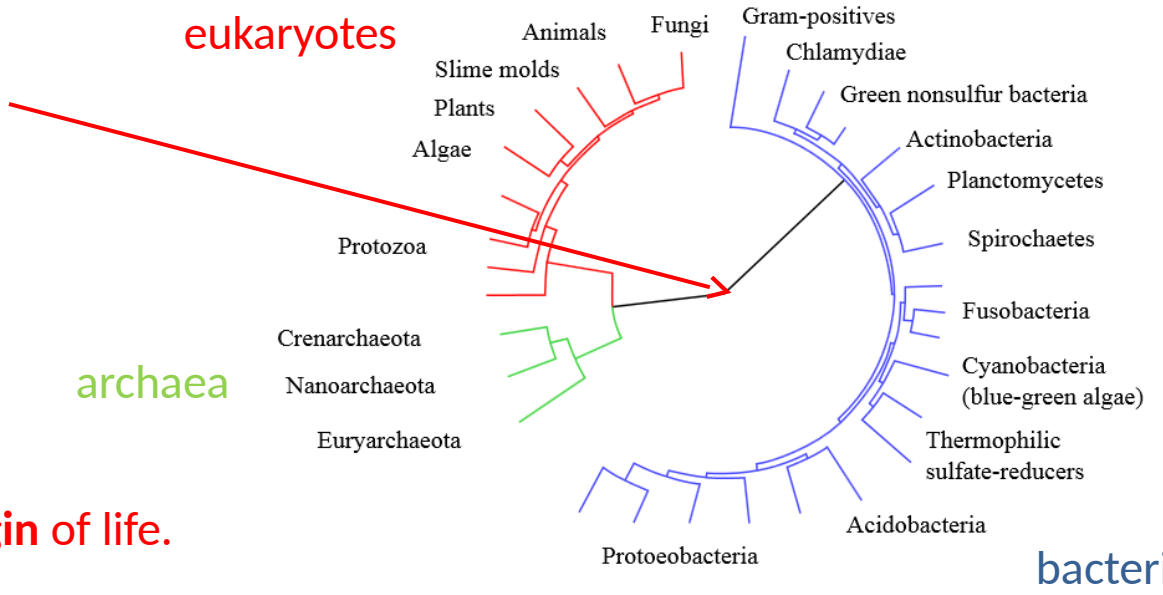
Schrodinger's apology (from his 1943 ***What is Life?***)

A scientist is supposed to have a complete and thorough knowledge, at first hand, of some subjects, and therefore he is usually expected not to write on any topic of which he is not a master. This is regarded as a matter of noblesse oblige. For the present purpose I beg to renounce the noblesse, if any, and to be freed of the ensuing obligation. My excuse is as follows. We have inherited from our forefathers the keen longing for unified, all-embracing knowledge. The very name given to the highest institutions of learning reminds us that from antiquity and throughout many centuries the universal aspect has been the only one to be given full credit. But the spread, both in width and depth, of the multifarious branches of knowledge during the last hundred odd years has confronted us with a queer dilemma. We feel clearly that we are only now beginning to acquire reliable material for welding together the sum-total of what is known into a whole; but, on the other hand, it has become next to impossible for a single mind fully to command more than a small specialized portion of it. I can see no other escape from this dilemma (lest our true aim be lost for ever) than that some of us should venture to embark on a synthesis of facts and theories, albeit with second-hand and incomplete knowledge of some of them, and at the risk of making fools of themselves. So much for my apology.

"**Evolution** is a cornerstone of modern science, accepted as one of the most reliably established of all facts and theories of science, based on evidence not just from the biological sciences but also from anthropology, psychology, astrophysics, chemistry, geology, physics, mathematics, and other scientific disciplines, as well as behavioral and social sciences."
—Wikipedia

LUCA (Last Universal Common Ancestor)



…but it does not explain the **origin** of life.

Introduction

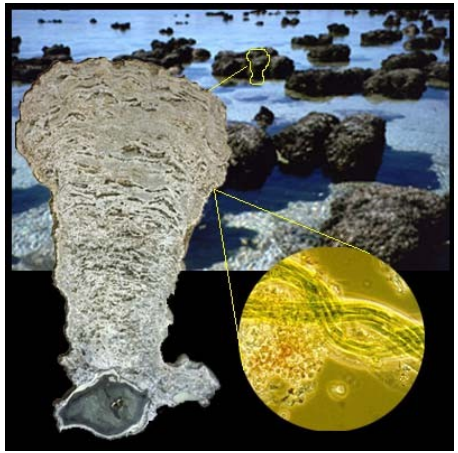
The **origin** of life on Earth remains a deep mystery.

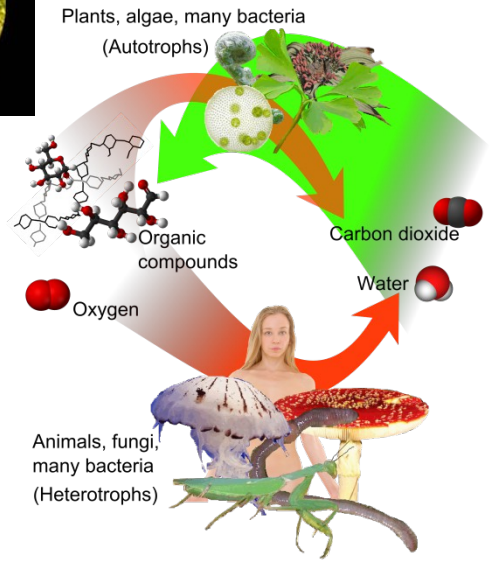
We'll discuss:

- **When** did life begin?
- **Where** did life begin?
- **How** did life begin?

Living Stromatolites

- Layers of sediment intermixed with different types of microbes
- “Autotrophs” (**photosynthesising** cyanobacteria “phototrophs”) near the top of a layer produce organic compounds…
- …“heterotrophs” beneath consume this organic “waste”, in a cycle that represents a **microcosm of life on Earth today**
- As sediment deposits, the microbes migrate up ⎵ layering

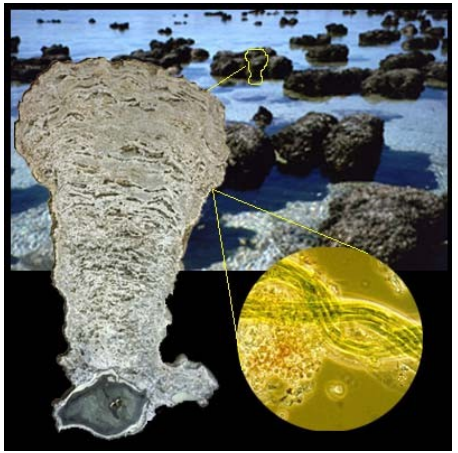




Fossilized Stromatolites?

- Similarity of layering structure suggests similar origin
- But is the layering biological or geological in origin?
- Wide variety of structures & isotopic analysis* favour a **biological** origin

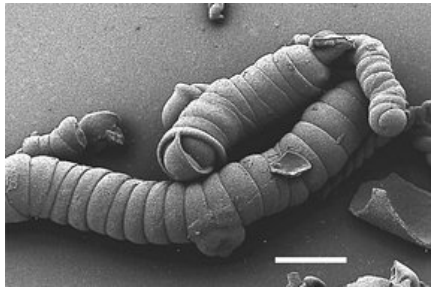
*Normal ratio of C-12 to C-13 is 89 to 1. But life metabolizes C-12 slightly more readily than C-13 ⎵ a C-12/C-13 ratio *higher* than 89 to 1 is evidence for "organic carbon"—life



- **So what?**
  - ✓ Fossilized stromatolites date back to 3.5 BYA
  - ✓ Photosynthesis is a complex metabolic process
  - ⎵ origin of life substantially predates this

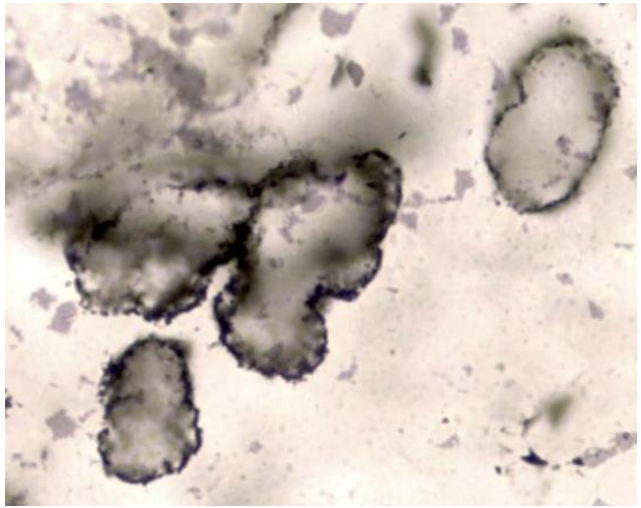
Microfossils

- It would be nice to find **individual fossilized cells**
- **Challenges**:
  - ✓ Old rocks, not changed by geological processes that destroy microfossils, are rare
  - ✓ Is the structure biological or mineral in origin?



Fake fossil: barium carbonate crystal

- **Oldest** microfossil (3.4 BYA)? Evidence:
  - ✓ Biological-like behaviour: clustering & habitat
  - ✓ Higher carbon-12/13 ratio in apparent cell wall
  - ✓ Different isotope of sulfur inside and around the cell wall (metabolizing sulfur for energy?)



Oldest Isotopic Evidence?

- Higher carbon-12/13 ratio is found in 3.85 billion year old rock on the island of Akilia

  (Unfortunately, this is *metamorphic* rock, i.e., rock transformed by high heat & pressure, which destroys microfossils)

- Evidence supported by:
  - ✓ Similar evidence elsewhere
  - ✓ Bio-altering isotopic ratios of other elements like iron, nitrogen, and sulfur

Ancient rock on island of Akilia, off the coast of Greenland, may hold oldest known evidence for life

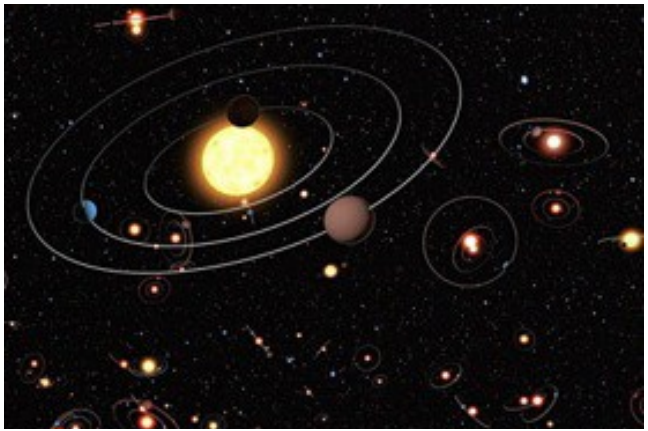
When did life begin?

Punchline:

- *Relatively complex* life was widespread on Earth at least 3.5 BYA (stromatolites), and possibly as far back as 3.85 BYA. Maybe 4.1 BYA (2015 article)?

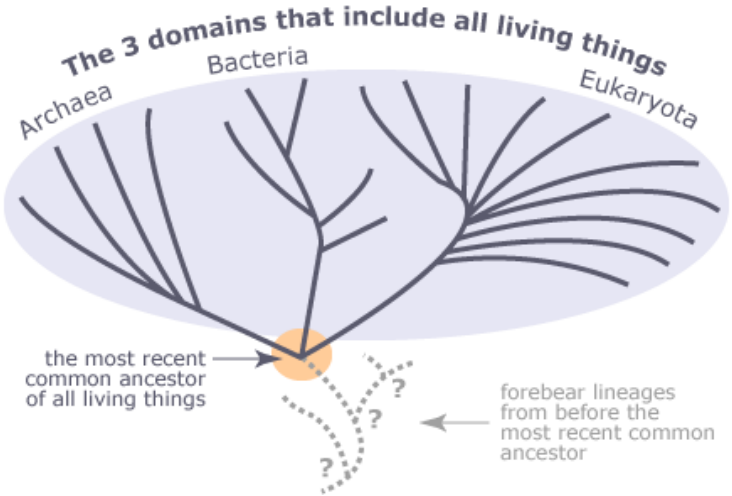
- **So what?**
  - ✓ This means life arose considerably earlier than 3.85 BYA, i.e., quite early in Earth's history, as soon as conditions allowed (after the "late heavy bombardment")
  - ✓ If life arose through a simple natural process (vs. a lucky event), then **life might be quite common in the universe!**

But the exact date when life began is still a mystery…



Genetic Evidence:

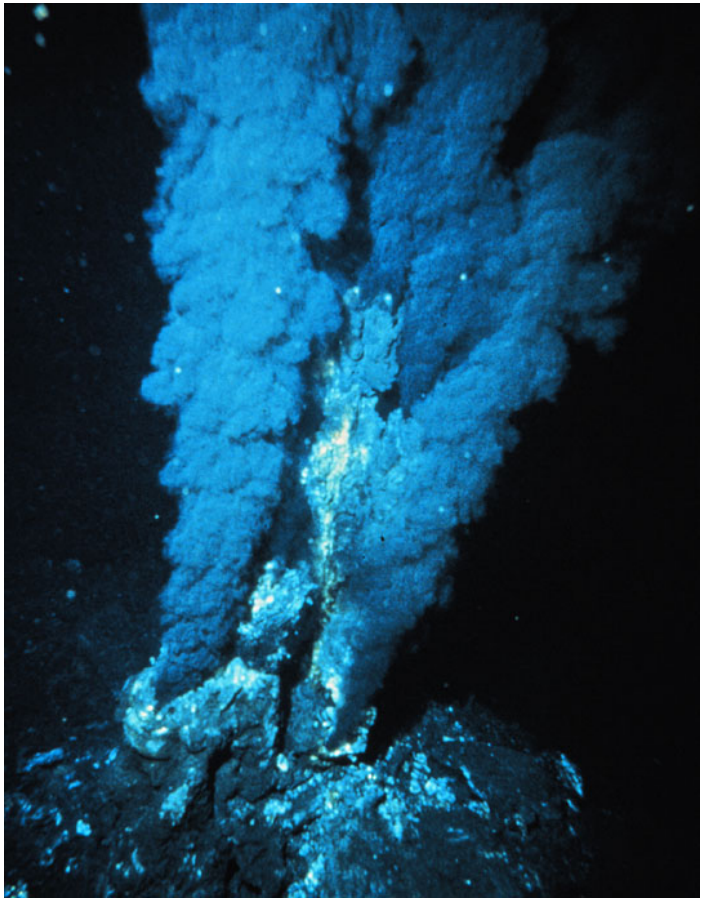
- Evolution works **slowly** by random **mutation** and (non-random) **natural selection**
- Starting with the DNA of the Last Universal Common Ancestor of all life today, mutations slowly accumulate as species differentiate
- Comparing amongst the DNA of species alive today allows biologist to map evolutionary history:
  - Two species with very similar DNA
    - more recent divergence
  - Two species with very different DNA
    - more ancient divergence
- E.g., plants and animals are actually quite similar (recently diverged)!



Genetic Evidence:

- Just as **sharks** branched off earlier than **primates** (as the geological/fossil record confirms), some **modern microbes** are more closely related to the **earliest organisms** than others

- Unfortunately, the evidence about the nature of the organisms near the root of the tree is still not clear:
  - ✓ Initially, they were thought to be ***extremophiles***, like those living today near deep-sea hydrothermal vents, or deep underground
  - ✓ But recently, evidence emerged for ***non-*** **extremophiles**, like certain living archaea



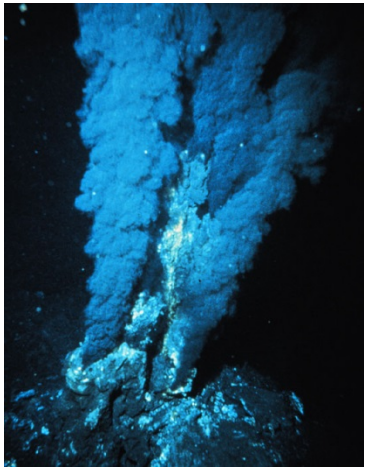
Geological Evidence:

- Did life originate on **land**? Unlikely:
  - ✓ All life today requires **water** as a solvent for chemical reactions. Cell = "bag of water"
  - ✓ Early atmosphere had no O_2 ⇨ no ozone (O_3) layer to protect from Sun's **intense UV**

- Did life originate in Darwin's "**warm little pond**"?
  - ✓ Organic compounds can form spontaneously…
  - ✓ Tides (bigger back then!) and wetting/evaporation would have increased their concentration, spurring reactions that may have led to life
  - ✓ Perhaps volcanic hot springs offered the energy to support an origin of life?
  - ✓ **Problem:** not much protection from UV…

Geological Evidence:

- Back to deep-sea vents or underground:
  - ✓ Protection from Sun's UV
  - ✓ Plenty of chemical energy to fuel reactions that may have led to life (for underground hypothesis: reactions between water & minerals in rock)
  - ✓ Even if life arose in "Darwin's ponds", lunar evidence of asteroid/comet impacts of the "late heavy bombardment" would have destroyed all life that didn't migrate to the deep-sea (or underground)



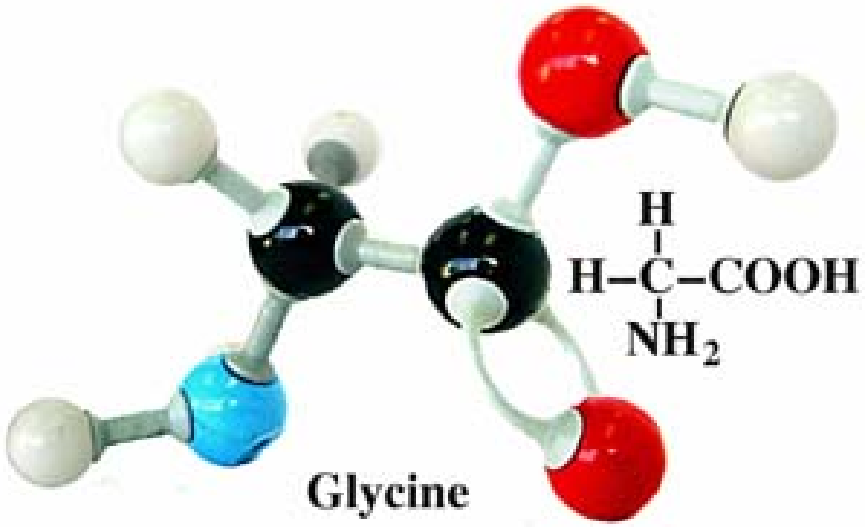
So exactly where life began is still a mystery…

Life is (at least) very complex chemistry:

Amino acids are the building blocks of life. More than 100 amino acids occur in bacteria and plants, but only about 20 are commonly found in animals.

12 can be synthesized by the human body. The remaining 8 must come from our diet (they are called *essential* amino acids).

Amino acids make up **proteins**, the second-largest component of human muscles, cells and other tissues (water is the largest)



N=blue, C=black, O=red, H=white

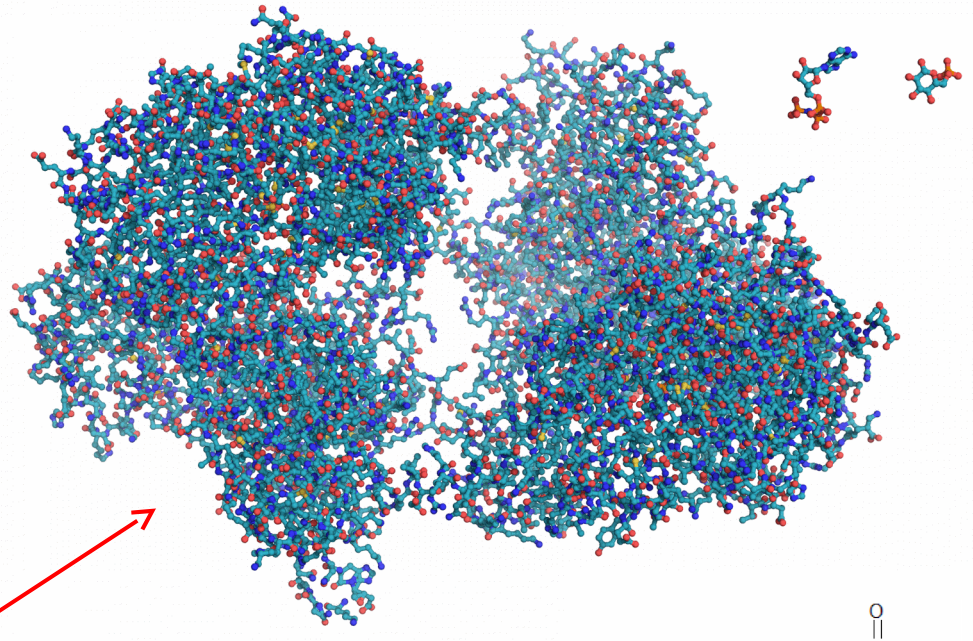
Life is very complex chemistry:

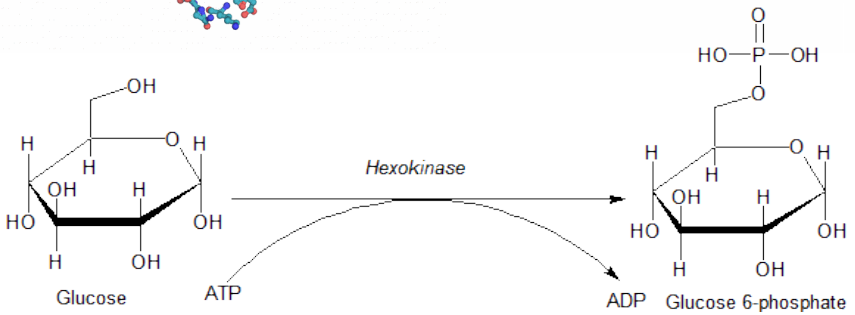
Proteins are **long chains** of amino acids, folded up in a complicated **3D structure**, both of which determine the protein's function.

Functions include:

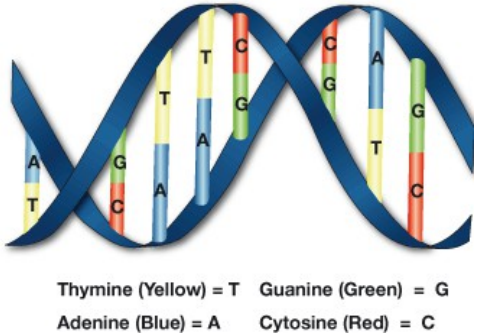
- Catalyzing metabolic reactions (enzyme)
- DNA replication
- Responding to stimuli (e.g., tissue repair)
- Transporting molecules around

Typical example of an enzyme (hexokinase) … involved in converting glucose to glucose 6-phosphate

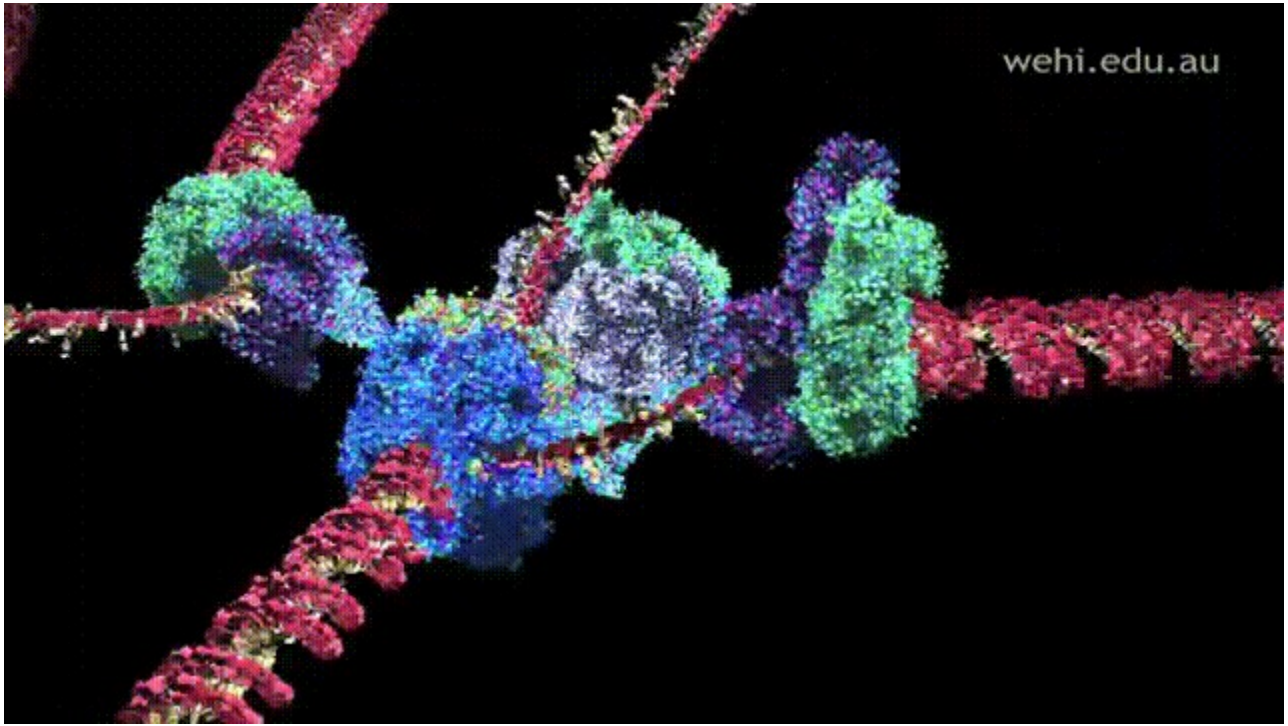




Life is very complex chemistry:



DNA replication: More than a dozen enzymes are involved in unzipping the DNA, checking and correcting errors, and re-zipping the duplicated DNA



Initial Puzzles:

- At the very least we need:
  - ✓ **Amino acids** (building blocks of proteins)—where do these come from?
  - ✓ **Lots of time** (for something interesting to happen)
- …then we can start to think about how simple organic compounds gave rise, over time, to complex, replicating life. **Having the notes is not the same as having the music!**

Early Earth

- Age of the Earth & concept of "deep time":
  - ✓ Theology ▭ a few thousand years to infinite, or cyclical; commonly 5,000–10,000 years
  - ✓ Starting in 1700s: **Rock erosion, sedimentation**, **salt in oceans** ▭ 10–100 million
  - ✓ 1856—Helmholtz: Assume Sun's energy from **gravitational collapse** ▭ 22 million
    Too small because it ignored the real energy source of the Sun: **fusion**
  - ✓ 1862—Lord Kelvin: **Cooling of initially molten Earth** ▭ 20–400 million
    Too small because it ignored heating due to **radioactivity** of the rocks
  - ✓ By later 1800s, **geology & evolution** argued for much older (billions) ▭ bitter disputes…

[In first version of *On Origin of Species*, removed by Kelvin, head of Royal Society]

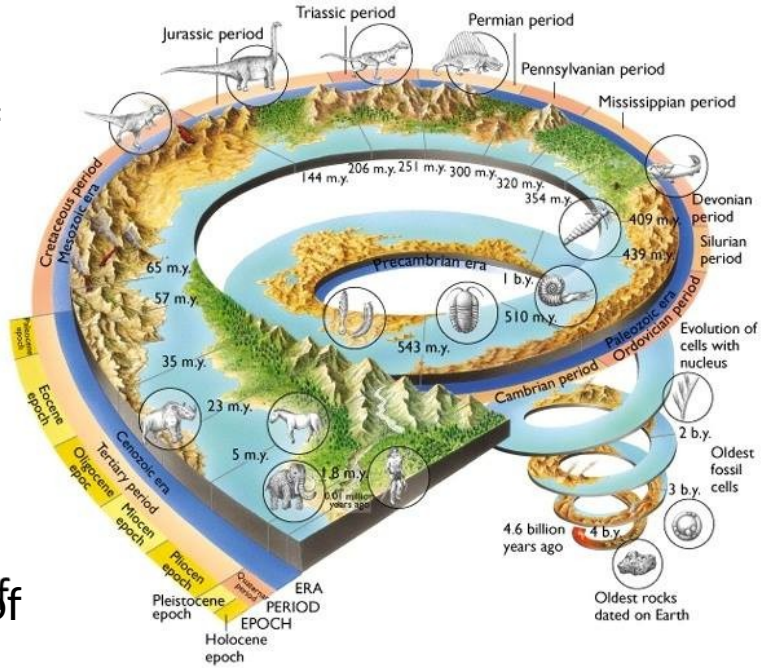
Early Earth

- Age of the Earth & concept of “deep time”:
  - ✓ 1904—Ernest Rutherford:
    - Realized **radioactivity** could heat the Earth (age could be much greater than Kelvin’s 1897 revised estimate of 20 million)
    - Took first step towards **radiometric dating** of the Earth
  - ✓ 1927—Arthur Holmes: “The Age of the Earth, an Introduction to Geological Ideas” gets 1.6-3.0 billion years…

Early Earth

- Today we know Earth is **4.54 ± 0.05 BYO**:
  - ✓ Radiometric dating (e.g., Potassium-40 to Argon-40) of **meteorites** left over from Solar System formation → 4.567 BYO
  - ✓ ...consistent with **radiometric dating of oldest Earth rocks** (zircon crystals in Australia) → 4.404 BYO
  - ✓ ...consistent with radiometric dating of the **oldest Apollo Moon rocks**
  - ✓ ...consistent with comparing the mass and luminosity of Sun to those of **other stars**

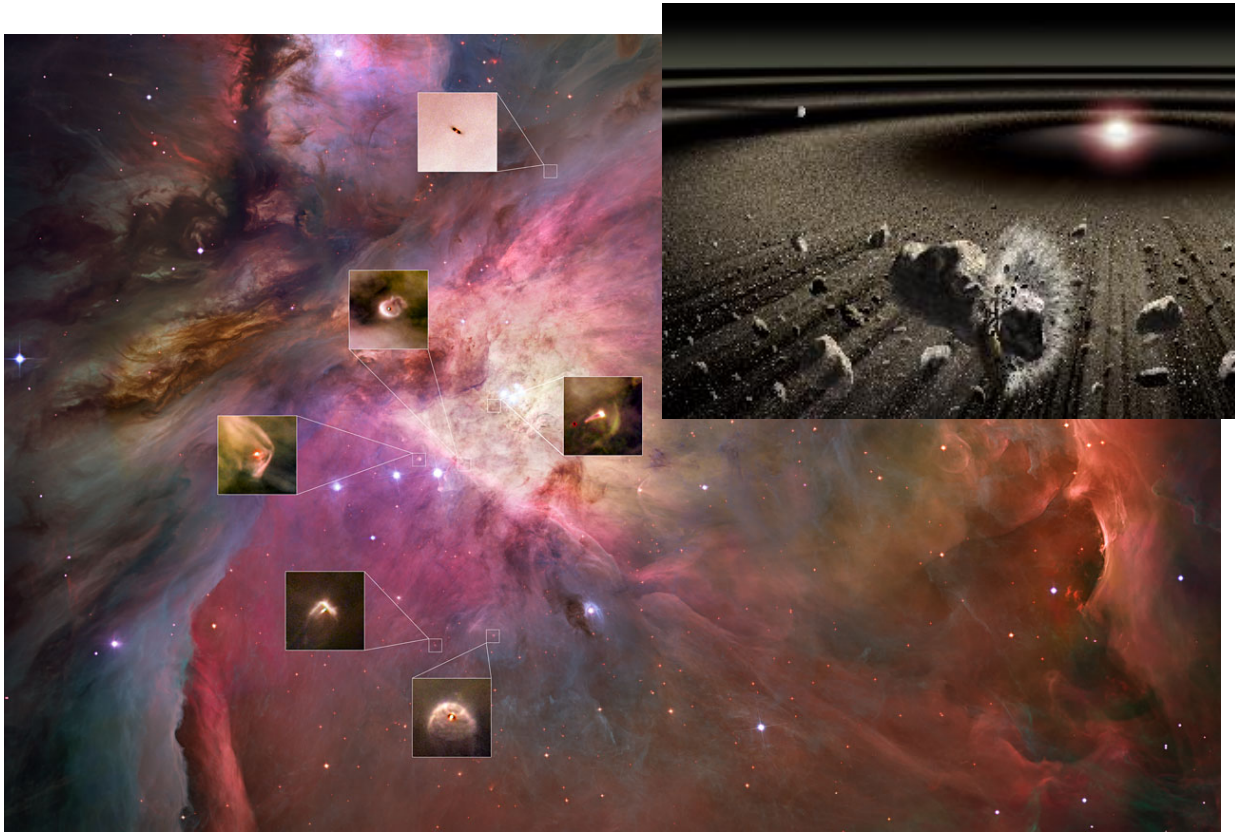
Mind Warp: Deep Time!



Early Earth

The **Sun formed** from the gravitational collapse of a small part of a giant molecular cloud (H + He + heavier elements a.k.a. “dust”, i.e., “stardust”)

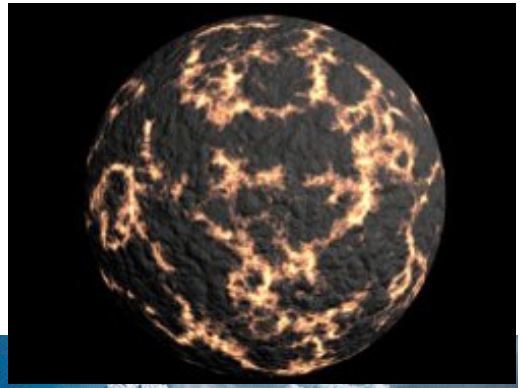
The **Earth formed** in a few million years by electrostatic then gravitational accretion of this dust into grains ▭ clumps of grains ▭ planetesimals (~10 km) ▭ planet size



Embryonic solar systems in the Orion Nebula

Early Earth

- Initially the Earth had **no oceans or atmosphere**:
  - ✓ Made from **rocky/metallic** planetisimals (icy planetisimals formed further out from Sun)
  - ✓ To small & warm to hold onto H or He gasses, and too little other gasses around
- Current models suggest:
  - ✓ **Rocky/icy** planetesimals far from Sun later flung inward by gravitational encounters
  - ✓ Trapped water and gas in this rock was later outgassed by volcanos (when Earth cooler)
  - ✓ Water vapor condensed to form oceans
  - ✓ Gasses (mainly CO_2; also N_2, H_2S, SO_2, H_2) formed <u>early</u> atmosphere



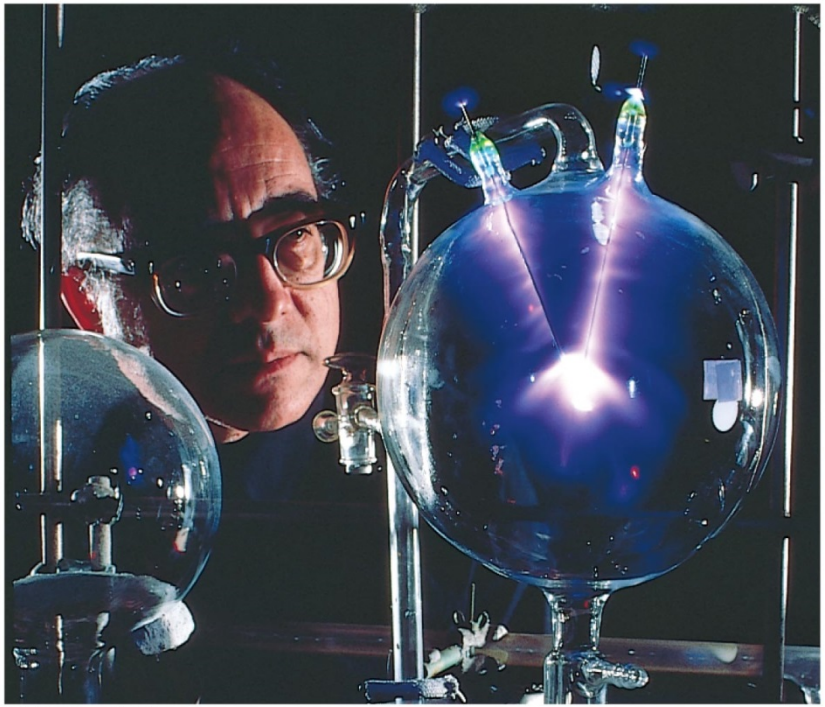
Early Earth

- Zircon evidence suggests Earth possibly had **continents, oceans and atmosphere** as soon as 100 million years after the planet first formed (!)
  - ✓ U-Pb dating ▭ solid zircon 4.4 BYA
  - ✓ O isotopes ▭ solidified in presence of water
  - ✓ Radioactive rocks, or impact that made Moon ▭ accelerated heating ▭ outgassing?

- **Note:** Life arose in a nearly **oxygen-free** environment
  - ✓ O_2 is highly reactive ▭ prevents complex organic molecules forming outside cells
  - ✓ So “life as we know it” **could not form** in the **present** environment on Earth

Origin of Organic Molecules

- Famous **Miller-Urey experiment**:
  - ✓ Assumed (wrongly) early Earth atmosphere was methane and ammonia, and energy drivi the chemical reactions was lightning
  - ✓ Readily synthesized **amino acids** (building blocks of life) and other organic molecules
  - ✓ Similar experiments today…problem: Don't know exact composition of the early atmosphere, especially H_2 content



- Other sources:
  - ✓ Chemical reactions between water and minerals near deep-sea vents
  - ✓ Material from space: Asteroids & comets, UV from Sun acting on dust in solar nebula

Chemistry ⊟ Biology?

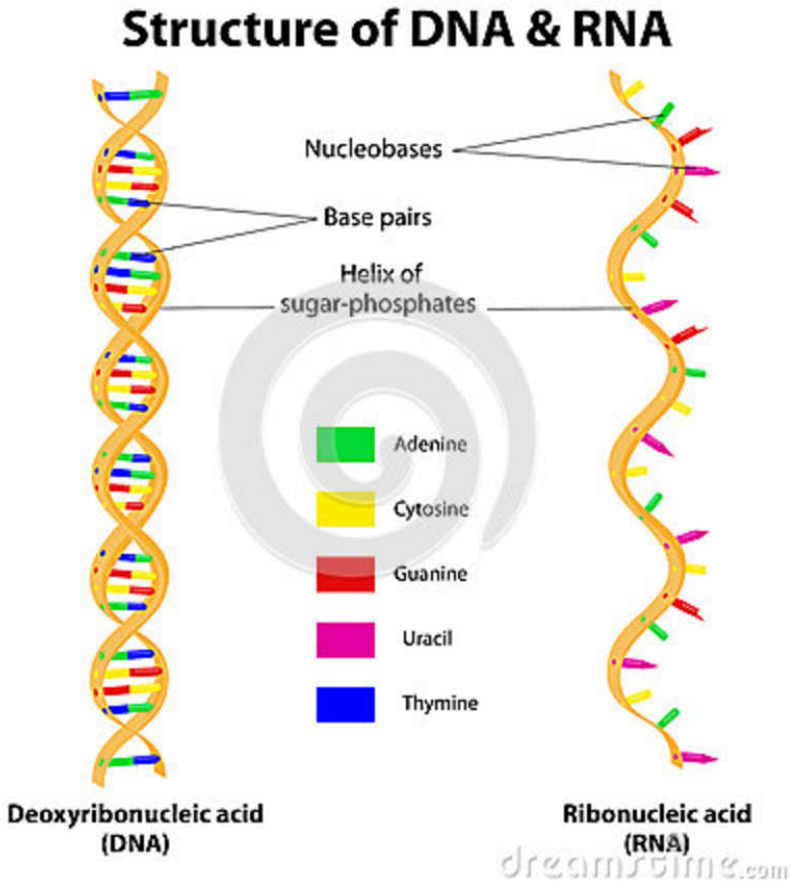
- Plenty of organic molecules around, but how do these form living/replicating cells?
- **Random chance is virtually impossible ⊟ must be a *natural mechanism*. But what?**
- Looking for high probability “chemical pathways”…

Chicken & Egg Paradox #1

- **Problem:** Modern DNA cannot replicate without catalysing proteins (enzymes), and enzymes cannot be made without DNA. **Which came first?**

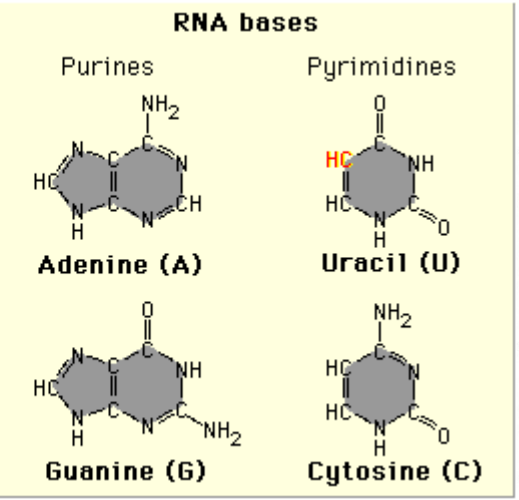
- **Possible Solution:** 1980s (Thomas Cech and colleagues—Nobel prize 1989): RNA *itself* can catalyse many cellular biochemical reactions, including (partially) *their own replication*!

- This supports the idea of an earlier "**RNA World**", where RNA serves as **both** genetic *and* catalysing molecule

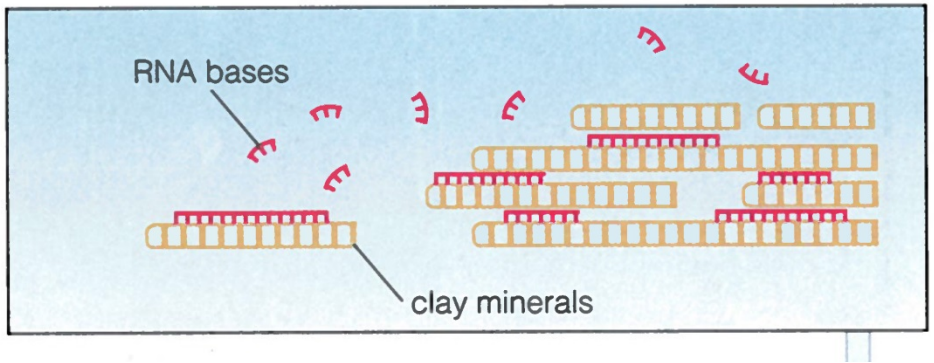


RNA World

- **Experiment:**
  - ✓ Inorganic minerals (a kind of “clay”) can facilitate self-assembly of RNA bases
  - ✓ Quickly and easily produces RNA strands up to **a few dozen** bases in length
    (Note: zircon grain analysis suggests “clay” was widespread 4.4 billion years ago)

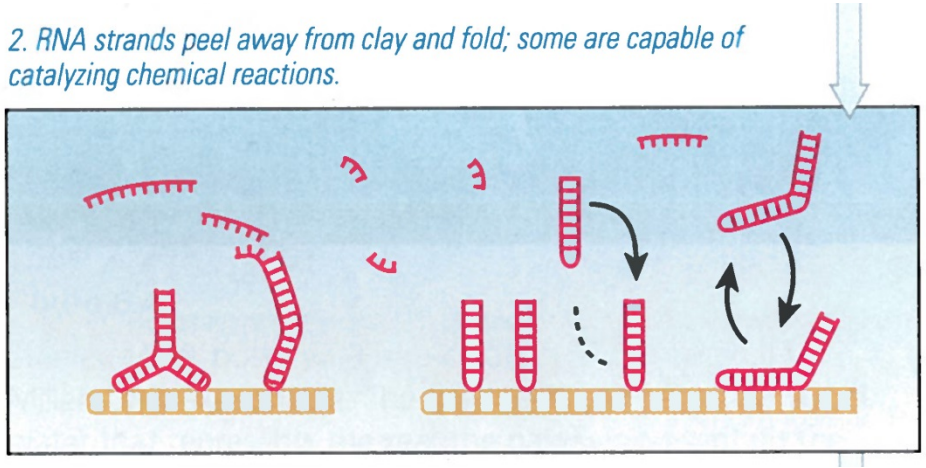


1. Clay minerals catalyze the formation of RNA strands up to a few dozen bases long.



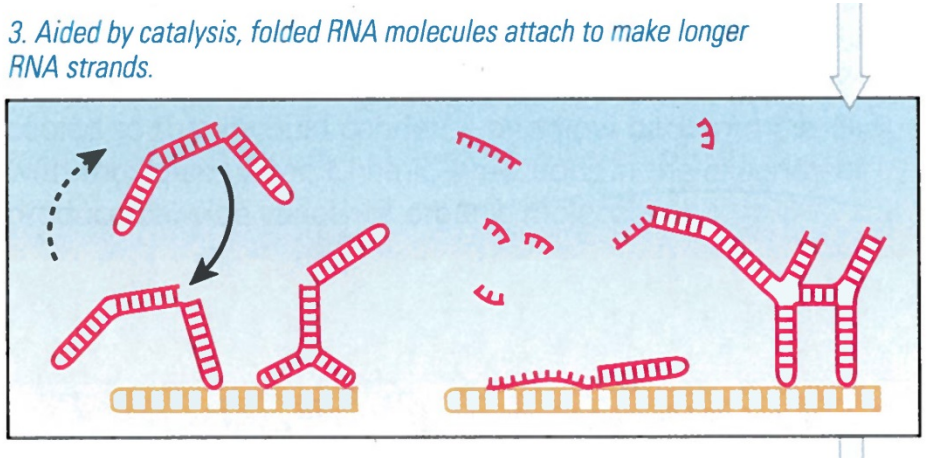
RNA World

- **Experiment:**
  - ✓ But need **length > 165 bases** for RNA to be able to catalyse its own replication
  - ✓ Note 1: Short strands easily peel away from the clay & fold in ways that promote joining
  - ✓ Note 2: Strands as small as 5 bases are able to catalyse various chemical reactions



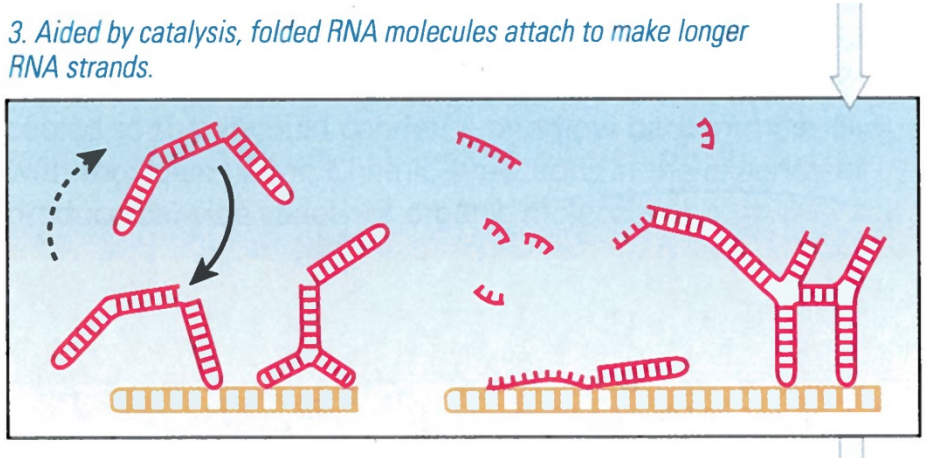
RNA World

- **Experiment:**
  - ✓ But need **length > 165 bases** for RNA to be able to catalyse its own replication
  - ✓ Note 1: Short strands easily peel away from the clay & fold in ways that promote joining
  - ✓ Note 2: Strands as small as 5 bases are able to catalyse various chemical reactions
    …like joining short strands into longer strands



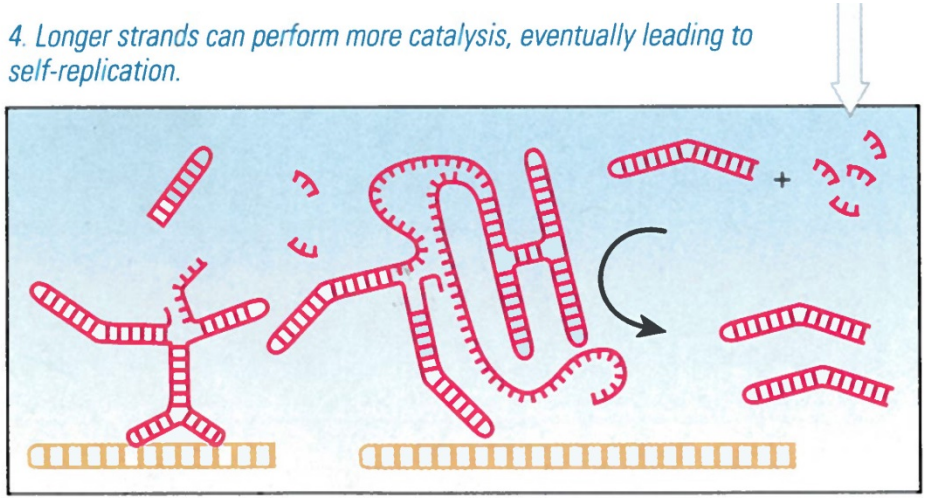
RNA World

- **Experiment:**
  - ✓ Given the countless clay grains, and that the RNA enzyme for joining is very simple, it is not unreasonable to expect very long RNA strand to form *naturally* (**spontaneously**)



RNA World

- **Experiment:**
  - ✓ This natural mechanism for creating longer RNA strands would have dramatically increased the chance of getting an RNA molecule **long enough to self-replicate**
  - ✓ Once this happens, growth is exponential…



These diagrams show steps through which self-replicating RNA may have originated as RNA bases (created by mechanisms like those in the Miller–Urey experiment) and interacted with clay minerals. (Adapted from Briones, Stich, and Manrubia, "The Dawn of RNA World," *RNA Journal*, May 2009.)

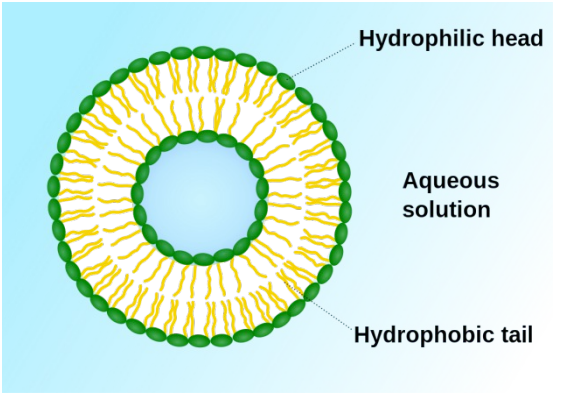
Exponential Growth

- Once you have **one** self-replicating molecule, its numbers grow **exponentially**:
  - ✓ 1 ␣ 2 ␣ 4 ␣ 8 ␣ 16 ␣ 32 ␣ 64 ␣ etc.
  - ✓ After only a few hundred self-replications, they could (given enough “raw material”) fill the entire volume of the Earth’s oceans!
  - ✓ Even with minutes, hours, days, or even years between self-replications, this would be a “blink of an eye” on geological timescales (“deep time”)
  - ✓ Exponential growth starts slowly, but in not too long it “skyrockets”

Chicken & Egg Paradox #2

- **Problem:** Which came first: the **cell membrane**, or its **contents:** genes (RNA/DNA) and proteins?

- **Possible Solution:** Scientists have known for decades that cooling a warm-water **solution of amino acids** can cause them to bond to form a spherical shell "**pre-cell**". **Lipids** (fats) in water also form pre-cells on the surface of the **same clay minerals** that help assemble RNA molecules. Some pre-cell membranes exhibit **real cell membrane behaviors** like:
  - ✓ Selective molecule transport across the membrane
  - ✓ Electrostatic energy storage and discharge
  - ✓ Growth and splitting into "daughter" spheres



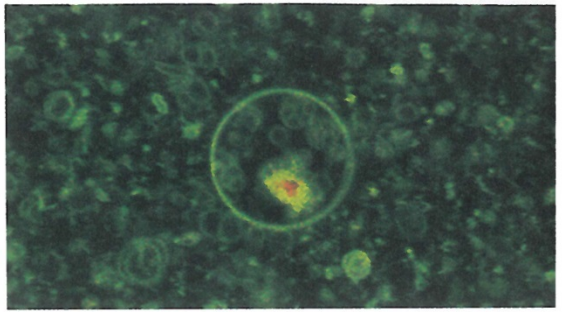
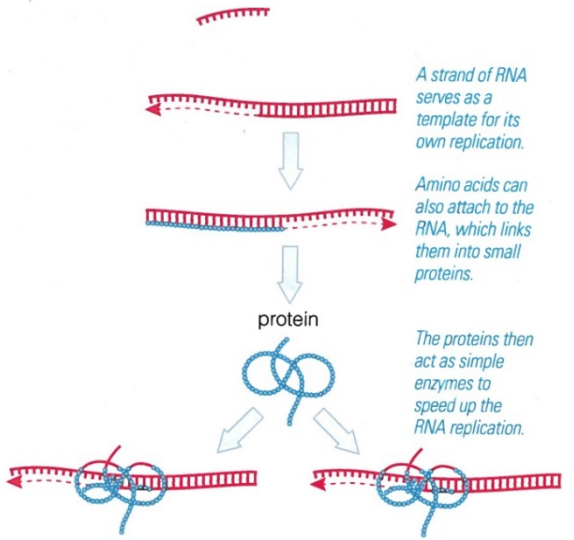


Figure 6.6

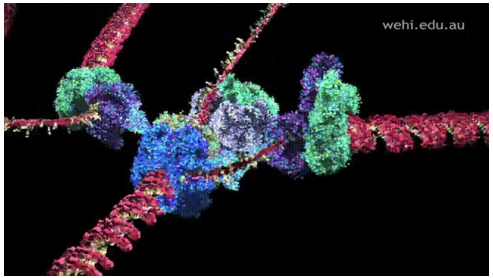
This microscopic photo (made with the aid of fluorescen dyes) shows short strands of RNA (red) contained within lipid pre-cell (green circle), both of which formed with th aid of catalysis by clay minerals beneath them.

Chicken & Egg Paradox #2

- **Confining** RNA & other organic molecules in pre-cells would **facilitate** the origin of life:
  - ✓ Keeping molecules concentrated **increases reaction rates** and likelihood of creating a self-replicating RNA
  - ✓ Suppose a self-replicating RNA emerges that codes for a **replicating enzyme**. The pre-cell would keep this enzyme inside where it would help this particular RNA (and no others) to replicate faster ⇨ **dominate**.
  - ✓ Experiments suggest relatively high early RNA mutation rates ⇨ many opportunities for **natural selection** of more efficient self-replication pathways and increased complexity



a This diagram shows a self-replicating RNA molecule that has evolved the capability to produce a primitive enzyme that helps its own replication.

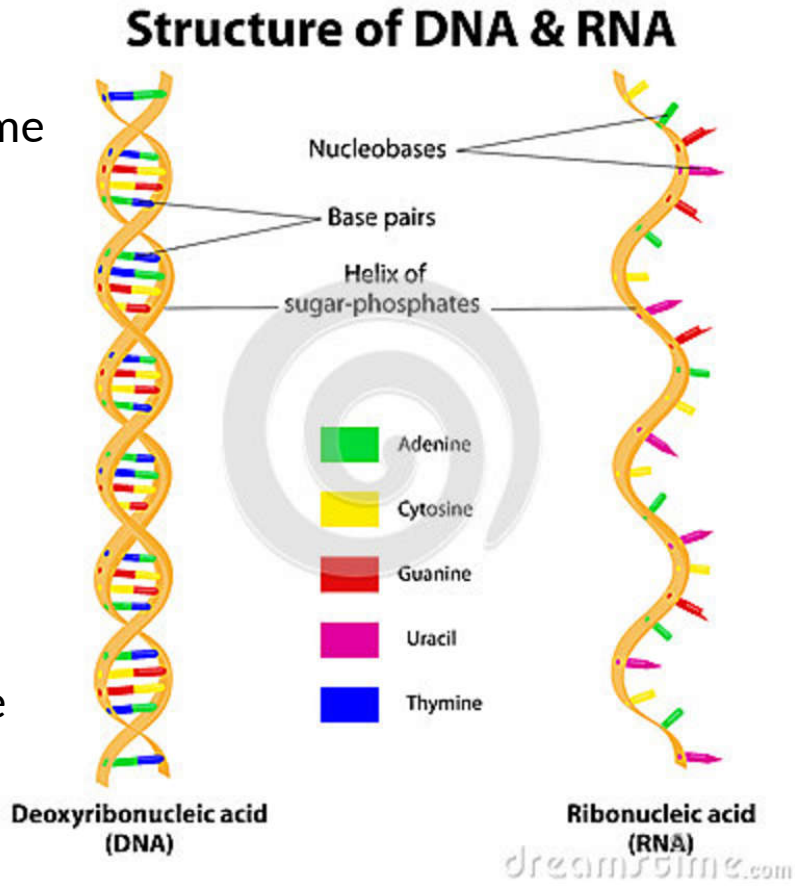


RNA World ⊟ DNA World

- ***Gradually***, these “RNA organisms” would have become “alive”, or “biological”, in the sense we think of now

- Biological natural selection could then take over, resulting eventually in a “DNA World”:
  - ✓ Similarity between RNA & DNA
  - ✓ DNA is a more durable hereditary material
  - ✓ DNA is less prone to copying errors

- RNA also served other functions in the cell, and so would stay, with now DNA serving the hereditary role



Summary of "RNA World"

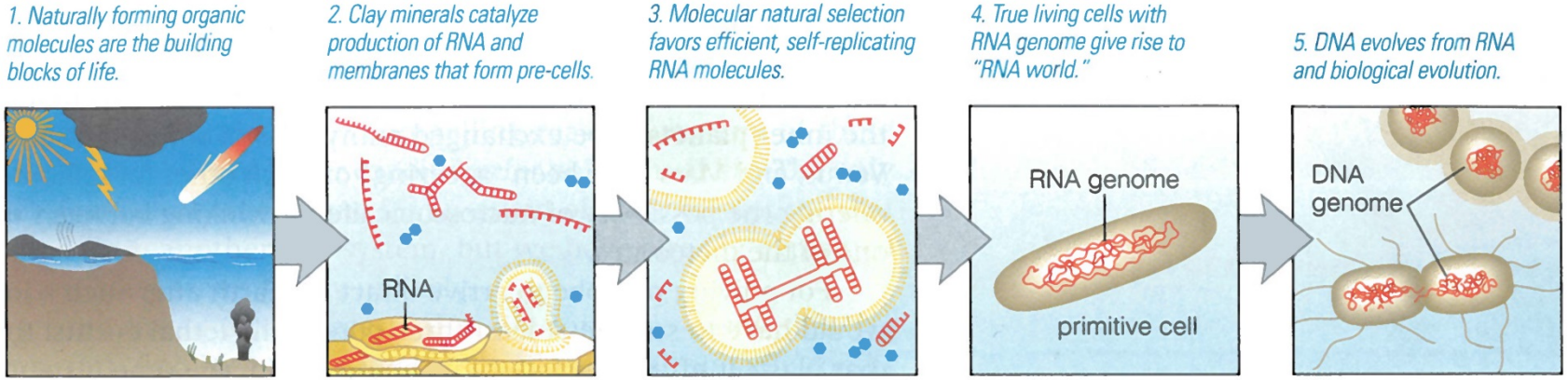


Figure 6.8

A summary of the steps by which chemistry on the early Earth may have led to the origin of life. (Adapted from Campbell, Reece, Simon, *Essential Biology*.)

...and the research continues:

- E.g.: "Researchers may have solved origin-of-life conundrum" (March 2015):
  - "...a pair of simple compounds, which would have been abundant on early Earth, can give rise to a network of simple reactions that produce the three major classes of biomolecules—**nucleic acids, amino acids, and lipids**"
  - If true, it might solve **both** chicken and egg paradoxes!

Summary

- We still do not know how life started on Earth, and we might never know for sure
- We have constructed one ***plausible*** model (RNA World), backed up at many points by experiments, and scientists are working on others
- But much work remains to unravel this mystery, and this is good. Science thrives on mysteries!

So exactly how life began is still a mystery…

Main Point

- The origin of life seems like a ***plausible/likely*** consequence of conditions on the early Earth, and the laws of nature (chemistry ⊂ biology)

- The next question is: Is life a ***necessary*** consequence of the laws of nature at the most elementary level, i.e., physics? (physics ⊂ chemistry ⊂ biology)