

Physics/Biology/Computation: setting the stage

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DIPARTIMENTO DI FISICA



SAPIENZA
UNIVERSITÀ DI ROMA

Who am I?

Teaching

Computational Biophysics (LM Fisica)

Data Analysis (LM Genetica e Biologia Molecolare
+ Neurobiologia)

Algoritmi e piattaforme per le decisioni d'impresa
(LM MANIMP, fac. Economia)

CONTACTS

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Research Activity

- have a look at pubmed
- <https://pubmed.ncbi.nlm.nih.gov/>
- or to BioRxiv (Giansanti A)
- <https://www.biorxiv.org/>

WHAT IS COMPUTATIONAL SCIENCE?

Based on **models** / numerical data / algorithms (to do what? See e.g. preceding Slide)

Someone (not necessarily a dummy) thinks we have no need of laws, principles

We need just ...predictive correlations, and that's all folks (The big data solution)

But, ordinarily:

- i) assume a model – not necessarily a mechanical one;
- ii) define a problem within the semantics of the model;
- iii) look for solutions, provided solutions do exist
- iv) compute them through sufficiently rapid, convergent, **algorithms**
- v) (finite sets of instructions to get a solution, steps to converge)
- vi) Sometimes recursive instructions)

Example: Ising model. Is not mechanical, but used to model: phase transitions (order/disorder: e.g. ferromagnetism); disordered - **complex** - systems: spin glasses, where J_{ik} are random quenched variables, that are used to model systems with single/degenerate ground states (see e.g. the problem of protein folding, IDPs. See also the **inverse statistical mechanical problem**: swarms, flocks in animal aggregates; I. Giardina's Course)

BIG DATA VS MODELS- THEORY

- A manifesto (Anderson 2008)
- <https://www.wired.com/2008/06/pb-theory/>

But, REMEMBER that, for many, **computational biophysics** is still

ATOMISTIC SIMULATION

See e.g. Oren M. Becker, Alexander MacKerrel, Jr. Benoit Roux,
Masakatsu Watanabe (Eds.) *Computational Biochemistry and Biophysics*
M. Dekker New York 2001.

GALILEI'S REMOVAL OF THE ANIMAL

Therefore I say that upon conceiving of a material or corporeal substance, I immediately feel the need to conceive simultaneously that it is bounded and has this or that shape; that it is in this place or that at any given time; that it moves or stays still; that it does or does not touch another body; and that it is one, few, or many. I cannot separate it from these conditions by any stretch of my imagination. But that it must be white or red, bitter or sweet, noisy or silent, of sweet or foul odor, my mind feel no compulsion to understand as necessary accompaniment. Indeed, without the senses to guide us, reason or imagination alone would perhaps never arrive at such qualities. For that reason, I think that tastes, odors, colors, and so forth are no more than mere names so far as pertains to the subject wherein they reside, and that they have their habitation only in the sensorium. Thus, if the living creature were removed, all these qualities would be removed and annihilated. [. . .]

[. . .] I do not believe that, for exciting in us tastes, odors, and sounds there are required in external bodies anything but sizes, shapes, numbers, and slow or fast movements; and I think that if ears, tongues, and noses were taken away, shapes and numbers and motions would remain but not odors or tastes or sounds. These, I believe, are nothing but names, apart from the living animal—just as tickling and titillation are nothing but names when armpits and the skin around the nose are absent [. . .]

From: *Il Saggiatore* (1623),

- The galilean paradigm: based on the “removal of the animal”
- What is physics: the study of material bodies, localized in space and time
- Reference frames + clocks (newtonian time, not percolating, it uniformly flows, always at the same rate)
- Biology is based on the careful observation of single cases, then correlated in a qualitative way, based on senses, into classes (classification) (e.g. species)
- The darwinian shift biological time vs physical time
- The molecular revolution (Watson & Crick) Macroscopic genetic laws can be explained by looking at molecular materials

Phylogenetic trees: evolutionary vs newtonian time

(A)

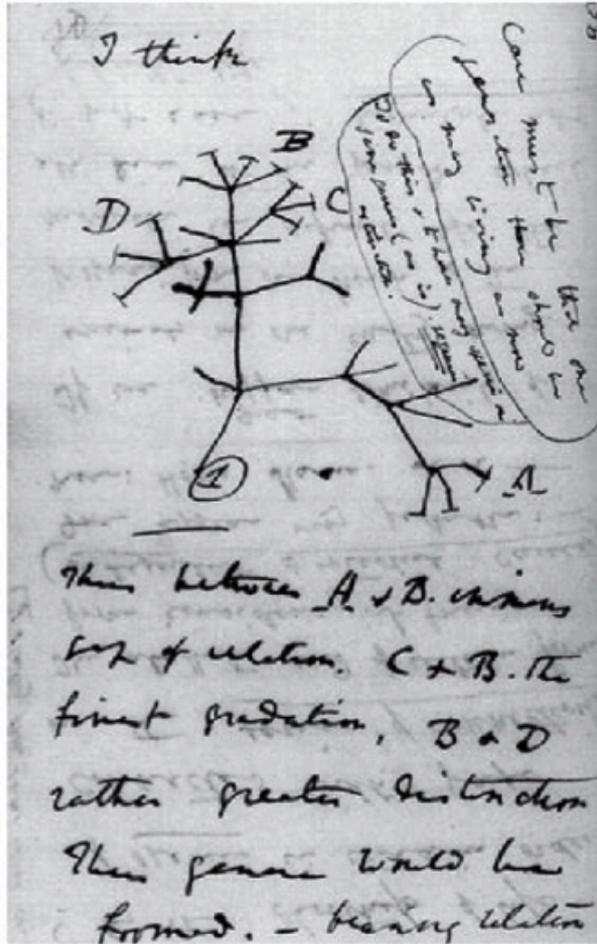


Figure 3.4 Physical Biology of the Cell (© Garland Science 2009)

(B)

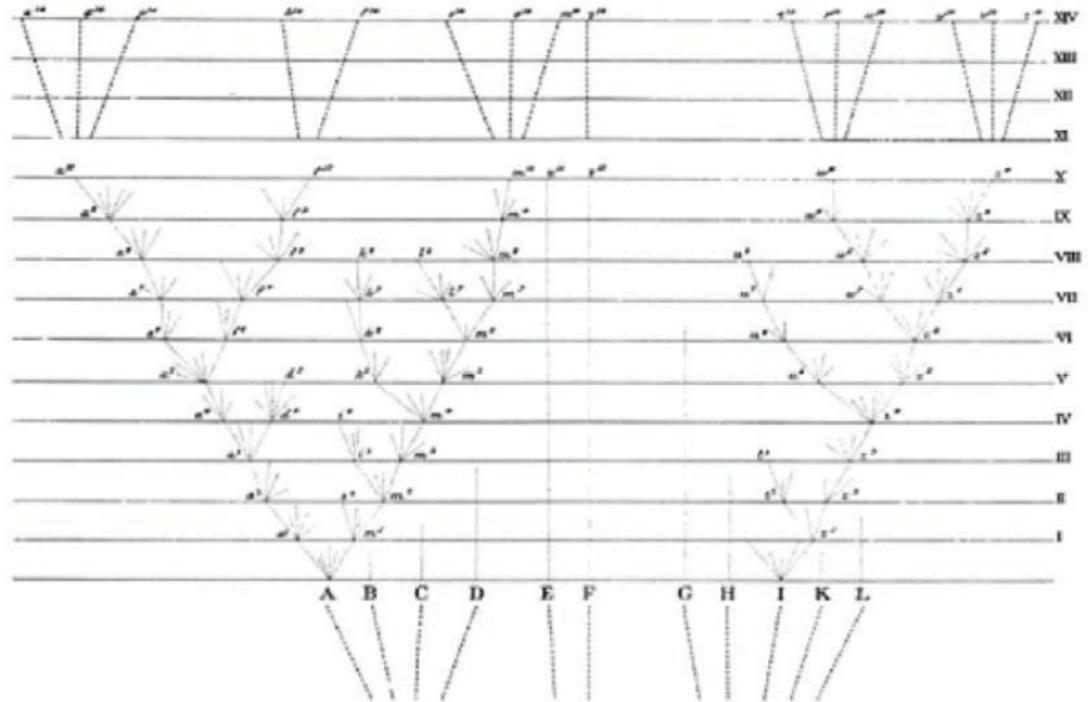


Figure 3.4 Two versions of Darwin's phylogenetic tree. (A) In his notebooks, Darwin drew the first version of what we now recognize as a common schematic demonstrating the relatedness of organisms. He introduced this speculative sketch with the words "I think" as his theory was beginning to take form. (B) In the final published version of *On the Origin of Species*, the tree had assumed more detail showing the passage of time and explicitly indicating that most species have gone extinct. (Adapted from C. Darwin, *On the Origin of Species*, London, John Murray, 1859. Courtesy of The American Museum of Natural History.)

we need, operationally, another unit, e.g. number of mutations per residue between coding sequences

THERE IS NO MOLECULAR CLOCK!

BIOPHYSICS

A basic critical , distinction when reading the leaflet of the Biophysical Society:

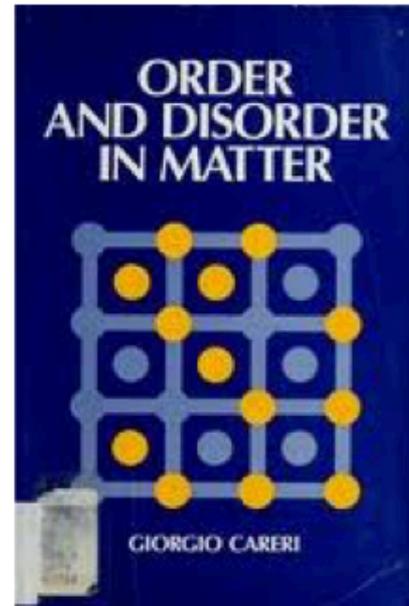
Physics of Living systems (cell biophysics, integrative biophysics, systems biology, e.g. physics of living plants at the blackboard)

Physics of parts of living systems (molecular biology/biophysics, Biomaterials, biophysical chemistry, in vitro, diluted solutions single molecule experiments, also x-ray cristallography is single molecule experiment)

Note: there is also a **Biological Physics** and **Physical Biology**
[**homework for next thursday**]

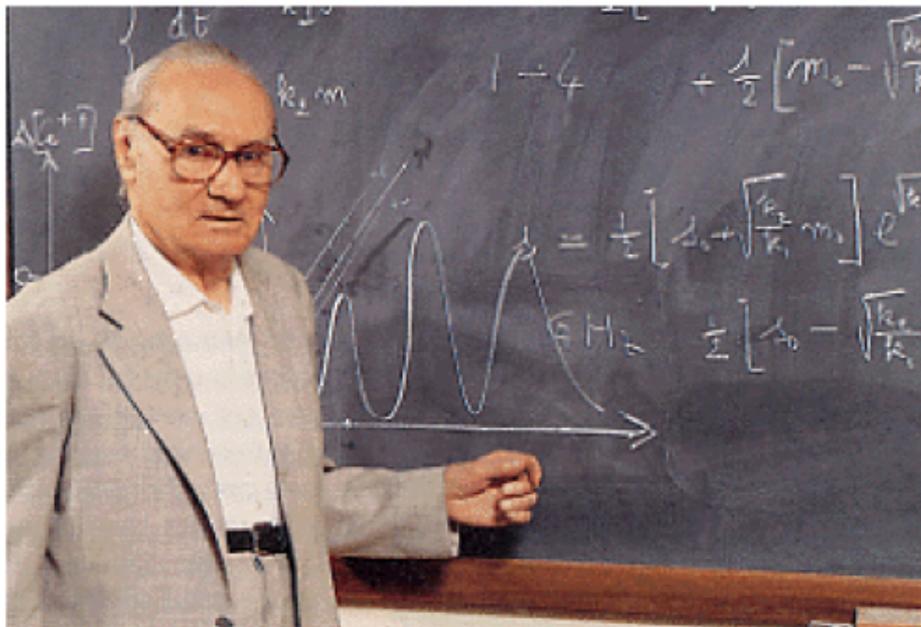
TWO DISTINGUISHED ROMAN SCHOOLS OF BIOPHYSICS

**molecular biophysics / biophysical chemistry / molecular biology/critical phenomena/
superfluids/ superconductors**

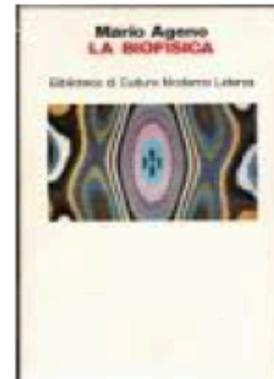


Giorgio Careri 1922-2008

Evolutionary biology/cell biophysics/ integrative biophysics/systems biology



Mario Ageno 1915-1992



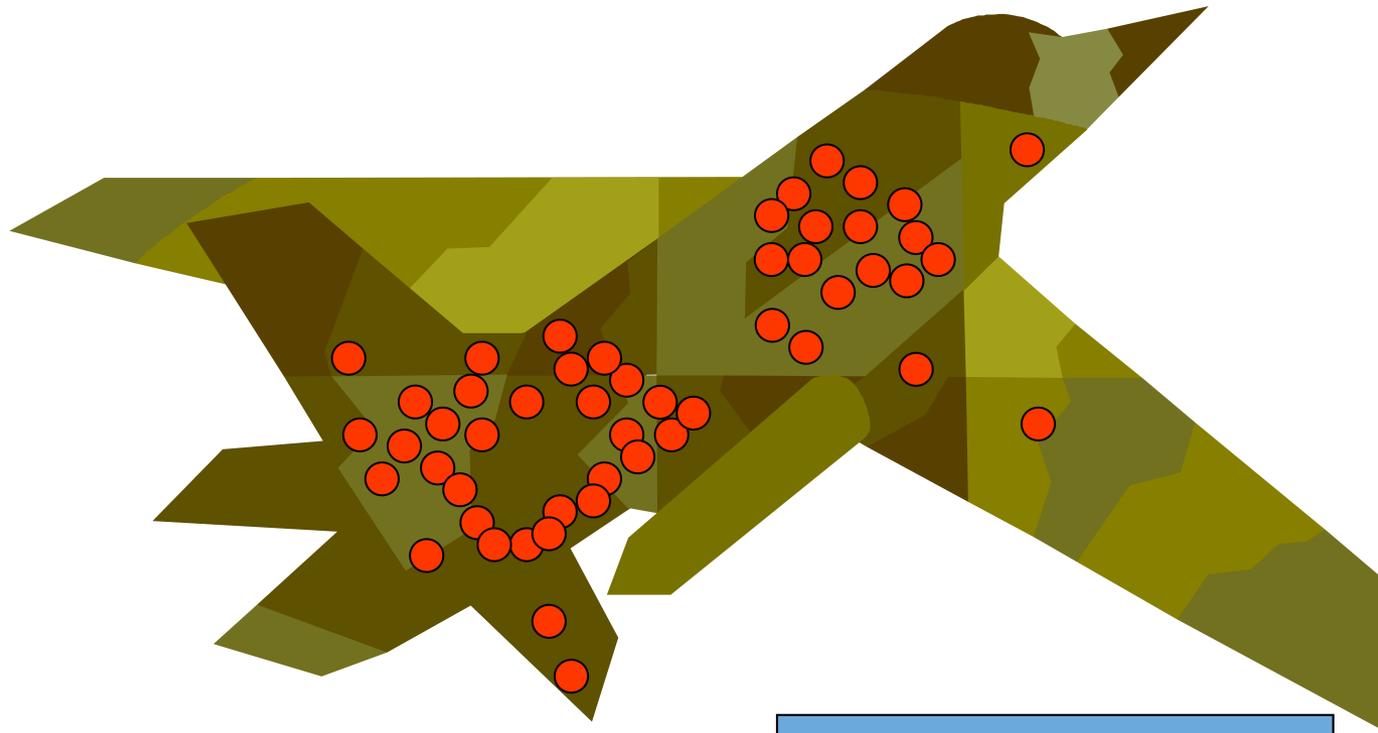
What is Terry Hwa doing?

- [http://biology.ucsd.edu/research/faculty/
thwa](http://biology.ucsd.edu/research/faculty/thwa)

Example of an *ostensive* definition: *particle physics is what particle physicists do...* (less stupid than it might seem, in a nutshell is an historical definition)

Biophysics, as part of biology, became an **evolutionary** science, in recent years and here is evolution in a nutshell Evolution in a nutshell (remembering Anna Tramontano, pioneer of bioinformatics)

The case of density bullet-holes in surviving war planes



Manguel M, Samaniego F.J.,
Abraham Wald's Work on Aircraft Suvivability,
J. American Statistical Association. 79, 259-270, (1984)

Outline of the next discussions

- Computational science
- networks (as a proxy model of complexity)
- Molecular evolution
- Substitution patterns in genes
- Estimation of the number of substitutions
- Differences in the gene evolutionary speed
- Molecular clocks
- Sequences/structures
- From the B. O. approximation to Molecular Dynamics

COMPUTATIONAL BIOPHYSICS

PROSPECTIVE PROGRAM

(CB_22_23)

doing physical biology with models and computers: from the Born-Oppenheimer approximation to molecular dynamics; from the space of biological sequences to integrative modelling of systems biology; the role of machine learning

Academic Year 2022-2023, fall semester, 6 ECTS.

The 20022-2023 Computational Physics Course is dedicated to the memory of Jacques Monod and Giuseppe Briganti

This is a course for the Master Program in Physics given in the **1st semester** as a part of an integrated set of courses in *biosystems*, comprehending: BIOCHEMISTRY, MOLECULAR BIOLOGY, BIOPHYSICS, THEORETICAL BIOPHYSICS, SOFT AND BIOLOGICAL MATTER.

The course starts on the 26th of September 2022. The class meets in presence, three times per week in the Rasetti Room (2nd floor, Marconi Building): i) Mondays, from 8 am to 9 am; ii) Tuesdays, from 2 pm to 4 pm; iii) Fridays, from 8 am to 10 am.

Instructor: prof. Andrea Giansanti, office room n. 211 (2nd floor, Marconi Building) tel. 06.49914367 (cell. 3385075611) andrea.giansanti@uniroma1.it

Description/Objectives. The course provides a compact introduction to modern computational (*in silico*, as opposed to *in vivo/in vitro*) biophysics/biology, in an evolutionary perspective. Expected audience: physics students enrolled in the biosystems and theoretical curricula. Students from other curricula: chemistry, mathematics, engineering. The course requires from the students an active participation, through questions, statements, written essays and collaborative projects. The style of teaching will be mainly by illustration and only partly by exhaustive demonstration. The main pedagogical intention is, besides competences, to discuss, correct and propagate ideas. Ideas are the wings of innovation, competences implement novelties (...elementary, Watson). Extensive reference and critical introductions to the literature and to many specialized texts will be offered as a thread for personal study. An effort will be made to locate each discussed topic in a clear framework of references, useful to prepare the final exam. In a nutshell, the objective of this course is to narrow the gap between the institutional level of training and that of research. Guest invited lectures by young researchers and reknown experts will be offered alongside.

Requirements. Enrolled students should have taken the basic courses of a BA program in physics, mathematics and engineering. In particular, basic competence in classical mechanics, thermodynamics, chemical equilibrium and quantum mechanics is required together with basic programming skills (possibly using Python). Biological facts will be discussed as needed along the course.

Evaluation: based on written essays, written tests, home-works and participation to projects and discussions: 40%. Final oral exam: 60%.

Recommended reference texts and textbooks of impact.

[MON] Jacques Monod, *Chance and Necessity: An Essay on the Natural Philosophy of Modern Biology*, New York, Alfred A. Knopf, 1971.

[CH] N Cristianini and MW Hahn, *Introduction to Computational genomics, a case studies approach*, Cambridge University Press (CUP), 2006.

[F] D Forsdyke, *Evolutionary bioinformatics*, Springer 2016.

[HA] PG Higgs and TK Attwood, *Bioinformatics and Molecular Evolution*, Blackwell, 2006.

[DU] R Durbin, Eddy, Krogh, Michison. *Biological Sequence Analysis*. CUP, 1999.

[V] E Voit, *A First Course in Systems Biology*, Garland Science, 2012.

[PPF] T Parr, G Pezzulo and LJ Friston, *Active Inference: the free energy principle in mind, brain and behaviour*, MIT press, 2022.

Note: outlines of lectures and themes and study materials will be made available in the e-learning Moodle platform of Sapienza University of Rome at: <https://elearning.uniroma1.it/course/view.php?id=15504>

THEMES

- 1. PHYSICS, BIOLOGY, MODELLING, COMPUTATION: SETTING THE STAGE**
- 2. APPROXIMATIONS: FROM THE SCHRÖDINGER EQUATION TO MOLECULAR DYNAMICS**
- 3. COMPLEXITY: ELEMENTS OF NETWORKS**
- 4. INTRODUCTION TO THE SYSTEMIC MODELLING OF BIOLOGICAL SYSTEMS**
- 5. PROBABILISTIC REASONING (BAYES REDUX)**
- 6. INTRODUCTION TO DATA SCIENCE (CLASSIFICATION: CLUSTERING AND NETWORKS)**
- 7. ELEMENTS OF PROTEIN STRUCTURES AND DATABASES**
- 8. INTRODUCTION TO MOLECULAR DYNAMICS OF PROTEINS**
- 9. MODELS OF SEQUENCE EVOLUTION**
- 10. SEQUENCE ALIGNMENT ALGORITHMS**
- 11. MACHINE LEARNING METHODS**
- 12. ACTIVE INFERENCE AND THE BAYESIAN BRAIN**
- 13. MAX ENT INFERENCE (THE TOLOMEO PLATFORM)**