

Preface

Before diving head to feet into the subject matter, a few words are in order to provide the moral excuse for writing this book and to give me the opportunity to tell a story that goes back to the year 2006.

When I arrived as a full professor in the Department of Physics of the University of Lille, the Director of that time, Michel Foulon, wanted the newly hired professor (it would be great if I could add “young” here, but I was already 45 at that time) to break some walls and open some original routes in research and teaching. I will always express my warmest thanks and deepest gratitude to Michel, for the wide freedom he allowed me in the choice and organisation of the new enterprise.

A quick look around Lille, a medium-sized, very lively city in the upper north of France, right next to the border with Belgium, gave me the obvious answer. With its about seventy institutes and laboratories revolving around biology, genetics, biotechnology, medical and clinical R&D, especially (but not exclusively) focussed on cancer research and therapy, *biophysics* was the way to go. It would have been a somewhat new field for me, but not far from my scientific interests at that time.

Thus, I started assembling an undergraduate school (‘master’, according to European nomenclature) with some colleagues from the Institut Pasteur, the Institut de Biologie and the Interdisciplinary Research Institute from CNRS, of course the Department of Physics, and my own CNRS Institut de Microélectronique et Nanotechnologie. The key idea was to shake up a cocktail of fundamental research in biophysics and applications in medical physics. The latter had its stronghold in the Oscar Lambret Cancer Therapy Center, just at the opposite end of the subway from the university. It was there that I met the brilliant Thierry Sarrazin, soon to become my best partner in crime, with whom I could put together a master programme in medical physics to be coupled with the programme in biophysics. Since its opening in 2010, this has been a successful story. Our new master in Biological and Medical Physics has attained a stable number of students, improving both the teaching throughput of the Department and the research potential of the laboratories, which now have a privileged route to attract some of our best students to the enormously exciting area of biophysical research.

Then, what is the place of this book? Already before the formal creation of the master course, I had started teaching biophysics units at various levels. As a theorist, I had chosen this way to learn about the basics, while increasingly redirecting my own research interests towards two main subjects: molecular mechanics of cell constituents, and microscopic radiation effects on the nucleic acids DNA and RNA. However, since the very beginning I realised that it was the very youngest students, second- or third-year undergraduate, who had to be exposed to introductory subjects of biophysics as early as possible. Without such an early exposure, there would be no ‘feeding’ for the students towards the more advanced subjects, and the master courses of the 4th and 5th years would have fallen from the sky, onto the shoulders of completely unprepared students. For that reason, I created from scratch a course of Introduction to the Physics of Living Systems for the physics sophomore. The idea was not to introduce much new physics for these students, but rather use their already acquired, albeit still elementary, knowledge about thermodynamics, mechanics, fluid physics, and electricity, to start *seeing* the physics behind the biology. Second-year students are still enough close to the high school to have some basic biology in their backpack, and that’s all that was needed. The course was original in its layout, trying not to follow the much abused path of ‘unveiling hidden physical principles underlying biological facts’. Rather, in the footsteps of D’Arcy Thompson, J.S.B. Haldane, Archibald Hill, and the more modern Knut Schmidt-Nielsen, Steven Vogel, J.C. Pennycuik and few others, I wanted to *start from physics* and show how living organisms *must conform* to the inevitable bounds imposed by gravity, light, temperature, atmosphere, oceans of the Earth, and by the more general constraints deriving from such life-setting variables as the water phase diagram, oxygen diffusivity, molecular elasticity, to name just a few.

This book evidently stems from the lecture notes for that course. Clearly, this is not a book for the research scientist in biophysics: the level is too elementary, the maths goes little beyond high school basics (at least for the *franco-français* students), and the subjects are well assessed and could not truly represent the last cry in biophysics research. It is primarily intended as a biophysics primer for young students, and, by just skipping a few pages too dense in formal math developments, it should be a pleasurable reading also for educated professionals working in the area of life sciences.

The physics inherent to living systems is immense and challenging. Where a physicist seeks mathematical rigour and experimental repeatability under extremely well-controlled conditions, the biologist rather seeks inductive proof, statistical correlations and performs hugely complex experiments with a whole bunch of competing (and often ill-known) free parameters. Biophysics is sometimes considered with a bit of a raised eyebrow by ‘purist’ colleagues: it may be felt that it requires sometimes too simple experiments, and too little theory, to keep the pace with ‘big-time’ physics such as superstring theory, tokamak magnetohydrodynamics, or the quest for the Higgs boson. However, the more I delve into the subject, the more interesting questions and puzzling connections I discover. To me, the fact that a simple experiment assembled in the backyard of the laboratory, or a

crystal clear piece of non-quantum, non-relativistic theory, or even a back-of-the-envelope calculation of a dimensionless number, could reveal a crucial information about the living, represents instead a great advantage and a fascinating opportunity.

Experienced readers will notice that the subject matter treated in this book is partly covered, and often with much deeper scope, in several other texts, such as (to cite just a few prominent ones) *Physics of life* by Clas Blomberg, *Biological physics* by Philip Nelson, *How animals work* by Knut Schmidt-Nielsen, *Comparative biomechanics, or Life's physical world* by Steven Vogel, *Physical biology of the cell* by Phillips, Kondev & Theriot, *Newton rules biology* by C.J. Pennycuick.

However, both the breadth of subjects touched upon and the pedagogical approach followed here should be unlike any of the above, highly commendable and respected works. The keywords behind the present effort can be summarised in the following three concepts:

1. use the least possible amount of mathematics and molecular chemistry, and provide a minimum necessary knowledge of cell and structural biology;
2. propose a wide subject coverage, with a macro \rightarrow micro \rightarrow macro logical path: start from the macroscopic world, namely the thermodynamics of the Universe and the Solar system, and, via such subjects as the greenhouse effect and energetics of metabolism, step down to the microscopic world (physics of bacteria and unicellular life, cells and tissues, biomolecules); hence, move again upwards in length- and timescales to the physics of organs and whole organisms, and end up with subjects in zoology (e.g. simplified aerodynamics of insect flight, energy budget for the survival and reproduction of a flock of animals), and planetary ecology (species competition in the Biosphere, limits of ecosystems);
3. exploit as much as possible the physics knowledge base of second-year undergraduate students (elementary thermodynamics, classical mechanics and electrokinetics, elementary fluid mechanics), without need to introduce more complex notions, unless strictly necessary.

The book can be approached at least at two different levels, by different groups of readers, namely: as an undergraduate textbook in introductory biophysics and as a “case of curiosities” for professionals working in the vast life sciences and biomedical domains. For the first approach, each chapter contains the necessary background and tools, including exercises and Appendices, to form a progressive course. In this case, the chapters can be used in the order proposed by the index, eventually split over two semesters (Chaps. 5–9 covering somewhat more advanced subjects, susceptible of further developments). For the second approach, the curious but less physics-oriented reader might skip the first chapter (if school memories of thermodynamics are still haunting his/her dreams), as well as all the grey boxes containing the more formal developments, and create his/her own menu of chapters *à la carte* (with the only author’s suggestions of reading Chap. 8 before Chap. 9, and Chap. 10 before Chap. 11). Also, note that the bibliographical references at the end of each chapter are not intended to provide a fully detailed support for all the

subjects treated, as it would be the case for a scientific paper, but rather to merely propose some possible directions of development.

No book will ever be complete and definitive, and this one can be no exception. In particular this one, I should say. The material has been expanding over the years, some subjects leaving the place to newer ones according to my own curiosity, or to the discovery of interesting scientific papers amenable to an easily accessible level. Had I kept going with including any new items that came to my attention as a teacher, I would have never written this book. However, one has to stop somewhere, to give account of the state of the house at a given point. Hopefully, others will continue this effort and provide it with more motivation, better writing, deeper substance, nicer examples and smarter problems. Hopefully, among these there could be one of my former students or one of the readers of this book. In any case, it is my hope that in reading this book, be it for an introductory course as a student, or for a curiosity refresher as a practicing life scientist, your interest and attention towards biophysics could only increase.

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Fabrizio Cleri

This work has been possible also thanks to the many colleagues and students with whom I have been interacting, during all these years. Whereas discussing with colleagues is (almost) always a pleasure and a good occasion for funny jokes, the daily exchange with students is definitely the most refreshing and challenging moment. I am grateful to all those people who had the patience of listening to me, advising and correcting my mistakes, and helping me to find better and better ways to transmit the message. And I know it is not over yet.

Special thanks are in order for those colleagues and friends who took the burden of reading early versions of the various chapters and could bring their precious comments, criticisms, enlightenments to my ongoing, often immature work. In alphabetical order: Angela Bartolo, Bruno Bastide, Ralf Blossey and Jean Cosleou (Lille), Enrico Carlon (Leuven), Dominique Collard (Tokyo), Luciano Colombo (Cagliari), Antonio Di Carlo (Rome), Bahram Djafari-Rouhani, Alessandro Faccinnetto, Stefano Giordano and Frank Lafont (Lille), Rob Phillips (Pasadena), Felix Ritort (Barcelona), Paola Salvetti (Dubai). However, for any error, imprecision or misprint still lurking in the text, the responsibility must be fully charged to the author.

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