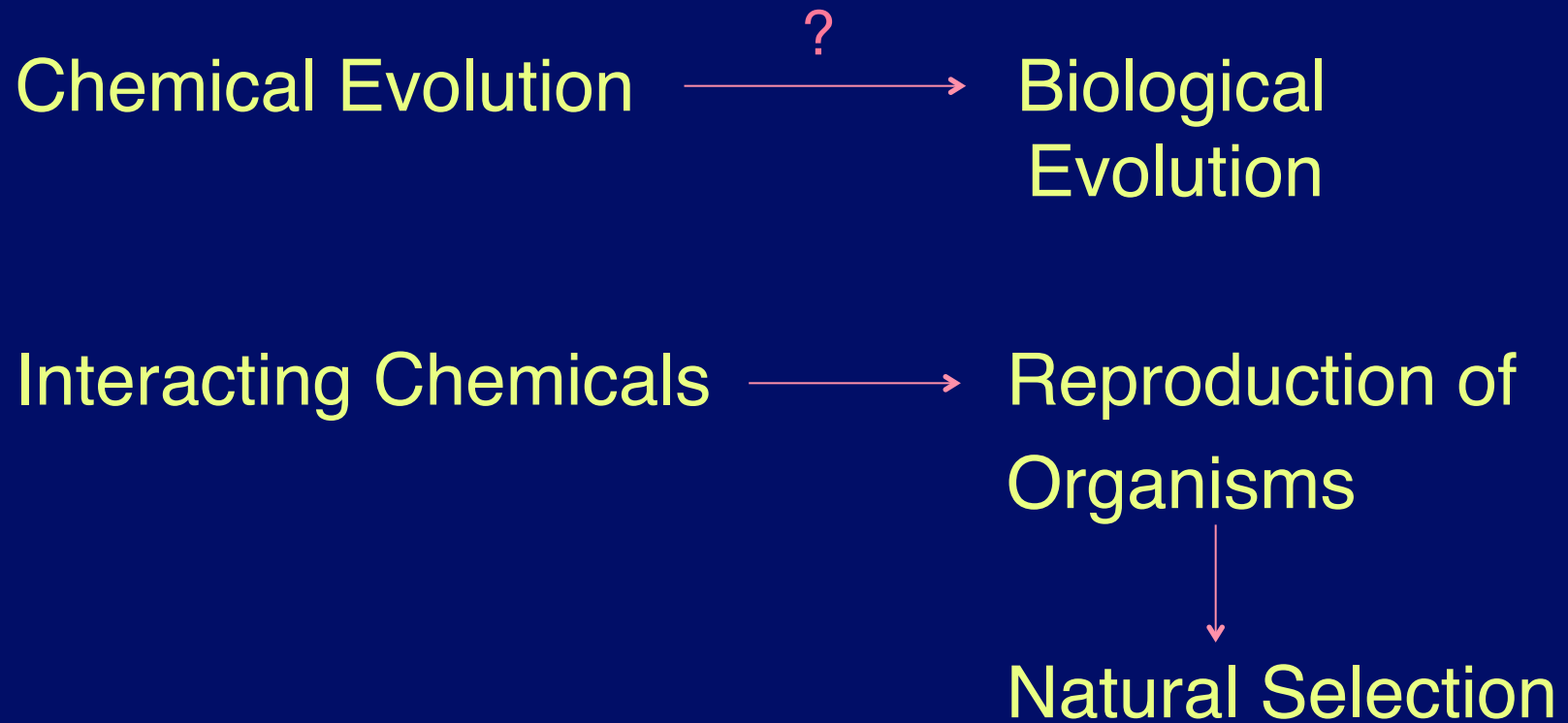


The Transition to Life

The Transition to Life



Based on Simplest Life Now:

Need:

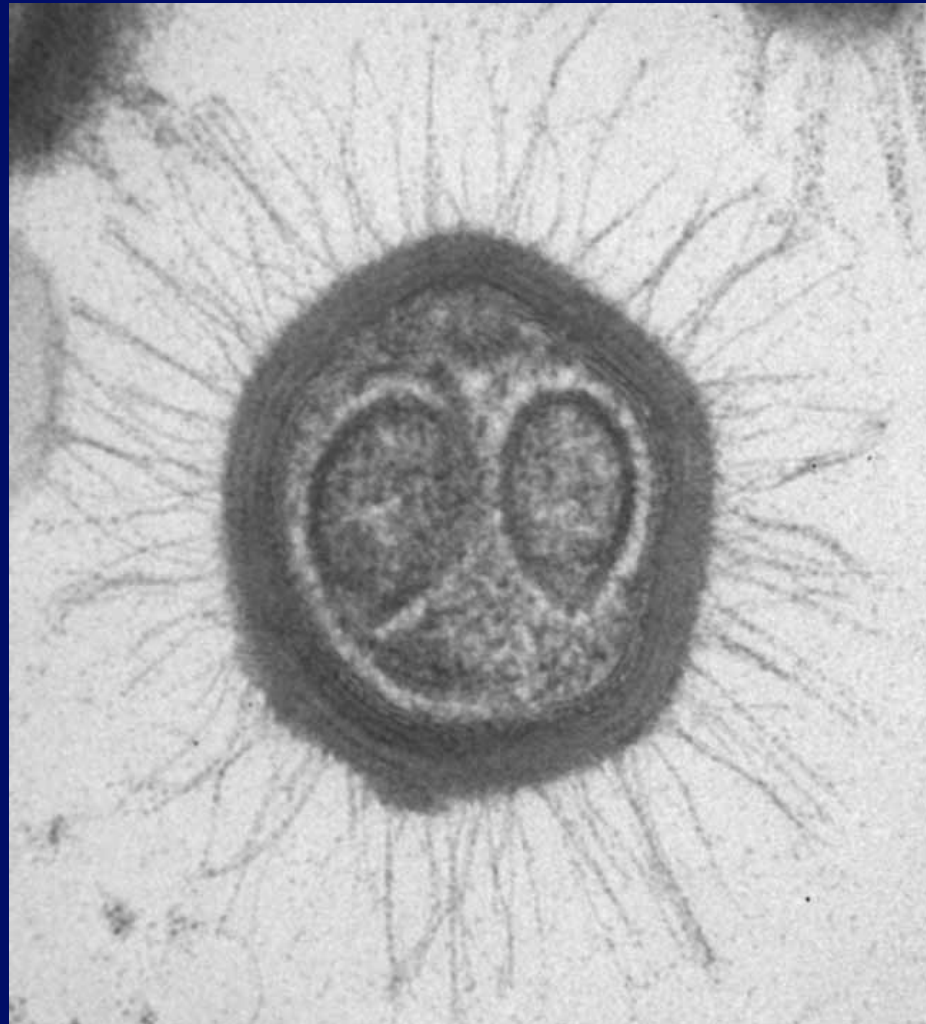
- | | |
|--------------------------------|---------------------------------------|
| 1. Nucleic Acids | Replicable Information |
| 2. Proteins | Enzymes (Catalysts) |
| 3. Lipids | Membranes (Enclosure) |
| 4. Carbohydrates
(Pigments) | Energy Storage
(Energy Conversion) |

Too much to ask of chemical evolution
⇒ 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 (Controversial)
 - Some may be ancient lineages
 - Remnants of RNA world
 - Precursors to bacteria, or eukaryotes

Image of Mimivirus



Protolife

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

Protein + Nucleic Acid + Supply by Environment



Genetic Code

2. Protein Protolife

Protein \longrightarrow Self Replication?

3. Nucleic Acid Protolife

RNA \longrightarrow 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

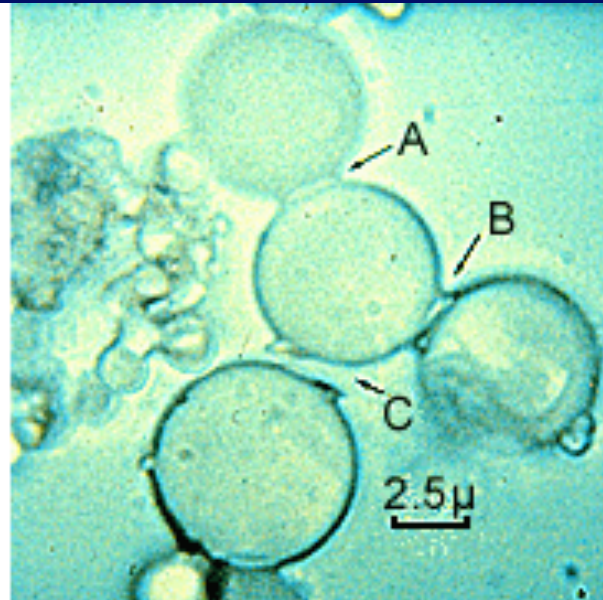


FIGURE 5.15 — Photograph of proteinoid microspheres produced by repeated energizing and dehydrating the primordial soup. The main features of this figure can be simulated by shaking a mixture of oil and water and watching the globs of oil cluster on the surface of the water. Seen here through a microscope, each microsphere contains a large concentration of amino acids. (The scale shown, 2.5 microns, equals 2.5×10^{-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)

⇒ 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

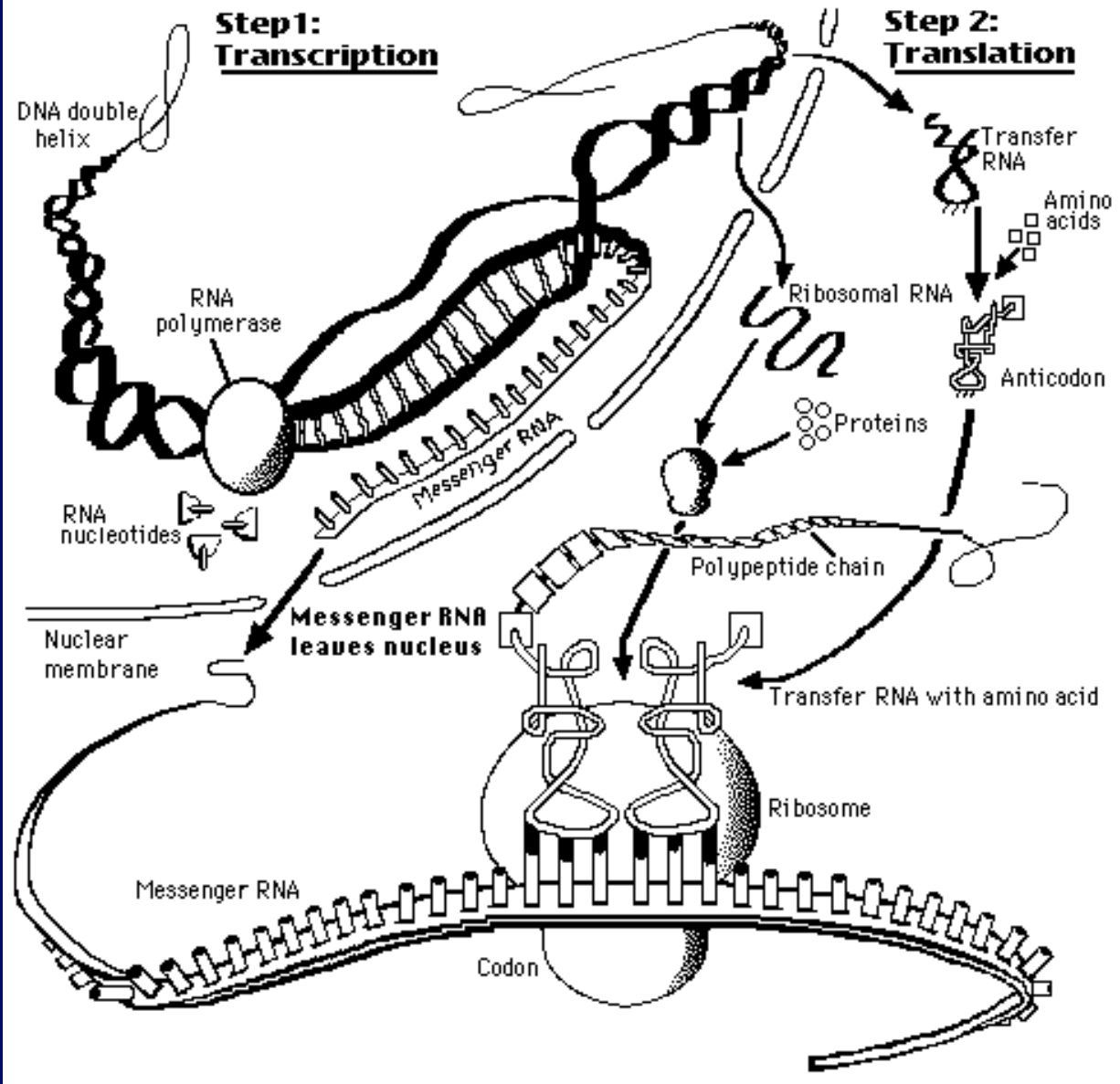
1. A replicating RNA molecule forms by chance (random replicator - not a gene)
ribozyme (catalyst, made of RNA)
2. Family of **similar** RNA's develops (quasispecies)
3. Connection to proteins
(quasispecies specialize to make parts of protein)

4. Complex interactions (cycles) between RNA and proteins
5. Use lipids to make protocells
6. Competition leads to biological evolution

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



Shapiro's Fable

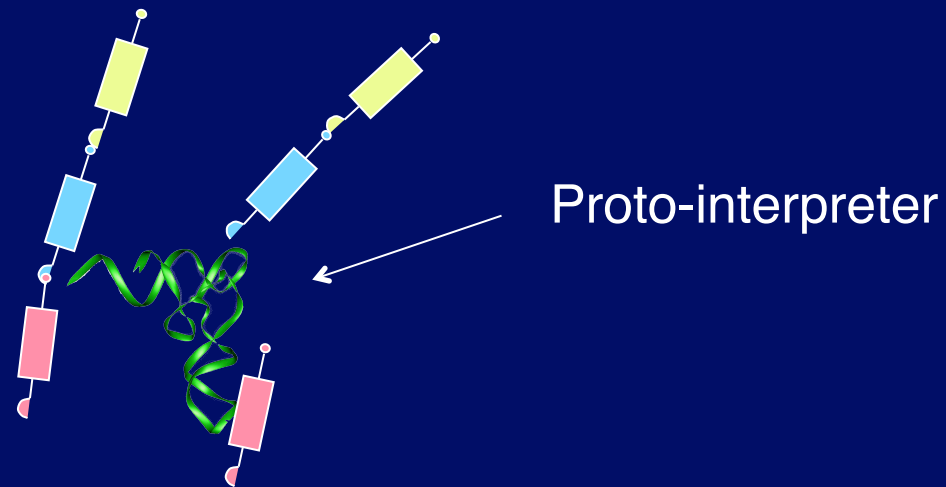
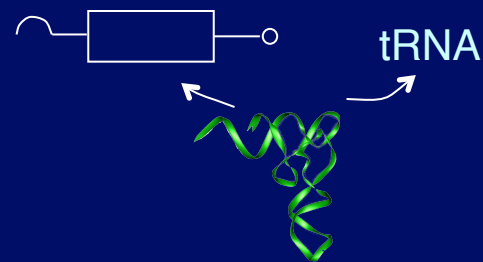
The case for the “chicken”

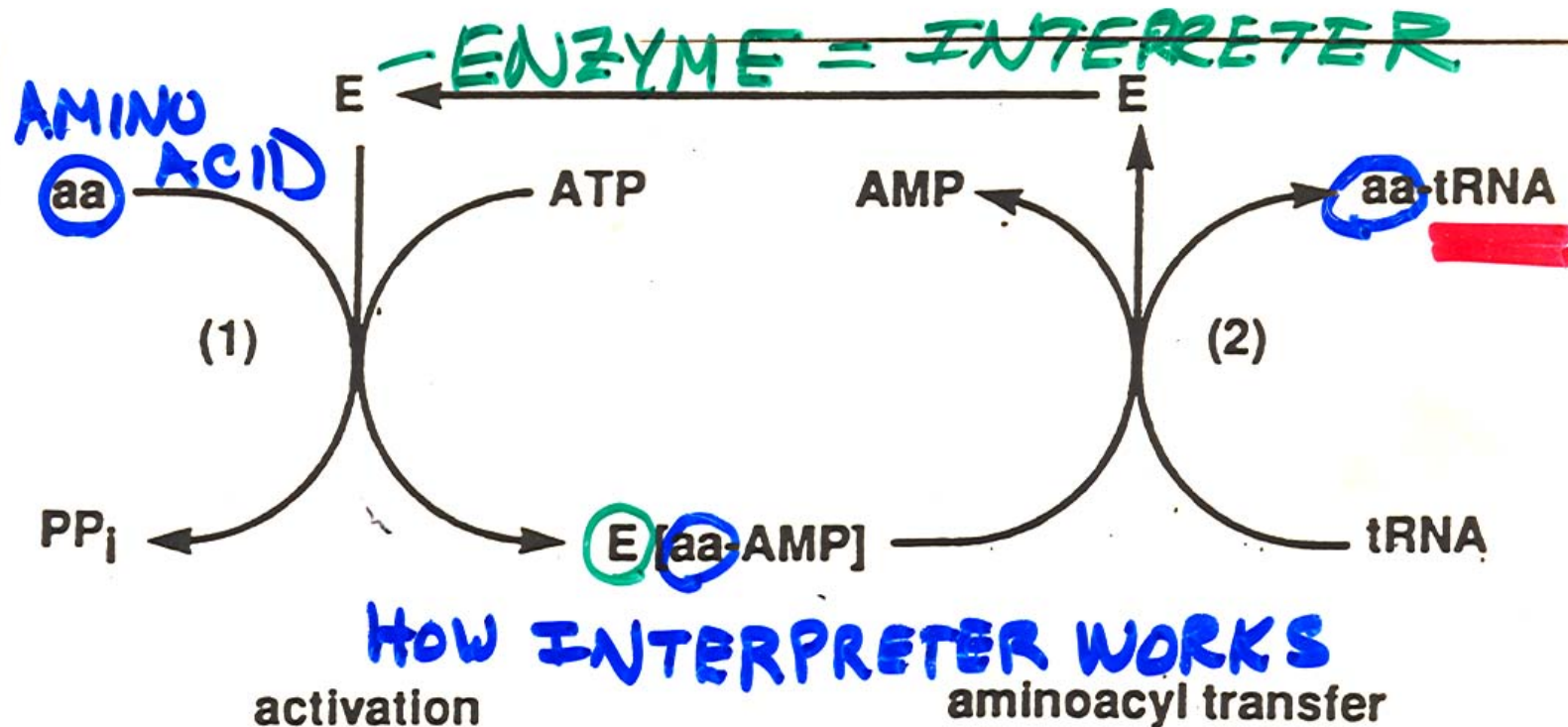
Protein first \Rightarrow replication problem

“interpreters” aminoacyl tRNA synthetases

Match tRNA &
Amino acids

Could an earlier version have copied proteins directly?





amino acid recognition

tRNA recognition

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 \longrightarrow 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) $\sim 1/2$
 - 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 that some RNA can catalyze
Non-RNA reactions

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

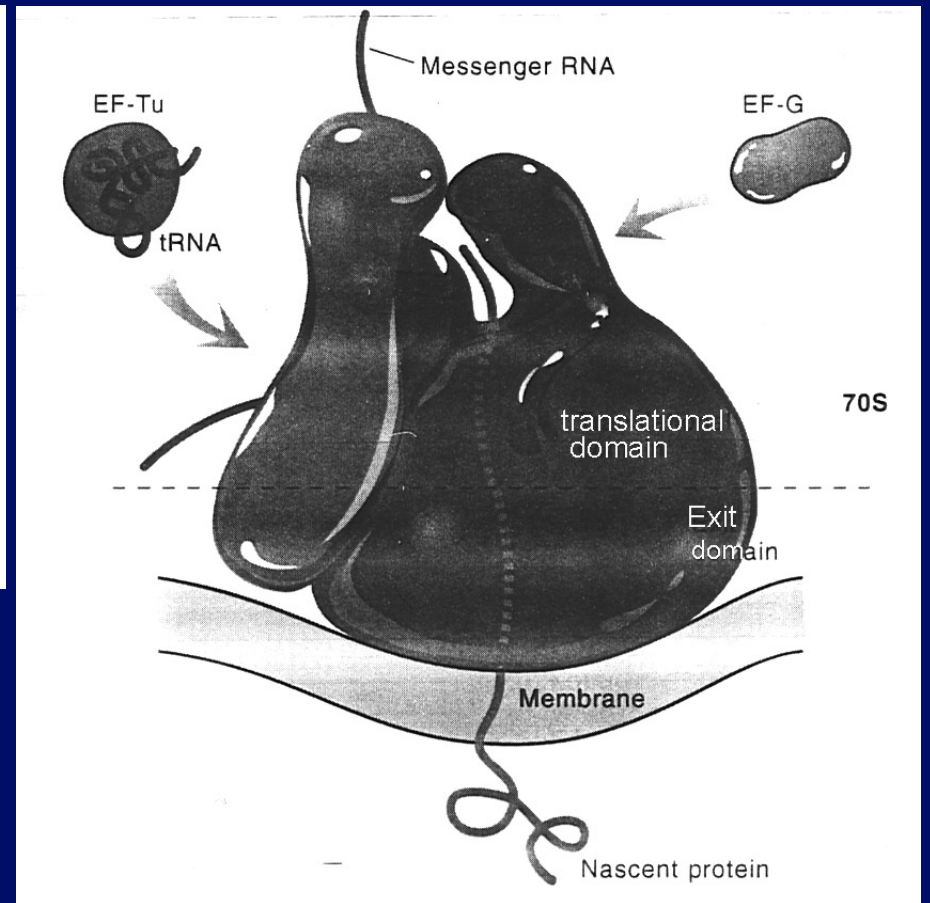
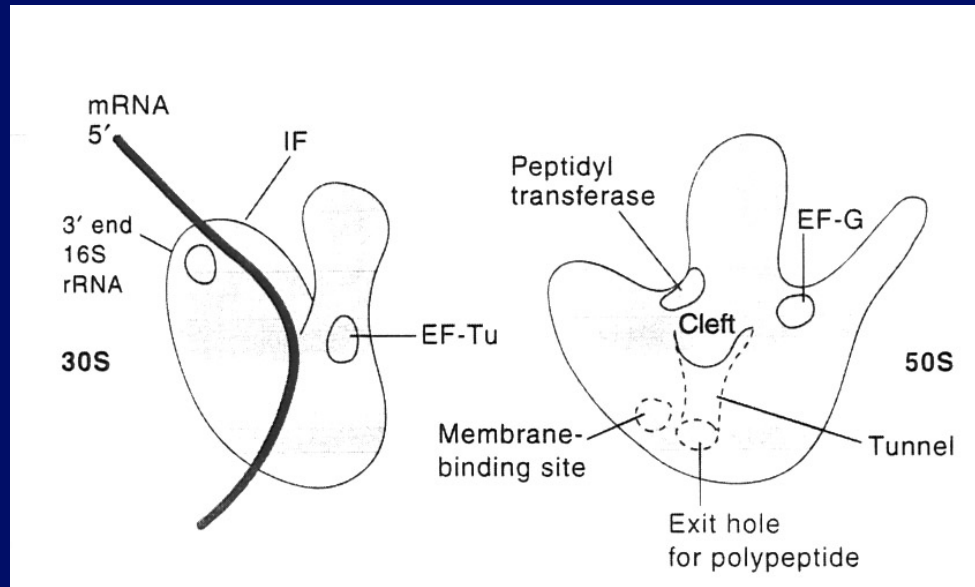
Noller, et al. 1992, *Science*, 256, 1416

2. RNA “ribozyme” catalyzes reactions between amino acids and tRNAs

First “interpreter” may have been RNA

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

Translation



New Work

- Progress in RNA copying (Szostak)
- Need Mg^{+2} ions, but they can be destructive
- Add citrate, avoids harmful effects of Mg^{+2} while keeping good effects
- Need a “leaky” lipid membrane to enclose, but let building blocks in, but keep RNA inside
- Need RNA and lipids
- Science Nov 29, 2013, News Focus

Origin of the Genetic Code

Crucial step in any theory

Allows communication

Nucleic Acids \longleftrightarrow 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

Some evidence for RNY and G - C more stable

Purine Either
| /
RNY
| \
Pyrimidine

⇒ 4 codons GGC glycine
 GCC alanine
 GAC aspartic acid
 GUC valine

} Common in
Miller-Urey
and Meteorites

Others added later

Evolution of Genetic Code

Gaining specificity

If early tRNAs carried more than 1 kind of amino acid

e.g.

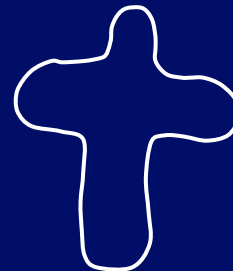
Glycine or alanine



CGG
GCC
—
mRNA

Mutation
→

Glycine



CCG
GGC
—
mRNA

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

Only one better at minimizing bad effects of mutations

⇒ 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