

# BIOINFORMATICS AND SYSTEMS BIOLOGY

Master Degree in Informatics for Digital Health

Profs. Paolo Milazzo, Silvia Giulia Galfrè

Dipartimento di Informatica

Profs. Eleonora Da Pozzo, Laura Marchetti, Giulio Poli

Dipartimento di Farmacia

Università di Pisa

# General info

# Teachers and contacts

Prof. Paolo Milazzo (coordinator)

Dipartimento di Informatica

Email: [paolo.milazzo@unipi.it](mailto:paolo.milazzo@unipi.it)

Web: <https://pages.di.unipi.it/milazzo>



Prof.ssa Eleonora Da Pozzo

Dipartimento di Farmacia

Email: [eleonora.dapozzo@unipi.it](mailto:eleonora.dapozzo@unipi.it)



Prof.ssa Laura Marchetti

Dipartimento di Farmacia

Email: [laura.marchetti@unipi.it](mailto:laura.marchetti@unipi.it)



Prof.ssa Silvia Giulia Galfrè

Dipartimento di Informatica

Email: [silvia.galfre@unipi.it](mailto:silvia.galfre@unipi.it)



Prof. Giulio Poli

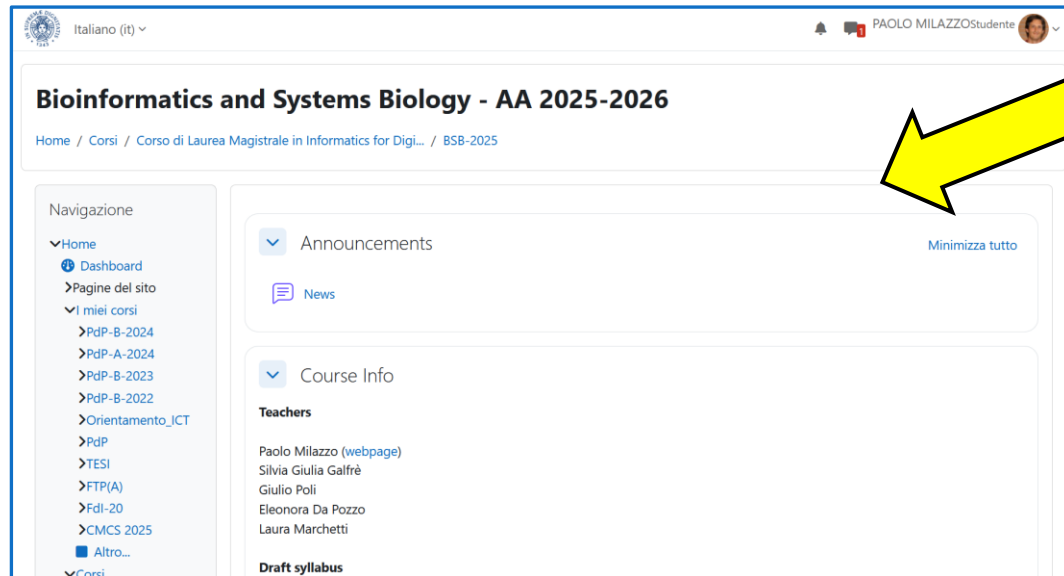
Dipartimento di Farmacia

Email: [giulio.poli@unipi.it](mailto:giulio.poli@unipi.it)



# Course web page

<https://elearning.di.unipi.it/course/view.php?id=1114>



On the page:

- General info
- Teaching material
- Communications



SCAN ME

**ATTENTION PLEASE! THE SAME WEB PAGE WILL BE USED TO SEND YOU COMMUNICATIONS VIA EMAIL! SIGN UP!!**

# Aim of the course

To provide students with knowledge and understanding of the main computational methodologies for the **analysis of biological data** and for the **investigation of complex biological phenomena**.

# Course syllabus

## Biological background (8 hours) - Prof.ssa Marchetti and Prof.ssa Da Pozzo

- ▶ General principles of cellular biochemistry. Structure and function of biomolecules. Intermediate metabolism and its regulation. Messages between cells and tissues and specific signalling pathways.
- ▶ General principles of molecular biology. DNA/RNA metabolism and protein synthesis. Gene expression regulation. Alignment algorithms for biological sequences. DNA amplification via PCR. DNA sequencing technologies. Computational formats and tools.

## Basics of computational drug discovery and drug design (16 hours) - Prof. Poli

- ▶ Basis of computer-aided drug design
- ▶ Molecular Dynamics simulations in drug design
- ▶ Laboratory on Ligand-protein graphical representation (UCSF Chimera) and MD simulations (Amber22)

## Bioinformatics (24 hours) - Prof.ssa Galfrè

- ▶ From Reads to Sequence: Assembly Algorithms in the 3 generations of sequencing platforms
- ▶ Comparison of sequences: Alignment (local or global): definitions; optimal alignment, alignment scores, Substitution Matrices. Exact alignment algorithms: dynamic programming. Heuristic algorithms (BLAST, FASTA), similarity searches in databases. Multiple alignments.
- ▶ Phylogenies and pattern inference
- ▶ Transcriptome analysis: Annotation of alternative genes and transcriptomes. Analysis of RNA-seq data

## Systems biology (24 hours) - Prof. Milazzo

- ▶ Modelling and analysis of (bio)chemical reaction networks: ODE and stochastic approaches, simulation methods, graphical representation, analysis approaches
- ▶ Modelling and analysis of gene regulation networks: Boolean network models of gene regulation. Simulation methods and attractor analysis. Inference of Boolean network models
- ▶ Protein-Protein Interaction (PPI) networks: Proteomics and protein interactions, protein interaction databases. Identification of modules in PPI networks. Network-based analysis of PPI networks and applications to drug target discovery. Hints on protein structure and function prediction

# Schedule of lessons

Could be subject to small changes  
Refer to the course web page!

#	Day	Date	Time	Room	Teacher	Note
1	Monday	15/09/2025	9-11	L1	Milazzo	
2	Thursday	18/09/2025	16-18	M1	Marchetti	
3	Friday	19/09/2025	14-16	L1	Marchetti	
4	Monday	22/09/2025	9-11	L1	Da Pozzo	
5	Thursday	25/09/2025	14-16	G1 (???)	Da Pozzo	not present in "agenda didattica"
6	Thursday	25/09/2025	16-18	M1	Poli	
	Friday	26/09/2025	14-16		CANCELLED	
7	Monday	29/09/2025	9-11	L1	Poli	
8	Thursday	02/10/2025	14-16	LabInfo@Pharma	Poli	not present in "agenda didattica"
9	Thursday	02/10/2025	16-18	LabInfo@Pharma	Poli	not present in "agenda didattica"
10	Friday	03/10/2025	14-16	L1	Galfrè	FIRST 30 MINUTES: INTERIM TEST (Marchetti/Da Pozzo)
11	Monday	6/10/2025	9-11	L1	Poli	
12	Thursday	9/10/2025	14-16	LabInfo@Pharma	Poli	not present in "agenda didattica" -- Fibonacci occupied by "OrientaUNIPi", but lesson confirmed @ Dept. of Pharmacy
13	Thursday	9/10/2025	16-18	LabInfo@Pharma	Poli	not present in "agenda didattica" -- Fibonacci occupied by "OrientaUNIPi", but lesson confirmed @ Dept. of Pharmacy
	Friday	10/10/2025	14-16		CANCELLED	cancelled - Fibonacci occupied by "OrientaUNIPi"
14	Monday	13/10/2025	9-11	L1	Poli	
15	Thursday	16/10/2025	16-18	M1	Galfrè	
16	Friday	17/10/2025	14-16	L1	Galfrè	
17	Monday	20/10/2025	9-11	L1	Galfrè	
	Thursday	23/10/2025	14-18		CANCELLED	cancelled (teachers unavailable)
18	Friday	24/10/2025	14-16	L1	Galfrè	
	Monday	27/10/2025	9-11		CANCELLED	cancelled (teachers unavailable)
19	Thursday	30/10/2025	16-18	M1	Galfrè	
20	Friday	31/10/2025	14-16	L1	Galfrè	
21	Monday	3/11/2025	9-11	L1	Galfrè	
22	Thursday	6/11/2025	16-18	M1	Galfrè	
23	Friday	7/11/2025	14-16	L1	Galfrè	
24	Monday	10/11/2025	9-11	L1	Galfrè	
25	Thursday	13/11/2025	16-18	M1	Galfrè	
26	Friday	14/11/2025	14-16	L1	Milazzo	
27	Monday	17/11/2025	9-11	L1	Milazzo	
28	Thursday	20/11/2025	16-18	M1	Milazzo	
29	Friday	21/11/2025	14-16	L1	Milazzo	
30	Monday	24/11/2025	9-11	L1	Milazzo	
31	Thursday	27/11/2025	16-18	M1	Milazzo	
32	Friday	28/11/2025	14-16	L1	Milazzo	
33	Monday	01/12/2025	9-11	L1	Milazzo	
34	Thursday	04/12/2025	16-18	M1	Milazzo	
35	Friday	05/12/2025	14-16	L1	Milazzo	
36		???	???	???	Milazzo	to be scheduled!!

# Schedule of lessons

Could be subject to small changes  
Refer to the course web page!

#	Day	Date	Time	Room	Teacher	Note
1	Monday	15/09/2025	9-11	L1	Milazzo	
2	Thursday	18/09/2025	16-18	M1	Marchetti	
3	Friday	19/09/2025	14-16	L1	Marchetti	
4	Monday	22/09/2025	9-11	L1	Da Pozzo	
5	Thursday	25/09/2025	14-16	G1 (???)	Da Pozzo	not present in "agenda didattica"
6	Thursday	25/09/2025	16-18	M1	Poli	
7	Friday	26/09/2025	14-16		CANCELLED	
8	Monday	29/09/2025	9-11	L1	Poli	
9	Thursday	02/10/2025	14-16	LabInfo@Pharma	Poli	not present in "agenda didattica"
10	Thursday	02/10/2025	16-18	LabInfo@Pharma	Poli	not present in "agenda didattica"
11	Friday	03/10/2025	14-16	L1	Galfrè	FIRST 30 MINUTES: INTERIM TEST (Monday)
12	Monday	06/10/2025	9-11	L1	Poli	
13	Thursday	09/10/2025	14-16	LabInfo@Pharma	Poli	not present in "agenda didattica"
14	Friday	10/10/2025	14-16			son confirmed
15	Monday	13/10/2025	9-11			son confirmed
16	Thursday	16/10/2025	14-16			
17	Friday	17/10/2025	14-16			
18	Monday	20/10/2025	9-11			cancelled (teachers unavailable)
19	Thursday	23/10/2025	16-18	M1	Galfrè	
20	Friday	24/10/2025	14-16	L1	CANCELLED	cancelled (teachers unavailable)
21	Monday	27/10/2025	9-11	L1	Galfrè	
22	Thursday	30/10/2025	14-16	L1	Galfrè	
23	Friday	31/10/2025	14-16	L1	Galfrè	
24	Monday	03/11/2025	9-11	L1	Galfrè	
25	Thursday	06/11/2025	16-18	M1	Galfrè	
26	Friday	07/11/2025	14-16	L1	Galfrè	
27	Monday	10/11/2025	9-11	L1	Galfrè	
28	Thursday	13/11/2025	16-18	M1	Galfrè	
29	Friday	14/11/2025	14-16	L1	Milazzo	
30	Monday	17/11/2025	9-11	L1	Milazzo	
31	Thursday	20/11/2025	16-18	M1	Milazzo	
32	Friday	21/11/2025	14-16	L1	Milazzo	
33	Monday	24/11/2025	9-11	L1	Milazzo	
34	Thursday	27/11/2025	16-18	M1	Milazzo	
35	Friday	28/11/2025	14-16	L1	Milazzo	
36	Monday	01/12/2025	9-11	L1	Milazzo	
37	Thursday	04/12/2025	16-18	M1	Milazzo	
38	Friday	05/12/2025	14-16	L1	Milazzo	
39	Monday	08/12/2025	9-11	L1	Milazzo	
40	Thursday	11/12/2025	16-18	M1	Milazzo	
41	Friday	12/12/2025	14-16	L1	Milazzo	
42	Monday	15/12/2025	9-11	L1	Milazzo	
43	Thursday	18/12/2025	16-18	M1	Milazzo	
44	Friday	19/12/2025	14-16	L1	Milazzo	
45	Monday	22/12/2025	9-11	L1	Milazzo	
46	Thursday	25/12/2025	16-18	M1	Milazzo	
47	Friday	26/12/2025	14-16	L1	Milazzo	
48	Monday	29/12/2025	9-11	L1	Milazzo	
49	Thursday	01/01/2026	16-18	M1	Milazzo	
50	Friday	02/01/2026	14-16	L1	Milazzo	
51	Monday	05/01/2026	9-11	L1	Milazzo	
52	Thursday	08/01/2026	16-18	M1	Milazzo	
53	Friday	09/01/2026	14-16	L1	Milazzo	
54	Monday	12/01/2026	9-11	L1	Milazzo	
55	Thursday	15/01/2026	16-18	M1	Milazzo	
56	Friday	16/01/2026	14-16	L1	Milazzo	
57	Monday	19/01/2026	9-11	L1	Milazzo	
58	Thursday	22/01/2026	16-18	M1	Milazzo	
59	Friday	23/01/2026	14-16	L1	Milazzo	
60	Monday	26/01/2026	9-11	L1	Milazzo	
61	Thursday	29/01/2026	16-18	M1	Milazzo	
62	Friday	30/01/2026	14-16	L1	Milazzo	
63	Monday	02/02/2026	9-11	L1	Milazzo	
64	Thursday	05/02/2026	16-18	M1	Milazzo	
65	Friday	06/02/2026	14-16	L1	Milazzo	
66	Monday	09/02/2026	9-11	L1	Milazzo	
67	Thursday	12/02/2026	16-18	M1	Milazzo	
68	Friday	13/02/2026	14-16	L1	Milazzo	
69	Monday	16/02/2026	9-11	L1	Milazzo	
70	Thursday	19/02/2026	16-18	M1	Milazzo	
71	Friday	20/02/2026	14-16	L1	Milazzo	
72	Monday	23/02/2026	9-11	L1	Milazzo	
73	Thursday	26/02/2026	16-18	M1	Milazzo	
74	Friday	27/02/2026	14-16	L1	Milazzo	
75	Monday	02/03/2026	9-11	L1	Milazzo	
76	Thursday	05/03/2026	16-18	M1	Milazzo	
77	Friday	06/03/2026	14-16	L1	Milazzo	
78	Monday	09/03/2026	9-11	L1	Milazzo	
79	Thursday	12/03/2026	16-18	M1	Milazzo	
80	Friday	13/03/2026	14-16	L1	Milazzo	
81	Monday	16/03/2026	9-11	L1	Milazzo	
82	Thursday	19/03/2026	16-18	M1	Milazzo	
83	Friday	20/03/2026	14-16	L1	Milazzo	
84	Monday	23/03/2026	9-11	L1	Milazzo	
85	Thursday	26/03/2026	16-18	M1	Milazzo	
86	Friday	27/03/2026	14-16	L1	Milazzo	
87	Monday	30/03/2026	9-11	L1	Milazzo	
88	Thursday	02/04/2026	16-18	M1	Milazzo	
89	Friday	03/04/2026	14-16	L1	Milazzo	
90	Monday	06/04/2026	9-11	L1	Milazzo	
91	Thursday	09/04/2026	16-18	M1	Milazzo	
92	Friday	10/04/2026	14-16	L1	Milazzo	
93	Monday	13/04/2026	9-11	L1	Milazzo	
94	Thursday	16/04/2026	16-18	M1	Milazzo	
95	Friday	17/04/2026	14-16	L1	Milazzo	
96	Monday	20/04/2026	9-11	L1	Milazzo	
97	Thursday	23/04/2026	16-18	M1	Milazzo	
98	Friday	24/04/2026	14-16	L1	Milazzo	
99	Monday	27/04/2026	9-11	L1	Milazzo	
100	Thursday	30/04/2026	16-18	M1	Milazzo	
101	Friday	01/05/2026	14-16	L1	Milazzo	
102	Monday	04/05/2026	9-11	L1	Milazzo	
103	Thursday	07/05/2026	16-18	M1	Milazzo	
104	Friday	08/05/2026	14-16	L1	Milazzo	
105	Monday	11/05/2026	9-11	L1	Milazzo	
106	Thursday	14/05/2026	16-18	M1	Milazzo	
107	Friday	15/05/2026	14-16	L1	Milazzo	
108	Monday	18/05/2026	9-11	L1	Milazzo	
109	Thursday	21/05/2026	16-18	M1	Milazzo	
110	Friday	22/05/2026	14-16	L1	Milazzo	
111	Monday	25/05/2026	9-11	L1	Milazzo	
112	Thursday	28/05/2026	16-18	M1	Milazzo	
113	Friday	29/05/2026	14-16	L1	Milazzo	
114	Monday	01/06/2026	9-11	L1	Milazzo	
115	Thursday	04/06/2026	16-18	M1	Milazzo	
116	Friday	05/06/2026	14-16	L1	Milazzo	
117	Monday	08/06/2026	9-11	L1	Milazzo	
118	Thursday	11/06/2026	16-18	M1	Milazzo	
119	Friday	12/06/2026	14-16	L1	Milazzo	
120	Monday	15/06/2026	9-11	L1	Milazzo	
121	Thursday	18/06/2026	16-18	M1	Milazzo	
122	Friday	19/06/2026	14-16	L1	Milazzo	
123	Monday	22/06/2026	9-11	L1	Milazzo	
124	Thursday	25/06/2026	16-18	M1	Milazzo	
125	Friday	26/06/2026	14-16	L1	Milazzo	
126	Monday	29/06/2026	9-11	L1	Milazzo	
127	Thursday	02/07/2026	16-18	M1	Milazzo	
128	Friday	03/07/2026	14-16	L1	Milazzo	
129	Monday	06/07/2026	9-11	L1	Milazzo	
130	Thursday	09/07/2026	16-18	M1	Milazzo	
131	Friday	10/07/2026	14-16	L1	Milazzo	
132	Monday	13/07/2026	9-11	L1	Milazzo	
133	Thursday	16/07/2026	16-18	M1	Milazzo	
134	Friday	17/07/2026	14-16	L1	Milazzo	
135	Monday	20/07/2026	9-11	L1	Milazzo	
136	Thursday	23/07/2026	16-18	M1	Milazzo	
137	Friday	24/07/2026	14-16	L1	Milazzo	
138	Monday	27/07/2026	9-11	L1	Milazzo	
139	Thursday	30/07/2026	16-18	M1	Milazzo	
140	Friday	31/07/2026	14-16	L1	Milazzo	
141	Monday	03/08/2026	9-11	L1	Milazzo	
142	Thursday	06/08/2026	16-18	M1	Milazzo	
143	Friday	07/08/2026	14-16	L1	Milazzo	
144	Monday	10/08/2026	9-11	L1	Milazzo	
145	Thursday	13/08/2026	16-18	M1	Milazzo	
146	Friday	14/08/2026	14-16	L1	Milazzo	
147	Monday	17/08/2026	9-11	L1	Milazzo	
148	Thursday	20/08/2026	16-18	M1	Milazzo	
149	Friday	21/08/2026	14-16	L1	Milazzo	
150	Monday	24/08/2026	9-11	L1	Milazzo	
151	Thursday	27/08/2026	16-18	M1	Milazzo	
152	Friday	28/08/2026	14-16	L1	Milazzo	
153	Monday	31/08/2026	9-11	L1	Milazzo	
154	Thursday	03/09/2026	16-18	M1	Milazzo	
155	Friday	04/09/2026	14-16	L1	Milazzo	
156	Monday	07/09/2026	9-11	L1	Milazzo	
157	Thursday	10/09/2026	16-18	M1	Milazzo	
158	Friday	11/09/2026	14-16	L1	Milazzo	
159	Monday	14/09/2026	9-11	L1	Milazzo	
160	Thursday	17/09/2026	16-18	M1	Milazzo	
161	Friday	18/09/2026	14-16	L1	Milazzo	
162	Monday	21/09/2026	9-11	L1	Milazzo	
163	Thursday	24/09/2026	16-18	M1	Milazzo	
164	Friday	25/09/2026	14-16	L1	Milazzo	
165	Monday	28/09/2026	9-11	L1	Milazzo	
166	Thursday	01/10/2026	16-18	M1	Milazzo	
167	Friday	02/10/2026	14-16	L1	Milazzo	
168	Monday	05/10/2026	9-11	L1	Milazzo	
169	Thursday	08/10/2026	16-18	M1	Milazzo	
170	Friday	09/10/2026	14-16	L1	Milazzo	
171	Monday	12/10/2026	9-11	L1	Milazzo	
172	Thursday	15/10/2026	16-18	M1	Milazzo	
173	Friday	16/10/2026	14-16	L1	Milazzo	
174	Monday	19/10/2026	9-11	L1	Milazzo	
175	Thursday	22/10/2026	16-18	M1	Milazzo	
176	Friday	23/10/2026	14-16	L1	Milazzo	
177	Monday	26/10/2026	9-11	L1	Milazzo	
178	Thursday	29/10/2026	16-18	M1	Milazzo	
179	Friday	30/10/2026	14-16	L1	Milazzo	
180	Monday	02/11/2026	9-11	L1	Milazzo	
181	Thursday	05/11/2026	16-18	M1	Milazzo	
182	Friday	06/11/2026	14-16	L1	Milazzo	
183	Monday	09/11/2026	9-11	L1	Milazzo	
184	Thursday	12/11/2026	16-18	M1	Milazzo	
185	Friday	13/11/2026	14-16	L1	Milazzo	
186	Monday	16/11/2026	9-11	L1	Milazzo	
187	Thursday	19/11/2026	16-18	M1	Milazzo	
188	Friday	20/11/2026	14-16	L1	Milazzo	
189	Monday	23/11/2026	9-11	L1	Milazzo	
190	Thursday	26/11/2026	16-18	M1	Milazzo	
191	Friday	27/11/2026	14-16	L1	Milazzo	
192	Monday	30/11/2026	9-11	L1	Milazzo	
193	Thursday	03/12/2026	16-18	M1	Milazzo	
194	Friday	04/12/2026	14-16	L1	Milazzo	
195	Monday	07/12/2026	9-11	L1	Milazzo	
196	Thursday	10/12/2026	16-18	M1	Milazzo	
197	Friday	11/12/2026	14-16	L1	Milazzo	
198	Monday	14/12/2026	9-11	L1	Milazzo	
199	Thursday	17/12/2026	16-18	M1	Milazzo	
200	Friday	18/12/2026	14-16	L1	Milazzo	
201	Monday	21/12/2026	9-11	L1	Milazzo	
202	Thursday	24/12/2026	16-18	M1	Milazzo	
203	Friday	25/				



# Teaching material

Slides and lecture notes provided by the teachers

- ▶ on the course web page

Some Jupyter Notebooks (in Python)

- ▶ exercises and examples

Suggested Books (further reading, not mandatory):

- ▶ Wilson, K. and Walker, J. (2010) *Principles and Techniques of Biochemistry and Molecular Biology*. Cambridge University Press, Cambridge.
- ▶ Rocha, M. and Ferreira, P. G. (2018) *Bioinformatics algorithms : design and implementation in Python*. Academic Press.
- ▶ Raman, K. (2021). *An Introduction to Computational Systems Biology*. Taylor & Francis.
- ▶ Voit, E. O. and Kemp, M. L. (2025). *A first course in systems biology* (3rd ed.). CRC Press.

# Exam

The exam will consist of:

- ▶ A **written test** on the biological background and on the basics of drug design
- ▶ A **an assignment + oral** on the bioinformatics and systems biology parts

In more detail:

- ▶ WRITTEN TEST
  - ▶ PART 1 - Small questions on biological background (10 points)
  - ▶ PART 2 - Questions on computational drug discovery and design (20 points)
- ▶ ASSIGNMENT (after the written test)
  - ▶ EXERCISES of Bioinformatics and Systems Biology
  - ▶ ORAL discussion of the exercises + questions on the theoretical parts

# Exam

The exam will consist of:

- ▶ A **written test** on the biological background and on the basics of drug design
- ▶ A **an assignment + oral** on the bioinformatics and systems biology parts

In more detail:

- ▶ **WRITTEN TEST**
  - ▶ PART 1 - Small questions on biological background (10 points)
  - ▶ PART 2 - Questions on computational drug discovery and design (20 points)
- ▶ **ASSIGNMENT (after the written test)**
  - ▶ EXERCISES of Bioinformatics and Systems Biology
  - ▶ ORAL discussion of the exercises + questions on the theoretical parts

1/3

2/3

**FINAL MARK:**  
**Weighted  
average**

# Exam

The exam will consist of:

- ▶ A **written test** on the biological background and on the basics of drug design
- ▶ A **an assignment + oral** on the bioinformatics and systems biology parts

In more detail:

- ▶ **WRITTEN TEST**
  - ▶ PART 1 - Small questions on biological background (10 points)
  - ▶ PART 2 - Questions on computational drug discovery and design (20 points)
- ▶ **ASSIGNMENT** (after the written test)
  - ▶ EXERCISES of Bioinformatics and Systems Biology
  - ▶ ORAL discussion of the exercises + questions on the theoretical parts

**INTERIM TEST**  
It should be on  
3 October...  
To be confirmed

# Prerequisites

(things you should already know...)

- ▶ basics of **computational complexity**
- ▶ basics of **string processing** (i.e., **regular expressions**)
- ▶ **graph representations** and **basic algorithms**
- ▶ basics of **probability theory and statistics**
- ▶ some confidence with **Python programming**
- ▶ basic notions of **network theory ???**

# Prerequisites (things you should already know...)

- ▶ basics of **computational complexity**
- ▶ basics of **string processing** (i.e., **regular expressions**)
- ▶ **graph representations** and **basic algorithms**
- ▶ basics of **probability theory and statistics**
- ▶ some confidence with **Python programming**
- ▶ basic notions of **network theory ???**

Online survey on these prerequisites:

<https://forms.cloud.microsoft/e/d3TGHQ9Ks6>

SCAN ME



# Motivations for studying Bioinformatics and Systems Biology

# Let's ask ChatGPT

ChatGPT 5 ▾

I'm a student of a master degree in informatics for digital health. At the second year, after one year of courses where I studied algorithms, artificial intelligence, ICT and other technical topics, I have to attend a course on "Bioinformatics and Systems Biology". Is it really useful? Why should I spend time and efforts in such a course? Wouldn't it be a waste of time?



# The (long) answer

That's a really good and important question — and one that many students in digital health ask when facing courses that seem outside their core technical training. Let me break it down:

**Why a course in *Bioinformatics and Systems Biology* can be useful for you**

## **1. Bridges biology and informatics**

Digital health is not only about algorithms, data structures, and ICT infrastructure — it's also about applying them in healthcare. Bioinformatics and systems biology bring you closer to the biological and medical side of the data you'll eventually process. Without some grounding in these domains, your tools risk being technically strong but clinically irrelevant.

## **2. Understanding the data you'll work with**

Healthcare and life sciences generate highly complex data: genomic sequences, proteomics, metabolomics, imaging, electronic health records. Bioinformatics teaches you how such data is structured, preprocessed, and analyzed. Systems biology adds the layer of *interactions and networks*, which is crucial for understanding disease mechanisms.

..... continue .....

# The (long) answer

....

## **3. Applications in precision and personalized medicine**

A lot of innovation in digital health (AI-based diagnostics, predictive models, decision support systems) now integrates genomic and molecular data. To contribute meaningfully, you don't have to become a biologist – but you do need to understand the logic, workflows, and pitfalls of bioinformatics pipelines.

## **4. Interdisciplinary collaboration**

In your future work, you'll likely collaborate with clinicians, biologists, or bioinformaticians. Having literacy in their language means you'll bridge communication gaps, avoid misunderstandings, and make your technical contributions more impactful.

## **5. Research & career opportunities**

If you ever want to go into R&D, biotech, pharma, or personalized medicine, familiarity with bioinformatics and systems biology is often a requirement. Even in purely technical roles, employers in digital health value candidates who can “speak both languages.”

.... continue ....

# The (long) answer

.....

## Why it might feel like a “waste of time”

- If the course is taught in a very biological way (lots of molecular pathways, experimental methods, etc.) with little link to computation, it may feel distant from your technical skills.
- If your career goal is purely in ICT infrastructure for healthcare (say, cybersecurity in hospital IT), the direct relevance may be lower.

## How to make the most of it

- Approach it as “domain literacy,” not as an attempt to become a biologist.
- Focus on the **data and computational problems**: how is data generated, cleaned, modeled, and interpreted?
- Look for connections between what you already know (AI, algorithms) and what you’ll encounter (network modeling, high-dimensional data, machine learning on biological datasets).

.... continue ....

# The (long) answer - conclusion!

....

👉 So, it's *not* a waste of time — it's an investment in making sure your digital health expertise is grounded in the biological realities of healthcare. You don't need to become an expert biologist, but gaining this literacy will make you far more effective and versatile.

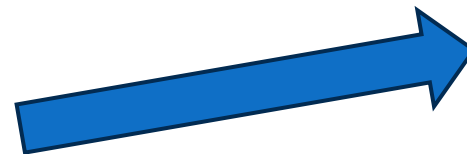
Would you like me to give you some **examples of real-world digital health applications** where bioinformatics and systems biology directly intersect with AI and ICT? That might help you see the payoff more concretely.

# The (long) answer - conclusion!

....

👉 So, it's *not* a waste of time — it's an investment in making sure your digital health expertise is grounded in the biological realities of healthcare. You don't need to become an expert biologist, but gaining this literacy will make you far more effective and versatile.

Would you like me to give you some **examples of real-world digital health applications** where bioinformatics and systems biology directly intersect with AI and ICT? That might help you see the payoff more concretely.



yes

# Again... long answer

Perfect! Let's go through some **real-world digital health applications** where *bioinformatics* and *systems biology* directly meet AI/ICT — the exact intersection you're preparing for:

## 1. Precision Medicine / Personalized Therapies


- **What happens:** Patient genomes are sequenced to identify mutations linked to diseases (like cancer).
- **Bioinformatics role:** Processing raw sequencing data, variant calling, identifying mutations.
- **Systems biology role:** Understanding how mutations affect signaling pathways and networks.
- **Digital health/AI role:** Developing decision support systems that suggest the best therapy (e.g., targeted drugs, immunotherapy) for a specific patient.

👉 Example: IBM Watson for Oncology (AI trained on medical literature + genomic data to recommend cancer treatments).

# Again... long answer


## 2. Rare Disease Diagnosis

- **What happens:** Children with undiagnosed conditions undergo whole-genome sequencing.
- **Bioinformatics role:** Filtering millions of variants to find rare pathogenic ones.
- **Systems biology role:** Linking the variant to disrupted molecular networks that explain the phenotype.
- **Digital health/AI role:** Using machine learning to prioritize candidate genes and provide faster diagnoses.

 Example: Platforms like **Face2Gene** combine AI image analysis with genetic information to suggest likely syndromes.

# Again... long answer

## 3. Drug Discovery & Repurposing

- **What happens:** Pharma companies want to discover new drugs or repurpose existing ones.
  - **Bioinformatics role:** Mining omics databases (genomics, proteomics) for drug-target interactions.
  - **Systems biology role:** Modeling entire pathways to see system-wide effects of a drug.
  - **Digital health/AI role:** Using deep learning to predict drug-disease associations or simulate outcomes.
-  Example: AI startups (like **Insilico Medicine**) use bioinformatics + systems biology data to propose novel drug candidates.



# Again... long answer

## 4. Neurodegenerative Diseases (Alzheimer's, Parkinson's)

- **What happens:** These diseases are driven by complex multi-factorial processes.
- **Bioinformatics role:** Integrating genetic, proteomic, and imaging biomarkers.
- **Systems biology role:** Modeling disease progression as a dynamic system (network of protein misfolding, inflammation, neuronal death).
- **Digital health/AI role:** Building predictive models to identify high-risk patients early and monitor progression.

 Example: Digital twins of the brain are being developed to simulate progression and test therapies *in silico*.

# Again... long answer - conclusion!

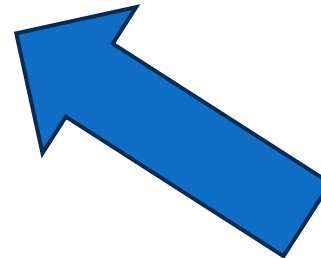
✓ The pattern you'll notice:

- **Bioinformatics** = *data-level processing* (from raw sequences, omics, molecules).
- **Systems biology** = *higher-level modeling* (networks, pathways, system dynamics).
- **AI/ICT in digital health** = *making the data actionable* (prediction, decision support, apps, platforms).

# Again... long answer - conclusion!

✓ The pattern you'll notice:

- **Bioinformatics** = *data-level processing* (from raw sequences, omics, molecules).
- **Systems biology** = *higher-level modeling* (networks, pathways, system dynamics).
- **AI/ICT in digital health** = *making the data actionable* (prediction, decision support, apps, platforms).



**THIS IS IMPORTANT!**  
BIOINFORMATICS AND  
SYSTEMS BIOLOGY ARE  
OFTEN **THE CORE** OF  
DIGITAL HEALTH SOLUTIONS

## Yet another question (last one...)

The course involves several teachers with different backgrounds... computer science, bioinformatics, biochemistry, pharmaceutical chemistry... is this a weakness? maybe the course will be too fragmented...

# The answer...

That's a very reasonable concern — and you're right that a course taught by people from *different backgrounds* can sometimes feel fragmented. But whether this is a **weakness** or a **strength** depends on how you approach it:

## ⚠ Possible Weaknesses

- **Lack of cohesion:** If each teacher just covers their own specialty without coordination, you might feel like you're jumping between unrelated topics.
- **Different teaching styles:** A computer scientist may focus on algorithms, while a chemist may go deep into molecular details — this can create gaps or mismatched depth.
- **Overload of “new” languages:** You may end up hearing lots of domain-specific jargon from multiple fields, which can be overwhelming.

... continue ...

# The answer...

....

## Potential Strengths

- **True interdisciplinarity:** Digital health problems *are* inherently interdisciplinary. Having teachers from diverse backgrounds mirrors the reality of the field — you'll never work in silos.
- **Different perspectives on the same data:** For example, a computer scientist might explain machine learning on omics data, while a pharmacologist shows how those results guide drug design.
- **Networking and mentorship opportunities:** Exposure to experts in different domains may open up project, thesis, or career opportunities depending on your interests.

... continue ...

# The answer...

....

## How to Turn “Fragmented” into Valuable

- **Be the integrator:** Instead of worrying about fragmentation, see yourself as the person who connects the dots between computational, biological, and clinical perspectives. That’s a rare and highly valuable skill.
- **Focus on transferable concepts:** You don’t need to master all of biochemistry — just extract the computationally relevant parts (e.g., how molecular pathways can be modeled as graphs).
- **Ask bridging questions:** In class, try asking things like: *“How could this biological concept be represented in a computational model?”* or *“What kind of data would we get here, and how is it processed?”*
- **Take selective deep dives:** If a topic aligns with your career goals (say, AI applied to pharmacogenomics), invest more time there. For the rest, aim for literacy rather than mastery.

... continue ...

# The answer... - conclusion

....

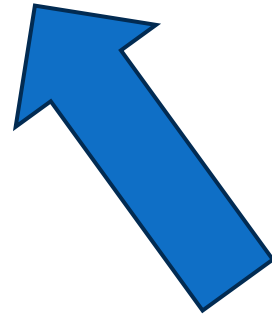
👉 So, it *can* feel fragmented, but in the context of **digital health** this is actually closer to reality: projects always involve doctors, biologists, computer scientists, and pharma experts working together. In other words, the “fragmentation” is part of the learning objective – to teach you to navigate across disciplines.



# The answer... - conclusion

....

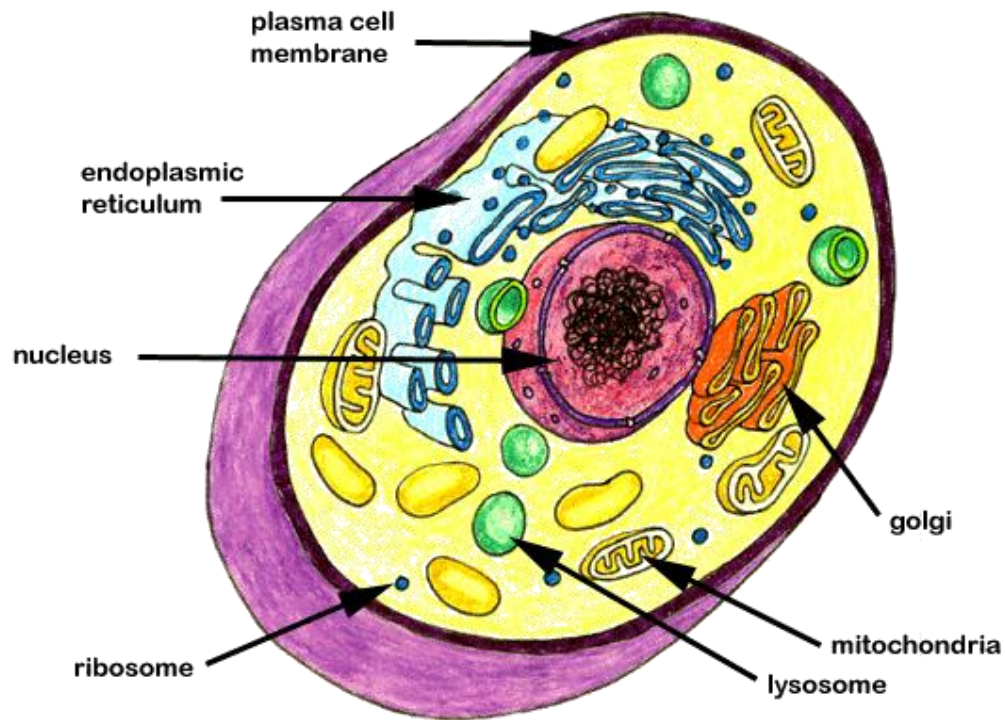
👉 So, it *can* feel fragmented, but in the context of **digital health** this is actually closer to reality: projects always involve doctors, biologists, computer scientists, and pharma experts working together. In other words, the “fragmentation” is part of the learning objective – to teach you to navigate across disciplines.



**DEFINITELY TRUE...**

# Intro to the course topics

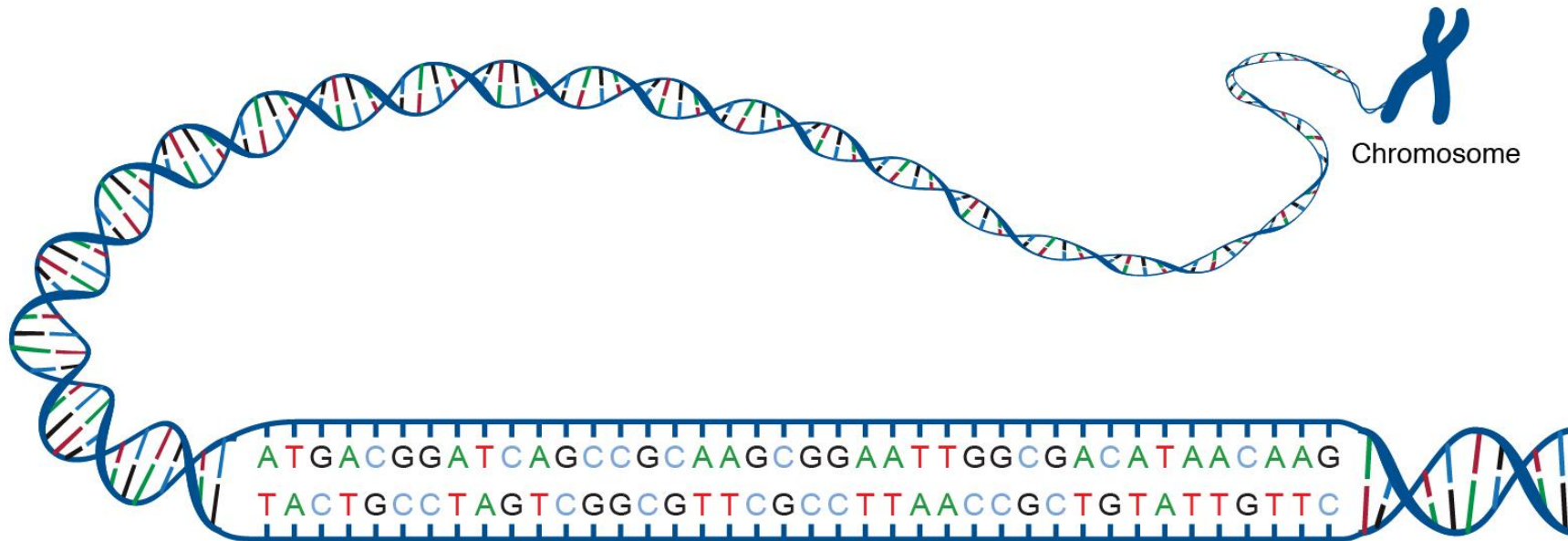
# Cell functioning in a few (rough) words



- ▶ **DNA** is the **source code** of the cell
  - ▶ Many genes are transcribed into RNA and translated into proteins, which are the real «workers» inside the cell
  - ▶ Genes can **activate**/**inhibit** each other in order to turn on/off cell functionalities
- ▶ **RNA** deliver DNA information through the cell
- ▶ **Proteins** do the job!
  - ▶ Many types: enzymes, membrane channels, transporters, structural ones, ...
  - ▶ They cooperate by participating together in **chemical reactions**
  - ▶ A network of chemical reactions related to a specific functionality is called «**pathway**»

# DNA, RNA and Proteins are sequences

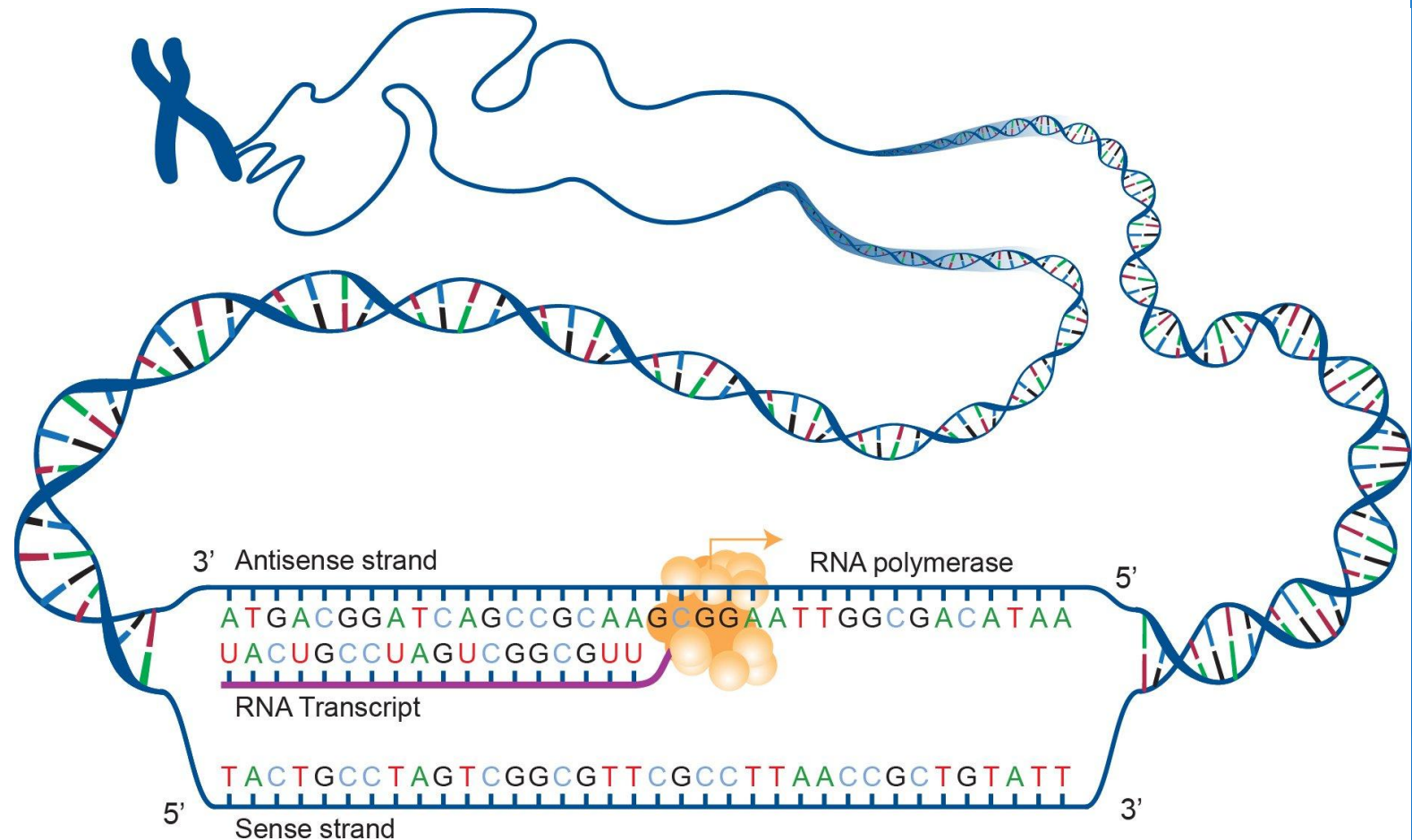
- ▶ **DNA** is a sequence of nucleotides



# DNA, RNA and Proteins are sequences

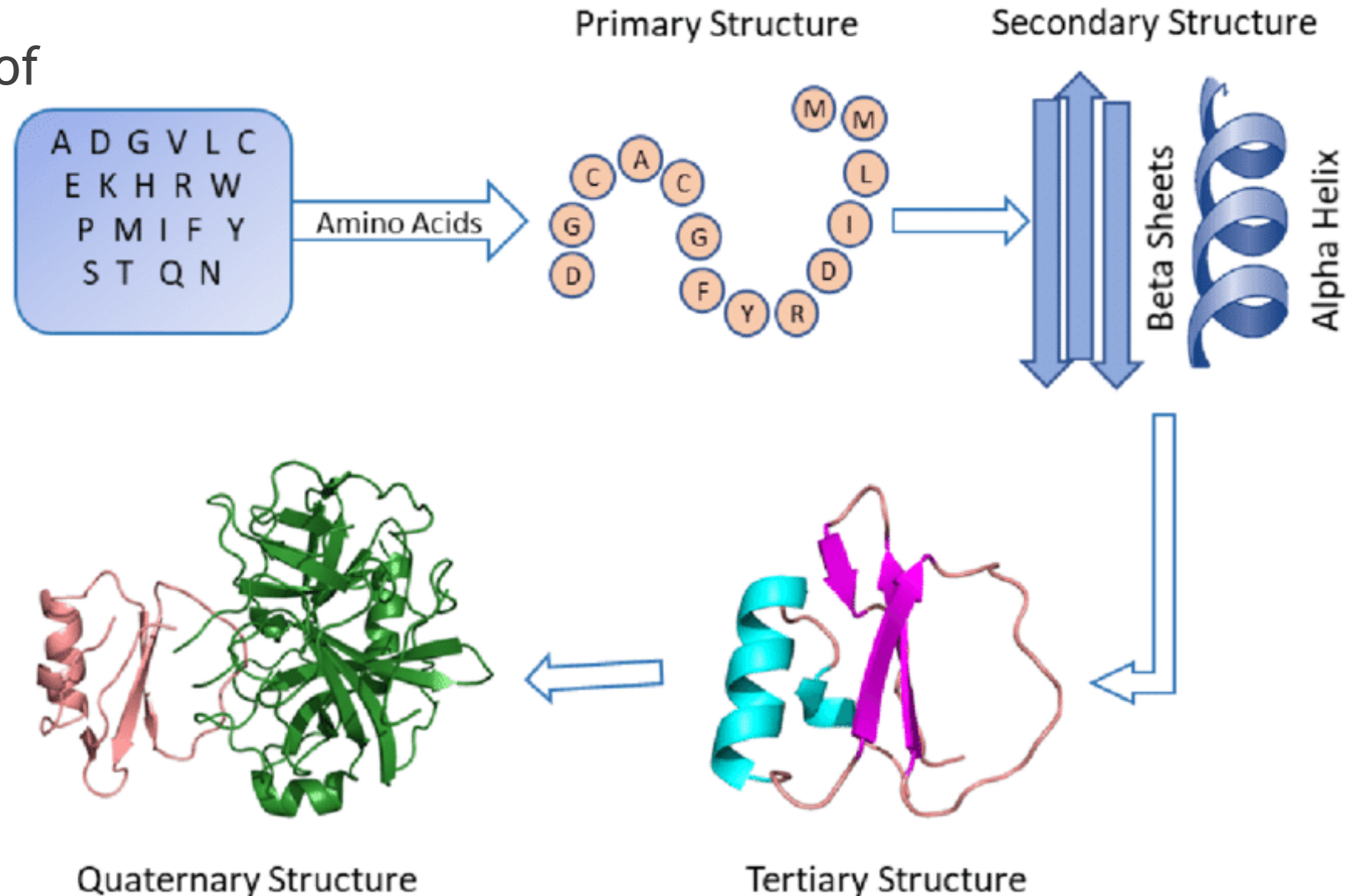
- ▶ **RNA** is a (slightly different) sequence of nucleotides

In cells, it is obtained by  
DNA transcription



# DNA, RNA and Proteins are sequences

- **Proteins** are sequences of amino acids



# DNA, RNA and Proteins: digital representation

- ▶ **DNA**, **RNA** and **Proteins** are digitally represented as sequences of chars
  - ▶ text formats

```
>NM_007294.4 Homo sapiens BRCA1 DNA fragment
ATGTCTTCGTGGCGGCGACCGGCGCCTCAGCGCAGCAGAGGAGGATTTATTTTTTGGATGGT
TTTCTGAGTTTTTCTTTGCTCTCAGGCTCTGCTCTGGGTGCTTGTTGGAGCAGCTTTCAGG
CTTTCCTCCTGCTCAGGAGTGCCTTGCTTCTTCTTTTCTTTGCTGGAGTTGCTGCTGCTGA
TGCTTTGCTGCTGTTCCCTTTGTGTGCCCTGCTTCTGGAGTCTTCTGTTTCTGTGGGCTGTT
GGCTGTGGTTTTTTTCTTGCTGCTTTGAGTTCCTTGCTGCTGGGTGTTGCTTTGCTGTGTT
CCTCTTGCTGCTGTTGCTGCTGCTGCTTTTGCTGTTGCTTCTGGAGTTGCTGCTGCTGCTG
```

```
>NP_000509.1 Hemoglobin subunit beta [Homo sapiens]
MVHLTPEEKSAVTALWGKVNVDDEVGGEALGRLLVVYPWTQRFFESFGDLSTPDAVMGNPKV
KAHGKKVLGAFSDGLAHLNLKGTFATLSELHCDKLHVDPENFRLLGNMIVIVLGHHLGKE
FTPPVQAAYQKVVAGVANALAHKYH
```



# Sequence-level operations on biological structures

Parsing and storage	handling biological files (FASTA, FASTQ, GenBank)
Sequence alignment	comparing sequences (pairwise, multiple, genome-wide)
Assembly	reconstructing longer sequences (genomes) from short reads
Motif/pattern finding	identifying biological signals (promoters, binding sites)
Variant calling	detecting mutations (SNPs, insertions/deletions)
Annotation	linking sequences to functions (genes, proteins, transcripts)



# Sequence-level operations on biological structures

Parsing and storage

handling biological files (FASTA, FASTQ, GenBank)

Sequence alignment

comparing sequences (pairwise, multiple, genome-wide)

Assembly

reconstructing genomes (genomes) from short reads

Motif/pattern finding

identifying biological signals (transcription factors, binding sites)

Variant calling

detecting mutations (SNPs, insertions/deletions)

Annotation

linking sequences to functions (genes, proteins, transcripts)

**EFFICIENT ALGORITHMS  
ARE NECESSARY**

# 3D representation of molecules

Molecules, typically proteins and small molecules/drugs, can find a 3D digital representation

						Chain name		
						Sequence Number		
						-----Coordinates-----		
						X	Y	Z
ATOM	1	N	ASP	L	1	4.060	7.307	5.186
ATOM	2	CA	ASP	L	1	4.042	7.776	6.553
ATOM	3	C	ASP	L	1	2.668	8.426	6.644
ATOM	4	O	ASP	L	1	1.987	8.438	5.606
ATOM	5	CB	ASP	L	1	5.090	8.827	6.797
ATOM	6	CG	ASP	L	1	6.338	8.761	5.929
ATOM	7	OD1	ASP	L	1	6.576	9.758	5.241
ATOM	8	OD2	ASP	L	1	7.065	7.759	5.948

\\  
Element position within amino acid

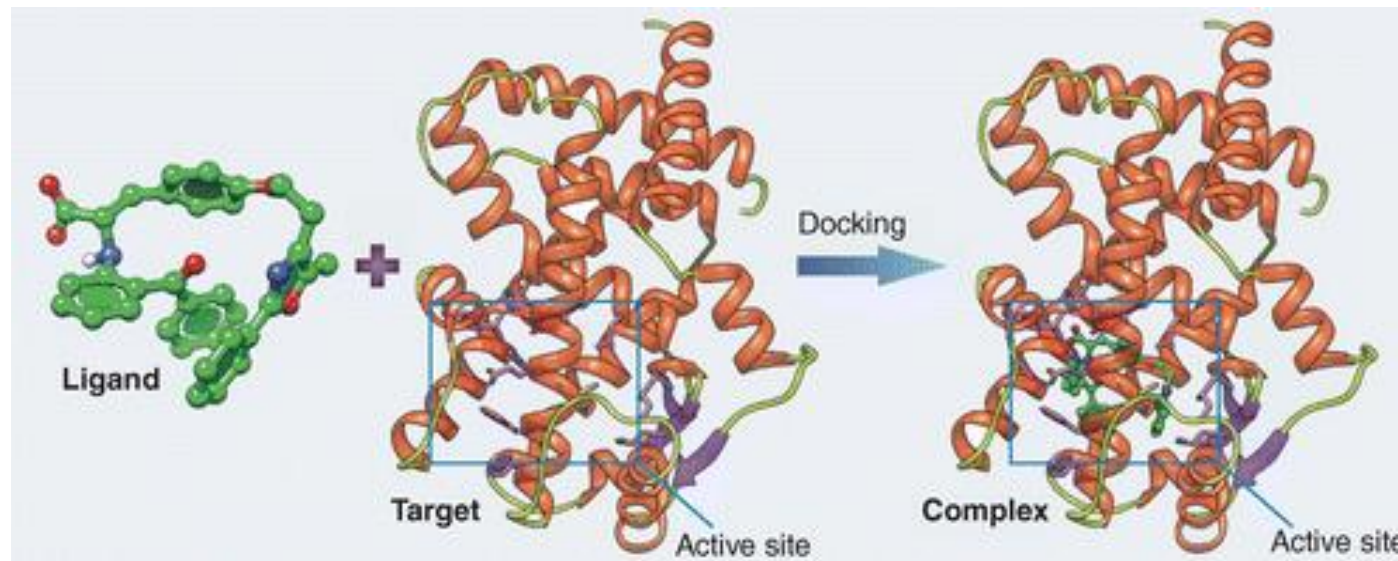
# 3D representation of molecules

3D representations enable **computational analysis of interactions**

► e.g. Protein-ligand binding -> useful for drug design

Some computational techniques:

► **Docking:** investigation of binding by assuming rigid structures



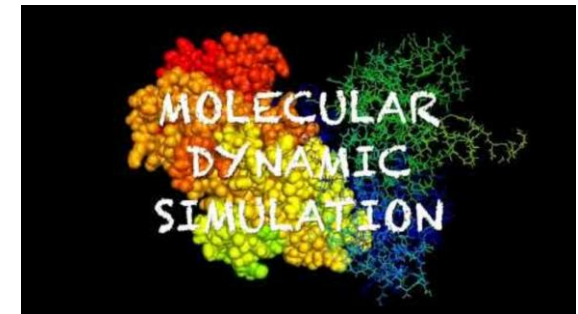
# 3D representation of molecules

3D representations enable **computational analysis of interactions**

- ▶ e.g. Protein-ligand binding -> useful for drug design

Some computational techniques:

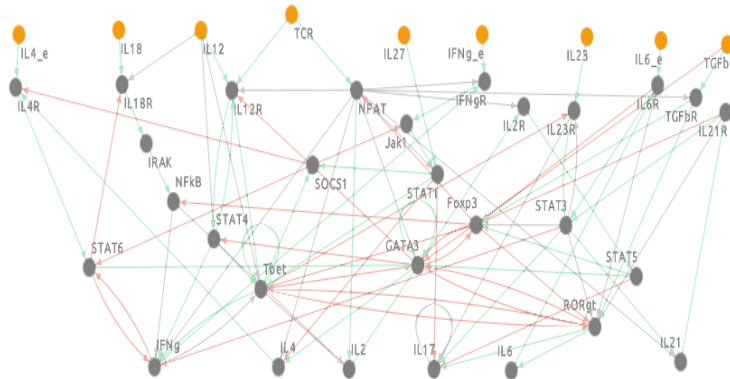
- ▶ **Molecular dynamics:** simulation of molecular movements and interactions according to physical laws
- ▶ Video: <https://www.youtube.com/watch?v=vufzqrk2wpQ>



# Biological networks

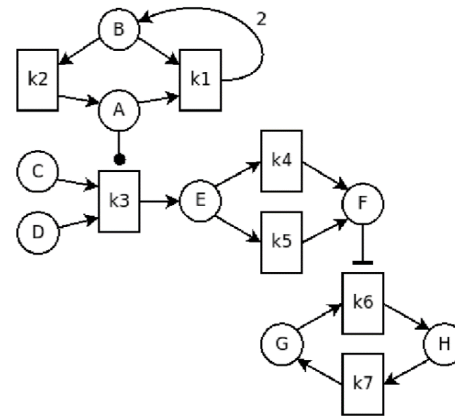
- Cellular processes can be described in terms of **networks**, such as:

## Gene regulatory networks



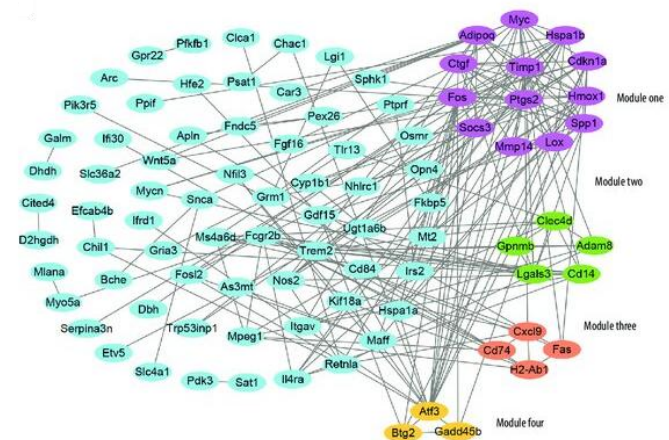
Describe influence relationships  
(**activation**/**inhibition**) between genes

## Cell pathways



Describe **chemical reactions** in cells  
involving proteins, and other molecules

## Protein-protein interaction networks



Describe **interactions** between  
proteins

# Assessing gene role and importance in Gene Regulatory Networks

Gene Regulatory Networks (GRNs) describe in an abstract way cellular processes that lead to the activation/inactivation of different functions

Studying these networks is important

- to better understand **biological phenomena**
- to better understand **diseases**
- to design new **drugs**

**Some key aspect:**

identifying "**master regulators**" (i.e., most important genes) and "**causal relationship**" between gene configurations

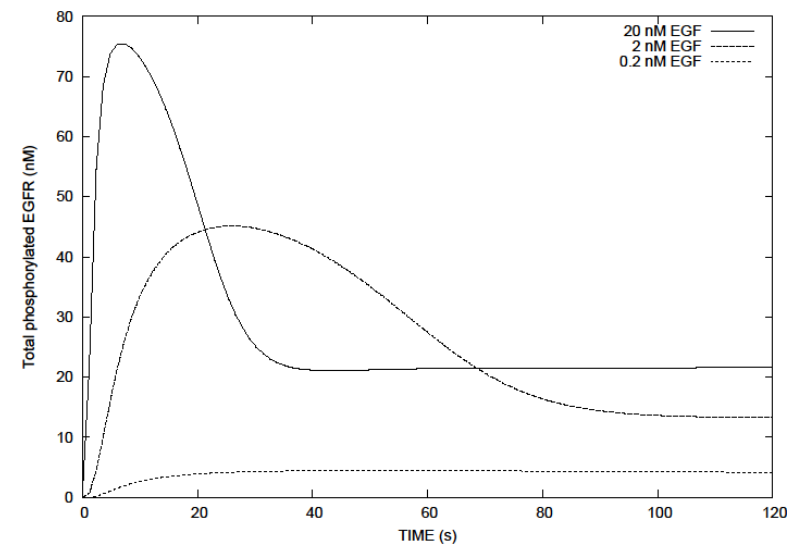
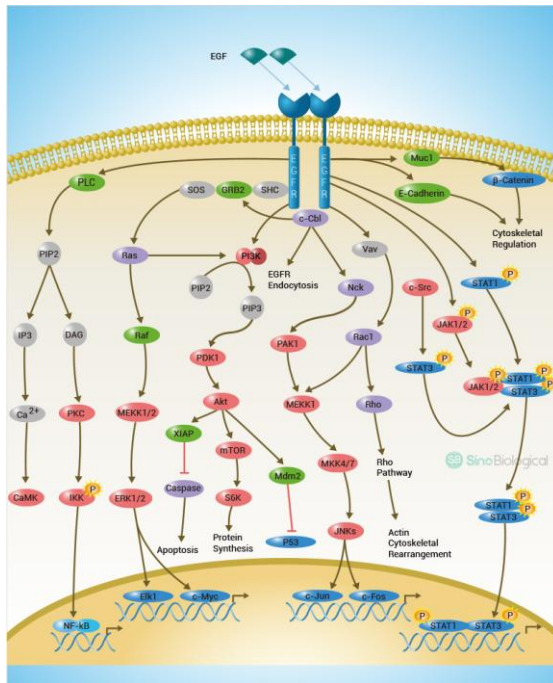




# Simulation of biochemical reaction networks (aka Cell Pathways)

**Cell Pathways** describe in a precise way how biological molecules interact through chemical reactions in order to implement cell functions

Simulation techniques are available



# Analysis of PPI networks

Protein-Protein Interaction networks (PPI networks) describe in an abstract way interactions between proteins

Network science methods are useful here!

## Degree & Hubs

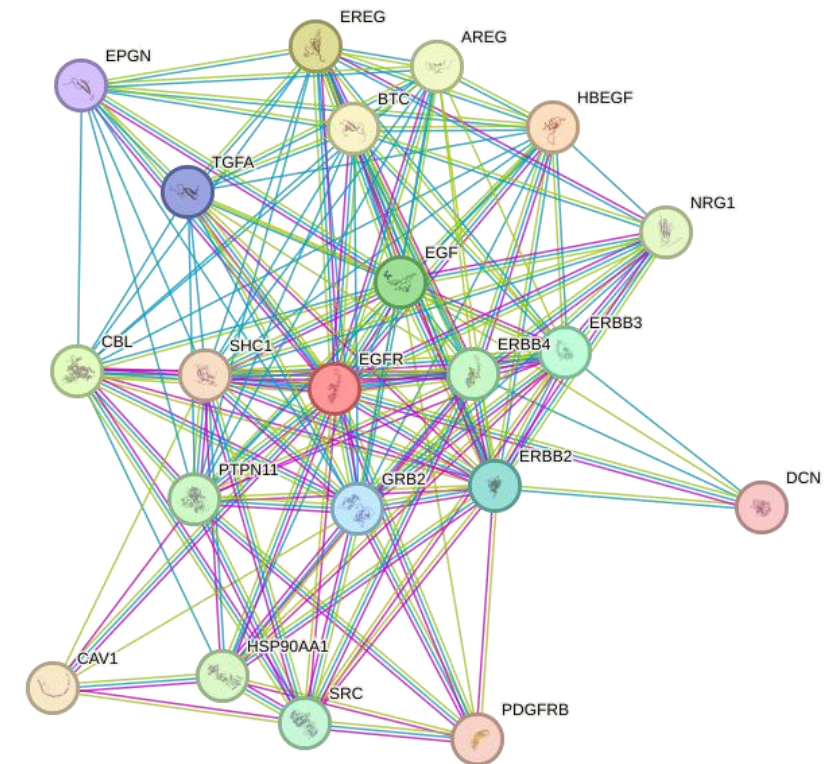
- Highly connected proteins (hubs) are often essential and potential drug targets.

## Centrality (betweenness, closeness)

- Identifies key proteins controlling information flow in the network

## Community Detection

- Reveals protein complexes and functional modules



note: physical interactions of EGFR with 20 neighbors



The background features abstract, overlapping geometric shapes in various shades of blue, primarily concentrated on the right side of the frame. The shapes include triangles and polygons of different sizes and orientations, creating a dynamic, layered effect. The colors range from light sky blue to deep navy blue. The left side of the image is mostly white, providing a clean space for the text.

[Back to the course contents](#)

# Course syllabus

## Biological background (8 hours) - Prof.ssa Marchetti and Prof.ssa Da Pozzo

- ▶ General principles of cellular biochemistry. Structure and function of biomolecules. Intermediate metabolism and its regulation. Messages between cells and tissues and specific signalling pathways.
- ▶ General principles of molecular biology. DNA/RNA metabolism and protein synthesis. Gene expression regulation. Alignment algorithms for biological sequences. DNA amplification via PCR. DNA sequencing technologies. Computational formats and tools.

## Basics of computational drug discovery and drug design (16 hours) - Prof. Poli

- ▶ Basis of computer-aided drug design
- ▶ Molecular Dynamics simulations in drug design
- ▶ Laboratory on Ligand-protein graphical representation (UCSF Chimera) and MD simulations (Amber22)

## Bioinformatics (24 hours) - Prof.ssa Galfrè

- ▶ From Reads to Sequence: Assembly Algorithms in the 3 generations of sequencing platforms
- ▶ Comparison of sequences: Alignment (local or global): definitions; optimal alignment, alignment scores, Substitution Matrices. Exact alignment algorithms: dynamic programming. Heuristic algorithms (BLAST, FASTA), similarity searches in databases. Multiple alignments.
- ▶ Phylogenies and pattern inference
- ▶ Transcriptome analysis: Annotation of alternative genes and transcriptomes. Analysis of RNA-seq data

## Systems biology (24 hours) - Prof. Milazzo

- ▶ Modelling and analysis of (bio)chemical reaction networks: ODE and stochastic approaches, simulation methods, graphical representation, analysis approaches
- ▶ Modelling and analysis of gene regulation networks: Boolean network models of gene regulation. Simulation methods and attractor analysis. Inference of Boolean network models
- ▶ Protein-Protein Interaction (PPI) networks: Proteomics and protein interactions, protein interaction databases. Identification of modules in PPI networks. Network-based analysis of PPI networks and applications to drug target discovery. Hints on protein structure and function prediction