How reproduction differs from chemical reaction networks

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Origins of Life and Its Search in the Universe

Madrid, 16.– 17.11.2016

Web-Page for further information:

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

Peter Schuster. Some mechanistic requirements for major transitions. *Phil. Trans. R. Soc.B* 371:e20150439, 2016

Peter Schuster. Increase in complexity and information through molecular evolution. *Entropy* 18:397, 2016

1. Chemical and biochemical reaction networks
2. Autocatalysis and replication
3. A simple model of evolution
4. Mutation and quasispecies
5. Cooperation and major transitions
6. Can mutations counteract extinction ?

1. **Chemical and biochemical reaction networks**
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Martin Feinberg, 1942 -

Martin Feinberg,
F.J.M. Horn,
Roy Jackson

$$\mathsf{A} \xrightarrow{k_1} \mathsf{2B} ,$$
$$\mathsf{2B} \xrightarrow{l_1} \mathsf{A} ,$$
$$\mathsf{A} + \mathsf{C} \xrightarrow{k_2} \mathsf{D} ,$$
$$\mathsf{D} \xrightarrow{l_2} \mathsf{A} + \mathsf{C} ,$$
$$\mathsf{D} \xrightarrow{k_3} \mathsf{B} + \mathsf{E} ,$$
$$\mathsf{B} + \mathsf{E} \xrightarrow{k_4} \mathsf{A} + \mathsf{C} .$$

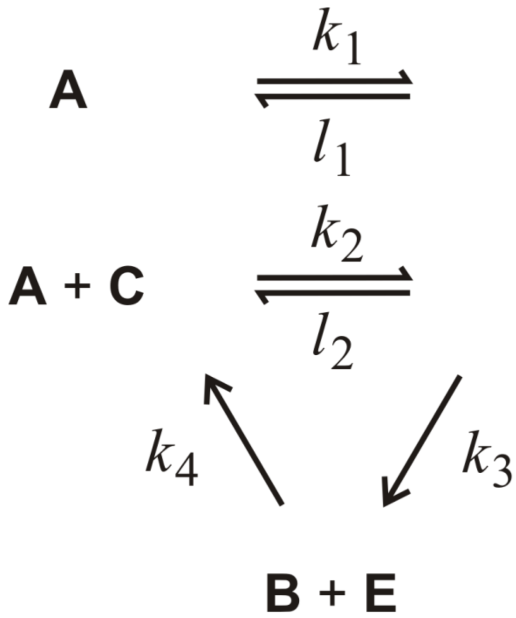
The Feinberg model mechanism

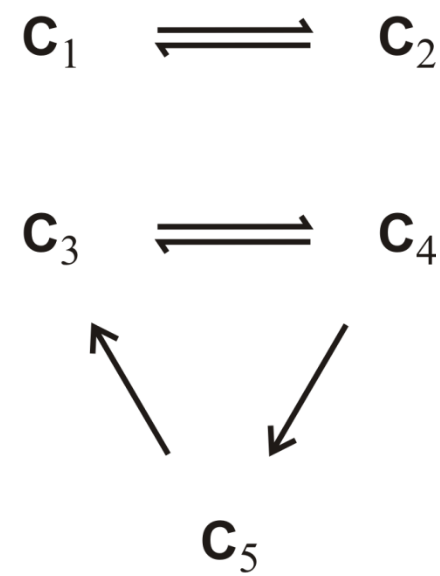
Martin Feinberg, Chemical reaction network structure and the stability of complex isothermal reactors I. The deficiency zero and deficiency one theorems.

Chem.Engineerin Science 42:229-2268, 1987

Martin Feinberg, Chemical reaction network structure and the stability of complex isothermal reactors II. Multiple steady states for networks of deficiency one.
Chem.Engineerin Science 43:1-25, 1988

Chemical reaction network theory





$$\mathcal{S} = \{\mathsf{A},\ \mathsf{B},\ \mathsf{C},\ \mathsf{D},\ \mathsf{E}\}$$

$$\mathcal{C} = \{\mathsf{C}_1 = \mathsf{A},\ \mathsf{C}_2 = 2\mathsf{B},\ \mathsf{C}_3 = \mathsf{A} + \mathsf{C},\ \mathsf{C}_4 = \mathsf{D},\ \mathsf{C}_5 = \mathsf{B} + \mathsf{E}\}$$

$$\begin{aligned}\mathcal{R} = \{&\mathbf{R}_1 = \mathsf{C}_1 \to \mathsf{C}_2,\ \mathbf{R}_2 = \mathsf{C}_2 \to \mathsf{C}_1,\ \mathbf{R}_3 = \mathsf{C}_3 \to \mathsf{C}_4,\\ &\mathbf{R}_4 = \mathsf{C}_4 \to \mathsf{C}_3,\ \mathbf{R}_5 = \mathsf{C}_4 \to \mathsf{C}_5,\ \mathbf{R}_6 = \mathsf{C}_5 \to \mathsf{C}_3\}\end{aligned}$$

Deficiency: $\delta = N - L - R$

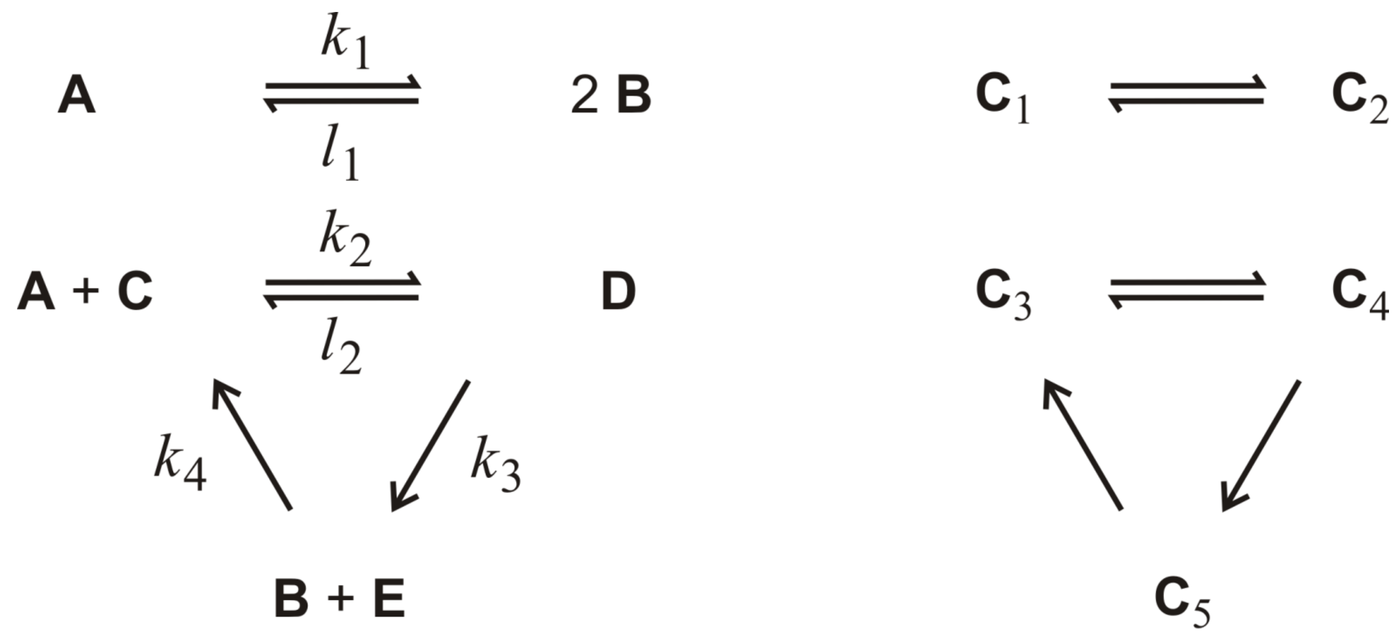
N … number of complexes

L … number of linkage classes

R … number of the degrees of freedom,
rank of the reaction kinetics

$\boldsymbol{\delta}$ **= 0**: unique and asymptotically stable equilibrium state,
no multiple steady states,
no oscillations, no deterministic chaos

Deficiency zero



L = 2

$$\mathcal{S} = \{\mathsf{A},\ \mathsf{B},\ \mathsf{C},\ \mathsf{D},\ \mathsf{E}\}$$

$$\mathcal{C} = \{\mathsf{C}_1 = \mathsf{A},\ \mathsf{C}_2 = 2\mathsf{B},\ \mathsf{C}_3 = \mathsf{A} + \mathsf{C},\ \mathsf{C}_4 = \mathsf{D},\ \mathsf{C}_5 = \mathsf{B} + \mathsf{E}\}$$

N = 5

$$\mathcal{R} = \{\mathbf{R}_1 = \mathsf{C}_1 \to \mathsf{C}_2,\ \mathbf{R}_2 = \mathsf{C}_2 \to \mathsf{C}_1,\ \mathbf{R}_3 = \mathsf{C}_3 \to \mathsf{C}_4,\ \mathbf{R}_4 = \mathsf{C}_4 \to \mathsf{C}_3,\ \mathbf{R}_5 = \mathsf{C}_4 \to \mathsf{C}_5,\ \mathbf{R}_6 = \mathsf{C}_5 \to \mathsf{C}_3\}$$

R = 3

Deficiency: δ = N – L – R

N … number of complexes

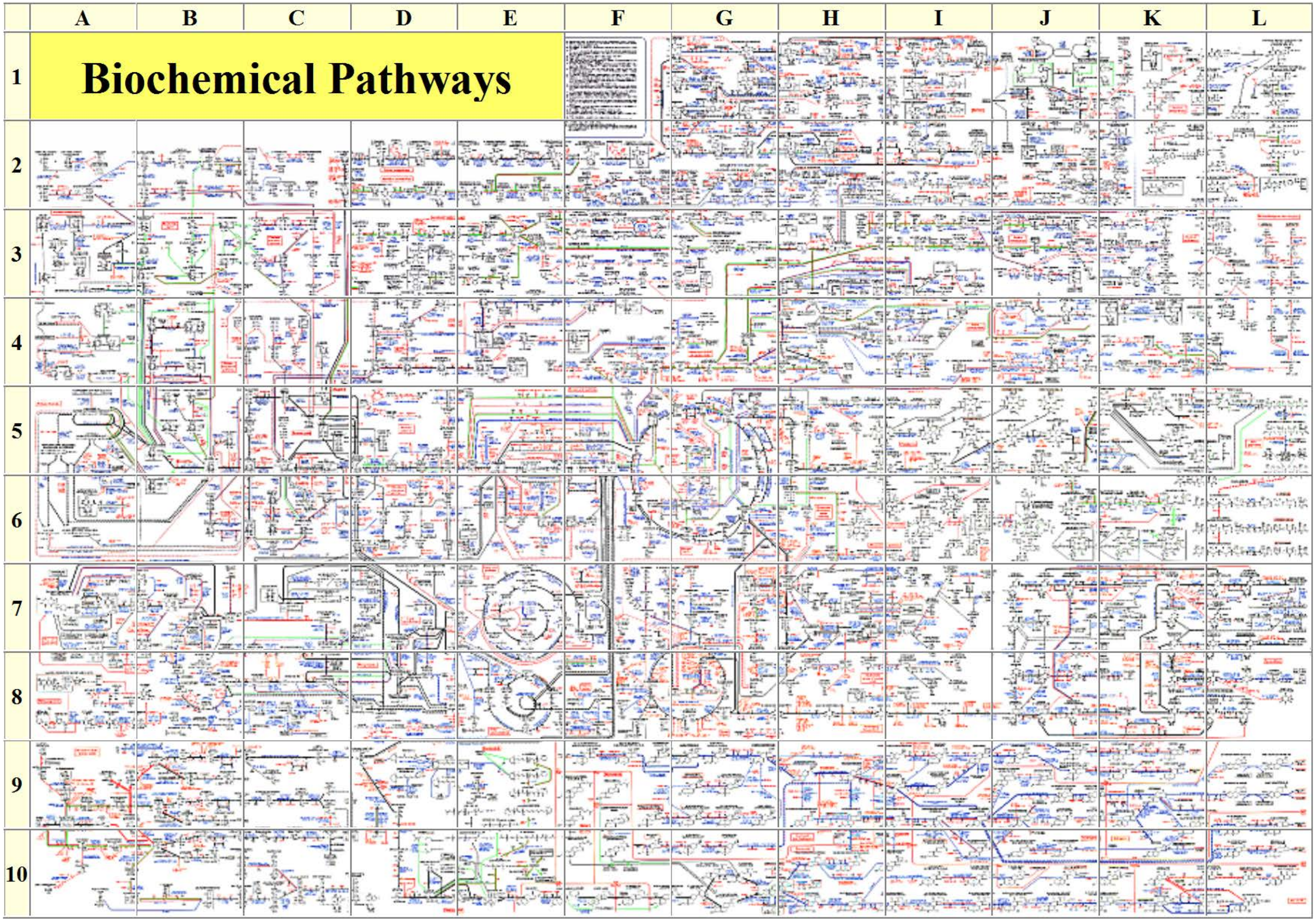
L … number of linkage classes

R … number of the degrees of freedom,
rank of the reaction kinetics

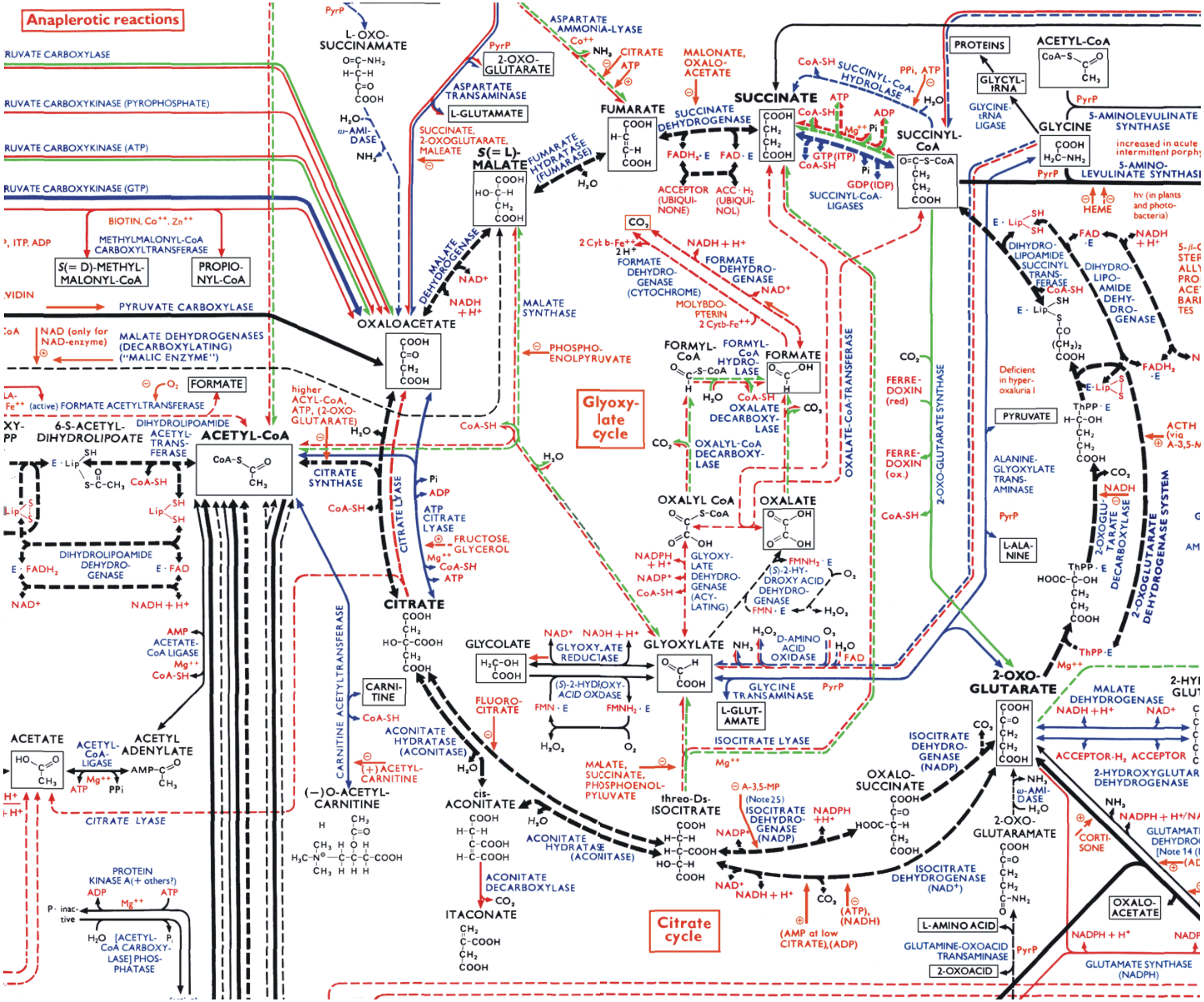
Feinberg mechanism: **N = 5**, **L = 2**, **R = 3** $\Rightarrow$ **δ = 0**

δ = 0: unique and asymptotically stable equilibrium state,
no multiple steady states,
no oscillations, no deterministic chaos

Deficiency zero



The reaction network of cellular metabolism published by Boehringer-Mannheim.



Anaplerotic reactions
PYRUVATE CARBOXYLASE
PYRUVATE CARBOXYKINASE (PYROPHOSPHATE)
PYRUVATE CARBOXYKINASE (ATP)
PYRUVATE CARBOXYKINASE (GTP)
BIOTIN, Co++, Zn++
METHYLMALONYL-CoA CARBOXYLTRANSFERASE
S(= D)-METHYL-MALONYL-CoA
PROPIONYL-CoA
AVIDIN
PYRUVATE CARBOXYLASE
NAD (only for NAD-enzyme)
MALATE DEHYDROGENASES (DECARBOXYLATING) ("MALIC ENZYME")
FORMATE
(active) FORMATE ACETYLTRANSFERASE
6-S-ACETYL-DIHYDROLIPOATE
DIHYDROLIPOAMIDE ACETYL-TRANSFERASE
ACETYL-CoA
CoA-SH
DIHYDROLIPOAMIDE DEHYDRO-GENASE
E · FADH2
E · FAD
NAD+
NADH + H+
AMP
ACETATE-CoA LIGASE
Mg++
CoA-SH
ACETATE
ACETYL-CoA LIGASE
ACETYL ADENYLATE
ATP
PPi
CITRATE LYASE
PROTEIN KINASE A (+ others?)
ADP
ATP
P · inactive
H2O
[ACETYL-CoA CARBOXYLASE] PHOSPHATASE
Pi
PyrP
L-OXO-SUCCINAMATE
H2O
ω-AMIDASE
NH3
2-OXO-GLUTARATE
ASPARTATE TRANSAMINASE
L-GLUTAMATE
SUCCINATE, 2-OXOGLUTARATE, MALEATE
S(= L)-MALATE
MALATE DEHYDROGENASE
NAD+
NADH + H+
OXALOACETATE
PHOSPHOENOLPYRUVATE
MALATE SYNTHASE
higher ACYL-CoA, ATP, (2-OXO-GLUTARATE)
H2O
CITRATE SYNTHASE
CoA-SH
CITRATE LYASE
Pi
ADP
ATP CITRATE LYASE
FRUCTOSE, GLYCEROL
Mg++
CoA-SH
ATP
CITRATE
CARNITINE ACETYLTRANSFERASE
CARNITINE
CoA-SH
(−)O-ACETYL-CARNITINE
(+) ACETYL-CARNITINE
ACONITATE HYDRATASE (ACONITASE)
FLUORO-CITRATE
H2O
cis-ACONITATE
ACONITATE DECARBOXYLASE
CO2
ITACONATE
ASPARTATE AMMONIA-LYASE
Co++
NH3
CITRATE
ATP
FUMARATE
FUMARATE HYDRATASE (FUMARASE)
H2O
MALONATE, OXALOACETATE
SUCCINATE DEHYDROGENASE
FADH2 · E
FAD · E
ACCEPTOR (UBIQUINONE)
ACC · H2 (UBIQUINOL)
SUCCINATE
CoA-SH
SUCCINYL-CoA HYDROLASE
PPi, ATP
H2O
ATP
ADP
Mg++
Pi
GTP (ITP)
GDP (IDP)
SUCCINYL-CoA LIGASES
SUCCINYL-CoA
CO2
2 Cyt b-Fe++
2 H+
FORMATE DEHYDROGENASE (CYTOCHROME)
NADH + H+
FORMATE DEHYDROGENASE
NAD+
MOLYBDOPTERIN
2 Cytb-Fe+++
Glyoxylate cycle
FORMYL-CoA
FORMYL-CoA HYDROLASE
FORMATE
H2O
CoA-SH
OXALATE DECARBOXYLASE
CO2
OXALYL-CoA DECARBOXYLASE
OXALYL CoA
OXALATE
NADPH + H+
NADP+
CoA-SH
GLYOXYLATE DEHYDROGENASE (ACYLATING)
FMNH2 · E
(S)-2-HYDROXY ACID DEHYDROGENASE
FMN · E
H2O2
O2
OXALATE-CoA-TRANSFERASE
GLYCOLATE
NAD+
NADH + H+
GLYOXYLATE REDUCTASE
GLYOXYLATE
(S)-2-HYDROXY-ACID OXIDASE
FMN · E
FMNH2 · E
H2O2
O2
NH3
D-AMINO ACID OXIDASE
FAD
GLYCINE TRANSAMINASE
L-GLUTAMATE
PyrP
ISOCITRATE LYASE
Mg++
MALATE, SUCCINATE, PHOSPHOENOLPYRUVATE
A-3,5-MP
threo-Ds-ISOCITRATE
ISOCITRATE DEHYDROGENASE (NADP)
NADP+
NADPH + H+
NAD+
NADH + H+
CO2
ISOCITRATE DEHYDROGENASE (NAD+)
(AMP at low CITRATE), (ADP)
(ATP), (NADH)
Citrate cycle
PROTEINS
GLYCYL-tRNA
GLYCINE-tRNA LIGASE
GLYCINE
ACETYL-CoA
PyrP
5-AMINOLEVULINATE SYNTHASE
increased in acute intermittent porphyria
5-AMINO-LEVULINATE SYNTHASE
HEME
hν (in plants and photo-bacteria)
FERREDOXIN (red)
FERREDOXIN (ox.)
2-OXO-GLUTARATE SYNTHASE
CoA-SH
DIHYDROLIPOAMIDE SUCCINYLTRANSFERASE
DIHYDROLIPOAMIDE DEHYDROGENASE
FAD · E
NADH + H+
FADH2 · E
Deficient in hyperoxaluria I
PYRUVATE
ALANINE-GLYOXYLATE TRANSAMINASE
PyrP
L-ALANINE
ACTH (via A-3,5-MP)
ThPP · E
2-OXOGLUTARATE DECARBOXYLASE
2-OXOGLUTARATE DEHYDROGENASE SYSTEM
Mg++
2-OXO-GLUTARATE
MALATE DEHYDROGENASE
NADH + H+
NAD+
ACCEPTOR-H2
ACCEPTOR
2-HYDROXYGLUTARATE DEHYDROGENASE
ISOCITRATE DEHYDROGENASE (NADP)
OXALO-SUCCINATE
NH3
ω-AMIDASE
H2O
2-OXO-GLUTARAMATE
L-AMINO ACID
GLUTAMINE-OXOACID TRANSAMINASE
2-OXOACID
CORTISONE
NADPH + H+
GLUTAMATE DEHYDROGENASE
OXALO-ACETATE
NADPH + H+
GLUTAMATE SYNTHASE (NADPH)

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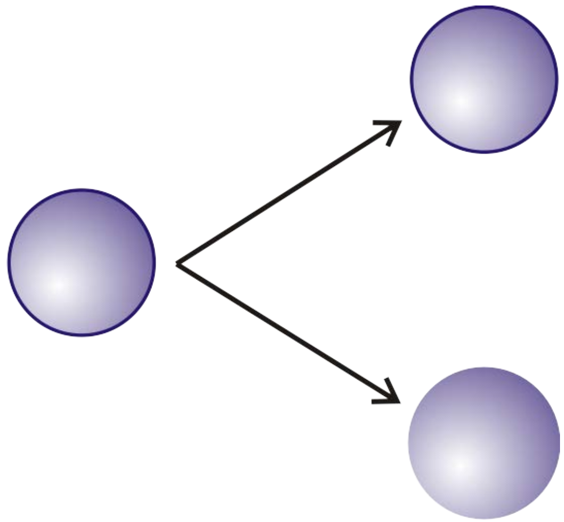
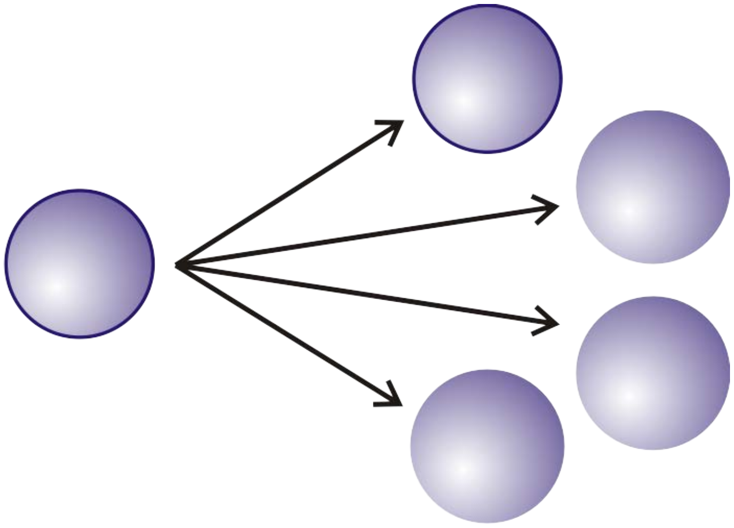


(A) + X = 2 X

$$\frac{dx}{dt} = fx \quad \Rightarrow \quad x(t) = x(0)\, e^{ft}$$

exponential growth

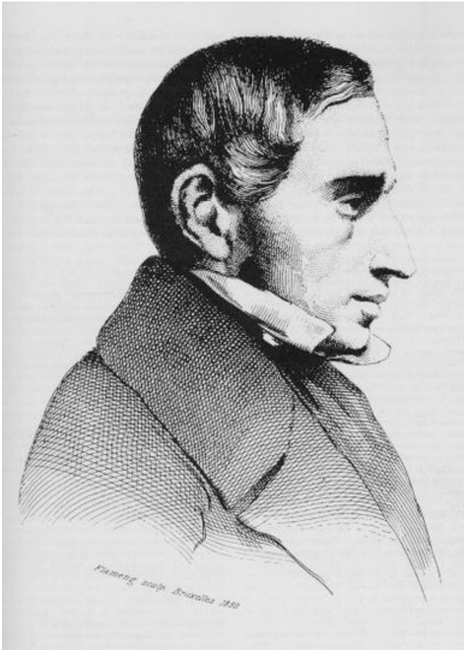


(A) + X = 4 X

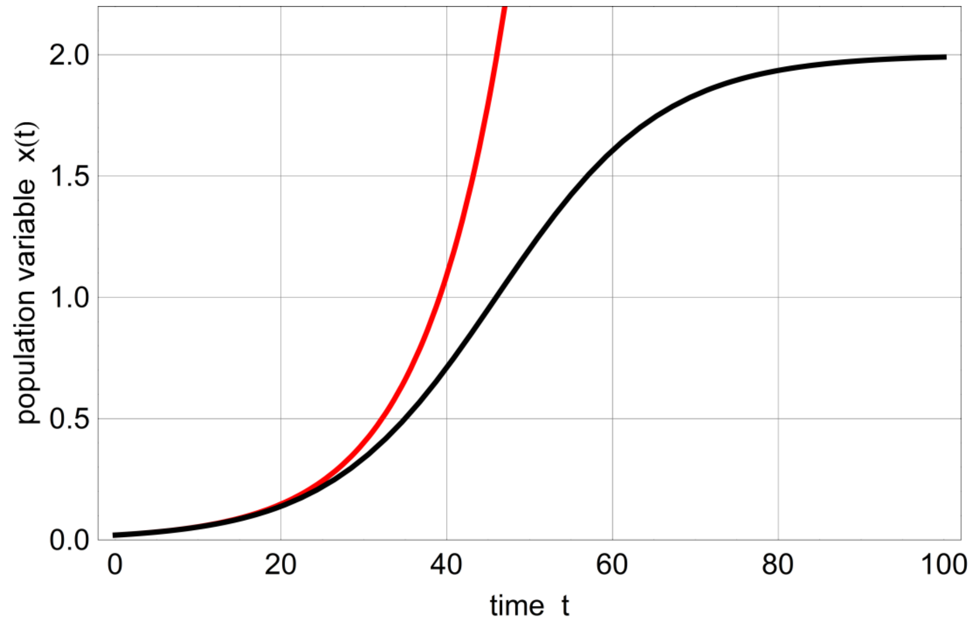
(A) + X = n X

$$\frac{1}{s}\cdot\frac{dx}{dt}=\frac{1}{n-1}\cdot\frac{dx}{dt}=f\,x \quad\Rightarrow\quad x(t)=x(0)\,e^{(n-1)\,f\,t}$$

exponential growth



Pierre-François Verhulst,
1804 - 1849

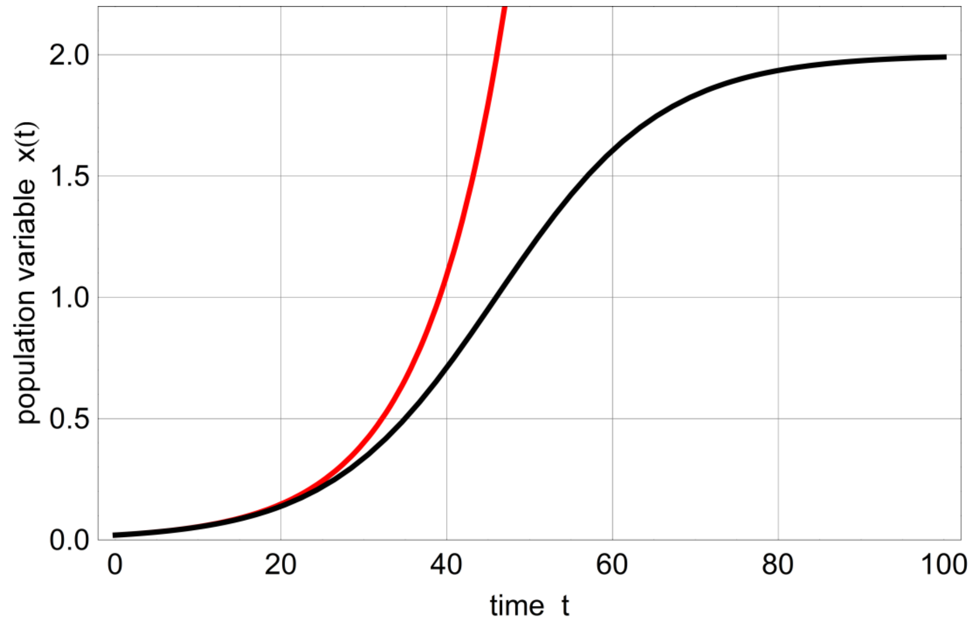


$$\frac{dx}{dt} = f\,x\left(1 - \frac{x}{C}\right) \quad \Rightarrow \quad x(t) = \frac{x(0)\,C}{x(0) + \big(C - x(0)\big)e^{-f\,t}}$$

C …… carrying capacity of the ecosystem

The logistic equation has been conceived in the year 1828.

Pierre-François Verhulst,
1804 - 1849



Has been known 30 years before the publication of the 'Origin of Species' !

The logistic equation has been conceived in the year 1828.

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

$$\mathrm{A} + \mathrm{X}_i = 2\,\mathrm{X}_i\,; \quad i = 1, 2\,, \ldots, n; \;\; f_1, f_2, \ldots, f_n$$

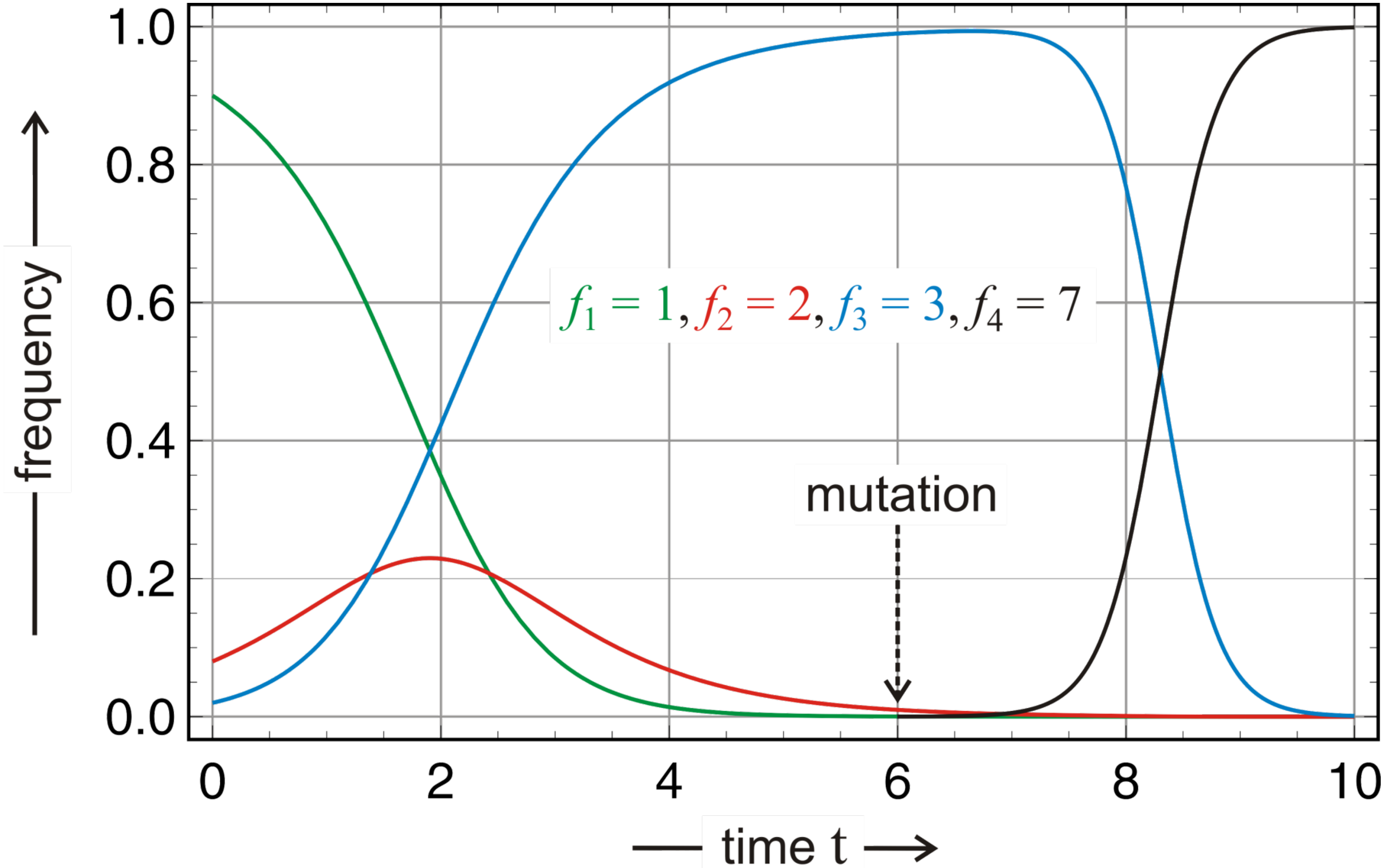
$$\mathrm{X}_1, \mathrm{X}_2, \ldots, \mathrm{X}_n : \quad [\mathrm{X}_i] = x_i\,; \quad \sum_{i=1}^{n} x_i = C = 1; \quad f_i = f(\mathrm{X}_i)$$

$$\frac{\mathrm{d}x_j}{\mathrm{dt}} = x_j \left(f_j - \sum_{i=1}^{n} f_i\, x_i \right) = x_j \left(f_j - \Phi \right) \; ; \quad \Phi = \sum_{i=1}^{n} f_i\, x_i$$

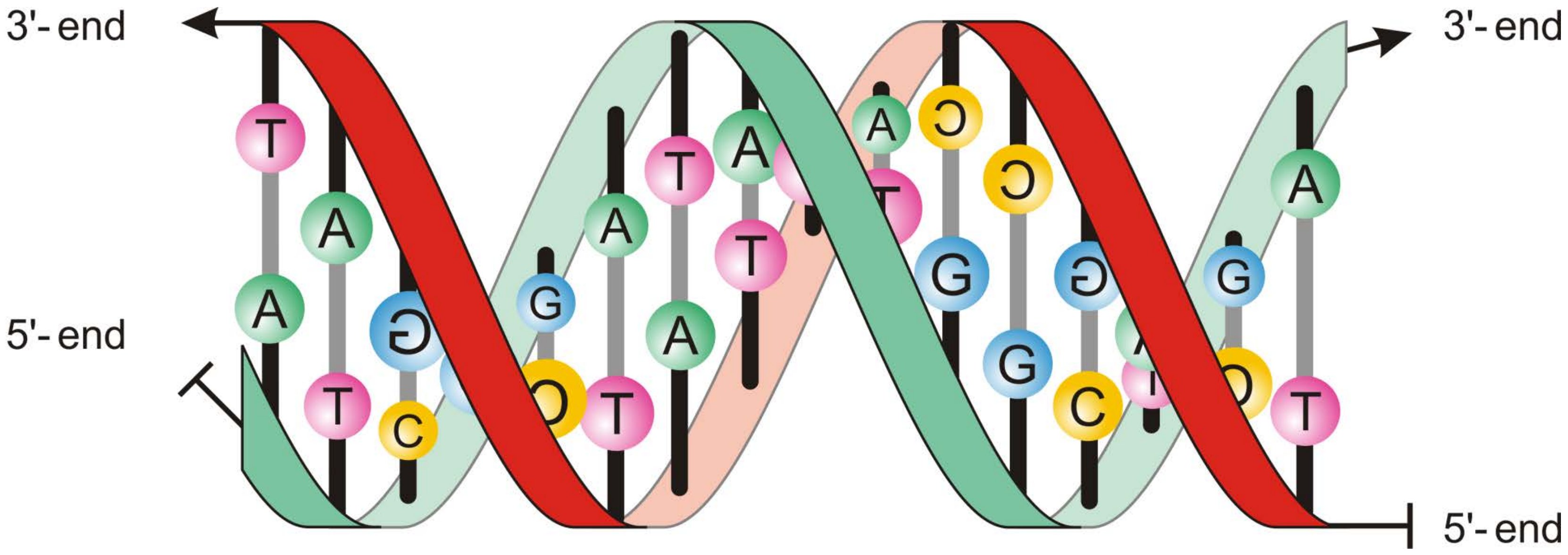
Darwin

$$\frac{\mathrm{d}\Phi}{\mathrm{dt}} = \langle f^{2} \rangle - \langle \bar{f} \rangle^{2} = \mathrm{var}\{f\} \geq 0$$

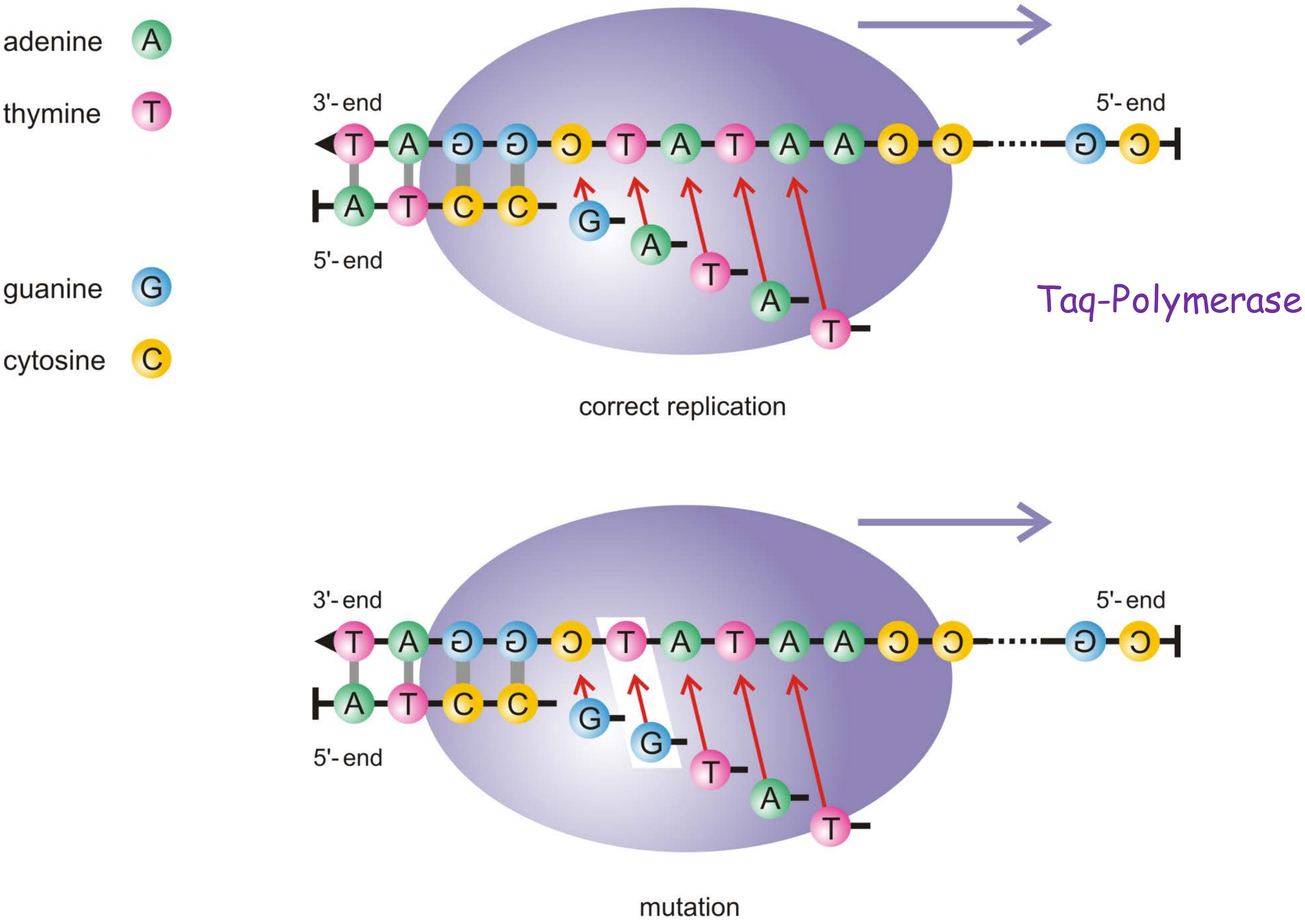
Generalization of the logistic equation to *n* variables yields selection



Selection of the fittest variant



B-conformation of the DNA double helix



Correct replication and point mutation

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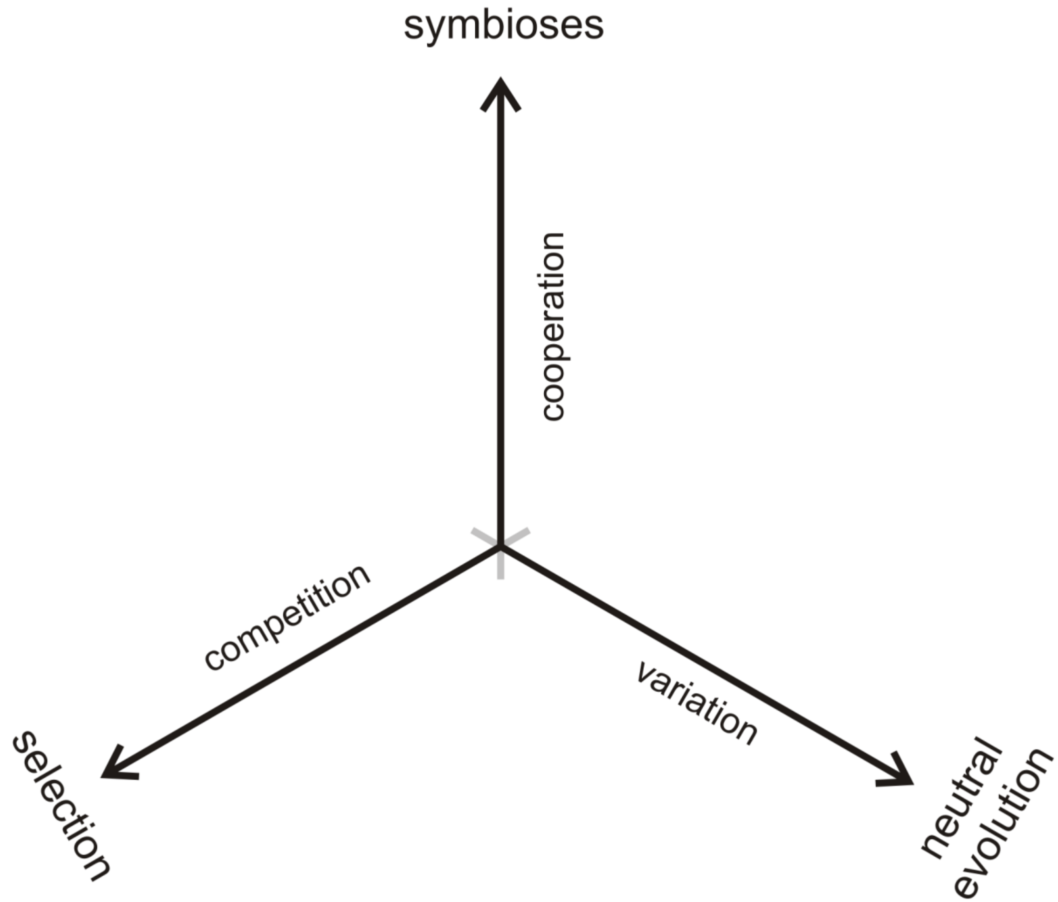
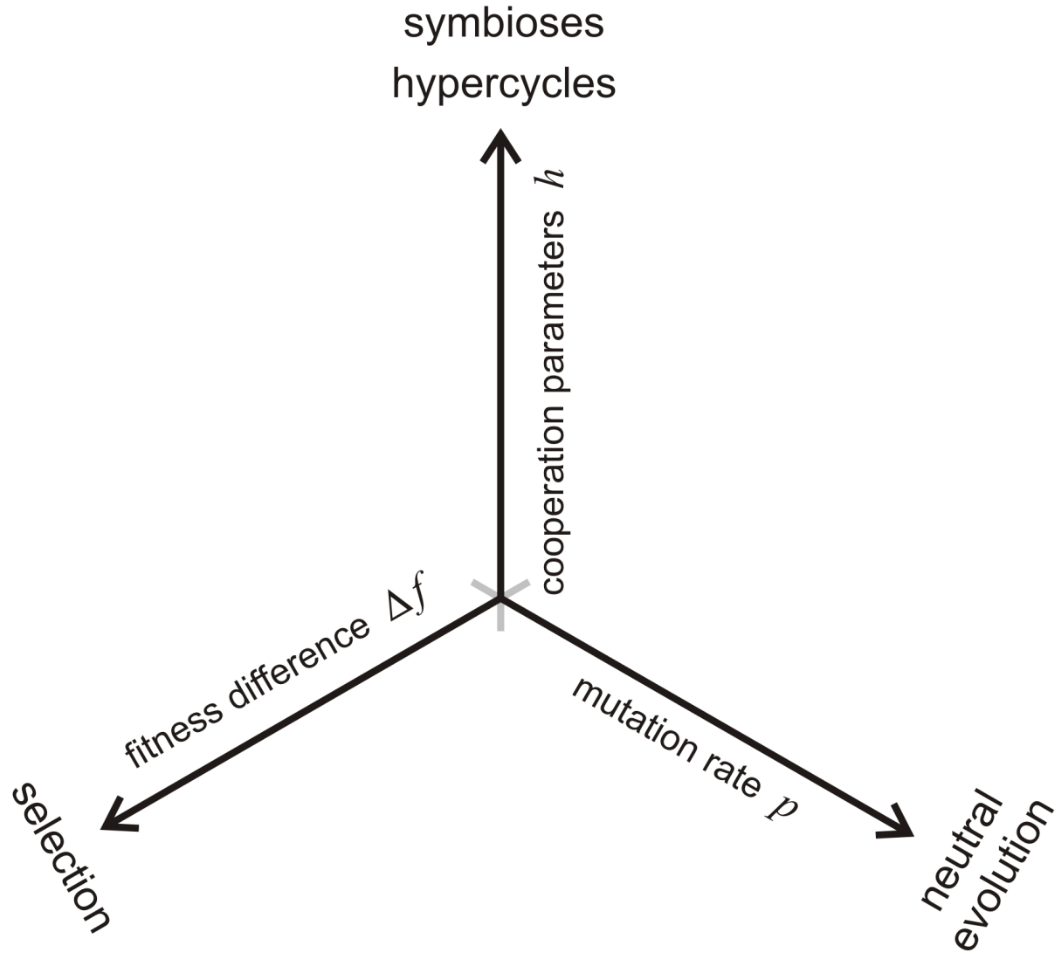
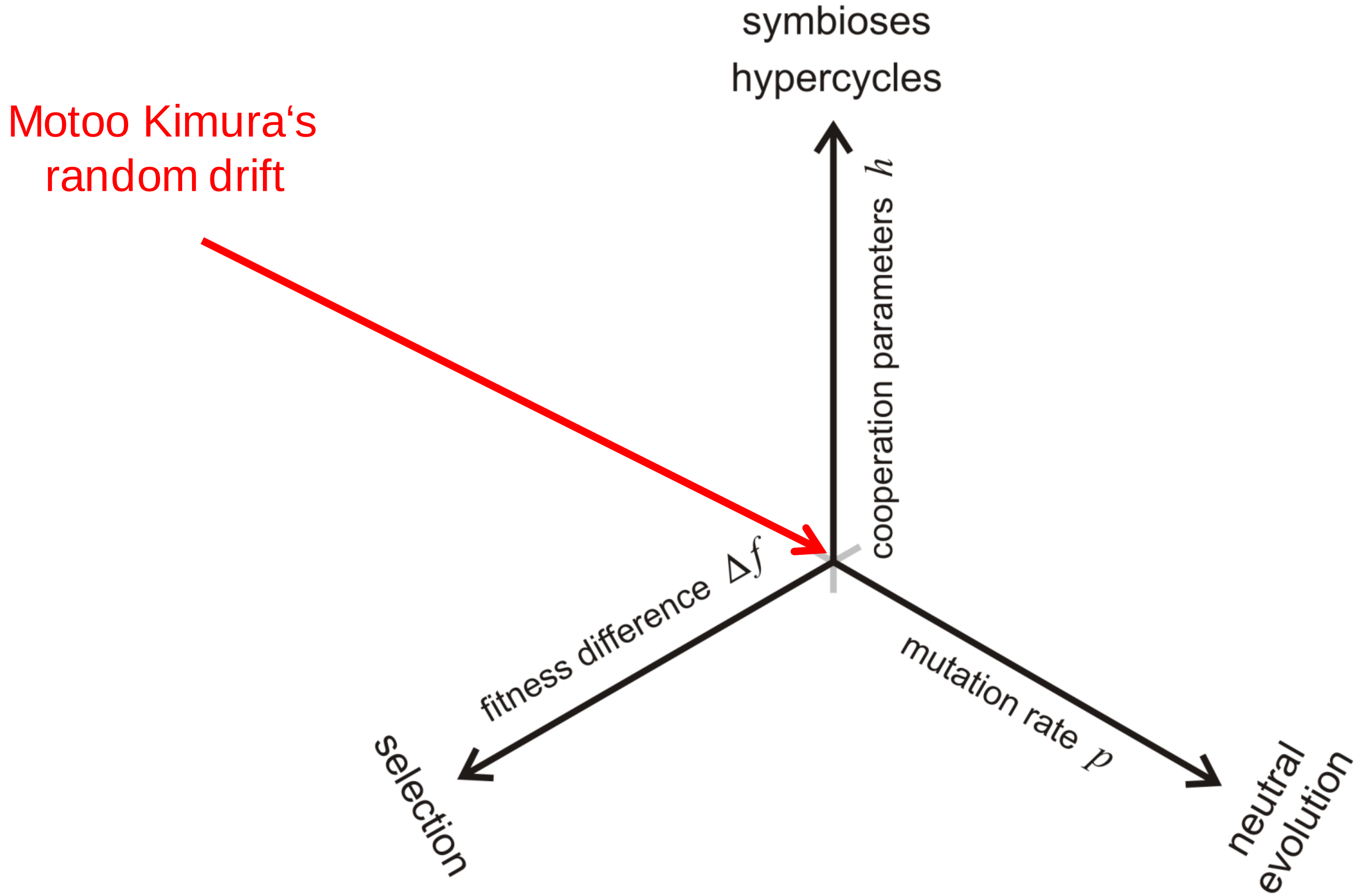


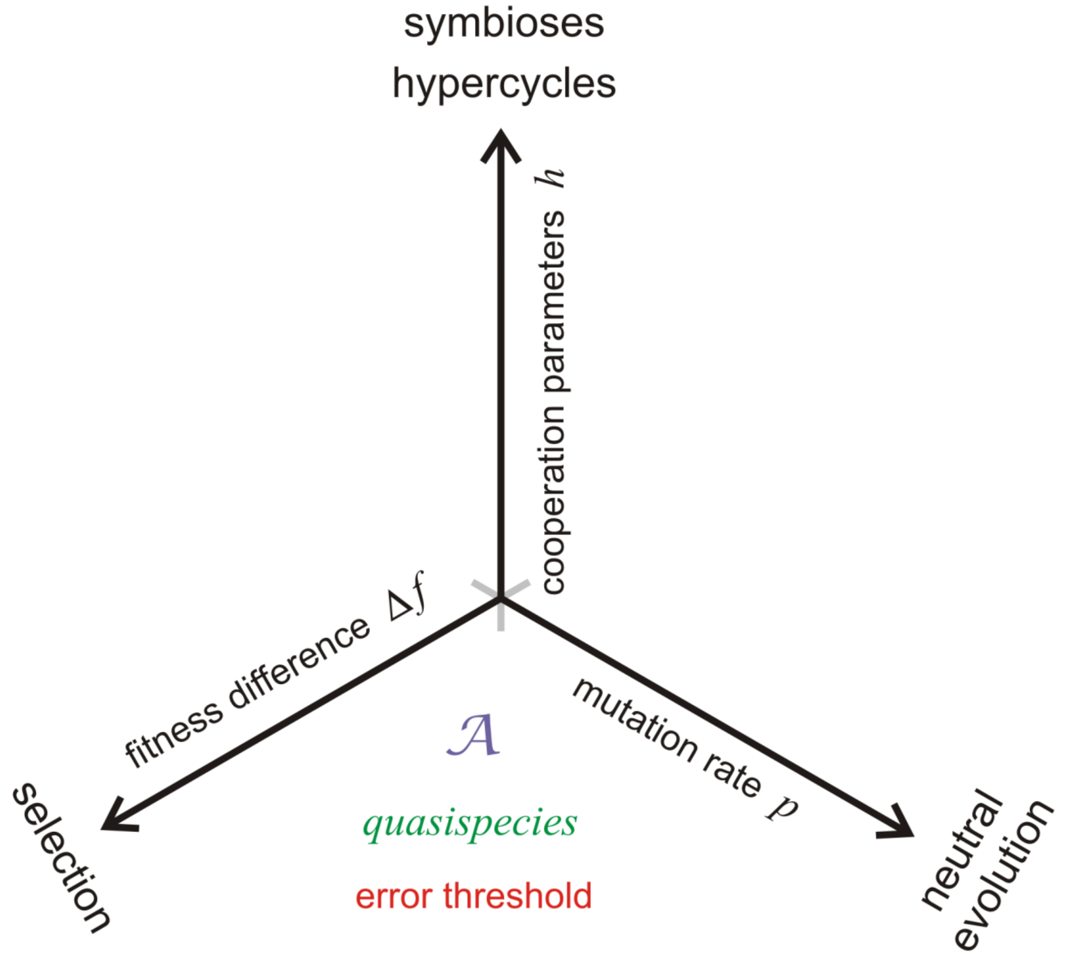
The three major processes driving evolution



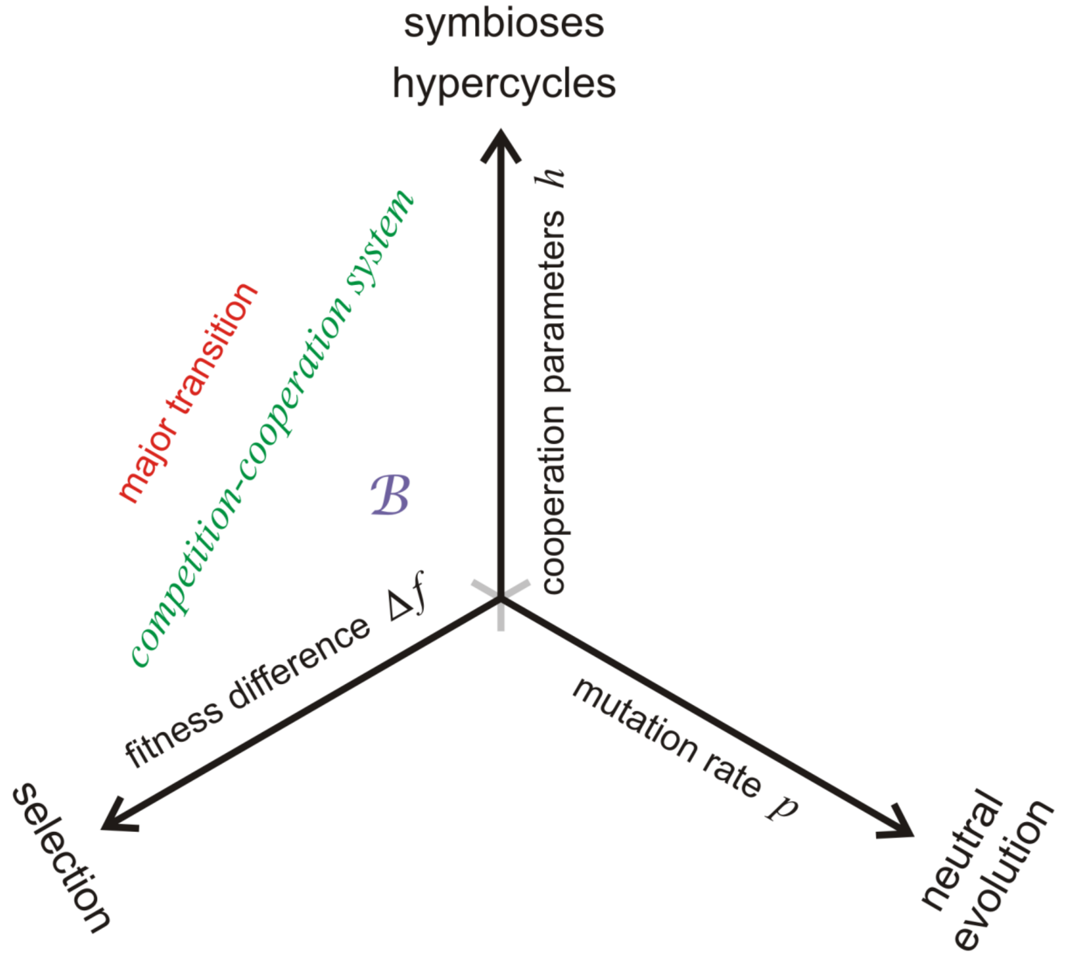
Three internal parameters driving evolution



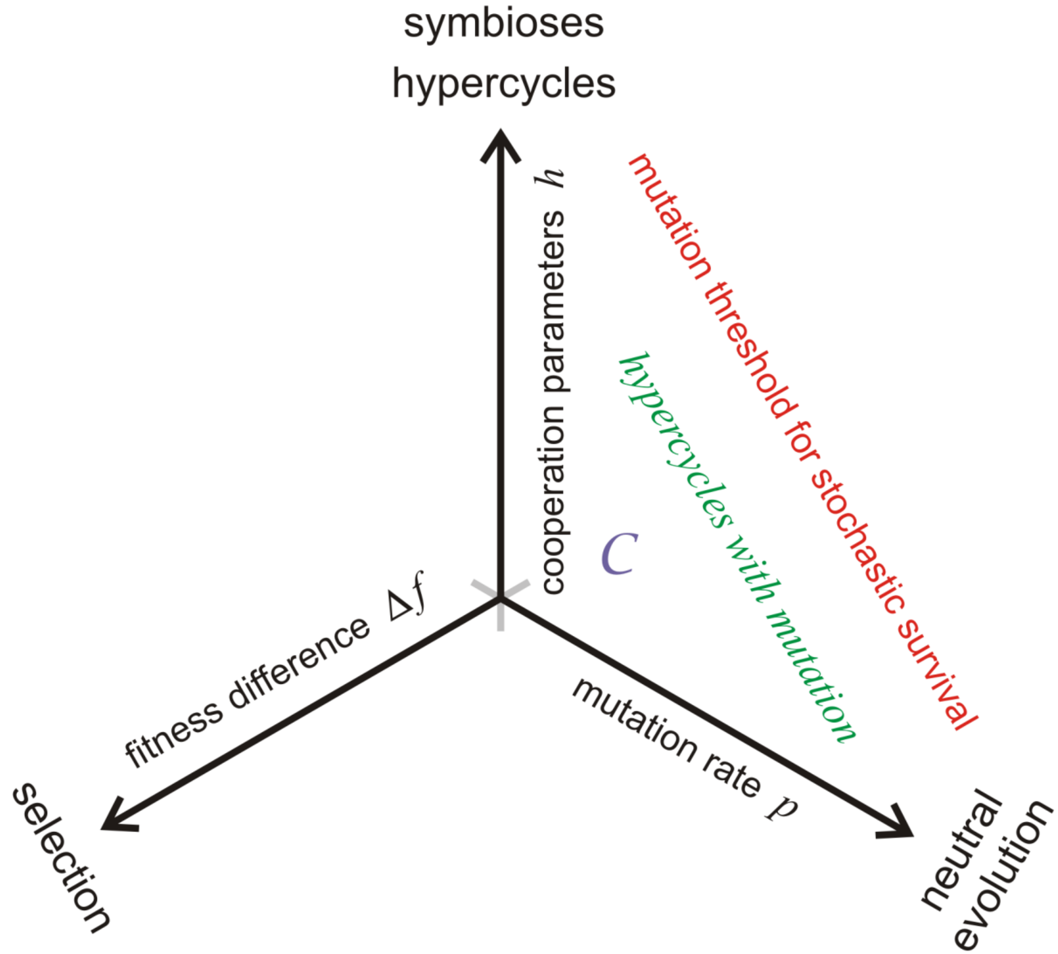
Three internal parameters driving evolution



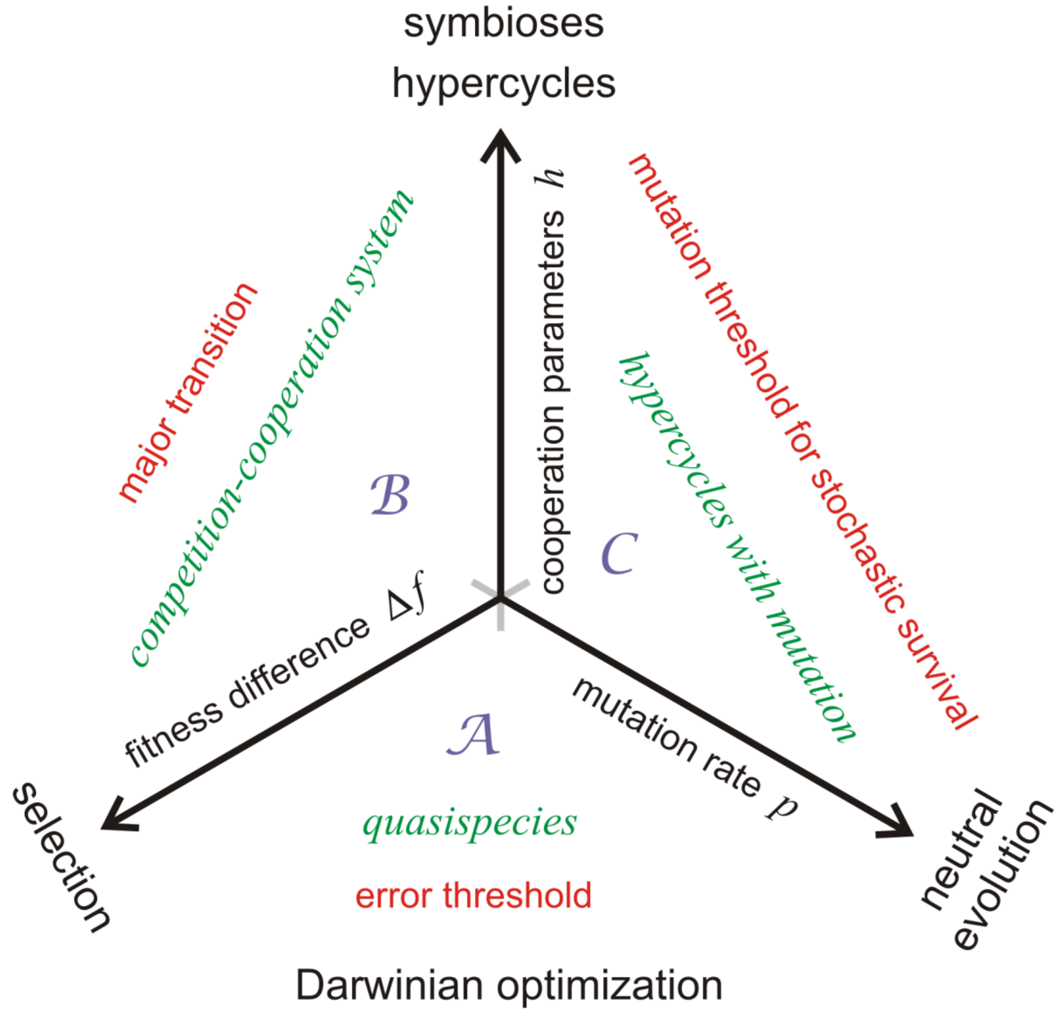
Competition and variation: error threshold



Competition and cooperation: major transition

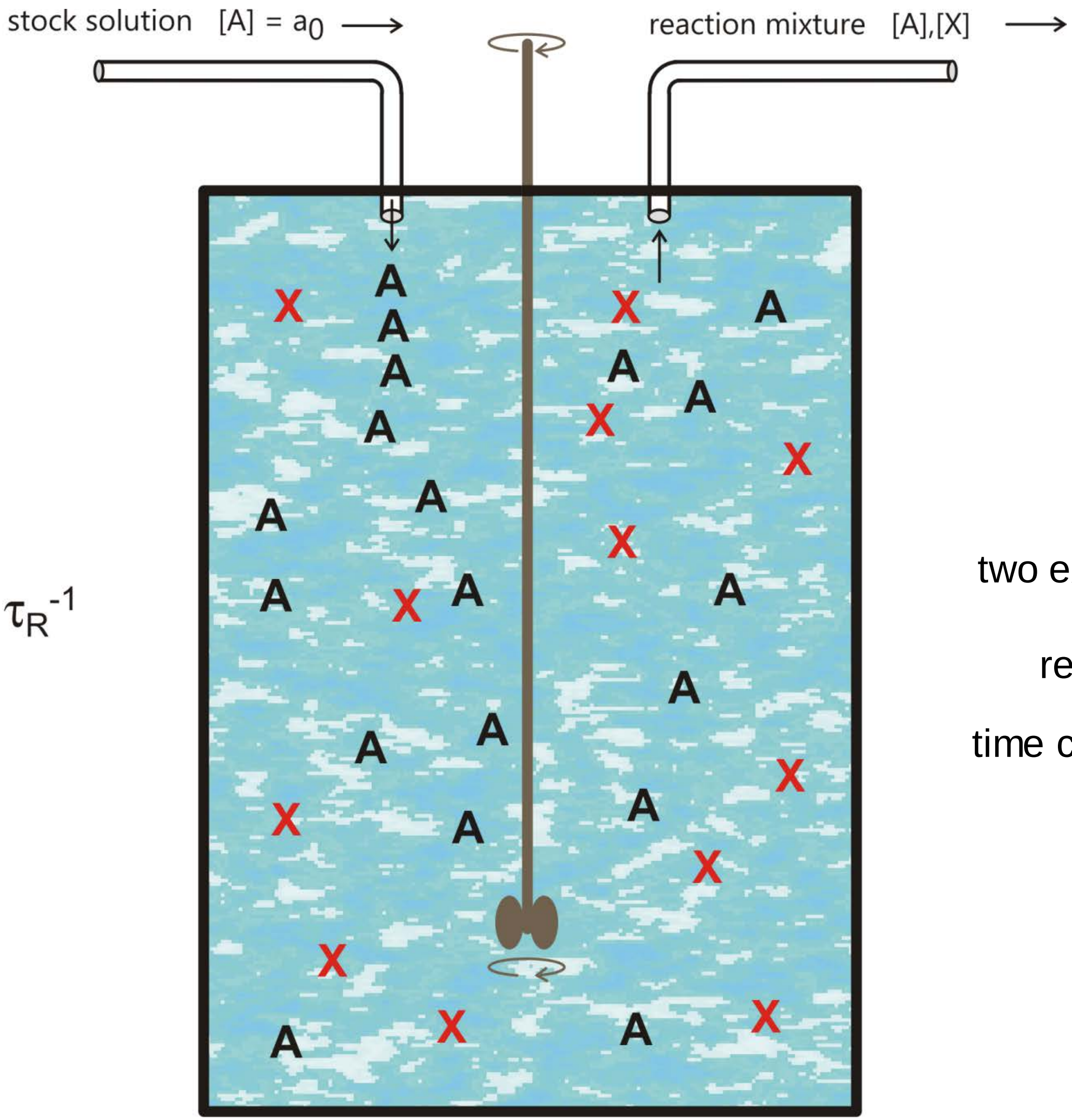


Cooperation and variation: survival threshold



The minimal model of evolution

flow rate $r = \tau_R^{-1}$



two external parameters:

resources **A** … a_0

time constraint … $\tau_R = r^{-1}$

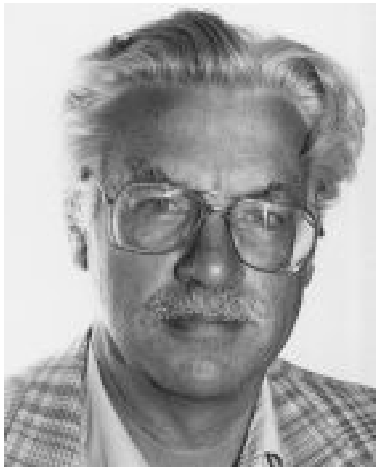
The continuously fed stirred tank reactor (CFSTR)

$$
\begin{aligned}
* \quad &\xrightarrow{a_0\, r} \quad \mathbf{A} \ , \\
\mathbf{A} + \mathbf{X}_i \quad &\xrightarrow{k_i\, Q_{ji}} \quad \mathbf{X}_i + \mathbf{X}_j \ ; \quad i,j = 1,\ldots,n \ ,
\end{aligned}
$$

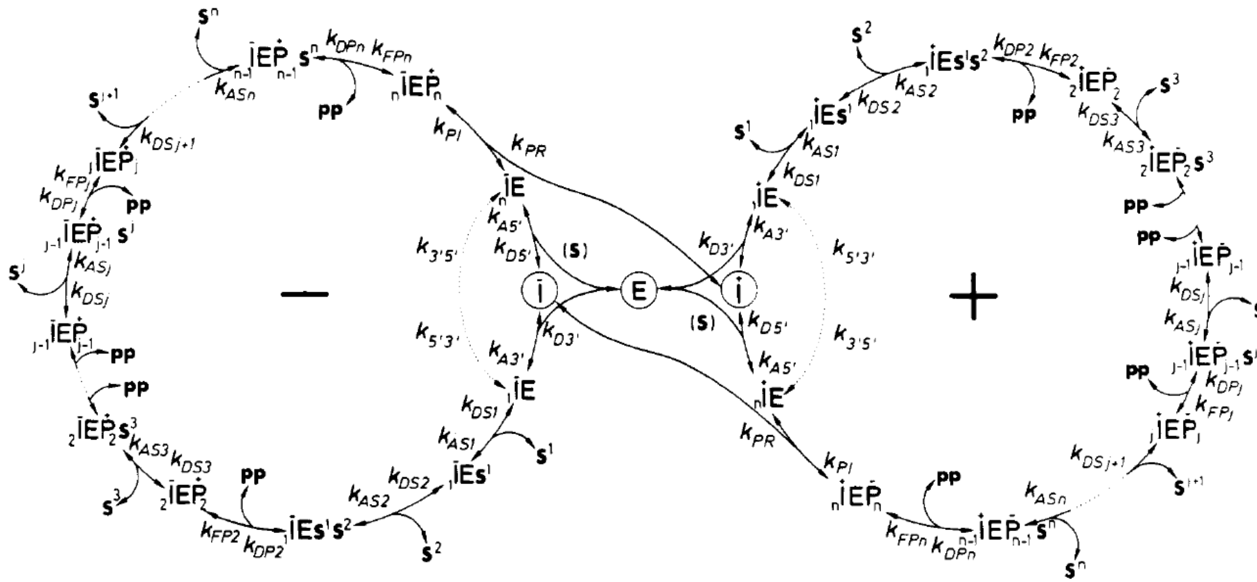
$$
\begin{aligned}
\mathbf{A} \quad &\xrightarrow{r} \quad \varnothing \ , \quad \text{and} \\
\mathbf{X}_i \quad &\xrightarrow{r} \quad \varnothing \ ; \ i = 1,\ldots,n \ .
\end{aligned}
$$

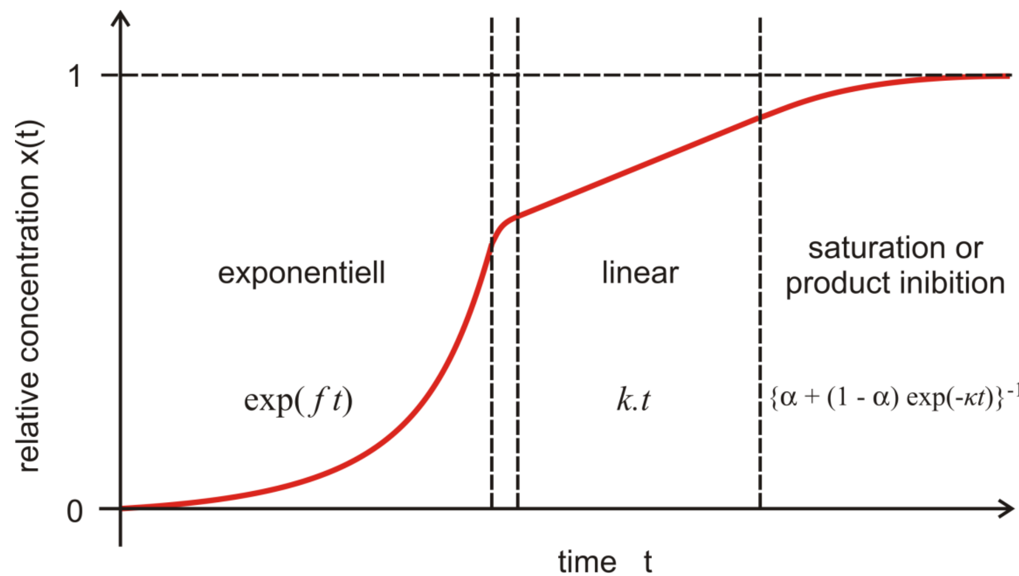
chemical reaction equations: k_i … reaction rate parameters

Q_{ji} … elements of the mutation matrix



Christof K. Biebricher,
1941-2009





Kinetics of RNA replication with Qβ-replicase

C.K. Biebricher, M. Eigen, W.C. Gardiner, Jr.
Biochemistry **22**:2544-2559, 1983

$$* \xrightarrow{a_0\, r} \mathbf{A} \; ,$$

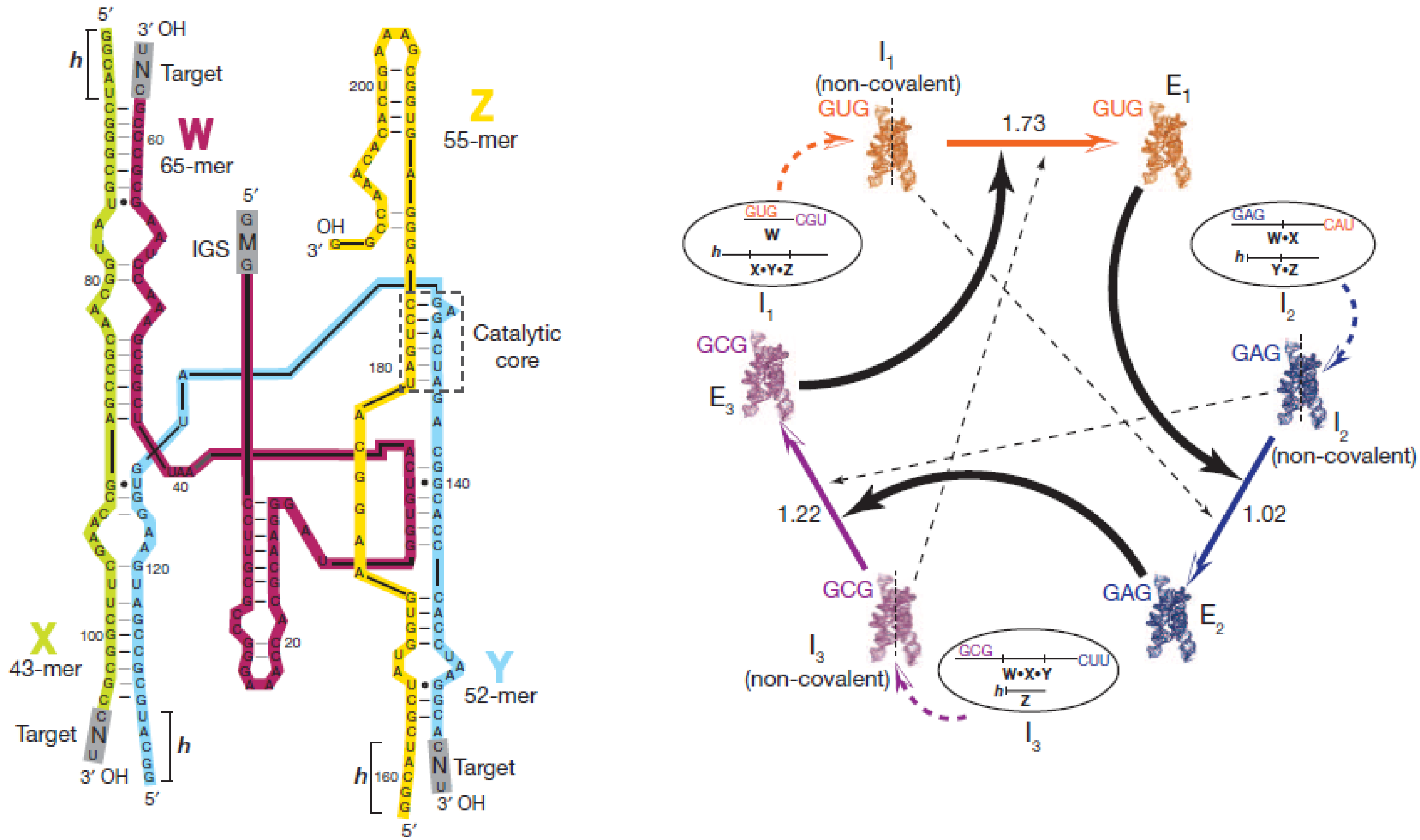
$$\mathbf{A} + \mathbf{X}_i + \mathbf{X}_{i+1} \xrightarrow{l_i\, Q_{ji}} \mathbf{X}_i + \mathbf{X}_j + \mathbf{X}_{i+1} \; ; \; i,j = 1,\ldots,n; \; i \bmod n \; ,$$

$$\mathbf{A} \xrightarrow{r} \varnothing \; , \quad \text{and}$$

$$\mathbf{X}_i \xrightarrow{r} \varnothing \; ; \; i = 1,\ldots,n \; .$$

chemical reaction equations: l_i … reaction rate parameters

Q_{ji} … elements of the mutation matrix



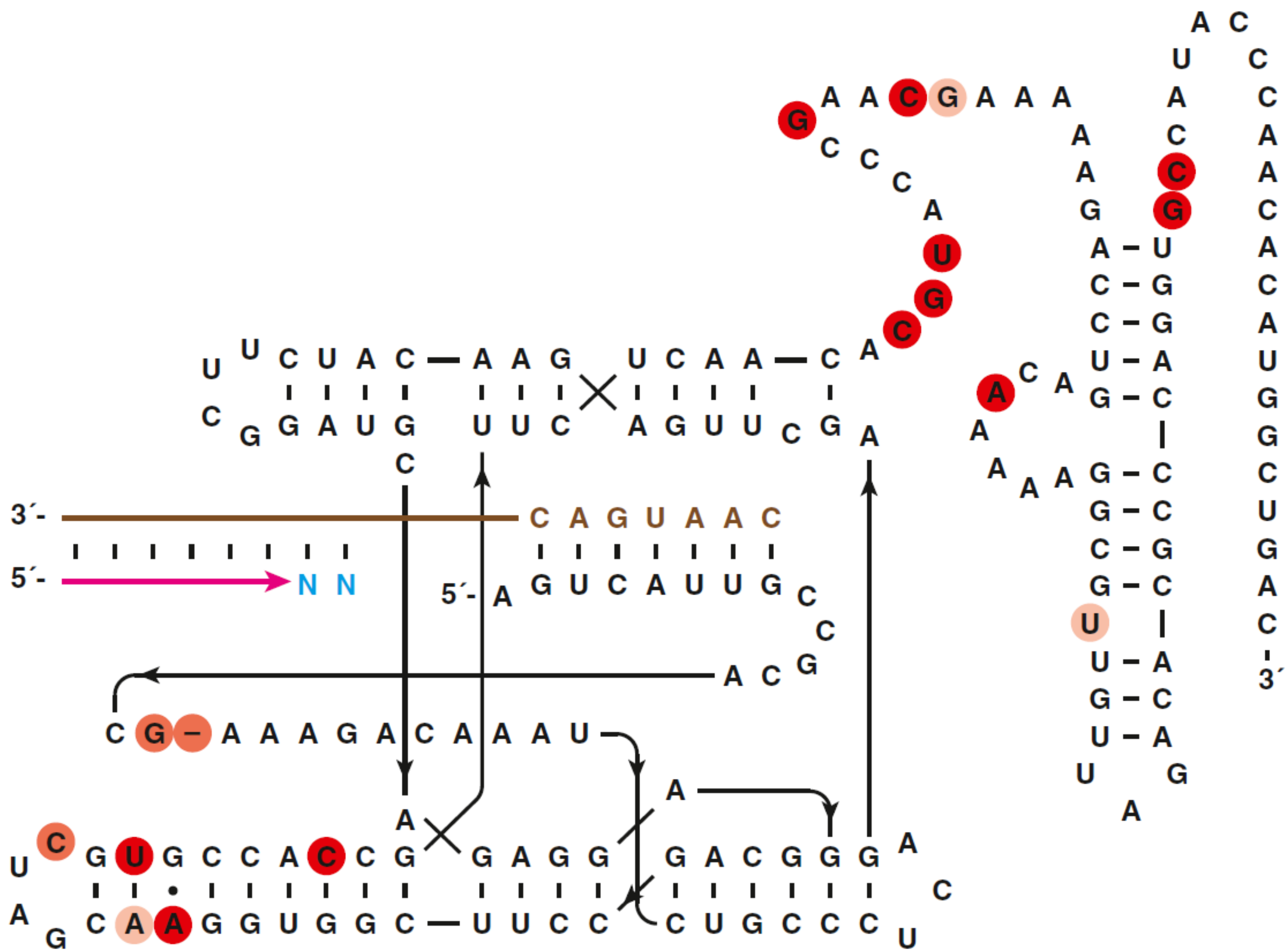
Nilesh Vaidya, Michael L. Manapar, Irene A. Chen, Ramon Xulvi_Brunet, Eric J. Hayden and Niles Lehman. Spontaneous network formation among cooperative RNA replicators. Nature 491:73-77, 2012

Cooperative RNA replicators

$$
\begin{aligned}
* \quad &\xrightarrow{a_0\, r} \quad \mathbf{A}\ , \\
\mathbf{A} + \mathbf{X}_i \quad &\xrightarrow{k_i\, Q_{ji}} \quad \mathbf{X}_i + \mathbf{X}_j\ ; \quad i,j = 1,\ldots,n\ , \\
\mathbf{A} + \mathbf{X}_i + \mathbf{X}_{i+1} \quad &\xrightarrow{l_i\, Q_{ji}} \quad \mathbf{X}_i + \mathbf{X}_j + \mathbf{X}_{i+1}\ ;\ i,j = 1,\ldots,n;\ i \bmod n\ , \\
\mathbf{A} \quad &\xrightarrow{r} \quad \varnothing\ , \quad \text{and} \\
\mathbf{X}_i \quad &\xrightarrow{r} \quad \varnothing\ ;\ i = 1,\ldots,n\ .
\end{aligned}
$$

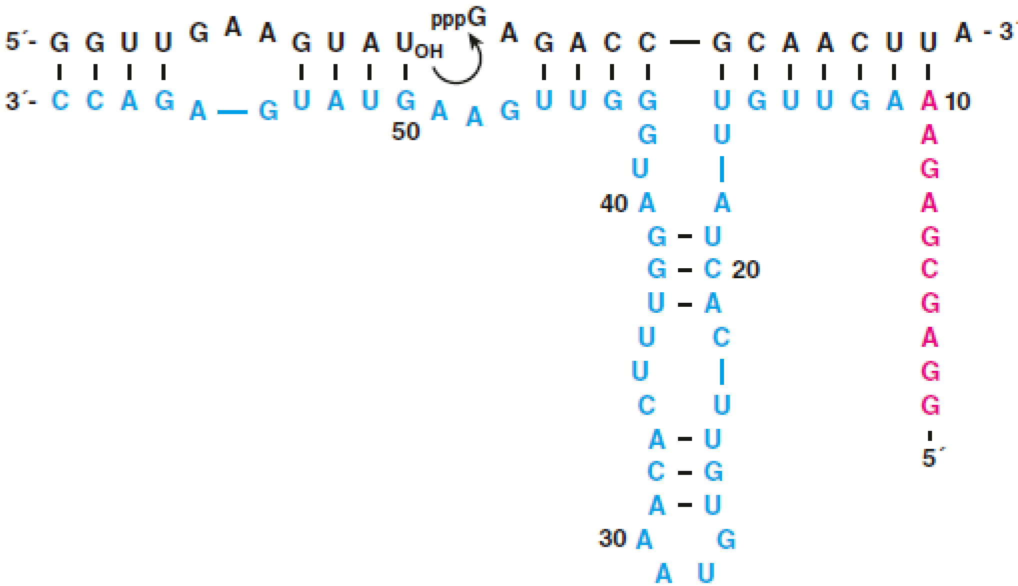
chemical reaction equations: k_i, l_i … reaction rate parameters

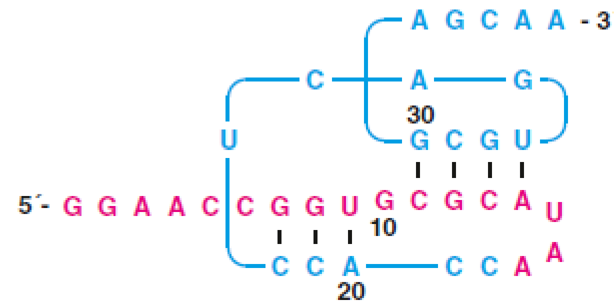
Q_{ji} … elements of the mutation matrix

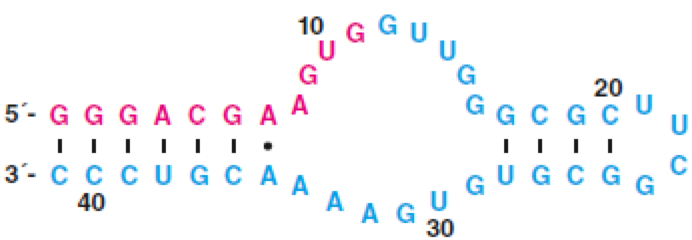


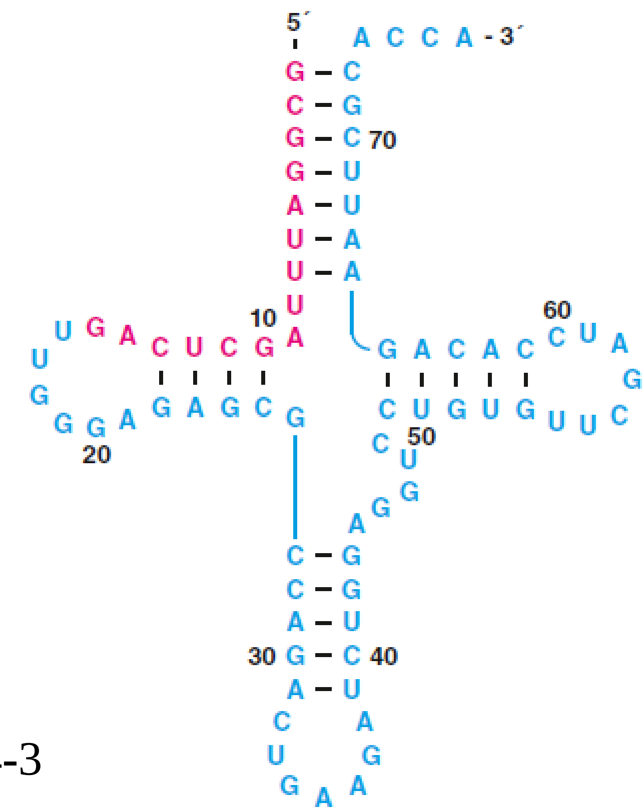
David P. Horning, Gerald F. Joyce. Amplification of RNA by an RNA polymerase ribozyme. Proc.Natl.Acad.Sci.USA 113:9786-9791, 2016

RNA polymerase ribozyme

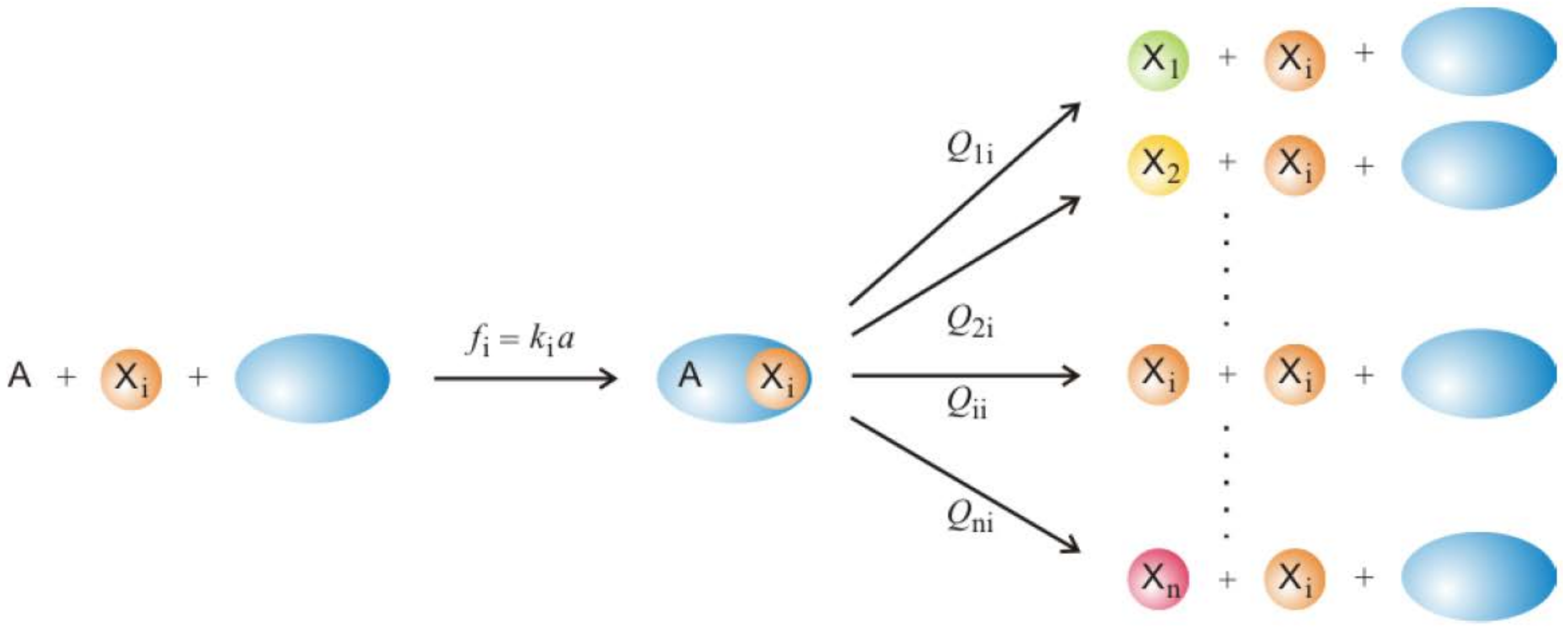








Functional molecules replicated by RNA polymerase 24-3



A molecular mechanism for mutation

$$\frac{\mathrm{d}a}{\mathrm{dt}} = -a \sum_{j=1}^{n} x_j \big(k_j + l_j x_{j+1}\big) + r\,(a_0 - a) \;\text{ and}$$

$$\frac{\mathrm{d}x_i}{\mathrm{dt}} = a\Big(\sum_{j=1}^{n} Q_{ij}(k_j + l_j x_{j+1})x_j\Big) - r x_i;\; i,j = 1\ldots,n;\; j \bmod n$$

$$Q_{ij}(p) = Q\,\varepsilon^{d_{\mathrm{H}}(\mathsf{X}_i,\mathsf{X}_j)} \;\text{ with }\; Q = (1-p)^{\nu} = Q_{ii}\;\forall\, i = 1,\ldots,n \;\text{ and }\; \varepsilon = \frac{p}{1-p}\,.$$

uniform error rate model

kinetic differential equations

$$\frac{\mathrm{d}P_{\mathbf{m}}}{\mathrm{d}t} = a_0\, r\, P_{(\mathbf{m};m-1)} + r\Big((m+1)P_{(\mathbf{m};m+1)} + \sum_{j=1}^{n}(s_j+1)P_{(\mathbf{m};s_j+1)}\Big) +$$

$$+ (m+1)\sum_{j=1}^{n}\Big((k_j + l_j\, s_{j+1})(s_j-1)P_{(\mathbf{m};m+1,s_j-1)}\Big) -$$

$$- \Big(r\Big(a_0 + m + \sum_{j=1}^{n} s_j\Big) + m\Big(\sum_{j=1}^{n}(k_j + l_j\, s_{j+1})\, s_j\Big)\Big)P_{\mathbf{m}} \,.$$

$$\mathbf{m} = (m, s_1, \ldots, s_n) \text{ and } (\mathbf{m}; m-1) = (m-1, s_1, \ldots, s_n), \text{etc.}$$

reactions $\mathbf{m} \rightarrow \mathbf{m}'$:

$$\mathbf{m}' = (\mathbf{m}' = m \pm 1, s_1, \ldots, s_n) \equiv (\mathbf{m}; m \pm 1)$$

$$\mathbf{m}' = (\mathbf{m}' = m, s_1, \ldots, s_k - 1, \ldots, s_n) \equiv (\mathbf{m}; s_k - 1)$$

$$\mathbf{m}' = (\mathbf{m}' = m - 1, s_1, \ldots, s_k' = s_k + 1, \ldots, s_n) \equiv (\mathbf{m}; m-1, s_k + 1)$$

Peter Schuster. Stochasticity in Processes. Fundamentals and Applications in Chemistry and Biology. Springer-International, Cham, CH, 2016

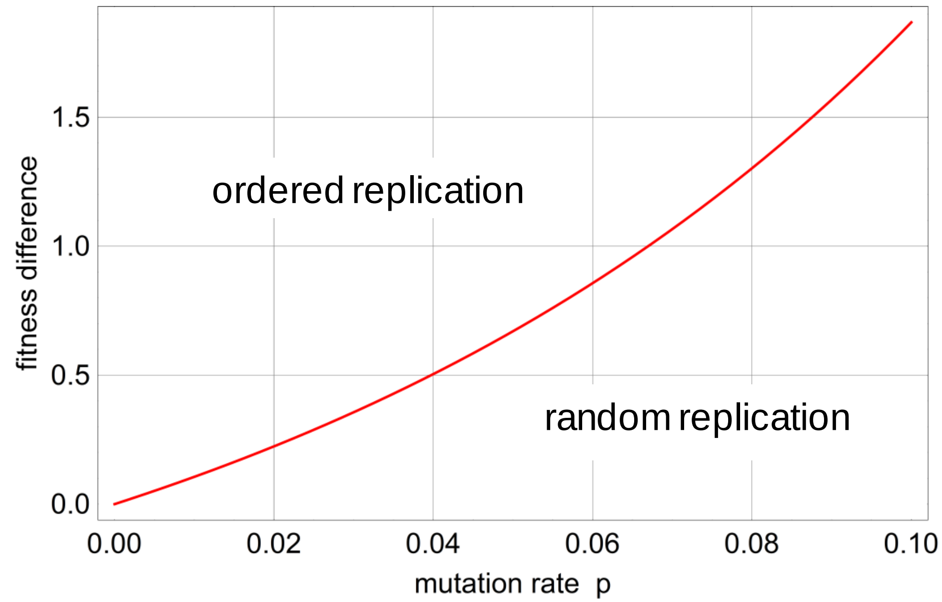
Master equation of the evolution model

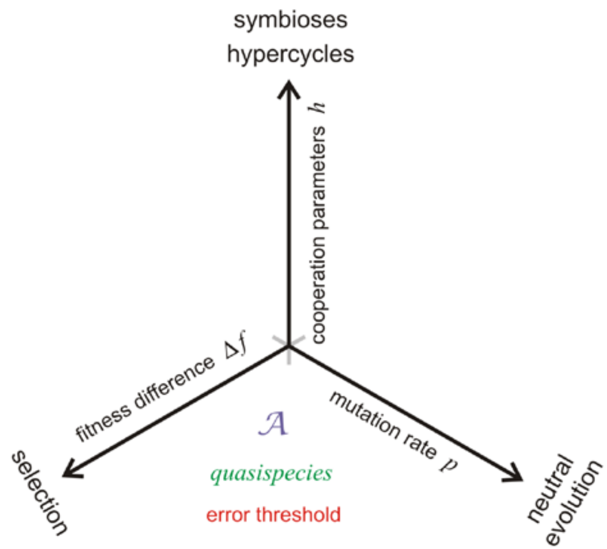
1. Chemical and biochemical reaction networks
2. Autocatalysis and replication
3. A simple model of evolution
4. **Mutation and quasispecies**
5. Cooperation and major transitions
6. Can mutations counteract extinction ?

Manfred Eigen
1927 -

$$p_{cr} = 1 - \sigma^{-1/l}$$

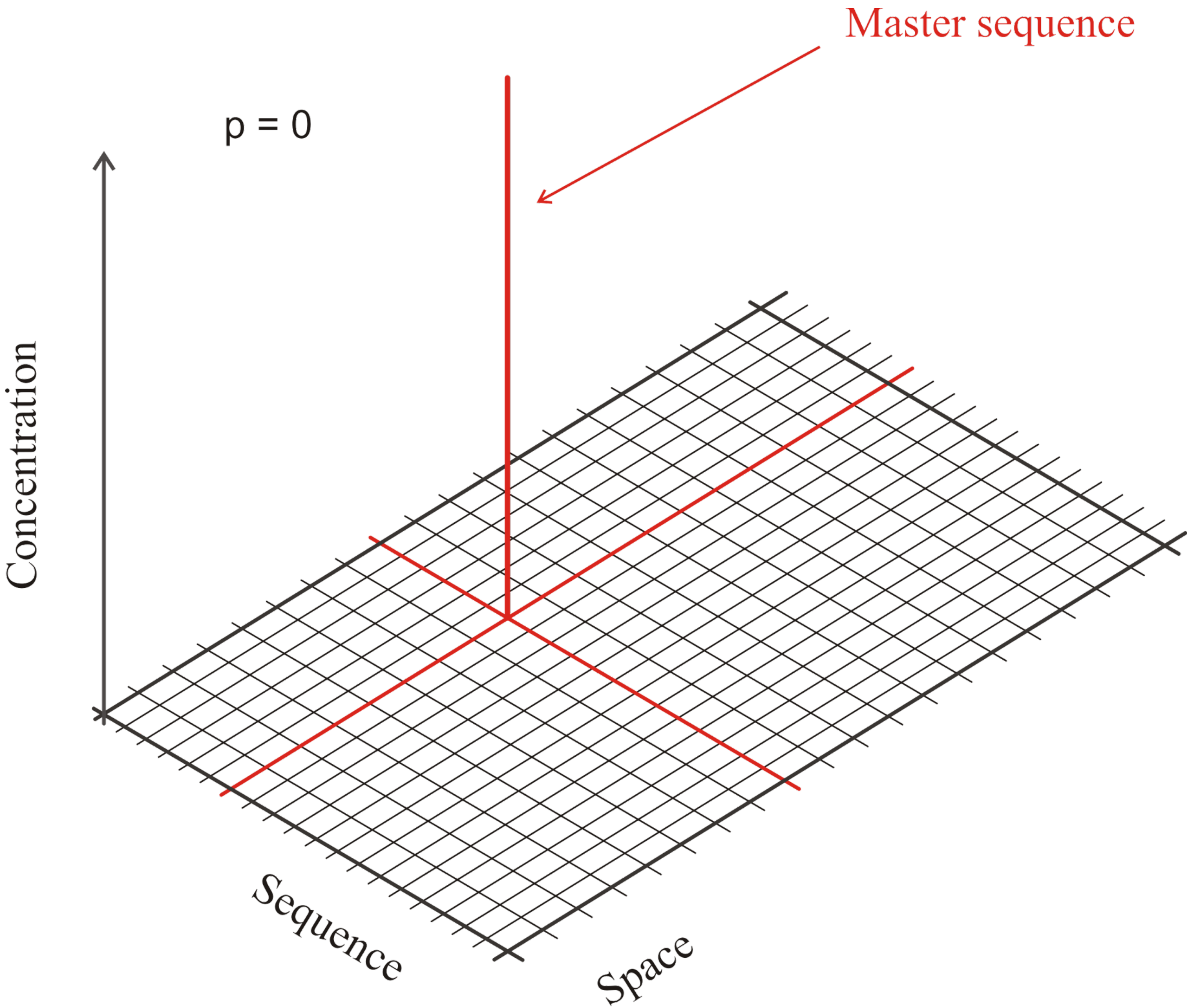
$$\sigma - 1 = \frac{\Delta f}{f} = (1-p)^{-l} - 1$$

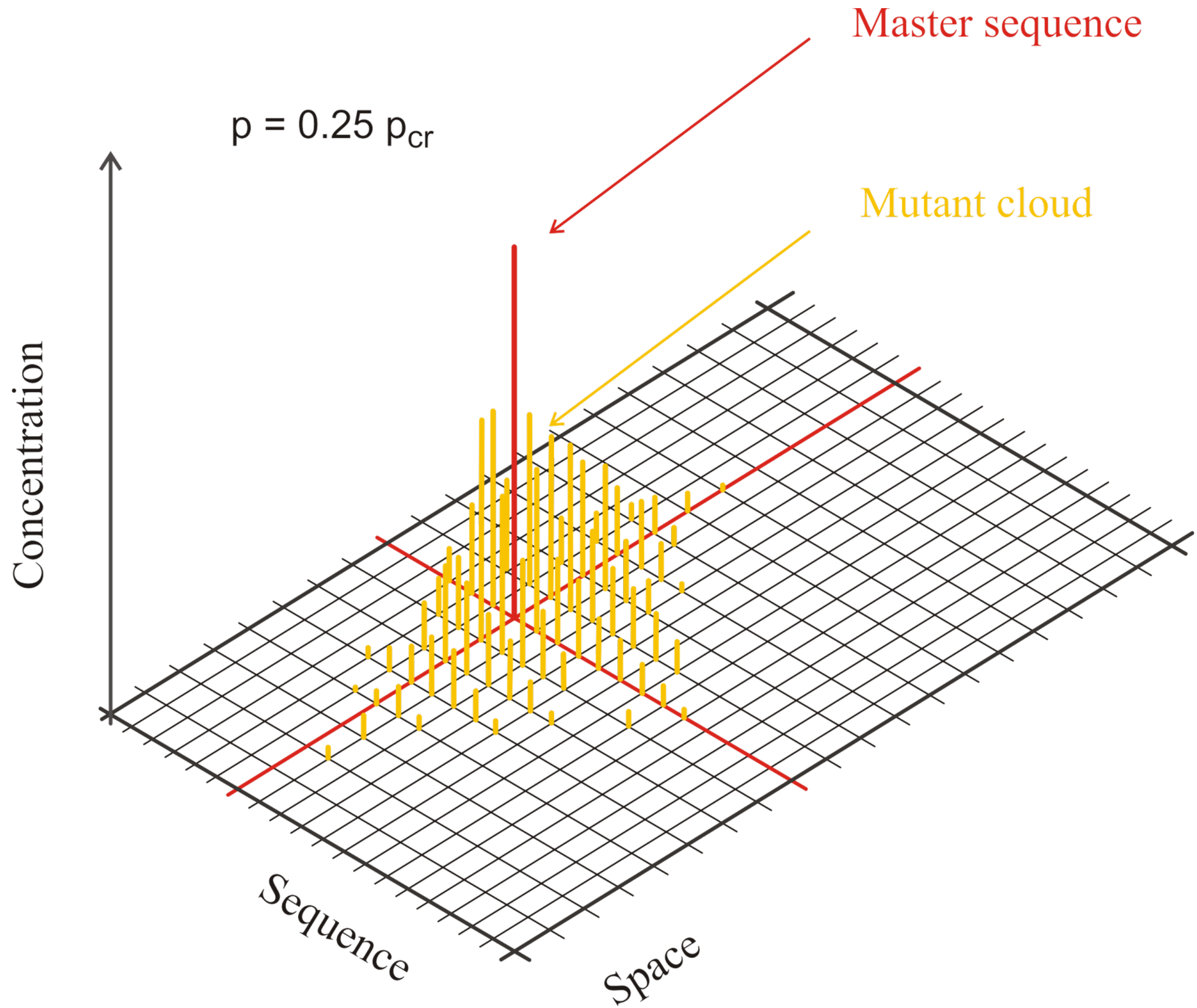




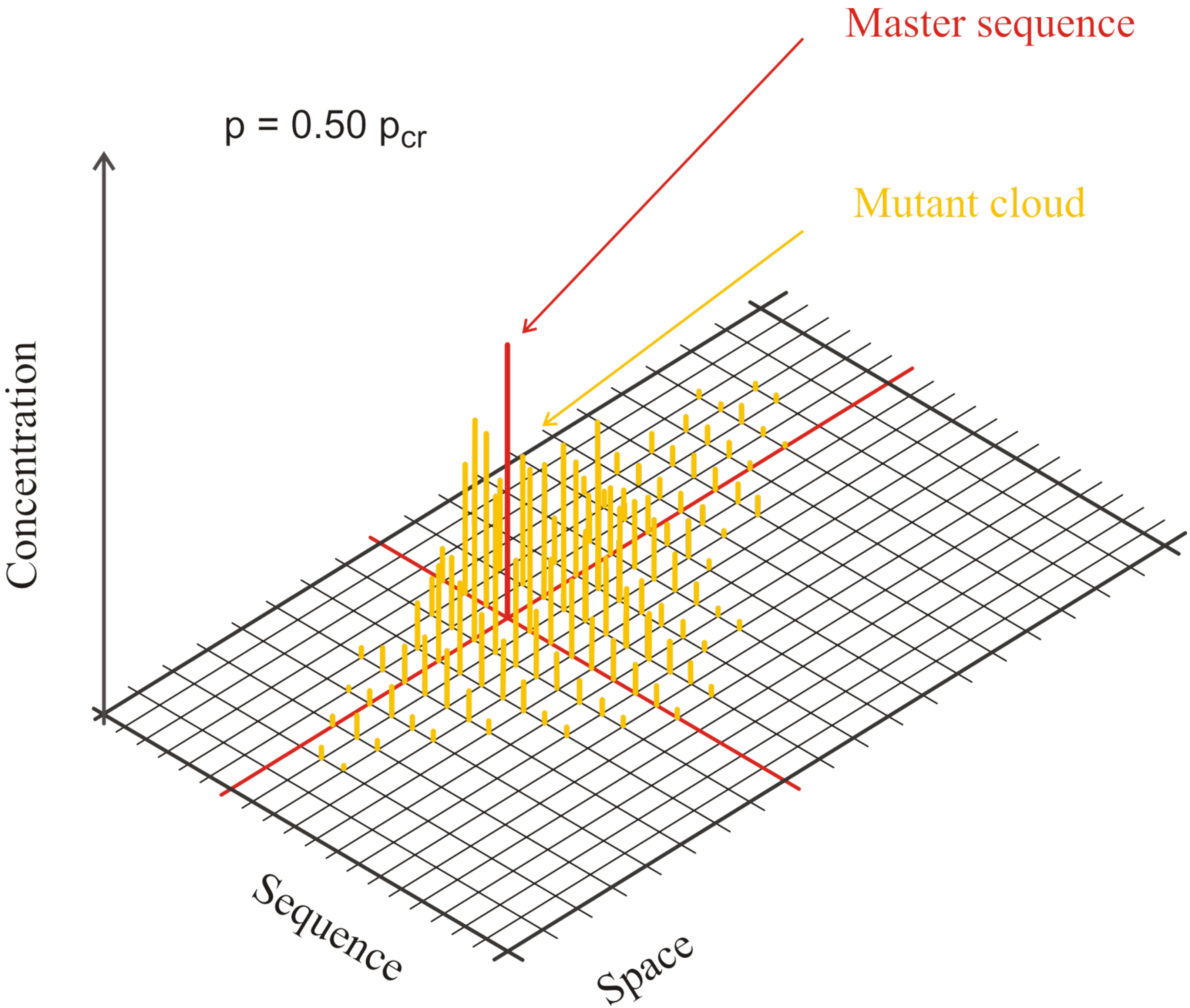
Esteban Domingo, Peter Schuster, eds. Quasispecies: From Theory to Experimental Systems
Current Topics in Microbiology and Immunology, Vol.392
Springer International, Cham, CH, 2016

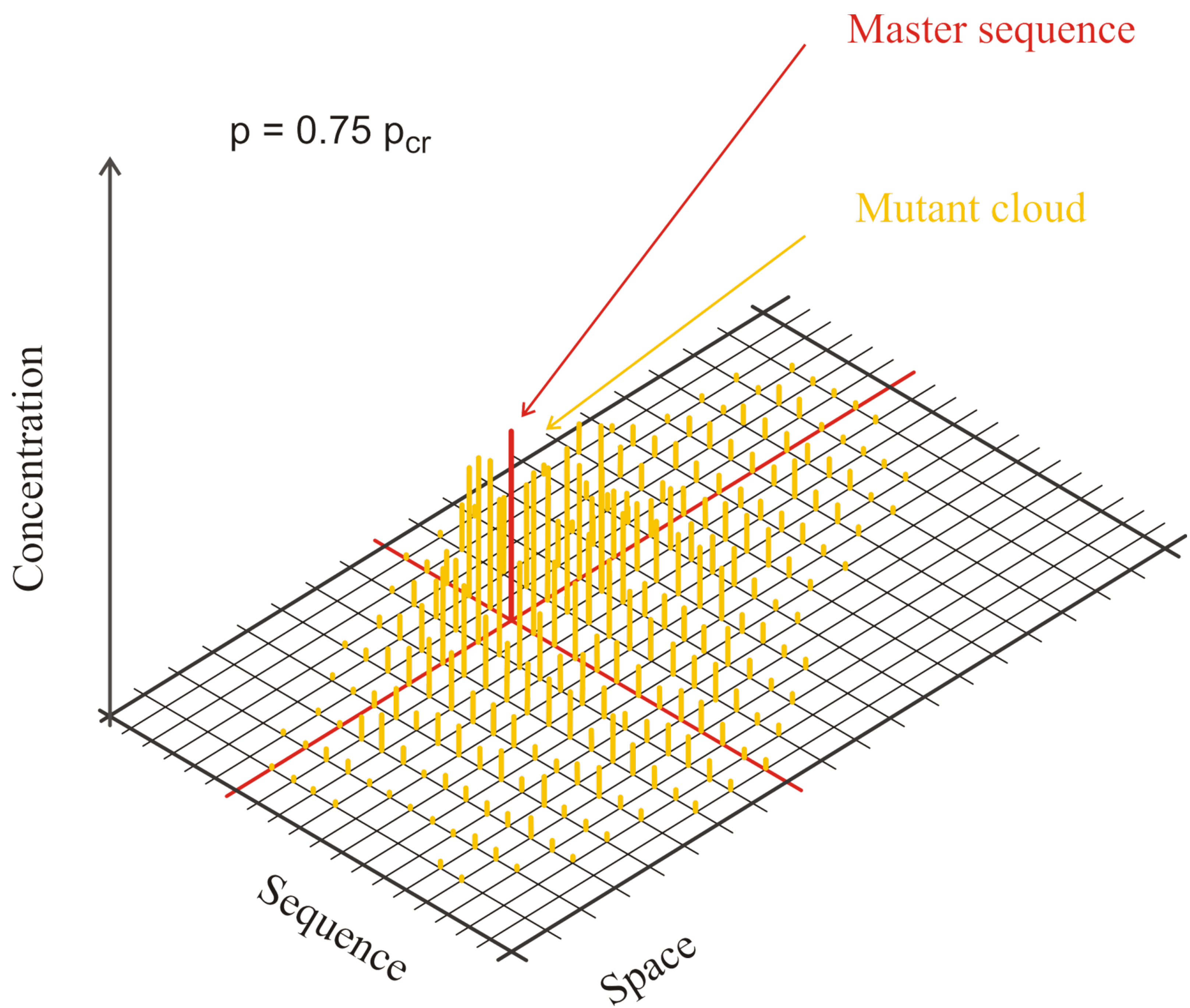
Competition and variation: error threshold


Master sequence
p = 0
Concentration
Sequence
Space

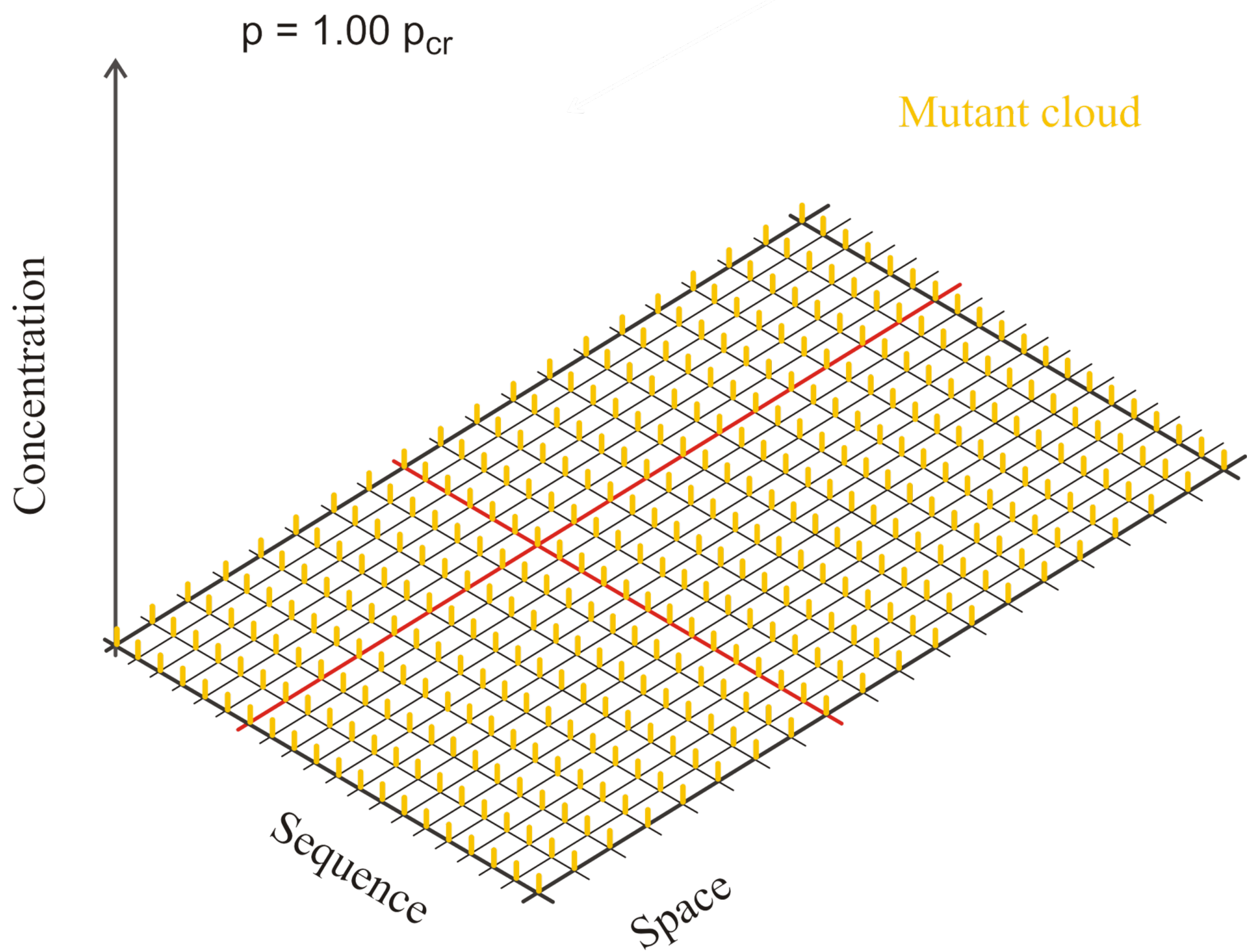


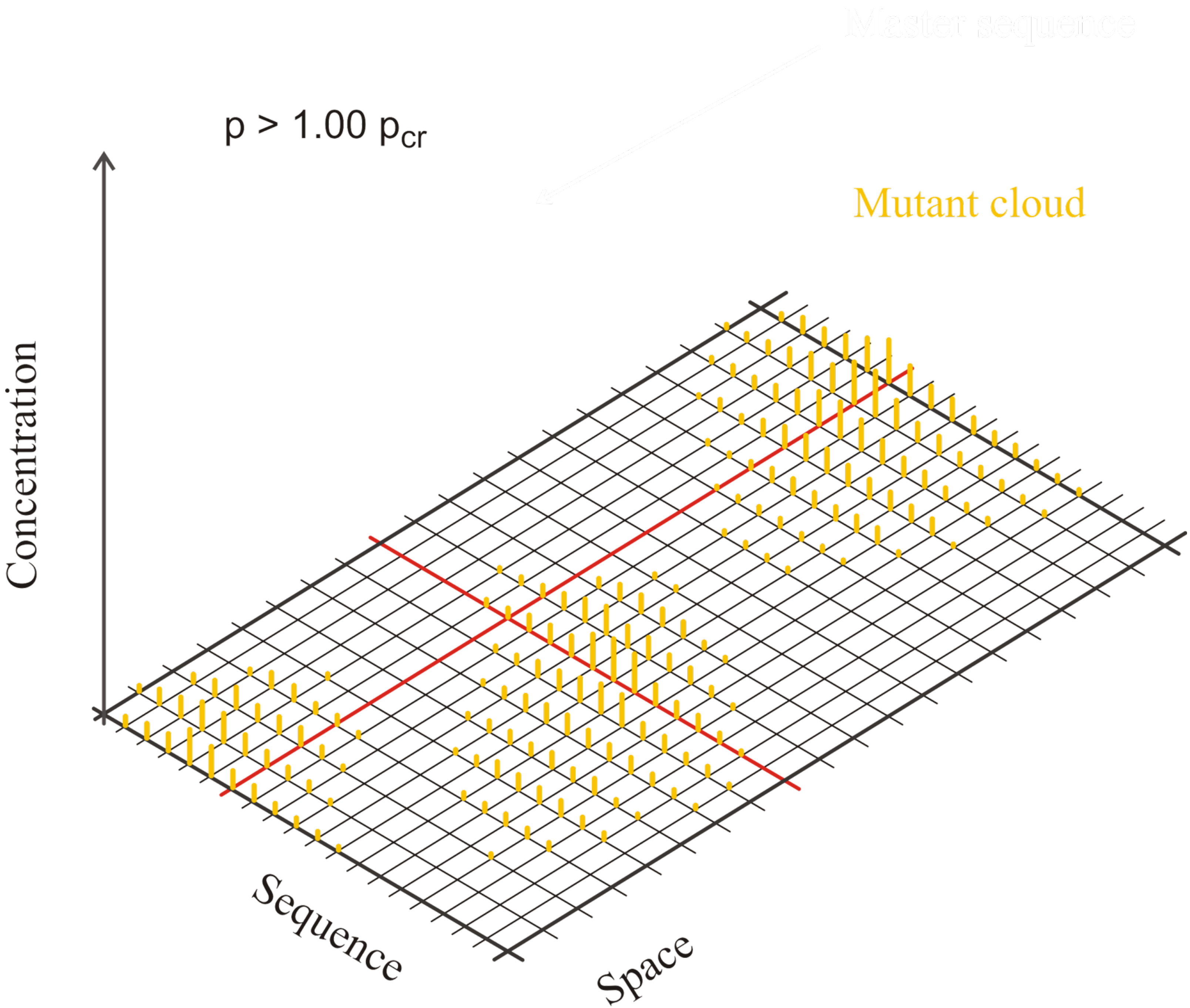
Master sequence
p = 0.25 p_cr
Mutant cloud
Concentration
Sequence
Space


Master sequence
p = 0.50 p_{cr}
Mutant cloud
Concentration
Sequence
Space

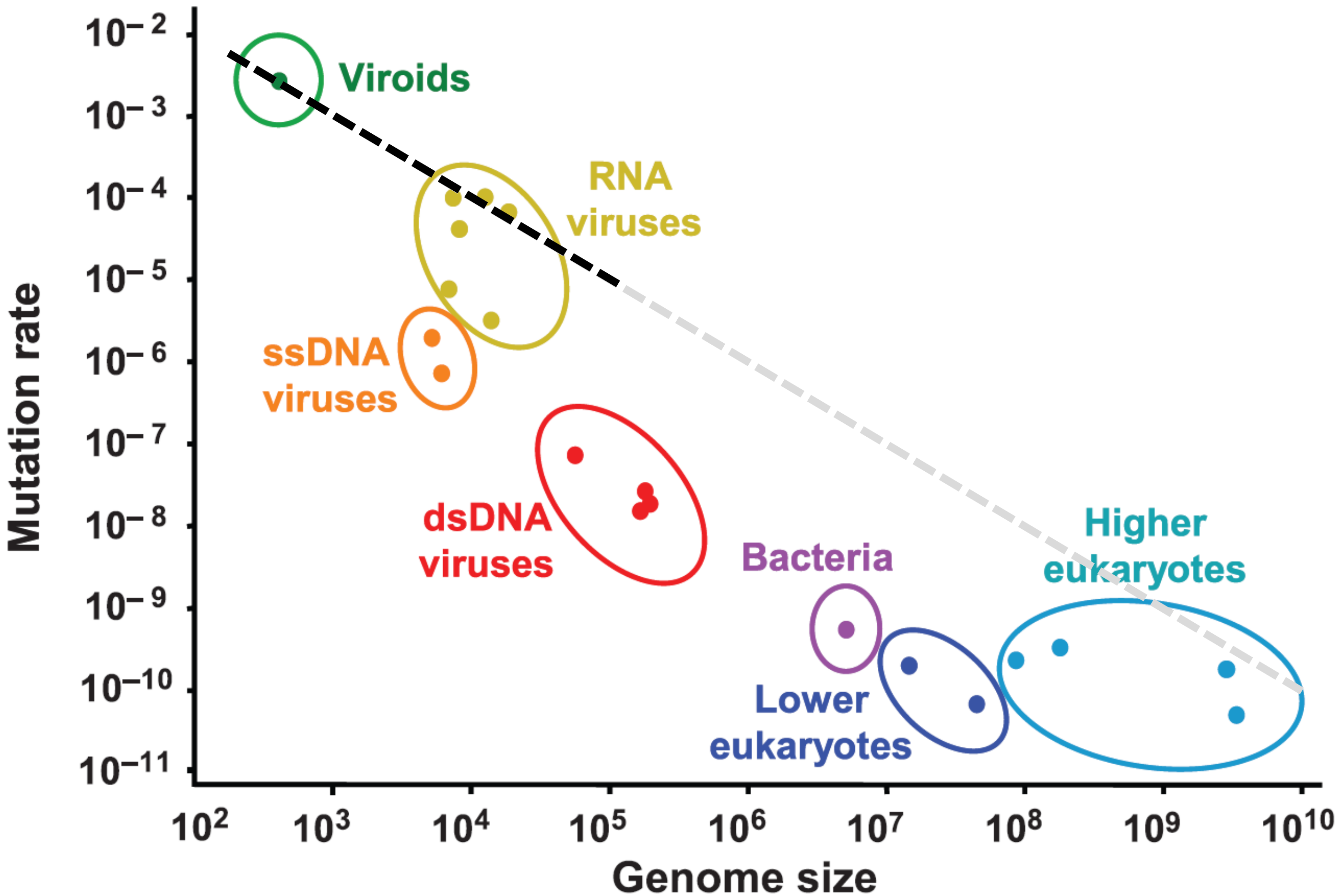


Master sequence
Mutant cloud
p = 0.75 pcr
Concentration
Sequence
Space


p = 1.00 pcr
Mutant cloud
Concentration
Sequence
Space



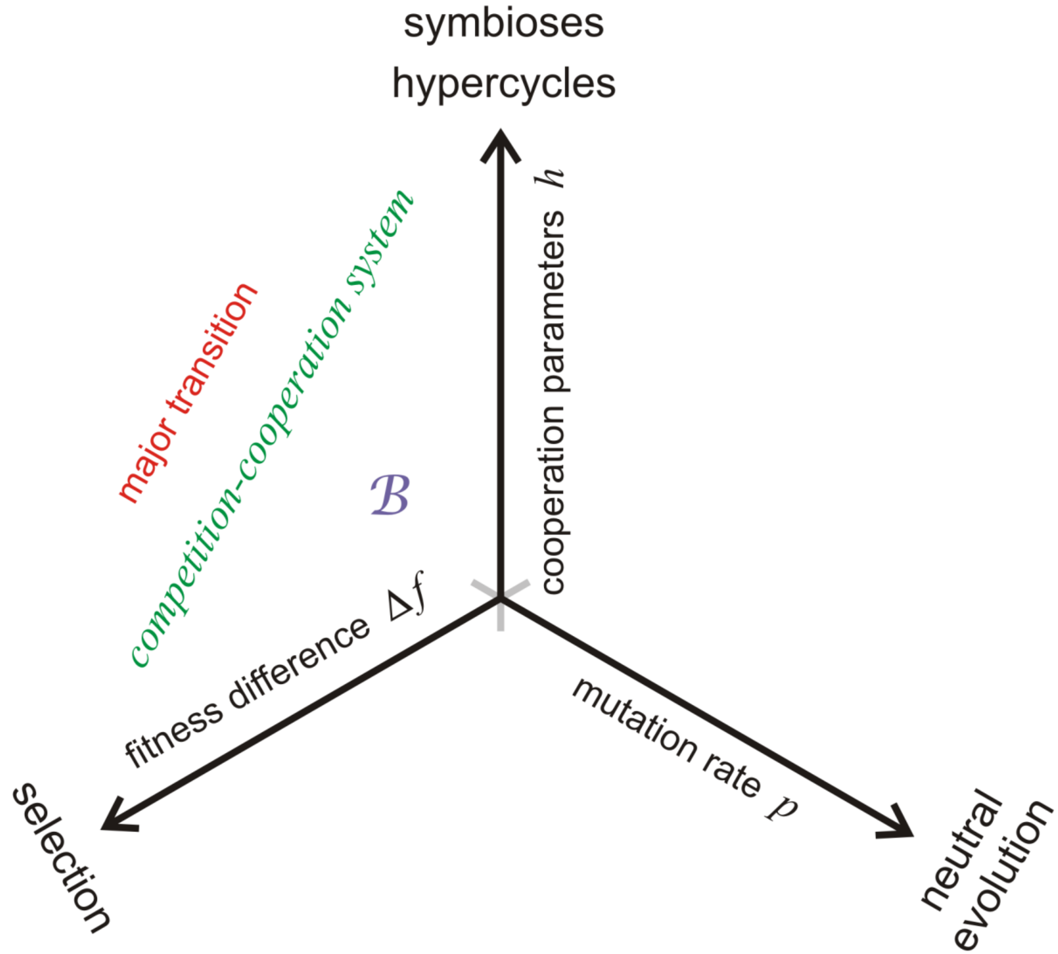
Master sequence
p > 1.00 p_cr
Mutant cloud
Concentration
Sequence
Space



Selma Gago, Santiago F. Elena, Ricardo Flores, Rafael Sanjuán. 2009. Extremely high mutation rate of a hammerhead viroid. Science 323:1308.

Mutation rate and genome size

1. Chemical and biochemical reaction networks
2. Autocatalysis and replication
3. A simple model of evolution
4. Mutation and quasispecies
5. **Cooperation and major transitions**
6. Can mutations counteract extinction ?



Competition and cooperation: major transition

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

$$\mathbf{A} + \mathbf{X}_j \xrightarrow{k_j} 2\,\mathbf{X}_j \, ; \quad j = 1, \ldots, n \, ,$$

$$\mathbf{A} + \mathbf{X}_j + \mathbf{X}_i \xrightarrow{l_{ji}} 2\,\mathbf{X}_j + \mathbf{X}_i \, ; \; i, j = 1, \ldots, n$$

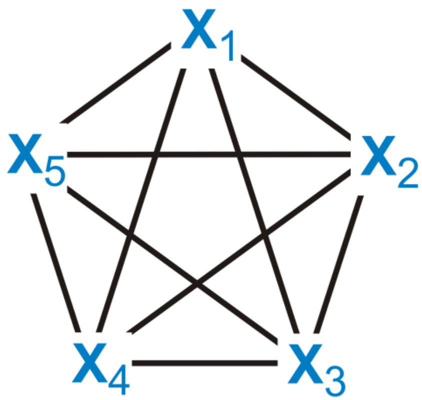
$$\mathbf{A} \xrightarrow{r} \varnothing \, , \quad \text{and}$$

$$\mathbf{X}_j \xrightarrow{r} \varnothing \, ; \; j = 1, \ldots, n \, .$$

A simple model for the analysis of competition and cooperation

$$\mathbf{A} + \mathbf{X}_j + \mathbf{X}_i \xrightarrow{l_{ji}} 2\,\mathbf{X}_j + \mathbf{X}_i \;;\; i,j = 1,\ldots,n$$

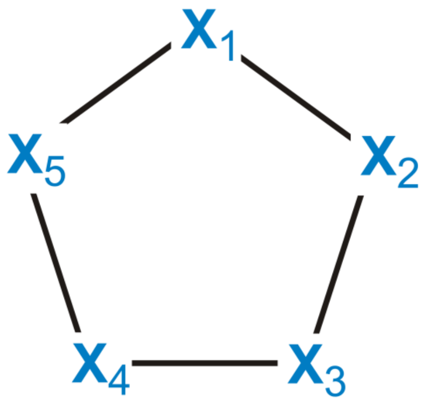
n^2 catalytic terms



A simple model for the analysis of competition and cooperation

$$\mathbf{A} + \mathbf{X}_i + \mathbf{X}_{i+1} \xrightarrow{\;l_i\;} 2\,\mathbf{X}_i + \mathbf{X}_{i+1}\,;\; i,j = 1,\ldots,n$$

n catalytic terms



$$\mathbf{X}_n \Leftarrow \mathbf{X}_1 \Leftarrow \mathbf{X}_2 \Leftarrow \cdots \Leftarrow \mathbf{X}_{n-1} \Leftarrow \mathbf{X}_n$$

A still simpler model for the analysis of competition and cooperation

$$
\begin{aligned}
* \quad &\xrightarrow{a_0\, r} \quad \mathbf{A}\ , \\
\mathbf{A} + \mathbf{X}_i \quad &\xrightarrow{k_i} \quad 2\,\mathbf{X}_i\ ; \quad i = 1, \ldots, n\ , \\
\mathbf{A} + \mathbf{X}_i + \mathbf{X}_{i+1} \quad &\xrightarrow{l_i} \quad 2\,\mathbf{X}_i + \mathbf{X}_{i+1}\ ;\ i, j = 1, \ldots, n \\
\mathbf{A} \quad &\xrightarrow{r} \quad \varnothing\ , \quad \text{and} \\
\mathbf{X}_i \quad &\xrightarrow{r} \quad \varnothing\ ;\ i = 1, \ldots, n\ .
\end{aligned}
$$

A still simpler model for the analysis of competition and cooperation

$$[\mathbf{A}] \;=\; a \quad \text{and} \quad [\mathbf{X}_j] \;=\; x_j\;; \quad j = 1, \ldots, n$$

$$\frac{\mathrm{d}a}{\mathrm{d}t} \;=\; -\,a\left(\sum_{j=1}^{n}\left(k_j + l_j x_{j+1}\right) x_j + r\right) + a_0\, r$$

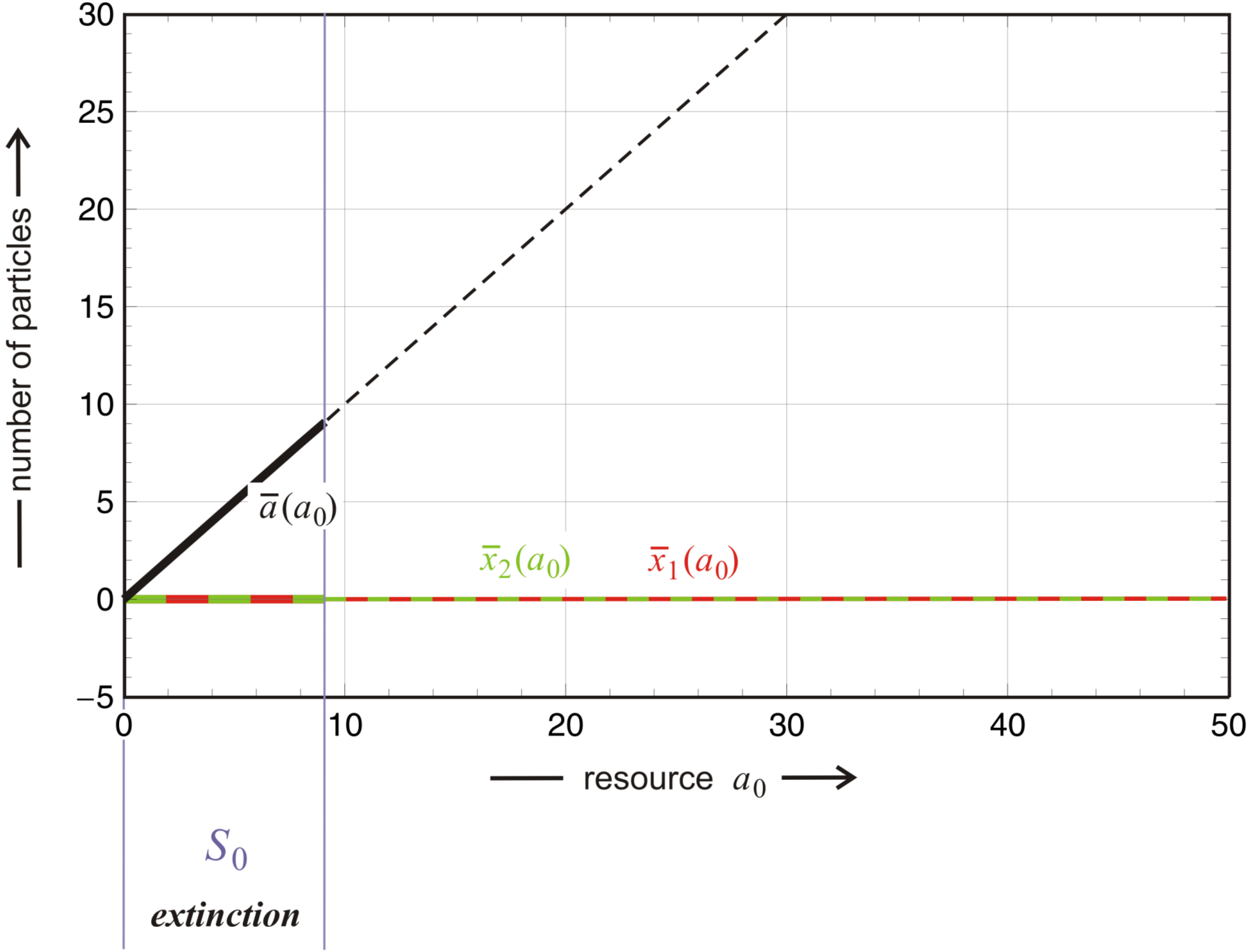
$$\frac{\mathrm{d}x_j}{\mathrm{d}t} \;=\; x_j\Big(\left(k_j + l_j x_{j+1}\right) a - r\Big)\;;\; j = 1, \ldots, n\;;\; j \mod n$$

quasi-stationary solutions: (i) $\overline{x}_j = 0\;;\; j = 1, \ldots, n$

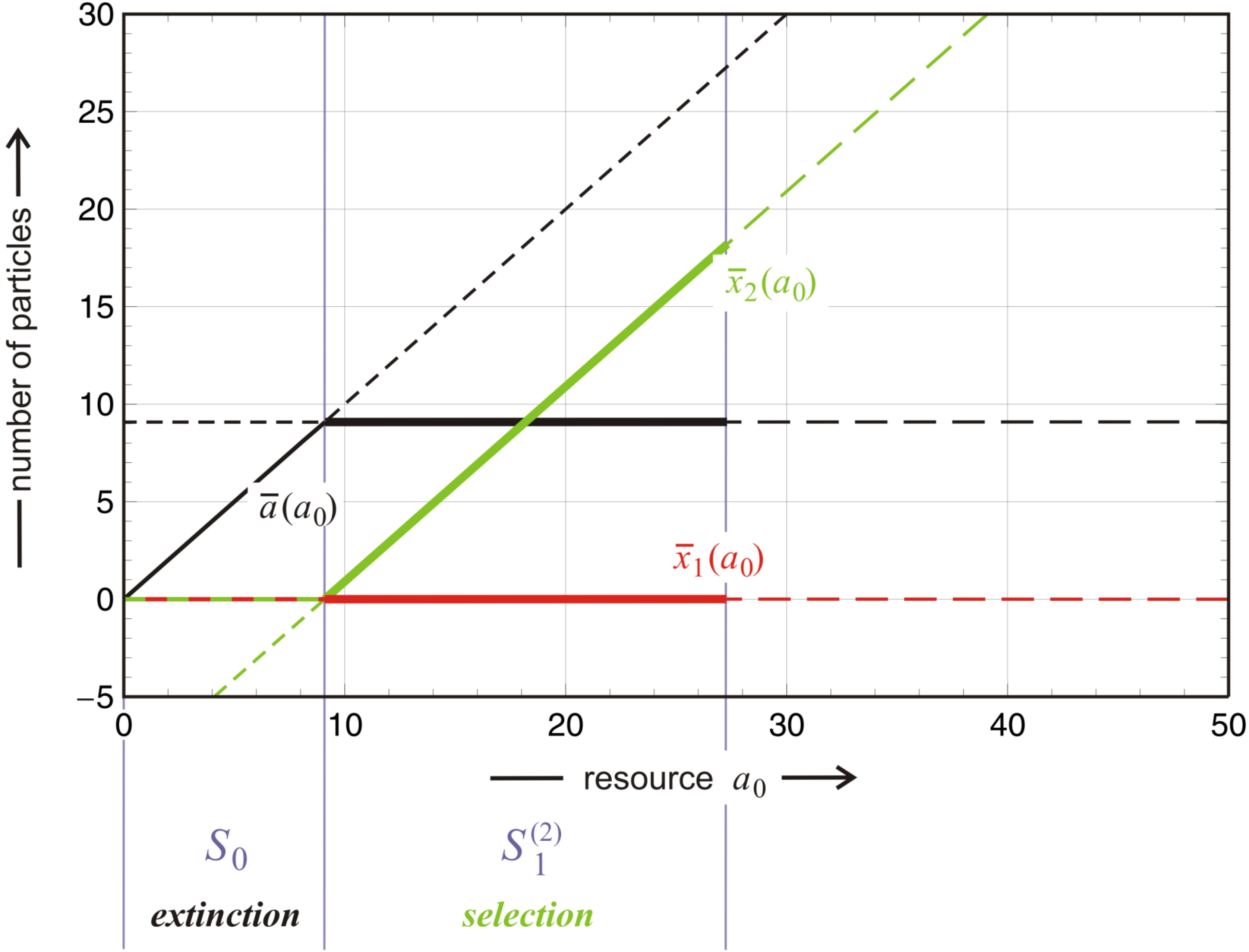
(ii) $\left(k_j + l_j \overline{x}_{j+1}\right) \overline{a} - r = 0\;;\; j \mod n$

In case of compatibility and linearity the number of stationary solutions is 2^n.

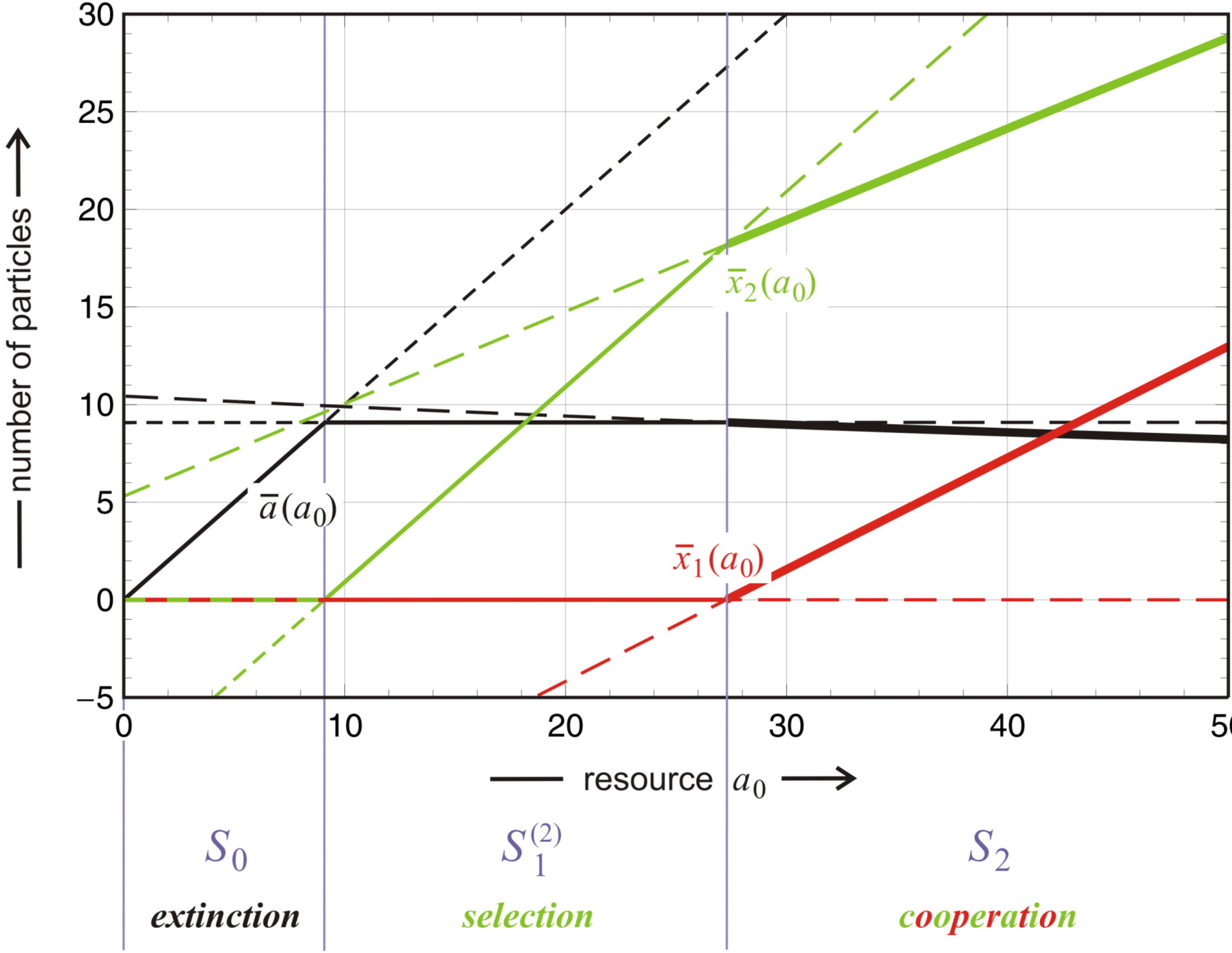
Kinetic differential equations and stationary solutions



30
25
20
15
10
5
0
−5
0
10
20
30
40
50
number of particles
resource a_0
$\bar{a}(a_0)$
$\bar{x}_2(a_0)$
$\bar{x}_1(a_0)$
S_0
extinction



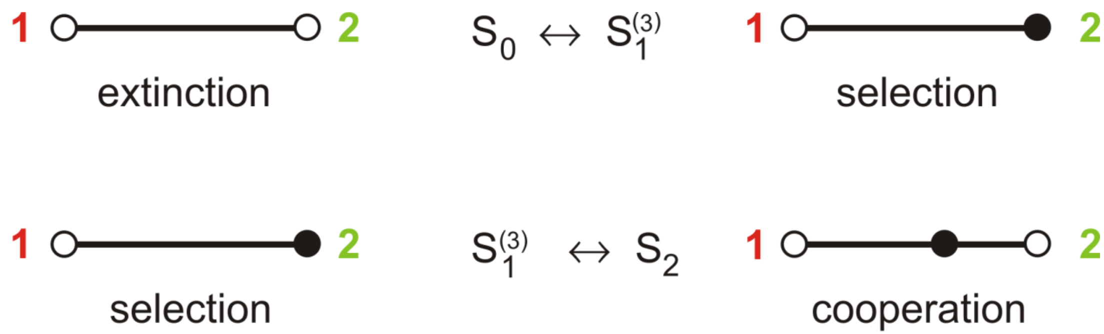
number of particles
resource a_0
$\bar{a}(a_0)$
$\bar{x}_2(a_0)$
$\bar{x}_1(a_0)$
S_0
$S_1^{(2)}$
extinction
selection



30
25
20
15
10
5
0
−5
number of particles
0
10
20
30
40
50
resource a_0
$\bar{x}_2(a_0)$
$\bar{a}(a_0)$
$\bar{x}_1(a_0)$
S_0
$S_1^{(2)}$
S_2
extinction
selection
cooperation

increasing a_0-values

$k_1 < k_2$ and $l_1 > l_2$



Name	Symbol	Stationary Values $\bar{a}$	$\bar{x}_1$	$\bar{x}_2$	Stability Range
extinction	S_0	a_0	0	0	$0 \leq a_0 \leq \frac{r}{k_2}$
selection	$S_1^{(2)}$	$\frac{r}{k_2}$	0	$a_0 - \frac{r}{k_2}$	$\frac{r}{k_2} \leq a_0 \leq \frac{r}{k_2} + \frac{k_2 - k_1}{l_1}$
cooperation	S_2	α	$\frac{r - k_2\alpha}{l_2\alpha}$	$\frac{r - k_1\alpha}{l_1\alpha}$	$\frac{r}{k_2} + \frac{k_2 - k_1}{l_1} \leq a_0$

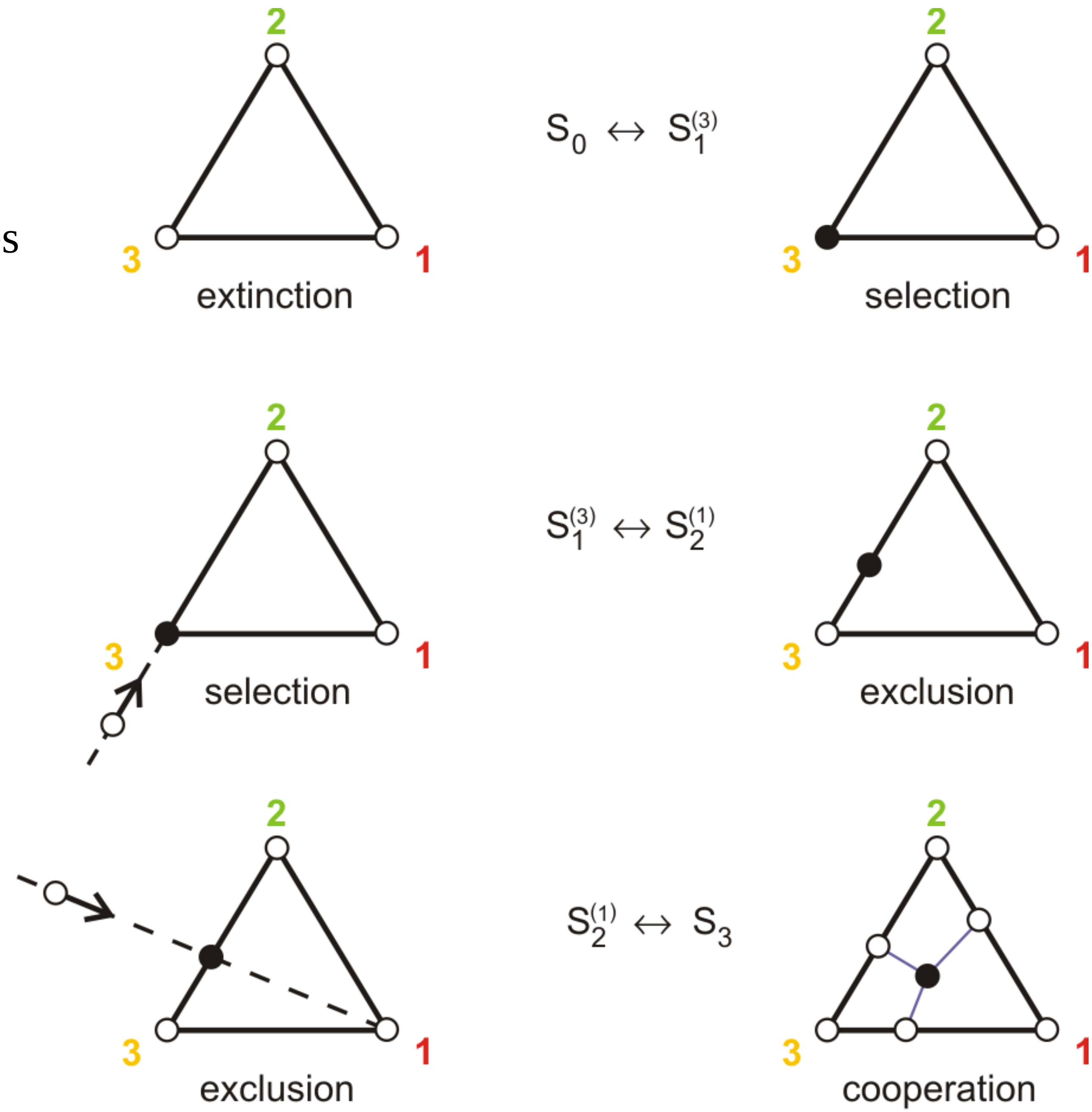
$$\bar{a}_{S_2} = \alpha = \frac{1}{2}\left(a_0 + \psi - \sqrt{(a_0+\psi)^2 - 4r\phi}\right) \text{ with } \psi = \sum_{i=1}^{n} \frac{k_i}{l_i}, \ \phi = \sum_{i=1}^{n} \frac{1}{l_i}$$

$$r \leq \frac{1}{4\phi}(a_0 + \psi)^2$$

$k_1 < k_2 < k_3$

$l_1 > l_2 > l_3$

increasing a_0-values



$$k_1 < k_2 < k_3 \text{ and } l_1 > l_2 > l_3$$

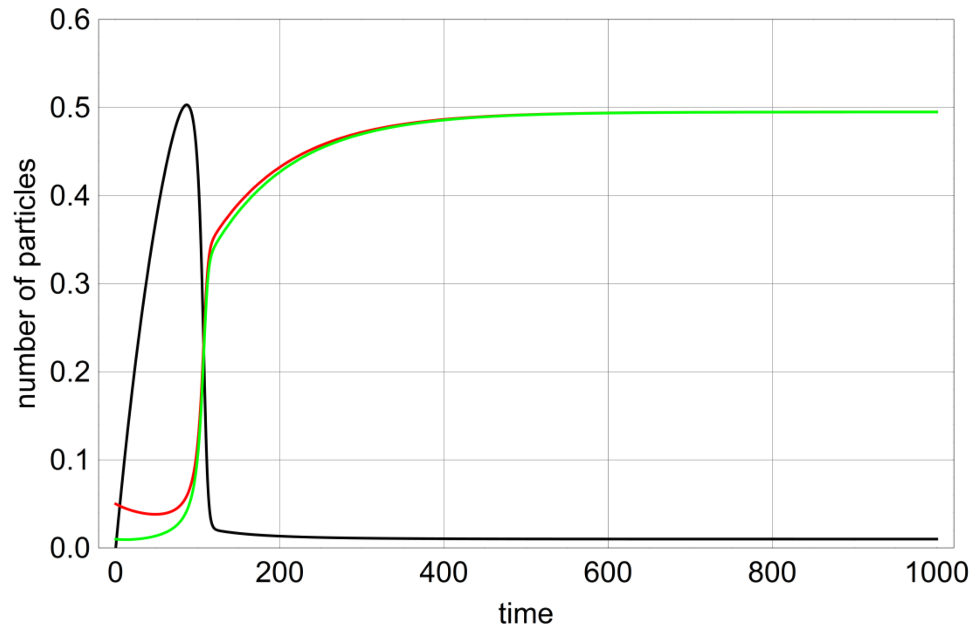
increasing a_0-values

Name	Symbol	Stationary Values				Stability Range
		$\overline{a}$	$\overline{x}_1$	$\overline{x}_2$	$\overline{x}_3$	
extinction	S_0	a_0	0	0	0	$0 \leq a_0 \leq \frac{r}{k_3}$
selection	$S_1^{(3)}$	$\frac{r}{k_3}$	0	0	$a_0 - \frac{r}{k_3}$	$\frac{r}{k_3} \leq a_0 \leq \frac{r}{k_3} + \frac{k_3-k_2}{l_2}$
exclusion	$S_2^{(1)}$	$\frac{r}{k_3}$	0	$a_0 - \frac{r}{k_3} - \frac{k_3-k_2}{l_2}$	$\frac{k_3-k_2}{l_2}$	$\frac{r}{k_3} + \frac{k_3-k_2}{l_2} \leq a_0 \leq \frac{r}{k_3} + \frac{k_3-k_2}{l_2} + \frac{k_3-k_1}{l_1}$
cooperation	S_3	α	$\frac{r-k_3\alpha}{l_3\alpha}$	$\frac{r-k_1\alpha}{l_1\alpha}$	$\frac{r-k_2\alpha}{l_2\alpha}$	$\frac{r}{k_3} + \frac{k_3-k_2}{l_2} + \frac{k_3-k_1}{l_1} \leq a_0$

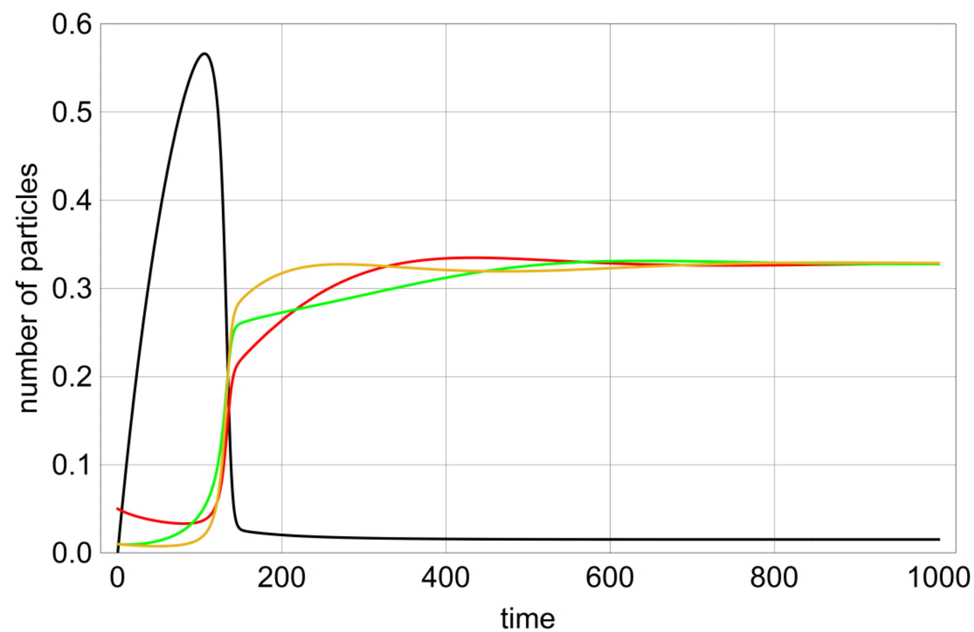
$$\overline{a}_{S_2} = \alpha = \frac{1}{2}\left(a_0 + \psi - \sqrt{(a_0+\psi)^2 - 4r\phi}\right) \text{ with } \psi = \sum_{i=1}^{n} \frac{k_i}{l_i}, \; \phi = \sum_{i=1}^{n} \frac{1}{l_i}$$

$$r \leq \frac{1}{4\phi}(a_0+\psi)^2$$

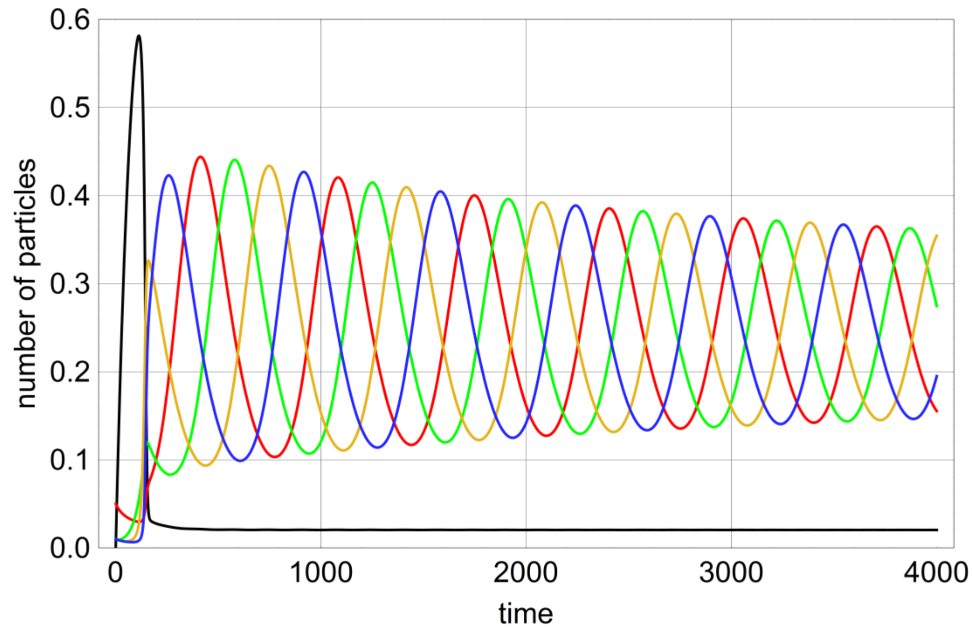
$n = 2$
$l_1 = l_2 = 2$, $r = 0.01$, $a_0 = 1$
$a(0) = 0$, $x_1(0) = 0.05$, $x_2(0) = 0.01$



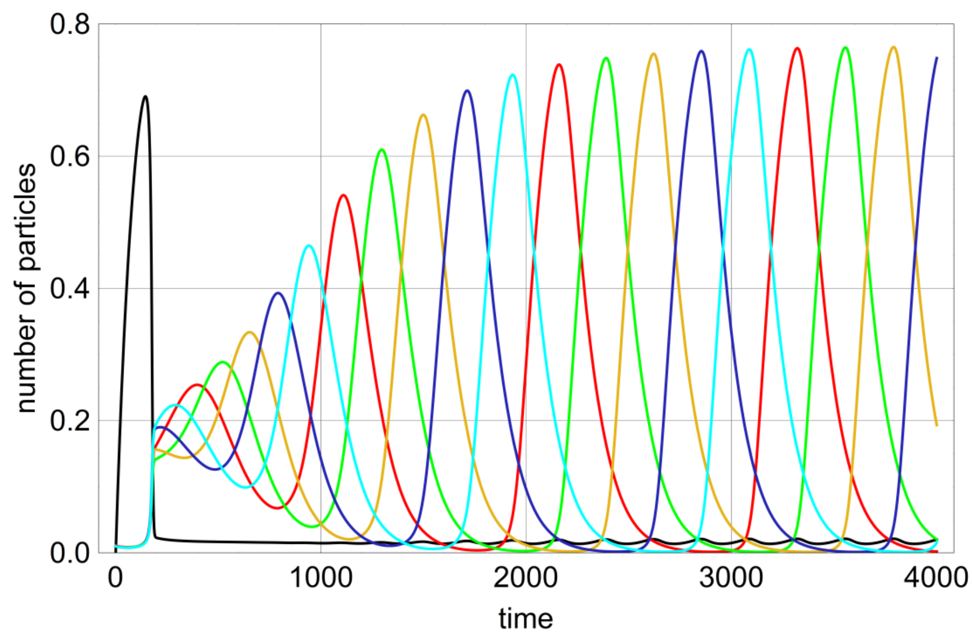
$n = 3$
$l_1 = l_2 = l_3 = 2$, $r = 0.01$, $a_0 = 1$
$a(0) = 0$, $x_1(0) = 0.05$,
$x_2(0) = x_3(0) = 0.01$



$n = 4$
$l_1 = l_2 = l_3 = l_4 = 2$, $r = 0.01$, $a_0 = 1$
$a(0) = 0$, $x_1(0) = 0.05$,
$x_2(0) = x_3(0) = x_4(0) = 0.01$



$n = 5$
$l_1 = l_2 = l_3 = l_4 = l_5 = 3$,
$r = 0.01$, $a_0 = 1$
$a(0) = 0$, $x_1(0) = 0.011$,
$x_2(0) = x_3(0) = x_4(0) = x_5(0) = 0.01$



$$[\mathsf{A}] = \mathrm{m}\,,\ [\mathsf{X}_j] = \mathrm{s}_j\,;\ j = 1,\ldots,n$$

$$\mathbf{X} = (\mathrm{m}, \mathrm{s}_j; j = 1,\ldots,n)$$

$$(\mathbf{X}; \mathrm{s}'_k) = (\mathrm{m}, \mathrm{s}_1, \ldots, \mathrm{s}_k = k', \ldots, n) = (\mathrm{s}'_k)$$

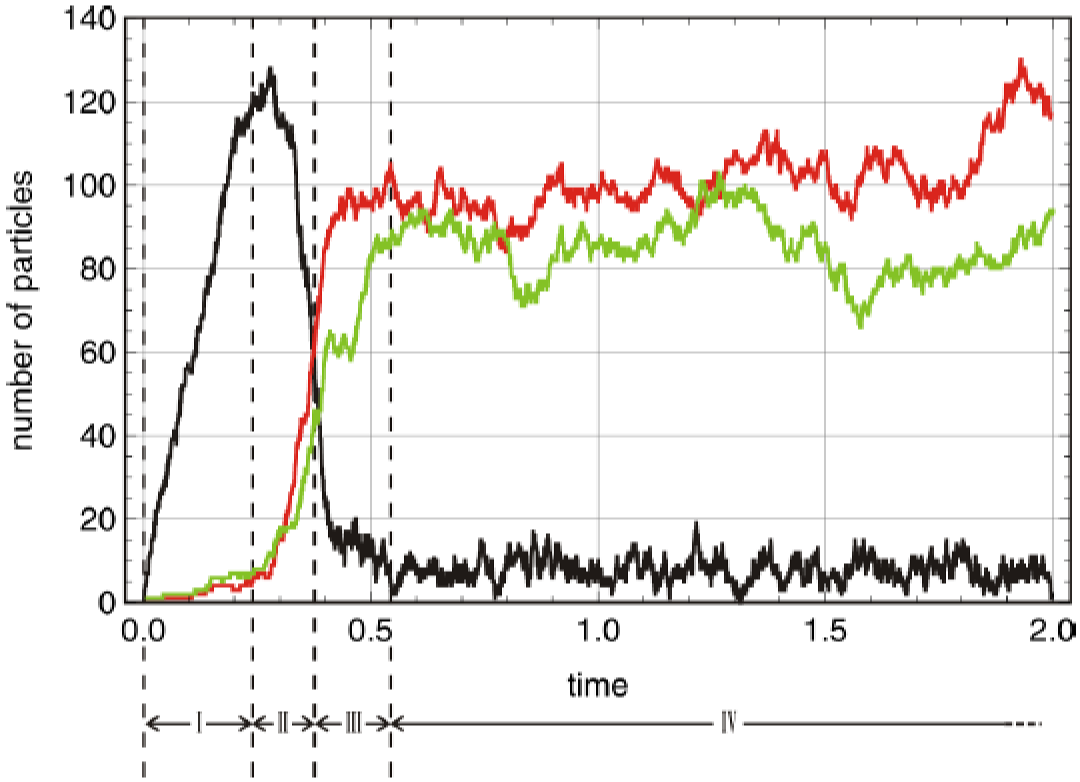
$$P_{\mathbf{X}}(t) = \mathrm{Prob}\Big([\mathsf{A}(t)] = \mathrm{m}, [\mathsf{X}_j(t)] = \mathrm{s}_j\,;\ j = 1,\ldots,n\Big)$$

$$\frac{\mathrm{d}P_{\mathbf{X}}}{\mathrm{dt}} = a_0\, r\, P_{(\mathrm{m}-1)} + r\Big((\mathrm{m}+1)P_{(\mathrm{m}+1)} + \sum_{j=1}^{n}(\mathrm{s}_j+1)P_{(\mathrm{s}+1)}\Big) +$$

$$+ (\mathrm{m}+1)\sum_{j=1}^{n}\Big((k_j + l_j\,\mathrm{s}_{j+1})(\mathrm{s}_j - 1)P_{(\mathrm{m}+1,\mathrm{s}_j-1)}\Big) -$$

$$- \Big(r\Big(a_0 + \mathrm{m} + \sum_{j=1}^{n}\mathrm{s}_j\Big) + \mathrm{m}\Big(\sum_{j=1}^{n}(f_j + k_j\,\mathrm{s}_{j+1})\,\mathrm{s}_j\Big)\Big)P_{\mathbf{X}}$$

The master equation for competition and cooperation



Daniel T. Gillespie, 1938 –

D.T. Gillespie, Annu.Rev.Phys.Chem. 58:35-55, 2007

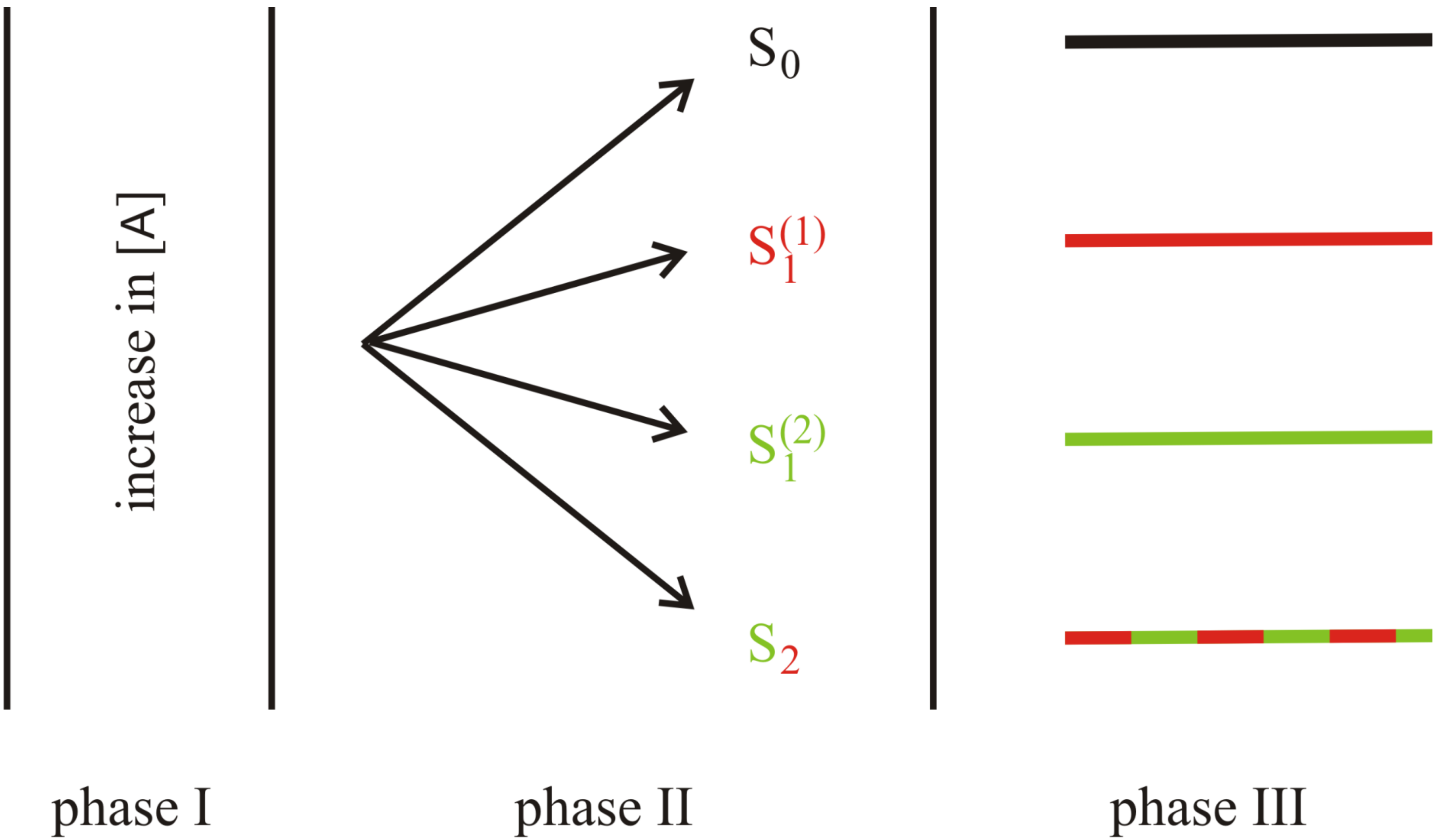
phase I: raise of [**A**] ;

phase II: random choice of convergence to a quasi-stationary state ;

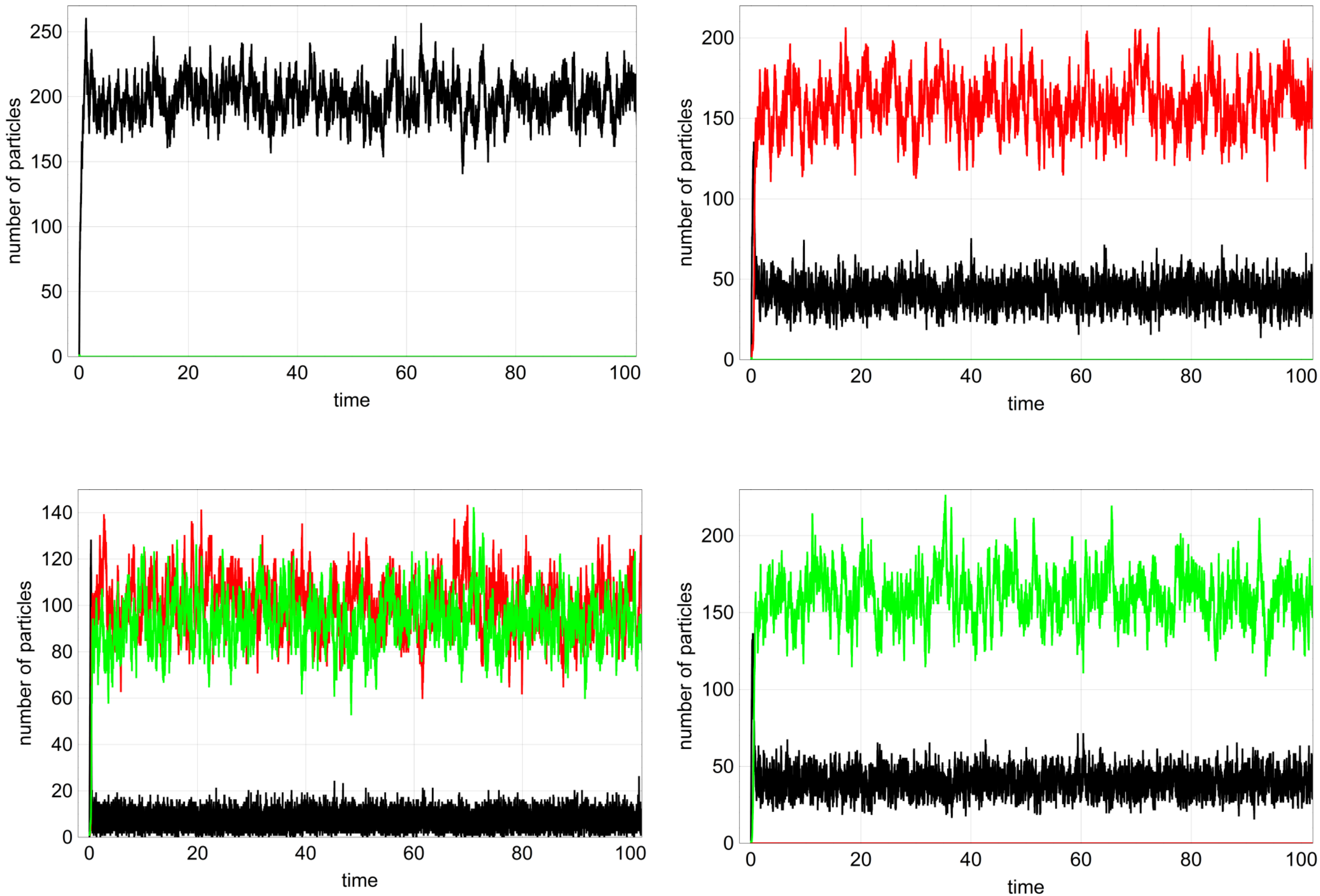
phase III: convergence to the quasi-stationary state;

phase IV: fluctuations around the values of the quasi-stationary state

Gillespie simulation of individual trajectories

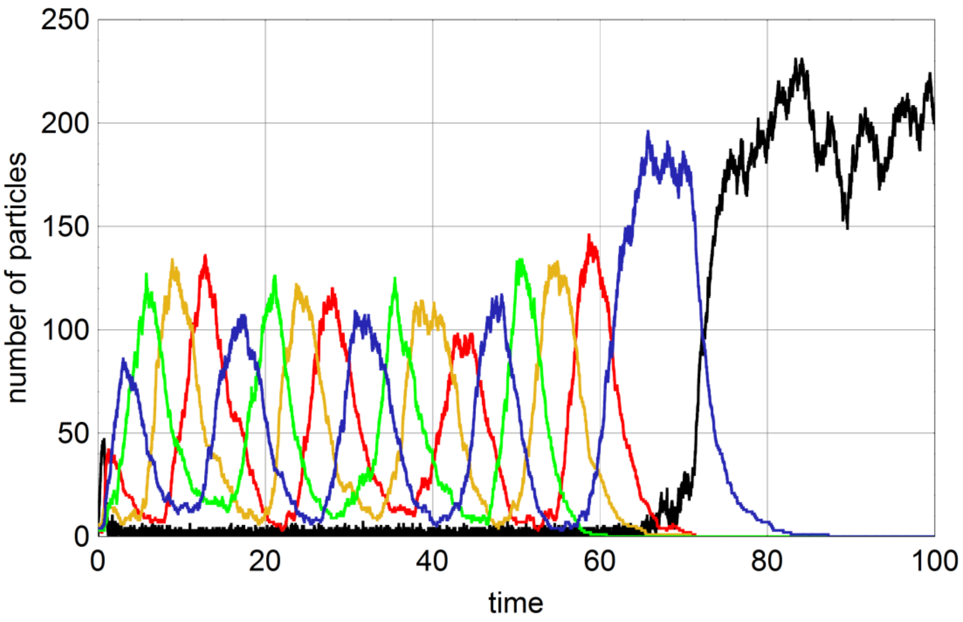


Random decision in the stochastic process

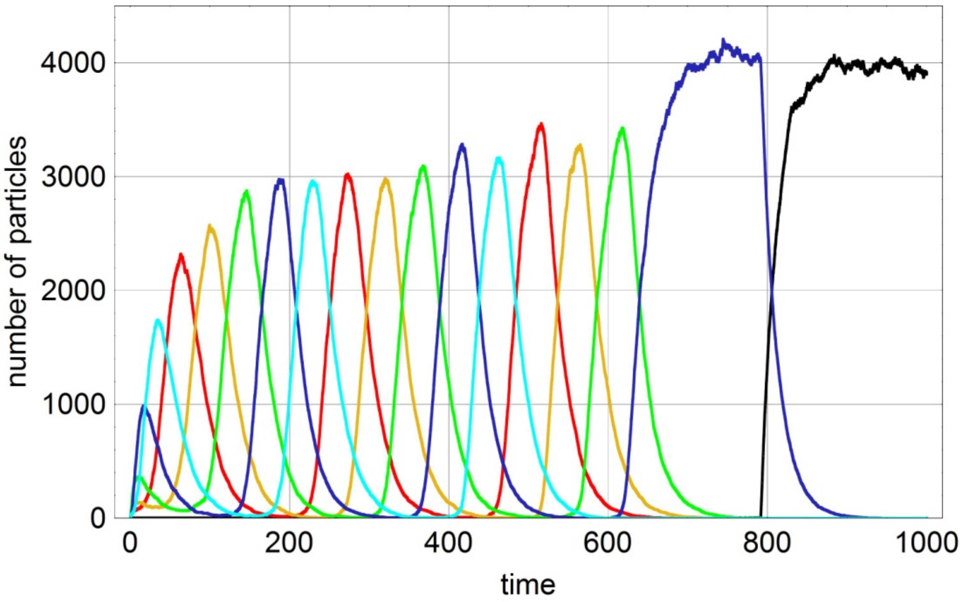


The four long-time solutions for competition and cooperation with $n = 2$

stochastic hypercycles with $n = 4$



stochastic hypercycles with $n = 5$



$$\frac{dx_i}{dt} = l_i \; x_i \;\; x_{i+1} - r \; x_i$$

$$x_{i+1} = 0 \quad \Rightarrow \quad \frac{dx_i}{dt} = -r \, x_i \leq 0 \quad \Rightarrow \quad x_i \to 0$$

Stochastic extinction of hypercycles

$$X_n \Leftarrow X_1 \Leftarrow X_2 \Leftarrow X_3 \Leftarrow X_4 \Leftarrow \cdots \Leftarrow X_{n-1} \Leftarrow X_n$$

$$X_n \Leftarrow X_1 \Leftarrow X_2 \Leftarrow X_3 \Leftarrow X_4 \Leftarrow \cdots \Leftarrow X_{n-1}$$

$$\downarrow$$
$$\downarrow$$

$$X_n \Leftarrow X_1 \Leftarrow X_2 \Leftarrow X_3 \Leftarrow X_4$$

$$X_n \Leftarrow X_1 \Leftarrow X_2 \Leftarrow X_3$$

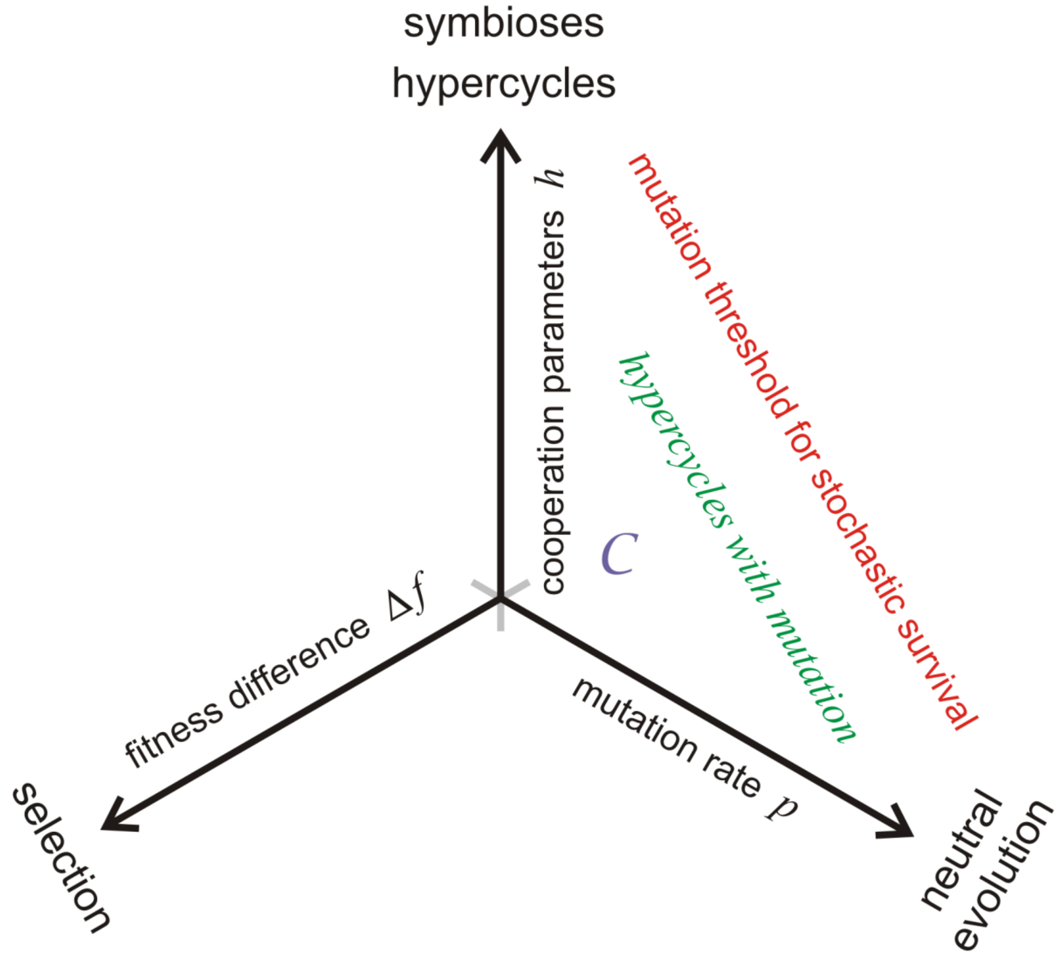
$$X_n \Leftarrow X_1 \Leftarrow X_2$$

$$X_n \Leftarrow X_1$$

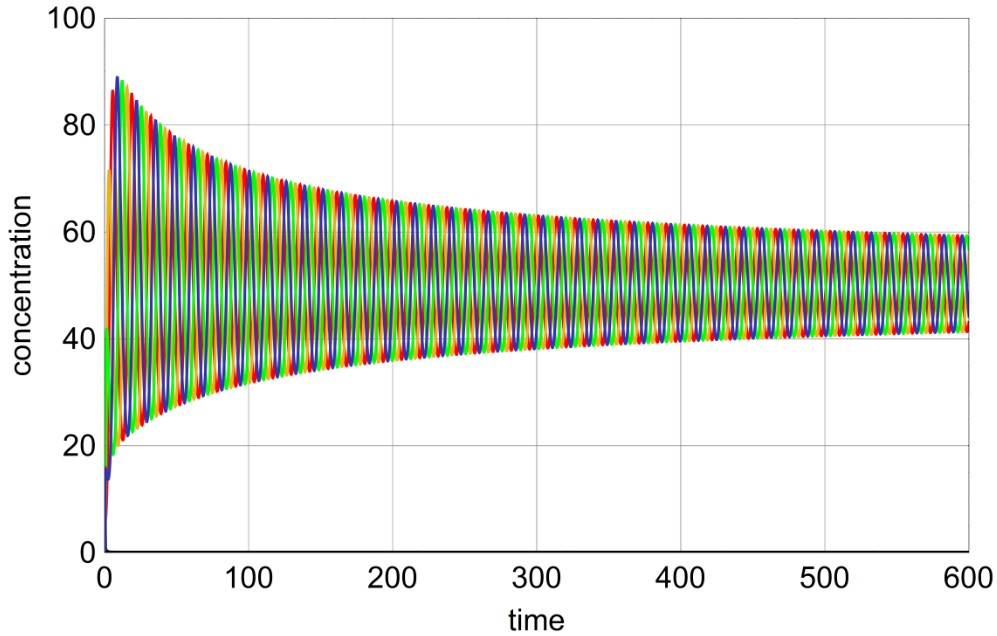
$$X_n$$

Stepwise consecutive extinction of a hypercycle

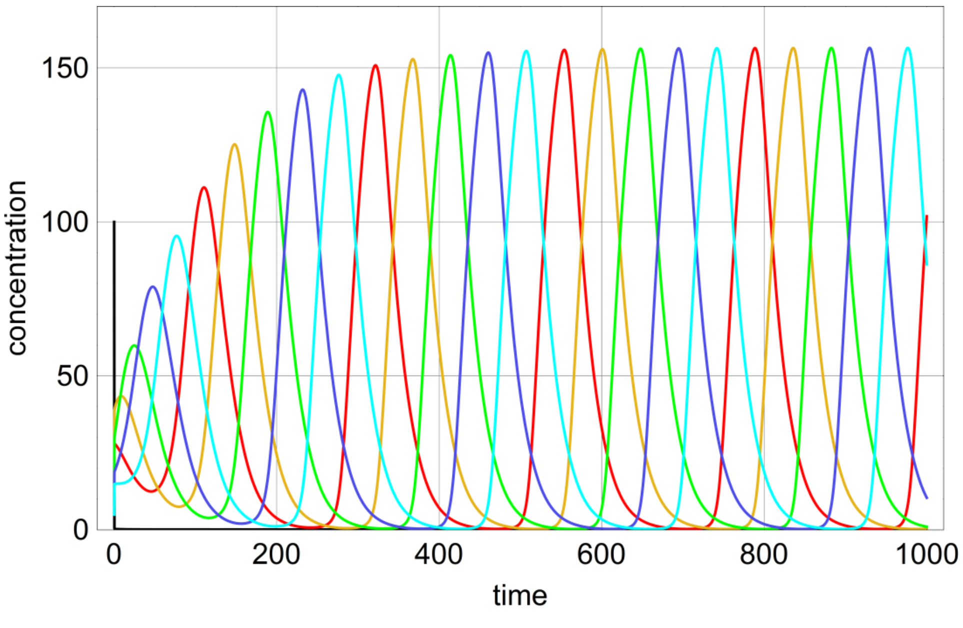
1. Chemical and biochemical reaction networks
2. Autocatalysis and replication
3. A simple model of evolution
4. Mutation and quasispecies
5. Cooperation and major transitions
6. **Can mutations counteract extinction ?**



Cooperation and mutation: stochastic escape from extinction n = 4

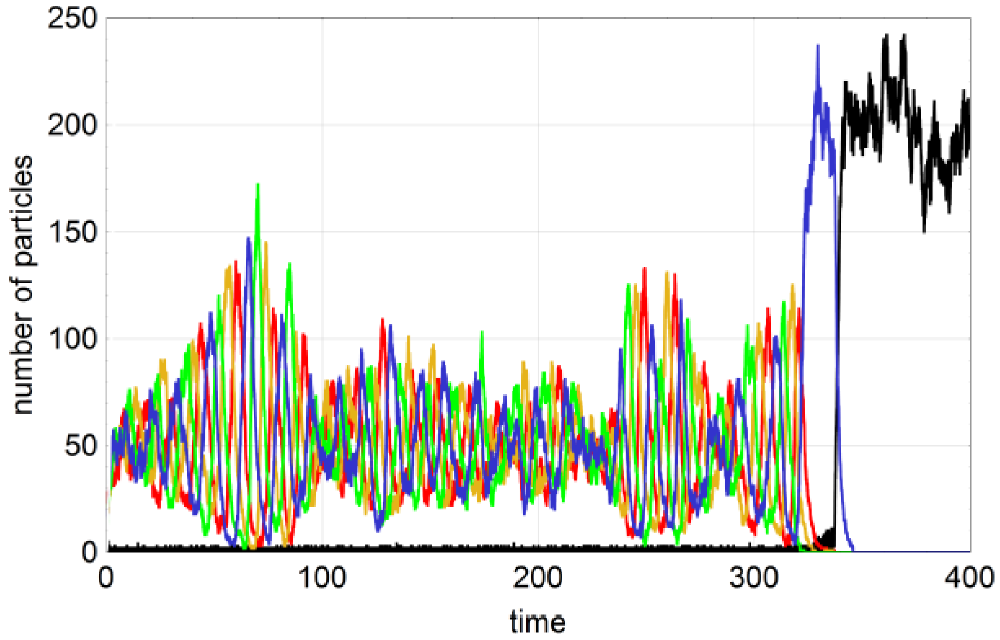


n = 5

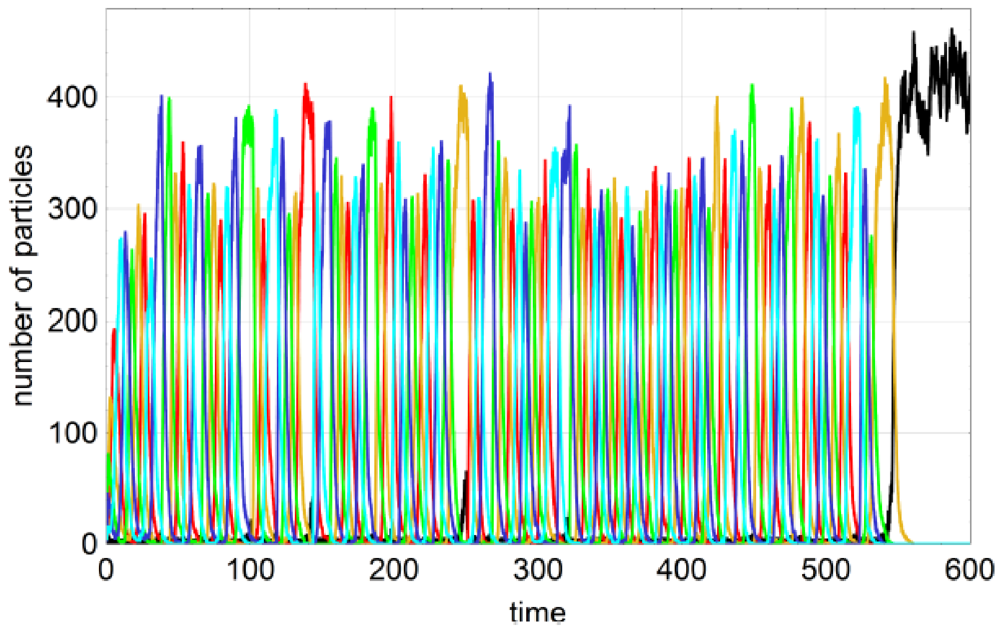


oscillatory hypercycles: ODE solutions

n = 4

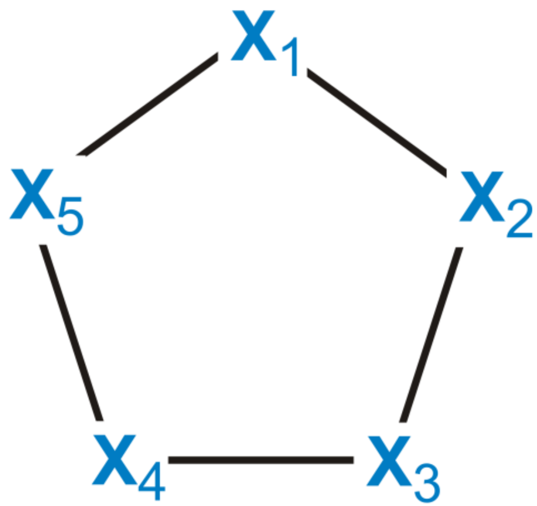


n = 5



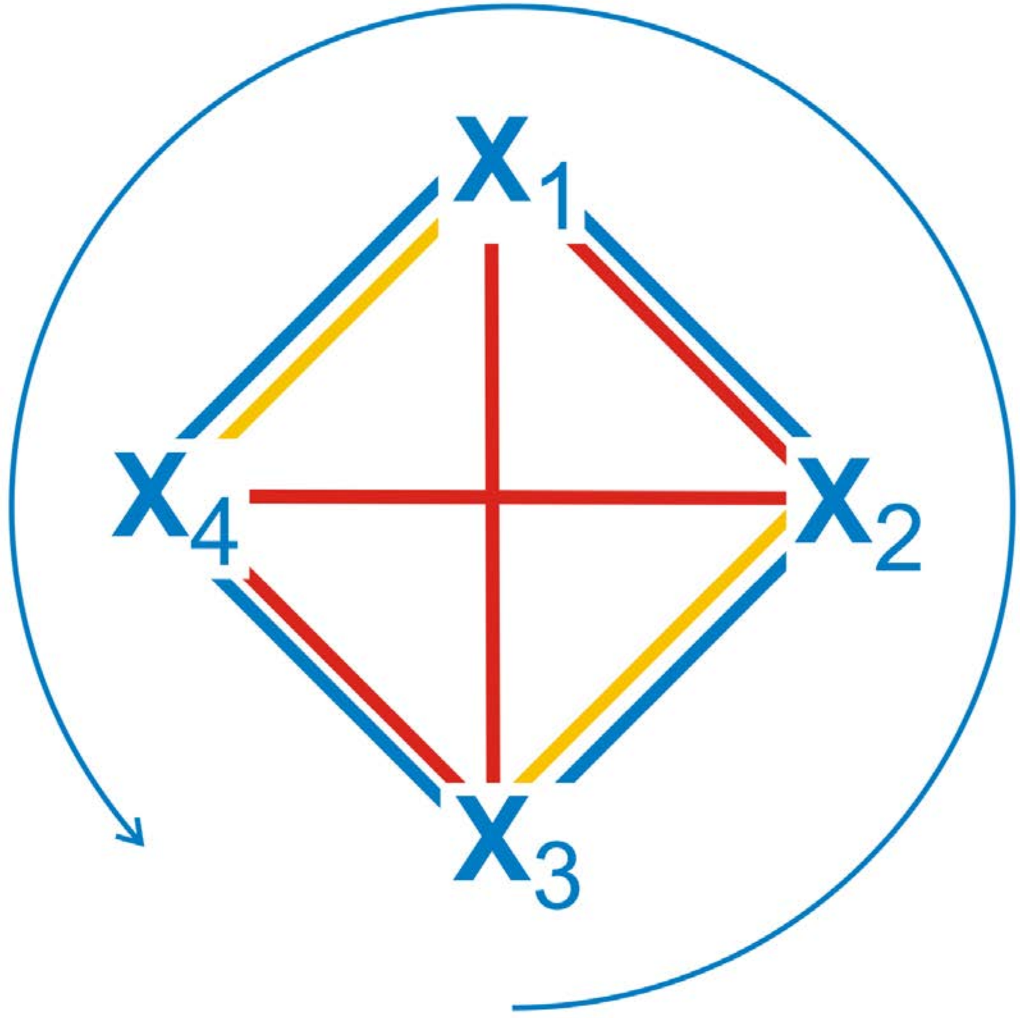
oscillatory hypercycles: simulations

$$\mathbf{A} + \mathbf{X}_j + \mathbf{X}_{j+1} \xrightarrow{l_j} 2\,\mathbf{X}_j + \mathbf{X}_{j+1}\,;\; j = 1, \ldots, n;\; j \bmod n$$

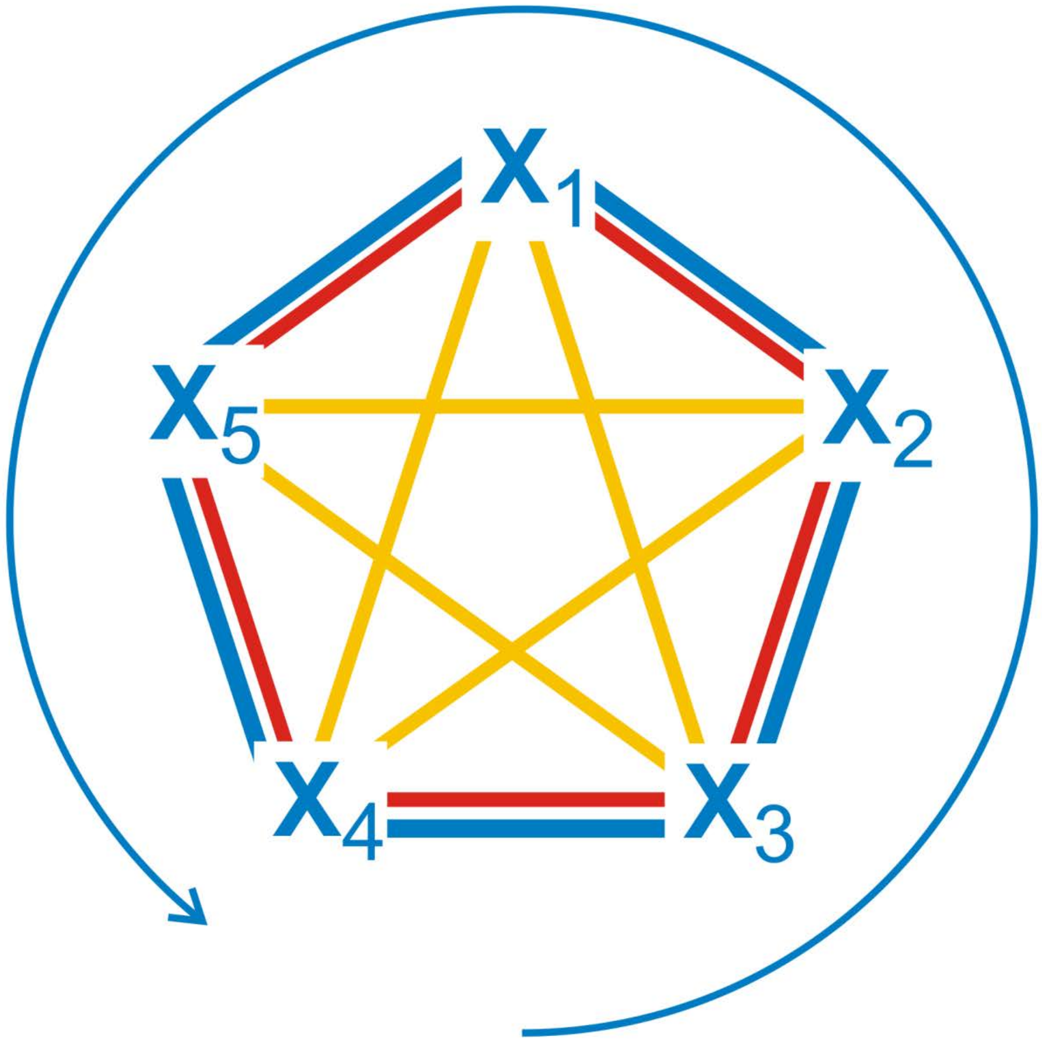


$$\mathbf{X}_n \Leftarrow \mathbf{X}_1 \Leftarrow \mathbf{X}_2 \Leftarrow \cdots \Leftarrow \mathbf{X}_{n-1} \Leftarrow \mathbf{X}_n$$

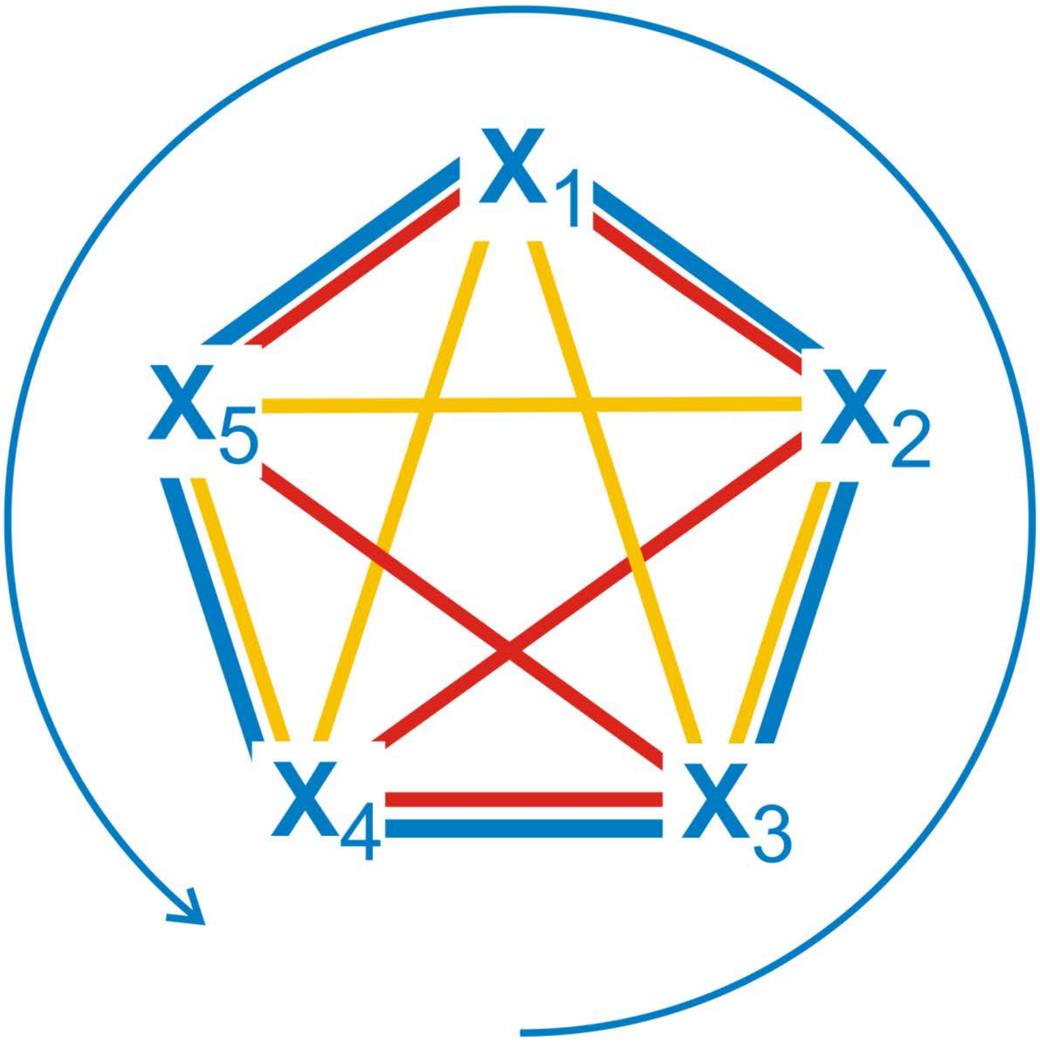
Catalytic hypercycles



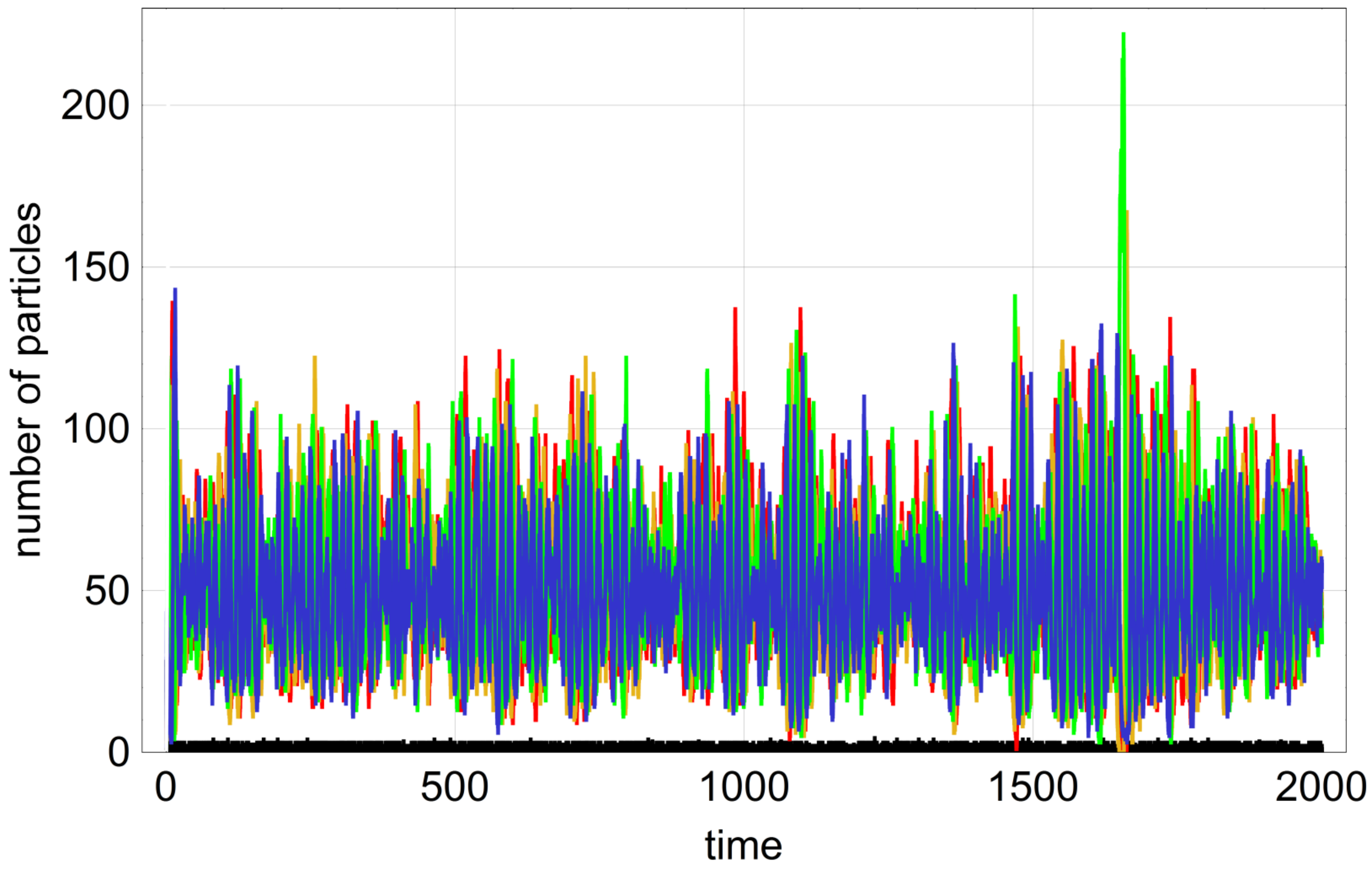
mutation mechanism, n = 4: ‚sequence space‘



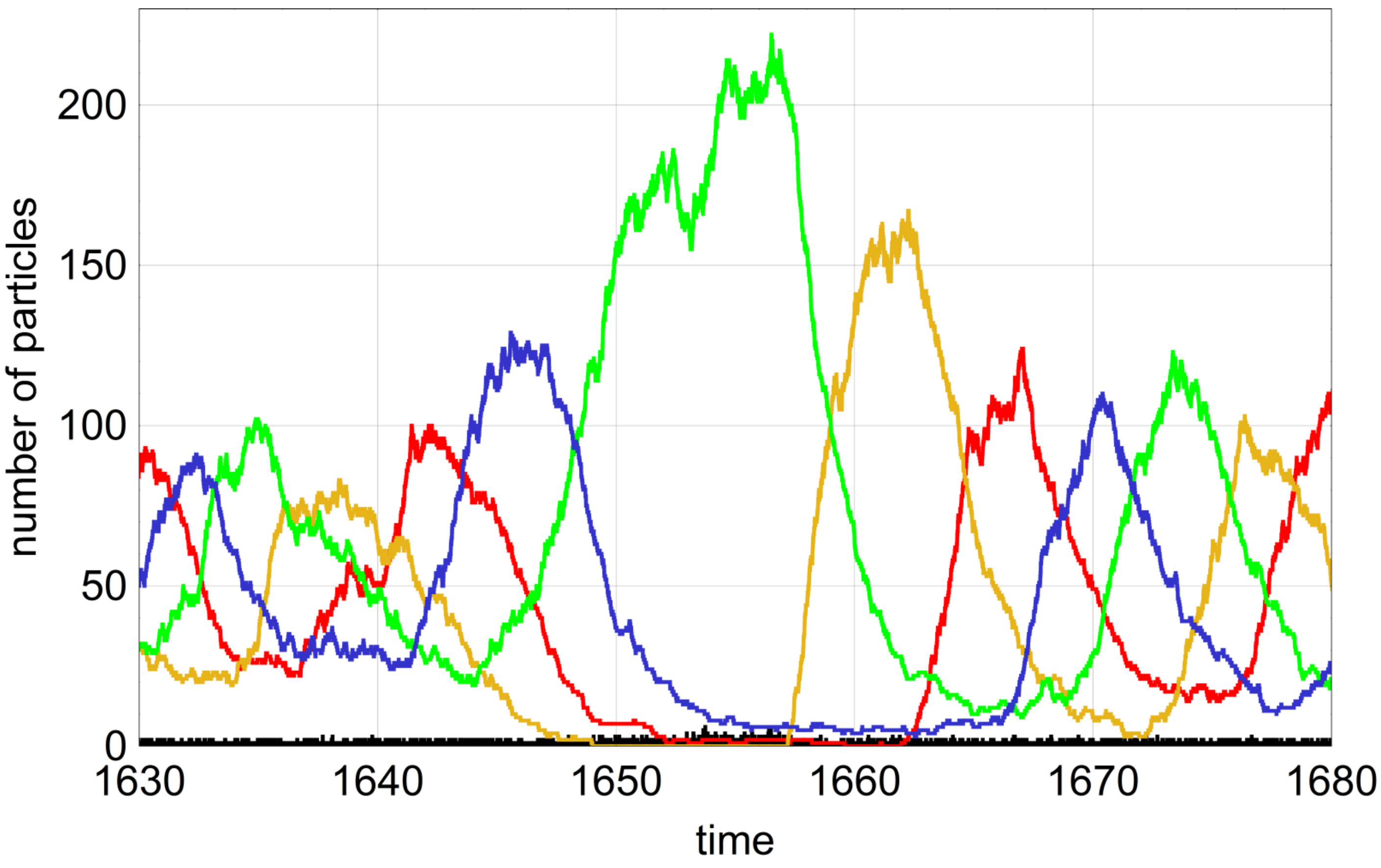
mutation mechanism, n = 5: ‚pentagram‘



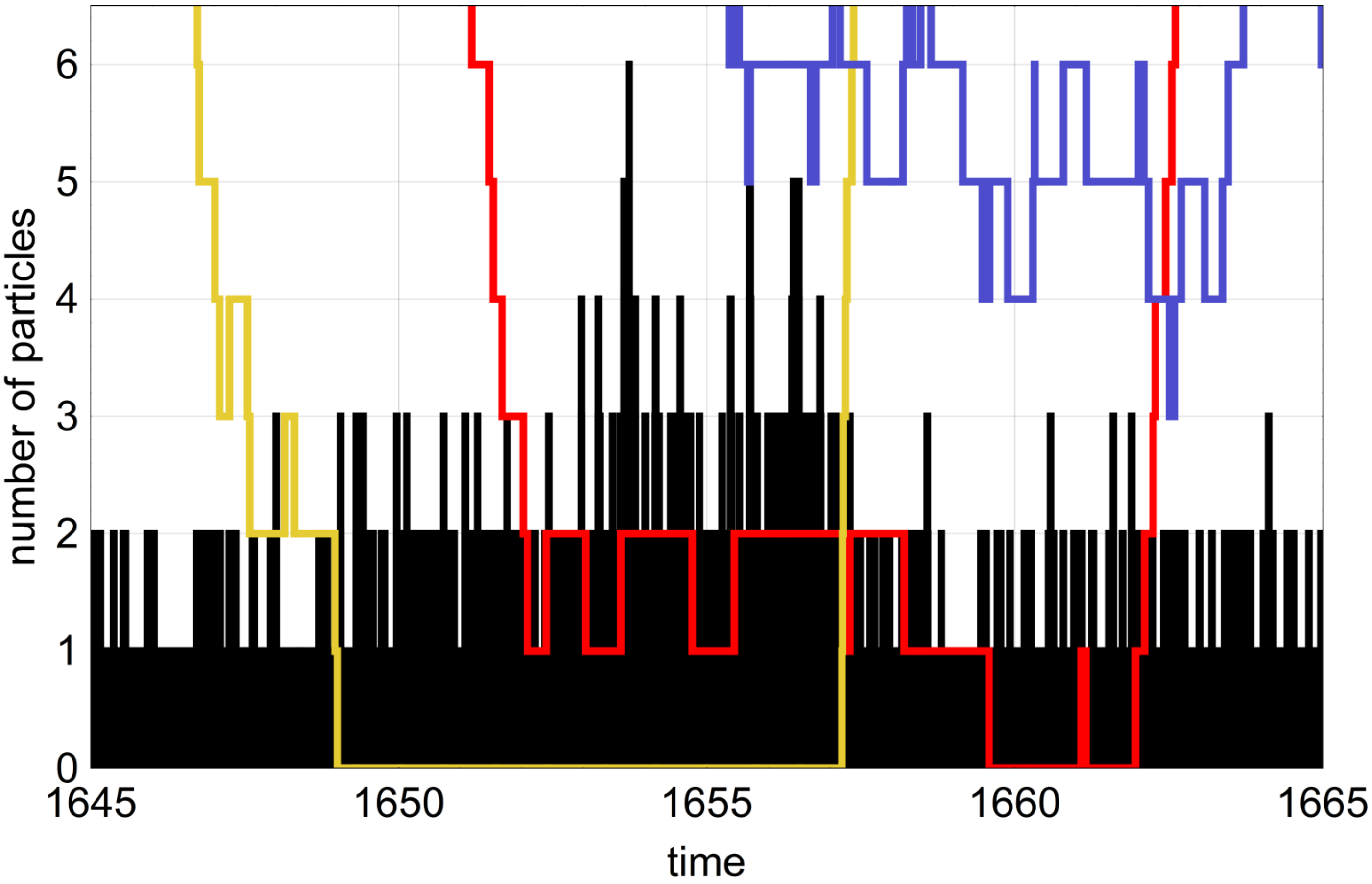
mutation mechanism, n = 5: ‚pentagramvariant‘



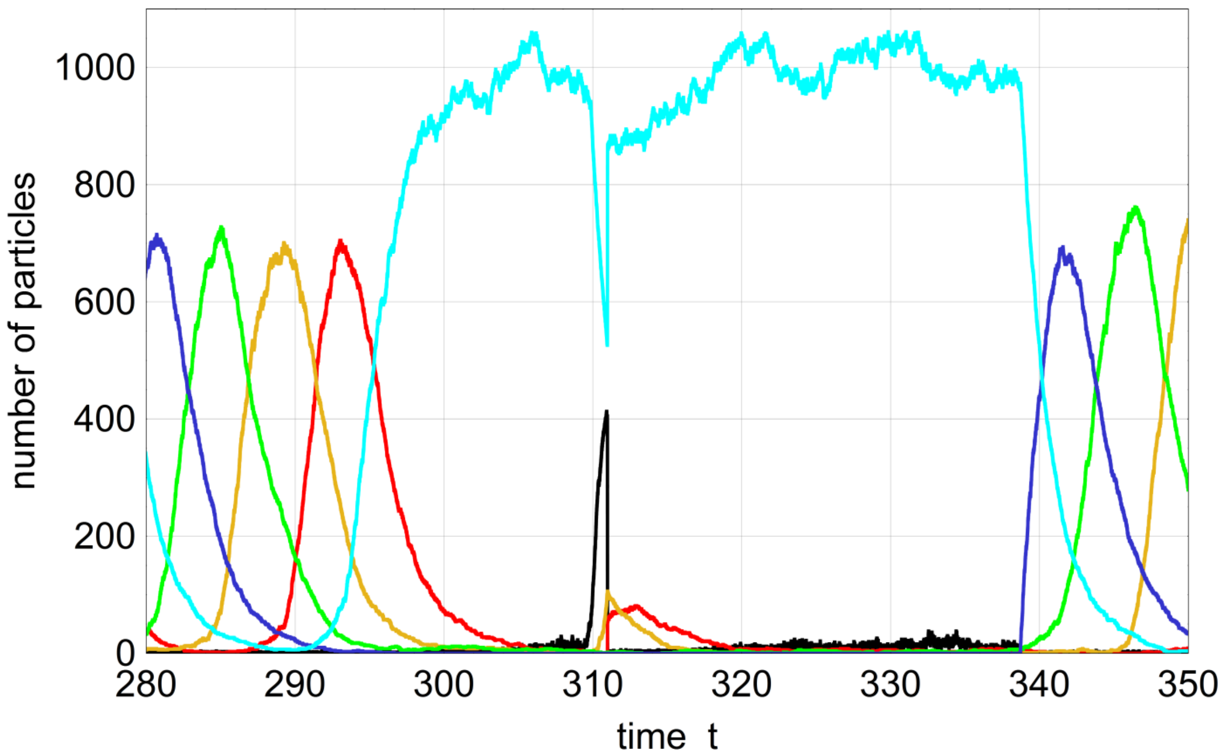
Oscillatory hypercycles:simulation for n=4



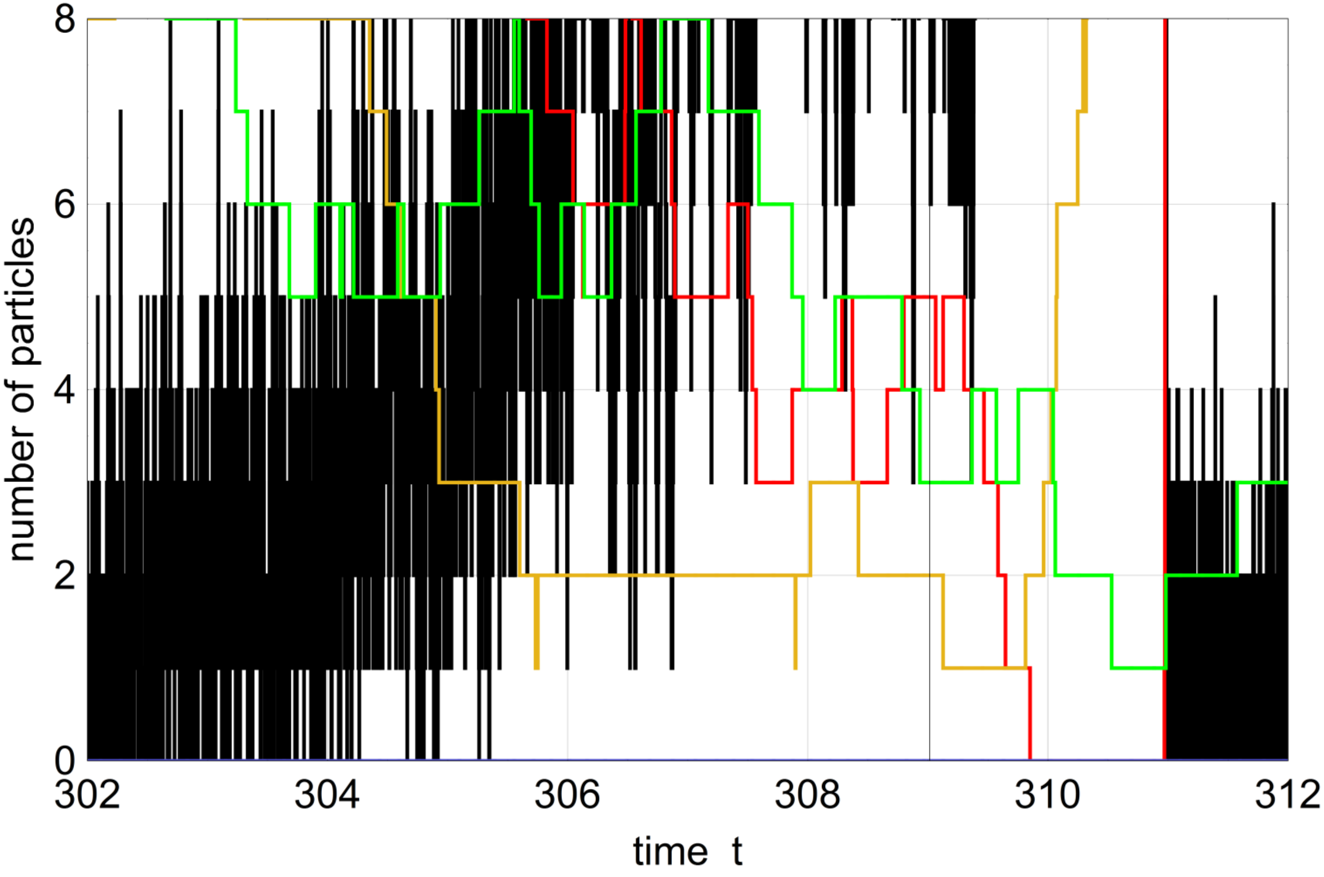
Oscillatory hypercycles:simulation for n=4, enlargement



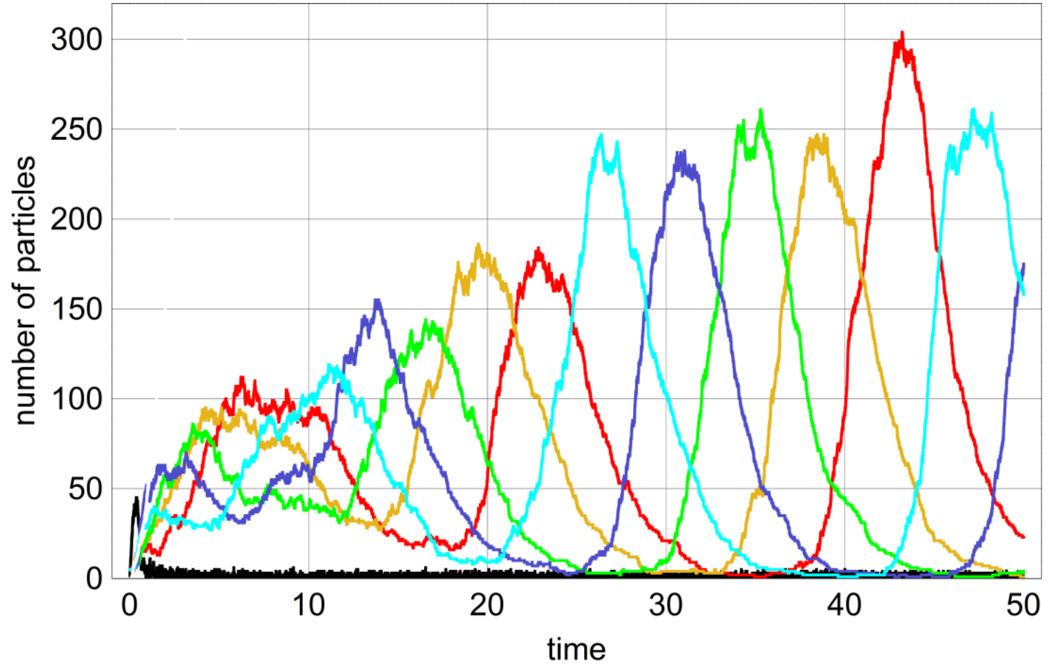
Oscillatory hypercycles:simulation for n=4, enlargement

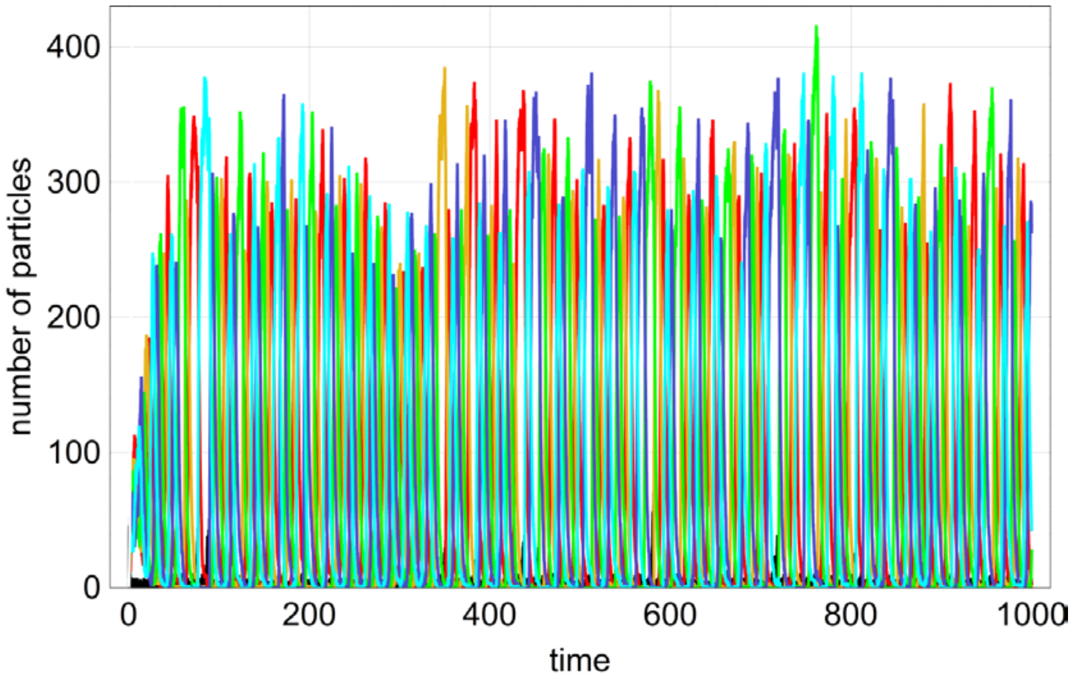


„Last minute mutation“ restores oscillations

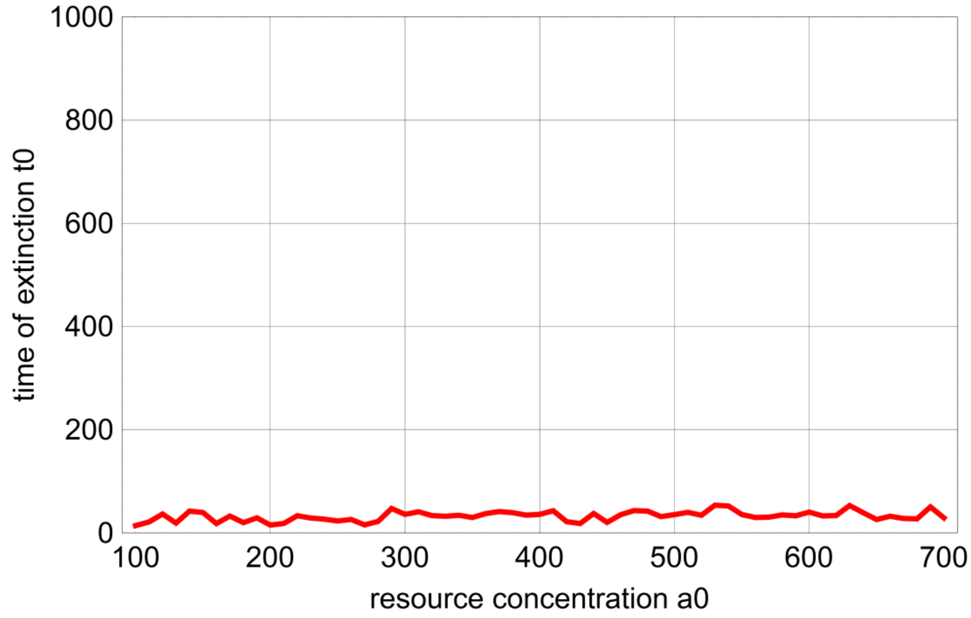


„Last minute mutation“ restores oscillations



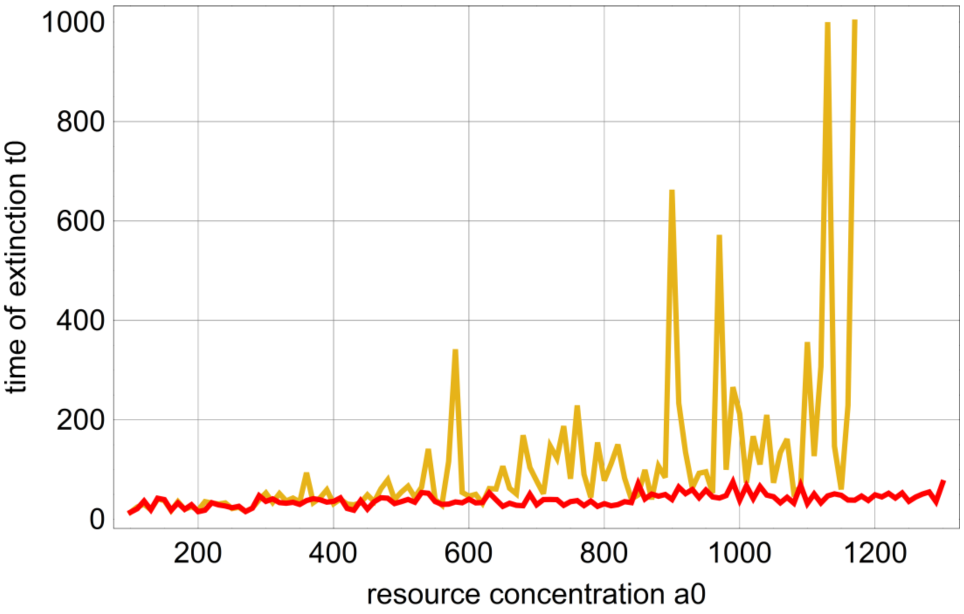


Oscillatory hypercycles:
simulation for n = 5



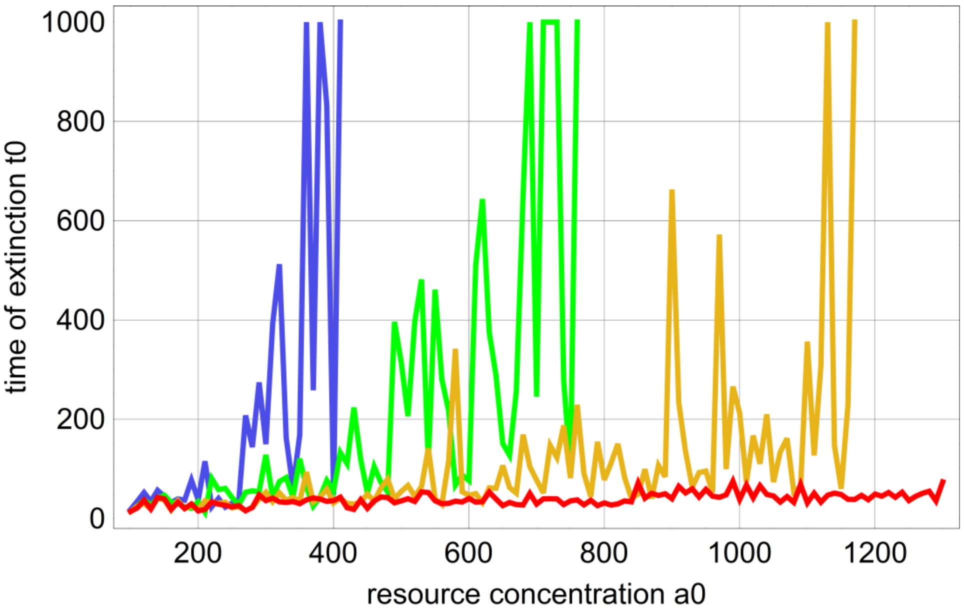
mutation rate: p = **0.0000**

Oscillatory hypercycles: simulation for n = 5



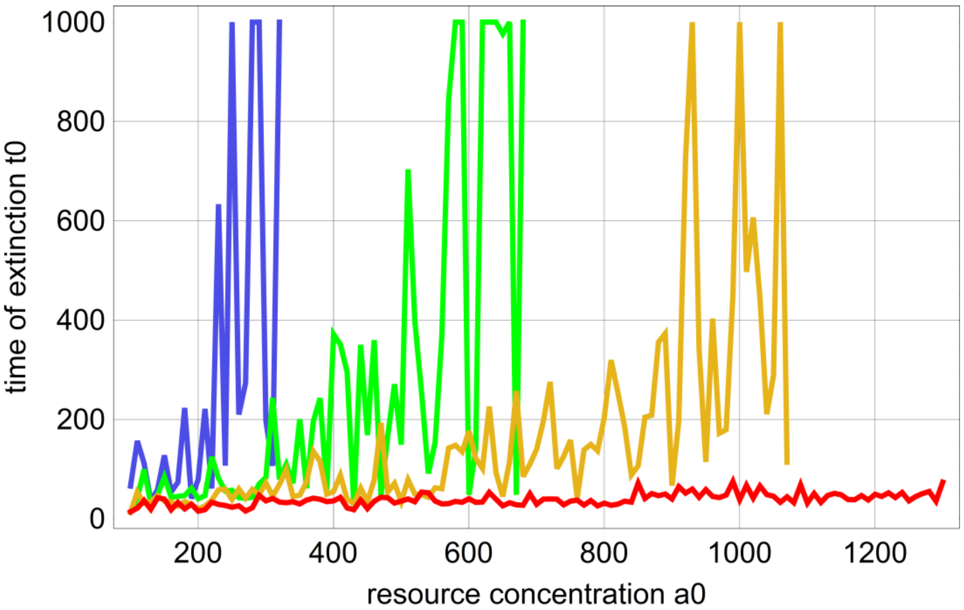
mutation rate: p = **0.0005**

Oscillatory hypercycles: simulation for n = 5,‘pentagram‘



mutation rate: p = **0.0000**, p=**0.0005**, p = **0.0010** and p = **0.0020**

Oscillatory hypercycles: simulation for n = 5, ‚pentagram'



mutation rate: p = **0.0000**, p=**0.0005**, p = **0.0010** and p = **0.0020**

Oscillatory hypercycles: simulation for n = 5, ‚pentagramvariant'

Some concluding remarks

The model despite its simplicity illustrates and provides explanations for features observed in real biology.

A Cartesian space with competition, cooperation, and variation plotted on the axes is used to classify processes that lead to transition phenomena. Commonly - but not always - these transitions are sharp in the sense of 'phase transitions' in finite systems or they are represented by bifurcations.

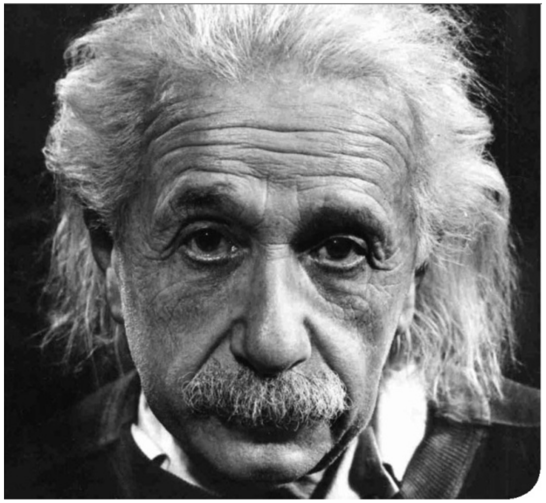
These transitions are:

i. A transition from ordered reproduction to random replication on the face constituted by differential fitness and mutation.
ii. A transition from selection to cooperation in the sense of the initiation of a 'major transition' driven by the availability of resources on the face of differential fitness and cooperation.
iii. A transition from stochastic extinction to survival on the face of cooperation and mutation.

A conjecture states that all transitions smoothen out in the interior of the Cartesian space.

Insofern sich Sätze der Mathematik auf die Wirklichkeit beziehen, sind sie nicht sicher, und insofern sie sicher sind, beziehen sie sich nicht auf die Wirklichkeit.

As far as the laws of mathematics refer to reality, they are not certain, and as far as they are certain, they don't refer to reality.



Albert Einstein. Geometrie und Erfahrung. Sitzungsberichte der Preussischen Akademie der Wissenschaften, 1921 (1), 123-130

Motto: Occam‘s razor in the twentieth century

Everything should be made as simple as possible, but not simpler.

Attributed to Albert Einstein

Thank you for your attention!

Web-Page for further information:

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

Peter Schuster. Some mechanistic requirements for major transitions. *Phil. Trans. R. Soc.B* 371:e20150439, 2016

Peter Schuster. Increase in complexity and information through molecular evolution. *Entropy* 18:397, 2016