

Origin of Life Scenarios

BASIC IDEA (hope) : once we begin investigating the processes available on early earth it will be found that everything just "falls together"

Time for life to arise : \approx 200 Myrs.

Views

1950's, 1960's : life was a happy accident

- life will be rare

Since then : life was the inevitable result of natural laws.

- life will be common
- SETI
NASA programs

BASIC SCENARIO

atmosphere + energy
(UV, lightning, volcanic
heat etc) + comets
& meteorites

"prebiotic soup"

amino acids,
nucleotides,
other useful small
molecules in
earth's oceans

spontaneous
polymerization
(catalyzed?)

crude metabolism
self-replication

peptides, proteins,
nucleic acids, etc
CATALYSTS

competition
for resources,
Darwinian
"chemical
evolution"

GENETIC SYSTEM?

ribosomes/translation?

photosynthesis?

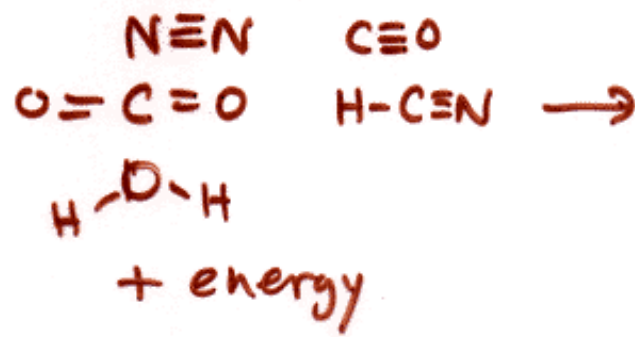
- more sophisticated
metabolism
- more efficient
replication

lipids or
something

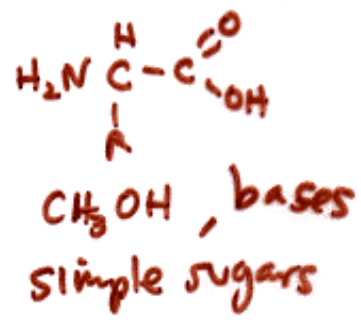
encapsulation, first cells

diversification into
new environments

tiny stuff



little stuff



↓
polymers, bigger stuff



big stuff interacting so as to replicate



↓ competition, selection



simple cells

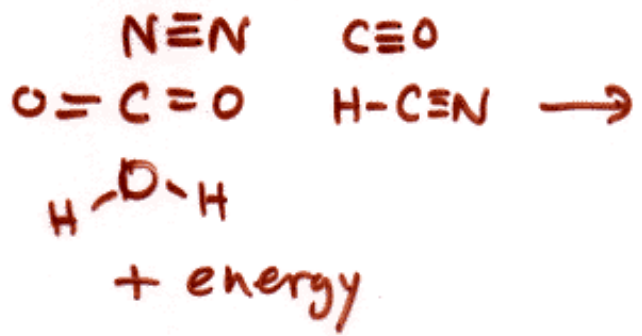
encapsulation?

genetic system?

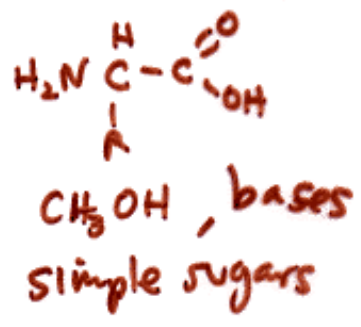
⇒ How can we make these vague ideas concrete?

↙ ↓ ↓ ↘
diversification

tiny stuff



little stuff



↓
 polymers, bigger stuff

big stuff interacting so as to replicate



↓ competition, selection



simple cells

↓ diversification



encapsulation?

genetic system?

⇒ How can we make these vague ideas concrete?

Sources of Biogenic Molecules

All present day life depends on

Amino acids

Sugars

Lipids

Nucleotides

{ Proteins

{ Nucleic acids

lots of other stuff

Where did it all come from?

HYPOTHESIS

- 1) synthesis from atmospheric molecules
- 2) synthesis in space, transport to earth on comets, meteors, asteroids.

BASIC GOAL

Find a simple self-replicating system, rely on "Chemical Evolution" to build it up to life.

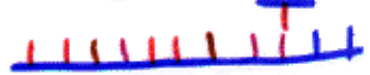
SIMPLE systems

RNA

RNA World Hypothesis

can carry genetic info
can act as a catalyst (machine)

can be replicated by templating



(simple, intrinsic mode for "reproduction")

plays several very basic roles in cells

self-recognition based on hybridization



 recognition

Holy Grail

An RNA-based, efficient, selective, polymerase

Protein
Replicators

simpler monomers
proteins crucial to all
life

Protein First
Scenario

Clay/Mineral
replicators

minerals as catalysts, OR
replicating organics
stuck to mineral surfaces
OR
mineral atomic arrangements
as genetic systems
themselves.

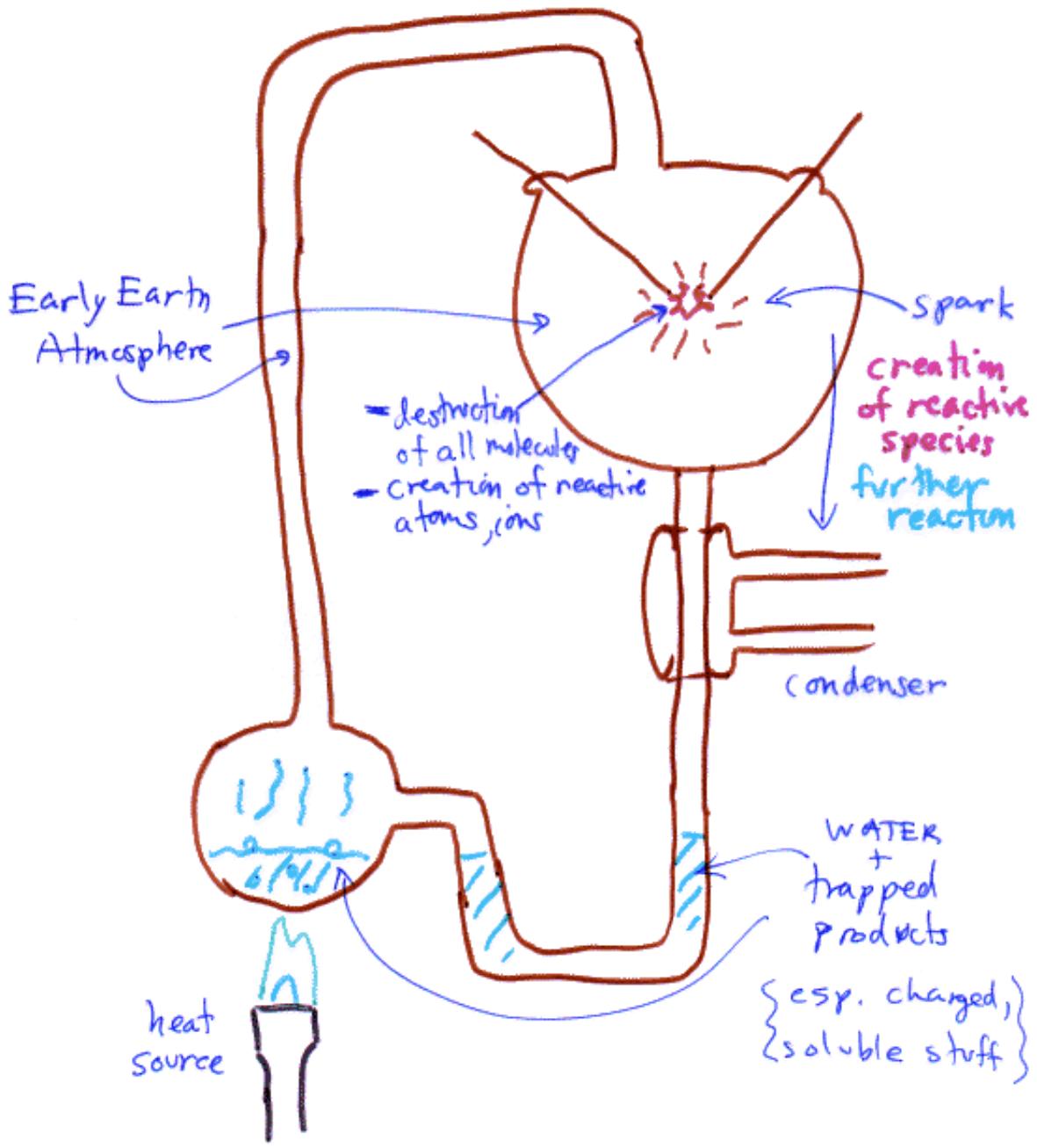
Collectively
Autocatalytic
Sets/Systems

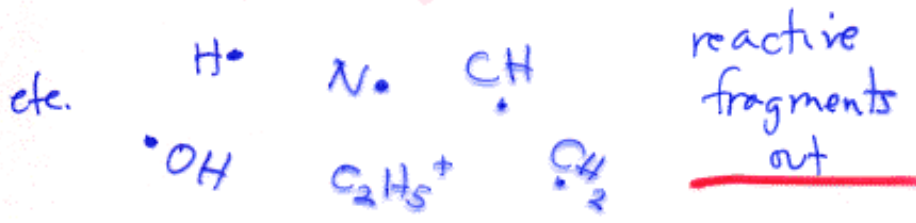
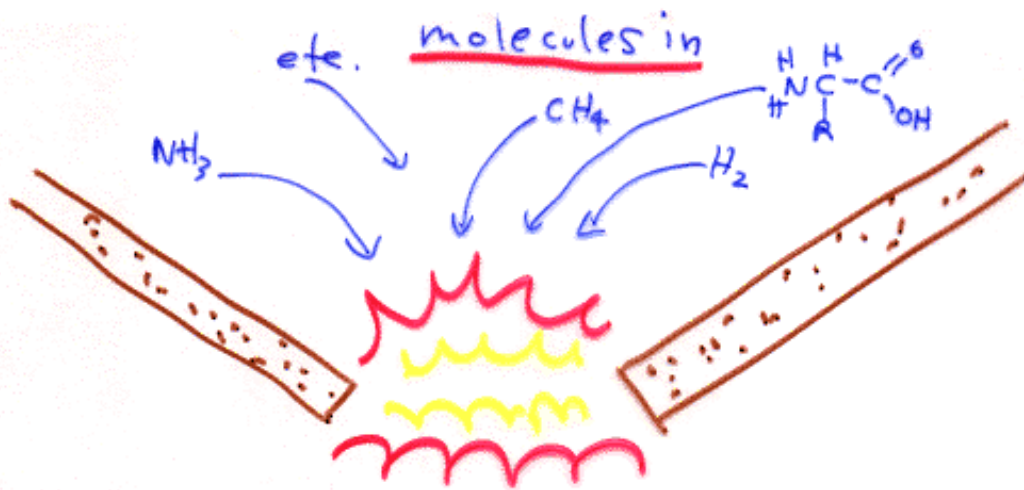
on paper only so far

Comments

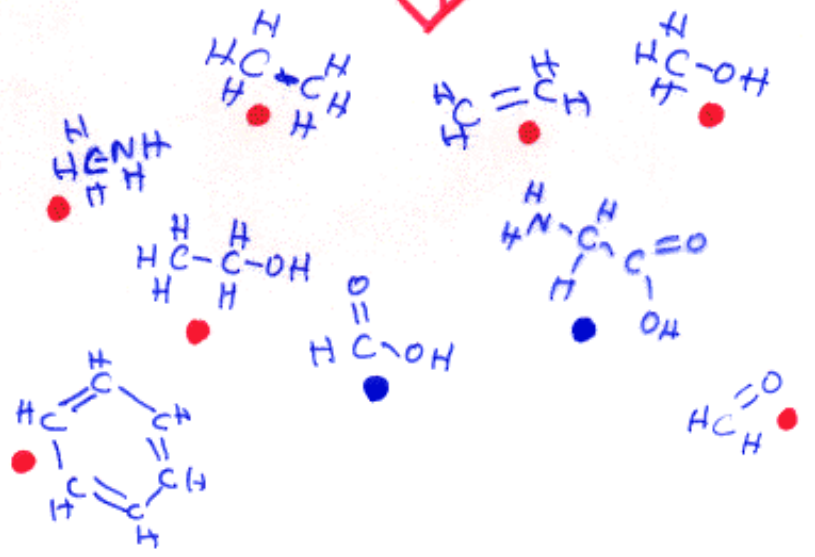
1. We will see that even "simple" replicators are very hard to get
2. The presence of many scenarios means no one of them is considered satisfactory
3. No even partial scenario that I am aware of gets you from the simple replicator to the DNA/RNA/protein/molecular machine form of life we actually know of.

Miller-Urey-Type "Simulation" Experiments





\Downarrow recombination (random)



- **volatile**
subject to destruction
- **non-volatile**
preserved in water trap

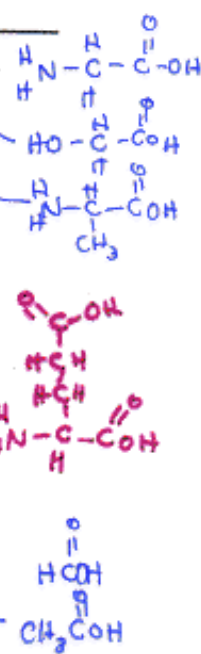
Best Yield Ever strongly reducing CH₄, NH₃, H₂ atm

The endogenous synthesis of organic compounds

- not relevant to earth, but maybe to comets

Table 3.2. Yields from sparking a mixture of CH₄, NH₃, H₂O, and H₂. The percentage yields are based on carbon (59 mmols [710mg] of carbon was added as CH₄).

Tar Compound	YIELD	
	(μmoles)	%
• Glycine	630	2.1
Glycolic acid	560	1.9
Sarcosine	50	0.25
• Alanine	340	1.7
Lactic acid	310	1.6
N-Methylalanine	10	0.07
α-Amino-n-butyric acid	50	0.34
α-Aminoisobutyric acid	1	0.007
α-Hydroxybutyric acid	50	0.34
β-Alanine	150	0.76
Succinic acid	40	0.27
• Aspartic acid	4	0.024
• Glutamic acid	6	0.051
Iminodiacetic acid	55	0.37
Iminoacetic-propionic acid	15	0.13
→ Formic acid	2,330	4.0
Acetic acid	150	0.51
Propionic acid	130	0.66
Urea	20	0.034
N-Methyl urea	15	0.051
Total		15.2



All strongly water soluble; most acids simple compounds favored.

0 °C, and 4×10^{-6} atm at 25 °C). Thus, at least a small amount of atmospheric NH₃ would seem necessary for amino acid synthesis. A similar estimate of the NH₄⁺ concentration in the primitive ocean can be obtained from the equilibrium decomposition of aspartic acid, a prebiotically produced amino acid (Bada and Miller 1968). Ammonia would have been decomposed in the early environment by ultraviolet light, but mechanisms for its resynthesis are also known. The details of the ammonia balance on the primitive Earth remain to be worked out.

In a typical electric discharge experiment, the partial pressure of CH₄ is 0.1–0.2 atm. This pressure is used for convenience, and it is likely (but has never been demonstrated) that organic compound synthesis would work at much lower partial pressures of methane. There are no estimates available for pCH₄ on the primitive Earth, but low levels (10^{-5} to 10^{-3} atm) seem plausible.

Stanley Miller, in The Molecular Origin of Life p59

Table 3.3. Yields from sparking CH_4 (336 mmoles), N_2 , and H_2O , with traces of NH_3 *

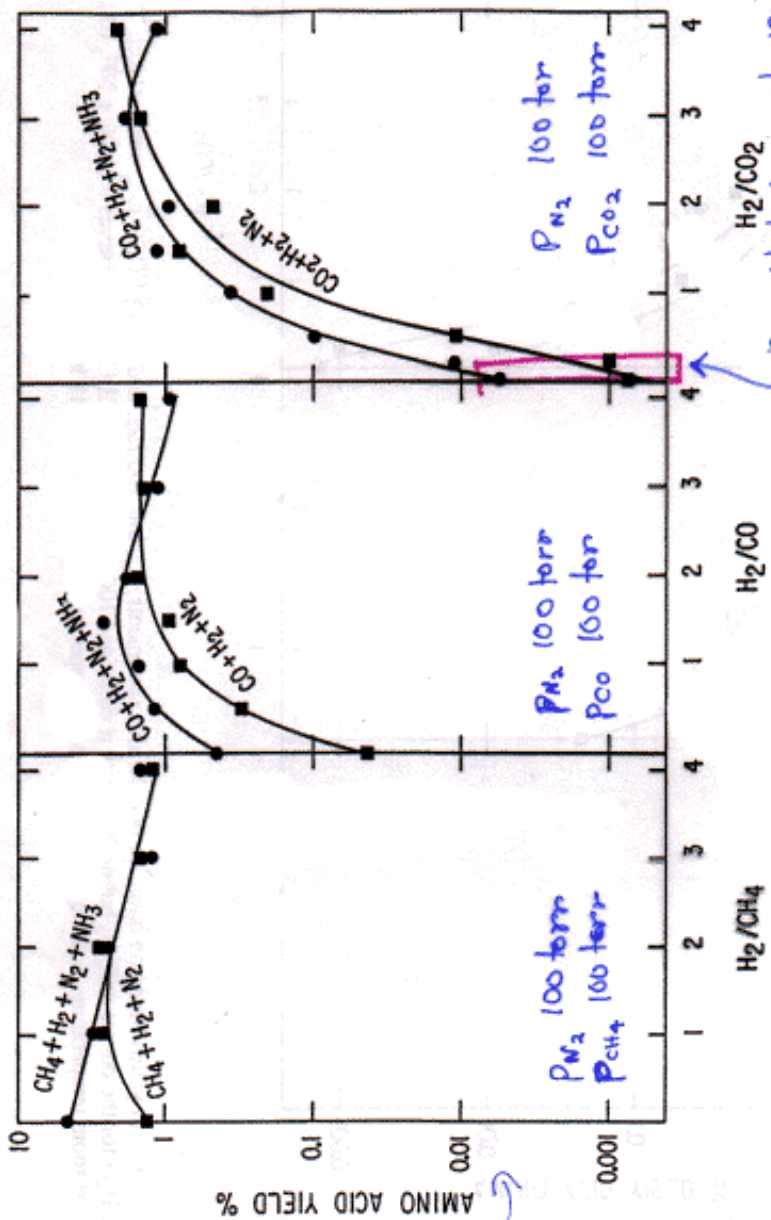
	μ moles		
● Glycine	440	0.26%	all AA's 1.9%
● Alanine	790	0.71%	
α -Amino- <i>n</i> -butyric acid	270		
α -Aminoisobutyric acid	-30		
● Valine	19.5	0.01%	
Norvaline	61		
Isovaline	-5		
● Leucine	11.3	0.005%	
Isoleucine	4.8	0.002%	
Alloisoleucine	5.1		
Norleucine	6.0		
<i>tert</i> -leucine	<0.02		
● Proline	1.5	small	
● Aspartic acid	34	0.015%	
● Glutamic acid	7.7	0.003%	
● Serine	5.0	0.002%	
● Threonine	-0.8	small	
Allothreonine	-0.8		
α,γ -Diaminobutyric acid	33		
α -Hydroxy- γ -aminobutyric acid	74		
α,β -Diaminopropionic	6.4		
Isoserine	5.5		
Sarcosine	55		
<i>N</i> -Ethylglycine	30		
<i>N</i> -Propylglycine	-2		
<i>N</i> -Isopropylglycine	-2		
<i>N</i> -Methylalanine	-15		
<i>N</i> -Ethylalanine	<0.2		
β -Alanine	18.8		
β -Amino- <i>n</i> -butyric acid	-0.3		
β -Aminoisobutyric acid	-0.3		
γ -Aminobutyric acid	2.4		
<i>N</i> -Methyl- β -alanine	-5		
<i>N</i> -Ethyl- β -alanine	-2		
Pipecolic acid	0.05		

* Yield based on the carbon added as CH_4 . Glycine = 0.26%; alanine = 0.71%; total yield of amino acids in the table = 1.90%.

ained 100 ml H_2O for the curves with N_2 but no NH_3 , and it contained 100 ml of 0.05 M NH_4Cl for the curves with N_2 + NH_3 (0.2 torr). The flask was kept at room temperature, and the spark generator was operated continuously for 48 hours.

reducing conditions

oxidizing conditions



Thought to be most realistic

Figure 3.3. Amino acid yields based on initial carbon. In all experiments, P_{N₂} was 100 torr, and P_{CH₄}, P_{CO}, or P_{CO₂} was 100 torr. The flask contained 100 ml H₂O for the curves with N₂ but no NH₃, and it contained 100 ml of 0.05 M NH₄Cl for the curves with N₂ + NH₃ (0.2 torr). The flask was kept at room temperature, and the spark generator was operated continuously for 48 hours.

CAVEATS

The spark is just a way to create highly reactive stuff

Not especially like lightning
(real lightning doesn't work well)

Distribution of products depends on experimental details

- spark vs pulse
- shape of chamber
- arrangement of trap etc

Most experiments designed to optimize yields, not to be plausibly prebiotic.

Many other energy sources utilized:
UV, heat, glow discharge/plasmas, chemistry, shock waves, ~~the~~ radiation, electron beams, etc.

Other Simulation Results

Many AA's (all but lysine, arginine, glutamine) from HCN, H₂CO atmospheres

Nucleotide bases A, G, C, T, U

from HNC solutions

H₂CO solutions

~~cyanoacetate~~ $\text{HC}\equiv\text{C}-\text{C}\equiv\text{N}$
cyanate NCO^-

Ribose ~~from~~ (and many other sugars)
from H₂CO atmospheres & solutions

Some nucleosides (base + sugar)
in mixtures of ribose + A
G etc.

Some things missing - lipids especially,

Basic conclusion

Most small molecules
can be made by relatively
simple processes.

all nucleotides
(base + sugar + phos.)

Another Source

Comets, meteorites, asteroids

■ Late heavy bombardment

Comets: ~ 50% rock, 50% water/organics

Meteorites: few percent carbonaceous material at best

Asteroids

- Space stuff thought to be source of much water, atmosphere
- Composition of organic material similar to results of simulation experiments with reducing atmospheres

Table 6.1. Carbon distribution in the Murchison meteorite.

Form	Amount
Total carbon	2.12%, 1.96% (1, 2)
<i>Interstellar grains</i>	
Diamond	400 ppm (3)
Silicon carbide	7 ppm (4)
Graphite	<2 ppm (5)
Carbonate minerals	2%–10% total C (6)
Macromolecular carbon (tar)	70%–80% total C
<i>Organic compounds</i>	
10%–20% total C	
Aliphatic hydrocarbons	++
Aromatic hydrocarbons	++
Polar hydrocarbons	+++
Volatile hydrocarbons	+
Aldehydes & ketones	++
Alcohols	++
Amines	+
Monocarboxylic acids	+++
Dicarboxylic acids	++
Sulfonic acids	+++
Phosphonic acids	+
N-heterocycles	+
Purines & Pyrimidines	+
Carboxamides	++
Hydroxy acids	++
Amino acids	++
+++ >100 ppm	++ >10 ppm
+ >1 ppm	

mixture
of a bit
of
everything

1. Jarosevich 1971. 2. Fuchs, Olsen and Jensen 1973. 3. Lewis et al. 1987;
Blake et al. 1988. 4. Tang et al. 1989. 5. Amari et al. 1990. 6. Grady et al. 1988.

Similar to Miller-Urey type stuff, but less concentrated

material. This macromolecular carbon, along with the exotic carbon phases, can be obtained by digesting the insoluble fraction with HF-HCl mixtures, a process that dissolves most inorganic minerals, including the carbonates.

Macromolecular carbon

The macromolecular carbon of the Murchison meteorite has been shown by both chemical degradation (Hayatsu et al. 1977, 1980) and ¹³C NMR (Cronin, Pizzarello and Frye 1987) to have both aliphatic and aromatic character and to be similar to the more aromatic (type III) terrestrial kero-gens (Miknis et al. 1984). High resolution electron microscopy (HREM) has shown this material to occur predominantly in irregular clumps having both amorphous and spiral layered structures (Lumpkin 1986). The clumps are composed of particles in the range 0.01 to <0.1 μm (Reynolds et al. 1978). Some portion of the macromolecular carbon may occur in fluores-

How Much?

Early claims: A prebiotic soup should have formed in the early oceans

- organic molecules at $\sim 1M$ conc.
 very concentrated.
- all the building blocks present in "reasonable" concentrations } still in textbooks

Present Consensus (see Shapiro, almost any review)

- no prebiotic soup ever existed
- concentrations $\sim 10^{-7}M$ more likely
aa's \leftarrow in oceans sub-reactive
~~must~~ other stuff
- no nucleotides at all

Some reasons for the change:

- Early atmosphere CH_4 $\overset{\text{then}}{\text{NH}_3}$ H_2 H_2O

$\overset{\text{now}}{\text{N}_2, \text{H}_2\text{O}, \text{CO}_2}$ ($\text{O}_2?$)

huge change in chemistry
much less reactive
much lower yields of all organics

↑
produced by
UV + water
vapor
**DEADLY to
all prebiotic
syntheses**

- Complete lack of geological evidence

Oceans full of stuff should have left
a record, even at 3.8-4.0 Bya.

- Better appreciation of destructive
processes

UV (huge, in absence of O_3)
hydrolysis, oxidation, adsorption
to minerals, tar formation,
precipitation to ocean bottom,
cycling of oceans through high T
vents, etc, etc.

Summary

Simulations, meteorite/comet data strongly suggest SOME "building blocks" on early earth.

"Prebiotic soup" scenario very unlikely, out of favor even in OoL field.

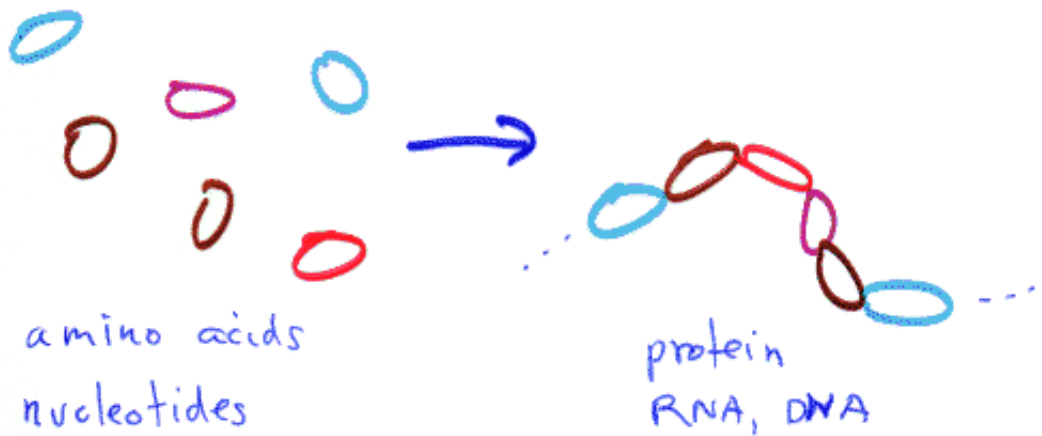
Some key molecules very unlikely

- nucleotides way too complicated
- complex aa's low concentrations at best
- lipids? (cell membranes never synthesized)
- "pure" sugars? mixtures, mainly no ribose, to speak of.

● Altogether, this is probably one of the stronger areas in OoL.

Formation of Polymers

Once you have the building blocks, you have to build up.



- No enzyme catalysts
- Water solutions (bad, usually)
- Mixtures of many things
- Cross reactions
- Destruction

Both protein and RNA, DNA formation are unfavorable in water

Cells do it by inputting ENERGY

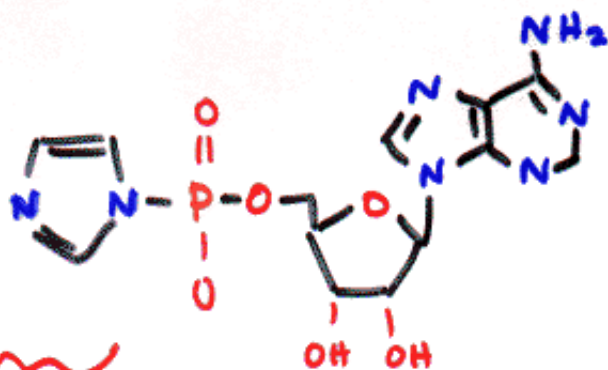
mainly from ATP (photosynthesis, etc).

— requires sophisticated enzymes, metabolism

anaerobic metabolism
oxidative phosphorylation

Solution for OOL purposes:

1. Don't use aa's or nucleotides — use "activated" building blocks

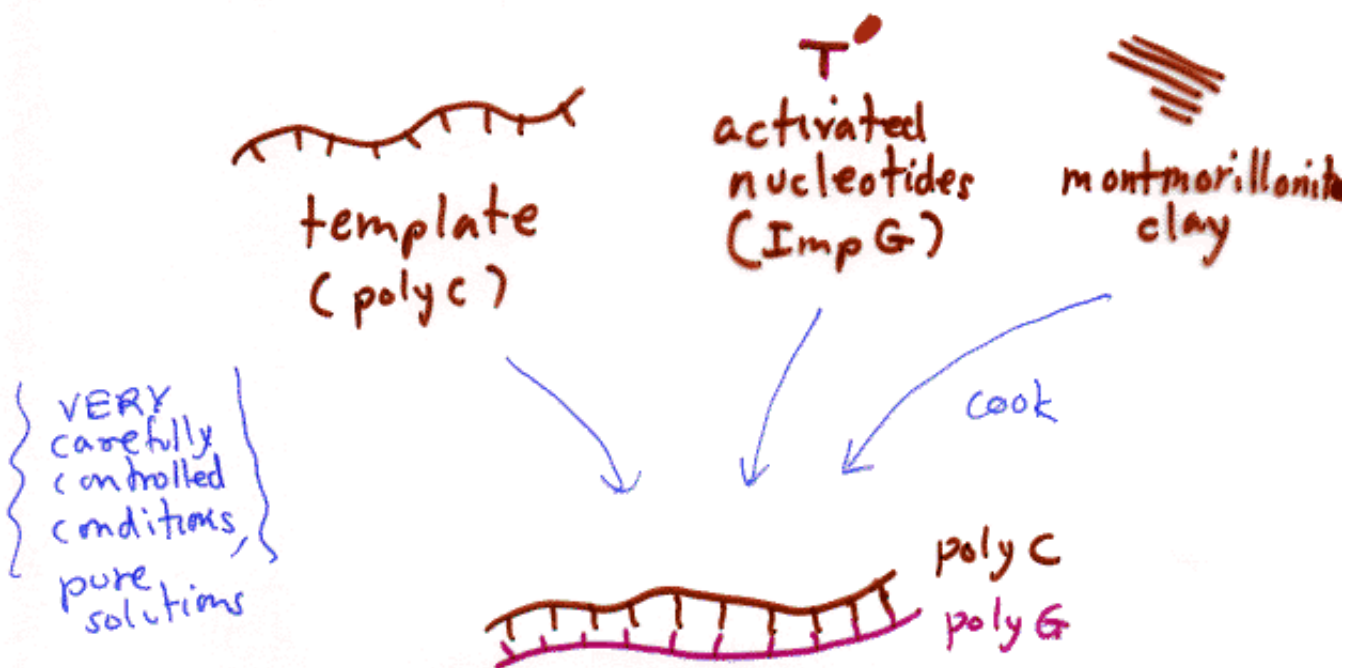


activating group

2. Look for a natural mineral catalyst

Some "success" by these methods:

EXAMPLE



Other successes

Montmorillonite catalyzes short (3-12) DNA, RNA's from nucleotides

Sydney Fox "proteinoids" with some "catalytic" activity formed by heat/drying of aa's

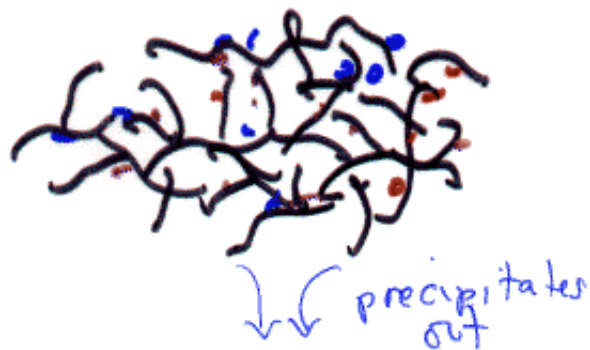
RNA catalysts can synthesize short DNAs, RNAs (3-6)

→ Basically, no real successes. Building blocks don't build up by themselves

Other problems

"Tar" formation is the norm in realistic solutions

- every reaction possible happens
you get crosslinked gunk
instead of nice clean polymer



Inhibition by contaminants (hence pure solutions in the experiments)

Hydrolysis back to building blocks (water again)

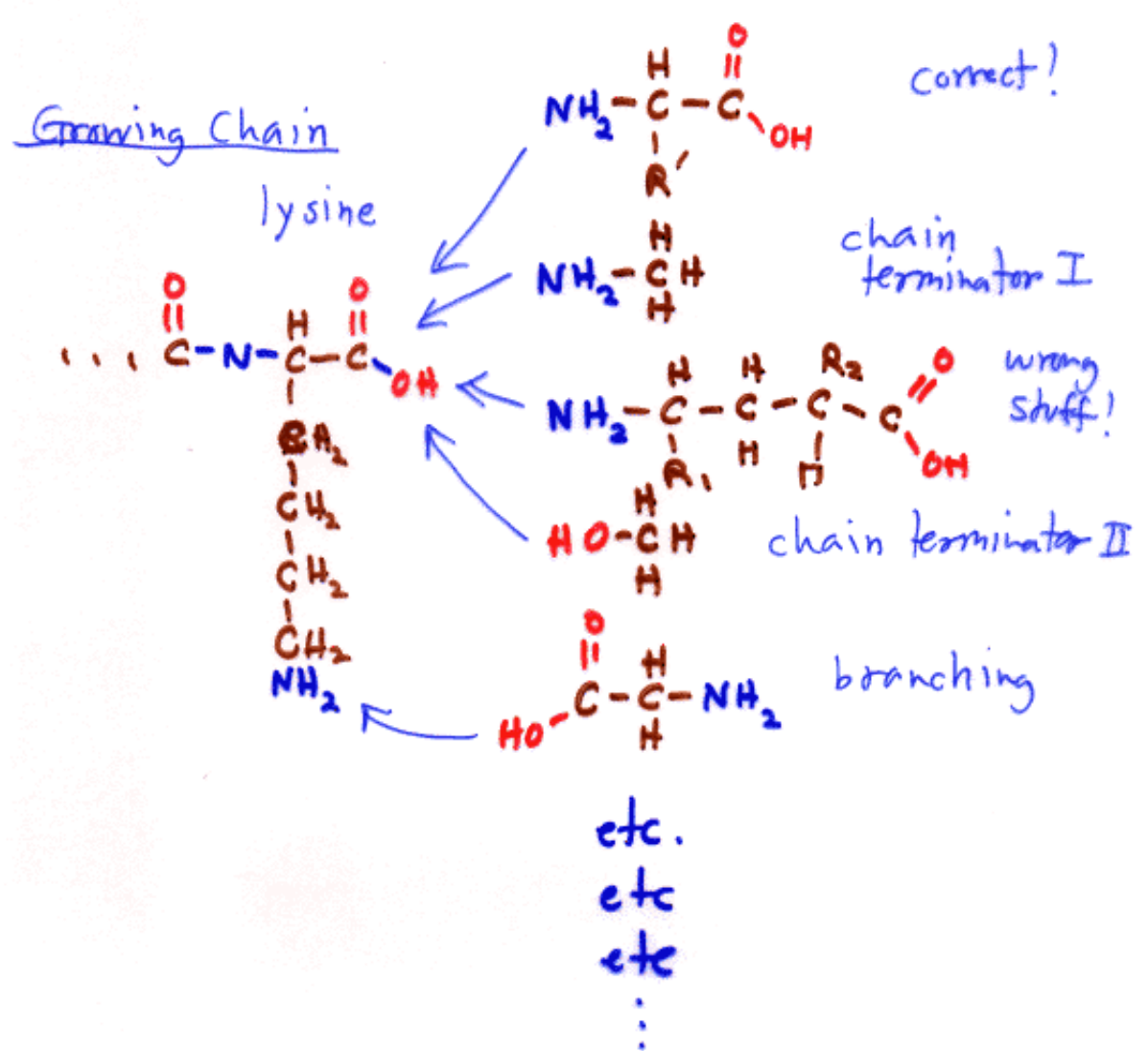
Inhibition by wrong chirality (mirror images)

Chain termination, branching

Need for high concentrations

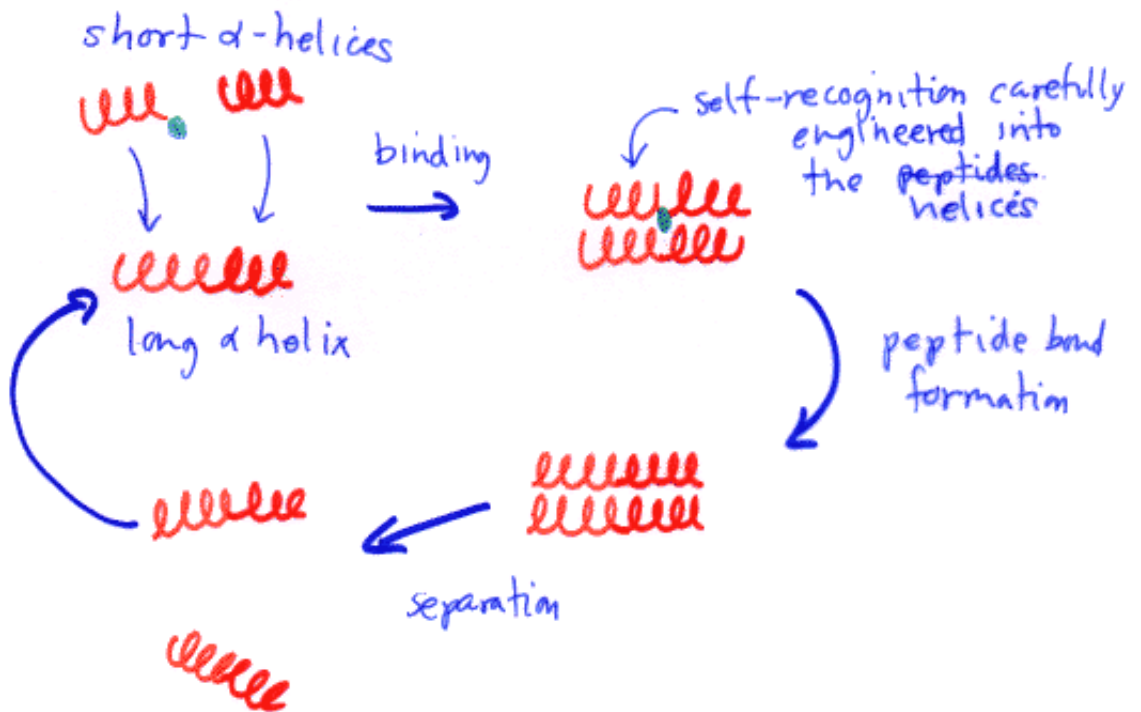
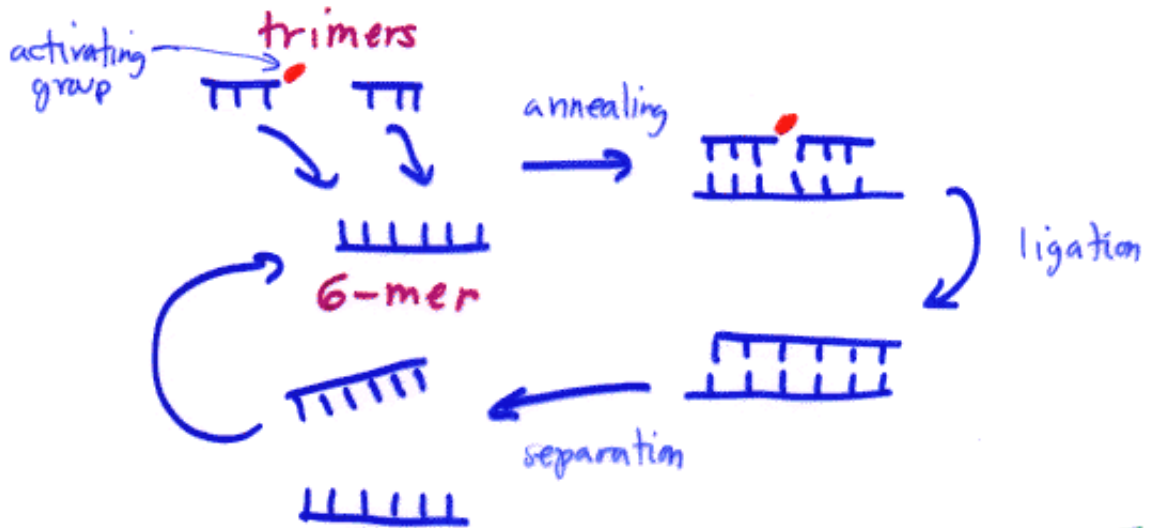
Etc, etc.

Next Subunit



Without the cell's machinery the odds of getting anything "nice" are 10⁻⁶ big.

Contrived "Replicators"



Comments

Very complicated starting points for both.

Unclear what effect impurities or competition would have

Not obvious that there is any potential for chemical evolution here

Significance for @oL unclear (but the chemistry is cool).

BASIC PROBLEM

These are not simple molecules,
Murphy's Law applies (ENTROPY)

If anything can go wrong, it will go
wrong

→ Many things can go wrong.

So, if trying to get a SPECIFIC thing
won't work, maybe we don't need one

self-organizing criticality

collectively autocatalytic ~~steps~~ sets

Stuart Kauffman

"Metabolism First" approach

Basic Claim:

Gather together enough molecular diversity of any sort and by pure chance it will inevitably form a collectively autocatalytic set

- no one molecule replicates itself, but all molecules TOGETHER replicate the whole system
 - there is a critical threshold of diversity above which collective autocatalysis becomes automatic.
- If true, this would solve many of the earlier troubles
 - Don't need anything specific, just a lot of SOMETHING.

There may be SOME cases where this is true BUT...
COUNTEREXAMPLES

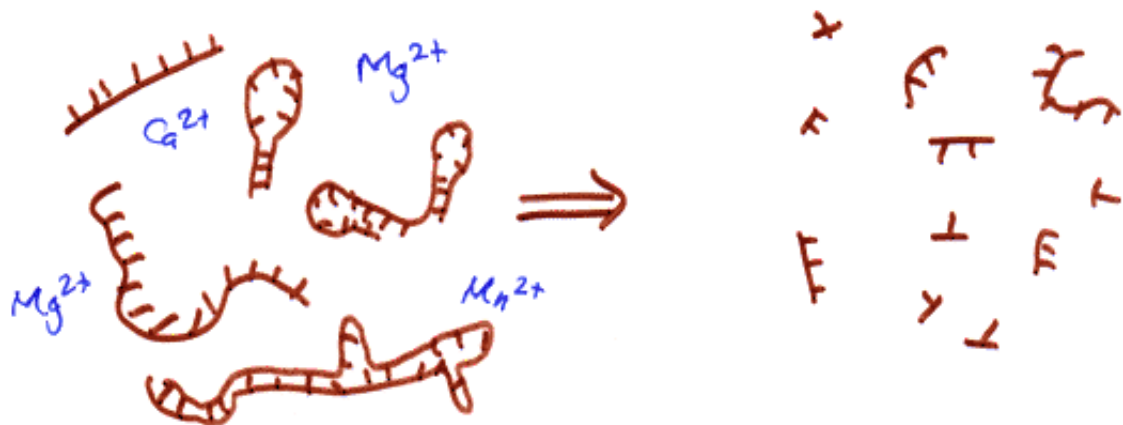
1. RNA molecules

- most common catalytic activity (by far, I believe) is cutting (nuclease)
w/ other RNA's.
- ligase activity (joining RNA's) much less common
- polymerase activity still less.

A collection of many RNA's is likely to just cut itself to bits

(This is often observed, in fact).
One of the main objections to RNA World scenario)

The kind of catalytic activity matters.



2. More generally

- for every replication process there will be competing destruction processes



- The rates for all these processes depend on CONCENTRATIONS of:

- enzymes (catalysts)
- food
- fuel
- substrates

Example:
remove all fuel and replication stops but destruction continues.

Whether replication wins or destruction wins depends on details of all the concentrations involved.

SUMMARY of OoL



1. A lot has been learned about:
 - early earth conditions
 - possible chemistries under such conditions
 - behavior of many candidate replicators, etc.
2. For OoL scenarios:
 - every stage has serious difficulties
 - where did building blocks come from?
 - how could they have built up?
 - how could they have been protected from destruction?
 - what environment could have been the "nursery"?

later stages really not
even addressed

— how could a ~~an~~ replicating RNA
evolve to life as we know it?

3. IMHO:

- RNA World scenario is impossible
(at least as an OoL scenario)
- Protein first is in worse shape
- "Metabolism first" approach still
has a shot (but will need to get
more concrete soon).

Final Comments

1. Watch out for hype in this field.

From Shapiro (readings)

"(Miller and Urey) simulated conditions on a primitive earth and created out of its atmospheric gases several organic compounds that are close to proteins... What they had done is to prove that complex organic compounds found in living matter can be formed... If their apparatus had been as big as the ocean, and if it had worked for a million years instead of one week, it might have created something like the first living molecule."

- pretty typical

The Voet & Voet picture is another example in another context.

2. The devil is in the details.

Eg: it sounds plausible that once you have the building blocks you can build up to proteins, DNA, RNA, etc., but it isn't when you look closer.

3. A modest proposal

If we really understand how life COULD HAVE arisen, it should be possible to reproduce it in the lab.

YES? Real science

NO? Not there yet.