Controversies in the Origins of Life: Metabolism-first or Replication-first?

Definitions

• Metabolism: the sum of anabolic and catabolic reactions in life
  – Catabolism: using matter to make energy (sugar $\rightarrow$ work)
  – Anabolism: using energy to make matter (light $\rightarrow$ sugar)

• Replication: When a molecule makes a copy of itself (DNA replicating)
• RNA: Ribonucleic Acid

• DNA: Deoxyribonucleic Acid
Evolution of Life Timeline

- Formation of Earth: 4.5 MY
- Stable hydrosphere: 4.2 MY
- Probiotic chemistry: 4.2-4.0 MY
- Pro-RNA world: 4.0 MY
- RNA world: 3.8 MY
- First DNA/protein life: 3.6 MY
- Diversification of life: 3.6-present

± 0.2 MY
Evolution of Life Timeline

Formation of Earth: 4.5 MY
Stable hydrosphere: 4.2 MY
Probiotic chemistry: 4.2-4.0 MY
Pro-RNA world: -4.0 MY
RNA world: -3.8 MY
First DNA/protein life: -3.6 MY
Diversification of life: 3.6-present

± 0.2 MY

Fossils / genetics
Evolution of Life Timeline

Chemical models from Stanley Miller and on
Evolution of Life Timeline

- Formation of Earth: 4.5 MY
- Stable hydrosphere: 4.2 MY
- Probiotic chemistry: 4.2-4.0 MY
- Pro-RNA world: -4.0 MY
- RNA world: -3.8 MY
- First DNA/protein life: -3.6 MY
- Diversification of life: 3.6-present

± 0.2 MY

Geological evidence

Biochemical evidence
Evolution of Life Timeline

- Formation of Earth: 4.5 MY
- Stable hydrosphere: 4.2 MY
- Probiotic chemistry: 4.2-4.0 MY
- Pro-RNA world: ±4.0 MY
- RNA world: ±3.8 MY
- First DNA/protein life: ±3.6 MY
- Diversification of life: ±3.6-present MY

Anyone’s guess
Evolution of Life Timeline

Chemistry: Origin of sugars, nucleotides, amino acids, phosphate, sulfides, etc.

Biochemistry: what can life do and what is most likely for life to do?

± 0.2 MY
RNA World

• RNA was dominant genetic material
  – Protein synthesis done by RNA
  – RNA may self-replicate (Spiegelman’s monster)

• RNA was catalytic material
  – Ribozymes (RNA enzymes) catalyze several biochemical reactions
  – RNA a substantial portion of coenzymes
Two Views on RNA World

• “Weak” RNA World
  – RNA was precursor to DNA/Protein as indicated by biochemical evidence
  – No idea on what preceded RNA
    • Either replication or metabolism first

• “Strong” RNA World
  – RNA or something very similar was \textbf{first} life
  – Replication-first
  – Provides elegant answer to origin of life
When did replication come on the scene?

• “Replication first”-er
• Evaluate metabolism-first ideas
  – Complex Systems:
    • Dyson, Kauffman
  – Membranes
    • Lancet, Deamer
  – Thioesters, Sulfides
    • De Duve, Wachtershauser, Russell, Lindhal, Morowitz
Complex systems

- Dyson’s Toy model based on ferromagnetic Systems

- Kauffman’s complexity model- Autocatalytic compounds eventually form complex systems
Anet’s criticism

- No real grounding in chemistry
- No experimental evidence
- Oversimplifications aren’t valid
- Errors?
Lipids membranes

- Vesicles form spontaneously under pH ~7-9, from fatty acids
- “Reproduce”, “Eat”, “Grow”
- Very easy to form, stable
Anet’s criticism

• Minimal information being passed from one to generation to the next
• Not related to replication as it’s known today
• Abstract model
Iron-Sulfur World

- Metabolism on a pyrite grain
- Mimics modern day metabolism (albeit in reverse)
- Metabolic processes fairly well thought out (Wachtershauser 1988)
- Well-liked by geologists
- Some experimental evidence for pathways
Anet’s criticism

- Spontaneous assembly a cyclical chemical reactions (vs. spontaneous assembly of polymer?)
- Catalyst is initial metabolic energy source
- “Magic” catalyst not so magical
- Metabolic reactions tend to go one way
General critique of Metabolism-first

• Most metabolism-first proposals aren’t founded in chemistry
  – Ideas from physicists, theoretical biologists, patent lawyers, geochemists
• Not much experimental work, most are model-based
• No means of passing genetic information?
Anet’s view

- RNA formed spontaneously through chemical processes, formed self-replicating catalyst, the rest is history
- Molecular midwives encourage base-pairing, help spontaneous assembly (shown experimentally)
Robert Shapiro (Quarterly Review of Biology)

• “Metabolism first”-er
• Author of “Skeptic’s guide to the origin of life”
• Focuses primarily on Ferris’ clay-catalyzed RNA polymerization experiment
• Has taken other paradigms to task as well
Clay and RNA polymerization

- Clay catalyzes the spontaneous polymerization of activated nucleosides to form strands of RNA (length ~50)
- Uses the natural chemical interactions between nucleosides and clay to form polymers
Shapiro’s criticism

- Didn’t use real clay (doesn’t work with natural clay)
- Methyladenine is not pre-biotic
- Doesn’t work with nucleoside triphosphates
- Polymers of length 40 wouldn’t really do much of anything
  - Unlikely to be autocatalytic
  - Random chirality
- More recent research suggests this last point may be less valid - the clays are selective, and can polymerize further
Other Critiques

- Nucleotide chemistry involves 3 parts:
  - CH$_2$O (formose) chemistry
    - Ribose not stable
    - Lots of chirality
  - HCN (cyanide) chemistry
    - HCN reacts with CH$_2$O to form tar
    - Nucleic bases low yields
  - PO$_4$ (phosphate) chemistry
    - Hard to condense phosphate

Environments don’t mix well!
Shapiro’s view

• Small molecule interactions led to origin of life
• Reaction coupling leads to increased complexity
• Metabolism yielded the necessary starting components for replication
Overview 1

- Neither metabolism-first or replication-first has the clear upper-hand
- Pushing realm of philosophy (causation arguments, Popper’s theory on science)
Overview 2

**Metabolism first**
- **Cons:**
  - Mostly model based, few experiments
  - Workers not always chemists
  - No known miracle catalysts
- **Pros**
  - Less worry for messy system
  - Metabolism less worried about chirality
  - Provides pure chemicals

**Replication first**
- **Cons**
  - Most systems not tolerant of dirt
  - “Prebiotic” chemistry isn’t so prebiotic
  - Reflective of “genes-first” biology
- **Pros**
  - Mostly experimental, done by chemists, biochemists
  - Provides easy answer for life
  - Provides easy route to evolution
Abundances of elements in metabolism very similar to elements of replication (RNA)

<table>
<thead>
<tr>
<th></th>
<th>Cosmic</th>
<th>Oceans</th>
<th>Bulk Bacteria</th>
<th>P-lipid</th>
<th>RNA</th>
<th>Metabolic Core</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>$2.8 \times 10^6$</td>
<td>$4.9 \times 10^7$</td>
<td>203</td>
<td>90</td>
<td>10</td>
<td>15.4</td>
</tr>
<tr>
<td>O</td>
<td>1400</td>
<td>$2.5 \times 10^7$</td>
<td>71.7</td>
<td>8</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>C</td>
<td>680</td>
<td>974</td>
<td>116</td>
<td>46</td>
<td>9.5</td>
<td>9.5</td>
</tr>
<tr>
<td>N</td>
<td>230</td>
<td>633</td>
<td>15.5</td>
<td>1</td>
<td>3.75</td>
<td>2</td>
</tr>
<tr>
<td>S</td>
<td>43</td>
<td>12,400</td>
<td>0.19</td>
<td>0</td>
<td>0</td>
<td>0.05</td>
</tr>
<tr>
<td>P</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
Replication and Metabolism are linked

- Coenzymes are small molecules that assist enzymatic (protein) chemical reactions
- Many coenzymes have RNA parts
  - Suggested to be artifacts of RNA world
  - RNA “tags” on important compounds
I. Condensed Phosphates (ATP)

NAD

FAD

Coenzyme A
I. Condensed Phosphates (ATP)

- OPO₃⁻ Adenosine
- PO₄⁻ Adenosine

Coenzyme A

NAD

FAD
I. Condensed Phosphates (ATP)

NAD

FAD

Coenzyme A
Coenzymes inform early metabolism?

• Coenzymes do majority of chemical work in metabolism
  – Not all coenzymes have RNA parts
  – RNA part doesn’t serve any purpose other than for enzyme placement
  – Actual work done by aromatic rings (HCN), metal ions, sulfides, and phosphate
  – Sugars are never involved though they could be

• Perhaps the origin of life was sugar-free?
WHAT IS EVOLUTION?

• Most non-scientists seem to be quite confused about precise definitions of biological evolution.
• When discussing evolution it is important to distinguish between the existence of evolution and various theories about the mechanism of evolution.
WHAT IS EVOLUTION?

One of the most respected evolutionary biologists has defined biological evolution as follows:

"In the broadest sense, evolution is merely change, and so is all-pervasive; galaxies, languages, and political systems all evolve.

_Biological evolution ... is change in the properties of populations of organisms that transcend the lifetime of a single individual._

The ontogeny of an individual is not considered evolution; individual organisms do not evolve. The changes in populations that are considered evolutionary are those that are inheritable via the genetic material from one generation to the next. Biological evolution may be slight or substantial; it embraces everything from slight changes in the proportion of different alleles within a population (such as those determining blood types) to the successive alterations that led from the earliest protoorganism to snails, bees, giraffes, and dandelions." - Douglas J. Futuyma in _Evolutionary Biology_, Sinauer Associates 1986

http://www.talkorigins.org/faqs/evolution-definition.html
WHAT IS EVOLUTION?

• It is important to note that biological evolution refers to populations and not to individuals and that the changes must be passed on to the next generation. In practice this means that,

*Evolution is a process that results in heritable changes in a population spread over many generations.*

This is a good working scientific definition of evolution; one that can be used to distinguish between evolution and similar changes that are not evolution.

• Another common short definition of evolution can be found in many textbooks:

• "*In fact, evolution can be precisely defined as any change in the frequency of alleles within a gene pool from one generation to the next.*" – (Helena Curtis and N. Sue Barnes, *Biology*, 5th ed. 1989 Worth Publishers, p.974)
Meaning of ALLELE

• Definition: [n] one of two alternate forms of a gene that can have the same locus on homologous chromosomes and are responsible for alternative traits; "some alleles are dominant over others"
Evolution (cont.)

- When biologists say that they have observed evolution, they mean that they have detected a change in the frequency of genes in a population.
POOR DEFINITIONS

The Oxford Concise Science Dictionary:

"evolution: The gradual process by which the present diversity of plant and animal life arose from the earliest and most primitive organisms, which is believed to have been continuing for the past 3000 million years."

This is poor because not only does this definition exclude prokaryotes, protozoa, and fungi, but it specifically includes a term "gradual process" which should not be part of the definition.

More importantly the definition seems to refer more to the history of evolution than to evolution itself. Using this definition it is possible to debate whether evolution is still occurring.

Also, this definition provides no easy way of distinguishing evolution from other processes. For example, is the increase in height among Caucasians over the past several hundred years an example of evolution? Are the color changes in the peppered moth population examples of evolution?
DEFINITION (CONT.)

• “Recently I read a statement from a creationist who claimed that scientists are being dishonest when they talk about evolution. This person believed that evolution was being misrepresented to the public. The real problem is that the public, and creationists, do not understand what evolution is all about. This person's definition of evolution was very different from the common scientific definition and as a consequence he was unable to understand what evolutionary biology really meant. This is the same person who claimed that one could not "believe" in evolution and still be religious! But once we realize that evolution is simply "a process that results in heritable changes in a population spread over many generations" it seems a little silly to pretend that this excludes religion! “

• Laurence Moran, January 22, 1993
BAD DEFINITIONS

Standard dictionaries are even worse:

"evolution: ...the doctrine according to which higher forms of life have gradually arisen out of lower.." - Chambers

"evolution: ...the development of a species, organism, or organ from its original or primitive state to its present or specialized state; phylogeny or ontogeny" - Webster's

These definitions are simply wrong. Unfortunately it is common for non-scientists to enter into a discussion about evolution with such a definition in mind. This often leads to fruitless debate since the experts are thinking about evolution from a different perspective. When someone claims that they don't believe in evolution they cannot be referring to an acceptable scientific definition of evolution because that would be denying something which is easy to demonstrate. It would be like saying that they don't believe in gravity!
Chapter 3. Evolution

• Charles Darwin & Natural Selection
• Evidence of evolution – the fossil record
• Mechanism of evolution – DNA
• A modification - Punctuated Equilibrium
• Creationism – a formidable opponent
Fossils

• Evolution is a fact, not a theory

• Evidence comes from the fossil record, but also from biology, anthropology

• What is the fossil evidence? Petrified remains of earlier life that records systematic changes
Fossil hominid skulls – missing links no longer missing?

Some of the figures have been modified for ease of comparison Smithsonian Institution.)
Fossil hominid skulls.

(A) *Pan troglodytes*, chimpanzee, modern
(B) *Australopithecus africanus*, STS 5, 2.6 My
(C) *Australopithecus africanus*, STS 71, 2.5 My
(D) *Homo habilis*, KNM-ER 1813, 1.9 My
(E) *Homo habilis*, OH24, 1.8 My
(F) *Homo rudolfensis*, KNM-ER 1470, 1.8 My
(G) *Homo erectus*, Dmanisi cranium D2700, 1.75 My
(H) *Homo ergaster* (early *H. erectus*), KNM-ER 3733, 1.75 My
(I) *Homo heidelbergensis*, “Rhodesia man,” 300,000 - 125,000 y
(J) *Homo sapiens neanderthalensis*, La Ferrassie I, 70,000 y
(K) *Homo sapiens neanderthalensis*, La Chappelle-aux-Saints, 60,000 y
(L) *Homo sapiens neanderthalensis*, Le Moustier, 45,000 y
(M) *Homo sapiens sapiens*, Cro-Magnon I, 30,000 y
(N) *Homo sapiens sapiens*, modern
EVIDENCE OF EVOLUTION

• The best arguments for evolution include:
  • Branching organization of life
  • Homology
  • Vestigial structures and imperfections
  • Embryonic history
  • Biogeography
Homology of forelimbs of various vertebrates, similar bones have similar colors. Although the functions are different the bones are structurally similar and develop from similar embryonic tissues. Simplest explanation is that all evolved from a common ancestor, the lobe-finned fish.

Homology: organs with different functions are built with same basic parts.
C. Panda’s thumb. Their true thumb has fused into a digit, but because they need a functional thumb, a modified wrist bone serves as one. A classic example of an imperfection.