Multilevel evolution & Major transitions
Evolution of DNA in RNA world

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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/stochaisticy
- Evolution of DNA in the RNA world: complexity as conflict
  resultion

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
  $dX/dt = -vX + aXX - cX \;\; dY/dt = -vY + aXY$
  (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)

A Theory of Group Selection 145

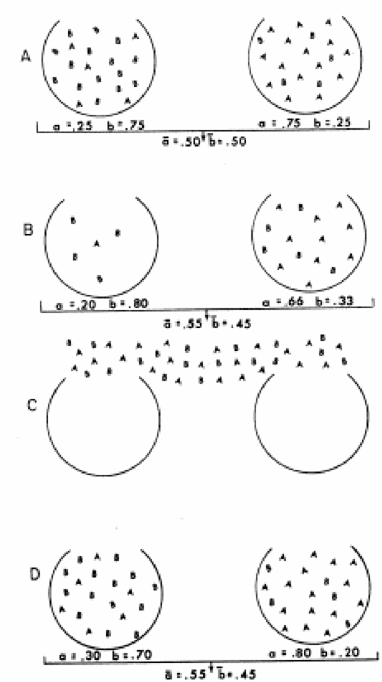


FIG. 2. Illustration of the group selection process. See *text* for explanation.

(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)

$$dX/dt = aX(XY)^{1/4} - dX - X((X+Y)/K)$$
$$dY/dt = bY(XY)^{1/4} - dY - Y((X+Y)/K)\ ;\ \mathbf{a > b}$$

(fastest growth iff X = Y)

(X outcompetes Y in ODE;
discrete stochastic version: master equation $->$
prob. distribution of mol after time=τ)

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

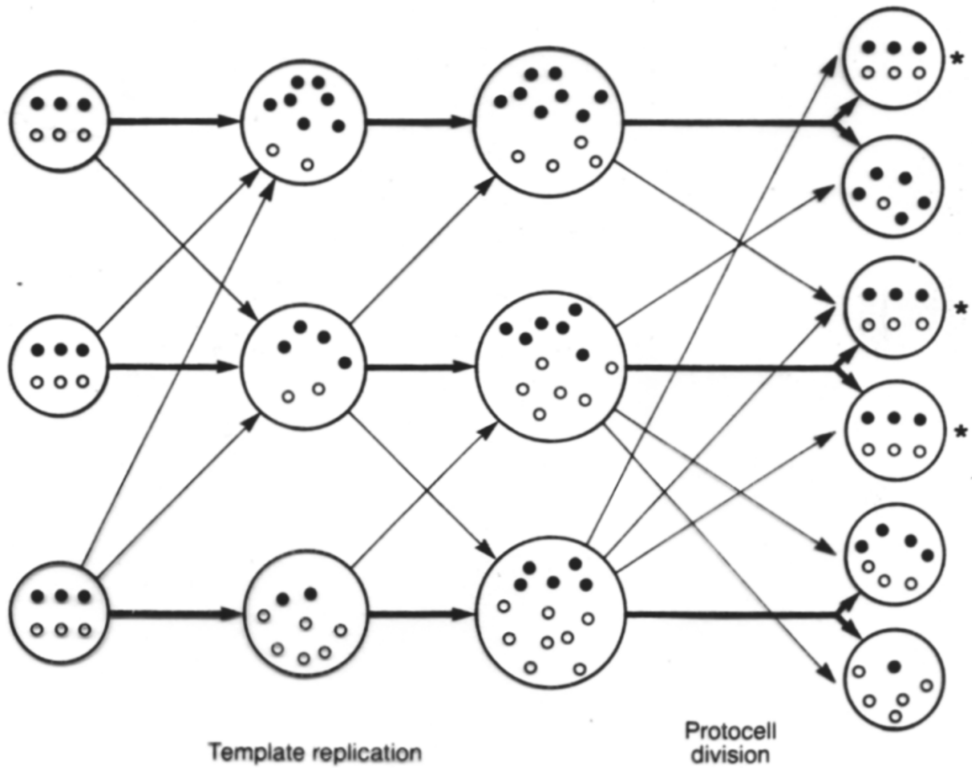
Result: master cell ($x_i = y_j$) persists!

(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 stochistcity)
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



NB timescales of micro vs macro dynamics

Micro and Macro level dynamics: intricate implicit mutual interactions
Takeuchi and Hogeweg 2009

Micro level:
RP (replicator parasite system);
Parasite 2 states:
template (1-l), enzyme (l);
Evolutionary Unstable

Macro level:
(1) implicit: waves
(2) explicit vesicles:
— folded l $->$ vesicle growth
— "modified" fixed size
death: # mols

Vesicles: CPM cells: volume
replicators at microlevel

$$(a) \quad R+R \underset{1-k_R}{\overset{k_R}{\rightleftharpoons}} C_R \overset{\kappa\theta}{\rightarrow} 2R+R,$$

$$L+R \underset{1-k_L}{\overset{k_L(1-l)}{\rightleftharpoons}} C_L \overset{\kappa\theta}{\rightarrow} 2L+R,$$

$$(b) \quad R,L \overset{d}{\rightarrow} \theta,$$

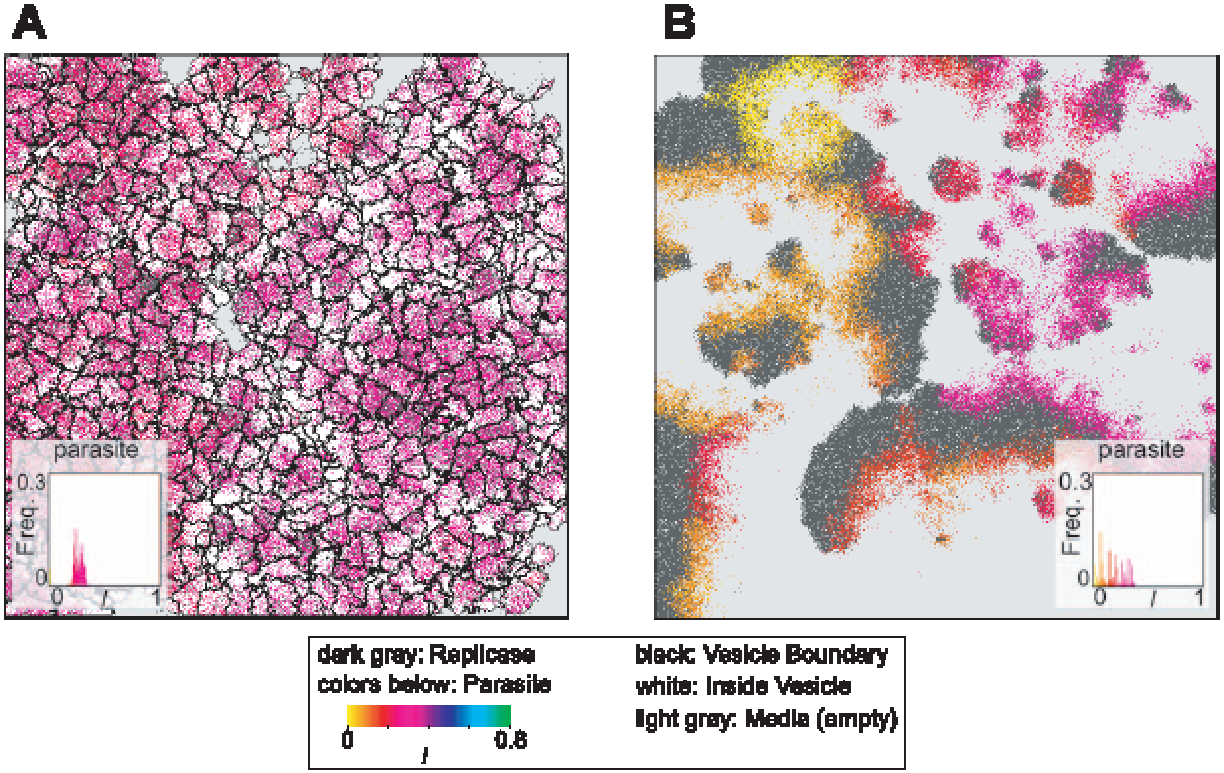
$$C_R \overset{2d}{\rightarrow} R+\theta,$$

$$C_L \overset{d}{\rightarrow} R+\theta,$$

$$C_L \overset{d}{\rightarrow} L+\theta,$$

$$(c) \quad L \overset{ml}{\rightarrow} L+x,$$

the 2 models

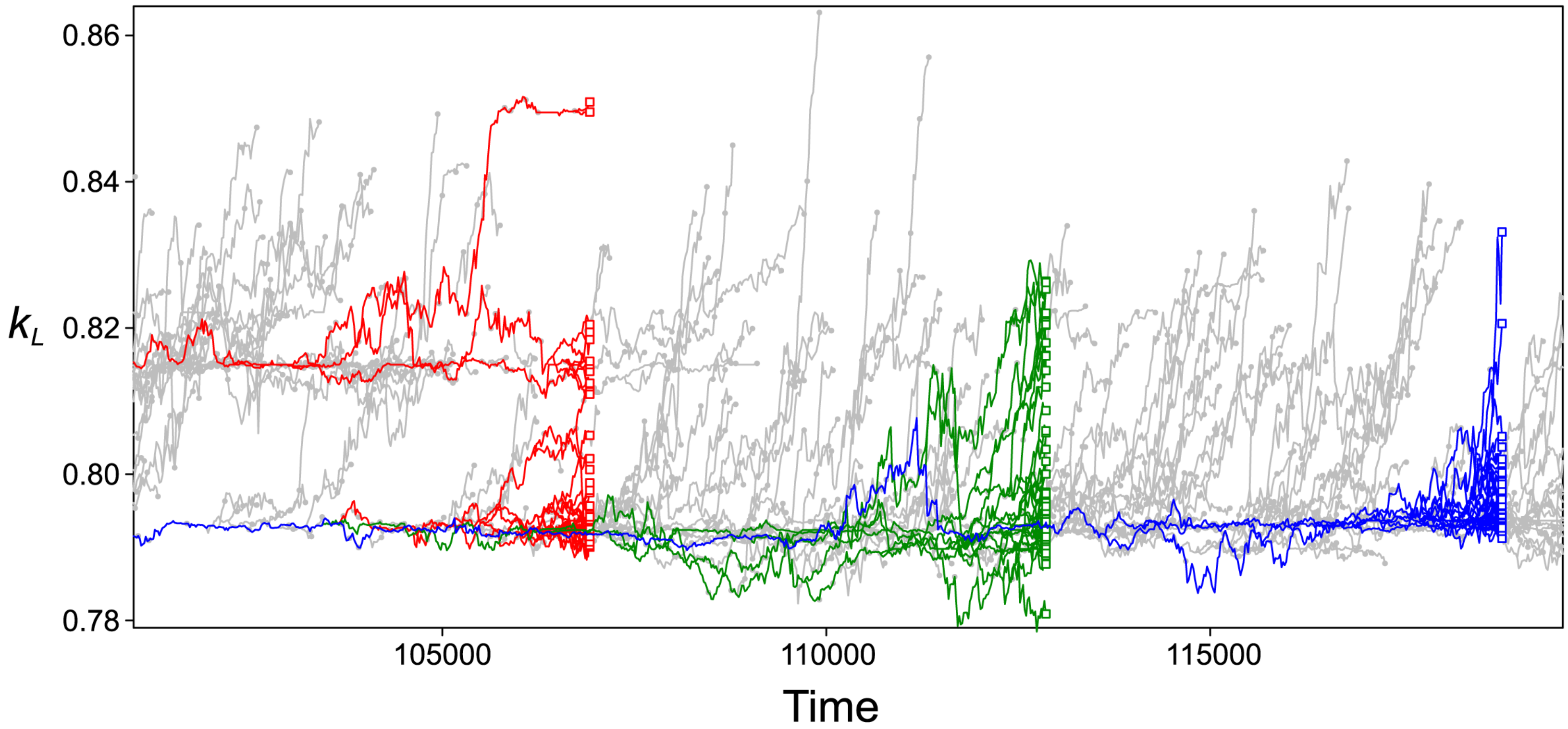


evolutionary dynamics

minimizes death rate
of vesicles

maximizes birth rate
of waves

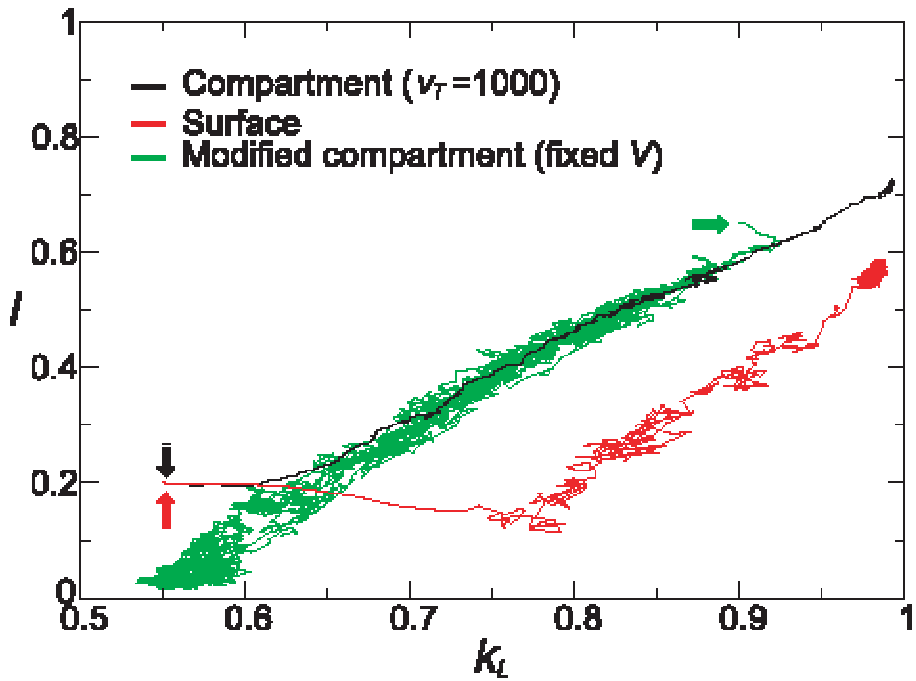
vesicle model: micro vs macro level selection

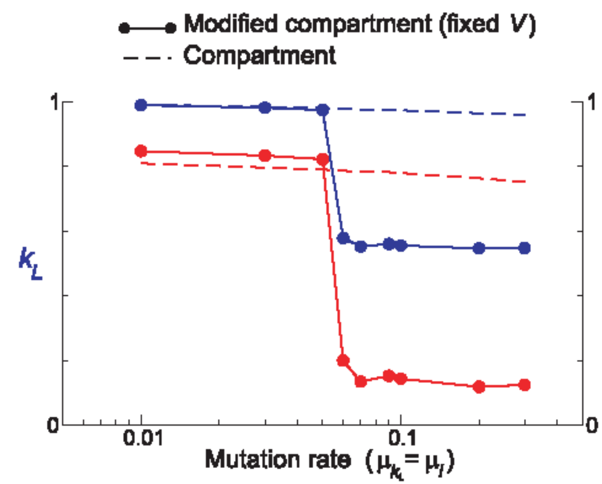


Only K_L evolves; l=0.5 vT=1000 $K_R = .6; d = 0.02$

evol rate of microsystem FAST relative to vesicle lifetime

evolutionary trajectories: emergent trade-off and long term evolution

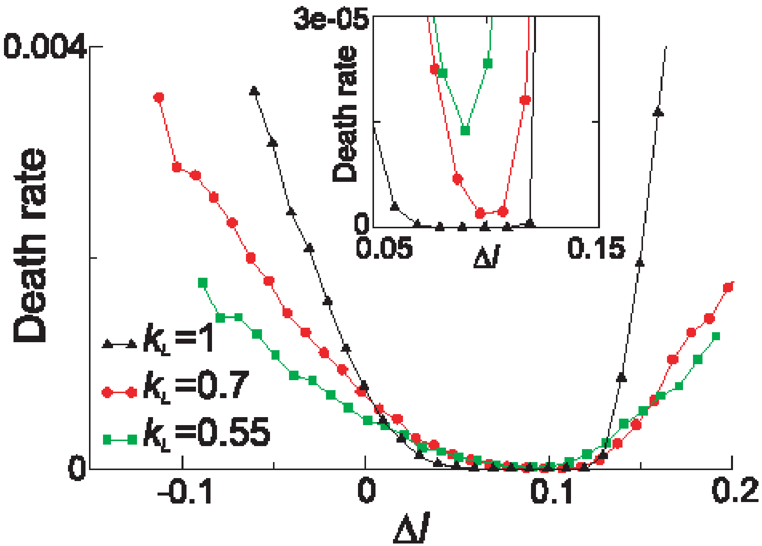


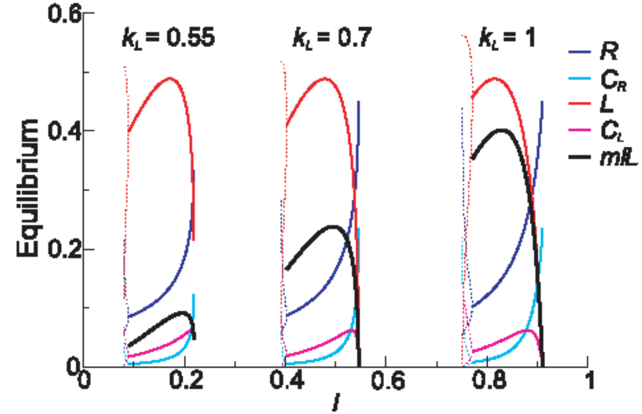


If lipid NOT needed for vesicle growth reversal of long term evolution trend *at high mutation rates*

'modified' vesicles
death rate of vesicles vs distance to replicator bifurcation

(constant vesicle size; death if no mol. or no L in vesicle)





Δl from bifurcation point

survival of the FLATTEST at high mutation rates

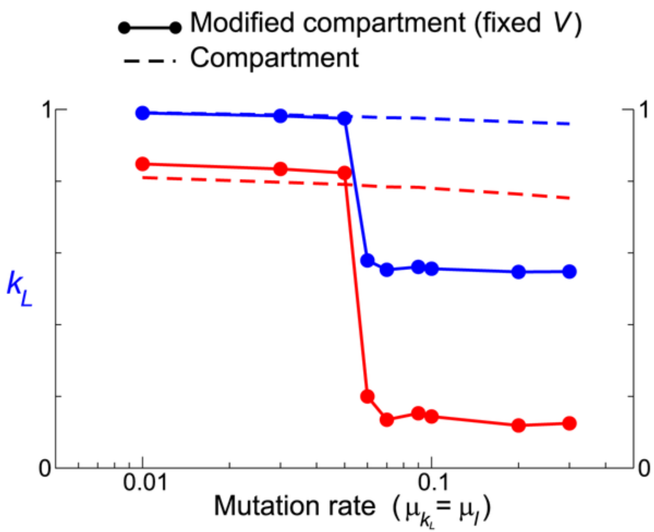
minimization of Death rate - max. of stoch.

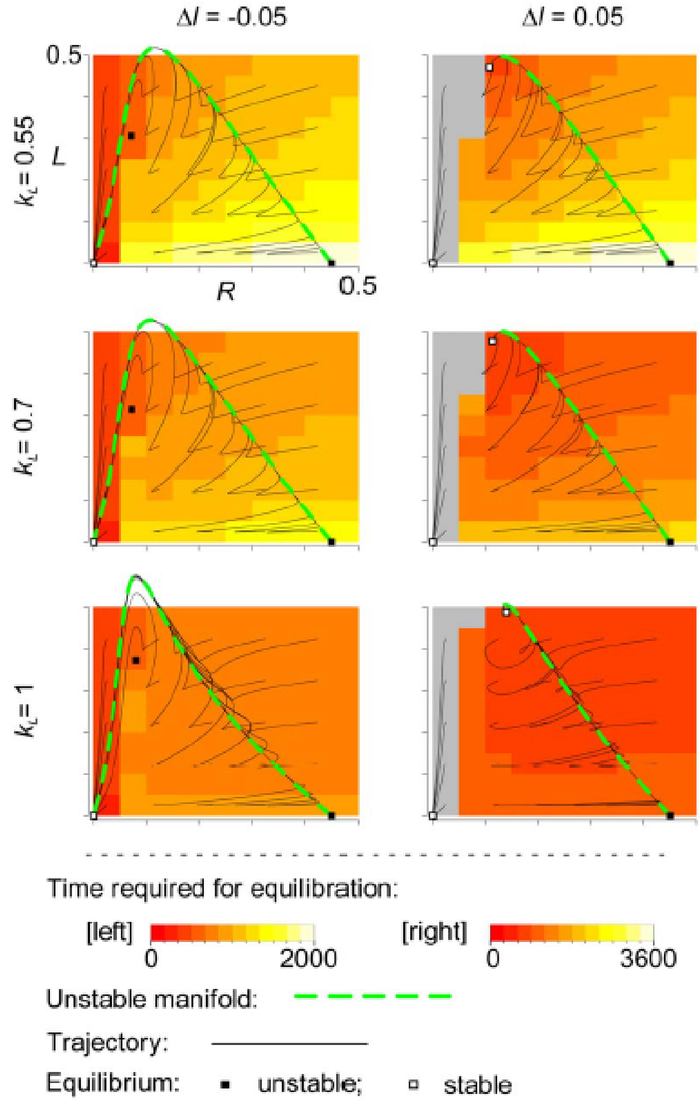
internal dynamics $->$ vesicle death rate

Modified vesicles:
Evolution of the flattest at high μ
evolution of the fittest at low μ

High μ cells are in unstable regime
evolve slow deterministc dynamics
$->$ high stochisticity - correction

Low μ stoch corrector keeps cells
in stable regime; fast dynamics minizes
stochisticity/death





maximization of stochasticity!

conclusion: comparison emergent and imposed levels of selection

- Higher level of selection: waves or vesicles
- Emergent trade-off for both models
- self-organized levels of selection more stable(!)
  $->$ Maximize birthrate (= rate of growth of replicators alone
- imposed higher levels: less stable
  especially at high mutation rates
  – slow down internal dynamics – minimize death rate
  – maximize stochasticity $->$ Stochastic correction

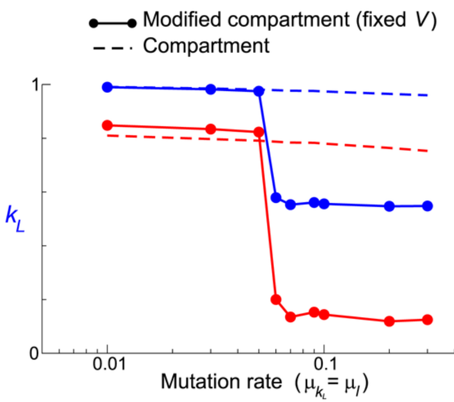
Implicit interactions in explicit multilevel models automatically mutually tunes "parameters"

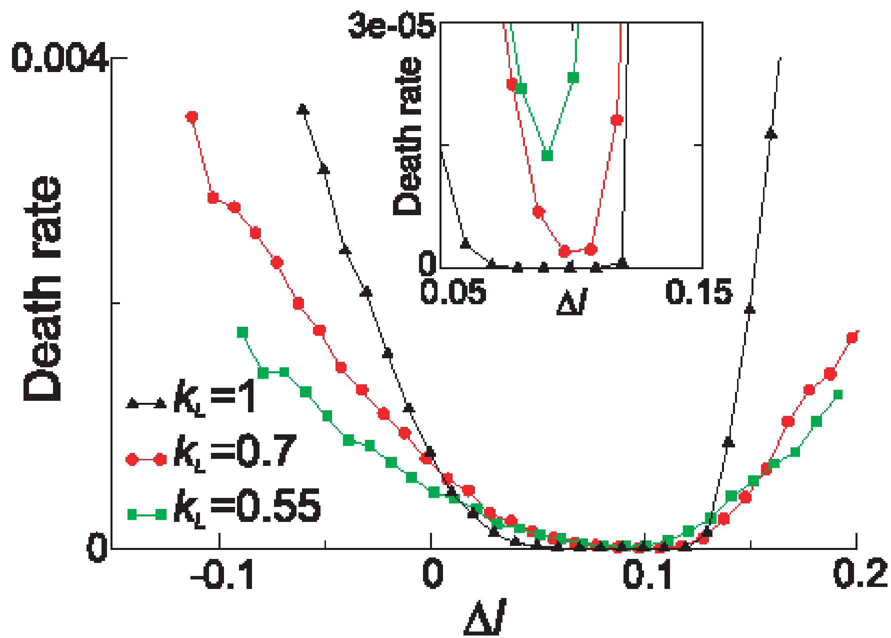
Evolution of the flattest at high μ .—. Evolution of the fittest at low μ

Automatic tuning of timescales by evolution in RP model in (CPM) vesicles

internal dynamics $->$ **vesicle death rate** High μ cells are in unstable regime
evolve slow deterministc dynamics
v $->$ high stochisticity - correction

Low μ stoch corrector keeps cells in stable regime; fast dynamics minimizes stochisticity/death





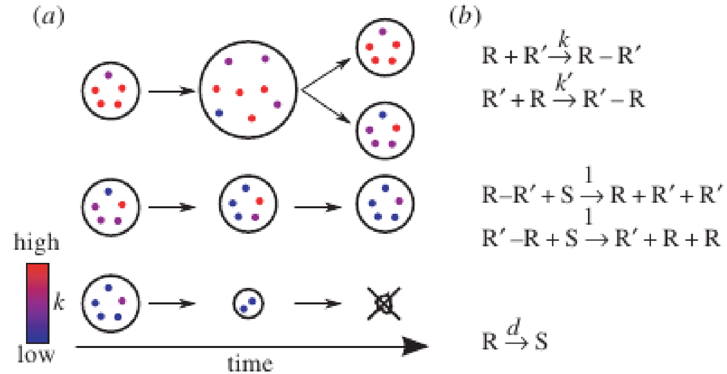
stable disequilibrium: endless dynamics of evolution in a stationary population (Takeuchi et al 2016)

Replicator model within cell
(:NO parasites)

Minimization of catalysis
within cell

Maximization of cat. between cell

Internal dynamics: $-- >$ extinctio



competition for substrate
high diffusion between cells

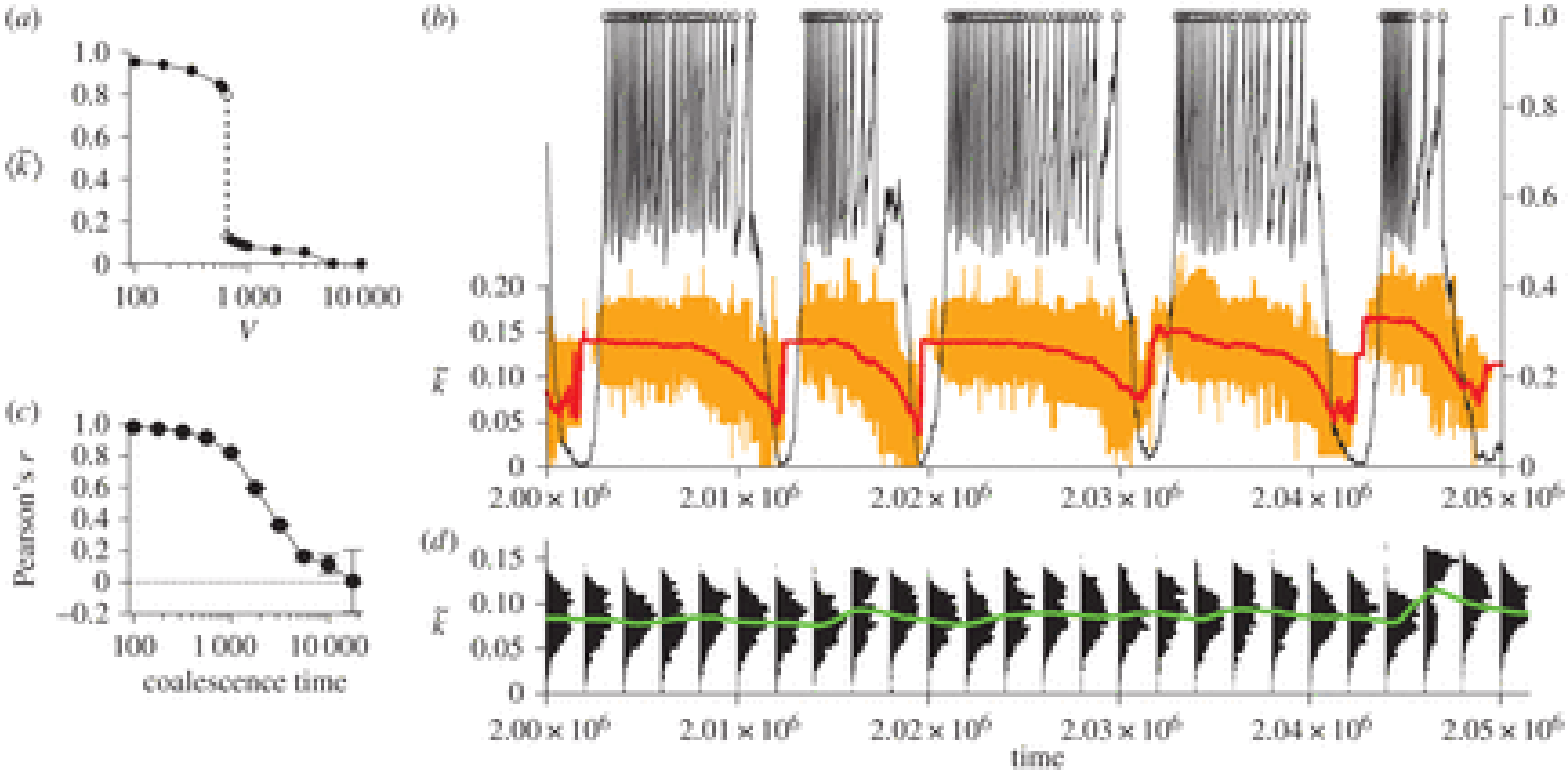
individual based, non-spatial model

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)

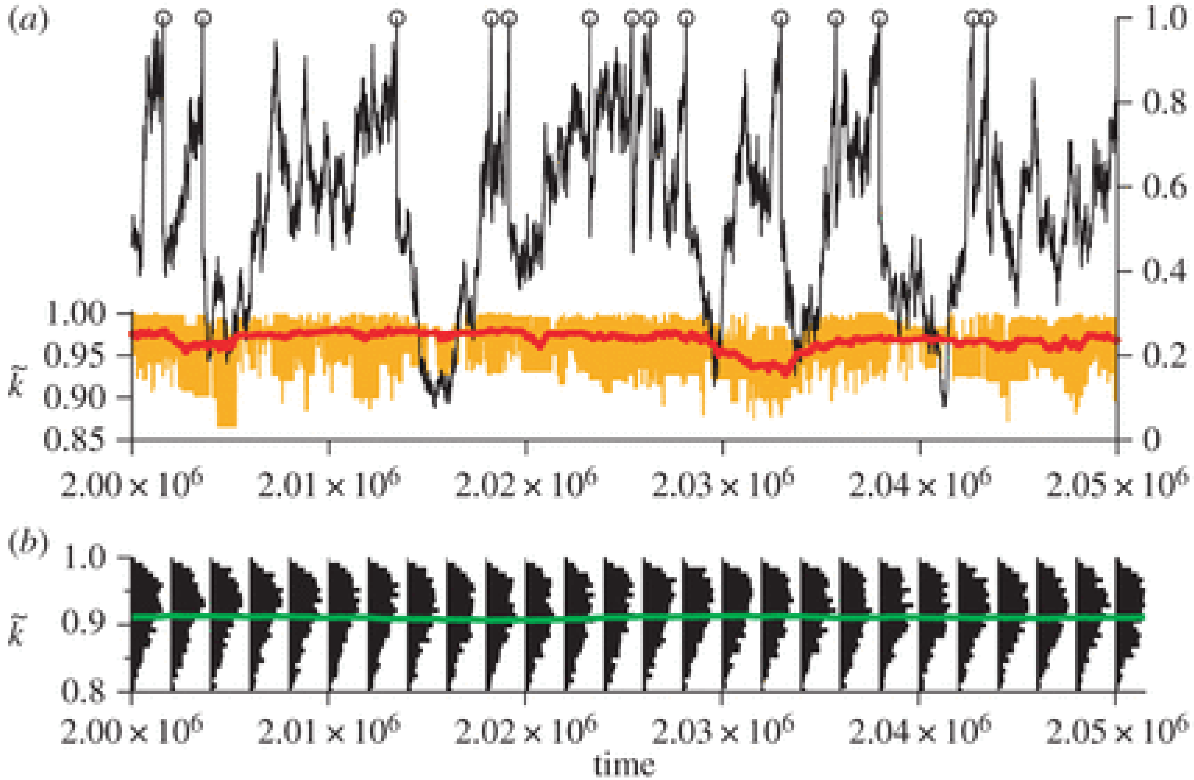
How does evolutionary dynamics cope with large cells?

Evolutionary dynamics along line of decent: evolutionary stable disequilibrium for large cells



V=1000

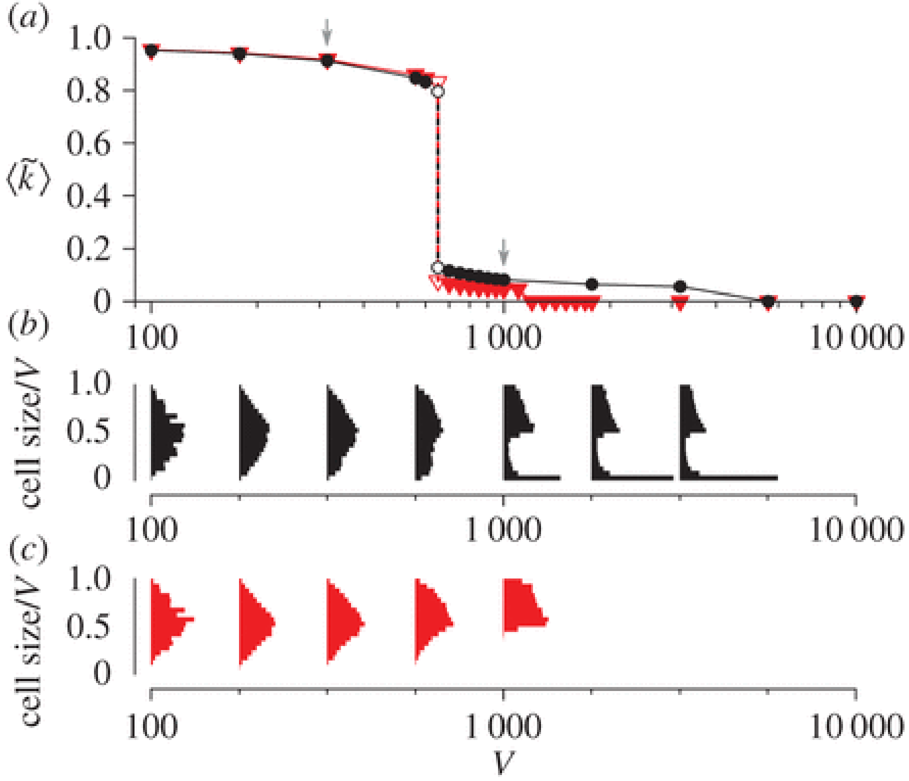
Evolutionary dynamics along line of decent: stochastic correction for small cells



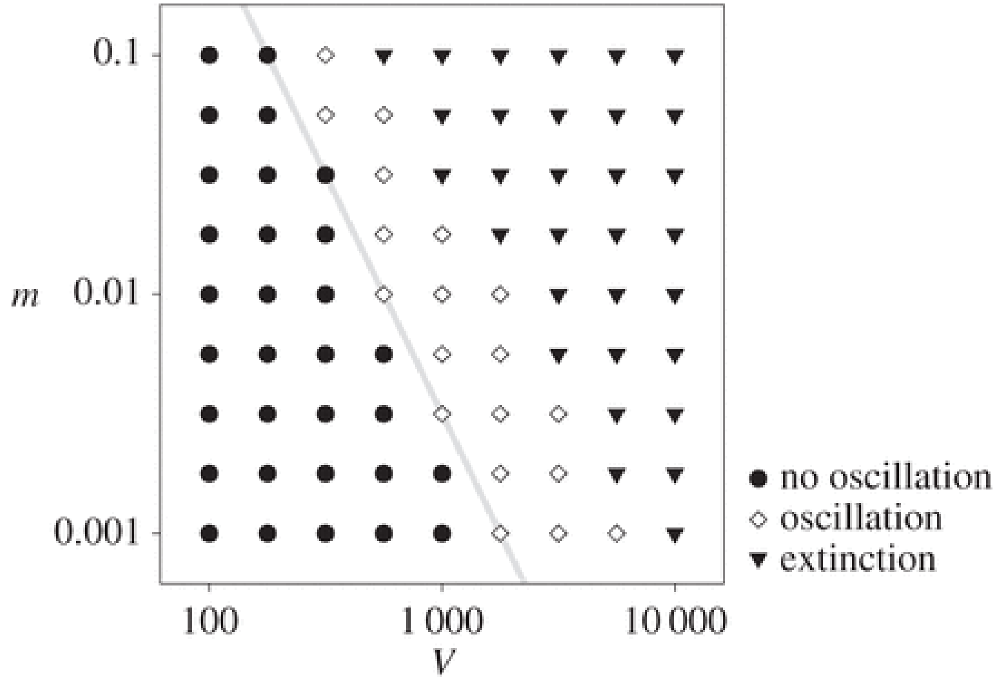
V=317

Coping with large cells by becoming small increase stochasiticy

Add extra selection
by killing small cells
only smaller cells survive



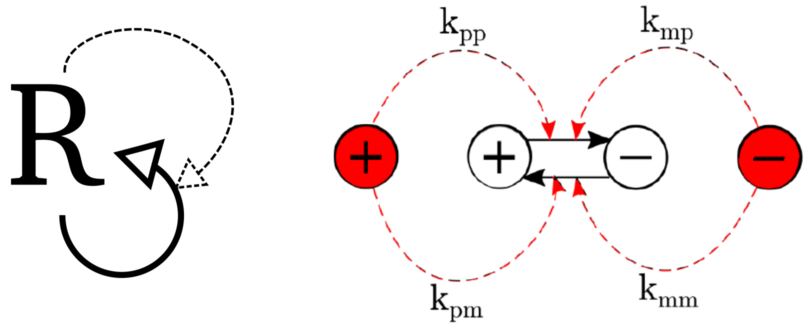
conclusion: conflict of levels of selection
if similar strength: "creative solution"



Within vesicle selection strength mV
Between vesicle selection strength 1/V
If mV $1/V$ $->$ $mV^2 = C$ - oscillating internal dynamics.

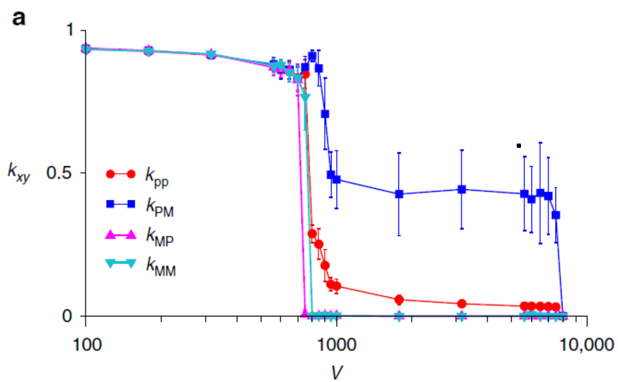
exploring evolutionary properties/advantages of more RNA-like replicators in RP systems (i.e. more degrees of freedom)

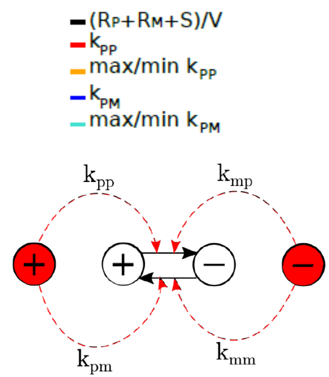
- **Direct replication vs Complementary replication**

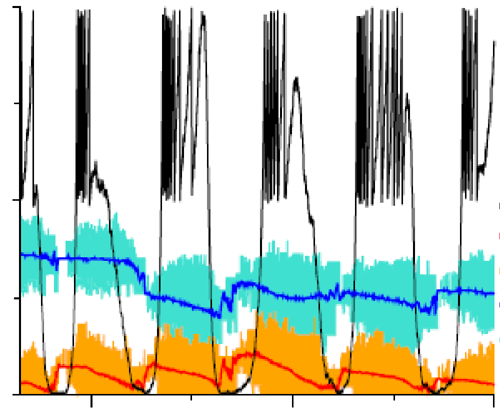


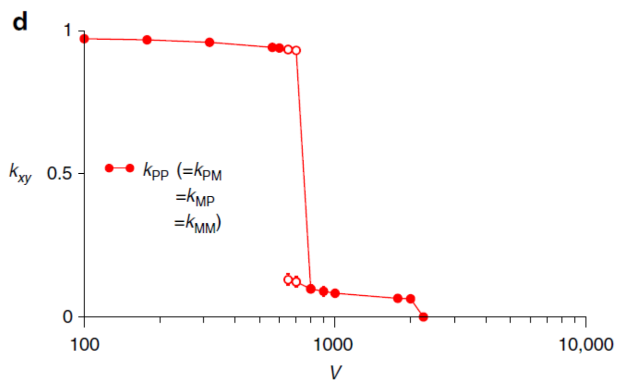
imposed levels of selection: protocells
direct vs complementary replication
symmetry breaking and robustness to larger cells

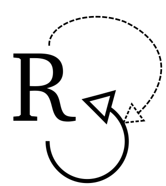
evolutionary attractors — **ancestor trace: bottlenecks**

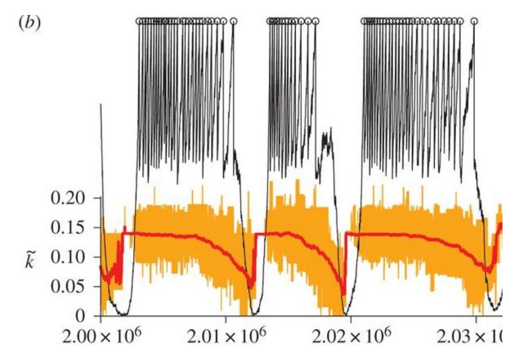






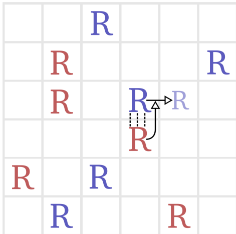




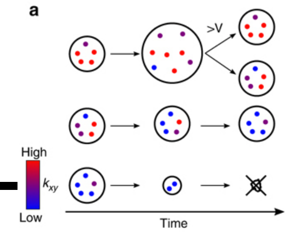


Evolutionary stable disequilibrium, and origin of 'primordial genome'

Takeuchi et al 2016, 2017;

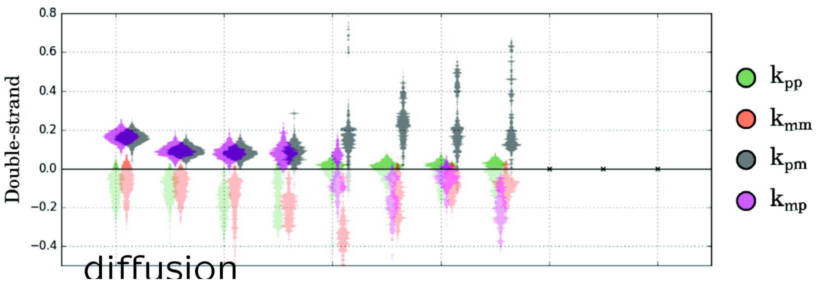


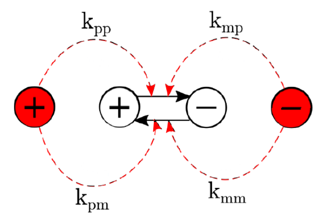
(emergent) multilevel evolution division of labor

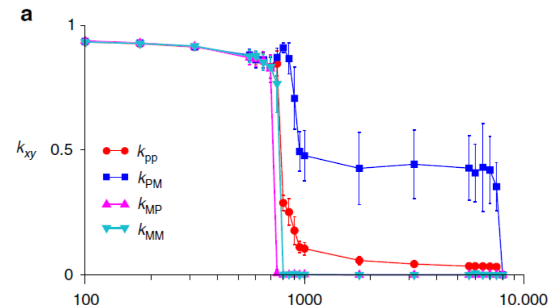


SPACE

Protocells

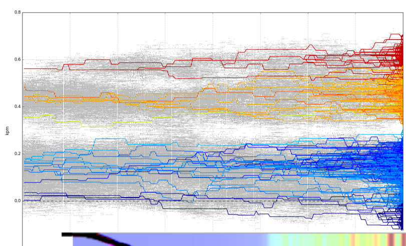


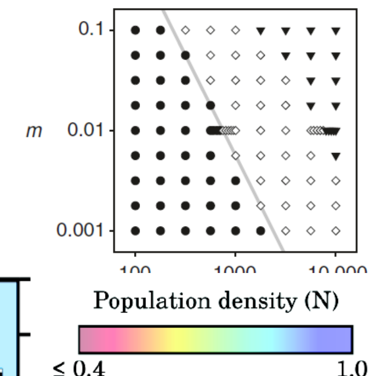


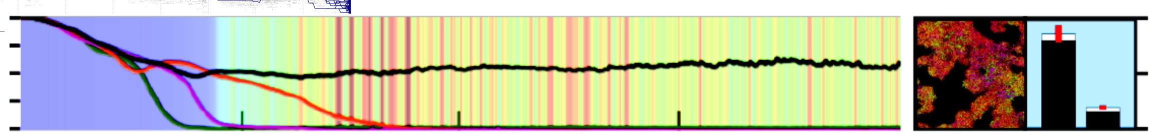


V

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

Multilevel evolution and replicator strategies protocells vs spatial self-organization

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

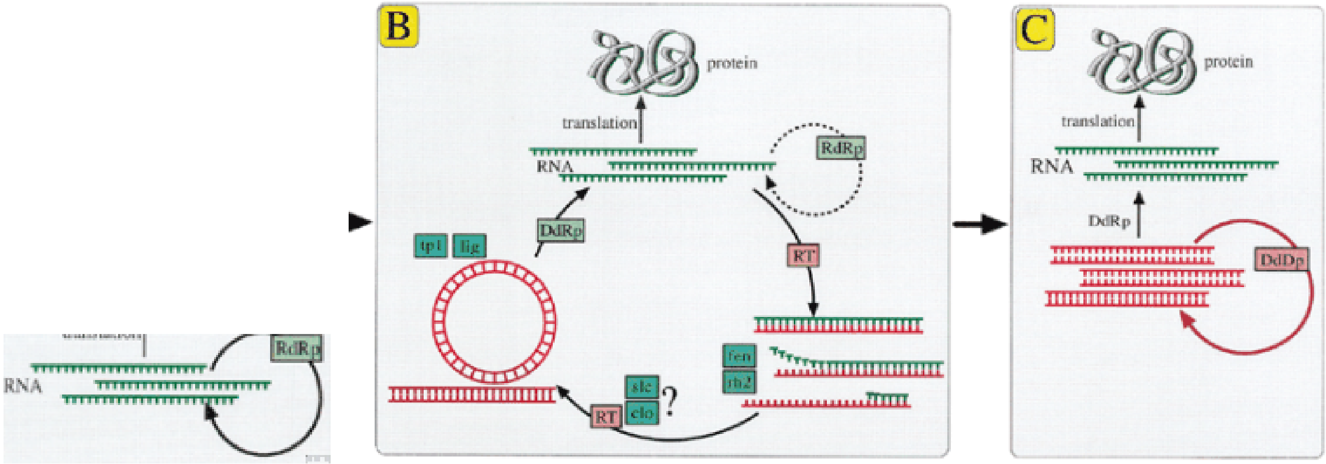
Template in Minority

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-sufficieny - selfreplication (?)
- Evolution of slower replication cycle

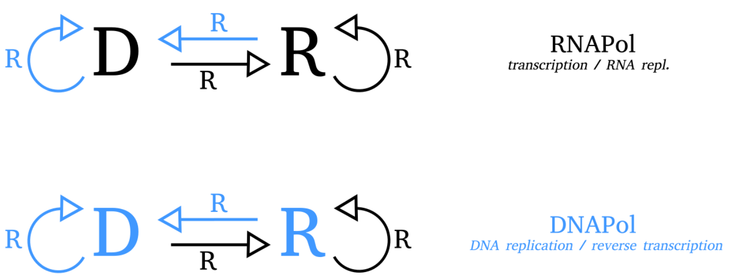
Takeuchi et al 2011 On the Origin of DNA Genomes: Evolution of the Division of Labor between Template and Catalyst in Model Replicator Systems

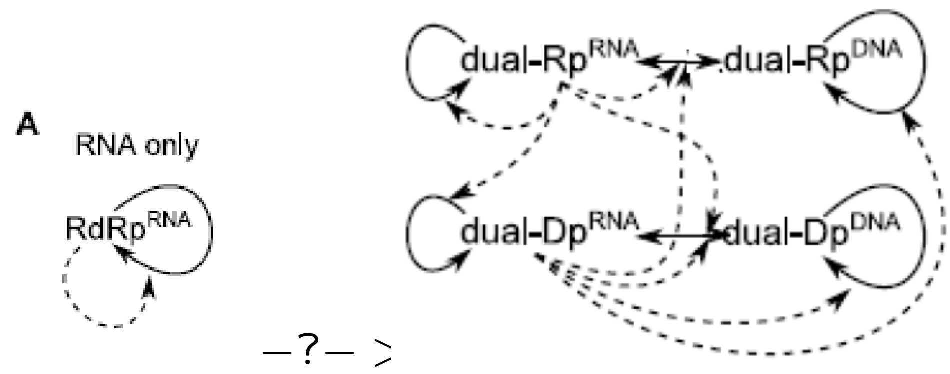
the model

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

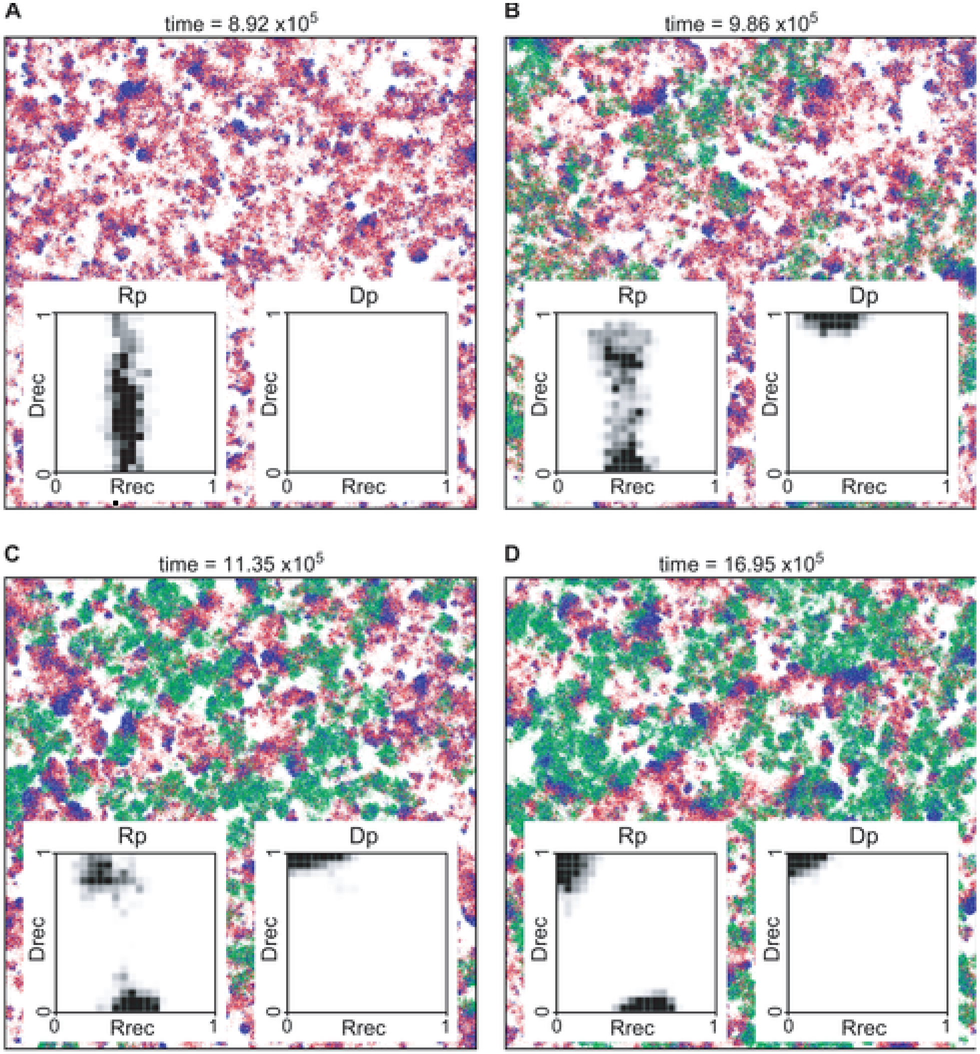
both can recognition RNA and/or DNA (binding evolvable parameter)

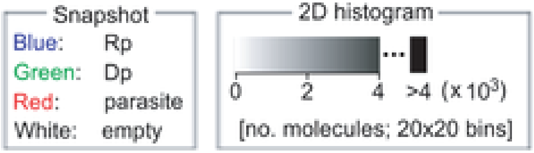


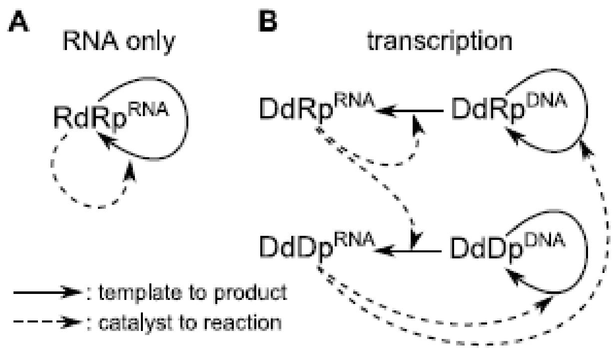


- **Can DNA establish itself in an RNA world** *in evolutionary equilibrium*
- **If so WHY (longer replication cycle)**
- **Which type of specificity evolves?**

evolutionary trajectory in spatial system





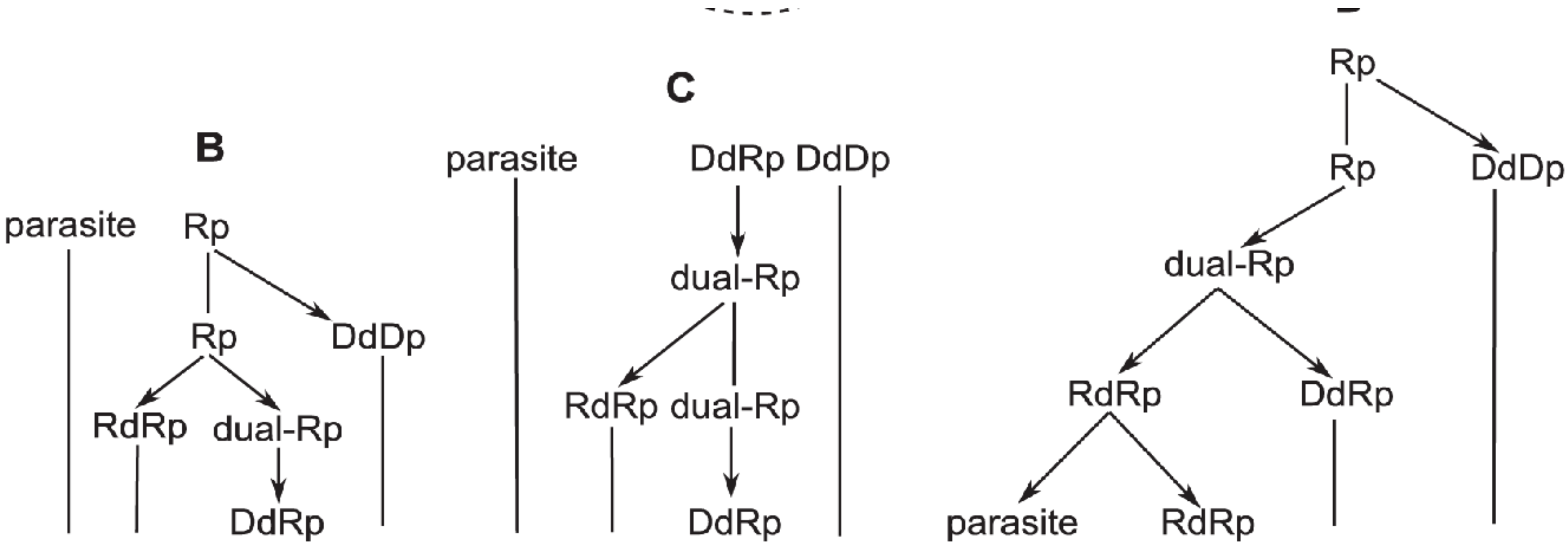


Experiments to test causes and consequences

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

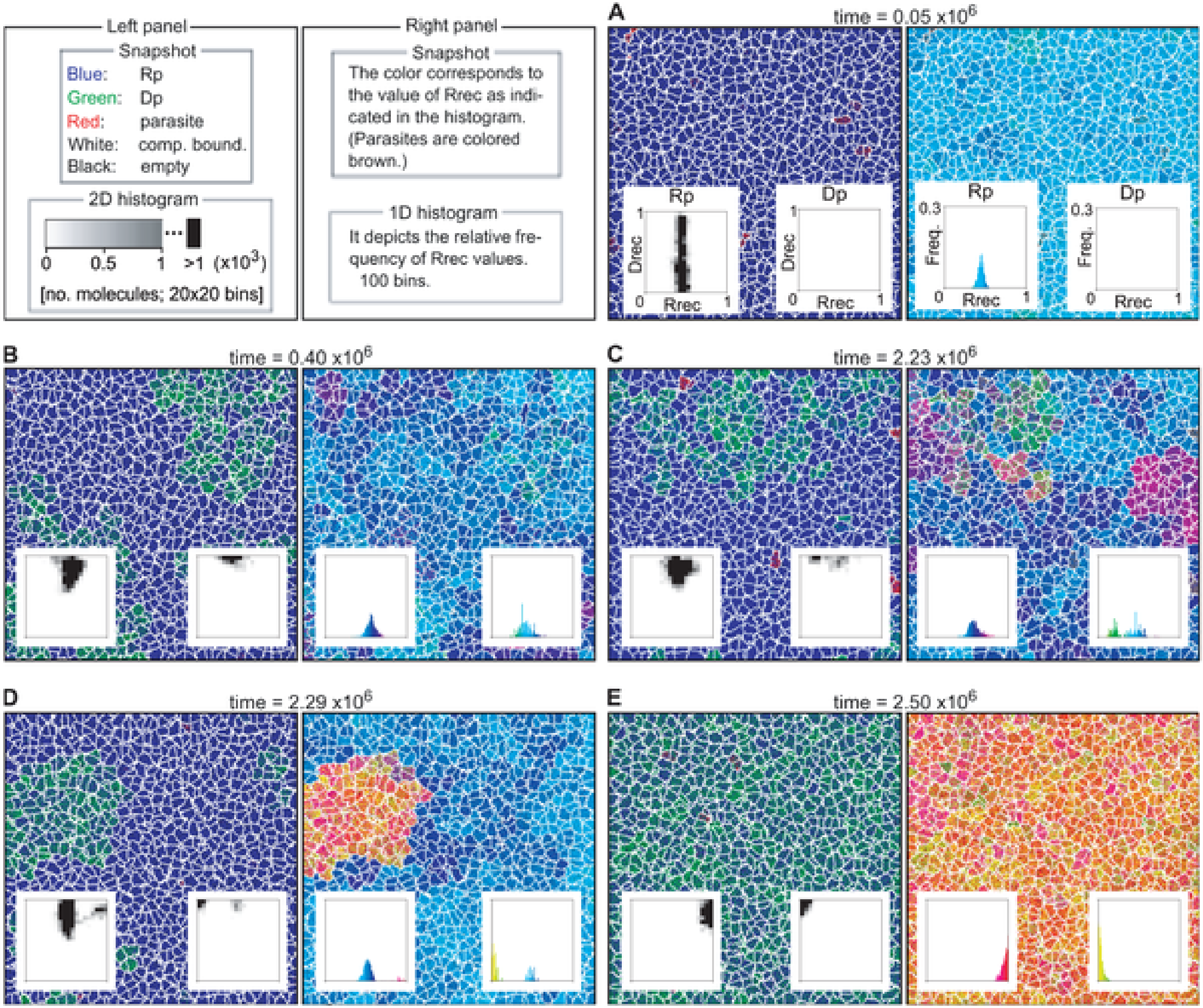
doi:10.1371/journal.pcbi.1002024.t001

alternative routes to same evolutionary attractor transcription system + RNA selfreplication

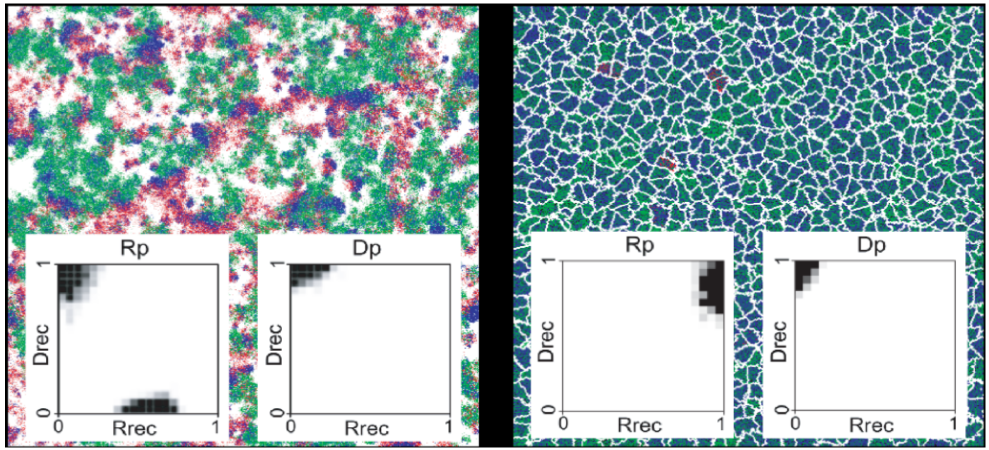


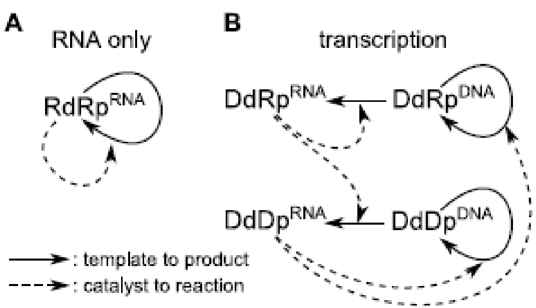
- evolved transcription system **B** killed when parasites are removed However when started without parasites **D** transciption system evolves and finally evolves parasite lineage as well.
- Transciption system without selfreplication **C** re-evolves selfreplications system. Without reverse transcriptase stable attractor.

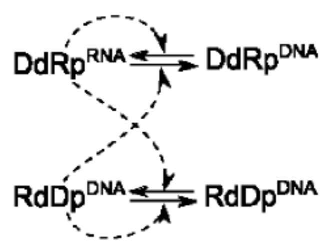
Evolutionary trajectory in vesicle system (CPM)

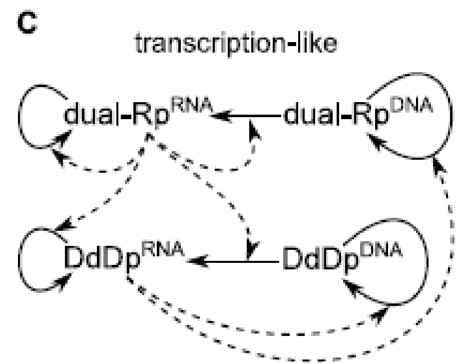


RNA replication AND + Transcription system in vesicles and in surface system however dual functional RNA polymerses in vesicles





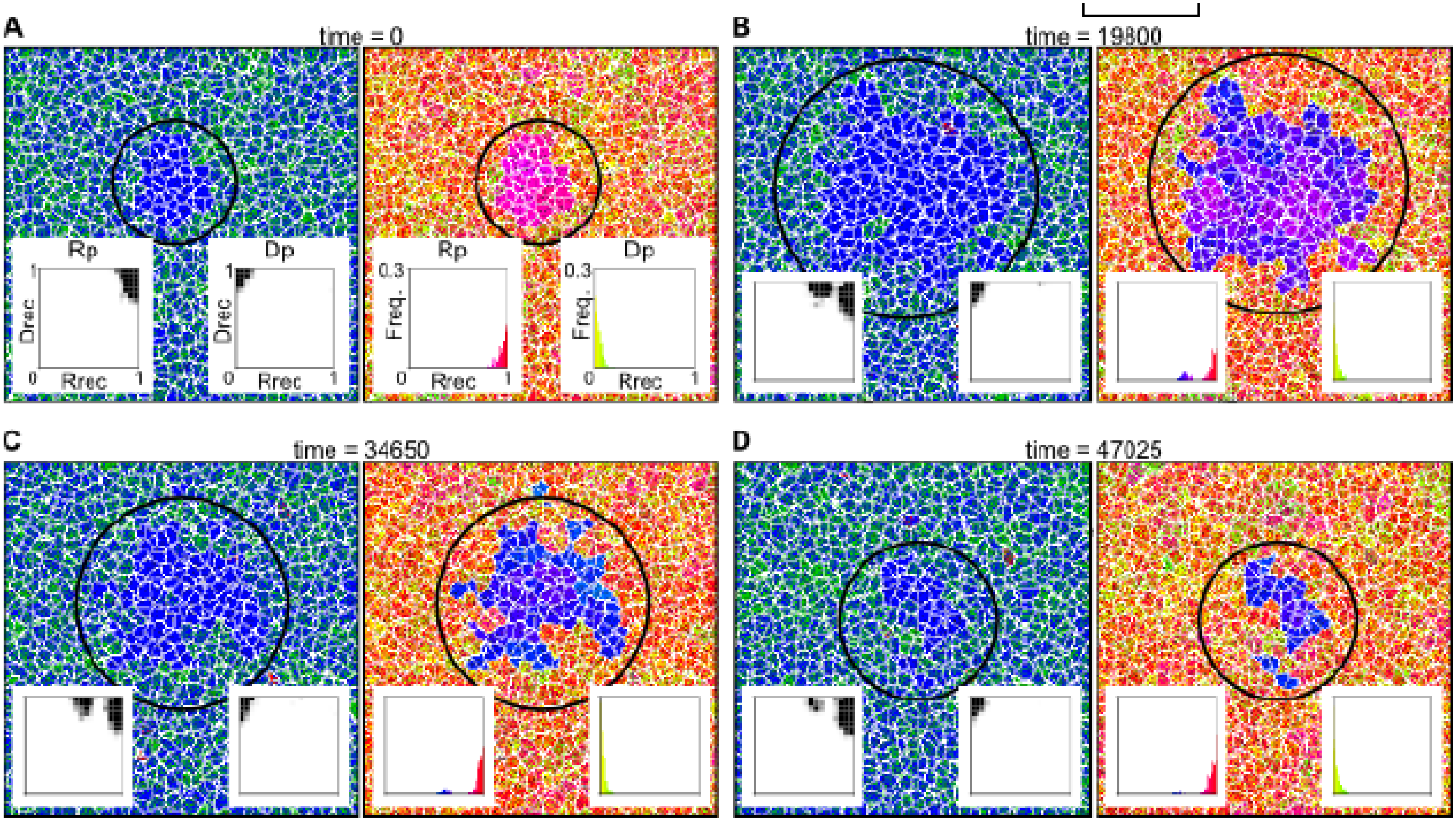




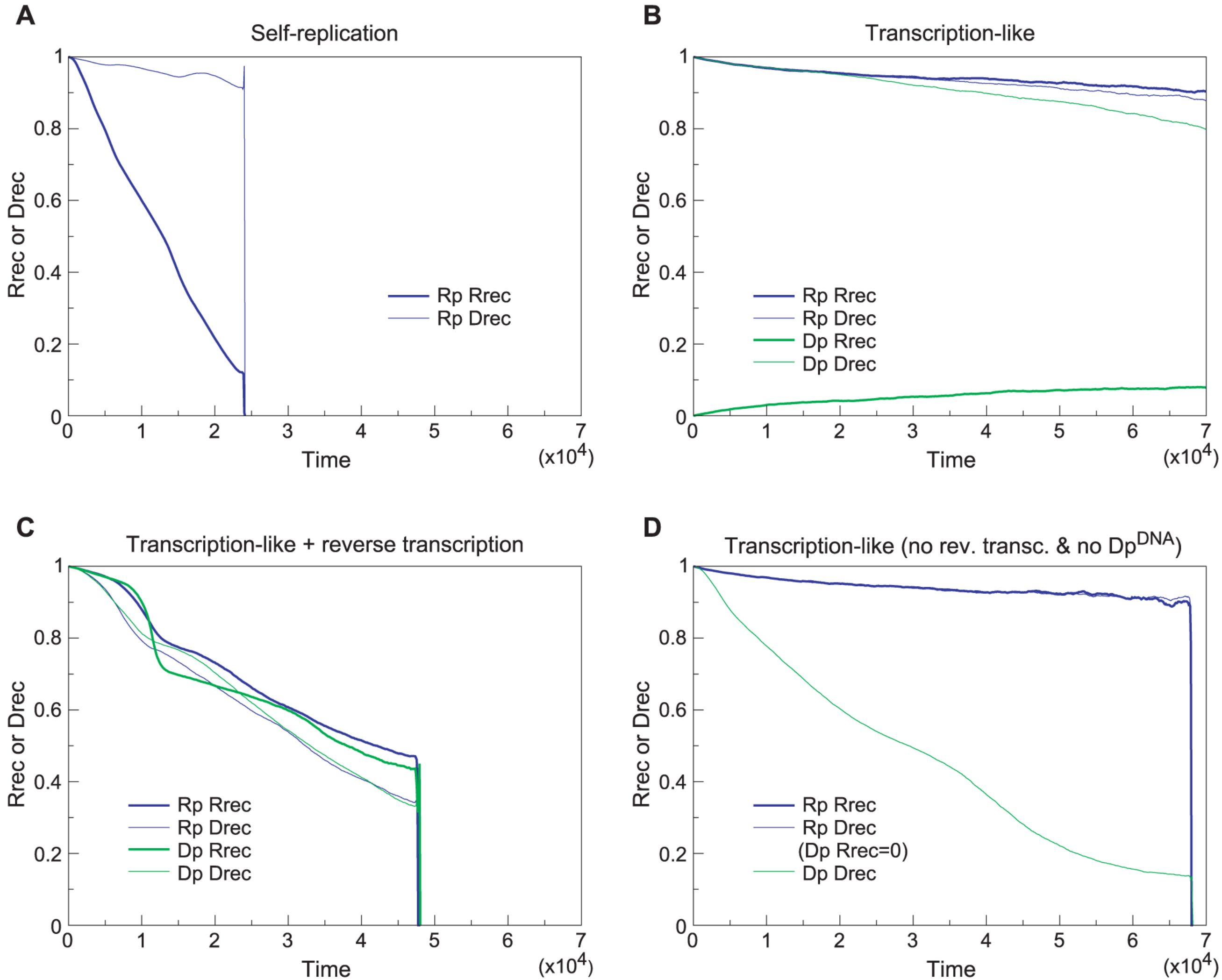
. **NO (minimal)** reverse transcription: DNA common ancestor

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 stabilsation of NON-catalytic DNA in RNA world

Toward similar attractor when started with fully symmetric system?

Unidirectional information flow?

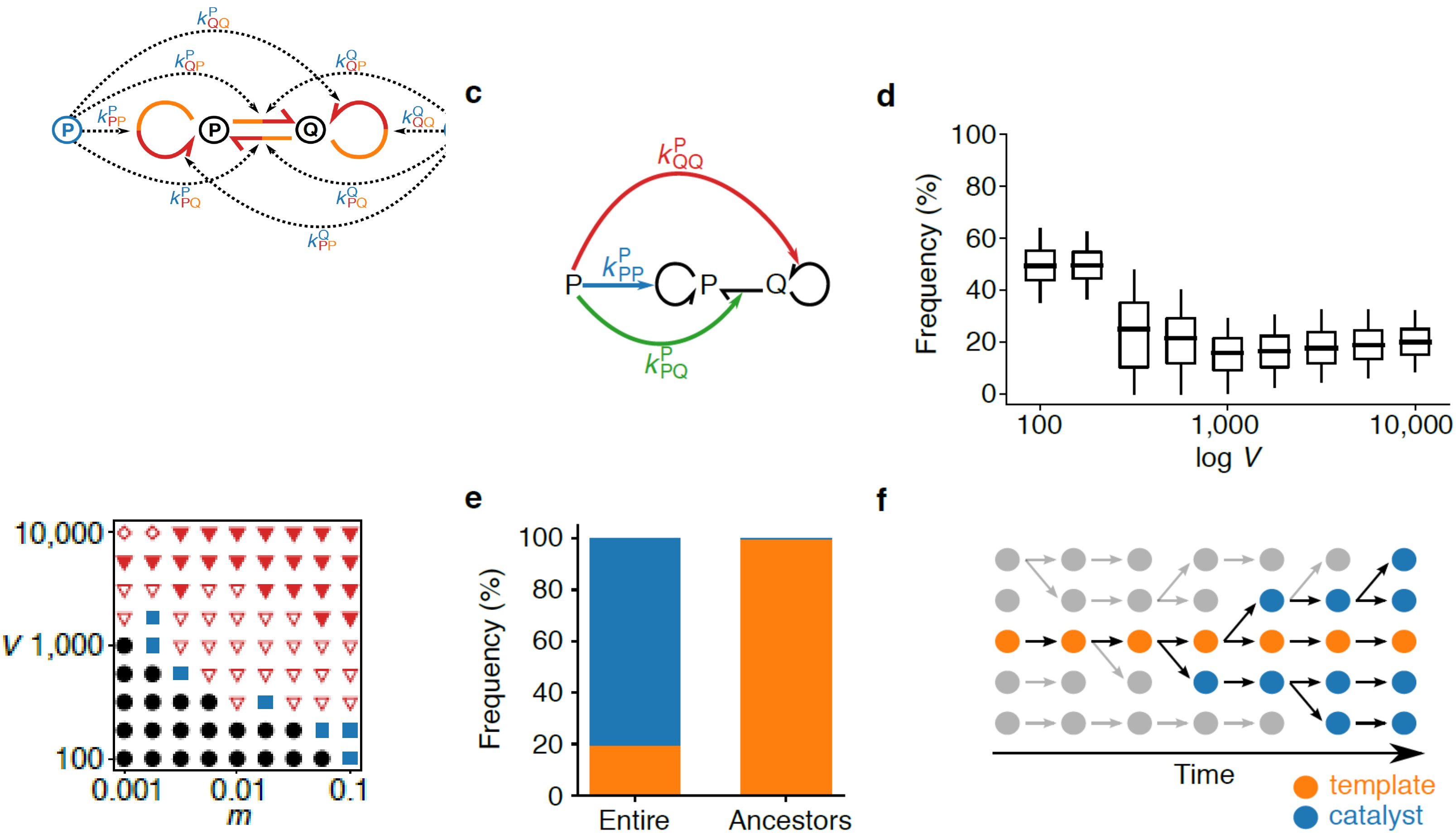
"Crick's dogma "from DNA to RNA to proteins" is not a dogma anymore" (Nobuto Takeuchi)

The origin of the central dogma through conflicting multi-level selectio Nobuto Takeuchi and Kunihiko Kaneko 2019

symetric
Initial catlysis

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.

hierarchy		**differentiation**	
whole	**parts**	**information**	**other**
cell	molecules	genome	enzyme
symbiont population*	prokaryotic cells	transmitted	non-transmitted
ciliate	organelles	micronucleus	macronucleus
multicellular organism	eukaryotic cells	germline	soma
eusocial colony	animals	queen	worker

*Bacterial endosymbionts of ungulate lice (*Haematopinus*) and planthoppers (*Fulgoroidea*) [38].

Takeuchi & Kaneko 2019

conclusion: division of labor

Spatial systems with local interactions or imposed multilevel sytems prevent evolutionary collapse of cooperative replicating systems

but only to the level of 'viability': they do minimize contribution to 'common good' (in RNA world giving catalysis)

Such evolutionary minimization of 'work' can be prevented by division of labor

3 modes of Division of labor help cope with harsh circumstances

- Ecosystem based: evolution of "parasites"
- Individual based: evolution of template vs catalyst
- Unidirectional information flow: inheritance via non-worker (DNA).

  Evolutionary stabilization (a long term effect) can indeed evolve! (even if lower replication rate)

  Conflict resolution between levels of evolution

Slower replicators "out-evolve" faster ones
complexity evolves because of evolutionary "benefit"