# From Belief to Facts in the Theory of Evolution

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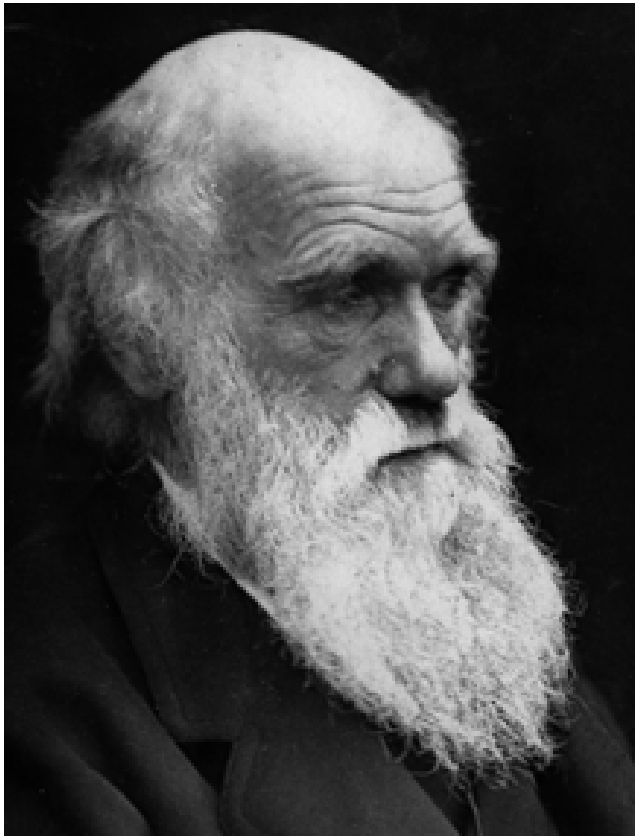
http://www.tbi.univie.ac.at/~pks

1. **Theory of evolution, science, and religion**

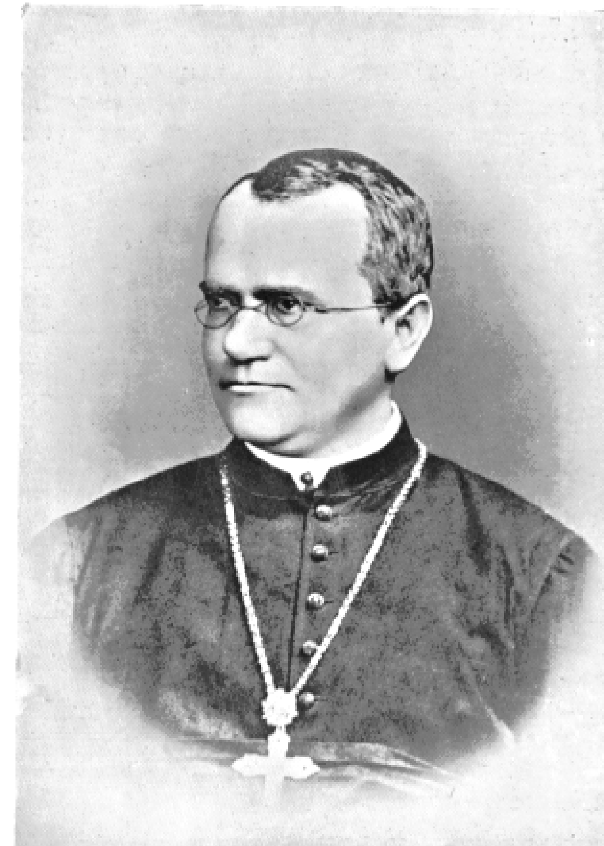
2. **Genetics and the theory of evolution**

3. **Evolution experiments in the laboratory**

4. **Molecular genetics and the tree of life**



Charles Robert Darwin, 1809-1882

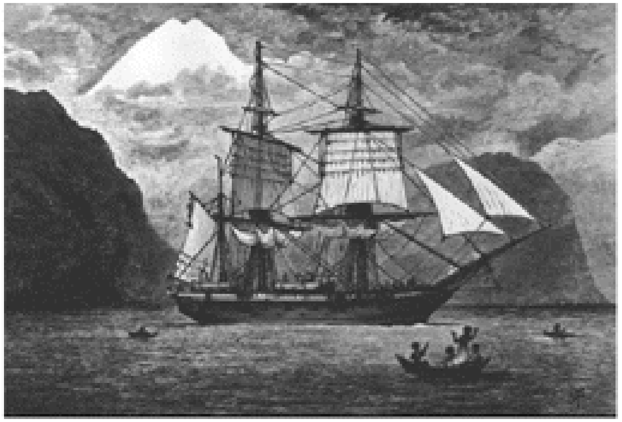


Gregor Mendel, 1822-1884,
Abbot of the Augustinian Monastery in Brünn

The two great scholars in nineteenth century biology

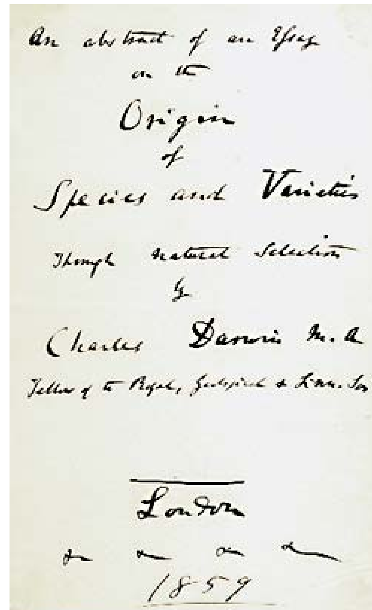

The University of Chicago Press: Chicago, 1979

The publication of the „Origin of Species“ was well prepared by Charles Darwin and his scientific friends. The conclusions of Alfred Russel Wallace drawn from observations made in Brazil (Amazon territory, 1848-1852) and in Indonesia (Malayan Archipelago, 1854-1862) were close to Darwin‘s thoughts, who did his systematic studies during the voyage around the world on HMS Beagle (1831-1836). Competition with Wallace urged Darwin to publish his comprehensive book.



HMS Beagle

Charles Robert Darwin, 1809-1882


An abstract of an Essay
on the
Origin
of
Species and Varieties
Through natural Selection
by
Charles Darwin M.A.
Fellow of the Royal, Geological & Linn. Soc.
London
1859

Earlier abstract of the ‚Origin of Species‘

Alfred Russell Wallace, 1823-1913

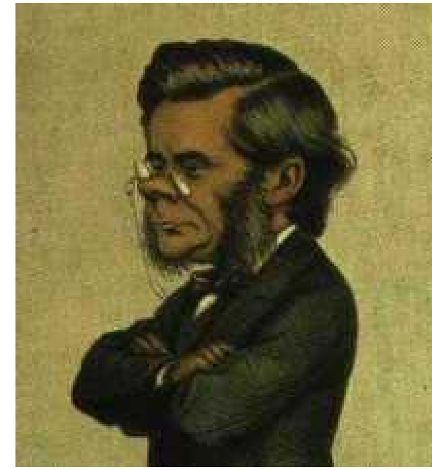
The two competitors in the formulation of evolution by natural selection

Samuel Wilberforce, 1805-1873,

asked Huxley whether it was through his grandfather or his grandmother that he claimed descent from monkeys.

British Association for the Advancement of Science: Meeting, Oxford 1860

Darwin, 1809-1882,
On the Origin of Species by Means of Natural Selection; or the Preservation of Favored Races in the Struggle for Life,
First edition, 24.11.1859,
London: John Murray, Albemarle Street



Thomas Henry Huxley, 1825-1895,

replied that if faced with the question, „would I rather have a miserable ape for a grandfather, or a man highly endowed by nature and possessed of great means and influence, and yet who employs these faculties and that influence to the mere purpose of introducing ridicule into a grave scientific discussion – I unhesitatingly affirm my preference for the ape.“

The Bishop Wilberforce –Huxley debate: Oxford, 30.06.1860

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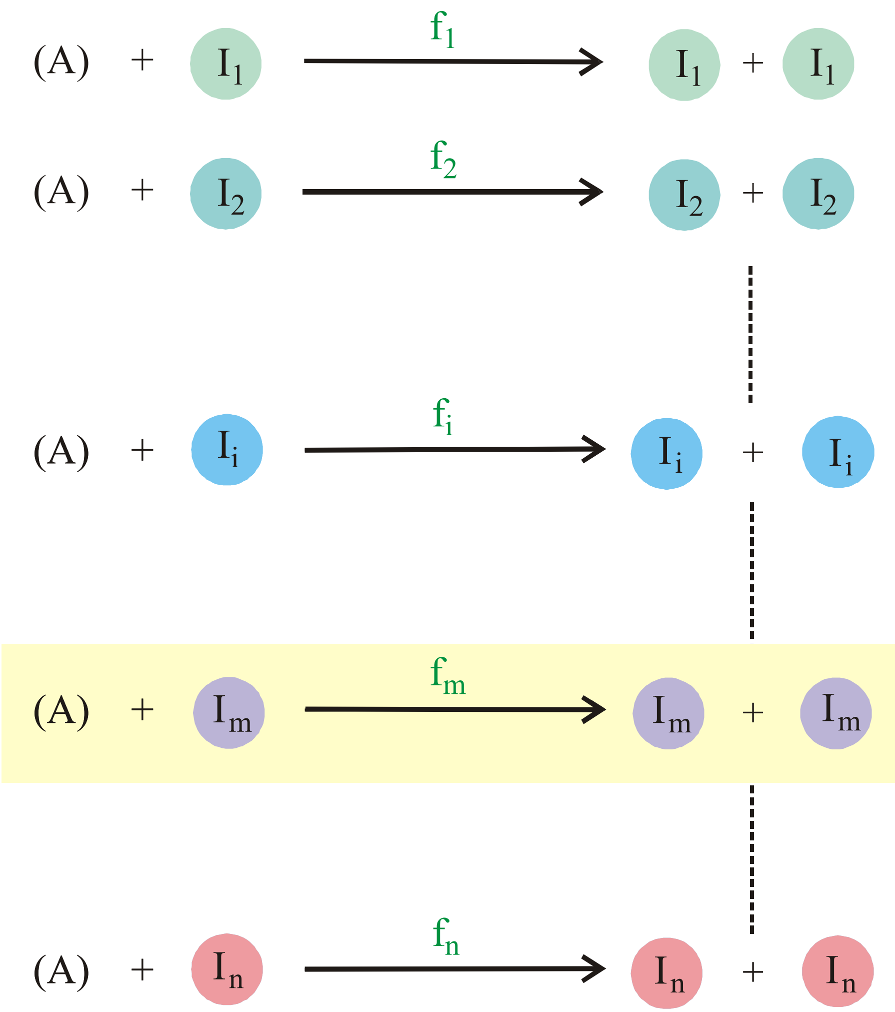



$dx_i / dt = f_i x_i - x_i \Phi = x_i (f_i - \Phi)$

$\Phi = \Sigma_j f_j x_j$ ; $\Sigma_j x_j = 1$ ; $i,j = 1,2,\ldots,n$

$[I_i] = x_i$ Æ 0 ; $i = 1,2,\ldots,n$ ;

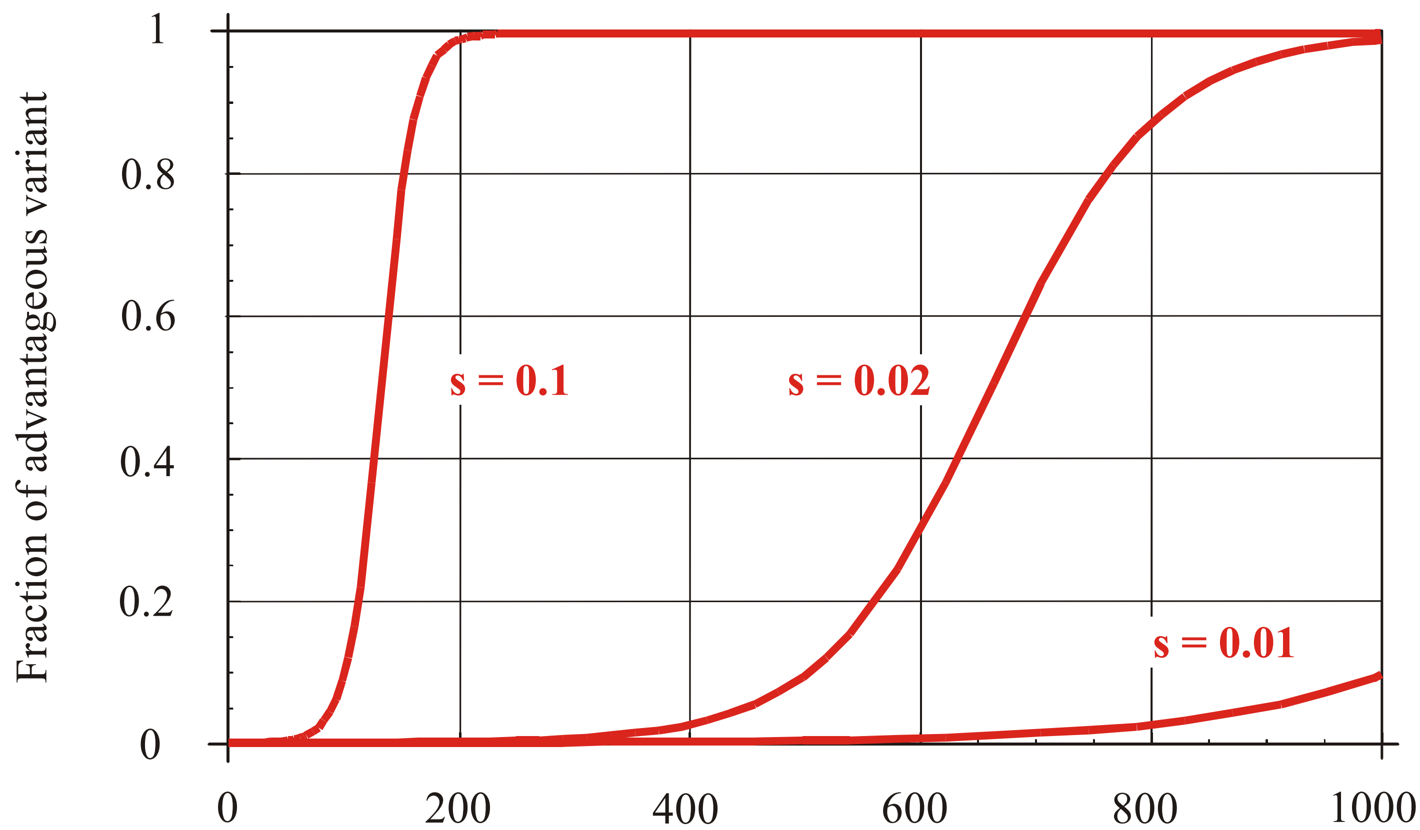
$[A] = a =$ constant

$f_m = \max \{f_j ; j=1,2,\ldots,n\}$

$x_m(t)$ Á 1 for t Á ¸

**Reproduction of individuals** as basis of selection

$\mathbf{s} = (f_2 - f_1)\,/\,f_1;\ f_2 > f_1\ ;\ x_1(0) = 1 - 1/N\ ;\ x_2(0) = 1/N$



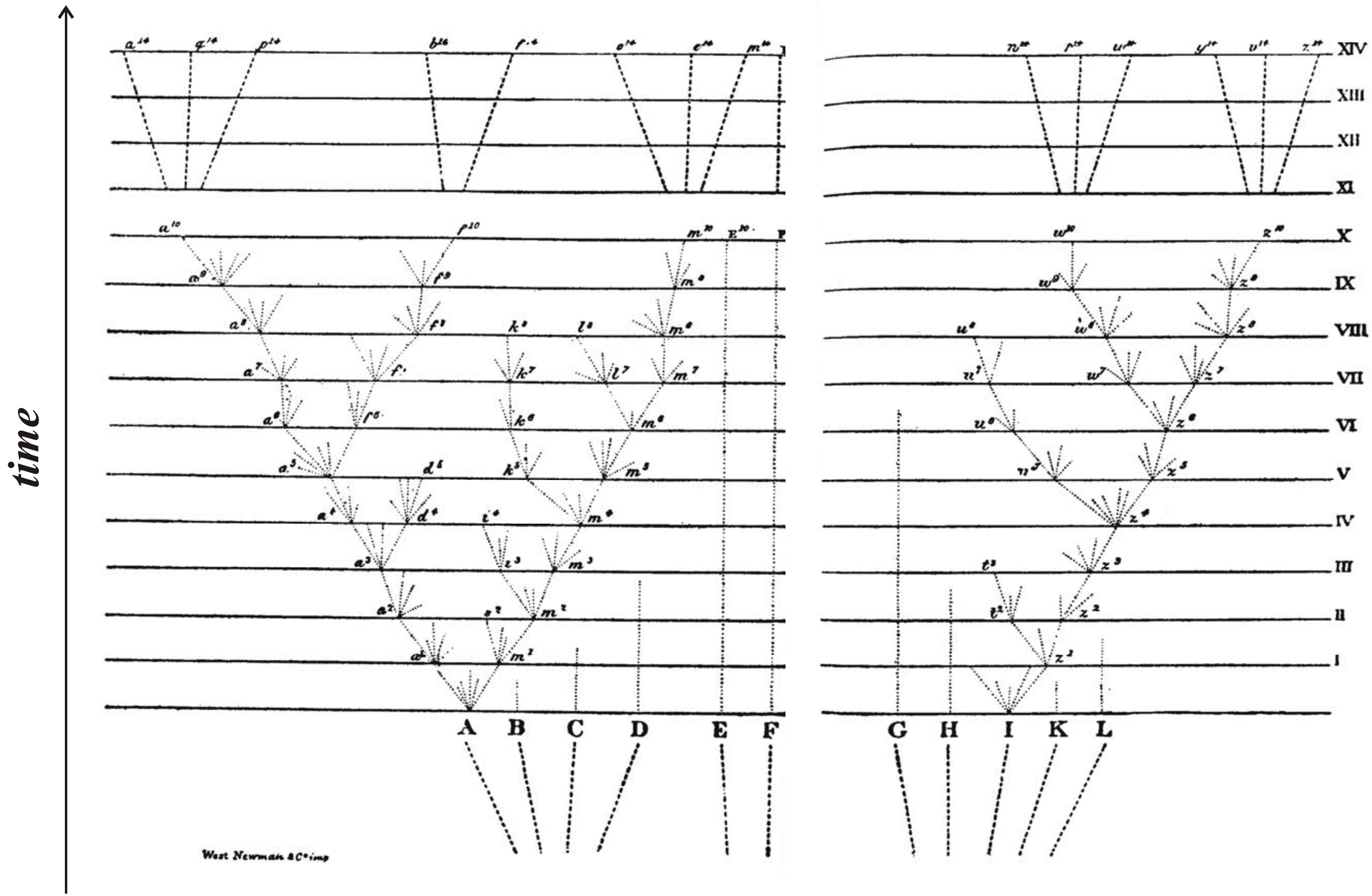

Selection of advantageous mutants in populations of N = 10 000 individuals

**Key ingredients in Darwin's theory of evolution are**:

(i) **Variations** occurring spontaneously and not themselves produced by the environment,

(ii) **Competition** for resources, so that only the best adapted survive to reproduce, and, therefore

(iii) **Selection** by the environment, of which variants will survive and increase in number.




Charles Darwin, *The Origin of Species*, 6th edition.
Everyman's Library, Vol.811, Dent London, pp.121-122.

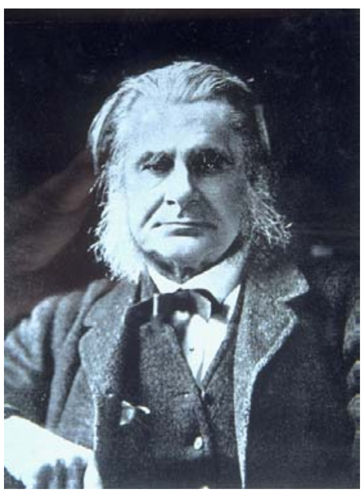
Etienne Geoffroy Saint-Hillaire, 1772-1844

Charles Robert Darwin, 1809-1882

Erasmus Darwin, 1731-1802

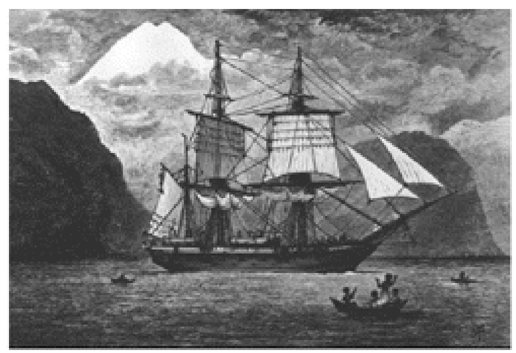
Alfred Russel Wallace, 1823-1913

Jean Baptiste Pierre Antoine de Monet, Chevalier de Lamarck, 1744-1829



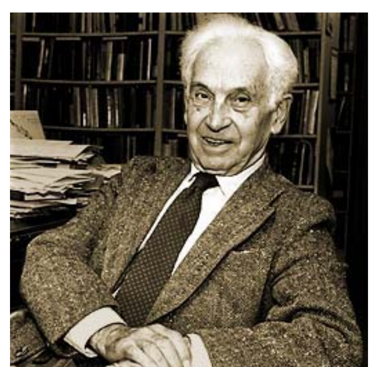
Thomas Henry Huxley, 1825-1895

HMS Beagle, 1831-1836



Joseph Dalton Hooker, 1817-1911

# The ‚Evolutionists‘



Ernst Mayr, 1904 -

John Frederick William Herschel, 1792-1871

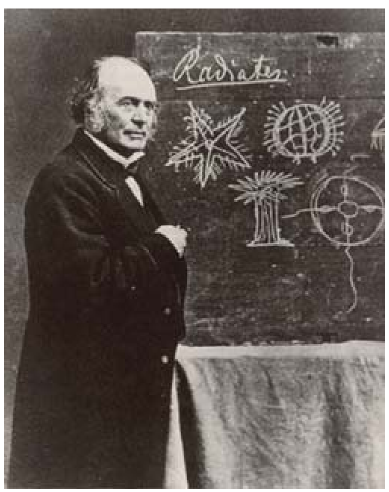
Sir Charles Lyell, 1797-1875

‚Borderline Evolutionists‘ (Michael Ruse, The Darwinian Revolution, 1979)

Georges Cuvier, 1769-1832

Bishop Samuel Wilberforce, 1805-1873

Richard Owen, 1804-1892

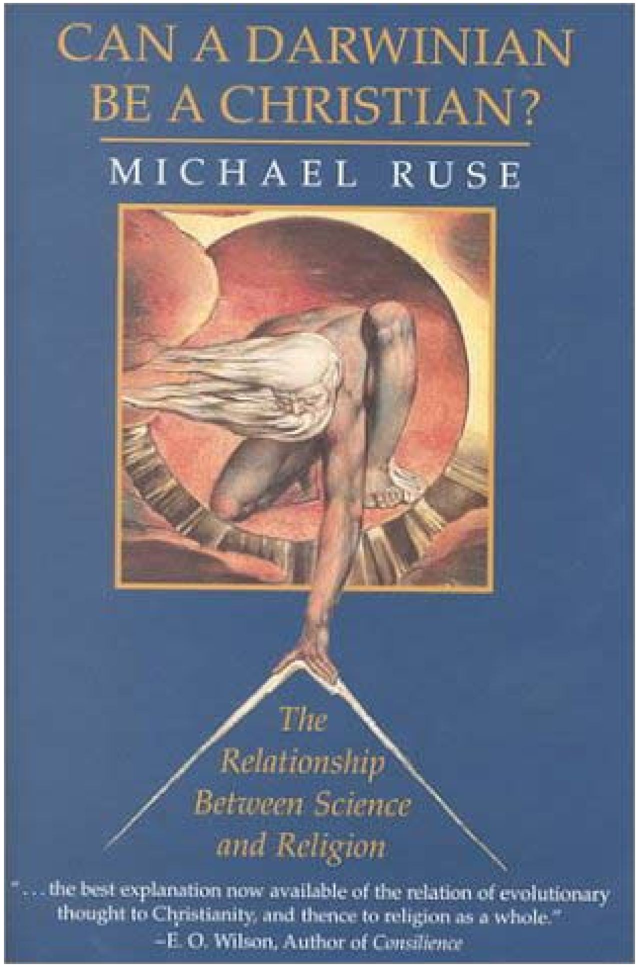



Jean Louis Rodolphe Agassiz, 1807-1873

Adam Sedgwick, 1785-1873

William Whewell, 1794-1866

The ‚Anti-Evolutionists‘




Cambridge University Press,
New York 2002

Science – Religion debate in the 21st Century:

| **Science** | **Religion** |
| --- | --- |
| Richard Dawkins,<br>Stephen J. Gould,<br>E.O. Wilson | Arthur Peacocke,<br>Robert J. Russell,<br>Keith Ward |

Michael Ruse argues, that although it is at times difficult for a Darwinian to embrace Christian belief, it is by no means inconceivable. At the same he suggests ways in which a Christian believer should have no difficulty accepting evolution in general, and Darwinism in particular.

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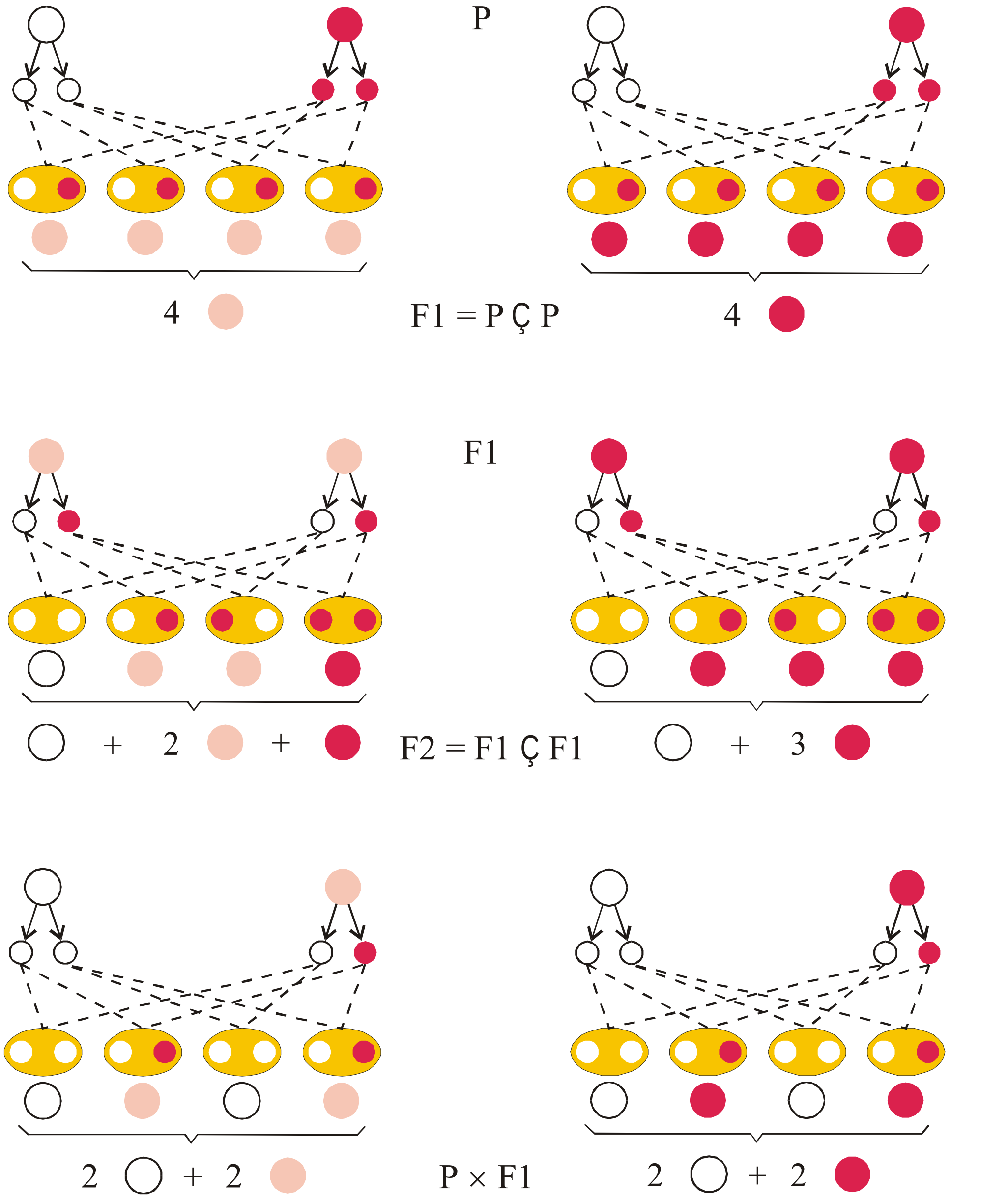
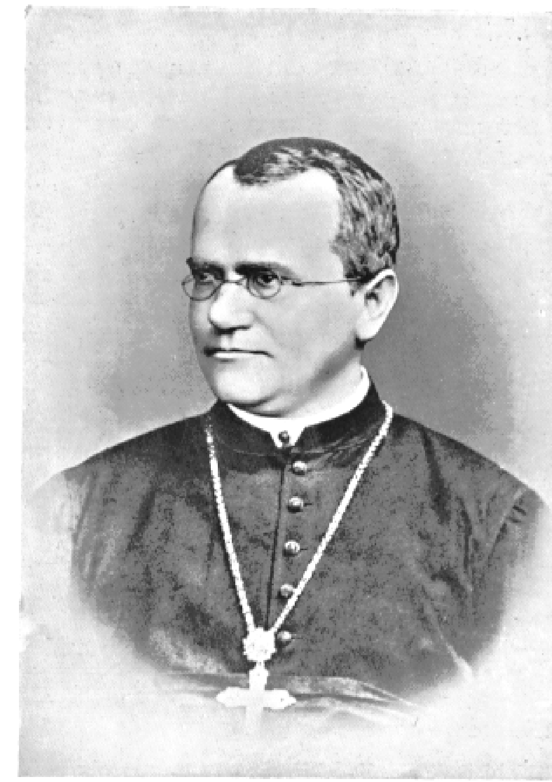


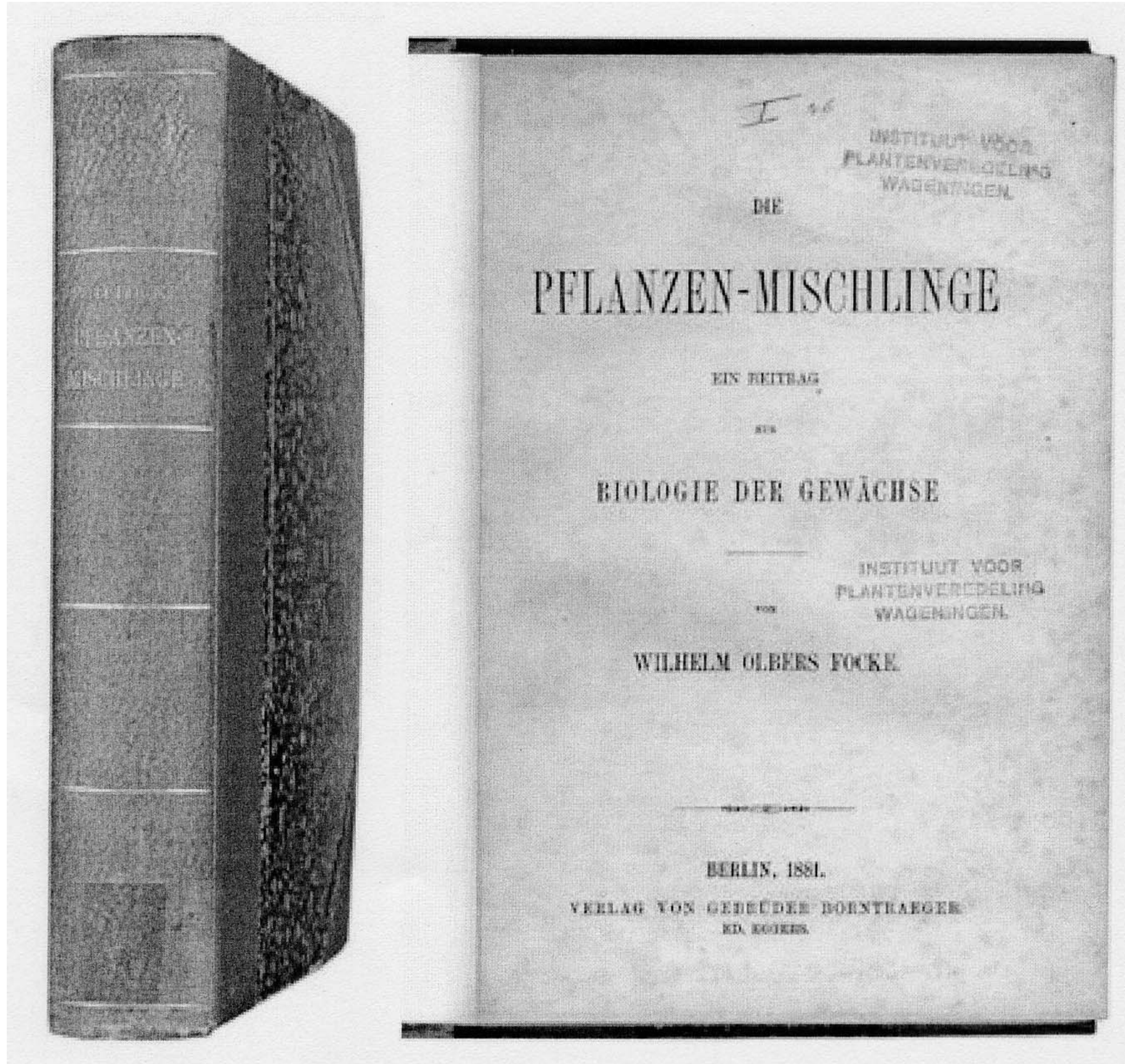

Intermediate pair of alleles

Dominant/recessive pair of alleles



## Gregor Mendels laws of inheritance:

Versuche über Pflanzen-Hybriden.
*Verhandlungen des naturforschenden Vereins in Brünn*, **4**: 3-47 (1865)
Presented at the Meetings of 08.02. and 08.03.1965




Mendel‘s work cited 1881
in W.O. Focke‘s
„*Die Pflanzen-Mischlinge*“

Sir Ronald Aylmer Fisher, 1890-1962

John Burdon Sanderson Haldane, 1892-1964

Sewall Wright, 1889-1988

The three scholars of theoretical population biology

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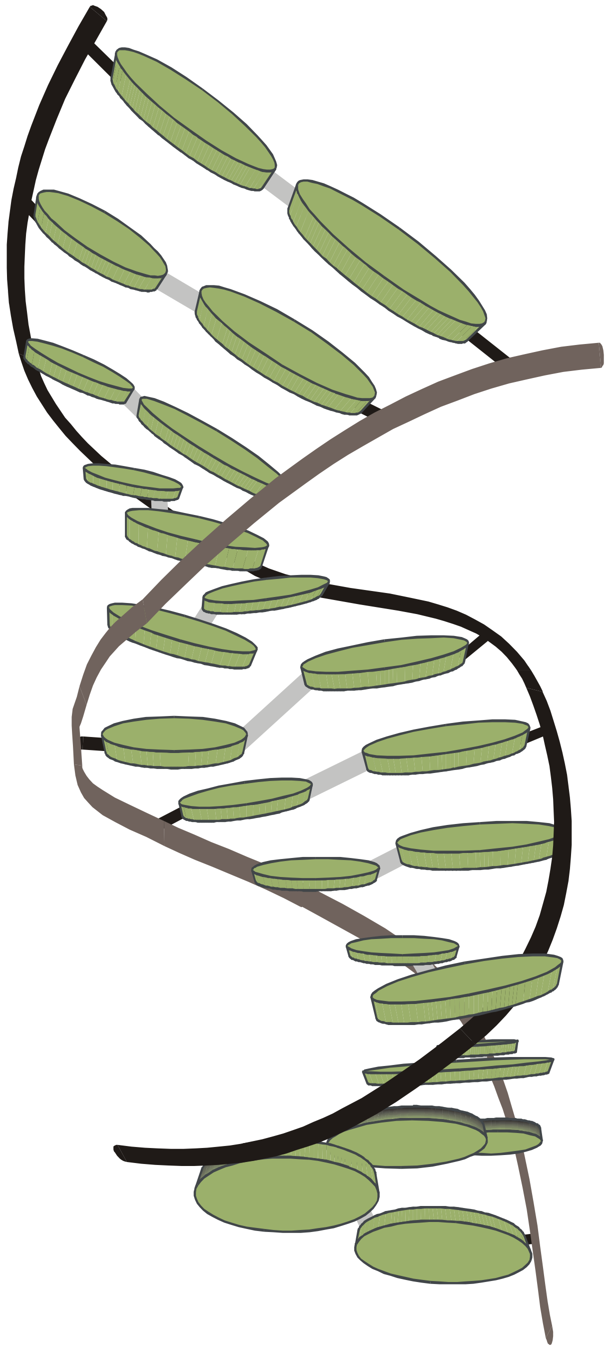
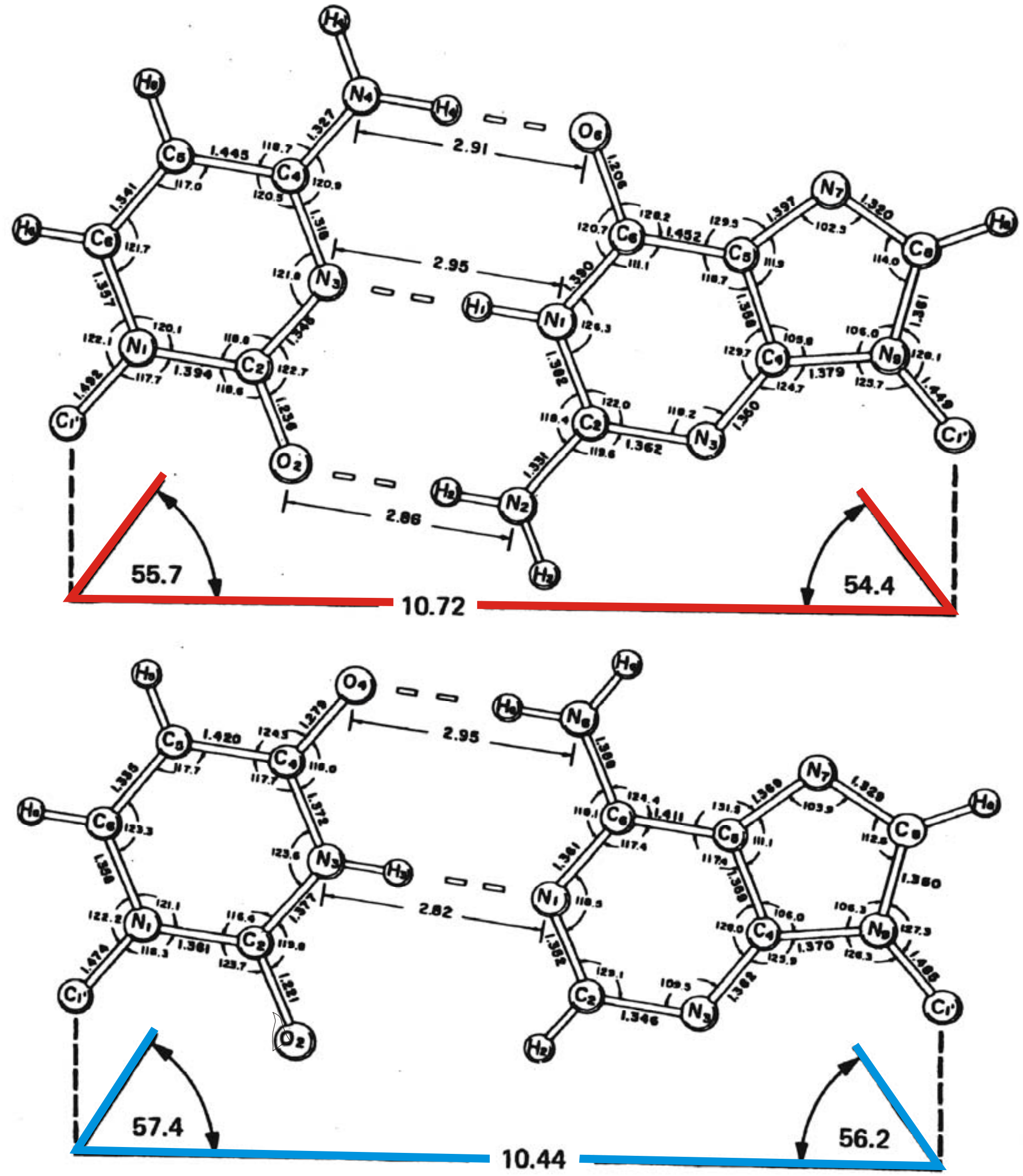


James D. Watson, 1928- , and Francis Crick, 1916- ,
Nobel Prize 1962

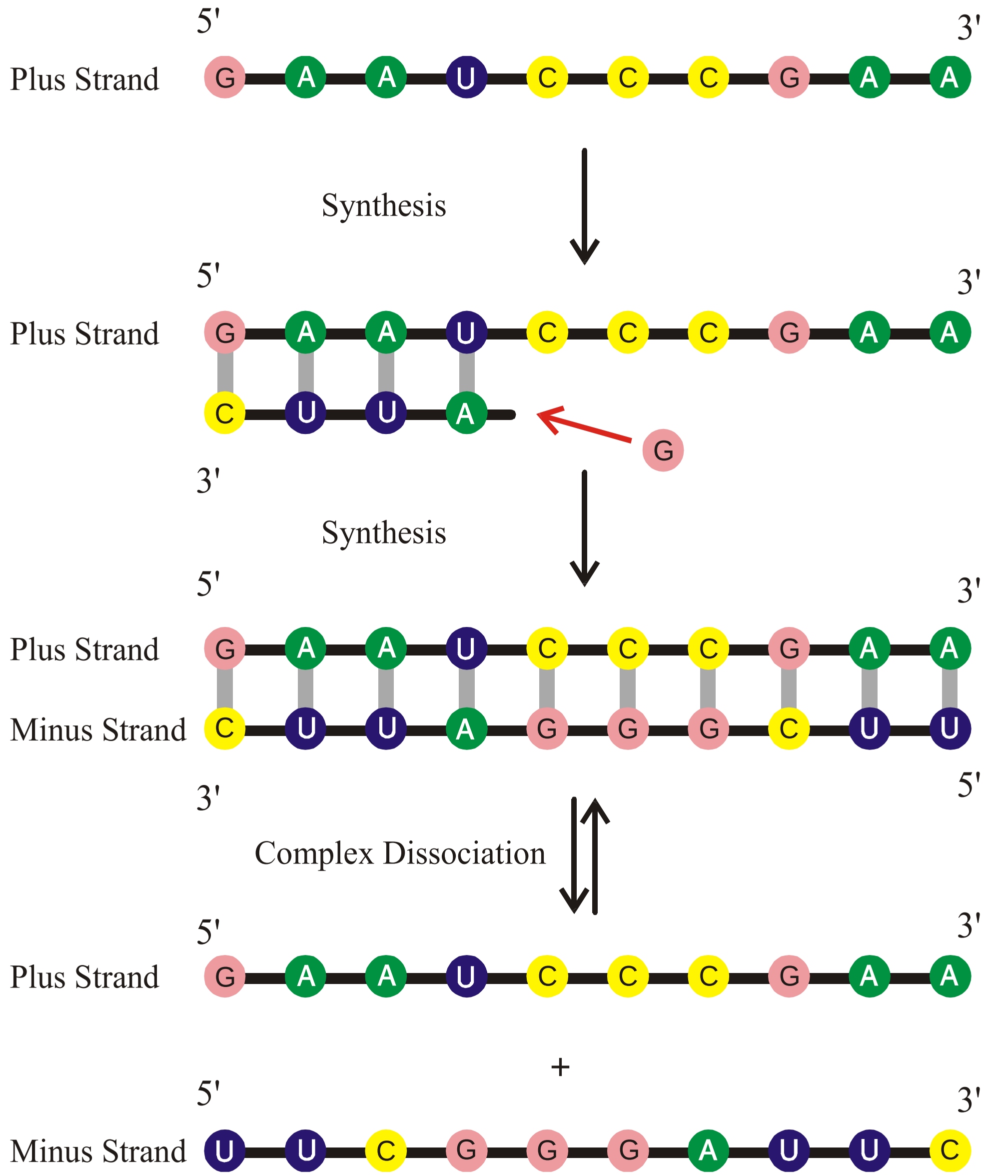
The three-dimensional structure of a short double helical stack of B-DNA




Canonical Watson-Crick base pairs:

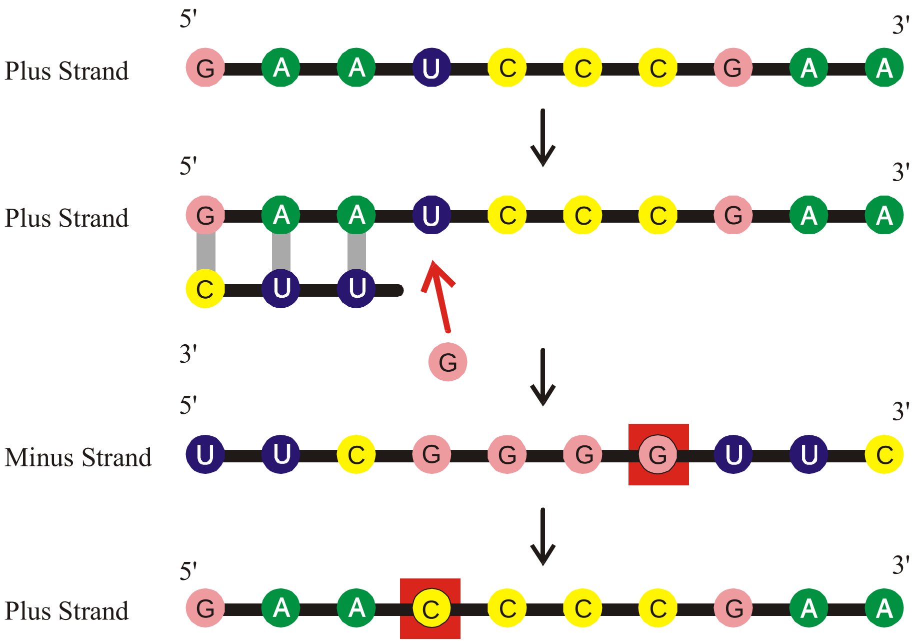
cytosine – guanine
uracil – adenine

W.Saenger, Principles of Nucleic Acid Structure, Springer, Berlin 1984




**Complementary replication** as the simplest copying mechanism of RNA Complementarity is determined by Watson-Crick base pairs:

G Í C and A=U




**Point Mutation**

GAAUCCCGAA → GAAUCCCGUCCCGAA

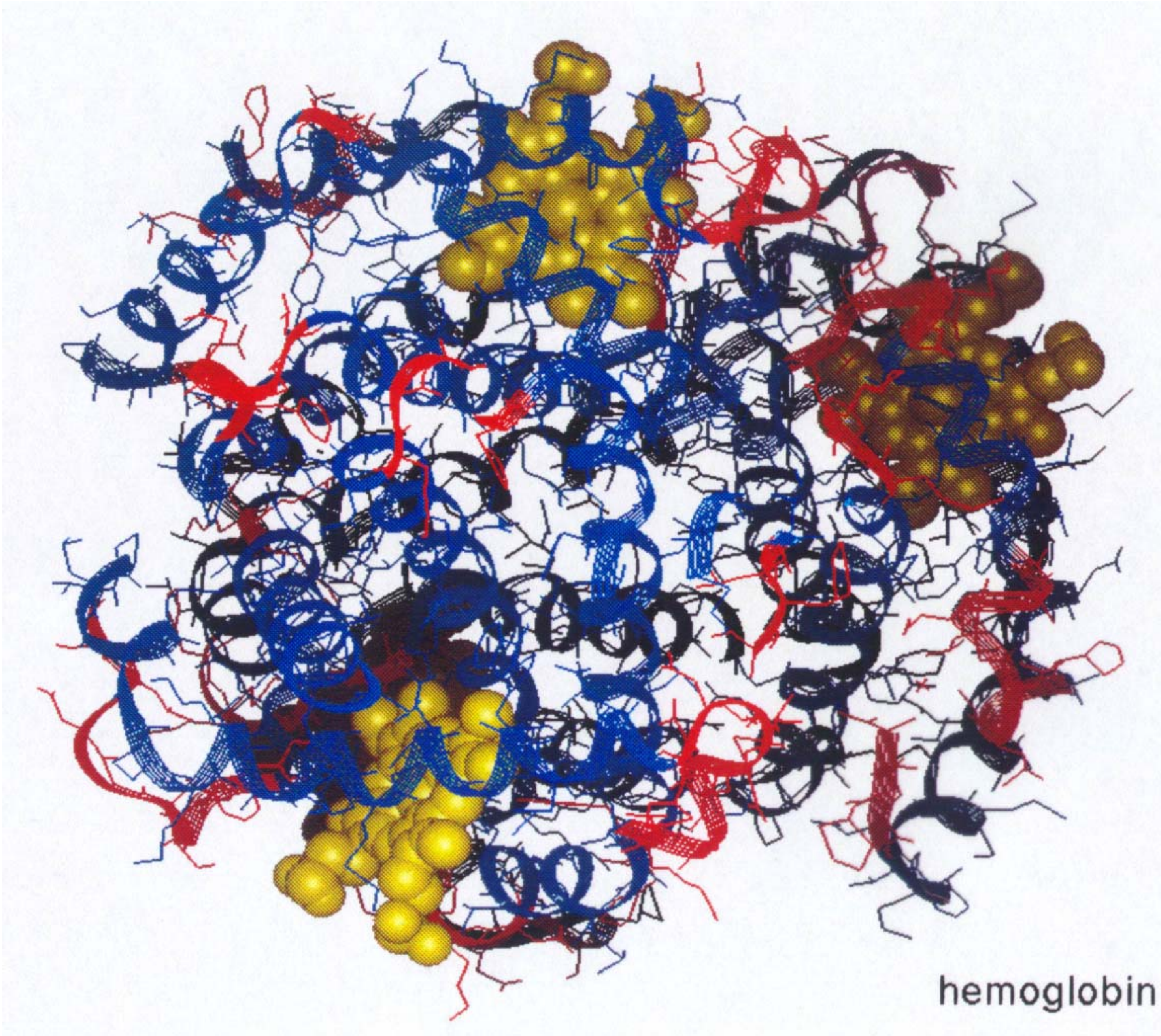
**Insertion**

GAAUCCCGAA → GAAUCCA

**Deletion**

**Mutations** in nucleic acids represent the mechanism of **variation** of **genotypes**.

Max Perutz, 1914-2002, at the opening
of the Max Perutz-Library, Vienna
BioCenter, in 1994
Nobel Prize 1962


hemoglobin

## Evolution of RNA molecules based on Qβ phage


D.R.Mills, R.L.Peterson, S.Spiegelman, ***An extracellular Darwinian experiment with a self-duplicating nucleic acid molecule***. Proc.Natl.Acad.Sci.USA **58** (1967), 217-224

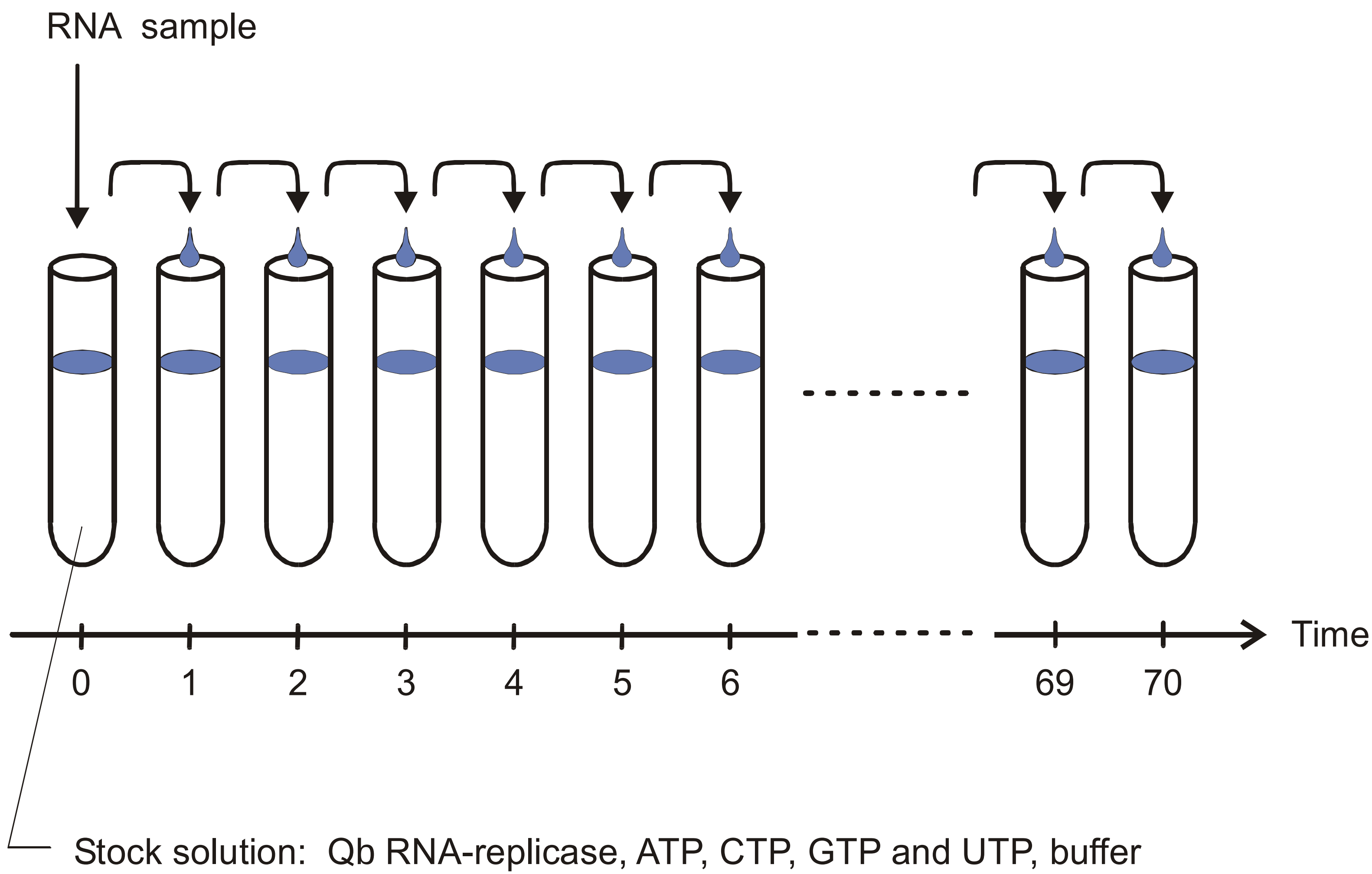
S.Spiegelman, ***An approach to the experimental analysis of precellular evolution***. Quart.Rev.Biophys. **4** (1971), 213-253

C.K.Biebricher, ***Darwinian selection of self-replicating RNA molecules***. Evolutionary Biology **16** (1983), 1-52

G.Bauer, H.Otten, J.S.McCaskill, ***Travelling waves of*** **in vitro** ***evolving RNA.*** *Proc.Natl.Acad.Sci.USA* **86** (1989), 7937-7941

C.K.Biebricher, W.C.Gardiner, ***Molecular evolution of RNA*** **in vitro**. Biophysical Chemistry **66** (1997), 179-192

G.Strunk, T.Ederhof, ***Machines for automated evolution experiments*** **in vitro** ***based on the serial transfer concept***. Biophysical Chemistry **66** (1997), 193-202




The serial transfer technique applied to RNA evolution ***in vitro***

Reproduction of the original figure of the serial transfer experiment with Qβ RNA

D.R.Mills, R,L,Peterson, S.Spiegelman, *An extracellular Darwinian experiment with a self-duplicating nucleic acid molecule*. Proc.Natl.Acad.Sci.USA **58** (1967), 217-224

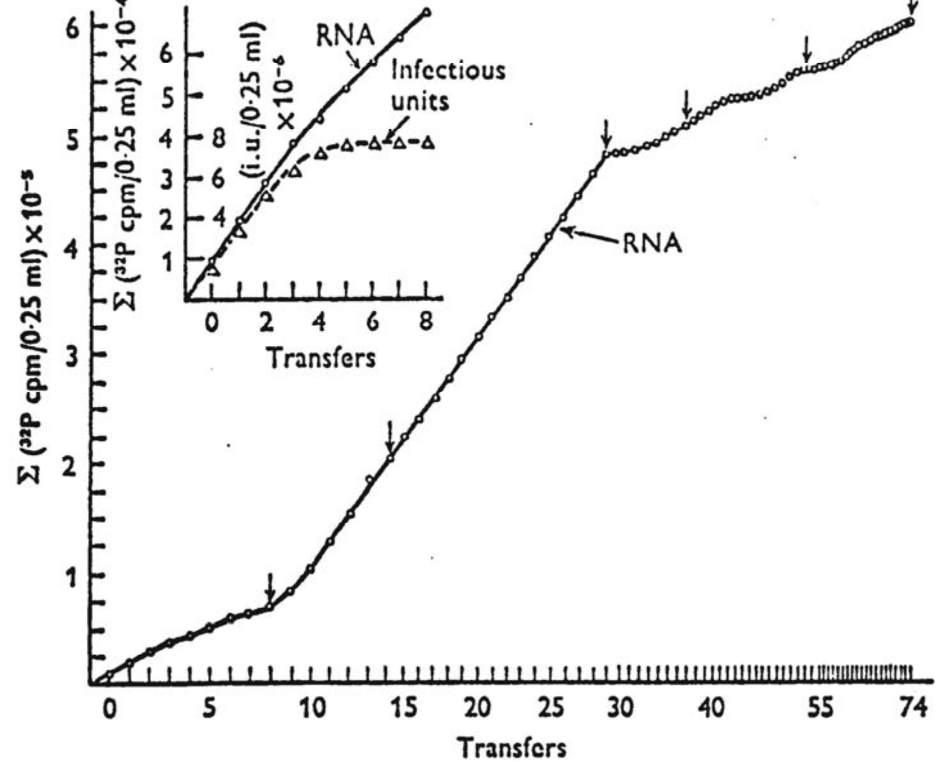
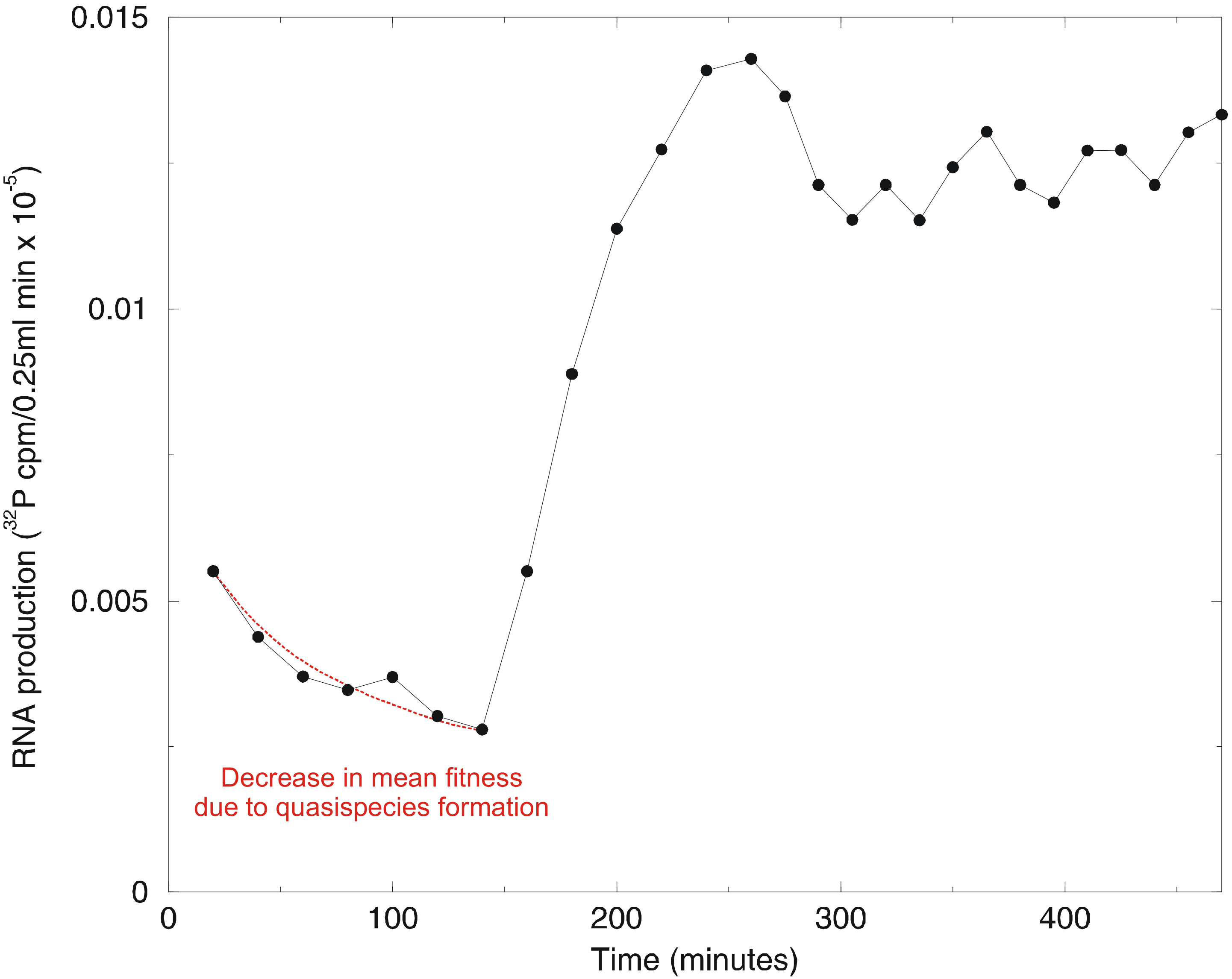



Fig. 9. Serial transfer experiment. Each 0·25 ml standard reaction mixture contained 40 μg of Qβ replicase and ³²P-UTP. The first reaction (0 transfer) was initiated by the addition of 0·2 μg ts-1 (temperature-sensitive RNA) and incubated at 35 °C for 20 min, whereupon 0·02 ml was drawn for counting and 0·02 ml was used to prime the second reaction (first transfer), and so on. After the first 13 reactions, the incubation periods were reduced to 15 min (transfers 14–29). Transfers 30–38 were incubated for 10 min. Transfers 39–52 were incubated for 7 min, and transfers 53–74 were incubated for 5 min. The arrows above certain transfers (0, 8, 14, 29, 37, 53, and 73) indicate where 0·001–0·1 ml of product was removed and used to prime reactions for sedimentation analysis on sucrose. The inset examines both infectious and total RNA. The results show that biologically competent RNA ceases to appear after the 4th transfer (Mills *et al.* 1967).




The increase in RNA production rate during a serial transfer experiment

## Bacterial Evolution

S. F. Elena, V. S. Cooper, R. E. Lenski. ***Punctuated evolution caused by selection of rare beneficial mutants***. Science **272** (1996), 1802-1804

D. Papadopoulos, D. Schneider, J. Meier-Eiss, W. Arber, R. E. Lenski, M. Blot. ***Genomic evolution during a 10,000-generation experiment with bacteria***. Proc.Natl.Acad.Sci.USA **96** (1999), 3807-3812

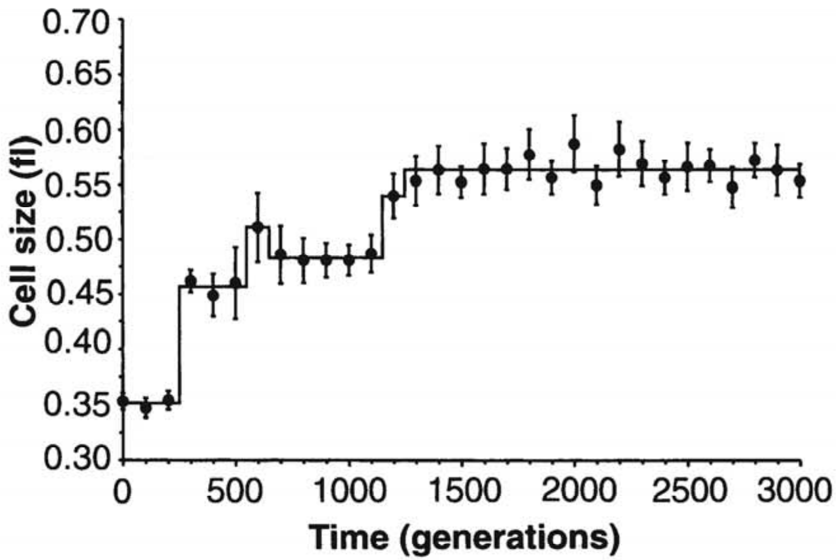



**Fig. 1.** Change in average cell size (1 fl = $10^{-15}$ L) in a population of *E. coli* during 3000 generations of experimental evolution. Each point is the mean of 10 replicate assays (*22*). Error bars indicate 95% confidence intervals. The solid line shows the best fit of a step-function model to these data (Table 1).

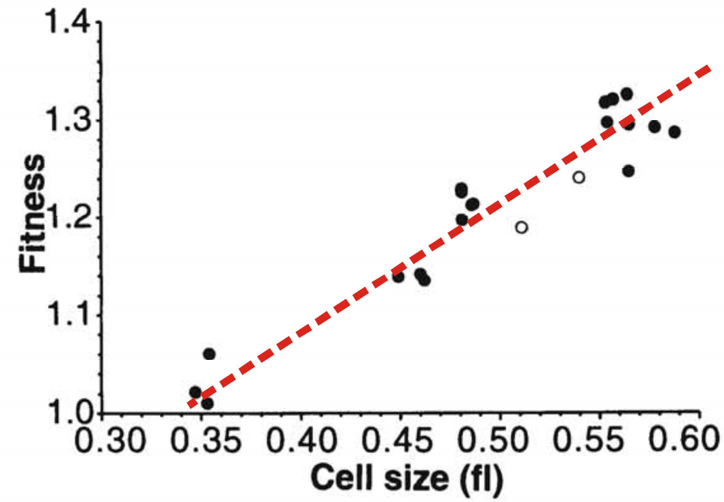



**Fig. 2.** Correlation between average cell size and mean fitness, each measured at 100-generation intervals for 2000 generations. Fitness is expressed relative to the ancestral genotype and was obtained from competition experiments between derived and ancestral cells (*6, 7*). The open symbols indicate the only two samples assigned to different steps by the cell size and fitness data.

Epochal evolution of bacteria in serial transfer experiments under constant conditions

S. F. Elena, V. S. Cooper, R. E. Lenski. *Punctuated evolution caused by selection of rare beneficial mutants*. Science **272** (1996), 1802-1804

# Evolutionary design of RNA molecules

D.B.Bartel, J.W.Szostak, **In vitro** ***selection of RNA molecules that bind specific ligands***. Nature **346** (1990), 818-822

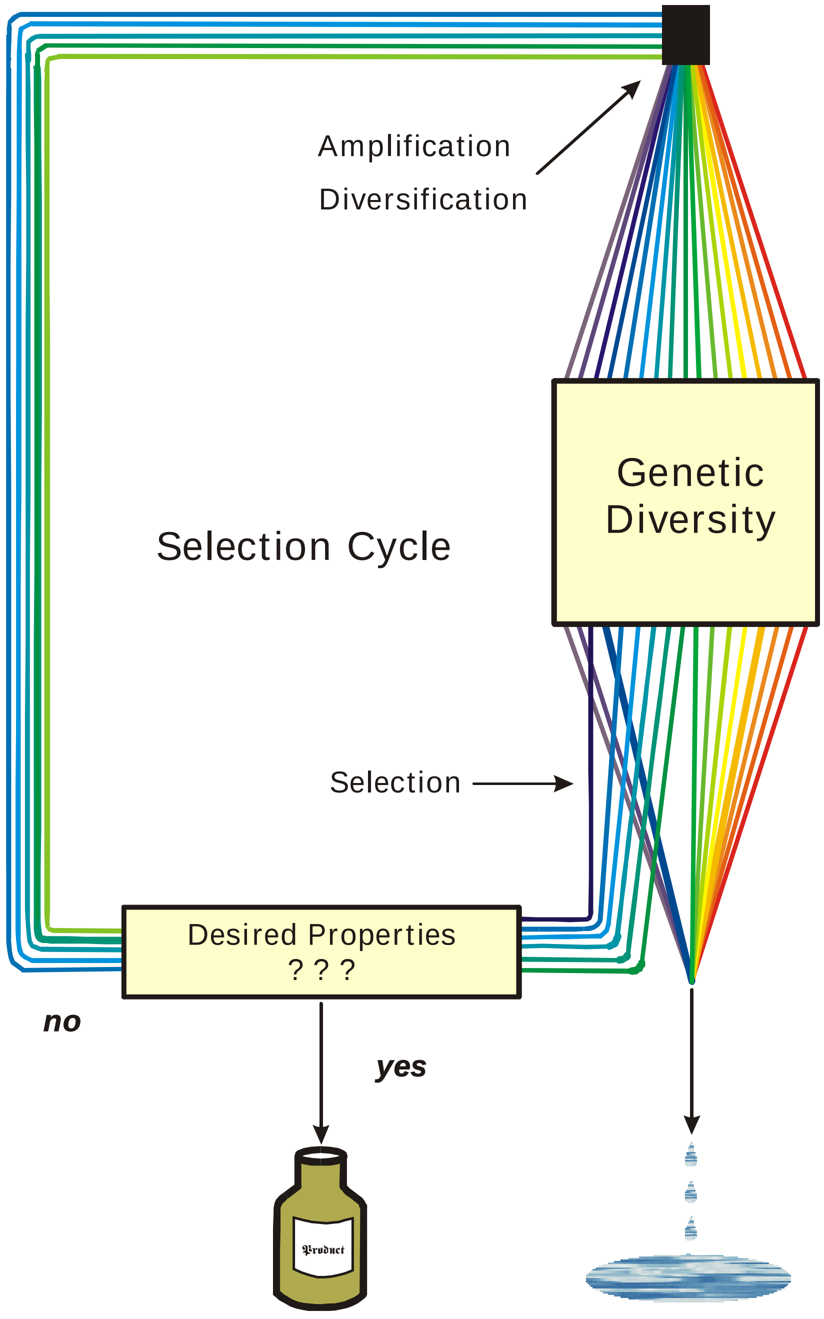
C.Tuerk, L.Gold, **SELEX** - ***Systematic evolution of ligands by exponential enrichment: RNA ligands to bacteriophage*** **T4** ***DNA polymerase***. Science **249** (1990), 505-510

D.P.Bartel, J.W.Szostak, ***Isolation of new ribozymes from a large pool of random sequences***. Science **261** (1993), 1411-1418

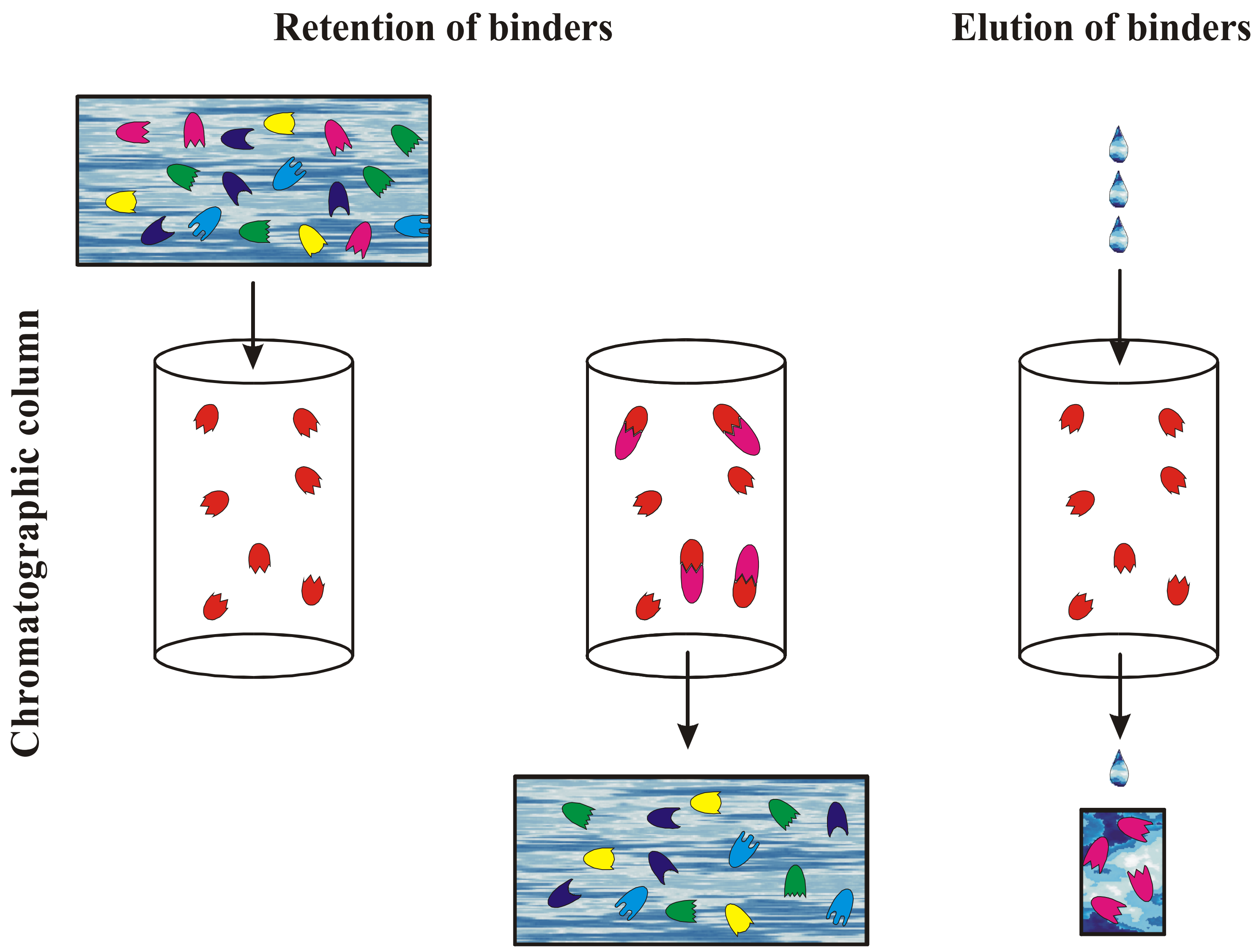
R.D.Jenison, S.C.Gill, A.Pardi, B.Poliski, ***High-resolution molecular discrimination by RNA***. Science **263** (1994), 1425-1429

Y.Wang, R.R.Rando, ***Specific binding of aminoglycoside antibiotics to RNA***. Chemistry & Biology **2** (1995), 281-290

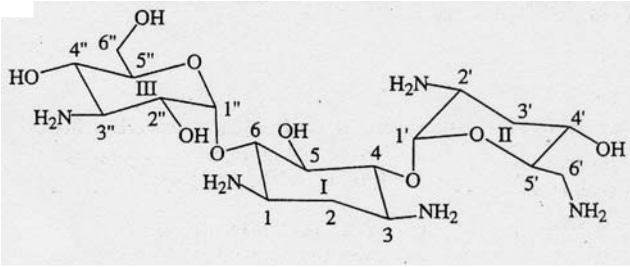
L.Jiang, A.K.Suri, R.Fiala, D.J.Patel, ***Saccharide-RNA recognition in an aminoglycoside antibiotic-RNA aptamer complex***. Chemistry & Biology **4** (1997), 35-50



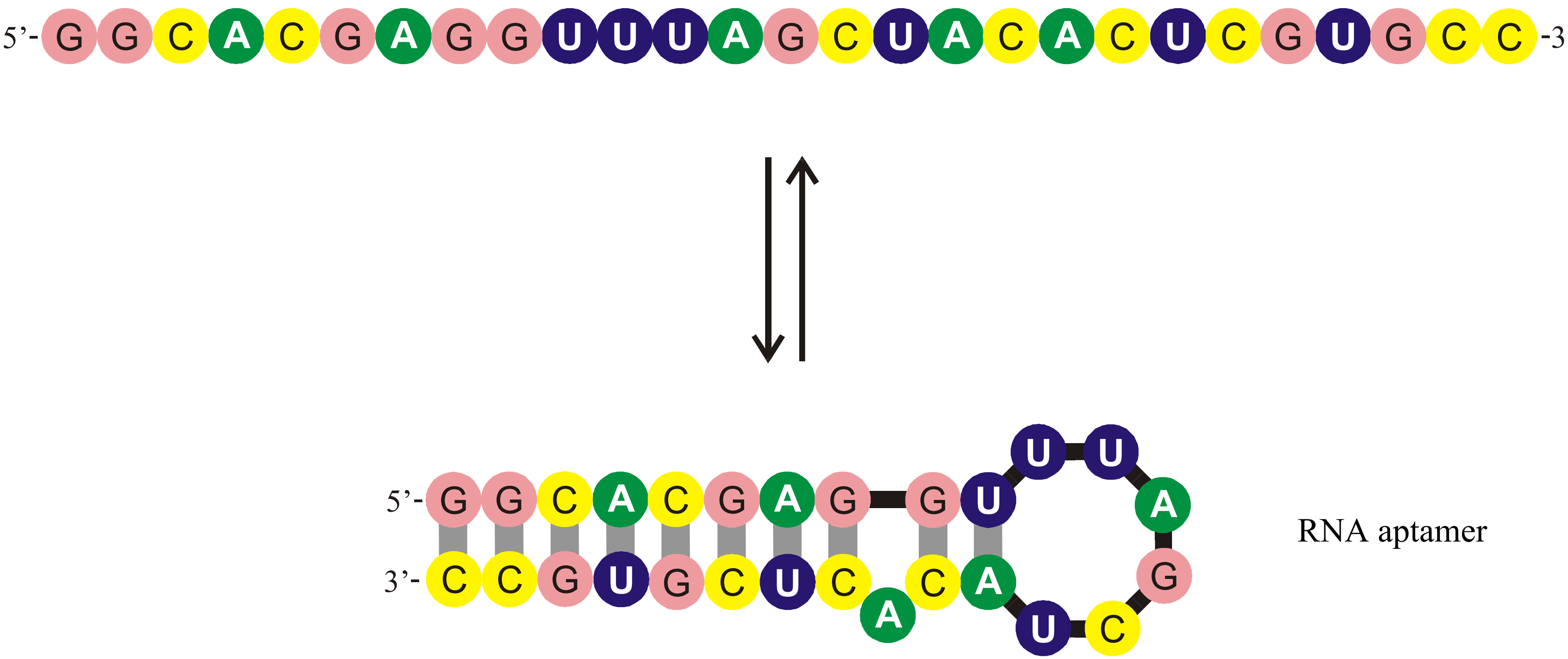

Selection cycle used in applied molecular evolution to design molecules with predefined properties




The SELEX technique for the evolutionary design of ***aptamers***



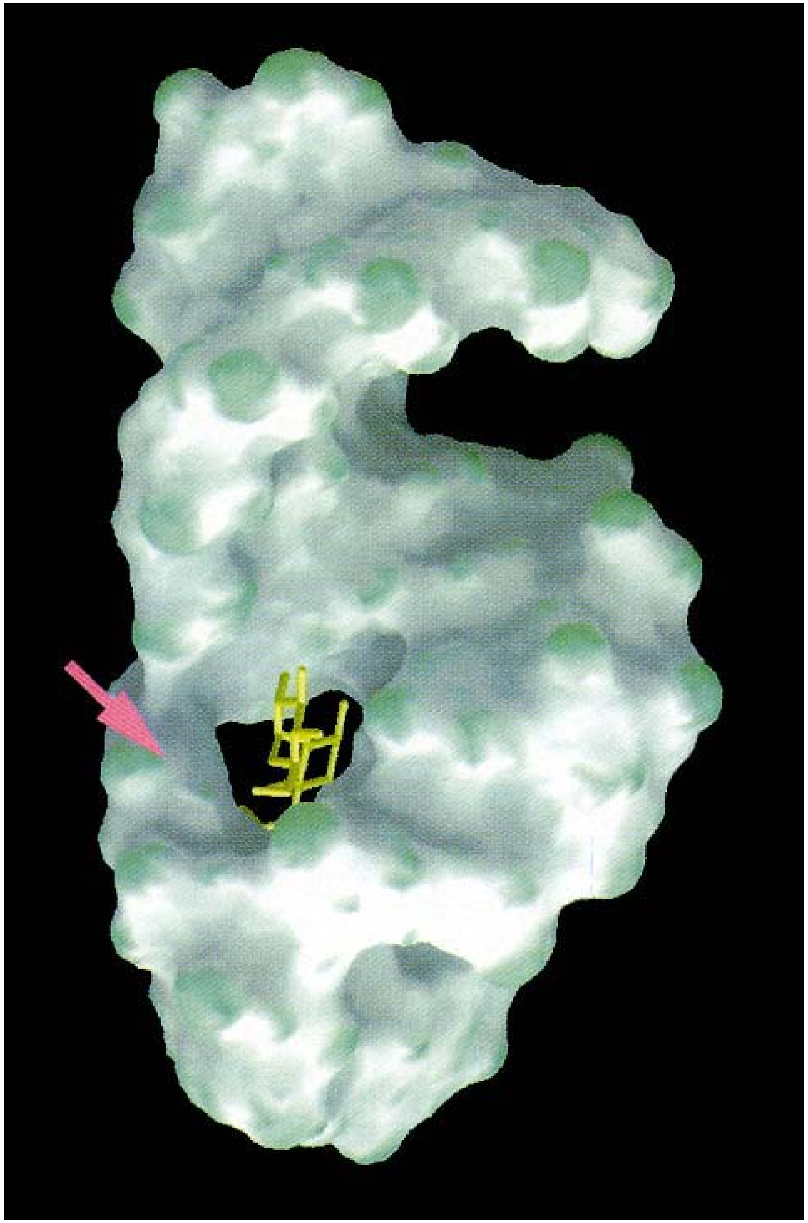

tobramycin




RNA aptamer

Formation of secondary structure of the tobramycin binding RNA aptamer

L. Jiang, A. K. Suri, R. Fiala, D. J. Patel, ***Saccharide-RNA recognition in an aminoglycoside antibiotic-RNA aptamer complex.*** Chemistry & Biology **4**:35-50 (1997)



The three-dimensional structure of the tobramycin aptamer complex

L. Jiang, A. K. Suri, R. Fiala, D. J. Patel, Chemistry & Biology **4**:35-50 (1997)

***No new principle will declare itself from below a heap of facts.***

Sir Peter Medawar, 1985

# Theory of molecular evolution

M.Eigen, ***Self-organization of matter and the evolution of biological macromolecules***. Naturwissenschaften **58** (1971), 465-526

C.J. Thompson, J.L. McBride, ***On Eigen's theory of the self-organization of matter and the evolution of biological macromolecules***. Math. Biosci. **21** (1974), 127-142

B.L. Jones, R.H. Enns, S.S. Rangnekar, ***On the theory of selection of coupled macromolecular systems.*** Bull.Math.Biol. **38** (1976), 15-28

M.Eigen, P.Schuster, ***The hypercycle. A principle of natural self-organization. Part A: Emergence of the hypercycle***. Naturwissenschaften **58** (1977), 465-526

M.Eigen, P.Schuster, ***The hypercycle. A principle of natural self-organization. Part B: The abstract hypercycle***. Naturwissenschaften **65** (1978), 7-41

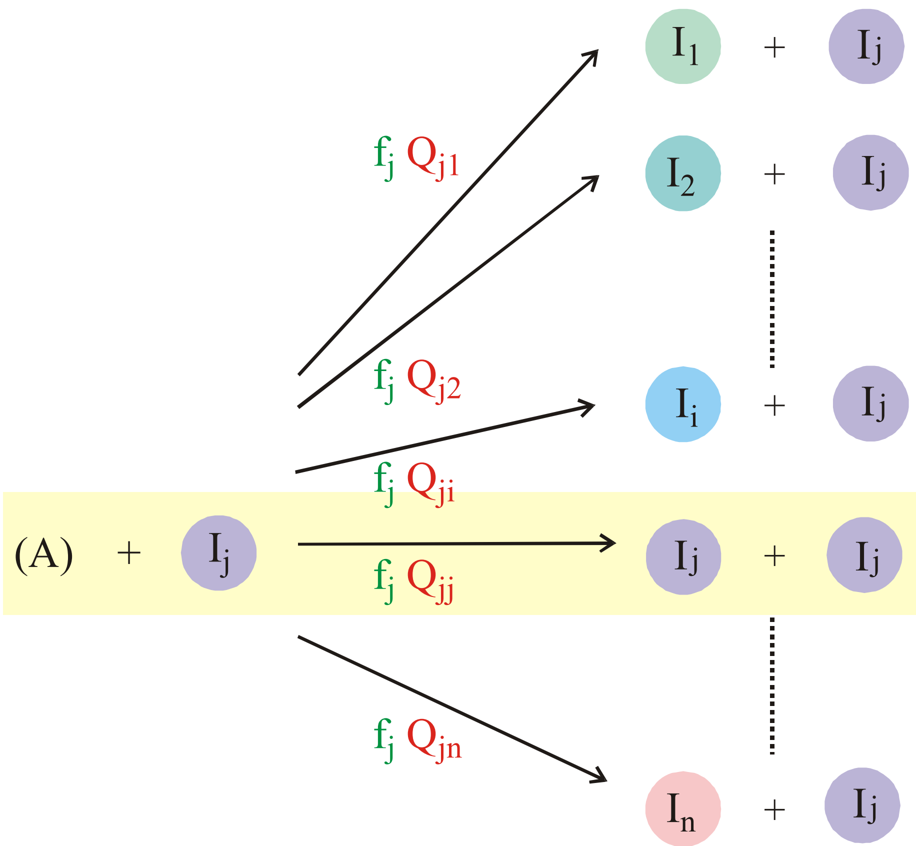
M.Eigen, P.Schuster, ***The hypercycle. A principle of natural self-organization. Part C: The realistic hypercycle***. Naturwissenschaften **65** (1978), 341-369

J. Swetina, P. Schuster, ***Self-replication with errors - A model for polynucleotide replication.*** Biophys.Chem. **16** (1982), 329-345

J.S. McCaskill, ***A localization threshold for macromolecular quasispecies from continuously distributed replication rates***. J.Chem.Phys. **80** (1984), 5194-5202

M.Eigen, J.McCaskill, P.Schuster, ***The molecular quasispecies***. Adv.Chem.Phys. **75** (1989), 149-263

C. Reidys, C.Forst, P.Schuster, ***Replication and mutation on neutral networks***. Bull.Math.Biol. **63** (2001), 57-94




$$dx_i / dt = \Sigma_j f_j Q_{ji} x_j - x_i \Phi$$

$\Phi = \Sigma_j f_j x_i$ ; $\Sigma_j x_j = 1$ ; $\Sigma_i Q_{ij} = 1$

$[I_i] = x_i$ Æ 0 ; i =1,2,...,n ;

[A] = a = constant

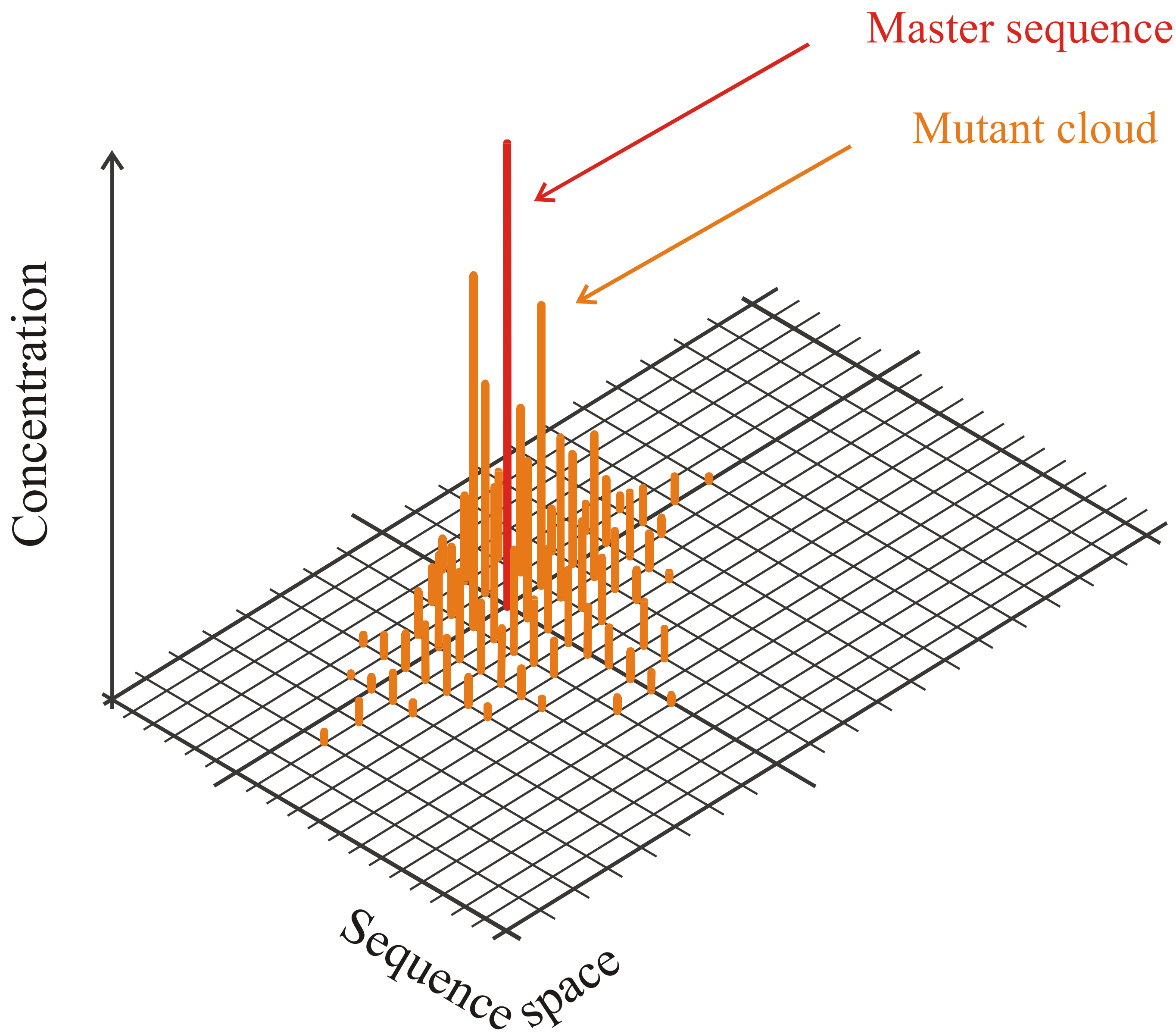
$$Q_{ij} = (1-p)^{\ell - d(i,j)}\ p^{d(i,j)}$$

p .......... Error rate per digit

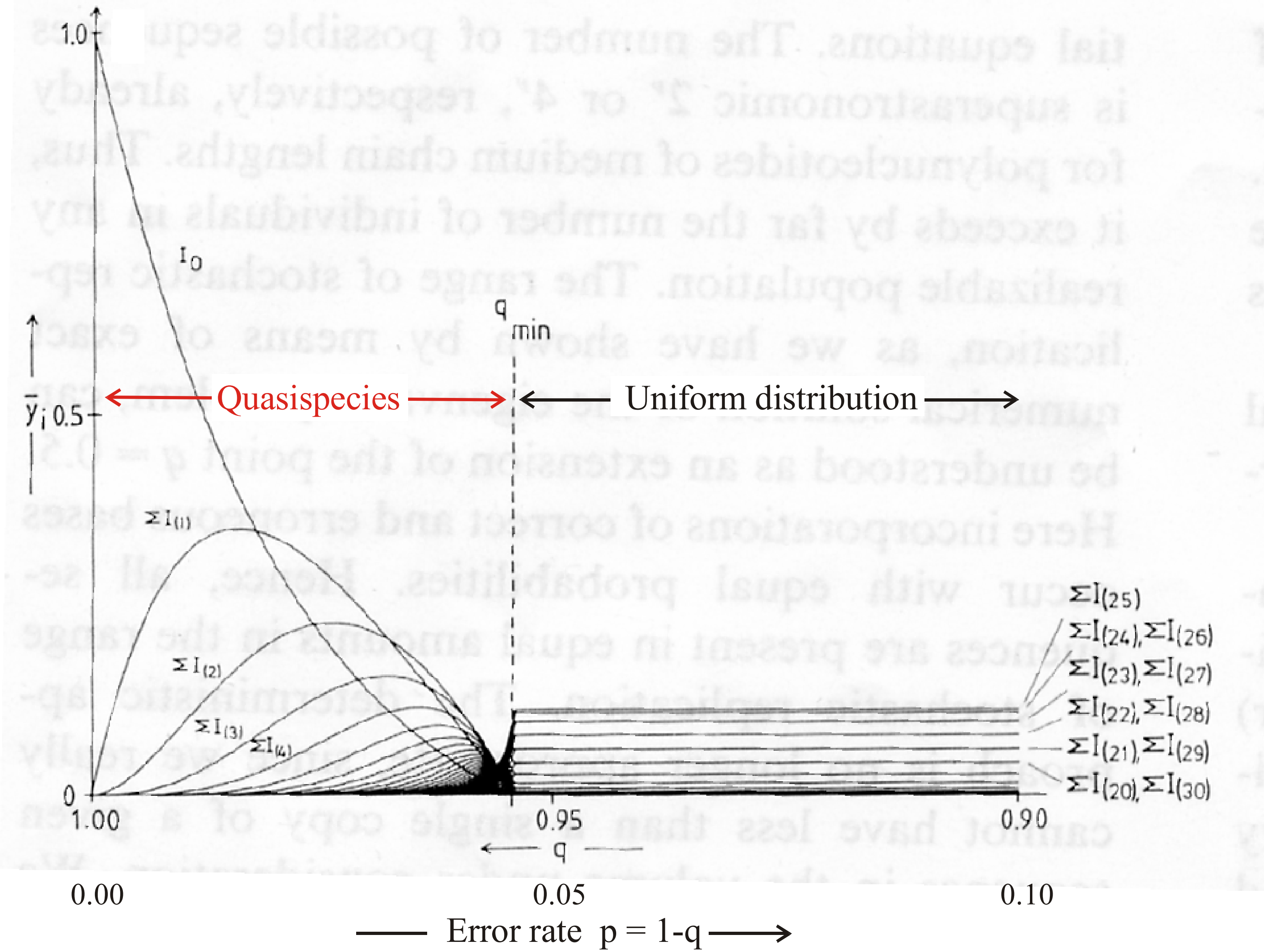
$\ell$ ........... Chain length of the polynucleotide

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

Chemical kinetics of replication and mutation as parallel reactions




The molecular quasispecies in sequence space




**Quasispecies** as a function of the replication accuracy q

## Optimization of RNA molecules *in silico*

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

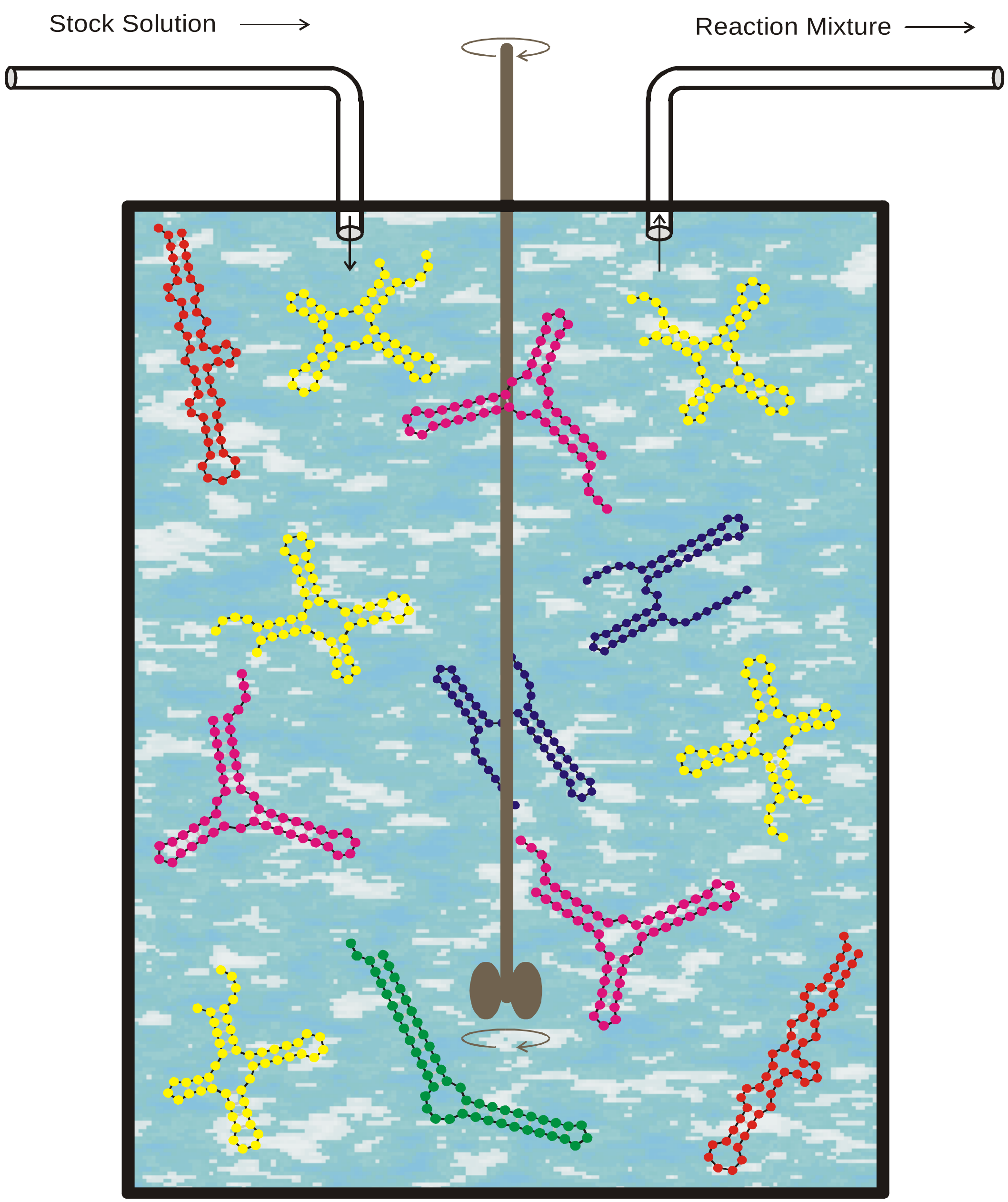
W.Fontana, W.Schnabl, P.Schuster, ***Physical aspects of evolutionary optimization and adaptation***. Phys.Rev.A **40** (1989), 3301-3321

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

B.M.R.Stadler, P.F.Stadler, G.P.Wagner, W.Fontana, ***The topology of the possible: Formal spaces underlying patterns of evolutionary change.*** J.Theor.Biol. **213** (2001), 241-274

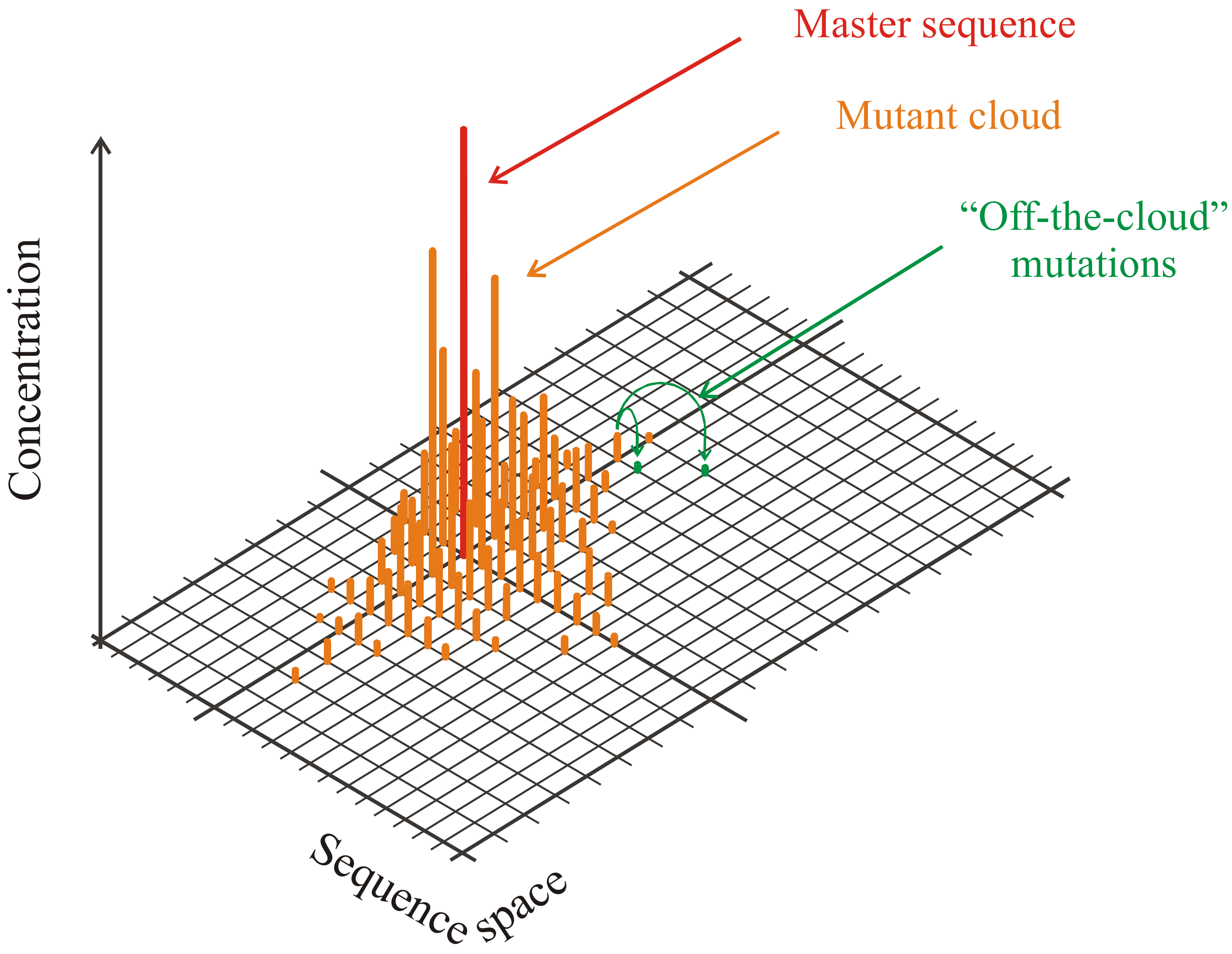



Fitness function:

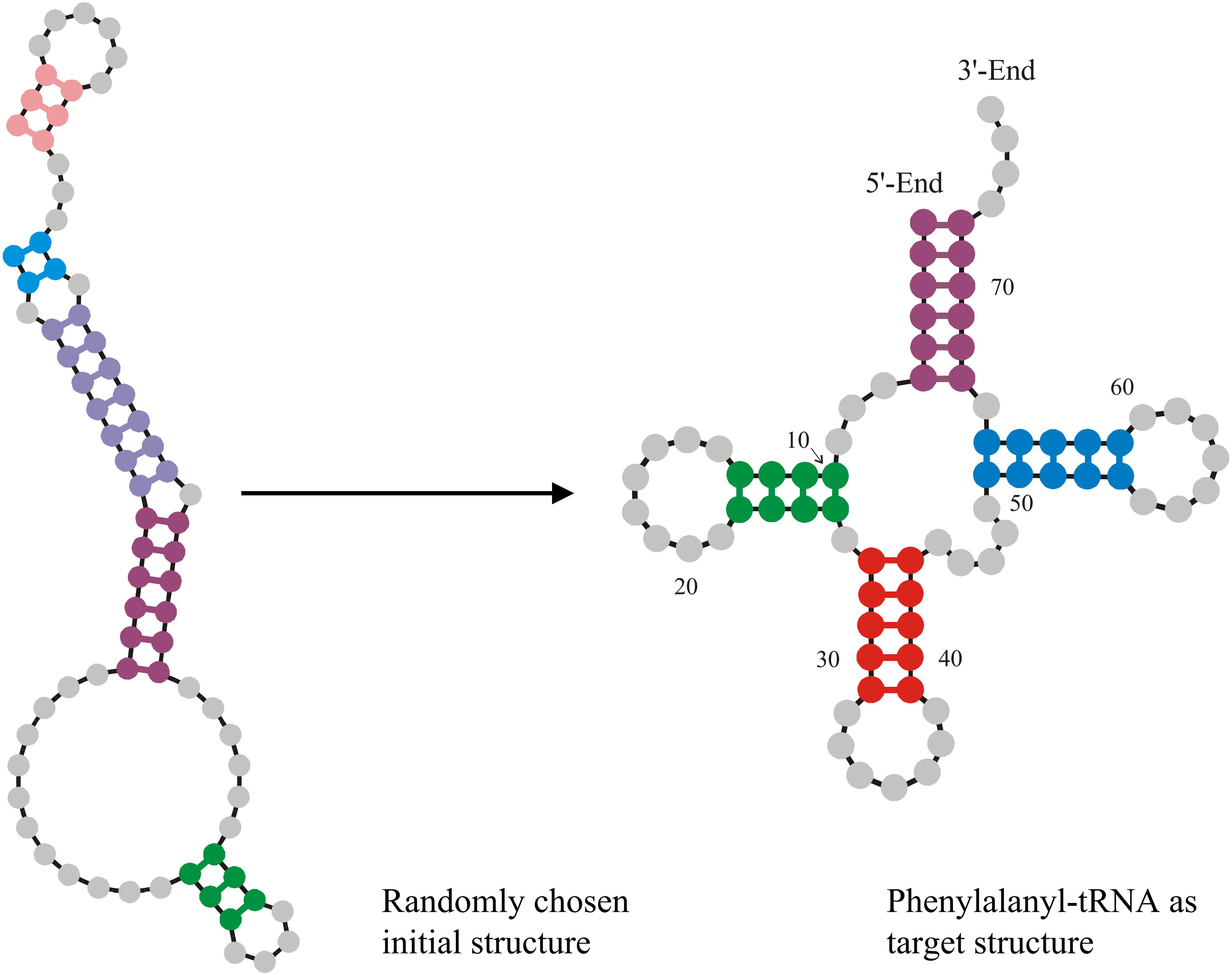
$f_k = \gamma / [\alpha + \Delta d_S^{(k)}]$

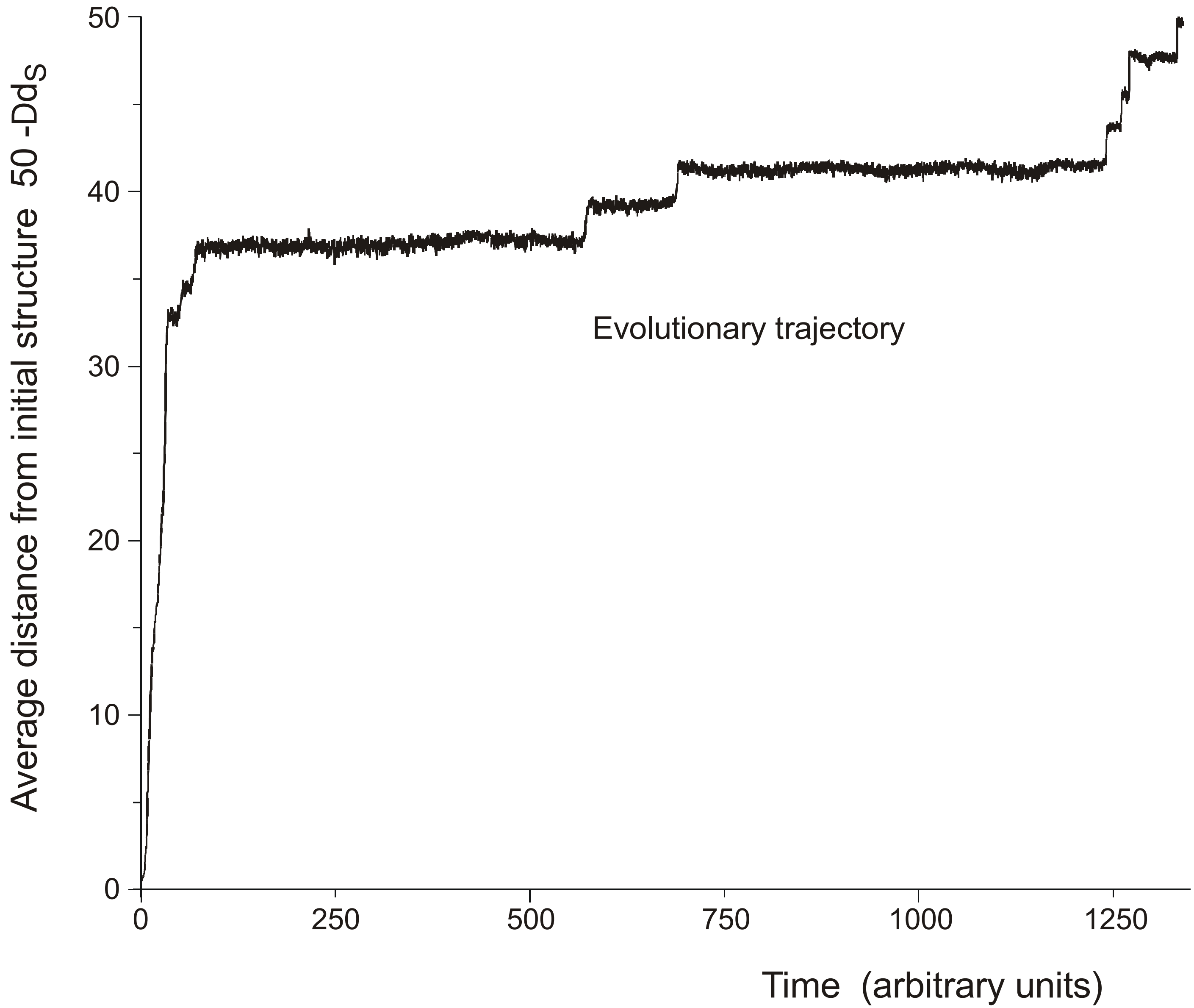
$\Delta d_S^{(k)} = d^s(I_k, I_t)$

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

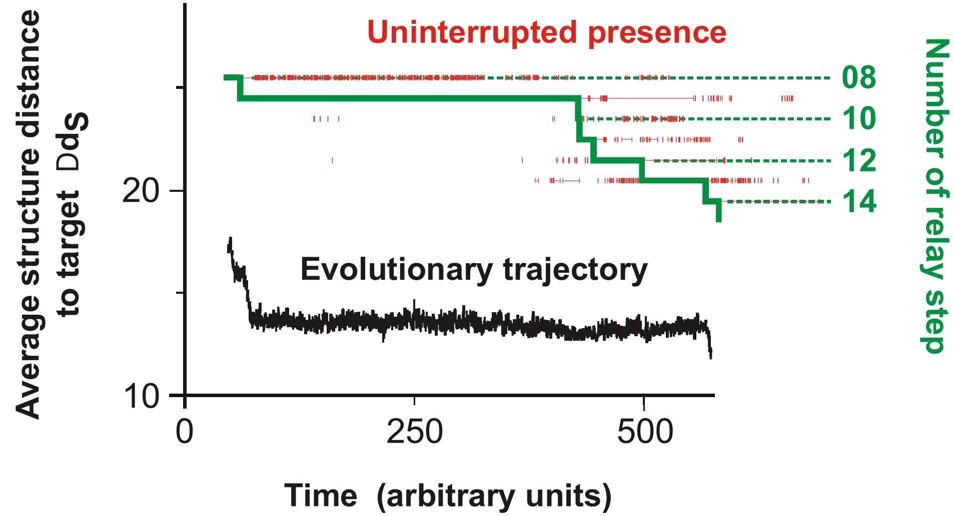



The molecular quasispecies
in sequence space


3'-End
5'-End
70
60
10
50
20
30
40
Randomly chosen initial structure
Phenylalanyl-tRNA as target structure




***In silico*** optimization in the flow reactor: Trajectory (**biologists' view**)




| | |
|---|---|
| entry | GGUAUGGGCGUUGAAUAGUAGGGUUUAAACCAAUCGGCCAACGAUCUCGUGUGCGCAUUUCAUAUCCCGUACAGAA |
| 8 | .(((((((((((........(((....)))........))))).....(((((.......)))))))))))....  |
| exit | GGUAUGGGCGUUGAAUAAUAGGGUUUAAACCAAUCGGCCAACGAUCUCGUGUGCGCAUUUCAUAUCCCAUACAGAA |
| entry | GGUAUGGGCGUUGAAUAAUAGGGUUUAAACCAAUCGGCCAACGAUCUCGUGUGCGCAUUUCAUAUACCAUACAGAA |
| 9 | .((((((.(((((........(((....)))........))))).....(((((.......))))).)))))).... |
| exit | UGGAUGGACGUUGAAUAACAAGGUAUCGACCAAACAACCAACGAGUAAGUGUGUACGCCCCACACACCGUCCCAAG |
| entry | UGGAUGGACGUUGAAUAACAAGGUAUCGACCAAACAACCAACGAGUAAGUGUGUACGCCCCACACAGCGUCCCAAG |
| 10 | .(((((..(((((........(((....)))........))))).....(((((.......)))))..))))).... |
| exit | UGGAUGGACGUUGAAUAACAAGGUAUCGACCAAACAACCAACGAGUAAGUGUGUACGCCCCACACAGCGUCCCAAG |

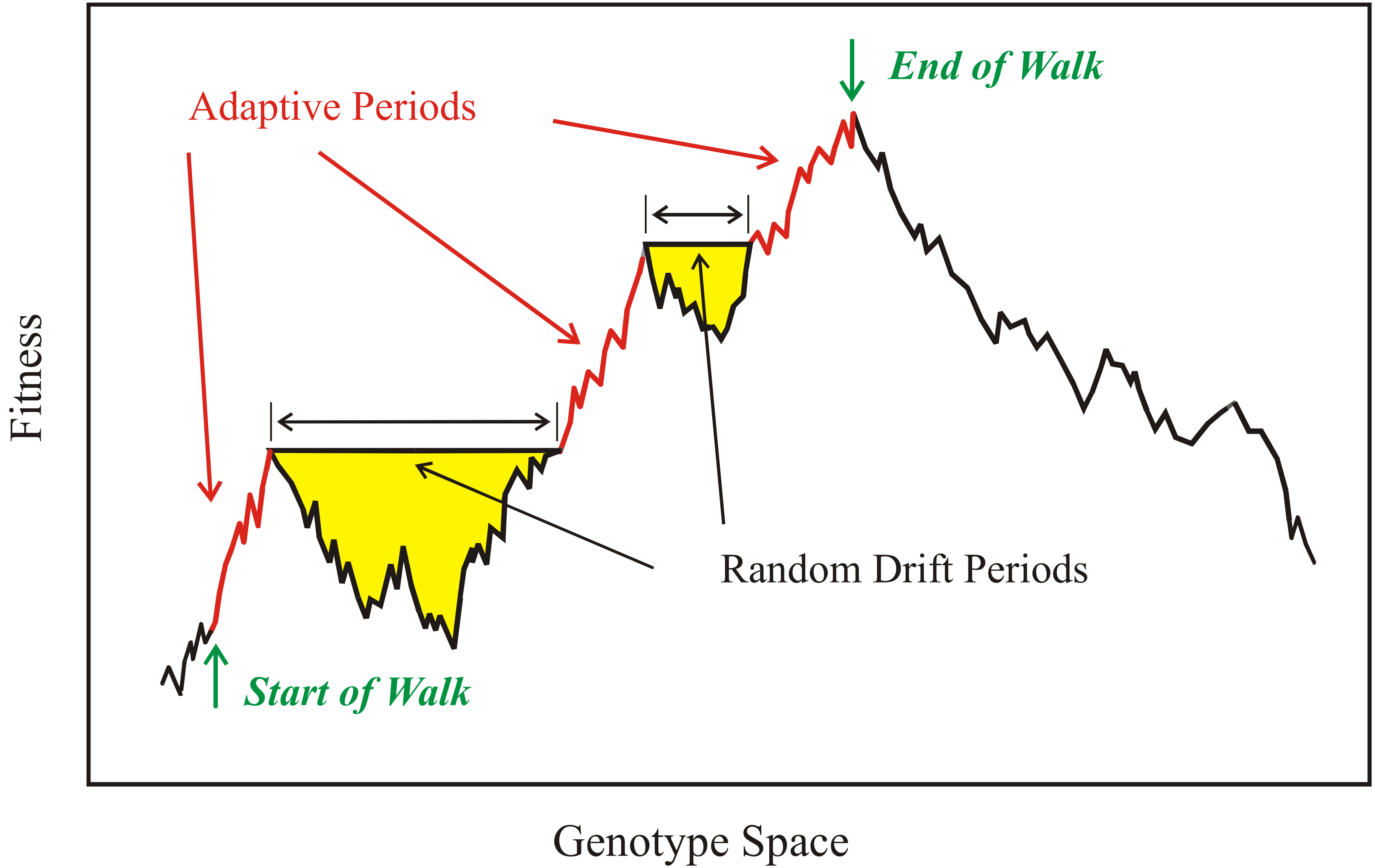
Transition inducing point mutations

Neutral point mutations

**Neutral genotype evolution** during phenotypic stasis

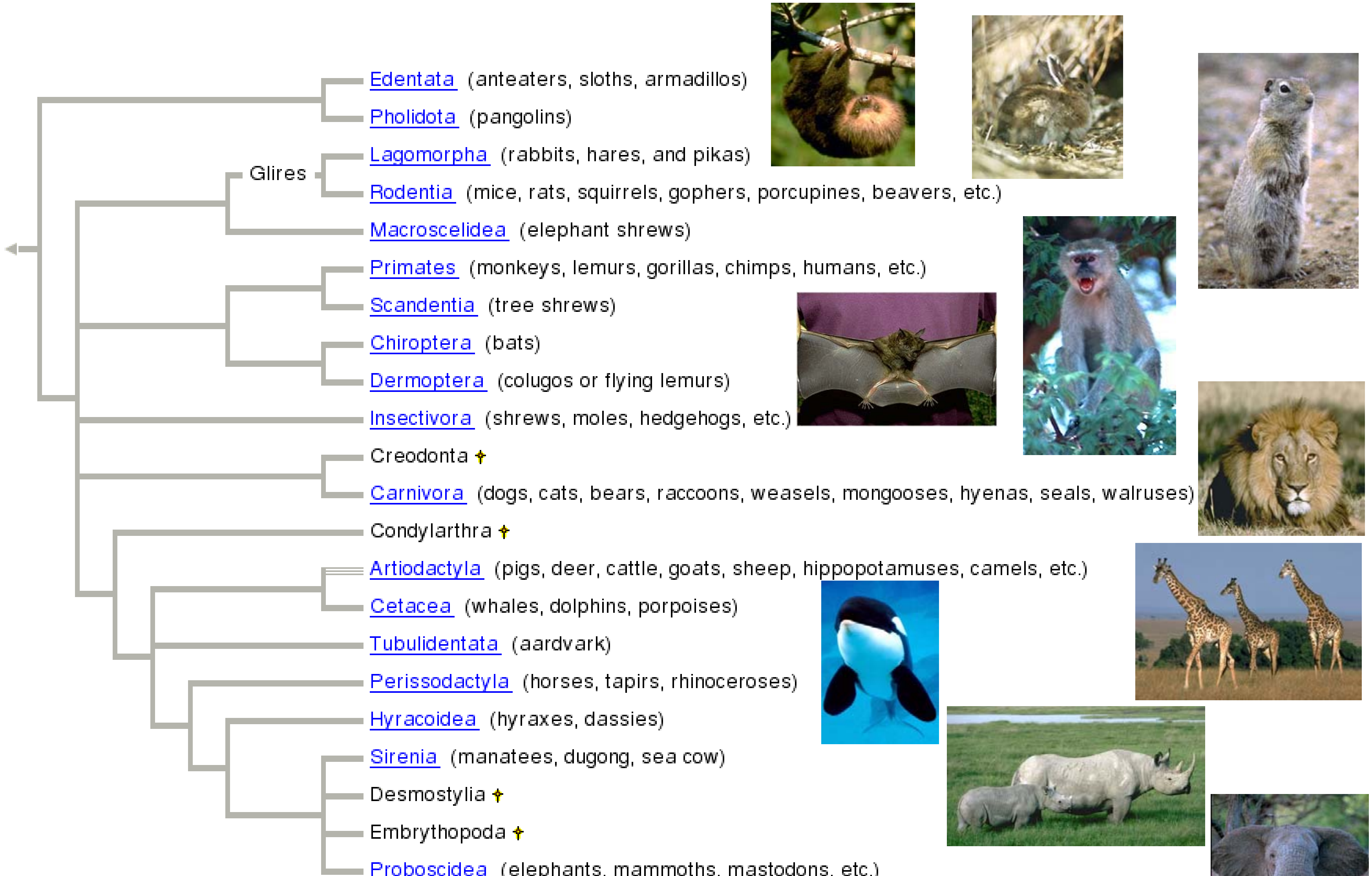
„…Variations neither useful not injurious would not be affected by natural selection, and would be left either a fluctuating element, as perhaps we see in certain polymorphic species, or would ultimately become fixed, owing to the nature of the organism and the nature of the conditions. …“

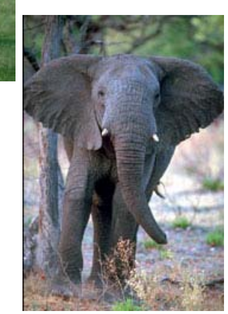
Charles Darwin, Origin of species (1859)




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

1. **Theory of evolution, science, and religion**
2. **Genetics and the theory of evolution**
3. **Evolution experiments in the laboratory**
4. **Molecular genetics and the tree of life**





The phylogeny of placental mammals: The ‚Tree of Life‘ Program

Gerhard Braunitzer, 1929 - 1989

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| | | | | A | | | | | | | | | | | | | | | | | B | | | | | | | | | |
| α | Val | | Leu | Ser | Pro | Ala | Asp | Lys | Thr | Asp | Val | Lys | Ala | Ala | Try | Gly | Lys | Val | Gly | Ala | His | Ala | Gly | Glu | Tyr | Gly | Ala | Glu | Ala | Leu |
| β | Val | His | Leu | Thr | Pro | Glu | Glu | Lys | Ser | Ala | Val | Thr | Ala | Leu | Try | Gly | Lys | Val | Asp | | | Val | Asp | Glu | Val | Gly | Gly | Glu | Ala | Leu |
| I | | | | | | | | | | | | | | | | | | | | | | | | | | Gly | | | | |

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| | | | | | | | C | | | | | | | CD | | | | | | | | D | | | | | | | E | |
| α | Glu | Arg | Met | Phe | Leu | Ser | Phe | Pro | Thr | Thr | Lys | Thr | Tyr | Phe | Pro | His | Phe | | Asp | Leu | Ser | His | | | | | | Gly | Ser | Ala |
| β | Gly | Arg | Leu | Leu | Val | Val | Tyr | Pro | Try | Thr | Glu | Arg | Phe | Phe | Glu | Ser | Phe | Gly | Asp | Leu | Ser | Thr | Pro | Asp | Ala | Val | Met | Gly | Asp | Pro |
| I | | | | | | | | Pro | | | | | | Phe | | | | | | | | | | | | | | | | |

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| | | | | | | | | | | | | | | | | | | EF | | | | | | | | F | | | | | |
| α | Glu | Val | Lys | Gly | His | Gly | Lys | Lys | Val | Ala | Asp | Ala | Leu | Thr | Asp | Ala | Val | Ala | His | Val | Asp | Asp | Met | Pro | Asp | Ala | Leu | Ser | Ala | Leu | Ser | Asp |
| β | Lys | Val | Lys | Ala | His | Gly | Lys | Lys | Val | Leu | Gly | Ala | Phe | Ser | Asp | Gly | Leu | Ala | His | Leu | Asp | Asp | Leu | Lys | Gly | Thr | Phe | Ala | Thr | Leu | Ser | Glu |
| I | | | | | His | | | | | | | | | | | | | | | | | | | | | | | | | Leu | | |

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| | | | | FG | | | | | G | | | | | | | | | | | | | | | | | | | GH | | | | |
| α | Leu | His | Ala | His | Lys | Leu | Arg | Val | Asp | Pro | Val | Asp | Phe | Lys | Leu | Leu | Ser | His | Cys | Leu | Leu | Val | Thr | Leu | Ala | Ala | His | Leu | Pro | | Ala | Glu |
| β | Leu | His | Cys | Asp | Lys | Leu | His | Val | Asp | Pro | Glu | Asp | Phe | Arg | Leu | Leu | Gly | Asp | Val | Leu | Val | Cys | Val | Leu | Ala | His | His | Phe | Gly | | Lys | Glu |
| I | | His | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

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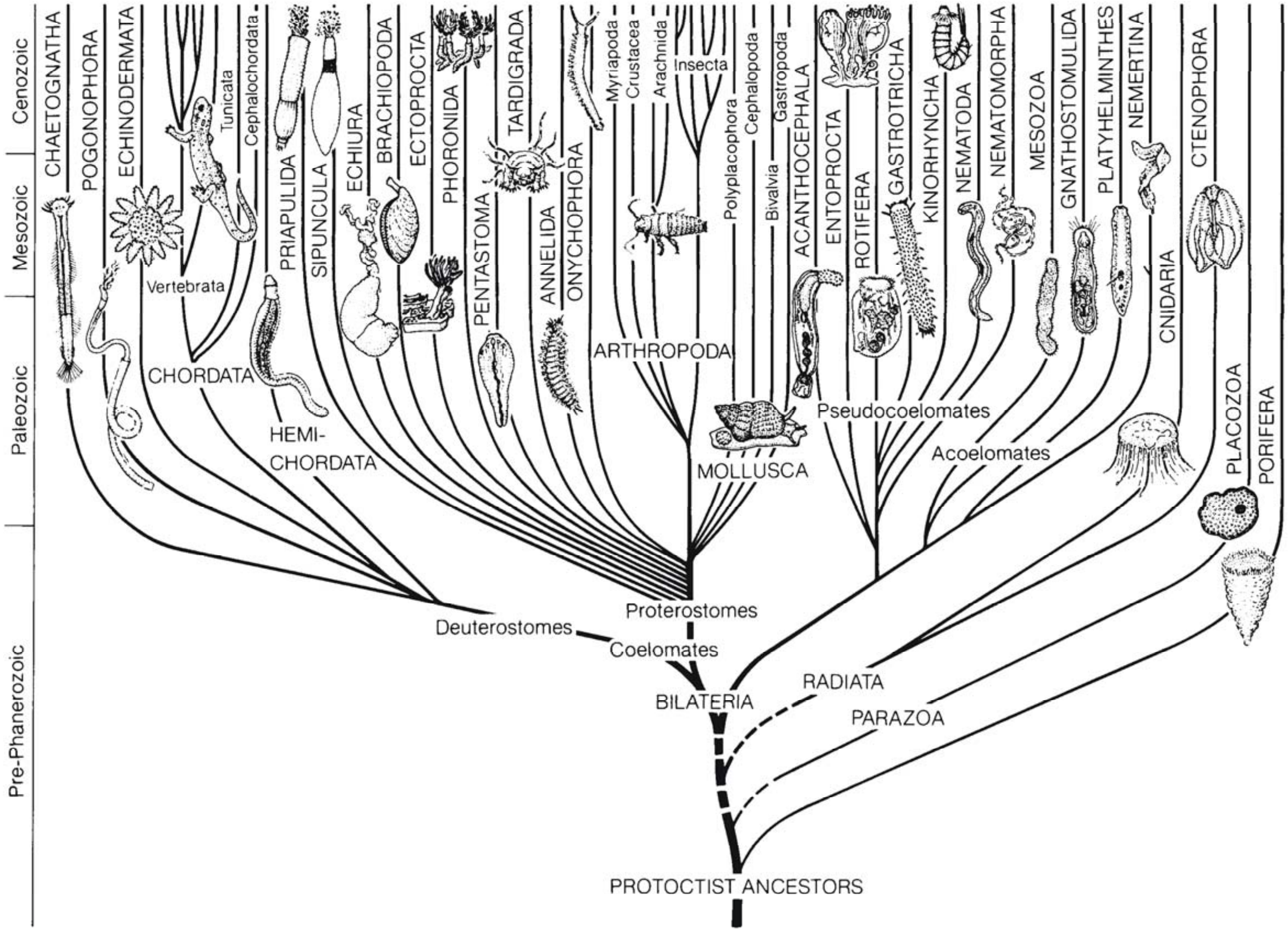
| | | H | | | | | | | | | | | | | | | | | | | | | | | |
| α | Phe | Thr | Pro | Ala | Val | His | Ala | Ser | Leu | Asp | Lys | Phe | Leu | Ala | Ser | Val | Ser | Thr | Val | Leu | Thr | Ser | Lys | Tyr | Arg |
| β | Phe | Thr | Pro | Pro | Val | Glu | Ala | Ala | Tyr | Glu | Lys | Val | Val | Ala | Gly | Val | Ala | Asp | Ala | Leu | Ala | His | Lys | Tyr | His |
| I | | | | | | | | | | | Lys | | | | | | | | | | | | | Tyr | |

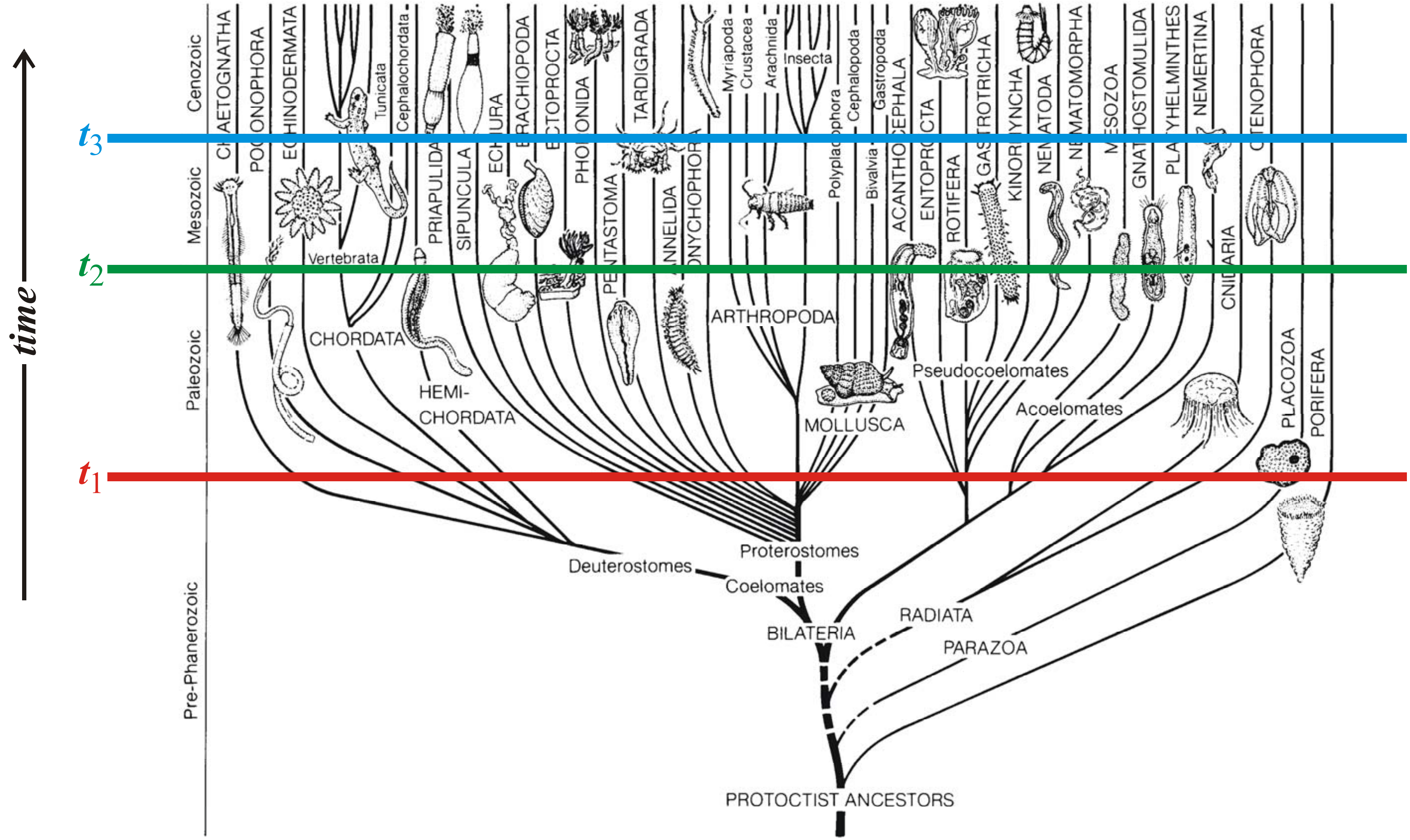
Tab. 4: Die invarianten Reste (I) der Hämoglobine der Vertebraten.

Hemoglobin sequences in different vertebrates




**Phylogenetic tree of animal kingdom**

Lynn Margulis & Karlene V. Schwarz, *Five Kingdoms. An illustrated guide to the Phyla of Life on Earth*. W.H. Freeman & Co., San Francisco, 1982, p. 160.




**Phylogenetic tree of animal kingdom**

Lynn Margulis & Karlene V. Schwarz, *Five Kingdoms. An illustrated guide to the Phyla of Life on Earth*. W.H. Freeman & Co., San Francisco, 1982, p. 160.

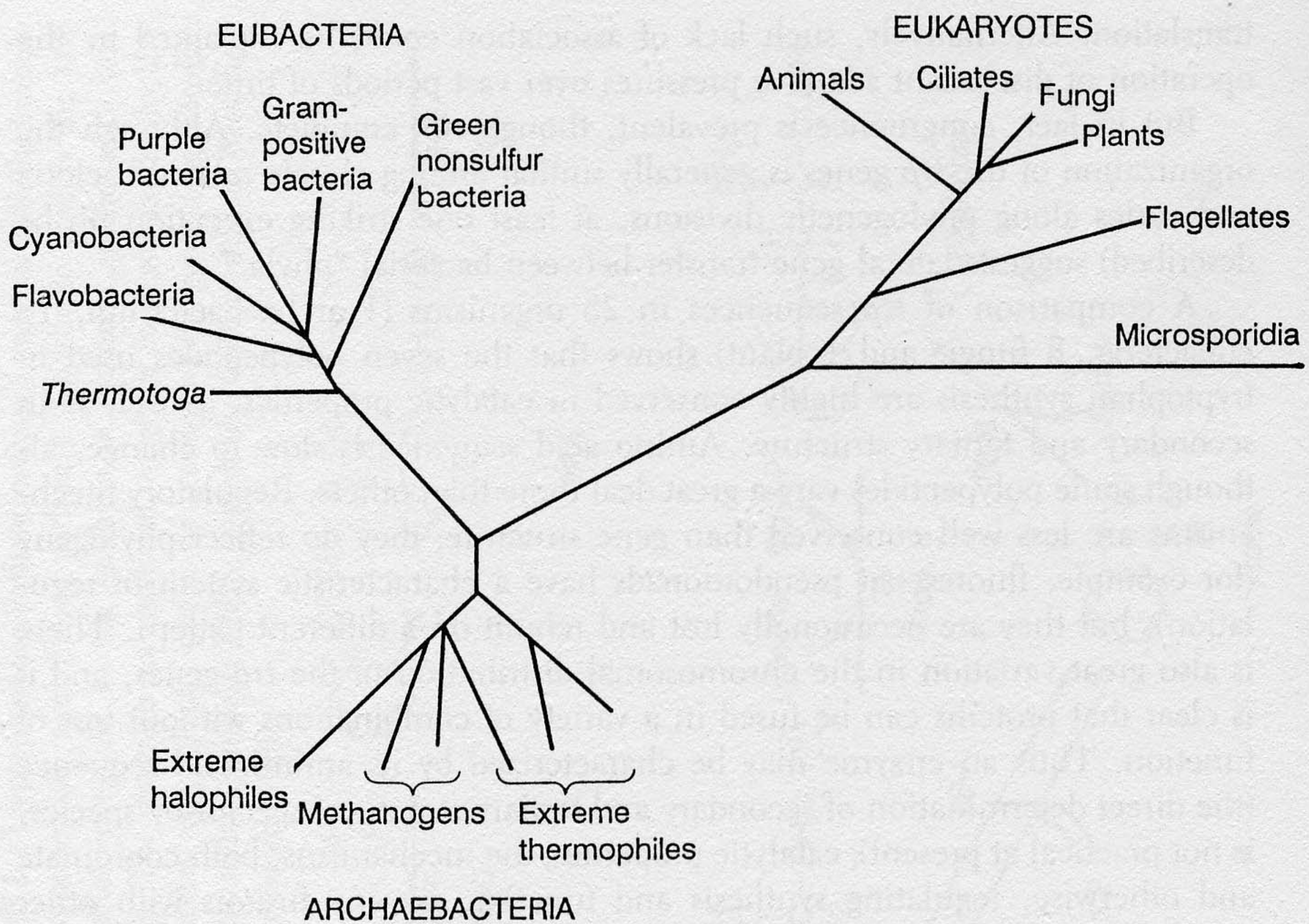
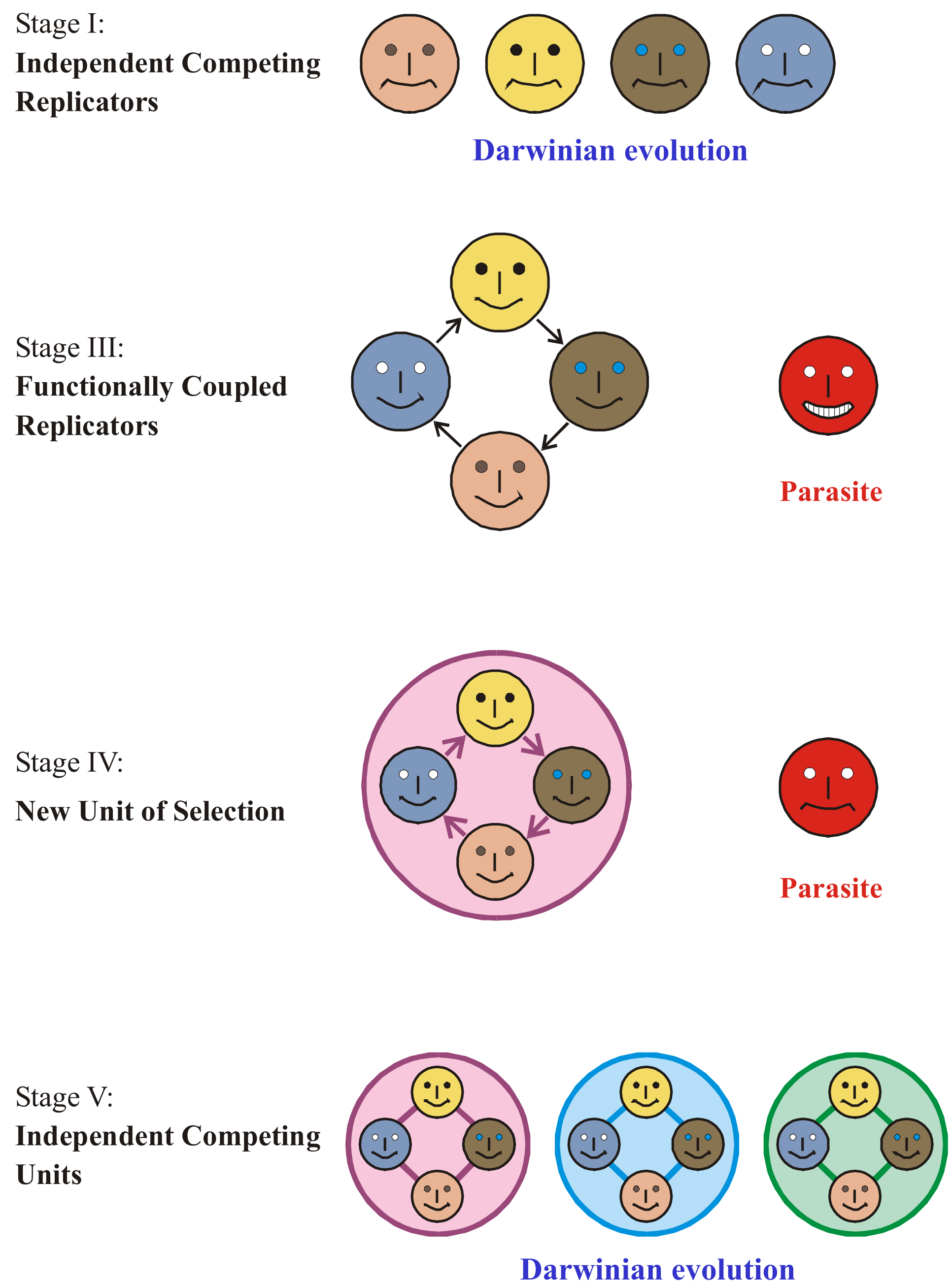



**FIGURE 2.** The two bacterial phylogenies, taken from the universal phylogenetic tree determined from rRNA sequence comparisons (Woese, 1987).

Evolution at the molecular level.

R.K. Selander, A.G. Clark, T.S. Whittam, eds. Sinauer Associates, 1991.




A mechanism for major transitions in evolution

Zur gleichen Zeit schreien viele nach einer neuen Biologie. Man liest, sie wollen „Integrative Biologie" machen, oder „Systembiologie". Kaum einer nennt es beim richtigen Namen: Theoretische Biologie. Weil diese einen schlechten Klang hat. Ich jedoch denke, ich kann die Sünden der Vergangenheit vergeben und nehme das Wort: Wir brauchen eine Theorie, die das alles einschließt. Stellen Sie sich doch nur mal vor, wir müssen am Ende all dieses Zeug nicht nur unter Fachleuten besprechen, sondern müssen es an Universitäten lehren, in der Schule, und es der Öffentlichkeit erklären. Wie sollen wir das machen ohne umfassende Theorie? Das, denke ich, ist die Herausforderung, der wir uns stellen müssen.

At the same time people are crying for a new biology. They say, they want to make "Integrative Biology" or "Systems Biology". Hardly anyone calls it by its proper name: Theoretical Biology. Because it has a bad reputation. I think, however, I can remit the sins of the past and declare: We need a theory, which comprises all that (*Molecular, Structural, Cellular, Developmental, …… , and Evolutionary Biology*). Imagine, eventually, we not only need to discuss all this stuff with our expert colleagues, but we have to teach it at universities, at schools, and to the public. How could we manage without a comprehensive theory? This is the challenge we have to meet.

**Sydney Brenner, Nobelpreisträger 2002, im Gespräch: „*Eine einsame Stimme aus der Prägenomik Ära*". Laborjournal 2002, Heft 4:28 – 33.**

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