Von der Chemie zur Biologie

Ein paar Gedanken zum Ursprung des Lebens

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Gesundheitstage 2014

Kötschach-Mauten, 07.11.2014

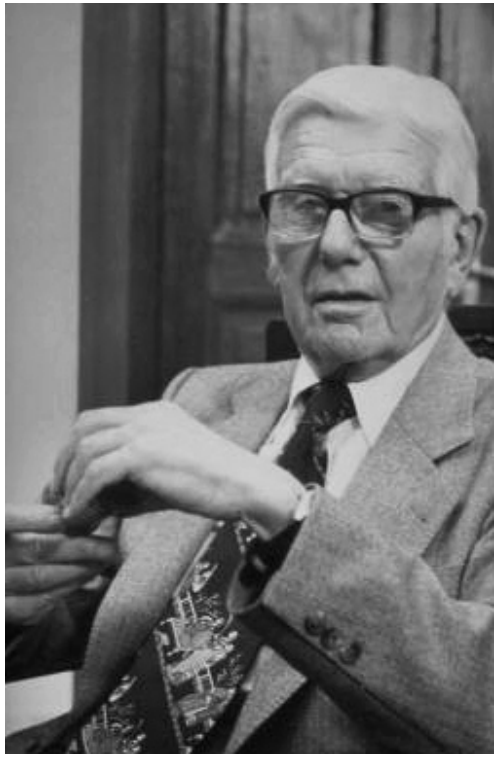
Web-Page für weitere Informationen:

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

Biologie und Chemie

Alles Leben ist Chemie.

Eine zehnteilige Fernsehreihe des Österreichischen Fernsehens im Jahre 1978 von Hermann Mark und Hellmut Andics.

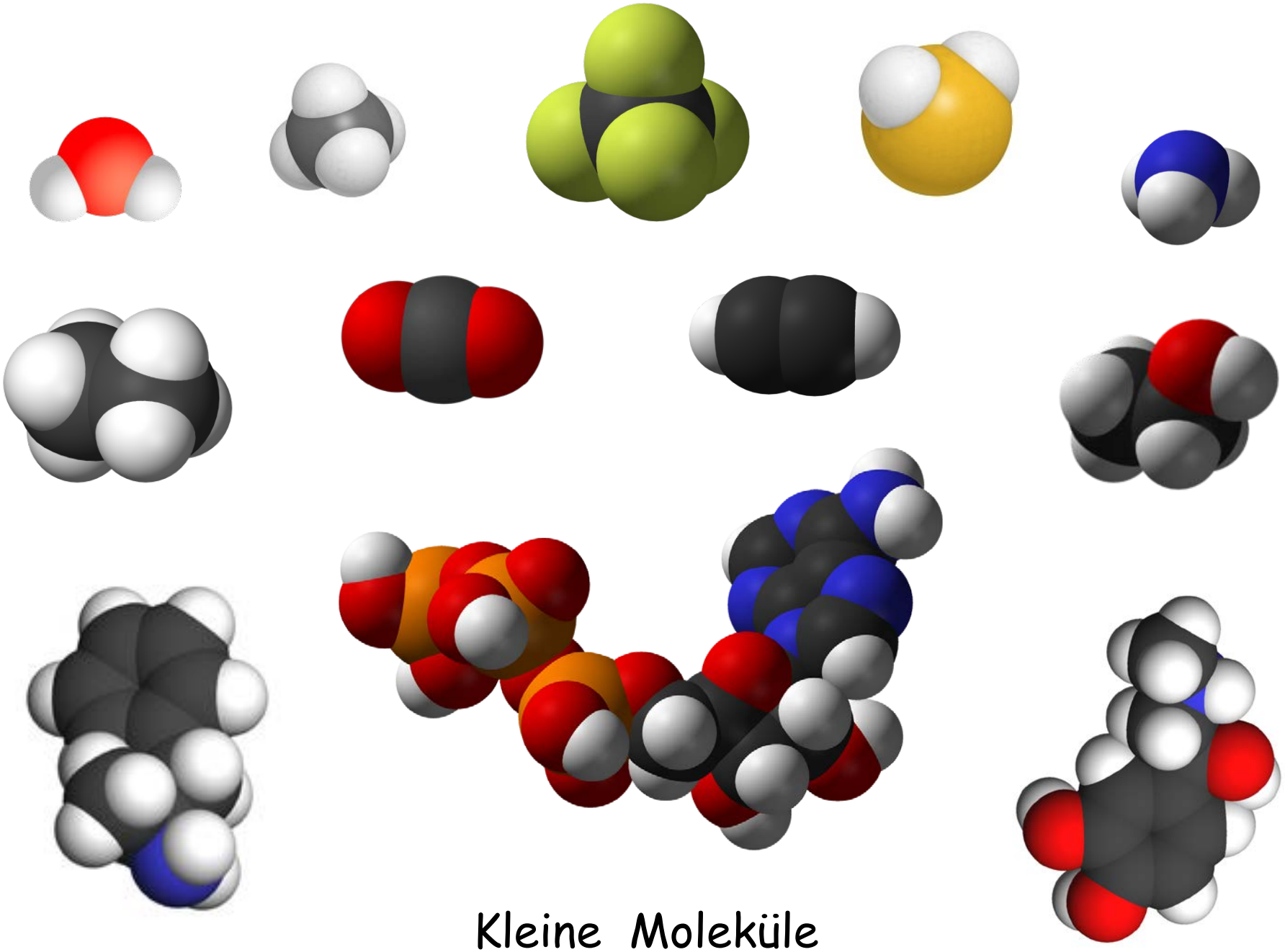


Hermann F. Mark, 1895 - 1992

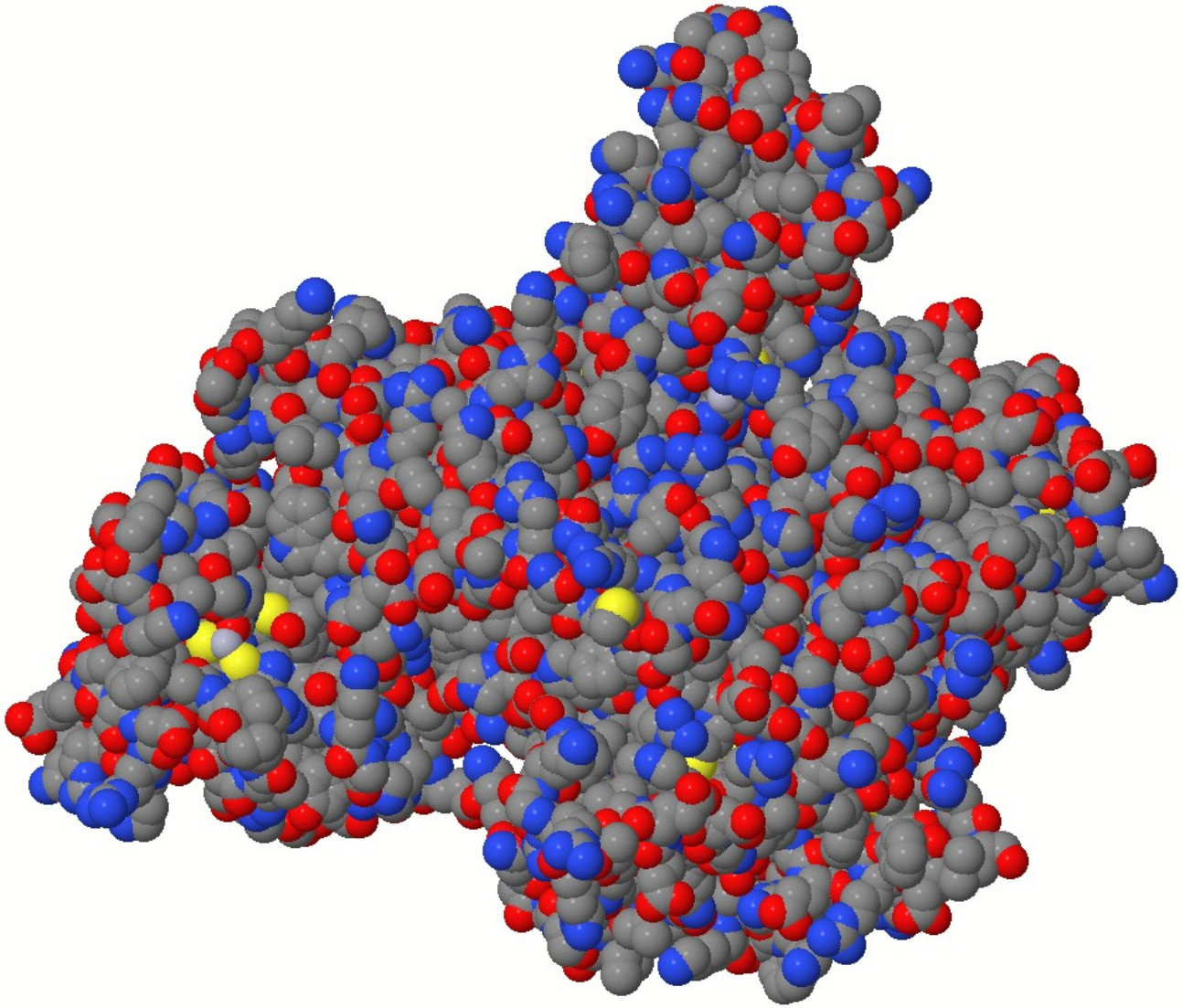
Alles Leben ist Chemie. Der Begriff des „Lebens" fokussiert auf das individuelle Tun eines Lebewesens und das Geschehen, in das es involviert ist.

Der Begriff „Chemie" verweist auf die Art und Weise der Funktionen und Strukturen, die Leben ausmachen.

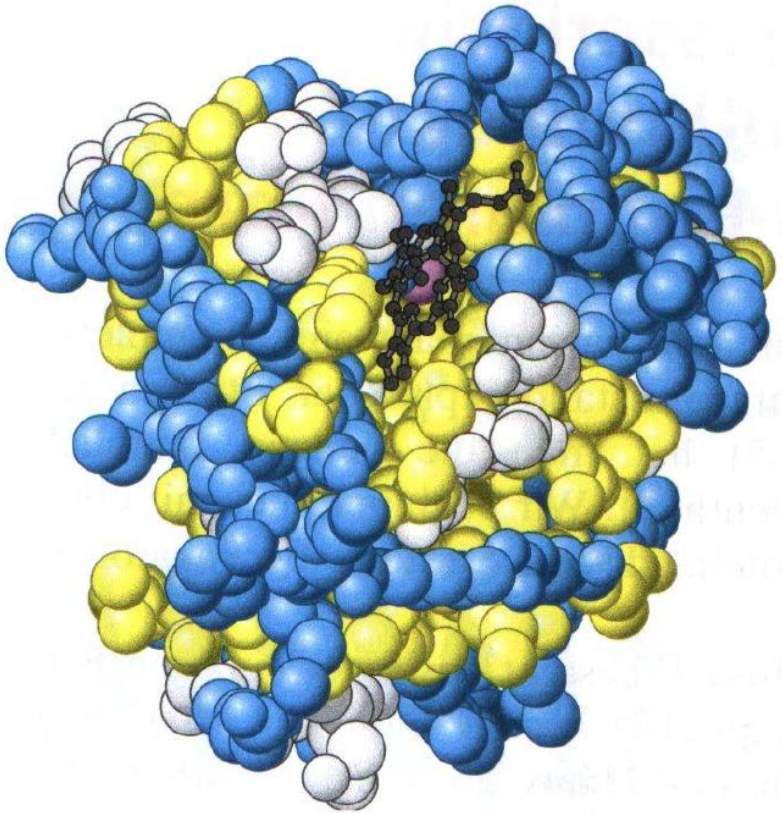
Wiener Vorlesungen, 18.10.2011 im Internationalen Jahr der Chemie

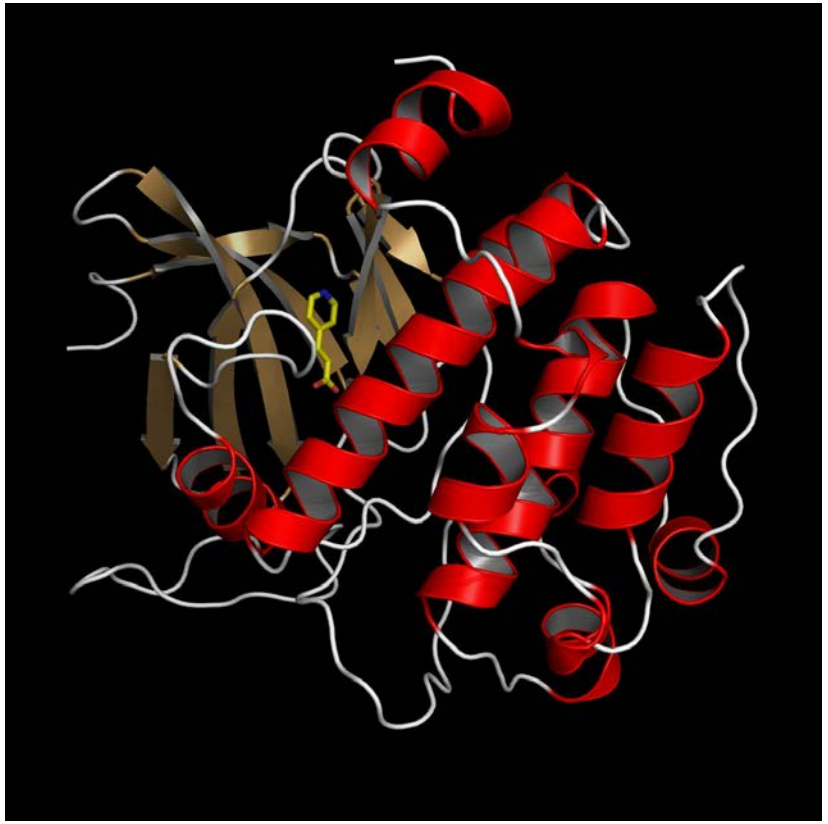


Kleine Moleküle

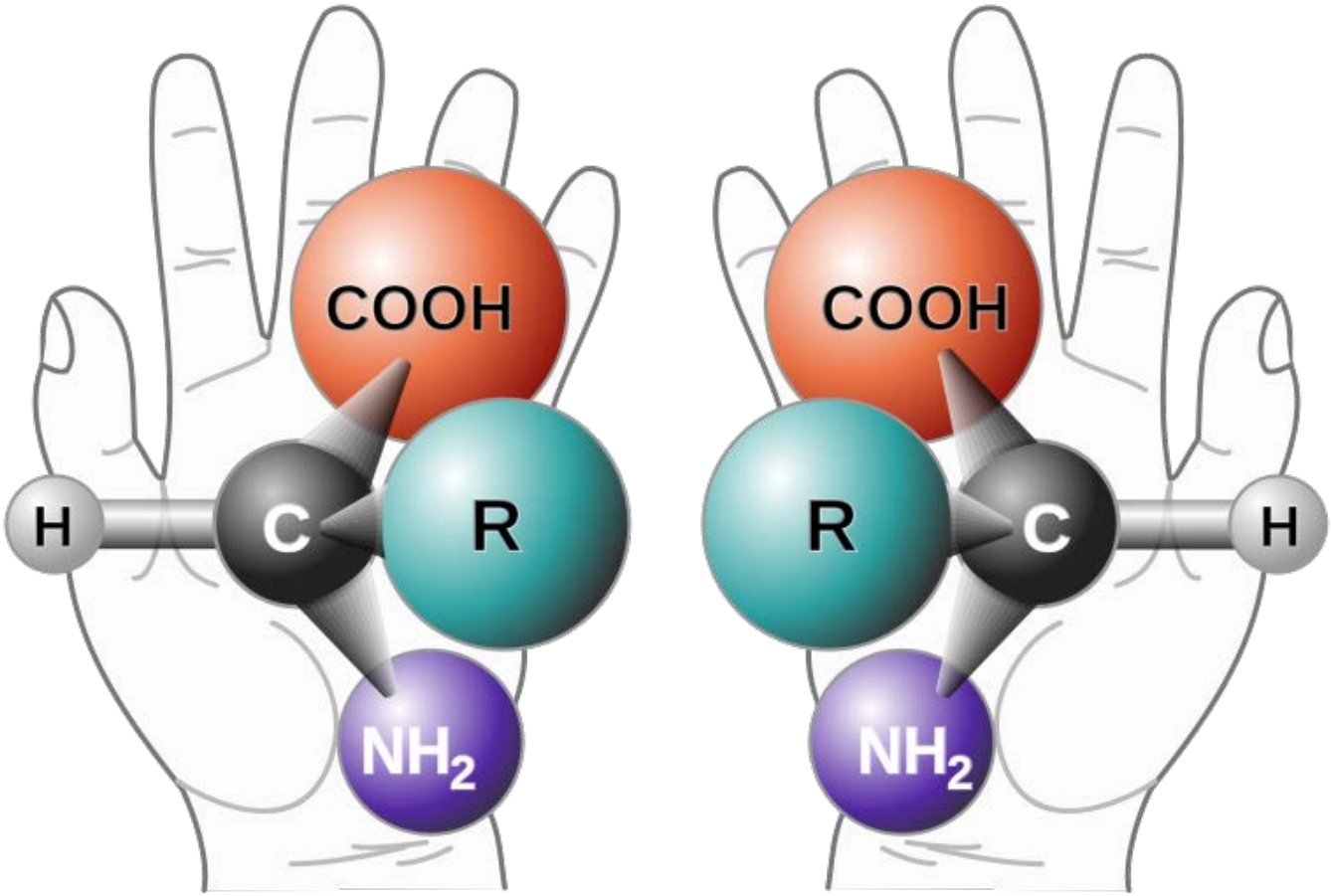


Transkriptionsenzym: DNA → RNA



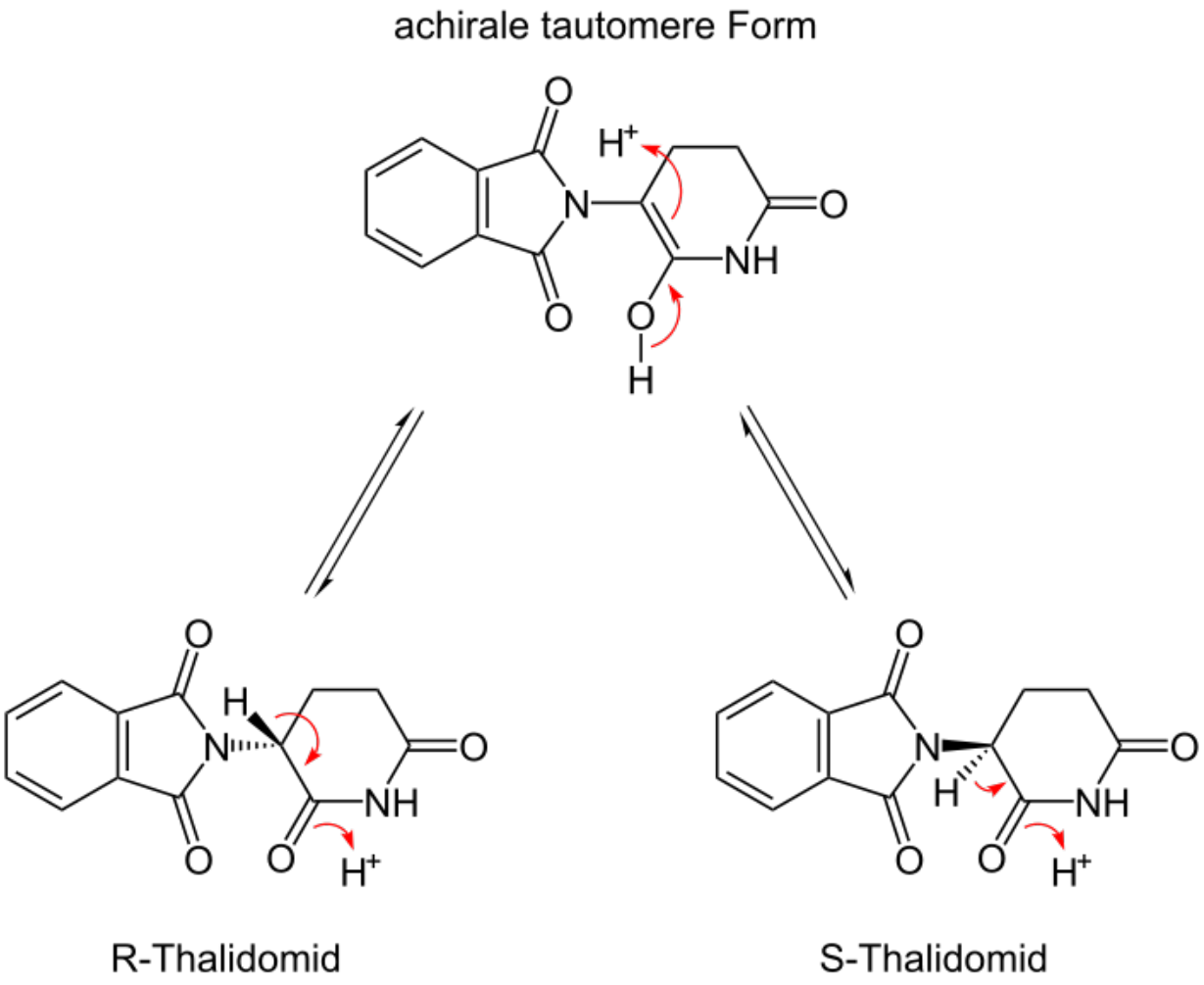


Proteinstrukturen



L-Aminosäure **D-Aminosäure**

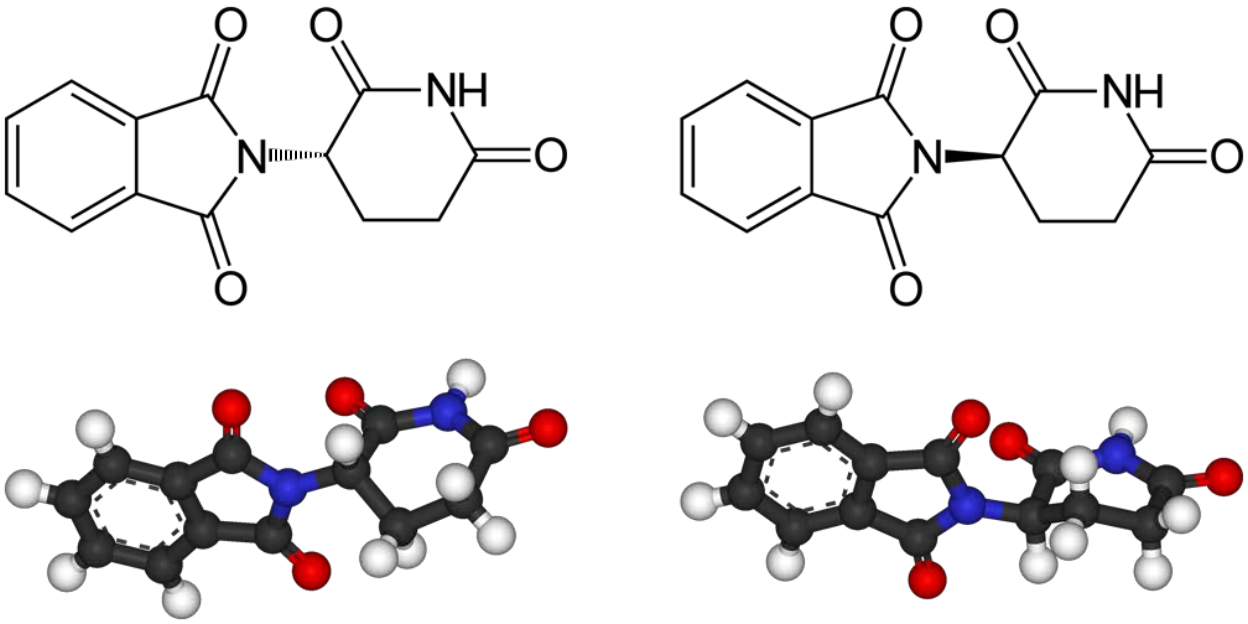
Chiralität der Biomoleküle



Sedativum

teratogene Wirkung

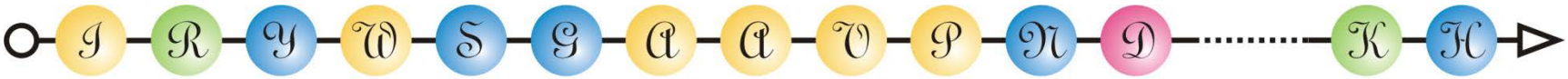
Thalidomid (Contergan)



Sedativum

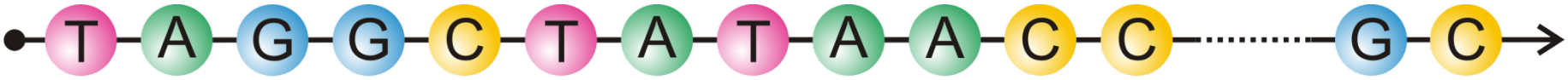
teratogene Wirkung

Thalidomid (Contergan)



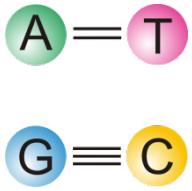
A ≡ **ala**nine	G ≡ **gly**cine	M ≡ **met**hionine	S ≡ **ser**ine
C ≡ **cys**teine	H ≡ **his**tidine	N ≡ **asparagine**	T ≡ **thr**eonine
D ≡ **asp**artic acid	I ≡ **iso**l**e**ucine	P ≡ **pro**line	V ≡ **val**ine
E ≡ **glu**tamic acid	K ≡ **lys**ine	Q ≡ **gl**utamin**e**	W ≡ **tryp**tophane
F ≡ **phe**nyl alanine	L ≡ **leu**cine	R ≡ **arg**inine	Y ≡ **tyr**osine

Protein

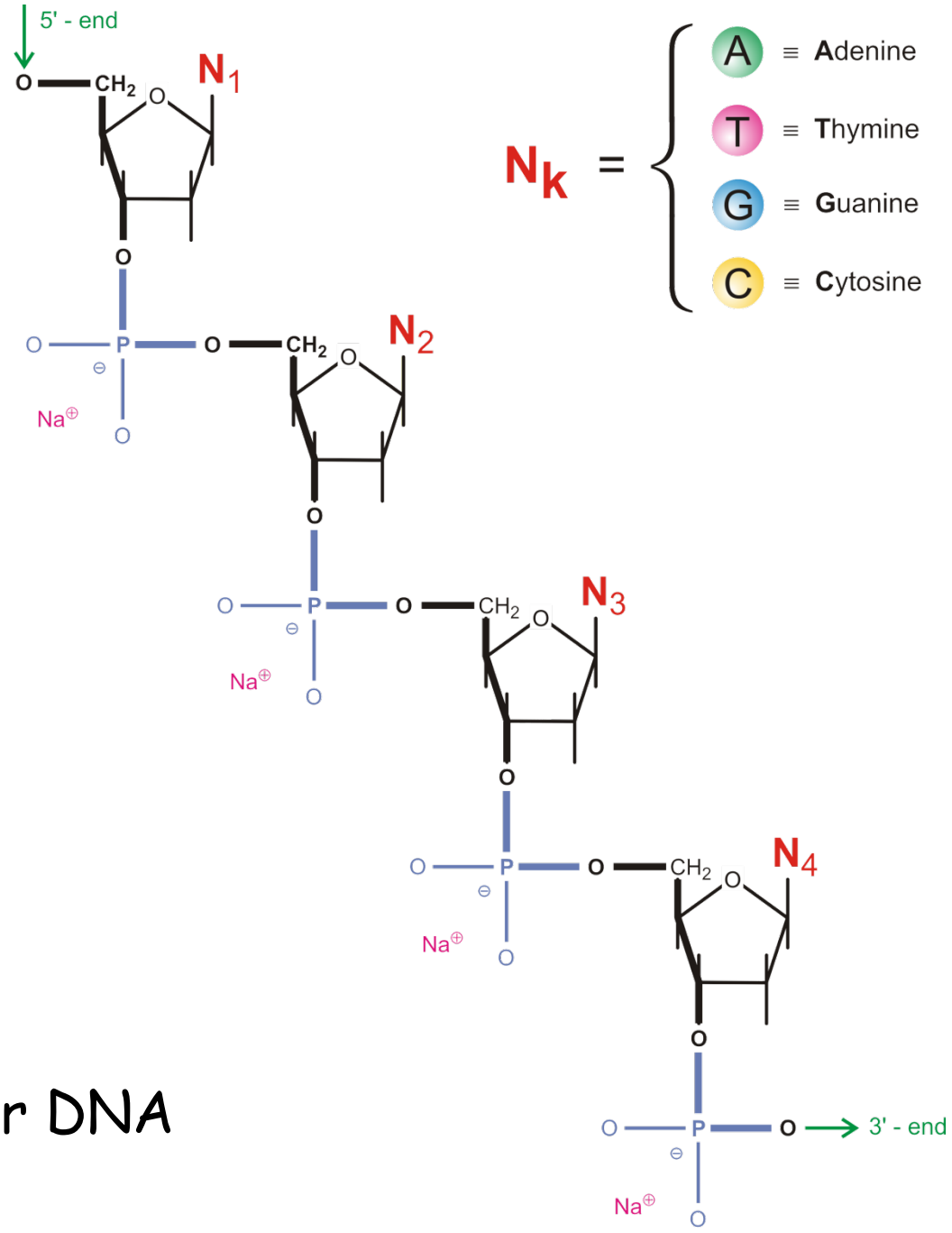


A ≡ **A**denin T ≡ **T**hymin G ≡ **G**uanin C ≡ **C**ytosin

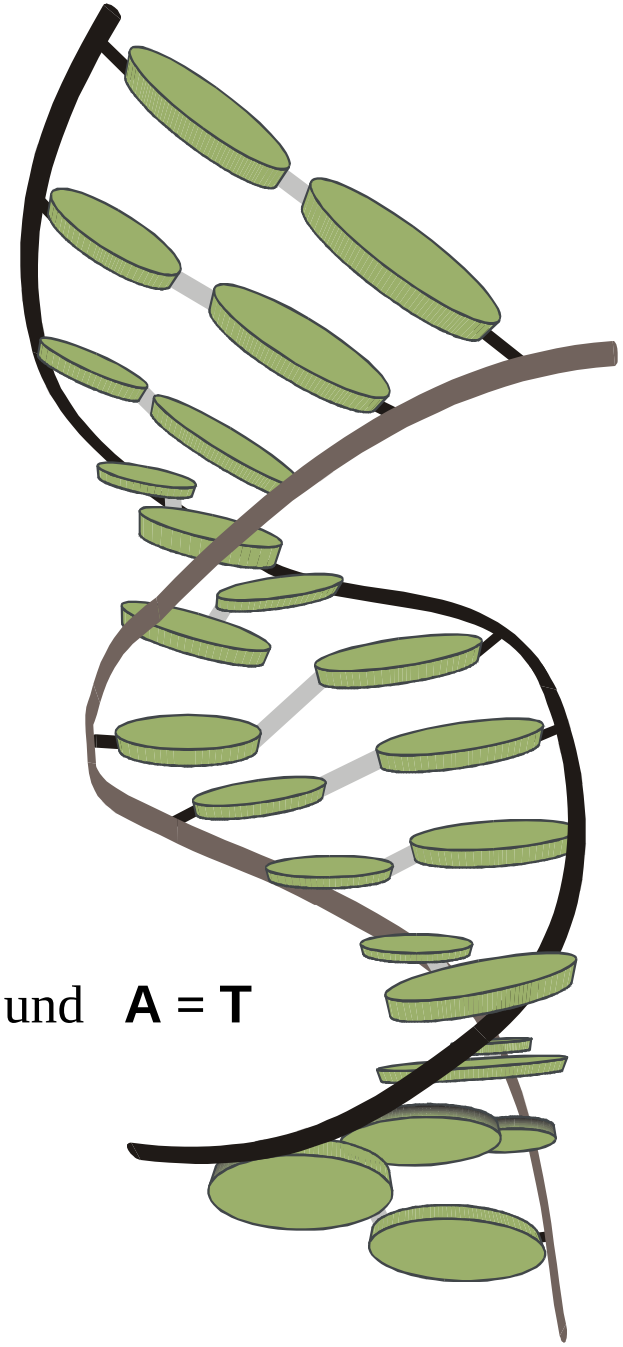
Desoxyribonucleinsäure DNA



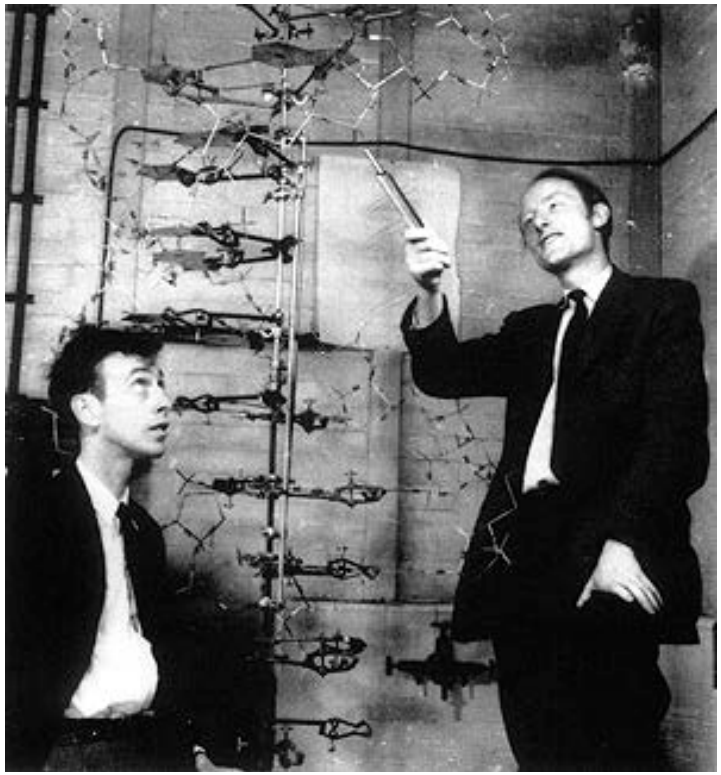
Nucleotidpaare



Chemische Formel der DNA

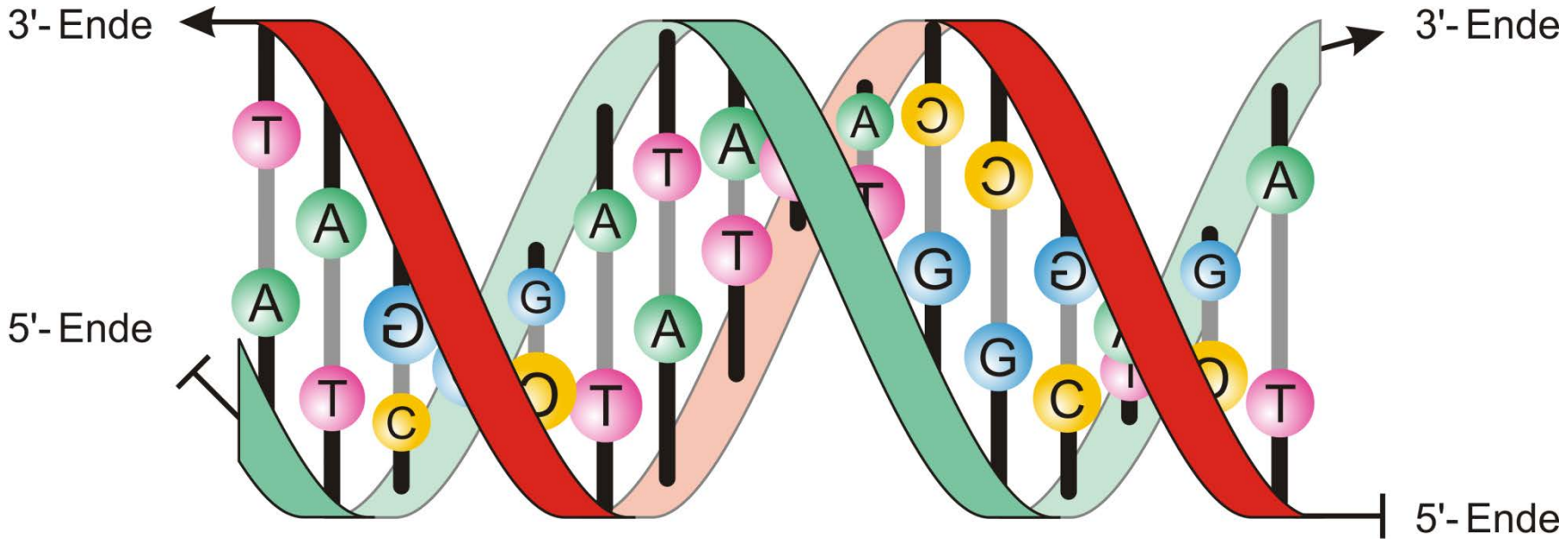


G ≡ C und **A = T**

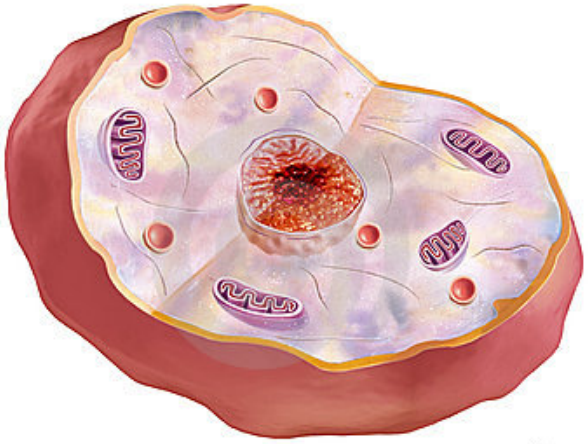


James D. Watson, 1928- , and Francis Crick, 1916-2004,
Nobel Preis 1962

Die dreidimensionale Struktur eines kleinen Stückes der B-DNA



Die B-Form der DNA-Doppelhelix



Zelldurchmesser

0,01 mm

DNA-Länge

1 m

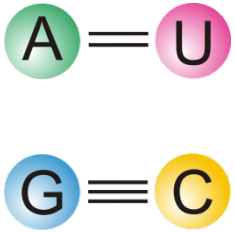
Vergrößerung 1 : 100 000

1 m

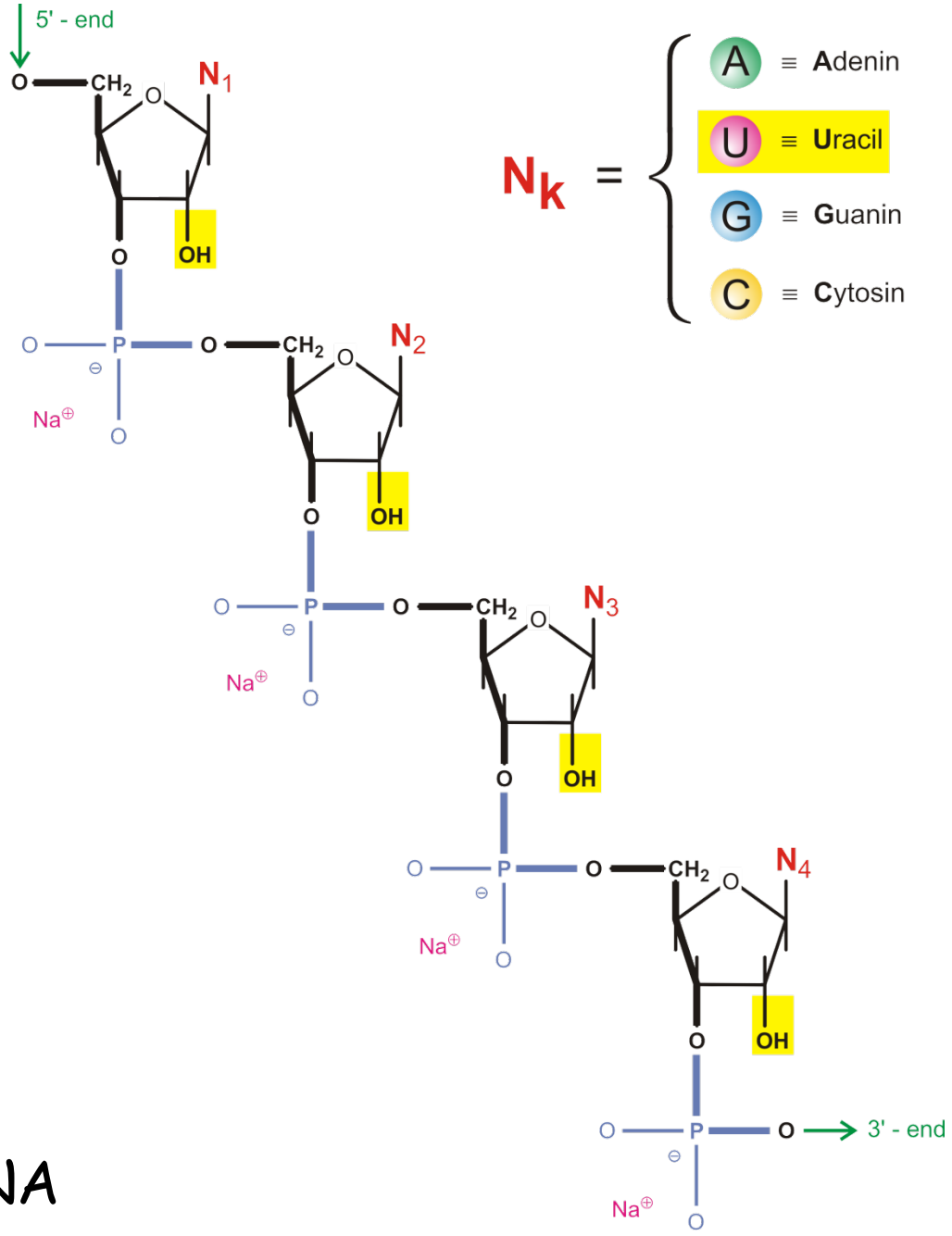
100 km

die menschliche DNA ist 3 Milliarden Basenpaare lang

Größenverhältnisse



Nucleotidpaare



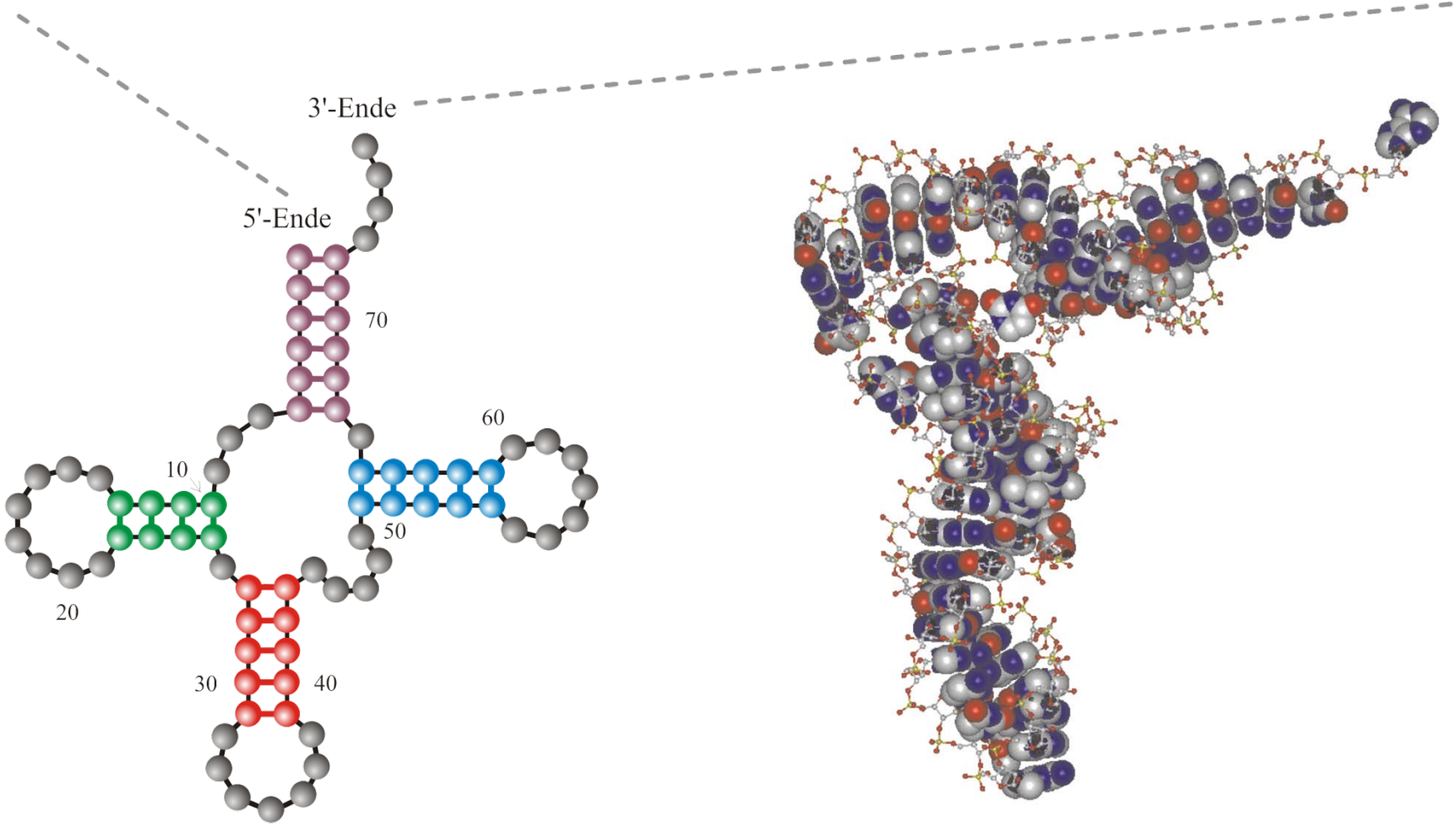
Ribonucleinsäure RNA

Sequenz

5'-Ende

3'-Ende

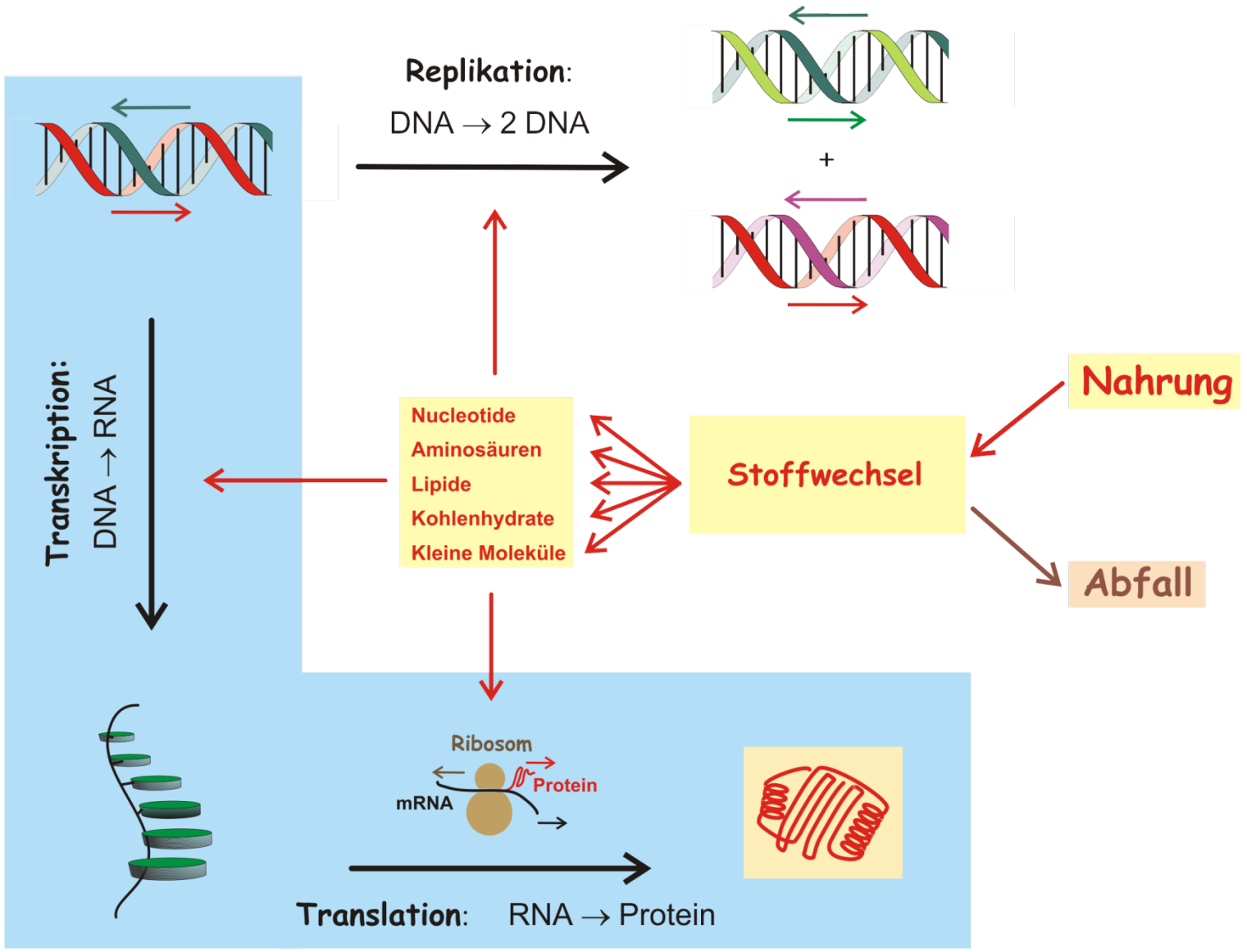
GCGGAUUUAGCUCAGDDGGGAGAGCMCCAGACUGAAYAUCUGGAGMUCCUGUGTPCGAUCCACAGAAUUCGCACCA



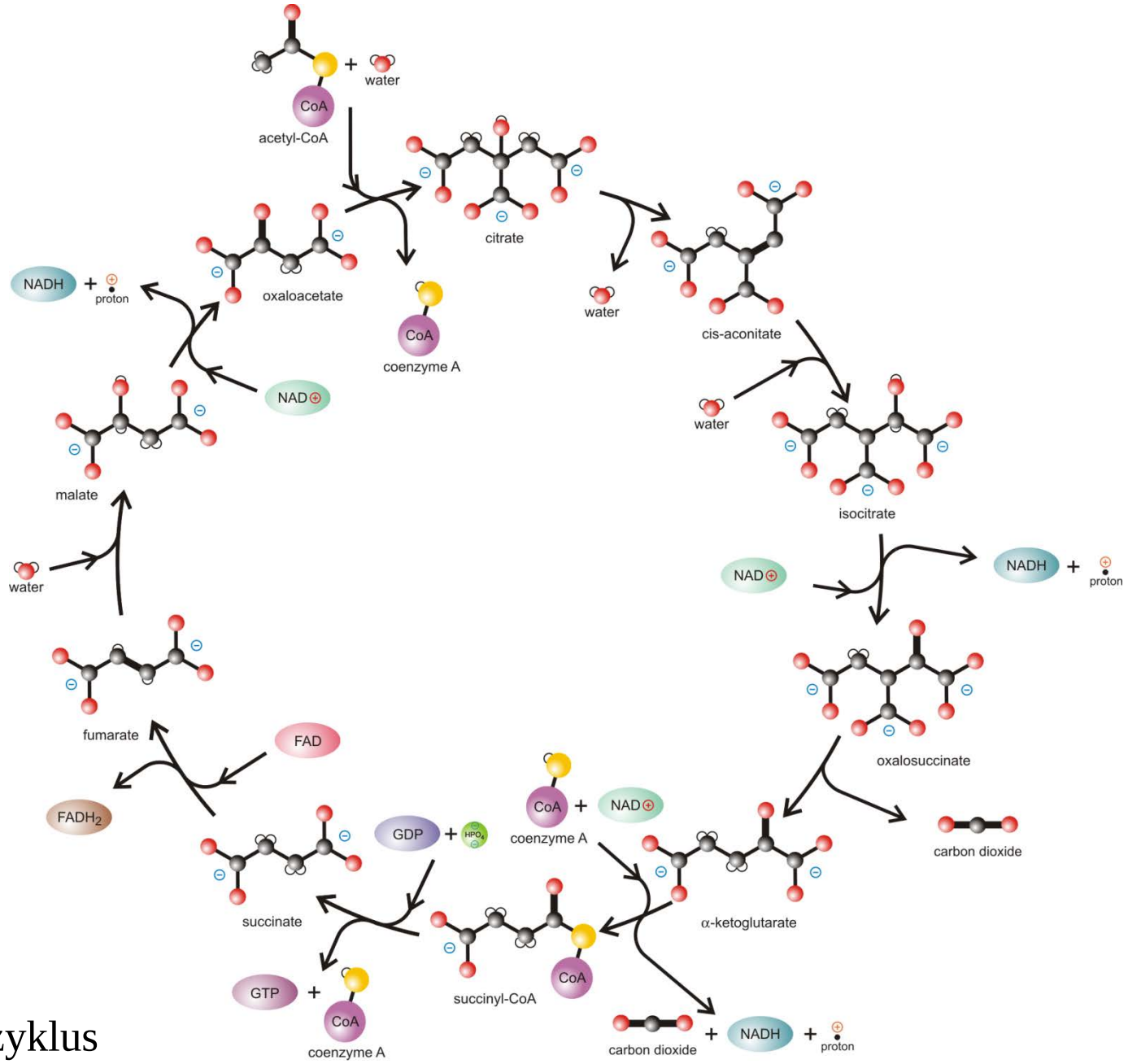
Sekundärstruktur

räumliche Struktur

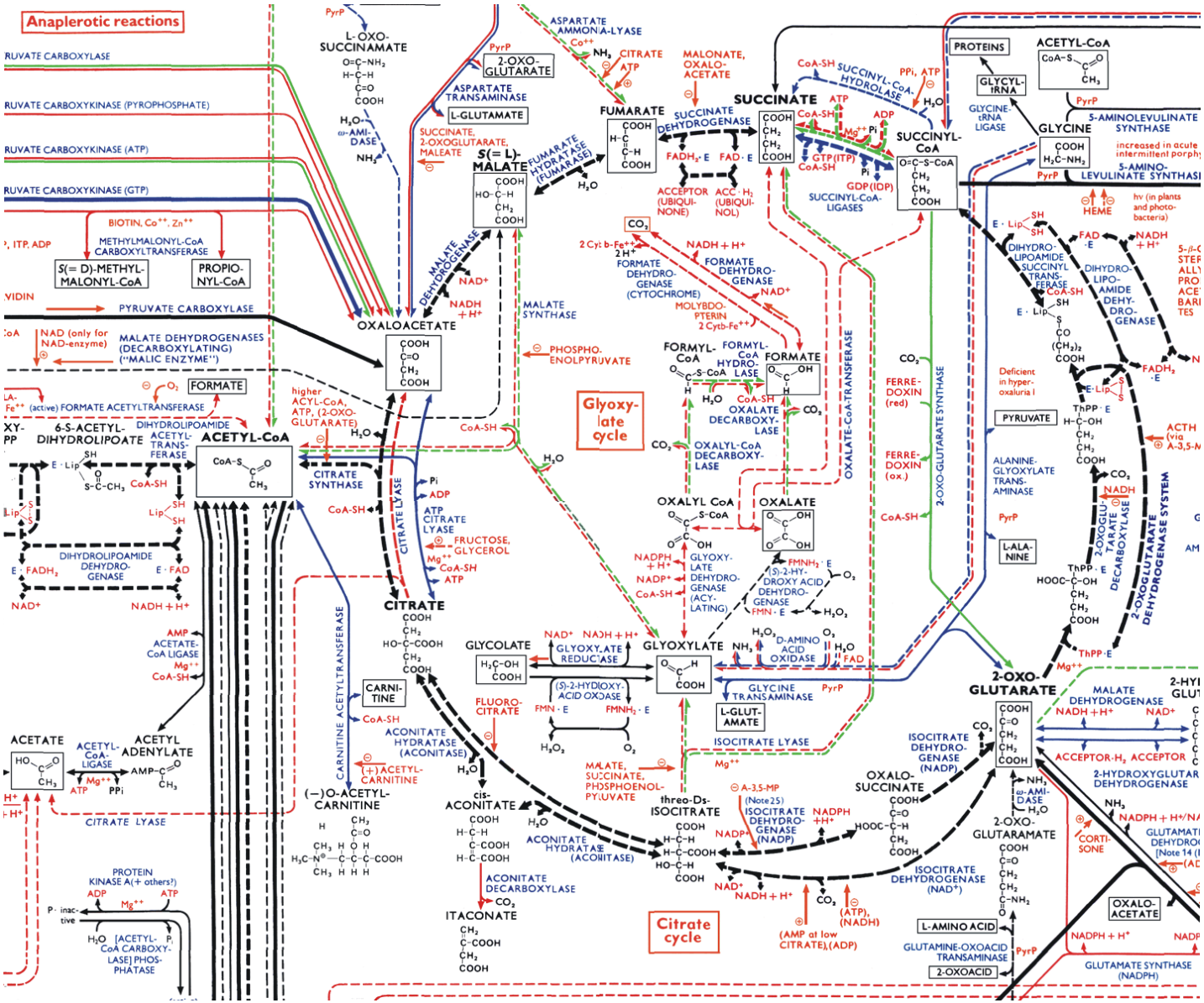
Ribonucleinsäure RNA

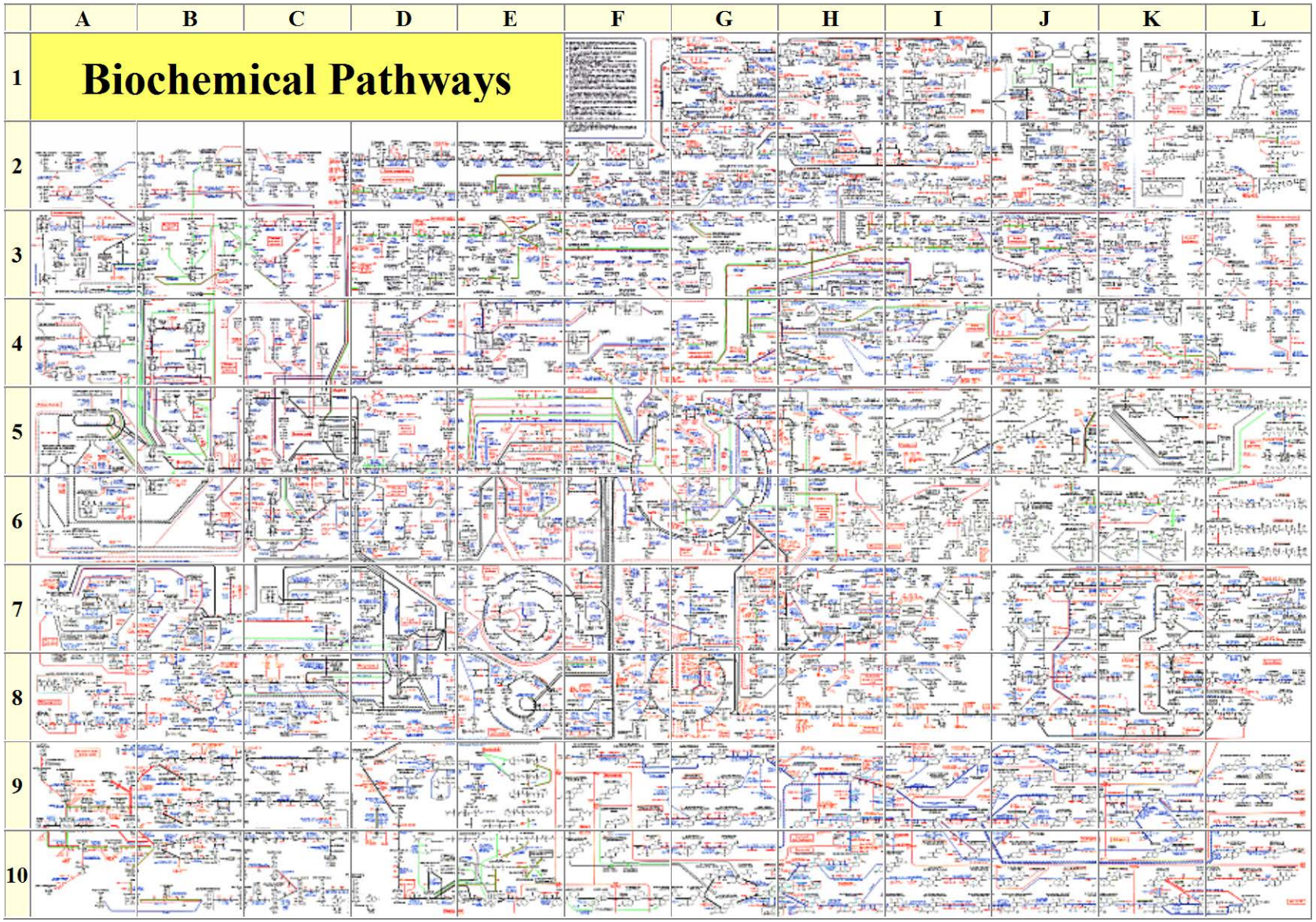

Replikation:
DNA → 2 DNA
+
Transkription:
DNA → RNA
Nucleotide
Aminosäuren
Lipide
Kohlenhydrate
Kleine Moleküle
Stoffwechsel
Nahrung
Abfall
Ribosom
Protein
mRNA
Translation: RNA → Protein

Funktionelle Komplexität



Der Zitronensäurezyklus


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



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.

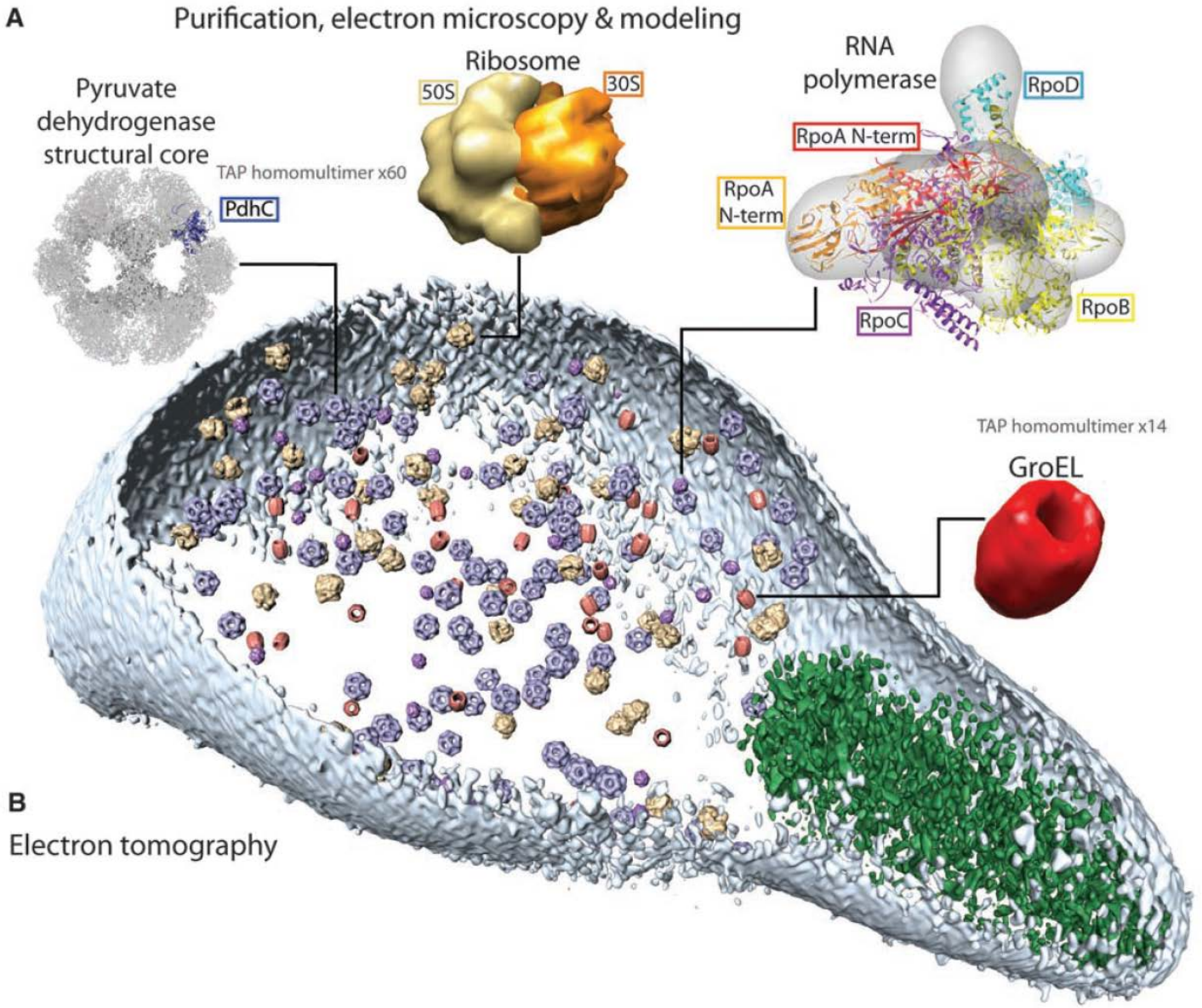


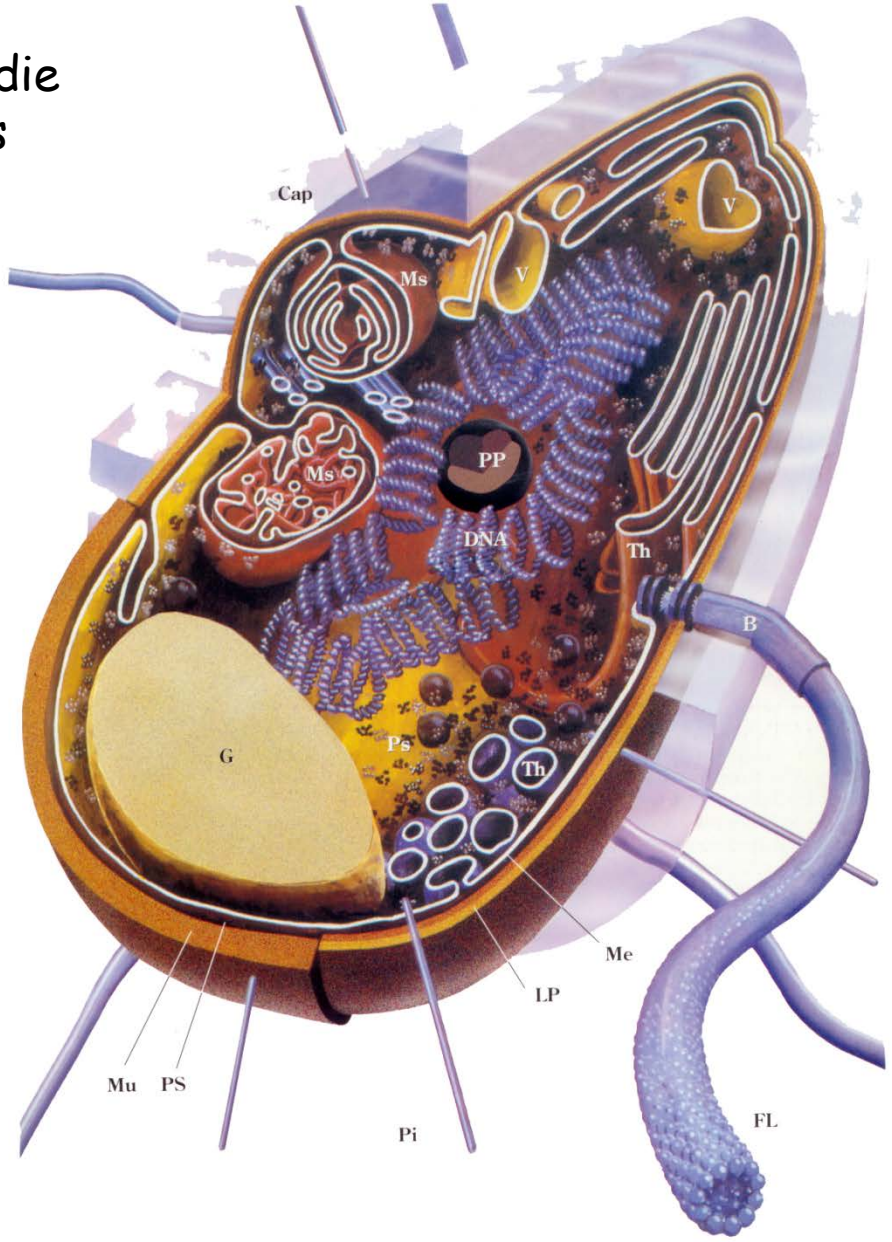
Fig. 4. From proteomics to the cell. By a combination of pattern recognition and classification algorithms, the following TAP-identified complexes from *M. pneumoniae*, matching to existing electron microscopy and x-ray and tomogram structures (**A**), were placed in a whole-cell tomogram (**B**): the 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:

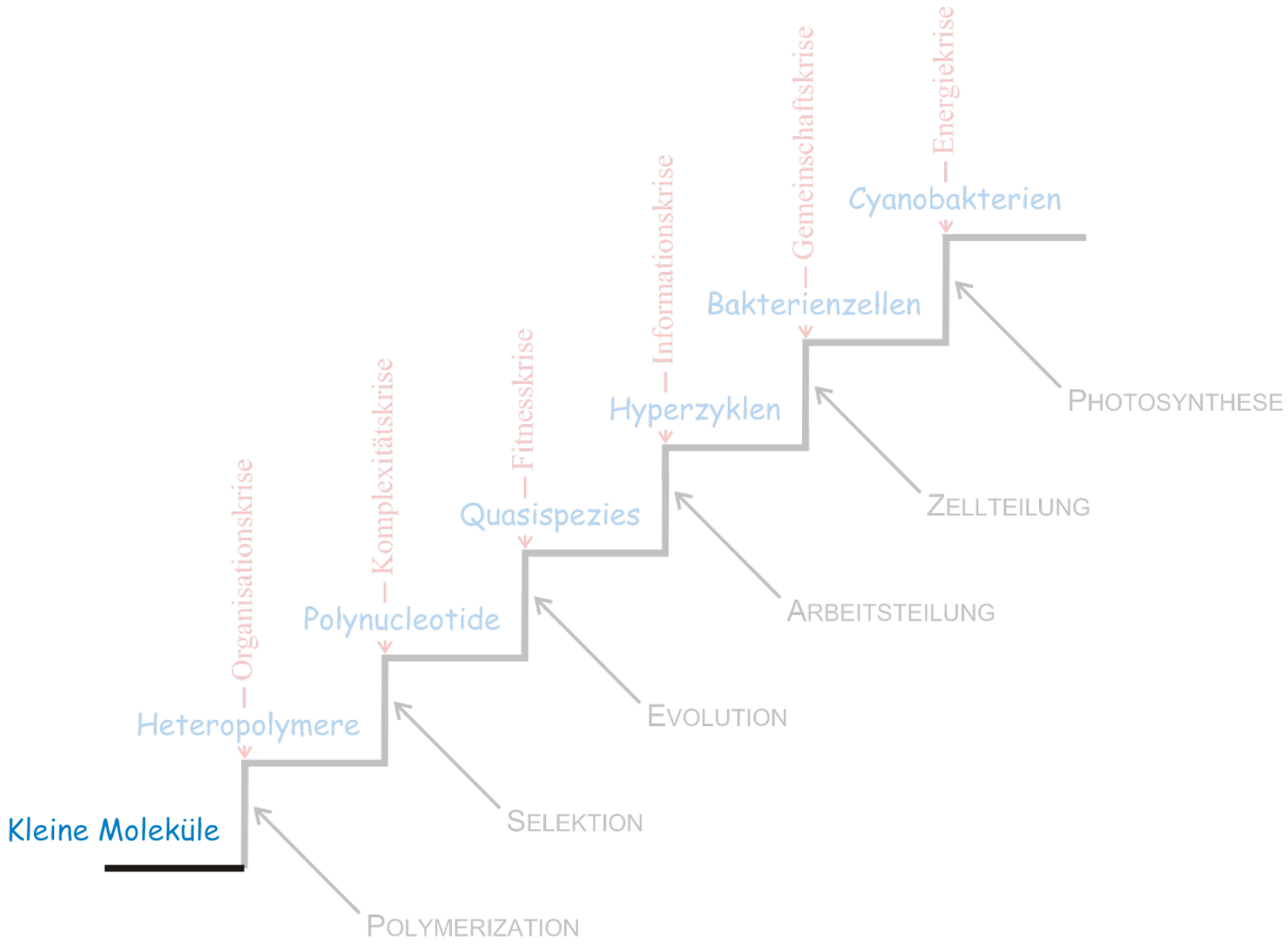
4 Millionen Nukleotide

4460 Gene



Die räumliche Struktur des Bakteriums *Escherichia coli*

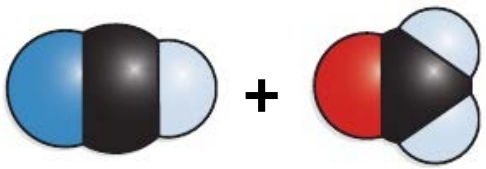
Stufen zum Leben


Kleine Moleküle
Heteropolymere
Polynucleotide
Quasispezies
Hyperzyklen
Bakterienzellen
Cyanobakterien
Organisationskrise
Komplexitätskrise
Fitnesskrise
Informationskrise
Gemeinschaftskrise
Energiekrise
POLYMERIZATION
SELEKTION
EVOLUTION
ARBEITSTEILUNG
ZELLTEILUNG
PHOTOSYNTHESE

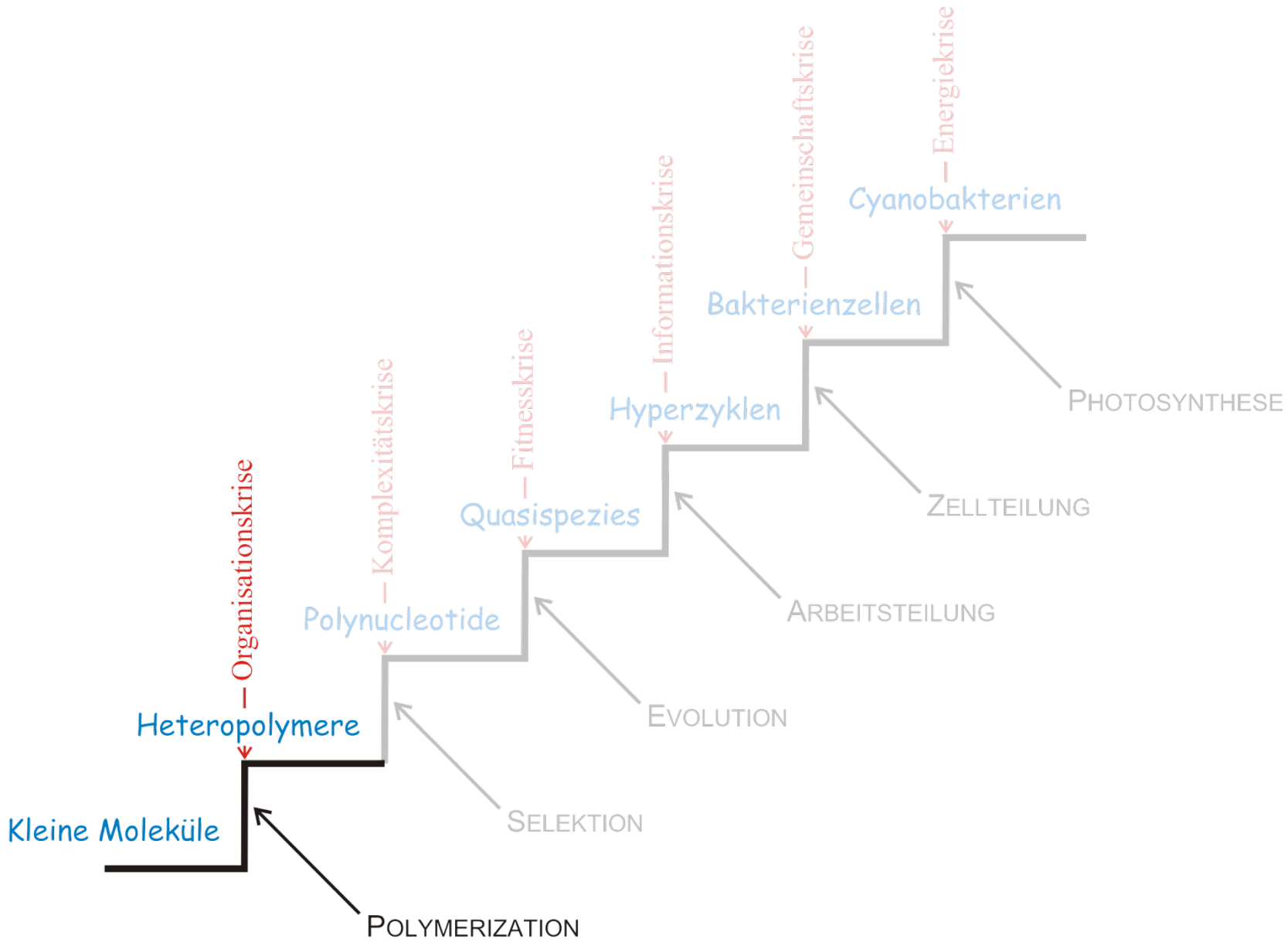
Aminosäuren

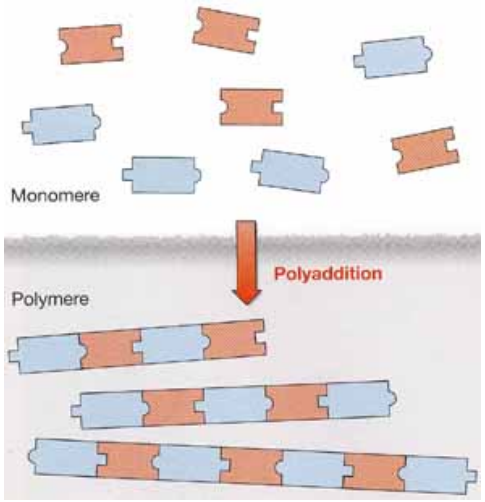
Nucleobasen

Kohlenhydrate

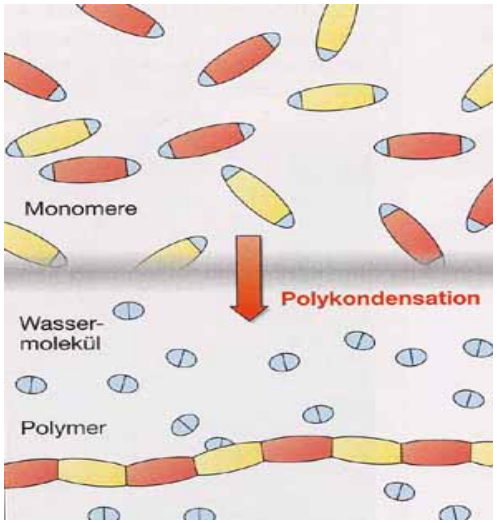


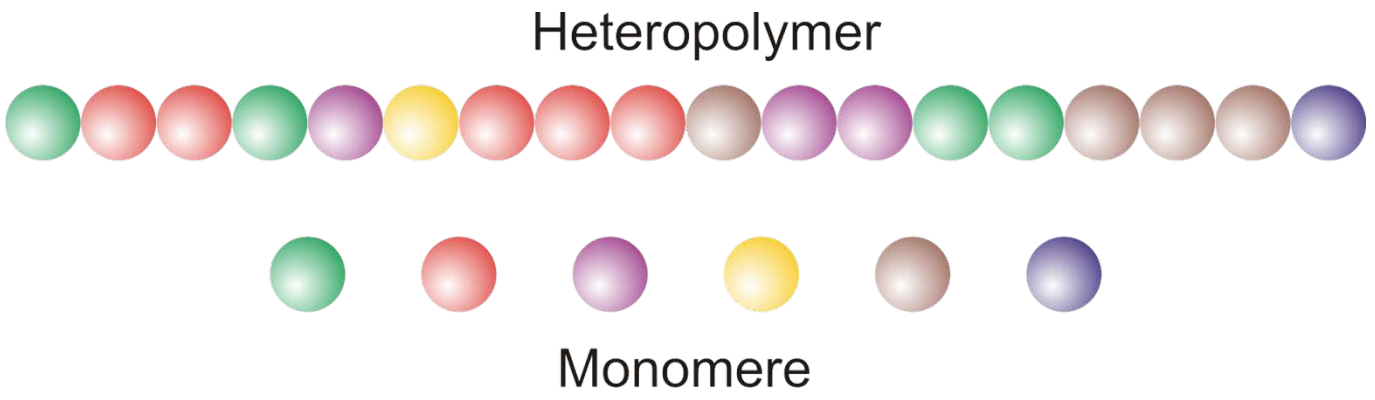
Kleine Moleküle


Kleine Moleküle
Organisationskrise
Heteropolymere
Komplexitätskrise
Polynucleotide
Fitnesskrise
Quasispezies
Informationskrise
Hyperzyklen
Gemeinschaftskrise
Bakterienzellen
Energiekrise
Cyanobakterien
POLYMERIZATION
SELEKTION
EVOLUTION
ARBEITSTEILUNG
ZELLTEILUNG
PHOTOSYNTHESE

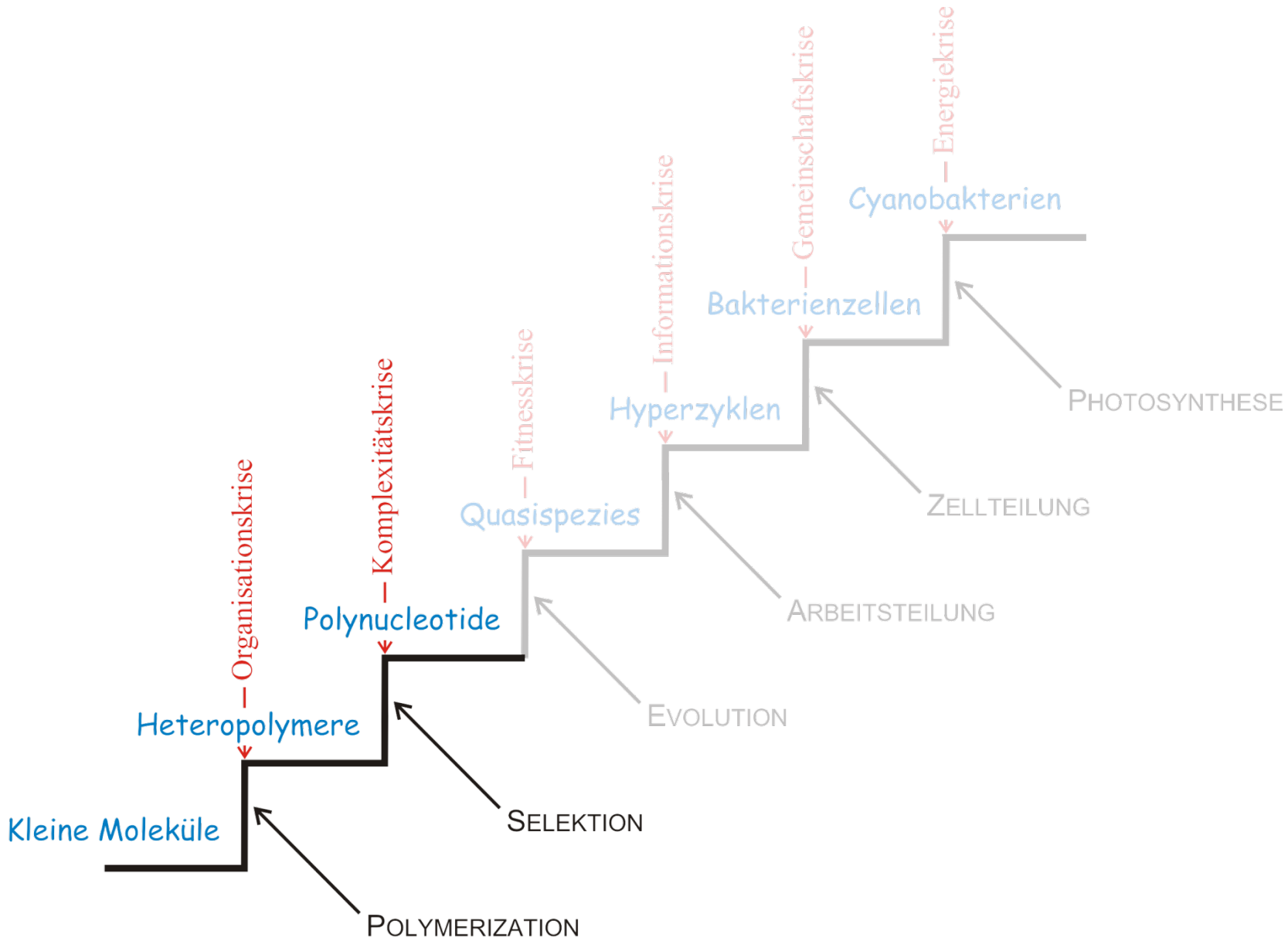


geordnete
Heteropolymere

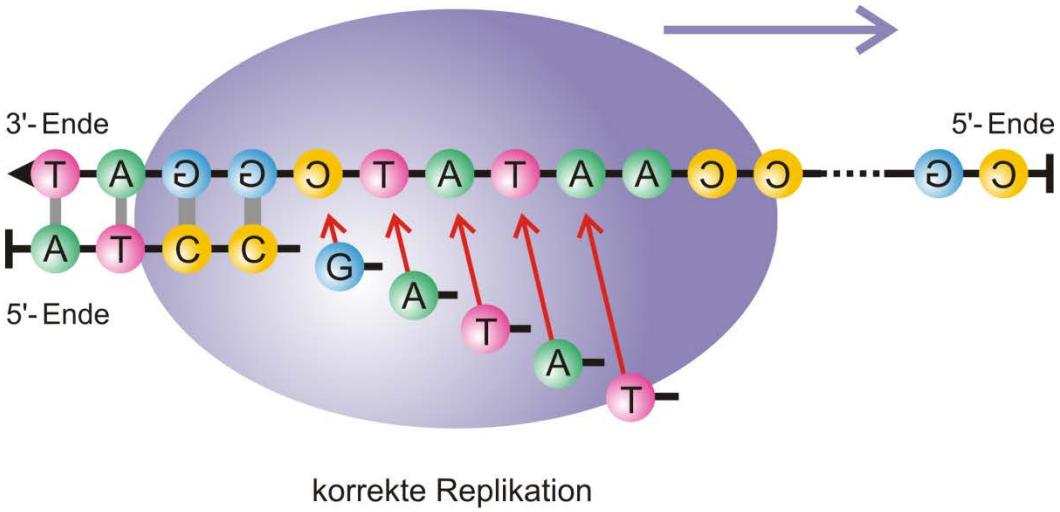




Heteropolymer mit zufälliger Sequenz der Monomeren


Kleine Moleküle
Heteropolymere
Polynucleotide
Quasispezies
Hyperzyklen
Bakterienzellen
Cyanobakterien
Organisationskrise
Komplexitätskrise
Fitnesskrise
Informationskrise
Gemeinschaftskrise
Energiekrise
POLYMERIZATION
SELEKTION
EVOLUTION
ARBEITSTEILUNG
ZELLTEILUNG
PHOTOSYNTHESE

Taq-Polymerase



korrekte Replikation

Adenin A

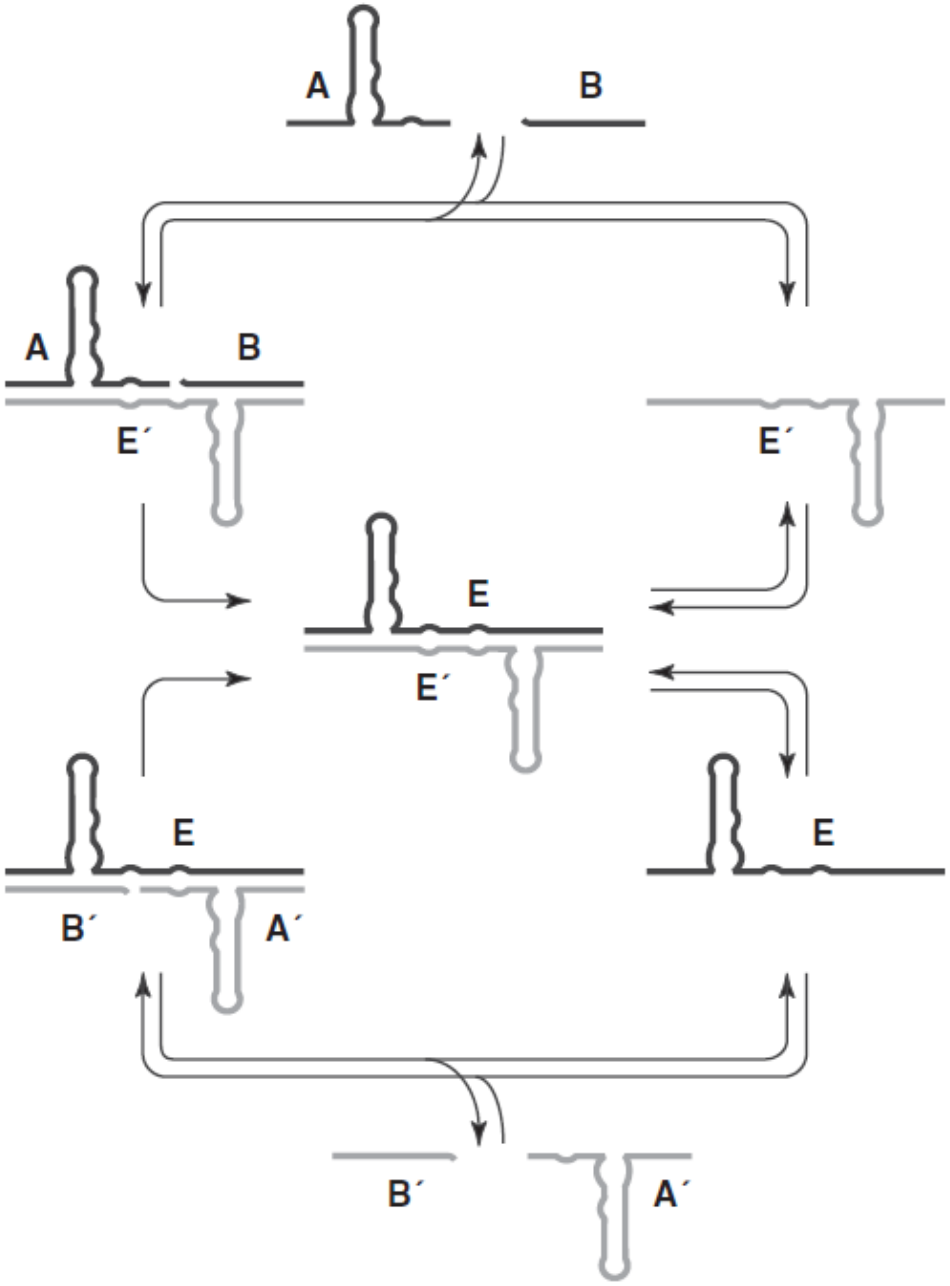
Thymin T

Uracil U

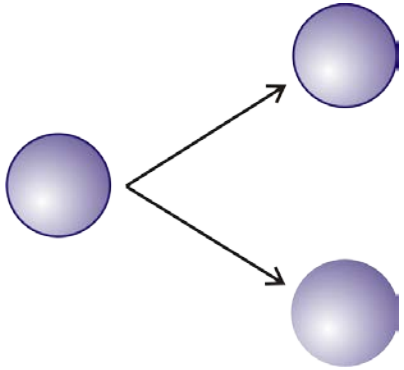
Guanin G

Cytosin C

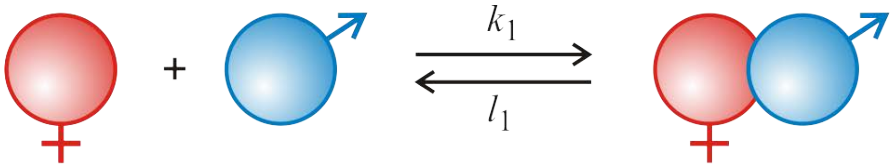
Replikation



Tracey A.Lincoln, Gerald F.Joyce. Self-sustained replication of an RNA enzyme. Science 323:1229-1232, 2009.

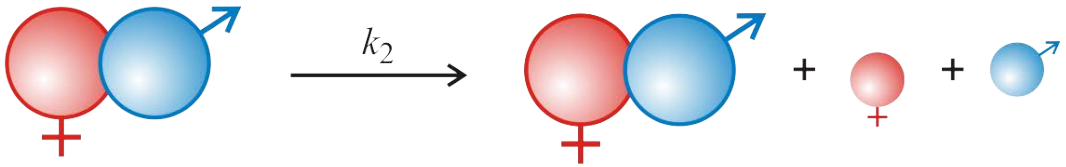


$$(A) + X = 2\,X$$

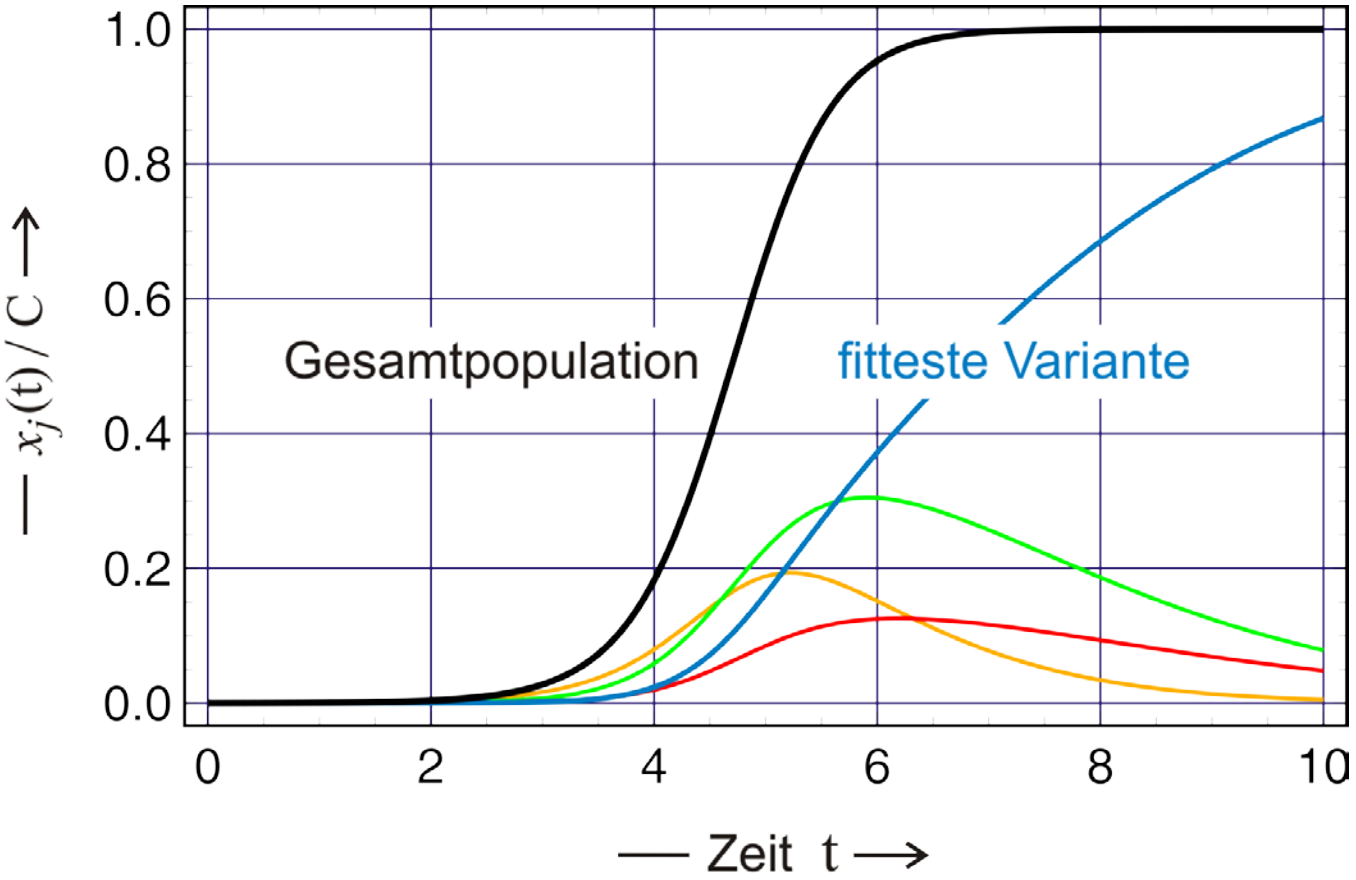


$$X + Y = X{\cdot}Y$$

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



Asexuelle und sexuelle Vermehrung

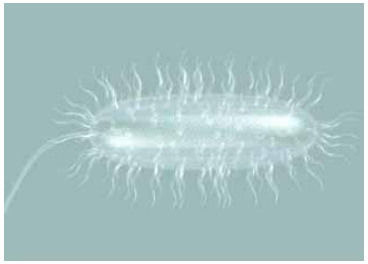


Fitness f = (**1.75**, **2.25**, **2.35** und **2.80**)

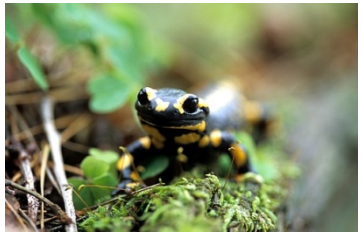
Selektion der fittesten Variante

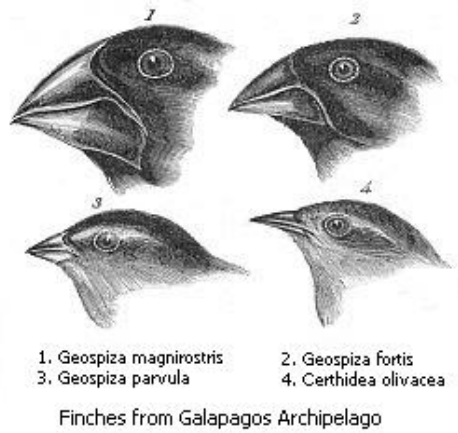
Charles Darwin, 1809 - 1882

Voyage on HMS Beagle, 1831 - 1836

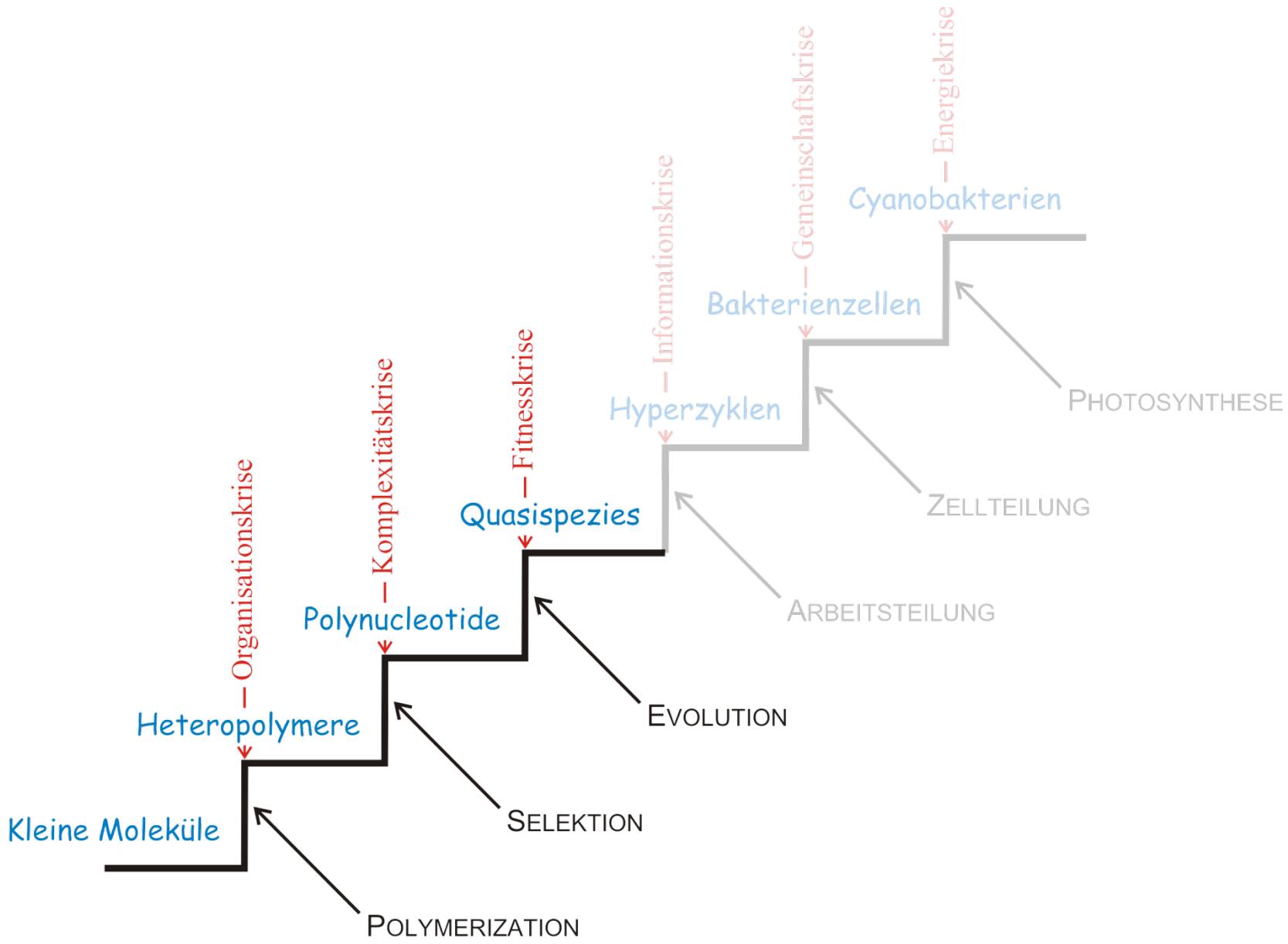


Phänotypen

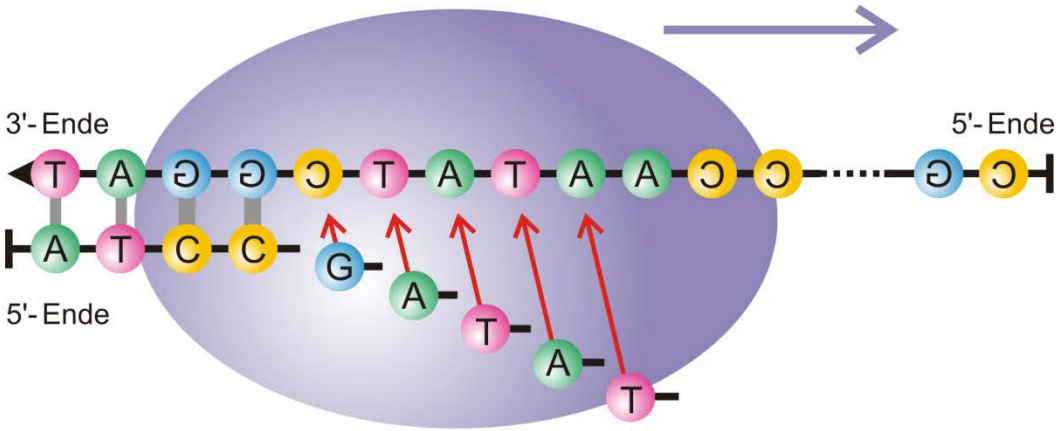




Finches from Galapagos Archipelago


Kleine Moleküle
Organisationskrise
Heteropolymere
Komplexitätskrise
Polynucleotide
Fitnesskrise
Quasispezies
Informationskrise
Hyperzyklen
Gemeinschaftskrise
Bakterienzellen
Energiekrise
Cyanobakterien
POLYMERIZATION
SELEKTION
EVOLUTION
ARBEITSTEILUNG
ZELLTEILUNG
PHOTOSYNTHESE

Taq-Polymerase



korrekte Replikation

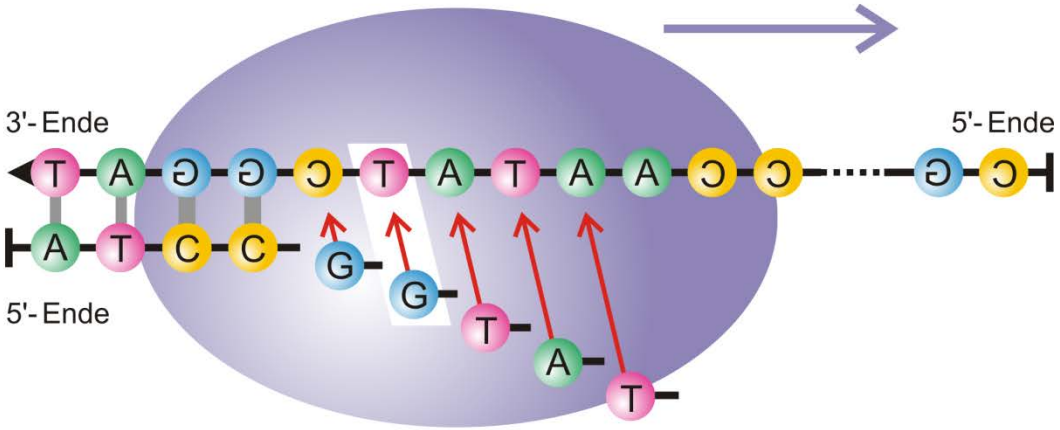
Adenin A

Thymin T

Uracil U

Guanin G

Cytosin C



Mutation

Korrekte Replikation und Punktmutation

Drei notwendige Bedingungen für Darwinsche Evolution sind:

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

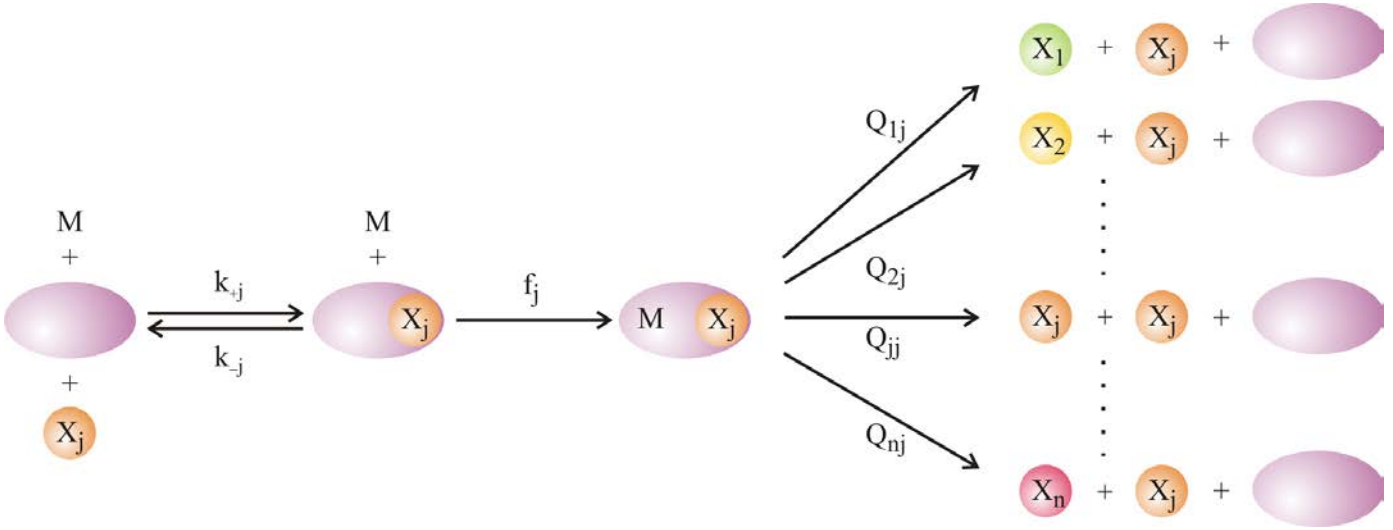
Vermehrung führt zu exponentiellem Wachstum und dieses stellt eine *conditio sine qua non* für Selektion dar.

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

Selektion ist eine Konsequenz exponentiellen Wachstums bei endlichen Ressourcen.

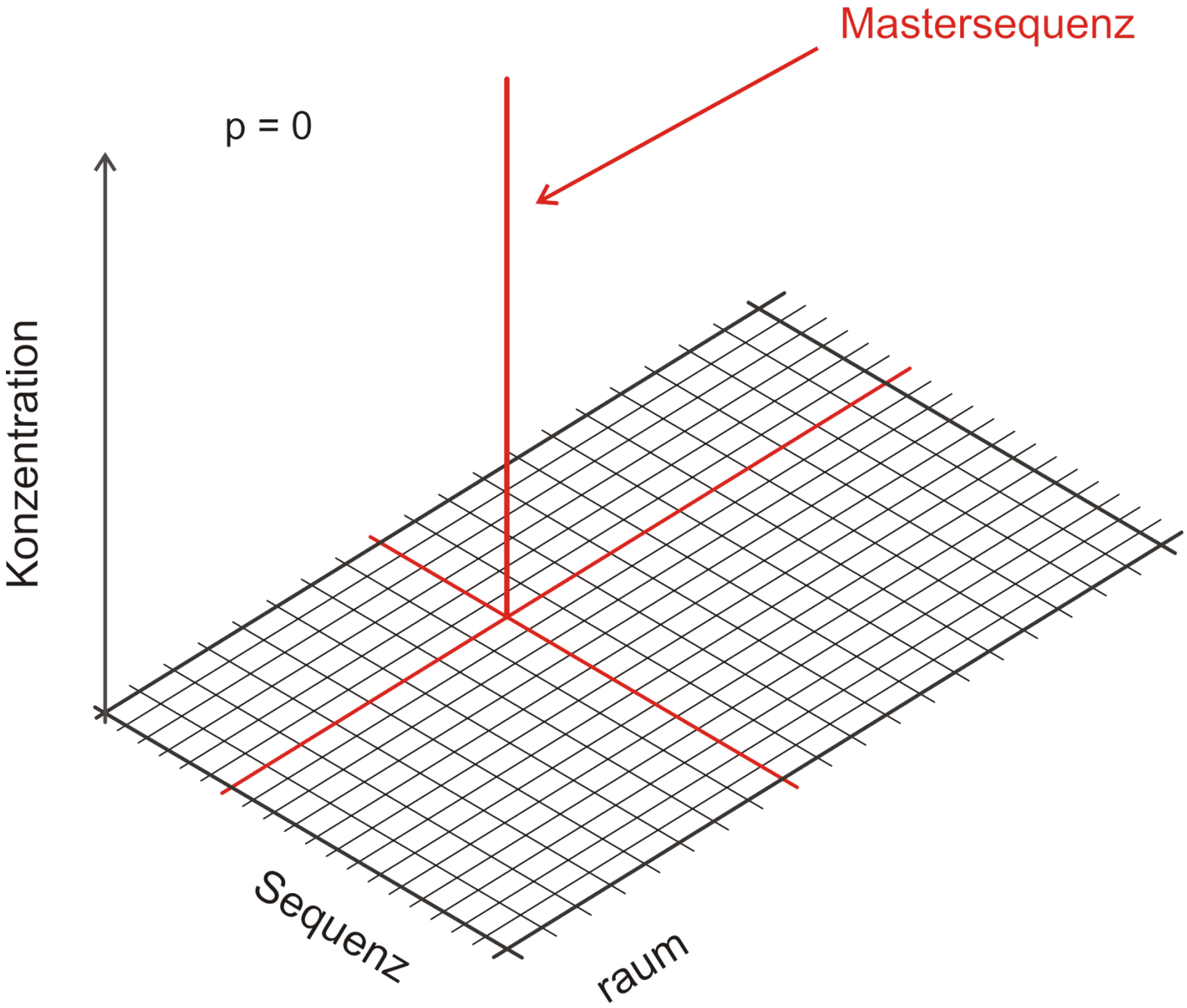
Da im Sinne der Optimierung von Fitness durch die Darwinsche Evolution nur Nachkommen gezählt werden, ist sie universell gültig, wenn die drei Bedingungen erfüllt sind.

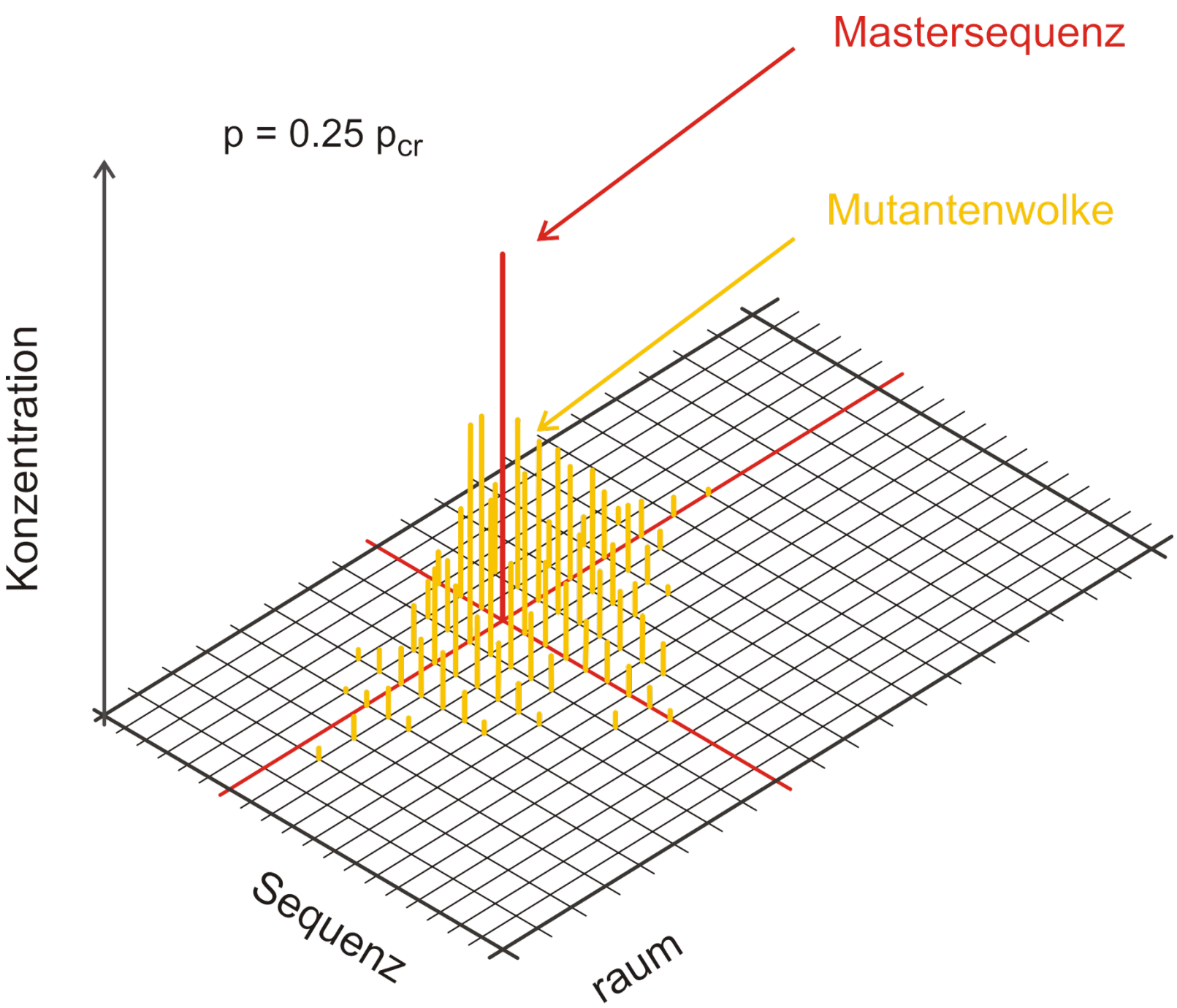
Manfred Eigen
1927 -

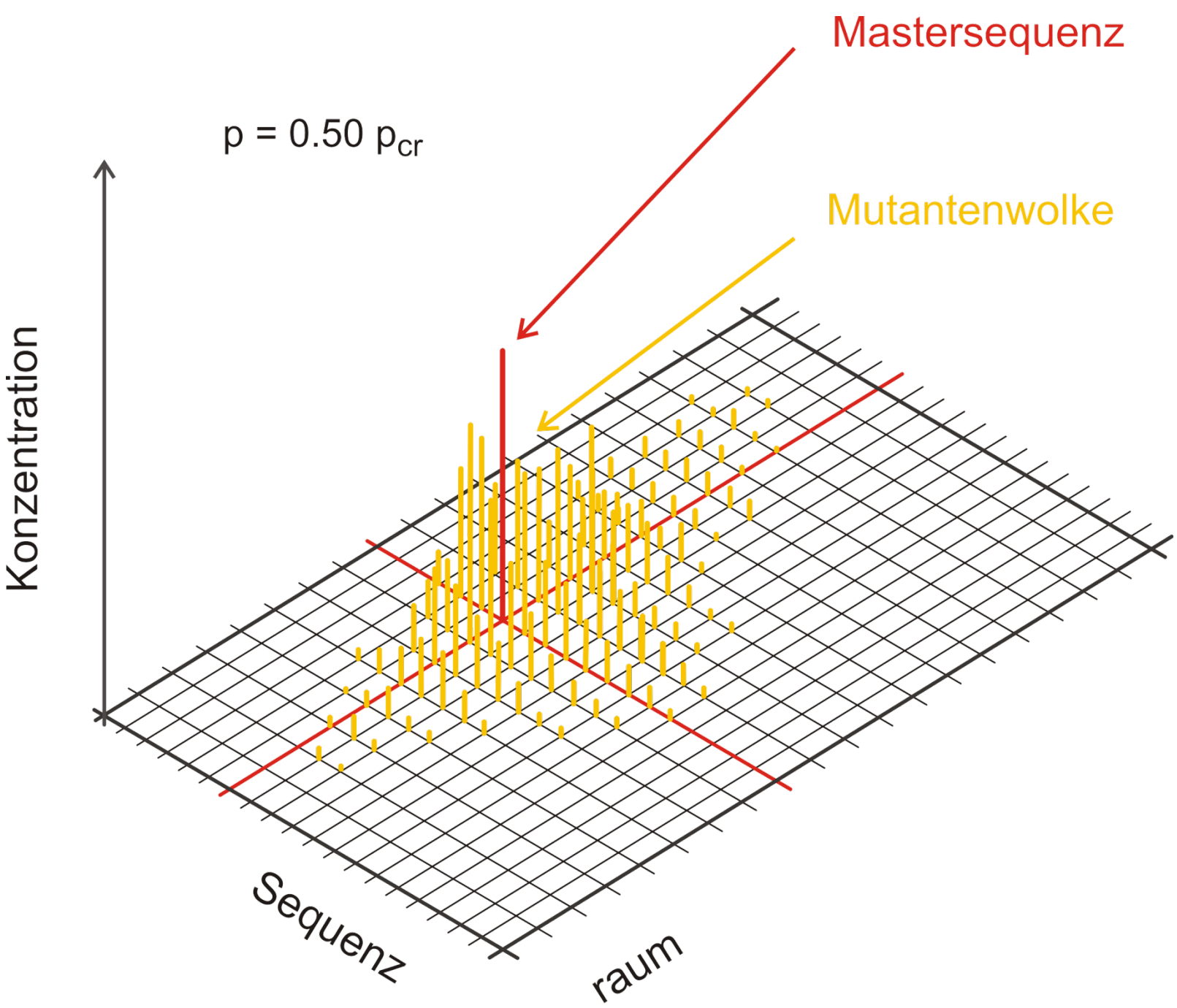


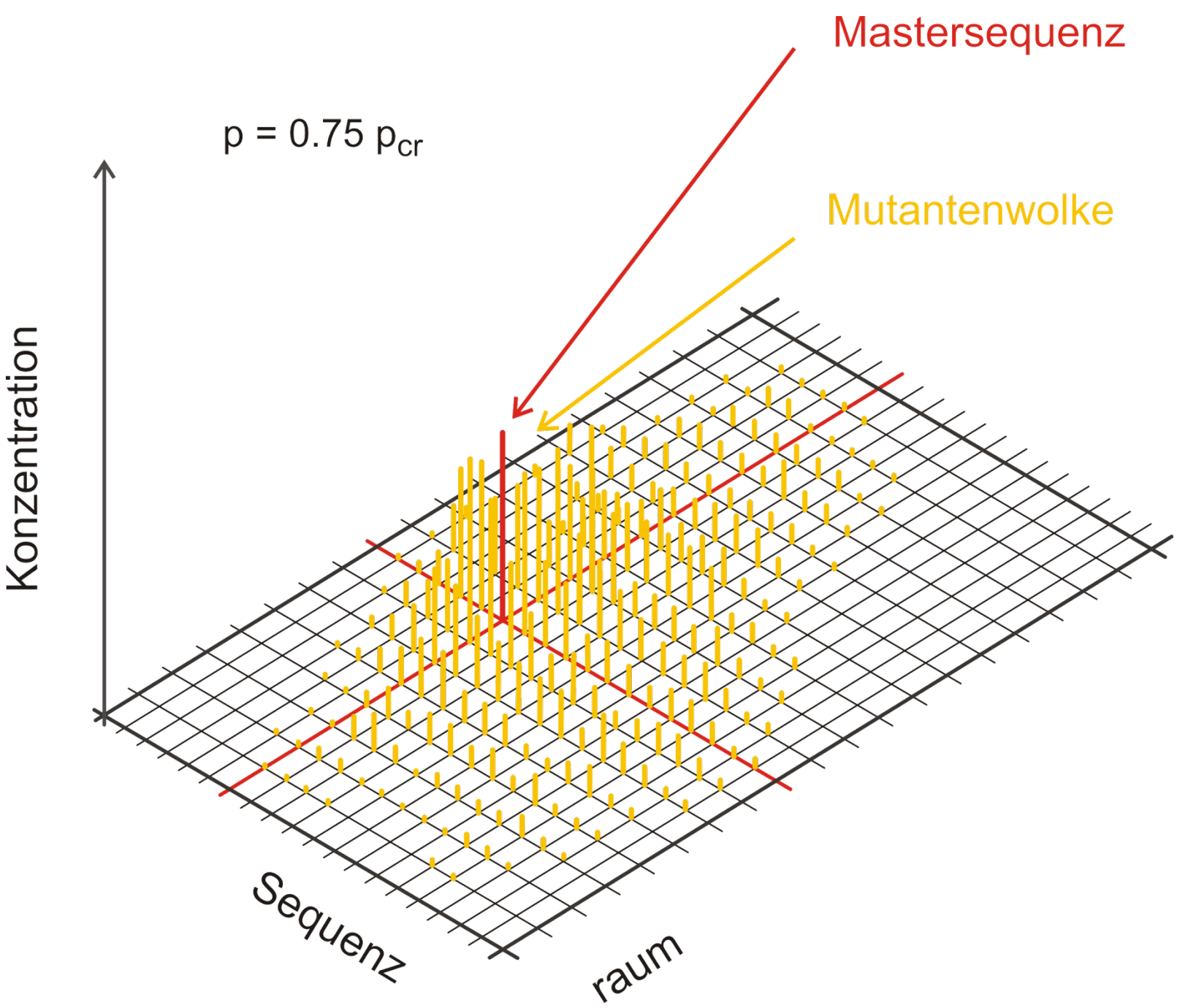
Korrekte Replikation und Mutation als parallele chemische Reaktionen

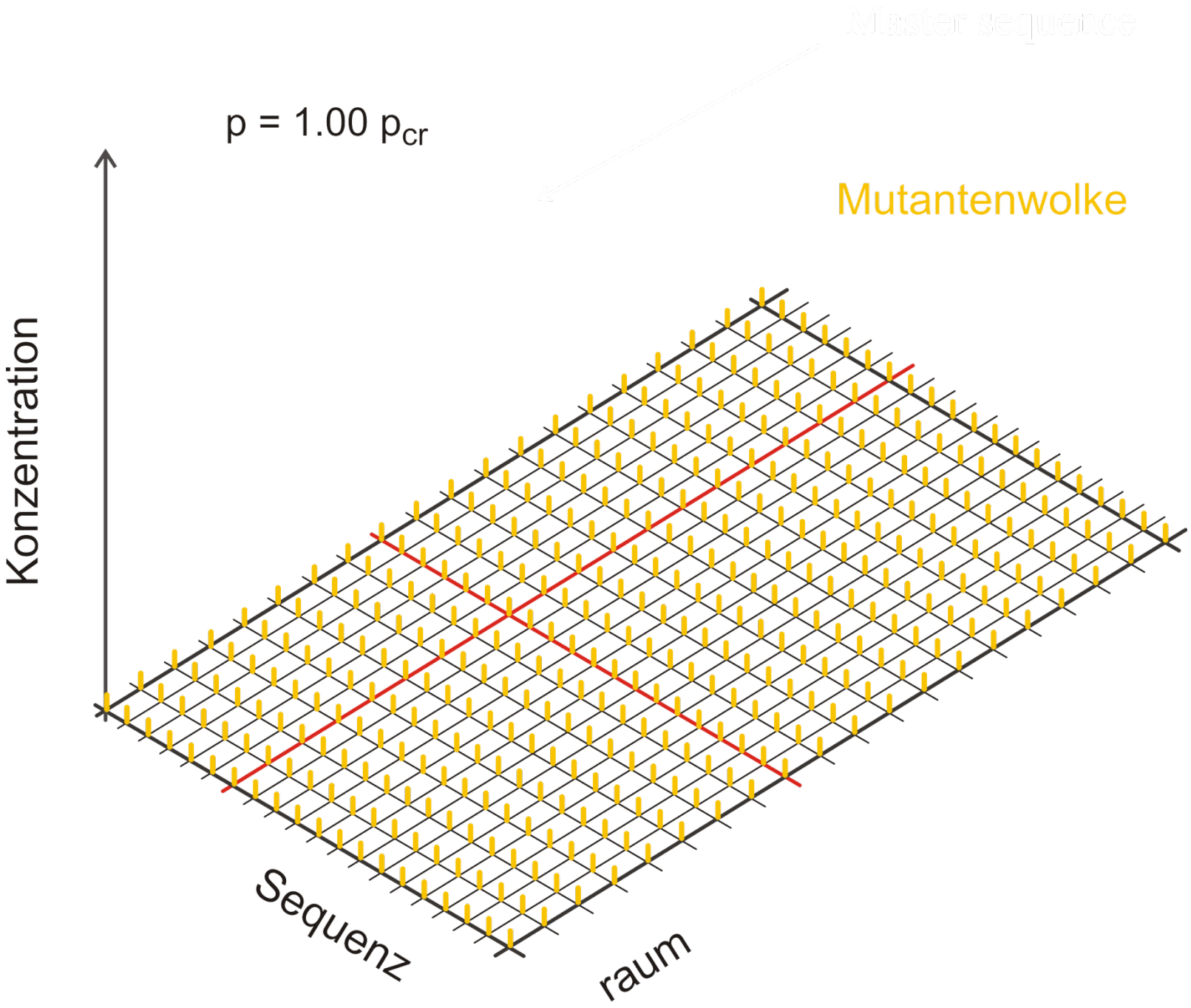
M. Eigen. 1971. *Naturwissenschaften* 58:465,
M. Eigen & P. Schuster.1977. *Naturwissenschaften* 64:541, 65:7 und 65:341

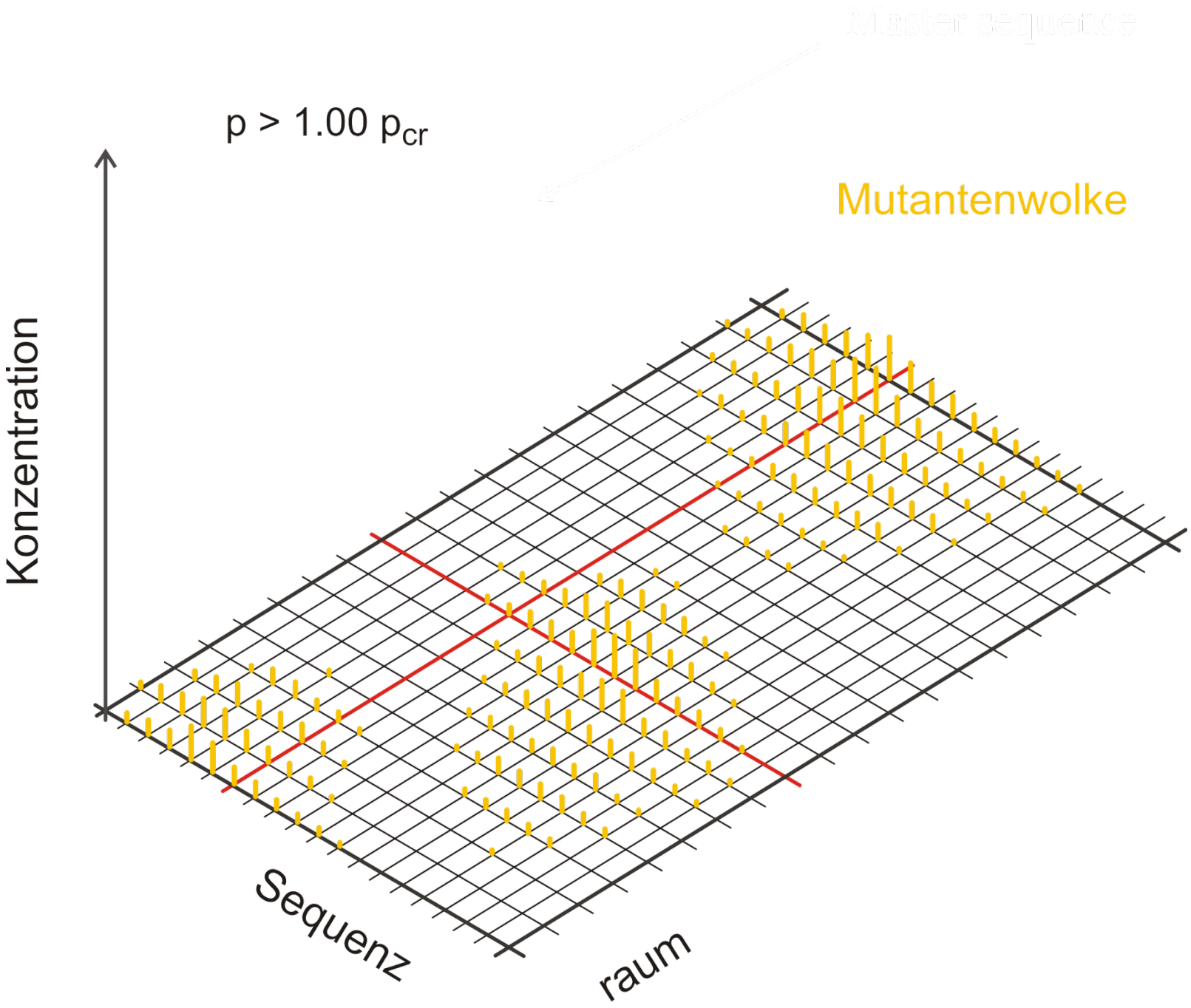

Mastersequenz
p = 0
Konzentration
Sequenz
raum

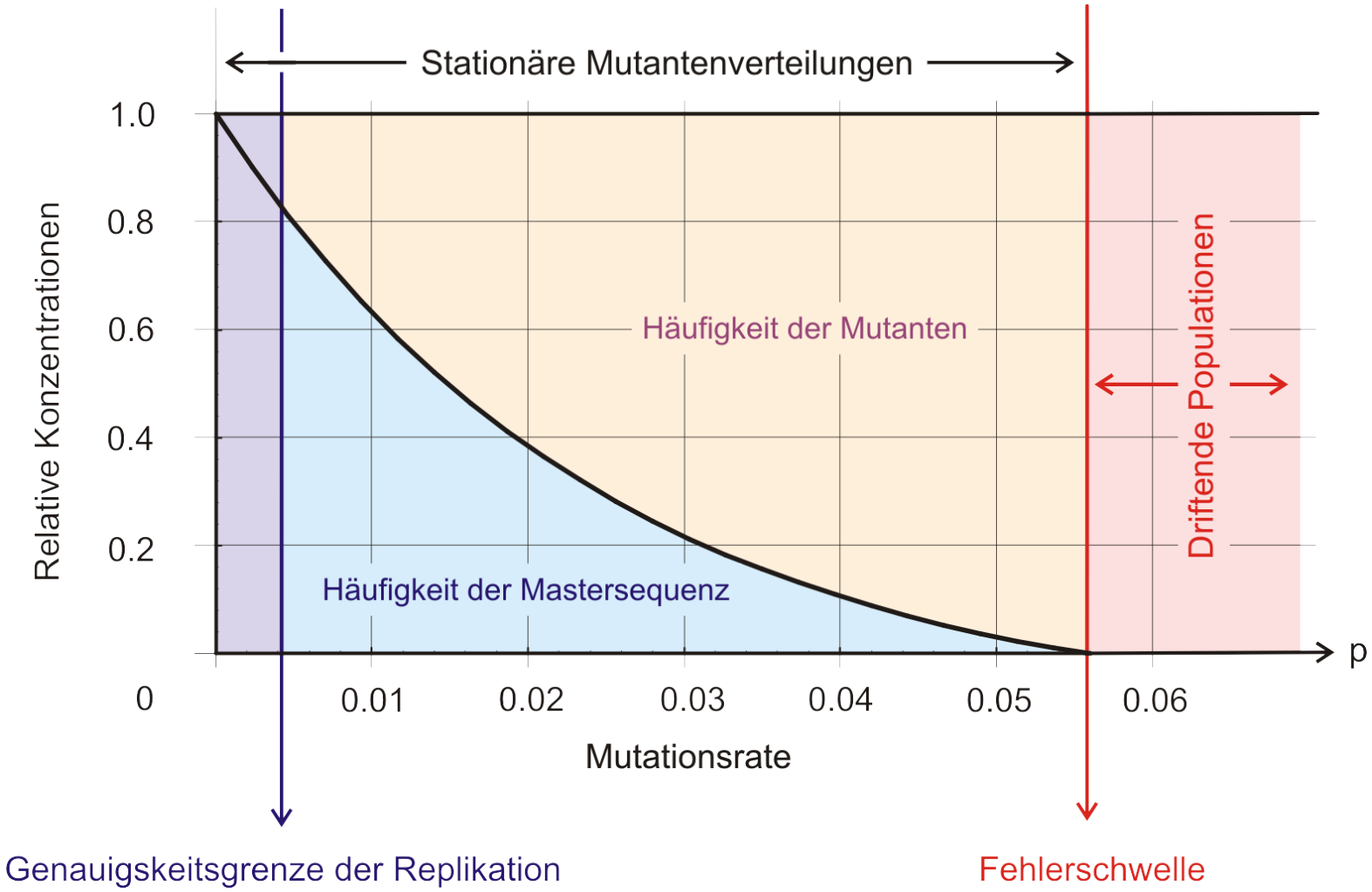

Mastersequenz
p = 0.25 p_cr
Mutantenwolke
Konzentration
Sequenz
raum


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

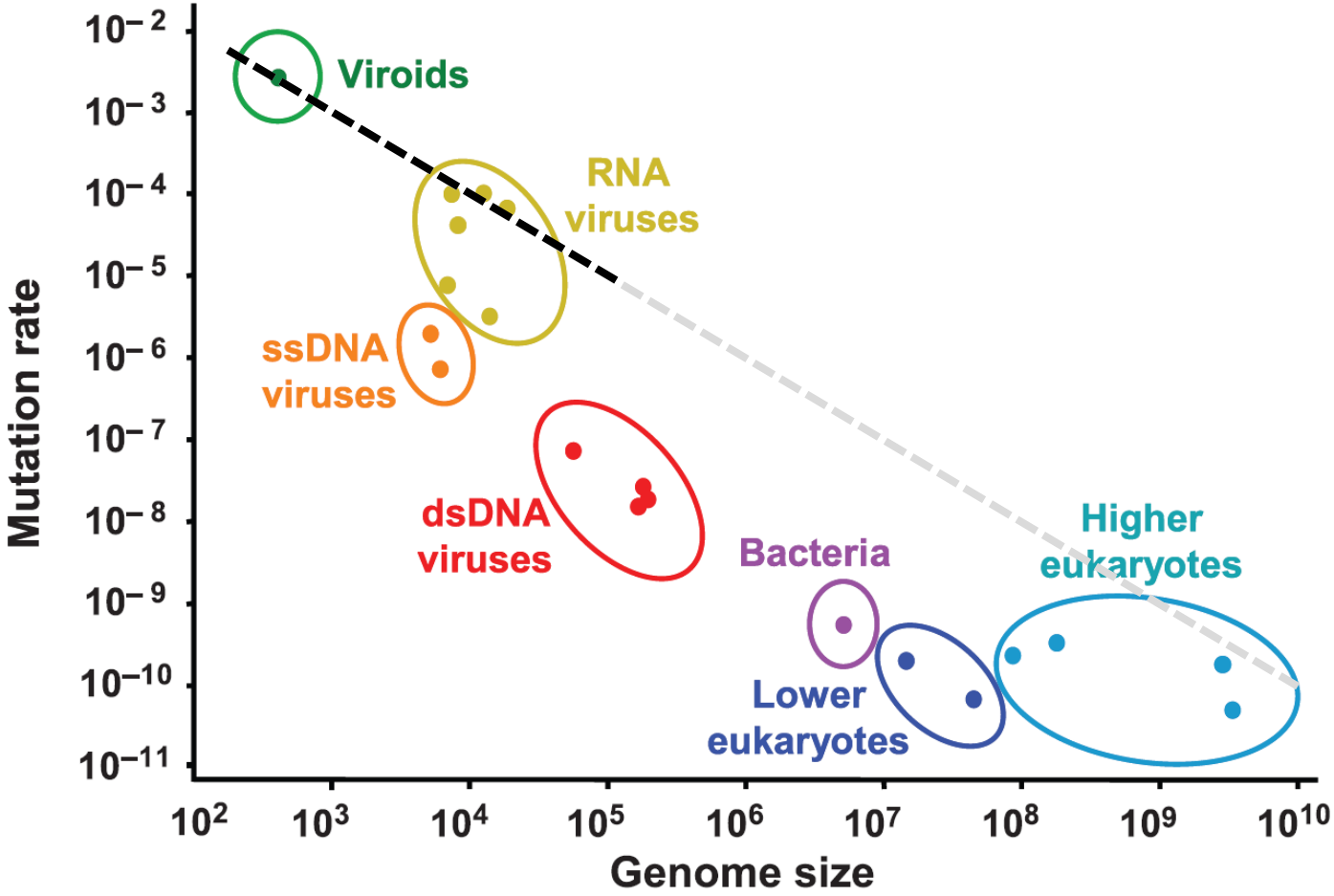

Mastersequenz
Mutantenwolke
p = 0.75 p_cr
Konzentration
Sequenz
raum


Master sequence
p = 1.00 p_{cr}
Mutantenwolke
Konzentration
Sequenz
raum


Master sequence
p > 1.00 p_{cr}
Mutantenwolke
Konzentration
Sequenz
raum

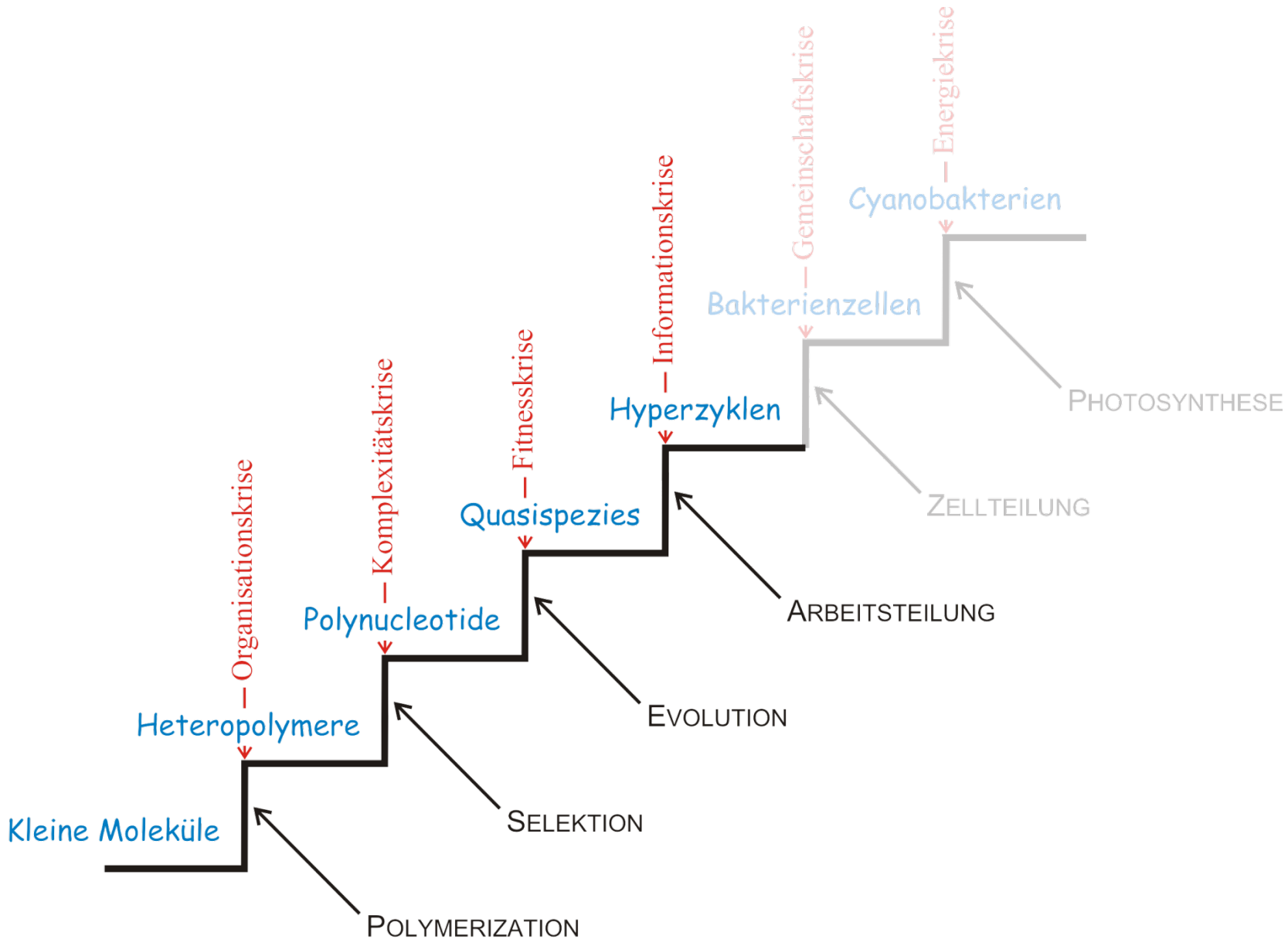


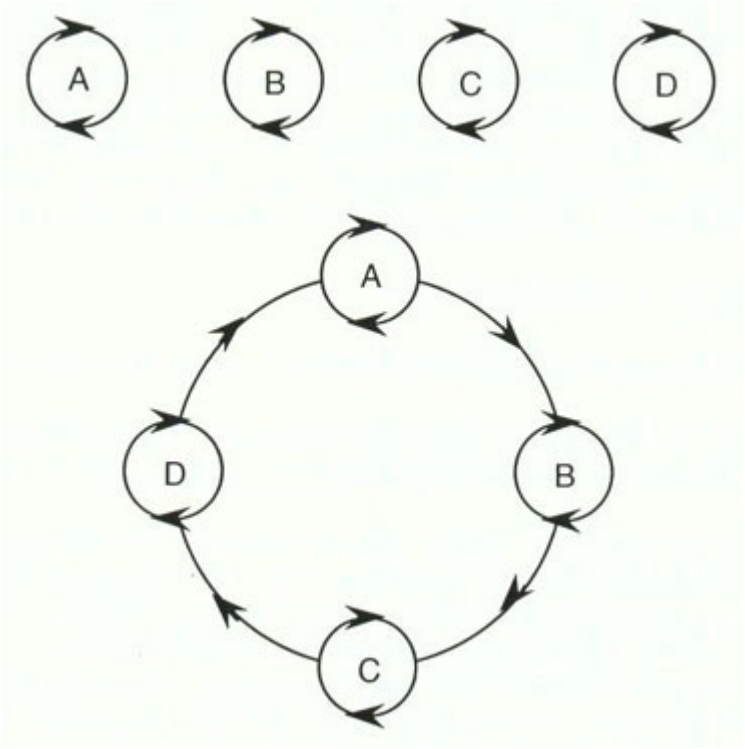
Die Fehlerschwelle bei Replikation und Mutation

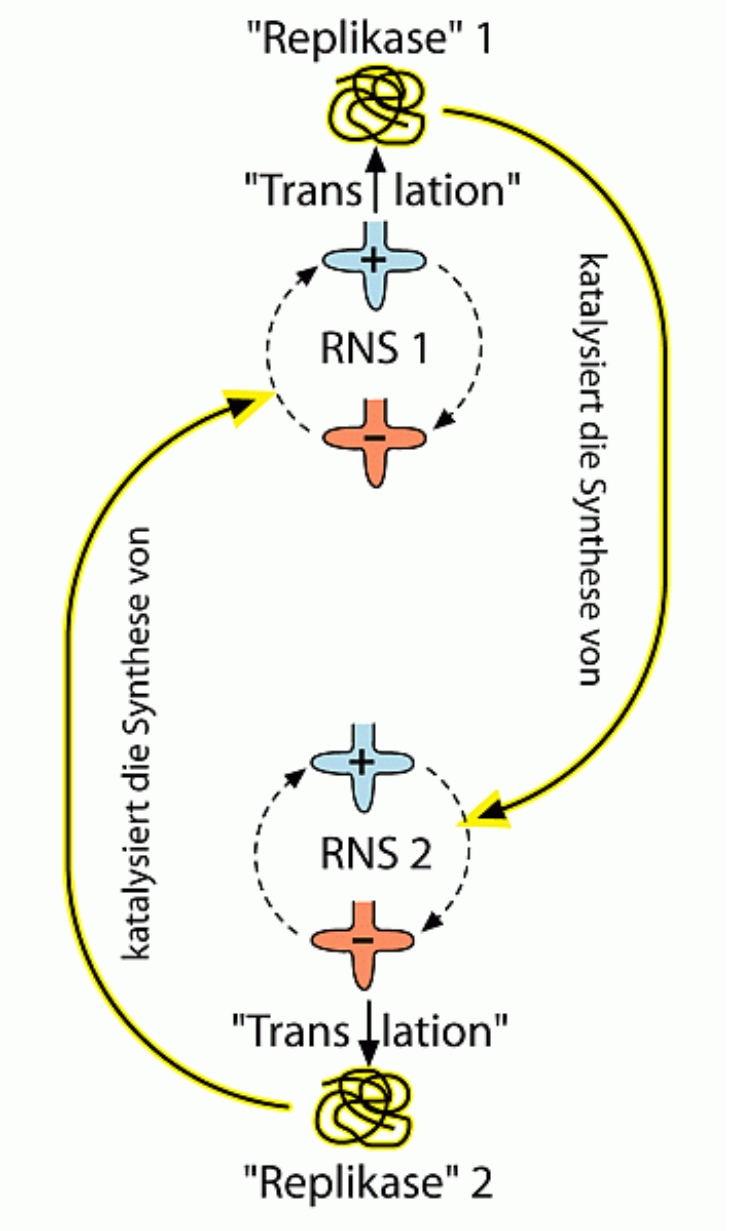


Selma Gago, Santiago F. Elena, Ricardo Flores, Rafael Sanjuán. 2009. Extremely high mutation rate of a hammerhead viroid. Science 323:1308.

Mutationsrate und Genomlänge

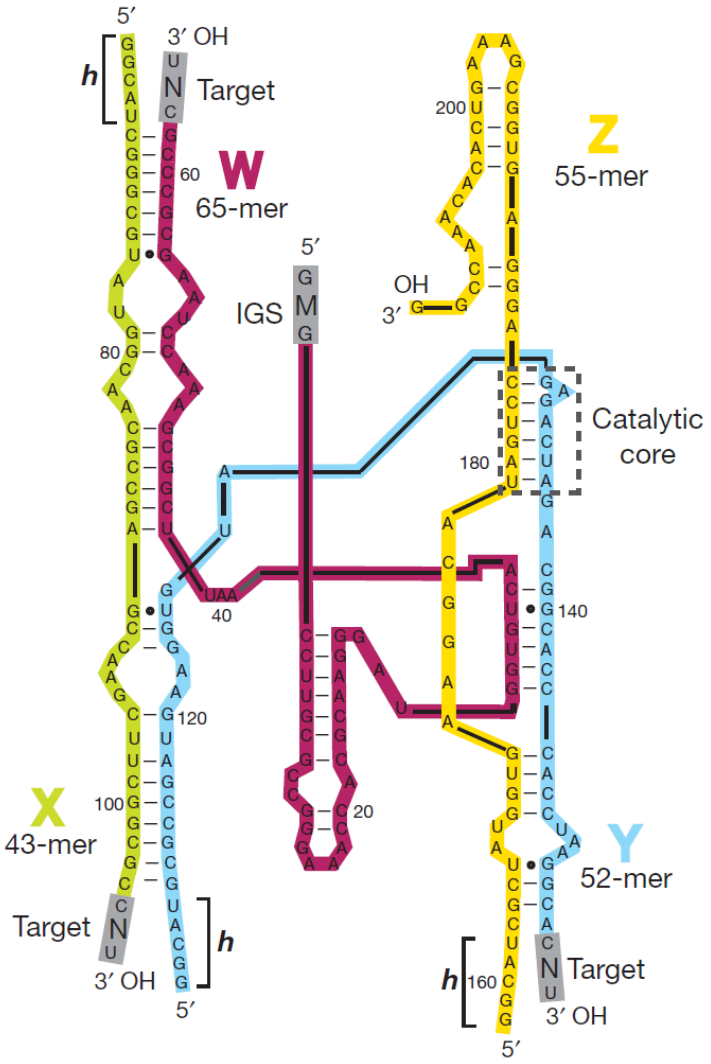

Kleine Moleküle
Organisationskrise
Heteropolymere
Komplexitätskrise
Polynucleotide
Fitnesskrise
Quasispezies
Informationskrise
Hyperzyklen
Gemeinschaftskrise
Bakterienzellen
Energiekrise
Cyanobakterien
POLYMERIZATION
SELEKTION
EVOLUTION
ARBEITSTEILUNG
ZELLTEILUNG
PHOTOSYNTHESE

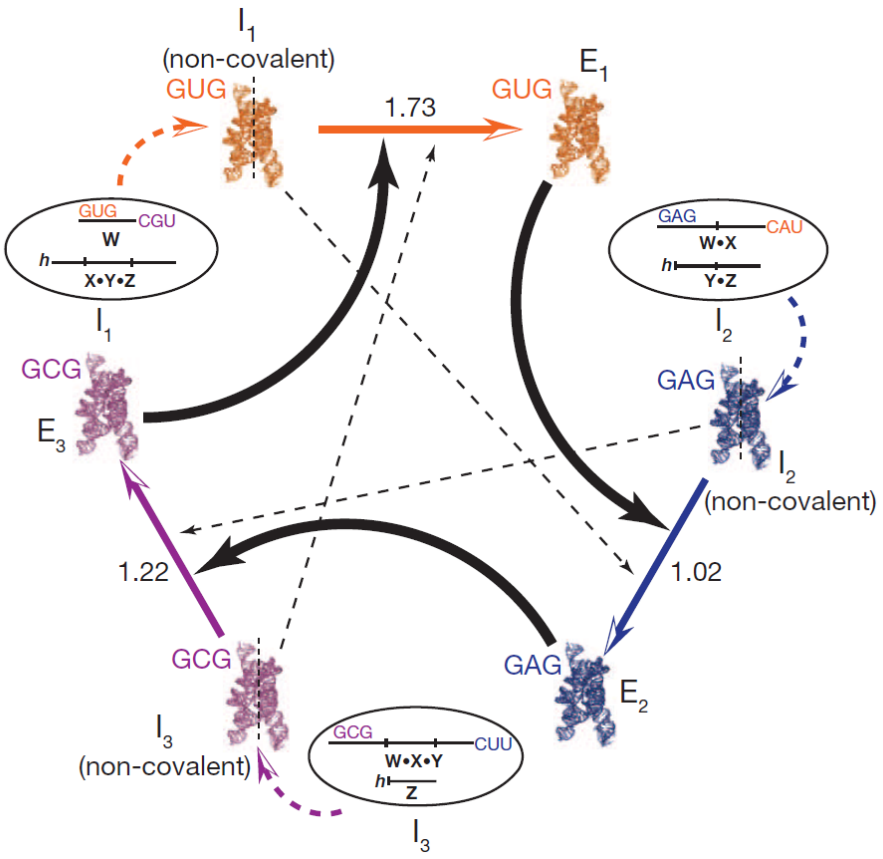




Kooperation zwischen Konkurrenten

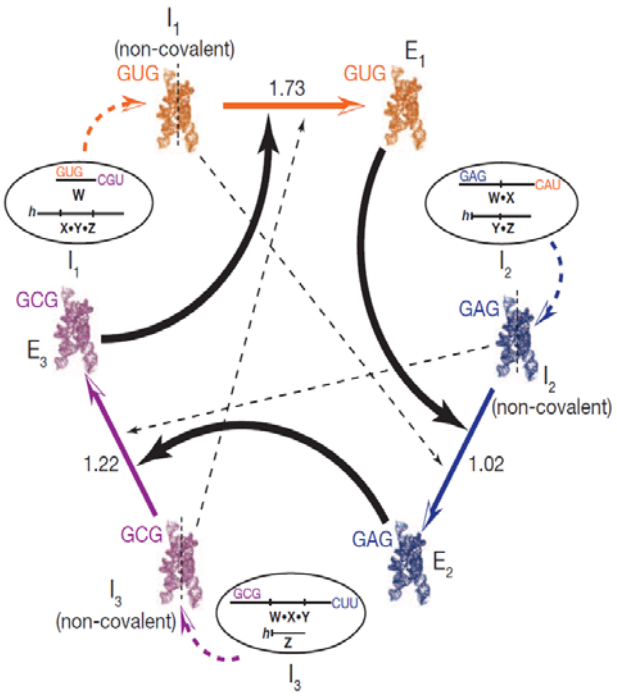
Hyperzyklen

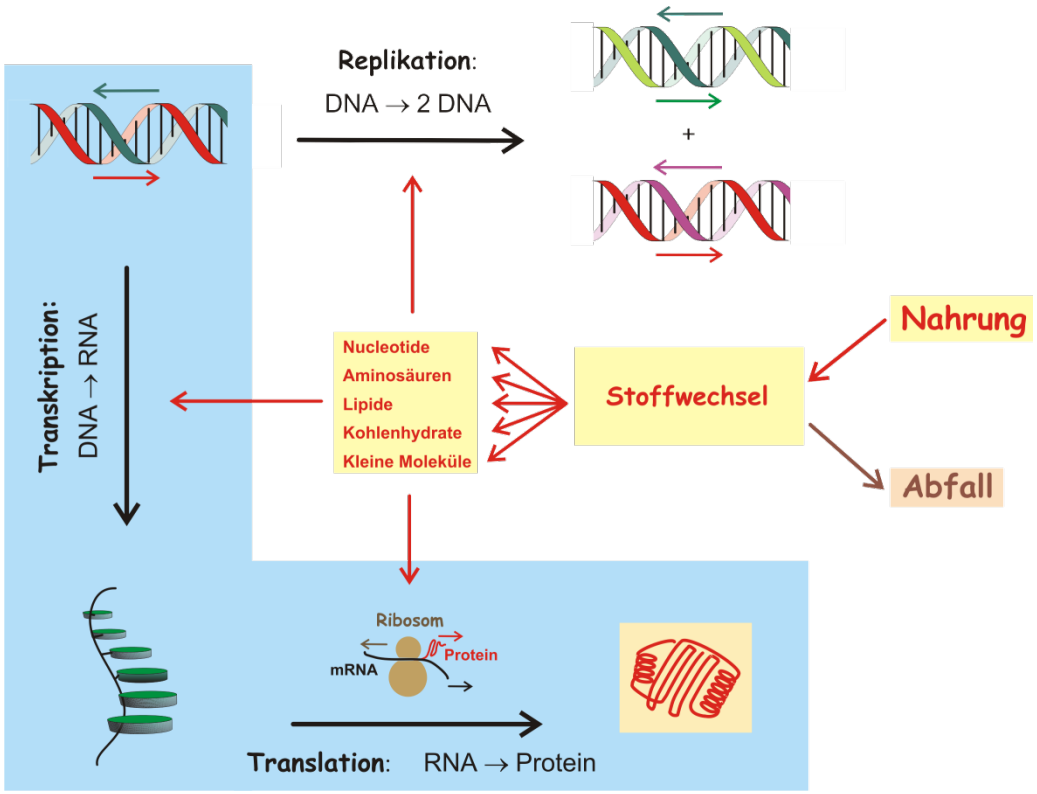




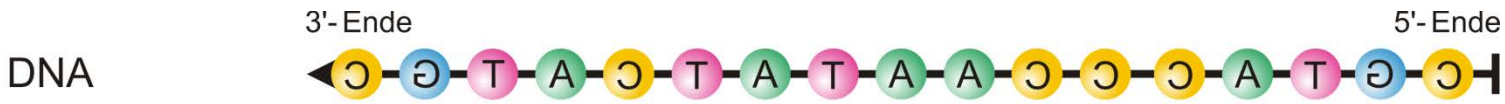
Kooperation von RNA Molekülen

Nilesh Vaidya, Michael L.Manpat, Irene A.Chen, Ramon Xulvi-Brunet, Eric J.Hayden, Niles Lehman. Spontaneous network formation among cooperative RNA replicators. Nature 491:72-77, 2012.





RNA-Welt ⇒ DNA & RNA & Protein-Welt

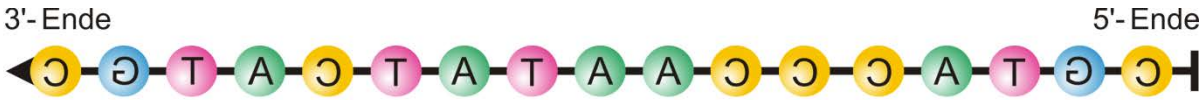


DNA ⇒ RNA

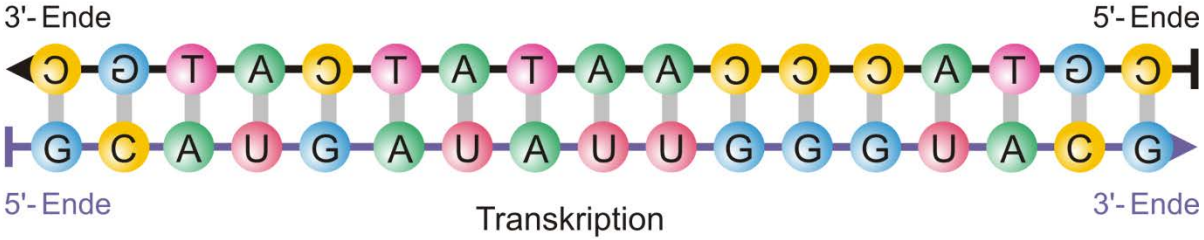
RNA ⇒ Protein

Transkription und Translation

DNA

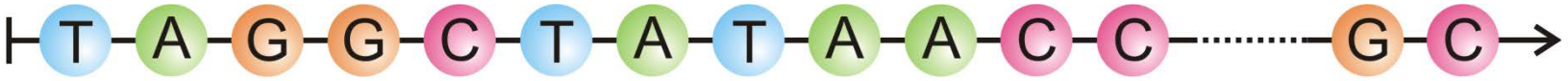


DNA ⇒ RNA



RNA ⇒ Protein

Transkription und Translation

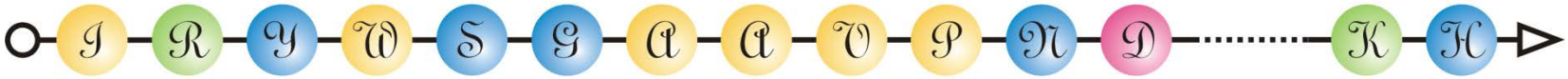


A ≡ Adenine

G ≡ Guanine

T ≡ Thymine

C ≡ Cytosine



𝔄 ≡ **ala**nine

𝔊 ≡ **gly**cine

𝔐 ≡ **met**hionine

𝔖 ≡ **ser**ine

ℭ ≡ **cys**teine

ℌ ≡ **his**tidine

ℜ ≡ **as**paragi**n**e

𝔗 ≡ **thr**eonine

𝔇 ≡ **as**partic acid

ℑ ≡ **i**so**l**eucine

𝔓 ≡ **pro**line

𝔙 ≡ **val**ine

𝔈 ≡ **glu**tamic acid

𝔎 ≡ **ly**sine

𝔔 ≡ **gl**utami**n**e

𝔚 ≡ **tryp**tophane

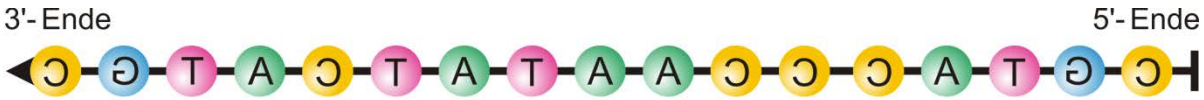
𝔉 ≡ **phe**nyl alanine

𝔏 ≡ **leu**cine

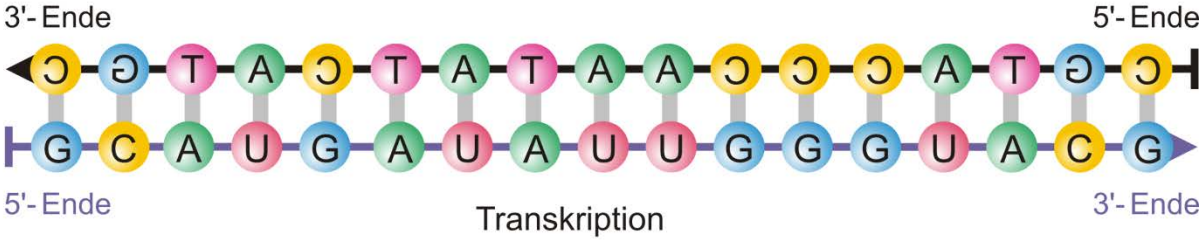
ℜ ≡ **arg**inine

𝔜 ≡ **tyr**osine

DNA

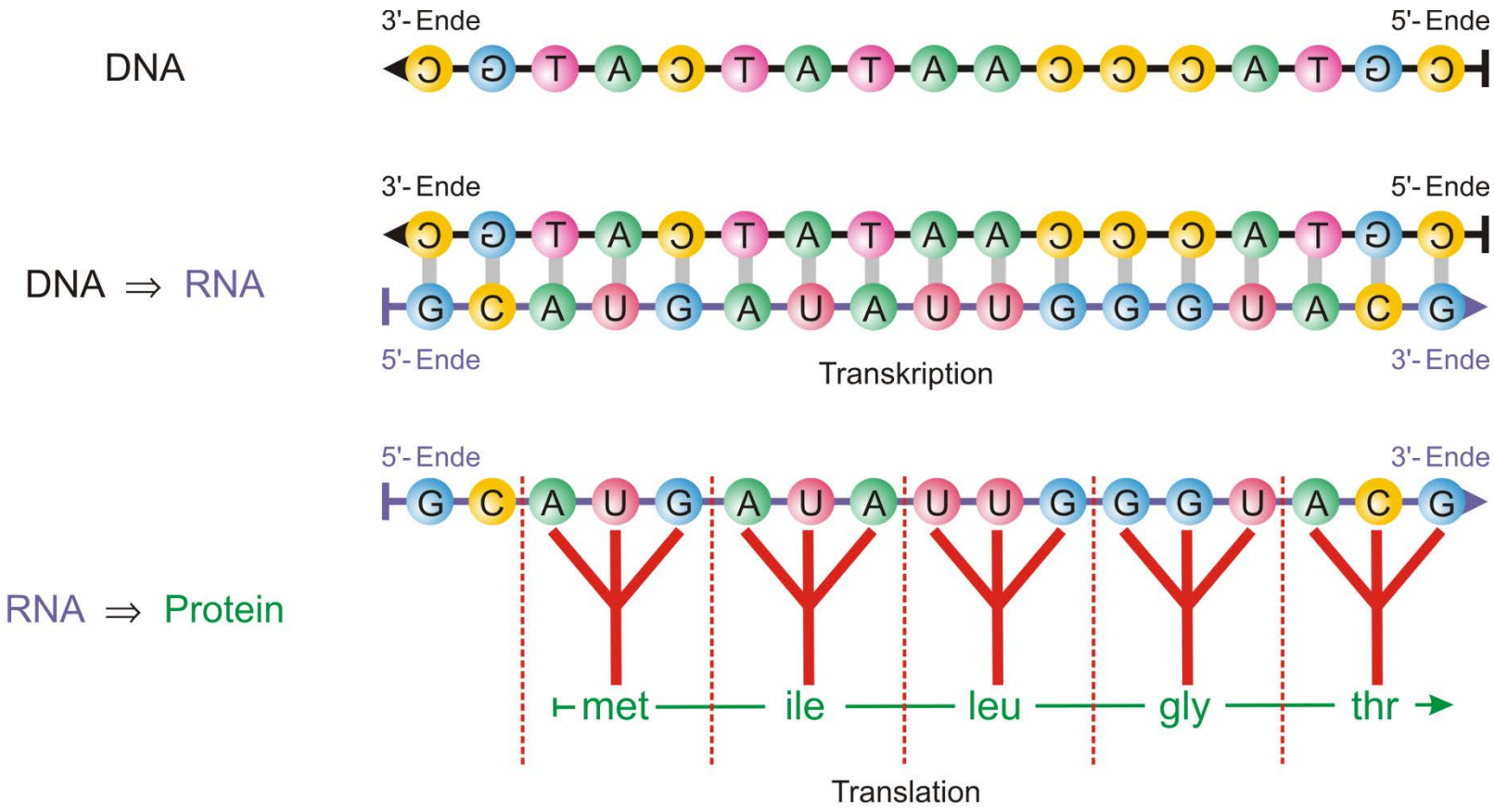


DNA ⇒ RNA

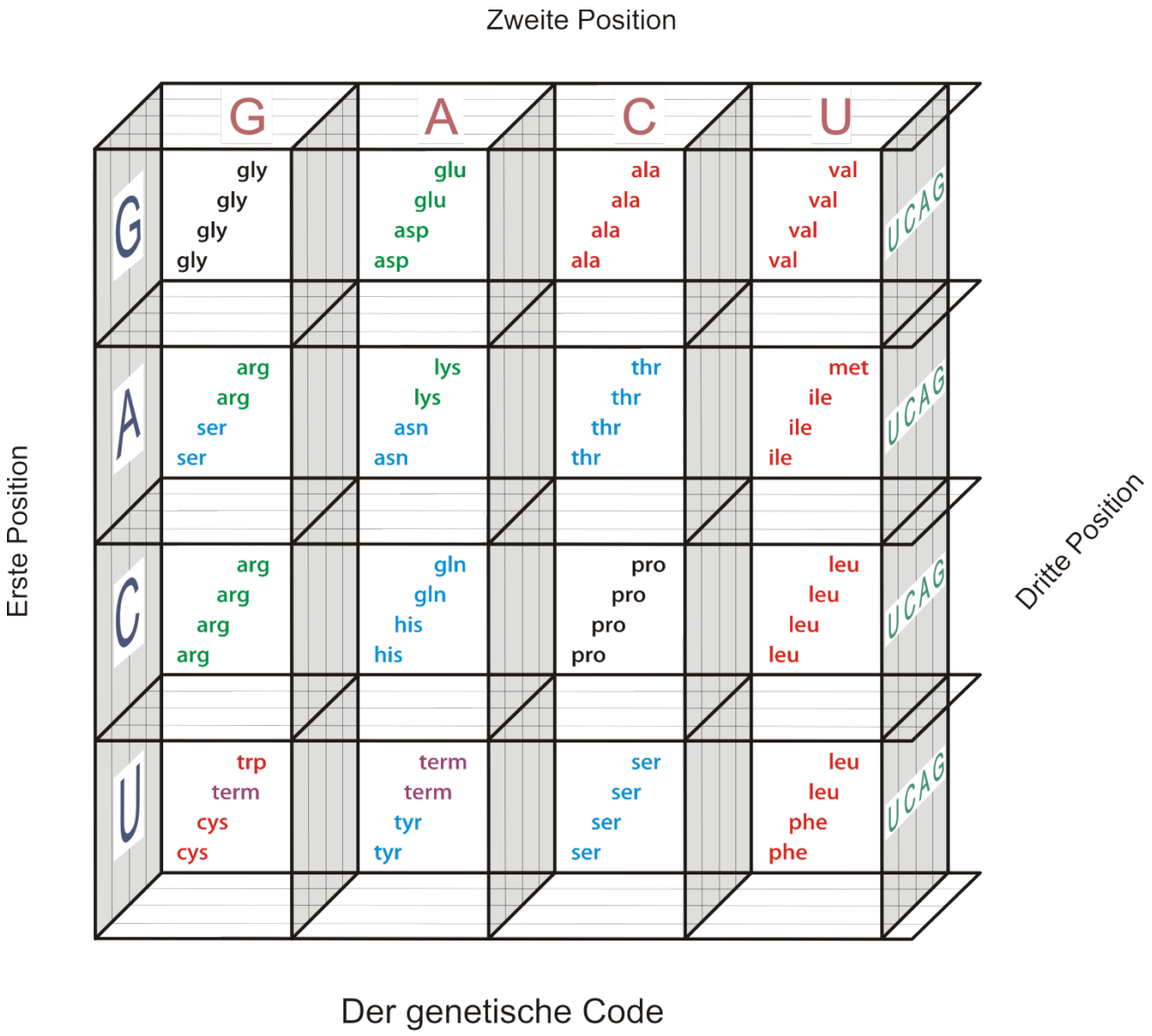


RNA ⇒ Protein

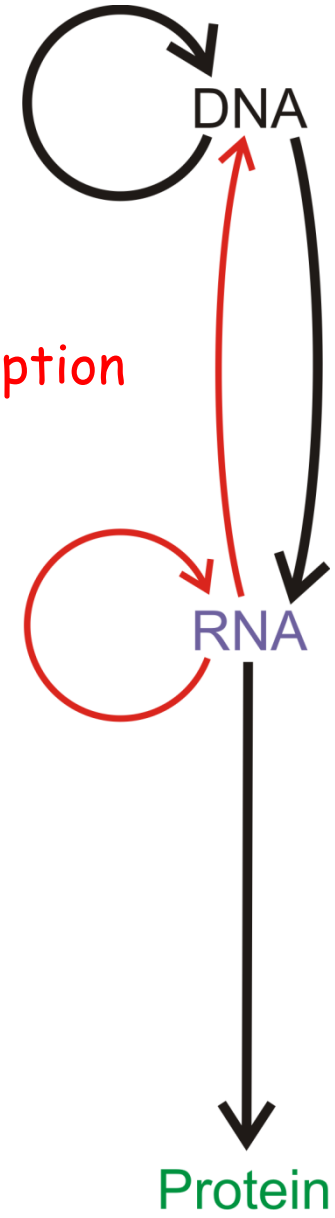
Transkription und Translation



Transkription und Translation



Der genetische Code



Replikation

Transkription

Reverse Transkription

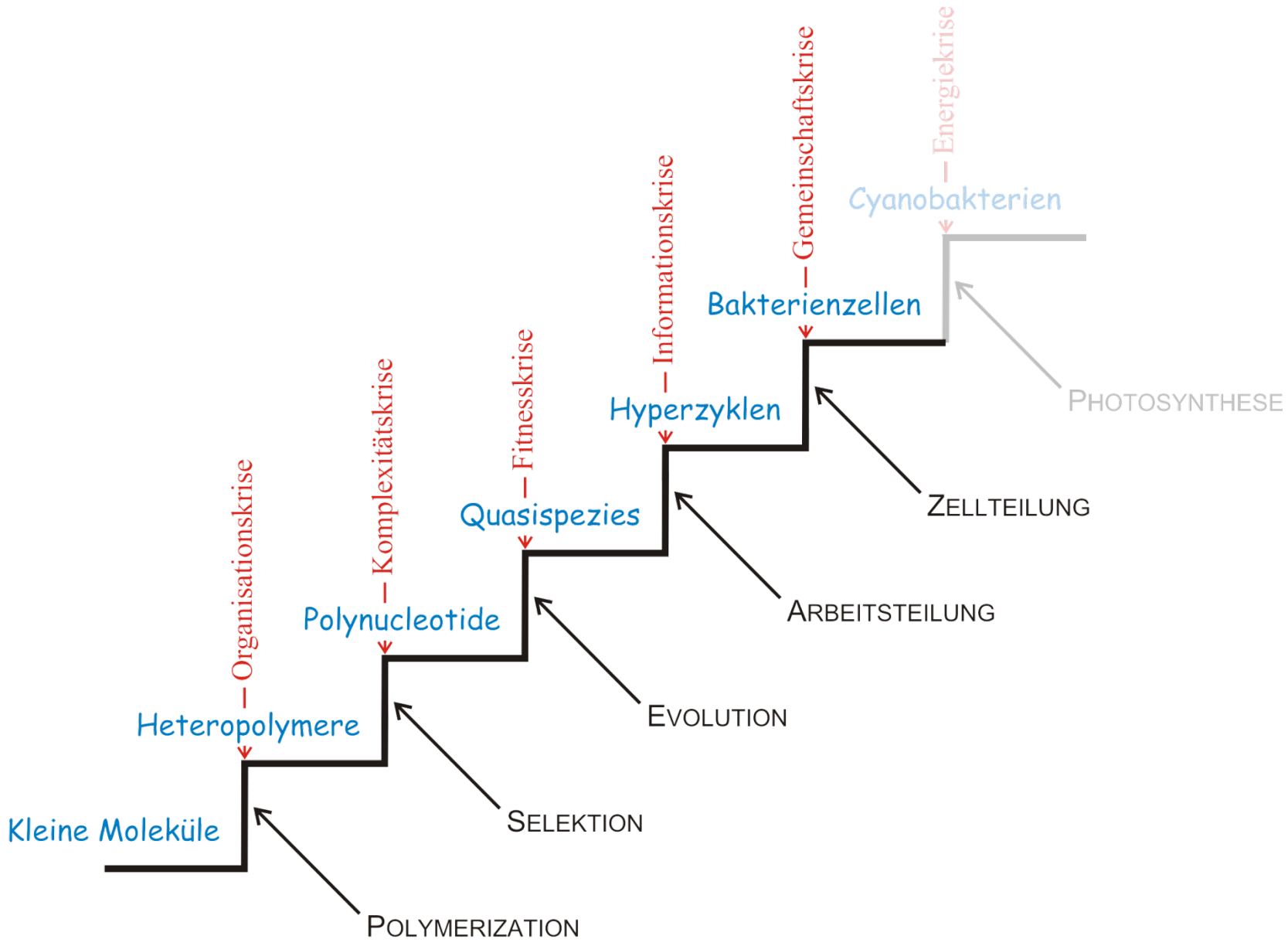
Replikation

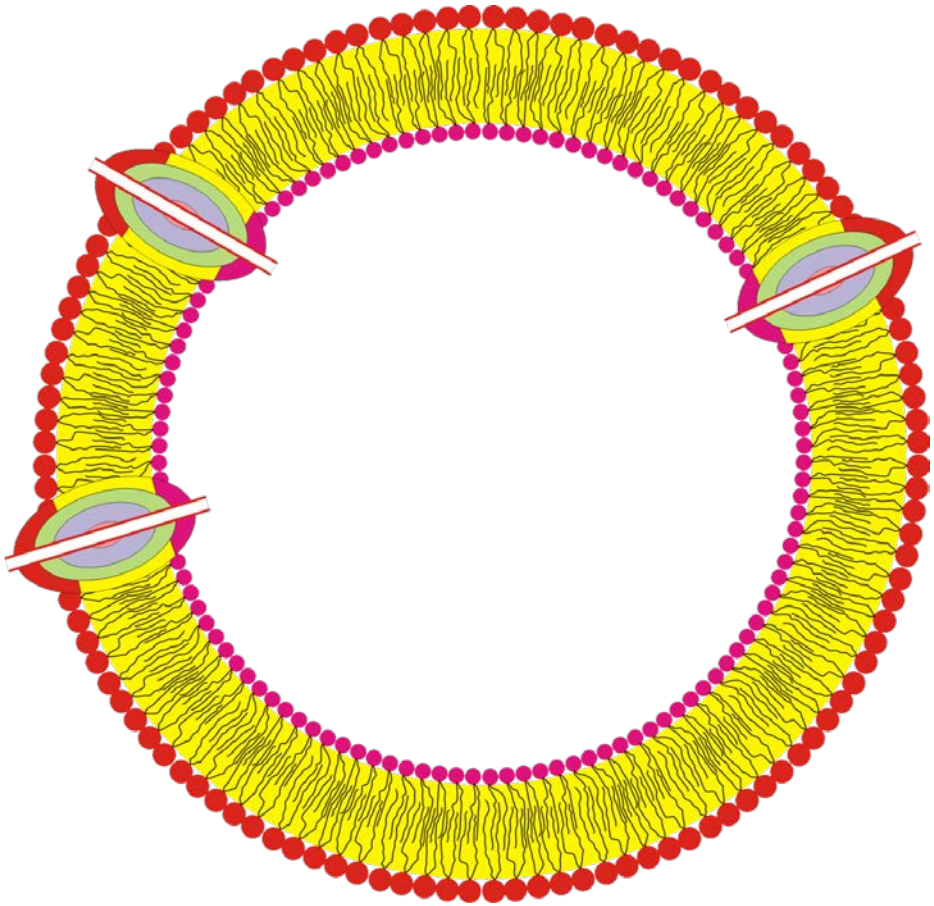
Translation

Die codierte genetische Information in der Biologie fließt von Nukleinsäure zu Nukleinsäure und von Nukleinsäure zu Protein.

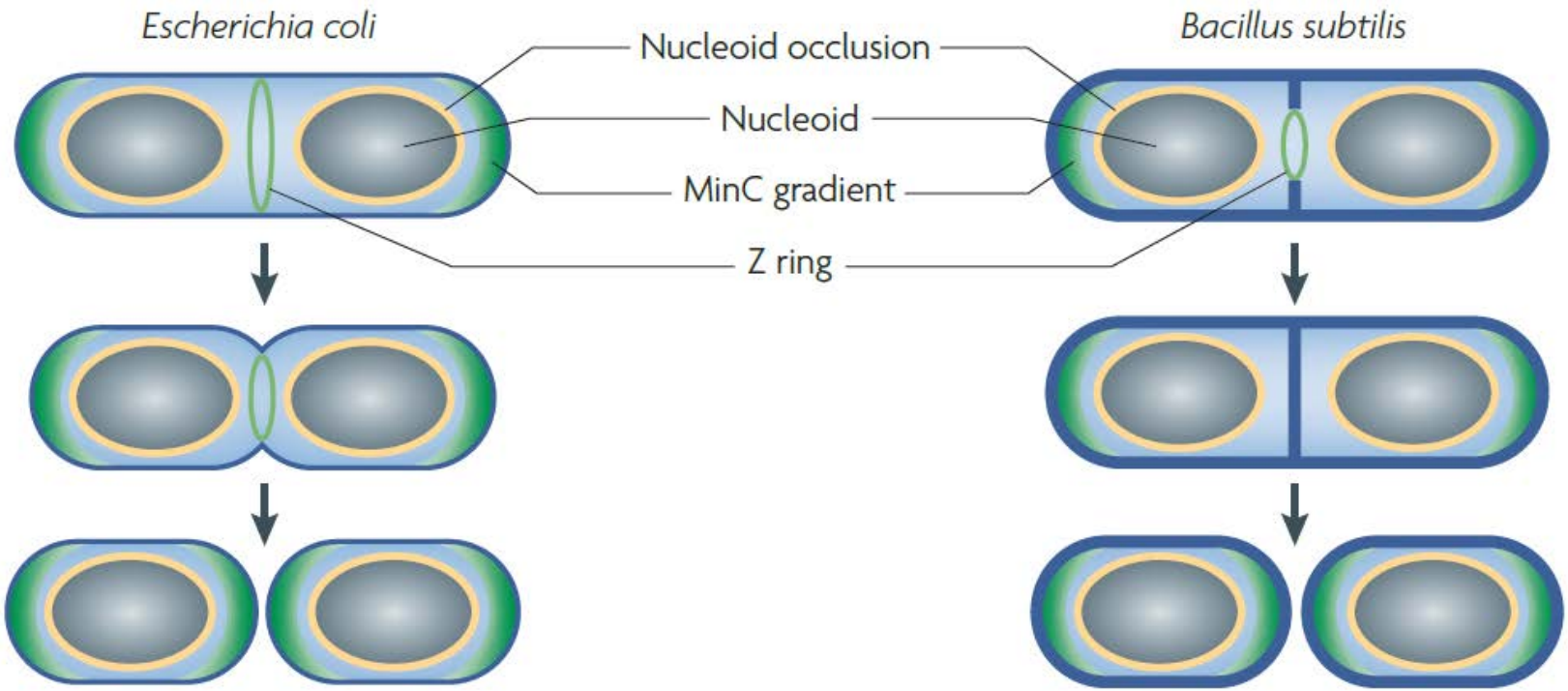
~~Die ein Gen ⇒ ein Protein Hypothese~~

Das zentrale „Dogma“ der Molekularbiologie

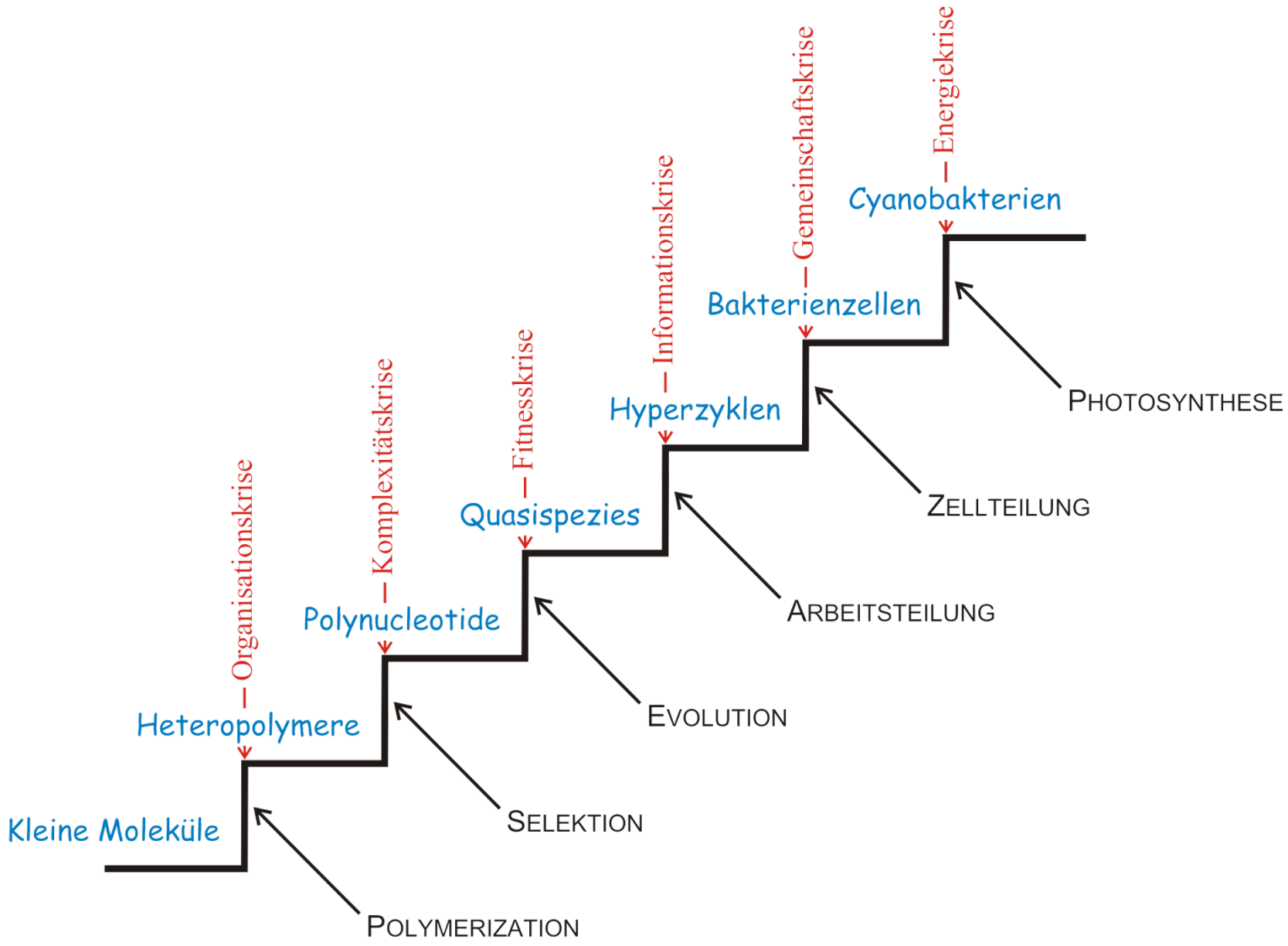

Kleine Moleküle
Heteropolymere
Polynucleotide
Quasispezies
Hyperzyklen
Bakterienzellen
Cyanobakterien
Organisationskrise
Komplexitätskrise
Fitnesskrise
Informationskrise
Gemeinschaftskrise
Energiekrise
POLYMERIZATION
SELEKTION
EVOLUTION
ARBEITSTEILUNG
ZELLTEILUNG
PHOTOSYNTHESE



Vesikel aus Lipidmembranen



Mechanismus der Zellteilung in Bakterien


Kleine Moleküle
Organisationskrise
Heteropolymere
Komplexitätskrise
Polynucleotide
Fitnesskrise
Quasispezies
Informationskrise
Hyperzyklen
Gemeinschaftskrise
Bakterienzellen
Energiekrise
Cyanobakterien
POLYMERIZATION
SELEKTION
EVOLUTION
ARBEITSTEILUNG
ZELLTEILUNG
PHOTOSYNTHESE

Blaualgen im Süßwasser

	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

Die großen Schritte der biologischen Evolution

Danke für die Aufmerksamkeit!

Web-Page für weitere Informationen:

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