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FROM INANIMATE MATTER

TO LIVING SYSTEMS

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INTRODUCTION

The history of science reveals that many of the most interesting advances emerged unexpectedly. They resulted from experiments designed to illuminate other phenomena. The results were thus the consequence of fundamental forces rather than of planning. Similarly, the origin and evolution of life on this planet appears to have occurred as inevitable manifestations of inanimate matter of the appropriate kind. Such developments were not the result of conscious planning. It is therefore logical that understanding of the attainments in such research have been, at each stage, well beyond what they were at first recognized to be. The consequences increasingly endorse the investigative approach that consists of attempting to retrace the steps in evolution itself.

METHODS OF STUDY

Information about the origin of life can be obtained in several ways. Microfossils (Schopf 1978) can give us direct awareness of morphology, and indirect understanding of geologic age and the original environment of the earliest cells. Since the fossils represent lithified matter and are static, they cannot be studied for chemical composition of the prefossilized organisms, nor for their biochemical capabilities (Fox 1980a).

Back-extrapolation of biosystematics of organisms can lead to suggestions of the locale of origin of protocells. Indeed, in an early but little-known monograph, Copeland (1936) suggested on that basis that life began in the waters of hot springs. This

idea is comparable to suggestions from knowledge from the Galapagos Rift (Waldrop 1980, 1980a). These concepts and a number of others, including those from experiments (Fox and Dose 1977), are consistent with the newer idea, based on thermodynamics (Fox and Dose 1977), that life began in some locale more limited than the traditional one of the open ocean.

Also consistent with the newer emphasis is a third type of inference, that derived from biochemical, rather than biological, systematics. Such studies, for example, have suggested early methanogenic bacteria (Woese 1979). In reality, we have no truly primitive living organisms available for biochemical comparisons. We have only modern descendants of organisms we infer to be primitive, and by which we mean relatively unevolved. If our inferences are correct, we learn about the type of organism the primitive cell was but, again, we do not learn from comparative biochemistry how the first cell came into existence.

The approach to that question most used by the now many theoretically interested scientists is the Aristotelean one, namely the inferring of origins from knowledge at hand, most expertly by Eigen and Schuster (1978) and by Crick et al. (1977). The applied theoretical knowledge at hand for such purpose has been largely that obtained by analysis of the modern cell.

Analytical knowledge of the modern cell can contribute, in at least two ways, to experiments designed for understanding of how life began. Such knowledge provides clues about what to experiment with as primordial cellular precursors in a

geological-type locale in the laboratory. It also provides standards against which to judge progress of experiments designed to simulate the spontaneous generation of the first cells. It does not, however, provide us with a mechanism that looks forward from the preliving side of the first cell.

The only known method for inferring how life began is that of attempting to simulate in the laboratory the assembly of precellular polymers to protocells under geologically relevant conditions. This requires empirical experiments and selection of those products that are most fit for the environment. In other words, experiments needed to be performed by essentially the same mechanisms in which evolution occurred on the developing Earth. Despite obvious difficulties, research in studies of origins do have the one unique advantage that we know the end products we seek before we begin the studies.

Such simulation experiments of the last twenty years have revealed a number of special processes and phenomena; these could not have been designated as essential steps in the sequence from analytical studies of modern living or fossil organisms. The total research has required more than 200 man-years of investigation in our laboratory plus uncounted effort in other laboratories. Just the main overviews are being discussed here. The extensive supporting details are found through the references, including that which was first presented in 1973 at the meeting of National Association of Biology Teachers (Fox 1974).

STATE OF THE ART

The flowsheet of Fig. 1 is the comprehensive sequence, derived from experiments, that models evolution from primordial matter to a protoreproductive protocell and beyond. Fig. 1 describes the origins of a protocell composed of ordered macromolecules and having numerous protobiological activities. The activities are of an enzymelike and protobehavioral kind (Fox and Nakashima 1980).

The performance of experiments in this area have been motivated especially by A. I. Oparin, who was a pioneer theorist in the origin of life from inanimate matter*. In addition to the ideas in his many books (e.g. 1957, 1968), he and his associates performed numerous experiments of one kind. These were experiments with coacervate droplets, which were used as models for the first cells on Earth. Oparin and associates made coacervate droplets from structural and enzymic polymers obtained from modern organisms. The basic question, however, is how primitive living structures and functions could have arisen from purely geochemical matter on the Earth more than three billion years ago (Dickerson 1978, Fox 1978a). Because of the modern materials used by Oparin, the coacervate droplets could not answer these questions, although they did contribute to some understanding of principles of cellular construction and behavior (Fox 1976, Fox and Nakashima 1980).

Basic questions of the protocell are answered by experiments

*The evidence for ordered and catalytically active molecules in the first cells was discussed by the author with A. I. Oparin in June 1979, ten months before death of the latter at the age of 86.

with the proteinoid microspheres (Florkin 1975, Fox 1978b). These remarkable (Lehninger 1975) bodies (Fig. 2) arise from copolyamino acids which were in turn formed by heating of sets of amino acids under geothermal conditions (Rohlfing 1976). The mixture must contain a minor proportion of trifunctional amino acid such as aspartic acid or glutamic acid (Fox and Dose 1977). The amino acids, aspartic acid and glutamic acid, have been found in virtually all extraterrestrial and terrestrial sources of amino acids examined and in the products of simulation experiments (Fox 1973a). The polymerization reactions occur over a wide range of ratios of amino acids, at 65°C or less.

The crucial finding from the copolymerization experiments is that the varied amino acids do not polymerize randomly; instead, they have much self-instructing ability. The sequences formed are highly specific (Table 1) and the polymers produced are of sharply limited heterogeneity (Fig. 3). Such data, collected in a number of laboratories, are obtained in varied analytical ways.

The self-ordered polymers yield in turn ordered populations of cell-like structures (microspheres) by the simplest of interactions - contact with water. These microspheres are almost uniform (Fig. 2). As expected theoretically, they are found by experiments to possess the properties that their polymers were independently shown to display (Fox 1980b), plus emergent properties as well (Fox and Nakashima 1980, Fox 1980a). They offer much opportunity for comprehending the early evolution of biochemical pathways (Hsu and Fox 1976, Fox 1980a).

Thus, the protocells were already remarkably well advanced in metabolic and other protoliving properties (Fox 1980b). This understanding, as explained, could not have been obtained from the conventional coacervate droplets. Also remarkable for some viewers of the scene is that these microspheres arose with no nucleic acids in their history.

The experiments were in one sense more like a sequence of dominoes than a staircase. The result of each experiment provided the matrix and yielded the information that led to the next experiment. This is the music from proceeding in a synthetic, or constructionistic, direction; it cannot be produced by analysis in the direction of disassembly.

The thick vertical line (Fig. 1) indicates the stage to which the laboratory experiments have quite fully carried the simulation of early evolution. Steps 1 and 2 involve inanimate matter preceding protocells. Step 3 results from interactions of a special kind of inanimate matter, thermal copolyamino acids (proteinoids). Of special significance is that the amino acids order themselves during their copolymerization into the macromolecular proteinoids in step 2.

The reactions are mechanistically complex, but operationally simple. They could have easily occurred spontaneously on the primitive Earth. They are fast and rugged. By estimate, tens of thousands of high school and undergraduate college students have repeated key experiments; the bibliography lists four of the sets of directions (Vegotsky 1972, Rhodes et al. 1975, Rauchfuss 1977, Fox and Dose 1977).

The significance of the sequence in Fig. 1 is of course dependent upon whether one accepts the implication of these experiments that catalytically active, ordered protocells having membranes and initial reproductivity were the beginning of cellular evolution (e.g. Fox 1959, cf. Lederberg 1959, cf. Calvin 1969, Black 1973, Dillon 1978). The alternative is the old, and still barren, idea of DNA-first, for which no experimental demonstration has materialized (Florkin 1975, Dillon 1978).

The concept of proteinoid protocells-first permits the origin of the genetic mechanism and code as a later evolutionary development. The modelling of this development has been extended since the earlier paper in this journal (Fox 1974, Fox et al. 1974).

By repeating the experiments in microsphere formation one can fully appreciate the utter simplicity and ruggedness of the phenomena yielding huge populations of almost uniformly sized microparticles. Other experiments have shown these to provide microenvironments highly adaptable to further evolution.*

FROM PROTOCELL TO MODERN CELL

The overall sequence of Fig. 1 consists of two main parts. The first is the succession of conversions from primordial matter to an ordered, protometabolic, infrastructured protoreproductive (Fox et al. 1967, Ambrose and Easty 1970, Fox and Dose 1977) protocell, as defined by experiments performed under geologically relevant conditions. (The steps are those through

*Any other imaginable primordial sequence such as protein → nucleic acid → cell or nucleic acid → protein → cell would presumably not compete with a protocell-first route, and has not even been modelled in the laboratory.

amino acid sets, ordered proteinoids, and to protocells.) The second main part of the sequence consists of steps 4 and 5.

A few years ago, the simulated protocell was already sufficiently well described that the salient properties could be subtracted from those of the modern cell. The differences accordingly defined the gap from protocell to a modern cell. The inference that the protocell, as described by the experiments, had many metabolic activities (Fox 1980b) gives us a new view on the course of development in bridging the gap between protocell and the modern cell. We see that the protocells had a good start biochemically and physiologically. Moreover, recent experiments have indicated that proteinoid inhibitors of enzymes were formed at the same time as proto-enzymes; the protocell could thus have contained control mechanisms (Fox 1980a). The experiments in crossing the gap between protocell and the modern cell have been done mostly since the earlier paper in this journal (Fox 1974). These experiments have not completely closed the gap, but no insurmountable difficulties are foreseen.

One of the gaps is the conversion of solar energy to biologically useful biochemical energy. The conversion of solar energy to cellular energy has however been modelled in laboratory experiments by the action of white light on ADP and inorganic phosphate in nonaqueous solution containing a quinone. It begins to appear that the answer may be like that of Atkinson (1977) for modern cells; ATP concentration is small but is maintained far-from-equilibrium and is constantly being replenished as energy stores, e.g. glycogen, are released. The dynamic

cellular situation can exist because ATP is constantly bled off into a number of reactions to which it is coupled.

One of the most significant single awarenesses since 1973 (Fox 1974) is of the multiple activity of lysine-rich proteinoid. Lysine-rich proteinoids catalyze the formation of both internucleotide and peptide bonds in aqueous suspension containing ATP. The microspheres that form from (undersaturated) solutions of lysine-rich proteinoid and acidic proteinoid resist dissolution at pH values representing a primitive alkaline ocean (Fox and Yuyama 1963, Snyder and Fox 1975). These particles in suspension also catalyze the formation of internucleotide and peptide bonds (Fox et al. 1974). When artificially fossilized (Francis et al. 1978), they resemble "fossils" of algae made in the laboratory, or natural fossils (Fox 1980a).

Earlier, lysine-rich proteinoids of various compositions were shown to interact selectively with polymers of various ribonucleotides (Yuki and Fox 1969, Lacey et al. 1979). While this may or may not be an essential model of part of the genetic code and its origin, it does support the view that the origin of the code was stereochemical.

The manifold activities of various lysine-rich proteinoids do not mean that extensive time elapsed for such evolution. More likely, extra time was of value in permitting a number of natural experiments (Wald 1954).

We can now see that the sequence: (a) self-instructing

(nonrandom polymerization) of amino acids, (b) formation of lysine-rich proteinoids, and (c) assembly of lysine-rich and acidic proteinoids into microspheres contributed to the inanimate → animate link which for so long was missing from the picture of cosmic evolution from primordial matter to modern life, a conceptualization that has been developing since early in the century. The idea that astronomical and geological events were a prelude to biological evolution was stated by Oparin (1924).

Fig. 4 ramifies part of Fig. 1. A principal advantage of Fig. 4 is that it explains more fully how an initial proteinoid mechanism evolved into the modern mechanism of coded genetics utilizing nucleic acids.

The experiments yielding simple proteinoid microspheres and the subsequent structures, plus the numerous studies on disassembly and reassembly of modern organelles, have led to a definition of evolution enlarged from that of Darwin by constructionistic processes (Fox 1980b). Assembly processes in evolution can be thought of as vertical evolution (Fig. 1) whereas natural selection from a population of variants on any horizontal plane can be thought of as horizontal evolution.

"WHEN WILL WE SEE SYNTHETIC LIFE?"

A favorite question of journalists, beginning students, and others is some version of "When can we expect a living

organism to be produced in the laboratory?"

Such questions lack scientific focus because of difficulties related to defining life. Calvin said (1962) that a definition of life is a matter of "subjective arbitrariness". F. Jacob, in his book Logic of Life, said in 1974, "Biologists no longer - - - attempt to define it (life)."

Fig. 1 makes this clearer. The onset of life does not appear as a one-time phenomenon occurring out of the void. Part of the difficulty in defining life is that it arose step-by-step. The right steps, from our current point of view, plus the right intermediates had to emerge, each from its predecessor. It is in this context that the full significance of self-instructing (self-ordering) processes can be seen.

According to the stepwise emphasis, however, one cannot specify which stage was first alive. There were, instead, stages of aliveness (Asimov 1967). Recent examination of the overall findings nevertheless continues to emphasize the formation of a phase-separated protocell as a dramatic step (Fox 1960). This is increasingly so because several laboratories have learned, in the last fifteen years, that varied proteinoids possess a range of biological activities; each of these activities tends to be incorporated into cellular structures when proteinoid molecules aggregate into such structures. Such active protocells, let it again be emphasized, are still <u>not</u> modern cells. For example, they lack highly efficient phospholipid membranes, DNA, and the genetic coding mechanisms.

The dramatic nature of microsphere formation is the emergence from inanimate matter (of the right kind) of a cellular structure having already a primitive membrane that sets it off from the environment, the ability to participate in proliferation, and a number of (mostly weak) enzymelike activities (Fox 1980b). While the units arose on the Earth spontaneously, and could do so without nucleic acids, the origin had to occur in steps. The amino acids, then the proteinoid, and then the "protocells" had to emerge in an evolutionary sequence. A further dramatic step in the laboratory will have occurred when proteinoid microspheres are constructed so as to make enough of their own polyamino acid that daughter organisms result, in other words when organized structures convert amino acids to polymers which aggregate to form new "organisms". Even so, feeding will have been seen to be essential at all stages - whether the food was preformed proteinoid for proliferating protocells, or whether the food was free amino acids or digestible combinations of amino acids, as is the case for modern organisms.

As Kornberg (1976) pointed out, the original Watson-Crick formulation of DNA replication did not mention enzymes. It is especially the work of Kornberg (1979) that enumerates the many "replication proteins" that have been found to participate in DNA processes (cf. Dillon 1978). Since we now see that protocells did not require nucleic acids in their history, one can contemplate the possibility that a "synthetic protocell" had already been made in the laboratory - more than twenty years ago (Fox 1960, 1969).

SCIENTIFIC OBJECTIONS TO THE PROTEINOID THEORY

The presentation of a balanced view of understanding on any question benefits from an exposition of all alternative theories when that is possible. So far, however, there are no connected, experimentally modelled, alternatives to the proteinoid theory for the origin of a protoreproductive protocell. If, as is often stated by biologists, it be correct that a model for life's origin is either on the evolutionary track or not on it, the proteinoid theory may in the future, as in the present, be the only one. It is to date the only one that defines the span of evolutionary progression described in Figs. 1 and 4.

Another avenue for testing a balanced understanding is through criticism of the single theory itself. Such criticisms have been freely available for the proteinoid theory. Many of the criticisms and unfocussed comments have been answered (Fox 1973b, Florkin 1975, Fox 1976, Fox 1977, Fox and Dose 1977, Fox 1980a).

A stream of objections seems to be normal for an evolutionary theory. Darwin, for example, dealt with criticisms of the principle of natural selection in many of the passages in his Origins of Species. In addition, he included a thirty-page chapter (Chapter VII) titled Miscellaneous Objections to the Theory of Natural Selection. An assessment of his sensitivity, as well as the breadth of the objections, is illustrated by his comment that "it would be useless to discuss all of them, as many have been made by writers who have not taken the trouble to understand the subject " (Darwin, undated). In reaffirming his claim that the theory of evolution is more than simply

natural selection (a point which needs analytical restatement today) Darwin said, "Great is the power of steady misrepresentation."

The most common source of controversies in the entire problem of origins is that in which an armchair thinker argues, in essence, that the model of the primitive should have all of the qualities of, or each quality in as full measure as, the modern cell. In other words, this difficulty is an inability or unwillingness to recognize the evolutionary truism that that which is already here evolved from something simpler and more primitive. It fails to recognize that what is here is still evolving and incidentally cannot, strictly speaking, be primitive.

For the proteinoid theory specifically, one of the two mos common criticisms is the temperature necessary for polymerization of amino acids (Miller and Orgel 1974). Given enough time, the polymerization theoretically should occur at any terrestrial temperature (Rohlfing 1976); 65° has been demonstrated to be high enough in a period of two weeks without added catalysts (Rohlfing 1976). A requirement of highly special conditions (Gish 1972) is easily seen to be invented if one reads the literature. What is needed is a mixture of α-amino acids containing a minor proportion of trifunctional amino acid (aspartic acid, glutamic acid, or lysine) and any climatic conditions in which water is barely present or can evaporate,

and a few hours to several weeks of heat or warmth, respectively.

The main criticism of the proteinoid theory is of the self-ordering of amino acids which in turn permits the concept of proteinoid protocells-first. The self-ordered nonrandomness is an empirical fact easily confirmed in any biochemical laboratory (Dose and Rauchfuss 1972, Nakashima et al. 1977).

The DNA-first view, which relies on ordering of amino acids through an outside agent, DNA, has a logical initial appeal since instructions for the modern cell are lodged in the DNA. What is often not recognized is that those instructions are read into the modern genome by protein enzymes (polymerase), they are reproduced by protein enzymes (replicase), and are later read out by protein enzymes (transcriptase). Moreover, the members of each of these classes are, like other enzymes, specific (Lagerkvist 1980). The instructions for the overall modern mechanism may thus be said to require proteins (Dillon 1978), as well as nucleic acids.

Even were this not all true, the requirements for the primordial mode of molecular replication, or of system replication, need not have been the same as for the modern cell. We cannot defend a premise that the modern evolved from the modern.

When the primitive world evolved from a chemical one to a biochemical one, a main feature was that some bidirectional, reversible reactions were supplanted by unidirectional reactions

(Atkinson 1977). The biochemistry of the inheritance mechanism was undoubtedly subject to this evolution to unidirectionalism.

Resolution of the dilemma of the DNA-protein "chicken-egg" problem emerged from the finding that amino acids contain their own instructions for their own sequence. This new view is based on data from many laboratories. These self-instructing forces have proved to be powerful, as well as consistent with evolutionary tenets. Nothing as complex as the orchestration of incoding, replication, transcription, translation, etc. was essential at the outset. The simplicity of self-ordering of amino acids is the reason that experimental support of proteinoid protocells-first could be obtained, whereas the DNA-first idea remains as a fuzzy, unparticularized concept. Indeed, DNA coding has sometimes been regarded positively as an evolutionary development that overcame the restrictions of self-ordering set by proteinoid synthesis.

Proponents of DNA-first do not provide an explanation of how functional DNA arose, whereas demonstrated synthesis of internucleotide bonds by proteinoids (Jungck and Fox 1973) support the concept of DNA as a later product of evolution (Fox 1959).

CREATIONISM AND SCIENCE

Whereas biblical treatments of the appearance of various kinds of life ordinarily do not belong in a scientific paper, they belong in any paper read by teachers who are confronted with related questions from students, students who have not experienced

decades of mental set and who do not yet have exposure to the scientific findings.

Before beginning school, almost every child has asked "Where did I come from?" The answer usually provided to the child in this society is that life was created by God. He or she learns the biblical sequence of events in simple, flowing narrative. God thus created life in a succession of grass, trees, fowl, beasts, and cattle, followed by man.

At some grade in school, the growing student is presented with aspects of the natural explanation. The concept of evolution from lower to higher forms is introduced. Since about 1965, the evolutionary interpretation of how life evolved has been fortified by the developing information on how life first began from inanimate matter (Biological Sciences Curriculum 1963).

Some beginning students have become aware of yet another answer - that seeds of life arrived on Earth from some unspecified corner of the Universe. The explanation is widely regarded by scientists as mythological, but it does not invoke supernatural events. This proposal, also, fails to answer the basic questions of how life arose and what were the material precursors of life. The overall trend in thinking, however, has historically been toward a natural interpretation.

While virtually all scientists agree that the Bible contains valuable guidelines for personal conduct today, and much beautiful prose, very few see it as providing scientific, i.e. natural, answers to scientific questions such as the origin and evolution of life. The majority of scientists recognize that scientific

knowledge is subject either to repeatable experiments or to explaining how that knowledge conforms with other understanding gained by scientific processes. Few biblical assertions, on the other hand, can be tested.

Scientific criticisms of the theory of life's origin are used by creationists. When scientists disagree about the scientific answers on any aspect of evolution, or when the explanation is incomplete, the Ph.D. creationists then state, or imply, that the biblical answer is the only acceptable alternative. They attempt to justify a mixed context of biblicism and science by such means as referring to their intellectualisms as "scientific creationism".

That confusion between creationism and science can exist for students at all may be the price we are paying for our having deferred education in the history and methods of science for beginning students. The history of science is important to students at all levels because the lessons of that history reveal that all new scientific ideas had to survive a period of challenge. Those challenges activate the self-correcting mechanism to operate in science. The student needs to know the importance of self-correction in the scientific method and that all knowledge is subject to refinement. A true sense of the nature of scientific advance may be more important to the student, and to the citizen that he later becomes, than most of the memorizable facts (Welch 1972).

The aspects of evolution that Darwin recognized as most

needed to flesh out a theory of evolution were those of design and direction (Gillespie 1979). This is the kind of understanding that self-ordering principles are beginning to provide through interpretations of the demonstrated nonrandom sequences (Fox 1980b). These are also aspects of evolution most often attributed instead to divine guidance. As such they have received the strongest attack from creationists (who used to be called fundamentalists).

The fundamentalists' opposition to the teaching of evolution lapsed at the end of the third decade of this century. Only one antievolution bill was introduced in a state legislature in 1930-1963 (Wilhelm 1978). Often referred to now as creationists, fundamentalists began again in 1964 to attempt to influence the teaching of evolution. It is significant that it was in 1963 that the BSCS blue version on Molecules to Man (Biological Sciences Curriculum 1963) included, for the first time in high school texts, a discussion of the origin of life by natural causes, as suggested by experiments.

As an example of the differences between creationism and science, the former emphasizes a one-time making of life, because that's what the Bible says. The inferences from experiments designed on the action of natural processes indicate that life arose innumerable times, and it emerged in steps, not all at once. It is true, even so, that numerous scientists proceed on the initial premise that life arose once; it seems reasonable that some of them hold this view because it has long been part of established thinking (Gillespie 1979). Were such

an assumption correct, the emergence of life would have been a very chancy event, the result of statistically random processes. The experiments indicate, rather, nonrandom processes, but the assumption of random events is very deeply rooted and very widespread. If these roots are not religious, they are often held in place with all the strength of religious conviction. DNA-first and random synthesis are also linked concepts, in that each connotes an outside agent to direct, or select, the adapted form.

The natural processes are interpreted as having begun with microscopic cells. Evolution continued with unicellular forms for at least one-and-a-half billion years. At the time the Book of Genesis was committed to parchment, microscopes were unknown. So, too, was microscopic life unknown. We cannot expect, therefore, that the Bible would speak of a microscopic life that no one even knew existed at the time of writing of the Book of Genesis. As we proceed through other scientifically acquired knowledge of protobiology, we find other aspects that the most intelligent bibliophile of A.D. 1000 or earlier could not have even guessed at.

EPILOGUE AND SUMMARY

An answer to the question of the origin and evolution of life was narrated in the Book of Genesis many centuries ago. Since the early part of this century, the answer has been explained as an extrapolation of astronomical and geochemical processes. The essence of the answer to date is a proto-reproductive protocell of much biochemical and cytophysical

competence. The processes of its origin, molecular ordering, and its functions have been described. The scientific answer is incomplete and will benefit from further refinements, like other scientific theories. A crucial understanding is that of the nonrandomness of evolutionary processes at all stages (with perhaps a minor statistical component). In this way, evolution conflicts with statistical randomness; the latter is a favorite assumption of both scientific and creationistic critics of the proteinoid theory.

Nonrandomness has been extensively demonstrated by experiment, as well as by the classical process of self-organization. Also demonstrated is the more newly recognized possibility of lysine-rich proteinoid in protocellular synthesis of peptides.

A principal contribution of the proteinoid work to the understanding of general biology is to particularize the view that evolutionary direction is rooted in the shapes of molecules,in stereochemistry. After molecules of the right kind first assembled to protocells, life in its various stages of evolution was an inevitable consequence. Such molecules and new ones were the products of those functioning cells. It is molecules that continue to assemble as part of the living process and, in the role of enzymes, continue to direct the life cycle of the cell.

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Table 1

Tyrosine-Containing Tripeptides Expected from Random Polymerization of Glutamic Acid, Glycine, and Tyrosine and Those Found.

A priori expectations based on random hypothesis	Found
α-Glu-α-glu-tyr	
α-Glu-γ-glu-tyr	
γ-Glu-α-glu-tyr	
γ-Glu-γ-glu-tyr	
< Glu-α-glu-tyr	
< Glu-γ-glu-tyr	
α-Glu-gly-tyr	
γ-Glu-gly-tyr	
< Glu-gly-tyr	< Glu-gly-tyr
α-Glu-tyr-glu	
γ-Glu-tyr-glu	
< Glu-tyr-glu	
α-Glu-tyr-gly	
γ-Glu-tyr-gly	
< Glu-tyr-gly	< Glu-tyr-gly
α-Glu-tyr-tyr	
γ-Glu-tyr-tyr	
< Glu-tyr-tyr	
Gly-α-glu-tyr	
Gly-α-glu-tyr	
Gly-gly-tyr	
Gly-tyr-glu	
Gly-tyr-gly	
Gly-tyr-tyr	
Tyr-α-glu-glu	
Tyr-γ-glu-glu	
Tyr-α-glu-gly	
Tyr-γ-glu-gly	
Tyr-α-glu-tyr	
Tyr-γ-glu-tyr	
Tyr-gly-glu	
Tyr-gly-gly	
Tyr-gly-tyr	
Tyr-tyr-glu	
Tyr-tyr-gly	
Tyr-tyr-tyr	

< = pyro

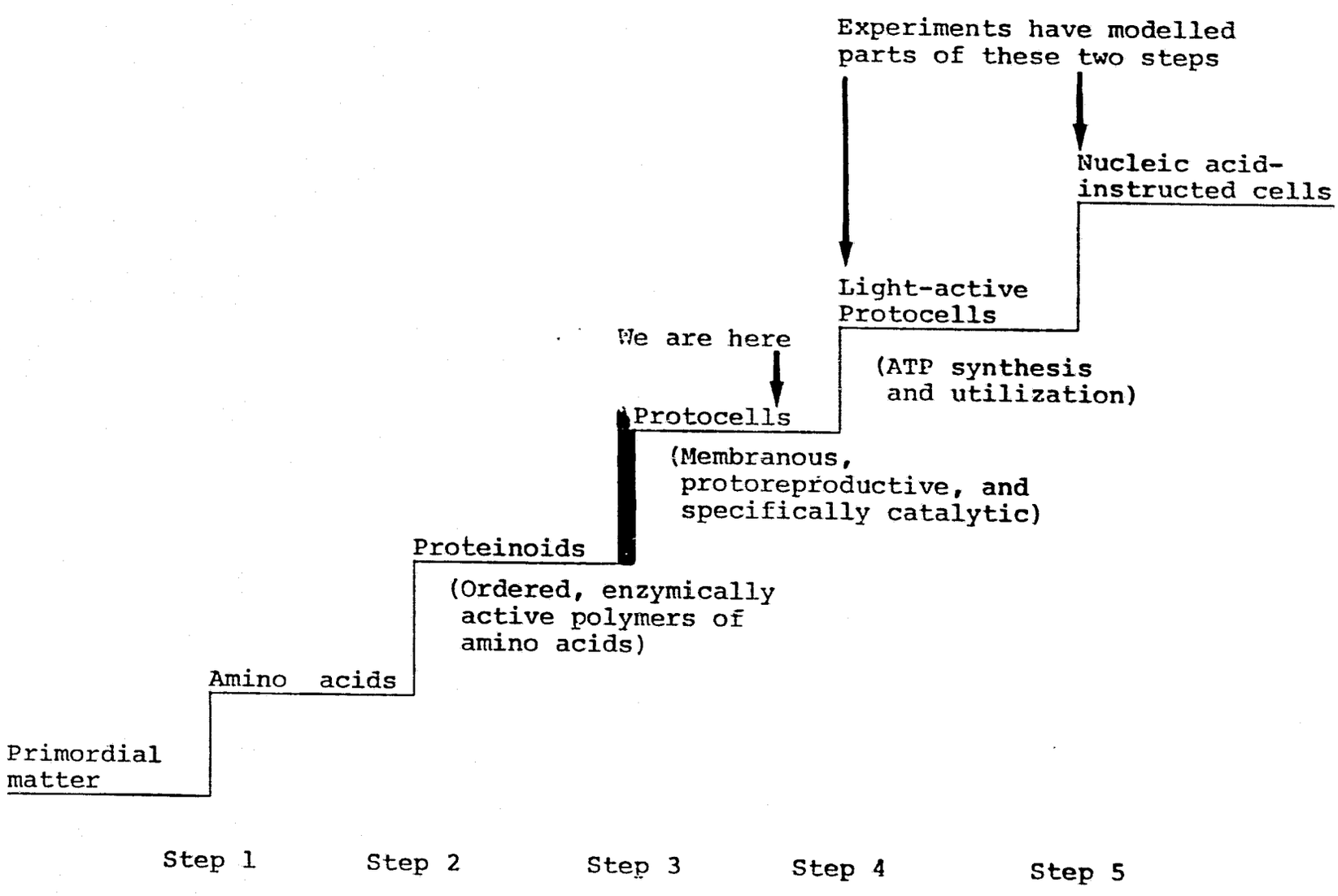

Fig. 1. Stepwise emergence of living organisms, as modelled in the laboratory.

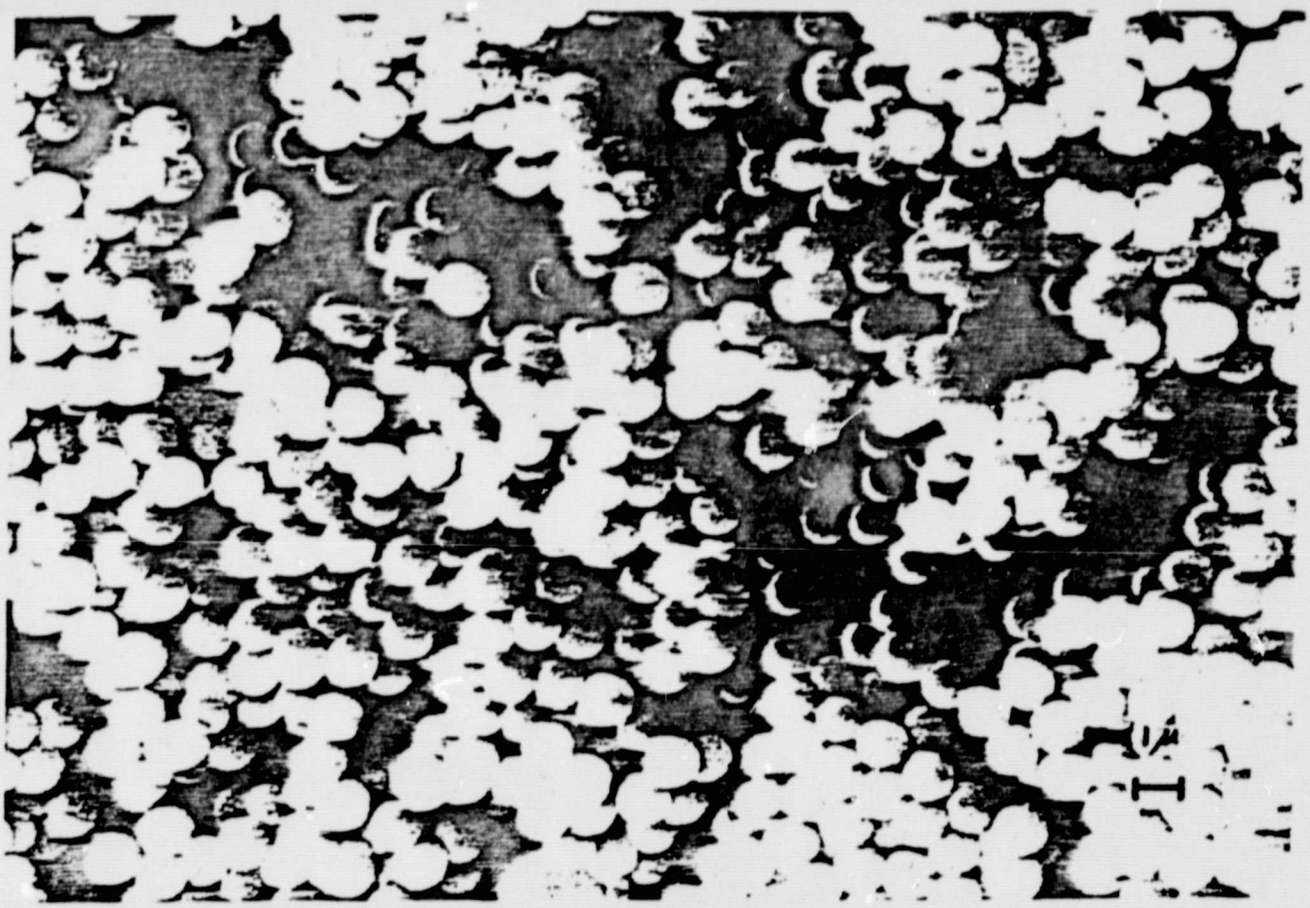

Fig. 2. Scanning electron micrograph of proteinoid microspheres. Uniformity of size and numerousness are evident. Original prepared by Mr. Steven Brooke.

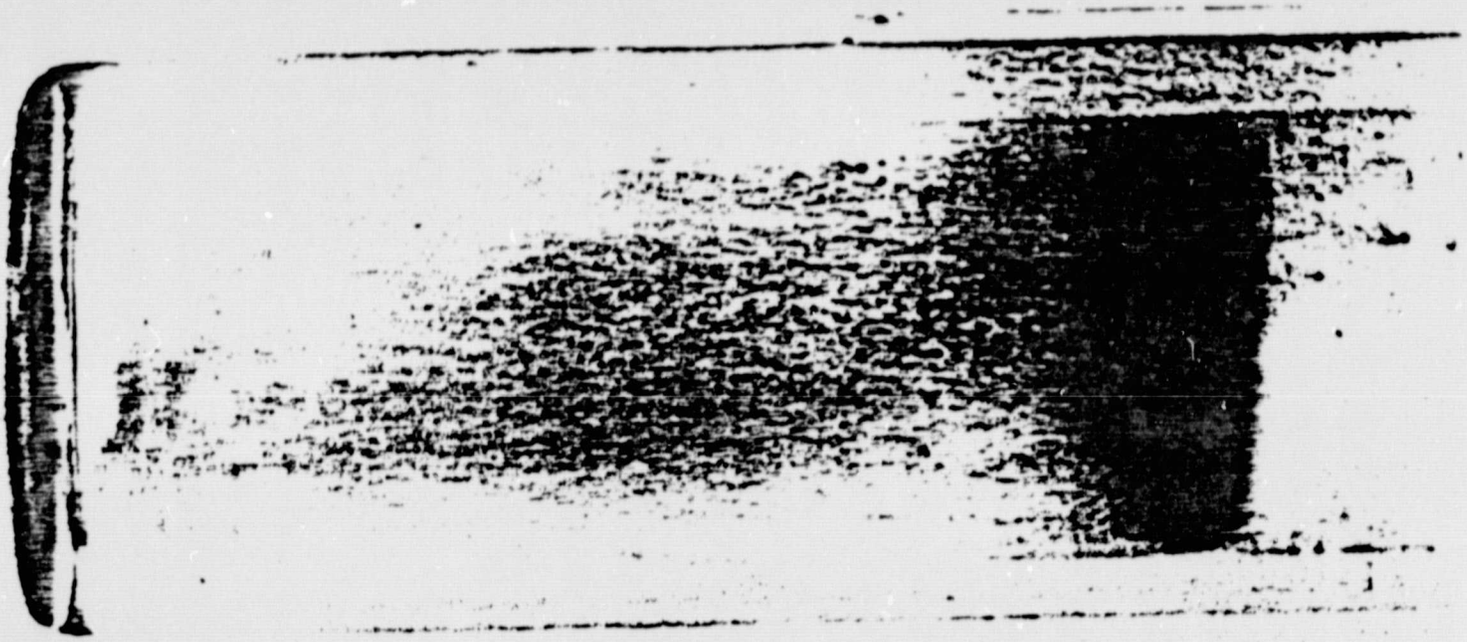

Fig. 3. Acrylamide gel electrophoresis of hemoproteinoid 83a at pH 8.6, stained with Amido Black 10 B. By electrophoresis at pH 4.5 and gel filtration, also, the preparation appears homogeneous. Courtesy of Dr. Klaus Dose.

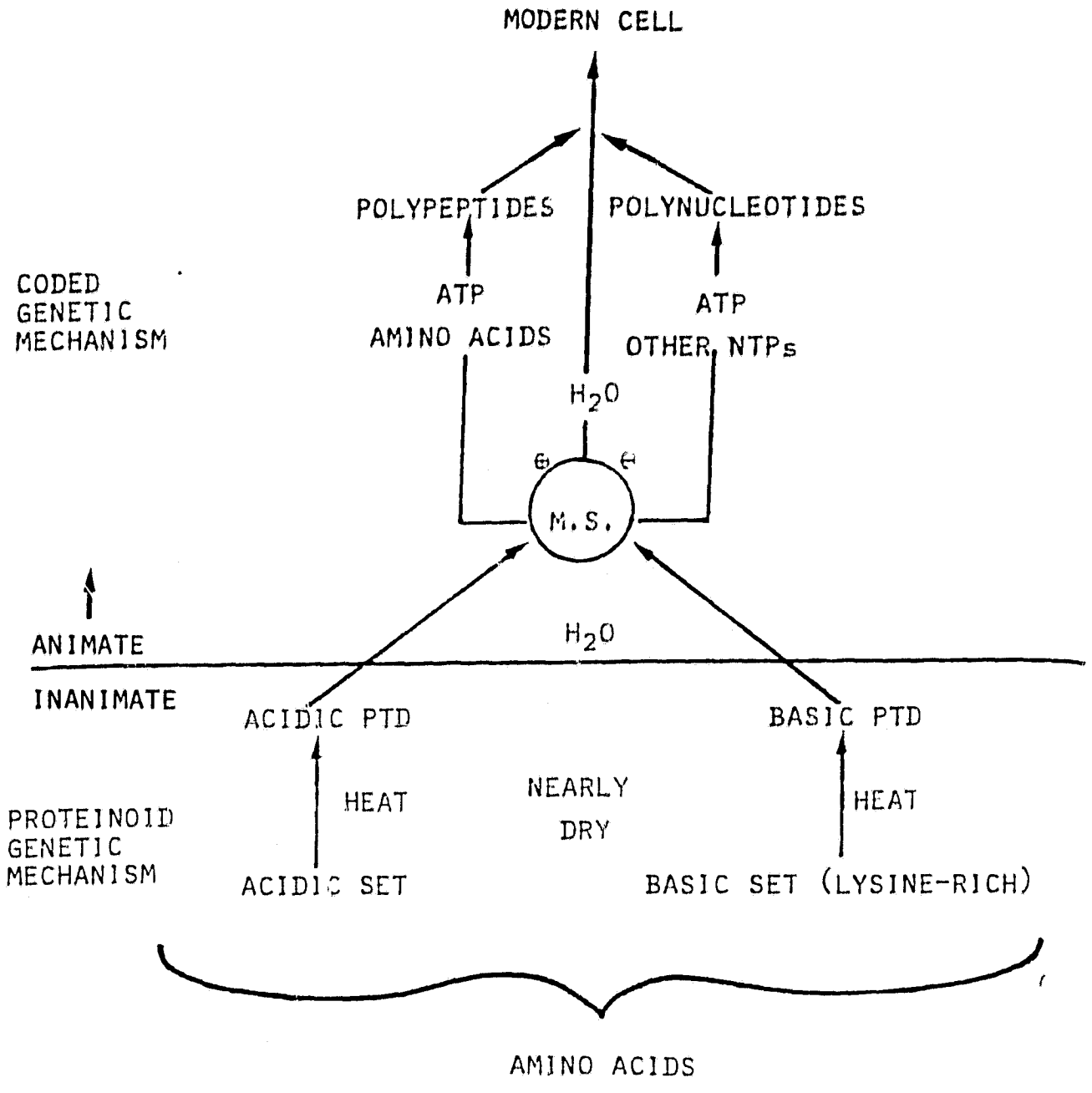

Fig. 4. Interpretation of recent experiments suggesting how a proteinoid mechanism evolved to a coded genetic mechanism containing nucleic acids. NTP = nucleoside triphosphates.