Evolution and Thermodynamics
Useful and Misleading Analogies

Peter Schuster

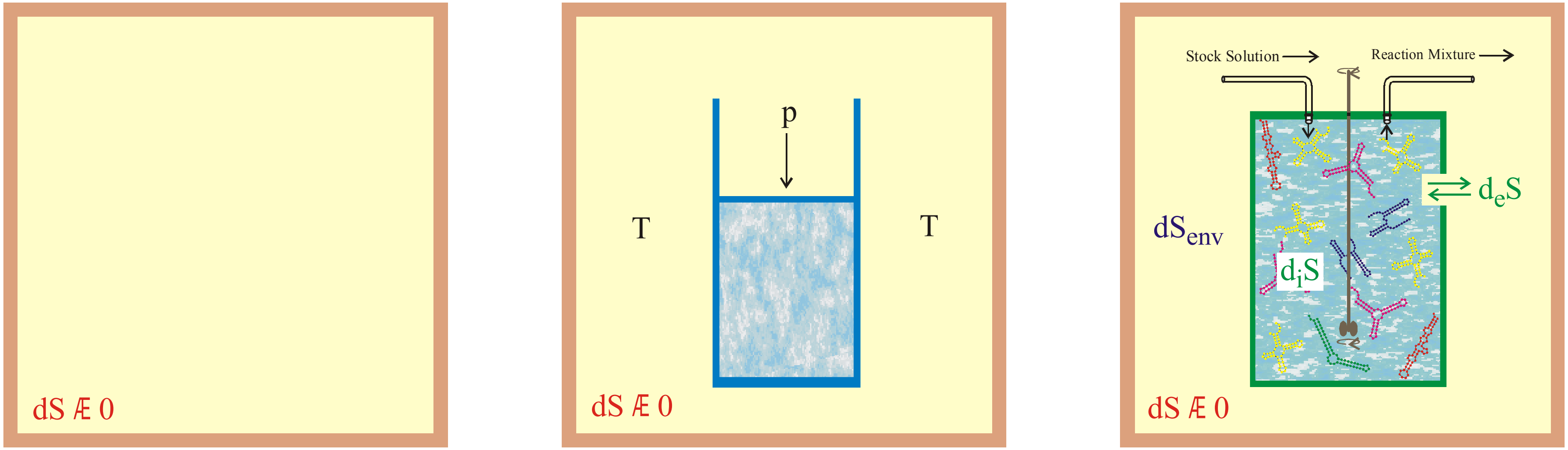
From Thermodynamics to Dynamical Systems
Emmerich Wilhelm‘s 60th Birthday
Universität Wien, 17.05.2002

Equilibrium thermodynamics is based on two major statements:

1. The energy of the universe is a constant (first law).
2. The entropy of the universe never decreases (second law).

Carnot, Mayer, Joule, Helmholtz, Clausius, ……

D.Jou, J.Casas-Vázquez, G.Lebon, *Extended Irreversible Thermodynamics*, 1996



Isolated system

U = const., V = const.,

$dS \geq 0$

Closed system

T = const., p = const.,

$dG = dU - pdV - TdS \leq 0$

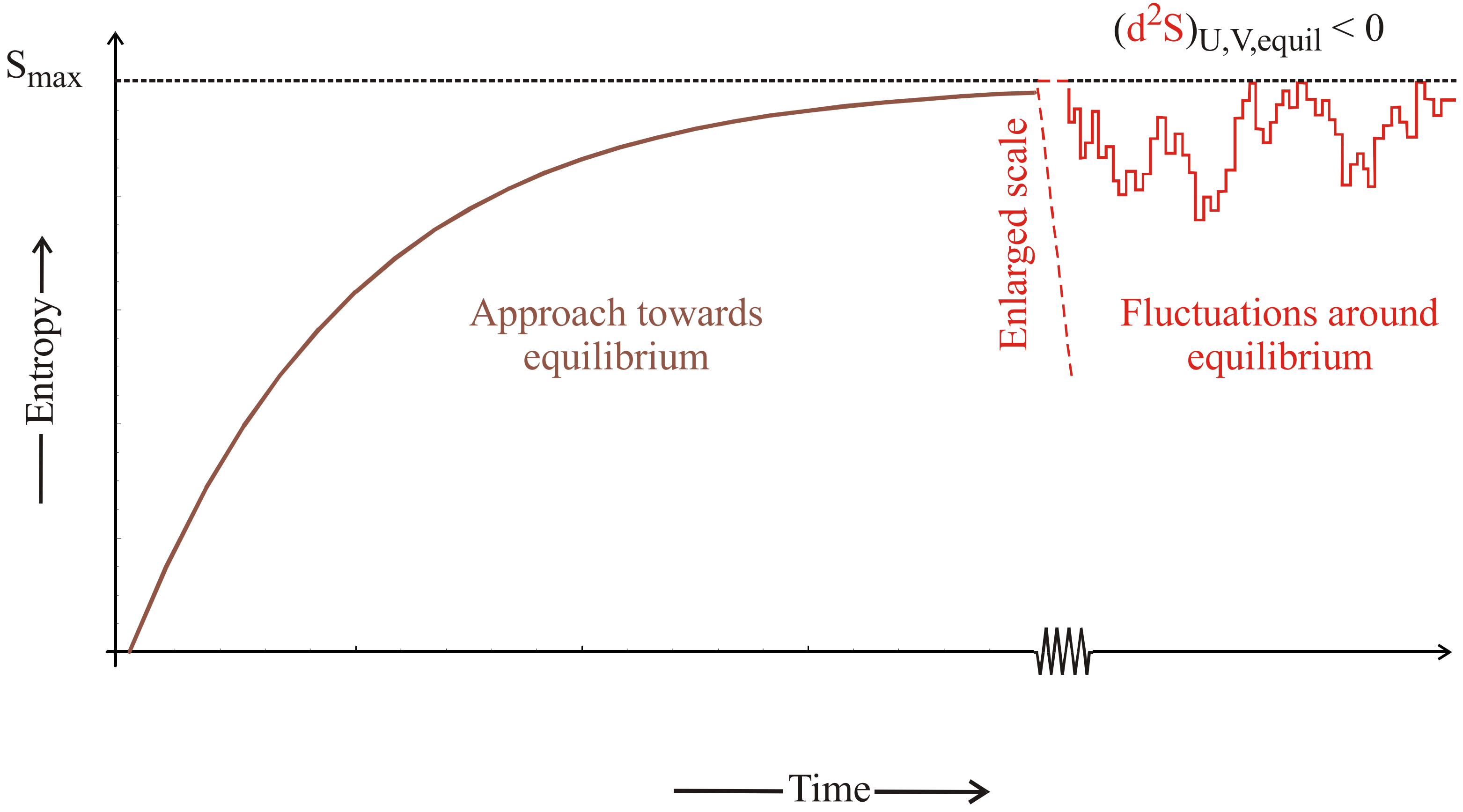
Open system

$dS = dS_{env} + dS \geq 0$

$dS = d_iS + d_eS$

$d_iS \geq 0$

Entropy changes in different thermodynamic systems

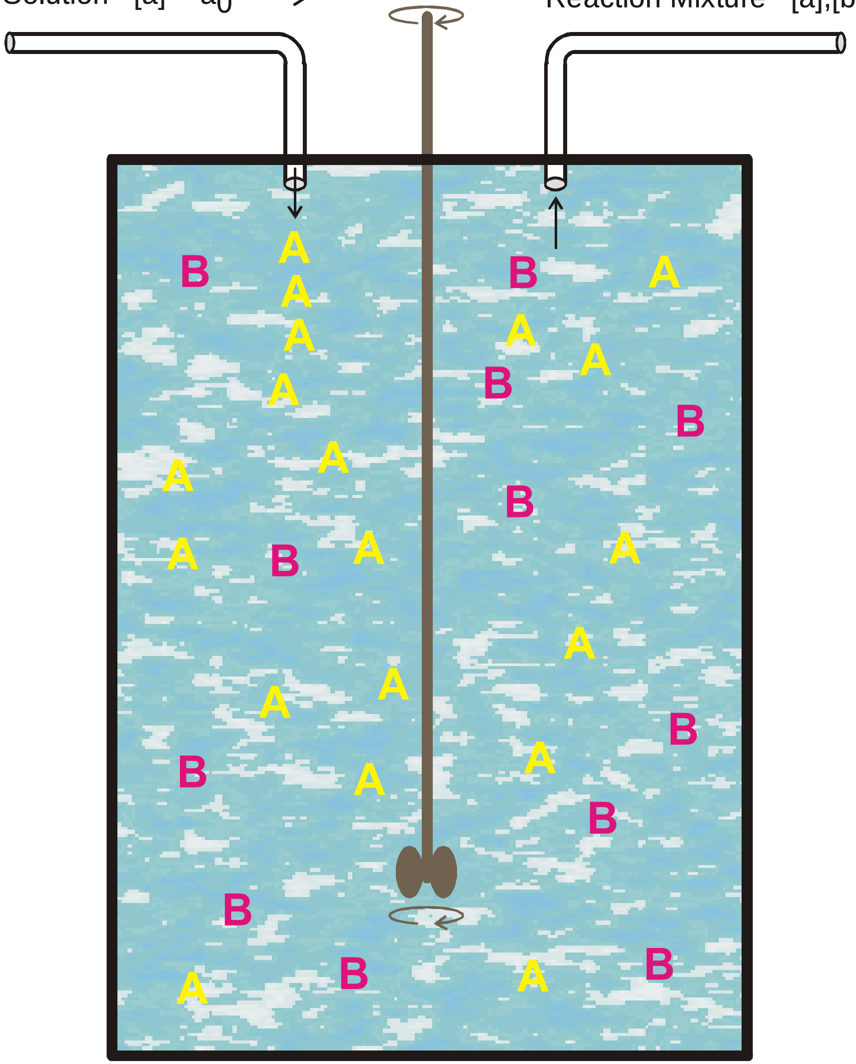


Entropy and fluctuations at equilibrium

Thermodynamics of closed systems:	Entropy is a non-decreasing function
Second law	$S(t) \rightarrow S_{max}$
Evolution of Populations:	Mean fitness is a non-decreasing function
Ronald Fisher's conjecture	$f(t) = S_k\, x_k(t)\, f_k \,/\, S_k\, x_k(t)\ \text{Á}\ f_{max}$

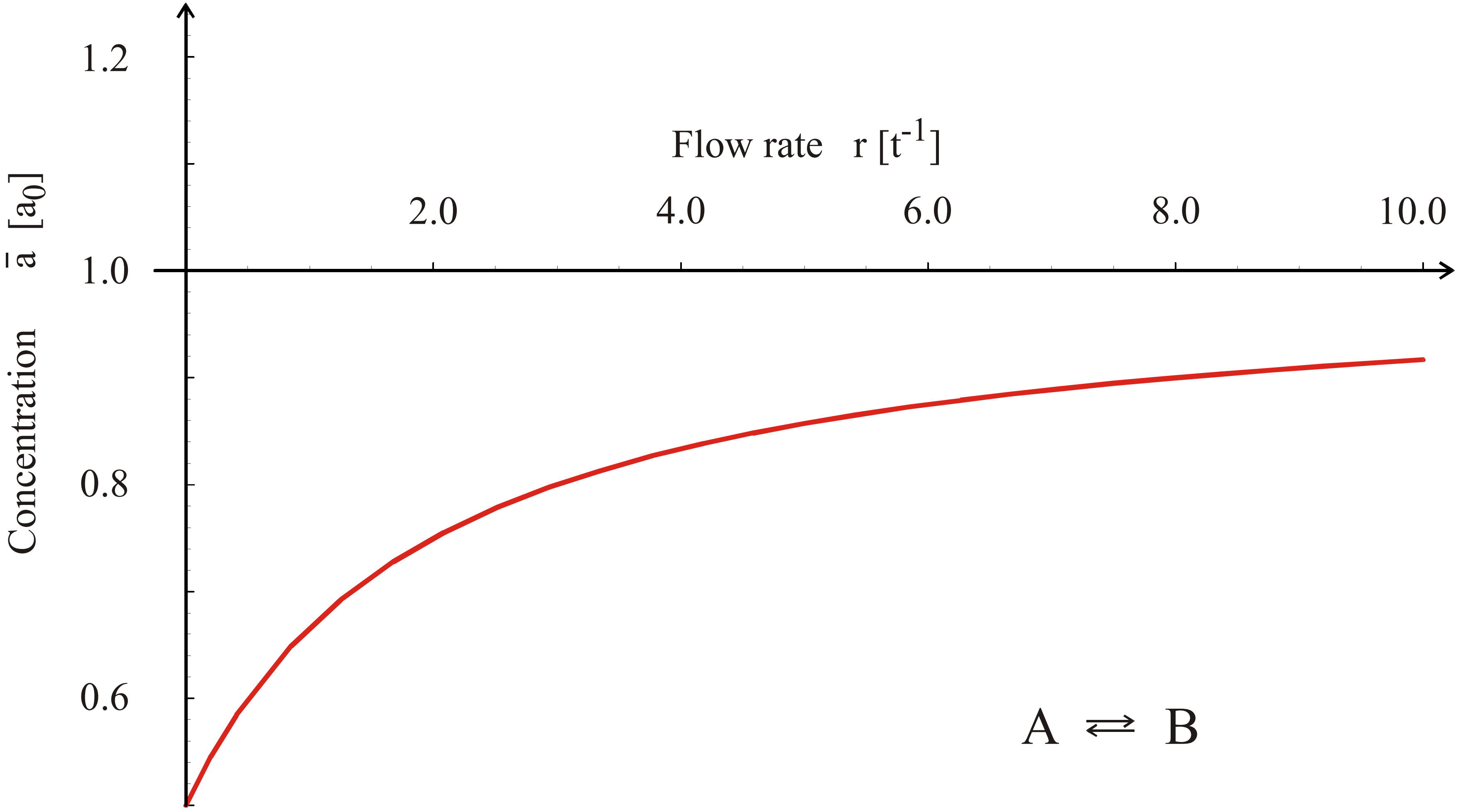
Stock Solution [a] = a_0 →

Reaction Mixture [a],[b] →

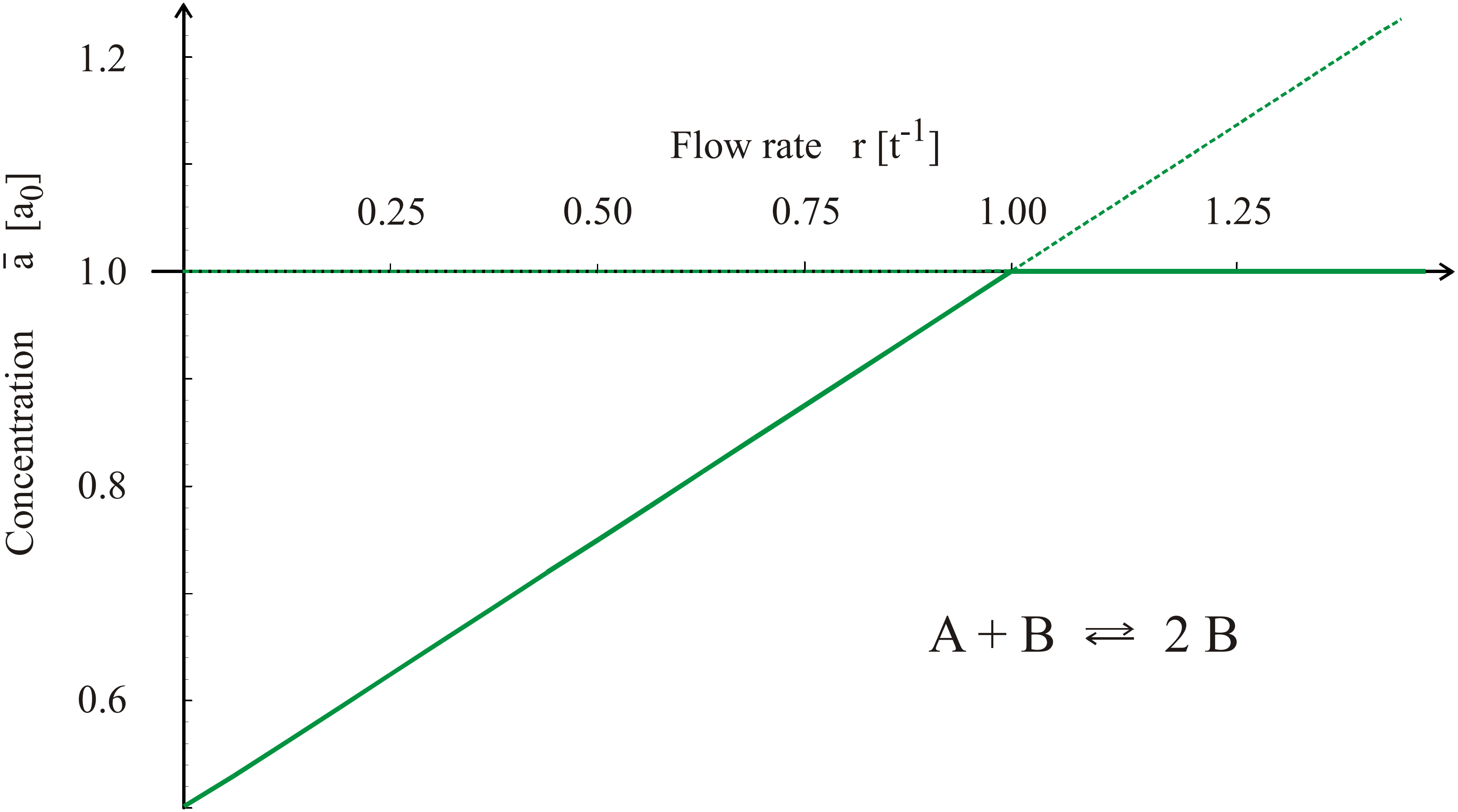


Flow rate $r = t_R^{-1}$

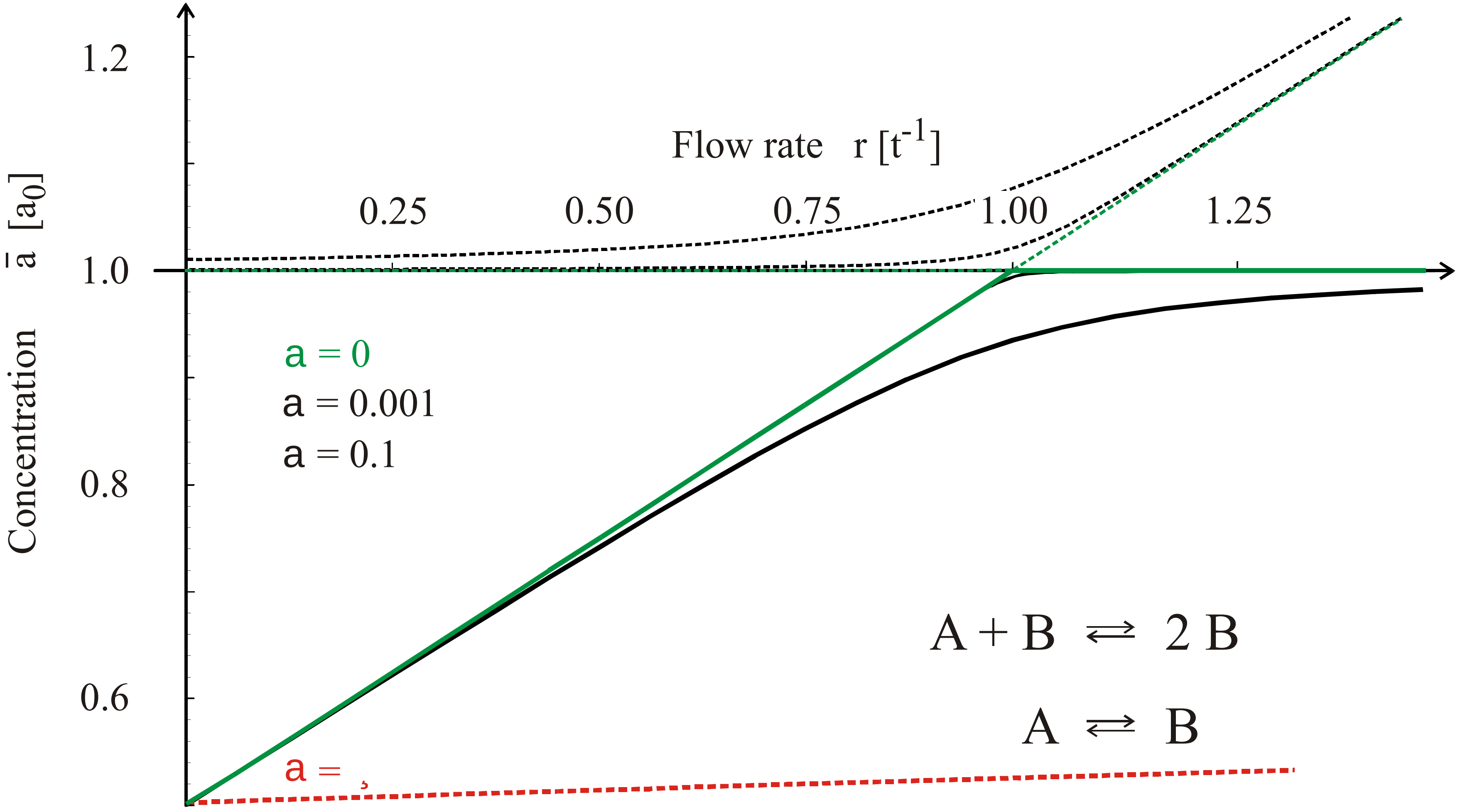
Reactions in the continuously stirred tank reactor (CSTR)



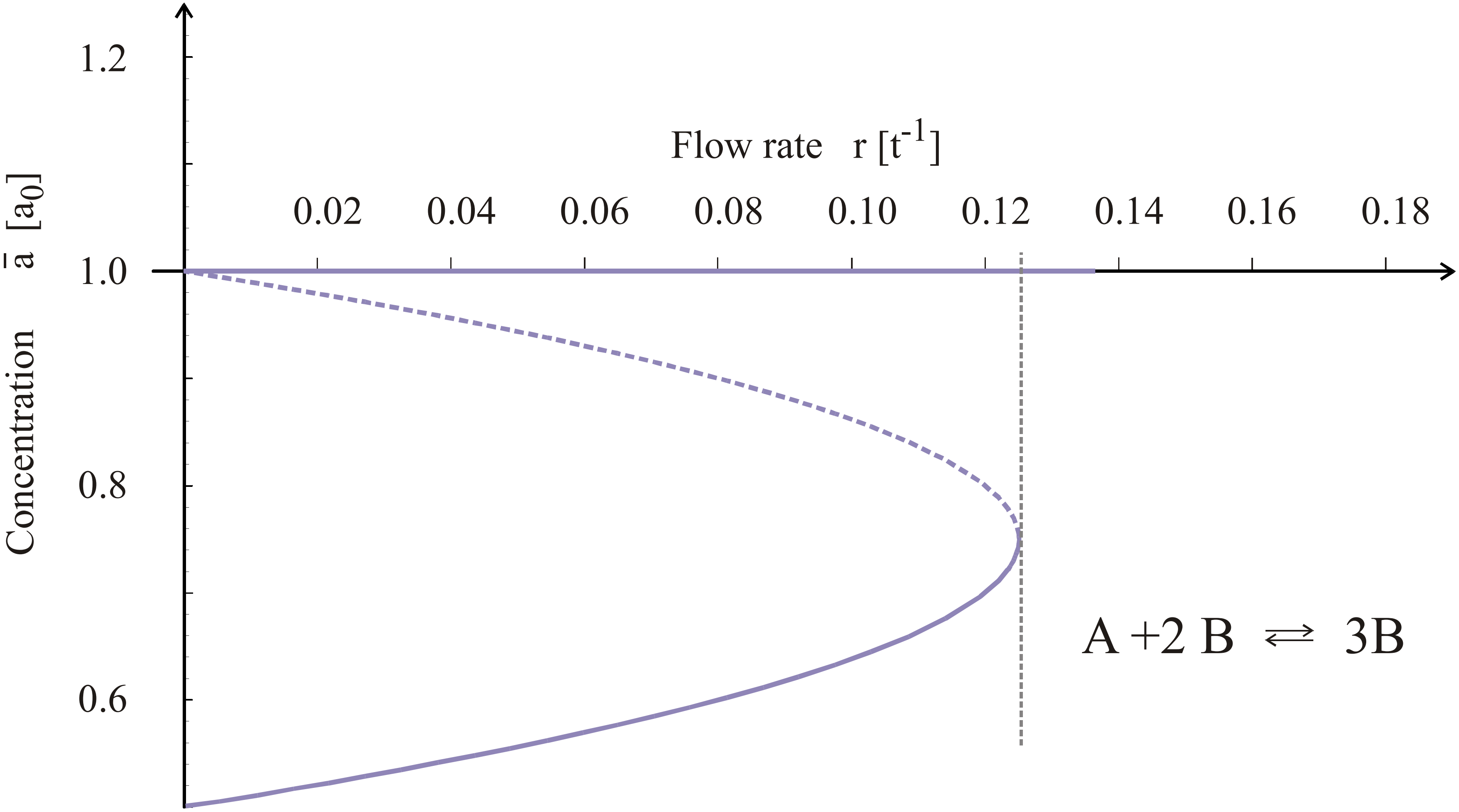
Reversible first order reaction in the flow reactor



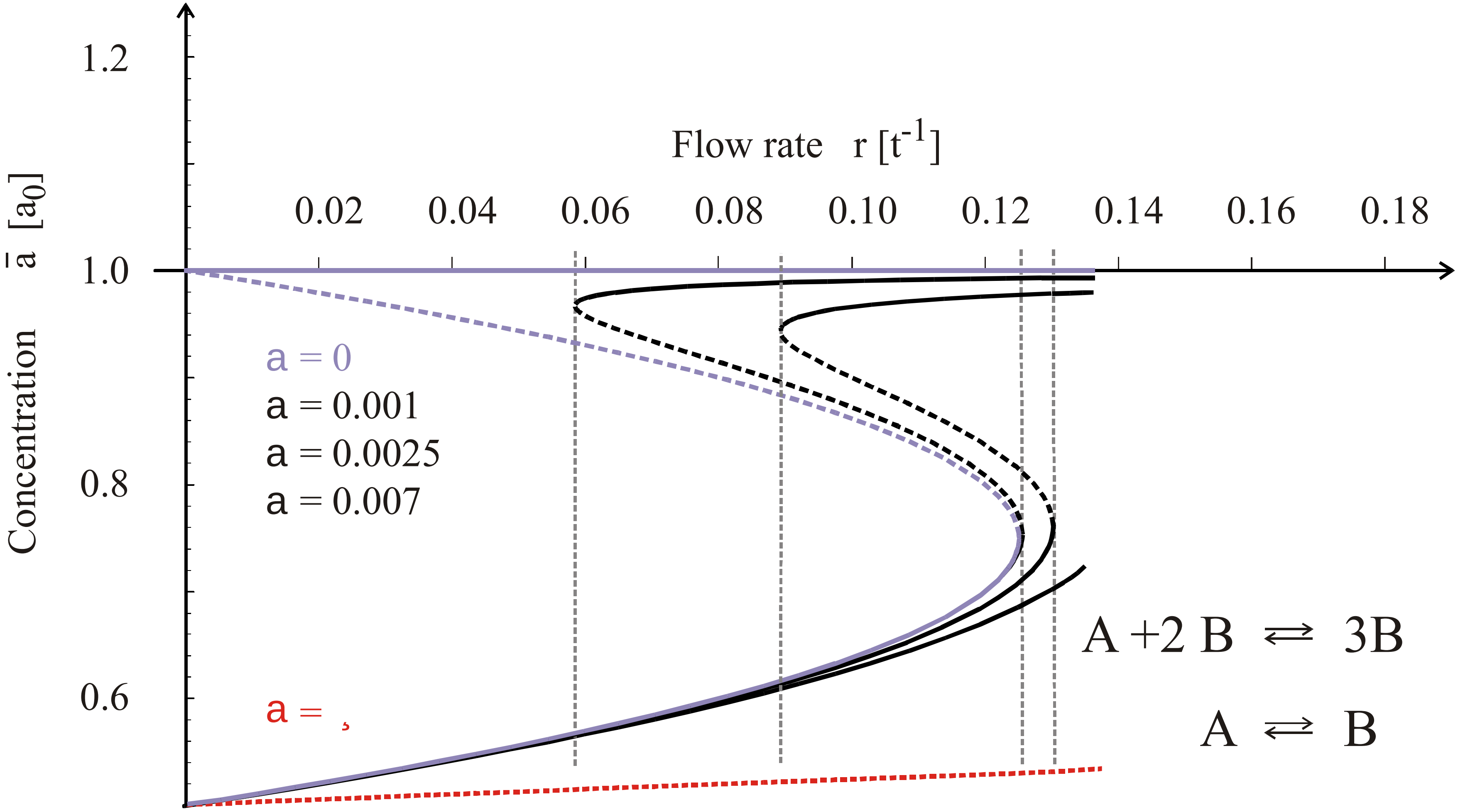
Autocatalytic second order reaction in the flow reactor



Autocatalytic second order and uncatalyzed reaction in the flow reactor



Autocatalytic third order reaction in the flow reactor



$A + 2B \rightleftarrows 3B$

$A \rightleftarrows B$

Autocatalytic third order and uncatalyzed reaction in the flow reactor

Autocatalytic third order reactions

Direct, $A + 2X \rightleftharpoons 3X$, or hidden in the reaction mechanism (Belousow-Zhabotinskii reaction).

Multiple steady states

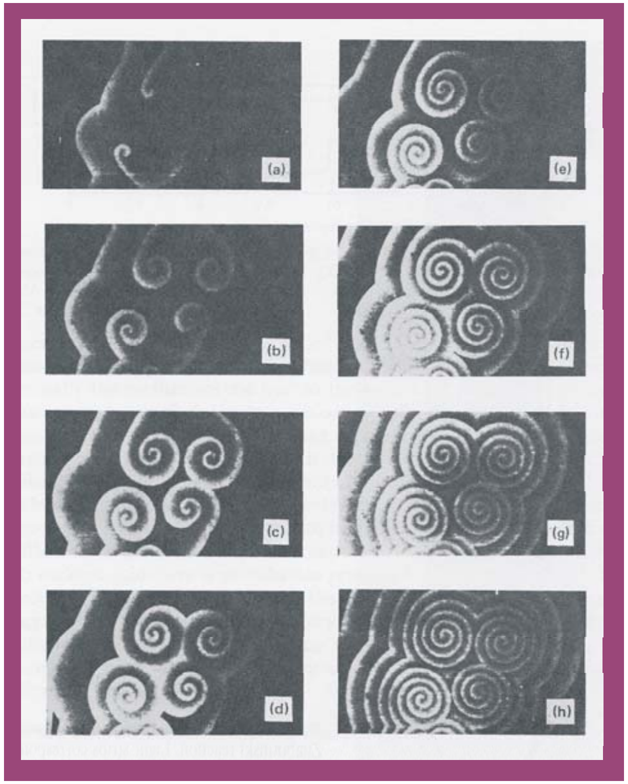
Oscillations in homogeneous solution

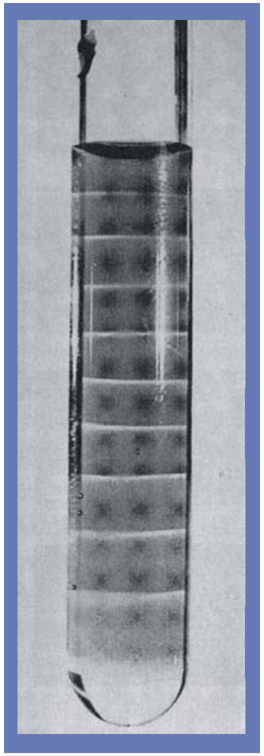
Deterministic chaos

Turing patterns

Spatiotemporal patterns (spirals)

Deterministic chaos in space and time





Pattern formation in autocatalytic third order reactions

G.Nicolis, I.Prigogine. *Self-Organization in Nonequilibrium Systems. From Dissipative Structures to Order through Fluctuations*. John Wiley, New York 1977

Autocatalytic second order reactions

Direct, $\mathbf{A + I \rightarrow 2\,I}$, or hidden in the reaction mechanism

Chemical self-enhancement

Combustion and chemistry of flames

Selection of laser modes

Selection of molecular or organismic species competing for common sources

Autocatalytic second order reaction as basis for selection processes.

The autocatalytic step is formally equivalent to replication or reproduction.

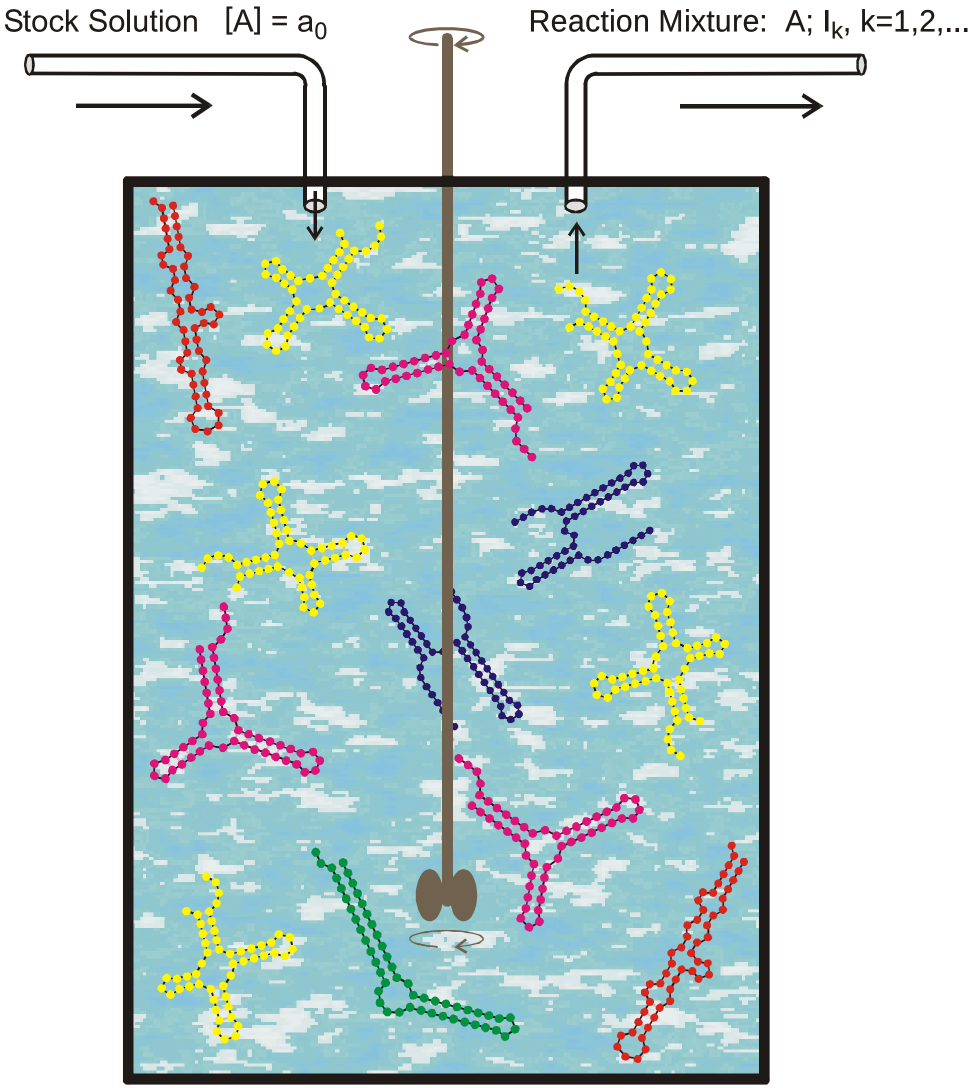
$$A + I_1 \underset{d_1}{\overset{k_1}{\rightleftharpoons}} 2\, I_1$$

$$A + I_2 \underset{d_2}{\overset{k_2}{\rightleftharpoons}} 2\, I_2$$

$$A + I_3 \underset{d_3}{\overset{k_3}{\rightleftharpoons}} 2\, I_3$$

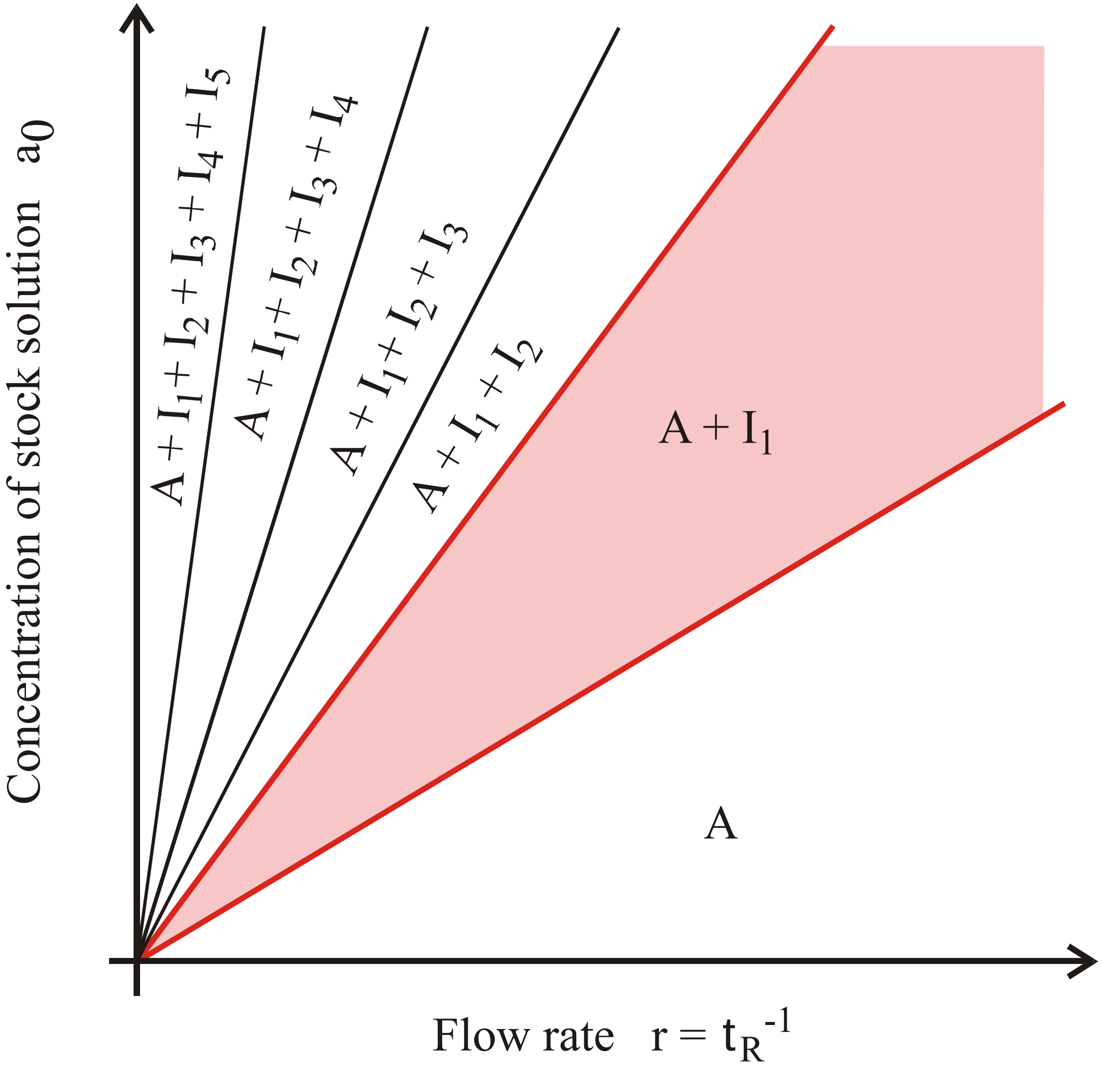
$$A + I_4 \underset{d_4}{\overset{k_4}{\rightleftharpoons}} 2\, I_4$$

$$A + I_5 \underset{d_5}{\overset{k_5}{\rightleftharpoons}} 2\, I_5$$



Replication in the flow reactor

P.Schuster & K.Sigmund, Dynamics of evolutionary optimization, *Ber.Bunsenges.Phys.Chem.* **89**: 668-682 (1985)



$A + I_1 \rightleftarrows 2\, I_1$

$A + I_2 \rightleftarrows 2\, I_2$

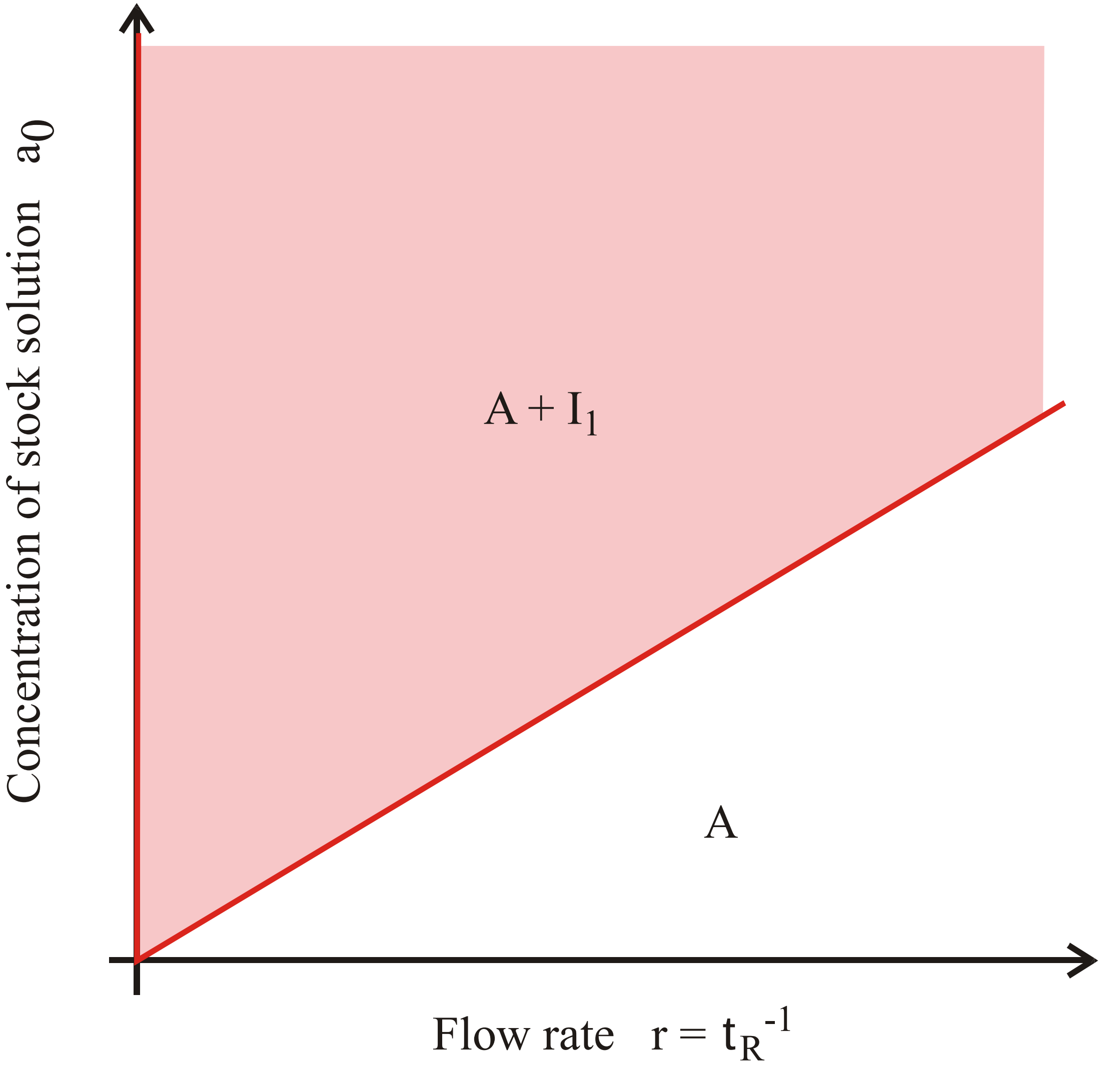
$A + I_3 \rightleftarrows 2\, I_3$

$A + I_4 \rightleftarrows 2\, I_4$

$A + I_5 \rightleftarrows 2\, I_5$

$k_1 > k_2 > k_3 > k_4 > k_5$

Selection in the flow reactor: Reversible replication reactions



$$A + I_1 \longrightarrow 2\,I_1$$

$$A + I_2 \longrightarrow 2\,I_2$$

$$A + I_3 \longrightarrow 2\,I_3$$

$$A + I_4 \longrightarrow 2\,I_4$$

$$A + I_5 \longrightarrow 2\,I_5$$

$$k_1 > k_2 > k_3 > k_4 > k_5$$

Selection in the flow reactor: Irreversible replication reactions

$$(A) + I_1 \xrightarrow[k_1]{} I_1 + I_1$$

$$(A) + I_2 \xrightarrow[k_2]{} I_2 + I_2$$

$$(A) + I_j \xrightarrow[k_j]{} I_j + I_j$$

$$(A) + I_m \xrightarrow[k_m]{} I_m + I_m$$

$$(A) + I_n \xrightarrow[k_n]{} I_n + I_n$$

$$dx_j / dt = \Sigma_i k_i x_i - x_j \Phi$$

$\Phi = \Sigma_i k_i x_i$; $\Sigma_i x_i = 1$

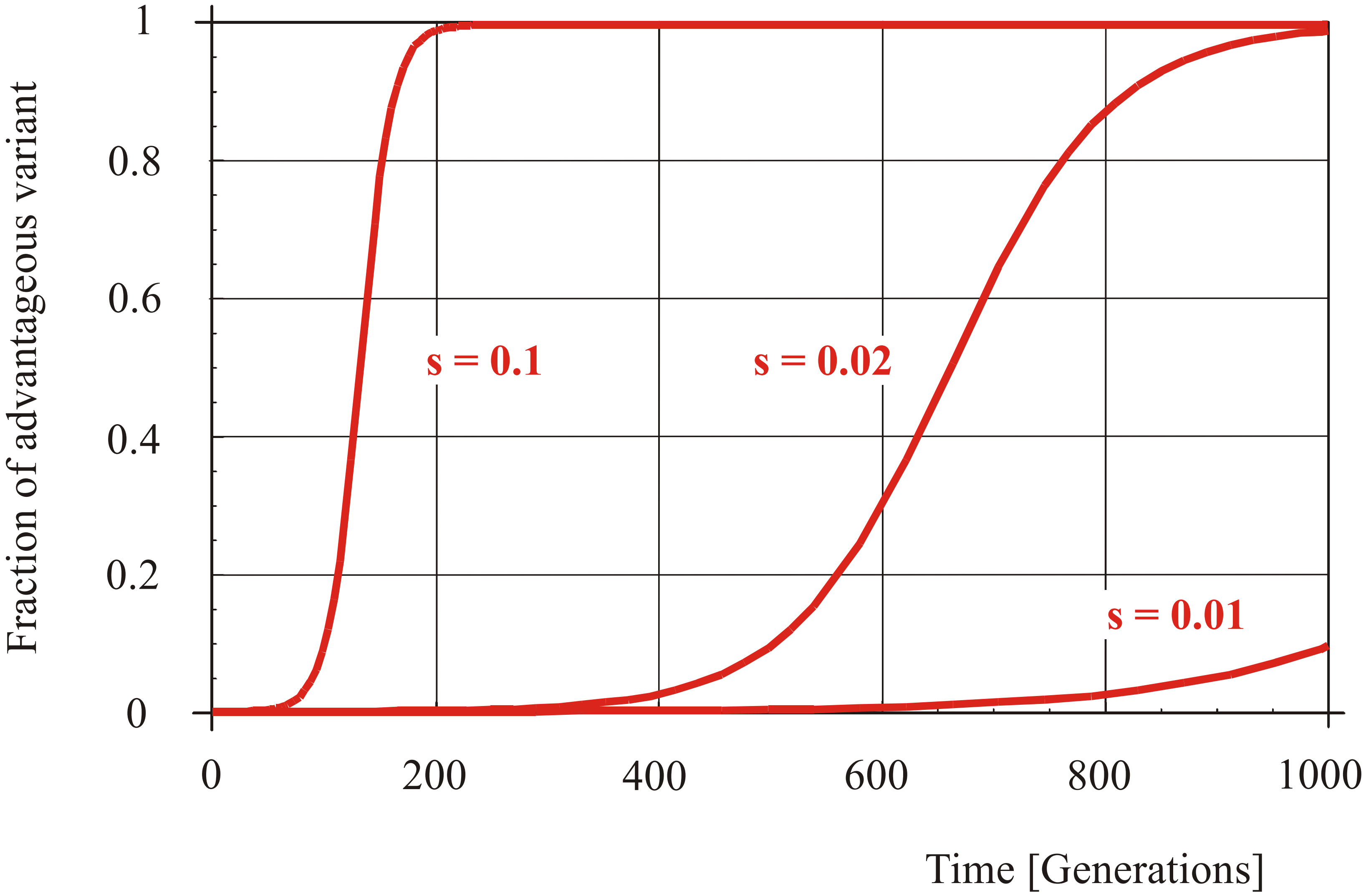
$[A] = a =$ constant

$k_m = \max \{k_j; j=1,2,...,n\}$

$x_m(t)$ Á 1 for t Á ¸

$s = (k_{m+1} - k_m)/k_m$

Selection of the „fittest“ or fastest replicating species



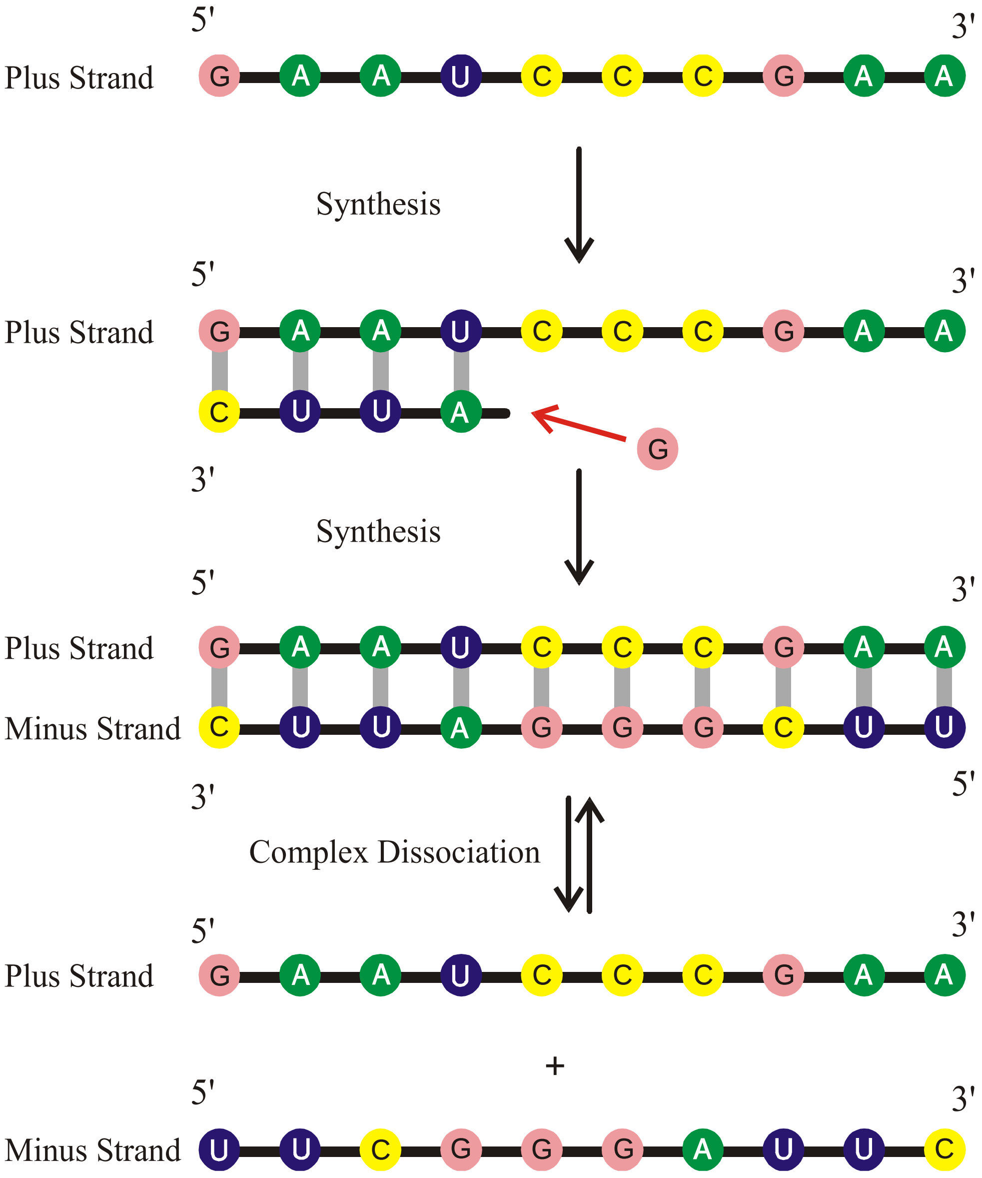
Selection of advantageous mutants in populations of N = 10 000 individuals

4^{27} = 1.801 Ç 10^{16} possible different sequences

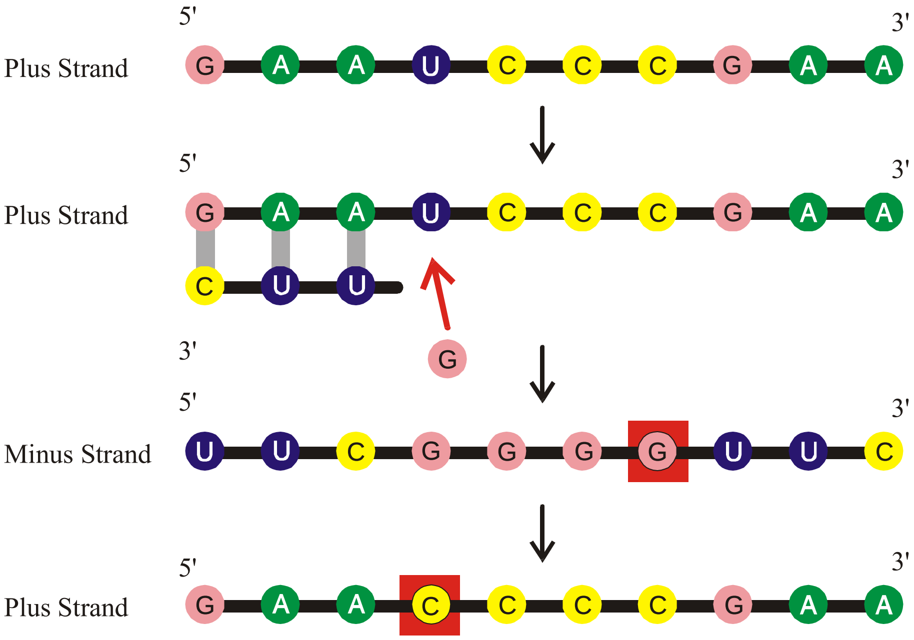
Combinatorial diversity of sequences: $N = 4^{\{}$

A = adenylate
U = uridylate
C = cytidylate
G = guanylate

Combinatorial diversity of heteropolymers illustrated by means of an RNA aptamer that binds to the antibiotic tobramycin



Complementary replication as the simplest copying mechanism of RNA



Point Mutation

GAAUCCCGAA → GAAUCCCGUCCCGAA

Insertion

GAAUCCCGAA → GAAUCCA

Deletion

Mutations represent the mechanism of variation in nucleic acids

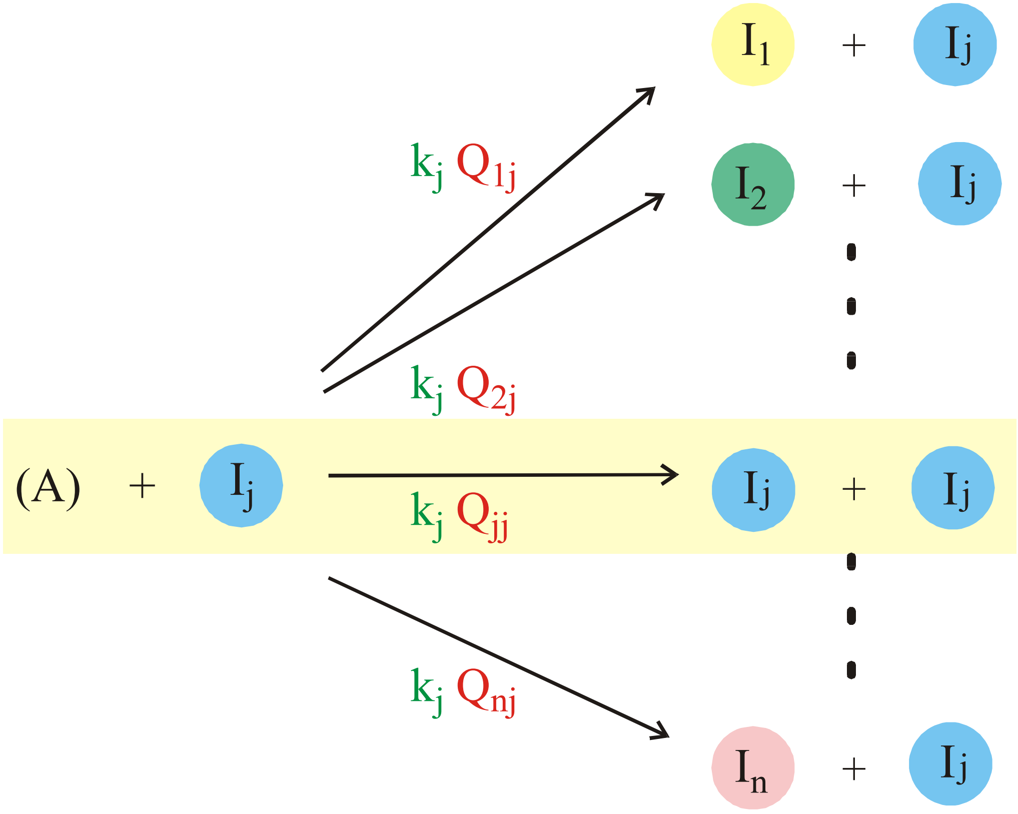
$$dx_j / dt = \Sigma_i k_i Q_{ji} x_i - x_j \Phi$$

$$\Phi = \Sigma_i k_i x_i \; ; \quad \Sigma_i x_i = 1 \; ; \quad \sum_i Q_{ij} = 1$$

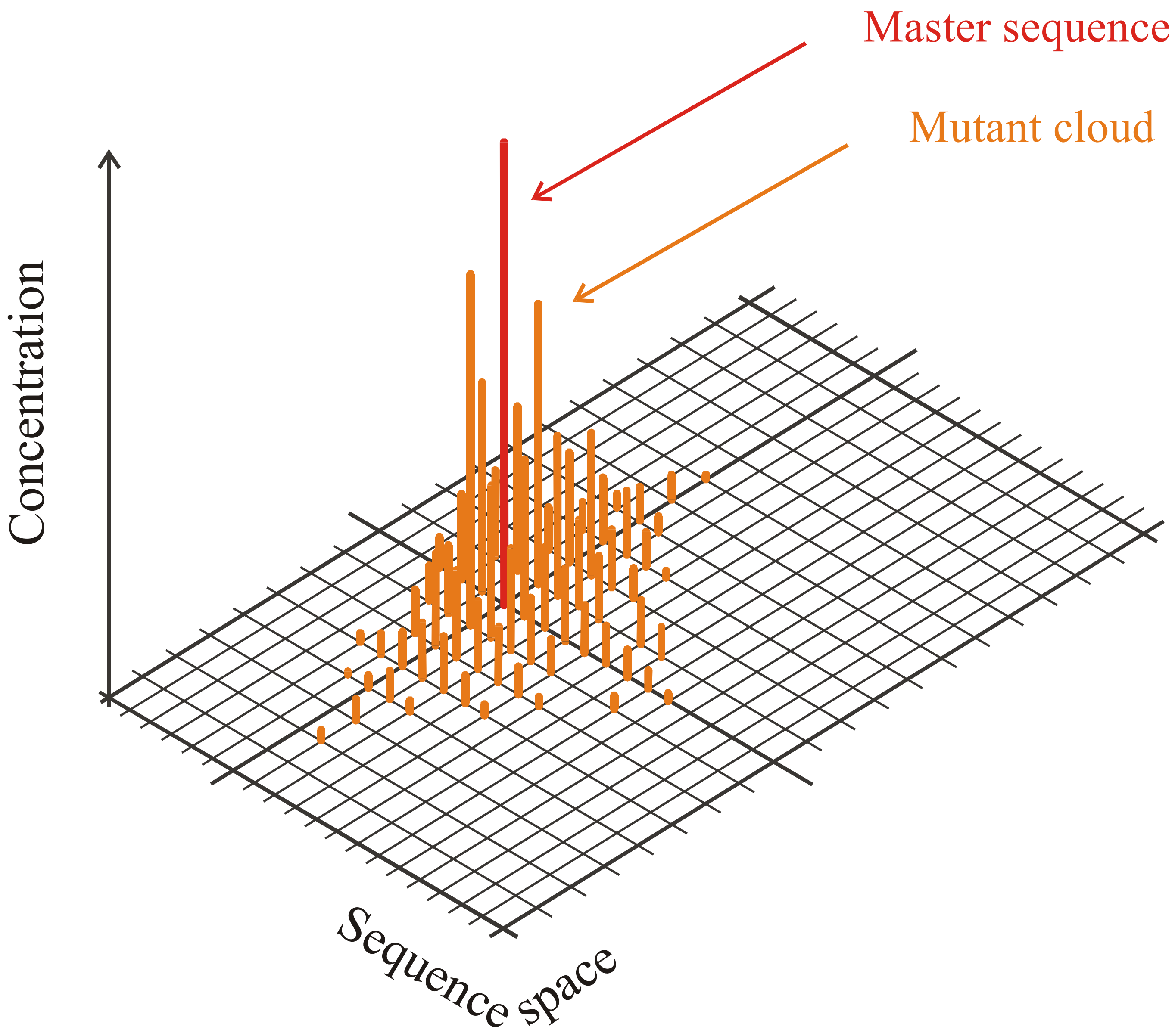
$$Q_{ij} = (1-p)^{n-d(i,j)} p^{d(i,j)}$$

p .... Error rate per digit

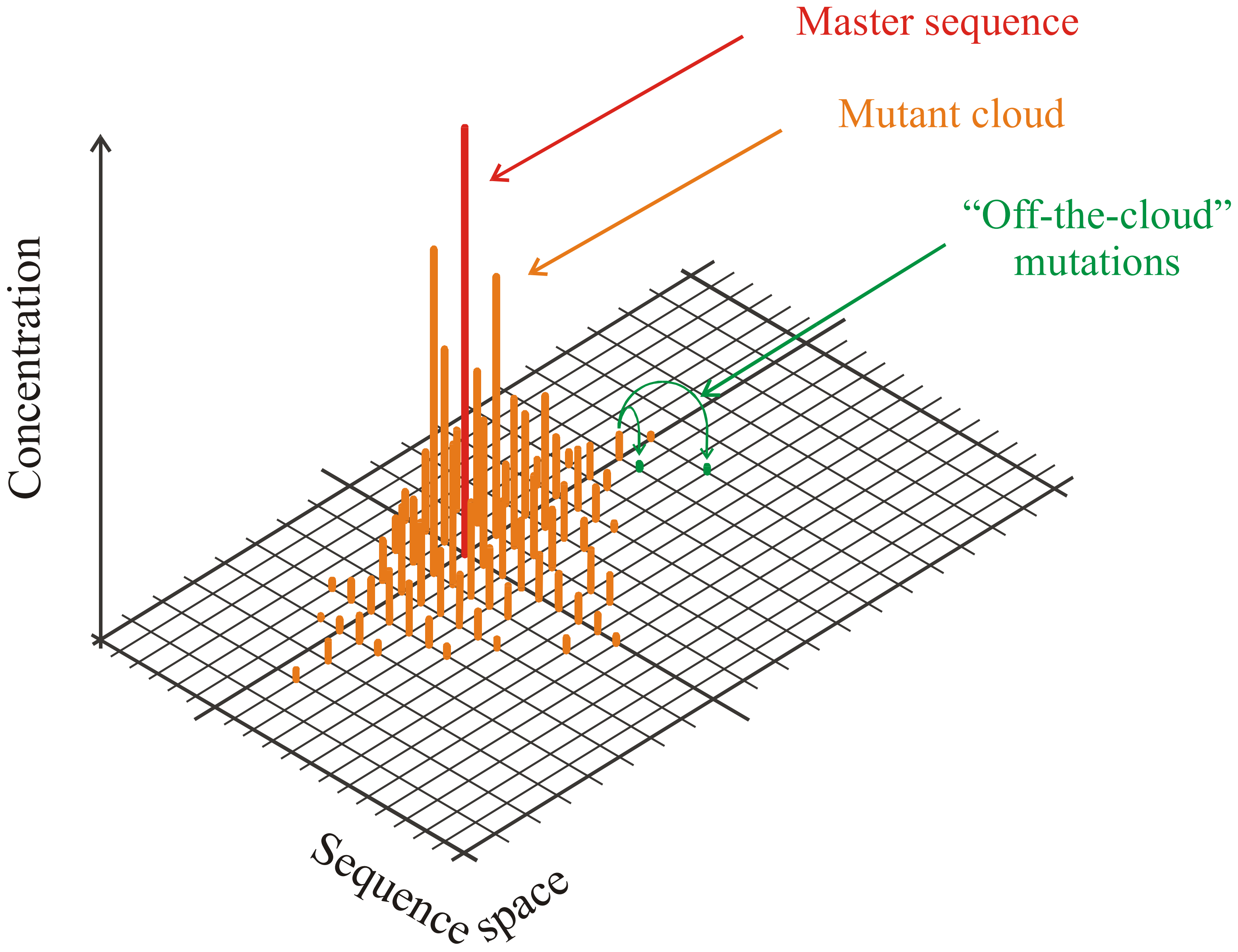
d(i,j) .... Hamming distance between I_i and I_j



Chemical kinetics of replication and mutation



The molecular quasispecies in sequence space



The molecular quasispecies and mutations producing new variants

Ronald Fisher‘s conjecture does not hold in general for **replication-mutation systems**: In general evolutionary dynamics the mean fitness of populations may also decrease monotonously or even go through a maximum or minimum. It does also not hold in general for **recombination of many alleles** and general multi-locus systems in population genetics.

Optimization of fitness is, nevertheless, fulfilled in most cases, and can be understood as a useful heuristic.

Optimization of RNA molecules *in silico*

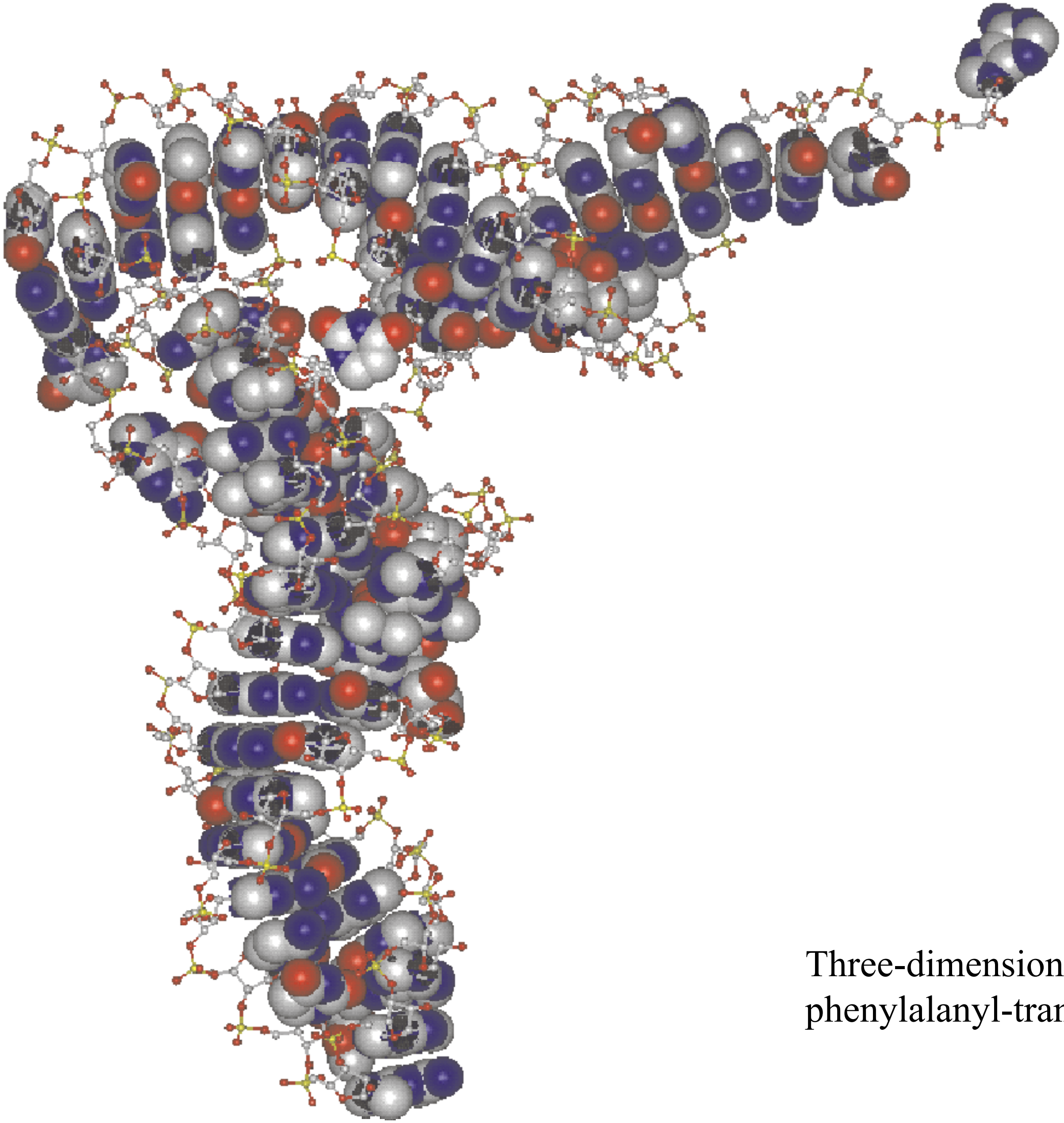
W.Fontana, P.Schuster, ***A computer model of evolutionary optimization***. Biophysical Chemistry **26** (1987), 123-147

W.Fontana, W.Schnabl, P.Schuster, ***Physical aspects of evolutionary optimization and adaptation***. Phys.Rev.A **40** (1989), 3301-3321

M.A.Huynen, W.Fontana, P.F.Stadler, ***Smoothness within ruggedness. The role of neutrality in adaptation***. Proc.Natl.Acad.Sci.USA **93** (1996), 397-401

W.Fontana, P.Schuster, ***Continuity in evolution. On the nature of transitions***. Science **280** (1998), 1451-1455

W.Fontana, P.Schuster, ***Shaping space. The possible and the attainable in RNA genotype-phenotype mapping***. J.Theor.Biol. **194** (1998), 491-515

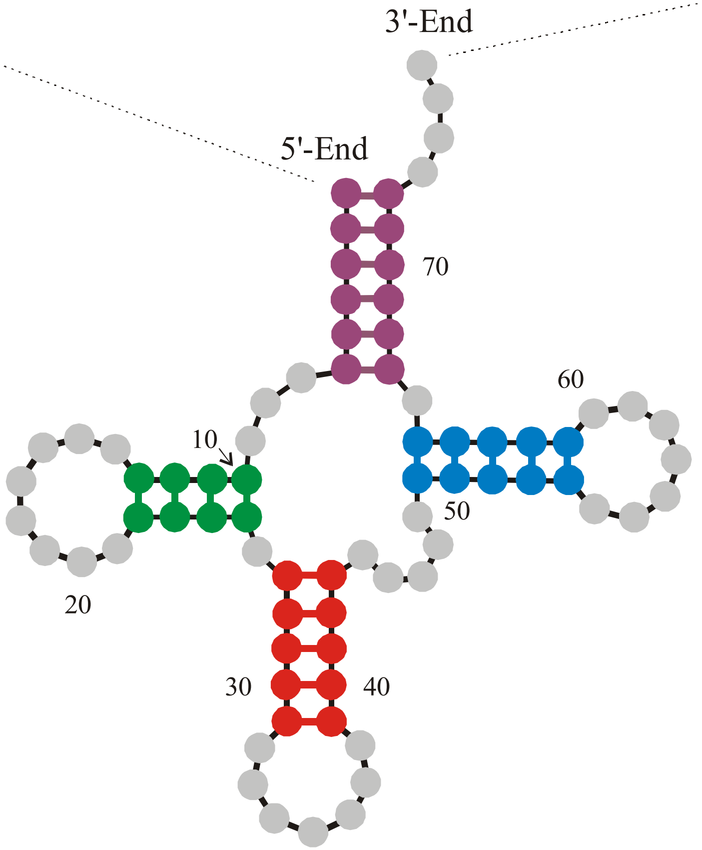


Three-dimensional structure of
phenylalanyl-transfer-RNA

5'-End 3'-End

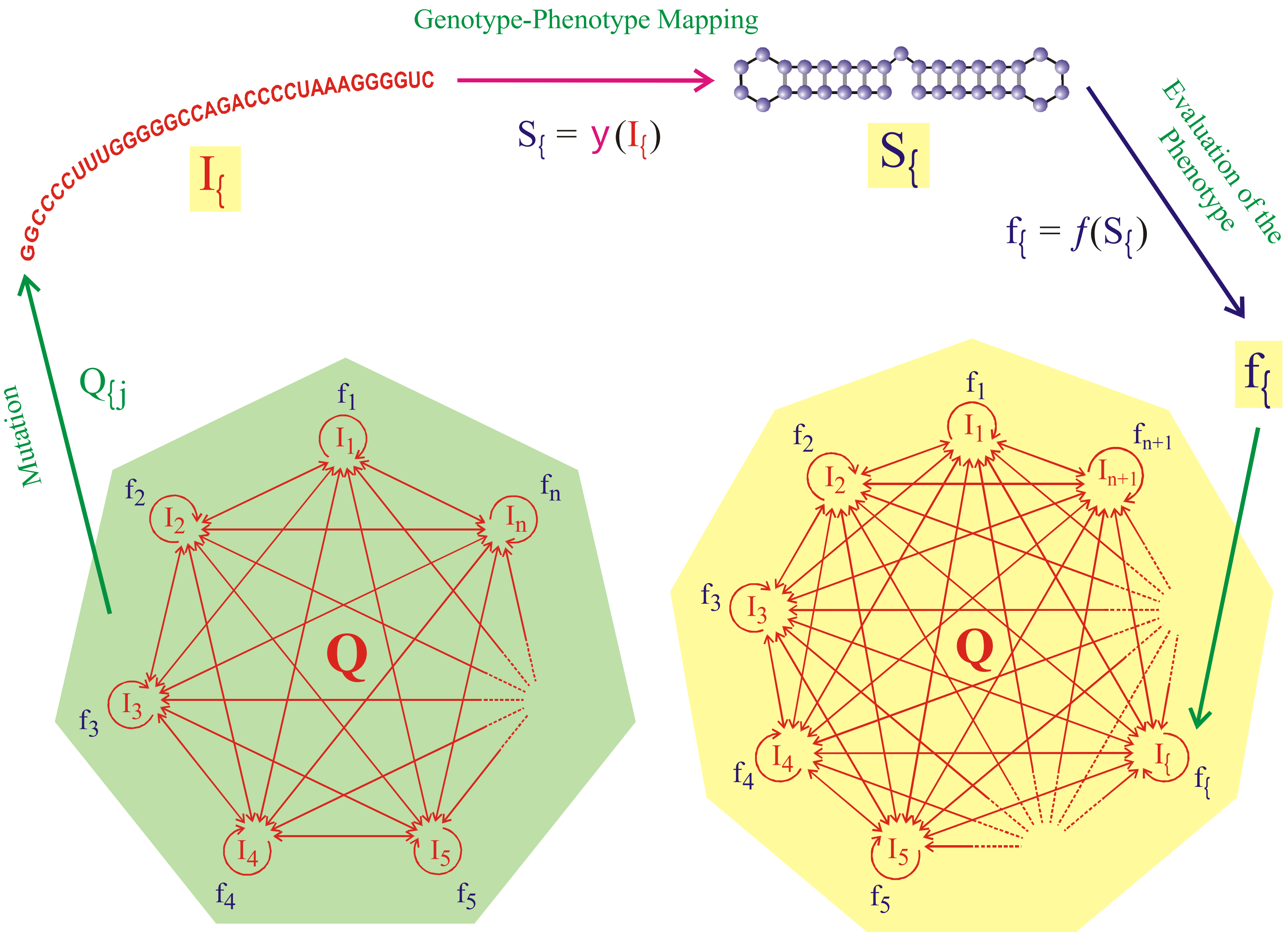
Sequence GCGGAUUUAGCUCAGDDGGGAGAGCMCCAGACUGAAYAUCUGGAGMUCCUGUGTPCGAUCCACAGAAUUCGCACCA

Secondary Structure



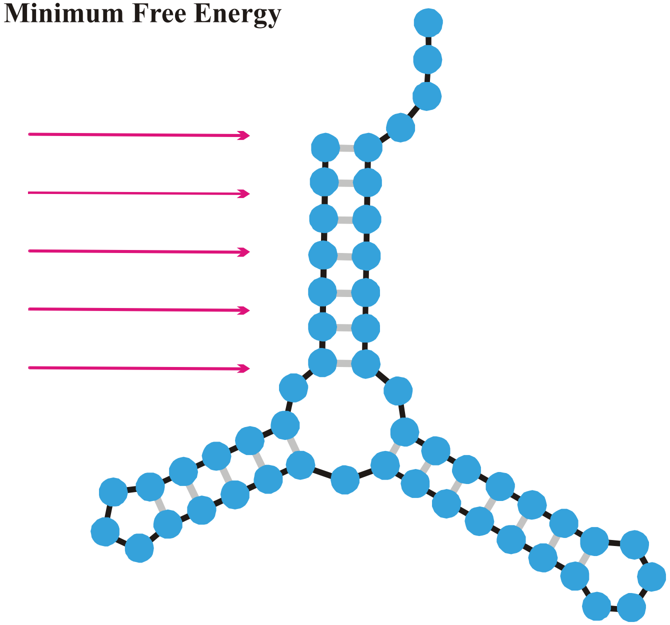
Symbolic Notation 5'-End ((((((···((((········))))·(((((·······)))))·····(((((·······)))))·))))))···· 3'-End

Definition and formation of the secondary structure of phenylalanyl-tRNA



Evolutionary dynamics
including molecular phenotypes

Criterion of
Minimum Free Energy



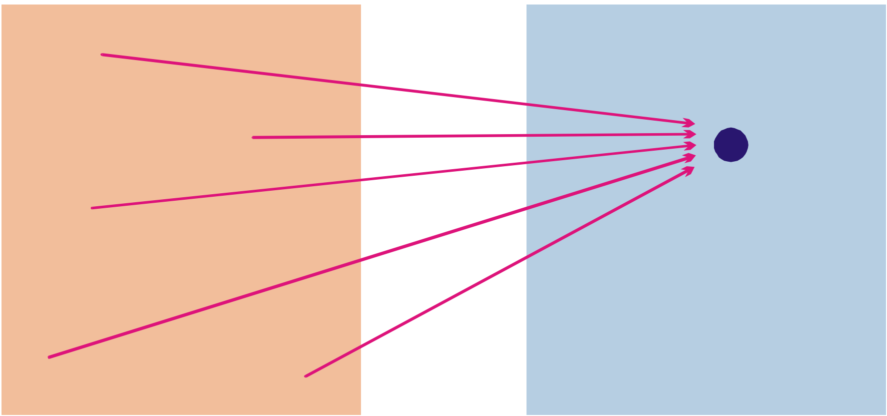
UUUAGCCAGCGCGAGUCGUGCGGACGGGGUUAUCUCUGUCGGGCUAGGGCGC

GUGAGCGCGGGGCACAGUUUCUCAAGGAUGUAAGUUUUUGCCGUUUAUCUGG

UUAGCGAGAGAGGAGGCUUCUAGACCCAGCUCUCUGGGUCGUUGCUGAUGCG

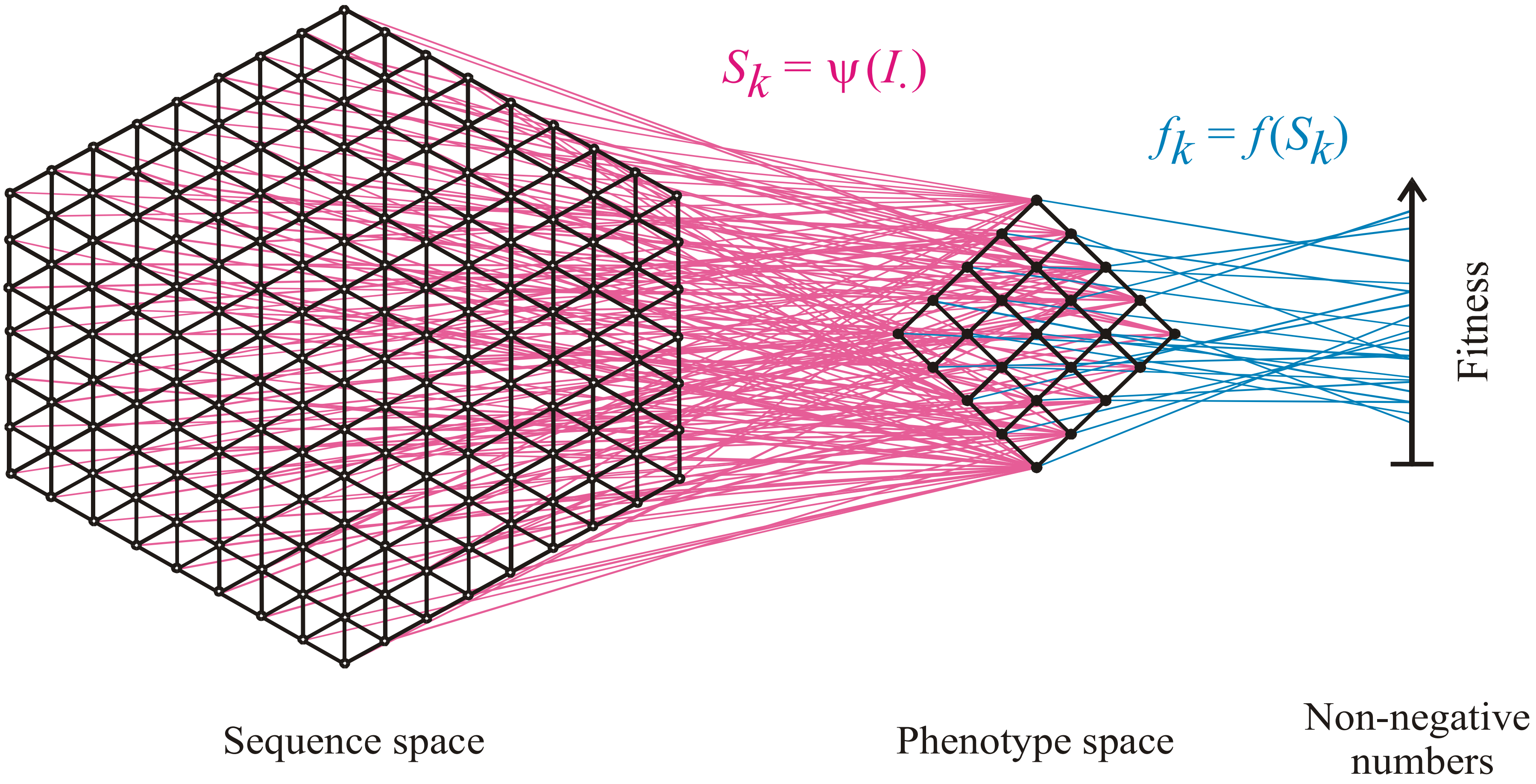
CAUUGGUGCUAAUGAUAUUAGGGCUGUAUUCCUGUAUAGCGAUCAGUGUCCG

GUAGGCCCUCUUGACAUAAGAUUUUUCCAAUGGUGGGAGAUGGCCAUUGCAG

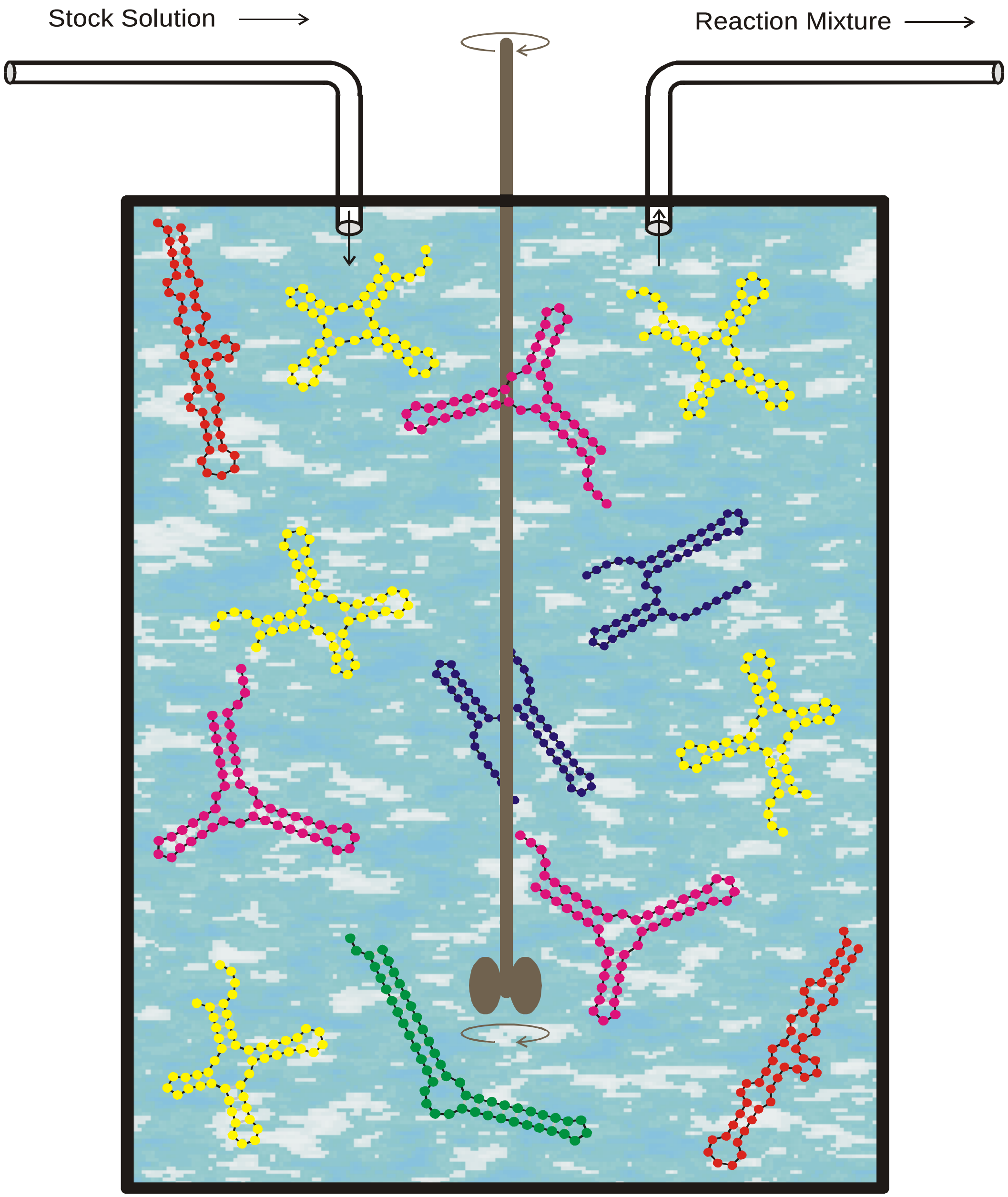


Sequence Space

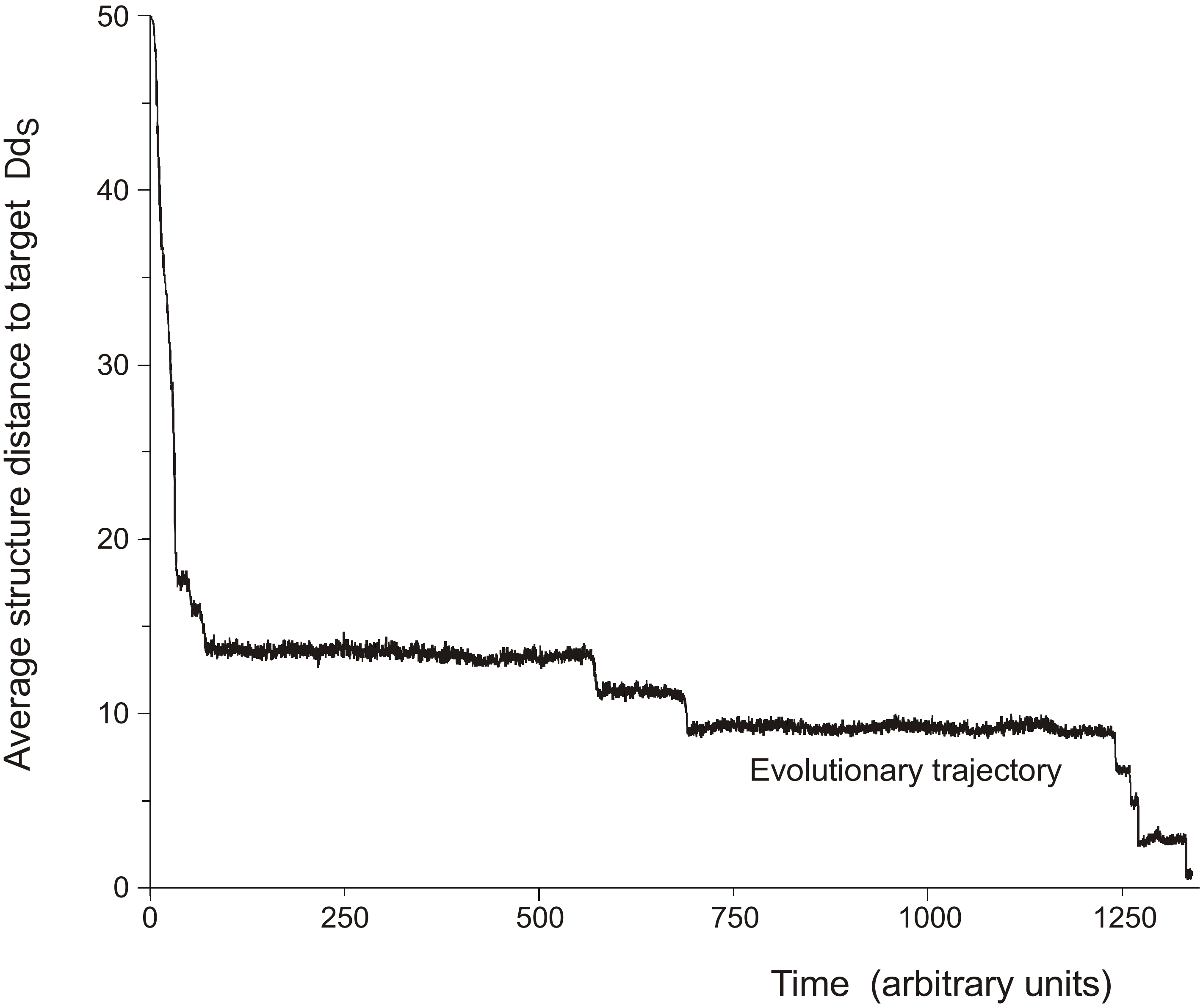
Shape Space



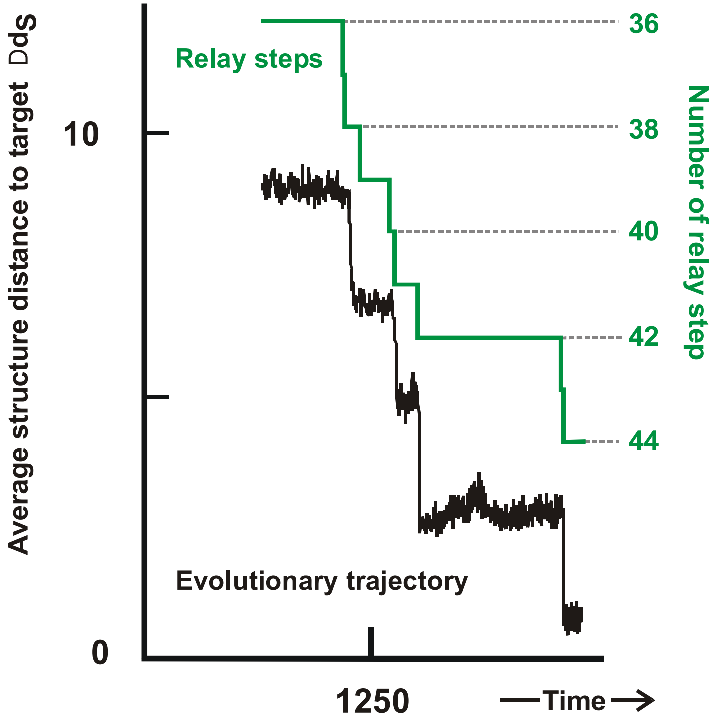
Mapping from sequence space into phenotype space and into fitness values

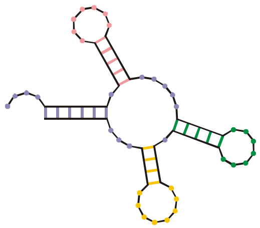


The flowreactor as a device for studies of evolution ***in vitro*** and ***in silico***



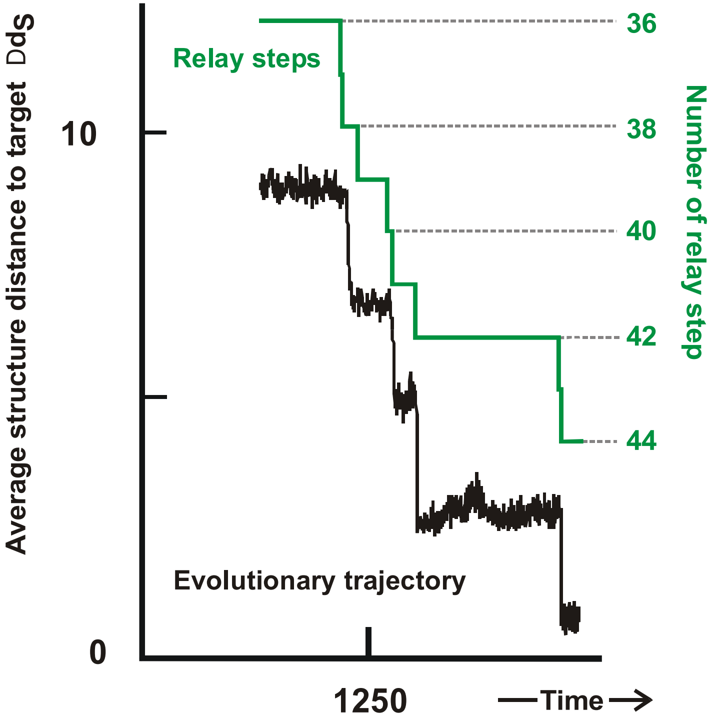
In silico optimization in the flow reactor: Trajectory

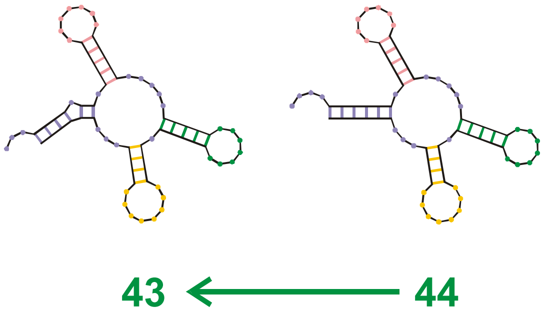




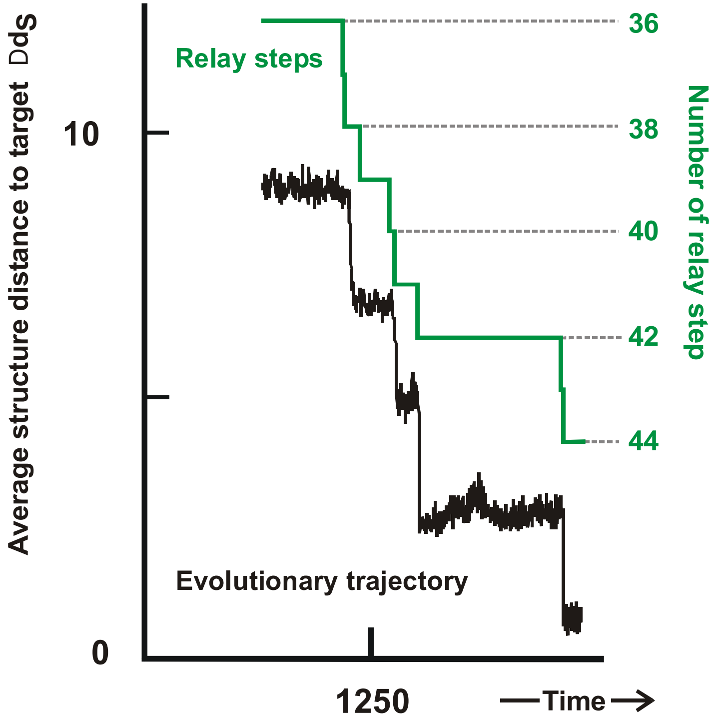
44

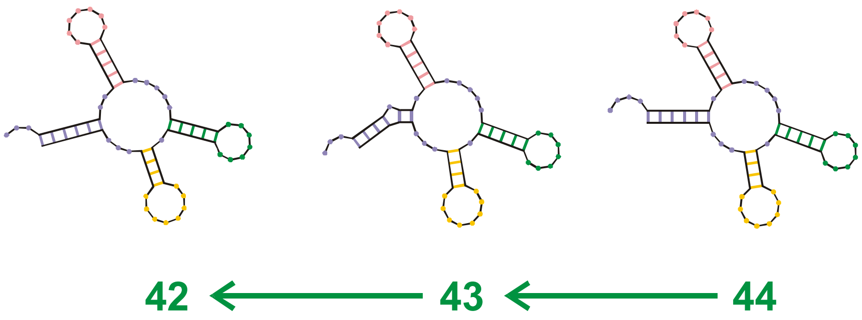
Endconformation of optimization



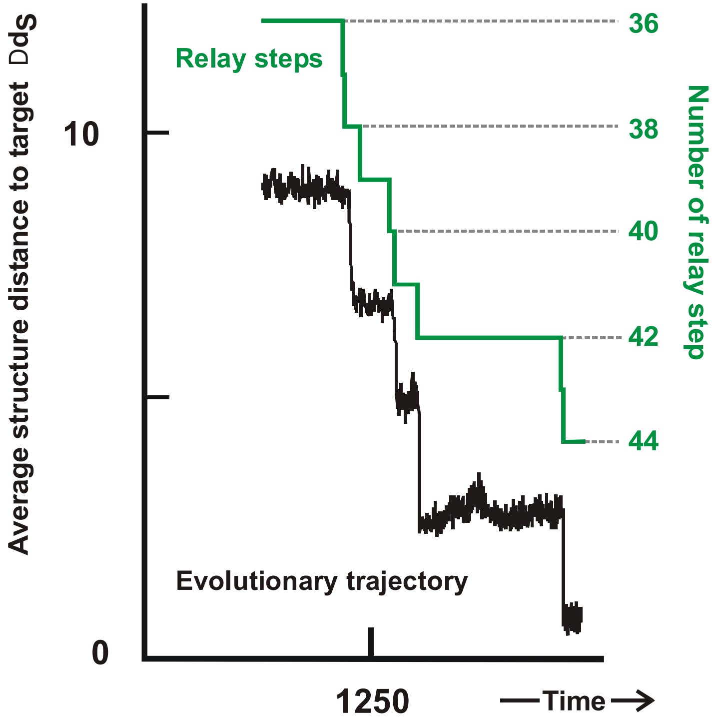


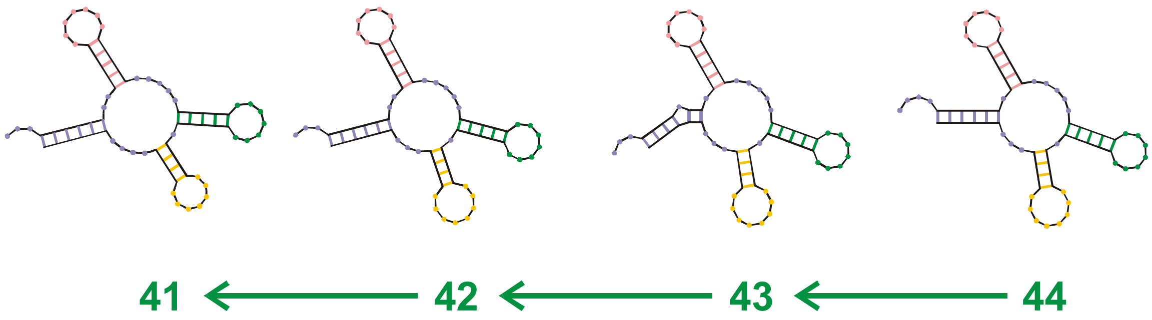
Reconstruction of the last step 43 Á 44



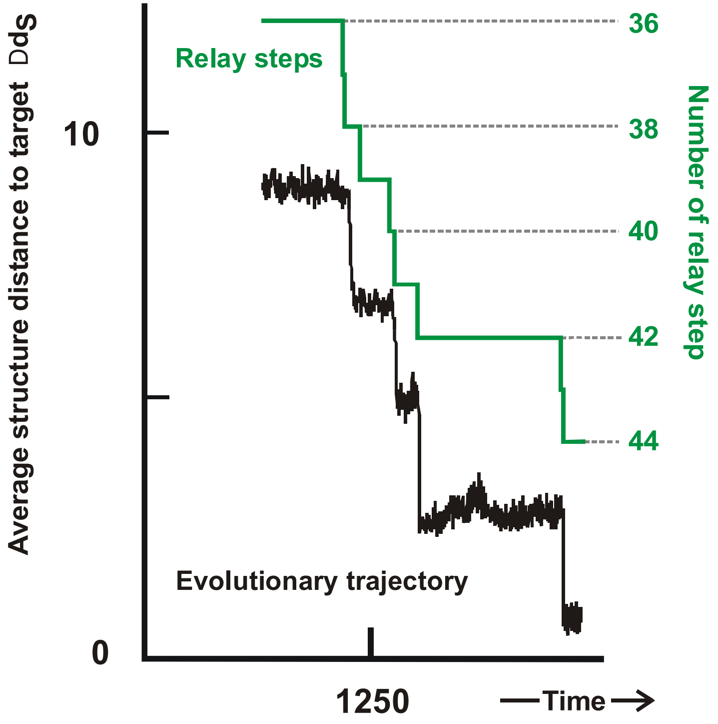


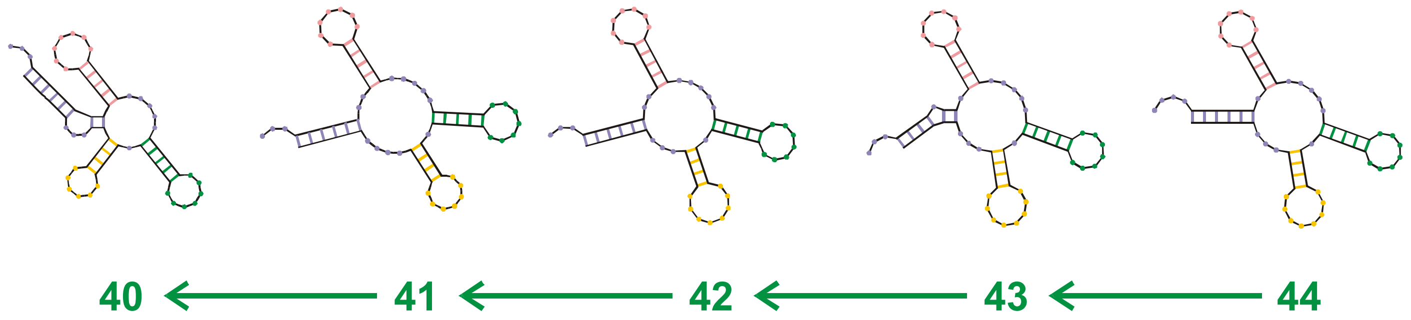
Reconstruction of last-but-one step 42 Á 43 (Á 44)



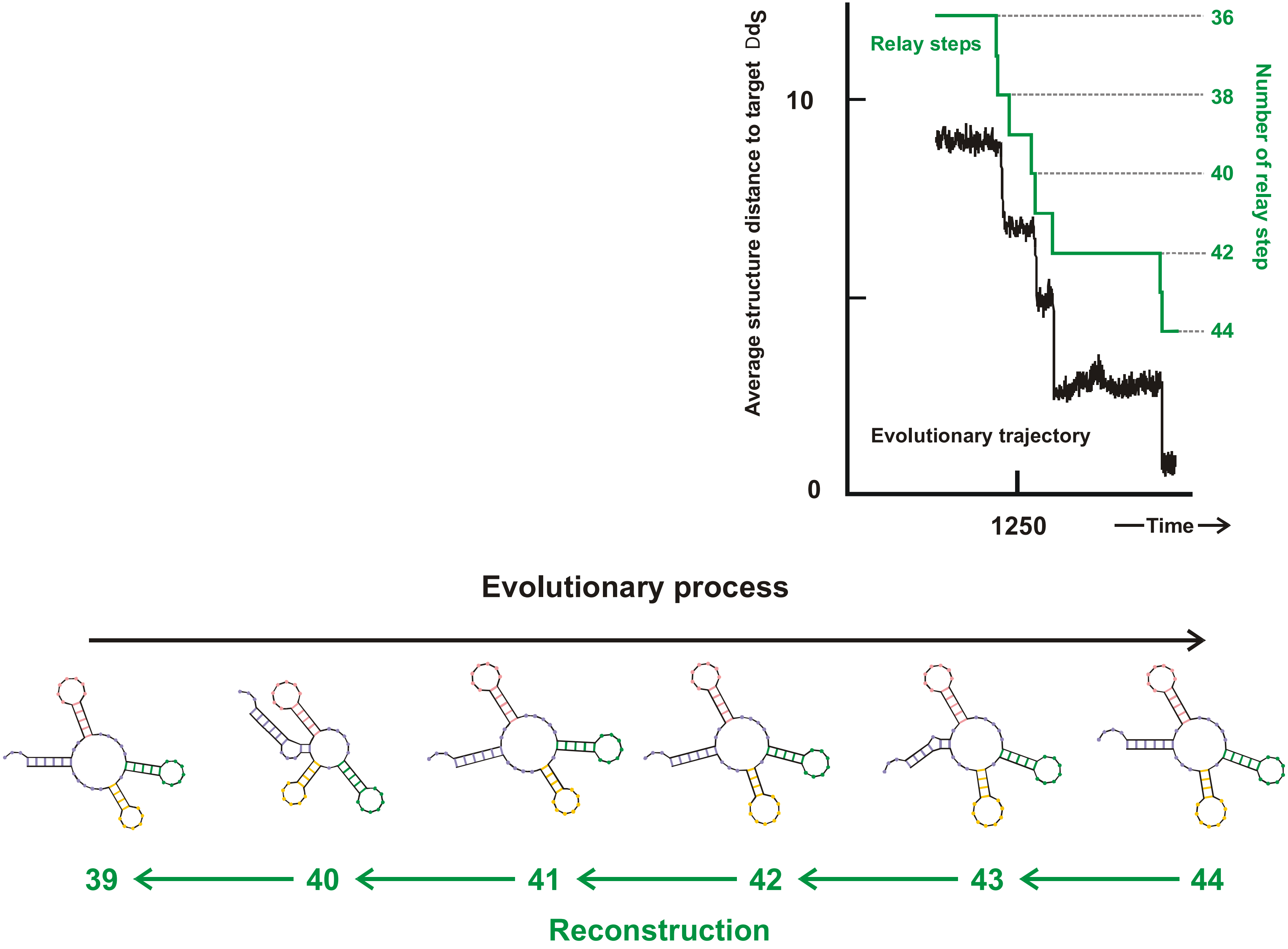


Reconstruction of step 41 Á 42 (Á 43 Á 44)

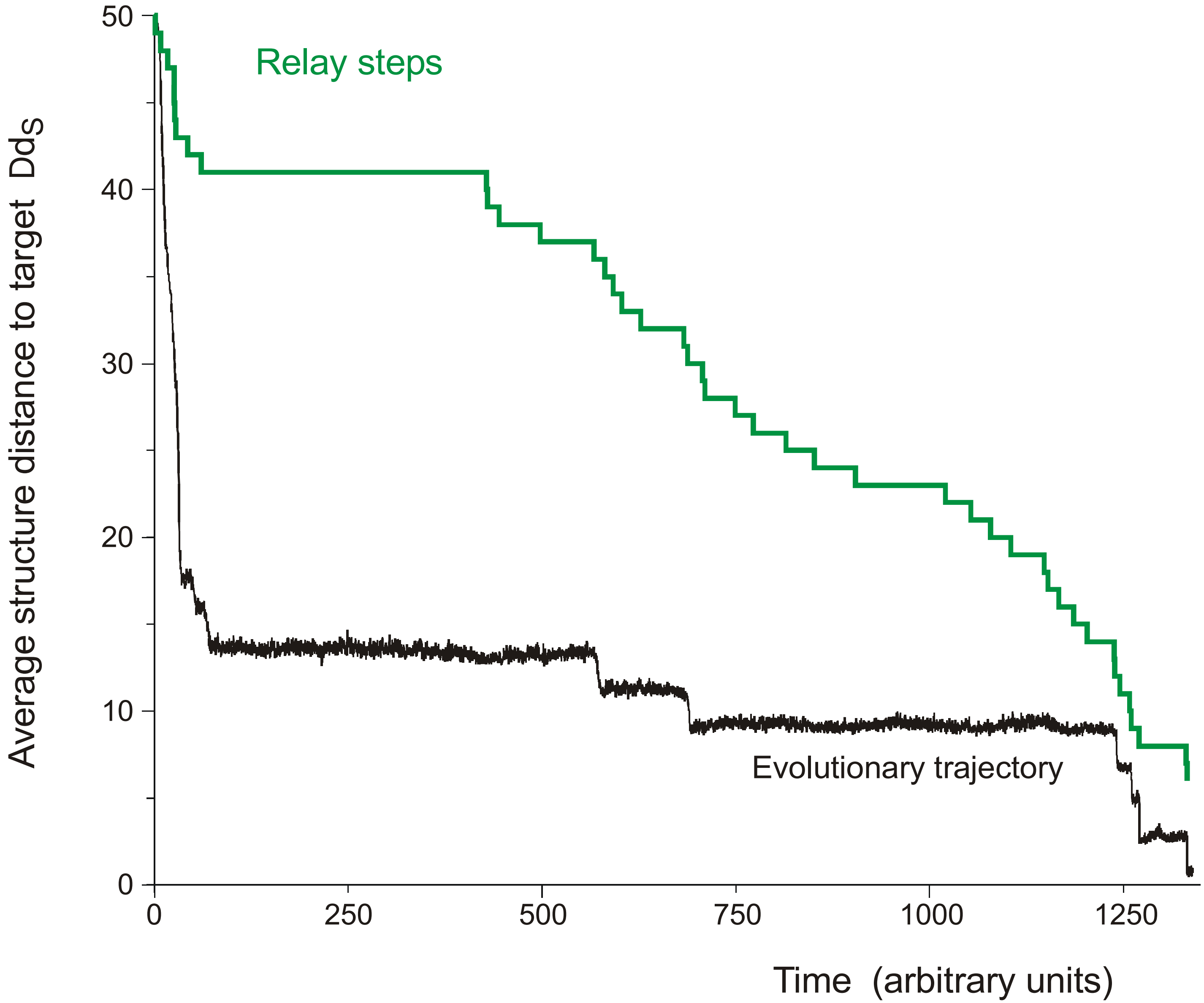




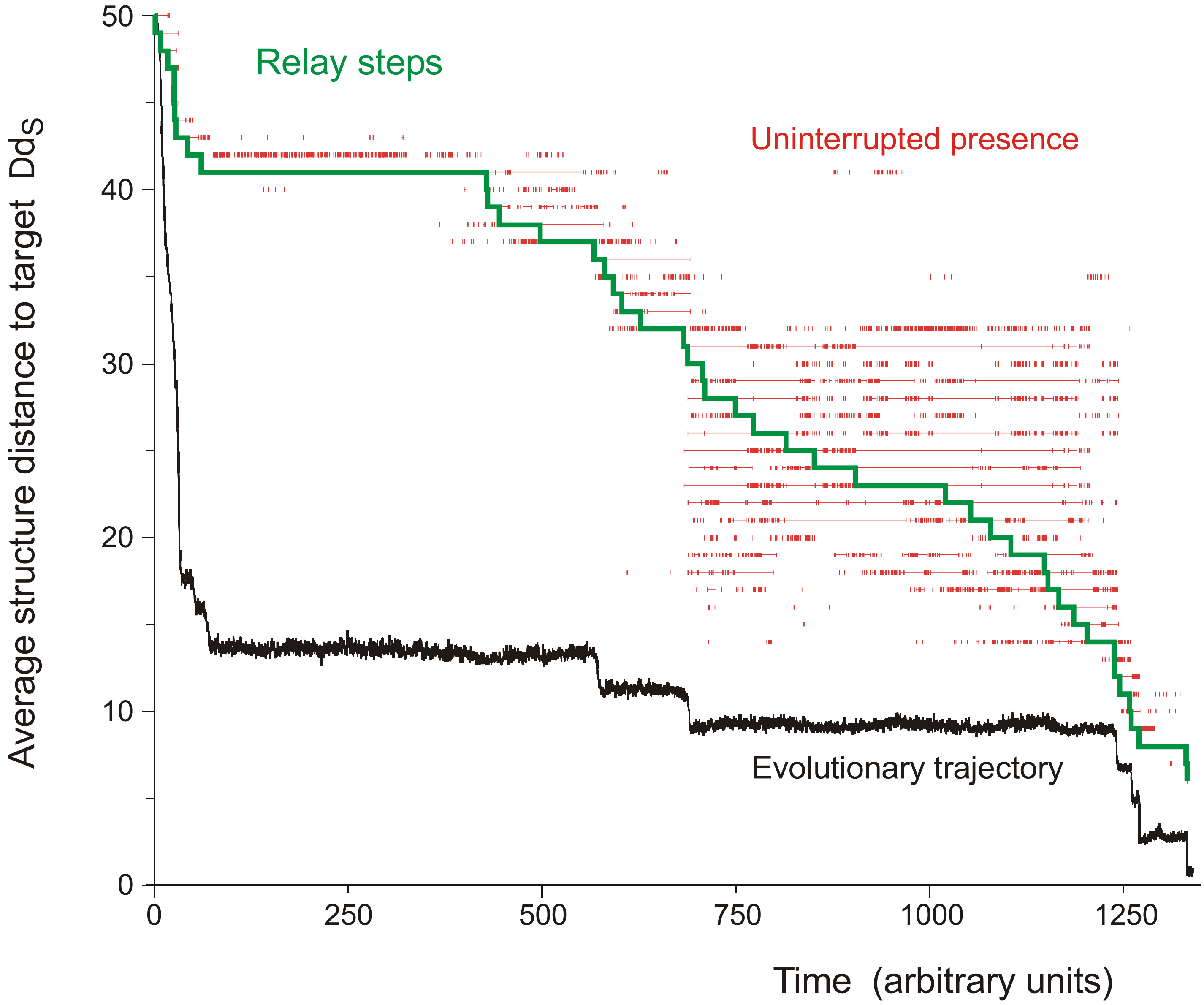
Reconstruction of step 40 Á 41 (Á 42 Á 43 Á 44)



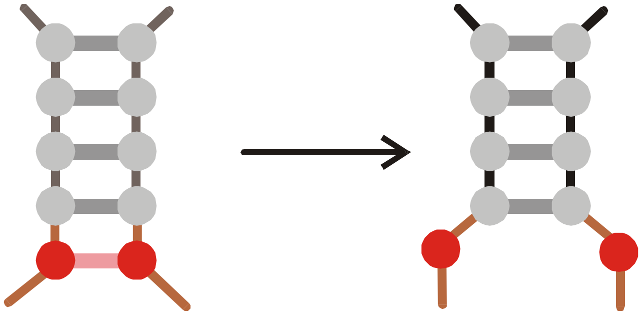
Reconstruction of the relay series



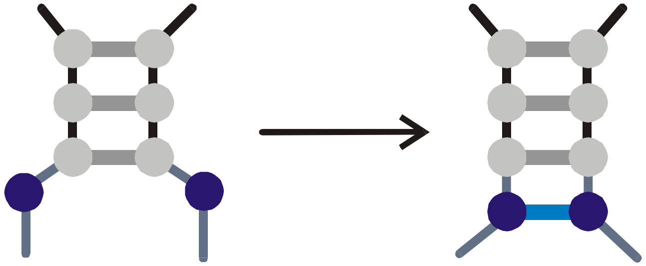
In silico optimization in the flow reactor: Trajectory and relay steps



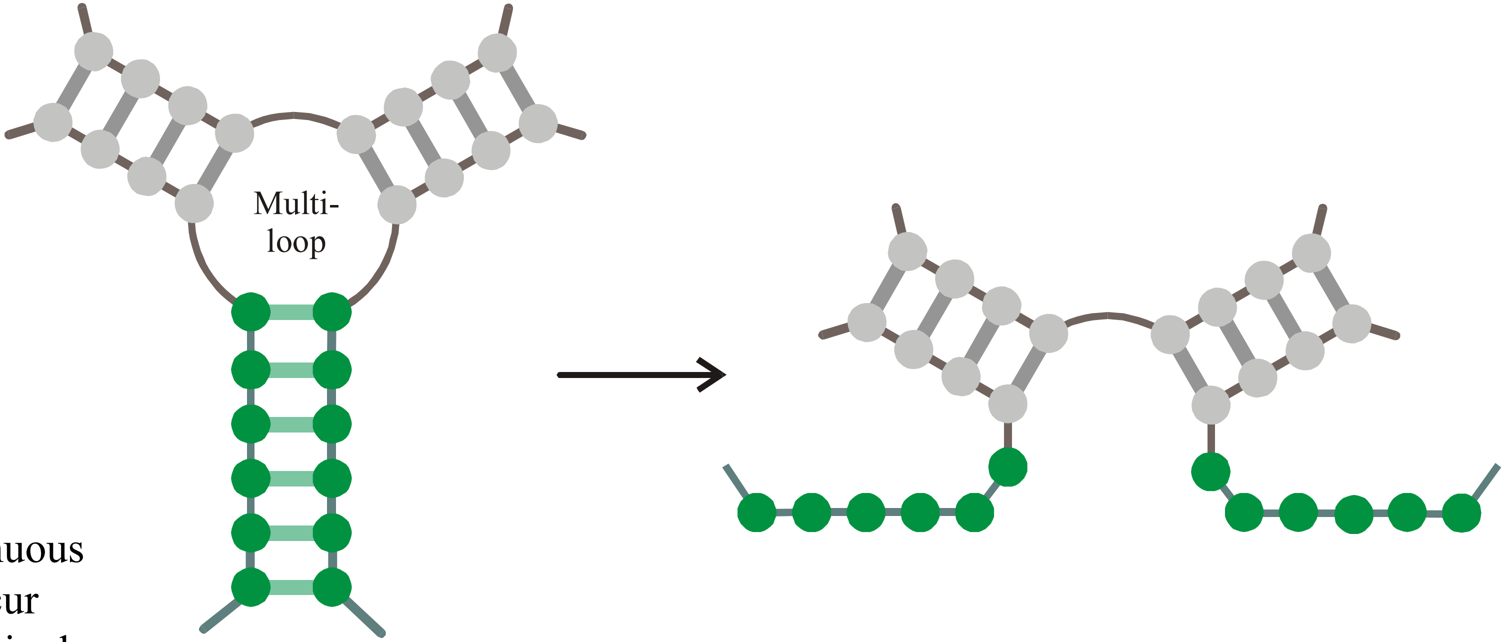
In silico optimization in the flow reactor: Uninterrupted presence



Shortening of Stacks

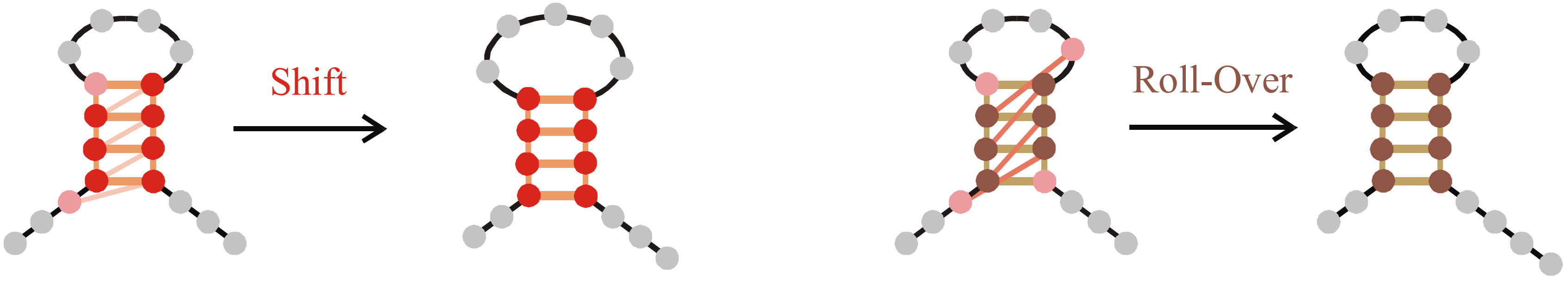


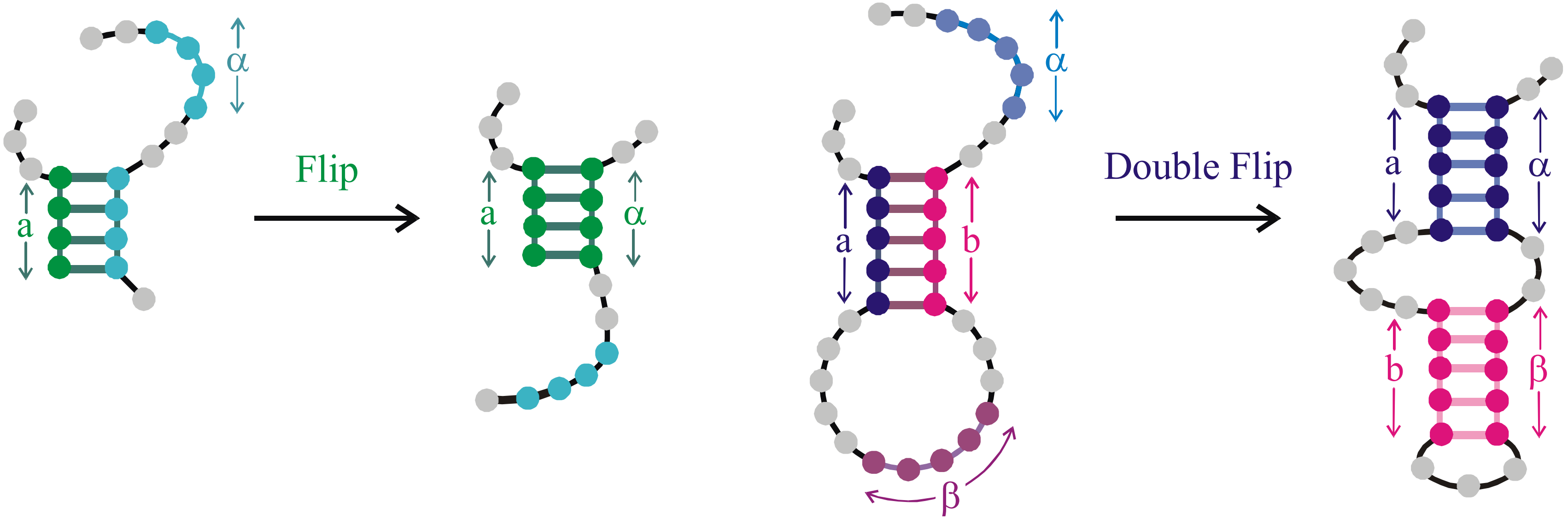
Elongation of Stacks



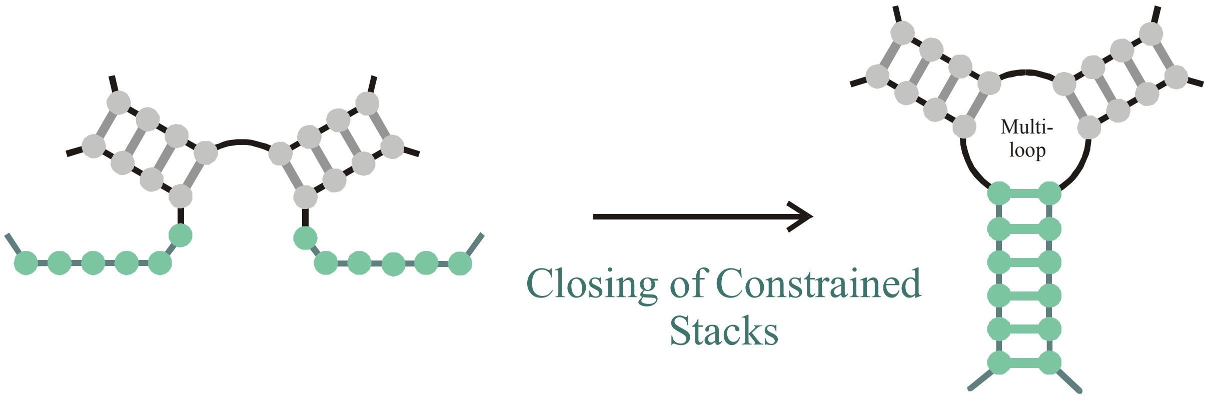
Minor or continuous transitions: Occur **frequently** on single point mutations

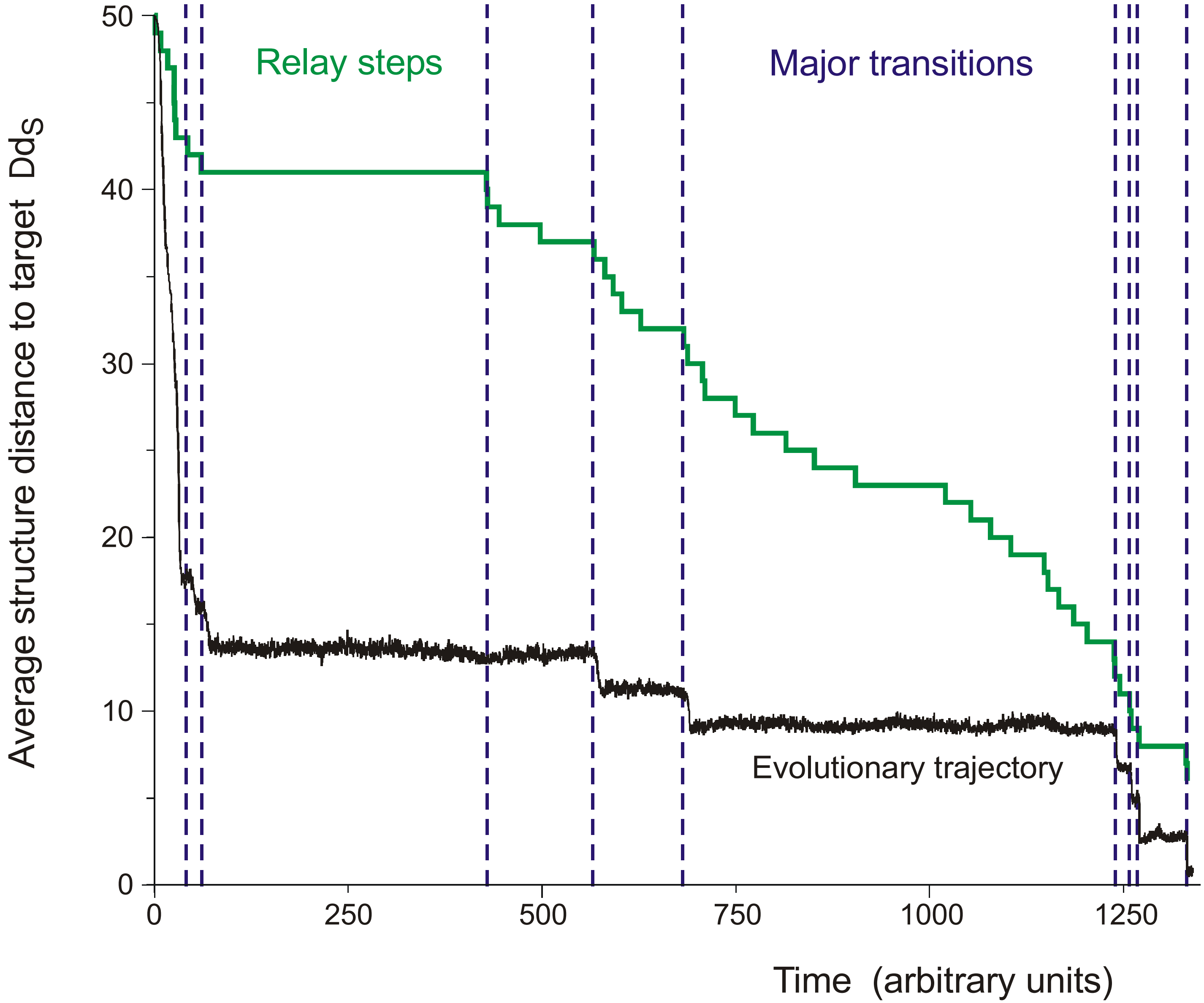
Opening of Constrained Stacks





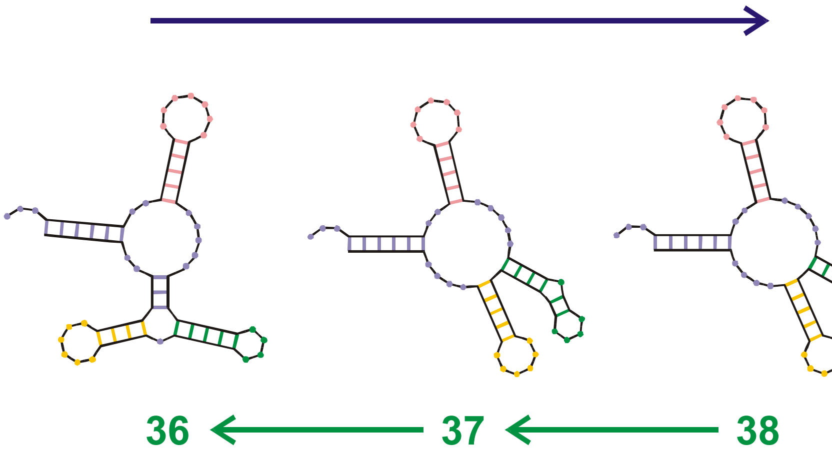
Major or discontinuous transitions: ***Structural innovations***, occur **rarely** on single point mutations

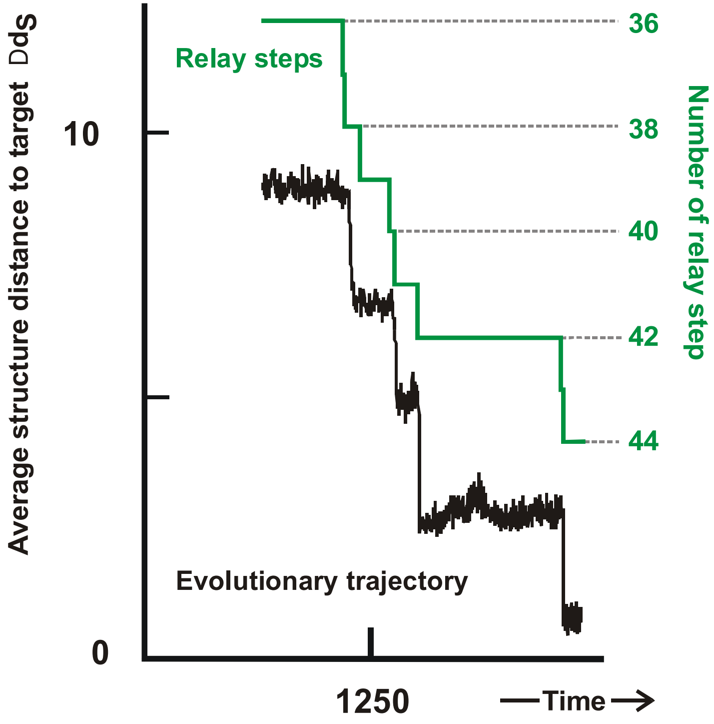




In silico optimization in the flow reactor: Major transitions

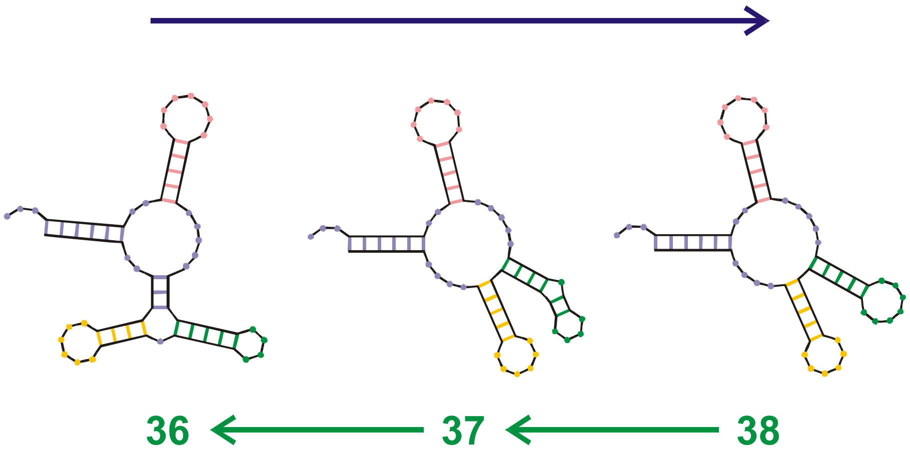
Major transition leading to clover leaf

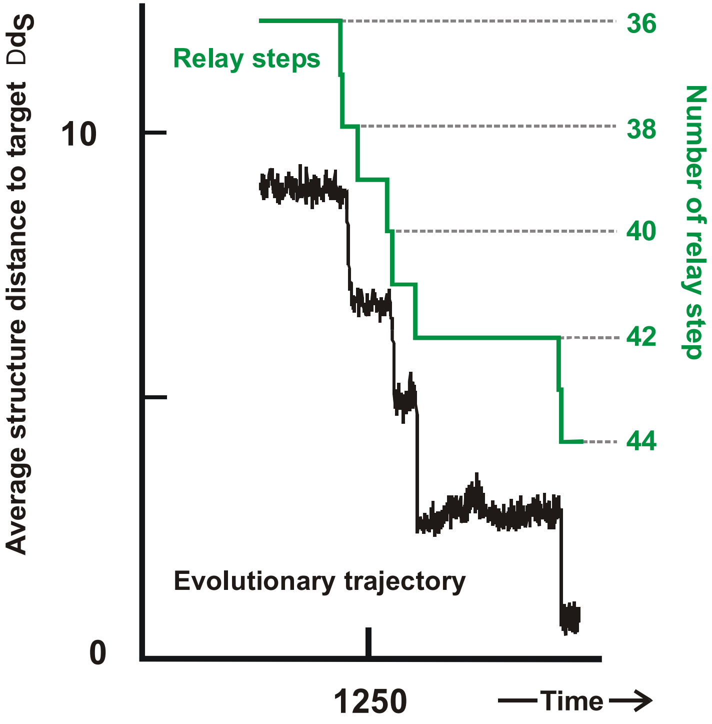




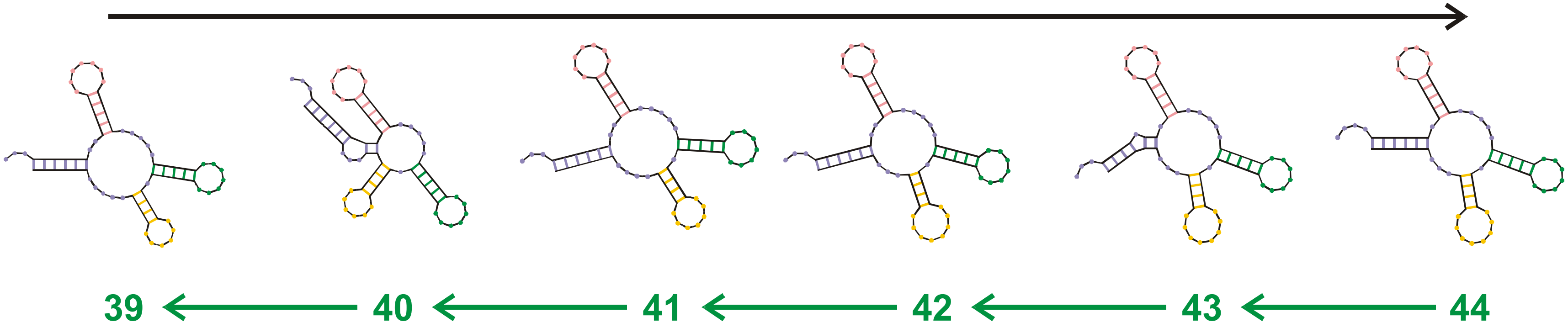
Reconstruction of a major transitions 36 Á 37 (Á 38)

Major transition leading to clover leaf



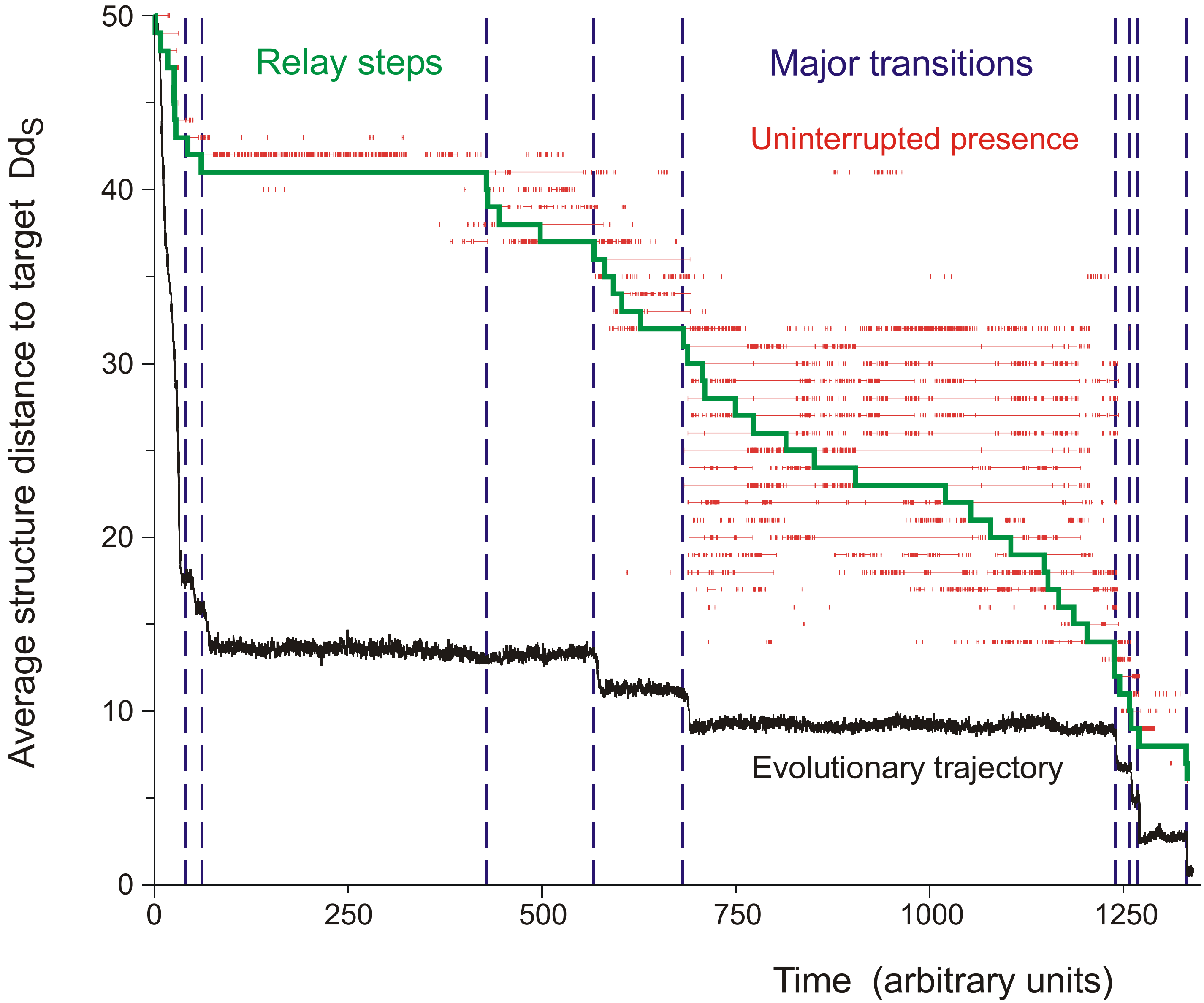


Evolutionary process

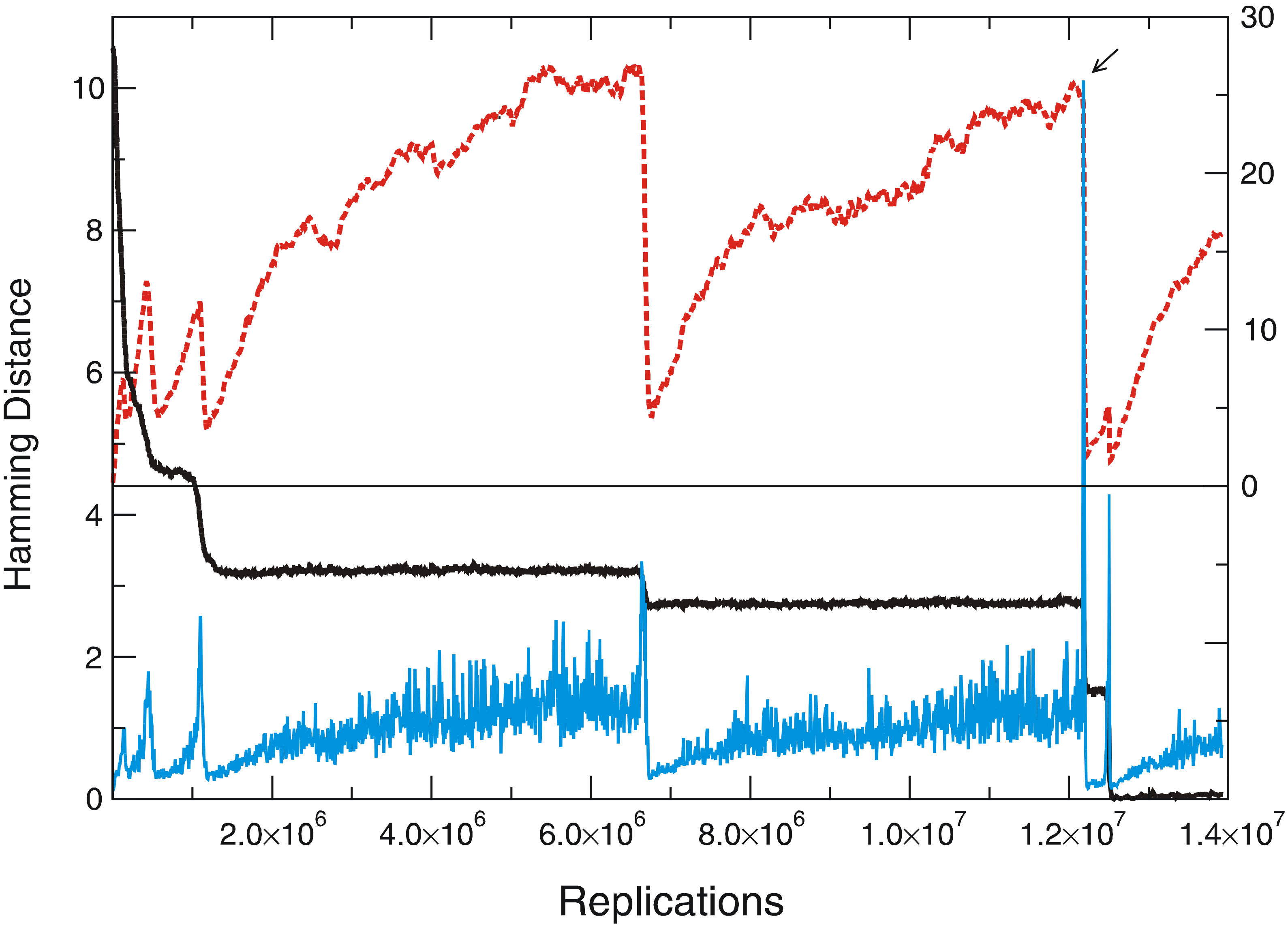


Reconstruction

Final reconstruction 36 Á 44



In silico optimization in the flow reactor



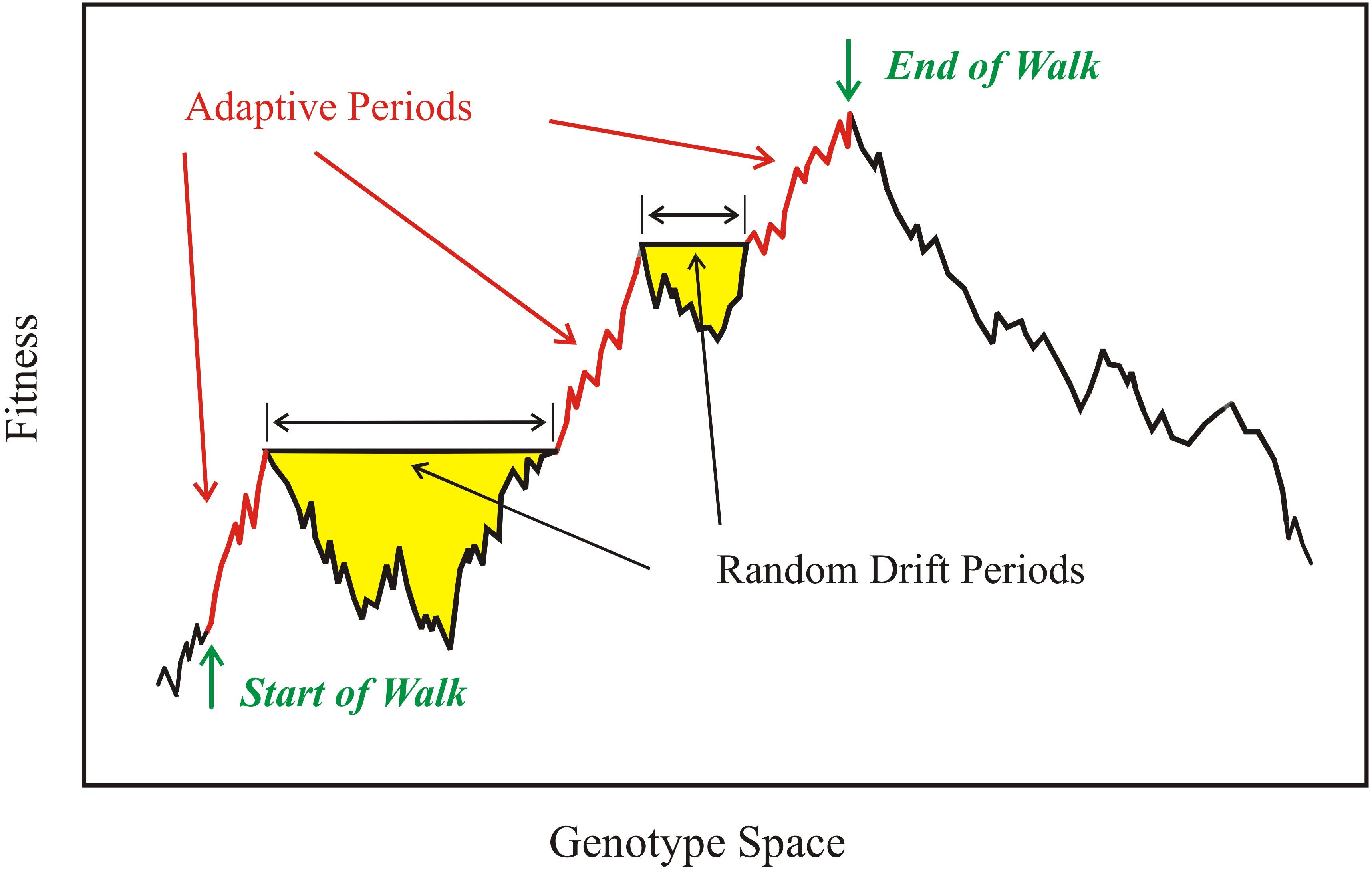
Variation in genotype space during optimization of phenotypes

Statistics of evolutionary trajectories

Population Size N	Number of Replications $< n_{\text{rep}} >$	Number of Transitions $< n_{\text{tr}} >$	Number of Major Transitions $< n_{\text{dtr}} >$	Epochal Phase $< d_{\tau}^{s}(t_{\text{ep}}) >$
1 000	$(5.5 \pm [6.9, 3.1]) \times 10^7$	$92.7 \pm [80.3, 43.0]$	$8.8 \pm [2.4, 1.9]$	$23.7 \pm [5.0, 4.1]$
2 000	$(6.0 \pm [11.1, 3.9]) \times 10^7$	$55.7 \pm [30.7, 19.8]$	$8.9 \pm [2.8, 2.1]$	$22.2 \pm [5.1, 4.2]$
3 000	$(6.6 \pm [21.0, 5.0]) \times 10^7$	$44.2 \pm [25.9, 16.3]$	$8.1 \pm [2.3, 1.8]$	$20.9 \pm [2.4, 2.2]$
10 000	$(1.2 \pm [1.3, 0.6]) \times 10^8$	$35.9 \pm [10.3, 8.0]$	$10.3 \pm [2.6, 2.1]$	$18.4 \pm [2.3, 2.1]$
20 000	$(1.5 \pm [1.4, 0.7]) \times 10^8$	$28.8 \pm [5.8, 4.8]$	$9.0 \pm [2.8, 2.2]$	$17.5 \pm [2.5, 2.2]$
30 000	$(2.2 \pm [3.1, 1.3]) \times 10^8$	$29.8 \pm [7.3, 5.9]$	$8.7 \pm [2.4, 1.9]$	$16.7 \pm [2.0, 1.8]$
100 000	$(3 \pm [2, 1]) \times 10^8$	$24 \pm [6, 5]$	9 ± 2	17 ± 1

„...Variations neither useful not injurious would not be affected by natural selection, and would be left either a fluctuating element, as perhaps we see in certain polymorphic species, or would ultimately become fixed, owing to the nature of the organism and the nature of the conditions. ...“

Charles Darwin, Origin of species (1859)



Evolution in genotype space sketched as a non-descending walk in a fitness landscape

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