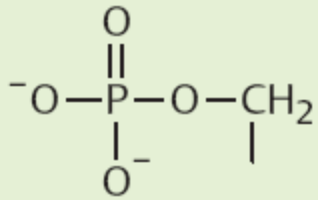


# **Prinzipien der Protein-DNA-Interaktionen**

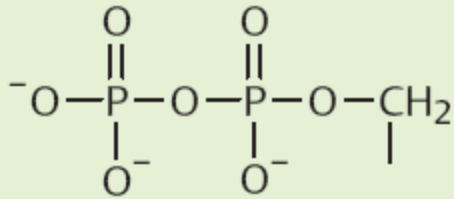
**Dr. Kristian M. Müller  
Institut für Biologie III  
Albert-Ludwigs-Universität Freiburg**

**Gene und Genome, WiSe 2007/2008**

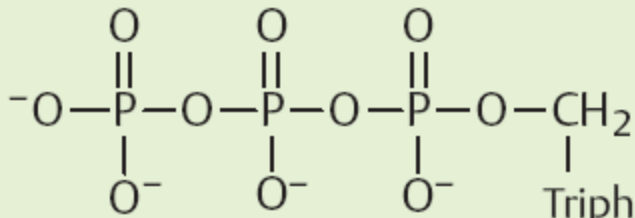
# Phosphat und Zucker



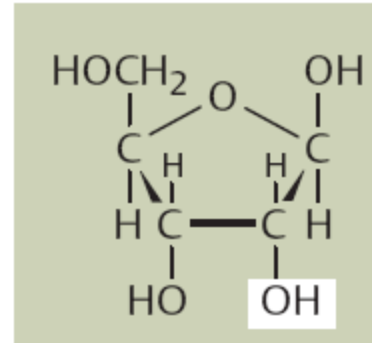
Monophosphate



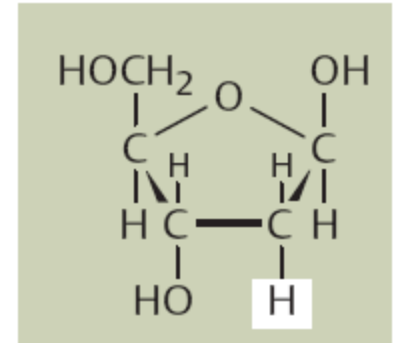
Diphosphate



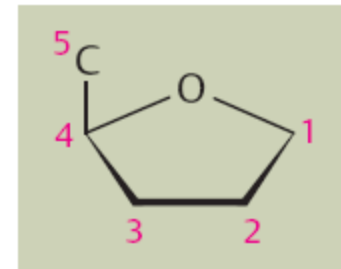
Triphosphate



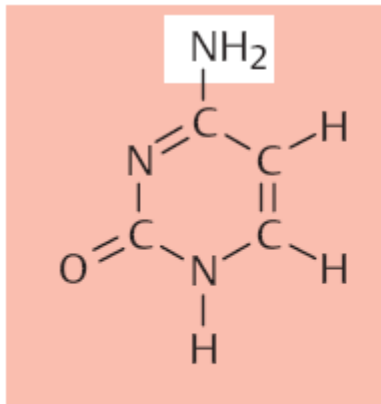
$\beta$ -D-Ribose



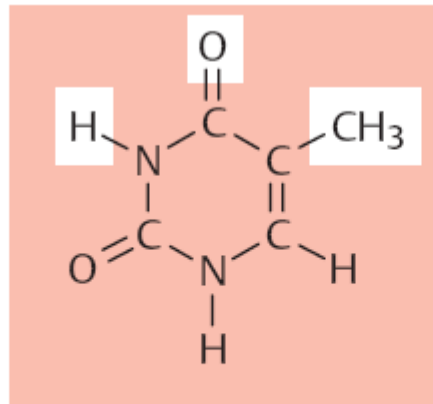
$\beta$ -D-Deoxyribose



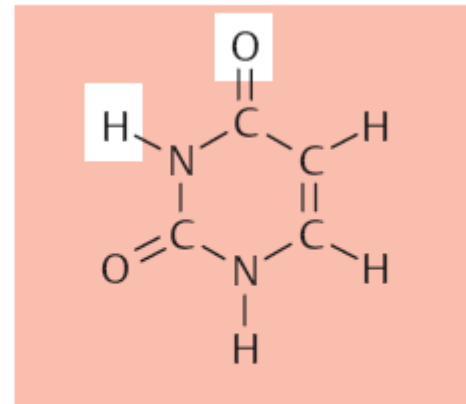
# Die Basen



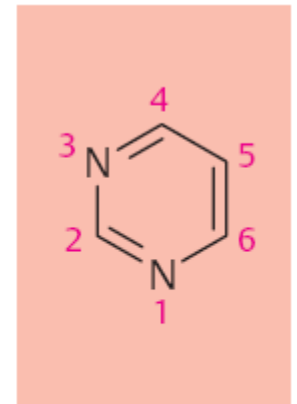
Cytosine (C)



Thymine (T)

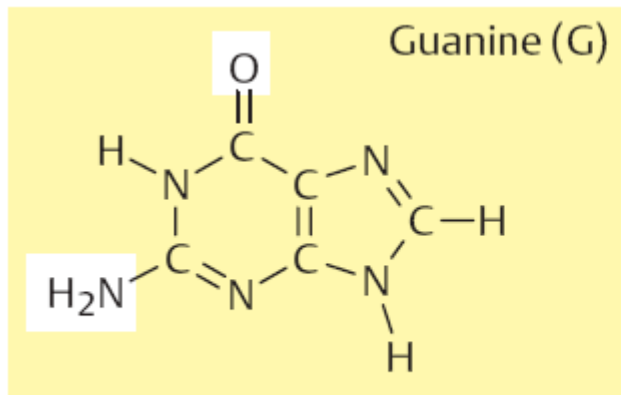


Uracil (U)

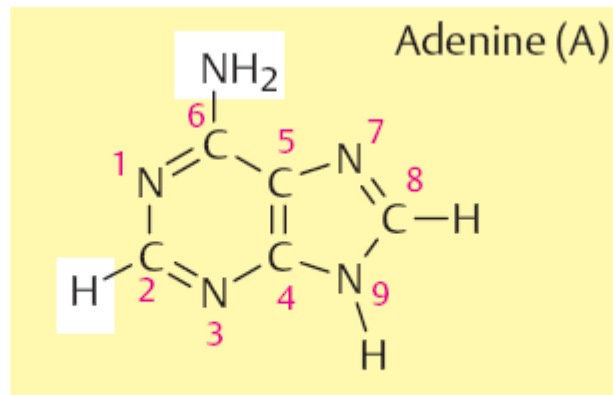


Pyrimidine

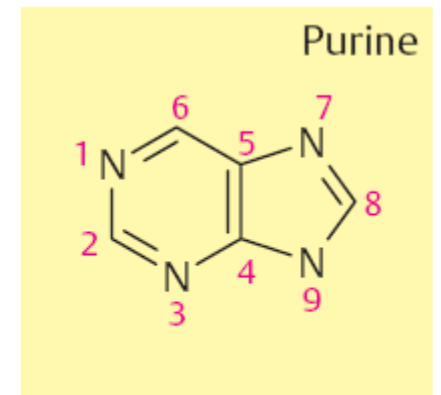
## C. Nucleotide bases of pyrimidine



Guanine (G)



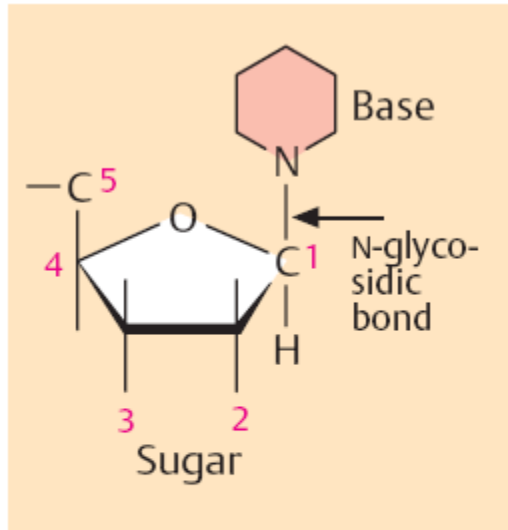
Adenine (A)



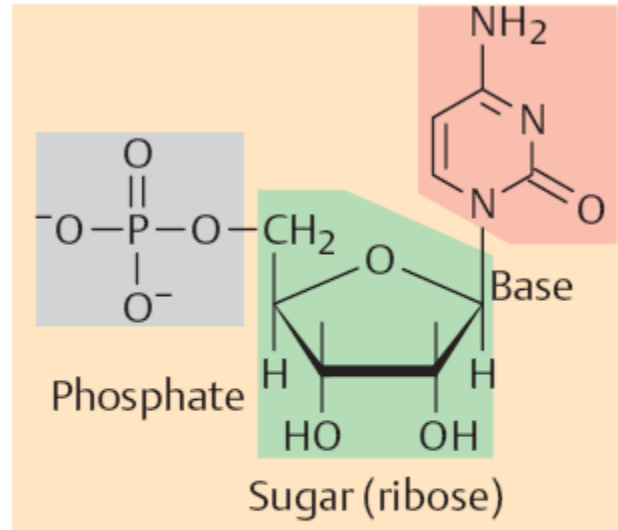
Purine

## D. Nucleotide bases of purine

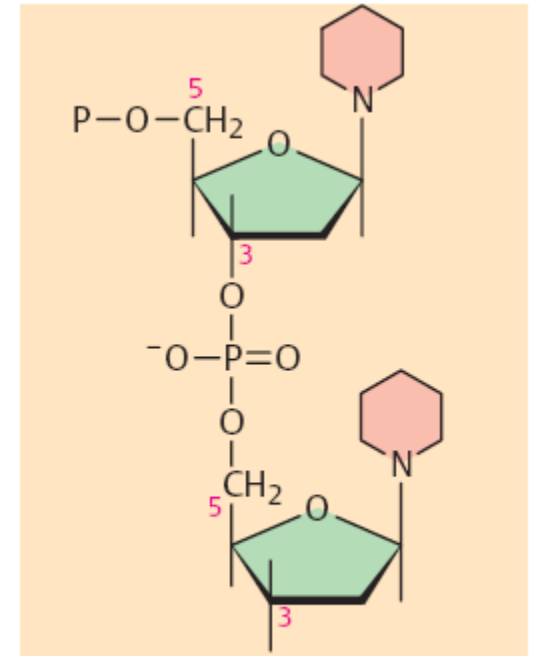
# Nucleosid, Nucleotid und Nukleinsäure



**E. Nucleoside**  
(base and sugar)



**F. Nucleotide**  
(base + sugar + phosphate)

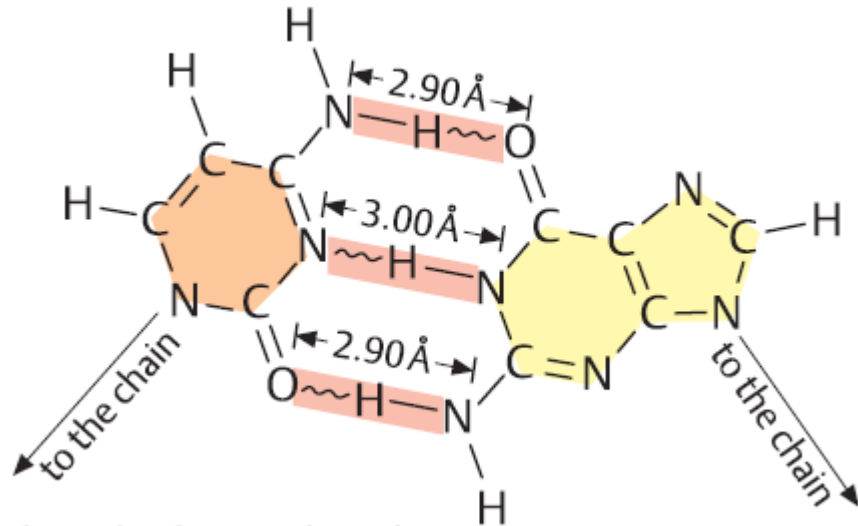


**G. Nucleic acid**

# Basenpaarung

Cytosine

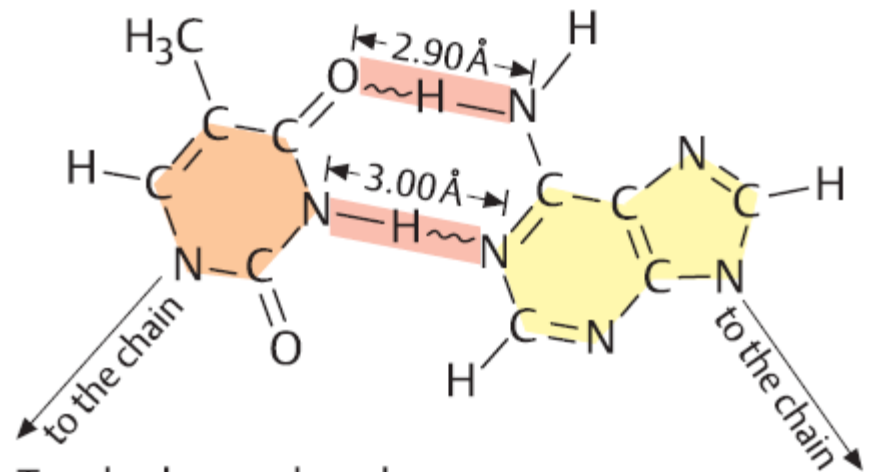
Guanine



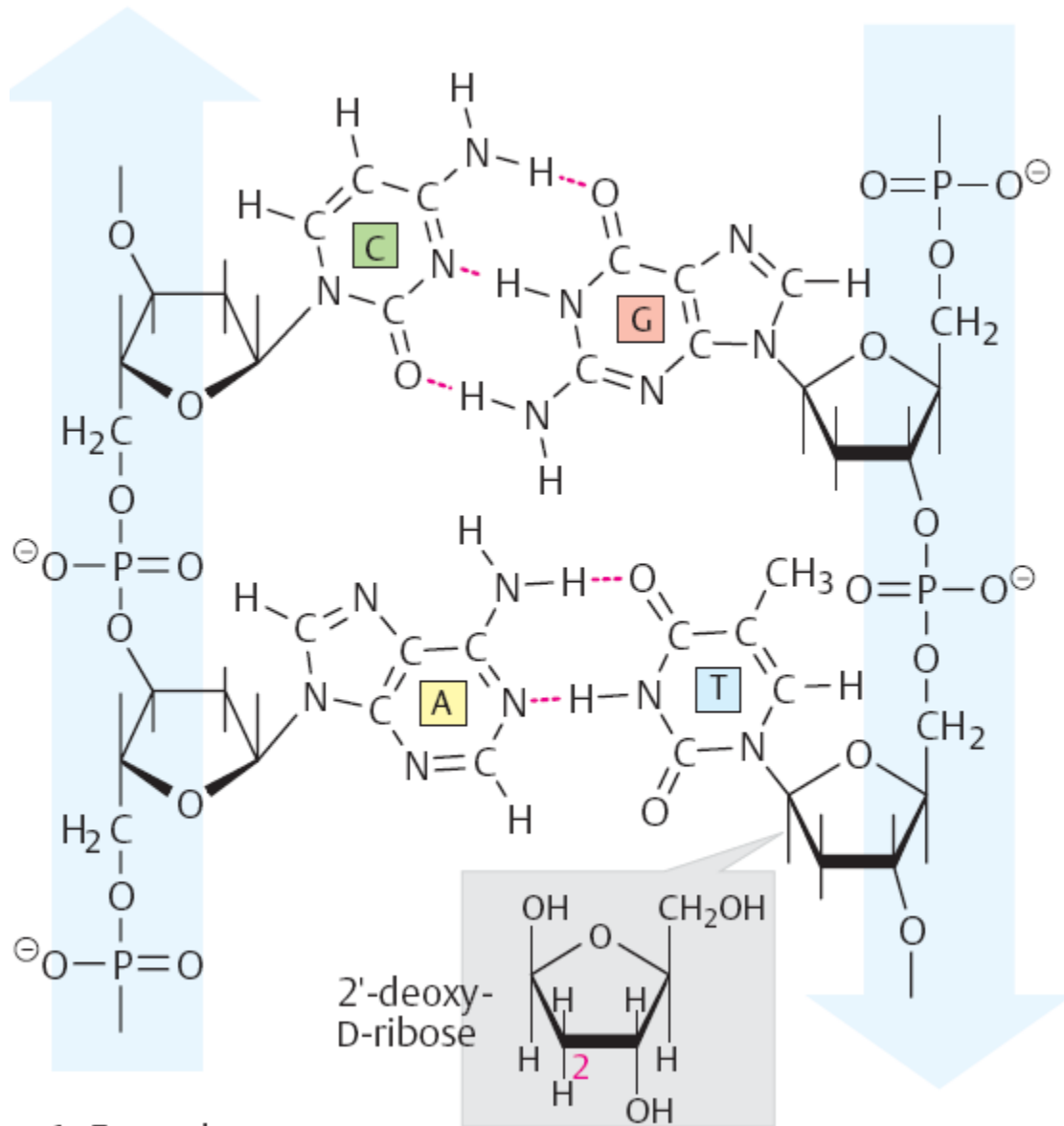
Three hydrogen bonds

Thymine

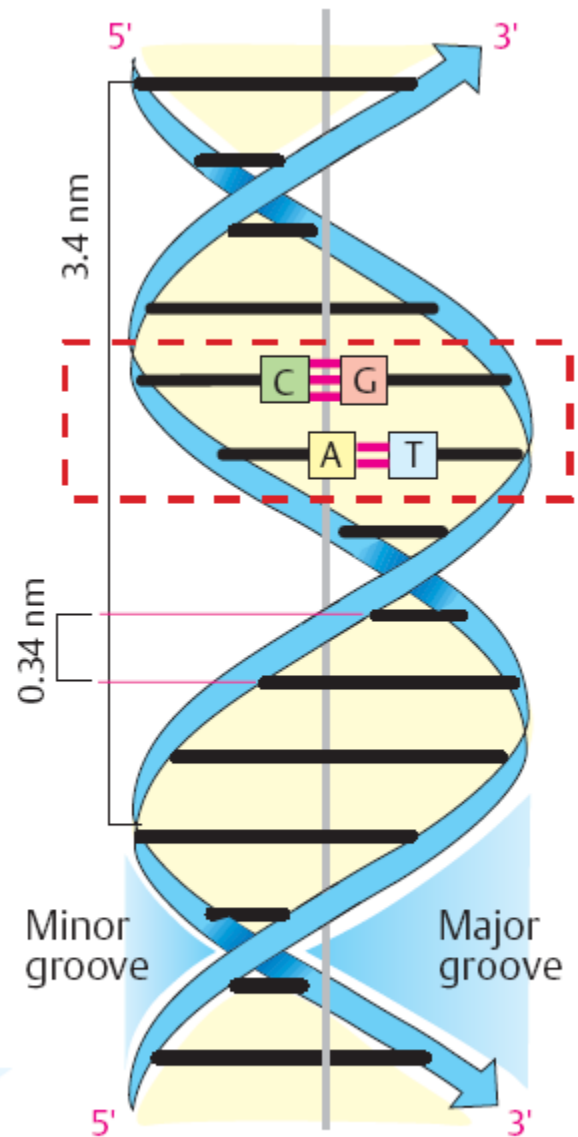
Adenine



Two hydrogen bonds

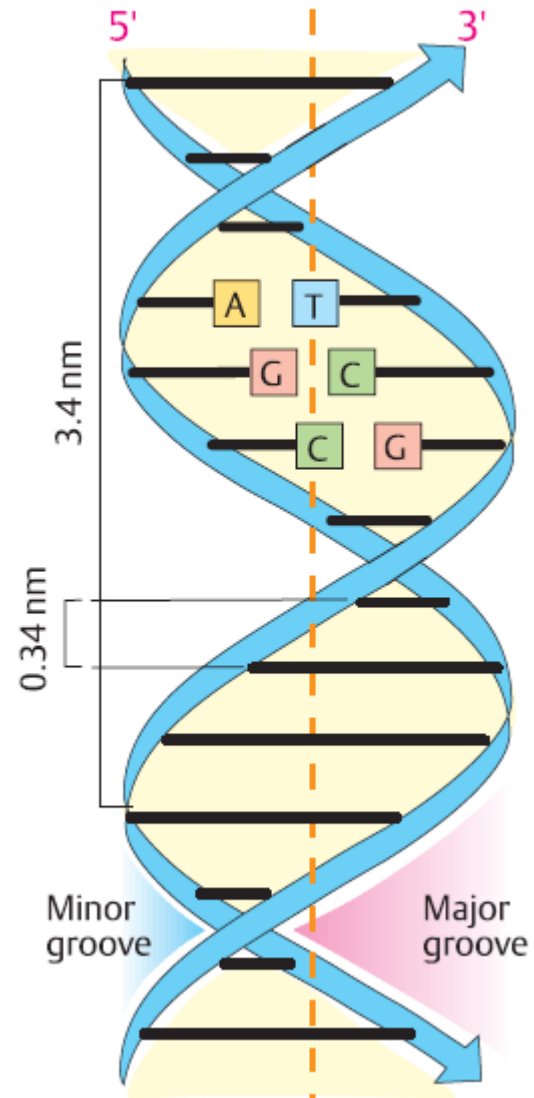
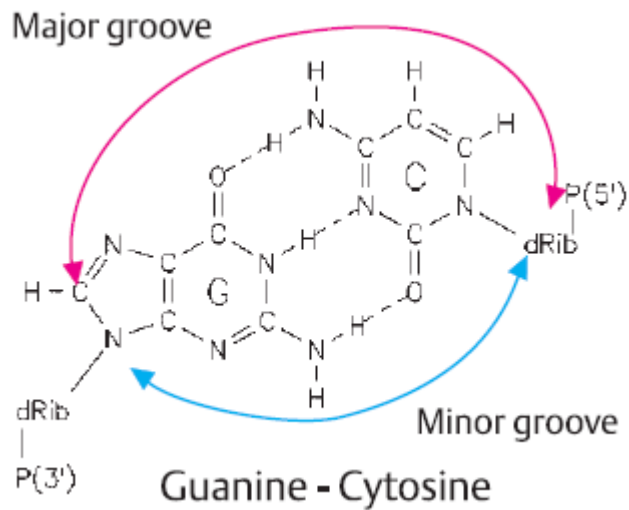
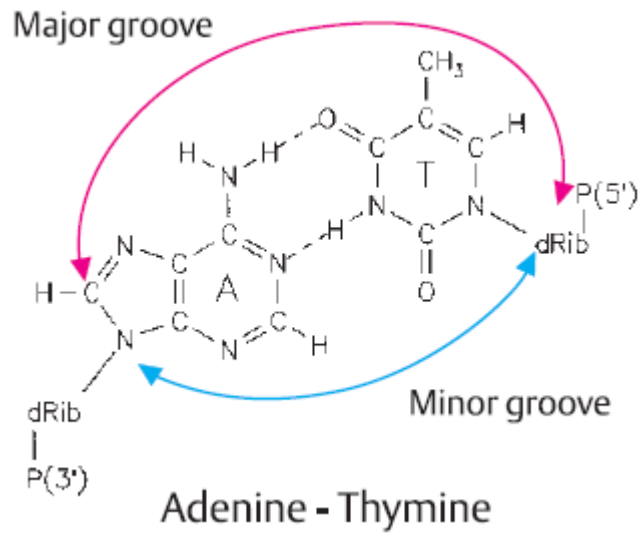


1. Formula

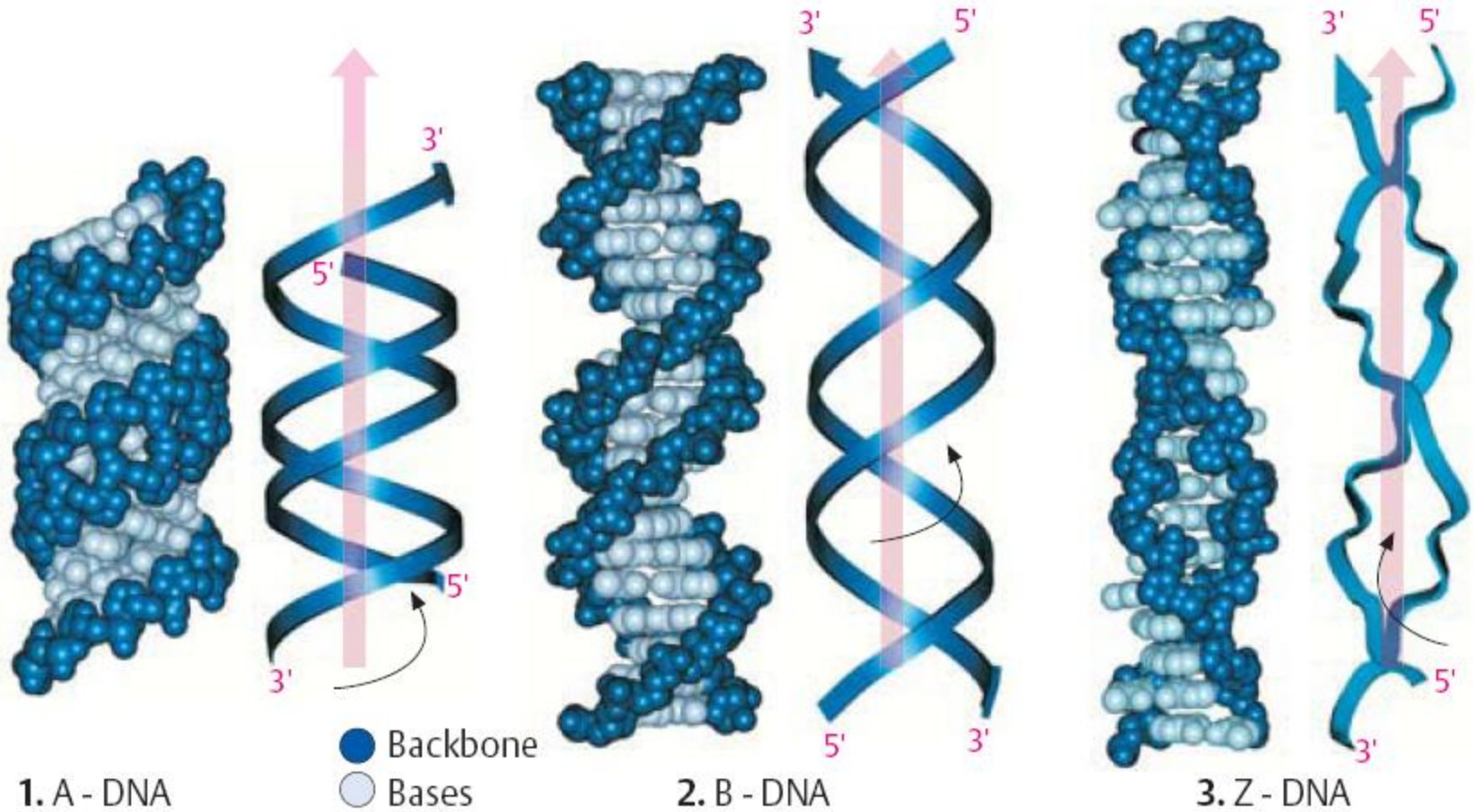


2. Double strand

# Die DNA Doppelhelix

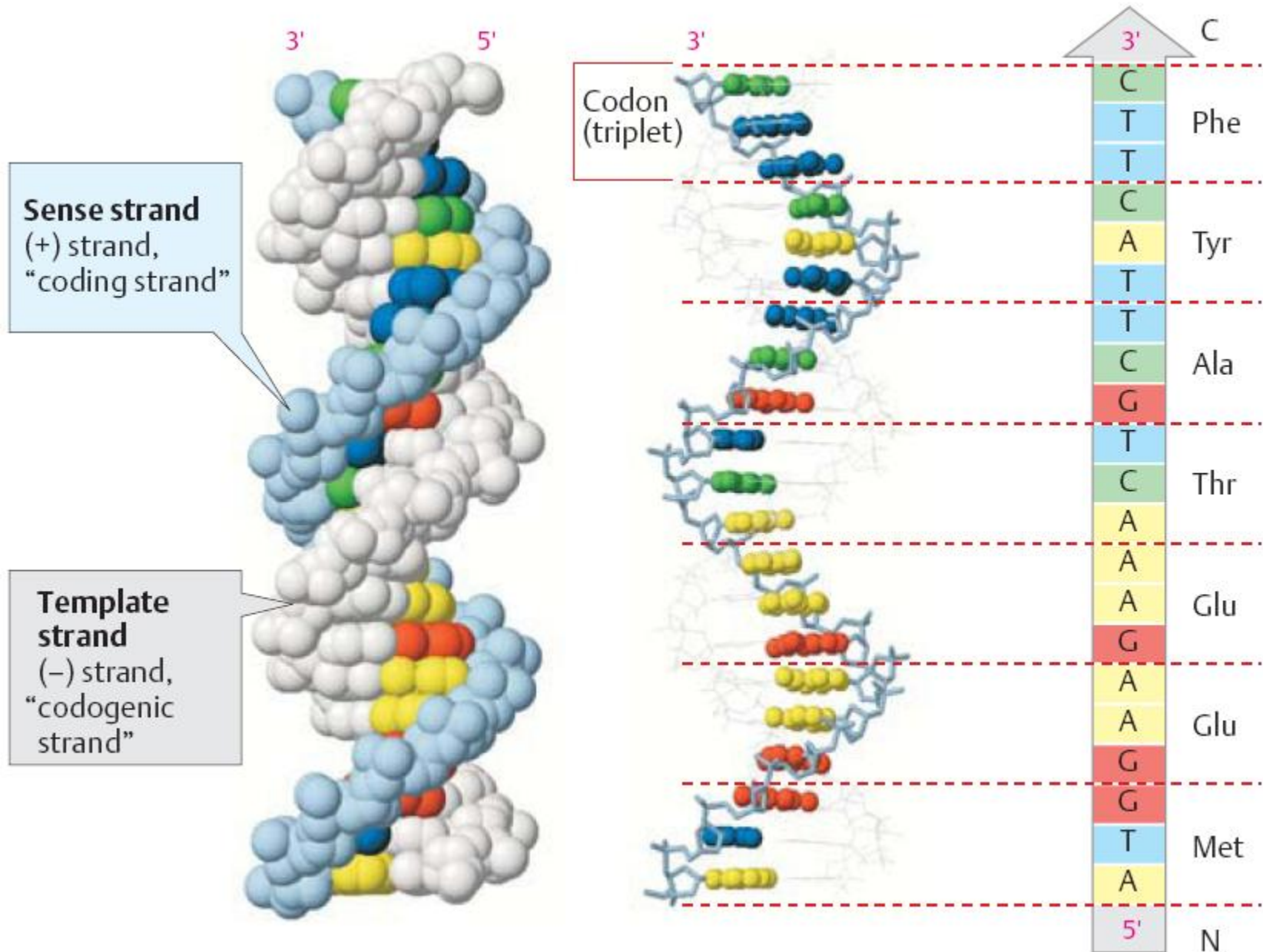


# DNA Formen

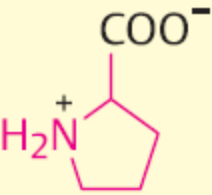




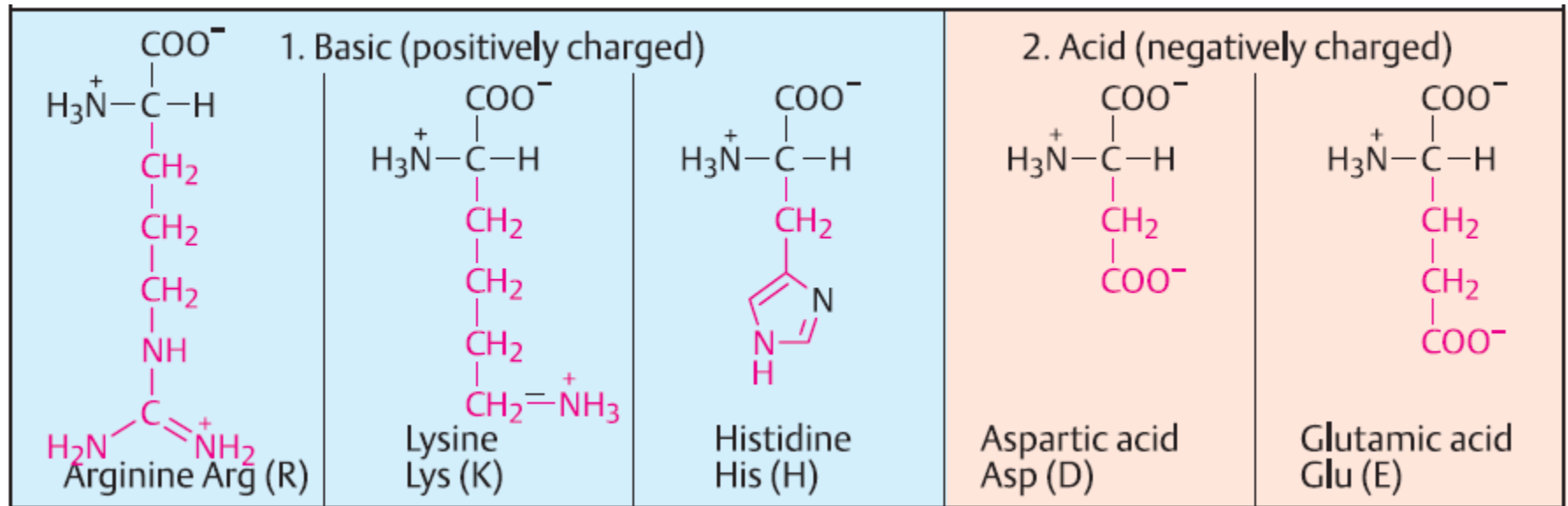
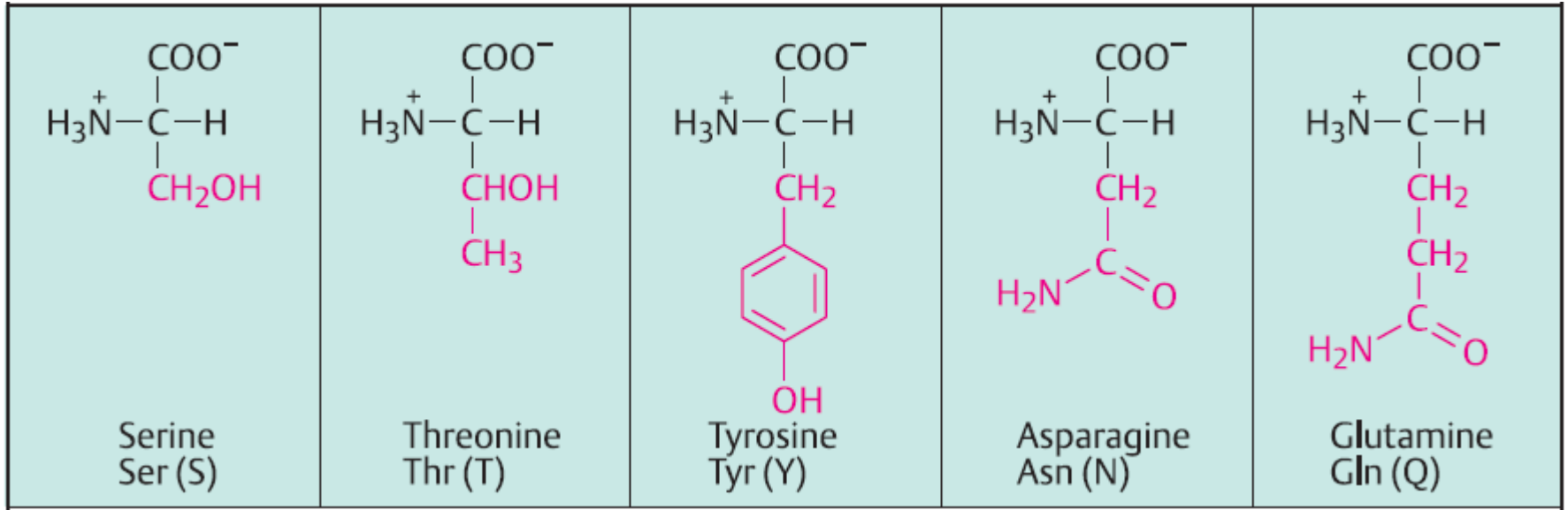
# Kodierender und Matrizen -Strang



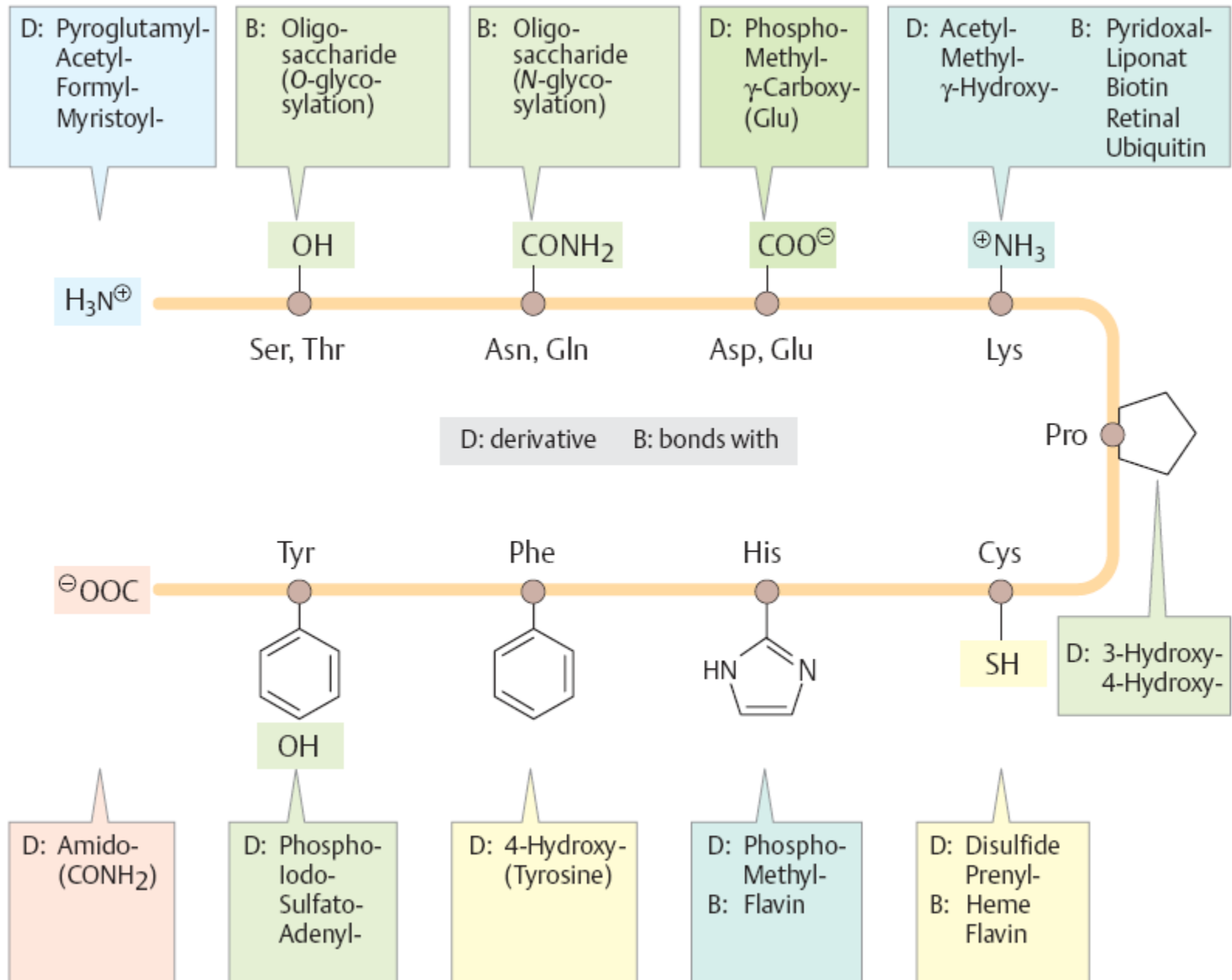
# Hydrophobe Aminosäuren

$  \begin{array}{c}  \text{COO}^- \\    \\  \text{H}_3\text{N}^+ - \text{C} - \text{H} \\    \\  \text{H}  \end{array}  $ <p>Glycine Gly (G)</p>	$  \begin{array}{c}  \text{COO}^- \\    \\  \text{H}_3\text{N}^+ - \text{C} - \text{H} \\    \\  \text{CH}_3  \end{array}  $ <p>Alanine Ala (A)</p>	$  \begin{array}{c}  \text{COO}^- \\    \\  \text{H}_3\text{N}^+ - \text{C} - \text{H} \\    \\  \text{CH} - \text{CH}_3 \\    \\  \text{CH}_3  \end{array}  $ <p>Valine Val (V)</p>	$  \begin{array}{c}  \text{COO}^- \\    \\  \text{H}_3\text{N}^+ - \text{C} - \text{H} \\    \\  \text{CH}_2 \\    \\  \text{CH} - \text{CH}_3 \\    \\  \text{CH}_3  \end{array}  $ <p>Leucine Leu (L)</p>	$  \begin{array}{c}  \text{COO}^- \\    \\  \text{H}_3\text{N}^+ - \text{C} - \text{H} \\    \\  \text{CH} - \text{CH}_2 \\    \quad   \\  \text{CH}_3 \quad \text{CH}_3  \end{array}  $ <p>Isoleucine Ile (I)</p>
 <p>Proline Pro (P)</p>	$  \begin{array}{c}  \text{COO}^- \\    \\  \text{H}_3\text{N}^+ - \text{C} - \text{H} \\    \\  \text{CH}_2 \\    \\  \text{C}_6\text{H}_5  \end{array}  $ <p>Phenylalanine Phe (F)</p>	$  \begin{array}{c}  \text{COO}^- \\    \\  \text{H}_3\text{N}^+ - \text{C} - \text{H} \\    \quad \text{CH} \\  \text{CH}_2 \\    \\  \text{C} = \text{CH} \\    \quad   \\  \text{C}_6\text{H}_4 \quad \text{NH}  \end{array}  $ <p>Tryptophan Trp (W)</p>	$  \begin{array}{c}  \text{COO}^- \\    \\  \text{H}_3\text{N}^+ - \text{C} - \text{H} \\    \\  \text{CH}_2 \\    \\  \text{SH}  \end{array}  $ <p>Cysteine Cys (C)</p>	$  \begin{array}{c}  \text{COO}^- \\    \\  \text{H}_3\text{N}^+ - \text{C} - \text{H} \\    \\  \text{CH}_2 \\    \\  \text{CH}_2 \\    \\  \text{S} \\    \\  \text{CH}_3  \end{array}  $ <p>Methionine Met (M)</p>

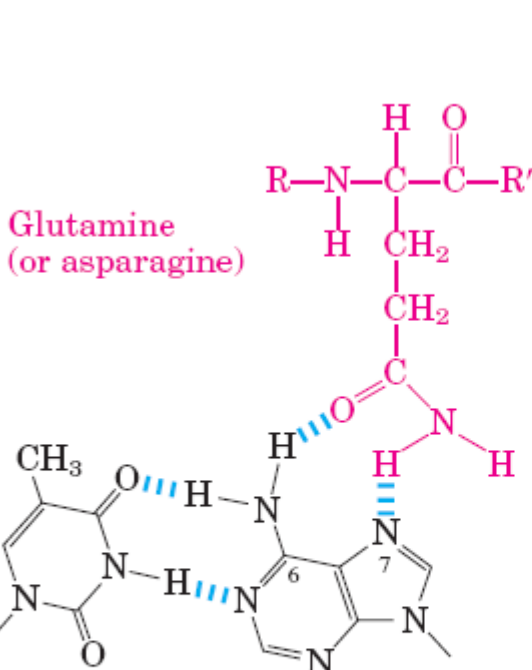
# Polare und geladene Aminosäuren



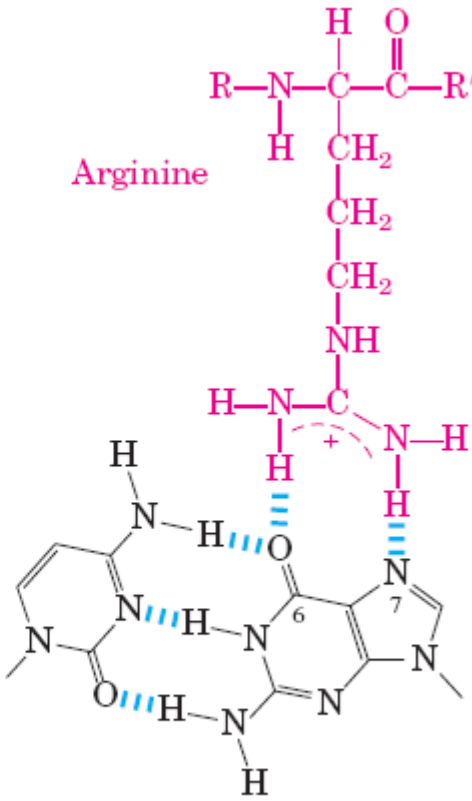
# Posttranslationale Modifikationen



# Typische Protein -DNA Interaktion



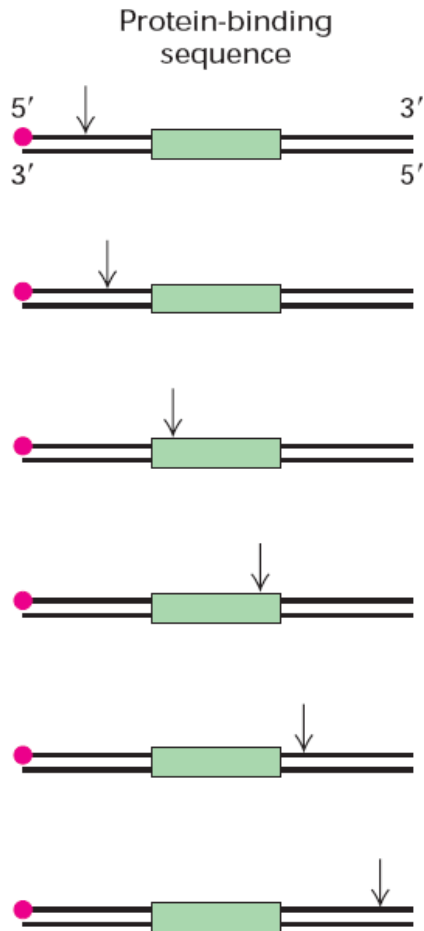
Thymine=Adenine



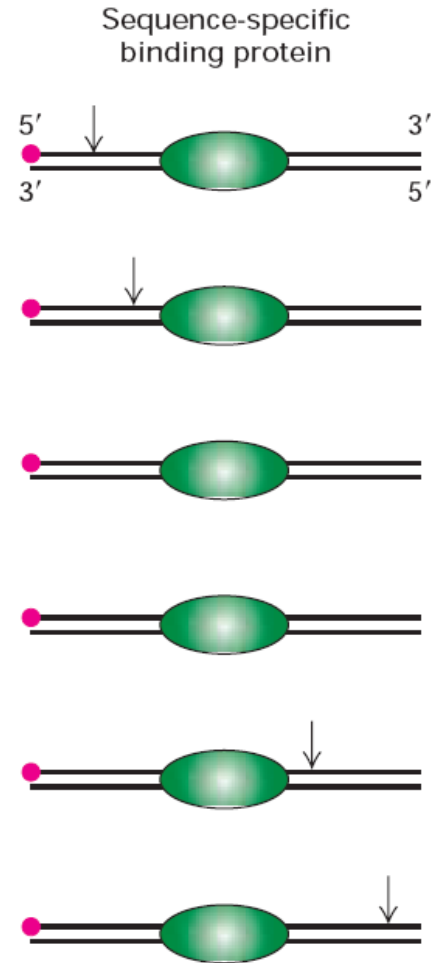
Cytosine≡Guanine

# Protein-DNA Interaktion: DNase footprinting

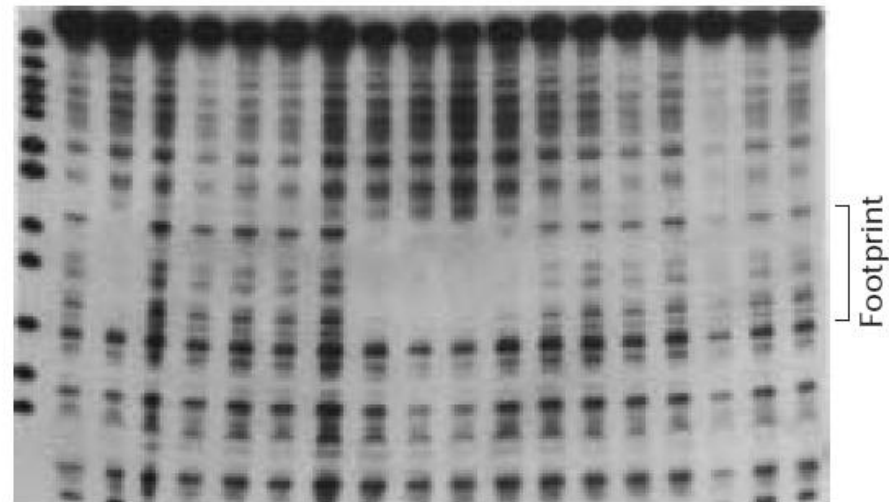
**Sample A**  
(DNA-binding protein absent)



**Sample B**  
(DNA-binding protein present)



Fraction  
M NE O FT 1 6 7 8 9 10 11 12 13 14 15 16 18 20 22



Proteinfractionen getestet auf DNA Bindung

M Marker

NE kein Extrakt

O Säulenauftrag

FT Durchlauf

1 ... 22 Fraktionen

# Gen Ontologie: DNA Bindung Teil I

- [DNA binding \(GO ID:3677\)](#)
  - DNA bending activity (GO ID:8301)
  - [damaged DNA binding \(GO ID:3684\)](#)
    - alkylated DNA binding (GO ID:32131)
      - O6-alkylguanine-DNA binding (GO ID:32132)
    - oxidized DNA binding (GO ID:32356)
      - oxidized purine DNA binding (GO ID:32357)
      - oxidized pyrimidine DNA binding (GO ID:32358)
  - [sequence-specific DNA binding \(GO ID:43565\)](#)
    - AT DNA binding (GO ID:3680)
    - [DNA replication origin binding \(GO ID:3688\)](#)
    - P-element binding (GO ID:3693)
    - centromeric DNA binding (GO ID:19237)
    - methyl-CpG binding (GO ID:8327)
    - purine-rich negative regulatory element binding (GO ID:32422)
    - rDNA binding (GO ID:182)
    - replication fork barrier binding (GO ID:31634)
      - rDNA spacer replication fork barrier binding (GO ID:43110)
    - satellite DNA binding (GO ID:3696)
    - sterol response element binding (GO ID:32810)
    - [telomeric DNA binding \(GO ID:42162\)](#)
      - double-stranded telomeric DNA binding (GO ID:3691)
      - single-stranded telomeric DNA binding (GO ID:43047)
    - unmethylated CpG binding (GO ID:45322)

# Gen Ontologie: DNA Bindung Teil II

- [structure-specific DNA binding \(GO ID:43566\)](#)
  - DNA end binding (GO ID:45027)
  - DNA secondary structure binding (GO ID:217)
    - DNA hairpin binding (GO ID:32448)
    - Y-form DNA binding (GO ID:403)
    - bubble DNA binding (GO ID:405)
    - double-strand/single-strand DNA junction binding (GO ID:406)
    - four-way junction DNA binding (GO ID:400)
      - » crossed form four-way junction DNA binding (GO ID:402)
      - » open form four-way junction DNA binding (GO ID:401)
  - G-quadruplex DNA binding (GO ID:51880)
  - bent DNA binding (GO ID:3681)
  - chromatin DNA binding (GO ID:31490)
    - chromatin insulator sequence binding (GO ID:43035)
  -



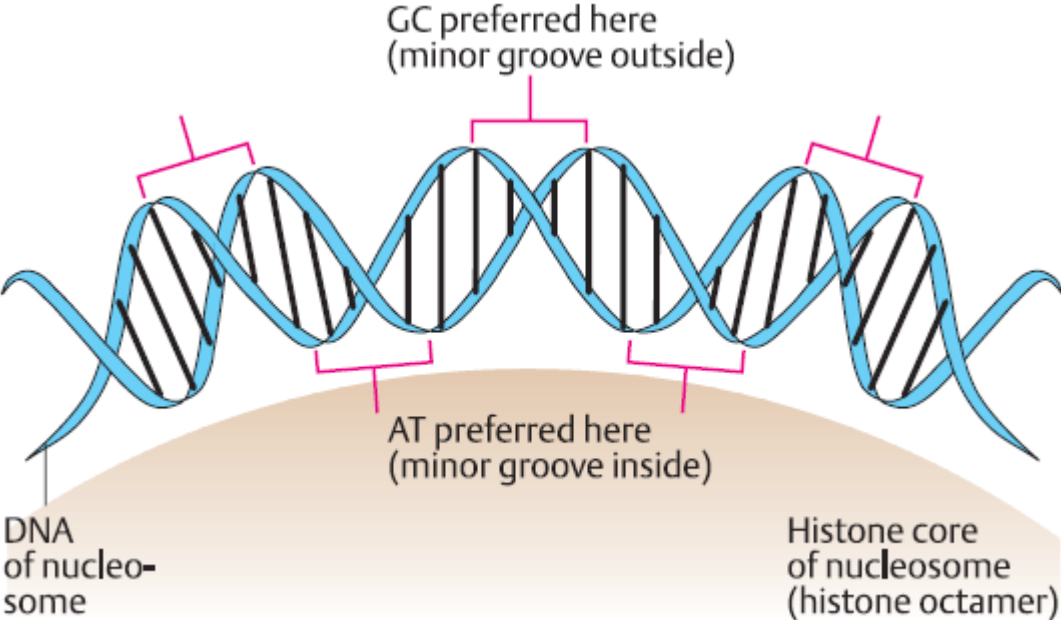
# Gen Ontologie: DNA Bindung Teil III

- [double-stranded DNA binding \(GO ID:3690\)](#)
  - double-stranded methylated DNA binding (GO ID:10385)
  - [mismatched DNA binding \(GO ID:30983\)](#)
    - » DNA insertion or deletion binding (GO ID:32135)
      - dinucleotide insertion or deletion binding (GO ID:32139)
        - dinucleotide repeat insertion binding (GO ID:32181)
      - loop DNA binding (GO ID:404)
      - single base insertion or deletion binding (GO ID:32138)
        - single adenine insertion binding (GO ID:32140)
        - single cytosine insertion binding (GO ID:32141)
        - single guanine insertion binding (GO ID:32142)
        - single thymine insertion binding (GO ID:32143)
    - » mispaired DNA binding (GO ID:32134)
      - adenine/cytosine mispair binding (GO ID:32136)
      - guanine/thymine mispair binding (GO ID:32137)
- left-handed Z-DNA binding (GO ID:3692)
- random coil DNA binding (GO ID:3695)
- [single-stranded DNA binding \(GO ID:3697\)](#)
  - DNA strand annealing activity (GO ID:739)
- triplex DNA binding (GO ID:45142)

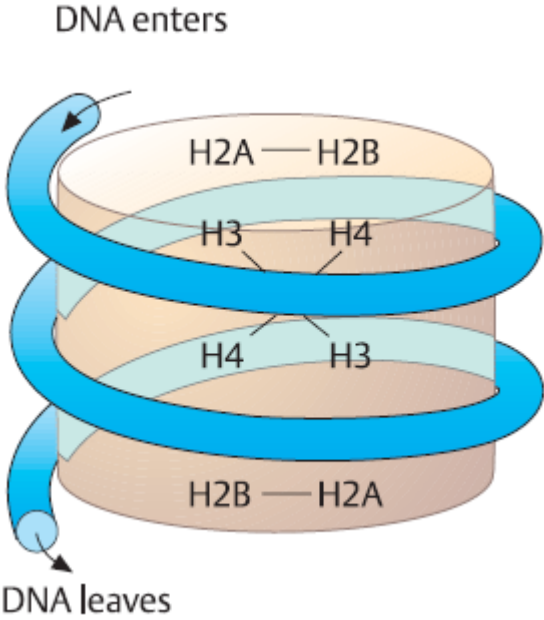
# Übersicht

- Histone
- B-ZIP Familie
- HLH Familie
- RHH Familie
- Zinc-Finger Familie
- Restriktionsenzyme

# Chromatin



DNA und Histon



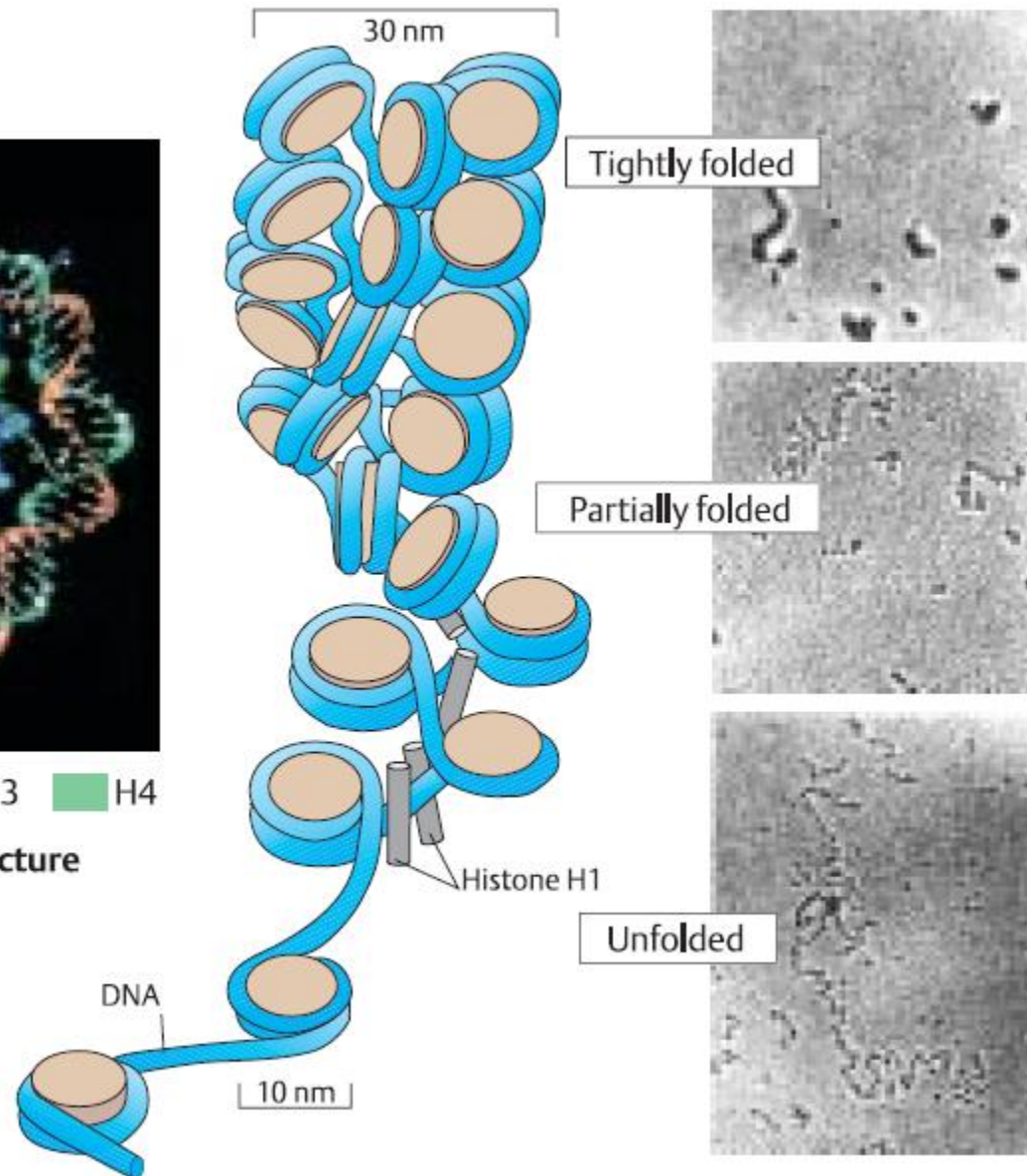
Nucleosom

# Chromatin Struktur



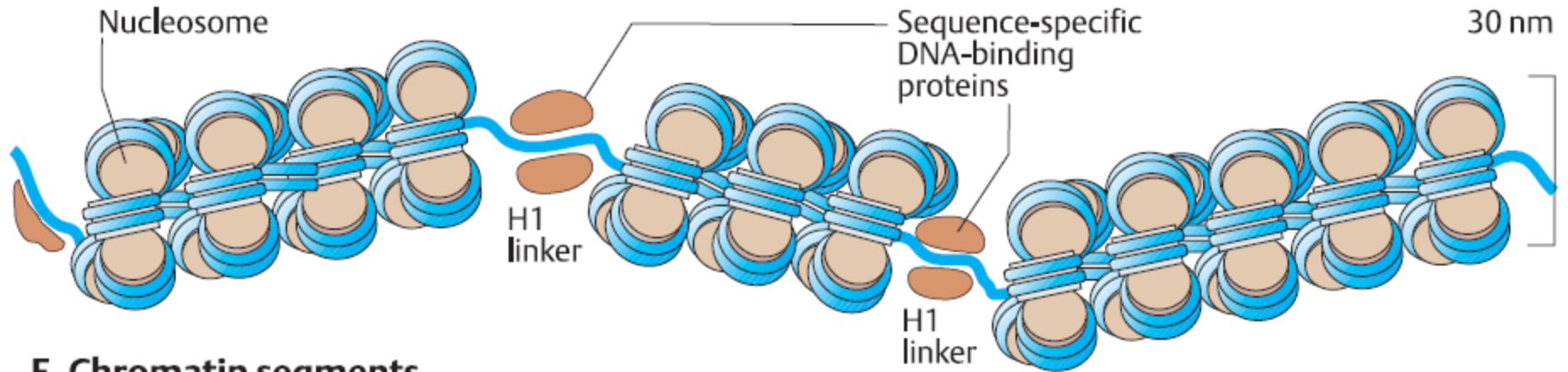
■ H2A ■ H2B ■ H3 ■ H4

C. Three-dimensional structure of a nucleosome



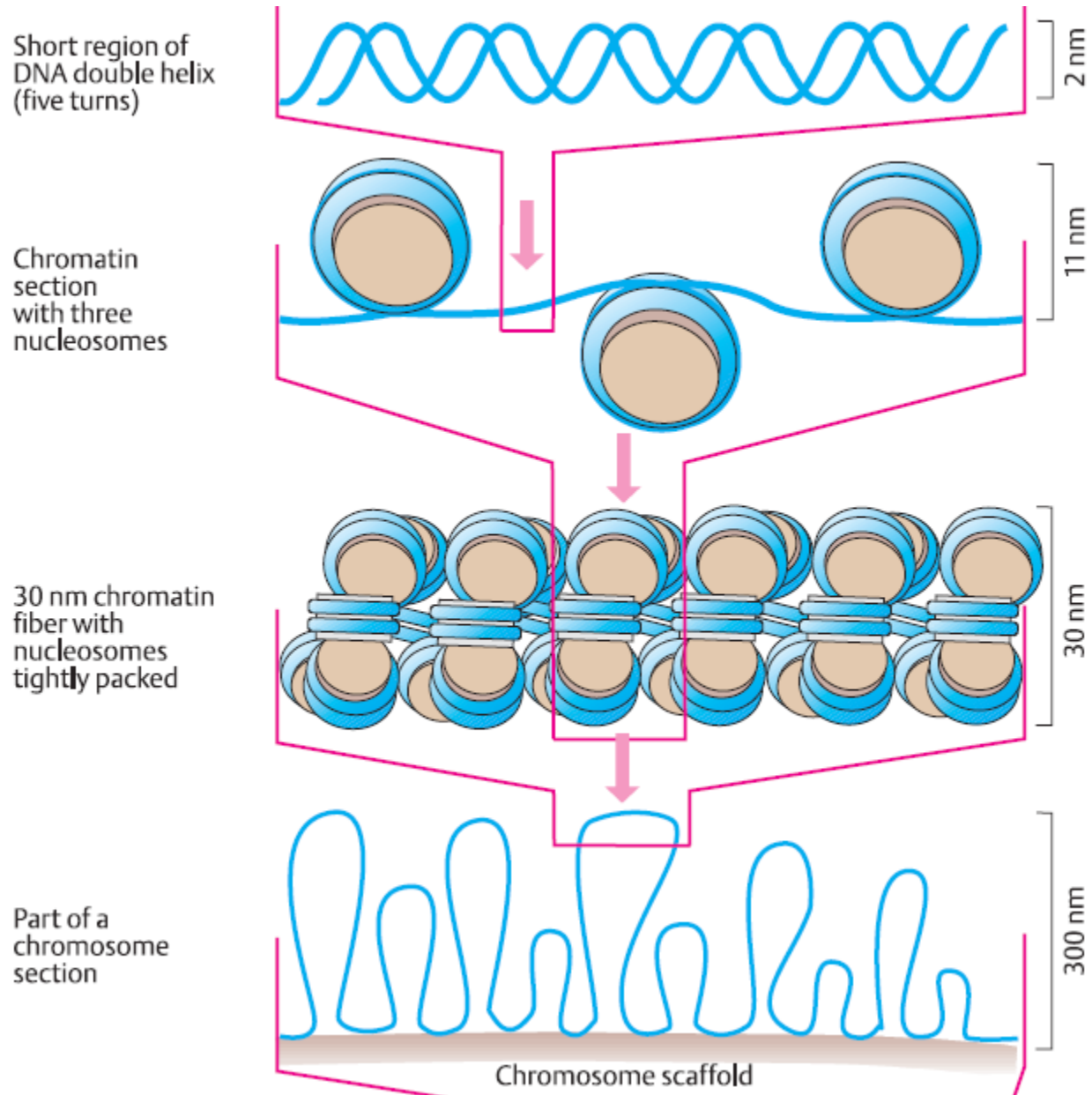
D. Chromatin structures

# Chromatin Segmente

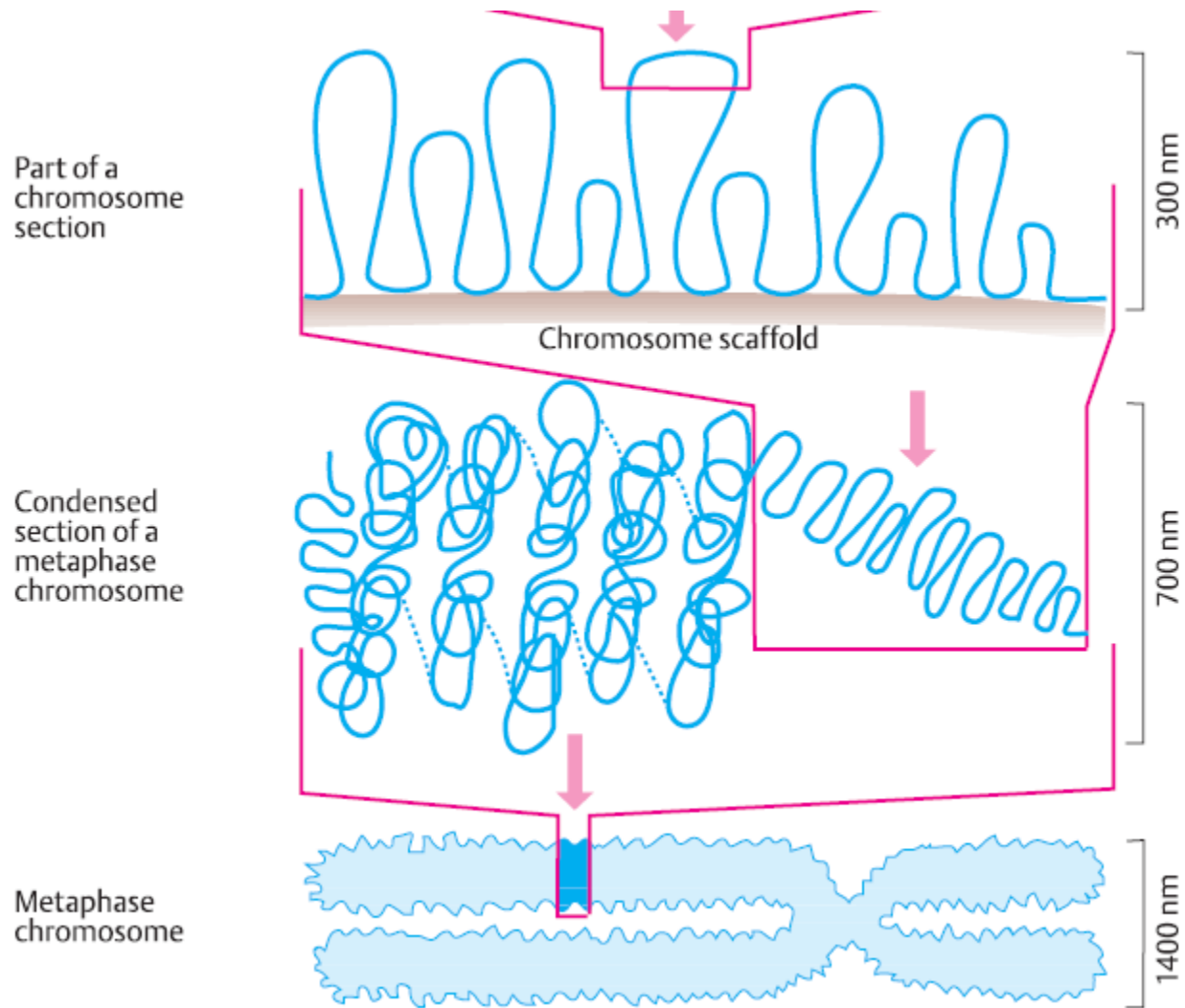


**E. Chromatin segments**

# Vom Chromatin zum Chromosom

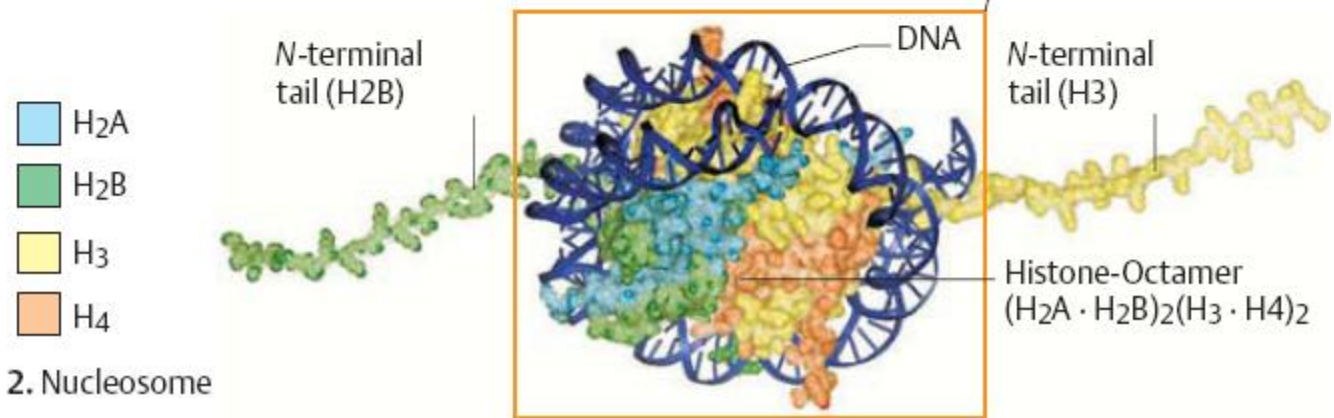
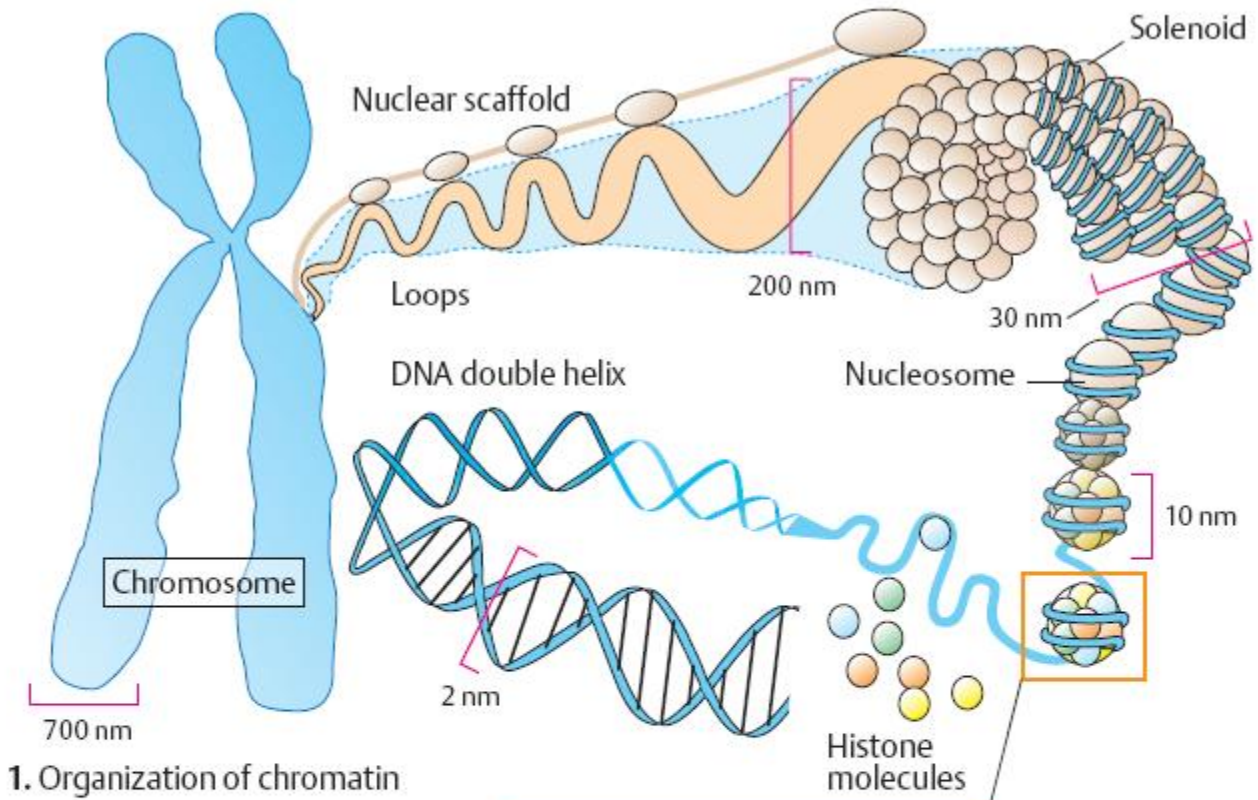


# Vom Chromatin zum Chromosom





# Gesamtübersicht



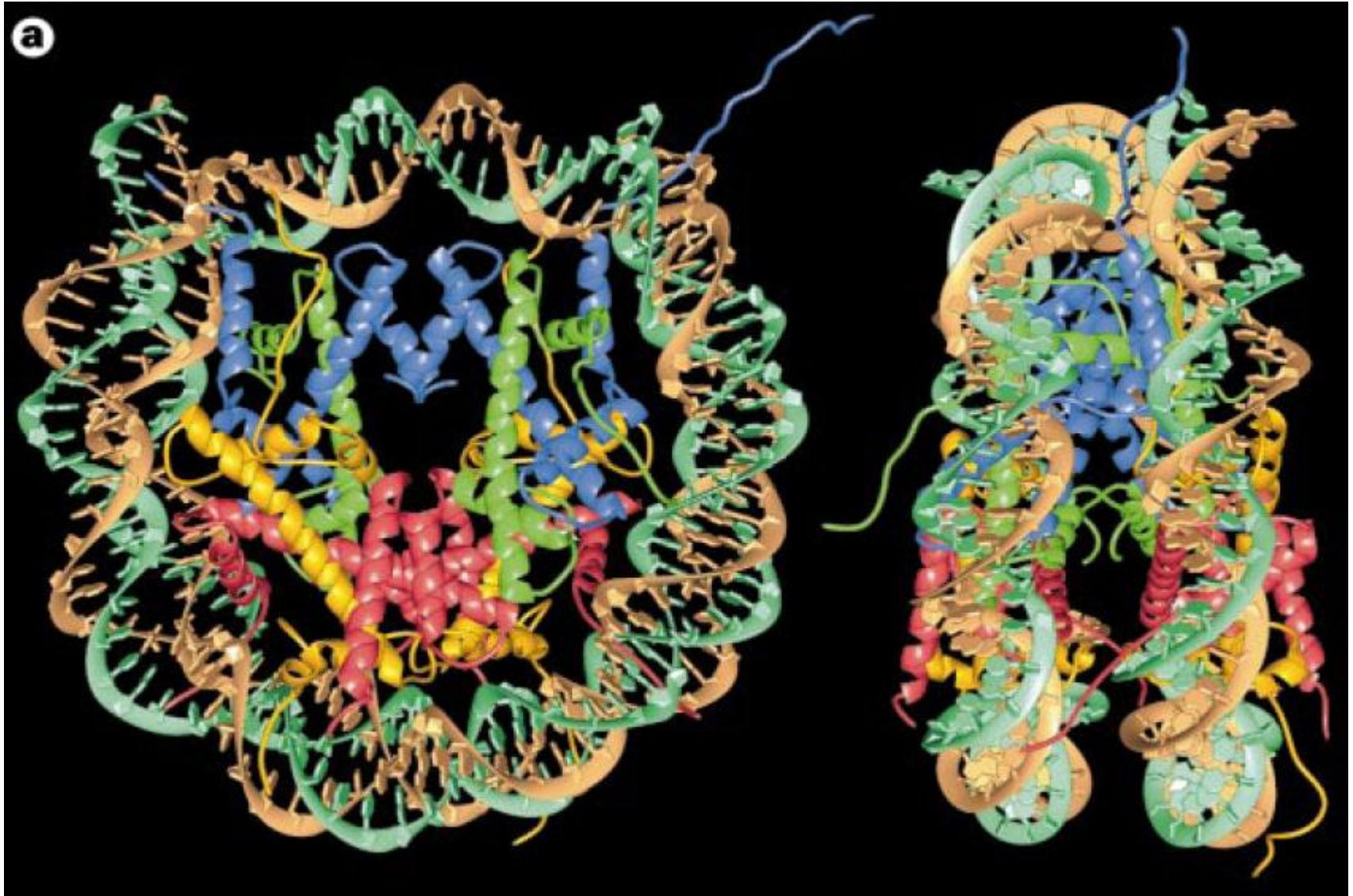


# Histone

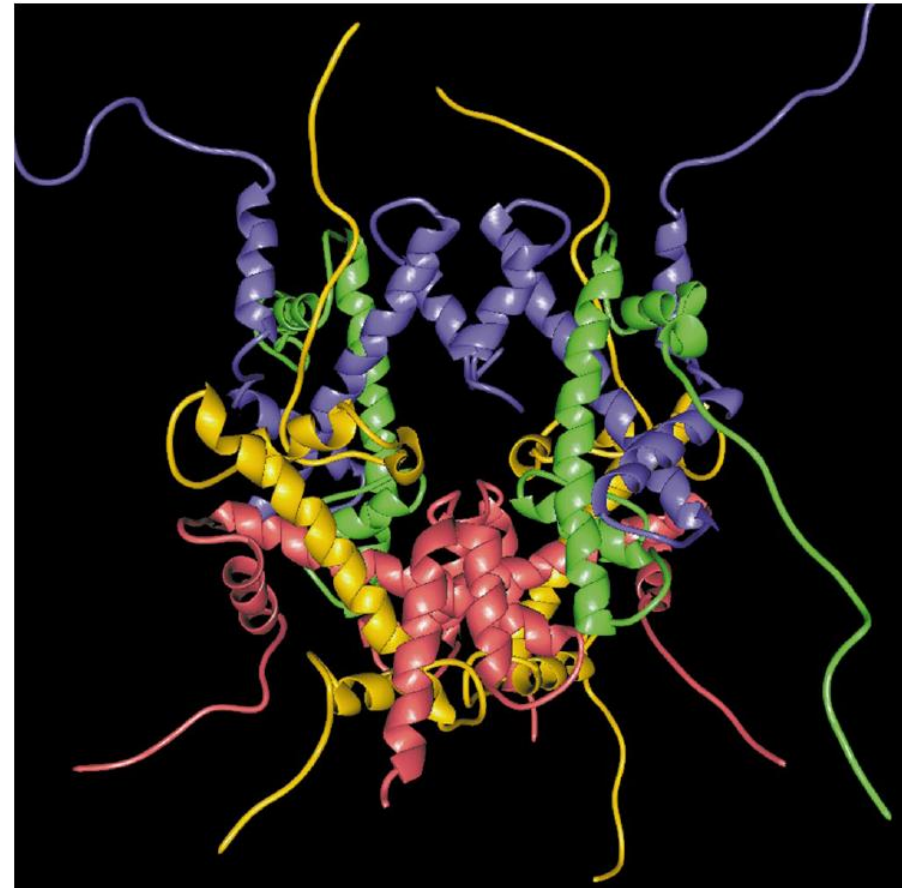
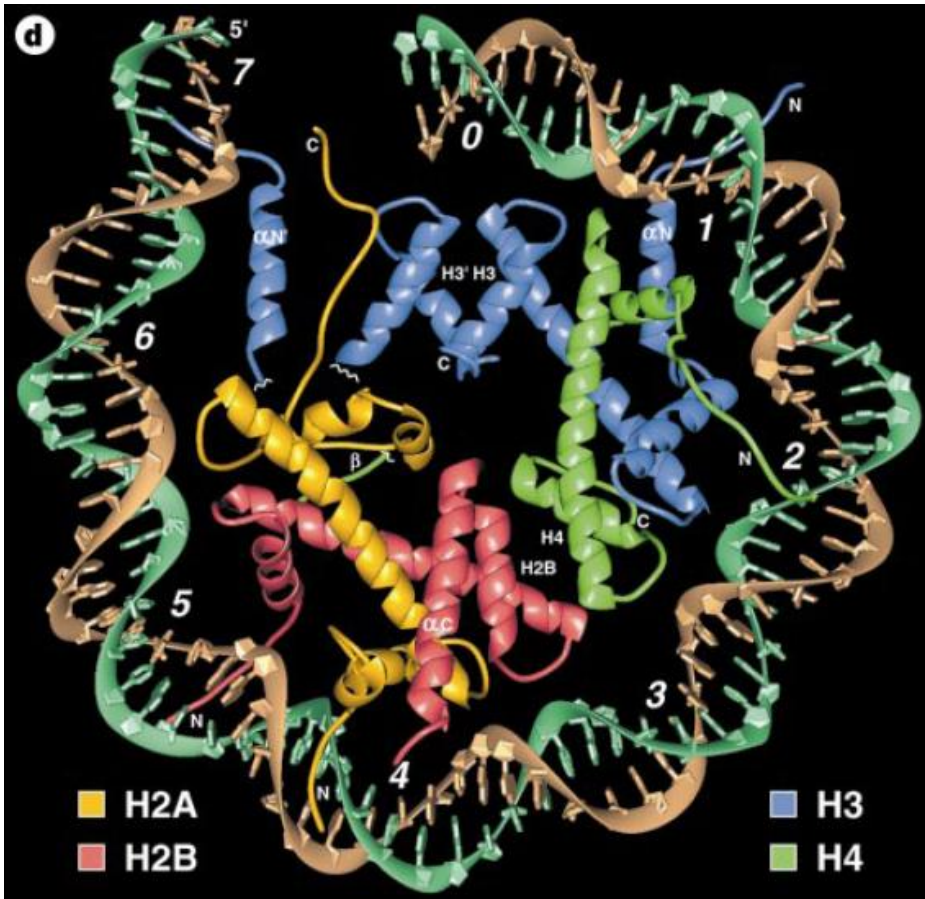
## Originalliteratur:

- Luger K, Mader AW, Richmond RK, Sargent DF, Richmond TJ “Crystal structure of the nucleosome core particle at 2.8 Å resolution.” *Nature*. 1997 Sep 18;389(6648):251-60
- Richmond TJ, Davey CA “The structure of DNA in the nucleosome core.” *Nature*. 2003 May 8;423(6936):145-50
- Schalch T, Duda S, Sargent DF, Richmond TJ “X-ray structure of a tetranucleosome and its implications for the chromatin fibre.” *Nature*. 2005 Jul 7;436(7047):138-41.

# Übersicht: Histon Octamer mit DNA

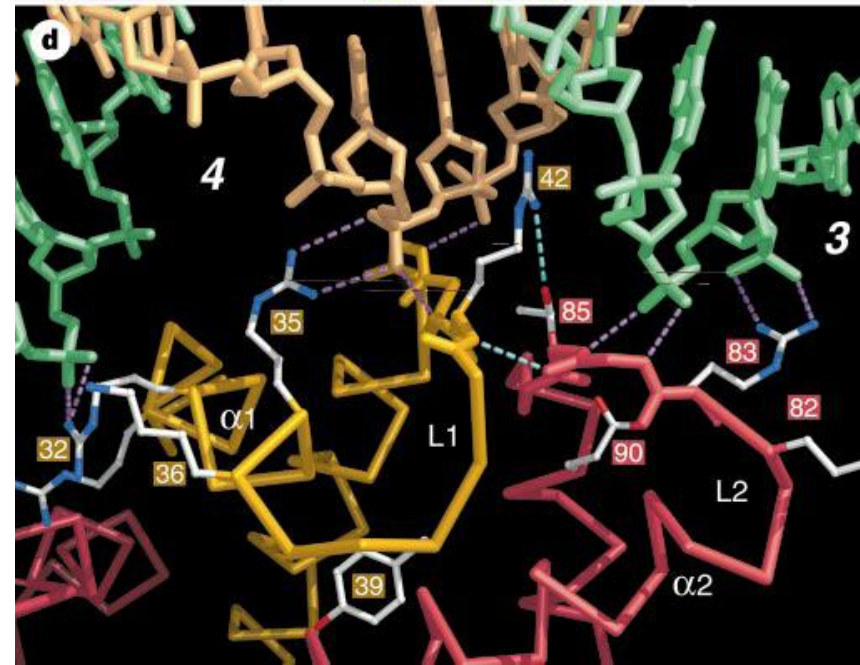
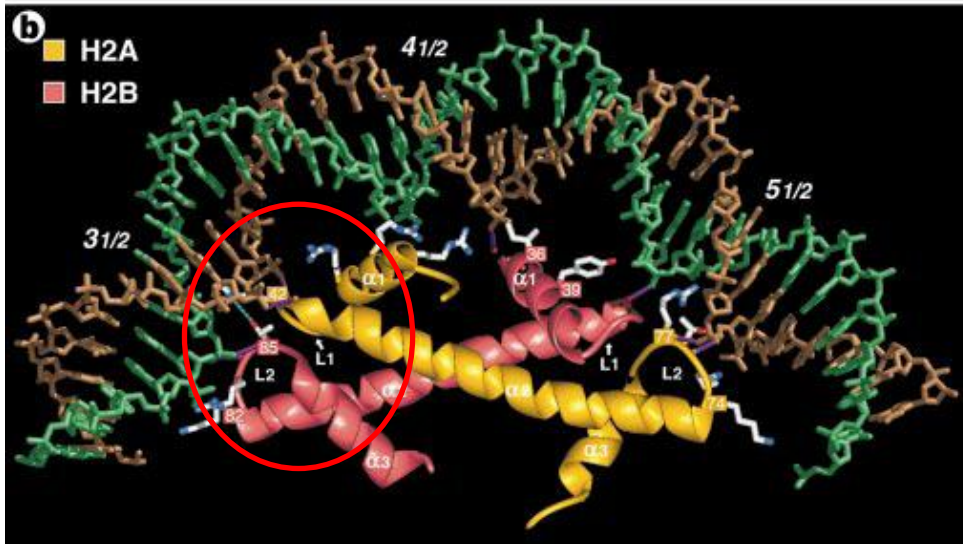
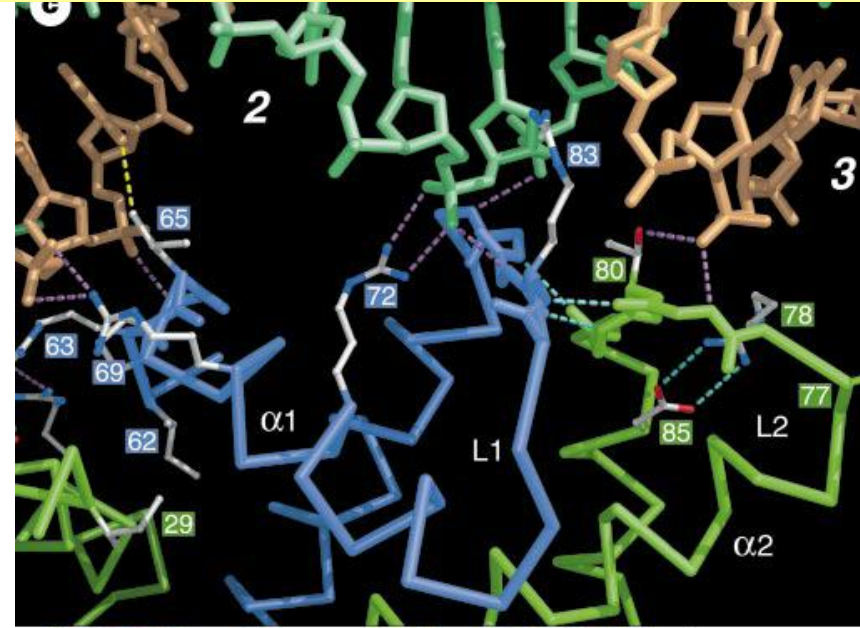
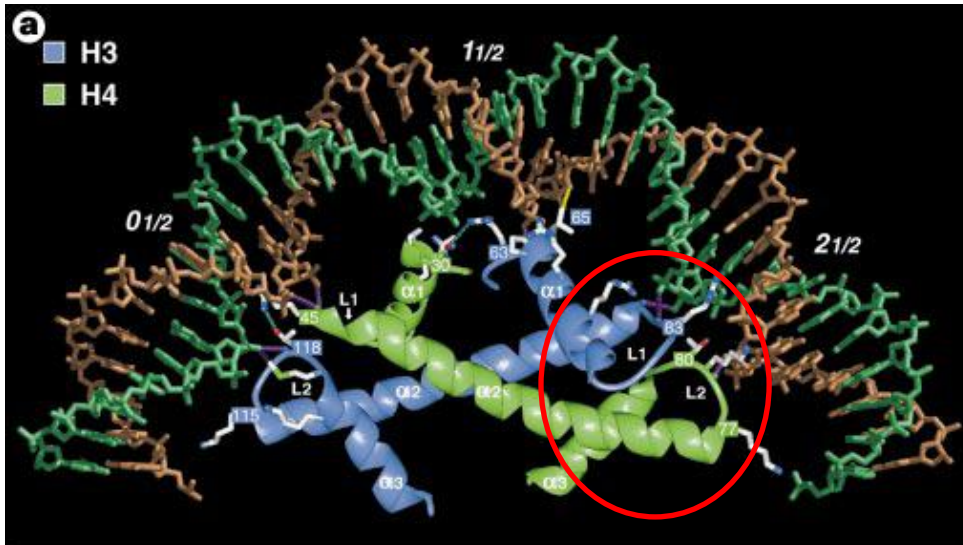


# Histone mit und ohne DNA

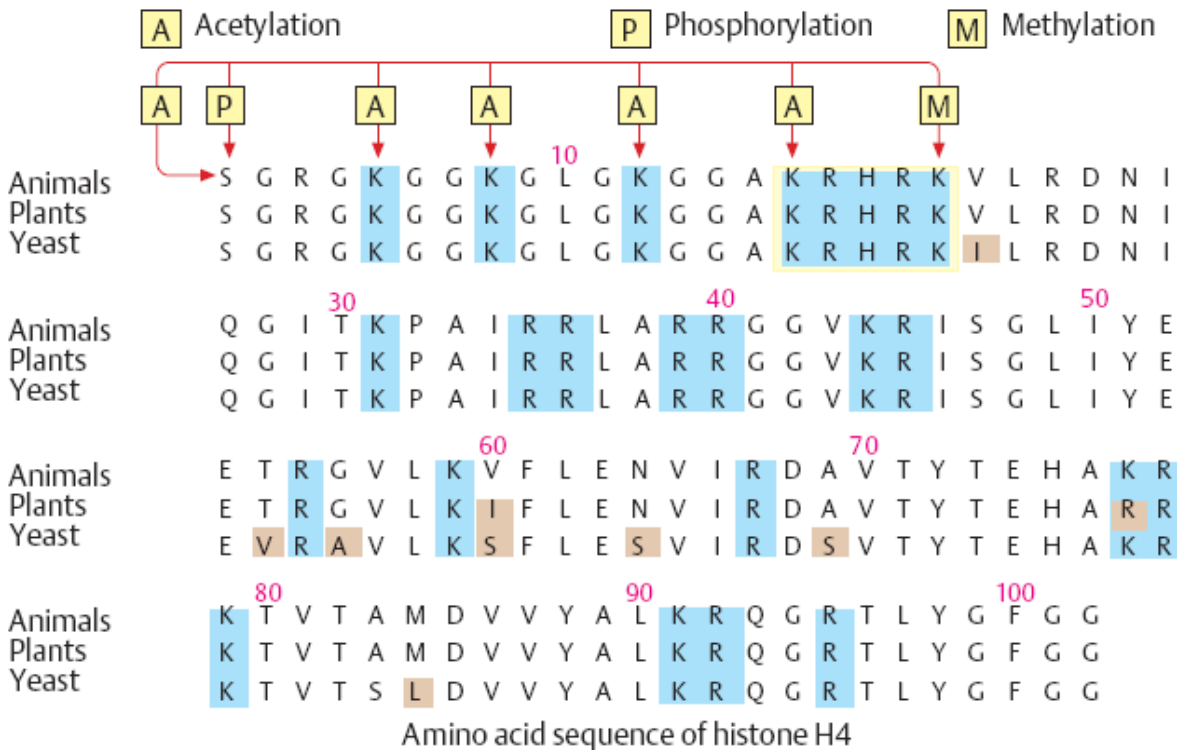
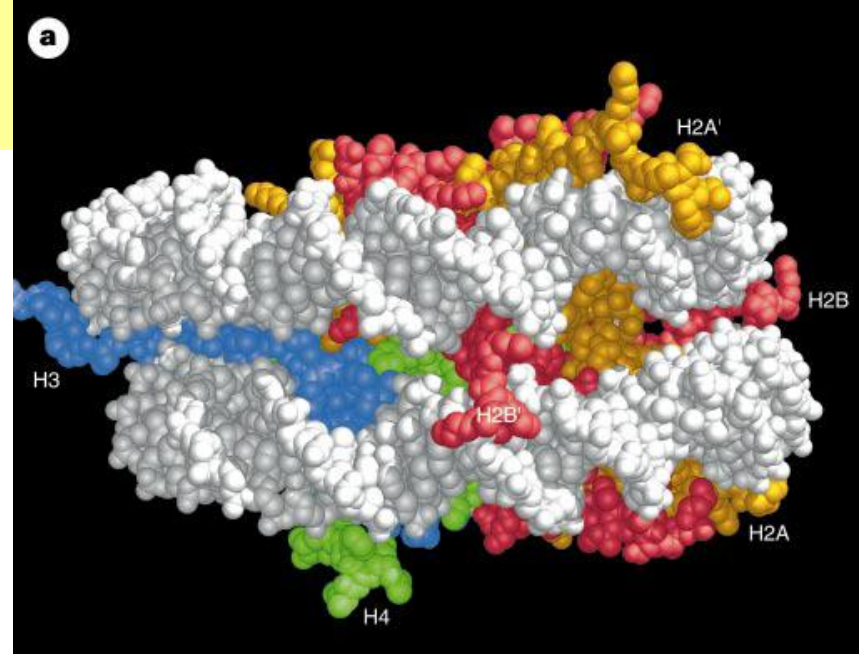




# Details der Protein DNA-Interaktion

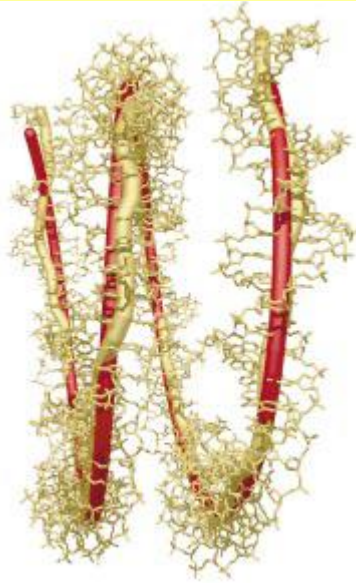
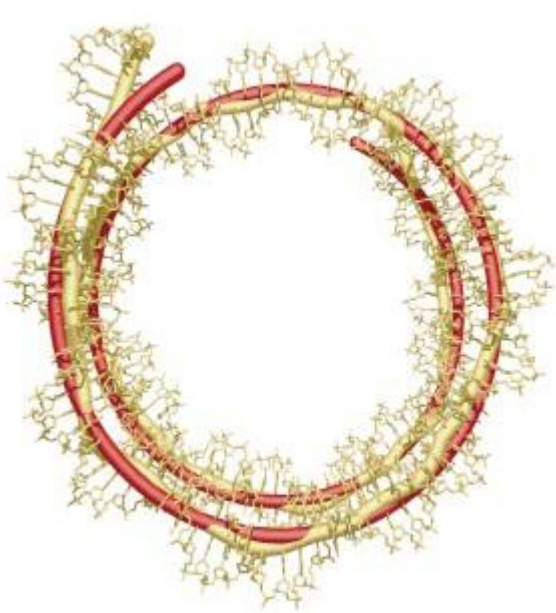


# Histon Modifikationen

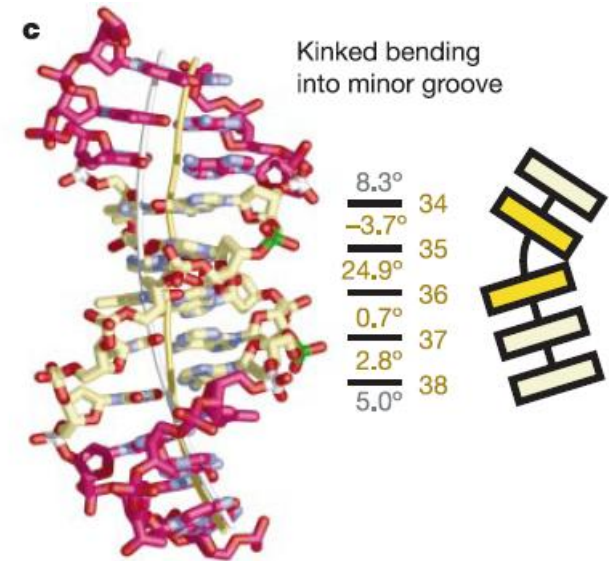
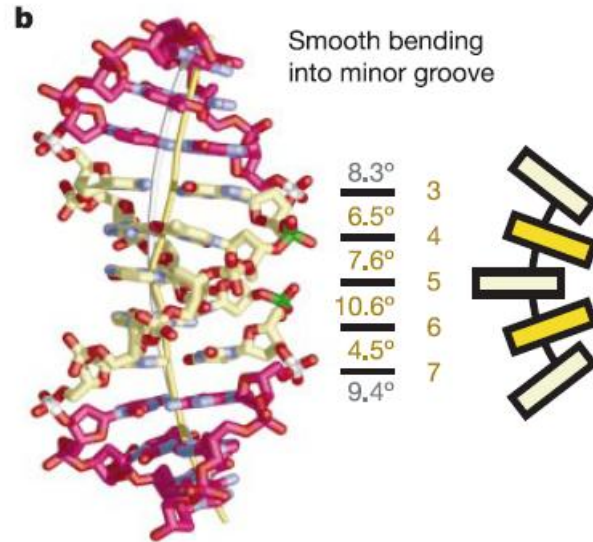
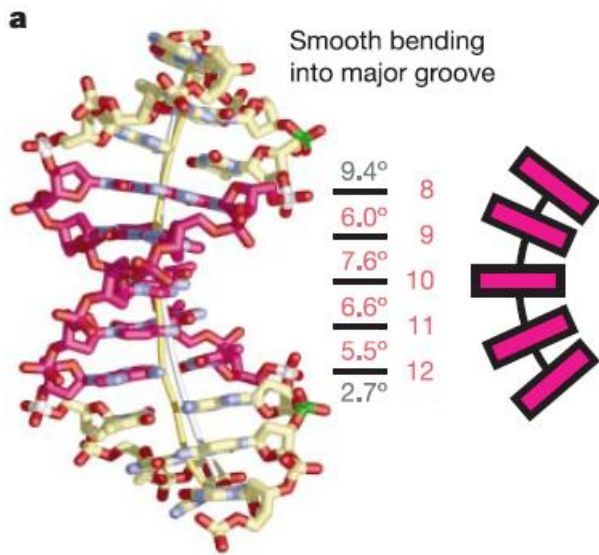




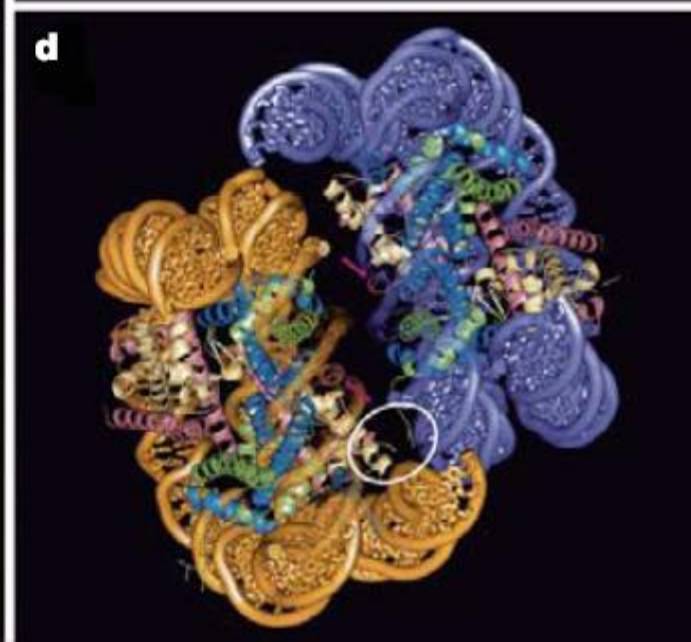
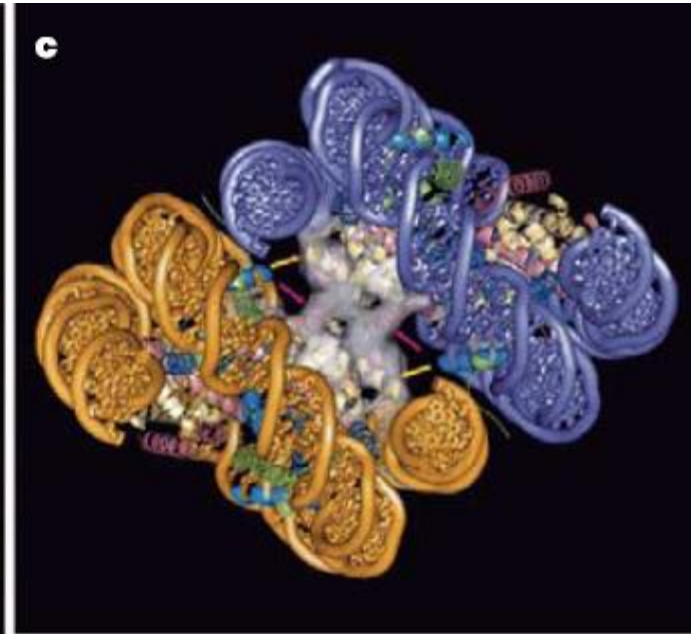
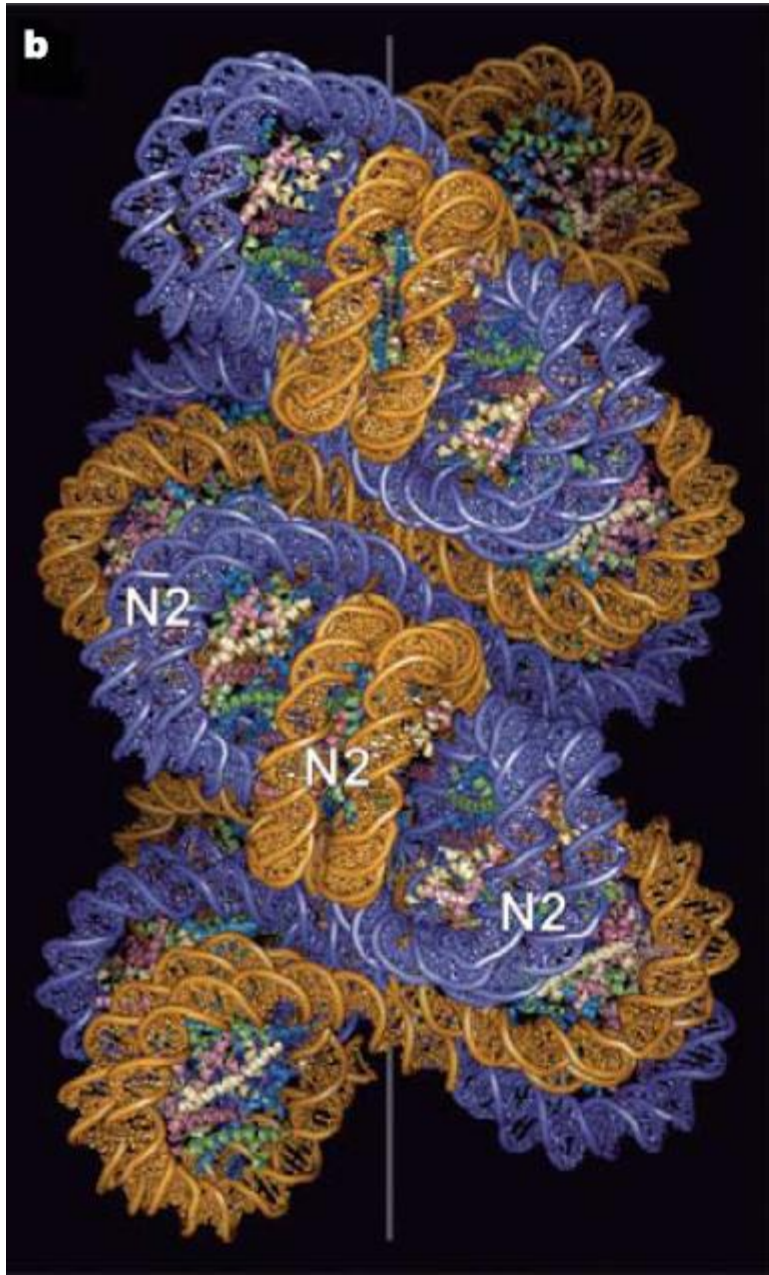
# Histone können die DNA Struktur verzerren



rot: ideale Superhelix  
gelb: gefundene Struktur

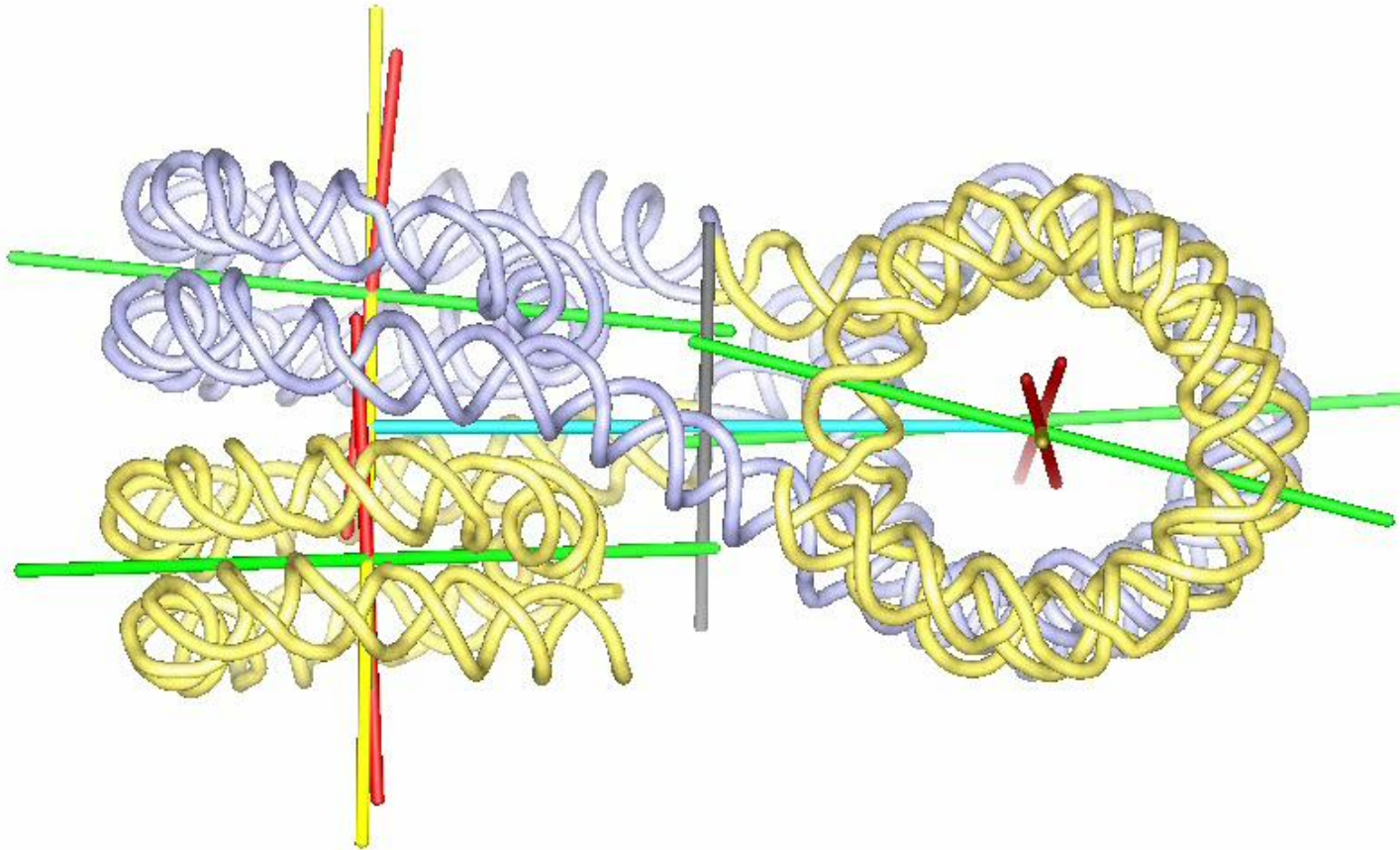


# Struktur eines Tetranukleosoms





# Packung im Tetranukleosom



(Animation)

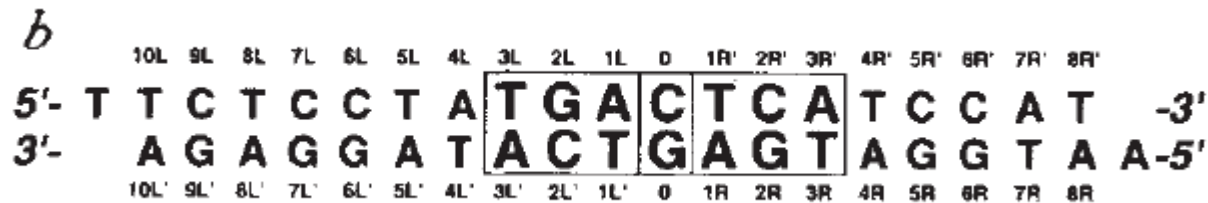
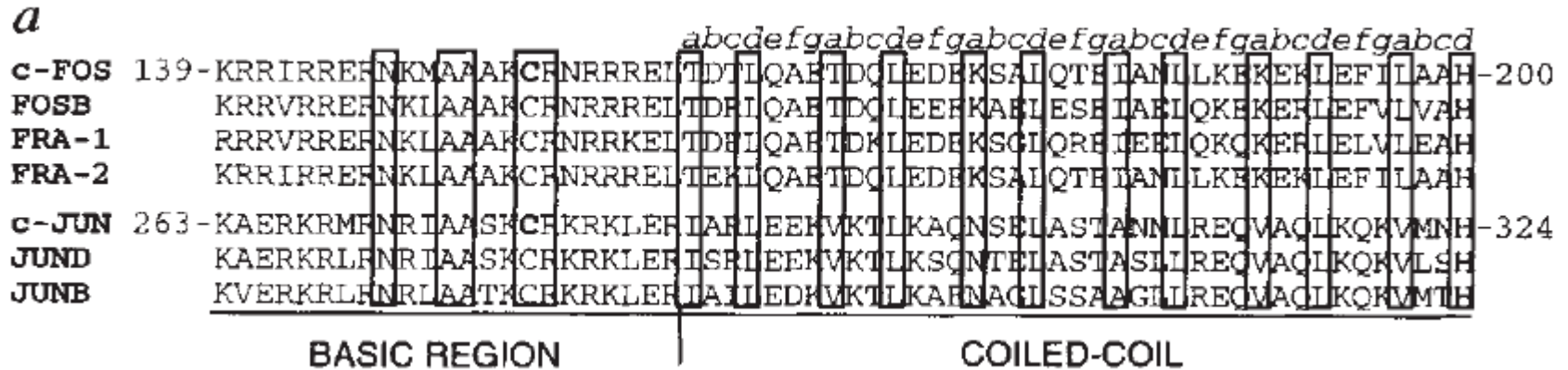


# Übersicht

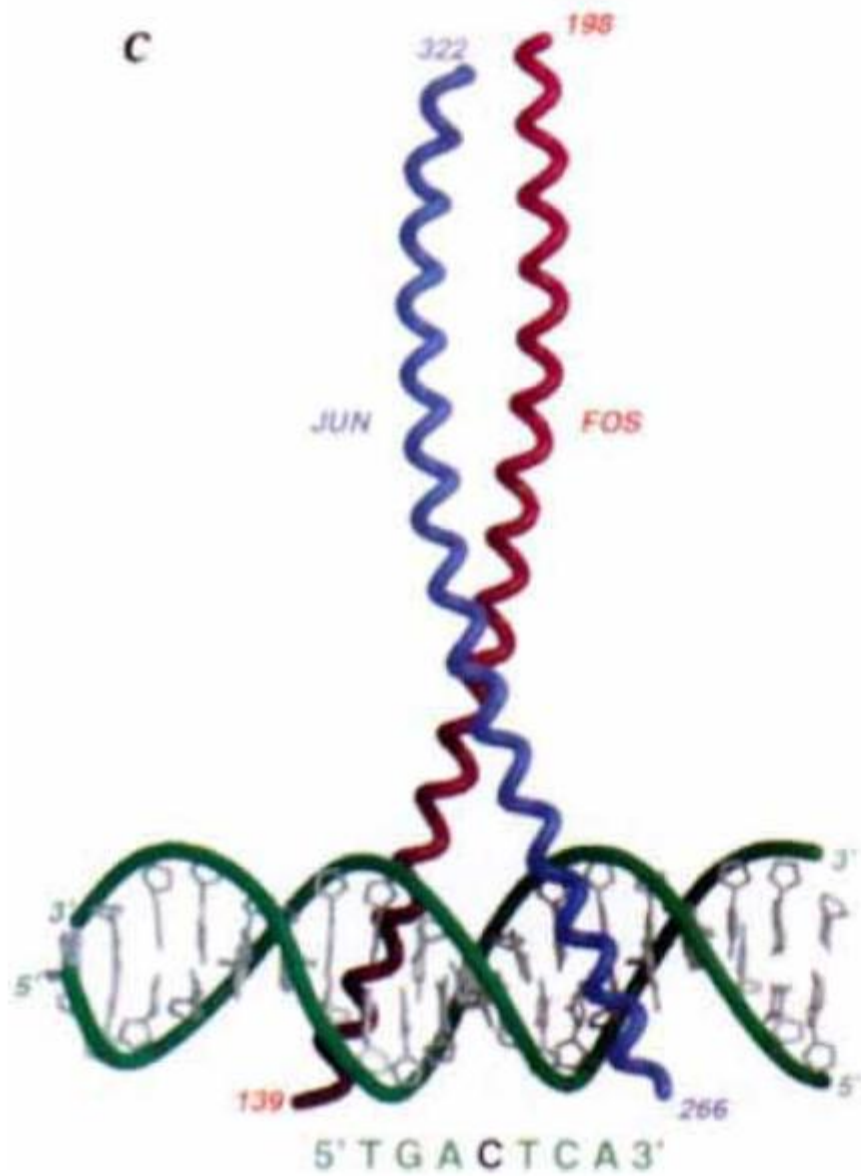
- Histone
- B-ZIP Familie
- HLH Familie
- HTH Familie
- RHH Familie
- Zinc-Finger Familie
- Restriktionsenzyme

# Basic Zipper (bZIP) Familie

Literatur: Glover JN, Harrison SC "Crystal structure of the heterodimeric bZIP transcription factor c-Fos-c-Jun bound to DNA." Nature. 1995 Jan 19;373(6511):257-61

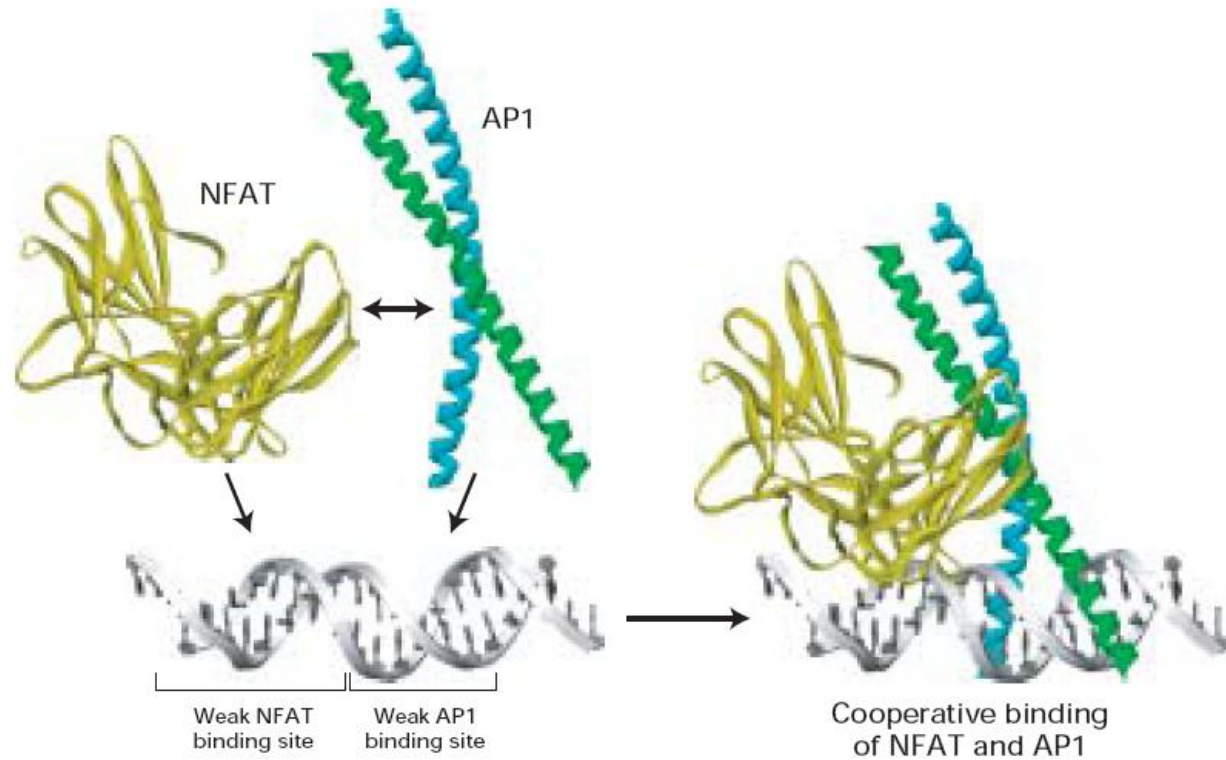


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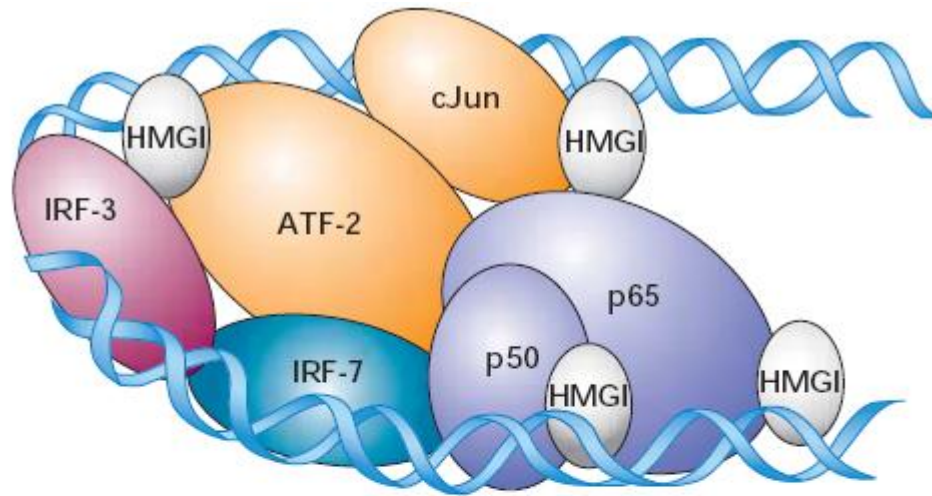


# Kooperative DNA Bindung

► **FIGURE 11-24 Cooperative binding of two unrelated transcription factors to neighboring sites in a composite control element.** By themselves, both monomeric NFAT and heterodimeric AP1 transcription factors have low affinity for their respective binding sites in the *IL-2* promoter-proximal region. Protein-protein interactions between NFAT and AP1 add to the overall stability of the NFAT-AP1-DNA complex, so that the two proteins bind to the composite site cooperatively. [See L. Chen et al., 1998, *Nature* **392**:42.]



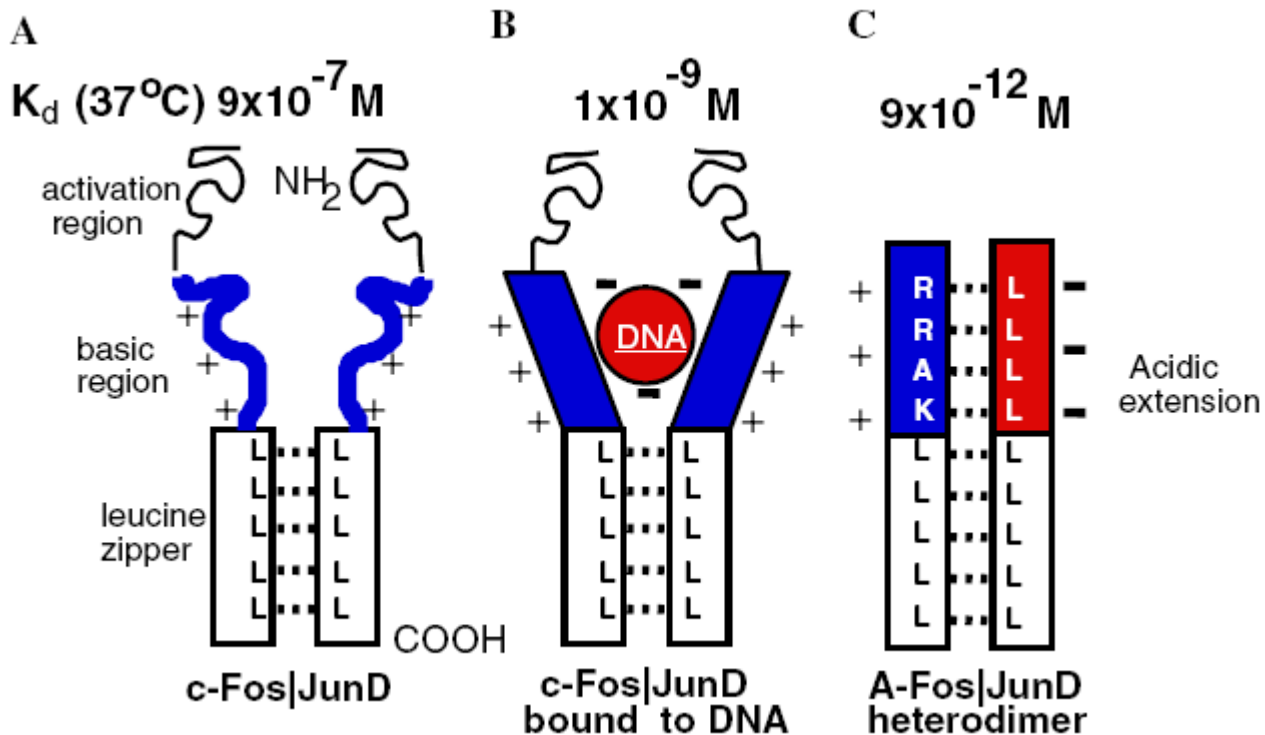
# Regulation erfordert komplexe Strukturen



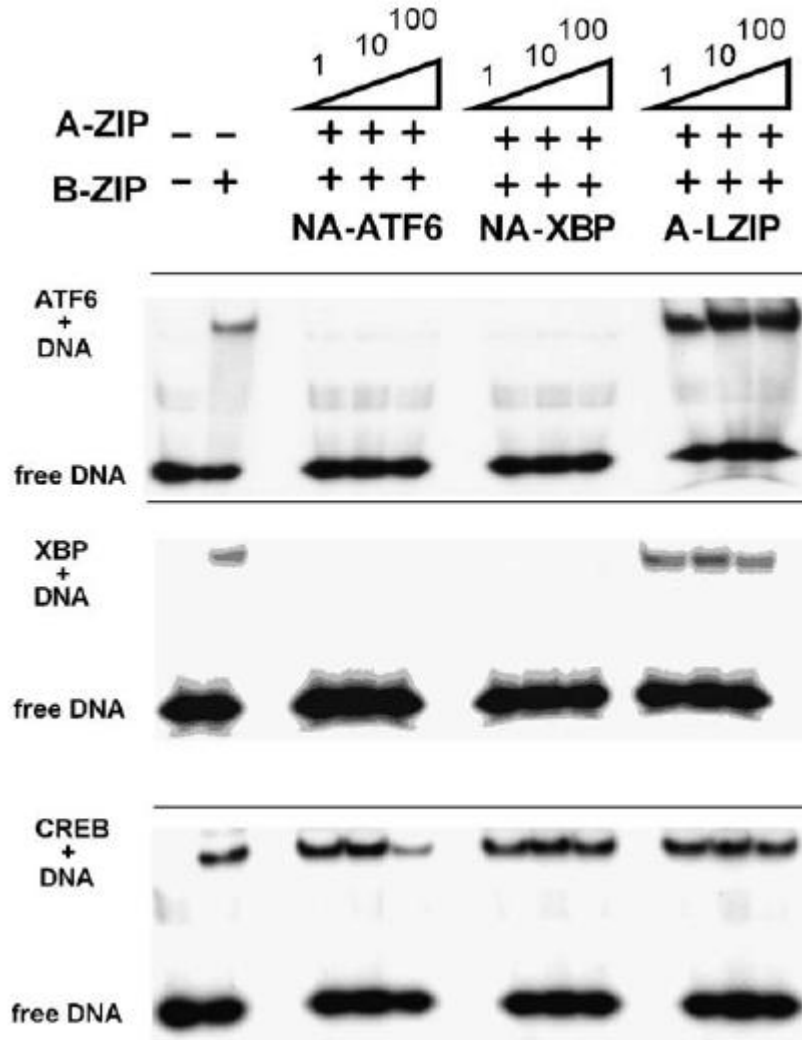
**▲ FIGURE 11-26 Model of the enhancesome that forms on the  $\beta$ -interferon enhancer.** Two monomeric transcription factors, IRF-3 and IRF-7, and two heterodimeric factors, Jun/ATF-2 and p50/ p65 (NF- $\kappa$ B) bind to the four control elements in this enhancer. Cooperative binding of these transcription factors is facilitated by HMGI, which binds to the minor groove of DNA and also interacts directly with the dimeric factors. Bending of the enhancer sequence resulting from HMGI binding is critical to formation of an enhancesome. Different DNA-bending proteins act similarly at other enhancers. [Adapted from D. Thanos and T. Maniatis, 1995, *Cell* **83**:1091, and M. A. Wathel et al., 1998, *Mol. Cell* **1**:507.]

# Künstliche Inhibitoren

Literatur: Acharya A, Rishi V, Moll J, Vinson C "Experimental identification of homodimerizing B-ZIP families in Homo sapiens." J Struct Biol. 2006 Aug;155(2):130-9.



# Inhibition im „EMSA“



Elektrophoretic Mobility Shift Assay

Oligos markiert (z.B. Kinasierung mit radioaktivem ATP), mischen mit Proteinen, Auftrennung im Polyacrylamidgel (6%).



# basic Helix-Loop-Helix Zipper (bHLHz) Familie

Literatur: Nair SK, Burley SK „X-ray structures of Myc-Max and Mad-Max recognizing DNA. Molecular bases of regulation by proto-oncogenic transcription factors.“  
Cell. 2003 Jan 24;112(2):193-205.

**A**



```

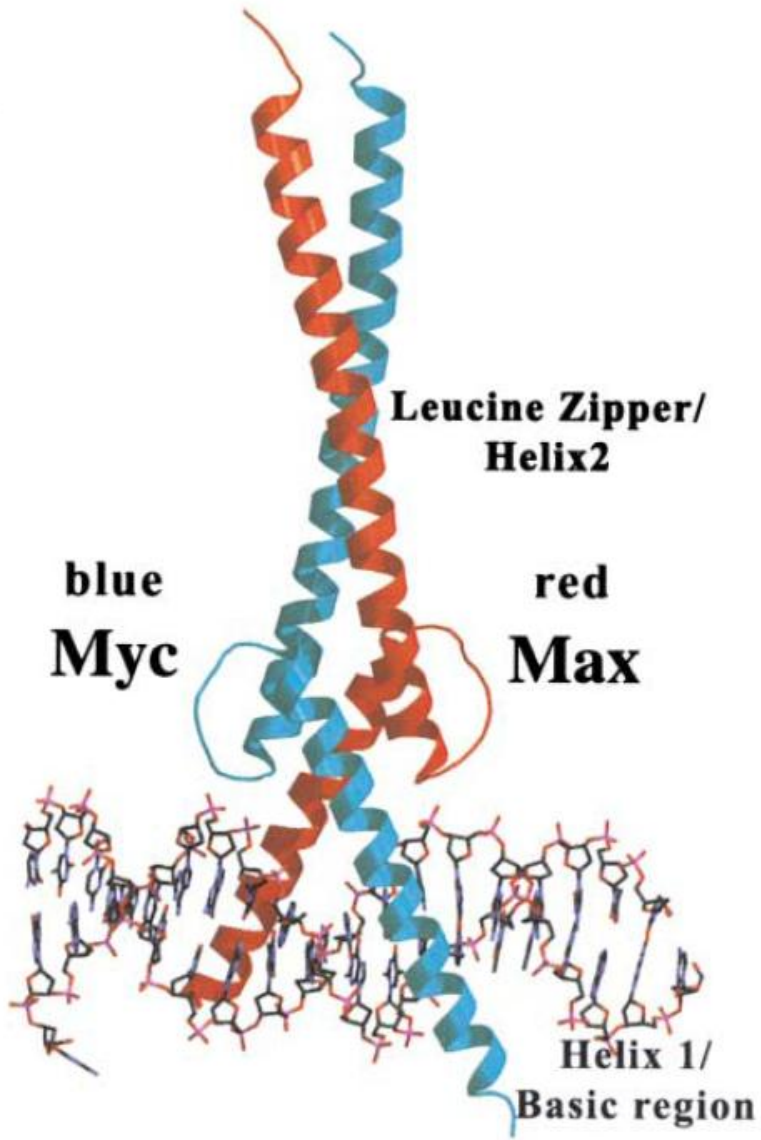
cMYC  NVKRRTHNVLERQRRNELKRSFFALRDQIP----ELENNEKAP-KVVILKKATAYILSVQAEQQLISEEDLLRKRREQLKHKLEQL
MAX    ADKRAHHNALERKRRDHIKDSFHSRLRDSVP-----SLQGEKAS-RAQILDKATEYIQYMRRKNDTHQQDIDDLKRQNALLEQQVRL
MAD    SSSRSTHNEMEKNRRAHLRLCLEKLGKGLVP----LGPSSSRHT-TLSLLTKAKLHIKKLEDCDRKAVHQIDQLQREQRHLKRQLEKL

nMYC   SESRRNHNILERQRNDLRSSFLLTRDHVP----ELVKNEKAA-KVVILKKATEYVHSLQAEHQLLLEKEKQLQARQQQLLKKIEHA
lMYC   VTKRKNHNFLEKRRNDLRSRFLALRDQVP----TLASCSKAP-KVVILSKALEYLQALVGAEKRMATEKRQLRCRQQQLQKRIAYL
USF    EKRRAQHNEVERRRRDKINNWIVQLSKIIP-DCSMESTKSGQS-KGGILSKACDYIQELRQSNHRLSEELQGLDQLQLDNDVLRQQV
E47    RERRMANNARERVVRDENEAFRELGRMCQ---MHLKSDKAQT-KLLILQQAVQYILGLEQQVRENLNP
MyoD   ADRRKAATMRERRRLSKVNEAFETLKRCTS----FMPKNRKLK-KVEILRNAIRYIEGLQALLRDQDAAP
Pho4   DDKRESHHKAEQARRNRLAVALHELASLI PAEWKQQNVSAAPS-KATIVEAACRYIRHLQQNGST
  
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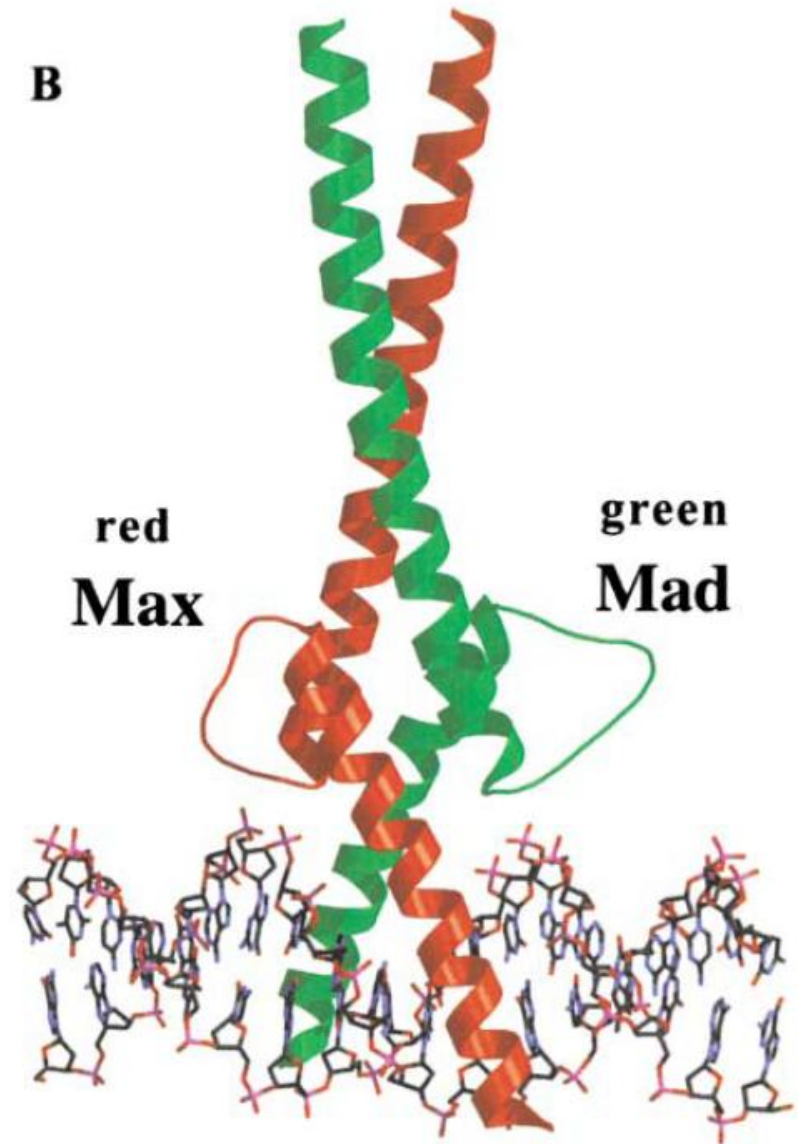


# Struktur der Heterodimeren

**A**

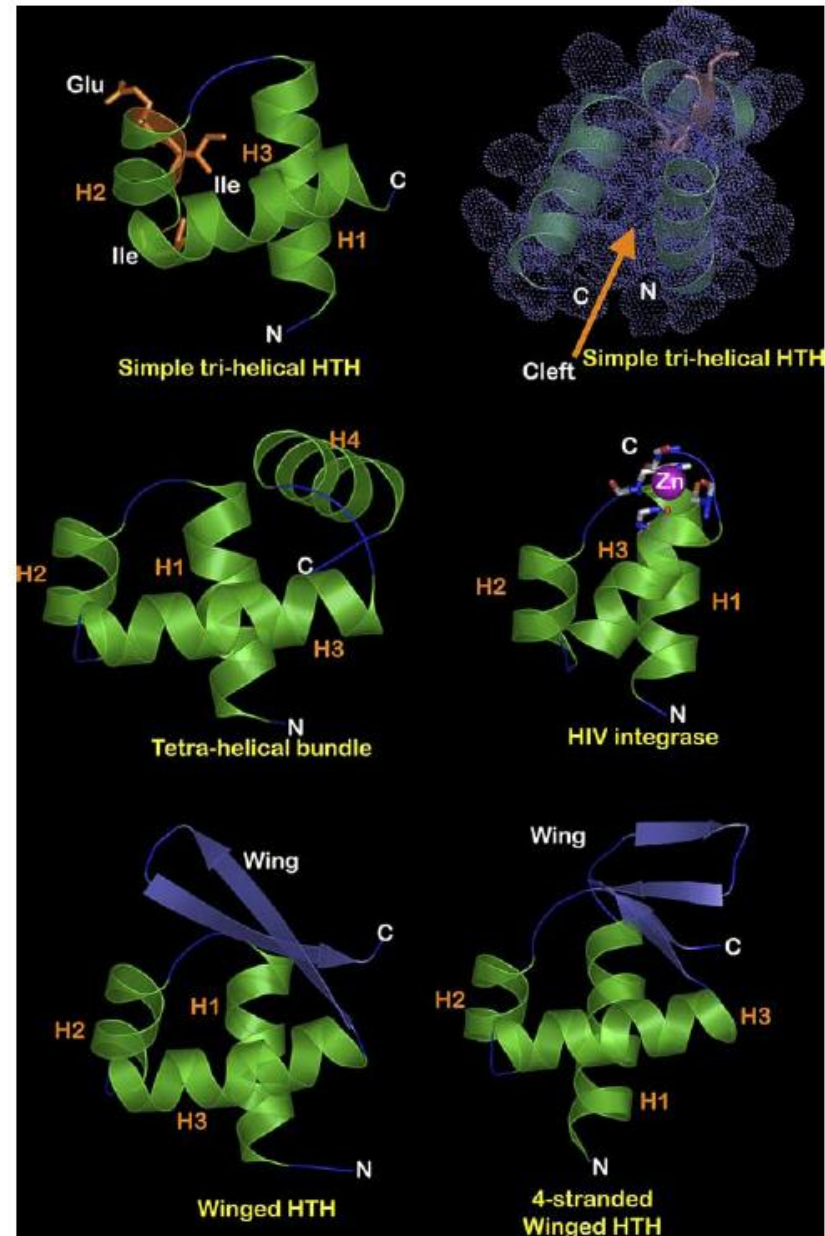
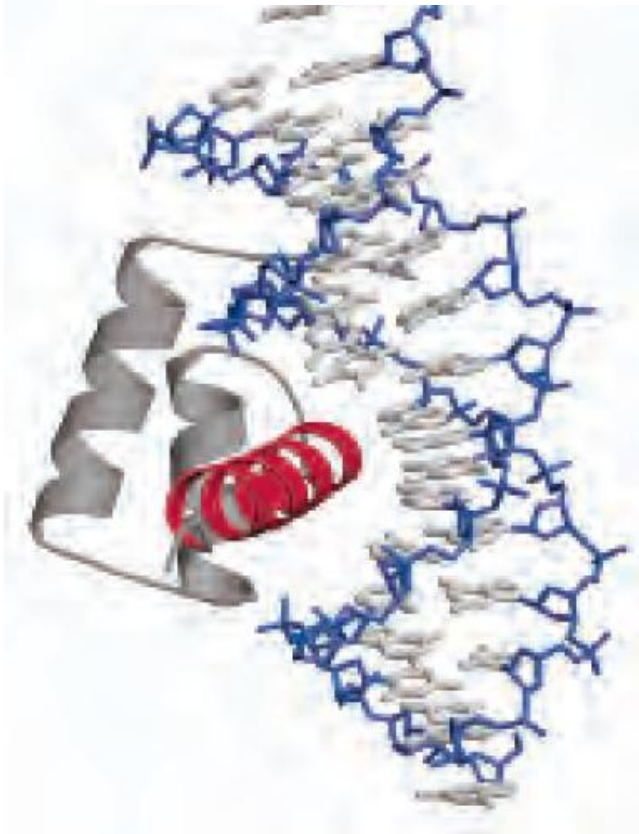


**B**



# Helix-Turn-Helix (HTH) Familie

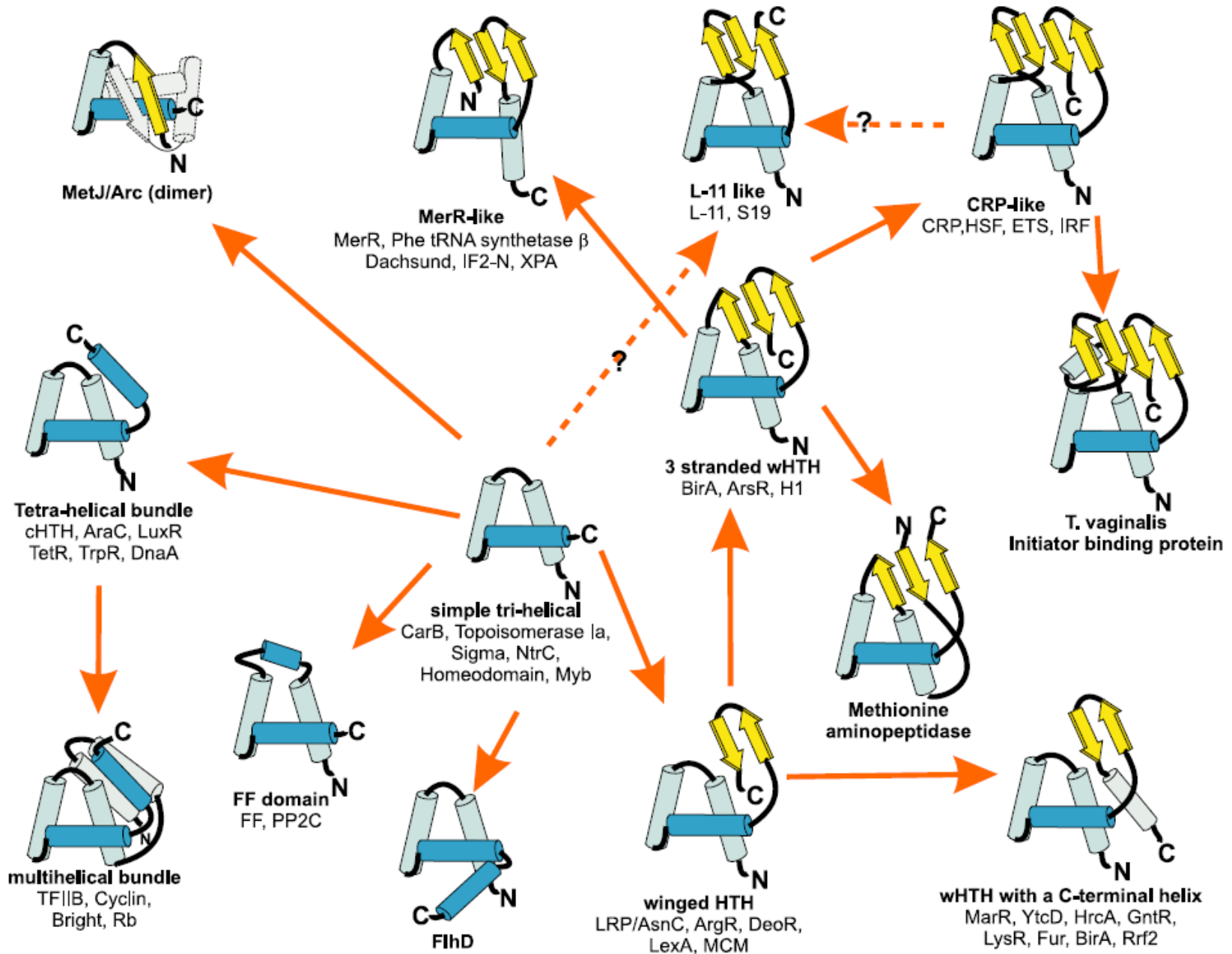
Aravind L, Anantharaman V, Balaji S, Babu MM, Iyer LM "The many faces of the helix-turn-helix domain: transcription regulation and beyond." FEMS Microbiol Rev. 2005 Apr;29(2):231-62



(Lehninger)

**FIGURE 28-13 Homeodomain.** Shown here is a homeodomain bound to DNA; one of the  $\alpha$  helices (red), stacked on two others, can be seen protruding into the major groove (PDB ID 1B8I). This is only a small part of the much larger protein Ultrabithorax (Ubx), active in the regulation of development in fruit flies.

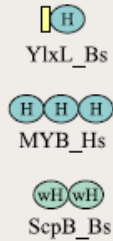
# Entwicklung der HTH Familie



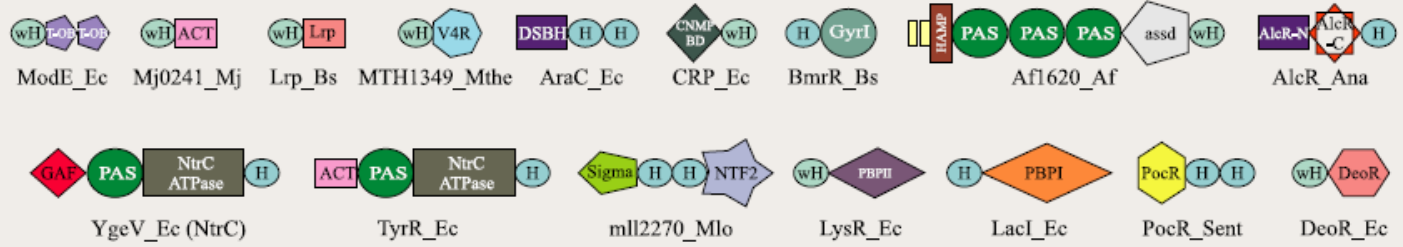


# HTH: Verbindung der DNA Bindung mit Funktion

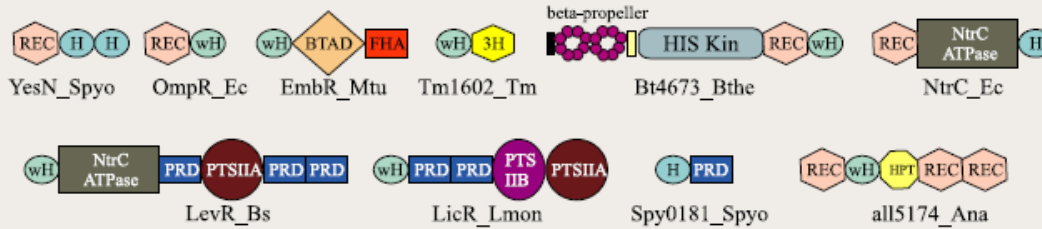
## Simple Architectures



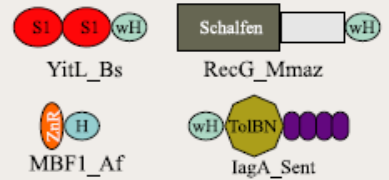
## One Component Systems and Fusions to Small Molecule Binding Domains



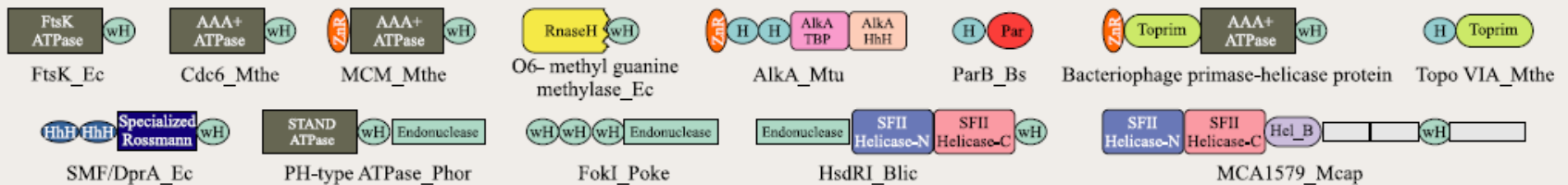
## Two Component Systems



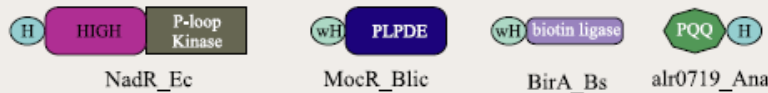
## Fusions to Adaptor and other Nucleic Acid-binding Domains



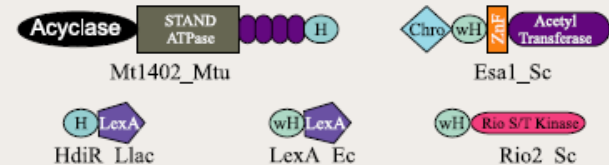
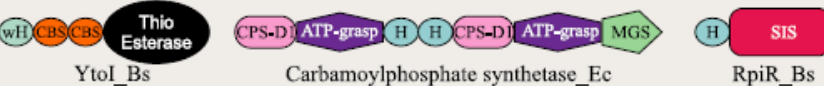
## Fusions to Catalytic Domains



## DNA Repair, Replication and Restriction Modification



## Translation and RNA Metabolism

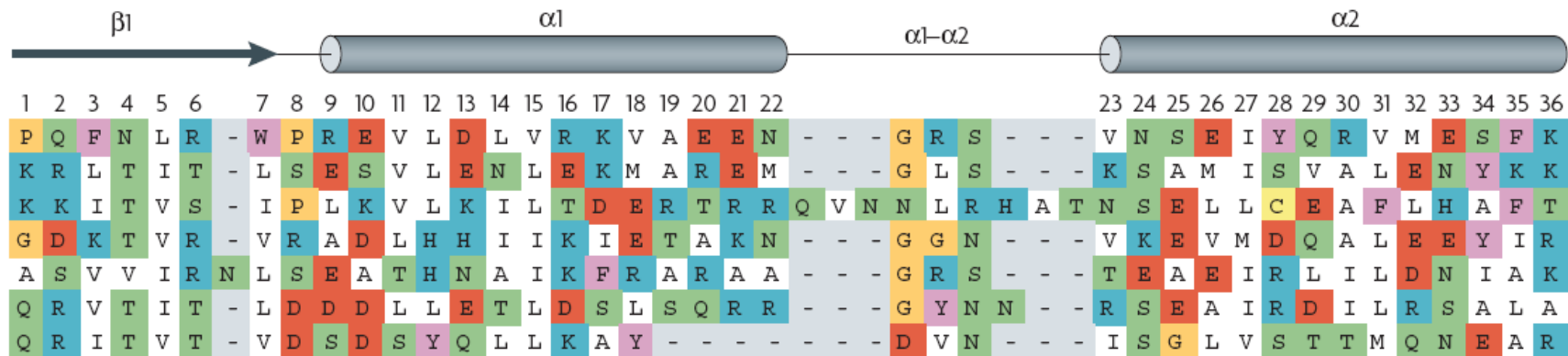


## Metabolism

## Other Fusions to Catalytic Domains

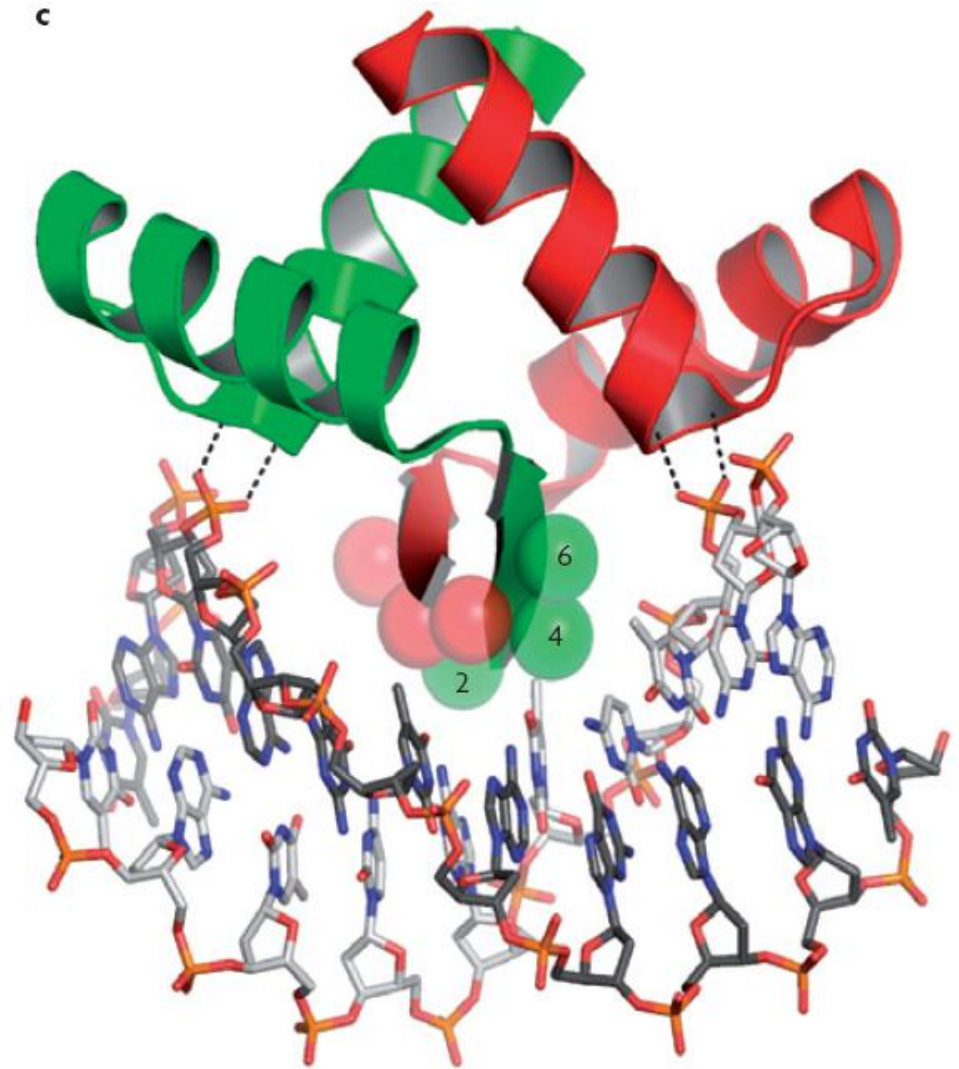
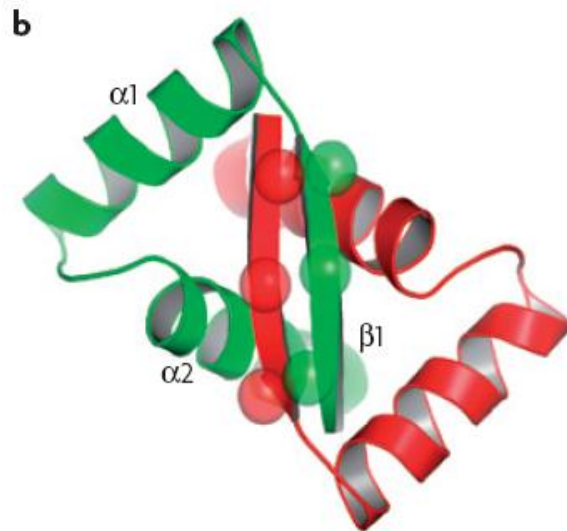
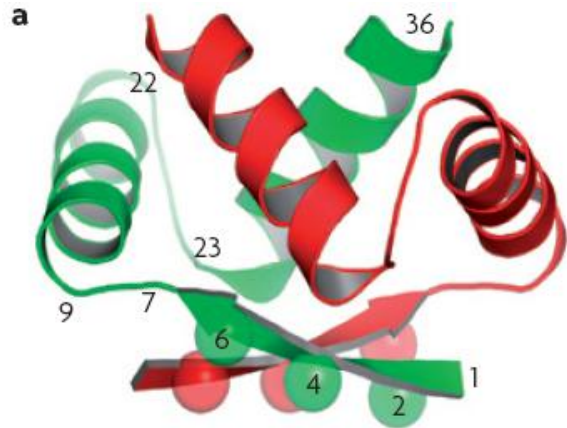
# Ribbon-Helix-Helix (RHH) Familie

Literatur: Schreiter ER, Drennan CL „Ribbon-helix-helix transcription factors: variations on a theme.“ Nat Rev Microbiol. 2007 Sep;5(9):710-20



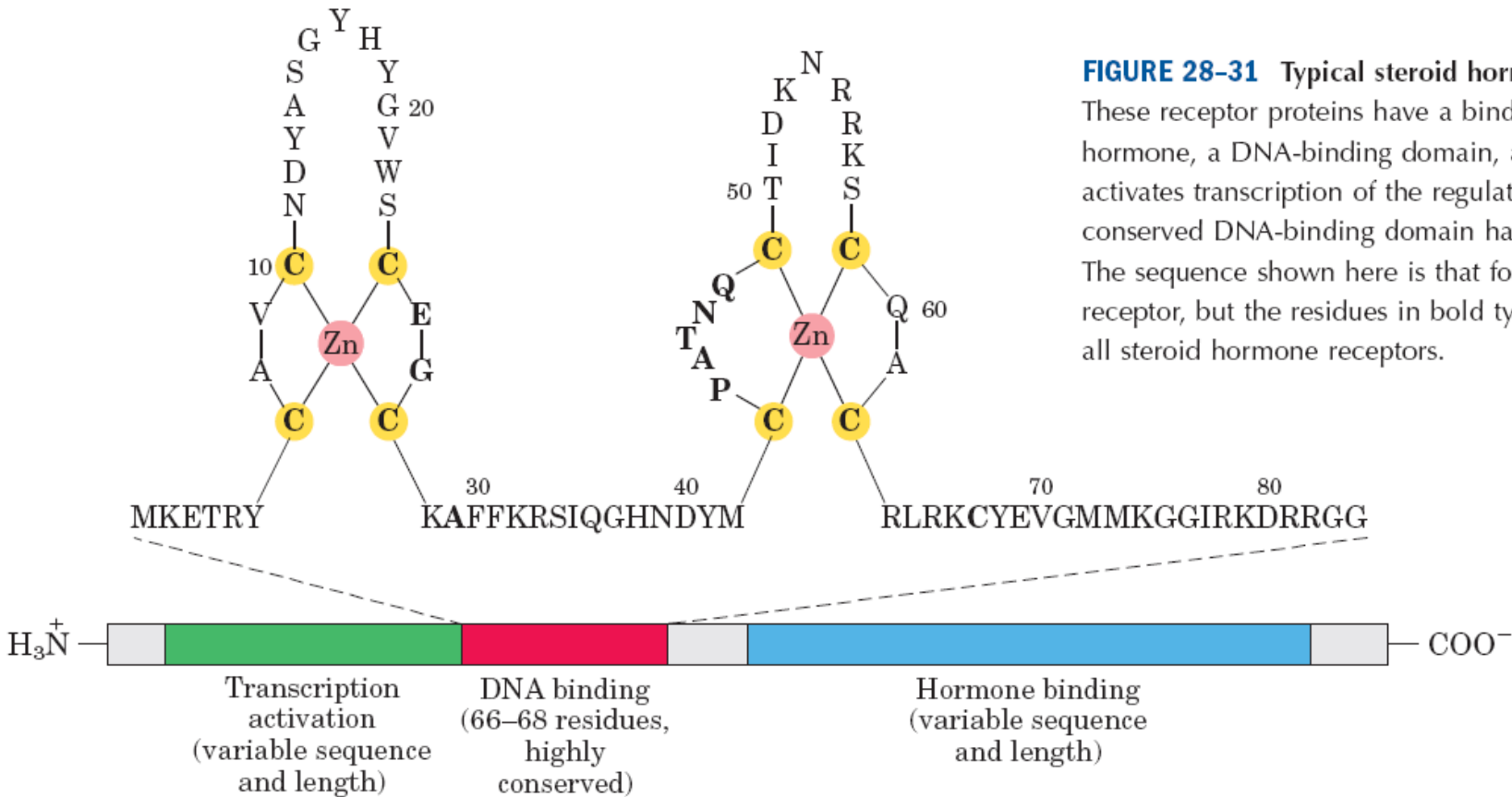


# Faltblatt Einlagerung in die DNA



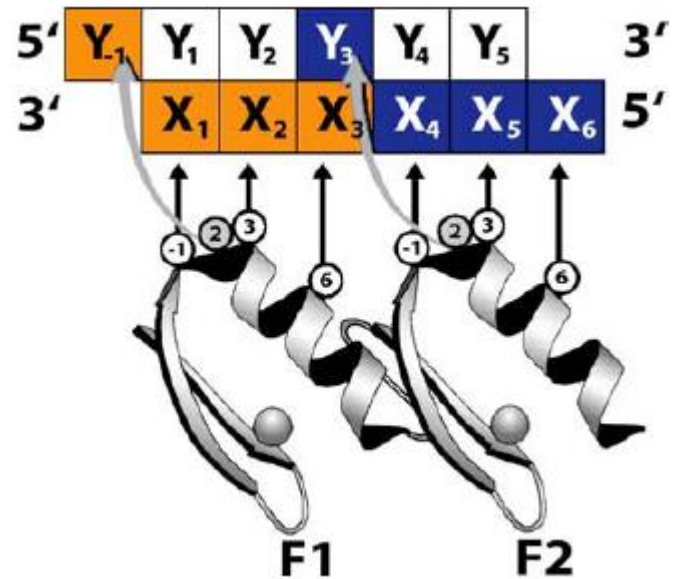
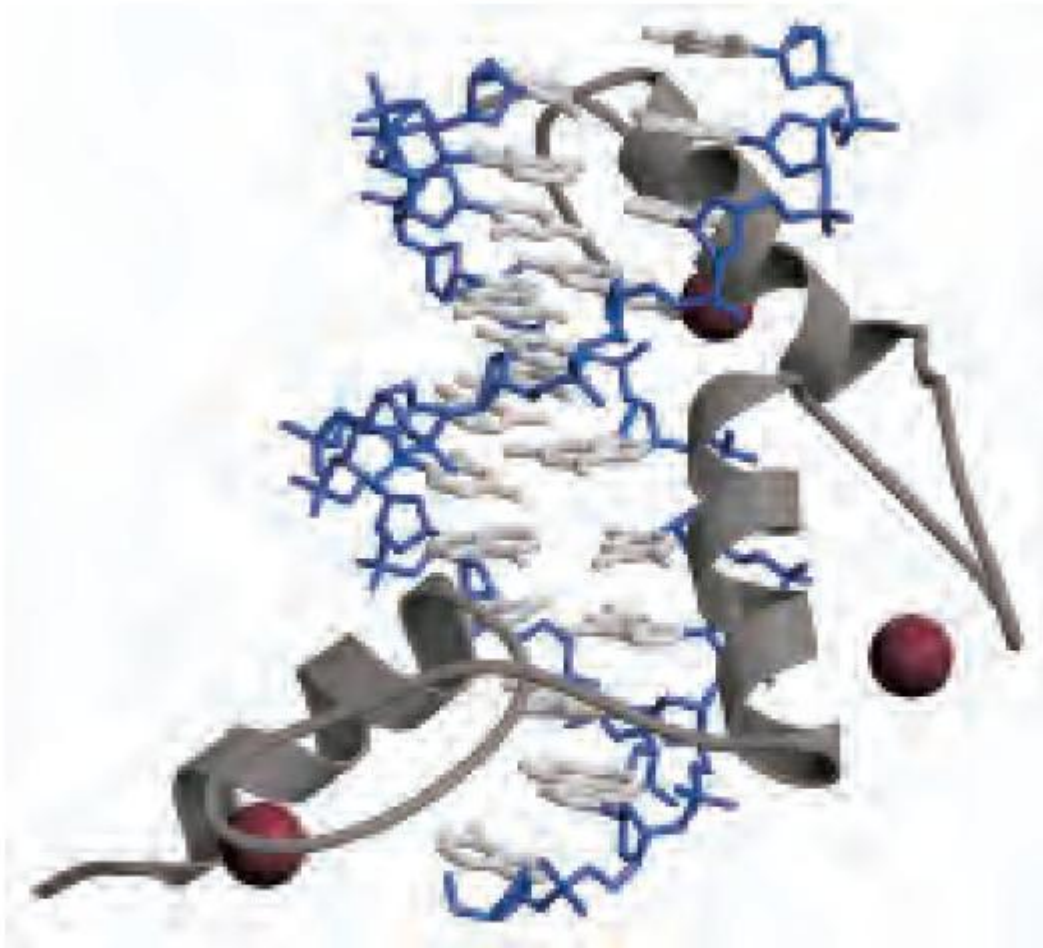
Reste „2“, „4“, „6“ bilden spezifische Kontakte mit der DNA

# Zinc Finger



**FIGURE 28-31** Typical steroid hormone receptors. These receptor proteins have a binding site for the hormone, a DNA-binding domain, and a region that activates transcription of the regulated gene. The highly conserved DNA-binding domain has two zinc fingers. The sequence shown here is that for the estrogen receptor, but the residues in bold type are common to all steroid hormone receptors.

# Zinc Finger DNA Bindung

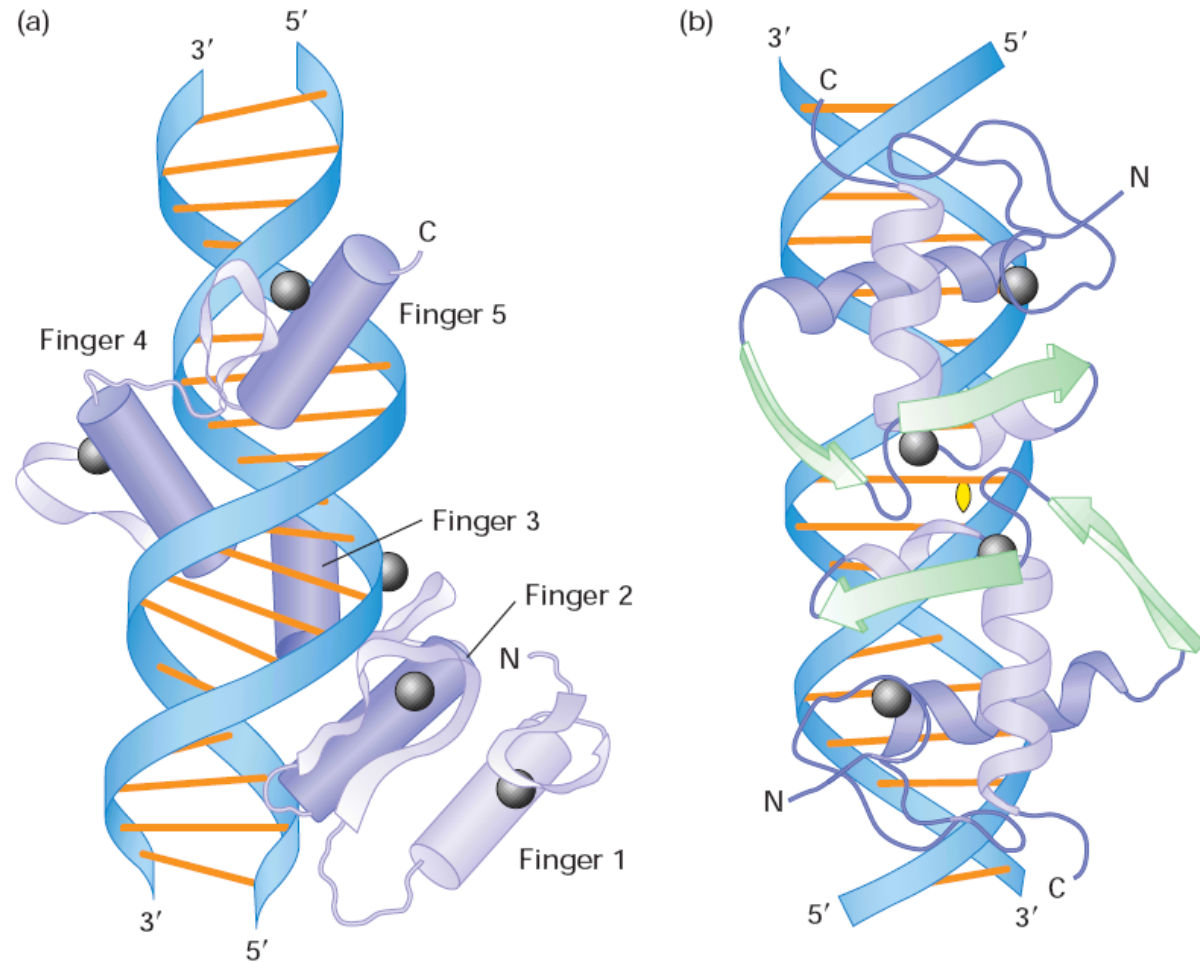


**FIGURE 28-12** Zinc fingers. Three zinc fingers (gray) of the regulatory protein Zif268, complexed with DNA (blue and white) (PDB ID 1A1L). Each Zn<sup>2+</sup> (maroon) coordinates with two His and two Cys residues (not shown).

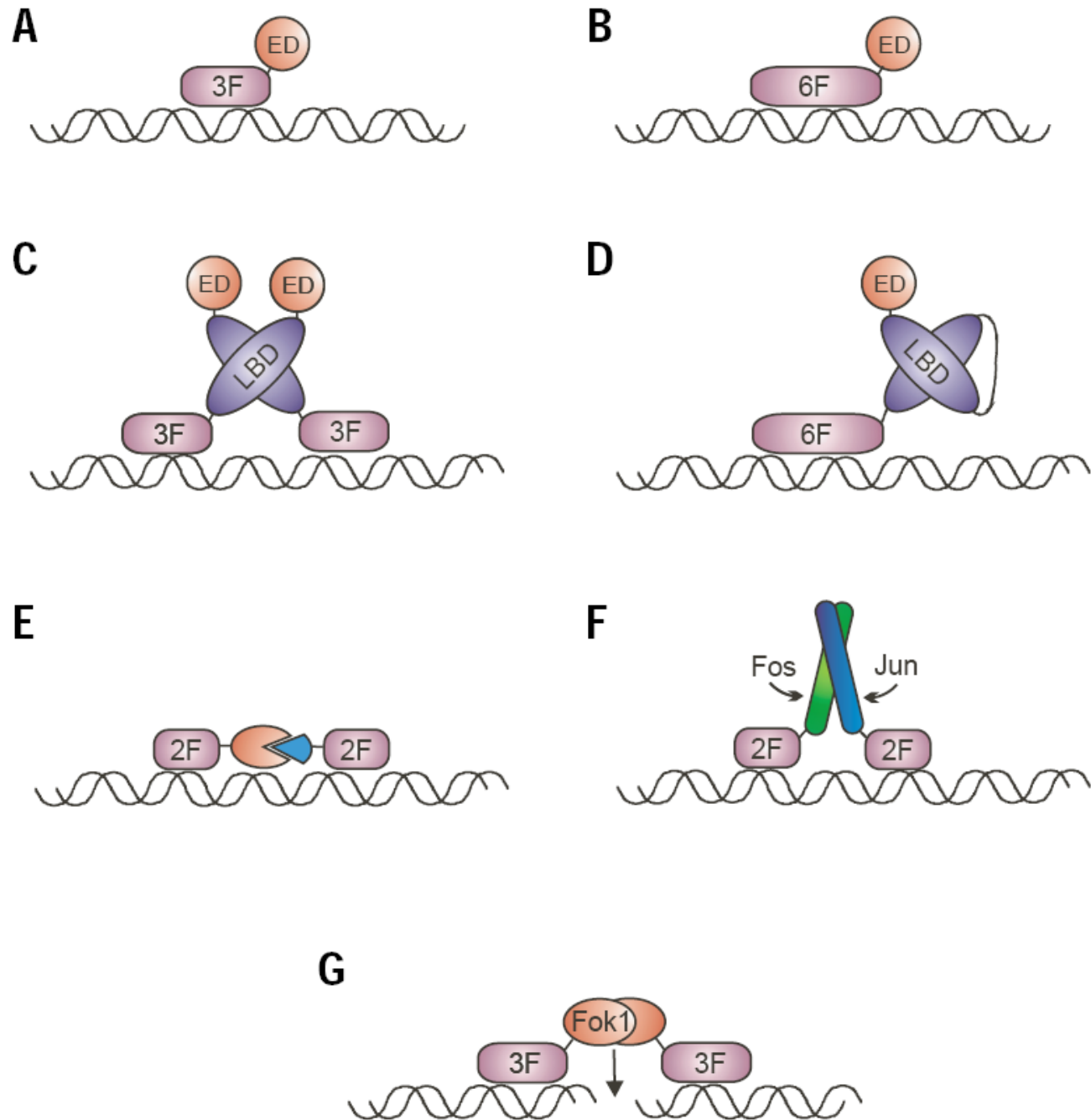
# Verknüpfung mehrerer Finger

## ► FIGURE 11-21 Interaction between DNA and proteins containing zinc fingers.

(a) GL1 is a monomeric protein that contains five  $C_2H_2$  zinc fingers.  $\alpha$ -Helices are shown as cylinders,  $Zn^{+2}$  ions as spheres. Finger 1 does not interact with DNA, whereas the other four fingers do. (b) The glucocorticoid receptor is a homodimeric  $C_4$  zinc-finger protein.  $\alpha$ -Helices are shown as purple ribbons,  $\beta$ -strands as green arrows,  $Zn^{+2}$  ions as spheres. Two  $\alpha$  helices (darker shade), one in each monomer, interact with the DNA. Like all  $C_4$  zinc-finger homodimers, this transcription factor has twofold rotational symmetry; the center of symmetry is shown by the yellow ellipse. In contrast, heterodimeric nuclear receptors do not exhibit rotational symmetry. [See N. P. Pavletich and C. O. Pabo, 1993, *Science* **261**:1701, and B. F. Luisi et al., 1991, *Nature* **352**:497.]



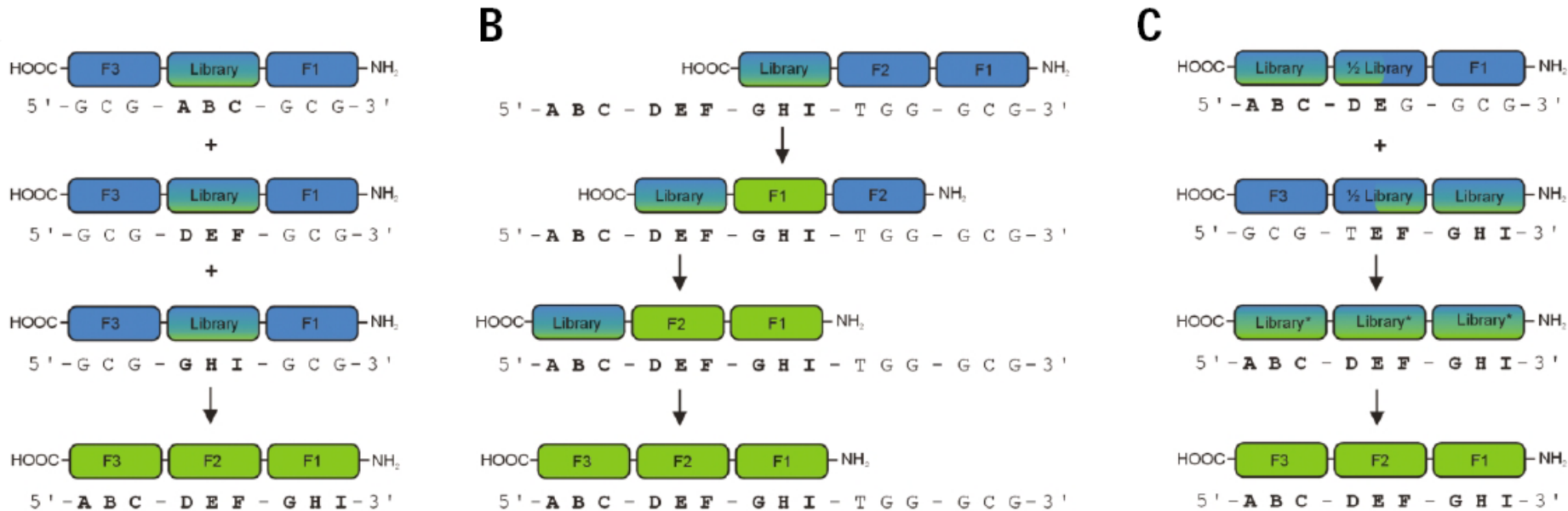
# Künstliche Zinc Finger



Beerli RR, Barbas CF 3rd.  
"Engineering polydactyl  
zinc-finger transcription  
factors." *Nat Biotechnol.*  
2002 Feb;20(2):135-41.



# Entwicklung künstlicher Zinc Finger



**Figure 2.** Strategies for the production of ZFPs with desired DNA-binding specificity. (A) Parallel selection. (B) Sequential selection. (C) Bipartite selection. Asterisks indicate preselected libraries. See text and references for

Anwendung:

Urnov FD, Miller JC, Lee YL, Beausejour CM, Rock JM, Augustus S, Jamieson AC, Porteus MH, Gregory PD, Holmes MC

**“Highly efficient endogenous human gene correction using designed zinc-finger nucleases.”**

Nature. 2005 Jun 2;435(7042):646-5

# Restriktionsenzyme

Roberts et al. "A nomenclature for restriction enzymes, DNA methyltransferases, homing endonucleases and their genes."  
Nucleic Acids Res. 2003 Apr 1;31(7):1805-12

**Table 1.** Subtypes of Type II REases

Subtype <sup>a</sup>	Defining feature	Examples	Recognition sequence
A	Asymmetric recognition sequence	FokI AciI	GGATG (9/13) CCGC (-3/-1)
B	Cleaves both sides of target on both strands	BcgI	(10/12) CGANNNNNNTGC (12/10)
C	Symmetric or asymmetric target. R and M functions in one polypeptide	GsuI HaeIV	CTGGAG (16/14) (7/13) GAYNNNNNRTC (14/9)
E	Two targets; one cleaved, one an effector	BcgI EcoRII NaeI	(10/12) CGANNNNNNTGC (12/10) ↓CCWGG GCC↓GGC
F	Two targets, both cleaved coordinately	SfiI SgrAI	GGCCNNNN↓NGGCC CR↓CCGGYG
G	Symmetric or asymmetric target. Affected by AdoMet	BsgI Eco57I	GTGCAG (16/14) CTGAAG (16/14)
H	Symmetric or asymmetric target. Similar to Type I gene structure	BcgI AhdI	(10/12) CGANNNNNNTGC (12/10) GACNNN↓NNGTC
M	Subtype IIP or IIA. Require methylated target	DpnI	Gm6 A↓TC
P	Symmetric target and cleavage sites	EcoRI PpuMI BslI	G↓AATTC RG↓GWCCY CCNNNNN↓NNGG
S	Asymmetric target and cleavage sites	FokI MmeI	GGATG (9/13) TCCRAC (20/18)
T	Symmetric or asymmetric target. R genes are heterodimers	Bpu10I BslI	CC <sup>+</sup> TNAGC (-5/-2) <sup>b</sup> CCNNNNN↓NNGG

<sup>a</sup>Note that not all subtypes are mutually exclusive. E.g. BslI is of subtype P and T.

# Restriktionsenzym Datenbank: REBASE



REBASE<sup>®</sup>

The Restriction Enzyme Database

<http://rebase.neb.com> - [Citing REBASE...](#)

Choose search category and enter keyword:

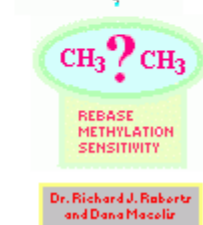
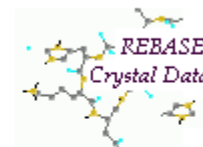
use percent sign as wildcard and quotes around phrases

author starting with

Go Clear

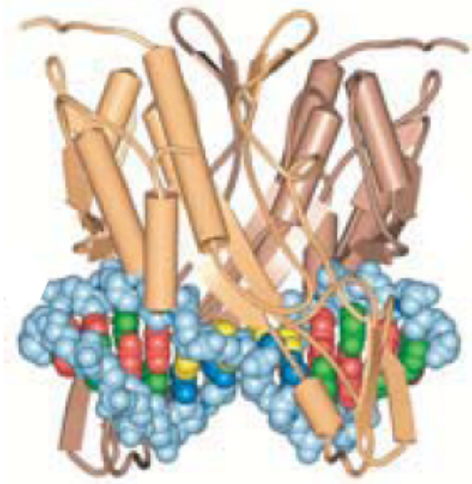
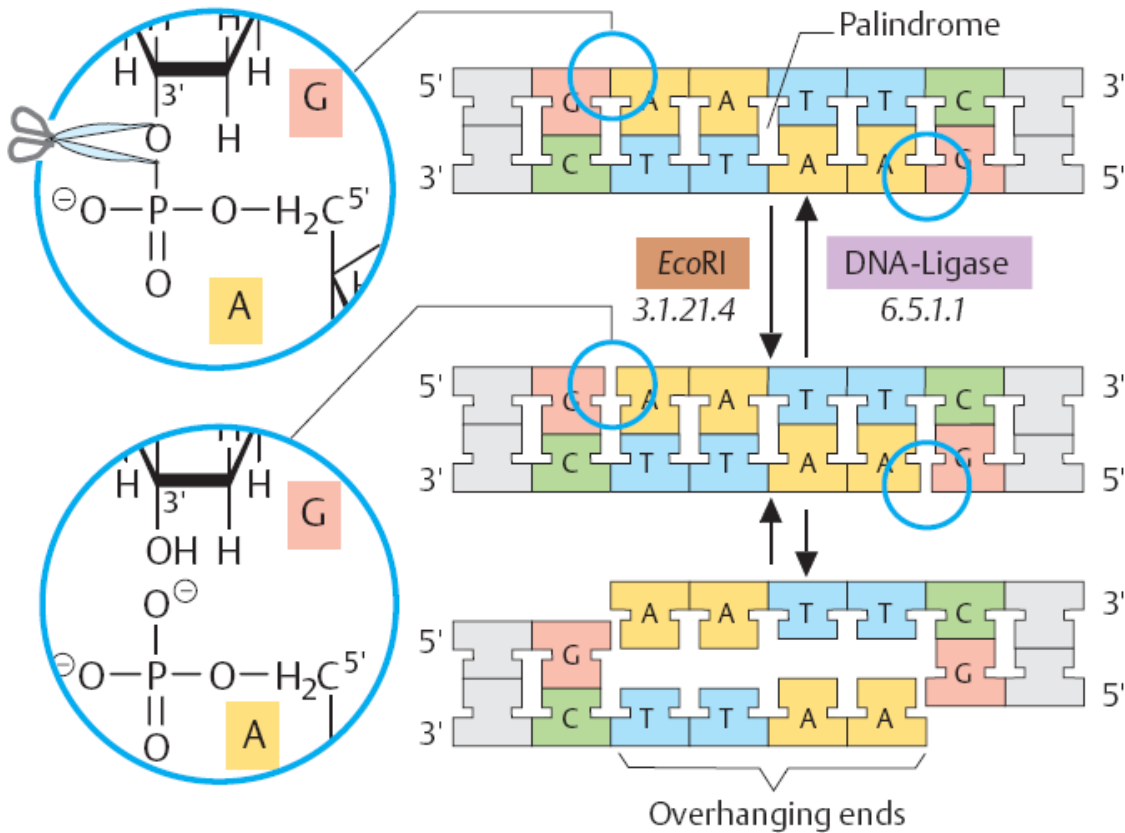
Or go directly to enzyme name or #:

Go Clear



Dr. Richard J. Roberts  
and Dana MacCallis

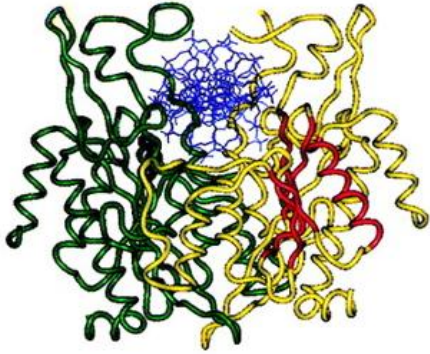
# Restriktionsenzym EcoRI



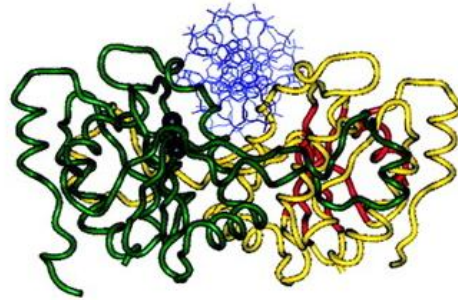
EcoRI + DNA

# Type II, EcoRI Familie

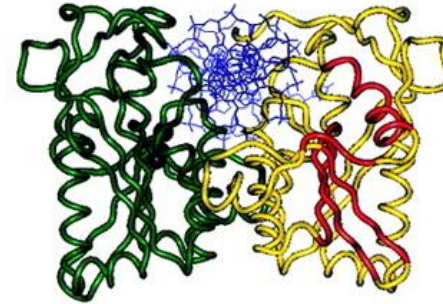
*EcoRI*



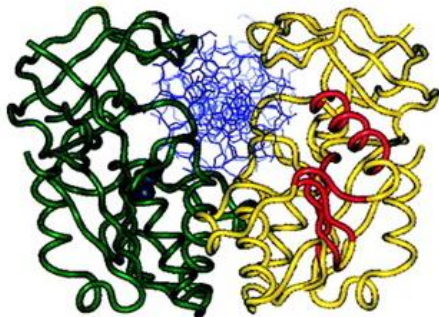
*MunI*



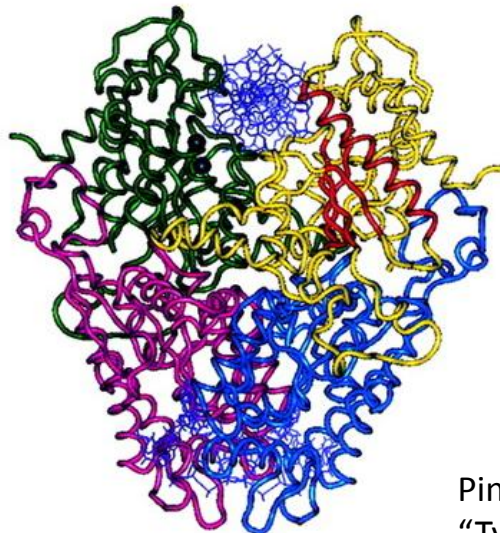
*BamHI*



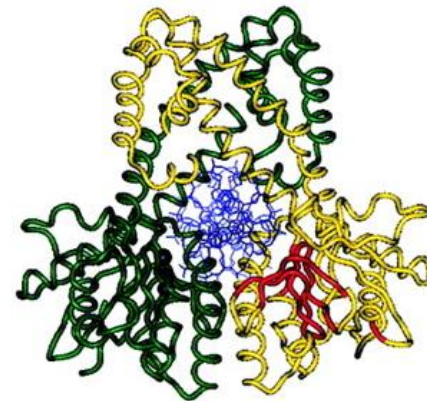
*BglII*



*NgoMIV*



*BsoBI*

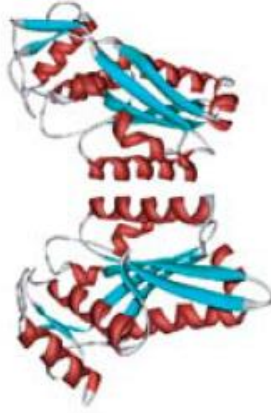


Pingoud A, Fuxreiter M, Pingoud V, Wende W.  
"Type II restriction endonucleases: structure and  
mechanism." Cell Mol Life Sci. 2005 Mar;62(6):685-707.

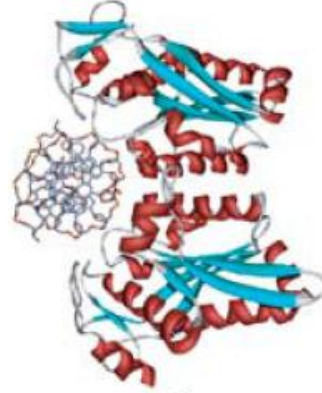


# Enzym-DNA Strukturen

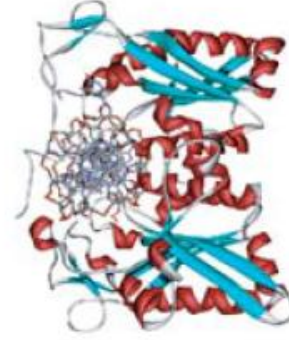
BamHI



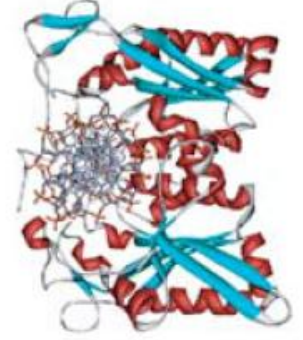
apo protein



complex with  
noncognate DNA

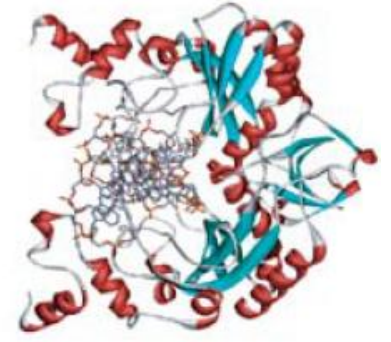
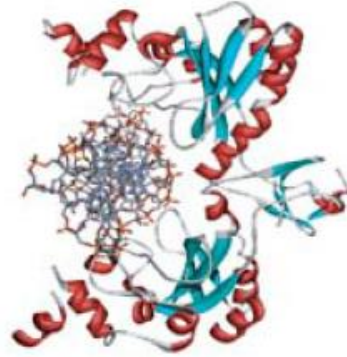
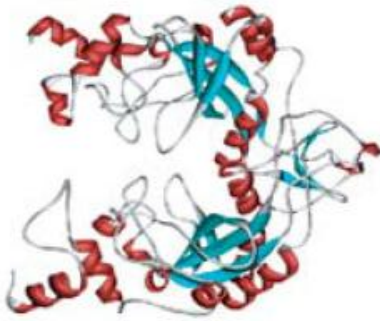


complex with  
cognate DNA



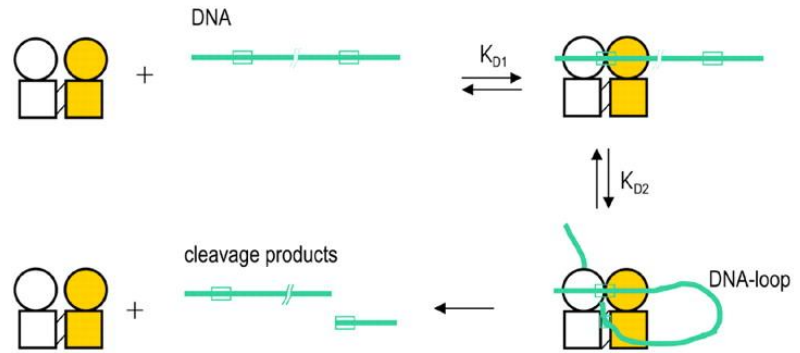
complex with  
product DNA

EcoRV

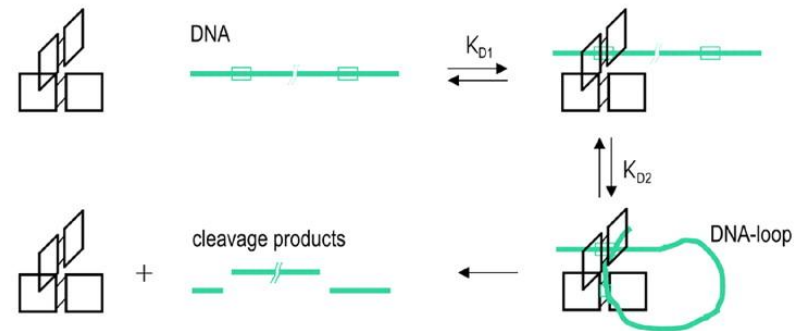


# Interaktion mit zwei Bindungsstellen

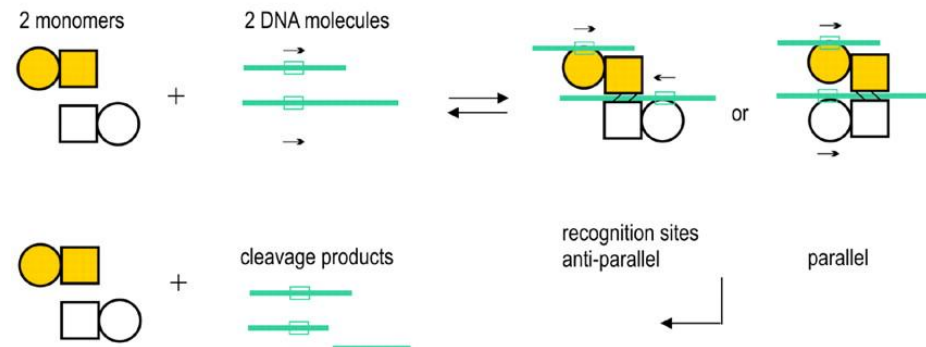
## A) Type IIE



## B) Type IIF

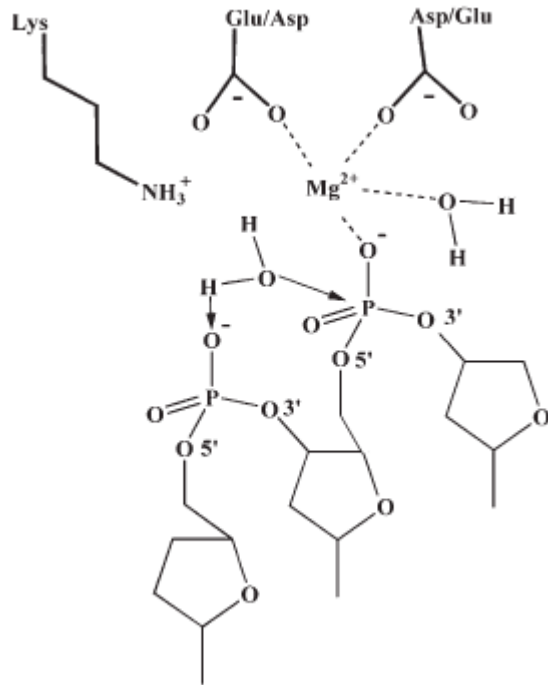


## C) Type IIS, Fok I



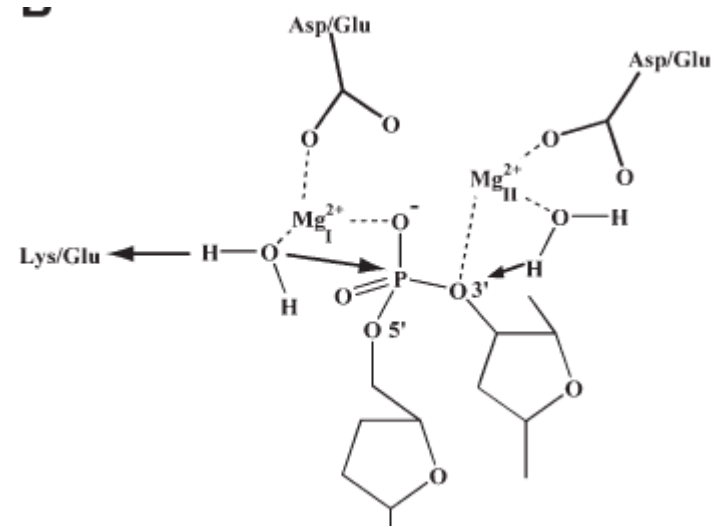
# Mechanismus der DNA Spaltung

Spaltung mit einem Metallion



Vermutlich bei EcoRI , BglIII

Spaltung mit zwei Metallionen



Vermutlich bei BamHI, BglI, NgoMIV and PvuII

# Literatur

- **Taschenatlas der Biochemie, Thieme (Color Atlas of Biochemistry, 2nd Ed., J. Koolman, K.H. Röhm)**
- **Taschenatlas der Genetik, Thieme (Color Atlas of Genetics)**
- **Genes, Lewin**
- **Principles of Biochemistry, Lehninger**
- **Molecular Cell Biology, Lodish et al.**
- **Molekulare Genetik, Knippers**