Origin of Life: I
Monomers to Polymers

Synthesis of Monomers

Life arose early on Earth (within 0.7×10^9 y)

1. Conditions
   1. Liquid Water
   2. Reducing or Neutral Atmosphere
   3. Energy Sources

2. Originally thought atmosphere was
NH_3, CH_4, H_2O, H_2

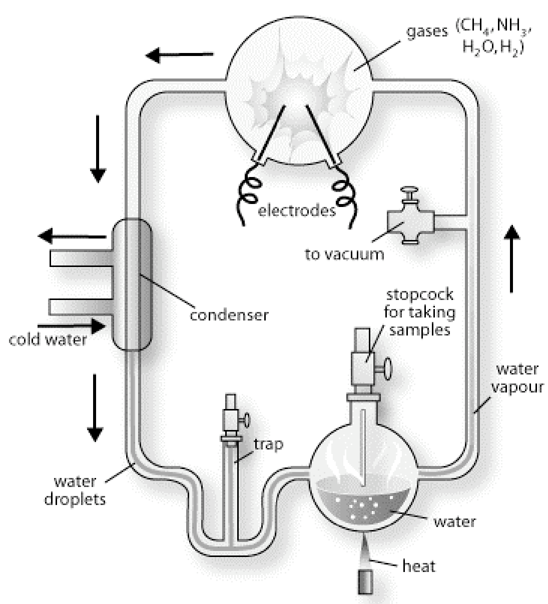
Miller -Urey Experiment

Now Believe CO_2, H_2O, N_2

3. Energy Sources

Ultraviolet Light (No Ozone)
Lightning
Geothermal (Lava, Hot Springs, Vents, …)

Miller -Urey Experiment



COMPOUND	Relative Yield
Glycine	270
Sarcosine	21
Alanine	145
N-methylalanine	4
Beta-alanine	64
Alpha-amino-n-butyric acid	21
Alpha-aminoisobutyric acid	0.4
Aspartic acid	2
Glutamic acid	2
Iminodiacetic acid	66
Iminoacetic0propionic acid	6
Lactic acid	133
Formic acid	1000
Acetic acid	64
Propionic acid	56
Alpha-hydroxybutyric acid	21
Succinic acid	17
Urea	8
N-methyl urea	6

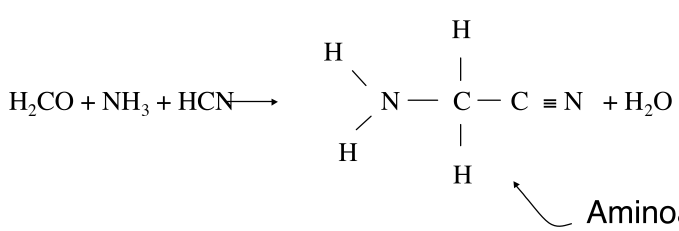
How did Amino Acids form in Miller -Urey Experiment?

Strecker Synthesis

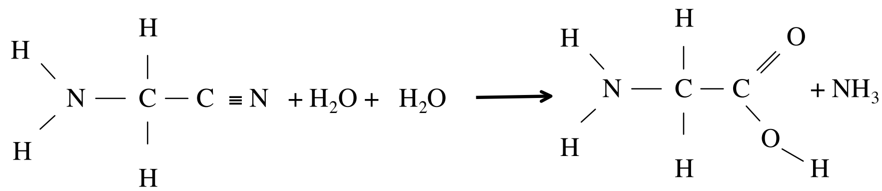
CH_4, H_2, NH_3 + Energy → H_2CO, HCN, HC_3N, Urea (H_2NCONH_2)

e.g. Glycine Synthesis

Reactive

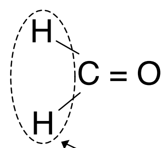


Aminoacetonitrile



glycine

H_2CO



form Aldehyde

More complex group - other aldehydes

↓

more complex amino acids

Lower yield if atmosphere was N_2, CO_2, H_2O

(If H_2/CO_2 > 2, get good yield)

Problems with Miller - Urey

Atmosphere was N_2, CO_2, H_2O

NH_3, CH_4 would react ⟶ N_2, CO_2

Try N_2, CO_2, H_2O in Miller - Urey simulation

Only get trace amounts of glycine
Need CH_4 to get more complex amino acids

Need $H_2/CO_2 > 2$ to get much of any amino acid

Miller - Urey with Cosmic Rays

A group in Japan has obtained good yields of amino acids from slightly reducing gases (CO_2, CO, N_2, H_2O)

When they used high energy protons (simulate cosmic rays)

Apparently not Strecker Synthesis (Low abundance of aminoacetonitrile)

Building Blocks of Nucleic Acids

Not formed in Miller - Urey But some intermediates were

1. Ribose Sugar:

   $5 \cdot H_2CO + \text{Heat} \longrightarrow H_{10}C_5O_5$

   [Clay Catalyst]

2. Bases

   a) Purines $5\ HCN \rightarrow H_5C_5N_5$

   (Adenine)

   b) Pyrimidines

   $HC_3N + \text{Urea} \longrightarrow H_5C_4N_3O$

   (Cytosine)

   (1995) Cyanoacetaldehyde + Urea $\longrightarrow$ Uracil

3. Phosphate
   Rock Erosion

Less understood than amino acids

<u>Other Possibilities:</u>

Seafloor Vents

Interstellar Molecules

Comets

<u>Alternative Delivery</u>

Molecular clouds - strongly reducing, contain many molecules used in Miller-Urey (H_2, NH_3, H_2O, CH_4) and intermediates (HCN, H_2CO, HC_3N) and possibly glycine

Problem: These would not have survived in part of disk where Earth formed

But interstellar ices ⟶ comets
Evidence from similar molecules
(e.g. C_2H_2, CH_4, HNC, …)
Clearly indicates interstellar chemistry

Cratering record on moon, …

$\Rightarrow$ heavy bombardment early in history

Comets and their debris could have brought large amounts of “organic” matter to Earth

(and maybe oceans)

Some evidence for non-biological amino acids in layer depostied after asteroid impact 65 million years ago

Sources of Organic Molecules

Quantitative comparison by Chyba & Sagan, Nature 1992, Vol. 355, p. 125

Currently, Earth accretes ~ 3.2×10^6 kg y^{-1} from interplanetary dust particles (IDP)

~ 10 % organic carbon $\Rightarrow$ 3.2×10^5 kg y^{-1}

~ 10^3 kg y^{-1} comets

~ 10 kg y^{-1} meteorites

~ $10^3 \times$ more at 4.5×10^9 yr ago (?)

(cratering record)

UV + reducing atmosphere 2×10^{11} kg y^{-1}

But if $H_2/CO \lesssim 0.1$ IDP’s dominant source

So if atmosphere very neutral, IDP's

Most of mass in IDP's in range of size ~ 100 m

mass ~ 10^{-5} g

Complex structure - composites of smaller grains
some carbon rich

Enhanced deuterium ⟶ low T

Also found in interstellar molecules

? connection back to interstellar chemistry

2 kinds (mass ranges) can supply organic matter

1. Interplanetary dust particles ($m \lesssim 10^{-5}$ g)

2. Smaller meteorites ($m \lesssim 10^{8}$ g)

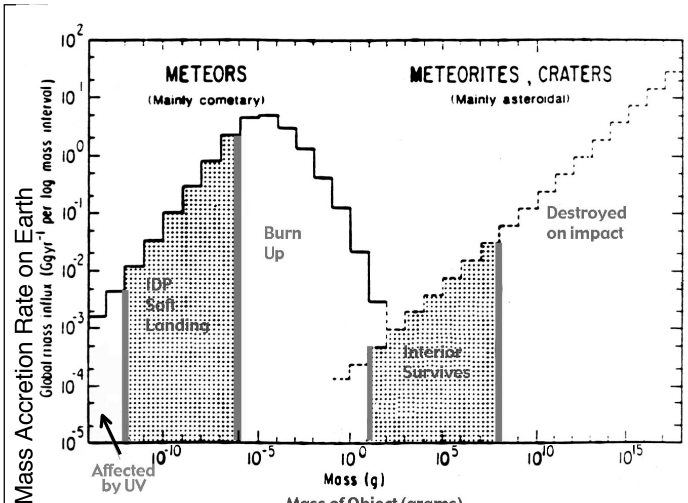


FIG. 1 Infall rate of meteoritic matter on Earth (adapted from ref. 5). Intervals where organic matter can survive passage through atmosphere are shaded. The curve on the right is based on the relation[5] $N = 0.54\, r^{-2.1}$ (N = number of impacts per Myr, r = radius in km), for an assumed density of 3 g cm^{-3}. The corresponding mass accretion rate (Gg yr^{-1}) between r_1 and r_2 is 15.83 $(r_2^{0.9} - r_1^{0.9})$.

E. Anders (1989) Nature, 342, 255

Alternative Sites

Locally reducing environments

1. Ocean vents
   Sources of CH_4 and H_2S
   Current Vents have ecosystems based on energy from chemicals - not photosynthesis
   $H_2S \longrightarrow$ Bacteria $\rightarrow$ Clams, Tube Worms
   Pre-biotic amino acid synthesis?

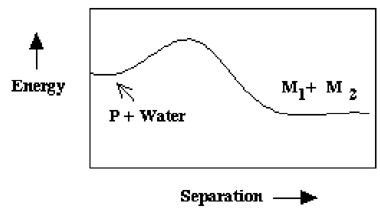
2. Inside Earth
   Many bacteria now known to live deep (~ 2 miles) in Earth. Again, on chemicals, adapted to high temperature genetic makeup very ancient

3. Hot Springs
   Bacteria may be important in precipitating minerals. again adapted to high T and ancient

Synthesis of Polymers

$M_1 + M_2 \longrightarrow P + H_2O$

$\longleftarrow$ more likely in liquid H_2O



Solutions Remove H_2O (Drying, Heat)

Sydney Fox $\longrightarrow$ Proteinoids

Energy Releasing Reactions (H_2NCN or HC_3N)

Catalysts: Clays

Monomers $\longrightarrow$ polymers

A problem:

Peptide bond requires removal of H_2O

This would be hard in primordial sea

Need special molecules to do what Ribosome does in living cells

Input of energy

or

Dry environment (dry land)

Imagine drying tidepool + geothermal heat

Heat + amino acids $\longrightarrow$ peptide bonds

Sidney Fox "proteinoids"

or catalyst - clay, energy-rich bonds…

Problem greater for nucleic acids

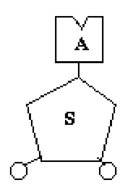
Sugar + base + heat $\longrightarrow$ some nucleosides

Activated nucleosides + phosphoric acid + Zn^{+2}

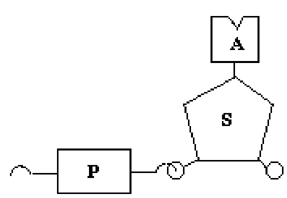
$\longrightarrow$ polymers up to 50 nucleotides

linkages (mostly) correct

Nucleic acids more complex



nucleoside



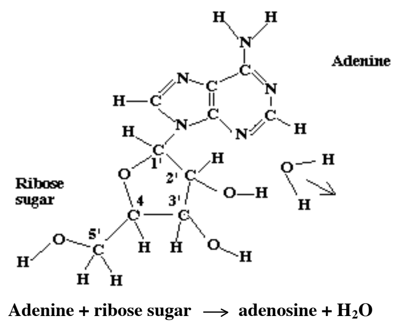
nucleotide

↑

Monomers of nucleic acids

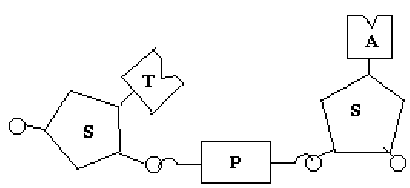
Synthesis of Adenosine

Base on 1' Carbon Why?



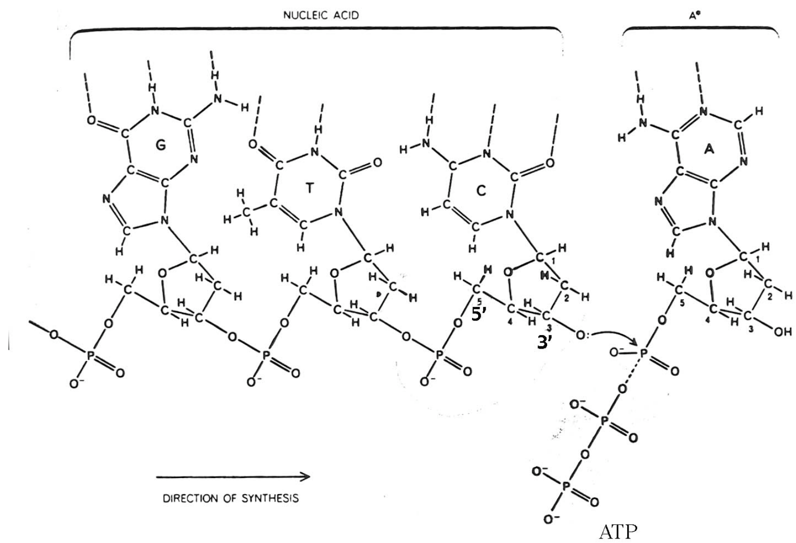
Also phosphates 3' & 5' carbons

Otherwise ↓ Misalignment



Leslie Orgel has had some success in getting high percentage of correct linkages, in presence of Zinc ions.

KORNBERG • THE SYNTHESIS OF DNA 233



SYNTHESIS OF DNA involves the stepwise addition of activated nucleotides to the growing polymer chain. In this illustration eoxyadenosine 5'-triphosphate (A*) is being coupled through a phosphodiester bond that links the 3' carbon in the deoxyribose portion of the last nucleotide in the growing chain to the 5' carbon in the deoxyribose portion of the newest member of the chain.

The Odds

- We need to get an "interesting" polymer
  - Enzyme
  - Self replicator
- Properties of polymer depend on
  - Order in which monomers combine
- If we combine monomers at random,
  - How likely to get something interesting?

Statistics of an unlikely event

Random reactions in primordial soup?

Unlikely event versus many trials

Probability ⟶ Consider tossing 10 coins

Probability of all heads = product of prob.

$$P = \left(\frac{1}{2}\right)\left(\frac{1}{2}\right)\left(\frac{1}{2}\right)\left(\frac{1}{2}\right)\left(\frac{1}{2}\right) \cdots \left(\frac{1}{2}\right)^{10} = \frac{1}{1024}$$

Probability of getting 10 amino acids ⟶ protein

Chosen from 20 in a particular <u>order</u>

$$\left(\frac{1}{20}\right)^{10} = \frac{1}{1 \times 10^{13}}$$

But if you try many times, the chance of success is higher

$$P(r) = \frac{n!}{r!\,(n-r)!}\, p^r\,(1-p)^{n-r}$$

r = # of successes p = prob. Of success on each trial

n = # of trials

n! = n (n-1) (n-2) … 1

e.g. make $n = \frac{1}{p}$ (flip all 10 coins 1024 times)

$$P(1) = \frac{n!}{1!\,(n-1)!}\left(\frac{1}{n}\right)\left(1-\frac{1}{n}\right)^{n-1} = 0.37$$

Chance of one or more successes = 0.63

For reasonable chance need $n \sim \frac{1}{p}$

How many do we have to get right?

1. How many atoms?

Lipids	10^2 - 10^3
Enzymes, RNA	10^3 - 10^5
Bacterial DNA	10^8 - 10^9
Bacterium	10^{11} - 10^{12}
Human Being	10^{27} - 10^{28}

If we choose from H,C, N, O (ignore S,P)

probability of right choice 1/4

So for enzyme: $\left(\frac{1}{4}\right)^{10^3} \sim 10^{-600}$

# of trials: Shapiro computes

$N = 2.5 \times 10^{51}$ (surely an overestimate)

$n \ll \frac{1}{p}$ for <u>simple</u> enzyme

2. What if we start with amino acids?
   Need ~ 10^{13} trials to get 10 amino acid protein

To get 200 amino acids in right order

$$\left(\frac{1}{20}\right)^{200} = 10^{-260}$$ Hopeless!

Need something besides random combinations

Selection (Natural?)

Improving the Odds

Many proteins composed of interchangeable segments (Domains)

10 -250 amino acids

One domain found in ~ 70 different proteins

Intermediate building blocks?

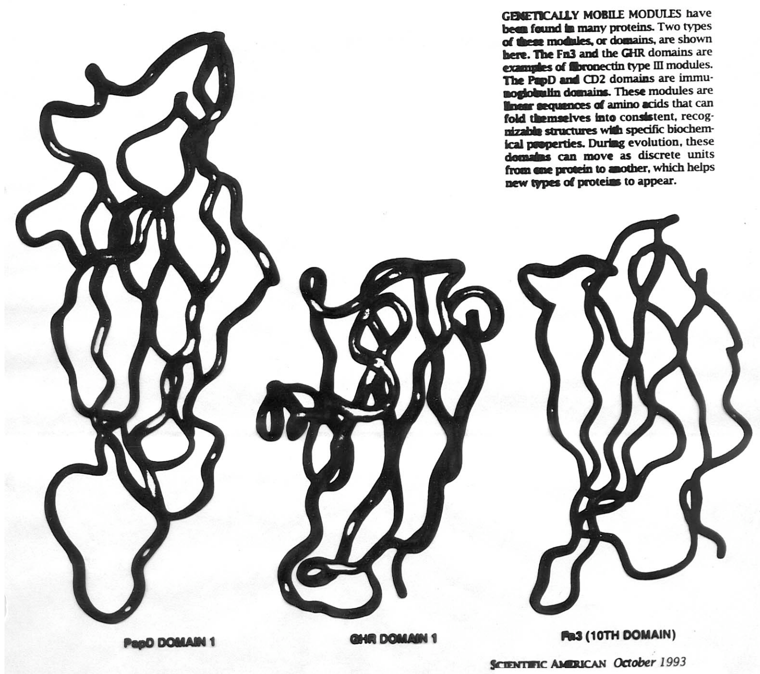
If so, may only need to get enough amino acids in right order for a domain

e.g. 18 amino acid domain

$P = \left(\frac{1}{20}\right)^{18}$ 10^{-23}

Also, many variations in amino acids don't destroy function

and many different sequences may be interesting



Scientific American Doolittle & Bork
Oct. 1993, pg. 50

Proteins made of domains, assembled in various ways
10-250 amino acids for ones containing disulfide bonds

18 - 100 for those without

Of all amino acids available

$$\left(\frac{1}{20}\right)^{40} \quad \text{or} \quad \left(\frac{1}{20}\right)^{18}$$

$\log_{10} = 40 \log 20$	$-18 \log 20$
$= -52$	$= -23.4$
so 10^{-52}	$10^{-23.4}$

Interesting fact on how the improbable happens

1st winner of Texas Lotto lottery
Picked all 6 numbers correctly in the same order as they were drawn.

Each number runs from 1 to 50, and once chosen, cannot be repeated (balls are taken from a box).

So the odds against getting them in order is

$$\left(\frac{1}{50}\right)\left(\frac{1}{49}\right)\left(\frac{1}{48}\right)\left(\frac{1}{47}\right)\left(\frac{1}{46}\right)\left(\frac{1}{45}\right) = \frac{1}{11,441,304,000}$$

You don't need to get them in the same order to win - odds against winning include any combination, so 1 in 16 million