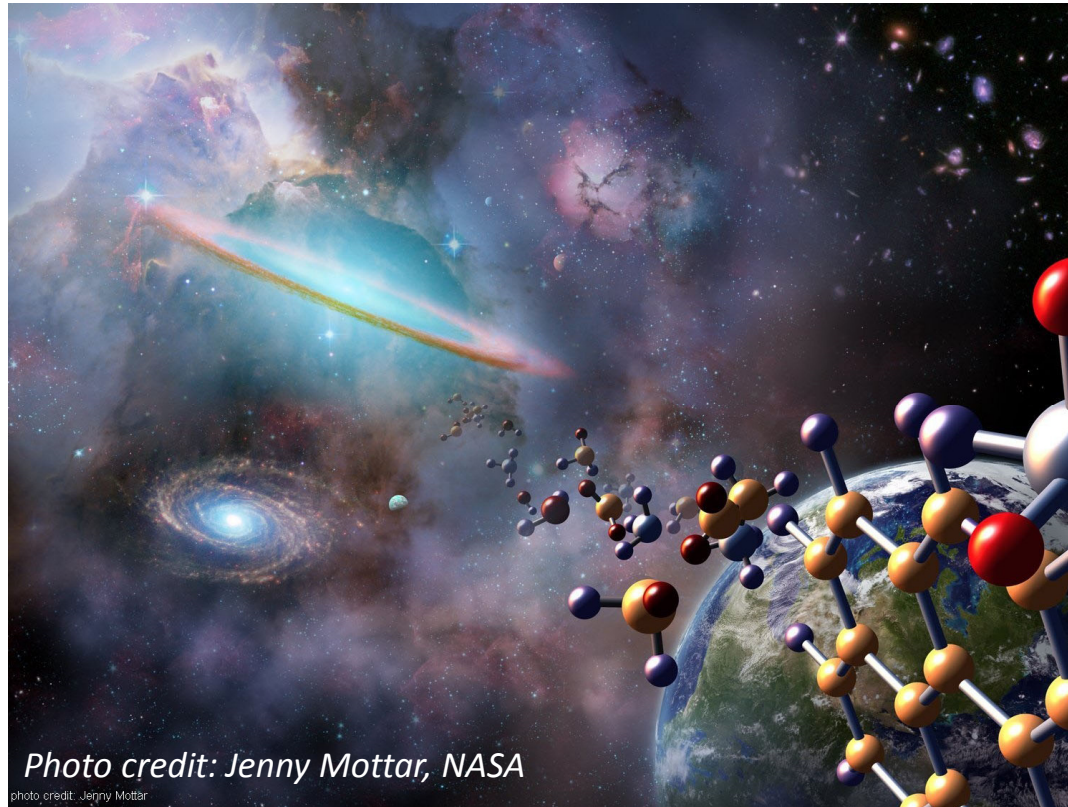


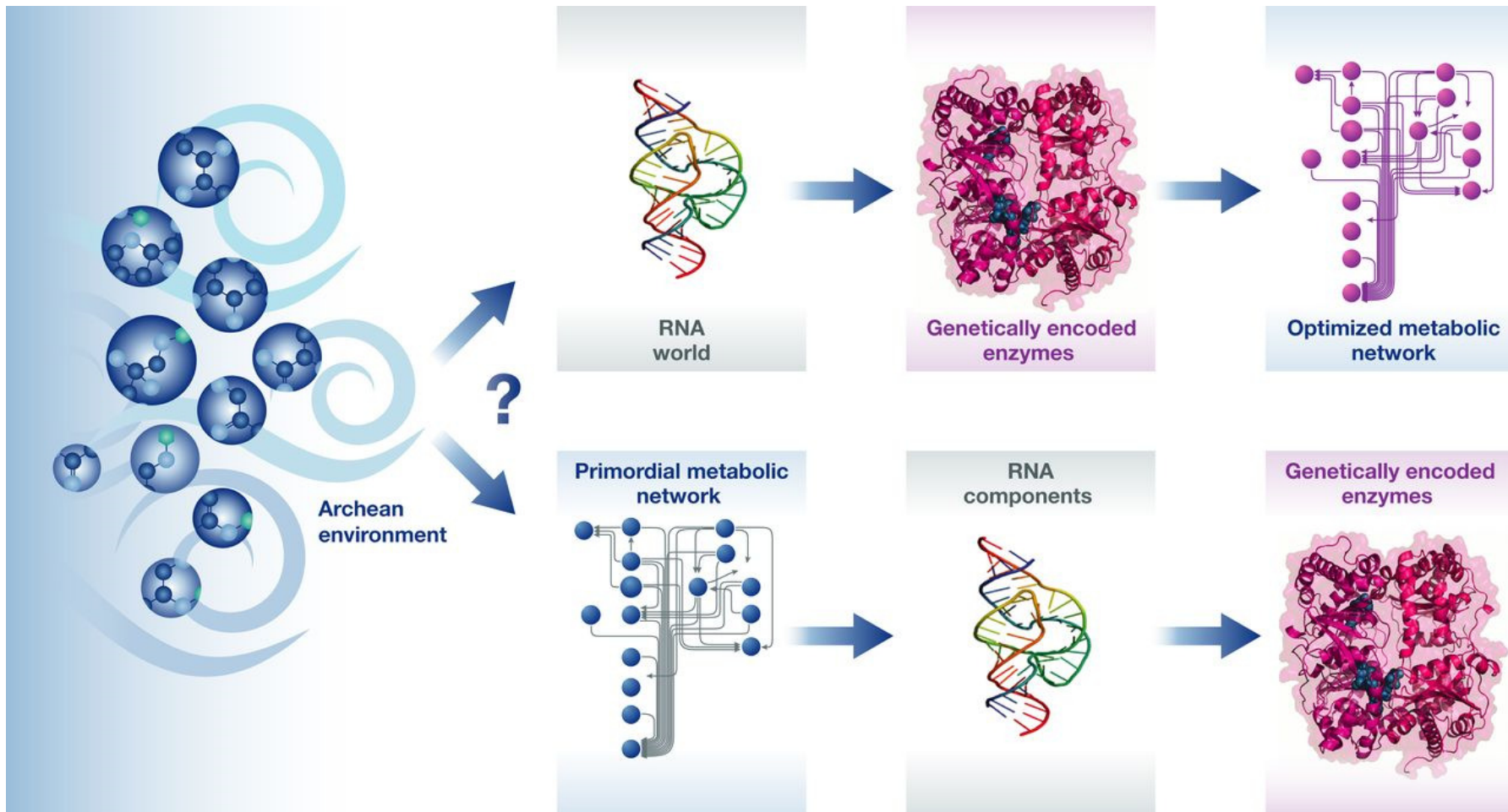
The molecular origins of life

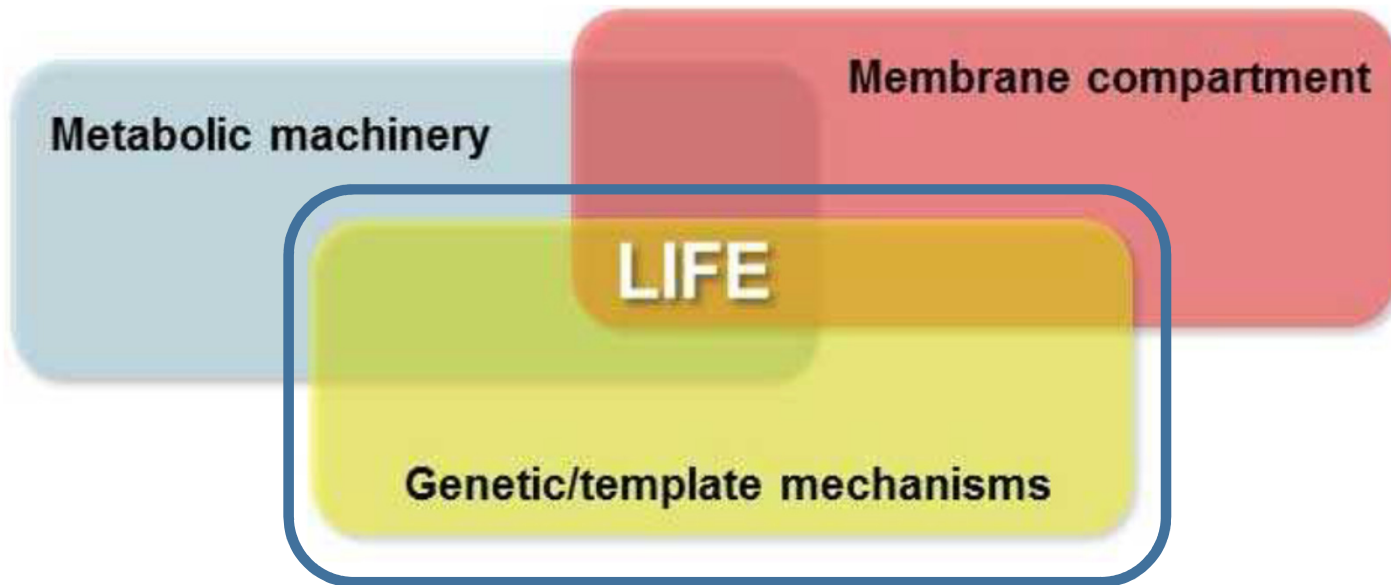


L7 SoSe 2020

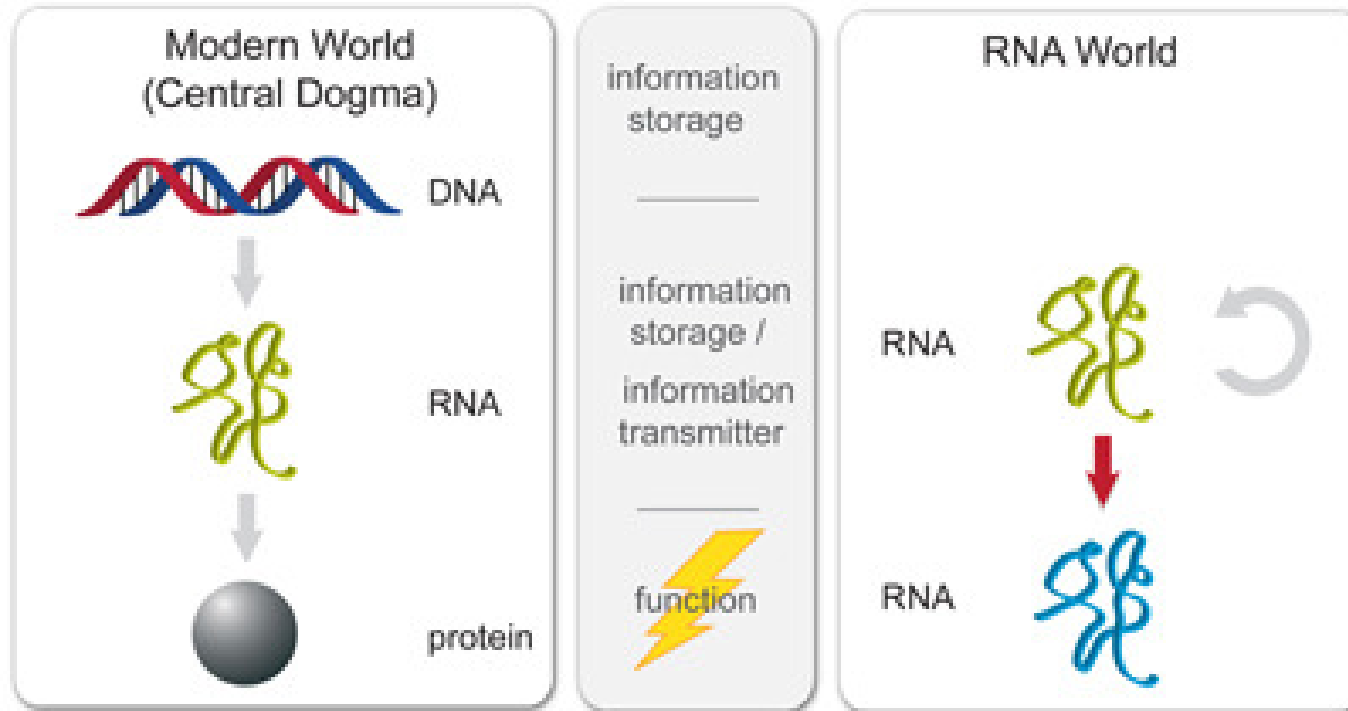
Zbigniew Pianowski

Route to life by chemical networks



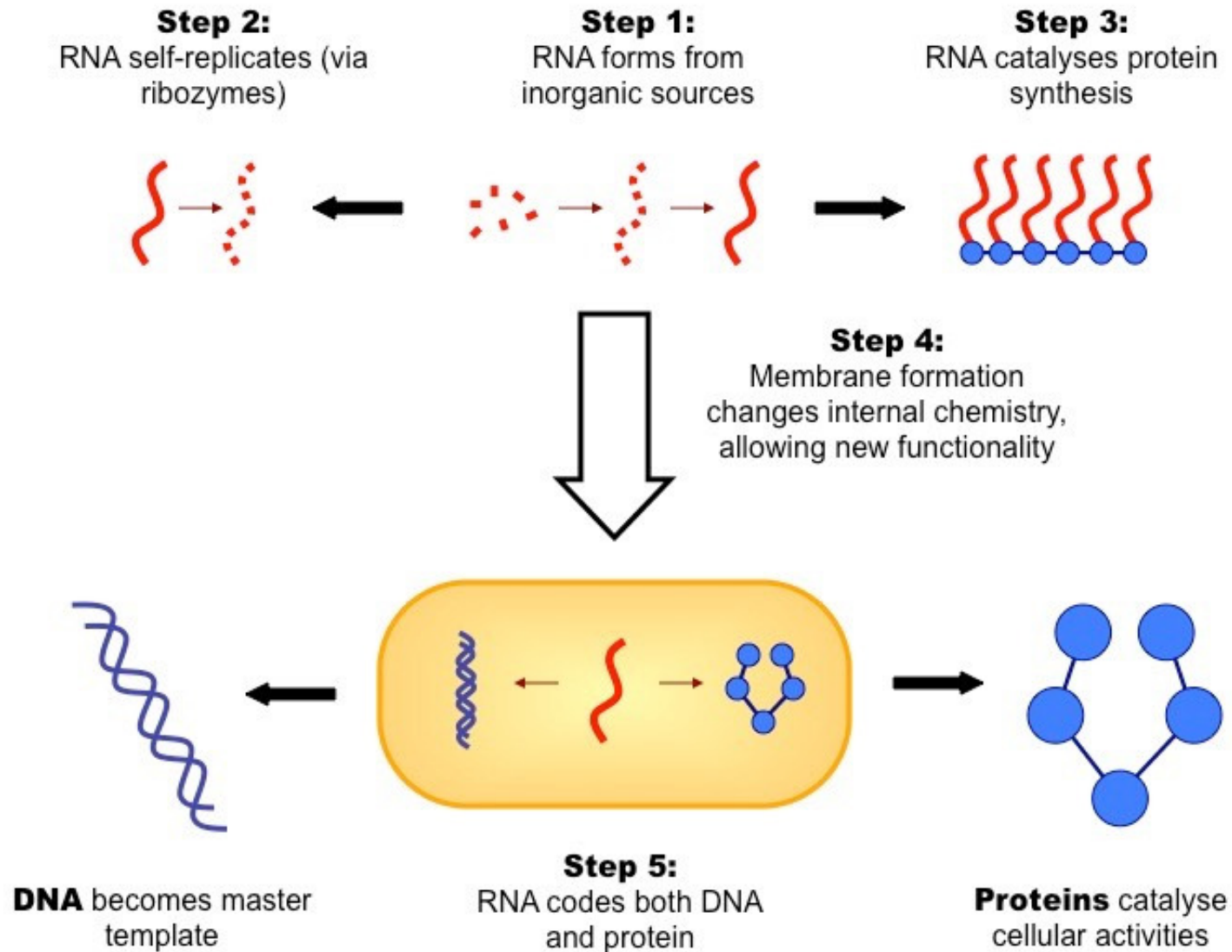


The RNA world



Conceptual idea that there was a period in the early history of life on Earth when RNA (or its structurally simplified analogue) carried out most of the information processing and metabolic transformations needed for biology to emerge from chemistry

The RNA world



The RNA world

RNA as catalyst

Currently known co-enzymes

Ribozymes, Riboswitches

Ribosome

Evolvability of RNA

Spiegelman's Monster

Aptamers

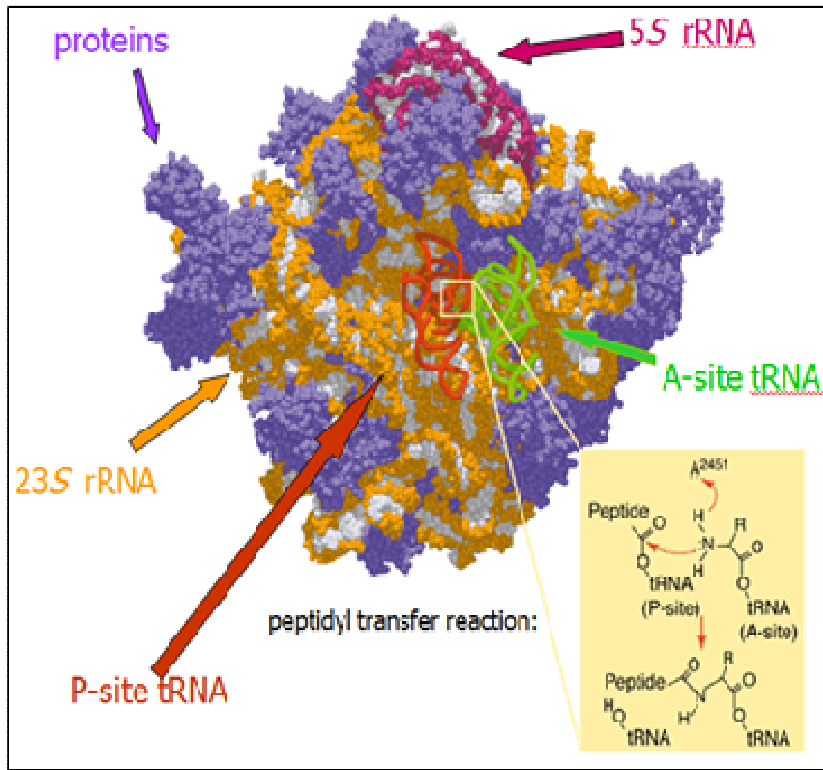
RNA (self)-replication

Replicase ribozymes – no self-replication yet, but replicate sequences longer than themselves

Replicating RNA networks

Ribosome – the ,smoking gun’

Ribosome is a ribozyme!

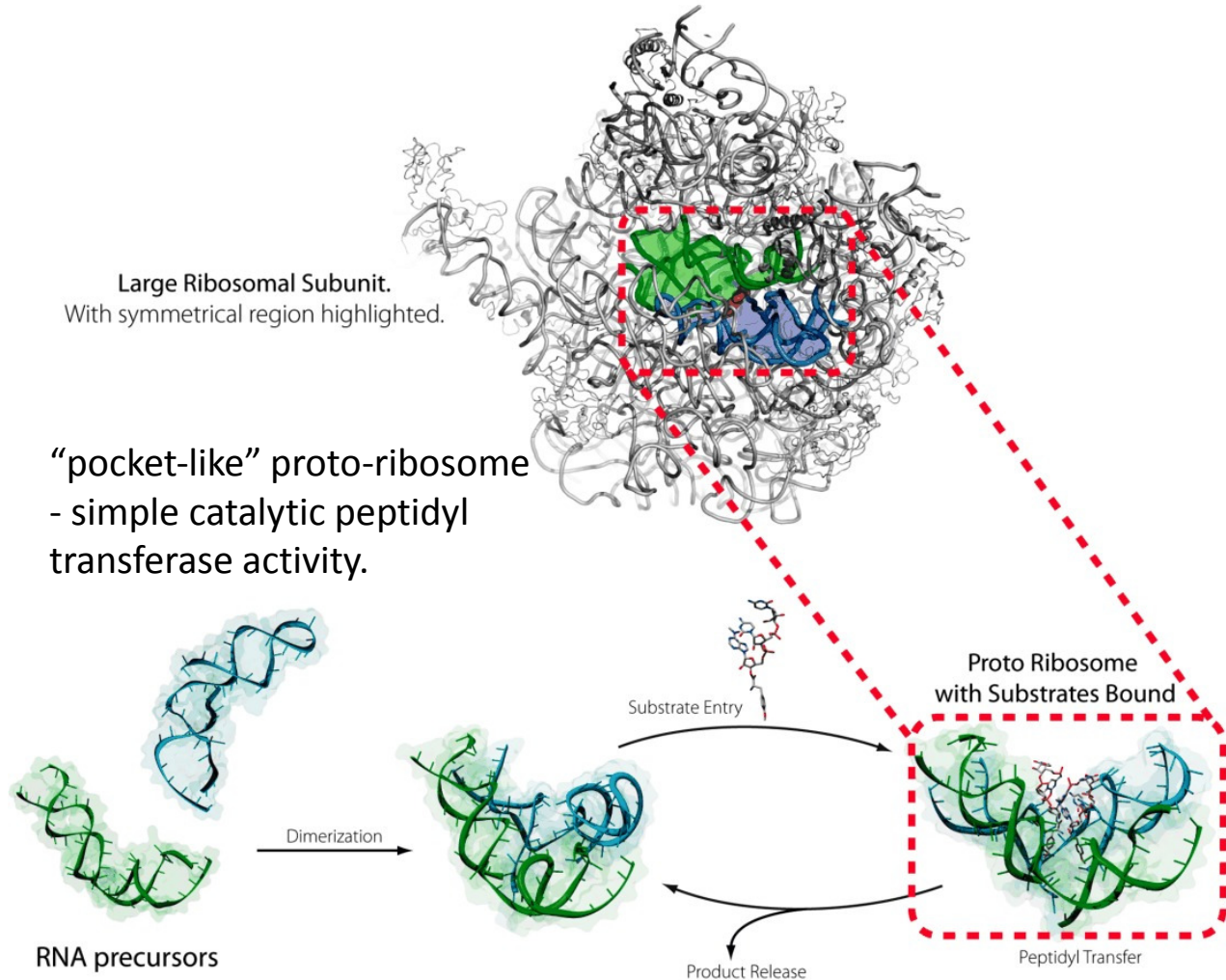


No protein is present within 18 Angstroms from the active site → **proteins** play a structural role, but **DO NOT CATALYZE THE ACYL TRANSFER PROCESS**

T. Gech *Science*. 2000, 289, 878-879

Large Ribosomal Subunit.
With symmetrical region highlighted.

“pocket-like” proto-ribosome
- simple catalytic peptidyl
transferase activity.



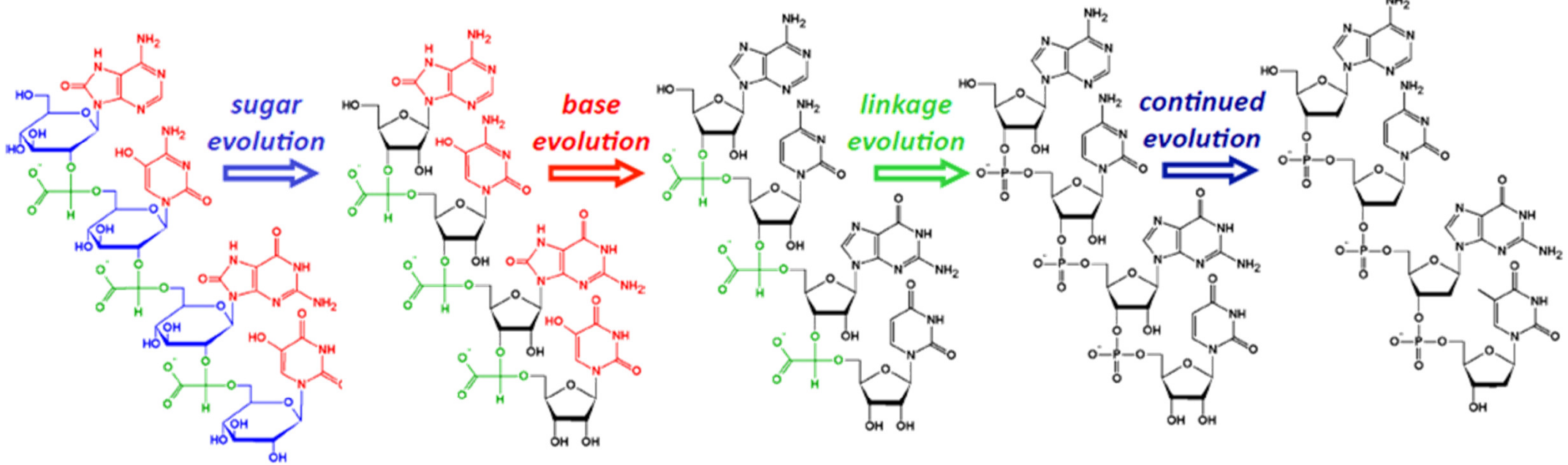
A. Yonath *et al. Israel Journal of Chemistry*, 2010, 50, 29-35

„RNA-second“

proto-RNA

RNA

DNA



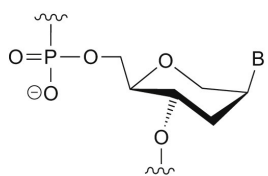
Easy to assemble



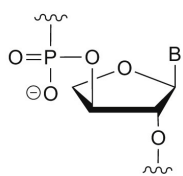
Functionally superior

Proto-RNA evolution: According to the protoRNA theory, each of the components of RNA — sugar, base and phosphate backbone — may have originally taken different forms.

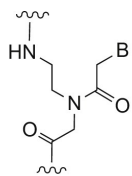
XNA – Xeno Nucleic Acids



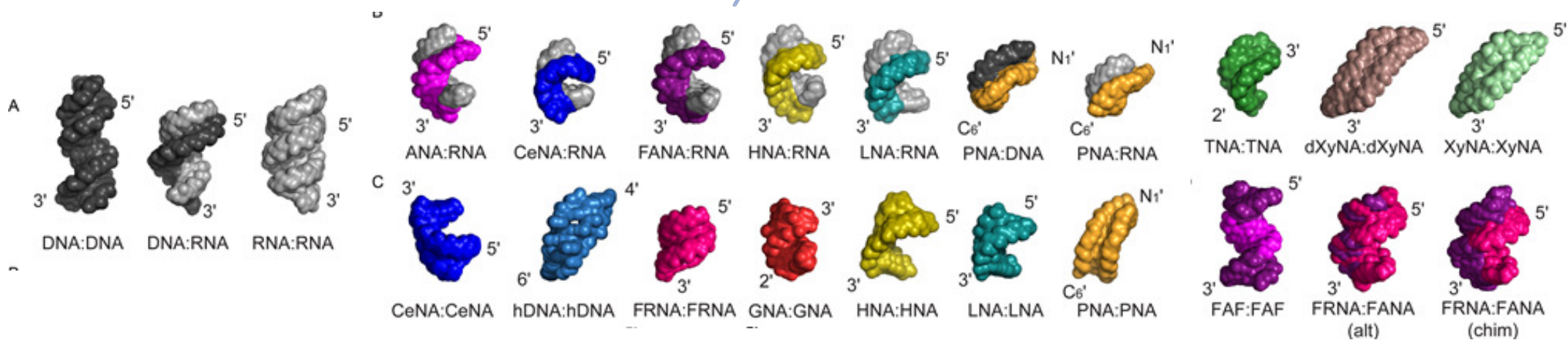
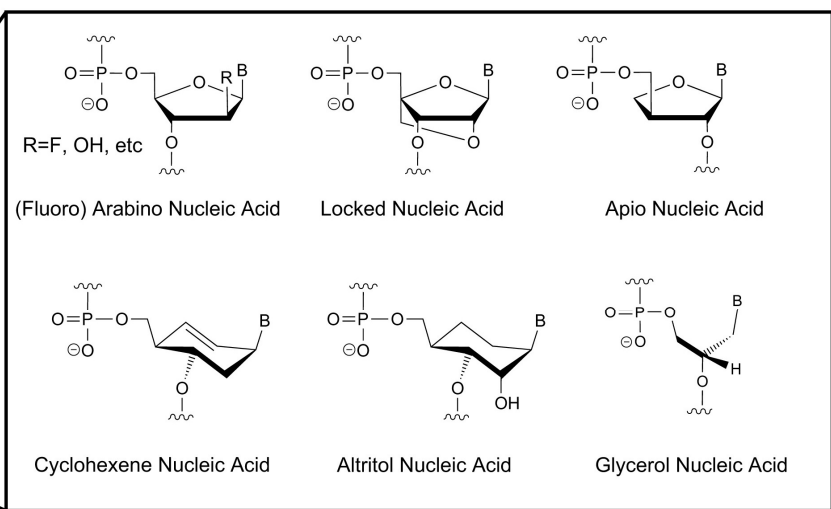
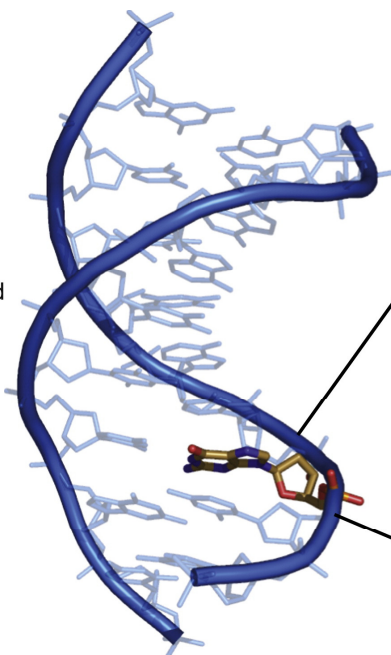
Hexitol Nucleic Acid (HNA)

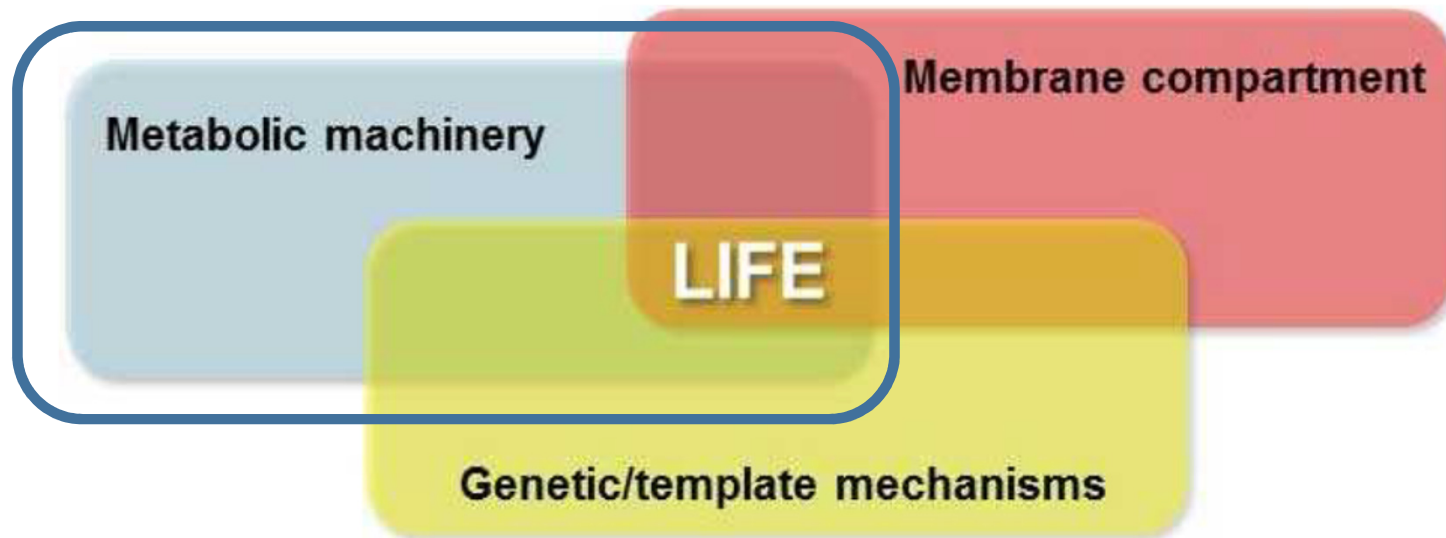


Threose Nucleic Acid (TNA)

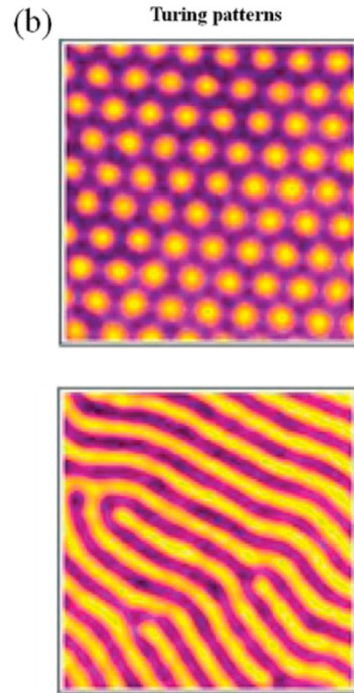
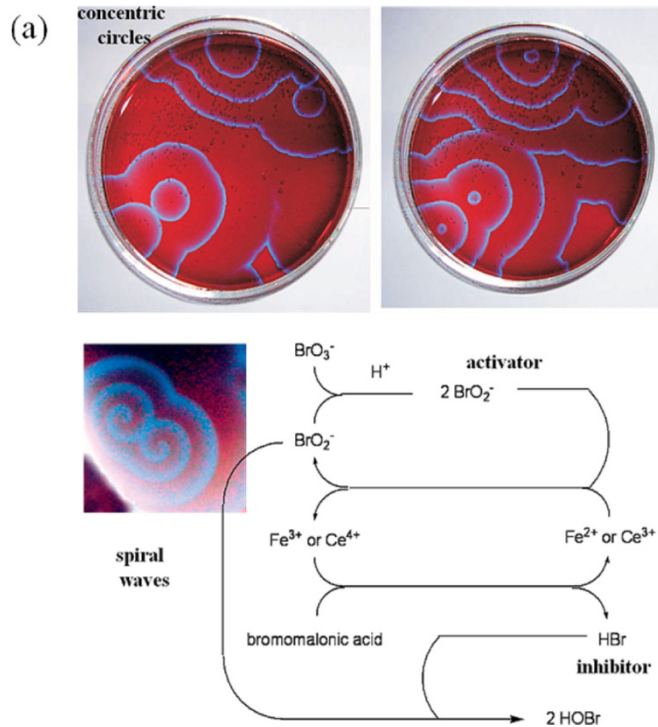


Peptide Nucleic Acid (PNA)





BZ and CIMA reactions – chemical models for metabolism



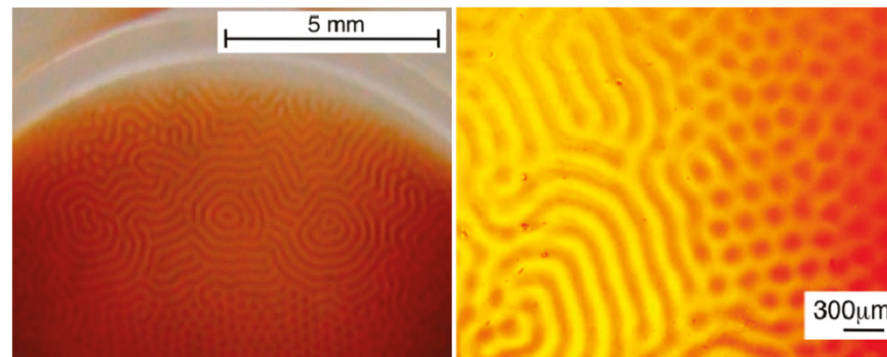
Turing patterns also observed in metabolic reactions (glycolysis)
 PLoS ONE 2007, 2(10):e1053



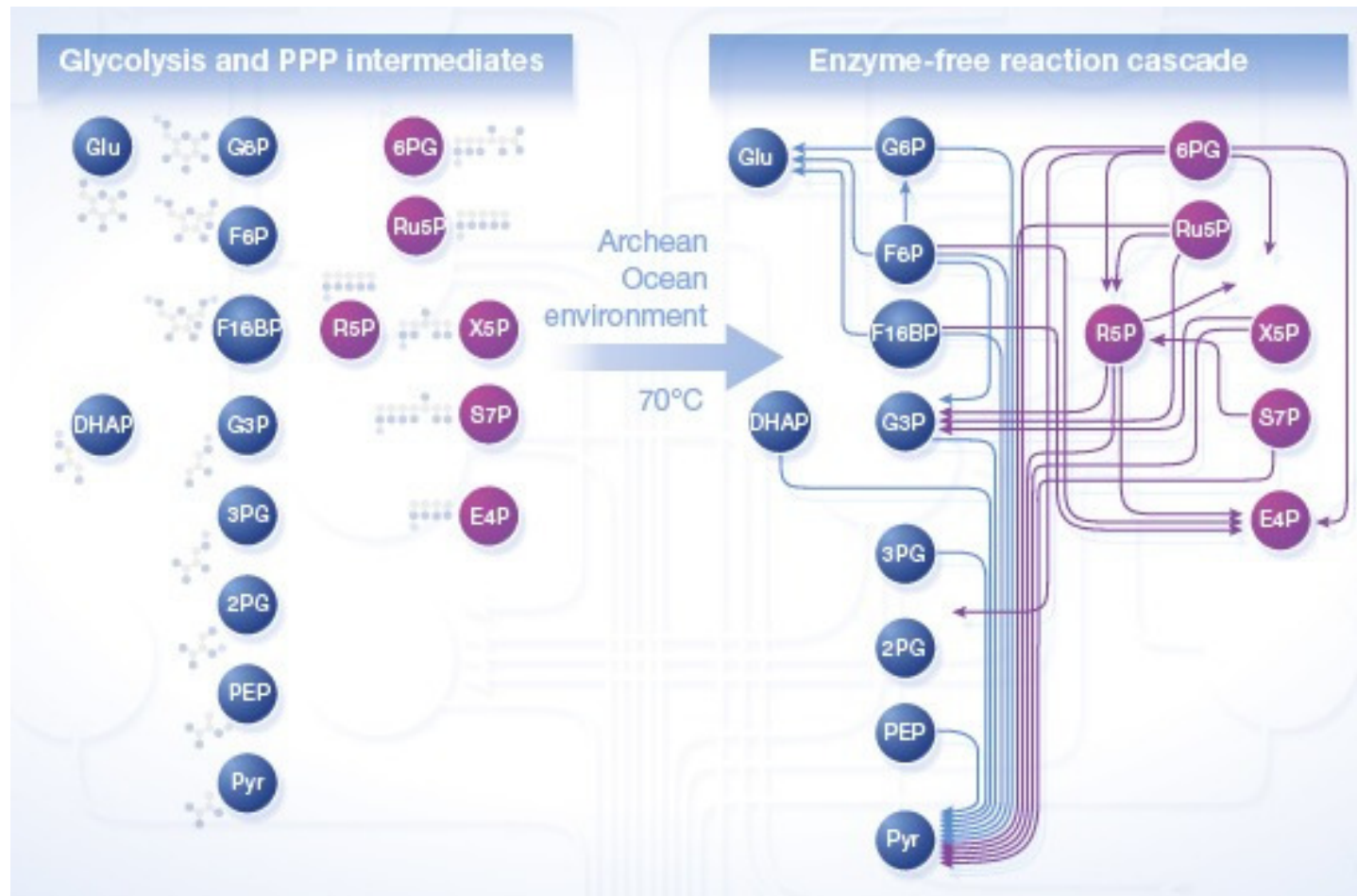
„Rosette” spots of a jaguar can be reproduced by two coupled activator/inhibitor processes

Turing patterns – BZ and CIMA, but also formation of zebra stripes or arrangement of leaves in plants

J. Phys. Chem. B 115(14):3959-63

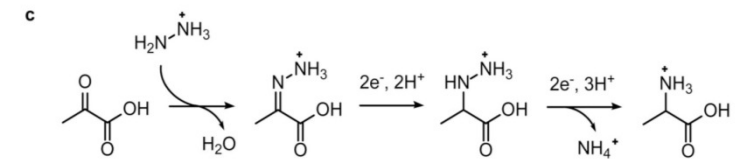
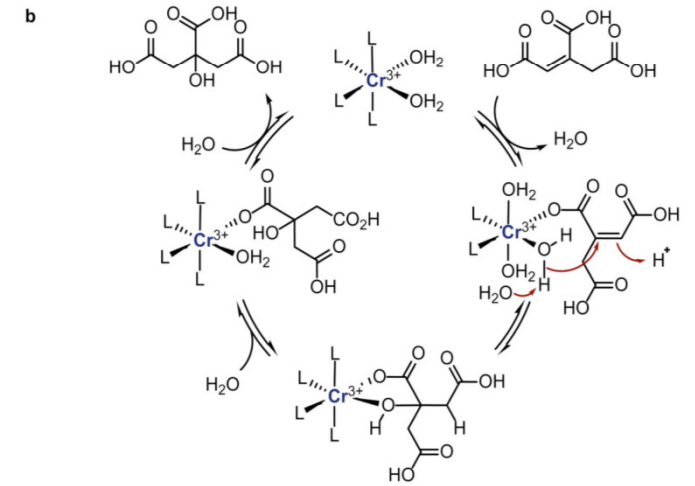
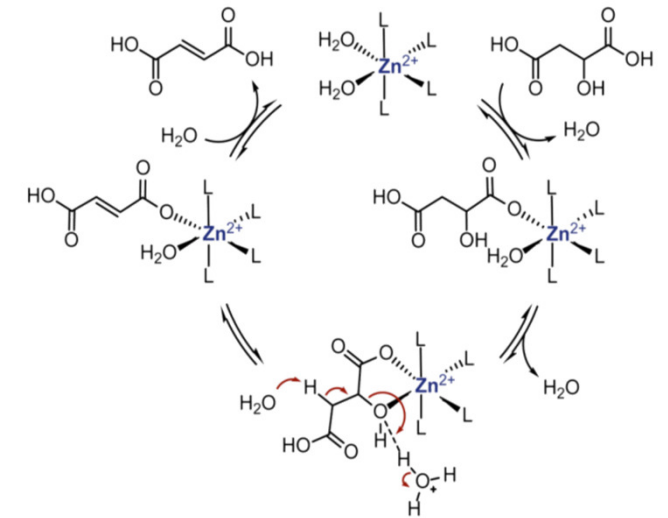
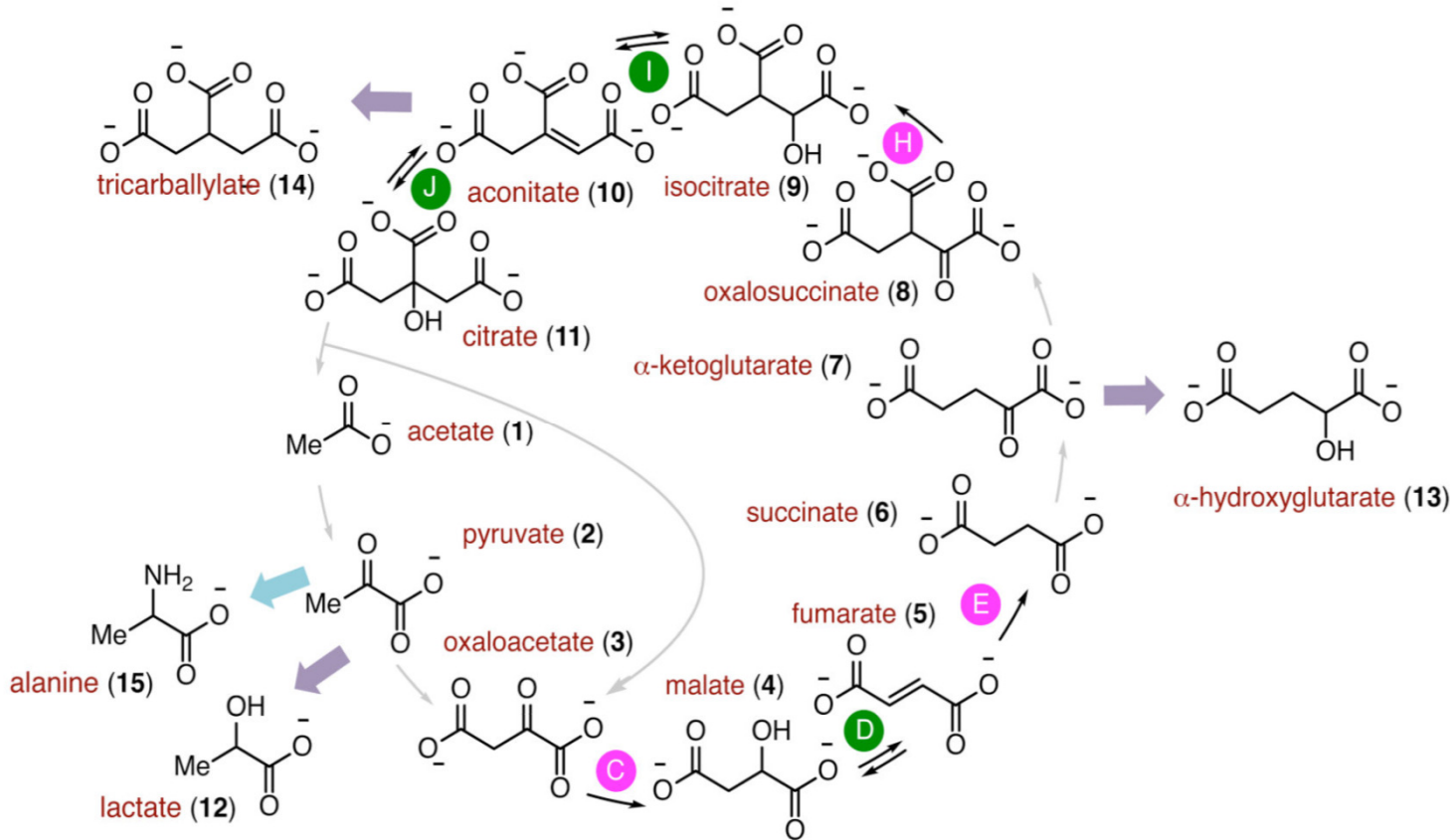


Nonenzymatic sugar phosphate interconversion in a plausible Archean ocean environment



M. Keller *et al.* *Molecular Systems Biology* **2014**, *10*, 725-737

Metals promote sequences of the reverse Krebs cycle

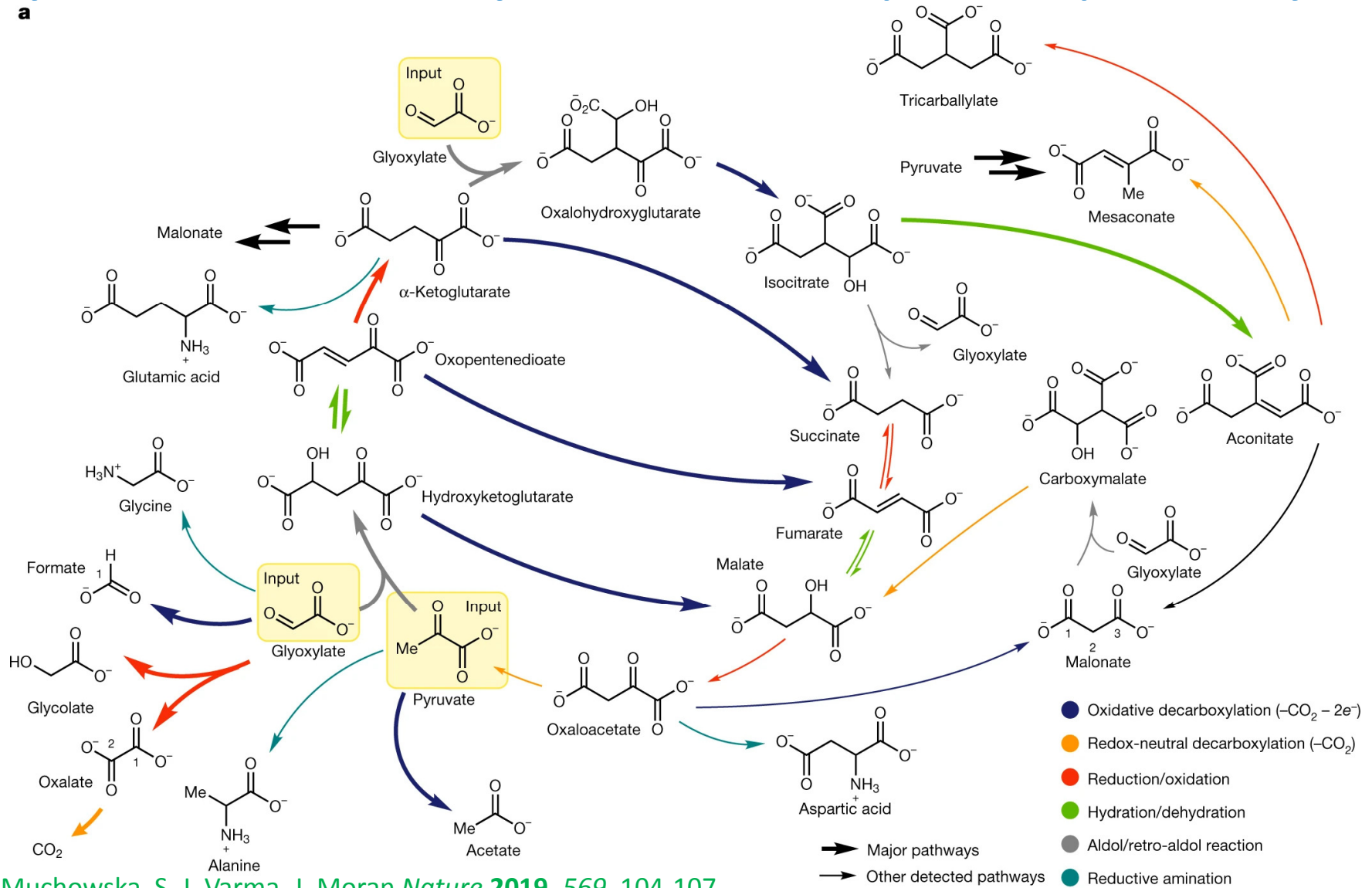


Prebiotic reaction network showing the rTCA cycle, reductive amination (light blue arrow) and potential off-cycle reductions (mauve arrows).

J. Moran et al. *Nat Ecol Evol.* **2017**, 1(11), 1716–1721

Synthesis and breakdown of universal metabolic precursors promoted by iron

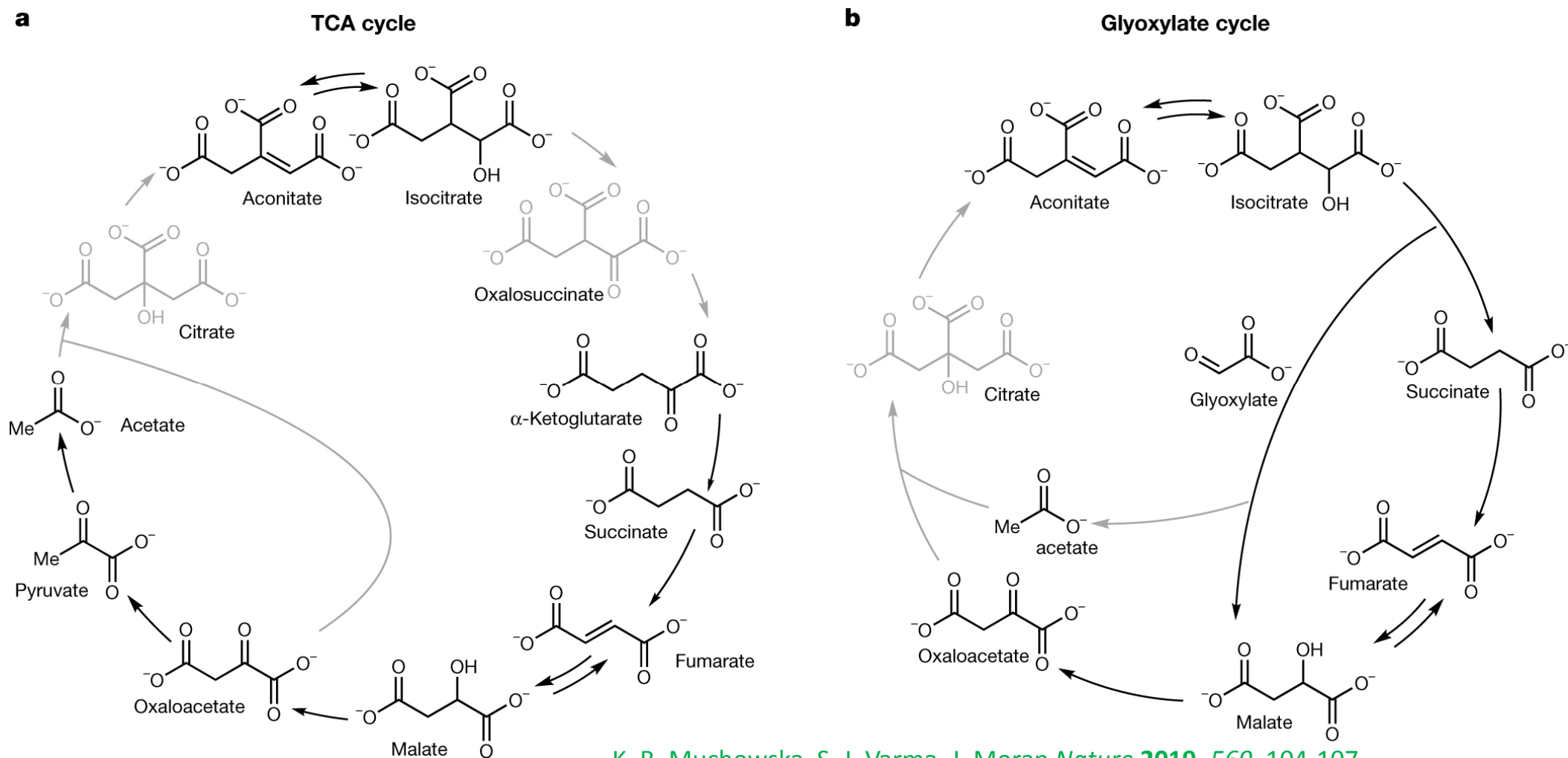
a



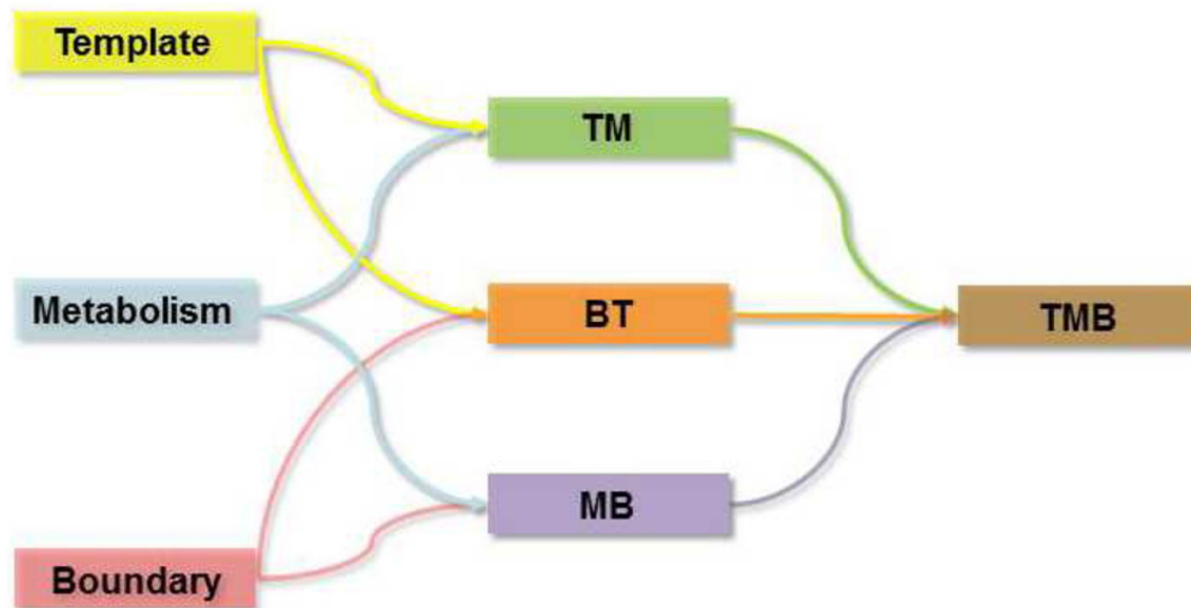
K. B. Muchowska, S. J. Varma, J. Moran *Nature* 2019, 569, 104-107

Synthesis and breakdown of universal metabolic precursors promoted by iron

Comparison of the observed reaction network with the TCA and glyoxylate cycles. Intermediates and reactions found in both the biological cycle and the synthetic reaction network shown in black. Those found only in the biological cycle - in grey.



K. B. Muchowska, S. J. Varma, J. Moran *Nature* 2019, 569, 104-107



Origin of the Universe – stars, planets, elements

Origin of biorelevant monomers – primordial soup

Complex chemical processes on the way to living systems

Protocells and LUCA

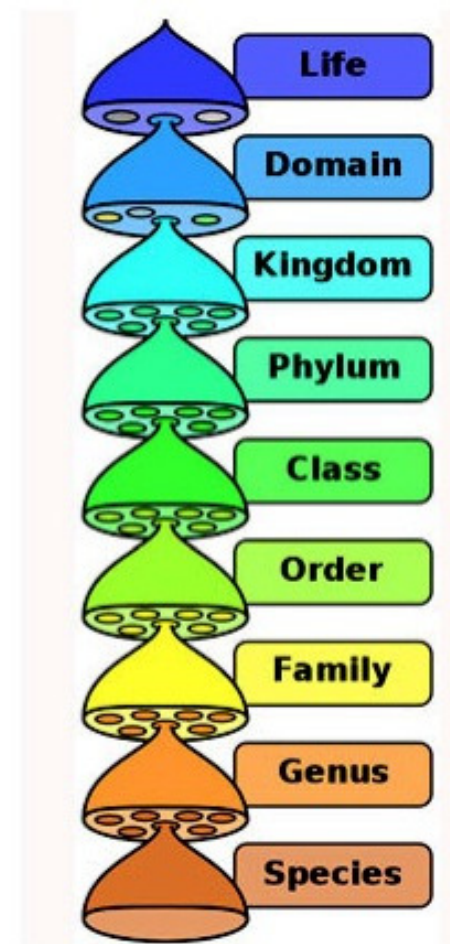
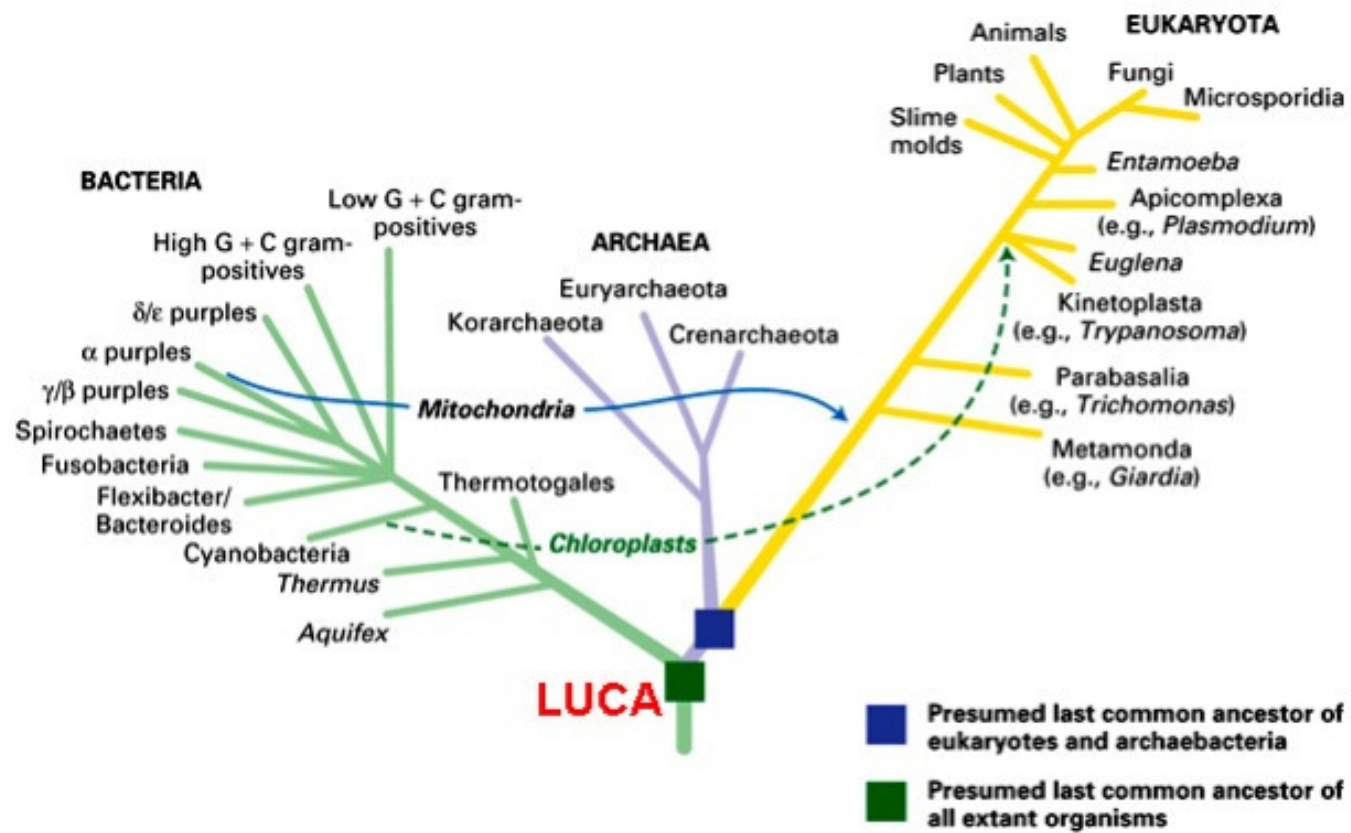
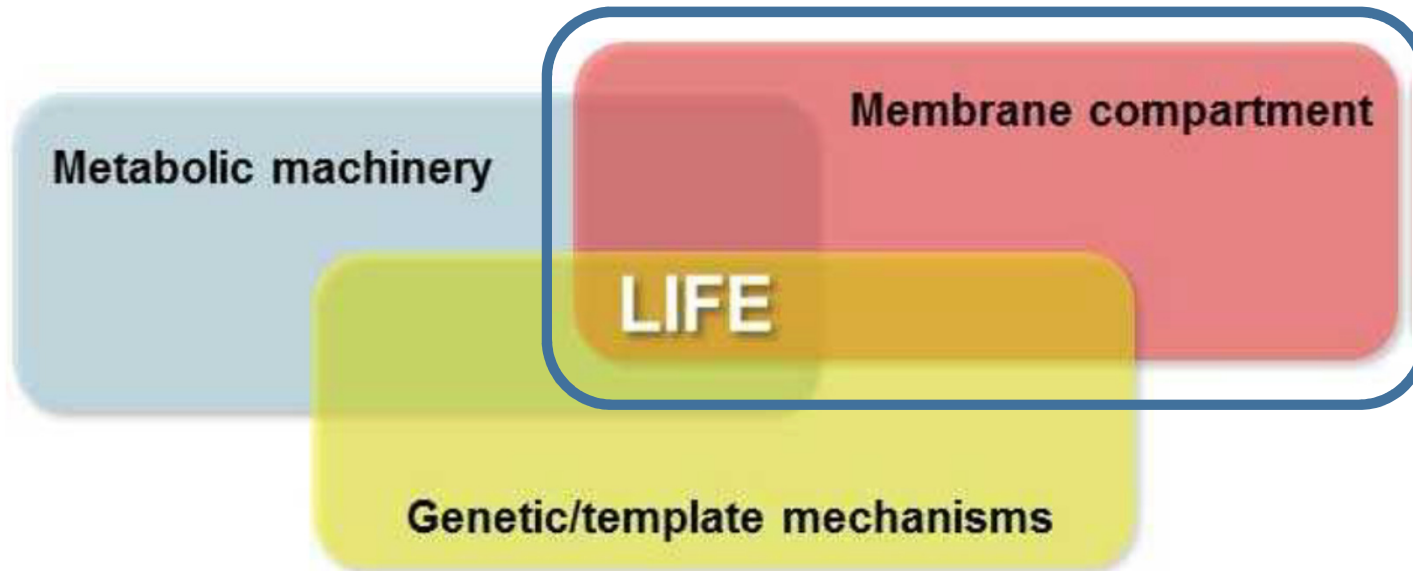
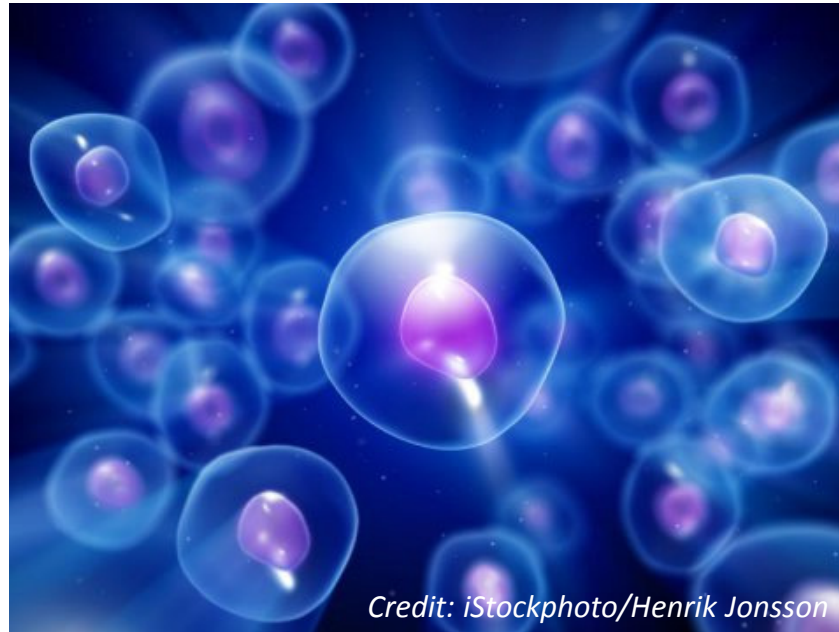


Figure 1.1a
Molecular Cell Biology, Seventh Edition
 © 2013 W.H. Freeman and Company



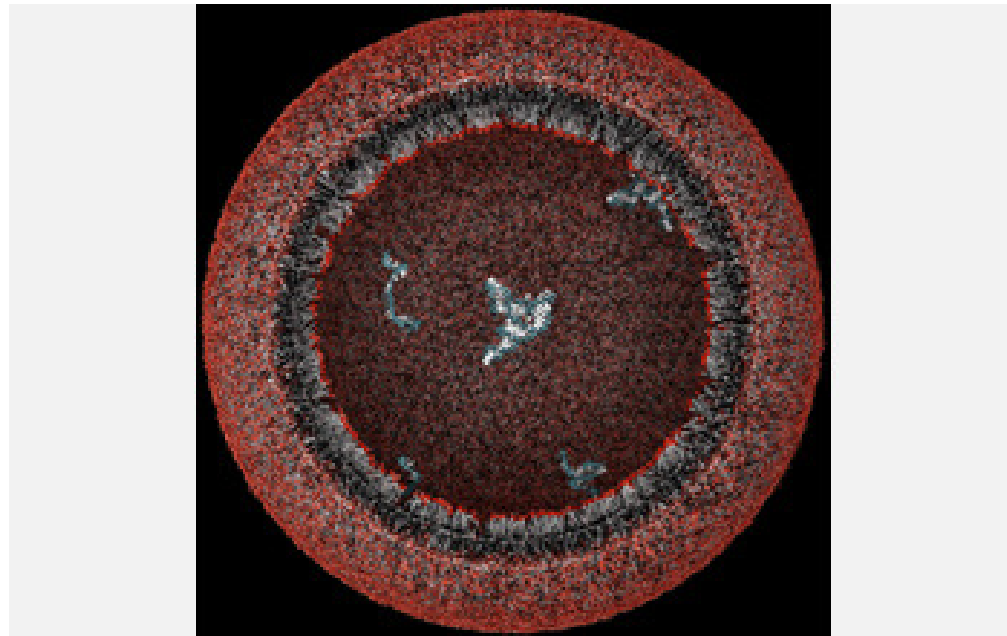
Encapsulation – essential for life



Credit: iStockphoto/Henrik Jonsson

Membrane compartments

Assembly of amphiphilic monomers into protocellular compartments

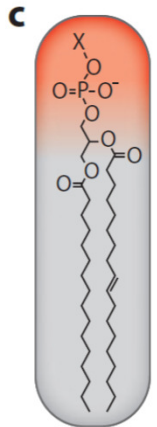
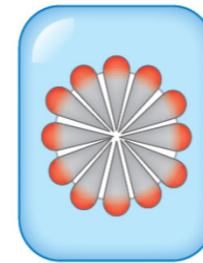
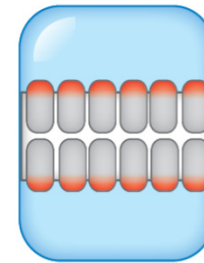
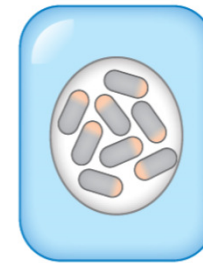
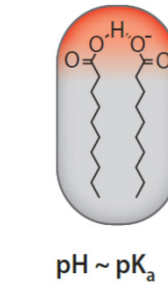
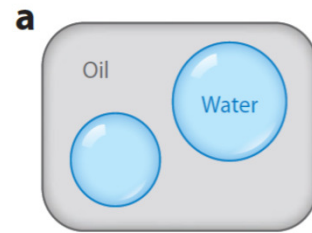
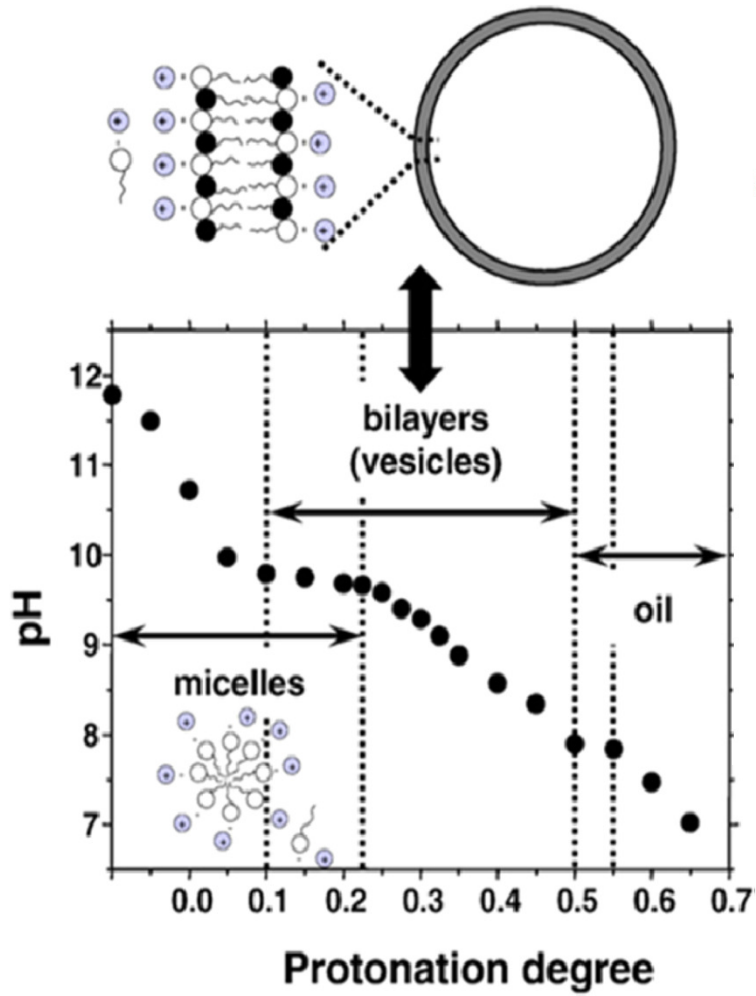


Credit: *Janet Iwasa*

A three-dimensional view of a model protocell (a primitive cell) approximately 100 nanometers in diameter.

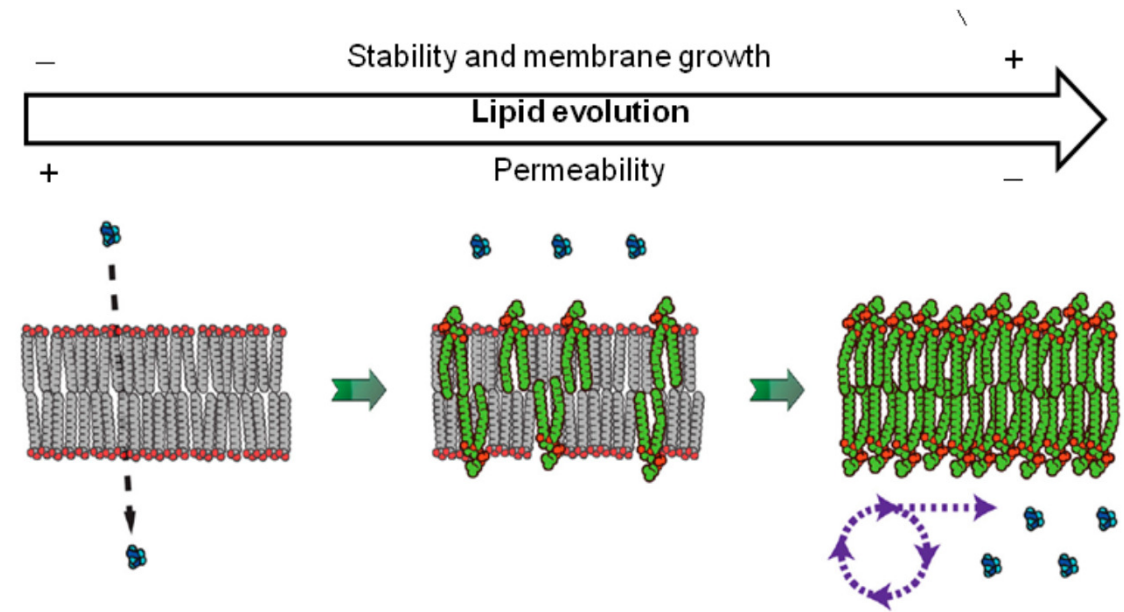
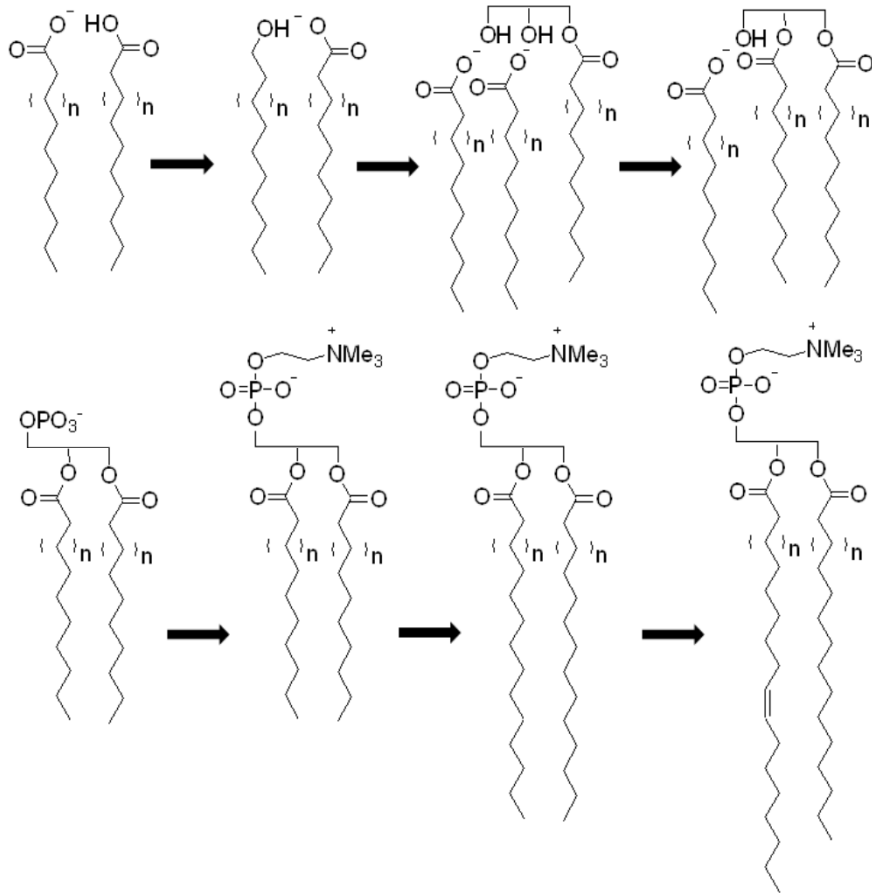
The protocell's fatty acid membrane allows nutrients and DNA building blocks to enter the cell and participate in non-enzymatic copying of the cell's DNA. The newly formed strands of DNA remain in the protocell

pH-dependent phase behavior of fatty acids in water



80 mM oleic acid/sodium oleate in water

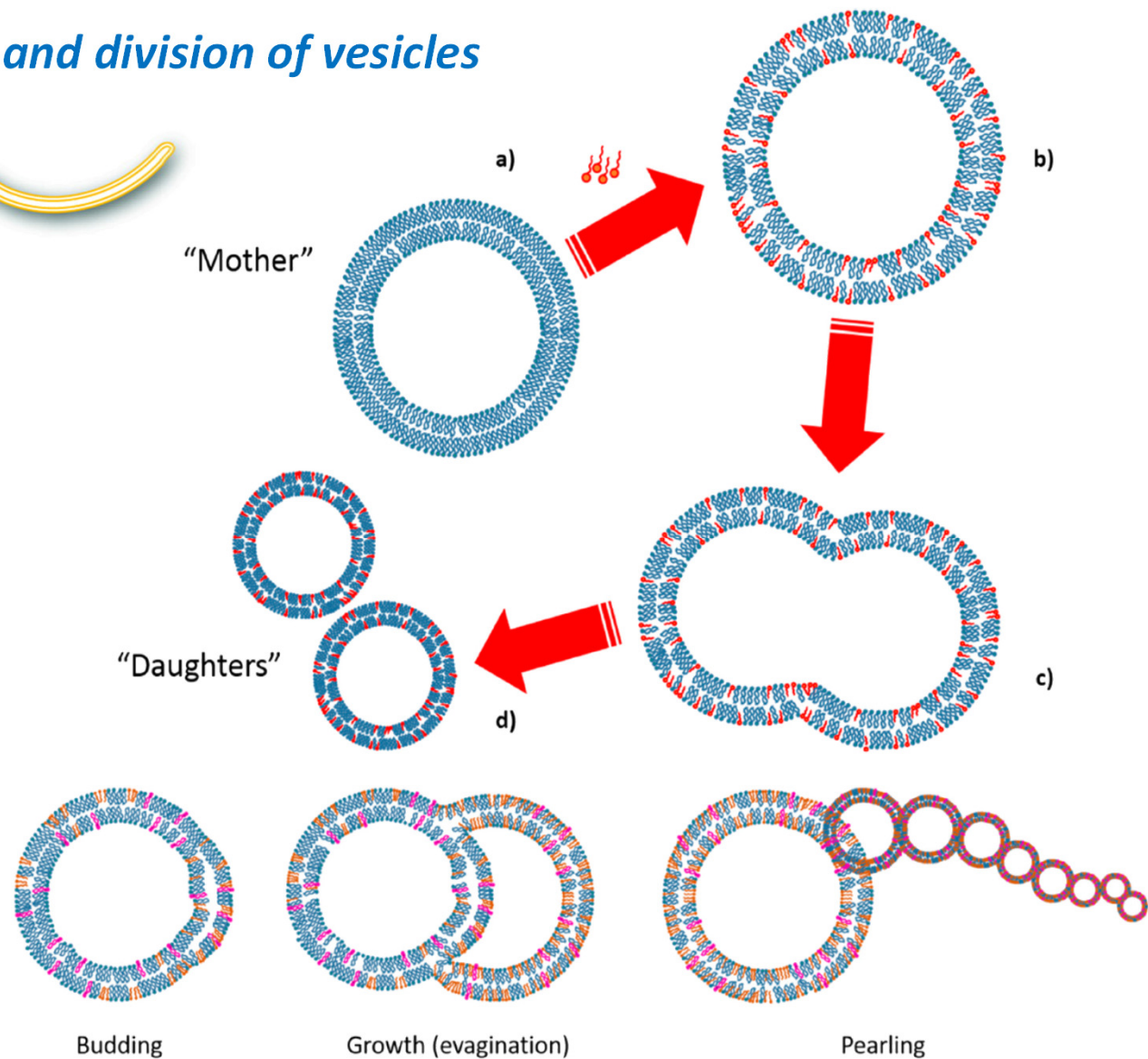
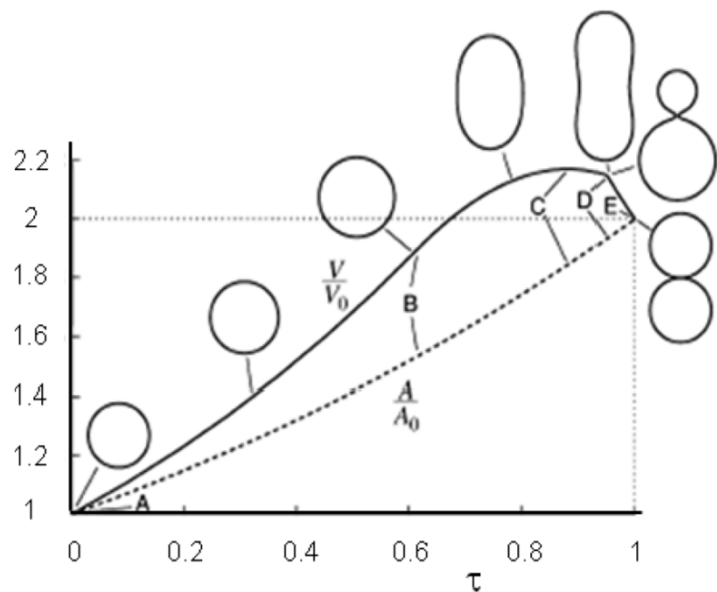
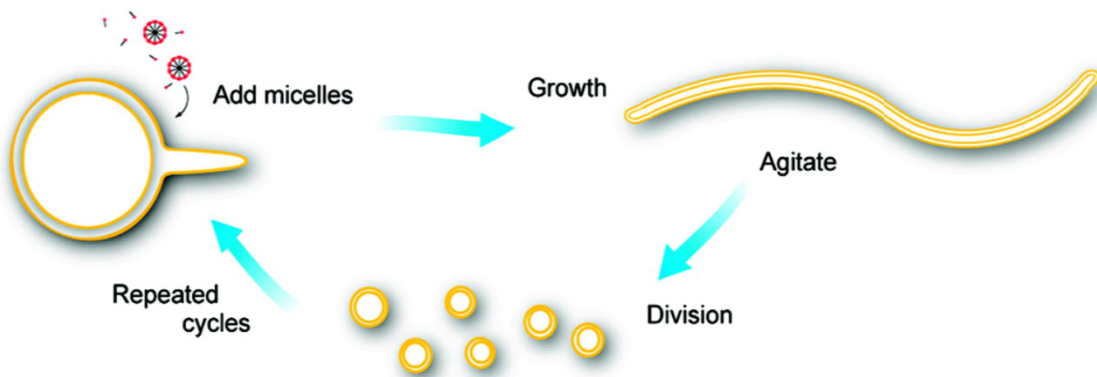
Scheme of the membrane evolution



More complex components lead to slower amphiphile desorption and thus faster growth of the protocell. Decreasing permeability is a selective pressure for the emergence of internalized metabolic and transport machinery in the system

Chemical evolution of membrane components

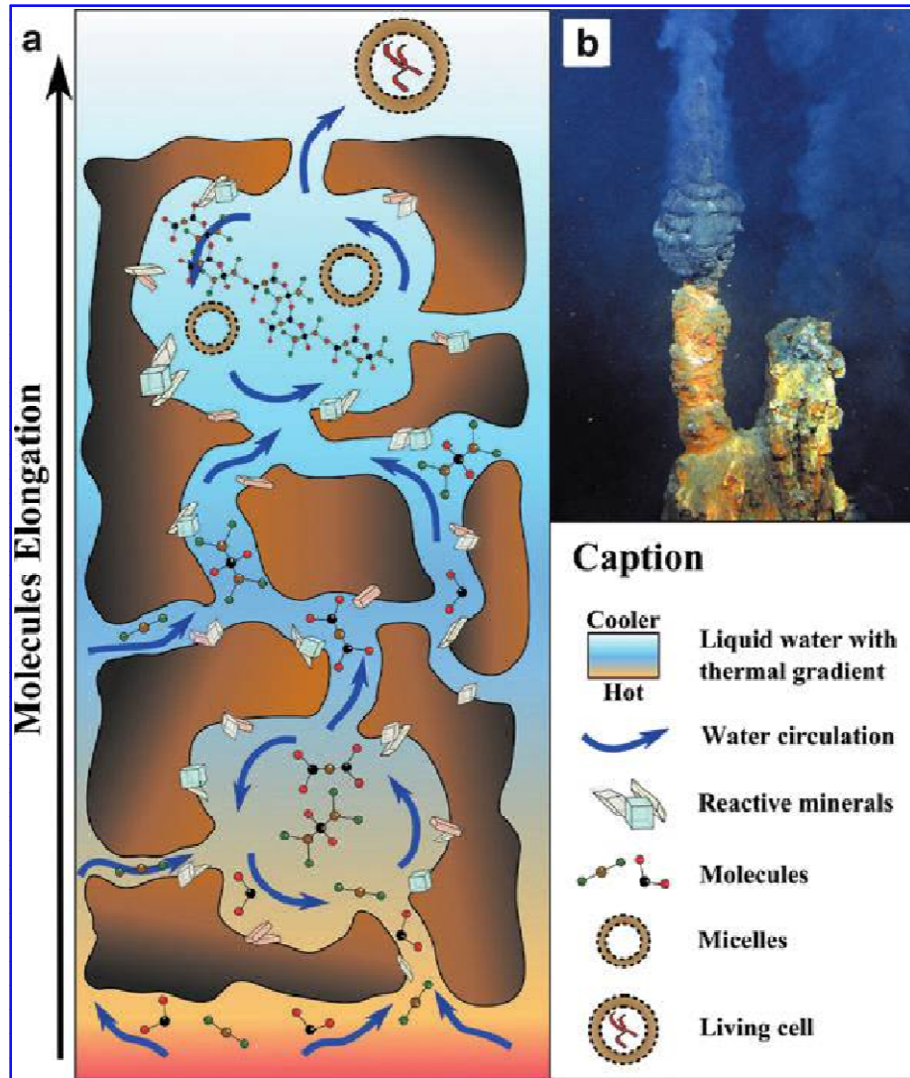
Growth and division of vesicles



Ting F. Zhu, and Jack W. Szostak
J. Am. Chem. Soc., **2009**, 131 (15), 5705-5713

A. Lopez, M. Fiore *Life* **2019**, 9(49), doi:10.3390/life9020049

Deep sea vent origin of life



Possible origin of life in porous hydrothermal vents.

(a) Sketch showing a porous beehive structure where hydrothermal fluids and seawater can circulate, leading to the accumulation of organic molecules. The reduced mineral surfaces within the vent pores could be favorable locations for the structural organization of macromolecules. We hypothesize the formation of lipid micelles in these environments and the incorporation of information-transferring molecules within the micelles, perhaps due to moderate agitation of the hydrothermal effluent.

(b) Image of a modern black smoker

(image credit: National Oceanographic and Atmospheric Administration). Color images available online at www.liebertonline.com/ast

F. Westall et al., *Astrobiology* **2013**, *13*(9), 887-897

Transition from the RNA world to LUCA

Ribozymes – self-acting → metabolic

Evolution of ribosome

Incorporation of aminoacids and peptides

The genetic code and archival storage

Enzyme-driven metabolism and membranes

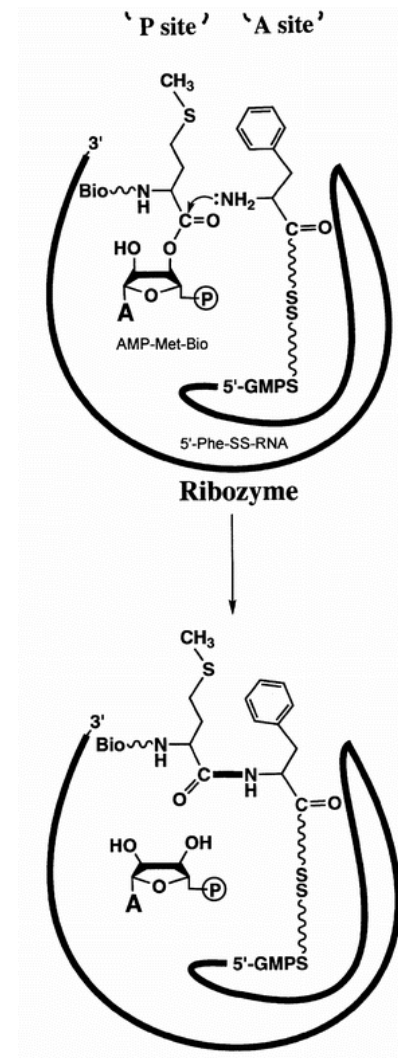
Ribozymes

Initially only self-processing ribozymes (introns, RNAses) discovered.

1992 – first ribozyme isolated capable to cleave the bond of methionine with its tRNA (also the reverse reaction – transacylation – is catalysed)

1995 (Yarus) – a random RNA sequence found capable of attaching an activated aminoacid to itself

1997 (Szostak) – an RNA sequence that transfers one aminoacid to another one, forming a dipeptide → analogue of the peptidetransferase center of the ribosome



Ribozymes

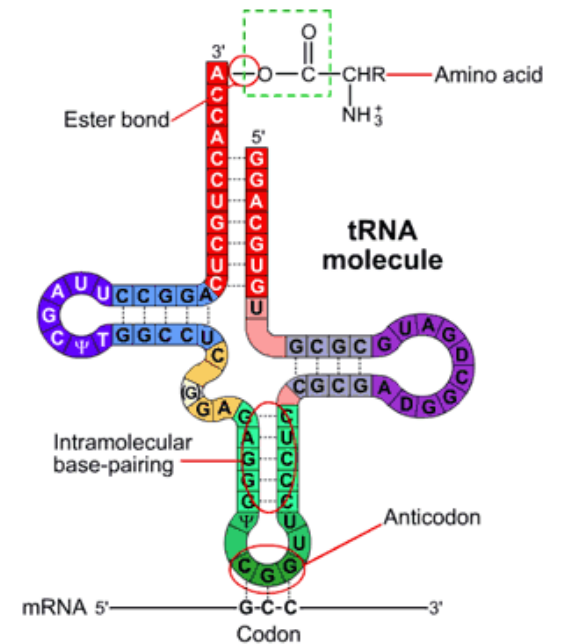
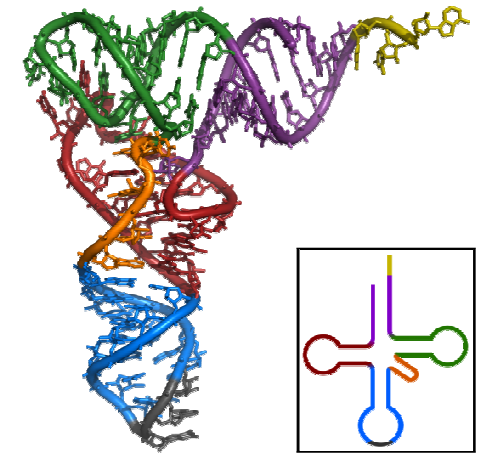
Ribozymes incorporate amino acids to enhance their catalytic abilities

It opens ways to improved metabolism and provides evolutionary advantage in receiving energy from outside

Initially incorporation of amino acids may have improved synthesis of nucleotides to produce more RNA

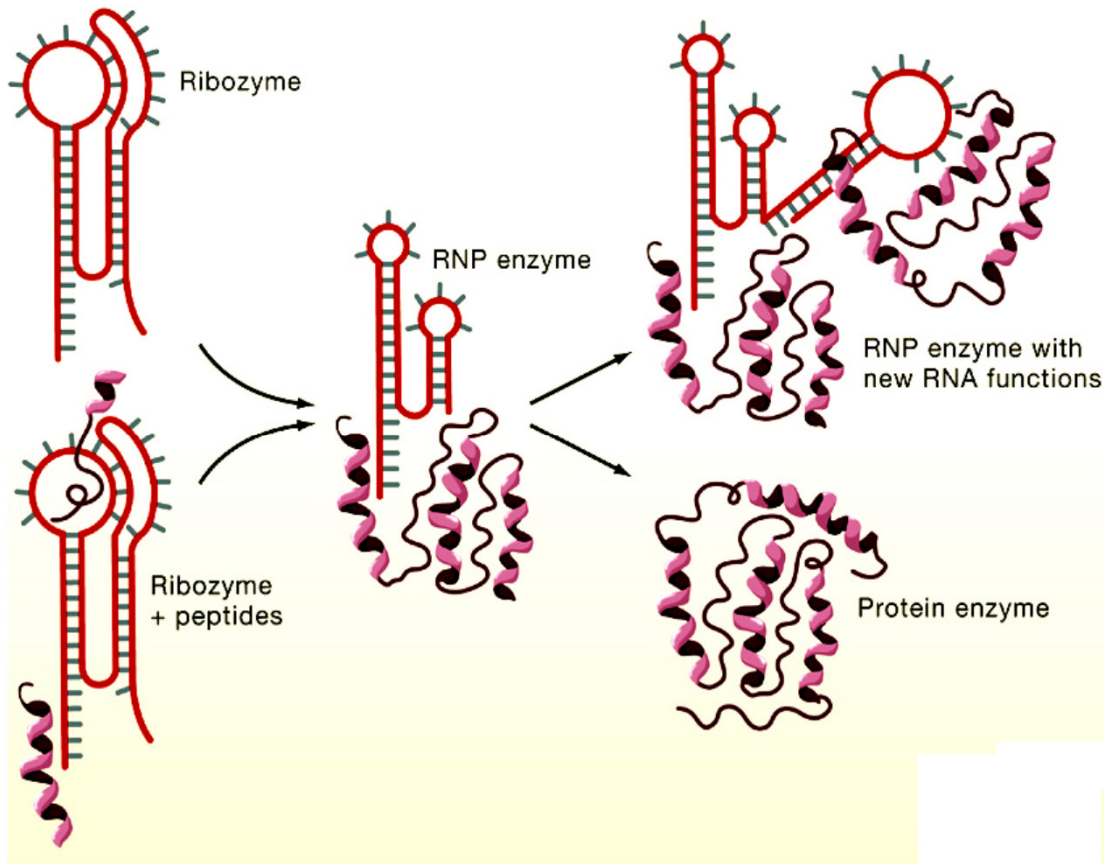
Primordial tRNAs were most likely self-charging, today special enzymes do it (tRNA synthetases)

Peptide chains increase in size, the RNA part decrease → non-covalent binding of nucleoside cofactors to contemporary enzymes



aminoacyl-tRNA

Evolution of biocatalysis



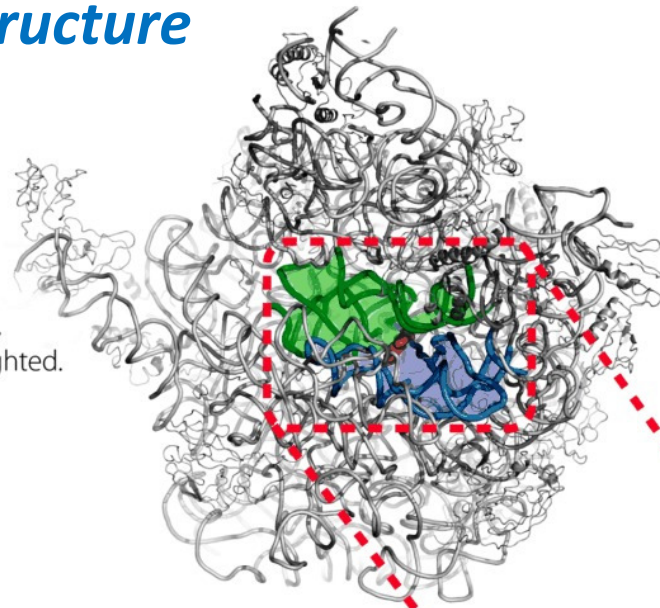
Primordial **RNA-only ribozymes** as well as **complexes of ribozymes and random peptides** could have acted as catalysts during the first steps of the RNA world.

In a more advanced stage, upon the advent of peptidyltransferase ribozymes, the availability of RNA-coded proteins allowed the assembly of **ribonucleoprotein (RNP) complexes**.

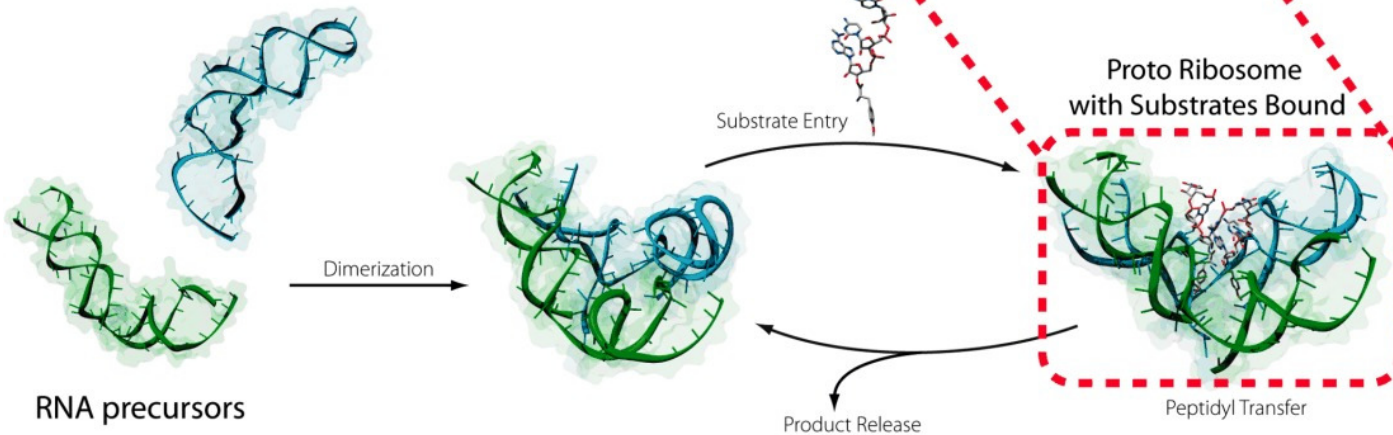
Some of the RNPs could have shown novel or improved catalytic activities, ultimately including the translation of mRNA on protoribosomes. Later, some **RNP enzymes** (upper right) evolved by adding or discarding some RNA subunits and fine-tuning their catalytic activity. In parallel, most RNP complexes (lower right) evolved to **protein-only enzymes**.

Ribosome structure

Large Ribosomal Subunit.
With symmetrical region highlighted.



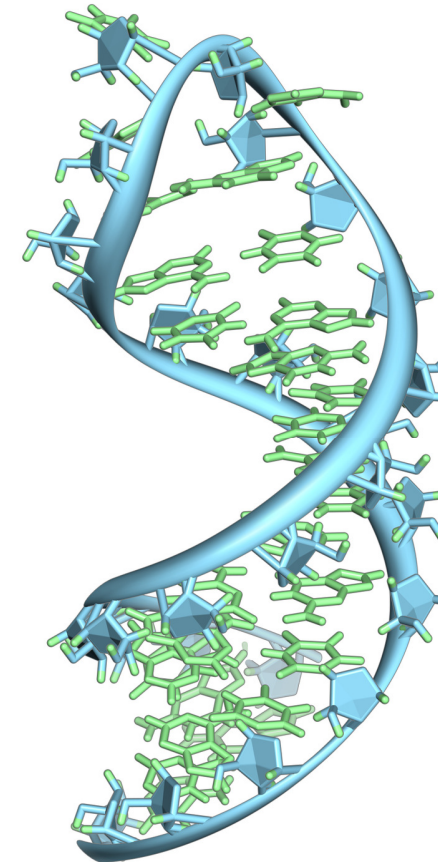
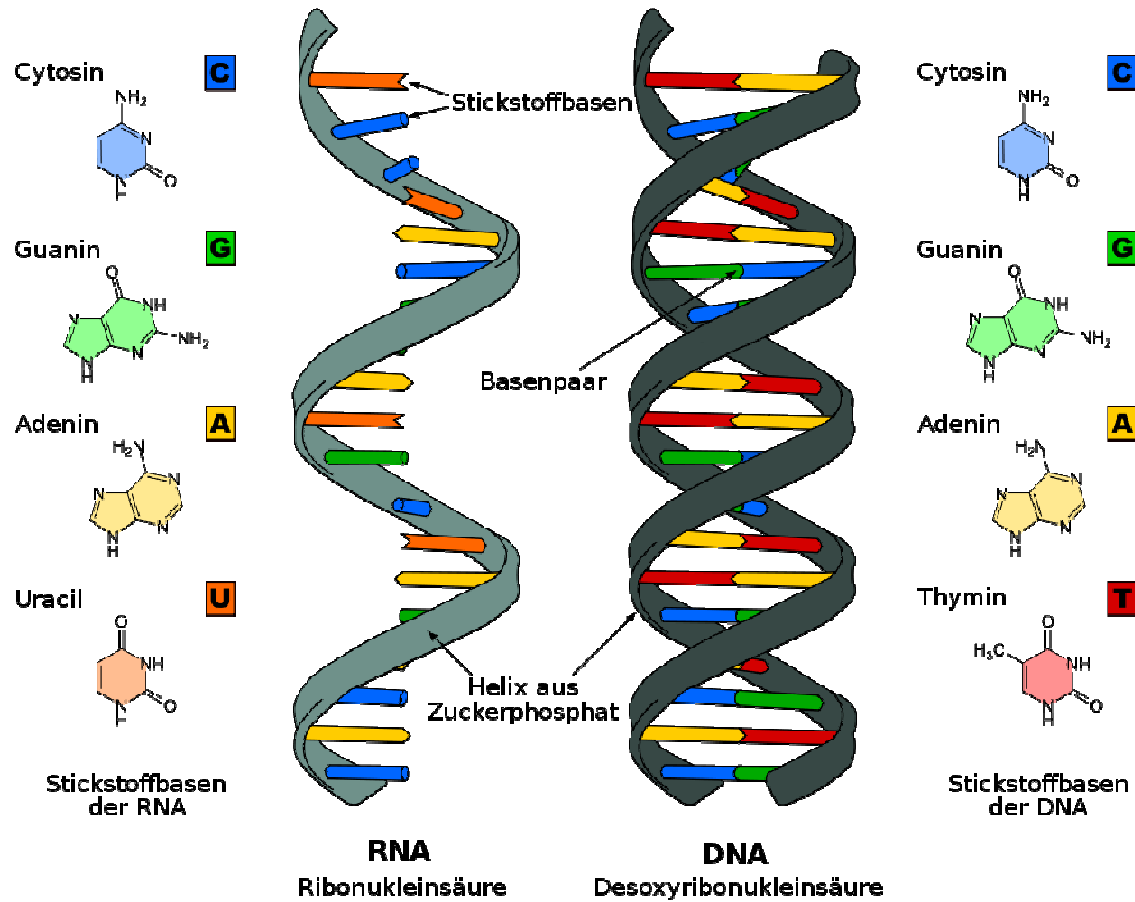
The symmetrical region within
the large ribosomal subunit.



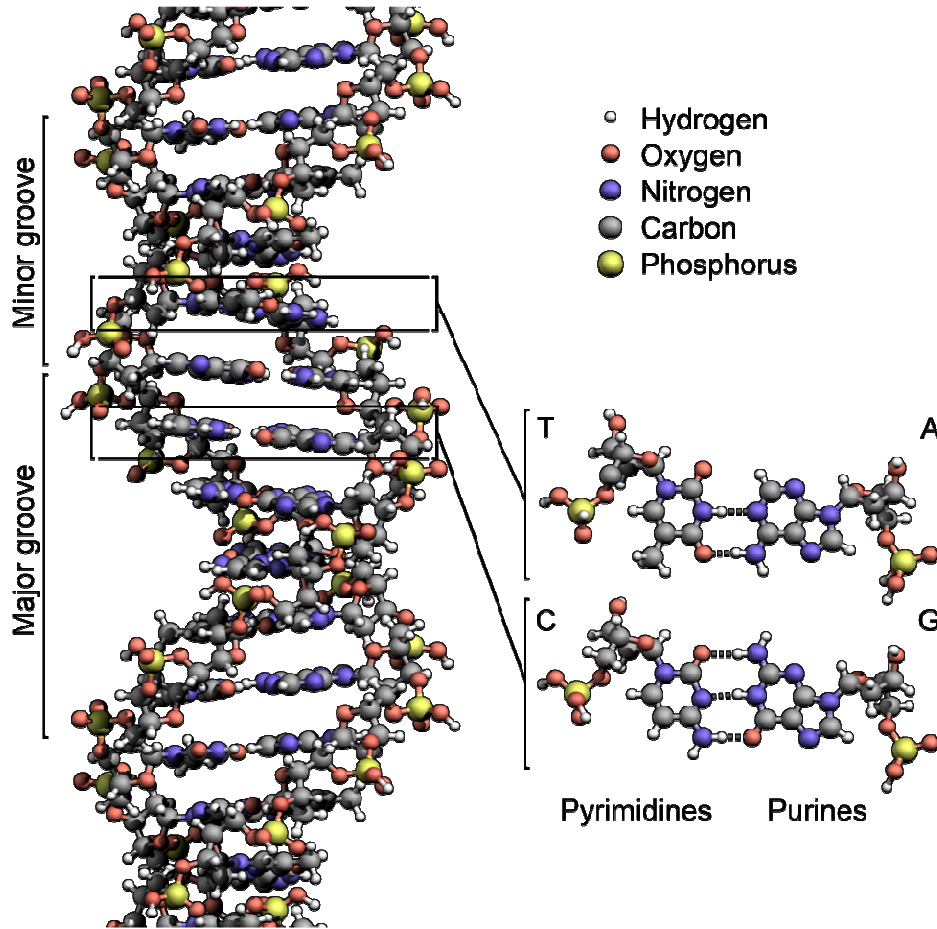
Schematic representation of
“pocket-like” proto-ribosome
formation from a RNA precursor,
showing simple catalytic peptidyl
transferase activity.

A. Yonath *et al.* *Israel Journal of Chemistry*, 2010, 50, 29-35

The origin of DNA



The origin of DNA



Maximal size of RNA-based genome: 3000-5000 bases
(HIV, West Nile virus)

Reason: above that, statistically certain to generate at least one self-cleaving RNA sequence (ribozyme)

Maximal DNA size – unlimited

- no self-cleaving DNazymes,
- tight storage as dsDNA,
- methylated uracil (thymine) → no accidental C-to-U mutations

The genetic code

		2nd base			
		U	C	A	G
1st base	U	UUU (Phe/F) Phenylalanine <chem>Nc1ccc(cc1)C(C)C(=O)O</chem>	UCU (Ser/S) Serine	UAU (Tyr/Y) Tyrosine	UGU (Cys/C) Cysteine <chem>Nc1ccccc1SC(C)C(=O)O</chem>
		UUC (Phe/F) Phenylalanine	UCC (Ser/S) Serine <chem>Nc1ccccc1C(C)C(=O)O</chem>	UAC (Tyr/Y) Tyrosine <chem>Nc1ccc(cc1)C(C)C(=O)O</chem>	UGC (Cys/C) Cysteine
		UUA (Leu/L) Leucine	UCA (Ser/S) Serine	UAA Ochre (Stop)	UGA Opal (Stop) β-Thalassaemia
		UUG (Leu/L) Leucine	UCG (Ser/S) Serine	UAG Amber (Stop)	UGG (Trp/W) Tryptophan <chem>Nc1ccc2c(c1)c(c[nH]2)C(C)C(=O)O</chem>
	C	CUU (Leu/L) Leucine <chem>Nc1ccccc1C(C)C(=O)O</chem>	CCU (Pro/P) Proline	CAU (His/H) Histidine <chem>Nc1ccc[nH]1</chem>	CGU (Arg/R) Arginine <chem>Nc1ccc(cc1)C(C)C(=O)O</chem>
		CUC (Leu/L) Leucine	CCC (Pro/P) Proline <chem>N1CC[C@H](C)C1</chem>	CAC (His/H) Histidine	CGC (Arg/R) Arginine
		CUA (Leu/L) Leucine	CCA (Pro/P) Proline	CAA (Gln/Q) Glutamine <chem>Nc1ccc(cc1)C(=O)O</chem>	CGA (Arg/R) Arginine
		CUG (Leu/L) Leucine	CCG (Pro/P) Proline	CAG (Gln/Q) Glutamine	CGG (Arg/R) Arginine
	A	AUU (Ile/I) Isoleucine <chem>Nc1ccc(cc1)C(C)C(=O)O</chem>	ACU (Thr/T) Threonine <chem>Nc1ccc(O)cc1</chem>	AAU (Asn/N) Asparagine <chem>Nc1ccc(cc1)C(=O)O</chem>	AGU (Ser/S) Serine
		AUC (Ile/I) Isoleucine	ACC (Thr/T) Threonine	AAC (Asn/N) Asparagine	AGC (Ser/S) Serine
		AUA (Ile/I) Isoleucine	ACA (Thr/T) Threonine	AAA (Lys/K) Lysine <chem>Nc1ccc(cc1)CCCC(=O)O</chem>	AGA (Arg/R) Arginine
		AUG (Met/M) Methionine <chem>CSCCNC(=O)O</chem>	ACG (Thr/T) Threonine	AAG (Lys/K) Lysine	AGG (Arg/R) Arginine
G	GUU (Val/V) Valine <chem>Nc1ccc(O)cc1</chem>	GCU (Ala/A) Alanine Colorectal cancer	GAU (Asp/D) Aspartic acid <chem>Nc1ccc(O)cc1</chem>	GGU (Gly/G) Glycine	
	GUC (Val/V) Valine	GCC (Ala/A) Alanine	GAC (Asp/D) Aspartic acid	GGC (Gly/G) Glycine	
	GUA (Val/V) Valine	GCA (Ala/A) Alanine	GAA (Glu/E) Glutamic acid <chem>Nc1ccc(O)cc1</chem>	GGA (Gly/G) Glycine	
	GUG (Val/V) Valine	GCG (Ala/A) Alanine	GAG (Glu/E) Glutamic acid	GGG (Gly/G) Glycine	

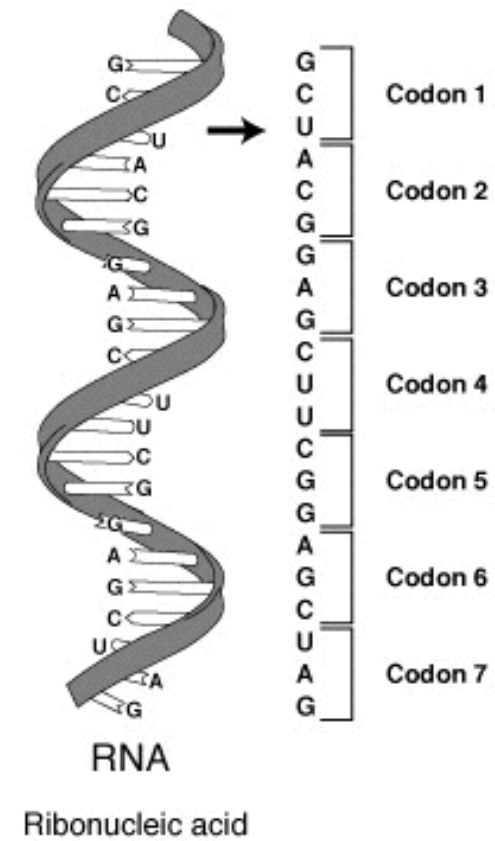
ΔF508 deletion in cystic fibrosis

- Myotonic dystrophy
- SCA 8

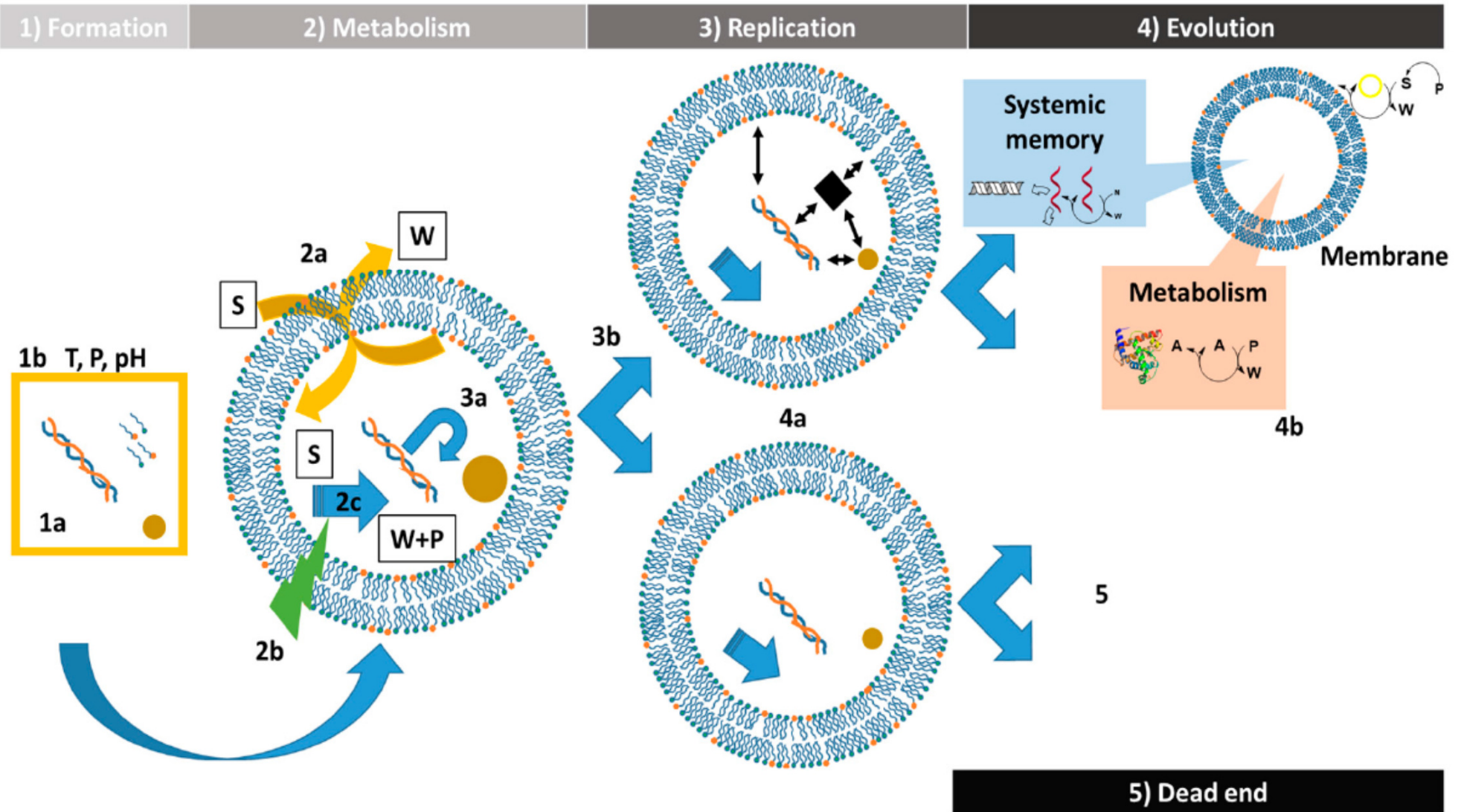
Prostate cancer

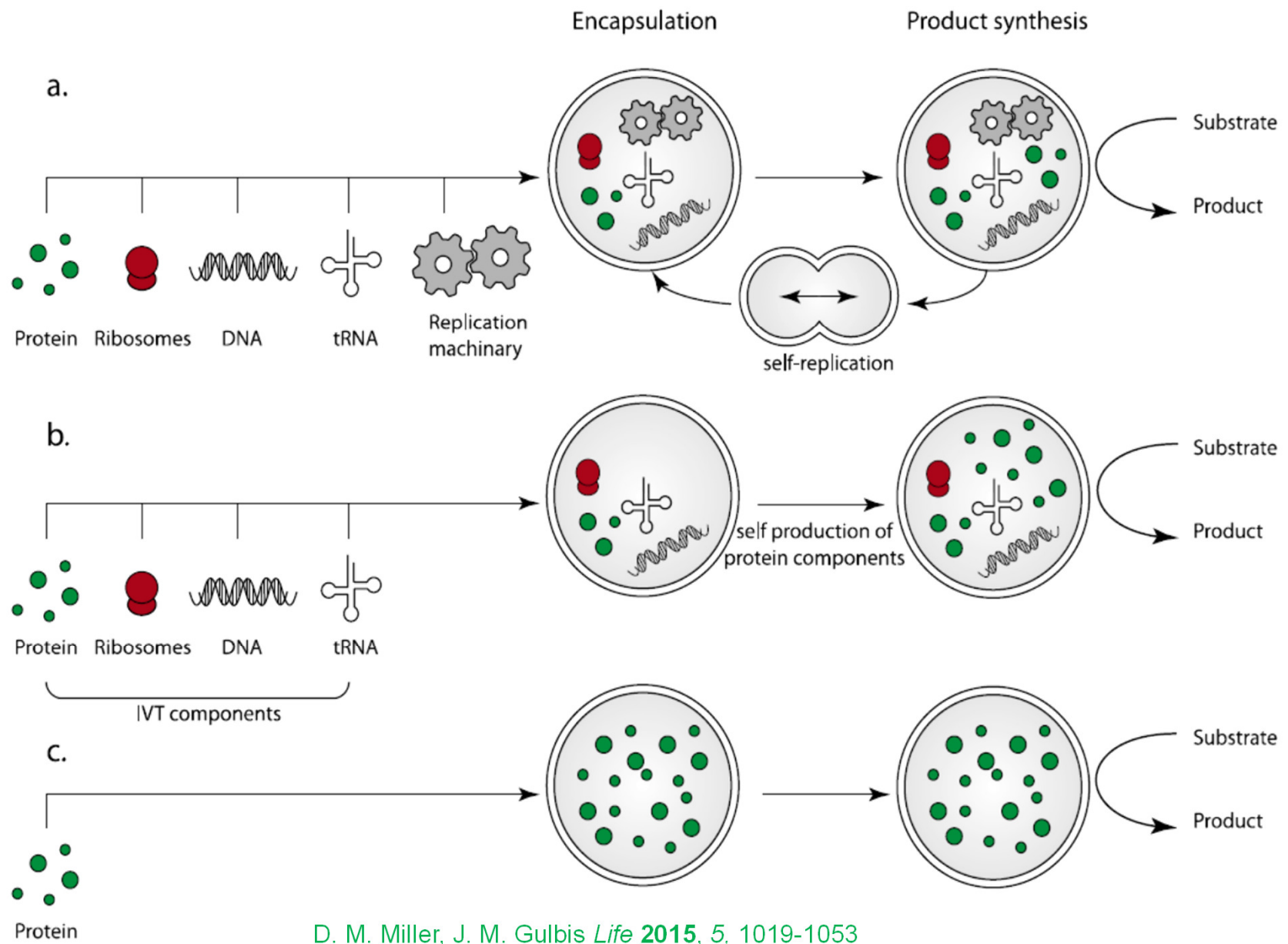
Sickle-cell disease

Friedreich's ataxia



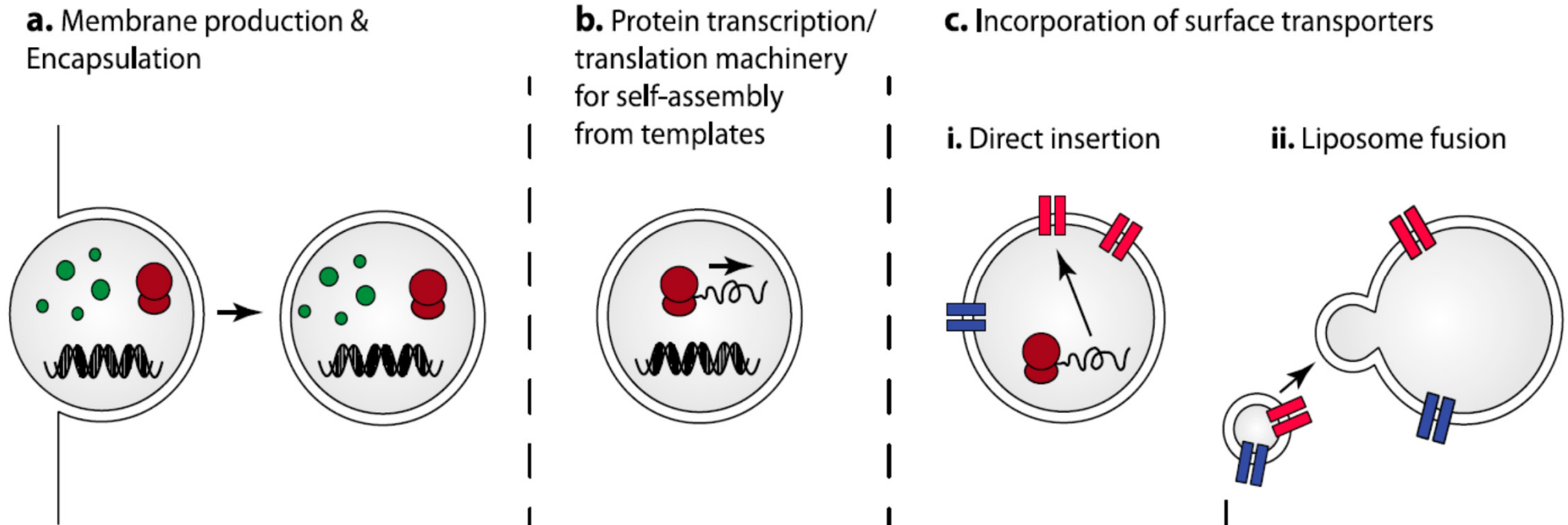
Increasing complexity of the protocells





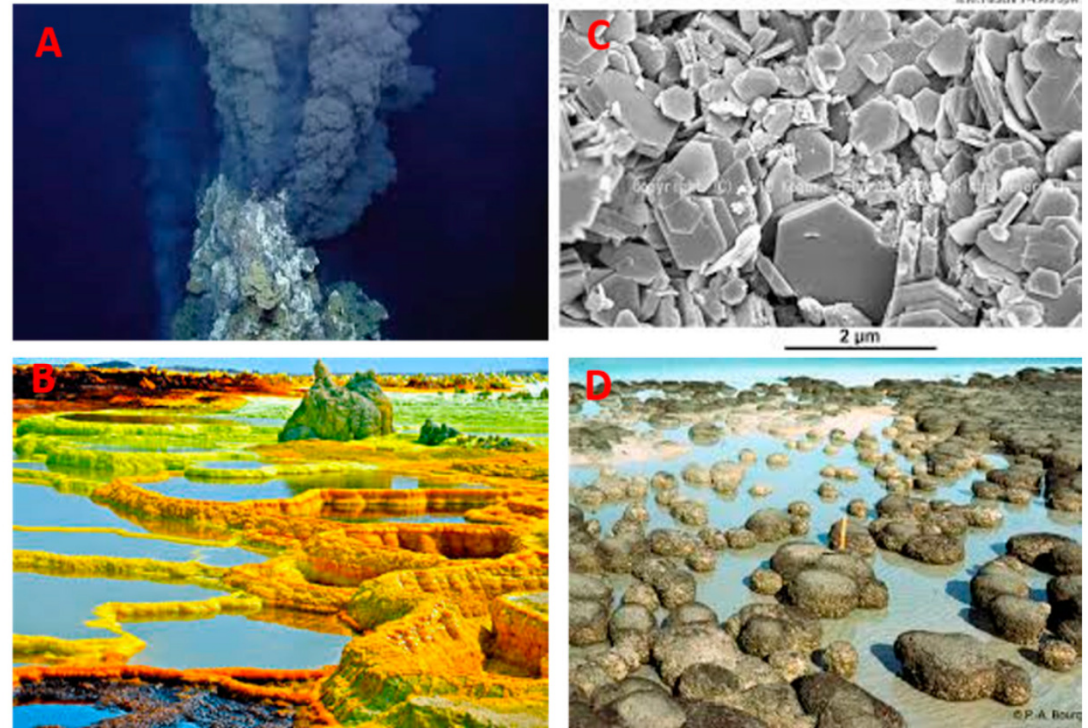
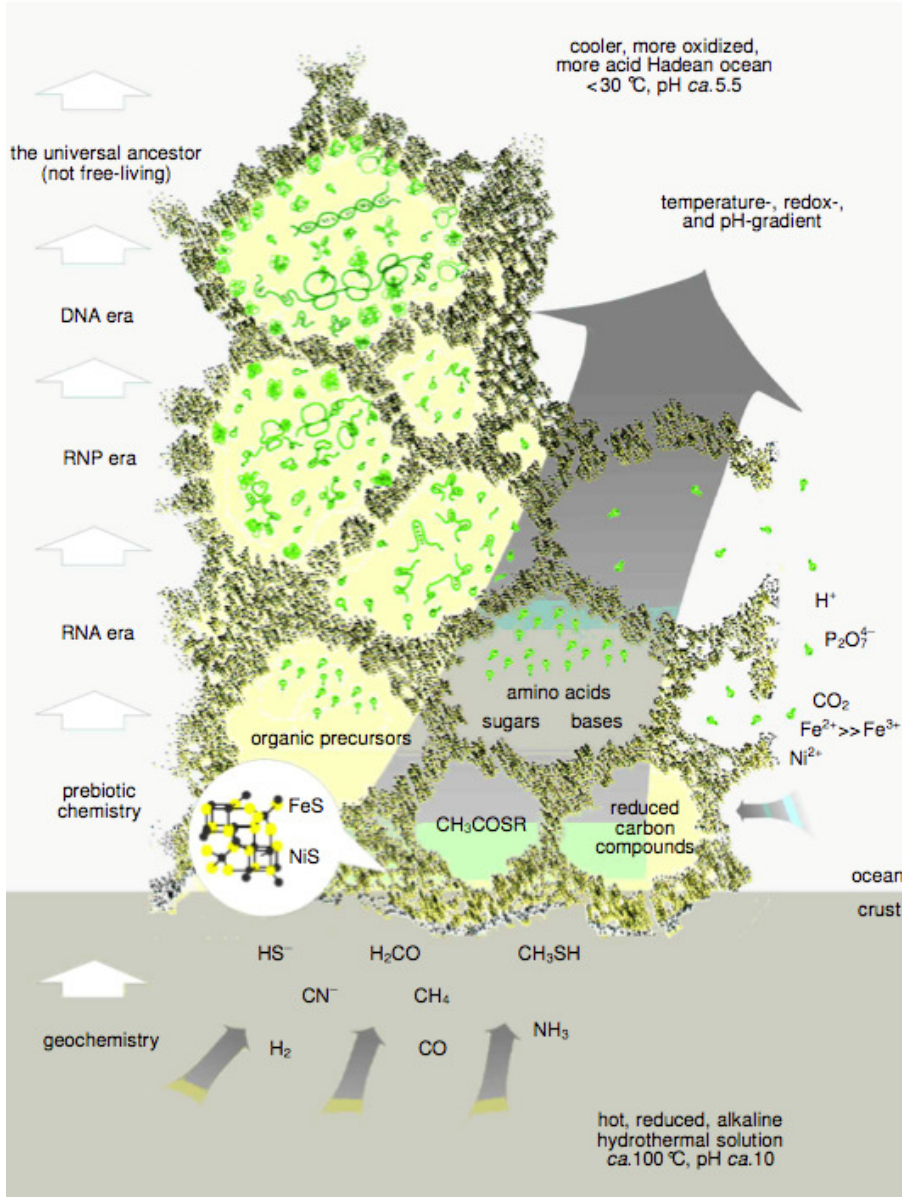
D. M. Miller, J. M. Gulbis *Life* 2015, 5, 1019-1053

Increasing complexity of the protocells



Compartments in hydrothermal vents?

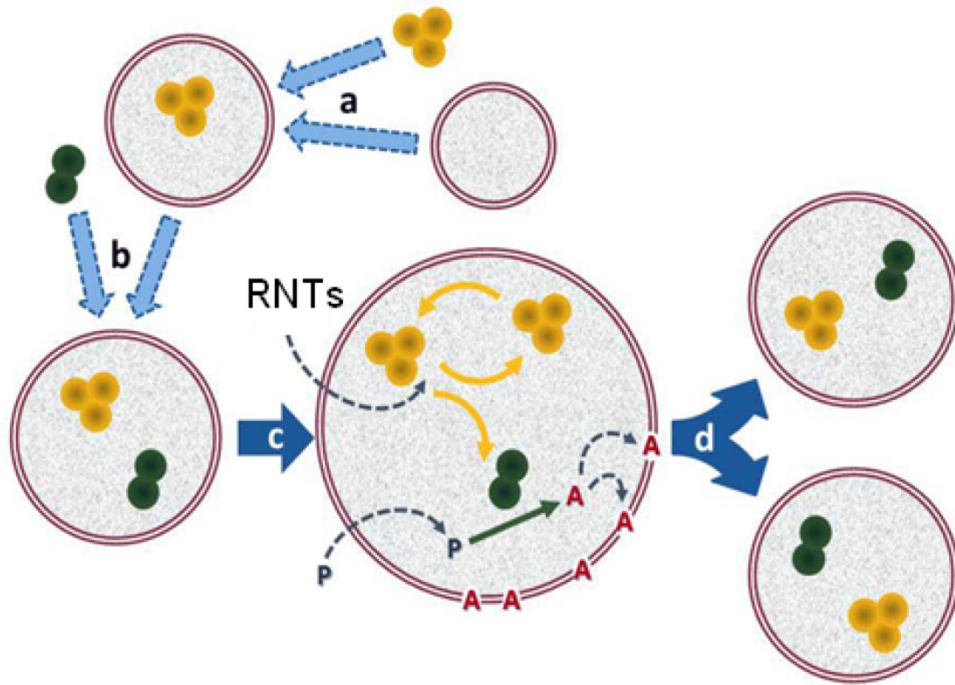
Complex metabolic machinery closed in the same compartment that genetic polymers (RNA) which generated it.



A. Lopez, M. Fiore *Life* 2019, 9(49), doi:10.3390/life9020049

We don't see ribozyme-based metabolism today anymore, because protein catalysts (enzymes) for the same reactions are orders of magnitude faster than the ribozymes

Primordial synthesis of an RNA-based protocell



(a) A self-reproducing vesicle is combined with an RNA replicase (yellow).

(b) This system is further combined with a second ribozyme (green) that is able to synthesize amphiphilic molecules (A) from precursor substrates (P), thus leading to an RNA protocell containing two ribozymes.

(c) In such a “ribocyte”, the RNA replicase is capable of replicating itself and also making copies of the membrane-forming ribozyme, provided that ribonucleotides (RNTs) are available in the surrounding medium and can permeate the vesicle membrane.

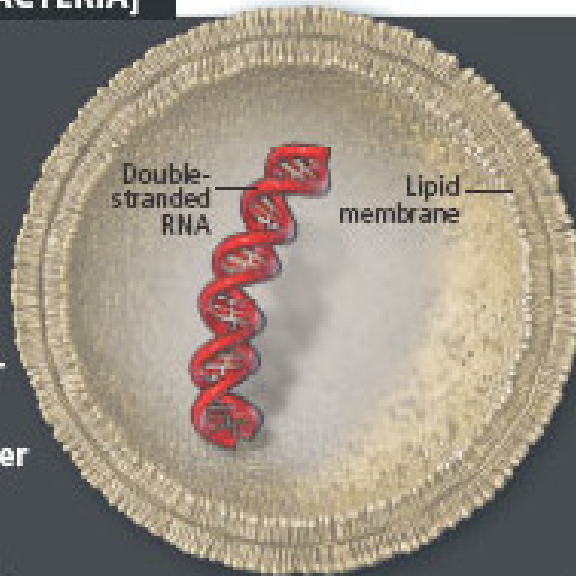
(d) Activity of the second ribozyme converts the previously internalized precursors into amphiphiles, which are further incorporated into the membrane; this leads to a progressive increase of the vesicle size and its subsequent division into two daughter vesicles, thus triggering Darwinian evolution of the whole (membrane–genome coupled) system

From RNA world to bacteria

[FROM RNA WORLD TO BACTERIA]

Journey to the Modern Cell

After life got started, competition among life-forms fueled the drive toward ever more complex organisms. We may never know the exact details of early evolution, but here is a plausible sequence of some of the major events that led from the first protocell to DNA-based cells such as bacteria.

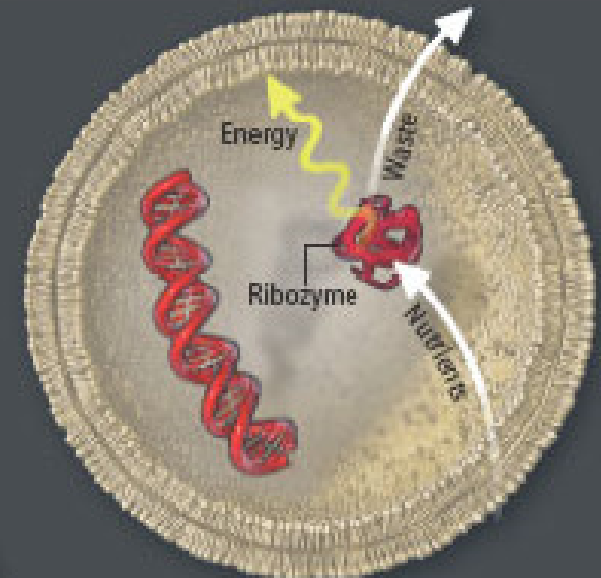
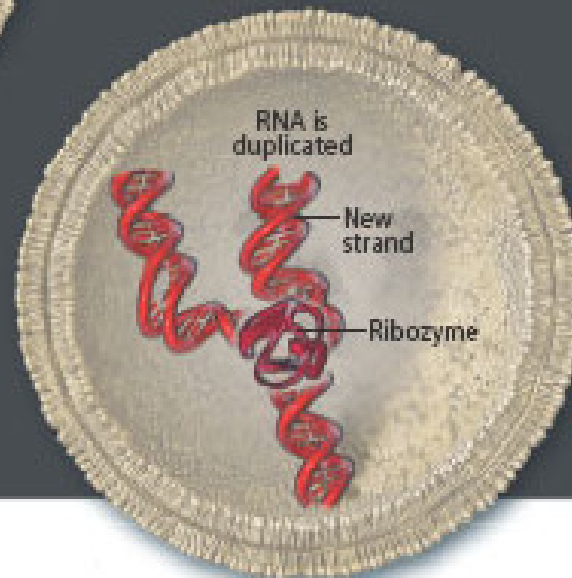


1 EVOLUTION STARTS ▲

The first protocell is just a sac of water and RNA and requires an external stimulus (such as cycles of heat and cold) to reproduce. But it will soon acquire new traits.

2 RNA CATALYSTS ▼

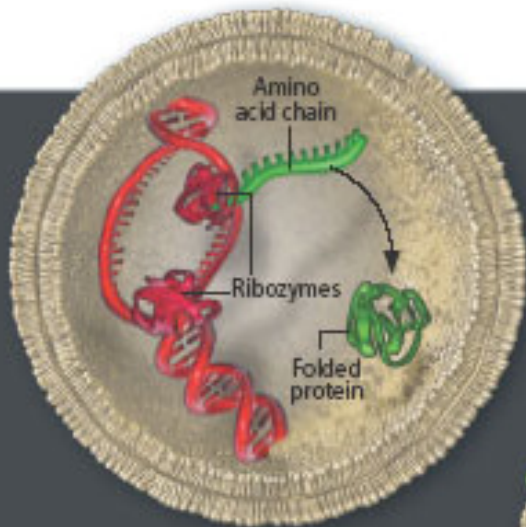
Ribozymes—folded RNA molecules analogous to protein-based enzymes—arise and take on such jobs as speeding up reproduction and strengthening the protocell's membrane. Consequently, protocells begin to reproduce on their own.



3 METABOLISM BEGINS ▲

Other ribozymes catalyze metabolism—chains of chemical reactions that enable protocells to tap into nutrients from the environment.

From RNA world to bacteria

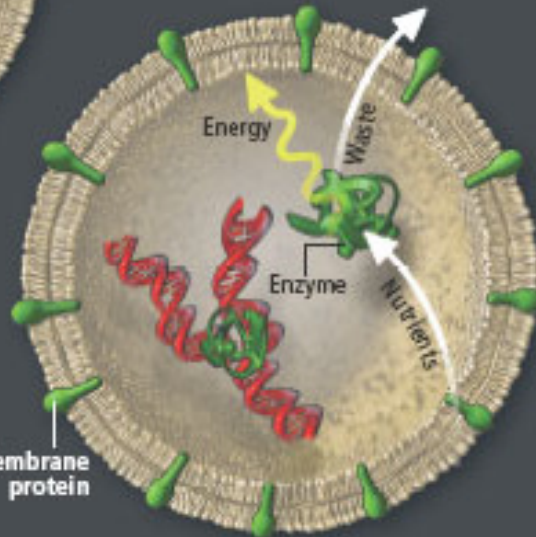


4 PROTEINS APPEAR ▲

Complex systems of RNA catalysts begin to translate strings of RNA letters (genes) into chains of amino acids (proteins). Proteins later prove to be more efficient catalysts and able to carry out a variety of tasks.

5 PROTEINS TAKE OVER ▼

Proteins take on a wide range of tasks within the cell. Protein-based catalysts, or enzymes, gradually replace most ribozymes.



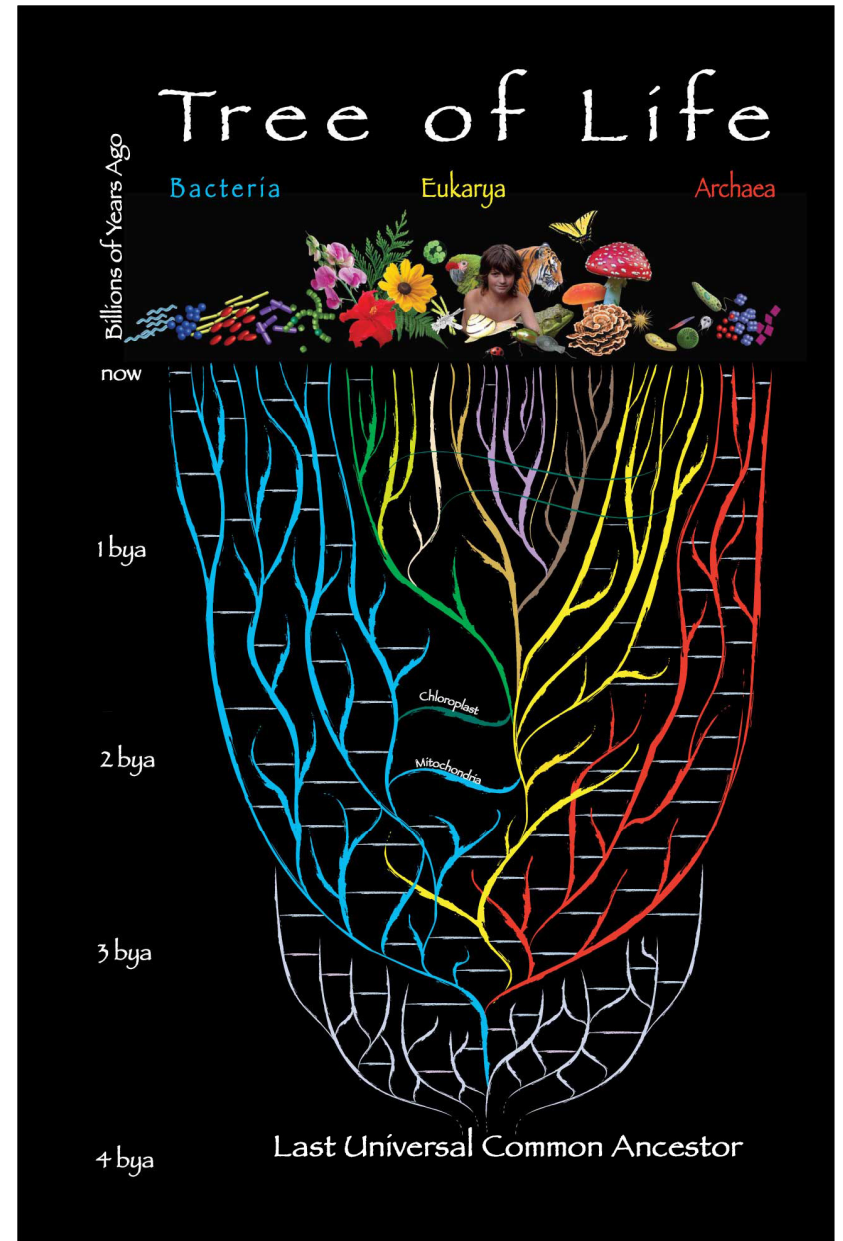
6 THE BIRTH OF DNA ▲

Other enzymes begin to make DNA. Thanks to its superior stability, DNA takes on the role of primary genetic molecule. RNA's main role is now to act as a bridge between DNA and proteins.

7 BACTERIAL WORLD ▲

Organisms resembling modern bacteria adapt to living virtually everywhere on earth and rule unopposed for billions of years, until some of them begin to evolve into more complex organisms.





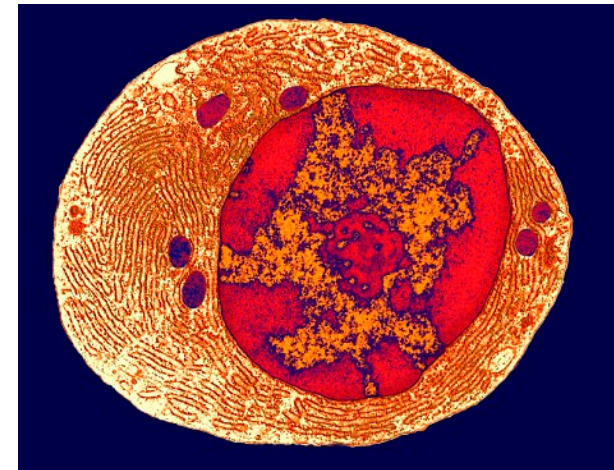
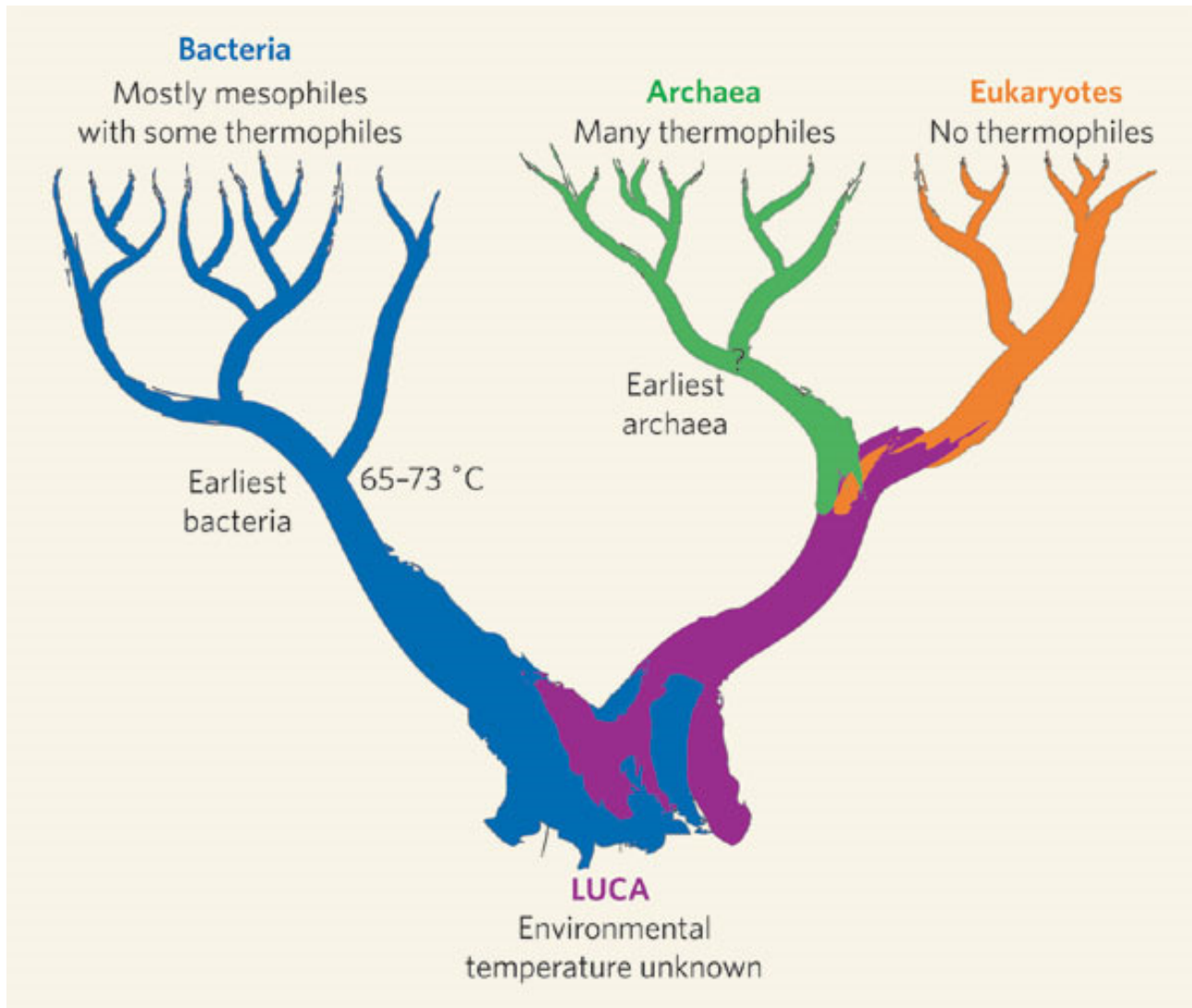
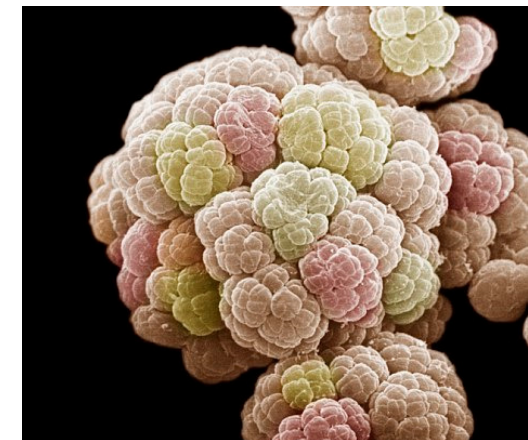


Image of a eukaryotic cell contains numerous organelles, which are now thought to be present in the last universal common ancestor

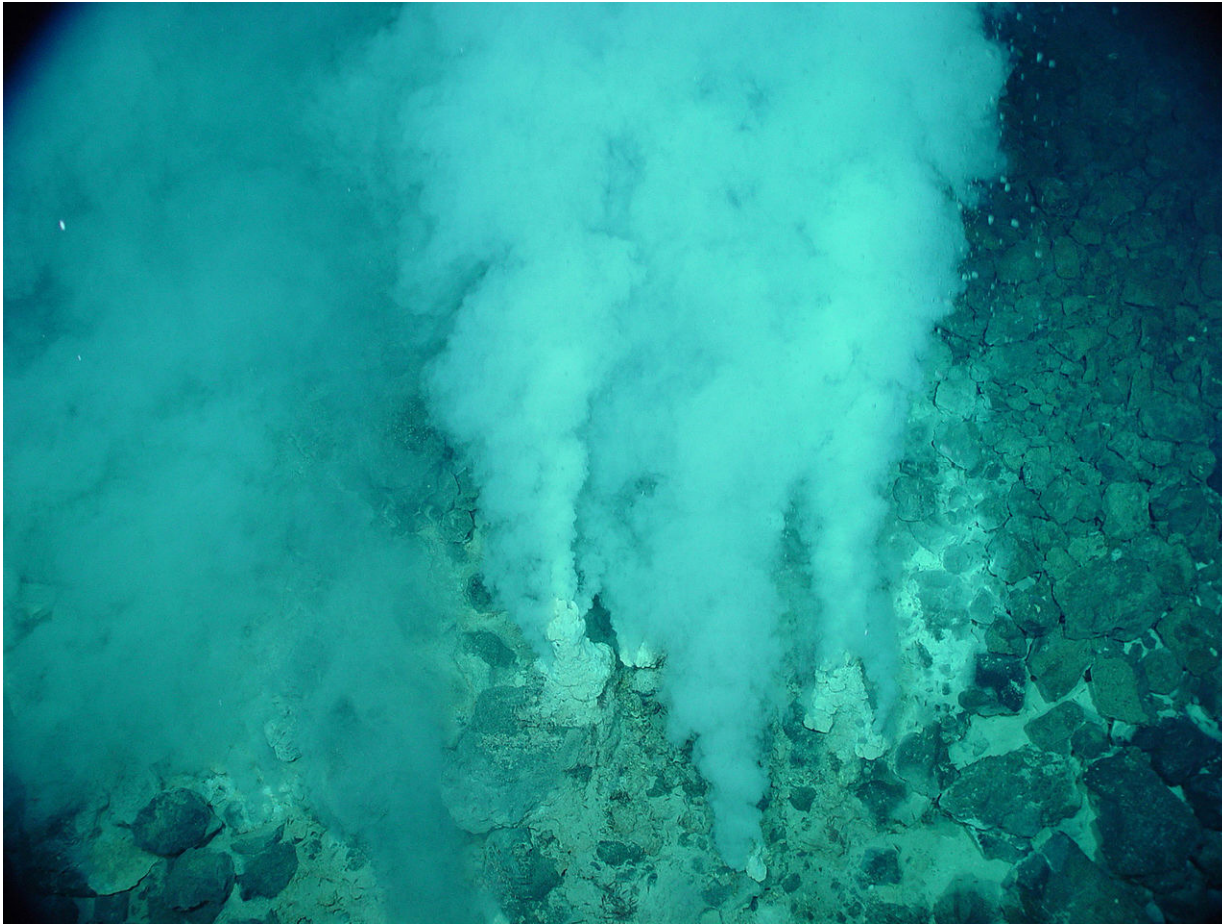


A colony of the archaea, which form one of the three lines of the tree of life in evolutionary history

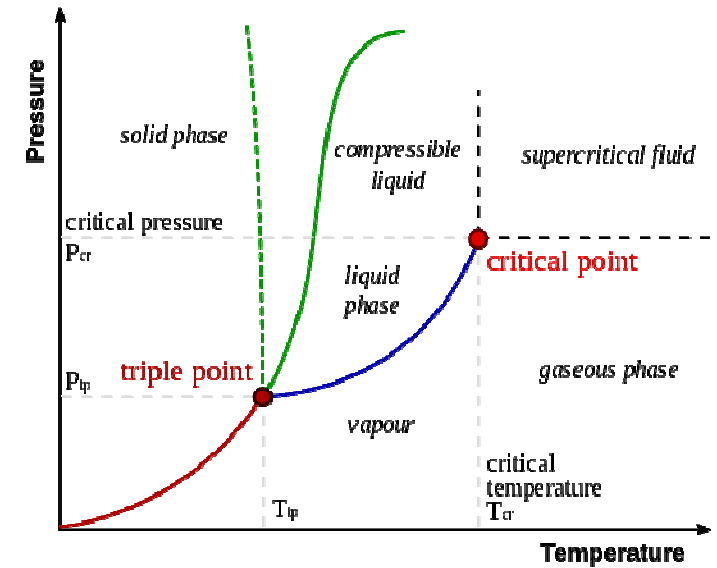
The Origin of Life near Deep Sea Hydrothermal vents?



Hydrothermal vents

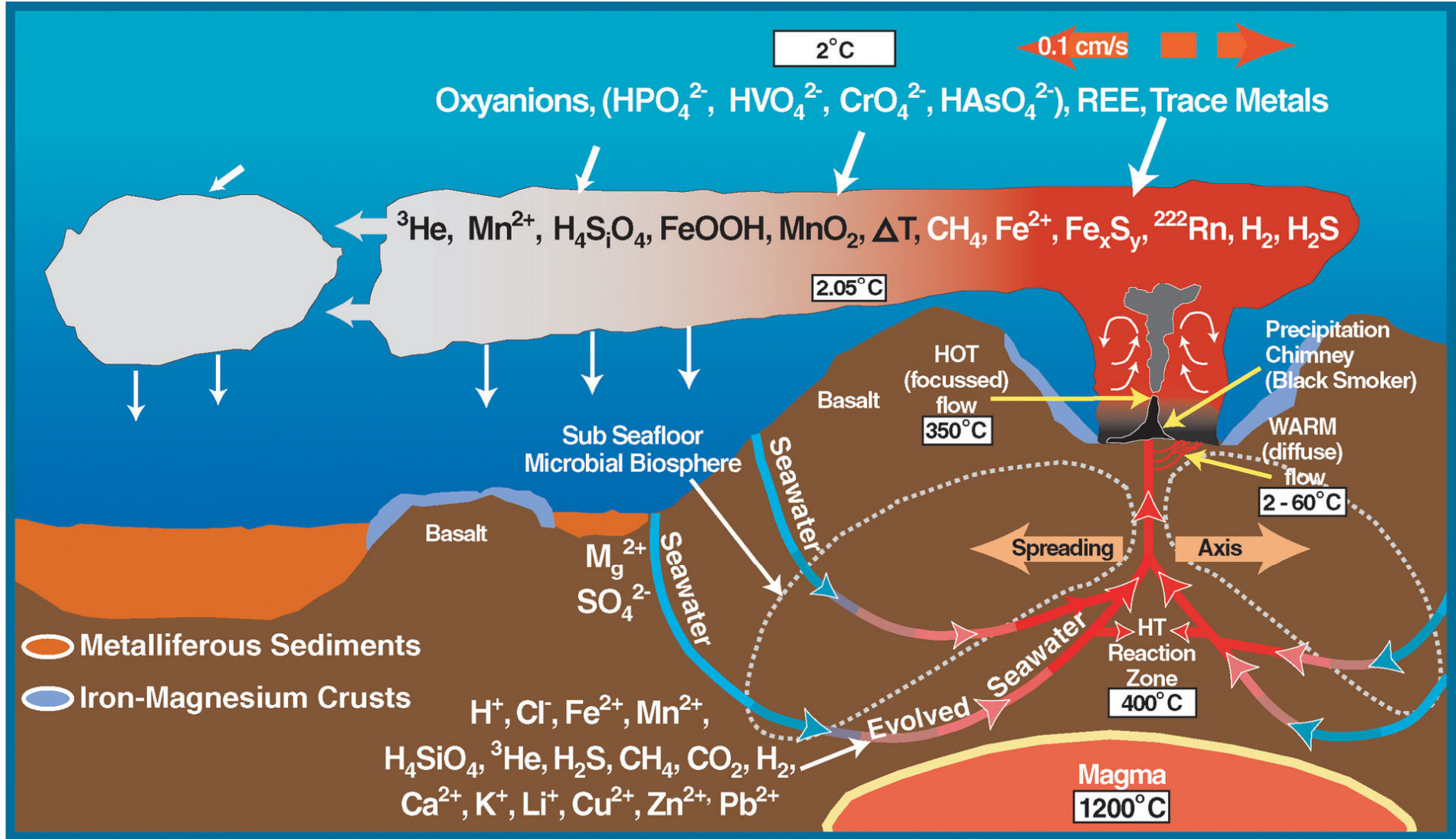


White flocculent mats in and around the extremely gassy, high-temperature ($>100^{\circ}\text{C}$, 212°F) white smokers at Champagne Vent.

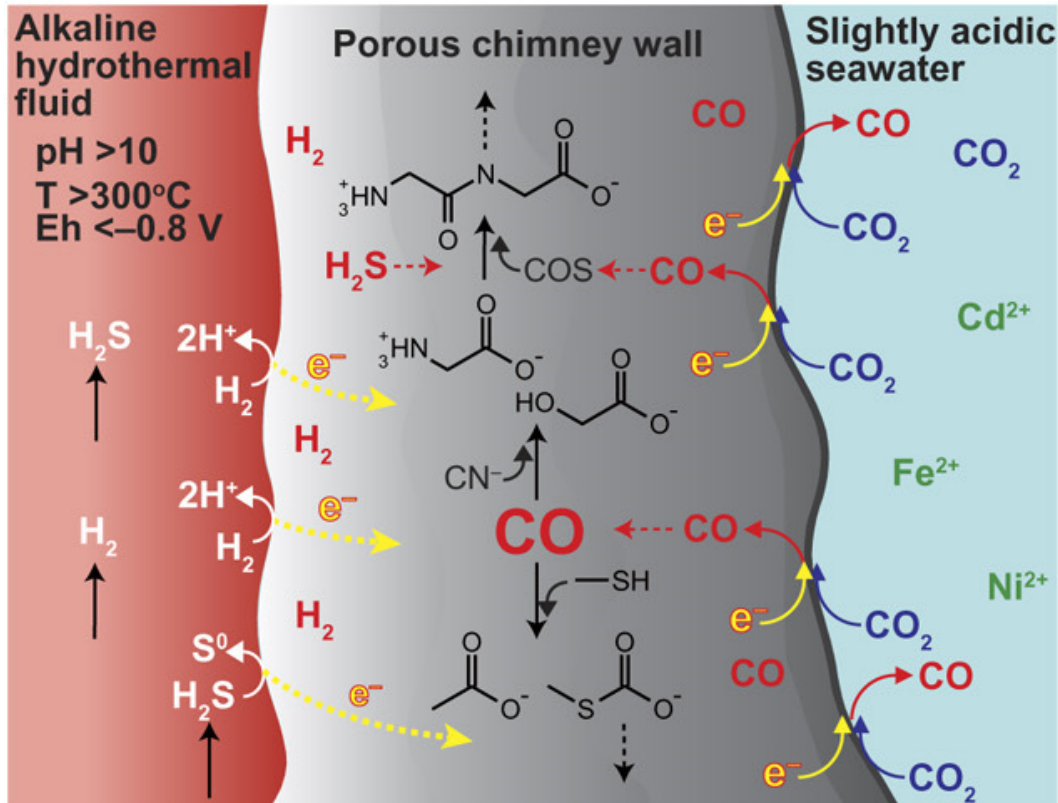


Alkaline hydrothermal vents consist of microscale caverns coated by thin membraneous metal sulfide walls \rightarrow ,Iron-sulfur world'

Deep sea vent biogeochemical cycle diagram



Deep sea vent origin of life

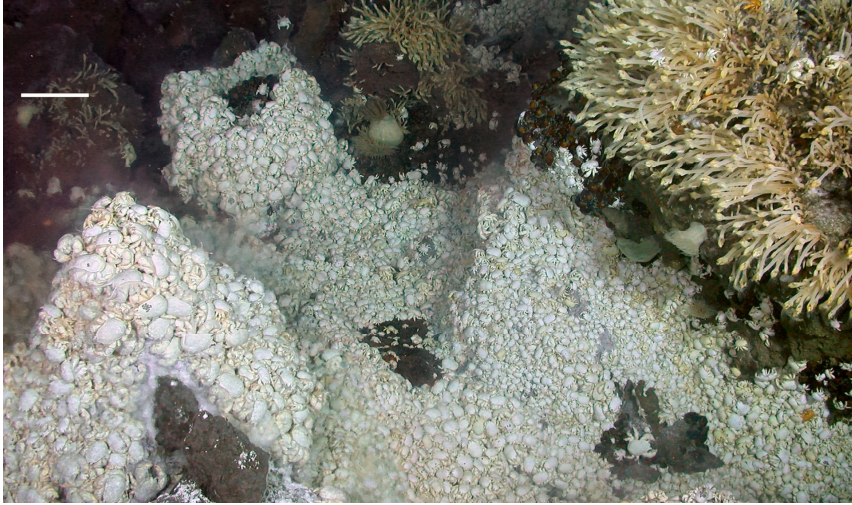


Abiotic carbon fixation in the primitive hydrothermal system.

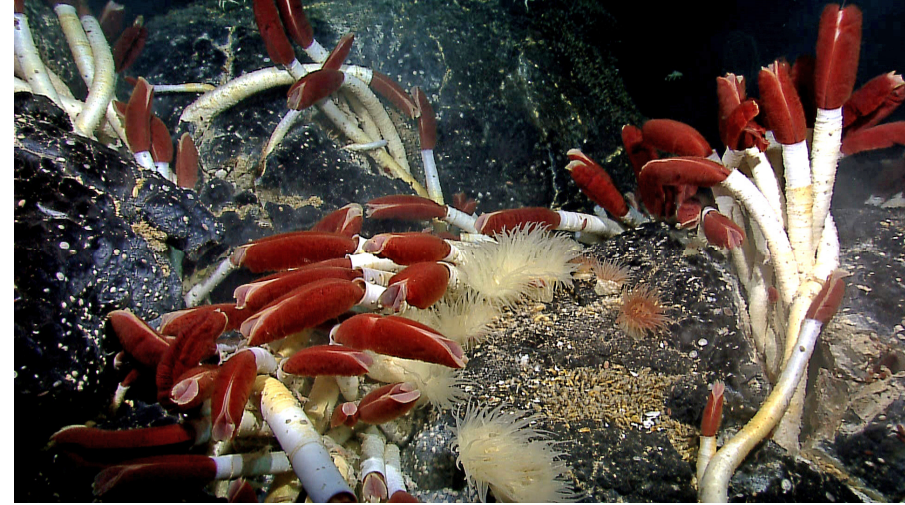
On the ocean floor, mixing of the hydrothermal fluids and seawater generated sulfide-rich chimneys, and the potential gradient across the chimney drove a continuous electron flow. The electric potential at the chimney-seawater interface could reach less than -1 V (versus SHE) in alkaline hydrothermal vent environments. The low potential, in the presence of sulfides rich in Cd^{2+} and Ag^+ , allowed the electrochemical CO_2 reduction to CO with the FE as high as dozens of percent, together with H_2 evolution. The produced CO served as a driving force for the subsequent abiotic organic synthesis that preceded the origin of life as schematically indicated in the figure

Kitadai et al., *Sci. Adv.* **2018**; 4: eaao7265

Deep sea vent fauna

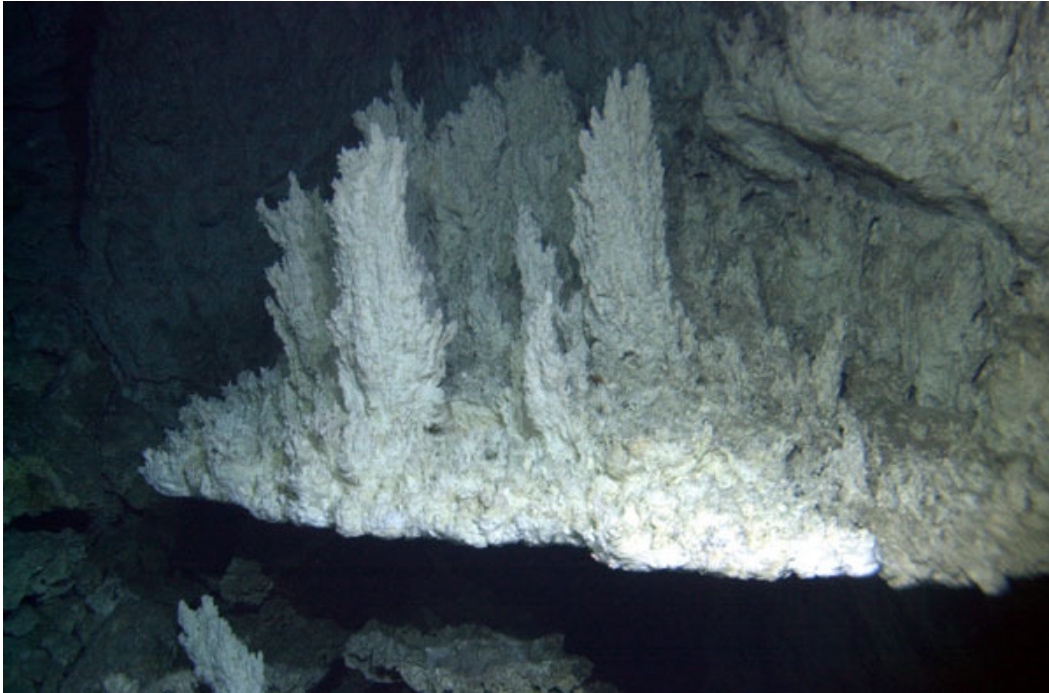


A dense fauna (*Kiwa anomurans* and *Vulcanolepas* like stalked barnacles) near East Scotia Ridge vents



Giant tube worms (*Riftia pachyptila*) cluster around vents in the Galapagos Rift

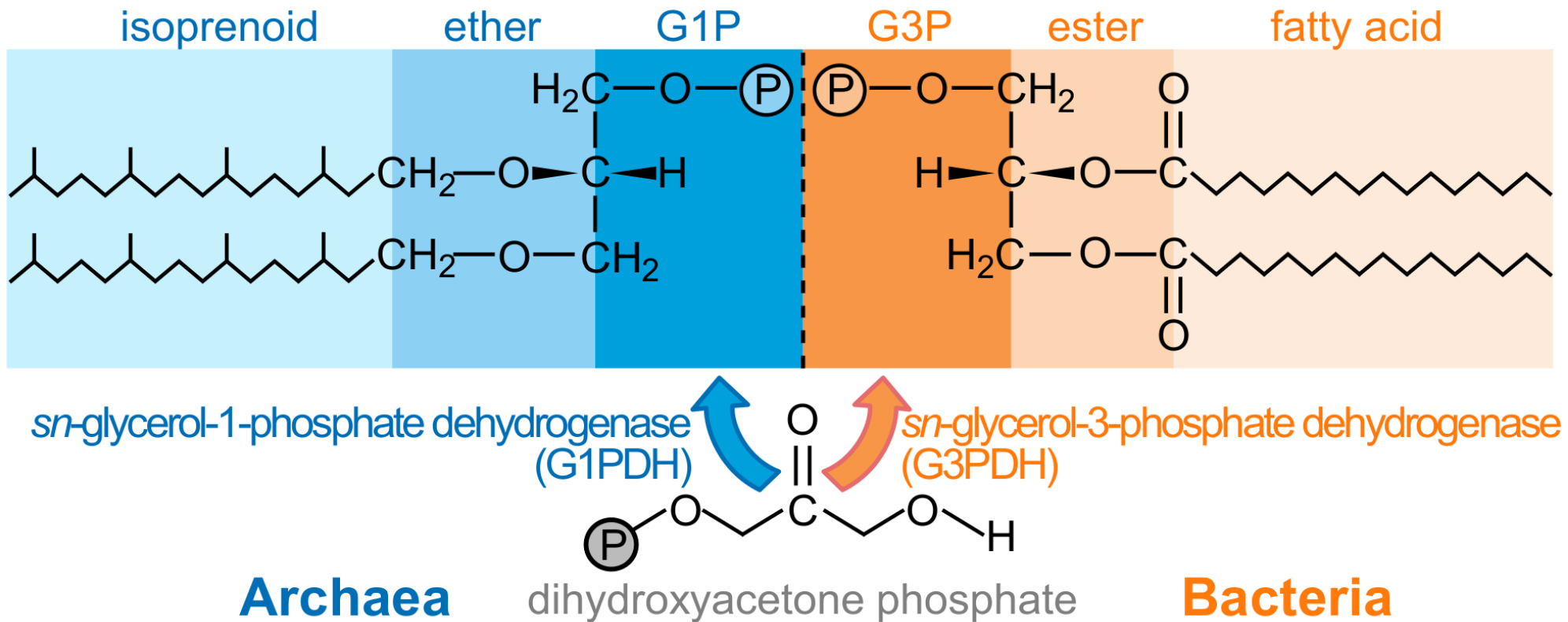
„Lost city” – white smokers: alkaline hydrothermal vents



A 1.5-meter-wide ledge on the side of a chimney is topped with dendritic carbonate growths that form when mineral-rich vent fluids seep through the flange and come into contact with the cold seawater.



A carbonate chimney more than 9 meters (30 feet) in height. The white, sinuous spine is freshly deposited carbonate material. The top shows evidence of collapse and re-growth, as indicated by the small newly developed cone on its top

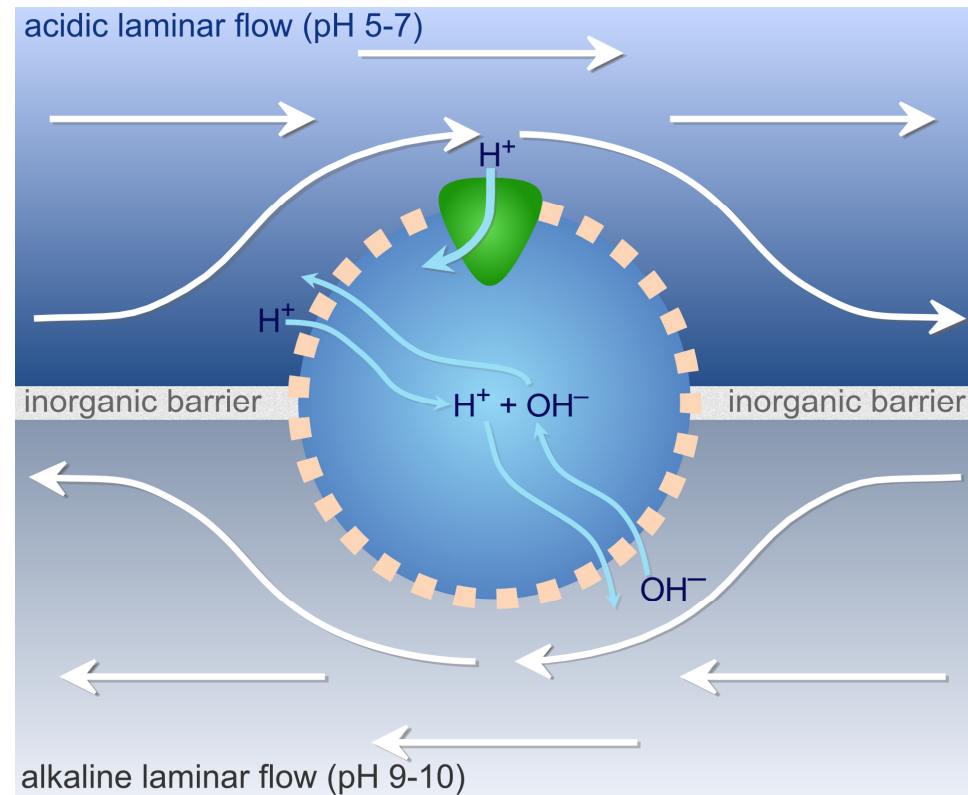


Archaeal lipids: isoprenoid chains + ether bonds + *sn*-glycerol-1-phosphate (G1P) backbone.

Bacterial lipids: fatty acids + ester linkage + *sn*-glycerol-3-phosphate (G3P) skeleton.

Despite widespread horizontal gene transfer, no bacterium has been observed with the archaeal enantiomer, or vice versa. (ether linkages have been observed in bacterial membranes and isoprenoids are common to all three domains)

V. Sojo, A. Pomiankowski, N. Lane *PLOS Biology*, 2014, 12(8), e1001926



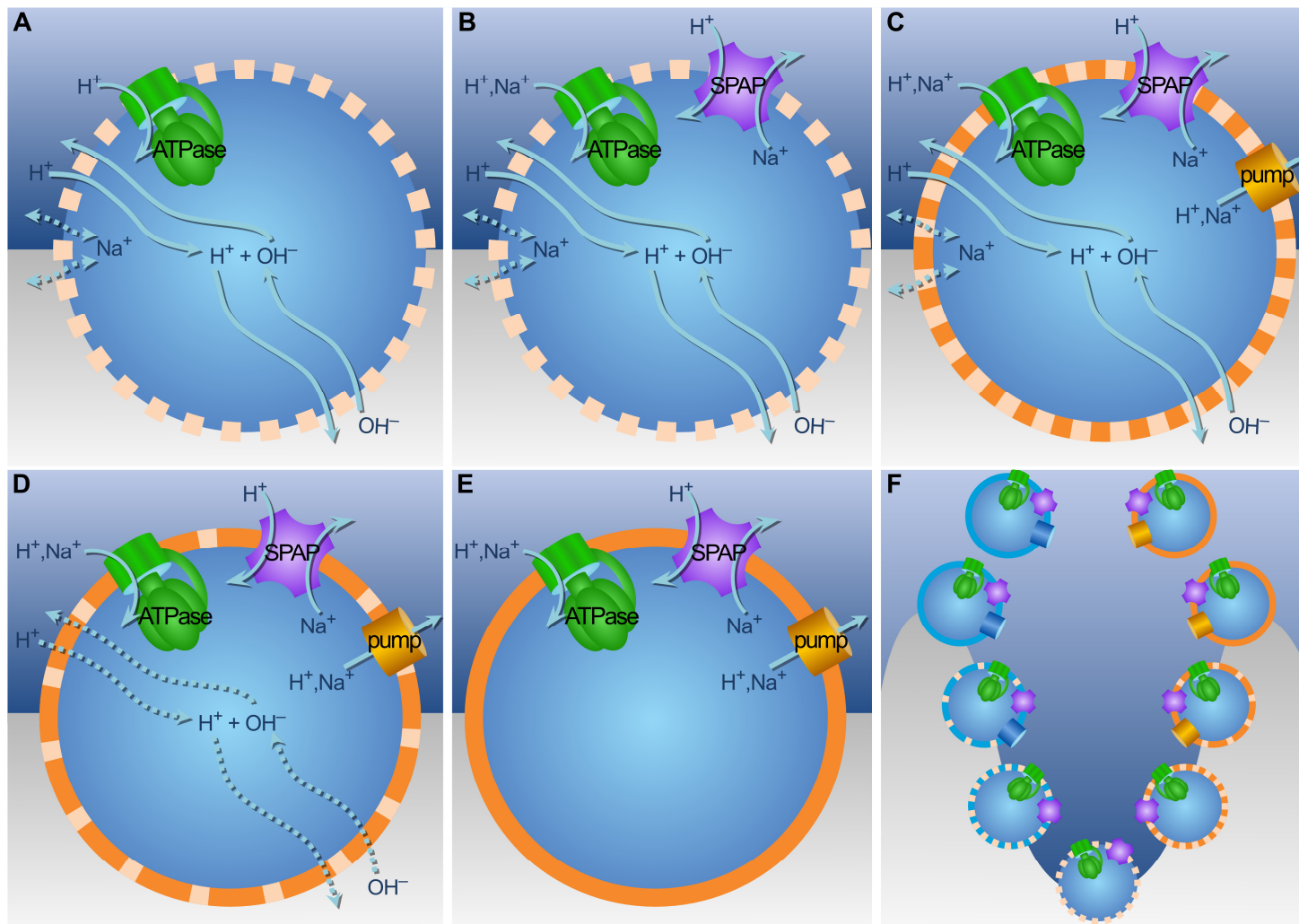
A cell with a semi-permeable membrane at the interface between an alkaline and an acidic fluid (separated elsewhere with an inorganic barrier). H^+ , OH^- , Na^+ , K^+ , Cl^- and other ions flow according to their natural gradients.

Inside the protocell, H^+ and OH^- can neutralize into water, or leave towards either side.

A protein capable of exploiting the natural proton gradient sits on the acidic side, allowing energy assimilation via ATP production, or carbon assimilation via CO_2 fixation.

V. Sojo, A. Pomiankowski, N. Lane *PLOS Biology*, 2014, 12(8), e1001926

The role of sodium-proton antiporter (SPAP)



A) H^+ gradient drives energy metabolism (ATPase) or carbon metabolism (Ech)

B) SPAP generates Na^+ from H^+ gradient

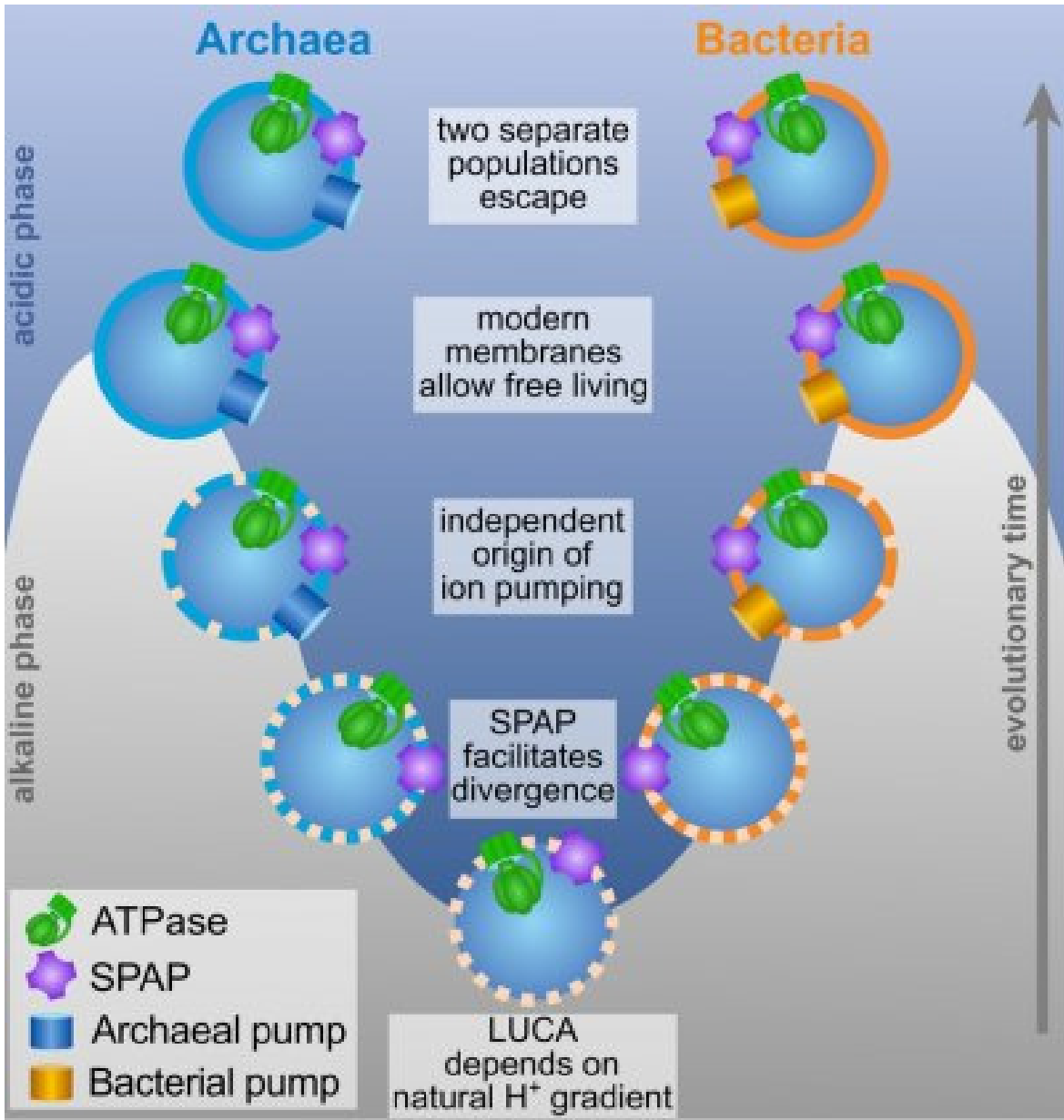
C) Membrane pumps secrete H^+ and Na^+

D) Tighter membranes are now produced, to colonize less alkaline environments

E) Impermeable membranes \rightarrow gradients created by proteins, independently from the natural environmental gradients

F) SPAP favors divergence, selection for active pumping and tighter membranes; independent evolution of archaea and bacteria

V. Sojo, A. Pomiankowski, N. Lane
PLOS Biology, 2014, 12(8), e1001926



Origin of autotrophy and development of cell membrane

Ion pumping and phospholipid membranes evolved independently in bacteria and archea.

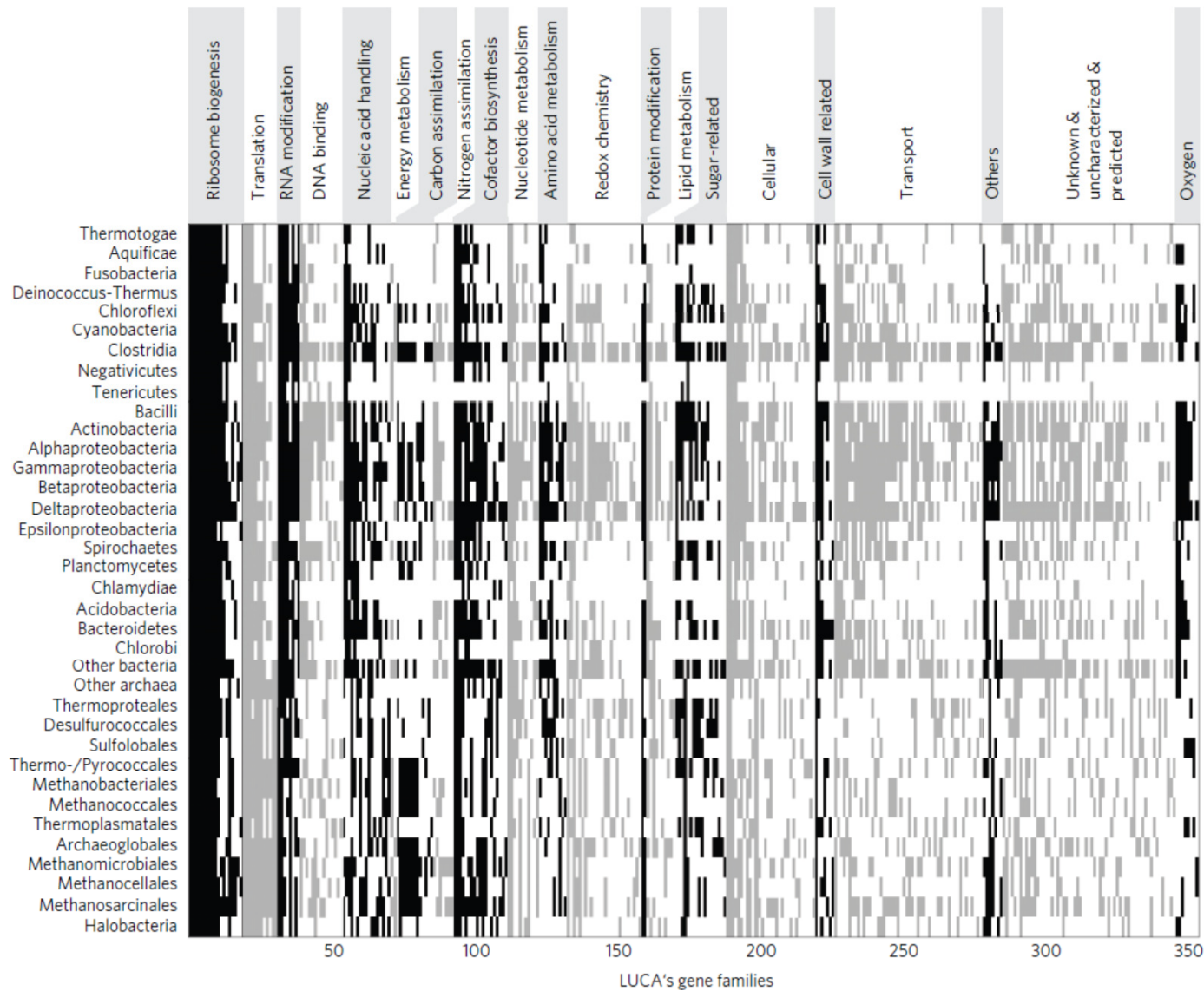
Energy could have been delivered by the natural proton gradient in alkaline hydrothermal vents, if the membrane was much more leaky than contemporary ones.

Development of proton pumping allowed for escape from the vent environment.

sodium-proton antiporter (SPAP)

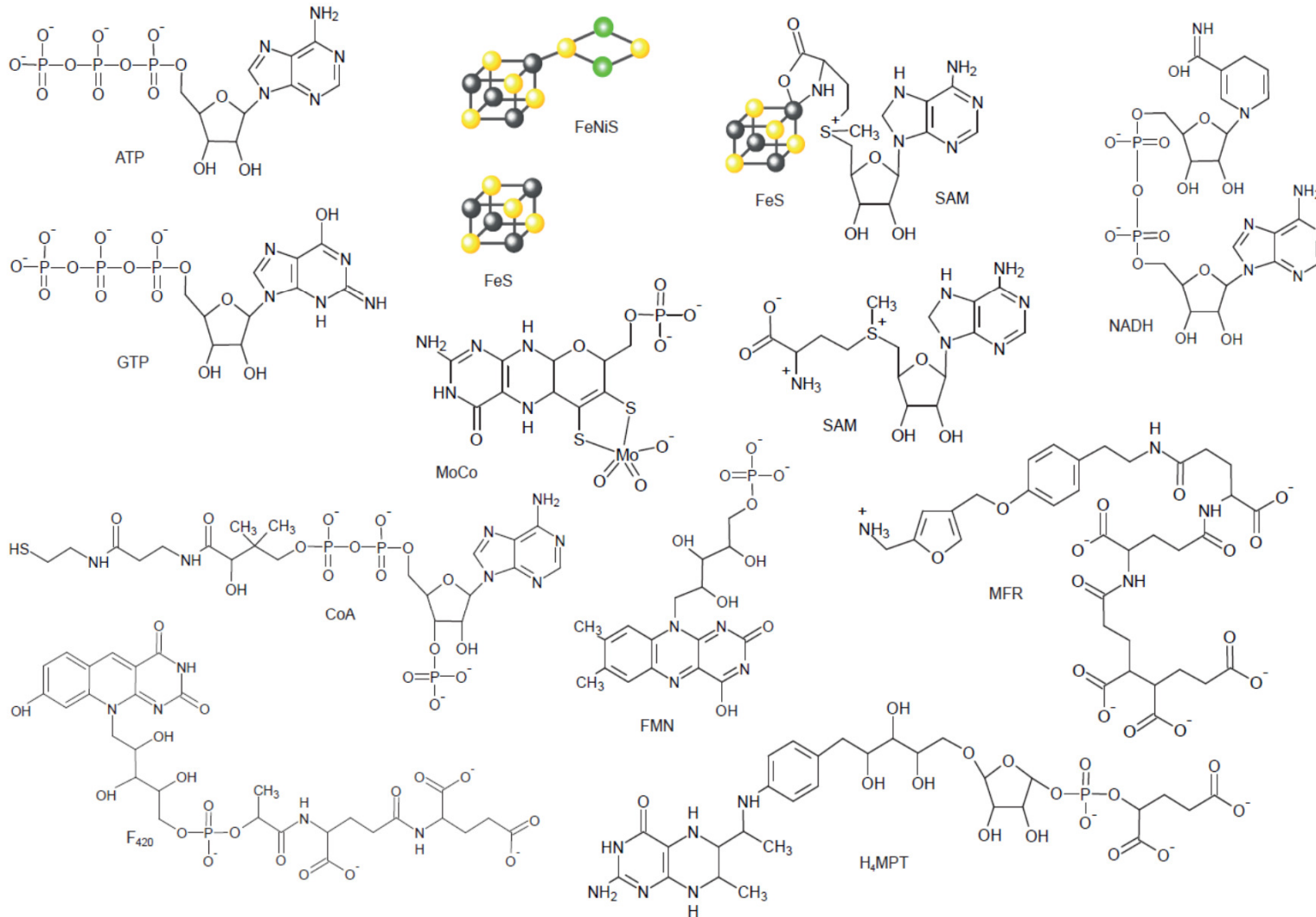
V. Sojo, A. Pomiankowski, N. Lane
PLOS Biology, 2014, 12(8), e1001926

Taxonomic distribution of LUCA's genes grouped by functional categories



M.C. Weiss et al. *Nature Microbiology*,
2016, Article 16116

Structures of the cofactors found in LUCA's protein set.



FeNiS – nickel-iron-sulfur cluster

FeS – iron-sulfur cluster

MoCo – molybdenum cofactor

SAM – S-adenosylmethionine

CoA – coenzyme A

MFR – methanofuran

H4MPT – tetrahydromethanopterin

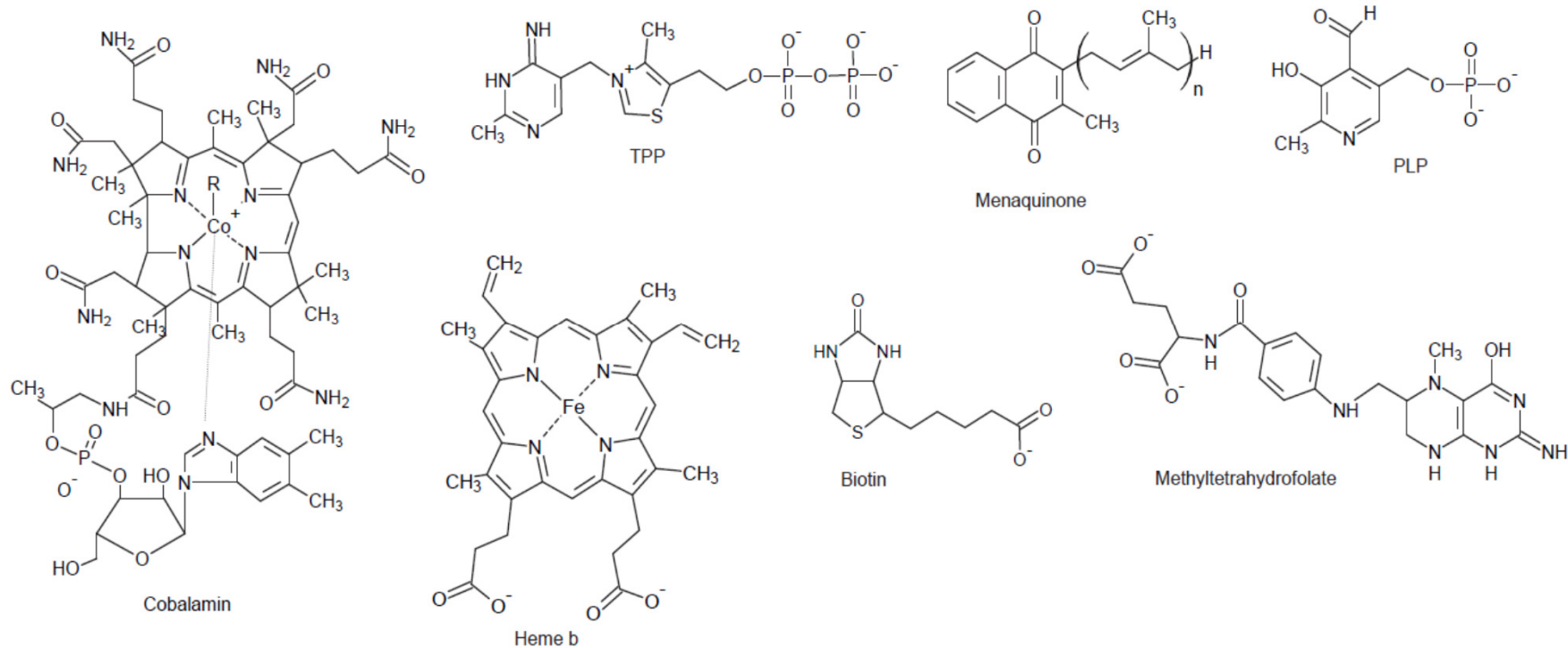
TPP - thiamine pyrophosphate

PLP - pyridoxal phosphate

NTP – nucleoside triphosphate.

M.C. Weiss et al. *Nature Microbiology*,
2016, Article 16116

Structures of the cofactors found in LUCA's protein set.



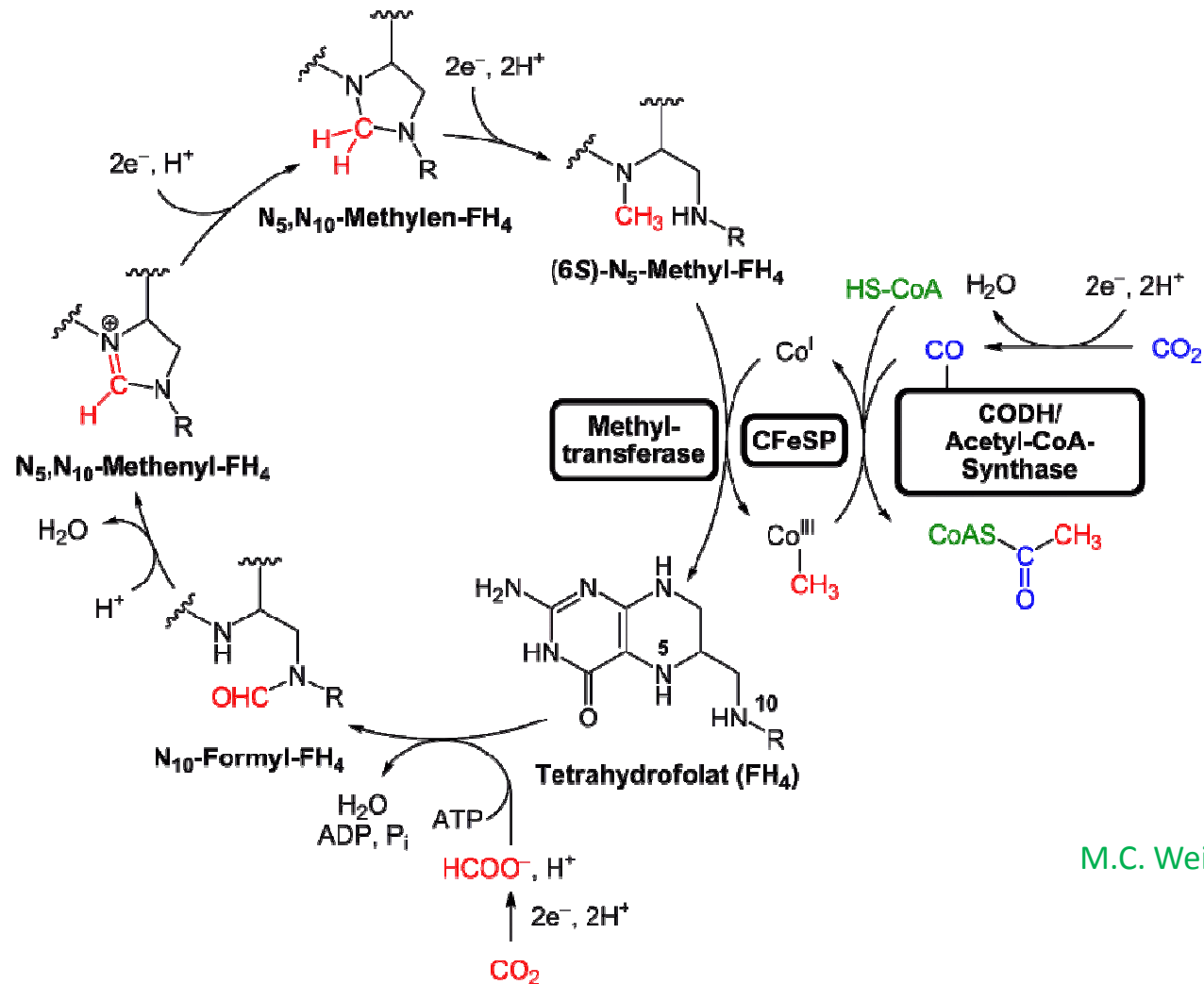
Mononuclear metal centers (Fe and Cu) and the non-standard amino acid selenocysteine are not shown, nor are small protein electron carriers such as ferredoxin or rubredoxin. NTP is also listed as a cofactor, but not shown here as it stands for any of the nucleoside triphosphates in those cases when it's not known which one is bound by the enzyme, or when more than one nucleoside triphosphate can be used

Phylogenetic identification of LUCA's proteome

355 protein families shared among contemporary *archaea* and *bacteria*, including:

- 19 proteins involved in ribosome biogenesis
- 8 aminoacyl tRNA synthetases
- proteins for carbon, energy, and nitrogen metabolism
- rotor-stator ATP synthase subunit (ion gradients were likely supplied geochemically)
- substrate-level phosphorylation (acetylphosphate from acetyl-CoA)
- reverse gyrase – specific for currently living hyperthermophilic organisms
- chemolithoautotrophy enzymes present (WL pathway), chemoorganoautotrophy enzymes absent

Wood-Ljungdahl (WL) anaerobic pathway of carbon fixation



M.C. Weiss et al. *Nature Microbiology*,
2016, Article 16116

A primitive metabolic pathway for carbon fixation, still used by some contemporary chemoautotrophic organisms

Metabolism of LUCA

Among six currently known pathways of CO₂ fixation, only WL pathway was present in LUCA:

The relevant enzymes are packed with FeS and FeNiS centres

They require cofactors: flavin, F₄₂₀, methanofuran, two pterins and corrins

Hydrogenases also present in LUCA's genome → electrons likely obtained from hydrogen, as in modern microbes using the WL pathway

Nitrogenase and glutamine synthetase serve for nitrogen fixation

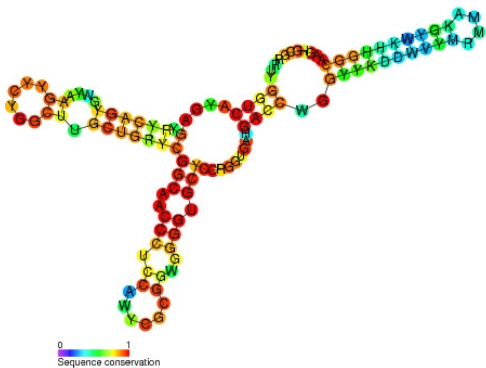
WL pathway, nitrogenase and hydrogenases are very oxygen-sensitive
→ LUCA was an anaerobic autotroph that could live from gases H₂, CO₂, and N₂.

Metabolism of LUCA

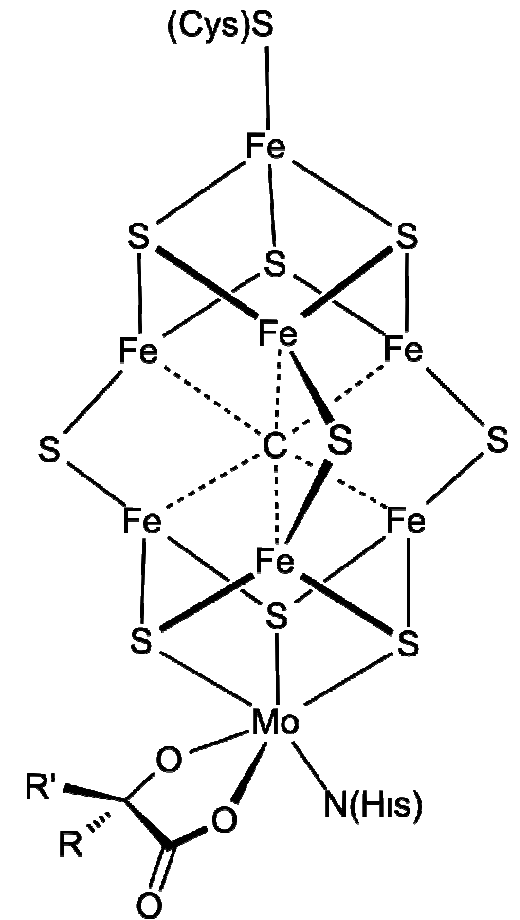
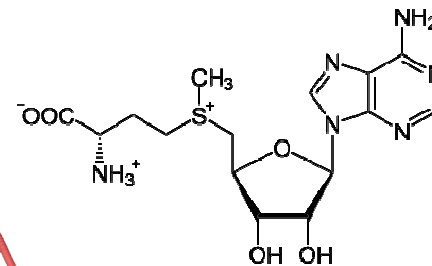
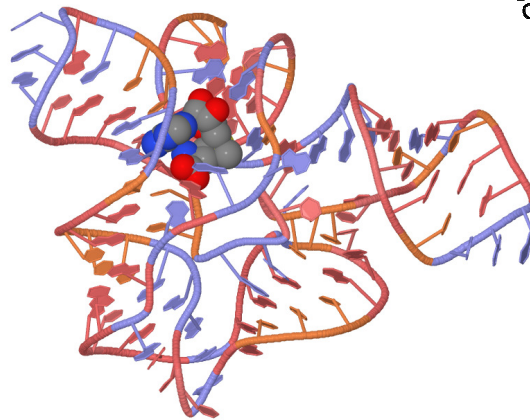
Enzymes for cofactor biosynthesis, including pterins, MoCo, cobalamin, siroheme, TPP, CoM and F₄₂₀, are also conserved.

Many of them are S-adenosyl methionine(SAM)-dependent

SAM chemistry is based on oxygen-sensitive FeS-containing proteins that initiate radical-dependent methylations.

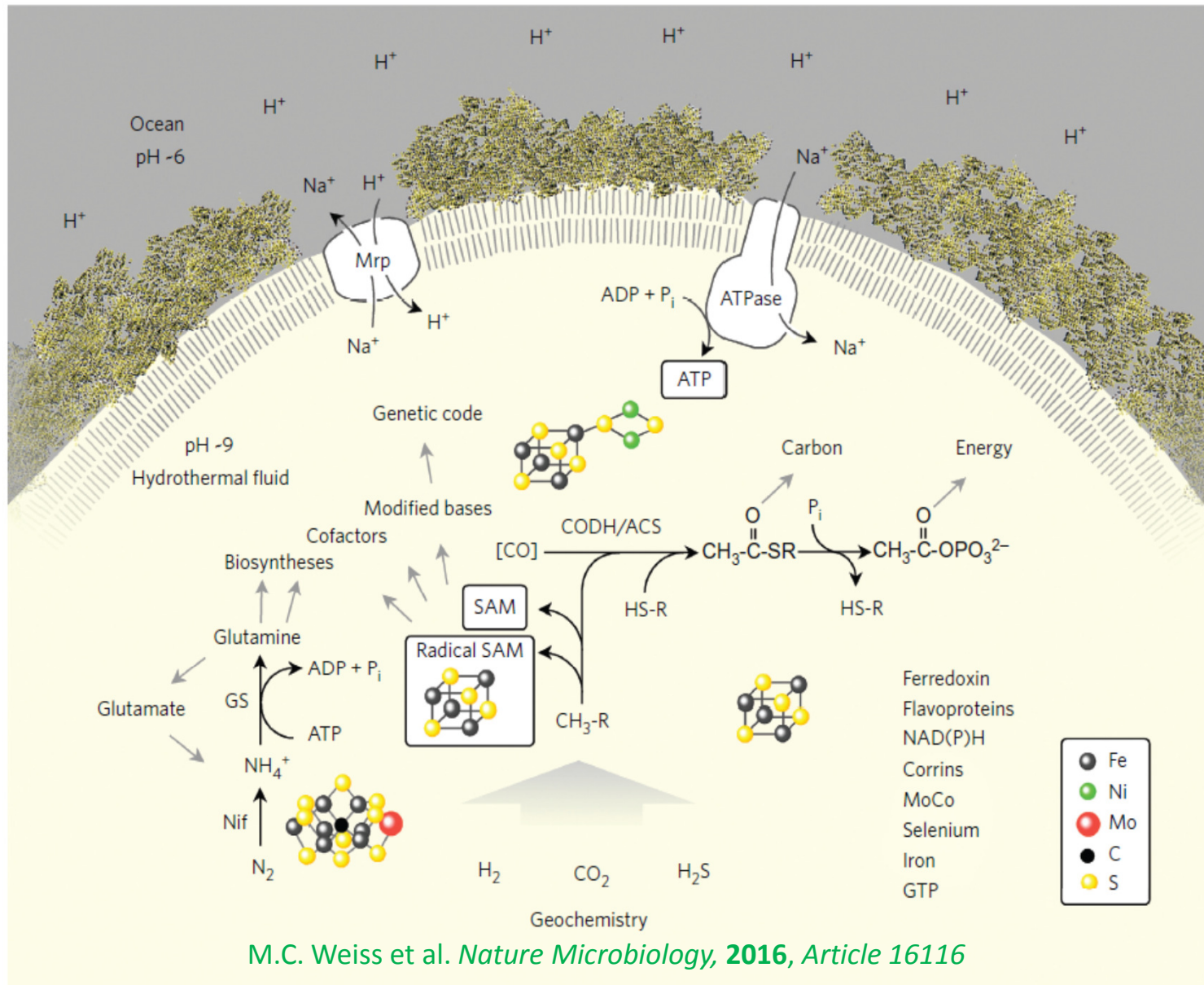


SAM-binding riboswitches



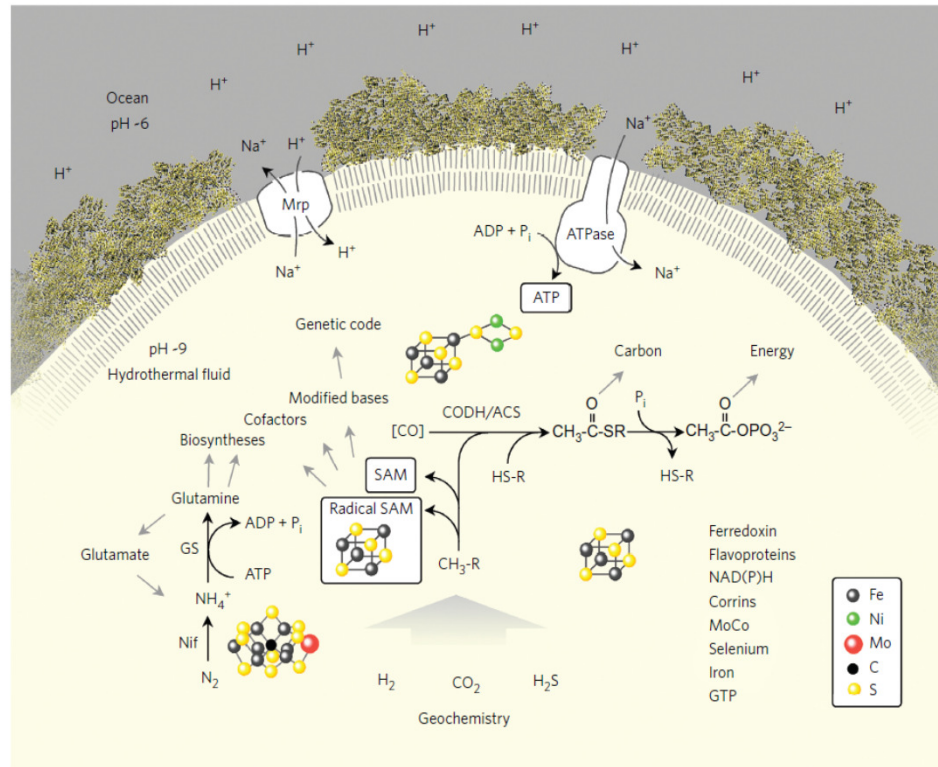
FeMo cofactor of nitrogenase

M.C. Weiss et al. *Nature Microbiology*,
2016, Article 16116



LUCA reconstructed from the genome data

Summary of the main interactions of LUCA with its environment, a vent-like geochemical setting as inferred from genome data.



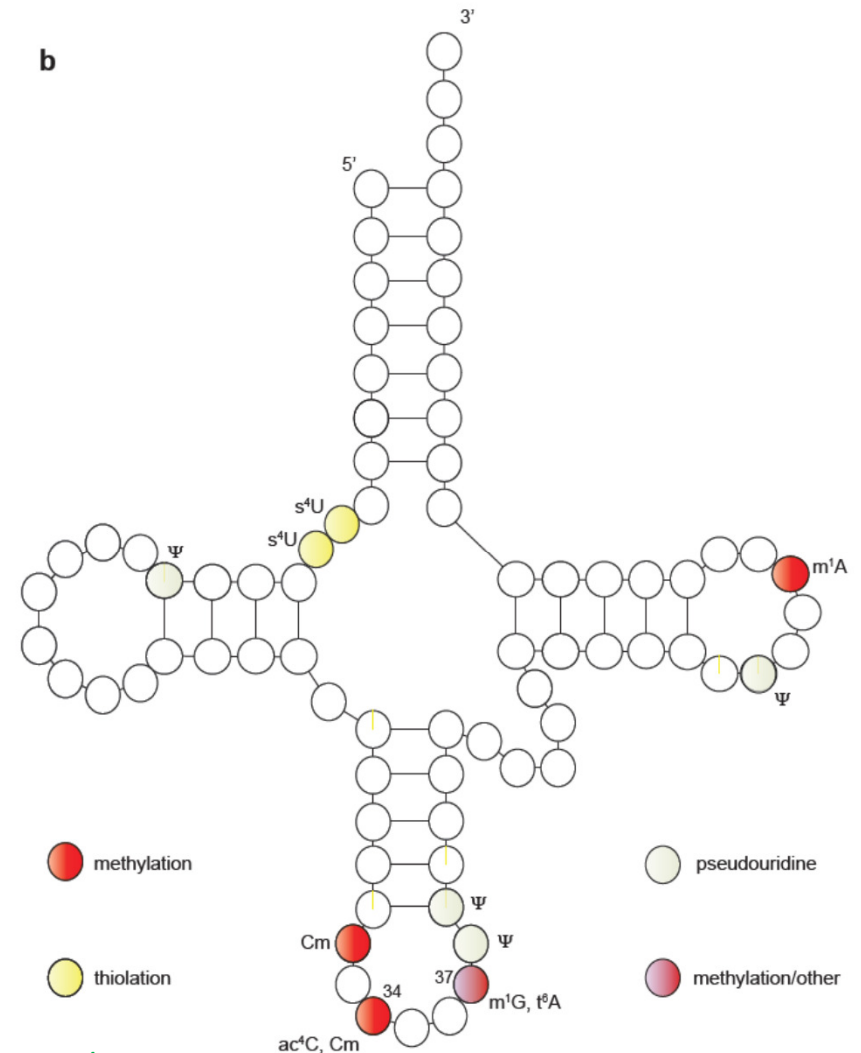
CO source unknown: In modern CODH/ACS complexes, CO is generated from CO₂ and reduced ferredoxin. In primordial metabolism, CO can appear uncatalysed *via* the gas water shift reaction or catalysed *via* transition metals.

A Na⁺/H⁺ antiporter could transduce a geochemical pH gradient (indicated on the left) inherent in alkaline hydrothermal vents into a more stable Na⁺ gradient to feed a primordial Na-dependent ATP synthase.

Modified nucleosides and the genetic code

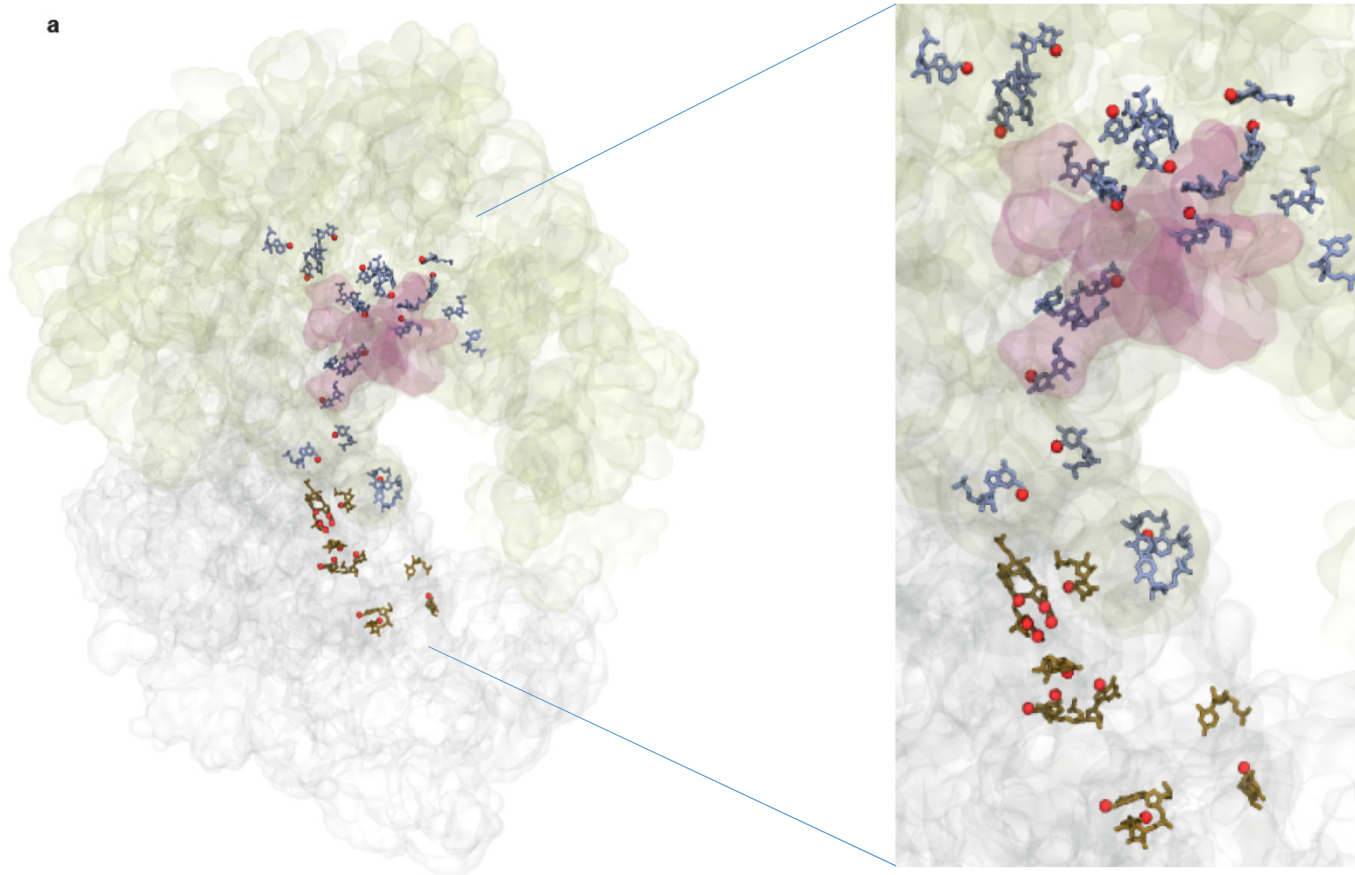
LUCA had also genes involved in RNA nucleoside modifications (mainly methylations and thiomethylations) still required today e.g. for the anticodon recognition process.

Cloverleaf secondary structure representation of tRNA showing only those posttranscriptional nucleoside modifications that are conserved among bacteria and archaea in both identity and position. (5-methoxyuridine at position 34 in archaea has been disputed).



M.C. Weiss et al. *Nature Microbiology*, 2016, Article 16116

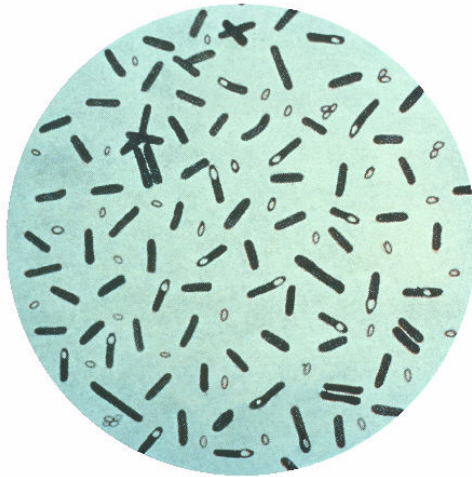
Modified nucleosides and the genetic code



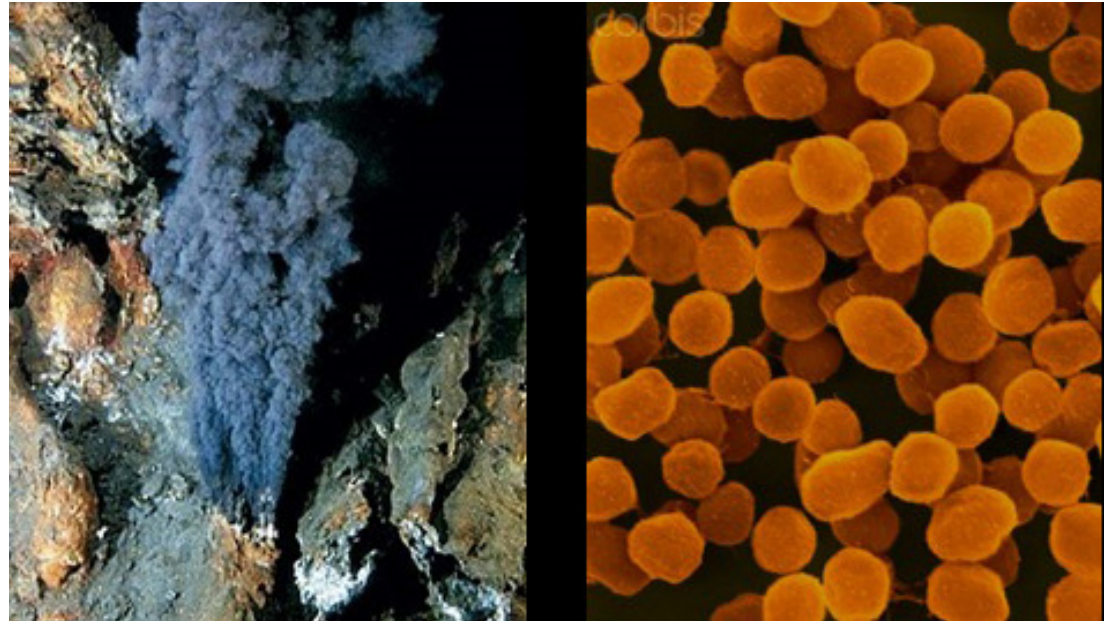
M.C. Weiss et al. *Nature Microbiology*,
2016, Article 16116

Structure of the *E. coli* ribosome (PDB ID: 4YBB), with the large and small subunits shown in green and silver, respectively. The peptidyl-transferase site is shaded pink. The modified nucleosides of 23S rRNA are depicted in icy blue, while in 16S rRNA they are ochre. Modification of C2501 to 5-hydroxycytidine is not present in the structure. Methyl group carbons are shown as red balls.

Closest living relatives of LUCA



clostridia
anaerobic bacteria
(botulin, gangrene, tetanus)

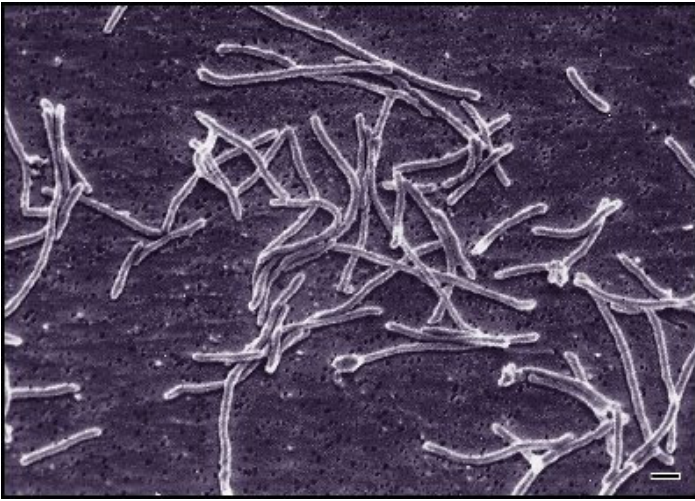


Deep ocean vent - home to the extremophilic archeon
Methanococcus jannaschii

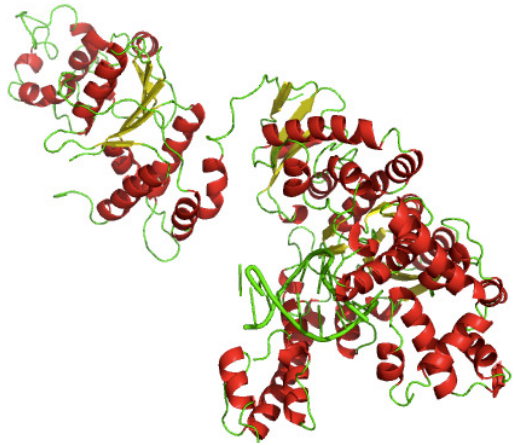
They use the WL pathway, abundant also today, some species can live from methyl groups (methane gas on marshes and wetlands), and they depend on H₂ (from geology or H₂-producing fermentation)

Geological source of hydrogen: serpentinization (iron + hot water, anoxic) $\text{Fe}^{2+} + \text{H}_2\text{O} \rightarrow \text{Fe}_3\text{O}_4 + \text{H}_2$

Thermophiles



Thermus aquaticus

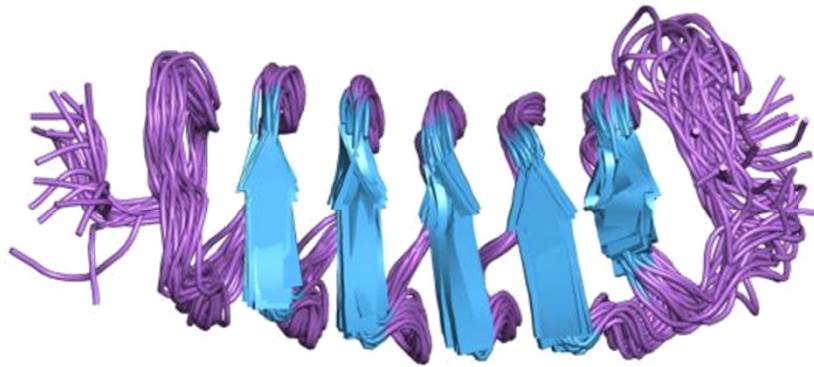


3D structure of Taq Polymerase.

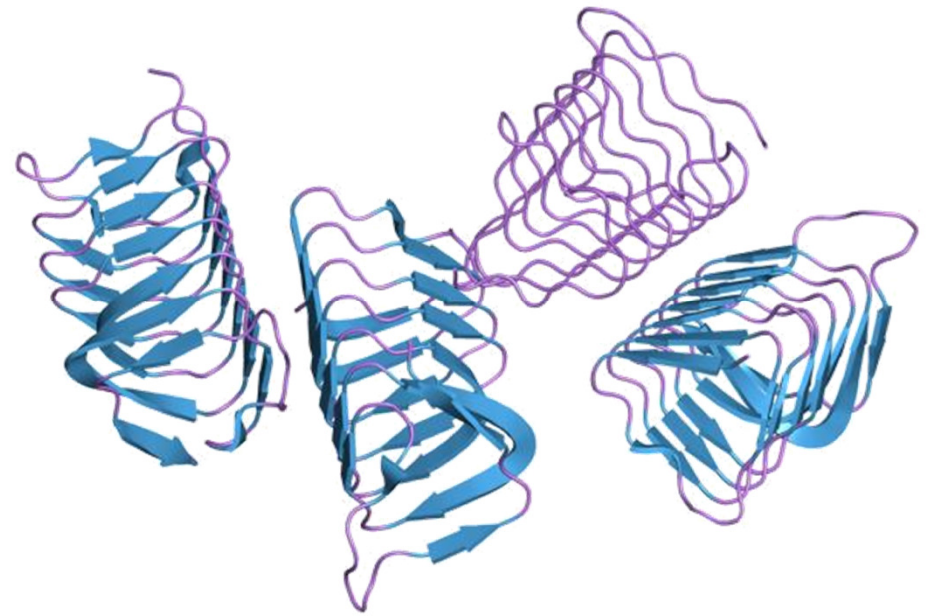


Hot springs with algae and bacteria in Yellowstone National Park

Cold adaptation

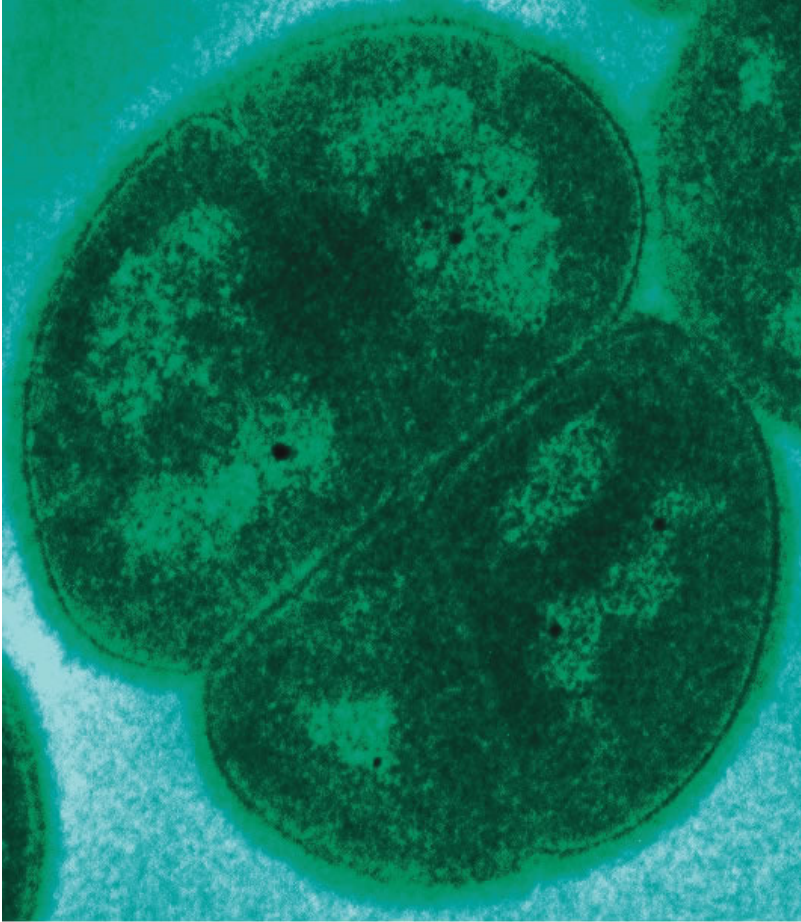


Structure of the *Tenebrio molitor* beta-helical antifreeze protein



Structure of *Choristoneura fumiferana* (spruce budworm) beta-helical antifreeze protein

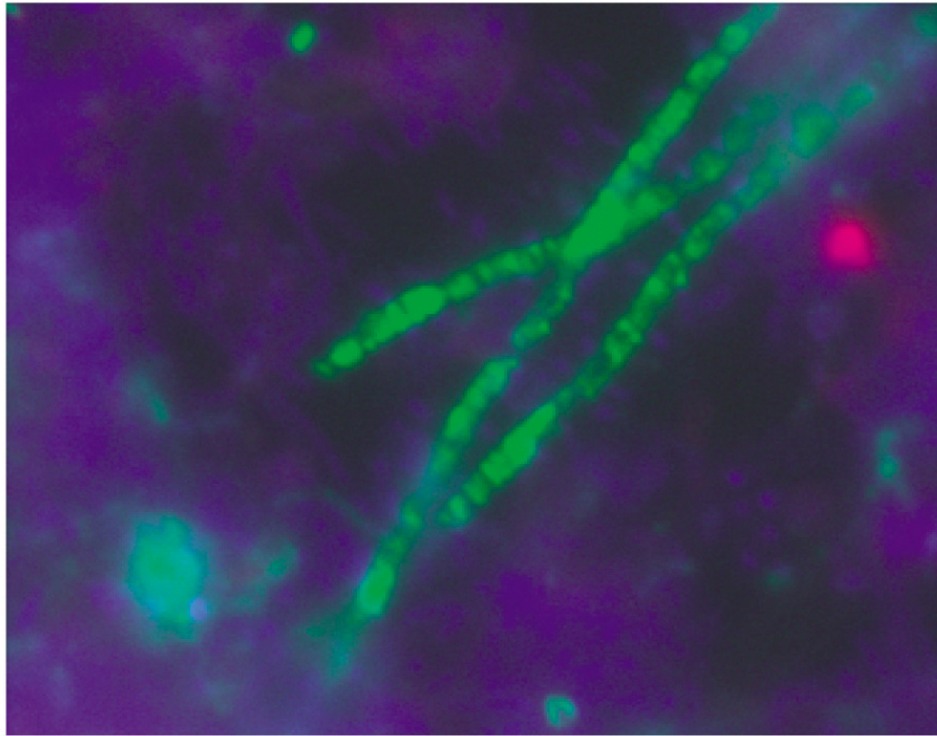
Drought, salinity, radiation



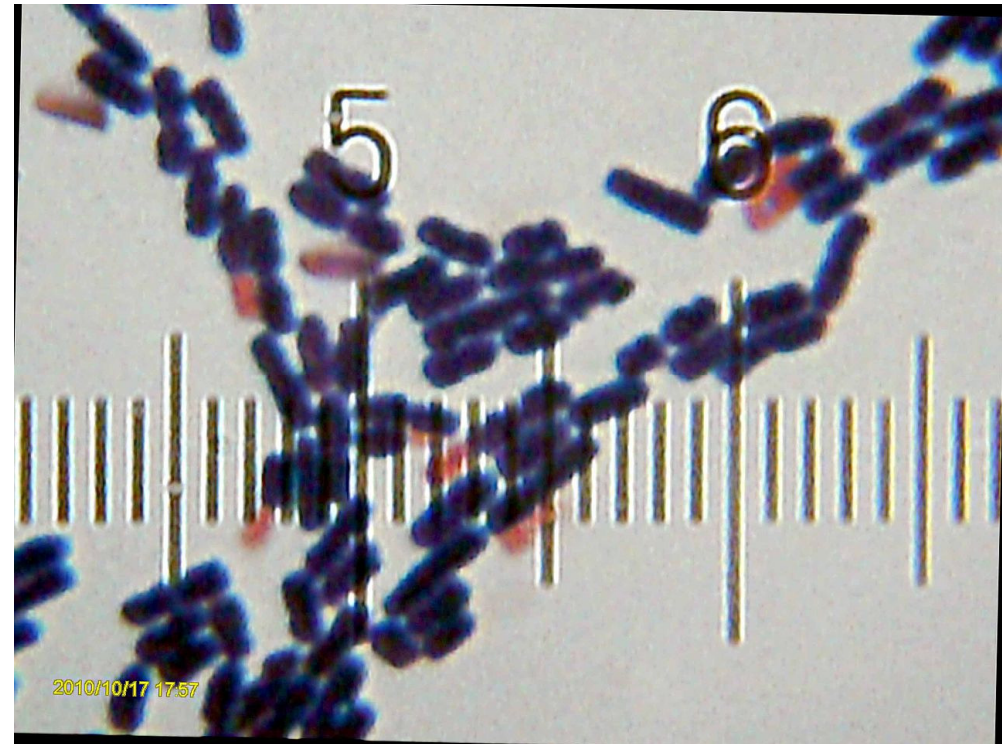
A tetrad of *D. radiodurans*

Efficient DNA damage repair,
Trehalose as the main sugar – glass solid, no crystallization

Acid, base



Acidobacterium



A typical *bacillus* culture. Many alkaliphiles possess a *bacillus* morphology



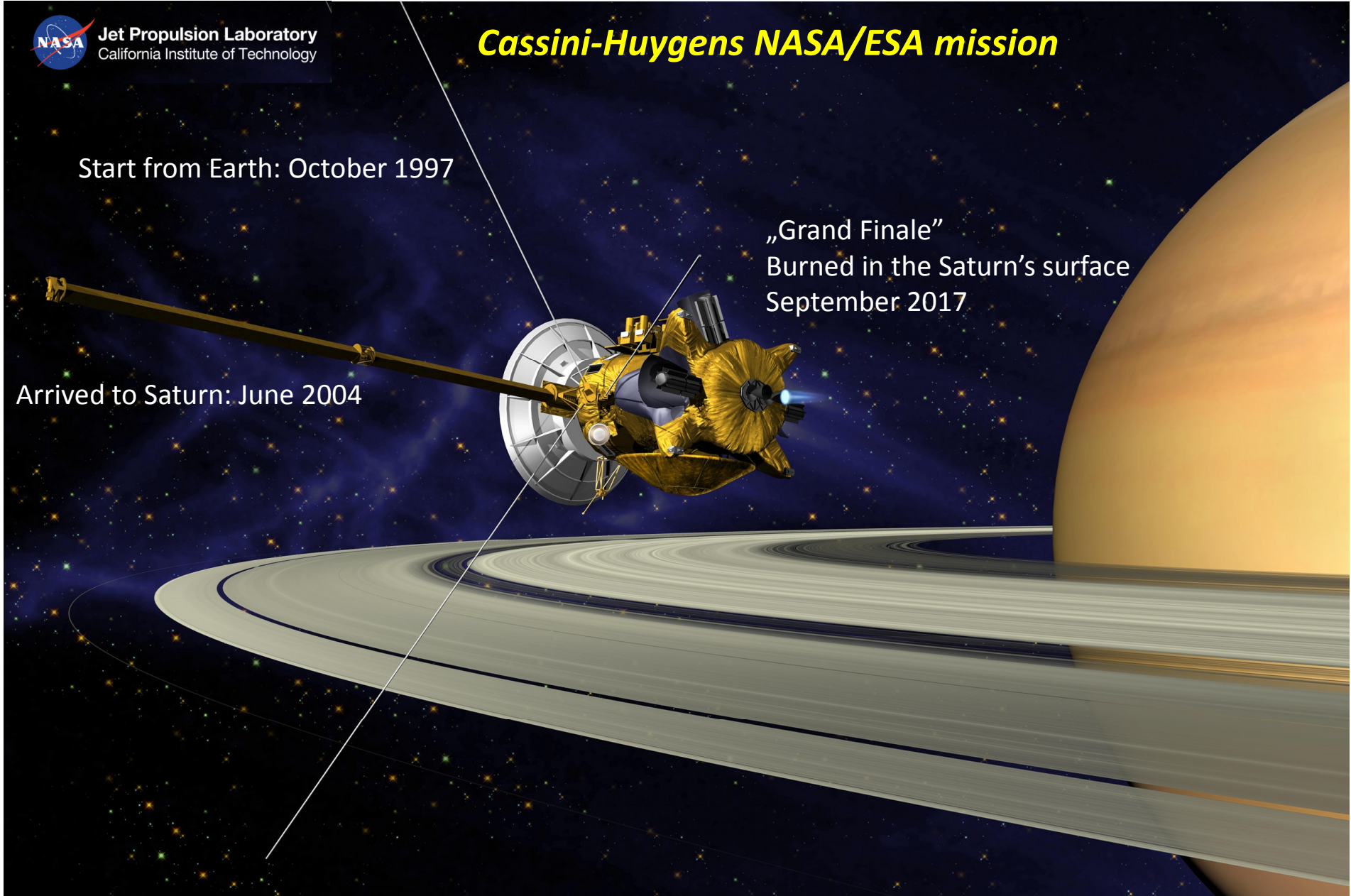
Jet Propulsion Laboratory
California Institute of Technology

Cassini-Huygens NASA/ESA mission

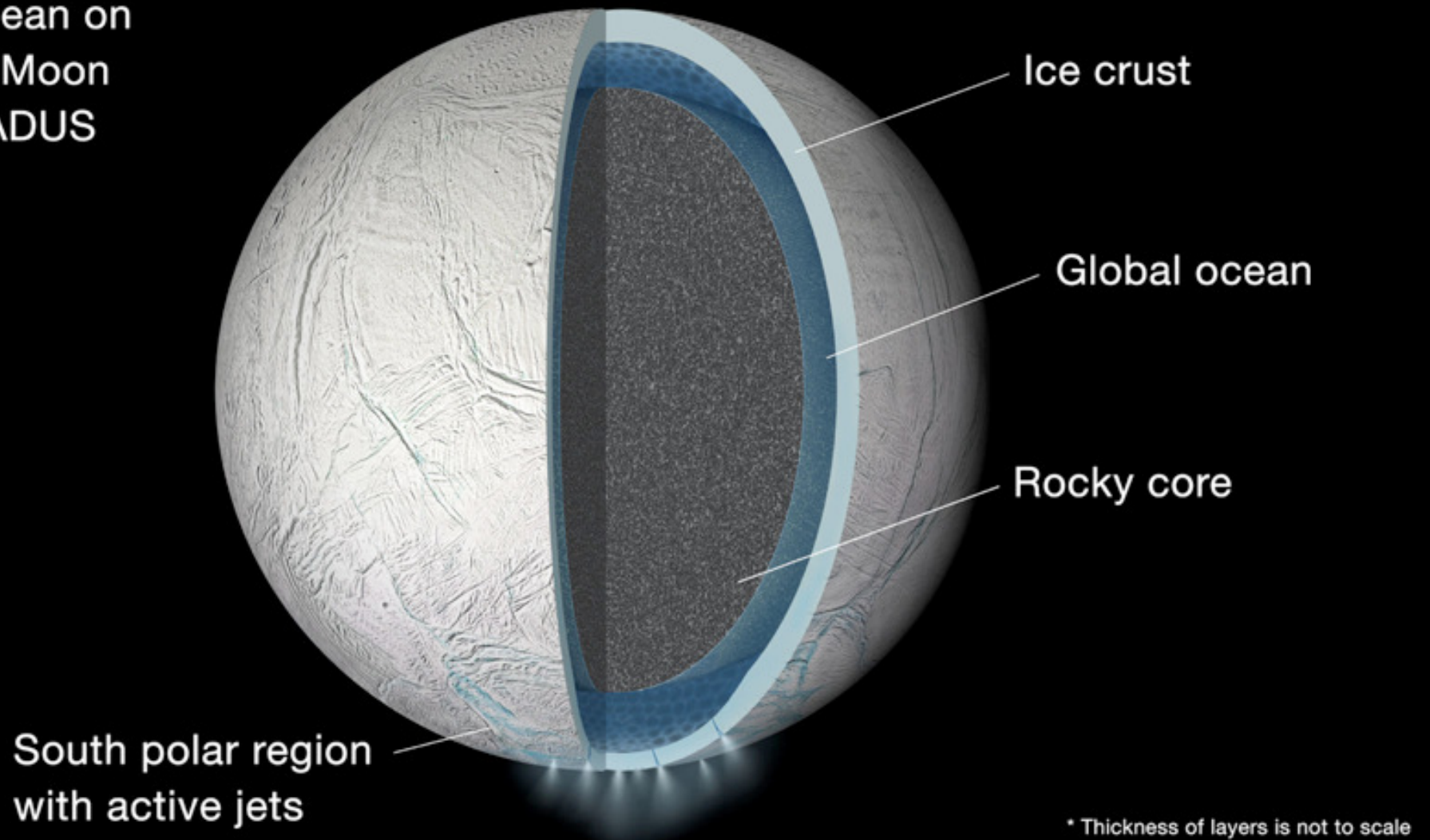
Start from Earth: October 1997

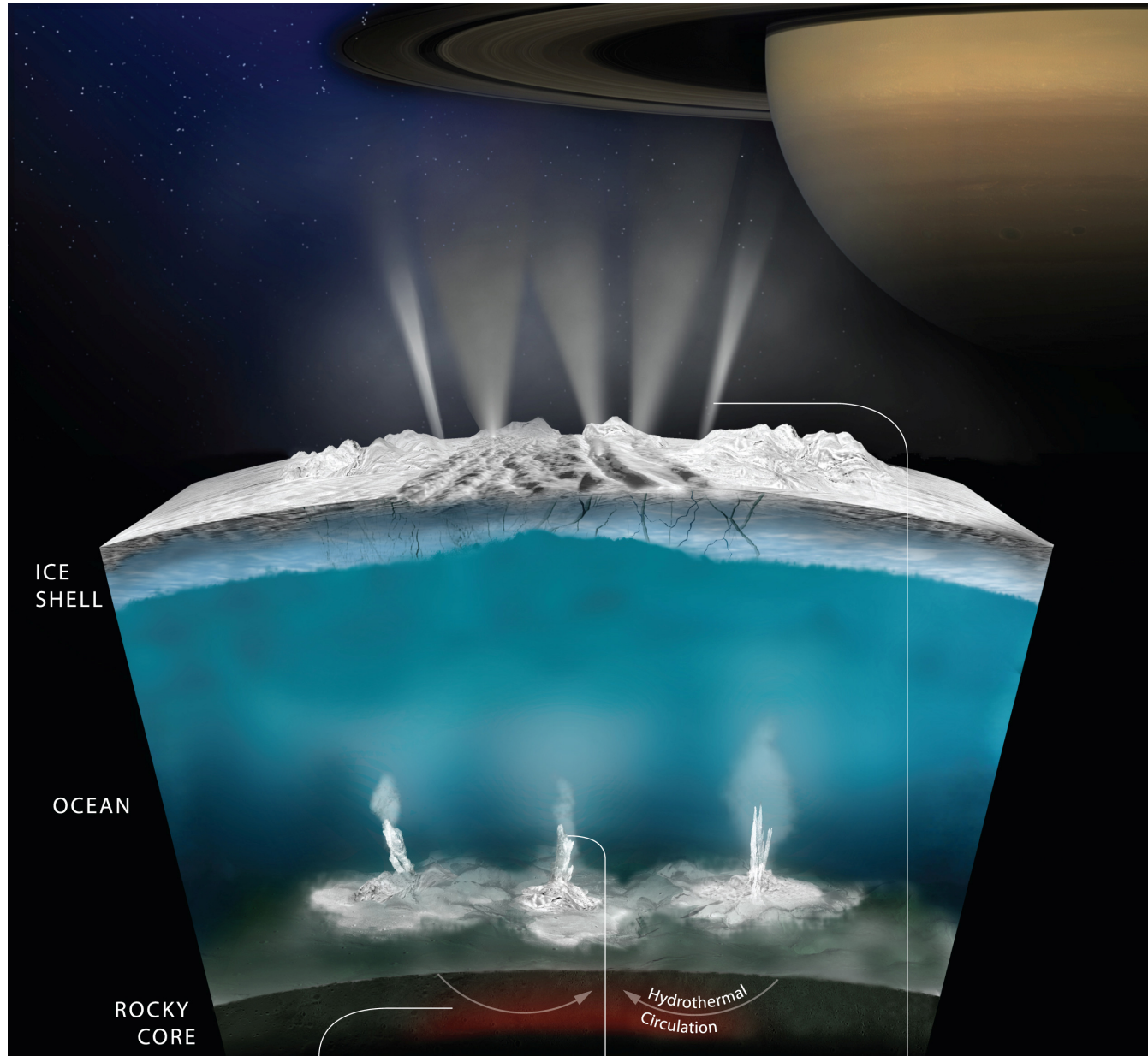
„Grand Finale“
Burned in the Saturn's surface
September 2017

Arrived to Saturn: June 2004



Global Ocean on
Saturn's Moon
ENCELADUS

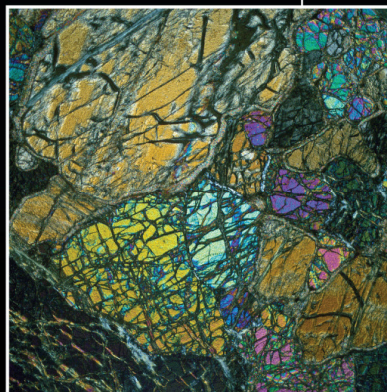




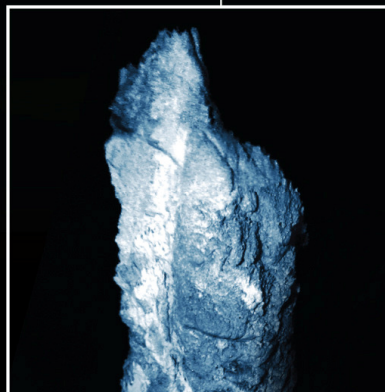
OCEAN

ROCKY
CORE

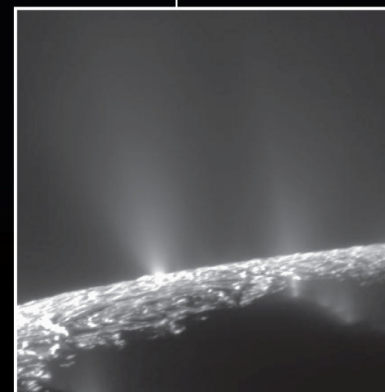
Hydrothermal
Circulation



WATER-ROCK REACTIONS



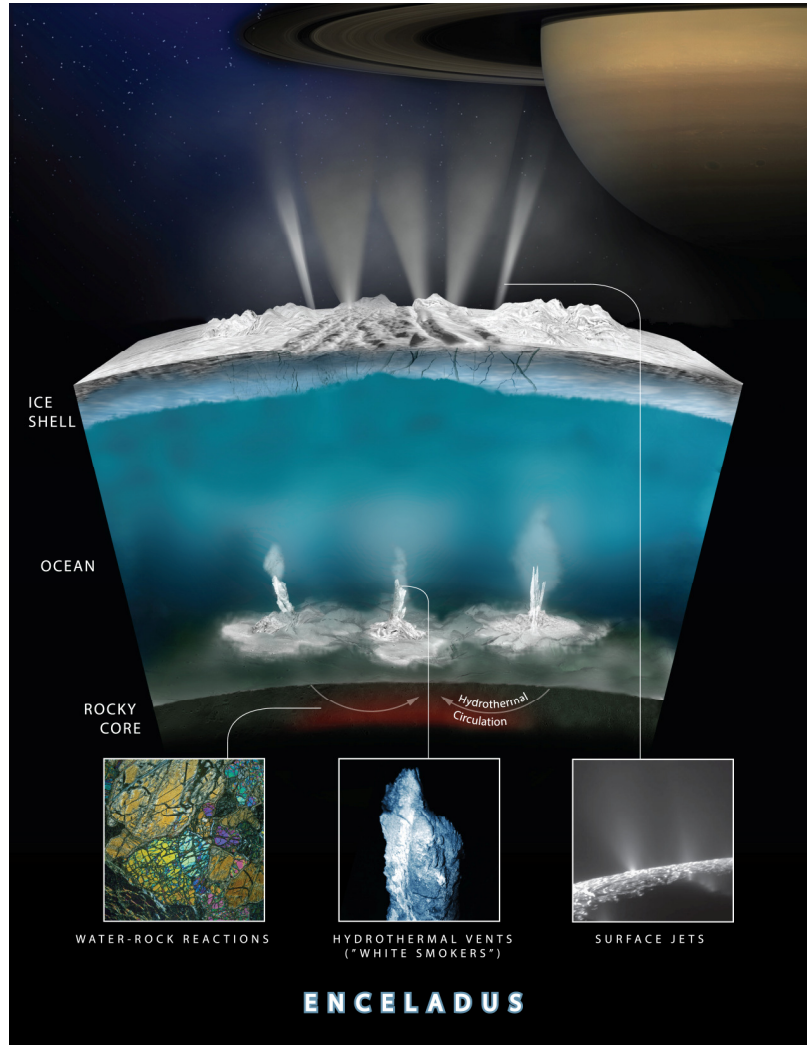
HYDROTHERMAL VENTS
("WHITE SMOKERS")



SURFACE JETS

ENCELADUS

Can (and does?) Enceladus host (microbial) life?



Fuels for life on one of Saturn's moons

NASA's Cassini spacecraft has discovered hydrogen and carbon dioxide erupting from Saturn's moon Enceladus – critical ingredients that sustain microbial life in extreme environments on Earth

ENCELADUS
Diameter: 504km

Rocky core
Ocean
Ice crust

CASSINI

2015: During Cassini's deepest-ever dive into plume of spray, instruments detected presence of organic chemicals in plume vapour

Geysers erupting from cracks in south polar region

Methanogenesis: Process by which microorganisms on Earth obtain energy by using hydrogen to produce methane from carbon dioxide

Hydrogen and carbon dioxide...
...produce methane and water

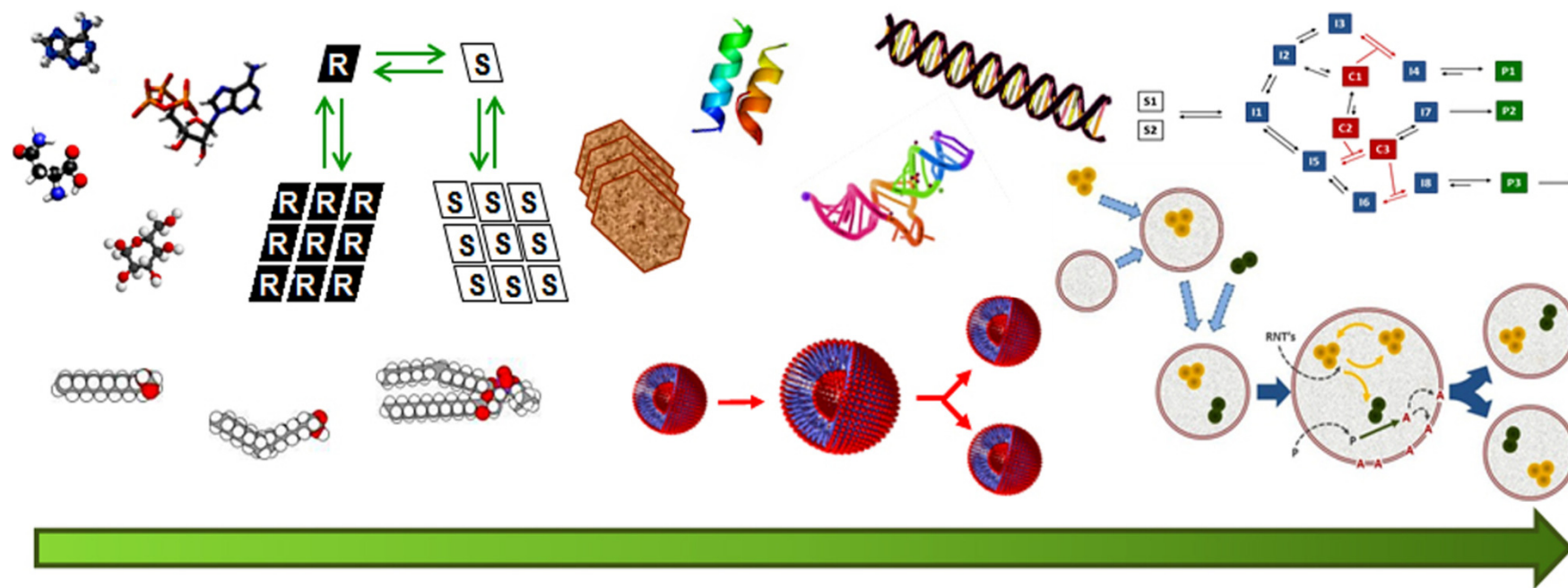
Hydrothermal vent: Molecular hydrogen most likely formed by chemical reactions between hot rocks and water in ocean

Ice
Ocean
Core

Sources: Science, Jet Propulsion Laboratory, Hunter Waite and colleagues © GRAPHIC NEWS

The molecular origins of life – important stages

biomolecules – biopolymers – self-replication – metabolism - compartmentalization



Increasing complexity from molecules to systems