Multilevel evolution & Major transitions
Evolution of DNA in RNA world
explicit higher levels of selection
coupling between levels

• Classical (ecological group selection model (DS Wilson)
  passive higher levels; no mutations
• Classical prebiotic evolution model
  Stochastic corrector model (Szathmary)
  coupling lower to higher levels; no mutations
• evolutionary replicator models in vesicles
  –RP model: minimization of deathrate of vesicals
    tuning internal dynamics
  –Evolutionary stable disequilibrium: tuning volume/stochaistics
• Evolution of DNA in the RNA world: complexity as conflict
  reslution

mutual tuning of dynamics of levels of selection
(1) Static multilevel evolutionary modeling

Classical theory of group selection (DS Wilson 1975, Michod)

- vs kin selection - >
- construct model without kinselection
- large number of predefined “compartments/patches” (leaves)
- confined selection
- within each compartment “altruist” (X) loses
  \[ \frac{dX}{dt} = -vX + aXX - cX \]
  \[ \frac{dY}{dt} = -vY + aXY \]
  (HOWEVER finite number!)
- random dispersal after growth/competition
- binomial distribution of X,Y in patches
- if \( c < a \) trait increases (cf single level)
- statistically same environment: higher level
  selection compensates for lower level
- more than random variation (clumping)
  also 'strong' altruist can evolve

NB patches do not react on lower level

NB Mathematically Kinselection == Groupslection

covariance between trait and fitness
(Compare Simpson paradox)

Fig. 2. Illustration of the group selection process. See text for explanation.
(2) (population) dynamics of macro-level (cells) explicitly modeled using param’s derived from micro level

vesicle-based ’solution’ of information threshold:
**Stochastic Corrector model** (Szathmary and Demeter 1987)
- higher level selection imposed as vesicles (cf waves)
- (like hypercycle) study ’ecological dynamics’ (without mutations)
- 2 mol. form together ’replicase’ (or produce metabolite)
  (cf RP model)

**Micro level (within vesicles)**

\[
\begin{align*}
\frac{dX}{dt} &= aX(XY)^{1/4} - dX - X((X + Y)/K) \\
\frac{dY}{dt} &= bY(XY)^{1/4} - dY - Y((X + Y)/K) \quad ; \quad a > b
\end{align*}
\]

(fastest growth iff \(X = Y\))

\((X\ \text{outcompetes}\ Y\ \text{in ODE};\ \text{discrete stochastic version: master equation} \rightarrow \text{prob. distribution of mol after time} = \tau\) )
Macrolevel dynamics: vesicles
Quasispecies equation.
Species: cells with $x_i, y_j$ molecules
“Mutations” probability to change from $x_i, y_j$ to $x_k, y_l$ cell

Result: master cell ($x_i = y_j$) persists!

(like group selection) can persist by stochastic fluct. in vesicle occupation (here dynamics).

NOTE: no evolution of internal replicators!

NOTE: scaling problems:
size of vesicle (should be small enough (enough stochasticity)
size of vesicle (should be large enough to prevent random extinction)
number of different molecules should be small enough
timescales of vesicle level and internal dynamics should 'match'.

scheme of stochastic corrector model

\[ \text{Template replication} \quad \text{Protocell division} \]

NB timescales of micro vs macro dynamics
Automatic tuning of timescales by evolution in RP model in (CPM) vesicles

**internal dynamics \(\rightarrow\) vesicle death rate**

Evolution of the flattest at high \(\mu\). \(\rightarrow\). Evolution of the fittest at low \(\mu\)

High \(\mu\) cells are in unstable regime

evolve slow deterministic dynamics

\(\nu \rightarrow\) high stochasticity - correction

Low \(\mu\) stoch corrector keeps

cells in stable regime;

fast dynamics minimizes

stochasticity/death
Evolutionary stable disequilibrium: endless dynamics of evolution in a stationary population (Takeuchi et al 2016)

Replicator model within cell (:NO parasites)

Minimization of catalysis within cell

Maximization of cat. between cells

Internal dynamics: $\rightarrow$ extinction

competition for substrate

high diffusion between cells

rate depends on mutation rate (not evolvable)

and Vesicle size (predefined at division) (not evolvable)

Vesicle level selection depends on variability (scales with $i/V$)

How does evolutionary dynamics cope with large cells?
Evolutionary dynamics along line of decent: evolutionary stable disequilibrium for large cells

\( V = 1000 \)
Evolutionary dynamics along line of decent: stochastic correction for small cells
Coping with large cells by becoming small
increase stochasiticy

Add extra selection
by killing small cells
only smaller cells survive
conclusion: conflict of levels of selection
if similar strength: “creative solution”

Within vesicle selection strength  $mV$
Between vesicle selection strength  $1/V$
If  $mV \frac{1}{V} > mV^2 = C$ - oscillating internal dynamics.
exploring evolutionary properties/advantages of more RNA-like replicators in RP systems (i.e. more degrees of freedom)

- Direct replication vs Complementary replication
imposed levels of selection: protocells
direct vs complementary replication
symmetry breaking and robustness to larger cells

**evolutionary attractors**

**ancestor trace: bottlenecks**

Evolutionary stable disequilibrium, and origin of 'primordial genome'
Takeuchi et al 2016, 2017;
(emergent) multilevel evolution
division of labor

SPACE

Protocells

RNA compl. repl.

Takeuchi, Hogeweg, Kaneko 2017: *The origin of a primordial genome through spontaneous symmetry breaking*

Von der Dunk, Colizzi, Hogeweg, 2017: *Evolutionary Conflict Leads to Innovation: Symmetry Breaking in a Spatial Model of RNA-Like Replicators*
Both models:

**Exploit “near death” for evolving new replication strategies**

*Protocells:* enhanced drift in bottlenecks of dying cells

*in space:* creation of wave-fronts and positive selection for more catalysis (wave-level+individual level)

Parasite lineage essential for survival: enabling wave-formation

**Exploit complementary replication for “division of labor”**

*protocells:* symmetry-breaking iff levels of selection similar strength decreases within cell mutational pressure to low catalysis

One catalytic strand (†), strongly favors complementary strand (‡)

Many †, few ‡ strands (Genome-like)

maintains more catalysis in bottle necks

*in space:* Always symmetry breaking, different kinds

At high diffusion similar to protocells and few ‡ strands many † strands optimizes both availability as template and amount of catalysis (wave front/wave back)

Evolution of multiple lineages (speciation)

**mutual dependence (feedback) higher level/lower level evolution**
bottom line

Division of labor: template and catalysis

Template in Minority

generic property Protocells and in space

multiple specific models converge to similar result
evolution of DNA in the RNA world
phylogenetic evidence

evolution of DNA replication late
core enzyme domains for DNA replicases
non-homologous between Prokaryotes and Eukaryotes
(reverse) transcriptases are homologous.

cf Leipe, Aravind and Koonin, NAR 1999
Conflict resolution between levels of selection
“major transitions in evolution”

- Decoupling of information storage and function:
  Evolution of DNA in RNA world
- RNA: information storage (template) AND ribozym;
  DNA only information storage (template)
  (Note in vitro DNA can also be catalyst but here defined as only template)
- Evolution of DNA in the RNA world: “division of labor”
- RNA “giving up” self-sufficiency - selfreplication (?)
- Evolution of slower replication cycle

the model

RNA world: minimal RP system (replicase (Rp) - parasite)

assume 2 types of polymerases: DNA pol. (Dp) and RNA pol. (Rp)
can exits as RNA and DNA

both can recognition RNA and/or DNA (binding evolvable parameter)

- Can DNA establish itself in an RNA world in evolutionary equilibrium
- If so WHY (longer replication cycle)
- Which type of specificity evolves?
evolutionary trajectory in spatial system
# Experiments to test causes and consequences

<table>
<thead>
<tr>
<th>No.</th>
<th>Purpose of simulation</th>
<th>Setting of simulation</th>
<th>Ref.</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Standard simulation. Point of reference</td>
<td>Starting with self-replication system</td>
<td>Fig. 2 &amp; Fig. 6B</td>
<td>Transcription system evolved, and it coexisted with self-replication system.</td>
</tr>
<tr>
<td>2</td>
<td>To observe the short-timescale dynamics of transcription system evolved in No. 1</td>
<td>Idealized transcription system (no mutation)</td>
<td>Fig. 3</td>
<td>Transcription system was resistant against parasites, but produced many empty regions.</td>
</tr>
<tr>
<td>3</td>
<td>To examine the role of parasites for the coexistence observed in No. 1</td>
<td>Parasites were removed in No. 1 after reaching equilibrium (no mutation)</td>
<td></td>
<td>Transcriptase (DdRp) went extinct: transcription system was destabilized.</td>
</tr>
<tr>
<td>4</td>
<td>To examine the role of self-replication system for the evolutionary stability of system</td>
<td>Self-replication system was removed in No. 1 after reaching equilibrium</td>
<td>Fig. 4 &amp; Fig. 6C</td>
<td>Transcription system regenerated self-replication system: DdRp became evolutionary unstable and diverged into RdRp &amp; DdRp via dual-Rp.</td>
</tr>
<tr>
<td>5</td>
<td>To examine the role of reverse transcription activity for the evolutionary destabilization of transcription system</td>
<td>The same as No. 4, except that reverse transcription was completely suppressed</td>
<td>Text S1, Note 4</td>
<td>Transcription system did not regenerate self-replication system: DdRp remained evolutionarily stable.</td>
</tr>
<tr>
<td>6</td>
<td>To examine the role of parasites for the evolution of transcription system</td>
<td>The same as No. 1, except that the model excluded the predefined parasite</td>
<td>Fig. 5 &amp; Fig. 6D</td>
<td>Transcription system evolved, enabling self-replication system to diverge into a catalytic and parasitic species.</td>
</tr>
<tr>
<td>7</td>
<td>To examine the effect of complex formation on the evolution of DNA</td>
<td>The model assumed that replication was an instantaneous process.</td>
<td></td>
<td>DNA did not evolve: complex formation is important for the evolution of DNA</td>
</tr>
</tbody>
</table>

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alternative routes to same evolutionary attractor
transcription system + RNA selfreplication

- evolved transcription system B killed when parasites are removed. However when started without parasites D transcription system evolves and finally evolves parasite lineage as well.
- Transcription system without selfreplication C re-evolves selfreplications system. Without reverse transcriptase stable attractor.
Evolutionary trajectory in vesicle system (CPM)

Left panel:
- **Snapshot**
  - Blue: Rp
  - Green: Dp
  - Red: parasite
  - White: comp. bound
  - Black: empty
- **2D histogram**
  - [no. molecules; 20x20 bins]
  - 0 0.5 1 >1 (x10^3)

Right panel:
- **Snapshot**
  - The color corresponds to the value of Rrec as indicated in the histogram.
  - (Parasites are colored brown.)
- **1D histogram**
  - It depicts the relative frequency of Rrec values.
  - 100 bins.

A, B, C, D, E:
- **time**
  - A: 0.05 x 10^6
  - B: 0.40 x 10^6
  - C: 2.23 x 10^6
  - D: 2.29 x 10^6
  - E: 2.50 x 10^6
RNA replication AND Transcription system in vesicles and in surface system however dual functional RNA polymerses in vesicles.

NO (minimal) reverse transcription: DNA common ancestor
DNA stabilizes high catalytic RNA because division of labor of information storage and catalysis vesicles without DNA first win, later lose competition
Slow down of Evolutionary Degradation of catalysis in evolved system (B); Tested in ODE
SO FAR:
Invasion and stabilization of NON-catalytic DNA in RNA world

Toward similar attractor when started with fully symmetric system?

Unidirectional information flow?

“Crick’s dogma “from DNA to RNA to proteins” is not a dogma anymore” (Nobuto Takeuchi)
The origin of the central dogma through conflicting multi-level selection

Nobuto Takeuchi and Kunihiko Kaneko 2019

Symmetric Initial catalysis

Specialized evolved

“DNA” minority
unidirectional information flow and inheritance of minority species seen at many levels of biological organization

Table 1. Division of labour between information transmission and other functions transcends the levels of biological hierarchy.

<table>
<thead>
<tr>
<th>hierarchy</th>
<th>parts</th>
<th>differentiation</th>
<th>other</th>
</tr>
</thead>
<tbody>
<tr>
<td>whole</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cell</td>
<td>molecules</td>
<td>genome</td>
<td>enzyme</td>
</tr>
<tr>
<td>symbiont population*</td>
<td>prokaryotic cells</td>
<td>transmitted</td>
<td>non-transmitted</td>
</tr>
<tr>
<td>ciliate</td>
<td>organelles</td>
<td>micronucleus</td>
<td>macronucleus</td>
</tr>
<tr>
<td>multicellular organism</td>
<td>eukaryotic cells</td>
<td>germline</td>
<td>soma</td>
</tr>
<tr>
<td>eusocial colony</td>
<td>animals</td>
<td>queen</td>
<td>worker</td>
</tr>
</tbody>
</table>

*Bacterial endosymbionts of ungulate lice (*Haematopinus*) and planthoppers (*Fulgoroidea*) [38].
结论：劳动分工

空间系统中局部交互或强加多级系统可以防止演化崩溃，但仅限于‘生存’水平：它们确实最小化了对‘公共利益’的贡献（在RNA世界中给予催化）。

这样的演化最小化‘工作’可以被劳动分工所防止。

3种劳动分工模式有助于应对恶劣环境

- 生态系统基的：‘寄生虫’的进化
- 个体基的：模板与催化剂的进化
- 单向信息流：非工人的继承（DNA）。

演化稳定化（一个长期效应）确实可以进化！（即使复制速度较低）。

冲突解决于不同水平的演化之间

较慢的复制者‘超越’更快的。

复杂性因为演化‘收益’而演化

较慢的复制者“超越”更快的。

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