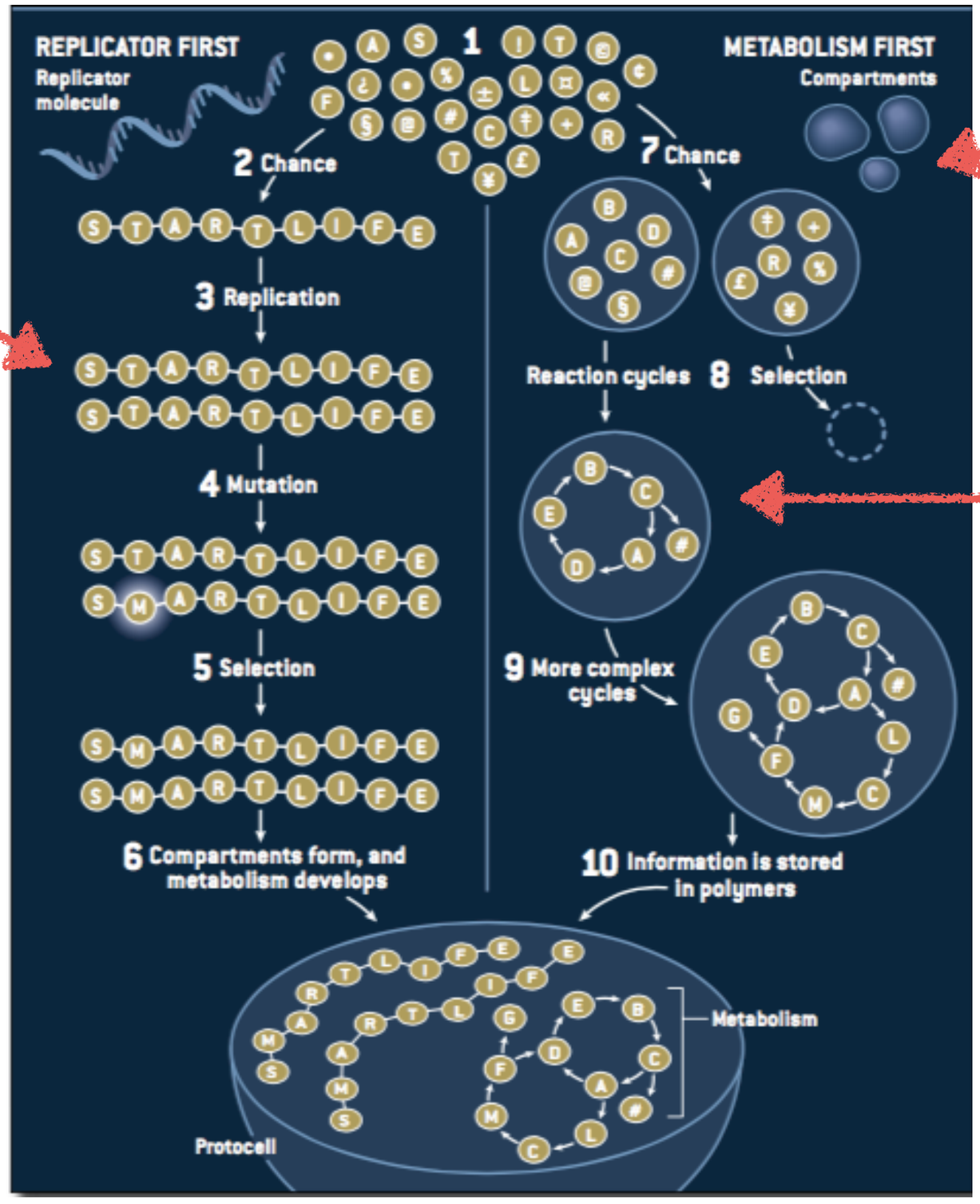
Summing up a

origin of replication

origin of compartments



origin of metabolism

QUESTION 1 - Replication, metabolism or compartments first?

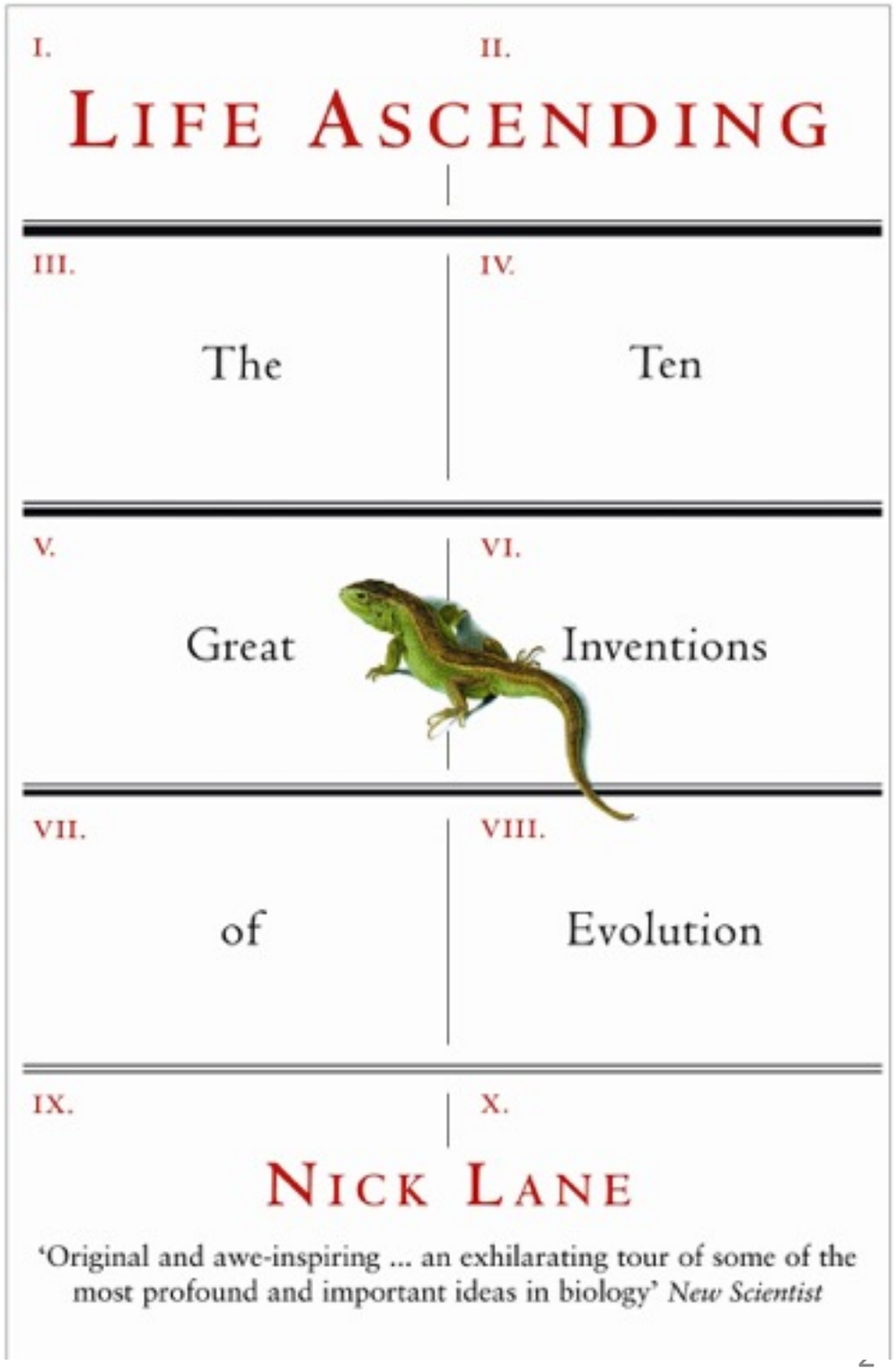
QUESTION 2 - What kind of biological system can be ascribed the property of living?

Summing up b

QUESTION 1 - Replication, metabolism or compartments first?

Replication-first scenario as conceptually unsatisfying: “The idea that replicators like RNA were the first figments of life, predating any thermodynamic driving force, is, in Mike Russell’s words, ‘*like removing the engine from an automobile and expecting the regulating computer to do the driving*’.”
Lane 2010, p. 14

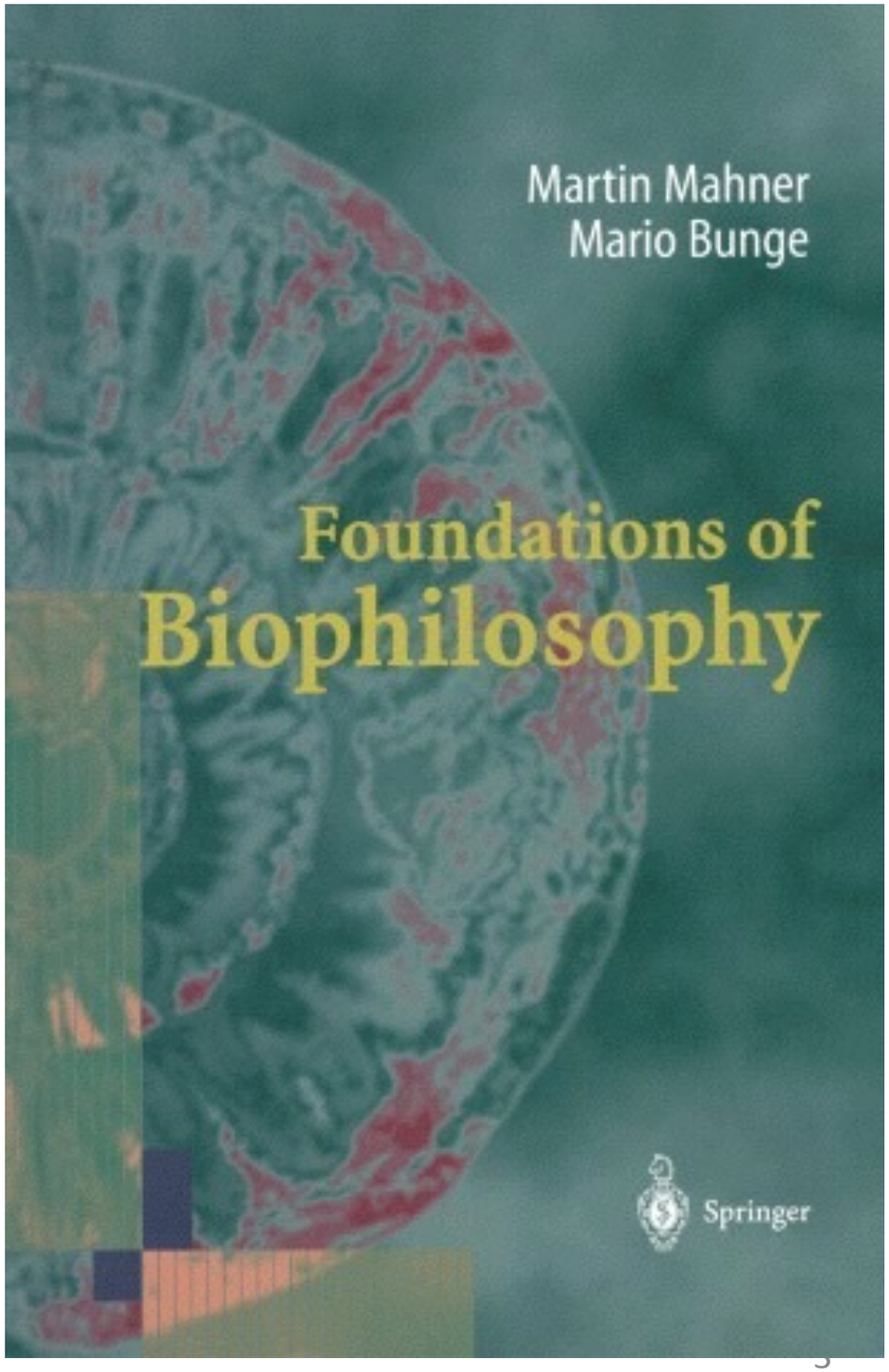
We have seen in last class that the “thermodynamic force” might have been the Wood–Ljungdahl metabolic pathway according to Martin & Russell.



Summing up c

One alternative is to assume that life requires replication and compartmentalised metabolism:

"… only the combination of nucleic acid molecules with metabolizing systems marks the '*beginning of life*' ….. Thus, the question of whether replicating molecules evolved first and metabolizing cells second, or whether the two originated the other way round, is irrelevant to the problem of life." Mahner & Bunge 1997 p. 145



Summing up d

The simultaneous emergence of replication and compartmentalised metabolism would provide an answer to the second question:

QUESTION 2 - What kind of biological system can be ascribed the property of living? A protocell.

Thus, **life = cell = cellular organisation**.

But if you do this, then the passage from non-life to life becomes **abrupt**, which is strange because many biological entities capable of some form of autonomous replication (e.g., autocatalytic chemical complexes, prions, viruses; see Dupré & O'Malley 2009), are then considered non-living by fiat.

Summing up e

Life ≠ cellular organisation ≠ organismality:

“Given the acceptance that life has evolved from a chemical context, ruling out self-replicating complexes of chemicals and molecules on the grounds that they are not cells seems misguided. A commitment to life as exclusively cellular and monogenomically organismal would mean that the origins of life must involve a single leap from fully non-living to fully living, something that is conceptually difficult to accept and, for that matter, provides a natural target for creationists to insist on the need for supernatural intervention.” Dupré & O’Malley 2009 p. 15

Consider prions and viruses. Prions: propagate without DNA involvement as templates for other prions; does the “self- propagational” status of prions gives them the status of being alive? What is self-replication in the first place (see slide 3.28-3.33)?

Summing up f

Life ≠ cellular organisation ≠ organismality:

Viruses: 1. they exhibit “developmental stages” (from inert virions or dormant provirus to active state, whether lytic or lysogenic or endogenous); 2. their evolutionary origin is unknown (primeval pre-cellular entities constituting a distinct super-domain vs. cellular parasites evolved after emergence of cellular life?); 3. they exhibit some form of autonomy; for instance, the mimivirus (Dupré & O’Malley 2009 p. 7) carries genes for translation and DNA repair, thus seemingly representing “ …. entities in transition from viruses to free-living organisms …”; 4. “They have their own evolution, which is independent, to some extent at least, of the evolution of organisms in which they reproduce (Luria et al. 1978, 481).”(Dupré & O’Malley 2009 p. 7); 5. some viruses are “infected” by virophages. Are they alive?

Summing up g

Dormant virions, dormant cells, dormant seeds, dormant spores and even dormant organisms such as tardigrades —> biochemically inert state = living?

“Not all of the functions (properties and activities) that we attribute to a biosystem are actually carried out by it at all times during its life history. Metabolism may be temporarily reduced or perhaps entirely suspended ….” Mahner and Bunge 1997 p. 143

“Life, according to our analysis, occurs at the intersection of lineage formation and (typically collaborative) involvement in metabolism. Entities that are problem cases, such as viruses, can be understood as alive when actively collaborating. When not collaborating, they have at most a potential for life.” Dupré & O’Malley 2009 pp. 14-15

Summing up h

One thing we can do is to reconstruct the genome of LUCA (i.e., last universal common ancestor). Of course, this research is already biased if only the genomes of extant cellular life forms are considered. But it is nonetheless relevant research because all conserved sequences are associated with translation and transcription.

Among the conserved translation-system components are, for instance, aminoacyl-tRNA synthetases (AARSs), enzymes that link tRNAs to the correct amino acid. How many genes? < 100. Significantly, it is genes for protein synthesis rather than DNA replication that are conserved, pointing to pivotal importance of metabolism (and RNA).

Metabolic definitions of life make this assumption: **life = cell = cellular organisation = organism.**

5.11 Definitions of life (from last class)

Metabolic definitions: emphasis on the self-maintenance.

1. Thermodynamic openness and possibility to make a living out of environmental acquisition of precursors of molecular components and energy (see this class's slides in section 3).

2. Autocatalytic network of reactions is maintained for a significant time. How is autocatalysis or "organisational closure" achieved?

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

5.12 Definitions of life (from last class)

A. Cornish-Bowden and M.L. Cárdenas

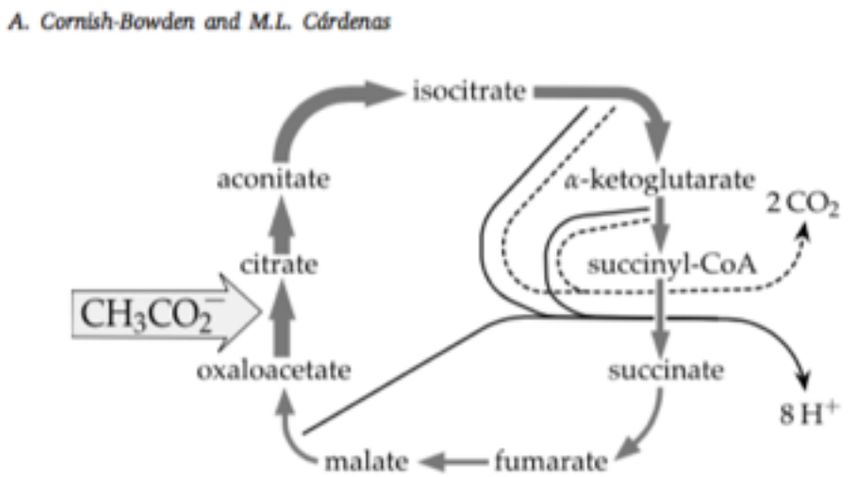


Fig. 20. Metabolic cycles. The tricarboxylate cycle (various coenzymes are not shown)

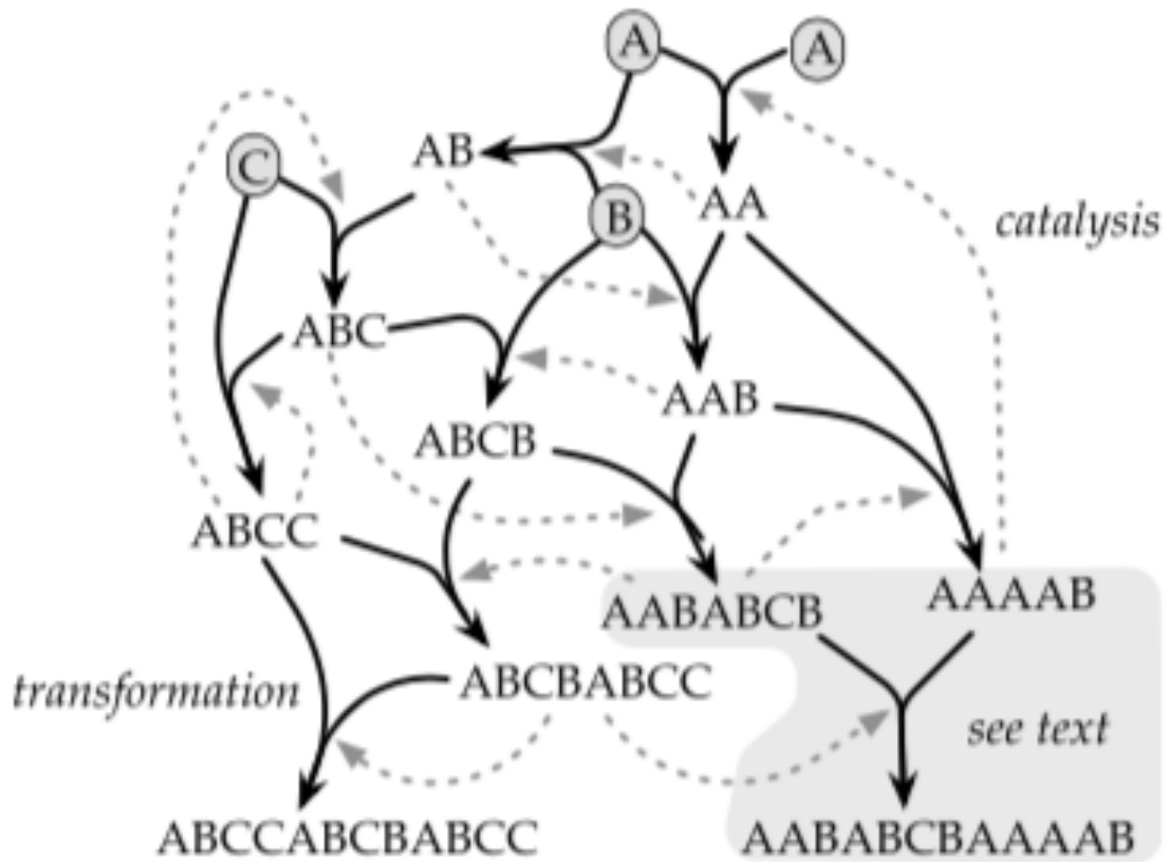
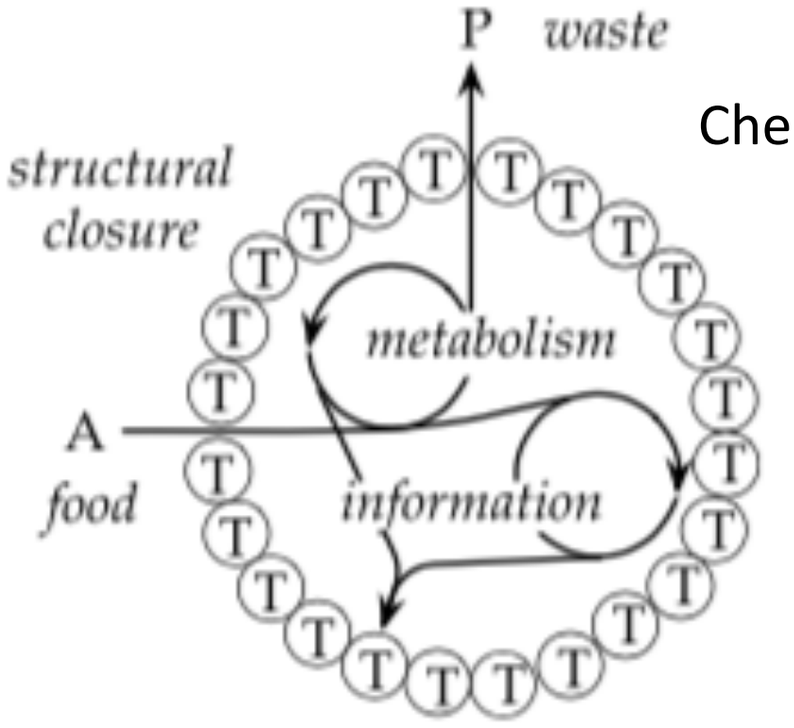


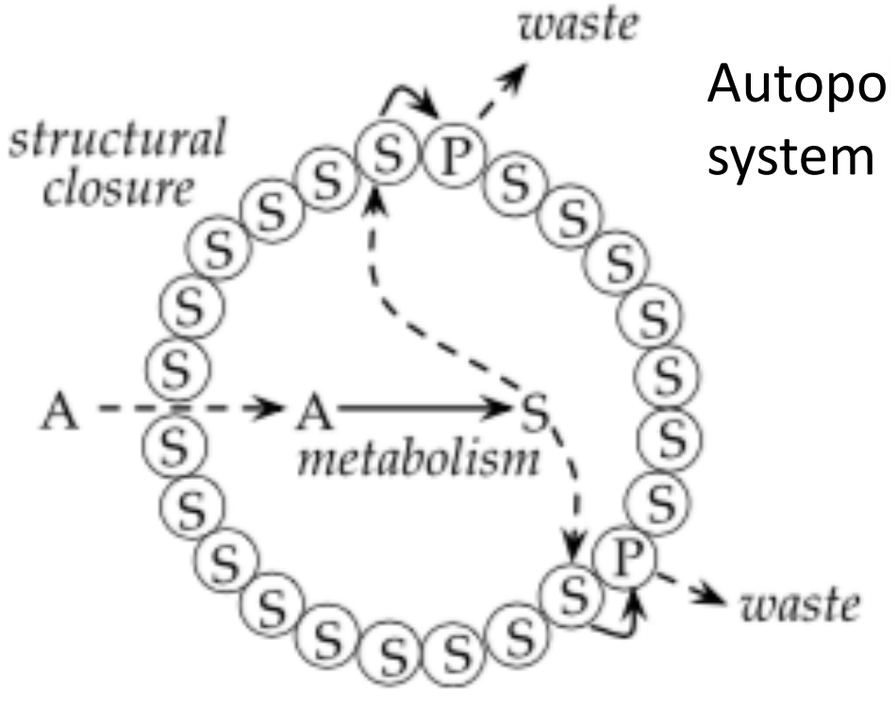
Fig. 34. An autocatalytic set as described by Kauffman (1986, 1993, pp. 298–341). The food molecules A, B and C shown in ovals are available in sufficient quantities from the environment. They can be amino acids, or RNA bases or other kinds of molecule that have some catalytic properties and are capable 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 (from last class)



Chemoton



Autopoietic system

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

5.15 Definitions of life (from last class)

"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 (from last class)

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 (see this class’s slides 3-19-3.27).

Physiological autonomy varies along a gradient (see this class’s slides in section 3 and 5). Ancestral life was probably much more dependent on environmental resources than extant life.

5.17 Definitions of life (from last class)

What Cornish-Bowden & Cardénas 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

<u>Life = organismality.</u>

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 (from last class)

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 this class.

CLASS 2 - 3 March: ORGANISM

1. A brief history of the organism concept
2. Autopoiesis
3. Organism = physiologically and reproductively autonomous biological system
4. Beyond autonomy: a realistic conception of paradigmatic organism
5. Organismality as a continuum: brief sketch of some criteria

Bibliography: at the end

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1.1 Organism concept history

General pattern of the development of the concept:

1. from denoting a kind of organisation to denoting a specific kind of entity;

2. from theological to metaphysical to scientific problem;

3. from immaterialism to materialism;

4. from immaterialistic vitalism to Aristotelian formalism to materialistic vitalism to organicism.

Starting point: the contrast between unorganised matter and biological organisms is phenomenologically evident.

1.2 Organism concept history

Until 1700, the term “organism” generally denoted a kind of order of the world, a specific kind of organisation, rather than individual organisms.

Francisco Suárez “ … referred around 1600 to the organized body of humans in which all parts are disposed for the expression of the proper activity of a (immaterial) soul which possesses regulating faculties.” Cheung 2010, p. 183

Theological and metaphysical problem.

Ontologically distinctiveness of individual biological organisms resides in coupling of immaterial substance and (lifeless) assemblage of organic parts.

The soul regulates and controls the body.

1.3 Organism concept history

With Georg Ernst Stahl (1708) the problem becomes different: distinction between *organismus materialis* (to be mechanically understood) and the *organismus formalis* (an organisational conception):

“It would be very strange to call the right disposition of the parts of the body, such as curves, laments, tendons, joints, beams, handles, small wheels, wells, pumps, canals, cataracts, aps, sieves, and who knows what, a vital principle. And it would also be strange to use only [the mechanism] of ... pneumatic or hydraulic machines to produce living bodies. This would result in an eternal confusion between mechanism and organism.” Cheung 2010, p. 167

“For Stahl, only ‘organisms’ live, and the categorical distinction between life and death can only be understood if the difference between the orders of organism and mechanism is clear.” Cheung 2010, p. 183

Organism ≠ machine (vs. Descartes).

1.4 Organism concept history

Georg Ernst Stahl starts to systematically use the term for both organisation and individual bodies (what we today call “organisms”).

The term was used by German *Naturalphilosophien* also as a principle of cosmological order (of which individual organisms are clearly part).

Later, in physiology, Christoph Wilhelm Hufeland (1795) re-proposed a dualistic position distinguishing organic “organization,” (mechanical and chemical, thus material) and “… the regulative, dynamic properties of the life forces of living beings, that are, as potentials, already activated in the egg..” and that cannot be reduced to their material organization. Cheung 2010, p. 174

1.5 Organism concept history

A similar distinction was endorsed by François-Joseph-Victor Broussais in the *Traité de physiologie appliquée à la pathologie* (1822) between the "… organized animal matter of an organism – that results from the interactions between the anatomical disposition of parts, a living chemistry (*chimie vivante*) and a set of vital forces –, the *Moi* or the rational soul as an agent that connects ideas through reflexive operations…" Cheung 2010, p. 178.

Physico-chemical explanation is sufficient to account for dead bodies.

It is unclear to me how Hufeland and Broussais were immaterial vitalists, Aristotelian formalists or materialistic vitalists.

1.6 Organism concept history

With Kant we have a deeper break with theological, immaterialistic and mechanistic traditions:

“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 [1987]: 221)

An organism is “cause and effect of itself”, a living entity is self-caused, and the causality involved cannot be understood mechanistically but only teleologically.

1.7 Organism concept history

Antinomy of the power of judgement (Critique of the Power of Judgment, Kant, 1790, cf. Watkins & Watkins & Marius 2014)

Thesis:
All generation of material things is possible in accordance with merely mechanical laws.

Antithesis:
Some generation of such things is not possible in accordance with merely mechanical laws.

- Note that the laws of mechanics are universal for Kant, so they must apply to biology. Ultimately, biology must comply with them in the sense that biological explanation must be mechanistic.

1.8 Organism concept history

Kant's aim was to understand all natural phenomena with a single mode of explanation (i.e., mechanistic) attributing a single fundamental causal power (i.e., motion) to a single fundamental kind of substance (i.e, matter).

He argued that we cannot understand the reciprocal causation - the fact that (multicellular) organisms are cause and effect of themselves - of ontogenetic phenomena such as metabolism, homeostasis, development and reproduction - unless we see organisms as products of purposive design, unless, that is, we postulate an immanent principle of order, a telos.

Organismal development is a process of generation of parts from other parts that cannot be understood unless a whole/an internal telos/an internal agent is postulated that regulates the generative process.

1.9 Organism concept history

However, the postulation of an immanent principle of order that controls, for instance, developmental stages by making parts differentiate and generate other parts (such as tissues and organs) and then organise the formed parts to act cooperatively by constituting an individual organism (i.e., self-organisation), for Kant contravenes at least the second law of mechanics.

First Law of Mechanics: the total quantity of matter remains the same throughout all changes in matter.

<u>Second Law of Mechanics: every change in matter has an external cause.</u>

Contrast with the ability of an organism to “determine” itself, to act according to an internal principle, to be the originator of motion.

Third Law of Mechanics: equality of action and reaction in the communication of motion.

1.10 Organism concept history

Kant's view was influential in biology. German physiologist and anatomist Johannes Müller (1838):

"Organic bodies differ from inorganic bodies not only through their specific composition of elements, but also through the activity that operates in the organic matter. This activity is productive according to the laws of a rational plan and its ends. It arranges parts for a whole, and this is exactly what is particular for an organism." Cheung 2010, p. 181

Again, the "essence" of life does not concern material composition but the form in which that material is arranged (i.e., a distinctive organisation). See slide 5.17 os last class.

1.11 Organism concept history

From 1830 “organism” denotes a kind of entity. The problem is transformed from being theological or metaphysical and it becomes a scientific problem.

With Kant it is clear that the substance dualism of Descartes and many previous “biologists” is overcome.

However, even though this means that immaterialistic vitalism is gradually abandoned, tendencies to think about organisms in Aristotelian formalistic or materialistic vitalistic terms remain.

1.12 Organism concept history

Kant concluded that, since living organisms cannot be explained mechanistically, the aim of understanding all natural phenomena with a single mode of explanation was bound to fail.

Kant had a very restrictive notion of mechanistic explanation; he has no concept of evolution; scientifically speaking his argument seems outdated.

Nonetheless, his argument has deeply influenced the history of biology.

2.1 Autopoiesis

Why is Kant relevant today? Let us take a deeper look at one “Kantian” view of the organism: Varela’s and Maturana’s autopoiesis.

Autopoiesis has Kantian roots in the following sense: it is an account of self-maintenance (which was Kant’s problems) based on the emergence of the organismal property of autonomy (see slides 5.13-5.15 of last class).

2.2 Autopoiesis

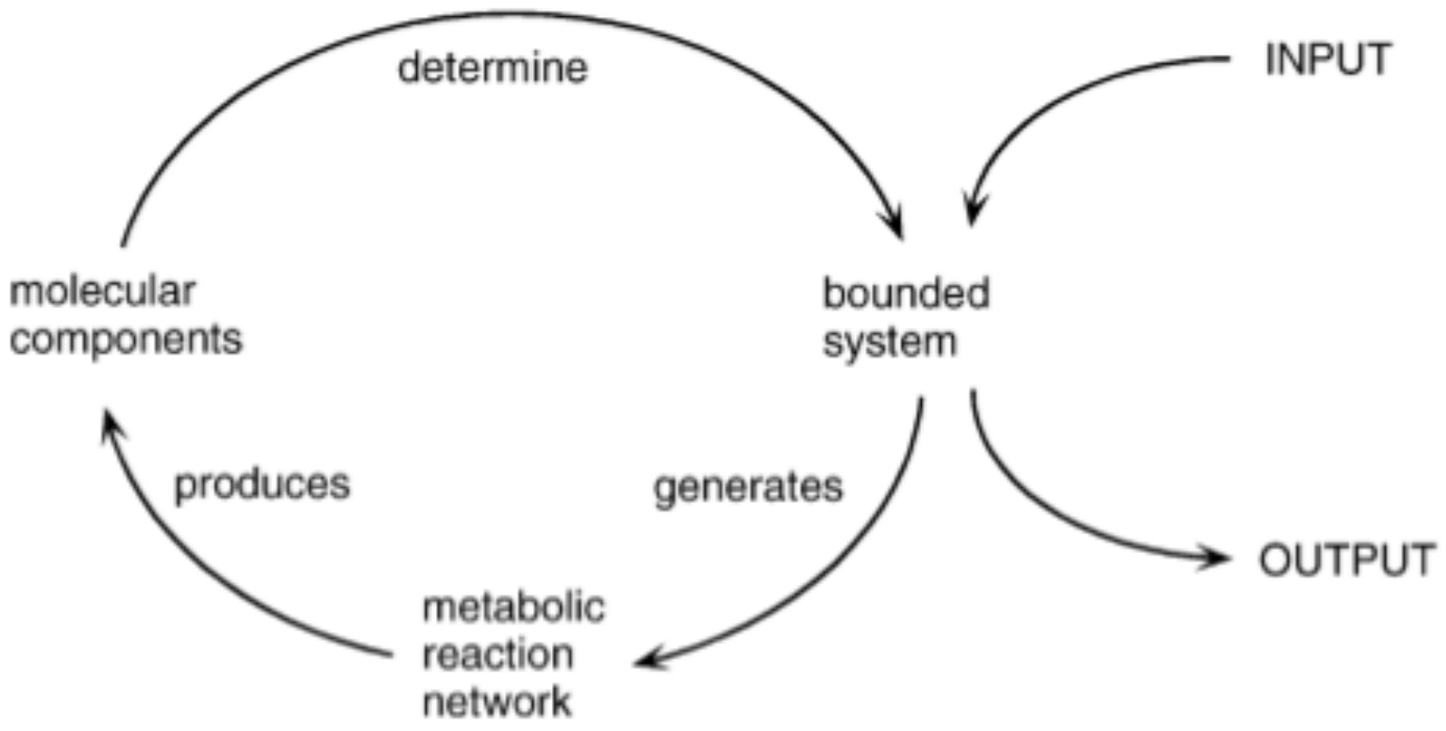
Autopoietic unit = minimal life form = most elementary organism = cell

Autopoiesis = emergent property = essence of the living = Kant's implicit idea of self-organisation interpreted in chemical terms

Autopoietic unit is capable of preserving its identity: "… system that is capable of self-sustaining owing to an inner network of reactions that re-generate **all the system's components** …. **The living is a factory that makes itself from within**. " Luisi 2003 p. 51-52

2.3 Autopoiesis

Life obeys a circular logic without an identified beginning and/or end. In order to ascertain whether an entity is living we need to verify: "…. (1) whether the system has a semipermeable boundary that (2) is produced from within the system and (3) that encompasses reactions that re-generate the components of the system." Luisi 2003, p. 51



2.4 Autopoiesis

Table 1 The game of the two lists

List of the living	List of the non living
The fly	The radio
The tree	The automobile
The mule	The virus
The baby	The crystal
The mushroom	The moon
The amoeba	The computer

What discriminates the living from the non-living?

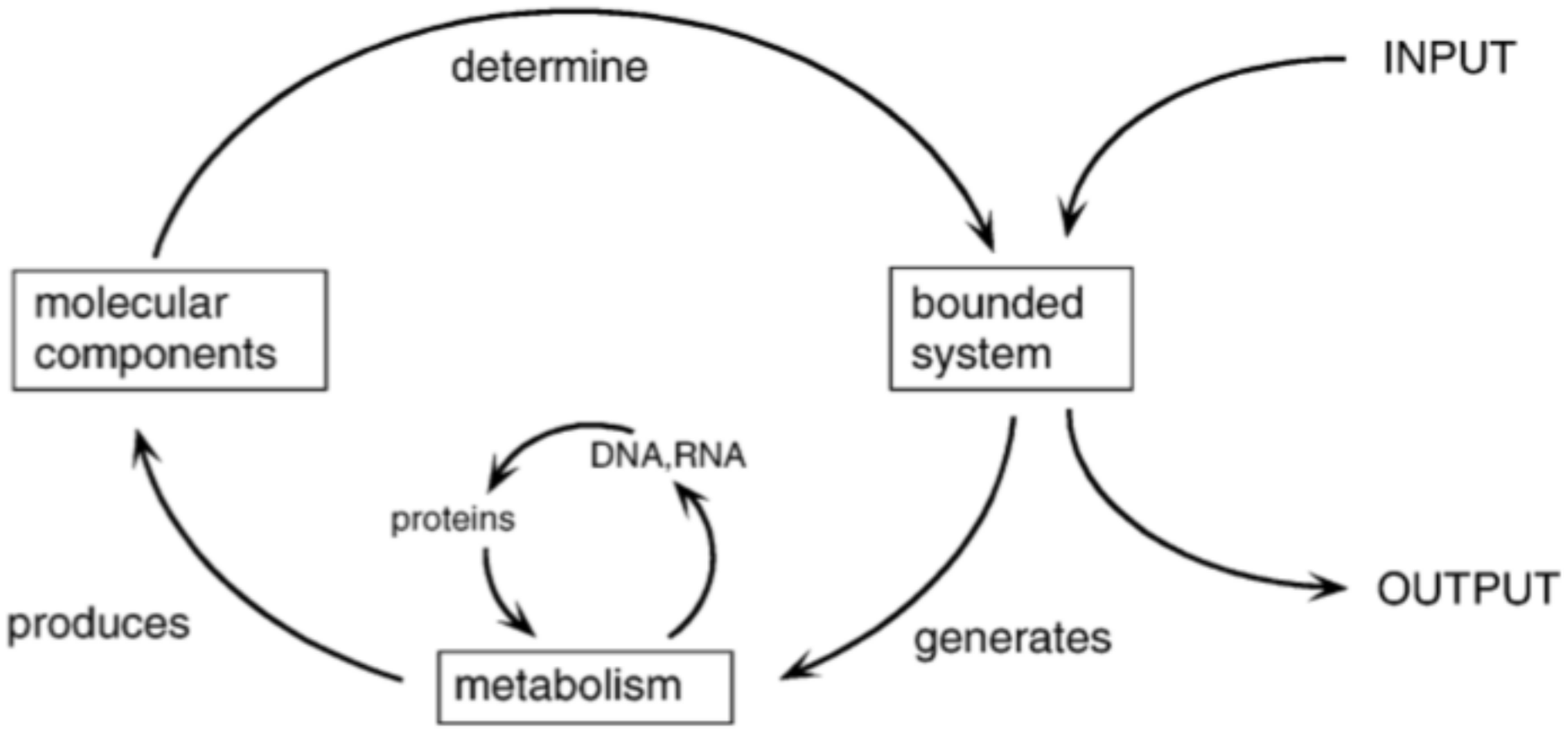
What is the quality (or qualities) which is present in all members of the "living list" and which is not and cannot be present in any of the elements of the "non-living" list?

(Luisi 2003, p. 51)

2.5 Autopoiesis

Characterisation does not take into account:

1. DNA (even though it is consistent with it, cf. Luisi 2003, p. 53);

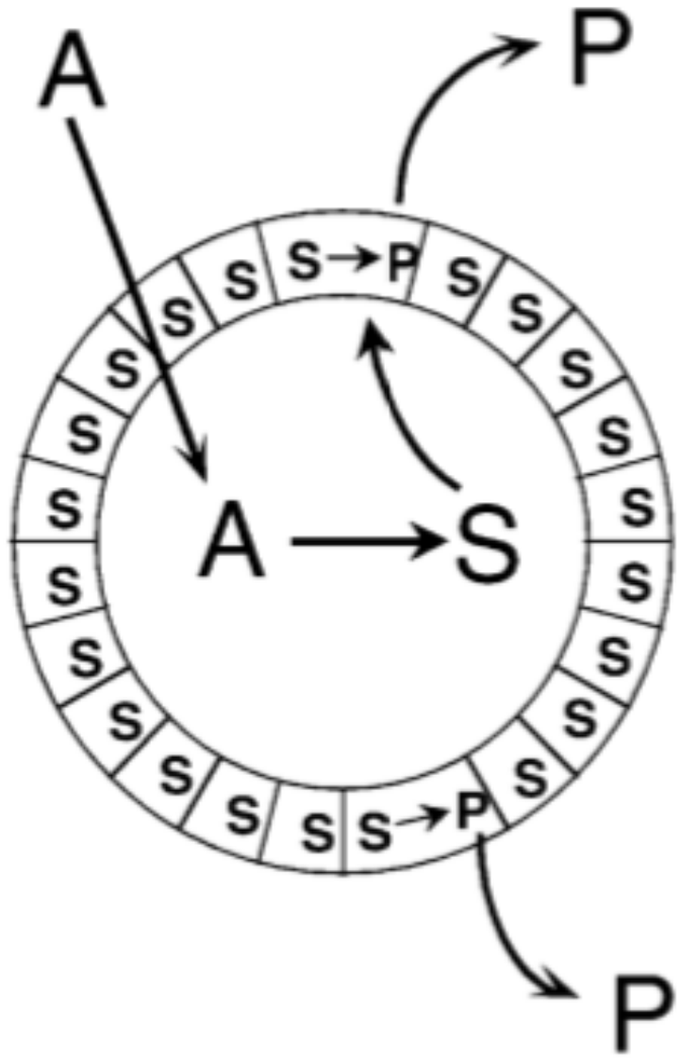


2.6 Autopoiesis

Characterisation does not take into account:
2. evolution and inheritance:

“Varela states that to include reproduction in the definition of the living would be ontologically wrong (Varela 2000), as “reproduction is a ...consequence of the existence of individuals. The difficult thing is to create an organism that is capable to self-reproduce with its own boundary. To divide it up in two is easy...”. And again (Varela and Maturana 1998), “In order to reproduce something, the unit must first be constituted as a unit, with an organization that defines this unit itself. This is simple common sense logic.” Luisi 2003, p. 53

2.7 Autopoiesis



$$v_{gen} = \frac{d[S]}{dt} \quad ; \quad v_{dec} = \frac{-d[S]}{dt}$$

if $v_{gen} = v_{dec}$ **homoestasis**

if $v_{gen} > v_{dec}$ **growth**

Growth —> reproduction (Luisi 2003, p. 53)

2.8 Autopoiesis

Characterisation does not take into account:

2. evolution and inheritance:

How can the existence of a rich variety of living things be accounted for? How can the evolution of new forms of organismality be explained?

Consider again Dupré & O'Malley's (2009) article: the history of life is a history of transformations in organismality: organelles such as mitochondria and plastids have been incorporated by eukaryotic cells, while multicellular organisms should more properly be considered holobionts (ecological unit = multicellular organism + microbiota).

3.1 Organismal autonomy

Autopoiesis has an important implication, i.e., the emergence of autonomy:

"… with life, an autopoietic unit acquires the singular property of becoming a **biologically autonomous system**, namely one that is capable of specifying its own rules of behavior …. **autopoiesis is the mechanism that imparts autonomy to the living**." Luisi 2003, p. 52

How is an organism autonomous? Physiologically and reproductively.

The notion of organism might be characterised most generally in terms of being a living casual agent with **physiological and reproductive autonomy**.

3.2 Organismal autonomy

Being a causal agent —> being capable of starting causal chains as autonomous source of activity = free will (clashes with deterministic outlook).

"The interaction with the environment, according to autopoiesis, is **seen from the internal logic of the living system**…. As Varela puts it, 'there is no particular nutrient value in sugar, except when the bacterium is crossing the sugar gradient and its metabolism utilizes the molecule so as to permit the continuity of its identity' (Varela 2000)." Luisi 2003, p. 54

3.3 Organismal autonomy

Thus, the interaction with the environment is "cognitive" because the environment "… induces a reaction in the organism, but the accepted changes are determined by the internal structure of the organism itself." Luisi 2003, p. 54

Life = cognition

The fundamental point is that "…the organism creates the environment with its own perceptory sensorium." Luisi 2003, p. 55 What does this mean?

3.4 Organismal autonomy

"…the organism creates the environment with its own perceptory sensorium." Luisi 2003, p. 55 What does this mean?

- Organisms are active "interpreters" of environmental stimuli;
- Organisms "enact", i.e., create their own "world" of meaning (the relevant portion of the environment with which they interact);

This is an account of the emergence not only of autonomy through self-production but also, implicitly, of the emergence of causal agency.

Varela drew this implication clearly: life = cognition = subjectivity = sentience = causal agency = free will.

3.5 Organismal autonomy

"… we wish our system to be able to 'choose,' in the sense that it can exhibit different and appropriate behaviors in the presence of different choice situations…. In an appropriately minimal sense of 'choice,' a system of this sort would be able to exercise choice. Real cells accomplish just such choice behavior."

Kauffman & Clayton 2006. pp. 507-8

3.6 Organismal autonomy

Let us now focus on physiological autonomy. What does this mean?

Autopoietic unit is capable of preserving its identity: "… system that is capable of self-sustaining owing to an inner network of reactions that re-generate **all the system's components** …. The living is a factory that makes itself from within. " Luisi 2003, p. 51 and 52 (slide 2.2)

What kind of self-production is needed for organismality?

3.7 Organismal autonomy

What kind of self-production is needed for organismality?

1. All parts of the organism?
2. A subset of the parts? If so, which subset?

What organismal components are self-produced? It crucially depends on the nature of the organism-environment interface.

Organisms constantly, opportunistically and contingently assimilate and functionally integrate components from the environment. This process has been called “entrenchment".

3.8 Organismal autonomy

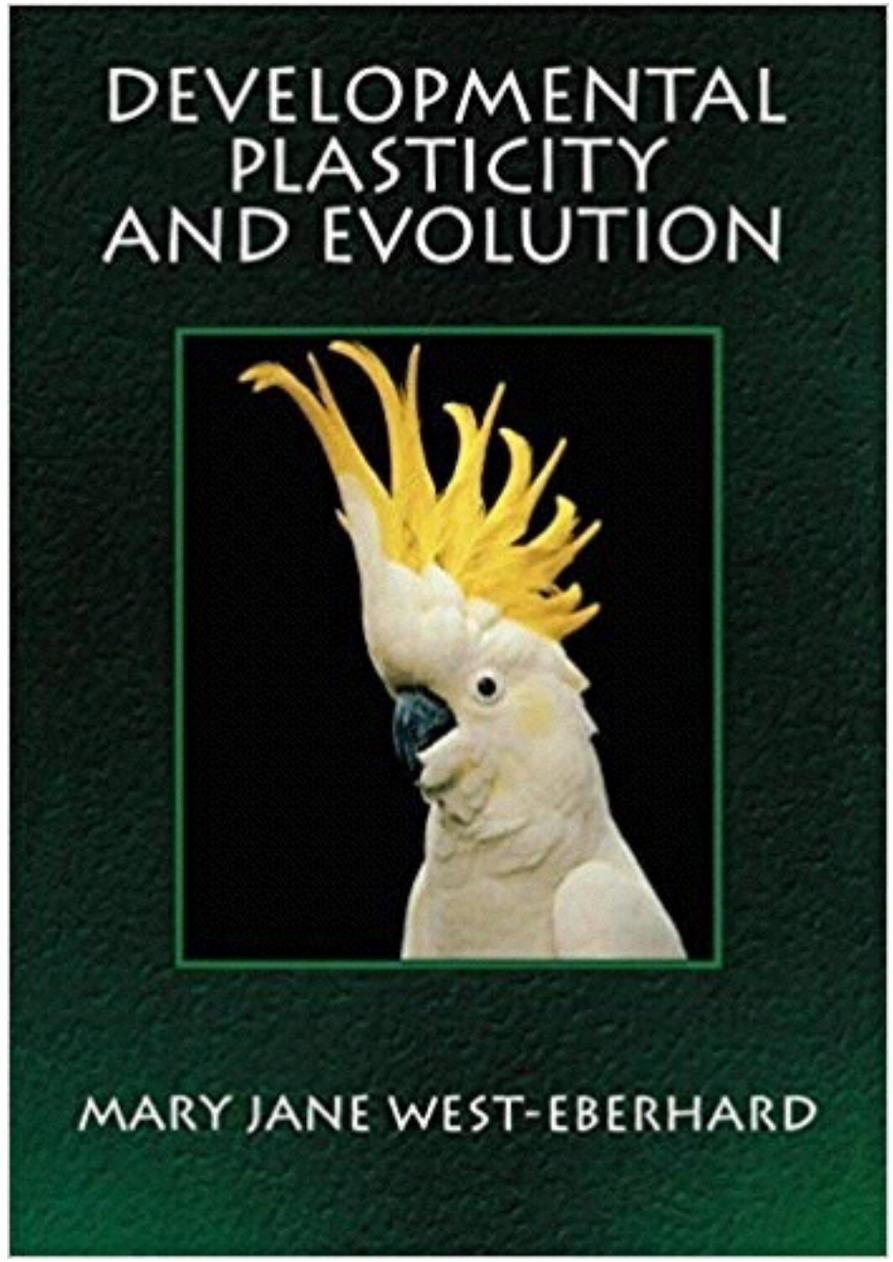
Entrenchment refers to the causal role of the environment:

1. in the regulation of development (as developmental signals);

2. in the production of the phenotype (as building blocks in phenotype construction or formation).

Focus on phenotype production.

“Entrenchment of some environmental elements is so thorough and widespread that we forget they were once evolutionary innovations.” West-Eberhard 2003, p. 500.



3.9 Organismal autonomy

Varieties of entrenchment:

1. <u>abiotic</u>: physical and chemical precursors of abiotic origin deployed for maintenance of metabolic capacities;

2. <u>biotic</u>:

2.1. of materials produced by other organisms (e.g., DNA, nutrition);

2.2 of entire organisms (e.g., symbionts).

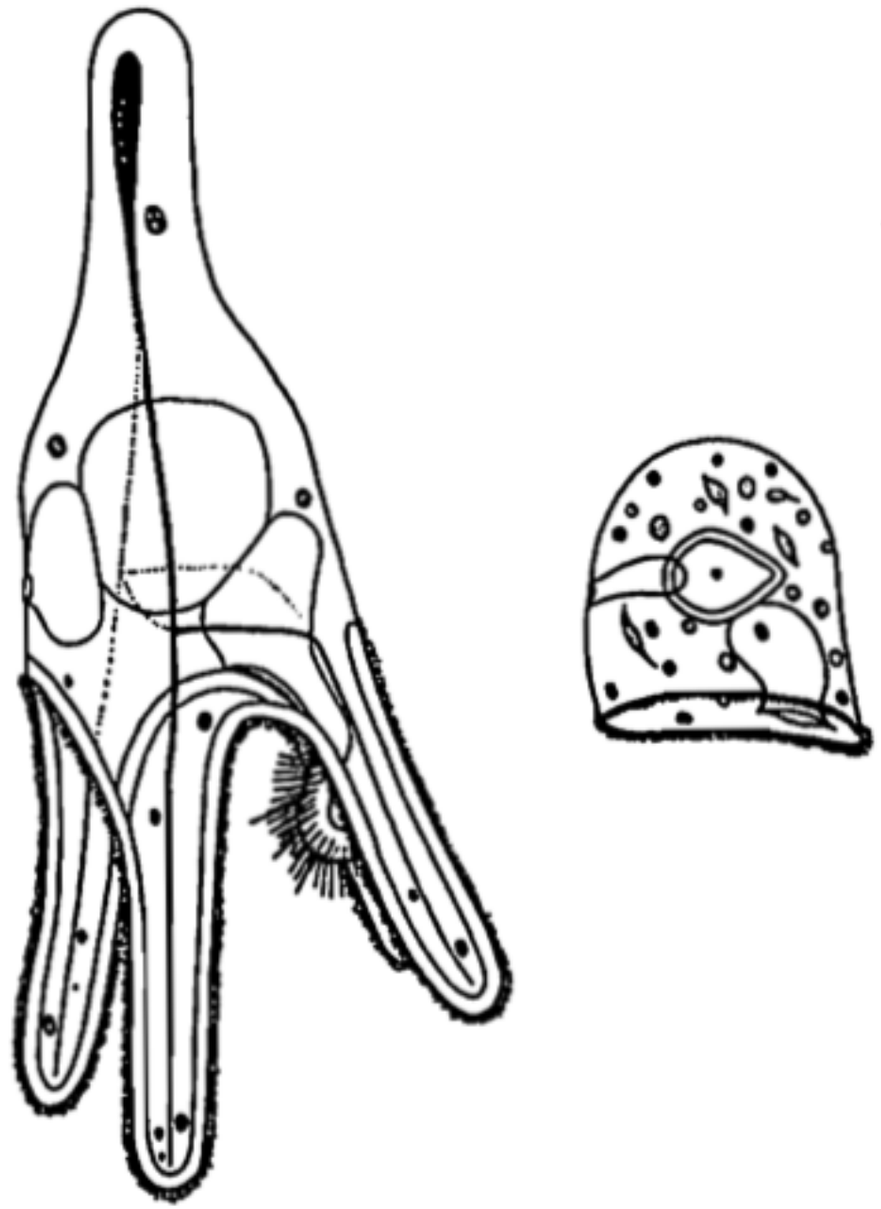


Fig. 26.2. Classical demonstration of environmental influence on larval development in a sea urchin:

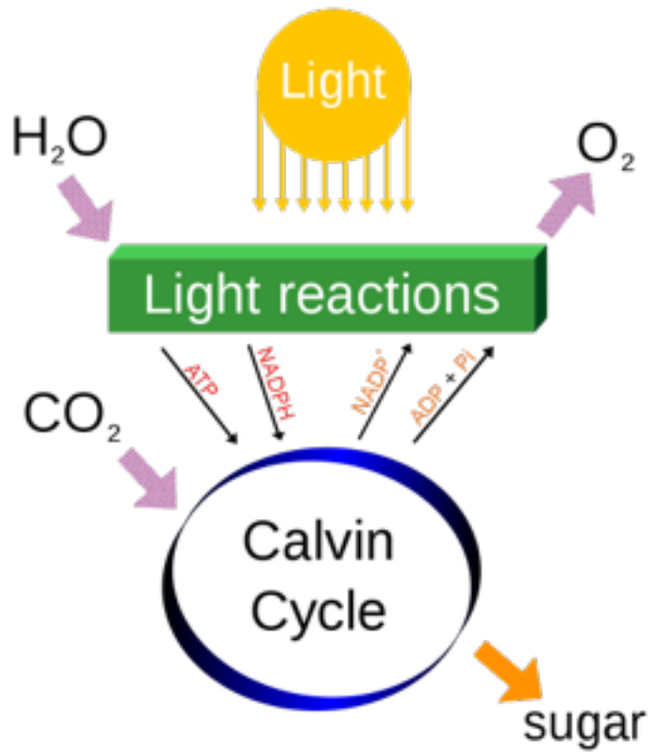
3.10 Organismal autonomy

1. abiotic entrenchment: physical and chemical precursors of abiotic origin deployed for maintenance of metabolic capacities.

Photosynthesis based on assimilation of photons.

Nucleotide synthesis (e.g., purines) based on assimilation of chemical precursors including carbon dioxide.

“…. nothing emanates from the genome without environmental materials...”. West-Eberhard (2003, p. 500)

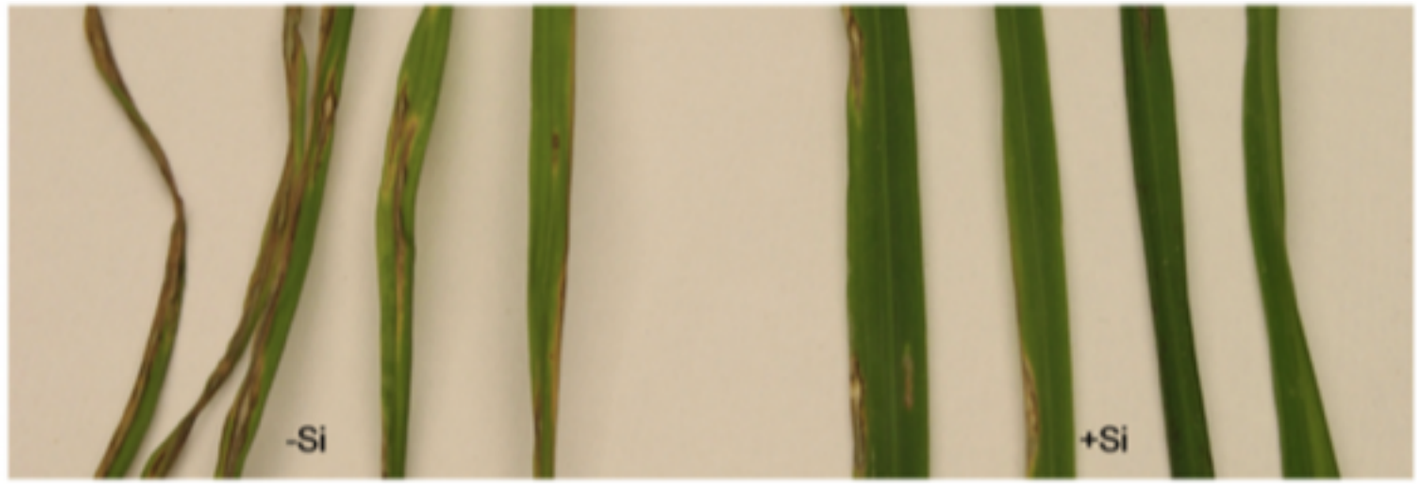


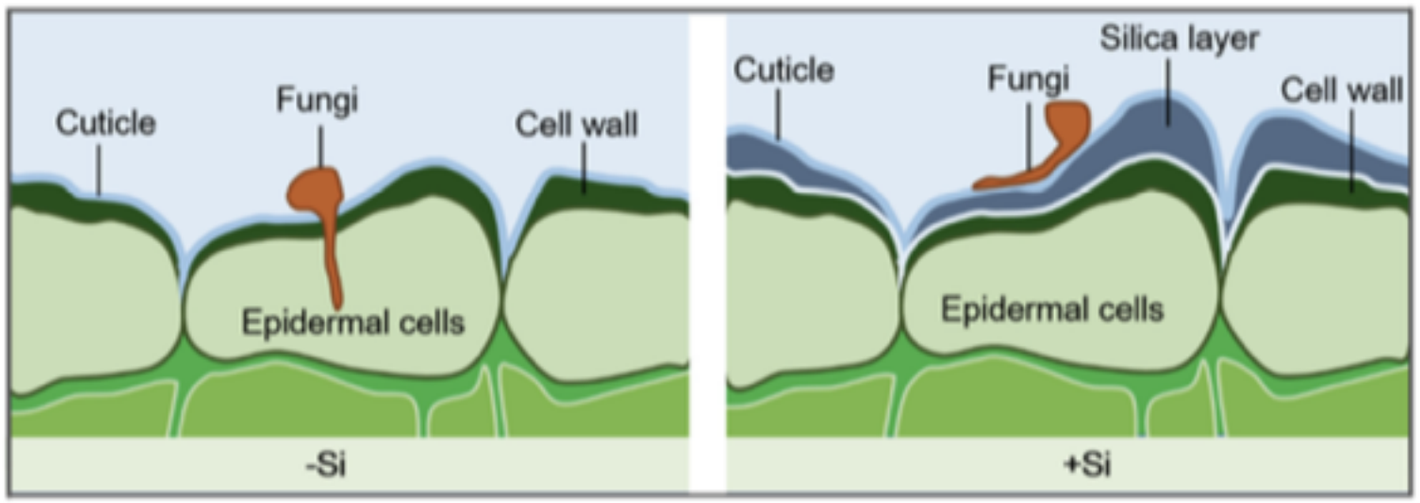
3.11 Organismal autonomy

1. abiotic entrenchment: physical and chemical precursors of abiotic origin deployed for maintenance of metabolic capacities.

Silicon was not considered a physiologically essential element (necessary to complete the plant's life cycle, cf. Epstein 1994).

But it nonetheless might play significant physiological roles (e.g., in cell walls, cf. Wang et al. 2017).

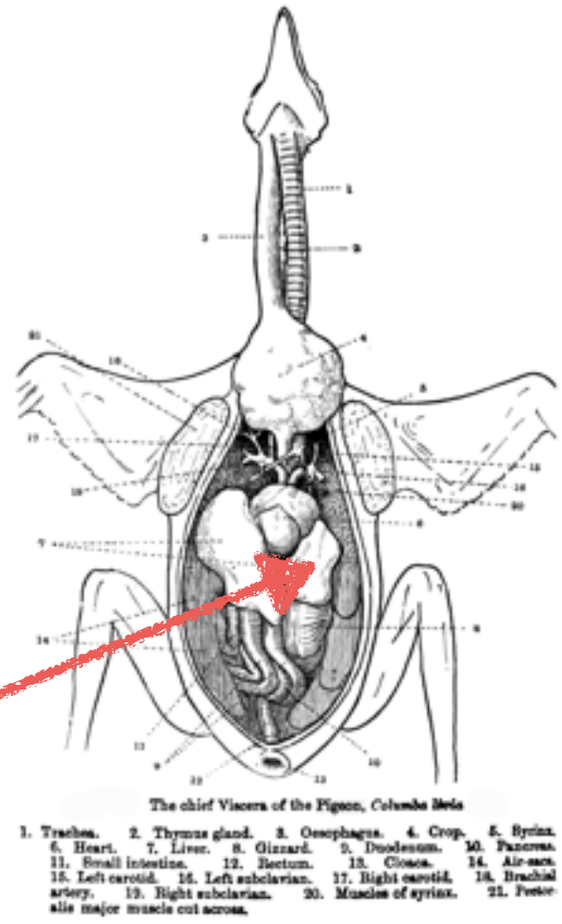




3.12 Organismal autonomy

1. abiotic entrenchment: physical and chemical precursors of abiotic origin deployed for maintenance of metabolic capacities.

Turkeys assimilate stones, which are functionally integrated as gastroliths; gastroliths located in the gizzard perform a function in digestion.



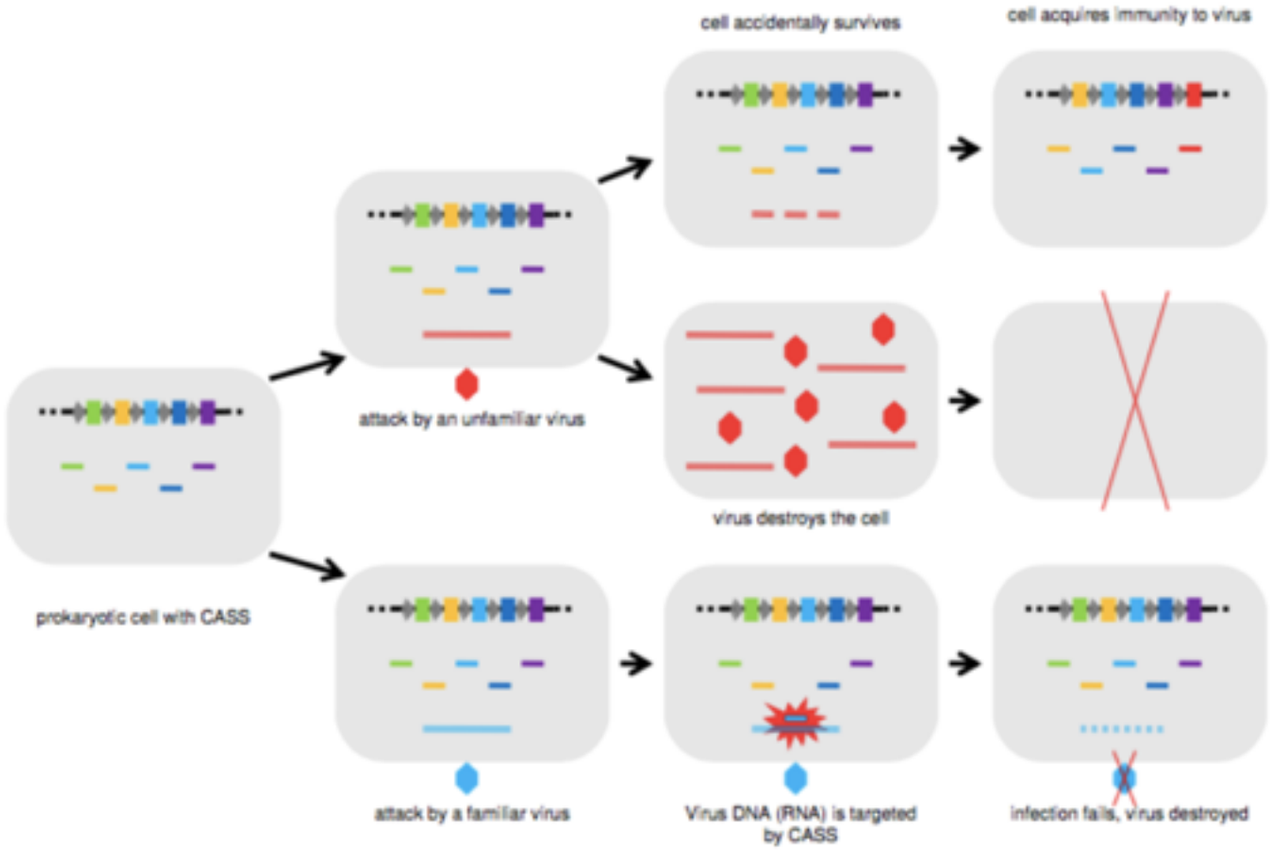
The chief Viscera of the Pigeon, *Columba livia*

1. Trachea. 2. Thymus gland. 3. Oesophagus. 4. Crop. 5. Syrinx. 6. Heart. 7. Liver. 8. Gizzard. 9. Duodenum. 10. Pancreas. 11. Small intestine. 12. Rectum. 13. Cloaca. 14. Air-sacs. 15. Left carotid. 16. Left subclavian. 17. Right carotid. 18. Brachial artery. 19. Right subclavian. 20. Muscles of syrinx. 21. Pectoralis major muscle cut across.

3.13 Organismal autonomy

Biotic entrenchment:

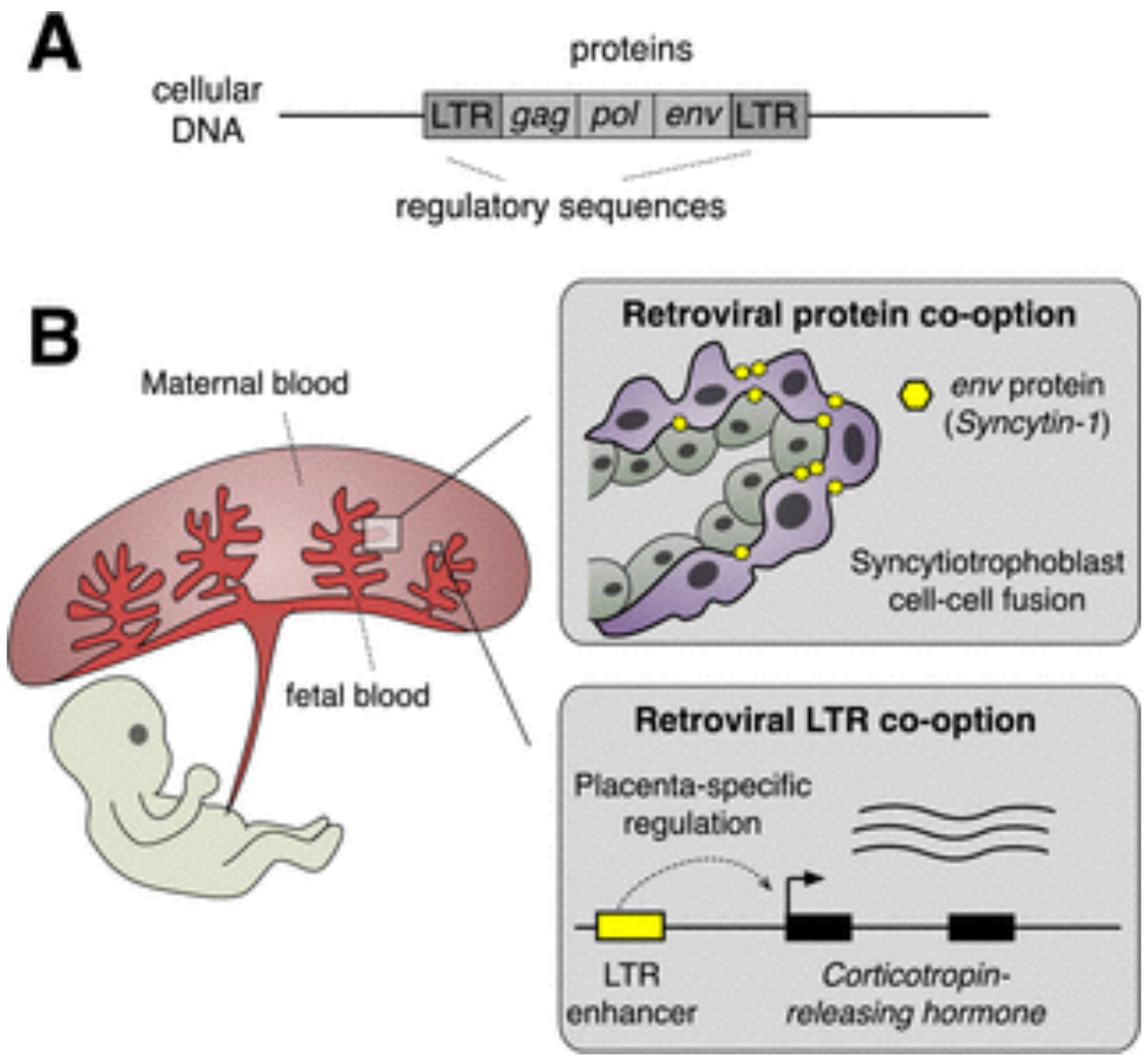
1. Lateral DNA transfer:
e.g., bacteria incorporate viral DNA sequences in their genomes as CRISPR cassettes which are then redeployed to destroy phage mRNAs (Koonin and Wolf 2009);



3.14 Organismal autonomy

Biotic entrenchment:

1. Lateral DNA transfer: origin of placental mammals likely due to the incorporation of retroviruses from other organisms (they allow the rewiring of cell circuitry to produce the progesterone-responsive uterine decidual cell as well as the syncytin fusion proteins of the mammalian placenta, (cf. Gilbert 2015 p. 616)

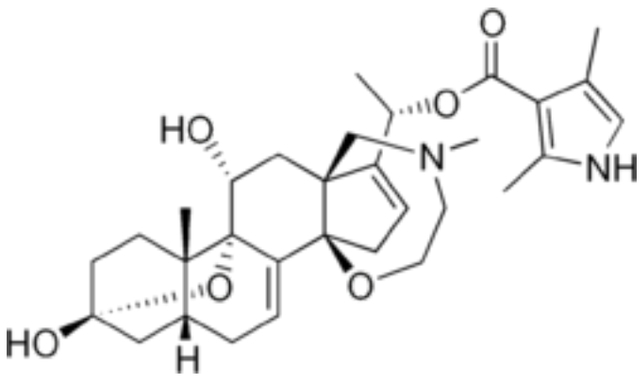


3.15 Organismal autonomy

Biotic entrenchment:

2. Nutrition: e.g., batrachotoxin - found, for instance, on the skin of several Colombian frogs (e.g., golden poison frog Phyllobates terribilis) - cannot be extracted from them when reared in captivity or in the laboratory.

These frogs assimilate it by eating batrachotoxin-containing insects (Dumbacher et al. 2004).



3.16 Organismal autonomy

Biotic entrenchment:

2. Nutrition: haemoglobin protein is produced through the environmental assimilation of iron and of amino acids.

Many animals are not physiologically autonomous and must assimilate “essential” amino acids because they cannot biosynthesise them.

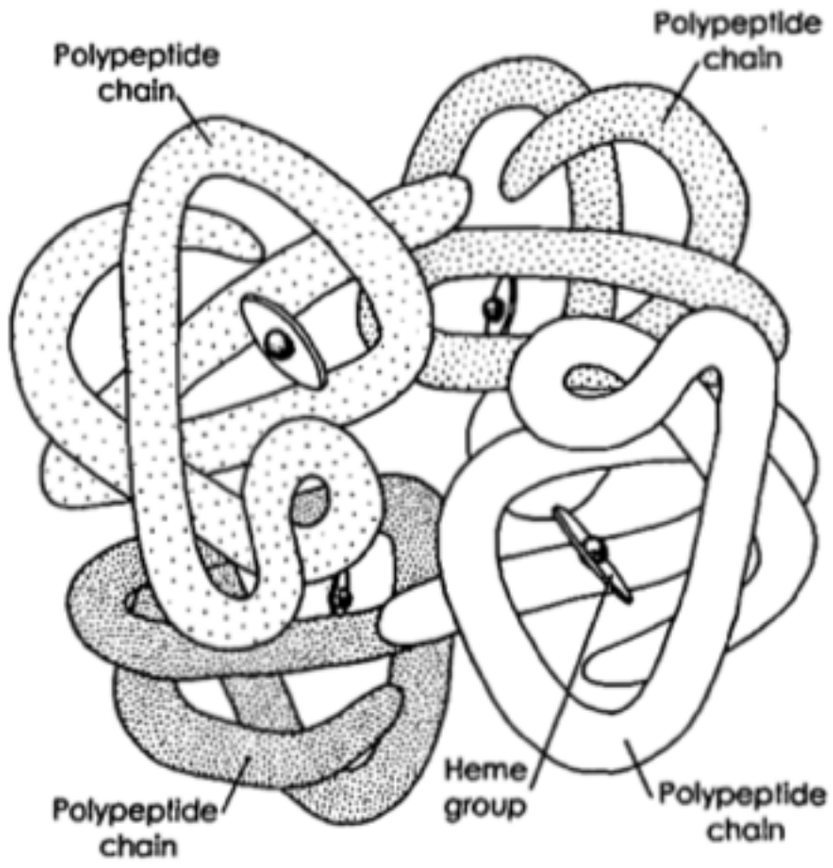


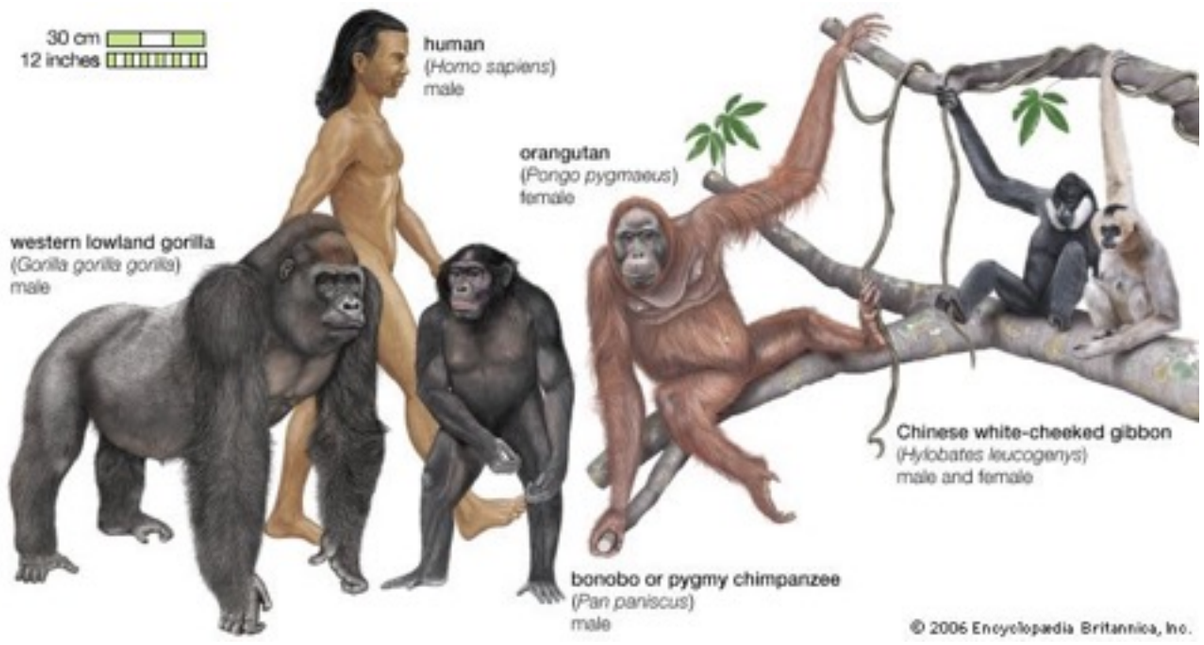
Fig. 26.1. Entrenchment of environmental elements in gene products. The hemoglobin molecule exemplifies the intimate connections between genetically specified elements (polypeptide chains) and elements of environmental origin (e.g., the iron in heme groups). Standard diagram, based on Dickerson and Geis (1969), Curtis (1983), and Bonner (1988).

West-Eberhard 2003, p. 500

3.17 Organismal autonomy

Biotic entrenchment:

2. Nutrition: the incapacity to convert 2-keto-L-gulonolactone to ascorbic acid (vitamin C) in primates and guinea pigs (note the phylogenetic pattern) was likely generated by originally fitness neutral mutations fixed by drift (King & Jukes 1969, p. 792). Assimilation from environment is generally simple.



3.18 Organismal autonomy

What kind of self-production is needed for organismality?

Entrenchment affects all organismal functions of all organisms. It is not a trivial phenomenon as it requires assimilation + functional integration + deployment of environmental resources.

Thus, **self-production is conditional on what is available in the environment**.

Organisms relinquish self-production capacities by assimilating abiotic elements of the environment or by assimilating the products of the self-production capacities of other organisms.

Entrenchment compensates lack of self-production capacities. **Hence, no self-produced physiological autonomy in the strict sense.**

~~1. All parts of the organism?~~

2. A subset of the parts? If so, which subset?

3.19 Organismal autonomy

What kind of self-production is needed for organismality?

~~1. All parts of the organism?~~

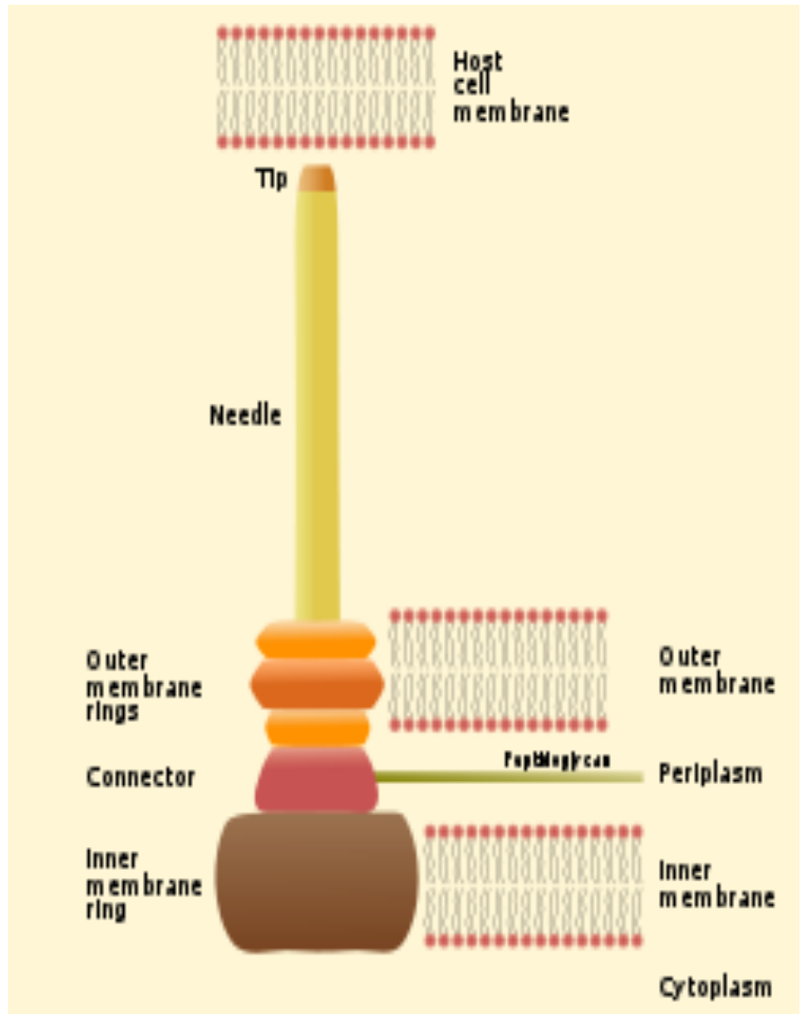
2. A subset of the parts? If so, which subset?

Cornish-Bowden & Cardénas (2020, p. 31, section 3.1.4): **all catalysts must be products of the system itself**.

Are all catalysts (e.g., enzymatic proteins) needed for host metabolism synthesised internally?

3.20 Organismal autonomy

Are all catalysts (e.g., enzymatic proteins) needed for host metabolism synthesised internally?



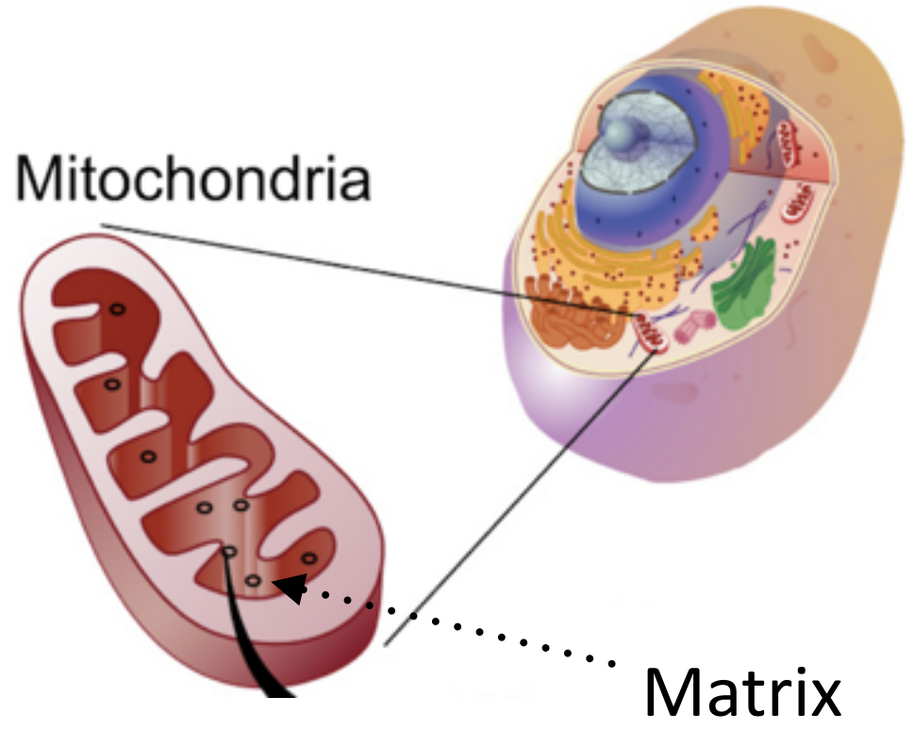
“Many enteric pathogens have developed a specialized secretion system, called type III secretion, to mediate the direct transfer of proteins into the host cell membrane. Through this mechanism, extracellular bacteria that are in close contact with eukaryotic cells can deliver bacterial proteins into the cytosol of these cells.”

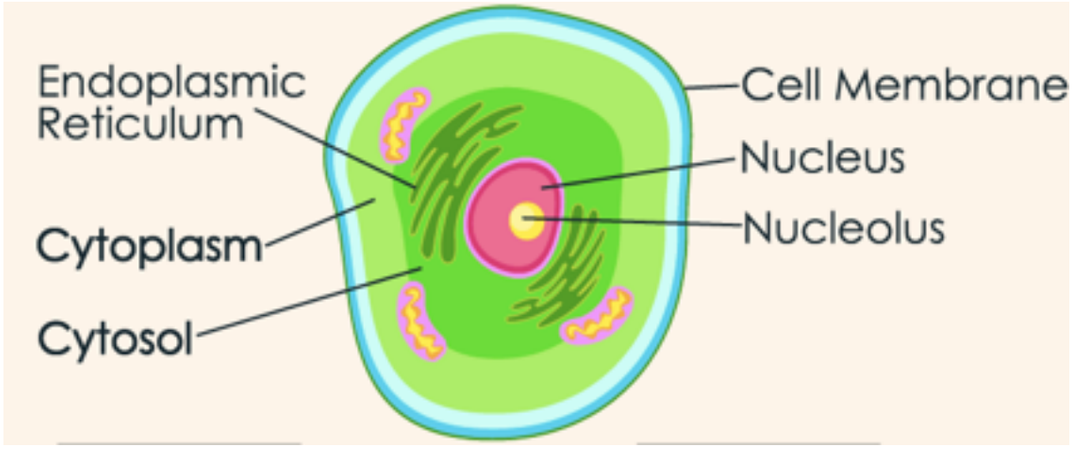
Lu et al. 2001 p. 1125S

3.21 Organismal autonomy

Are all catalysts (e.g., enzymatic proteins) needed for host metabolism synthesised internally?

Assembly of a functional mitochondrion requires import of proteins from the cytosol (of the cell) and export of proteins from the matrix (of the mitochondrion) ….. it is now clear that proteins encoded in the nucleus as well as those encoded in the mitochondrion also move from the matrix into and across the inner membrane, a process defined here as export. (Poyton et al. 1992).





3.22 Organismal autonomy

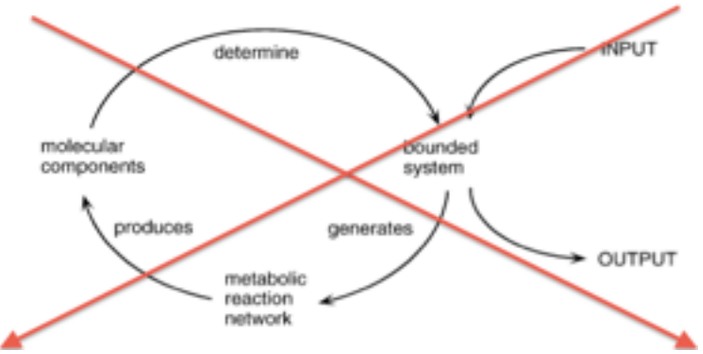
Relationship between a multicellular host (“Japanese” human), an endosymbiotic bacterium that is recruited to perform a novel metabolic role (*Bacteroides plebeius*) and a marine bacterium ingested by the host (*Zobellia galactanivorans*).

The endosymbiont controls an aspect of the metabolism of the host by using specific enzymes not explicitly coded in the host genome.

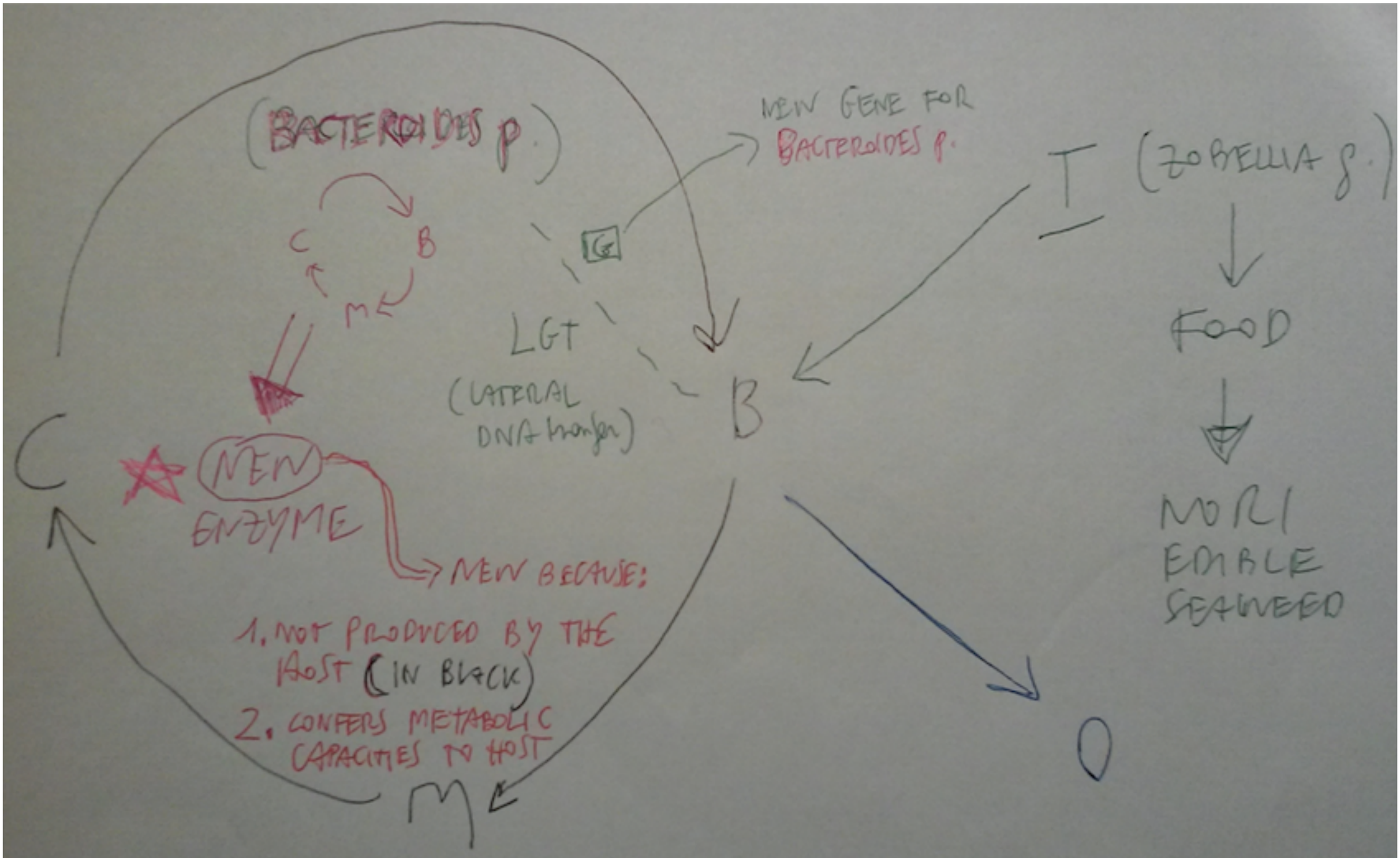
The transfer of the enzymes is first by lateral DNA transfer from marine bacteria and then “internalised” by the gut bacteria of “Japanese” people.

Algae-degrading enzymes (β-porphyranases) are new enzymes, not produced by the host.

Hehnemann et al. 2010

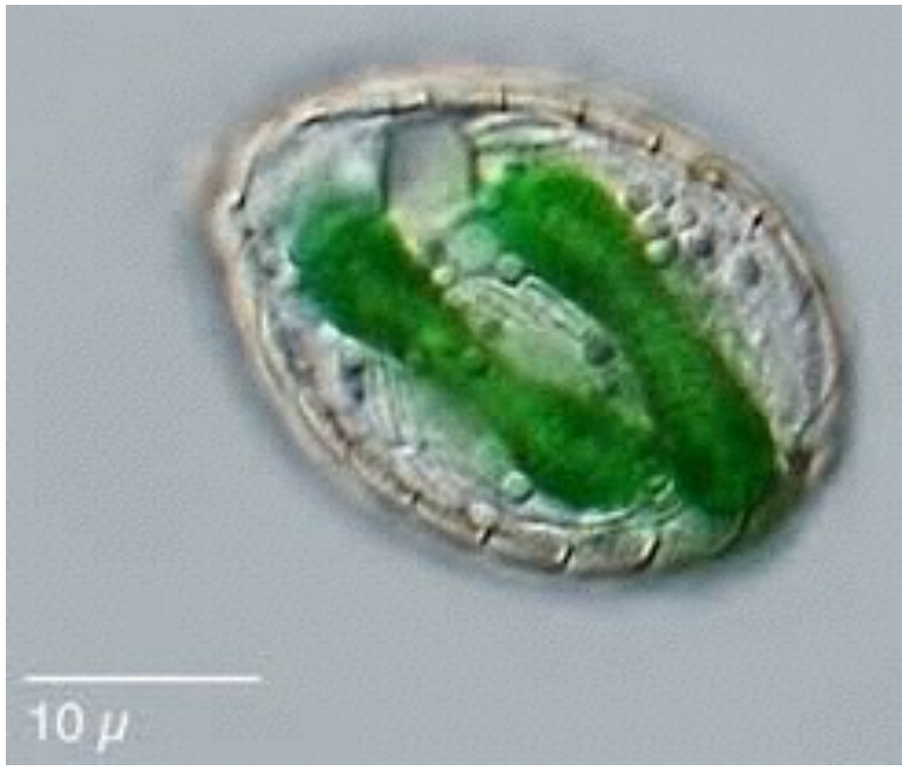


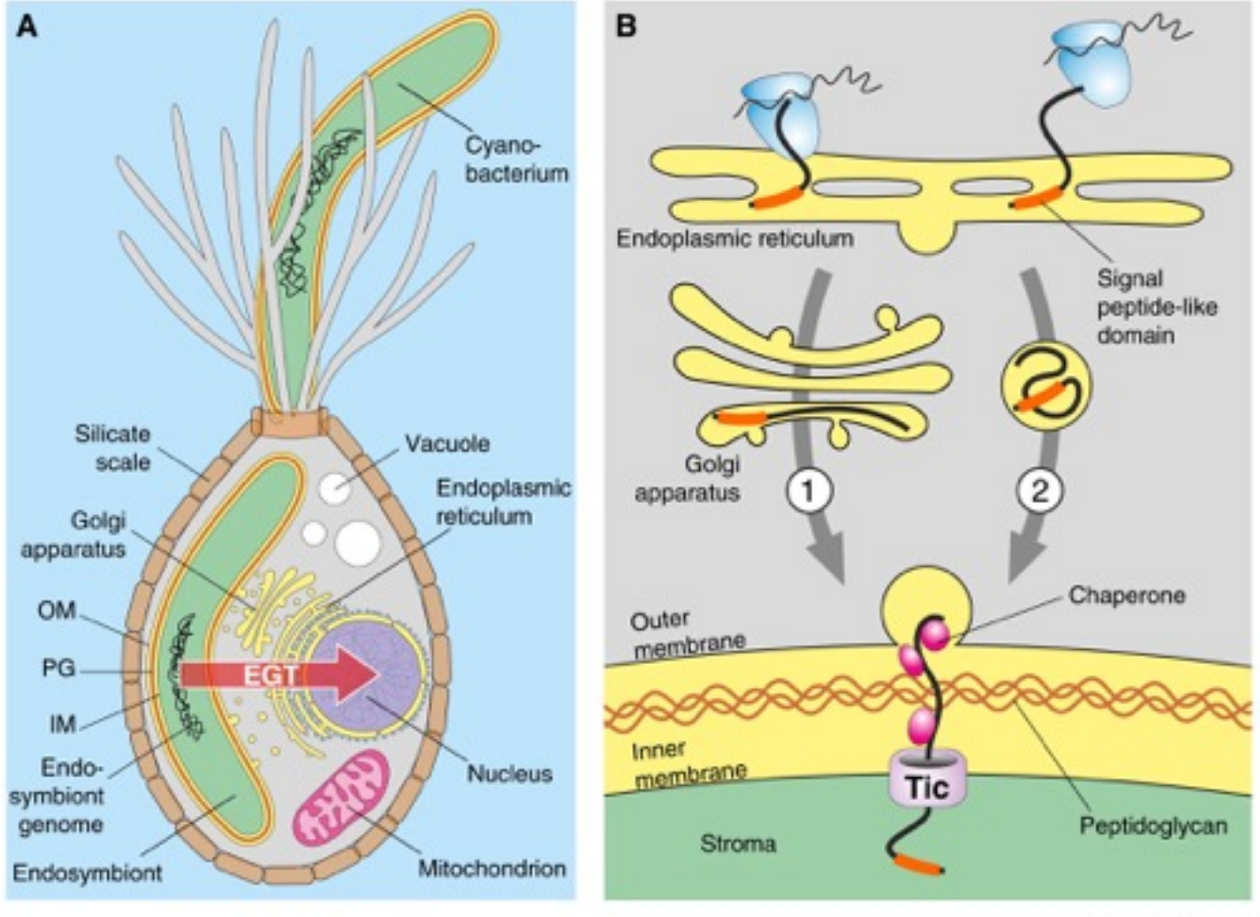
3.23 Organismal autonomy



3.24 Organismal autonomy

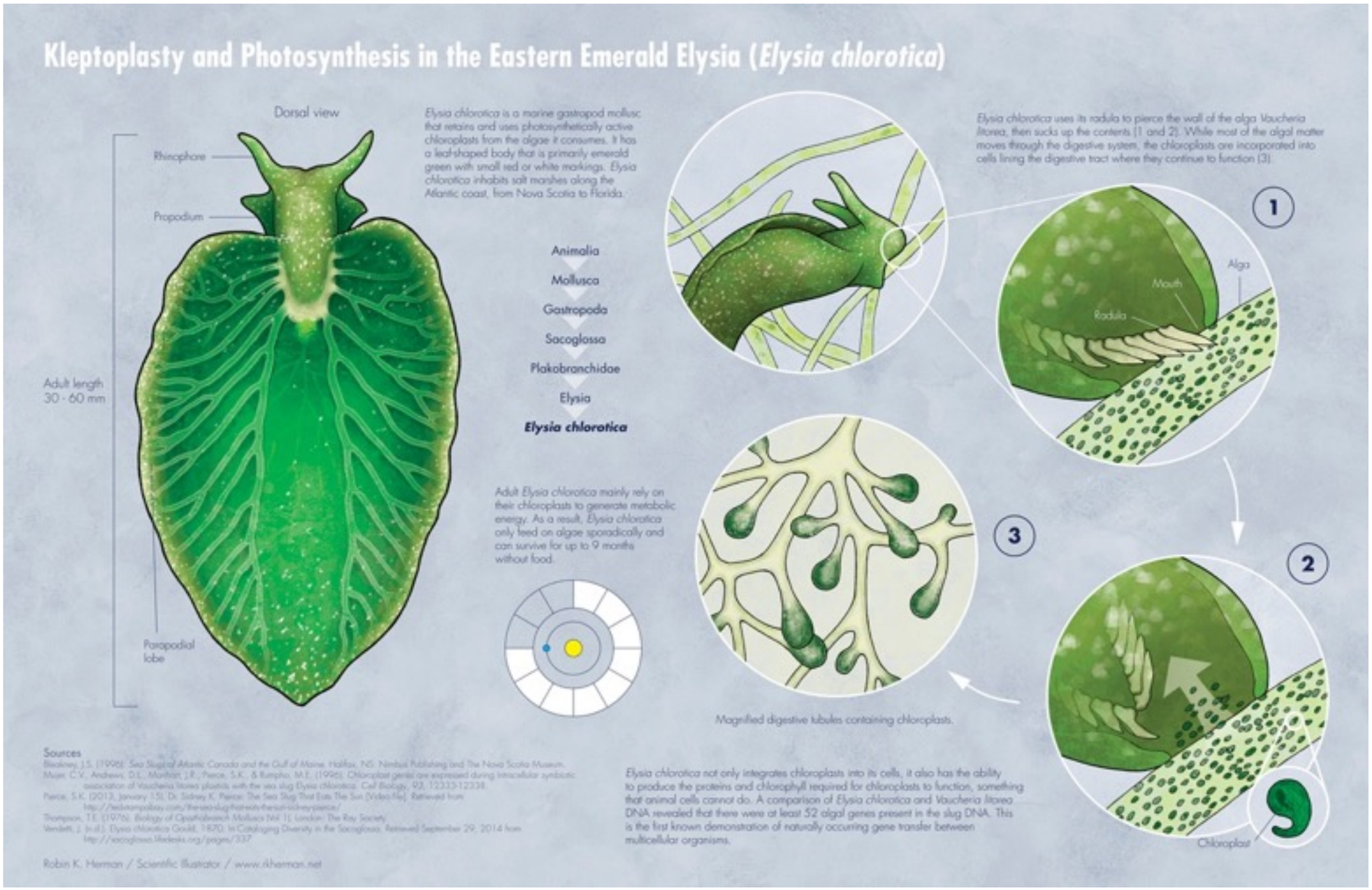
That self-production in the more limited sense of enzymatic or catalytic “closure” is problematic can be particularly seen in the case of “composite” organisms (see section 4) such as symbiotic associations. The amoeba *Paulinella chromatophora* has 2 chromatophore endosymbionts (unable to reproduce independently). Transfer of chromatophore genes coding for proteins involved in photosynthesis to host. Furthermore, cytosol-synthesized proteins are imported back into chromatophores (Bodył et al. 2012).





3.25 Organismal autonomy

Another clear case is that of *Elysia Chlorotica*.



3.26 Organismal autonomy

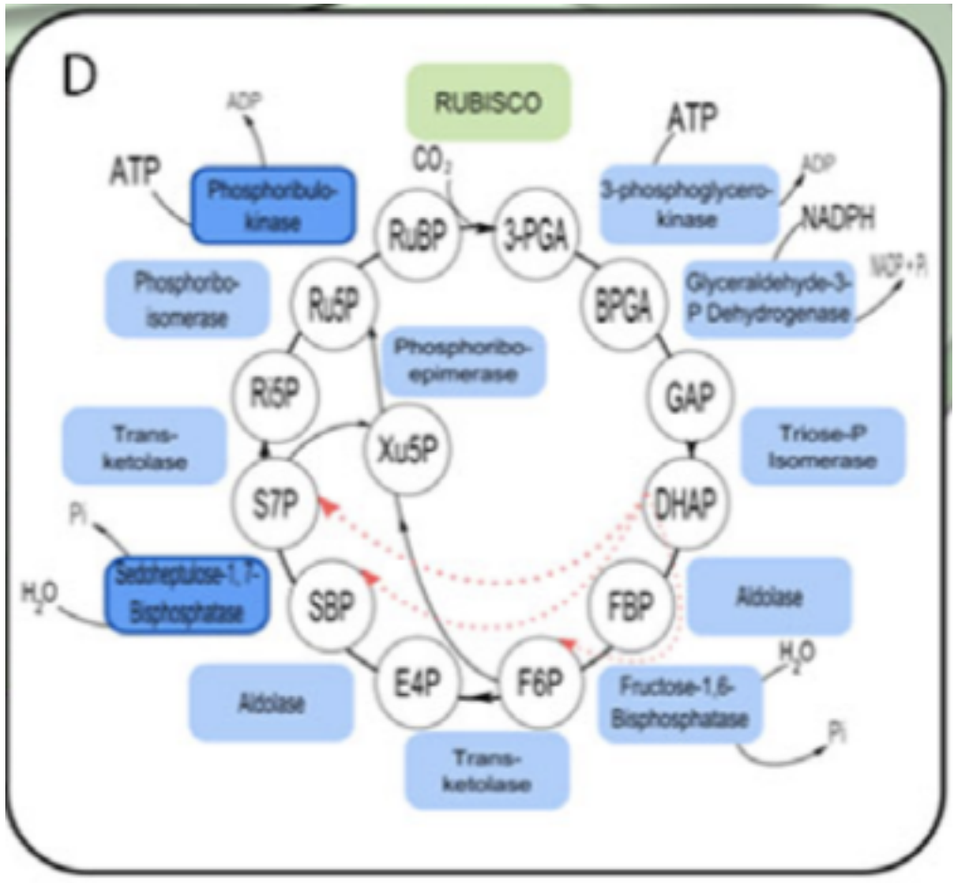
Slug-plastid relationship:

1. protein exchange from slug to plastid involves the simplification of the plastid membrane;

2. recruitment in plastid photosynthetic pathways of enzymes biosynthesised by slug;

3. redeployment and functional re-organisation of plastid photosynthetic pathways.

Elysia chlorotica becomes a photosynthetic animal by the increasing mutual dependence (genomic, metabolic, cellular and reproductive) between slug and plastids.



In green plastid encoded enzymes. In dark blue nuclear encoded ones unique to phototrophs. All others are nuclear encoded and have homologues in animals (Rumpho et al. 2011).

3.27 Organismal autonomy

That catalytic closure or self-sufficiency is problematic is not surprising in the face of entrenchment: **self-production is conditional on what is available in the environment** (slide 3.18).

Additionally, catalysis is not a fundamental property of life because:

1. catalytic enzymes are not necessary for chemical reactions: in the urea cycle, no catalytic enzymes are necessary to regulate this cycle, even though without them the chemical reactions are much slower; thus, the urea cycle (or the Wood–Ljungdahl metabolic pathway) can be given an interpretation purely in terms of chemical transformations by avoiding reference to catalysis;

2. from an evolutionary perspective, enzymatic catalysis is an acquired phenotype and chemical reactions were likely performed by much simpler molecules than proteins (see first class slides 4.13-4.14).

3.28 Organismal autonomy

In 3.6 we started to characterise physiological autonomy. We then saw that the idea of self-production and physiological autonomy are challenged by the varieties of entrenchment seen in slides 3.7-3.27.

But perhaps the proper sense of autonomy is reproductive: can we thus define reproductive autonomy more rigorously than physiological autonomy?

Reproduction cannot be intended in the sense of “self-replication”, which is a biological myth.

3.29 Organismal autonomy

DNA and genes do not self-replicate: "…. whatever sense we might try to make of the Dawkinsian idea of selfish genes, molecular replication is always, and has always been from the pre-cellular molecular community to the present, the achievement of ensembles of molecules, not of individual molecules …." p. 15 (reference to Dawkins, R. 1976. The selfish gene).

The same, by analogy, must be the case for prions and viruses.

What about paradigmatic organisms?

"….. it is doubtful whether even paradigmatic multicellular organisms can meet the criterion of lineage-exclusive autonomous reproduction." Dupré & O'Malley 2009, p.

3.30 Organismal autonomy

“Not even all organisms are capable of self-reproduction, such as certain hybrids or the members of certain insect castes. Moreover, the so-called sexually reproducing organisms are not really self-reproducing: it is not the individual but the mating-pair that produces offspring; and, in so doing, it does not really self-reproduce - it does not produce another mating-pair-but merely produces one or more organisms of the same species.” Mahner and Bunge 1997 p. 144

This leaves the possibility of unicellular organisms. But what kinds of unicellular organisms?

3.31 Organismal autonomy

Consider that reproduction is a physiological process: a cell dividing (by mitosis and meiosis) requires regulation of DNA replication, membrane formation etc.

Some unicellular organisms have - in evolutionary time - lost their reproductive autonomy.

Organelles (e.g., mitochondria and plastids, see slide 3.21 + 3.25-3.26): preserve partial control of reproductive process (e.g., their membranes are generally inherited from pre-existing membranes and are usually not constructed *de novo*, thus organelles are templated from pre-existing organelles) + their DNA is organelle-specific; <u>BUT, the control of the reproduction cycle requires developmental resources (e.g., genes and proteins) from the host; hence, no total reproductive autonomy</u>.

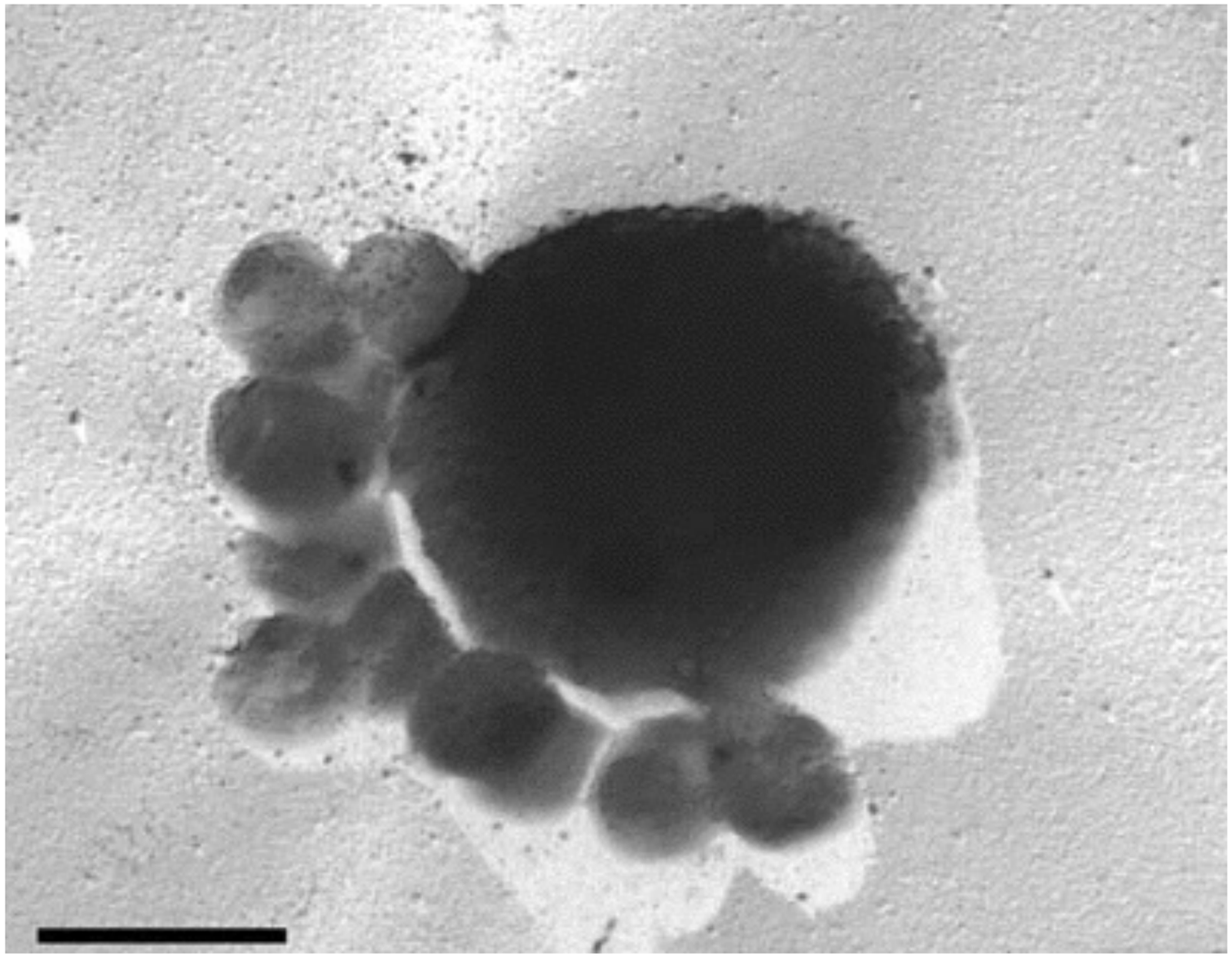
3.32 Organismal autonomy

Consider that reproduction is a physiological process: a cell dividing (by mitosis and meiosis) requires regulation of DNA replication, membrane formation etc. Such regulation is frequently “outsourced” to other organismal entities.

Analogous considerations apply for endosymbionts (such as the chromatophores in *Paulinella chromatophora*, see 3.24). Endosymbionts: they undergo genome reduction so that many of the developmental resources (e.g., genes and proteins) to regulate reproduction are supplied by the host.

3.33 Organismal autonomy

Some free-living (neither organelles or endosymbionts) unicellular organisms have lost their reproductive autonomy.



Nanoarchaeum equitans unable to metabolize, grow and reproduce independently of the other archaeon *Ignicoccus hospitalis*.

What's left of the idea of reproductive autonomy?

4.1 Beyond autonomy

Life as autonomy vs. life as collaboration: "…. metabolism is typically a collaborative activity involving many of the things that are generally supposed to be discrete living entities." Dupré & O'Malley 2009 p. 13

Analogous considerations apply to reproduction.

"Life, according to our analysis, occurs at the intersection of lineage formation and (typically collaborative) involvement in metabolism. Entities that are problem cases, such as viruses, can be understood as alive when actively collaborating. When not collaborating, they have at most a potential for life." Dupré & O'Malley 2009 pp. 14-15

4.2 Beyond autonomy

What to make of this conception? Are physiological and reproductive autonomy biological myths?

We have seen that physiological autonomy is challenged by entrenchment (slides 3.8-3.27). The same applies to reproductive autonomy: self-replication is a myth (3.28) while the regulation of the reproductive process - which is fundamentally physiological - often requires collaboration with other organisms (as in sexual reproduction, slide 3.30) or “outsourcing” (slides 3.31-3.33). Many times, when the units participating in physiology and reproduction are two or more organisms, the physiological and reproductive autonomy of the individual organisms are partially relinquished.

But this is not surprising if we consider the nature of life and the varieties of living things again.

4.3 Beyond autonomy

If we consider the entire spectrum of cellular life forms, we need to make a distinction between two types of organisms: **elementary and composite** (somehow based on Mahner & Bunge 1997 section 4.3).

All elementary organisms are cells (hence life begins at the cell level, cf. slide Summing up c). Cell = smaller unit of life.

Prokaryotic cells are elementary organisms (even the zygotes of multicellular organisms are not elementary because they are eukaryotic cells).

4.4 Beyond autonomy

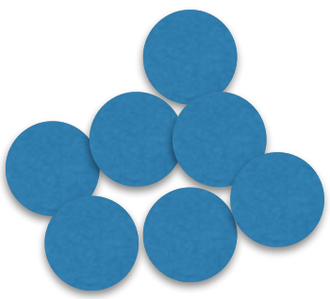
A composite organism is composed of elementary organisms, that is, either cells or other composite organisms made out of cells.

Eukaryotic cells (composed of two kinds of ancestral cells with different genomes) and multicellular organisms (taken as composed of eukaryotic cells with same genome) are composite organisms.

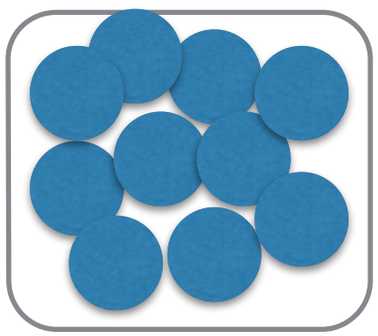
Then there exists a variety of other biological entities such as: biofilms, symbiotic associations (e.g., eukaryotic cells, lichens, multicellular organisms as holobionts), species, communities, ecosystems etc.

4.5 Beyond autonomy

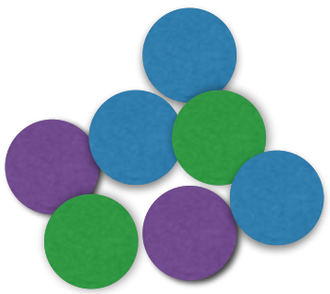
1. **Elementary organism** = prokaryotic cell (i.e., bacterium or archaeum).



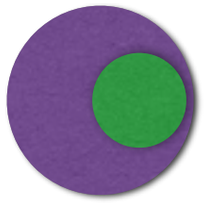
2. **Multi-cellular and mono-lineage composite organism without boundary** = 2 or more elementary organisms of the same species (e.g., mono-species bacterial biofilm).



3. **Multi-cellular and mono-lineage composite organism with boundary** = 2 or more elementary organisms of the same species (e.g., mono-species bacterial biofilm living in a self-synthesised extra-cellular matrix).



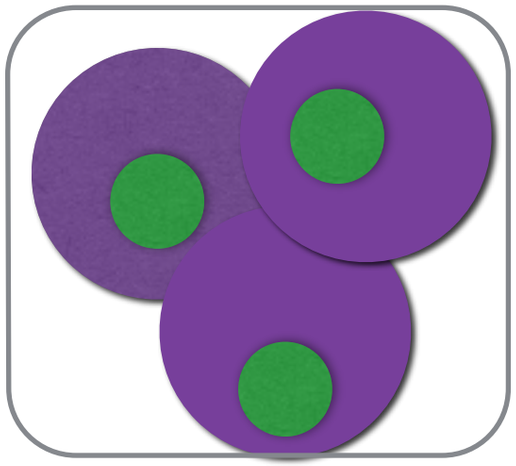
4. **Multi-cellular and multi-lineage composite organism without boundary** = 2 or more elementary organisms of different species (e.g., multi-species bacterial biofilm).



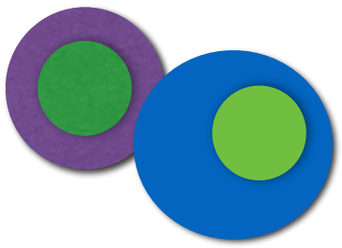
5. **Bi-cellular and multi-lineage composite organism with boundary and incorporation** = eukaryotic cell (e.g., host cell + mitochondrion) = 2 elementary organisms (if mitochondrion is only 1 as, probably, in the ancestral eukaryote).

This classification is not exhaustive (e.g., [4] might come with a kind of boundary). Furthermore, also consider that [2], [4] & [7} might not be considered organismal enough if a boundary is essential for organismality ascription. But I argue that organismality is a continuum (slide 5.1).

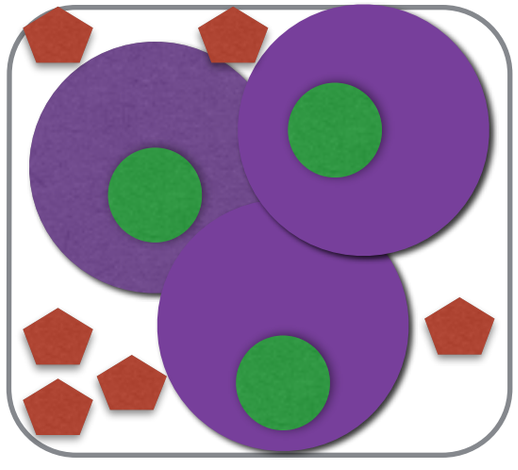
4.6 Beyond autonomy



6. **Multi-cellular and bi-lineage composite organism with boundary and two types of incorporation** = multicellular organism as set of eukaryotic cells surrounded by a boundary (epidermis) without microbiota.



7. **Multi-cellular and multi-lineage composite organism without boundary and only one kind of incorporation** = symbiotic association (e.g., lichen) of 2 or more composite organisms of different lineages.



8. **Multi-cellular and multi-lineage composite organism with boundary and two types of incorporation** = multicellular organism as set of eukaryotic cells surrounded by a boundary (epidermis) with incorporated (i.e., within epidermis) resident microbiota = 2 or more composite organisms + huge set of viruses and elementary organisms (many times called “holobiont”).

9. Then there are supra-organismal biosystems (i.e., whose level of physiological + reproductive integration is increasingly lower): e.g., populations of [8] or geographically dispersed species of [8], ecosystems made of different species of [1, 5 and 8] …. up to the entire biosphere.

4.7 Beyond autonomy

It is unsurprising, from this perspective, to find that elementary organisms posses the higher degree of physiological and reproductive autonomy.

This means that:

1. the prokaryotic organism living in a planktonic state (i.e., isolated from other organisms) possesses the highest level of physiological and reproductive autonomy (this view is evolutionary-based, as the last universal common ancestor was an elementary organism);

2. multicellular organisms are holobionts characterised by multi-genomic state because they are multi-lineage composites;

4.8 Beyond autonomy

What to make of the life = collaboration and life ≠ autonomy conception? Are physiological and reproductive autonomy biological myths?

More than myths, they are idealised states, probably not very common. The planktonic prokaryote approximates this autonomy state.

Planktonic prokaryotic organisms are paradigmatic organisms, not multicellular ones.

5.1 Organismality criteria

The upshot of all this analysis is that **organismality is a property that can be thought in terms of a continuum** ranging from higher levels of physiological and reproductive autonomy to lower levels.

This is particularly the case since we have discovered - thanks to symbiosis research - that eukaryotes and multicellular organisms are **multi-lineage composite organisms**.

5.2 Organismality criteria

The problem with composite organisms is that **organismality can be ascribed to both the sub-units** (i.e., the constituent elementary or composite organisms of the whole) **and the whole itself** (i.e., the composite bio-system).

The interesting point about composite organisms is that the physiological and reproductive autonomy of the sub-units is often relinquished.

The crux of the problem of conceptualising composite organisms is to think in terms of the **physiological and reproductive integration of the sub-units**.

This problem is particularly evident when we consider the organismal status of multi-lineage composite organisms ([4]-[8] in slides 4.5 and 4.6).

5.3 Organismality criteria

Physiological and reproductive integration between the sub-units of the composite organisms can be realised in multifarious ways and is highly idiosyncratic and contingent.

Furthermore, it changes through ontogenetic and evolutionary time.

From this, it follows that the organismality of the composite organism as a whole is a matter of degree because it depends on the ontogenetic and evolutionary stage considered.

5.4 Organismality criteria

Organismality criteria (based on Queller & Strassmann 2016):

1. Spatial proximity of the sub-units of the composite organism;

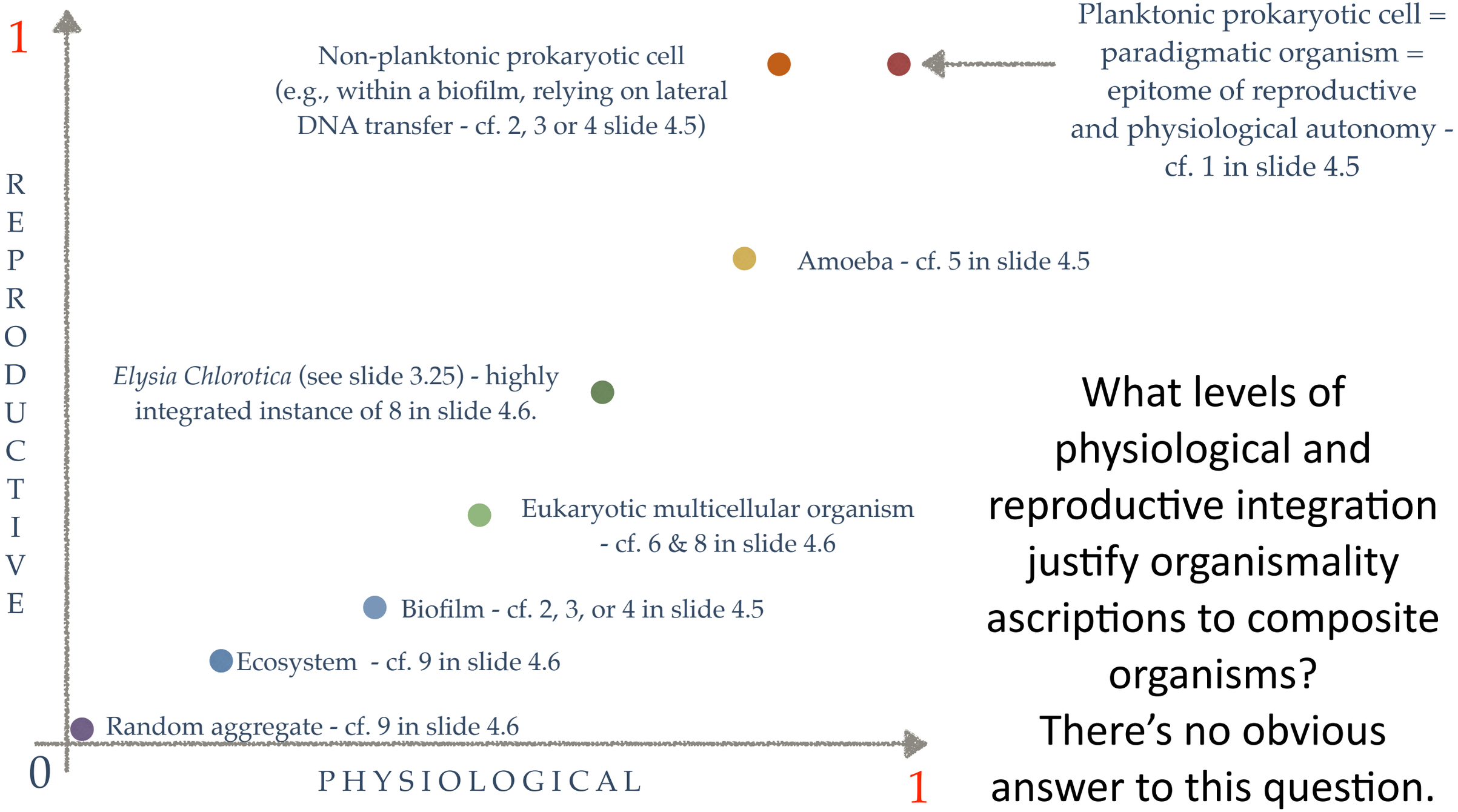
2. Temporal proximity of the sub-units of the composite organism and ontogenetic and evolutionary durability of the mutual dependence;

3. Partner fidelity of the sub-units of the composite organism;

4. Integration of physiology of the sub-units of the composite organism through genomic and metabolic material exchanges and the evolution of morphological structures;

5. Integration of the reproductive systems of the sub-units of the composite organism allowing some form of vertical transmission.

5.5 Organismality criteria



What levels of physiological and reproductive integration justify organismality ascriptions to composite organisms?
There's no obvious answer to this question.

Possible application along two axes of integration of the proposed organismality criteria (slide 5.4) to organismal systems (slides 4.5-4.6)

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CLASS 3 - 10 March: Development

Organism = unit of development

What is development: growth, differentiation and morphogenesis.
How to conceptualise development: epigenesis and preformation.
Causal role of DNA and environment in development.

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Chapter 8, pp. 271-287
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