Prebiotic evolution: replicator systems and information threshold
Life as evolved (evolving) complex multilevel information processing system

how to model it?

(1) how did it get started?/ bootstrap itself

Origin of life

studied by

• phylogenetic reconstruction (LUCA)
  quite complex - what before that?....
• Sufficient chemistry / environment
• experimental studies of minimal 'living' systems
  (re)constructing/engineering/evolving) such systems
• modeling studies of minimal 'living' systems

different approaches (focus) dependent on:

what is life?

including alternative forms (e.g. extra terrestrial / lab.)
Life is ....
Unique properties of life not shared by technological systems

'In stark contrast with current computer technology, biological cells compute in construction using molecular and spatial information, in order to delimit, organize, power, sustain, repair, move, communicate, reproduce, protect and evolve themselves robustly from simple and scarce material and energy resources in their complex environments'
J. McCaskill and S. Rasmussen EU report (2012)

not good starting point...
Hypothesized Environments of Prebiotic 'life' (metabolism)

Hydrothermal vents: (black smokers) energy/energy gradients for free compartments (concentration of ingredients) catalysis by metal sulphides; acetyl-coA pathway abiotic aminoacid synthesis Menez et al PNAS 2018

OR

Origin of first cells at terrestrial, anoxic geothermal fields Because of 'open' cell environment should match internal cell composition

“shallow ponds of condensed and cooled geothermal vapor that were lined with porous silicate minerals mixed with metal (primarily Zn) sulfides and enriched in K+, Zn2+, and phosphorous compounds.”

Armen Y........ Eugene V. Koonin, 2012 PNAS
(1) Life is energy/nutrient cycling

“The individual taxonomic units evolve and go extinct, yet the core machines survive surprisingly unperturbed.”

PG Falkowski et al, Science 2008
conserved metabolic pathway: glycolysis/gluconeogenesis

WHY??
“unique?” , “optimal?”
contingency? , (evolvability?)

Court, Waclaw & Allen 2015
Mapping all possible trunc pathways
Glyceraldehyde 3 phosphate to pyruvate

All (~1500) unbranched aliphatic CHOPN upto 4 carbon, negatively charged free energy for formation

All possible reaction

All possible pathways which produce (at least) 2 ATP
length 4,5 or 6 ->
1787 glycolysis pathways
6445 gluconeogenic pathways

<table>
<thead>
<tr>
<th>EC class</th>
<th>Reaction</th>
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<tbody>
<tr>
<td>1.1.1</td>
<td>Oxidation</td>
</tr>
<tr>
<td>1.2.1</td>
<td>phosphorylation</td>
</tr>
<tr>
<td>1.3.1</td>
<td>Deamination</td>
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<td>1.4.1</td>
<td>Transamination</td>
</tr>
<tr>
<td>2.6.1</td>
<td>Phosphate transfer</td>
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<td>2.7.1</td>
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<td>6.3.1</td>
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optimality of alternative pathways (maximal flux)

Sample 10000 conditions of
11 external metabolites + G3P and Pyruvate
(log sampling around typical existing levels)

Limit internal metabolite conc. 0.1-100mM

average relative flux in all samples
different optima for different conditions

alternative 'bests'

c

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Range sampled</th>
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<tr>
<td>[source]/[product]</td>
<td>0.01 to 100</td>
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<td>[ATP]/[ADP]</td>
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<td>[NAD]/[NADH]</td>
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<td>[AMP]</td>
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<td>[Pi]</td>
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<td>[PPI]</td>
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<td>[CO₂]</td>
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<tr>
<td>[2-OXO]</td>
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“Biological systems are distinguishable from chemical systems because they contain components that have many potential alternative compositions but adopt a particular composition based on the history of the system. In this sense biological systems have a molecular memory (genotype), which is shaped by experience (selection) and maintained by self-reproduction”

Joyce (2012) Bit by Bit: The Darwinian Basis of Life:

“How many heritable bits are involved, and where did they come from
Evolution-first scenario of the origin of life

RNA world

The RNA world hypothesis:

the worst theory of early evolution of life (except for all the others)
( Harold S Bernhardt, Biology Direct 2012)

- RNA for information storage and amplification
- (template and catalyst)
- potential 'generic' replication
- RNA in core processes of current biological systems
- New (old?) catalytic functions easily evolvable

HOWEVER
Many chemical caveats raised, and partially solved...

BUT

“The presumed RNA world should be viewed as a milestone, a plateau in the early history of life on Earth. So, too, the concept of an RNA world has been a milestone in the scientific study of life’s origins. Although this concept does not fully explain how life originated, it has helped to guide scientific thinking and has served to focus experimental efforts”

Protocells and RNA Self-Replication
Gerald F. Joyce1 and Jack W. Szostak nov 2020
review of and towards RNA world from chemical point of view.
RNA dependent RNA polymerase evolved from a ligase (Bartel & Szostak 1993), and improved by design and evolution to current form:

Replicated RNA's
Works also Reversed transcriptase!
RNA world hypothesis

here assumed as starting point for developing

bioinformatic theory prebiotic evolution

focusing on informatic rather than chemical constraints

AND as starting point for

modeling biotic systems as

evolving mutilevel information processing systems

Informatic potential and limitation of RNA world hypothesis

limited evolvability?
Minimal requirements for (Darwinian) evolution
(cf definition of life of Joyce)
“RNA world without chemical constraints”

• 'generic replicators'
• independent synthesis and decay
• mutation
• competition

Sufficient to bootstrap, from small RNA's?

Eigen: Replicator Equation (in chemostat)

\[ \frac{dX_i}{dt} = A_i Q_i X_i - d_i X_i + \sum w_{ij} X_j - \Omega_i \]

\[ \Omega_i = \left( \frac{X_i}{\sum X_j} \right) \sum (A_j - d_j) X_j \]

\[ E(t) = \frac{\sum (A_j - d_j) X_j}{\sum X_j} \]

\(--\rightarrow\) Quasispecies (=‘wildtype’)
\=
eigenvector of max eigenvalue of \( \hat{W} \)
\(--\rightarrow\) Information Threshold
Error Threshold and Information Threshold

“Survival of the fittest” only if mutation rate small enough.

Illustrate by simplifying to 2 equations + No ‘back-mutations’

\[ \frac{dX}{dt} = a_1 Q_1 X - d_1 X - X((a_1 - d_1)X + (a_2 - d_2)Y) \]
\[ \frac{dY}{dt} = a_2 Y - d_2 Y + a_1 (1 - Q_1) X - Y((a_1 - d_1)X + (a_2 - d_2)Y) \]

\[ X > 0 \text{ iff } \frac{dX}{dt} > 0 \text{ close to } X = 0 \]
\[ a_1 Q - d_1 > a_2 - d_2 \]
\[ Q > \frac{a_2}{a_1} = 1/\sigma \quad (\text{assuming } d_1 = d_2) \]

Error threshold $\rightarrow$ Information Threshold

\[ Q = q^L = e^{-L(1-q)} \]
\[ L < \ln\sigma/(1 - q) \]

Only limited information accumulation possible for given error rate
Error threshold / Information threshold

Takeuchi & Hogeweg (2007)
this is 'best' case scenario

• infinite population size
  - always to 'best' quasispecies
  - no stochastic population dynamics
  - no extinction (everybody viable-replicatable)

• strong selection, single peak landscape
  - therefore sharp transition (threshold)
  - delocalization vs threshold

• fixed length - no other constraints
  - NO negative selection on length (rate, energy)
Delocalization but no threshold for exponential fitness landscape

Takeuchi & Hogeweg (2007, BMC-evol)

However, if also lethal mutations - there is a sharp threshold