

WS 2018/19

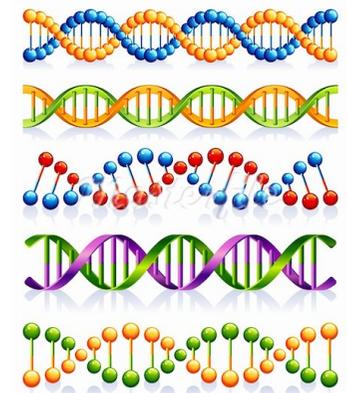
**Grundvorlesung Modul 8
„Allgemeine und Molekulare Genetik“**

- **Struktur und Funktion von Nukleinsäuren**
- **Chromosomen und Chromatin**
- **Replikation der DNA**
- **Transkription und Genregulation**
- **Gentechnologie**



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Aktualisierte Versionen der Vorlesung als PDF...



Institut für Organismische und Molekulare Evolutionsbiologie
Fachbereich Biologie
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AG Molekulargenetik und Genomanalyse

Informationen und Material zu Lehrveranstaltungen

- **MSc-Modul 7A/B „Genomforschung und Sequenzanalyse“ (AG Hankeln)**
Nächster Termin: Okt./Nov. 2017 (Anmeldung per JOGUstine)

PDFs zur Modul 7A-Vorlesung "Genomforschung und Sequenzanalyse" (T. Hankeln)

[\(1\)](#)[\(2\)](#)[\(3\)](#)[\(4\)](#) [\(5\)](#)[\(6\)](#)[\(7\)](#)[\(8\)](#)[\(9\)](#)[\(10\)](#)[\(11\)](#) [\(12\)](#) [Seq-Testfile zu VL1](#)

Ergänzende PDFs zum MSc-Modul 7A (F1-Praktikum „Genomforschung und Sequenzanalyse“)

[\(1\)](#)[\(2\)](#)[\(3\)](#)[\(4\)](#)[\(5\)](#)[\(6\)](#)

PDFs zur ergänzenden Vorlesung „Molekulare Evolution von Genen und Genomen“ (T. Hankeln)

[\(1\)](#) [\(2\)](#) [\(3\)](#) [\(4\)](#) [\(5\)](#) [\(6\)](#) [\(7\)](#) [\(8\)](#)

- **BSc-Modul 13/14 „Analyse von Eukaryotengeneten“ (AG Hankeln).**
Nächster Termin: 19.02.– 09.03. 2018, ganztags (Anmeldung per JOGUstine)

- **BSc-Modul 13/14 „Molekulargenetik der Eukaryoten“ (Hankeln, Kraemer).**
Nächster Termin: voraussichtlich Mai /Juni 2018, Durchführung halbtags (Anmeldung per JOGUstine)

- **BSc-Modul 8 Grundvorlesung & Grundpraktikum „Allgemeine und Molekulare Genetik“**
PDFs zur Grundvorlesung: [DNA Chromatin Replikation](#) [Genorganisation/Transkription1](#) [Transkription2](#) [Transkription3](#) [Gentechnologie](#)
PDFs zum Grundpraktikum: [\(Kurstag Chromosomen\)](#) [\(Kurstag DNA\)](#) [\(Kurstag Gentechnologie 1\)](#) [\(Kurstag Gentechnologie 2\)](#)

- **BSc MolBio Modul 10B (alte BSc-Ordnung) „Einführung in die Bioinformatik“**
PDF zur Vorlesung, Teil Hankeln [\(1\)](#) PDF zum Kursteil AG Hankeln [\(2\)](#)

- **BSc MolBio Modul 4-2 „Bioinformatik und Biostatistik“**
PDF zur Vorlesung, Teil Hankeln [\(A\)](#) [\(B\)](#)

- **PDF „Strahlenbiologie“ (T. Hankeln)** [VL Strahlenbiologie: PDF](#)

Oder im



<http://molgen.biologie.uni-mainz.de>



Für besonders Interessierte...



Also lautet ein Beschluss, dass der Mensch
was lernen muss...
(auch im Selbststudium)

Die PDFs auf Homepage/Reader enthalten bisweilen
Zusatzfolien als Erweiterung und zum tieferen Verständnis.

3

Aber: auch Vorlesung hat spezielles *Bonusmaterial*...😊

Struktur und Funktion von Nukleinsäuren

...von der DNA zum „Personal Genome“



An animated primer on the basics of DNA, genes, and heredity.

www.dnafb.org Kap. 17, 19, 31, 32, 39

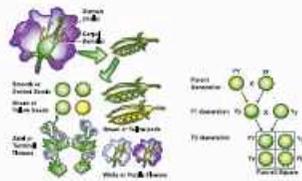
Zur historischen Einordnung....



Gene: An Evolving Concept



Gregor Mendel



The laws of inheritance were described.

1865

1869



The nucleic acids were isolated and studied by Friedrich Miescher.

The rediscovery of Mendel's work by Carl Correns, Erich von Tschermak-Seysenegg, and Hugo De Vries prompted the foundation of genetics.

1900

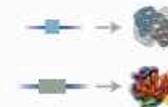


Thomas Morgan



Studies in *Drosophila melanogaster* suggest a linear model of genes on chromosomes, like 'beads on a string.'

1910



One gene, one enzyme; Then one gene, one protein.

Artificial transmutation of the gene by X-ray was reported by Hermann Müller.

1927



Francis Crick James Watson

The DNase experiment by Avery, MacLeod, and McCarty suggested transformation is induced by DNA.

1941

1944



The DNA double helix structure was solved.

1953

Gene as a discrete heredity unit

Gene as a distinct locus

Gene as a physical molecule

Gene as a protein blueprint

A term invented almost a century ago, 'gene,' with its beguilingly simple orthography, has become a central concept in biology. Given a specific meaning at its coinage, this word has evolved into something complex and elusive over the years, reflecting our ever-expanding knowledge in genetics and in life sciences at large. The stunning discoveries made in the ENCODE Project—like many before that significantly enriched the meaning of this term—are harbingers of another tide of change in our understanding of what a gene is.

The first appearance of the word 'gene,' derived from the Greek *genesis* or *genos*.

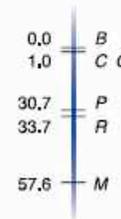


Wilhelm Johannsen

1909

1913

Alfred Sturtevant constructed the first genetic map.



Griffith's experiment demonstrating type-switching in *pneumococcus* suggested a transforming principle.

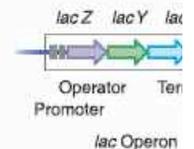
1928

Hershey and Chase determined that DNA is the genetic material.



Alfred Hershey Martha Chase

The operon, described by François Jacob Jacques Monod, demonstrated transcription control.



lac Operon

1952

ing Concept



James Watson

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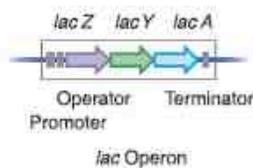
The **DNA double helix** structure was solved,

1944

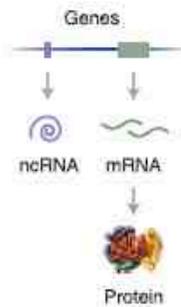
molecule
a protein blueprint

1952

The **operon**, described by François Jacob and Jacques Monod, demonstrated **transcriptional control**,



3SE



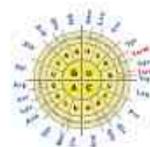
The '**Central Dogma**' of molecular biology was proposed by Francis Crick.

1958

Gene as transcribed code

1961

The **genetic code** was deciphered by Marshall Nirenberg, Har Gobind Khorana, and others.



1965



The **first sequence** of a gene, *COAT_BPMS2*, was determined.

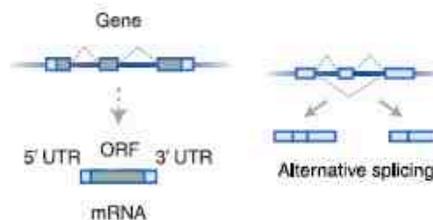
1972

The first large-scale **gene function** analysis using gene expression in yeast

Gene as ORF sequence pattern

1977

Introns and the mechanism of **RNA splicing** were discovered by Phillip Sharp and Richard Roberts demonstrating 'split gene structure.'



```

ATGCGTATA
ATGATCTGGCTT
TACCCCTCTATTT
CTTCTACAGCCCA
ACTGGTTGTTT
TTTCTCTGTA
    
```

GENSCAN, a computer program for **gene structure prediction**, became available.

1994

Gene as annotated genomic entity

1997

The **ENCODE Project** was launched.



2003

The drafts of the **human genome sequence** were published.

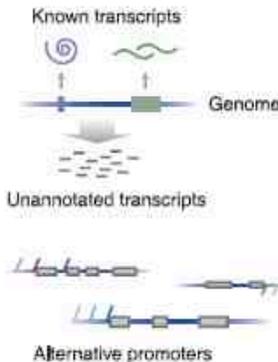
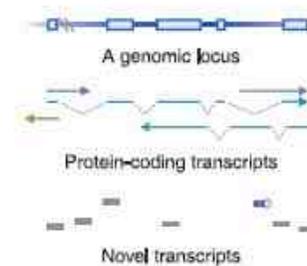
2001

The ENCODE Project highlighted the **complexity** of gene transcription and regulation.

Gene as ...

2007

The pilot phase of the ENCODE Project was finished. New gene models are proposed.



Unannotated transcripts

Alternative promoters

Zwei Typen...

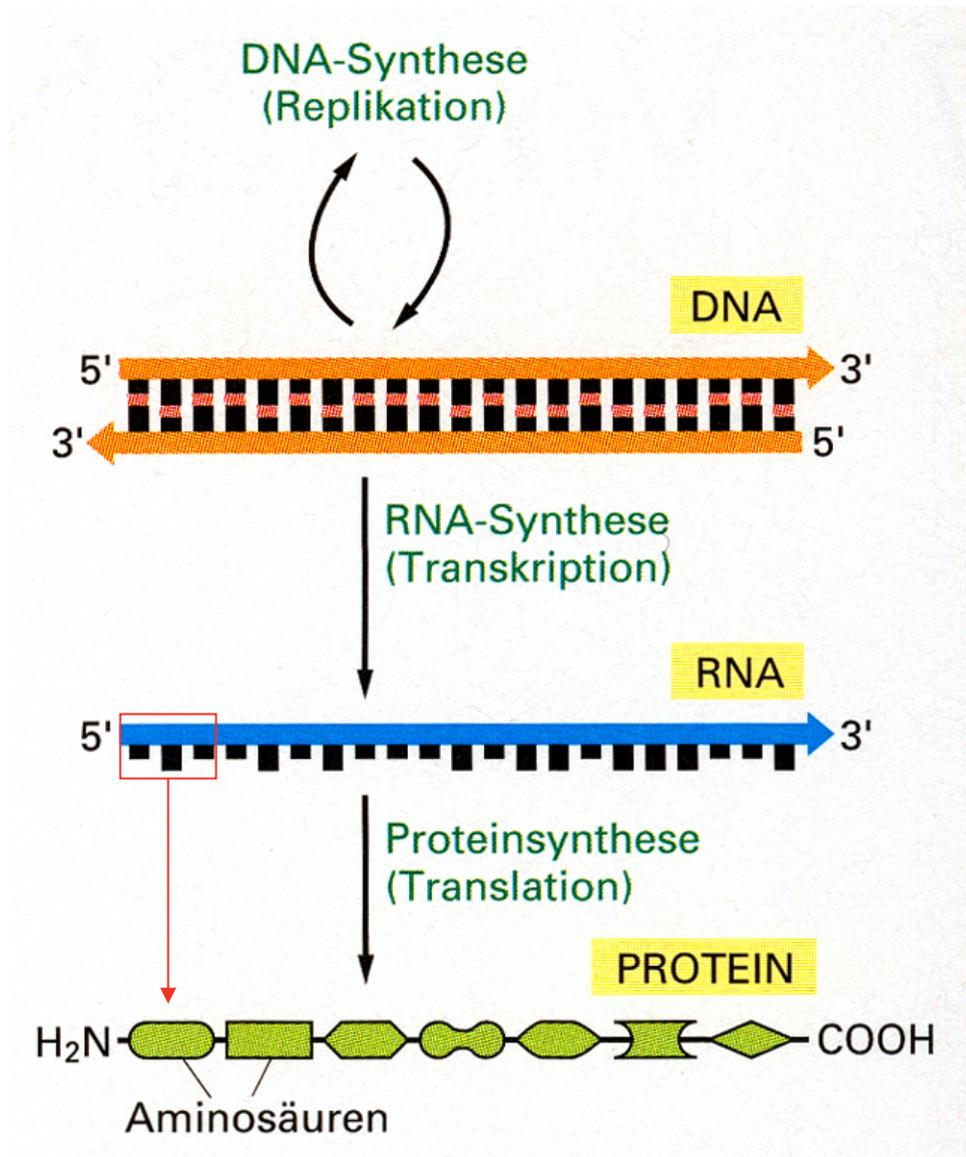


- Desoxyribonukleinsäure DNA
- Ribonukleinsäure RNA

Die Erbinformation aller Lebewesen ist die Desoxyribonukleinsäure (DNA).

(Viren können auch RNA haben)

Die Umsetzung der genetischen Information*

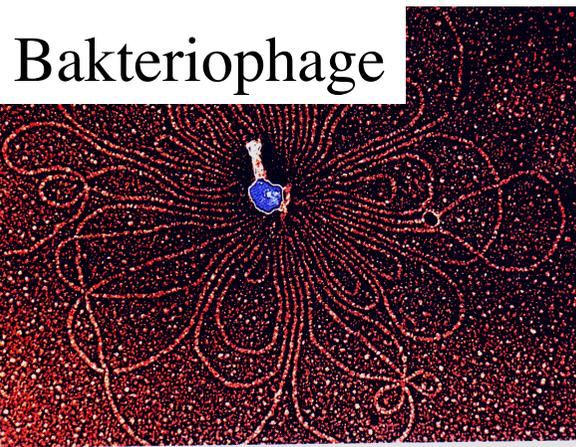
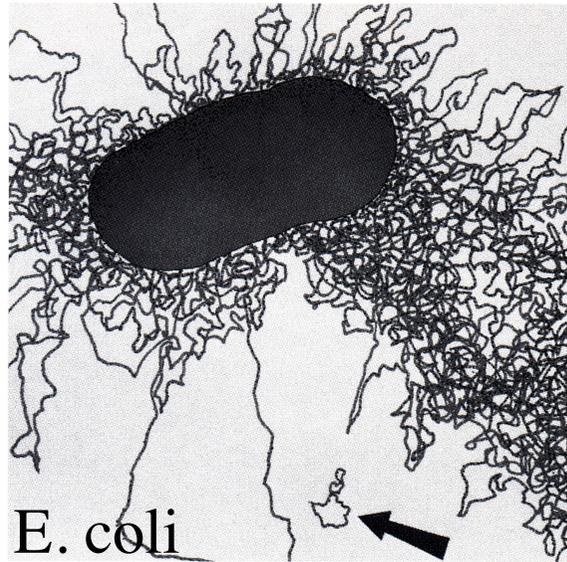


Informationsspeicher

Informationsabschrift

Genprodukt

DNA im Elektronenmikroskop



Gerüst („Scaffold“)

Friedrich Miescher (1844-1895)

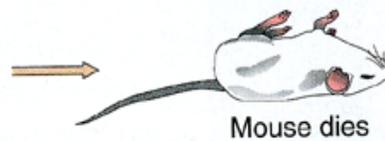


„Sofern wir annehmen wollten, dass eine einzelne Substanz auf irgendeine Art die spezifische Ursache der Befruchtung sei, so müsste man ohne Zweifel vor allem an das Nuklein denken.“ (1874)

Entdeckung der DNA als „Nuklein“ in Zellkernen von weißen Blutkörperchen (1869)

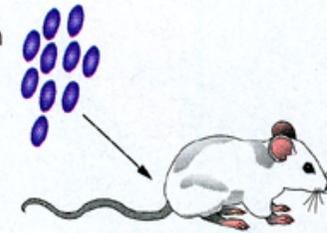
Griffith 1928: das Prinzip der „Transformation“

Streptococcus pneumoniae



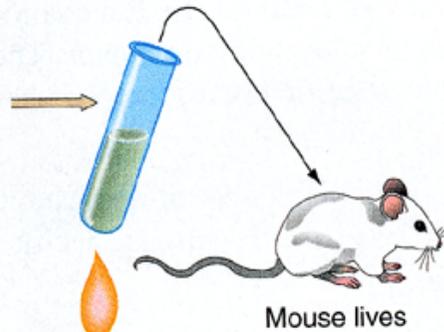
(a)

R strain

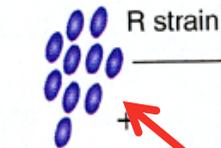


Mouse lives

(b)



(c)



Mouse dies

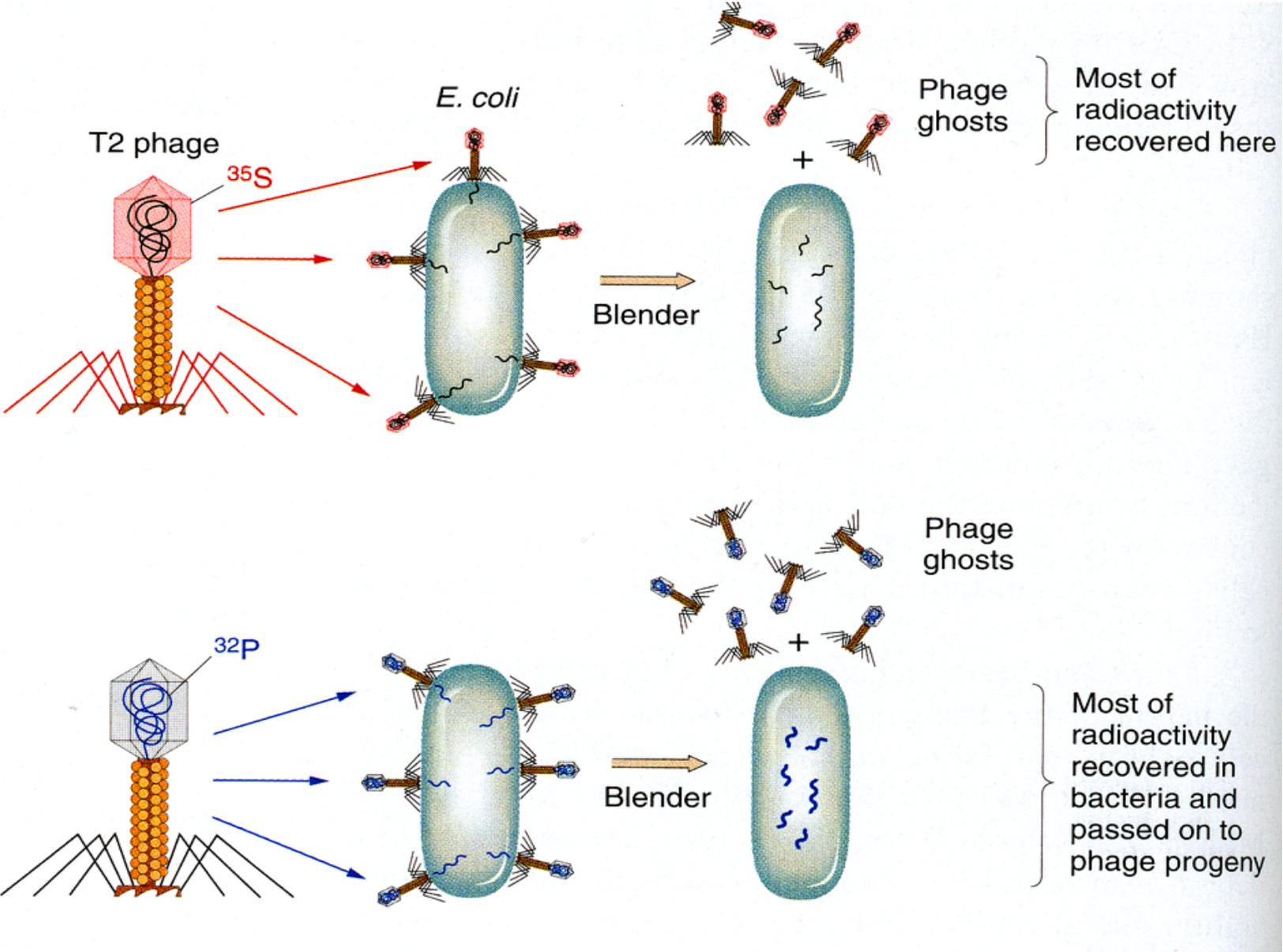
(d)

Avery, MacLeod & McCarty 1944

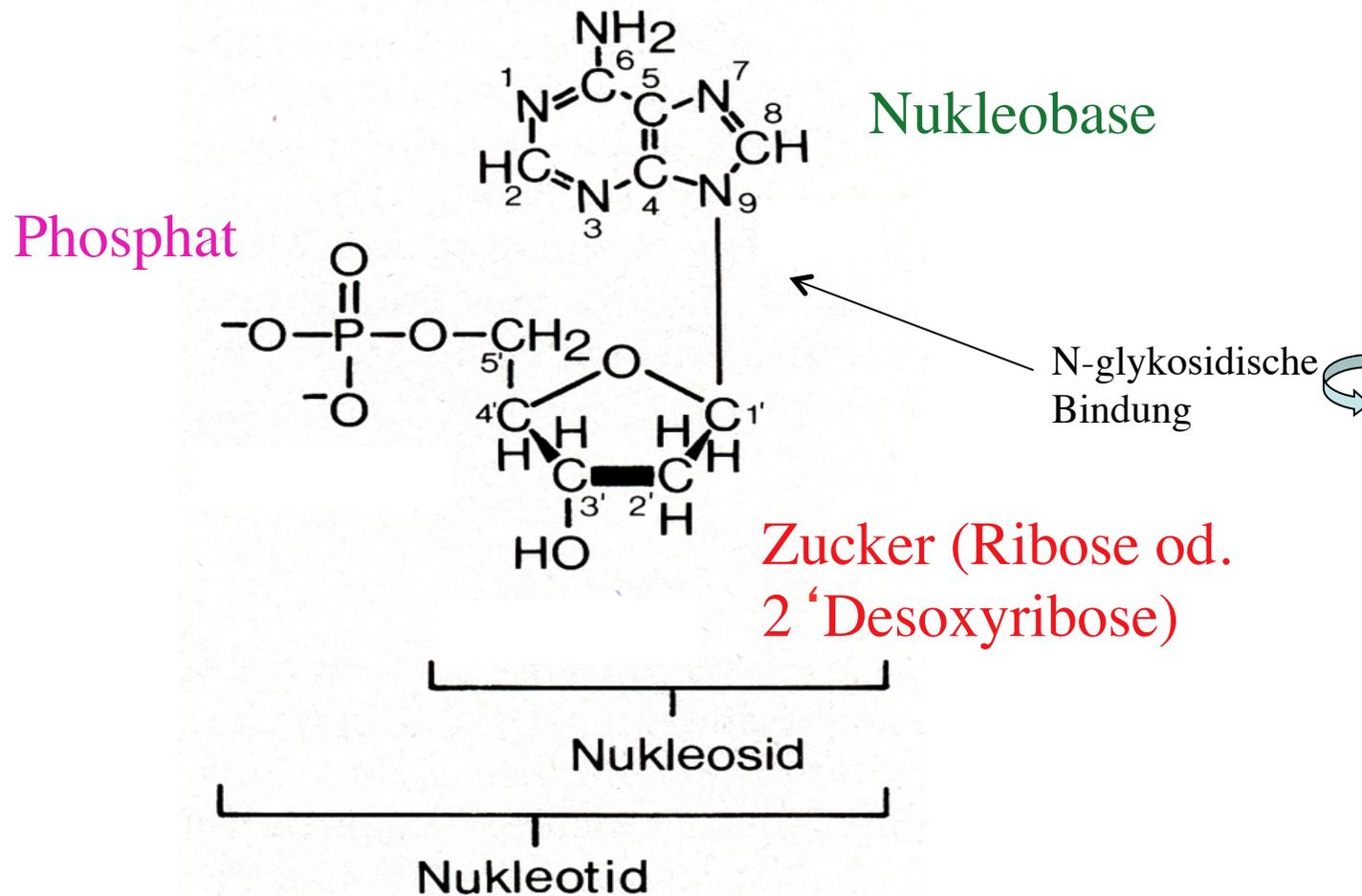
- „Verfeinerung“ des Griffith-Experiments durch Behandlung des virulenten Zellextrakts mit Nukleasen (DNasen oder RNasen) bzw. Proteasen
- Ergebnis: nur Behandlung mit **DNasen** verhindert Transformation!
Daher ist die DNA das „transformierende Prinzip“

„If the results of the present study on the chemical nature of the transforming principle are confirmed, then nucleic acids must be regarded as possessing biological specificity, the chemical basis of which is as yet undetermined“

Hershey & Chase 1952: „DNA ist die Erbinformation“



Die Bausteine von DNA/RNA sind die NUKLEOTIDE



Und dann kam sie, die Eine-Million-Euro-Frage.

Frage: „Welches zählt zu den fünf Elementen, die die Grundbausteine der menschlichen DNA sind?“

A: Phosphor

B: Neon

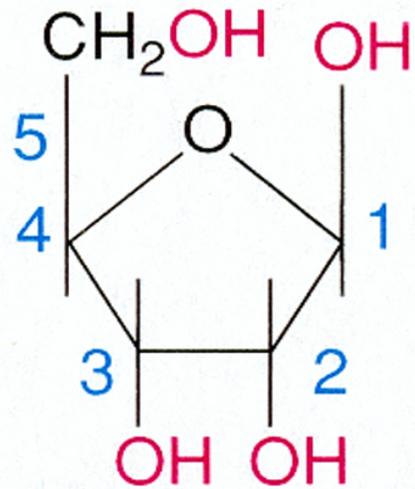
C: Magnesium

D: Chlor

Kaiser hielt kurz inne, wurde sich dann aber wohl ihres bisherigen Glücks bewusst. Sie nahm die 500.000 Euro und ging nach Hause. Was sie mit

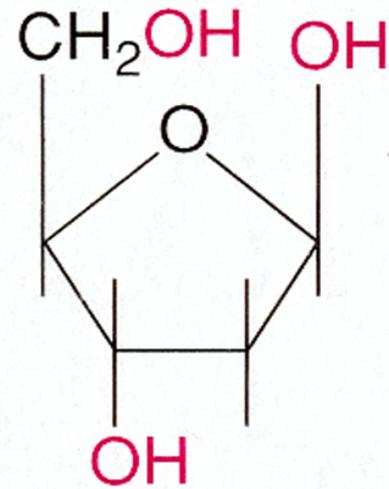


Zwei Typen von Pentose-Zuckern in Nukleinsäuren...



Ribose

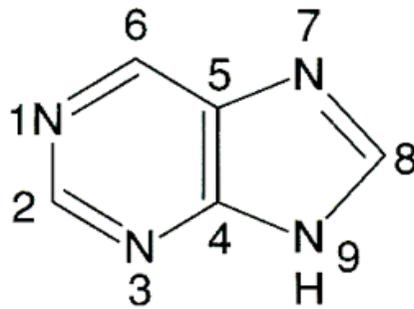
RNA



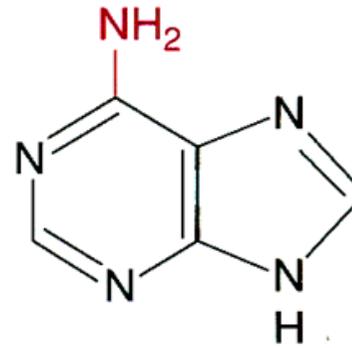
2-deoxyribose

DNA

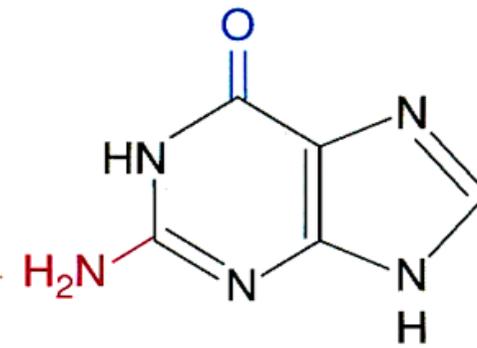
Die (häufigsten) Nukleobasen



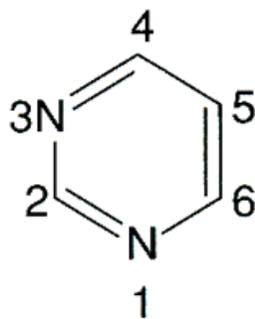
Purine



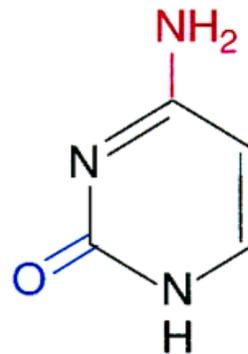
Adenine



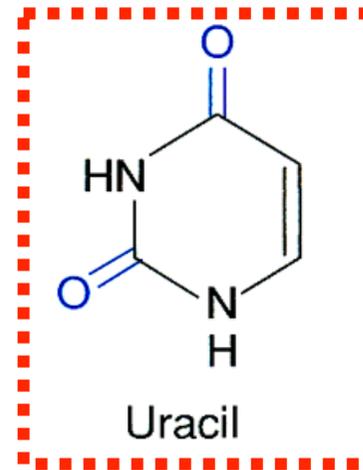
Guanine



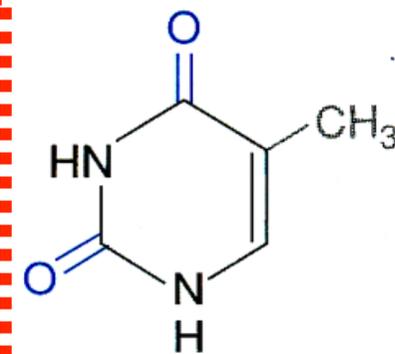
Pyrimidine



Cytosine



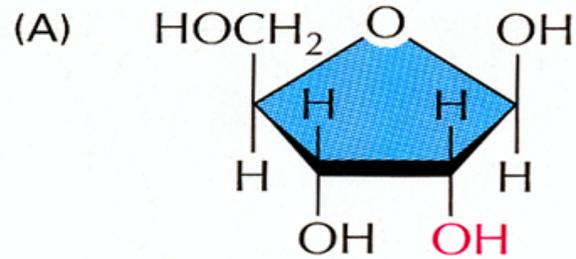
Uracil



Thymine

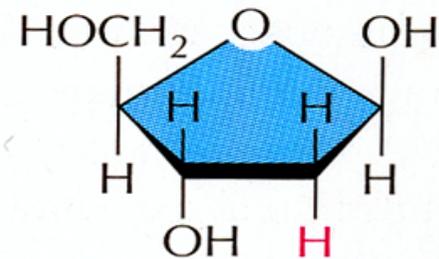
nur in RNA!
(statt Thymin)

DNA versus RNA



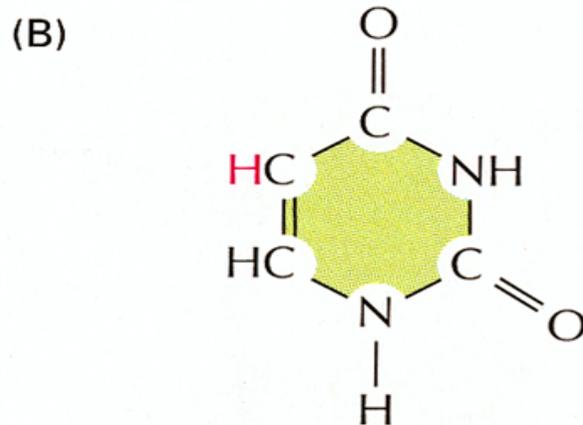
Ribose

Verwendung in
Ribonucleinsäure
(RNA)



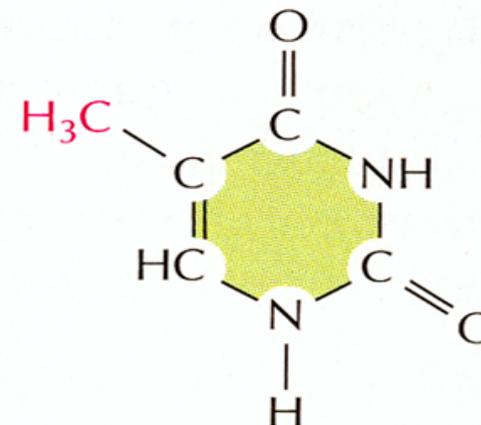
Desoxyribose

Verwendung in
Desoxyribonuclein-
säure (DNA)



Uracil

Verwendung in RNA

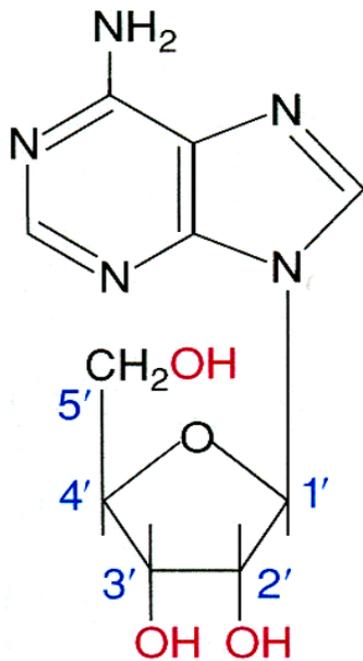


Thymin

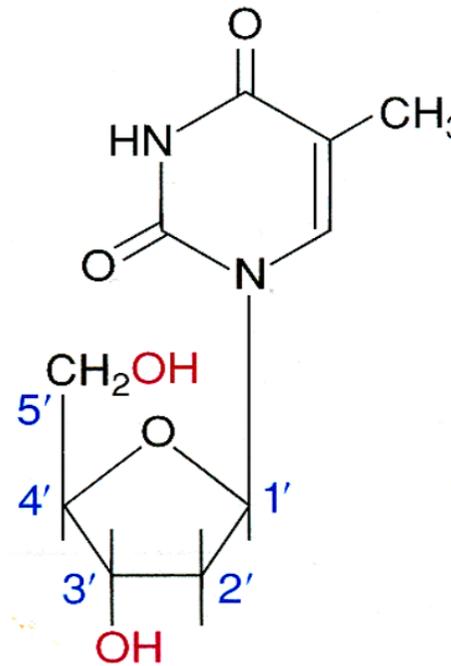
Verwendung in DNA

Die Nukleoside

- Adenin + Zucker > Adenosin
- Thymin + Zucker > Thymidin
- Guanin + Zucker > Guanosin
- Cytosin + Zucker > Cytidin
- Uracil + Zucker > Uridin

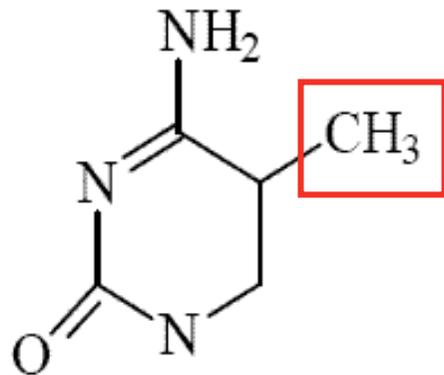


Adenosine



2' -deoxythymidine

Immer wichtiger: Die „*fünfte* Base der DNA“



5-Methylcytosin

- existiert als Modifikation in allen Lebewesen
- bei Säugetieren:
In „CpG“-Abfolge sind 60-80% der Cytosine methyliert

- Bedeutung für **Mutationsentstehung** („Hotspot“),
- **Genregulation** und Epigenetik (5mC korreliert mit Gen-**Inaktivität**)



...und die Nr. 6!



- bereits 1952 in Bakteriophagen-DNA erstmals entdeckt
- 2009: Säugetiere haben Gene für Hydroxylasen (Tet), die aus 5mC das 5hmC herstellen
- 2011: Tet wandelt 5mC in noch 2 weitere C-Basen-Intermediate um und bewirkt wohl damit **DEMETHYLIERUNG** von DNA (**>Genregulation**)

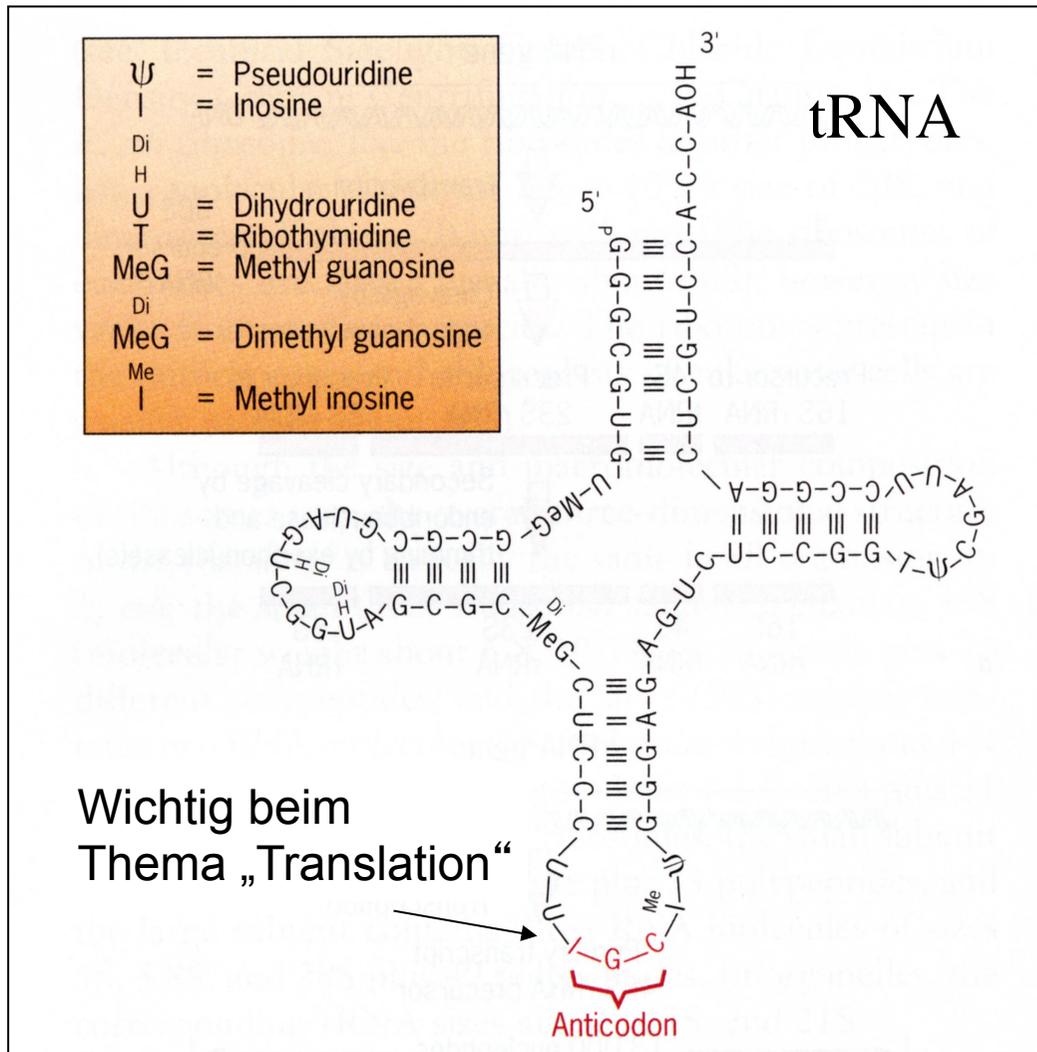


Tet-Mediated Formation of 5-Carboxylcytosine and Its Excision by TDG in Mammalian DNA

Yu-Fei He,^{1*} Bin-Zhong Li,^{1*} Zheng Li,¹ Peng Liu,¹ Yang Wang,¹ Qingyu Tang,² Jianping Ding,² Yingying Jia,² Zhangcheng Chen,² Lin Li,² Yan Sun,³ Xiuxue Li,³ Qing Dai,⁴ Chun-Xiao Song,⁴ Kangling Zhang,⁵ Chuan He,⁴ Guo-Liang Xu^{1†}

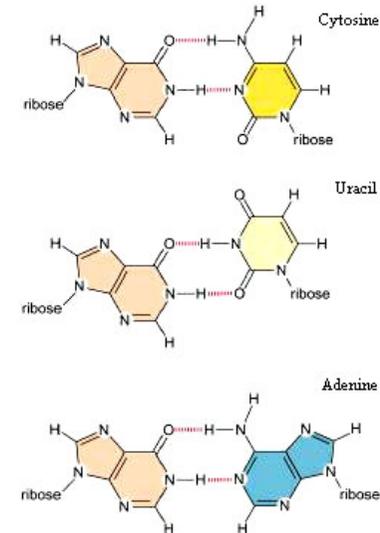
The prevalent DNA modification in higher organisms is the methylation of cytosine to 5-methylcytosine (5mC), which is partially converted to 5-hydroxymethylcytosine (5hmC) by the Tet (ten eleven translocation) family of dioxygenases. Despite their importance in epigenetic regulation, it is unclear how these cytosine modifications are reversed. Here, we demonstrate that 5mC and 5hmC in DNA are oxidized to 5-carboxylcytosine (5caC) by Tet dioxygenases in vitro and in cultured cells. 5caC is specifically recognized and excised by thymine-DNA glycosylase (TDG). Depletion of TDG in mouse embryonic stem cells leads to accumulation of 5caC to a readily detectable level. These data suggest that oxidation of 5mC by Tet proteins followed by TDG-mediated base excision of 5caC constitutes a pathway for active DNA demethylation.

Basen-Modifikationen gibt es auch in der RNA!



Inosin = Nukleosid der Purinbase ‚Hypoxanthin‘

I paart mit C/U/A

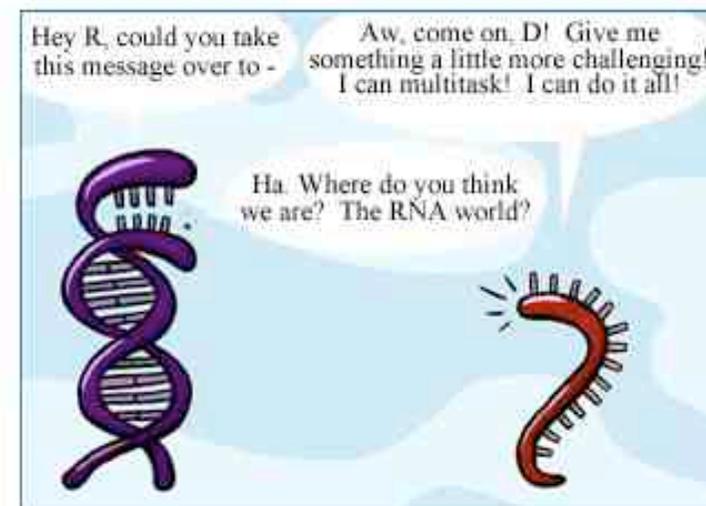
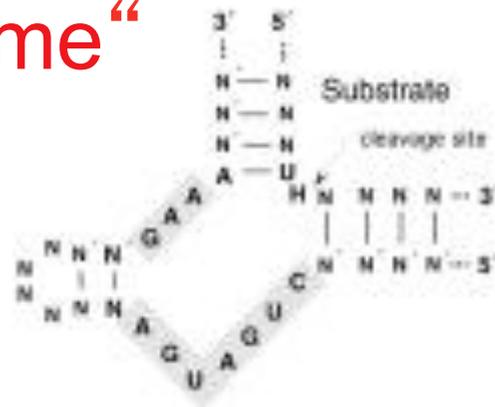


...und RNA bildet zudem mit sich selbst Doppelstränge!



RNA kann noch mehr...

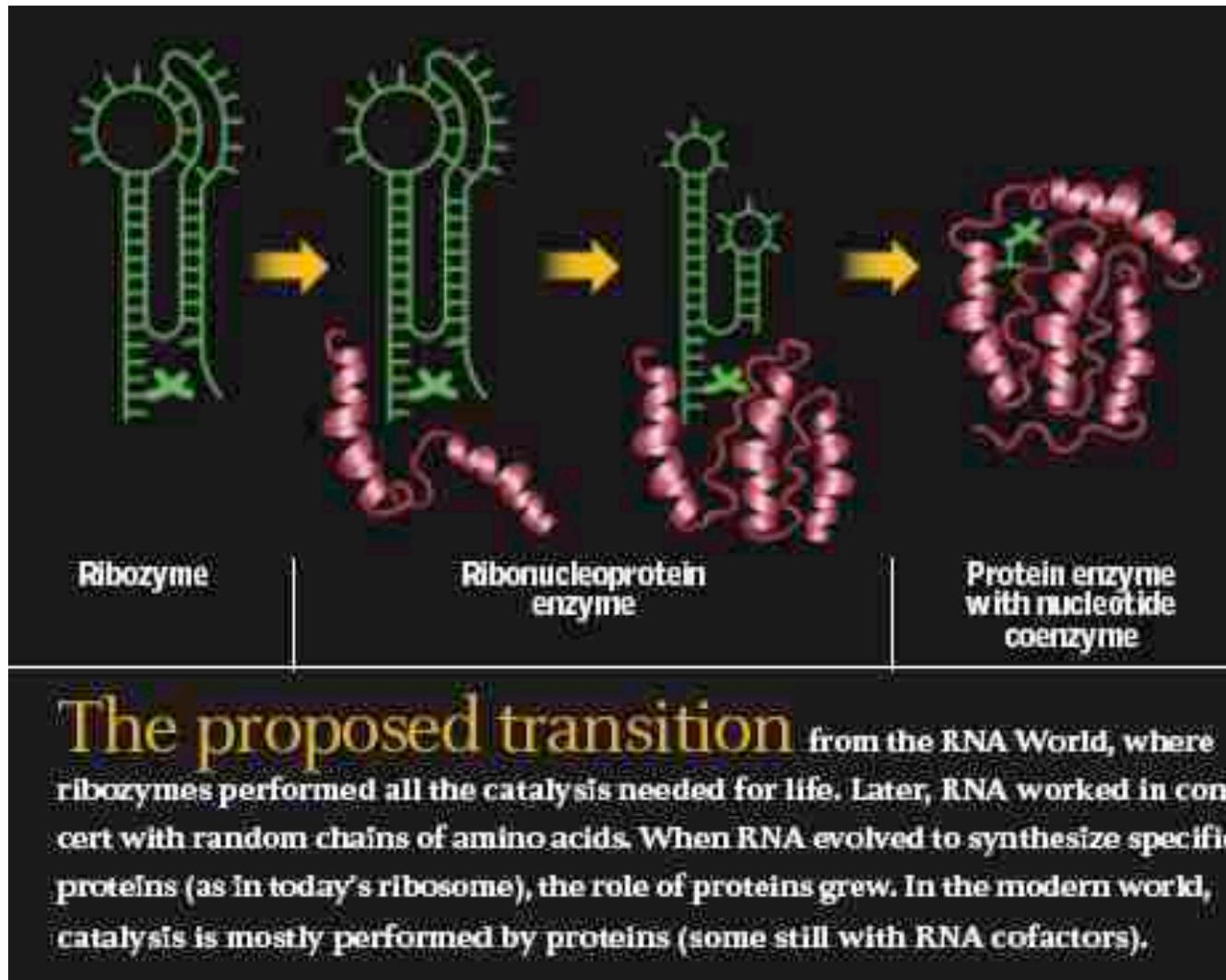
„Ribozyme“



RNA ist mehr als eine reine Abschrift:
Sie kann Information **speichern**, sich **replizieren**
und sogar Enzym-Funktionen **ausführen**!



Eine RNA-Welt?



Zurück zur DNA...

Die Chargaff-Regeln



TABLE ADAPTED FROM CHARGAFF'S 1949 PAPER

DNA SOURCE	ADENINE	THYMINE	GUANINE	CYTOSINE
Calf Thymus	1.7	1.6	1.2	1.0
Beef Spleen	1.6	1.5	1.3	1.0
Yeast	1.8	1.9	1.0	1.0
Tubercle Bacillus	1.1	1.0	2.6	2.4



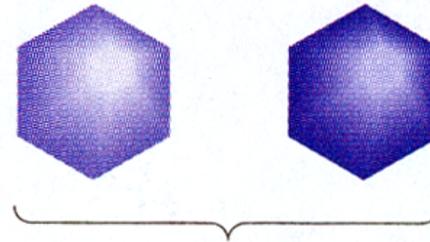
Die Basenzusammensetzung ist

- artspezifisch
- gleich in verschiedenen Geweben eines Individuums
- unabhängig von Faktoren wie Alter, Ernährung etc.

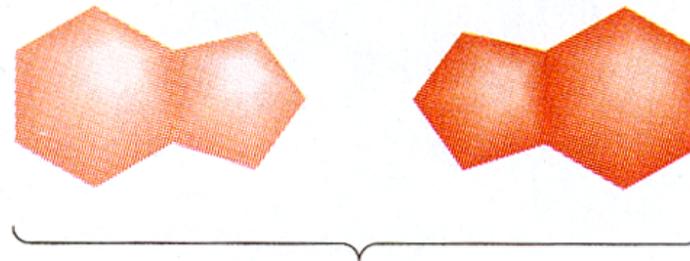
Mengenmäßig gilt $A = T$, $C = G$ und $A+G = T+C$

Röntgen-Strukturdaten zeigten...

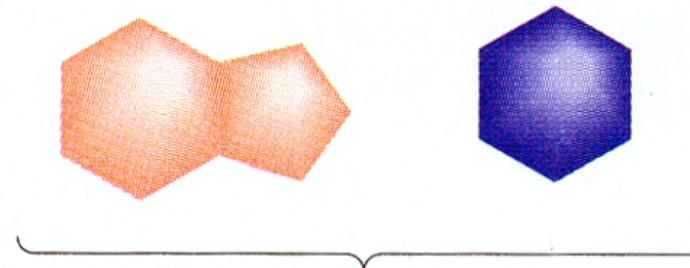
Pyrimidine + pyrimidine: DNA too thin



Purine + purine: DNA too thick

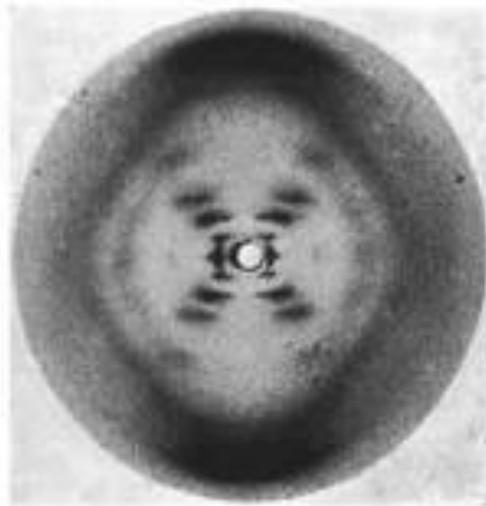


Purine + pyrimidine: thickness compatible with X-ray data



James Watson, *The Double Helix*:

„In dem Augenblick, als ich das Bild sah, klappte mir der Unterkiefer herunter, und mein Puls flatterte. Das Schema war unvergleichlich viel einfacher als alle, die man bis dahin erhalten hatte ... [Maurice Wilkins gab jedoch zu bedenken,] das eigentliche Problem sei noch immer das Fehlen einer Strukturhypothese, die gestatte, die Basen auf regelmäßige Weise auf der Innenseite der Spirale anzuordnen. Das setzte natürlich voraus, dass Rosy [Rosalind Franklin] recht hatte, wenn sie die Basen im Zentrum und das Skelett außen haben wollte! Obwohl Maurice mir versicherte, er sei jetzt völlig von der Richtigkeit ihrer Behauptungen überzeugt, blieb ich skeptisch, denn Francis [Crick] und ich konnten ihren Beweis noch immer nicht recht verstehen.“



ARTICLE & INTERVIEW

[Before Watson and Crick](#)

Brenda Maddox, author of *Rosalind Franklin: The Dark Lady of DNA*, describes the discoveries that lead scientists to focus on DNA as the secret behind life.



[Defending Franklin's Legacy](#)

Hear one biologist's perspective on why Rosalind Franklin should have shared the Nobel Prize for the discovery of DNA's structure.



SLIDE SHOW & INTERACTIVES

[Picturing the Molecules of Life](#)

Over the past 50 years, scientific images of DNA, ribosomes, and RNA have catalyzed our understanding of these amazing molecules.



[Anatomy of Photo 51](#)

When you know how to look at it, this shadowy X-ray photograph speaks volumes about the shape of DNA.



[Journey into DNA](#)

Where does DNA live inside the human body, and how is it packaged? Take an animated journey into the tiny world of DNA to find out.



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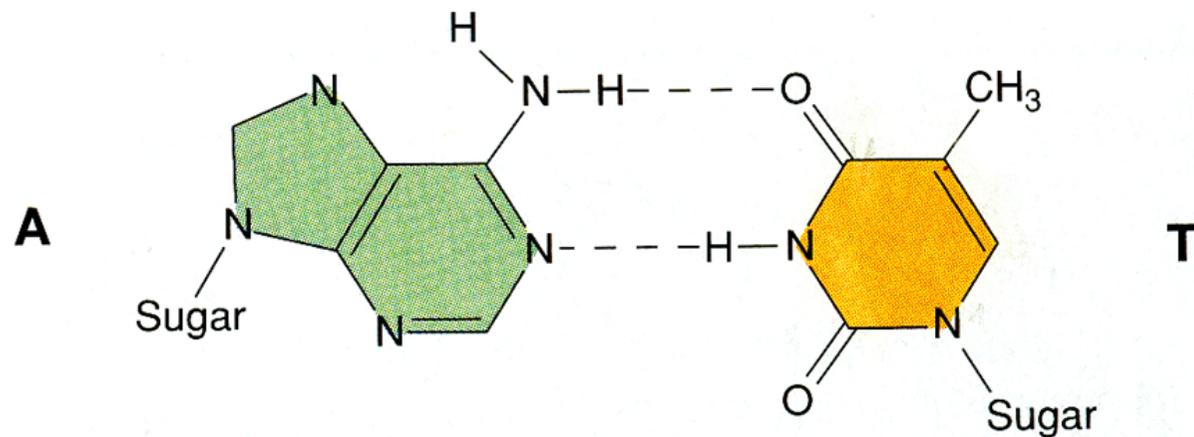
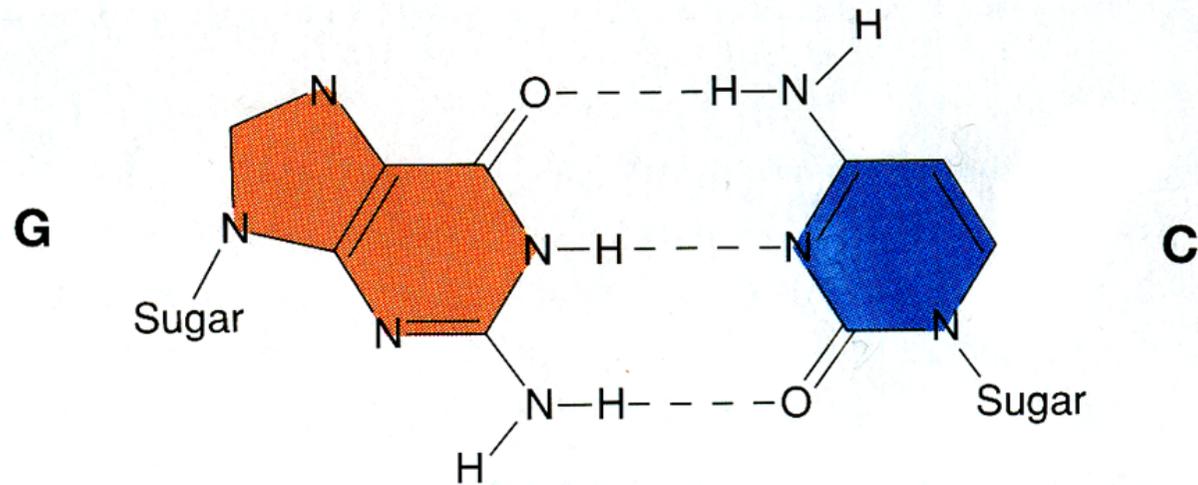
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Die Basenpaarungen in der DNA

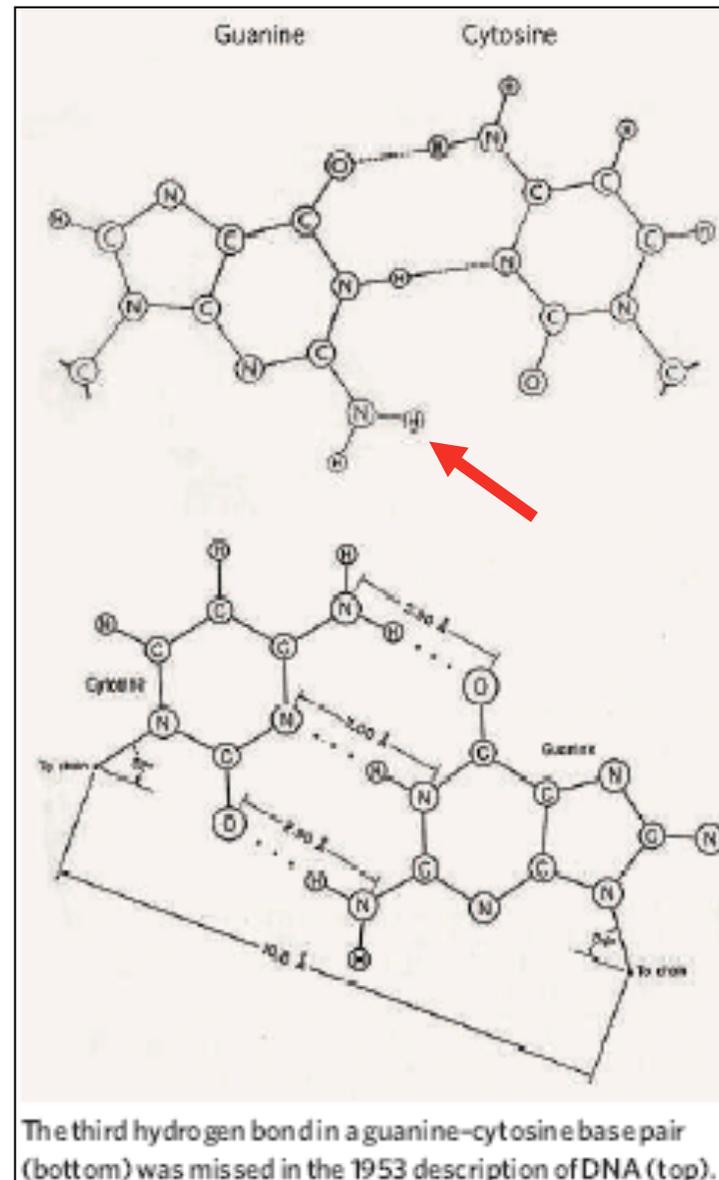
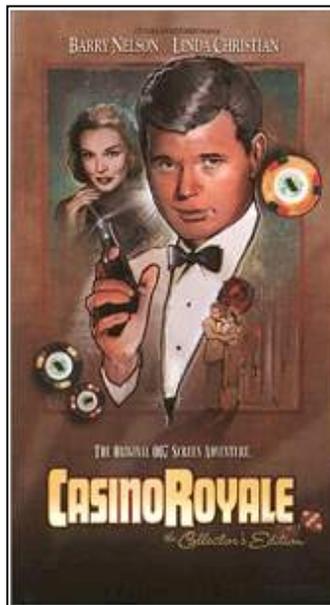




The 3rd bond...

The 1st Bond...

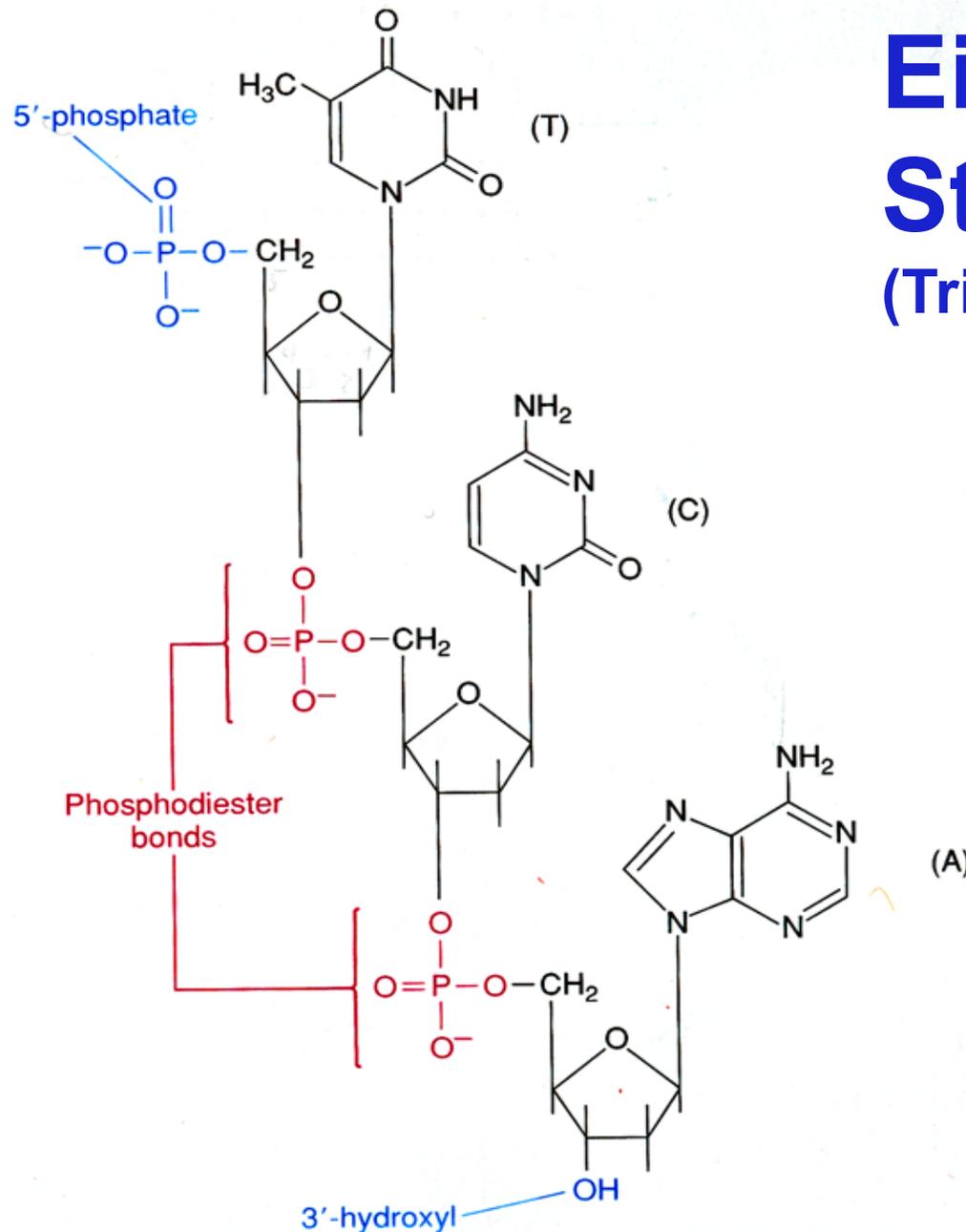
1953



1953
Watson
& Crick

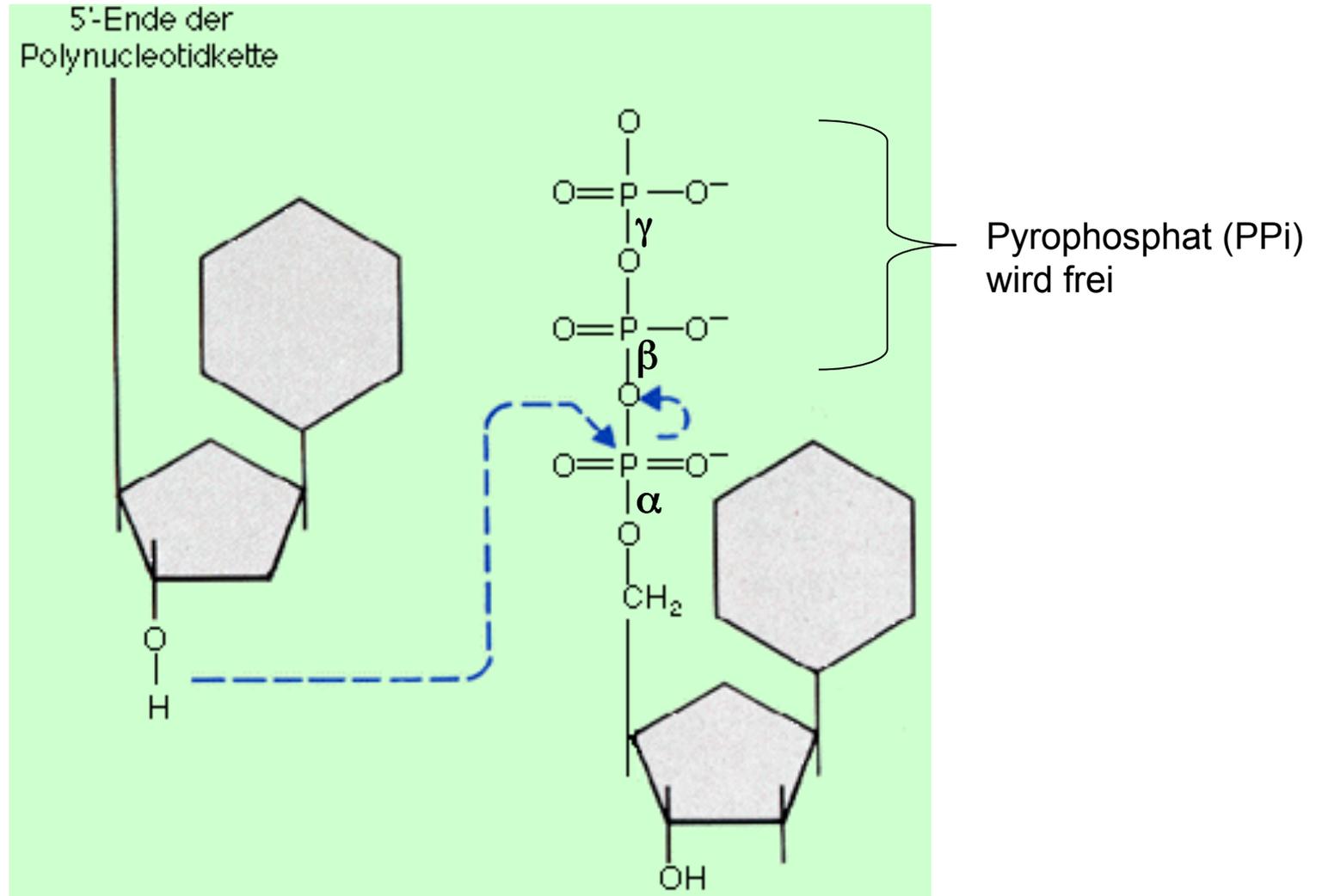
1956
Corey
& Pauling

Ein kurzes Stück DNA... (Trinukleotid, Einzelstrang)

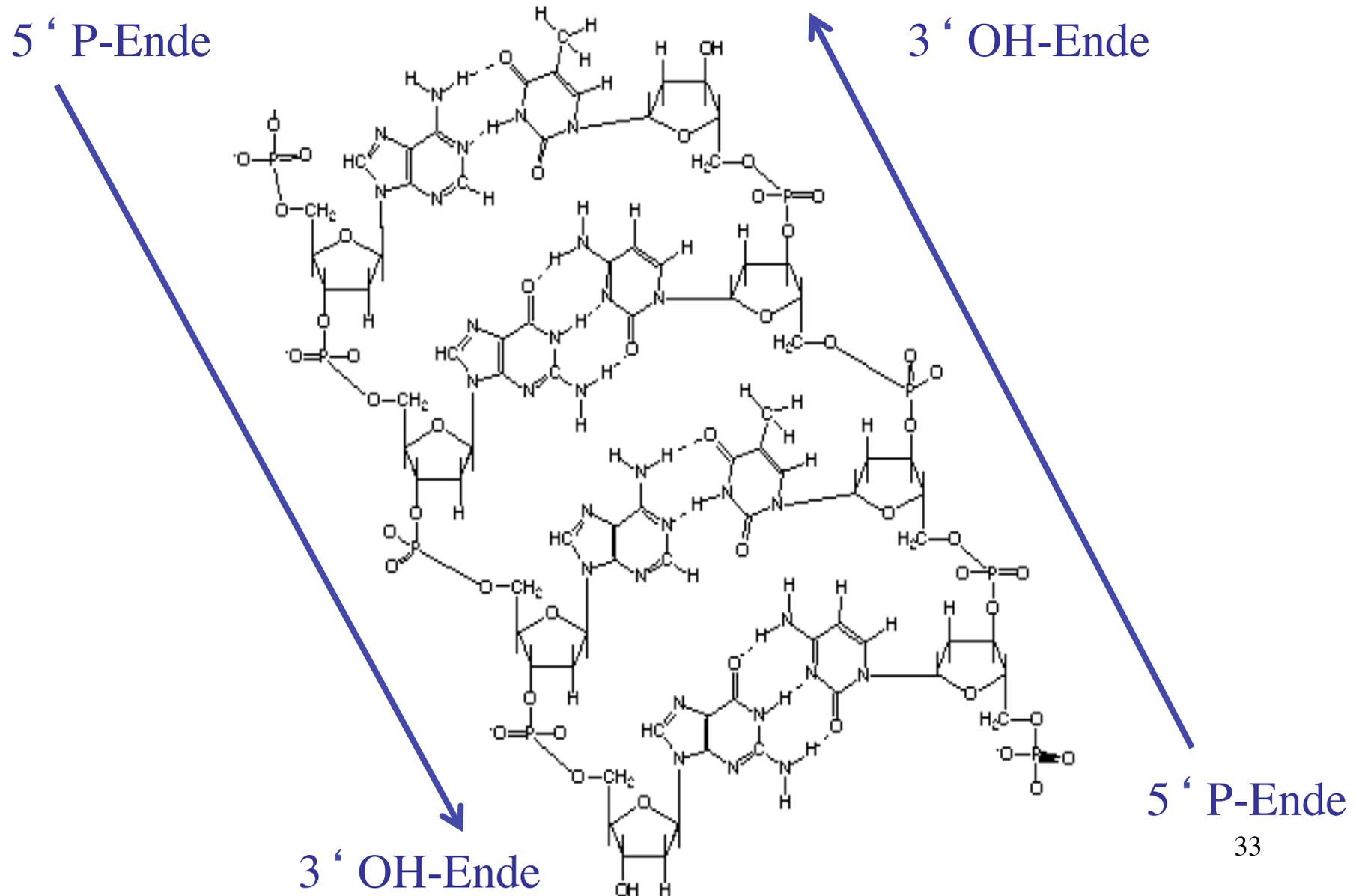


DNA-Moleküle haben unterschiedliche Enden (5' Phosphat bzw. 3' OH) und damit eine Richtung!

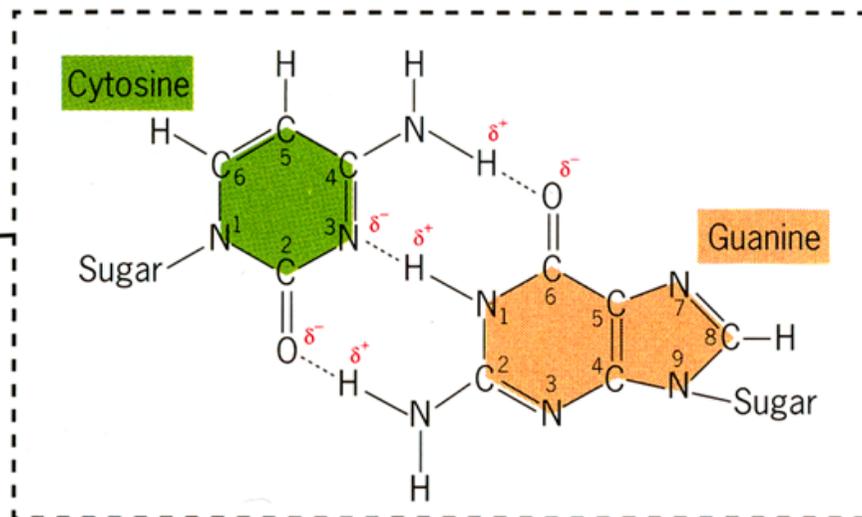
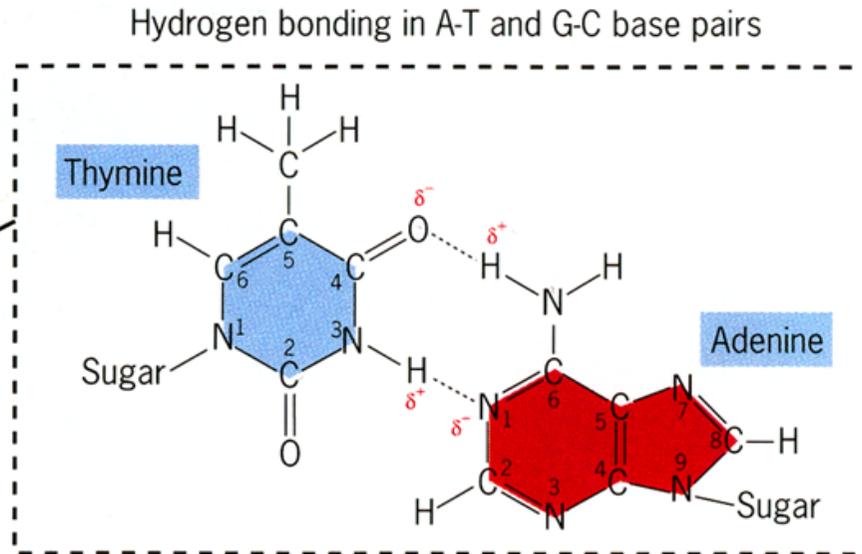
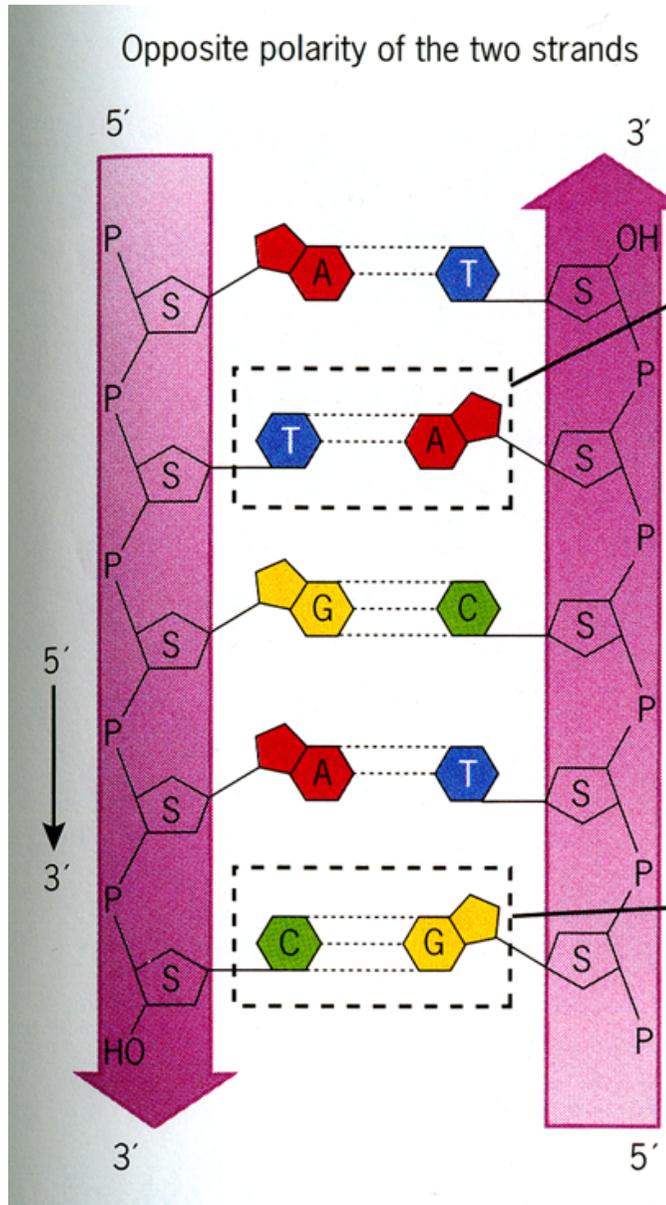
Die 3' - 5' - Phosphodiesterbindung



Die DNA-Stränge sind **anti-parallel** !



Der DNA-Doppelstrang



Schreiben einer DNA-Sequenz...

- immer von links (5 ' Ende) nach rechts (3 ' Ende)
- meist nur ein Strang („Watson“ oder „Crick“)

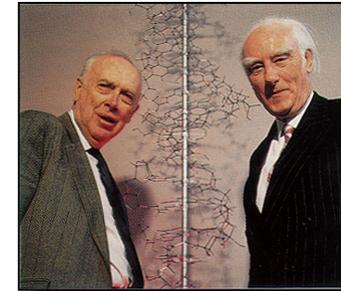
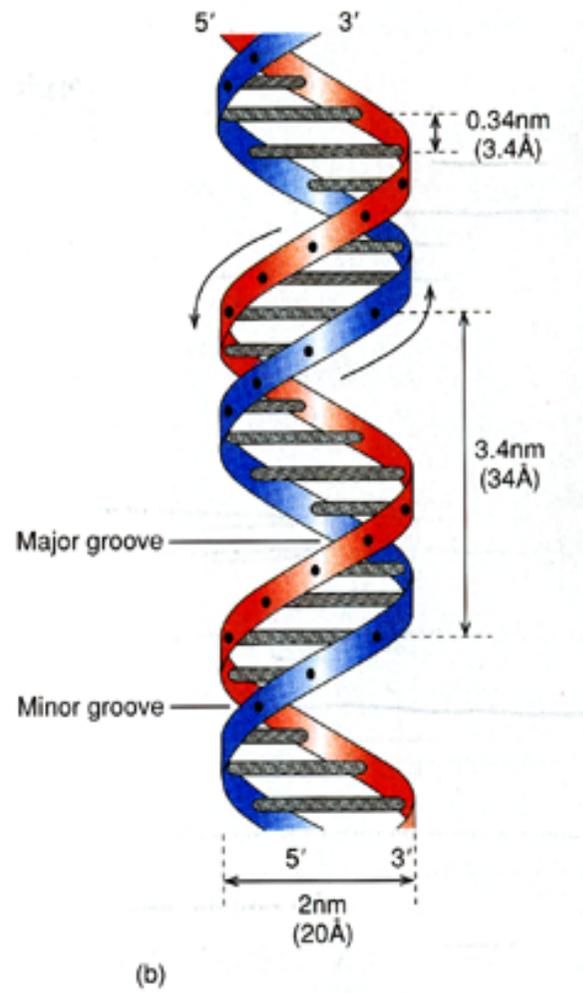
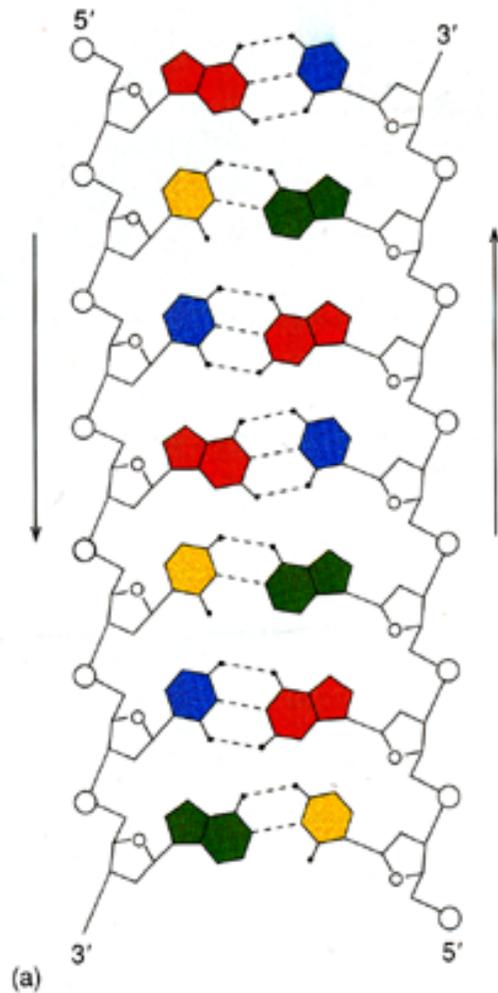
Beispiel:

5 '-**GAGGGCTACTGCA**-3 '

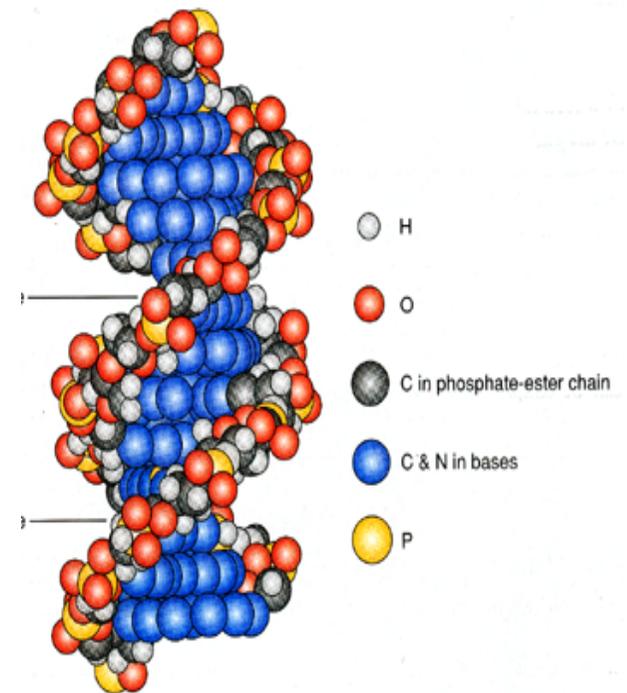
oder

5 '-**TGCAGTAGCCCTC**-3 '

Die Watson-Crick Doppelhelix (B-Helix)



+29.7.2004

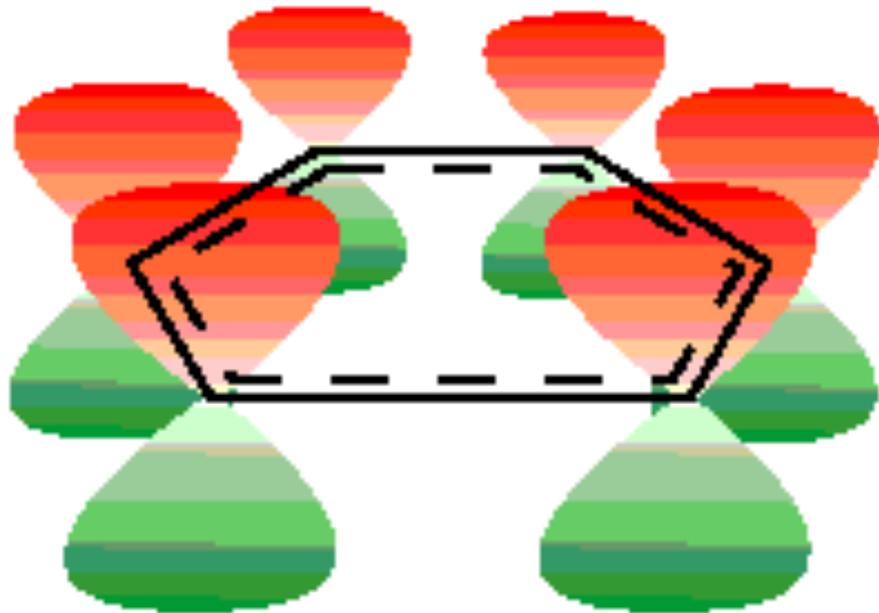




Die DNA...

- ist ein Polymer aus **Desoxy-Nukleotiden**, die über 3 ' -5 ' Phosphodiester-Brücken verbunden sind
- besteht aus **2 Einzelsträngen**, die über Wasserstoffbrücken-Bindungen zwischen den Basen zusammengehalten werden
- Die Einzelstränge sind **komplementär, antiparallel** und **plektonämisch** verwunden (= Doppelhelix)
- trägt ihre Information in der Abfolge der Basen!

Stapelkräfte stabilisieren die DNA

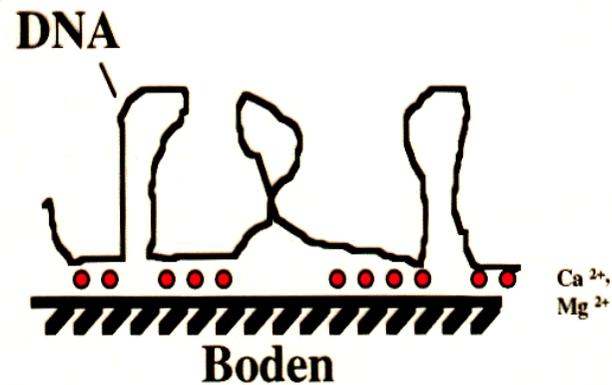


Ringsysteme mit
konjugierten
Doppelbindungen
haben π -Elektronen-
wolken

π -Elektronen der übereinander liegenden
Basen interagieren



DNA ist in der Umwelt stabil



DNA bindet an negativ geladene Bodenpartikel über Salzbrücken
➤ schützt sogar vor Abbau durch DNasen!

„Ancient DNA“ Science und Fiction





New insights into the Tyrolean Iceman's origin and phenotype as inferred by whole-genome sequencing

Andreas Keller^{1,2,*}, Angela Graefen^{3,*}, Markus Ball^{4,*}, Mark Matzas⁵, Valesca Boisguerin⁵, Frank Maixner³, Petra Leidinger¹, Christina Backes¹, Rabab Khairat⁴, Michael Forster⁶, Björn Stade⁶, Andre Franke⁶, Jens Mayer¹, Jessica Spangler⁷, Stephen McLaughlin⁷, Minita Shah⁷, Clarence Lee⁷, Timothy T. Harkins⁷, Alexander Sartori⁷, Andres Moreno-Estrada⁸, Brenna Henn⁸, Martin Sikora⁸, Ornella Semino⁹, Jacques Chirani¹⁰, Siiri Rootsi¹¹, Natalie M. Myres¹², Vicente M. Cabrera¹³, Peter A. Underhill⁸, Carlos D. Bustamante⁸, Eduard Egarter Vigl¹⁴, Marco Samadelli³, Giovanna Cipollini³, Jan Haas¹⁵, Hugo Katus¹⁵, Brian D. O'Connor^{16,17}, Marc R.J. Carlson¹⁸, Benjamin Meder¹⁵, Nikolaus Blin^{4,19}, Eckart Meese¹, Carsten M. Pusch⁴ & Albert Zink³

The Tyrolean Iceman, a 5,300-year-old Copper age individual, was discovered in 1991 on the Tisenjoch Pass in the Italian part of the Ötztal Alps. Here we report the complete genome sequence of the Iceman and show 100% concordance between the previously reported mitochondrial genome sequence and the consensus sequence generated from our genomic data. We present indications for recent common ancestry between the Iceman and present-day inhabitants of the Tyrrhenian Sea, that the Iceman probably had brown eyes, belonged to blood group O and was lactose intolerant. His genetic predisposition shows an increased risk for coronary heart disease and may have contributed to the development of previously reported vascular calcifications. Sequences corresponding to ~60% of the genome of *Borrelia burgdorferi* are indicative of the earliest human case of infection with the pathogen for Lyme borreliosis.



Adrian Mettauer

FORSCHUNG

DNA überlebt Flug ins All

27.11.2014 - Forscher haben Erbgut an die Außenwand einer Rakete geheftet. Ihren ersten Weltraumflug haben die unsichtbaren Passagiere bestens überstanden.

Die besten Aktionen entstehen aus spontanen Ideen – das gilt auch für Weltraumexperimente. Schweizer Forscher wollten ursprünglich nur die Rolle der Schwerkraft bei der Regulation der Genexpression in menschlichen Zellen untersuchen. Während der Vorbereitung dieser Weltraummission kam die Frage auf, ob sich die Außenstruktur der Rakete auch für Stabilitätstests von so genannten Biosignaturen eignet – also Molekülen, welche die Existenz von aktuellen oder früheren Lebensvorgängen belegen können. Die Forscher einigten sich auf ein Zusatzexperiment als Vortest, um die Stabilität von Biomarkern bei Raumflug und Wiedereintritt in die Atmosphäre zu prüfen. Vor dem Start der Forschungsmission TEXUS-49 platzierte das Team um Oliver Ullrich vom Anatomischen Institut der Universität Zürich kleine doppelsträngige DNA-Moleküle an verschiedene Stellen der Außenhülle des Nutzlast-Bereichs der Rakete. Im März 2011 wurden die unsichtbaren Weltalltouristen von der nordschwedischen Basis in Kiruna (siehe Bild) auf ihre Reise geschickt.

 PLOS ONE

RESEARCH ARTICLE

Functional Activity of Plasmid DNA after Entry into the Atmosphere of Earth Investigated by a New Biomarker Stability Assay for Ballistic Spaceflight Experiments

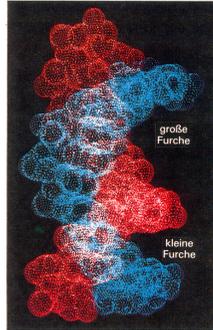
Cora S. Thiel^{1*}, Svantje Tauber^{1,2}, Andreas Schütte³, Burkhard Schmitz², Harald Nuesse⁴, Ralf Moeller⁵, Oliver Ullrich^{1,2,6*}

zurück zum Kerngeschäft...

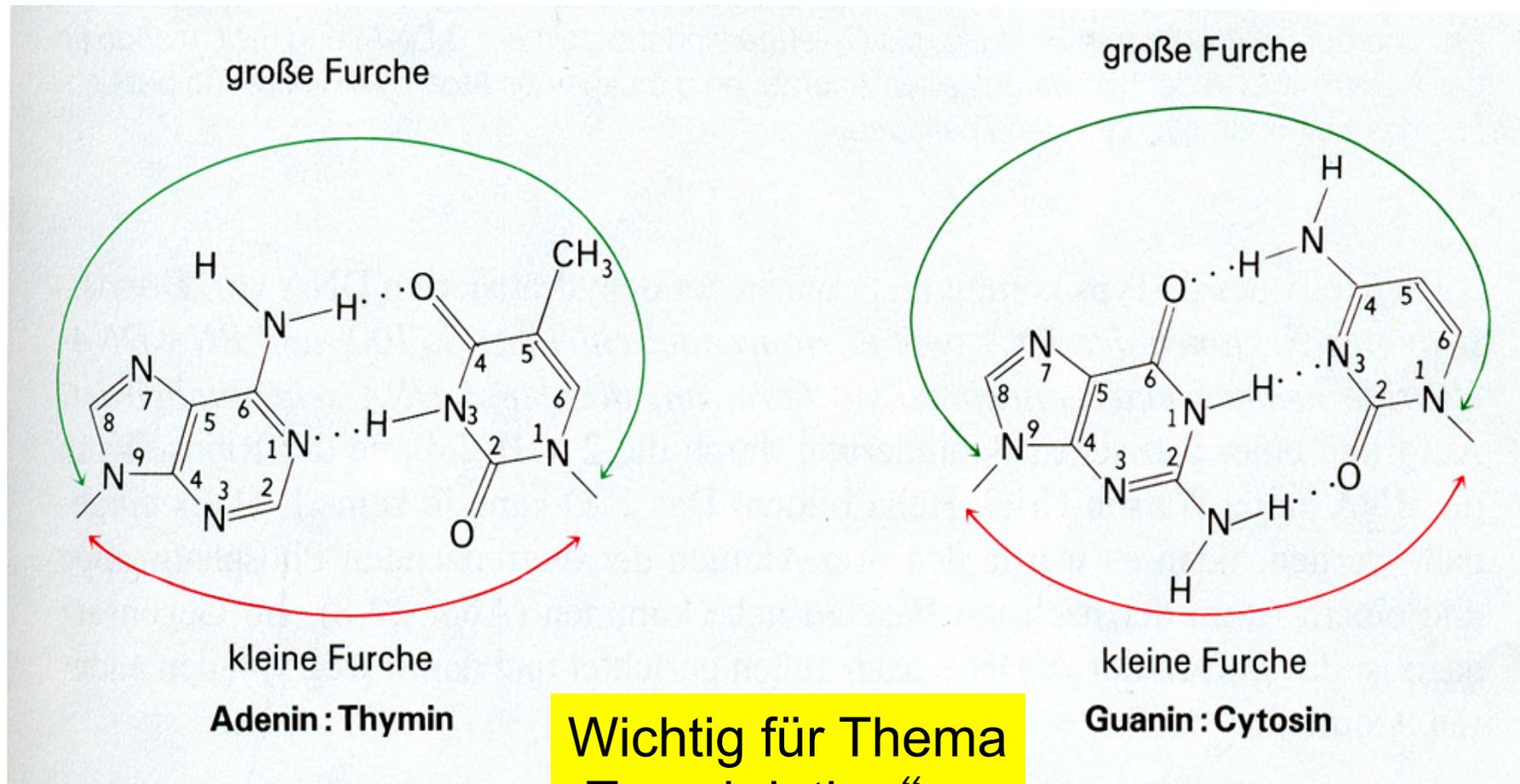


B-Helix Parameter

- rechtsgewunden
- ca. 10,4 Basenpaare pro Windung
- Abstand zwischen zwei Bp beträgt 3.4 Angstrom (10^{-10} m)
- Dicke der Helix beträgt 2 nm (= 20 A)



Die „Furchen“ der DNA bieten Proteinen Möglichkeiten zur basenspezifischen Erkennung und Bindung



Wichtig für Thema „Transkription“

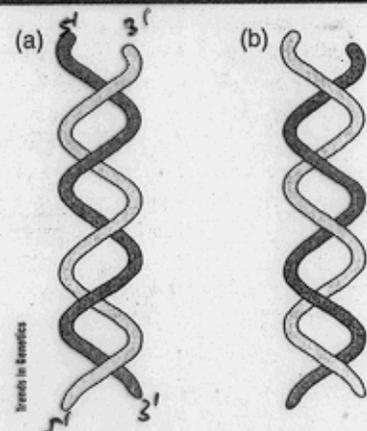
Sinister depictions of DNA

At the centre of molecular genetics stands the DNA molecule. Students learn about the structure of double-stranded DNA from textbooks and lectures. They are taught that the helical structure of DNA inside a living cell is in the right-handed or B-form. They also learn about left-handed DNA, termed Z-DNA, which was first proposed by Pohl and Jovin in 1972 (Ref. 1). Under certain circumstances, a transition from B- to Z-DNA can occur in stretches of alternating purine and pyrimidine residues. Whether Z-DNA has a biological function, however, is still not known.

B- and Z-DNA can easily be distinguished from each other in diagrams if the two strands are marked in different shades (Fig. 1). But wait – unexpected figures depicting left-handed DNA seem to be cropping up in unusual places. In Richard R. Sinden's textbook *DNA Structure and Function*², for example, one figure (5.7) intends to demonstrate that the formation of left-handed DNA depends on the topological state of the DNA molecule. However, the starting DNA molecule is already in the left-handed confirmation. Another prominent example is found on the cover of a recent issue of *Science* (23 October 1998). Even the next generation of molecular biologists is being prepared for an onslaught of left-handed DNA. In a textbook distributed by CSHL Press³, and designed to teach children 'the secret of DNA', most of the figures, including that on the cover, depict Z-DNA.

The most spectacular example of this sinister trend is found in the sixth edition of Benjamin Lewin's text book, *Genes VI* (Ref. 4). Most of the figures have been redone, but unfortunately so has the handedness of the DNA. In

FIGURE 1. The B to Z of DNA



(a) Right-handed (B-form) and (b) left-handed (Z-form) DNA.

176 of 179 figures, left-handed DNA is shown, instead of right-handed DNA. More curiously still, in some figures, DNA is neither right- nor left-handed; the two strands are not intertwined at all (e.g. Fig. 4.21). Most of the time the figures are just wrong without mechanistic consequences, but sometimes there is a consequence. For example, in Fig. 17.14 rotation of the DNA strands does not lead to strand separation, as indicated in the text (p. 551), but to DNA supercoiling. Beware students – these figures are sold as transparencies and are used in teaching! While preparing this brief note, it was brought to our attention that others too have been struck by the growing appearance of left-handed DNA.

In a beautifully illustrated homepage entitled *The left-handed hall of fame* (<http://www-lecb.ncifcrf.gov/~toms/LeftHanded.DNA.html>), Tom Schneider provides an impressive collection from the past 34 years of illustrations depicting left-handed DNA. Based on this sudden prevalence of left-handed DNA, it appears that more than 25 years after its discovery, Z-DNA has finally found its functional role, if only in text books and scientific journals.

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- 1 Pohl, F.M. and Jovin, T.M. (1972) Salt-induced co-operative conformational change of a synthetic DNA: Equilibrium and kinetic studies with poly (dG-dC). *J. Mol. Biol.* 67, 357-369
- 2 Sinden, R.R. (1994) *DNA Structure and Function*, Academic Press
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- 4 Lewin, B. (1997) *Genes VI*, Oxford University Press



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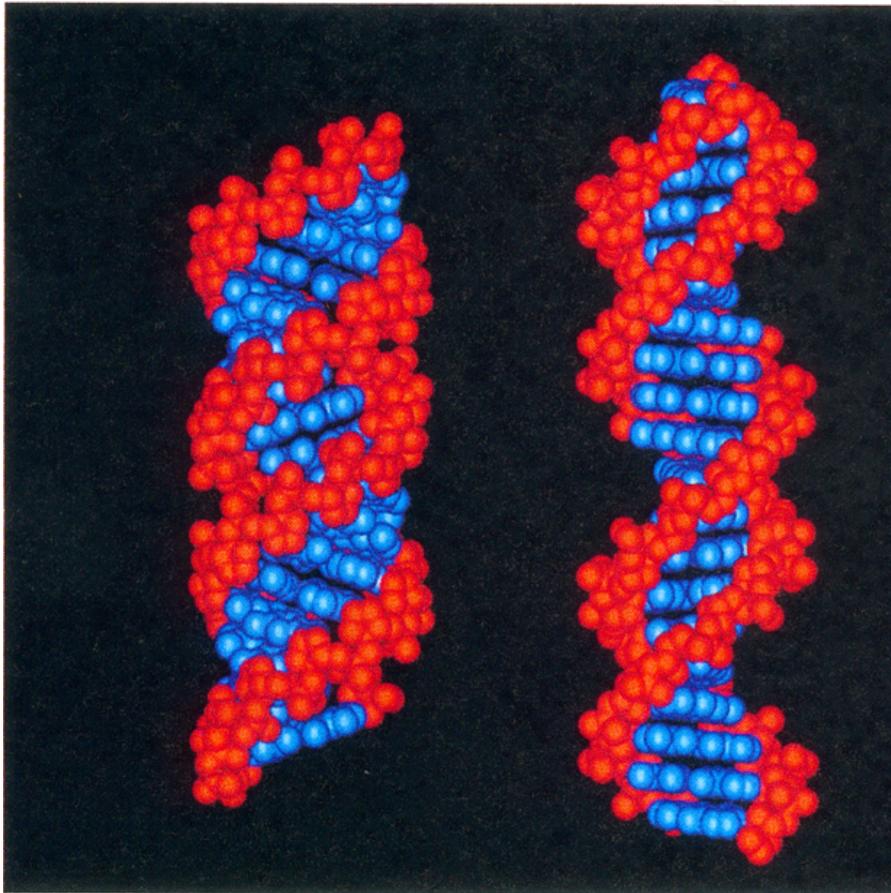
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Cologne, Germany.



Es gibt auch noch andere Helix-Formen!

z. B. abhängig von DNA-Sequenz, Nukleinsäuretyp
und Ionen-Milieu

Charakteristika der A-Helix

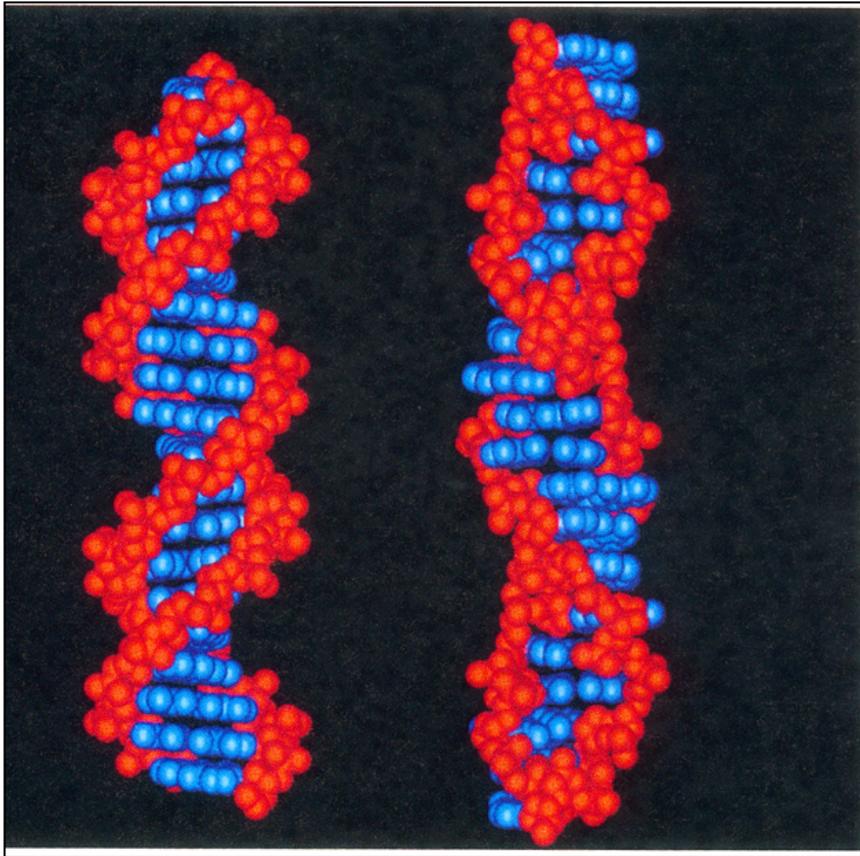


A

B

- rechtsgewunden
- Basen stehen im 20° -Winkel zur Achse
- Helix ist innen „hohl“
- Helix ist „dicker“
- 11 statt 10,4 Bp pro Windung

Charakteristika der Z-Helix



B

Z

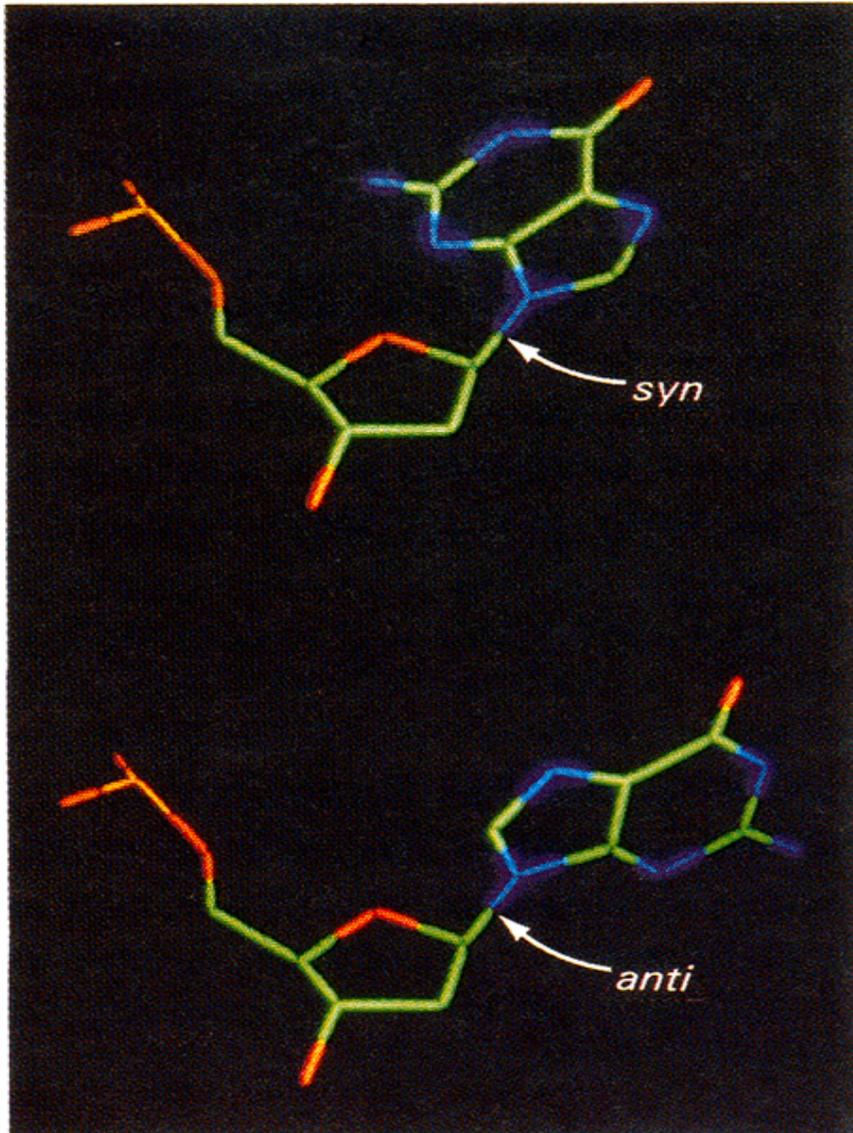
- bei alternierenden Purin/Pyrimidin-Folgen (z.B. GC oder AC)
- **links**gewunden !!!
- ‚major groove‘ nahezu verschwunden
- Helix ist „dünner“
- 12 statt 10,4 Bp pro Windung

Verschiedene DNA-Konformationen sind möglich durch...

- **‚syn‘** oder **‚anti‘** Stellung der Basen relativ zum Zucker
- **C2‘-endo** oder **C3‘-endo**-Konfiguration des Zuckers
- **‚Propeller-Twist‘** der Basen

Syn vs. Anti

Stellung der
Basen
relativ zum
Zucker



Einfluss der Zuckerkonformation auf den Abstand der 3'-5' Phosphodiester-Bindung

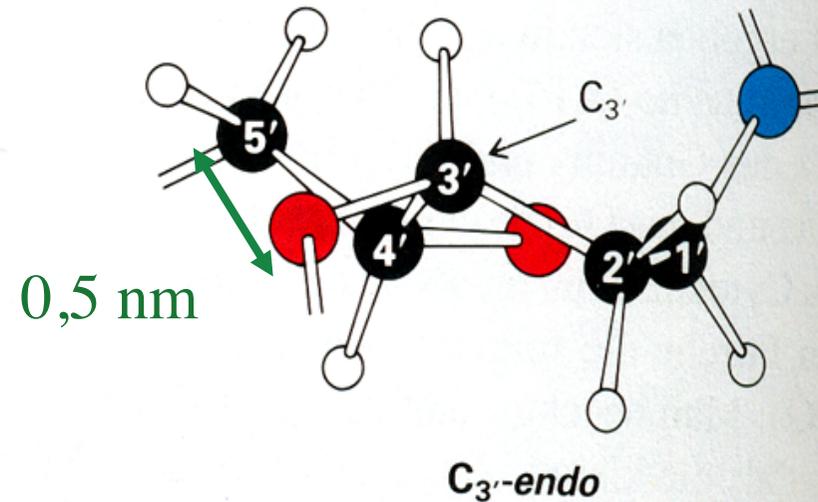
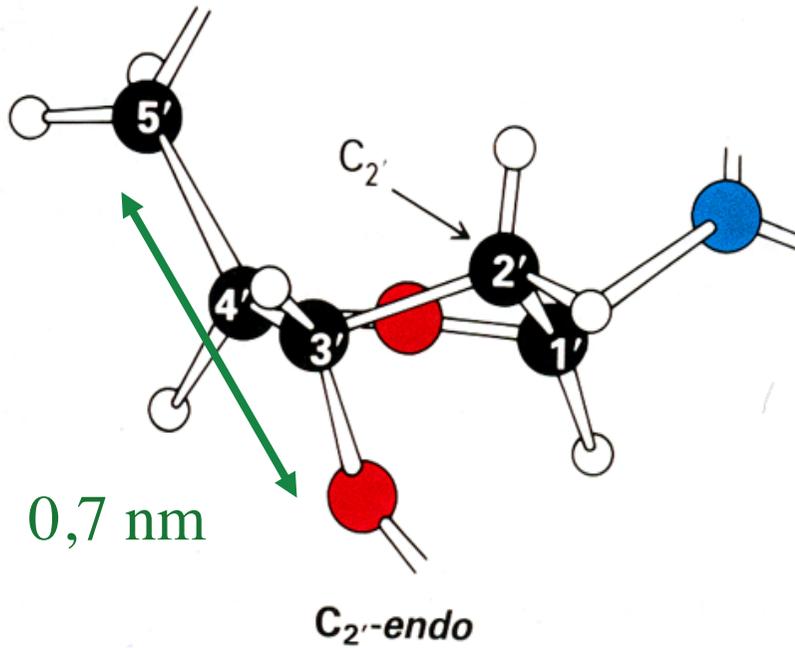


Tabelle 27.1: Vergleich von A-, B- und Z-DNA

	Helixtyp		
	A	B	Z
Gestalt	am breitesten	zwischen A- und Z-Typ	am längsten
Höhe pro Basenpaar	0,23 nm	0,34 nm	0,38 nm
Helixdurchmesser	2,55 nm	2,37 nm	1,84 nm
Verwindungsrichtung	rechtsgängig	rechtsgängig	<u>linksgängig</u>
Konformation der glykosidischen Bindung	<i>anti</i>	<i>anti</i>	<u><i>anti</i> bei C, T <i>syn</i> bei G</u>
Anzahl der Basenpaare pro Helixwindung	11	10,4	12
Ganghöhe	2,46 nm	3,32 nm	4,56 nm
Neigung der Basenpaare zur Helixachse	<u>19°</u>	1°	9°
große Furche	eng und sehr tief	breit und ziemlich tief	flach
kleine Furche	sehr breit und flach	eng und ziemlich tief	sehr eng und tief

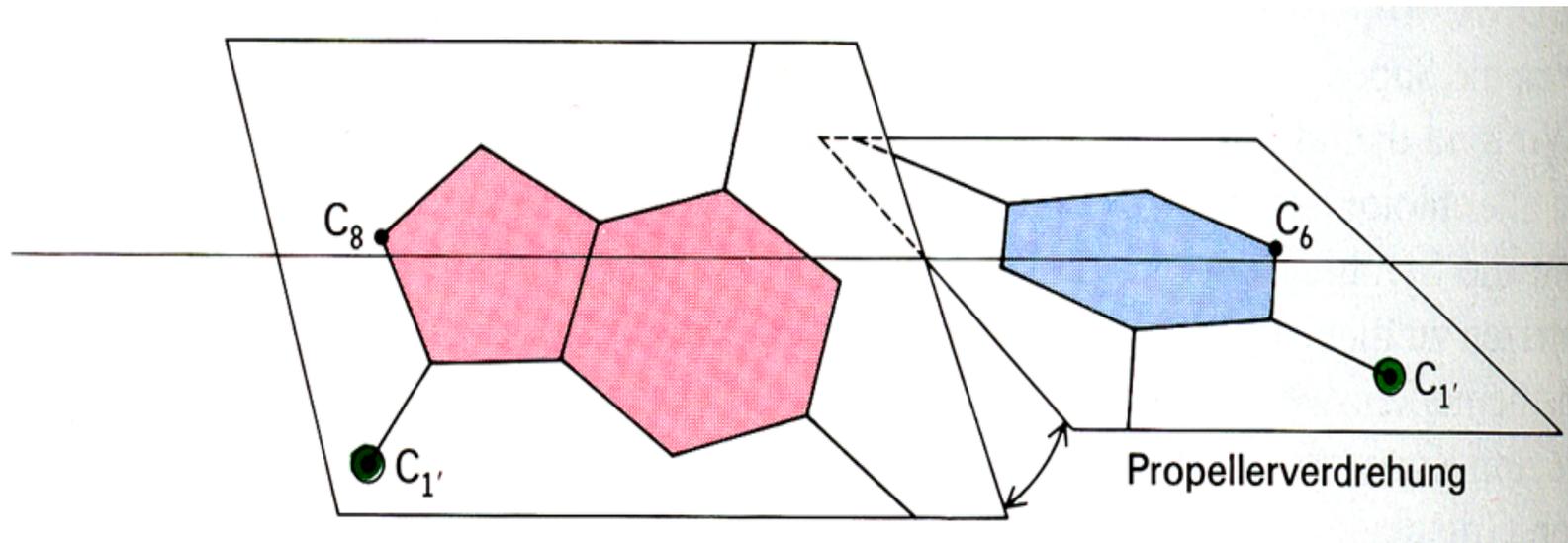
Zuckerkonformation

C3'endo

C2'endo

**G: C2'endo
C: C3'endo**

Propeller-Twist zwischen Basen





„curved DNA“

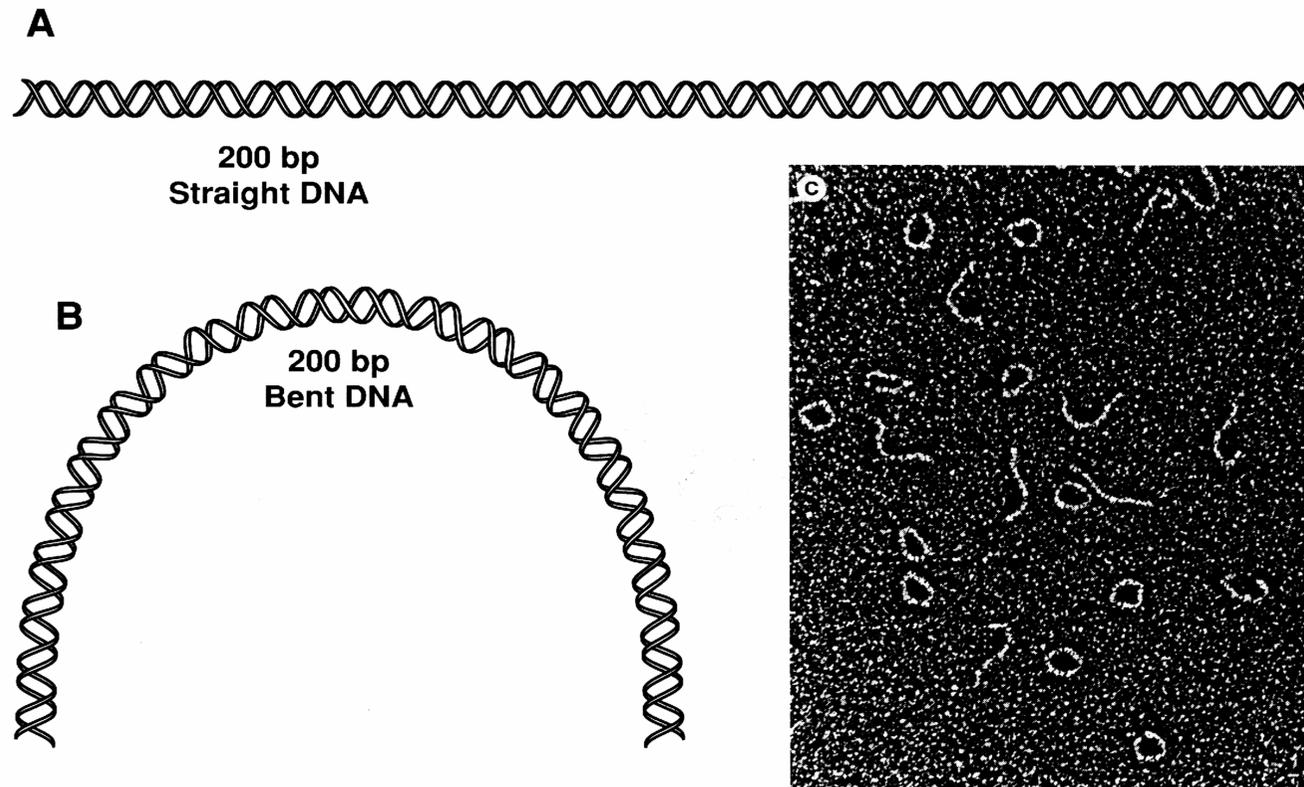
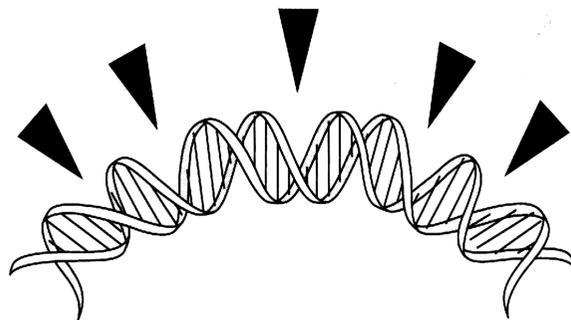


Figure 2.1 Straight DNA and bent DNA. (A) A representation of a 200-bp straight DNA molecule. The persistence length of DNA is 150–200 base pairs. Persistence length is the length of DNA that resists easy deformation, or a length that is not considered very flexible. DNA smaller than its persistence length cannot be easily bent into a circle. (B) A 200-bp piece of bent DNA is shown. Some DNAs, because of their primary base sequence, will adopt a stable bent or curved configuration. (C) The electron micrograph shows a 223-bp fragment of *Crithidia fasciculata* DNA containing 18 phased A₄ to A₆ tracts. Although the fragment is linear and is blunt ended, many molecules appear to be intact circles. Without the phased A tracts, the DNA would appear as linear, relatively straight molecules. Courtesy of Jack D. Griffith.



Änderung des Propellertwists führt zu DNA-Krümmung

Wedge Model



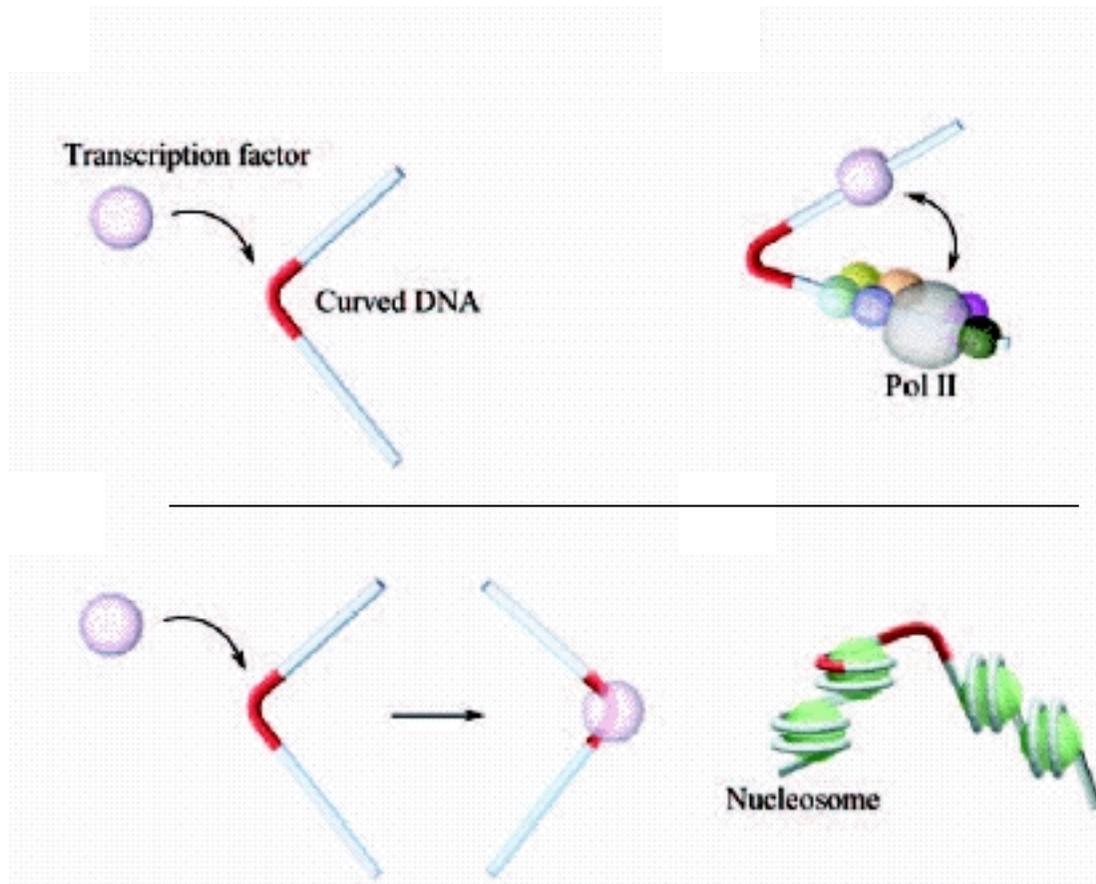
z.B. bei Wiederholung von $(A)_{n>3}$ im Abstand von ca. 10 Bp

AAA_gcatgacAAAA
gatcctAAAAAgcttg...

Propellertwist-Änderungen wiederholen sich ca alle 10 Bp und liegen so auf der gleichen Seite der Helix. Die Summe mehrerer kleiner Winkel führt zur sichtbaren Krümmung.

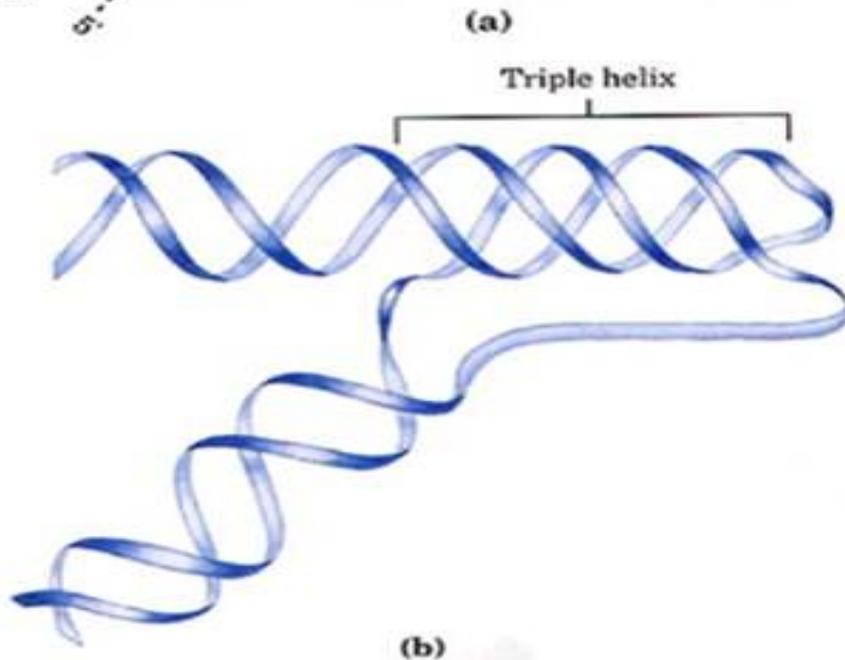
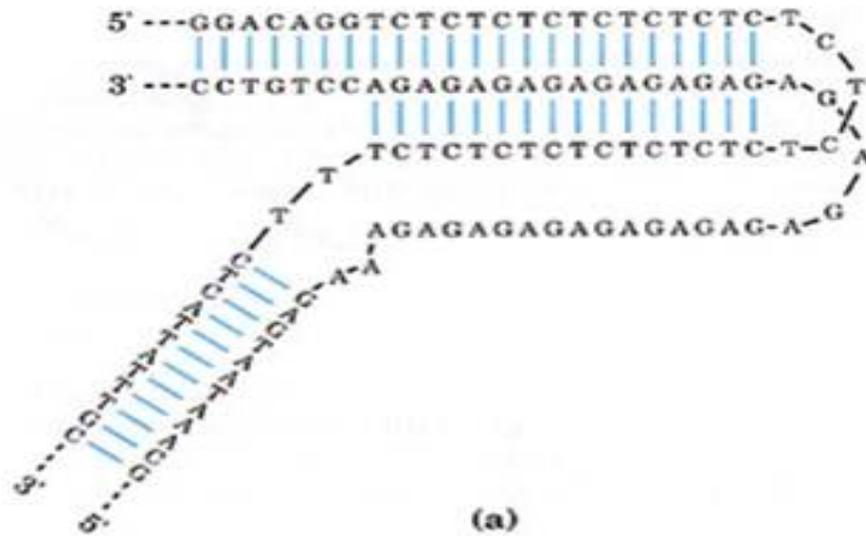


Curved DNA: Funktionen



Bei Bakterien
vielfach bestätigt...

H-DNA



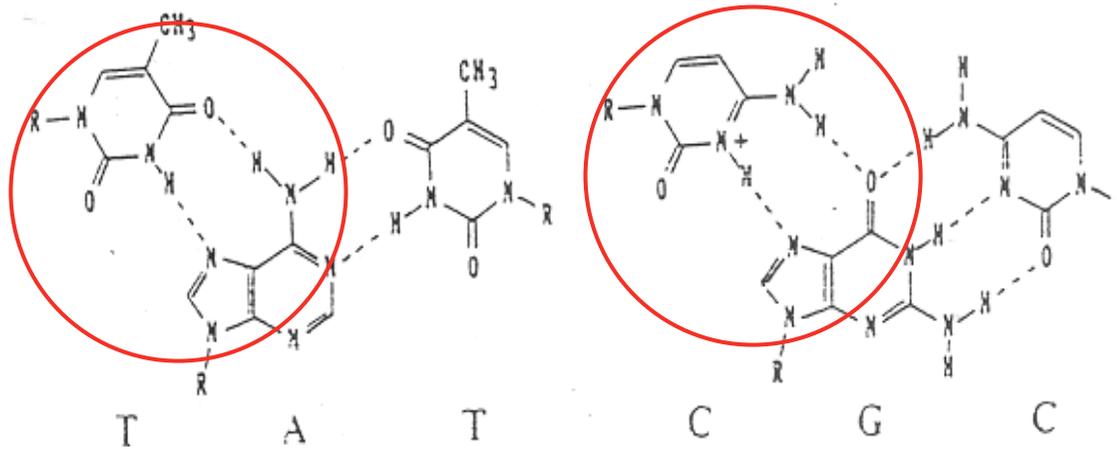
- **Triple**-Helix!!!!
- non-Watson/Crick-Basenpaarung („**H**oogsteen-Paarung“)
- in Bereichen mit alternierenden T/C- bzw. G/A-Abfolgen
- *in vivo* nachgewiesen in Gen-Promotern; im Human-genom häufig: 1/50000 Bp



H-DNA



FIG. 1. Model for intramolecular triplex (*Upper*). Watson-Crick paired duplexes of the vector (*Lower*). The strand containing the pyrimidine-rich sequence is shaded, whereas the strand containing the purine-rich sequences is unshaded. The 3'-half of the purine strand (termed second strand) of the insert remains Watson-Crick paired with the 5'-half of the pyrimidine strand. The 3'-half of the pyrimidine strand (termed third strand), after dissociating from its Watson-Crick complement, occupies the major groove of the duplex region described above and is specifically complexed with it through Hoogsteen base pairs (*Lower*). The mirror repeat and the oligopurine-oligopyrimidine nature of these sequences enable this specific association. The structure of the nonpaired 5'-half of the purine-rich strand is uncertain.





H-DNA: biologische Relevanz

MOLECULAR AND CELLULAR BIOLOGY, Jan. 2008, p. 863–872
0270-7306/08/\$08.00+0 doi:10.1128/MCB.00960-07
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Vol. 28, No. 2

Naturally Extended CT · AG Repeats Increase H-DNA Structures and Promoter Activity in the Smooth Muscle Myosin Light Chain Kinase Gene[∇]

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Received 30 May 2007/Returned for modification 12 July 2007/Accepted 25 October 2007

Naturally occurring repeat sequences capable of adopting H-DNA structures are abundant in promoters of disease-related genes. In support of this, we found (CT)₂₂ · (AG)₂₂ repeats in the promoter of smooth muscle myosin light chain kinase (smMLCK), a key regulator of vascular smooth muscle function. We also found an insertion mutation that adds another six pairs of CT · AG repeats and increases smMLCK promoter activity in spontaneously hypertensive rats (SHR). Therefore, we used the smMLCK promoters from normotensive and hypertensive rats as a model system to determine how CT · AG repeats form H-DNA, an intramolecular triplex, and regulate promoter activity. High-resolution mapping with a chemical probe selective for H-DNA showed that the CT · AG repeats adopt H-DNA structures at a neutral pH. Importantly, the SHR promoter forms longer H-DNA structures than the promoter from normotensive rats. Reconstituting nucleosomes on the promoters, in vitro, showed no difference in nucleosome positioning between the two promoters. However, chromatin immunoprecipitation analyses revealed that histone acetylations are greater in the hypertensive promoter. Thus, our findings suggest that the extended CT · AG repeats in the SHR promoter increase H-DNA structures, histone modifications, and promoter activity of the smMLCK, perhaps contributing to vascular disorders in hypertension.



A Four-Base Paired Genetic Helix with Expanded Size

Haibo Liu, Jianmin Gao, Stephen R. Lynch, Y. David Saito, Lystranne Maynard, Eric T. Kool*

We describe a new molecular class of genetic-pairing system that has a native DNA backbone but has all four base pairs replaced by new, larger pairs. The base pairs include size-expanded analogs of thymine and of adenine, both extended by the width of a benzene ring (2.4 Å). The expanded-diameter double helices are more thermodynamically stable than the Watson-Crick helix, likely because of enhanced base stacking. Structural data confirm a right-handed, double-stranded, and base-paired helical form. Because of the larger base size, all the pairs of this helical system are fluorescent, which suggests practical applications in detection of natural DNA and RNA. Our findings establish that there is no apparent structural or thermodynamic prohibition against genetic systems having sizes different from the natural one.

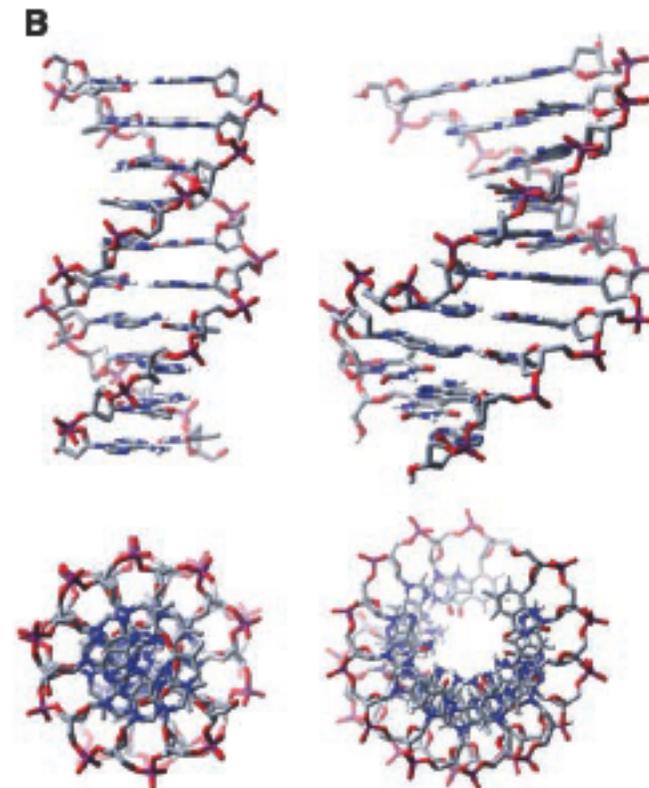
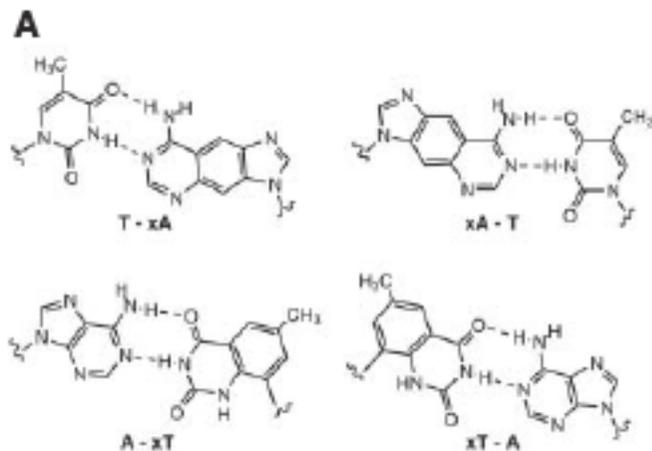


Fig. 4. Proposed structures of expanded base pairs and helices. (A) Structures of the four nonnatural base pairs of the mixed xDNA sequence, having interglycosidic distances of ~12.9 Å (compared with 10.7 Å for B-form DNA). (B) Side and end views of a plausible modeled structure of a 10-bp expanded DNA helix (right), consistent with NMR structural data; standard B-form DNA helix is shown for comparison at left.



Schlechte Zeiten für Diebe Künstliche DNA als Falle

Fingerabdrücke auf Möbeln und Türen? Es gibt Handschuhe. Die Polizei in Bremen geht den umgekehrten Weg: Wertsachen werden mit einer künstlichen DNA markiert. Werden sie gestohlen, kann das Diebesgut dem rechtmäßigen Besitzer zugeordnet werden. Das Pilotprojekt kann erste Erfolge vorweisen.

Als erstes Bundesland testet Bremen seit einigen Monaten künstliche DNA, um Dieben das Handwerk zu legen. Die Zahl der Einbrüche ist seitdem gesunken. "Es scheint so, als schreckt das ab", sagte Polizeisprecher Gundmar Köster. Während die Langfinger die an dem Pilotprojekt teilnehmenden Haushalte und Tankstellen verschonten, griffen sie in Schulen nach wie vor zu.



Gut markiert ist fast überführt - hofft die Bremer Polizei.
(Foto: picture alliance/ dpa)

Seit Ende vergangenen Jahres markieren alle Schulen, zahlreiche Bürger und drei Tankstellen ihre Wertsachen mit künstlicher DNA. Die Flüssigkeit trocknet zu einem farblosen Lack, der unter UV-Licht leuchtet. Dadurch kann die Bremer Polizei Diebesgut identifizieren. Außerdem enthält die künstliche DNA winzige Mikrochips, mit denen die Beamten den Besitzer von gestohlenem Schmuck, Computern oder Antiquitäten aus einer Datenbank ermitteln können.

Mit DNA-Hightech gegen Metallklau bei der Bahn

Die Eisenbahn besteht nicht nur aus Eisen, sondern auch aus Buntmetall, das immer teurer wird. Das lockt Diebe an, die gewaltige Schäden verursachen. Die Bahn reagiert mit Hightech aus dem Genlabor. Von Bernhard Sprengel

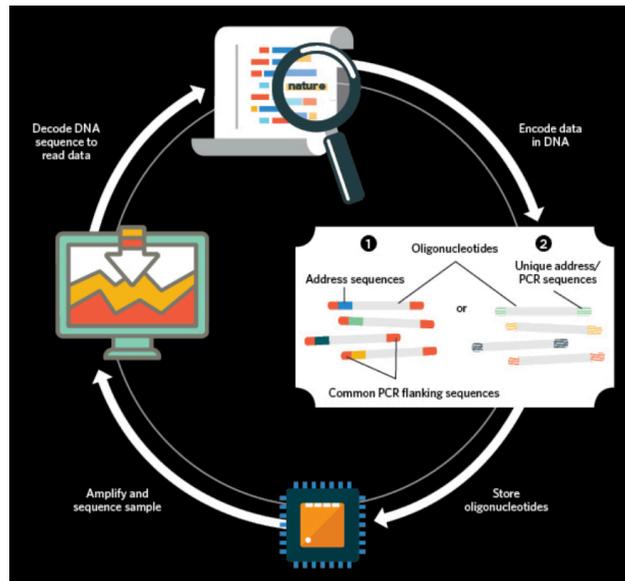
Die neue Methode gegen Metalldiebe

1/6 < >





DNA: Informationsspeicher für die Ewigkeit?



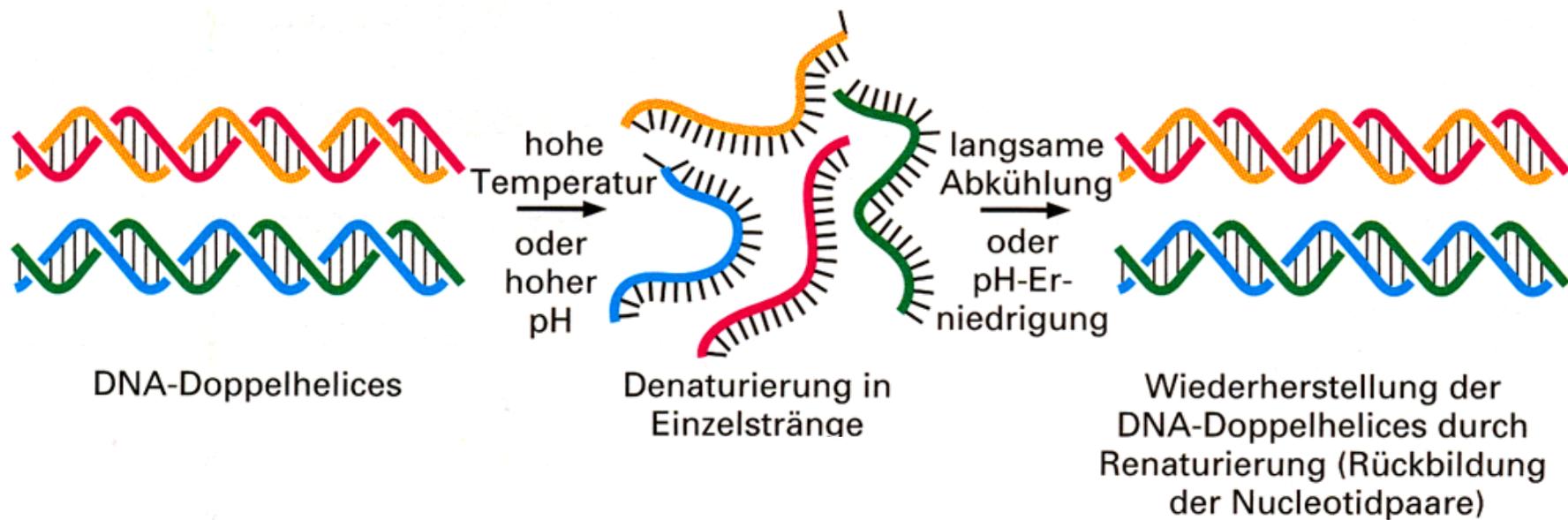
- Kodieren der Daten durch chemische DNA-Synthese
- Vermehrung (PCR!) und Lagerung der DNA
- Auslesen der Information durch DNA-Sequenzierung

215 Peta-Byte (10^{15}) pro g DNA !!

Erlich et al., Science 355, 950–954 (2017) 3 March 2017

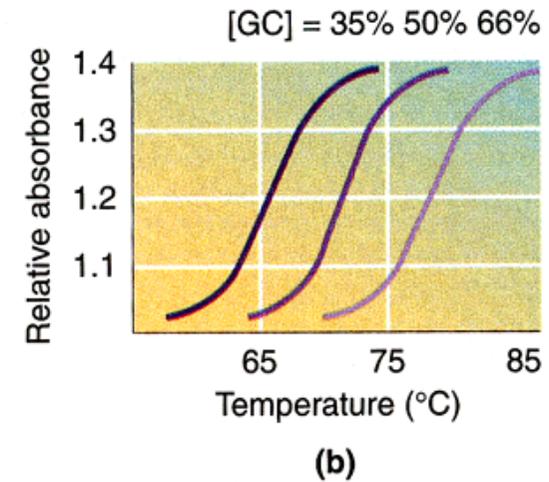
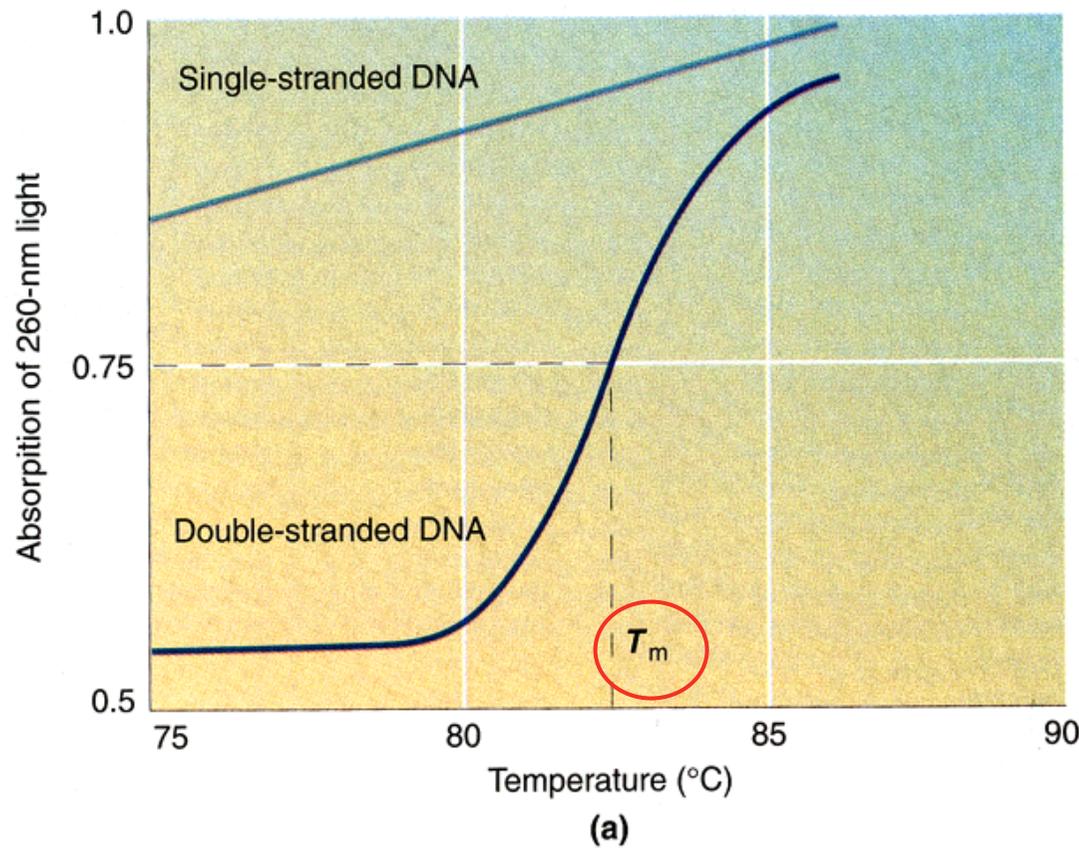
zurück ins Labor...

Denaturierung und Renaturierung von DNA



...und was man damit anfangen kann!

Bestimmung des Schmelzpunkts der DNA durch Denaturierung

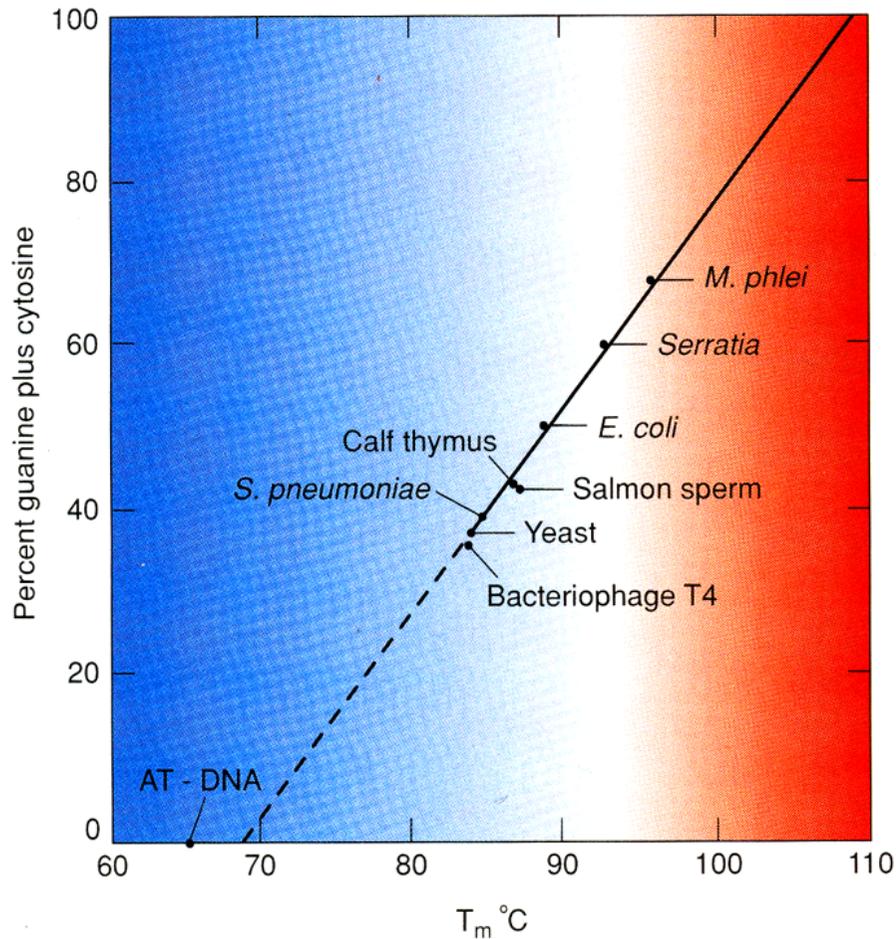




Der Schmelzpunkt der DNA

- T_m = Schmelzpunkt der DNA (50% einzelsträngig)
- $T_m = 69,3 + 0,41 (\%GC)$
- Hyperchromizität = Zunahme der Absorption von einzelsträngiger DNA bei OD_{260nm}

Der Schmelzpunkt der DNA ist mit ihrem GC-Gehalt korreliert

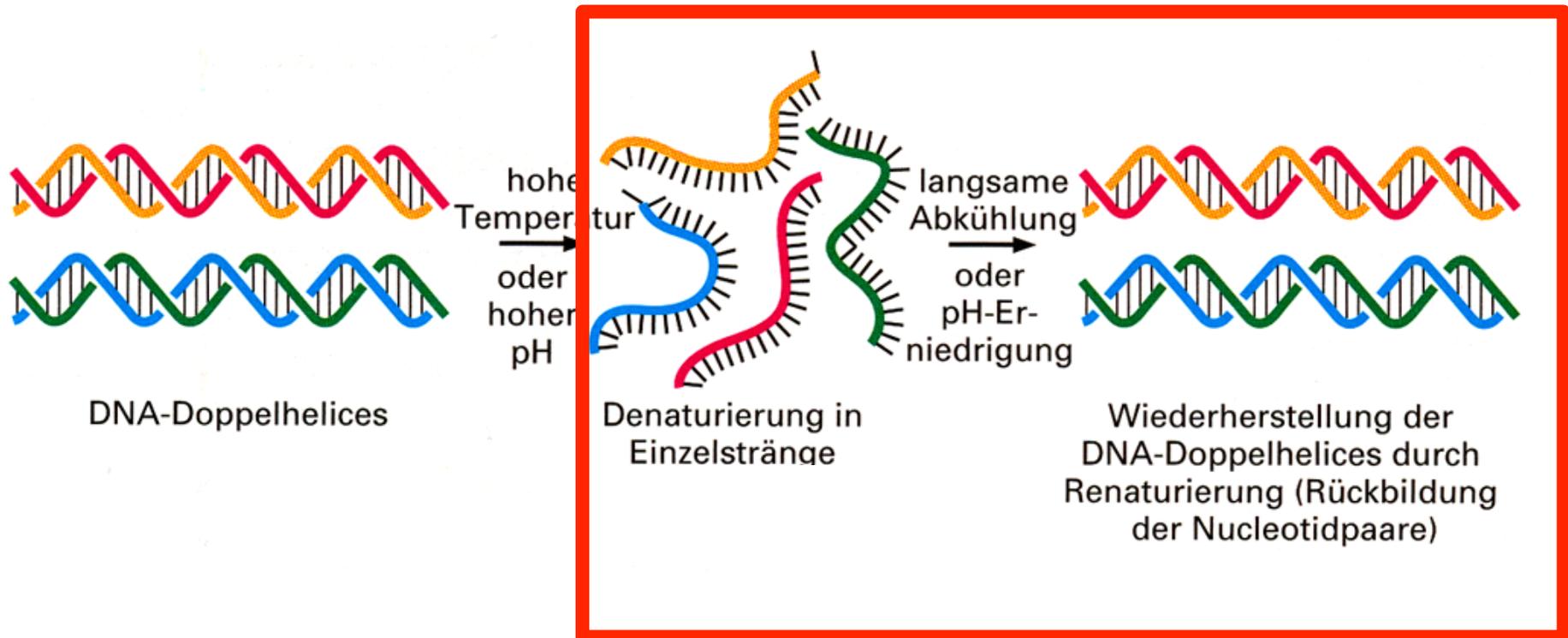


• Dictyostelium	22 % GC
• <i>S. cerevisiae</i>	39
• Maus, Mensch	44
• <i>E. coli</i>	51
• Pseudomonas	68
• Herpes simplex Virus	72

Unterschiedliche Mutationsrichtungen?

Auswirkungen auf DNA-Stabilität?

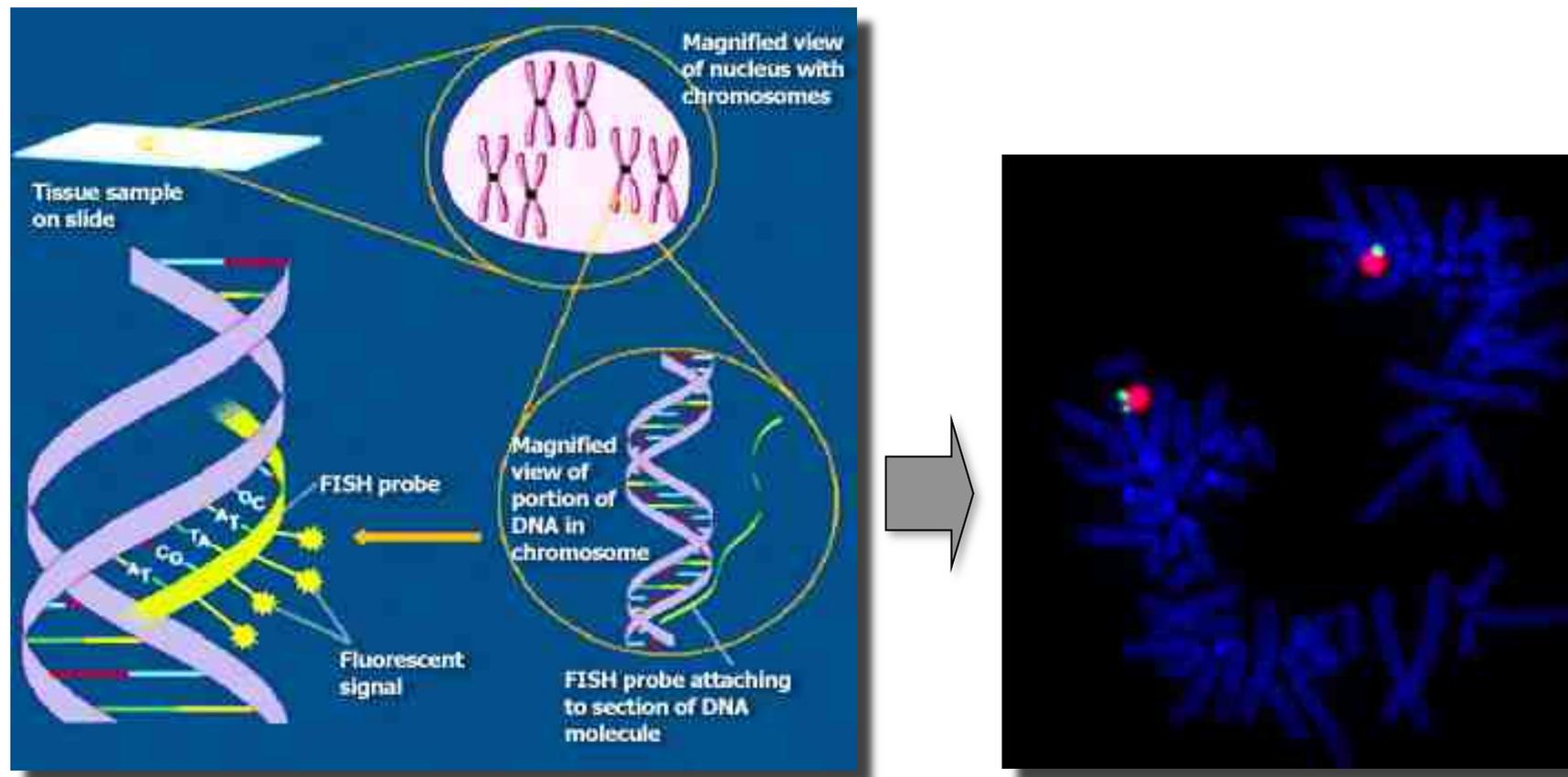
Denaturierung und Renaturierung von DNA





Hybridisierung

z. B: Wo liegt eine DNA-Sequenz/ein Gen auf den Chromosomen?





16 March 2006 | www.nature.com/nature | \$10 THE INTERNATIONAL WEEKLY JOURNAL OF SCIENCE

nature

DNA ORIGAMI

Nanoscale shapes the easy way

CLINICAL TRIALS
Can you believe what you read?

ALZHEIMER'S DISEASE
Catching it early

COSMIC ARCHITECTURE
A double helix in the stars

DNA ORIGAMI

By folding a long, single-stranded DNA scaffold using short, single-stranded "staples," researchers can build any shape they like. For example, researchers recently designed a three-dimensional bunny, using computer algorithms to determine the folding pathways and DNA sequences that would be required to create the desired shape.

DNA scaffold + Staple strands → DNA origami

3-D design plan

Wrapping of scaffold DNA

3-D origami model

50 nm

DNA AS BRICKS AND MORTAR

The straightforward and consistent pairing of DNA's nucleotide bases make the molecule a reliable building material. Depending on the sequence, DNA strands can crossover to adjacent helices, creating a branch point. Researchers can develop such connecting pieces, called branched DNA junctions, with 4, 5, 6, 8, or 12 arms, projecting from a central hub at various angles in three-dimensional space.

The ends of the molecules can be designed to contain single-stranded "sticky ends" that enable researchers to encode the predictable self-assembly of larger nanostructures.

DNA CROSSOVERS

Reciprocal exchange

Resolve

BRANCHED DNA JUNCTIONS

4-arm

5-arm

6-arm

8-arm

12-arm

STRUCTURAL GLUE

Sticky end

CAGTA

GTCA

DNA SELF ASSEMBLY

Self-assembly

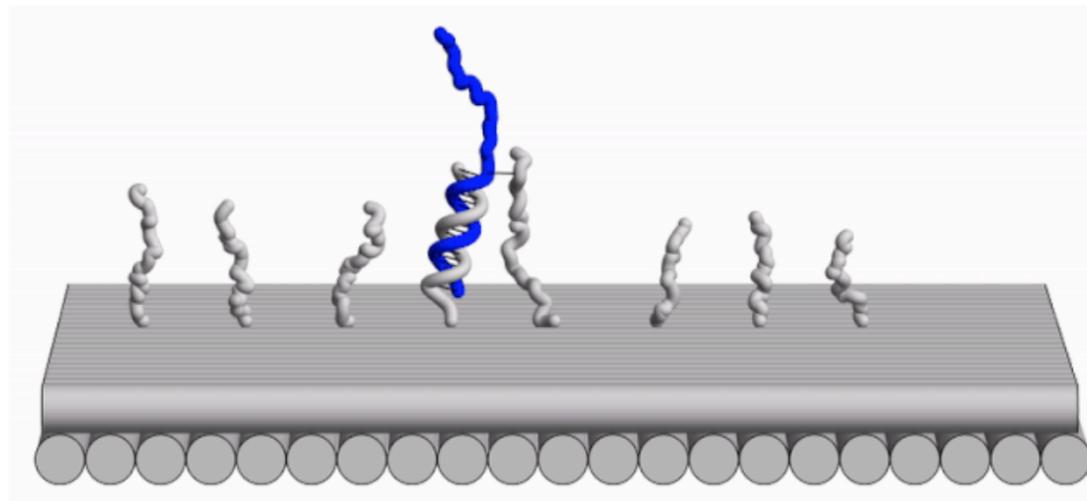
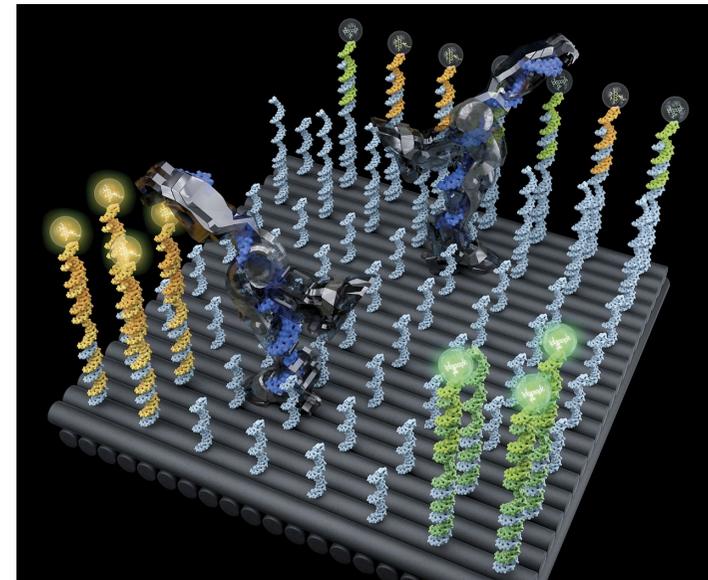


DNA NANOTECHNOLOGY

A cargo-sorting DNA robot

Anupama J. Thubagere,¹ Wei Li,¹ Robert F. Johnson,¹ Zibo Chen,¹ Shayan Doroudi,² Yae Lim Lee,³ Gregory Izatt,^{2,4} Sarah Wittman,² Niranjan Srinivas,⁴ Damien Woods,^{2*} Erik Winfree,^{1,2,4} Lulu Qian^{1,2†}

Two critical challenges in the design and synthesis of molecular robots are modularity and algorithm simplicity. We demonstrate three modular building blocks for a DNA robot that performs cargo sorting at the molecular level. A simple algorithm encoding recognition between cargos and their destinations allows for a simple robot design: a single-stranded DNA with one leg and two foot domains for walking, and one arm and one hand domain for picking up and dropping off cargos. The robot explores a two-dimensional testing ground on the surface of DNA origami, picks up multiple cargos of two types that are initially at unordered locations, and delivers them to specified destinations until all molecules are sorted into two distinct piles. The robot is designed to perform a random walk without any energy supply. Exploiting this feature, a single robot can repeatedly sort multiple cargos. Localization on DNA origami allows for distinct cargo-sorting tasks to take place simultaneously in one test tube or for multiple robots to collectively perform the same task.



Conceptual animation of a DNA robot (blue) taking a single step on a linear track (gray).
CALTECH



Renaturierung (Hybridisierung) von DNA

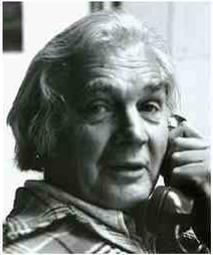
...ist abhängig von

- **Temperatur** (Optimum ist bei $T_m - 25^\circ\text{C}$)
- **Konzentration** der DNA in der Lösung
- erlaubter **Zeit** für die Renaturierung



Welchen Einfluss hat die **Konzentration der DNA** in der Lösung auf die Renaturierung?

- A. Bei hoher Konzentration geht Renaturierung schneller
- B. Hohe DNA-Konzentration verlangsamt die Renaturierung



Roy Britten

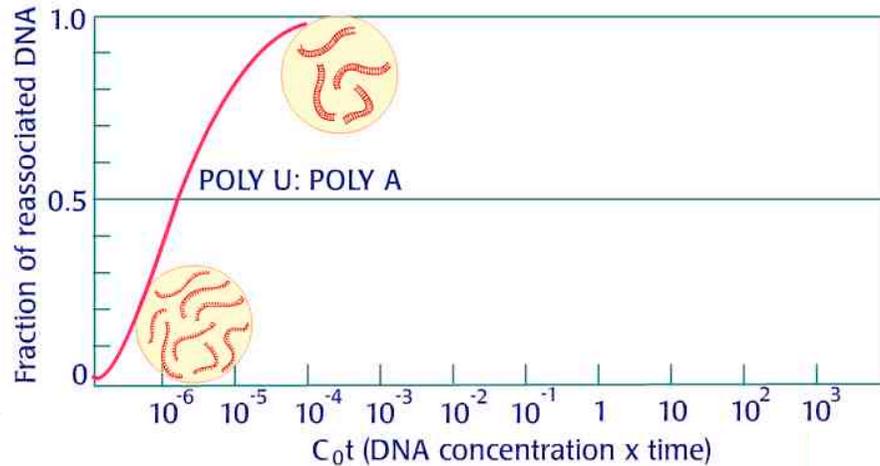
Renaturierungskinetik:

Bestimmung des $C_0t_{1/2}$ -Werts einer DNA

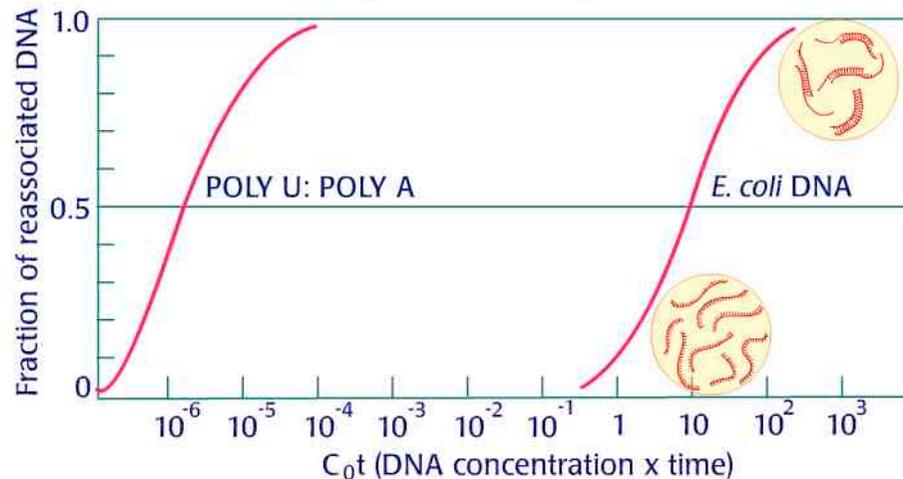
- Produkt aus Anfangs-DNA-Konz. , C_0 ‘ und der Zeit , t ‘
- beschreibt die Renaturierungseigenschaften einer DNA:

Punkt, an dem 50% der zuvor einzelsträngigen DNA wieder doppelsträngig geworden ist

Der $C_{0t}_{1/2}$ -Wert hängt von der Komplexität des Genoms ab

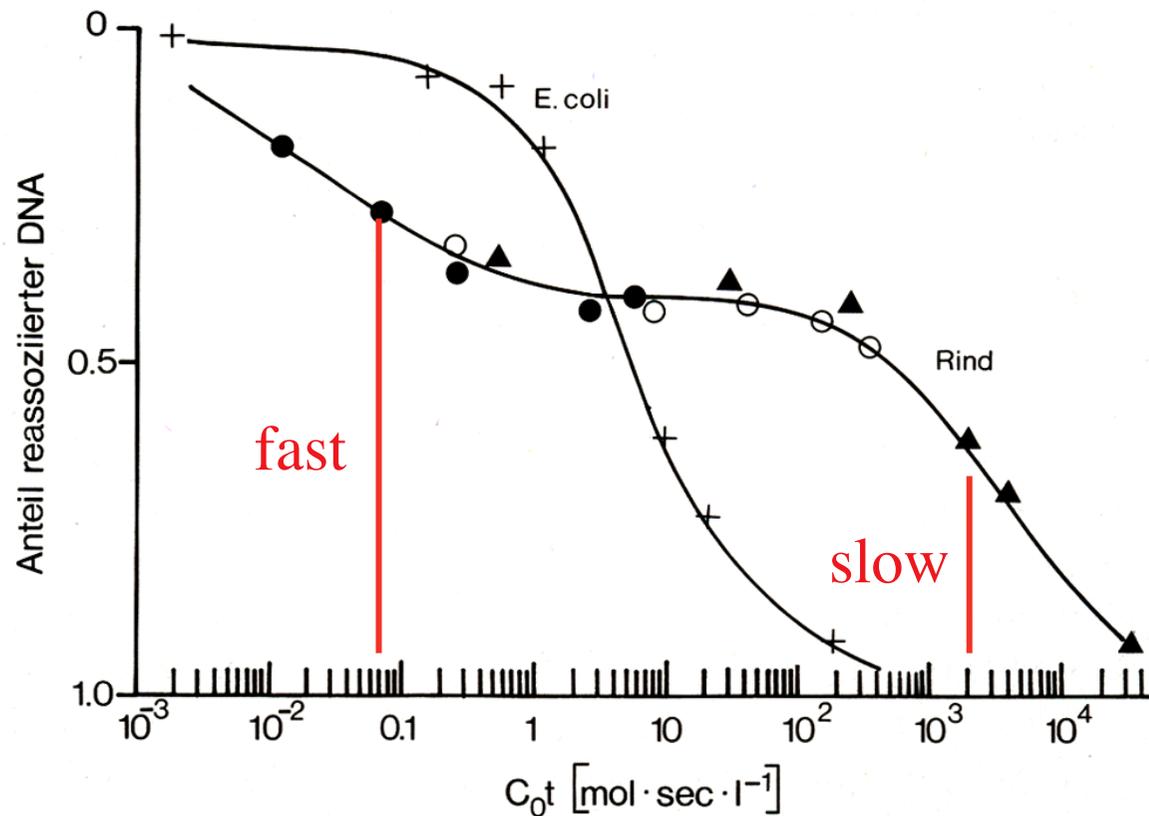


passende Partner-Stränge finden sich extrem schnell

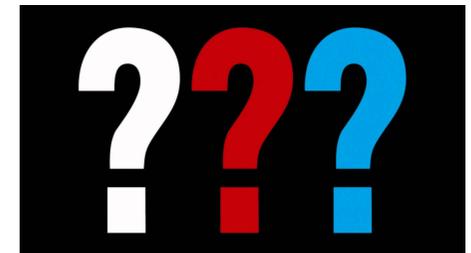


Je größer das Genom, desto mehr DNA-Stränge: Partnersuche verlängert!

Renaturierungskinetiken bei höheren Organismen



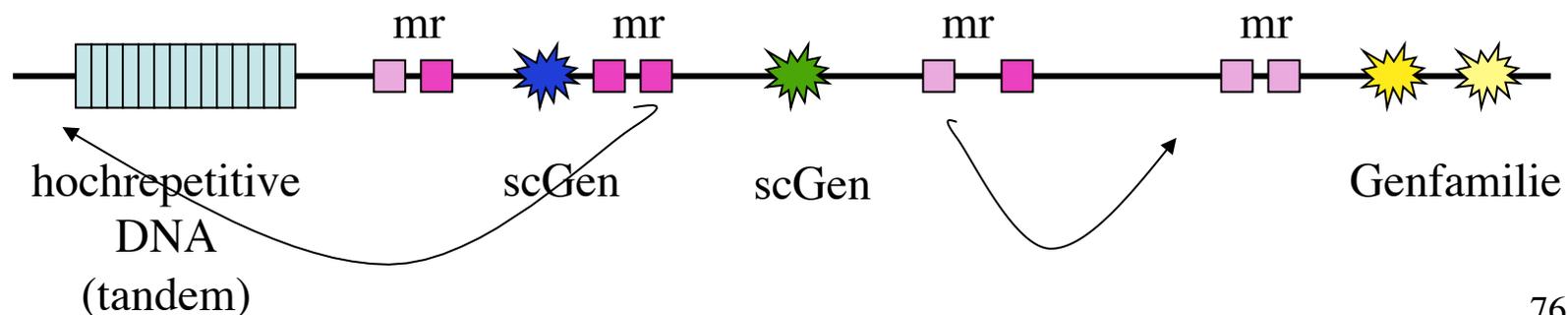
- mind. 2 Komponenten mit unterschiedlicher Reassoziationsgeschwindigkeit





Komponenten der Genome höherer Eukaryoten

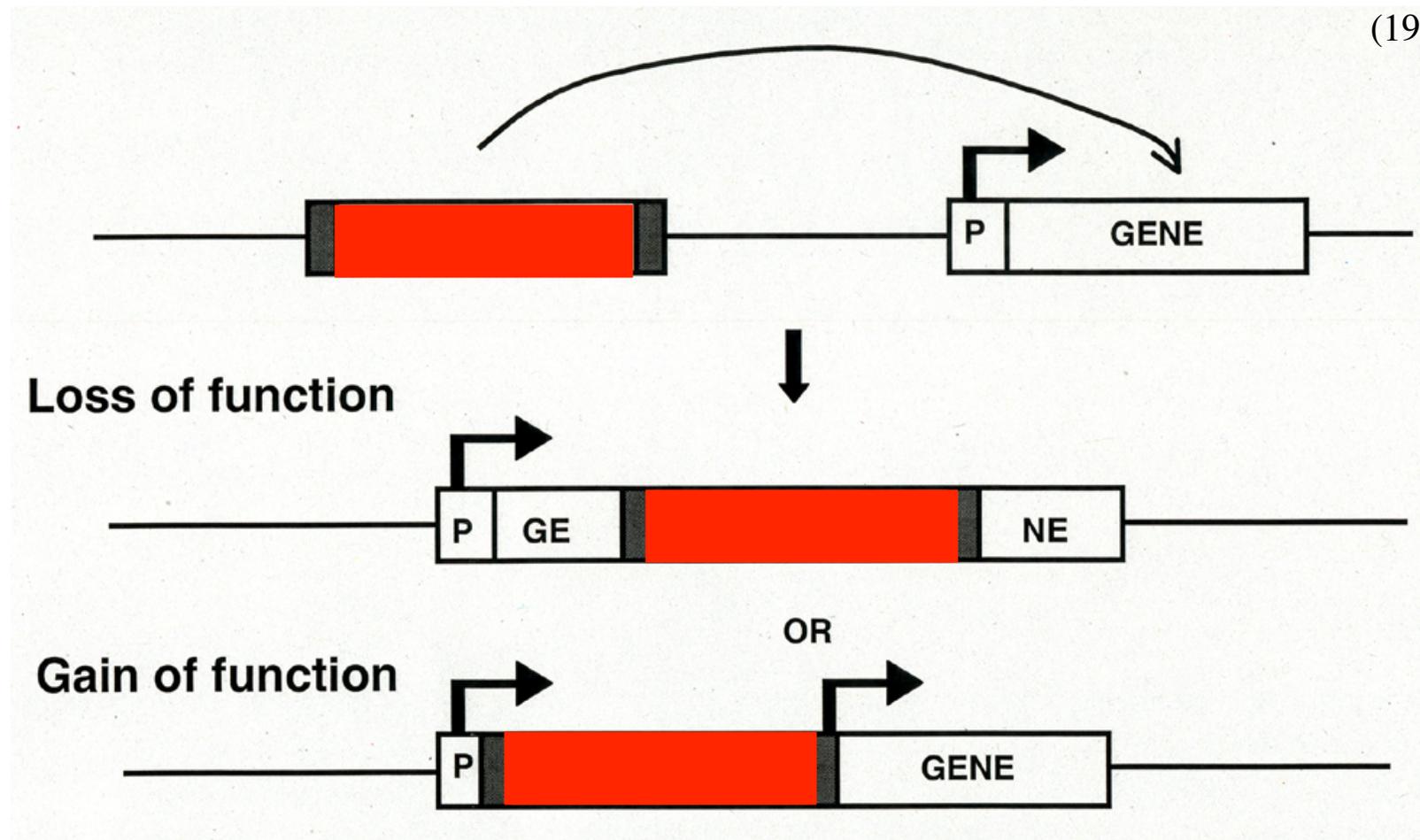
- hoch-repetitive DNA ca. 10% des Genoms; $C_0t_{1/2} = 0,001$
- mittel-repetitive DNA ca. 40% des Genoms; $C_0t_{1/2} = 0,04$
- ‚single copy‘ DNA ca. 50% des Genoms; $C_0t_{1/2} = 4000$



„Springende Gene“ machen Genome instabil!



Barbara McClintock
(1902-1992)





Genom-Komponenten

- **single copy DNA**
 - viele Gene und Intergenregionen
- **mittel-repetitive DNA** (ca. 10-1000; oft verstreut im Genom)
 - Genfamilien (z. B. Globin/Histon/rDNA-Gene)
 - Transposons (= springende DNA-Abschnitte!!)
- **hoch-repetitive DNA** (ca. 10^3 - 10^6 Kopien)
 - Satelliten-DNA der Centromer-Regionen (tandem)
 - sehr „mobile“ Transposons (stark verstreut)

Das Humangenom

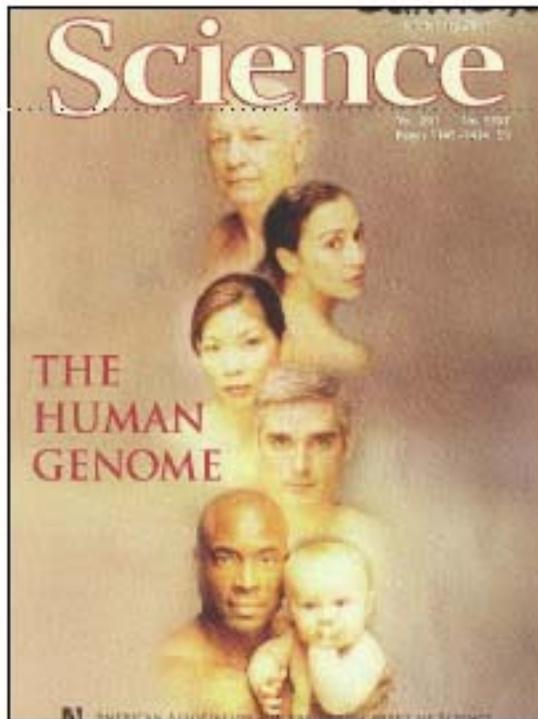
2001 : „working draft“

2003: „finished sequence“

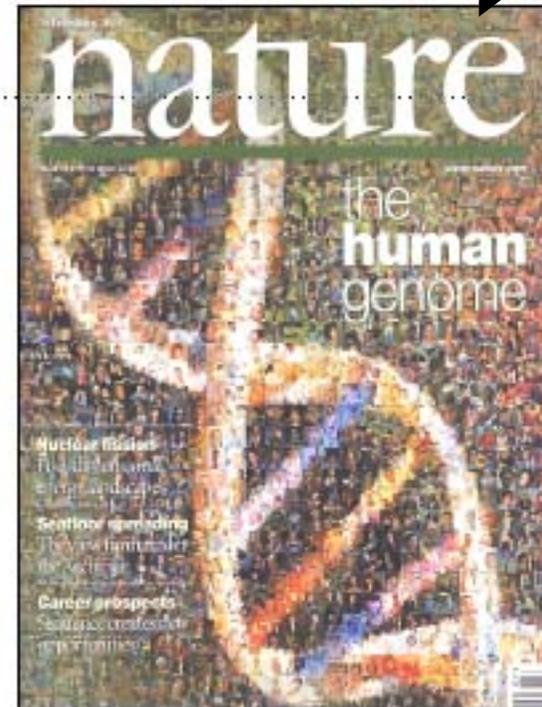


J. Craig Venter /
Fa. Celera

Francis Collins /
Human Genome Project



Celera



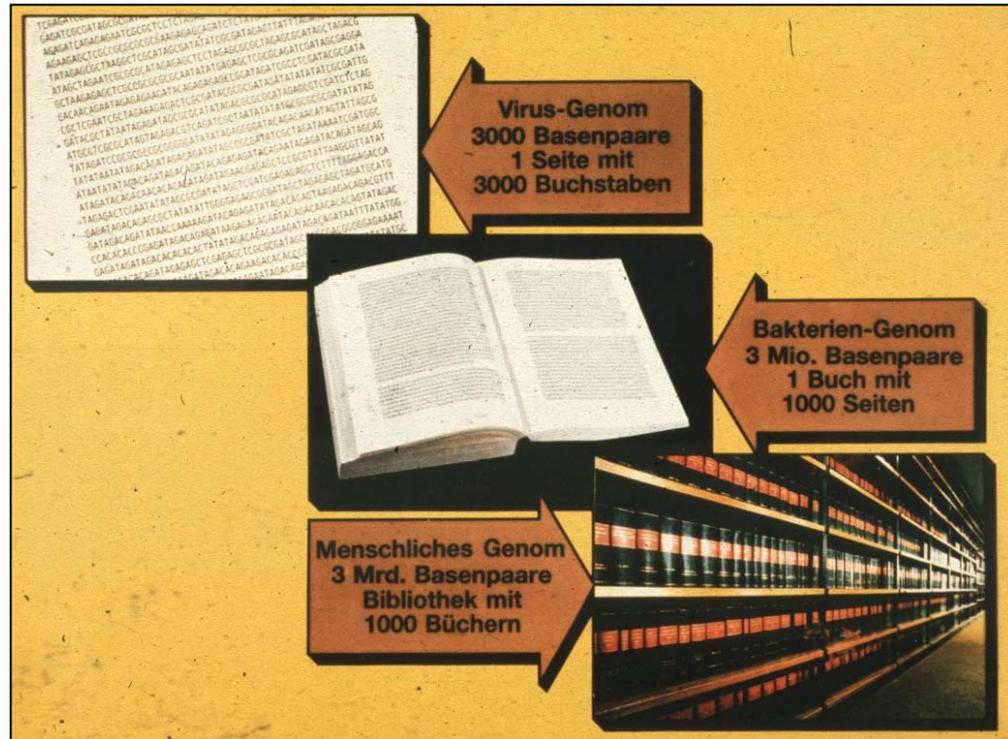
Int. Human Genome Sequencing Consortium

Genomgrößen bei Eukaryoten



• Encephalitozoon	3	MBp	2 000 Gene
• Saccharomyces cerevisiae	12	MBp	6 200 Gene
• Caenorhabditis elegans	97	MBp	19 000 Gene
• Drosophila melanogaster	137	MBp	14 000 Gene
• Gallus gallus	1 000	MBp	23 000 Gene
• Homo sapiens	>3 000	MBp	<25 000 Gene
• Arabidopsis thaliana	125	MBp	25 000 Gene
• Oryza sativa	400	MBp	>50 000 Gene
• Paris japonica	149 000	MBp	?

Das Säugerengenom



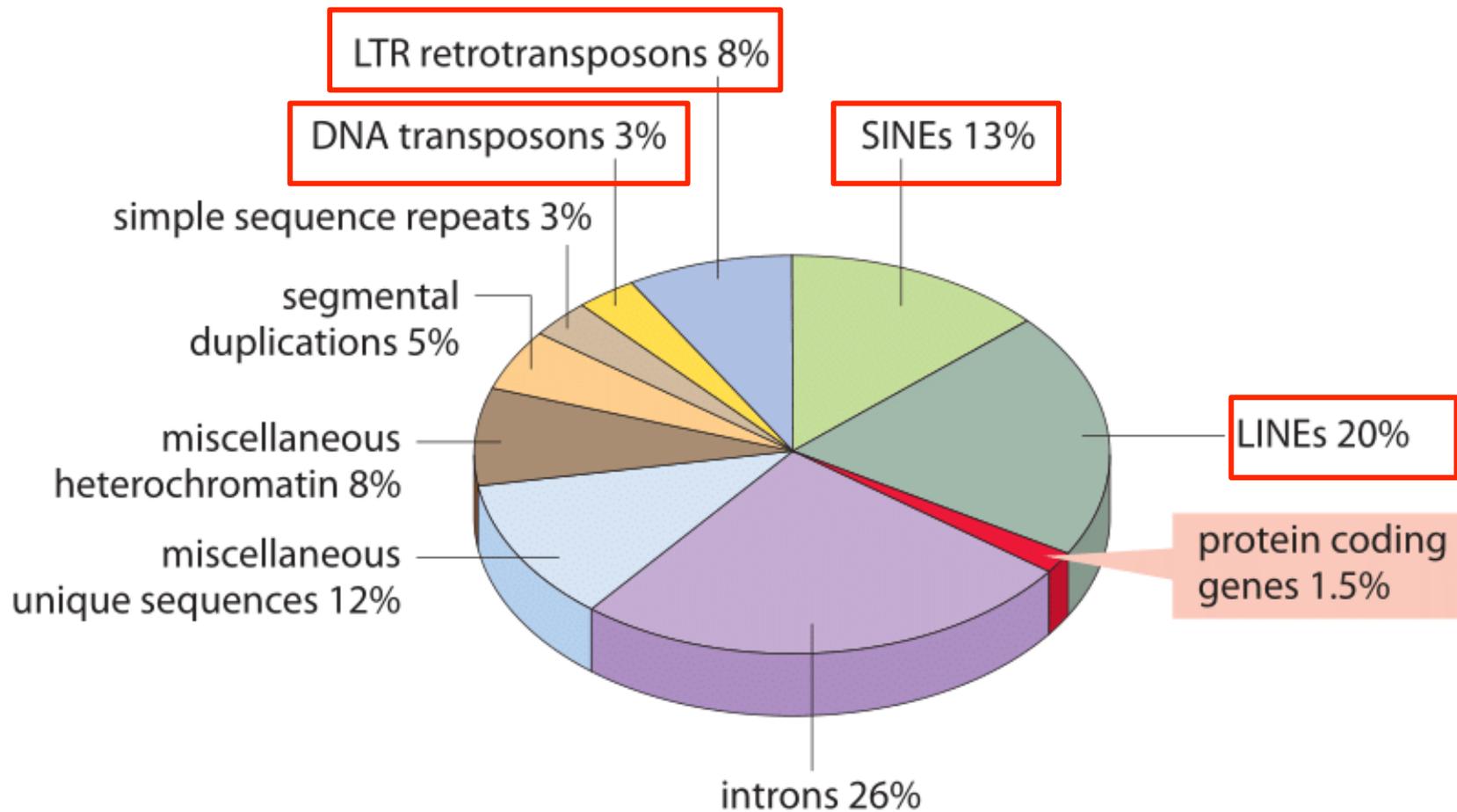
Genomgröße = C-Wert
(in bp/Kbp/Mbp oder in pg)

$$1 \text{ pg} = 0.965 \times 10^9 \text{ bp} \\ = 6.1 \times 10^{11} \text{ Da} = 34 \text{ cm}$$

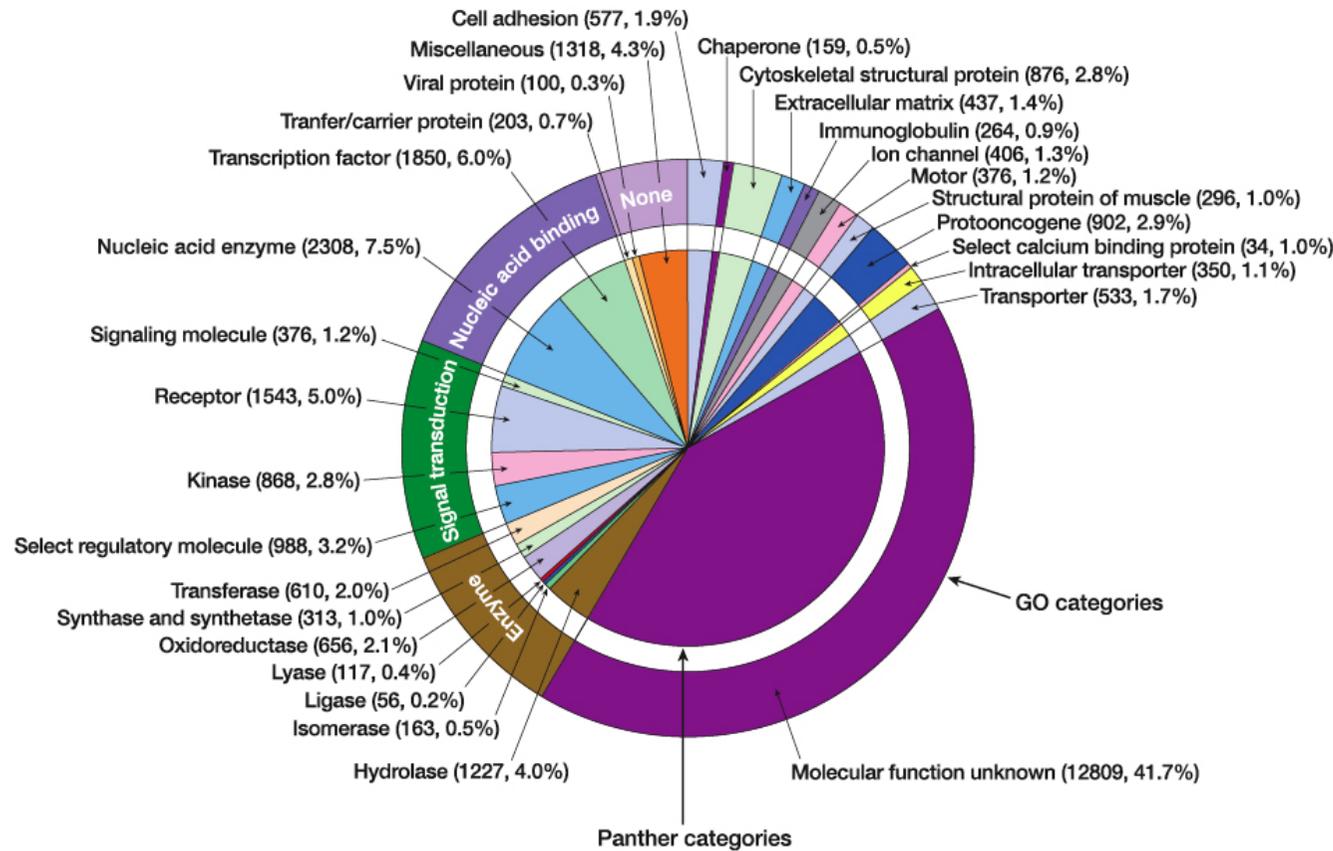
DOGS - Database Of Genome Sizes

<http://www.cbs.dtu.dk/databases/DOGS/>

Fast die Hälfte des menschlichen Genoms besteht aus **Transposons**



Viele Genfunktionen unbekannt...



Mindestens 2000 Gene sind an Erkrankungen beteiligt (OMIM Datenbank)

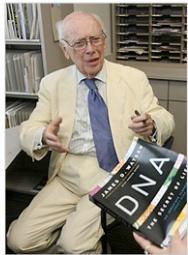
Figure 12.20: A preliminary functional classification of human polypeptide-encoding genes. Known or predicted functions for 26 383 human polypeptide-encoding genes. Classification is according to the GO molecular function categories as shown in the outer circle (Gene Ontology classification – see Section 8.3.6) or to Celera’s Panther molecular function categories (inner circle). Reproduced from Venter *et al.* (2001) *Science* **291**, 1304–1351, with permission from the American Association for the Advancement of Science.

Genome of DNA Discoverer Is Deciphered

By NICHOLAS WADE
Published: June 1, 2007

The full genome of James D. Watson, who jointly discovered the structure of DNA in 1953, has been deciphered, marking what some scientists believe is the gateway to an impending era of personalized genomic medicine.

Enlarge This Image



Richard Carson/Reuters
James D. Watson, co-discoverer of the DNA helix and father of the Human Genome Project, prepares to autograph his book at the Baylor College of Medicine's Human Genome Sequencing Center.

A copy of his genome, recorded on two DVDs, was presented to Dr. Watson yesterday in a ceremony in Houston by Richard A. Gibbs, director of the Human Genome Sequencing Center at the Baylor College of Medicine, and by Jonathan M. Rothberg, founder of the company 454 Life Sciences.

"I am thrilled to see my genome," Dr. Watson said.

Dr. Rothberg's company makes an innovative DNA sequencing machine, the latest version of which proved capable of decoding Dr. Watson's genome in two months at a cost of less than \$1 million, said Michael Egholm, 454's vice president for research. The sequence was verified and analyzed by Dr. Gibbs's center in Houston. It was Dr. Gibbs who proposed the idea of sequencing Dr. Watson's genome.

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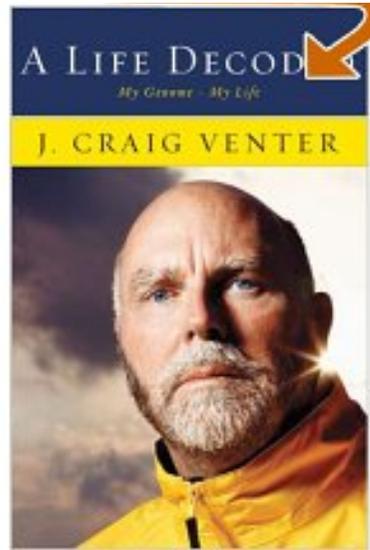
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Personal Genome Projects

ARTICLE

OPEN

doi:10.1038/nature15393

A global reference for human genetic variation

The 1000 Genomes Project Consortium*

1. Okt. 2015

The 1000 Genomes Project set out to provide a comprehensive description of common human genetic variation by applying whole-genome sequencing to a diverse set of individuals from multiple populations. Here we report completion of the project, having reconstructed the genomes of 2,504 individuals from 26 populations using a combination of low-coverage whole-genome sequencing, deep exome sequencing, and dense microarray genotyping. We characterized a broad spectrum of genetic variation, in total over 88 million variants (84.7 million single nucleotide polymorphisms (SNPs), 3.6 million short insertions/deletions (indels), and 60,000 structural variants), all phased onto high-quality haplotypes. This resource includes >99% of SNP variants with a frequency of >1% for a variety of ancestries. We describe the distribution of genetic variation across the global sample, and discuss the implications for common disease studies.

..ACGGC..
..TGCCG..

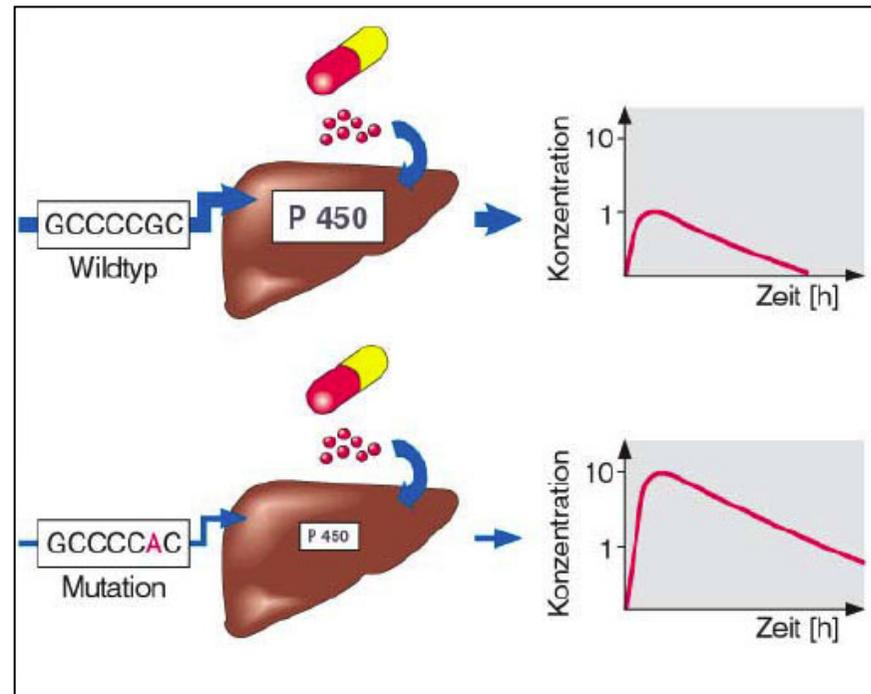
..ACTGC..
..TGACG..

Single Nucleotide Polymorphisms (SNPs)

Zwei beliebige Genome unterscheiden sich im Mittel alle **1000 Bp**.

Aus diesen etwa **3 Mio. Bp-Unterschieden** pro Genom resultiert ein Großteil unserer Individualität.

Auch die Reaktion auf Pharmazeutika!



Pharmakogenetik > personalisierte Medizin

Genomprojekte bei Modell-Organismen



Platypus
Ornithorhynchus anatinus



Dog
Canis familiaris
Photo: Courtesy of The Broad Institute of MIT and Harvard



African elephant
Loxodonta africana



Fruitfly
Drosophila melanogaster



Silkworm
Bombyx mori Daza
Photo: Alden M. Johnson, California Academy of Sciences



Cow
Bos taurus
Photo: Courtesy of Terri Hobbs (www.crazyforcows.com)



European rabbit
Oryctolagus cuniculus



Honey Bee
Apis mellifera
Photo: Courtesy of Scott Bauer, USDA/ARSLaboratories



Armadillo
Dasypus novemcinctus
Photo: Courtesy of B. Bagatto, Department of Biology, University of Akron



Guinea pig
Cavia porcellus



Roundworm
Caenorhabditis elegans
Photo: Courtesy of Erik Jorgensen, University of Utah



Zebrafish
Danio rerio



Mouse
Mus musculus
Photo: Courtesy of Jackson Laboratories



Chicken
Gallus gallus



Opossum
Monodelphis domestica
Photo: Courtesy of Don Sakaguchi



Cat
Felis domesticus
Photo: Courtesy of Dr. Kristina Narfstrom, University of Missouri-Columbia

Blindmulle
Spalax



Fang X et al. (2014)

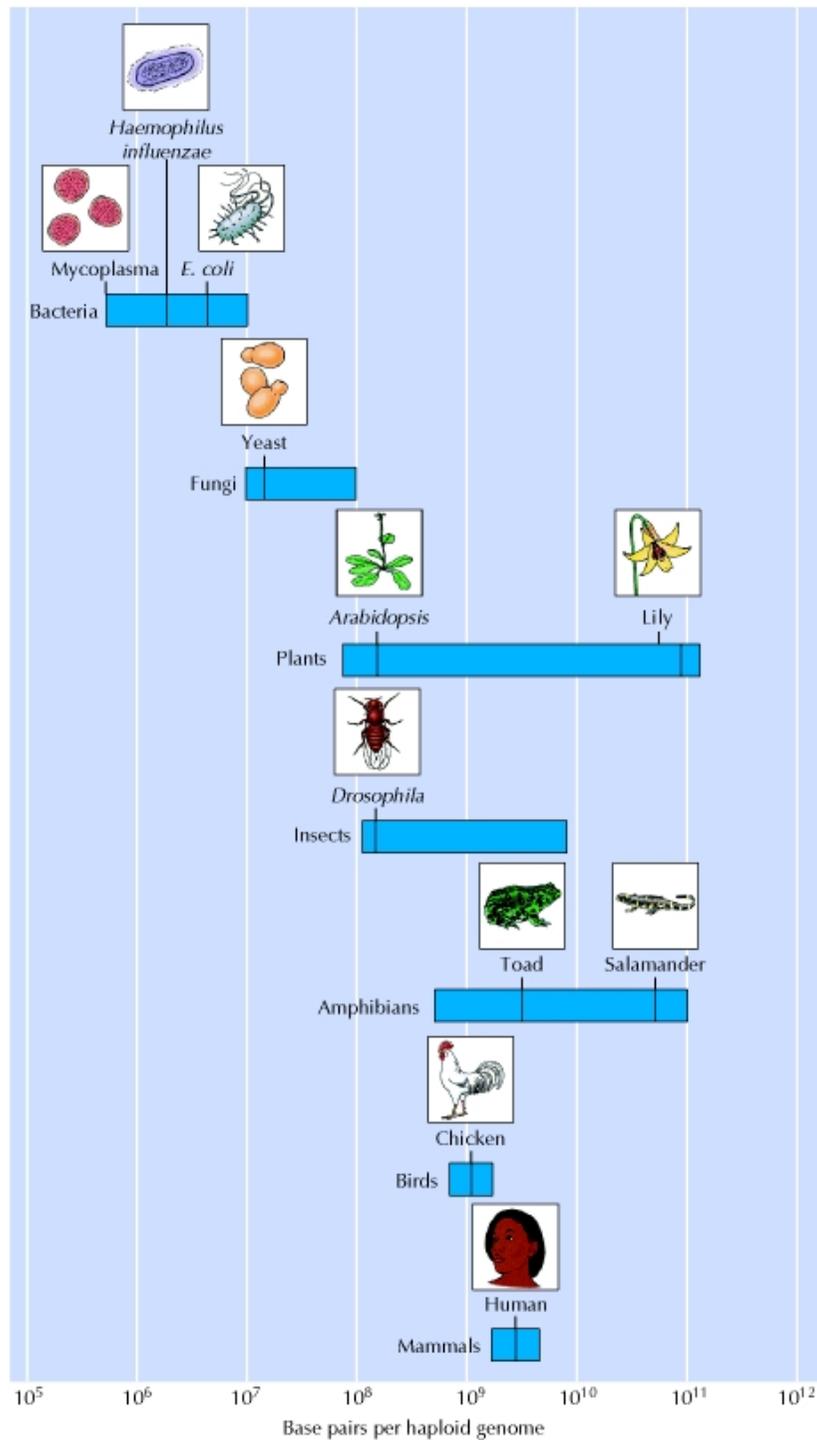
Politik, Forschung und Modellorganismen



<https://www.youtube.com/watch?v=Eg1vleuQT1s>

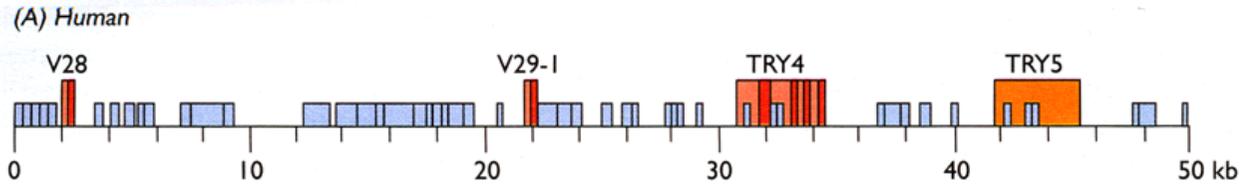
Das C-Wert-Paradoxon*

* Enorme Unterschiede in der Genomgröße trotz weitgehend ähnlicher Komplexität der Organismen

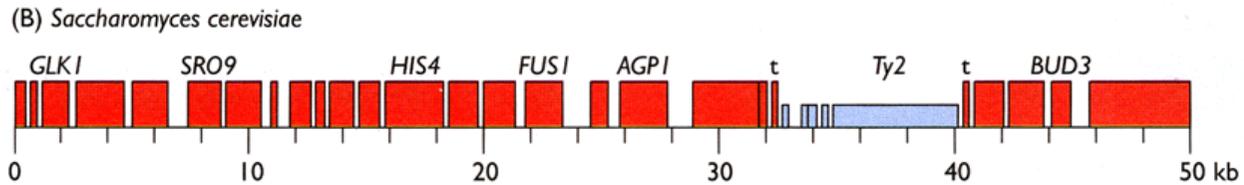


Die Genomstruktur ist artspezifisch

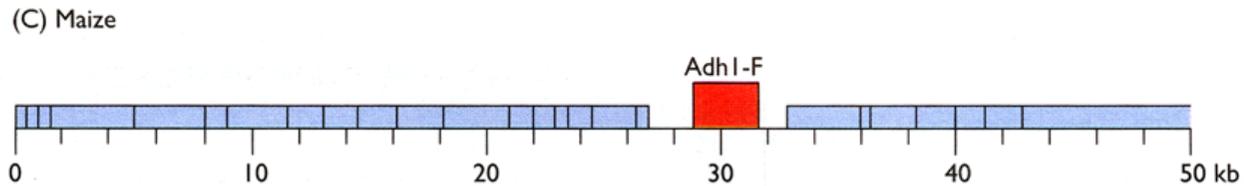
Mensch



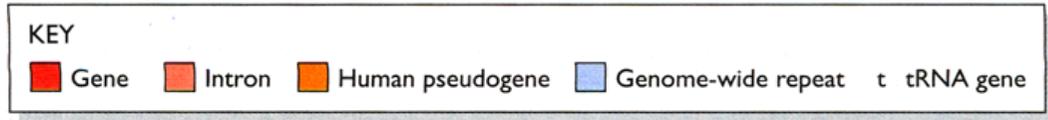
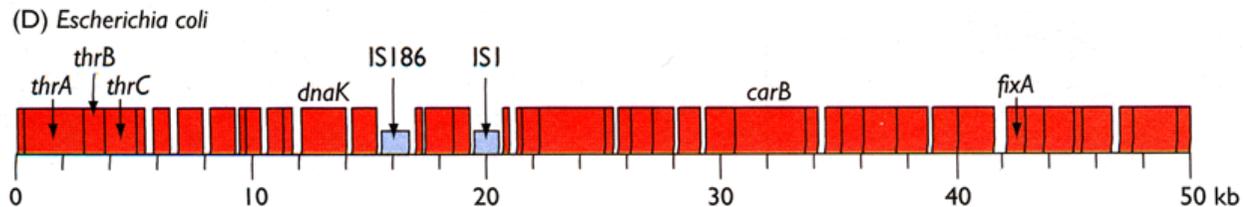
Hefe



Mais

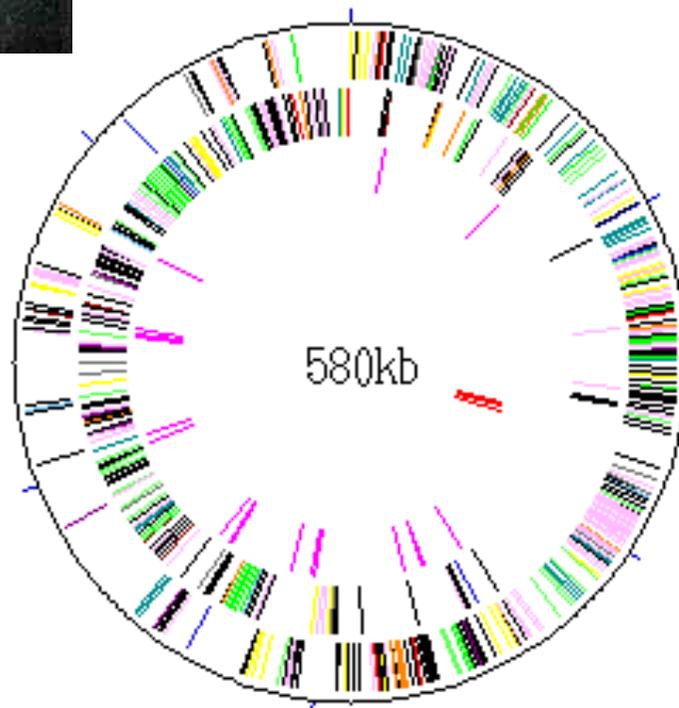


E. coli



Prokaryoten-Genome

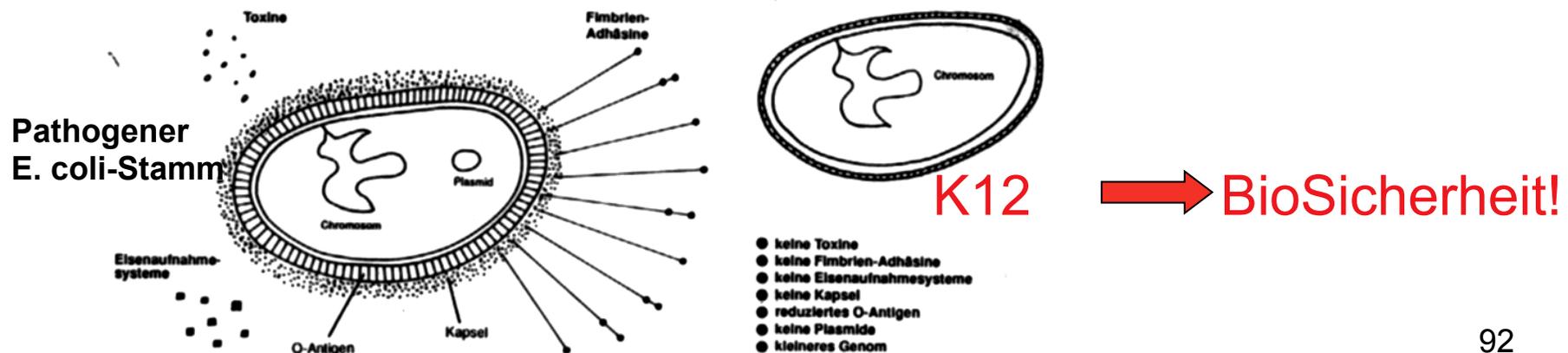
z. B. *Mycoplasma genitalium*: 582 970 Bp und 521 Gene



- meist ringförmig
- wenig repetitive DNA
- ‚dicht-gepackte‘ Gene, oft ca. 1 Gen/kb

Genomgrößen in Prokaryoten

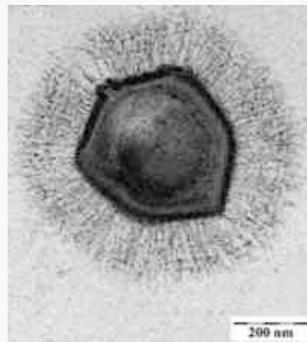
• Eubakterien:	Nasuia spec.	112 kb
	Mycoplasma genitalium	583 kb
	E. coli (K12)	4639 kb
	E. coli (O157:H7)	5529 kb
	Sorangium cellulosum	14782 kb





Tot oder lebendig?

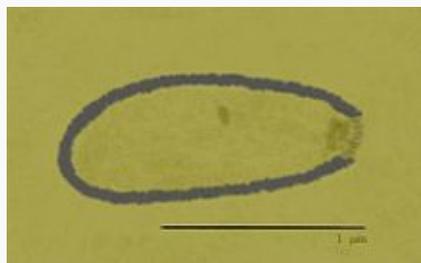
- Mimi*-Virus (befällt Amöben)



1.2 Mb DNA
1260 Gene
< 10% repetitive DNA

400 nm groß!

- Pithovirus sibericum (Bohrkern aus sibirischem Permafrost)



600 Kb DNA
470 Gene

1,5 µm groß !!

* **Microbe-mimicking**

Synthetische Biologie !



Science 2010

Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome

Daniel G. Gibson,¹ John I. Glass,¹ Carole Lartigue,¹ Vladimir N. Noskov,¹ Ray-Yuan Chuang,¹ Mikkel A. Algire,¹ Gwynedd A. Benders,² Michael G. Montague,¹ Li Ma,¹ Monzia M. Moodie,¹ Chuck Merryman,¹ Sanjay Vashee,¹ Radha Krishnakumar,¹ Nacyra Assad-Garcia,¹ Cynthia Andrews-Pfannkoch,¹ Evgeniya A. Denisova,¹ Lei Young,¹ Zhi-Qing Qi,¹ Thomas H. Segall-Shapiro,¹ Christopher H. Calvey,¹ Prashanth P. Parmar,¹ Clyde A. Hutchison III,² Hamilton O. Smith,² J. Craig Venter^{1,2*}

We report the design, synthesis, and assembly of the 1.08–mega–base pair *Mycoplasma mycoides* JCVI-syn1.0 genome starting from digitized genome sequence information and its transplantation into a *M. capricolum* recipient cell to create new *M. mycoides* cells that are controlled only by the synthetic chromosome. The only DNA in the cells is the designed synthetic DNA sequence, including “watermark” sequences and other designed gene deletions and polymorphisms, and mutations acquired during the building process. The new cells have expected phenotypic properties and are capable of continuous self-replication.

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It's time to play God

If Craig Venter's research leads to engineering new forms of life, mankind has hope for the future

