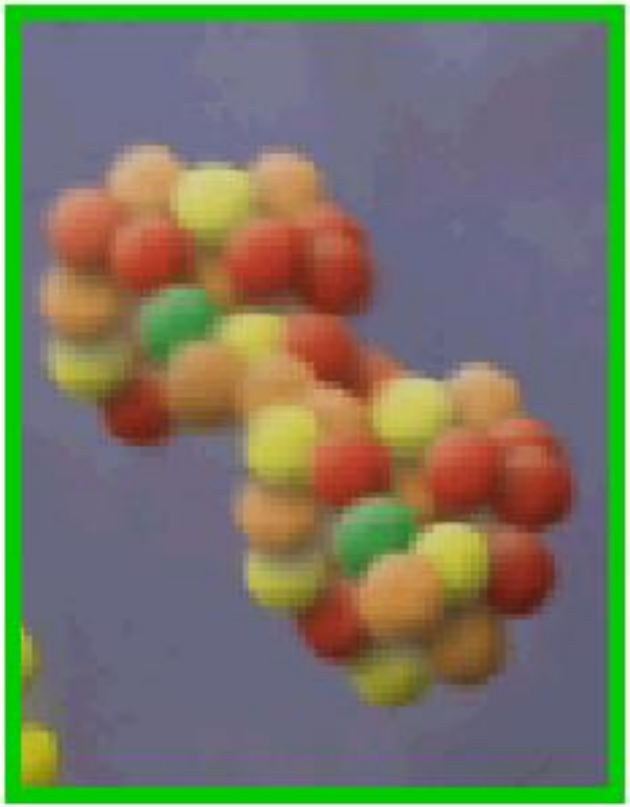
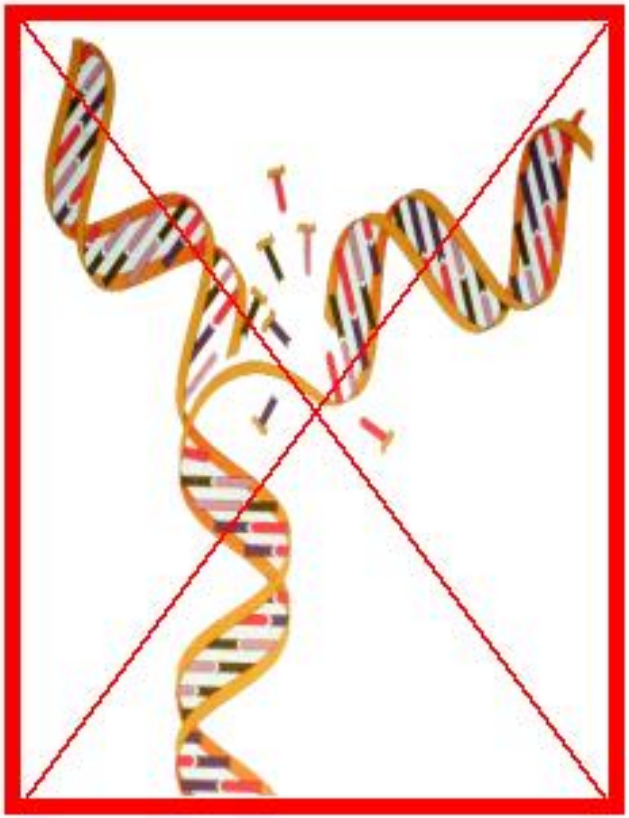
[01] Dr. D. Lancet, Weizmann (ITP 4/24/01) Origin of Life without Biopolymers

Origin of life without biopolymers

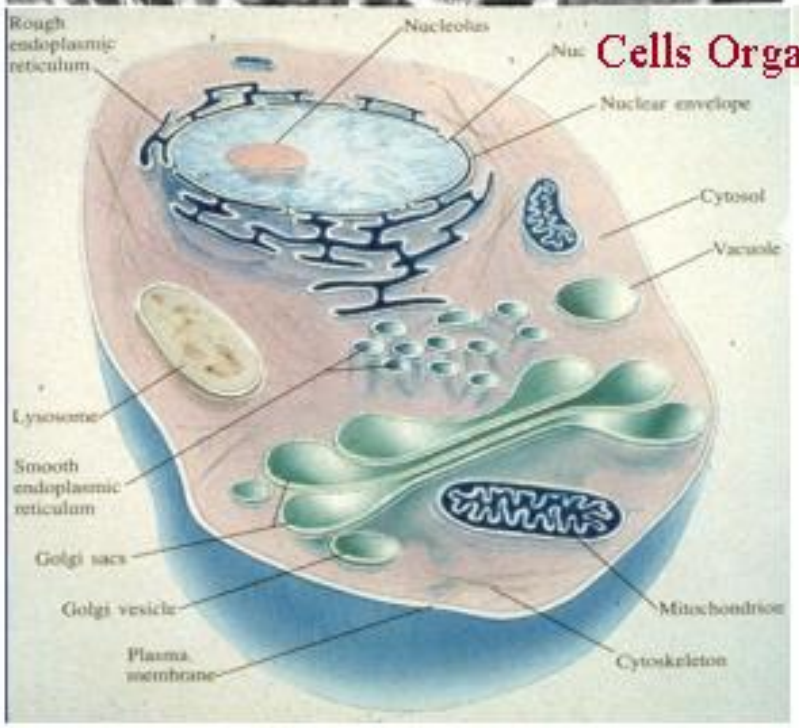


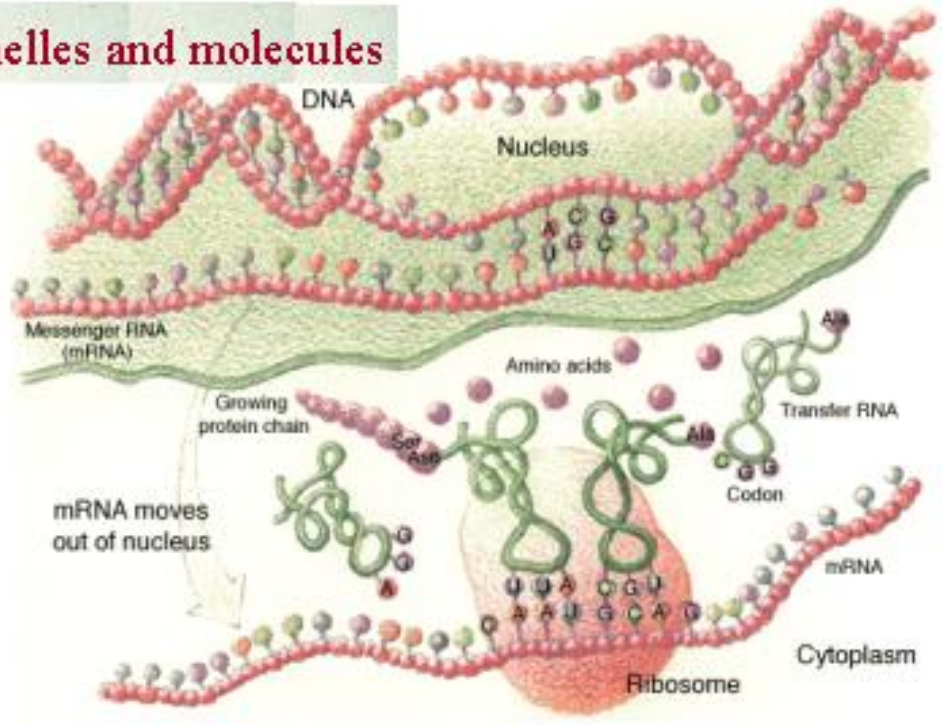


Doron Lancet, Crown Human Genome Center,
the Weizmann Institute of Science, Rehovot, Israel

Http://ool.weizmann.ac.il

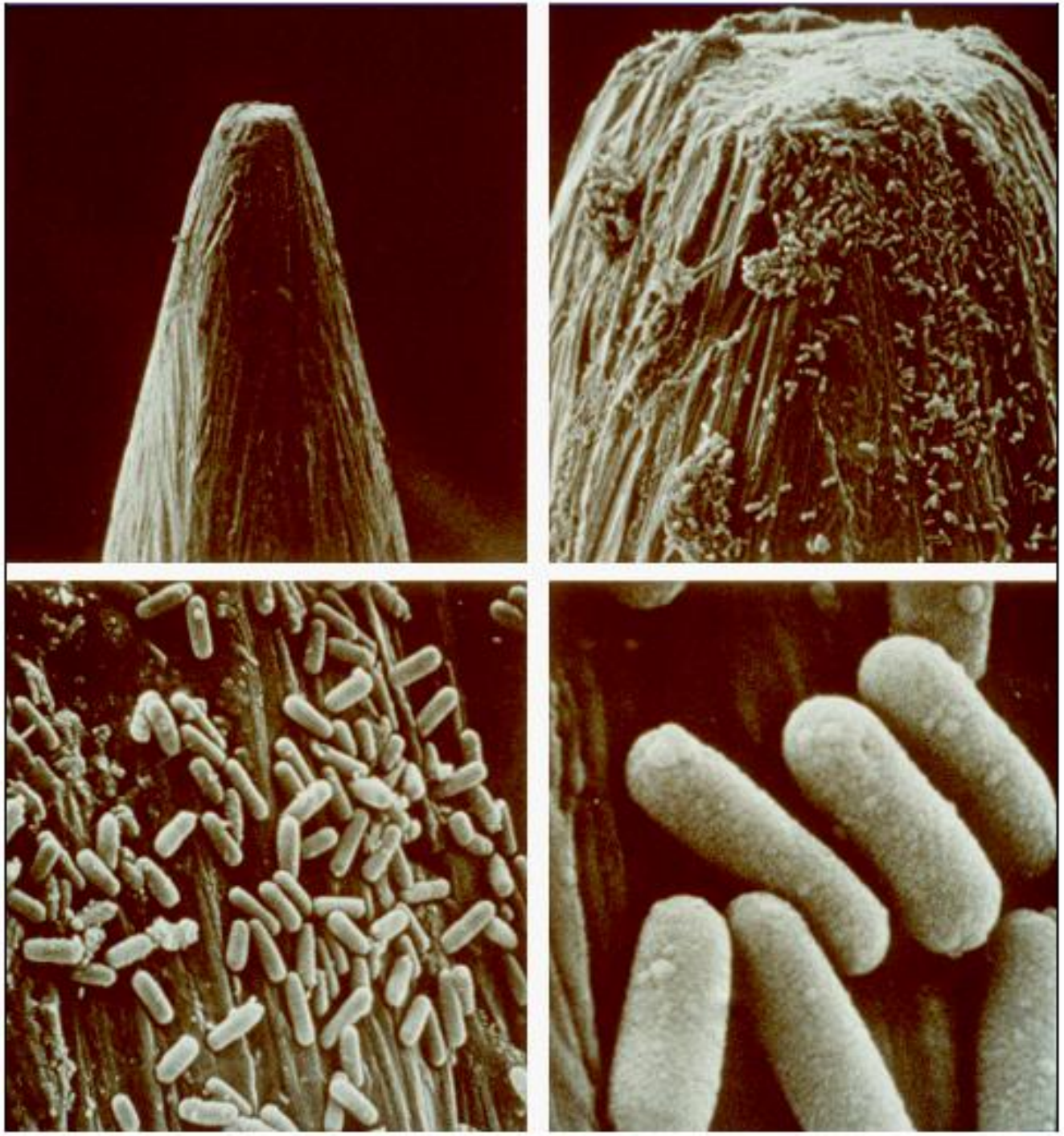
Life is complex!
How did it emerge?

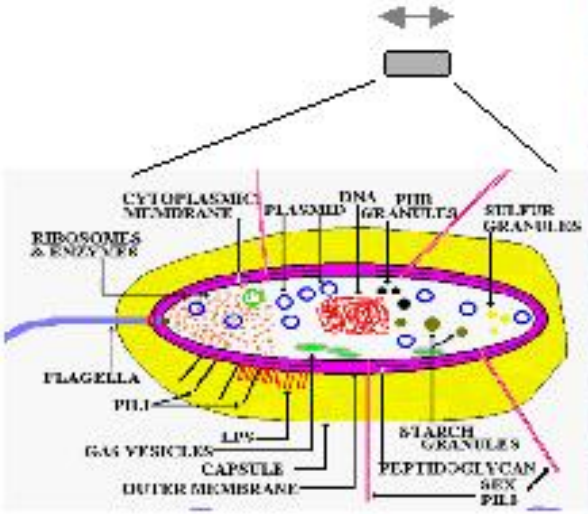




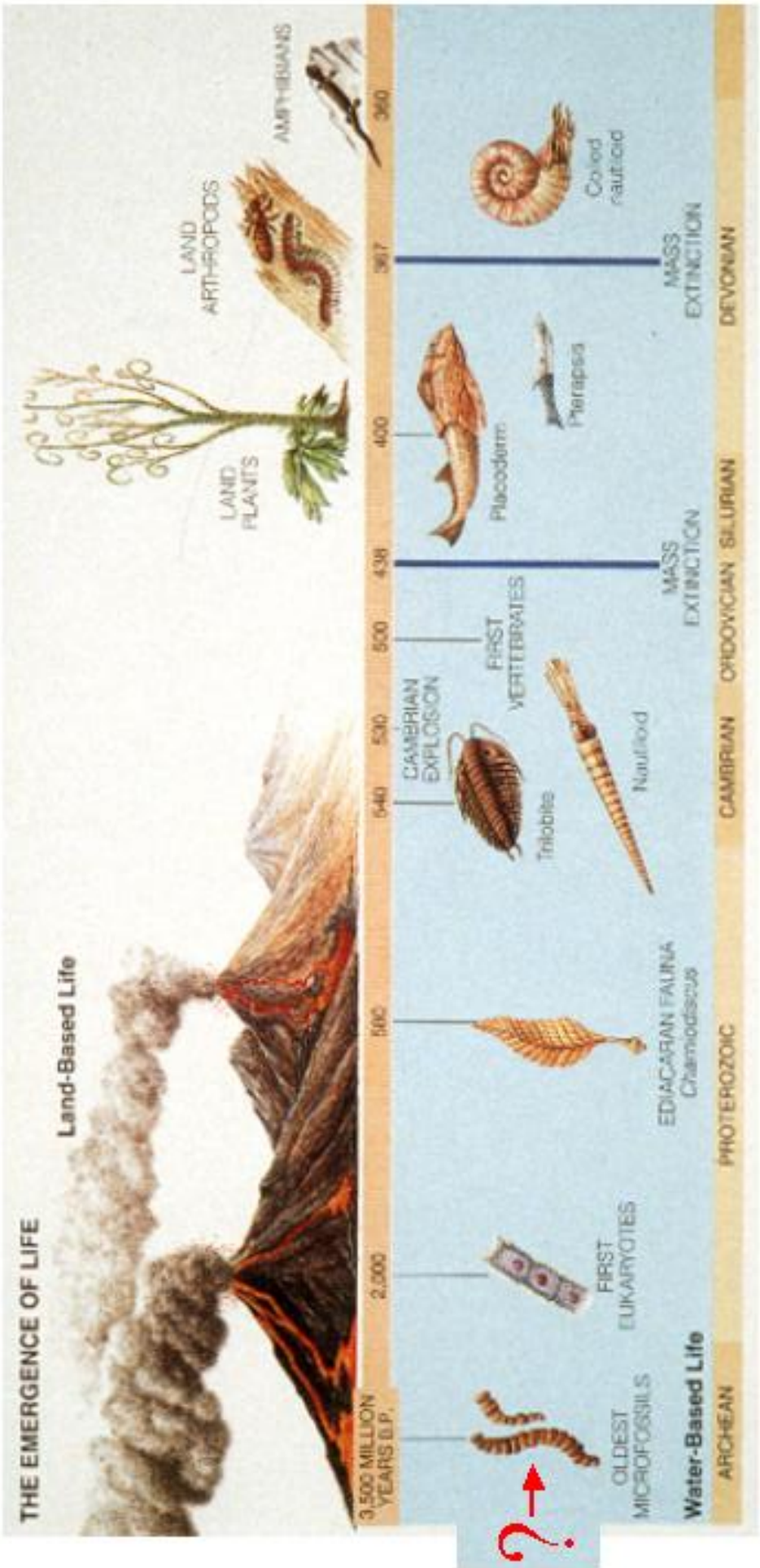
[04] Dr. D. Lancet, Weizmann (ITP 4/24/01) Origin of Life without Biopolymers

Life: a haystack at the point of a needle

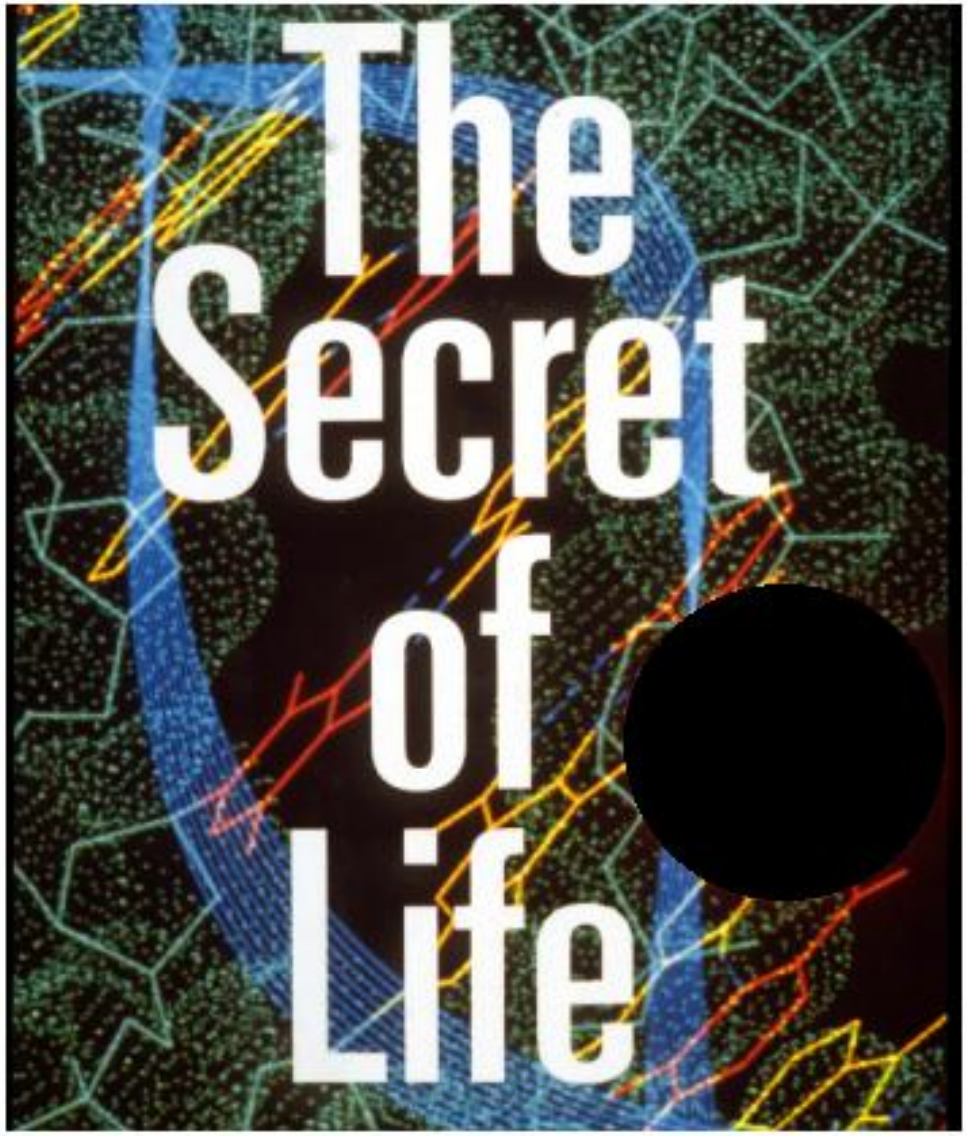




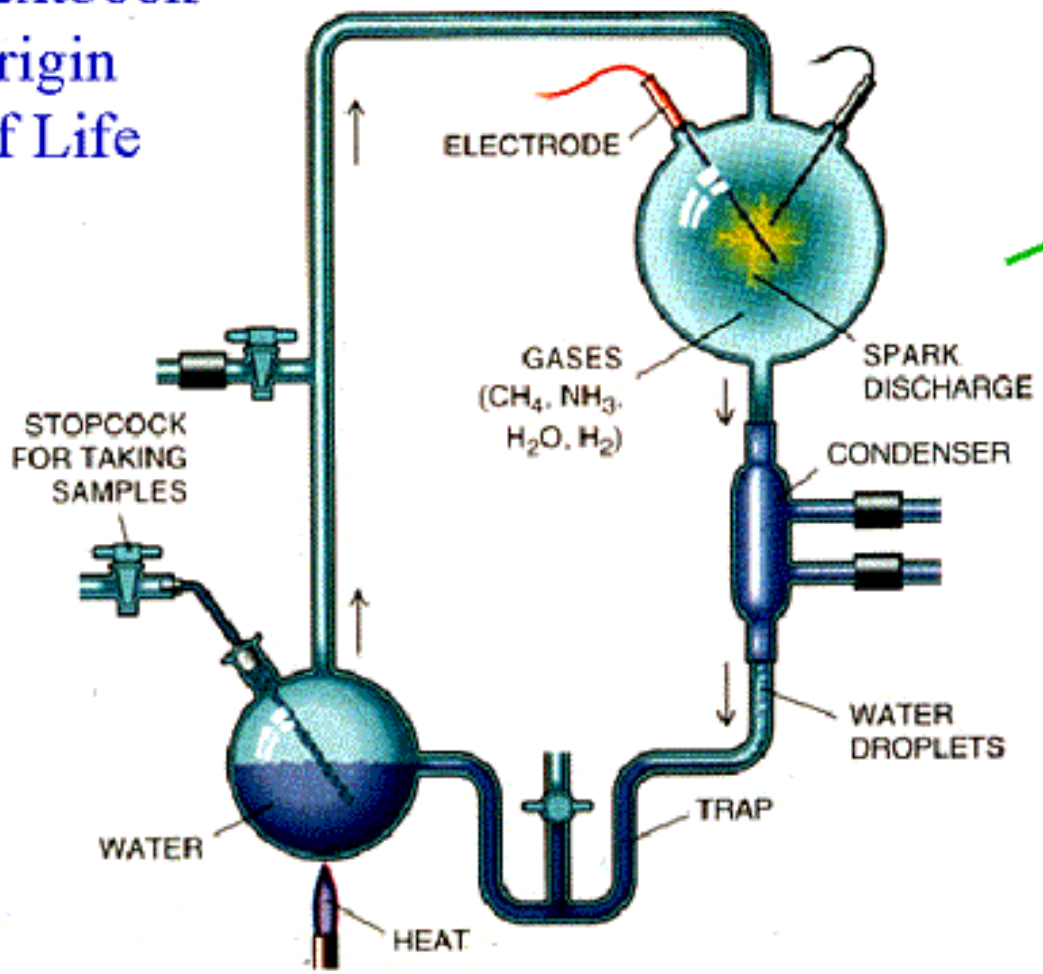
How to reconstruct the events preceding the fossil record?



Finding out about the Origin of Life may lead to a much better understanding of present-day life!



Textbook Origin Of Life



The Miller-Urey experiment (1953)

Amino acids, nucleotides

Polymerization Catalyzed by minerals

Proteins, RNA

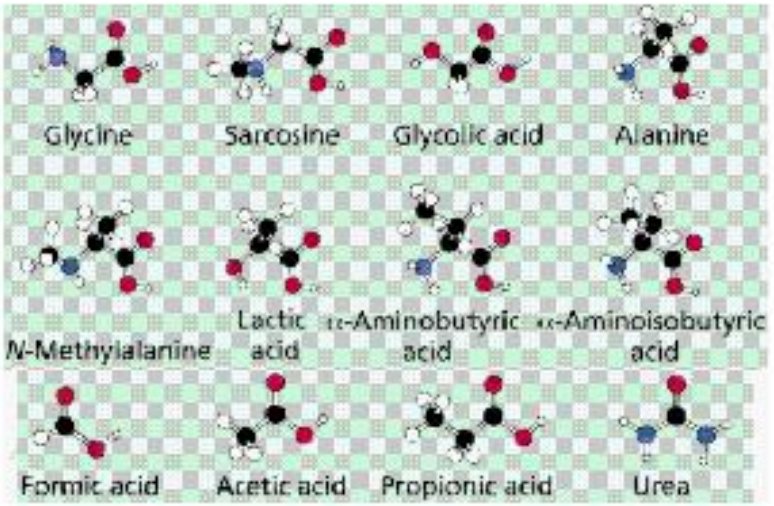
Molecular Evolution

Cells

Three proposed stage in the Origin of Life

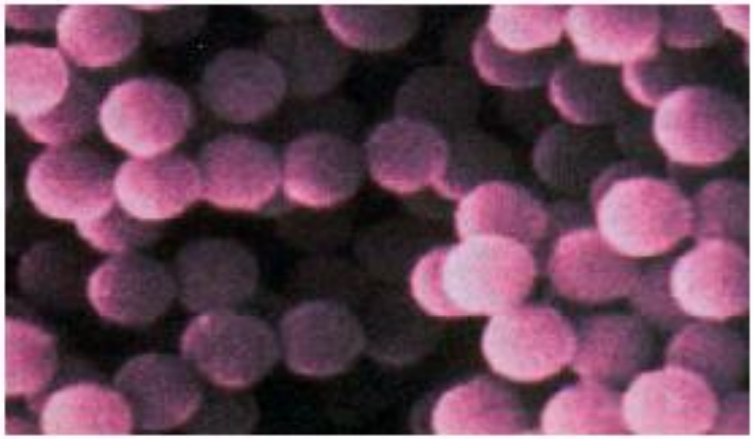
1) Origin of organic compounds

Understood in principle, need more details



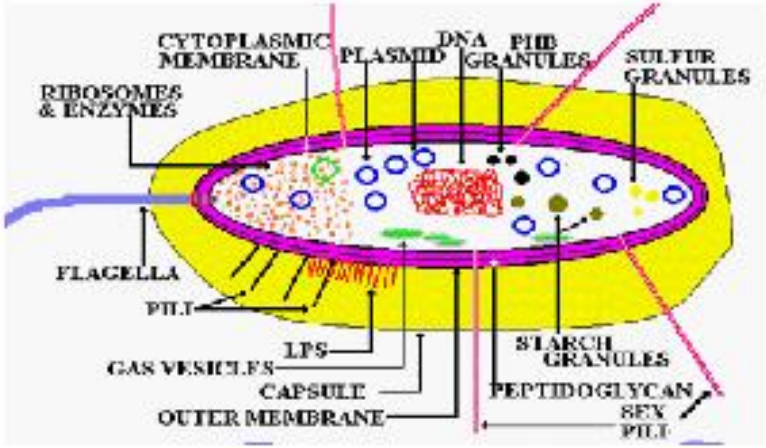
2) Origin of protocells (Morowitz, 1992)

Possible to model by general physicochemical reasoning

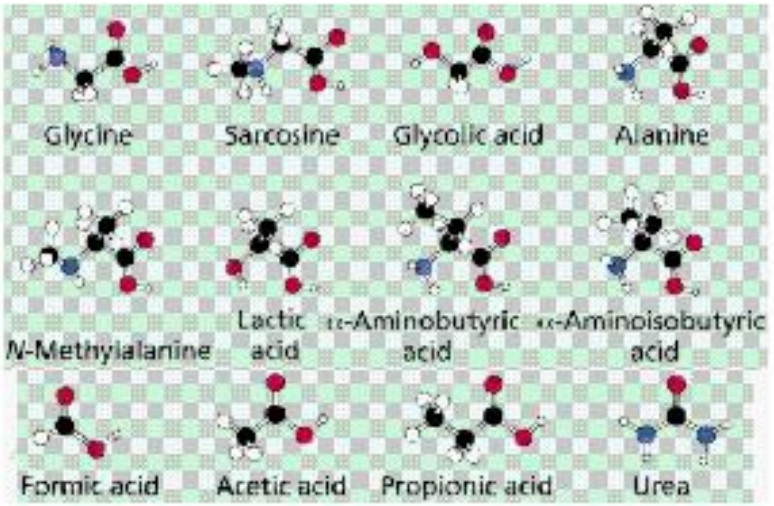


3) Origin of the Last Universal Common Ancestor (LUCA)

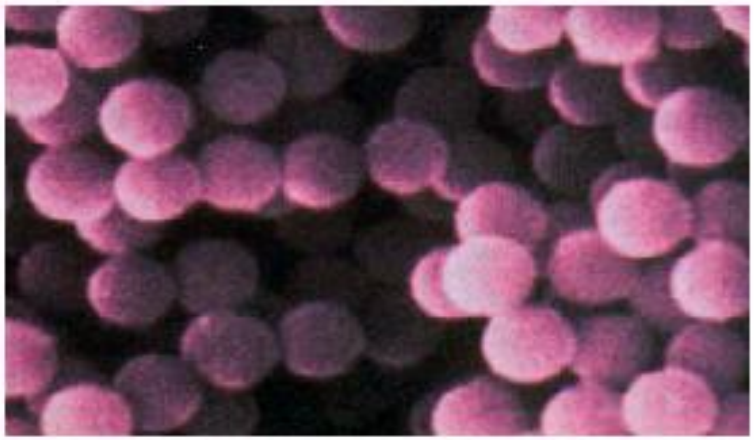
Much more difficult, requires detailed historical molecular-evolution scenarios



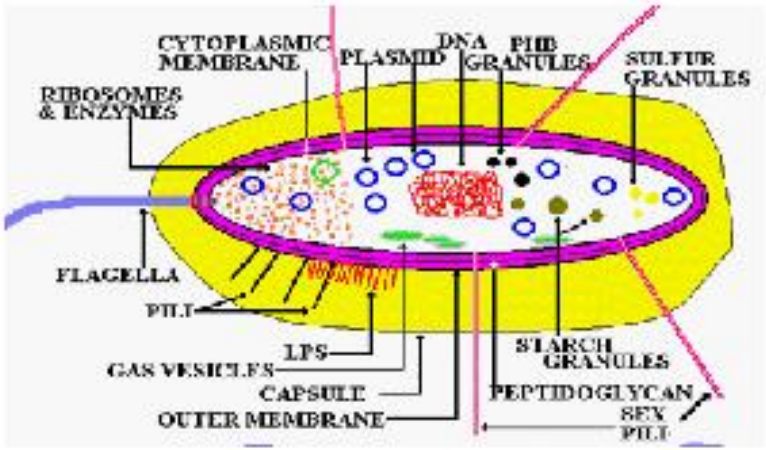
Organic compounds: form naturally by many different processes: UV, sparks, volcanoes, comets, meteorites



Protocell: must have rudimentary self-replication, free energy harvesting and capacity to evolve, but not necessarily RNA or proteins

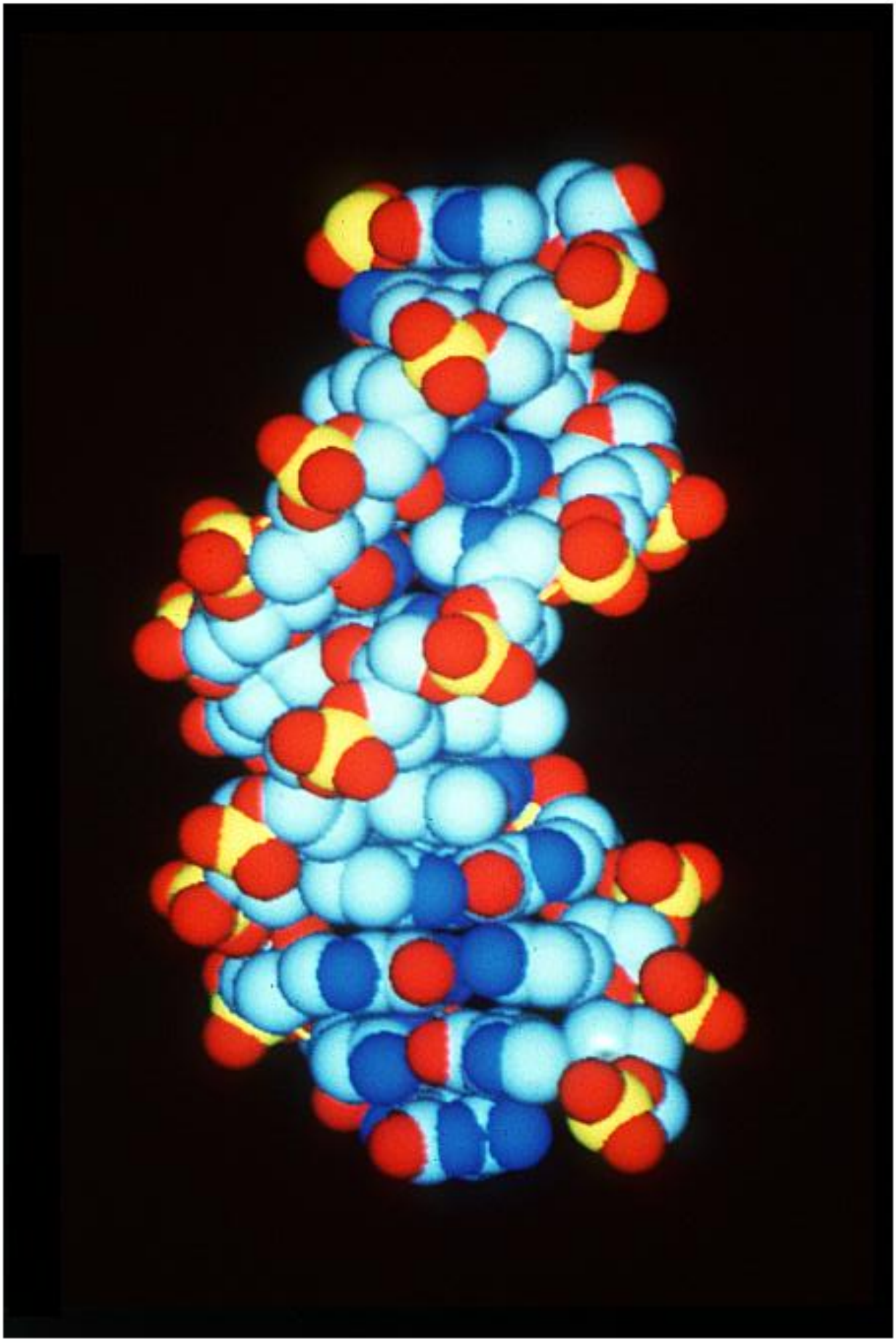


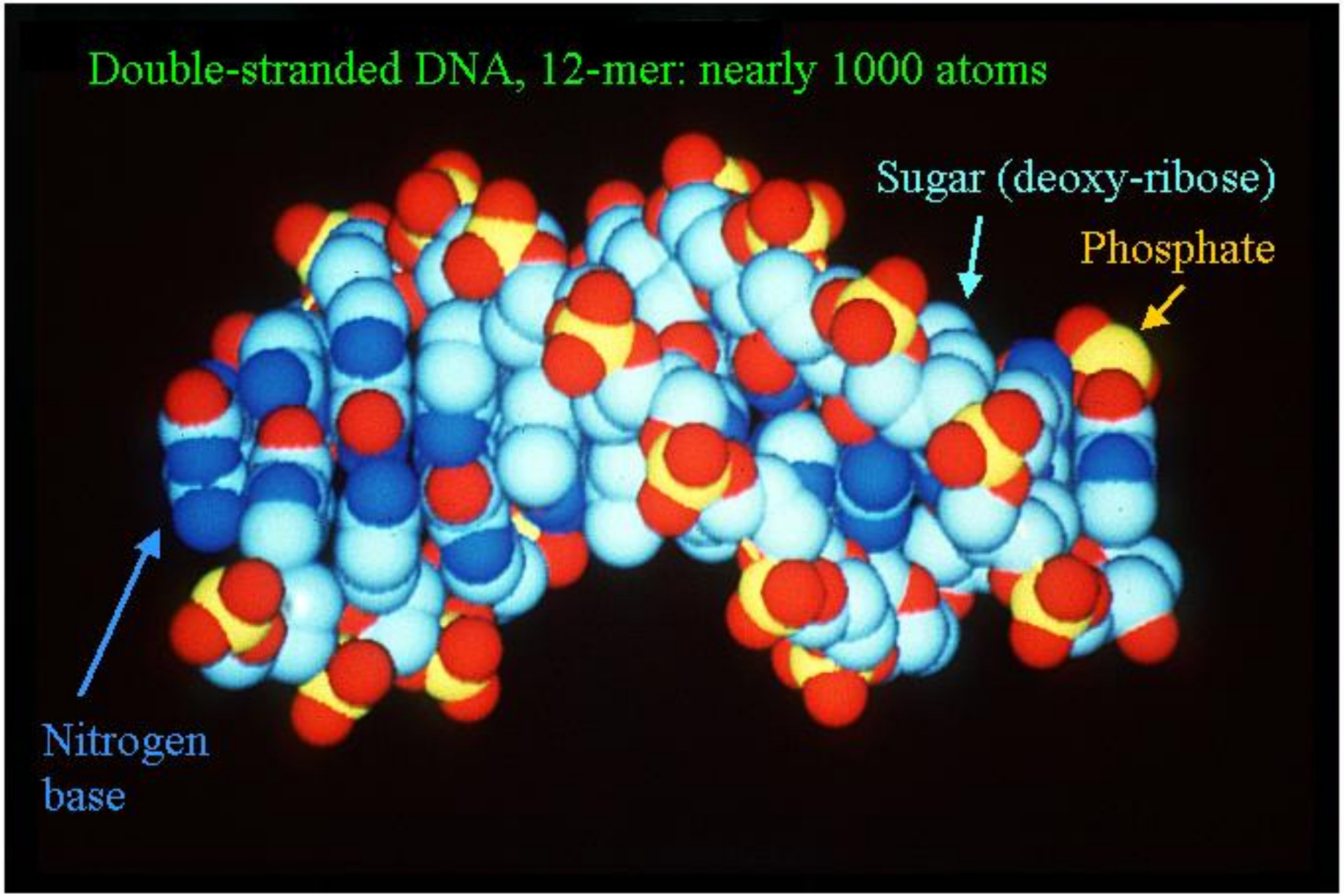
LUCA: has DNA, RNA, tRNA, ribosomes, proteins, membrane, elaborate metabolism, photosynthesis



[10] Dr. D. Lancet, Weizmann (ITP 4/24/01) Origin of Life without Biopolymers

What is that?

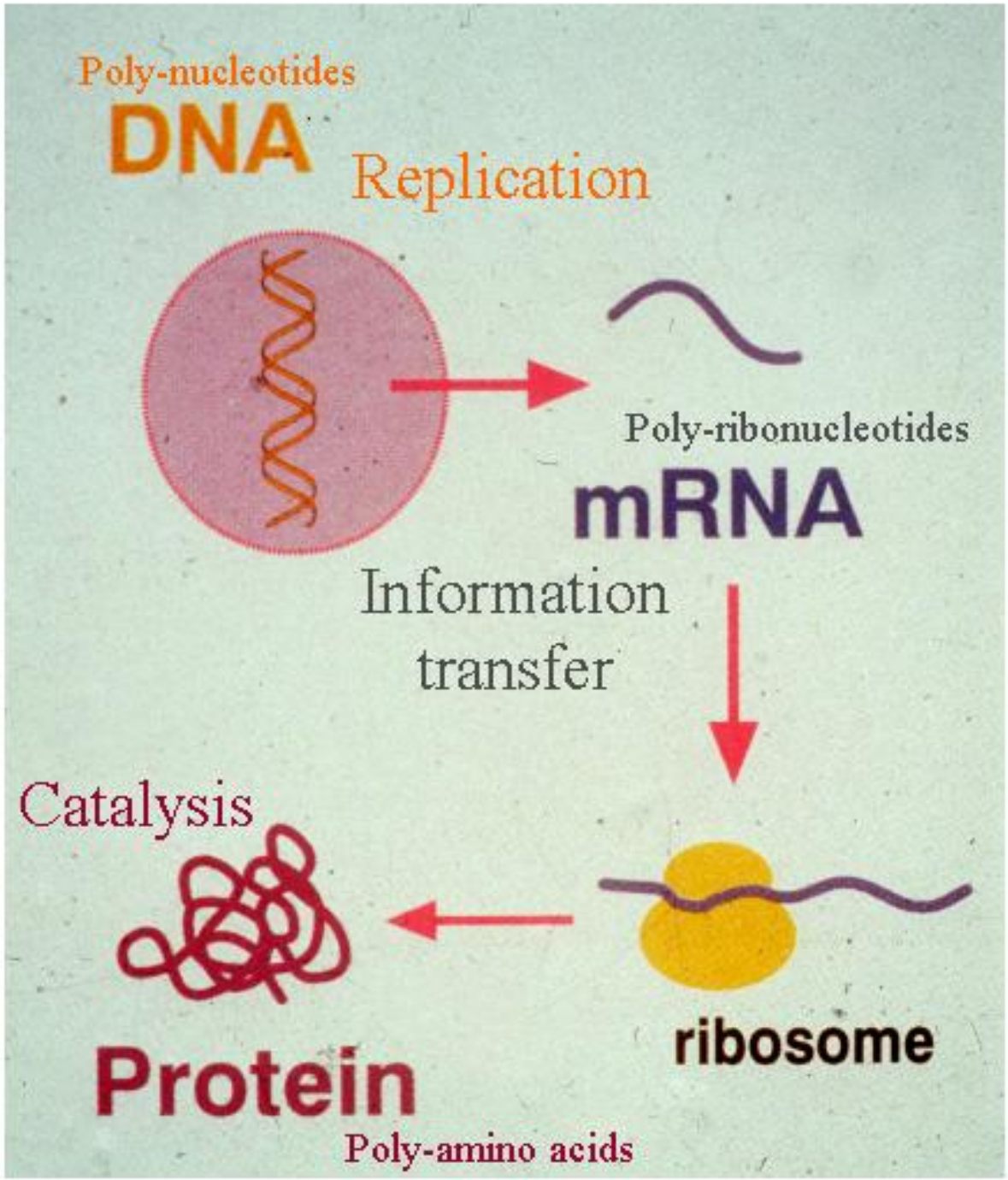




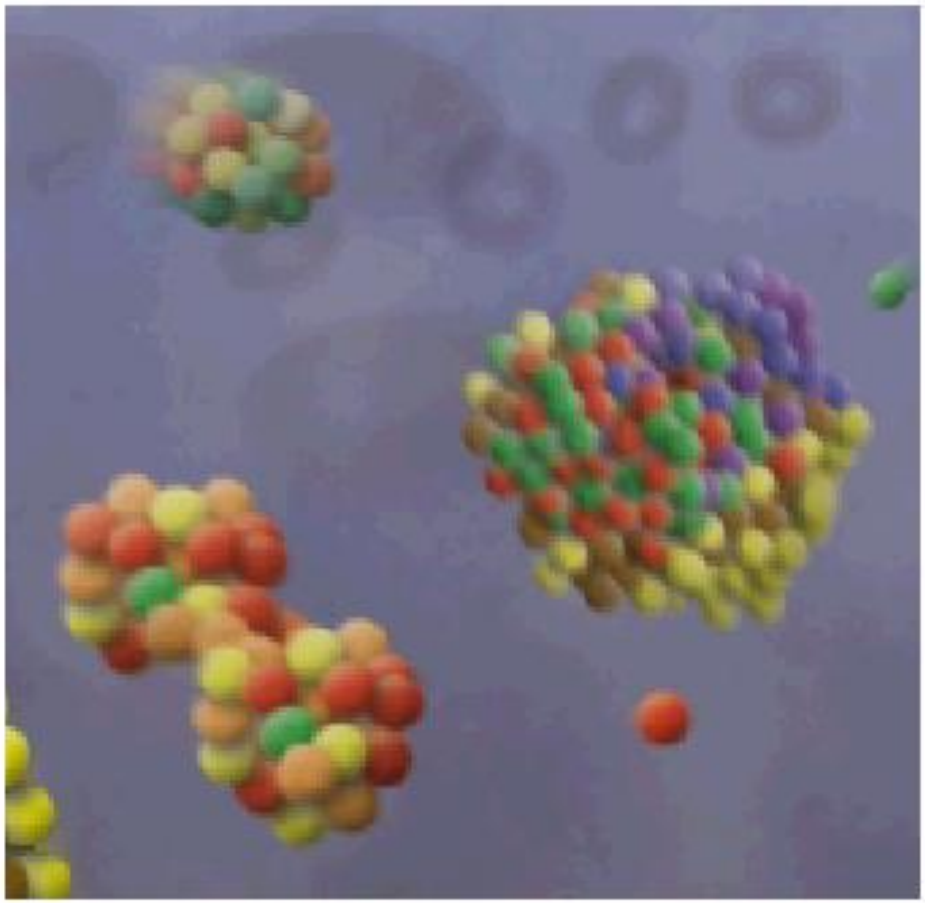
Polymers are too large, too complex. Need to focus on smaller molecules! ("monomers")

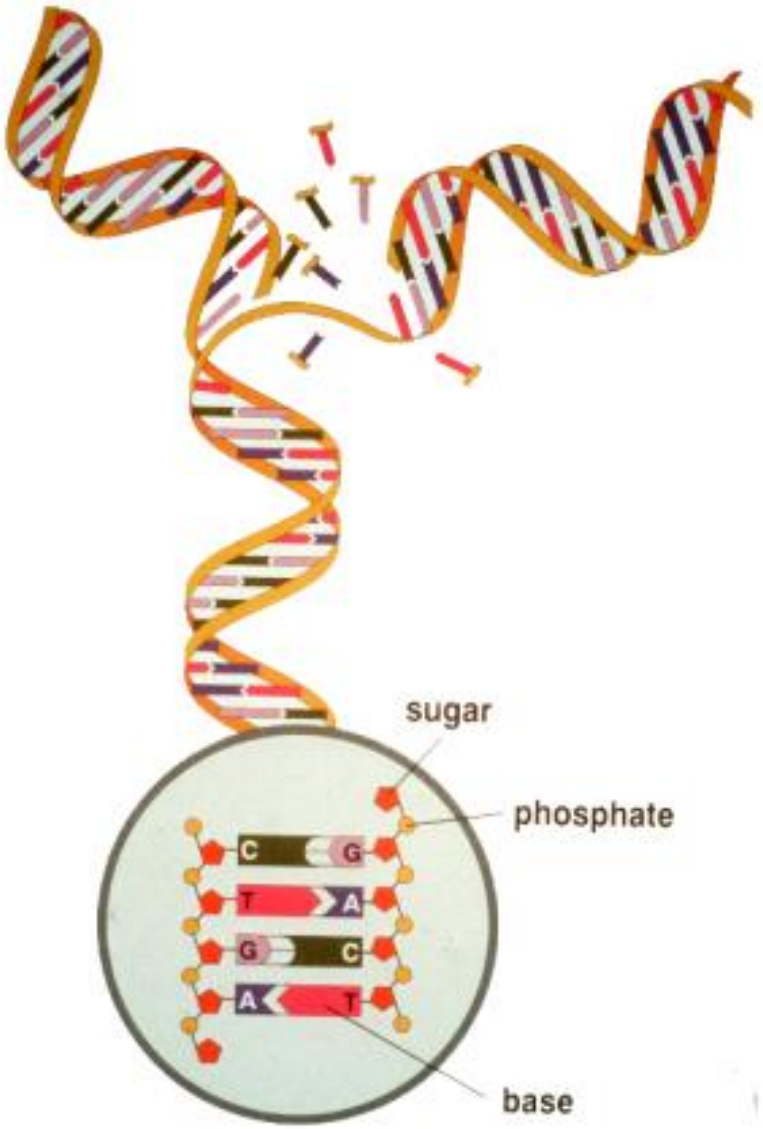
Present-day life is totally based on polymers.

But: did it start this way?

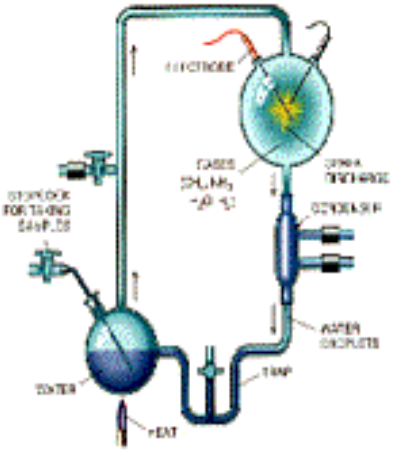


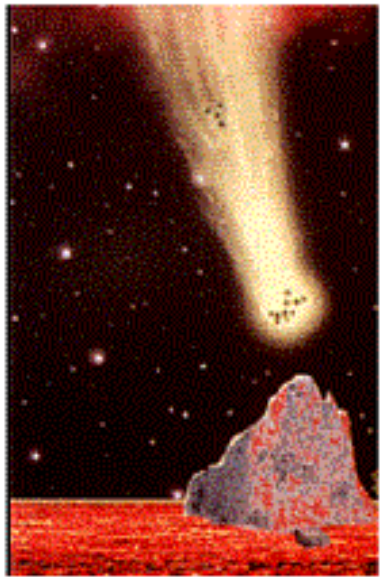
Non-covalent assemblies: the simple alternative.
But many questions need to be answered!





An alternative scenario: Origin of Life without polymers





A plethora of small organic compounds

↓ Spontaneous accretion

Non-covalent assemblies

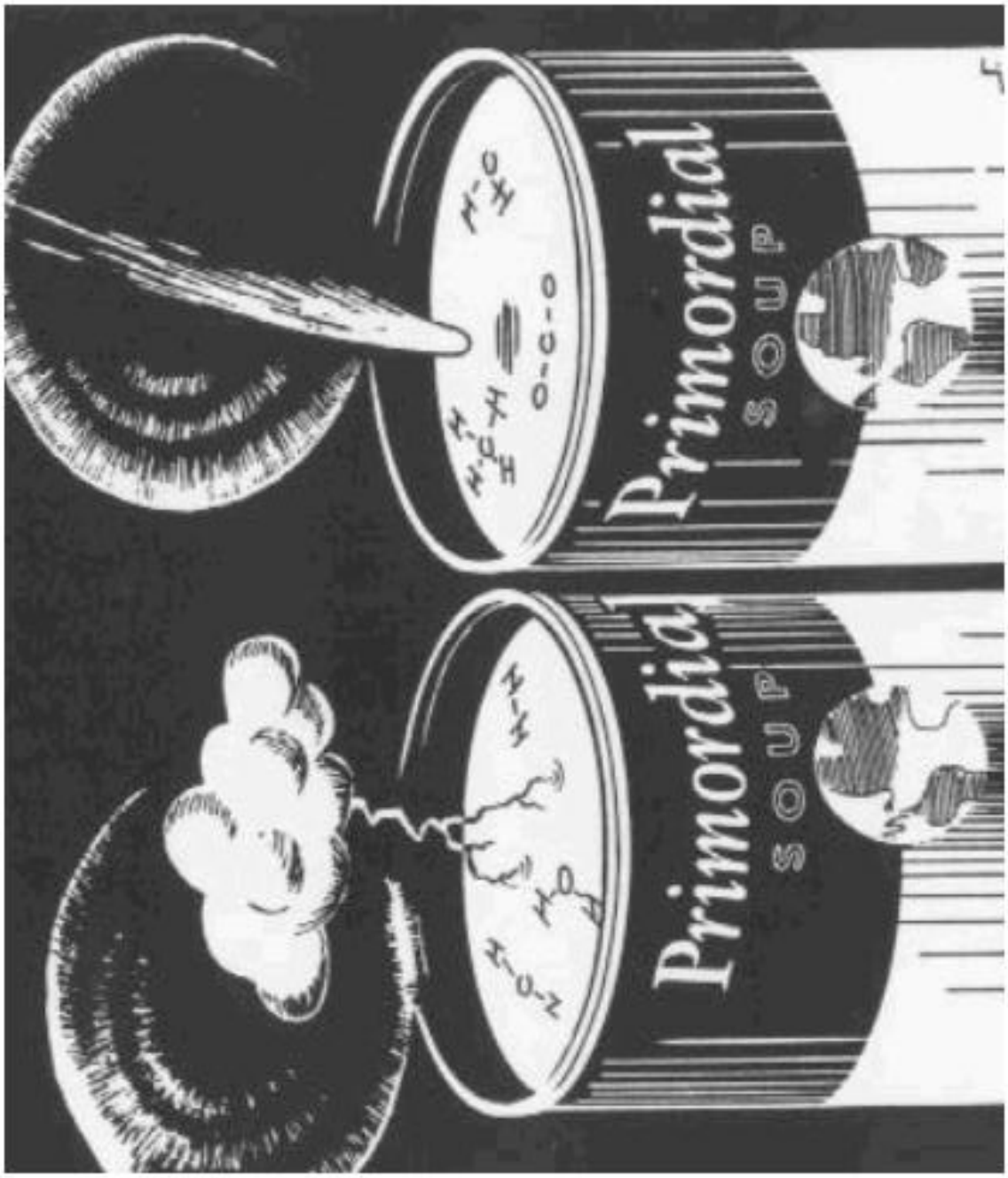
↓ Catalytic networks

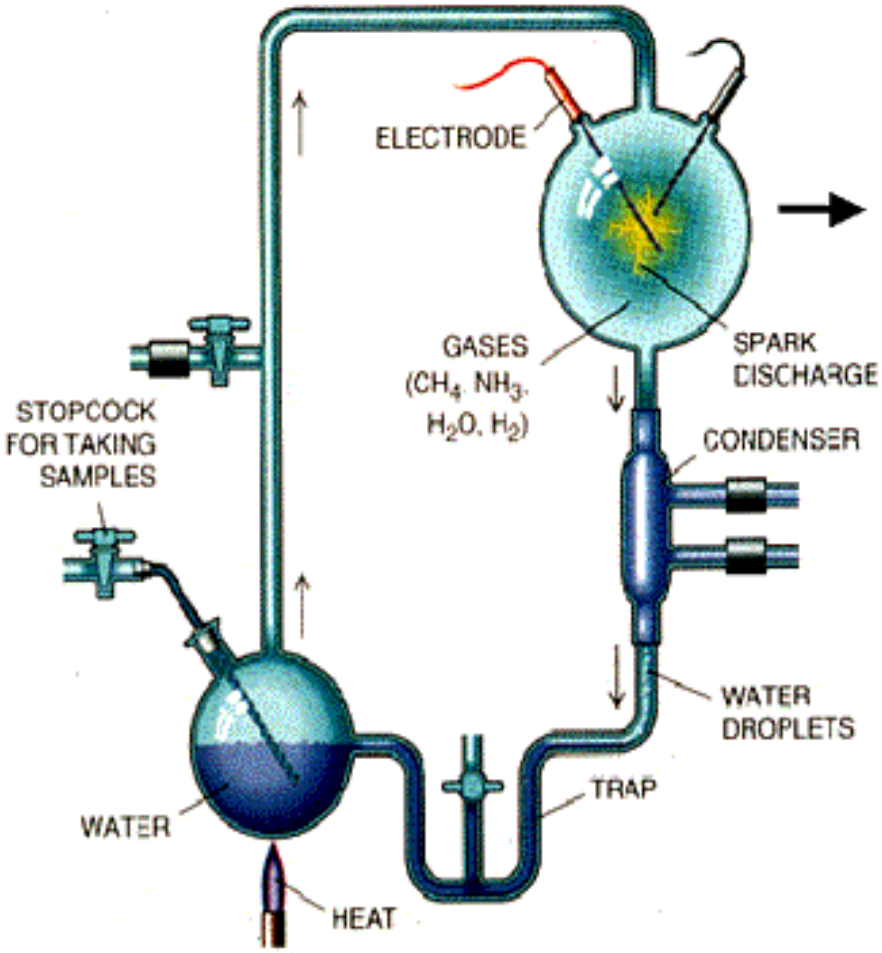
Protocells

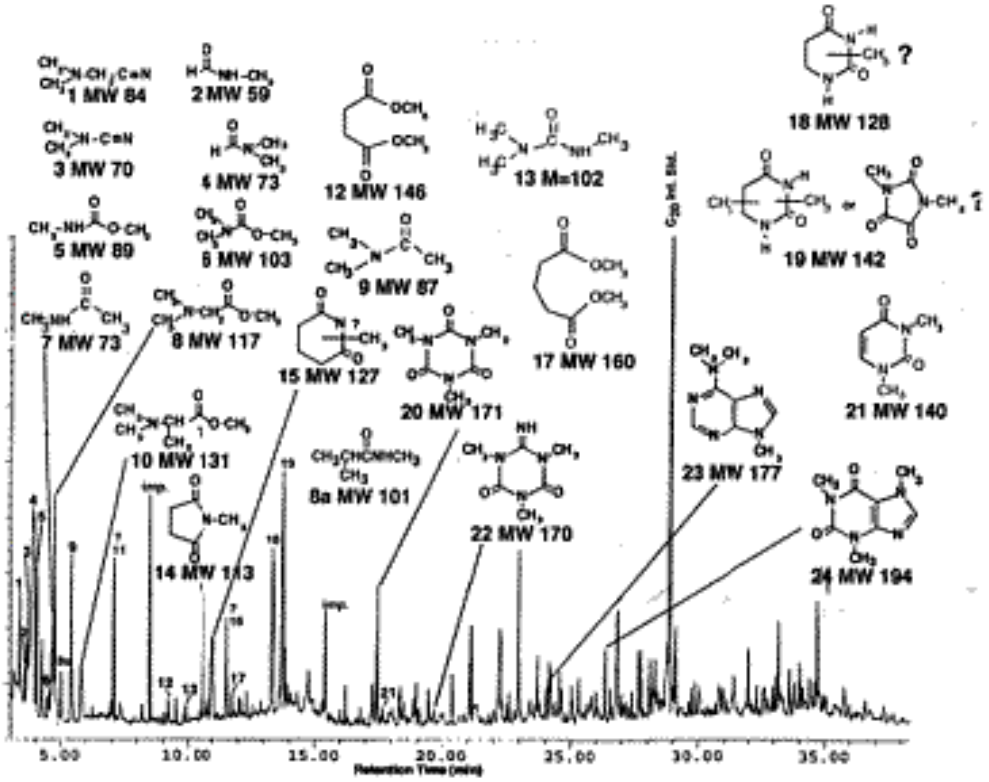
↓ Cellular evolution

LUCA, including biopolymers

The origin of life: a planet-scale random chemistry experiment







Two different questions:

1) Are compounds of life as we know it present in the mixture?

1) What is actually formed and how to get from such a mixture to the narrower assortment of present life forms?

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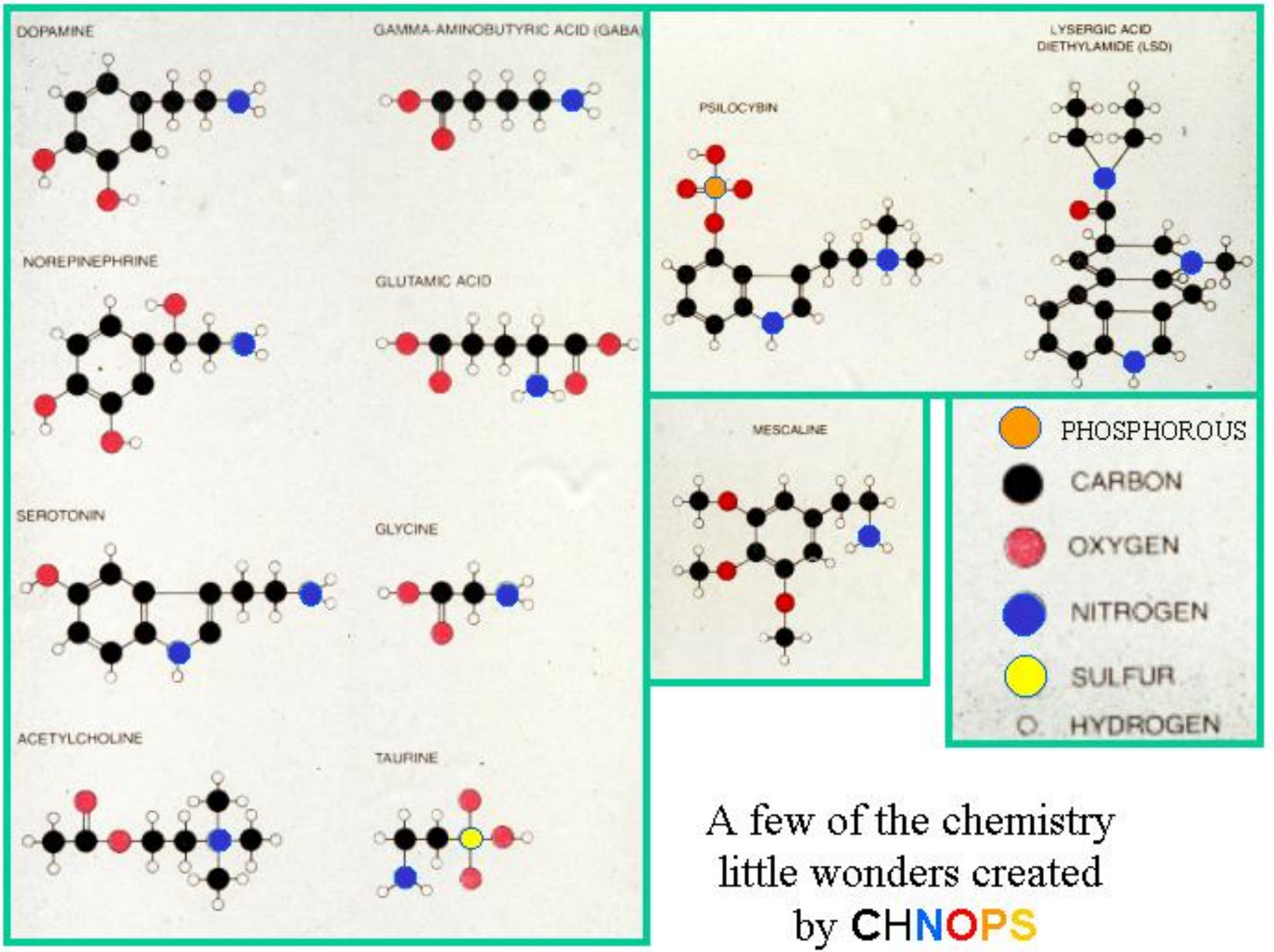
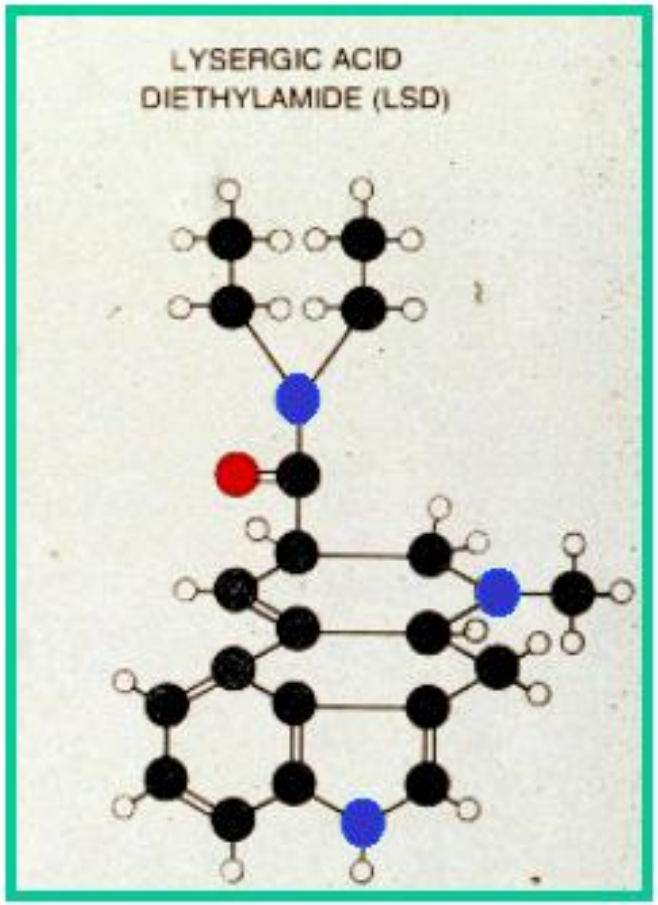
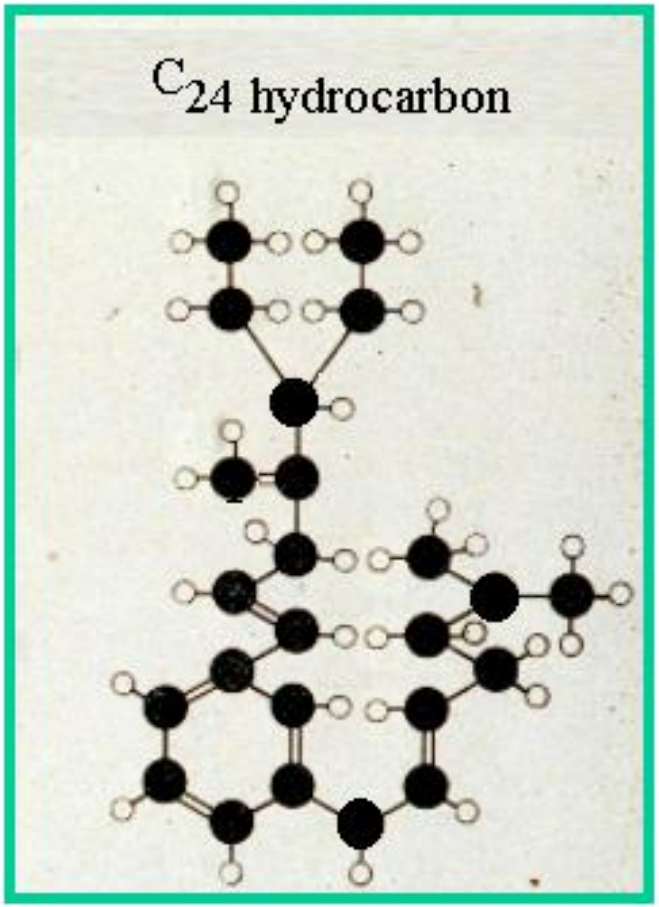


24 non-hydrogen atoms



24 carbon atoms



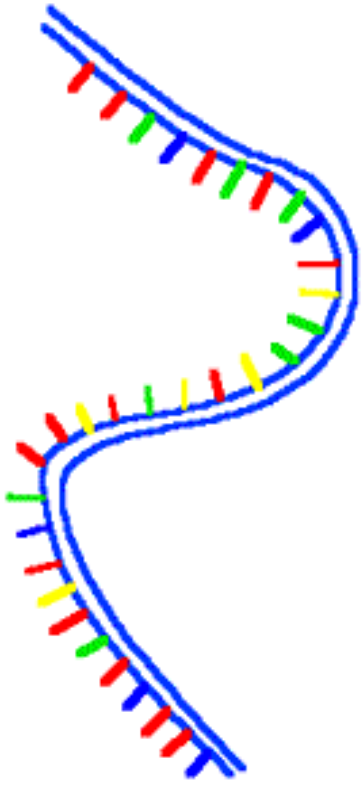
This has about 10,000,000 isomers!

In general, A C_n Compound has ~$0.01e^n$ isomers

With heteroatoms - at least 10^9 isomers

If let loose, **CHNOPS** can generate billions of compounds!

Which substances played the planet-scale random chemistry?



Lipid World:

Easy monomers

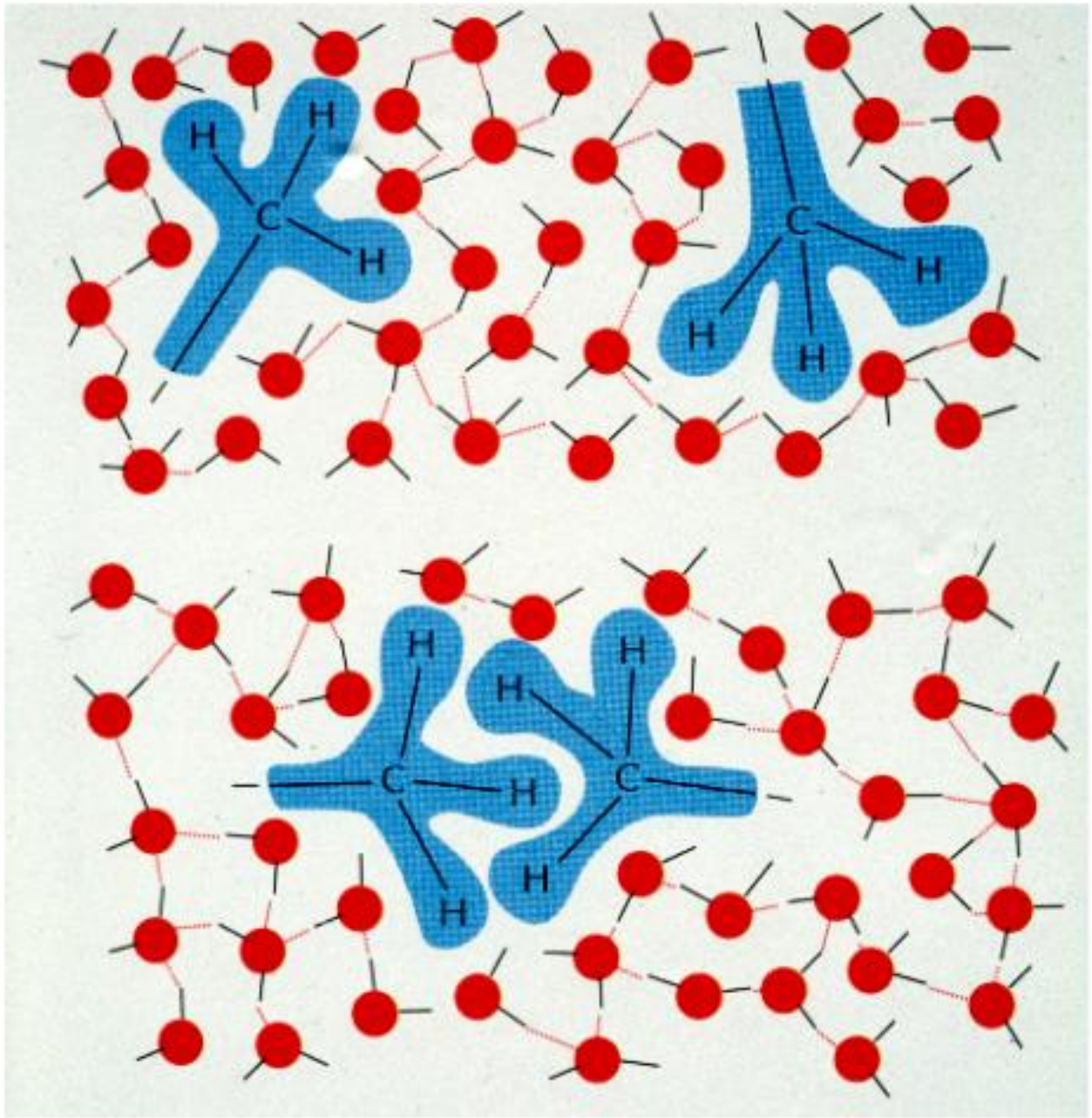
Easy non-covalent "polymers"

RNA World:

Rare monomers

Difficult covalent polymerization

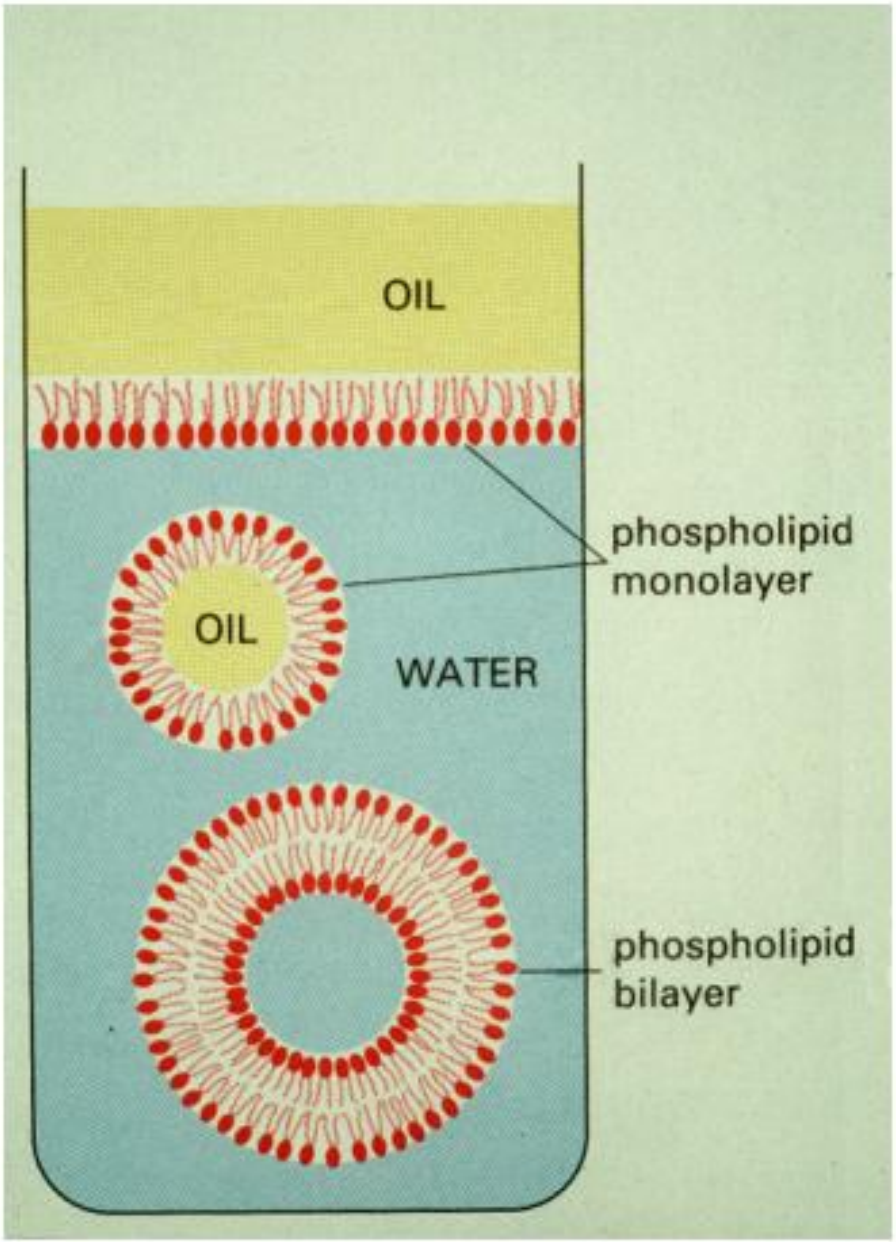
HYDROPHOBIC FORCES



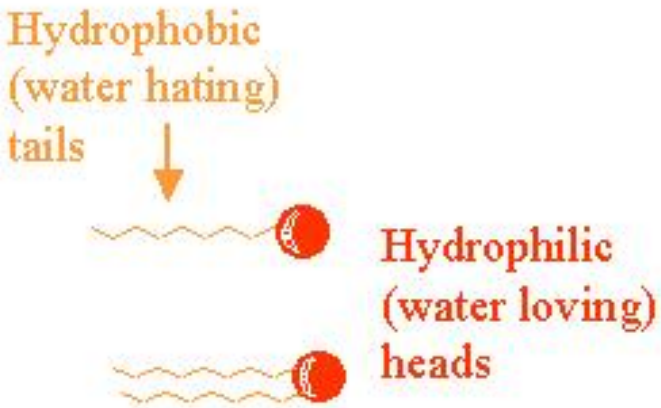
These interactions is driven by the increased entropy, due to disordering of water molecules, as they get released from the interface between two "oily" molecules

Micelle

Vesicle



Amphiphilic Molecules
(e.g. phospholipids)



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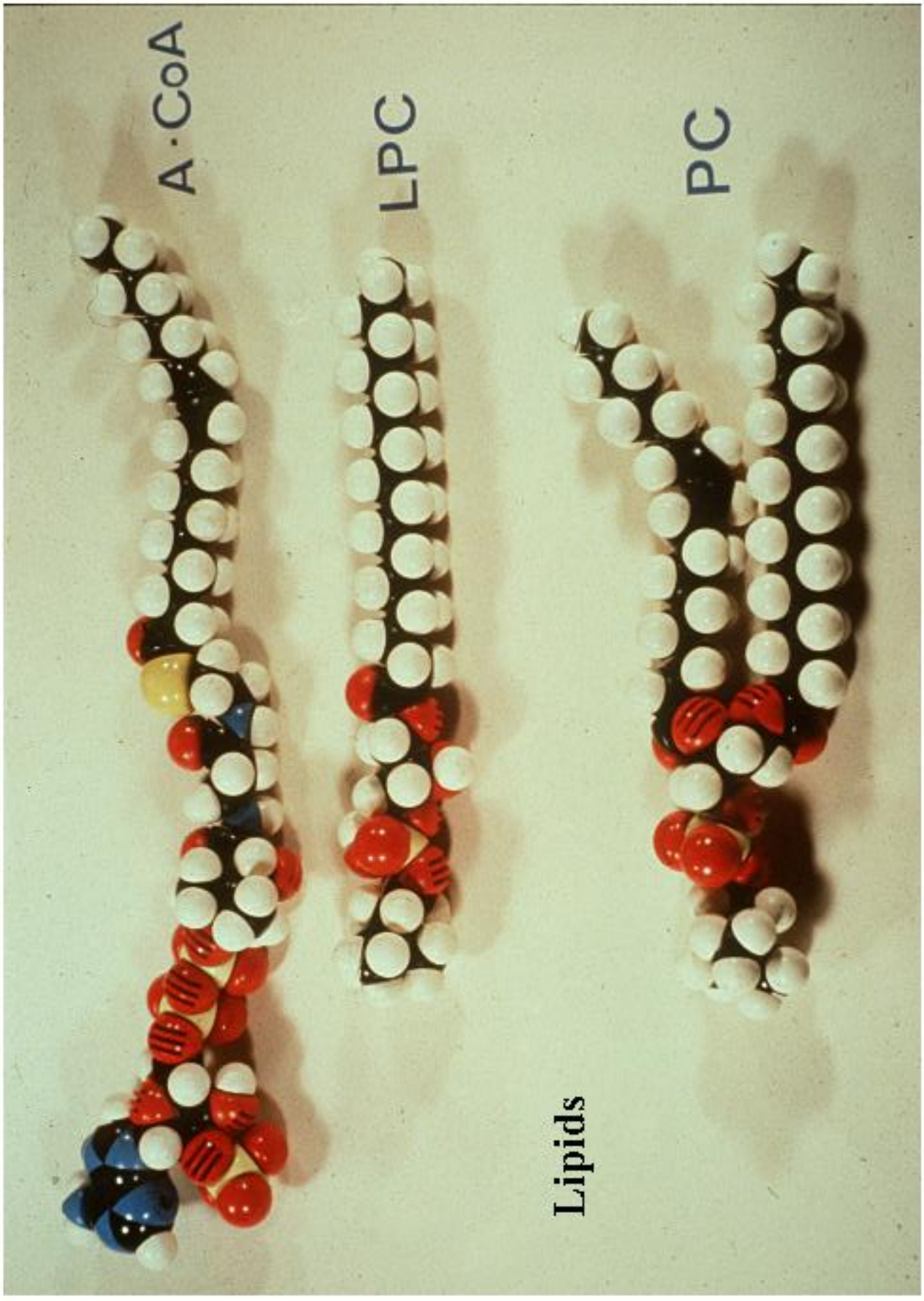
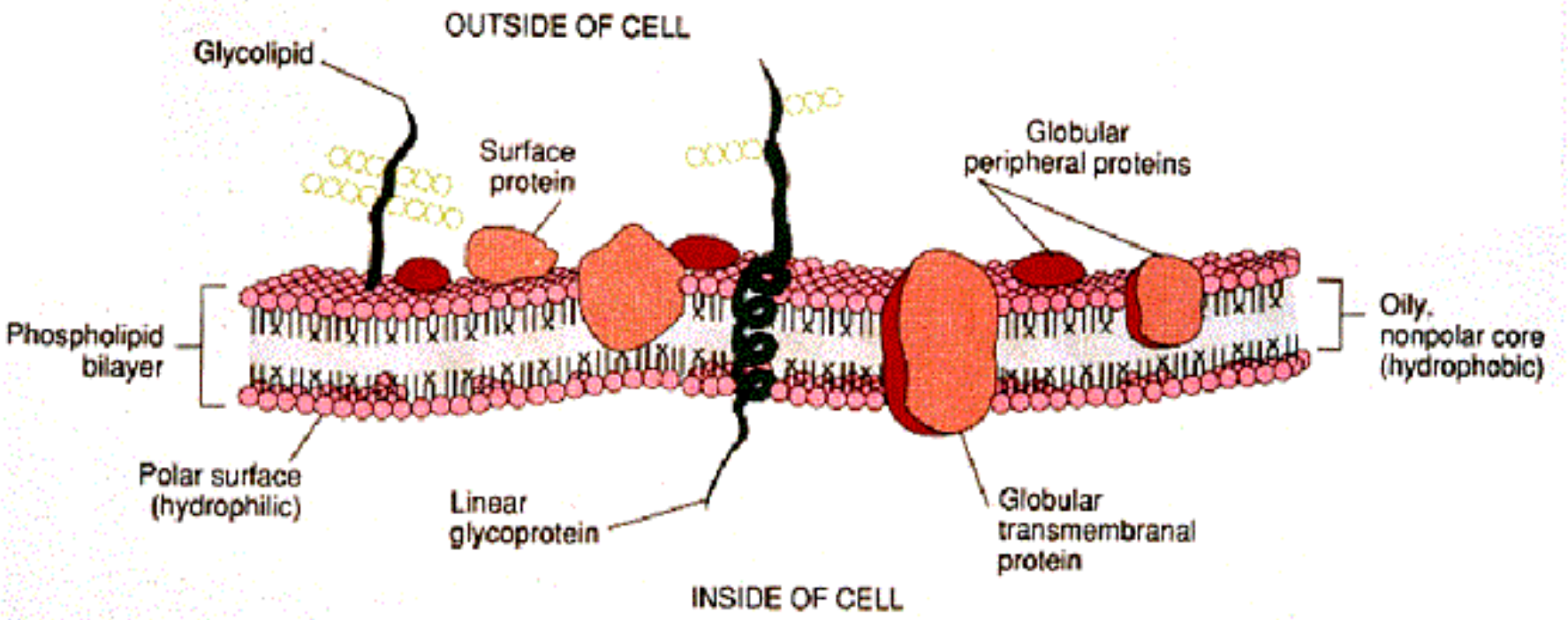
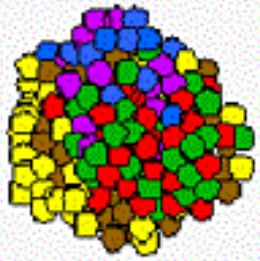


Present-day membranes are bustling places, where most of the business is carried out by proteins within or near the lipid bilayer



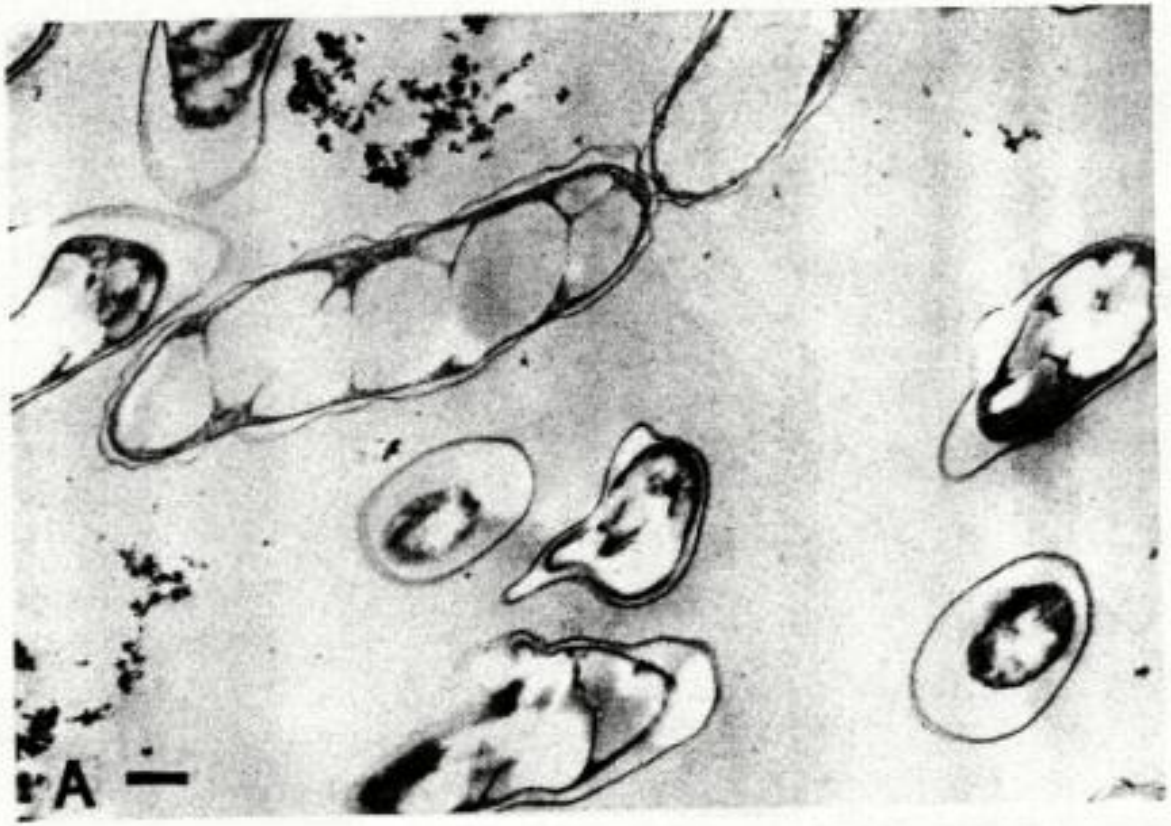
But could it have begun like this?



A complex aggregate of lipid-like molecules with diverse chemical groupings

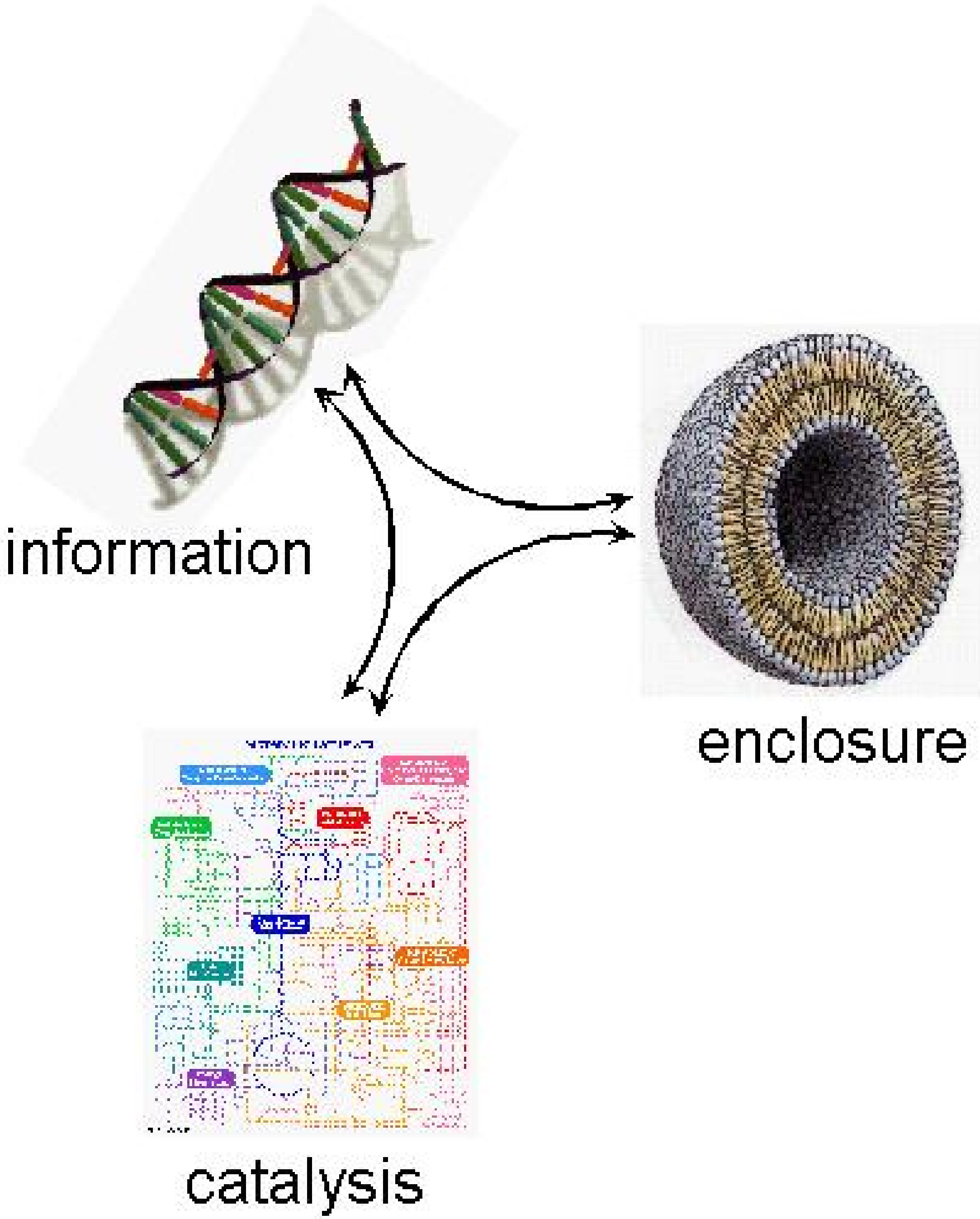
Lipids are abiotically available

AMPHIPHILIC COMPONENTS OF THE MURCHISON CARBONACEOUS CHONDRITE: SURFACE PROPERTIES AND MEMBRANE FORMATION



D. W. DEAMER R. M. PASHLEY

Origins of Life & Evolution of the Biosphere, Volume 19 (1989), pp. 21-38.



Primordially, lipids could do much more than they do in present-day cells

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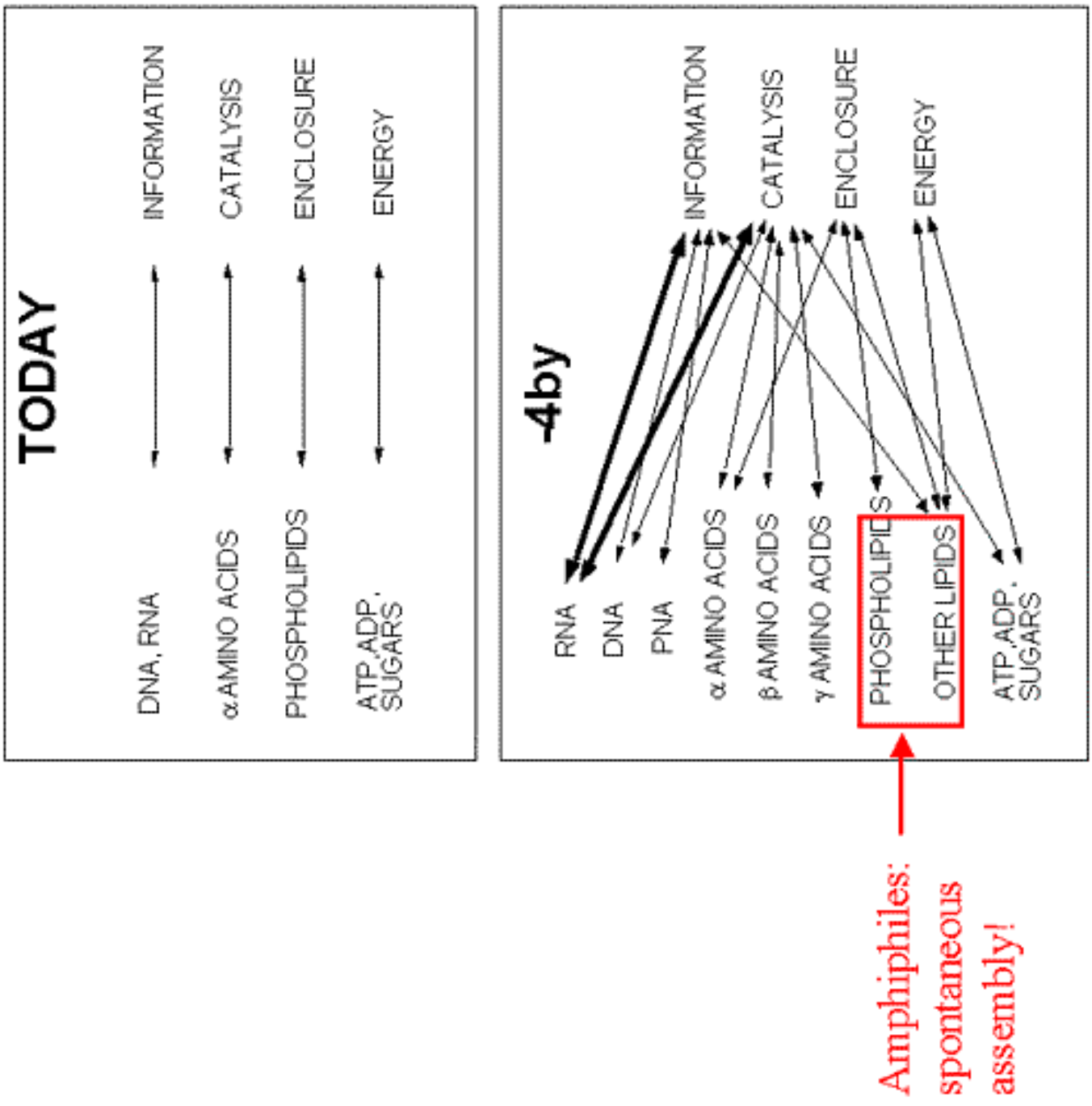
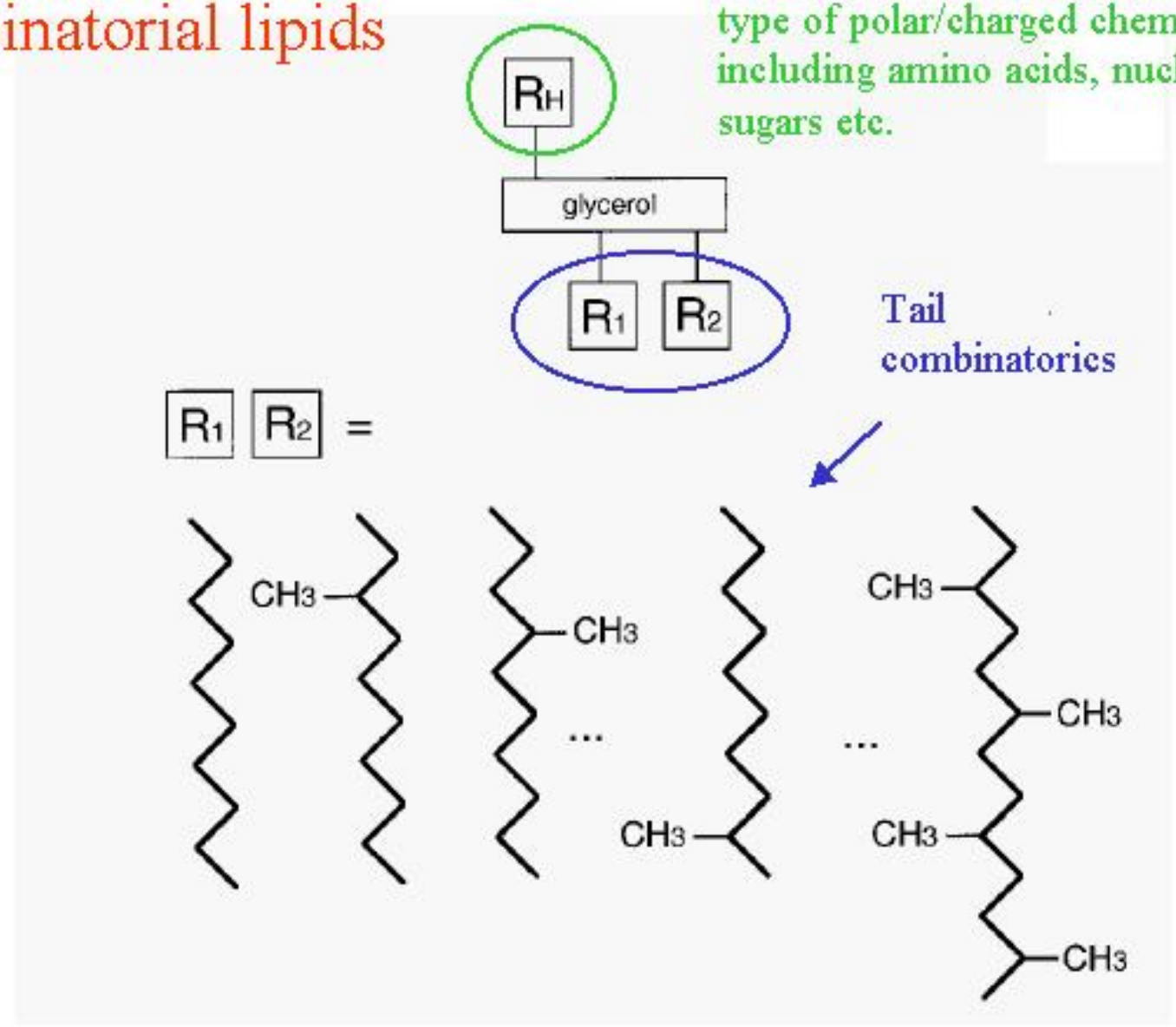
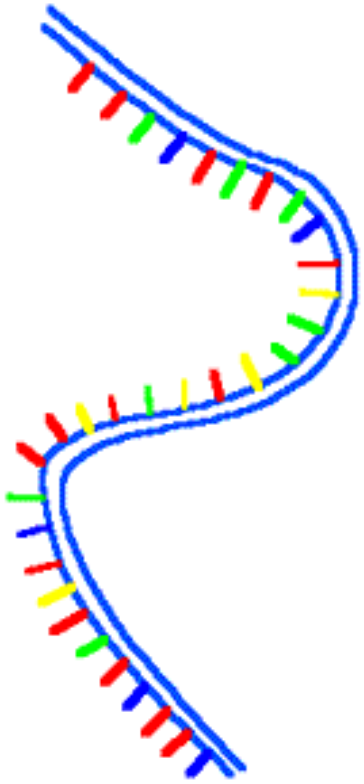


Combinatorial lipids



Where does information reside?



Lipid World:
Compositional diversity!
(A novel concept)

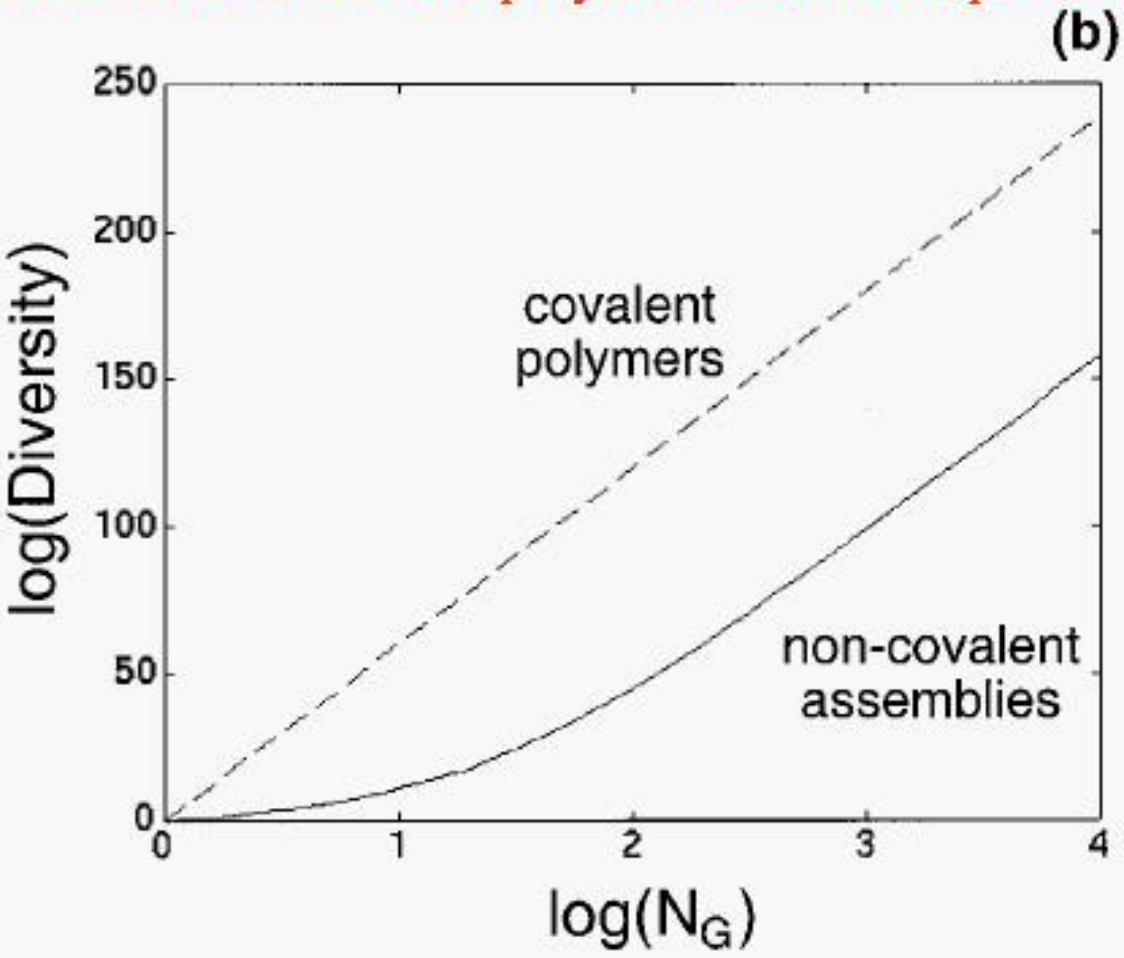
RNA World:
Sequence diversity

Both diversity (D) functions have the same limiting slope

Diversity is the number of different polymers/assemblies possible

N = number of monomers in a sequence or in an assembly

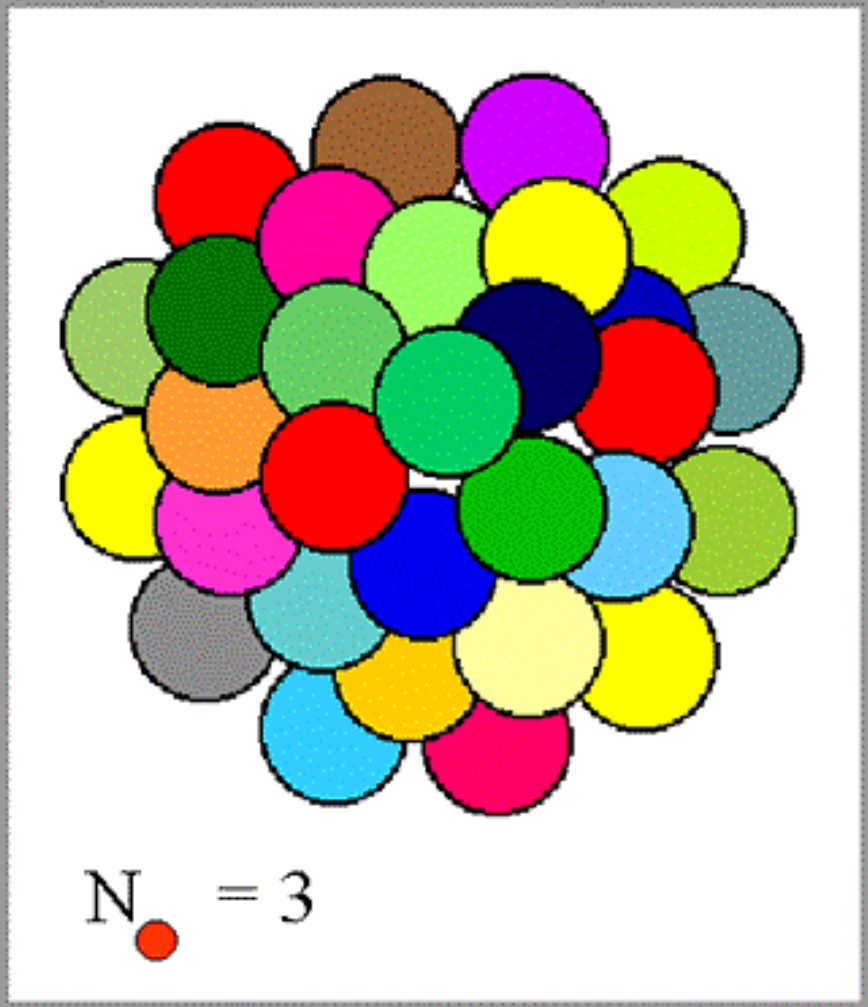
N_G = number of different types of monomers that exist



Polymers: $D = (N_G)^N$

Assemblies: $D = (N_G+N-1)!/(N!(N_G-1)!)$

Non-covalent assemblies have compositional information



n_i is the number of molecules of type i in the assembly

The vector **n** defines the Assembly's composition

The scalar product
$H = \mathbf{n'} \bullet \mathbf{n''}$
is the distance between compositions

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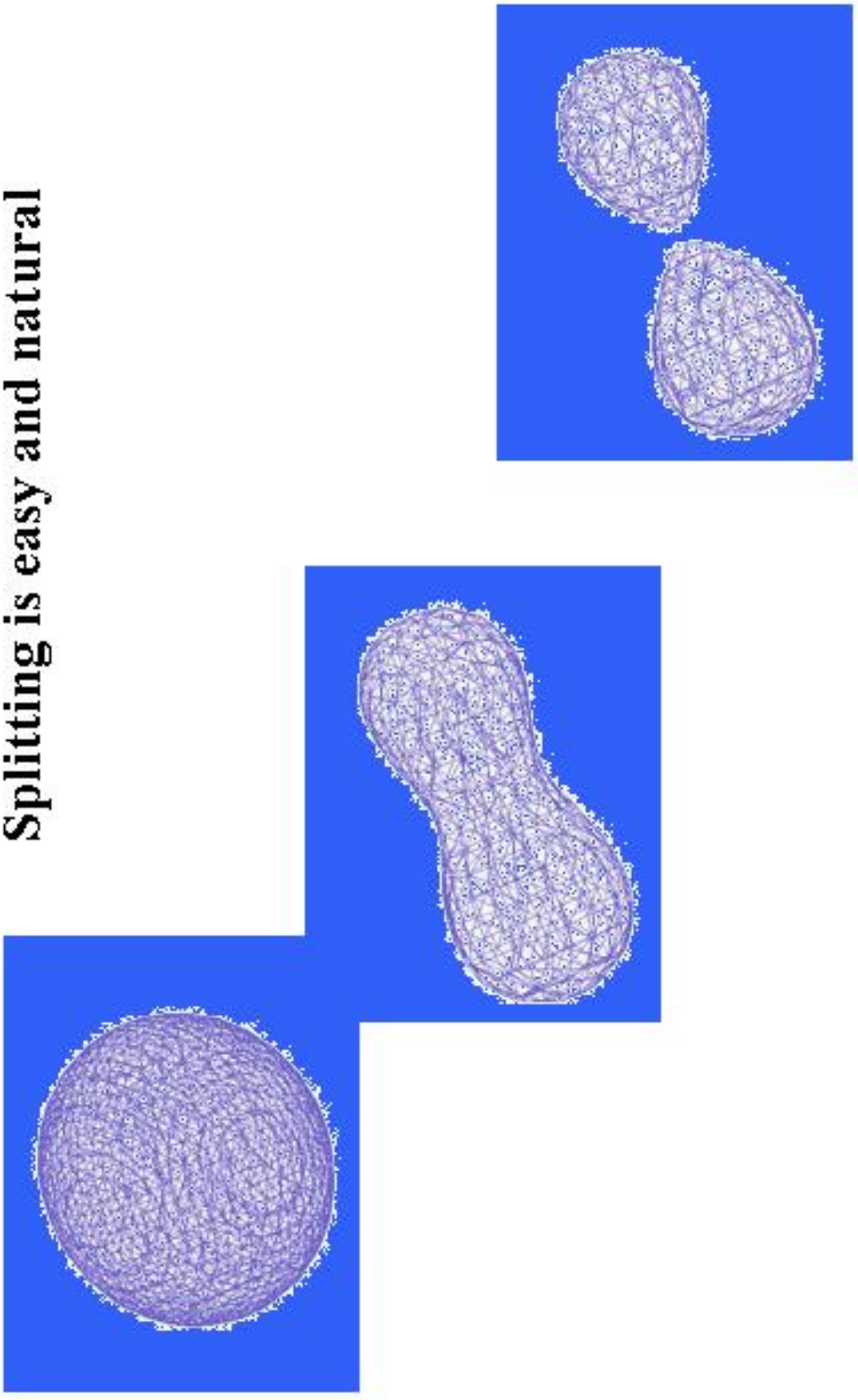
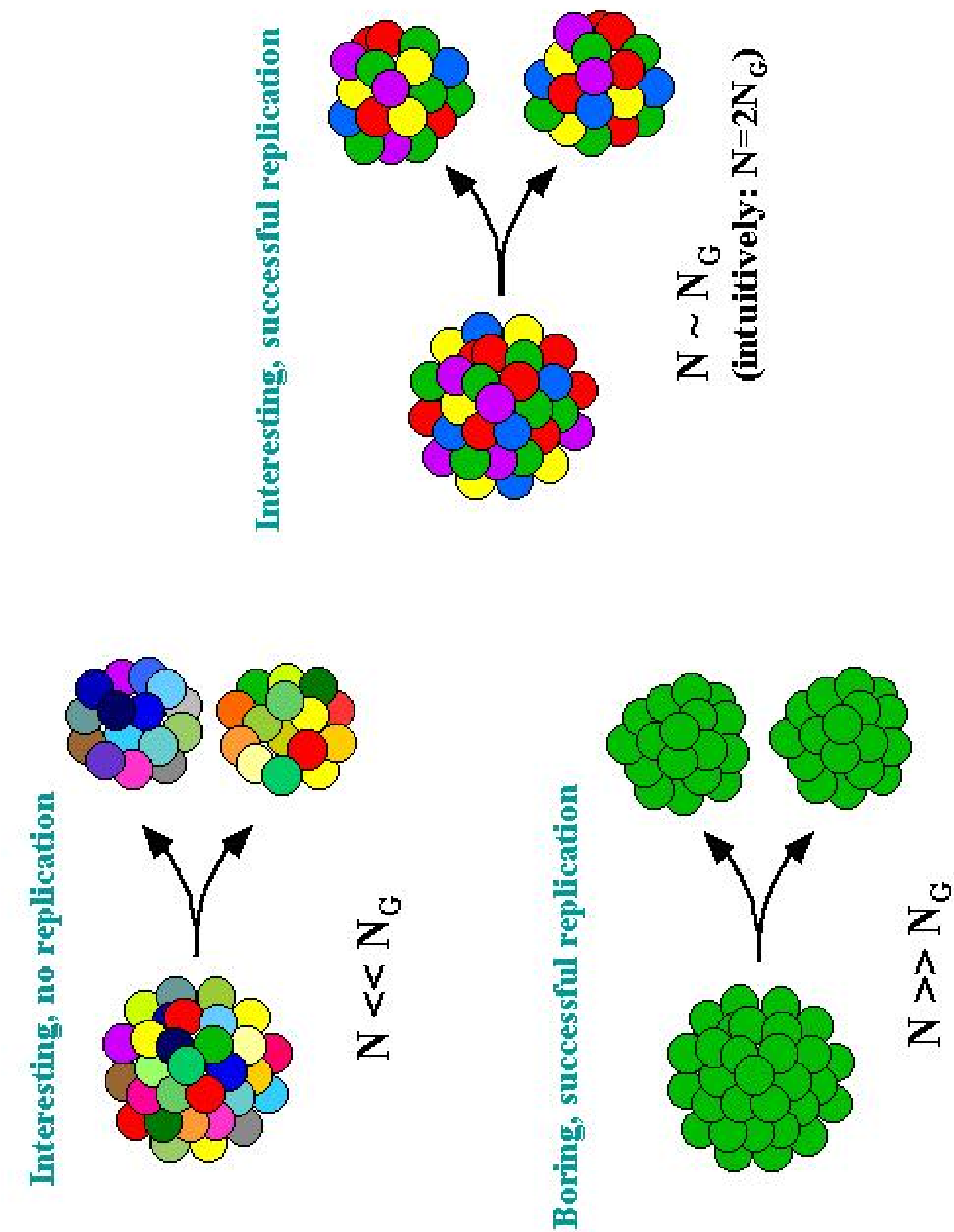
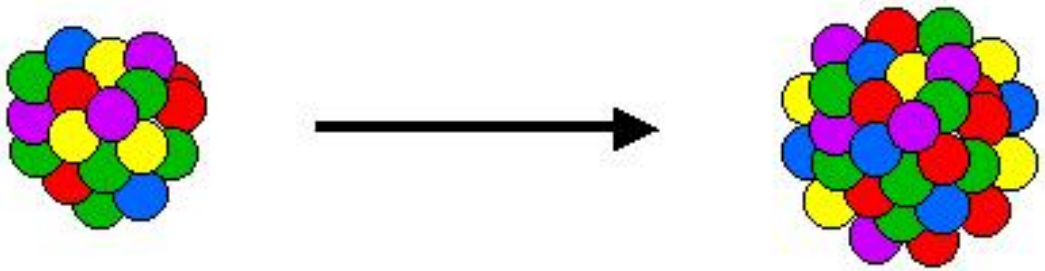
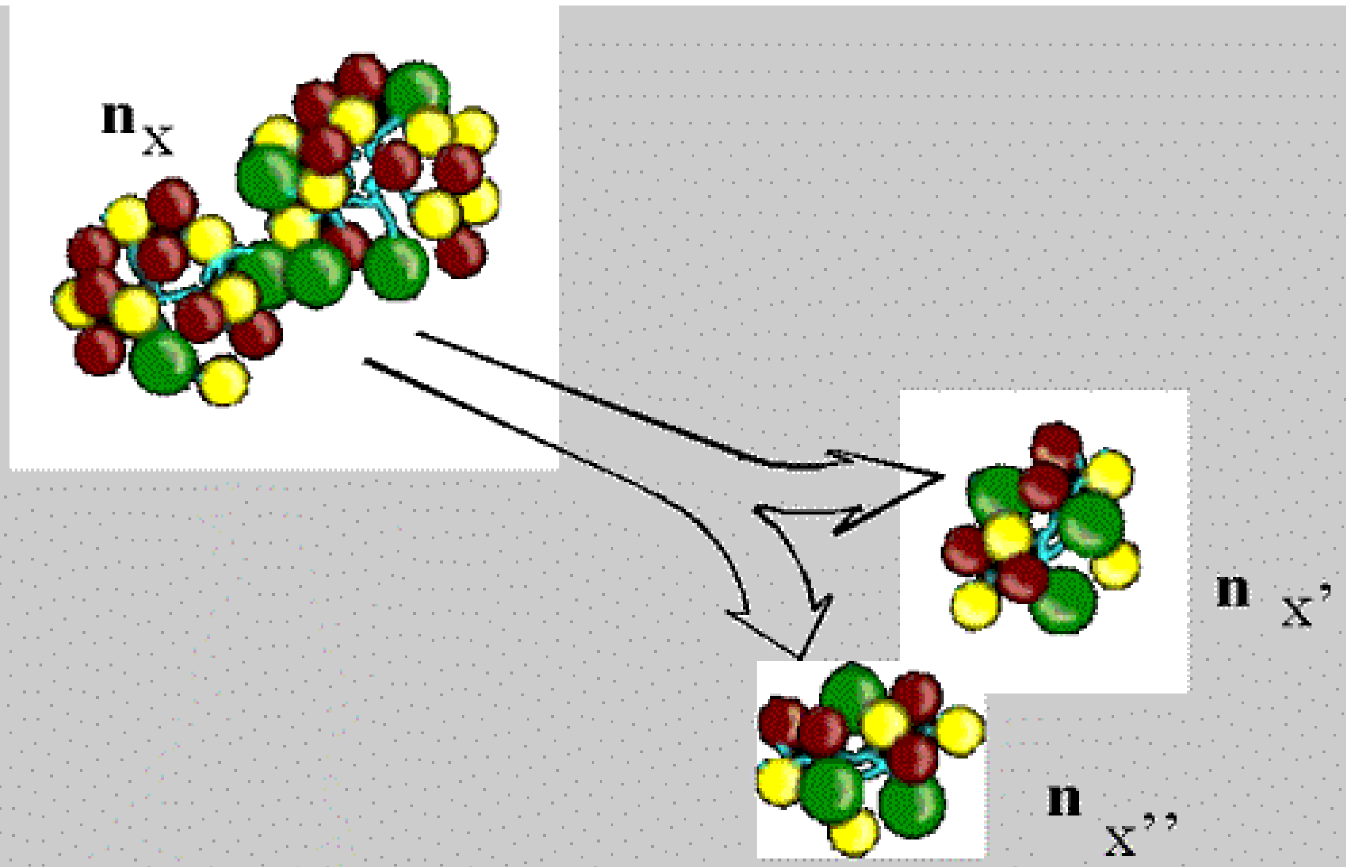



Interesting, successful replication
N ~ N_G
(intuitively: N=2N_G)
Interesting, no replication
N < N_G
Boring, successful replication
N >> N_G

How to achieve replication capacity?
By homeostatic growth! (time-invariable concentrations)



This may be mediated by mutually catalytic networks!
(see Freeman Dyson, Stuart Kauffman)



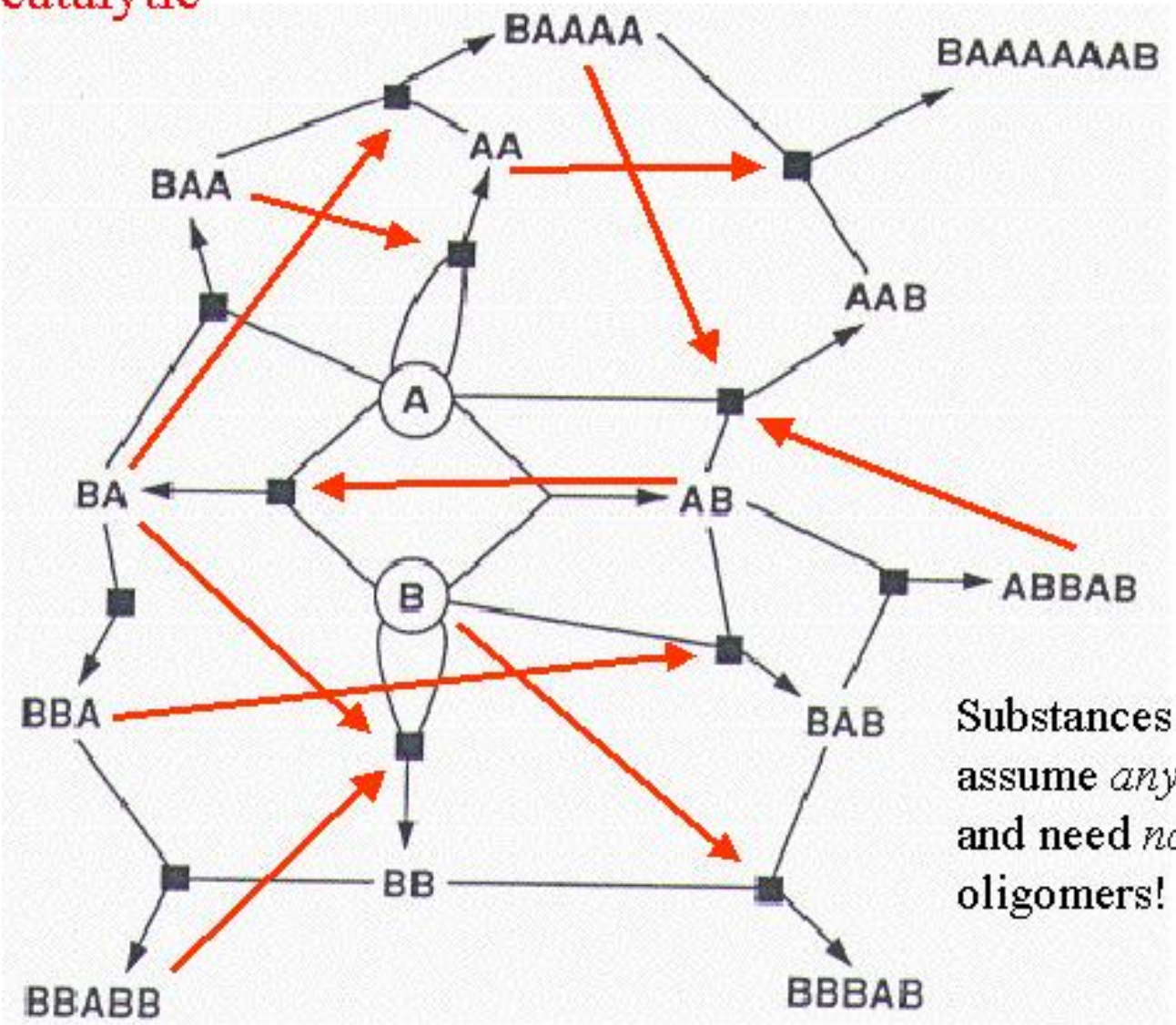
Requirements for successful replication:

1) Efficient catalytzed growth

2) Homeostatic preservation of composition

3) High inheritance fidelity upon splitting $n_X \sim n_{X'} \sim n_{X''}$

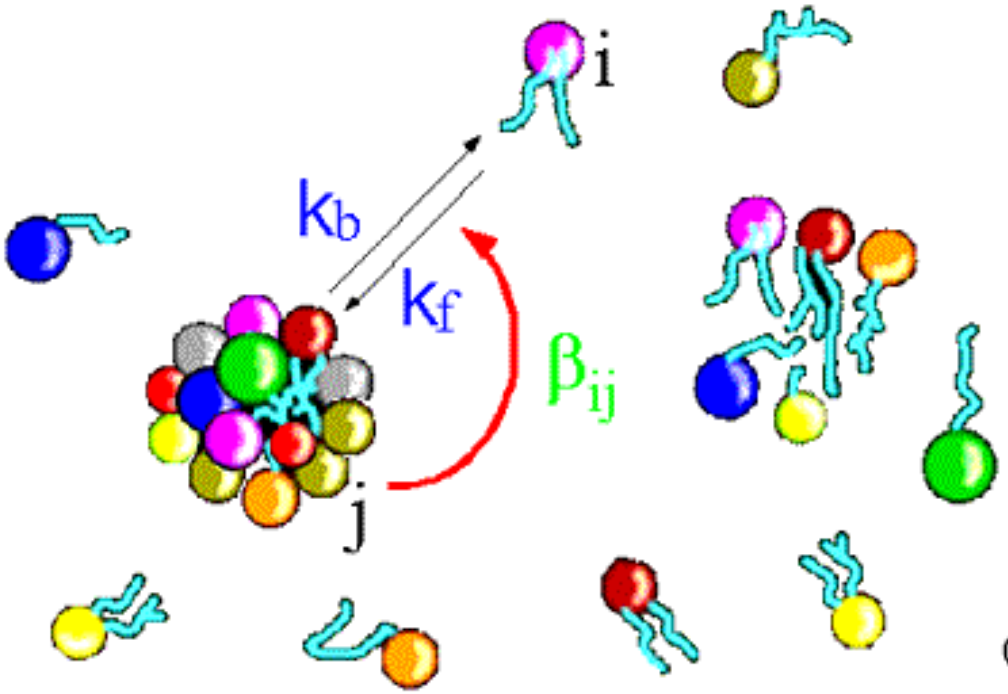
Kauffman/Dyson:
Mutually catalytic networks



Substances can assume *any* chemistry and need *not* be oligomers!

GARD: the Graded Autocatalysis Replication Domain model

(Segre, Ben-Eli and Lancet, PNAS 2000)



Spontaneous down hill assembly

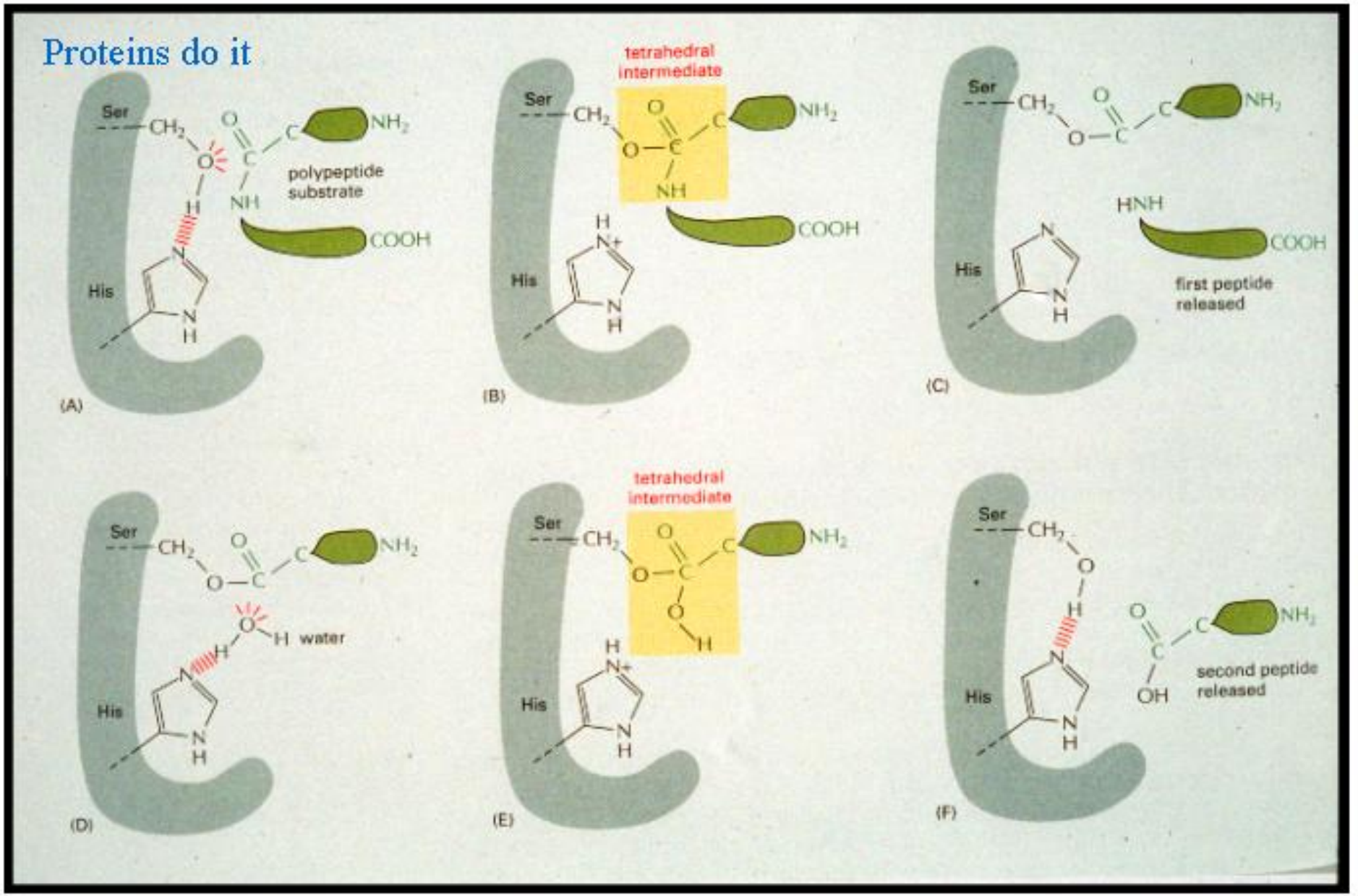
Growth by catalyzed joining or in-situ synthesis

Mutual catalysis defined by a beta matrix

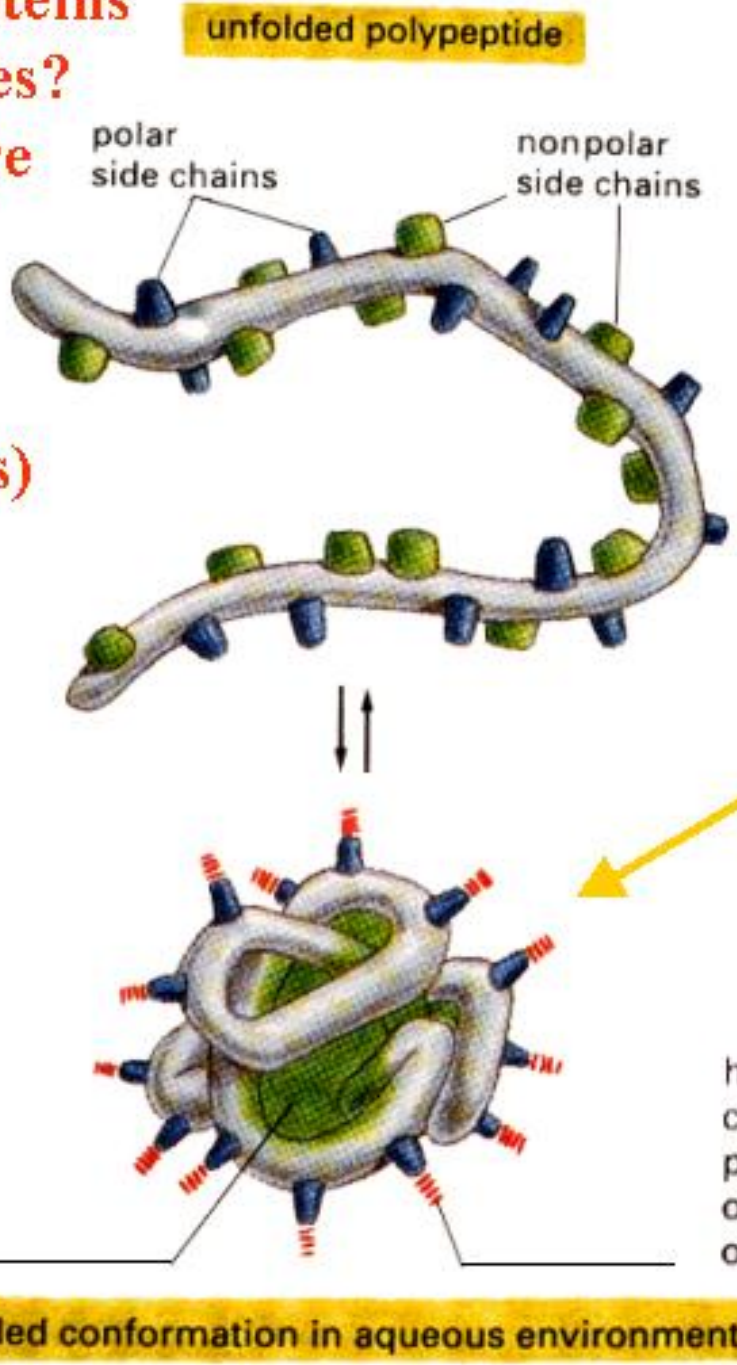
Complete heterotrophy (opposite of autotrophy)

But, are lipids catalytic at all?

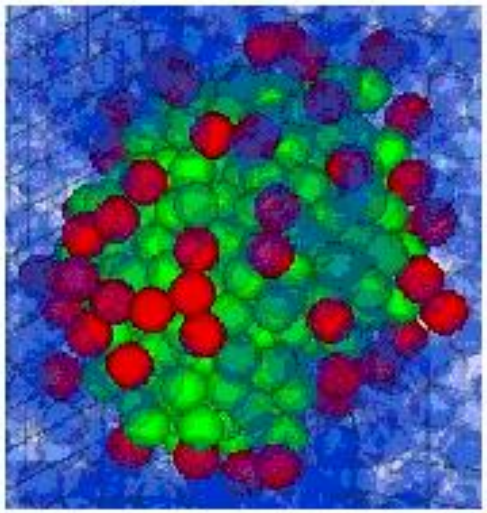
Enzyme catalysis = right chemical groupings in a correct, rigid orientation.
This allows concerted chemical action that lowers the activation energy



But are proteins the only ones? no, there are enzyme-mimetics (e.g. cage Compounds)

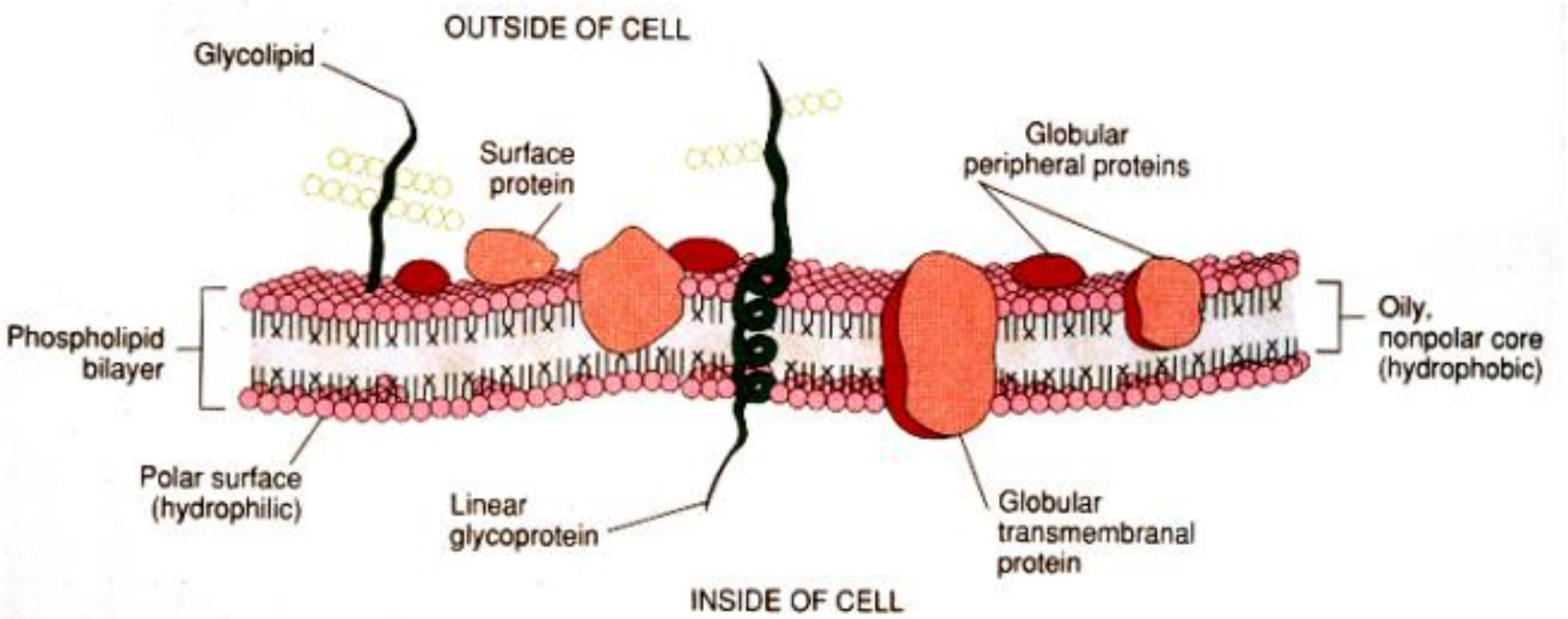


A heterogeneous lipid micelle may be viewed as a "disconnected" folded globular protein



(Lipowsky)

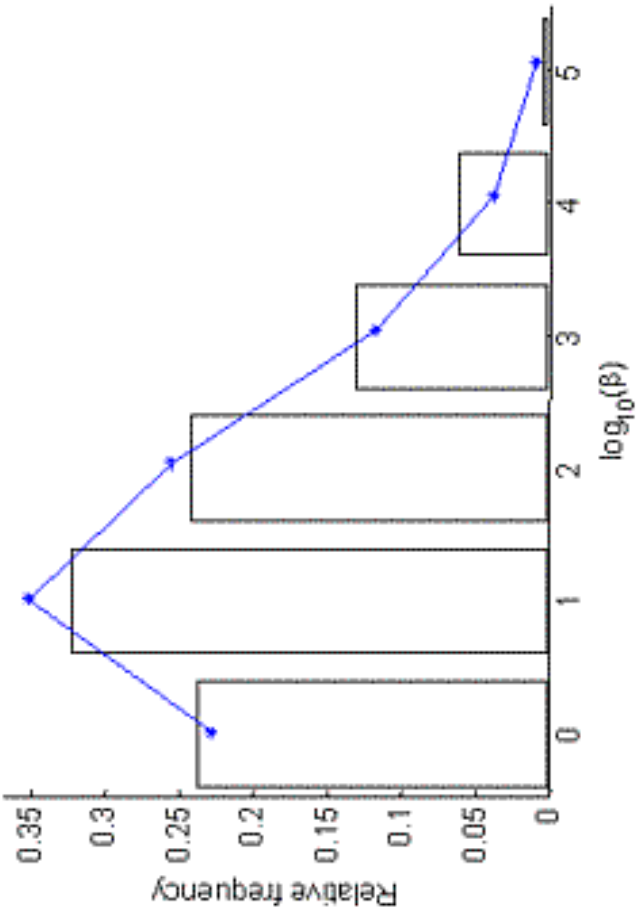
It could have enzyme mimetic properties



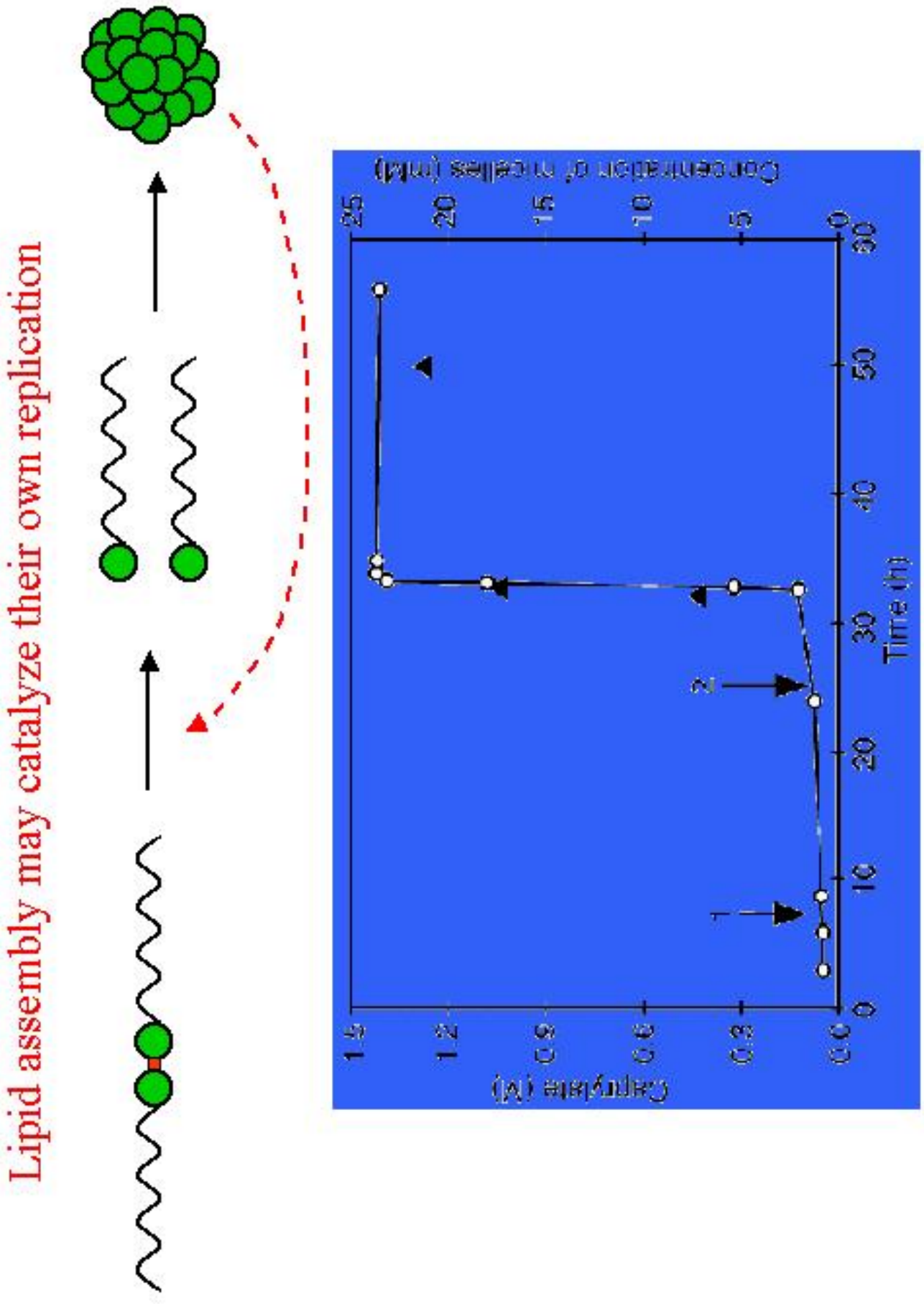
Lipids modulate enzymatic reactions in membranes

Lipid synthesis, insertion,
exchange and leaflet flipping may be catalyzed

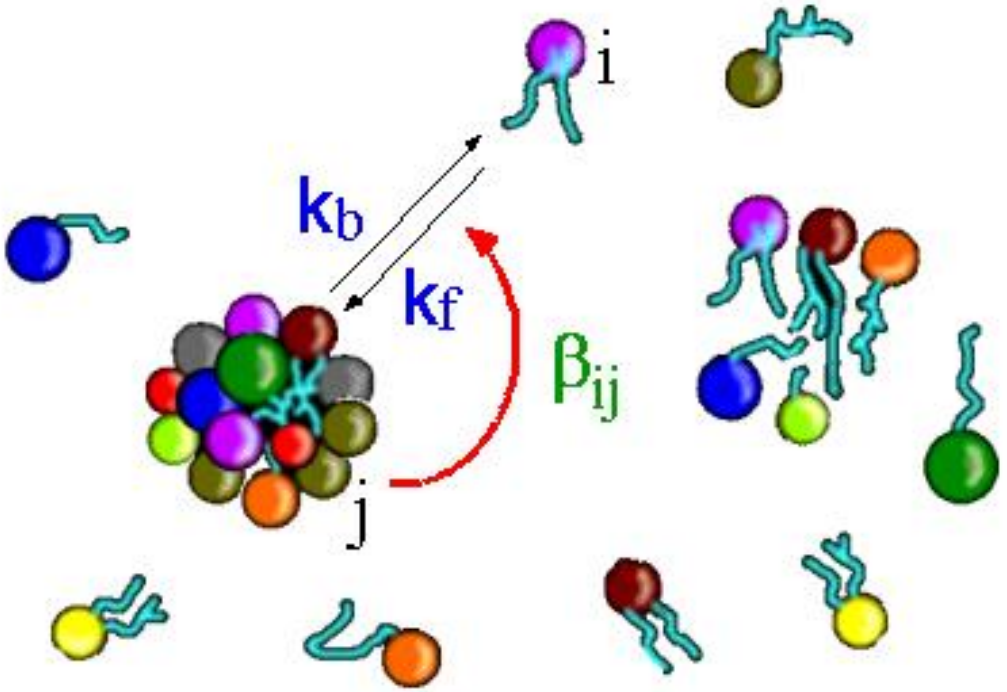
Lipid catalysis



Histogram of lipid catalytic rate enhancement values (from Fendler, Membrane Mimetic Chemistry)


Lipid assembly may catalyze their own replication
Concentration of micelles (mM)
Time (h)
Turbidity (V)
1
2
P.L.Luisi, Nature 1992

GARD: the Graded Autocatalysis Replication Domain model



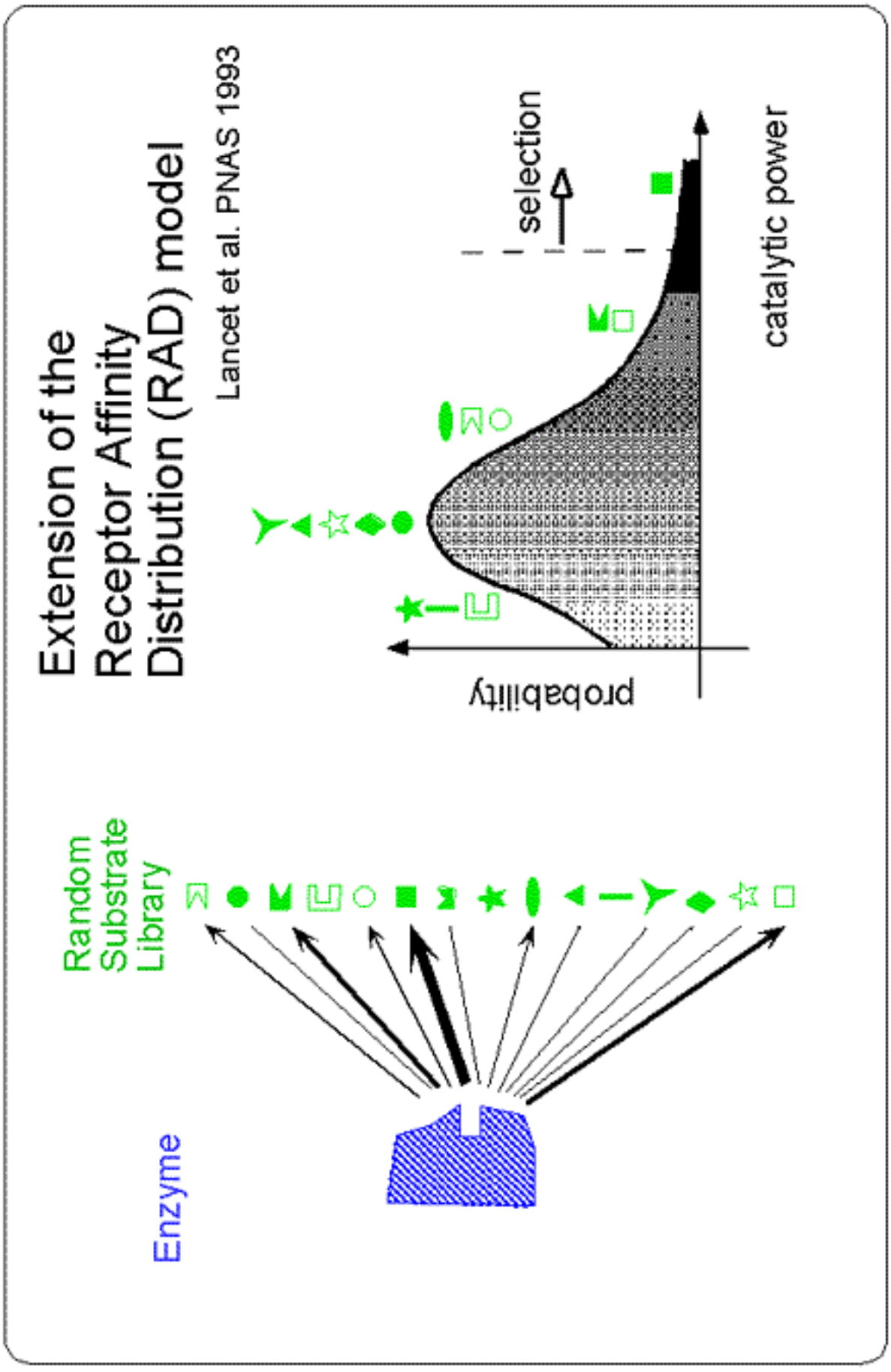
Spontaneous down hill assembly

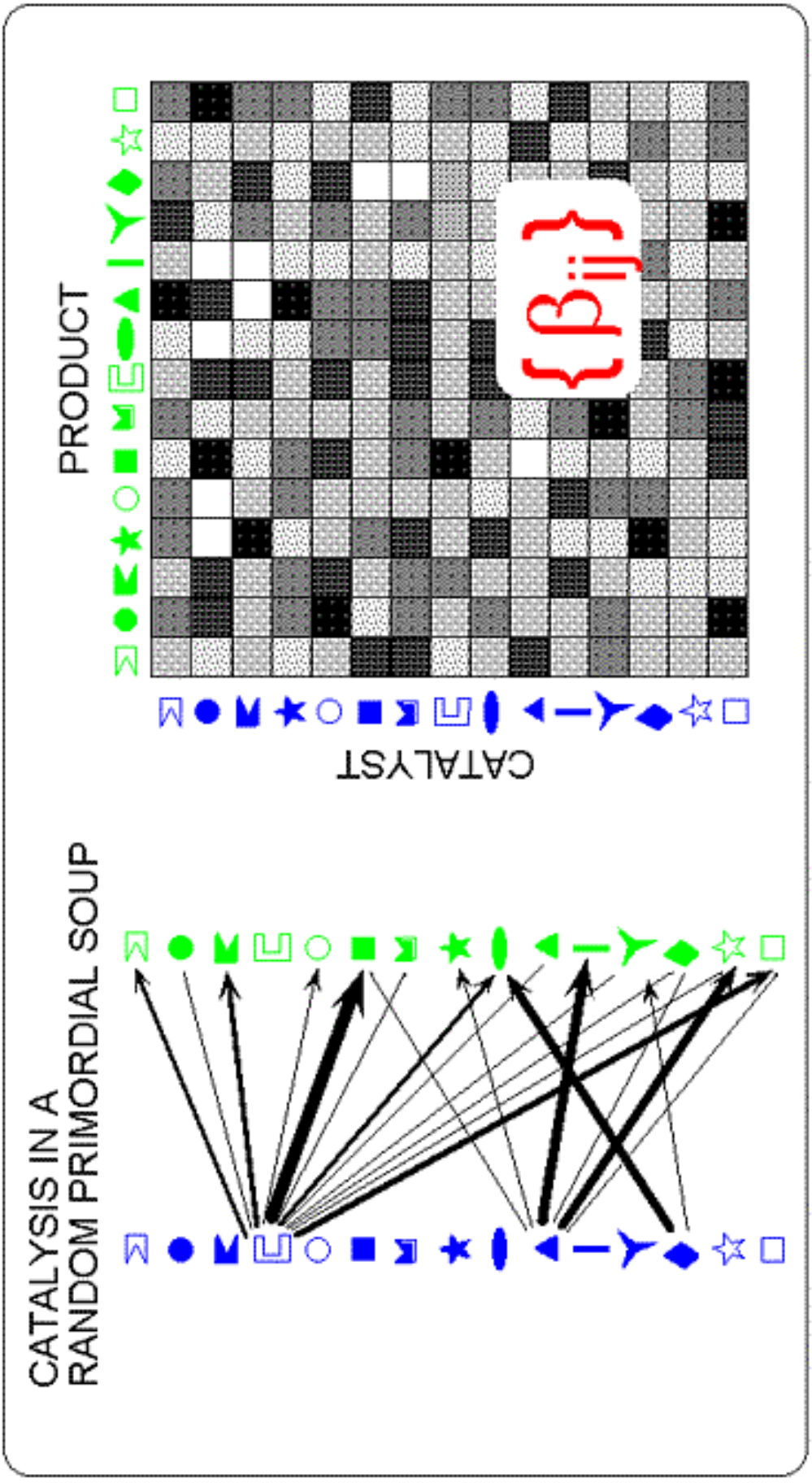
Growth by catalyzed joining or in-situ synthesis

Mutual catalysis defined by a beta matrix

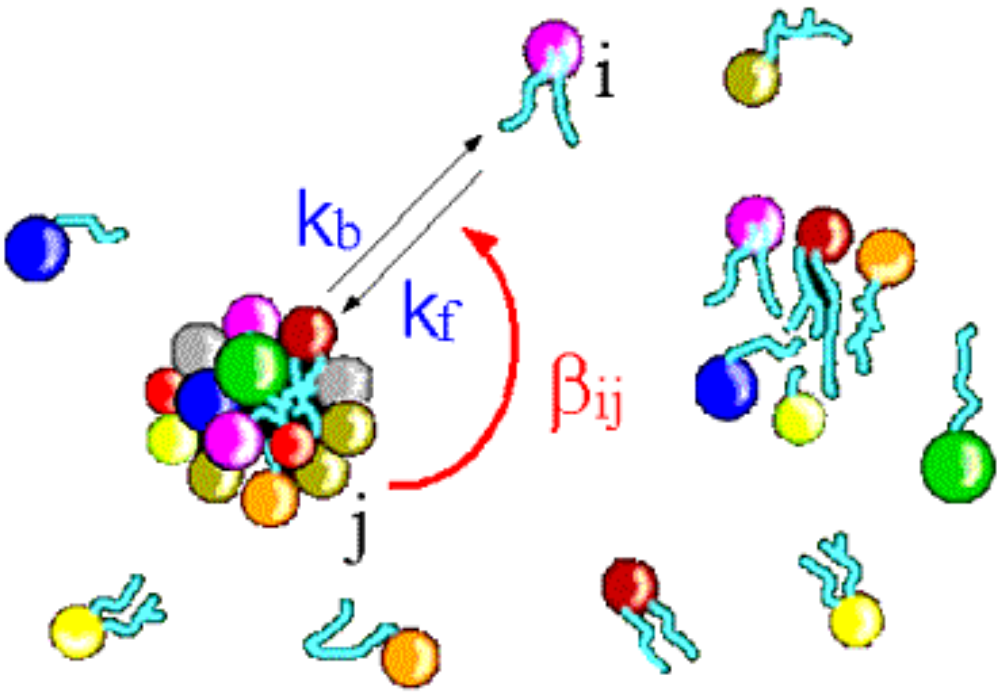
But how can one obtain the beta values for simulations?

[43] Dr. D. Lancet, Weizmann (ITP 4/24/01) Origin of Life without Biopolymers




PRODUCT
CATALYST
CATALYSIS IN A
RANDOM PRIMORDIAL SOUP

A kinetic model for the catalyzed growth of heterogeneous noncovalent assemblies



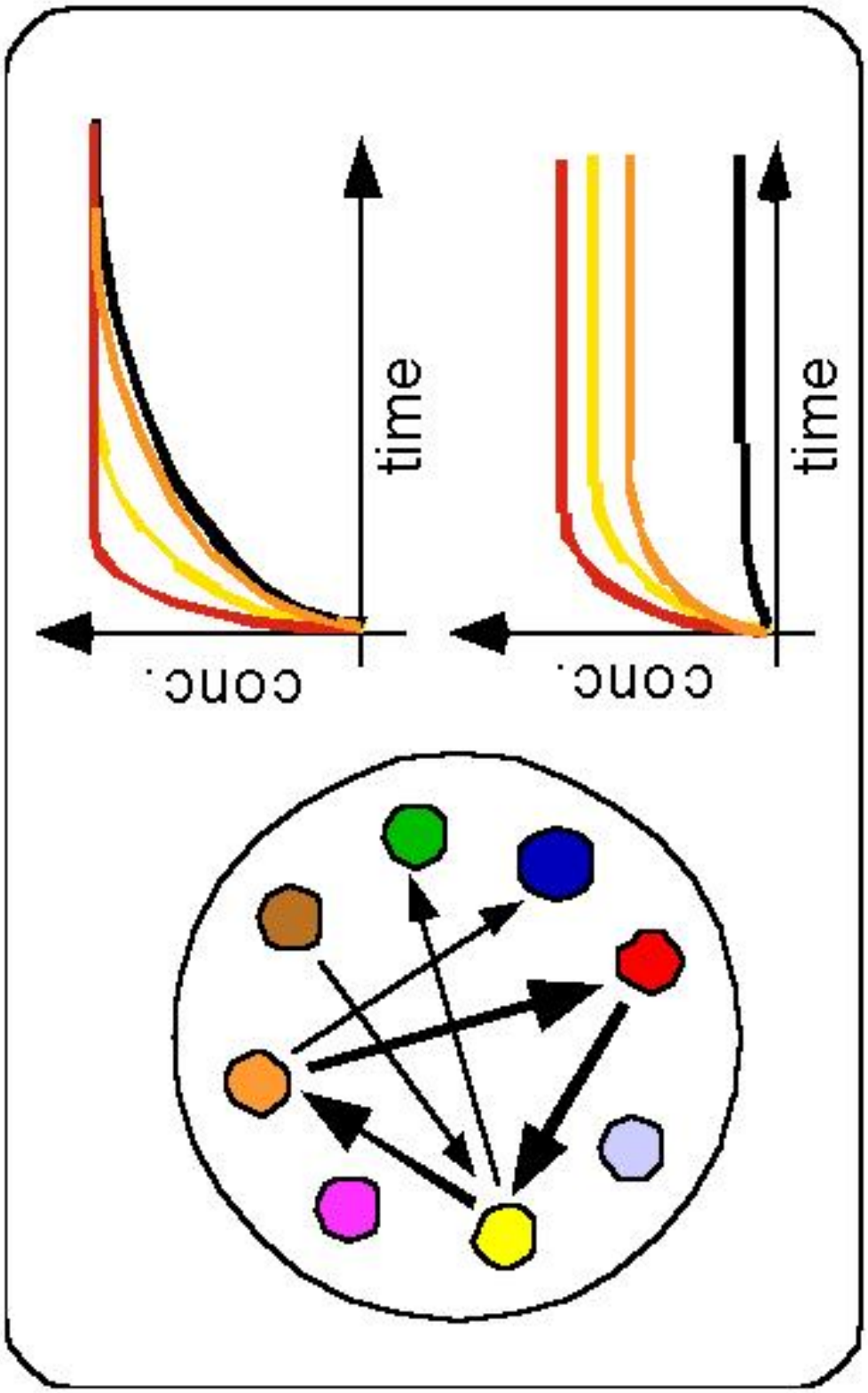
N_G = number of different kinds

n_i = count of molecules of kind i in the assembly

$N = \sum n_i$ (assembly size)

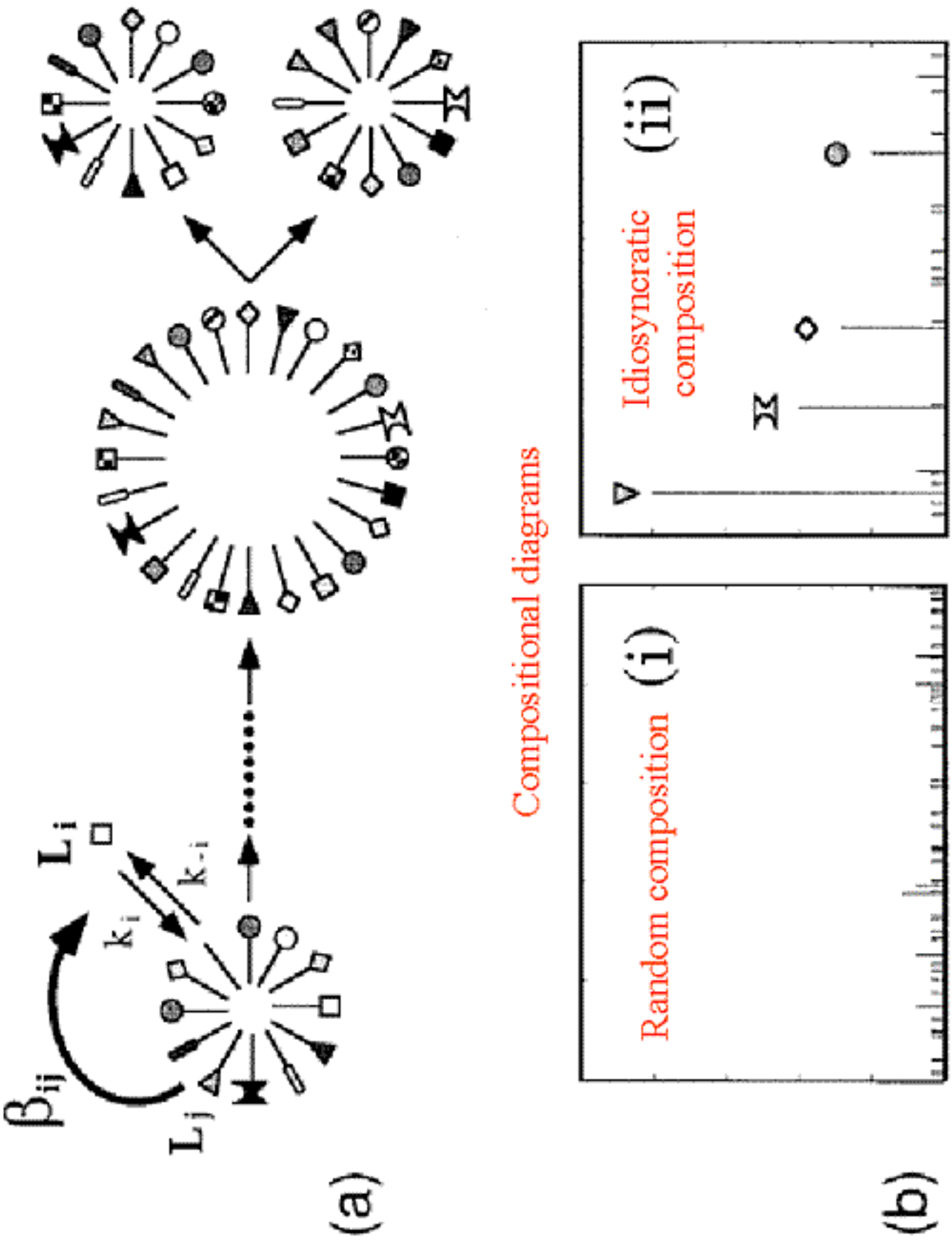
$$\frac{dn_i}{dt} = (\rho_i k_f N - k_b n_i)\left(1 + \sum_{j=1}^{N_G} \beta_{ij} \frac{n_i}{N}\right)$$

Forward reaction | Backward reaction | Catalytic enhancement

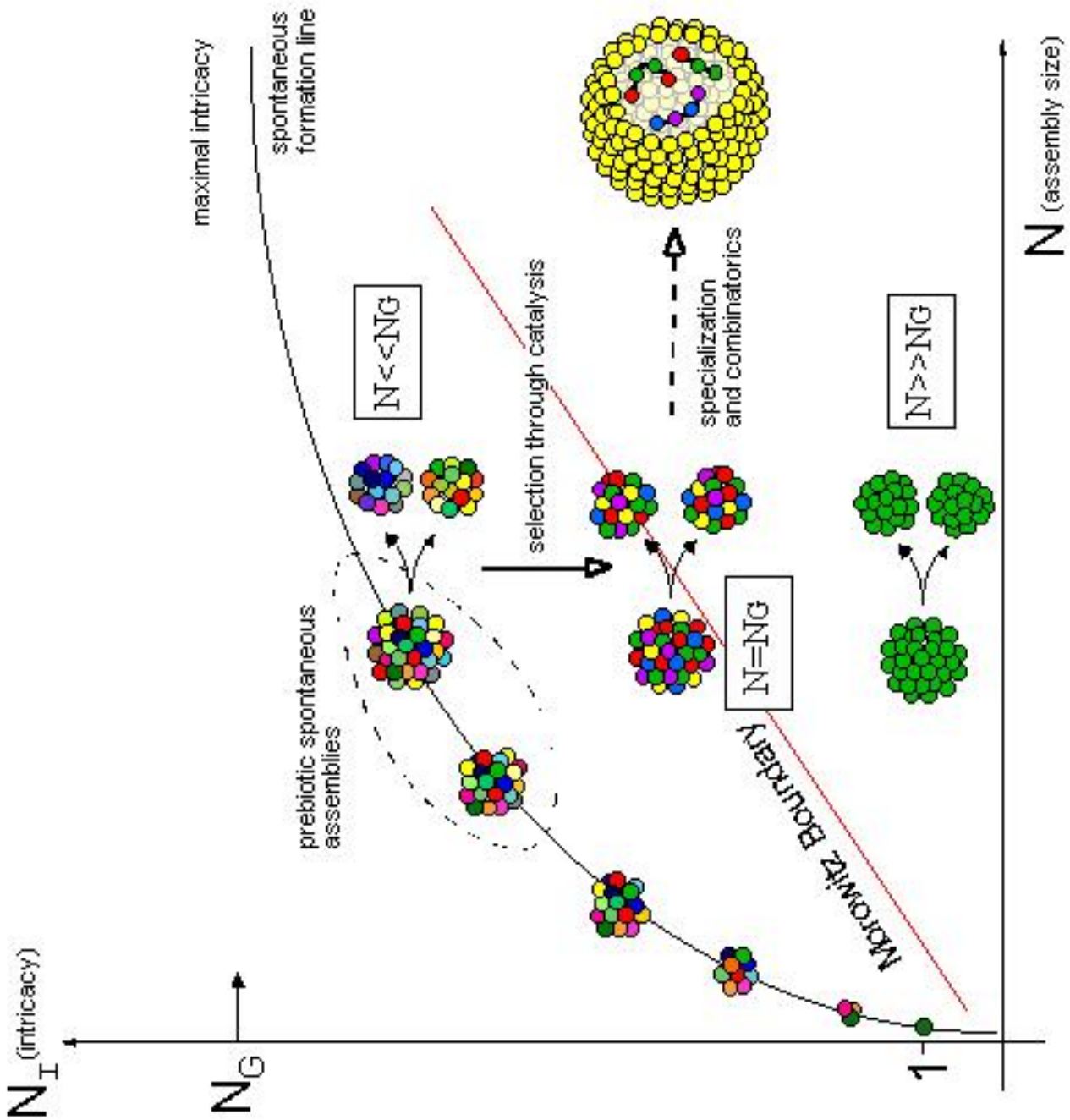


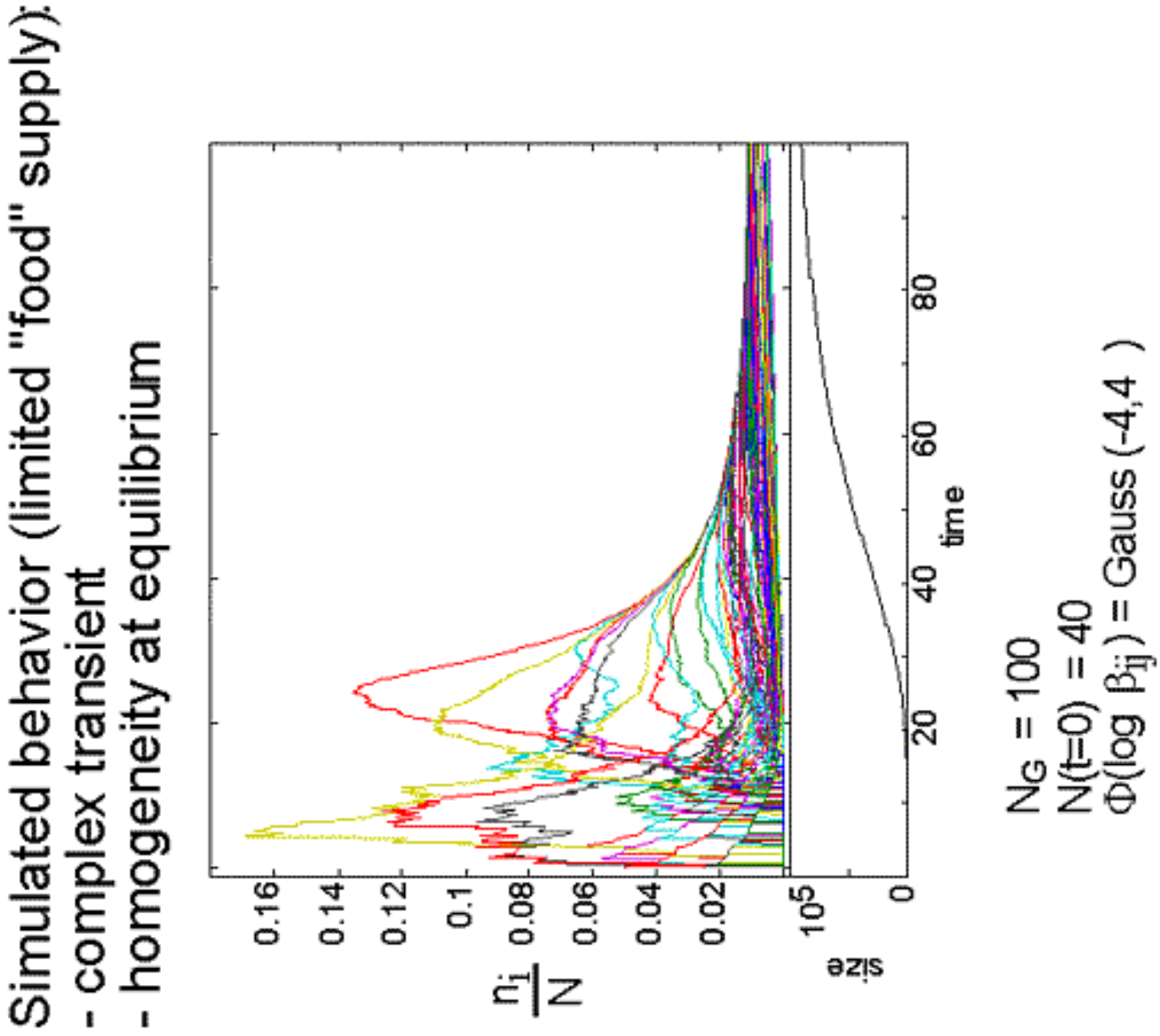
Lower panel – out of equilibrium

Network is established
(thicker arrows)

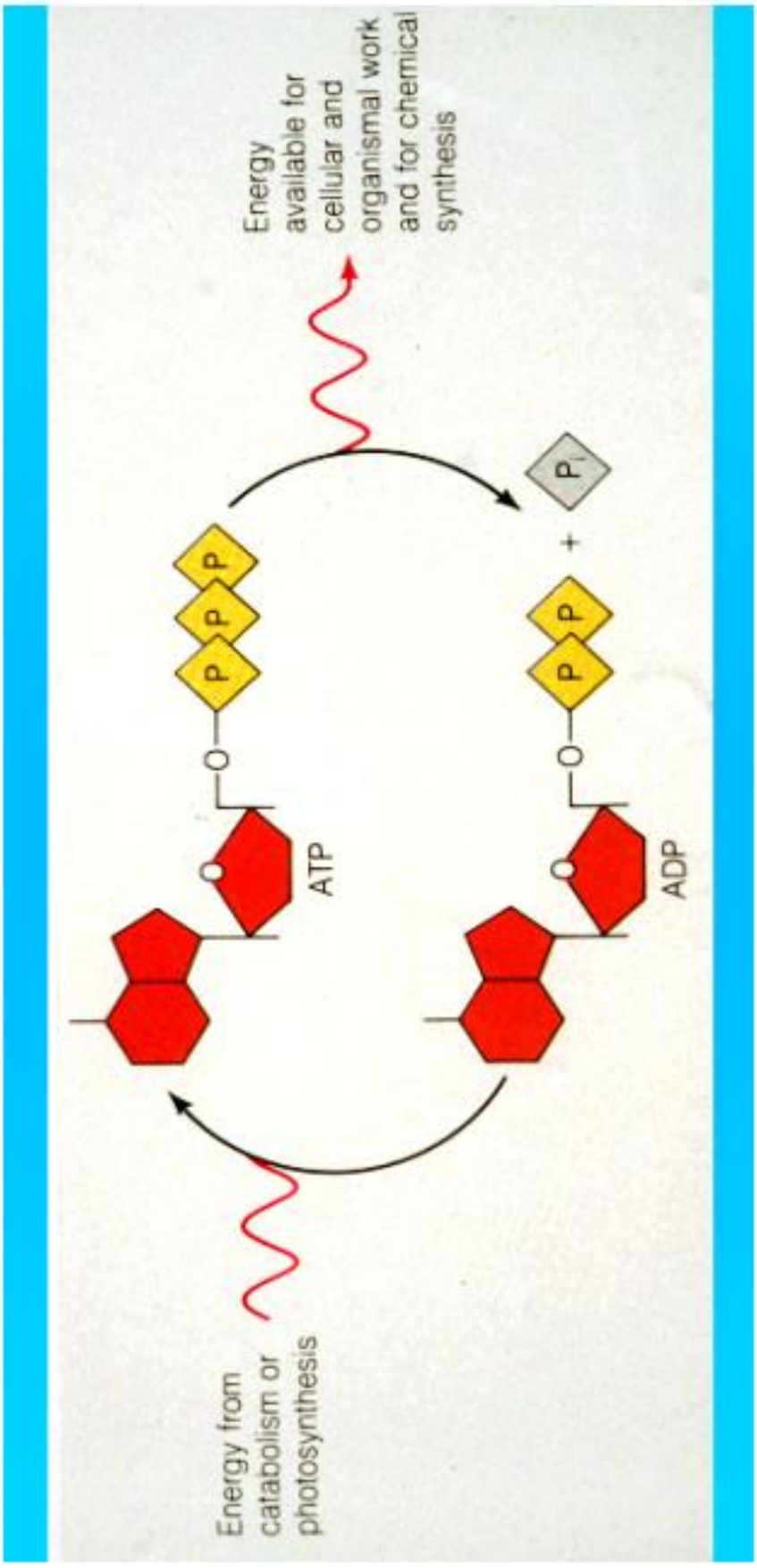

(a)
β_{ij}
L_j
L_i
k_i
k_{-i}
Compositional diagrams
(b)
Random composition (i)
Idiosyncratic composition (ii)

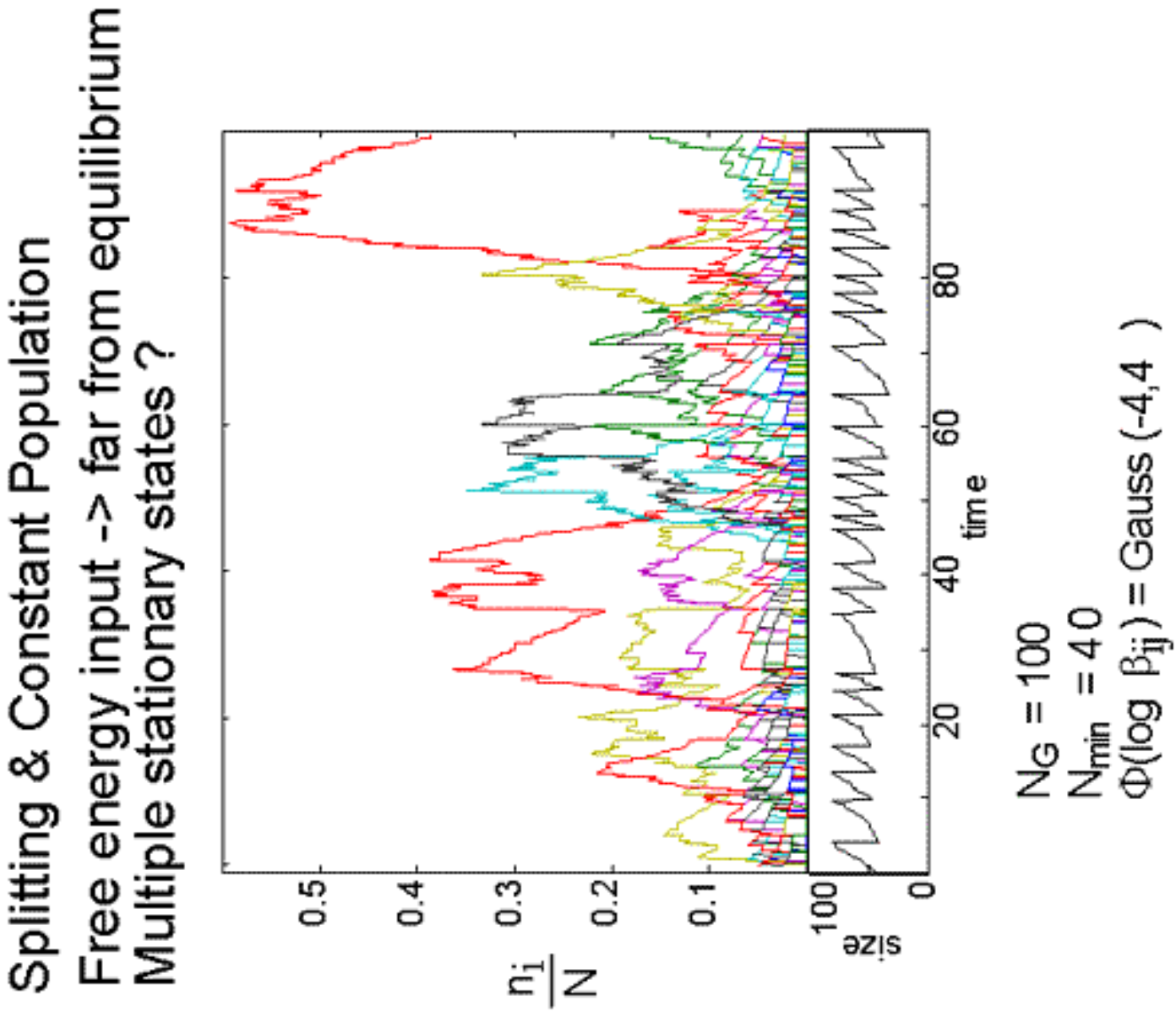
[48] Dr. D. Lancet, Weizmann (ITP 4/24/01) Origin of Life without Biopolymers




Simulated behavior (limited "food" supply):
- complex transient
- homogeneity at equilibrium
$\frac{n_i}{N}$
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
size
10^5
0
20
40
60
80
time
N_G = 100
N(t=0) = 40
$\Phi(\log \beta_{ij})$ = Gauss (-4,4)

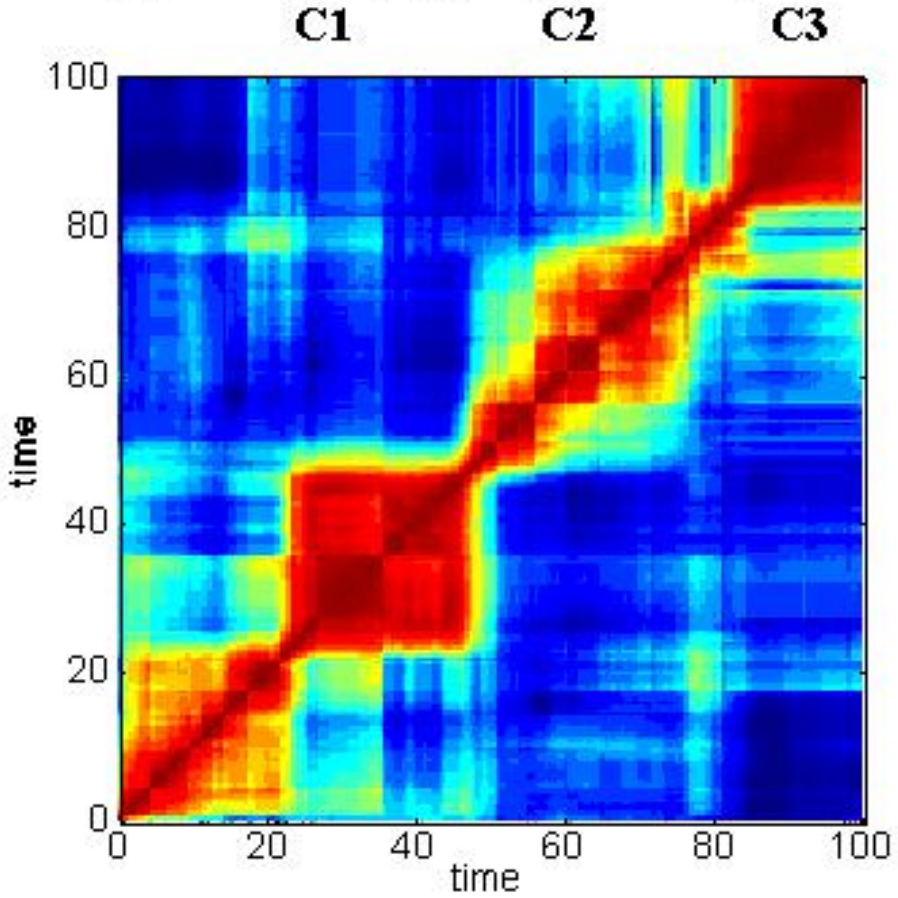
[50] Dr. D. Lancet, Weizmann (ITP 4/24/01) Origin of Life without Biopolymers




Splitting & Constant Population
Free energy input -> far from equilibrium
Multiple stationary states ?
$\frac{n_i}{N}$
0.5
0.4
0.3
0.2
0.1
size
100
0
20
40
60
80
time
$N_G = 100$
$N_{min} = 40$
$\Phi(\log \beta_{ij}) = \text{Gauss}(-4,4)$

DETECTION OF COMPOSITIONAL METASTABLE STATES (COMPOSOMES) IN COMPUTER SIMULATIONS OF THE LIPID WORLD

Metastable compositional states ("composomes") are detected by plotting H(**n**(t), **n**(t')) for all t,t' :

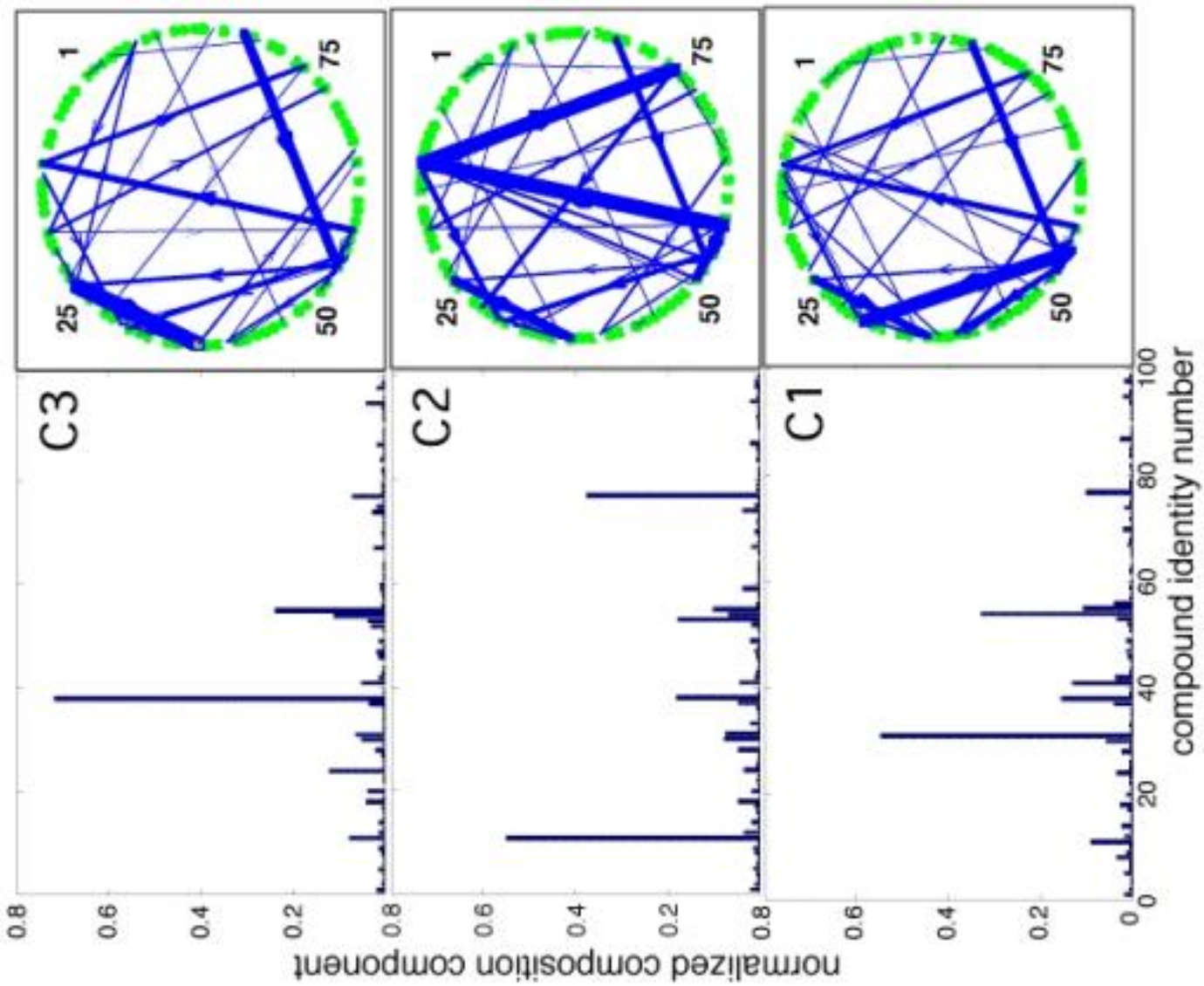


$$H(\mathbf{n},\mathbf{n}') = \frac{\mathbf{n}}{|\mathbf{n}|} \cdot \frac{\mathbf{n}'}{|\mathbf{n}'|}$$

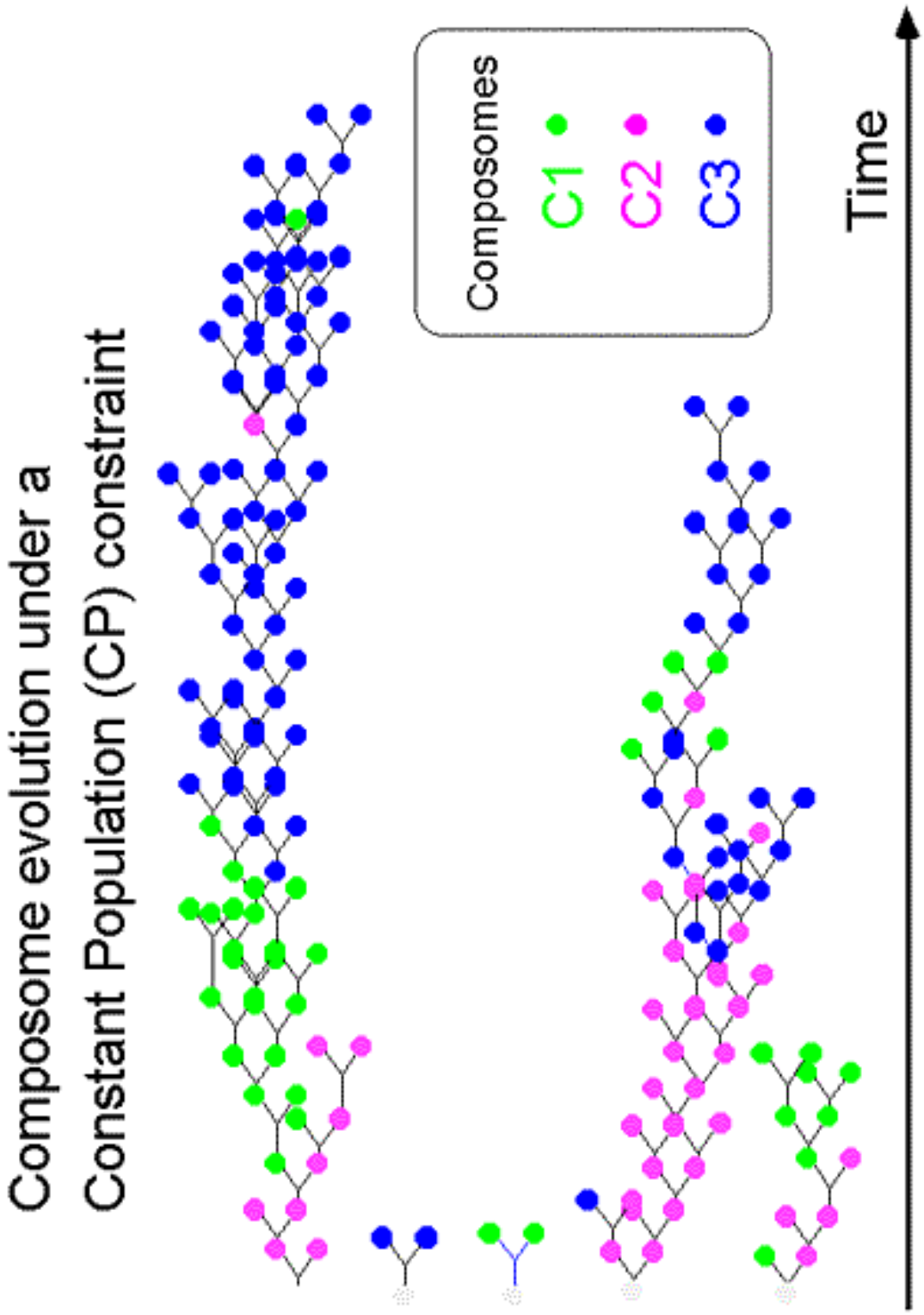
H=1 H=0

Segre, Ben-Eli and Lancet
PNAS 97:4112-7 (2000)

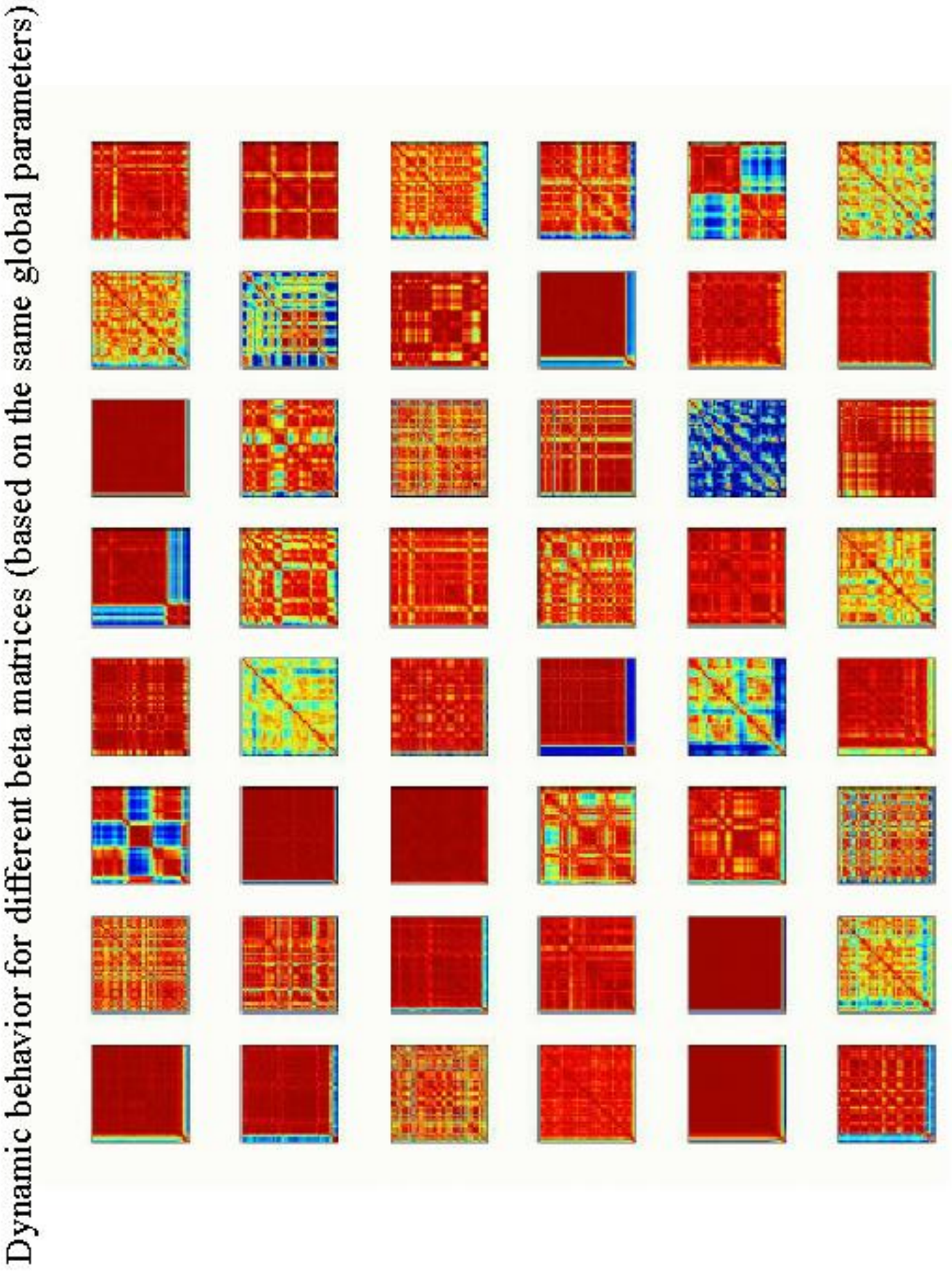
[53] Dr. D. Lancet, Weizmann (ITP 4/24/01) Origin of Life without Biopolymers

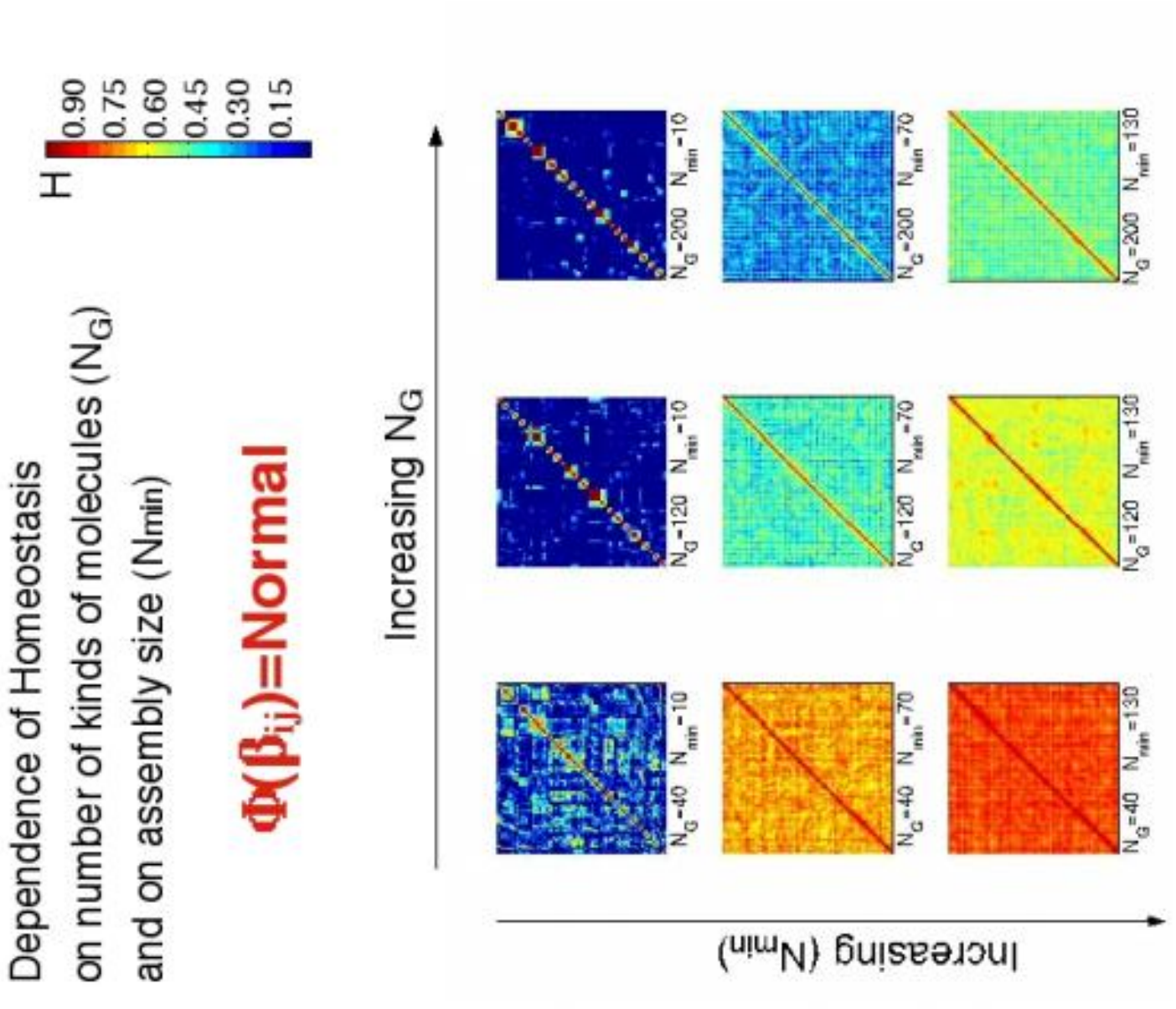


[54] Dr. D. Lancet, Weizmann (ITP 4/24/01) Origin of Life without Biopolymers

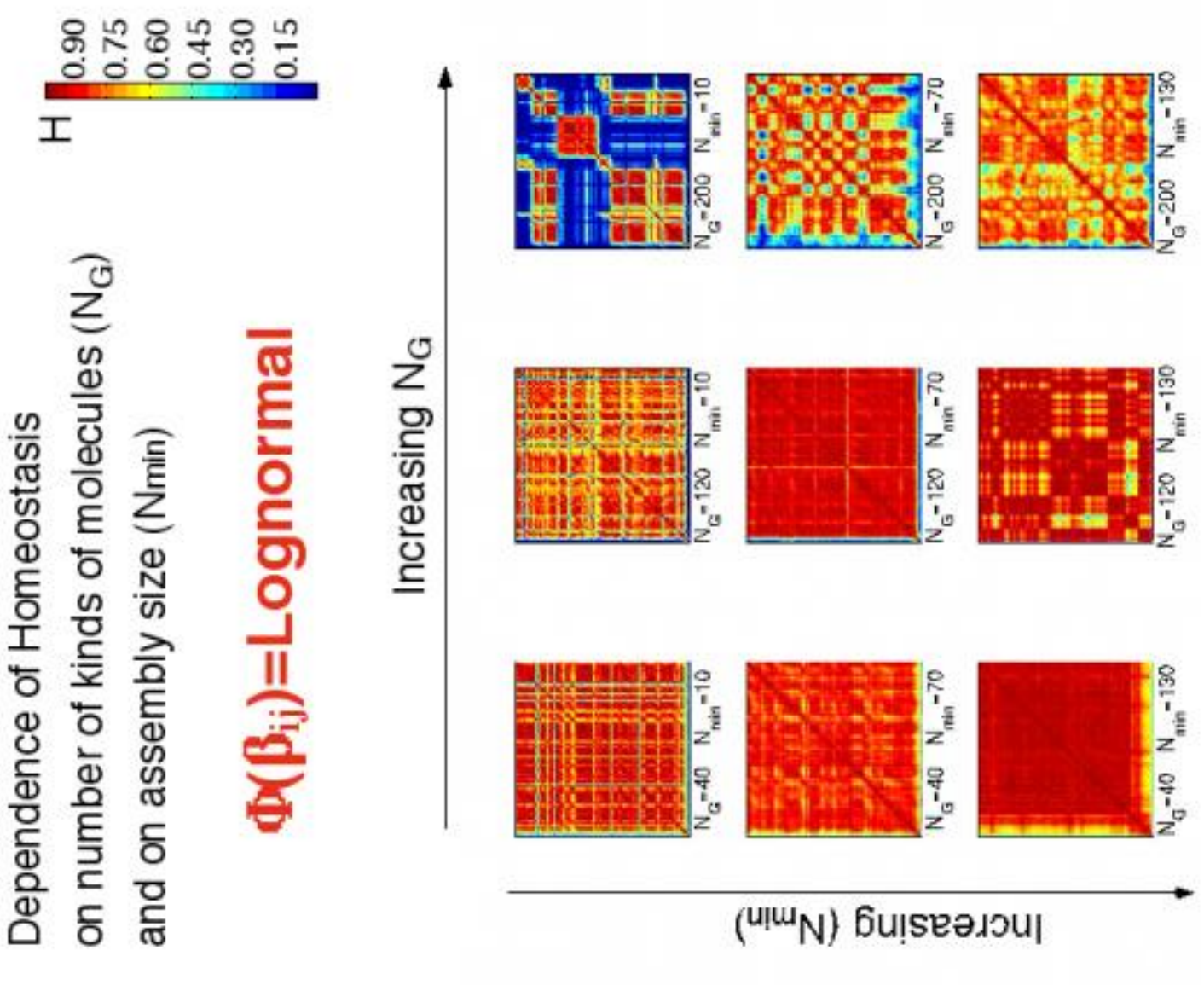


[55] Dr. D. Lancet, Weizmann (ITP 4/24/01) Origin of Life without Biopolymers

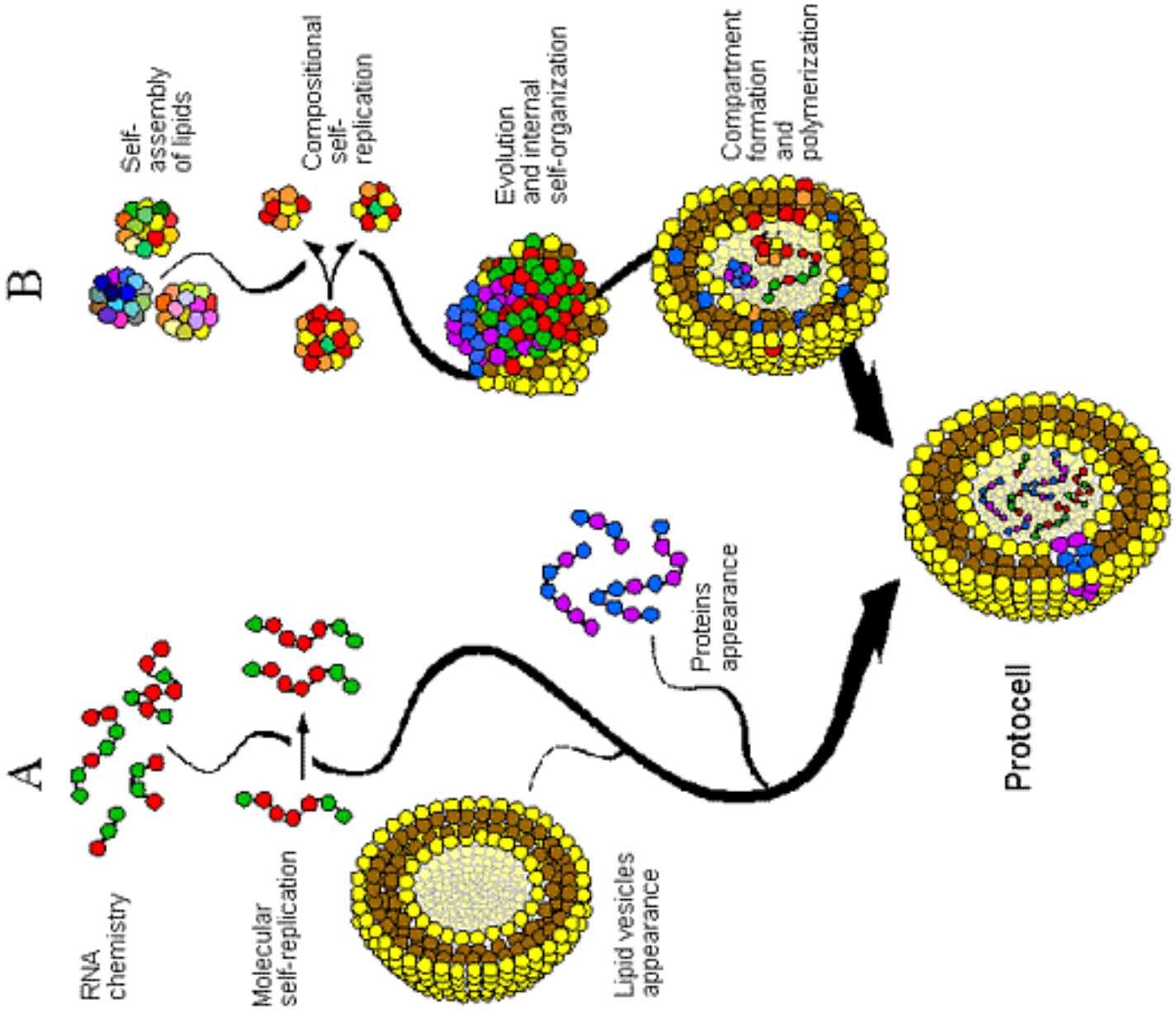



Dependence of Homeostasis
on number of kinds of molecules (N_G)
and on assembly size (N_{min})
$\Phi(\beta_{ij})$=Normal
H
0.90
0.75
0.60
0.45
0.30
0.15
Increasing N_G
Increasing (N_{min})
N_G=40 N_{min}=10
N_G=40 N_{min}=70
N_G=40 N_{min}=130
N_G=120 N_{min}=10
N_G=120 N_{min}=70
N_G=120 N_{min}=130
N_G=200 N_{min}=10
N_G=200 N_{min}=70
N_G=200 N_{min}=130

[57] Dr. D. Lancet, Weizmann (ITP 4/24/01) Origin of Life without Biopolymers

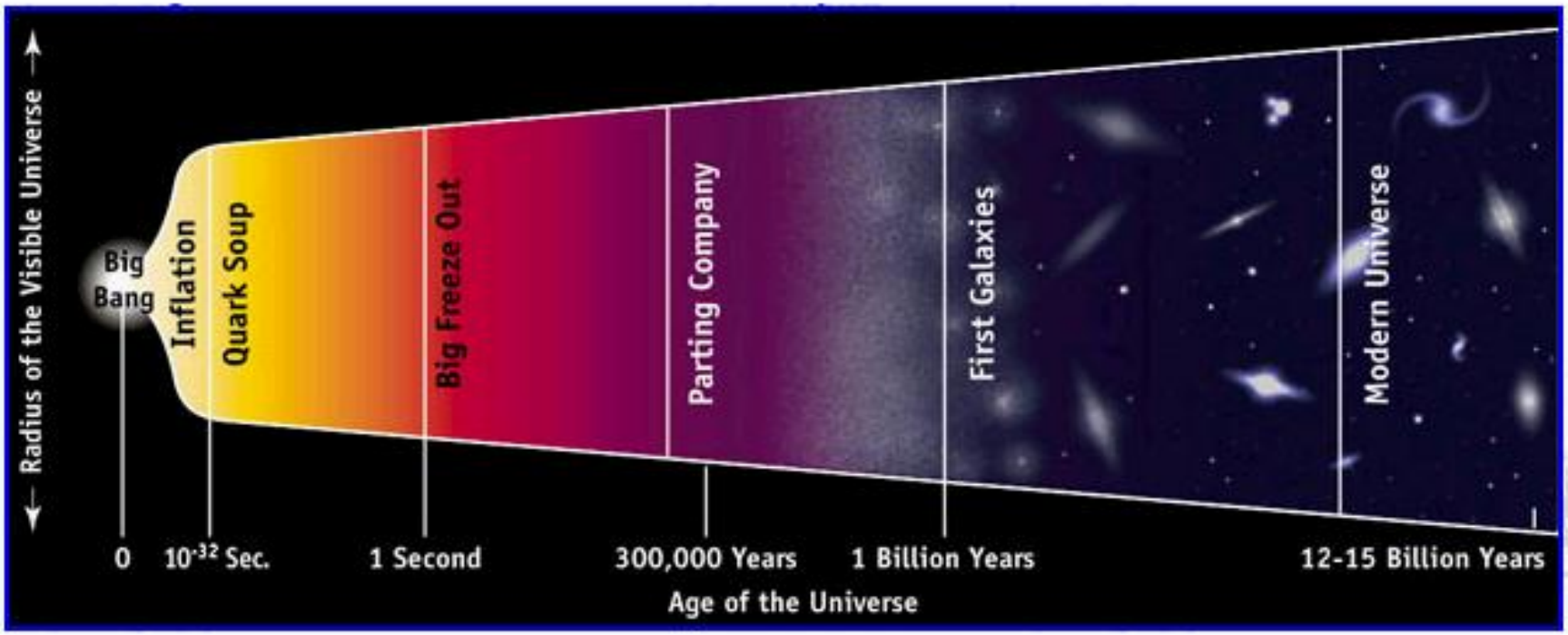


[58] Dr. D. Lancet, Weizmann (ITP 4/24/01) Origin of Life without Biopolymers



Experimental verification of the model:

1) Large scale computer simulations. The Origin of life is a planet-scale process that took millions of years to unravel. Shouldn't we attack it with tools similar to those used to study the origin of the universe or of galaxies and suns?

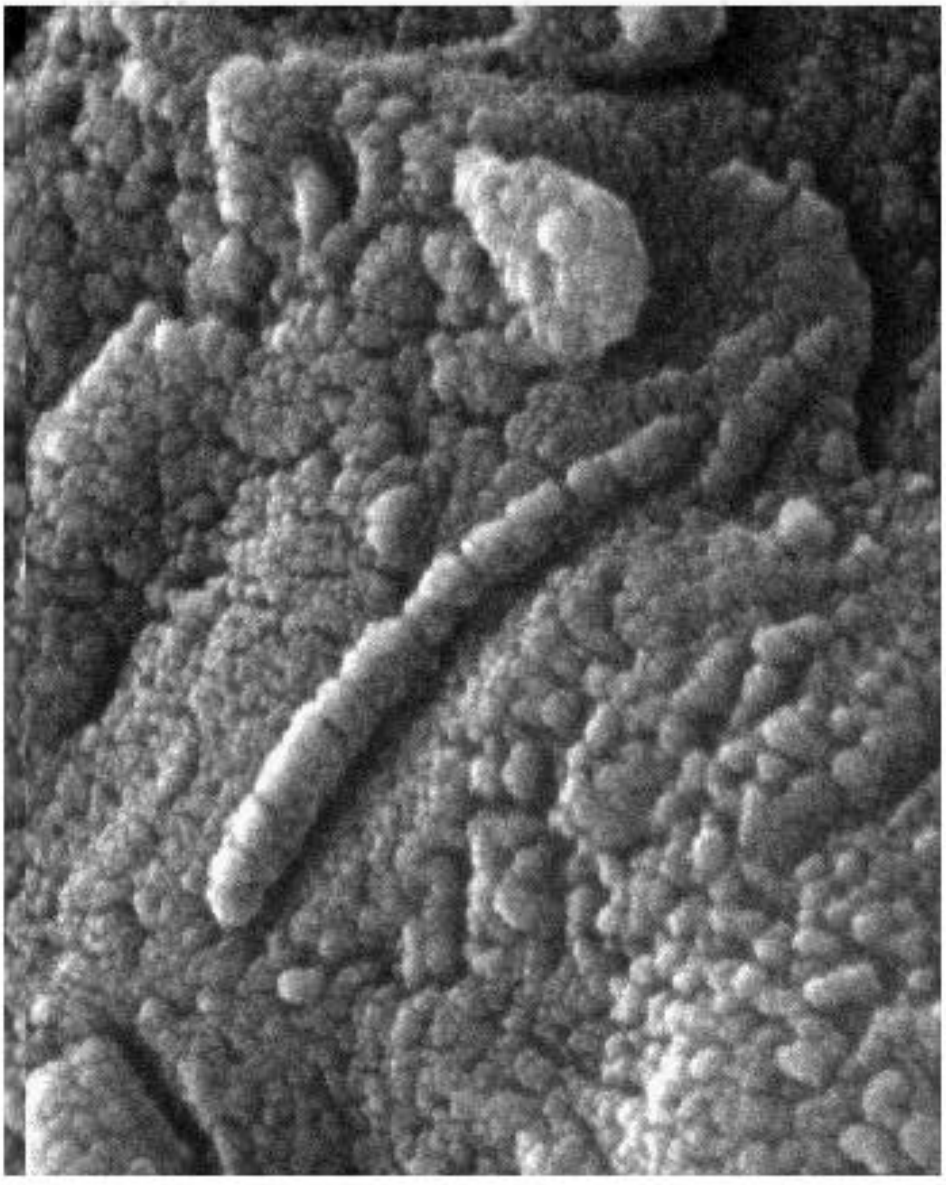


2) Microanalysis of individual assemblies in a very large scale/duration experiment

3) Galactic travel - know what to expect!

[60] Dr. D. Lancet, Weizmann (ITP 4/24/01) Origin of Life without Biopolymers

GARDobes on Mars??



Thanks to:

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RAD

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