The Principles of Life

Tibor Gánti

With a commentary by
James Griesemer and Eörs Szathmáry

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Preface

It was sometime around the autumn of 1974 that I saw Tibor Gánti for the first time. He was delivering a series of popular lectures about the basic characteristics of life and living processes at the centre of the Hungarian Organization for the Popularization of Science. Having just started the grammar school in Budapest, already with a well-developed interest in biology, I remember how struck I was by the extreme clarity and intelligibility of those lectures. The audience was mixed, but the vast majority were students (also from the university) and schoolteachers. By then many knew that Gánti had published a seminal book in Hungarian with the title *The Principle of Life* (*Az élet princípiuma*, Gondolat, 1971). It was a very serious book in a popular science disguise. It sought to establish the foundations of the theoretical biology of individual organisms.

Trained as a chemical engineer, Gánti has always been interested in biology. In fact by the time he went to university he was convinced that the basic characterization of living systems was impossible without a firm chemical grounding. For some time Gánti worked in areas of chemical industry close to applied biology. He has filed patents for the production of biochemicals by the directed use of enzymatic biochemical networks.

However, his interest in the basics of life has never wavered. He realized that the problem could not be solved without using the new results of molecular biology. He was the first author in Hungary to popularize molecular biology (*Forradalom az élet kutatásában* (*Revolution in Life Research*), Gondolat, 1966). But already in that book there is a chapter on the basic characterization of life. Gánti argued that life at its most fundamental was a combination of two different types of process: one responsible for homeostasis (keeping the status quo in some sense) and another ensuring the controlled succession of life history events (the 'main circle'). The first relates to metabolism, the second to DNA and the genes. This 'dual nature' of life has been independently realized by other outstanding scientists (such as Freeman Dyson and John Maynard Smith). However, Gánti went far beyond that.

When he published his pioneering book on molecular biology, he was afraid that he might have to go to prison. The atmosphere of Lysenkoism was still present in Eastern Europe in the late 1960s. He had similar worries when he decided to go public with his *chef d'ouvre: The Principle of Life*. Part of the text of this volume is an updated version of that landmark book.

Why has *The Principle* been so remarkable? There are, I think, a number of good reasons. First, it built on much of the new data of molecular biology. The first edition (in 1971) contained several chapters which could be seen as a revision of Gánti's first book. Second, it approached the problems of life characteristics and units of life with unprecedented rigour for the time and in a way that is still heuristically quite valuable. Third, Gánti recognized, and *The Principle* shows, how chemical cycles (and networks) of various kinds play a crucial role in living systems and that their exact description needs a new approach (later called cycle stoichiometry). Fourth, he borrowed some key concepts from cybernetics. Fifth, in sharp contrast to the first point, he omitted a sacrosanct assumption of molecular biology. Finally, the new conceptual framework was not only presented, but was also applied to a novel attack on the problem of the origin of life.

Let me elaborate on some of these key points. Why did he adopt this Janus-faced approach to molecular biology? What is the crucial omission? Gánti thought (and still thinks) that the elementary units of life (he calls them chemotons) could be described without the incorporation of enzymes. The first argument is that enzymes just facilitate what is otherwise possible, and it is the *regulated*, rather than the *regulating*, system that is of primary importance. The second argument states that experiments related to the origin of life suggest that non-enzymatic systems precede enzymatic systems not only logically, but also historically. I suspect that a much greater number of biologists would agree with the former argument than with the latter. The question of whether non-enzymatic living systems are feasible or not is open to theoretical and experimental investigation. But the ***chemoton theory*** (as it is now called) by no means excludes enzymes from its framework: it incorporates them logically and historically in a cardinal way, as we shall see shortly.

Cycle stoichiometry deserves special mention. Stoichiometry is the oldest exact branch of chemistry, and so it may come as a surprise that in the order to characterize chemical cycles properly it had to be developed in a special way. The main reason is that cycles act as catalysts, and catalysts cancel out from the overall balance equations of stoichiometry. Gánti realized that the problem could not be solved without the introduction of the 'turning number', appropriately displayed in the cyclic process sign that he introduced to replace the equality sign in the familiar mass-balance equations. Although it is true that the kinetic characterization is feasible using the traditional differential equations of chemical kinetics, the equations are non-linear in such a way that only numerical solutions are possible. The cyclic process sign combines stoichiometry with a dynamical element in a shrewd way.

Also historically, stoichiometry is not unrelated to the basics of biology. Mendel's revolutionary genetic paradigm is very stoichiometric in nature: if different heritable factors are combined in fixed amounts, certain qualities are obtained. Replace 'heritable factors' with atoms, and one has the stoichiometric description of molecules.

The later development of chemoton theory saw many revised and foreign editions of *The Principle*, together with the publication of many papers and some other books, most notably *Contra Crick, or the Essence of Life* (in Hungarian, 1989), parts of which are included in the present volume. There is one crucial development which should still be considered in this Preface, namely 'priority on the RNA world hypothesis'. Biologists credit this phrase and idea to Walter Gilbert's influential *News and Views* item in *Nature* in 1986. In a Hungarian specialist journal (*Biológia*, with English abstracts) in 1979 Gánti describes the same idea (but not the phrase) in more detail and in a manner much better integrated with other problems of the origin of life. He asks how the basic non-enzymatic units of life could have acquired the capacity of enzymatically controlled metabolism. Based on preliminary ideas promulgated in 1968 (by Crick and Orgel) and in 1972 (by White), he boldly draws the picture of metabolizing reproducing chemical systems where the reactions are catalysed by enzymatic RNA molecules (now called ribozymes). The enzymatic RNAs would have been replicated as well in these ancient, but already evolved, chemotons. The genetic code and translation could have come later. In 1983 (shortly after the discovery in the United States of ribozymes acting in modern organisms) Gánti described in the same Hungarian journal how ribozymes could have been assembled in a way guided by the substrates already present. The insight related to the RNA world alone would have deserved worldwide attention.

But why did the Anglo-Saxon world miss these results? The obvious answer is that they were not published in internationally known journals. Why not? There are a number of reasons. Gánti seems to have chosen a bad publication strategy. He has always tried to promote the *grand scheme* first, and to derive specific points from that. Now, the more revolutionary an idea is, the more difficult it is to sell it, unless it focuses on one timely and specific aspect. The second reason is that Gánti has not been well funded in Hungary, to put it mildly. He has been almost completely denied the possibility of attending meetings. It is true that his English (partly as a consequence of that) is not very good, but he has been a marvellous speaker in Hungarian and an acceptable one in English. More opportunity could have helped.

The aim of this volume is to compensate for outrageous fortune as much as it is possible today. Hopefully, the thoughts of Gánti, including his grand theme, may now become better known in the Anglo-Saxon world. It is my pleasure to acknowledge and to pay back (to a minor extent) my intellectual debt to Professor Gánti by contributing to this English edition with comments and some editing. I am overjoyed to be have been complemented in this task by my dear friend and colleague James Griesemer from Davis, California. It is my conviction that 30 years after their first publication, Gánti's thoughts will still be extremely stimulating.

Eörs Szathmáry

I first met Eörs Szathmáry in the autumn of 1992. We were both new Fellows of the Wissenschaftskolleg zu Berlin (Institute for Advanced Study). I had come to Berlin expecting to turn an essay I had written, 'The informational gene and the substantial body', into a book. I had been rethinking my views on units of evolution since 1989 in light of my recent recognition that Weismann—originator of the doctrine of germ-plasm continuity and somatic discontinuity—was no Weismannian and thus that theories of evolutionary units claiming to be Weismannian, such as Richard Dawkins' replicator theory, needed reassessment. Eörs was working on his book, *The Major Transitions of Evolution*, with John Maynard Smith. Those were wonderful times, although the great achievement of my year in Berlin turned out to be a delay of 10 years in writing my own book while I sorted out these new ideas. Eörs' ideas, and his introduction to Gánti's work, led me to believe that more than fixing up Weismannism was needed to clarify my thinking. Several years later, Eörs invited me to Budapest's sister institute to the Wissenschaftskolleg zu Berlin, Collegium Budapest, to continue my quest. I owe to Eörs and to Gánti (whom I had the great fortune and pleasure to meet in Hungary) the very exciting, challenging, and frustrating struggle that I have had over the last decade to articulate a new conception of the units of evolution. At the heart of 'my' perspective is Gánti's chemoton model.

Three features of Gánti's model are of fundamental importance philosophically. First, it is a *chemical* model. The importance of introducing a seriously chemical way of thought into the philosophy of biology should not be underestimated. These days, molecular biology is prominent in the thinking of many philosophers of biology, but we know from the many and various critical reviews of molecular biology as a history of 'informational macromolecules' that this molecular biology sustains a curiously un-chemical philosophy. Gánti's work opened my eyes to the real possibility of a philosophical rapproachment of biology and chemistry far more sophisticated than the tired debate over whether biology is 'reducible' to chemical laws or not.

Second, Gánti's model is a *stoichiometric* model. The idea of cycle stoichiometry at once captures a fundamental feature of biological systems—that they are organized in cycles—and at the same time offers a way of understanding what it is to think chemically. In my own case, the chemoton model resonates because I had turned away from Dawkins' copy metaphor for replicators as an inadequate way of understanding units of heredity, development, and evolution. In its place, I put 'reproducers', entities which form genealogies by 'material overlap' of parts—what once were parts of parents become parts of offspring. While the *relations* between parents and offspring might be understood in terms of copy-similarity, the *process* of reproduction is fundamentally different from copying processes. Since Gánti's cycle stoichiometry tracks the flow of *matter* (not only of information) through chemical processes, the chemoton model seems well suited to the kind of materialist (or better, Aristotelian) basis of all our biological thinking.

Third, Gánti's chemoton model helped me break out of the dualistic thinking enforced by that grand triumvirate of dichotomies in modern biology: Weismann's germ/soma, Mendel's factor/character, and

Johannsen's genotype/phenotype. The simple chemoton has three constituent stoichiometrically coupled subsystems: an autocatalytic metabolism, a 'genetic' polymer, and a 'genetic' membrane. We have known since the polymath Charles Saunders Peirce that 'three-ness' is far more conceptually productive than 'two-ness'—the complexity afforded by having *three* interrelated subsystems rather than two polar opposites has helped lead me to a more nuanced view of the nature of the processes of inheritance and development by showing how these processes need *not* be treated as causally or logically autonomous (as in Weismannism's distinction of a developmental process running from genotype to phenotype and an inheritance process running from genotype in one generation to genotype in the next).

Indeed, I find myself turning frequently to the chemoton model these days as a touchstone, a heuristic model to keep my new way of thinking on course and to prevent backsliding to old ideas that cannot easily be eliminated. While it has been my pleasure to contribute to the reissue of Gánti's work in this volume, in partial repayment of intellectual debts to my two Hungarian friends, I think that the greatest pleasure will be in making Gánti's work available to a new generation of readers. I hope that they will be as astonished as I have been that a book conceived in 1968 can continue to be heuristically fruitful despite the vast changes of chemical, molecular, and biological sciences since then.

James Griesemer

Organization of the book

This book is organized into five chapters. The first is a new essay by Professor Gánti, 'Levels of life and death', which introduces the reader to some of the concepts central to his main argument as well as illustrating how the core problem of the nature of the living state applies at many levels of life.

The second chapter, 'The nature of life', is a revised version of the second part ('Solutions') of Gánti's book *Contra Crick, or The Essence of Life*, published in Hungarian in 1989. Responding to Crick's 'panspermia' hypothesis in his book *Life Itself: Its Origin and Nature* (Simon and Schuster, New York, 1981), which attributes the chemical origin of life on Earth to innoculations of organic molecules from space, Gánti offers a set of reflections on the parameters of the problems to be solved in both origins of life research and, more broadly, in the search for principles governing the living state in general.

While it may well be true that life on Earth began by innoculation from space, the problem of finding general principles of the living state and the related problem of the chemical conditions for the origins of the living state are not solved by pointing to the *place* of origin. Gánti's meditations help to reorganize the problems in terms of his chemical way of thought. This is useful in light of the fact that the informational paradigm in molecular biology heralding from Crick's work with Watson as well as his development of the 'central dogma' of molecular genetics is something to be explained, not presupposed by a theory of the origin of life or the principles by which the living state is to be recognized. Thus, in this chapter, the reader is introduced to the chemoton, to cycle stoichiometry, and to a chemical way of thought that transcends whatever chemical model of the moment may be directing (or misdirecting) our attention to fundamental principles.

The third chapter, 'The unitary theory of life', comprises the majority of the much revised 6th edition (1987) of Gánti's book *The Principle of Life* (published in Hungarian in 1971). We owe a debt of gratitude to L. Vekerdi, who translated Gánti's *Principle* into English for the first time (as well as to Erzsébet Czárán for translating *Contra Crick* and Viktor Müller for translating the Introduction into English). In this chapter, Gánti develops his theory of the chemoton in accessible language and without all the technical details of chemical kinetics. Central to this is an account of 'life criteria' which builds as the reflections in chapter 2. The life criteria serve to articulate a basic philosophy of units of life which encompasses everything that philosophers have discussed under the restricted heading of 'units of selection'. He then extends and applies the theory of these fundamental units to considerations of conventional ways of organizing discussion of life principles, such as genetics, chemical synthesis, and the requirements of what he calls 'exact theoretical biology' generally.

Chapters 4 and 5 are essays by Eörs Szathmáry and James Griesemer on the biological and philosophical significance respectively of Gánti's work. In these essays we try to indicate not only how Gánti's work has proved significant to us personally, but why we think it has continuing relevance and heuristic power for theoretical biology. Finally, we include comments by each of us on Gánti's contributions throughout the book, bringing his work into relation with current literature in biology and philosophy. Comments by Eörs Szathmáry are identified by the prefix S and those by James Griesemer by the prefix G.

Eörs Szathmáry
James Griesemer

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