Selected topics in biological physics and advanced chemical kinetics

Prof. Francesco Piazza

Université d'Orléans, Centre de Biophysique Moléculaire, CNRS-UPR4301, Rue C. Sadron, 45071, Orléans, France
Tel. 0238255653

E-mail: Francesco.Piazza@cnrs-orleans.fr

1. Course synopsis

This course is intended to present some advanced material in physical biology and theory and simulation of chemical kinetics, covering mainly three topics:

(i) Coarse-grained models of protein dynamics

(ii) Diffusion-limited bimolecular reactions with an emphasis on diffusion in crowded and confined environments.

(iii) Advanced topics in chemical kinetics, free-energy transduction in chemical reaction networks. Stochastic simulation of chemical reaction networks and the Gillespie algorithm.

The course is open to all Ph.D. students in the scientific doctoral schools. A background in elementary statistical mechanics and calculus is required but no pre-requisite in molecular and cell biology is needed, as a basic introduction to this will be given. The most complex mathematical derivations are done in full length and at slow pace, covering all details in a self-contained manner. A full set of written hand-outs will be available soon for the students to familiarize with the course material, including a full list of references.

The course is structured in about 8 or 9 two-hours lectures. Depending on the students' interest, two of them can be organized as exercise classes, with the possibility of both supervised problem solving and running individual or group sessions of computer simulations and calculations, covering aspects treated during the lectures. The material for these (computer codes etc.) will be supplied by the instructor. Students will have the possibility to set up their personal laptops to use them for the exercise classes. The computer languages used for these demonstration are typically Fortran 90 and Python.

1.1. List of lecture content

Lecture 1 Introduction to the most important biomolecules in molecular and cell biology. A personal account on the basic building blocks of biological matter.

Lecture 2 Statistical physics models of DNA and basic concepts of polymer physics. The case of DNA pulling by optical tweezers.

Lecture 3 Modeling protein dynamics. Force fields and normal mode analysis. Elastic network models, an account on how exceedingly simple modeling schemes still teach a lot on biologically relevant issues.

Lecture 4 Diffusion-limited bimolecular reactions I. Modeling reactions in the liquid phase through boundary value problems. The classic Smoluchowski and Debye theories.

Lecture 5 Diffusion-limited bimolecular reactions II. Cells uniformly covered in receptors versus cells with a single, large cluster of receptors. Which is better? A (not so?) surprisingly simple answer from a complex (but instructive) mathematical model.

Lecture 6 Diffusion-limited bimolecular reactions III. The concept of *diffusive* interaction. Are two closely spaced receptors as effective as two separated ones, more or less effective?

Lecture 7 Diffusion-limited bimolecular reactions IV. Towards realistic modeling of transport in the cell. Selected topics in diffusion in crowded environments. What do simple stochastic processes teach us on this subject?

Lecture 8 Chemical reaction networks. Detailed balance and non-equilibrium steady states. Free energy transduction and Biochemical cycle kinetics. Hill diagrammatic techniques.

Lecture 9 Deterministic and stochastic chemical kinetics. Rate equations and exact stochastic simulation of chemical reaction networks. Master equation formulation and Gillespie algorithm. Worked examples and applications.

1.2. Suggested preliminary reading

One main reference for this course is the book *Physical biology of the cell* [1]. Selected papers pertinent to the first part of the course (there will be more in the hand-outs) are refs. [2], [3] and [4]. Some reading that is relevant to the second part are refs [5], [6], [7], [8], [9], [10] and [11]. References for the part on advanced topics in chemical kinetics are the book by Terrel. L. Hill [12]. The essential reading on stochastic simulation of chemical reactions is the original paper by Daniel T. Gillespie [13].

References

[1] Phillips R, Kondev J, Julie T and G G H 2013 *Physical Biology of the Cell* 2nd ed (Garland Science)

[2] Tozzini V 2005 *Current Opinion in Structural Biology* **15** 144–150

[3] Tirion M M 1996 *Phys. Rev. Lett.* **77** 1905–1908

[4] Atilgan A, Durell S, Jernigan R, Demirel M, Keskin O and Bahar I 2001 *Biophys. J.* **80** 505–515

[5] McGuffee S R and Elcock A H 2010 *PLoS Comput Biol* **6** e1000694 EP –

[6] Dix J A and Verkman A 2008 *Annual Review of Biophysics* **37** 247–263

[7] Konopka M C, Shkel I A, Cayley S, Record M T and Weisshaar J C 2006 *Journal of Bacteriology* **188** 6115–6123

[8] Agrawal M, Santra S B, Anand R and Swaminathan R 2008 *PRAMANA - Journal of Physics* **71** 359–368

[9] Fanelli D and McKane A J 2010 *Physical Review E* **82** 021113

[10] Kim J S and Yethiraj A 2009 *Biophysical journal* **96** 1333–1340

[11] Novak I L, Kraikivski P and Slepchenko B M 2009 *Biophysical Journal* **97** 758 – 767

[12] Hill T L 2005 *Free Energy Transduction and Biochemical Cycle Kinetics* (Dover Publications, Inc.)

[13] Gillespie D T 1977 *The Journal of Physical Chemistry* **81** 2340–2361