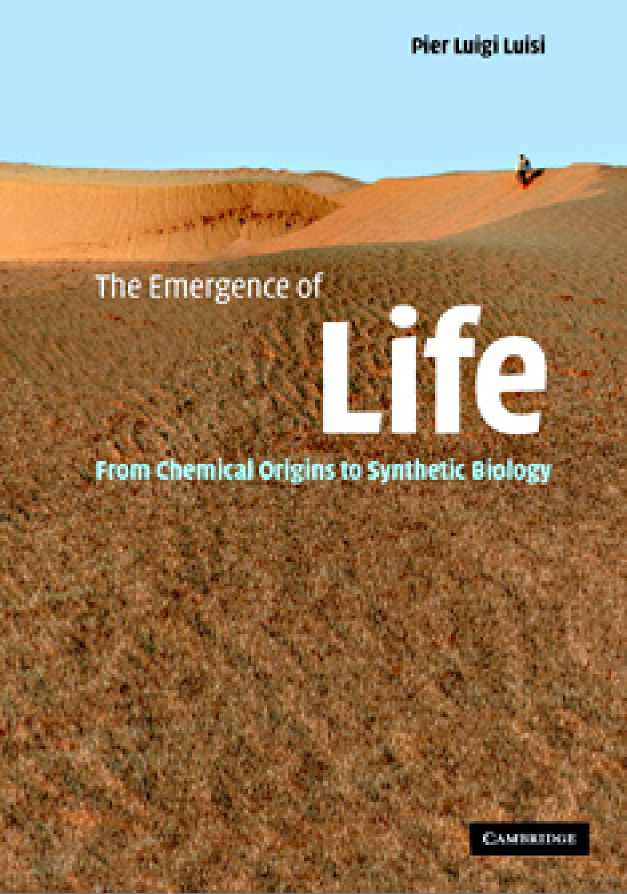
Pier Luigi Luisi

The Emergence of Life

From Chemical Origins to Synthetic Biology



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THE EMERGENCE OF LIFE

The origin of life from inert chemical compounds has been the focus of much research for decades, both experimentally and philosophically. Connecting both approaches, Luisi takes the reader through the transition to life, from prebiotic chemistry to synthetic biology. This book presents a systematic course discussing the successive stages of self-organization, emergence, self-replication, autopoiesis, synthetic compartments and construction of cellular models, in order to demonstrate the spontaneous increase in complexity from inanimate matter to the first cellular life forms. A chapter is dedicated to each of these steps, using a number of synthetic and biological examples. The theory of autopoiesis leads into the idea of compartments, which is discussed with an emphasis on vesicles and other orderly aggregates. The final chapter uses liposomes and vesicles to explain the synthetic biology of cellular systems, as well as describing attempts to generate minimal cellular life within the laboratory. With challenging review questions at the end of each chapter, this book will appeal to graduate students and academics researching the origin of life and related areas such as biochemistry, molecular biology, biophysics, and natural sciences. Additional resources for this title are available online at www.cambridge.org/9780521821179.

Pier Luigi Luisi became Professor Emeritus (Macromolecular Chemistry) at ETH-Zürich in 1982, where he also acted as Dean of the Chemistry Department; he is currently a professor of Biochemistry at the University of Rome 3. He has authored *c.* 300 papers in the fields of enzymology, molecular biology, peptide chemistry, self-organization and self-reproduction of chemical systems, and models for cells.

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To my wife Claudia

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Preface

There are already so many books on the origin of life, as listed on pages xiv–xi. Why then write another?

There are two answers to this question. The first comes from the desire to write a book for students – rather than a specialist book – in which the various phases of the transition to life would be laid out in a discursive way that illustrates the basic principles of self-organization, emergence, self-reproduction, autocatalysis, and their mutual interactions. Another important aspect of this teaching aim is to take into consideration the philosophical implications that are present, more or less consciously, in the field of the origin of life. I believe in fact that the younger generation of chemists and molecular biologists should be more cognizant of the connections between the biological and the philosophical quest, so as possibly to integrate the most basic language of epistemology, and see their science work in a broader dimension. This integration, when taken seriously, may also foster an interaction with the ethical and humanistic aspects of life. The age-old question: "what can science say about the domains of psyche, ethics, or consciousness?" is usually discarded by most scientists with a wave of the hand. This behavior is one of the main reasons why science has lost contact with the broad public – and again, it would be desirable that the younger generations take a different stand. Although this is not a central issue of this book, I hope to offer some hints on how this new approach might be defined.

While all these reasons are centered on the target of teaching, the other reason for the coming to being of this book is more subtle. It comes from the perception of a shift in the field of the origin of life, a new "Zeitgeist" (spirit of time), which makes it timely to propose a new discourse.

One aspect of the new Zeitgeist is the influence of system biology, a new operational framework where the behavior of an entire complex biological system is more important than – or as important as – the individual molecular events. Although the origin of this novel biology lies in the development of analytical tools, more than in a basic philosophical shift, the final consequence is an operational framework which is at some distance from the reductionistic approach of viewing life as a reaction based solely on nucleic acids. I believe that the exaggerated emphasis given until now to the prebiotic RNA world probably needs to be brought back into balance. And I believe the balance must be based on a more integrative view of cellular processes, even at the stage of the origin of life. Thus, I will give here proper emphasis to the autopoietic view of minimal life – which is generally not considered in other books. The latter chapters are devoted to the chemical and physical properties of compartments, vesicles in particular, and these are more technical in nature. In fact, this book suffers from that kind of heterogeneity that characterizes the field of the origin of life: on the one hand it thrives on epistemological concepts; and on the other hand it is based on experimental organic and physical chemistry. This double nature, far from being a problem, constitutes the very complexity and beauty of the field.

More generally, I will try to illustrate the different views on the origin of life and early evolution – notions like determinism and contingency will come into focus. All these scientific views are based on the postulate that life on Earth comes from inanimate matter; and a corollary of this postulate is that it might be possible to reconstitute life in the laboratory, at least in some elementary form. The ambition of understanding the prebiotic chemistry leading to the transition to life, and ultimately, to the Faustian dream of making life on the workbench, underlies the whole field – and is also the common thread of this book.

I do not know whether this dream will be fulfilled, but in closing I would like to cite Friedrich Rolle, a German philosopher and biologist, who, in 1863, writing about the hypothesis that life arose from inanimate matter, stated:

The general reasons for this assumption are really so impelling, that no doubt sooner or later it will be possible to show this in a clear and broadly scientific way, or even to repeat the process by experimentation.

This was written one and a half centuries ago and yet today we do not know whether we will ever get there. This book makes no pretence of showing the way, but as the pages unfold we will see some of the reasons why this enterprise is so difficult; and this in itself is a kind of positive knowledge.

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1

Conceptual framework of research on the origin of life on Earth

Introduction

The main assumption held by most scientists about the origin of life on Earth is that life originated from inanimate matter through a spontaneous and gradual increase of molecular complexity.

This view was given a well-known formulation by Alexander Oparin (Oparin, 1924, 1953 and 1957), a brilliant Russian chemist who was influenced both by Darwinian theories and by dialectical materialism. A similar view coming from a quite different context was put forward by J. B. Haldane (Haldane, 1929; 1954; 1967). By definition, this transition to life via prebiotic molecular evolution excludes panspermia (the idea that life on Earth comes from space) and divine intervention. If we look at Figure 1.1 without prejudice, we realize that Oparin's proposition is extremely bold. The idea that molecules, without the help of enzymes or DNA, could spontaneously assemble into molecular structures of increasing complexity, order, and functionality, appears at first sight to go against chemical and thermodynamic common sense. This view, which modern biology generally takes for granted, appears in most college textbooks, specialized literature, and mass media. The background of Figure 1.1 is the continuity principle (Oparin, 1924; De Duve, 1991; Morowitz, 1992; Crick, 1996; Eigen and Winkler-Oswatitisch, 1992; Orgel, 1973; 1994), which sets a gradual continuity from inorganic matter to organic molecules and from these to molecular complexes, up to the onset of cellular life, with no qualitative gap between each stage. In this sense, then, the view expressed in Figure 1.1 is the modern version of a kind of spontaneous generation, although on a sluggish time scale.

In recent times, the challenges of creationists and their attacks on educational institutions in the United States led to some novel scrutiny of this view. There is nothing new in the arguments of the creationists since the writing by William Paley, the Anglican priest who became famous for having introduced one of the

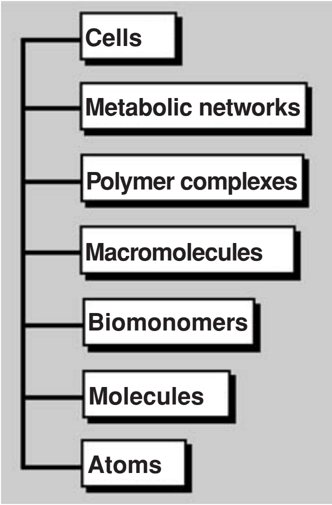

Figure 1.1 An arbitrary scale of complexity towards the emergence of life.

most famous metaphors in the philosophy of science, the image of the watchmaker (Paley, 1802):

> . . . when we come to inspect the watch, we perceive . . . that its several parts are framed and put together for a purpose, e.g. that they are so formed and adjusted as to produce motion, and that motion so regulated as to point out the hour of the day; that if the different parts had been differently shaped from what they are, or placed after any other manner or in any other order than that in which they are placed, either no motion at all would have been carried on in the machine, or none which would have answered the use that is now served by it . . . the inference we think is inevitable, that the watch must have had a maker – that there must have existed, at some time and at some place or other, an artificer or artificers who formed it for the purpose which we find it actually to answer, who comprehended its construction and designed its use.

Living organisms, Paley argued, are even more complicated than watches, thus only an intelligent Designer could have created them, just as only an intelligent watchmaker can make a watch. According to Paley (1802):

> That designer must have been a person. That person is GOD.

As already stated, modern science – even without reaching the extreme reductionism of Richard Dawkins and his Blind Watchmaker (Dawkins, 1990) – does not conform to this view. Paley's metaphor was already negated in his time by Hume and other contemporary philosophers. This does not mean that all scientists are necessarily atheist: the meeting point (the easy one) between science and religion is to accept the idea of a God, who created the beginning and the laws of nature, leaving them alone to do their job. We will come back to this argument a couple of times in this book.

Creationists apart, the view that life originates by itself from inanimate matter is rich with important implications for the philosophy of science and life at large. It is therefore important in our discussion to pause and consider this view, the underlying conceptual framework, as well as some of the consequences.

Let us start with the concept that is perhaps most important for lay people: it may at first sight appear that once divine intervention is eliminated from the picture, nothing remains except molecules and their interactions to arrive at life. Of course, evolution and interactions with the environment are very important factors, and they can take the fancy form of self-organization and emergence. However, all these factors appear to be based on, or caused by, molecular interactions. In other words, at first sight the acceptance of the view expressed in Figure 1.1 is tantamount to stating that life consists only of molecules and of their interactions.

Is it so? Does a rose consist only of molecules and their interactions? We can answer yes, but it is also fair to say that this would represent only a first, gross approximation. First of all, notice that the term "consists of" does not necessarily imply that life can be *explained* and *understood* in terms of molecules and their interactions. Here comes the age-old question of the discrimination between structure and properties, and whereas the structure per se can be seen as consisting of small parts, usually properties and behavior are not – or at least additional qualitative concepts are needed. In turn, this does not necessarily mean that life holds something intrinsically unexplainable or beyond the reach of science. This is an important and subtle point, and I hope to be able to offer some clarifying ideas about that in the chapter dealing with autopoiesis and cognition.

Let us consider some of the further implications of Figure 1.1. The view that cellular life can be arrived at from inanimate matter may imply in principle the possibility of reproducing it in the lab. Why not, if all we need is a bunch of molecules in a properly reactive environment? This way of thinking is the basis of the experimental work on the origin of life. In fact, the best way to demonstrate the validity of this view would be to make life in the laboratory – the age-old Faustian dream. We do not know how the process of the transition to life really occurred in nature, so how can we reproduce it in the laboratory? The answer to this question is conceptually simple, as pointed out by Eschenmoser and Kisakürek (1996):

> the aim of an experimental aetiological chemistry is not primarily to delineate the pathway along which our (natural) life on earth could have originated, but to provide decisive experimental evidence, through the realization of model systems ('artificial chemical life') that life can arise as a result of the organization of the organic matter.