



POLITÉCNICA

INTERNATIONAL  
CAMPUS OF  
EXCELLENCE

COORDINATION PROCESS OF  
LEARNING ACTIVITIES  
PR/CL/001



E.T.S. de Ingenieros  
Informáticos

# ANX-PR/CL/001-01

## LEARNING GUIDE

### SUBJECT

**103000363 - Programmable biology: dna computing and biocircuits engineering**

### DEGREE PROGRAMME

10AJ - Master Universitario En Inteligencia Artificial

### ACADEMIC YEAR & SEMESTER

2018/19 - Semester 1

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### Learning guide

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## 1. Description

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### 1.1. Subject details

|                                       |   |
|---------------------------------------|---|
| <b>Name of the subject</b>            | 103000363 - Programmable biology: dna computing amd biocircuits engineering |
| <b>No of credits</b>                  | 5 ECTS  |
| <b>Type</b>                           | Optional  |
| <b>Academic year of the programme</b> | First year  |
| <b>Semester of tuition</b>            | Semester 1  |
| <b>Tuition period</b>                 | September-January   |
| <b>Tuition languages</b>              | English   |
| <b>Degree programme</b>               | 10AJ - Master universitario en inteligencia artificial                      |
| <b>Centre</b>                         | 10 - Escuela Tecnica Superior de Ingenieros Informaticos                    |
| <b>Academic year</b>                  | 2018-19   |

## 2. Faculty

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### 2.1. Faculty members with subject teaching role

| <b>Name and surname</b>   | <b>Office/Room</b> | <b>Email</b>                       | <b>Tutoring hours *</b> |
|---|--------------------|------------------------------------|-------------------------|
| Alfonso Vicente Rodriguez-<br>Paton Aradas (Subject<br>coordinator) | 2106               | alfonso.rodriguez-<br>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 \*

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### 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

CEIA10 - Identificación de áreas de aplicación en las que se pueda utilizar las técnicas y métodos de la Inteligencia Artificial.

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.

CG11 - Adquirir conocimientos científicos avanzados del campo de la informática que le permitan generar nuevas ideas dentro de una línea de investigación.

CG12 - 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.

CG13 - Capacidad para valorar la importancia de las fuentes documentales, manejarlas y buscar la información para el desarrollo de cualquier trabajo de investigación.

CG14 - 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 cómo se pueden diseñar e implementar bioalgoritmos que emplean moléculas de ADN como sustrato (memoria).

RA91 - Diseñar circuitos lógicos biomoleculares sintéticos operando : (1) con ADN/ARN o (2) con proteínas

RA92 - Comprender cómo las células procesan información codificada en biomoléculas y toman decisiones.

RA4 - Valorar la importancia de las fuentes documentales y seleccionar aquellas 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

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### 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 these 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 opens 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 uses 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/0B1K8p9umsfI4WWWhUd1IMLTA0OVE/view>

## 4.2. Syllabus

### 1. DNA Computing

- 1.1. DNA structure and DNA operations
- 1.2. DNA Strand displacement-based biocircuits
- 1.3. 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: A toggle switch and an oscillator (repressilator)
- 2.4. Designing genetic circuits: Directed evolution
- 2.5. 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 and tissues with IBM: Gro and Morpheus
- 4.2. BioBlocks: programming experiments with blocks
- 4.3. Engineering portable biolabs with Arduino cards
- 4.4. Deep learning in SynBio

## 5. Schedule

### 5.1. Subject schedule\*

| Week | Face-to-face classroom activities   | Face-to-face laboratory activities | Other face-to-face activities | Assessment activities   |
|------|---|------------------------------------|-------------------------------|---|
| 1    | <b>Tema 1: DNA Computing 1.1: DNA structure and DNA operations</b><br>Duration: 02:00<br>Lecture                                      |                                    |                               | <b>Reading papers</b><br>Other assessment<br>Continuous assessment<br>Duration: 01:00 |
| 2    | <b>1.2 DNA Strand displacement-based biocircuits</b><br>Duration: 02:00<br>Lecture  |                                    |                               | <b>Reading papers</b><br>Other assessment<br>Continuous assessment<br>Duration: 01:00 |
| 3    | <b>1.3 Molecular automata and DNA origami</b><br>Duration: 02:00<br>Lecture   |                                    |                               | <b>Reading papers</b><br>Other assessment<br>Continuous assessment<br>Duration: 01:00 |
| 4    | <b>2. Synthetic Biology: unicellular genetic circuits. 2.1. Gene expression and regulation</b><br>Duration: 02:00<br>Lecture          |                                    |                               | <b>Reading papers</b><br>Other assessment<br>Continuous assessment<br>Duration: 01:00 |
| 5    | <b>2.2. Genetic Boolean logic gates</b><br>Duration: 02:00<br>Lecture   |                                    |                               | <b>Reading papers</b><br>Other assessment<br>Continuous assessment<br>Duration: 01:00 |
| 6    | <b>2.3. Basic genetic circuits: A toggle switch and an oscillator (repressilator)</b><br>Duration: 02:00<br>Lecture                   |                                    |                               | <b>Reading papers</b><br>Other assessment<br>Continuous assessment<br>Duration: 01:00 |
| 7    | <b>2.4. Designing genetic circuits: Directed evolution and 2.5 CRISPR-based devices and gene drives</b><br>Duration: 02:00<br>Lecture |                                    |                               | <b>Reading papers</b><br>Other assessment<br>Continuous assessment<br>Duration: 01:00 |
| 8    | <b>3.1 Bacterial cell-cell communication: quorum sensing based-circuits</b><br>Duration: 02:00<br>Lecture                             |                                    |                               | <b>Reading papers</b><br>Other assessment<br>Continuous assessment<br>Duration: 01:00 |
| 9    | <b>3.2. Bacterial cell-cell communication: conjugation and 3.3 Morphogenesis</b><br>Duration: 02:00<br>Lecture                        |                                    |                               | <b>Reading papers</b><br>Other assessment<br>Continuous assessment<br>Duration: 01:00 |
| 10   | <b>4.1: Gro and Morpheus. 4.2: BioBlocks and 4.3: Portable biolabs</b><br>Duration: 02:00<br>Lecture                                  |                                    |                               | <b>Reading papers</b><br>Other assessment<br>Continuous assessment<br>Duration: 01:00 |



|    |   |  |  |   |
|----|---|--|--|---|
| 11 | <b>4.4: Deep learning in SynBio</b><br>Duration: 02:00<br>Lecture               |  |  | <b>Reading papers</b><br>Other assessment<br>Continuous assessment<br>Duration: 01:00   |
| 12 | <b>iGEM groups presentations</b><br>Duration: 02:00<br>Lecture                  |  |  | <b>Reading papers</b><br>Other assessment<br>Continuous assessment<br>Duration: 01:00   |
| 13 | <b>Oral presentations students</b><br>Duration: 02:00<br>Cooperative activities |  |  |   |
| 14 | <b>Oral presentations of the students</b><br>Duration: 02:00<br>Lecture         |  |  |   |
| 15 | <b>Oral presentations of the students</b><br>Duration: 02:00<br>Lecture         |  |  | <b>Oral presentations</b><br>Individual presentation<br>Continuous assessment<br>Duration: 25:00  |
| 16 | <b>Review of general topics</b><br>Duration: 02:00<br>Problem-solving class     |  |  |   |
| 17 | <b>Written exam</b><br>Duration: 02:00<br>Additional activities                 |  |  | <b>Written exam</b><br>Written test<br>Continuous assessment<br>Duration: 14:00<br><br><b>Final written assay</b><br>Individual work<br>Continuous assessment<br>Duration: 50:00<br><br><b>Final written assay (for final evaluation)</b><br>Individual work<br>Final examination<br>Duration: 44:00<br><br><b>Written exam (for only final evaluation)</b><br>Written test<br>Final examination<br>Duration: 20:00 |

The independent study hours are training activities during which students should spend time on individual study or individual assignments.

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 subject schedule is based on a previous theoretical planning of the subject plan and might go through experience some unexpected changes along throughout the academic year.

## 6. Activities and assessment criteria

### 6.1. Assessment activities

#### 6.1.1. Continuous assessment

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

|    |                     |                         |               |       |     |        |  |
|----|---------------------|-------------------------|---------------|-------|-----|--------|--|
| 9  | Reading papers      | Other assessment        | No Presential | 01:00 | 2%  | 5 / 10 | CG11<br>CG15<br>CG9<br>CGI4  |
| 10 | Reading papers      | Other assessment        | No Presential | 01:00 | 2%  | 5 / 10 | CG11<br>CG15<br>CG9<br>CGI4  |
| 11 | Reading papers      | Other assessment        | No Presential | 01:00 | 2%  | 5 / 10 | CG11<br>CG15<br>CG9<br>CGI4  |
| 12 | Reading papers      | Other assessment        | No Presential | 01:00 | 2%  | 5 / 10 | CG11<br>CG15<br>CG9<br>CGI4  |
| 15 | Oral presentations  | Individual presentation | Face-to-face  | 25:00 | 25% | 5 / 10 |  |
| 17 | Written exam        | Written test            | Face-to-face  | 14:00 | 1%  | 5 / 10 | CG18<br>CEIA1<br>CGI1<br>CGI2<br>CEIA2<br>CEIA5<br>CG6<br>CG8<br>CG15<br>CG9<br>CGI4<br>CEIA10<br>CGI3 |
| 17 | Final written essay | Individual work         | No Presential | 50:00 | 50% | 5 / 10 |  |

### 6.1.2. Final examination

| Week | Description                                | Modality        | Type          | Duration | Weight | Minimum grade | Evaluated skills   |
|------|--|-----------------|---------------|----------|--------|---------------|--|
| 17   | Final written essay (for final evaluation) | Individual work | No Presential | 44:00    | 75%    | 5 / 10        | CEIA1<br>CG6<br>CGI3   |
| 17   | Written exam (for only final evaluation)   | Written test    | No Presential | 20:00    | 25%    | 5 / 10        | CG18<br>CGI1<br>CGI2<br>CEIA2<br>CEIA5<br>CG8<br>CG15<br>CG9<br>CGI4<br>CEIA10 |

### 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 2,5 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 5,5 puntos sobre 10.

La asistencia y participación activa en clase se valorará entre 0 y 2 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):<br /><br><a href="http://www.lia.upm.es">http://www.lia.upm.es</a>   |
| 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: <a href="https://github.com/liaupm/GRO-LIA">https://github.com/liaupm/GRO-LIA</a> <br /><br>Paper: <a href="https://pubs.acs.org/doi/abs/10.1021/acsynbio.7b00003">https://pubs.acs.org/doi/abs/10.1021/acsynbio.7b00003</a>               |
| BioBlocks                  | Web resource | Drag-and-drop software for describing biological protocols based on Scratch<br /><br>Paper: <a href="http://biorxiv.org/content/early/2016/10/14/081075">http://biorxiv.org/content/early/2016/10/14/081075</a> <br /><br>Link: <a href="https://github.com/liaupm">https://github.com/liaupm</a> |