The Transition to Life

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Chemical Evolution → ? → Biological Evolution

Interacting Chemicals
Reproduction of → Organisms
↘ Natural Selection

Based on Simplest Life Now:

Need:

1. Nucleic Acids Replicatable Information
2. Proteins Enzymes (Catalysts)
3. Lipids Membranes (Enclosure)
4. Carbohydrates Energy Storage
   (Pigments) (Energy Conversion)

Too much to ask of chemical evolution

$\Rightarrow$ Protolife?

Protolife

1. "Virus" Free living but equivalent in complexity

   Protein + Nucleic Acid + Supply by Environment

   Genetic Code

2. Protein Protolife

   Protein → Self Replication?

3. Nucleic Acid Protolife

   RNA → Self Catalysis?

4. Something Else

   Minerals

   Clay Layers

   Mineral - Molecule

   Pyrite

   Thioesters

Genetic Takeover

   ? → RNA → DNA

Protein-Based Protolife

1. Proteinoid microspheres - Sidney Fox

Amino Acids + Dry Heat ⟶ Proteinoids

(Hot Tidepool?) ↓ H_2O

(Tide)

Microspheres

Protocells

Protolife?

Can Add Proteinoid

Split

Bud

Form Chains

(Look like life)

Grow

Divide "Reproduce"

Bud

Like Bacteria

But "Reproduction" not exact

Later incorporate Nucleic Acids

Proteinoid ⟶ Cells ⟶ Genes

Nucleic Acid Based Protolife

RNA → Genes → Protein → Cells

Self-replicating RNA molecules

Experiment by Sol Spiegelman

RNA from Q_β Virus - parasite on bacteria

Injects RNA - Bacterium makes replicase

Enzyme to Replicate RNA

RNA multiplies, using activated nucleotides in

Bacterium → new viruses

In Test Tube: Template RNA, Replicase, Activated Nucleotides (ATP, CTP, GTP, UTP)

$\Rightarrow$ RNA copied <u>without</u> machinery of cell

Variation: <u>No</u> template RNA

Replicase made RNA from nucleotides

↑

Protein

Manfred Eigen - further experiments with RNA in test tube:

Mutant RNA strands compete

Degrade to smallest (~ 200 nucleotides)

RNA that replicase could recognize

(Monster - Selfish RNA)

RNA can do self-catalysis in some cases

Could this have led to self replication?

Eigen scenario

1. A replicating RNA molecule forms by chance (random replicator - not a gene)
   ribozyme (catalyst, made of RNA)

2. Family of **similar** RNA's develops (quasispecies)

3. Connection to proteins
   (quasispecies specialize to make parts of protein)

4. Complex interactions (hypercycles)

5. Use lipids to make protocells

6. Competition leads to biological evolution

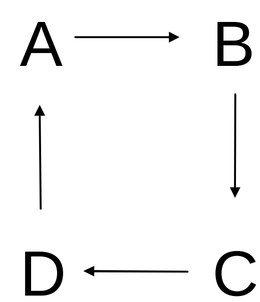
Problems with Nucleic Acid First Scenario

1. Hard to get monomers
2. Unlikely to link correctly
3. Need existing proteins and lipids
4. Hypercycles subject to instabilities

N = size of molecular population

If N small → Population Collapse

If N large → Selfish RNA, Short Circuit



If B $\longrightarrow$ D Short Circuit

$\Rightarrow$ Only narrow range of sizes works

The Origin of the Genetic Code

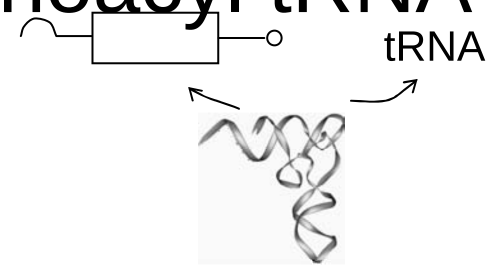
- We need more than **either** protein or RNA protolife
- Need interaction via genetic code
- Need **translation**
- Consider first a scenario by R. Shapiro

Shapiro’s Fable

The case for the “chicken”

Protein first $\Rightarrow$ replication problem

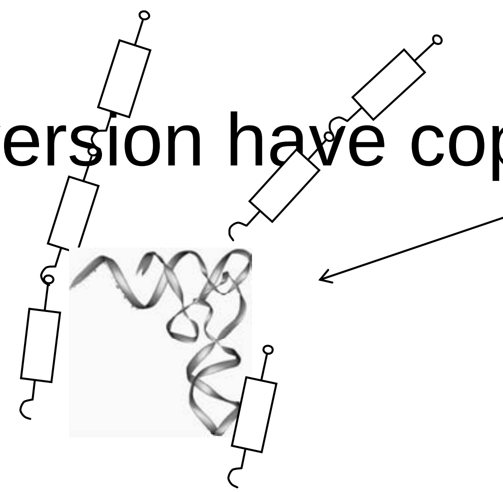
“interpreters” aminoacyl tRNA synthetases



Match tRNA &

Amino acids

Could an earlier version have copied proteins directly?



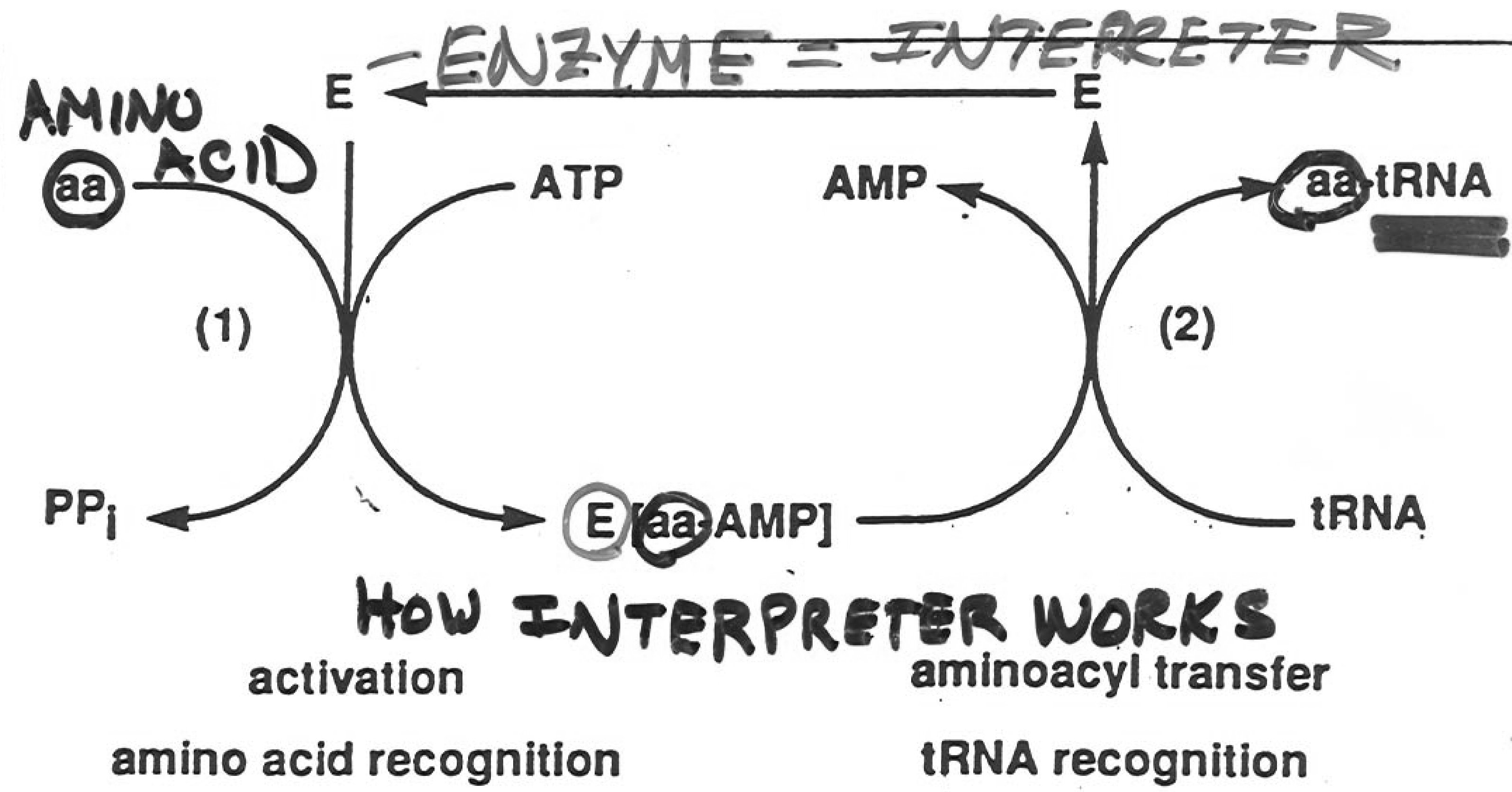


Fig. 1 The two steps of the reaction catalysed by aminoacyl-tRNA synthetases. The tRNA is recognized in the second step (through the features designated paracodon in this article) by the enzyme carrying a bound aminoacyl-AMP intermediate. Participation of the aminoacyl group in the recognition process is thus an attractive possibility.

1. Early Evolution: Start with 4-6 amino acid
   types, gradually add more
   enzymes increase in size and catalytic power
2. First use of phosphate as energy? (ATP)
   or sugar-phosphate chains for construction
   (Teichoic acids in membranes of some bacteria)
   (partial Q_β replicase)
3. Bases added for structure
   Support for protein synthesis ⟶ ribosome

4. Begin to copy RNA (Full Q_{β} replicase)
   Natural selection ⟶ better ribosome

5. Specialized, Short RNA aided attachment of

   amino acids to proteins; became tRNA

6. Then mRNA - to align tRNA's

   now a separate genetic system that evolves

7. DNA developed from RNA

Shapiro dates last step to prokaryote -eukaryote split (different ways of storing DNA info)

Tests:

1. Synthesize in lab? Not possible yet.
2. Molecular archaeology - vestigial ability of

   interpreters to recognize amino acids in proteins
3. Survivors of protein era? prions?

Support for the “chicken”

1. 1988 discovery that interpreter does not

   use tRNA codon to recognize correct tRNA

   (in some cases) ~ 1/2

   - instead a single base pair at the other end of tRNA

   ⇒ simpler, older code

   second genetic code

   ⇒ connection of interpreter and tRNA

   more primitive than current code

2. Dyson modeling of molecular “populations”

Transition from disorder to order

(non-life) (life)

Finds number of monomer types likely to be

9 - 11 (ok if used ~ 1/2 of modern proteins)

But nucleotides (only 4) - not enough

Favors protein first

The Egg Strikes Back

Other work shows some RNA can catalyze Non-RNA reactions

1. RNA in ribosome appears to be what catalyzes peptide bond formation

   Noller, et al. 1992, *Science*, **256**, 1416

2. RNA "ribozyme" catalyzes reactions between amino acids and tRNAs

   First "interpreter" may have been RNA

   Piccirilli, et al. 1992, *Science*, **256**, 1420

   ⟶

Origin of the Genetic Code

Crucial step in any theory

Allows communication

Nucleic Acids ⟷ Proteins

Early versions probably coded fewer amino acids - less specific

Purine Either

Some evidence for RNY and G - C more stable

Pyrimidine

⇒ 4 codons

GGC	glycine	Common in Miller Urey and Meteorites
GCC	alanine	
GAC	aspartic acid	
GUC	valine	

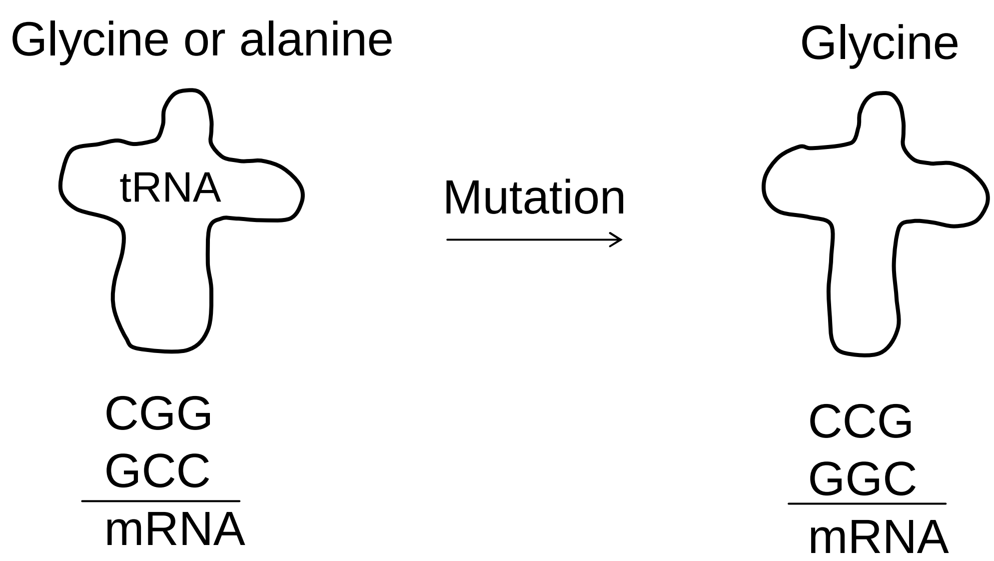
Others added later

Evolution of Genetic Code

Gaining specificity

If early tRNAs carries more than 1 kind of amino acid

e.g.



Evidence that code has evolved Freeland, et al. Tested 10^6 other codes

Only one better at minimizing bad effects of

mutations

$\Rightarrow$ Natural Selection

Still Evolving

Some organisms have slightly different codes in

mitochondria or in nucleus

Other Ideas

- Neither the chicken nor the egg came first
- Transitional forms that were later discarded

Or was it the "egkin"?

Some experiments with peptide nucleic acid (PNA).

PNA: <u>Peptide</u> backbone with bases

Can act as template for polymerization of RNA
From activated nucleotides

(Böhler, et al., *Nature*, **376**, 578
& comments by Piccirilli, pg. 548 } 17 Aug. 1995

PNA could be simpler to form under prebiotic conditions
Main point is that a simpler thing (not necessarily PNA)
could have preceded RNA

Membranes

- Membranes provide enclosure
  - Also fundamental for metabolism
- Membranes never arise from scratch
  - Always passed down and added to
  - All derived from ancestral cell
- T. Cavalier-Smith proposes membranes
  - Plus nucleic acid formed “ob-cell”
  - Merger of 2 ob-cells formed first cell

Summary of Proto-Life Development

Stage	**Proteins**	**Halfway # 1** Peptide Nucleic Acids	**Halfway # 2** RNA Ribozyme	**Nucleic Acids**
Monomers	Amino Acids	Bases Amino Acids	Ribose Sugars Bases Phosphates Amino Acids	Ribose Sugars Bases Phosphate
Polymerization	Proteinoids	Short strands of PNA's	Short strands of RNA + amino acids	Short strands of RNA
Replication	?	Affinity for complementary bases + ease of peptide bonding	Affinity for complementary bases	Affinity for complementary bases
Pre-life	Proteinoids + RNA?	Separation of proteins and nucleic acids	Separation of nucleic acids and protein parts	RNA adapts proteinoids as needed
Life	Proteins	Disappears	Disappears	DNA and RNA

Alternative Ideas

Alternative Ideas

A different initial genetic substance + genetic

takeover

e.g. clay life

Panspermia

Various versions

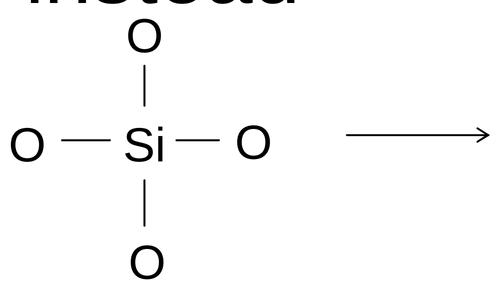
Creationism

Clay Life

A.G. Cairns - Smith

Silicate Life? Early Genetic Material

$O = Si = O$ but O can make another bond instead



great variety of minerals

Layers - clay

Also occasional impurity (Al, Mg, …)

Can grow by adding dissolved material

Tends to copy pattern of impurities in adjacent layers - reproduction?

Defects - different impurity, … (mutations?)

Sheets can separate - move - and then "reproduce"

Advantages	Problem
Clay clearly present	How to get to
Simpler genetic structure	life as we know it
Crystal growth occurs naturally	

Clay Life $\xrightarrow{?}$ Life

Clay life begins to synthesize, use "organic"

[carbon] molecules

Clays do have some catalytic activity

Genetic takeover

organics $\longrightarrow$ protein/RNA mechanisms

Clay discarded

Tests

1. Surviving clay life - unlikely

2. New clay life - maybe in some places

3. Demonstrate in lab

Focus on Energy

G. Wächtershäuser

Inorganic - organic connection

FeS_2 (Iron pyrite)

Attracts negatively charged molecules

Surface catalysis provides energy via formation from

$FeS + H_2S$

Scene is hot sulfur vents on sea floor

Some recent successes in simulations

Amino acids formed peptide bonds

Panspermia

- Life arose elsewhere and was delivered here
  - Original idea was bacterial spores
  - Hoyle and Wickramasinghe
    - Life originates on dust grains, comets, …
  - May be revived (meteorites from Mars)
- Directed panspermia
  - Crick and Orgel (tongue in cheek)
  - Earth seeded by intelligent ET

Exotic Life Forms?

Antidote to Earth Chauvinism

1. Different organic molecules (e.g., PNA)
   Rebek's variation $\longrightarrow$ self replication
   possibility of life based on other polymers

2. Not based on Carbon
   Silicon (Si) instead of Carbon?
   (also 4 bonds)
   & more (135 $\times$) more abundant on Earth

Negatives:

a. C - C bond $2 \times$ stronger than Si - Si

b. Si - O   stronger than Si - Si

$\longrightarrow$ silicates, not .. Si - Si - Si …

c. C forms multiple bonds   (e.g. $C \equiv N$)

Si rarely dies

d. C + O $\longrightarrow$ CO or CO_2 (gas - further reacts)

Si + O SiO_2 - silicate rocks

$\Rightarrow$ Si unlikely to replace C

SiO_2 (clay life)?

3. Other Solvents

Earth: Liquid water 273-373 K

Alternatives:		T_{freeze}	T_{boil}
Ammonia	NH_3	195	240
Methyl Alcohol	CH_3OH	179	338
Methane	CH_4	91	109
Ethane	C_2H_6	90	184

Water is better solvent

Also better for temperature regulation

But others could play a role in colder zones

extend CHZ?

4. Non-chemical life?

Disembodied intelligence

Black cloud life?

Other forces

Strong nuclear force? $\tau \sim 10^{-15}$ s

Gravity?

Estimates for f_l

- Possible range is very large
  - Perhaps 10^{-6} (one in a million) to 1 (all)
- Arguments for large value
  - Life part of overall evolution in complexity
  - Arises naturally from interplay of forces

Estimates for f_l

- Arguments for small value
  - May need more than liquid water
    - Large tides, so large moon
    - Dry land (for polymerization)
  - Life may be a fluke
    - A rare statistical event

Can we estimate f_l from early origin of life?

Very ancient microfossils (now disputed)

$\Rightarrow$ Life arose as early as 3×10^9 yr ago

[soon after end of heavy bombardment]

Lineweaver & Davis argued:

Early origin $\Rightarrow f_l > 0.33$

For suitable planets older than 1×10^9 yrs.

Statistics from <u>one</u> example!