HISTORICAL PERSPECTIVE: THE PROBLEM OF THE ORIGIN OF LIFE IN THE CONTEXT OF DEVELOPMENTS IN BIOLOGY

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Abstract. The structure of the history of scientific ideas on the origin of life, after Darwin's theory of evolution brought the problem into focus, is discussed. 19th-century theories in the mainstream of historical development already included some notion of chemical evolution. These theories were limited, however, by their reliance on a protoplasmic view of life, according to which the protoplasmic substance combines all vital properties.

It was only when this holistic concept of protoplasm was abandoned that a clear distinction between different vital functions such as metabolism and replication was made. This led to two schools of thought in the origin of life field, one inspired by biochemistry and one by genetics.

Oparin's theory, which was rooted in the metabolic traditions of biochemistry, provided a model which has had a lasting impact in methodological terms and which helped to transform the field from a largely theoretical one to an area of active research. Genetically based theories, on the other hand, had a delayed impact in this respect, because of long-lasting uncertainty regarding the structural basis of gene function.

1. Introduction

Conceptual developments in the field of the origin of life have been characterised by a rich interplay between philosophical assumptions regarding the nature of life, methodological issues concerning the investigation and explanation of vital behaviour and theoretical developments in the biological sciences. My aim here is to survey the main features of these interactions after 1860, not to present a detailed history of the subject*.

Figure 1 summarises the principal phases in the history of ideas on the origin of life on earth. Before the 1860s, the question was primarily of philosophical and religious interest and only exercised the minds of practising scientists in an incidental manner. This situation changed radically when Darwin's theory of evolution implicitly raised the question of life's beginnings within an historical perspective of life on earth. The main classes of 19th-century theories on the origin of life that were proposed as a result will be discussed briefly, with emphasis on those that were inspired directly by evolutionary thinking. It will be argued that these latter theories, although in the mainstream of historical development, were limited by the protoplasmic theory of life on which they were based.

* The full historical and philosophical study from which this account has been distilled was presented in a PhD thesis (H. Kamminga, 1980, *Studies in The History of Ideas on the Origin of Life, from 1860*, PhD thesis, University of London).

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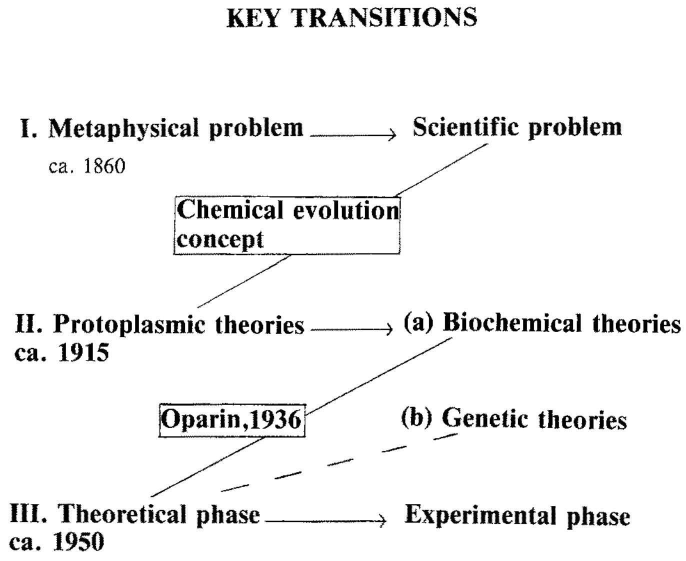

Fig. 1. Key transitions in the history of ideas on the origin of life, as discussed in the text.

The next important step was the formulation of theories founded on biochemistry and genetics, respectively, when these sciences began to flourish in the early decades of the 20th century. A major landmark during this phase was the publication in 1936 of Oparin's classic theory of the origin of life. As will be shown, Oparin's theory, with its strong roots in biochemistry, laid the foundations for modern approaches to the question, including some of the experimental approaches that have characterised the field since the 1950s. Theories based strictly on a genetic interpretation of life had a somewhat later impact on experimental work relating to the problem, for reasons that will be discussed.

2. The Impact of Darwin

The problem situation in the 1860s was created by the conjunction of Darwin's theory of evolution and Pasteur's work on spontaneous generation. Darwin's *On the Origin of Species* was published in 1859, causing much controversy and excitement. Here was a theory which explained the apparent purposiveness of living organisms in terms of purely natural causes, without appeal to divine intervention, vital forces or teleological concepts. It introduced a new perspective on the diversity of life and focussed attention on life as a historical phenomenon. There was an omission in the theory, however, in so far as it demanded some starting point, some type of primordial cell from which all extant forms of life had ultimately descended. In the *Origin of Species* Darwin cautiously refrained from offering an explanation of the initial generation of the ultimate ancestor, but his work encouraged a search for a naturalistic explana-

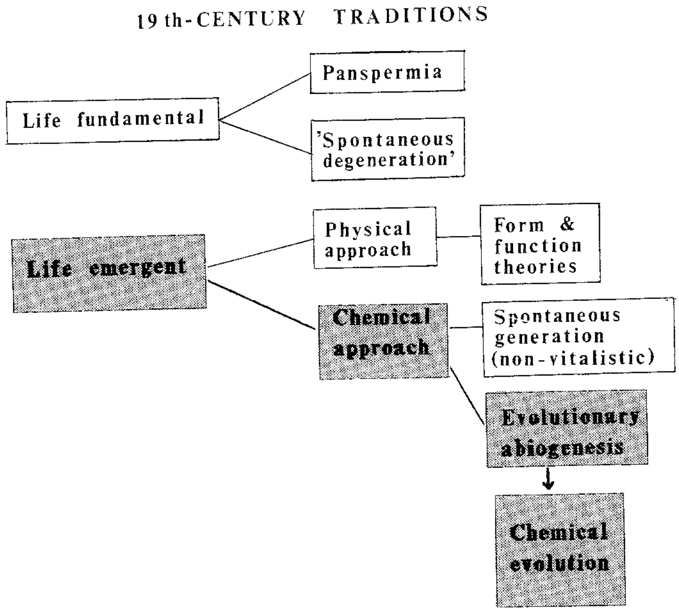

Fig. 2. Nineteenth-century traditions in the field of the origin of life (post-1860). The shaded boxes represent the dominant tradition.

tion of this question*. Among the many biologists who adopted the Darwinian perspective, the problem of the origin of life became a matter of acute interest.

By coincidence, it was at about the same time that explanations of life's origins in terms of spontaneous generation were firmly ruled out of court. Pasteur's famous experiments, which he began in 1860, suggested that even the simplest known organisms, i.e. bacteria, could not arise suddenly from non-living matter, independently of any parent. So how could life have come into being on a lifeless earth? This dilemma gave rise to a considerable literature on the origin of life in the remainder of the 19th century. It is a period of interest, because it was characterised by rival theories that differed strongly with respect to fundamental assumptions regarding the nature of life. Approaches to the problem were being worked out, with varying degrees of success in terms of lasting impact.

3. Nineteenth-century Traditions

As set out in Figure 2, post-1860 theories on the origin of life on earth fall into two main categories: those based on the assumption that life is an emergent feature of nature and those founded on the view that life is a fundamental feature of the universe. According to theories in the latter category, life was coeval with the

* Darwin himself discussed the question of the origin of life only in private correspondence and even then only rarely. The oft-quoted 'warm little pond' passage from his 1871 letter to Joseph Hooker is the prime example (reproduced in Calvin, 1969).

universe and the transition from non-living to living matter was held to be impossible in principle. Pasteur's results were interpreted literally: life was necessarily antecedent to life.

3.1. Panspermia

In this category we encounter 19th-century versions of the theory of panspermia, according to which organisms as we know them had always lived somewhere in the universe and had reached the earth from space when geological conditions were ripe for life. Both the universe and living organisms had existed for eternity on this view; different planets were simply seeded at different times, depending on local conditions. Life as such, then, had no origin and most proponents of panspermia were primarily concerned with proposing mechanisms for the inter-planetary transfer of viable germs.

These theories gained considerable popularity in the 19th century and are associated with a number of illustrious physicists and chemists, for example Kelvin, Helmholtz and Arrhenius (see Kamminga, 1982, for an assessment of their theories). Among biologists, however, theories of panspermia based on the idea of the eternity of life did not gain a firm foothold, because they erected an impassable barrier between the living and the non-living. This barrier was felt to have serious methodological implications for the biological sciences as it appeared to go against the dominant anti-vitalist trend in biology in the second half of the 19th century.

3.2. Spontaneous degeneration

There was a second class of rather curious theories based on the principle that life is a fundamental property of nature, according to which life actually predated the inorganic world. On this view, the inorganic domain represents the products of excretion and decay of organisms. Extant organisms on earth were, in effect, seen as the vital remains of a dying planet. This type of theory required a radical redefinition of the concept of life, which was given in terms of molecular motion. Originally, the cosmos itself and the planets, when they were still whirling nebulae, had been alive. Life here was characterised as a state of motion that was highly unstable and disordered, non-life as a stable, ordered state (see, for example, Fechner, 1873).

It was postulated in addition that there is a natural tendency towards stability in the universe. This underlying principle was in direct contradiction with the second law of thermodynamics and the triumphs of thermodynamics eclipsed the principle of the natural tendency towards stability as well as theories of the origin of life based upon it. These theories also offered a rather bleak prospect for the future: eventually all life in the universe would be extinguished purely by virtue of the natural transition from life to death. This implication was not congenial to evolutionary biologists; nor did it fit comfortably into the more general 19th-century ethos of progress.

3.3. Physical forces and morphology

Turning now to theories based on the assumption that life is an emergent feature of the universe, we distinguish two positions with respect to the question of what makes life into what it is. There were those who attached most importance to the physical form and functions of organisms, rather than their chemical make-up. On the other hand, there were those who characterised life in chemical terms and held that the structure-function relationships of living organisms are the outcome of the inherent properties of complex carbon compounds.

In the physical category were theories in which supposedly fundamental forces were proposed as the determinants of biological form and the functions that maintain it. Depending on the author, the physical basis of life was to be explained in terms of osmosis, surface tension, ionising forces, radioactivity and so on. However, ignoring the chemistry of life as it is generally understood begged the question. If osmosis, say, is both necessary and sufficient for life, why is it that this force has not generated forms of life based on a different chemistry as well as carbon-based life? If, on the other hand, the force is necessary but not sufficient, then the explanation is incomplete. Some authors tried to avoid this difficulty by attributing vitality to the entire domain in which the force of choice operates, i.e. the cosmos as a whole. But stretching the concept of life does not automatically provide us with an explanation of the origin of living things as they are conventionally defined. In the face of such problems, these theories failed to gain wide or lasting influence.

3.4. Spontaneous generation revisited

Among scientists who did take account of the chemical constitution of living organisms, there were a number who continued to look for instances of sudden spontaneous generation. They denied the validity of Pasteur's conclusions and tried out various conditions under which spontaneous generation supposedly occurred. The ensuing debates have been well documented by Farley (1977), who discusses the position of Pasteur's opponents with considerably sympathy. What should be pointed out, however, is the basic asymmetry between the explanatory strategies of Pasteur and those of his opponents.

Pasteur showed that careful elimination of microbial contamination prevents the growth of bacteria in organic infusions. Especially after the discovery of bacterial spores in the early 1870s, and the design of sterilisation methods which prevented their germination, Pasteur and his followers could explain and predict the presence or absence of bacterial growth in infusions in a systematic manner. His opponents, however, had no systematic, independent critera by which to explain the presence or absence of microbial growth under different conditions, or at different times under similar conditions. Unlike those who accepted the validity of Pasteur's conclusions, persistent advocates of spontaneous generation showed little concern about the lack of an explanatory basis for their demonstrations. Their position was a minority one, in terms of the impact it had on thinking about the origin of life on earth in the post-1860 period.

3.5. Evolutionary abiogenesis

Most popular among biologists were theories that were firmly rooted in the Darwinian tradition. From the 1860s ontwards many attempts were made to account for a natural transition from non-living to living matter, not by sudden spontaneous generation, but by a prolonged series of chemical transformations under the special, if unspecified, conditions of the early earth. In general terms, transformations from inorganic to organic matter and then to proteins and primitive living organisms were attributed to the properties of carbon compounds. This type of theory was based on a materialistic view of life and a unified view of nature: there were no impassable barriers in nature. The form of explanation, in terms of natural, non-purposive causes acting over prolonged periods, was directly inspired by Darwin's work.

These theories of evolutionary abiogenesis were not based on a denial of Pasteur's refutation of spontaneous generation in its traditional sense. Rather, they questioned whether this refutation was relevant to the question of the origin of extremely simple forms of life by a gradual increase in complexity of carbon compounds, under the special conditions of the earth in the long distant past. The idea that quite complex organisms might appear *de novo* over a matter of hours, days or weeks was unnecessary to those who adopted an evolutionary approach to the question of the origin of life.

Among the many authors who treated the problem in these terms were Ernst Haeckel, Thomas Huxley, Carl Nägeli, John Tyndall and August Weismann. Haeckel, who started writing on the subject in the 1860s, presented a popular account of the approach and its philosophical context in his book *The Riddle of the Universe* (Haeckel, 1900).

Eventually, theories of evolutionary abiogenesis came to include more or less precise notions of chemical evolution. It was the renowned physiological chemist Eduard Pflüger who first made a serious attempt to specify the mechanisms whereby certain constituents of organisms might have been formed and stipulated the conditions under which these processes would have taken place.

According to Pflüger (1875), live protoplasm is characterised by the presence of cyanogen groups and cyanogen compounds are easily formed under the hot conditions then believed to have prevailed on the primitive earth. He described the type of reactions which would have given rise to cyanogen compounds under these conditions and speculated how these might have gained in complexity by polymerisation reactions to form the first protoplasm. Although Pflüger's cyanogen theory was abandoned with advances in biochemistry, it was with this theory that the concept of chemical evolution was born. The term 'chemical evolution', incidentally, was used explicitly by the biochemist Benjamin Moore in his book *The Nature and Origin of Life* (1913).

These 19th-century theories of evolutionary abiogenesis suffered limitations because of their foundation on a protoplasmic theory of life. All vital behaviour was postulated to be the outcome of the properties of protoplasm and to require the integrity of protoplasm. In other words, protoplasm was regarded as a single, albeit highly complex, substance and the origin of life was equated with the origin of protoplasm in its primitive, undifferentiated form. In the absence of a more precise characterisation, protoplasm was thought to consist of protein and the problem of protein structure was believed to hold the key to the question of the nature and origin of life.

The protoplasmic view of life gradually lost its usefulness. Cytological studies using new staining techniques began to show up the cell substance as highly heterogeneous and revealed the relative autonomy of the cell nucleus during cell division. In addition, biochemical studies began to reveal the chemical complexity of the living cell and to undermine the idea that protoplasm as a whole is required for such vital processes as fermentation and metabolism. In particular, the isolation of different enzymes and the study of specific reactions catalysed by particular enzymes suggested that vital activity required the participation of a large number of individual proteins and other organic molecules.

Hence, early this century, the view that vital processes are the outcome of the properties of a single substance became untenable and the question of the origin of life had to be reformulated. What had to be explained was the origin of systems composed of many different molecules acting in coordination to express different vital functions. Not surprisingly, most biochemists at the time chose to avoid this complex question.

4. Oparin's Model

Thus an impasse was reached and for many years little progress of lasting influence was made on the problem of the origin of life. This situation changed with the publication of Oparin's classic book *The Origin of Life* in 1936. The publication of the English translation in 1938 gave the work international attention.

Oparin's theory gave a fresh impetus to the field in several respects. First, Oparin gave substance to the notion of chemical evolution by his very detailed consideration of the interactions between the environment and organic matter at successive stages of development. Secondly, he was the first in the field to draw extensively on independent evidence from a wide range of scientific disciplines to establish the plausibility of his model. Thirdly, he took into account the biochemical properties of living things in an original and fruitful way. And lastly, he presented a model that was partially testable, at least with respect to those stages which could be described in detail. Hence the importance of his work in stimulating an experimental approach to the problem.

Before discussing the main features of Oparin's theory, it is worth mentioning that Oparin's earlier booklet on the subject (Oparin, 1924) did not have a similar impact on future developments. Although the general plan of this work is similar to that of the 1936 book, it lacks the rich chemical and biochemical detail which gave the later theory its concrete content and heuristic value. Nor, being published in Russian only, did the booklet gain an international readership.

In addition, certain key concepts are missing in the early work, notably that of a reducing atmosphere in prebiotic times. This idea was proposed by Haldance (1929) and later independently by Oparin. Haldane's brief paper contained several interest-

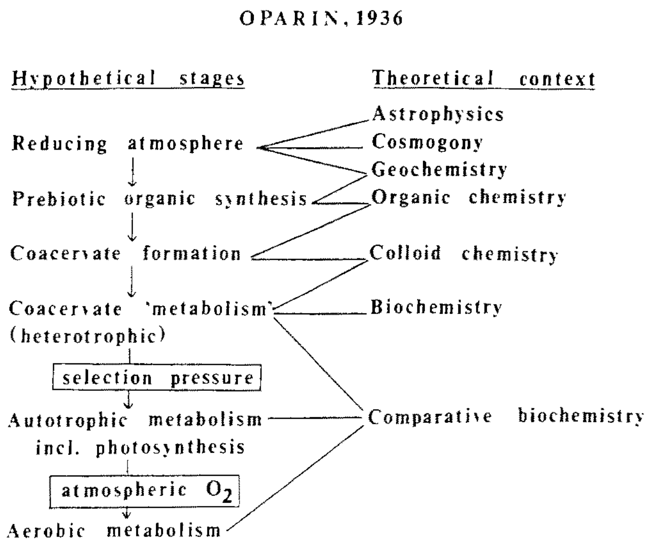

Fig. 3. Hypothetical stages in the development of matter on the prebiotic earth and during the earliest biological stages, as proposed by Oparin in 1936 (see Oparin, 1938). Supporting evidence was derived from the fields listed on the right.

ing ideas, but it also lacked sufficient detail to stimulate further developments at the time.

Turning now to Oparin's main work of 1936, the stages in the development of life on earth which he proposed are summarised in Figure 3, together with the fields of science from which he obtained supporting evidence. Geochemical studies, chemical and mineralogical analysis of meteorites and spectroscopic studies of stars, comets and planets suggested that the prebiotic earth had a reducing atmosphere. Under reducing conditions organic compounds would have formed readily as the earth cooled and then undergone progressive transformations according to reaction mechanisms well known in organic chemistry.

As the organic molecules became more complex, colloidal reactions came into play and organic matter became concentrated locally in the form of individual colloidal bodies called coacervates. Oparin's consideration of colloidal processes, although not in itself without precedence in the field, derived its concrete basis from investigations of the phenomenon of coacervation. The most striking feature of the coacervates was their capacity to absorb and assimilate organic matter from the aqueous environment and utilise this material in reactions leading to their growth and development, a feature strongly reminiscent of metabolism.

In general terms, therefore, the property of metabolism provided Oparin with a possible link between prevital coacervate bodies and primitive living organisms. Strongly within the biochemical traditions of his time, Oparin adopted the view that metabolism consists of a series of coupled oxidations and reductions involving intermolecular hydrogen transfer. This idea of the fundamental unity of metabolism provided him with the focus of his theory. At the same time, the diversity of metabolic patterns among extant organisms provided him with comparative data on which to base a possible sequence for the evolution of the earliest organisms, from anaerobic heterotrophs, to photo- and chemoautotrophs, to aerobic organisms. His choice of metabolism as the fundamental characteristic of living systems and his comparative approach to the early evolution of life constituted important innovations.

The comparative biochemical approach, which is now so well established in the field, was introduced in this context by Oparin. Moreover, his explanatory scheme demands consistency between theories about the atmosphere, hydrosphere and lithosphere and theories about chemical and biochemical transformations at each stage of development. This feature of his theory set methodological standards for all future work in the field and, as such, Oparin's work will continue to stand as an exemplar.

It is also worth stressing the open character of the theory. Further details, for example those relating to new findings in biochemistry and molecular biology, could be built into its structure without trouble. In fact, Oparin himself continued to extend and modify the theory for the rest of his life. Moreover, the theory's modular construction gives it an in-built flexibility. The model was useful even to those who had reservations about some of the stages described by Oparin. This very flexibility has encouraged a pluralistic approach to the problem of the origin of life, especially now that experimental work in the field has advanced well beyond exploration of the earliest stages of prebiotic chemistry.

5. Genes and Living Molecules

What Oparin did not consider in the 1936 book was any genetic basis of evolution, although he certainly did not ignore this subject in his later writings (see, for example, Oparin, 1957). Others before him, however, had formulated theories of the origin of life based on gene function. These theories came from within genetics, a science which developed largely independently from biochemistry until the rise of molecular biology.

The development of genetics, even during the first two decades of this century, was accompanied by attempts to explain the origin of life in terms of the origin of the gene. This approach was based on the assumption that, in modern terms, gene replication and gene expression are the fundamental features of life, over and above other vital functions such as metabolism. Like the biochemical approach, these theories represented a departure from the protoplasmic view of life, but they went further in reducing the question of the origin of life by equating it with the origin of 'living molecules' with the properties of genes (see Ravin, 1977, for a review of the early history of this approach).

These gene theories of the origin of life were modified with developments in genetics (see Table I), but here only their common characteristics will be considered (for

TABLE I
The 'living molecule' tradition

Minimum living system	Theoretical context	Principal proponents
Chromatin particle	Cytology	E. A. Minchin (ca. 1910)
Auto + heterocatalytic enzyme	Classical genetics	L. T. Troland (ca. 1915)
Auto + heterocatalytic molecule ('protogene')	(a) Chromosome genetics	H. J. Muller (1920s onwards)
	(b) Biochemical genetics (one gene/one enzyme theory)	G. W. Beadle (1940s onwards)
Self-replicating informational polymer	Molecular genetics	L. E. Orgel (1960s onwards)

'Naked gene' theories of the origin of life have traditionally characterised the first living entities as single molecules capable of both replication and expression. The nature of the original living molecule was redefined with developments in genetic theory (see Kamminga, 1986).

further details, see Kamminga, 1986). The gene was regarded as the fundamental unit of life and the nature of the gene was sought in terms of molecules with the dual function of self-replication and control over the formation of secondary products. It was assumed that these 'living molecules' were complex and that the original formation of a gene had been a chance event of low probability. This reliance on a lucky accident limited the heuristic value of these theories, as no testable models could be presented.

The main problem here was the lack of chemical precision in the characterisation of genes, which persisted until the molecular structure of DNA was deciphered in 1953. With the DNA double helix, a mechanism for self-replication was formulated, a template model for protein synthesis became dominant and there was a shift to informational concepts. Especially since the unravelling of the genetic code in the 1960s, molecular biologists have translated the older gene theories of the origin of life into structural terms. Attempts to explain the formation on the prebiotic earth of polynucleotides that were functional precursors of the genetic materials RNA and DNA have since also given rise to active experimentation.

Hence, it was only in the 1960s that gene theories of the origin of life could be given a concrete chemical content. Given the rich chemical and biochemical content of Oparin's 1936 theory, it is not so surprising that he showed little interest in the purely formal genetic theories of life's origins that were current at the time.

6. Conclusion

Basic philosophical approaches to the question of the origin of life on earth were formulated in the 19th century. It was the input from the biological sciences, however, which gave substance to these theories and in this respect the impact of evolutionary theory, biochemistry and molecular biology have been of prime significance. The history of the field suggests that it is the interplay of different traditions that has led to an enrichment of the problem. We have come a long way from the early theories of evolutionary abiogenesis and it is likely that this process will continue with further developments in our understanding of living organisms.

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