Mestrado e Doutorado em História e Filosofia das Ciências

Filosofia das Ciências da Vida (codes 585146, 485102)

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2nd semester 2020/2021

Sala: 8.2.02

Practicalities

Aims - In each class, the goal is to unravel the history and the philosophical significance of a particular theoretical and philosophical problem. This is an interdisciplinary course at the interface between the history of biology, the philosophy of biology and biology itself.

Teaching methodology - Three modules taught by three instructors that are at the same time partially independent and significantly overlapping.

Evaluation:

- 75 % - One 3.000 words well-structured essay (i.e., introduction, development of an argument and analysis, conclusion);
- 25 % - One 20-minutes class presentation on a topic of the course in the last class meeting.
- Distinct topics.

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

- Developmental biology, embryology (very old)
- Systematics (very old)
- Physiology (very old)
- Evolutionary biology (after Lamarck 1809 at least)
- Biochemistry (1838 Gerardus Johannes Mulder), molecular biology
- Virology (1892 Dmitry Ivanovsky or 1898 Martinus Beijerinck), microbiology (Antonie Van Leeuwenhoek 1673), botany, zoology
- Cell biology (Matthias Schleiden and Theodor Schwann 1839)
- Genetics (Mendel 1865), genomics (1990s)
- Ecology (oldish), conservation biology
- Synthetic biology (2000s) ….. etc.

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 1970 p. 303.

CLASS 1 THEME: Life

A. The domain and autonomy of biology;
B. Origin of life: from spontaneous generation to contemporary scenarios;
C. Definitions of life: compositional vs. organisational.

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.

Material

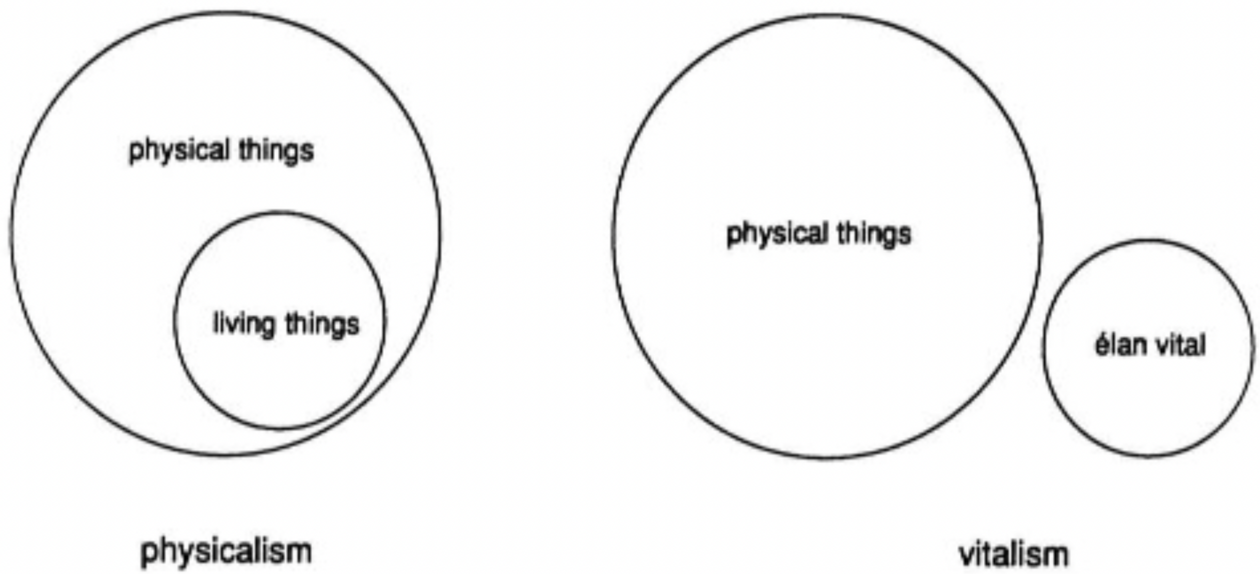
Cornish-Bowden, A. & María Luz Cárdenas, M.L. (2020). Contrasting theories of life: Historical context, current theories. In search of an ideal theory. Biosystems, 188:1-50. https://doi.org/10.1016/j.biosystems.2019.104063. (henceforth CBC)

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

Mayr, E. (1996). The Autonomy of Biology: The Position of Biology Among the Sciences. The Quarterly Review of Biology 71(1):97-106.

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

1.2 Life: the domain of biology



(a) biology and physics

Sober 1993

1.3 Life: the domain of biology

Physicalistic materialism = all living things are physical objects. If you take a living thing, 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.

* Non-materialistic vitalism as a form of substance dualism.

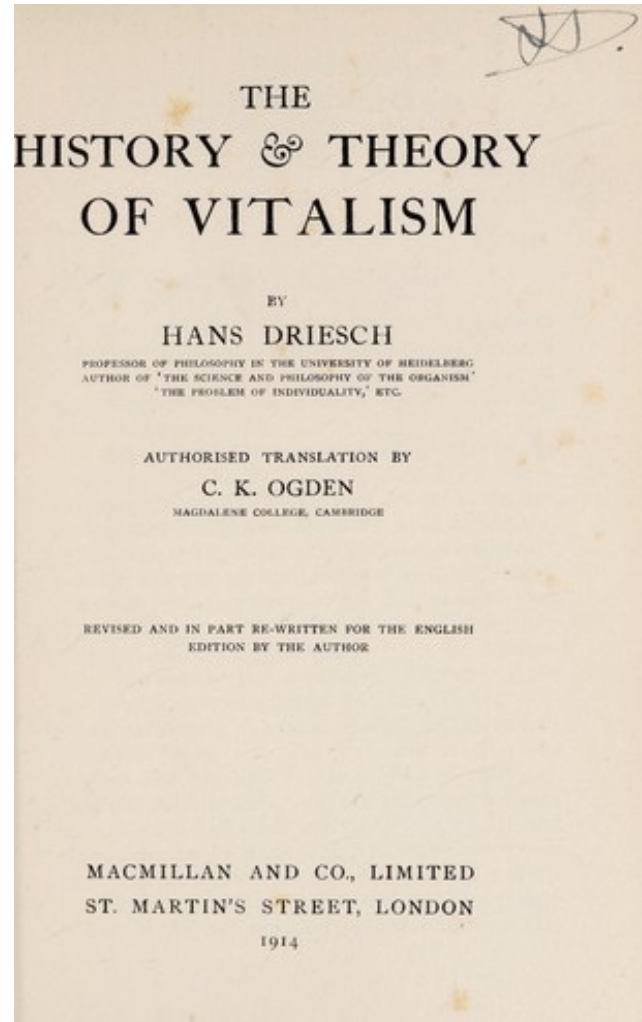
1.4 Life: the domain of biology

Non-materialistic vitalism: life is another substance distinct from physical stuff.

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)

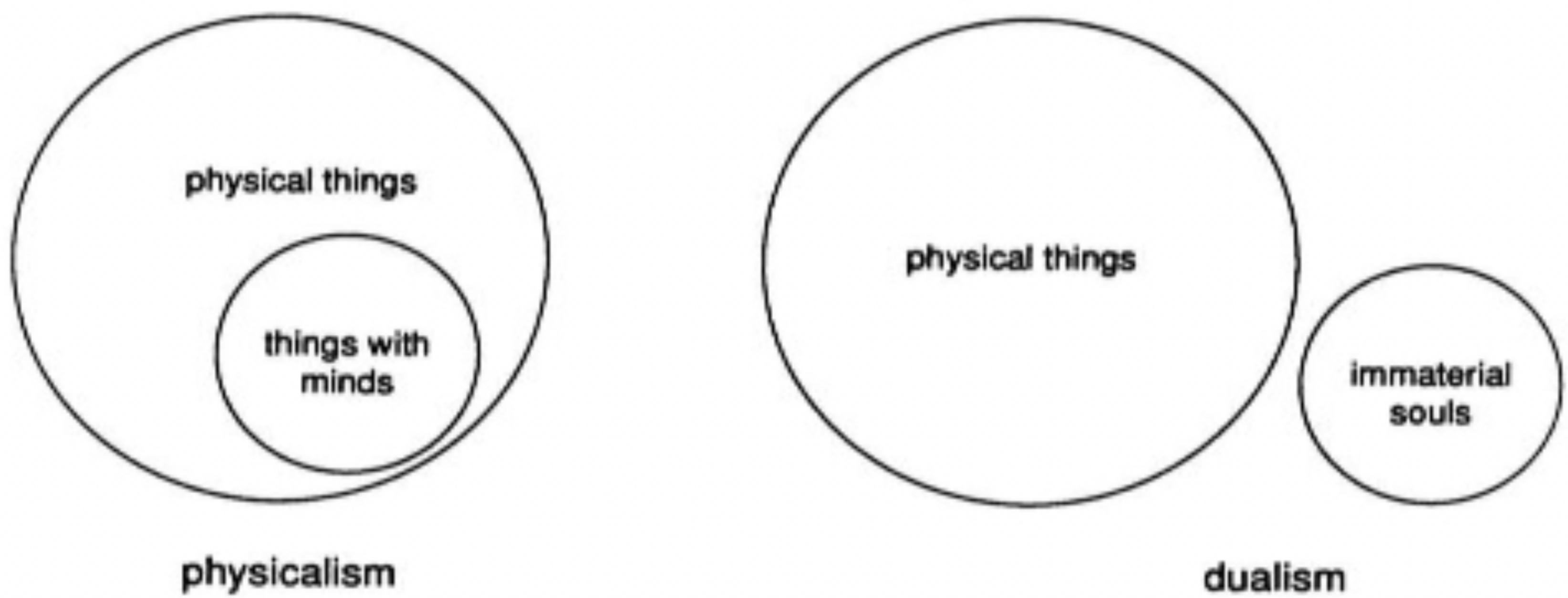
Buchner discovered that yeast extract with no living yeast fungi can form alcohol from a sugar solution. Thus, biochemical processes do not necessarily require living cells. They are rather governed by proteins.

In class 3 we shall speak of Driesch again. Note that he wrote after Buchner.



1.5 Life: the domain of biology

Parallel with psychology.



Sober 1993

1.6 Life: the domain of biology

Non materialistic vitalism = substance dualism (in analogy with Descartes, i.e., *elan vital* analogous to soul).

Cartesian substance dualism provided the foundation for the natural sciences, sharply “isolating” *res extensa* and *res cogitans.*

The first is to be studied through through mathematisation and measurement by focusing on primary qualities (independent of the observer, e.g., extension, motion, shape).

Cartesianism also lead to the expurgation of secondary qualities (dependent on the observer, e.g., colour, taste, smell) from the ontology of the natural sciences.

1.7 Life: the domain of biology

Cartesian substance dualism provided the foundation for the natural sciences, sharply “isolating” *res extensa* and *res cogitans.*

Cartesianism also generated two conundrums that still reverberate in the way we think about biological phenomena these days:

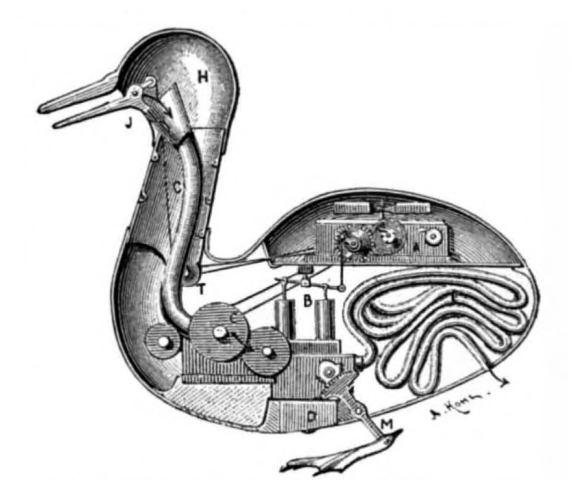
1. The so-called “mind-body” problem (how do the two substances causally interact?);

2. The phylogenetic spread of cognition, consciousness and sentience (assumed by Descartes to be confined to the solitary case of humans).

1.8 Life: the domain of biology

Ironically, Descartes also conveniently freed (non-human) biology of its ontological weight, introducing the mechanical interpretation of non-human organisms as reflex-driven machines.

Animals are, according to this view, merely complicated versions of the famous mechanical digesting duck created by Jacques de Vaucanson in 1739 in France.



INTERIOR OF VAUCANSON'S AUTOMATIC DUCK.
A, clockwork; *B*, pump; *C*, mill for grinding grain; *F*, intestinal tube; *J*, bill; *H*, head; *M*, feet.

1.9 Life: the domain of biology

“…. if one knew in detail all the parts of the seed of a particular species of animal, for instance, Man, one could deduce from that alone for reasons entirely mathematical and certain, the whole figure and conformation of each of its parts."

Descartes, René (1909 [1648]) ‘La Description du Corps Humain’, in Charles Adam and Paul Tannery (eds) Oeuvres de Descartes, vol. XI, Paris: Cerf.

1.10 Life: the domain of biology

So, we have a contrast between:

Physicalistic materialism = substance monism.

Non materialistic vitalism = substance dualism.

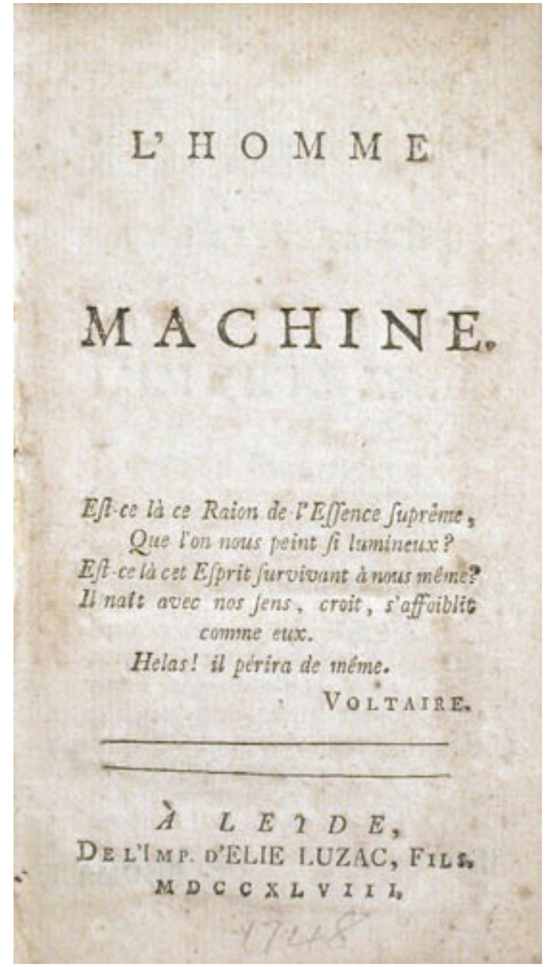
Other forms of monism possible?

More specifically, other types of monism that could be biologically relevant?

1.11 Life: the domain of biology

Materialistic vitalism (intuitively perceived as an oxymoron): “An obvious solution ….. was to see matter itself as inherently dynamic, capable of feeling, even intelligent. Motion and mind derive from some inherent powers of life or sentience that dwell in matter itself or in the organizational properties of matter.”

Skrbina, D. 2017. Panpsychism in the West. Cambridge, MA: MIT Press. p. 123



L'HOMME

MACHINE.

Est-ce là ce Raion de l'Essence suprême,
Que l'on nous peint si lumineux?
Est-ce là cet Esprit survivant à nous même?
Il naît avec nos sens, croît, s'affoiblit comme eux.
Helas! il périra de même.

VOLTAIRE.

À LEYDE,
DE L'IMP. D'ELIE LUZAC, FILS.
MDCCXLVIII.
1748

La Mettrie

1.12 Life: the domain of biology

The equation of materialism with mechanism is not necessary.

Kant was a materialist and (seemingly) also an anti-mechanist:

"An organized being is then not a mere machine, for that has merely moving power, but it possesses in itself formative power of a self-propagating kind which it communicates to its materials though they have it not of themselves; it organizes them, in fact, and this cannot be explained by the mere mechanical faculty of motion." (Immanuel Kant, Critique of Judgment 1790, SS65)

1.13 Life: the domain of biology

There is a general agreement today on a materialistic ontology (vs vitalism and dualism): living objects are made only of physical objects.

Substance dualism has been rejected.

The chief reason is the increasing knowledge concerning the chemical nature of life (e.g., nucleotides composing DNA and RNA, amino acids composing proteins, cells composing multicellular organisms).

However, the rejection of substance dualism leaves a host of ontological and epistemological issues concerning the domain of study of biology and its putative autonomy from the physico-chemical sciences open.

1.14 Life: the domain of biology

"Traditionally, the argument against an autonomy of biology was simple: Only Cartesian science (physicalism) is exact science, and only exact science is real science. Whatever in biology does not answer to the Cartesian concept has to be assigned to vitalism. Although this view has still been expressed rather recently (e.g., Crick 1966; Smart 1963), Nagel (1961) recognized perceptively that classical vitalism, such as that of Driesch, '*is now almost entirely a dead issue in the philosophy of biology . . . [but that] many outstanding biologists who find no merit in vitalism are equally dubious about the validity of the Cartesian program and . . . advance . . . reasons for affirming the irreducibility of biology to physics, and the intrinsic autonomy of biological methods*'. Mayr 1996 p. 103

1.15 Life: the domain of biology

The open ontological and epistemological issues can be classified in two interrelated categories:

1. The dispute between reductionism (physico-chemicalism or “machinism”) and organicism/holism: e.g., what counts as a satisfactory causal explanation in biology? What kinds of entities should be considered? What kinds of causal interaction?

2. The dispute concerning the autonomy of biology from physics and chemistry (e.g., nomological, methodological, explanatory): e.g., are there any laws in biology at all? Are there any laws irreducible to physics? Are evolutionary explanations reducible to biochemistry and molecular biology?

1.16 Life: the domain of biology

"…. reductionists usually adopt one of two strategies. They may say that 'vital processes' can be reduced to physicochemical processes, which obey universal laws, and that anything in biology that cannot be reduced in this manner is simply not part of science. And since the reduced portion of biology obeys the Cartesian program, there is no reason to acknowledge an autonomy of biology. The other option is not very different. It simply designates the part of biology that cannot be expressed in the terms of universal laws as natural history, and claims that natural history is not part of science." Mayr 1996 p. 103

1.17 Life: the domain of biology

In a sense, 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 2001 p. 1.

This view implies that biology is not an autonomous science because it has no independent domain of study, i.e., life.

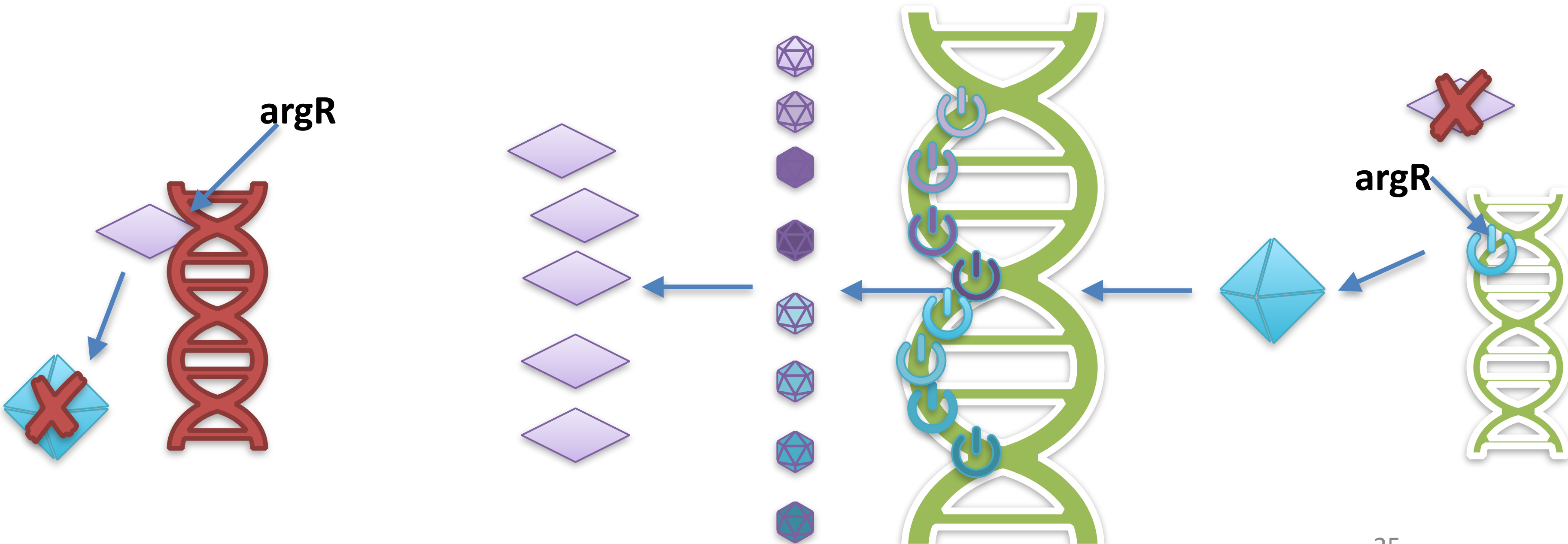
1.18 Life: the domain of biology

“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 CDC, p. 3])

1.19 Life: the domain of biology

Arginine biosynthesis pathway in bacteria: 8 metabolic steps catalysed by eight enzymes. The production of these enzymes is regulated by the arginine repressor (gene argR) “switching” off and on.

If arginine is present in the bacterial cell, it binds to argR, switching it off, repressing the 8 enzymes’ transcription. If arginine is absent in the bacterial cell, argR is switched on and all enzymes are transcribed.



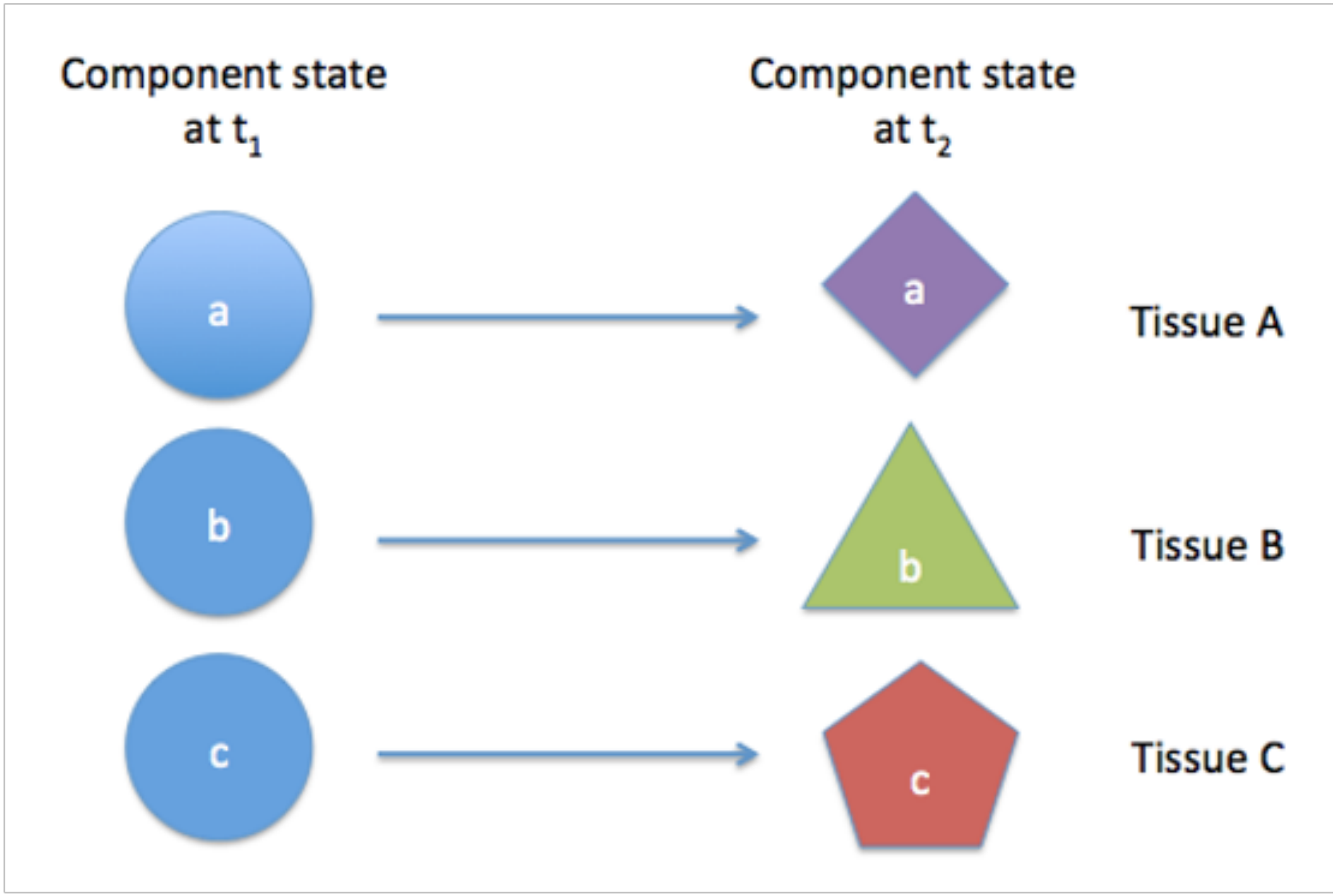
1.20 Life: the domain of biology

However, there is an alternative to reductionism:

"…. 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 2001 p. 1

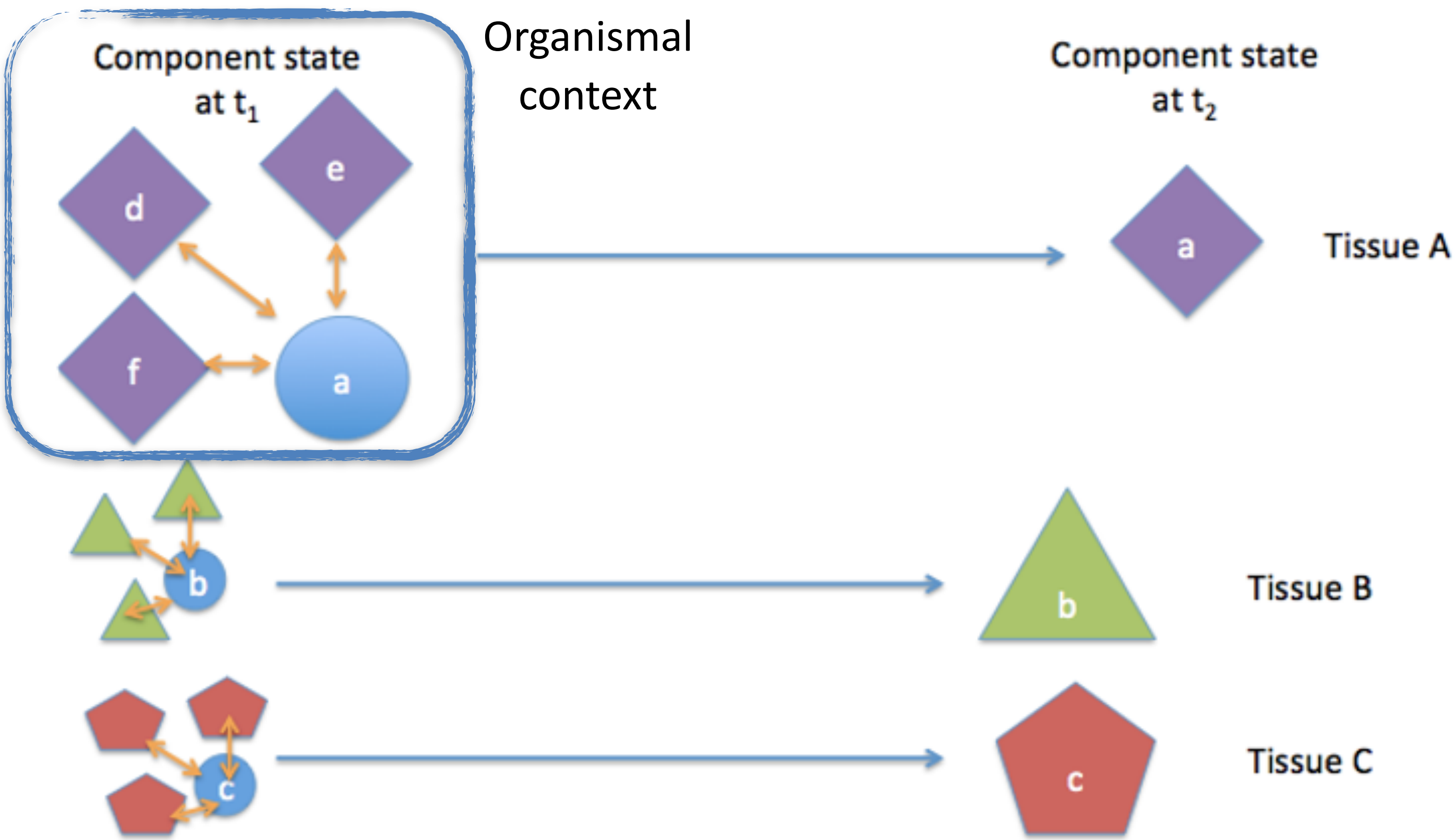
The difference between life and non-life concerns how parts are put together in a whole.

1.21 Life: the domain of biology



Cellular differentiation: reductionist explanation

1.22 Life: the domain of biology

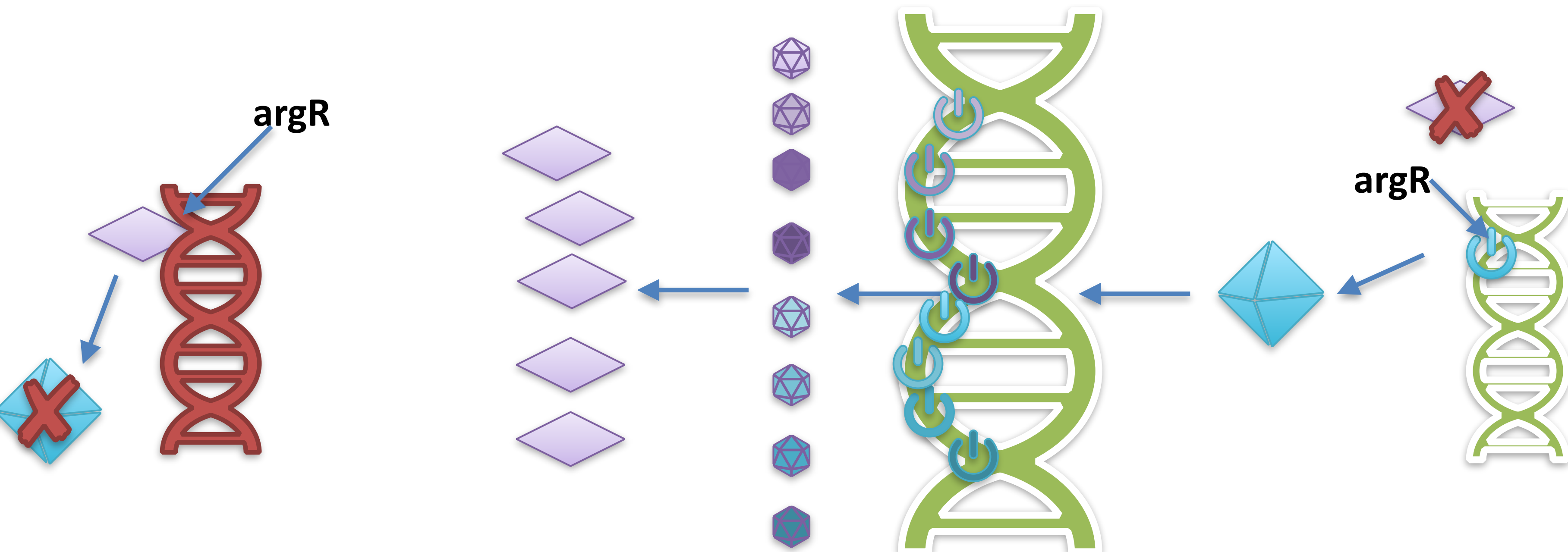


Cellular differentiation: organicist explanation

1.23 Life: the domain of biology

"Organicism has little to do with vitalism, except for the thesis that organisms are not simply inert matter. In other words, physicalism and vitalism are not the only two possible philosophies of biology: Organicism is a third option. If one wants to reject the autonomy of biology, it is no longer sufficient just to refute vitalism. Now it is necessary to prove that it is possible to reduce organicism to the Cartesian program, and no one has been able to do this." Mayr 1996 p. 103

1.24 Life: the domain of biology



Organicist explanation: how can context be important in this case?

1.25 Life: the domain of biology

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?

The first answer is that life has a peculiar chemistry.

The second answer is that life is organised matter.

One way to understand whether the first or second answer is correct is to enquire about life’s origin: how did life originate?

In the next part I shall show that the increasing knowledge concerning the chemical nature of life led to the rejection of the Aristotelian doctrine of spontaneous generation.

Then we shall move to contemporary origin scenarios.

2.1 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

2.2 Spontaneous generation

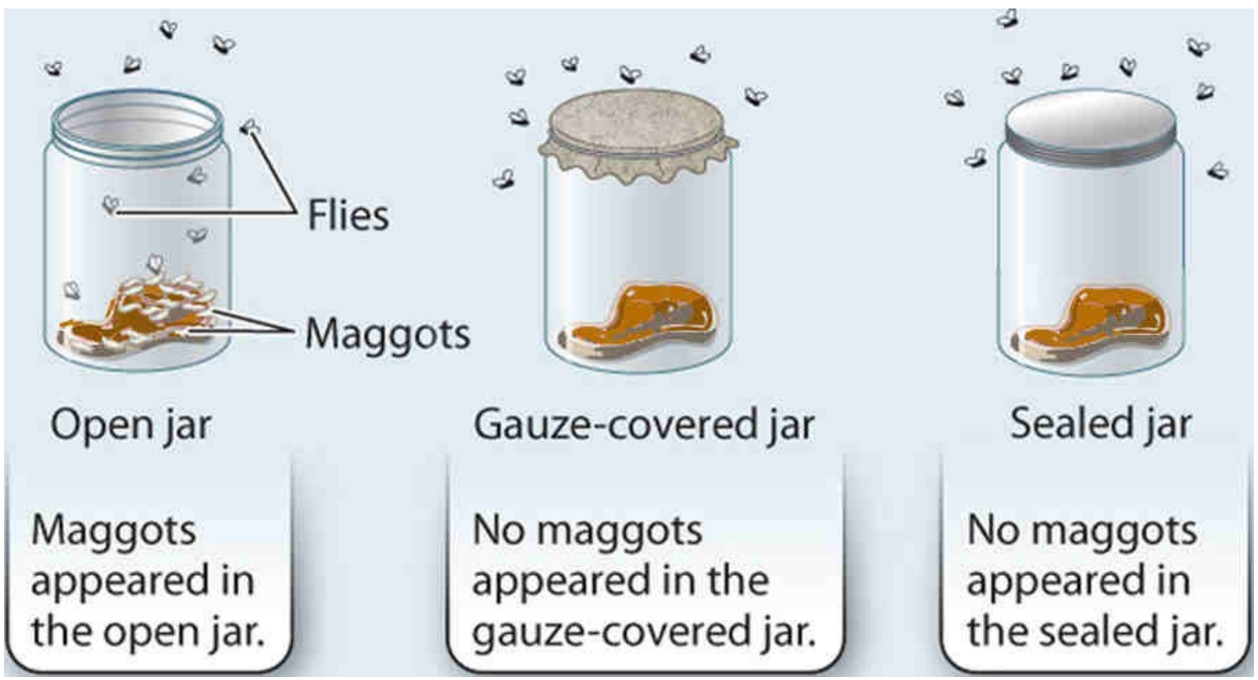
Why postulating spontaneous generation?

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

2.3 Spontaneous generation

William Harvey: *ex ovo omnia*.

Francesco Redi's experiments:



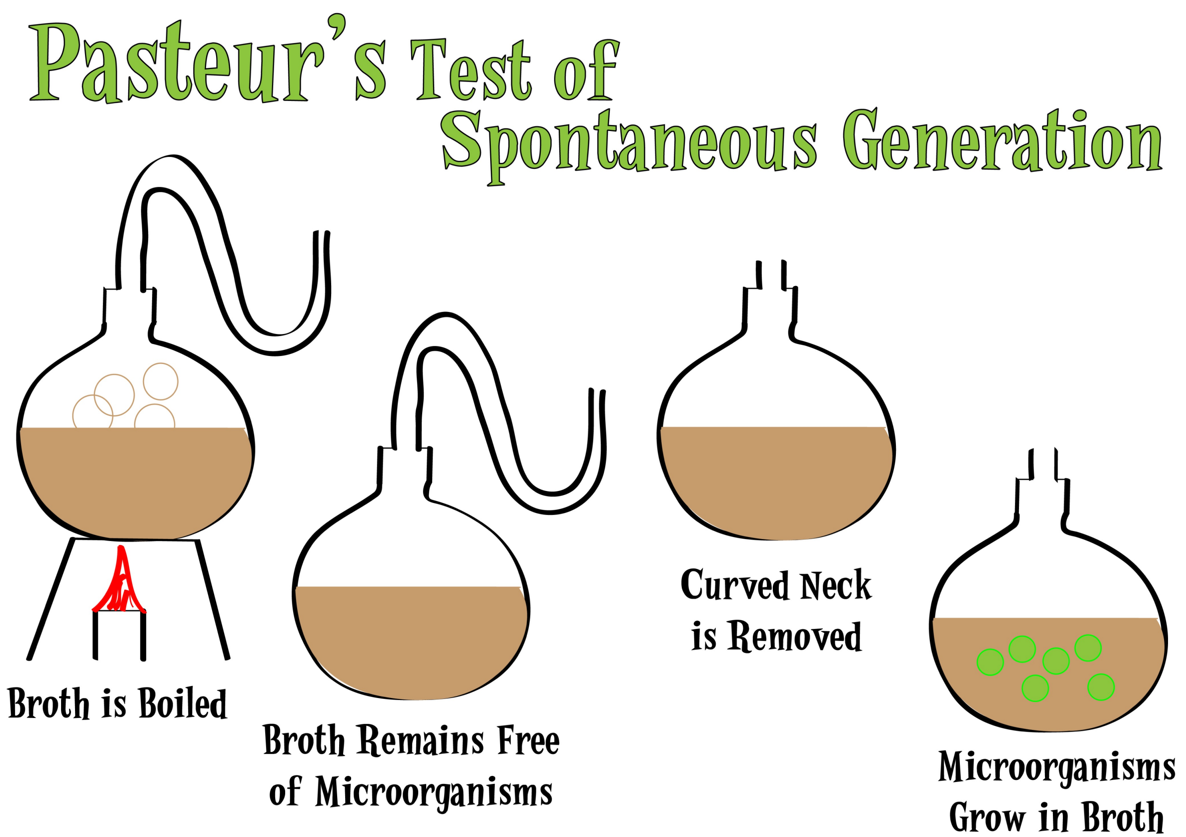
2.4 Spontaneous generation

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*.

2.6 Spontaneous generation

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



2.7 Spontaneous generation

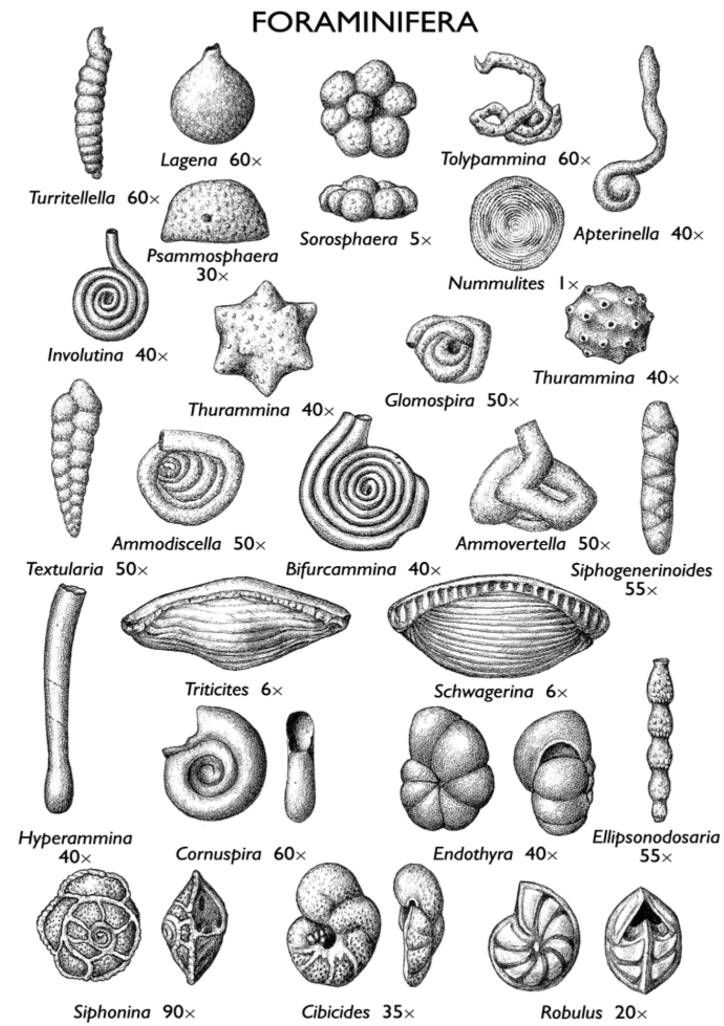
What did Pasteur prove? Did he prove that no life can ever come from non-living things? No, he didn't, and this is because you cannot disprove something like that experimentally.

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.

2.8 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.



2.9 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 (e.g., Harvey, Virchow).

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 (e.g., Pasteur, Buchner).

2.10 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.

2.10 Spontaneous generation

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.**

If not spontaneous generation, then what?

Let us now take a look at contemporary origin scenarios.

3.1 The origin of life

All abiogenetic (life from non-life, like spontaneous generation) scenarios: from prebiotic chemistry to life.

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

These are terrestrial abiogenetic scenarios, apart from ……

<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

3.2 The origin of life

…. panspermia: did life originate outside of our planet?

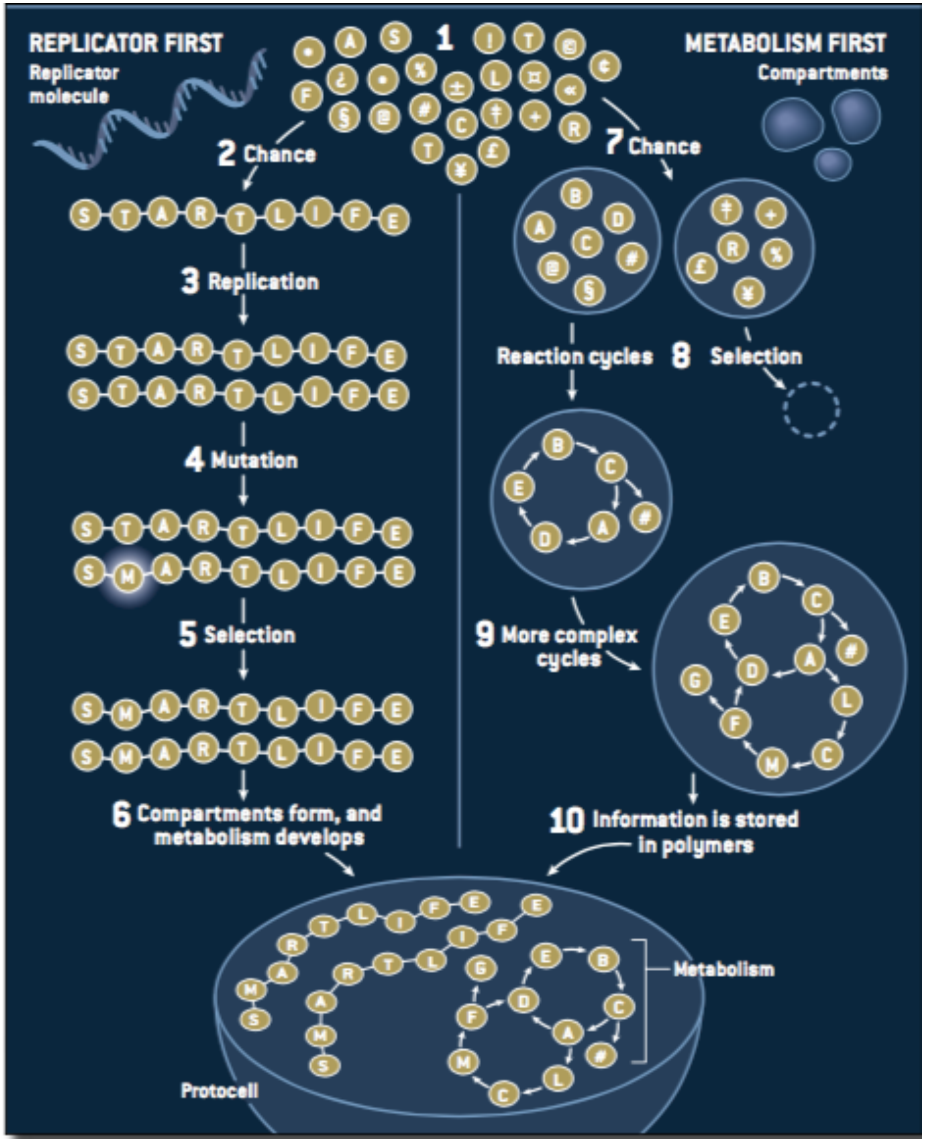
Some kind of regress implied, but it remains a possibility of course.

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.

3.3 The origin of life



Shapiro R. 2007. A simpler origin for life. Scientific American 296(6):46-53.

Note three elements:

1. Replicating entities capable of evolution (capacity to create lineages of biological entities of the same kind);
2. Metabolism (network of chemical reactions for self-preservation of the biological entity),
3. Cellular compartments (providing a protected environment for metabolic reactions).

Most important element? Actually, is there a most important element?

3.4 The origin of life

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 biochemistry of life and known biomolecules.

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

3.5 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

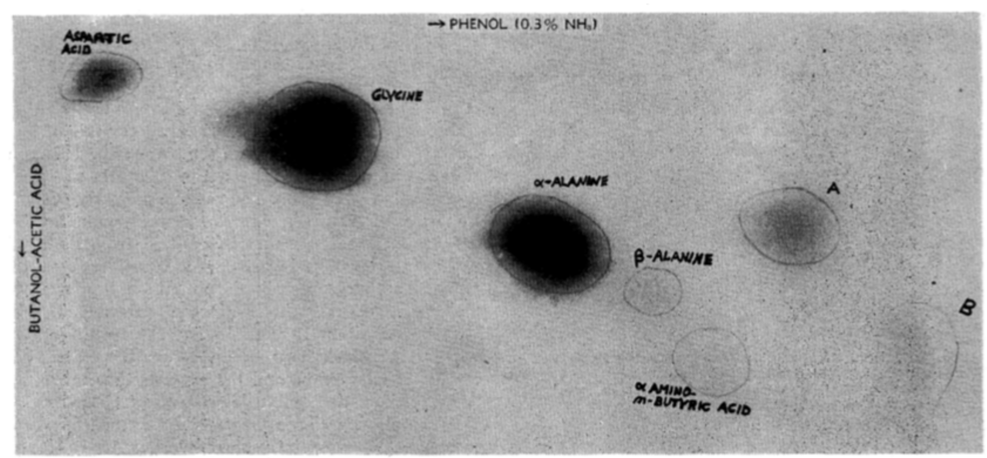
See also CDC pp. 8-9

3.6 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



3.7 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.

"Concentration problem": in oceans, organic molecules are much more probable to dissolve rather than forming polymers such as RNA. How can concentration problem be solved without compartments? Under what conditions can compartments be naturally formed?

Origin of compartmentalisation, metabolism and replication evaded: 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.

3.8 The origin of life

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

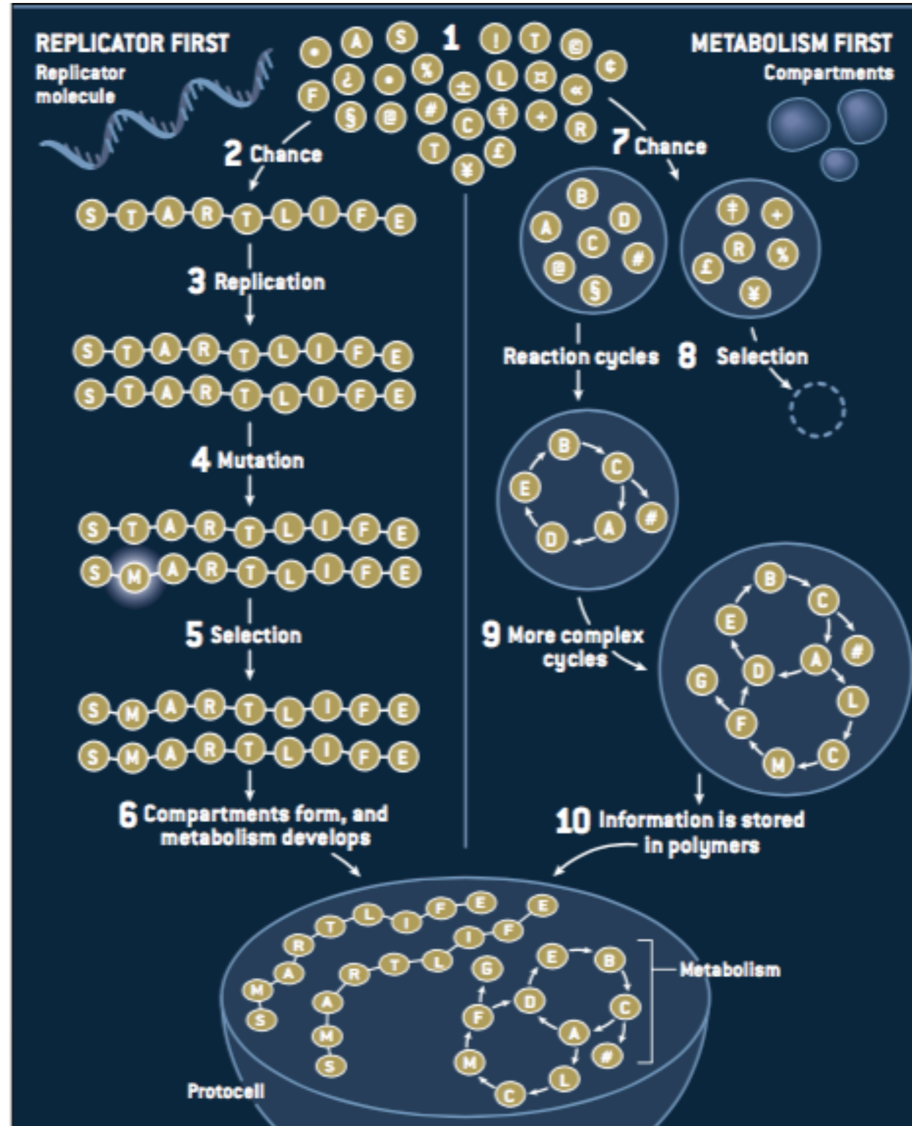
“… catalyse the synthesis of a new RNA molecule from precursors and an RNA template …. there is no need for protein enzymes at the beginning of evolution. One can contemplate an RNA world, containing only RNA molecules that serve to catalyse the synthesis of themselves…. The first stage of evolution 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 … 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 and rapidly, and hence will eventually dominate. … Finally, DNA appeared on the scene.”

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

3.9 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?



3.10 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 profound conceptual problem.

3.11 The origin of life

A. Cornish-Bowden and M.L. Cárdenas

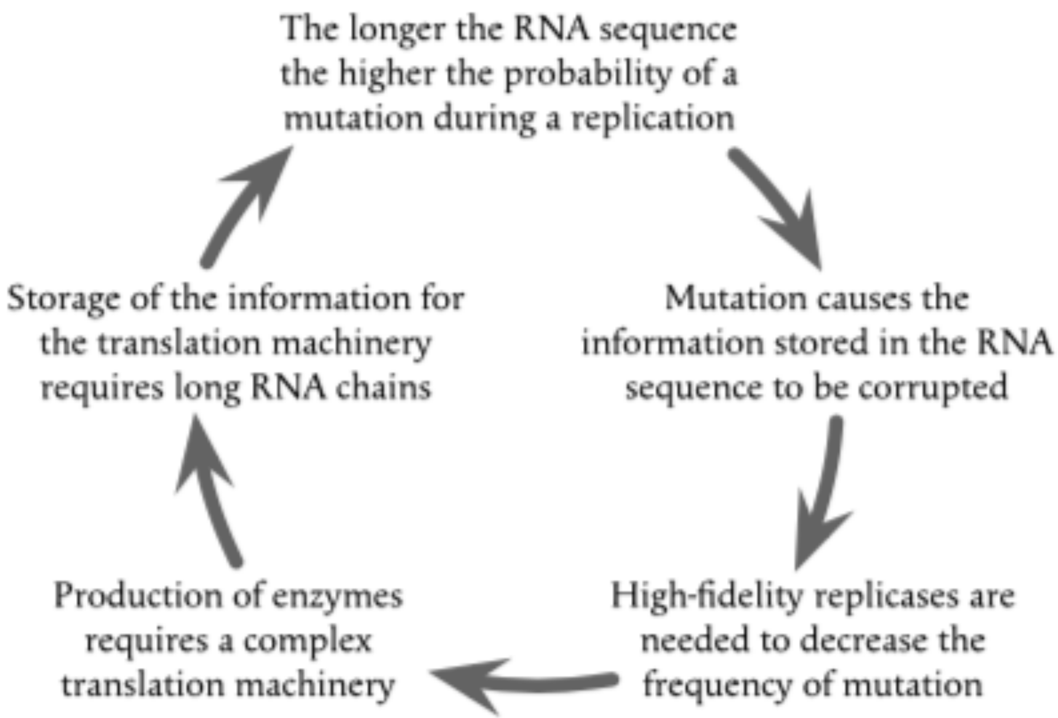


Fig. 15. Eigen's paradox. Following the arrows (starting anywhere) shows that a simple model in which the same kinds of molecules fulfil both functions cannot work: RNA does not have sufficient catalytic potential to provide the necessary specificity, and proteins alone cannot replicate. The scheme is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

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

3.12 The origin of life

Alkaline vent as location were abiogenesis might have occurred because:

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

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

3. it provides some hints concerning the origin of replication: 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.

3.13 The origin of life

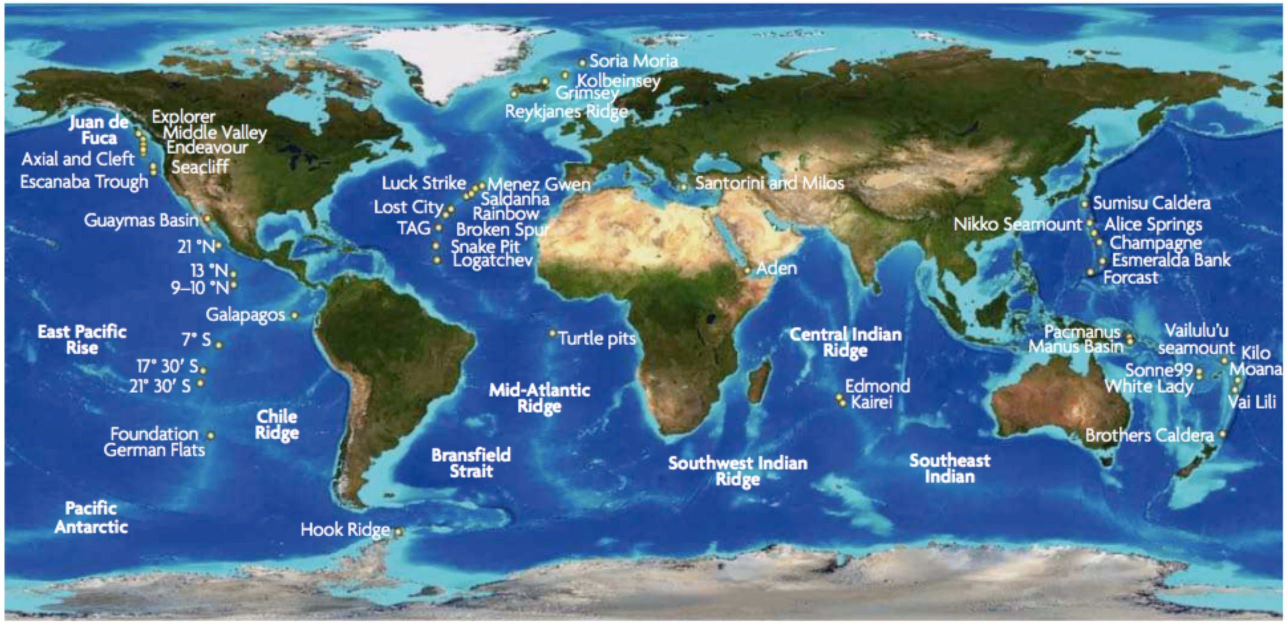
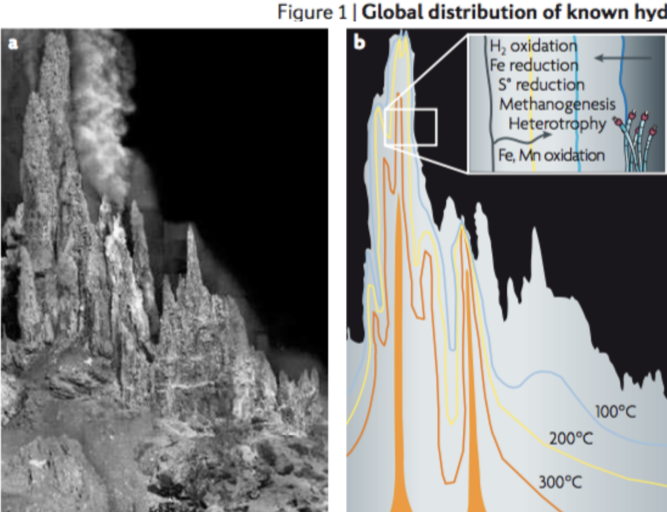


Figure 1 | **Global distribution of known hydrothermal vents.** Temperature and chemical anomalies hint that many
Data courtesy of D. Fornari and T. Shank, Woods Hole Oceanographic



Ancestral compartments or "inorganic cells:.

3.14 The origin of life

Organisational (rather than compositional) approach focused on metabolism and organisational features (rather than component molecules).

The RNA world hypothesis does not countenance the possibility of spontaneous catalysis (what Gilbert suggests 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 spontaneous chemical reactions, probably an ancestral version of the 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).

3.15 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.”

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

3.16 The origin of life

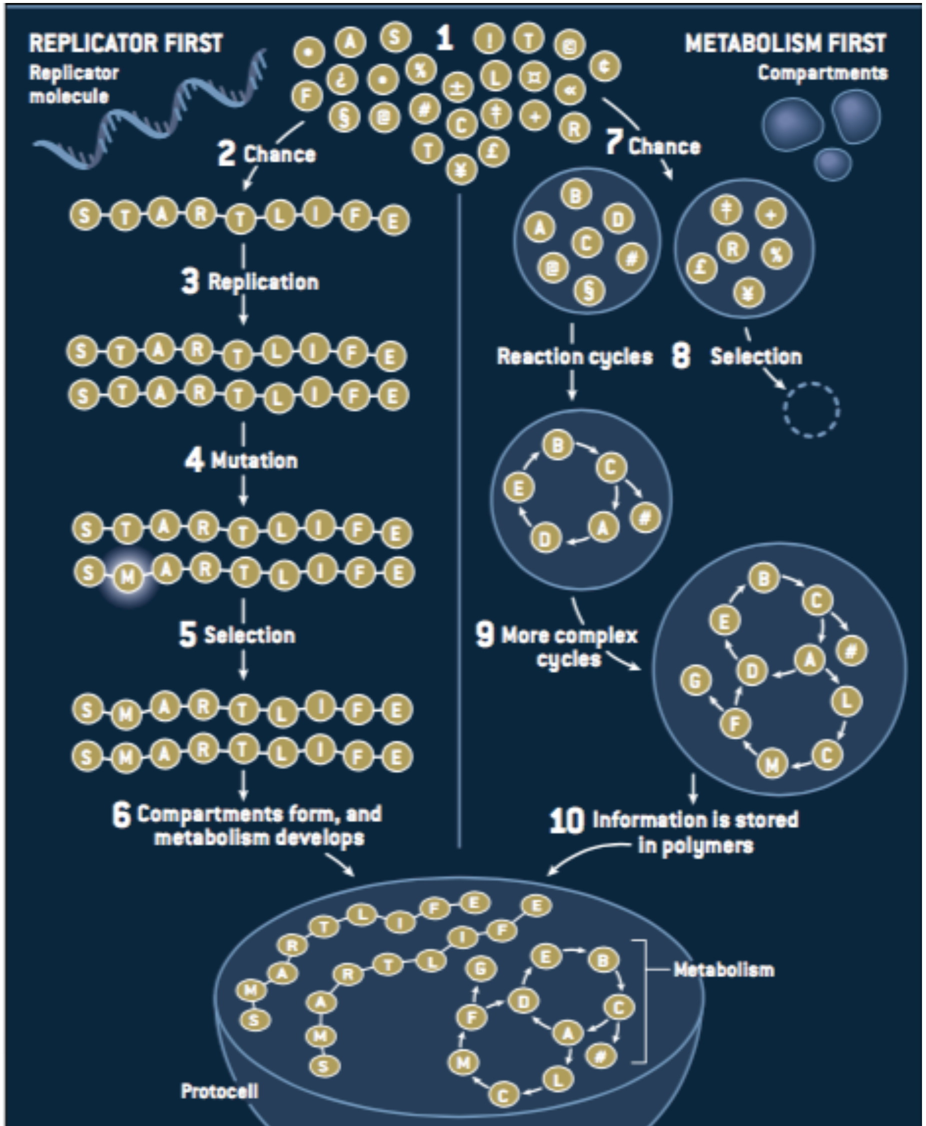
Basic suggestion: the ancestral Wood–Ljungdahl metabolic pathway was a spontaneous process energetically stable without need of protein-or-RNA-mediated catalysis.

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.

3.17 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., ancestral version of the Wood–Ljungdahl metabolic pathway) and chemical processes (e.g., chemiogenesis).

3.18 The origin of life

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?

The first answer is that life has a peculiar chemistry: RNA world hypothesis focused on peculiar properties of RNA, namely replication and their metabolic role;

The second answer is that life is organised matter: hydrothermal vent hypothesis focused on joint origin of autocatalysis and compartments.

Speculative hypotheses. So, what are the lessons of origin of life research for defining life as the object of study of biology?

4.1 Definitions of 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 p. 303.

"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 CDC - p. 3]

4.2 Definitions of life

What kind of definition of life should we seek? On what basis?

Does life have an essence? Is this essence compositional or organisational?

On what kind of information should an appropriate definition be sought? Inevitable terra-centric bias (perhaps artificial life and synthetic biology will help).

Material

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.

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

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

4.3 Definitions of life

"It is difficult to generalize from a single example, and in this respect the biologist is fundamentally handicapped ….. 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. 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 1970 p. 305.

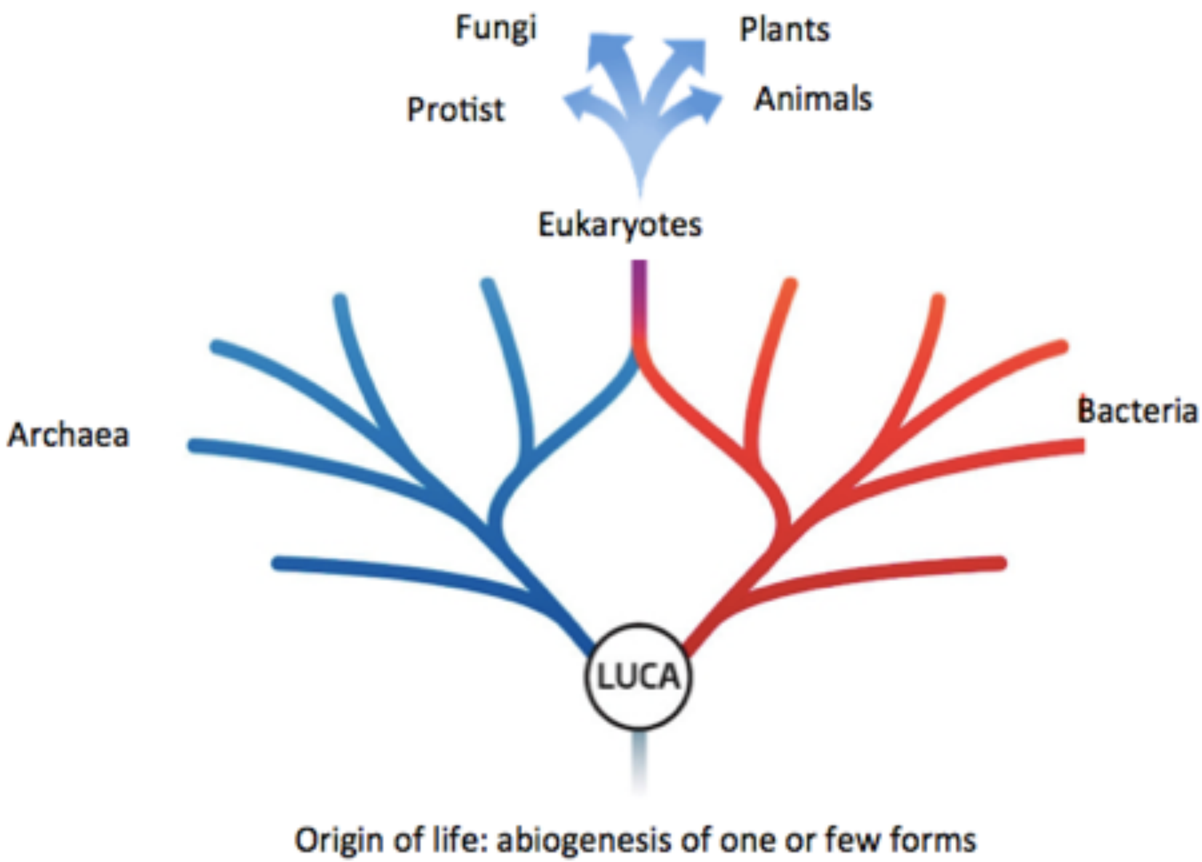
4.4 Definitions of life

What is known about extant life?

1. No special substance but material physico-chemical basis.
2. Common ancestry postulated (see class 4);
3. No spontaneous generation in the sense of a continuous process (vs. idea that spontaneous generation is now occurring);
4. Abiogenesis: life emerged from non-life (vs biogenesis); other possibility is panspermia (partial and complete);
5. Phylogenetically conserved biochemical components and organisational features (e.g., basic metabolic pathways).

How conserved?

4.5 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).

4.6 Definitions of life

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, 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.

In origin of life research, the central questions concern the origin of compartments, metabolism and replication: the extant details of compartmentalisation (i.e., nature of cellular membranes), metabolism (i.e., conserved biochemical pathways) and replication (i.e., DNA-based) might be different from those at the origin.

4.7 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?

Strong ontological definitions (necessary and sufficient conditions; discriminating life from non-life; fixed conditions) vs. operational definitions (focused on scientific practice, experimental research and model building).

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

4.8 Definitions of life

Essentialist definitions: a property set x is necessary and sufficient to define life.

Life = distinctive material constitution (i.e., specific "biomolecules", e.g., RNA)

Life = distinctive mode of organisation of material components (e.g., universal biochemical pathways or pathways with certain topological features).

Operational definition: "Life is a self-sustained chemical system capable of undergoing Darwinian evolution" (NASA). What kind of features has this definition?

4.9 Definitions of life

<u>Physiological</u>: system capable of performing functions such as metabolising, moving, growing, reproducing, and being responsive to external stimuli etc.

<u>Biochemical</u>: system that contains reproducible hereditary information coded in nucleic acid molecules and that metabolises by controlling the rate of chemical reactions using enzymes.

<u>Genetic</u>: system capable of evolution by natural selection.

<u>Metabolic</u>: system 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.

<u>Thermodynamic</u>: system that maintains order by being open, exploiting environmental energy flows.

(Sagan 1970)

4.10 Definitions of life

Compositional definitions: biochemical (material composition)
Structural definitions: metabolic (organisational requirements)
Functional definitions: all (functions performed)

Thermodynamic included in metabolic;
Genetic = physiological focusing on reproduction;
Genetic includes biochemical (focusing on hereditary material);
Metabolic = physiological focusing on metabolism.

Hence, physiological and thermodynamic definitions are parasitic on others.

4.11 Definitions of life

<u>Genetic definitions: emphasis on the function of replication, independently of the material nature of the hereditary material.</u>

(Linked to RNA world hypothesis).

Problems: what about putatively living entities that do not produce lineages? What about somatic cells of multicellular organisms, sterile organisms etc.?

Is reproduction (and subsequent lineage-generation) an essential property of life? "…. staying alive is the fundamental necessity. Reproduction is not …" CDC p. 29

4.12 Definitions of life

<u>Biochemical: emphasis on biochemical composition and the importance of replication.</u>

(Linked to RNA world and hydrothermal vent hypothesis).

Problems: extraterrestrial and artificial life would turn out not to be genuine life ("… 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).

Are DNA, RNA and proteins composed of amino-acids essential materials for life? They might be evolutionary accidents.

4.13 Definitions of life

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

~~Biochemical: system that contain reproducible hereditary information coded in nucleic acid molecules and that metabolise by controlling the rate of chemical reactions using enzymes.~~

~~Genetic: system capable of evolution by natural selection.~~

Metabolic: system 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.

~~Thermodynamic: system that maintain order by being open, exploiting environmental energy flows.~~

4.14 Definitions of life

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

<u>(Linked to hydrothermal vent hypothesis).</u>

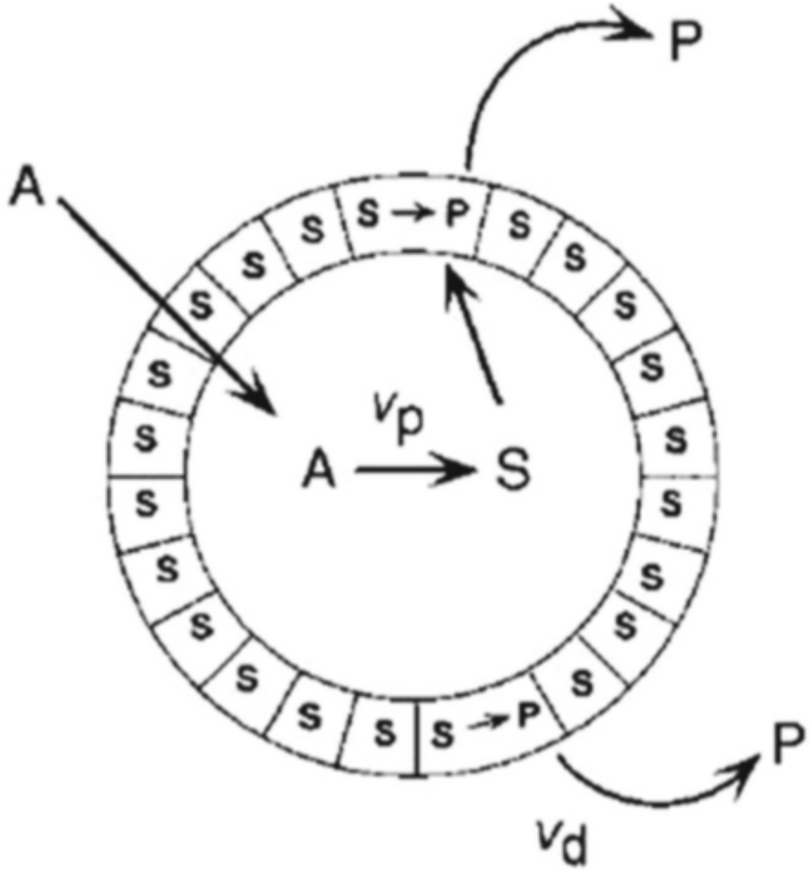
1. Thermodynamic openness and possibility to make a living out of environmental acquisition of precursors of molecular components and energy.

2. Autocatalytic network of reactions is maintained for a significant time.

3. Boundary enclosing the network.

"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 1998 p. 619

4.15 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.

4.16 Definitions of life

Focus is on membrane/boundary and metabolic activity, not on replication (which is a by-product of growth, see slide 4.15).

Boundary and other material components are self-produced from materials assimilated through environmental interaction (boundary must be semi-permeable).

Two features:

1. Essentialist definition: the “essence” of life concerns the distinctive organisation of metabolic processes.

2. This metabolic definition is a characterisation of physiological autonomy. This is a description of an organism: **life = organismality**.

So, what is an organism? Class 2.

Summing up

If life is not a special substance, what is it then?

A distinctive material constitution or a specific mode of organisation of material components?

The first answer is that life has a peculiar chemistry: the RNA world hypothesis and biochemical definitions betray this compositional bias. **This compositional ethos is more consistent with the spirit of reductionism.**

The second answer is that life is organised matter: the hydrothermal vent hypothesis and metabolic definitions betray this organisational bias. **This organisational ethos is more consistent with the spirit of organicism.**

One fundamental question is whether what Mayr (slides 1.16 + 1.23) calls the “Cartesian programme” (i.e., 1. organism = machine; 2. reductive explanation of the behaviour of the living thing in terms of its parts) is good enough for biology. We shall return to this in class 3.