Evolution gesehen durch die Brillen der Physiker und der Biologen

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Echophysics, Pöllauer Tage der Physikgeschichte

Pöllau, 26.– 27.09.2014

Web-Page für weitere Informationen:

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

Prolog aus dem 17. und 18. Jahrhundert

Gottfried Wilhem Leibniz,
1646 - 1716

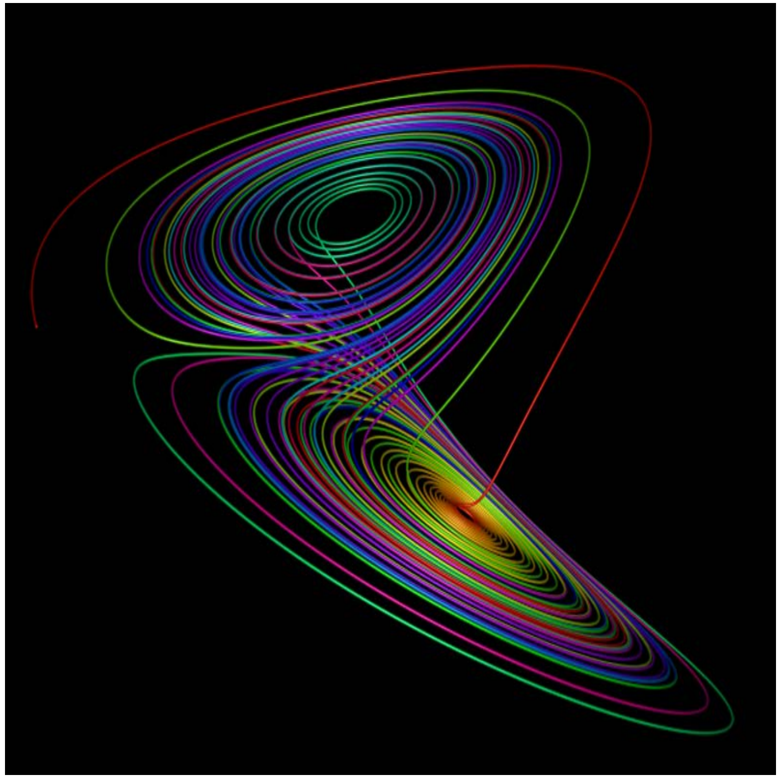
Leonhard Euler,
1710 - 1783

Isaac Newton,
1643 - 1727

$$\lim_{\Delta t \to 0} \frac{\Delta x}{\Delta t} = \frac{\mathrm{d}x}{\mathrm{d}t}$$

Grenzübergang vom Diskreten zum Kontinuum

Jules Henri Poincaré,
1854 – 1912



Edward N. Lorenz,
1917 – 2008

$$\frac{dx}{dt} = \mathrm{a}\,(y - x);\ \frac{dy}{dt} = x(\mathrm{b} - z) - y;\ \frac{dz}{dt} = xy - \mathrm{c}\,z$$

Deterministisches Chaos

„ … *Ich behaupte nur, dass in jeder besonderen Naturlehre nur so viel eigentliche Wissenschaft angetroffen werden könne, als darin Mathematik anzutreffen ist.*“

Immanuel Kant, 1724 - 1804

Kant über Mathematik und Naturwissenschaft

Kant, I. 1786. Metaphysische Anfangsgründe der Naturwissenschaft. Johann Friedrich Hartknoch, Riga.

1. Evolutionstheorie und Mathematik
2. Molekularbiologie: ‚Alles Leben ist Chemie'
3. Was zeichnet die Biologie heute aus?
4. Optimierung und historische Kontingenz
5. Die neue Biologie: Epigenetik und ‚Big-Data'
6. Perspektiven einer theoretischen Biologie

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„Biologie“

1797 Theodor Gustav August Roose
1802 Jean-Baptiste Lamarck

1802 Gottfried Reinhold Treviranus

„Biologie oder Philosophie der lebenden Natur für Naturforscher und Aerzte“

6 Bände, Röwer, Göttingen 1802-1822.

Ursprung des Begriffs „Biologie“

„ … *es ist für Menschen ungereimt,* …
zu hoffen, dass noch etwa dereinst
ein Newton aufstehen könne, der
auch nur die Erzeugung eines
Grashalms nach Naturgesetzen,
die keine Absicht geordnet hat,
begreiflich machen werde …“.

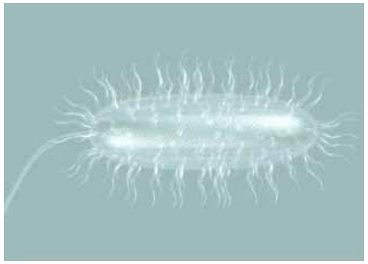
Immanuel Kant, Kritik der Urteilskraft. 1790

Immanuel Kant, 1724 - 1804

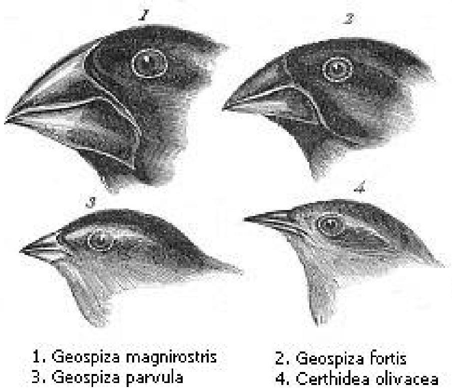
Der Newton des Grashalms

Charles Darwin, 1809 - 1882

Voyage on HMS Beagle, 1831 - 1836



Phänotypen



Finches from Galapagos Archipelago

Nothing in Biology Makes Sense Except in the Light of Evolution

THEODOSIUS DOBZHANSKY

As recently as 1966, sheik Abd el Aziz bin Baz asked the king of Saudi Arabia to suppress a heresy that was spreading in his land. Wrote the sheik:

"The Holy Koran, the Prophet's teachings, the majority of Islamic scientists, and the actual facts all prove that the sun is running in its orbit . . . and that the earth is fixed and stable, spread out by God for his mankind. . . . Anyone who professed otherwise would utter a charge of falsehood toward God, the Koran, and the Prophet."

The good sheik evidently holds the Copernican theory to be a "mere theory," not a "fact." In this he is technically correct. A theory can be verified by a mass of facts, but it becomes a proven theory, not a fact. The sheik was perhaps unaware that the Space Age had begun before he asked the king to suppress the Copernican heresy. The sphericity of the earth had been seen by astronauts, and even by many earth-bound people on their television screens. Perhaps the sheik could retort that those who venture beyond the confines of God's earth suffer hallucinations, and that the earth is really flat.

Parts of the Copernican world model, such as the contention that the earth rotates around the sun, and not vice versa, have not been verified by direct observations even to the extent the sphericity of the earth has been. Yet scientists accept the model as an accurate representation of reality. Why? Because it makes sense of a multitude of facts which are otherwise meaningless or extravagant. To nonspecialists most of these facts are unfamiliar. Why then do we accept the "mere theory" that the earth is a sphere revolving around a spherical sun? Are we simply submitting to authority? Not quite: we know that those who took time to study the evidence found it convincing.

The good sheik is probably ignorant of the evidence. Even more likely, he is so hopelessly biased that no amount of evidence would impress him. Anyway, it would be sheer waste of time to attempt to convince him. The Koran and the Bible do not contradict Copernicus, nor does Copernicus contradict them. It is ludicrous to mistake the Bible and the Koran for primers of natural science. They treat of matters even more important: the meaning of man and his relations to God. They are written in poetic symbols that were understandable to people of the age when they were written, as well as to peoples of all other ages. The king of Arabia did not comply with the sheik's demand. He knew that some people fear enlightenment, because enlightenment threatens their vested interests. Education is not to be used to promote obscurantism.

The earth is not the geometric center of the universe, although it may be its spiritual center. It is a mere speck of dust in cosmic spaces. Contrary to Bishop Ussher's calculations, the world did not appear in approximately its present state in 4004 B.C. The estimates of the age of the universe given by modern cosmologists are still only rough approximations, which are revised (usually upward) as the methods of estimation are refined. Some cosmologists take the universe to be about 10 billion years old; others suppose that it may have existed, and will continue to exist, eternally. The origin of life on earth is dated tentatively between 3 and 5 billion years ago; manlike beings appeared relatively quite recently, between 2 and 4 million years ago. The estimates of the age of the earth, of the duration of the geologic and paleontologic eras, and of the antiquity of man's ancestors are now based mainly on radiometric evidence—the proportions of isotopes of certain chemical elements in rocks suitable for such studies.

One of the world's leading geneticists, Theodosius Dobzhansky is professor emeritus, Rockefeller University, and adjunct professor of genetics, University of California, Davis 95616. Born in Russia, in 1900, he is a graduate of the University of Kiev and taught (with J. Philipchenko) at the University of Leningrad before coming to the U.S., in 1927; thereafter he taught at Columbia University and the California Institute of Technology before joining the Rockefeller faculty, in 1962. He has been president of the Genetics Society of America, the American Society of Naturalists, the Society for the Study of Evolution, the American Society of Zoologists, and the American Teilhard de Chardin Association. Among his many honors are the National Medal of Science (1964) and the Gold Medal Award for Distinguished Achievement in Science (1969). He holds 18 honorary doctorates from universities in this country and abroad. Among his well-known books are *The Biological Basis of Human Freedom* (1956) and *Mankind Evolving* (1963). The present paper was presented at the 1972 NABT convention.

Theodosius Dobzhansky,
1900 – 1975

Theodosius Dobzhansky. 1973. The American Biology Teacher **35**:125-129.

Despite Ernst Haeckel's enthusiams Darwin is no Newton of the grass blade. „ … Darwin himself has systematically avoided dwelling upon the question how life has originated from inanimate materials. Natural selection begins with a living cell."

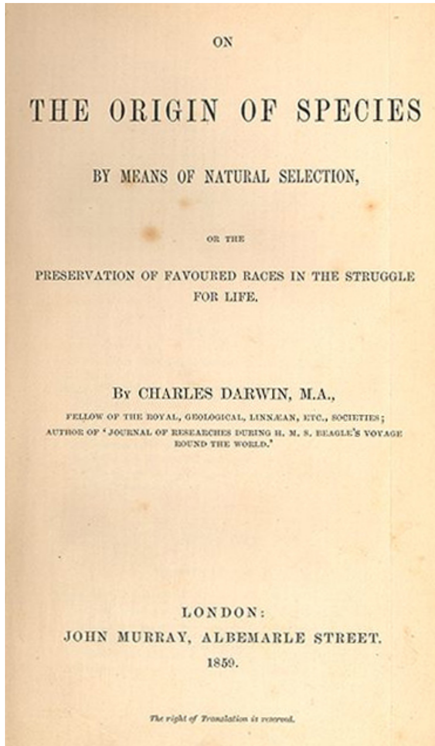
Evelyn Fox Keller, 1936 –

Die Brücke zwischen Physik, Chemie und Biologie

E. Fox Keller. 2010. Is Darwin a Newton of the grass blade? Lecture at University of Vienna, Physics Dept. Nov. 05, 2010.

P. Schuster. 2011. Is there a Newton of the grass blade? The complex relation between mathematics, physics and biology. Complexity **16**(6):5-9.

Charles Darwin,
1809 - 1882



ON

THE ORIGIN OF SPECIES

BY MEANS OF NATURAL SELECTION,

OR THE

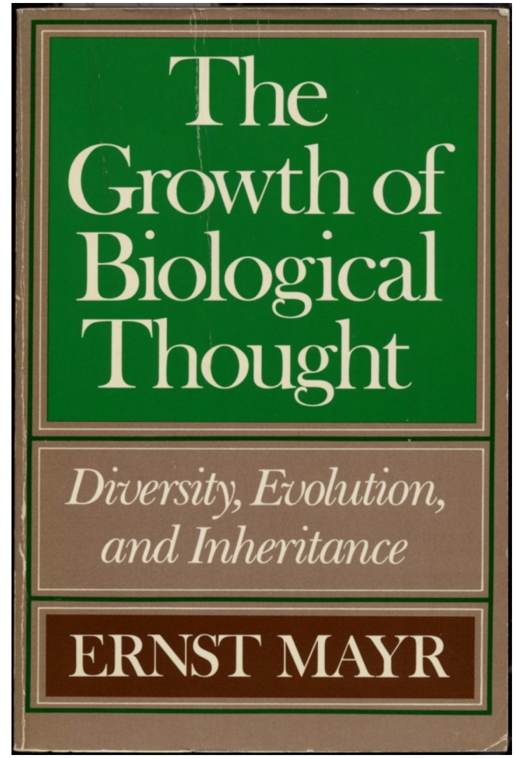
PRESERVATION OF FAVOURED RACES IN THE STRUGGLE FOR LIFE.

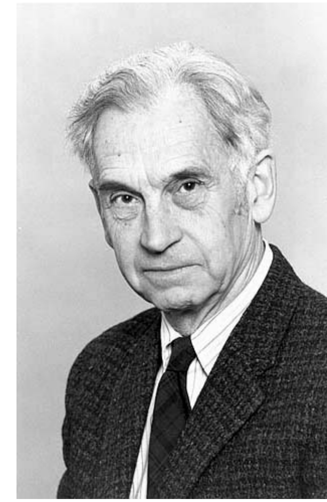
BY CHARLES DARWIN, M.A.,

FELLOW OF THE ROYAL, GEOLOGICAL, LINNÆAN, ETC., SOCIETIES;
AUTHOR OF 'JOURNAL OF RESEARCHES DURING H. M. S. BEAGLE'S VOYAGE ROUND THE WORLD.'

LONDON:
JOHN MURRAY, ALBEMARLE STREET.
1859.

The right of Translation is reserved.





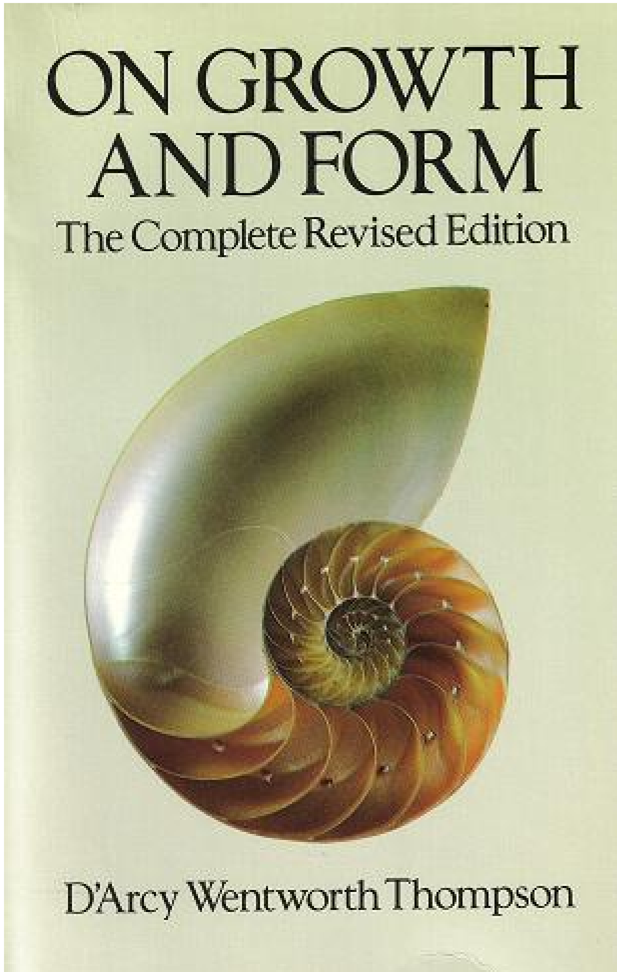
Ernst Mayr,
1904 - 2005

Theorie der natürlichen Auslese
1859

Synthetische Evolutionstheorie
1982

Grundlegende Werke über biologische Theorien enthalten nicht eine einzige Gleichung:

Zwei Beispiele.

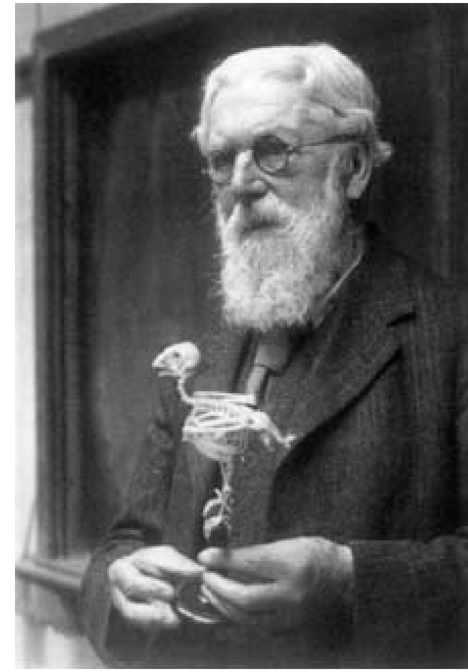


First edition: 1917,
847 pages

Second edition: 1942,
Cambridge Univ. Press,
1116 pages

Dover edition: 1992,
1116 pages

Further editions
until 2014



D'Arcy Thompson,
1860 – 1948

Der „Klassiker" am Beginn der Theoretischen Biologie

Drei notwendige Bedingungen für Darwinsche Evolution sind:

1. **Vermehrung** (mit Vererbung),
2. **Variation**, und
3. **Selektion**.

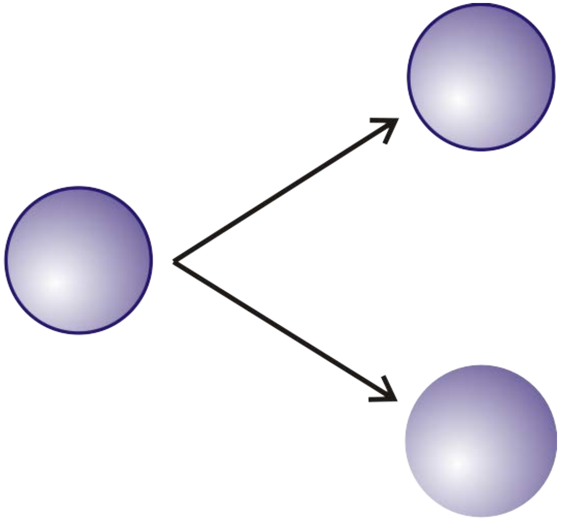
Vermehrung führt zu exponentiellem Wachstum und dieses stellt eine *conditio sine qua non* für Selektion dar.

Variation folgt als Begleiterscheinung des molekularen Mechanismus der Reproduktion und war Darwin unbekannt.

Selektion ist eine Konsequenz exponentiellen Wachstums bei endlichen Ressourcen.

Da im Sinne der Optimierung von Fitness durch die Darwinsche Evolution nur Nachkommen gezählt werden, ist sie universell gültig, wenn die drei Bedingungen erfüllt sind.

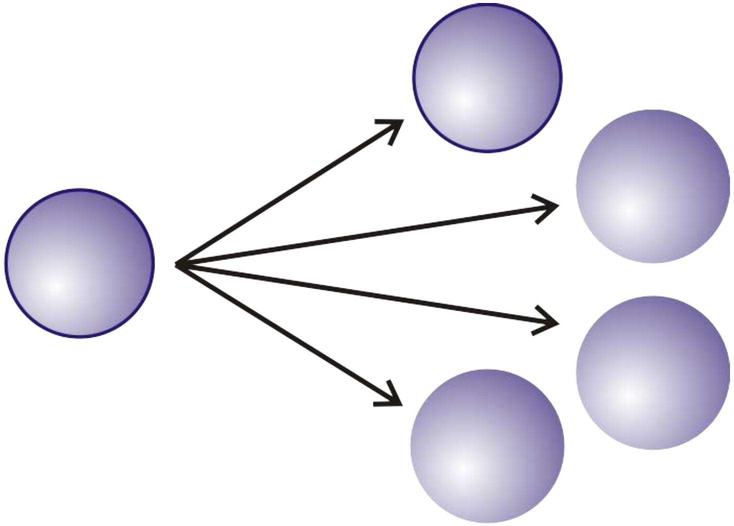
Vermehrung und Wachstum



$$(A) + X \rightarrow 2X$$

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

exponentielles Wachstum

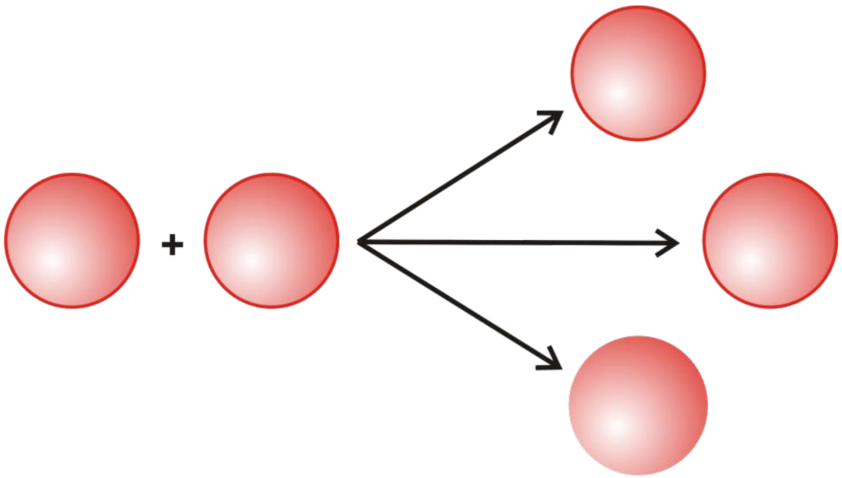


$$(A) + X \rightarrow 4\,X$$

$$(A) + X \rightarrow n\,X$$

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

exponentielles Wachstum

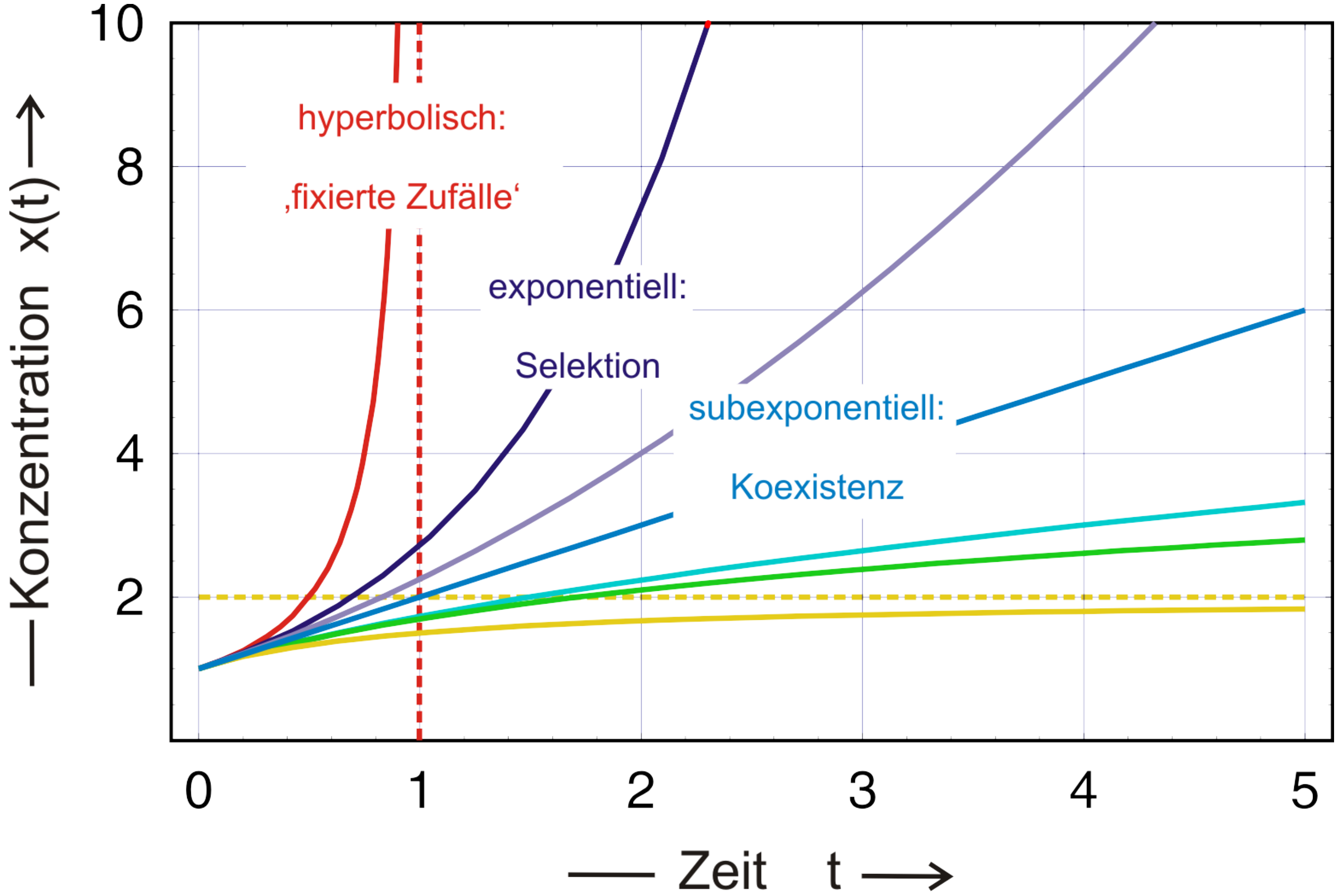


$$(A) + 2X \to 3X$$

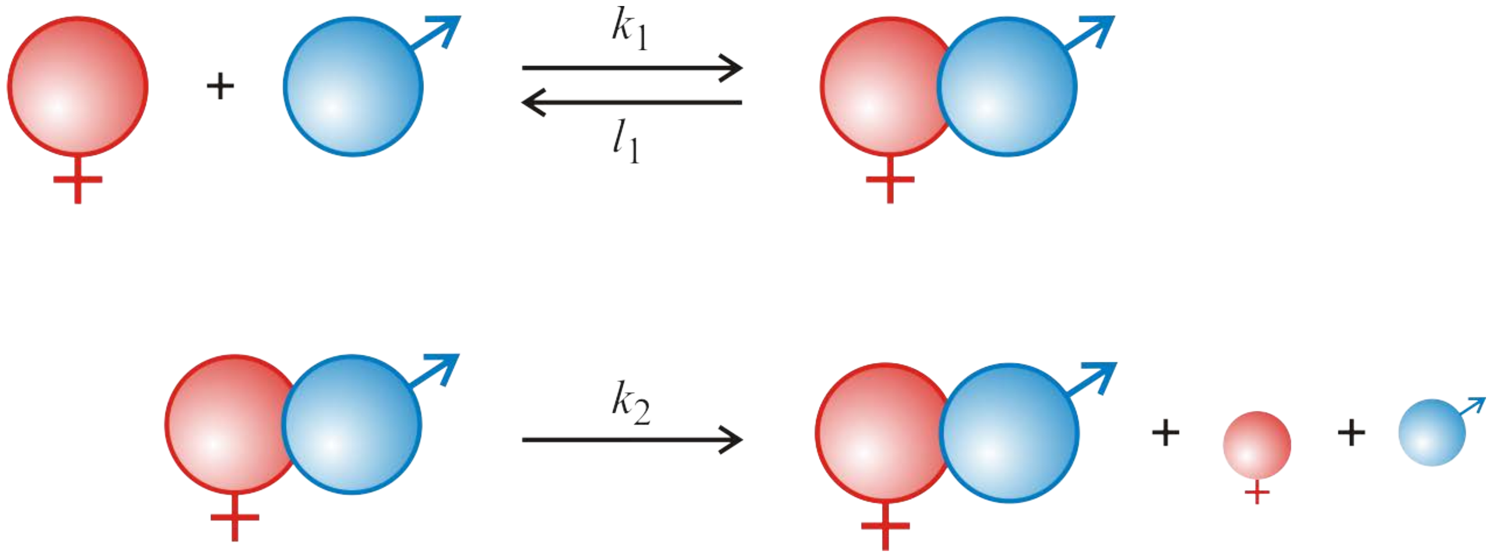
$$\frac{dx}{dt} = kx^2 \quad \Rightarrow \quad x(t) = x(0) \cdot \frac{1}{1 - x(0)kt}$$

hyperbolisches Wachstum

$$t_{cr} = 1/kx(0)$$



Verschiedene Formen des Wachstums



$$X + Y \leftrightarrow X{\cdot}Y$$

$$(A) + X{\cdot}Y \rightarrow X{\cdot}Y + X + Y$$

Sexuelle Reproduktion und exponentielles Wachstum

$[X] = x$; $[Y] = y$; $[X \cdot Y] = z$

$$\frac{dx}{dt} = -k_1\, x\, y + l_1\, z + k_2\, z = \frac{dy}{dt}$$

$$\frac{dz}{dt} = k_1\, x\, y - l_1\, z$$

$$\frac{d\hat{x}}{dt} = \frac{dx}{dt} + \frac{dz}{dt} = k_2\, z = \frac{dy}{dt} + \frac{dz}{dt} = \frac{d\hat{y}}{dt}$$

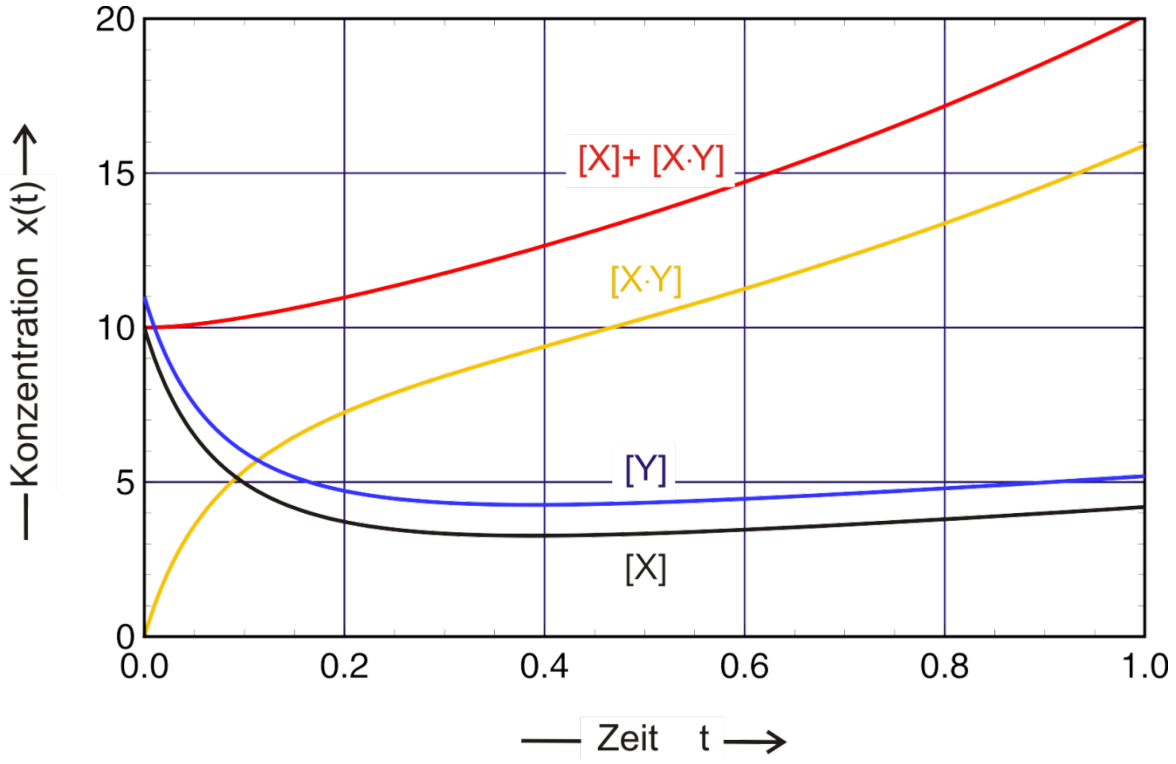
quasistationärer Zustand: $\dfrac{dz}{dt} = 0 = k_1 \cdot \bar{x} \cdot \bar{y} - l_1 \, \bar{z} \, ; \quad \bar{z} = \dfrac{k_1}{l_1} \bar{x} \cdot \bar{y}$

$$\bar{z} = \left(1 + K(2\,\hat{x} + \vartheta) - \sqrt{\left(1 + K(2\,\hat{x} + \vartheta)\right)^2 - 4K^2 \,\hat{x}\,(\hat{x} + \vartheta)} \right) \Big/ 2K$$

$$K = k_1 / l_1 \quad \text{und} \quad \vartheta = \hat{y} - \hat{x}$$

$$\bar{z} \approx \hat{x} \quad \text{für} \quad \hat{x} >> |\,\vartheta\,|$$

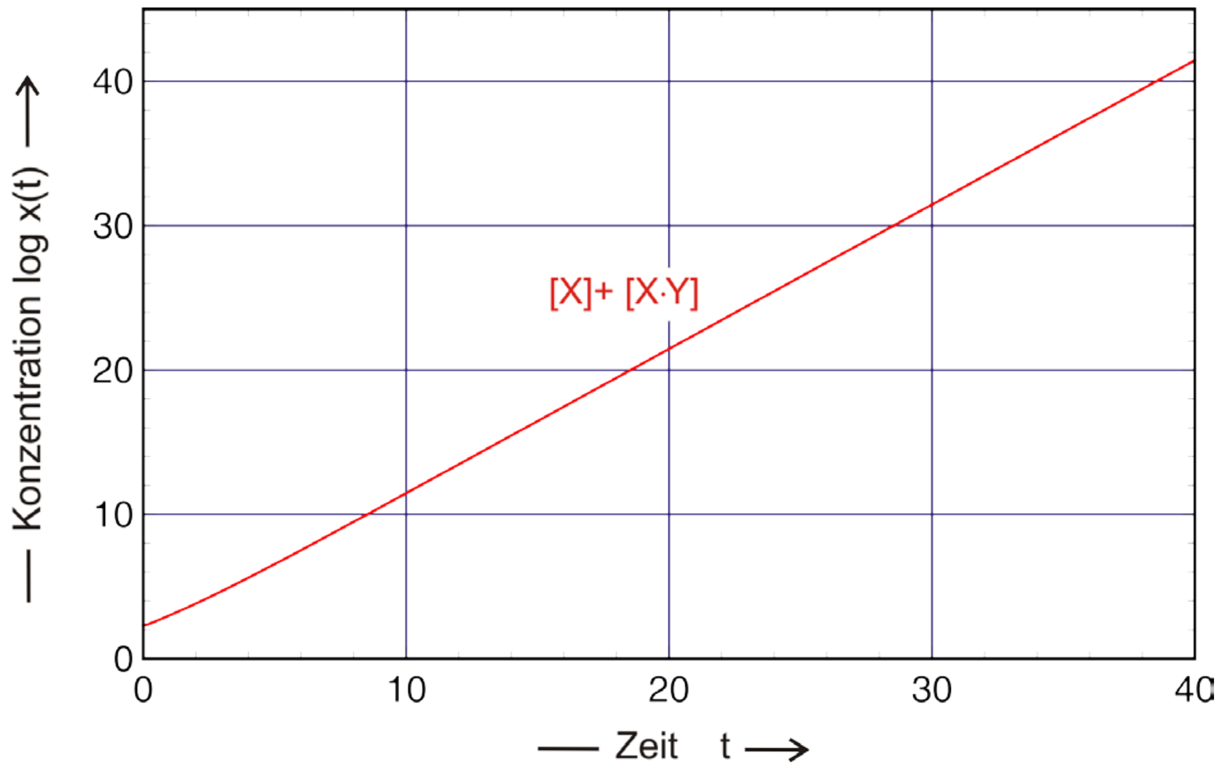
$\dfrac{d\hat{x}}{dt} = k_2 \, \bar{z} \approx k_2 \, \hat{x}$ …… exponentielles Wachstun



$$X + Y \leftrightarrow X{\cdot}Y$$

$$(A) + X{\cdot}Y \rightarrow X{\cdot}Y + X + Y$$

Sexuelle Reproduktion und exponentielles Wachstum



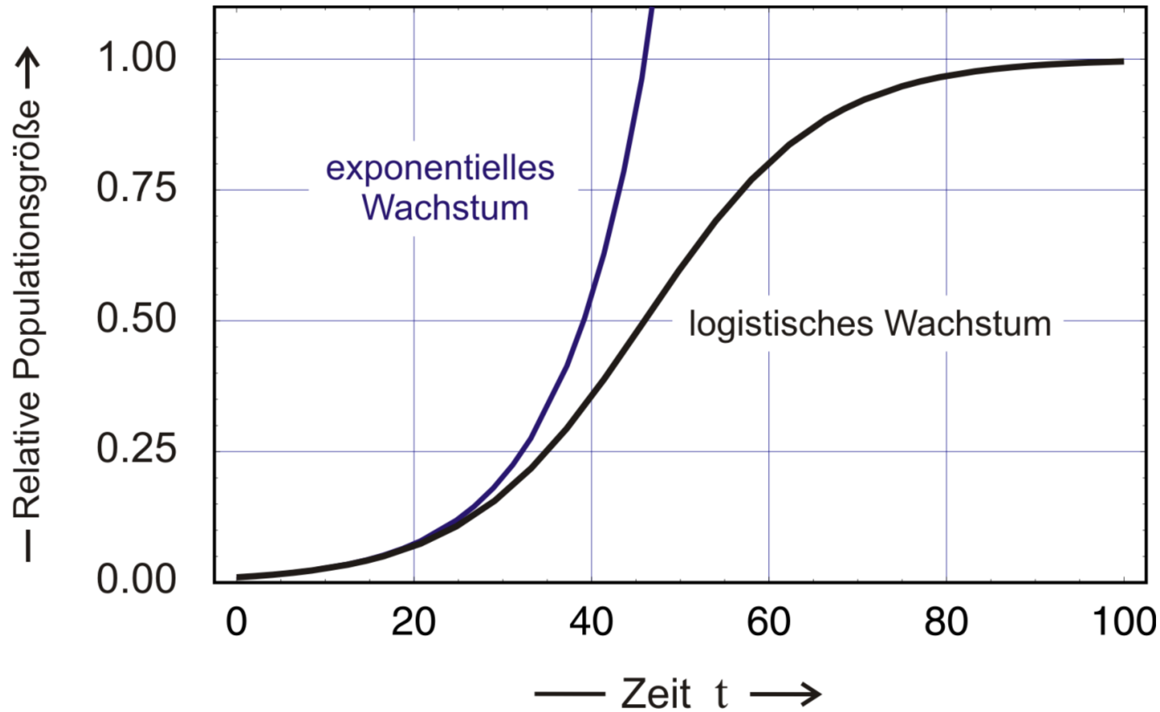
$$X + Y \leftrightarrow X{\cdot}Y$$

$$(A) + X{\cdot}Y \rightarrow X{\cdot}Y + X + Y$$

Sexuelle Reproduktion und exponentielles Wachstum

Beschränkte Ressourcen und Selektion

Pierre-François Verhulst,
1804 - 1849

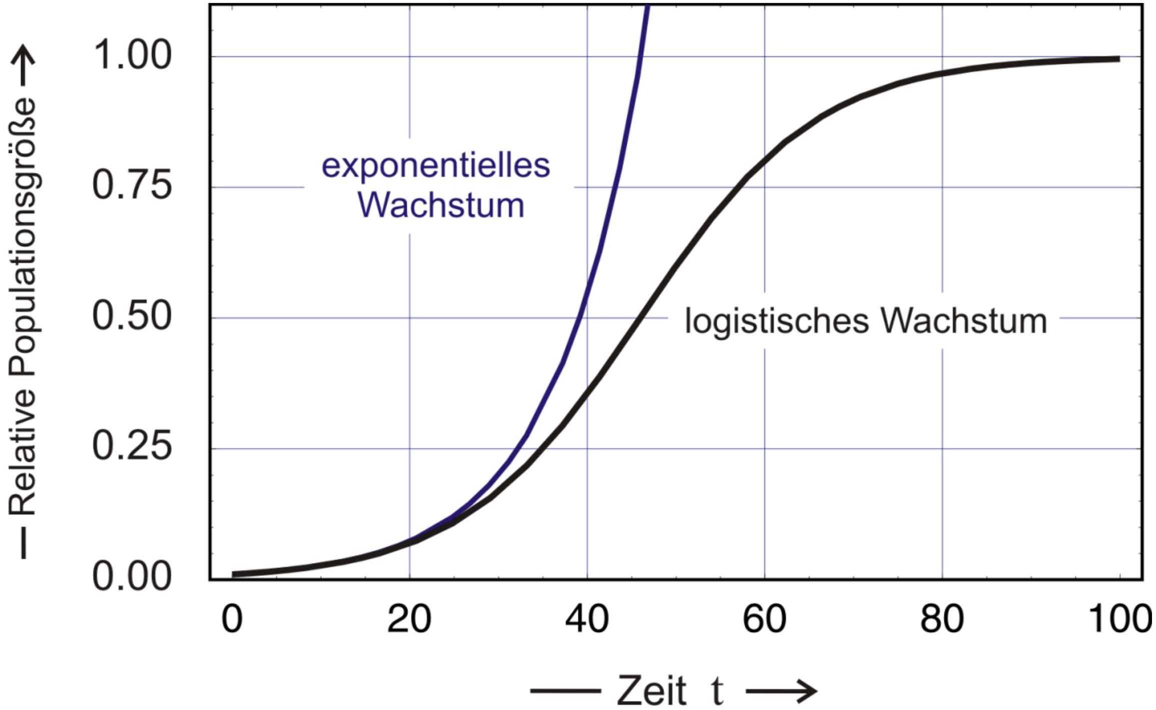


$$\frac{d\xi}{dt} = f\,\xi\left(1 - \frac{\xi}{C}\right) \quad \Rightarrow \quad \xi(t) = \frac{\xi(0)\,C}{\xi(0) + \left(C - \xi(0)\right)e^{-f\,t}}$$

C …… Kapazität des Ökosystems

Die logistische Gleichung wurde 1828 konzipiert.

Pierre-François Verhulst,
1804 - 1849



War 30 Jahre vor der Veröffentlichung der 'Origin of Species' bekannt

Die logistische Gleichung wurde 1828 konzipiert.

$$\frac{\mathrm{d}x}{\mathrm{dt}} = f\ x\left(1-\frac{x}{C}\right) \quad \Rightarrow \quad \frac{\mathrm{d}x}{\mathrm{dt}} = f\ x - \frac{x}{C}\ f\ x$$

$$f\ x \equiv \Phi(\mathrm{t})\,,\, C = 1: \quad \frac{\mathrm{d}x}{\mathrm{dt}} = x\left(f\ - \Phi\right)$$

Verallgemeinerung der logistischen Gleichung auf *n* Variable ergibt Selektion

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

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

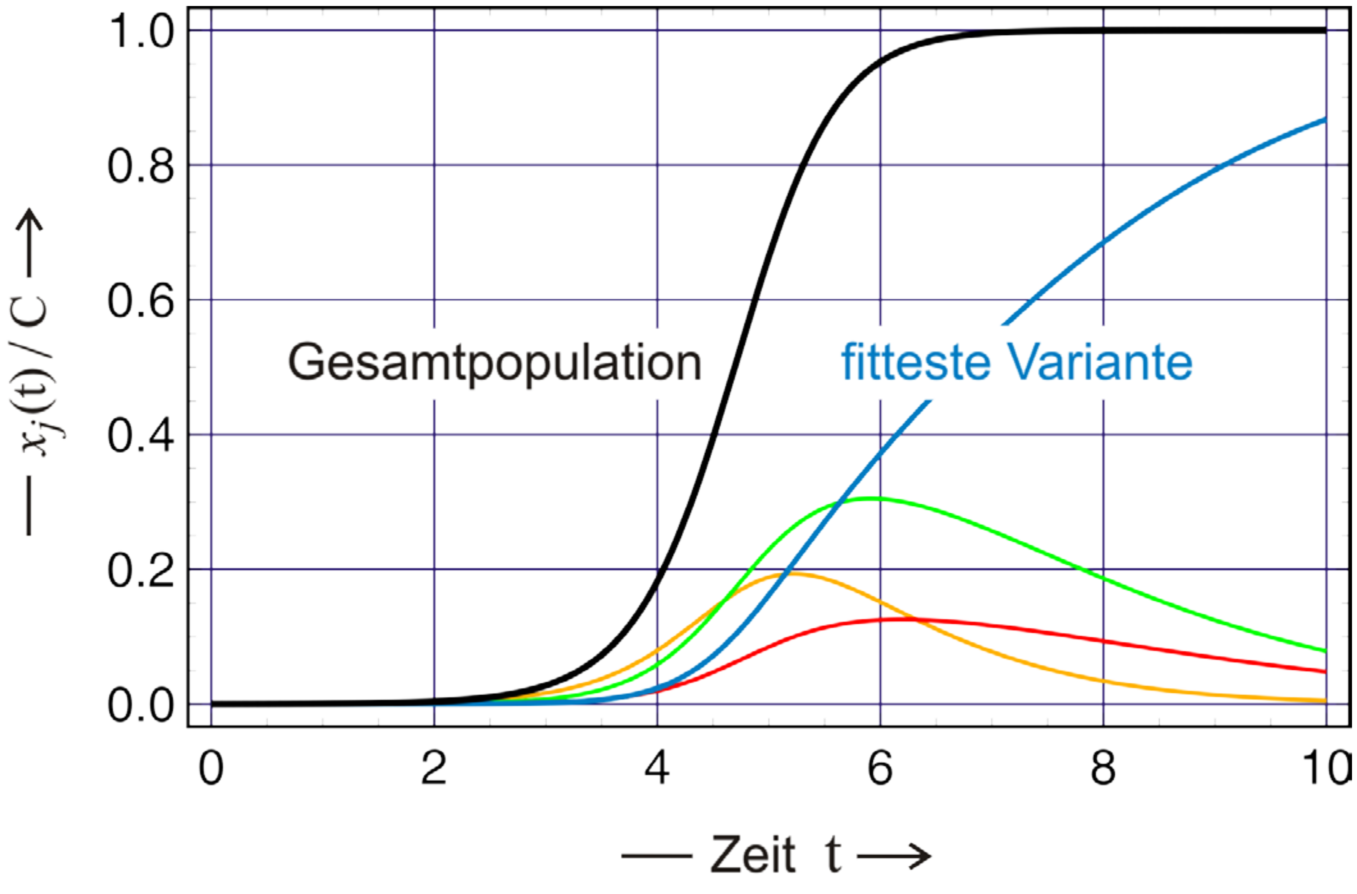
$$\mathrm{X}_1, \mathrm{X}_2, \ldots, \mathrm{X}_n : \quad [\mathrm{X}_i] = x_i\,; \quad \sum_{i=1}^{n} x_i = C = 1; \quad f_i = f(\mathrm{X}_i)$$

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

Darwin

$$\boxed{\frac{\mathrm{d}\Phi}{\mathrm{dt}} = \; < f^{\,2} > - < \bar{f} >^2 = \; \mathrm{var}\{f\} \geq 0}$$

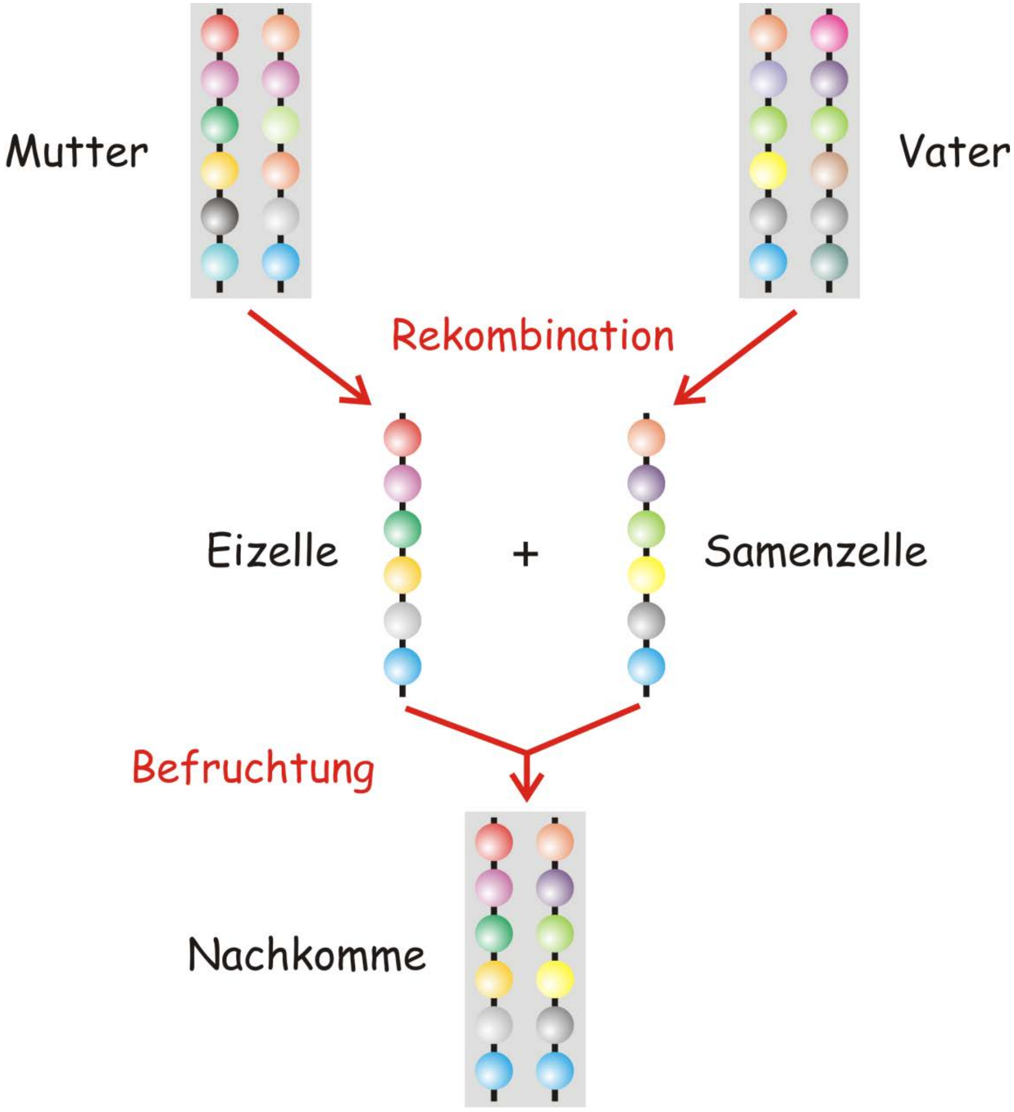
Verallgemeinerung der logistischen Gleichung auf *n* Variable ergibt Selektion



Fitness f = (**1.75**, **2.25**, **2.35** und **2.80**)

Selektion der fittesten Variante

Variation I: Gregor Mendels Genetik und Rekombination



Gregor Mendel
1822 - 1884

Rekombination in Mendels Genetik

Ronald Fisher (1890-1962)

Allele: $A_1, A_2, \ldots, A_n$

Häufigkeiten: $x_i = [A_i]$; Genotypen: $A_i \cdot A_j$

Fitnesswerte: $a_{ij} = f\,(A_i \cdot A_j),\ a_{ij} = a_{ji}$

Mendel

Darwin

$$\frac{\mathrm{d}x_j}{\mathrm{d}t} = \sum_{i=1}^{n} a_{ji}\, x_i\, x_j - \Phi\, x_j = x_j \left(\sum_{i=1}^{n} a_{ji}\, x_i - \Phi \right), \quad j = 1, 2, \ldots, n$$

$$\text{mit} \quad \Phi(\mathrm{t}) = \sum_{j=1}^{n} \sum_{i=1}^{n} a_{ji}\, x_i\, x_j \quad \text{und} \quad \sum_{j=1}^{n} x_j = 1$$

$$\frac{\mathrm{d}\Phi}{\mathrm{d}t} = 2\left(< \overline{a}^{\,2} > - < \overline{a} >^2 \right) = 2\,\mathrm{var}\{\overline{a}\} \geq 0$$

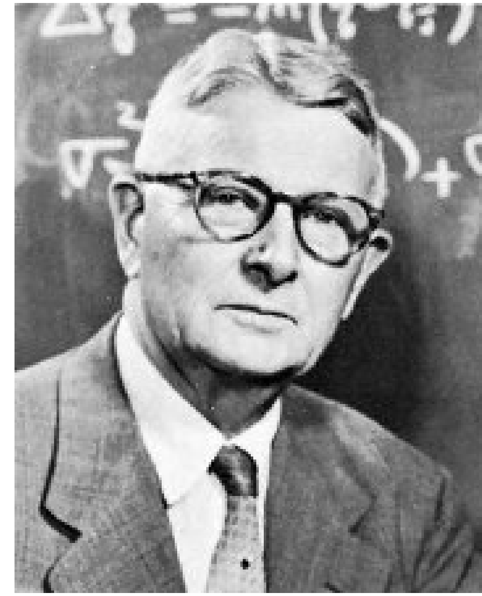
Ronald Fisher‘s Selektionsgleichung: The genetical theory of natural selection. Oxford, UK, Clarendon Press, 1930.

Theodosius Dobzhansky,
1900 – 1975

„Genetics is the first biological science which got in the position in which physics has been for many years. One can justifiably speak about such a thing as theoretical mathematical genetics, and experimental genetics, just as in physics. There are some mathematical geniuses who work out what to an ordinary person seems as a fantastic kind of theory. This fantastic kind of theory nevertheless leads to experimentally verifiable prediction, which an experimental physicist then has to test the validity of. Since the times of Wright, Haldane, and Fisher, evolutionary genetics has been in a similar position."

Ronald Fisher (1890-1962)

J. B. S. Haldane (1892-1964)



Sewall Wright (1889-1988)

Die drei Begründer der Populationsgenetik

1. Evolutionstheorie und Mathematik
2. **Molekularbiologie: ‚Alles Leben ist Chemie'**
3. Was zeichnet die Biologie heute aus?
4. Optimierung und historische Kontingenz
5. Die neue Biologie: Epigenetik und ‚Big-Data'
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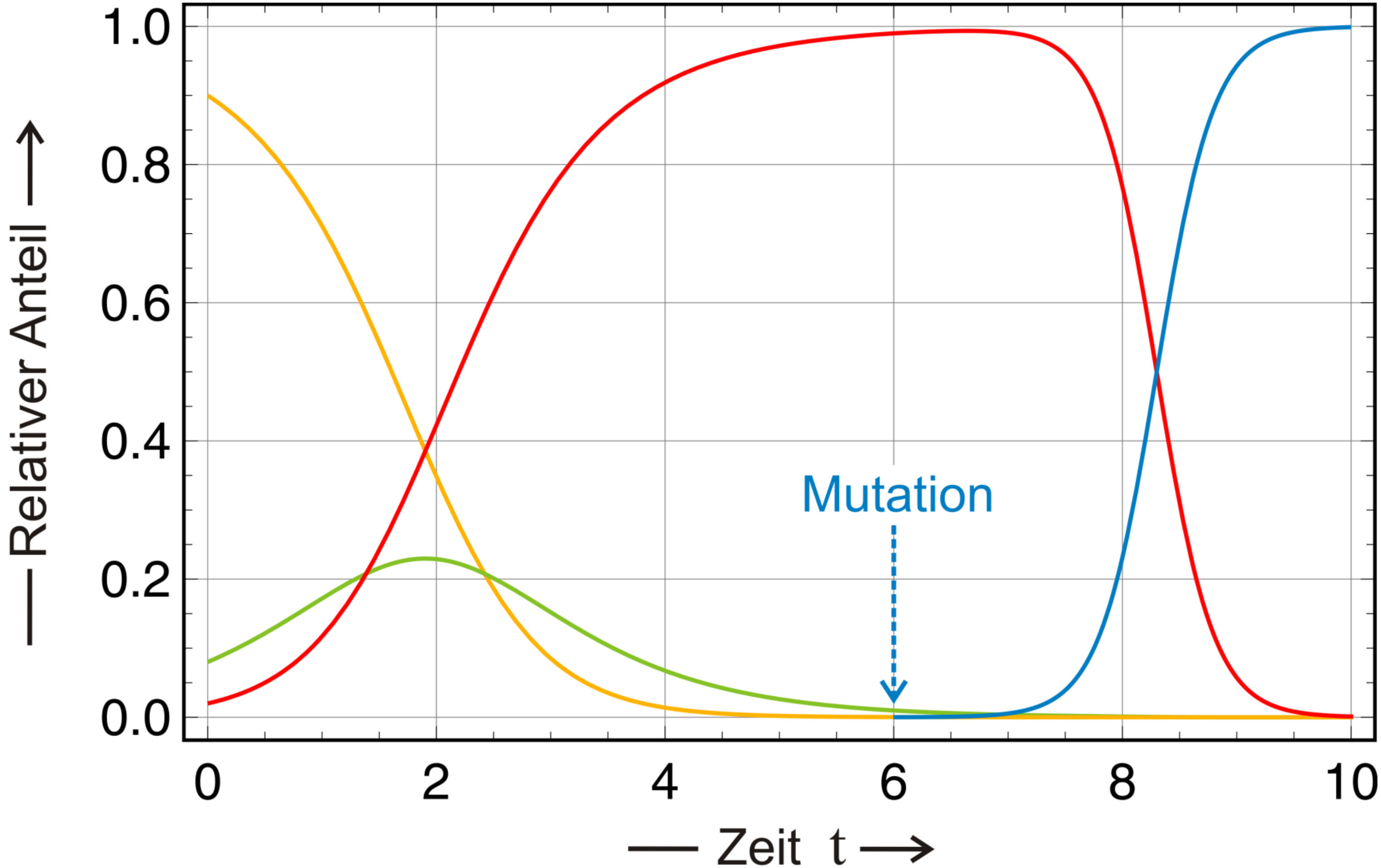
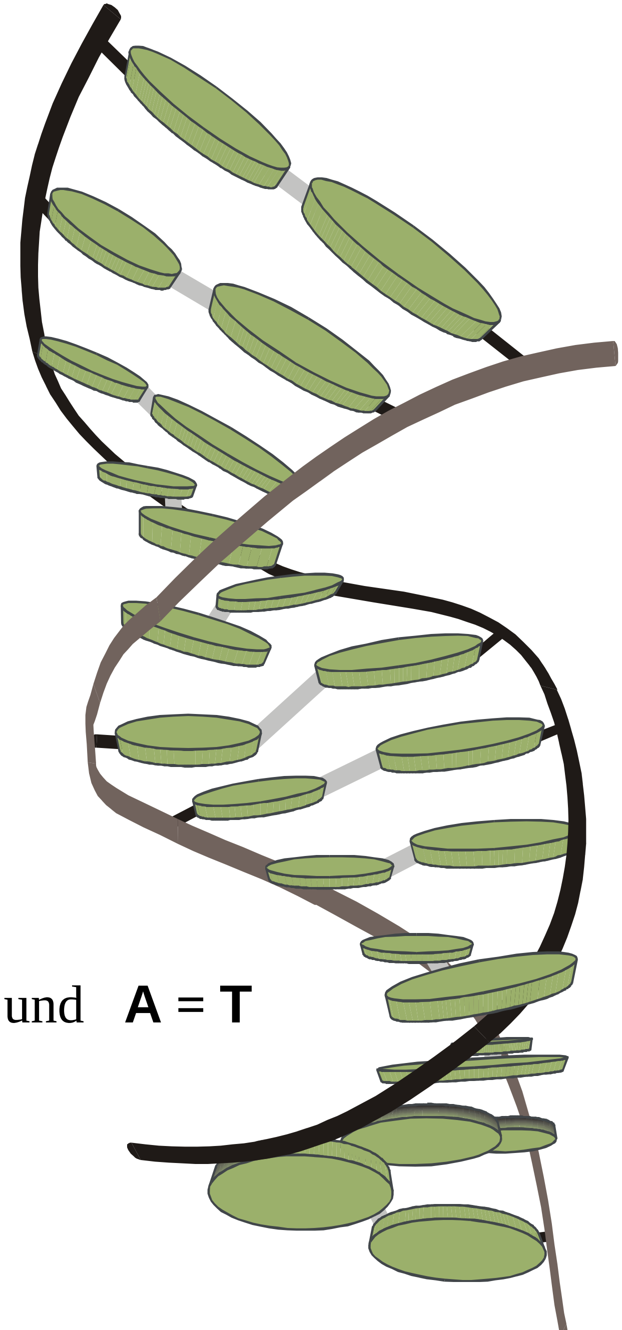
Variation II: Mutation

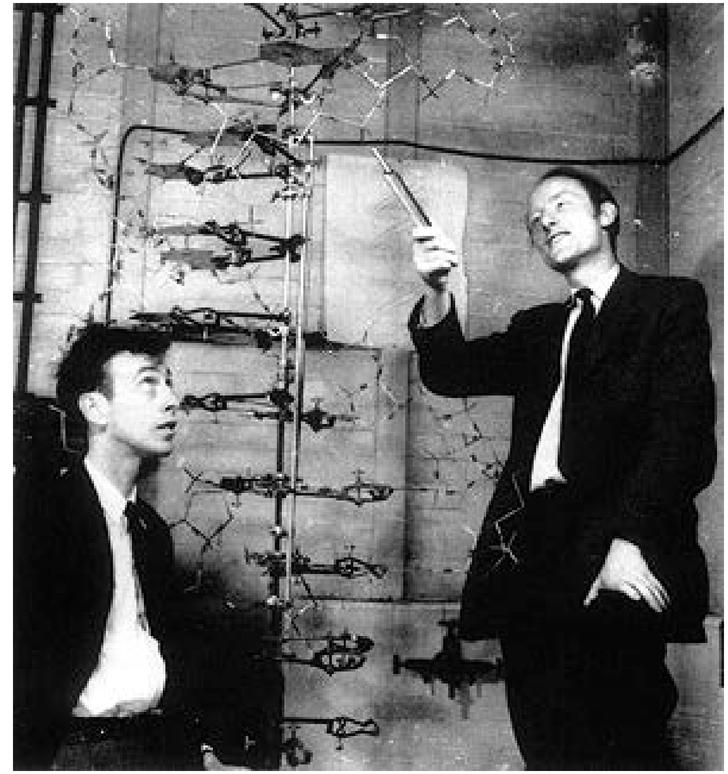


$f_1 = 1, f_2 = 2, f_3 = 3, f_4 = 7$

Vor der Entwicklung der Molekularbiologie wurde Mutation als ein "Deus ex Machina" behandelt

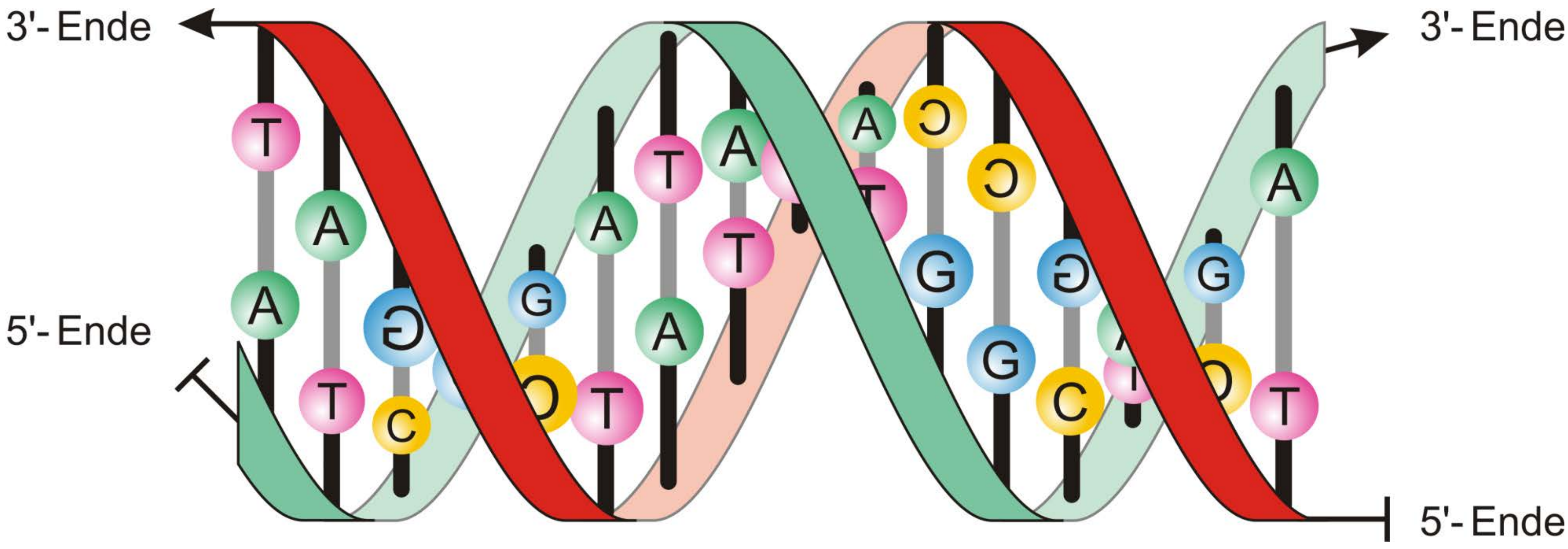


G ≡ C und A = T



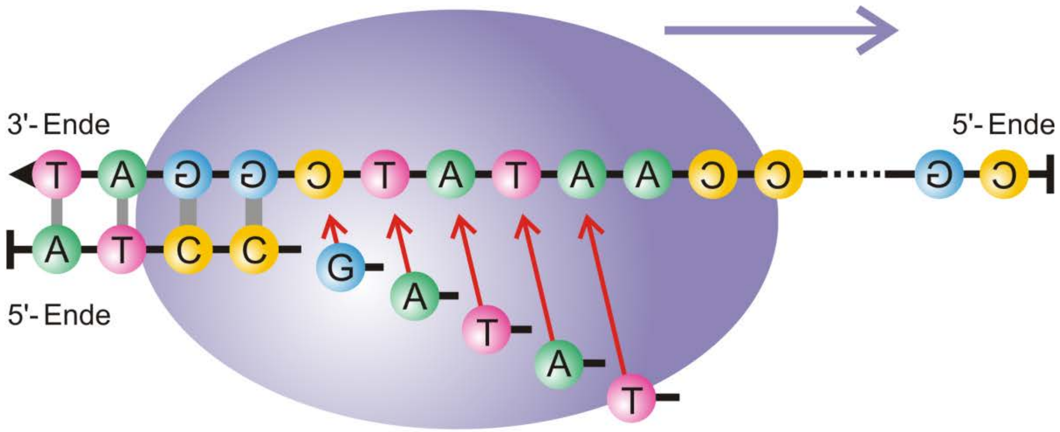
James D. Watson, 1928- , and Francis Crick, 1916-2004,
Nobel Preis 1962

Die dreidimensionale Struktur eines
kleinen Stückes der B-DNA



Die B-Form der DNA-Doppelhelix

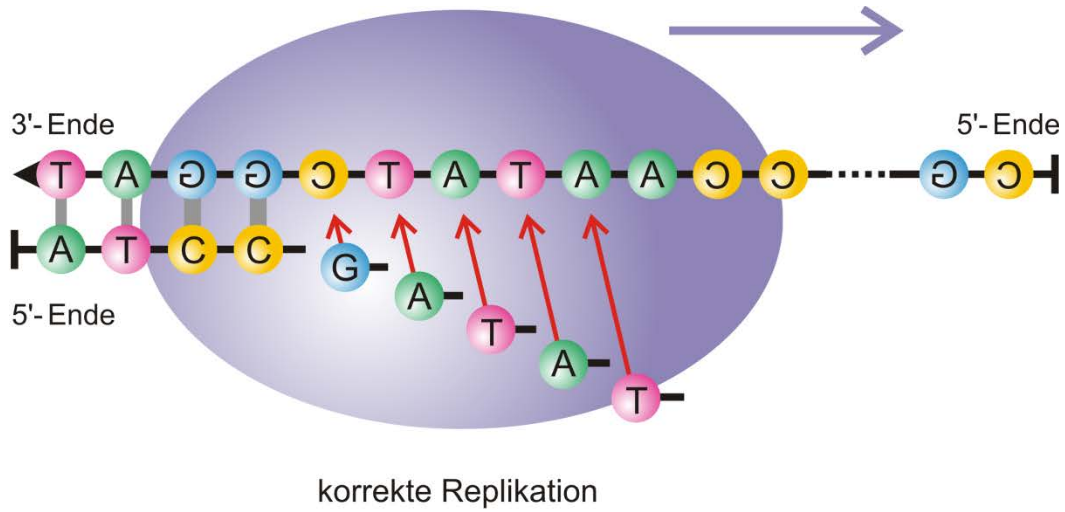
Taq-Polymerase

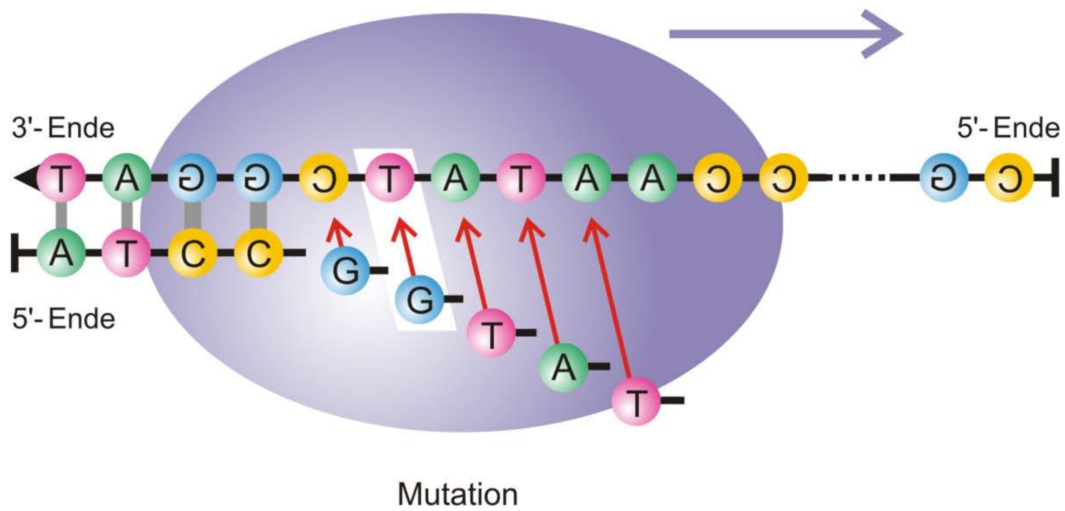


korrekte Replikation

Korrekte Replikation und Punktmutation

Taq-Polymerase



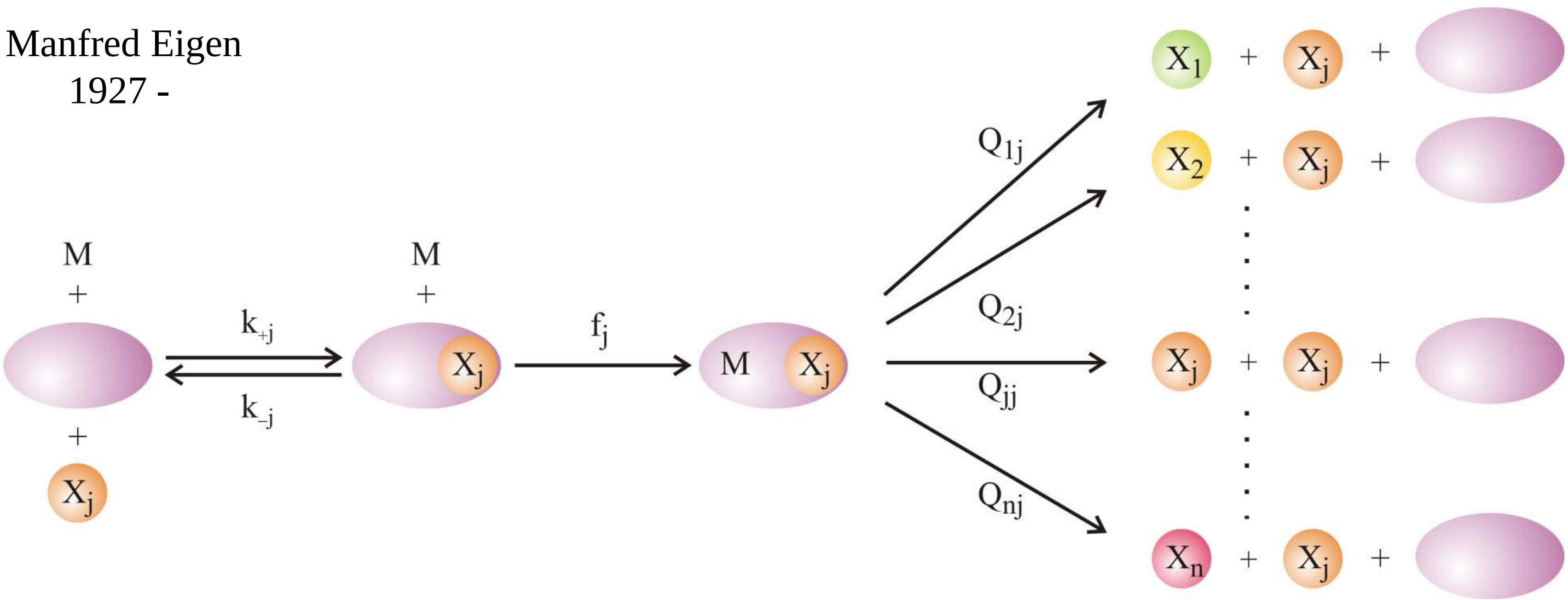


Korrekte Replikation und Punktmutation

Manfred Eigen
1927 -

$$\frac{\mathrm{d}x_j}{\mathrm{dt}} = \sum\nolimits_{i=1}^{n} W_{ji}\, x_i - x_j\, \Phi\, ; \quad j = 1, 2, \ldots, n$$

$$W_{ji} = Q_{ji}\, f_i\, , \quad \Phi = \sum\nolimits_{i=1}^{n} f_i\, x_i \Big/ \sum\nolimits_{i=1}^{n} x_i$$



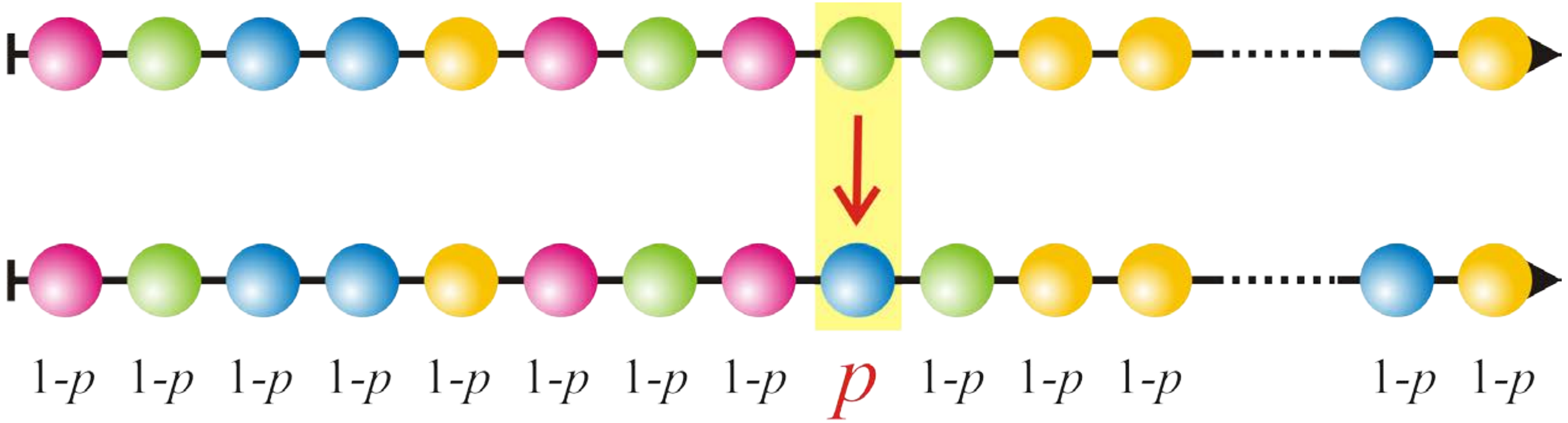
Mutation und (korrekte) Replikation als parallele chemische Reaktionen

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

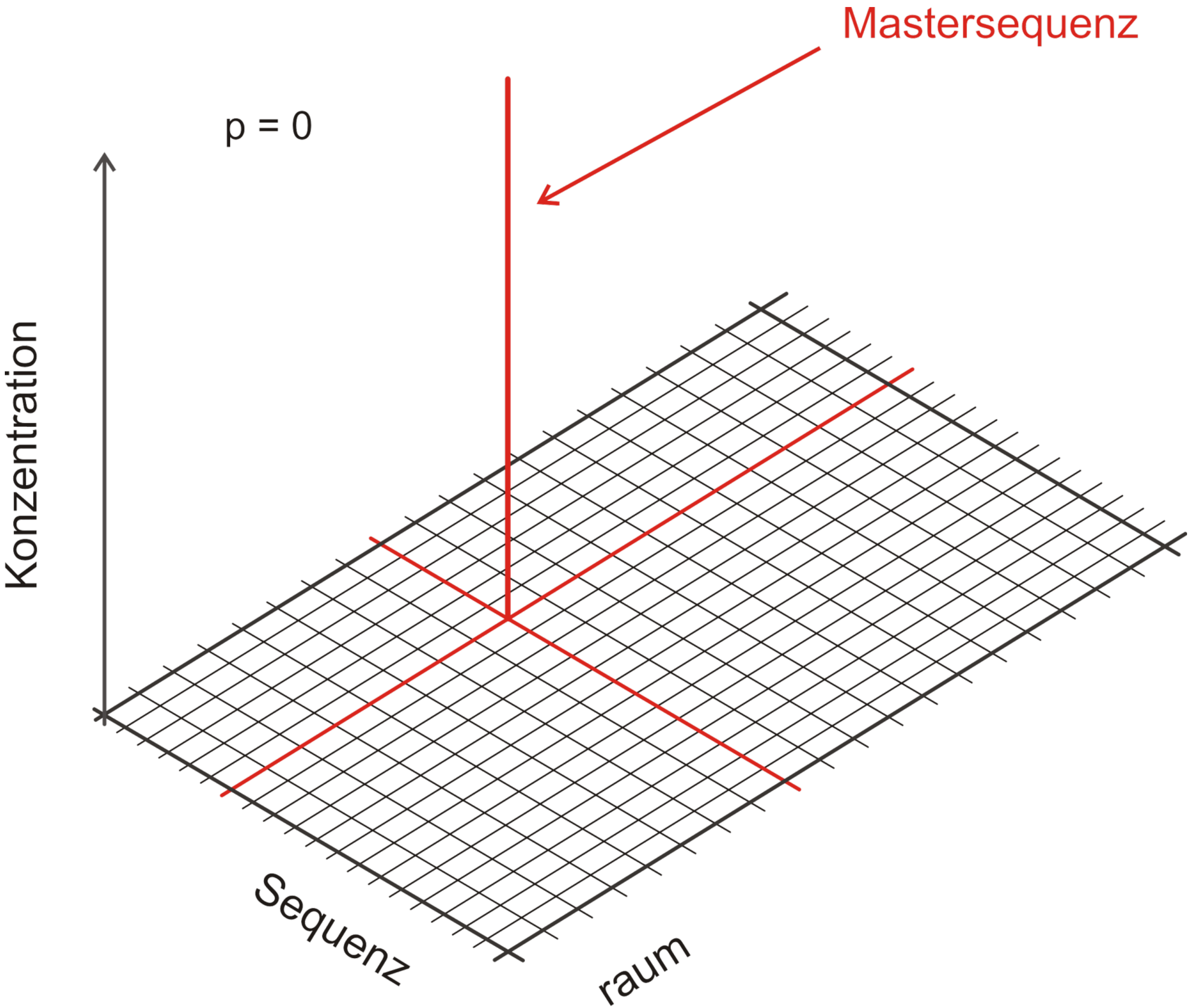
$$Q_{ij} = (1-p)^{n-d_{\mathrm{H}}(X_i,X_j)}\ p^{d_{\mathrm{H}}(X_i,X_j)}$$

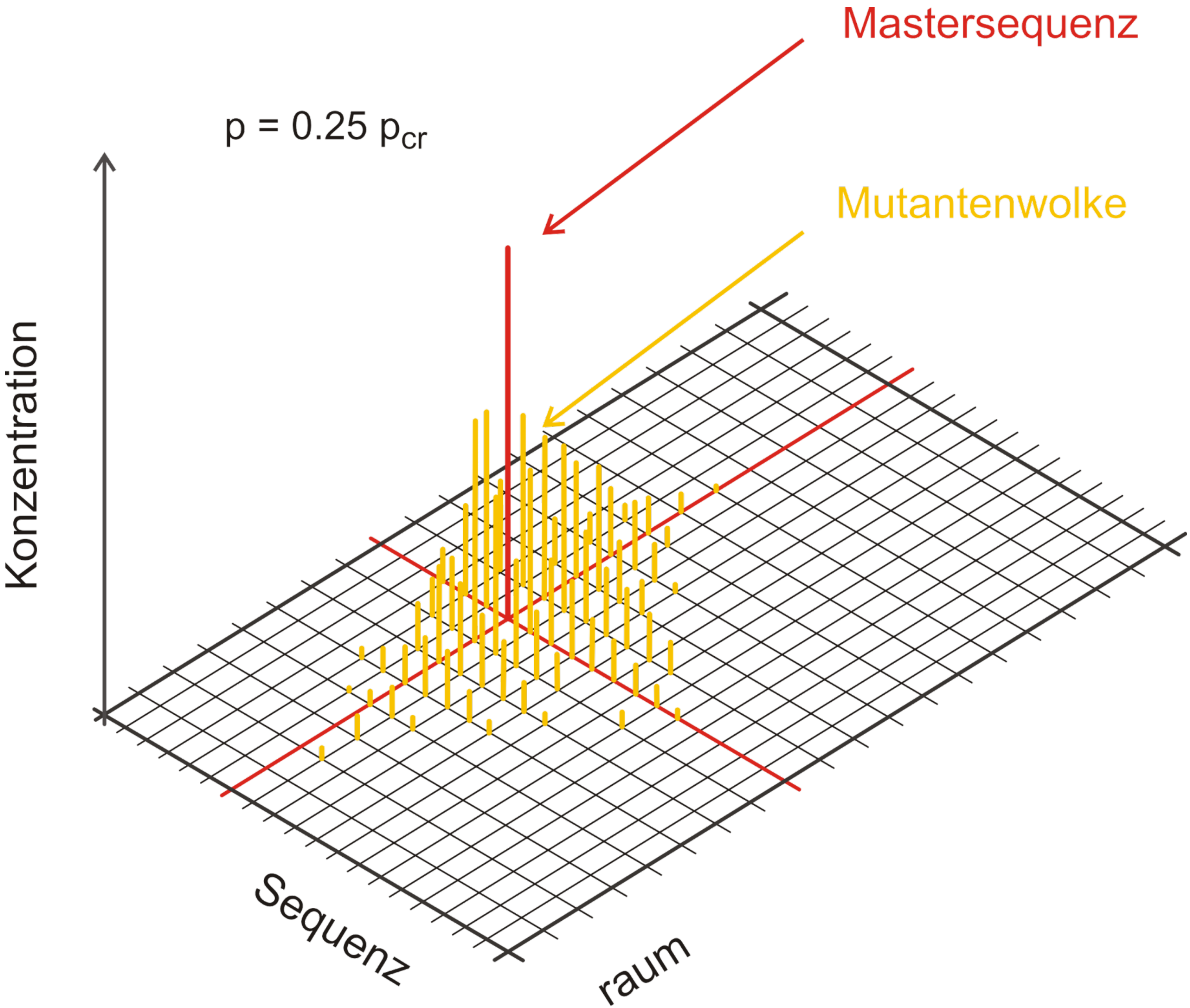
p = Fehler- oder Mutationsrate pro Replikation und Nukleotid

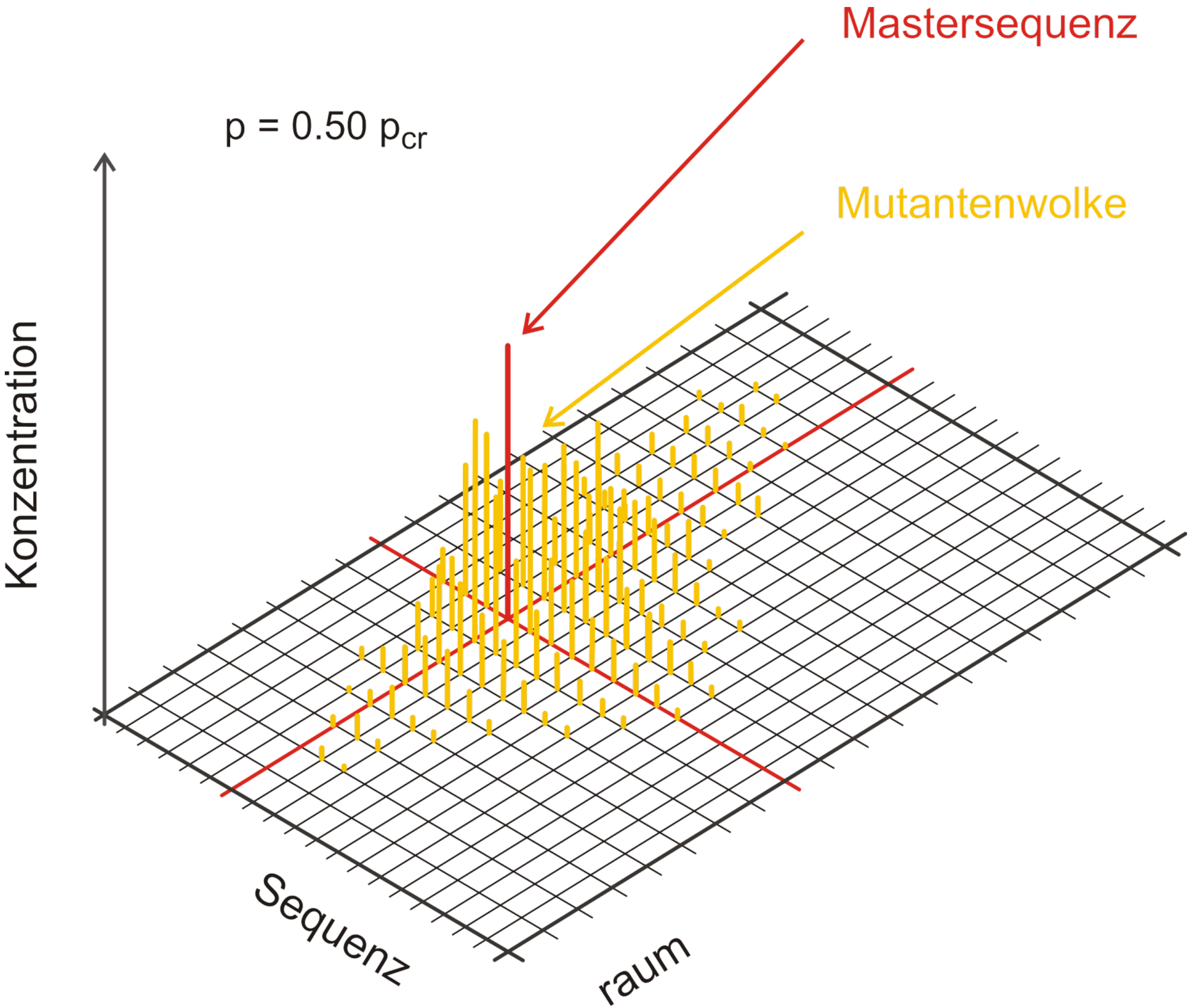
n = Kettenlänge und $d_{\mathrm{H}}(X_i,X_j)$ = Hammingabstand

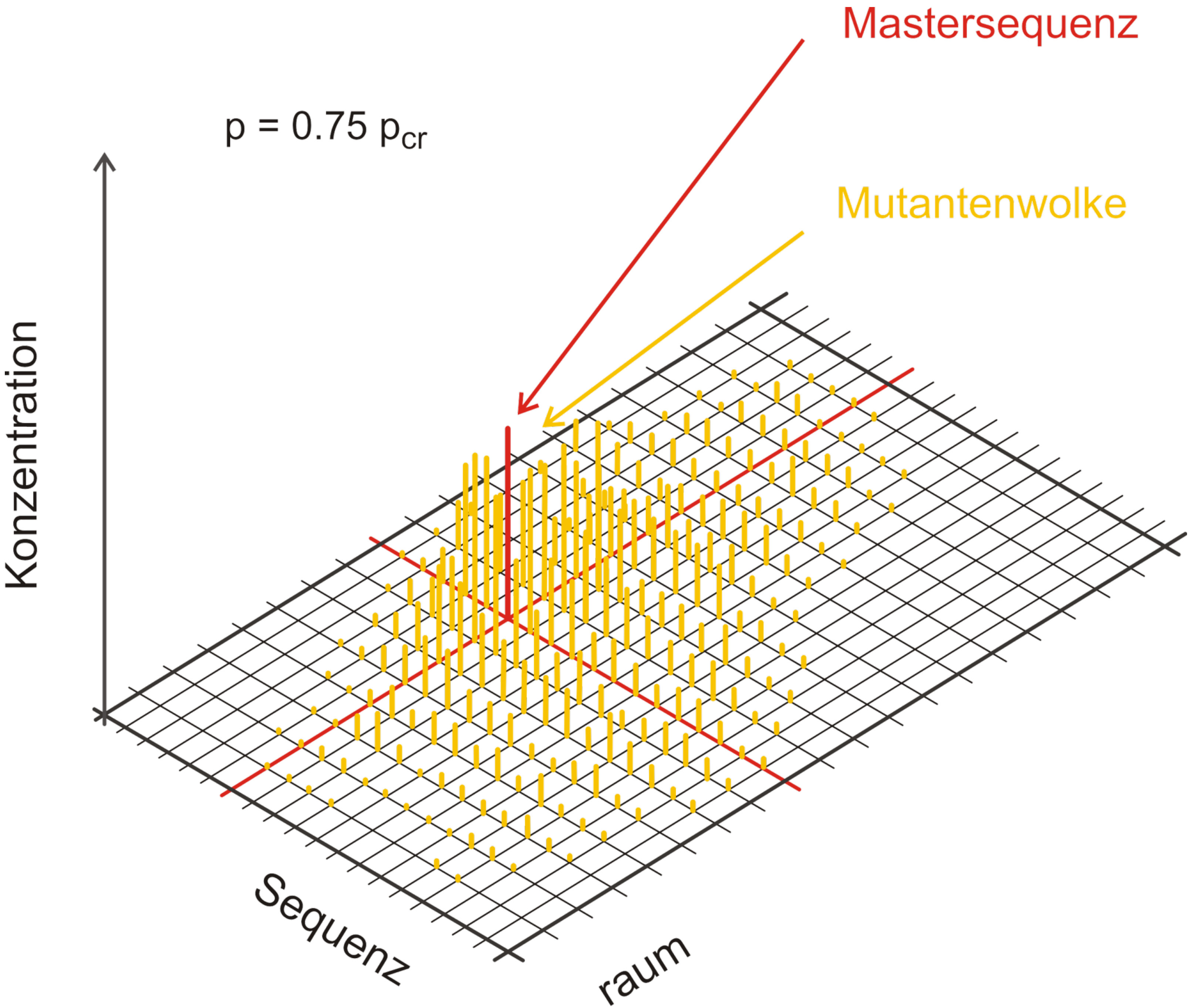


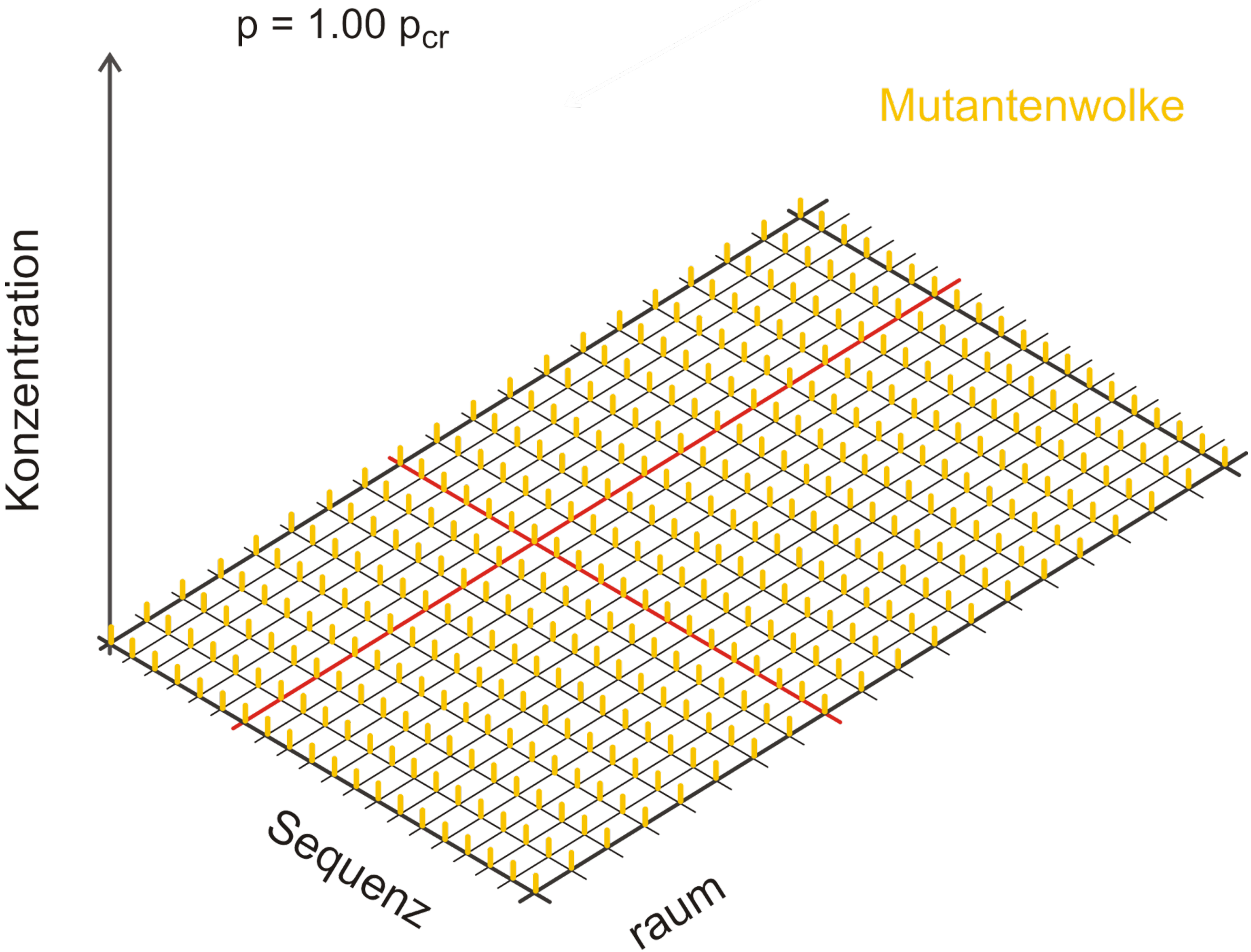
Punktmutation


Mastersequenz
p = 0
Konzentration
Sequenz
raum

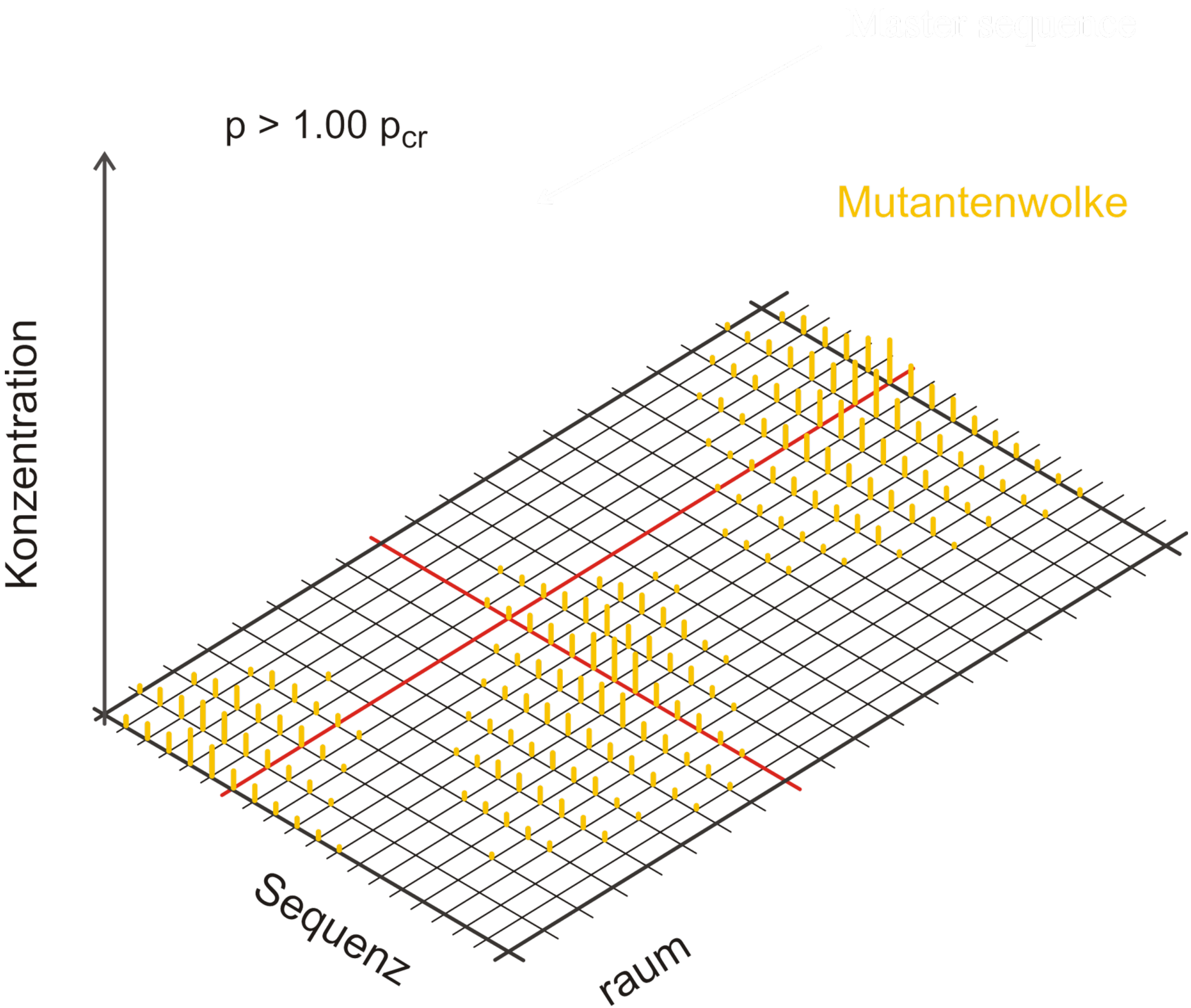

Mastersequenz
p = 0.25 p_cr
Mutantenwolke
Konzentration
Sequenz
raum


Mastersequenz
p = 0.50 p_{cr}
Mutantenwolke
Konzentration
Sequenz
raum

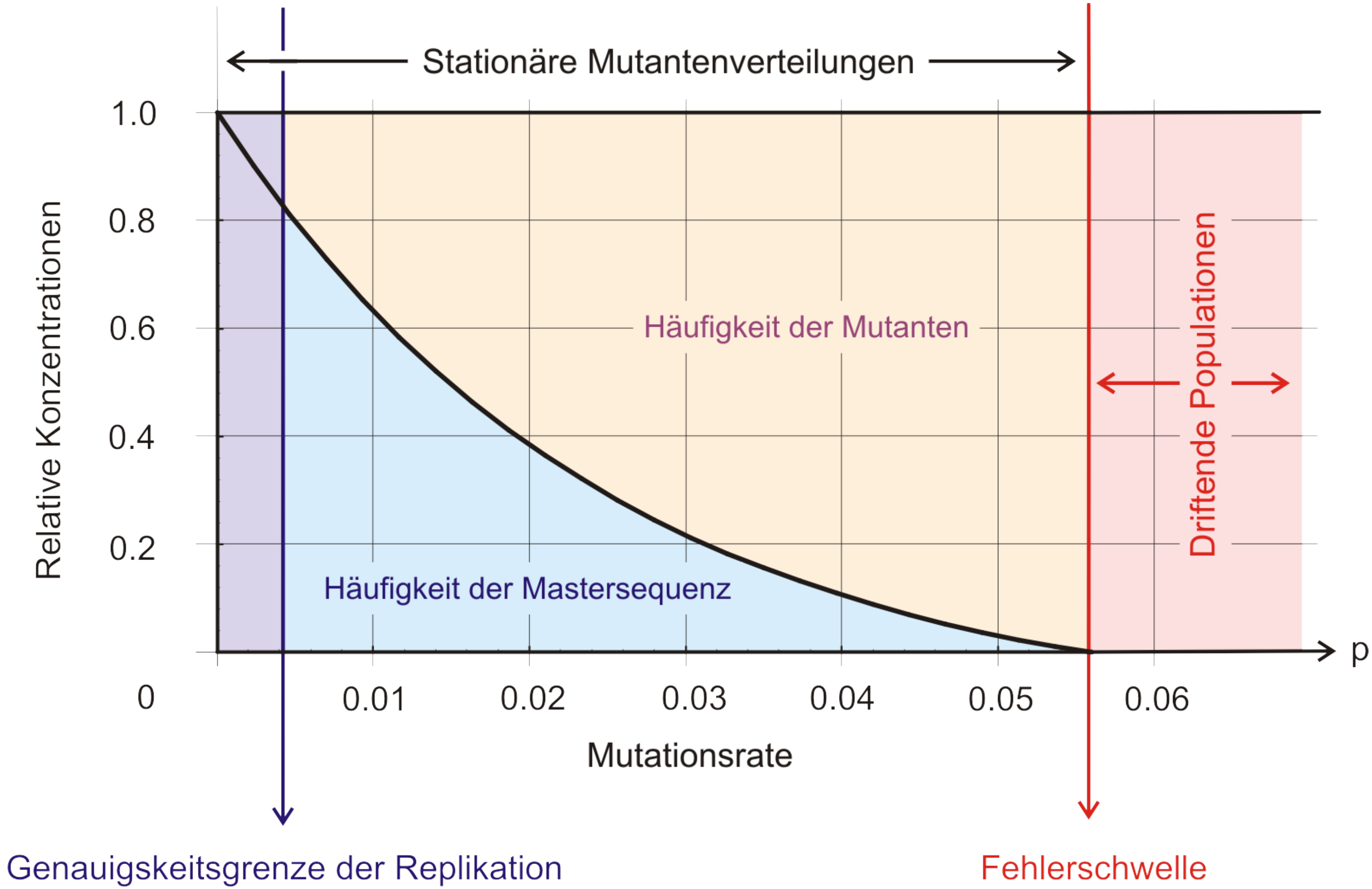

Mastersequenz
p = 0.75 p_cr
Mutantenwolke
Konzentration
Sequenz
raum



$p = 1.00\ p_{cr}$
Mutantenwolke
Konzentration
Sequenz
raum



Master sequence
p > 1.00 p_cr
Mutantenwolke
Konzentration
Sequenz
raum



Die Fehlerschwelle bei Replikation und Mutation

Ergebnisse der Quasispezies-Theorie:

1. Die Selektion führt zu uneinheitlichen Populationen, die aus einer Anzahl molekularer Varianten bestehen.
2. Die stationäre Population bildet das genetische Reservoir einer sich asexuell vermehrenden Spezies und wird deshalb als Quasispezies bezeichnet.
3. Eine Quasispezies enthält eine fitteste Variante, die sogenannte Mastersequenz und ihre nahe verwandten Mutanten.
4. Jedem Replikationsmechanismus entspricht eine maximale Mutationsrate, die Fehlerschranke, welche nicht überschritten werden kann, ohne dass die Vererbung zusammenbricht.

1. Evolutionstheorie und Mathematik
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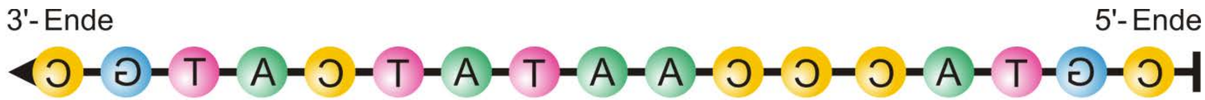
6. Perspektiven einer theoretischen Biologie

1. Digitale Codierung der genetischen Information
2. Überastronomische Vielfalt der Möglichkeiten
3. Komplexe Kinetik in großen Netzwerken
4. Komplexe räumliche Strukturierung
5. Komplexe Entwicklungsprozesse bei Vielzellern
6. Komplexe Umweltfaktoren

Digitale Codierung und überastronomische Vielfalt

DNA

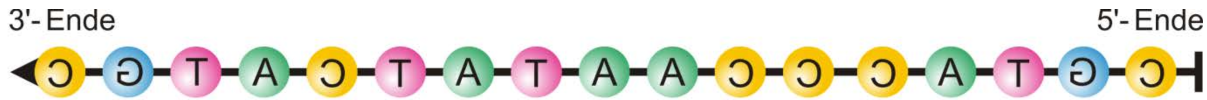


DNA ⇒ RNA

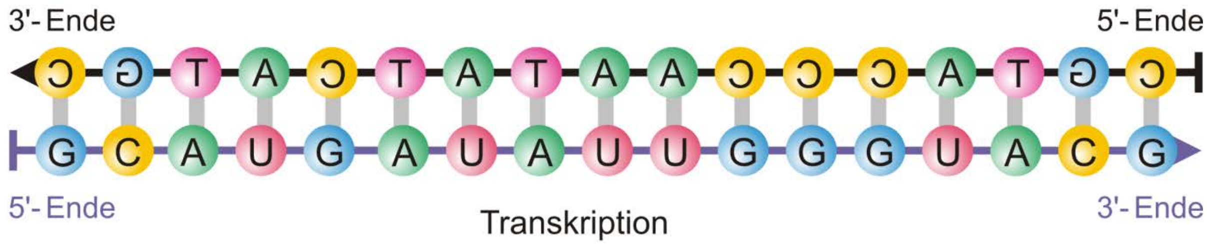
RNA ⇒ Protein

Transkription und Translation

DNA

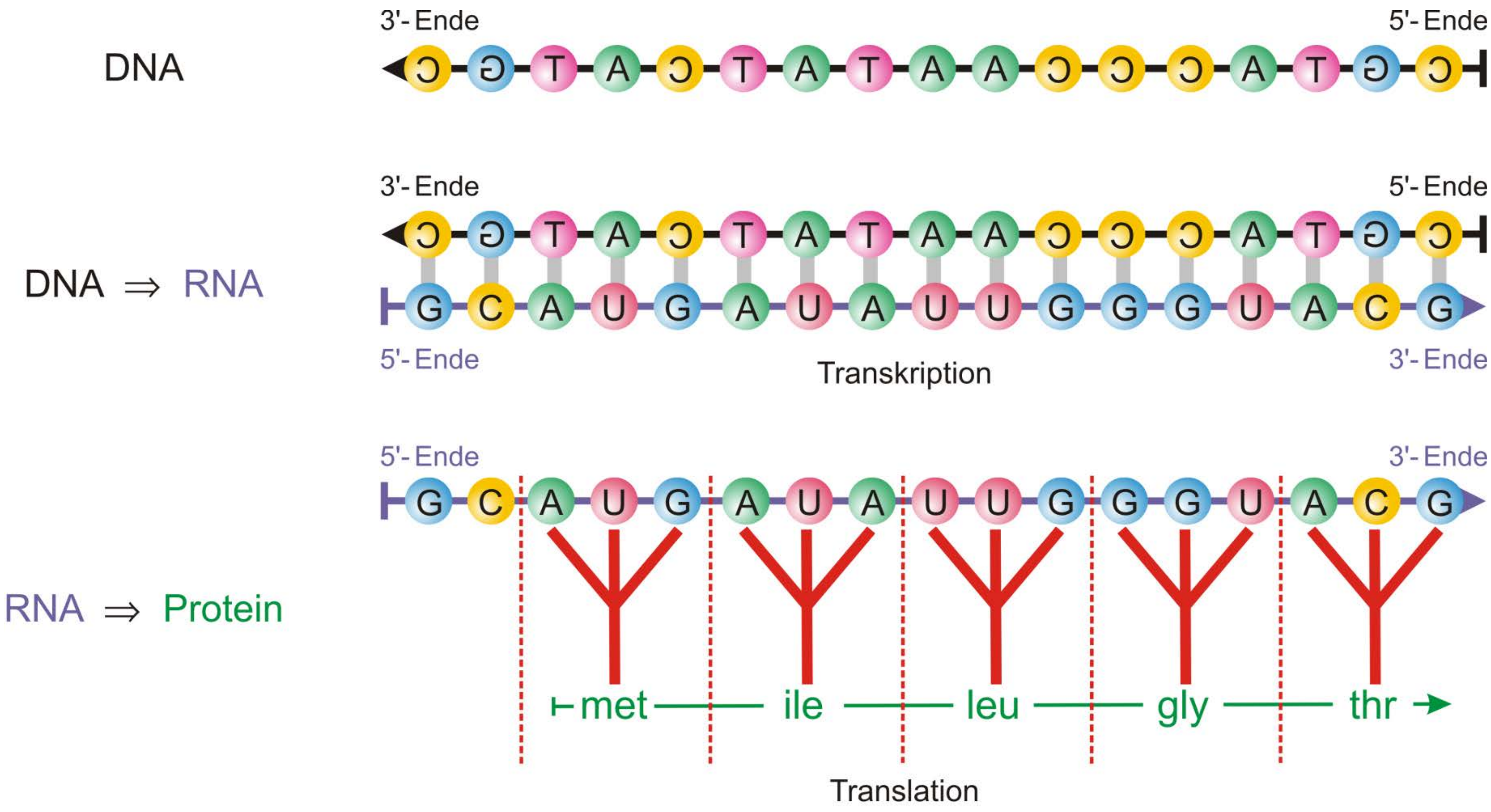


DNA ⇒ RNA



RNA ⇒ Protein

Transkription und Translation



Transkription und Translation

Zahl möglicher Sequenzen: 4^n

Viroide: $4^{300} = 4 \times 10^{180}$

Viren: $4^{5000} = 2 \times 10^{3010}$

Populationsgrößen:

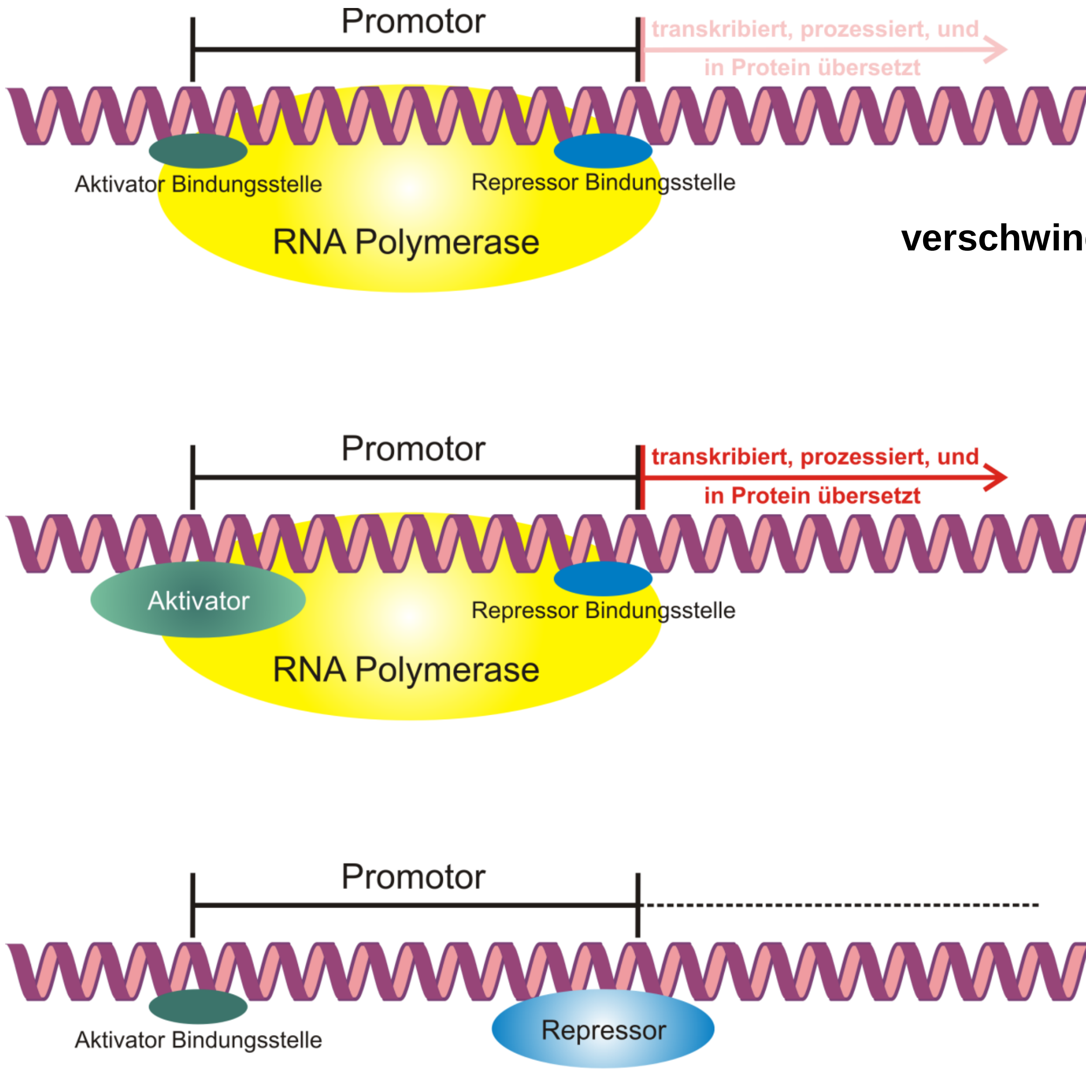
Weltbevölkerung: 7.2×10^9

Bakterien in Petrischale: 5×10^8

RNA-Moleküle im Laborexperiment: 1×10^{15}

Wassermoleküle in einem Mol (= 18 g): 6×10^{23}

Interne Regulation



Zustand I:

Grundzustand

verschwindend geringe RNA Synthese

Zustand II:

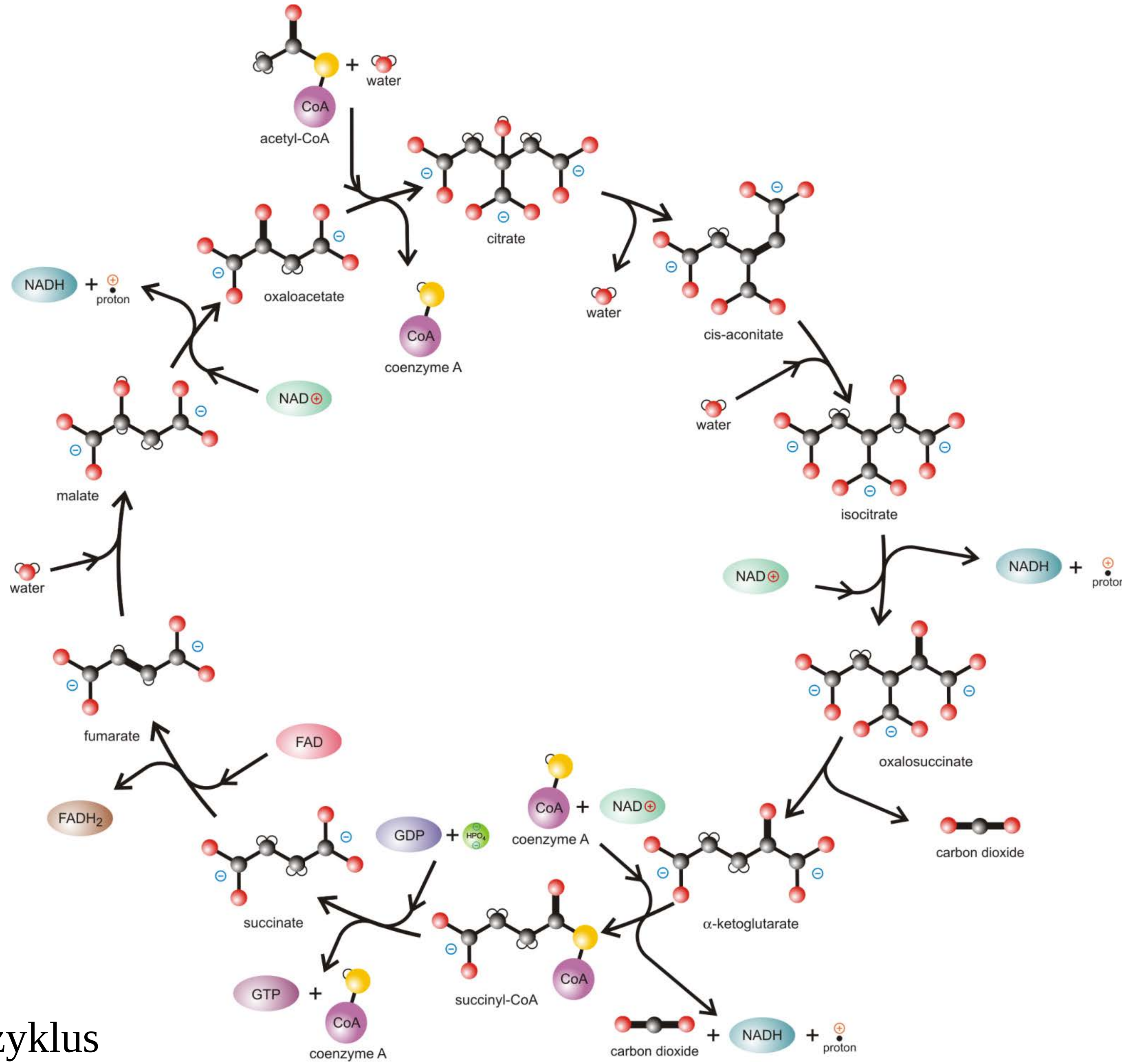
aktiver Zustand

Zustand III:

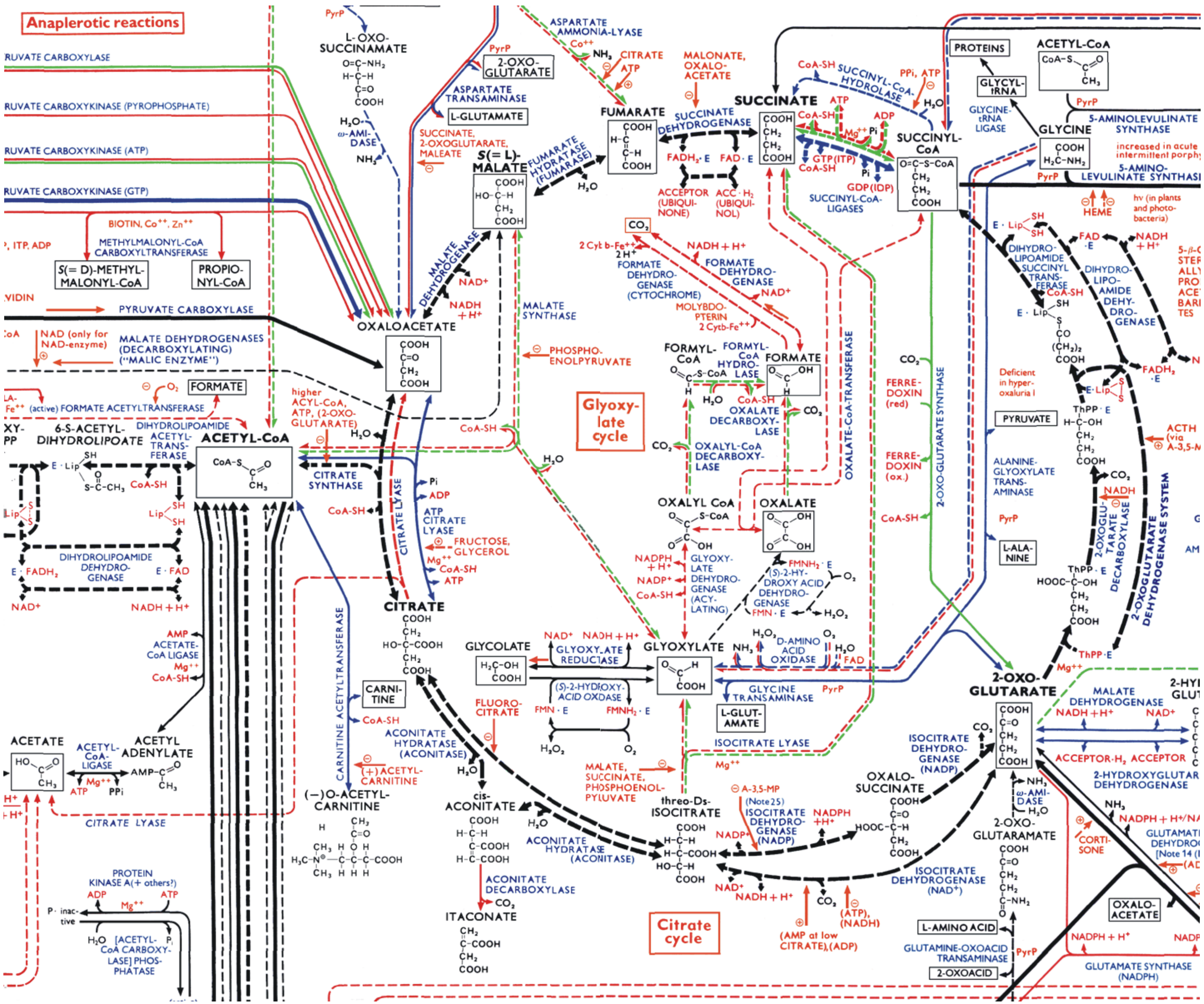
inaktiver Zustand

Regulation der Genexpression

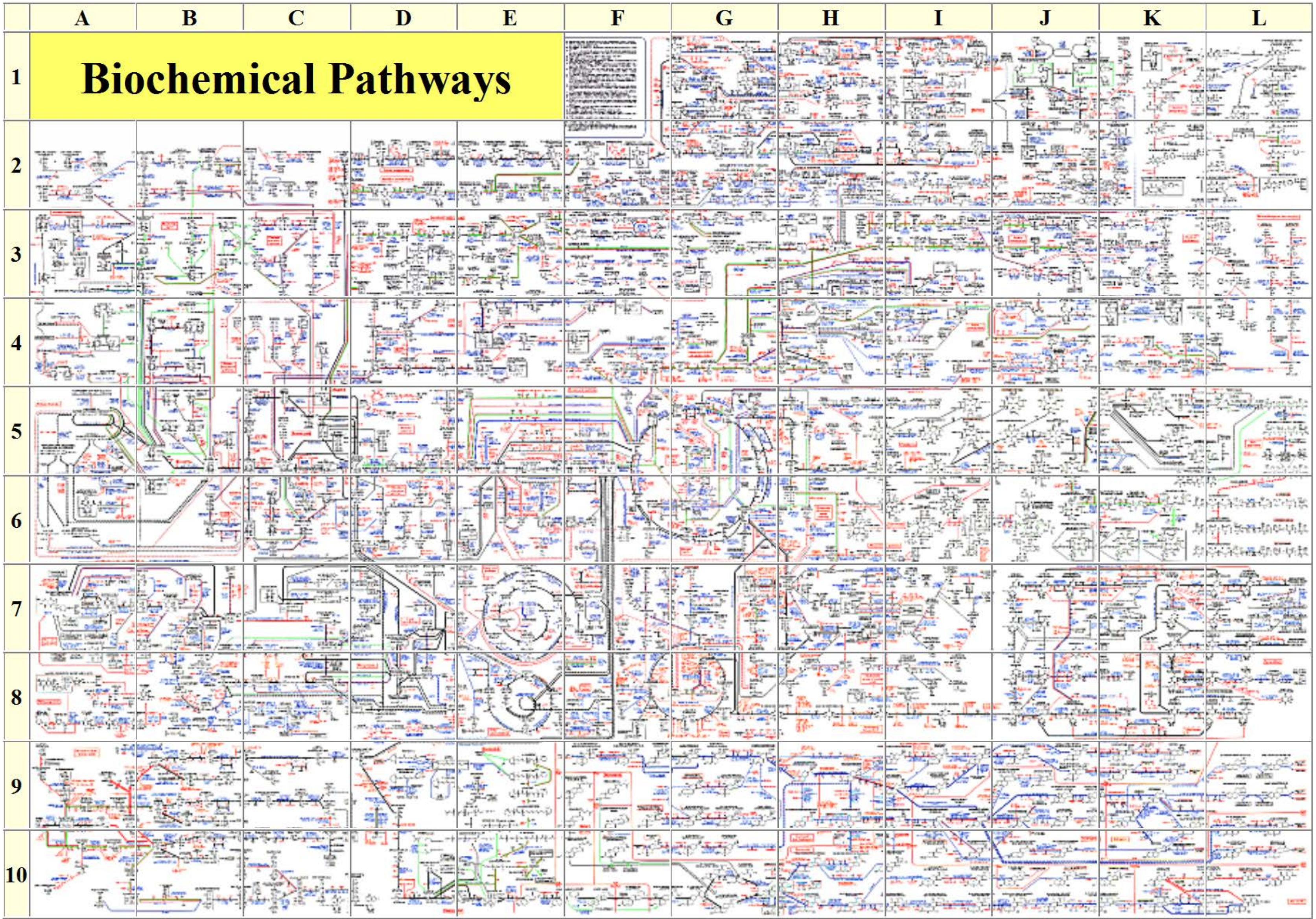
Funktionelle Komplexität



Der Zitronensäurezyklus



Anaplerotic reactions
PYRUVATE CARBOXYLASE
PYRUVATE CARBOXYKINASE (PYROPHOSPHATE)
PYRUVATE CARBOXYKINASE (ATP)
PYRUVATE CARBOXYKINASE (GTP)
BIOTIN, Co++, Zn++
METHYLMALONYL-CoA CARBOXYLTRANSFERASE
S(= D)-METHYL-MALONYL-CoA
PROPIO-NYL-CoA
AVIDIN
PYRUVATE CARBOXYLASE
NAD (only for NAD-enzyme)
MALATE DEHYDROGENASES (DECARBOXYLATING) ("MALIC ENZYME")
FORMATE
(active) FORMATE ACETYLTRANSFERASE
6-S-ACETYL-DIHYDROLIPOATE
DIHYDROLIPOAMIDE ACETYL-TRANS-FERASE
ACETYL-CoA
CoA-SH
DIHYDROLIPOAMIDE DEHYDRO-GENASE
E · FADH₂
E · FAD
NAD+
NADH + H+
AMP
ACETATE-CoA LIGASE
Mg++
CoA-SH
ACETATE
ACETYL-CoA-LIGASE
ACETYL ADENYLATE
ATP
PPi
CITRATE LYASE
PROTEIN KINASE A(+ others?)
ADP
ATP
P · inac-tive
[ACETYL-CoA CARBOXY-LASE] PHOS-PHATASE
L-OXO-SUCCINAMATE
ω-AMI-DASE
2-OXO-GLUTARATE
ASPARTATE TRANSAMINASE
L-GLUTAMATE
SUCCINATE, 2-OXOGLUTARATE, MALEATE
S(= L)-MALATE
MALATE DEHYDROGENASE
NAD+
NADH + H+
OXALOACETATE
MALATE SYNTHASE
PHOSPHO-ENOLPYRUVATE
higher ACYL-CoA, ATP, (2-OXO-GLUTARATE)
CITRATE SYNTHASE
CITRATE LYASE
ATP CITRATE LYASE
Pi
ADP
FRUCTOSE, GLYCEROL
CoA-SH
ATP
CITRATE
CARNI-TINE
CARNITINE ACETYLTRANSFERASE
(+) ACETYL-CARNITINE
(−)O-ACETYL-CARNITINE
ACONITATE HYDRATASE (ACONITASE)
cis-ACONITATE
ACONITATE DECARBOXYLASE
ITACONATE
FLUORO-CITRATE
ASPARTATE AMMONIA-LYASE
CITRATE
MALONATE, OXALO-ACETATE
FUMARATE
FUMARATE HYDRATASE (FUMARASE)
SUCCINATE DEHYDROGENASE
FADH₂ · E
FAD · E
ACCEPTOR (UBIQUI-NONE)
ACC · H₂ (UBIQUI-NOL)
SUCCINATE
SUCCINYL-CoA HYDROLASE
PPi, ATP
GTP (ITP)
GDP (IDP)
SUCCINYL-CoA-LIGASES
SUCCINYL-CoA
CO₂
2 Cyt b-Fe++
FORMATE DEHYDRO-GENASE (CYTOCHROME)
FORMATE DEHYDRO-GENASE
MOLYBDO-PTERIN
2 Cyt b-Fe+++
FORMYL-CoA
FORMYL-CoA HYDRO-LASE
FORMATE
OXALATE DECARBOXY-LASE
OXALYL-CoA DECARBOXY-LASE
Glyoxy-late cycle
OXALYL CoA
OXALATE
OXALATE-CoA-TRANSFERASE
GLYOXY-LATE DEHYDRO-GENASE (ACY-LATING)
(S)-2-HY-DROXY ACID DEHYDRO-GENASE
FMN · E
FMNH₂ · E
GLYCOLATE
GLYOXYLATE REDUCTASE
(S)-2-HYDROXY-ACID OXIDASE
GLYOXYLATE
D-AMINO ACID OXIDASE
FAD
GLYCINE TRANSAMINASE
L-GLUT-AMATE
ISOCITRATE LYASE
MALATE, SUCCINATE, PHOSPHOENOL-PYRUVATE
threo-Ds-ISOCITRATE
A-3,5-MP (Note 25)
ISOCITRATE DEHYDRO-GENASE (NADP)
ISOCITRATE DEHYDROGENASE (NAD+)
(AMP at low CITRATE), (ADP)
(ATP), (NADH)
Citrate cycle
OXALO-SUCCINATE
ISOCITRATE DEHYDRO-GENASE (NADP)
FERRE-DOXIN (red)
FERRE-DOXIN (ox.)
2-OXO-GLUTARATE SYNTHASE
2-OXO-GLUTARATE
PROTEINS
GLYCYL-tRNA
GLYCINE-tRNA LIGASE
ACETYL-CoA
GLYCINE
5-AMINOLEVULINATE SYNTHASE
increased in acute intermittent porphyria
5-AMINO-LEVULINATE SYNTHASE
HEME
hν (in plants and photo-bacteria)
DIHYDRO-LIPOAMIDE SUCCINYL TRANS-FERASE
DIHYDRO-LIPO-AMIDE DEHY-DRO-GENASE
Deficient in hyper-oxaluria I
PYRUVATE
ALANINE-GLYOXYLATE TRANS-AMINASE
L-ALA-NINE
2-OXOGLU-TARATE DECARBOXYLASE
2-OXOGLUTARATE DEHYDROGENASE SYSTEM
ACTH (via A-3,5-MP)
MALATE DEHYDROGENASE
ACCEPTOR-H₂ ACCEPTOR
2-HYDROXYGLUTARATE DEHYDROGENASE
ω-AMI-DASE
2-OXO-GLUTARAMATE
L-AMINO ACID
GLUTAMINE-OXOACID TRANSAMINASE
2-OXOACID
CORTI-SONE
GLUTAMATE DEHYDROGENASE [Note 14]
OXALO-ACETATE
GLUTAMATE SYNTHASE (NADPH)



Das Reaktionsnetzwerk des zellulären Stoffwechsels nach Boehringer-Mannheim

Räumliche Komplexität

Mycoplasma pneumoniae:	Genomelänge	820 000 bp
	# Gene:	733
	# Proteine (ORF):	689
	# tRNAs	37
	# rRNAs	3
	# andere RNAs	4

S. Kühner, V. van Noort, M. J. Betts, A. Leo-Macias, C. Batisse, M. Rode, T. Yamada, T. Maier, S. Bader, P. Beltran-Alvarez, D. Castaño-Diez, W.-H. Chen, D. Devos, M. Güell, T. Norambuena, I. Racke, V. Rybin, A. Schmidt, E. Yus, R. Aebersold, R. Herrmann, B. Böttcher, A. S. Frangakis, R. B. Russell, L. Serrano, P. Bork, and A.-C. Gavin. 2009.
Proteome organization in a genome-reduced bacterium. Science **326**:1235–1240.

E. Yus, T. Maier, K. Michalodimitrakis, V. van Noort, T. Yamada, W.-H. Chen, J. A. Wodke, M. Güell, S. Martínez, R. Bourgeois, S. Kühner, E. Raineri, I. Letunic, O. V. Kalinina, M. Rode, R. Herrmann, R. Gutiérez-Gallego, R. B. Russell, A.-C. Gavin, P. Bork, and L. Serrano. 2009.
Impact of genome reduction on bacterial metabolism and its regulation. Science **326**:1263–1268.

M. Güell, V. van Noort, E. Yus, W.-H. Chen, J. Leigh-Bell, K. Michalodimitrakis, T. Yamada, M. Arumugam, T. Doerks, S. Kühner, M. Rode, M. Suyama, S. Schmidt, A.-C. Gavin, P. Bork, and L. Serrano. 2009.
Transcriptome complexity in a genome-reduced bacterium. Science **326**:1268–1271.

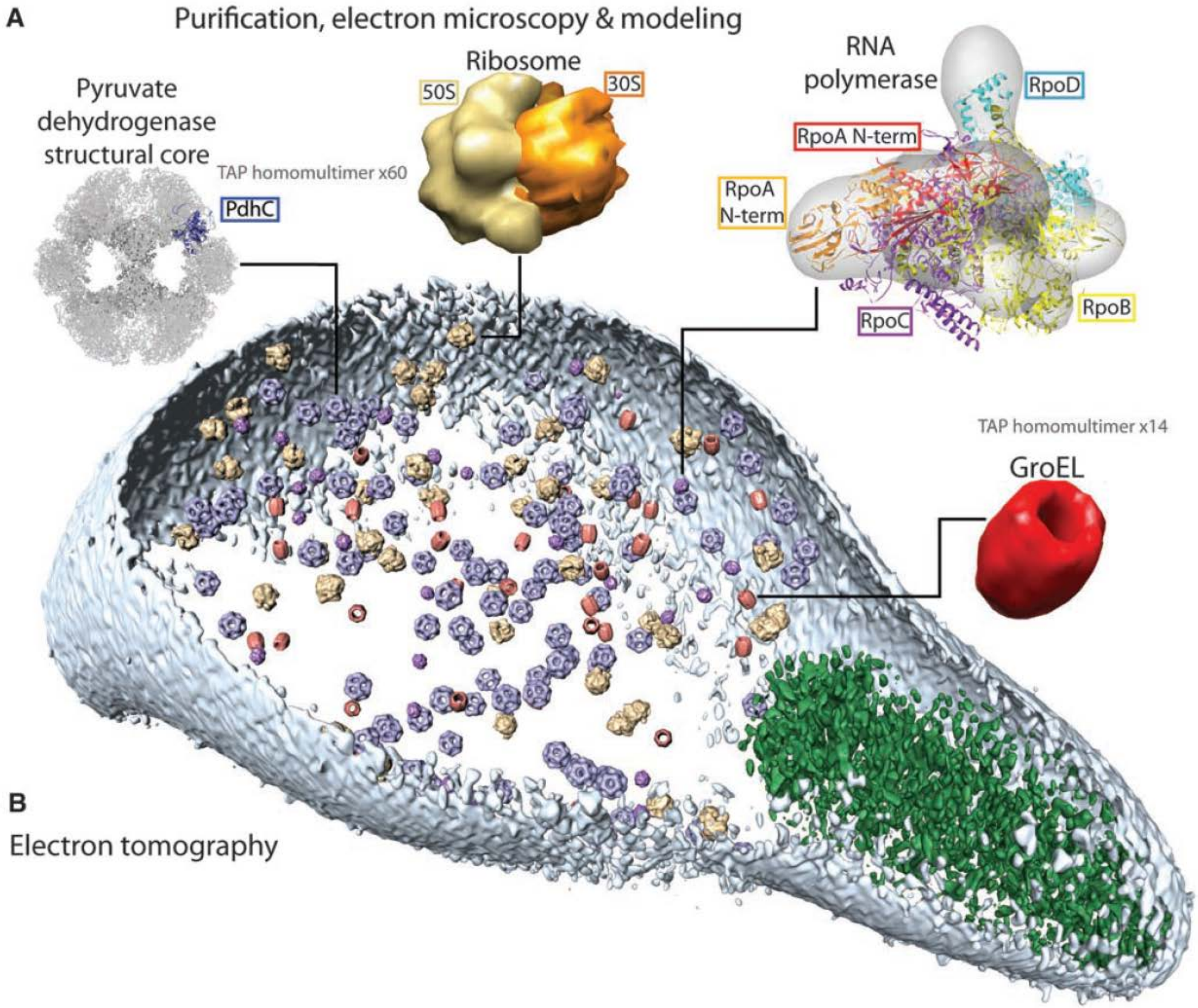
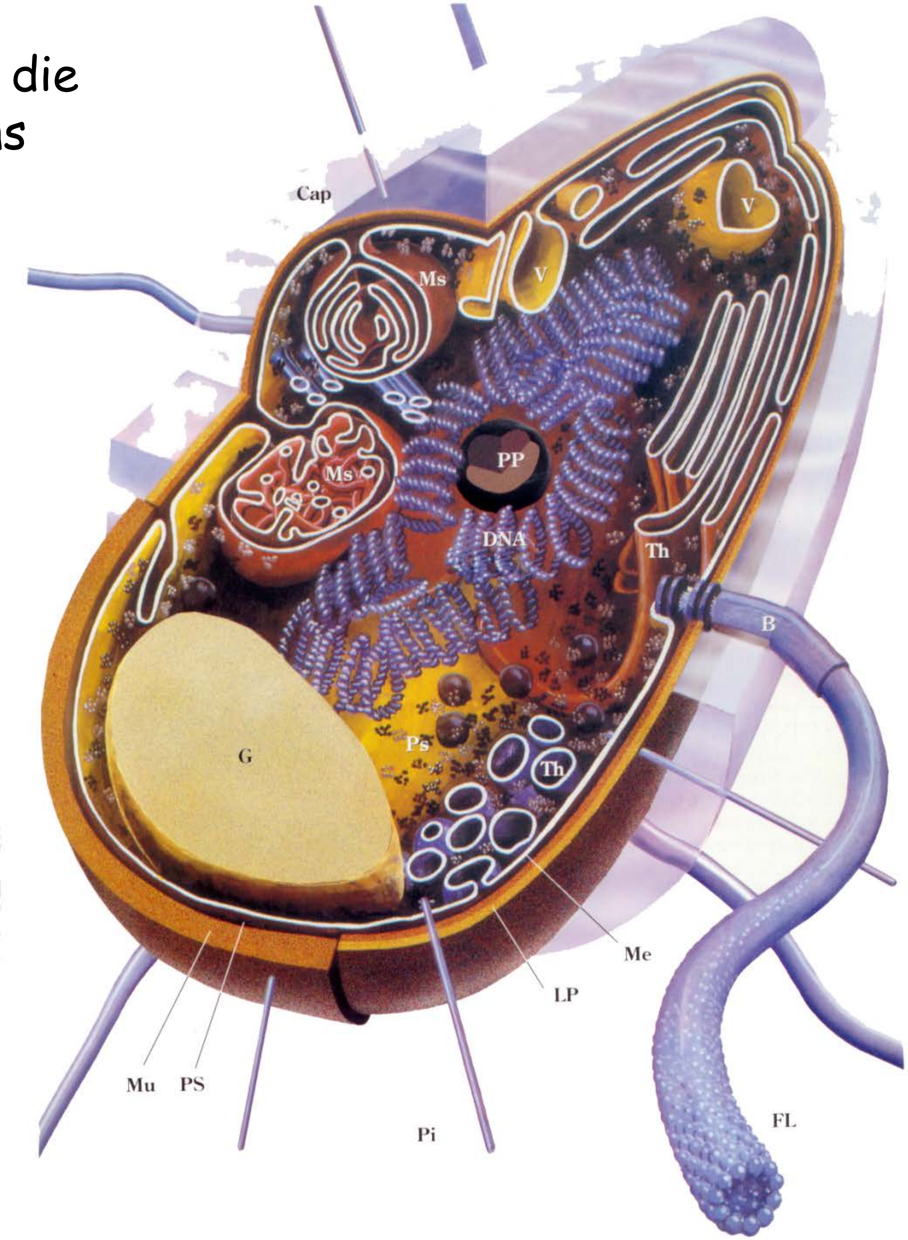


Fig. 4. From proteomics to the cell. By a combination of pattern recognition and classification algorithms, the following TAP-identified complexes from *M. pneumoniae*, matching to existing electron microscopy and x-ray and tomogram structures (**A**), were placed in a whole-cell tomogram (**B**): the structural core of pyruvate dehydrogenase in blue (~23 nm), the ribosome in yellow (~26 nm), RNA polymerase in purple (~17 nm), and GroEL homomultimer in red (~20 nm). Cell dimensions are ~300 nm by 700 nm. The cell membrane is shown in light blue. The rod, a prominent structure filling the space of the tip region, is depicted in green. Its major structural elements are HMW2 (Mpn310) in the core and HMW3 (Mpn452) in the periphery, stabilizing the rod (*42*).The individual complexes (A) are not to scale, but they are shown to scale within the bacterial cell (B).

Die Bakterienzelle als Beispiel für die einfachste Form autonomen Lebens



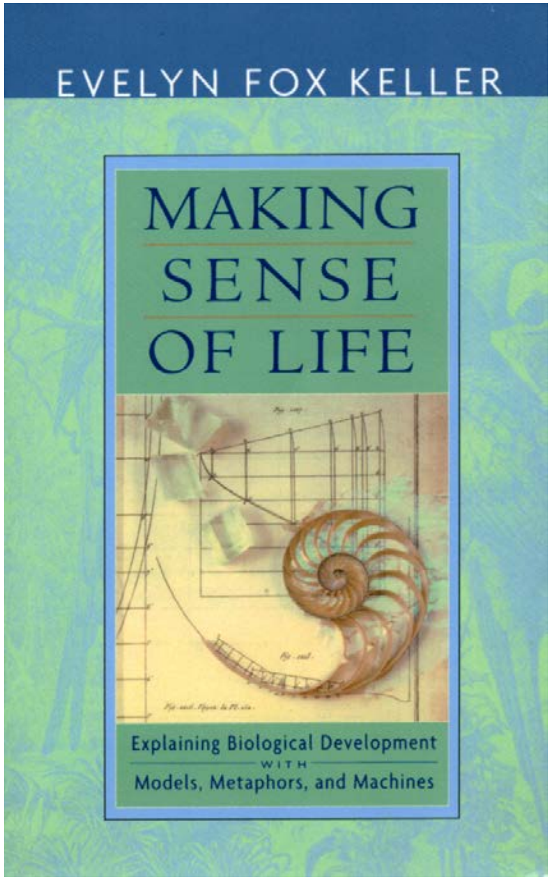
Das Escherichia coli Genom:

4 Millionen Nukleotide

4460 Gene

Die räumliche Struktur des Bakteriums *Escherichia coli*

Entwicklungsbiologie



Mathematical Models:
Explaining development
without the help of genes

„Untimely Birth of a
Mathematical Biology“

Evelyn Fox Keller, 1936 –

Fakten müssen der Theorienbildung vorausgehen

Keller, E.F. 2003. Making Sense of Life. Explaining Biological Development with Models, Metaphors, and Machines. Harvard University Press, Cambridge, MA

Es ist zumeist sehr schwierig geeignete einfache, aussagekräftige und experimentell überprüfbare Modellssysteme zu finden.

Es gibt eine Himmelsmechanik aber keine Himmelsbiologie!

1. Evolutionstheorie und Mathematik
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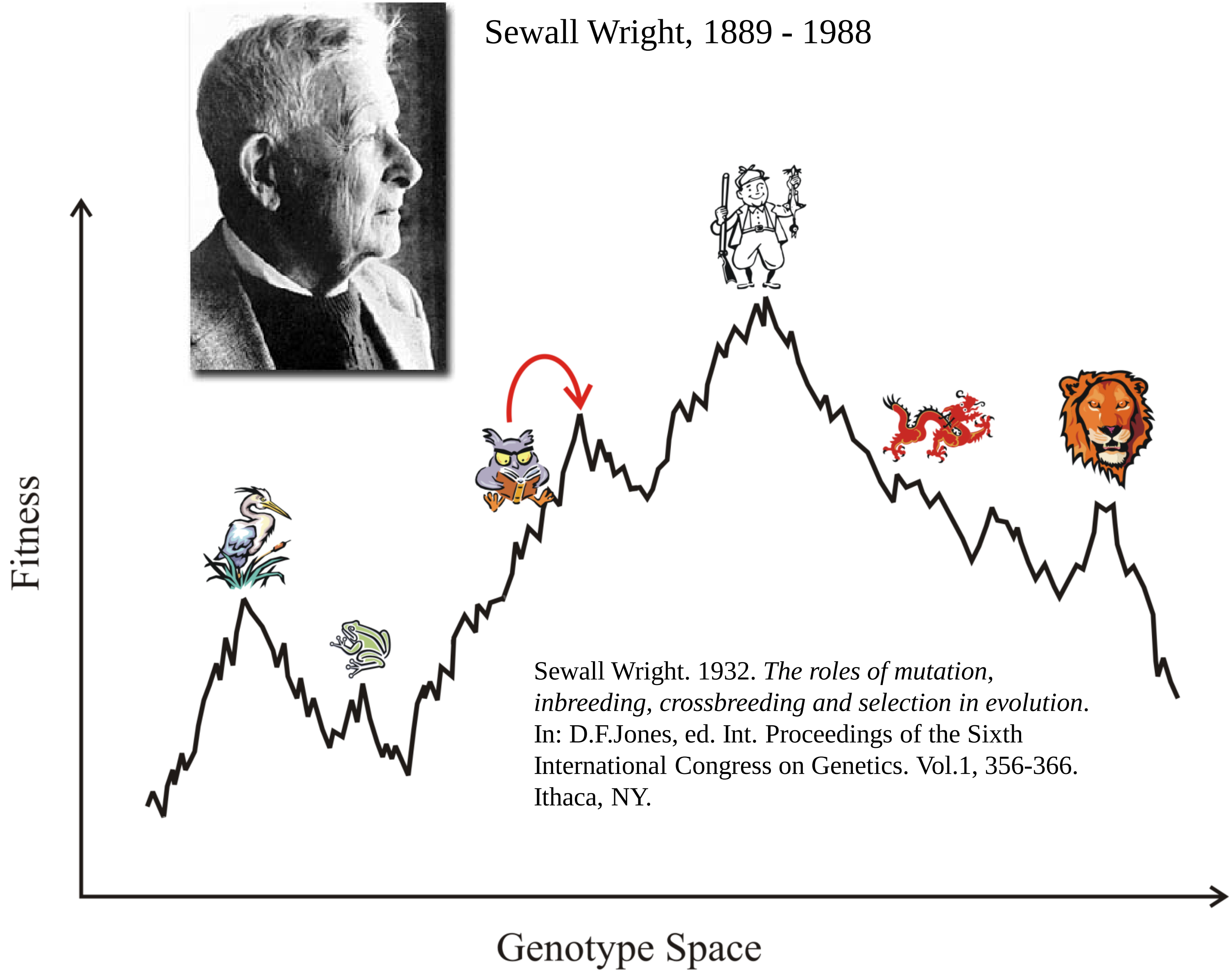
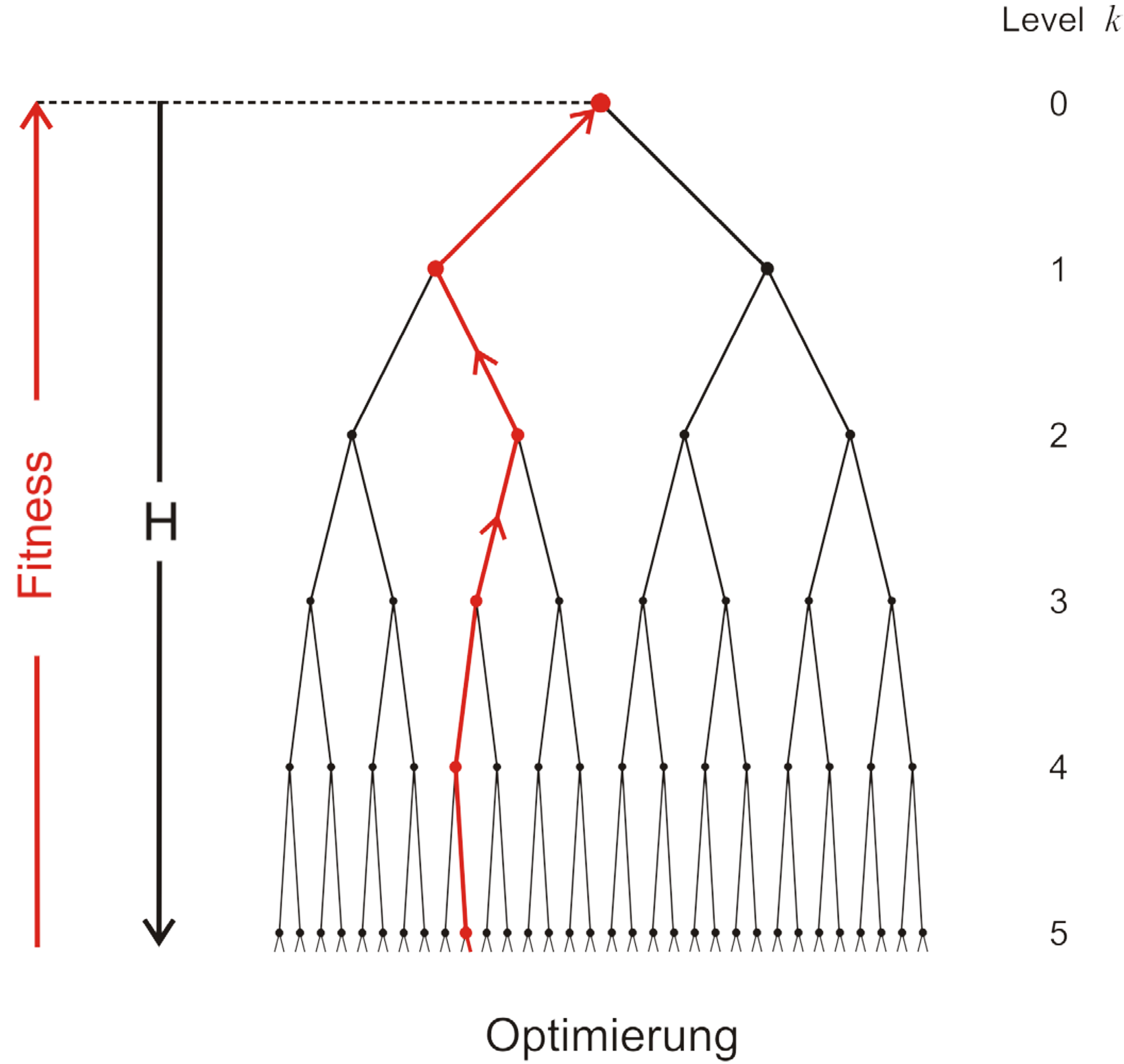
4. **Optimierung und historische Kontingenz**
5. Die neue Biologie: Epigenetik und ‚Big-Data'
6. Perspektiven einer theoretischen Biologie

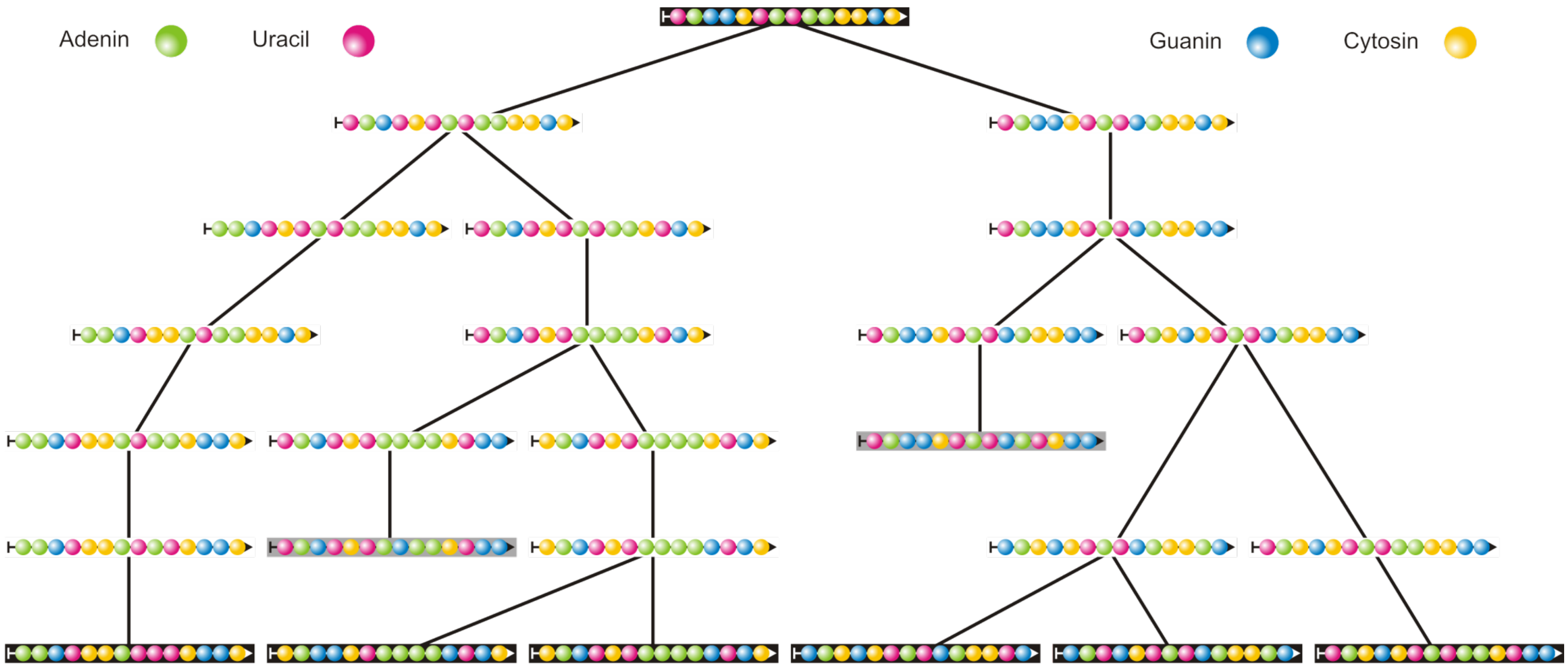


Sewall Wright, 1889 - 1988

Sewall Wright. 1932. *The roles of mutation, inbreeding, crossbreeding and selection in evolution*. In: D.F.Jones, ed. Int. Proceedings of the Sixth International Congress on Genetics. Vol.1, 356-366. Ithaca, NY.

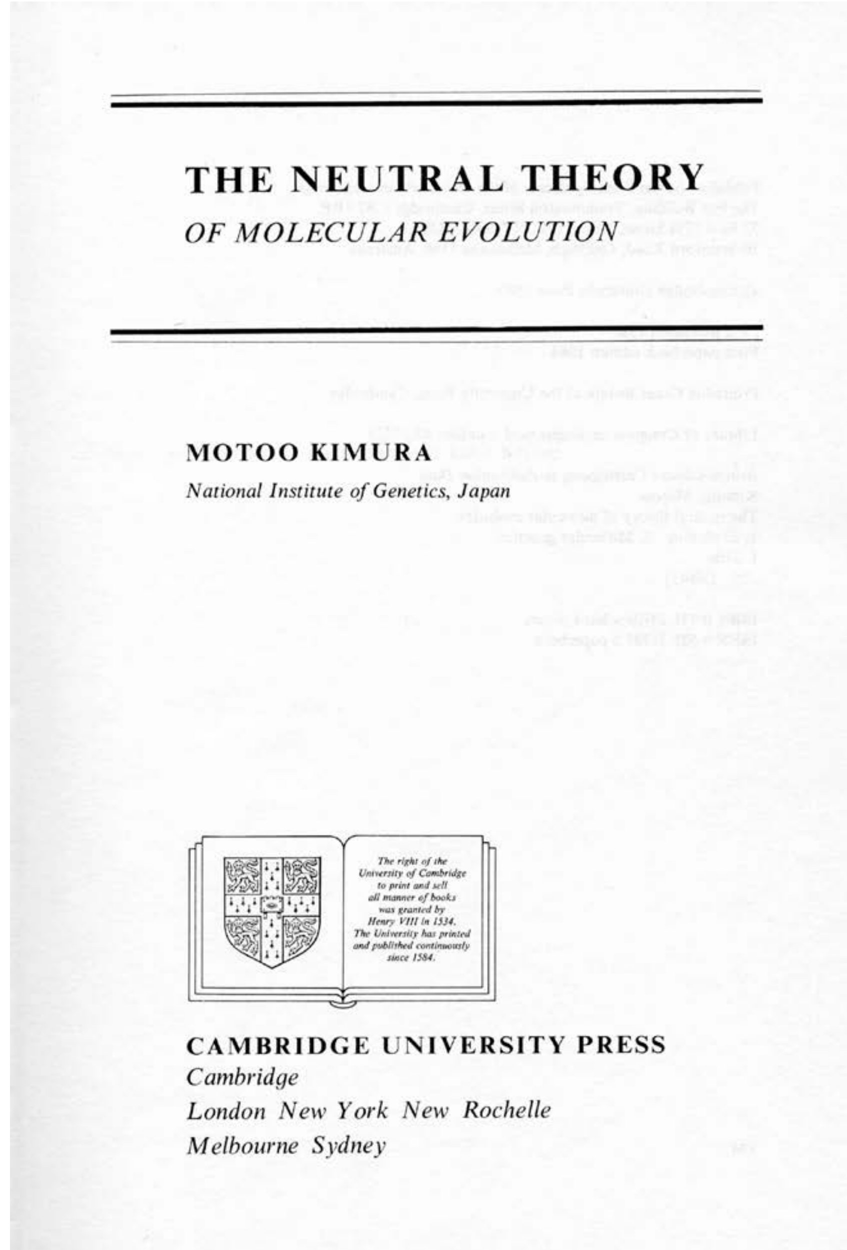
Sewall Wrights fitness landscape as metaphor for Darwinian evolution


Level k
0
1
2
3
4
5
Fitness
H
Optimierung



Rekonstruktion von Phylogenien aus heutigen Sequenzdaten

Motoo Kimura, 1924 - 1994



THE NEUTRAL THEORY

OF MOLECULAR EVOLUTION

MOTOO KIMURA

National Institute of Genetics, Japan

The right of the University of Cambridge to print and sell all manner of books was granted by Henry VIII in 1534. The University has printed and published continuously since 1584.

CAMBRIDGE UNIVERSITY PRESS

Cambridge

London New York New Rochelle

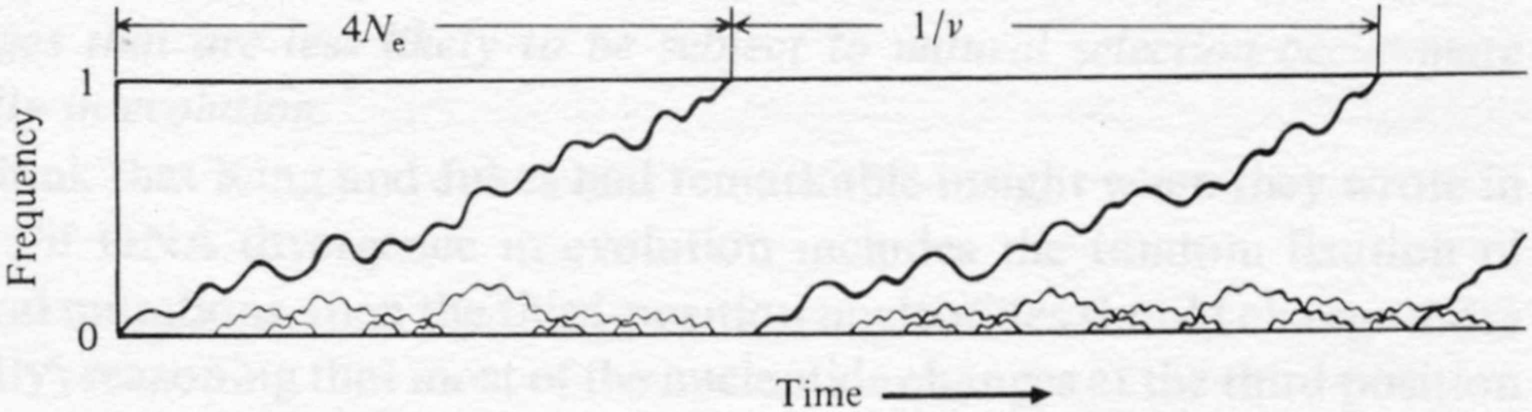
Melbourne Sydney

Motoo Kimuras Populationsgenetik der neutralen Evolution.

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

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

Fig. 3.1. Behavior of mutant genes following their appearance in a finite population. Courses of change in the frequencies of mutants destined to fixation are depicted by thick paths. N_e stands for the effective population size and v is the mutation rate.



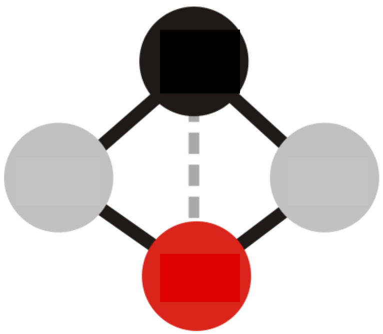
Motoo Kimura

Gilt das Kimura Szenario für häufige Mutationen wie bei Viren?

Muss es immer **eine** fitteste Variante sein?

$d_H = 1$

$$\lim_{p\to 0} x_1(p) = x_2(p) = 0.5$$



$d_H = 2$

$$\lim_{p\to 0} x_1(p) = \alpha/(1+\alpha)$$

$$\lim_{p\to 0} x_2(p) = 1/(1+\alpha)$$

$d_H \geq 3$

$$\lim_{p\to 0} x_1(p) = 1, \lim_{p\to 0} x_2(p) = 0 \quad \text{or}$$

$$\lim_{p\to 0} x_1(p) = 0, \lim_{p\to 0} x_2(p) = 1$$

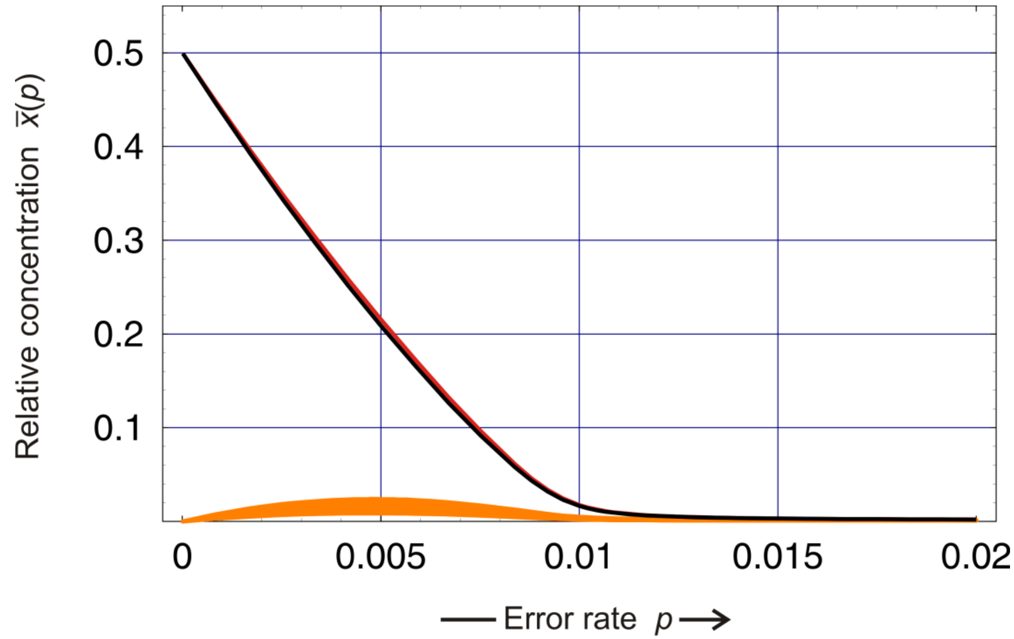
Zufallsselektion im Sinne von Motoo Kimura

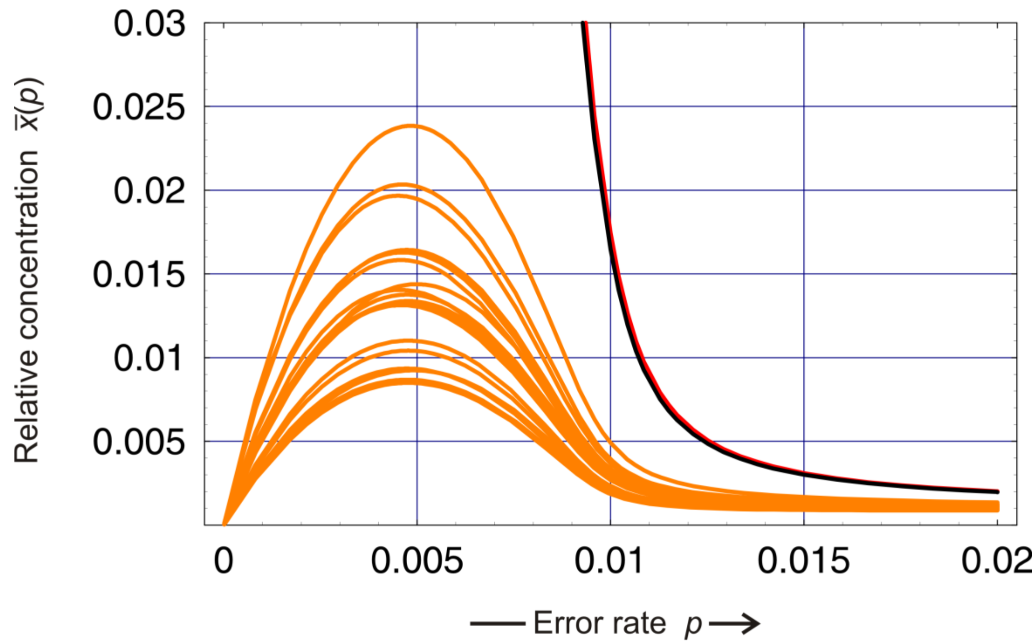
Paare neutraler Sequenzen in Replikationsnetzwerken

P. Schuster, J. Swetina. 1988. Bull. Math. Biol. 50:635-650

Neutral network

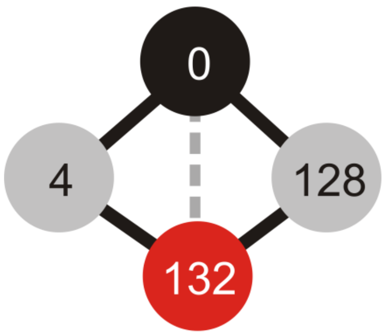
$\lambda = 0.01$, $s = 367$





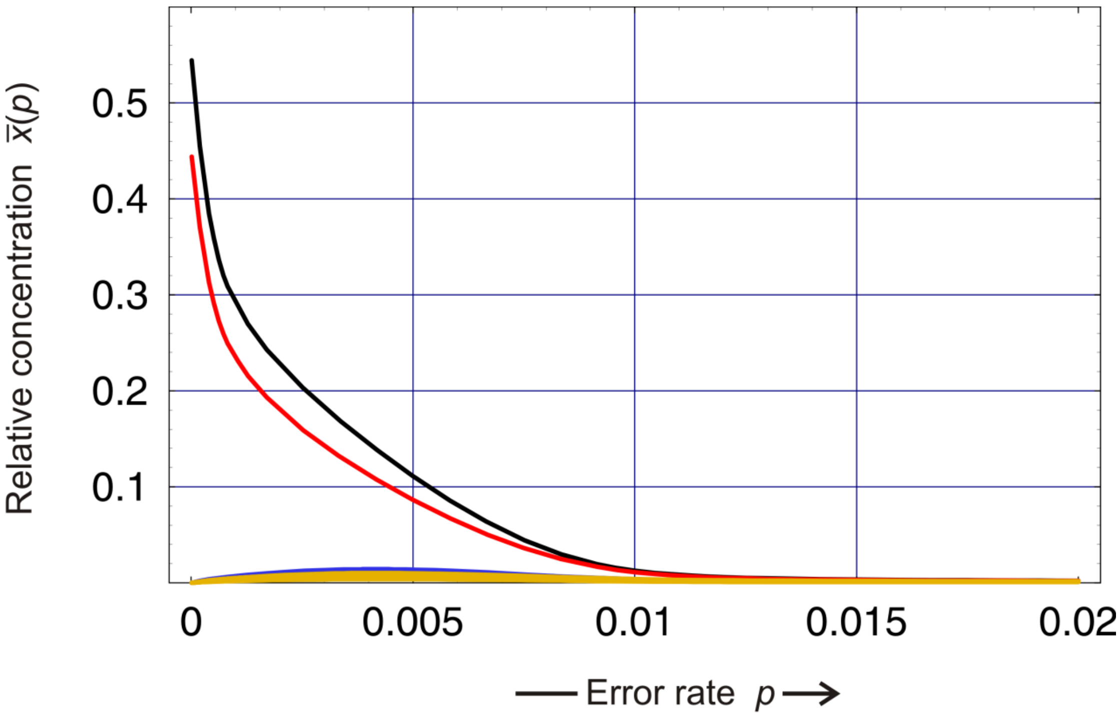
neutral network: individual sequences

$n = 10$, $\sigma = 1.1$, $d = 1.0$



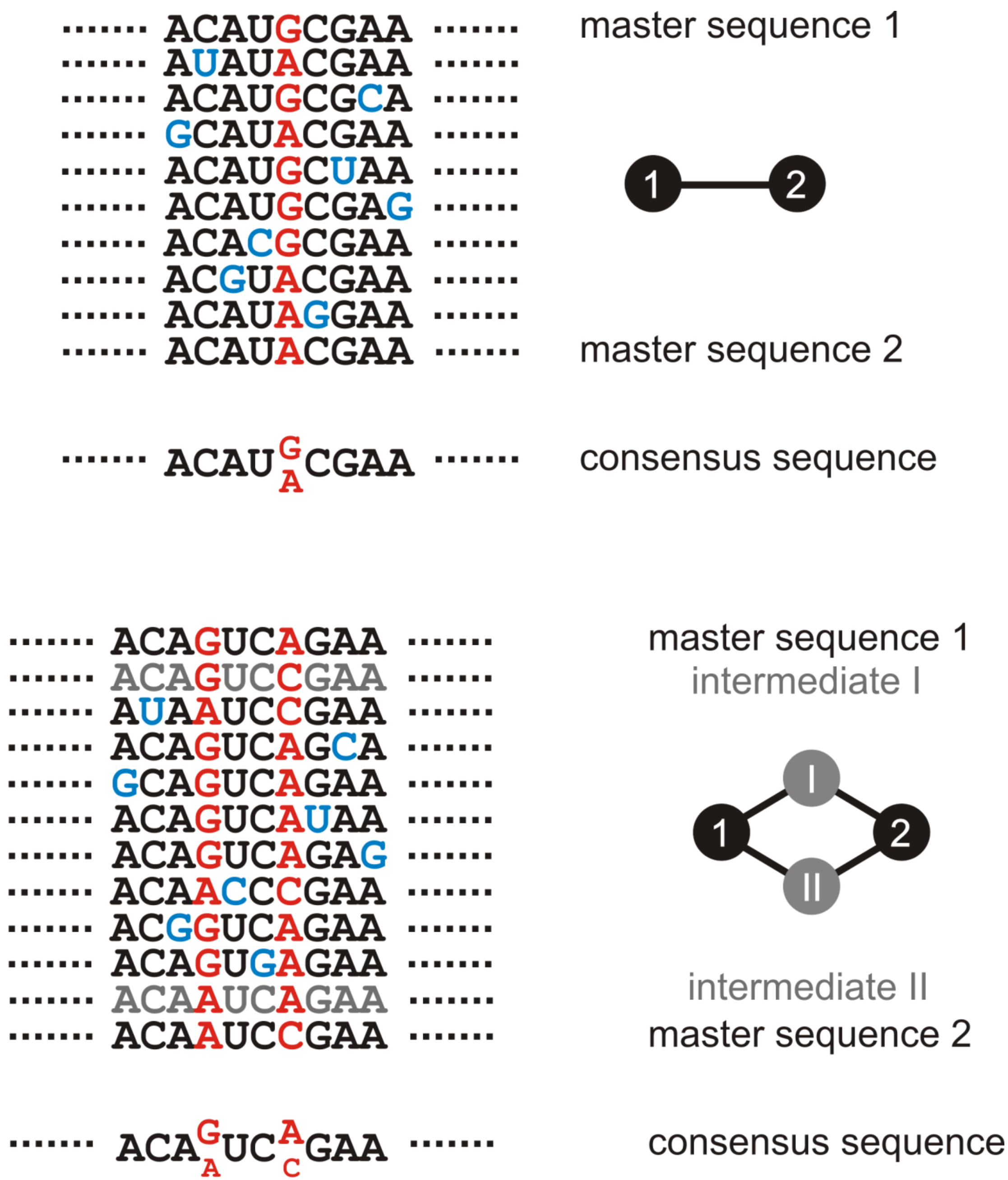
Neutral network

$\lambda = 0.01, \;\; s = 877$



neutral network: individual sequences

$n = 10, \sigma = 1.1, d = 1.0$



consensus sequences of a quasispecies of two strongly coupled sequences of Hamming distance $d_H(X_{i,},X_j) = 1$ and 2.

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Evolution im Licht der gegenwärtigen Molekulargenetik

1. Die Vorstellungen der konventionellen Genetik müssen hinsichtlich der Genregulation entscheidend erweitert werden.

2. Ein Gen wird im Vielzellerorganismus gewebsspezifisch in mehrere verschiedene Proteine übersetzt.

3. Umwelteinflüsse geben Anlass zu Veränderungen des Genoms, welche einige Generationen lang vererbbar sind.

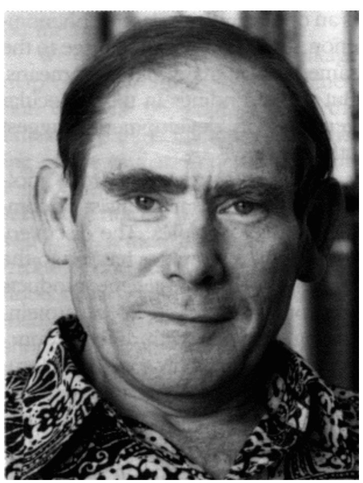
4. Komplexität, Robustheit und Plastizität der Organismen wird erst im Zusammenspiel von Genetik und Epigenetik verstehbar.

Vorteile der molekularen Betrachtungsweise

1. Komplexe Mechanismen der Vermehrung können ohne grundsätzliche Probleme berücksichtigt werden.

2. Genetische Regulation auf der Basis von DNA oder RNA ist nichts anderes als chemische Kinetik!

3. Eine adäquate Behandlung epigenetischer Phänomene erfordert **nur**(?) die Einbeziehung mehrerer Generationen und der Umwelt.

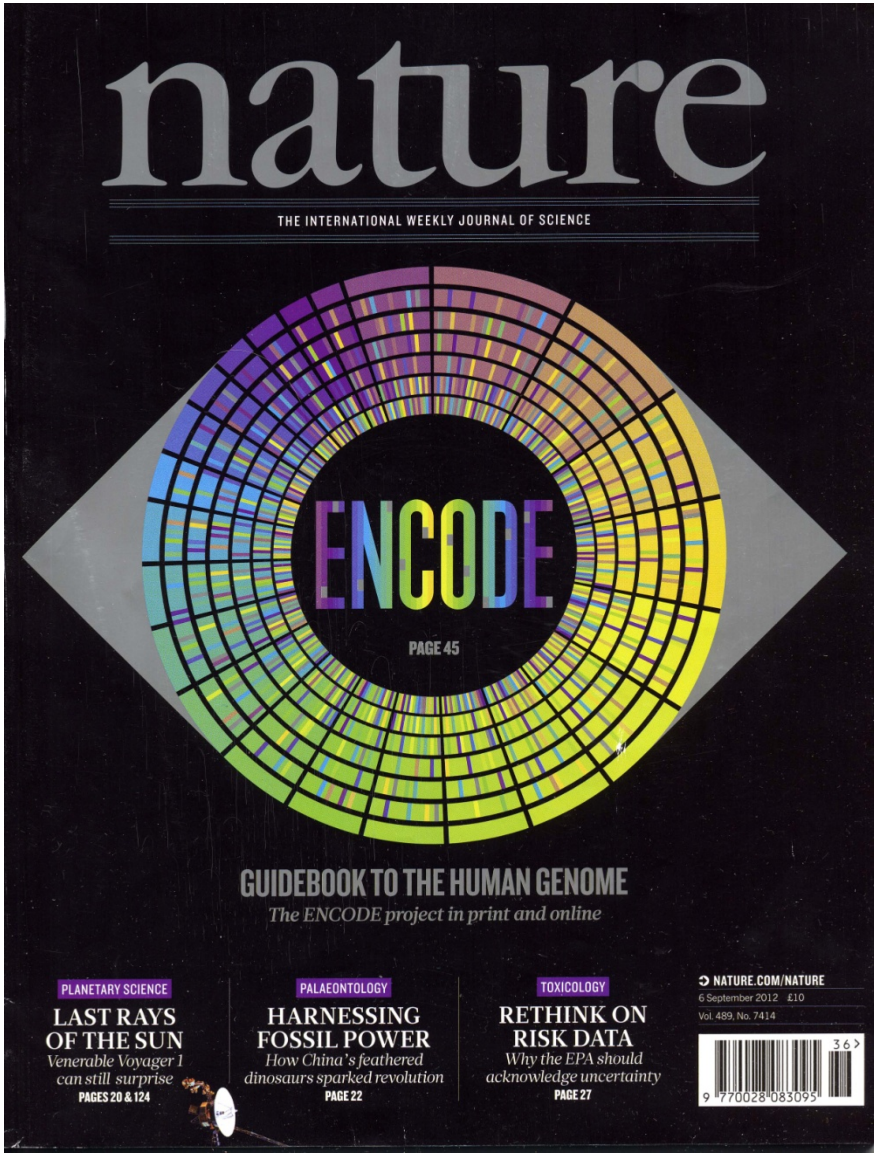


Sydney Brenner, 1927 -

What else is epigenetics than a funny form of enzymology ?

Each protein, after all, comes from some piece of DNA.

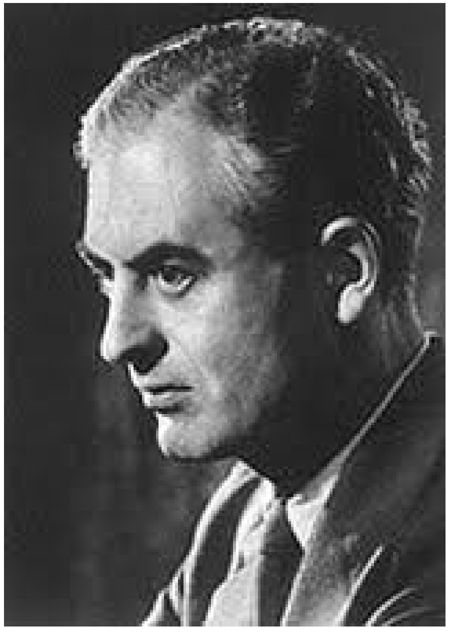
2007



2012

ENCyclopedia **O**f **D**NA **E**lements

„… no new principle will declare itself
from below a heap of facts.“

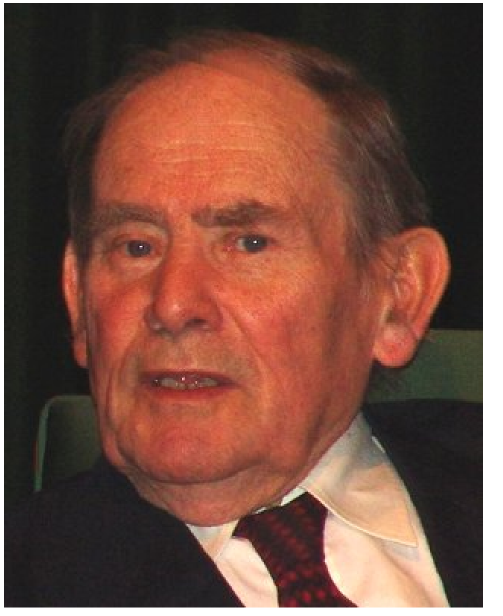


Peter Medawar,
1915 – 1987

T. Fagerström, P. Jagers, P. Schuster, and E. Szathmary.
Biologists put on mathematical glasses.
Science, *274:2039–2040, 1996.*

Theodosius Dobzhansky: Scientists often have a naive faith that if only they could discover enough facts about a problem, these facts would somehow arrange themselves in a compelling and true solution.

„I was taught in the pregenomic era to be a hunter. I learnt how to identify the wild beasts and how to got out, hunt them down and kill then. We are now, however, being urged to be gatherers, to collect everything lying about and put it into storehouses. Someday, it is assumed someone will come and sort through the storhouses, discard the junk and keep the rare finds. The only difficulty is how to recognize them."



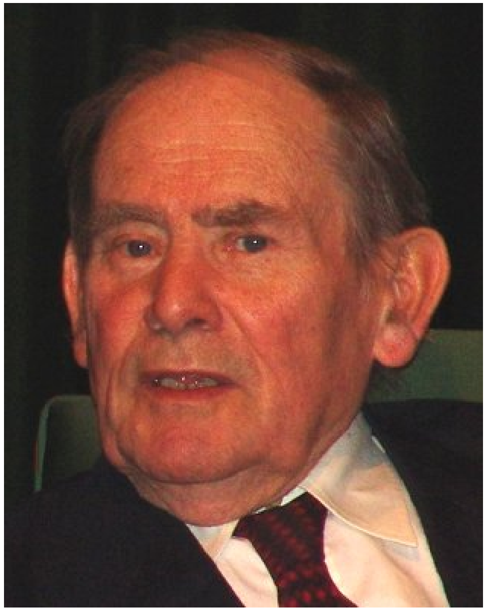
Sydney Brenner, 1927 –

Sydney Brenner über ‚Big-Data'

Sydney Brenner. 2002. Hunters and gatherers. The Scientist **16**(4): 14.

1. Evolutionstheorie und Mathematik
2. Molekularbiologie: ‚Alles Leben ist Chemie'
3. Was zeichnet die Biologie heute aus?
4. Optimierung und historische Kontingenz
5. Die neue Biologie: Epigenetik und ‚Big-Data'
6. **Perspektiven einer theoretischen Biologie**

„Unfortunately, theoretical biology has a bad name because of its past. Physicists were concerned with questions such as whether biological systems are compatible with the second law of thermodynamics and whether they could be explained by quantum mechanics. ……… Even though alternatives have been suggested, such as computational biology, biological systems theory and integrative biology, I have decided to forget and forgive the past and call it theoretical biology."



Sydney Brenner, 1927 –

Sydney Brenner über Theoretische Biologie

Sydney Brenner. 1999. Theoretical biology in the third millenium. Phil.Trans.Roy.Soc.London B **354**:1963-1965.

Danke für die Aufmerksamkeit!

Web-Page für weitere Informationen:

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