Oparin 2014
International Conference: The problem of the origin of life

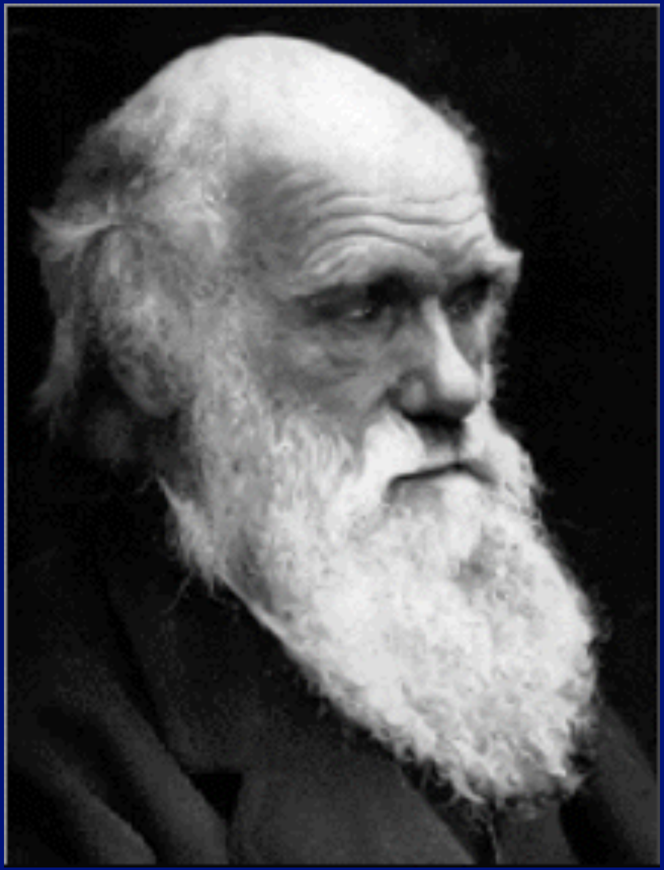
Oparin’s heterotrophic theory of the origin of life: a contemporary assessment

Antonio Lazcano

Miembro de El Colegio Nacional
Universidad Nacional Autónoma de México
Mexico

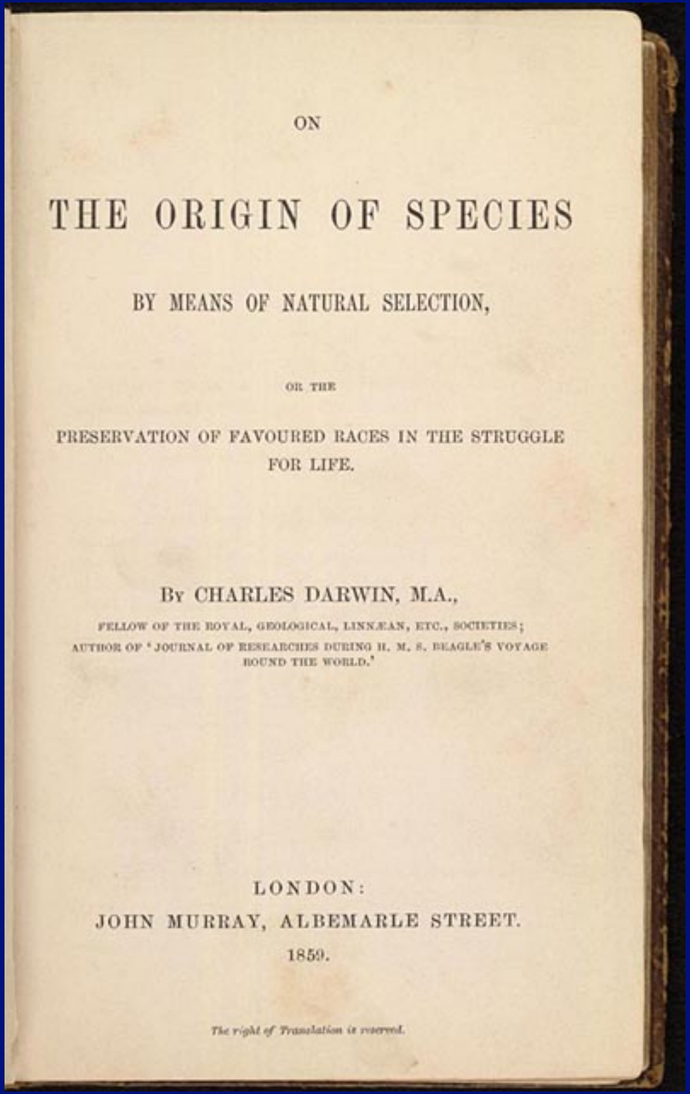
Moscow 2014

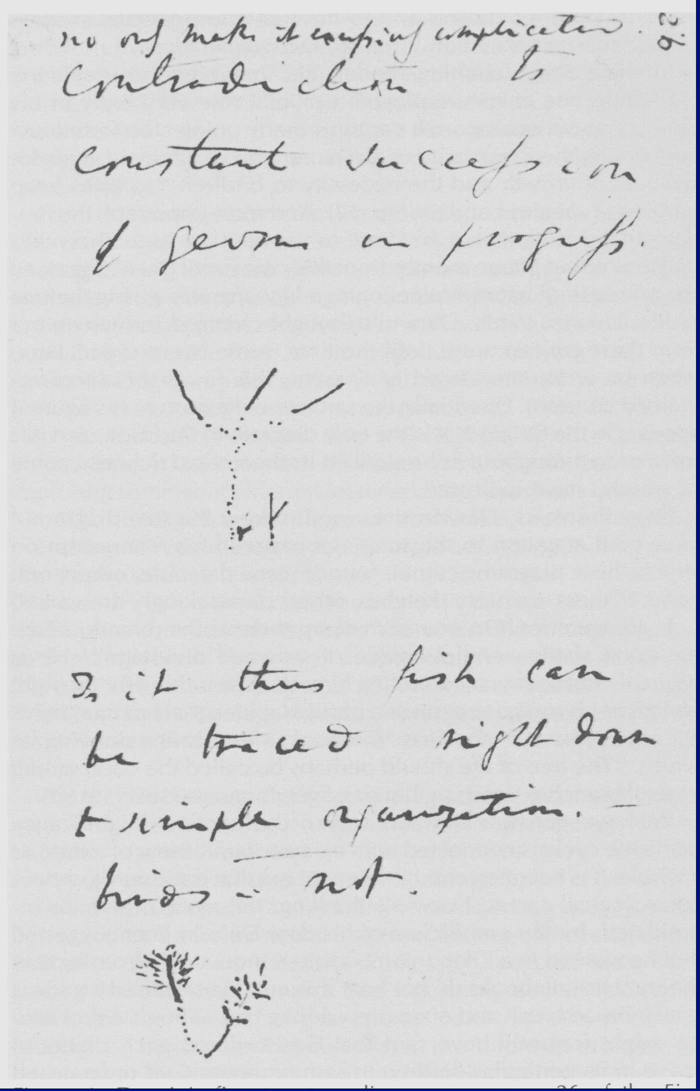
Darwin vs. Mendel?



Following the “rediscovery” of Mendel’s work, genetic mutations were considered as the fundamental source of evolutionary novelties in opposition to Darwin’s natural selection.

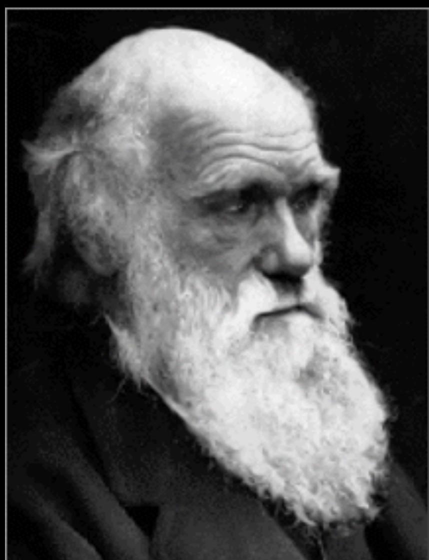
Darwin and the origin of life



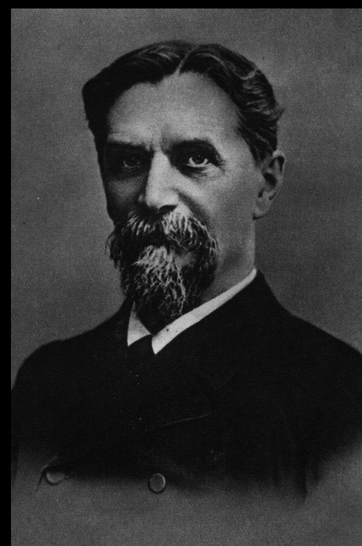


Peretó, Bada & Lazcano (2009) *Origins Life Evol Biosph* **39**: 395

Intellectual & scientific genealogies



Charles Darwin



Kliment A. Timiriazev

Alexandr I. Oparin

The times were ripe for a heterotrophic theory

the water which can not be eliminated. For oxidase activity, the oxidation of tetra methyl para phenylene diamine showed a slight activity. On the addition of hydrogen peroxide to this reagent a very active peroxidase action was shown. Catalase was determined by means of the Van Slyke apparatus commonly used for the determination of amino acids, the oxygen being liberated in the reaction vessel and measured in the burette. The material was collected from pure culture and the determinations were completed within a few minutes. No catalase activity was shown by the Phormidium filaments either suspended in water or after grinding for a long time in a mortar with fine quartz sand and calcium carbonate. The failure to decompose hydrogen peroxide was not due to any defect in the experiment or to poisonous substances in the spring water, since leaves of Iva xanthifolia treated in exactly the same manner with spring water showed high catalase activity at room temperature. It must be concluded, then, that this Phormidium possesses no catalase and little oxidase activity but shows a strong peroxidase and probably oxydo-reductase action.

Catalase previously has been found to be of universal distribution in living organisms. Czapek in his "Biochemie der Pflanzen" gives a bibliography of its distribution in various groups of plants and animals. Oscar Loew concluded that catalase was universally distributed, occurring in every organism and necessary in every living cell. This is the first instance of its absence from an organism having been demonstrated. G. B. Reed reported catalase activity in ripe and half ripe pineapples but found no activity in very green pineapples. No mention was made of controlling the acidity, so it seems probable that the catalase present in the green fruits was destroyed in the preparation. This enzyme, therefore, can not be required for the life activities of all organisms as has been suggested. The maximum temperature for the activity of catalase is low. Catalase derived from leaves of Iva xanthifolia was destroyed at the temperature of the spring water of Hymen Terrace (73° C.) by exposure for less than one minute. Oxydo-reductase is known to have a rather high optimum (57° C.) for its activity, and peroxidase activity is shown at the boiling temperature since it is thermostable, in fact, to such a degree that there is doubt that it should be included in the class of enzymes.

The fact that an organism can live at the temperature at which water boils at high altitudes demands that by some means it shall be able to carry on the hydrolytic cleavages or other chemical activities required for its metabolism. As the altitude increases there would be found a level at which water would maintain a constant temperature by boiling at a tem-

SPECIAL ARTICLES

ENZYMES OF THERMAL ALGAE

The algae of the hot springs in Yellowstone National Park offer good opportunity for a study of the distribution of enzymes in relation to the temperatures at which the organisms live. There is a complete series of thermal springs ranging in temperature from the boiling point (about 91° C) down to ordinary temperatures. Algae are found growing at a great many different temperatures within this range. One species of Phormidium was found growing at 89° C in Beryl Spring.

The action of some enzymes has been shown to be destroyed at temperatures much below the normal temperature range of some of these thermal algae. It seems of interest to determine at what range of temperature the thermolabile enzymes are present in the algae, and how the algae are able to conduct their metabolic processes at temperatures above the maximum for the activity of several important enzymes.

Phormidium laminosum was found growing in pure culture in Hymen Terrace spring at 73° C. to 65° C. Its range did not extend below 65° C. Possibly other factors than the temperature were concerned in this distribution, since the carbon dioxide and hydrogen sulfide used by this organism are quickly liberated from the water after it escapes. Possibly the temperatures below this range do not allow metabolic processes to proceed normally in the absence of certain enzymes.

Determinations on the catalase, oxidase, oxydo-reductase and peroxidase action of this Phormidium were made immediately at the spring. For oxydo-reductase activity the reduction of methylene blue in the presence of acetone was used. Strong reduction was shown by the preparation, some of which was probably due to the reducing substances present in

THE ORIGIN OF LIFE

By Professor CHARLES B. LIPMAN
UNIVERSITY OF CALIFORNIA

At the remotest frontiers of man's most penetrating and imaginative thought there has always lingered the dream—perhaps the hope—that the age-old mystery of the origin of life would some day be solved. The remarkable forward strides that have been taken in the physical sciences in the last two decades, replete with significance for the progress of biological thought and study, have strengthened rather than weakened that hope. It is my purpose in this brief paper to recall to your minds, among other things, some of the theories, or at least speculative hypotheses, which have been put forward in the past to account for the origin of life on our planet, but chiefly to review critically some of the consequences of these hypotheses in order to test the soundness of the latter and to propose a view of my own relative to the problem in hand. To the interested reader, it is probably superfluous to enter into a disquisition on the difficulties of the task in question. Needless to say, finality of judgment in the premises is proscribed and I do not seek to be dogmatic in any part of my discussion. Inconclusive indeed I must be, but I venture to hope that my analysis of the problem may contribute to progress, or at least to clarification of our thought.

The Aristotelian conception of the origin of many forms of

The Editor of "The Rationalist Annual" desires it to be understood that each contributor is alone responsible for the opinions he expresses, and that he in no way commits the R. P. A. or any of the other contributors to an endorsement of his views. The aim of the Editor is to provide a platform for all liberal thinkers in general agreement with Rationalism as defined in the Memorandum of the R. P. A.

THE ORIGIN OF LIFE

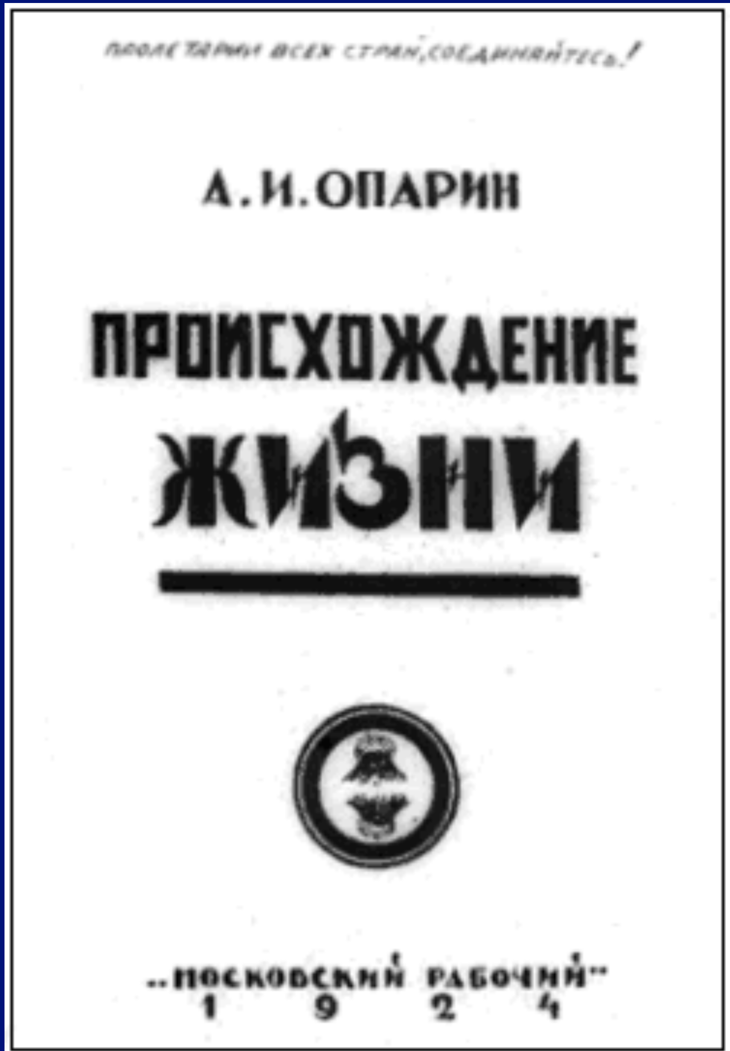
By J. B. S. HALDANE

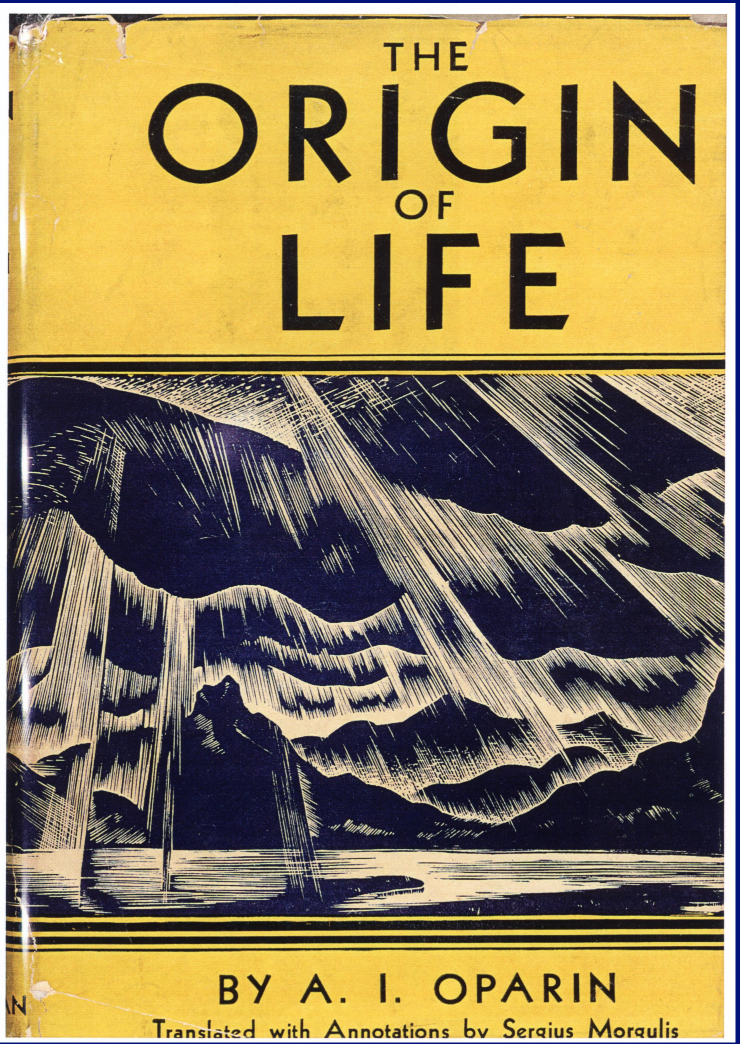
Until about 150 years ago it was generally believed that living beings were constantly arising out of dead matter. Maggots were supposed to be generated spontaneously in decaying meat. In 1668 Redi showed that this did not happen provided insects were carefully excluded. And in 1860 Pasteur extended the proof to the bacteria which he had shown were the cause of putrefaction. It seemed fairly clear that all the living beings known to us originate from other living beings. At the same time Darwin gave a new emotional interest to the problem. It had appeared unimportant that a few worms should originate from mud. But if man was descended from worms such spontaneous generation acquired a new significance. The origin of life on the earth would have been as casual an affair as the evolution of monkeys into man. Even if the latter stages of man's history were due to natural causes, pride clung to a supernatural, or at least surprising, mode of origin for his ultimate ancestors. So it was with a sigh of relief that a good many men, whom Darwin's arguments had convinced, accepted the conclusion of Pasteur that life can originate only from life. It was possible either to suppose that life had been supernaturally created on earth some millions of years ago, or that it had been brought to earth by a meteorite or by micro-organisms floating through interstellar space. But a large number, perhaps the majority, of biologists, believed, in spite of Pasteur, that at some time in the remote past life had originated on earth from dead matter as the result of natural processes.

The more ardent materialists tried to fill in the details of this process, but without complete success. Oddly enough, the few scientific men who professed idealism agreed with them. For if one can find evidences of mind (in religious terminology the finger of God) in the most ordinary events, even those which go on in the chemical laboratory, one can

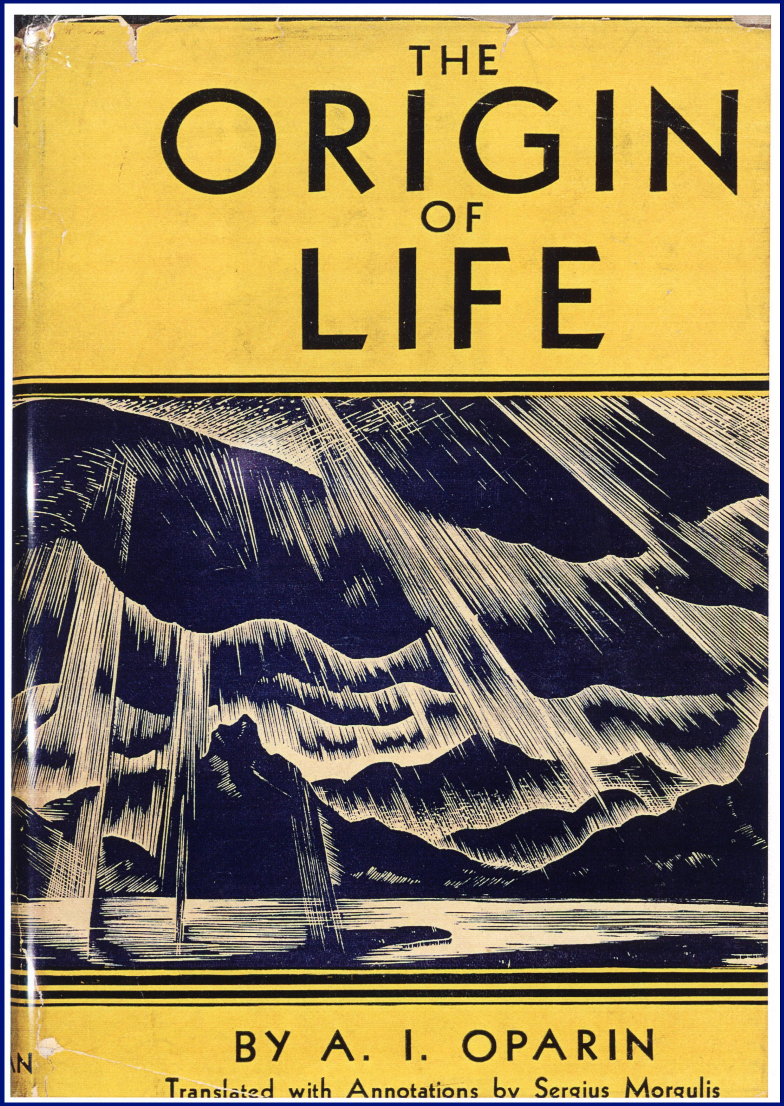
Bada & Lazcano, 2003

The evolution of Oparin's heterotrophic theory: what happened between 1924-1936?





Oparin's step-wise heterotrophic origin of life



reducing atmosphere

↓

synthesis and accumulation of organic compounds in the primitive oceans

↓

coacervates

↓

primordial anaerobic heterotrophic bacteria

It is surprising that Oparin's proposal did not include genes or nucleic acids?

1. Ernst Haeckel, who was a major influence in Oparin's work, had assumed that Monera lacked all traces of the hereditary substances found in other organisms

   E. Haeckel (1904) *The Wonders of Life*

2. "… bacteria have no genes in the sense of accurately quantized portions of hereditary substances; and therefore have no need for accurate division of the genetic system which is accomplished by mitosis."

   Julian Huxley (1942) *Evolution: the modern synthesis*

cf Lazcano (2010) *Cold Spring Harbor Perspectives in Biology: the origins of life* (CSHS Press): 1

Herman J. Muller's single gene theory of the origin of life

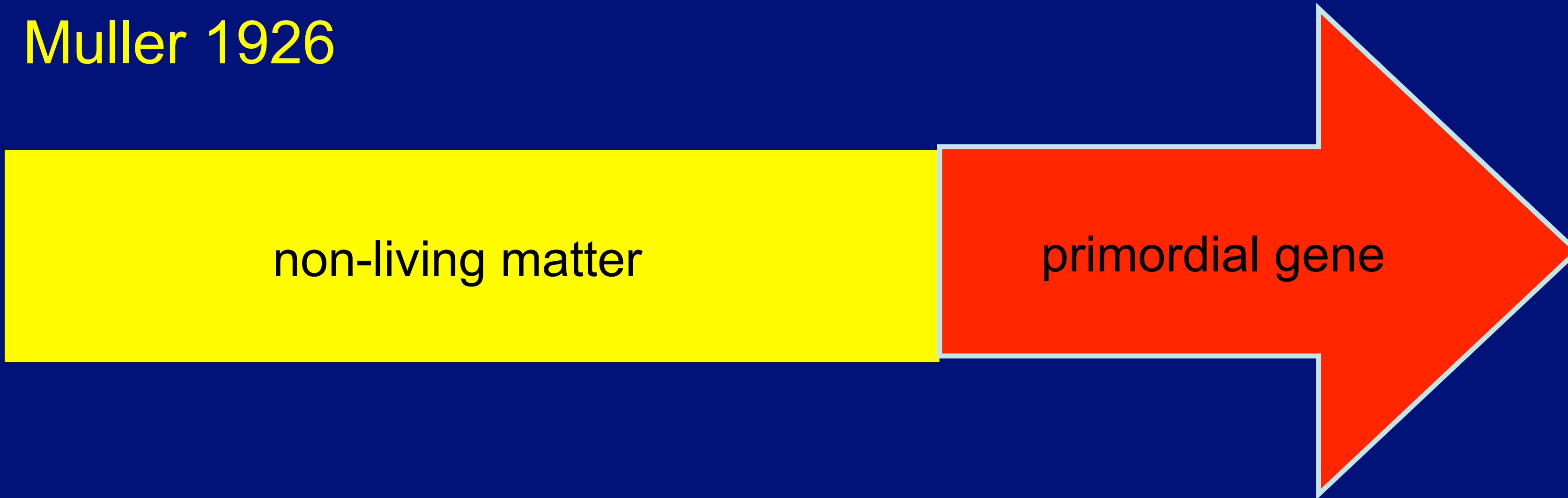
1. The first living being was a gene that appeared by chance in the primitive oceans;

2. The primordial gene was endowed with

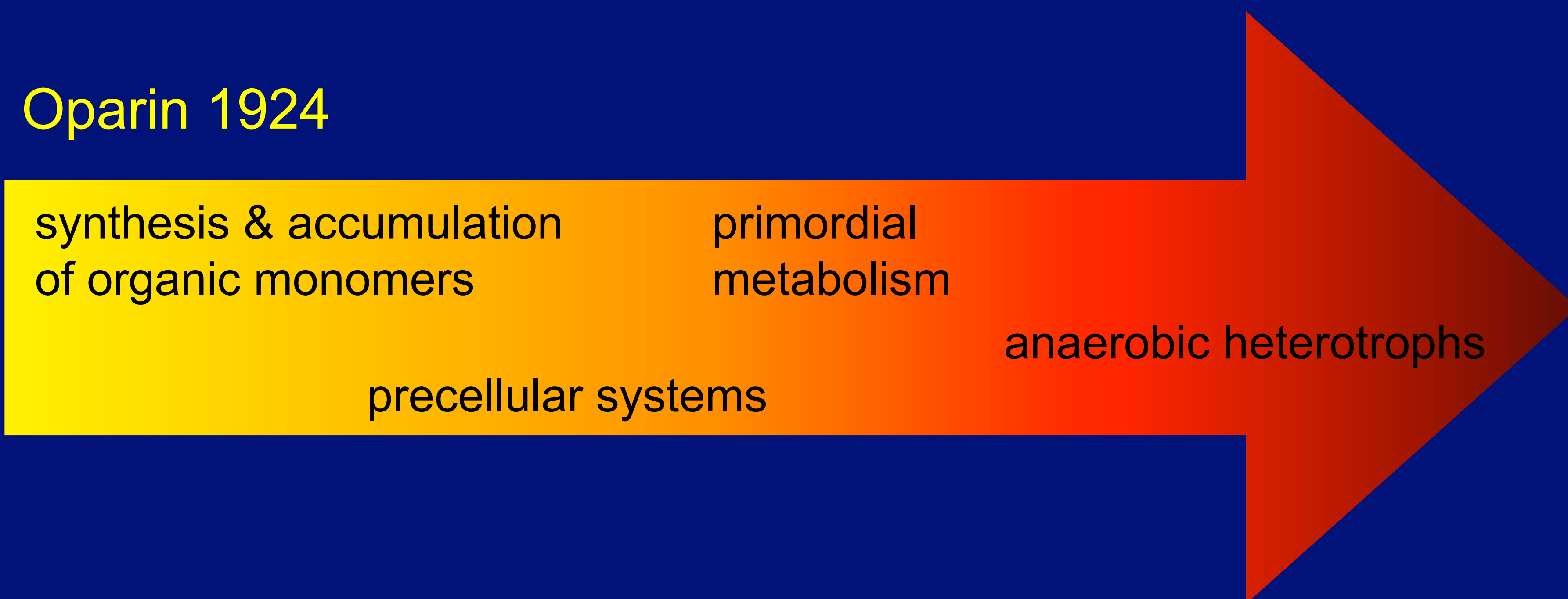
a) autocatalysis (replication)
b) heterocatalysis (metabolism)
c) mutability (evolvability)

Muller, 1926

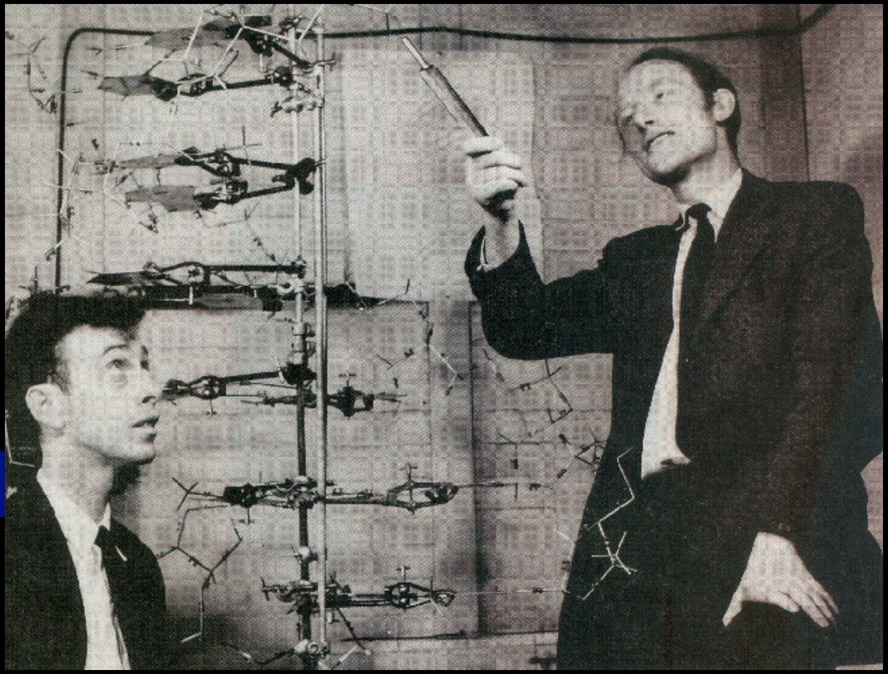
Muller 1926



Oparin 1924



The harvest of '53



Watson & Crick and the DNA double helix model

S. L. Miller and the prebiotic synthesis of amino acids

An insightful proposal…

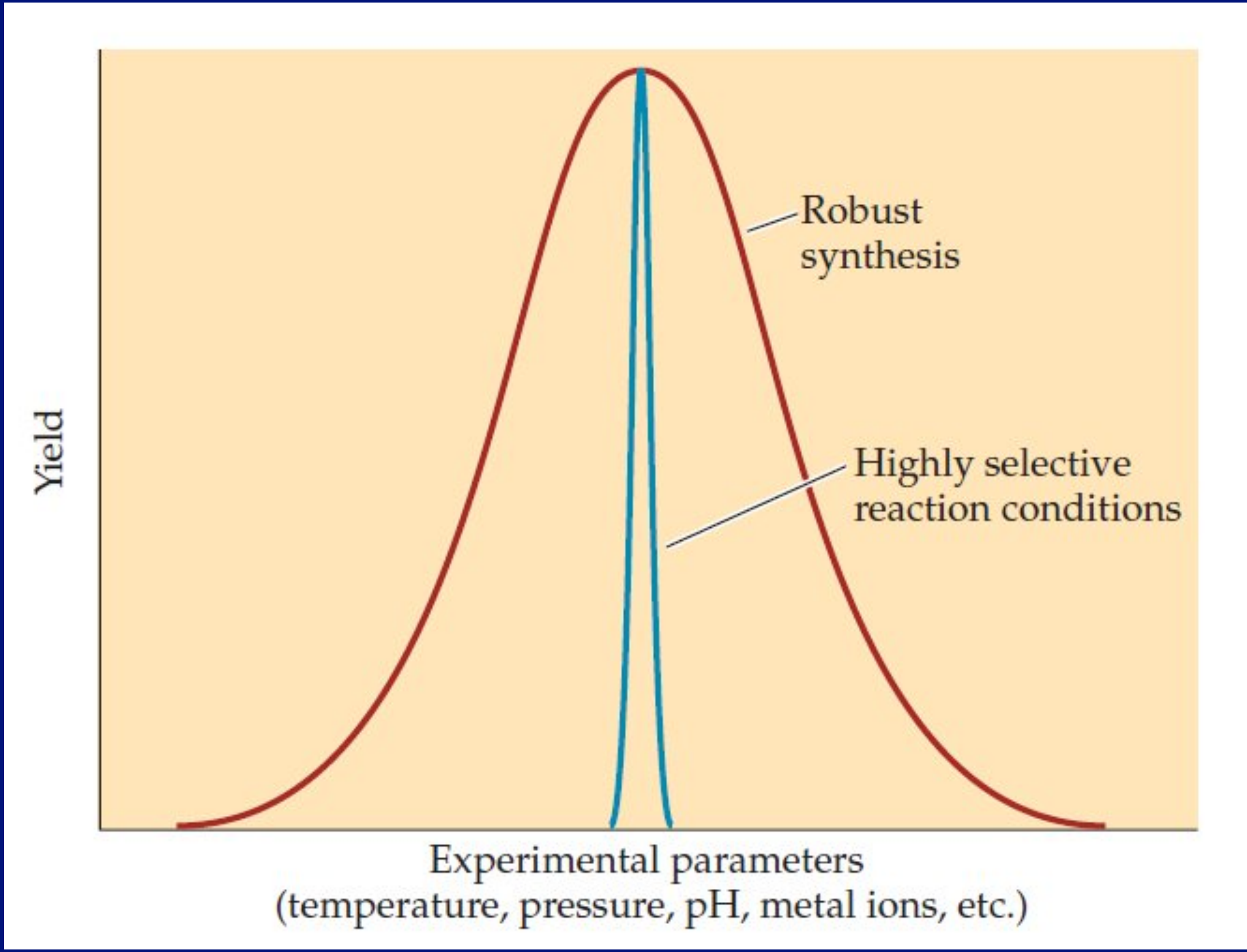
"The long-chain polymers found in living organisms have 'back-bones', composed of phosphate [i.e., nucleic acids], glycine or pentose residues. The first seem to be the most catalytically active, and may be the most primitive. The critical event which may have best be called the origin of life was the enclosure of several different self-reproducing polymers within a semipermeable membrane"

Haldane (1954) *New Biology* **16**: 12

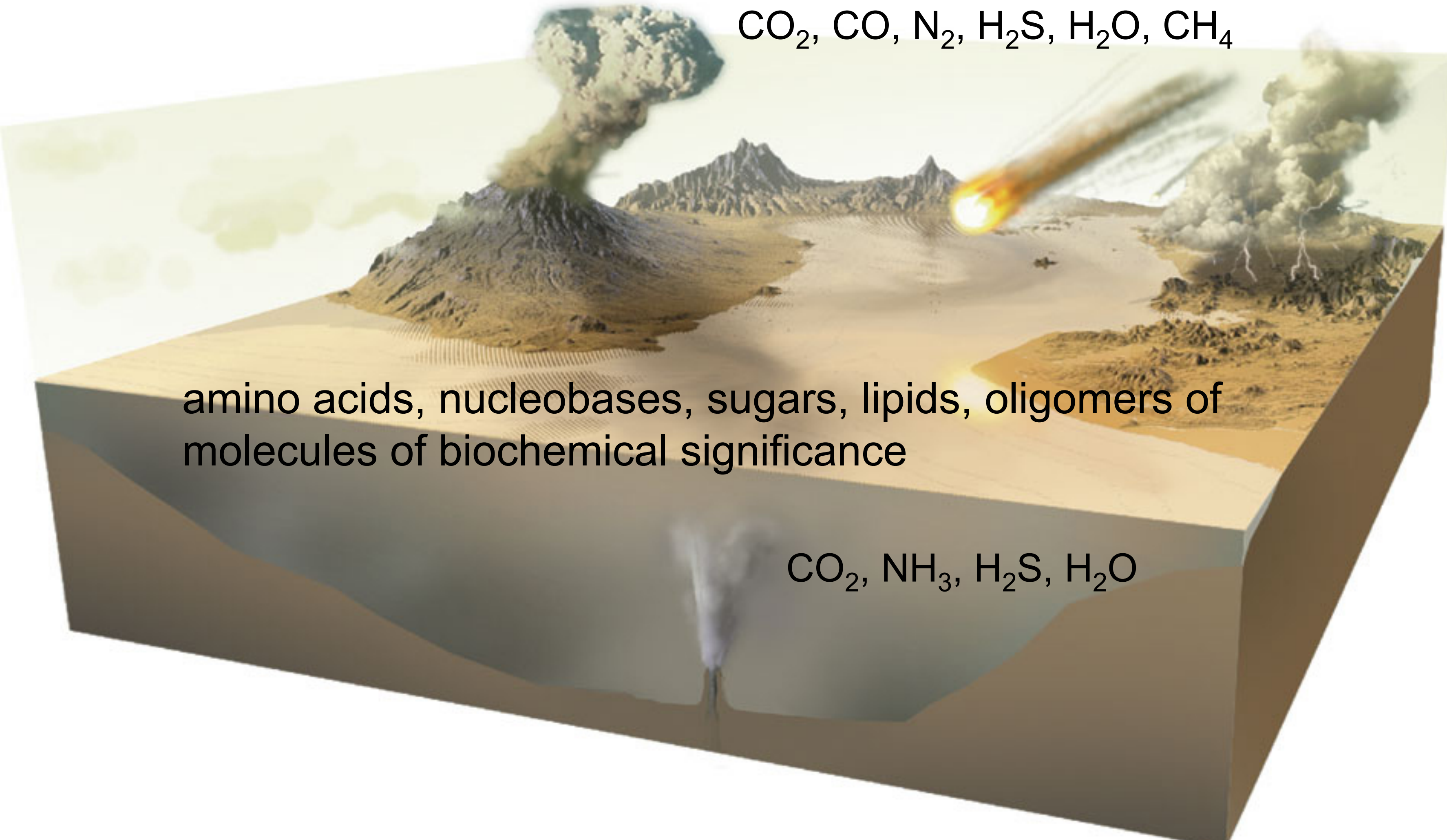
The evidence suggests that prior to the origin of life the primitive Earth already had:

- a wide array of organic compounds of biochemical significance –and not only proteinic amino acids
- many inorganic & organic catalysts
- many different purines & pyrimidines (the potential for template-directed polymerizations)
- membrane-forming compounds

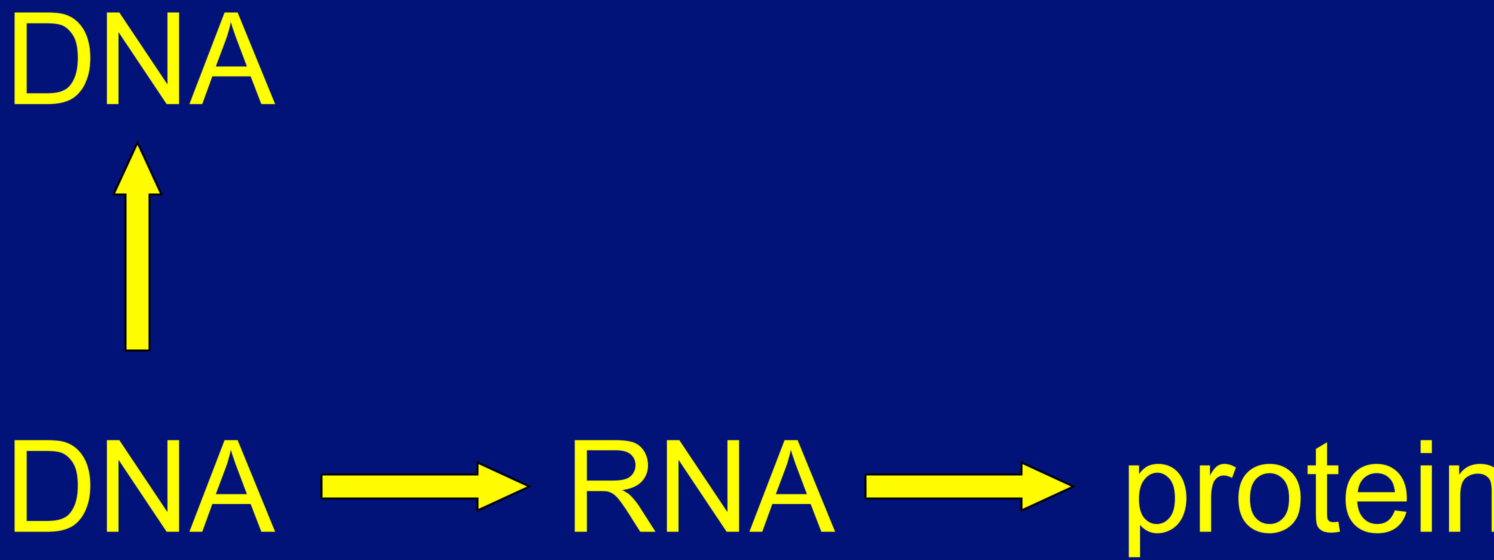
Synthesis of monomers under possible prebiotic conditions produce appreciable yields under a wide range of environmental settings*

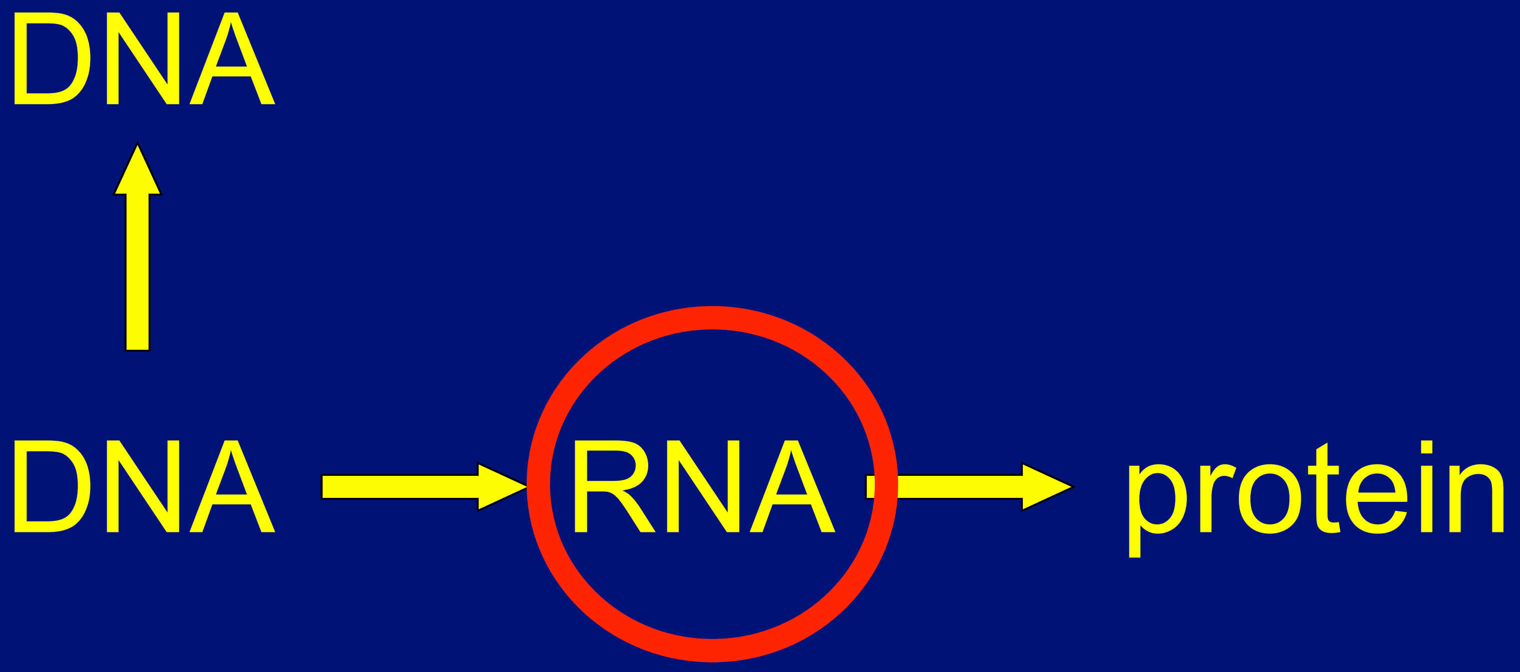


Miller & Lazcano, 2002

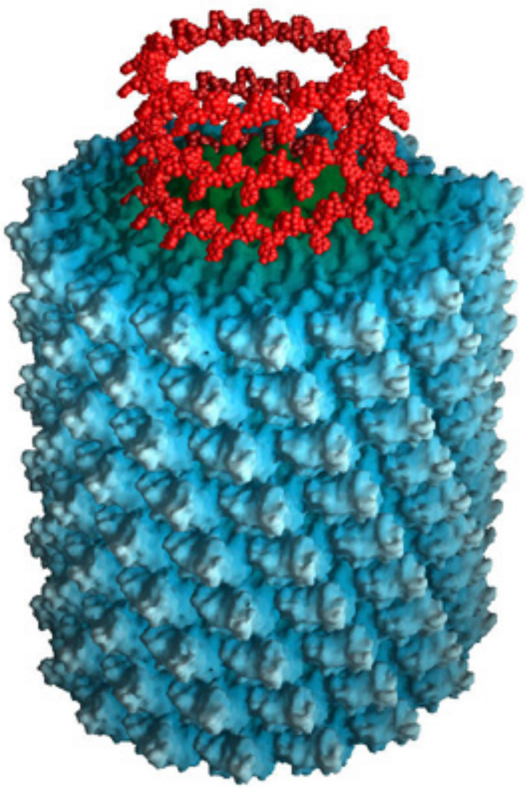


Lazcano 2006)


DNA
DNA
RNA
protein


DNA
DNA
RNA
protein

A broken watch gives the right time now and then…



In the early 1950s, it was argued that since

a) some viruses, like the tobacco mosaic virus, have RNA genomes; and

b) viruses can be crystalized, leading many to argue they may be at the threshold of life,

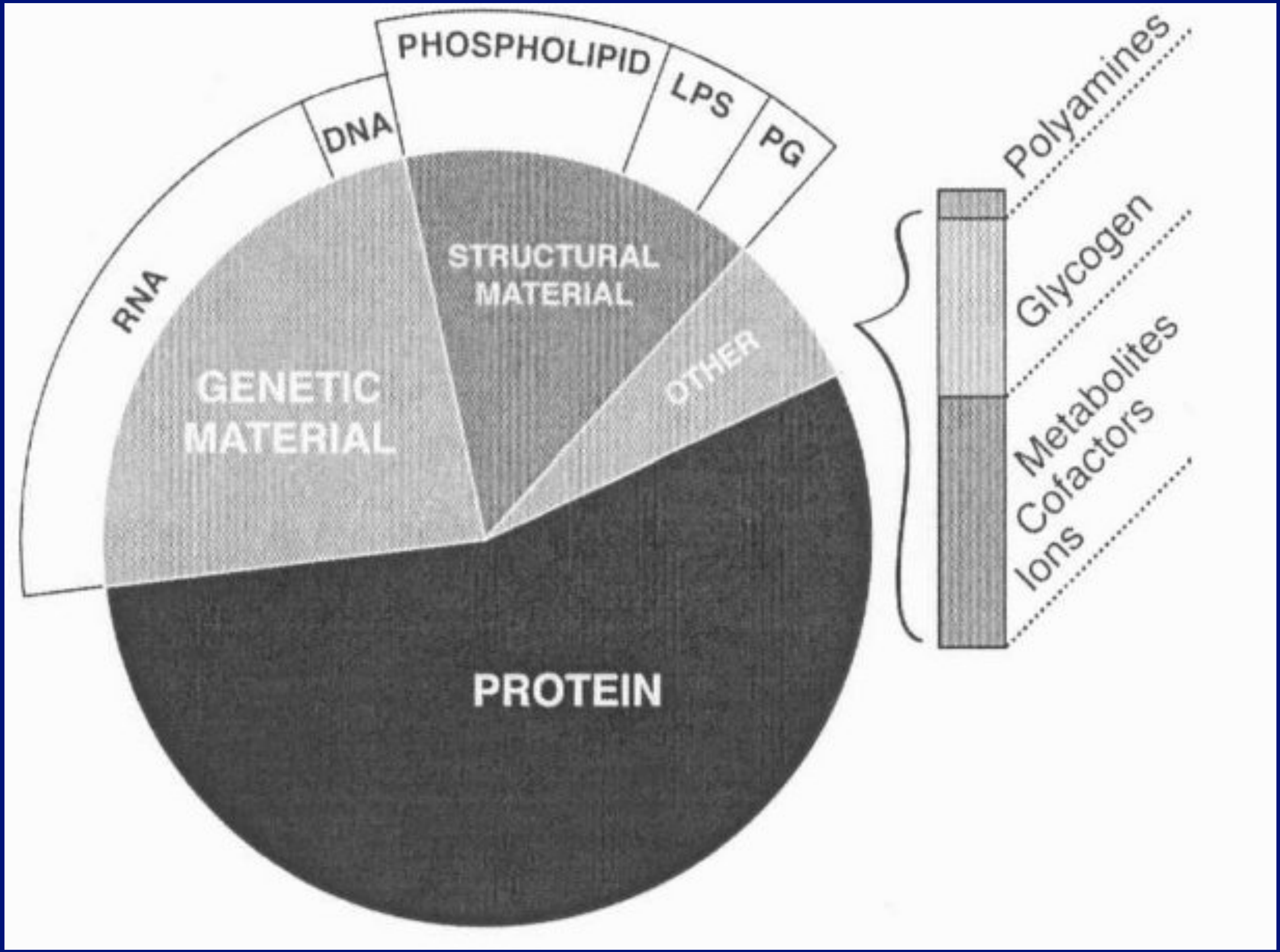
therefore, RNA genomes must be primitive

cf. Lazcano (2012) *Hist.Phil.Life Sci*. **34**: 407

In the 1950s, Brachet and Belozersky independently concluded that the abundance of RNA molecules was an indication of its antiquity

Andrei Nikolaevich Belozersky

Jean Louis Auguste Brachet

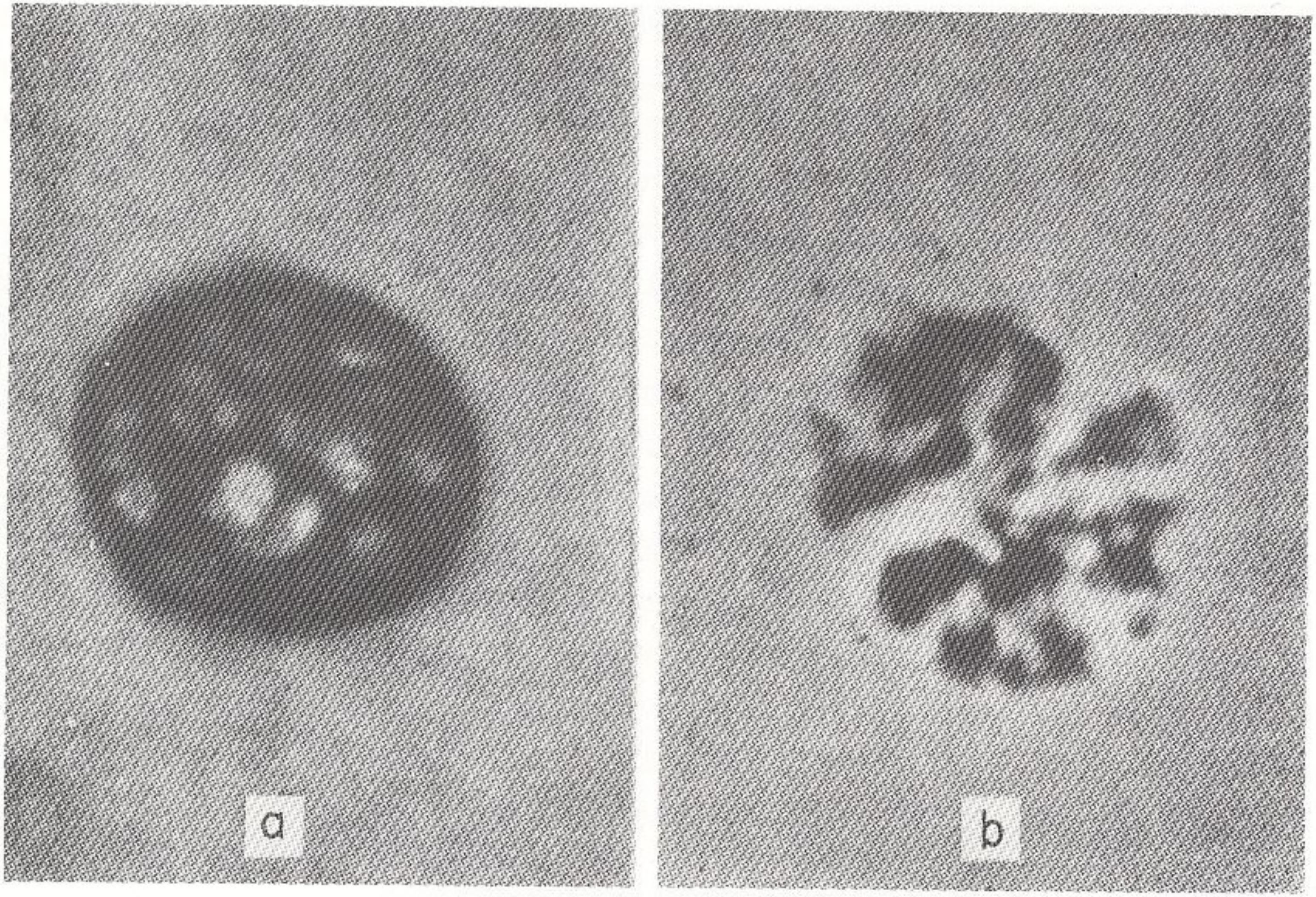


Neidhart, Ingraham & Schaechter (1990)

"…There is no doubt that nucleic acids played an important role in the evolution of the organic world and metabolic reactions. Yet both RNA and DNA could hardly arise simultaneously in the early evolution of life. It rather seems that ribonucleotides, and then RNA, originated first. DNA came into existence far more recently, as the protoplasm became more differentiated and its functions grew in complexity.

"It seems that RNA, being associated with the most general processes of life, was formed at an earlier evolutionary stage, while the origin of DNA was associated with the development of more specialized and phylogenetically later features of organisms"

A.N. Belozersky, 1957 (1959)



Coacervate droplet of serum albumin + gum arabic + RNA and the enzyme ribonuclease under the electron microscope. a. Before the beginning of breakdown. b. After a 15-minute breakdown period.

Oparin (1968) *Genesis and Evolutionary Development of Life* (Academic Press, New York)

From the early 1950s onwards the road to proposals of an RNA World was paved by

1) The embracement of the idea that primitive life had RNA genomes (Haldane, Bernal, Pirie, Oparin, Belozerki, Brachet, Lipmann);

2) Proposals of an ancestral metabolism catalyzed by ribonucleotidyl coenzymes (Eakin, Handler, Orgel, White III);

3) The awareness of the complex tertiary structures of RNAs and their key roles in protein biosynthesis (Smithies, Crick, Orgel)

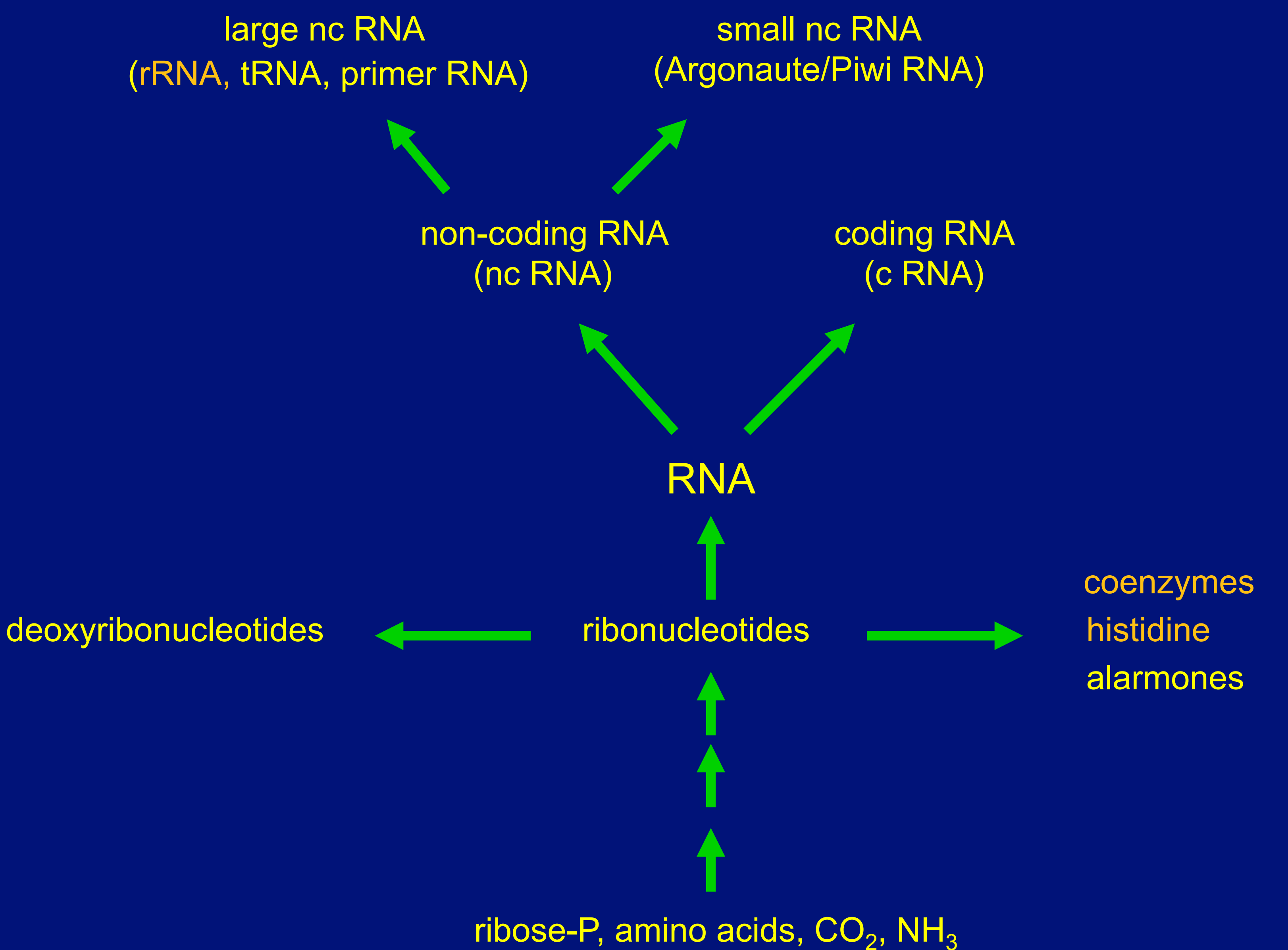
cf. Lazcano (2012) *Hist.Phil.Life Sci*. **34**: 407

In vivo & *in vitro* biochemical catalysis

Class	Enzymes	Ribozymes
EC1 Oxidoreductases	Dehydrogenases Oxidases, peroxidases Reductases Monooxygenases Dioxygenases	Dehydrogenases Peroxidases
EC2 Transferases	C1-Transferases Glycosyltransferases Aminotransferases Phosphotransferases	Methyltransferases Aminoacyltransferases Pentosyltransferases Phosphotransferases Nucleotidyltransferases
EC3 Hydrolases	Esterases Glycosidases Peptidases Amidases	Esterases Endodeoxyribonucleases Endoribonucleases Glycosylases Amidases Phosphoamidases
EC4 Lyases (synthases)	C-C-Lyases C-O-Lyases C-N-Lyases C-S-Lyases	Carboxylyases Aldehydelyases Ferrochelatases
EC5 Isomerases	Epimerases *cis trans* Lyases Intramolecular transferases	Methylmanolyl CoA epimerases
EC6 Ligases (synthetases)	C-C-Ligases C-O-Ligases C-N-Ligases C-S-Ligases	C-C-Ligases C-O-Ligases C-N-Ligases C-S-Ligases Phosphoric ester ligases

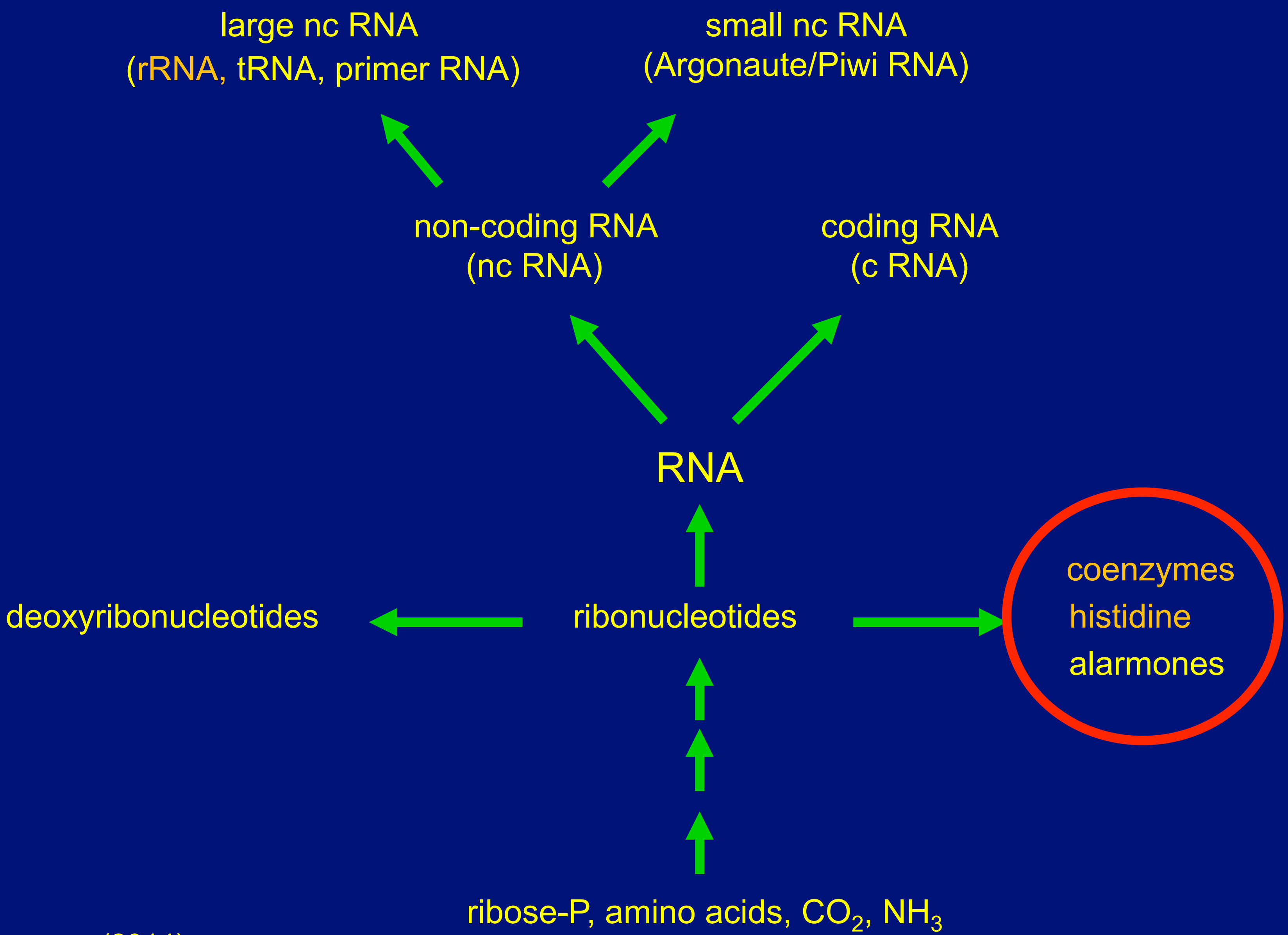
Hernández-Morales, Becerra & Lazcano 2014 (submitted)

RNA and ribonucleotides: stepping out of the shadows



Lazcano (2014)

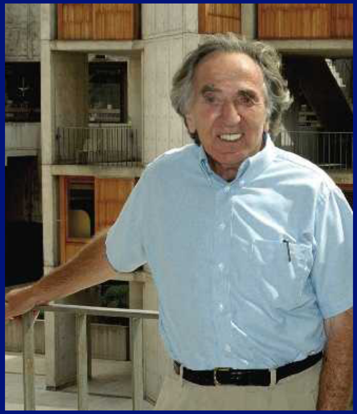
RNA and ribonucleotides: stepping out of the shadows



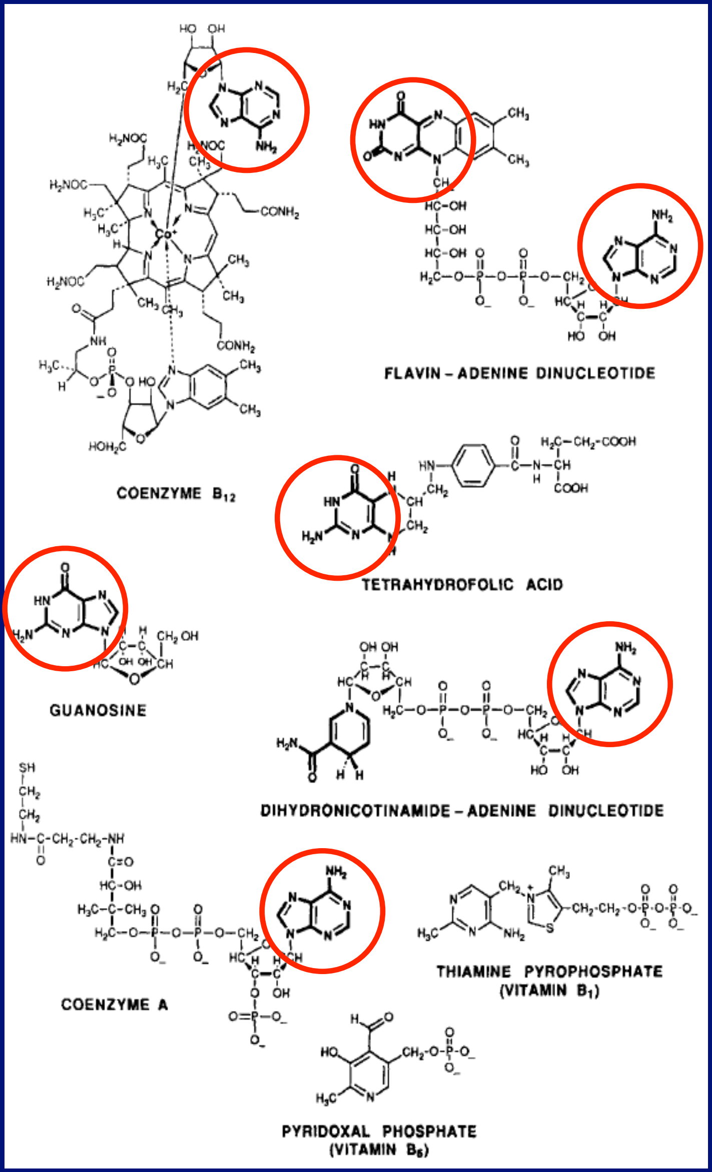
Lazcano (2014)

Coenzymes as primordial catalysts

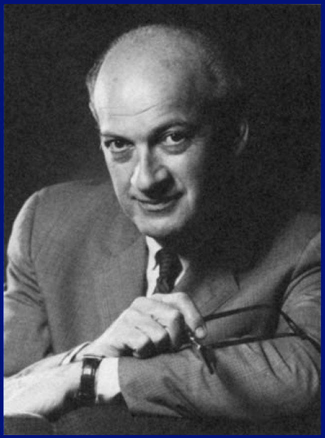
Robert E. Eakin (1916–1979)



Leslie E. Orgel (1927-2007)



Eschenmoser & Loewenthal 1992



Philip Handler (1917-1981)

Harold B. White III

Harold White's hypothesis: is histidine an evolutionary remmant of a catalytic ribonucleotide?

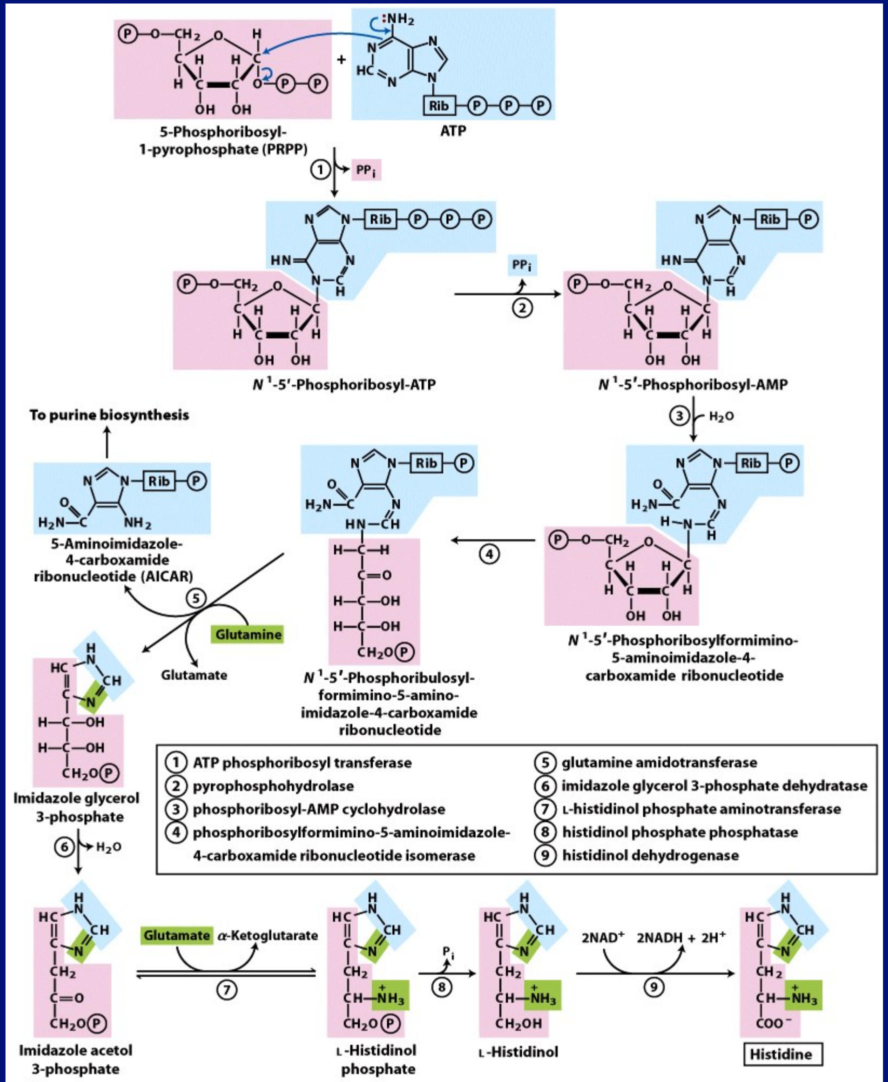
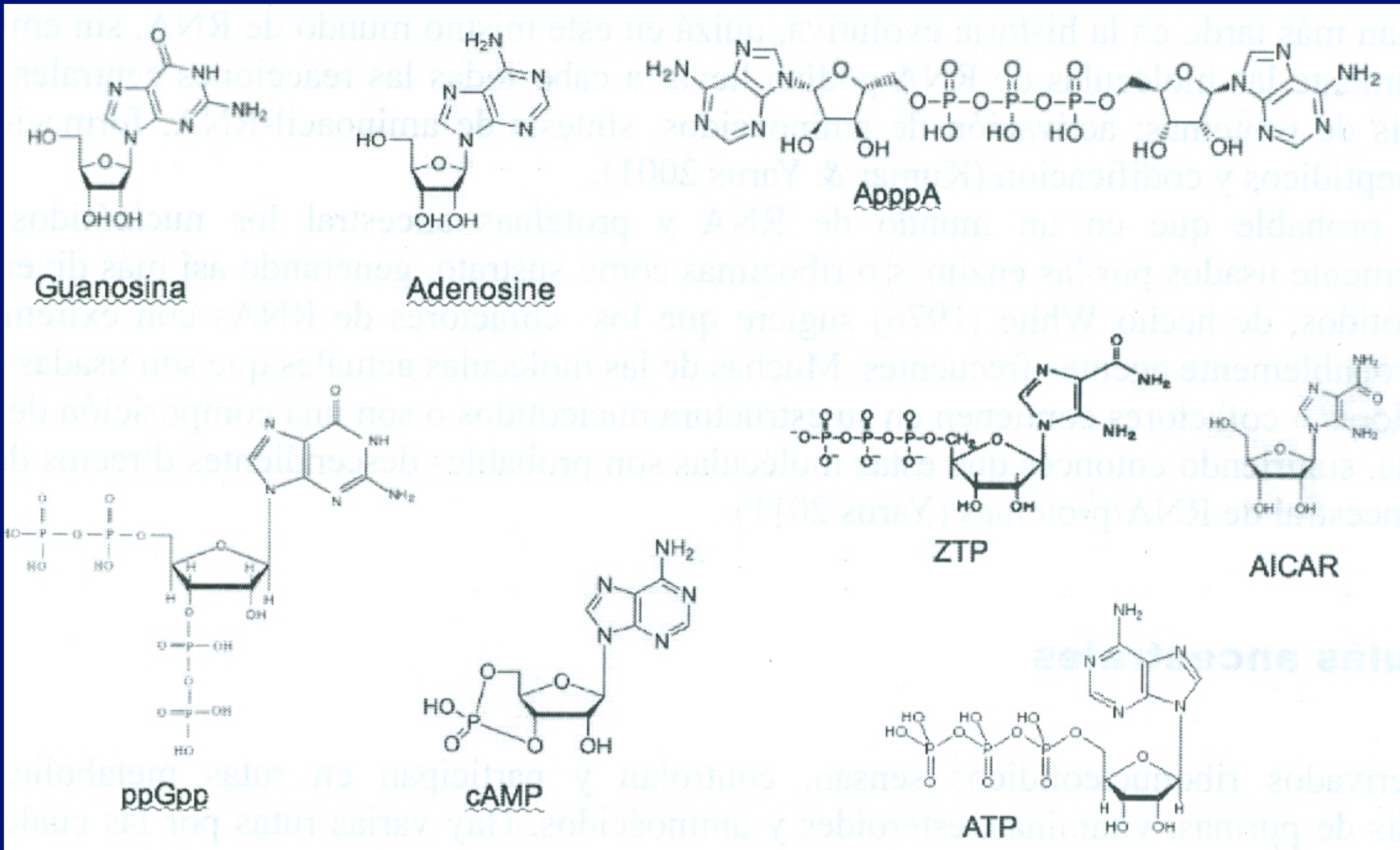


Figure 22-20

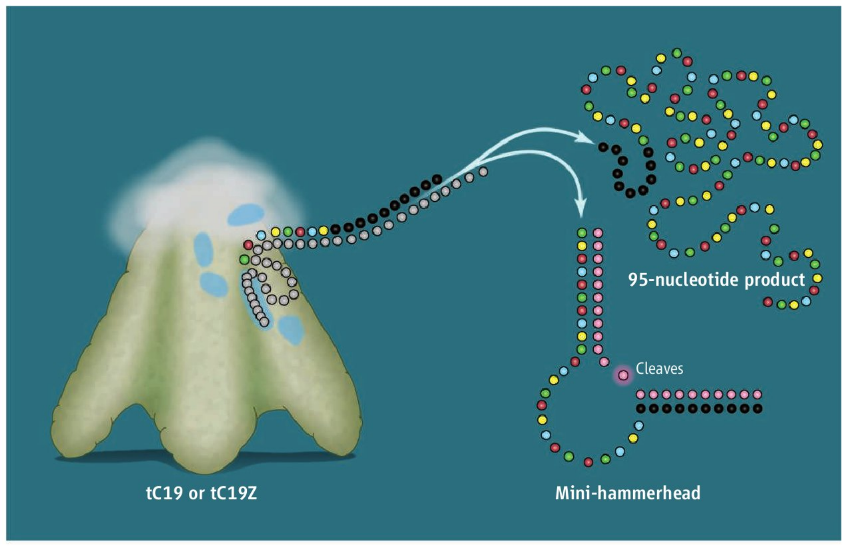
Lehninger Principles of Biochemistry, Fifth Edition

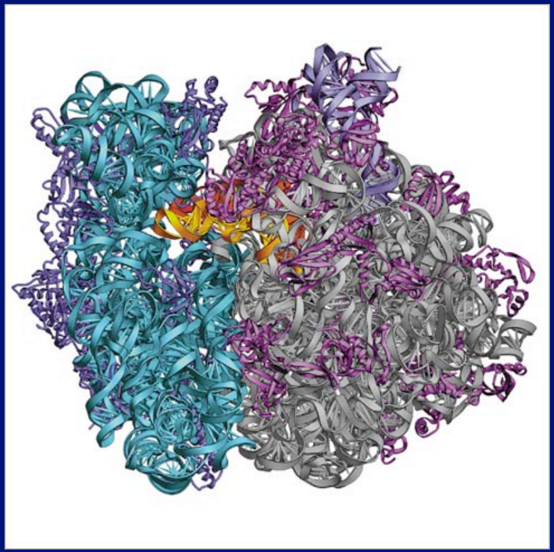
Alarmones: a vestigial regulatory and signaling system from the RNA World



Lazcano, Becerra & Delaye (2011)

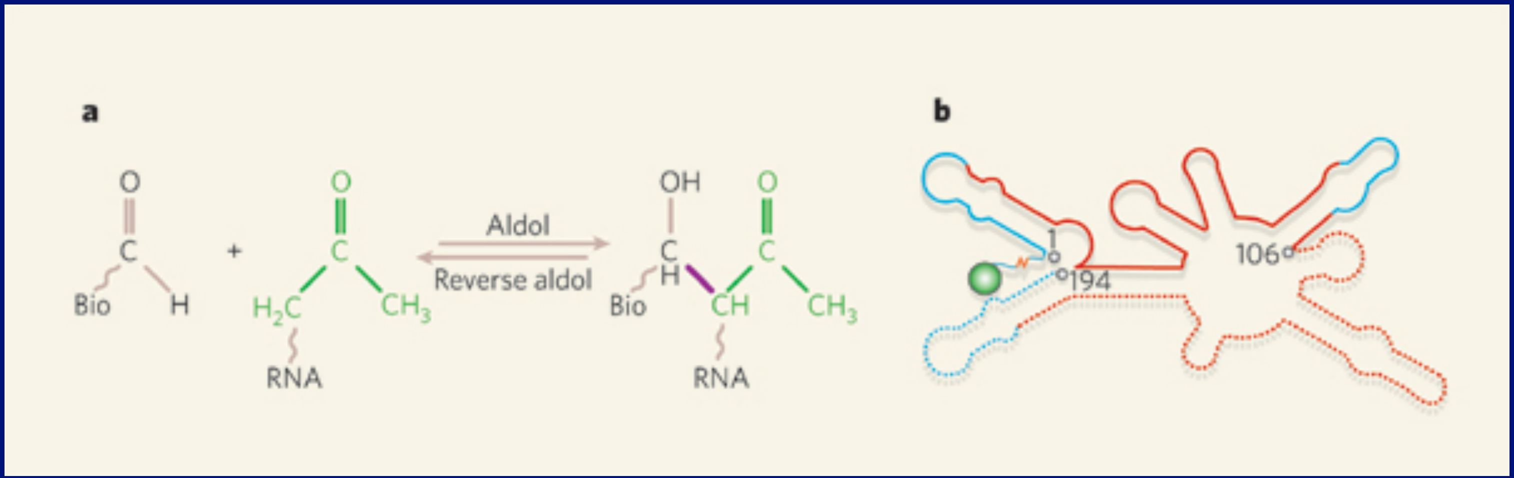
The robustness of the RNA world hypothesis



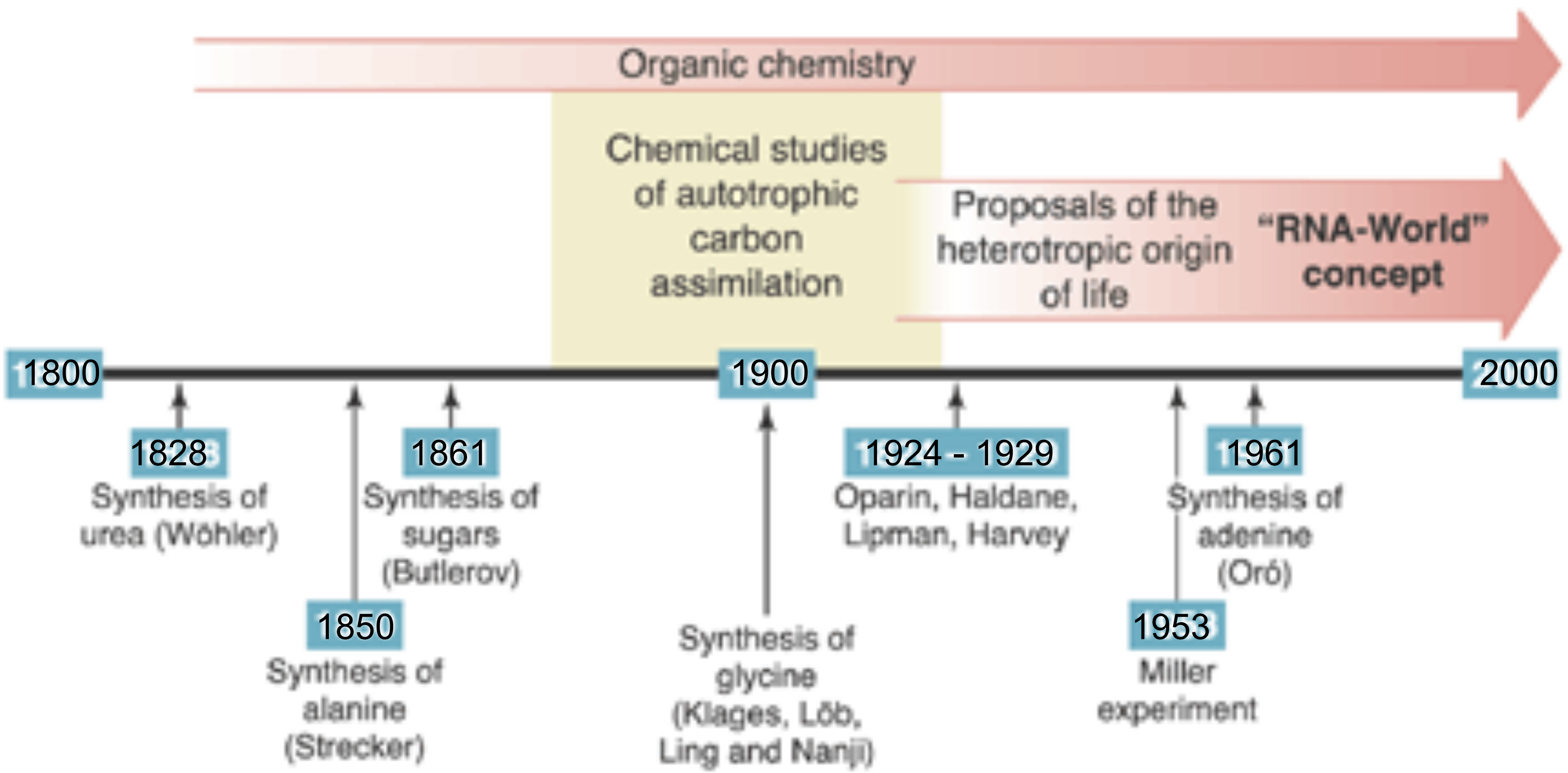


Self-sustained replication of RNA molecules Wochner et al. (2011)

RNA ribosomal catalyzes peptide-bond formation (Hsiao et al 2009)



Ribozymes catalyze metabolic reactions (Fusz *et al*, 2005, *Chem. Biol.* 12: 941)



Bada & Lazcano (2003) *Science* **300**: 745

What is the RNA World?

There are many definitions of the RNA World, including several contradictory ones. Any definition should recognize the role of ribonucleotides and modified ribonucleotides as part of the RNA World.

Recognition of the evolutionary significance of RNA catalytic activities implies that the origin of life is no longer synonymous to the origin of the genetic code

The heterotrophic theory of the origin of life: a contemporary reassessment

reducing atmosphere

↓

synthesis of organic compounds & formation of the primitive soup

↓

coacervates

↓

anaerobic heterotrophic bacteria

synthesis & accumulation of organic compounds

↓

RNA World

↓

DNA/RNA/protein cells

Consilience* and the heterotrophic theory of the origin of life

It is impossible to demonstrate that this is the evolutionary pathway that led to the origin and early evolution of life.

However, the available evidence from widely different scientific fields is consistent with the possibility that it happened this way.

* E. O. Wilson (1998) *Consilience: the unity of knowledge* (Knopf, New York)

The study of the origin and early evolution of life: some methodological issues

STAGE	METHODOLOGIES
synthesis & accumulation of organic molecules	characterization of extraterrestrial organic compounds Miller-Urey type model experiments
RNA World	characterization of ribozymes *In vitro* evolution of RNA-based systems theoretical models (v.gr., quasi-species) synthetic life experiments
RNA/protein cells	evolutionary biochemistry comparative genomics RNA viruses

Some examples of self-organization which may be relevant to the origin of life *

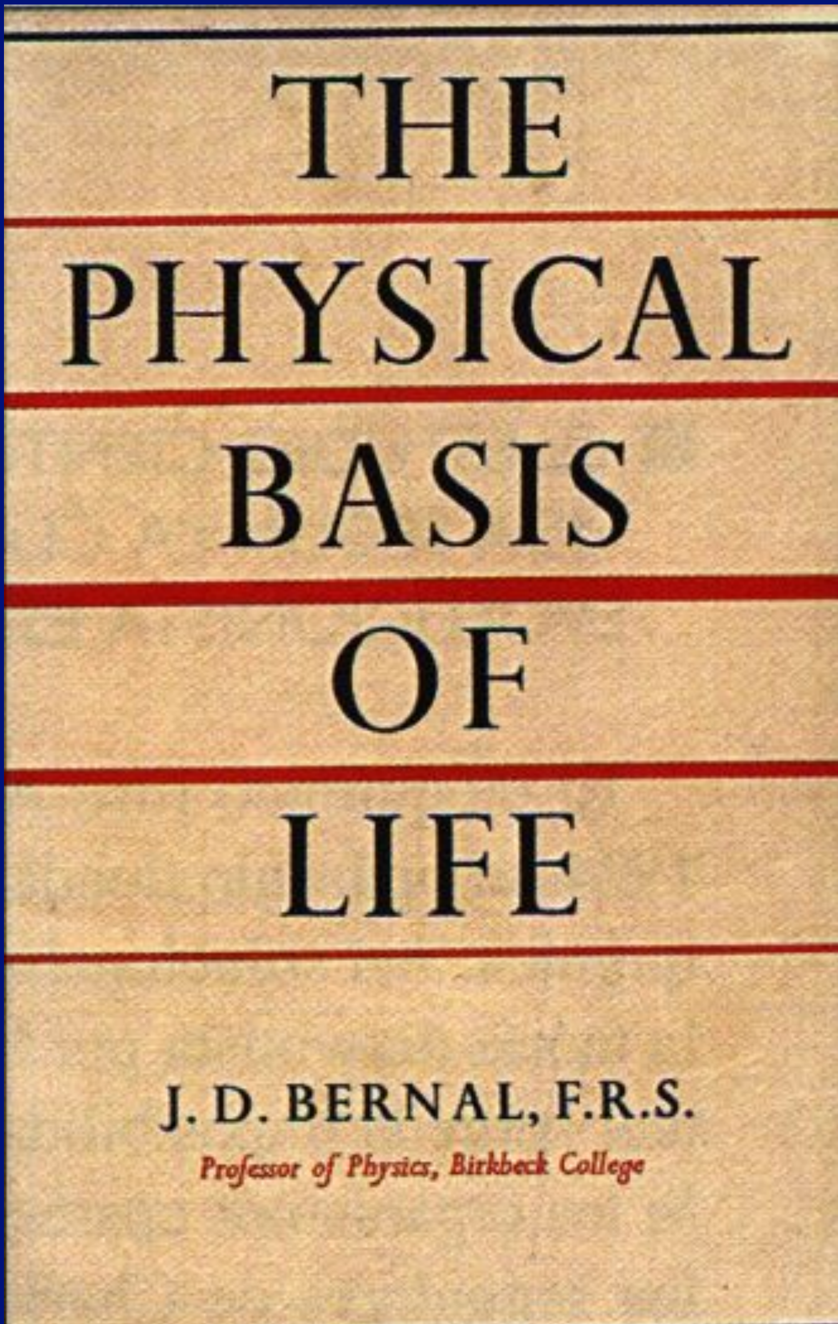
1. Formation of micelles, liposomes and lipid vesicles from prebiotic amphiphiles;
2. Self-assembly of nucleic acids (base-bearing polymers);
3. Fe-S catalytic clusters;
4. Mineral and organic compounds complexes (clays and bases); and
5. Autocatalytic synthetic reactions (formose reaction)

* Lehn 2002; Orgel 2008; Lazcano 2010; Budin & Szostak 2010

Evolutionary history or emergence of complexity?

To understand the nature of life, we must recognize both the limits imposed by the laws of physics and chemistry, as well as history's contingency. For instance, concepts like natural selection and endosymbiosis are consistent with physical laws, but cannot be deduced from them.

This is shown, for instance, in the different types of lipids found in archaeal and bacterial membranes. Both can self-organize and form liposomes or bilayers, but have different evolutionary histories.



"It is mere rubbish thinking at present of the origin of life; one might as well think of the origin of matter…"

Charles Darwin (1887)

"This does not mean that we should accept wild hypothesis of the origin of life or of matter, which simply conceal ignorance, but rather that we should attempt almost from the outset to produce careful and logical sequences in which we can hope to demonstrate that certain stages must have preceded certain others, and from these partial sequences gradually built up one coherent history. There are bound to be gaps where this cannot be done, but until the process is attempted these gaps cannot be located, nor can the attempt be made to fill them up…"

CONCLUSIONS….