computing, Synthetic Biology and Programmable Biology.

What is Synthetic Biology? It is the engineering of biology: the application of the engineering principles in biology to design and build biological systems.This field considers biology as a technology that can be programmed to manufacture new synthetic biological devices and systems. This field was born in 2000 in MIT Artificial Intelligence Lab where engineers, computer scientists, and physicists started to work jointly with biologists. Engineers asked this question: can we combine natural living hardware components (mainly genes) to build new synthetic biological systems? Can we design and write genetic programs in DNA (the software) to be run in a cellular processor (the hardware)? The answer was yes. The biotechnology and genetic engineering tools were already available. The first synthetic devices were developed in 2000: a genetic memory (Gardner, Cantor, & Collins, 2000), an oscillatory genetic circuit (Elowitz et al. 2000) and several genetic Boolean logic gates (Hasty, McMillen, & Collins, 2002; Weiss et al., 2003).

From single cell biocircuits to multicell biocircuits: recent efforts in synthetic biology are moving into the engineering of distributed biocircuits encoded in multicell populations. Multicellular synthetic circuits exploit the ability of the single cells to communicate with its peers to achieve robust dynamics in engineered populations. **Quorum sensing** circuits are the most noticeable example of this tendency, with great efforts going into the study of artificial pattern-formation, division of labour or bio-computation. We will also analyze software tools like **individual-based simulators** able to model multicellular bacterial programmed populations and tissues.

RNA Synthetic Biology: traditionally, transcriptional and translational RNA regulators have performed worse than protein regulators in terms of ON/OFF switching range. But recently, the engineering of new robust **RNA switches** have overcome this problem. These bio-switches can be flipped ON or OFF with high speed and high fidelity. Some of theses new synthetic RNA switches act transcriptionally (STARs and CRISPRi) and others act translationally (Toehold Switches). The results obtained in terms of dynamic range response and expression rates make them an interesting tool to reach robust and fast genetic circuits (Chappell, Takahashi, & Lucks, 2015; Green, Silver, Collins, & Yin, 2014) . On the other hand, RNA molecules can be used as effective and orthogonal wiring signals due to their size and to their high programmability. Moreover, RNA circuits are more compact than protein-based ones so that implies a reduced metabolic burden on the cell host and allow for faster propagation of signals. Finally, it is already known that **CRISPR** is not only a powerful gene-editing tool but it can also be used as a precise and programmable computing tool, so this open a new research line in the SynBio framework.

Biomolecular computing: is the term used for information processing encoded in biological macromolecules. A bio-molecular computer is a device made with these biomolecules that processes biological information, and use DNA, RNA, proteins, or their combination. We will describe only a few of the most relevant DNA and RNA-based computers developed so far and applied to in vivo diagnostic and drug delivery. The engineering of programmable biomolecular automata applied to the diagnosis/treatment in vitro of a disease is a promising application in the area of intelligent in situ drug delivery. This field started in 2001 with the first design of a DNA-based automaton operating in vitro (Benenson et al. 2001) applied to biomedical diagnosis in 2004 (Benenson et al. 2004). An automaton is a device that can operate in an autonomous way, sensing inputs, processing those inputs and emitting an output without external human interaction. Another important and widely used nucleic acid sensing technique is the so-called `competitive hybridization' or `DNA strand displacement' (Seelig et al., 2006). This technique is used in the design of DNA logic circuits for the intelligent sensing and processing of DNA and RNA molecules.

Programmable Biology and open-source portable biology labs: LIA group is developing code for programming portable biology labs run by Arduino cards. We want to make these biolabs easy to program and easy to engineer. This is why we are using BioBlocks language (a drag-and-drop visual language based on Scratch and Blockly). We

want to develop open-source versions of Bento.bio and Amino.bio.

More introductory info at: http://www.lia.upm.es

Also: Alfonso's talk in Valencia, Spain, in ISBBC Summer School, June 2017: Synthetic Biology for computer scientists in 2 hours. Slides available at: https://drive.google.com/file/d/0B1K8p9umsfI4WWhUd1lMLTA0OVE/view

Alfonso Rodríguez-Patón talk in CIB - CSIC, Dec. 2017 titled "Bioblocks and GRO: software tools for protocol and multicellular bacterial simulations": https://drive.google.com/open?id=1o2eX5O3SFhzk6yQvBzy7ks-2oRmnKmWZ

Programmable antibiotics: https://www.youtube.com/watch?v=H8WA_8Yfjno

http://www.upm.es/UPM/SalaPrensa/Noticias_de_investigacion?id=d780fb62f5b0a610VgnVCM10000009c7648a_____&fmt=detail&prefmt=articulo

Decrypting bacterial virulence networks: https://youtu.be/tPZ36vyzAUM

4.2. Syllabus

1. DNA Computing
    1.1. DNA Strand displacement-based biocircuits
    1.2. Molecular automata and DNA origami
2. Synthetic Biology: unicellular genetic circuits
    2.1. Gene expression and regulation
    2.2. Genetic Boolean logic gates
    2.3. Basic genetic circuits: toggle switch, oscillator (repressilator)
    2.4. CRISPR-based devices and gene drives
3. Synthetic Biology: multicellular genetic circuits
    3.1. Bacterial cell-cell communication: quorum sensing
    3.2. Bacterial cell-cell communication: conjugation
    3.3. Morphogenesis: engineering multicellular motifs

4. Programmable Biology

4.1. Simulating bacterial colonies with IBM: Gro simulator

4.2. Engineering portable biolabs with Arduino cards and software blocks

4.3. Deep learning in SynBio

5. Schedule

5.1. Subject schedule*

Week	Face-to-face classroom activities	Face-to-face laboratory activities	Distant / On-line	Assessment activities
1				
2	**1.2 DNA Strand displacement-based biocircuits** Duration: 02:00			**Reading papers** Continuous assessment Not Presential Duration: 00:30
3	**1.3 Molecular automata and DNA origami** Duration: 02:00			**Reading papers** Continuous assessment Not Presential Duration: 00:30
4	**2. Synthetic Biology: unicellular genetic circuits. 2.1. Gene expression and regulation** Duration: 02:00			**Reading papers** Continuous assessment Not Presential Duration: 00:30
5	**2.2. Genetic Boolean logic gates** Duration: 02:00			**Reading papers** Continuous assessment Not Presential Duration: 00:30
6	**2.3. Basic genetic circuits: A toggle switch and an oscillator (repressilator)** Duration: 02:00			**Reading papers** Continuous assessment Not Presential Duration: 00:30
7	**2.4. Designing genetic circuits: Directed evolution and 2.5 CRISPR-based devices and gene drives** Duration: 02:00			**Reading papers** Continuous assessment Not Presential Duration: 00:30
8	**3.1 Bacterial cell-cell communication: quorum sensing based-circuits** Duration: 02:00			**Reading papers** Continuous assessment Not Presential Duration: 00:30
9	**3.2. Bacterial cell-cell communication: conjugation and 3.3 Morphogenesis** Duration: 02:00			**Reading papers** Continuous assessment Not Presential Duration: 00:30

10	**4.1: Gro 4.2: BioBlocks and 4.3: Portable biolabs** Duration: 02:00			**Reading papers** Continuous assessment Not Presential Duration: 00:30
11	**4.4: Deep learning in SynBio** Duration: 02:00			**Reading papers** Continuous assessment Not Presential Duration: 00:30
12	**iGEM groups presentations** Duration: 02:00			**Reading papers** Continuous assessment Not Presential Duration: 00:30
13	**Oral presentations students** Duration: 02:00			
14	**Oral presentations of the students** Duration: 02:00			
15	**Oral presentations of the students** Duration: 02:00			**Oral presentations** Continuous assessment Not Presential Duration: 08:00
16	**Review of general topics** Duration: 02:00			
17	**Written exam** Duration: 01:00			**Written exam** Continuous assessment Not Presential Duration: 06:00 **Final written assay** Continuous assessment Not Presential Duration: 28:00 **Final written assay (for final evaluation)** Final examination Not Presential Duration: 36:00 **Written exam (for only final evaluation)** Final examination Not Presential Duration: 16:00

Depending on the programme study plan, total values will be calculated according to the ECTS credit unit as 26/27 hours of student face-to-face contact and independent study time.

* The schedule is based on an a priori planning of the subject; it might be modified during the academic year, especially considering the COVID19 evolution.

6. Activities and assessment criteria

6.1. Assessment activities

6.1.1. Continuous assessment

Week	Description	Modality	Type	Duration	Weight	Minimum grade	Evaluated skills
2	Reading papers		No Presential	00:30	2%	5 / 10	
3	Reading papers		No Presential	00:30	2%	5 / 10	
4	Reading papers		No Presential	00:30	2%	5 / 10	
5	Reading papers		No Presential	00:30	2%	5 / 10	
6	Reading papers		No Presential	00:30	2%	5 / 10	
7	Reading papers		No Presential	00:30	2%	5 / 10	
8	Reading papers		No Presential	00:30	2%	5 / 10	
9	Reading papers		No Presential	00:30	2%	5 / 10	
10	Reading papers		No Presential	00:30	2%	5 / 10	
11	Reading papers		No Presential	00:30	2%	5 / 10	
12	Reading papers		No Presential	00:30	2%	5 / 10	
15	Oral presentations		No Presential	08:00	25%	5 / 10	CT02 CE10 CG01 CE03 CG03
17	Written exam		No Presential	06:00	1%	5 / 10	CE10 CE05 CG01 CG03 CE03
17	Final written assay		No Presential	28:00	52%	5 / 10	CT02 CE02 CE10 CE05 CG01 CG03 CE03

6.1.2. Final examination

Week	Description	Modality	Type	Duration	Weight	Minimum grade	Evaluated skills
17	Final written assay (for final evaluation)		No Presential	36:00	75%	5 / 10	CT02 CE02 CE10 CE05 CG01 CG03 CE03
17	Written exam (for only final evaluation)		No Presential	16:00	25%	5 / 10	CE10 CE05 CG01 CG03 CE03

6.1.3. Referred (re-sit) examination

No se ha definido la evaluación extraordinaria.

6.2. Assessment criteria

Las presentaciones orales se valorarán y calificarán en función de la claridad y la profundidad a la hora de explicar los conceptos básicos del tema elegido, la extensión y adecuación de la bibliografía consultada, la concisión y el ajuste al tiempo asignado. La presentación oral individual es obligatoria para aprobar la asignatura y tiene un valor máximo de 2 puntos sobre 10.

El examen de conocimientos básicos se califica como Apto o No Apto. Si un alumno no obtiene la calificación de No-Apto puede presentarse a otro examen de recuperación. Es obligatorio superar este examen para aprobar la asignatura.

El trabajo escrito final tiene un valor máximo de 7,5 puntos sobre 10.

La asistencia y participación activa en clase se valorará entre 0 y 0,5 puntos.

Para superar la asignatura hay que obtener al menos 5 puntos sobre un total de 10 al sumar las tres calificaciones anteriores (presentación oral+trabajo escrito+participación presencial). Y aprobar el examen de conocimientos básicos.

Los alumnos deberán realizar un trabajo escrito al final del curso en el que estudiarán un problema o tópico

descrito en la asignatura y a definir previamente con el profesor. Este documento contendrá una descripción del problema o tópico elegido así como una reflexión crítica por parte del alumno sobre el tema y la bibliografía consultada por el alumno. El alumno deberá consultar al menos 5 artículos relevantes sobre el tema descrito. La memoria del trabajo deberá ser original y contener todas las citas y referencias bibliográficas utilizadas para su elaboración. El plagio de algún párrafo conlleva el suspenso automático en la asignatura. No se valora la cantidad escrita sino la calidad. Es decir, se valora la capacidad de síntesis, la capacidad de comprensión por parte del alumno del problema analizado, la profundidad del análisis y la crítica y la reflexión personal del alumno.Al tratarse de una asignatura de un Máster de investigación se valorará en gran medida cualquier aportación creativa o idea novedosa y original por parte del alumno.

Los alumnos que no realicen la evaluación continua (presentación oral + examen parcial + trabajo final) se pueden presentar a la convocatoria extraordinaria de julio en la que tendrán que realizar/entregar un trabajo escrito (sobre un tema que se debe acordar con el profesor no más tarde de principios/mediados de junio) y un examen de conocimientos sobre los contenidos y temas analizados a lo largo del curso. Para aprobar en la convocatoria de julio hay que aprobar tanto el trabajo escrito como el examen de conocimientos.

La metodología o modelo docente que se sigue en las clases es el denominado "Flipped Classroom" en el que los alumnos leen y consultan artículos y material docente previamente a la sesión presencial que se utiliza no de manera expositiva por parte del profesor sino interactiva para resolver dudas y analizar de manera conjunta los aspectos más relevantes o complejos que los alumnos se han encontrado al consultar el material docente (artículos de investigación).

7. Teaching resources

7.1. Teaching resources for the subject

Name	Type	Notes
Basic docs about synbio	Web resource	Consultar la web del grupo LIA (hay una sección con material introductorio a la Biología Sintética): http://www.lia.upm.es
Reading papers	Web resource	At the beginning of the course a link to the reading papers described during each class will be given to the students

GRO 2D bacterial simulator	Web resource	Software for simulating growing 2D bacterial colonies: https://github.com/liaupm/GRO-LIA Paper: https://pubs.acs.org/doi/abs/10.1021/acssynbio.7b00003
BioBlocks	Web resource	Drag-and-drop software for describing biological protocols based on Scratch Paper: http://biorxiv.org/content/early/2016/10/14/081075 Link: https://github.com/liaupm