

The Transition to Life

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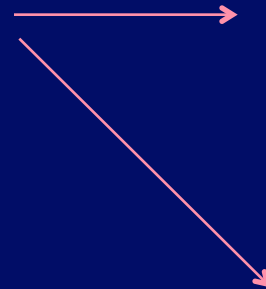
Chemical Evolution

— ? — Biological

Interacting Chemicals

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)

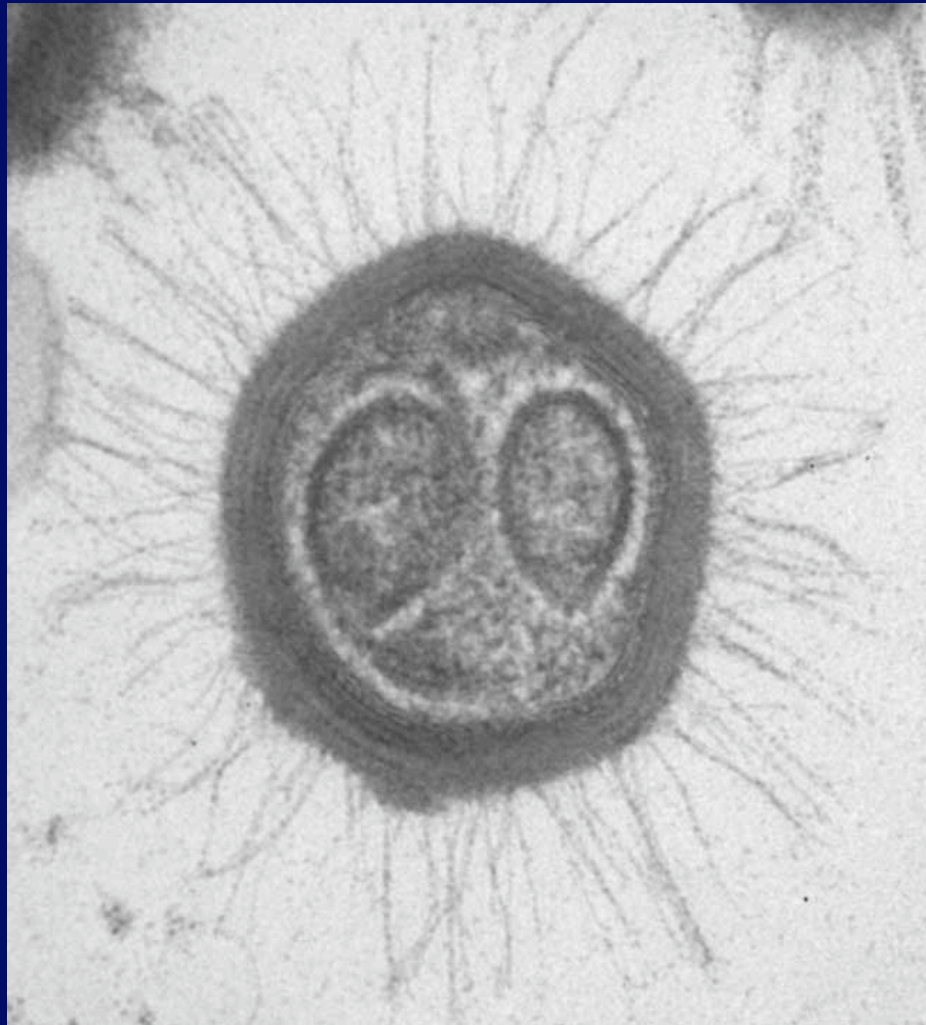
Too much to ask of chemical evolution

⇒ Protolife?

Update: Mimivirus

- A very large virus was discovered in 2003
- Both RNA and DNA
- More DNA than some bacteria
- Genes for translation, DNA repair enzymes
- Leading to reevaluation of viruses
- May be ancient lineages
 - Precursors to bacteria, etc.
 - Controversial

Image of Mimivirus



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 \longrightarrow 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

(Hot Tidepool?)

— Proteinoids

↓ H₂O (Tide)

Microspheres

Protocells

Protolife?

(Look like life)

Can Add Proteinoid

Grow

Split

Divide } "Reproduce"

Bud

Bud

Form Chains

Like Bacteria

But "Reproduction" not exact

Later incorporate Nucleic Acids

Proteinoid

→ Cells

→ Genes

Problem: How to incorporate Nucleic acids?

Picture of Proteinoid Microspheres

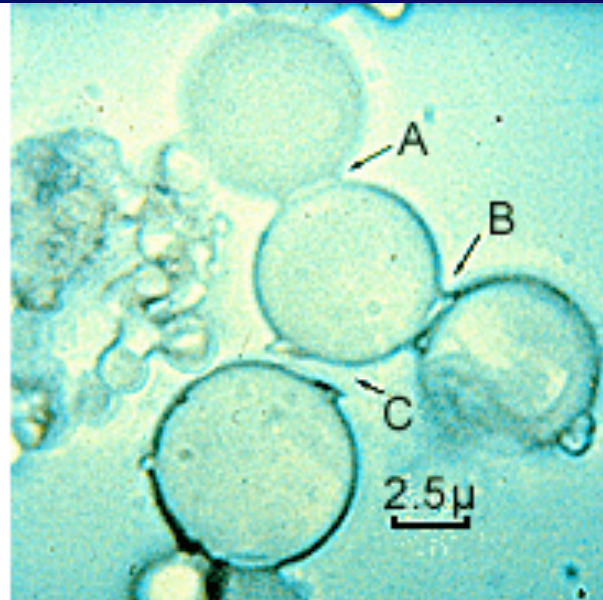


FIGURE 5.15 — Photograph of proteinoid microspheres produced by repeated energizing and dehydrating the primordial soup. The main features of this figure can be simulated by shaking a mixture of oil and water and watching the globs of oil cluster on the surface of the water. Seen here through a microscope, 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 (hypercycles)
6. Use lipids to make protocells
6. Competition leads to biological evolution

EXON1 **INTRON** **EXON2**

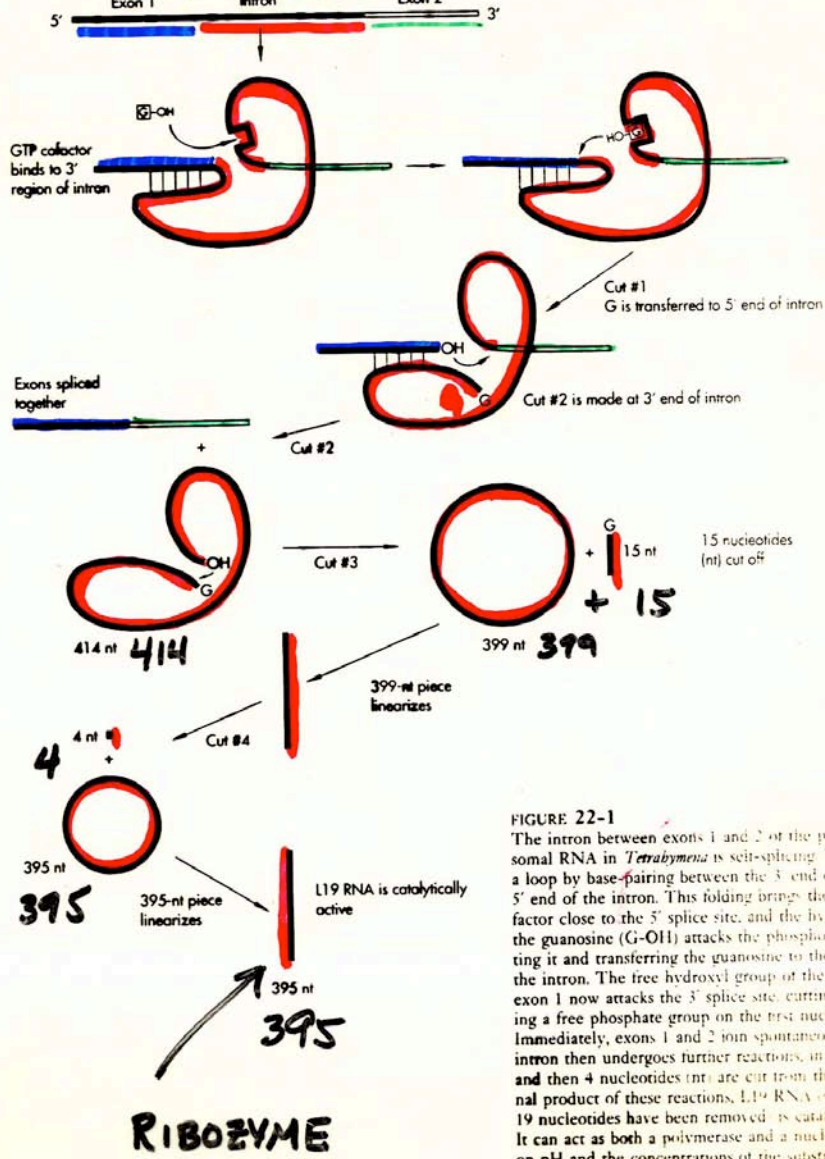


FIGURE 22-1

The intron between exons 1 and 2 of the pre-mRNA in *Tetrahymena* is self-splicing. The intron folds into a complex structure by base-pairing between the 3' end of the intron and the 5' end of the intron. This folding brings the GTP collector close to the 5' splice site, and the hydroxyl group of the guanosine (G-OH) attacks the phosphodiester bond, forming a cyclic intermediate and transferring the guanosine to the 5' end of the intron. The free hydroxyl group of the last exon 1 now attacks the 3' splice site, cutting it off and leaving a free phosphate group on the first nucleotide. Immediately, exons 1 and 2 join spontaneously. The intron then undergoes further reactions, in which 15 nucleotides are cut off from the 399-nt piece, and then 4 nucleotides are cut from the 395-nt piece. The final product of these reactions, L19 RNA (395 nucleotides), is catalytic. It can act as both a polymerase and a nuclease. The reaction is dependent on pH and the concentrations of the substrates.

RIBOZYME

HOW AN "INTRON" (NOT A GENE) CAN CUT, SPLICE & BECOME A CATALYST

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

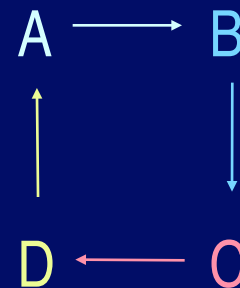
If N small

Population Collapse

If N large

Selfish RNA

Short Circuit



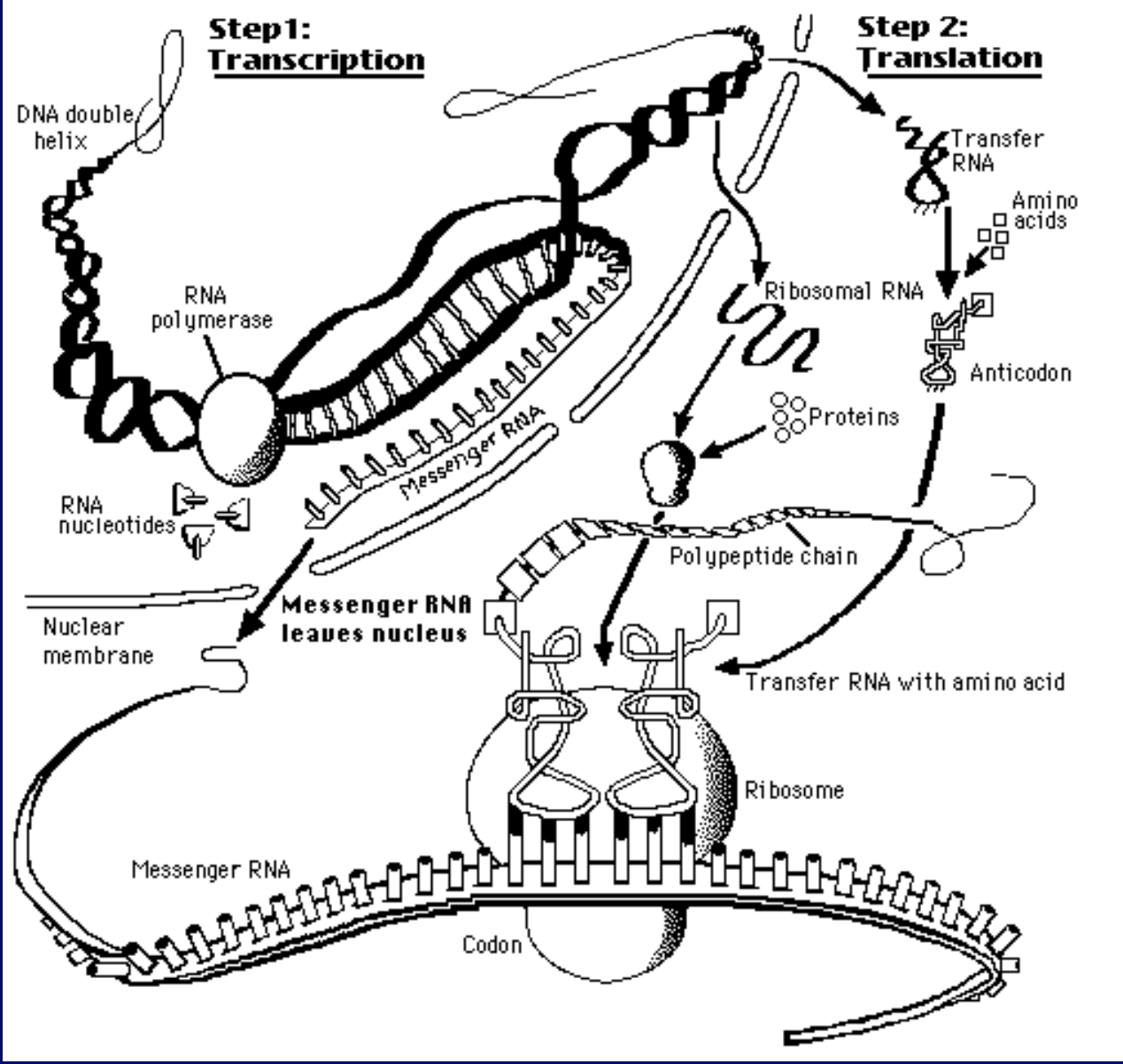
If B \rightarrow D Short Circuit

\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**
- Let's recall what is needed for translation...

PROTEIN SYNTHESIS



Shapiro's Fable

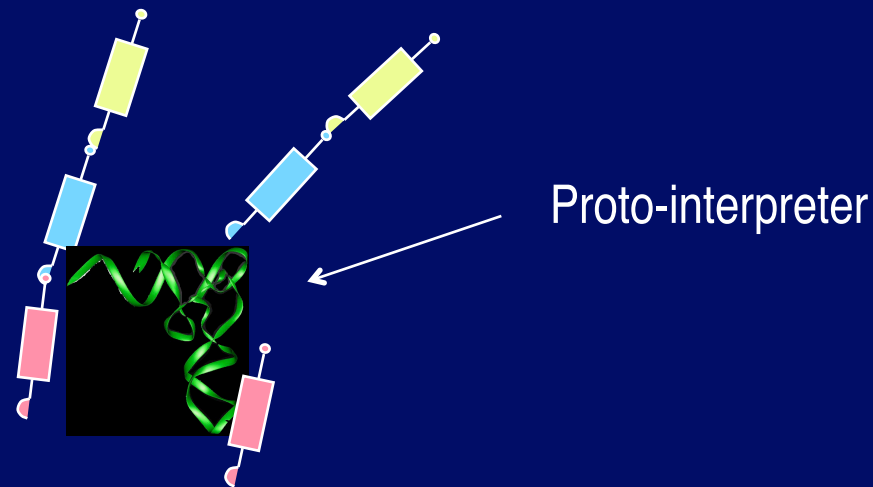
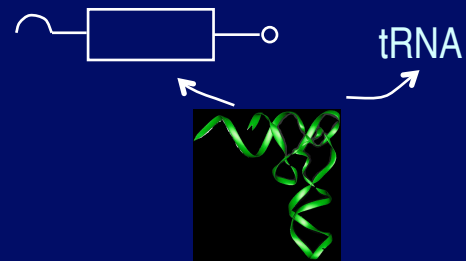
The case for the “chicken”

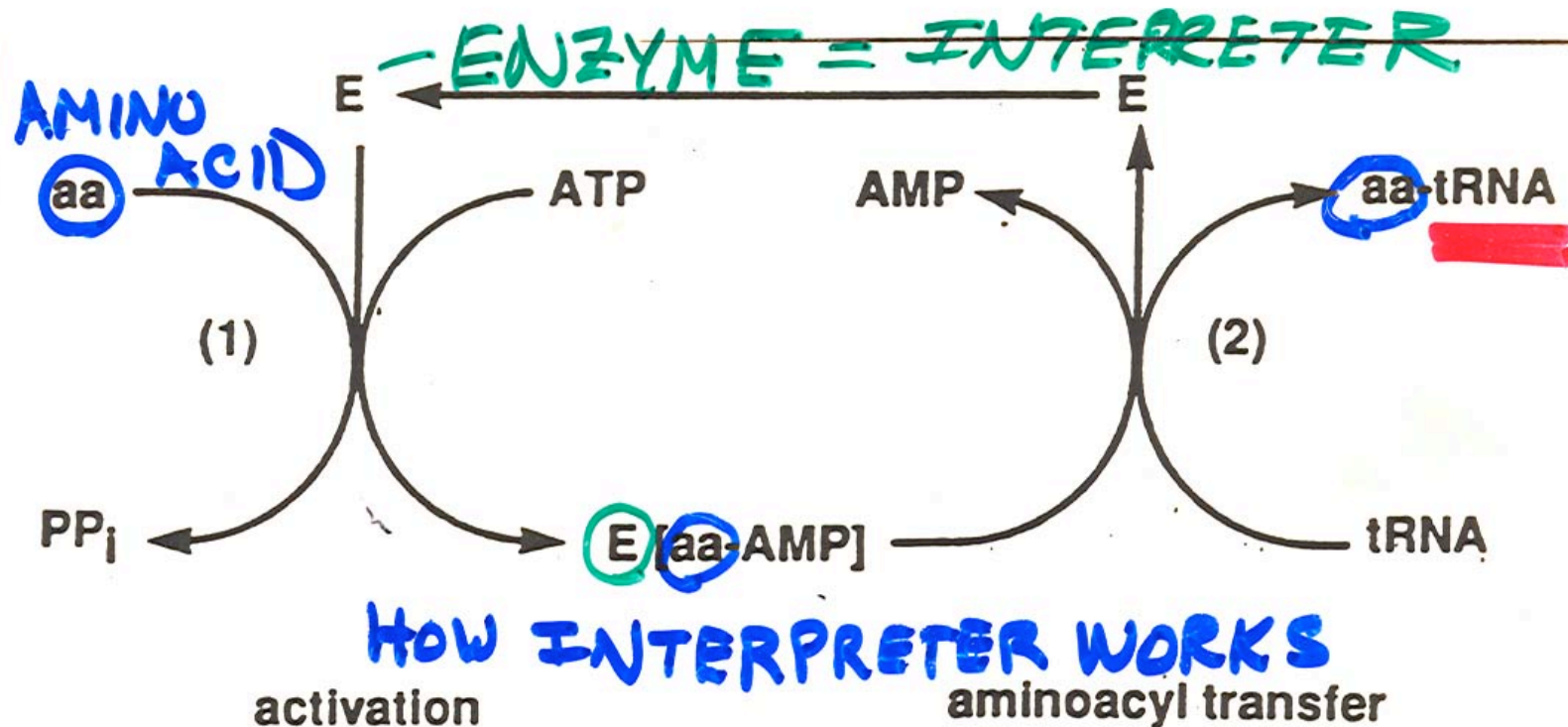
Protein first \Rightarrow replication problem

“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 ~~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.
3. 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
 - \Rightarrow simpler, older code
second genetic code

 - \Rightarrow connection of interpreter and tRNA
more primitive than current code

2. Dyson modeling of molecular “populations”

Transition from disorder to order

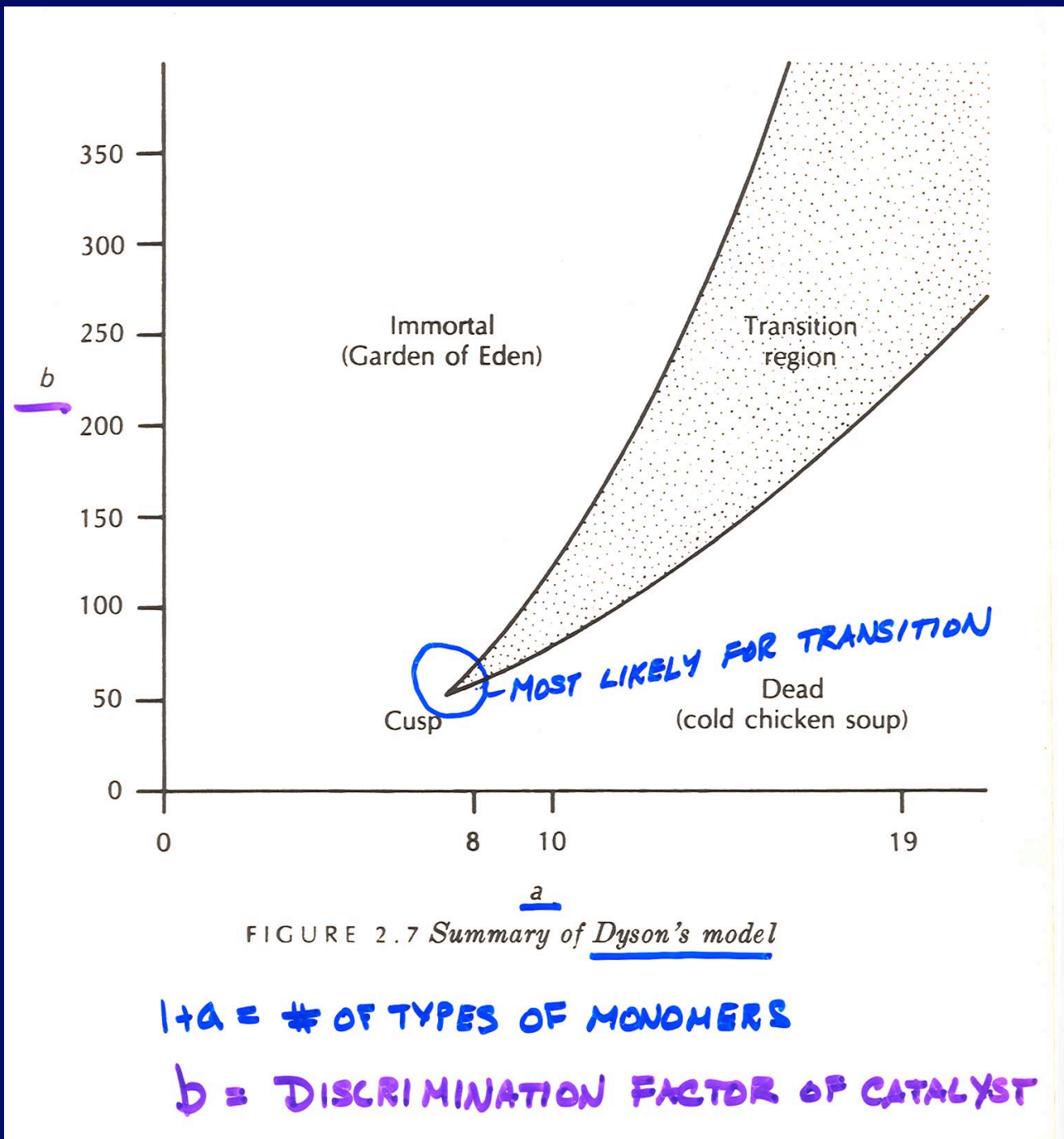
(non-life) (life)

Finds number of monomer types likely to be

9 - 11 (ok if used $\sim 1/2$ 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

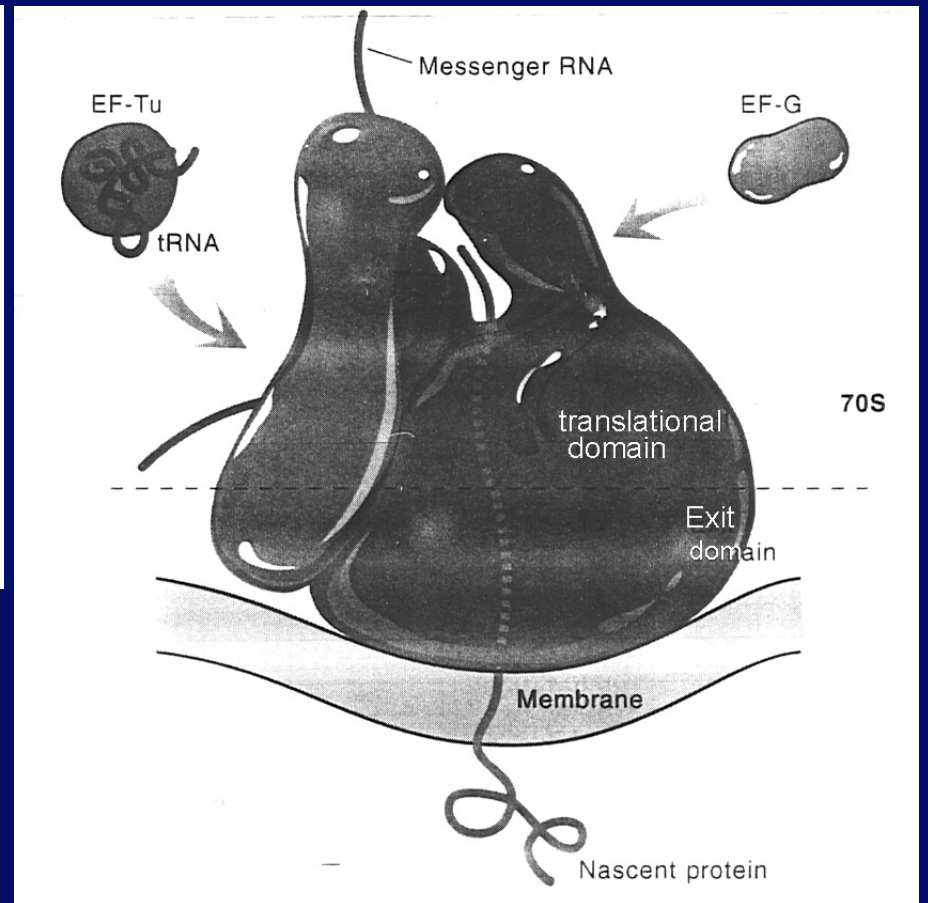
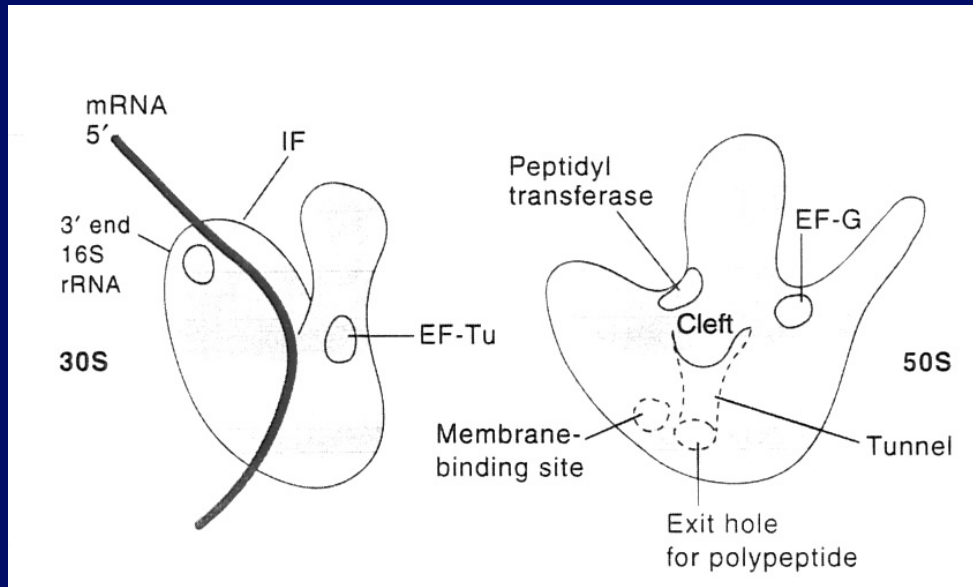
Noller, et al. 1992, *Science*, **256**, 1416

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

First “interpreter” may have been RNA

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

Translation



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
|
RNY
|
G - C
|
Pyrimidine

Either

⇒ 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



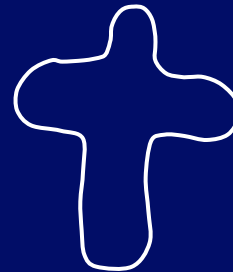
CGG

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?