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# THE EMERGENCE OF LIFE

Addressing the emergence of life from a systems biology perspective, this new edition has undergone extensive revision, reflecting changes in scientific understanding and evolution of thought on the question "what is life?" With an emphasis on the philosophical aspects of science, including the epistemic features of modern synthetic biology, as well as providing an updated view of the autopoiesis/cognition theory, the book gives an exhaustive treatment of the biophysical properties of vesicles, seen as the beginning of the "road map" to the minimal cell – a road map, which will develop into the question of whether and to what extent synthetic biology will be capable of making minimal life in the laboratory. Fully illustrated and accessibly written, *The Emergence of Life* challenges the reader directly with provocative questions, while also offering suggestions for research proposals taken directly from the author's bench experience. Dialogues with contemporary authors including Humberto Maturana, Albert Eschenmoser, and Harold Morowitz make this an ideal resource for researchers and students across fields including bioengineering, evolutionary biology, molecular biology, chemistry, and chemical engineering.

Pier Luigi Luisi is Professor Emeritus at the Swiss Federal Institute of Technology in Zurich, Switzerland (ETHZ), where he developed his professional career, notably initiating Cortona Week in 1985. He has also held the position of Professor in Biochemistry at the University of Rome 3. He has authored more than 500 peer-reviewed papers as well as a number of books, recently including *The Systems View of Life* with Fritjof Capra (2014).

# THE EMERGENCE OF LIFE

## From Chemical Origins to Synthetic Biology

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# Contents

# Acknowledgments

This book has been written immediately after the book with Fritjof Capra, *The Systems View of Life: A Unifying Vision* (2014), and the many fruitful discussions I had with Fritjof have helped to shape and enrich the new edition of the present book. I would also like to express my gratitude to Michel Bitbol, Rossella Mascolo, Michele Lucantoni, Angela Spaltro, and Pasquale Stano for their comments and continuous encouragement. The help of Pasquale Stano has been very important for the discussions in Part IV of this book. I would like to emphasize the collaboration with Angelo Merante, who was with me also in the first edition: he has been not only responsible for the many illustrations of the book, but also for the general organization of the various chapters, and for important critical comments and enrichments to the text.

# Introduction

The first edition of this book, published in 2006, was written about 10 years ago; a partial update was done in the Japanese edition, in the 2010 Spanish edition, and in the 2013 Portuguese edition. A more complete English update was deemed necessary. Not that something dramatic has taken place since the first edition: the origin of life remains an unsolved question. At the last 2004 ISSOL meeting in Nara, Japan, a discussion took place on the question “what is life?,” and this was conducted in similar terms and emphasis as the conversation 20 or 30 years back. Of course, in all these years, although not solving the core question, some particularly important research papers have appeared, and the corresponding update will be presented, to the best of my knowledge, in this second edition. However, this is not the main reason for this second edition.

Life on Earth is based on ordered sequences of proteins and nucleic acids, and on their mutual ordered interactions. And the solution to the quest for the origin of life is the answer to the question, of how this order came about. There are approaches to the origin of life that ignore this simple consideration and start from already pre-constituted ordered systems. This is the case of the (original) RNA-world, starting from a self-replicating RNA. This is a highly ordered, functional macromolecule, and to explain the origin of life from this ordered state would be akin to constructing a house roof first. The same can be said for those researchers who advocate viroids, or pristine forms of ribosomes, as the starting base to explain the origin of life. First, you should explain how this highly ordered state came about – and if you do so, perhaps, yes, you then have paved the way to explain the origin of life. To be clear on that: the research on the three areas mentioned above is often of the highest quality, and corresponds to the best pages of modern science. But in my view it will help very little to explain the origin of life on Earth.

The other approach to the origin of life starts from the opposite direction, namely from the disorder of monomers or low molecular weight compounds. The keywords here are hydrothermal sources, marine or volcanic smokes, endogenous prebiotic molecules, or molecules coming from space. Again, beautiful research is done on these areas, but you can have all the low molecular weight compounds of this world, in any quantity you wish, and you will never be able to make life. You cannot expect that a cathedral arises by simply having all the possible bricks. With 20 different bricks, you can construct a 100-bricks-long wall in an almost infinite number of ways; the question is to discover the principle that permits the construction of only a few ordered sequences.

This book starts from the consideration that we are still a long way from having a solution to this pristine problem of the origin of ordered structures (not that this is the only one in the origin of life). It attempts to analyze why this is so, indicating that one main reason may lie in the present-day reductionist (nucleic acid-centered) philosophical thinking in the field; and it then tries to propose some way to eliminate this shortcoming, emphasizing a systemic view of life and a corresponding systems view approach to its origin.

Part I of the book examines the various aspects of the bottom-up approach to the origin of life, as generally presented in the literature. This part also contains stringent criticism of the prebiotic RNA-world as origin of life, with an invitation to look at the origin of life from "ground zero." The discussion is enriched by a series of conversations with distinguished authors in the field, such as David Deamer, Albert Eschenmoser, Gerald Joyce, Doron Lancet, Harold J. Morowitz, Eörs Szathmáry, Sandra Pizzarello, and Nobelist Ada Yonath.

Part II is a detailed account of the theory of autopoiesis, as due to Maturana and Varela, who picture the cell as an open molecular system capable of self-maintenance, due to a regeneration of the components from within. This systems view is in sharp contrast with the reductionist, DNA- or RNA-centered visions of life according to which life is the result of the behavior of a single molecular species. Here, it is instead the system's organization of the internal web interactions that may cause cellular self-reproduction (eventually leading to Darwinian evolution) – and Darwinian evolution, being the result of that organization, cannot be seen obviously as the *prima causa* of life.

Also considered is the interaction of the living with the environment, which leads to the important notion of cognition with its epistemic and ecological aspects. Particularly in this part of the book, but then also as a general background framework, philosophical and biological aspects are strictly interwoven with each other, with the intention of showing that philosophy and biology should not be seen as two distinct disciplines, but as an integrated unity of the systems view of life: a message that should be given to all our students. Part II also includes the conversation with Humberto Maturana and – as a tribute to Francisco Varela's thought – the conversations with philosophically minded authors such as Amy Cohen Varela and Evan Thompson. Other enrichments of discussion on these arguments are a conversation with Denis Noble and a Side

Box concerning future developments of research on autopoiesis by Luisa Damiano.

With Part III, the book moves towards biological complexity, and here the two complementary notions of self-organization and emergence – from simpler molecular systems, as micelles and vesicles, to more complex structures (organized protein systems, ribosomes, viruses, and so on) – are presented in two distinct chapters. The following chapter concerns the most salient emergent property, namely self-replication/reproduction. Two side boxes, the first one concerning self-organization mechanisms in Hydra and the other focusing on the sciences of complexity – written by distinguished authors Giorgio Venturini and Stuart Kauffman – offer interesting points of view about the richness of the arguments handled in this section of the book.

The first chapter of Part IV concerns the world of surfactants and lipids, in particular the procedures for solute incorporation and questions about overall and local concentration. The other two chapters are focused on the world of vesicles, in particular their physical and chemical properties, with emphasis on their capability of entrapping biopolymers – whereby they are seen as the best models for the shell of biological membranes.

The information regarding the self-organization and self-reproduction of vesicles will be the basis for the last section of this book, Part V, which is devoted to synthetic biology and the attempts to construct the minimal living cell in the lab. First, general questions about synthetic biology – as today's most celebrated and ambitious laboratory approach to make new or alternative forms of life – are handled. The opening discussion about the epistemology of synthetic biology is enriched by two interesting conversations with relevant authors Paul Freemont and Sarah Lau. Then, a review of the experimental work carried out in my laboratory and others towards the synthetic biology of the minimal cells, which includes the new and unexpected finding of the spontaneous solute overcrowding in vesicles.

The general idea, the red thread that pervades this book, is to provide a unitarian view of life and its origin that departs from a reductionist, nucleic-acid-centered view, to favor instead a systems approach, in which the cellular organization, and its cognitive interaction with the environment, gives the basis for an understanding and, possibly, the reconstruction of life.