ANX-PR/CL/001-01
LEARNING GUIDE

SUBJECT

103000363 - Programmable Biology: Dna Computing Amd Biocircuits Engineering

DEGREE PROGRAMME

10AJ - Master Universitario En Inteligencia Artificial

ACADEMIC YEAR & SEMESTER

2023/24 - Semester 1

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1. Description

1.1. Subject details

Name of the subject	103000363 - Programmable Biology: Dna Computing Amd Biocircuits Engineering
No of credits	5 ECTS
Type	Optional
Academic year ot the programme	First year
Semester of tuition	Semester 1
Tuition period	September-January
Tuition languages	English
Degree programme	10AJ - Master Universitario en Inteligencia Artificial
Centre	10 - Escuela Tecnica Superior De Ingenieros Informaticos
Academic year	2023-24

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.

3. Skills and learning outcomes *

3.1. Skills to be learned

CEIA1 - Capacidad de integrar tecnologías y sistemas propios de la Inteligencia Artificial, con carácter generalista, y en contextos más amplios y multidisciplinares

CEIA2 - Capacidad de conectar la tecnología puntera en Inteligencia Artificial con las necesidades de los clientes

CEIA5 - Conocimiento las principales técnicas de computación natural, tanto a nivel simbólico como físico, e identificar su idoneidad para distintos tipos de problemas

CG15 - Capacidad para contribuir al desarrollo futuro de la informática.

CG18 - Capacidad de trabajar y comunicarse también en contextos internacionales

CG6 - Gestión de la información.

CG8 - Planteamiento y resolución de problemas también en áreas nuevas y emergentes de su disciplina

CG9 - Aplicación de los métodos de resolución de problemas más recientes o innovadores y que puedan implicar el uso de otras disciplinas.

CGI1 - Adquirir conocimientos científicos avanzados del campo de la informática que le permitan generar nuevas ideas dentro de una línea de investigación.

CGI2 - Comprender el procedimiento, valor y límites del método científico en el campo de la Informática, siendo capaz de identificar, localizar y obtener datos requeridos en un trabajo de investigación, de diseñar y guiar investigaciones analíticas, de modelado y experimentales, así como de evaluar datos de una manera crítica y extraer conclusiones.

CGI3 - Capacidad para valorar la importancia de las fuentes documentales, manejarlas y buscar la información para el desarrollo de cualquier trabajo de investigación.

CGI4 - Capacidad de leer y comprender publicaciones dentro de su ámbito de estudio/investigación, así como su catalogación y valor científico.

3.2. Learning outcomes

RA90 - Comprender co?mo se pueden disen?ar e implementar bioalgoritmos que emplean mole?culas de ADN como sustrato (memoria).

RA91 - Disen?ar circuitos lo?gicos biomoleculares sinte?ticos operando : (1) con ADN/ARN o (2) con protei?nas

RA92 - Comprender co?mo las ce?lulas procesan informacio?n codificada en biomole?culas y toman decisiones.

RA4 - Valorar la importancia de las fuentes documentales y seleccionar aquéllas que sean más interesantes para publicar sus trabajos

RA3 - Abordar los aspectos formales del proyecto inicial de una investigación

RA2 - 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

Towards programmable antibiotics and in silico microbiota: https://www.youtube.com/watch?v=b4ECvhXD5kg

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

¿Cómo funcionan los fármacos programables? https://youtu.be/RwAUjSLwXOc

4.2. Syllabus

1. DNA Computing
    1.1. DNA structure and DNA operations
    1.2. DNA Strand displacement-based biocircuits
    1.3. Molecular automata
2. Synthetic Biology: unicellular genetic circuits
    2.1. Gene expression and regulation
    2.2. Genetic Boolean logic gates
    2.3. Basic genetic circuits: A toggle switch and an 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	Classroom activities	Laboratory activities	Distant / On-line	Assessment activities
1	**Tema 1: DNA Computing 1.1: DNA structure and DNA operations** Duration: 02:00 Lecture			**Reading papers** Other assessment Continuous assessment Not Presential Duration: 01:00
2	**1.2 DNA Strand displacement-based biocircuits** Duration: 02:00 Lecture			**Reading papers** Other assessment Continuous assessment Not Presential Duration: 01:00
3	**1.3 Molecular automata** Duration: 02:00 Lecture			**Reading papers** Other assessment Continuous assessment Not Presential Duration: 01:00
4	**2. Synthetic Biology: unicellular genetic circuits. 2.1. Gene expression and regulation** Duration: 02:00 Lecture			**Reading papers** Other assessment Continuous assessment Not Presential Duration: 01:00
5	**2.2. Genetic Boolean logic gates** Duration: 02:00 Lecture			**Reading papers** Other assessment Continuous assessment Not Presential Duration: 01:00
6	**2.3. Basic genetic circuits: A toggle switch and an oscillator (repressilator)** Duration: 02:00 Lecture			**Reading papers** Other assessment Continuous assessment Not Presential Duration: 01:00
7	**2.4 CRISPR-based devices and gene drives** Duration: 02:00 Lecture			**Reading papers** Other assessment Continuous assessment Not Presential Duration: 01:00
8	**3.1 Bacterial cell-cell communication: quorum sensing based-circuits** Duration: 02:00 Lecture			**Reading papers** Other assessment Continuous assessment Not Presential Duration: 01:00
9	**3.2. Bacterial cell-cell communication: conjugation and 3.3 Morphogenesis** Duration: 02:00 Lecture			**Reading papers** Other assessment Continuous assessment Not Presential Duration: 01:00

10	**4.1: Gro. 4.2: Portable biolabs** Duration: 02:00 Lecture			**Reading papers** Other assessment Continuous assessment Not Presential Duration: 01:00
11	**4.4: Deep learning in SynBio** Duration: 02:00 Lecture			**Reading papers** Other assessment Continuous assessment Not Presential Duration: 01:00
12	**iGEM groups presentations** Duration: 02:00 Lecture			**Reading papers** Other assessment Continuous assessment Not Presential Duration: 01:00
13	**Oral presentations students** Duration: 02:00 Cooperative activities			
14	**Oral presentations of the students** Duration: 02:00 Lecture			
15	**Oral presentations of the students** Duration: 02:00 Lecture			**Oral presentations** Individual presentation Continuous assessment Presential Duration: 10:00
16	**Review of general topics** Duration: 02:00 Problem-solving class			**Oral Presentation** Individual presentation Final examination Presential Duration: 10:00
17	**Written exam** Duration: 02:00 Additional activities			**Written exam** Written test Continuous assessment Presential Duration: 14:00 **Final written assay** Individual work Continuous assessment Not Presential Duration: 50:00 **Final written assay (for final evaluation)** Individual work Final examination Not Presential Duration: 44:00 **Written exam (for only final evaluation)** Written test Final examination Not Presential Duration: 20:00

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. Assessment

Week	Description	Modality	Type	Duration	Weight	Minimum grade	Evaluated skills
1	Reading papers	Other assessment	No Presential	01:00	2%	5 / 10	CG15 CGI1 CG9 CGI4
2	Reading papers	Other assessment	No Presential	01:00	2%	5 / 10	CG15 CGI1 CG9 CGI4
3	Reading papers	Other assessment	No Presential	01:00	2%	5 / 10	CG15 CGI1 CG9 CGI4
4	Reading papers	Other assessment	No Presential	01:00	2%	5 / 10	CG15 CGI1 CG9 CGI4
5	Reading papers	Other assessment	No Presential	01:00	2%	5 / 10	CG15 CGI1 CG9 CGI4
6	Reading papers	Other assessment	No Presential	01:00	2%	5 / 10	CG15 CGI1 CG9 CGI4
7	Reading papers	Other assessment	No Presential	01:00	2%	5 / 10	CG15 CGI1 CG9 CGI4
8	Reading papers	Other assessment	No Presential	01:00	2%	5 / 10	CG15 CGI1 CG9 CGI4

9	Reading papers	Other assessment	No Presential	01:00	2%	5 / 10	CG15 CGI1 CG9 CGI4
10	Reading papers	Other assessment	No Presential	01:00	2%	5 / 10	CG15 CGI1 CG9 CGI4
11	Reading papers	Other assessment	No Presential	01:00	2%	5 / 10	CG15 CGI1 CG9 CGI4
12	Reading papers	Other assessment	No Presential	01:00	2%	5 / 10	CG15 CGI1 CG9 CGI4
15	Oral presentations	Individual presentation	Face-to-face	10:00	30%	5 / 10	
17	Written exam	Written test	Face-to-face	14:00	30%	3 / 10	CG18 CG6 CG8 CG15 CGI1 CGI2 CEIA1 CEIA2 CEIA5 CG9 CGI3 CGI4
17	Final written assay	Individual work	No Presential	50:00	40%	4 / 10	

6.1.2. Global examination

Week	Description	Modality	Type	Duration	Weight	Minimum grade	Evaluated skills
16	Oral Presentation	Individual presentation	Face-to-face	10:00	30%	4 / 10	CG18 CG6 CGI2 CG9 CGI3 CGI4
17	Final written assay (for final evaluation)	Individual work	No Presential	44:00	40%	3 / 10	CG6 CEIA1 CGI3

17	Written exam (for only final evaluation)	Written test	No Presential	20:00	30%	3 / 10	CG18 CG8 CG15 CGI1 CGI2 CEIA2 CEIA5 CG9 CGI4

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 3 puntos sobre 10.

El examen de conocimientos básicos se realiza al final del curso. Tiene un valor máximo de 3 puntos sobre 10.

El trabajo escrito final tiene un valor máximo de 4 puntos sobre 10.

Para superar la asignatura hay que obtener al menos 5 puntos sobre un total de 10 al sumar las dos calificaciones anteriores (presentación oral+trabajo escrito). Y llevar al menos un 4 sobre 10 en 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