Mestrado em História e Filosofia das Ciências

Filosofia das Ciências da Vida (codes 585145, 485102)

Teachers: Davide Vecchi, Maurizio Esposito & Lorenzo Baravalle

2nd semester 2020/2021

Sala: online (so far)

Practicalities

Course outline:

- Aims
- Teaching methodology
- Evaluation

CLASS 1 THEME: Life

A. The domain of biology
B. Two central questions
C. Origin of life: spontaneous generation and contemporary scenarios.
D. Definitions of life

PREAMBLE: “biology”

βίος, bios, "life" + λογία, -logia, "study of.”

Aristotle: 25 % of his books are on biology. Cf. https://www.bbc.co.uk/programmes/m0002cfd?fbclid=IwAR2xl65-Vl0owksAb_y_gHOUV1ANY-rKMTJP-1PEoGANzvPJvtaY7Mcyx2Q

First use: 1736 Carl Linnaeus used term “biologi” in *Bibliotheca botanica*.

Term becomes common with *Biologie, oder Philosophie der lebenden Natur* (1802–22) by Gottfried Reinhold Treviranus:

“The objects of our research will be the different forms and manifestations of life, the conditions and laws under which these phenomena occur, and the causes through which they have been effected. The science that concerns itself with these objects we will indicate by the name biology [Biologie] or the doctrine of life [Lebenslehre].”

PREAMBLE: (some of) the life sciences

- Biochemistry (1838 Gerardus Johannes Mulder), molecular biology
- Virology (1892 Dmitry Ivanovsky or 1898 Martinus Beijerinck), microbiology (1673 Antonie Van Leeuwenhoek), botany, zoology
- Developmental biology, embryology
- Systematics
- Evolutionary biology (after Lamarck 1809 at least)
- Ecology, conservation biology
- Cell biology (Matthias Schleiden and Theodor Schwann 1839), physiology
- Genetics, genomics
- Synthetic biology

PREAMBLE: what is life?

"…despite the enormous fund of information that each of these biological specialties has provided, it is a remarkable fact that no general agreement exists on what it is that is being studied."

Sagan, C. 1970. Life. Encyclopædia Britannica, pp. 1083–1083A, Chicago: Encyclopædia Britannica Incorporated.

<u>Can life be defined rigorously? What kind of definition should we seek? Is the lack of an agreed upon definition a obstacle to scientific research? Does life have an essence? Is this essence compositional or organisational?</u>

1.1 Life: the domain of biology

The domain of biology:

1. Physics is about any and all objects that are made of matter.
2. Biology is about objects that are alive.
3. Psychology is about objects that have minds.

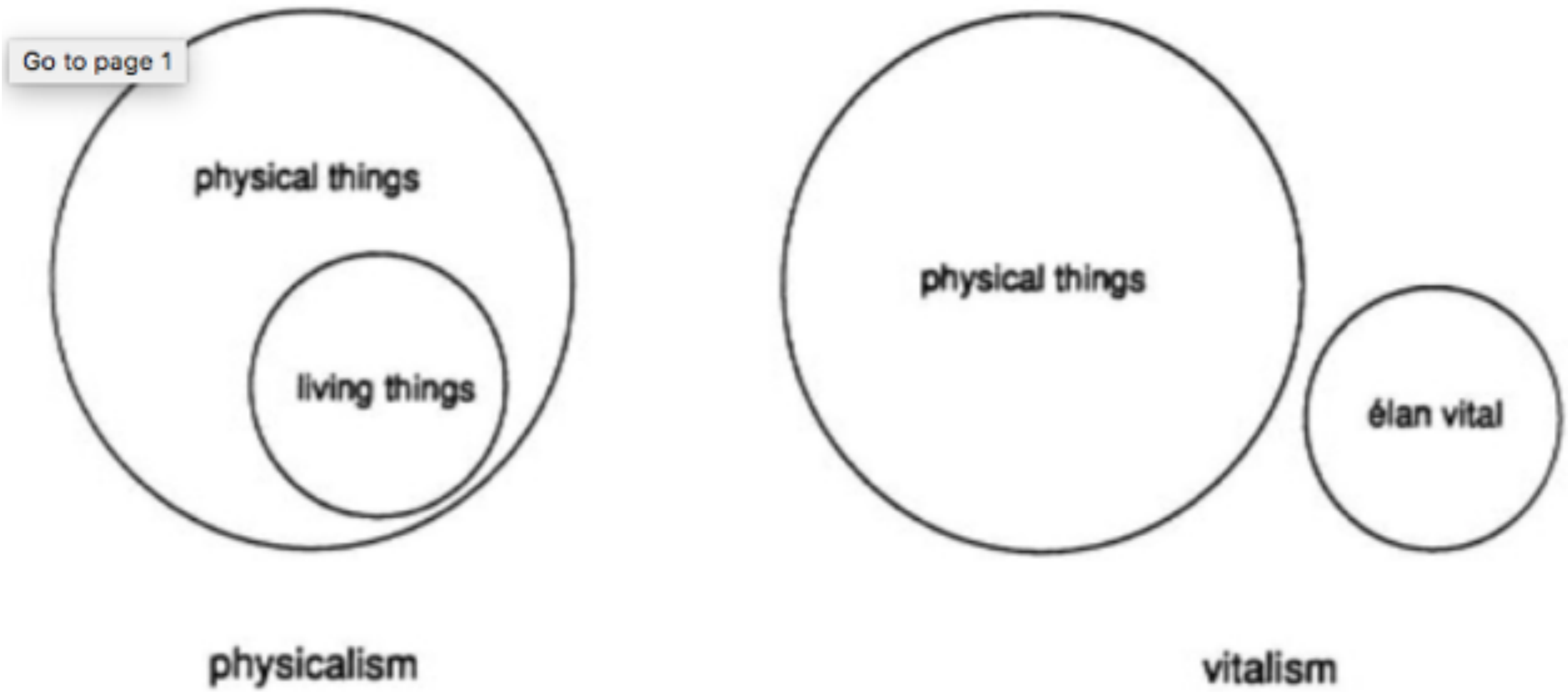
Relationship between physics, biology and psychology.

<u>Material</u>

Sober, E. (1993). Philosophy of Biology. Section 1.6.

Gilbert, S.F., and Sarkar, S. (2000). Embracing complexity: organicism for the 21st century. Developmental Dynamics, 219, 1–9.

1.2 Life: the domain of biology



(a) biology and physics

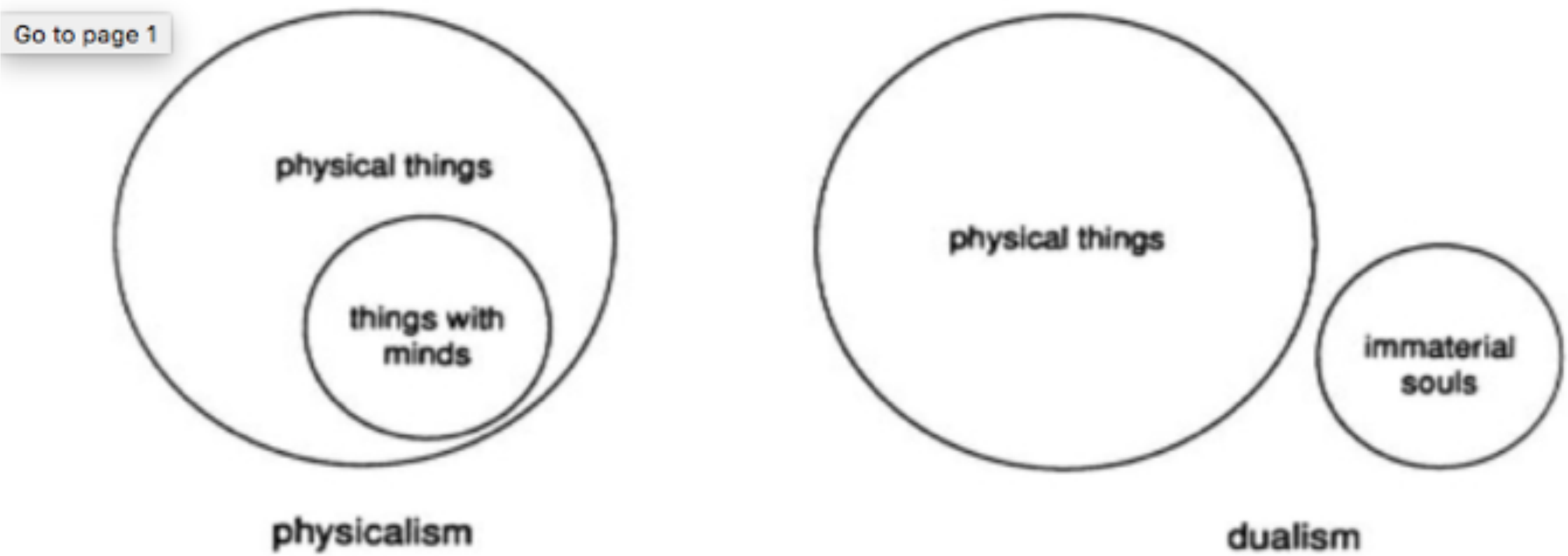
1.3 Life: the domain of biology

Physicalistic materialism = all living things are physical objects. If you take an organism, no matter how complex, and break it down into its constituents, you will find matter and only matter there. Living things are made of the same basic ingredients as nonliving things.

Vitalism rejects this physicalistic picture. It says that living things are alive because they contain an immaterial ingredient (*elan vital* in Henry Bergson, entelechy in Hans Driesch). According to vitalism, two objects could be physically identical even though one of them is alive while the other is not.

1.4 Life: the domain of biology

Parallel with psychology: vitalism as a form of dualism (an ontological thesis).



1.5 Life: the domain of biology

Materialistic physicalism implies a form of reductionism:

“By finding the parts that construct the whole, we will learn and explain everything about the whole, including how it functions. Biological functions of a system will be explained solely in terms of the chemical properties of its parts, and these chemical properties will, in turn, be explained by the physical properties of even smaller parts.” Gilbert and Sarkar, Embracing complexity, 2001

Materialistic physicalism implies some form of metaphysical fundamentalism and atomism.

1.6 Life: the domain of biology

Non-dualistic alternative: materialistic "holism" because life is *organised* matter. The difference between life and non-life concerns how parts are put together in a whole:

"…. complex wholes are inherently greater than the sum of their parts in the sense that the properties of each part are dependent upon the context of the part within the whole in which they operate. Thus, when we try to explain how the whole system behaves, we have to talk about the context of the whole and cannot get away talking only about the parts. This philosophical stance is variously called *wholism*, *holism*, or *organicism*." Gilbert and Sarkar, Embracing complexity, 2001

In what sense wholes are greater than the sum of their parts?

1.7 Life: the domain of biology

Agreement on materialistic ontology (vs vitalism and dualism): living objects are made only of physical objects.

<u>If life is not a special substance, what is it then? A distinctive material constitution (i.e., specific "biomolecules") or a specific mode of organisation of material components?</u>

Physicalist reductionism vs anti-reductionism (e.g., holism, emergentism, structuralism) debate.

One way to answer this question is to enquire about its origin: how did life originate?

2.1 Two central questions

“The basis of biology is physical chemistry. From the moment that one works in biochemistry and biophysics, and understands the physico-chemical mechanisms that account for the properties of living beings, life vanishes! Today molecular biologists have no need to use the word ‘life’ in their work.”

Atlan and Bousquet (1994) [quoted in Cornish-Bowden & Cárdenas 2020 - **henceforth CDC** - p. 3]

<u>Material</u>

Cornish-Bowden, A. & María Luz Cárdenas, M.L. 2020. Contrasting theories of life: Historical context, current theories. In search of an ideal theory. Biosystems, 188:1-50. https://doi.org/10.1016/j.biosystems.2019.104063.

2.2 Two central questions

1. Can we study the origin of life without a definition of what it is?

Cornish-Bowden & Cardenas 2020 p.(**henceforth CBC**): NO.

2. Can we study the definition of life without any knowledge of its origin?

CBC: YES.

Answer to 1: CBC: you need at least an operational definition (even though not an essentialist one in terms of necessary and sufficient conditions) of life if you want to answer questions like: is this object an item of life? The object could be terrestrial and natural (e.g., a brain-dead human or even a putative item of life with different biochemistry and metabolism), terrestrial and artificial (e.g., synthetic or even artificial life) or extraterrestrial. (NASA uses an operational definition: "Life is a self-sustained chemical system capable of undergoing Darwinian evolution").

The problem of this view is that it is local (based on extant life and terracentric).

2.3 Two central questions

1. Can we study the origin of life without a definition of what it is?

Cornish-Bowden & Cardenas 2020 p. (henceforth CBC): NO.

2. Can we study the definition of life without any knowledge of its origin?

CBC: YES.

Answer to 2: we can study the definition of life without knowledge of origins. Focus on putative universal features of extant life (e.g., cellular basis of all life; universality of DNA as material of inheritance; universality of the genetic code; ATP as energy currency; common core of metabolic reactions such as the Krebs cycle and chemical processes such as chemiosmosis; metabolic closure and autocatalysis etc.)

The problem of this view is that the origin of compartments, metabolism and replication are dependent on prebiotic chemistry: assuming that certain features of extant life are universal of all life is speculative.

2.4 Two central questions

Cutting corners:

1. question of whether artificial life is real life: is a robot or computer programme alive?;
2. question of whether synthetic life is real life;
3. vitalism: is life another substance distinct from physical stuff?
4. panspermia: did life originate outside our planet?
5. spontaneous generation: is abiogenesis continuously happening?

2.5 Two central questions

Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome

Daniel G. Gibson,[1] John I. Glass,[1] Carole Lartigue,[1] Vladimir N. Noskov,[1] Ray-Yuan Chuang,[1] Mikkel A. Algire,[1] Gwynedd A. Benders,[2] Michael G. Montague,[1] Li Ma,[1] Monzia M. Moodie,[1] Chuck Merryman,[1] Sanjay Vashee,[1] Radha Krishnakumar,[1] Nacyra Assad-Garcia,[1] Cynthia Andrews-Pfannkoch,[1] Evgeniya A. Denisova,[1] Lei Young,[1] Zhi-Qing Qi,[1] Thomas H. Segall-Shapiro,[1] Christopher H. Calvey,[1] Prashanth P. Parmar,[1] Clyde A. Hutchison III,[2] Hamilton O. Smith,[2] J. Craig Venter[1,2]*

We report the design, synthesis, and assembly of the 1.08–mega–base pair *Mycoplasma mycoides* JCVI-syn1.0 genome starting from digitized genome sequence information and its transplantation into a *M. capricolum* recipient cell to create new *M. mycoides* cells that are controlled only by the synthetic chromosome. The only DNA in the cells is the designed synthetic DNA sequence, including "watermark" sequences and other designed gene deletions and polymorphisms, and mutations acquired during the building process. The new cells have expected phenotypic properties and are capable of continuous self-replication.

SYNTHETIC BIOLOGY

Design and synthesis of a minimal bacterial genome

Clyde A. Hutchison III,*† Ray-Yuan Chuang,† Vladimir N. Noskov, Nacyra Assad-Garcia, Thomas J. Deerinck, Mark H. Ellisman, John Gill, Krishna Kannan, Bogumil J. Karas, Li Ma, James F. Pelletier, Zhi-Qing Qi, R. Alexander Richter, Elizabeth A. Strychalski, Lijie Sun, Yo Suzuki, Billyana Tsvetanova, Kim S. Wise, Hamilton O. Smith, John I. Glass, Chuck Merryman, Daniel G. Gibson, J. Craig Venter*

A. Cornish-Bowden and M.L. Cárdenas

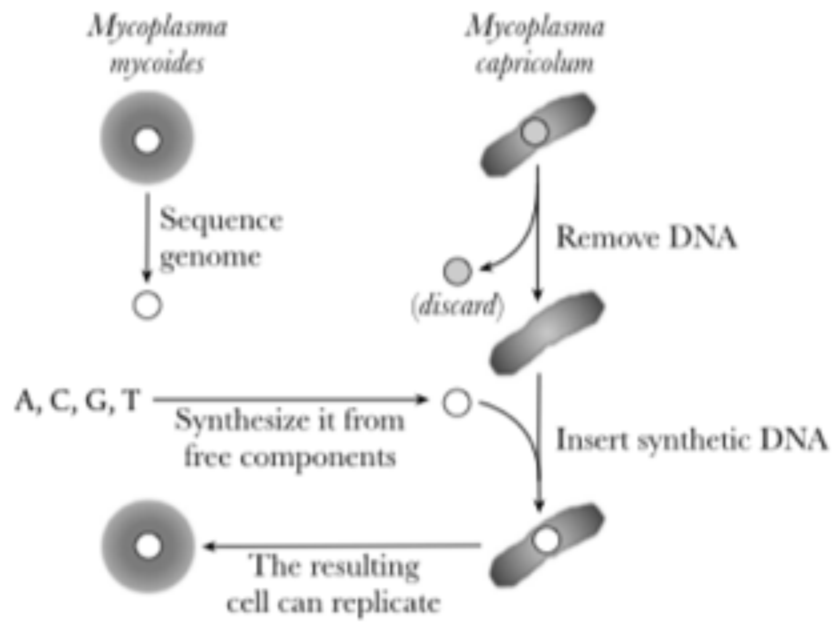


Fig. 6. Transfer of a genome from one bacterial species to another. Has a synthetic cell been created?.

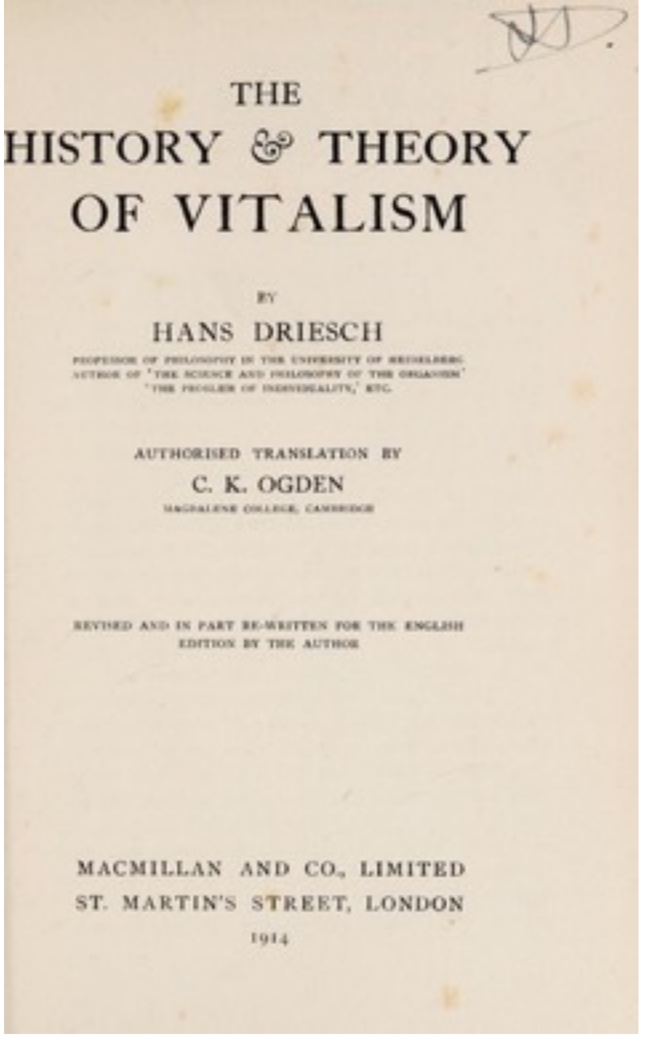
2.6 Two central questions

Vitalism: is life another substance distinct from physical stuff?

Ontological claim: incompatible with materialistic physicalism; so what? Hans Driesch's case significant.

Vitalism ".... was swept away by the discovery that a cell-free extract of yeast could catalyse fermentation, the conversion of glucose into ethanol and CO_2 (Buchner, 1897)." (CBC p. 11)

Epistemological claim: "It is perfectly possible that there may be physical laws necessary for understanding biology that cannot be revealed by studying physics alone, because the world that physicists study is too limited." (CBC p. 11)


THE HISTORY & THEORY OF VITALISM

BY HANS DRIESCH

AUTHORISED TRANSLATION BY C. K. OGDEN

MACMILLAN AND CO., LIMITED
ST. MARTIN'S STREET, LONDON
1914

2.7 Two central questions

Panspermia: did life originate outside of our planet?

Complexity issue drives this speculation (ignorance concerning origin of compartments, metabolism and replication).

Some kind of regress implied.

It remains a possibility of course. Eminent scientists such as Fred Hoyle, Leslie Orgel and Francis Crick proposed panspermia hypotheses.

Essential building blocks of life were synthesised extra-terrestrially and reached early Earth by comets or meteorites (de Duve, C. 1995. Vital Dust: Life as a Cosmic Imperative. Basic Books, New York). Indeed, some meteorites show presence of amino acids.

2.8 Two central questions

1. Can we study the origin of life without a definition of what it is?

2. Can we study the definition of life without any knowledge of its origin?

<u>The two questions are inextricably linked: we cannot know about anything else apart from extant life, but life at the origin might have been compositionally and organisationally different.</u>

2.9 Two central questions

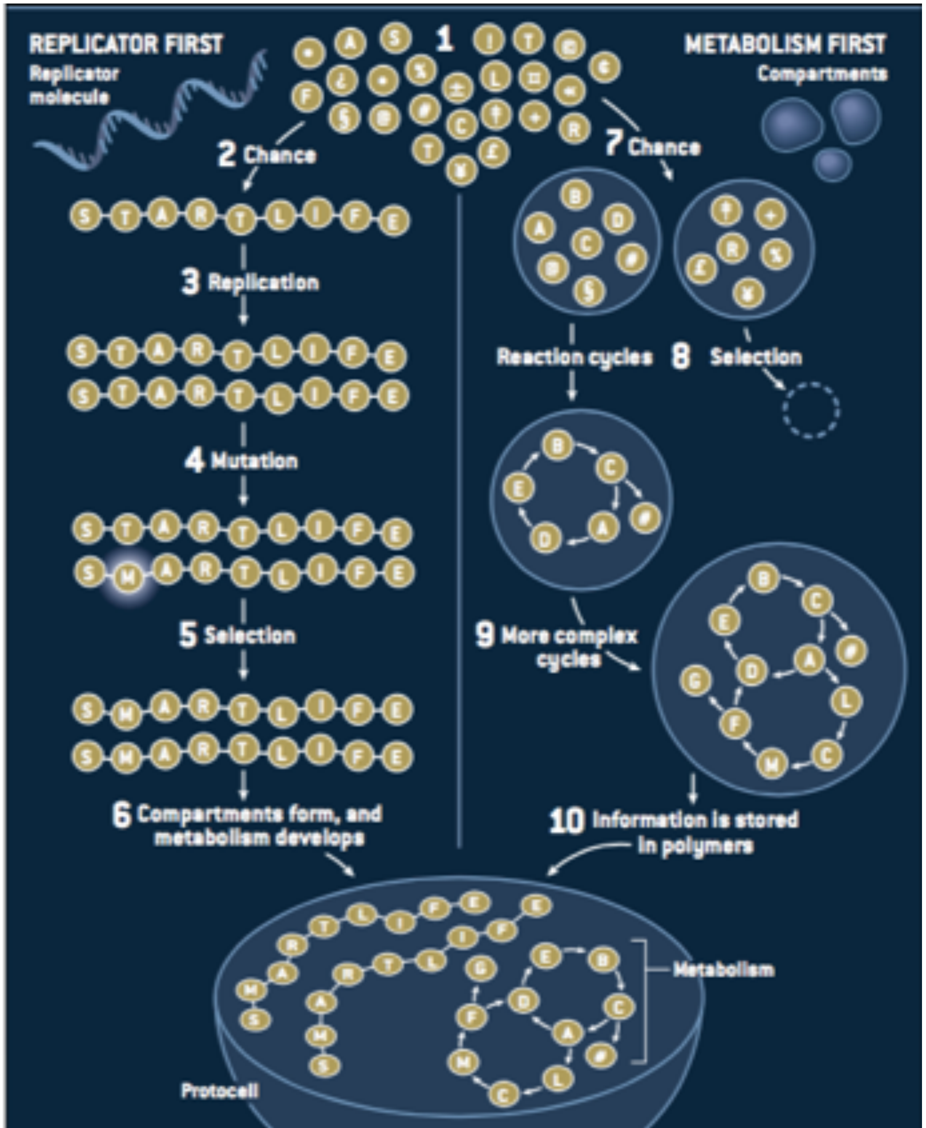
Working assumptions:

1. terracentric bias: can we extrapolate a definition from what we know about extant living forms? There's nothing else we can do until we know about extraterrestrial living forms. But, of course, <u>this extrapolation is local, based on particular biochemical details that might be contingent. That's why knowing the origin is important, because some of these details might have changed</u>;

2. abiogenesis happened at some point but, so far as we know, is not happening at this moment;

3. the central questions concern the origin of compartments, metabolism and replication: <u>the extant details of compartmentalisation (e.g., cellular membranes), metabolism (i.e., autocatalysis) and replication (e.g., DNA-based) might be different from those at the origin</u>.

2.10 Two central questions



<u>Life at the origin might have been compositionally and organisationally different; so in order to define life and ascertain whether life depends on a distinctive material constitution or a specific mode of organisation of material components, we need to study its origin.</u>

3.1 Spontaneous generation

"So with animals, some spring from parent animals according to their kind, whilst others grow spontaneously and not from kindred stock; and of these instances of spontaneous generation some come from putrefying earth or vegetable matter, as is the case with a number of insects, while others are spontaneously generated in the inside of animals out of the secretions of their several organs."

Aristotle, History of Animals, 539a18-26

<u>Material</u>

Wilkins, J.S. (2004). Spontaneous Generation and the Origin of Life. http://www.talkorigins.org/faqs/abioprob/spontaneous-generation.html

3.2 Spontaneous generation

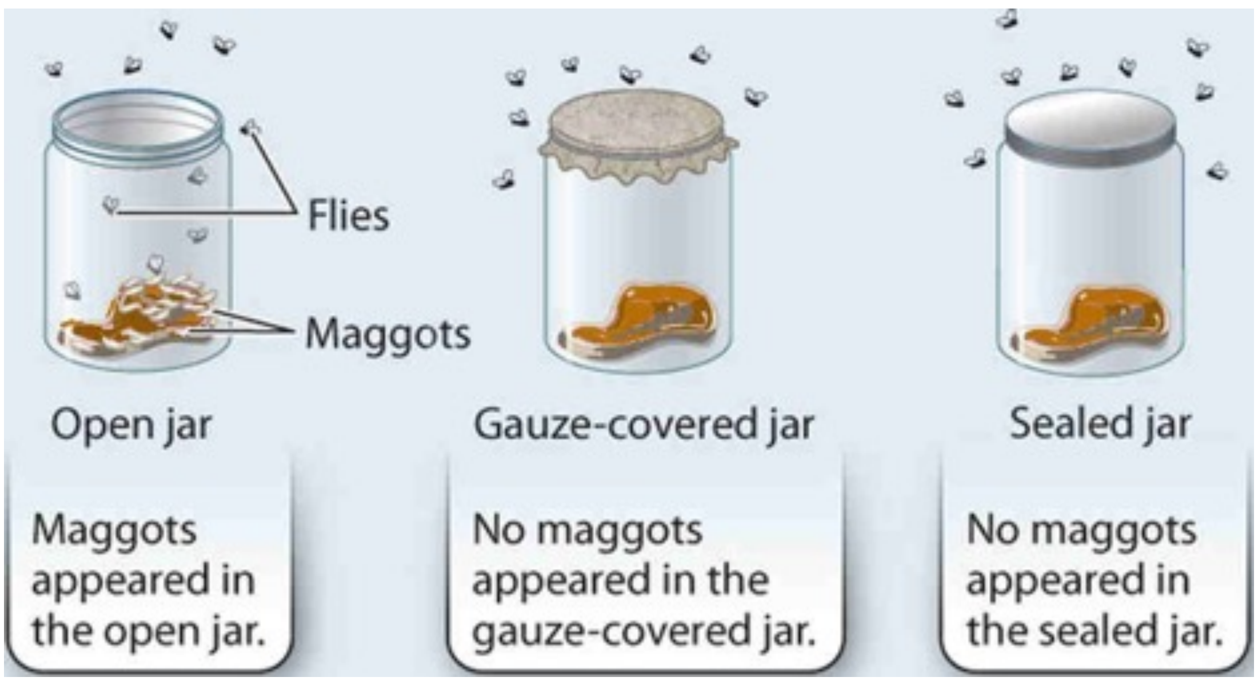
Why postulating spontaneous generation?

1. Unobservable phenomena (particularly the mode of reproduction);
2. Consistency with idea that universe was not created: spontaneous generation is a continuous process.

3.3 Spontaneous generation

William Harvey: *ex ovo omnia*.

Francesco Redi's experiments:

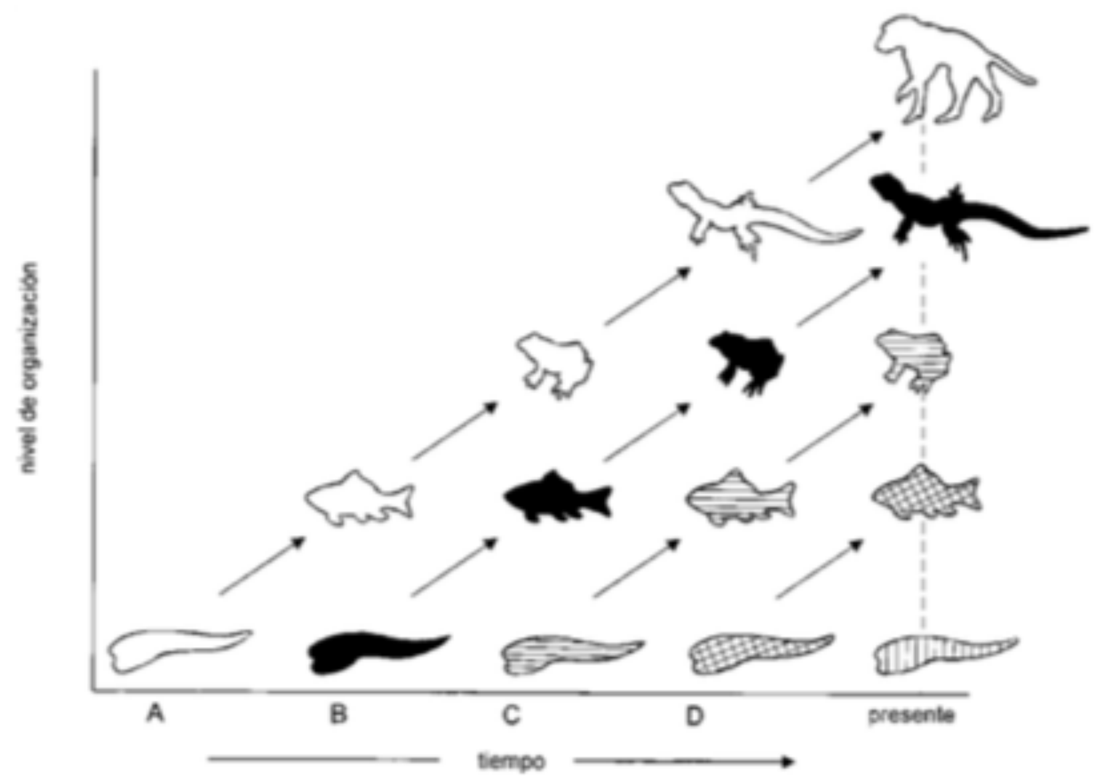


3.4 Spontaneous generation

Redi did not disprove spontaneous generation as such, but his experiments did "shrink the battle from the generation of macroscopic creatures to the small new world of infusoria and animalcules discovered by van Leeuwenhoek” (Magner, Lois N. 1994. A history of the life sciences. 2nd ed. New York: Marcel Dekker, Inc. 267).

Eventually, Virchow: *omnis cellula e cellula*.

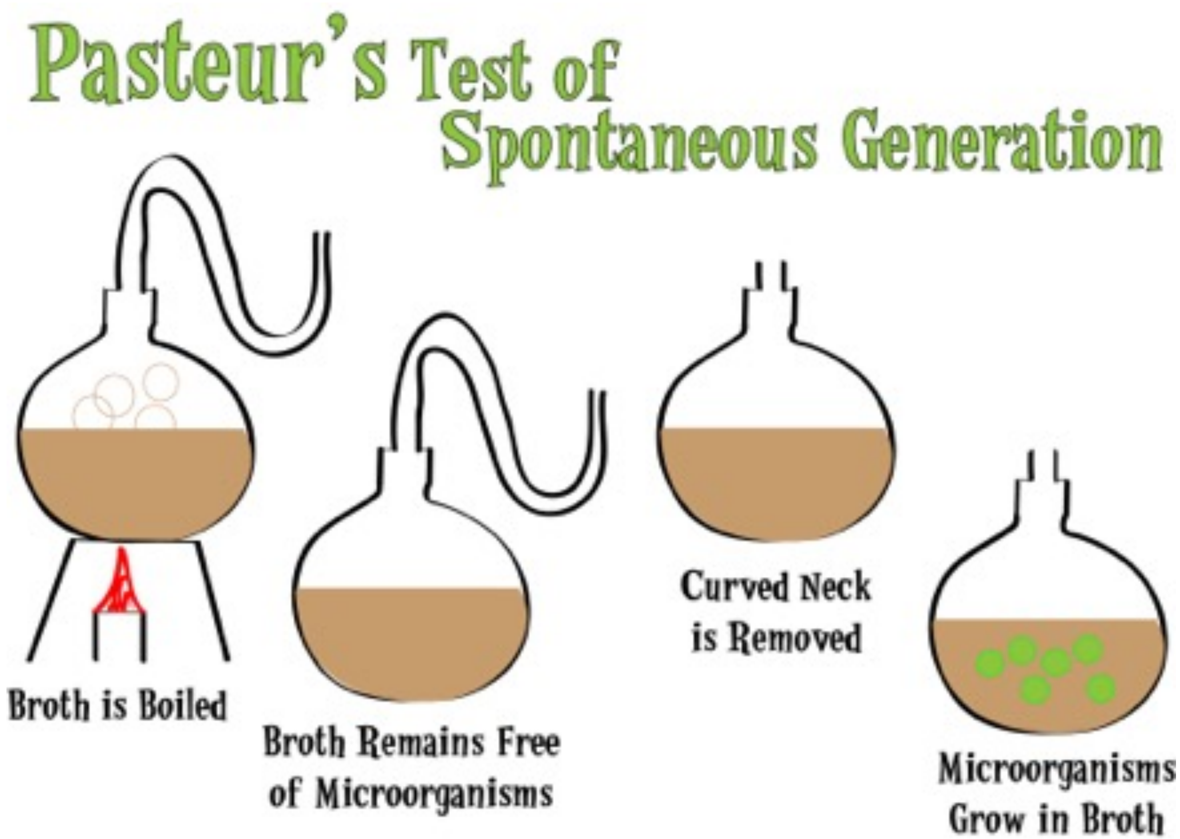
3.5 Spontaneous generation



Lamarck's view

3.6 Spontaneous generation

Pasteur: *Omne vivum ex vivo;* does it mean that biogenesis is true (and that abiogenesis is false)?



3.7 Spontaneous generation

What did Pasteur prove? Did he prove that no life can ever come from non-living things? No, he didn't, and this is because you cannot disprove something like that experimentally.

What he showed was that it was highly unlikely that modern living organisms arose from non-living organic material. This is a much more restricted claim than that primitive life once arose from non-living non-organic material.

The claims "all life from egg", "all cell from cell" and "all life from life" are generalisations with limited scope.

3.8 Spontaneous generation

In an essay to the Atheneum in 1863, Darwin wrote upon heterogeny "as the old doctrine of spontaneous generation is now called", in which he noted that a "mass of mud with matter decaying and undergoing complex chemical changes is a fine hiding-place for obscurity of ideas". He argued that while it is true that "there must have been a time when inorganic elements alone existed on our planet", "our ignorance is as profound on the origin of life as on the origin of force or matter", and denies that the theory of evolution requires that life continuously arises. So-called "primitive" life forms as Foraminifera are well adapted to their conditions, and are not evidence of on-going heterogenesis.

3.9 Spontaneous generation

1. In the initial period of the history of biology it was assumed that life was a special substance, and that it could generate living beings directly. As research into the lifecycles of animals, plants and microorganisms progressed, it became obvious that modern living forms were always observed to form from existing living forms, and that cells always came from existing cells.

2. At the same time, it became increasingly obvious that the gap between living things at the chemical level and non-living molecules was decreasing, until it became clear in the mid-20th century that all processes of living things were chemical, and there was no "vital principle" needed for life.

3.10 Spontaneous generation

3. None of the people who did crucial experiments on spontaneous generation disproved abiogenesis. At best, they strongly confirmed the hypothesis that extant organisms (mice, maggots, or “germs”) did not arise in ordinary cases out of nonliving material as hypothesised by Aristotle. Most of the experiments against spontaneous generation were posed against heterogenesis, the doctrine that life could form from the decayed products of living organisms.

4. Pasteur did not disprove the origin of life by natural means, and the saying "all cell from cell" was not intended to cover the initial period of life on earth.

5. Darwin did not propose a theory of the origin of life. Evolutionary theory was not proposed to account for the origins of life, but only to account for the process of change once life exists. However, the theory of evolution logically requires a beginning of life.

4.1 The origin of life

If not spontaneous generation, then what? Let us now take a look at contemporary scenarios.

All abiogenetic scenarios: from prebiotic chemistry to life.

How to conceptualise this passage is key.

<u>Compositional approaches</u>: focus on components such as biomolecules. Prebiotic soup scenarios. Start from what is known about extant life and known biomolecules.

<u>Organisational approaches</u>: focus on metabolism and organisational requirements. Origin of autocatalysis and compartments.

<u>Material</u>

Cornish-Bowden, A. & María Luz Cárdenas, M.L. 2020. Contrasting theories of life: Historical context, current theories. In search of an ideal theory. Biosystems, 188:1-50. https://doi.org/10.1016/j.biosystems.2019.104063.

Gilbert, W. 1986. Origin of life: The RNA world. Nature 319:618. https://www.nature.com/articles/319618a0

Martin et al. 2008. Hydrothermal vents and the origin of life. Nat. Rev. Microbiol 6 (11), 805–814. p. 811.

Miller, S. L. 1953. A Production of Amino Acids Under Possible Primitive Earth Conditions. Science 117(3046): 528-529. DOI: 10.1126/science.117.3046.528

4.2 The origin of life

Compositional approaches: focus on components such as molecules. Prebiotic soup scenarios.

Darwin's "warm little pond":

"But if (and oh what a big if) we could conceive in some warm little pond with all sorts of ammonia and phosphoric salts, light, heat, electricity etcetera present, that a protein compound was chemically formed, ready to undergo still more complex changes …." Charles Darwin, letter to Joseph Hooker (1871). Cf. https://www.darwinproject.ac.uk/letter/DCP-LETT-7471.xml

See also CDC pp. 8-9

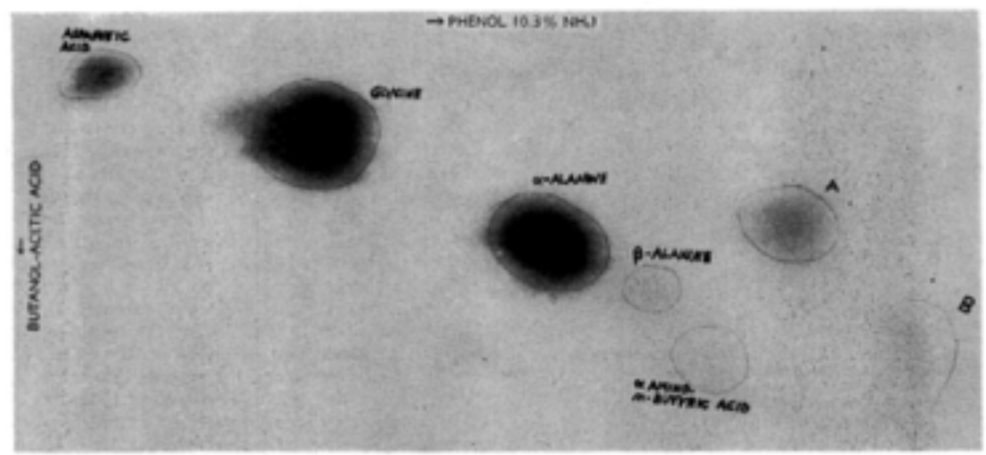
Also Haldane and Oparin (CDC p. 6)

4.3 The origin of life

Miller-Urey experiment: primordial composition of the earth’s atmosphere (in analogy to those present on Jupiter and known through spectroscopy): ammonia, hydrogen and methane —> electric sparks emulating lightning —> amino acids used to build proteins by extant life forms, i.e., the “building blocks” of life.

A Production of Amino Acids Under Possible Primitive Earth Conditions

Stanley L. Miller[1, 2]
G. H. Jones Chemical Laboratory, University of Chicago, Chicago, Illinois



4.4 The origin of life

Primordial soup fell out of favour because original soup was not rich in those elements, even though meteorites showed presence of amino acids.

<u>"Concentration problem"</u>: in oceans, organic molecules are much more probable to dissolve rather than form polymers such as RNA.

How can concentration problem be solved without compartments? Under what conditions can compartments be naturally formed?

<u>Origin of compartmentalisation, metabolism and replication completely evaded</u>: the passage from amino acids to proteins and the origin of nucleotides and membranes remain mysterious.

Discovery that RNA molecules are both "self-replicating" and enzymes (ribozymes) and that ribosomes and other major cellular components operating in basic cellular processes are made out predominantly of RNA changed origin of life research.

4.5 The origin of life

RNA world hypothesis: emergence of a self-replicating system from a “soup” of nucleotides. RNA can:

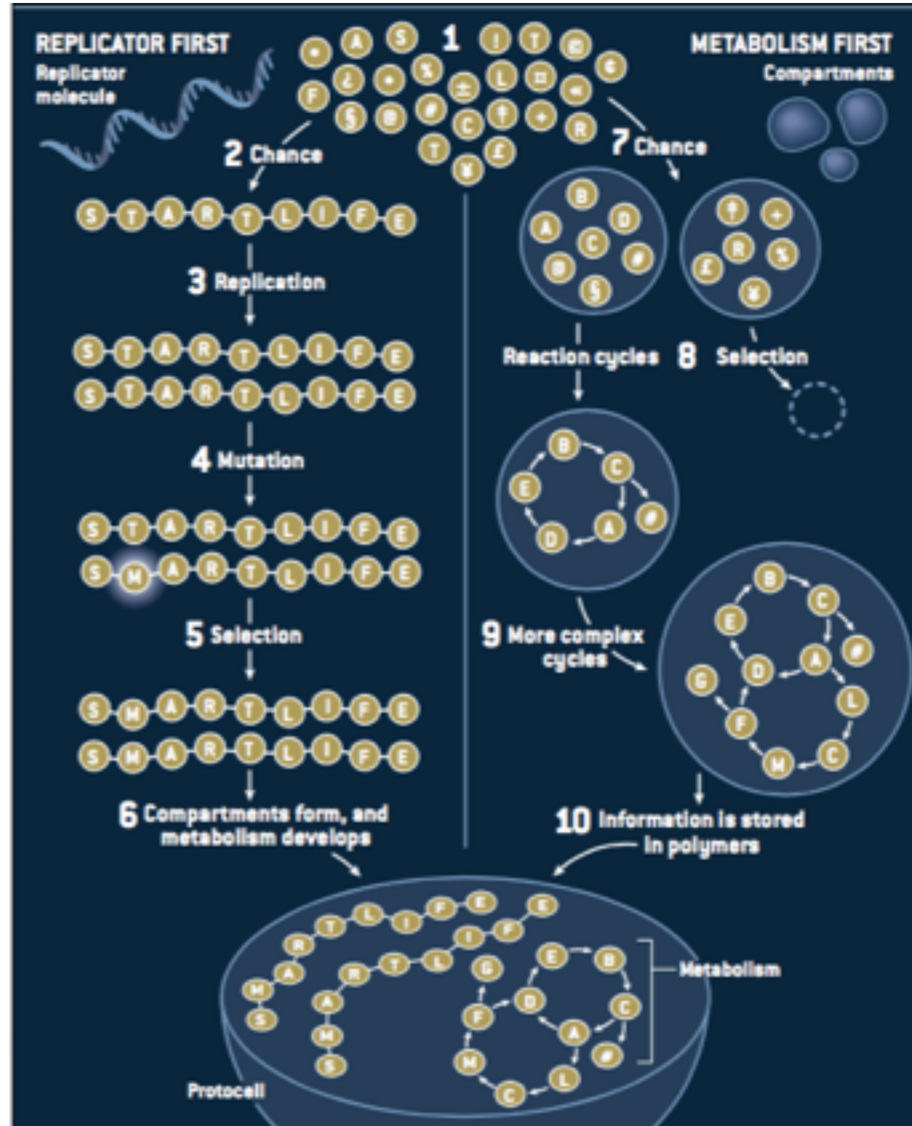
“… catalyse the synthesis of a new RNA molecule from precursors and an RNA template …. <u>there is no need for protein enzymes at the beginning of evolution</u>. One can contemplate an RNA world, containing only RNA molecules that serve to catalyse the synthesis of themselves…. The first stage of evolution proceeds, then, by RNA molecules performing the catalytic activities necessary to assemble themselves from a nucleotide soup …. they then develop an entire range of enzymic activities. At the next stage, RNA molecules began to synthesize proteins … <u>I suggest that protein molecules do not carry out enzymic reactions of a different nature from RNA molecules but are able to perform the same reactions more effectively</u> and rapidly, and hence will eventually dominate. … <u>Finally, DNA appeared on the scene</u>.”

Gilbert, W. 1986. The RNA World. Nature. 319 (6055): 618. doi: 10.1038/319618a0.

4.6 The origin of life

RNA world hypothesis:

1. replication first scenario;
2. metabolism initially RNA-based (but nothing proposed about nature of chemical reactions catalysed);
3. and how can an RNA-based metabolism be stable without compartments?



4.7 The origin of life

Advantages of RNA world hypothesis (CDC p. 19):

1. RNA can in principle encode protein sequences in the same way as DNA;
2. It can form base pairs and replicate in the same way as DNA;
3. It can fold into three-dimensional structures that would be very difficult for DNA, but analogous to those of proteins;
4. It can recognize and interact specifically with other molecules;
5. It can act as a specific catalyst for chemical reactions.

At the same time, it faces a series of profound conceptual problems.

4.8 The origin of life

A. Cornish-Bowden and M.L. Cárdenas

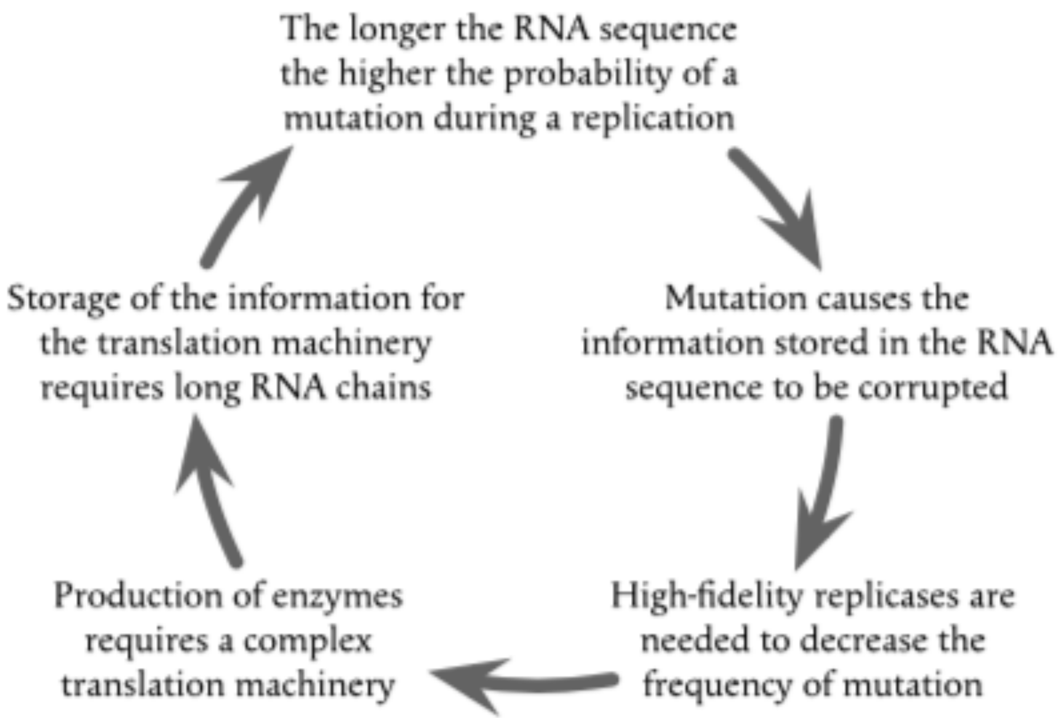


Fig. 15. Eigen's paradox. Following the arrows (starting anywhere) shows that a simple model in which the same kinds of molecules fulfil both functions cannot work: RNA does not have sufficient catalytic potential to provide the necessary specificity, and proteins alone cannot replicate. The scheme is based on Fig. 2 of Szostak et al. (2016).

Which came first: nucleotide/ information or protein/ enzyme? Insoluble conceptual problem.

4.9 The origin of life

"As one of the most esteemed proponents of the RNA world hypothesis, the late Leslie E. Orgel, once pointed out: "[w]hile acceptance of an RNA World greatly simplifies the problem of the origin of life, it also has a negative aspect. <u>If the origin of the RNA World preceded the origin of protein synthesis, little can be learned about the chemistry of the origin of life from the study of protein enzyme mechanisms</u> …. If the RNA World originated *de novo* on the primitive Earth, it erects an almost opaque barrier between biochemistry and prebiotic chemistry."

Martin et al. 2008. Hydrothermal vents and the origin of life. Nat. Rev. Microbiol 6 (11), 805–814. p. 811

4.10 The origin of life

Bottom-up approach: focus on geochemical conditions. Alkaline vent as location were abiogenesis might have occurred because:

1. <u>it provides a possible solution to the problem of origin of compartments</u>: the first ancestral cells arose spontaneously and were porous rocky structures or mineral cells with iron-sulphur wall composition;

2. <u>it provides a possible solution to the origin of metabolism</u>: such compartments offered an ideal vehicle to concentrate chemical reactions and organic molecules and thus perform autocatalysis;

3. <u>it provides some hints concerning the origin of replication</u>: hydrogen and carbon dioxide are components freely available in such vents and through some chemical reactions production of complex organic molecules (such as nucleotides) might ensue.

4.11 The origin of life

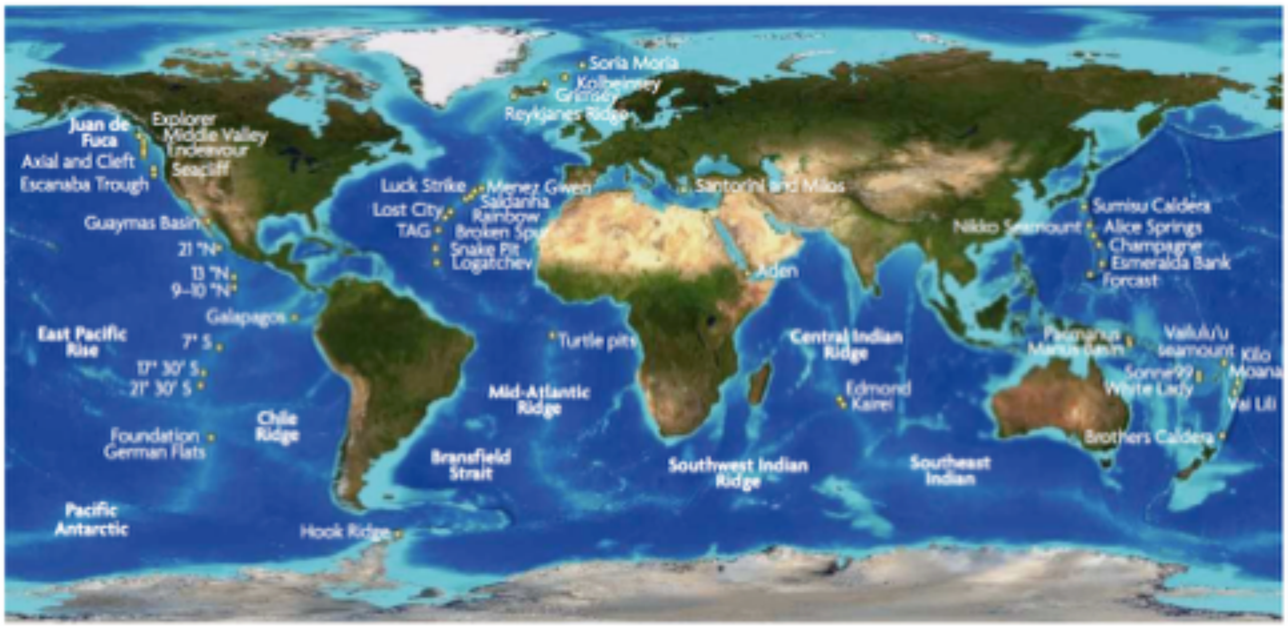
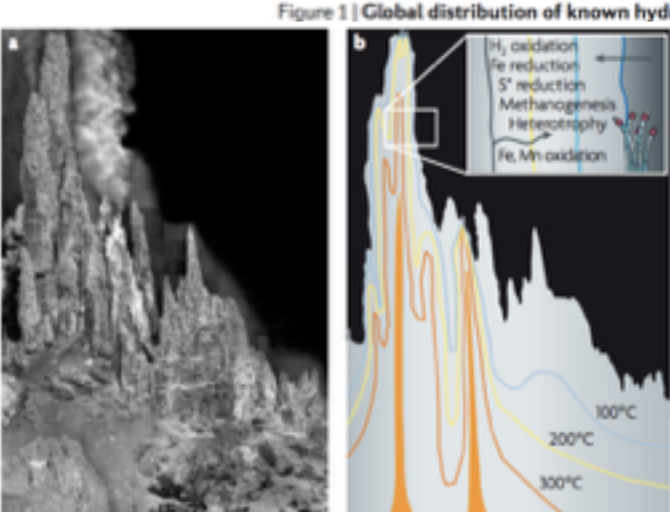


Figure 1 | Global distribution of known hydrothermal vents. Temperature and chemical anomalies hint that many
Data courtesy of D. Fornari and T. Shank, Woods Hole Oceanographic



Ancestral compartments
or “inorganic cells:.

4.12 The origin of life

This bottom-up approach has been merged with an organisational (rather than compositional) approach focused on metabolism and organisational features (rather than molecules).

The RNA world hypothesis does not countenance the possibility of spontaneous catalysis (what Gilbert says is that protein enzymes are substituted by RNA catalysts). But some metabolic pathways occur spontaneously in certain environmental contexts.

Ancestral metabolism was probably based on the spontaneous Wood–Ljungdahl metabolic pathway (Martin, W., Russell, M.J., 2007. On the origin of biochemistry at an alkaline hydrothermal vent. Phil. Trans. R. Soc. B 362, 1887–1925).

4.13 The origin of life

"Did enzymes invent all biochemical reactions or did chemistry (similar to some biochemical reactions) naturally exist before the assistance of enzymes? Enzymes do not perform feats of magic, but merely allow chemical reactions that have a tendency to occur anyway to occur more rapidly …. the first step of biological methanogenesis, the formation of a carbamate, is spontaneous and requires no protein at all. Of course, it remains within the realm of possibilities that modern microbial metabolism holds no relics of the chemistry that preceded the origin of genetic material."

Martin et al. 2008. Hydrothermal vents and the origin of life. Nat. Rev. Microbiol 6 (11), 805–814. p. 811

4.14 The origin of life

Basic point: the ancestral Wood–Ljungdahl metabolic pathway was a spontaneous process energetically stable without need of protein-or-RNA-mediated catalysis.

It was not invented by genes; only later on during evolution gene-protein regulation emerged.

The pathway was internalised in the rocky compartments earlier than DNA and proteins were invented.

Eigen problem is dissolved because basic metabolism was not gene-protein-mediated.

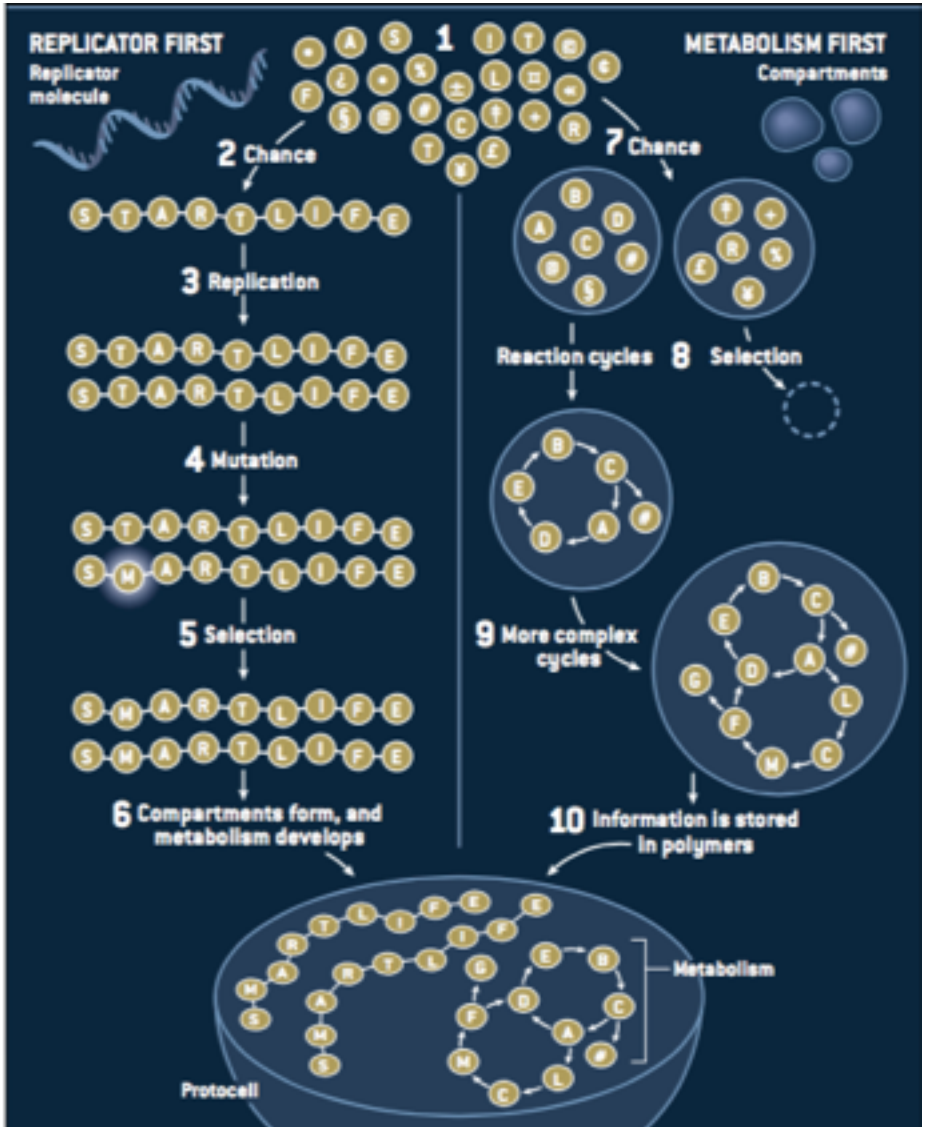
4.15 The origin of life

LUCA was not a free living cell but a rocky labyrinth of mineral cells with walls composed of iron, sulphur and nickel and energised by proton gradients. <u>Can we call this life?</u>

Remember the quotation in slide 2.1:

"The basis of biology is physical chemistry. From the moment that one works in biochemistry and biophysics, and understands the physico-chemical mechanisms that account for the properties of living beings, <u>life vanishes</u>! Today molecular biologists have no need to use the word 'life' in their work." Atlan and Bousquet (1994) [quoted in **CDC** - p. 3]

4.16 The origin of life



Life at the origin was, according to Martin et al. (2007, 2008), compositionally and organisationally different:

1. compartments were not like extant membranes;
2. metabolism was not gene-protein-based;
3. replication evolved afterwords (metabolism first scenario).

However, there was an <u>important organisational similarity: </u>the harnessing of basic autocatalytic chemical reactions (i.e., Wood–Ljungdahl metabolic pathway) and chemical processes (e.g., chemiogenesis).

5.1 Definitions of life

<u>What is known about extant life?</u>

Common ancestry (vs Lamarck's view) postulated;

Common core of conserved biochemical components and organisational features (basic metabolic reactions);

No spontaneous generation in the sense of a continuous process; but it happened somehow at least once (vs. idea that spontaneous generation is now occurring);

Abiogenesis: life emerged from non-life (vs biogenesis); other possibility is panspermia (partial and complete).

<u>Material</u>

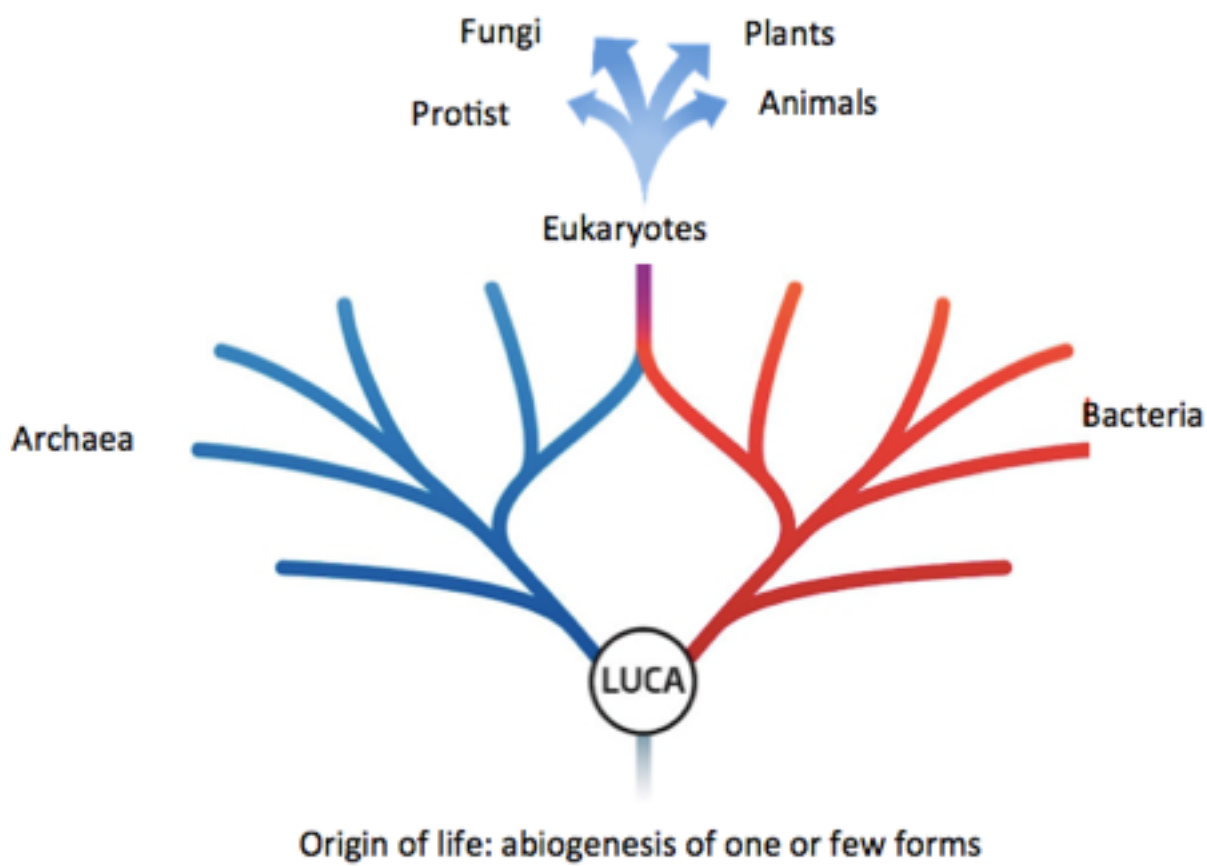
Bedau, M. (1997). Four Puzzles about Life. Artificial Life 4:125-140.

Bich and Green. 2018. Is defining life pointless? Operational definitions at the frontiers of biology. Synthese (2018) 195:3919–3946.

Cornish-Bowden, A. & María Luz Cárdenas, M.L. 2020. Contrasting theories of life: Historical context, current theories. In search of an ideal theory. Biosystems, 188.https://doi.org/10.1016/j.biosystems.2019.104063.

Sagan, C. 2010. Definitions of life. In M. Bedau & C. Cleland (Authors), The Nature of Life: Classical and Contemporary Perspectives from Philosophy and Science (pp. 303-306). Cambridge: Cambridge University Press. doi:10.1017/CBO9780511730191.029

5.2 Definitions of life



Schematic representation of the common ancestry of all life forms descended from LUCA. Before LUCA there might have been a plurality of life forms that have not left any genomic trace in extant organisms. The origins of life and LUCA are not the same (CDC p. 27).

5.3 Definitions of life

"It is difficult to generalize from a single example, and in this respect the biologist is fundamentally handicapped ….. <u>It is not known what aspects of living systems are necessary in the sense that living systems everywhere must have them; it is not known what aspects of living systems are contingent in the sense that they are the result of evolutionary accident, so that somewhere else a different sequence of events might have led to different characteristics</u>. In this respect the possession of even a single example of extraterrestrial life, no matter how seemingly elementary in form or substance, would represent a fundamental revolution in biology."

Sagan, C. (1970). Life. Encyclopedia Britannica, pp. 1083–1083A, Chicago: Encyclopædia Britannica Incorporated.

5.4 Definitions of life

Given the speculations about the origin of life and what is known about extant life, what kind of definition should we seek?

Can life be defined in essentialist terms?

Strong ontological definitions (necessary and sufficient conditions; discriminating life from non-life; fixed conditions) vs operational definitions (focus on scientific practice; content of definitions used in experimental research and model building).

Is life a distinctive material constitution (i.e., specific "biomolecules", e.g., RNA) or a specific mode of organisation of material components (e.g., universal biochemical pathways)? Does this question require an essentialist definition?

5.5 Definitions of life

Does lack of an agreed definition impair scientific research? And applied research? Operational definitions abound:

Origin of life research: what is the minimal biochemical life?

Astrobiology: how can we detect life?

Artificial life: what are the organisational requirements of life?

Synthetic biology: when is designed life new life and real life?

(Bich and Green. 2018. Is defining life pointless? Operational definitions at the frontiers of biology. Synthese (2018) 195:3919–3946)

5.6 Definitions of life

Is life a "Boolean" property (either yes or no, dichotomous)?

"… the common sense view [that life is a Boolean property] is put under stress by various borderline cases like viruses which are unable to replicate without a host and spores or frozen sperm which remain dormant and unchanging indefinitely but then 'come back to life' when conditions become suitable."

Bedau, M. (1997). Four Puzzles about Life. Artificial Life 4:125-140.

At which stage of evolution (think about both the RNA world hypothesis and the Martin-Russell hypothesis) are the biological system evolving alive?

5.7 Definitions of life

Physiological: any system capable of performing functions such as eating, metabolising, excreting, breathing, moving, growing, reproducing, and being responsive to external stimuli etc.

Biochemical: systems that contain reproducible hereditary information coded in nucleic acid molecules, and that metabolise by controlling the rate of chemical reactions using proteinaceous catalysts, i.e., enzymes.

Genetic: emphasis on the importance of replication, independently of the material nature of the hereditary material.

Metabolic: a living system as an object with a definite boundary, continually exchanging some of its materials with its surroundings, but without altering its general properties, at least over some period of time.

Sagan, C. (1970). Life. Encyclopedia Britannica, pp. 1083–1083A, Chicago: Encyclopædia Britannica Incorporated.

5.8 Definitions of life

Physiological: any system capable of performing functions such as eating, metabolising, excreting, breathing, moving, growing, reproducing, and being responsive to external stimuli.

Problem: folk biology based. Many of these properties are either present in machines (e.g., thermostats, robotic vacuum cleaners, cars) that nobody is willing to call alive, or absent from biological entities that could be considered alive (e.g., viruses, anaerobic bacteria).

5.9 Definitions of life

<u>Biochemical: systems that contain reproducible hereditary information coded in nucleic acid molecules, and that metabolise by controlling the rate of chemical reactions using enzymes.</u>

Problems: extraterrestrial, artificial ("… were man able to construct a system that had all the functional properties of life, it would still not be alive if it lacked the molecules that earthly biologists are fond of …" Sagan p. 304) and synthetic life unaccounted for.

Focus on material composition rather than functional organisation might be unjustified: some compositional biochemical aspects are evolutionarily contingent.

5.10 Definitions of life

<u>Genetic definitions (subset of biochemical): emphasis on the importance of replication, independently of the material nature of the hereditary material.</u>

Problems: what about non-replicating biological entities, entities that are not reproductively autonomous etc.?

“We have not forgotten evolution and reproduction, but …. we regard them as consequences of life, not prerequisites. A self-organizing system in a constant environment could sustain itself for ever if it made no mistakes, even if it was unable to grow. However, no chemical reaction is 100% specific: ‘‘mistakes’’ always occur, in consequence the system evolves. If it grows it will inevitably reach a size where it needs to divide, and, because of ‘‘mistakes’’ the resultant entities will not be identical, and so reproduction implies a capacity for evolution. In summary, staying alive is the fundamental necessity. Reproduction is not …” CDC p. 29

5.11 Definitions of life

<u>Metabolic definitions: emphasis on the self-maintenance.</u>

1. Thermodynamic openness and possibility to make a living out of environmental acquisition of precursors of molecular components and energy.

2. Autocatalytic network of reactions is maintained for a significant time. <u>How is autocatalysis or “organisational closure” achieved?</u>

3. Boundary enclosing the network (structural closure). <u>Must the boundary be self-produced?</u>

5.12 Definitions of life

A. Cornish-Bowden and M.L. Cárdenas

A. Cornish-Bowden and M.L. Cárdenas

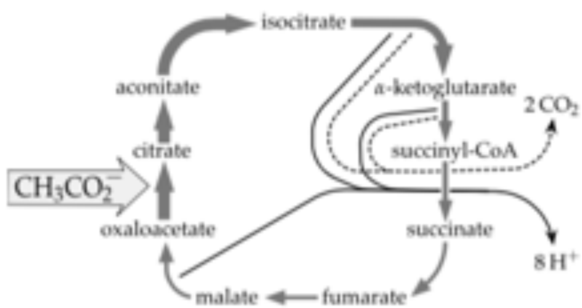


Fig. 20. Metabolic cycles. The tricarboxylate cycle (various coenzymes are not shown)

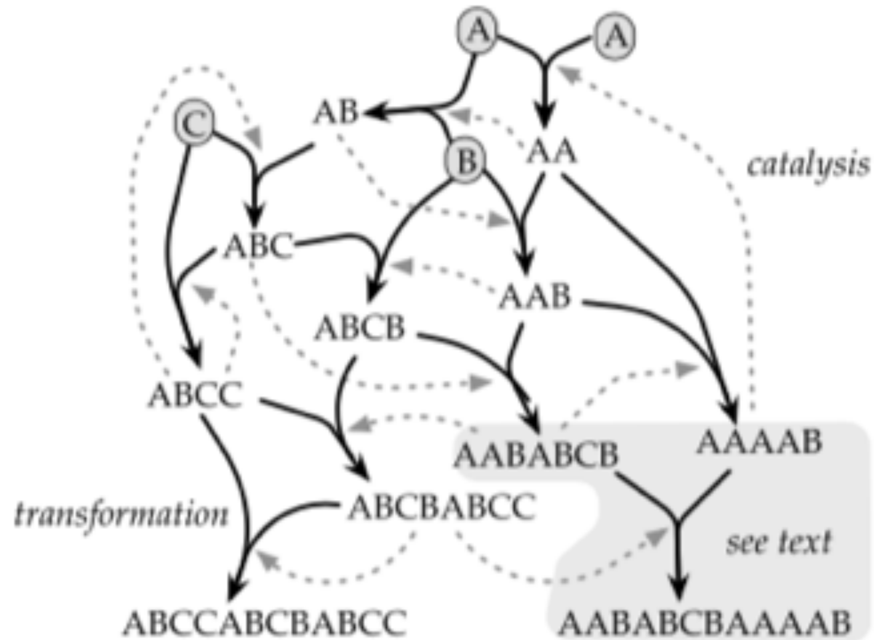
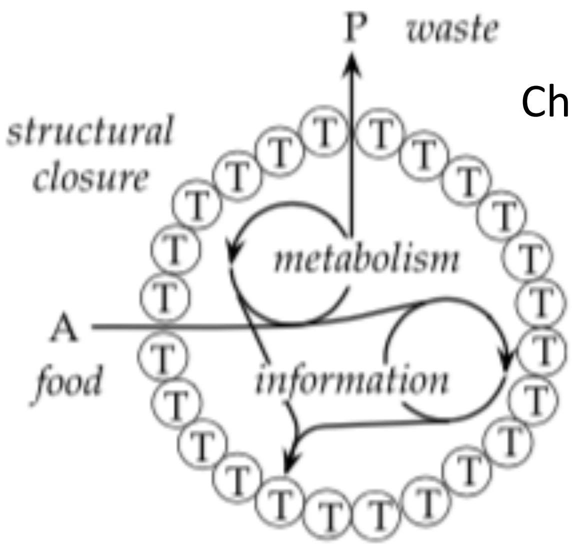


Fig. 34. An autocatalytic set as described by Kauffman (1986, 1993, pp. 298–341). The food molecules A, B and C shown in ovals are available in sufficient quantities from the environment. They can be amino acids, or RNA bases or other kinds of molecule that have some catalytic properties and are capable of polymerizing into chains of indefinite length. Full arrows represent chemical transformations, and broken grey arrows identify their catalysts. All of the intermediates can be generated from the food molecules by series of catalysed reactions. The shaded part of the diagram is discussed in the text.

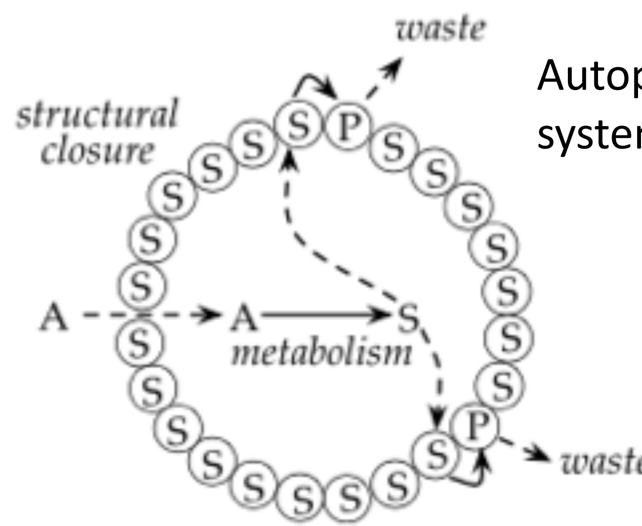
- Arising spontaneously by self-organisation and predating gene-protein regulation?
- Autocatalysis must be achieved and then maintained.

5.13 Definitions of life



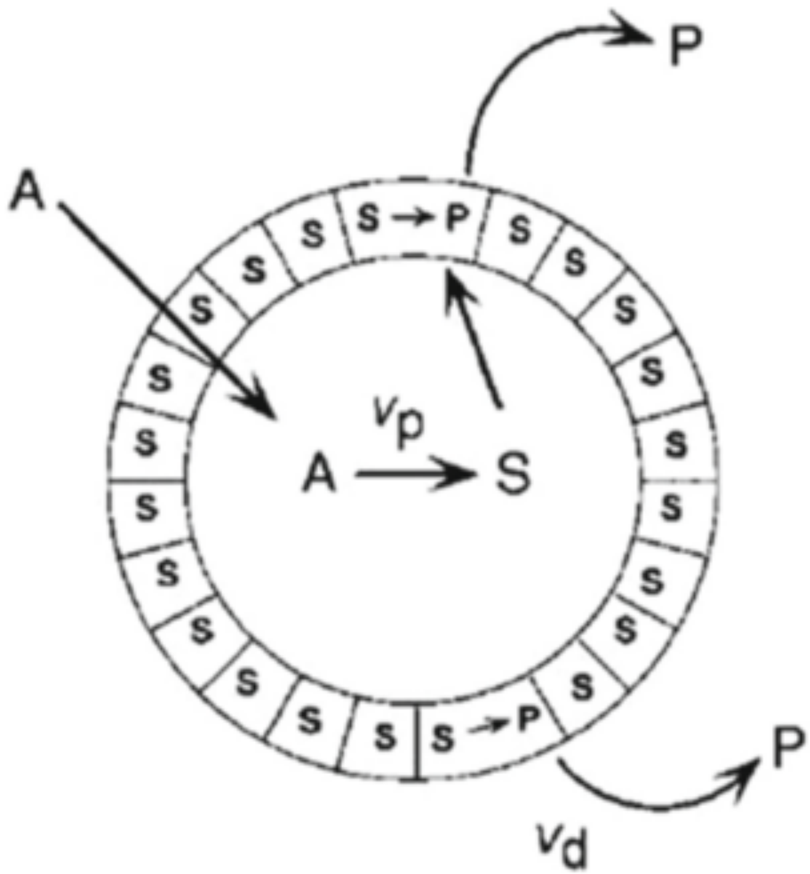
Chemoton

Autopoietic
system



Is self-produced boundary needed?
Is an information cycle needed?
Is self-production needed?
Is catalytic closure needed?

5.14 Definitions of life



$$v_p = \frac{d[S]}{dt} \quad ; \quad v_d = -\frac{d[S]}{dt}$$

if $v_p = v_d$ homoestasis

if $v_p > v_d$ self-reproduction

Zepik, H. H., Blöchliger, E., & Luisi, P. L. (2001). A chemical model of homeostasis. Angewandte Chemie, 113, 205–208.

5.15 Definitions of life

"A living system is spatially defined by a semipermeable compartment of its own making and which is self-sustaining by transforming external energy/nutrients by its own process of component production."

Luisi, P. L. (1998). About various definitions of life. Origins of Life and Evolution of the Biosphere, 28, 613–622. p. 619

Integration of metabolism and self-produced compartmentalisation from environment.

Biochemically-based, but focus is on membrane/boundary and metabolic activity, not on replication (which is a by-product of growth).

5.16 Definitions of life

Must the boundary be self-produced? "Martin and Russell (2007)… argue strongly against such theories [making a self-produced boundary a prerequisite] on various grounds ….. We find their arguments persuasive, and accordingly do not regard the lack of membranes fabricated internally …. as long as alternative natural compartments are available." CDC p. 32

The need for all catalysts to be products of the metabolism of the system itself is, analogously, not necessary if catalysts can be "developmentally entrenched" from the environment.

Physiological autonomy varies along a gradient. Ancestral life was probably much more dependent on environmental resources than extant life.

5.17 Definitions of life

What CDC do is adopting a conception of extant organism in order to define the essence of life:

"Can any of the current theories be considered to be an ideal theory of life? To answer that we need to begin by listing the characteristics that an ideal theory ought to have. A **living organism** must then have the following characteristics …." CDC p. 29

Life = organismality.

Does the "essence" of life concern the material out of which it is composed (i.e., a distinctive material constitution) or the form in which that material is arranged (i.e., a distinctive organisation)?

A distinctive organisation.

5.18 Definitions of life

Nothing wrong with this, but:

1. extant organisms are different from ancestral ones (that's why origin of life research is so important for defining life);

2. what is an organism in the first place?Many biological systems can display some form of "organismality": where do we draw the line?

We shall see in the next class.

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