Evolution und Design

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Treffen S. H. Benedikt XVI mit seinen Schülern

Castelgandolfo, 01.09.2006

Vorbemerkungen

• Das Referat beschränkt sich auf die Naturwissenschaft mit heutigem Wissensstand.

• Die Vorstellung der biologischen Evolution ist eine empirisch begründete, naturwissenschaftliche Theorie.

• Die Evolutionstheorie ist in einigen wesentlichen Aussagen experimentell prüfbar und überprüft und baut auf Tatsachen aus mehreren Teildisziplinen auf.

• Die Evolutionstheorie ist daher vom selben Rang wie physikalische Theorien, etwa die Newtonsche Mechanik, die Relativitätstheorie oder die Quantentheorie.

• Wie die meisten naturwissenschaftlichen Theorien kann die biologische Evolutionstheorie nicht alle beobachteten Einzelheiten erklären insbesondere, da die Biologie zur Zeit in einer faszinierenden und raschen Entwicklung steht.

• Die Molekularbiologie führt die biologischen Befunde auf Gesetzmäßigkeiten aus Physik und Chemie zurück, ohne dadurch die Eigenständigkeit der Biologie in Frage zu stellen.

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2. Wahrscheinlichkeit und Zufall in der Biologie
3. Komplexes Verhalten aus einfachen Regeln
4. Evolutionsmechanismen
5. Molekularbiologie und Evolutionsexperimente
6. Ursprung komplexer Organe – Das Auge als Beipiel

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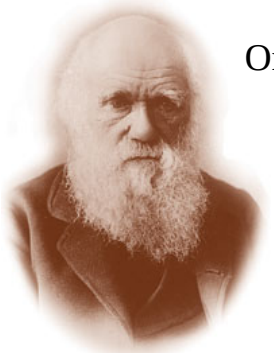

Charles Darwin

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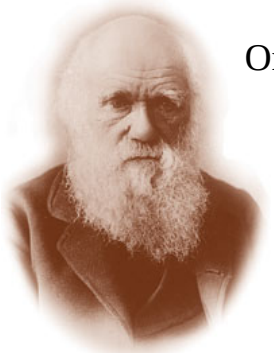
1859

Origin of genetics
1865

Gregor Mendel



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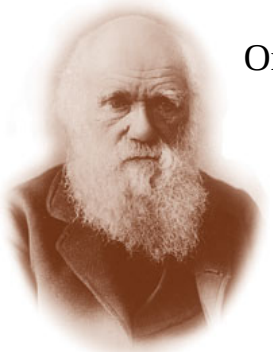

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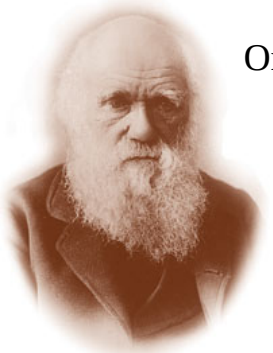
Ronald Fisher

JSB Haldane

Sewall Wright



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Ernst Mayr

Theodosius
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Synthetic or
Neo-Darwinian theory
1940 - 1950

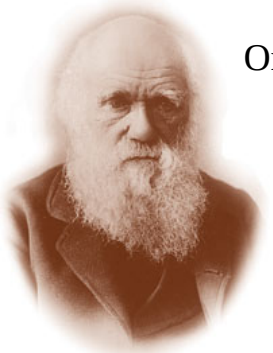
Ernst Mayr und andere Evolutionsbiologen:

Können die Beobachtungen in der Biologie ohne die Annahme einer **Causa finalis** erklärt werden?

Die Antwort der Evolutionsbiologen ist "**Ja**": Adaptation durch Variation und Selektion führt zum gleichen Resultat wie das rationale Design.

"**Teleonomie ersetzt Teleologie**"

In der evolutionären Biotechnologie war es möglich diese Behauptung an Hand von Molekülen zu verifizieren. An Hand von molekularen Systemen kann man rationales Design und evolutionäre Optimierung vergleichen.



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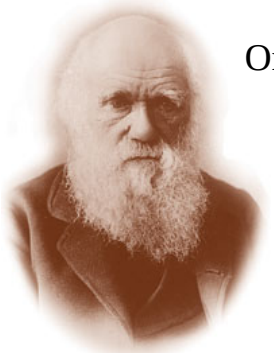

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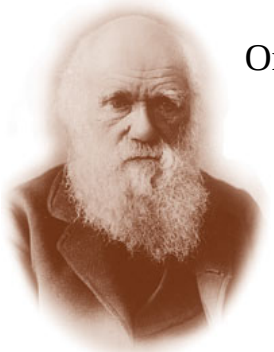

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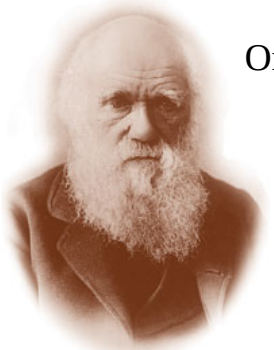
Biology of the 21st century



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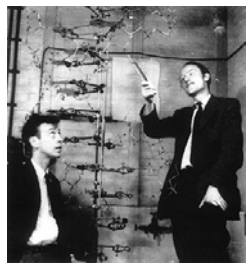

James Watson and
Francis Crick

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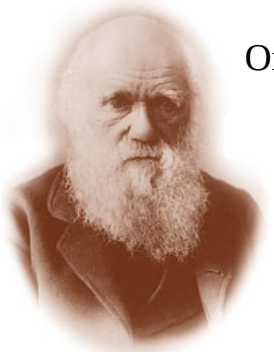

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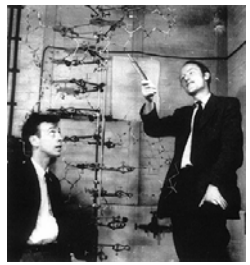

James Watson and Francis Crick

François Jacob

Max Perutz

Manfred Eigen

Sydney Brenner

John Kendrew

Biology of the 21st century

Biomathematics, bioinformatics, … , biophysics, biochemistry, … , molecular genetics, … , systems biology, biomedicine, macroscopic biology, evolutionary biology, sociobiology, anthropology, …

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Eugene Wigner's argument applied to a bacterium:

All genomes have equal probability

5'-end GCGGATTTAGCTCAGTTGGGAGAGCGCCAGACTGAAGATCTGGAGGTCCTGTGTTCGAUCCACAGAATTC.....GCACCA 3'-end

Alphabet size: 4

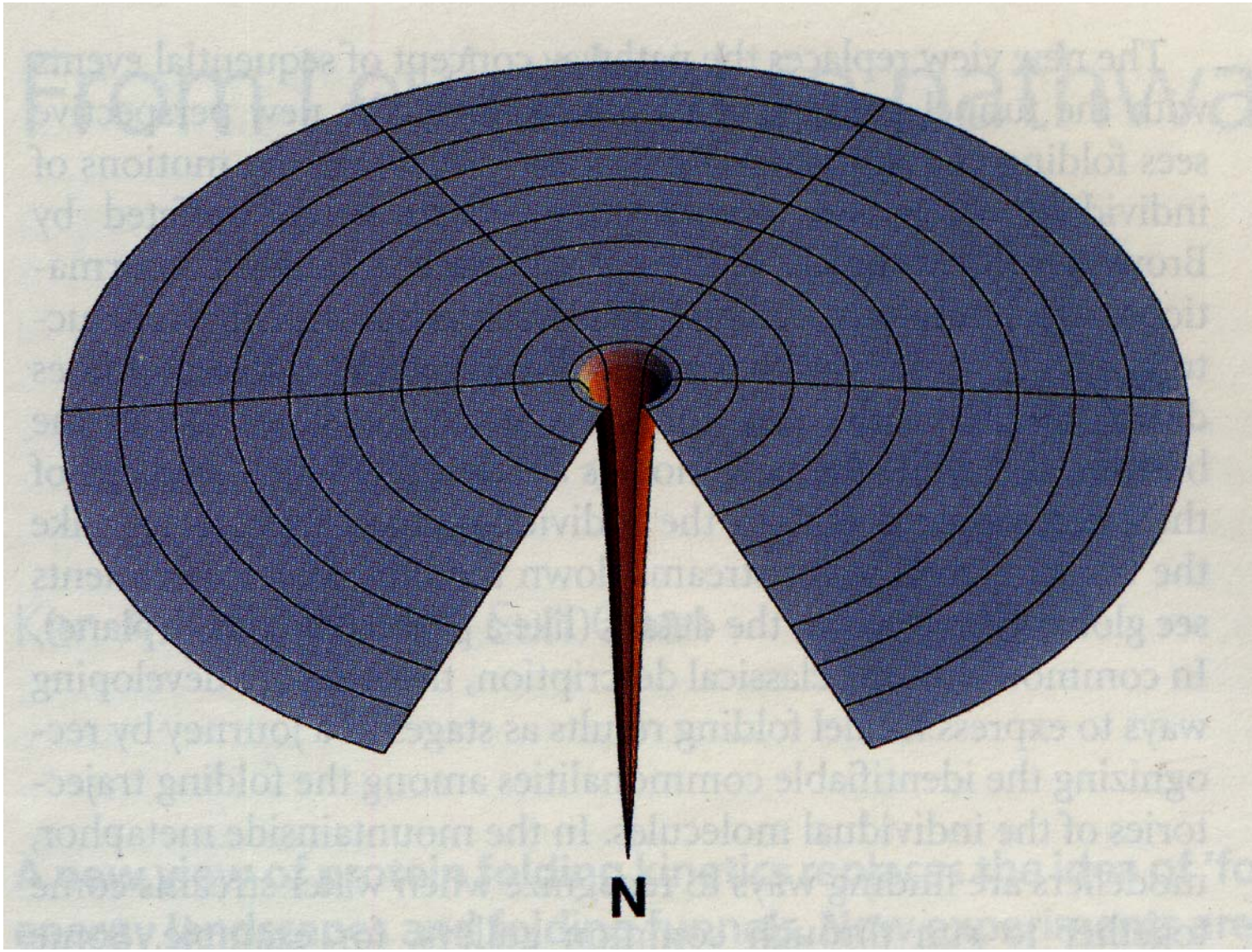
Chain length: ≈ 1 000 000 nucleotides

Number of possible genomes: $4^{1\,000\,000}$

Probability to find a given bacterial genome:

$$4^{-1\,000\,000} \approx 10^{-600\,000} = 0.000\ldots\ldots001$$

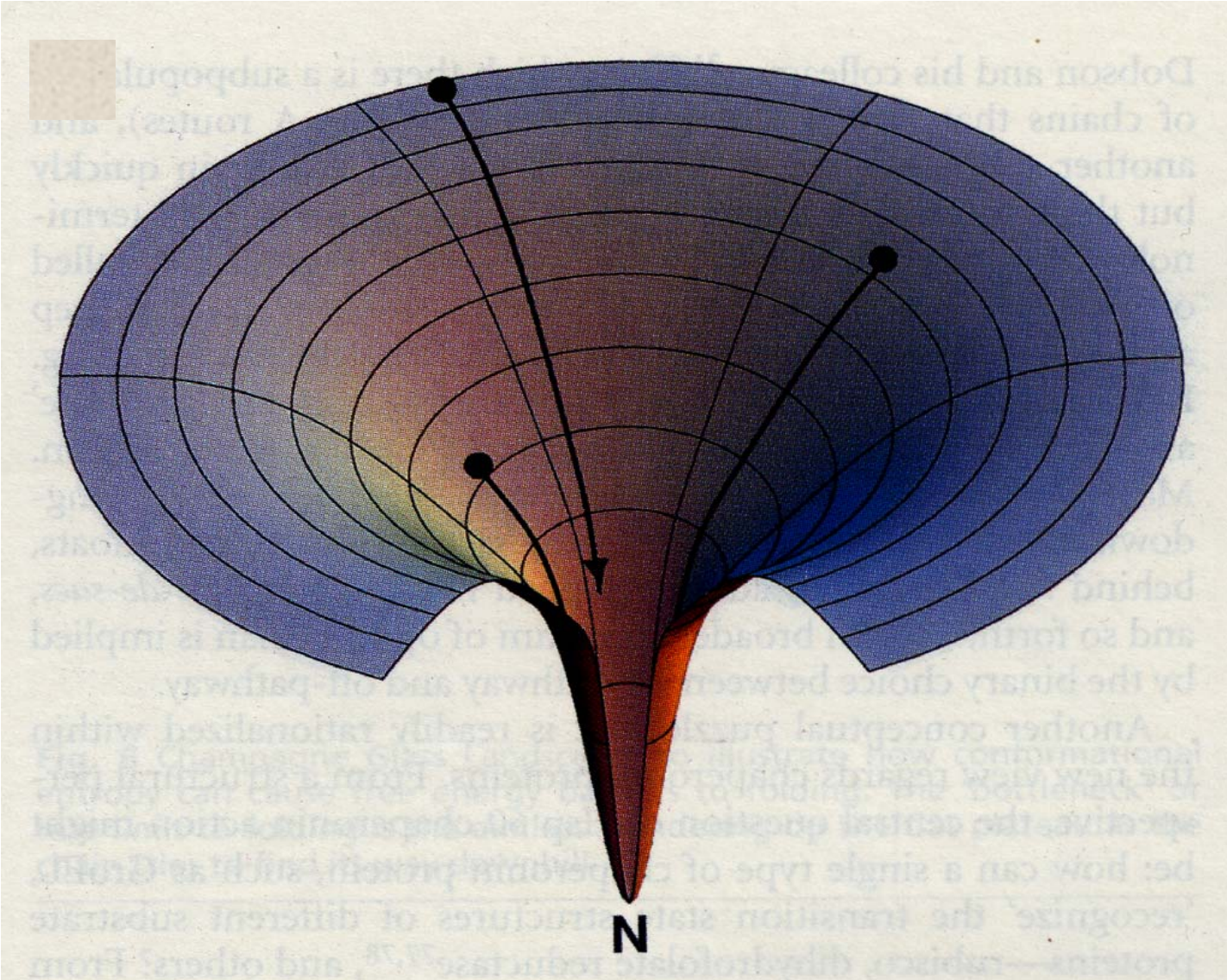
← 600000 →



The golf course landscape

Wigner’s paradox

Picture: K.A. Dill, H.S. Chan, Nature Struct. Biol. 4:10-19



The funnel landscape

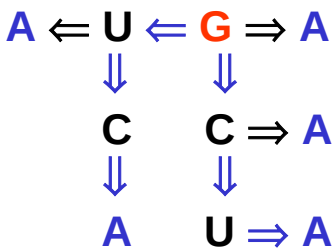
Solution to Wigner’s paradox

Picture: K.A. Dill, H.S. Chan, Nature Struct. Biol. 4:10-19

Eugene Wigner's argument revisited:

Every single point mutation leads to an improvement and is therefore selected

5'-end GCGGATTTAGCTCAGTTGGGAGAGCGCCAGACTGAAGATCTGGAGGTCCTGTGTTCGAUCCACAGAATTC.....GCACCA 3'-end



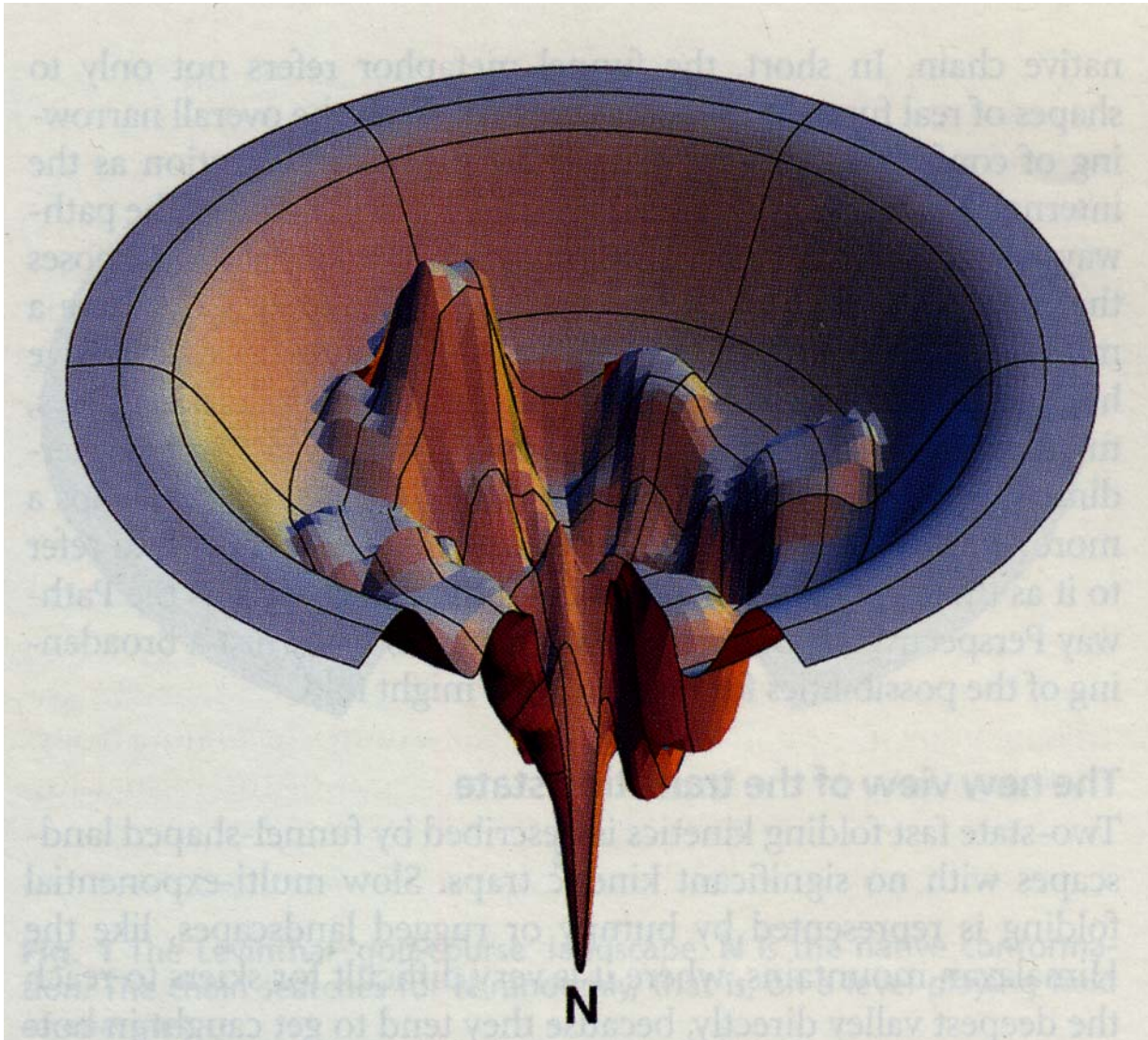
Alphabet size: 4

Chain length: ≈ 1 000 000 nucleotides

Length of longest path to the optimum: 3×1000000

Probability to find the optimal bacterial genome:

$$0.333.. \times 10^{-6} = 0.000000333..$$



The structured funnel landscape

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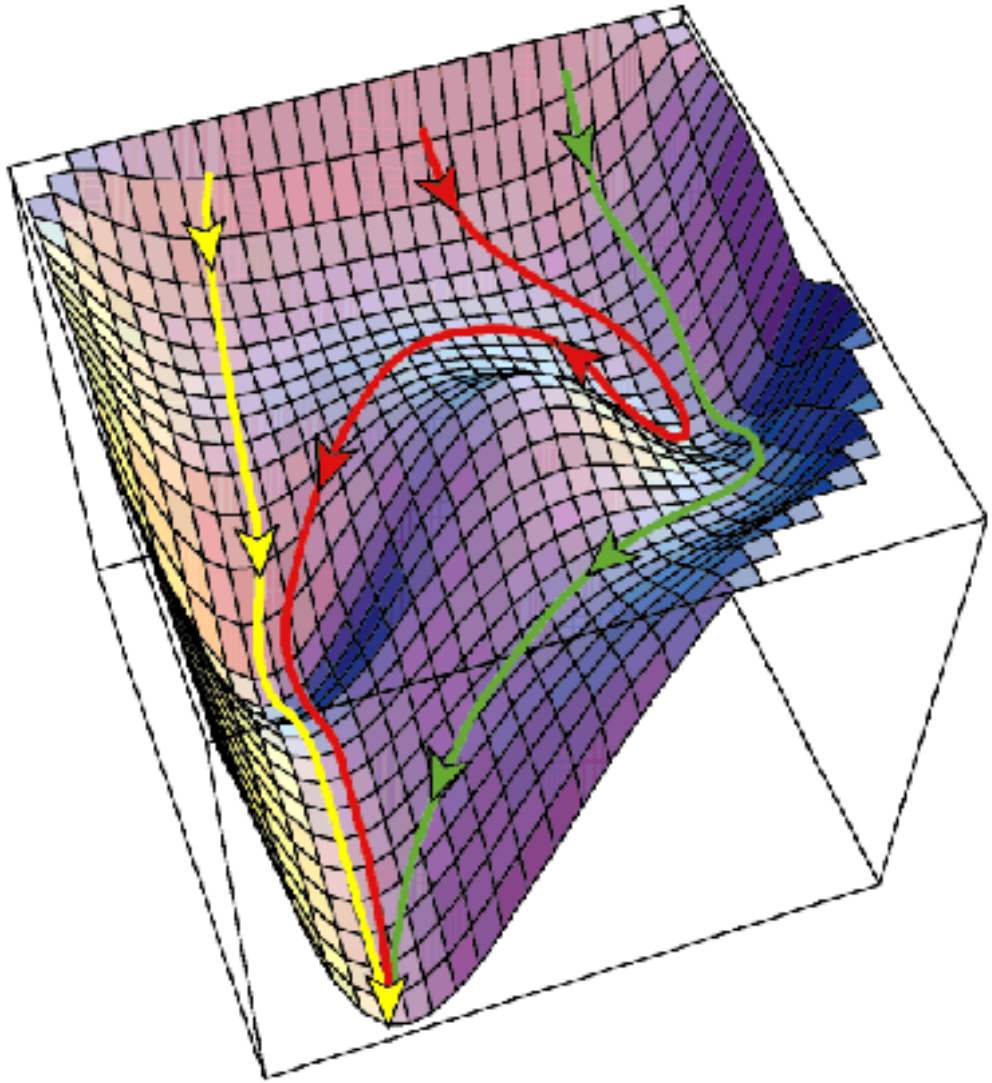
Picture: K.A. Dill, H.S. Chan, Nature Struct. Biol. 4:10-19

An “all-roads-lead-to-Rome” landscape



The reconstructed folding landscape
of a real biomolecule: “Lysozyme”

Picture: C.M. Dobson, A. Šali, and M. Karplus, Angew.Chem.Internat.Ed. 37: 868-893, 1988

Aber (!) die Landschaften, auf denen die Evolution in der Natur und im Laborexperiment stattfindet, sehen ganz anders aus als die vier hier gezeigten einfachen Beispiele !

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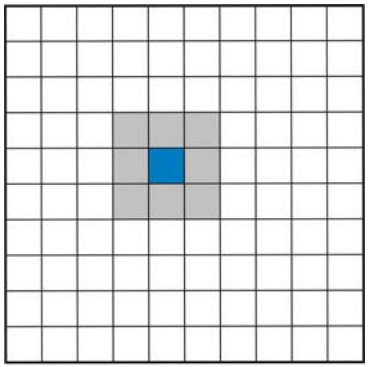
John Horton Conway's Game-of-Life



Cell and neigborhood

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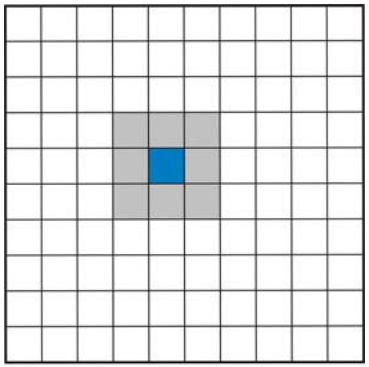

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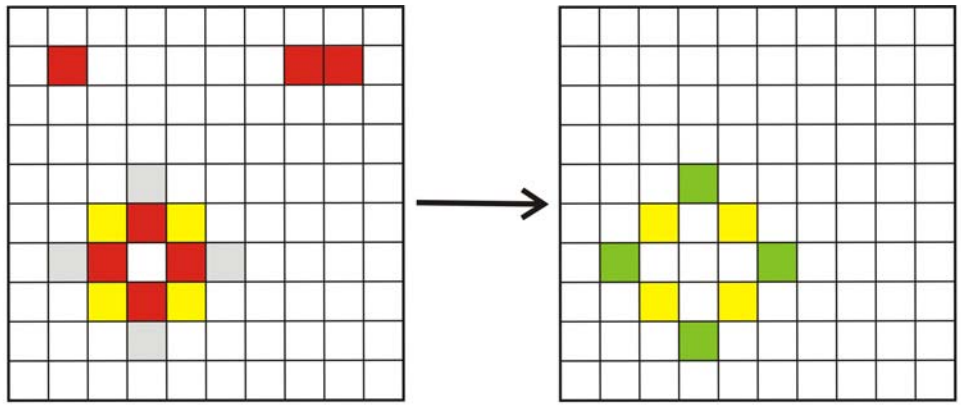

Populated cell: (1) each cell with one or no neighbors dies
(2) each cell with two or three neighbors suvives
(3) each cell with four or more neighbors dies

Empty cell: (4) each empty cell with three neighbors becomes populated.

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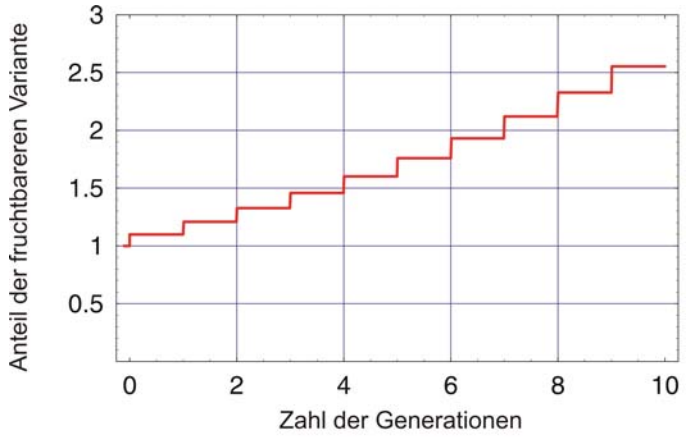
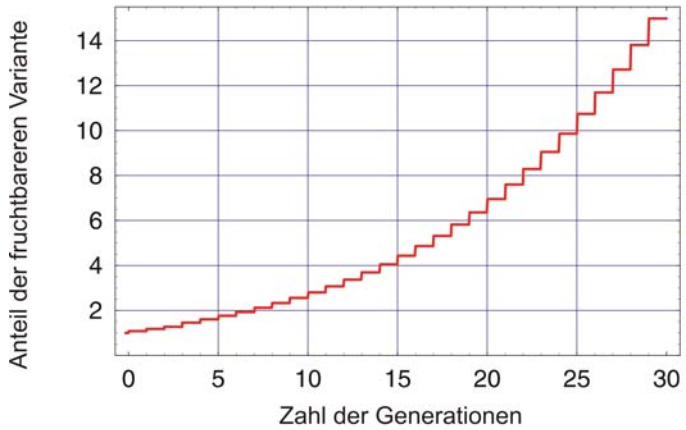
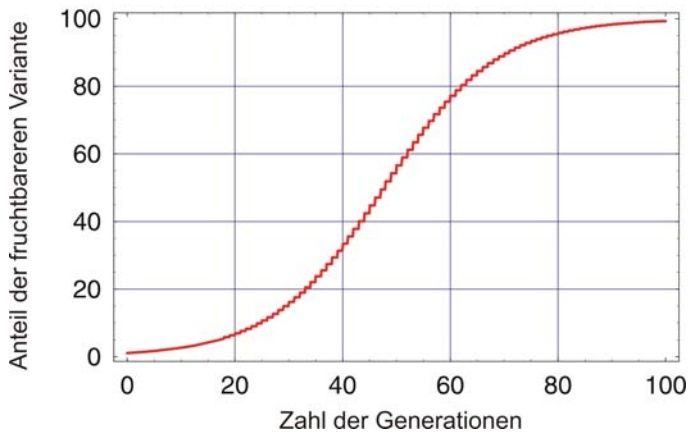
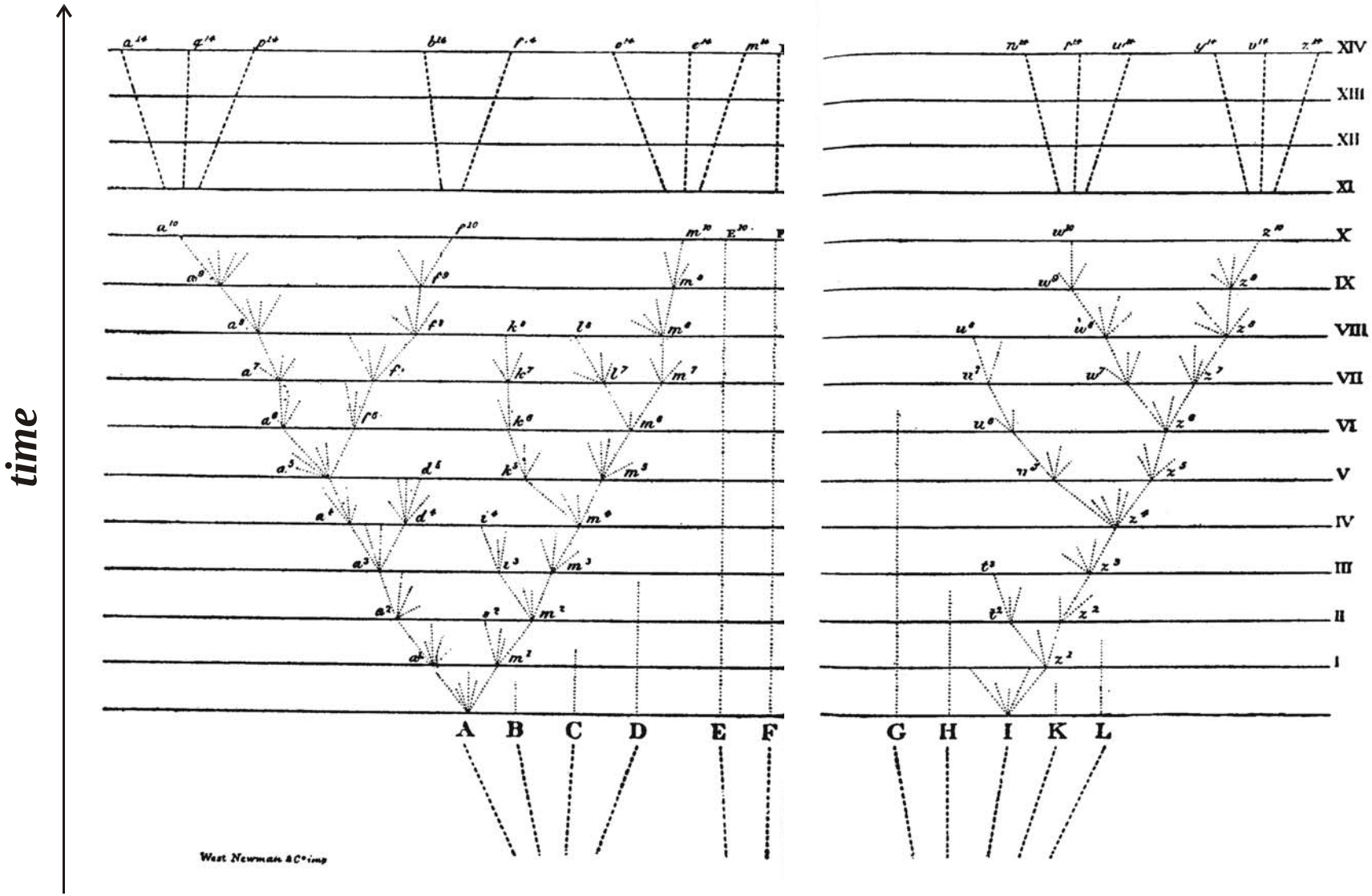




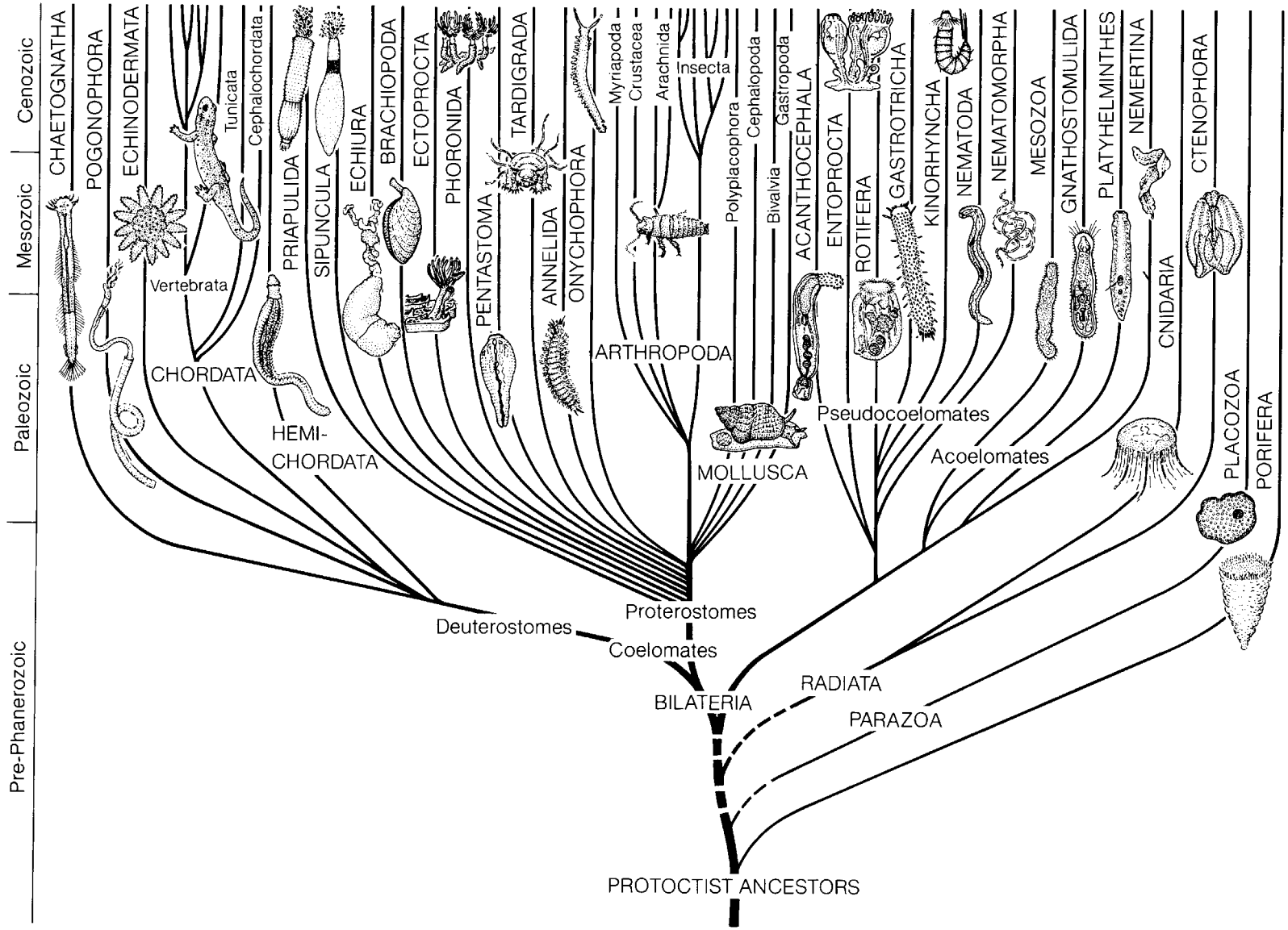
Die Effizienz des Selektionsmechanismus:

Verglichen sind zwei Varianten mit nur 10% Unterschied in der Fertilität – 10 und 11 Nachkommen im Mittel. Die Anfangsgeneration besteht aus 99 weniger fruchtbaren Individuen und einem einzigen Vertreter der fruchtbareren Variante. Die Vemehrung erfolgt asuexuell.



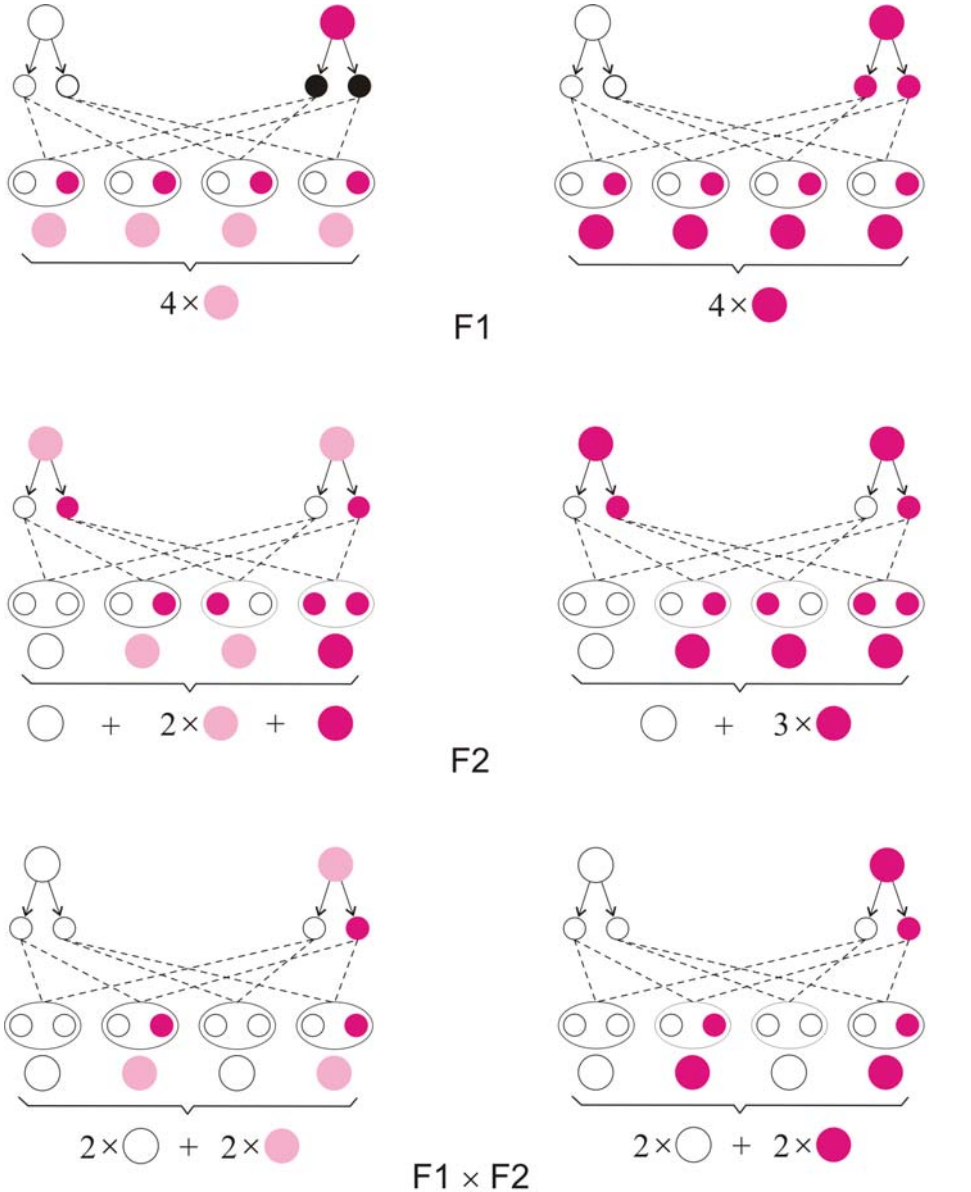


Charles Darwin, *The Origin of Species*, 6th edition.
Everyman‘s Library, Vol.811, Dent London, pp.121-122.



Modern phylogenetic tree: Lynn Margulis, Karlene V. Schwartz. *Five Kingdoms. An Illustrated Guide to the Phyla of Life on Earth*. W.H. Freeman, San Francisco, 1982.

Die Mendelschen Gesetze der Vererbung

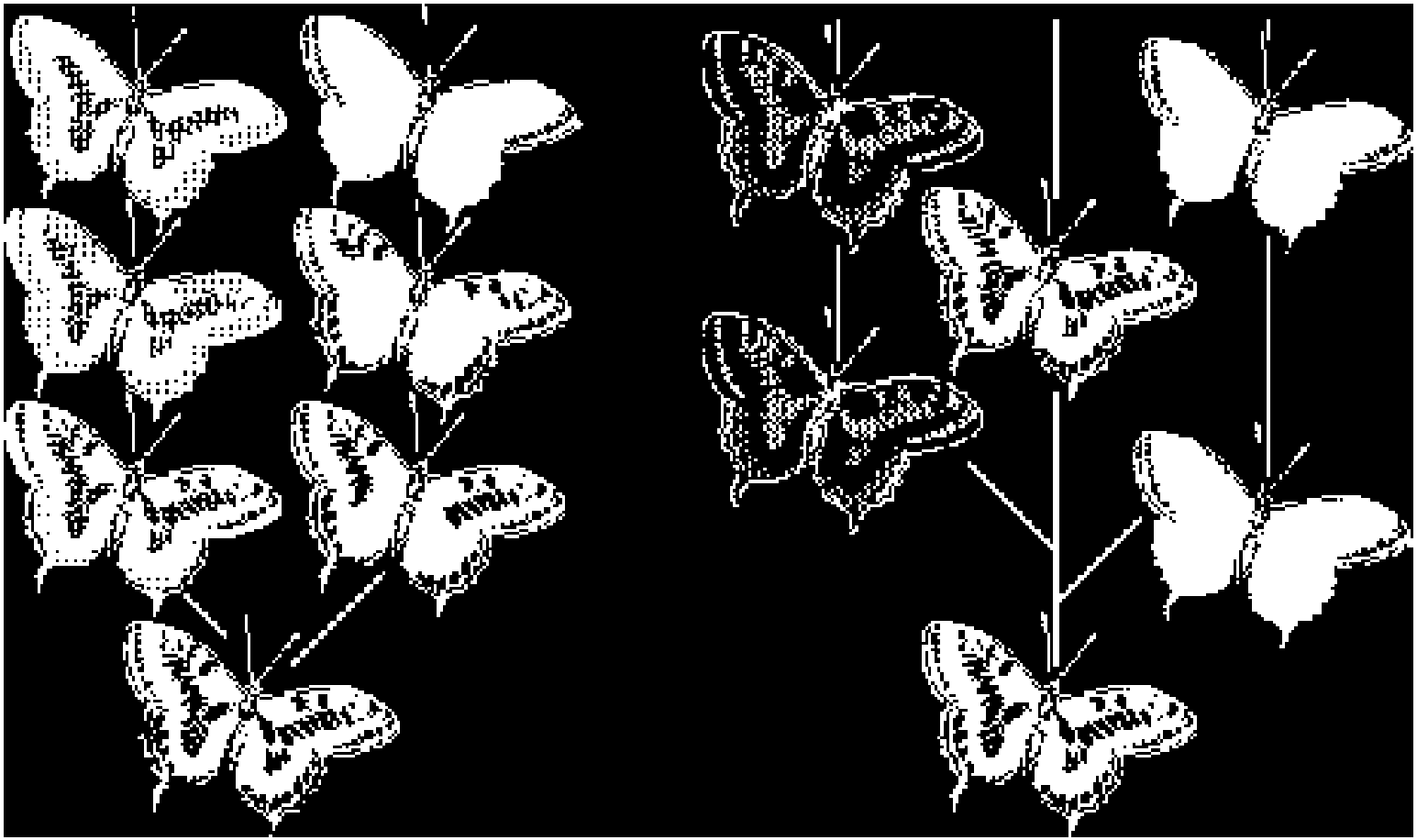


Stephen Jay Gould, 1941 – 2002

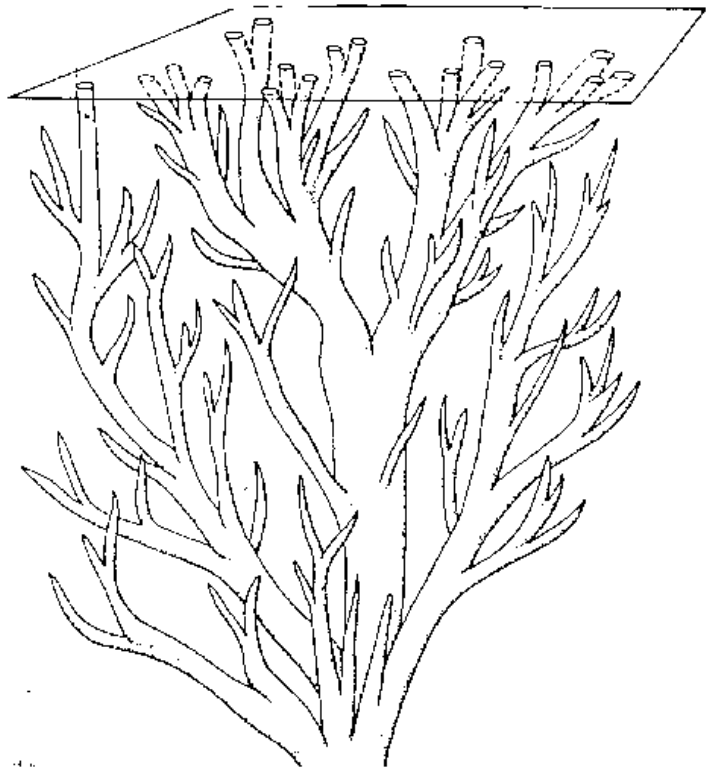
"**Punctuated Equilibrium**":

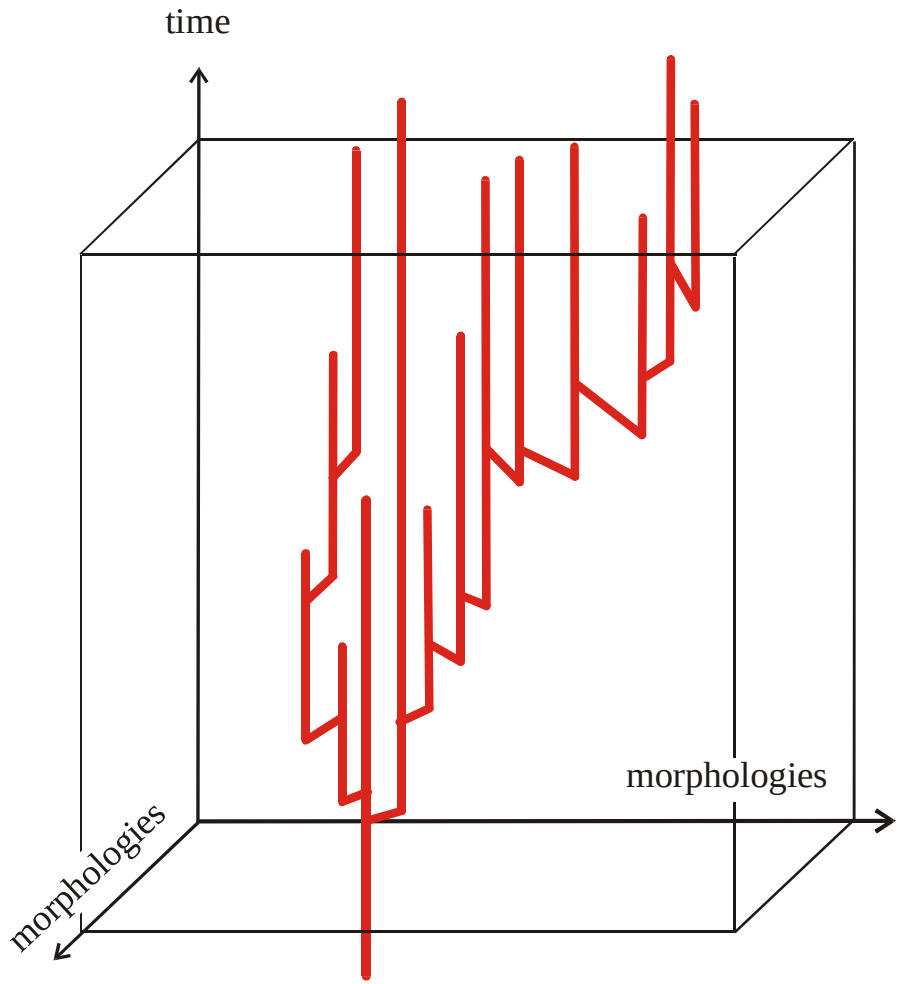
Die Evolution erfolgt in abrupten Sprüngen und nicht durch (unmerkbar) kleine Schritte.

Niles Eldredge, 1943 –

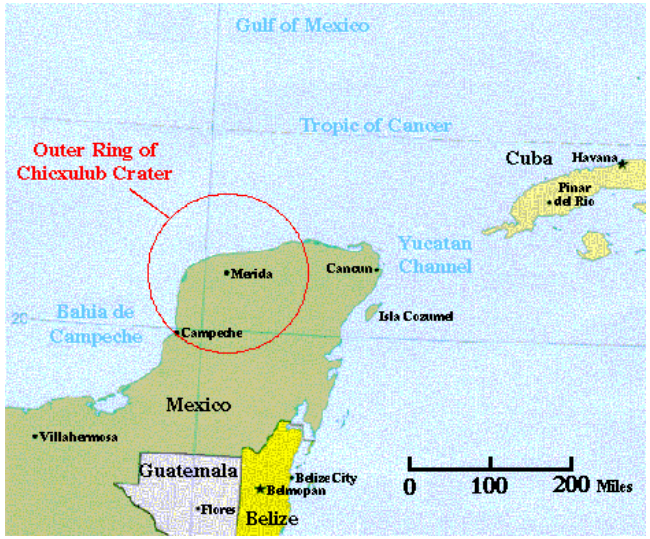


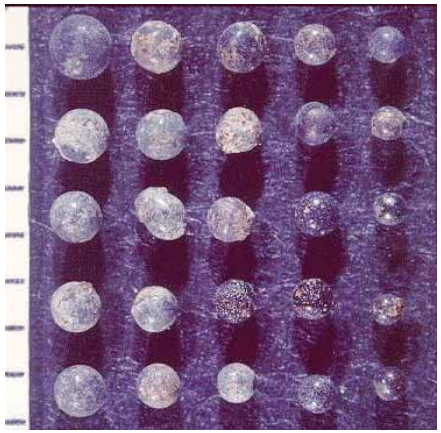
Graduelle Veränderung und “Punctuated Equilibrium” auf Schmetterlingsflügeln

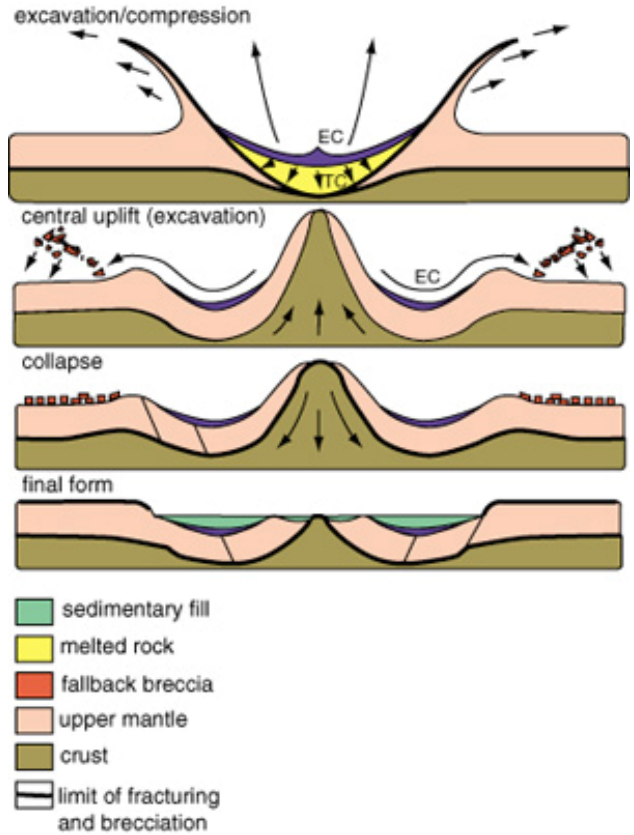




Phylogenetische Bäume aus der Sicht der “Gradualisten” und des “Punctuated Equilibrium”







Falling meterorites:
An example is the Chicxulub crater in Mexico dated 65 million years ago

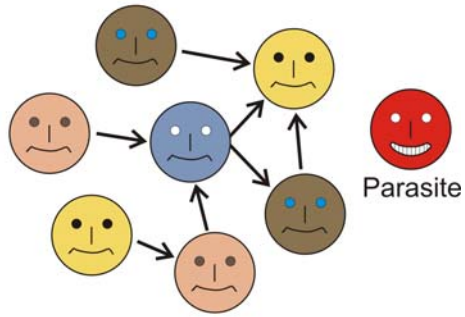
L.W.Alvarez, *Mass Extinctions caused by large bolide impacts*. Physics Today **40**: 24-33, 1987

Die großen Evolutionssprünge (nach John Maynard Smith und Eörs Szathmáry)

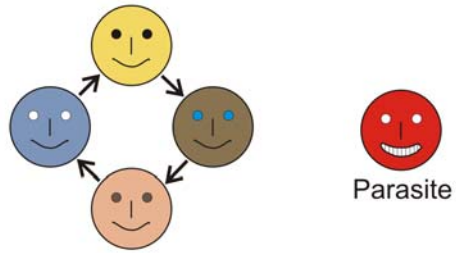
	Membranen, organisierte Teilung		
Replizierende Moleküle	⇒	Moleküle in Kompartments	
	Molekülverkettung, gemeinsame Replikation		
Unabhängige Replikatoren	⇒	Chromosomen	
	genetischer Code, Ribosom		
RNA als Gen und Enzyme	⇒	DNA und Protein	
	Zusammenschluß durch Endosymbiose		
Prokaryoten	⇒	Eukaryoten	
	Ursprung der sexuellen Vermehrung		
Asexuell vermehrende Klone	⇒	Sexuell vermehrende Populationen	
	Zelldifferenzierung und Entwicklung		
Protisten	⇒	Pflanzen, Pilze und Tiere	
	Entstehung nicht-reproduktiver Kasten		
Einzeln lebende Individuen	⇒	Tierkolonien	
	Sprache, Schrift, Kultur, …		
Primatengesellschaften	⇒	menschliche Gesellschaften	

Stufe I:
Unabhängige Replikatoren
in Konkurrenz

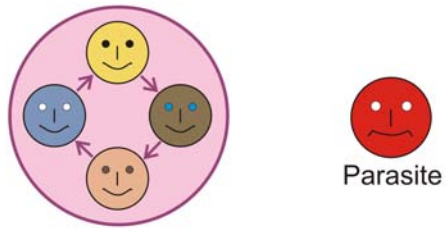
Stufe II:
Katalyse und Konkurrenz
bei der Replikation



Stufe III:
Funktionell verknüpfte
Replikatoren



Stufe IV:
Neue Einheit der
Selektion



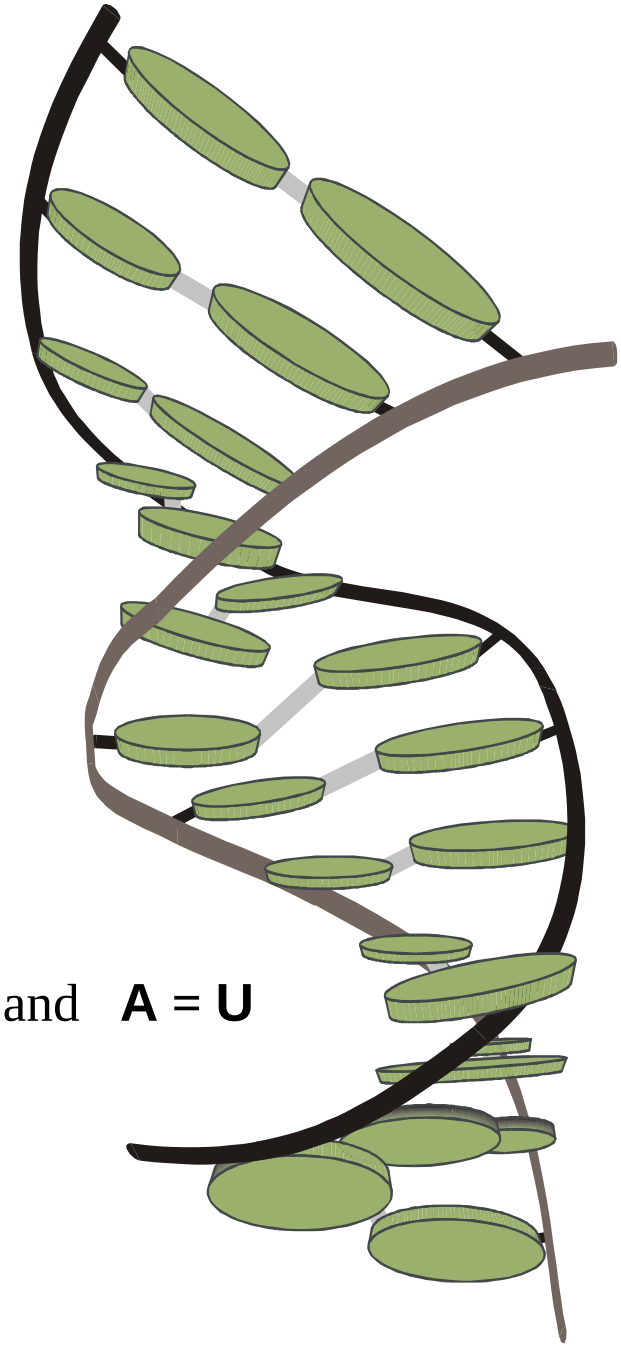
Stufe V:
Unabhängige Einheiten
in Konkurrenz

Ein Mechanismus zur Überwindung
hierarchischer Stufen in der Evolution
(nach Manfred Eigen und Peter Schuster)

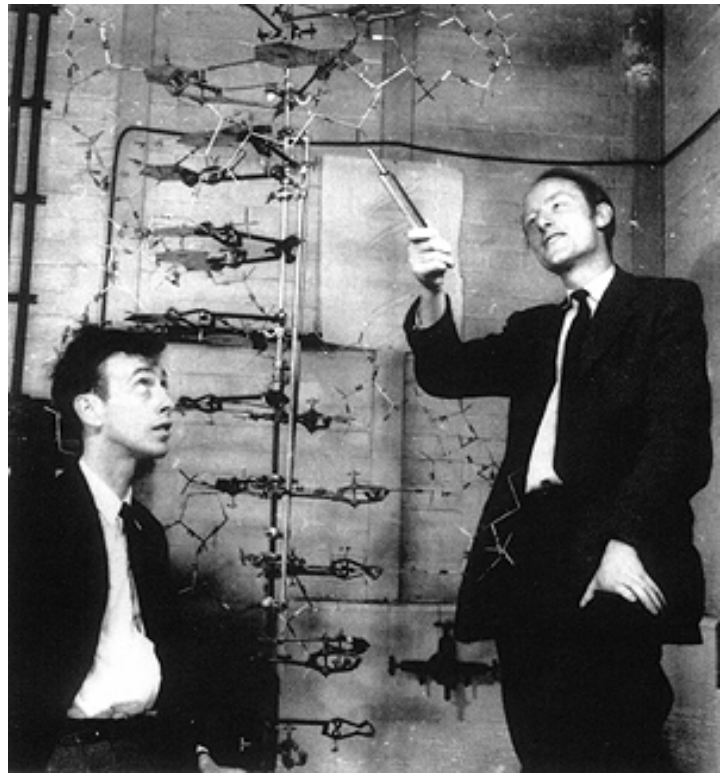
1. Geschichte des Evolutionsgedankens
2. Wahrscheinlichkeit und Zufall in der Biologie
3. Komplexes Verhalten aus einfachen Regeln
4. Evolutionsmechanismen
5. **Molekularbiologie und Evolutionsexperimente**
6. Ursprung komplexer Organe – Das Auge als Beipiel

	Generation time	Selection and adaptation 10 000 generations	Genetic drift in small populations 10^6 generations	Genetic drift in large populations 10^7 generations
RNA molecules	10 sec 1 min	27.8 h = 1.16 d 6.94 d	115.7 d 1.90 a	3.17 a 19.01 a
Bacteria	20 min 10 h	138.9 d 11.40 a	38.03 a 1 140 a	380 a 11 408 a
Multicelluar organisms	10 d 20 a	274 a 20 000 a	27 380 a 2×10^7 a	273 800 a 2×10^8 a

Time scales of evolutionary change

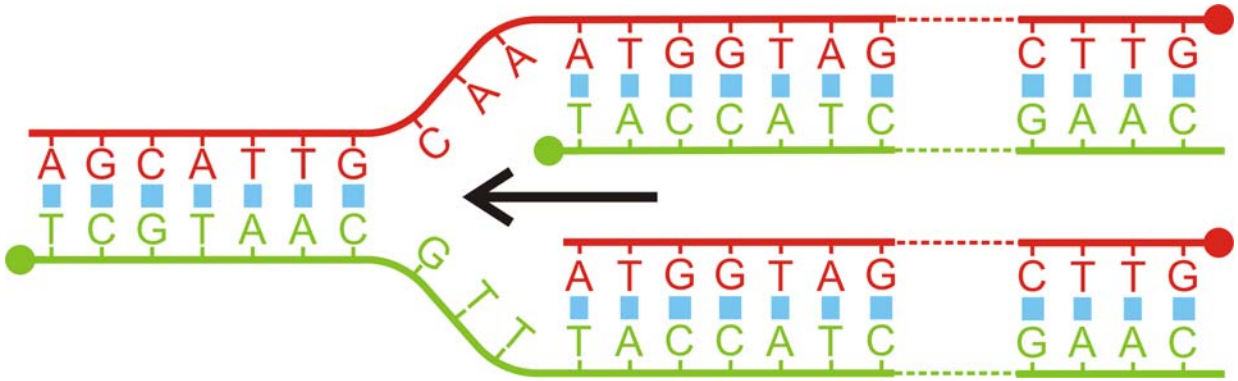


G ≡ C and **A = U**



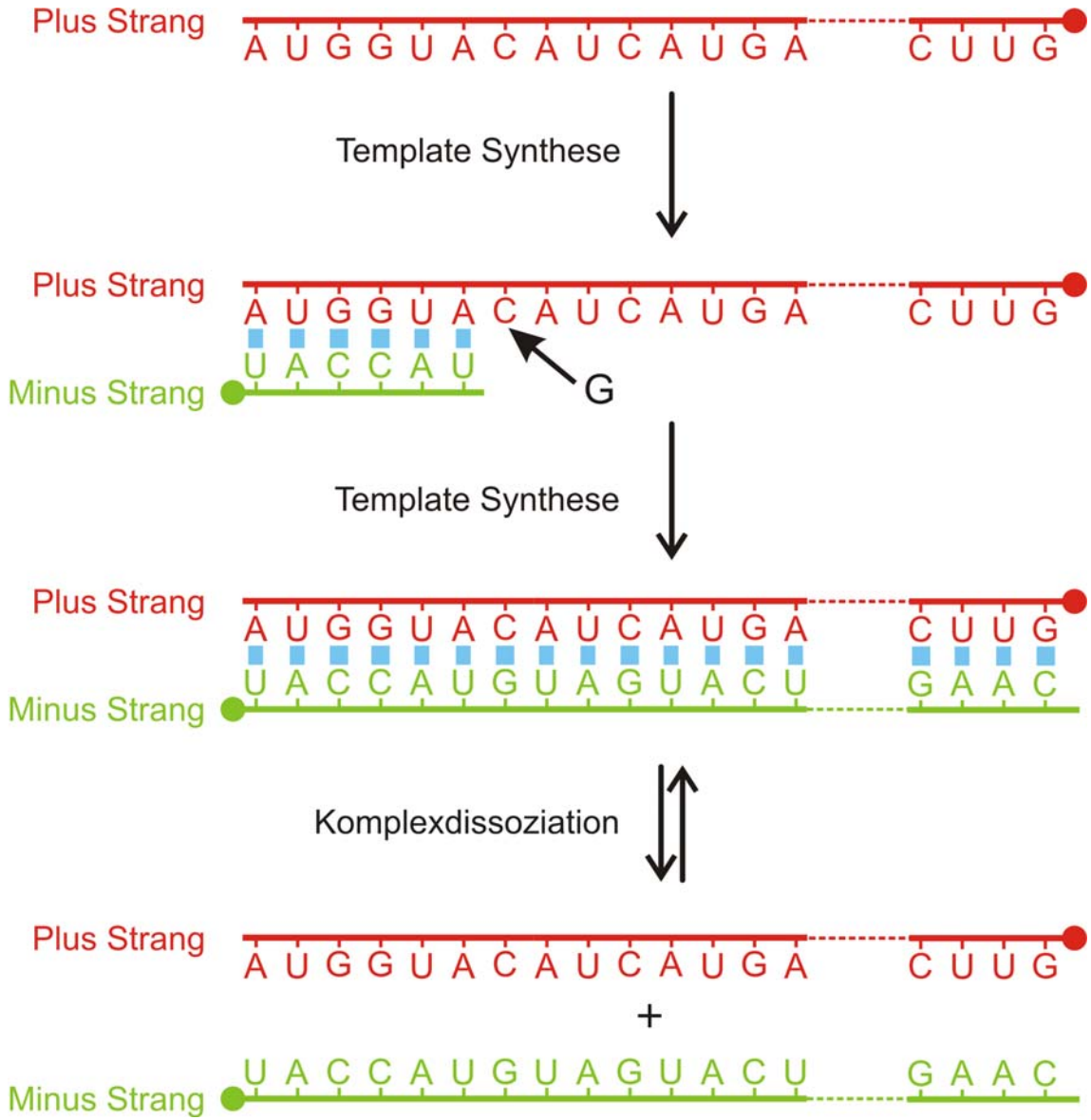
James D. Watson, 1928- , and Francis Crick, 1916-2004,
Nobel Prize 1962

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

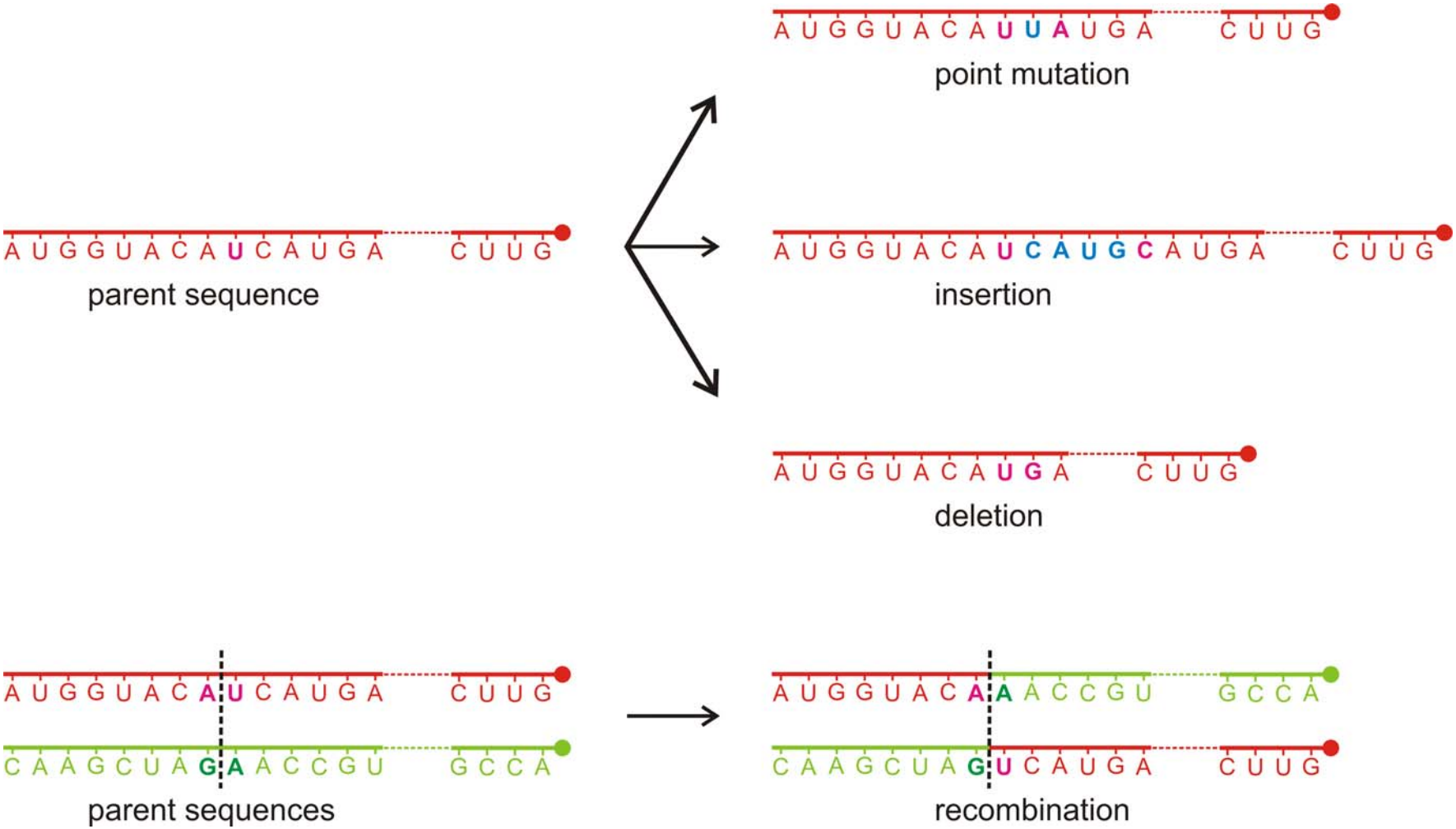


Die “Replikationsgabel”

Mechanismus der Replikation von doppelsträngigen DNA-Molekülen



Der Mechanismus der Replikation einsträngiger RNA-Moleküle



Ursachen der Variation der genetischen Information: Mutation und Rekombination

Molekulare Evolutionsforschung durch DNA-Sequenzierung

Aus dem Vergleich der heutigen DNA-Sequenzen kann die geschichtliche Abfolge der Mutationen rekonstruiert werden und diese ergibt phylogenetische Bäume, die jenen aus der vergleichenden Morphologie, welche durch Betrachtung von Formen und Gestalten gewonnen wurden, weitest gehend entsprechen.

Eine in der Vergangenheit postulierte **molekulare Uhr der Evolution** verlangt, dass die Mutationshäufigkeiten auf den verschiedenen Ästen der phylogenetischen Bäume gleich groß sind (**???**).

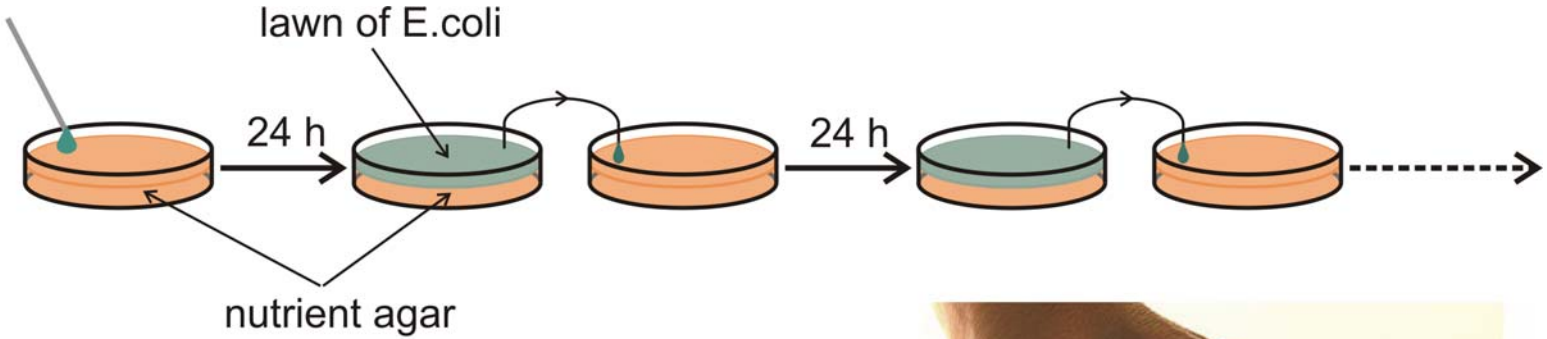
Bacterial Evolution

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

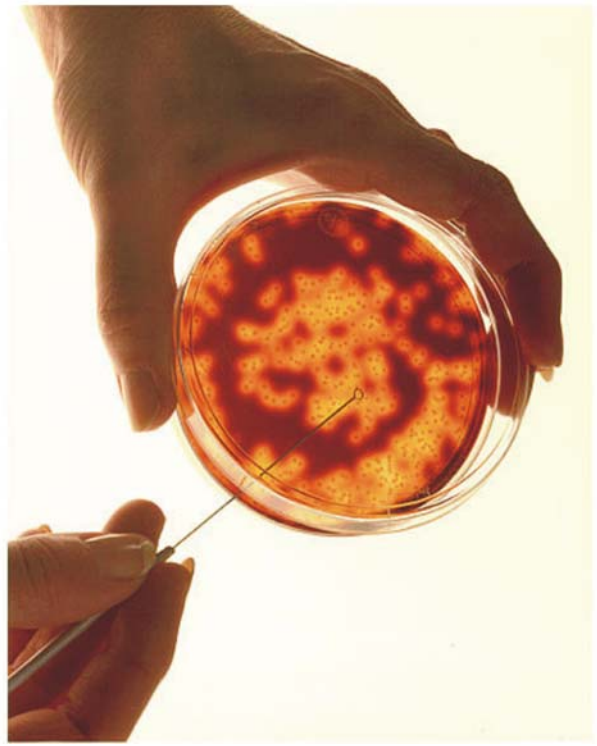
D. Papadopoulos, D. Schneider, J. Meier-Eiss, W. Arber, R. E. Lenski, M. Blot. ***Genomic evolution during a 10,000-generation experiment with bacteria***. Proc.Natl.Acad.Sci.USA **96** (1999), 3807-3812

S. F. Elena, R. E. Lenski. ***Evolution experiments with microorganisms: The dynamics and genetic bases of adaptation***. Nature Review Genetics **4** (2003), 457-469

C. Borland, R. E. Lenski. ***Spontaneous evolution of citrate utilization in* Escherichia coli *after 30000 generations***. Evolution Conference 2004, Fort Collins, Colorado



1 day » 6.67 generations
1 month » 200 generations
1 year » 2400 generations



Serial transfer of Escherichia coli cultures in Petri dishes

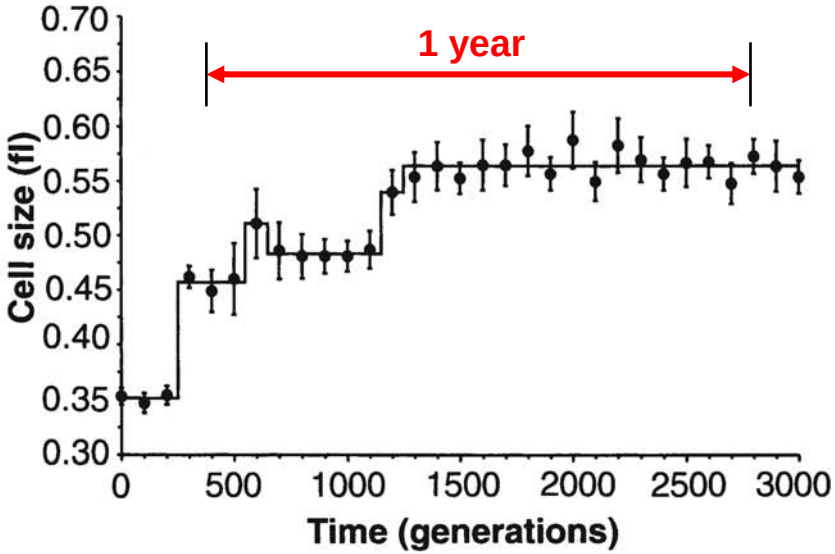


Fig. 1. Change in average cell size (1 fl = 10^{-15} L) in a population of *E. coli* during 3000 generations of experimental evolution. Each point is the mean of 10 replicate assays (*22*). Error bars indicate 95% confidence intervals. The solid line shows the best fit of a step-function model to these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

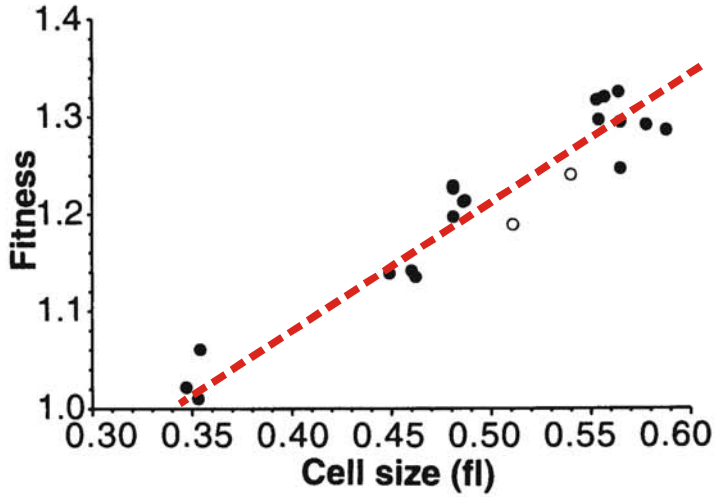
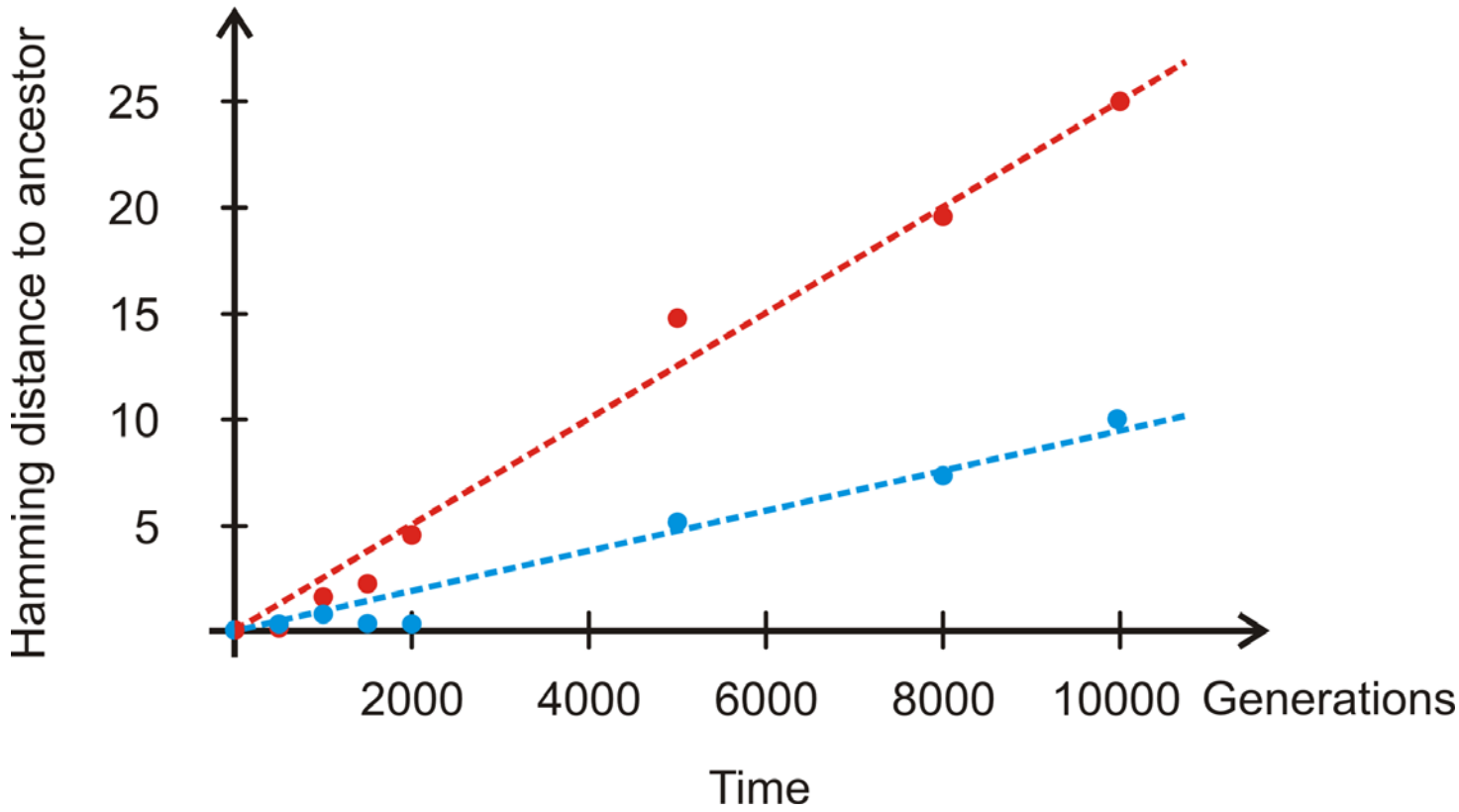


Fig. 2. Correlation between average cell size and mean fitness, each measured at 100-generation intervals for 2000 generations. Fitness is expressed relative to the ancestral genotype and was obtained from competition experiments between derived and ancestral cells (*6*, *7*). The open symbols indicate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



Variation of genotypes in a bacterial serial transfer experiment

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

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

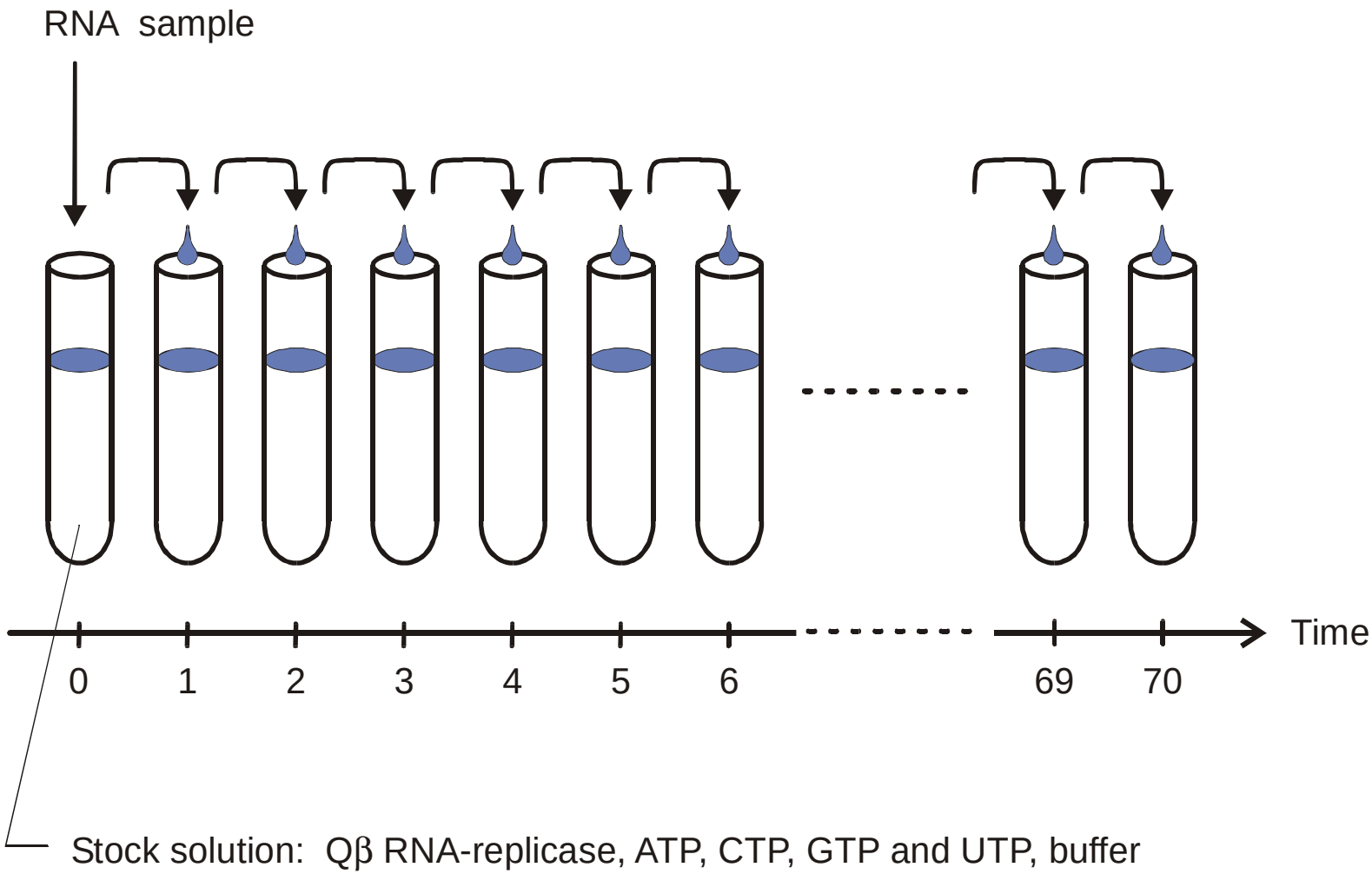
S.Spiegelman, ***An approach to the experimental analysis of precellular evolution***. Quart.Rev.Biophys. **4** (1971), 213-253

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

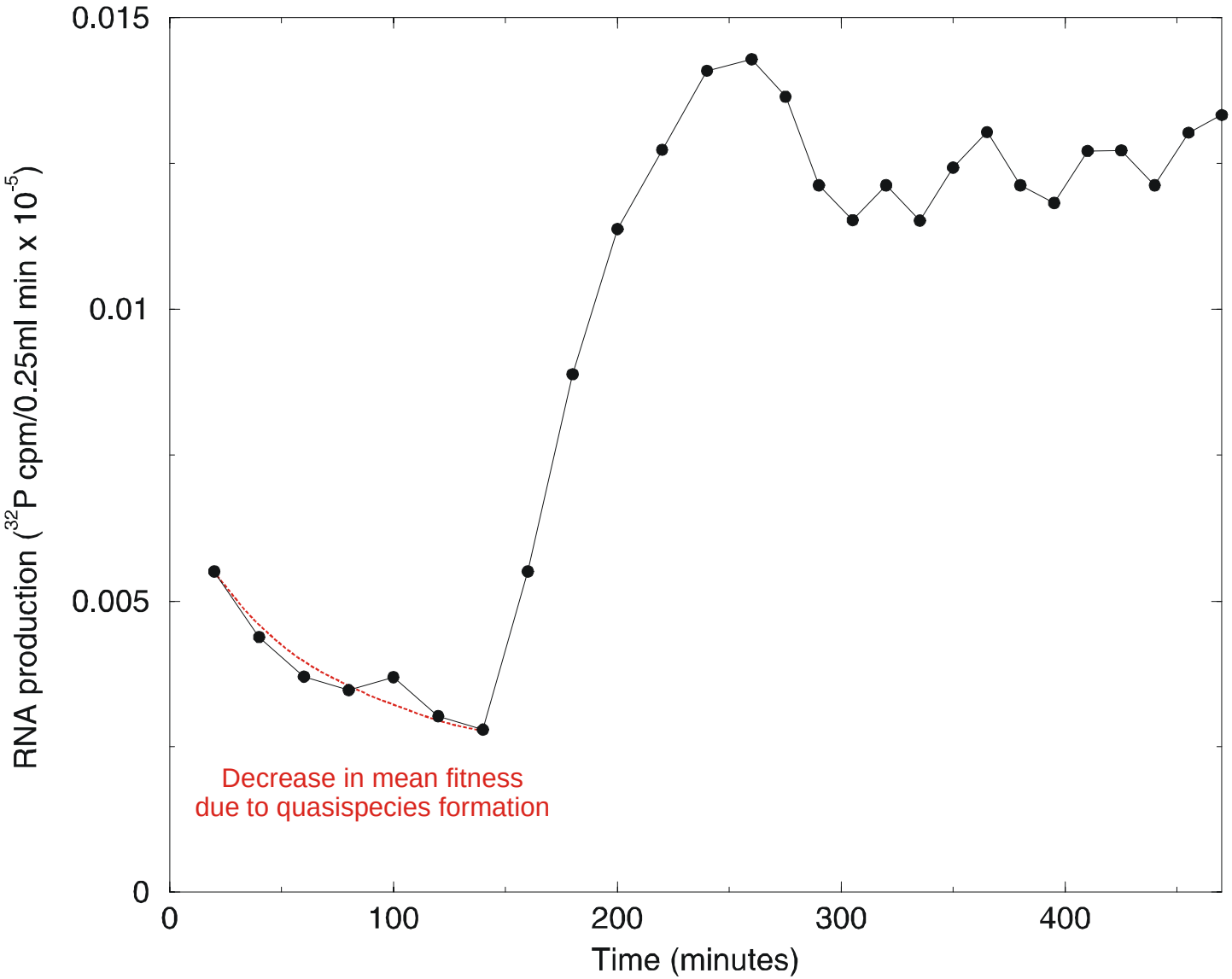
G.Bauer, H.Otten, J.S.McCaskill, ***Travelling waves of* in vitro *evolving RNA.*** *Proc.Natl.Acad.Sci.USA* **86** (1989), 7937-7941

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***



The increase in RNA production rate during a serial transfer experiment

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

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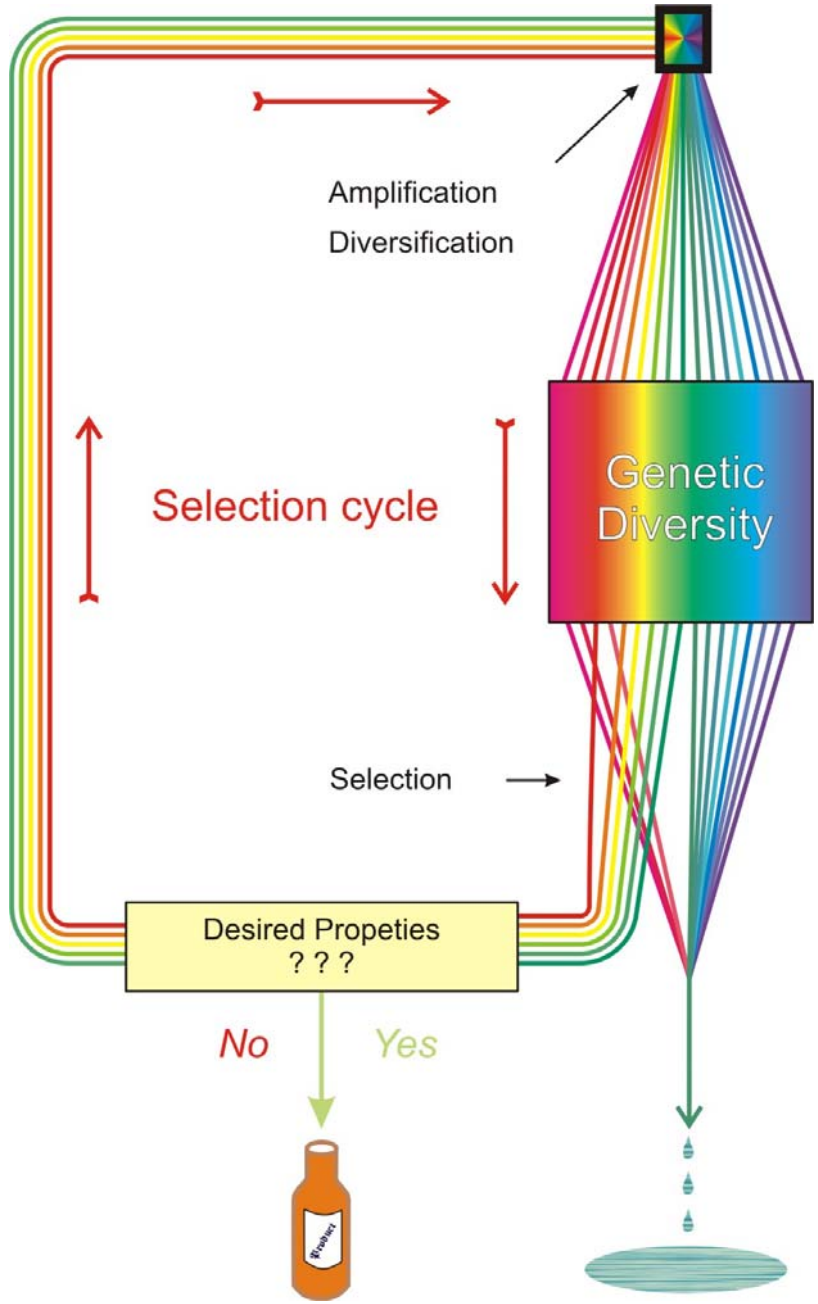
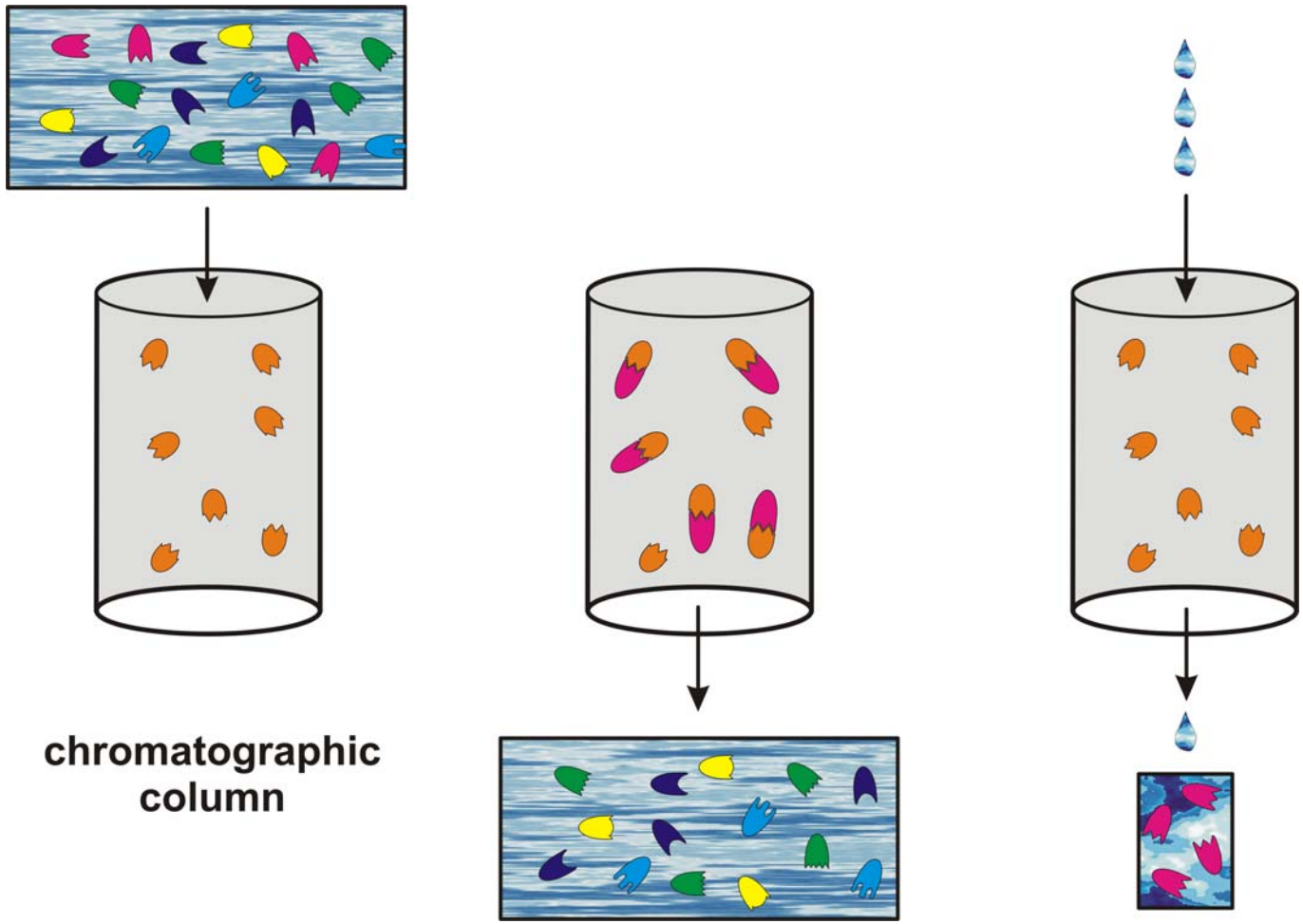
R.D.Jenison, S.C.Gill, A.Pardi, B.Poliski, ***High-resolution molecular discrimination by RNA***. Science **263** (1994), 1425-1429

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

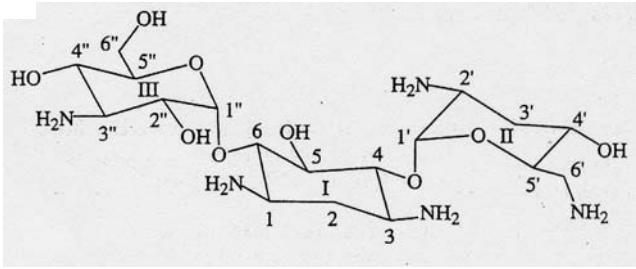
Jiang, A. K. Suri, R. Fiala, D. J. Patel, ***Saccharide-RNA recognition in an aminoglycoside antibiotic-RNA aptamer complex***. Chemistry & Biology **4** (1997), 35-50

An example of ‘artificial selection’ with RNA molecules or ‘breeding’ of biomolecules

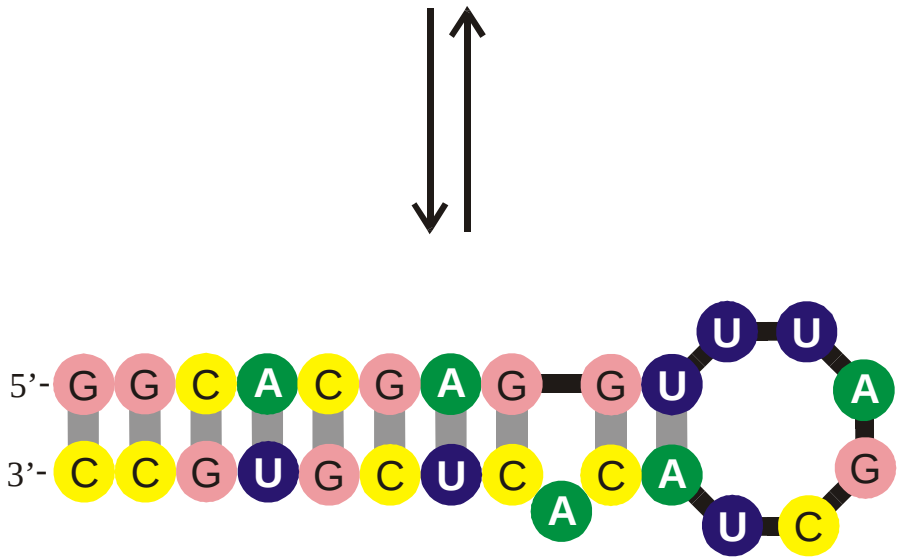




The SELEX technique for the evolutionary preparation of aptamers



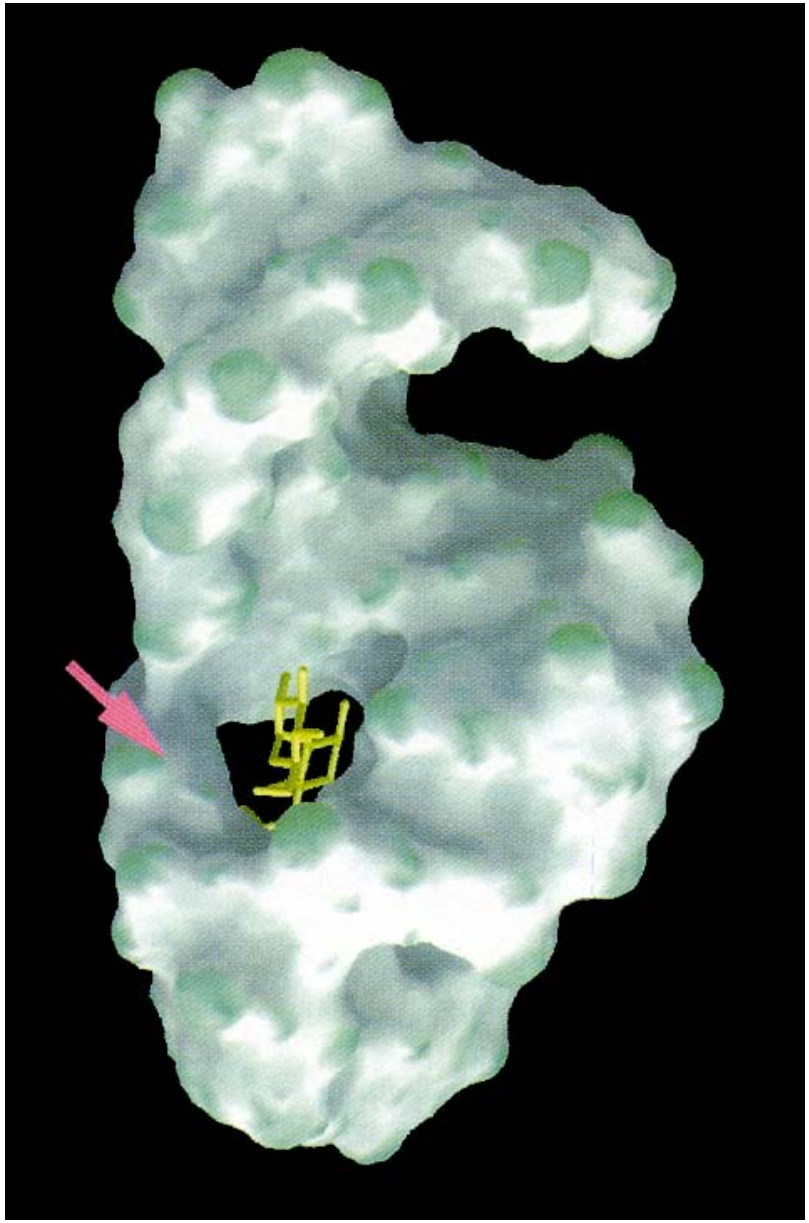
tobramycin



RNA aptamer

Formation of secondary structure of the tobramycin binding RNA aptamer with **K_D = 9 nM**

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)

Evolution *in silico*

W. Fontana, P. Schuster,
Science **280** (1998), 1451-1455

random individuals. The primer pair used for genomic DNA amplification is 5′-TCTCCCTGGATTCT-CATTTA-3′ (forward) and 5′-TCTTTGTCTTCTGT-TCCACC-3′ (reverse). Reactions were performed in 25 μl using 1 unit of Taq DNA polymerase with each primer at 0.4 μM; 200 μM each dATP, dTTP, dGTP, and dCTP; and PCR buffer [10 mM tris-HCl (pH 8.3), 50 mM KCl_2,1.5 mM $MgCl_2$] in a cycle condition of 94°C for 1 min and then 35 cycles of 94°C for 30 s, 55°C for 30 s, and 72°C for 30 s followed by 72°C for 6 min. PCR products were purified (Qiagen), digested with Xmn I, and separated in a 2% agarose gel.

32. A nonsense mutation may affect mRNA stability and result in degradation of the transcript [L. Maquat, *Am. J. Hum. Genet.* **59**, 279 (1996)].
33. Data not shown; a dot blot with poly (A)$^+$ RNA from 50 human tissues (The Human RNA Master Blot, 7770-1, Clontech Laboratories) was hybridized with a probe from exons 29 to 47 of *MYO15* using the same condition as Northern blot analysis (*13*).
34. Smith–Magenis syndrome (SMS) is due to deletions of 17p11.2 of various sizes, the smallest of which includes *MYO15* and perhaps 20 other genes [(*6*); K-S Chen, L. Potocki, J. R. Lupski, *MRDD Res. Rev.* **2**, 122 (1996)]. *MYO15* expression is easily detected in the pituitary gland (data not shown). Haploinsufficiency for *MYO15* may explain a portion of the SMS phenotype such as short stature. Moreover, a few SMS patients have sensorineural hearing loss, possibly because of a point mutation in *MYO15* in trans to the SMS 17p11.2 deletion.
35. R. A. Fridell, data not shown.
36. K. B. Avraham *et al.*, *Nature Genet.* **11**, 369 (1995); X-Z. Liu *et al.*, *ibid.* **17**, 268 (1997); F. Gibson *et al.*, *Nature* **374**, 62 (1995); D. Weil *et al.*, *ibid.*, p. 60.
37. RNA was extracted from cochlea (membranous labyrinths) obtained from human fetuses at 18 to 22 weeks of development in accordance with guidelines established by the Human Research Committee at the Brigham and Women's Hospital. Only samples without evidence of degradation were pooled for poly (A)$^+$ selection over oligo(dT) columns. First-strand cDNA was prepared using an Advantage RT-for-PCR kit (Clontech Laboratories). A portion of the first-strand cDNA (4%) was amplified by PCR with Advantage cDNA polymerase mix (Clontech Laboratories) using human *MYO15*-specific oligonucleotide primers (forward, 5′-GCATGACCTGCCGGCTAAT-GGG-3′; reverse, 5′-CTCACGGCTTCTGCATGGT-GCTCGGCTGGC-3′). Cycling conditions were 40 s at 94°C; 40 s at 66°C (3 cycles), 60°C (5 cycles), and 55°C (29 cycles); and 45 s at 68°C. PCR products were visualized by ethidium bromide staining after fractionation in a 1% agarose gel. A 688-bp PCR product is expected from amplification of the human *MYO15* cDNA. Amplification of human genomic DNA with this primer pair would result in a 2903-bp fragment.

38. We are grateful to the people of Bengkala, Bali, and the two families from India. We thank J. R. Lupski and K.-S. Chen for providing the human chromosome 17 cosmid library. For technical and computational assistance, we thank N. Dietrich, M. Fergusson, A. Gupta, E. Sorbello, R. Torkzadeh, C. Varner, M. Walker, G. Bouffard, and S. Beckstrom-Sternberg (National Institutes of Health Intramural Sequencing Center). We thank J. T. Hinnant, I. N. Arhya, and S. Winata for assistance in Bali, and T. Barber, S. Sullivan, E. Green, D. Drayna, and J. Battey for helpful comments on this manuscript. Supported by the National Institute on Deafness and Other Communication Disorders (NIDCD) (Z01 DC 00035-01 and Z01 DC 00038-01 to T.B.F. and E.R.W. and R01 DC 03402 to C.C.M.), the National Institute of Child Health and Human Development (R01 HD30428 to S.A.C.) and a National Science Foundation Graduate Research Fellowship to F.J.P. This paper is dedicated to J. B. Snow Jr. on his retirement as the Director of the NIDCD.

9 March 1998; accepted 17 April 1998

Continuity in Evolution: On the Nature of Transitions

Walter Fontana and Peter Schuster

To distinguish continuous from discontinuous evolutionary change, a relation of nearness between phenotypes is needed. Such a relation is based on the probability of one phenotype being accessible from another through changes in the genotype. This nearness relation is exemplified by calculating the shape neighborhood of a transfer RNA secondary structure and provides a characterization of discontinuous shape transformations in RNA. The simulation of replicating and mutating RNA populations under selection shows that sudden adaptive progress coincides mostly, but not always, with discontinuous shape transformations. The nature of these transformations illuminates the key role of neutral genetic drift in their realization.

A much-debated issue in evolutionary biology concerns the extent to which the history of life has proceeded gradually or has been punctuated by discontinuous transitions at the level of phenotypes (*1*). Our goal is to make the notion of a discontinuous transition more precise and to understand how it arises in a model of evolutionary adaptation.

We focus on the narrow domain of RNA secondary structure, which is currently the simplest computationally tractable, yet realistic phenotype (*2*). This choice enables the definition and exploration of concepts that may prove useful in a wider context. RNA secondary structures represent a coarse level of analysis compared with the three-dimensional structure at atomic resolution. Yet, secondary structures are empirically well defined and obtain their biophysical and biochemical importance from being a scaffold for the tertiary structure. For the sake of brevity, we shall refer to secondary structures as "shapes." RNA combines in a single molecule both genotype (replicatable sequence) and phenotype (selectable shape), making it ideally suited for in vitro evolution experiments (*3*, *4*).

To generate evolutionary histories, we used a stochastic continuous time model of an RNA population replicating and mutating in a capacity-constrained flow reactor under selection (*5*, *6*). In the laboratory, a goal might be to find an RNA aptamer binding specifically to a molecule (*4*). Although in the experiment the evolutionary end product was unknown, we thought of its shape as being specified implicitly by the imposed selection criterion. Because our intent is to study evolutionary histories rather than end products, we defined a target shape in advance and assumed the replication rate of a sequence to be a function of the similarity between its shape and the target. An actual situation may involve more than one best shape, but this does not affect our conclusions.

An instance representing in its qualitative features all the simulations we performed is shown in Fig. 1A. Starting with identical sequences folding into a random shape, the simulation was stopped when the population became dominated by the target, here a canonical tRNA shape. The black curve traces the average distance to the target (inversely related to fitness) in the population against time. Aside from a short initial phase, the entire history is dominated by steps, that is, flat periods of no apparent adaptive progress, interrupted by sudden approaches toward the target structure (*7*). However, the dominant shapes in the population not only change at these marked events but undergo several fitness-neutral transformations during the periods of no apparent progress. Although discontinuities in the fitness trace are evident, it is entirely unclear when and on the basis of what the series of successive phenotypes itself can be called continuous or discontinuous.

A set of entities is organized into a (topological) space by assigning to each entity a system of neighborhoods. In the present case, there are two kinds of entities: sequences and shapes, which are related by a thermodynamic folding procedure. The set of possible sequences (of fixed length) is naturally organized into a space because point mutations induce a canonical neighborhood. The neighborhood of a sequence consists of all its one-error mutants. The problem is how to organize the set of possible shapes into a space. The issue arises because, in contrast to sequences, there are

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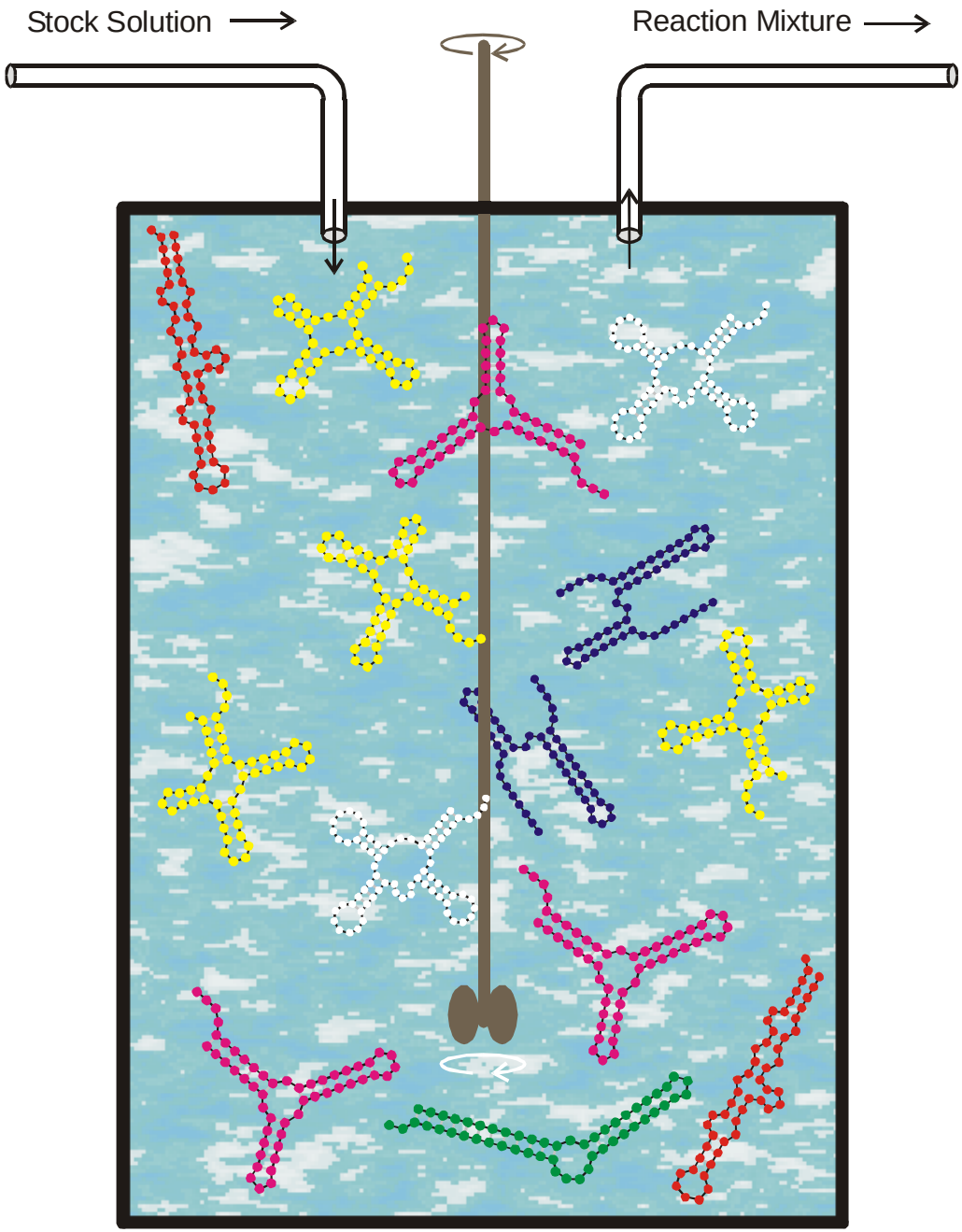


Replication rate constant:

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

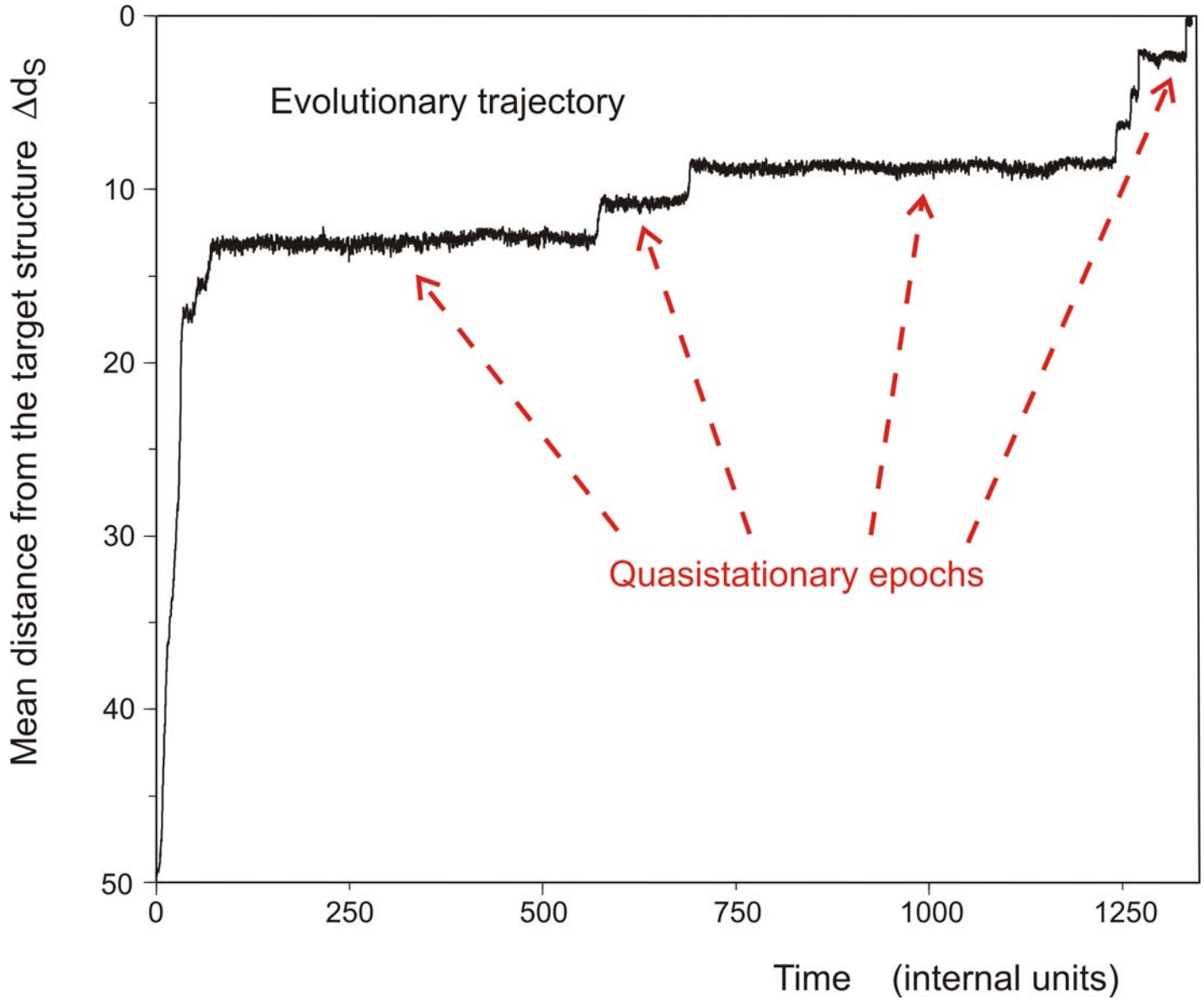
$$\Delta d_S{}^{(k)} = d_H(S_k, S_\tau)$$

Selection constraint:

RNA molecules is controlled by the flow

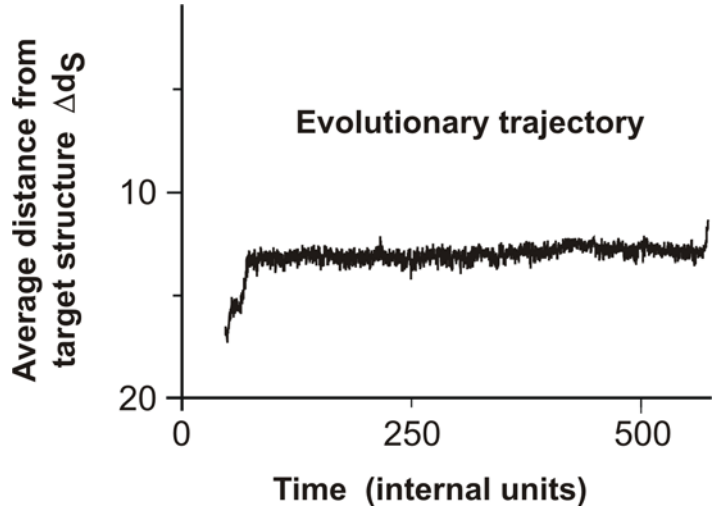
$$N(t) \approx \overline{N} \pm \sqrt{\overline{N}}$$

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



In silico optimization in the flow reactor: Evolutionary Trajectory

28 neutral point mutations during a long quasi-stationary epoch




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

Transition inducing point mutations change the molecular structure

Neutral point mutations leave the molecular structure unchanged

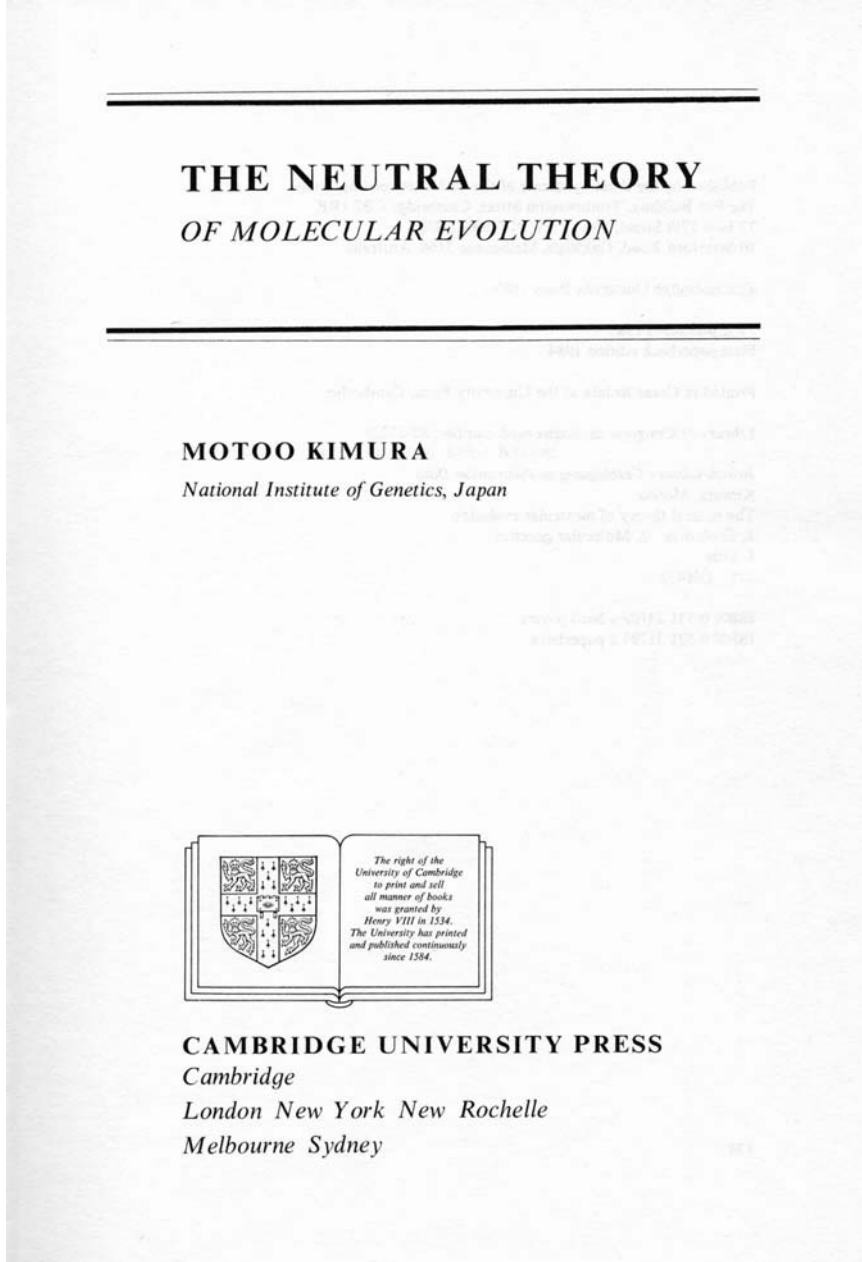
Neutral genotype evolution during phenotypic stasis

MOTOO KIMURA

Motoo Kimura's Population genetics of neutral evolution.

Evolutionary rate at the molecular level. *Nature* **217**: 624-626, 1955.

The Neutral Theory of Molecular Evolution. Cambridge University Press. Cambridge, UK, 1983.



THE NEUTRAL THEORY

OF MOLECULAR EVOLUTION

MOTOO KIMURA

National Institute of Genetics, Japan

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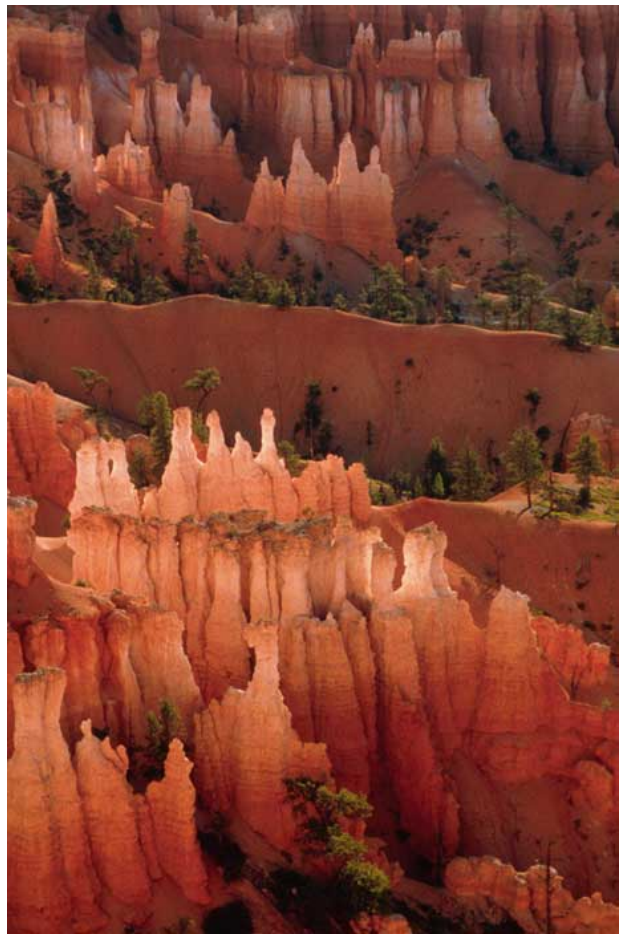
Melbourne Sydney

Mount Fuji

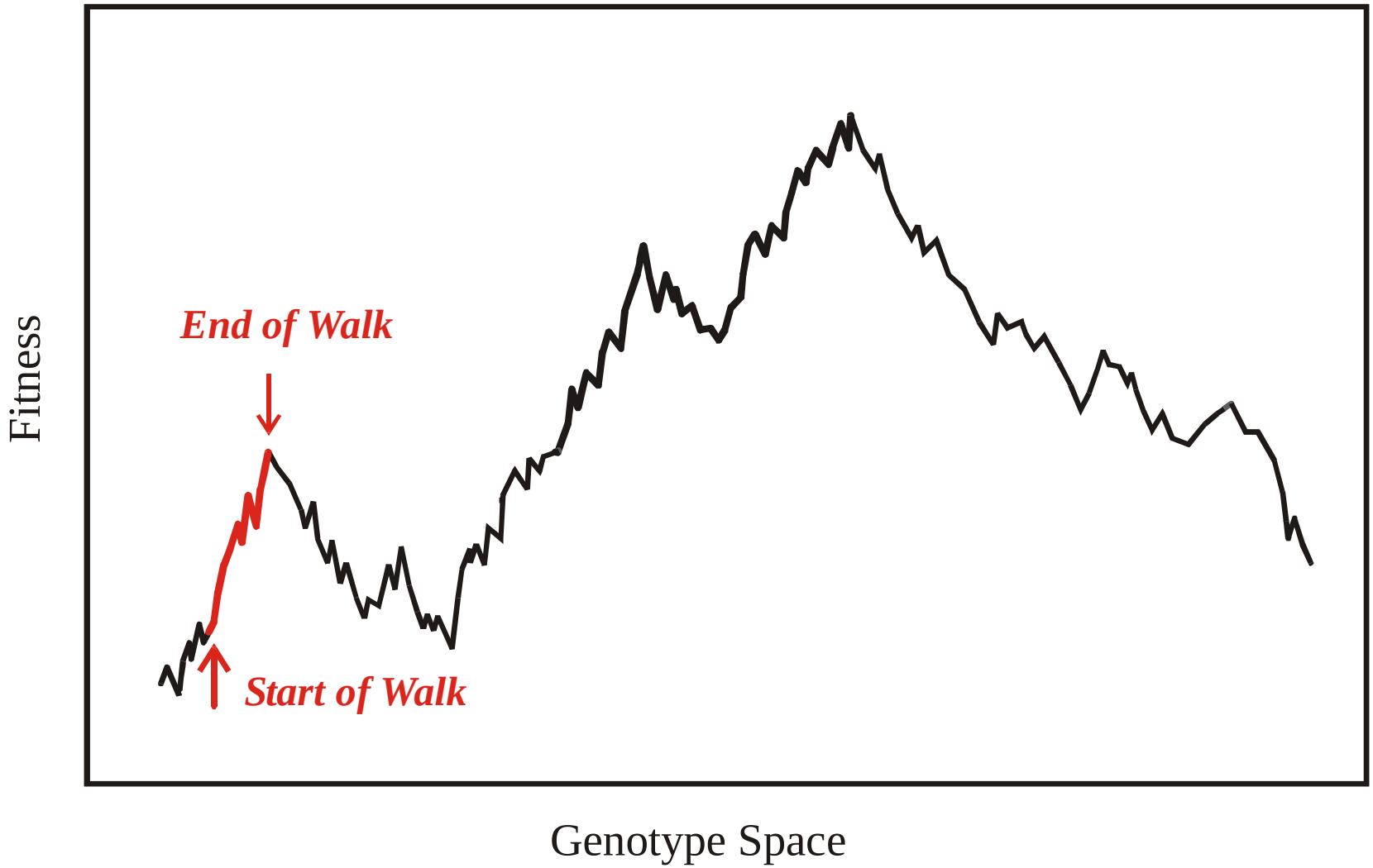
Example of a smooth landscape on Earth

Dolomites

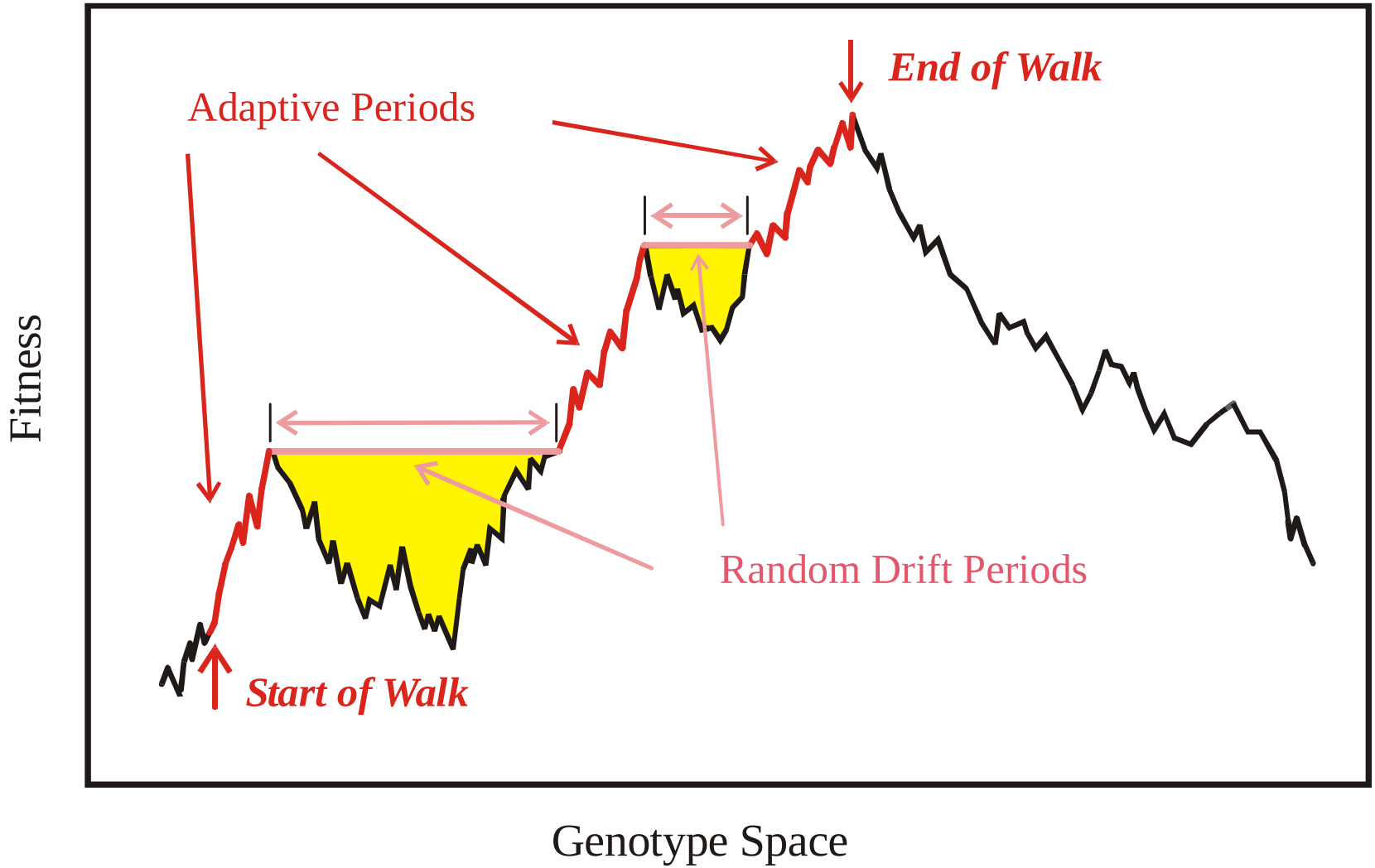


Bryce Canyon

Examples of rugged landscapes on Earth



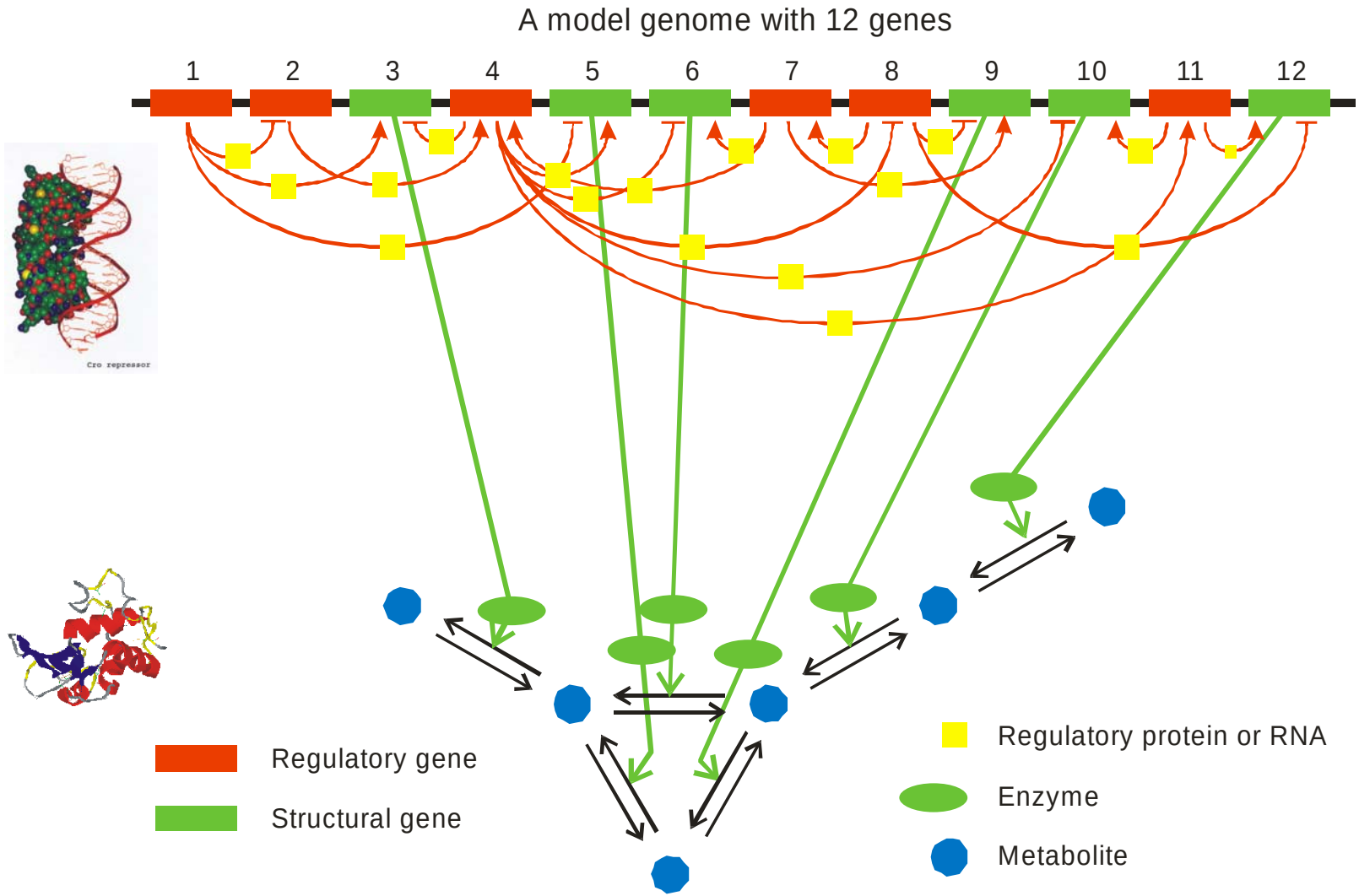
Evolutionary optimization in absence of neutral paths in sequence space



Evolutionary optimization including neutral paths in sequence space

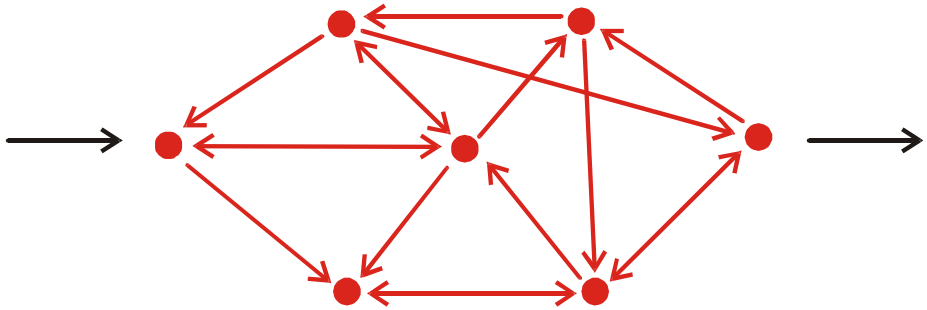
Grand Canyon

Example of a landscape on Earth with ‘neutral’ ridges and plateaus



Skizze eines einfachen genetisch-metabolischen Regulationsnetzwerkes

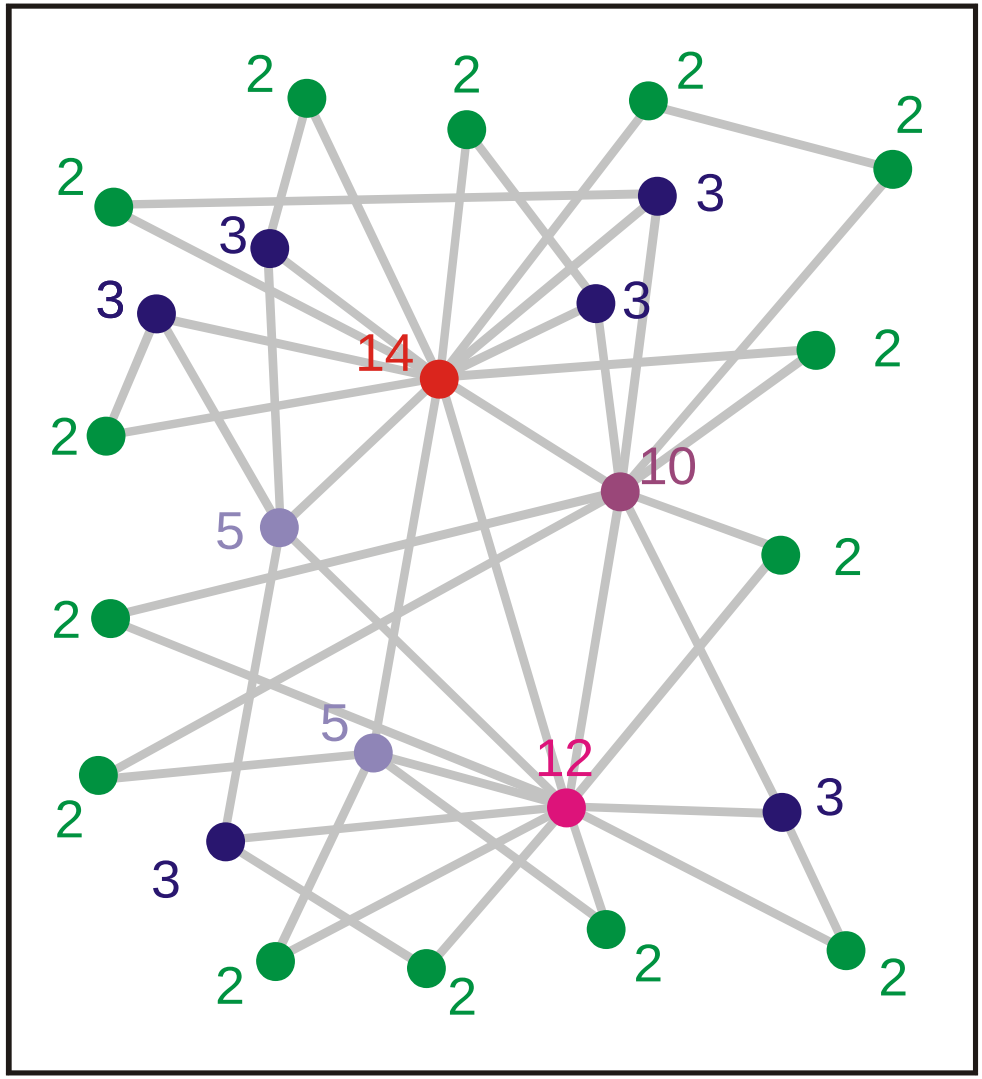
Linear chain



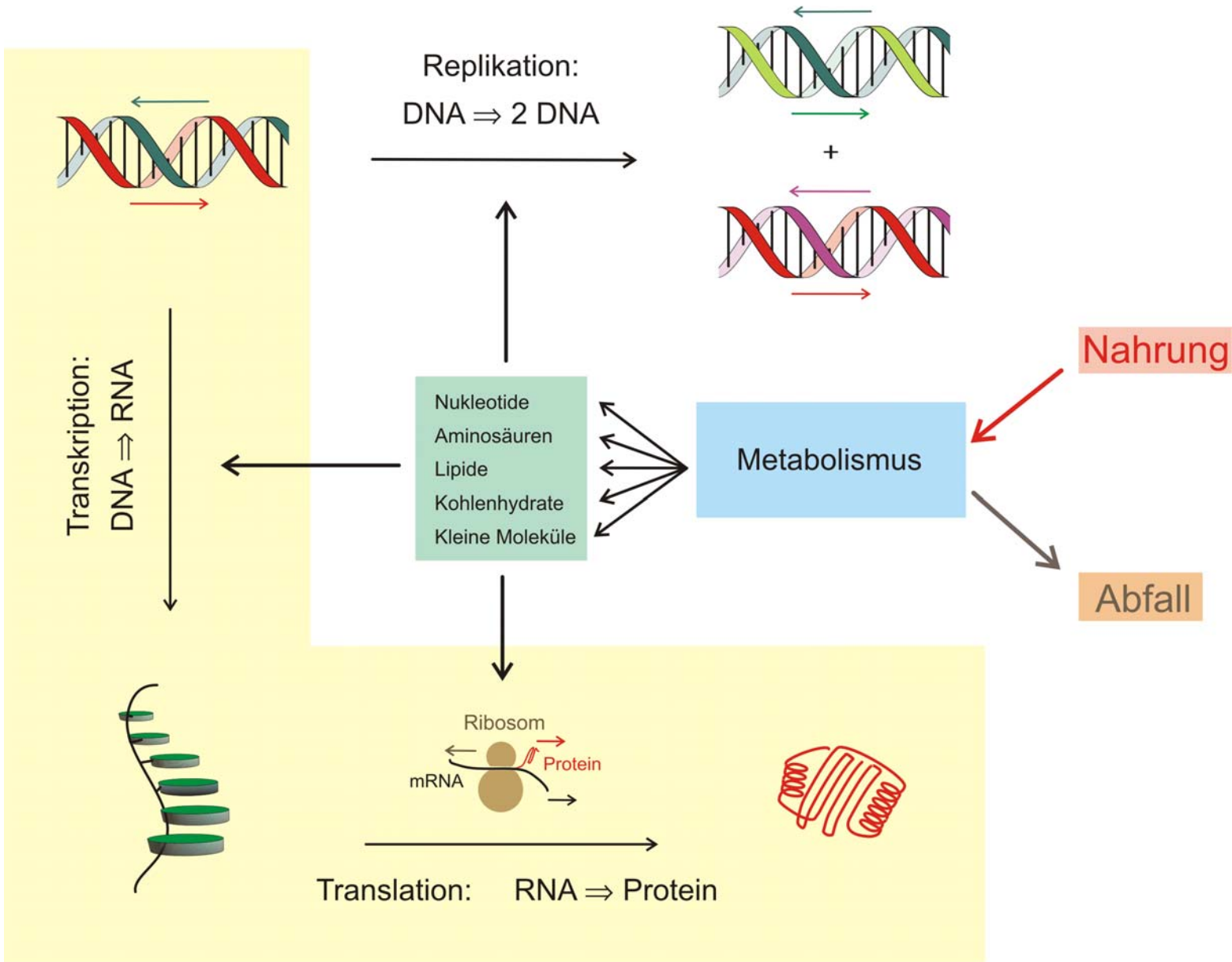
Network

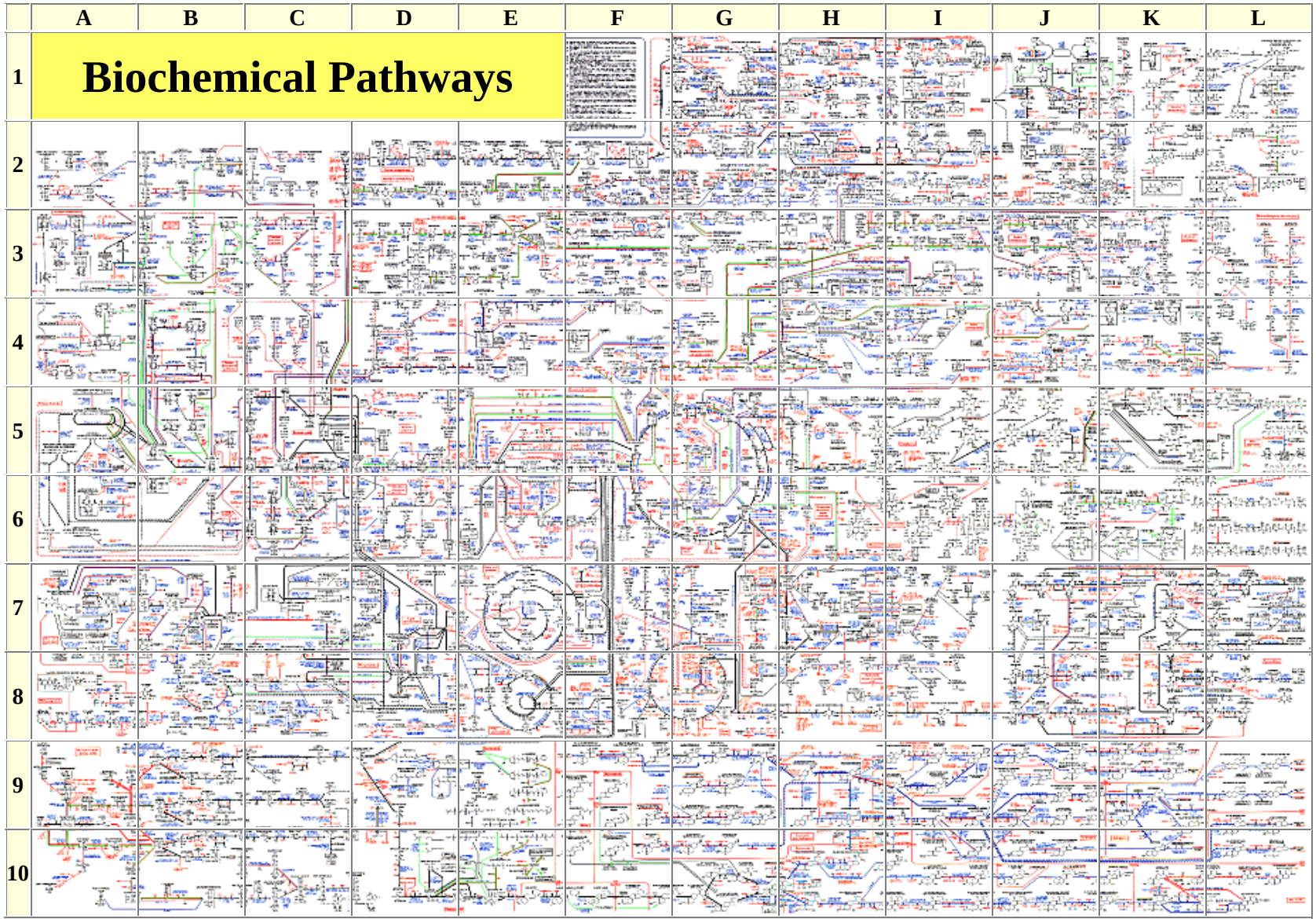
Processing of information in cascades and networks

links	# nodes
2	14
3	6
5	2
10	1
12	1
14	1



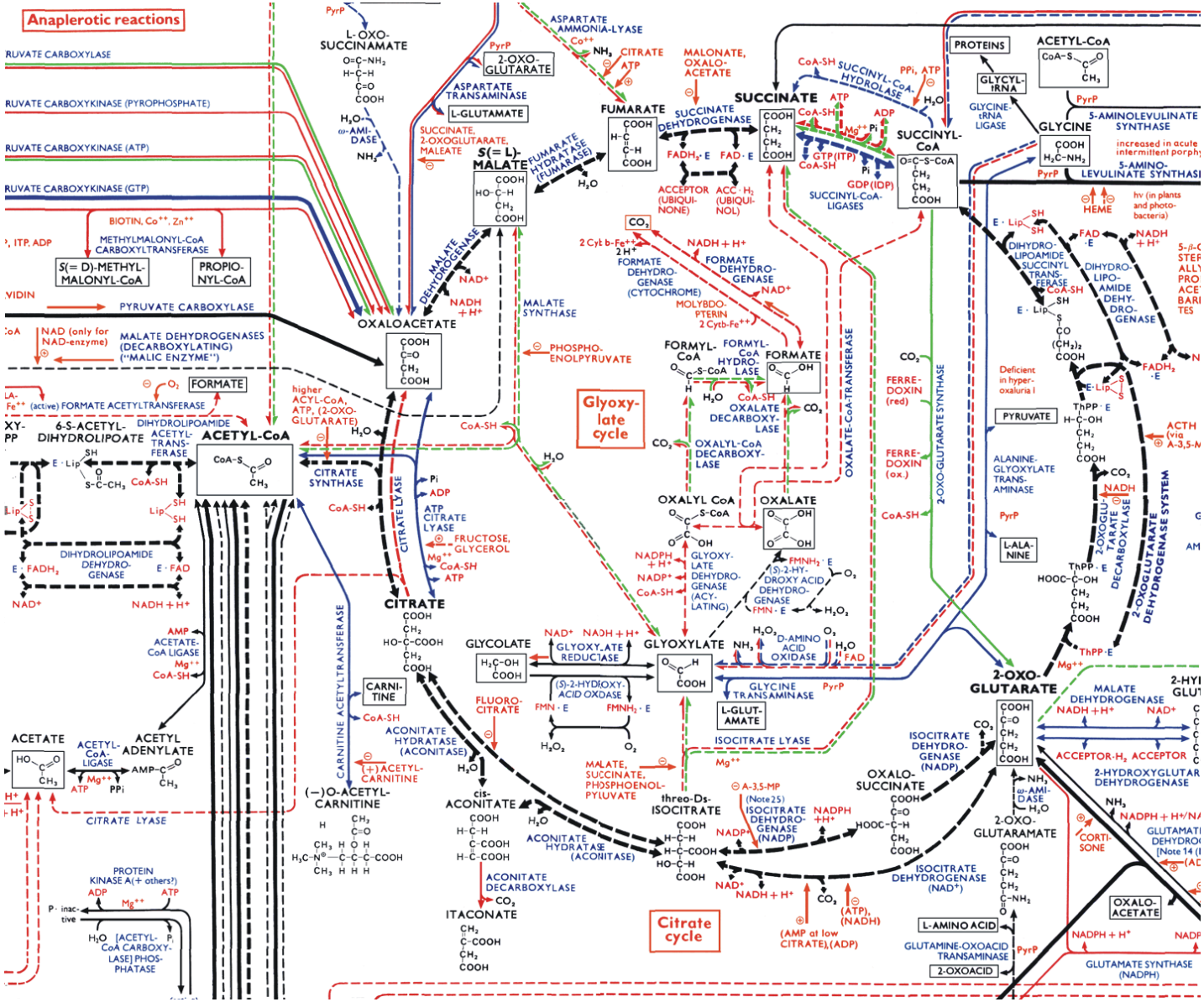
Analysis of nodes and links in a step by step evolved network

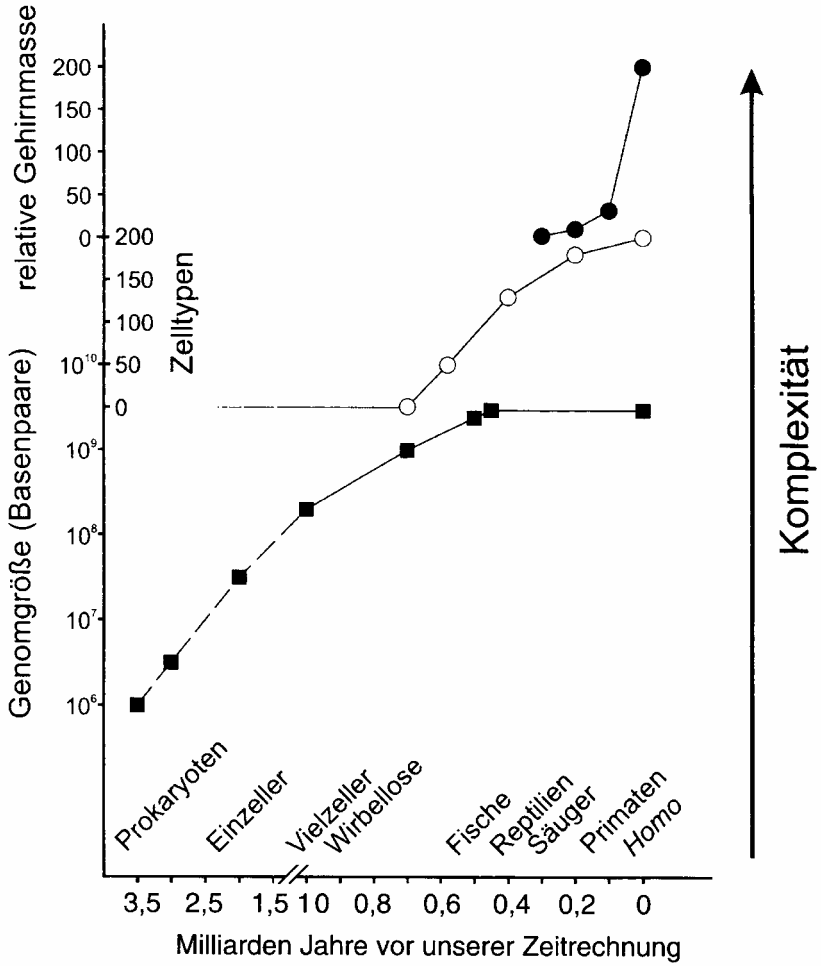

Replikation:
DNA ⇒ 2 DNA
+
Transkription:
DNA ⇒ RNA
Nukleotide
Aminosäuren
Lipide
Kohlenhydrate
Kleine Moleküle
Metabolismus
Nahrung
Abfall
Ribosom
mRNA
Protein
Translation: RNA ⇒ Protein



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

The citric acid or Krebs cycle (enlarged from previous slide).



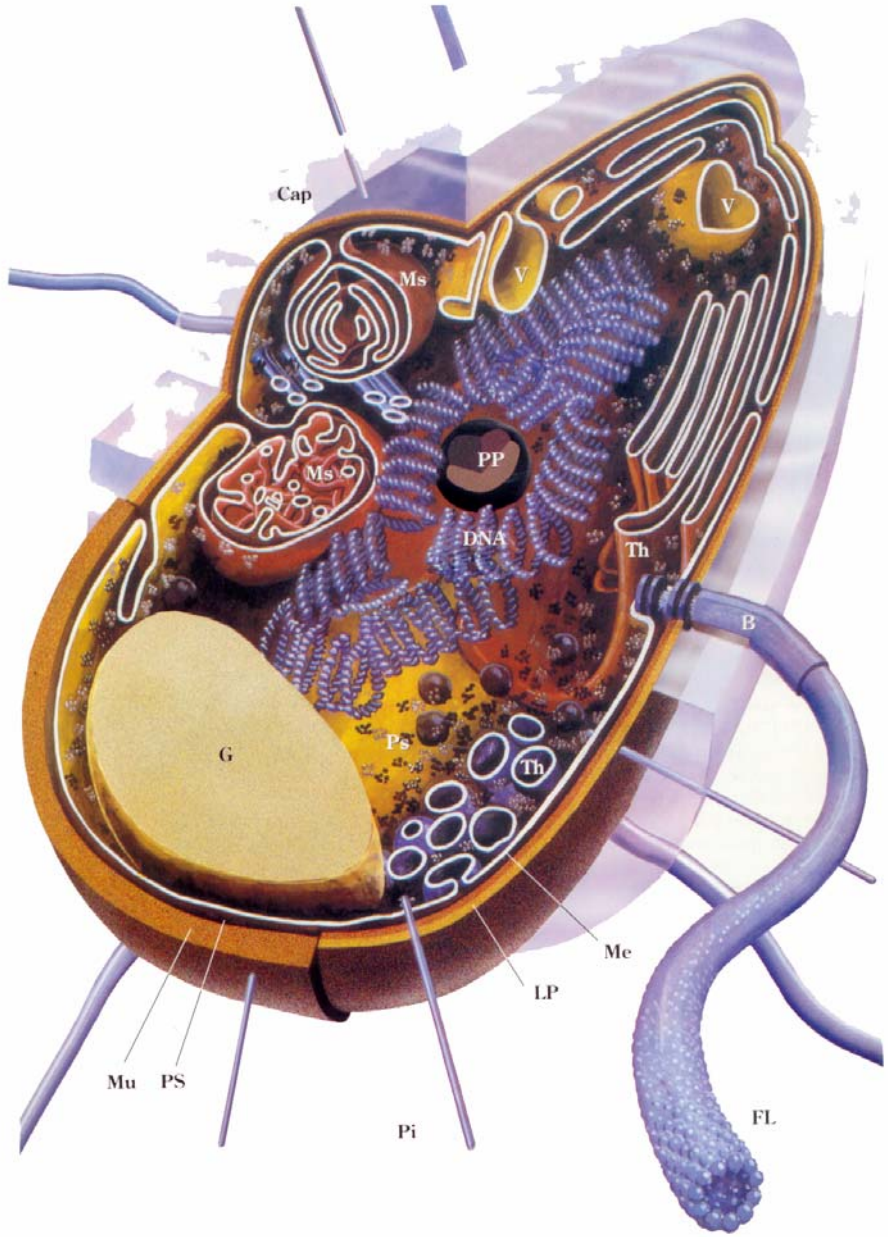


4.10 Die Zunahme der Komplexität ist ein wesentlicher Aspekt der biologischen Evolution, wobei höhere Komplexität sowohl durch Vergrößerung der Zahl von miteinander in Wechselwirkung stehenden Elementen als auch durch Differenzierung der Funktionen dieser Elemente entstehen kann. In dieser Abbildung wird zwischen drei Phasen oder Strategien der Evolution von Komplexität unterschieden. *Untere Kurve*: Zunahme der Genomgröße; logarithmische Auftragung der Zahl der Basenpaare im Genom von Zellen seit Beginn der biologischen Evolution (Daten aus Abbildung 2.3). *Mittlere Kurve*: Zunahme der Zahl der Zelltypen in der Evolution der Metazoa (Daten aus Abbildung 4.8). *Obere Kurve*: Zunahme des relativen Gehirngewichts (bezogen auf die Körperoberfläche) bei Säugetieren (Daten aus Wilson 1985). Für die Abszisse wurden zwei Skaleneinteilungen verwendet, eine für den Zeitraum $>10^9$ Jahre, eine andere für den Zeitraum $<10^9$ Jahre vor der Gegenwart. Oberhalb der Abszisse sind die Namen einiger wichtiger taxonomischer Einheiten angeführt, deren Evolution in etwa beim jeweiligen Wortbeginn einsetzt.

Wolfgang Wieser. *Die Erfindung der Individualität oder die zwei Gesichter der Evolution*. Spektrum Akademischer Verlag, Heidelberg 1998.

A.C.Wilson. *The Molecular Basis of Evolution*. Scientific American, Oct.1985, 164-173.

Die Bakterienzelle als ein Beispiel für die einfachste Form autonomen Lebens.



Der menschliche Körper:

10^{14} Zellen =
10^{13} eukaryotische Zellen +
$\approx 9 \times 10^{13}$ prokaryotische Bakterienzellen

$\approx$ 200 Eukaryotische Zelltypen

1. Geschichte des Evolutionsgedankens
2. Wahrscheinlichkeit und Zufall in der Biologie
3. Komplexes Verhalten aus einfachen Regeln
4. Evolutionsmechanismen
5. Molekularbiologie und Evolutionsexperimente
6. **Ursprung komplexer Organe – Das Auge als Beipiel**

Walter Gehring, Biozentrum, Universität Basel

Molecular genetics shows that the developments of all different forms of eyes have the same evolutionary origin, which can be traced back to a simple form of light-sensitive pre-organ found already in primitive bacteria.

W. J. Gehring. The genetic control of eye development and its implications for the evolution of the various eye-types. *Zoology* **104** (2001):171-183

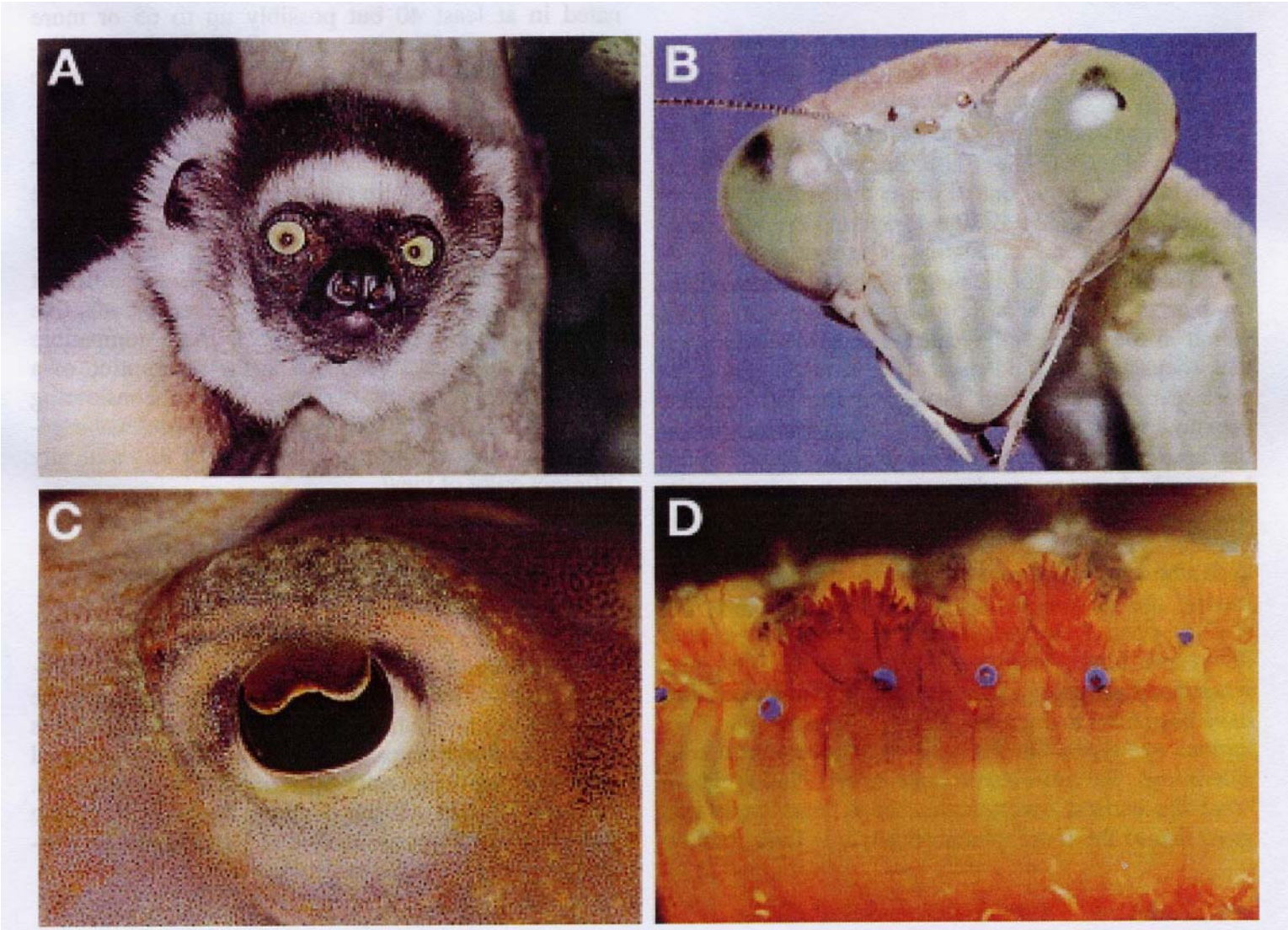


Fig. 1. Different types of eyes. **(A)** Camera-type eye from the Lemur *Propithecus verrauxi.* **(B)** Compound eye of the praying *Mantis.* **(C)** Camera-type eye from the Cephalopod *Sepia erostrata.* **(D)** Mirror eye from the clam *Chlamys nobilis.* (Courtesy of Dr. Kazuto Kato; photographs kindly provided by Masahiro Iijima, Susumu Yamaguchi and Isamu Soyama).

Walter J. Gehring, The genetic control of eye development and its implications for the evolution of the various eye-types. *Zoology* **104** (2001), 171-183

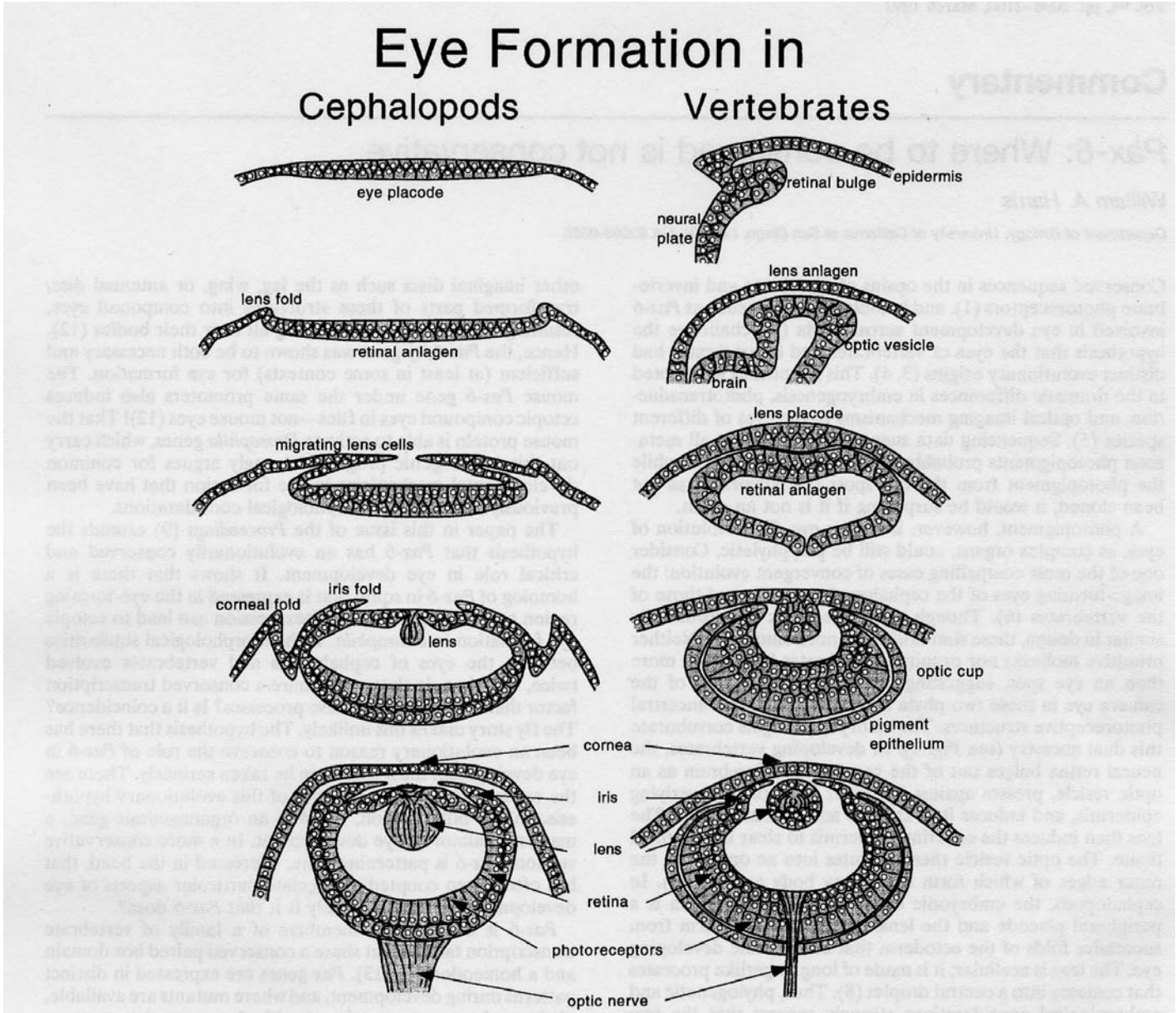


FIG. 1. Schematic diagram of cephalopod eye development (*Left*) and vertebrate eye development (*Right*) as explained in more detail in refs. 7 and 8. Development proceeds from top to bottom. Even though the adult structures are fairly similar, excepting certain obvious features such as the placement of the photoreceptors and lentigenic cells, the development is very different. The cephalopod eye forms from an epidermal placode through a series of successive infoldings, while the vertebrate eye emerges from the neural plate and induces the overlying epidermis to form the lens.

William A. Harris,
Proc.Natl.Acad.Sci.USA
94 (1997), 2098-2100

Schlußbemerkungen

Darwin hatte in folgenden Punkten **nicht recht**:

• Der Darwinsche Vererbungsmechanismus war falsch. Mendel hatte die korrekte Lösung.

• Mutation und Rekombination können gar keine, kleine und große Auswirkungen haben und es besteht kein Grund, dass die biologische Evolution quasikontinuierlich nur in kleinen Schritten erfolgt.

• Im Verlaufe der biologischen Evolution gab es auch katastrophenartige Ereignisse terrestrischen und extraterrestrischen Ursprungs.

• Die Komplexität der höheren Lebewesen ist so groß, dass ihre Eigenschaften nicht voll optimiert sein können.

Schlußbemerkungen

Darwins Theorie wurde in folgenden Punkten **voll bestätigt**:

•Das Auftreten von Varianten bei der Reproduktion wurde durch die Aufklärung der molekularen Mechanismen von Rekombination und Mutation auf eine solide wissenschaftliche Basis gestellt.

• Das Darwinsche Prinzip der Optimierung durch Variation und Selektion in endlichen Populationen gilt nicht nur in der Biologie sondern auch in der unbelebten Welt.

• Die natürliche Entstehung der Arten und die daraus resultierenden phylogenetischen Stammbäume wurde durch die Vergleiche der genetischen Informationsträger heute lebender Organismen voll bestätigt.

Web-Page für weitere Informationen:

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