The Transition to Life

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Chemical Evolution → ? → Biological Evolution

Interacting Chemical → Reproduction of Organisms

↓

Natural Selection

Based on Simplest Life Now:

Need:

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

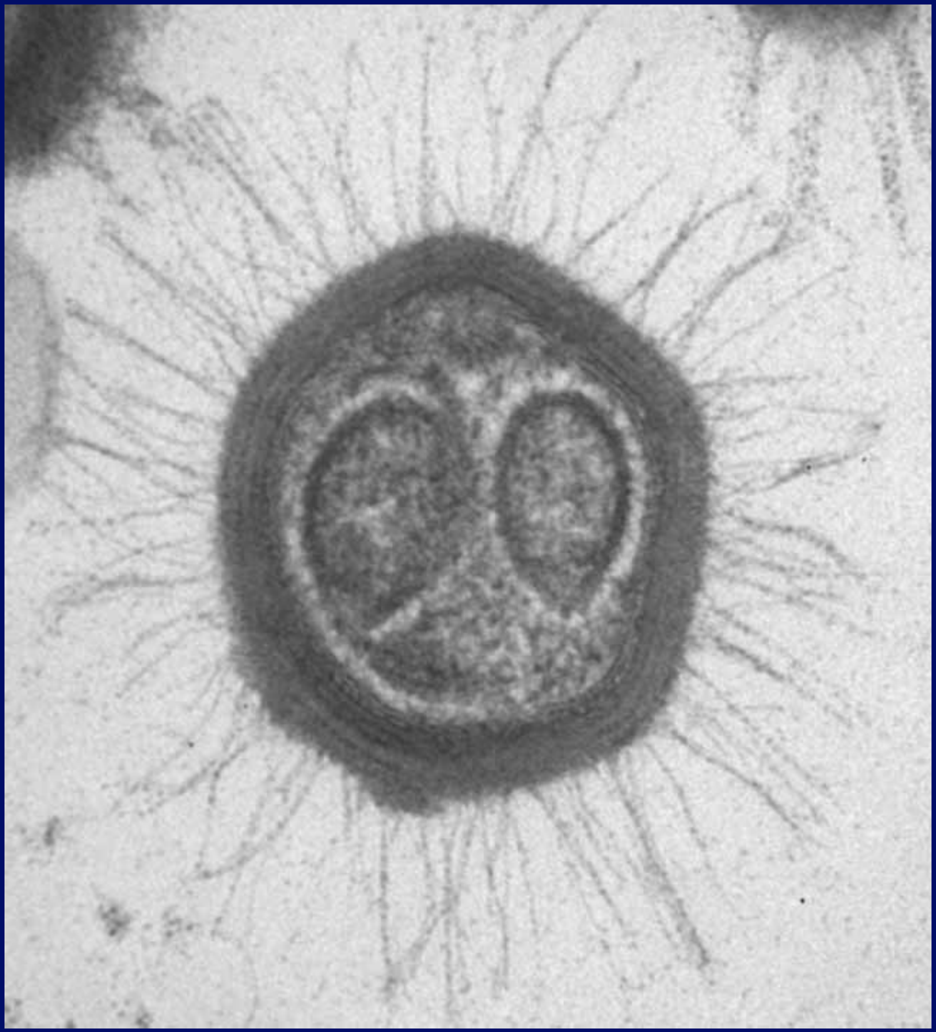
Too much to ask of chemical evolution

$\Rightarrow$ Protolife?

Mimiviruses: A Model for protolife?

- A very large virus (mimivirus) was discovered in 2003
- Now part of a group of such viruses
- Both RNA and DNA
- More DNA than some bacteria (> 1000 genes)
- Genes for translation, DNA repair enzymes
- Still needs ribosome of a host cell
- Leading to reevaluation of viruses
- May be ancient lineages
  - Precursors to bacteria, or eukaryotes
  - Controversial

Image of Mimivirus



Protolife

1. “Virus” equivalent in complexity, but free-living

Protein + Nucleic Acid + Supply by Environment

(Protein + Nucleic Acid: 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

- Experiments by Sidney Fox
- Amino acids + dry heat led to proteinoids
- Addition of water produced microspheres
- They can grow, bud, form chains, divide
- But no nucleic acids, so not reproduction
- Could be model for protocells
- Consider “evolution” to life later

Picture of Proteinoid Microspheres

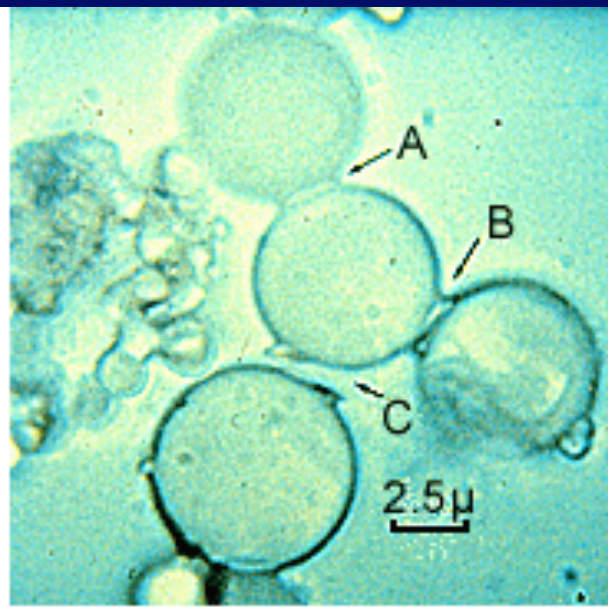


FIGURE 5.15 — Photograph of proteinoid microspheres produced by repeated energizing and dehydrating the primordial soup. The main features of this figure can be simulated by shaking a mixture of oil and water and watching the globs of oil cluster on the surface of the water. Seen here through a microscope, each microsphere contains a large\ concentration of amino acids. (The scale shown, 2.5 microns, equals 2.5x10-4 cm.) (Sidney Fox)

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 to copy RNA and make new viruses

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

$\Rightarrow$ RNA copied **without** machinery of cell

Variation: **No** 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

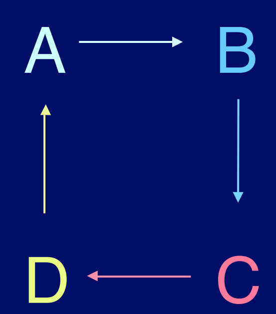
Problems with Nucleic Acid First Scenario

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

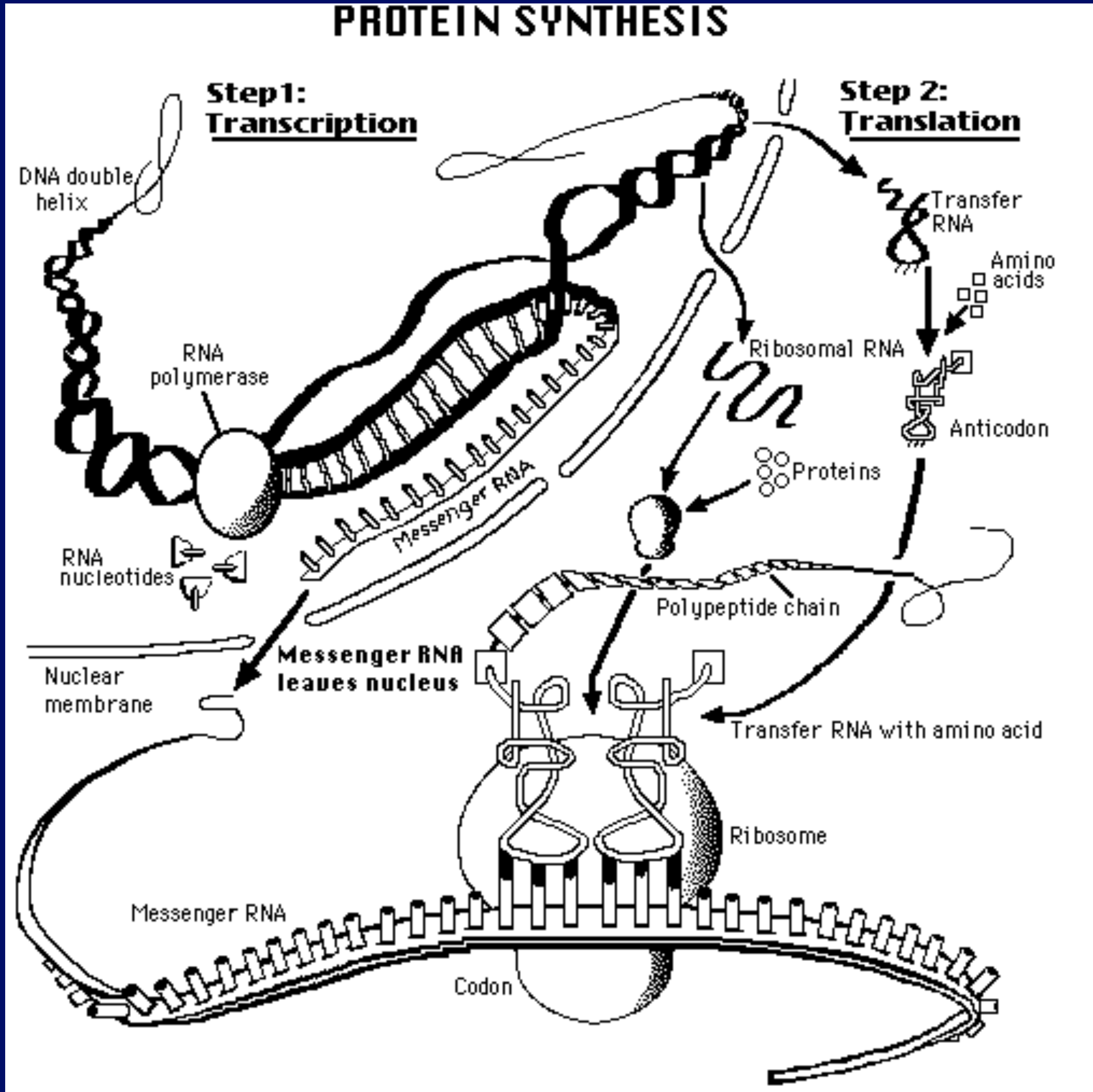


If B $\longrightarrow$ D Short Circuit

$\Rightarrow$ Only narrow range of population sizes works

The Origin of the Genetic Code

- We need more than **either** protein or RNA protolife
- Need interaction via genetic code
- Need **translation**
- Let's recall what is needed for translation…

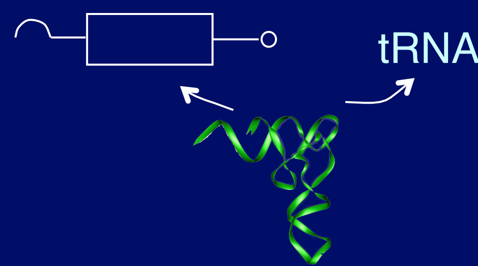

PROTEIN SYNTHESIS
Step1: Transcription
Step 2: Translation
DNA double helix
RNA polymerase
Messenger RNA
RNA nucleotides
Messenger RNA leaves nucleus
Nuclear membrane
Transfer RNA
Amino acids
Ribosomal RNA
Anticodon
Proteins
Polypeptide chain
Transfer RNA with amino acid
Ribosome
Messenger RNA
Codon

Shapiro's Fable

The case for the "chicken"

Protein first ⇒ replication problem

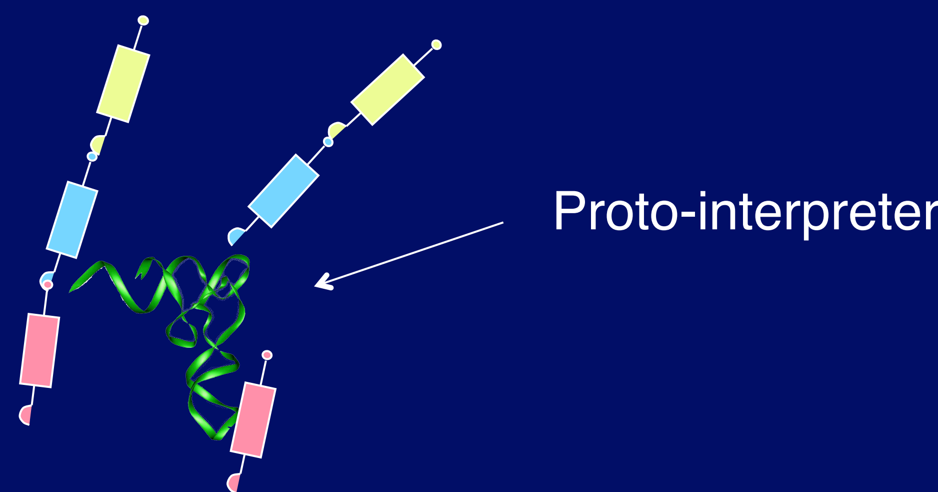
"interpreters" aminoacyl tRNA synthetases



Match tRNA &

Amino acids

Could an earlier version have copied proteins directly?



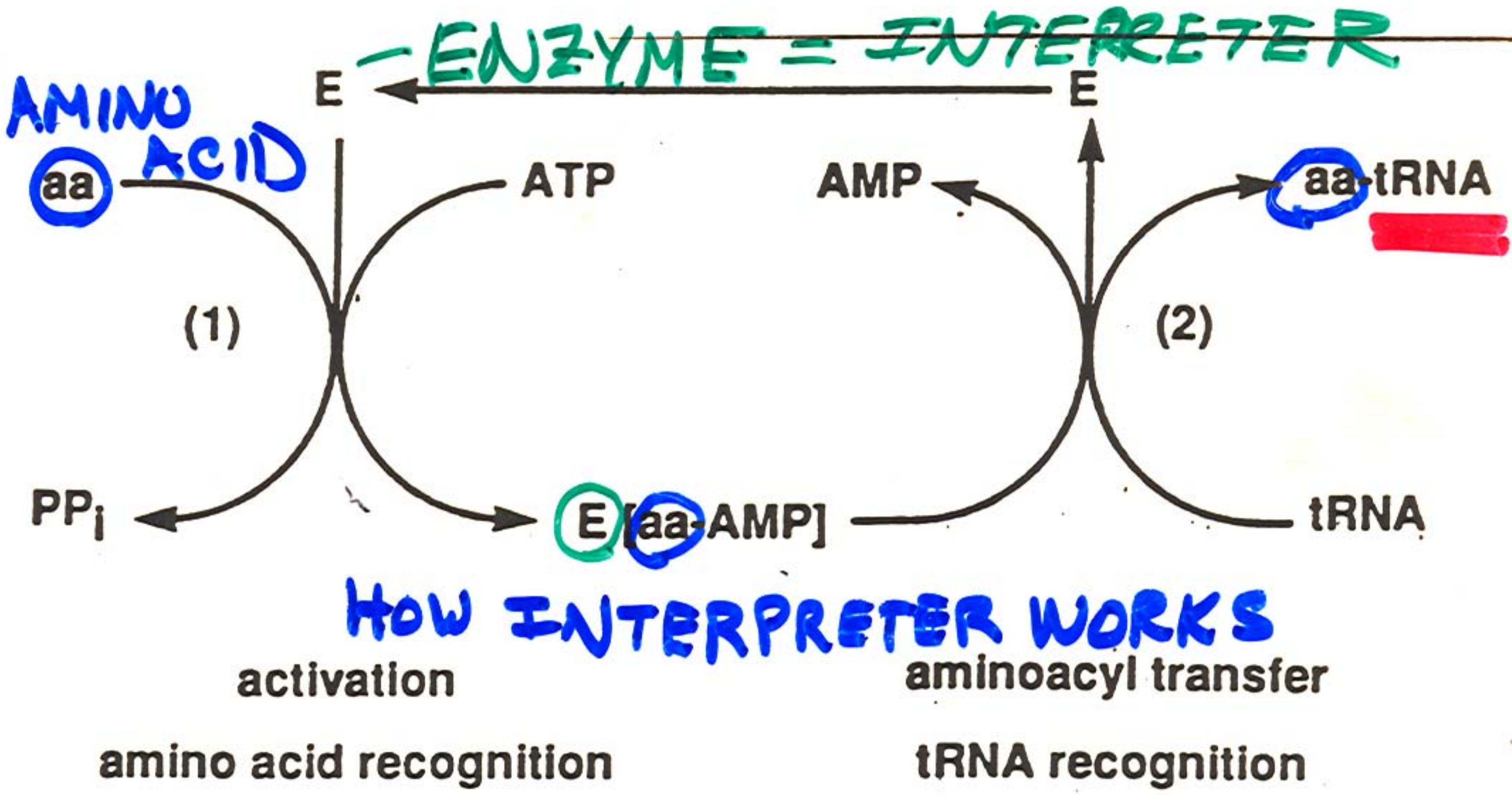


Fig. 1 The two steps of the reaction catalysed by aminoacyl-tRNA synthetases. The tRNA is recognized in the second step (through the features designated paracodon in this article) by the enzyme carrying a bound aminoacyl-AMP intermediate. Participation of the aminoacyl group in the recognition process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

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

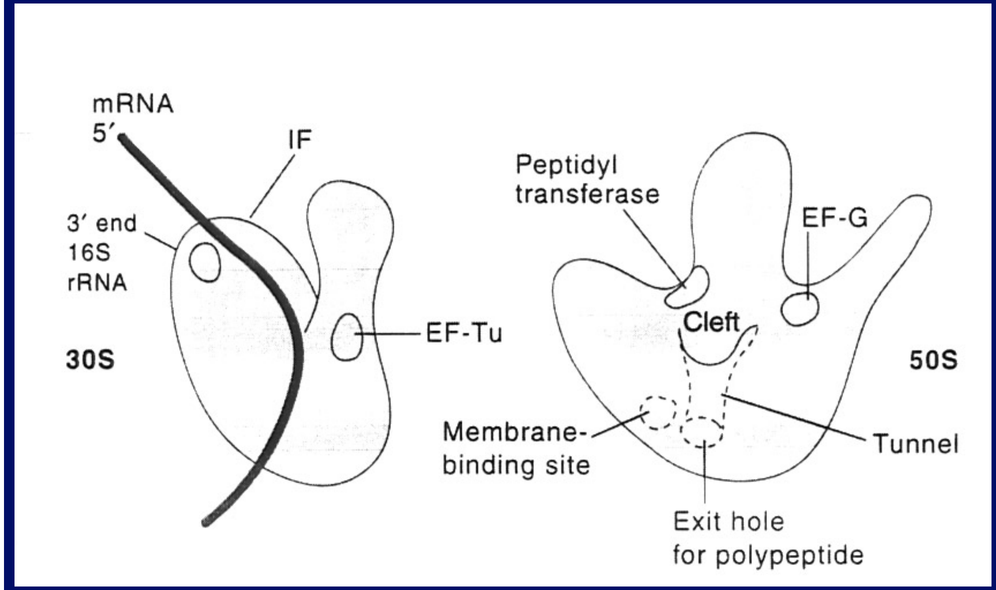
   Noller, et al. 1992, *Science*, **256**, 1416

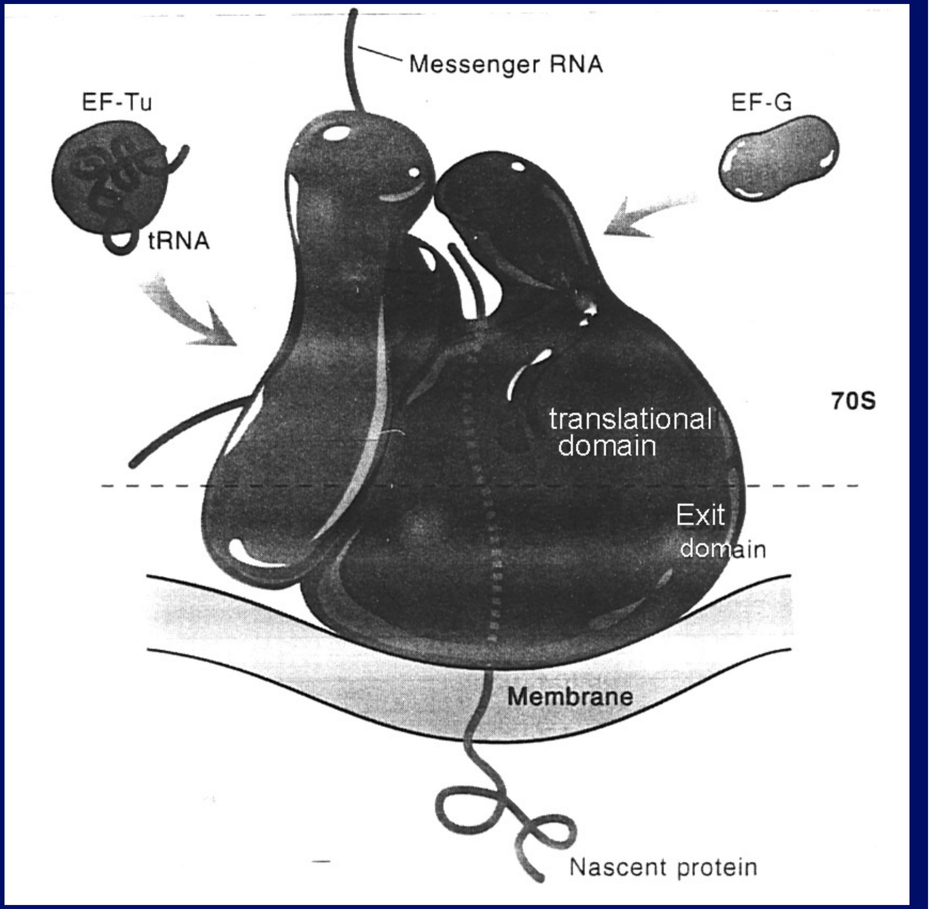
2. RNA "ribozyme" catalyzes reactions between amino acids and tRNAs

   First "interpreter" may have been RNA

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

Translation





Origin of the Genetic Code

Crucial step in any theory

Allows communication

Nucleic Acids ⟷ Proteins

Early versions probably coded fewer amino acids - less specific

For mRNA

Genetic Code

First RNA Base	U	C	A	G	Third RNA BASE
U	Phenylalanine	Serine	Tyrosine	Cysteine	U
	Phenylalanine	Serine	Tyrosine	Cysteine	C
	Leucine	Serine	Stop	Stop	A
	Leucine	Serine	Stop	Tryptophan	G
C	Leucine	Proline	Histidine	Arginine	U
	Leucine	Proline	Histidine	Arginine	C
	Leucine	Proline	Glutamine	Arginine	A
	Leucine	Proline	Glutamine	Arginine	G
A	Isoleucine	Threonine	Asparagine	Serine	U
	Isoleucine	Threonine	Asparagine	Serine	C
	Isoleucine	Threonine	Lysine	Arginine	A
	Start/Methionine	Threonine	Lysine	Arginine	G
G	Valine	Alanine	Aspartic Acid	Glycine	U
	Valine	Alanine	Aspartic Acid	Glycine	C
	Valine	Alanine	Glutamic Acid	Glycine	A
	Valine	Alanine	Glutamic Acid	Glycine	G

Amino Acids

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	

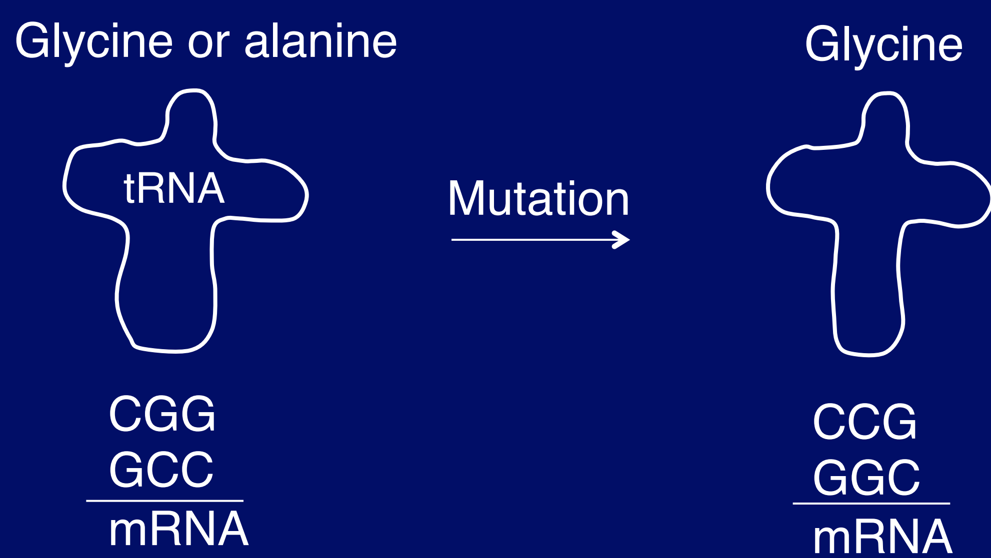
Others added later

Evolution of Genetic Code

Gaining specificity

If early tRNAs carried 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

Summary

- Transition to life is poorly understood
- Need to consider “protolife”
- Can we get by with only one polymer?
  - If so, protein or RNA?
  - If so, how do we get genetic code going?
  - Translation is key
- Most work now focused on nucleic acids
  - Ribozymes can play role of proteins