Karl Sigmund‘s Birthday

Peter Schuster

Institut für Theoretische Chemie, Universität Wien, Austria
and
The Santa Fe Institute, Santa Fe, New Mexico, USA

Symposium in Honor of Karl Sigmund

Wien, 29. - 30.10.2015

Web-Page for further information:

http://www.tbi.univie.ac.at/~pks

Happy
birthday

ad multos
annos

Karl Sigmund

Bulletin of Mathematical Biology, Vol. 40, pp. 743–769
Pergamon Press Ltd. 1978. Printed in Great Britain

DYNAMICAL SYSTEMS UNDER CONSTANT ORGANIZATION I. TOPOLOGICAL ANALYSIS OF A FAMILY OF NON-LINEAR DIFFERENTIAL EQUATIONS —A MODEL FOR CATALYTIC HYPERCYCLES†

■ P. Schuster, K. Sigmund and R. Wolff
Institute of Theoretical and
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The paper presents a qualitative analysis of the following systems of n differential equations: $\dot{x}_i = x_i x_j - x_i \sum_{r=1}^{n} x_r x_s$ $(j = i - 1 + n\delta_{i1}$ and $s = r - 1 + n\delta_{r1})$, which show cyclic symmetry. These dynamical systems are of particular interest in the theory of selforganization and biological evolution as well as for application to other fields.

SEMINAR

Mathematische Methoden in der Theoretischen Chemie

25.-30.März 1984
Barbarahaus
Turracher Höhe 176, 9565 Ebene Reichenau

Montag, 26.3.1984

P.Schuster,	Stochastische Prozesse in der Chemie - die Anwendbarkeit von Master-, Langevin- und Fokker-Planck-Gleichungen
K.Sigmund,	Stochastische und deterministische Analyse der Selektionsgleichung
W.Fontana,	Replikation als stochastischer Prozeß

Dienstag, 27.3.1984

B.Gassner,	Lösung einer Mastergleichung für die fehlerhafte, molekulare Replikation mit Hilfe der Erzeugenden-Funktion
J.Hofbauer,	Bifurkationstheorie und Anwendungen auf nichtlineare Reaktionsmechanismen
F.Kemler,	Stochastische und deterministische Analyse von dynamischen Systemen mit Autokatalyse höherer Ordnung

Mittwoch, 28.3.1984

H.P.Kauffmann,	Inkohärente Energiewanderung zwischen identischen Chromophoren - Stochastische Variable und transientes Verhalten
O.Steinhauser,	Molekulare Dynamik im Feld von stochastischen Kräften - eine molekulare Analyse der Brown'schen Bewegung
A.Beyer,	Proteindynamik

Donnerstag, 29.3.1984

J.Swetina,	Über das asymptotische Verhalten von Eigenfunktionen von 1-Teilchen Schrödingeroperatoren
M.Hoffmann-Ostenhof,	Asymptotisches Verhalten von Eigenfunktionen von n-Teilchen Schödingeroperatoren in Zusammenhang mit dem Spektrum des Operators
T.Hoffmann-Ostenhof,	Über Triplettzustände von atomaren Systemen mit 2 Elektronen

SEMINAR

Mathematische Methoden in der Theoretischen Chemie
Reaktions-Diffusionsgleichung

24.-30.März 1985
Barbarahaus
Turracher Höhe 176, 9565 Ebene Reichenau

Sonntag,24.3.1985

P.Schuster, Die Reaktions-Diffusionsgleichung und einige Anwendungen in Chemie und Biologie (mit Film)

Montag, 25.3.1985

T.Hoffmann-Ostenhof, Elliptische Differentialgleichungen

M.Hoffmann-Ostenhof, Parabolische Differentialgleichungen

J.Swetina, Vergleichssätze für Reaktions-Diffusionsgleichungen

Dienstag,26.3.1985

H.Muthsam, Zur numerischen Behandlung partieller Differentialgleichungen

R.Bürger und W.Fontana, Populationsgenetik und Diffusion (M.Kimuras "Neutrale Theorie"

Mittwoch,27.3.1985

K.Sigmund, Topologische Methoden für Reaktions-Diffusionssysteme

J.Hofbauer, Methoden der Bifurkationstheorie für partielle Differentialgleichungen

J.Hofbauer, "Travelling Waves"

Donnerstag,28.3.1985

T.Hoffmann-Ostenhof, Regularitätseigenschaften und Eigenschaften der Nullstellen von Lösungen 2-dimensionaler Schrödingergleichungen in der Nähe von unendlich

K.Sigmund, Stabile und instabile Mannigfaltigkeiten für Reaktions-Diffusionsgleichungen

H.Kauffmann, Zeitabhängige Diffusion in excitonischen Transportvorgängen

B.Rupp, Pilzgifte und Giftpilze

Café Stadlmann, Währingerstraße 26, 1090 Wien

The interior of Café Stadlmann
in the 1930th

Café Stadlmann before it was closed for ever

Modeling Cooperation

From Molecules to Man

Peter Schuster

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1. Hypercycles – 1975
2. Hypercycles – 40 years later
3. How important is recycling?
4. RNA replication without protein enzymes
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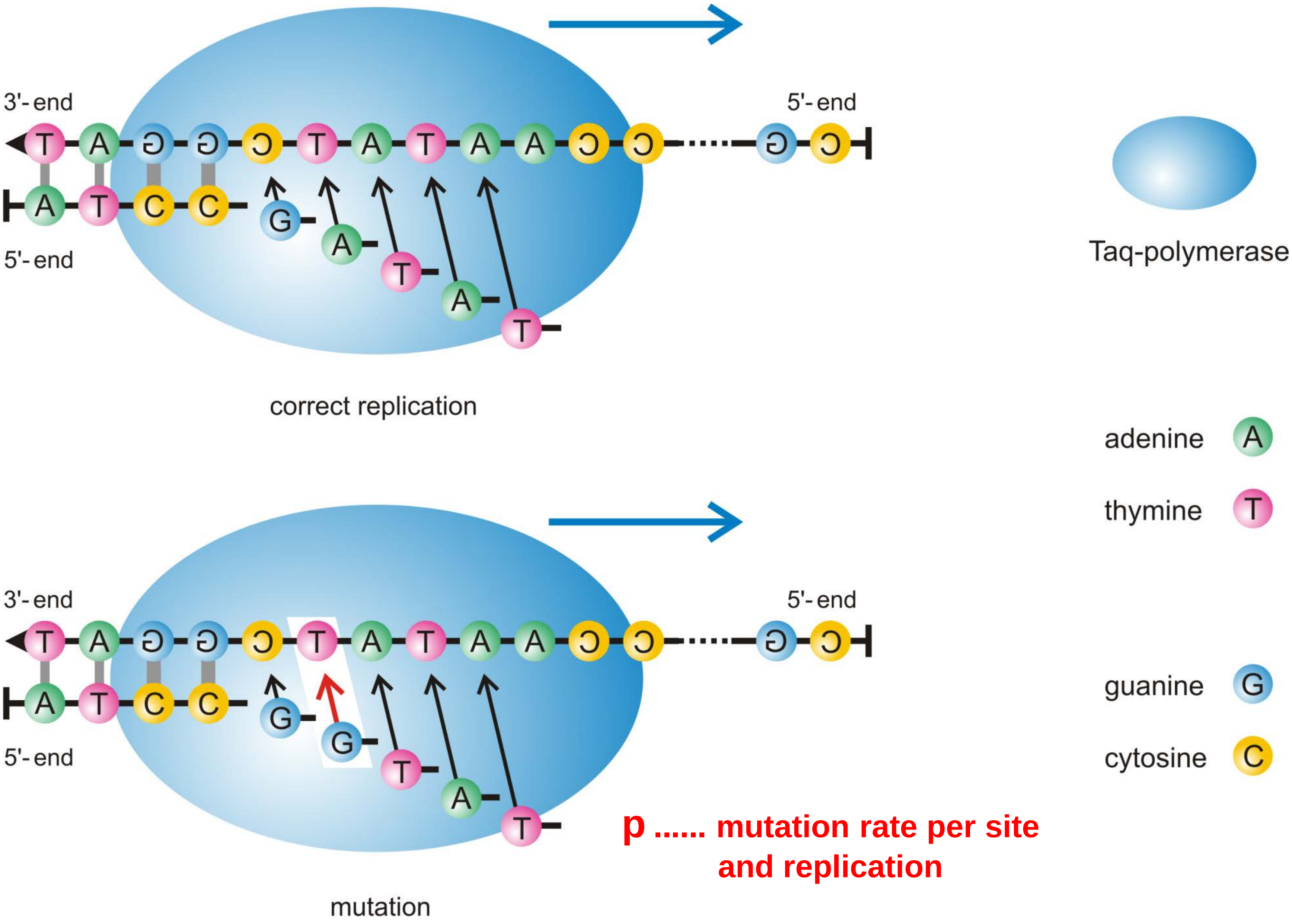


p ...... mutation rate per site and replication

DNA replication and mutation

RNA or DNA replication dynamics is now fully resolved in chemical kinetic terms but highly complicated and involving thousands of elementary steps.

Albert Einstein (?): *„Things should be made as simple as possible but not simpler!“*

first order autocatalysis

$\mathbf{X}_i$ …… template

$$
\begin{array}{c}
(\mathbf{A}) + \mathbf{X}_1 \xrightarrow{\;f_1\;} 2\,\mathbf{X}_1 \\
\vdots \\
(\mathbf{A}) + \mathbf{X}_i \xrightarrow{\;f_i\;} 2\,\mathbf{X}_i \\
\vdots \\
(\mathbf{A}) + \mathbf{X}_n \xrightarrow{\;f_n\;} 2\,\mathbf{X}_n
\end{array}
$$

simple, „linear“ dynamics

competition and selection

second order autocatalysis

$\mathbf{X}_i$ … template, $\mathbf{X}_j$ … catalyst

$$(\mathbf{A}) + \mathbf{X}_i + \mathbf{X}_j \xrightarrow{\;a_{ij}\;} 2\,\mathbf{X}_i + \mathbf{X}_j$$

$$i = 1, 2, \ldots, n; \;\; j = 1, 2, \ldots, n$$

rich dynamics including oscillations.
multiple stationary states, and
deterministic chaos

competition and **cooperation**

$$(\mathbf{A}) + \mathbf{X}_1 + \mathbf{X}_2 \xrightarrow{f_2} \mathbf{X}_1 + 2\,\mathbf{X}_2$$

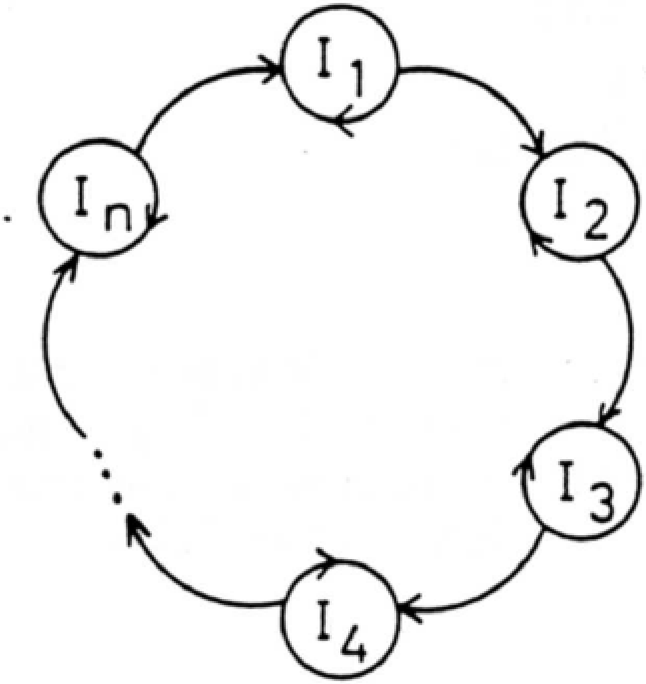
$$(\mathbf{A}) + \mathbf{X}_2 + \mathbf{X}_3 \xrightarrow{f_3} \mathbf{X}_2 + 2\,\mathbf{X}_3$$

$$(\mathbf{A}) + \mathbf{X}_3 + \mathbf{X}_4 \xrightarrow{f_4} \mathbf{X}_3 + 2\,\mathbf{X}_4$$

$$\vdots$$

$$(\mathbf{A}) + \mathbf{X}_{n-1} + \mathbf{X}_n \xrightarrow{f_n} \mathbf{X}_{n-1} + 2\,\mathbf{X}_n$$

$$(\mathbf{A}) + \mathbf{X}_n + \mathbf{X}_1 \xrightarrow{f_1} \mathbf{X}_n + 2\,\mathbf{X}_1$$



The catalytic hypercycle a model for cooperation

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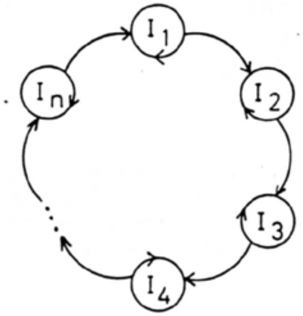


Figure 1. Catalytic hypercycle (closed cycles ↻ represent self-instructed replication, arrows ⟶ pointing from one cycle to another correspond to the catalytic terms $x_i x_j$, $j=i-1+n\delta_{i1}$)

$$\frac{\mathrm{d}x_1}{\mathrm{dt}} = f_1\,x_1\,x_n - x_1\,\Phi = x_1\big(f_1\,x_n - \Phi\big)$$

$$\frac{\mathrm{d}x_2}{\mathrm{dt}} = f_2\,x_2\,x_1 - x_2\,\Phi = x_2\big(f_2\,x_1 - \Phi\big)$$

$$\vdots$$

$$\frac{\mathrm{d}x_n}{\mathrm{dt}} = f_n\,x_n\,x_{n-1} - x_n\,\Phi = x_n\big(f_n\,x_{n-1} - \Phi\big)$$

$$\sum_{i=1}^{n} x_i = c_0 = 1 \quad \text{and} \quad \Phi = \sum_{i=1,\,i \bmod n}^{n} f_i\,x_i x_{i-1}$$

special case: $f_1 = f_2 = \ldots = f_n$

central fixed point

$$\mathbf{x} = (x_1, x_2, \ldots, x_n) = \left(\tfrac{1}{n}, \tfrac{1}{n}, \ldots, \tfrac{1}{n}\right)$$

eigenvalues and eigenvectors

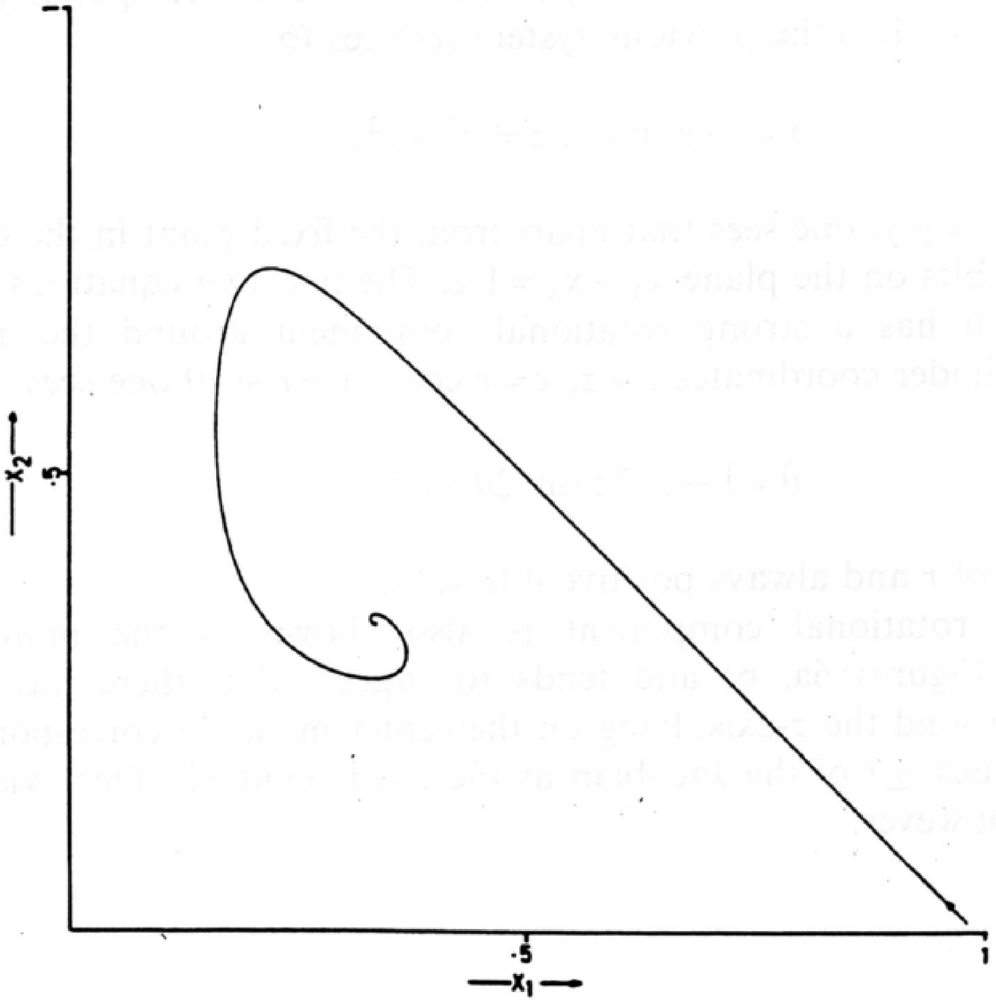
$$\omega_0^{(1)} = -1; \quad \xi_0^{(1)} = (1, 1 \ldots 1)$$

$$\omega_0^{(j)} = \exp\left\{\frac{2\pi i}{n}(j-1)\right\} = \lambda_j;$$

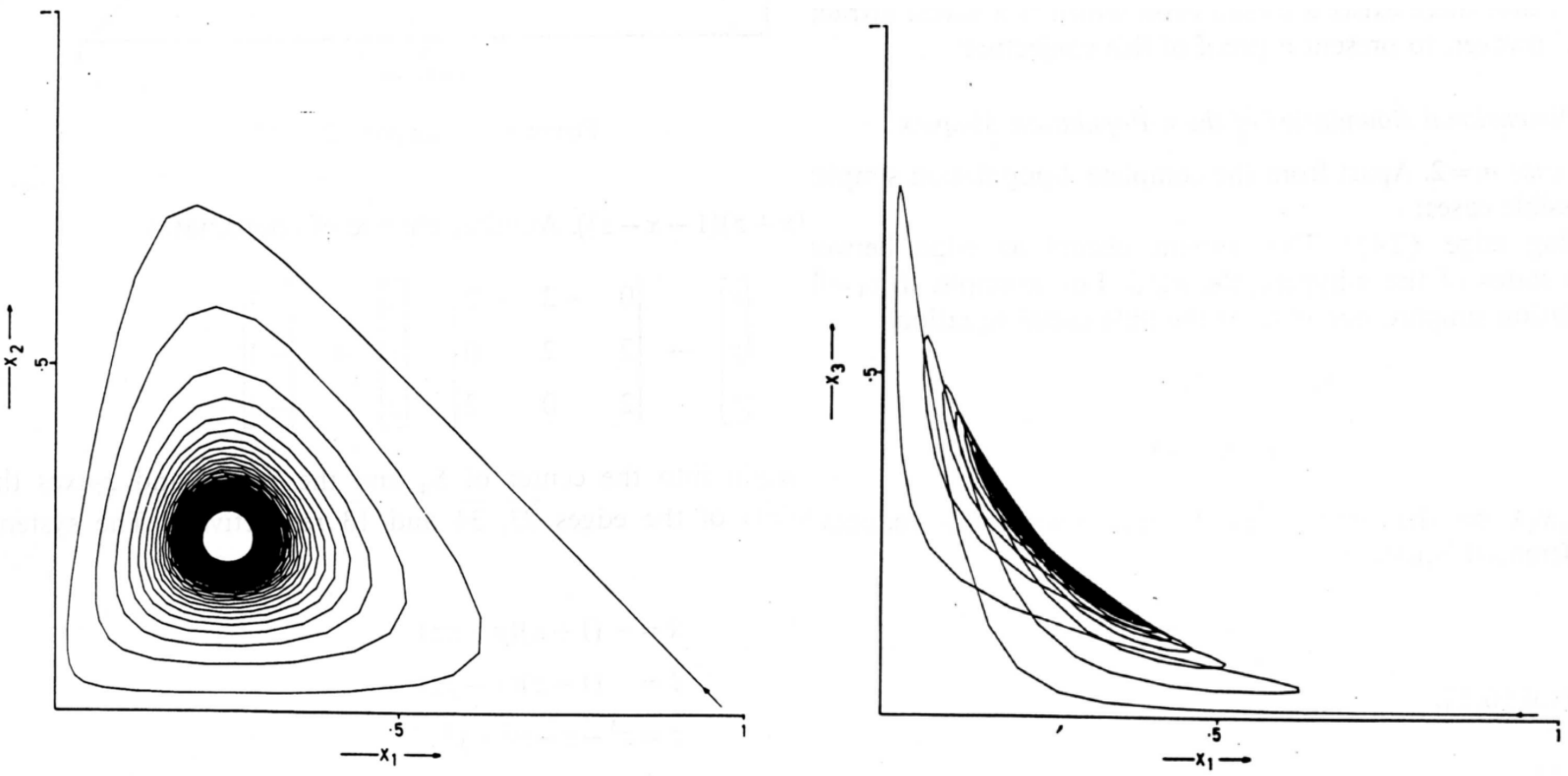
$$j = 2, 3, \ldots, n;$$

$$\xi_0^{(j)} = (1, \lambda_j^{-1}, \lambda_j^{-2}, \ldots, \lambda_j^{-n+1})$$

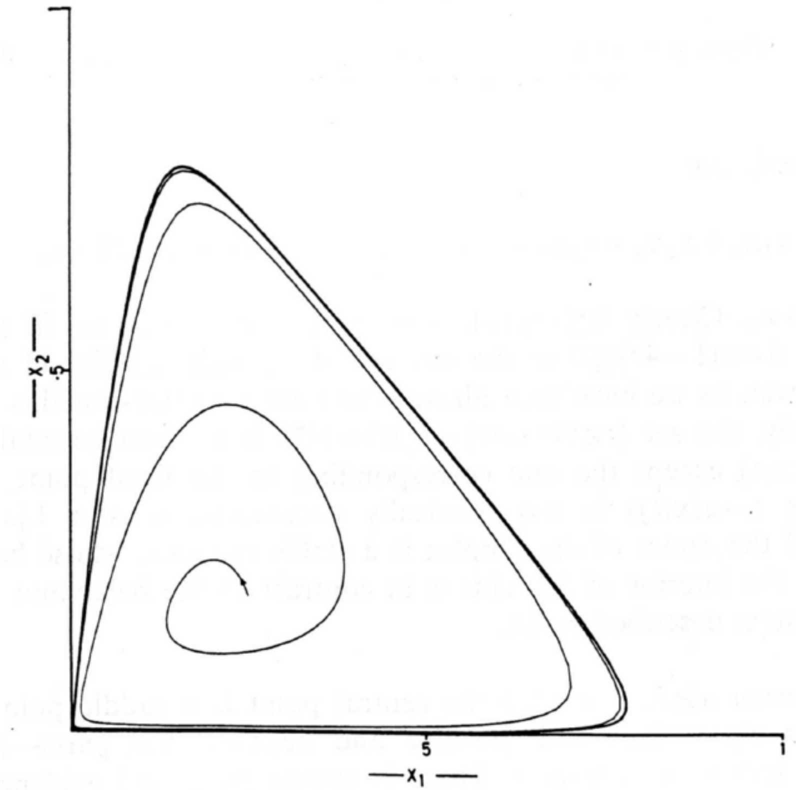
qualitative analysis of hypercycle dynamics

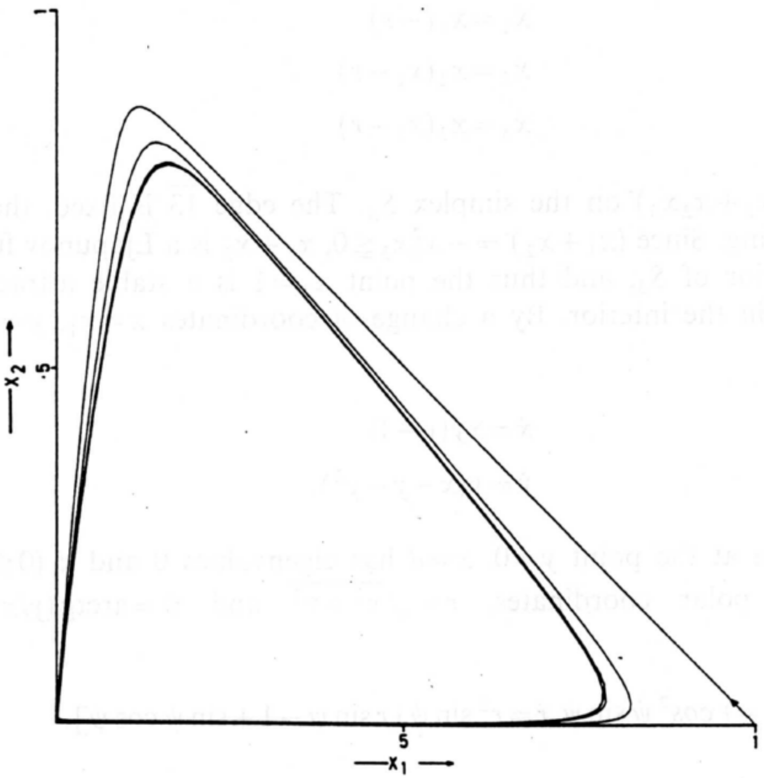


$n = 3$: eigenvalues $\lambda_{2,3} = (-1 \pm i\sqrt{3}) / 2$

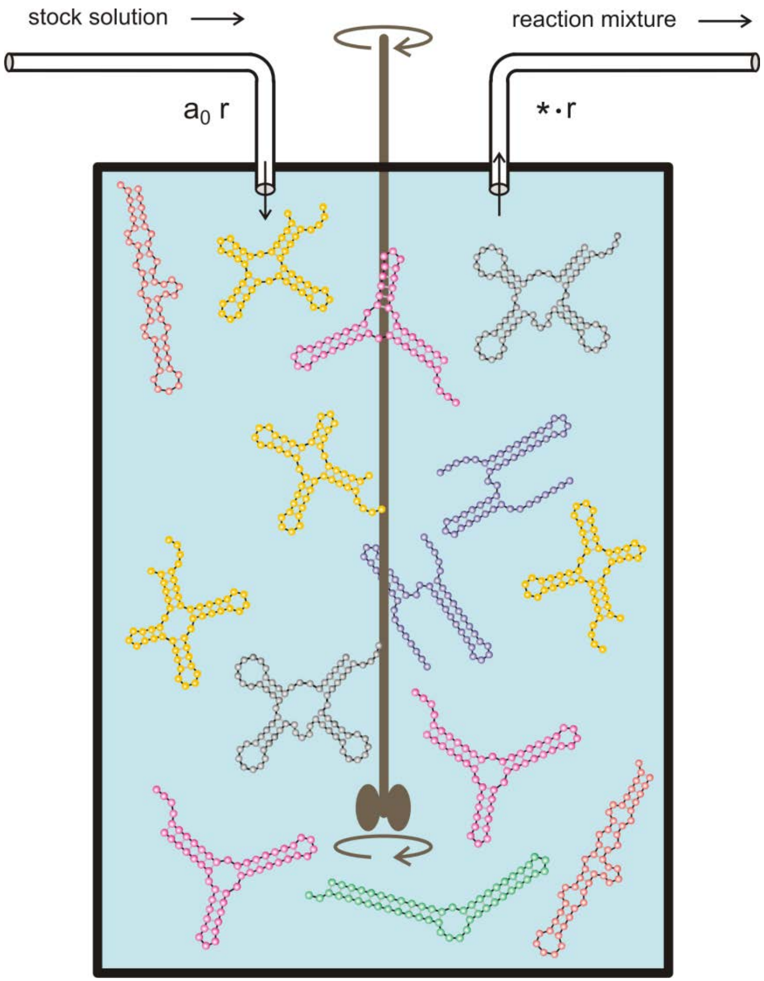


$n = 4$: eigenvalues $\lambda_{2\text{-}4} = (i\ ,\ -1,\ -i)$



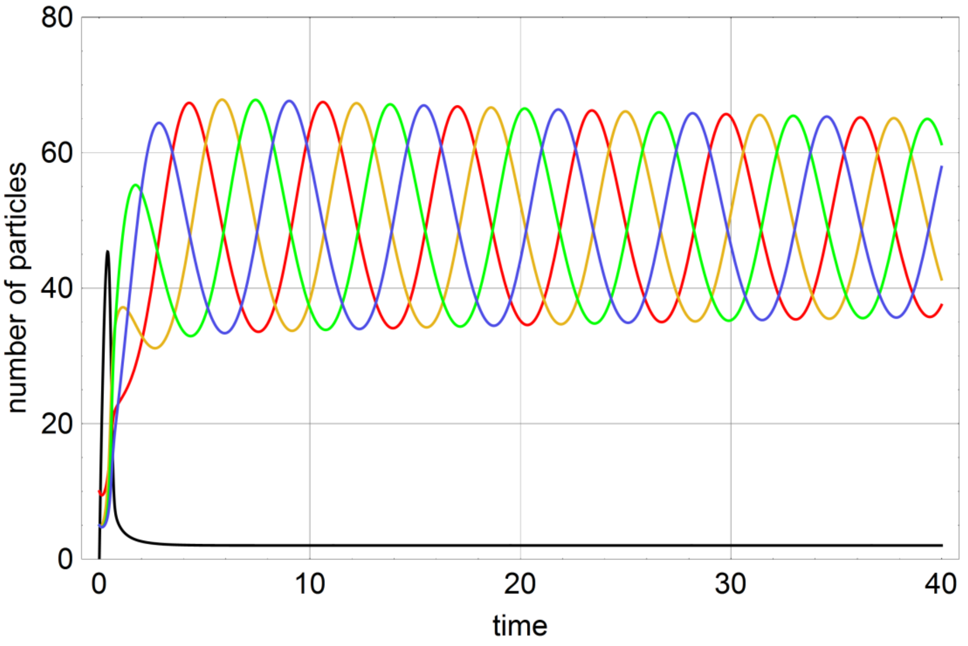


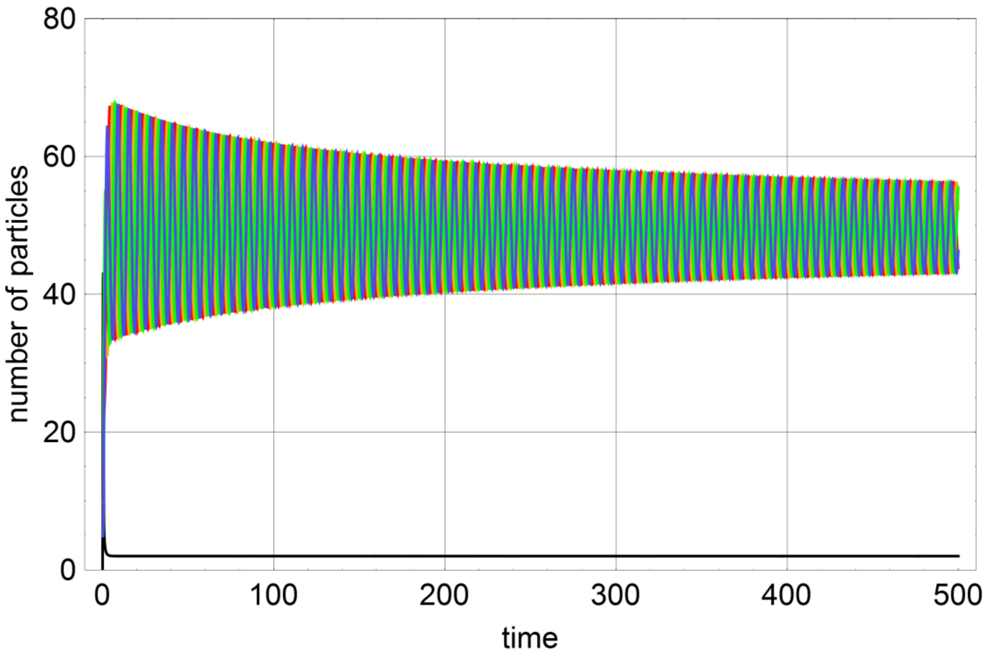
$n = 5$: eigenvalues $\lambda_{2\text{-}5} = (\pm \surd 5 - 1 \mp \surd(5 \pm \surd 5)/2))/4$



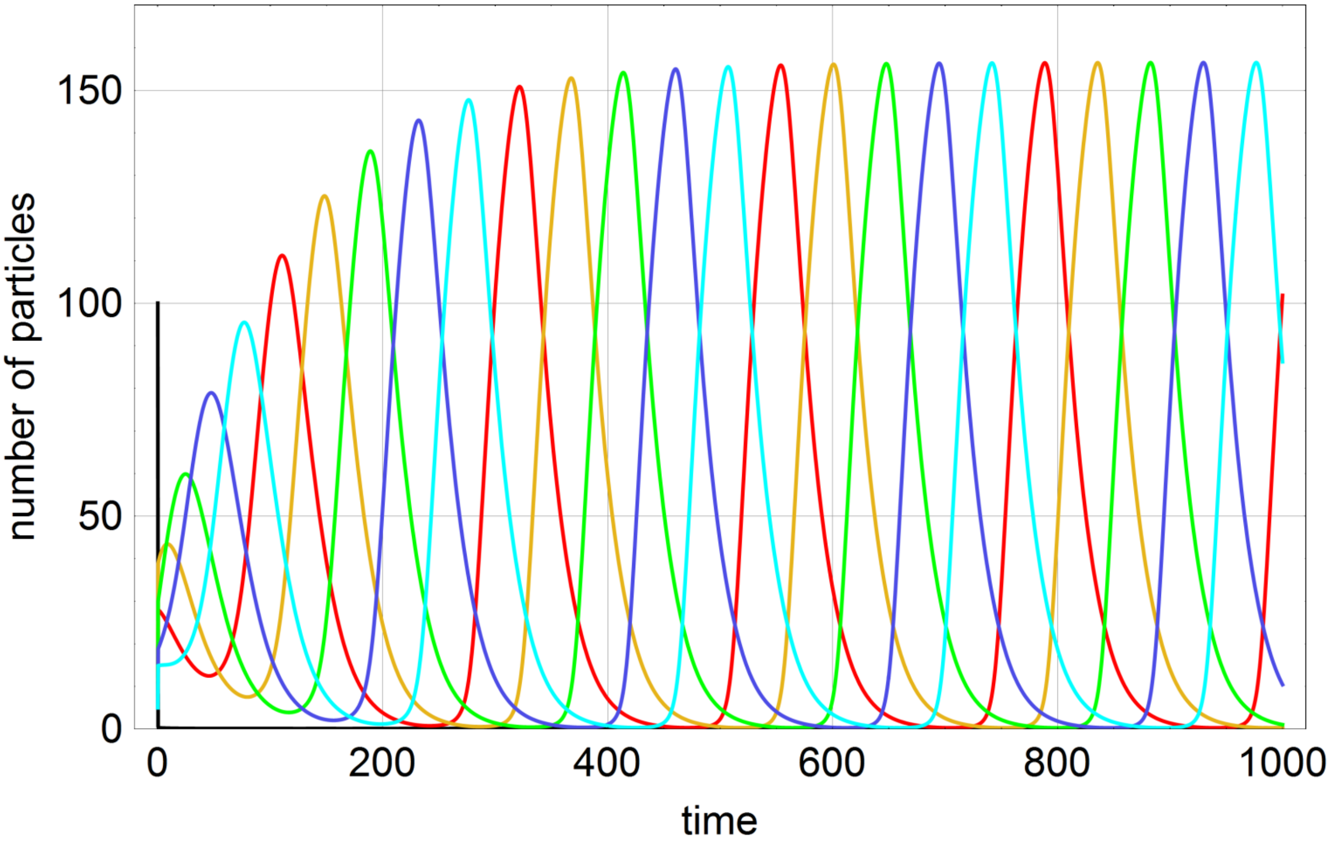
$$\begin{array}{rcl}
* & \xrightarrow{a_0\cdot r} & \mathbf{A} \\
\mathbf{A} + \mathbf{X}_1 + \mathbf{X}_2 & \xrightarrow{f_2} & \mathbf{X}_1 + 2\,\mathbf{X}_2 \\
\mathbf{A} + \mathbf{X}_2 + \mathbf{X}_3 & \xrightarrow{f_3} & \mathbf{X}_2 + 2\,\mathbf{X}_3 \\
\mathbf{A} + \mathbf{X}_3 + \mathbf{X}_4 & \xrightarrow{f_4} & \mathbf{X}_3 + 2\,\mathbf{X}_4 \\
 & \vdots & \\
\mathbf{A} + \mathbf{X}_{n-1} + \mathbf{X}_n & \xrightarrow{f_n} & \mathbf{X}_{n-1} + 2\,\mathbf{X}_n \\
\mathbf{A} + \mathbf{X}_n + \mathbf{X}_1 & \xrightarrow{f_1} & \mathbf{X}_n + 2\,\mathbf{X}_1 \\
\mathbf{A} & \xrightarrow{r} & \varnothing \\
\mathbf{X}_1 & \xrightarrow{r} & \varnothing \\
 & \vdots & \\
\mathbf{X}_n & \xrightarrow{r} & \varnothing\ .
\end{array}$$

hypercycle in the flow reactor





flow reactor: $n = 4$



flow reactor: $n = 5$

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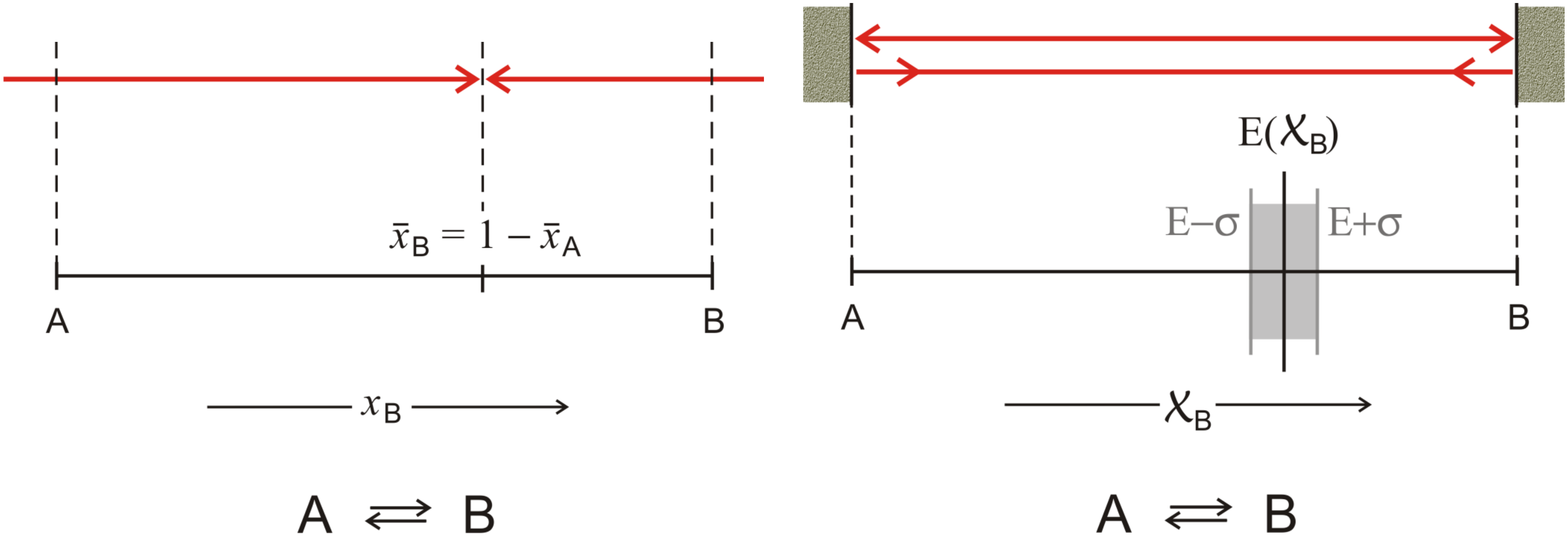


thermodynamic equilibrium

deterministic and stochastic chemical reaction A ↔ B

$$P_n(t) \;=\; P\big(\mathcal{X}_{\mathrm{A}}(t) = n\big)$$

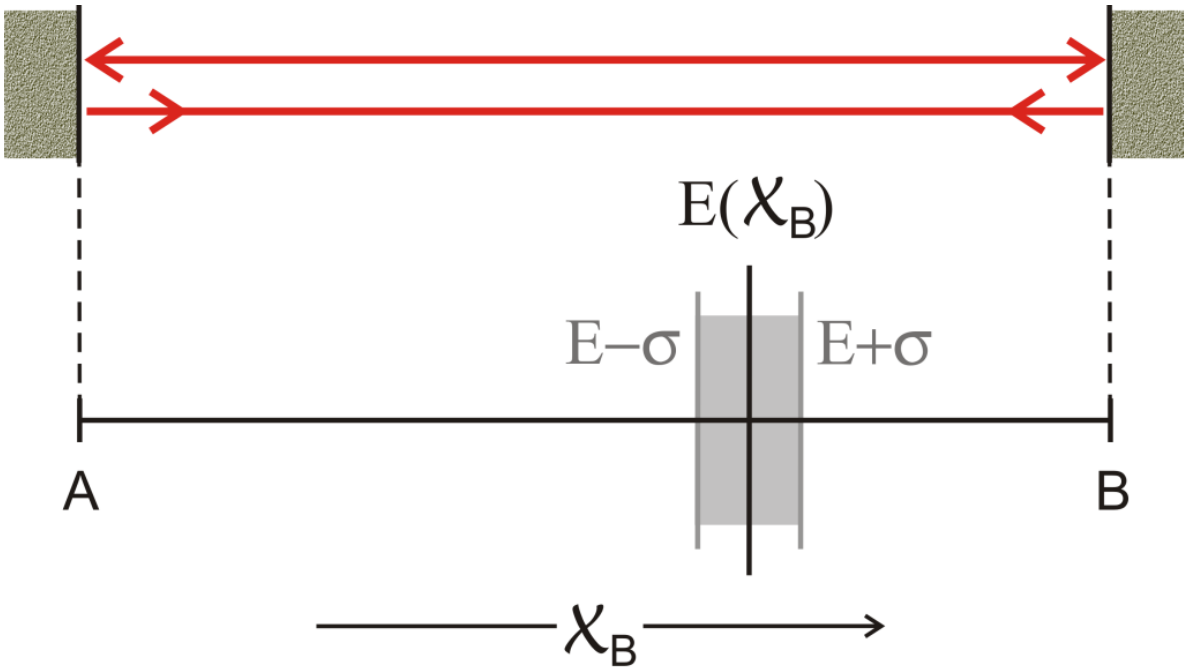
$$\begin{aligned}\frac{\partial P_n(t)}{\partial t} \;&=\; l(n_0 - n + 1)P_{n-1}(t) \;+\; k(n+1)P_{n+1}(t) - \\ &\quad - \Big(kn + l(n_0 - n)\Big)P_n(t)\;.\end{aligned}$$

$$P_n(t) \;=\; \binom{n_0}{n} \frac{1}{(1+K)^{n_0}} \,\left(Ke^{-\kappa t} + 1\right)^n \Big(K(1 - e^{-\kappa t})\Big)^{n_0 - n}$$

$$\mathrm{E}\big(\mathcal{X}_A(t)\big) \;=\; \frac{n_0}{1+K}\,\omega(t)\;,\;\; K \;=\; \frac{k}{l}\;\;,\;\;\; \omega(t) = K\exp\left(-\kappa t\right) + 1$$

$$\mathrm{var}\big(\mathcal{X}_A(t)\big) \;=\; \frac{n_0\,\omega(t)}{1+K}\left(1 - \frac{\omega(t)}{1+K}\right)$$

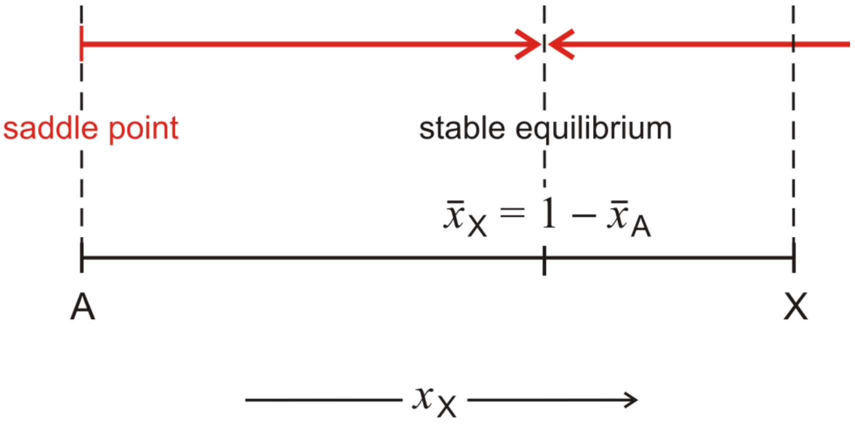
$$\mathbf{A} \;\underset{l}{\overset{k}{\rightleftharpoons}}\; \mathbf{B}$$



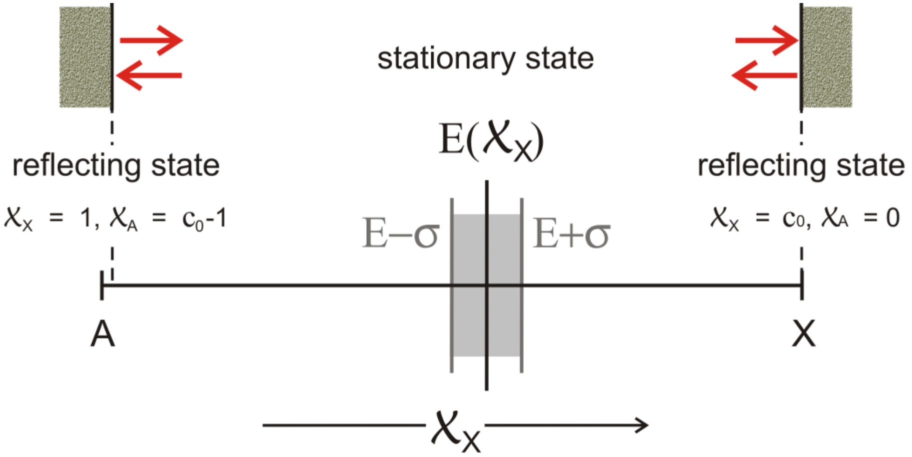
$$\mathrm{A} \rightleftarrows \mathrm{B}$$

$$\lim_{t\to\infty} P_n(t) = \overline{P}_n = \binom{n_0}{n}\frac{K^{n_0-n}}{(1+K)^{n_0}} = \binom{n_0}{n}\frac{1}{(k+l)^{n_0}}\, k^{n_0-n}\, l^n$$

$$\lim_{t\to\infty} \mathrm{E}\big(\mathcal{X}_A(t)\big) = n_0\,\frac{l}{k+l} \qquad \lim_{t\to\infty} \sigma\big(\mathcal{X}_A(t)\big) = \sqrt{n_0}\,\frac{\sqrt{k\,l}}{k+l}$$



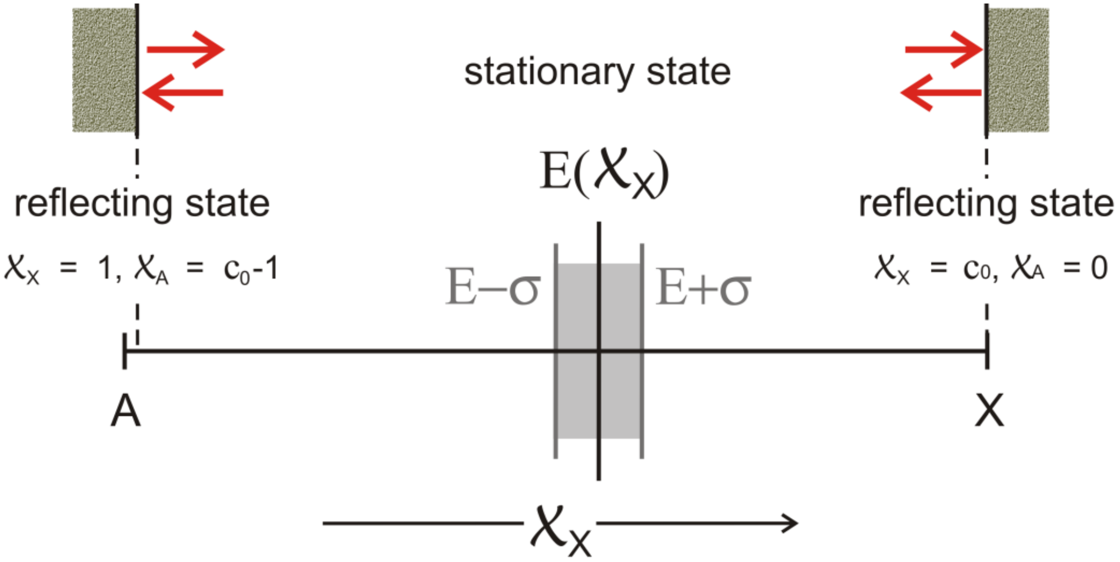
$A + X \rightleftarrows 2X$



$A + X \rightleftarrows 2X$

thermodynamic equilibrium

deterministic and stochastic chemical reaction $A + X \leftrightarrow 2X$



stationary state

reflecting state

$\chi_X = 1, \chi_A = c_0 - 1$

$E(\chi_X)$

$E-\sigma$

$E+\sigma$

reflecting state

$\chi_X = c_0, \chi_A = 0$

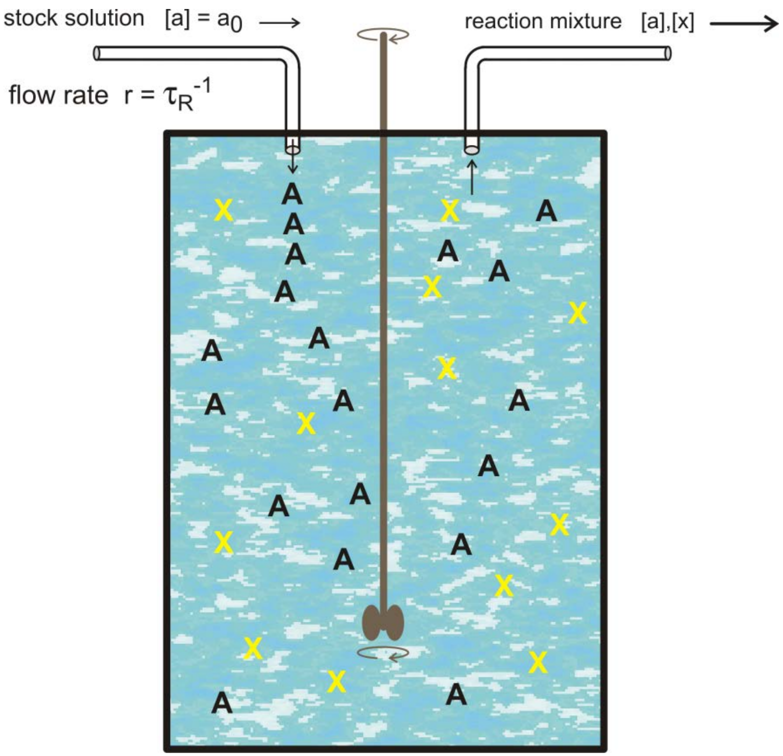
A

X

χ_X

$$A + X \rightleftarrows 2\,X$$

$$\bar{P}_n = \binom{n_0}{n} \frac{K^n}{(1+K)^{n_0} - K^{n_0}}$$



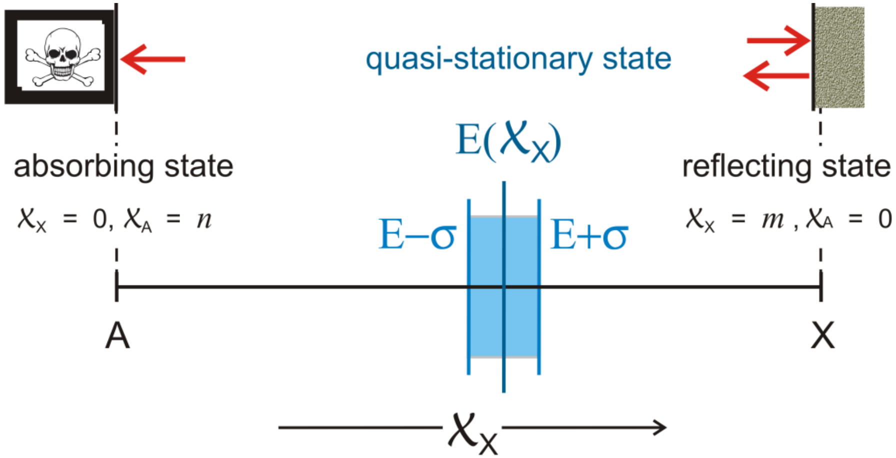
$$* \xrightarrow{a_0 \cdot r} \mathbf{A}$$

$$\mathbf{A} + \mathbf{X} \xrightarrow{k} 2\,\mathbf{X}$$

$$2\,\mathbf{X} \xrightarrow{l} \mathbf{A} + \mathbf{X}$$

$$\mathbf{A} \xrightarrow{r} \varnothing$$

$$\mathbf{X} \xrightarrow{r} \varnothing$$



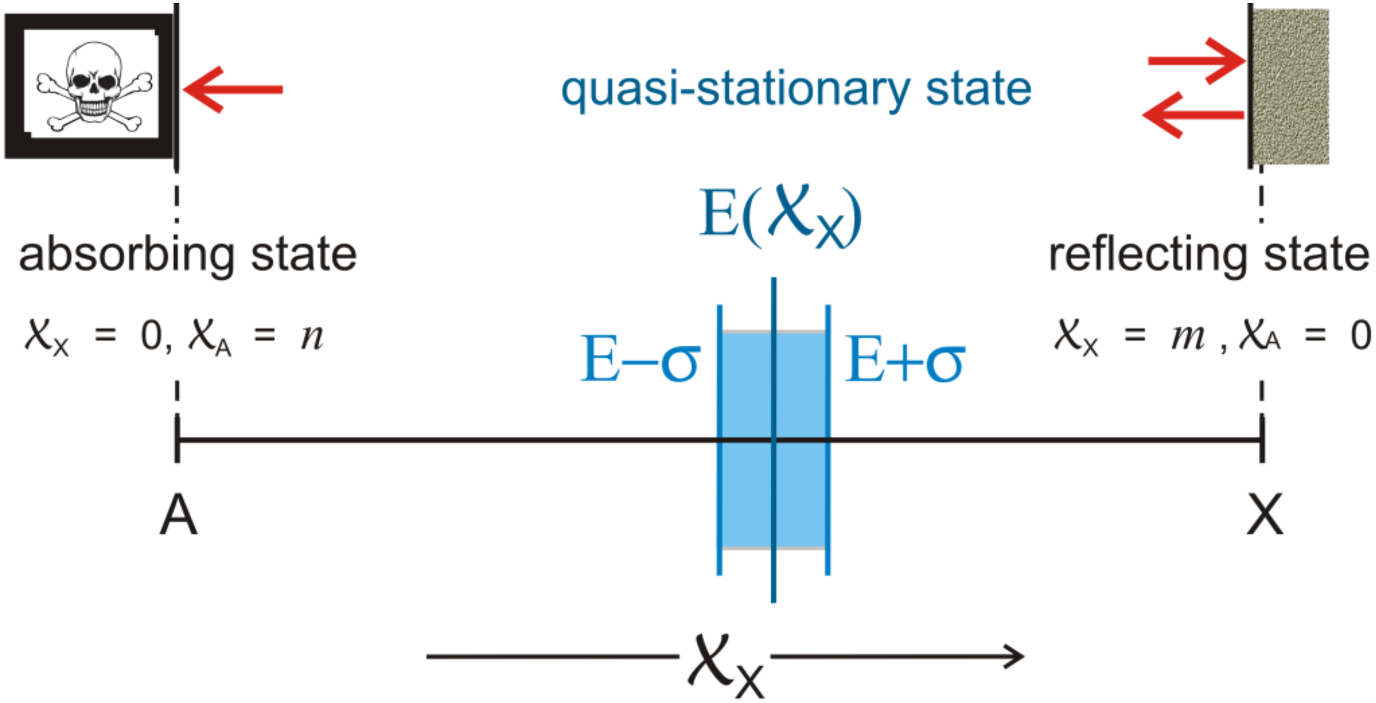
autocatalysis in the flow reactor

$$\mathrm{A} + \mathrm{X} \rightleftarrows 2\,\mathrm{X}$$

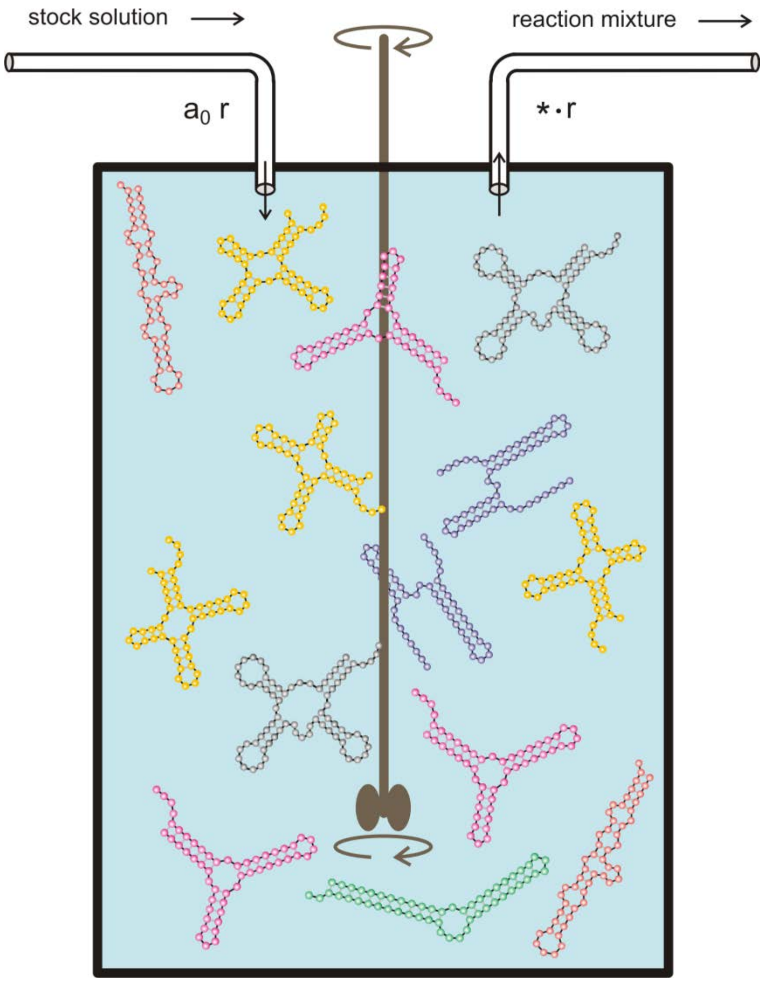
$$P_n(t) \;=\; P\big(\mathcal{X}_{\mathsf{A}}(t) = n\big)\,,\;\; P_m(t) \;=\; P\big(\mathcal{X}_{\mathsf{X}}(t) = m\big)$$

$$\begin{aligned}\frac{\mathrm{d}P_n(t)}{\mathrm{dt}} &= r\,a_0\,P_{n-1}(t) \;+\; (f\,n\,m - r\,a_0 - r\,n)\,P_n(t) - \\ &\quad - \;\big(f\,(n+1)(m-1) - r\,(n+1)\big)\,P_{n+1}(t)\end{aligned}$$

$$\begin{aligned}\frac{\mathrm{d}P_m(t)}{\mathrm{dt}} &= f\,(n+1)(m-1)\,P_{m-1}(t) \;-(f\,n\,m + r\,m)\,P_m(t) + \\ &\quad + \;r\,(m+1)\,P_{m+1}(t)\end{aligned}$$



$$A + X \rightleftarrows 2\,X$$



$$
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\mathbf{A} + \mathbf{X}_3 + \mathbf{X}_4 &\xrightarrow{f_4} \mathbf{X}_3 + 2\,\mathbf{X}_4 \\
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\mathbf{A} + \mathbf{X}_n + \mathbf{X}_1 &\xrightarrow{f_1} \mathbf{X}_n + 2\,\mathbf{X}_1 \\
\mathbf{A} &\xrightarrow{r} \varnothing \\
\mathbf{X}_1 &\xrightarrow{r} \varnothing \\
&\vdots \\
\mathbf{X}_n &\xrightarrow{r} \varnothing \,.
\end{aligned}
$$

hypercycle in the flow reactor

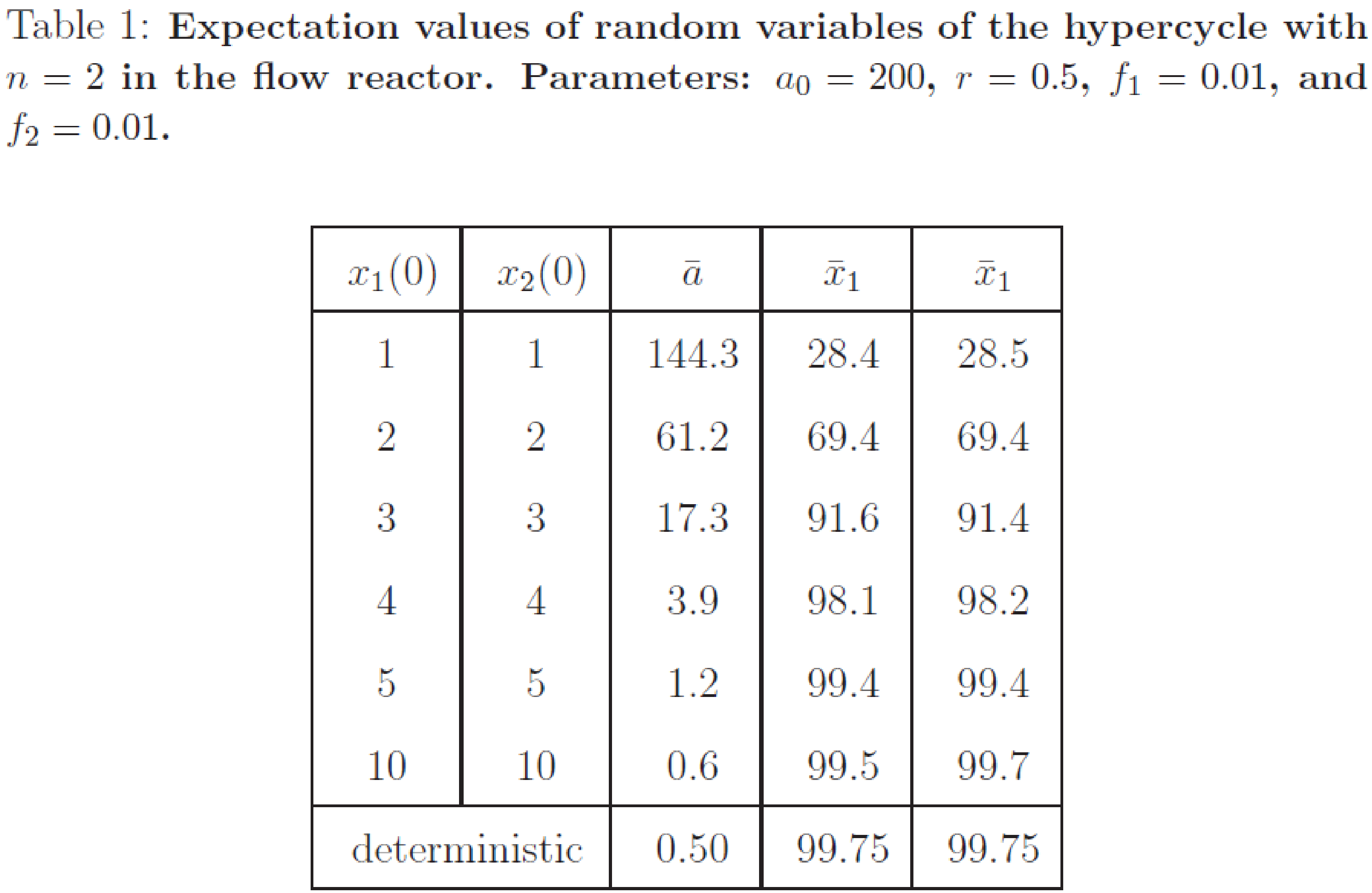
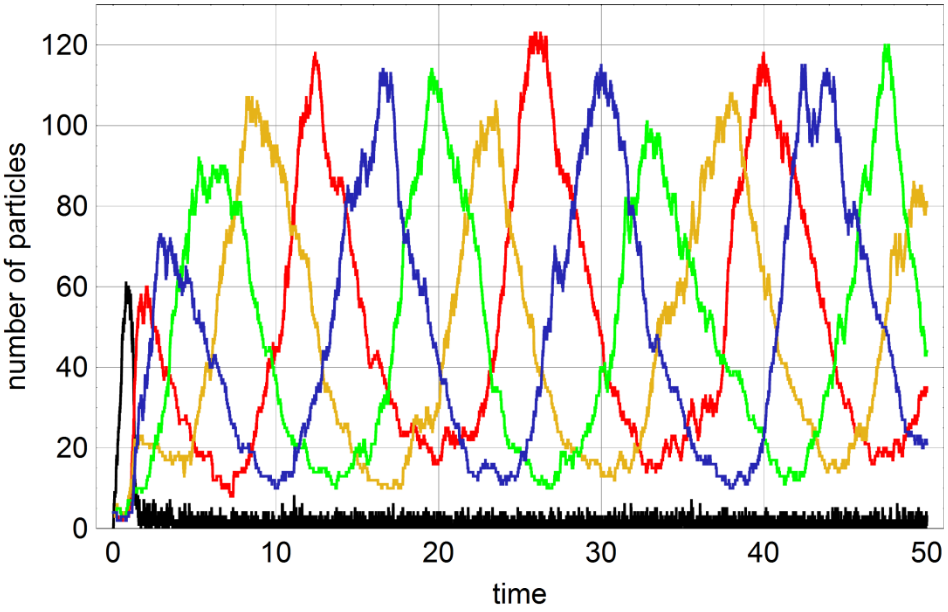
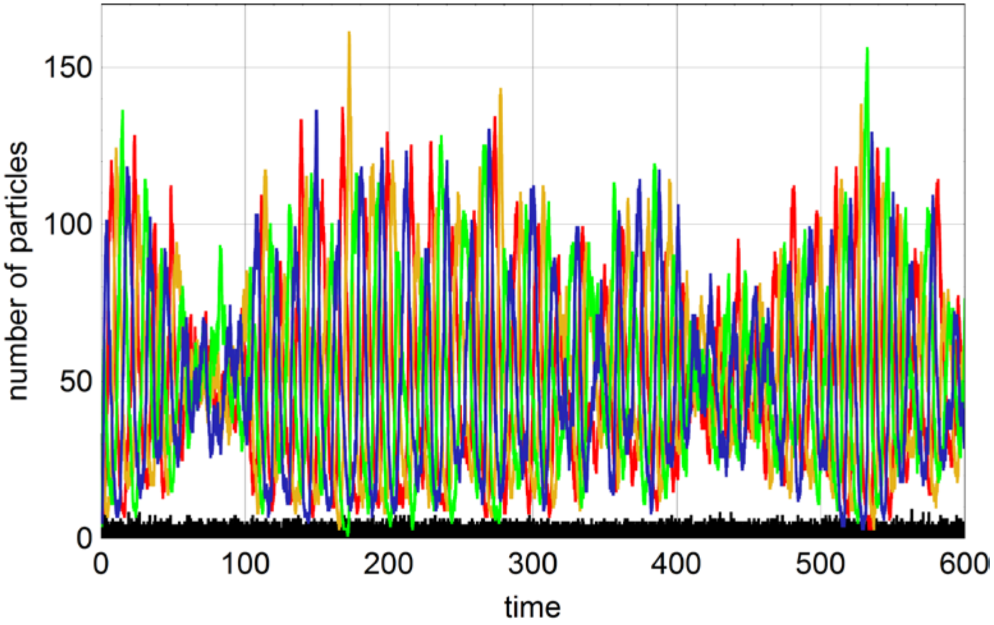


Table 1: **Expectation values of random variables of the hypercycle with $n = 2$ in the flow reactor. Parameters: $a_0 = 200$, $r = 0.5$, $f_1 = 0.01$, and $f_2 = 0.01$.**

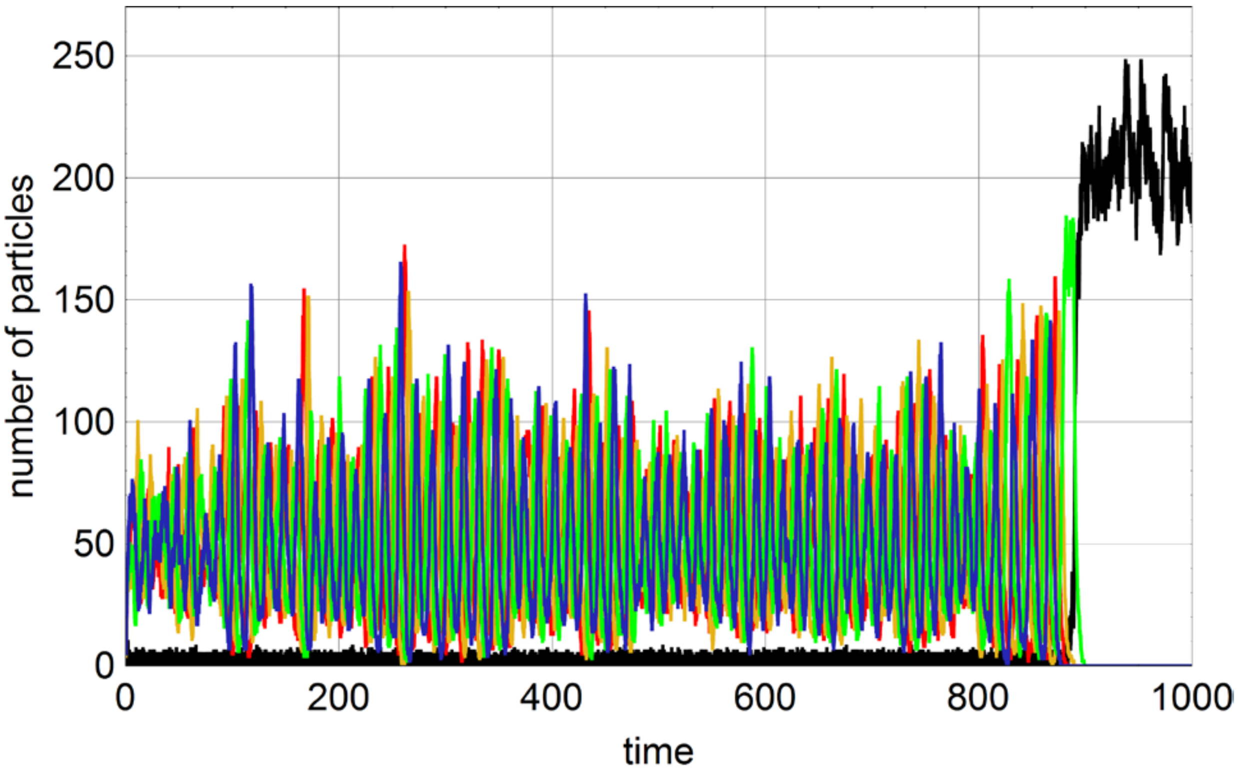
$x_1(0)$	$x_2(0)$	$\bar{a}$	$\bar{x}_1$	$\bar{x}_1$
1	1	144.3	28.4	28.5
2	2	61.2	69.4	69.4
3	3	17.3	91.6	91.4
4	4	3.9	98.1	98.2
5	5	1.2	99.4	99.4
10	10	0.6	99.5	99.7
deterministic		0.50	99.75	99.75

Competition between the absorbing and the quasi-stationary state





flow reactor: $n = 4$



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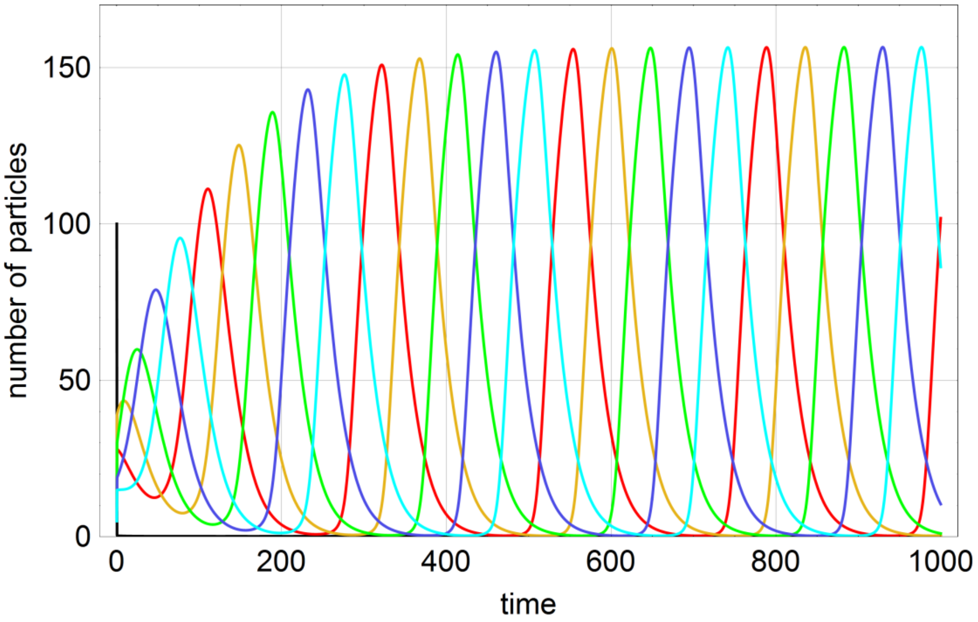

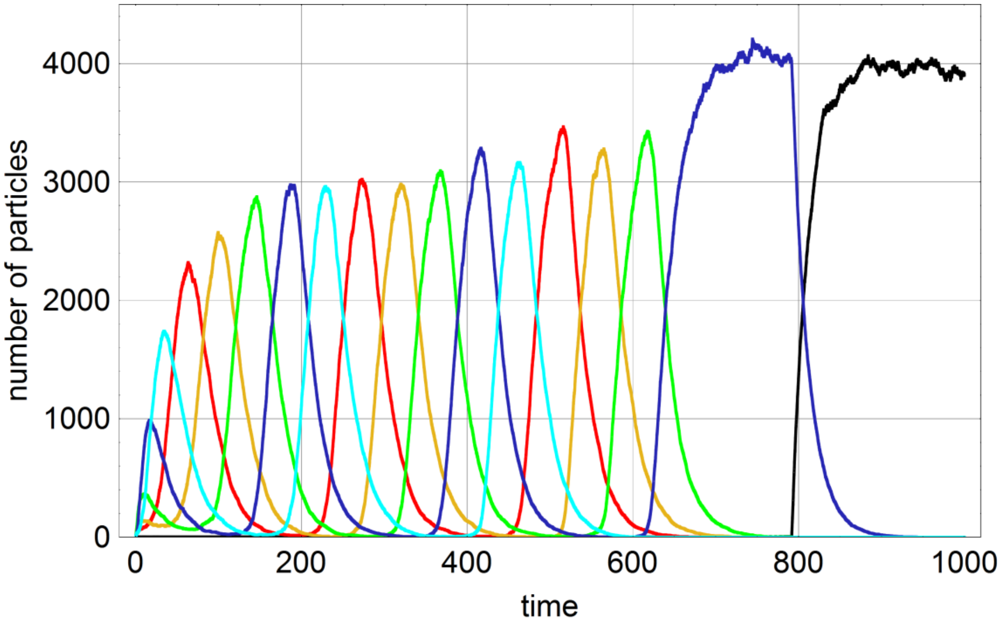

flow reactor: $n = 5$

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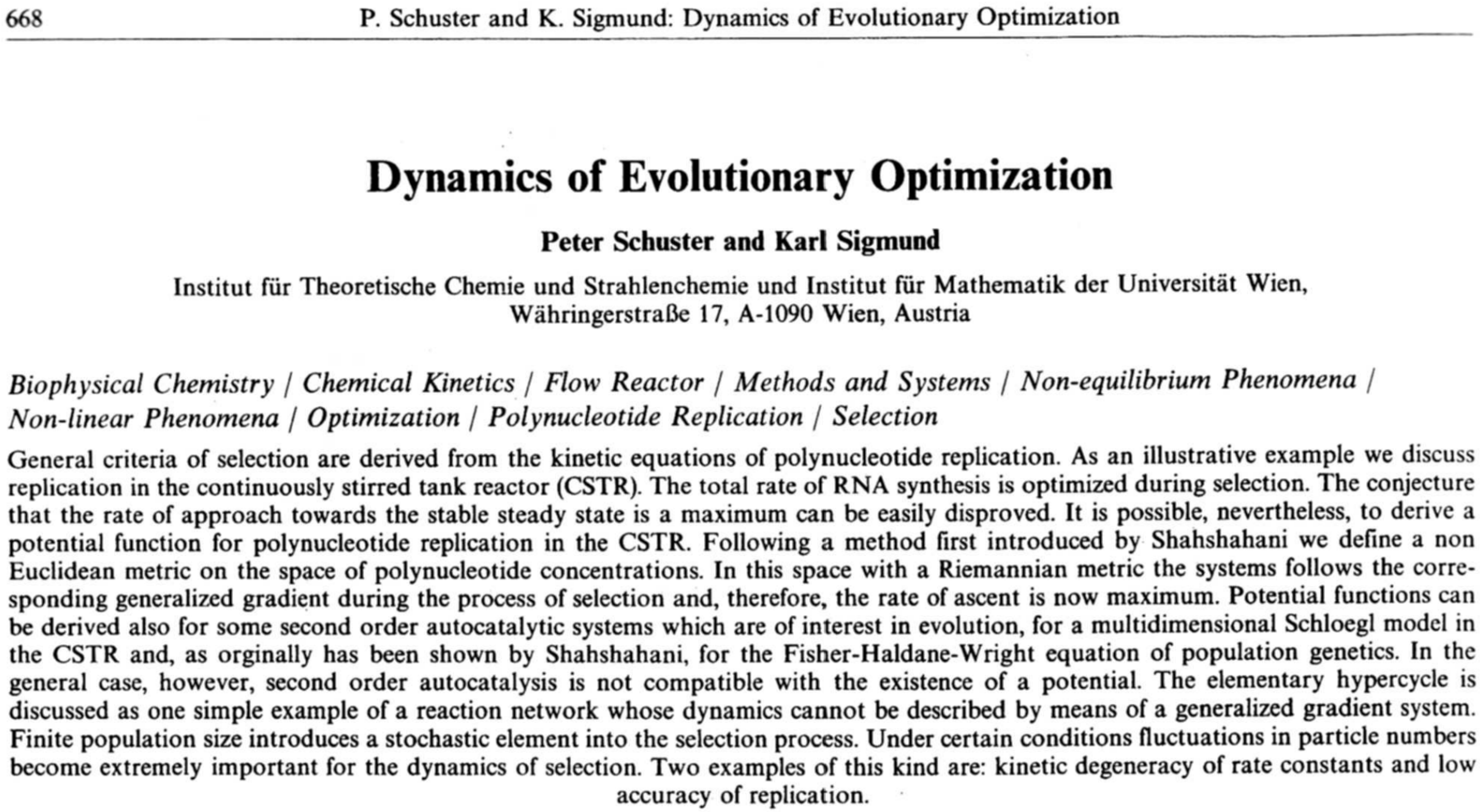

Dynamics of Evolutionary Optimization

Peter Schuster and Karl Sigmund

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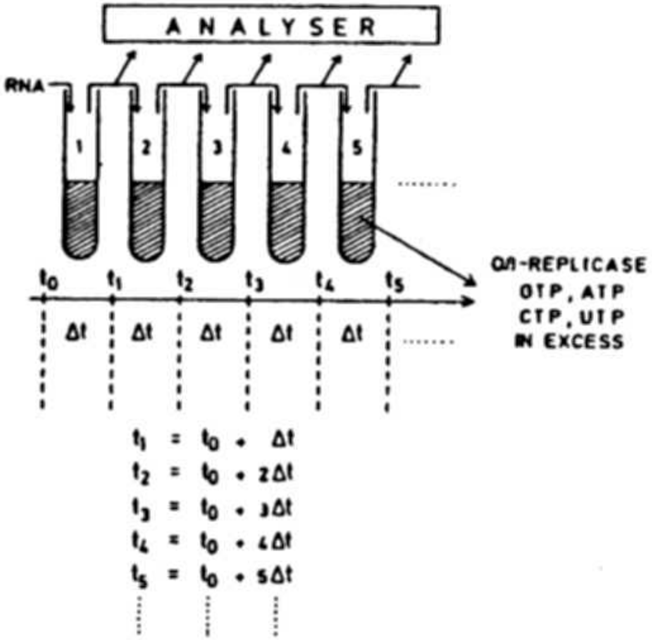
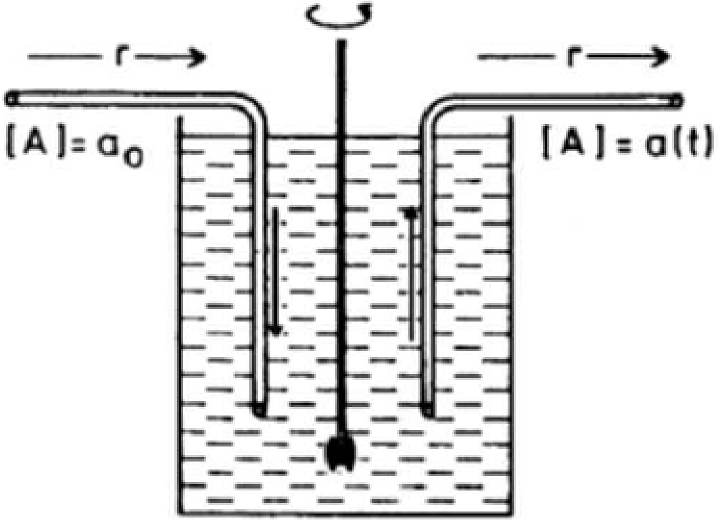
Biophysical Chemistry / Chemical Kinetics / Flow Reactor / Methods and Systems / Non-equilibrium Phenomena / Non-linear Phenomena / Optimization / Polynucleotide Replication / Selection

General criteria of selection are derived from the kinetic equations of polynucleotide replication. As an illustrative example we discuss replication in the continuously stirred tank reactor (CSTR). The total rate of RNA synthesis is optimized during selection. The conjecture that the rate of approach towards the stable steady state is a maximum can be easily disproved. It is possible, nevertheless, to derive a potential function for polynucleotide replication in the CSTR. Following a method first introduced by Shahshahani we define a non Euclidean metric on the space of polynucleotide concentrations. In this space with a Riemannian metric the systems follows the corresponding generalized gradient during the process of selection and, therefore, the rate of ascent is now maximum. Potential functions can be derived also for some second order autocatalytic systems which are of interest in evolution, for a multidimensional Schloegl model in the CSTR and, as orginally has been shown by Shahshahani, for the Fisher-Haldane-Wright equation of population genetics. In the general case, however, second order autocatalysis is not compatible with the existence of a potential. The elementary hypercycle is discussed as one simple example of a reaction network whose dynamics cannot be described by means of a generalized gradient system. Finite population size introduces a stochastic element into the selection process. Under certain conditions fluctuations in particle numbers become extremely important for the dynamics of selection. Two examples of this kind are: kinetic degeneracy of rate constants and low accuracy of replication.

Replicator equations in different environments

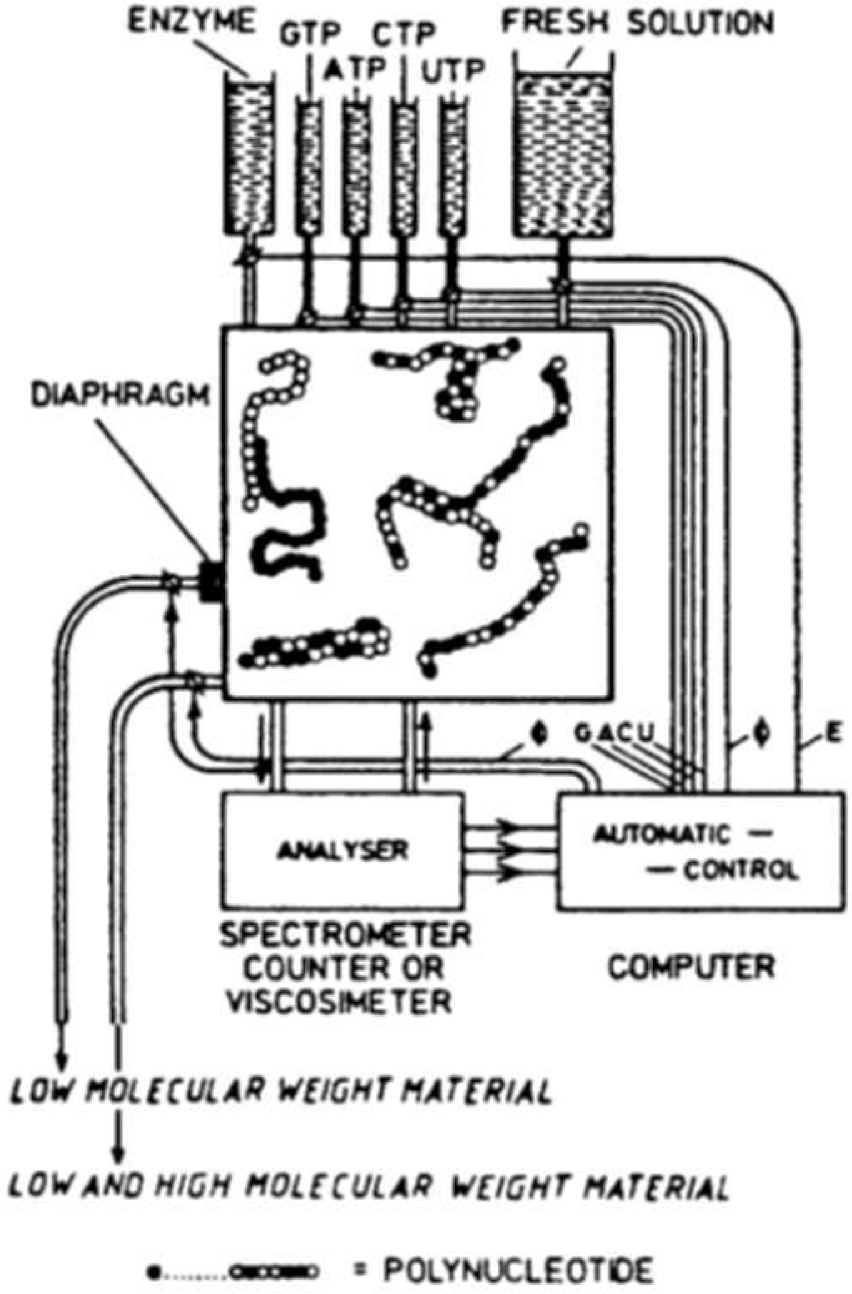


serial transfer

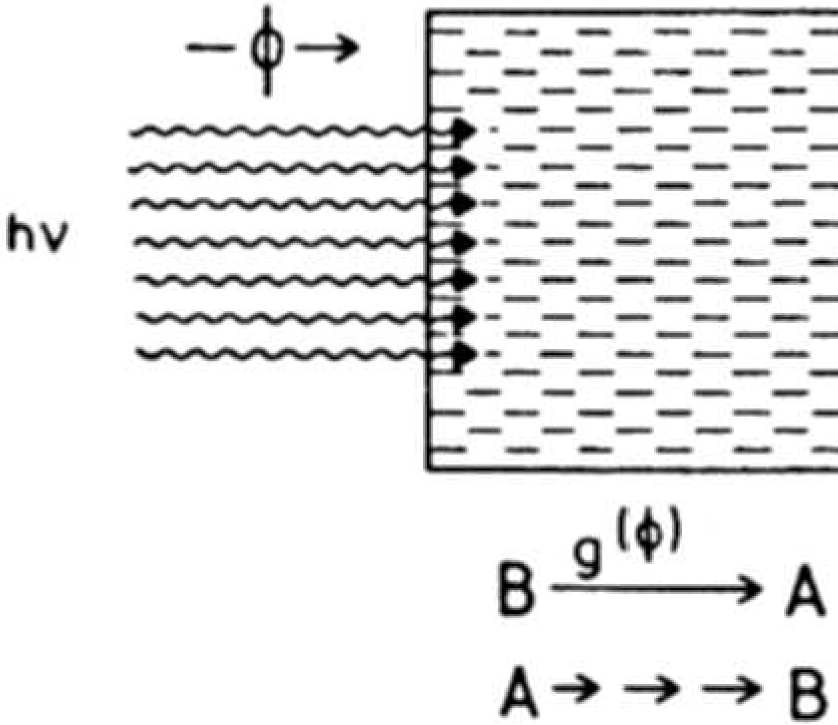


flow reactor

open systems for studying evolution in vitro I

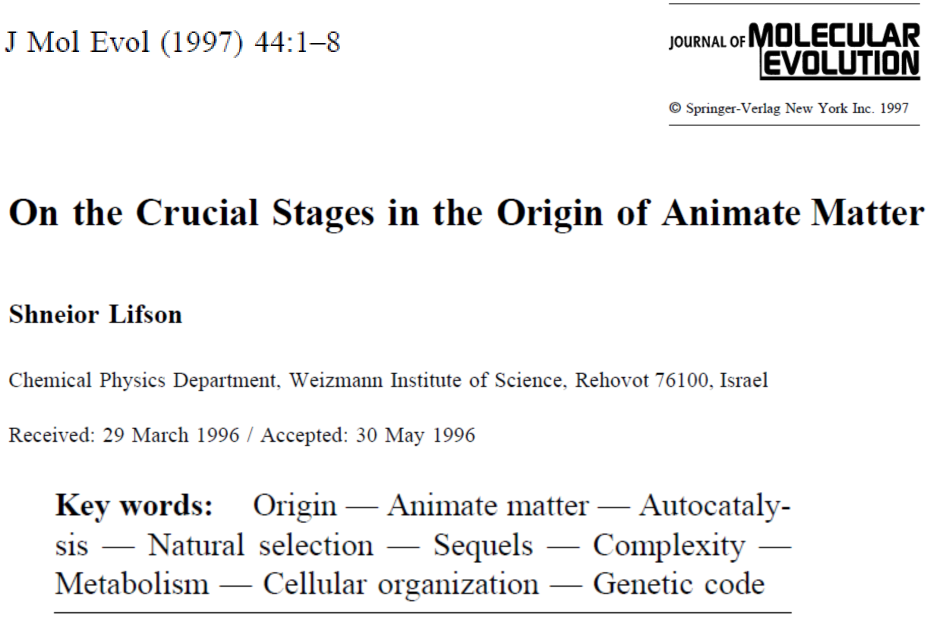


open systems for studying evolution in vitro II



„Los Alamos bug"

recycling open systems for studying evolution in vitro



J Mol Evol (1997) 44:1–8

JOURNAL OF MOLECULAR EVOLUTION

On the Crucial Stages in the Origin of Animate Matter

Shneior Lifson

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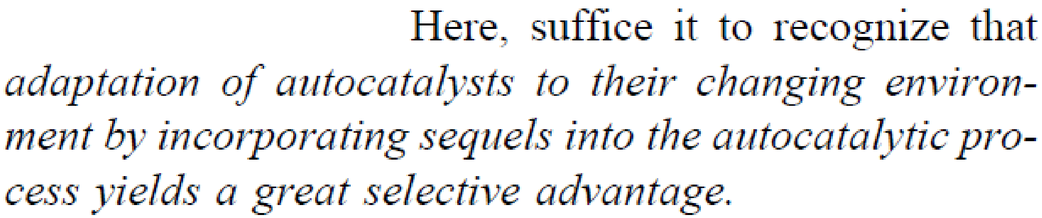
Received: 29 March 1996 / Accepted: 30 May 1996

Key words: Origin — Animate matter — Autocatalysis — Natural selection — Sequels — Complexity — Metabolism — Cellular organization — Genetic code

Shneior Lifson, 1914 - 2001

$$A + X \rightarrow 2X ;\ X \rightarrow D$$



Here, suffice it to recognize that *adaptation of autocatalysts to their changing environment by incorporating sequels into the autocatalytic process yields a great selective advantage.*

$$A + X \rightarrow 2X ;\ X \rightarrow D ;\ D \rightarrow A$$ ← recycling

Shneior Lifson and recycling in origin of life models

$$\dot{x}_i = \Gamma_i(\mathbf{x}) - \frac{x_i}{c(t)}\,\phi(t)$$

$$\phi(t) = \sum_{i=1}^{n} \Gamma_i(\mathbf{x}) - \frac{\mathrm{d}c}{\mathrm{d}t} \qquad \text{or} \qquad c(t) = c_0 + \int_0^t \left\{ \sum_{i=1}^{n} \Gamma_i(\mathbf{x}) - \phi(\tau) \right\} \mathrm{d}\tau$$

$$\boldsymbol{\xi} = \frac{1}{c}\,\mathbf{x} \quad \longrightarrow \quad \dot{\xi}_i = \frac{1}{c(t)}\,\{\Gamma_i(\mathbf{x}) - \xi_i \Sigma_j \Gamma_j(\mathbf{x})\}$$

$$\Gamma_i(\mathbf{x}) = \Gamma_i(c\,\boldsymbol{\xi}) = c^{\lambda}\,\Gamma_i(\boldsymbol{\xi}) \qquad\qquad \dot{\xi}_i = c^{\lambda-1} \left\{ \Gamma_i(\boldsymbol{\xi}) - \xi_i \sum_{j=1}^{n} \Gamma_j(\boldsymbol{\xi}) \right\}$$

$\lambda = p = 1$ ⟶ identical solution curves in growing and stationary systems

dynamics in growing system

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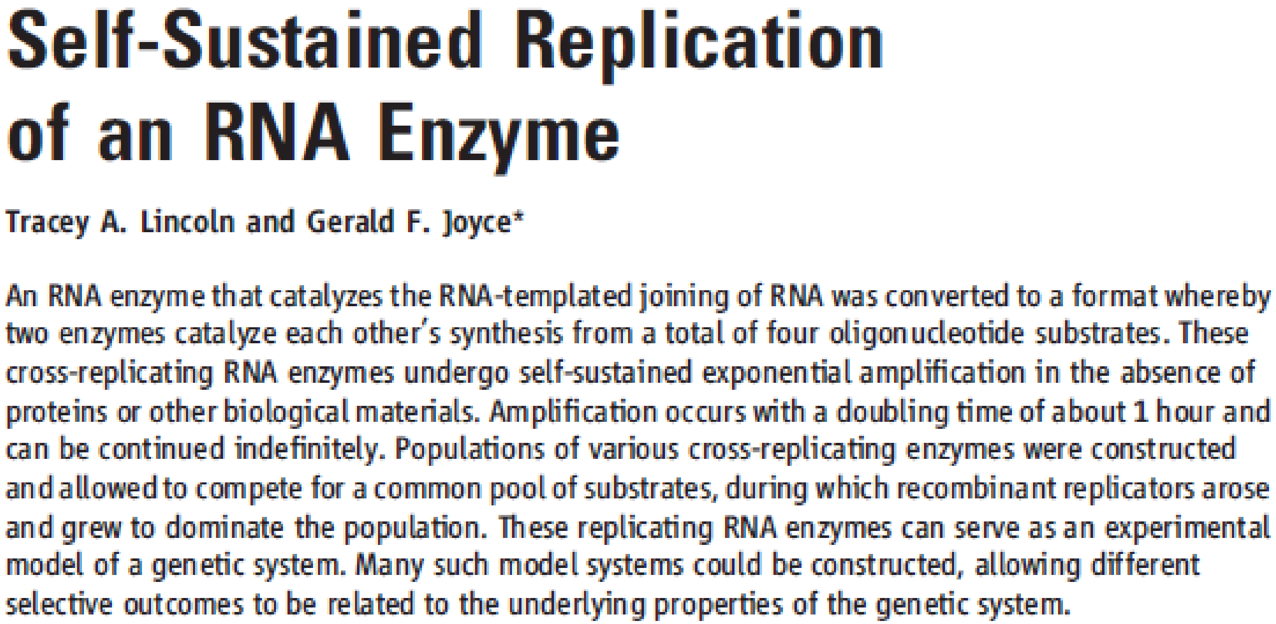
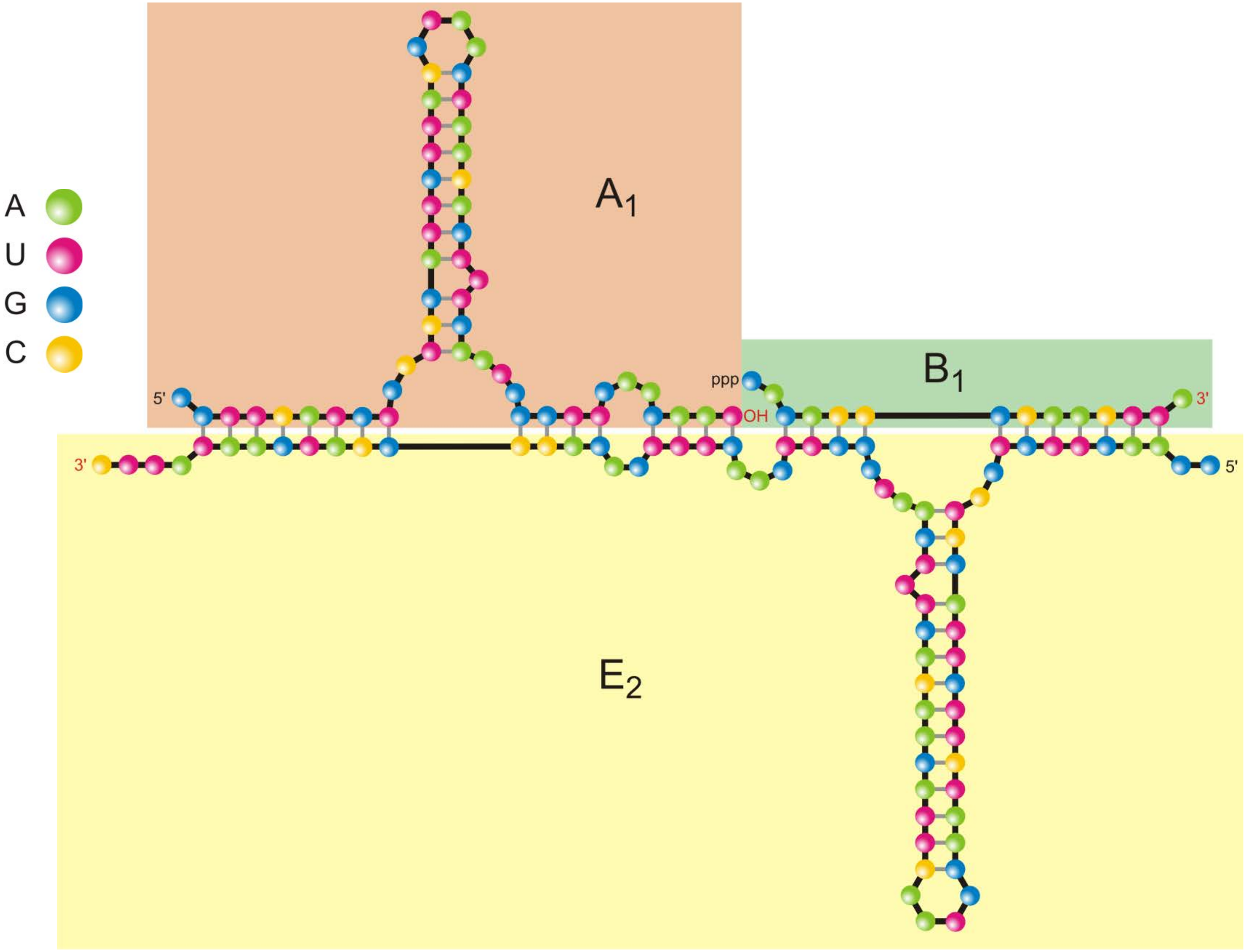


Self-Sustained Replication of an RNA Enzyme

Tracey A. Lincoln and Gerald F. Joyce*

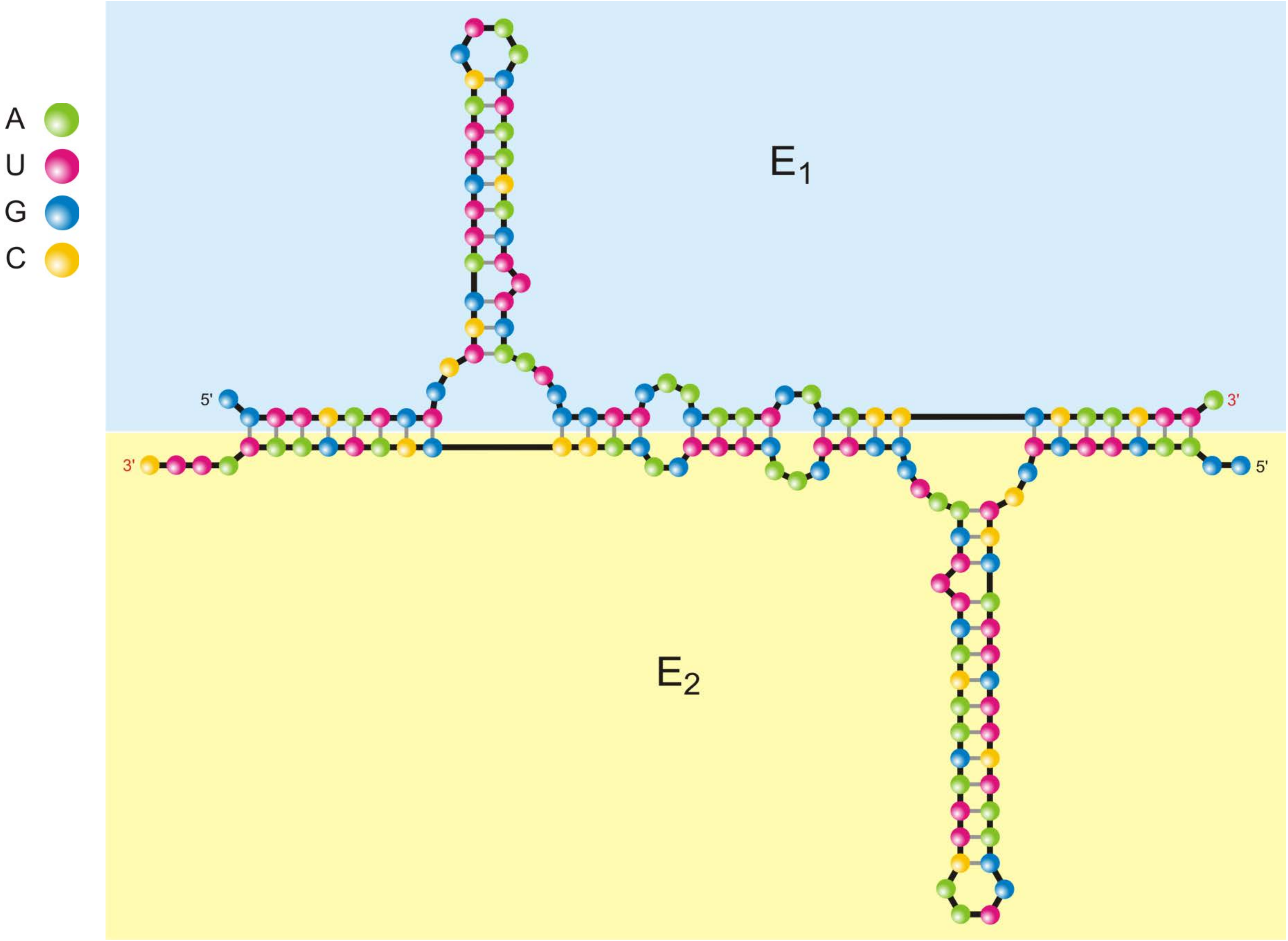
An RNA enzyme that catalyzes the RNA-templated joining of RNA was converted to a format whereby two enzymes catalyze each other's synthesis from a total of four oligonucleotide substrates. These cross-replicating RNA enzymes undergo self-sustained exponential amplification in the absence of proteins or other biological materials. Amplification occurs with a doubling time of about 1 hour and can be continued indefinitely. Populations of various cross-replicating enzymes were constructed and allowed to compete for a common pool of substrates, during which recombinant replicators arose and grew to dominate the population. These replicating RNA enzymes can serve as an experimental model of a genetic system. Many such model systems could be constructed, allowing different selective outcomes to be related to the underlying properties of the genetic system.

Science 2009, 323:1229 - 1232



An example of two ribozymes growing exponentially by cross-catalysis.

T.A. Lincoln, G.F. Joyce. 2009. Self-sustained replication of an RNA enzyme. Science 323:1229-1232



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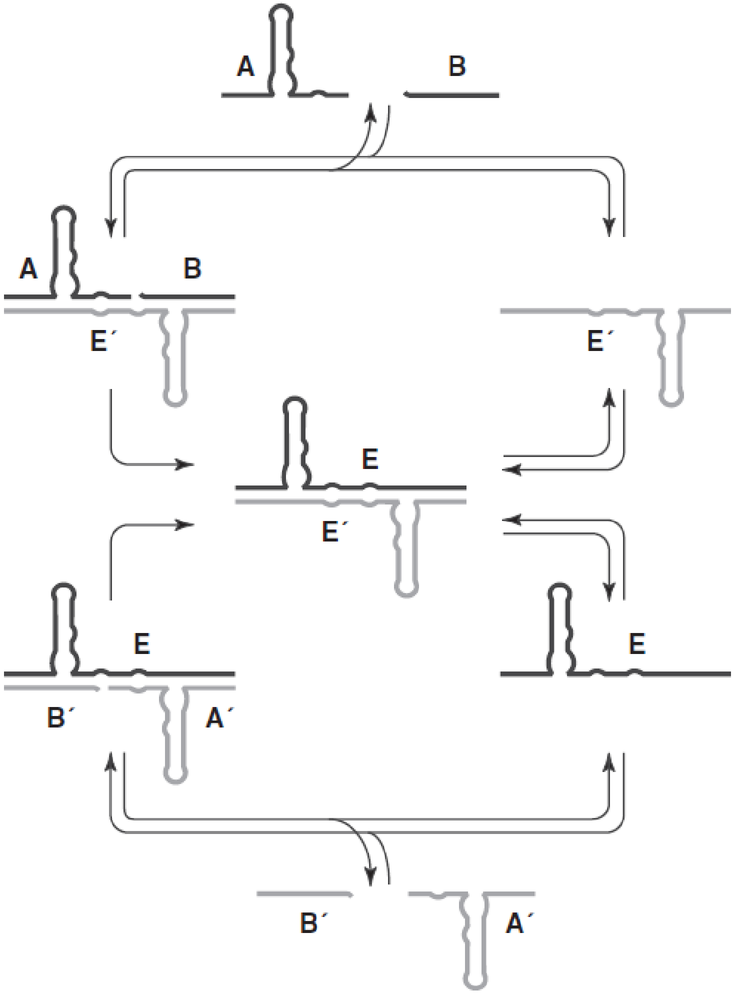
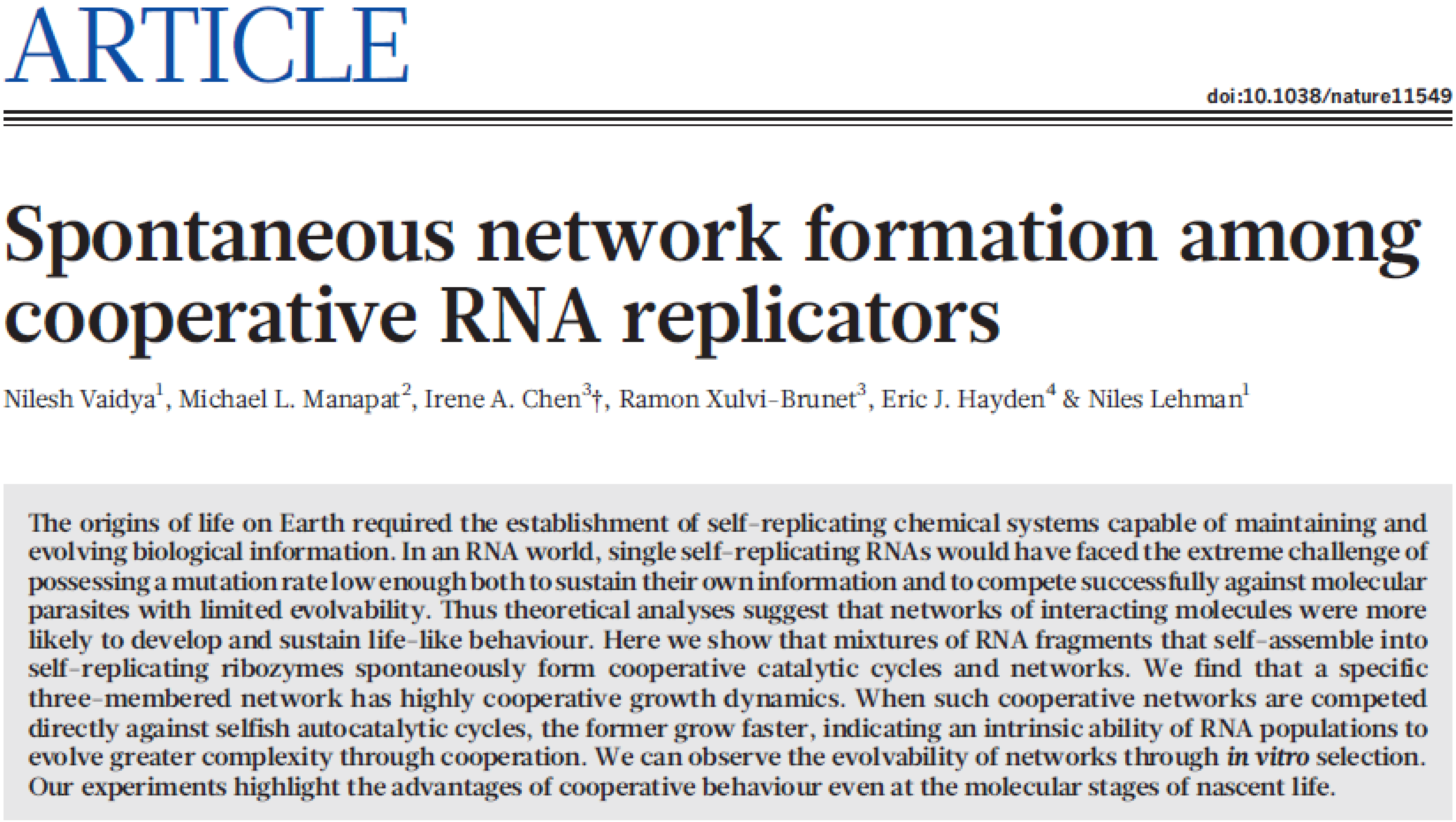


Fig. 1. Cross-replicating RNA enzymes. (**A**) The enzyme E′ (gray) catalyzes ligation of substrates A and B (black) to form the enzyme E, whereas E catalyzes ligation of A′ and B′ to form E′. The two enzymes dissociate to provide copies that can catalyze another reaction. (**B**) Sequence and secondary structure of the complex formed between the enzyme and its two substrates (E′, A, and B are shown; E, A′, and B′ are the reciprocal). The curved arrow indicates the site of ligation. Solid boxes indicate critical wobble pairs that provide enhanced catalytic activity. Dashed boxes indicate paired regions and catalytic nucleotides that were altered to construct various cross replicators. (**C**) Variable portion of 12 different E enzymes. The corresponding E′ enzymes have a complementary sequence in the paired region and the same sequence of catalytic nucleotides (alterations relative to the E1 enzyme are highlighted).



ARTICLE

doi:10.1038/nature11549

Spontaneous network formation among cooperative RNA replicators

Nilesh Vaidya[1], Michael L. Manapat[2], Irene A. Chen[3]†, Ramon Xulvi-Brunet[3], Eric J. Hayden[4] & Niles Lehman[1]

The origins of life on Earth required the establishment of self-replicating chemical systems capable of maintaining and evolving biological information. In an RNA world, single self-replicating RNAs would have faced the extreme challenge of possessing a mutation rate low enough both to sustain their own information and to compete successfully against molecular parasites with limited evolvability. Thus theoretical analyses suggest that networks of interacting molecules were more likely to develop and sustain life-like behaviour. Here we show that mixtures of RNA fragments that self-assemble into self-replicating ribozymes spontaneously form cooperative catalytic cycles and networks. We find that a specific three-membered network has highly cooperative growth dynamics. When such cooperative networks are competed directly against selfish autocatalytic cycles, the former grow faster, indicating an intrinsic ability of RNA populations to evolve greater complexity through cooperation. We can observe the evolvability of networks through *in vitro* selection. Our experiments highlight the advantages of cooperative behaviour even at the molecular stages of nascent life.

Nature 2012, 491:72 - 77

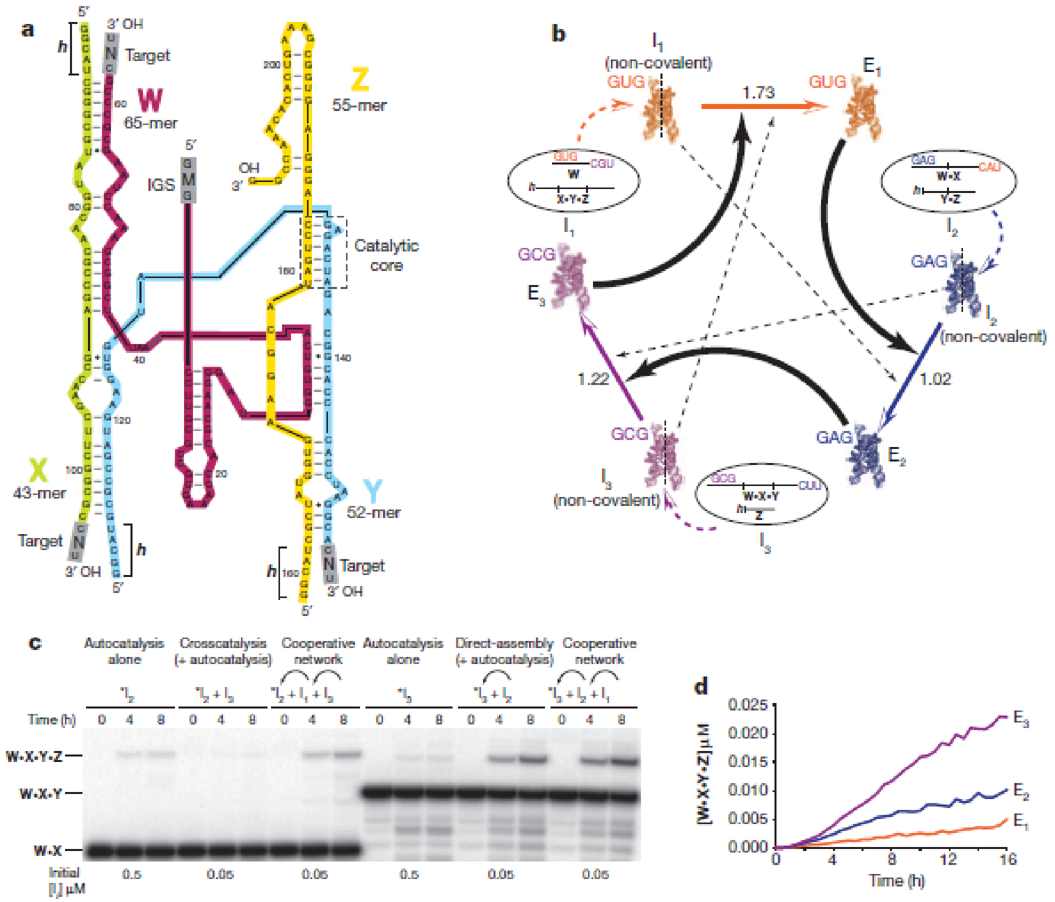


Figure 1 | Cooperative covalent assembly of recombinase ribozymes. **a**, Design of recombinase ribozymes capable of spontaneous cooperative covalent assembly from fragments. The *Azoarcus* ribozyme[25] can be broken at three loop regions to obtain four oligomers capable of self-assembling into a full-length molecule[26,27]. The grey box in **W** (magenta) is the internal guide sequence (IGS), whereas those at the 3′ ends of the **W**, **X** (lime) and **Y** (blue) fragments are recombination targets (tags) recognized by the IGS, which guides the catalysis of a covalent closure (•) of the loops. **b**, A cooperative system comprised of three subsystems, each created from partitioning the molecule into two pieces at different junctions: I_1 (**W** + ***h*•X•Y•Z**), I_2 (**W•X** + ***h*•Y•Z**) and I_3 (**W•X•Y** + ***h*•Z**). Numbers over arrows estimate the cooperative advantage for each step (see text). **c**, Electrophoretic observation of assemblies of E_2 and E_3. The 5′ fragments of I_2 or I_3 were independently 5′-radiolabelled with ^{32}P (that is, $*I_2$ or $*I_3$). The reactions were performed by incubating 0.5 μM (for autocatalysis) or 0.05 μM (for direct assembly, cross catalysis and cooperation) of each fragment for 8 h. Where appropriate, the arrows identify the subsystems being assembled by the previous subsystems in the network, where the IGS and recombination tags match. **d**, Yields of individual E_i ribozymes over time, measured every 30 min for 16 h when all six I_i RNA fragments are co-incubated at 0.05 μM.

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How Does Complexity Arise in Evolution

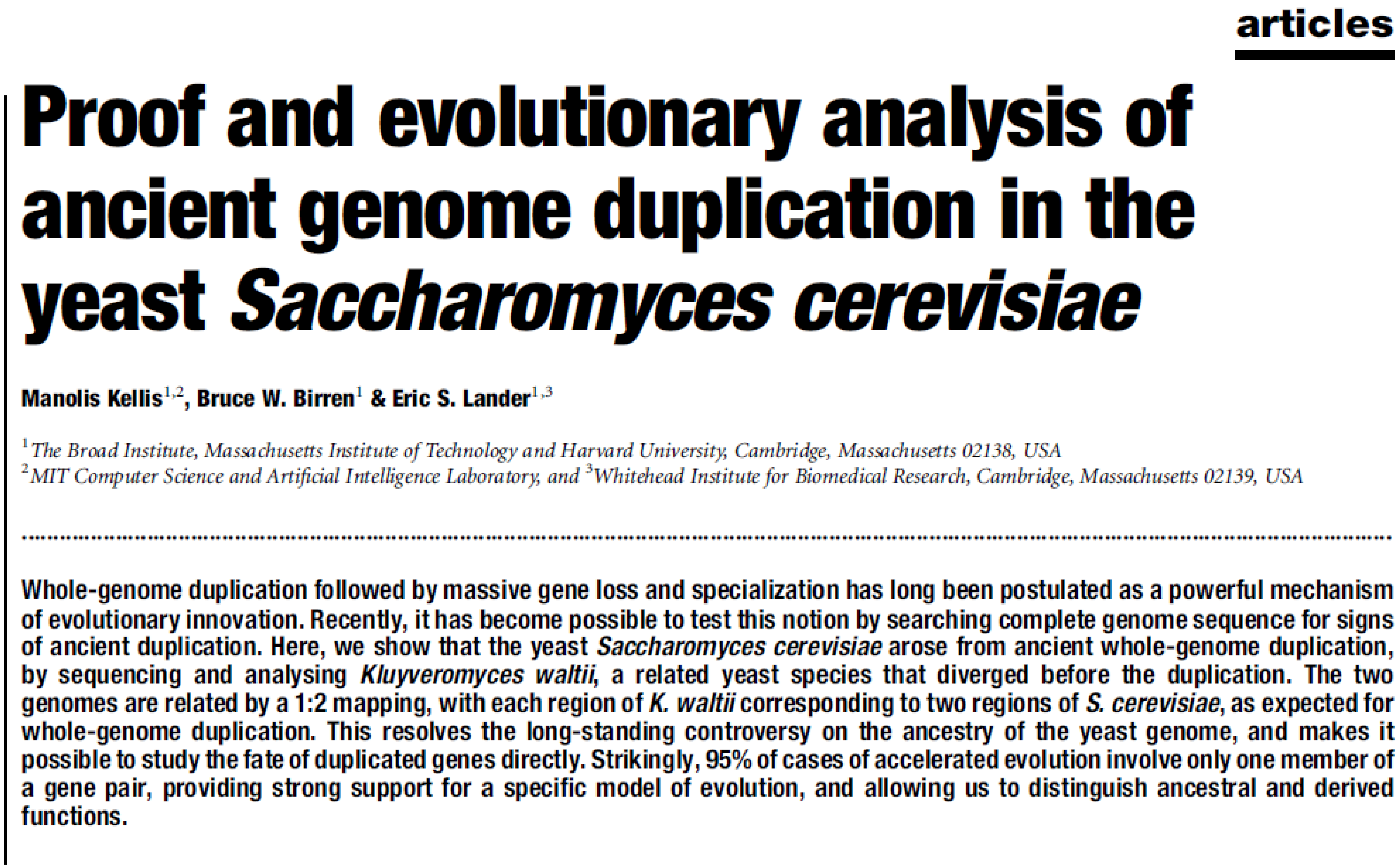
Nature's recipe for mastering scarcity, abundance, and unpredictability

PETER SCHUSTER

Scarcity drives optimization in Darwin's sense

Abundance is required for innovation
and major transitions

Complexity 1996, 2(1):22 - 30



articles

Proof and evolutionary analysis of ancient genome duplication in the yeast *Saccharomyces cerevisiae*

Manolis Kellis[1,2], **Bruce W. Birren**[1] **& Eric S. Lander**[1,3]

[1] *The Broad Institute, Massachusetts Institute of Technology and Harvard University, Cambridge, Massachusetts 02138, USA*
[2] *MIT Computer Science and Artificial Intelligence Laboratory, and* [3] *Whitehead Institute for Biomedical Research, Cambridge, Massachusetts 02139, USA*

Whole-genome duplication followed by massive gene loss and specialization has long been postulated as a powerful mechanism of evolutionary innovation. Recently, it has become possible to test this notion by searching complete genome sequence for signs of ancient duplication. Here, we show that the yeast *Saccharomyces cerevisiae* arose from ancient whole-genome duplication, by sequencing and analysing *Kluyveromyces waltii*, a related yeast species that diverged before the duplication. The two genomes are related by a 1:2 mapping, with each region of *K. waltii* corresponding to two regions of *S. cerevisiae*, as expected for whole-genome duplication. This resolves the long-standing controversy on the ancestry of the yeast genome, and makes it possible to study the fate of duplicated genes directly. Strikingly, 95% of cases of accelerated evolution involve only one member of a gene pair, providing strong support for a specific model of evolution, and allowing us to distinguish ancestral and derived functions.

A model for the genome duplication in yeast 100 million years ago

Manolis Kellis, Bruce W. Birren, and Eric S. Lander. Proof and evolutionary analysis of ancient genome duplication in the yeast *Saccharomyces cerevisiae*. *Nature* **428**: 617-624, 2004

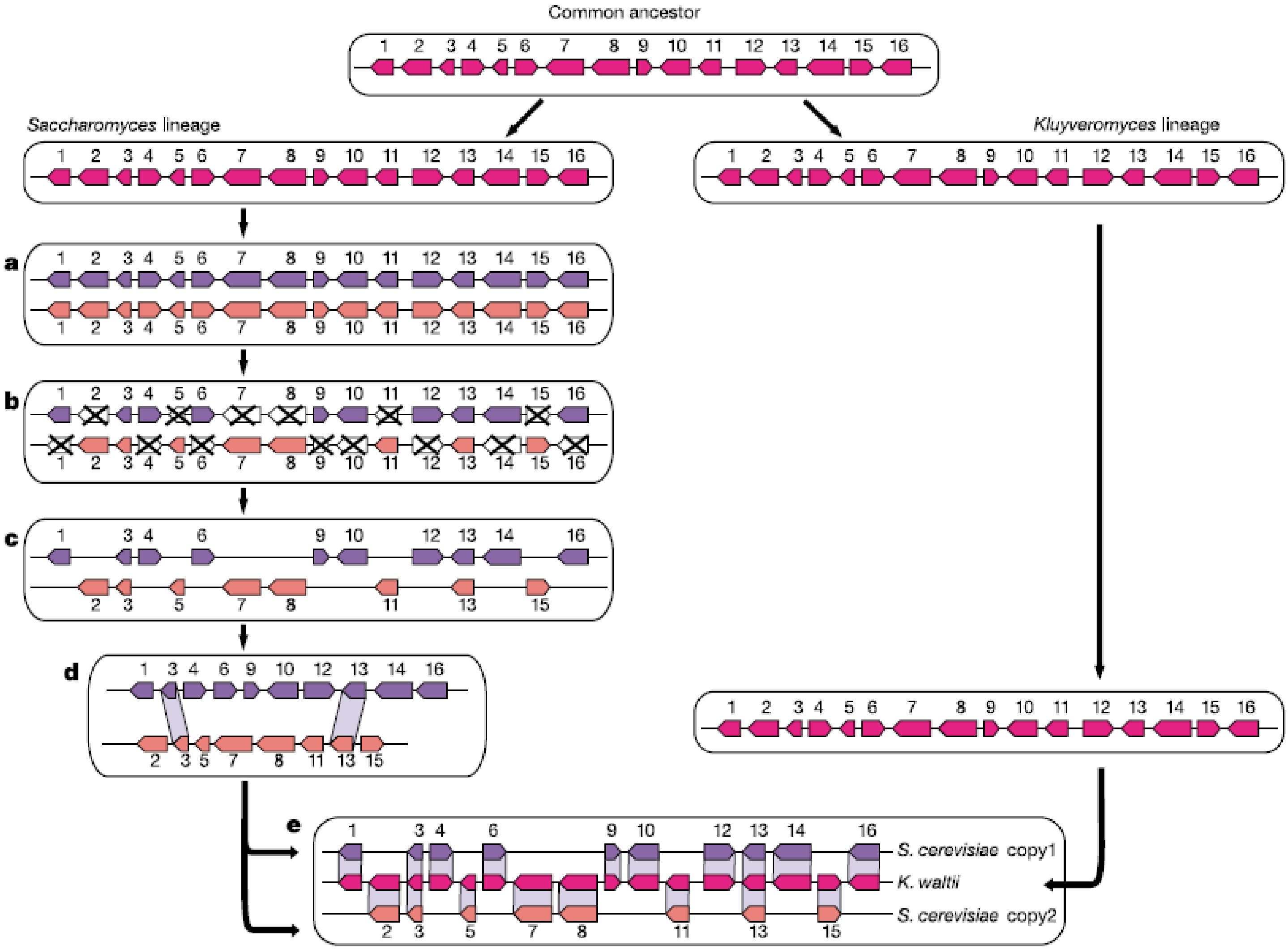
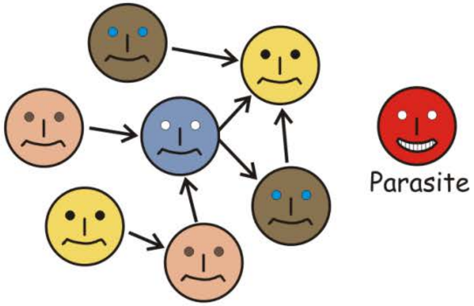


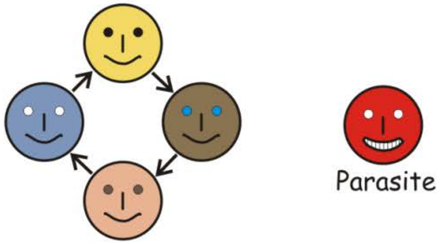
Figure 1 Model of WGD followed by massive gene loss predicts gene interleaving in sister regions. **a**, After divergence from *K. waltii*, the *Saccharomyces* lineage underwent a genome duplication event, creating two copies of every gene and chromosome. **b**, The vast majority of duplicated genes underwent mutation and gene loss. **c**, Sister segments retained different subsets of the original gene set, keeping two copies for only a small minority of duplicated genes, which were retained for functional purposes. **d**, Within *S. cerevisiae*, the only evidence comes from the conserved order of duplicated genes (numbered 3 and 13) across different chromosomal segments; the intervening genes are unrelated. **e**, Comparison with *K. waltii* reveals the duplicated nature of the *S. cerevisiae* genome, interleaving genes from sister segments on the basis of the ancestral gene order.

Stage I:
Independent competing replicators

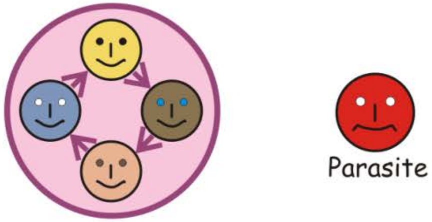
Stage II:
Catalysis and competition in replication



Stage III:
Functionally coupled replicators



Stage IV:
New unit of selection



Stage V = Stage I:
Independently competing units

Thank you for your attention!

Web-Page for further information:

http://www.tbi.univie.ac.at/~pks