Whence the demise and fall of the RNA world?

Ask me.

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Abstract

A widely promulgated concept for the fundamental ancestor-descendent relationship in the origin of life (OoL), and hence the inception of **Darwinian Evolution**, is the **RNA World hypothesis**. Even if life on Earth began with a simple RNA molecule that had the ability to replicate itself, it did not stay that way. DNA emerged and became the preferred informational molecule, leading to the establishment of the **contemporary DNA+Peptide World.** Understanding what could have driven the transition from an RNA(+/- Peptide) to DNA World **necessitates a biogeodynamic contextualization of the co-evolution of the early Earth environment with, for example, the evolution of key metabolic styles.**

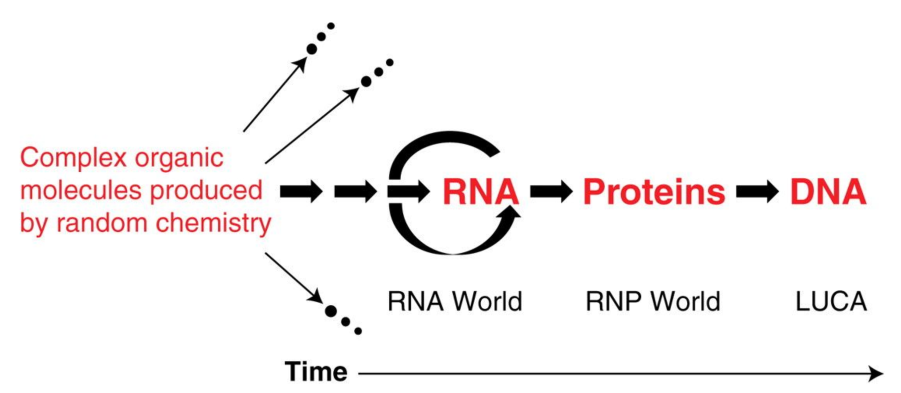


Figure 1

Generalised model of the **RNA(+/- Peptide) World** concept. The timeline here is *arbitrary* owing uncertainties over the nature and timing of this transition. Along with RNA, Peptides may have been present in these early mixtures, but they were likely short polymers at best and unlike the complicated functional proteins of today. LUCA (last universal common ancestor**s**) were already a DNA organisms with RNP and RNA enzymes (Cech 2012).

The RNA World - a biogeodynamic perspective

potentials & pitfalls

- Biological entities exhibit (Ganti 1997): **Metabolism, encapsulation, information**
  - Each can, arguably, be the starting point (ex. lipid world hypothesis)
  - **But, only *information* is capable of Darwinian Evolution**
- DNA is self-catalytic and highly stable, but fabulously complex (not at OoL)
- **RNA can self-replicate!**
- Shorter, one strand - simpler molecule
  - Non-linear - highly folded
- Extremely high mutation rate
  - Possibility of rapid selection
- Good likelihood for abiogenesis

- **Plausible remnants of an RNA World** in the contemporary DNA+Peptide biosphere:
  * ribosome is composed mostly of RNA
  * ribonucleotide moieties exist in many co-enzymes such as **acetyl-CoA**, NADH, FADH and F420

RNA viruses have RNA genomes!

→ **Acetyl-CoA** may be a remnant of a covalently bound coenzyme in an RNA world (Brabender+ 2024; White 1976)

- RNA by itself is flimsy compared to DNA
  - breaks down at temperature (>50° C); loose incorporation of wild peptides?
  - sensitive to pH (>8); 5.5-7 ideal?
  - unstable at seawater salinity (viz. Mg^{2+}, Ca^{2+}, Mn^{2+}, Fe^{2+}); freshwater origin?
  - high mutation rate (i.e. "junk" products)
  - ineffective repair mechanisms
- **The Pre-biotic Chemist's Nightmare**

→ prebiotic catalytic reactions left unattended yield asphalt (Benner 2023)
→ how to form & stabilize RNA polymers? (Jerome+ 2022; Šponer+2023)
→ external source of nucleotides needed
- RNA catalyzed reactions are limited
- **Eigen-Threshold** - strict limit to information RNA can code (Wolf and Koonin 2007, Eigen 1971)

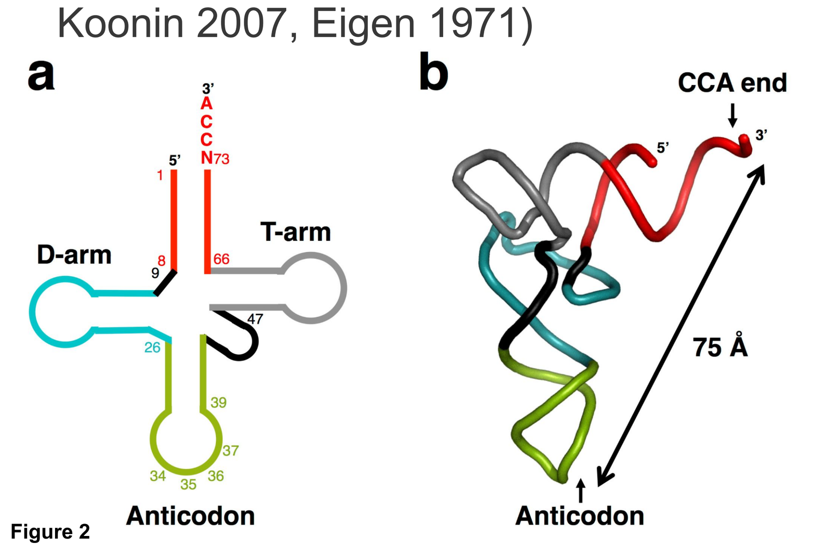


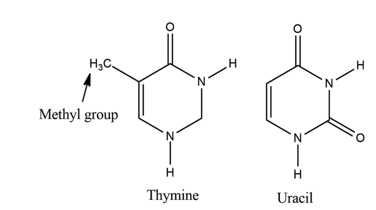
Figure 2

Generalized secondary and tertiary structures of tRNA (Tamura 2015)

The transition from an RNA World to the DNA World

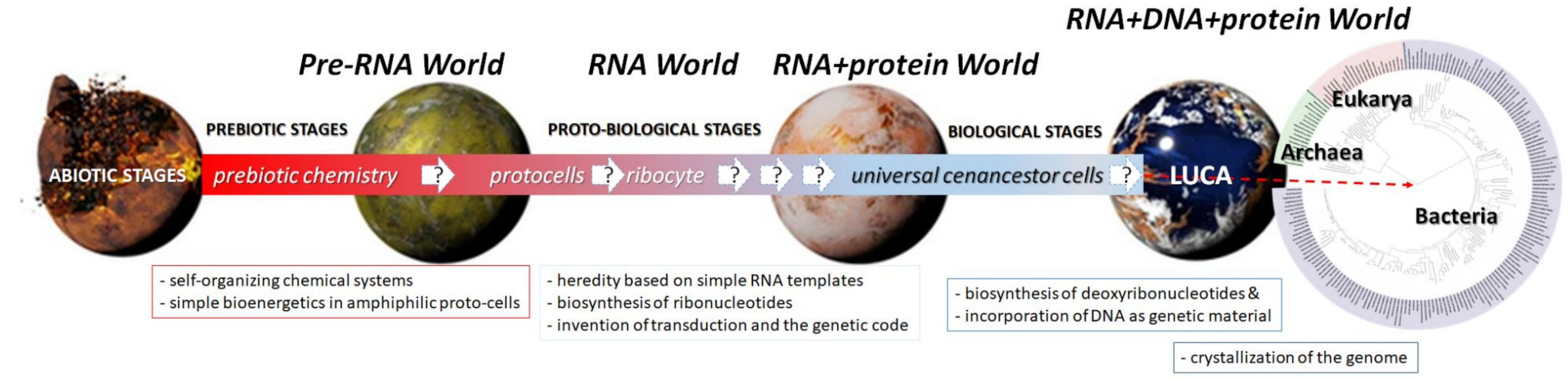
The nature of the steps leading to the takeover of an RNA(+/-Peptide) World (RNA/RNP) by DNA remain generally uninvestigated. It seems that RNA cannot encode the enzymes needed for the formation of DNA; there is a vast difference in the amount of information encoded by the two molecules. Several steps are required from RNA/RNP to DNA that involve intermediates like methyl-RNAs. These include:

[1] **reduction of ribonucleotides** (to form deoxyribonucleotides)
[2] the **formation of a double-strand** (later the helix, spontaneously?), and
[3] the **replacement of the nucleotide uracil** with **thymine**.



Again, DNA is much more stable than RNA. It is less sensitive to heat, stable in seawater salinity, and proteins with 20 amino acids that can catalyze a much larger variety of chemical reactions

Why is DNA *fitter* than RNA? When and why did all life become DNA based?



Tracking down the transition (e.g. Co, Ni, Fe, S & co-factors)

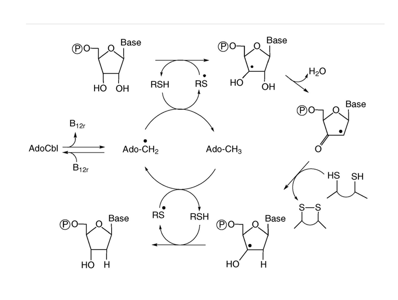


Figure 3. The model of the Class II type of RNRs, which use adenosylcobalamin as their cofactor (Gruber+ 2011)

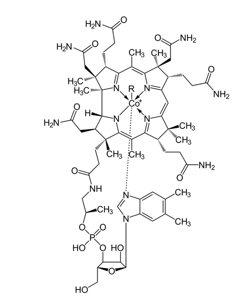


Figure 4. Chemical structure of cobalamin (vitamin B12) - Co^{+} ion is in the ring. Cobalamin is a complicated vitamin B structure, but nevertheless can be formed under pre- or proto-biotic conditions. (Monteverde+ 2016)

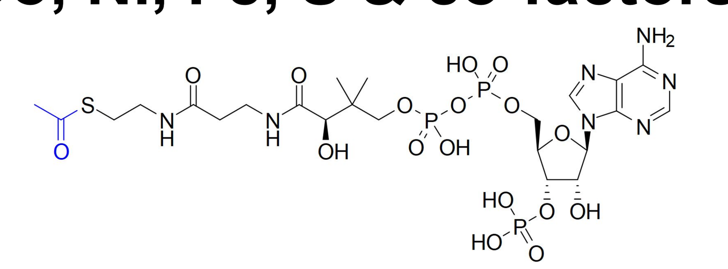
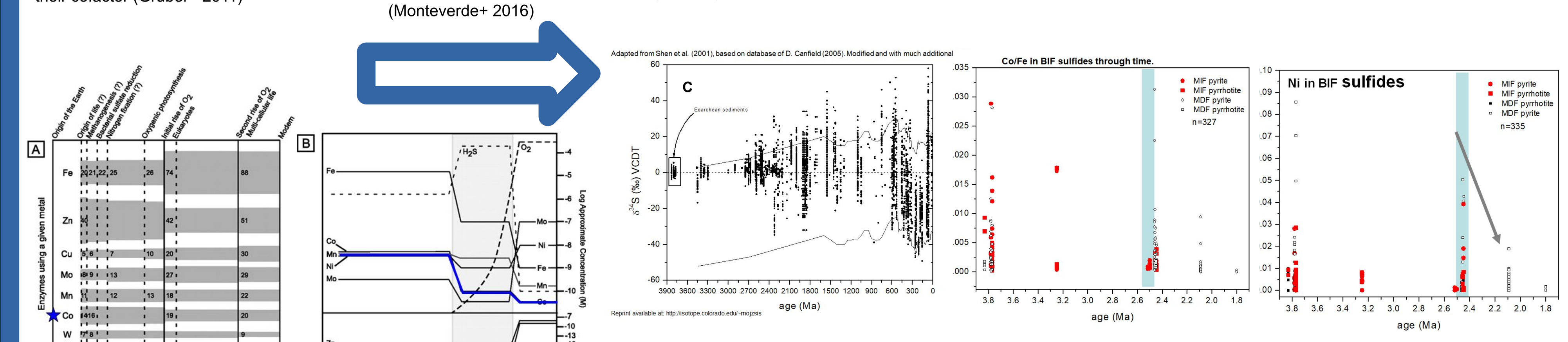


Figure 5. The reductive acetylcoenzyme A (Acetyl-CoA), or Wood–Ljungdahl (W–L) pathway (e.g. Braakman and Smith 2012; Ragsdale and Pierce 2008). Biosynthesis via the autotrophic acetyl-CoA pathway uses free hydrogen from the environment as an electron donor, and carbon dioxide as an electron acceptor. LUCA (AFTER the RNA/RNP World!) used this W–L pathway in a primordial H_2-powered biosphere, perhaps at mildly alkaline hydrothermal settings (e.g. Brabender+ 2024).



Models of Saito et al. (2003); Zerkle, House and Brantley (2005); adapted by Anbar (2008)

Figure 6. (A & B). Evolution of key metals found in metallo-enzyme active centers vs. time and as a function of calculated concentration in marine waters. **(C)**. Mass-Dependent Sulfur isotope fractionations (MDF) in sediments with time. Note changes in range of MDF at different times. Compare this to **(D & E)**: Records of trace Co and Ni in banded iron-formation (BIF) sulfides with time. Note the general decrease in Co and Ni content at time of GOE (vertical blue bar) which we attribute to changes in the geodynamic regime of crust formation (transition from ultramafic to mafic crust, cf. Konhauser+ 2009, 2011).

- Our search for the RNA to DNA World transition envisions **two key components**, to inform us about the timing of this fundamental event in the history of life before the LUCA:
  - **Environmental changes leading to the transition (bio-GEODYNAMICS part)**
  - **Biochemical changes to the biosphere as a result of the transition (BIO-geodynamics part)**

Here we focus on the BIO- GEO aspects

- Reduction of ribonucleotides (*Ror*) means that **an early form of RNRs** (ribonucleotide reductases) **played a part in the transition process. What evidence could exist for this evolution?**
  - Out of the three classes of RNRs, **the simplest that requires no free oxygen is the class II type** (Dickman, 1977)
  - ***Ror* must happen before oxygenation of the environment and thus before the GOE ca. 2.42 Ga**
  - Class II type of RNRs use **cobalamin** (adenosylcobalamin) as a cofactor
  - **Cobalt** (and judging by its presence in riboswitches, possibly **Nickel**) played a role in the transition
- **Cobalamin** is heat stable, but sensitive to UV, alkalic environments and oxidation

*Cobalt, Nickel and Iron are all scavenged by Sulfides in the geologic record (**Figure 6**).

→ If these cofactors were switched with more favorable ones (like **Iron**) before the time of GOE, changes in the S isotopes might be accompanied by changes in **Co** (and **Ni**) content of sulfides in ancient rocks.

Conclusions and Future Prospects

The RNA World hypothesis is a temporary phase in the origin of life. If this is correct, it means that from an RNA World origin life ultimately went through a transition into a DNA+peptide World.

→ Absence of a fossil record from this transition calls for a **new approach - biogeodynamics**
- **Trace metals** can yield some clues and the transition likely happened in several steps.

→ One of the most important of these steps would be the **reduction of ribonucleotides (Ror)**!
- The key enzyme for this is **ribonucleotide reductase - RNR**

→ **Class II RNR uses cobalamin** (adenosylcobalamin) as a cofactor in the absence of free oxygen
- **Cobalt is the active metal center** of cobalamin
- Rise in free oxygen (Great Oxidation Event), mantle cooling and changes in the geodynamics of the crust (ultramafic to mafic; initiation of plate tectonics, etc.) = **replacement of Co with Fe** in enzymatic systems. This chemical evolution continues apace with Cu, Zn and others.

Ongoing work poses the following questions:

- What other enzymatic processes played a role? Were there other metals in the active centers like cobalt and nickel?
- How can we narrow down the time frame of the transition in relation to GOE?
- Can we model the earliest enzymes? What coding capacity was needed for their appearance?

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