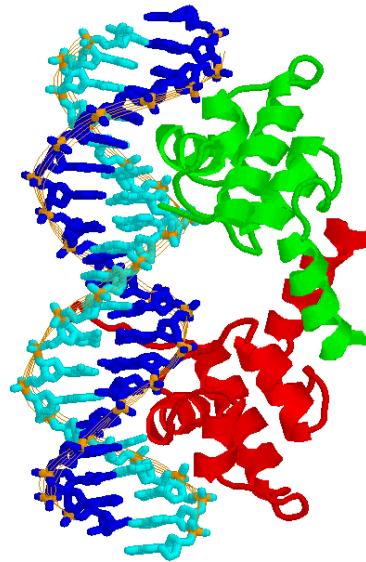


# Molekulargenetik der Eukaryoten

## WS 2006/7



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# Molekulargenetik der Eukaryoten

- Teilnahme an Vorlesung und „Quicktests“ ist Voraussetzung für Platz in F1-Praktikum Molekulargenetik der Eukaryoten
- ECTS-Punkte (2) nur bei regelmäßiger Teilnahme (Anwesenheitsliste)
- Ergebnis aus 12 Quicktests entscheidet über Platz in F1-Praktikum
- F1-Praktikum vom 19. 2. – 10. 03. 2007

# Literaturempfehlungen

- Watson, Baker, Bell, Gann, Levine, Losick: Molecular Biology of the Gene, Int. Ed. CSHL-Press 2004, ISBN 0-321-22368-3, 63,90€
- Graw, Genetik, 4. Auflage, Springer Heidelberg 2006, ISBN 3-540-24096-9
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## Speziell für DNA-Freunde

Calladine, Chris R., Drew, Horace, R., Luisi, Ben F.,  
Travers, Andrew A.: DNA Das Molekül und seine  
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R. R. Sinden: DNA Structure and Function,  
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ISBN 0-12-645750-6

D. A. Micklos, G. A. Freyer: DNA-Science, A First Course,  
CSHL-Press N.Y. 2003  
ISBN 0-87969-636-2

# Themen der heutigen Vorlesung

- Präbiotische Evolution
- Nukleotide und Nukleinsäuren, RNA/DNA
- Von der RNA zur DNA-Welt
- Unterschiede Pro- und Eukaryoten
- Genomstruktur der Eukaryoten

# „Präbiotische Evolution“

- Alles, was wir heute Leben nennen, spielt sich in **Zellen** ab
- Aber auch in abiotischem Milieu entstehen typische „Biomoleküle“, oder wenigstens deren Bausteine
- Manche dieser Moleküle sind sogar im Weltraum nachgewiesen worden

# Die präbiotische Evolution:

- Die wichtigsten Moleküle des Lebens:
- Zucker
- Aminosäuren
- Nucleotide
- Fettsäuren
- U.a.

# Extrazelluläre „Biomoleküle“ aus der Retorte (Miller-Experiment)

Tabelle 6.1: Präbiotische Bausteine, die entstehen, wenn man  $\text{CH}_4 + \text{NH}_3 + \text{H}_2\text{O} + \text{H}_2$  entzündet.

Verbindung	% Kohlenstoff aus $\text{CH}_4$
Ameisensäure	4,0
Glycin	2,1
Glycolsäure	1,9
Alanin	1,7
Milchsäure	1,6
$\beta$ -Alanin	0,76
Propionsäure	0,66
Essigsäure	0,51
Iminodiessigsäure	0,37
$\alpha$ -Aminobuttersäure	0,34
$\alpha$ -Hydroxybuttersäure	0,34
Bernsteinsäure	0,27
andere	0,62

Nach Miller (110, 111).

# Aminosäuren aus dem Weltraum

Aminosäure	Meteorit von Murchison	elektrische Entladung
Glycin	++++	+++
Alanin	++++	+++
$\alpha$ -Amino- <i>n</i> -Buttersäure	+++	+++
$\alpha$ -Isoaminobuttersäure	++++	++
Valin	+++	++
Norvalin	+++	+++
Isovalin	++	++
Prolin	+++	+
Pipecolinsäure	+	<+
Asparaginsäure	+++	+++
Glutaminsäure	+++	++
$\beta$ -Alanin	++	++
$\beta$ -Amino- <i>n</i> -Buttersäure	+	+
$\beta$ -Isoaminobuttersäure	+	+
$\gamma$ -Aminobuttersäure	+	++
Sarkosin	++	+++
<i>N</i> -Ethylglycin	++	+++
<i>N</i> -Methylalanin	++	++

Nach Miller (110, 111).

# Die präbiotische Evolution: Zucker

„Formose-Reaktion“

*Präbiotische Evolution:  
Entstehung von Zuckern*

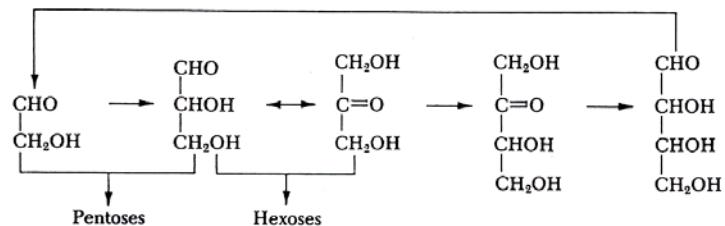
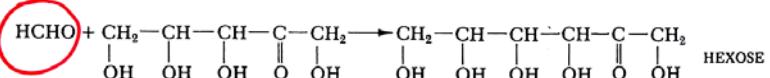
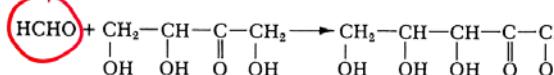
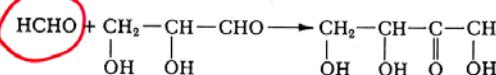
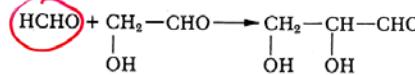
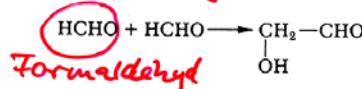


Figure 11. Formation of sugars. Sequential condensations of formaldehyde generate trioses, tetroses, pentoses, and hexoses. Five- and six-carbon sugars are quite unstable in aqueous solutions and break down into alcohols and organic acids, but trioses and tetroses are more stable and can accumulate for hundreds of years. The reactions are autocatalytic, proceeding through glycoaldehyde, glyceraldehyde, and the various sugars to finally generate hexoses such as glucose and fructose. Clays will catalyze some of these reactions.

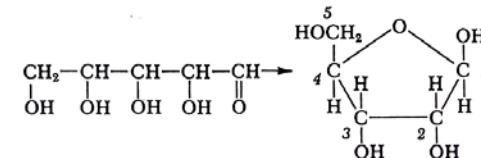


Figure 12. Ribose. This pentose preferentially takes up a 5-membered ring structure, referred to as a furanose structure. The configuration of the hydroxyl group at the C1 position (carbon on the right hand side of the ring) determines whether the furanose is referred to as  $\alpha$  or  $\beta$ . The structure shown is a  $\beta$ -D-ribofuranose.

# Die präbiotische Evolution: Aminosäuren

## Entstehung von Aminosäuren:



Blausäure (Cyanid)

Figure 3. Methane and ammonia are transformed into cyanide and hydrogen under conditions where electric discharge provides the activating energy for the reaction. Spark discharges in atmospheres of hydrogen, ammonia, and either carbon monoxide or carbon dioxide also generate cyanide.

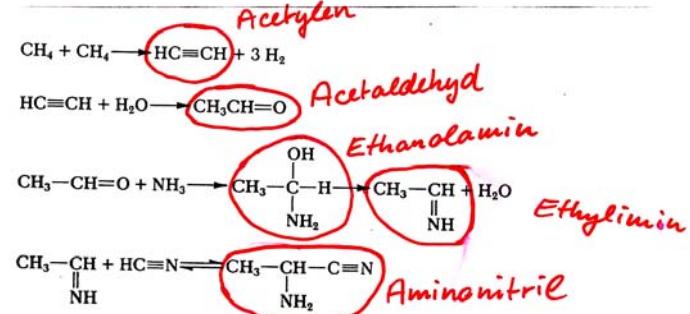


Figure 4. Electric discharges can excite methane to form acetylene, which spontaneously reacts with water to form acetaldehyde. Acetaldehyde and ammonia react to form ethanolamine, which will spontaneously dehydrate to give ethylimine. Imines and cyanide are thought to have been prevalent in the prebiological environment and to have reacted to form aminonitriles whenever electric energy was available.

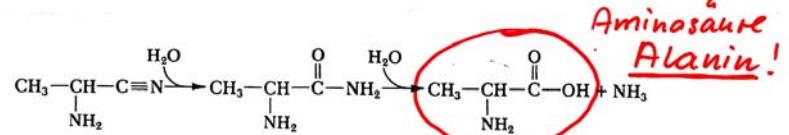


Figure 5. Formation of alanine. Water spontaneously reacts with the nitrile to generate the amino acid alanine in two steps.

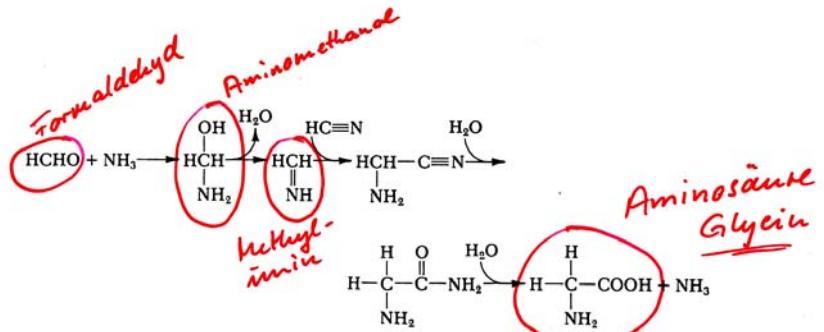


Figure 6. Synthesis of glycine. Formaldehyde and ammonia react to form aminomethanol that spontaneously dehydrates to give methylimine. Addition of cyanide and hydration generates glycine. This is the simplest and one of the most prevalent amino acids in the prebiological mix.

# Die präbiotische Evolution: Heterozykl. Basen Nukleotide

## Präbiotische Evolution Entstehung von Nukleobasen

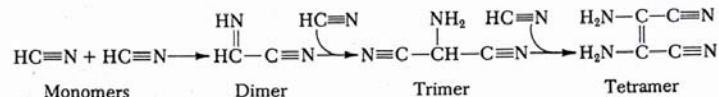


Figure 7. Polymerization of hydrogen cyanide. Cyanide readily dimerizes. Addition of another cyanide molecule generates the trimer, aminomaleonitrile. Further addition of a molecule of cyanide forms diaminomaleonitrile, the tetramer.

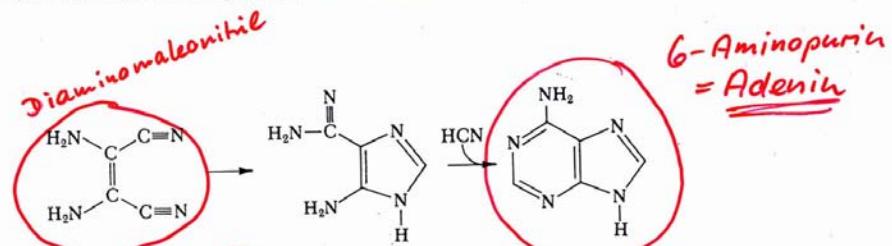


Figure 8. Formation of adenine. Prebiological reactions of diaminomaleonitrile and cyanide activated by ultraviolet light generate such complex molecules as the purine nucleic acid base, adenine. Yields of 0.5% adenine have been obtained when solutions of ammonium cyanide are refluxed for several days.

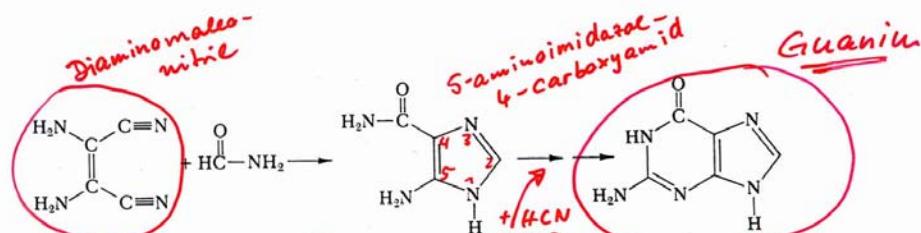


Figure 9. Formation of guanine. The tetramer of cyanide, diaminomaleonitrile, gives rise to 5-aminoimidazole-4-carboxamide in the presence of a concentrated solution of ammonia in water. Further reaction with cyanide, hydrolysis and cyclization can lead to formation of guanine in 30% yields. Several different chemical pathways starting with the polymerization of cyanide lead to the synthesis of guanine.

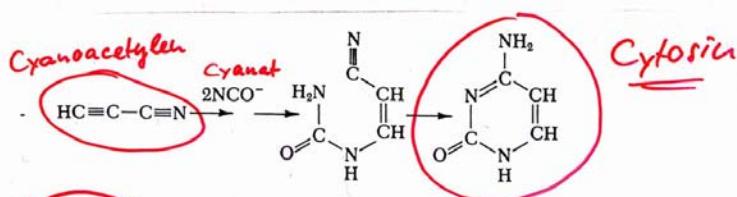


Figure 10. Cytosine formation. Cyanoacetylene reacts with aqueous cyanate to give cytosine in about 29% yields. The reaction appears to proceed by ring closure of ureidoacrylonitrile. Other routes of chemical synthesis also lead to pyrimidines, including the reaction of aminoacrylonitrile with cyanogen or cyanamide.

# Die Nukleotide sind die Bausteine der Nukleinsäuren

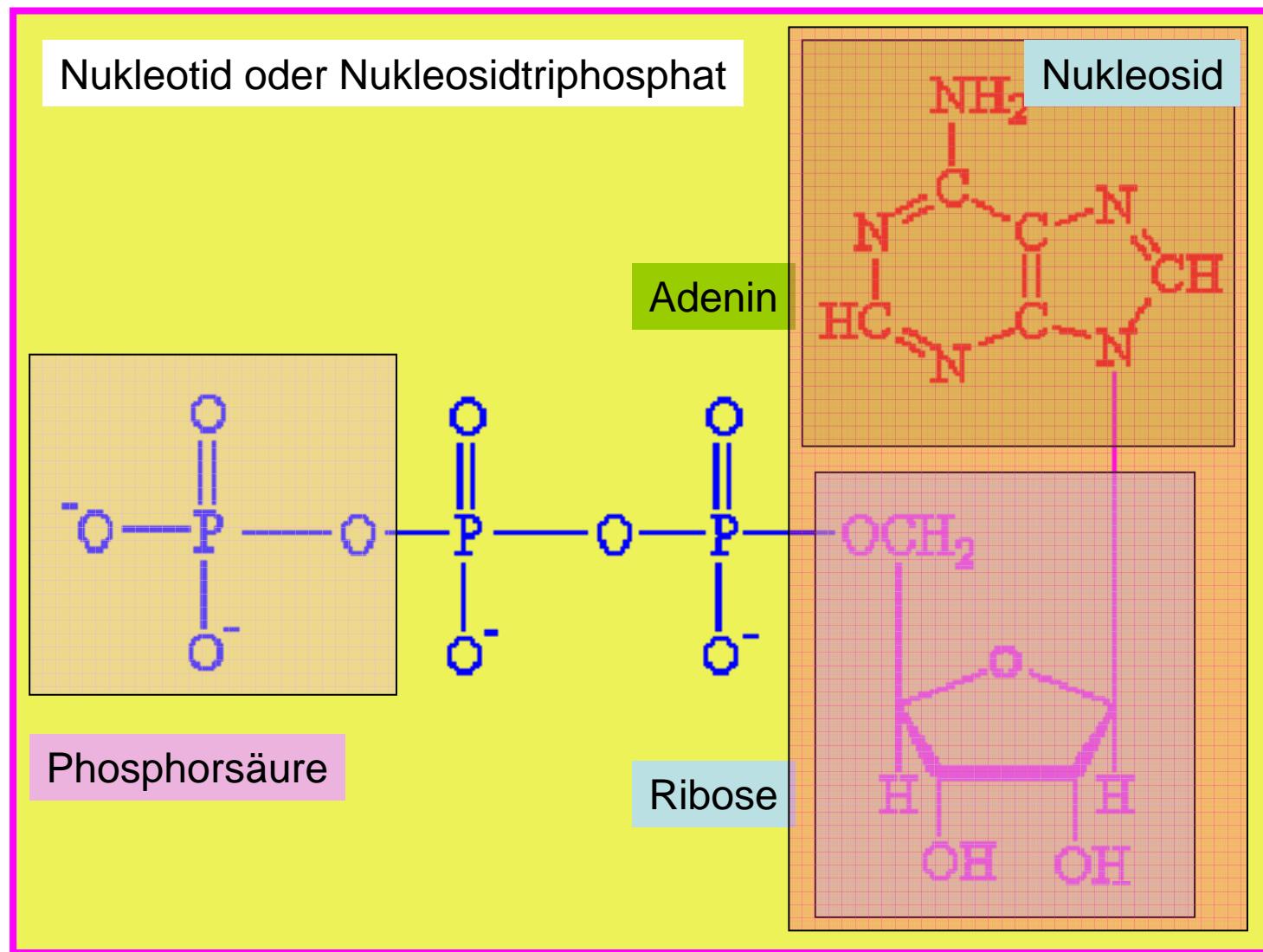
Die wichtigste Stoffklasse für die Molekulargenetik  
sind die **Nukleinsäuren**

Nukleinsäuren sind **Polynukleotide**  
**RNA**  
**DNA**

# Nukleotide

- Ein Nukleotid besteht aus drei einfachen Komponenten:
- Phosphatrest
- Pentose (Ribose oder 2'-Deoxy-Ribose)
- Nukleobase (Purinbase: Adenin oder Guanin; Pyrimidinbase Cytosin, Uracil oder Thymin =5-Methyl-Uracil)

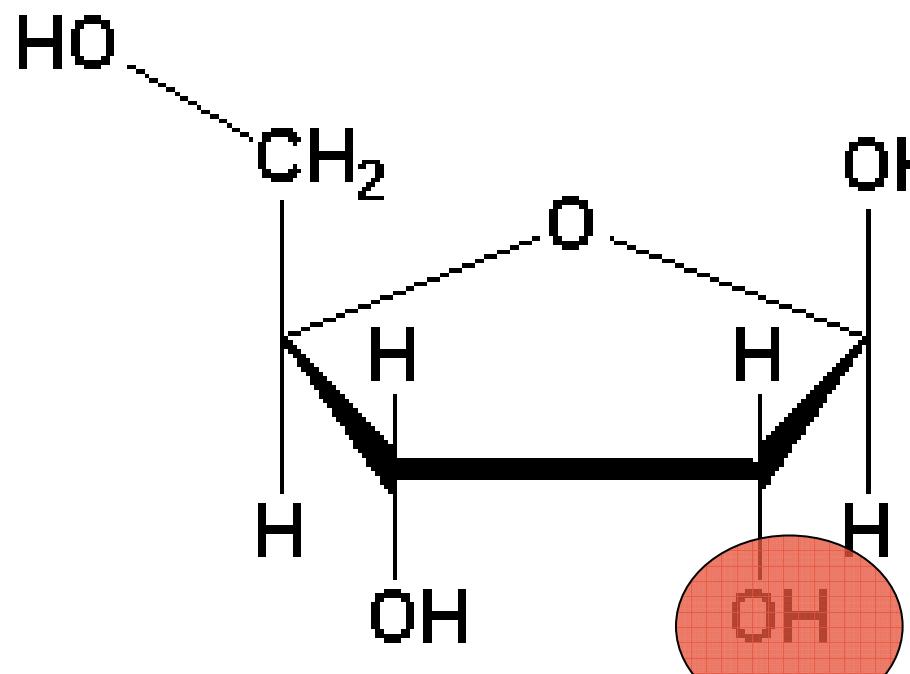
# z. B. Adenosintriphosphat (ATP)



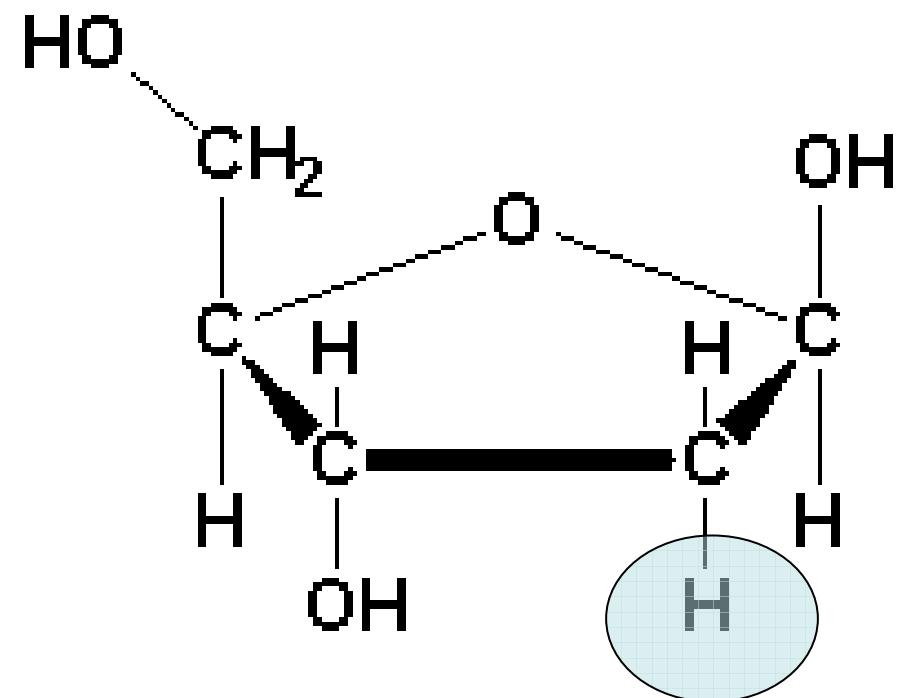
Ein wichtiger Unterschied wird durch den Zucker bestimmt:

- Ribose kommt nur in der RNA (=Ribonukleinsäure) vor
- 2'-Deoxyribose kommt nur in der DNA (Deoxyribonukleinsäure) vor

# Ribose und 2-Deoxy-Ribose

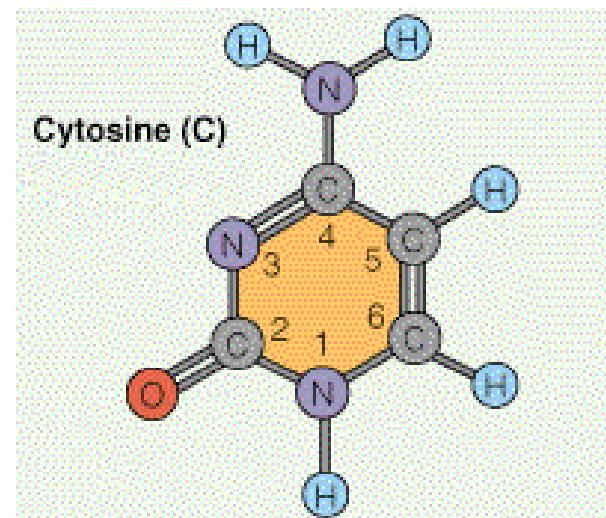
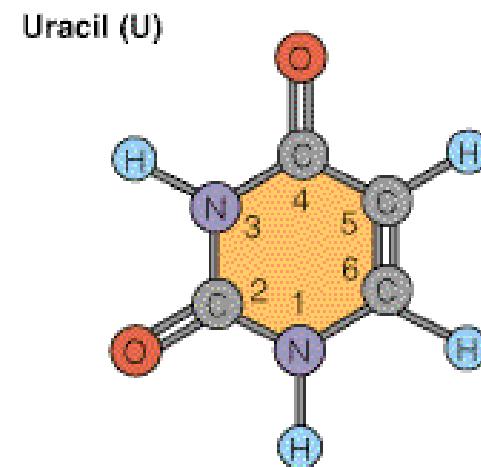
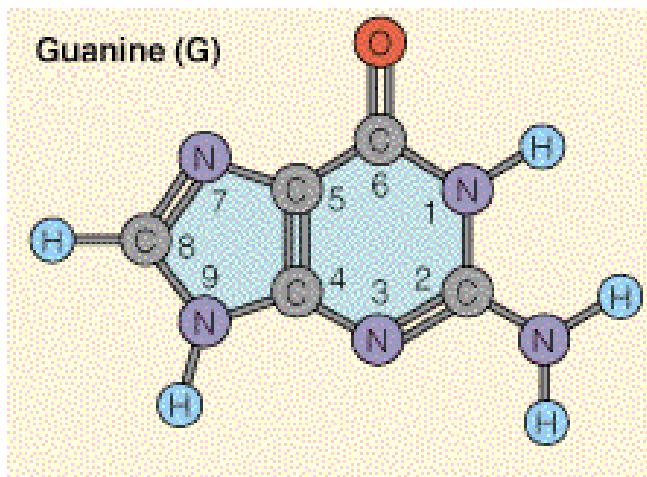
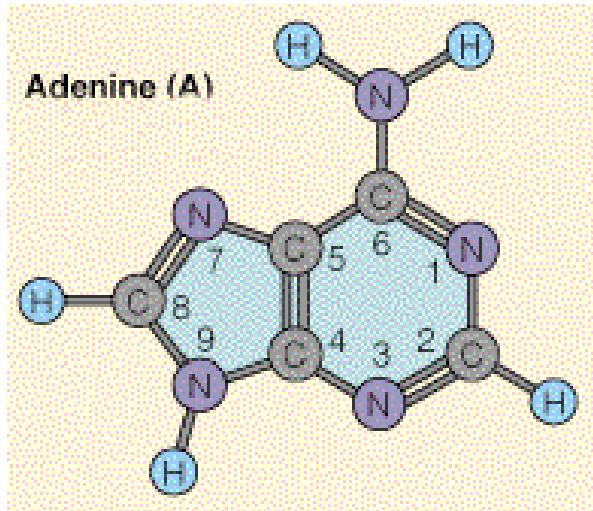


D-Ribose

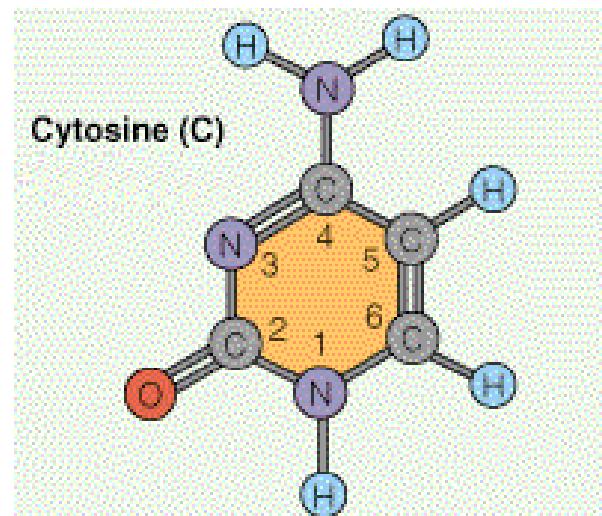
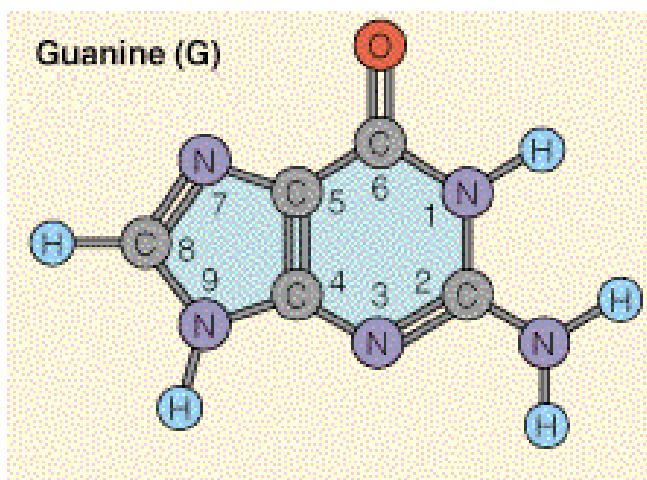
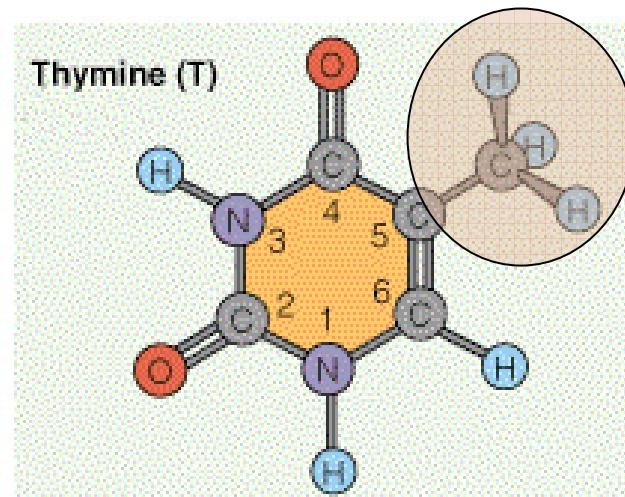
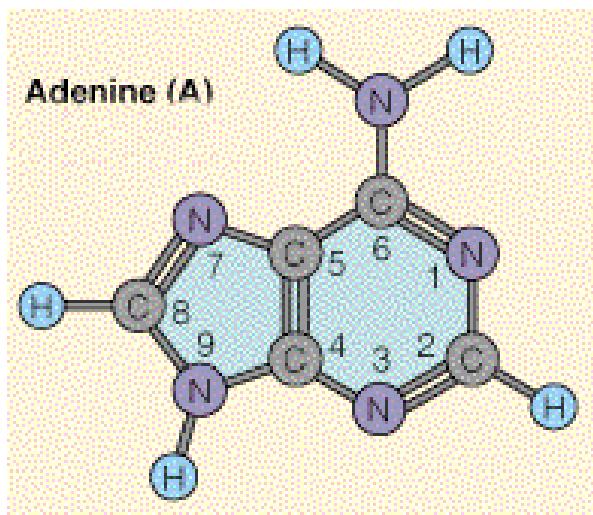


Deoxyribose

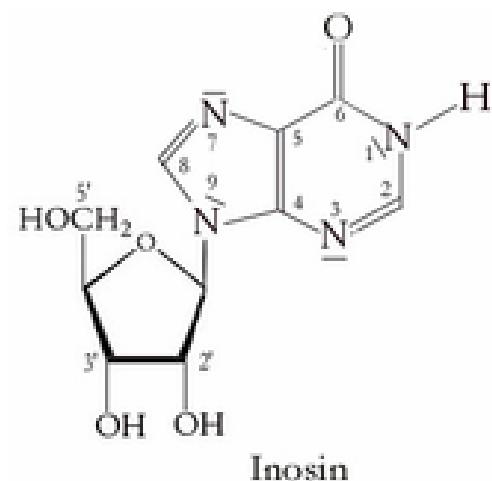
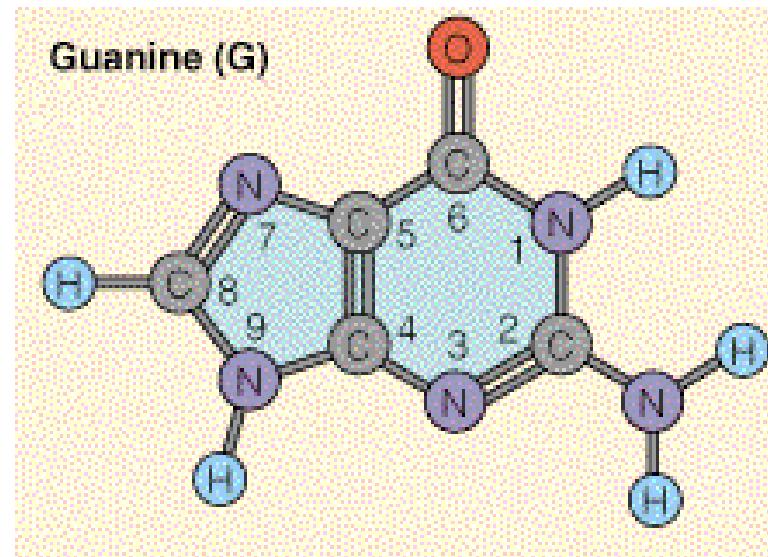
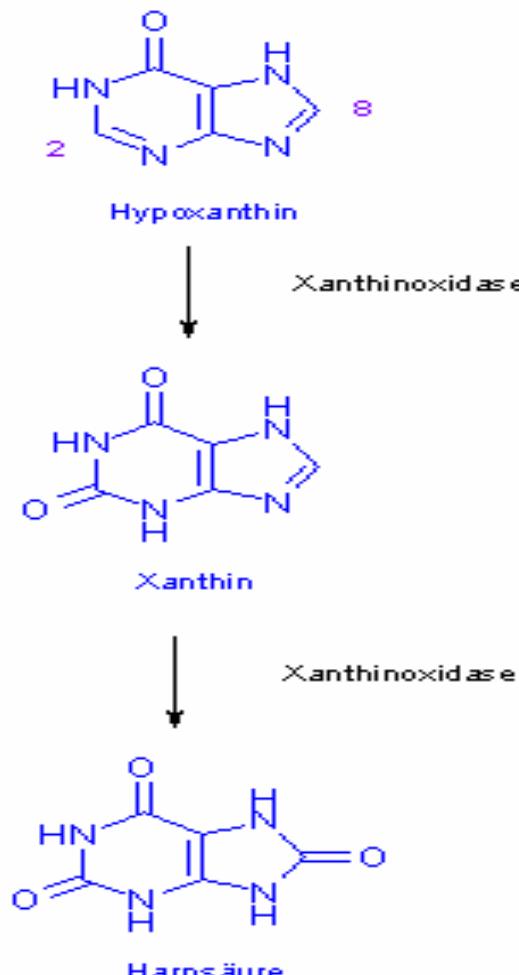
# Die Nukleobasen der RNA



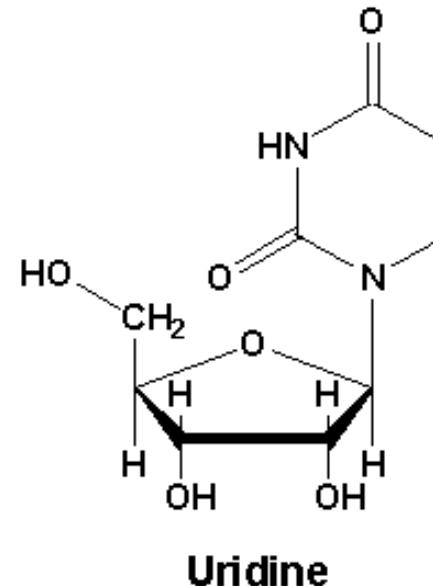
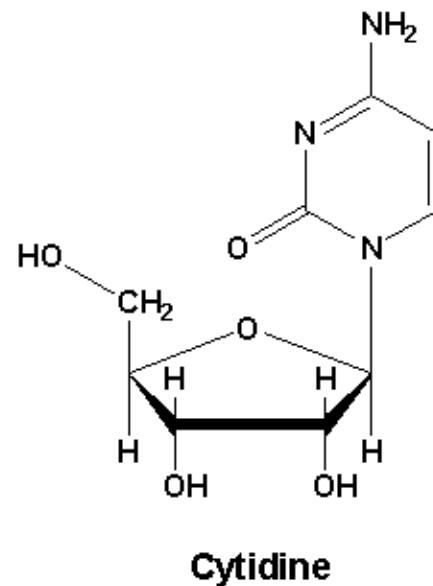
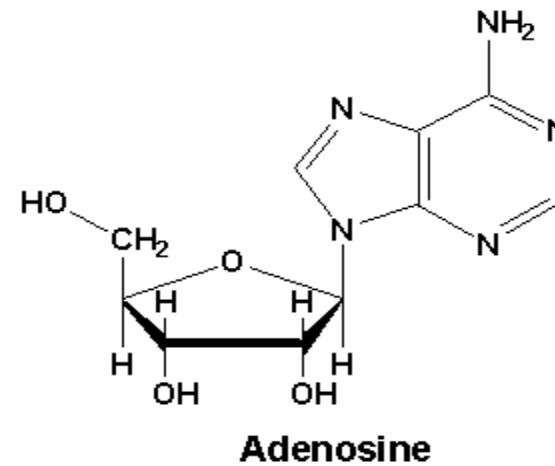
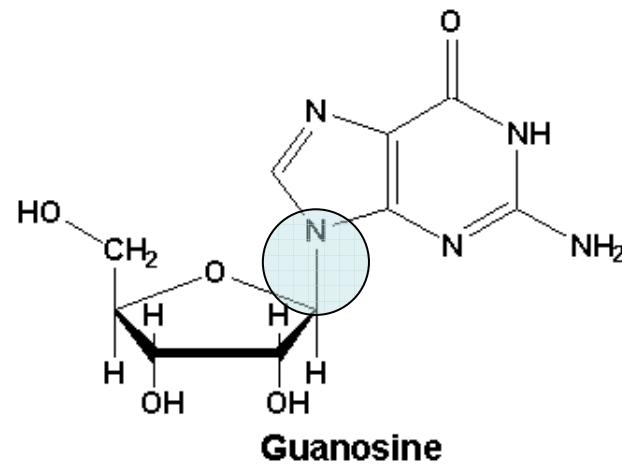
# Die Nukleobasen der DNA



# Seltene Basen in der RNA/DNA

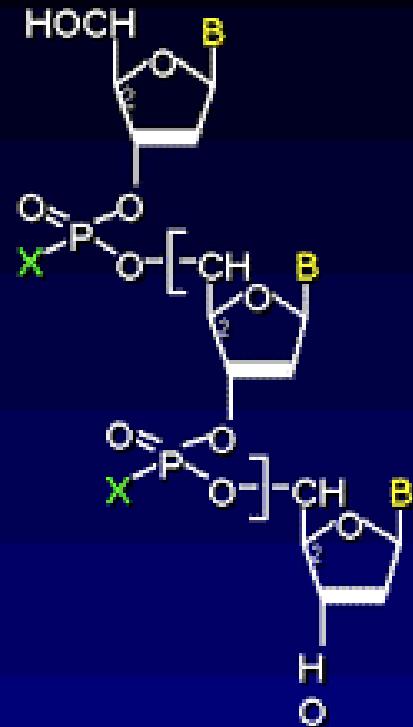


# Die Nukleobasen werden mit der Pentose über N-glycosidische Bindungen zu „Nucleosiden“ verknüpft



Zwei Nukleotide werden über Phosphodiester-Bindungen zu Oligo- und Polynukleotiden verknüpft

## Oligonucleotide

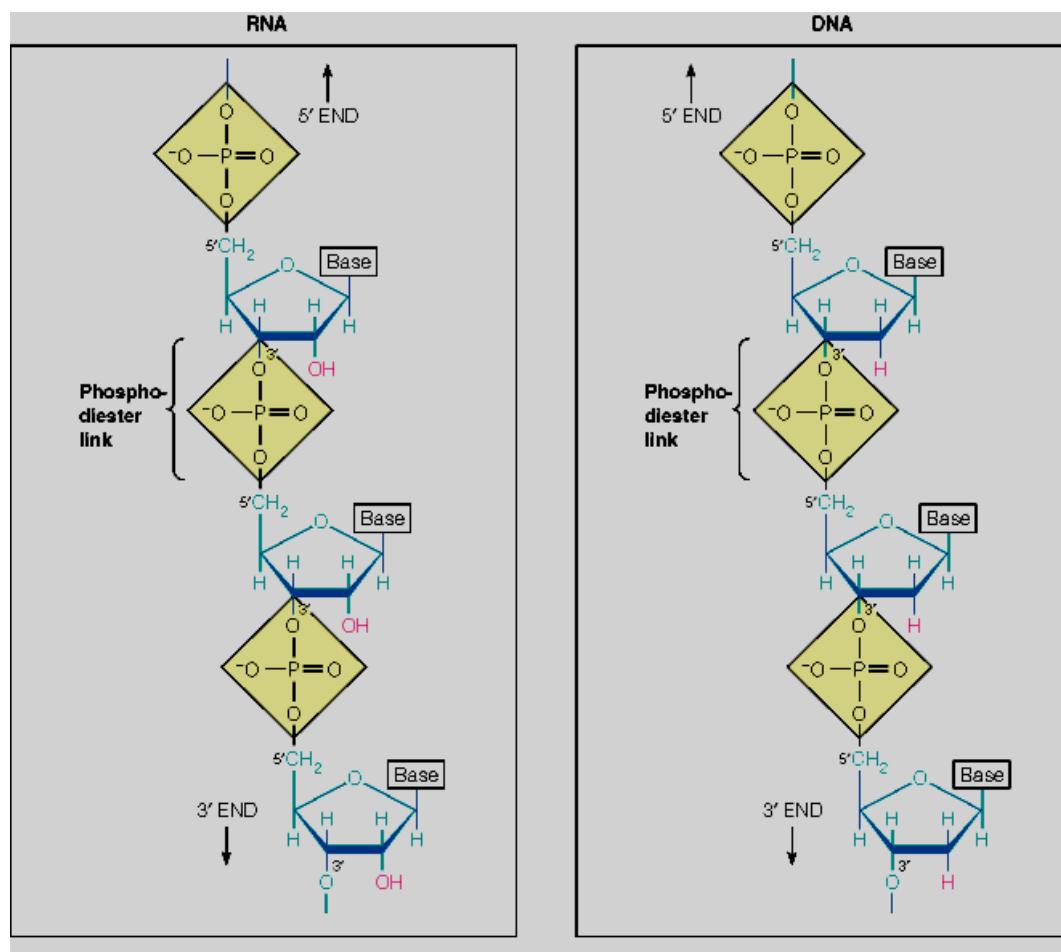


X
I    O <sup>-</sup>
II   OEt
III   Me
IV   S <sup>-</sup>

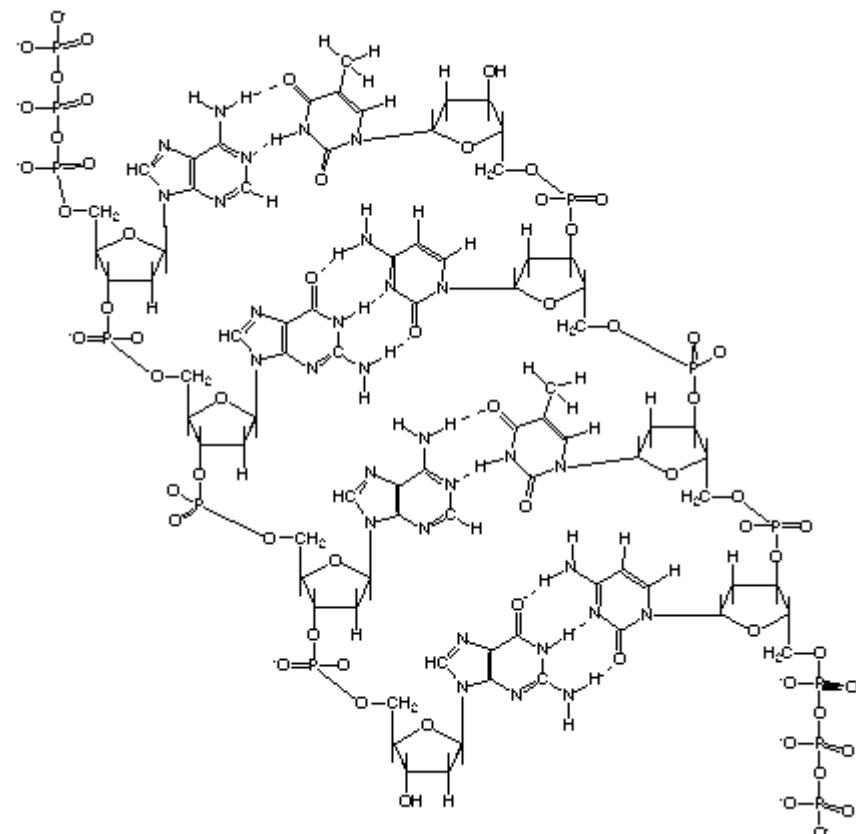
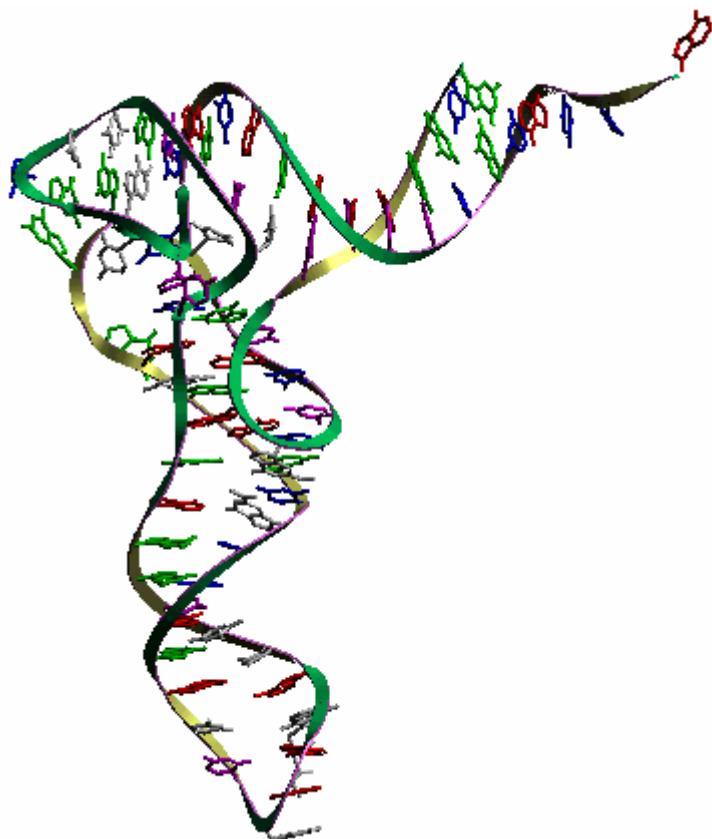
B= Base(A,T,U,G,C)



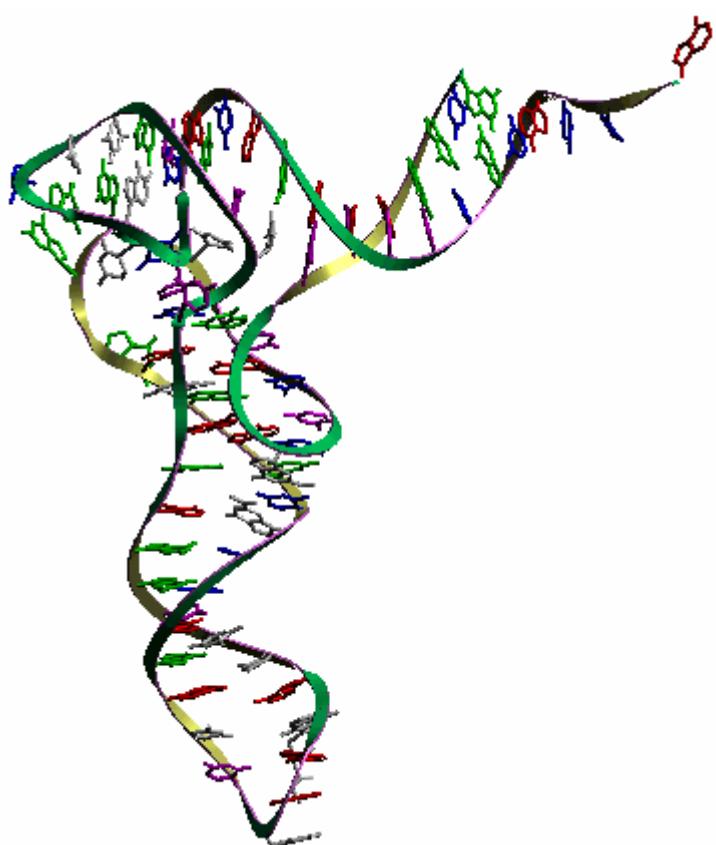
# Polynukleotide entstehen durch Bildung von Phosphodiesterbindungen zwischen Zucker und Phosphat



RNAs sind i. A. einkettige Moleküle  
DNAs zweikettig



Sowohl RNAs als auch DNAs haben eine ausgeprägte Sekundärstruktur

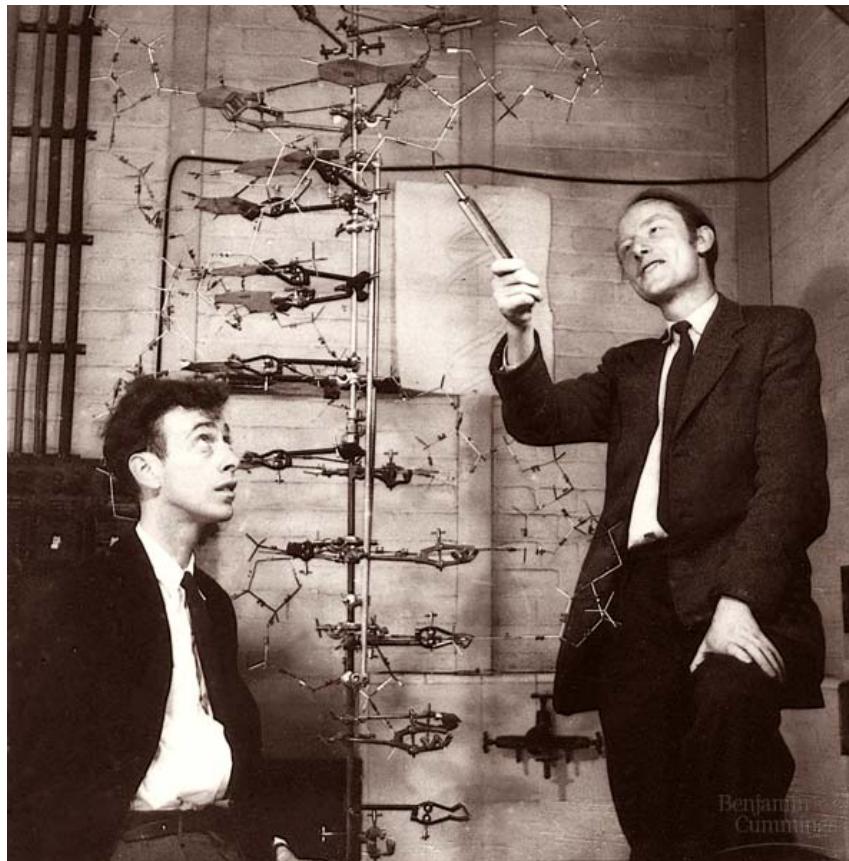


tRNA



B-DNA

# Die typische Struktur ist die „Doppelhelix“

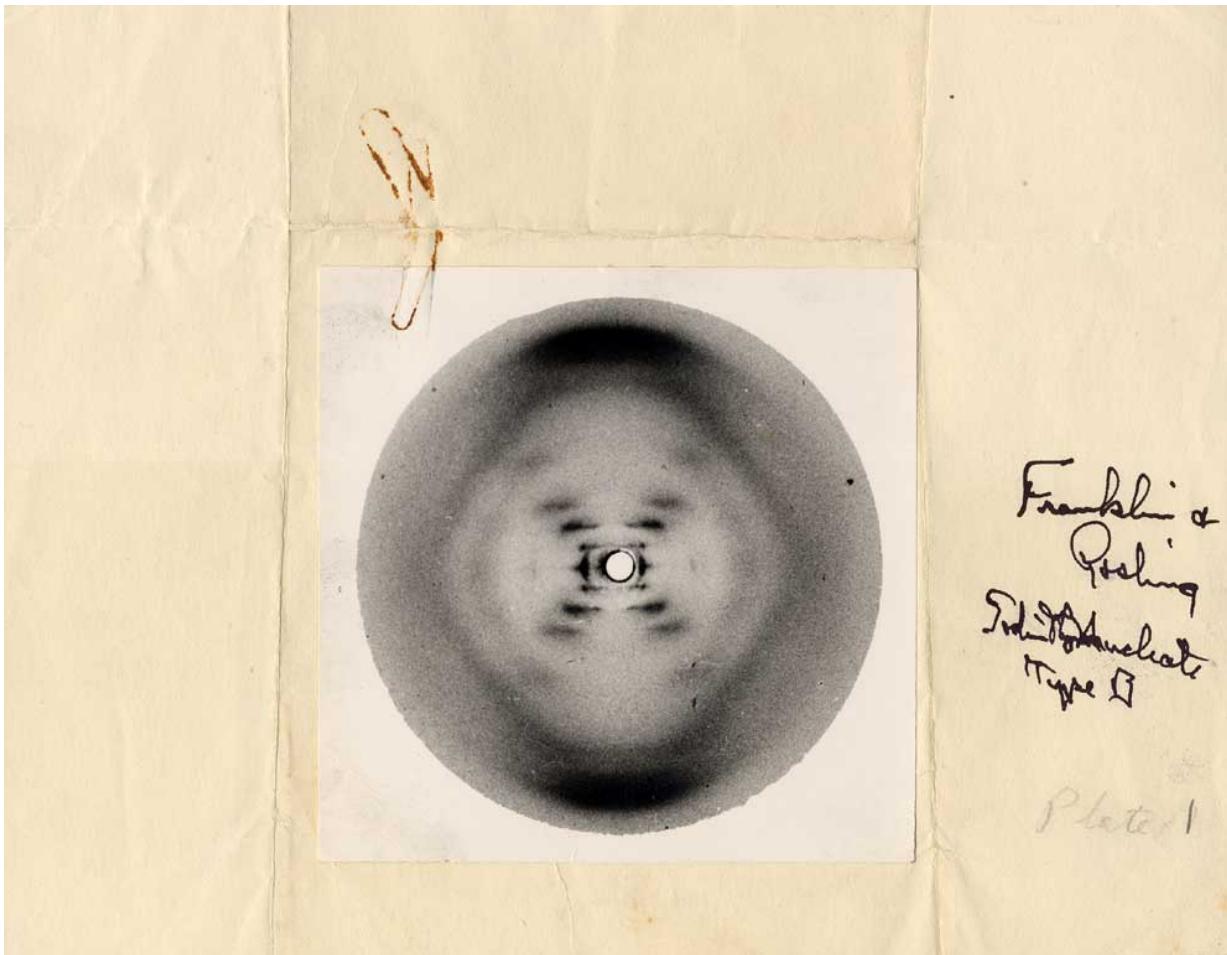


Watson und Crick, DNA-Modell 1953

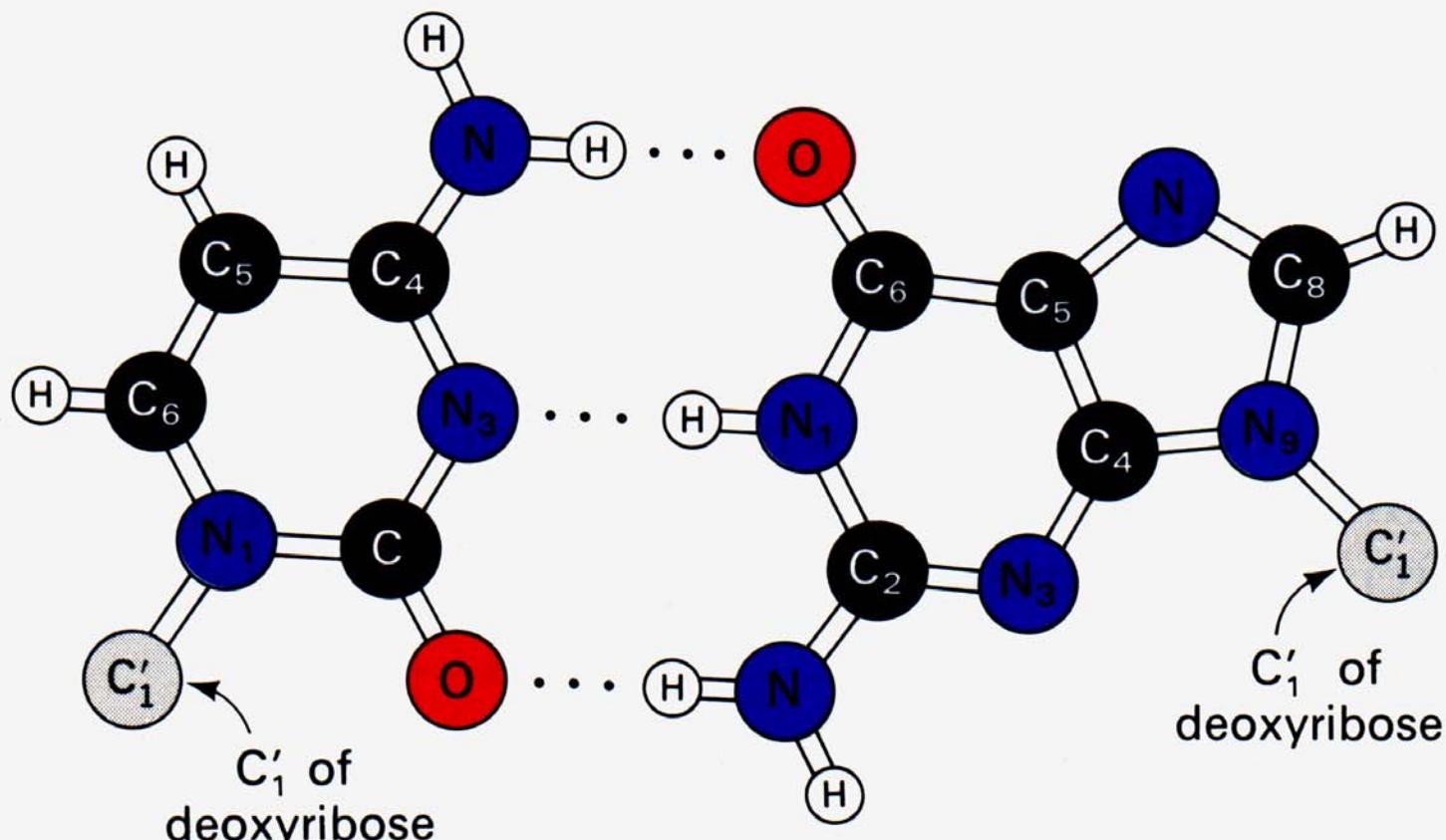


B-DNA

# Röntgenstreuung zeigt Helix an

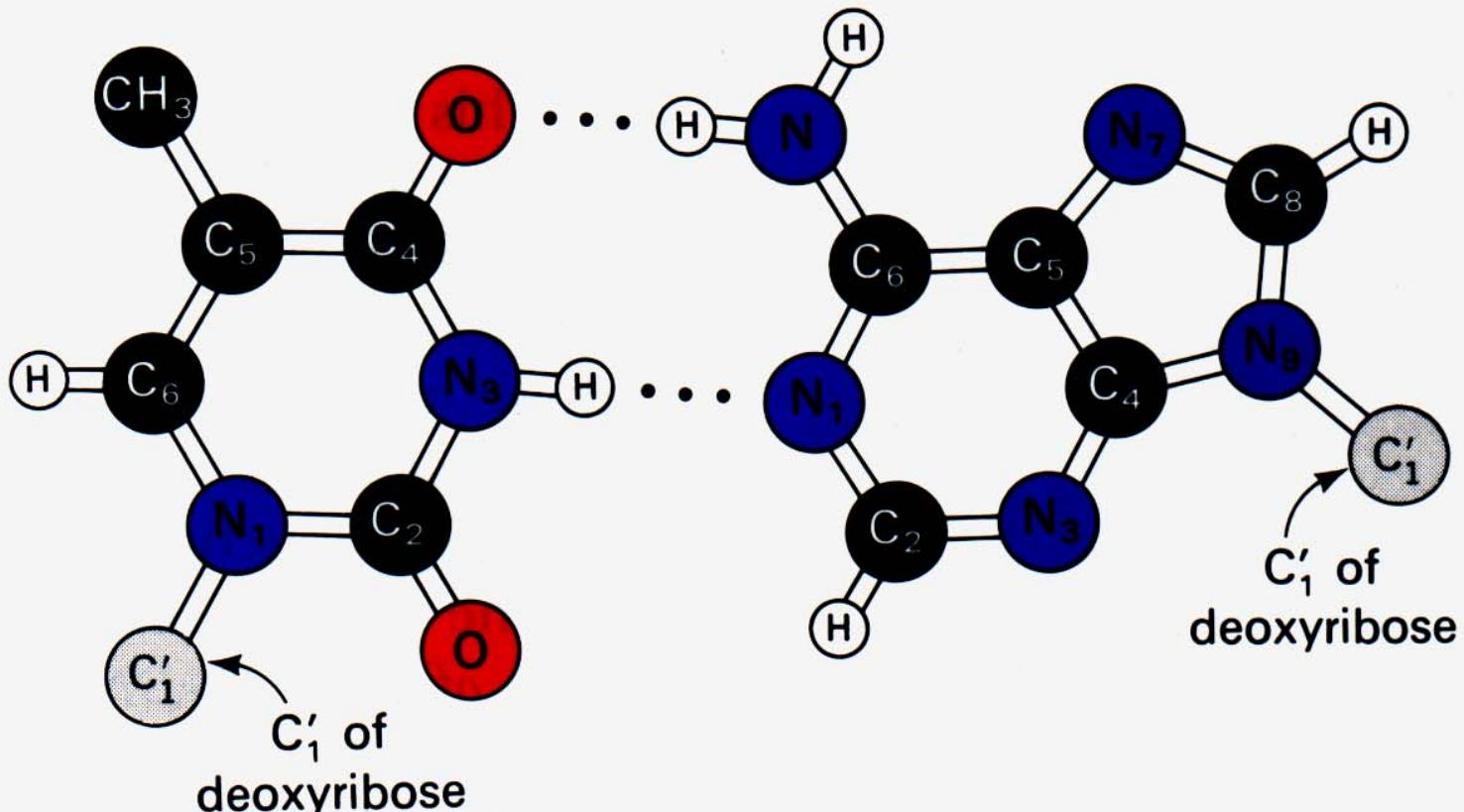


# Die Sekundärstruktur wird über Wasserstoff-Brückenbindungen stabilisiert



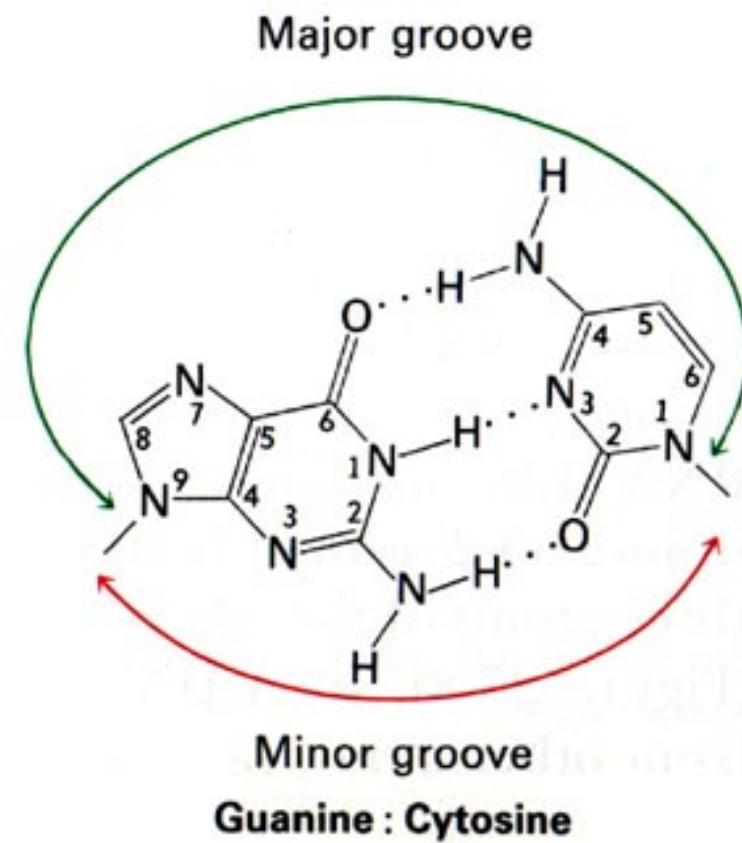
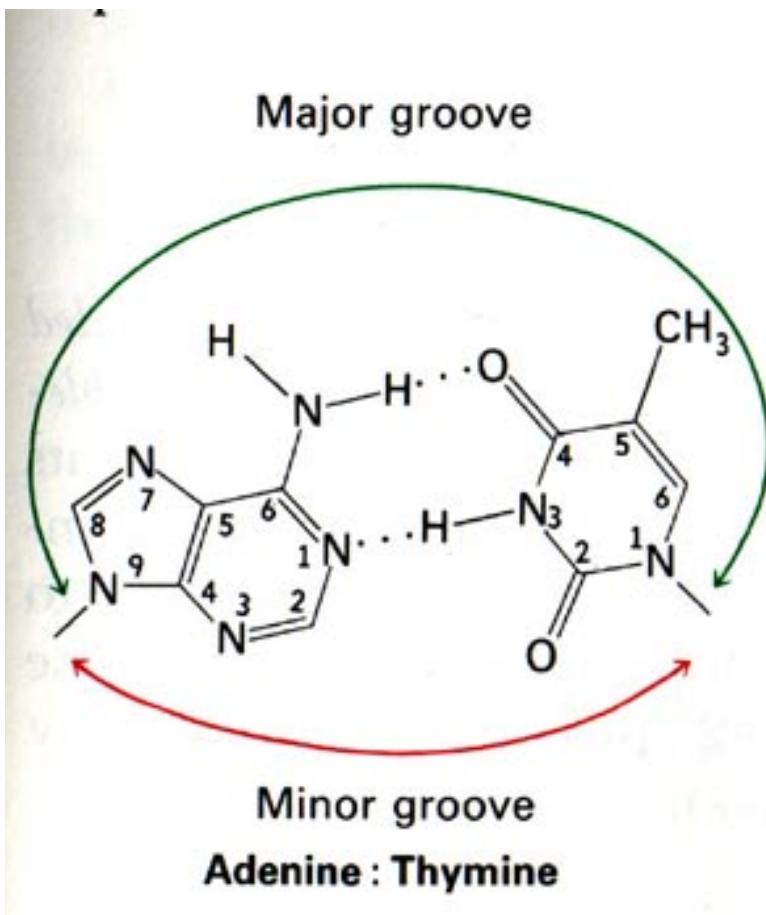
Cytosin-Guanin

## Die Sekundärstruktur wird über Wasserstoff-Brückenbindungen stabilisiert



Thymin-Adenin

# Die Basenpaare haben „zwei Seiten“



# „stacking forces“ – Stapelkräfte

## Beispiel AT-GC stacking

