Selection Dynamics in Transient Compartmentalization

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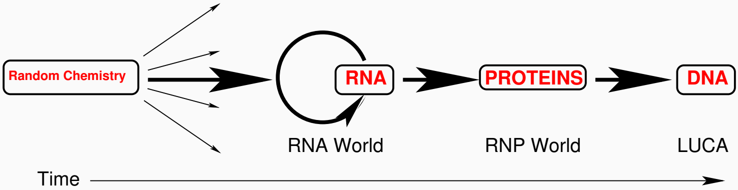
Motivation

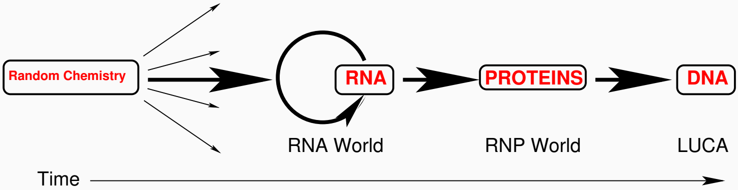
The RNA World hypothesis



- How could self-replicating molecules maintain their activity, in spite of inevitable replication errors?
- How could functional molecules overcome their disadvantages wrt non-functional (but faster-replicating) mutants?

Motivation

The RNA World hypothesis



- How could self-replicating molecules maintain their activity, in spite of inevitable replication errors?
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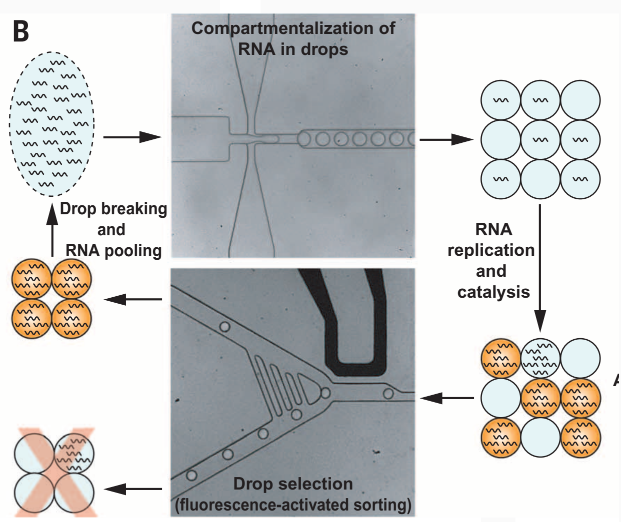
COMPARTMENTALIZATION

The Questions

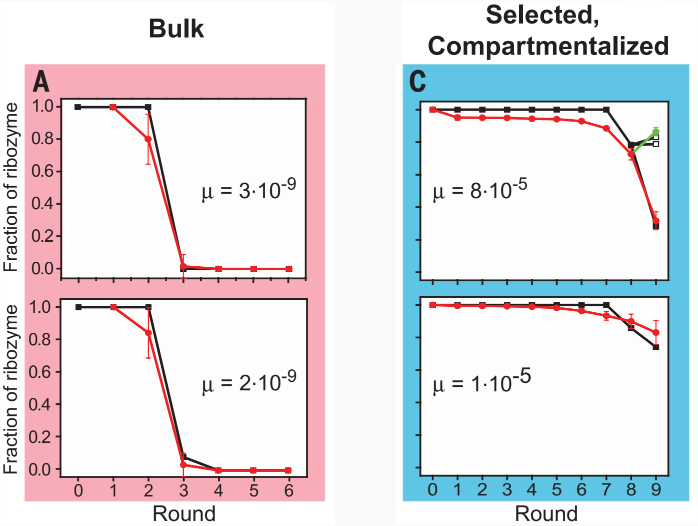
- Can transient compartmentalization be sufficient to maintain active ribozymes in the presence of fast-replicating parasites?
- Which quantities determine success or failure of the process?

Experiment Scheme



MATSUMURA ET AL., 2016

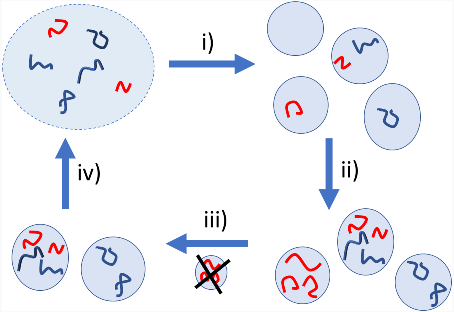
Experiment Results



Matsumura et al., 2016

The process

i) Inoculation
ii) Maturation
iii) Selection
iv) Pooling



Inoculation

- Droplets are initialized with a large number (N_{e}) of Qβ enzymes, and activated nucleotides
- Droplets are seeded with n RNA templates: n is Poisson-distributed with average λ
- RNA templates come in two kinds: ribozymes and parasites
- In a given droplet there are initially m ribozymes and $y = (n - m)$ parasites (m is random, of average λx)
- x: fraction #ribozymes/#RNAs in the solution (at the end of the previous round)
- We neglect mutations producing new parasites (mutation rate is very small)

Maturation

- RNAs initially replicate autocatalytically: $n(t) \sim \exp(t)$ (*exponential phase*)
- Parasites replicate faster than ribozymes: $m(t) \simeq m\,\mathrm{e}^{\alpha t}$, $y(t) \simeq y\,\mathrm{e}^{\gamma t}$, $\gamma > \alpha$
- When $n(t) \simeq N_{\mathrm{e}}$, Q$\beta$ is the growth-limiting factor: further growth is linear with time (*linear phase*)
- In the linear phase, the ratio $y(t)/m(t) =$ #parasites/#ribozymes remains constant
- At the end of the maturation phase, we have $m(t) = \bar{m}$, $y(t) = \bar{y}$, with

$$\frac{\bar{y}}{y} = \Lambda\,\frac{\bar{m}}{m} \qquad \Lambda > 1$$

- Thus given (x, m, n), one has

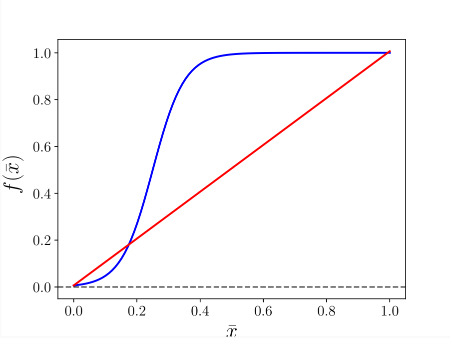
$$\bar{m} = \frac{N \cdot m}{n\Lambda - (\Lambda - 1)m} = N\bar{x}$$

$$\bar{y} = N - \bar{m}$$

Selection

- Droplets are selected according to the number $\bar{m}$ of ribozymes contained
- N: number of RNAs at the end of the maturation phase
- $\bar{x} = \bar{m}/N$: fraction of ribozymes
- Selection function:

$$f(\bar{x}) = \frac{1}{2}\left(1 + \tanh\left(\frac{\bar{x} - x_{\mathrm{th}}}{x_{\mathrm{w}}}\right)\right)$$



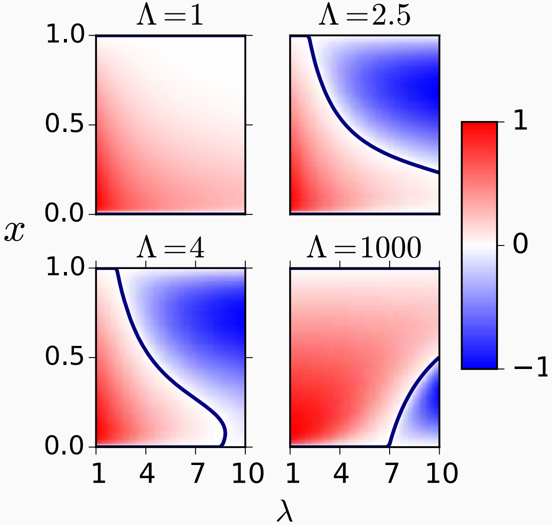
Pooling

- Each round k yields $x \longrightarrow x'$:

$$x' = \frac{\sum_{m,n} \bar{x}(m,n)\, f(\bar{x}(m,n))\, P(x|m,n;\lambda,\Lambda)}{\sum_{m,n}\, f(\bar{x}(m,n))\, P(x|m,n;\lambda,\Lambda)}$$

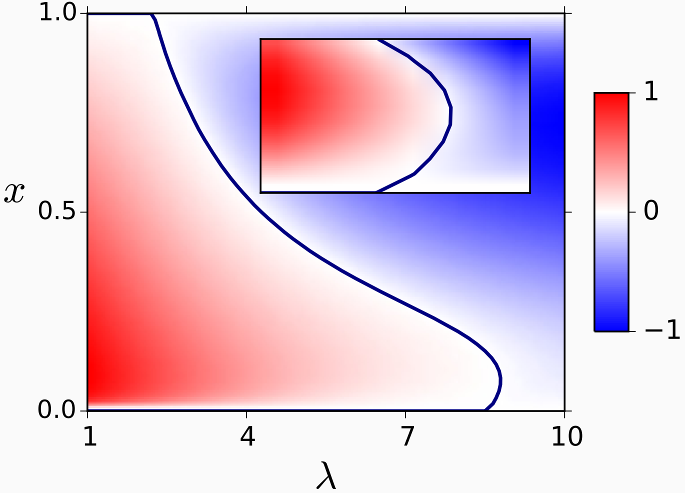
- Does x reach a fixed point as $k \to \infty$?
- Evaluate $\Delta x = x' - x$ vs. (λ, x) for fixed Λ

Δx vs. (λ, x)

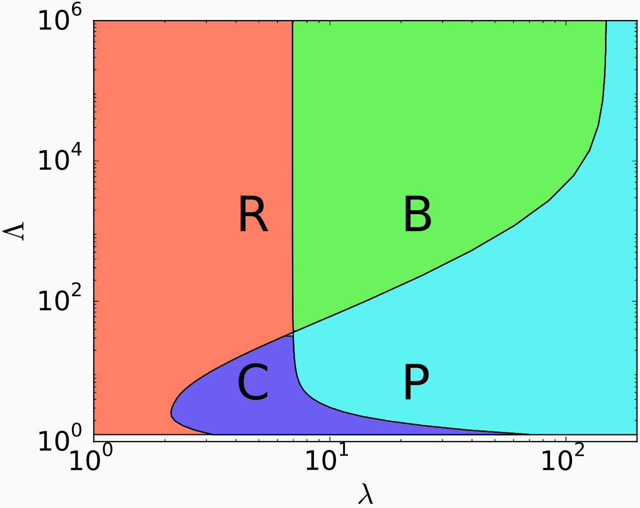


Dynamics

Δx vs. (λ, x) $\Lambda = 4$



Phase diagram



Asymptotes

$\Lambda \gg 1$: R-B line at λ_0: $\lambda_0 f(1) = \left(e^{\lambda_0} - 1\right) f(0)$ $(\lambda_0 \simeq 6.95)$

B-P line at λ_1: $\lambda_1 f(0) = \left(e^{\lambda_1} - 1\right) f(1)$ $(\lambda_1 \simeq 1.49 \cdot 10^2)$

$\lambda \gg 1$: R-C line at $\Lambda = 1 + (f'(1)/(f(1)\lambda)) + O(\lambda^{-2})$

C-P line at $\Lambda = 1 + (f'(0)/(f(0)\lambda)) + O(\lambda^{-2})$

The exact shape of $f(x)$ is not important

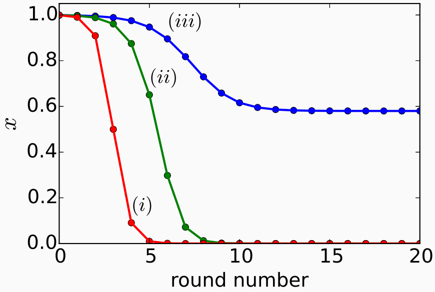
Population dynamics

$\lambda = 5$, $\Lambda = 10$ (C)

(i) No compartments

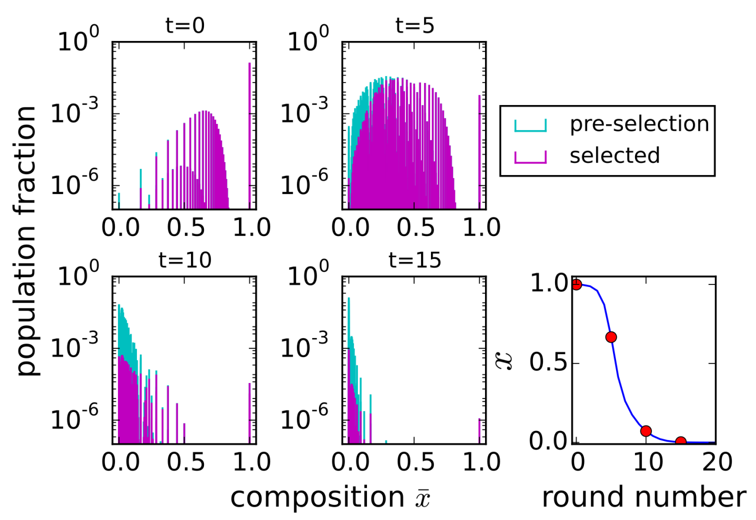
(ii) Compartments, no selection

(iii) Compartments with selection

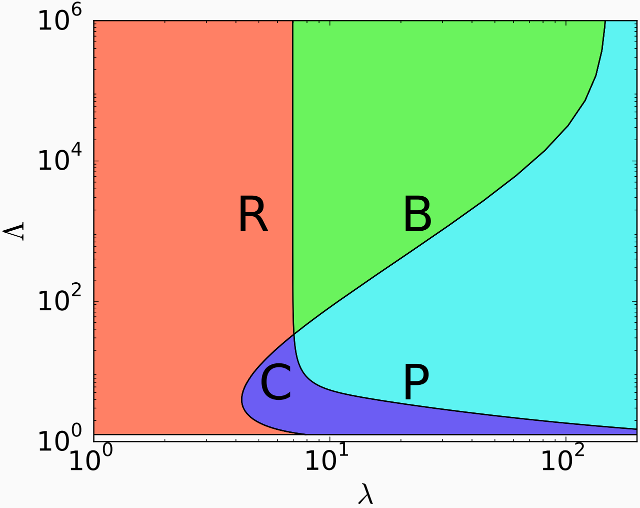


Population dynamics

$\lambda = 10$, $\Lambda = 5$ (P)



Linear Selection Function



Summary

- Transient compartmentalization with selection may succeed in purging parasites, provided λ is small enough (and selection is strong enough)
- Here selection is extrinsic but the same scenario applies to intrinsic selection (due, e.g., to cooperativity)
- Transient compartments may bridge the gap between metabolism-based (Oparin, Dyson) and information-based (Eigen, Schuster) scenarios for the origin of life

Acknowledgments

ArXiv 1802.00208

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EDUCATION SCIENCE INNOVATION

Thank you!

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