

Evolution of asexually reproducing populations

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Eröffnung des CD-Labors zur Produktion neuartiger
Biopharmazeutika in *Escherichia coli*

Wien, 10.05.2017

Web-Page for further information:

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

Current Topics in Microbiology and Immunology

Esteban Domingo
Peter Schuster *Editors*

Quasispecies: From Theory to Experimental Systems

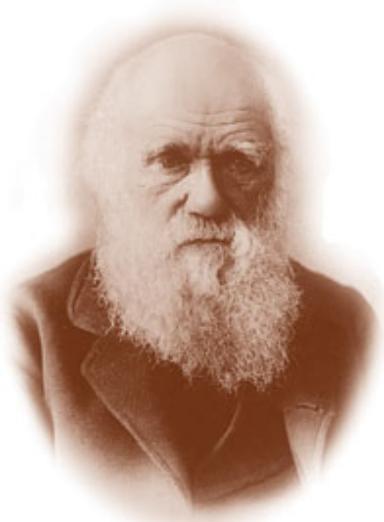
 Springer

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Volume 392

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1. Darwinian evolution
2. Quasispecies and error thresholds
3. Rugged and neutral biopolymer landscapes
4. Antiviral strategies and lethal mutagenesis

Darwinian evolution



Three necessary conditions for Darwinian evolution are:

1. Multiplication,
2. Variation, and
3. Selection.

Charles Darwin, 1809-1882

Variation through mutation and recombination operates on the genotype whereas the phenotype is the target of selection.

One important property of the Darwinian scenario is that variations in the form of mutations or recombination events occur uncorrelated with their effects on the selection process.



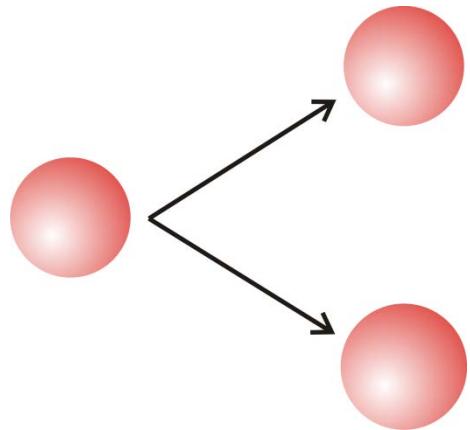
Three necessary conditions for Darwinian evolution are:

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All three conditions are fulfilled not only by cellular organisms but also by **nucleic acid molecules** - DNA or RNA - **in** suitable **cell-free experimental assays**:

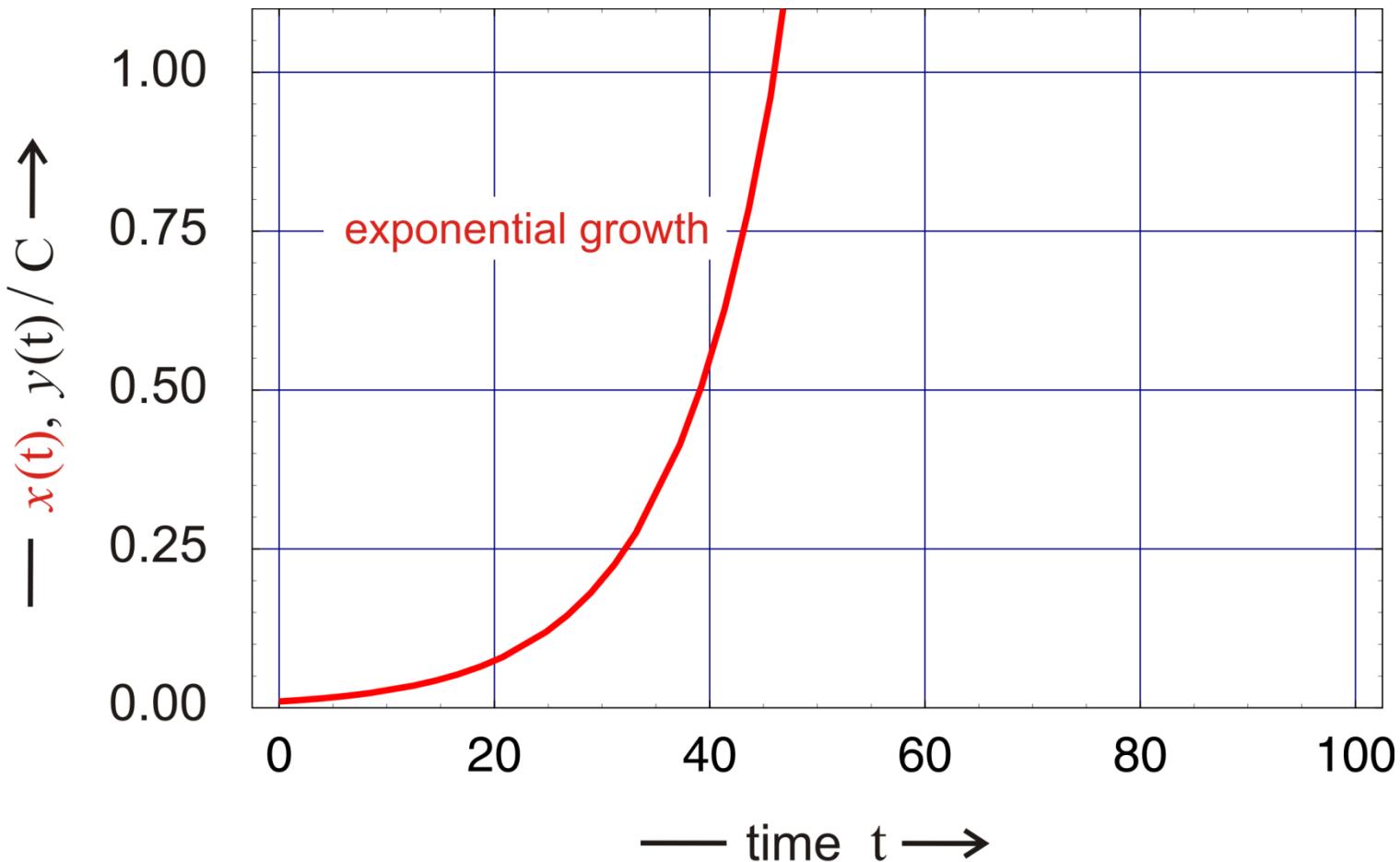
Darwinian evolution in the test tube

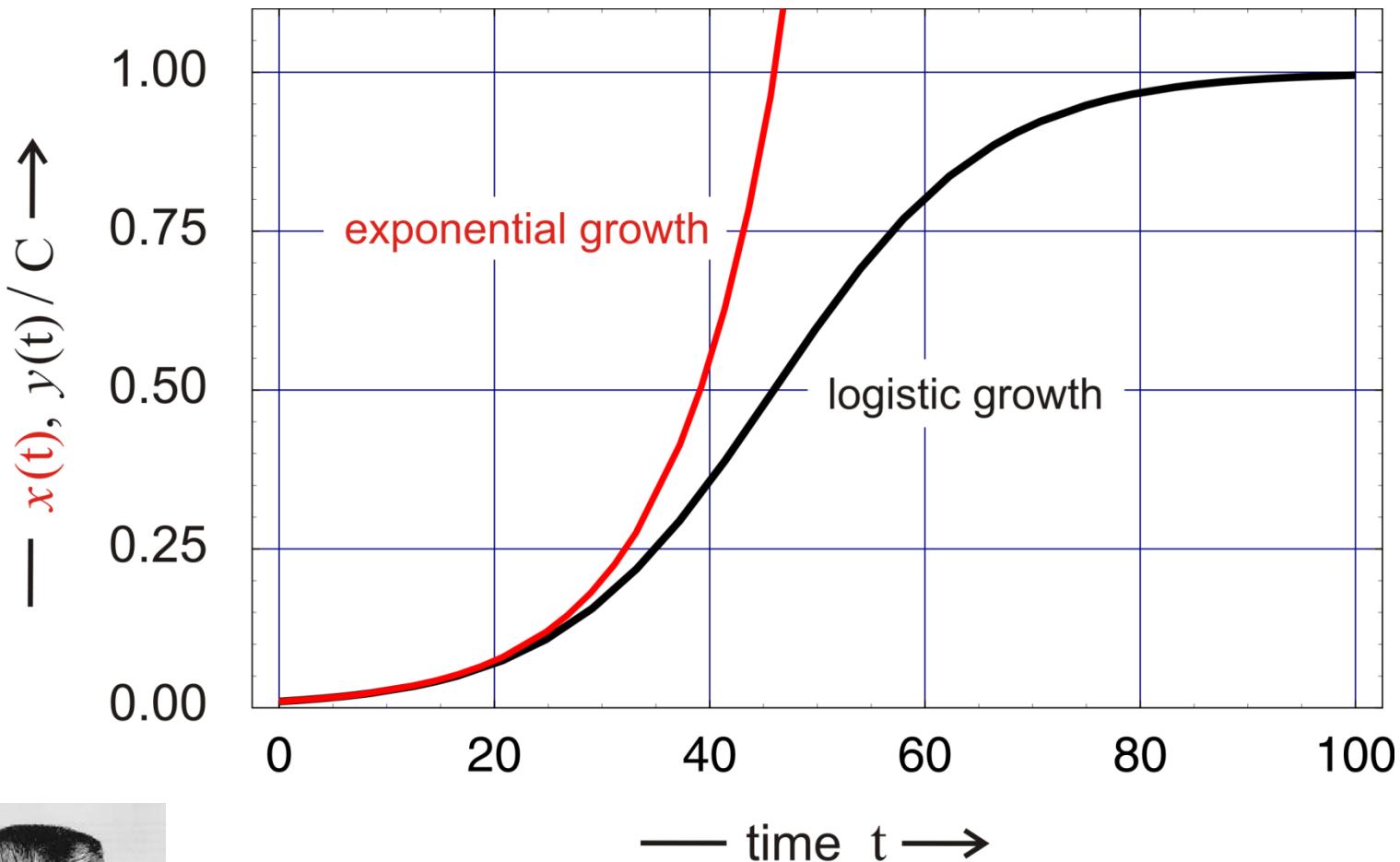


$$(A) + X = 2X$$

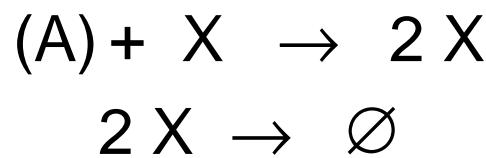
$$\frac{dx}{dt} = f x \quad \Rightarrow \quad x(t) = x(0) e^{f t}, \quad f \dots \text{fitness parameter}$$

exponential growth

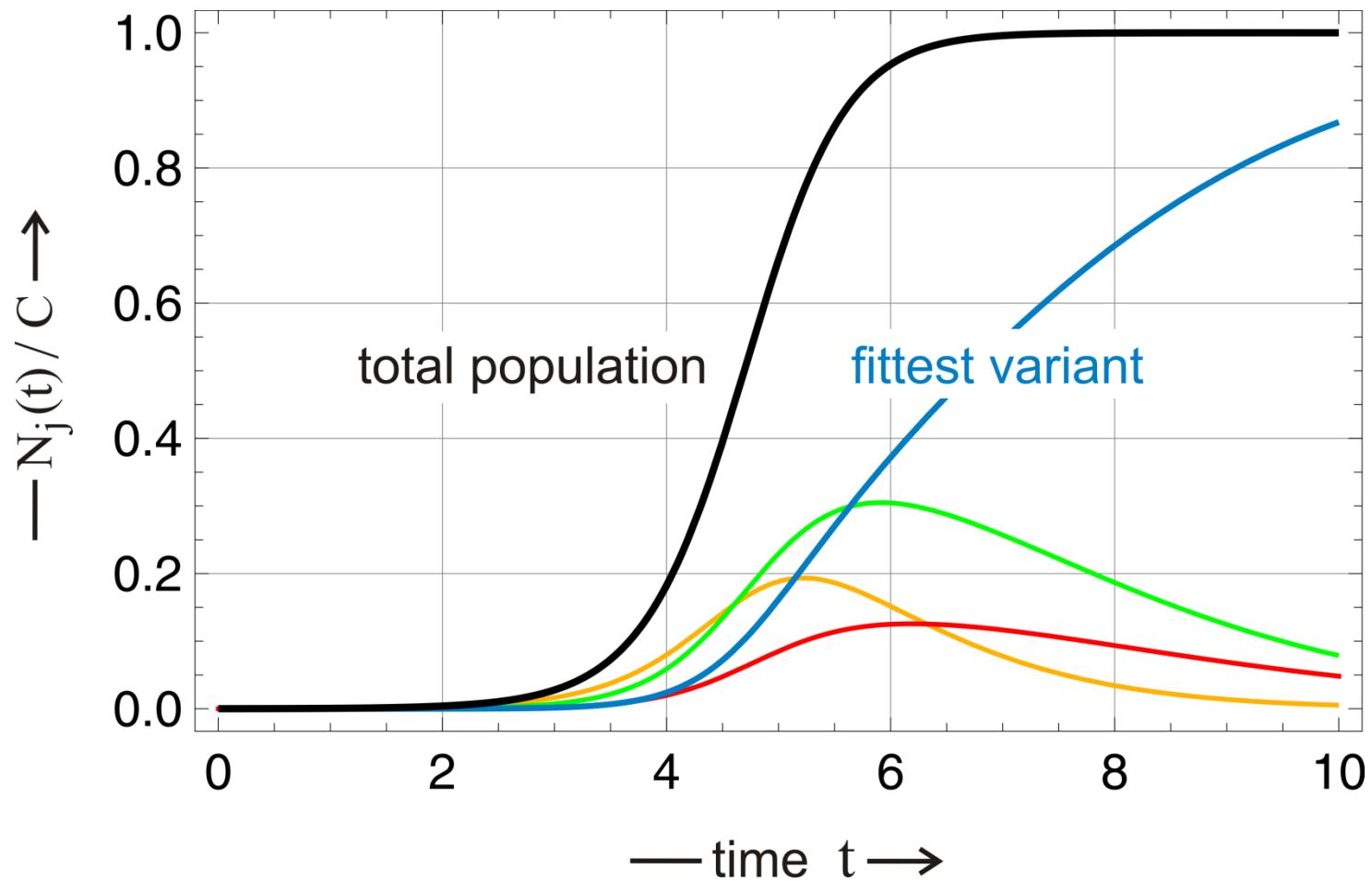




Pierre-François
Verhulst,
1804-1849

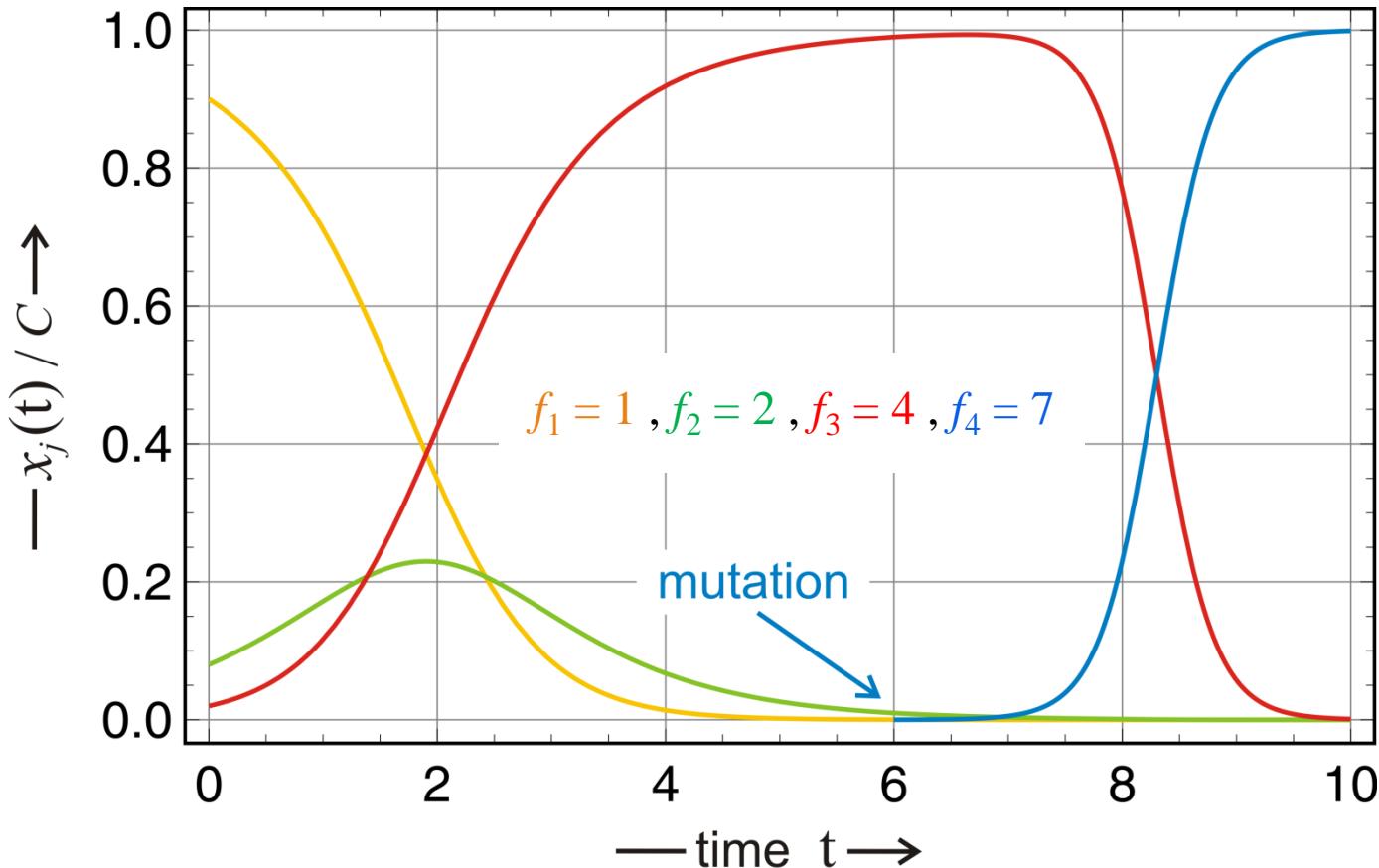


Was known 30 years
before the
'Origin of Species'



$$f_1 = 1, f_2 = 2, f_3 = 3, f_4 = 4$$

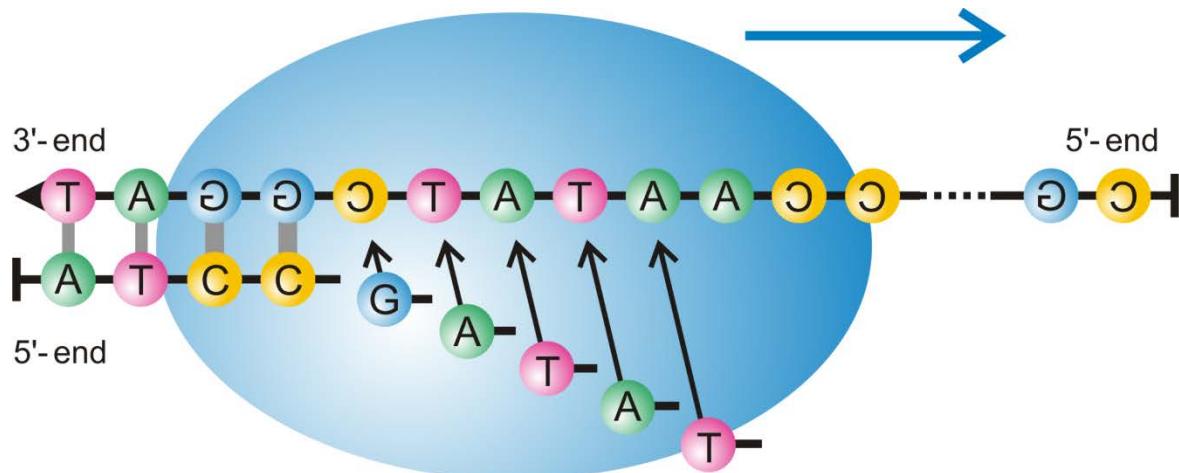
Limited resources and different fitness values f_k lead inevitably to natural selection



The strong-selection - weak-mutation scenario

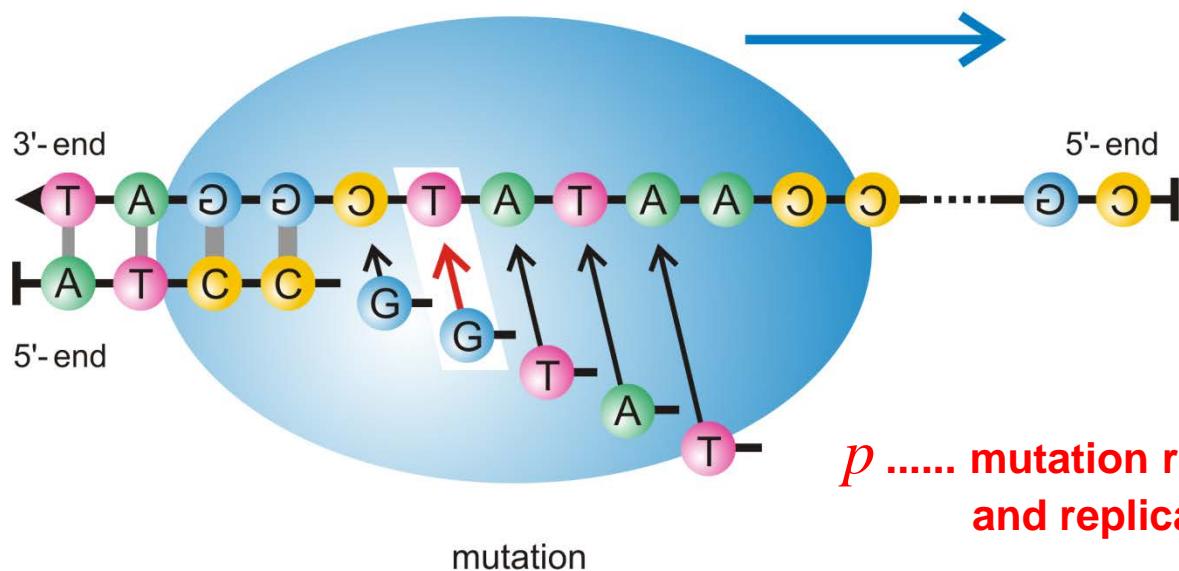
Before the development of molecular biology mutation was treated as a “*deus ex machina*”

quasispecies and error thresholds



Taq-polymerase

correct replication



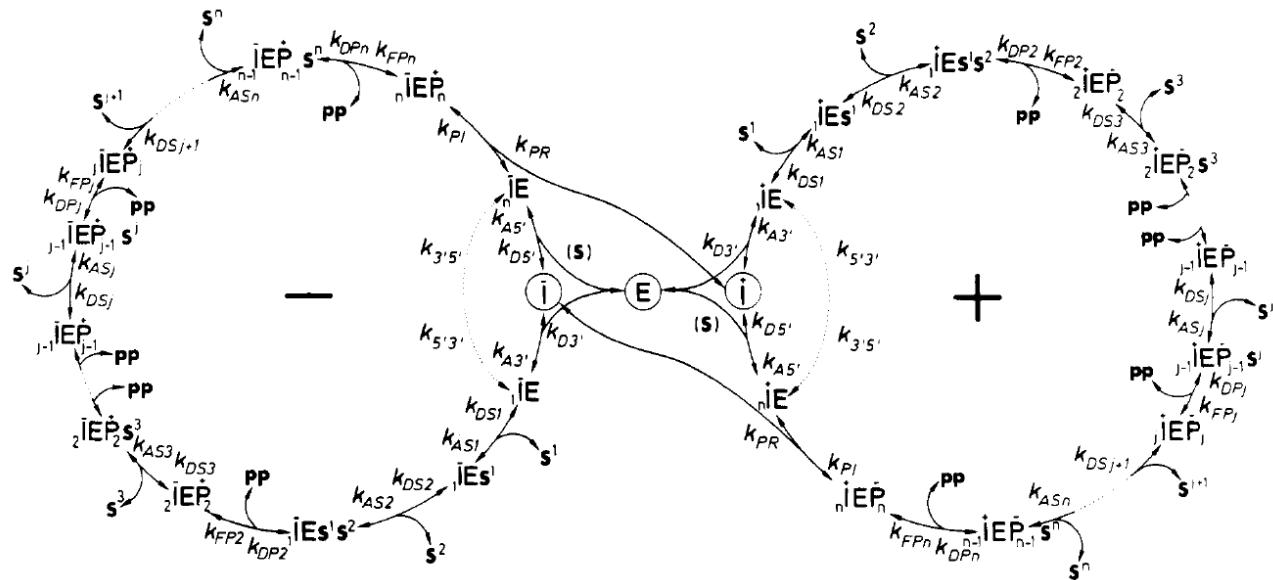
adenine	A
thymine	T
guanine	G
cytosine	C

p mutation rate per site
and replication

DNA replication and mutation

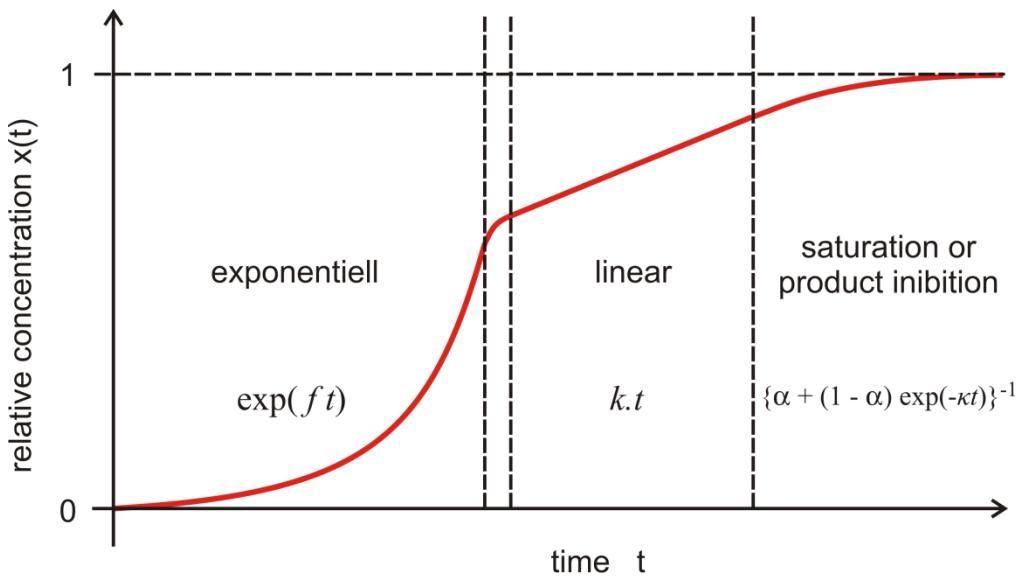


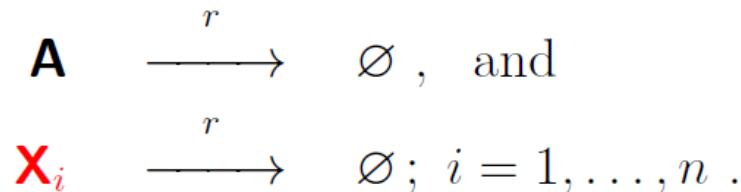
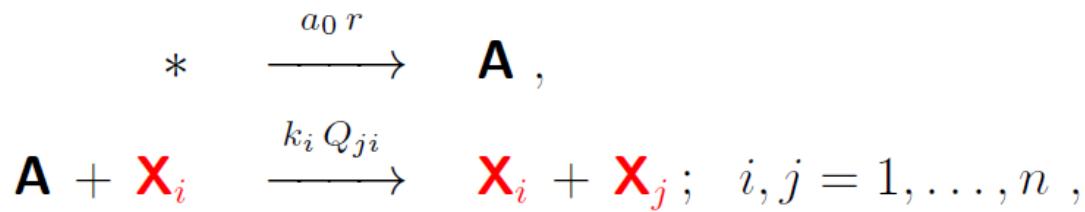
Christof K. Biebricher,
1941-2009



Kinetics of RNA replication with Q β -replicase

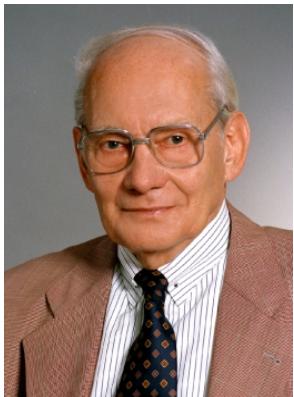
C.K. Biebricher, M. Eigen, W.C. Gardiner, Jr.
Biochemistry 22:2544-2559, 1983





chemical reaction equations: k_i ... reaction rate parameters

Q_{ji} ... elements of the mutation matrix



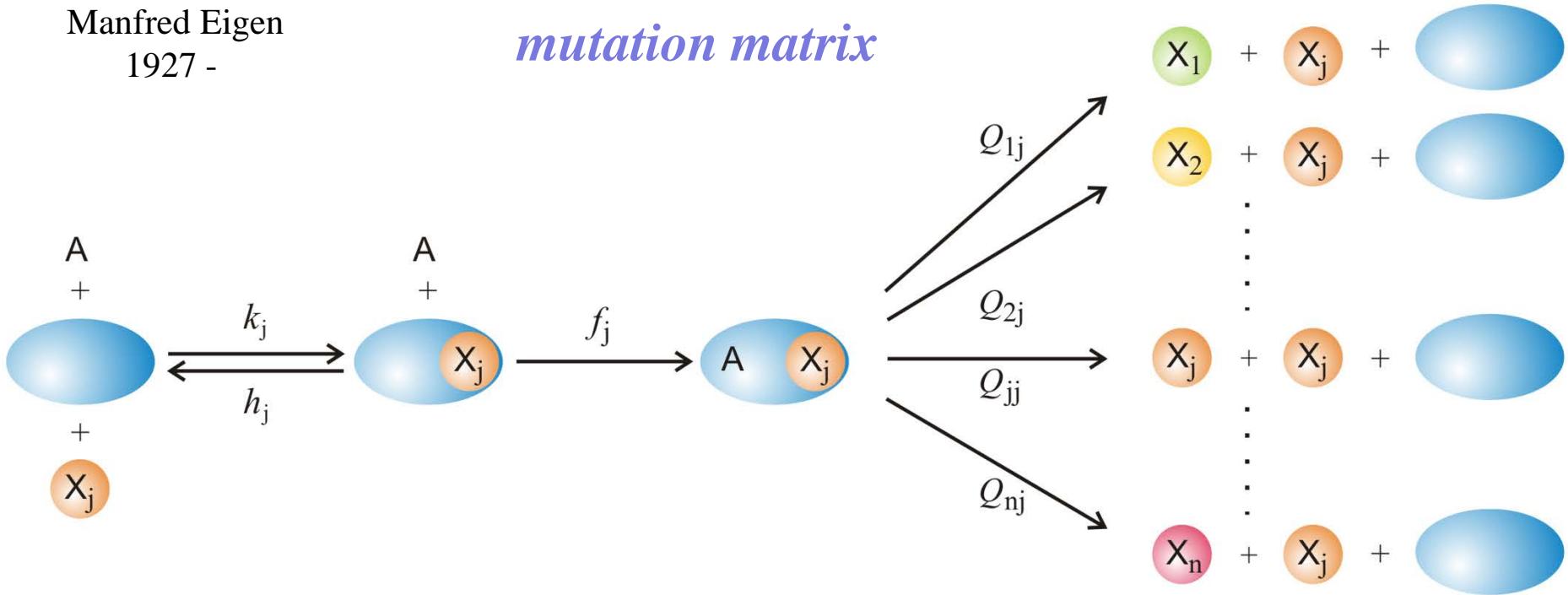
Manfred Eigen
1927 -

$$\frac{dx_j}{dt} = \sum_{i=1}^n W_{ji} x_i - x_j \Phi; \quad j = 1, 2, \dots, n$$

$$W_{ji} = Q_{ji} \cdot f_i, \quad \sum_{i=1}^n x_i = 1, \quad \Phi = \sum_{i=1}^n f_i x_i$$

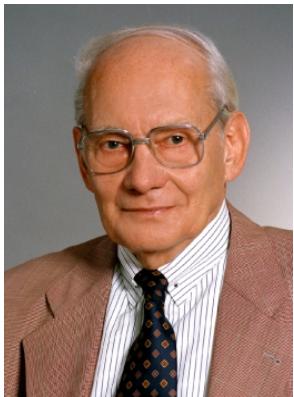
fitness landscape

mutation matrix



Mutation and (correct) replication as parallel chemical reactions

M. Eigen. 1971. *Naturwissenschaften* 58:465,
M. Eigen & P. Schuster. 1977-78. *Naturwissenschaften* 64:541, 65:7 und 65:341



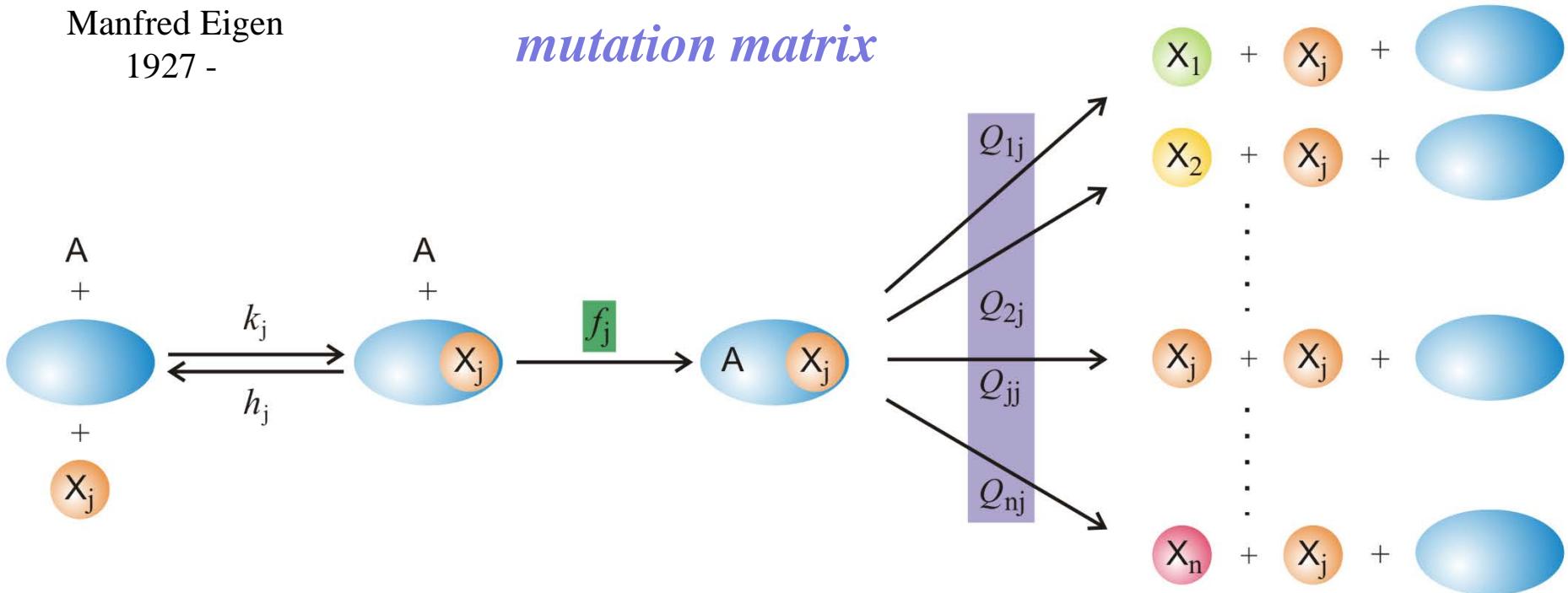
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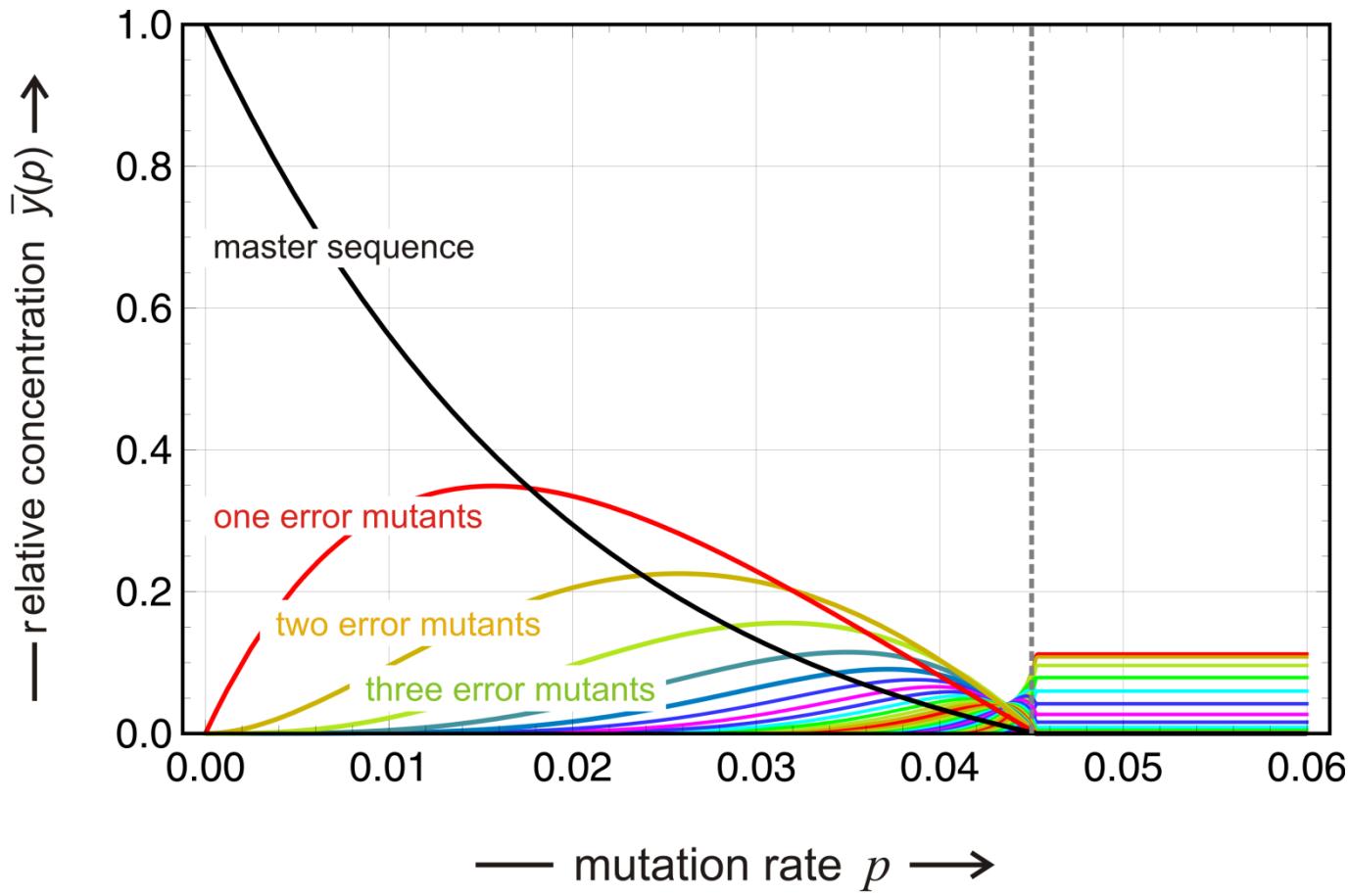
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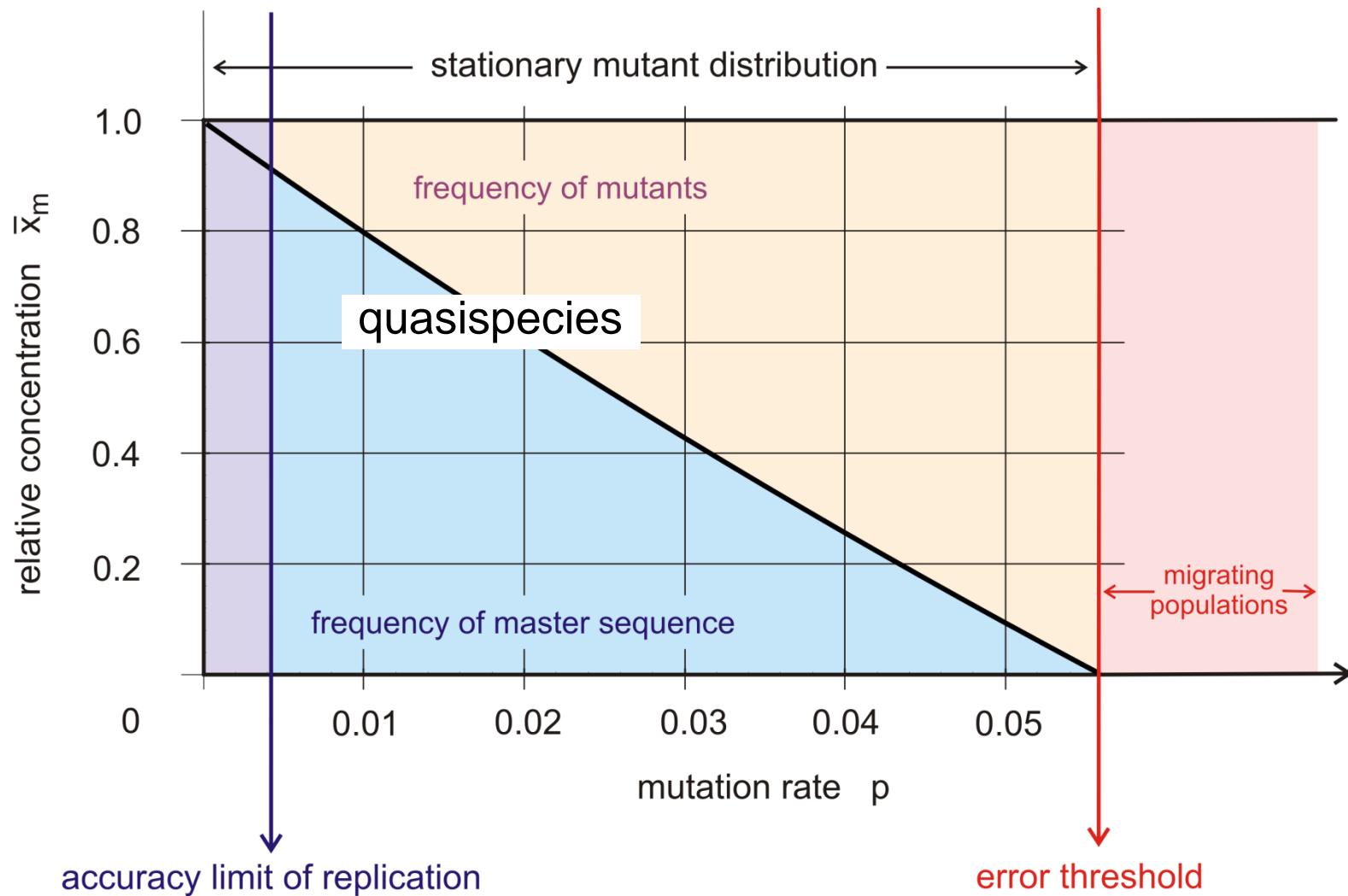
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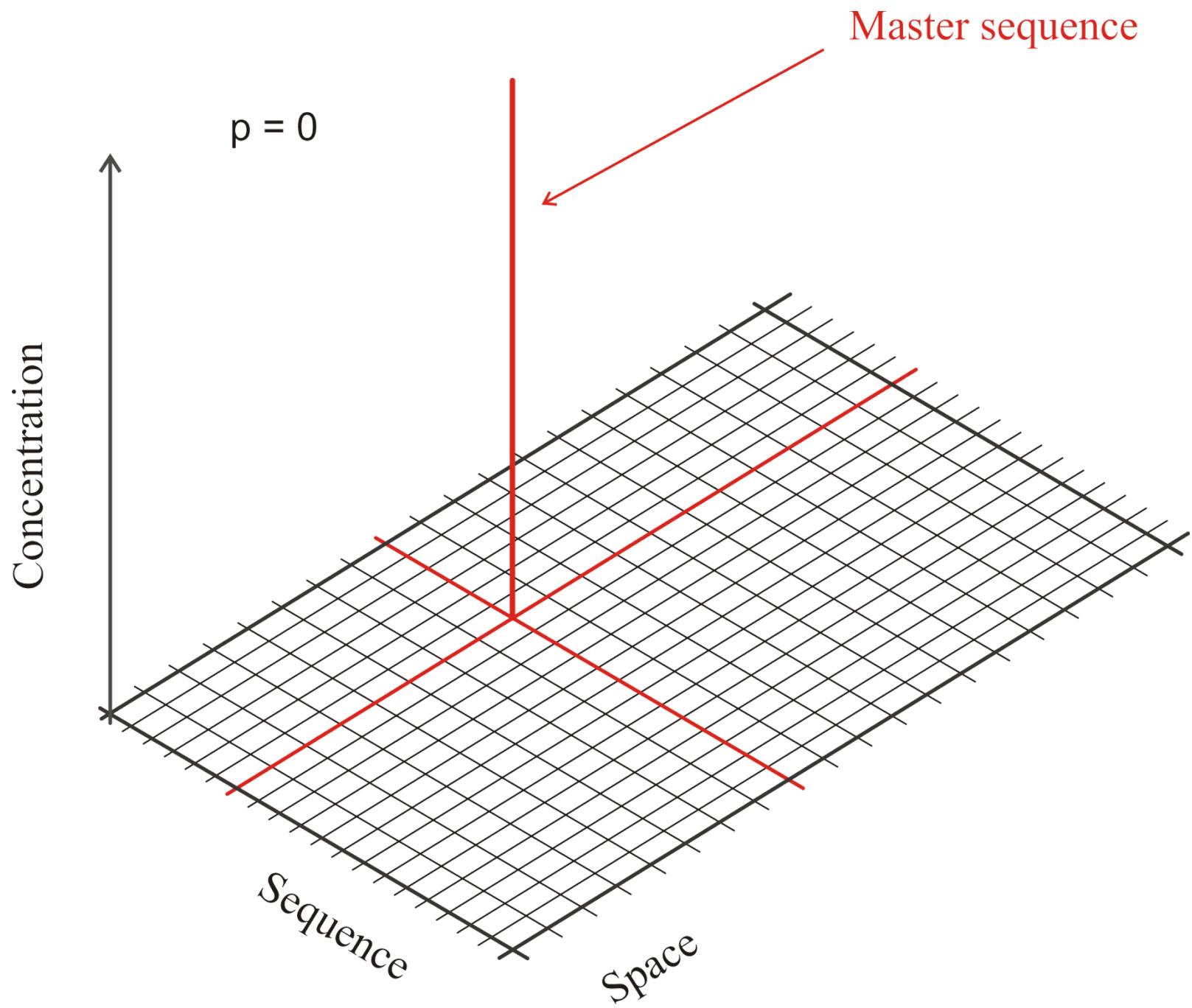


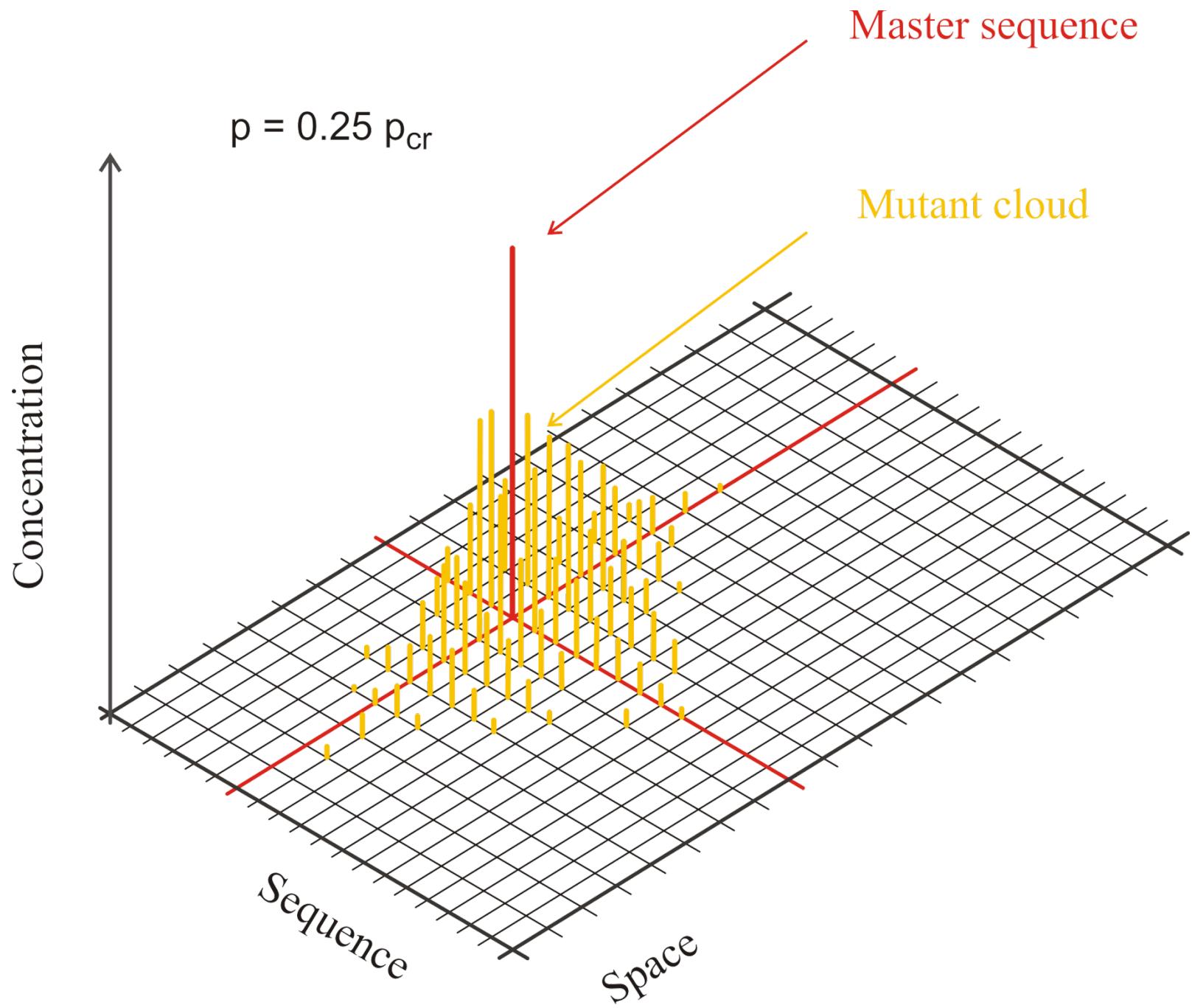
quasispecies as a function of the error rate parameter p

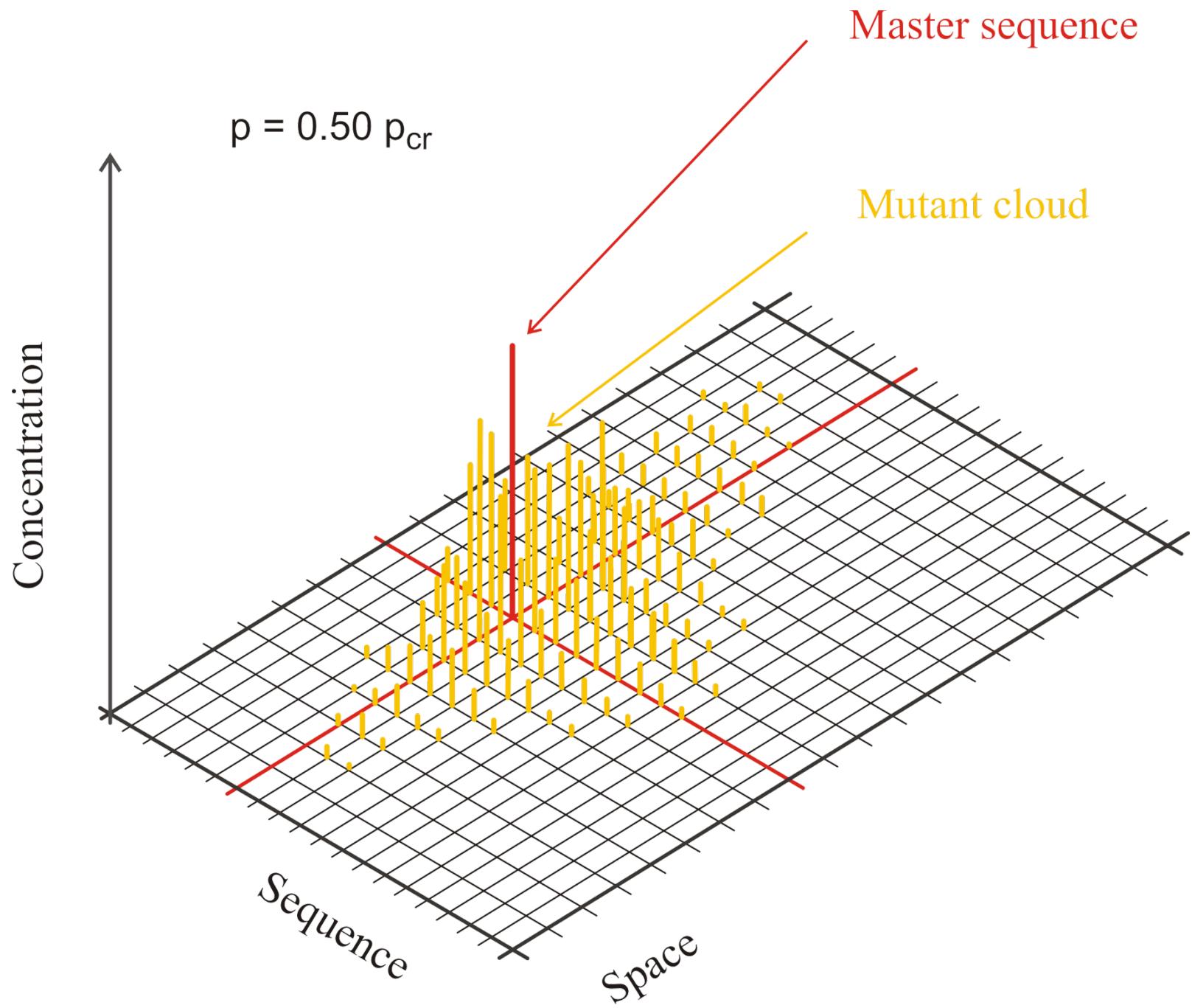
a quasispecies is the stationary mutant distribution of a population

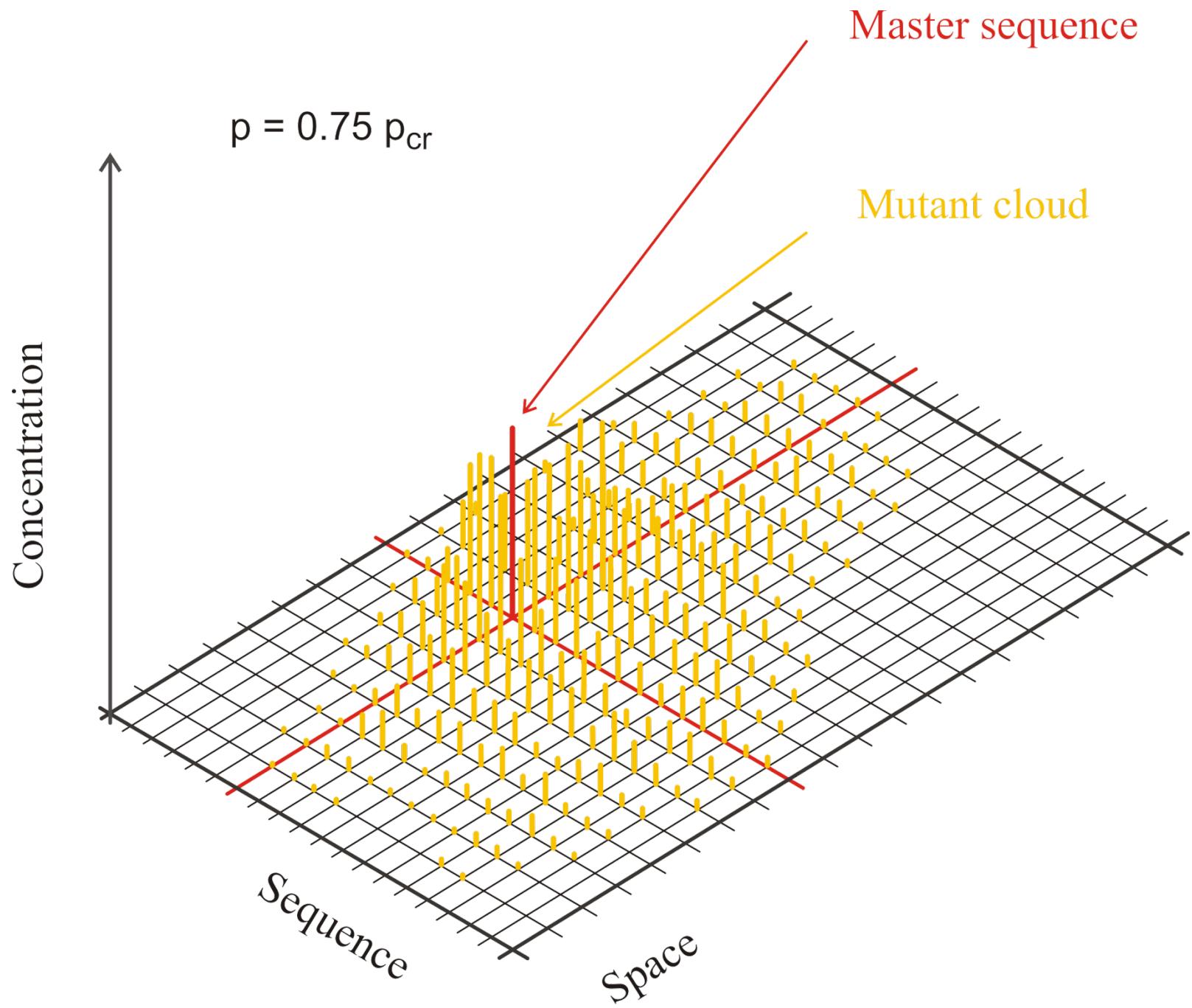


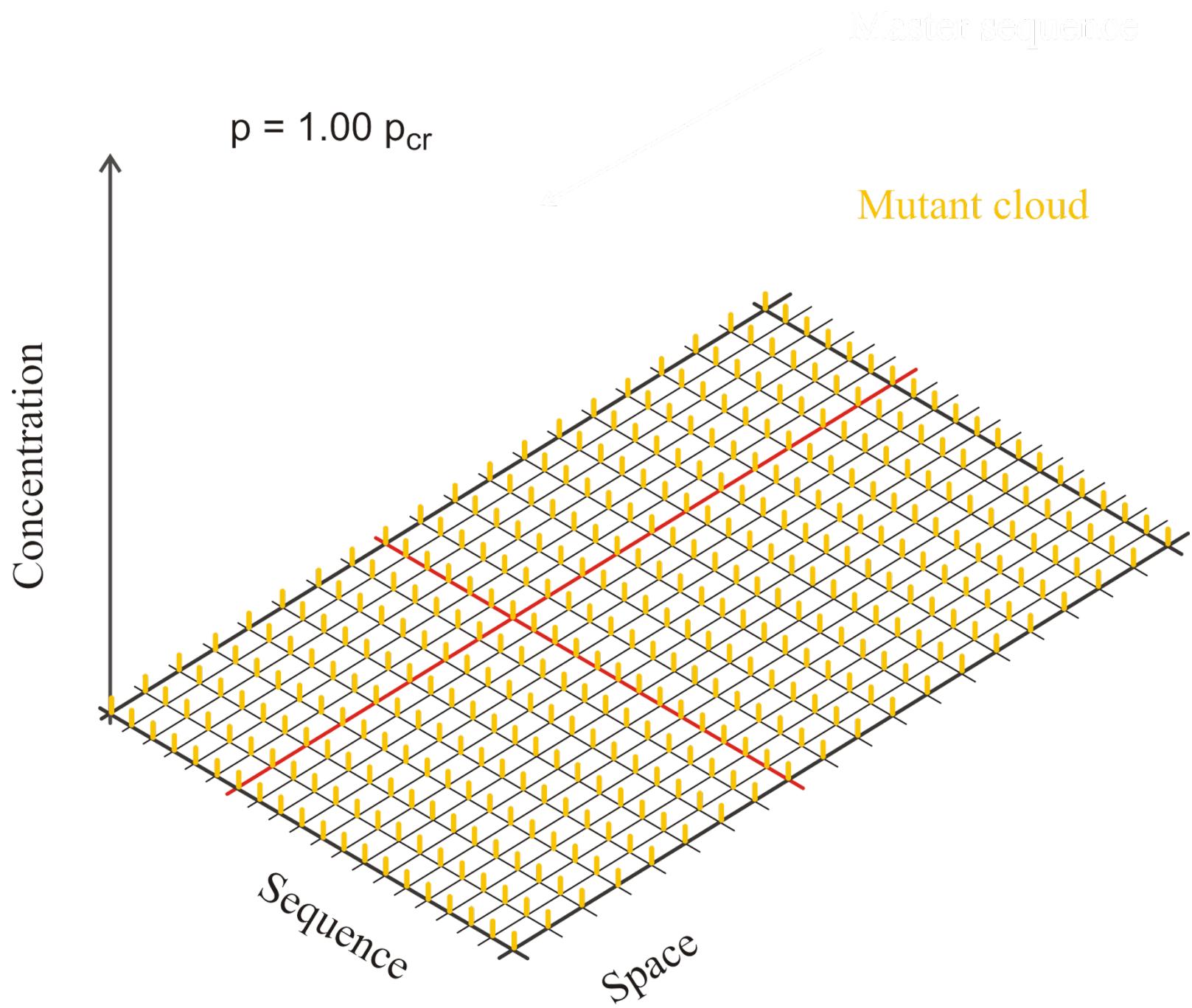
The error threshold in replication and mutation

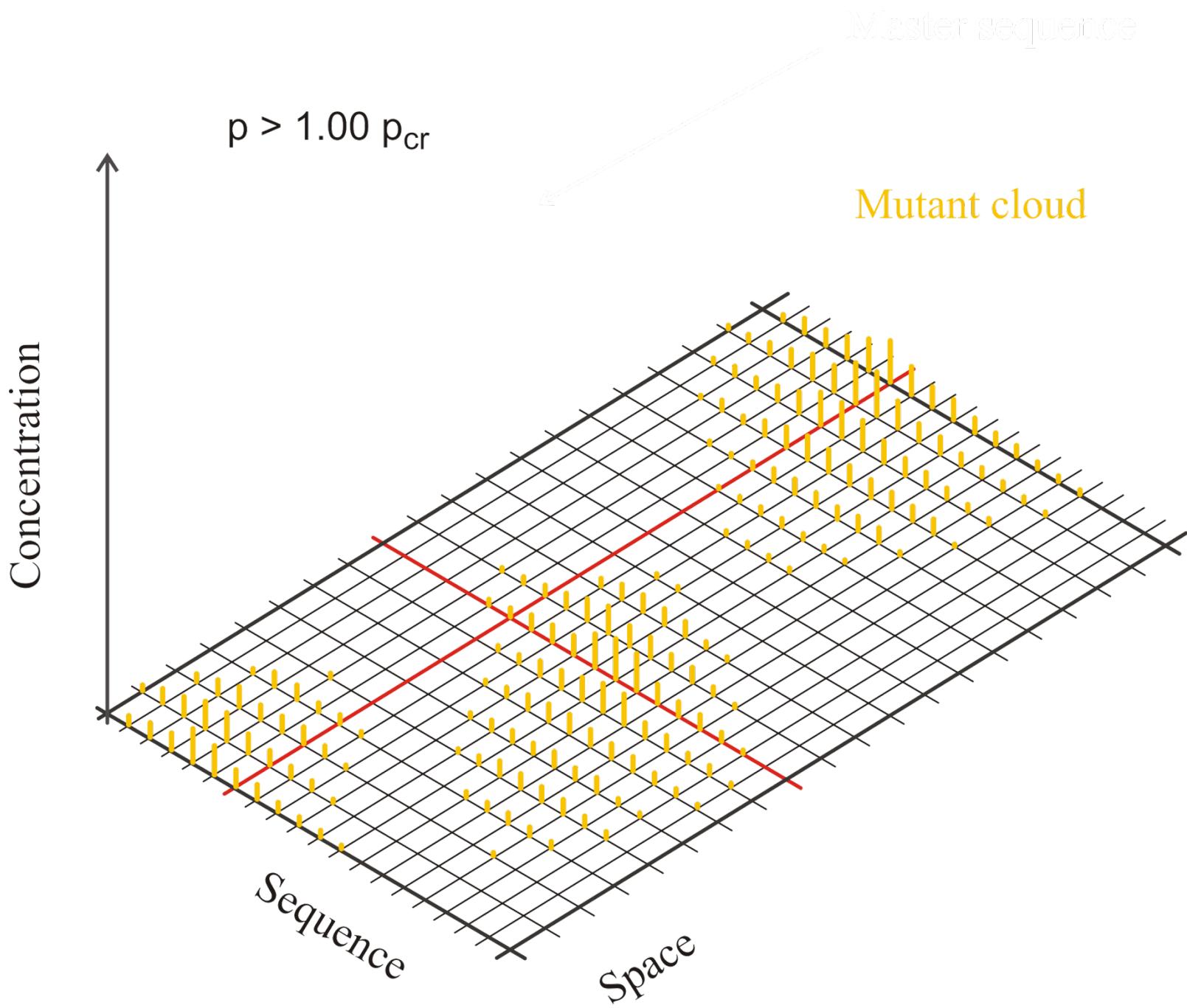


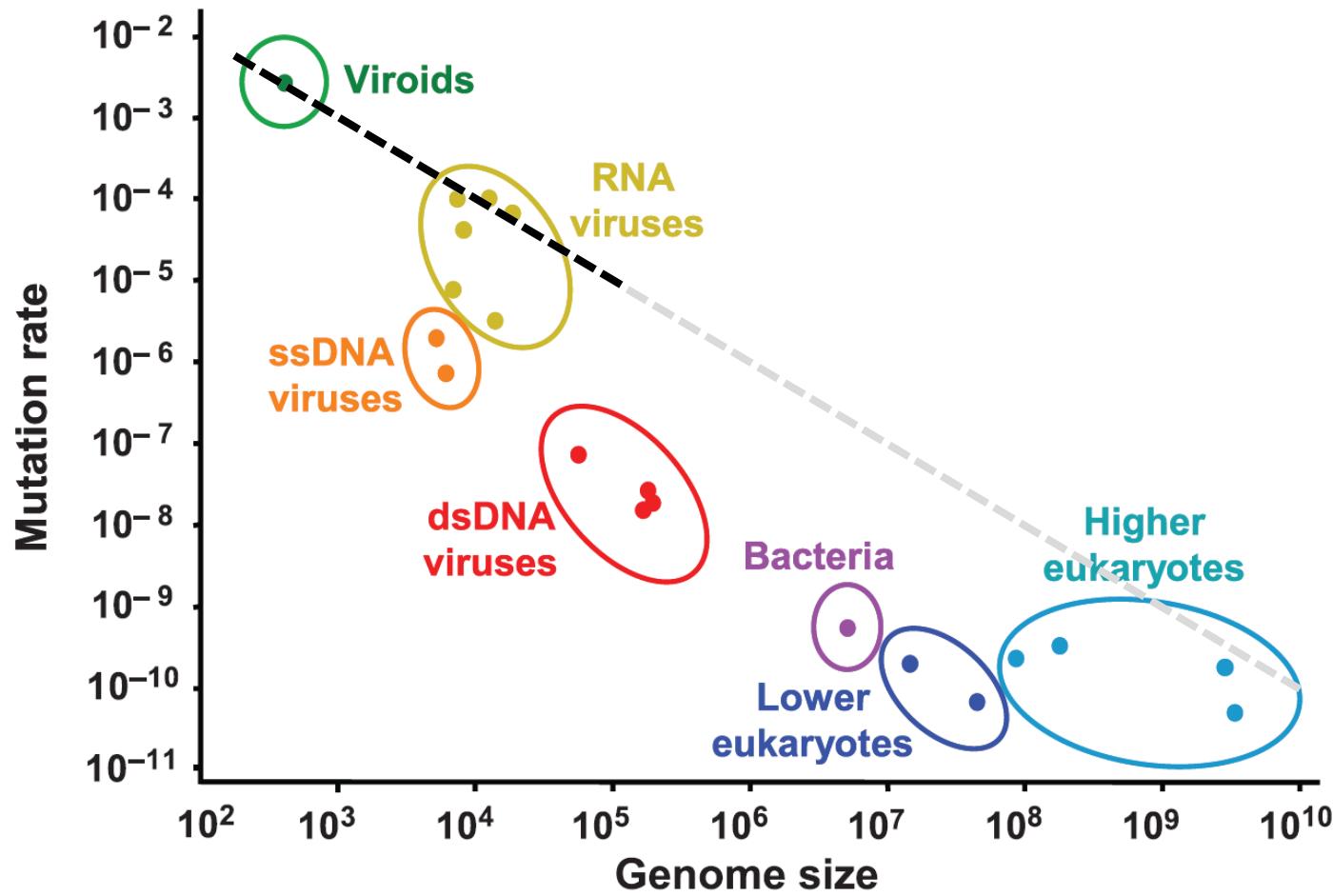








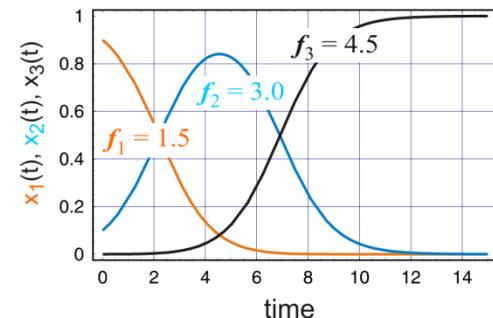
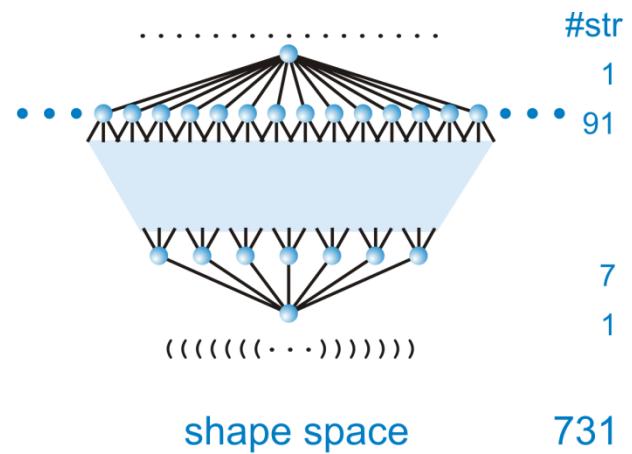
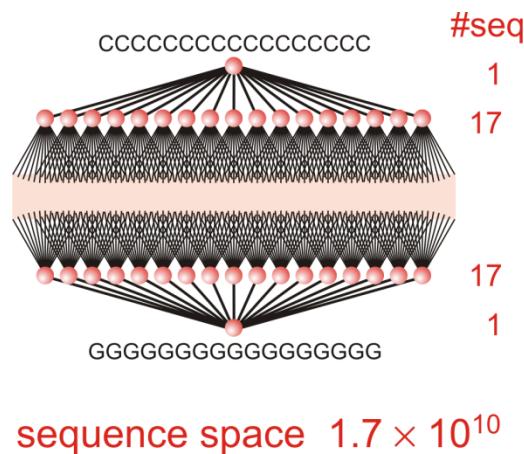




Selma Gago, Santiago F. Elena, Ricardo Flores, Rafael Sanjuán. 2009. Extremely high mutation rate of a hammerhead viroid. Science 323:1308.

mutation rate and genome size

rugged and neutral biopolymer landscapes



sequence space 1.7×10^{10}

shape space

731

parameter space

The diagram illustrates a sequential process. It starts with a red 'X' labeled 'sequence' followed by a thick black arrow pointing right. To its right is a blue 'S' labeled 'structure' followed by another thick black arrow pointing right. Finally, a green 'f' labeled 'fitness' is shown.

genotype → phenotype → selection

Evolutionary searches in sequence space

AGCUUAACUUAGUCGCU

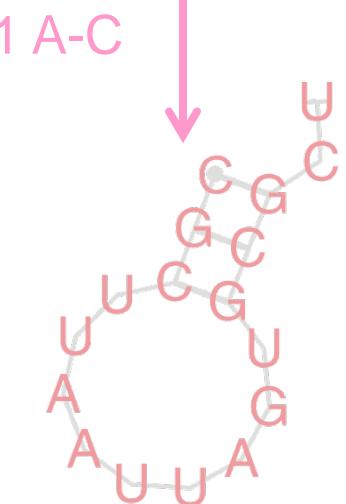


1 A-U

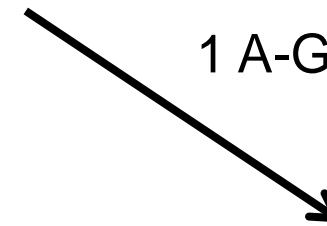


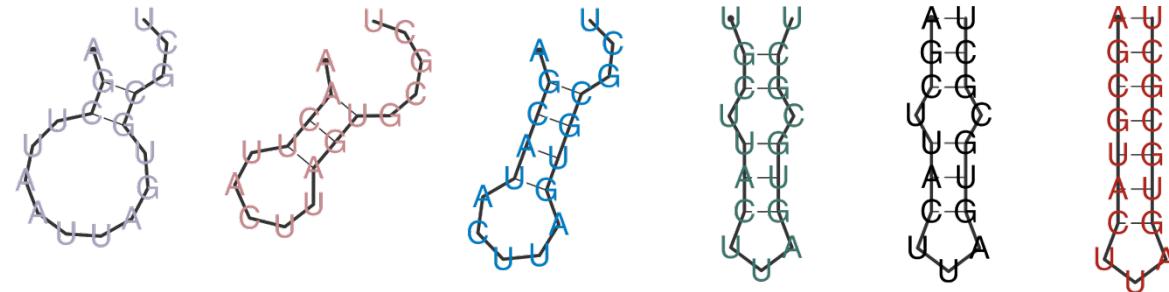
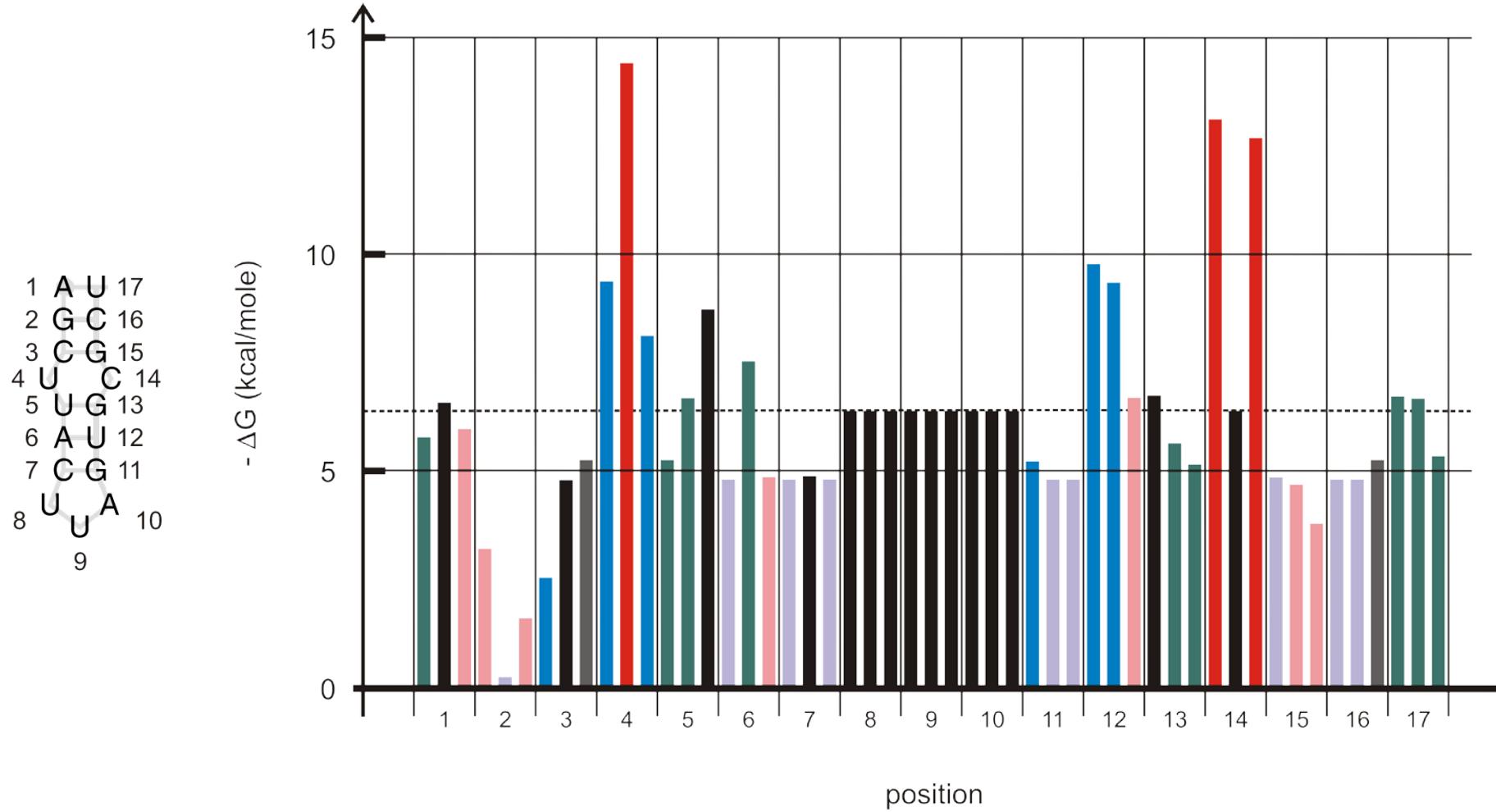
1 A-U 17
2 G C 16
3 C G 15
4 U C 14
5 U G 13
6 A U 12
7 C G 11
8 U U A 10
9

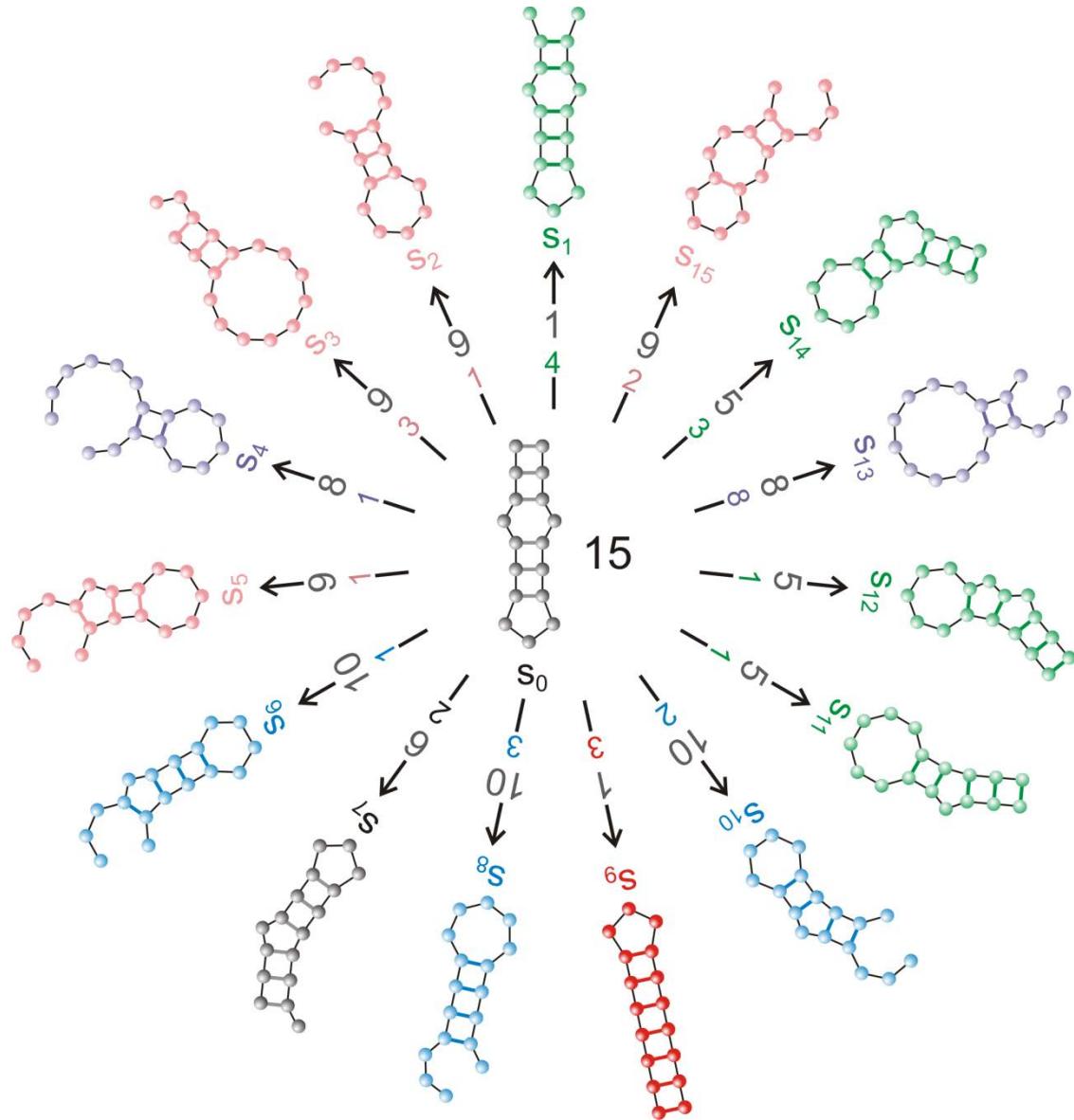
1 A-C



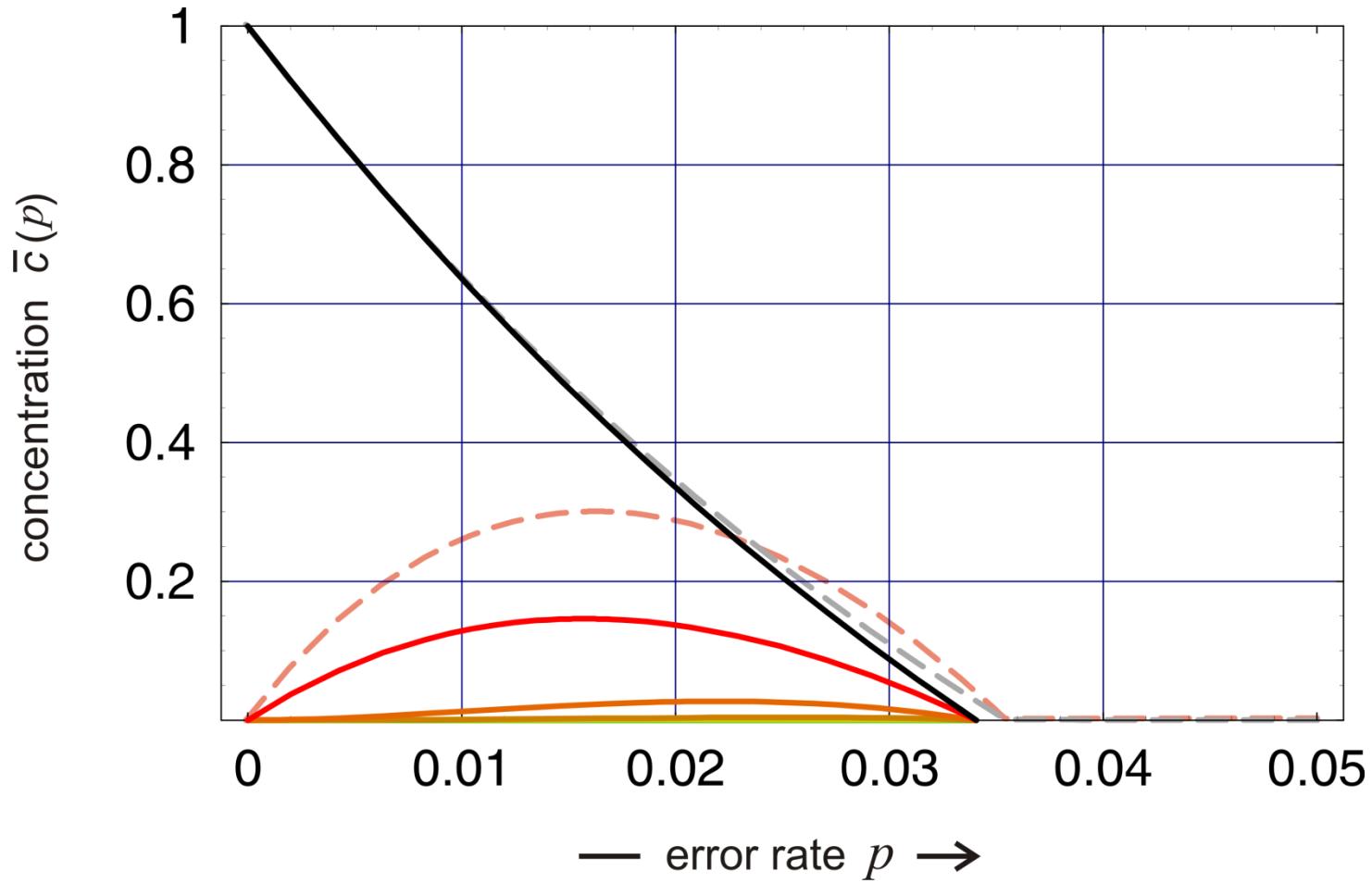
1 A-G



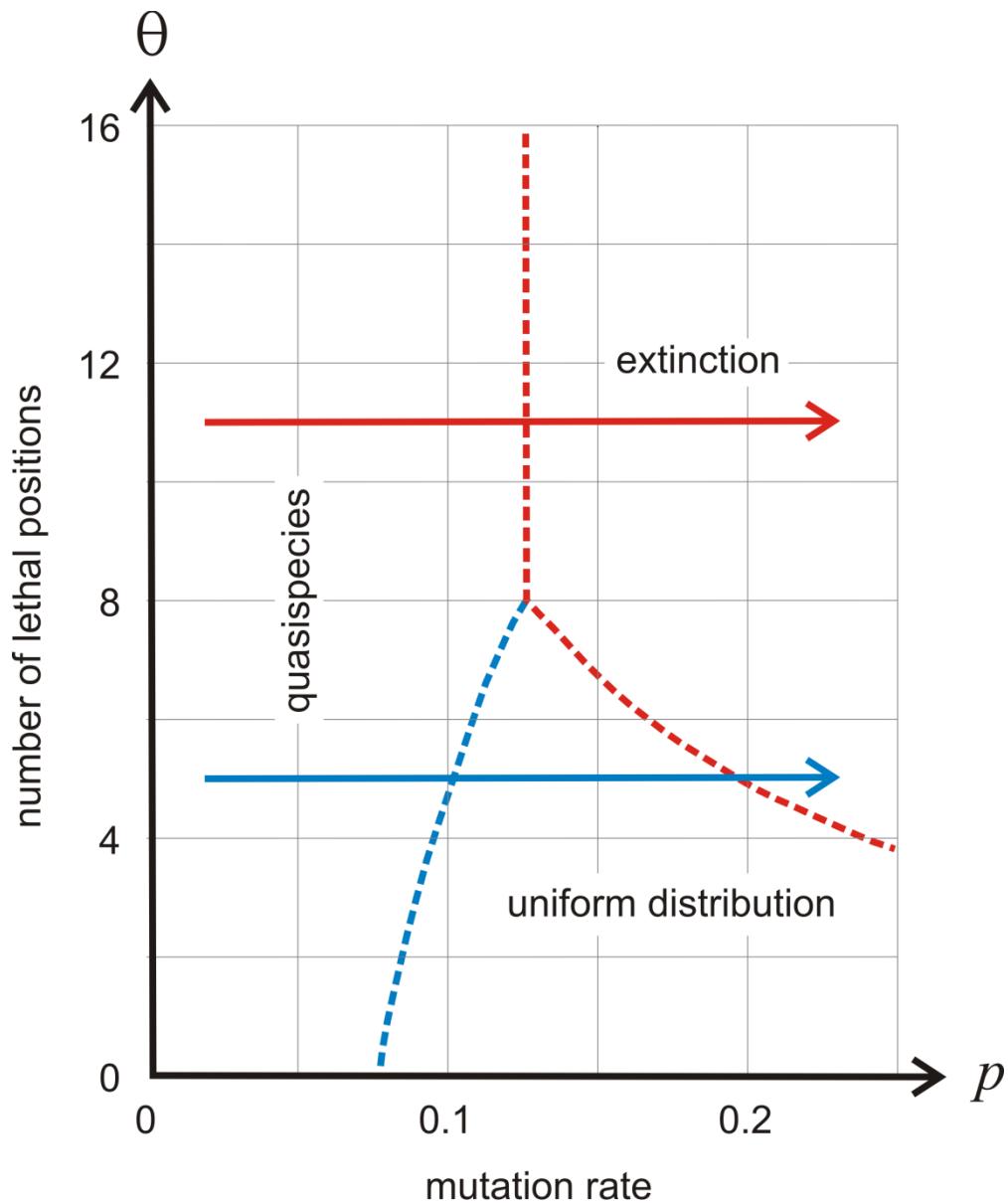




antiviral strategies and lethal mutagenesis



lethality threshold and quasispecies



H.Tejero, A.Marín, F.Moran. 2010.
Effect of lethality on the extinction and on
the error threshold of quasispecies.
J.Theor.Biol. **262**:733-741.

quasispecies, error threshold, and lethal mutagenesis

Thank you for your attention!

Web-Page for further information:

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

