Emergence of life in an inflationary universe

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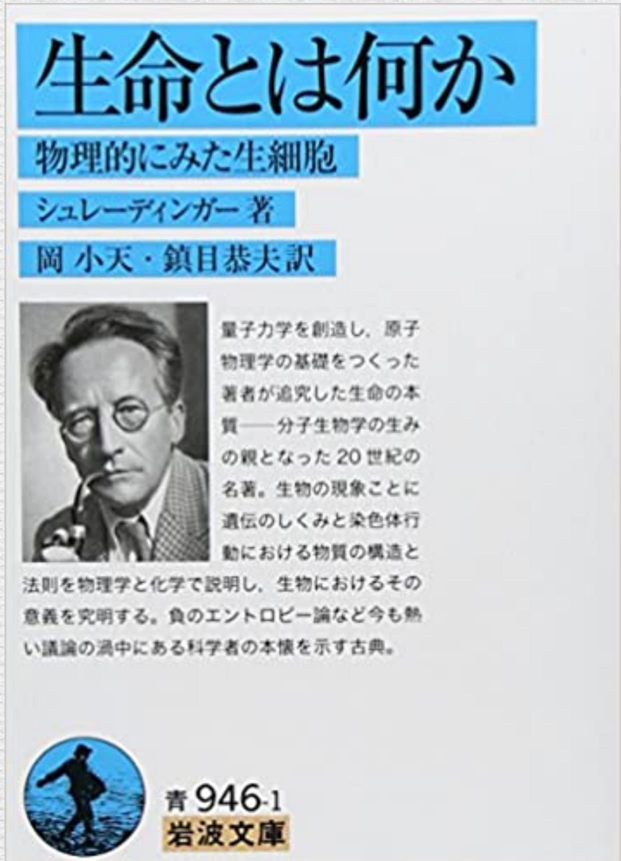
How an astrophysicist started to think about the origin of life?

- Some people say…
  - Sometimes a senior scientist starts a crazy study…
  - When a physicist starts to study about life, it is the end of his/her carrier…

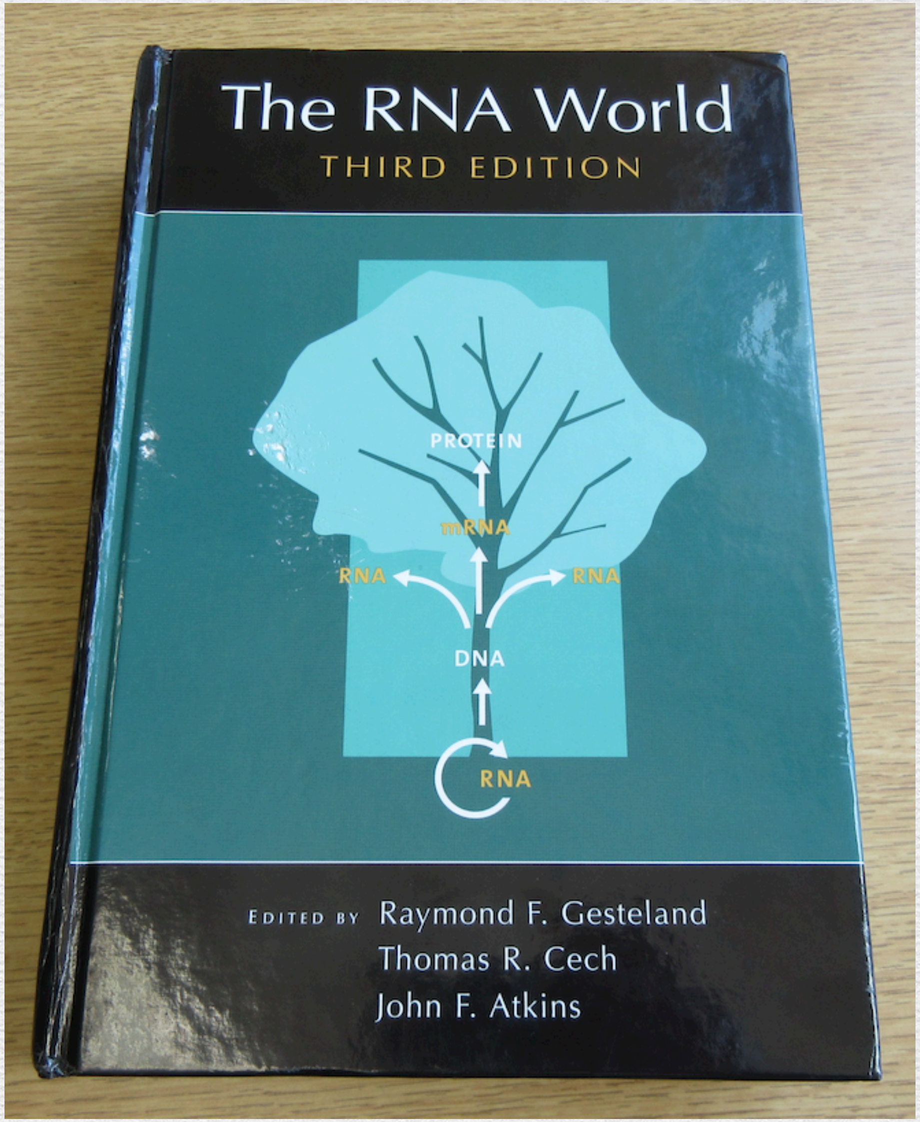
- Some famous people in astronomy/physics started to think about life
  - E. Schrodinger
  - F. Hoyle
  - … and more?



An example of a cosmologist turned into a biologist

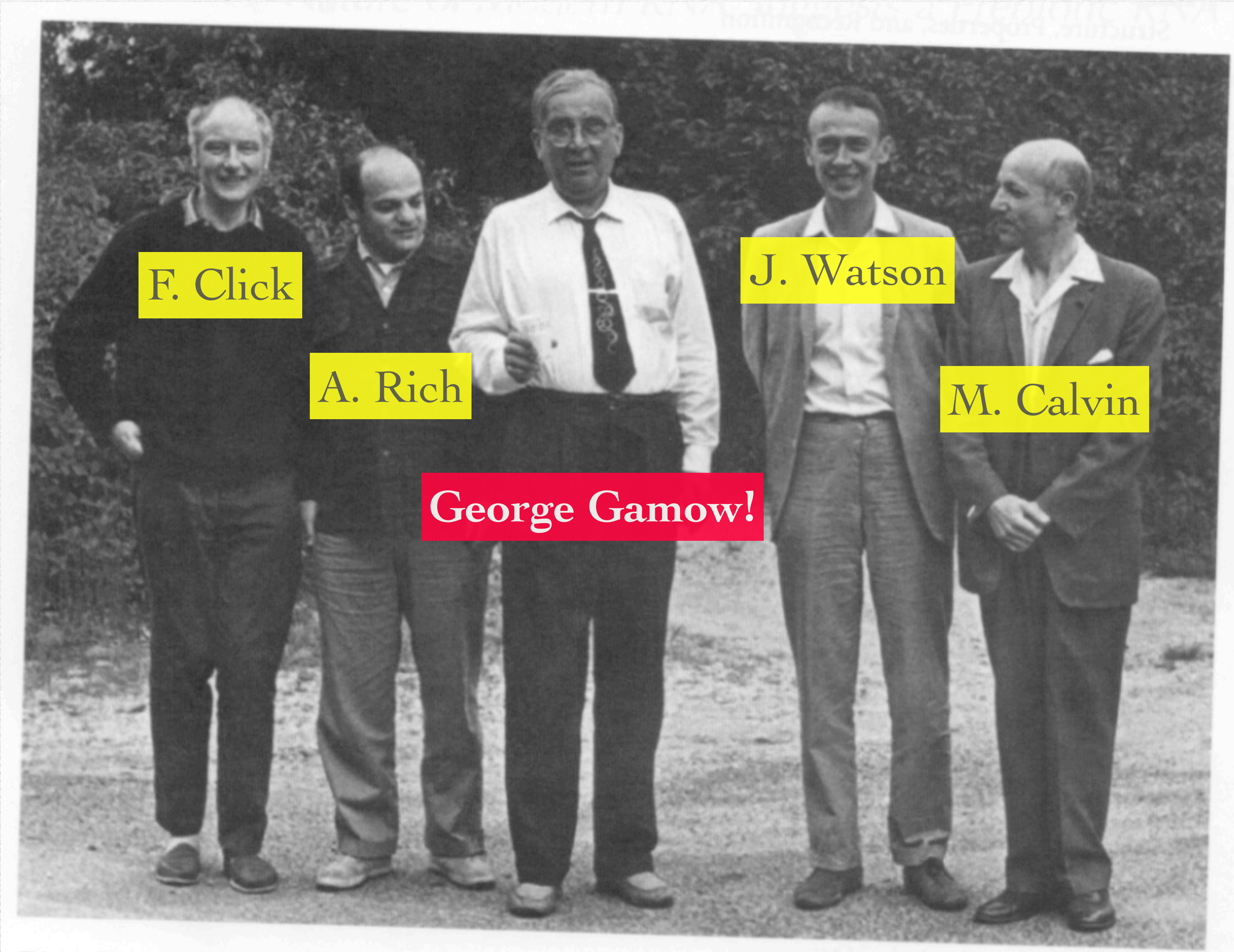
- One day, I wanted to read a chapter of a book “the RNA world (3rd edition, 2006)

- Only in the library of School of Medicine in my university!
    - For the first time I visited the medicine library…



An example of a cosmologist turned into a biologist

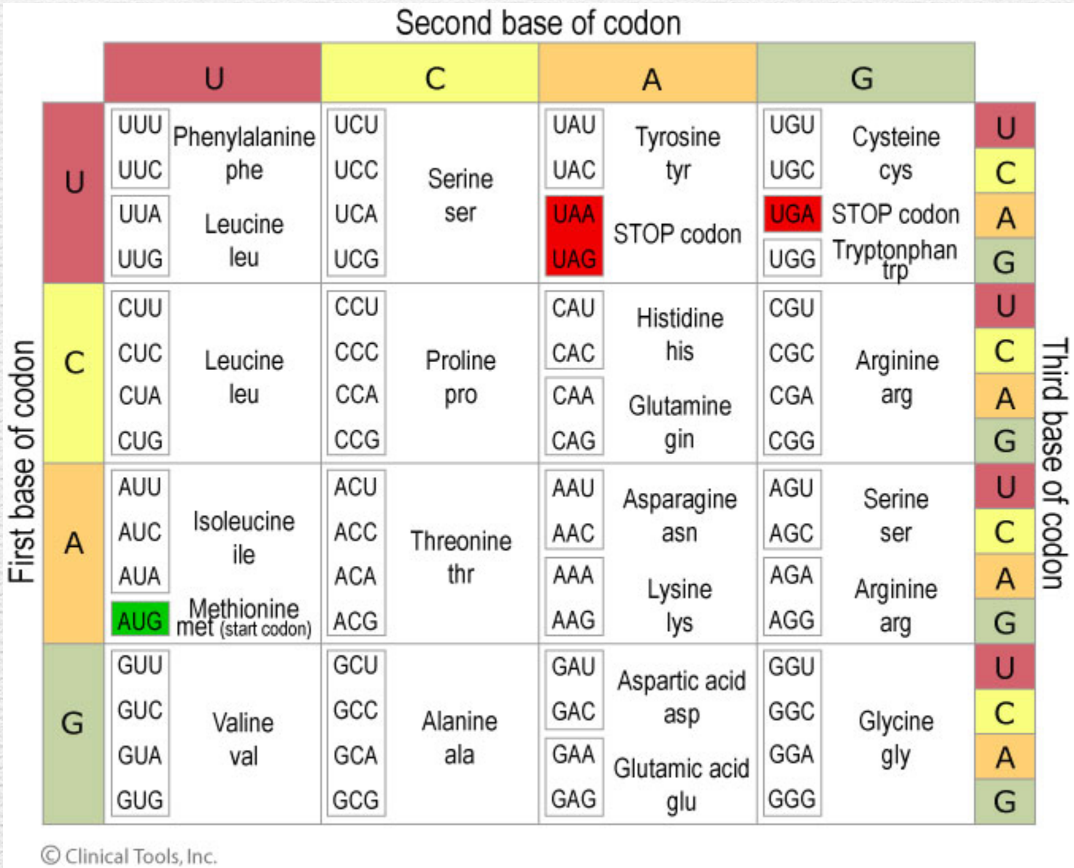
- On the first page of the book, there is a photo
- Titled "the RNA Tie Club Members", taken in 1963



An example of a cosmologist turned into a biologist

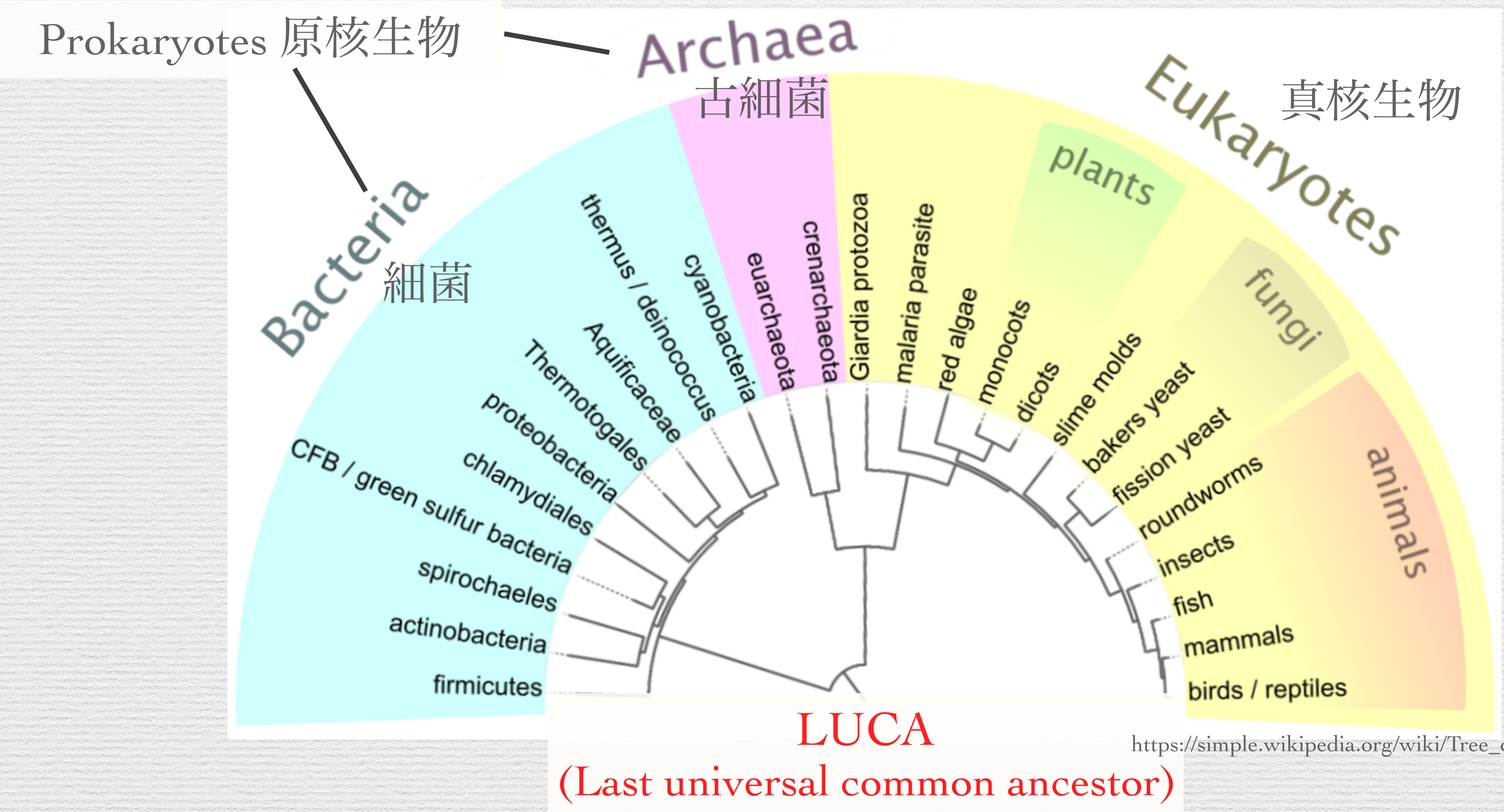
- According to Wikipedia
  - Gamow & Watson co-founded the RNA Tie Club (1954)
  - Crick said that Gamow's suggestions helped him in his own thinking about the protein formation by DNA information
  - 3 nucleotides with 4 different base types (4^3=64 combinations) code 20 different amino acids
  - Gamow pointed out: if the order of 3 nucleotides is irrelevant, the different combinations reduce to $(4+3-1)!/3! = 20$ = types of amino acids!
  - This was incorrect, but contributed to giving rise to models of "biological degeneracy"

The standard genetic code (codon)



Evolutionary history of life on Earth

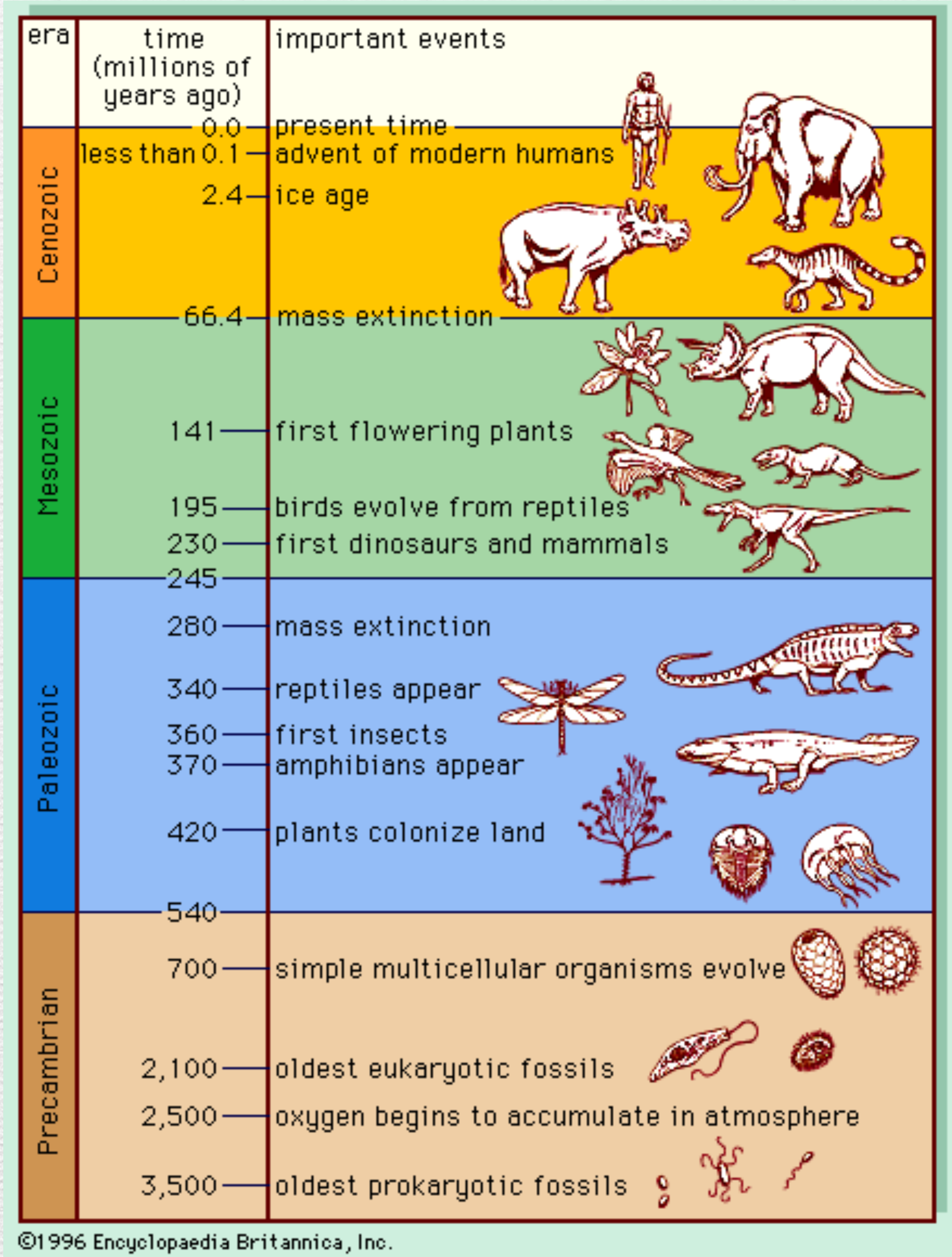
- All cellular life on Earth has evolved from the single last universal common ancestor (LUCA)
- No evidence for another independent abiogenesis event
  - "abiogenesis" = emergence of life from abiotic (=non-biotic) processes



https://simple.wikipedia.org/wiki/Tree_of_life_(biology)

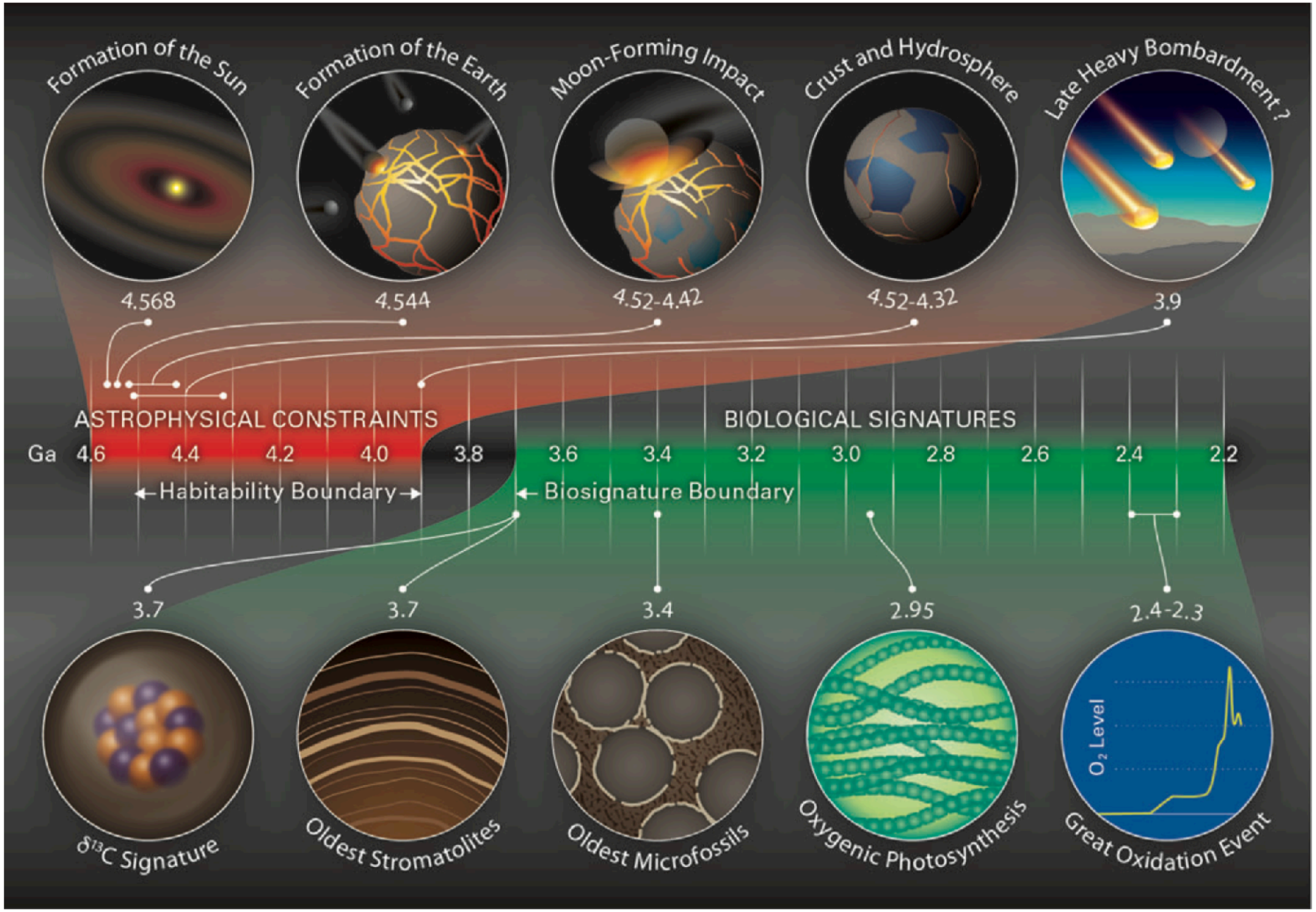
Evolutionary history of life on Earth

- >3.5 Ga (Gyr ago)
  - The first life
- 2.1 Ga
  - The oldest eukaryote fossils
- 0.7 Ga
  - Appearance of multicellular organisms
- 0.5 Ga
  - Increase of oxygen level
  - Plants colonize land
  - Diverse multicellular organisims



When the first life appeared on Earth?

- Older than 3.7 Ga from Fossil records / carbon isotope
- Appearance of the earliest crust & hydrosphere: 4.5 Ga (soon after the Earth formation)
- Life may be possible only after late heavy bombardment (3.9 Ga)
- The time taken for life to appear: 0.2-0.8 Ga (4-18% of the Earth current age)



Pearce+'18

Abiogenesis probability on a planet?

- The early emergence of life in the Earth history implies a high probability?
  - (the only one) argument that favors a high probability
  - An immediate counter argument: no evidence for multiple abiogenesis events

- No strong conclusions can be derived for the moment (Lineweaver+02; Spiegel+12)
  - Early appearance may be just by chance (4-18% chance probability)
  - Early Earth may have been more favorable environment for abiogenesis
    - e.g. higher geological activities, more hydrothermal vents, …
  - Anthropic effect: an intelligent life must appear before the end of the Earth habitability
    - Increase of solar luminosity may cause the end of habitability in 1 Gyr?

- Arbitrarily small abiogenesis probability cannot be excluded
  - We do not know any other life of a different origin in Earth or in the universe
  - We will find ourselves on a planet where abiogenesis happened

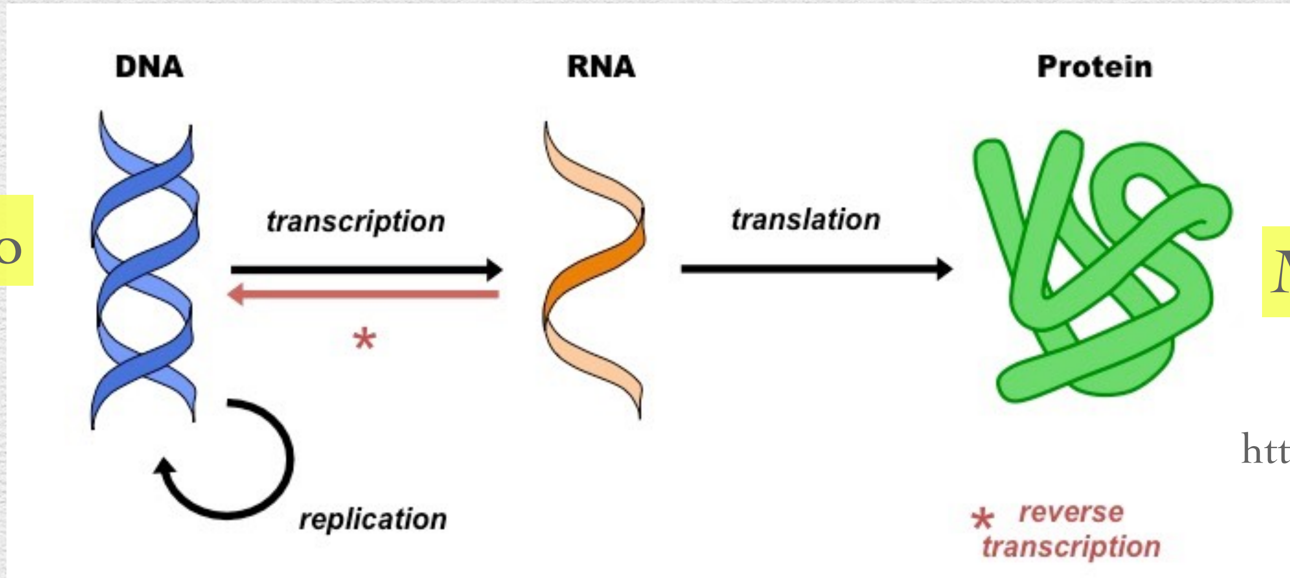
What is life actually?

- Definition of life?
  - The NASA Astrobiology Institute Definition of Life: “self-sustaining chemical system capable of Darwinian evolution.”

- Essential aspects of life
  - Self-replication with genetic information
  - Metabolism (take energy from outside for necessary chemical reactions)
  - Compartmentalized by lipid membrane from outside as a cell

- The central dogma of the life on Earth

genetic info

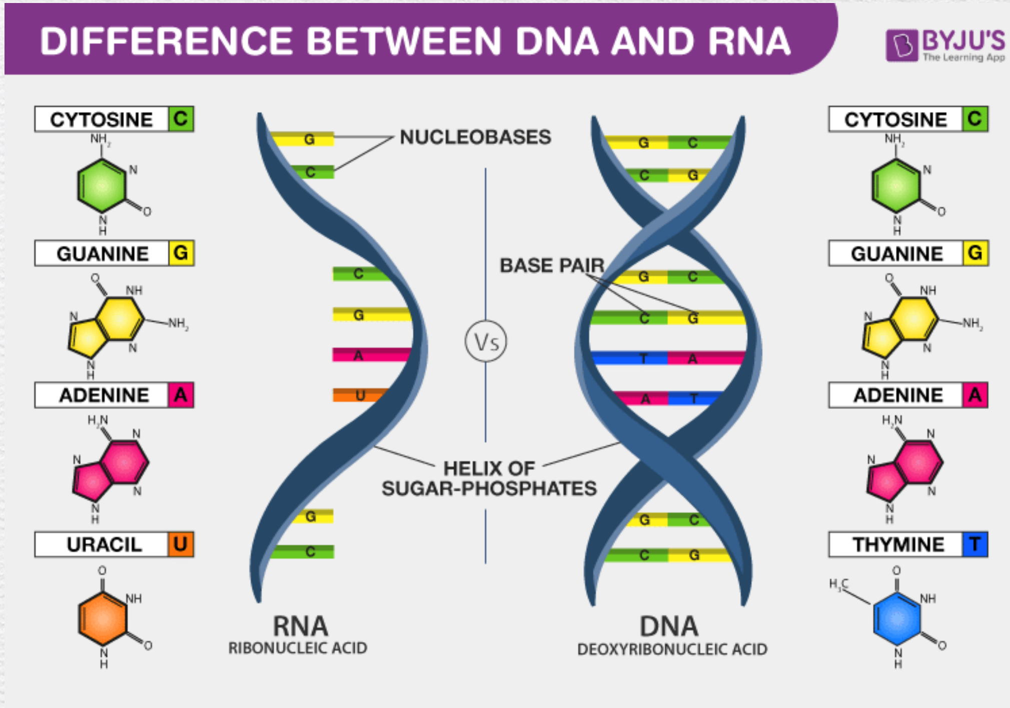


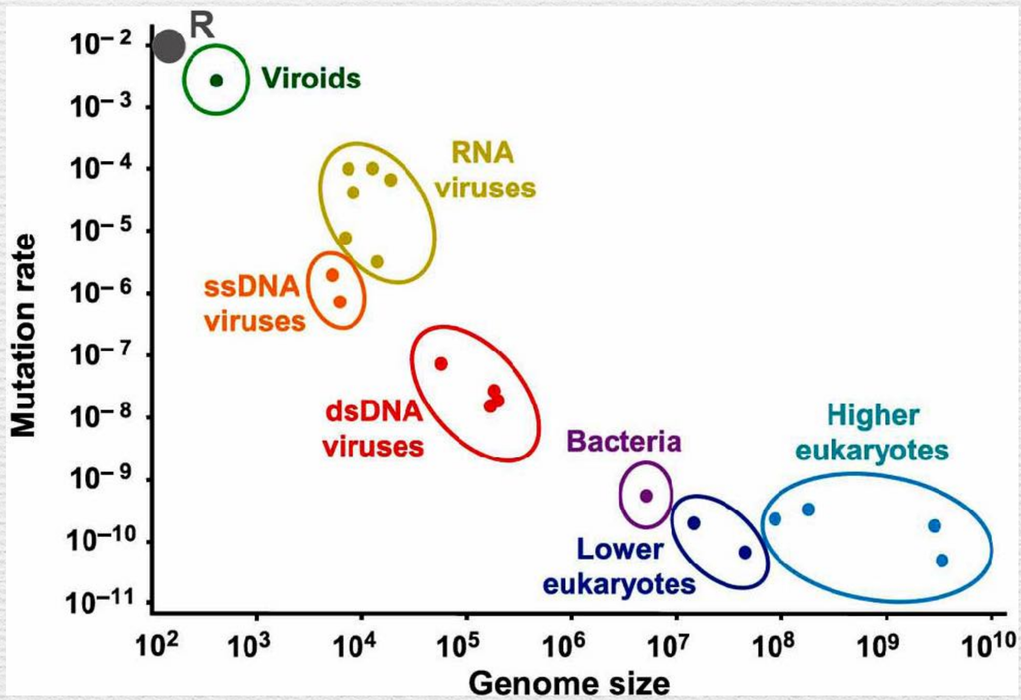
Metabolism

https://ib.bioninja.com.au

Genome in Life

- Genome size (in DNA length [base-pair])
  - Polychaos dubium (a sort of amoeba) 6.7×10^{11} (the biggest size in all organisms)
  - Human 3.0×10^{9}
  - Bacteria/Archaea 1.1×10^{5} — 1.6×10^{7}
  - Virus 1759 — 2.5×10^{6}
  - Viroid 246
  - RNA polymerase ribozyme in in-vitro experiments ~100





Gago+'09; Ruiz-Mirazo+'14

How did the first life appear?

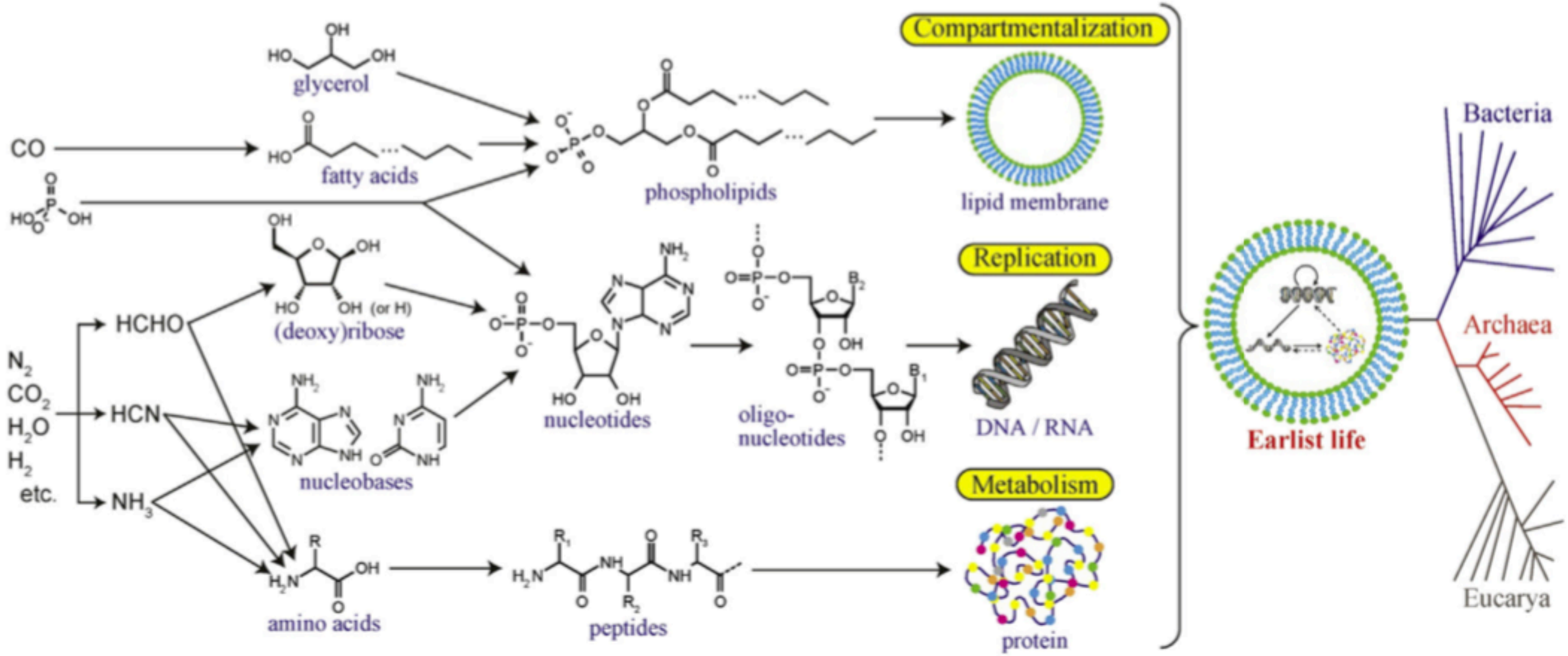
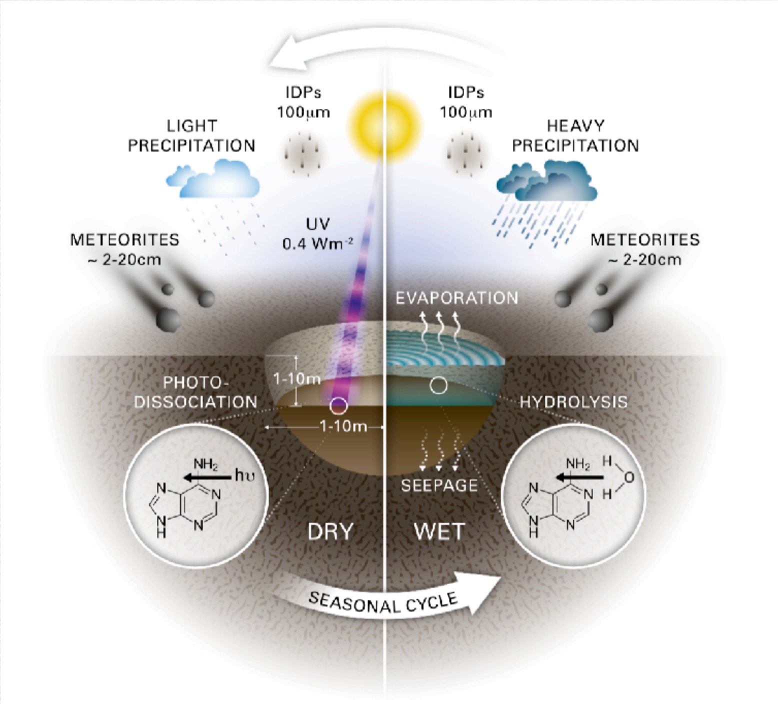


Figure 2. Structures, components, and abiotic synthetic pathways of bio-macromolecules operating three fundamental functions of life (replication, compartmentalization, and metabolism).

Kitadai+'18

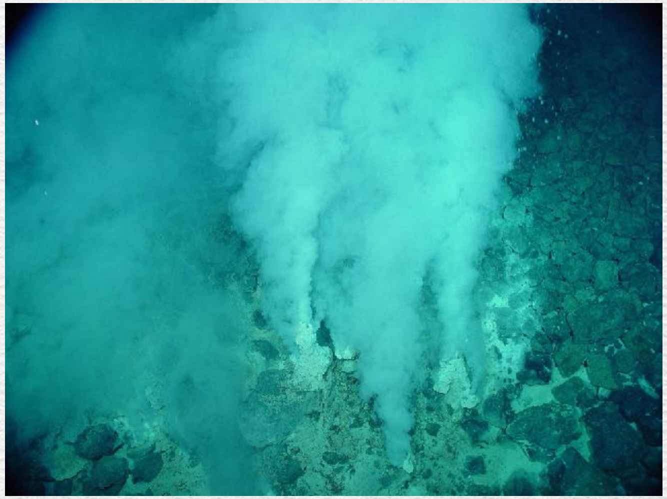
Possible sites of abiogenesis

Warm little ponds?



Pearce+'17

Hydrothermal vents?



https://en.wikipedia.org/wiki/Hydrothermal_vent

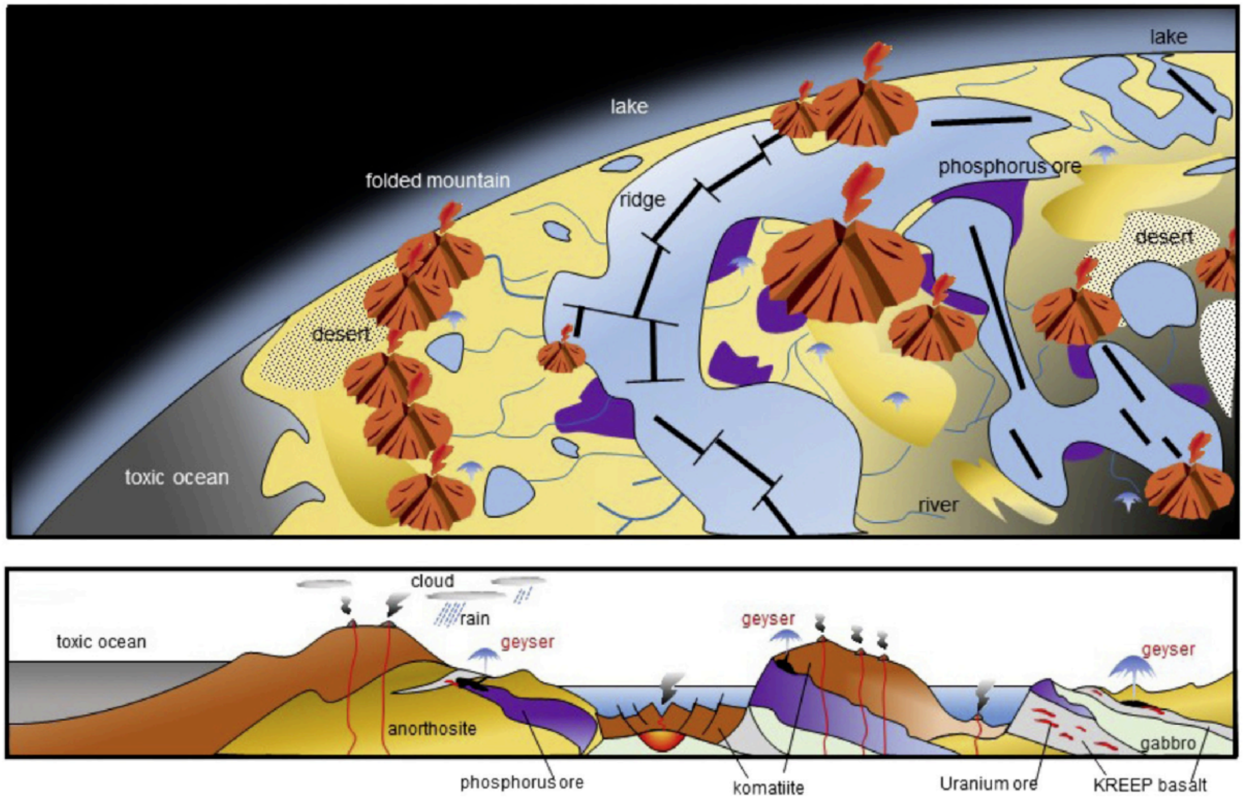
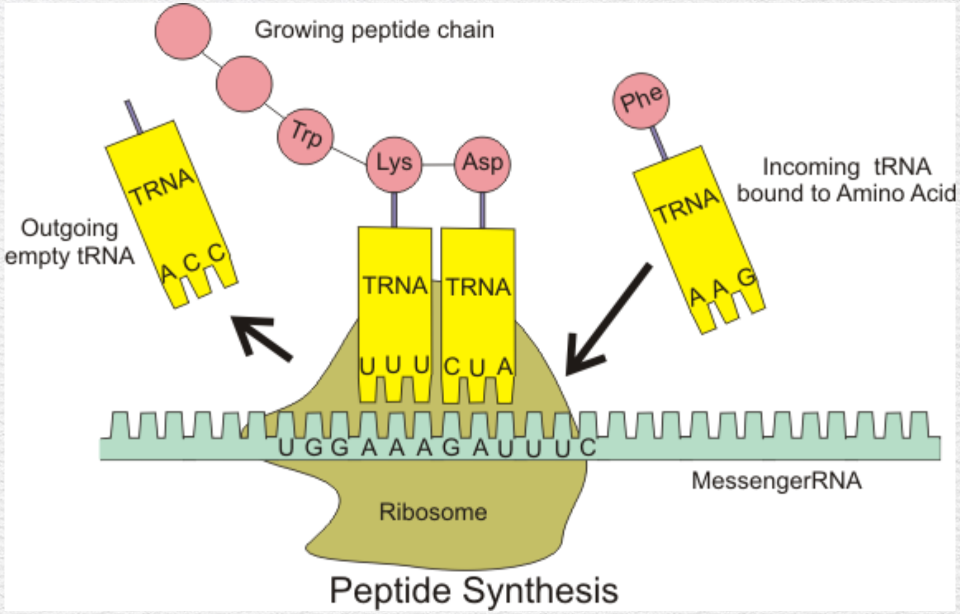


Figure 1. Schematic diagram of a Hadean surface environment proposed by Maruyama et al. (2013) and Santosh et al. (2017).

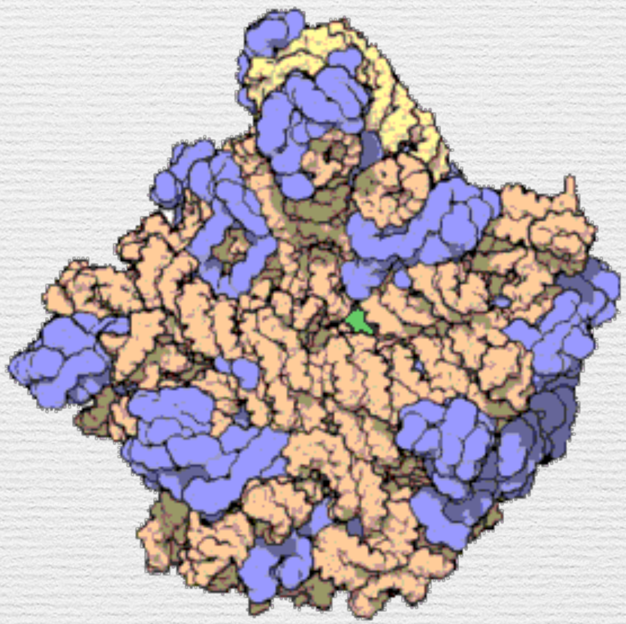
Kitadai+'18

The RNA world hypothesis

- A chicken-and-egg problem:
  - Protein is assembled based on the genetic information coded in DNA
  - DNA needs protein for their self-replication
- DNA vs. proteins: which was the first?
  - A solution: RNA was the first!
- RNA can catalyze some biological reactions like protein enzymes — "ribozyme"
  - The central part of a ribosome (the machine producing protein from RNA) is made of RNA
- The RNA world hypothesis: self-replicating RNA polymerase ribozyme was the earliest form of life
  - It does not reject a pre-RNA world with different types of molecules
- The most popular hypothesis in the origin-of-life studies

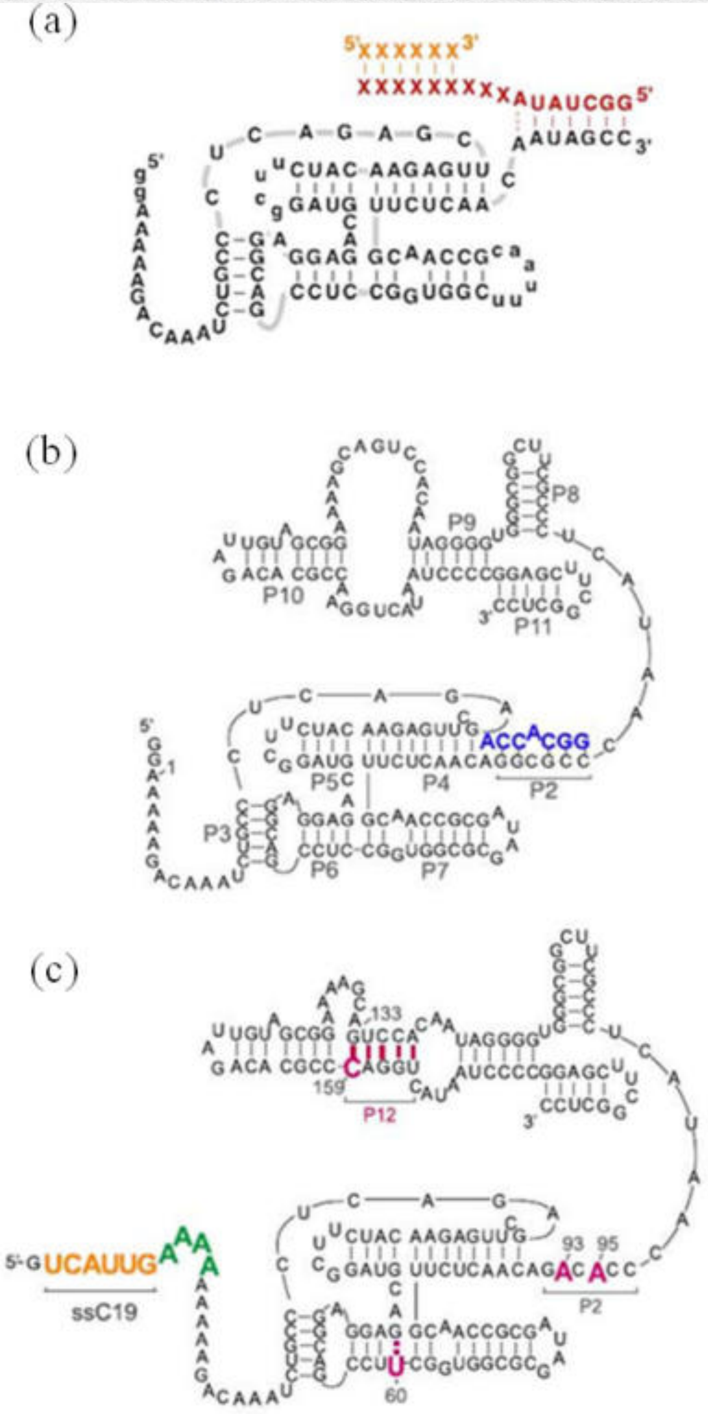


https://en.wikipedia.org/wiki/Ribosome



What did the first RNA polymer look like?

- The RNA world hypothesis does not give any explanation of the first self-replicating RNA polymer
- *In vitro* evolution experiments have produced ribozymes with template-dependent RNA polymerase activity
  - Typically 100-200 nt (nucleotides)
- How short can the first self-replicating RNA be? According to expert biologists (Szostak '93; Robertson+'12):
  - RNA shorter than 25-nt do not show a specified function
  - A reasonable hope of RNA replicase ribozyme with a length of 40-60 nt



Ruiz-Mirazo+'14

The first key step to abiogenesis

- A polymer of RNA (or its precursor) longer than 40-100 nt needs to be produced abiotically, with a particular nucleotide sequence (genetic info) allowing a self-replicating activity

- Not just one, but a pair of identical RNA strand may be required
    - One acts as a ribozyme, and the other as a template
    - Then the required length would be twice longer

- The first big step for abiogenesis
    - Generation of biological information as an ordered sequence from zero
    - Statistically the biggest barrier (in my view)

- After that, the Darwinian evolution is triggered toward the first cell
    - Encapsulation by membrane
    - Incorporating protein and DNA

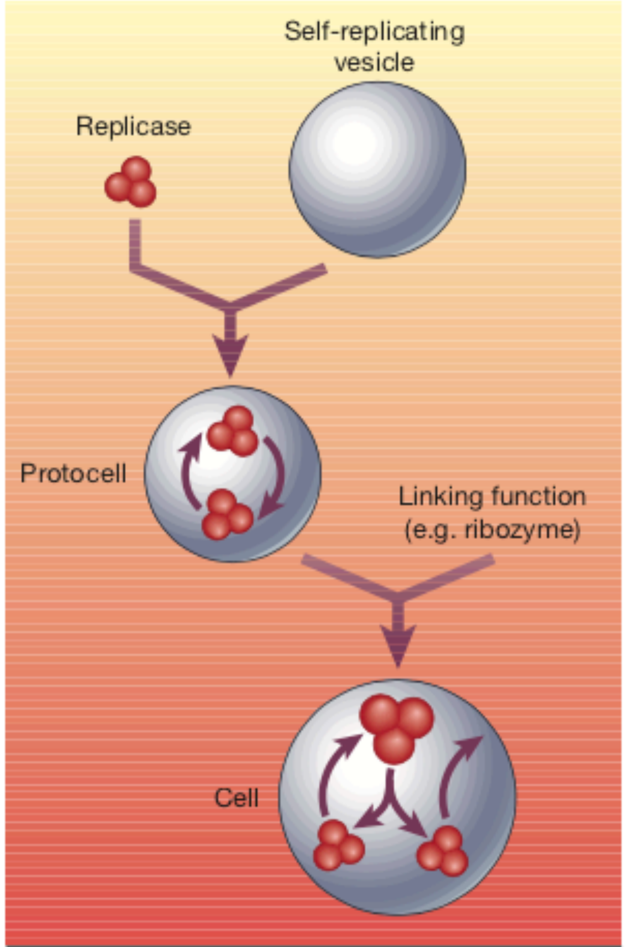


Figure 2 **Outline of proposed pathway for synthesis of a cell. The first major synthetic intermediates are an RNA replicase and a self-replicating vesicle. These are combined into a protocell, enabling rapid evolutionary optimization of the replicase. Addition of an RNA-coded linking function, such as a lipid-synthesizing ribozyme, completes the cellular structure.**

Szostak '01

How was the first active RNA built abiotically?

Kawamura+'94

- RNA polymerization experiments
  - polymerization occurs by reactions of activated monomers
  - can be accelerated on catalyzer (e.g. clay mineral surface) (e.g. Ferris+'06)
  - consistent with statistical adding of monomers randomly
    - Yields rapidly decrease with polymer length, up to ~10 nt (Kawamura+'94, Cafferty+14)
  - Some reports reporting >30-nt polymer production remain controversial, possibly misidentifying polymers and aggregates
    - Huang+03, Costanzo+09, Burcar+13

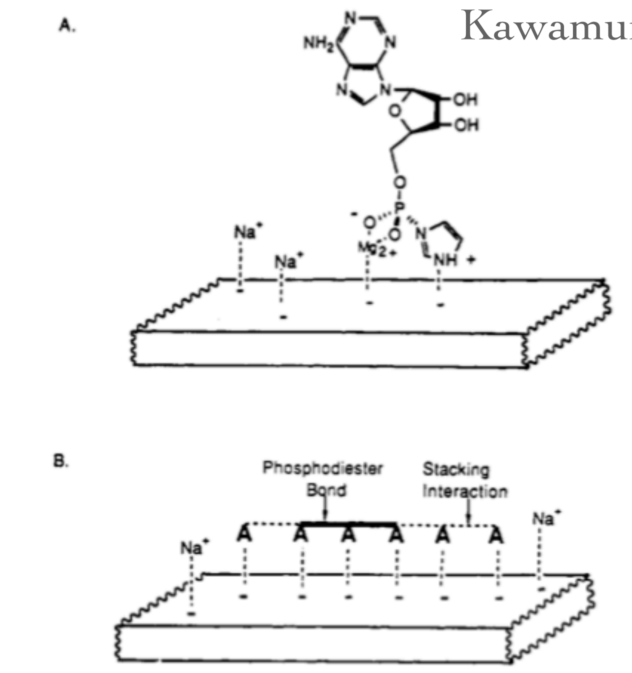


Figure 7. (A) Proposed binding of ImpA to negative sites on the surface of Na^+-Vol. (B) Proposed model for elongation of $(pA)_3$ by reaction with ImpA at the negative sites on the surface of Na^+-Vol: $(pA)_3$ = A A A and ImpA = A.

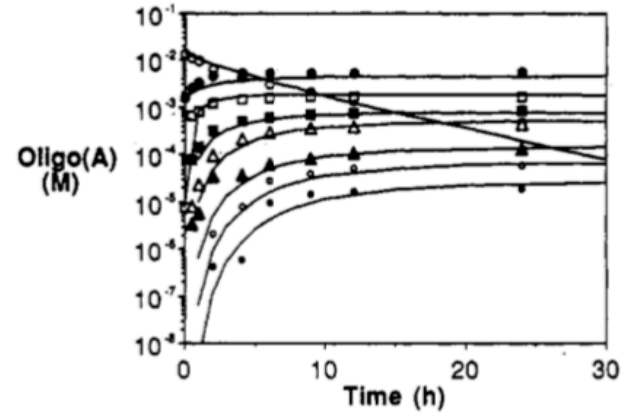
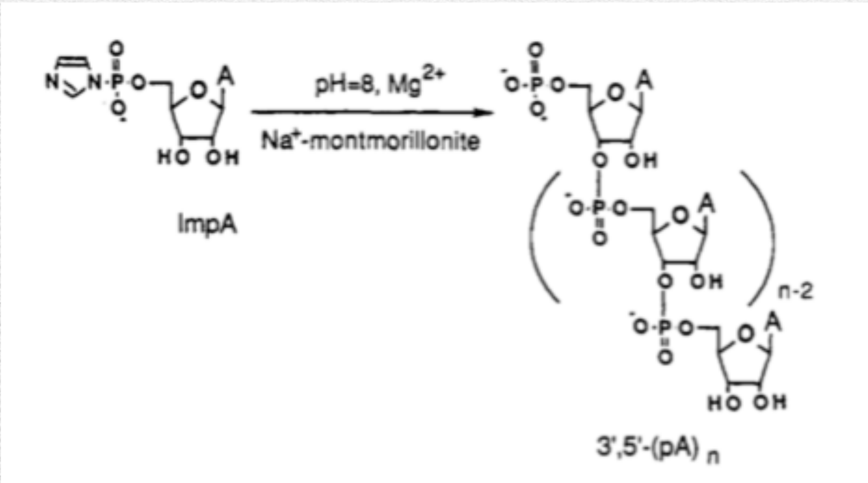


Figure 5. Reaction curve for the loss of 15 mM ImpA and the formation of oligo(A)s in the presence of Na^+-Vol. Total concentrations of the oligomer in the aqueous phase and bound to the Na^+-Vol are plotted. The lines drawn through the experimental points were fit by SIMFIT: ○, ImpA; ●, pA; □, 2-mer; ■, 3-mer; △, 4-mer; ▲, 5-mer; ∘, 6-mer; ·, 7-mer.

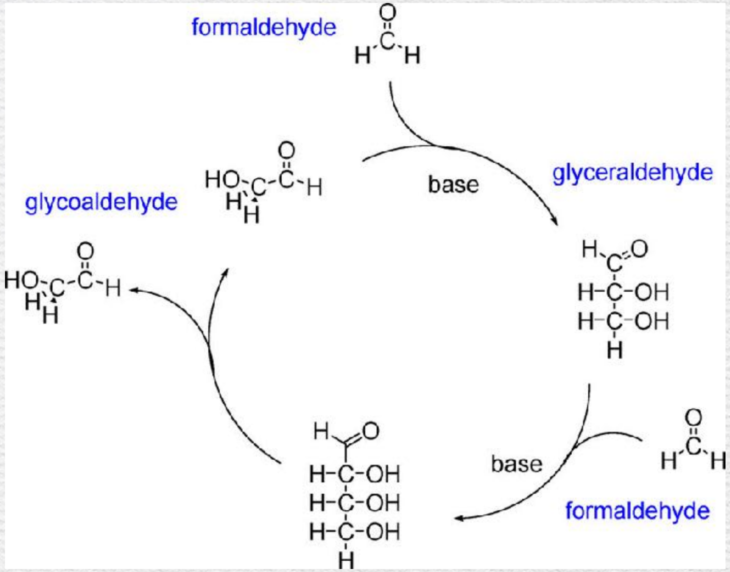


More efficient processes to the first RNA?

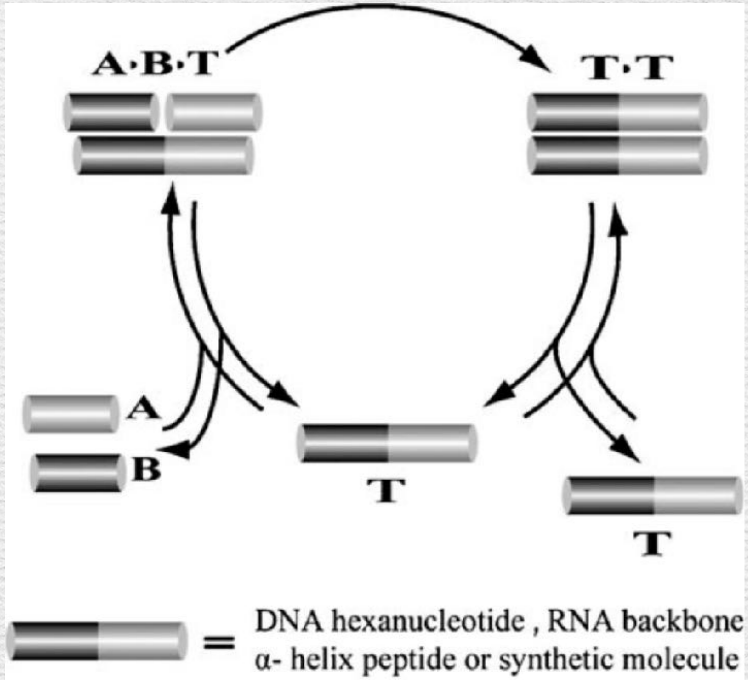
- More efficient processes than randomly adding monomers?
  - Cyclic (auto- or cross-catalytic) reaction network has been considered in the context of abiogenesis (Coveney+'12; Hordijk+'18)
  - Mostly theoretical, but some experimental demonstrations for basic reactions
    - e.g. template-directed ligation of short oligomer fragments
  - No experimental proof for such reactions actually working at the abiogenesis

- Such a reaction network may be useful for self-replication of necessary molecules (building blocks), but unlikely useful for template-independent polymerization of the first long polymer at the starting point of abiogenesis

- Conservatively, the simplest polymerization by adding monomers is the only one path that certainly exists



Ruiz-Mirazo+'14



Dadon+'08

How small can the abiogenesis probability be?

- Abiogenesis by statistically adding monomers looks extremely unlikely
  - Can a monkey hitting a keyboard at random type a complete work of Shakespeare?
  - "The probability of abiogenesis is comparable to the chance that a tornado sweeping through a junkyard might assemble a Boeing *747*" (F. Hoyle)

- In literature, a small abiogenesis probability is often considered as that in the whole Galaxy, or in the observable universe (13.8 billion light year radius including 10^{22} Sun-like stars and 10^{11} galaxies)

- From a viewpoint of cosmology, considering abiogenesis probability in the observable universe is almost nonsense!
  - The size of the observable universe is determined by the light travel distance since the Big Bang
  - "the cosmic horizon" in which we can directly see

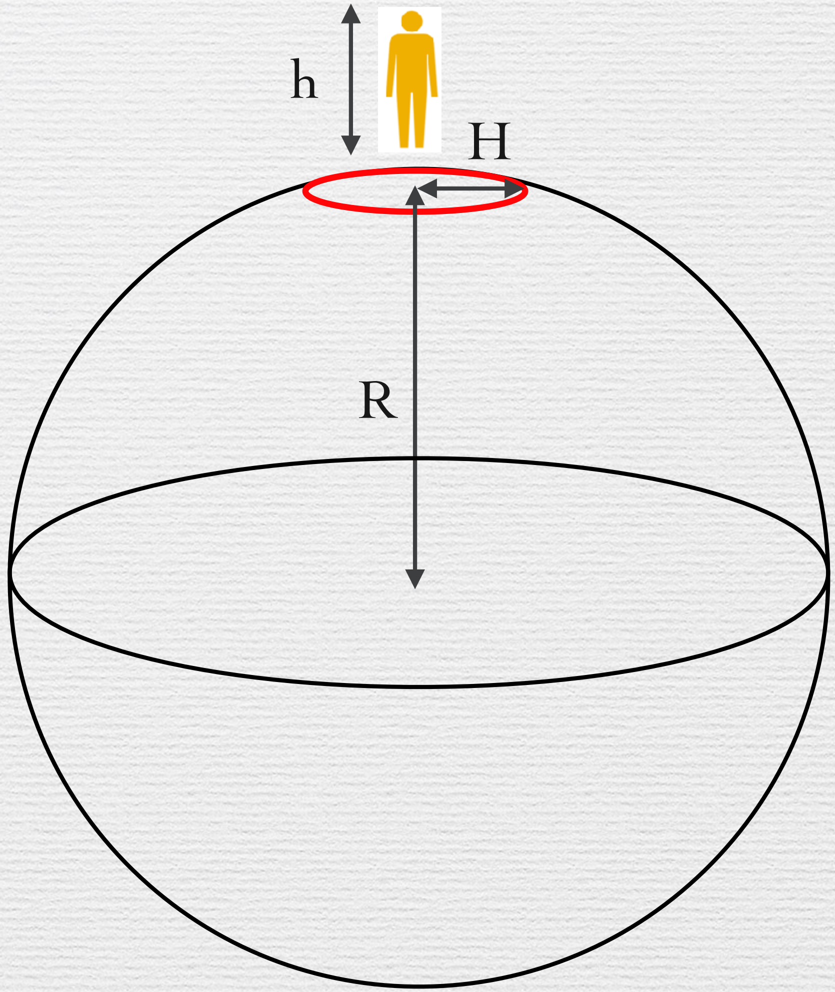
The horizon on the Earth surface

- Horizon length for a person (height h) is:
  - $H = [2 h (R + h)]^{1/2}$
  - R=Earth radius= 6371 km
  - H ~ 5 km for a h=1.7m person

- Suppose you are considering on the abiogenesis probability on Earth. How do you feel if somebody considers about the probability within one's horizon

- "abiogenesis probability in the observable universe" is similar to this

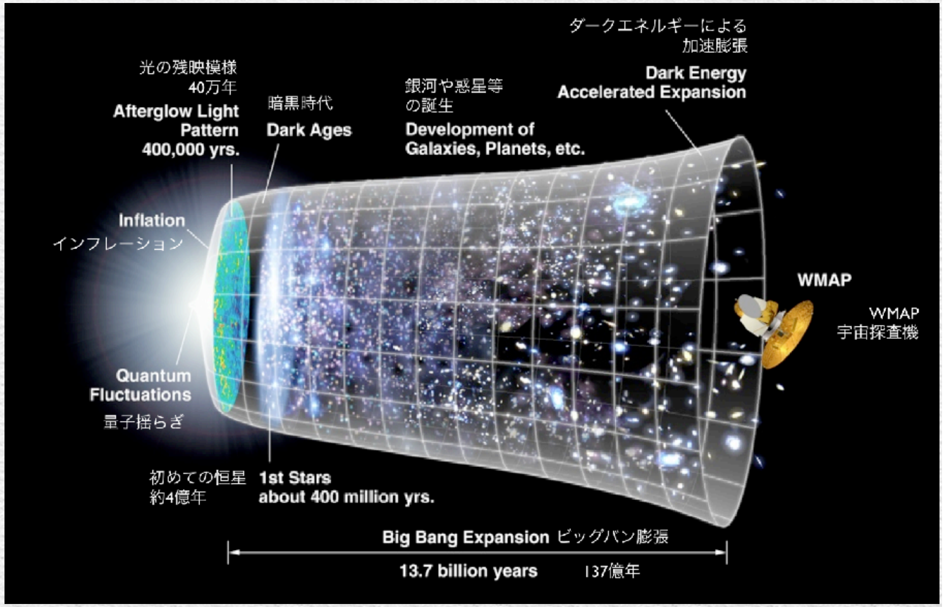
- Then, how large is the real physical universe?



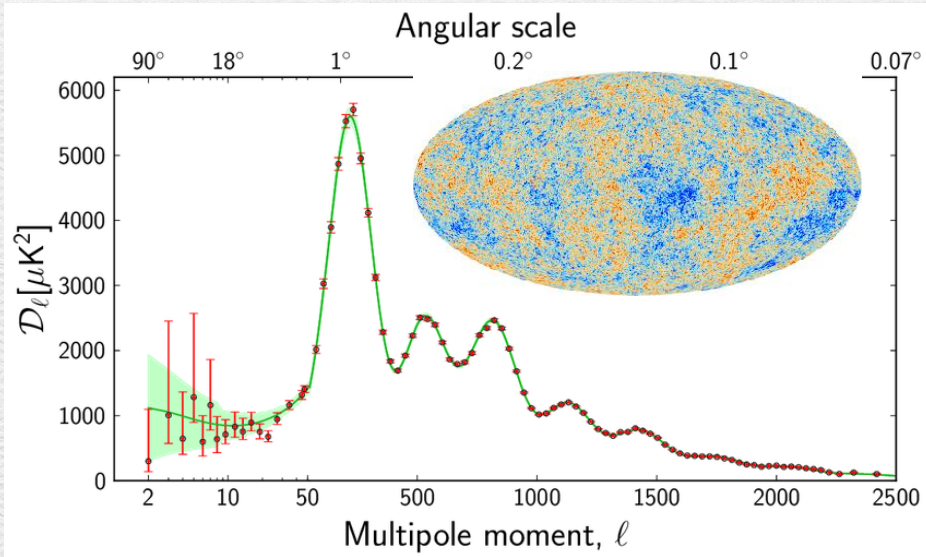
The inflationary universe

- The observable universe now is
  - extremely homogeneous
  - spatially flat

  far beyond the horizon at the early universe



- The widely accepted solution: cosmic inflation
  - The universe experienced an exponential expansion in the early universe (typically $t < 10^{-37}$ s, $kT > 10^{16}$ GeV)
  - Such an expansion provides a flat and homogeneous universe beyond the horizon
  - The minimum expansion factor required:
    - $\exp(N_i)$ with $N_i > 60$
    - 3×10^{-27} cm → ~1 cm (our observable universe at the end of inflation)



- Further observational support:
  - Scale-invariant matter density fluctuations in the universe (power spectrum ∝ 1/λ)
  - Confirmed at a high precision by the cosmic microwave background radiation

How large is the inflationary universe?

- The minimum requirement to solve the homogeneity/flatness problems:
  - $N_i > N_{i,min} \sim 60$
  - No observational upper bound on N_i
  - $N_i \propto$ inflation duration

- If you change some model parameters of inflation, the duration easily changes, say, by a factor of a few

- It would be a fine tuning if the actual N_i is very close to $N_{i,min}$
  - Rather, we expect $(N_i - N_{i,min}) \gtrsim N_{i,min}$

- If inflation duration is twice, three, and four times larger than $N_{i,min} \sim 60$:
  - The physical size of the universe is exp(60), exp(120), and exp(180) times larger than the observable universe now
  - 10^{78}, 10^{156}, and 10^{234} times larger in volume
  - contains 10^{100}, 10^{178}, 10^{256} Sun-like stars

- If abiogenesis occurs many times in an inflationary universe, it is consistent with our existence even if the abiogenesis probability is negligibly small in the observable universe (10^{22} stars)

This work

T. Totani 2020, Scientific Reports 10, 1671

- Examine whether life can emerge by the most conservative process (random reactions of monomers) in the total volume of an inflationary universe
  - Derive a quantitative relation between:
    - The minimum length of RNA (or its precursor) required to trigger an abiogenesis event
    - The universe size necessary to expect the formation of such a long RNA by random adding of monomers

- Koonin (2008) considered abiogenesis in the universe assuming "the eternal inflation scenario"
  - In this scenario, multi-verses are produced by repeated inflation events
  - Predicts a infinite volume of the universe, thus abiogenesis is possible with an infinitely small probability
  - Quantitative discussion impossible
  - Eternal inflation is difficult to confirm observationally

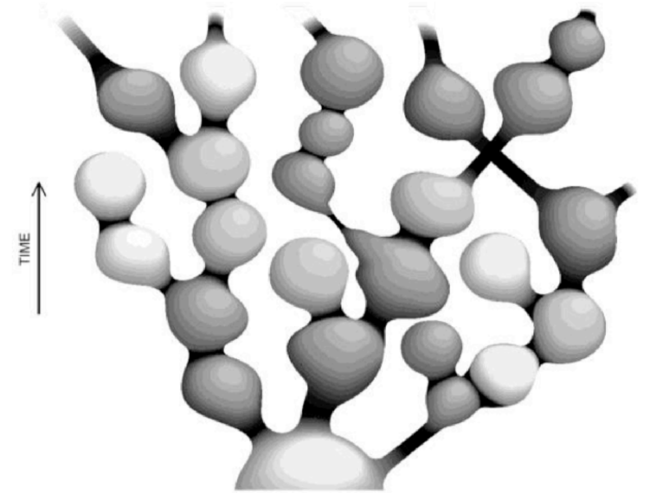


Fig. 4 - Global structure of the chaotic self-replicating multiverse. The different gray hues symbolize "mutations" in the physics laws in the domains, as compared to the parent island universes.
Adapted from Linde (2014; 2015)

- This work assumes the minimal inflation to explain observations:
  - A homogeneous region created by a single inflation event, including our observable universe
  - Thus a quantitative discussion becomes possible

Poissonian RNA polymerization

- Suppose a cycle of polymerization, where activated monomers are injected into a reaction site

- Polymerization by adding monomers
  - Basic equations for the abundance of l-length RNA, x_l

$$\dot{x}_{l+1} = \kappa \ x_l - \kappa \ x_{l+1}$$

  - κ : the reaction probability per unit time
  - solving with a condition of $x_l << x_{l+1}$, abundance at a time t is:

$$x_l = \frac{p_r^{l-1}}{(l-1)!} x_1$$

    - $p_r = \kappa t$
    - can also be derived from the Poisson distribution

- We only consider the regime of $p_r = \kappa t < 1$
  - Beyond $t > 1/\kappa$, a significant amount of activated monomers would be lost, so the above simple formula does not hold

- $p_r \sim 1$ can be achieved if polymerization in a cycle continues up to $t \sim 1/\kappa$
  - Experiments on clay surface found $p_r \sim 1$ is achieved with $\kappa \sim (\text{hour})^{-1}$
  - The reaction rate $\kappa \propto$ (monomer concentration)
    - High monomer concentration necessary. Dry-wet cycle in warm little ponds?

Equation of abiogenesis probability

- The expected number of abiogenesis events in a region including N$*$ stars

$$N_{\rm life} = N_* \, f_{pl} \; t_d \; r_p \; P_{ac} \; P_{ev}$$

  - f_{pl} : mean number of habitable planets per star
  - t_d : duration of polymerization cycles continue
  - r_p : production rate of a l_{min}-length RNA polymer on a planet
    - N_m: the number of activated monomers on a planet
    - t_c: time interval between cycles

$$r_p = N_m \frac{p_r^{l_{\rm min}}}{l_{\rm min}!} t_c^{-1}$$

  - P_{ac} : probability of active nucleobase sequences among all sequences
    - N_{ac}: number of active sequences, N_{nb} (=4): number of nucleobase types

$$P_{ac} = \frac{N_{ac}}{N_{nb}^{l_{\rm min}}} = \frac{1}{N_{nb}^{l_{\rm min}-\Delta l}} \qquad N_{ac} \equiv N_{nb}^{\Delta l}$$

    - N_{ac} is uncertain, but perhaps 10^4 sequences among all sequences of 40-mer ($4^{40} \sim 10^{24}$ sequences), i.e. Δl=6.6 for l_{min}=40 (Robertson & Joyce '12)
    - Assume Δl = 0 in the baseline model
  - P_{ev} : probability that an active RNA polymer evolves to life (=1)
    - very uncertain, can be much smaller

lg N∗ vs. l_{min}

- Requiring N_{life} = 1, and taking a logarithm

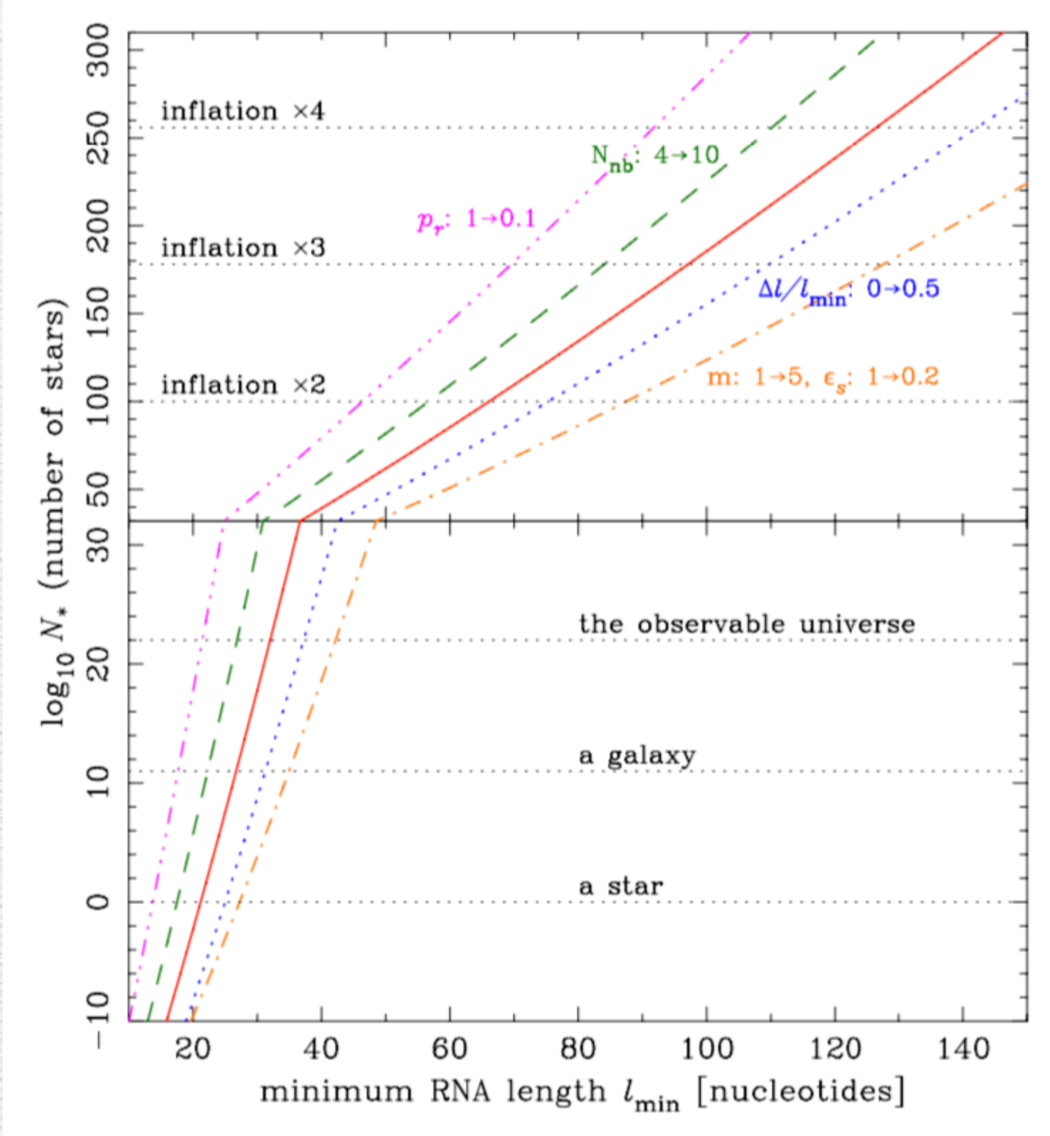
$$2.3\,\mathrm{lg}N_* = \ln(l_{\min}!) - l_{\min}\ln p_r + (l_{\min} - \Delta l)\ln N_{nb} - \ln C$$

$$C \equiv f_{pl}\ N_m\ t_d\ t_c^{-1}\ P_{ev}$$

- Non-logarithmic main terms: lgN∗ ($\propto N_i$) and l_{min}
- Other parameters appear only logarithmically, though some of them are very uncertain
  - C is uncertain probably by more than 10 orders of magnitude
- Baseline estimate of C:
  - f_{pl} = 0.1 (from exoplanet observations)
  - t_d = 0.5 Gyr (time scale from Earth formation to abiogenesis)
  - t_c = 1 yr (assuming a seasonable cycle, 1 day may also be good for day-night cycle)
  - $N_m = 10^{25}$ (~ 1 kg)(very uncertain, from a model of nucleobase delivery by meteorites)
    - $N_m \sim 10^{38}$ for the total biomass on the present Earth
  - ln C = 75.3

Results

- l_{min} vs lgN∗
  - l_{min} = 21 for lgN∗ = 0 (a star)
  - l_{min} = 27 for lgN∗ = 11 (a galaxy)
  - l_{min} = 31 for lgN∗ = 22 (the observable universe)
  - c.f. l_{min} > 40-100 required for a biological self-replicating activity
  - lgN∗ = 39 for l_{min} = 40
- Inflationary universe:
  - l_{min} = 66, 97, 127 for lgN∗ = 100, 178, 256 (×2, ×3, ×4 longer inflation than the minimum)
- lgN∗ changes by 10 when C is changed by $\times 10^{10}$
  - Not a large effect especially in the large limit of l_{min} and lgN∗



Discussion & Conclusions (1/2)

- A long (>40-100nt) and biologically active RNA can be produced in the total volume of an inflationary universe only by random reactions of adding monomers
    - A (currently the only) solution to the initial abiotic polymerization problem about the origin of life
    - Life can emerge in the framework of science, and we do not have to consider something beyond science (e.g. intelligent design)

- The expected number of abiogenesis events is small even in the observable universe, but it does not contradict with available observational facts
    - The observable universe is just a tiny part (likely less than $1/10^{78}$) of the real universe size
    - No strong reason to expect more than one abiogenesis events in the observable universe
    - Giving an explanation to the Fermi's paradox

- Implication for the homochirality of life:
    - Life uses only L-chiral (left-handed) amino acids and D-chiral (right-handed) sugers in DNA/RNA
    - The l_{min} vs $\lg N_*$ statistics does not significantly change when N_{nb} (base types) increased by ×2
    - If homochirality is a necessary condition for a biological activity, simply a bit larger volume of inflationary universe is required to expect an abiogenesis event

Discussion & Conclusions (2/2)

- Implications for extraterrestrial life search:
  - I regret that, but I bet on negative results in future searches in the Solar system or nearby exoplanets!
  - If discovered, I would first consider the possibility of interplanetary/interstellar traveling of microorganisms (i.e., the common origin with the life on Earth)
  - Caveat: a much more efficient process of RNA polymerization may change this conclusion, but in my view, no such convincing process is known yet
    - … and we do not need such a hypothetical process to explain the origin of life

- Ultimate mystery of life?
  - I assumed that life can emerge if a sufficiently long RNA polymer is abiotically assembled
  - This may be trivial under the physical laws that we know, because we know the phenomenon of life (esp. ribozyme) on Earth
  - But does it easily occur when the physical laws are arbitrarily made?
    - This may be the ultimate mystery about life, which is not answered at all by this work