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Physics of Life

The Physicist's Road to Biology

$$\mathcal{E} = n\cdot h\cdot \nu$$

$$S = k_B\cdot ln(\Omega)$$

Clas Blomberg

PHYSICS OF LIFE

The Physicist's Road to Biology

by

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Preface

For me, the journey to the physics of life began in the sixties when I was a theoretical physics student searching for a proper subject for a continued carrier. I started with statistical thermodynamics and with lattice models. A great challenge at that time was to provide a proper theory of phase transitions. At the same time I enjoyed reading about the progress and development of molecular biology, in particular, through articles in *Scientific American*. I read these articles with a physicist's mind and thought I saw a lot of physics aspects. This was exciting. I had and still have a great interest in Nature and biology, a form of which can be seen on the cover of this book.

Then, from some different directions I found that statistical thermodynamics and the models I had started to work with had potential applications in polymer science and in molecular biology. With a support from the growing discipline of biophysics and Rudolf Rigler, Anders Ehrenberg and Måns Ehrenberg, I dared to take the step to begin research in "theoretical biological physics" as it is called nowadays. I got resources to form a small group, which I think became quite successful.

This book can be characterised as a mixture of my experience with the field, influences from all co-workers at The Royal Institute of Technology in Stockholm and elsewhere at different times, teaching at different levels and inspirations from numerous discussions on deep questions from those on organisation and the second law of thermodynamics to the esoteric ones about consciousness, determinism and free will. Important inspiration sources for the book are the activities in Agora of biosystems together with Peter Århem and Hans Liljenström as well as the recent discussion group at the Karolinska Institue around Ingemar Ernberg.

I want to mention two prominent physicists, whose works are of significant importance to biology. One is Edmé Mariotte, a 17th century French scientist. He among other things, studied pressure and is often mentioned together with the British scientist Robert Boyle for the relation between pressure and volume, often called the Boyle–Mariotte's law. His physics activities comprised studies in hydrodynamics with applications on the importance of pressure for raising the sap in trees. He also considered vision, found the blind spot in our eyes, and had ideas on colours and paintings, ideas that are still applicable and are referred to at the internet. The other person, Albert Einstein, is maybe the best-known physicist of all times besides Newton. He is famous for the relativity theories, which do not play much role in biological physics. However, he did much more than this, in particular, he made important progress in statistical thermodynamics. In his remarkable year 1905, he had two papers, which were as pioneering as relativity theory. He gave a basis for Brownian motion, and by that could show how the irregular movements of atoms provide observable effects, a very important finding at that time. This is still an important theme that takes a prominent part in my book. He also laid the foundation of quantum mechanics, probably the greatest achievement of the 20th century. By this, he solved some severe dilemmas of light effects and of statistical thermodynamics, which I discuss here as a particular path to quantum mechanics, maybe not the commonest one. He gave the relation between radiation frequency and energy, a relation that is crucial for understanding the effects of light and radiation, effects that are very relevant for all life, for instance, in maybe the most important process of life: photosynthesis.

On the cover I show two basic formulas. One is the formula by Einstein about the relation between energy quanta and radiation frequency, a formula as important as the well-known $E = mc^2$, but much more relevant for daily life. That formula is here found on page 47. The other formula is Boltzmann's formula for the entropy, which comprises a basic starting point for the statistical thermodynamics that plays a principal role in the development of this book. This is in the text formula (8.1) on page 73.

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* Sections marked by an asterisk are mainly of a mathematical-formula character. Other sections are more or less descriptive.

Part I

General introduction

§ 1 INTRODUCTION: THE AIM AND THE SCOPE OF THE BOOK

Physics of life. What physics, what biology? I think it is important to pose these questions before going further. Often, it is suggested that an aim of physics is to accomplish an explanation of everything by some kind of basic theories of everything. I don't think that is a proper way in general. I don't think one gets a better explanation of life by string theory. (In the next chapter I will discuss the meaning of "explanation" and "understanding".) Life could not really be explained from the knowledge of atoms. It must be necessary to see everything from its appropriate level description. Life is as we will call it in this book, a "macroscopic phenomenon", a phenomenon at a high level. Is it also appropriate to investigate to which degree one can follow the features at that high level down to lower levels, to the atoms and the atomic forces. Now, we shall consider biology. Isn't biology very different from physics? Yes, it is. It is certainly very varying, more complicated than the questions traditionally taken up by physics. But why shouldn't physics be able to handle also complicated things. Physics should be a proper science to describe nature. No part of nature is really simple and pure. I can agree that physics often tries to simplify very far, to regard isolated phenomena, purified described by simple laws. I will not say that this is not a possible way for biological physics, but one must always know what one is doing and what is an appropriate way of regarding phenomena. What concerns biology, it is necessarily the lowest level biological phenomena that are most appropriately attacked by physics analysis. Indeed, there is also a biological reductionism to basic molecule processes, where physics appears as a natural instrument. That is the way we shall go.

Our basic aim will be to investigate the relevance and importance of basic physical ideas to questions of biology. In doing this, I think it is important to specify and to some extent adjust physical principles to be appropriate for biological applications. A point is also that some of our comprehensions of Nature has a biological basis, not generally acknowledged. The view we have about the world is created in our brains with a primary aim to be appropriate for our survival. This is important for grasping concepts of comprehension. We most easily "understand" features that are important for our lives in this world. This is further discussed in the next chapter.

My starting point is the recognition that the study of Nature implies an identification of various levels, each with its own prominent features. Often, one regards reductionism as a central theme of physics, where an aim may be to reduce all features to basic laws at the lowest possible level. I will partially, but only partially follow such a path. When we regard high-level objects as those around me at this moment, it is relevant to acknowledge that they all are composed by atoms that are coupled together in certain ways to provide their properties, their forms, colour, brightness and so on. The atoms in their turn are composed by still smaller entities, going down perhaps to superstrings. For biological objects, we may most appropriately finish at atoms.

The kind of reductionism that goes back to lowest possible levels does not provide the whole truth when studying the world around us and in particular the biological world. The higher level objects (in what we called the macro-world) get features of their own. These may be related to the atomic structure, but this cannot be anticipated in a simple way solely from the low-level description (which we call the micro-world). We then speak about large-scale properties and what we see as *emergent concepts*. I see this as very relevant for physics although there are also claims that emergence does not belong to physics. [*cf.* Mayr, 2004]

This identification of concepts at different levels, their relations, but also apparent contrasts is here a basic theme. This is also related to the second law of thermodynamics and the arrow of time, which features will be thoroughly investigated.

The aim is to discuss this together with certain examples from molecular biology and cell-biological processes, although the ambition is not to do that in a systematic, exhaustive manner. Rather, the discussion will be centred on concepts as order and disorder, determinism and randomness. One point is that the high-level description, relevant for biological questions, is basically indeterministic (in some sense), irrespective of what we believe about basic physical laws.

The ambition is to see certain basic biological concepts in a physical framework. Biology implies great variety, while traditional physics mainly concerns simple, often idealised situations. Thus physics has to be generalised in that respect, and I will discuss what that means for evolutionary paths, both biological and non-biological. The aim is also to get to what we may regard as "deep biological functions", learning, thinking and at the end, the mind. What may physics say about the concept of consciousness? Some people claim that physics is very relevant; some may say that physics is totally irrelevant. At that stage, we may not completely abandon the physicists' search for simplicity, and look for such aspects. How simple can a living system be? What was required to start life, and how can that be understood from a physicists' point of view? Are there basic biological laws?

I also have an ambition to follow up the principles of the second law and the arrow of time and see that in a cosmological, scope. Which may lead to the question: What are the particular properties of our universe to lead to life?

This is not intended as a textbook for, e.g. a biological physics. There are good examples of that. Neither have I wanted to provide an exhaustive account of the latest achievements of a particular subject. Rather, my ambition is to provide a view about how physical principles relevant for and biological applications can be seen in a large framework. The arguments shall be deep, but with a hope that this may be attractive both to biologists and physicists at a research level, I try to work out arguments from a basic starting point. With this aim, I think the book could well be read by a general scientifically inclined public. The chapters here are intentionally of two kinds. I have a number of purely descriptive parts, where I try to describe principles without mathematical formulas. Then I also have chapters full with mathematical formulas for those who want to go deeper, sometimes quite deep. My ambition is also to be self-contained, to start everything as basically as possible. For that reason, an aim is that much shall be possible to read without much previous knowledge.

The plans I have described here are inspired by numerous discussions with colleagues from various scientific disciplines, also in the form of regular seminar series.

A book like this is necessarily limited in scope. There are many very interesting properties that are not taken up, and I have no ambition of being exhaustive. Instead, I concentrate on certain subjects and also certain important lines: thermodynamics, stochastic processes, non-linear theories.

The book contains nine main parts. The first one is the present one with this introduction and an introductory chapter on my views of physics, the reductionism and the level structure of nature, which I think have to be at the basis of a full physics of life.

The second part takes up the basic physics. There is a chapter on the concepts of classical physics, followed by chapters on electromagnetism and on quantum mechanics. These chapters as much of the book contain both descriptive parts with attempts to show the general features and formula sections, where I go in some detail. The principles of these chapters will not be followed up in the rest, and they serve as reference to later developments. This part also contains the basics of thermodynamics and statistical physics, here in a descriptive style. These parts will be developed further in later parts, and shall be regarded as important main threads throughout the book.

The third part in a purely descriptive manner takes up general trends of physics, which are of relevance for applications to biology, and there is also a preliminary chapter to provide the relevant molecular biological background. One chapter shows the analogy view I find important, and takes up physics models, mainly of magnetic systems, that have been generalised to describe also molecular biological problems and concepts, such as spin glass, which has been very useful as metaphor. In another chapter, we at this early stage take up the question "What is life?", unavoidable in a book like this, and here serving as a starting point. All these ideas of these chapters will be followed up in later parts.

Thermodynamics is further developed in the fourth part, which to a large extent takes up mathematical formalisms. Here, the thermodynamic and the statistical formalisms are further developed. This part also takes up the principles of linear non-equilibrium thermodynamics with discussions about possibilities of further generalisations. One chapter discusses the entropy concept and can be regarded as a key chapter for grasping the basic concepts of order and disorder. That chapter is based on combinatorial expressions with an aim to show the very large numbers already appearing at not too large systems. There are examples from shuffling a pack of cards and the sometimes cited monkey library, a library consisting of pages unintentionally, randomly written by monkeys on typewriters or, less spectacular but maybe more relevant, produced systematically to cover all combinations of characters on one page and then saved in a fictitious library. Finally, that part takes up the proposed physics models in a more elaborate way. All the concepts of that part will be followed up in later chapters.

The fifth part is about probability and stochastic processes, important for the applications. A first chapter is descriptive, presenting the general ideas, while the rest contains much, but self-contained, mathematical formalism, to some parts quite deep. The concepts are presented in an introductory chapter and in the rest I take up a number of examples. One chapter takes up step processes, processes that are characterised by a number of discrete steps, with random transitions between the steps. The physical–mathematical treatment is based on what we in physics call "master equations", of which there are many examples. Other chapters consider continuous, random movements, based on differential equations that describe random movements. An archetype is provided by Brownian motion, which is covered quite comprehensively, also for describing a barrier passage due to random influences and, related to that, the background to what is called stochastic synchronisation. I also take up diffusion with some applications and the continuous correspondence of the step processes and the so-called Fokker–Planck equations. Fokker–Planck equations are also used for the Brownian motion and the barrier passage problem.

In the sixth part, we get to the more proper applications, and the chapters there concern questions associated with protein structure, recognition and kinetics. They rely much on the developments in Parts IV and V. Main states of a protein can be considered according to the random processes, which provide important aspects. Thermodynamic step models can be relevant for the folding process of proteins, and they also to some extent can be regarded as an analogy to a spin glass discussed in Part IV. Thermodynamic principles are relevant for all kinds of chemical kinetics as well as for the recognition of molecules in a cell. All that comprise the basis of the control of enzyme kinetics.

In the seventh part, we go further to non-linear problems and some biological applications. This was preliminarily discussed in Part III. We go deeper here and discuss general aspects. In one chapter, I consider generation of pulses, oscillations and waves with examples, in particular as used for describing oscillating cell processes, generation of chemical signals between cells and generation of nerve signals. Although the basic applications are different, the formalisms can be of quite similar structures. One chapter is about what is called "deterministic chaos", the possibility that relatively simple sets of (deterministic) differential equations provide solutions that give rise to irregular, non-predictable features. I take up the basic aspects without going too deep into the mathematics. There are many suggestions that such processes are applicable to biological phenomena, which is discussed. What certainly is relevant is that they, in an elucidative manner, show that even simple mathematical–physical relations can provide an irregular, non-predictive behaviour, a fact that is conceptually important in discussions about determinism. I also in that part have a chapter on the effects of random influences on non-linear phenomena. As randomness (noise, fluctuations) play a large role in cell processes, this is an important point, but this provides a science area where still many important questions are still unclear. There are few possibilities to make systematic studies and to achieve analytic results. (The Brownian motion studies in Part V are among the successful examples). In many cases, it is not even clear how to make proper numerical calculations. (There exist calculations that do not take these difficulties into account.) I take up such questions at this point.

Part VIII goes entirely to applications. Here are certain points taken up here where the physics aspects, I think, are very important. One concerns the selection of units in the systematic synthesis of macromolecules, nucleic acids or proteins. These are very accurate in a cell, but also controlled by molecular mechanisms. Thermodynamics play a role and there are thermodynamic limits on how accurate selection can be. Indeed apart from being an important cell biological problem, this provides important thermodynamic questions, as the outcome depends on how far from equilibrium the selection mechanisms are driven. Basic thermodynamics also play a role for the next problem, that of unidirectional motion, getting ions to go in one direction or moving a unit, for instance muscle parts, in a particular direction. Again, these depend on processes driven from equilibrium. A metaphor is what is called "Brownian ratchet". A Brownian particle normally goes randomly in any direction, and a primary question is whether there exist possibilities for the particle to proceed in only one direction. Another application here is about the neural system and the basic function of the neural network and its signals. Again, here we see a very complicated system where the concept of a spin glass is a useful metaphor, relating to other questions of the book. We follow up network ideas in questions on gene regulations and the immune system, where again recognition questions play an important role. Finally, in that part, there is a large chapter about the origin of life, where first general ideas of early molecule synthesis are discussed with some recent ideas on how the first cells might have been developed. That chapter also takes up some mathematical models used for discussing selection processes and possible difficulties of an early stage without proper control mechanisms.

Finally, Part IX provides a summary and also widens the scope by going further with some deeper questions that are briefly dealt with previously in the book, and where the physics aspects are extended. In one chapter, I take up physics aspects on evolution. Evolution may be considered a main core of biology, but it is also made clear at many points that the basis of evolution theory is easily reconciled with a rational physics view. The basis of evolution—genetic variation and selection are themes that are taken up in other chapters. There is here also a chapter which sums up a general view on determinism and randomness, again aspects that have appeared in other chapters, but here deeper analysed. Then, we go to the deep questions on what can be considered higher functions: thinking, mind with all that implies and the free will, concepts that have been discussed since the beginning of a scientific view without any clear agreement. Here, I discuss these aspects together with the general multi-level basis and with ideas on how such concepts shall be interpreted. The preceding question on determinism provides central aspects. Then, in the last chapters, we extend the physics. In one chapter, we take up the question on time and its direction, closely related to thermodynamics and the entropy aspects that form important themes throughout the book. That also mean that we extend this aspect to ideas about the "end of time", what may happen in a distant future? What is meant by heat death? There is here also a highly speculative but nonetheless intriguing question on how long life can survive. And then, I also take up somewhat related questions, not completely unmotivated here about the elusive anthropic principle, the fact that natural laws and their parameters are as they must be to provide the world we live in with the right kind of elements that are suited for forming life. I will analyse this principle, which certainly is striking, although it is difficult to make any firm conclusions.

§ 2 THE PHYSICS OF LIFE: PHYSICS AT SEVERAL LEVELS

Physics of life. Is that a preposterous dream of an arrogant physicist, believing that the whole world is nothing but strict, mechanistic laws, which also enter the almost sacral phenomenon of life? Or is it an expression of a powerful tool to understand also living organisms? Can physics and biology be unified into an all-embracing natural science? Well, that is my view and what I want to discuss in this book.

Today, there exist a very optimistic view among many physicists and some biologists that physics really can provide a deeper understanding of biological systems and what we call life. At the same time, there are critical voices that the typical features of physics, to reduce processes to underlying basic laws and also to simplify phenomena, cannot be applicable to the diversity of life.

There are many "jokes" that go around about physicists, and which have an undeniable kernel of truth. Physicists always strive for the simplest descriptions. There is the speaker who starts a lecture by saying that a cow can be approximated by a sphere. There is the circulating story about the shepherd meeting a wanderer who in varying stories has different occupations, but here he is of course a physicist. The shepherd promises the wanderer one of his sheep if he can tell how many there are. Of course the physicist can tell that, and he takes his promised animal. The shepherd is then allowed to get it back if he can guess the occupation of the wanderer. Which the shepherd can do, and why? Well, the physicist had taken the dog.

There is an undeniable arrogance among some physicists who may claim that physics is at the top of all science. Everything is basically physics. There are physicists who apply established methods to biology without understanding that they oversimplify or that the methods are not relevant to biology. Shall physics be applied to biology, one has to understand the biological background and also to look for the relevant physical description. One has to ask "What biology?" and "What physics?".

There are obvious biological systems where physics in a significant way has contributed to clarifying and deepening our understanding. Most clearly, this concerns the structure and function of the biological macromolecules, such as proteins and nucleic acids. Here, physical principles and physical experimental methods are fundamental for our understanding of their properties. Processes in a cell as well as transport of various substances through cell membrane can be comprehended as governed by physical principles. Can we go further?

Ernest Rutherford, one of the most important physicists in the early 20th century is often cited (by physicists of course) as having said "all science is either physics or stamp collecting". Again physical arrogance? One may identify some biology as "stamp collecting", but is the rest physics? Again I think we must ask "What physics?".

Clearly, we must see physics in a greater scope than often is done. For me, physics is essentially about mechanisms, to understand how things work, to ask questions about how and why. (And we need some idea of the meaning of "understand".) Physics shall not only be about simplified systems, it must be able to cope with complicated ones. The physicist who shall contribute to biology must learn the difference between a dog and a sheep. At the same time, the aim of simplification can be useful. In some cases, it would not matter if it is a dog or a sheep, and there are problems where it is a practical simplification to treat a cow as a sphere. All the time, we must know what we do.

A first step is to recognise a certain level structure of the world where our relevant physics will fit in. We can identify a low-level world with the atoms themselves that move and bind together to form larger entities according to well-studied natural laws. We may go even deeper, to the constituents of the atoms, but in most of the cases that we take up, this will not provide any further insight. The low-level atomic world is very detailed. The number of atoms in a room may be expressed by a number of 29 digits. It is not possible to keep track of all these atoms and how they move, although if we wanted a complete description, that should be necessary.

Rather, we will have another level of description, the world as we see it with ourselves and objects such as we apprehend them. The description at that level is necessary for our comprehension. We could never grasp a 29-digit number of atoms, and the situation is indeed still worse than that as the number of various combinations to distribute energy among the atoms may even be numbers with 10^{29} digits, totally incomprehensible. (There will be many discussions later about such features.) That view leads to some necessary concepts that will be important for out presentation. One is that the objects as we see them cannot be completely well determined. There is a necessary indeterminacy due to the atomic structure. (This is not the same indeterminacy as appears in quantum mechanics, and which we also will consider). Atoms move incessantly and thus the atomic basic structure of the objects changes all the time. What also is important at the higher level is that its aspects and concepts are based upon how we apprehend the world. There is no easy way to deduce all that from the underlying atomic structure, although one goal of physics might have been to understand everything from the basic laws. It is very important that the high-level structure involves "emergent" features, not anticipated from the low level.

It is also important to go downwards, and consider how the high-level concepts are related to the low-level atomic structure. In particular, this concerns the interpretation of what usually are called secondary features, or qualities, emergent features. In traditional physics, this has been a very powerful way to interpret concepts like colours (why is grass green and gold yellow?), as they can be associated to the features of the atomic structures.

My view is thus that we have basic laws at a low level, which for our purposes means the quantum mechanical description of atoms, of atomic forces and how atoms build up larger units, in particular the macro-molecules. The basis of that picture is very well studied, very well accepted, and I see no reason to question it. When going to higher levels, we follow a path from the atoms, how they form the large molecules, how the molecules become important units in their own rights that can bind to and influence each other, and then we go further upwards to the cell units and to the cells that build up biological organisms and individuals like ourselves. At that stage we are units that in turn influence each other. The view is that there are no basically new physical laws when we go upwards; everything is built up by the same basic physics laws. However, the higher units are built up and act in ways that are not anticipated form the lowest level vies. This is what see interpret as *emergence*.

So, I don't think there are any new principles entering when going to the higher levels. The high-level objects are built up by the basic atomic principles. Their features, their properties are due to their structures and special properties of the large objects. One may put the question, and many people have done that, whether the basic atomic laws already at the lowest level contain anything that points to the development of life and still more, to the development of a mind. We cannot deny that the main elements in the world, hydrogen, carbon, oxygen, nitrogen are perfect for building up the complexity that is needed for life, and we cannot deny the importance of liquid water, which is formed by the two most abundant elements in the universe which form compounds, and the distinction between water and organic compounds that are perfect for building up demarcated units that as cells act in an autonomous manner. All this depends on the particular possibilities for compounds of carbon, oxygen and hydrogen. And the possibilities of cell function are due to the structure of the macromolecules (proteins, DNA and so on) built up according to the basic principles. These properties appear, emerge as the higher order units are built up, they are not apparent in the basic