Erasmus Intensive Program 2014:
Origin, Evolution and Future of the Biosphere

The biochemical roots of the RNA World: the history of a concept

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Banuyls 2014

The emergence of life in the Universe

The possibility that other planets were inhabited was discussed in the past, sometimes in considerable detail, by naturalists and philosophers alike. More often than not, these were speculations that rested on the idea of a uniform Universe but with little or no empirical basis. How life had appeared in other bodies was not discussed.

Despite claims on the contrary, there is little or no epistemological continuity of these ideas with contemporary attempts to study life in the Universe.

Our current understanding and efforts to study the origin of life resulted from the 19th century development of evolutionary theory, first with Lamarck and then by Darwin.

At the turn of the 20th century,

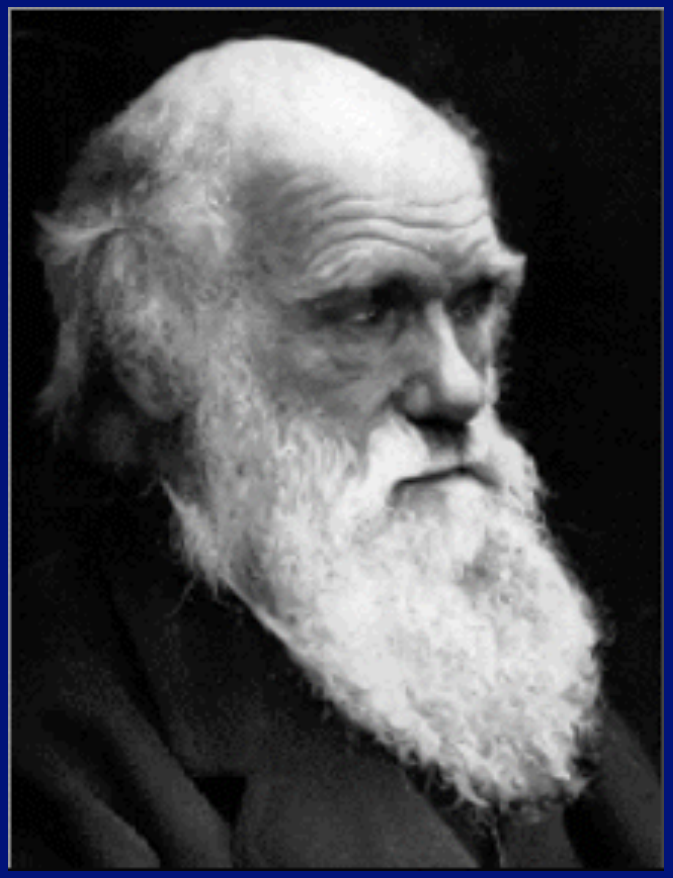
1. The trend towards a chemical description of living phenomena had led both to the identification of protoplasm as basis of life and to the development of biochemistry;

2. Viruses seem to confirm the existence of subcellular entities for the basis of life;

3. Mendel's laws were "rediscovered"; and

4. Many accepted the idea of evolution, but Darwinian explanations based on natural selection were rejected

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.

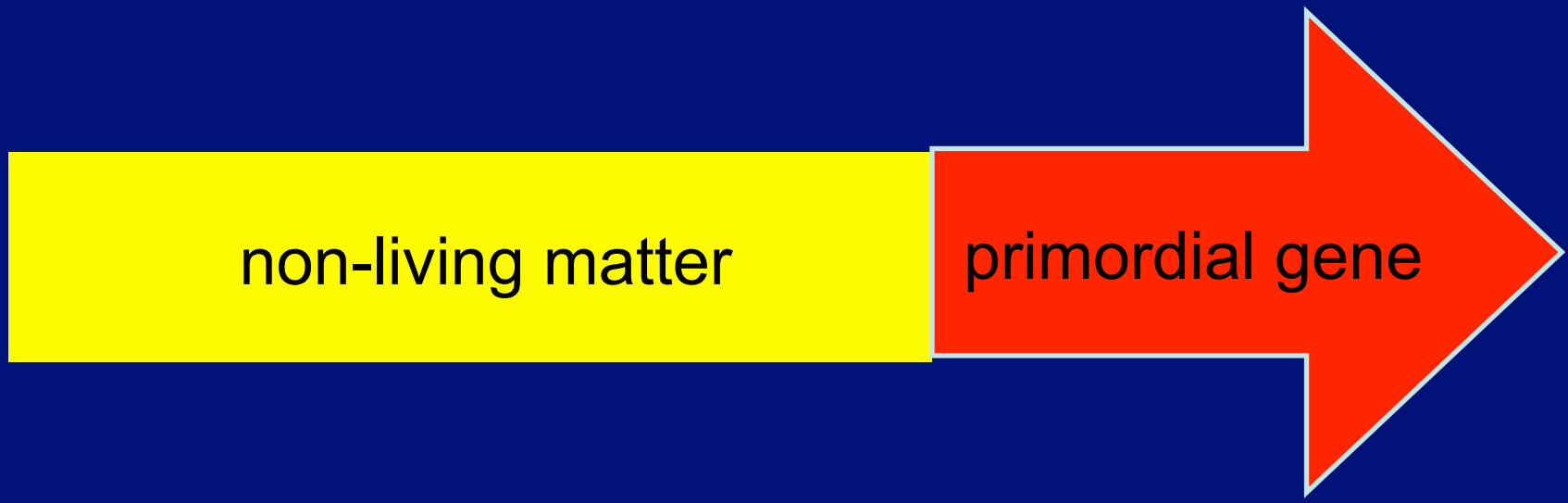
Herman J. Muller's single gene theory of the origin of life

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


non-living matter
primordial gene

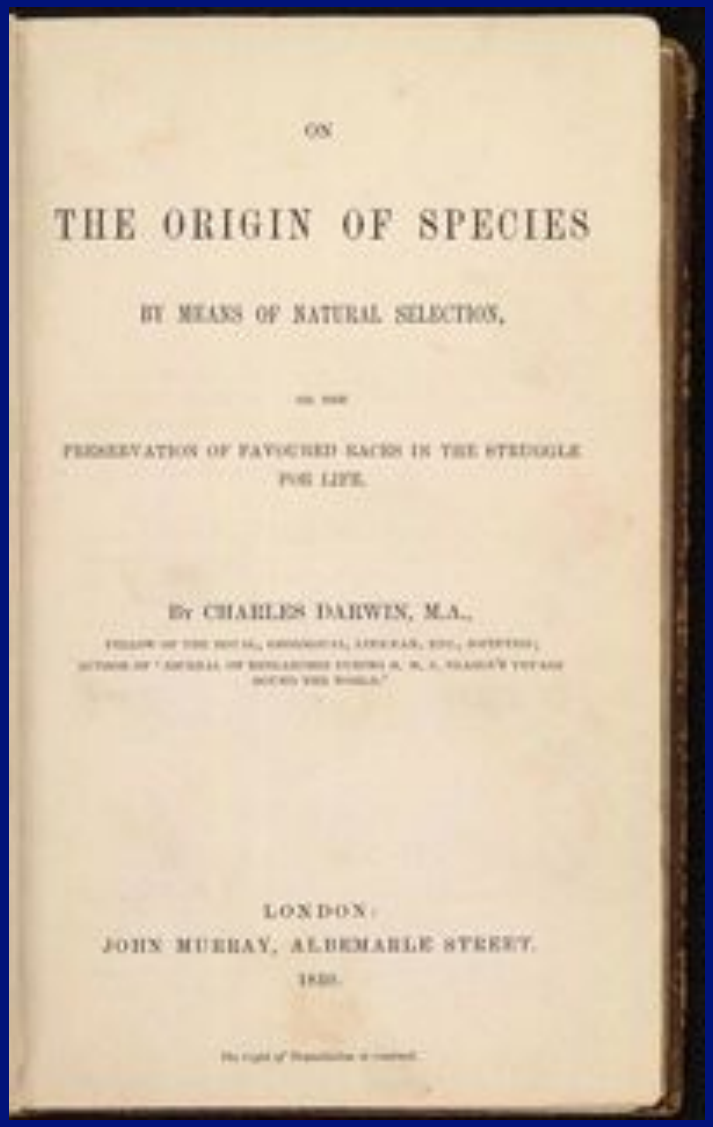
Intellectual and scientific genealogies: Herman Muller and the primordial gene as the origin of life

Gregor Mendel

Thomas Hunt Morgan

Hermann J. Muller

Darwin and the origin of life



ON

THE ORIGIN OF SPECIES

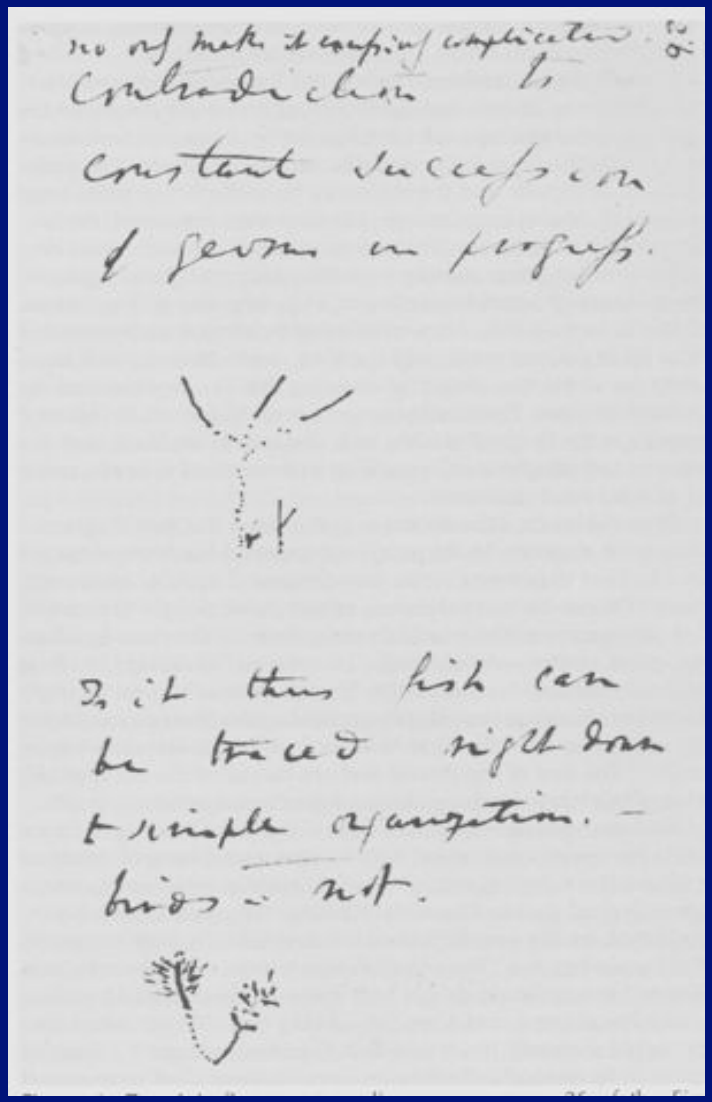
BY MEANS OF NATURAL SELECTION,

OR THE

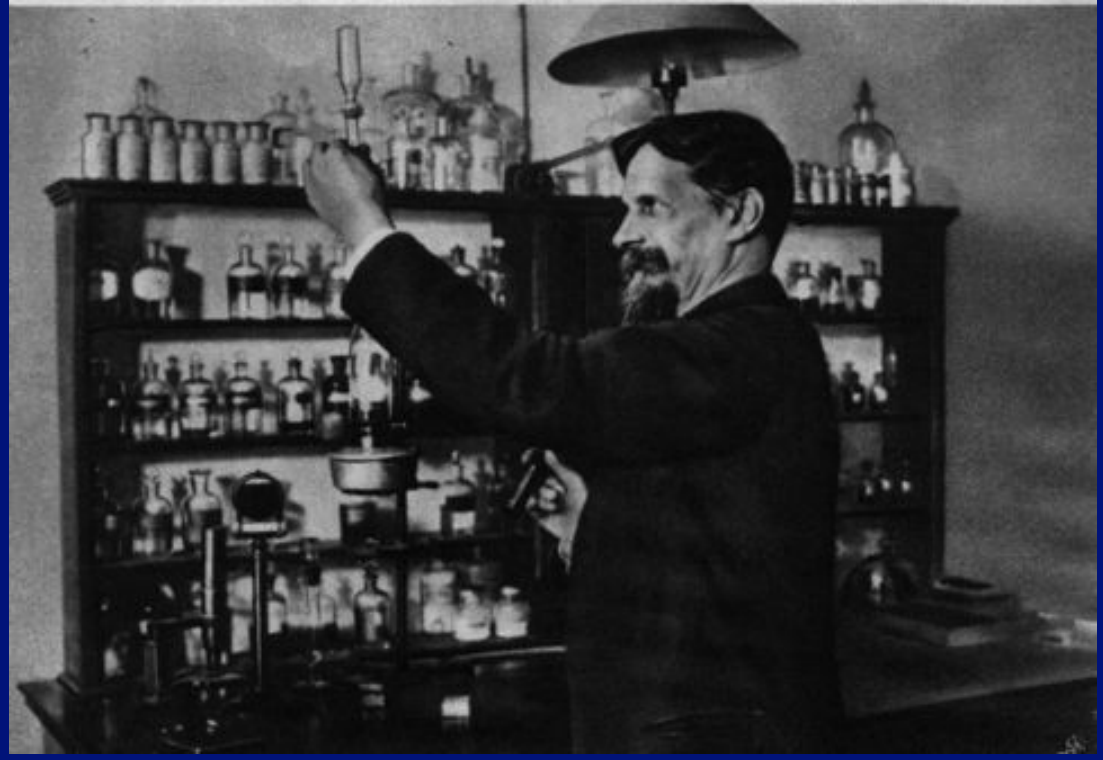
PRESERVATION OF FAVOURED RACES IN THE STRUGGLE FOR LIFE.

By CHARLES DARWIN, M.A.,

LONDON:
JOHN MURRAY, ALBEMARLE STREET.
1859.



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



Starting in 1865, Arkadi K. Timiriazev starts promoting Darwin's ideas, an effort that would play a significant role in the secularization of Russian culture (cf. Vucinich, A.,1988)

A number of historians, sociologists, philosophers and, of course, left-wing politicians are attracted to Darwinism. They include Kropotkin, Plekhanov and many others.

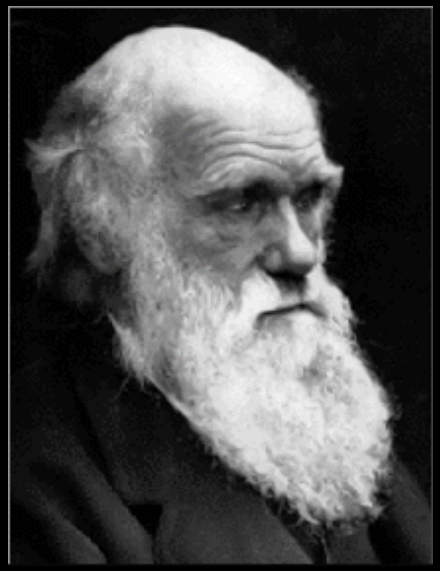
Some important traits of Russian/Soviet Darwinism

1. From 1880 onwards a number of conservative thinkers like Strajov, Merscherski and Danilievski (a staunch defensor of monarchic absolutism) start a campaign against Darwin's ideas;

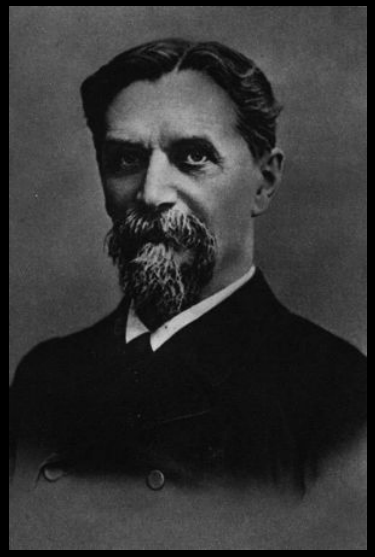
2. The "rediscovery" of Mendel's ideas and the role of mutation was seen by many as an attack against Darwinism.

   This will lead Tymiriazev (1912) to state that Mendelists and mutationists are the principal enemies in the struggle against anti-darwinists.

Intellectual & scientific genealogies



Charles Darwin

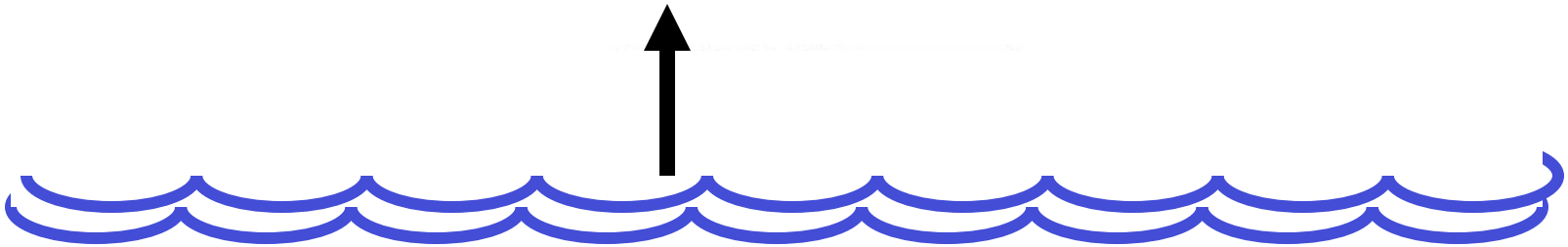


Kliment A. Timiriazev

Alexandr I. Oparin

CO_2 and H_2O- rich atmosphere

primitive heterotrophic cells



primitive soup

Haldane, 1929

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

CE 481

ie water which can not be eliminated. For oxidase tivity, the oxidation of tetra methyl para phenylene iamine showed a slight activity. On the addition f hydrogen peroxide to this reagent a very active eroxidase action was shown. Catalase was determined by means of the Van Slyke apparatus commonly used for the determination of amino acids, he oxygen being liberated in the reaction vessel and easured in the burette. The material was collected rom pure culture and the determinations were completed within a few minutes. No catalase activity as shown by the Phormidium filaments either suspended in water or after grinding for a long time in 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. At the altitude increases there would be found a level at which water would maintain a constant temperature by boiling at a tem-

THE ORIGIN OF LIFE 357

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 animal life from de
during the greater
man. In fact, the th
its death-blow until
arrived. But befor
Pasteur had put th
generation, many inv
Before the last third
strated that maggots
from flies, and that o
in the meat were m
were challenged by
by the high authority
to be specious by the
of Cagniard de la To
the solid foundation

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.

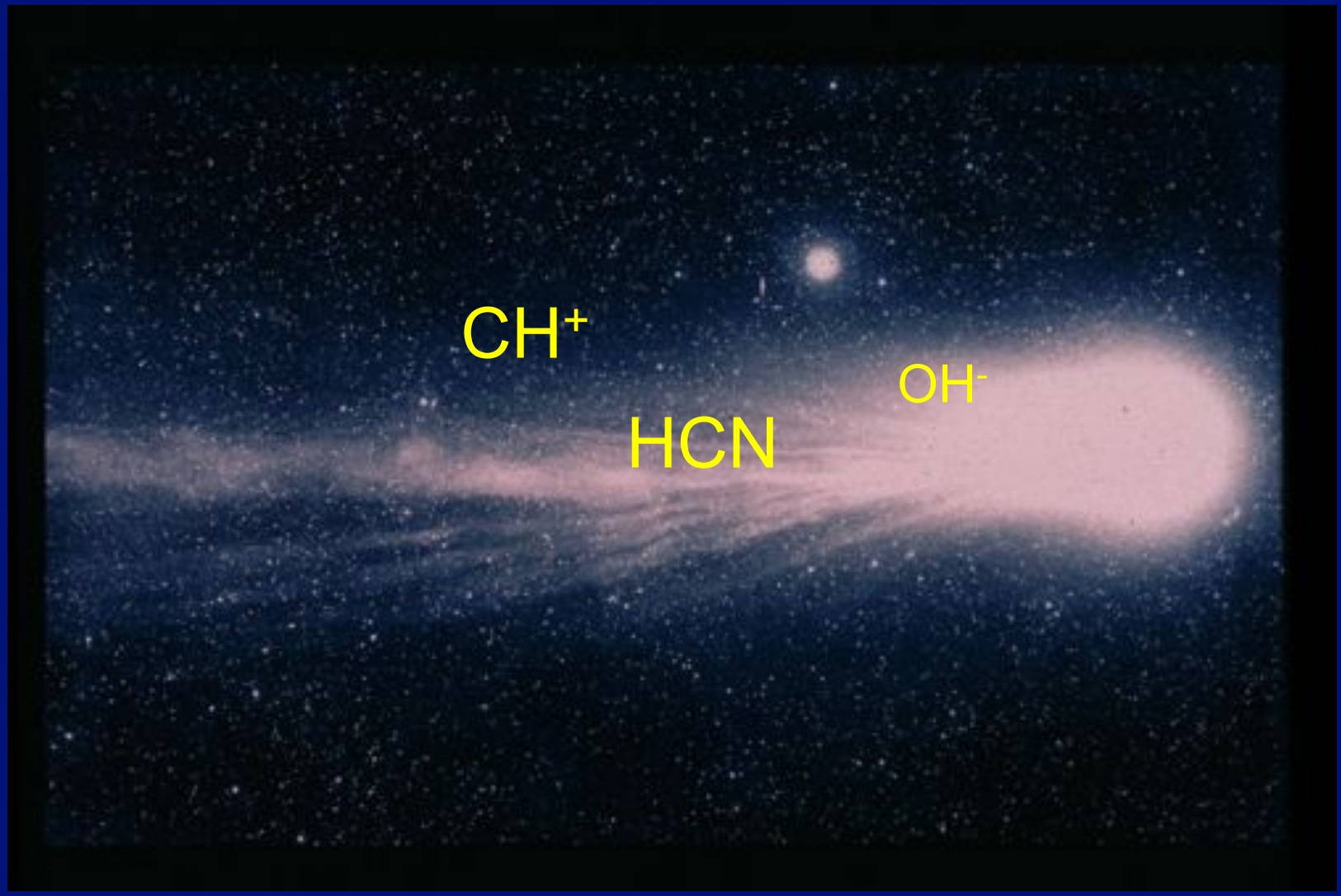
The more ardent materialists tried to fill in the details of this process, but without complete success. Oddly enough, the few scientific men who professed idealism agreed with them. For if one can find evidences of mind (in religious terminology the finger of God) in the most ordinary events, even those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

3

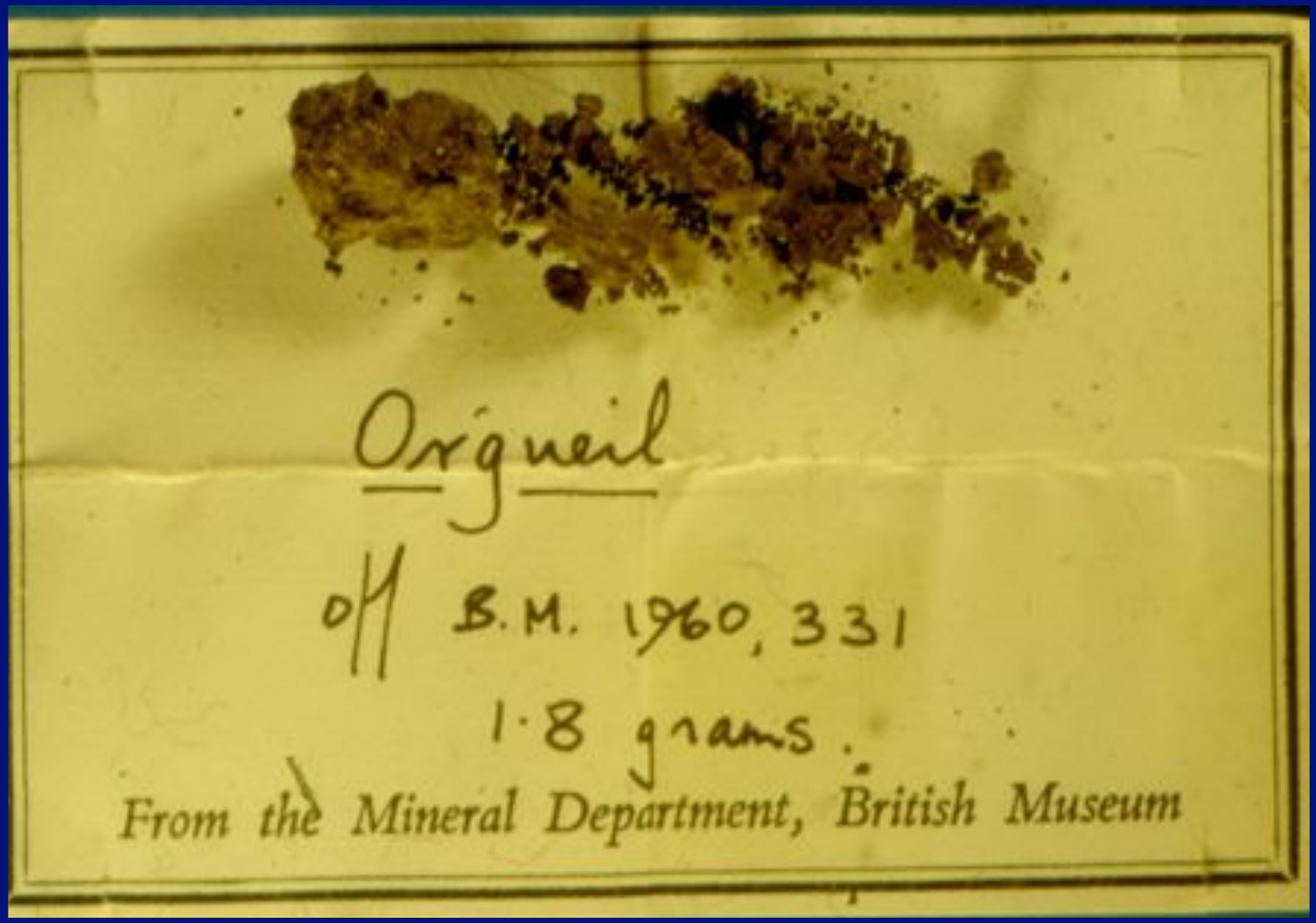
Bada & Lazcano, 2003

How did Oparin support his assumption of prebiotic organic synthesis as a prerequisite for the origin of life?

Organic compounds in cometary spectra



…and in carbonaceous meteorites



Early abiotic synthesis of biochemical monomers

1) Proust 1807

HCN $\xrightarrow{OH^-}$ polymer + adenine (?)

2) Wöhler 1828

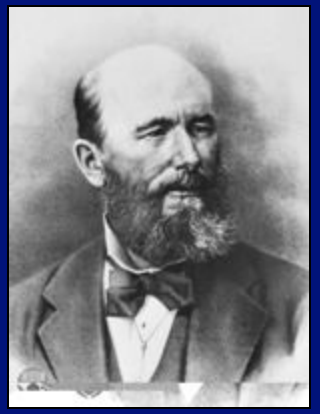
$NH_4NCO \rightarrow$ urea

3) Strecker 1850

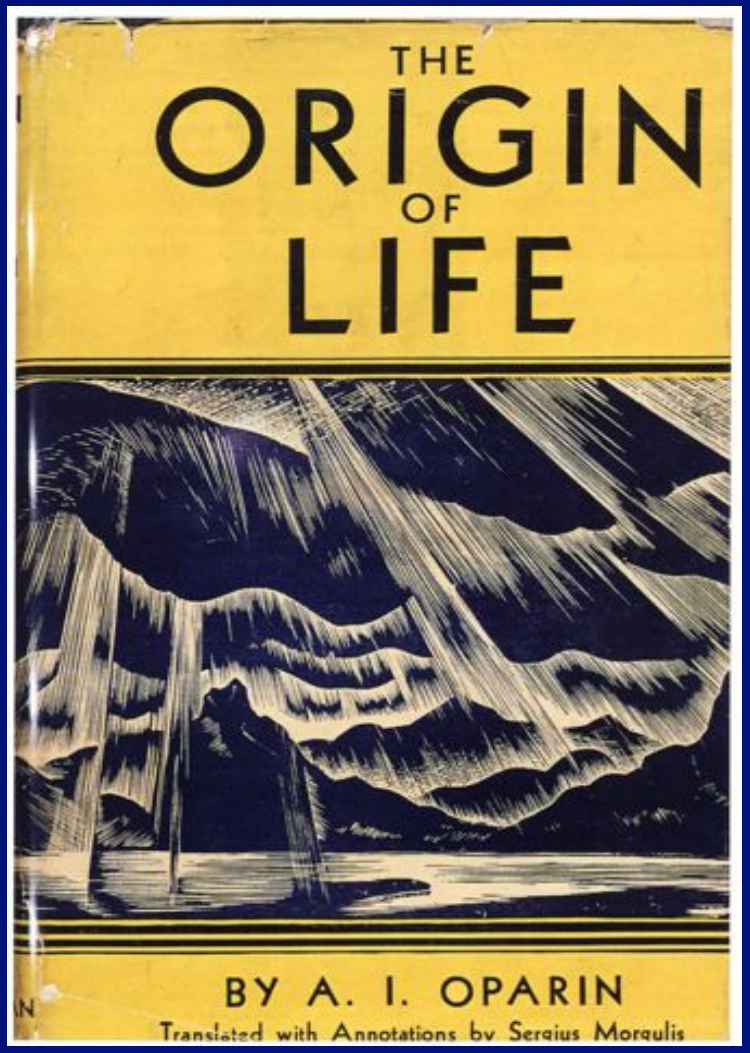
$CH_3CHO + NH_3 + HCN \rightarrow$ alanine

4) Butlerow 1861

HCHO $\xrightarrow{OH^-}$ sugars



Heterotrophic origin of life



reducing atmosphere

↓

synthesis of organic compounds & formation of the primitive soup

↓

coacervates

↓

primordial heterotrophic anaerobic bacteria

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

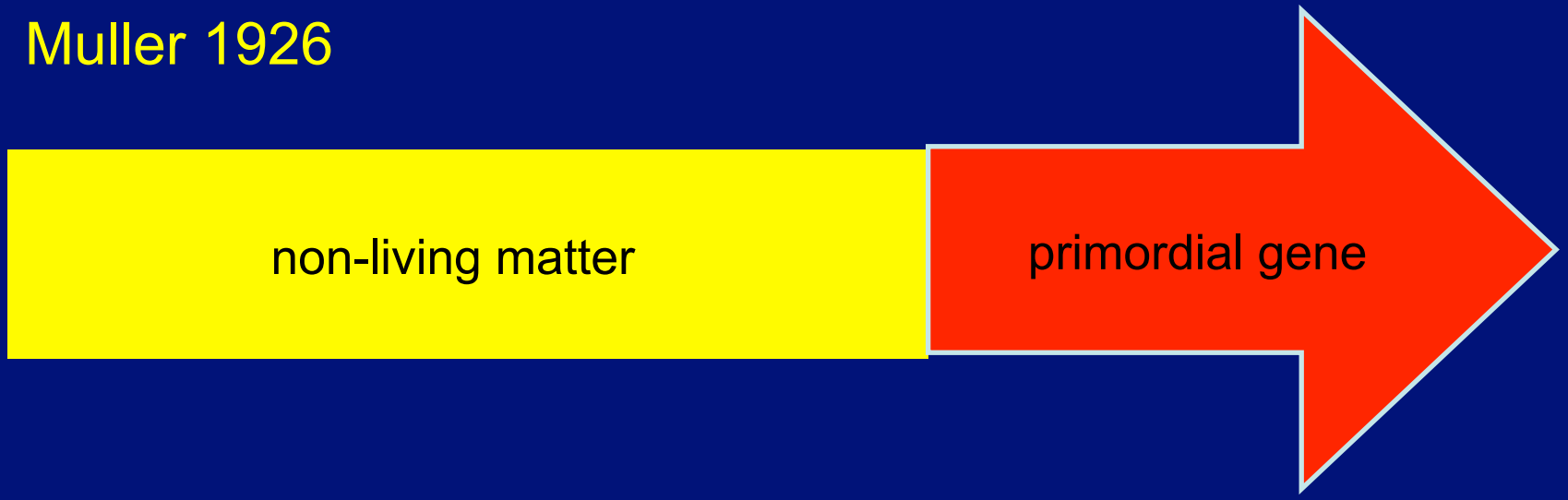
1. Ernst Haeckel, who was a major influence in Oparin's work, had assumed that Monera lacked all traces of the hereditary substances of other organisms

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

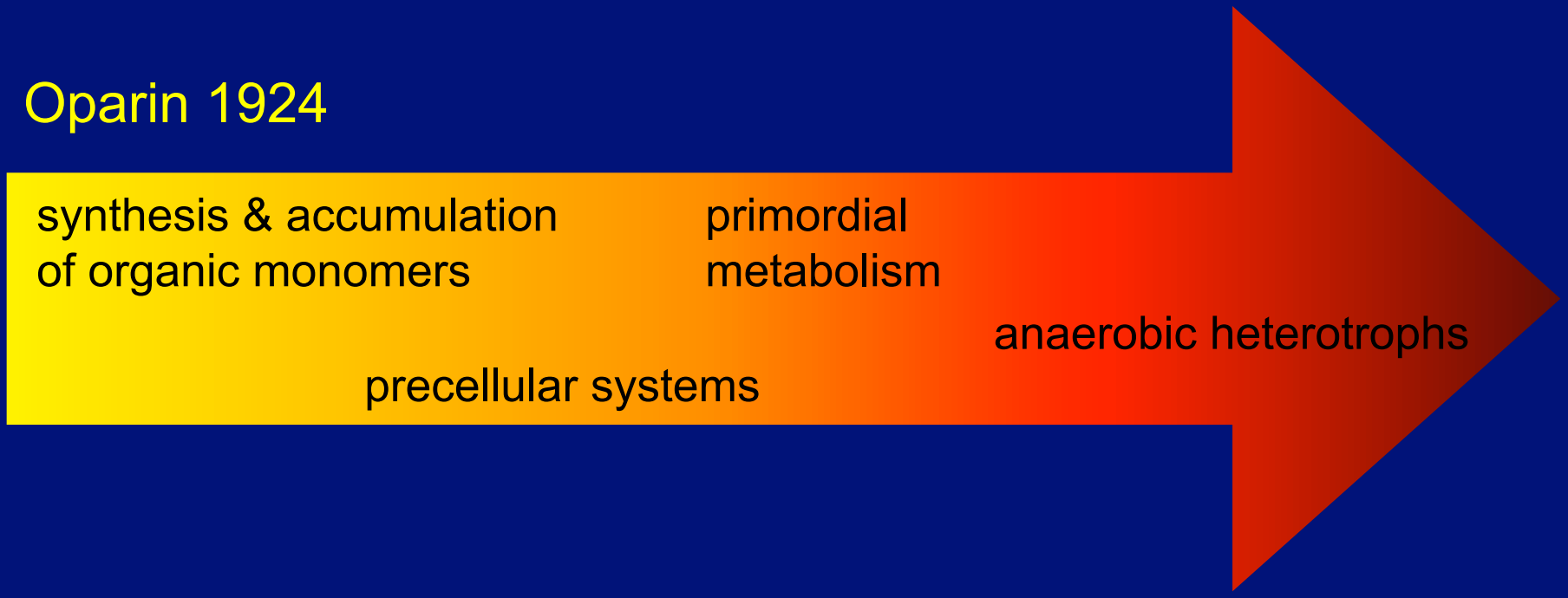
2. "… bacteria have no genes in the sense of accurately quantized portions of hereditary substances; and therefore have no need for accurate division of the genetic system which is accomplished by mitosis."

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

Muller 1926



Oparin 1924



Harold C. Urey's primitive terrestrial atmosphere

$C + 2H_2 \rightarrow CH_4$

$N_2 + 3H_2 \rightarrow NH_3$

$O_2 + 2H_2 \rightarrow H_2O$

$S + H_2 \rightarrow H_2S$

$CO_2 + 6H_2 \rightarrow CH_4 + 2H_2O$

In the early 1950's, it was generally accepted that:

a) living beings could be divided into three major (Haeckelian) kingdoms (plants, animals and microbes);

b) the earliest traces of life were about 600 million years old;

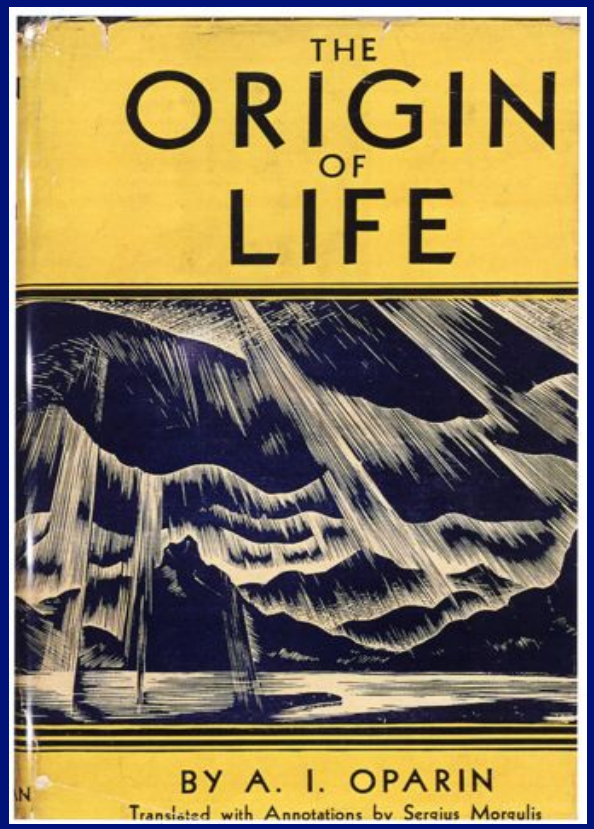
c) the emergence of the biosphere had been a lengthy process involving billions and billions of years;

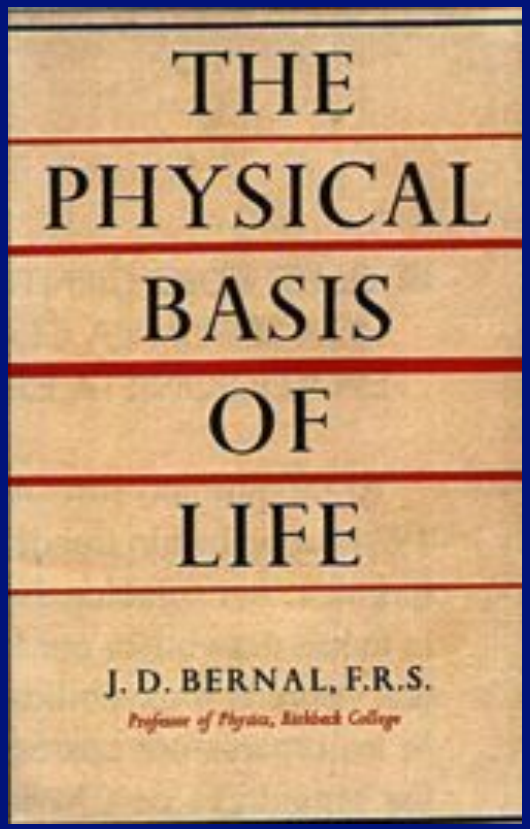
d) proteins played a major role in genetic continuity;

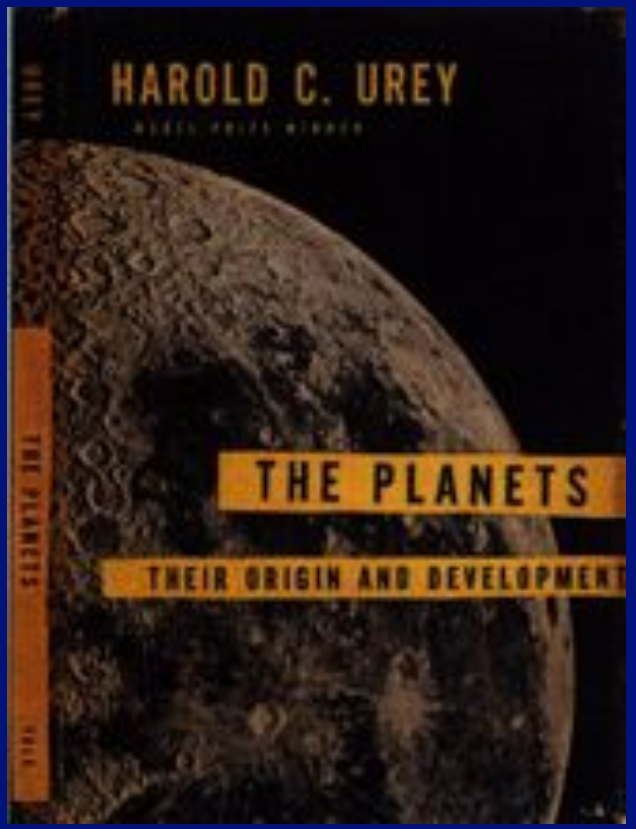
e) the formation of planetary systems was rare; and

f) space exploration was unlikely, among other misconceptions

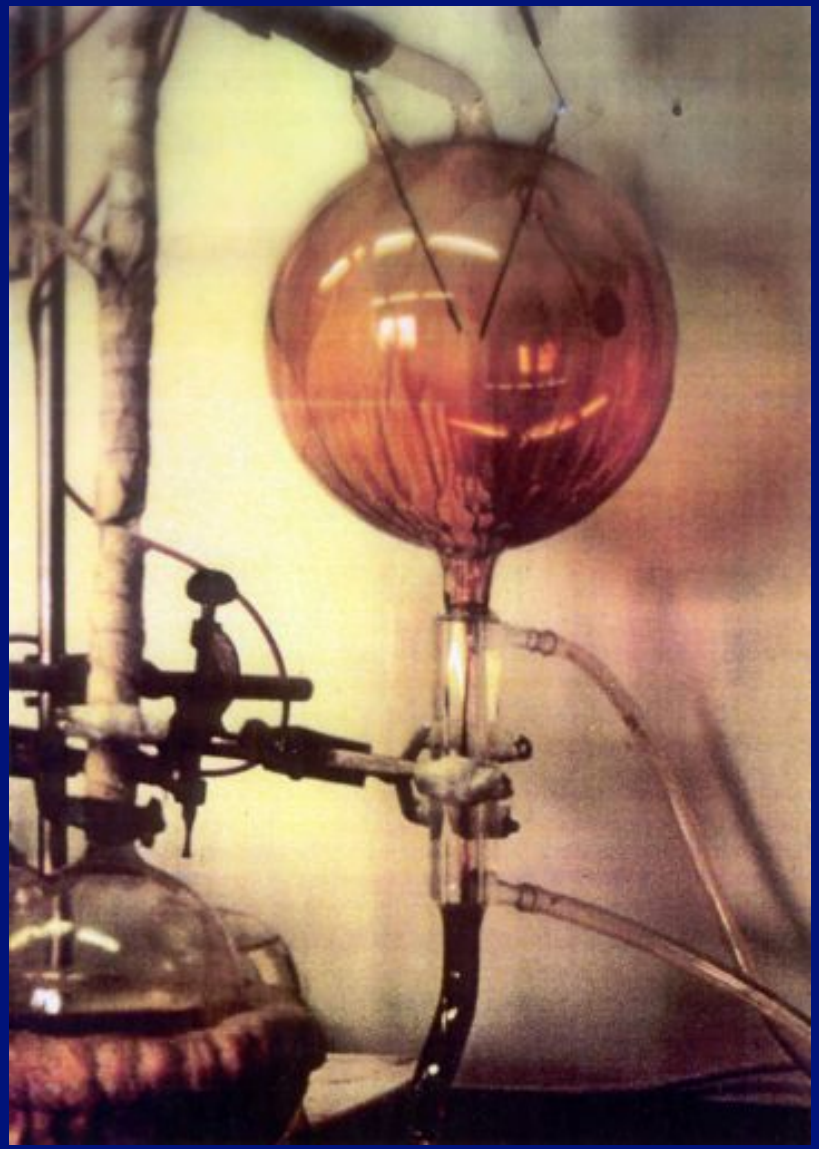
The authors that shaped S. L. Miller's ideas on the origin of life

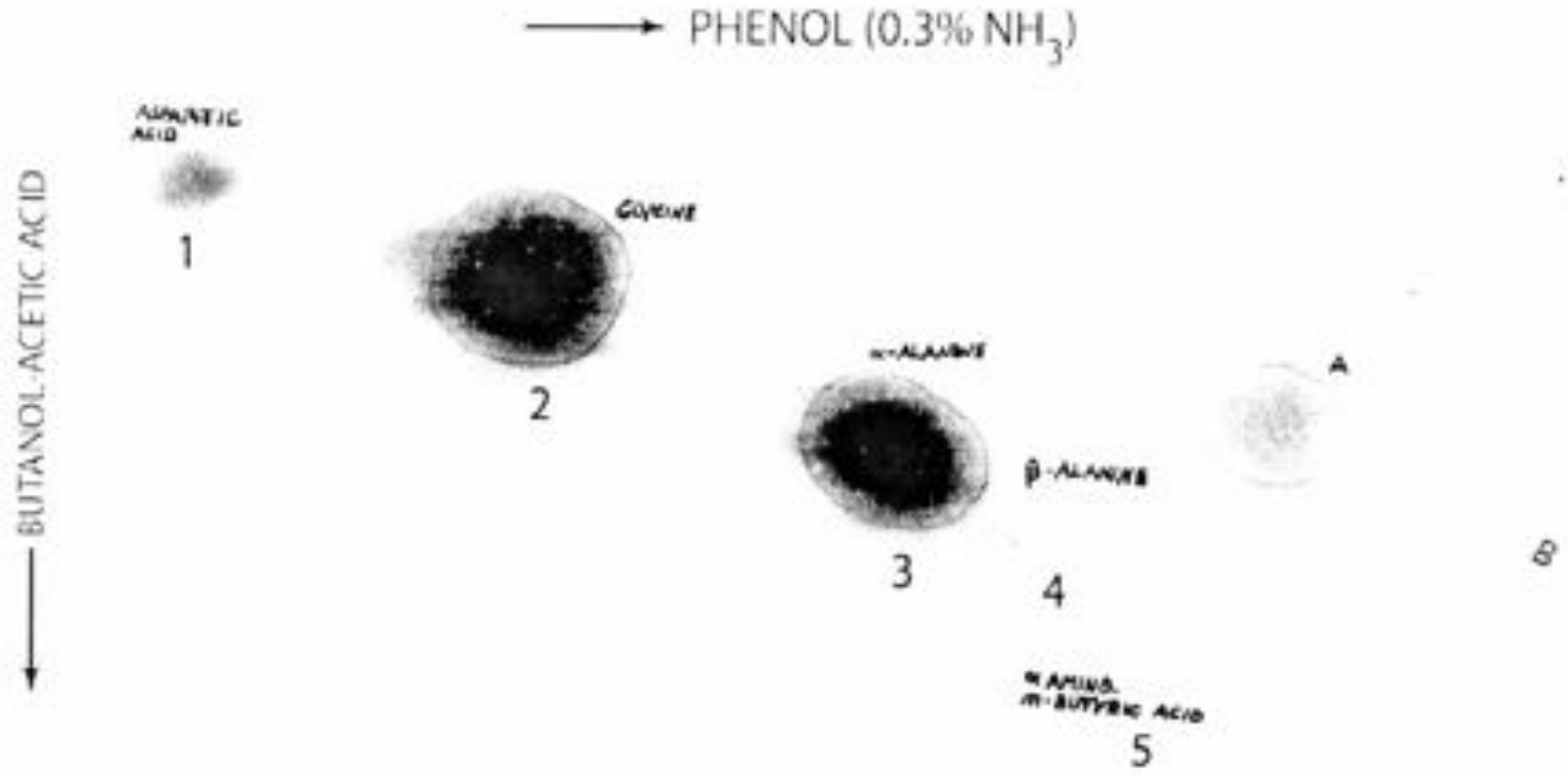






The 1953 Miller-Urey experiment




PHENOL (0.3% NH3)
BUTANOL-ACETIC ACID
1
2
3
4
5
6

Los Angeles Examiner
Wed., Apr. 1, 1953 Sec. I—5

UREY COSMIC THEORY TOLD

Life on this earth could have had its inception when light-ning ...

SCIENCE

Amino Acids Produced from CH_4, NH_3, H_2O, and H_2

How life may have started

An experiment showing how ... gun on the earth has been per... year-old University of Chicago ... ing under Nobel Prize-win... Stanley Miller built ... containing ... monia—the ... scientists beli... phere of ...

Scientific American, July, 1953

Los Angeles Times 19
MONDAY, JUNE 8, 1953—Part I

Many Doubt Science Can Create Life

Yes, will be
No, will not
No opinion

N. Y. HERALD TRIBUNE
May 15, 1953

Scientist, 23, Hailed

Test Backs Theory Life Began as Chemical Act

Genesis by Lightning

A NEW way to make organic compounds was reported last ... young chemist at the U... Chicago. But perhaps "ne..." right word, for some s... that this method is bi... of years old; that it ... od used by natu... started life on t...

Notes of the W...

Prof. Harold C. Urey ... that life on ... through spont...

Semi-Creation

Many scientists think that life appeared on earth when the atmosphere, instead of being its present mixture of oxygen, nitrogen and carbon dioxide, contained methane, ammonia and hydrogen. These ingredients, still to be found in the atmospheres of Jupiter and Saturn, slowly combined into larger and larger (carbon-containing) molec... in the ...

STUDENT MILLER
A million years to go.

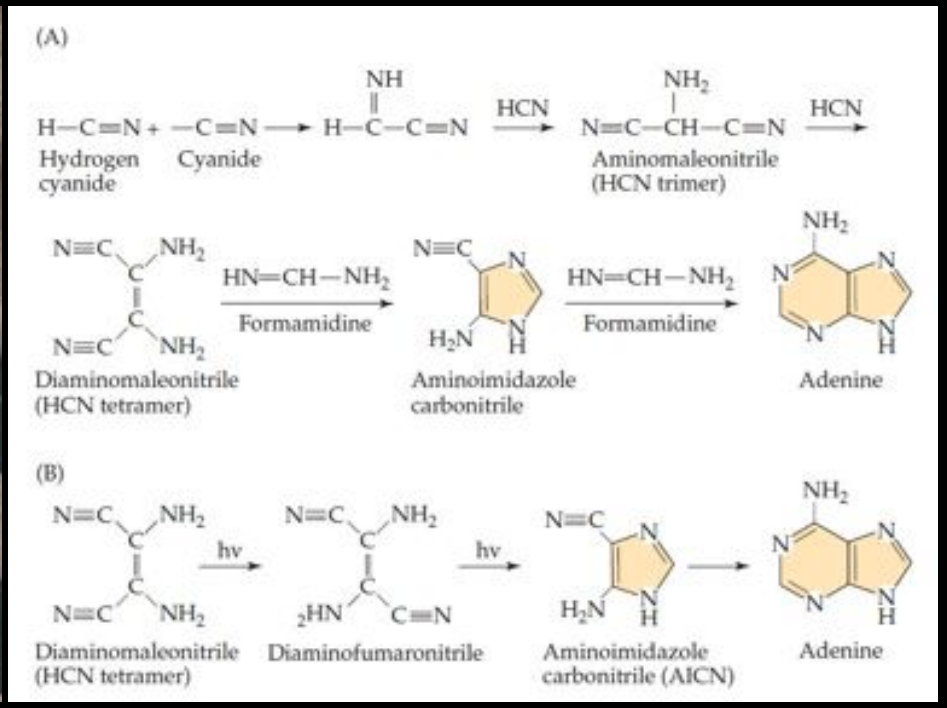
TIME, MAY 25, 1953

The harvest of ‘53

Watson & Crick and the DNA double helix model

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

Molecular biology and the origins of life: the prebiotic synthesis of adenine*



a) Oró, 1960; b) Ferris & Orgel, 1966

* Did DNA form in the prebiotic soup?

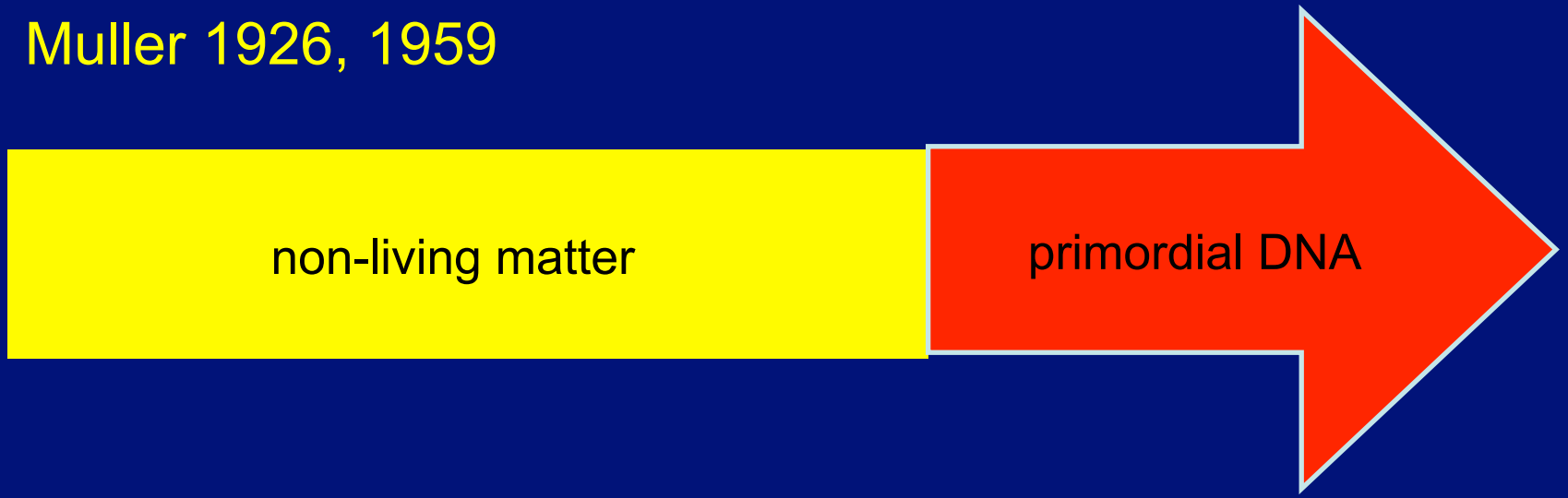
Did life appear with the spontaneous formation of DNA in the primitive soup?

Hermann J. Muller (1890-1967)

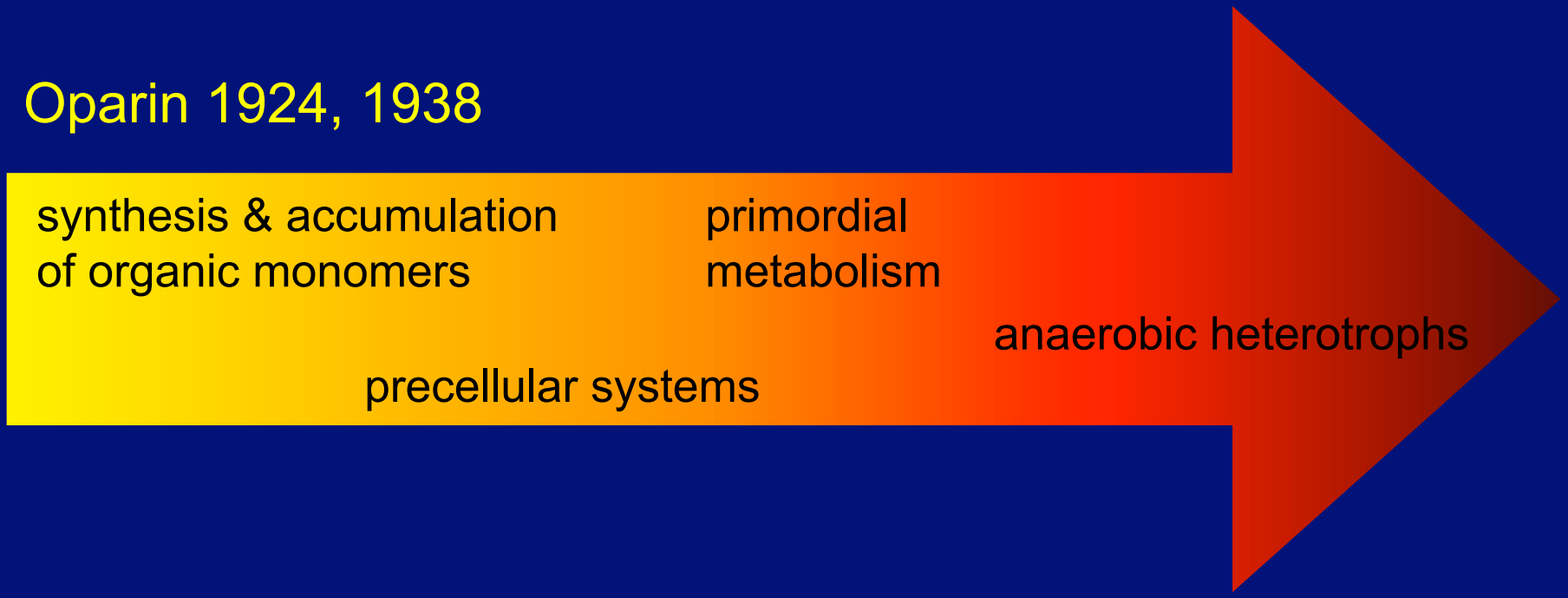
catalytic & autocatalytic primordial gene (1926)

catalytic & autocatalytic primordial DNA (1959)

Muller 1926, 1959



Oparin 1924, 1938



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

During the first twenty years following the 1953 Miller experiment, attempts to understand the origin of life were shaped, to a considerable extent,

1) scientifically,

   * by the fact that since the late 1940´s, evolutionary biology became an established field of research;

   * the unraveling of the details of DNA replication & protein biosynthesis; and

   * the development of space programs

2) in socio-political terms, by the atmosphere created by Cold War tensions.

A painful, excruciating situation: Cold War politics, ideology and science

"[the suggestion based on Haeckel that] protoplasm had originated first and had the capability of manufacturing not only the genetic material but also its own complex organization… The Russian Oparin has since the early 1930's espoused this view and has followed the official Communist Party line by giving the specific genetic materials a back seat."

H. J. Muller 1961

cf. Falk & Lazcano (2012)

АКАДЕМИК
АЛЕКСАНДР ИВАНОВИЧ ОПАРИН

Москва, Б. Калужская ул., д. 33.

Телефоны: В 2-34-61,
В 2-36-74

15 March 1956 г.

Professor L.Miller
California Institute
of Technology ,
California, USA.

Dear Colleague,

As you will see from the attached material in August 1957 in Moscow there will be held the International Symposium on the Origin of Life, which is convened in connection with the desire expressed by many prominent scientists working in various fields and in various countries, to meet and exchange opinion on the mentioned above complex and interesting question.

Taking into consideration your interest to the problem of the Origin of Life, expresed, in particular, in your excellent works on synthesis of amino acides in electrical discharges, I permit myself to hope that you will agree to participate in the work of the Symposium and will be good enough to deliver a report on your works.

Your early reply will be greatly appreciated.

Truly yours,

A.I.Oparin.

April 13, 1957.

Dr. Stanley L. Miller,
Columbia University,
College of Physicians and Surgeons,
630 West 168th Street,
New York 32, N. Y.

Dear Miller,

Thanks for your letter of April 10 in regard to the trip to Russia. I think I shall not go to this meeting. I am not going to put it on the basis of the things that you say, but just on the basis that I must get back to Chicago to look after my work. I have been away all year and I just cannot pull up again and travel off to Moscow within such a short time. I would like to go to Moscow, but I would much rather look after my research than make trips. I have not sent in any manuscript. The reason is that I have been working here on a paper on the atmospheres of the planets for seven months, and wish to put into the paper my general conclusions in regard to atmospheres as a result of that study, and it has only been completed a couple of weeks ago.

I am very put out by the behavior of the Russians and do not feel like doing anything to indicate any acquiescence in their treatment of Hungary but to the Russians I probably will not say this since I think it would do no good.

I do not know how to advise you. I think each of us must make up his own mind about this. The nuclear scientists went some time ago, and if they will let nuclear scientists go in the United States without stigmatizing them, I should think that innocent people like us might also go. But one never knows what a McCarthy will do in the future. It is a very sad situation.

Please give my best regards to Rittenberg.

Very sincerely,

Harold Urey

In sociopolitical terms….

"I do not know how to advise you. I think each of us must make his own mind about this. The nuclear scientists went some time ago, and if they will let the nuclear scientists go in the United States without stigmatizing them, I should think that innocent people like us might also go, but one never knows how what a McCarthy will do in the future. It is a very sad situation."

Harold C. Urey to Stanley L. Miller, April 13, 1957

UNITED STATES
ATOMIC ENERGY COMMISSION
NEW YORK OPERATIONS OFFICE
70 COLUMBUS AVENUE
NEW YORK 23, NEW YORK

TELEPHONE NO.:
PLaza 7-3600

Refer to:
SS:MJK

June 19, 1957

Mr. Stanley Lloyd Miller
50 Haven Avenue
New York 32, N. Y.

Dear Sir:

In accordance with your proposed foreign travel, transmitted herewith for your completion and return are five foreign travel forms.

You are advised at this time of your responsibilities under the Atomic Energy Act of 1954:

1. To report any significant changes in your itinerary.

2. To avoid disclosure of any Restricted Data to which you have had access under our program to any unauthorized person.

3. To report to this office, by mail or by telephone, upon your return to the United States.

If, while on foreign travel, you feel that your safety is in jeopardy at any time, please contact the nearest U. S. Diplomatic Representative.

Your security clearance will be terminated if you will be out of the United States beyond six months unless your travel is in connection with United States Government business.

Thank you for your cooperation in this matter.

Very truly yours,

Harry R. Walsh

HARRY R. WALSH
Director, Security Division

Enclosure:
AEC-290 (5)

August 6, 1956

Mr. Frederick T. Merrill
Special Assistant to the
Assistant Secretary for Public Affairs,
Room 107, State Dept., Annex 5,
United States Department of State
Washington 25, D. C.

Dear Mr. Merrill:

Dr. Consolazio of the National Science Foundation suggested that I inform you of an invitation from A. I. Oparin I received to attend a symposium on the Origin of Life to be held in Moscow on August 19-24, 1957. The conference is being sponsored by the International Union of Biochemistry and the U.S.S.R. Academy of Sciences.

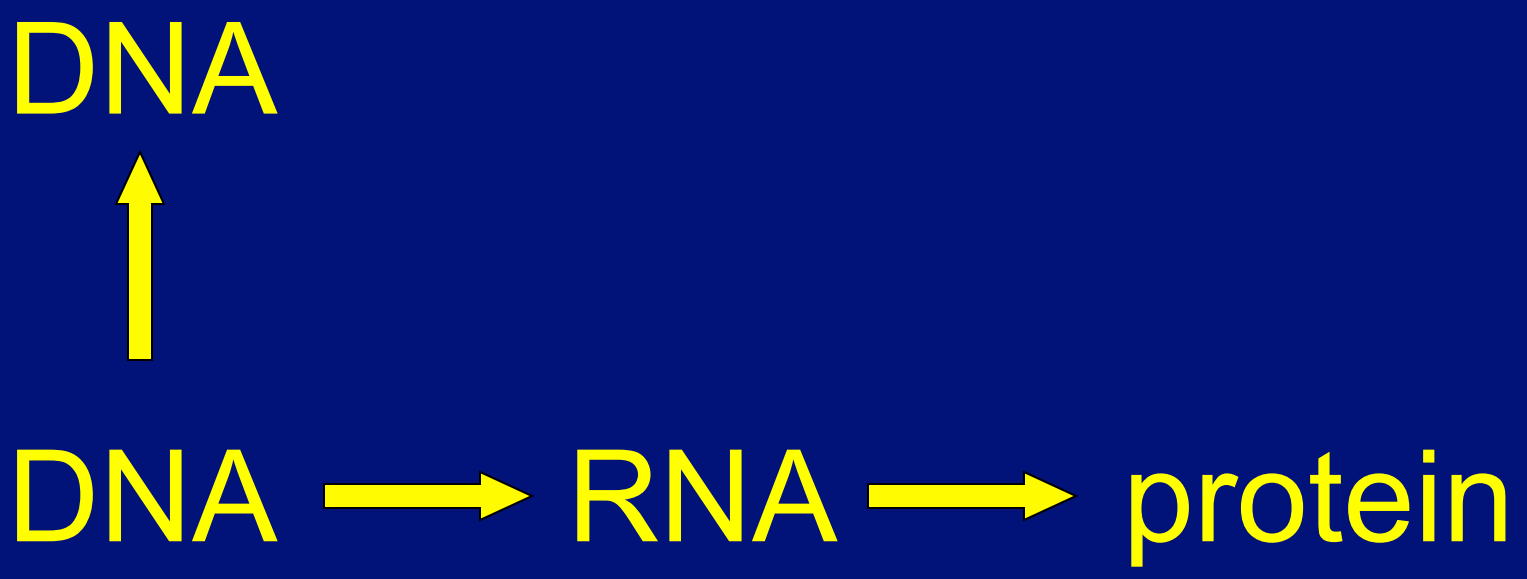
The invitation was extended to me because of my research on the synthesis of organic compounds on the Earth before life began. I believe that several other Americans have been invited to this conference including Professor E. Chargaff of this department.

I would like to know if there are any steps I should take at this time concerning this invitation.

Very sincerely yours,

Stanley L. Miller

rh


DNA
DNA
RNA
protein

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

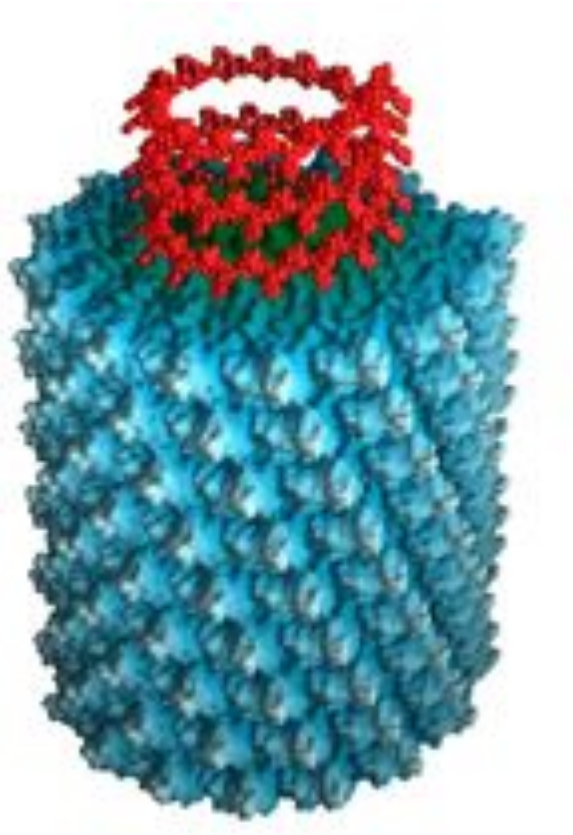
Some viruses have RNA

Analysis of TMV show a preparation that contained “0.5 per cent phosphorus and 2.5 per cent carbohydrate. The last two constituents can be isolated as nucleic acid of the ribose type from protein denatured by heat.”

C. F. Bawden, C. F., Pirie, N. C., J. D. Bernal, J. D. and I Frankuchen (1936) Liquid crystalline substances from virus-infected plants. *Nature* **138**: 1051

This is followed by the demonstration that the infectivity of the TMV was due to RNA by Fraenkel-Conrat, Schramm and others

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,

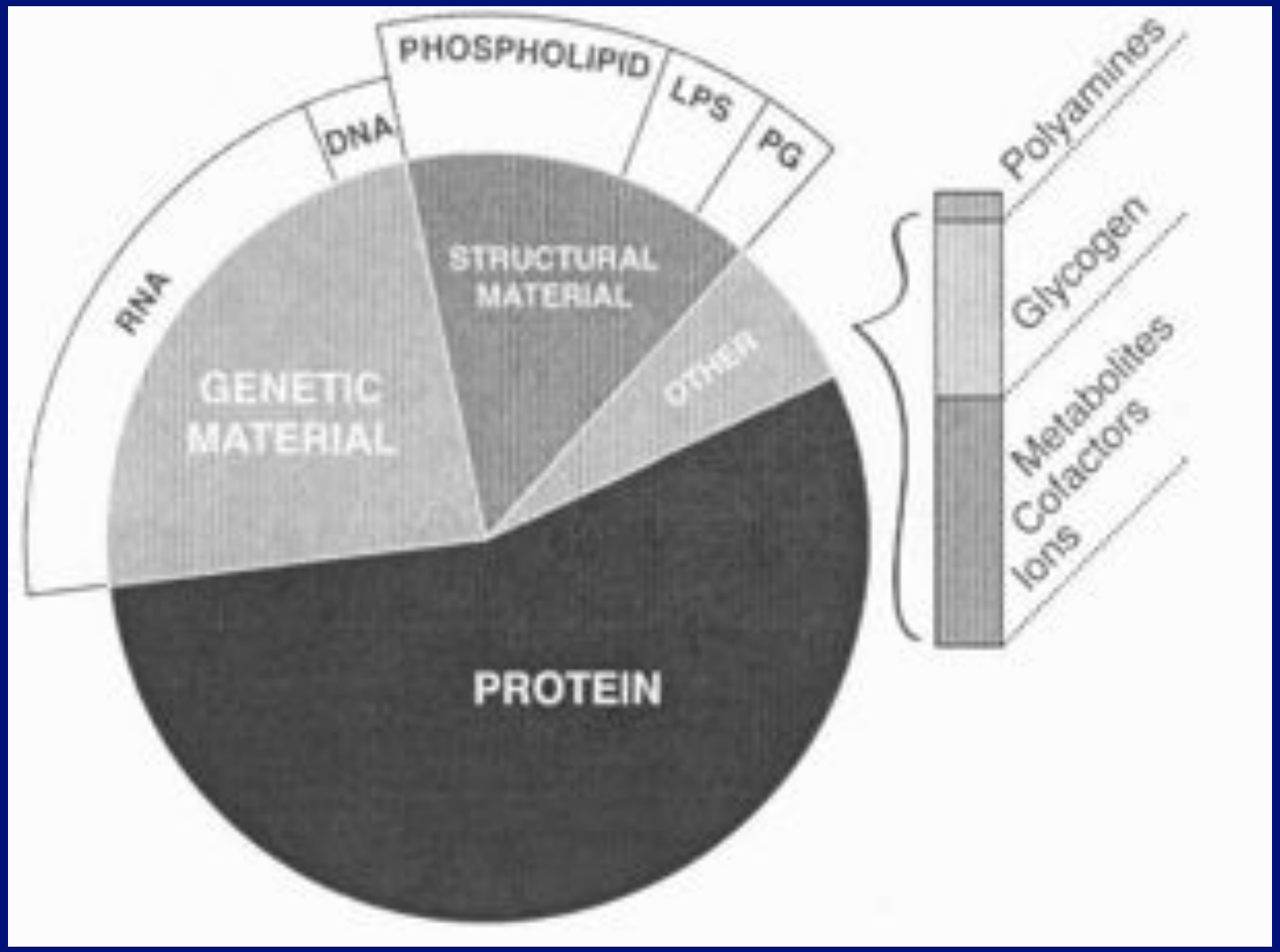
therefore, RNA genomes must be primitive

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)

August 22, Thursday

… Next we visited the Biochemical Institute and spent most of our time in BELOZERKY's lab. He studies plan biochemistry and antibiotics. We saw his office with a rug on the floor and the his lab for students. The apparatus was not bad, about 10 to 15 years behind our biochemical labs….

… We talked with two of Belozerky's students. One has just completed his candidates degree (equivalent to Ph.D.). His dissertation was on the polyphosphates in microorganisms. He said that the polyphosphates were discovered in 1887 but not studied again until 1936 when a little work was done. Then in 1946 work began again. The polyphosphates are not meta phosphates which are cyclic structures, but rather stright (sic) chain polymers. This students was rather heavy set and one could see that he was no moron…

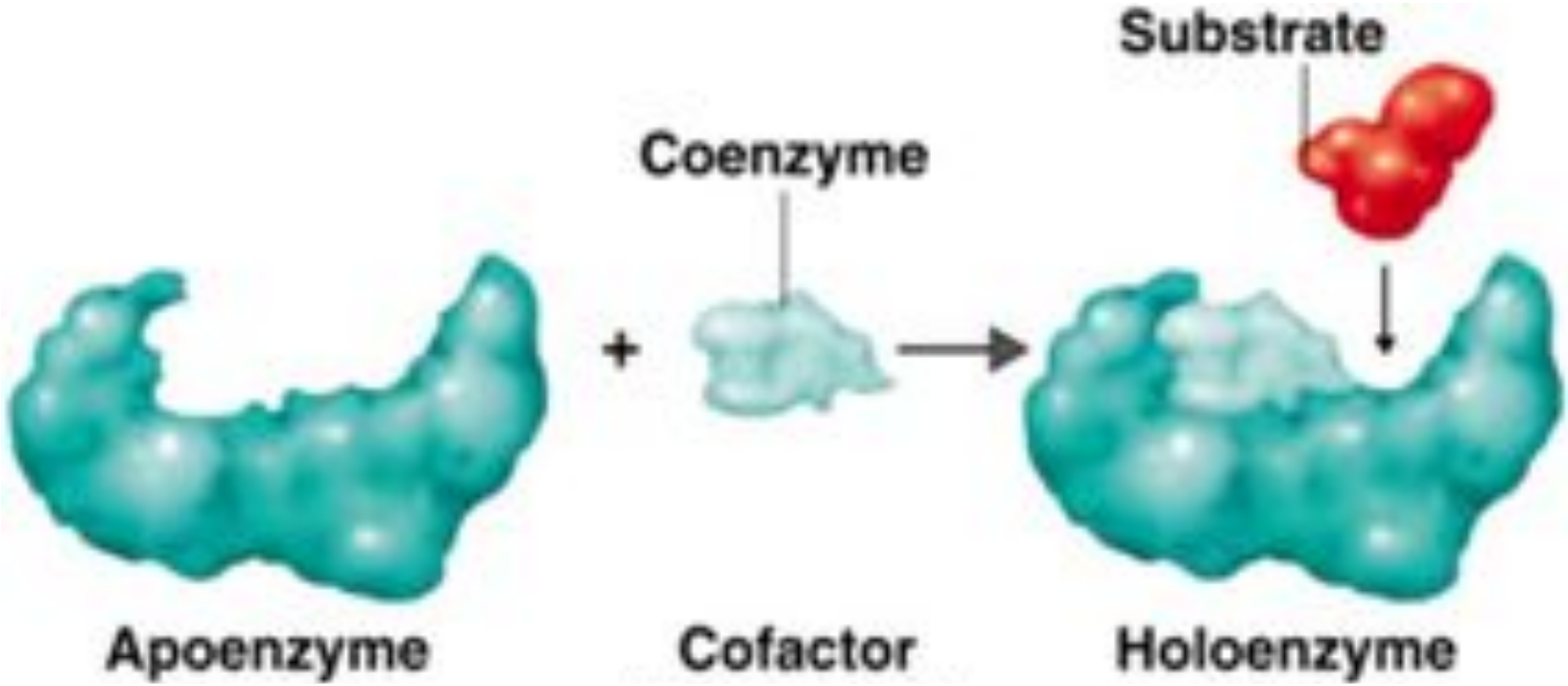
Stanley L. Miller, Notes on the "Trip to Moscow for the First International Symposium on the Origin of Life, August 18-30, 1957", S. L. Miller Archives, Mandeville Special Collections in the Geisel Library, UCSD campus

"…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.

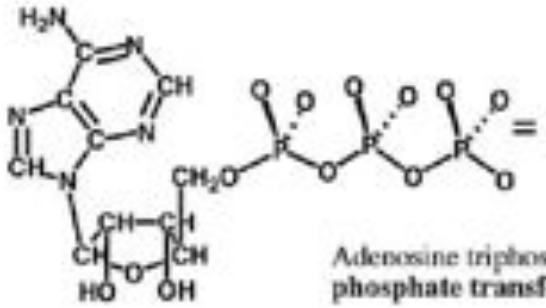
"It seems that RNA, being associated with the most general processes of life, was formed at an earlier evolutionary stage, while the origin of DNA was associated with the development of more specialized and phylogenetically later features of organisms"

A.N. Belozersky, 1957 (1959)

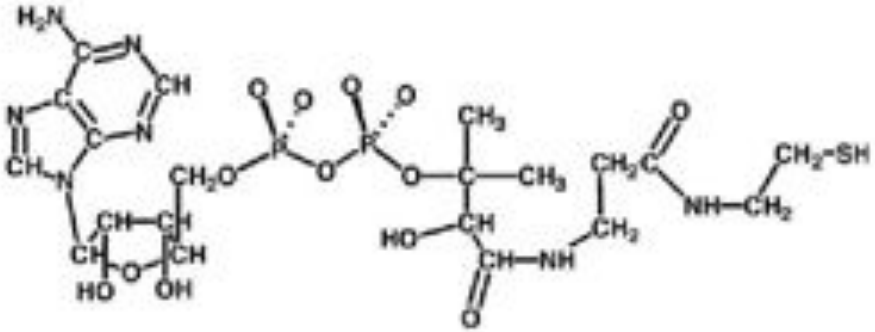
Coenzymes play a key role in many enzyme-mediated catalytic processes



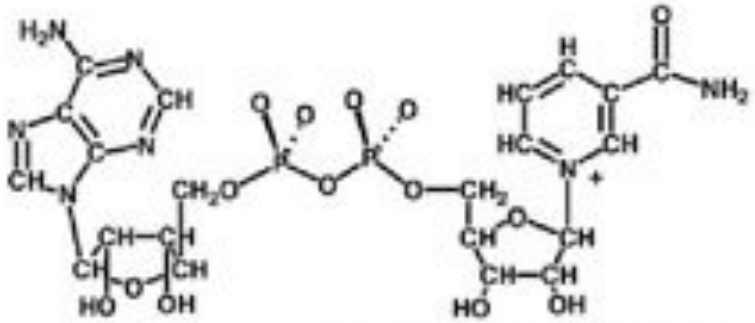
Some ribonucleotidyl coenzymes



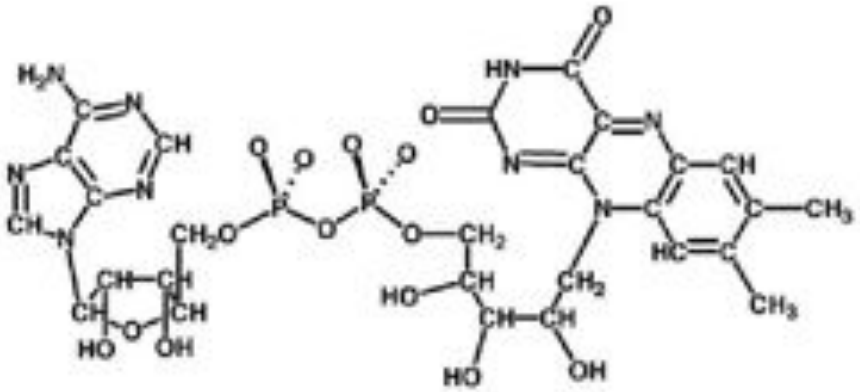
Adenosine triphosphate (ATP)
phosphate transfer energy transfer



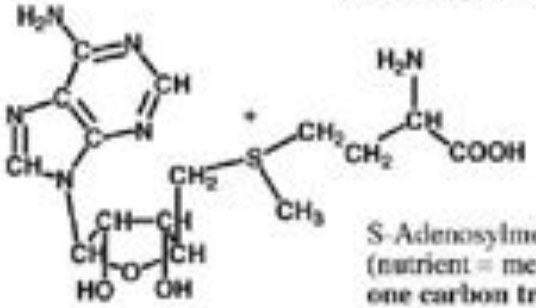
Coenzyme A
(vitamin = pantothenic acid)
carbon-carbon bond formation



Nicotinamide adenine dinucleotde
(vitamin = niacin)
oxidation, reduction



Flavin adenine dinucleotide
(vitamin = riboflavin)
oxidation, reduction

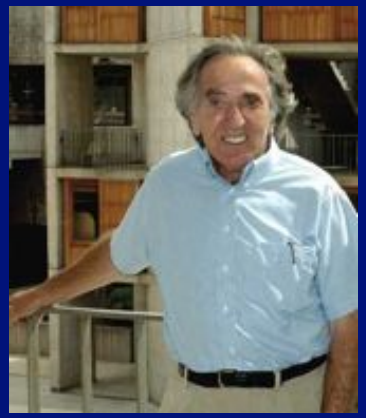


S-Adenosylmethionine
(nutrient = methionine)
one carbon transfer

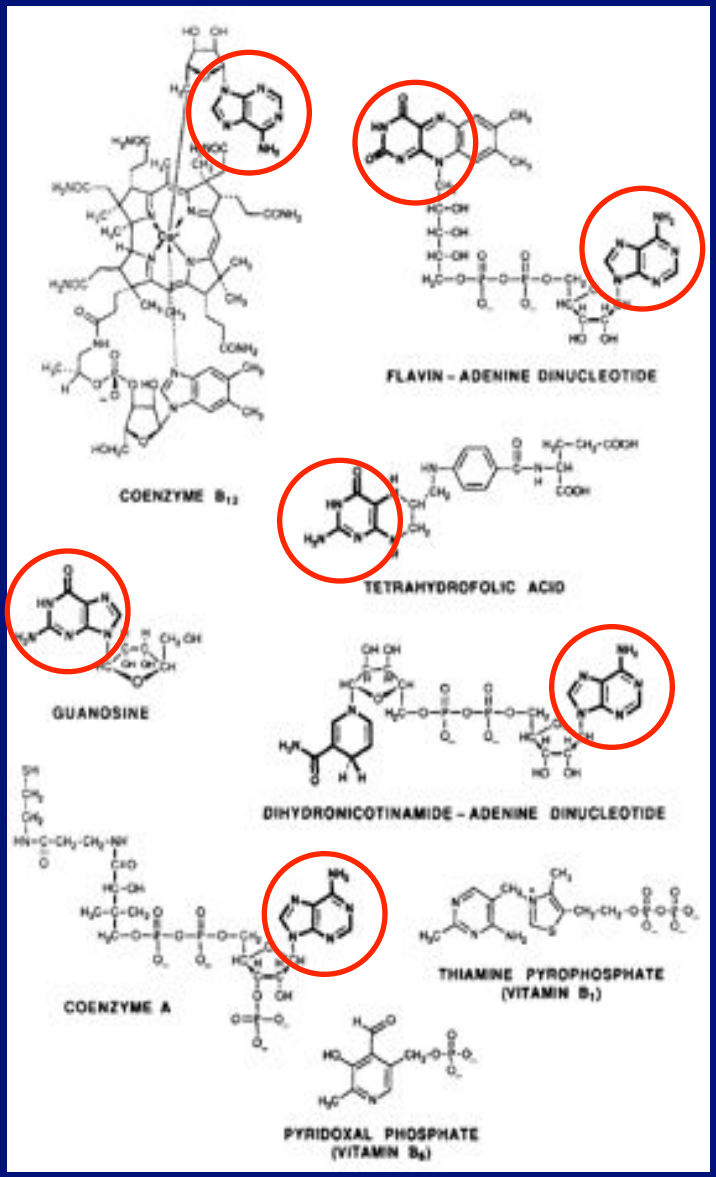
Neveu, Kim & Benner, 2013

Coenzymes as primordial catalysts

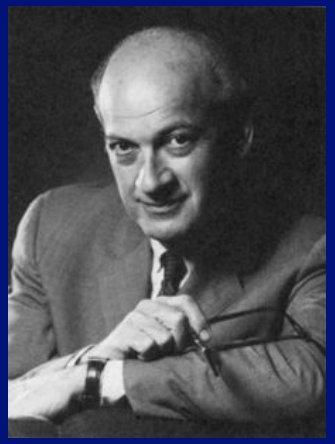
Robert E. Eakin (1916–1979)



Leslie E. Orgel (1927-2007)



Eschenmoser & Loewenthal 1992



Philip Handler (1917-1981)

Harold B. White III

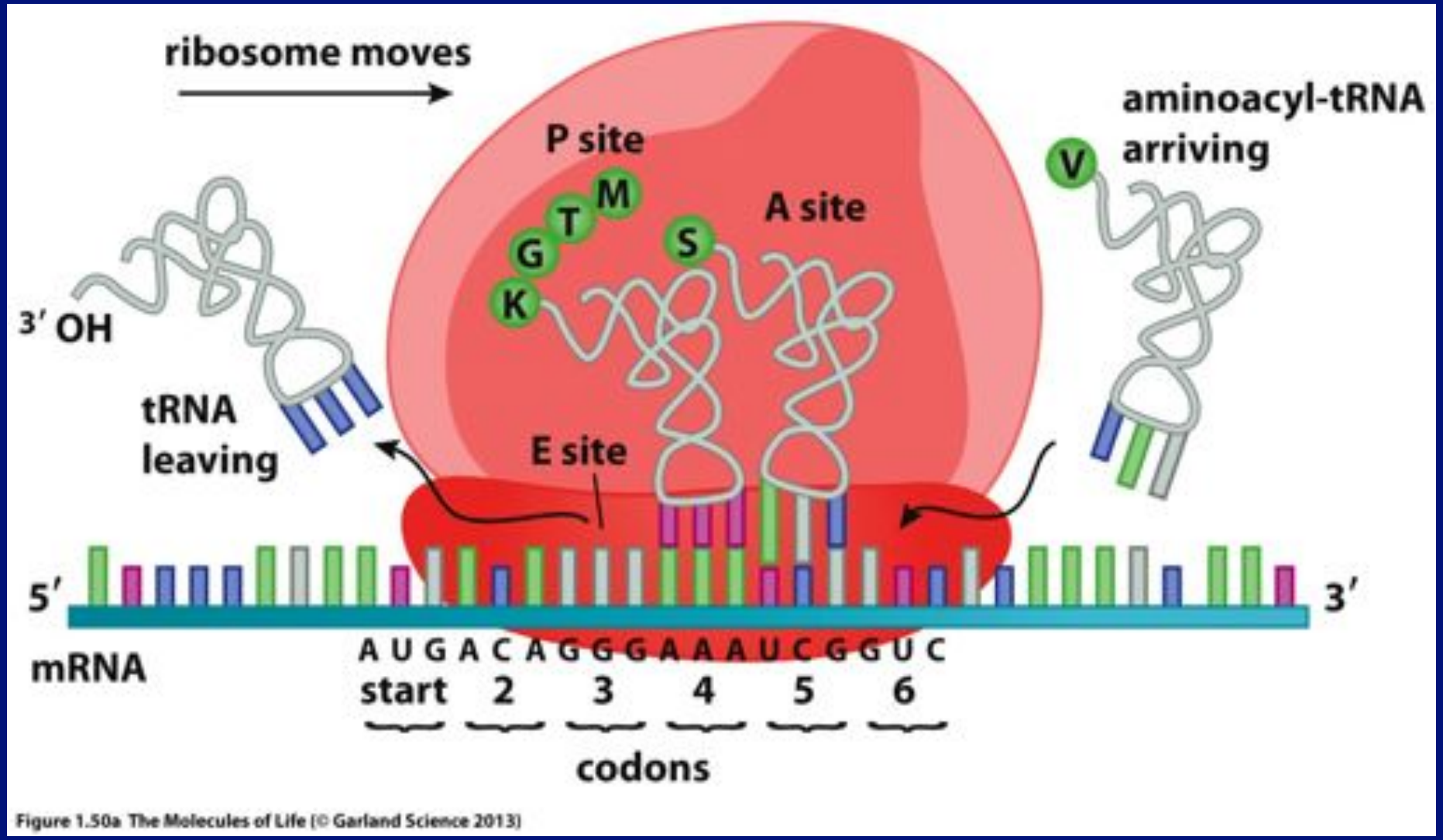
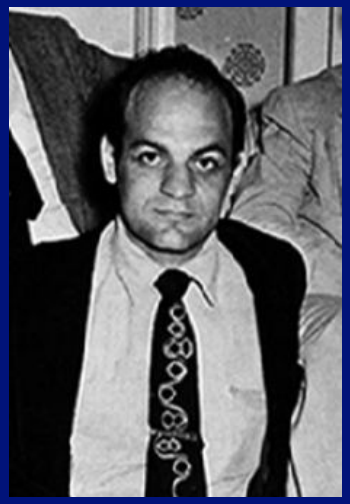
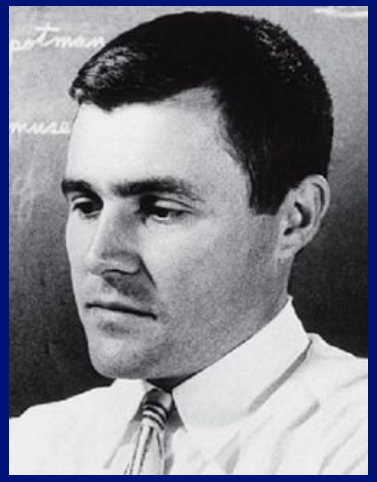


Figure 1.50a The Molecules of Life (© Garland Science 2013)

Early proposals of an RNA World



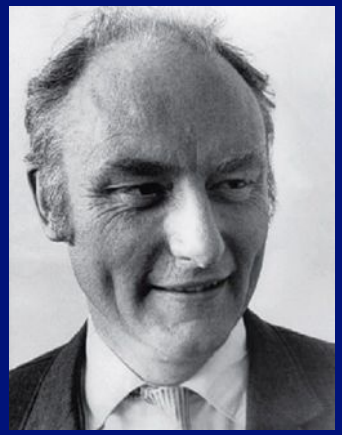
Alex Rich (1962)



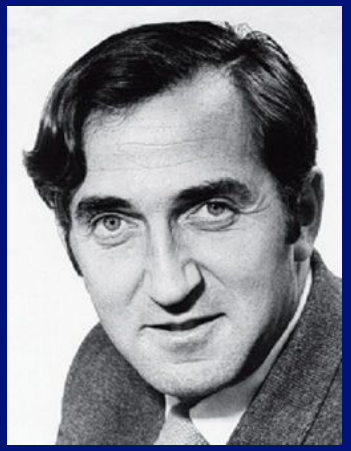
Carl R. Woese (1967)

replicative RNA

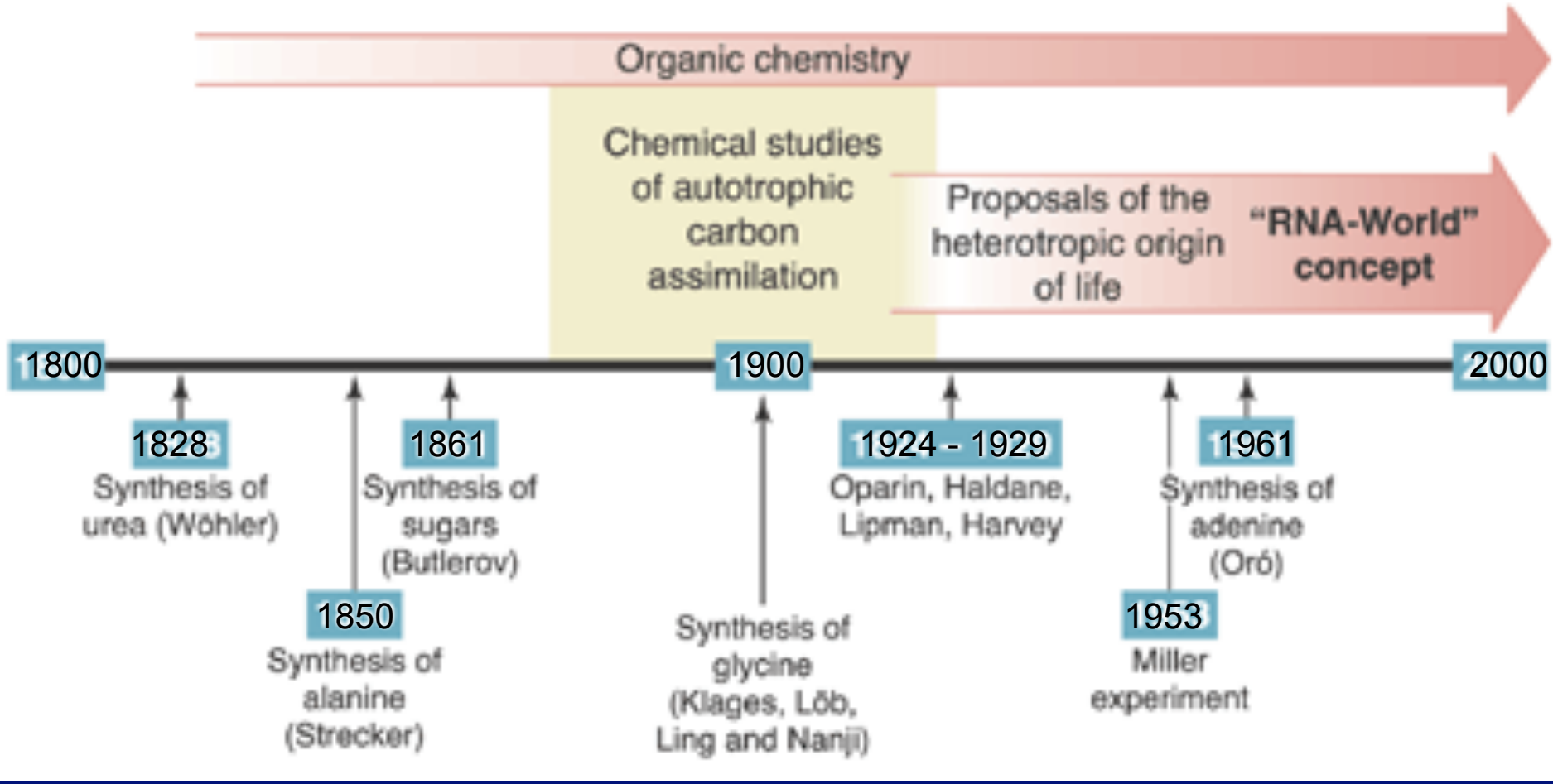
catalytic RNA



Francis H. Crick (1968)



L. E. Orgel (1968)



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

During the two decades following the first suggestion of an RNA World,

a) Many accepted the idea that RNA genomes came prior to DNA cell genomes;

b) Many accepted the possibility that coenzymes were vestiges of an RNA World stage (but few worked on it);

c) Some accepted the idea that histidine was a molecular vestige of an RNA World stage (but no one worked on this possibility);

d) No one was really working on the possible catalytic properties of RNA molecules

RNA has catalytic properties

Cell, Vol. 35, 849–857, December 1983 (Part 2), Copyright © 1983 by MIT

0092-8674/83/130849-09 $02.00/0

The RNA Moiety of Ribonuclease P Is the Catalytic Subunit of the Enzyme

Cecilia Guerrier-Takada,* Katheleen Gardiner,† Terry Marsh,† Norman Pace,† and Sidney Altman*
*Department of Biology
Yale University
New Haven, Connecticut 06520
†Department of Molecular and Cellular Biology
National Jewish Hospital and Research Center
and Department of Biochemistry, Biophysics and Genetics
University of Colorado Medical Center
Denver, Colorado 80206

Summary

The RNA moieties of ribonuclease P purified from both E. coli (M1 RNA) and B. subtilis (P-RNA) can cleave tRNA precursor molecules in buffers containing hydrogen bonded nucleotide pairs with tRNA precursor molecules (Reed et al., 1982). The RNA moiety alone, in RNAase P or any other ribonucleoprotein aggregate, was not believed to be capable of performing the catalytic function presumed to be governed by the complex. Recently, however, Cech and coworkers showed that the precursor rRNA found in T. thermophila carries out self-splicing and circularization reactions (Kruger et al., 1982) in the absence of protein.

In this paper we present evidence that RNA may possess a wider range of catalytic capabilities than previously expected. In buffers containing high concentrations of Mg^{2+} the RNA subunits of RNAase P alone are sufficient to carry out the catalytic cleavage of tRNA precursor molecules. However, the protein subunit is required for cleavage activity in standard buffers and in combination with M1 RNA has the ability to cleave one other type of precursor molecule—namely, the precursor to the small,

Cell, Vol. 31, 147–157, November 1982, Copyright © 1982 by MIT

Self-Splicing RNA: Autoexcision and Autocyclization of the Ribosomal RNA Intervening Sequence of Tetrahymena

Kelly Kruger, Paula J. Grabowski, Arthur J. Zaug, Julie Sands, Daniel E. Gottschling and Thomas R. Cech
Department of Chemistry
University of Colorado
Boulder, Colorado 80309

Summary

In the macronuclear rRNA genes of Tetrahymena thermophila, a 413 bp intervening sequence (IVS) interrupts the 26S rRNA-coding region. A restriction linear IVS RNA has a 5′-terminal guanosine residue that is not encoded by the DNA (Zaug and Cech, 1982; Kan and Gall, 1982) but that is added to the RNA during excision (Cech et al., 1981). The requirement for the guanosine cofactor and the lack of an energy requirement for the reaction led us to propose a topoisomerase-like phosphoester transfer mechanism for pre-rRNA splicing (Cech et al., 1981). We have recently found that cyclization of the IVS also involves linked cleavage and ligation of RNA, providing strong support for the phosphoester transfer mechanism (A. J. Zaug, P. J. Grabowski and T. R. Cech, manuscript submitted).

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)

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

What is the RNA World?

There are many definitions of the RNA World, including several contradictory ones.

The available evidence suggest that during early stages of biological evolution RNA molecules played a much more conspicuous role in genetic and catalytic processes.

Acknowledgement of the antiquity of RNA must also recognize its coexistence with many other compounds, including the products of reactions of ribonucleotides with other molecules. Nowadays these are best represented by histidine, many coenzymes, and alarmones.

The heterotrophic origin of life: a contemporary reassessment

synthesis & accumulation of organic compounds

RNA World

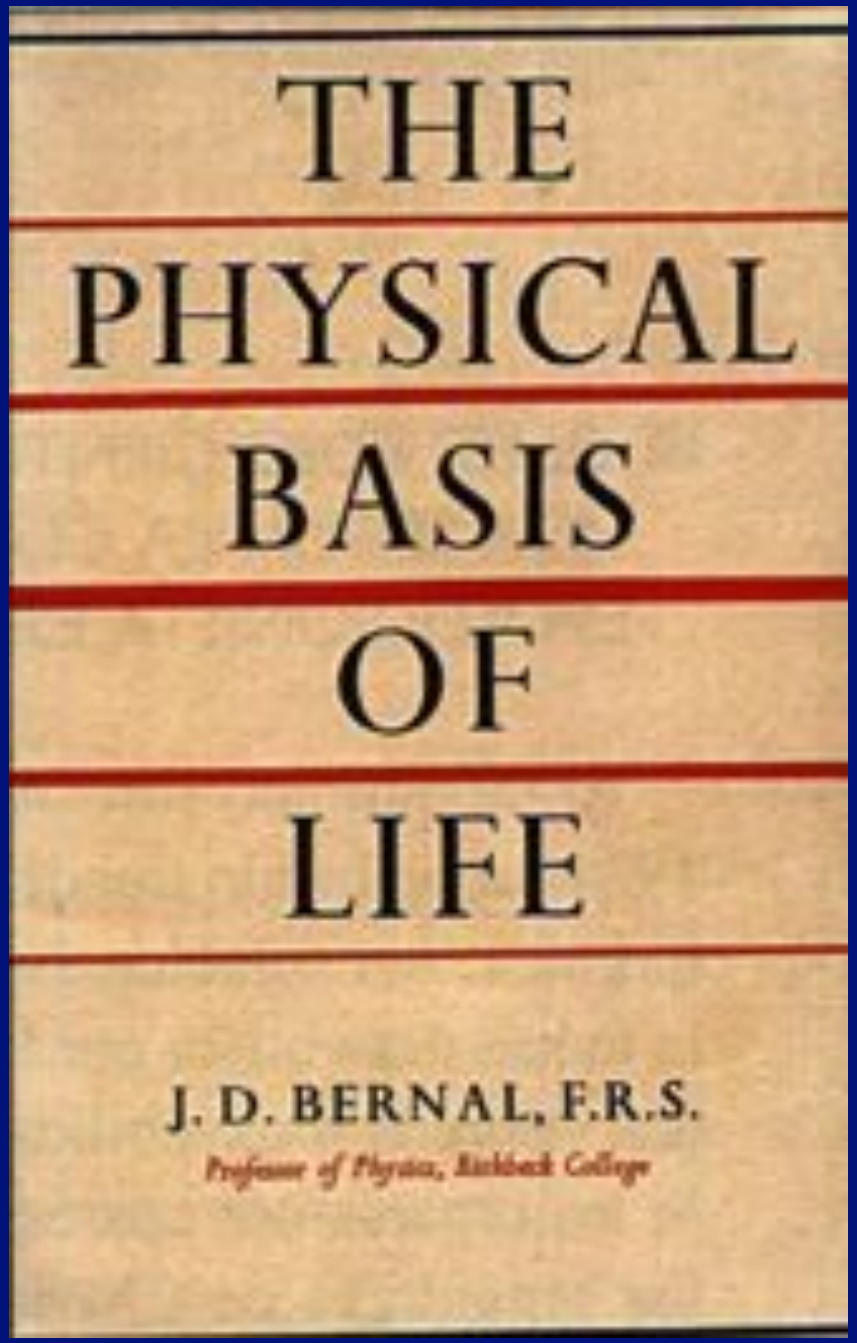
RNA/protein cells

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)



"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…"