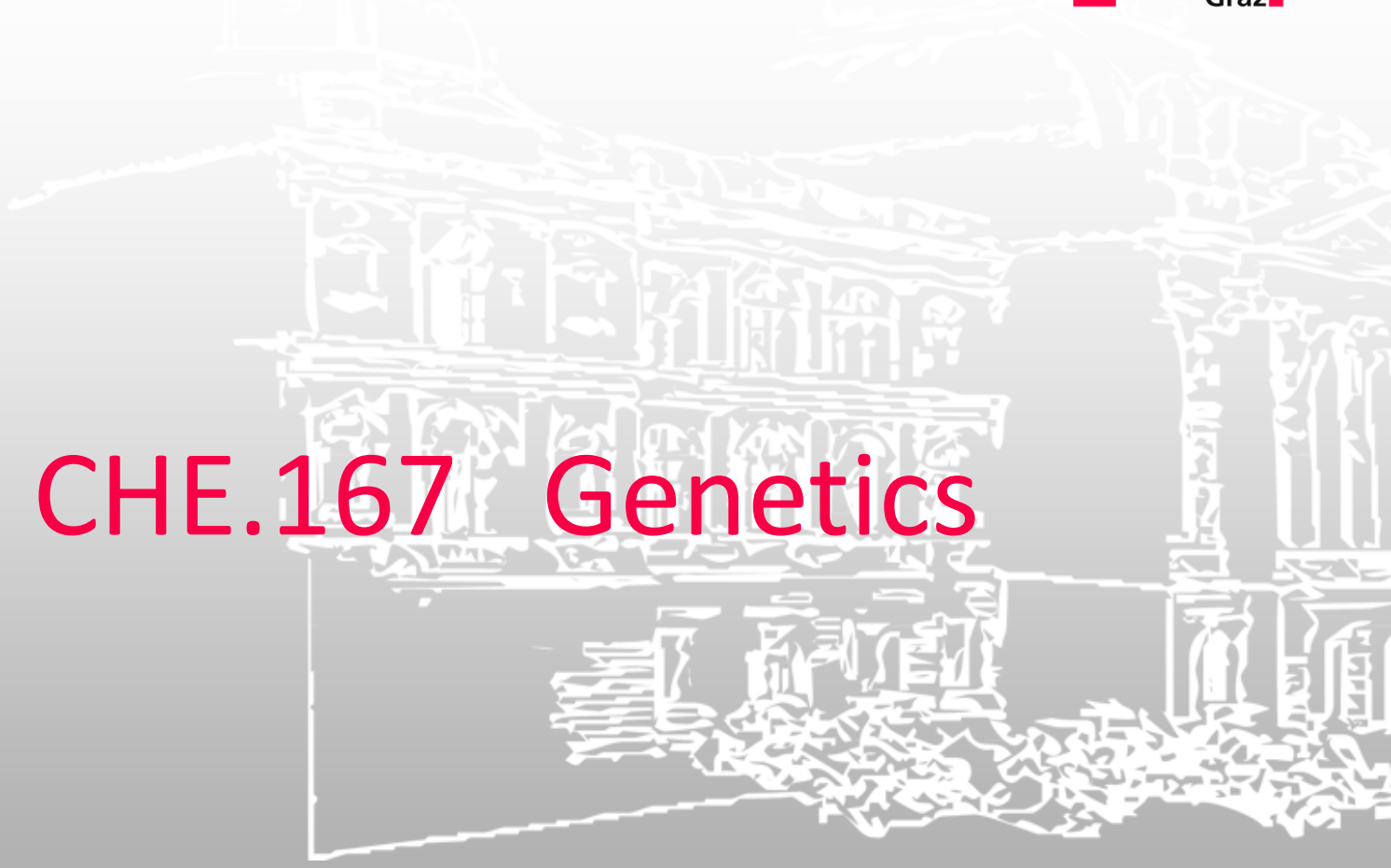


CHE.167 Genetics

OVERVIEW

Topics	Contents
Introduction	Historical facts
„Classical“ Genetics	Mendel
DNA	Composition, higher-level structure, configurations, cellular organisation, chromatin, chromosome structure, genome
Extrachromosomal elements, mobile DNA (Is, Tn), repetitive DNA	
Replication	Basic concept, uni-bi, rolling circle, telomeres
Segregation - Partitioning	
Cell cycle	Meiosis, Mitosis
Gene expression	Transcription: promoters, termination, mRNA processing, mRNA stability; translation initiation
Regulation of gene expression	Regulation of transcription in prokaryotes/eukaryotes, operons, regulatory proteins, regulation on translational level, regulation on DNA level
Changing genetic information	Mutation, recombination, genetic engineering, gene transfer (parasexual mechanisms)
Genetic analysis	Crossing analyses, molecular analyses

Presentations: in TUG online (link to FTP server)

Essential books:

Benjamin Lewin
Genes XI
Pearson Education Inc. 2008

Benjamin Lewin
Essential Genes
Intern. Edition
Pearson,2006

Klug, Cummings, Spencer, Palladino
Concepts of Genetics, 9th Edition
Pearson Int. Edition, 2009

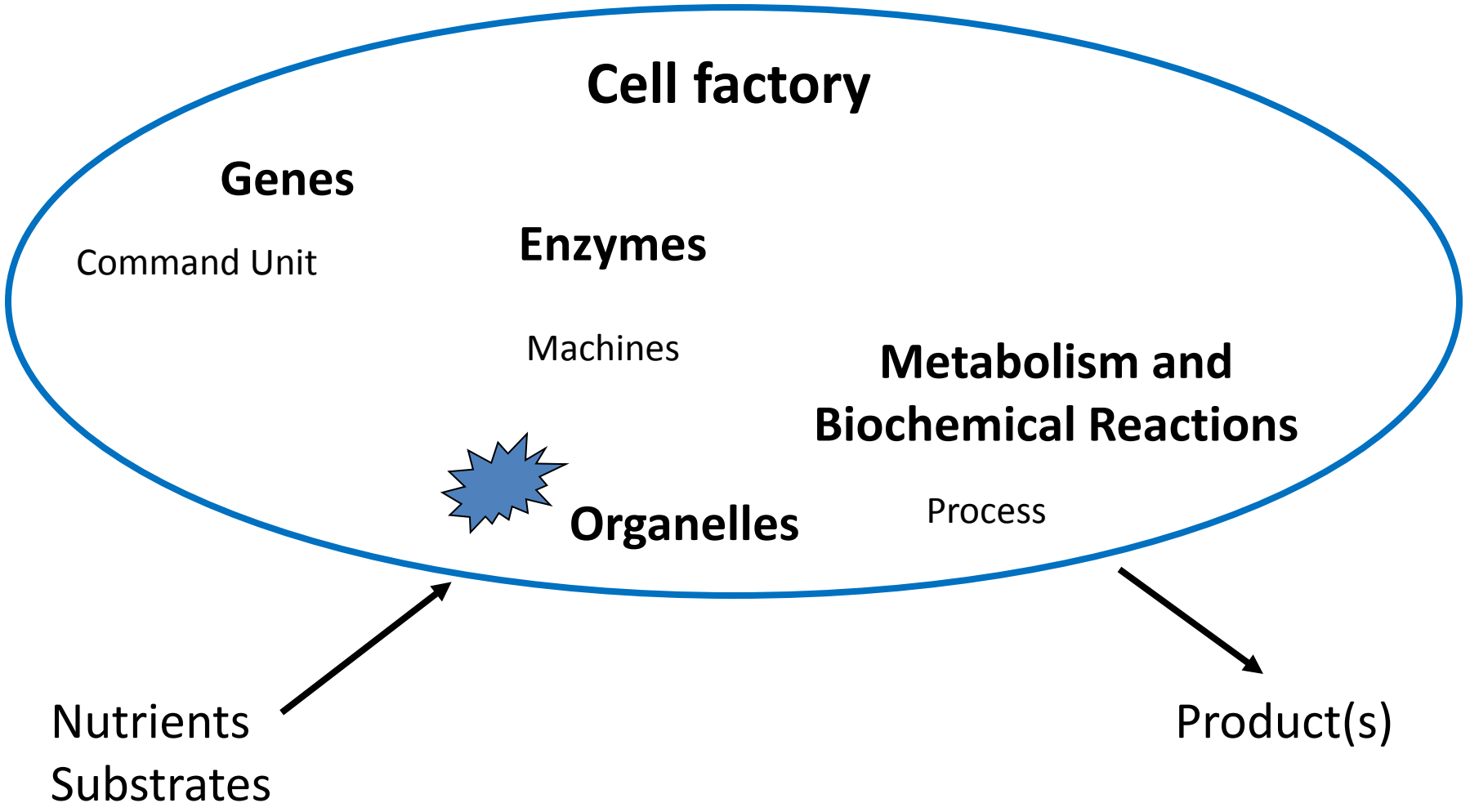
Additional literature:

Rolf Knippers
Molekulare Genetik, 9. Auflage
Thieme Verlag, 2006

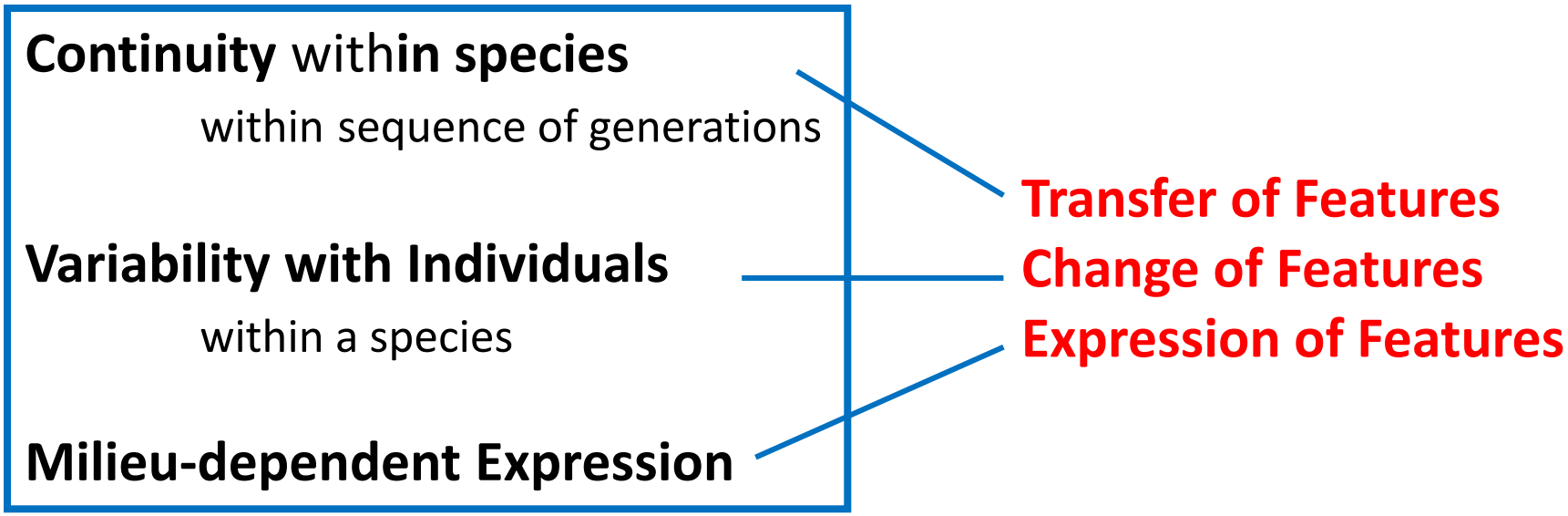
D.L. Hartl, E.W. Jones
Genetics: Analysis of Genes and Genomes. 6th Edition
Jones and Bartlett, 2005

Jochen Graw
Genetik, 4. Auflage
Springer 2006

T.A. Brown
Genomes 3, Garland Science (3rd Edition, 2006)


Cell factory
Genes
Command Unit
Enzymes
Machines
Metabolism and
Biochemical Reactions
Process
Organelles
Nutrients
Substrates
Product(s)

Phenotype of Organisms



Genetics:

Deals with Inherited Features

Includes Environment-determined Features

What is genetic information?
How can genetic information be maintained?
How is genetic information transferred to progeny?
How can genetic information be altered?
How is genetic information transmitted into features?

How can one manipulate organisms at the gene level?

Basic Science

Applied Research

Tools

Gregor Mendel
~ 1860

Genes determine features of living organisms

Taken from: A.J.F Griffiths, J.H. Miller, D.T. Suzuki, R.C. Lewontin, W.M. Gelbart; An Introduction to Genetic Analysis, 5th Edition; W.H. Freeman and Company, NY

Mendel´s seven traits:

Traits	Dominant allele	Recessive allele
Seed shape	round, roundish	wrinkled, angular
Endosperm colour	pale yellow, light yellow, orange	more or less intensively green
Seed coat colour	grey, greyish brown or leather brown with or without violet dotting; violet leaf banner, purple blossom leaves and reddish stems at the leaf axes	white with white blossoms
Pod shape	arched , inflated	Constricted and more or less wrinkled
Pod colour	light to dark green	vibrant yellow
Flower and pod position	axial	terminal
Stem length	long	short

→ Clearly defined traits that behave equally stable over generations
→ Traits are independent from environmental factors

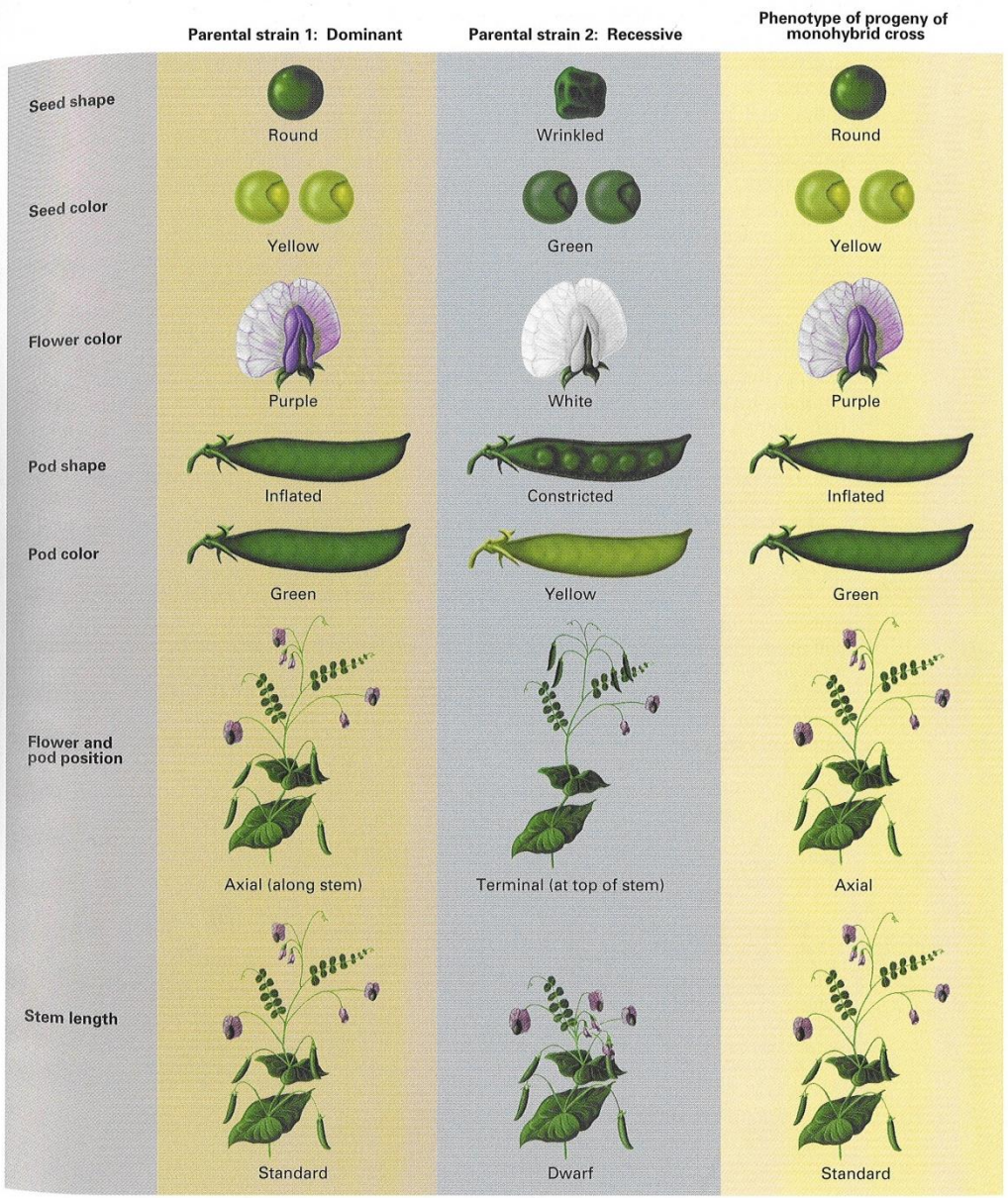
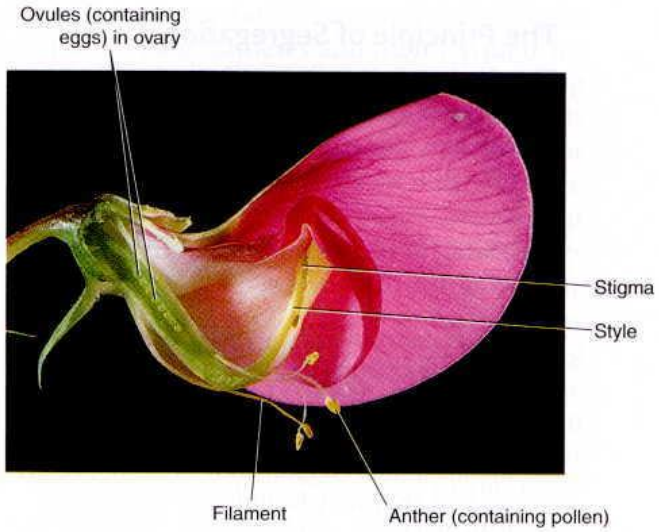


Figure 3.1 The seven different traits in peas studied by Mendel. The phenotype shown at the far right is the dominant trait, which appears in the hybrid produced by crossing.



The anatomy of a pea plant makes it easy to work with. Mendal chose the pea plant because it is small, easy to grow, and has a short generation time. [Jean-Michel Labat/Ardea.]

Taken from: Daniel L. Hartl & Elizabeth W. Jones, Genetics: Analysis of Genes and Genomes, 6th Edition, Jones and Bartlett Publishers

Targeted fertilizations

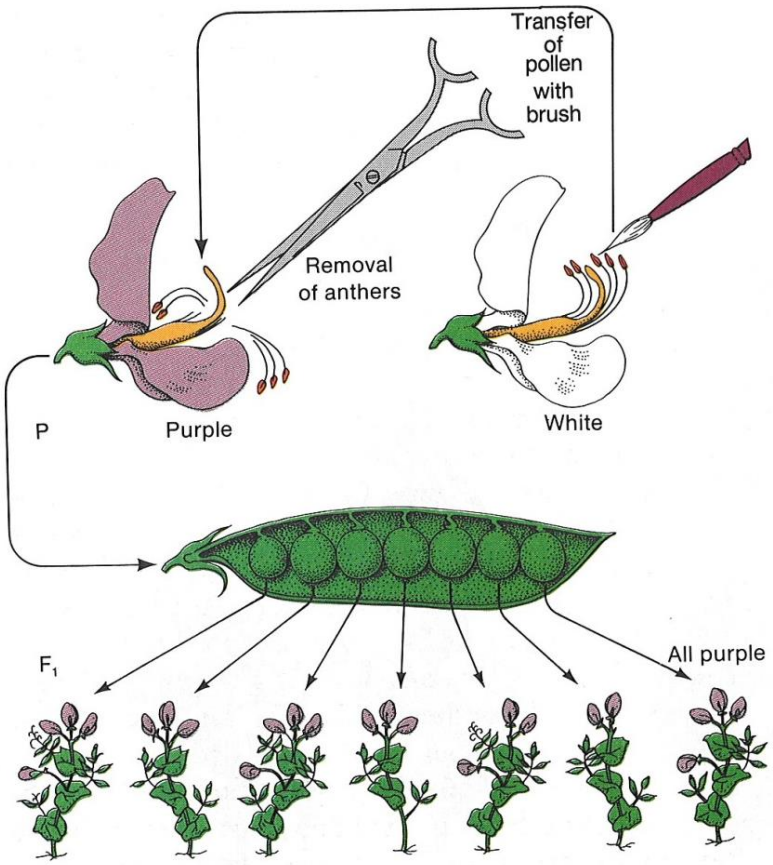


Figure 2-4 Mendel's cross of purple-flowered ♀ × white-flowered ♂.

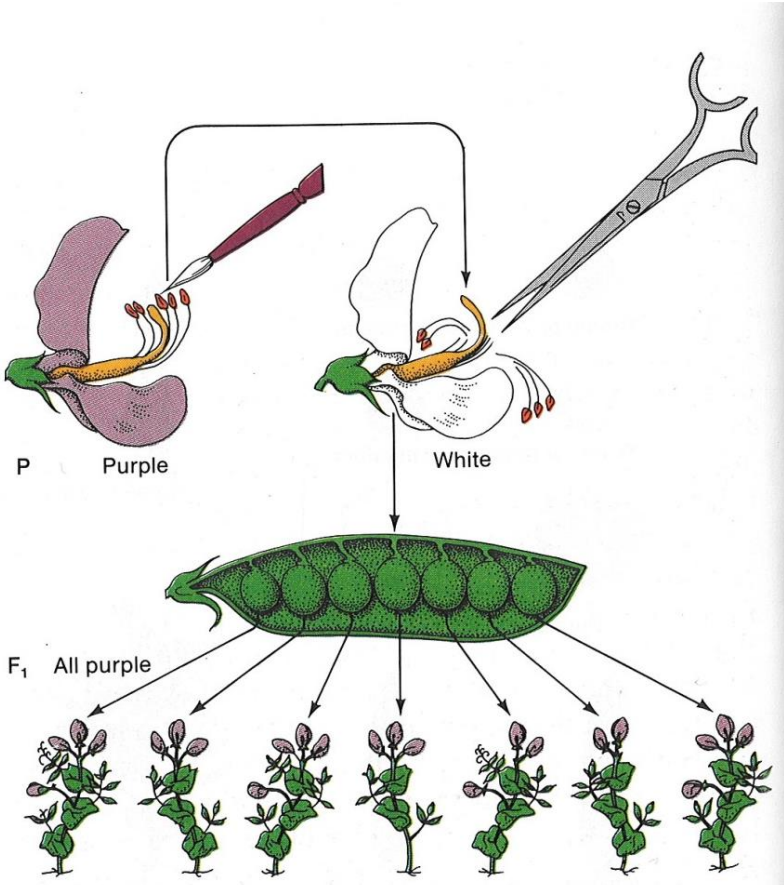


Figure 2-5 Mendel's cross of white-flowered ♀ × purple-flowered ♂.

Trait is independent of the sexual origin.

Taken from: A.J.F Griffiths, J.H. Miller, D.T. Suzuki, R.C. Lewontin, W.M. Gelbart; An Introduction to Genetic Analysis, 5th Edition; W.H. Freeman and Company, NY

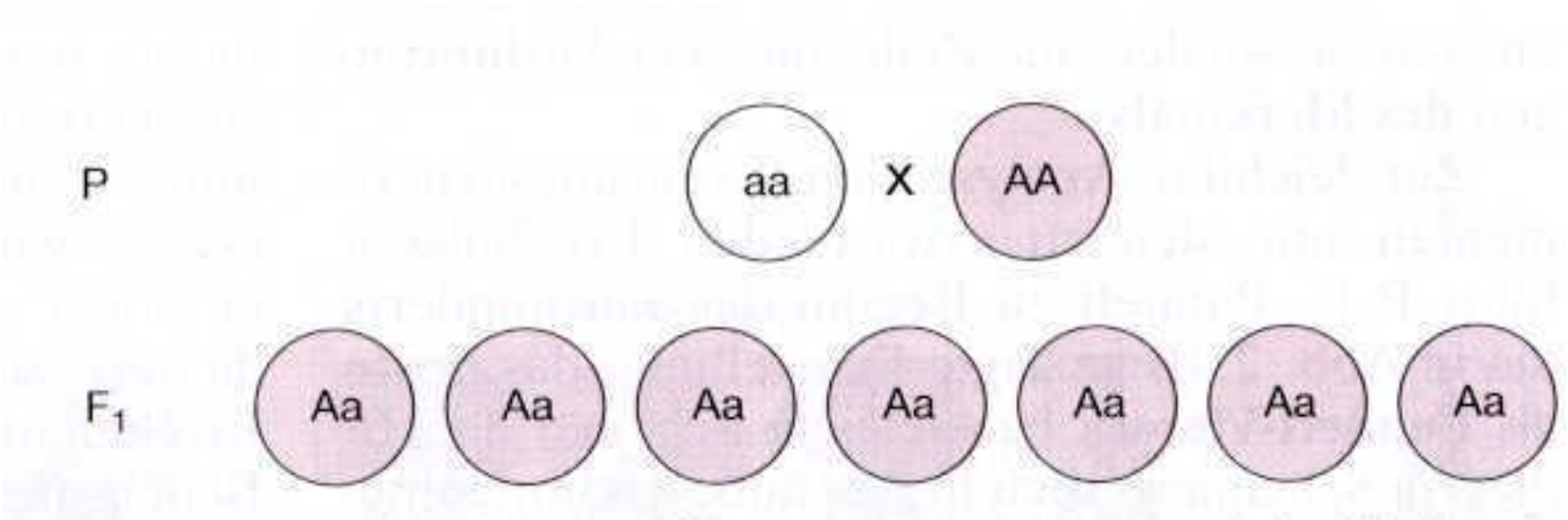
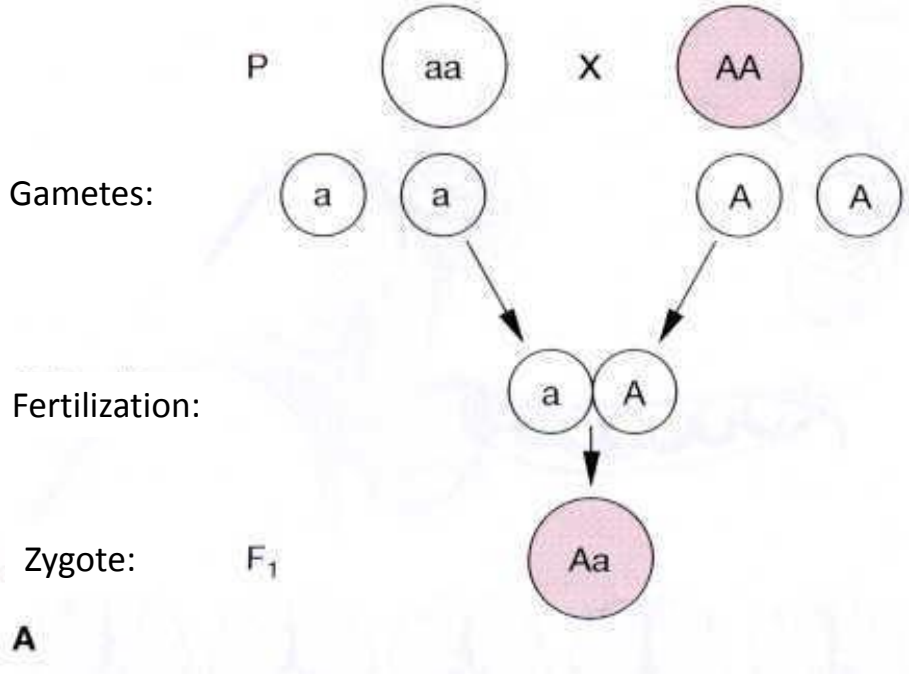


Fig. 2.3. Mendel's interpretation of the results of the monohybrid cross: schematic depiction of the distribution of characteristics on cellular level. The dominant traits (flower colour purple) are characterized with capital letters, recessive traits (flower colour white) with small letters. Mendel assumed, that each ordinary plant cell contains two variants of each trait which are separated during germ cell development and distributed to single gametes (haploidy). The status of two traits (diploidy) is reconstituted during fertilization.

Taken from: Wolfgang Hennig; Genetik, 3rd Edition; Springer



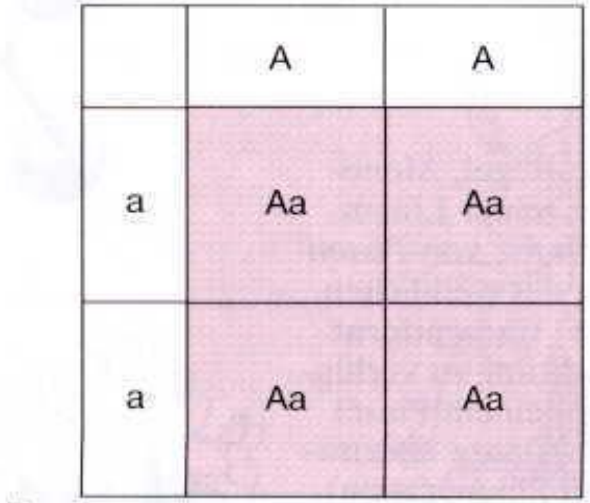
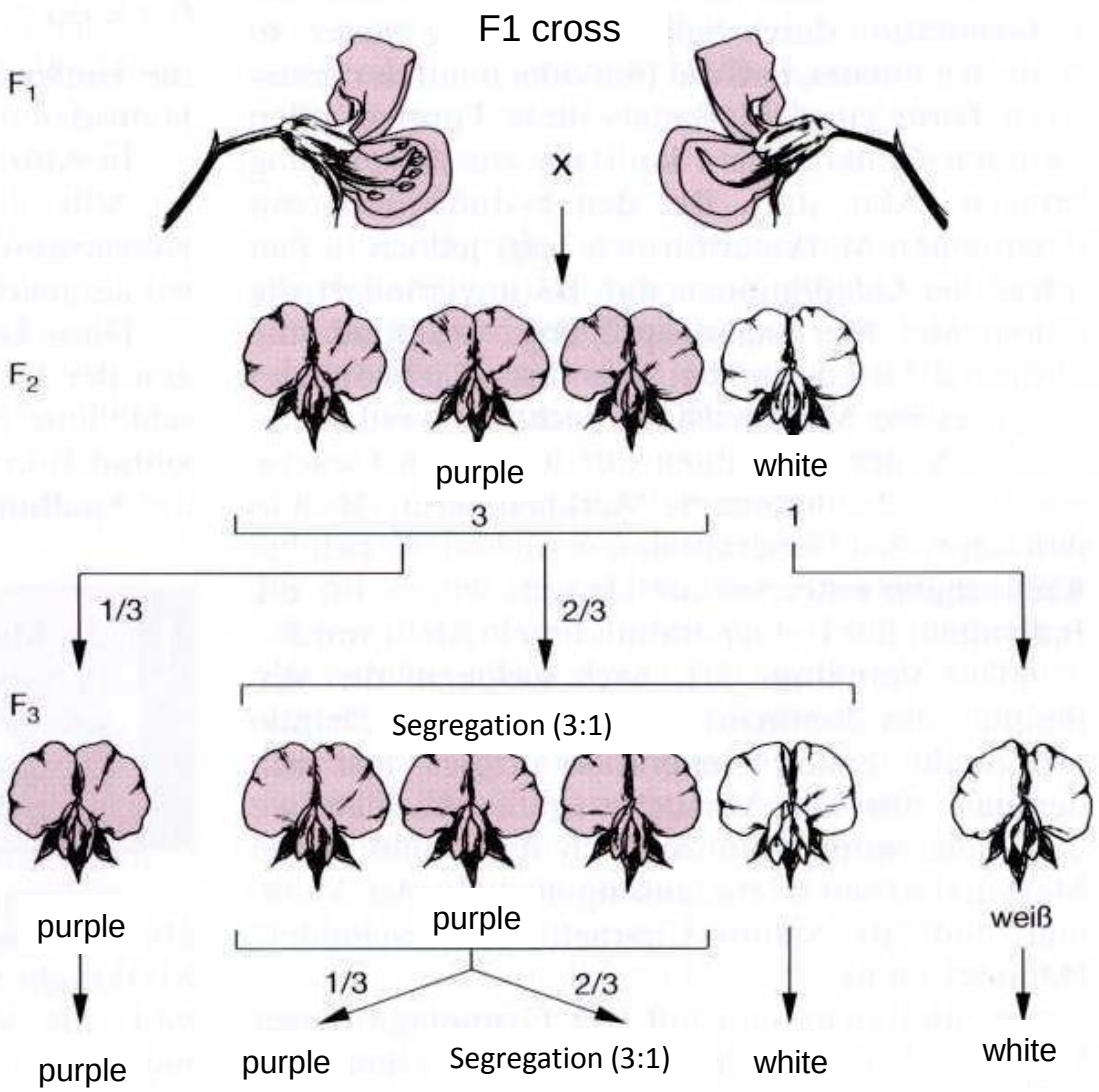


Fig. 2.4. **A** The clear lineages of the parental generation (P) carry each homozygously either the dominant (AA) or the recessive trait (aa). The filial generation (F1) has a heterozygous constitution based on the segregation of the gametes. Only the dominant allele A characterizes the phenotype. **B** The Punnett square of the cross and its results. The gamete constitution of the parents is depicted in the horizontal and vertical outer lines. The genetic constitution of the progeny and its frequencies can be deduced from the inside of the square.

Taken from: Wolfgang Hennig; Genetik, 3rd Edition; Springer

Fig. 2.5 2nd Mendelian Law. Cross of the F1 individuals resulting from the former cross by self-fertilization. The progeny (F2) segregate in a 3:1 ratio and 25% of the individuals show the recessive trait of the parental generation (white flowers). Those individuals keep their recessive phenotype when crossed with other individuals of the recessive phenotype. Thus, they are homozygous for the recessive trait. Whereas, in case they are further crossed with a dominant phenotype (purple flowers) by self-fertilization, 2/3 of the following F3 progeny is segregated into the recessive/dominant phenotype in a 1:3 ratio. The remaining 1/3 of the individuals with a dominant phenotype keep their phenotype unaltered even in the following generations. The genetic constitution of the F2 individuals is thus 25% homozygous for the recessive trait (white:aa), 25% homozygous for the dominant trait (purple:AA) and 50% heterozygous (Aa) (see Fig. 2.6).



Segregation of heterozygous traits

Taken from: Wolfgang Hennig; Genetik, 3rd Edition; Springer

F2 generation of a monohybrid cross

TABLE 3.1 **Results of Mendel's monohybrid experiments**

Parental traits	F_1 trait	Number of F_2 progeny	F_2 ratio
Round × wrinkled (seeds)	Round	5474 round, 1850 wrinkled	2.96 : 1
Yellow × green (seeds)	Yellow	6022 yellow, 2001 green	3.01 : 1
Purple × white (flowers)	Purple	705 purple, 224 white	3.15 : 1
Inflated × constricted (pods)	Inflated	882 inflated, 299 constricted	2.95 : 1
Green × yellow (unripe pods)	Green	428 green, 152 yellow	2.82 : 1
Axial × terminal (flower position)	Axial	651 axial, 207 terminal	3.14 : 1
Long × short (stems)	Long	787 long, 277 short	2.84 : 1

Important experimental basis: statistical treatment of data

Taken from: Daniel L. Hartl & Elizabeth W. Jones, Genetics: Analysis of Genes and Genomes, 6th Edition, Jones and Bartlett Publishers

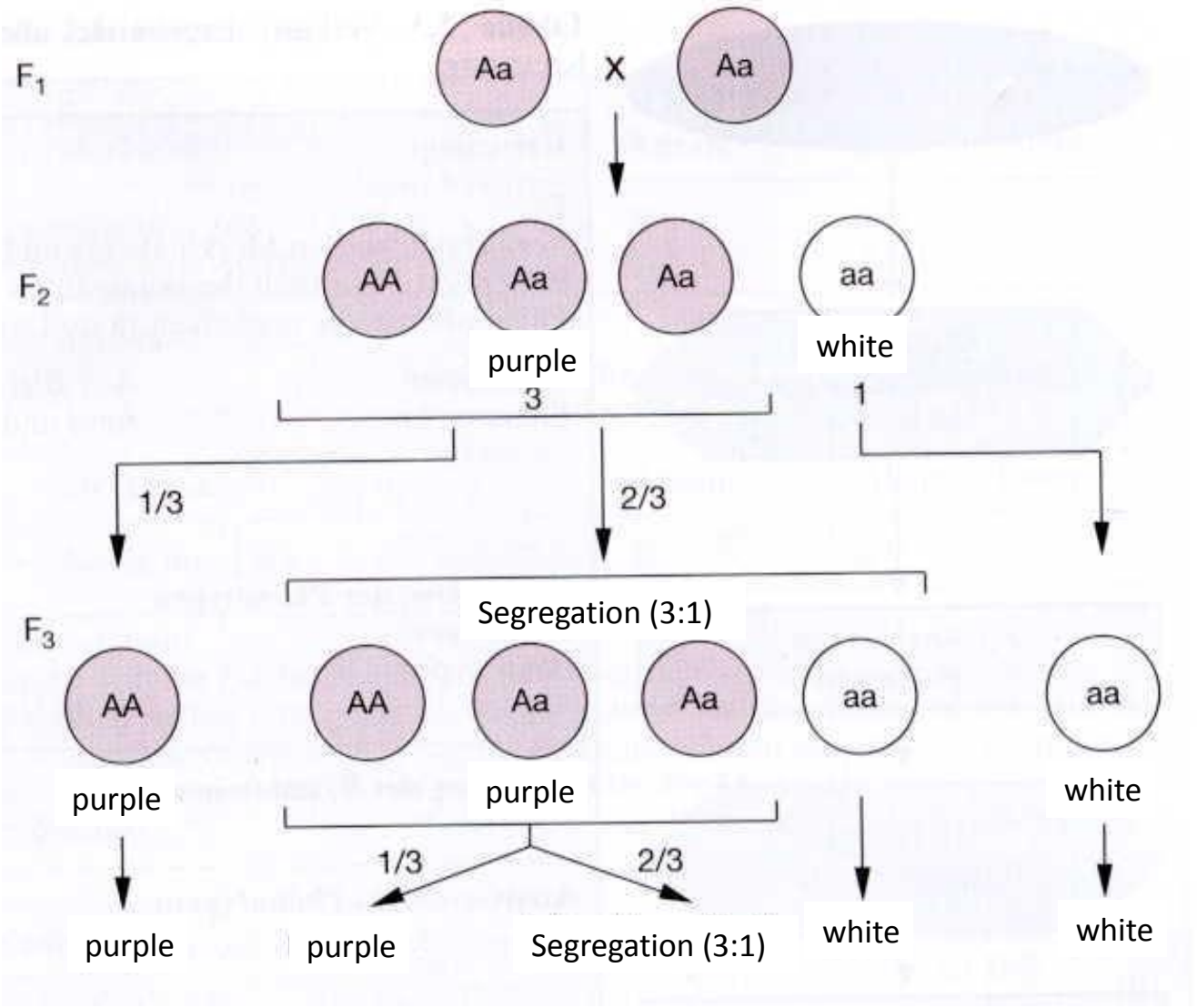
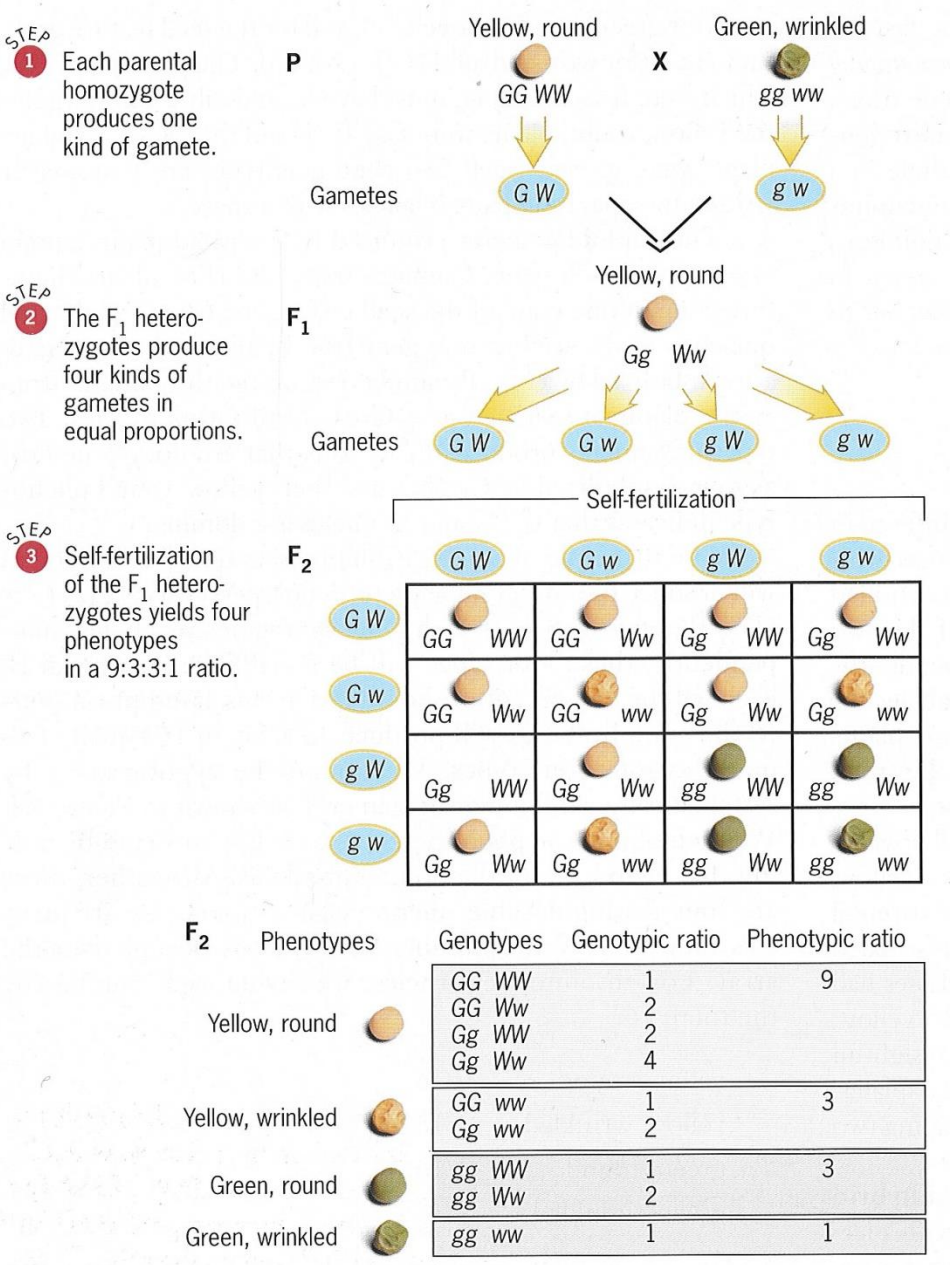


Fig. 2.6. Mendel´s interpretation of the monohybrid cross results: Scheme of the distribution of the cross traits shown in Fig. 2.5 on a cellular level.

Taken from: Wolfgang Hennig; Genetik, 3rd Edition; Springer

Symbolic representation of Mendel´s dihybrid cross

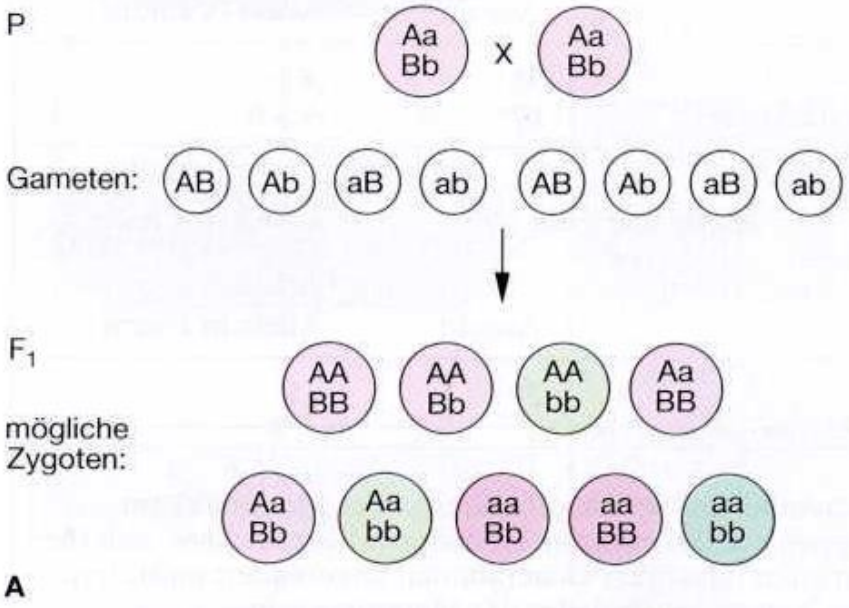


F_2	Phenotypes	Genotypes	Genotypic ratio	Phenotypic ratio
	Yellow, round	GG WW	1	9
		GG Ww	2	
		Gg WW	2	
		Gg Ww	4	
	Yellow, wrinkled	GG ww	1	3
		Gg ww	2	
	Green, round	gg WW	1	3
		gg Ww	2	
	Green, wrinkled	gg ww	1	1

Taken from: D. P. Snustad, M.J. Simmons; Principles of Genetics, 5th Edition; John Wiley & Sons, Inc.

Combination independent of original constellation

Two Markers (=Genes)



	AB	Ab	ab	aB
AB	AABB	AABb	AaBb	AaBb
Ab	AABb	AAbb	Aabb	AaBb
ab	AaBb	Aabb	aabb	aabB
aB	AaBB	AaBb	aaBb	aaBB

B

Fig. 2.7A, B: **3rd Mendelian Law**. Dihybrid cross. Parents are heterozygous for 2 different traits (*A* and *B*). **A** The figure shows the inheritance on cellular level, according to Fig. 2.3, 2,4 and 2.6. The gamete´s constitution of the P generation represents all possible combinations of all existing alleles in the diploid cells. By an accidental combination of gametes in the zygote, nine different genotypes can be generated. **B** Depiction of the cross in a Punnett square. Out of this, the characteristic phenotype ratio for the dihybrid cross of two heterozygous parents – 9:3:3:1 – can be easily deduced.

Taken from: Wolfgang Hennig; Genetik, 3rd Edition; Springer




F_2 phenotypes	Observed Number	Observed Proportion	Expected Number	Expected Proportion
Yellow, round	315	0.567	313	0.563
Green, round	108	0.194	104	0.187
Yellow, wrinkled	101	0.182	104	0.187
Green, wrinkled	32	0.057	35	0.063
Total	**556**	**1.000**	**556**	**1.000**

Figure 3.5 ▶ Comparing the observed and expected results of Mendel's dihybrid cross.

Taken from: D. P. Snustad, M.J. Simmons; Principles of Genetics, 5th Edition; John Wiley & Sons, Inc.

yellow, round	315	9
yellow, wrinkled	101	3
green, round	108	3
green, wrinkled	32	1

round	315 + 108	423	3
wrinkled	101 + 32	133	1

yellow	315 + 101	416	3
green	108 + 32	140	1

Question:
Is the genetic information Nucleic Acid or protein??

1928: Griffith – Experiments with *Diplococcus pneumoniae*

S-form: lethal
R-form: no effect

Extract of S-form + viable R-Form: lethal
viable S-form present

1944: Avery, MacLeod, McCartney: Nucleic acid of desoxyribose type is responsible for transformation

New Systems in genetics

Microorganisms

Fungi

Bacteria (E.coli)

Phages

Labeling techniques

radioactivity

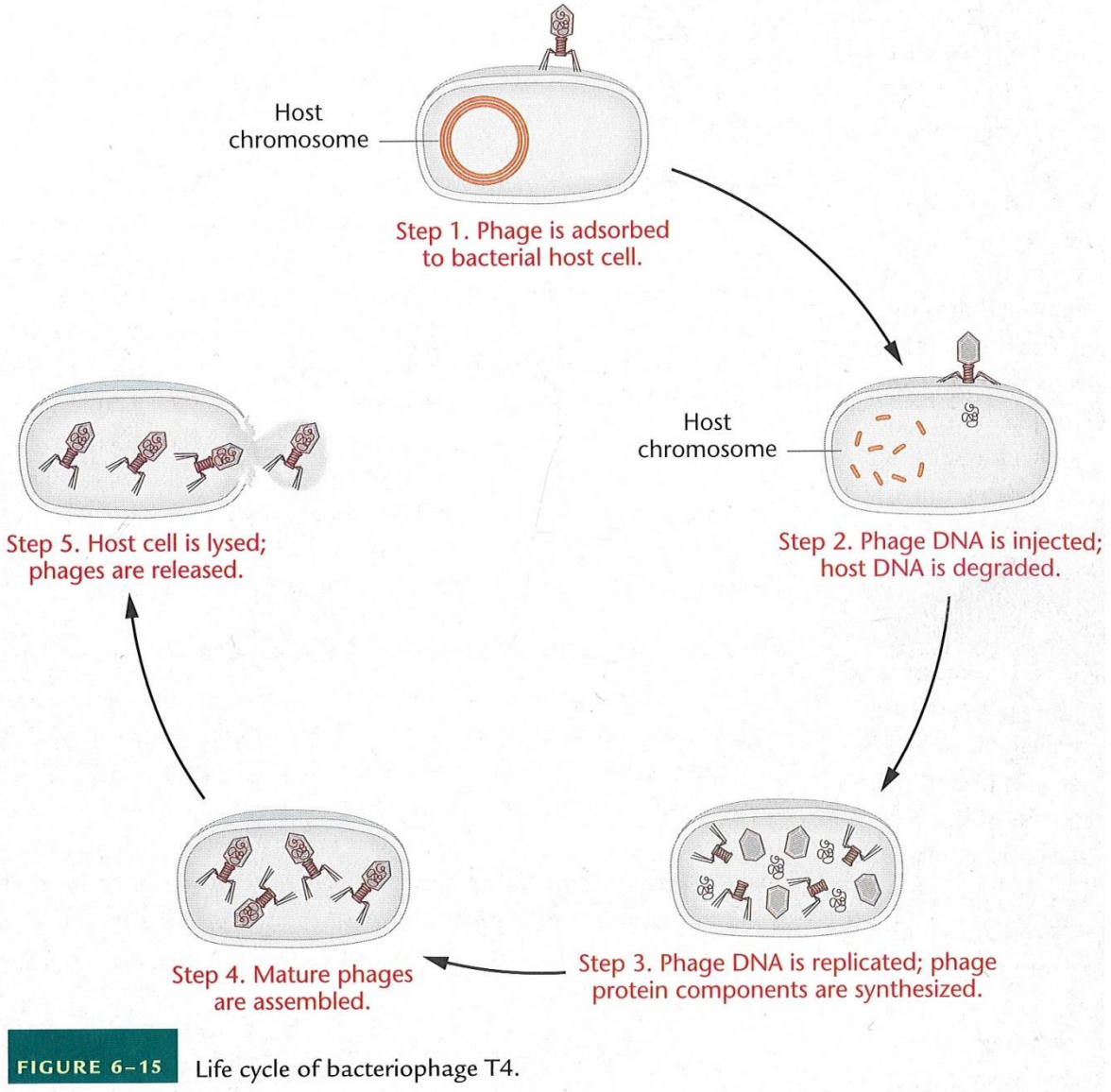


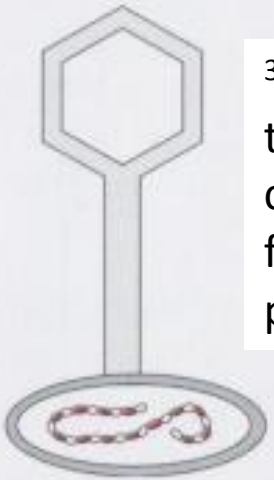
FIGURE 6–15 Life cycle of bacteriophage T4.

Taken from: W.S. Klug, M. R. Cummings, C.A. Spencer, M.A. Palladino; Concepts of Genetics, 9th Edition; Pearson Benjamin Cummings

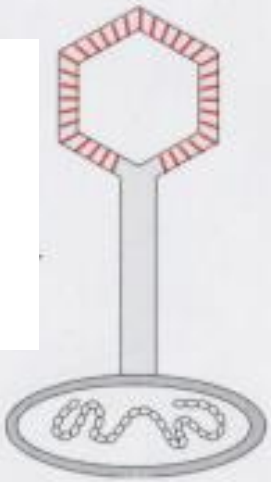
Hershey – Chase („blender“) Experiment (1952)

T4 phage with ^{32}P labeled DNA

T4 phage with ^{35}S labeled protein



^{32}P-DNA enters the host cell and causes the formation of phage progeny

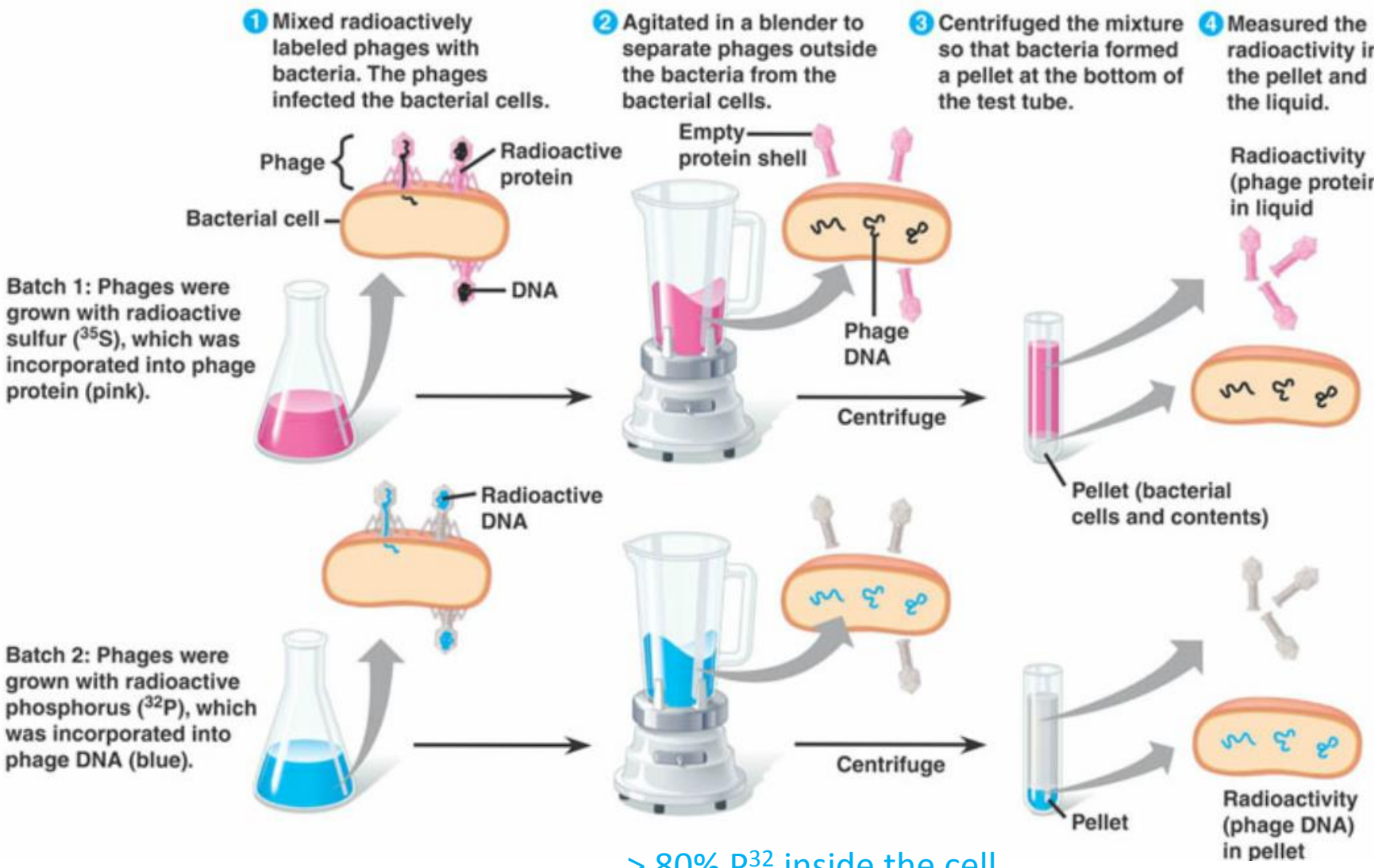


^{35}S-protein sticks to the surface of the host cells and can be removed by shearing in a blender. The infection process takes place normally.

> 80% P^{32} inside the cell
> 80% S^{35} outside the cell

Quelle???

Hershey – Chase („blender“) Experiment (1952)



> 80% P^{32} inside the cell

> 80% S^{35} outside the cell

https://prezi.com/cws9dhcj34m-/griffith-hershey-and-chase/

1950: Chargaff – nucleic acids are long molecules with 4 nucleotides in random order
- A:T and C:G = 1

1953: James Watson and Francis Crick - Double Helix Model of DNA

1956: A. Kornberg – DNA Synthesis in vitro

1958: Meselson, Stahl – DNA replication

1961: Brenner, Jacob, Meselson – m-RNA as template for protein synthesis

1961: Jacob, Monod – Operon model, regulation of gene expression

1961-1966 Nirenberg, Matthaei, Khorana, Crick – Genetic Code

1965: Spiegelman – in vitro synthesis of RNA genome , Phage $Q_{ß}$ biologically active RNA

1969: Beckwith, Shapiro – Isolation of a gene

1970: Khorana: Gene synthesis by reverse transcription

1973: Cohen, Boyer, Berg – DNA Cloning

1973 → now: enormous development of molecular techniques

6.10.15

DNA is the molecule for storage of genetic information

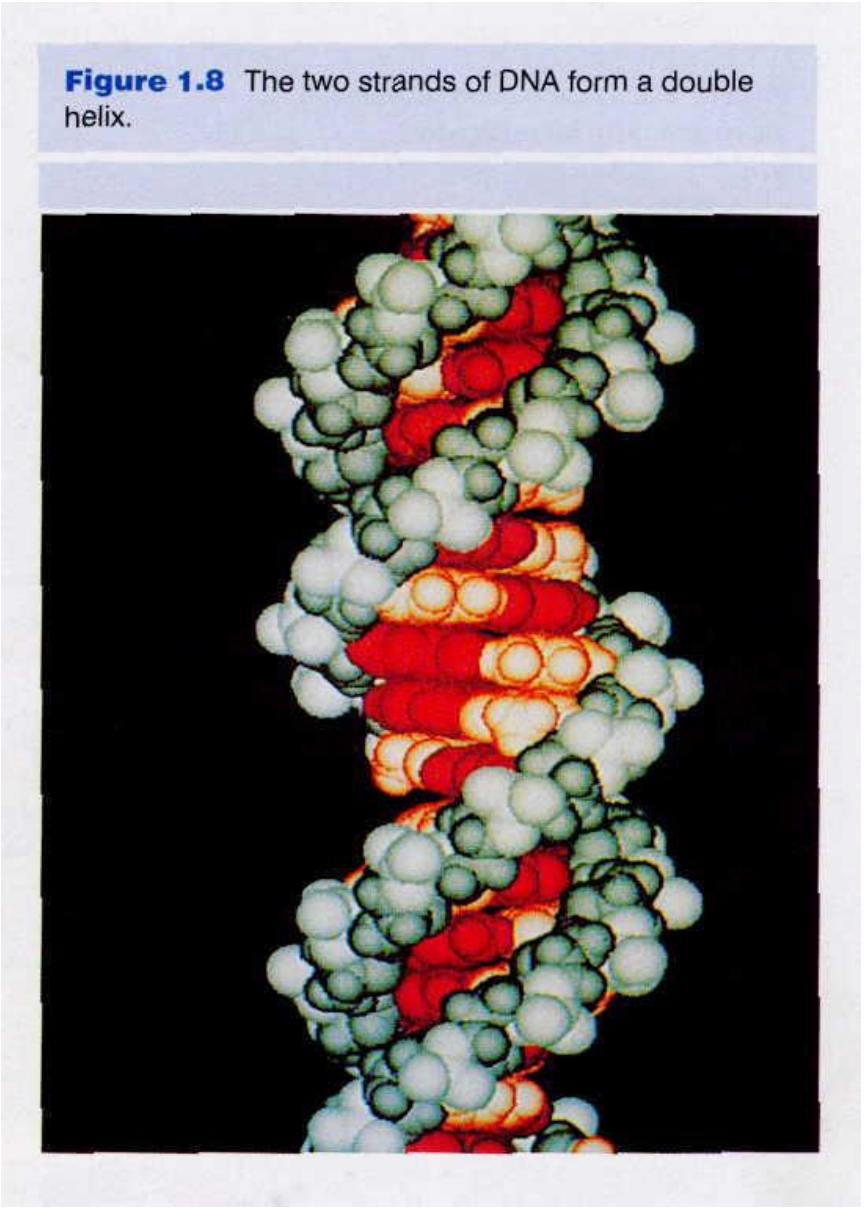
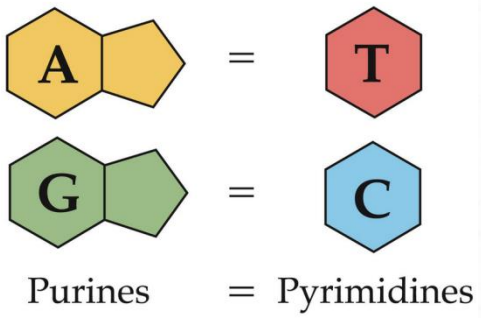


Figure 1.8 The two strands of DNA form a double helix.

Quelle???



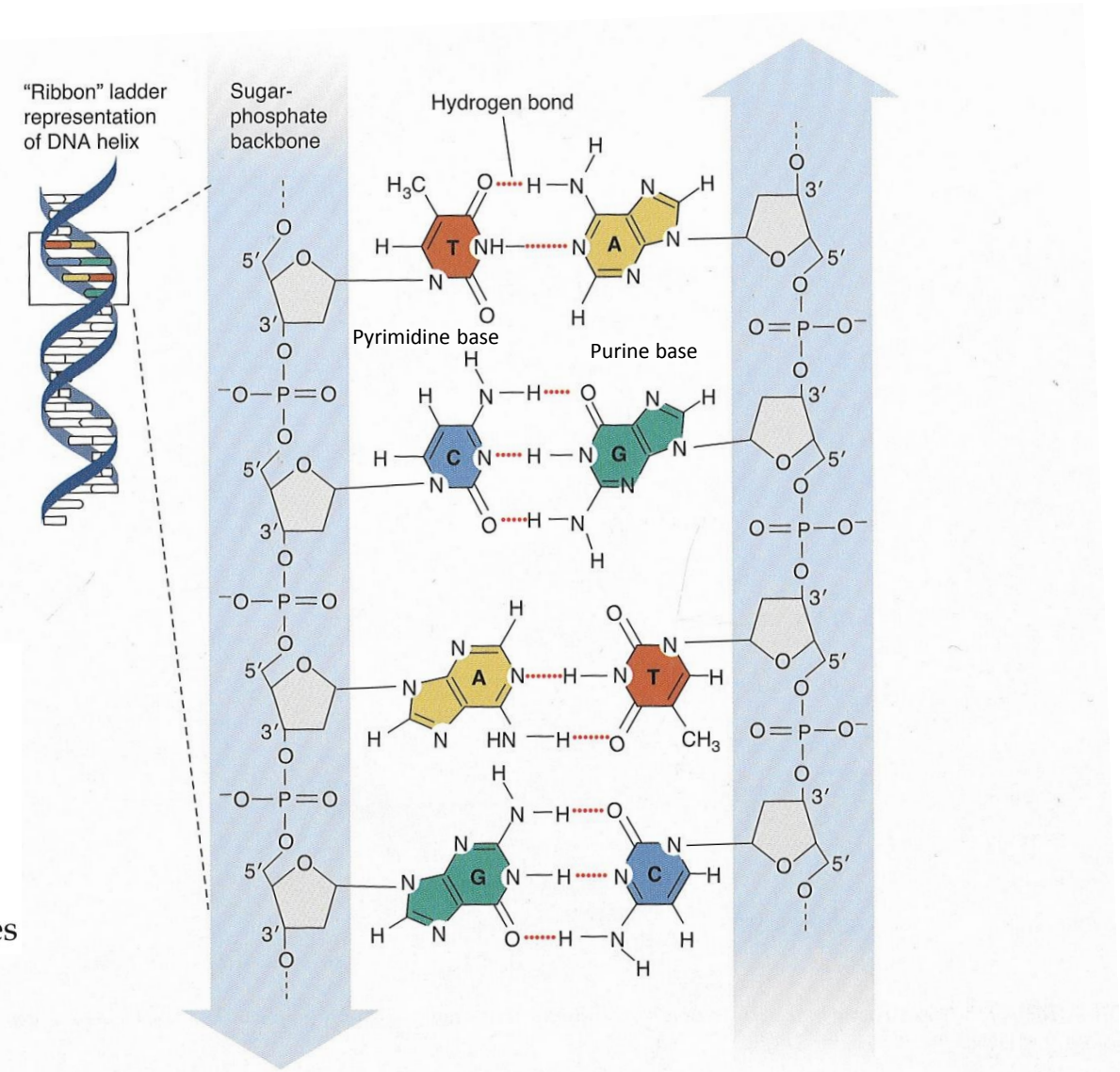
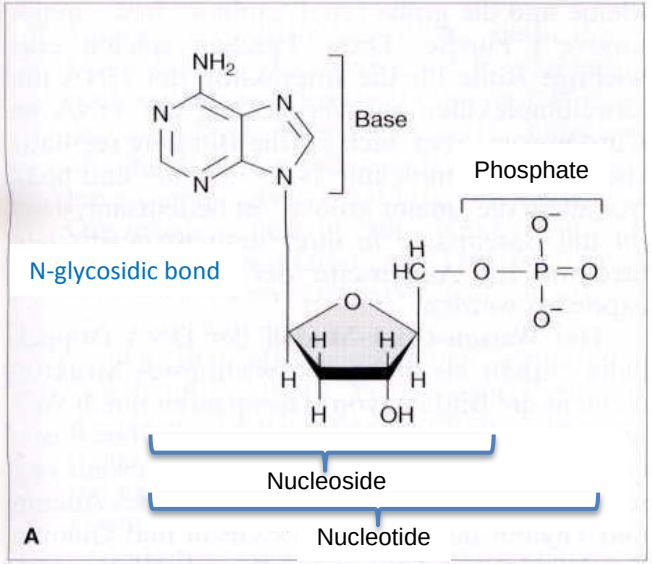


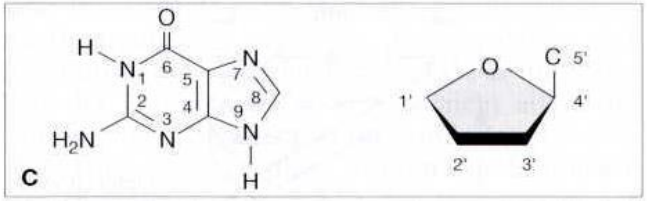
FIGURE A1.5 A view of unwound DNA exhibits the sugar-phosphate backbones and rungs containing nitrogenous base pairs connected via hydrogen bonds.

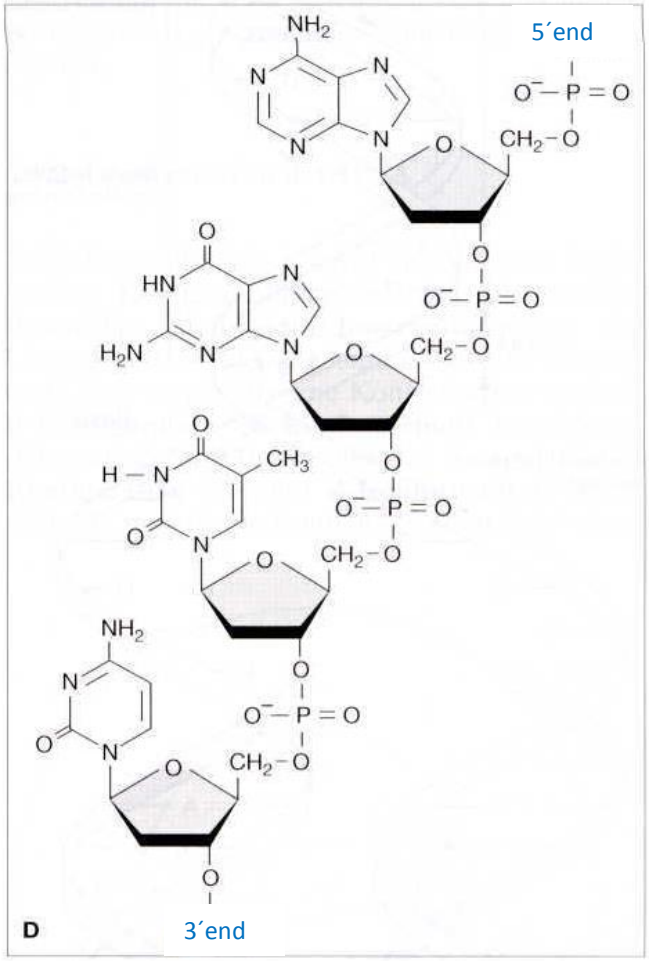
Taken from: C.A. Dehlinger, Molecular Biotechnology, Jones & Bartlett Learning

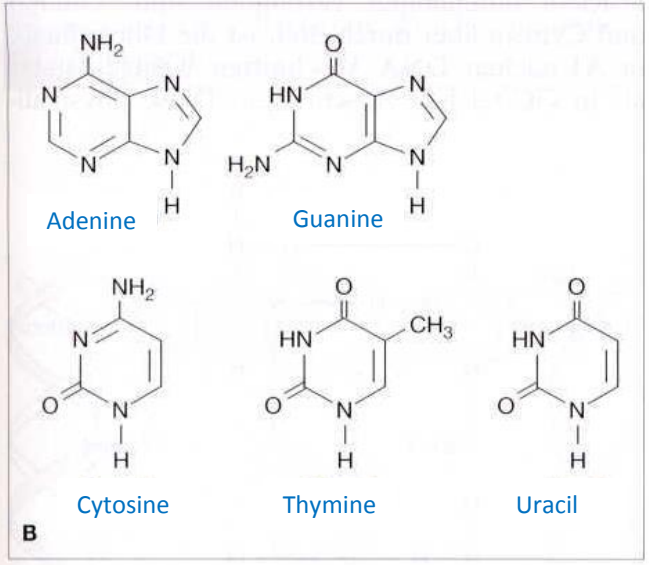
DNA and RNA components:

A The **Nucleotide** is the basic building block, consisting of a deoxyribose molecule (or ribose molecule for RNA), a heterocyclic organic base, which is connected by a N-glycosidic bond to the C^1 atom of the (deoxy)ribose and phosphate group linked to the C^5 atom of the (deoxy)ribose. If the phosphate group is missing, the molecule is called **Nucleoside**. **B** The organic bases are either the purines adenine (A) or guanine (G) or the pyrimidines cytosine (C), thymine (T) or in case of RNA uracil (U) instead of thymine. **C** Numbering of the bases and the ribose atoms. **D** Nucleotides linked via 3´-5´-phosphate-diesterbonds between the sugar units build the macromolecules of the nucleic acids. They can be distinguished chemically only by the sequence of the organic bases.

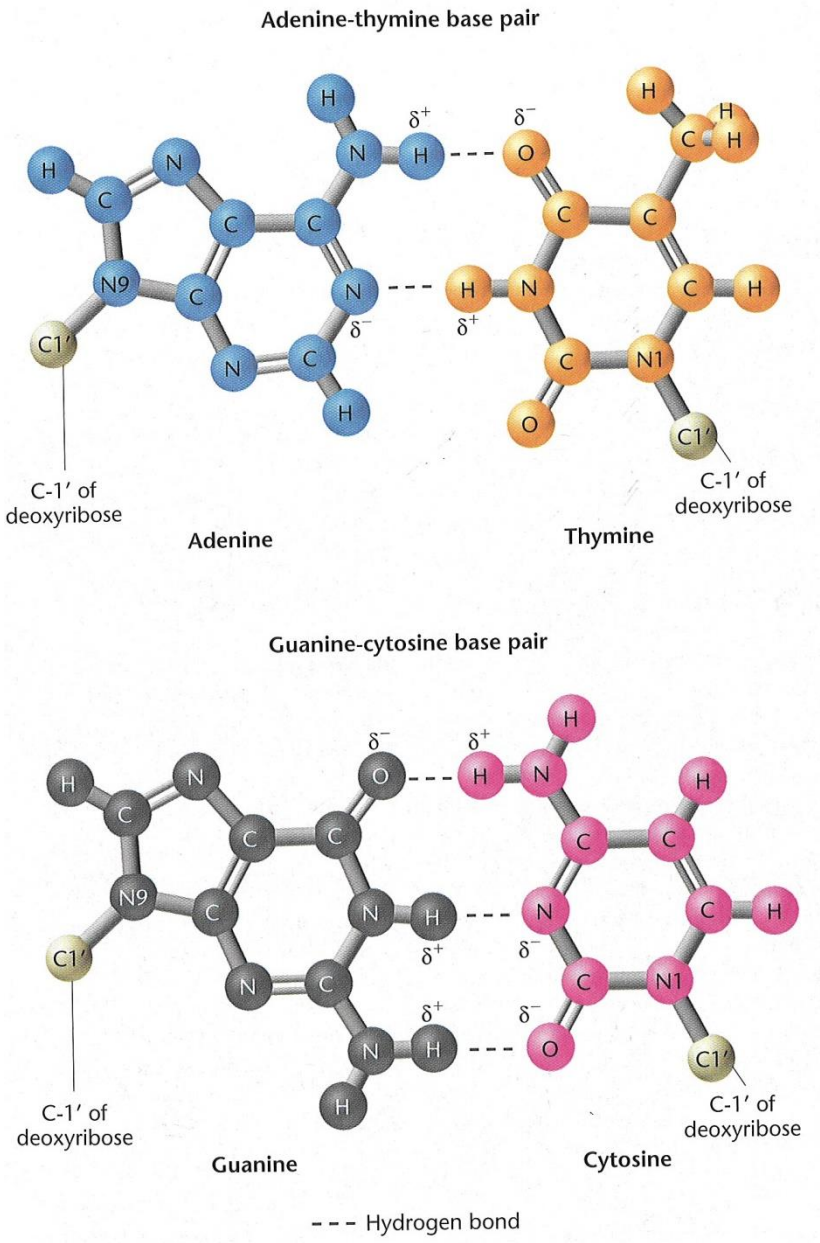








Watson Crick base pairing



Taken from: W.S. Klug, M. R. Cummings, C.A. Spencer, M.A. Palladino; Concepts of Genetics, 9th Edition; Pearson Benjamin Cummings

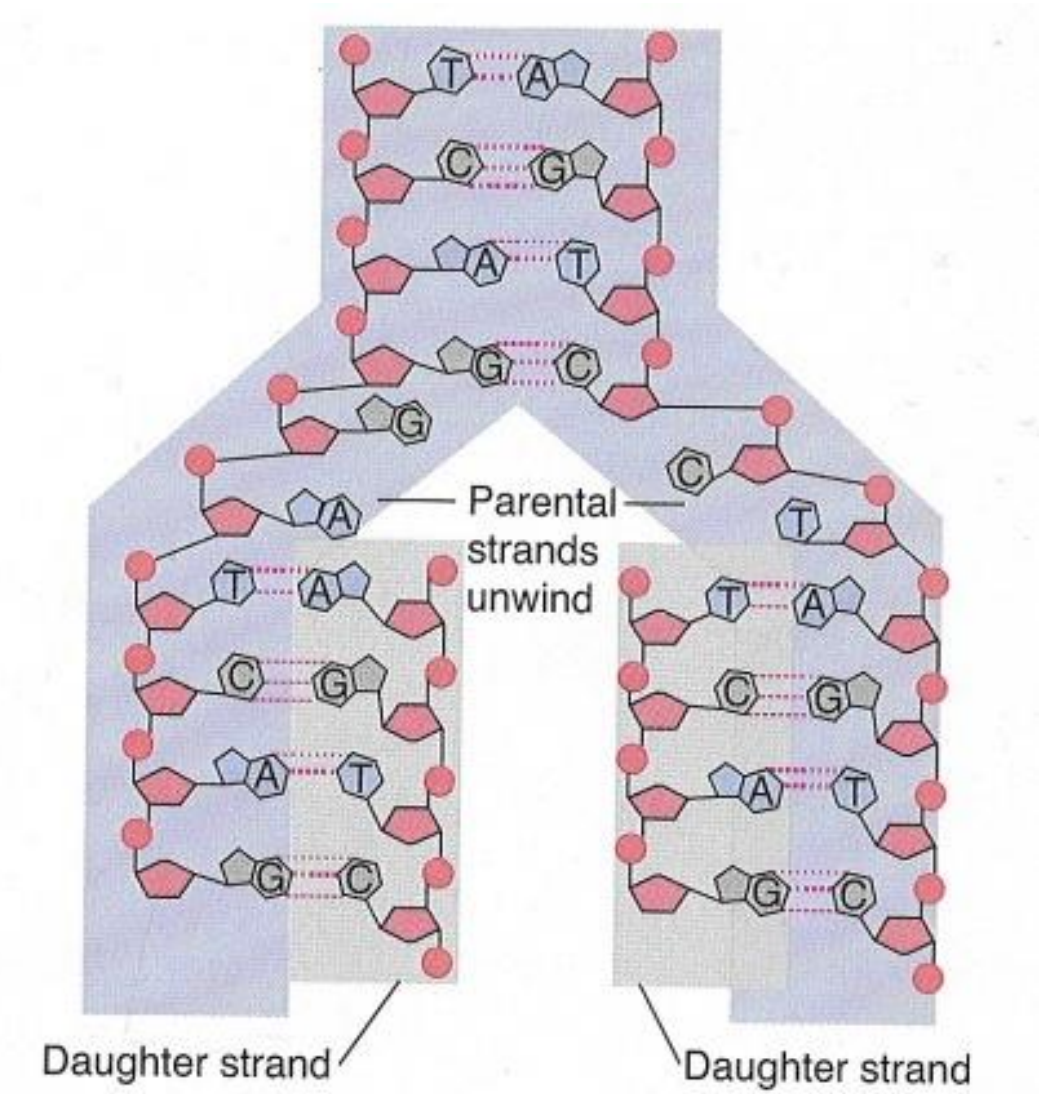
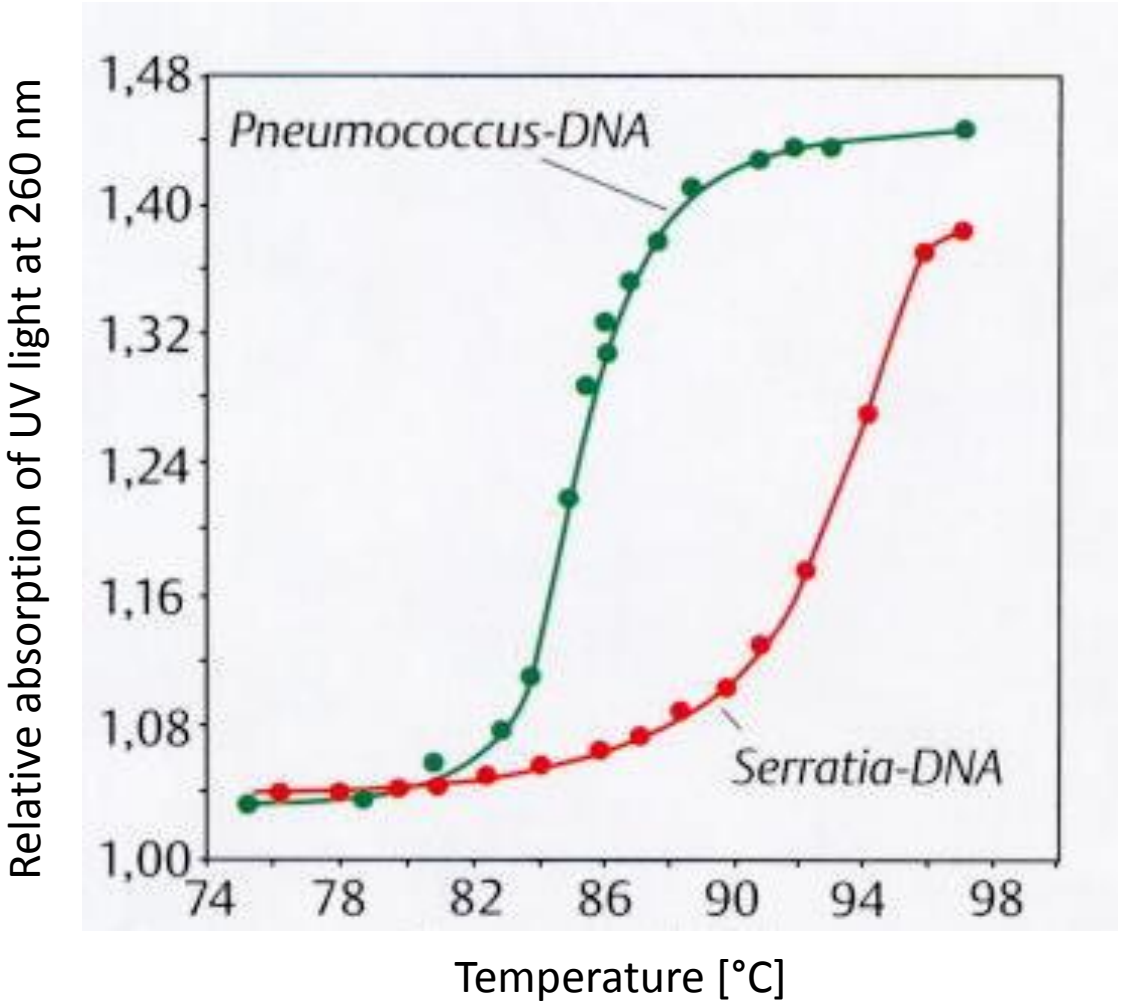
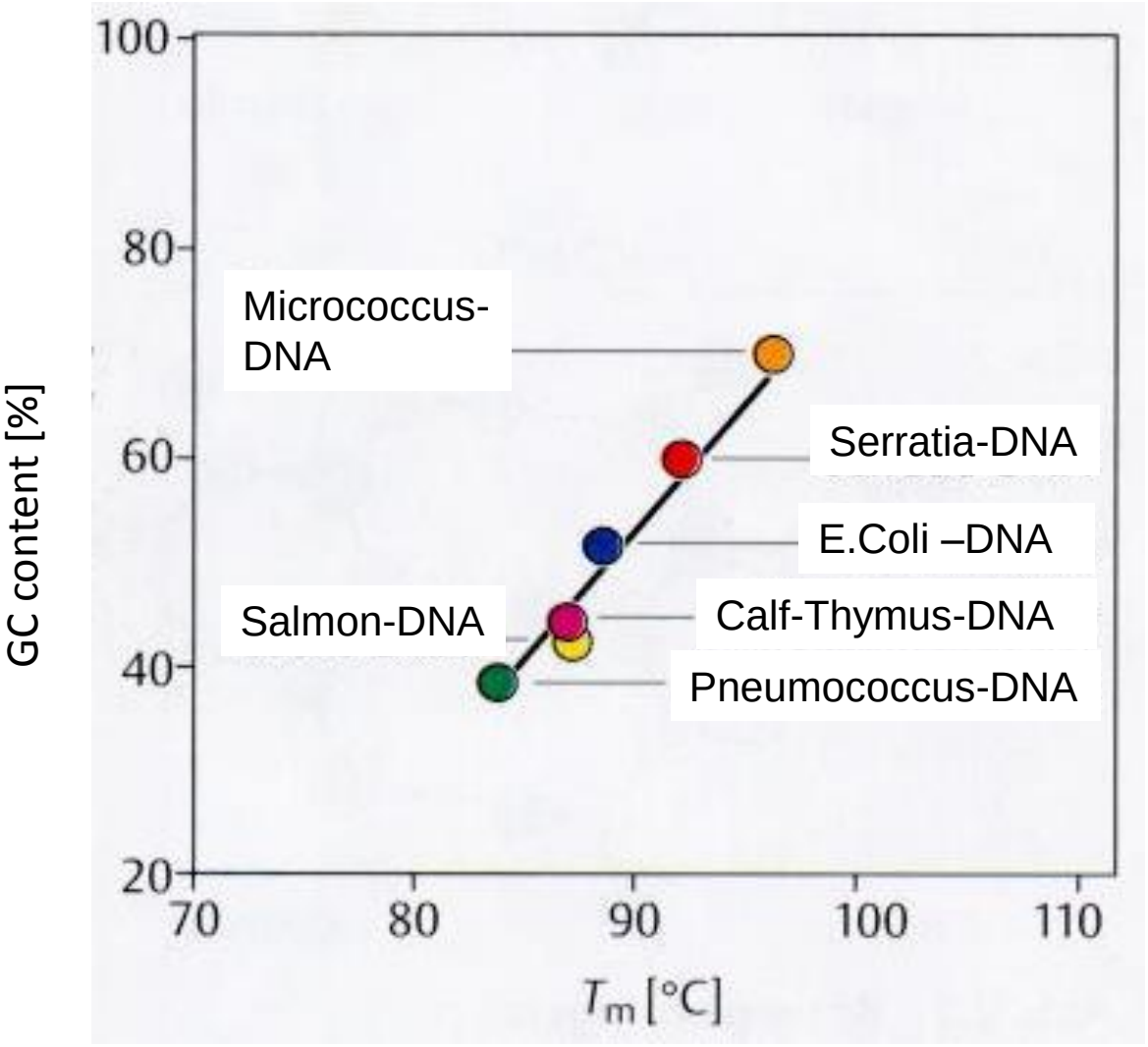


FIGURE 1.14 Base pairing provides the mechanism for replicating DNA.

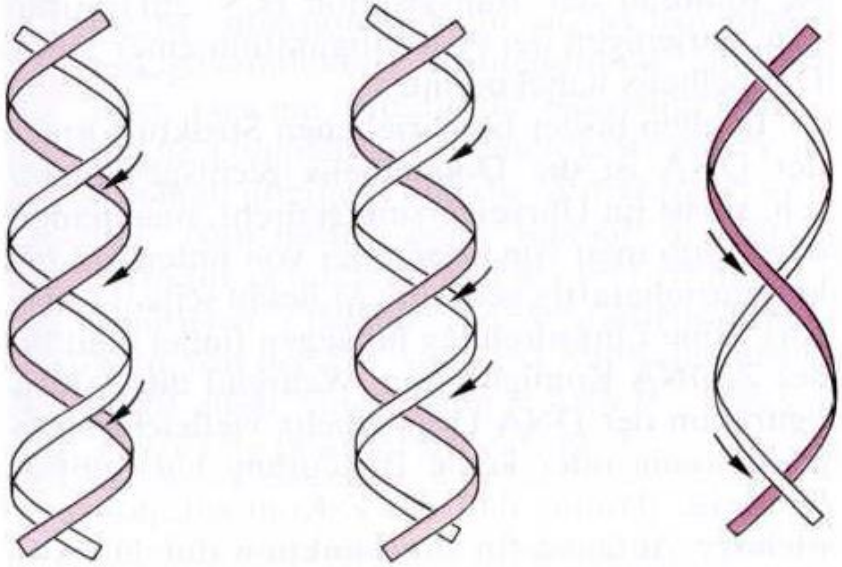
Taken from: J.E. Krebs, E.S. Goldstein, S.T. Kilpatrick; Lewin´s Genes XI; Jones & Bartlett Learning, 2014



Absorption rises with increasing temperature.

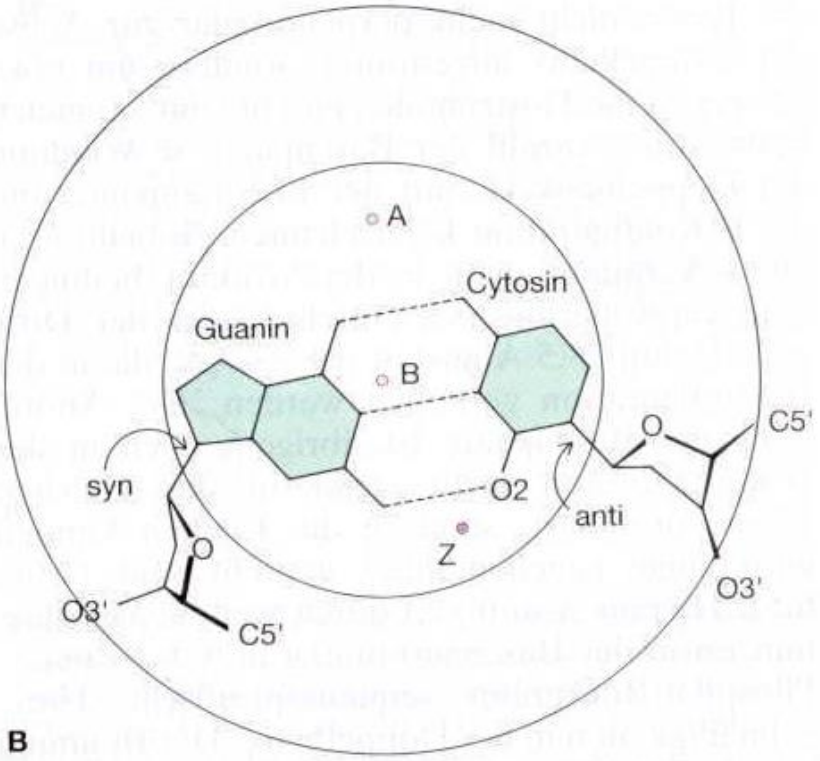


The average melting point depends on the GC content of the DNA.



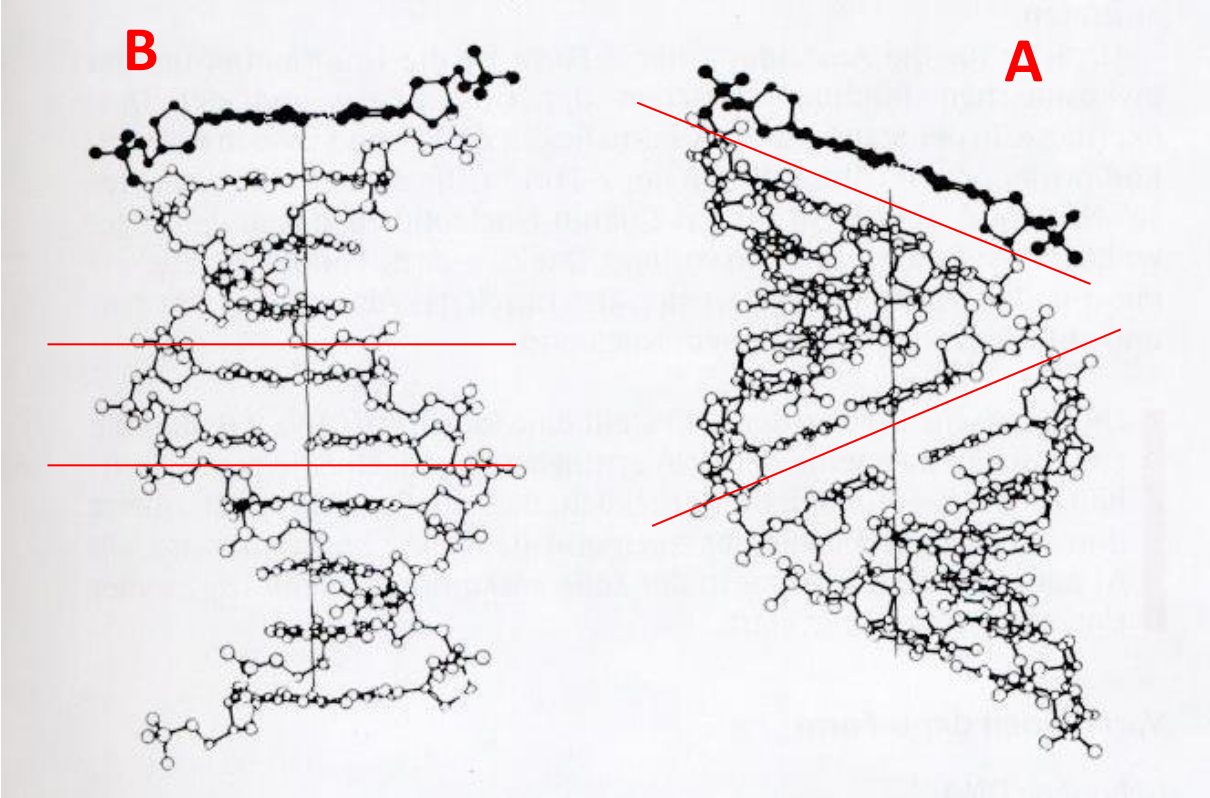
A - conformation B - conformation Z - conformation

A



B

A A - and B – DNA are right-handed helices (twisted clockwise), whereas Z – DNA is a left-handed helix (twisted counter-clockwise). Additionally, Z –DNA is less twisted and has a reduced diameter, causing changes in the „major“ and „minor groove“. **B** Double helix top view. The axis of B – DNA double helix (B) is central (inner circle), base pairs are in the centre and the sugar-phosphate backbone twists round the central area (outer circle). The axis of the A – and Z – conformations (A, Z) are located asymmetrically and cause structural changes of the grooves. (A: Weaver & Hendrick, 1992; B: Watson et al. 1987)

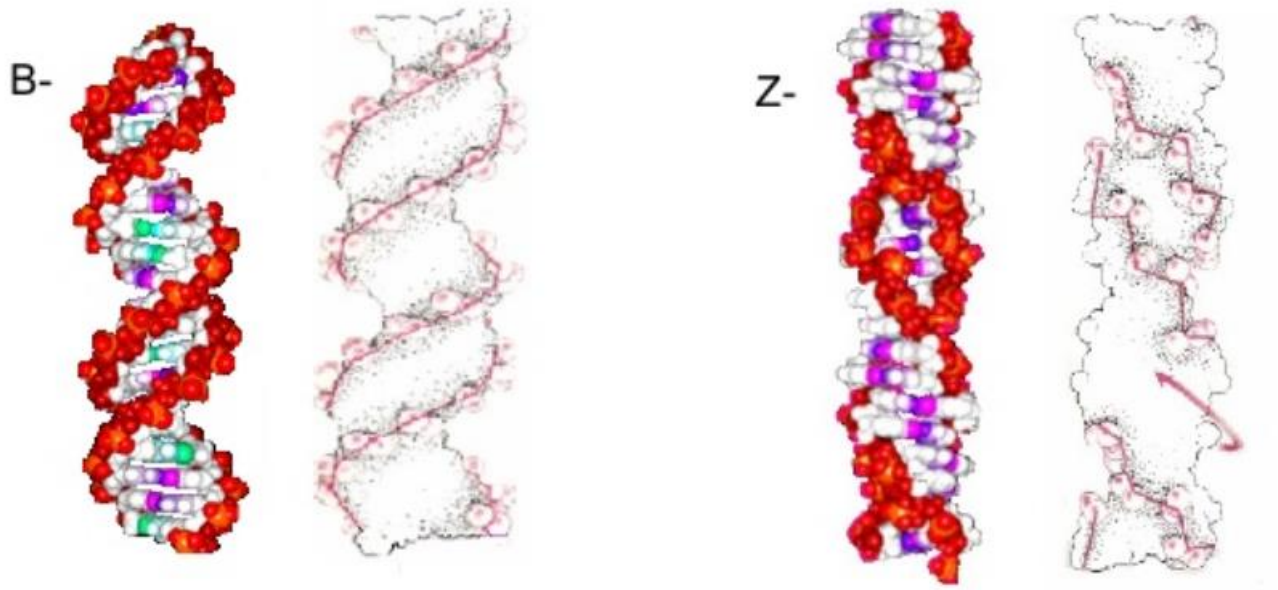


Dehydrogenation causes a change from B form DNA into the rigid A form. In both cases, the double helix is right-handed but shows structural differences. Concerning the B form, base pairs are located vertical to the central axis whereas in the A form base pairs are inclined at an angle of ~ 70° and displaced from the central axis to the major groove. This creates an open space inside of the molecule and the occurrence of a deep, but narrow major groove.

Z-DNA

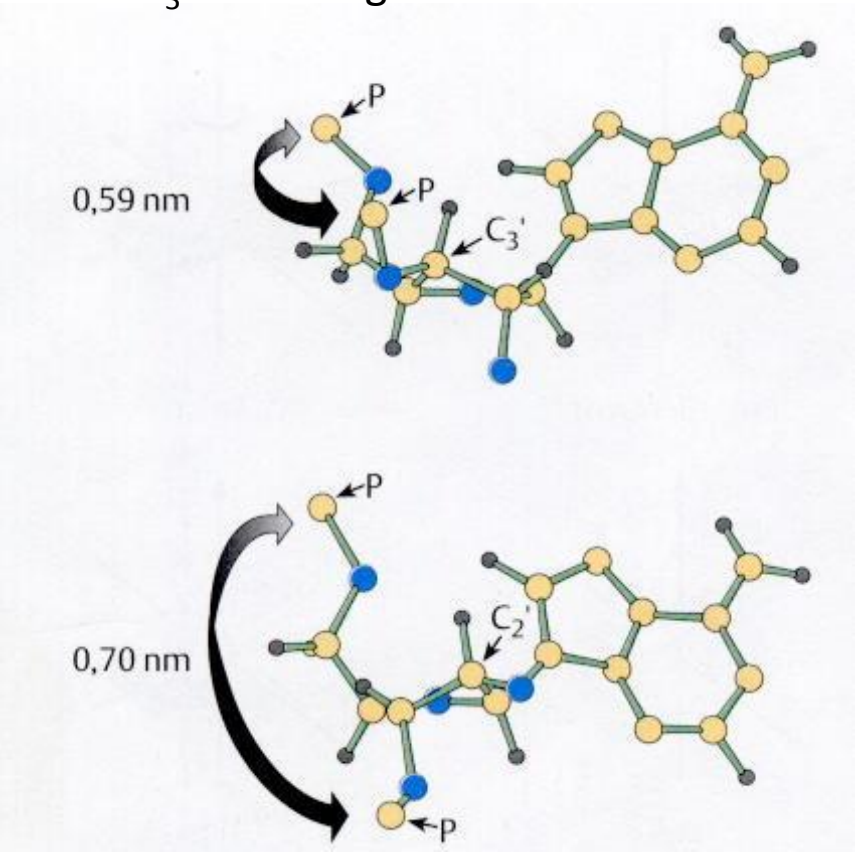
is **a left-handed double helix** that has 12 Watson-Crick base pairs per turn. The line joining successive phosphate groups follows a zig-zag path around the helix (hence the name Z-DNA); the major groove is broad and flat and the minor groove very narrow so that it can be hardly discerned.

Z-form occurs always in segments with alternating purine-pyrimidine base sequences. High ionic strength stabilizes Z-form, the methylation of cytosine residues promotes Z-DNA formation and initiates the separation of DNA strands.

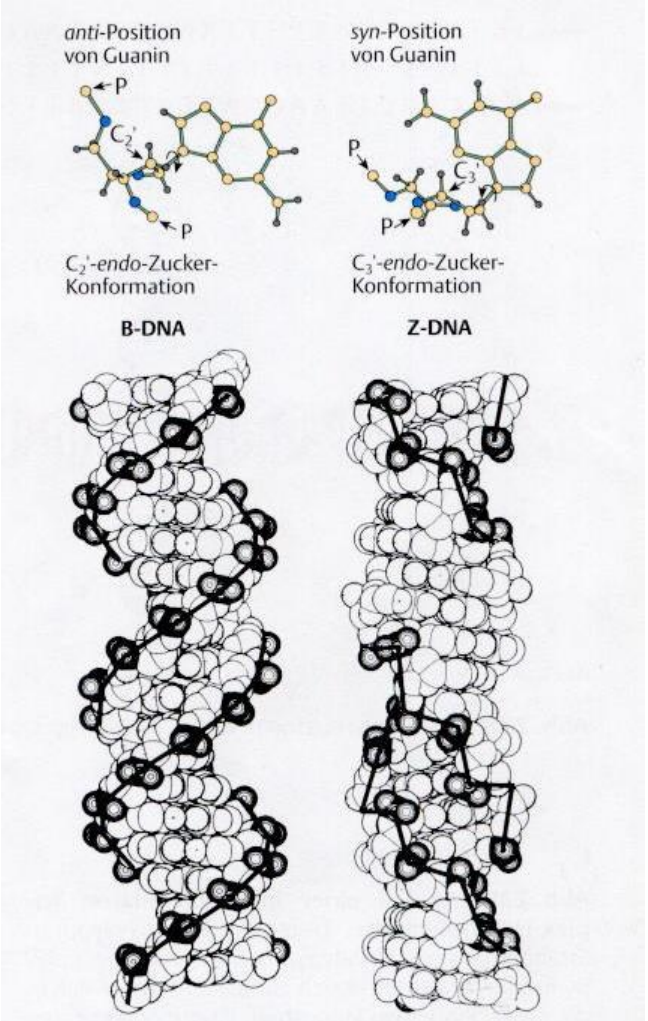


Taken from: http://de.slideshare.net/MUBOSScz/10-polysacch-heteroglycosidesnucleicacids

C_3´-endo sugar conformation



C_2´-endo sugar conformation

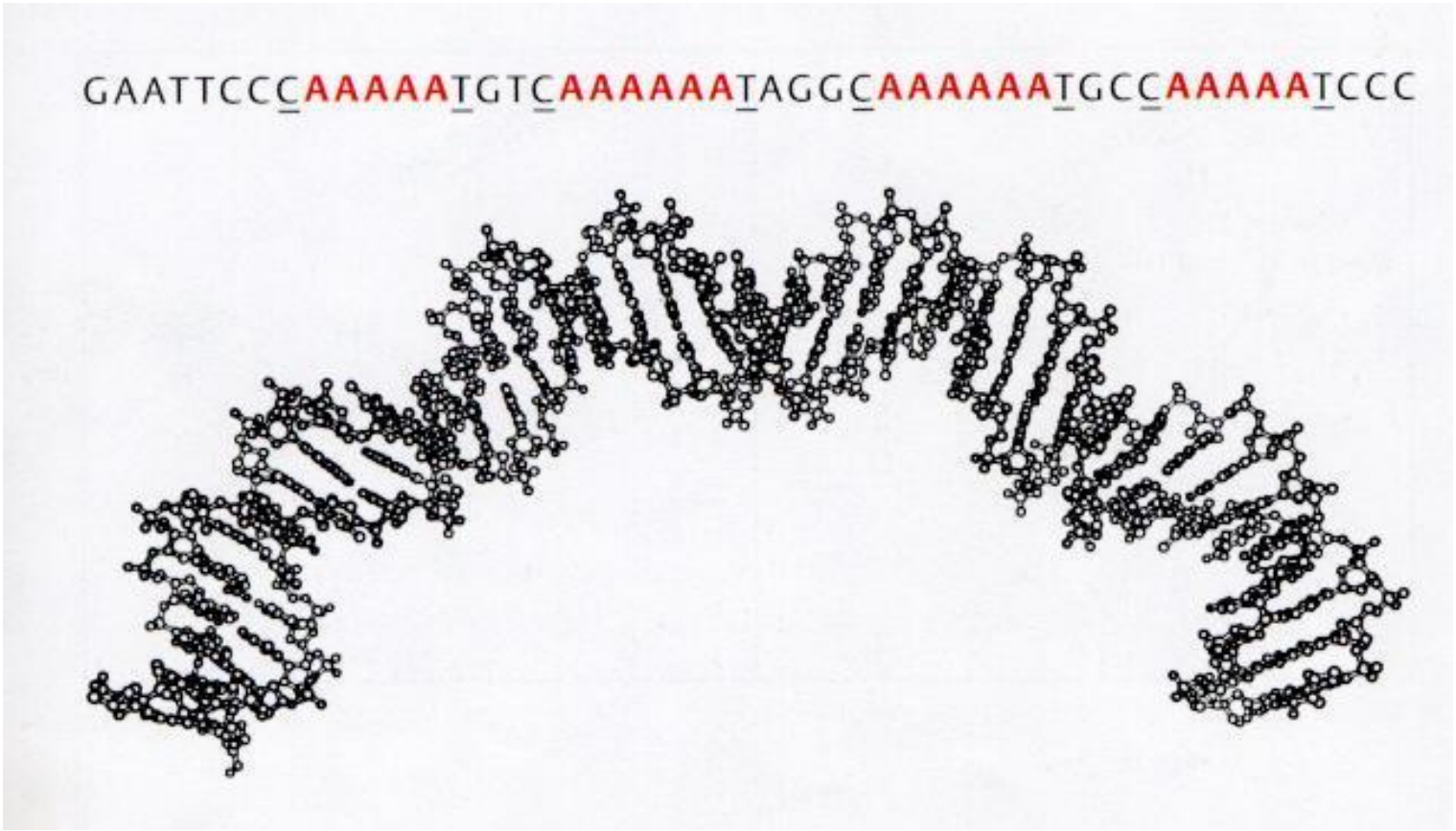


B – DNA compared to Z – DNA. The phosphate sugar backbone in the Z – DNA follows a zig-zag path around the helix.

dsDNA	B form	A form	Z form
Helical sense	**right-handed**	right handed	left-handed
Diameter	**20 nm**	26 nm	18 nm
Base pairs per helical turn	**10**	11	12
Helical twist per bp	**36°**	33°	30°
Helical pitch (rise per turn)	**34 nm**	28 nm	45 nm
Base tilt from normal to the helix axis	**1° - 6°**	20°	7
Major groove	**wide and deep**	narrow and deep	flat
Minor groove	**narrow and deep**	broad and shallow	narrow and deep
Sugar pucker	**C(2´)-endo**	C(3´)-endo	C(2´)-endo for Py C(3´)-endo for Pu

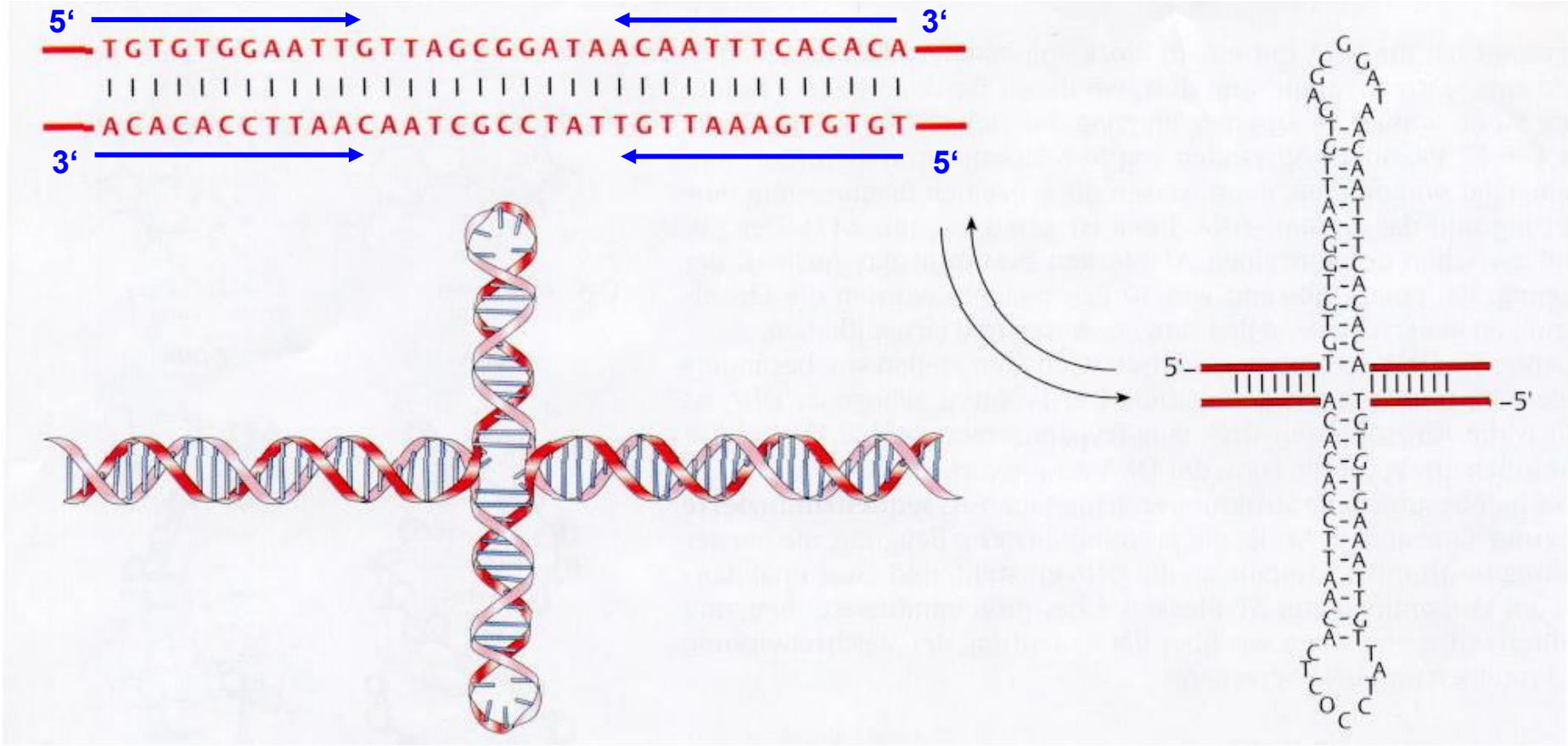
Taken from: http://de.slideshare.net/MUBOSScz/10-polysacch-heteroglycosidesnucleicacids

Fixed bent structure caused by specific primary sequence structure



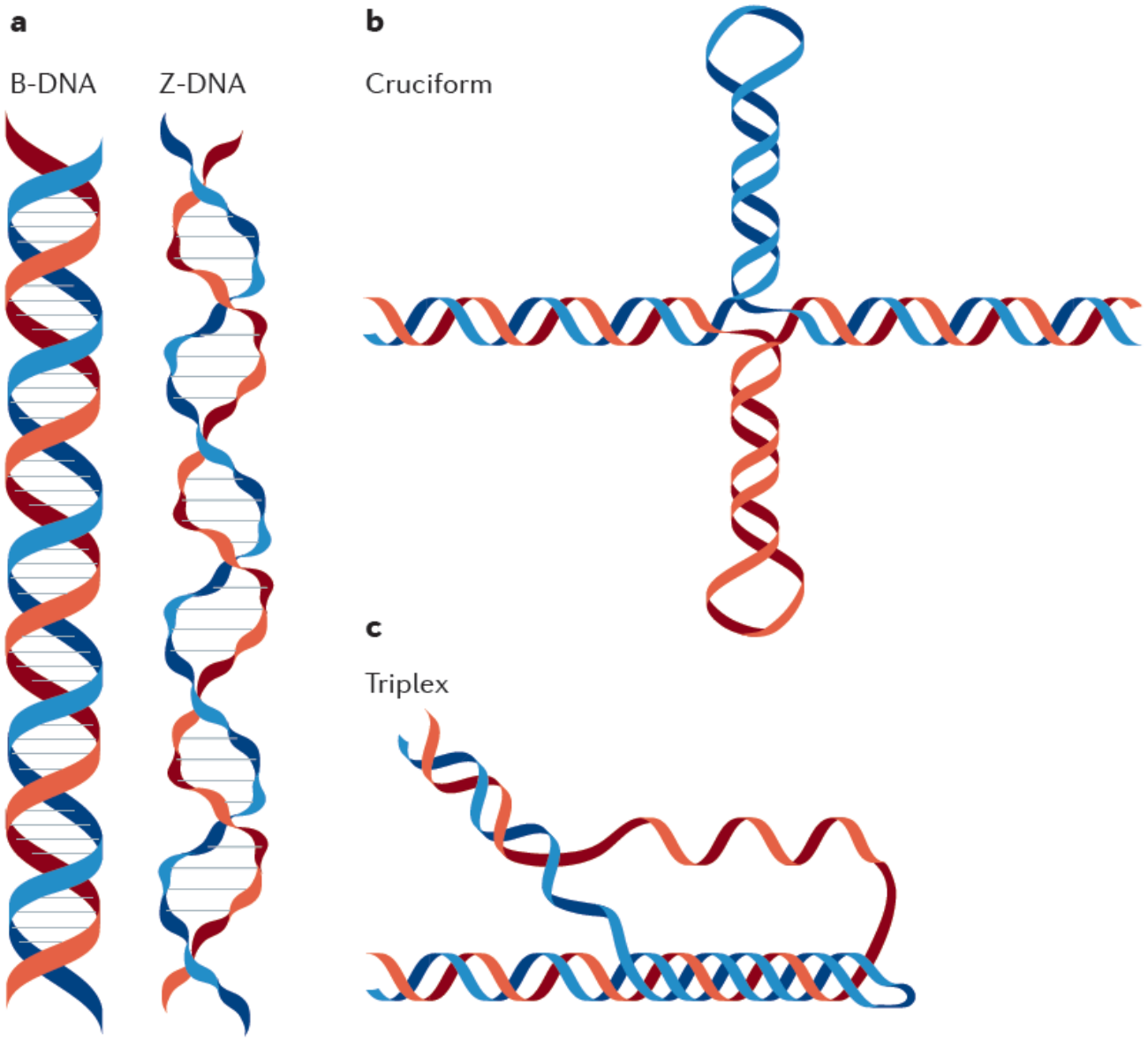
Kinetoplast DNA of Trypanosoma. Blocks of adenine residues succeed each other in distance of a helix turn (10-11 base pairs).

Cruciform DNA



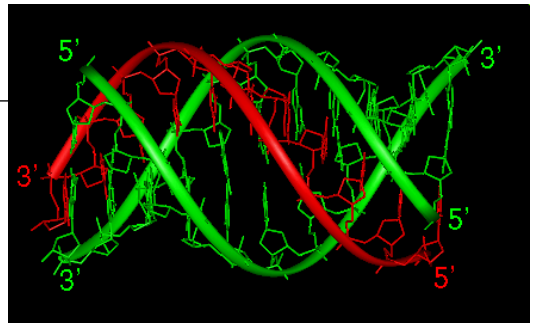
Left: *lac* operon DNA (*E.coli*); right: cruciform DNA model

Box 1 | **Other non-B-form DNA secondary structures**

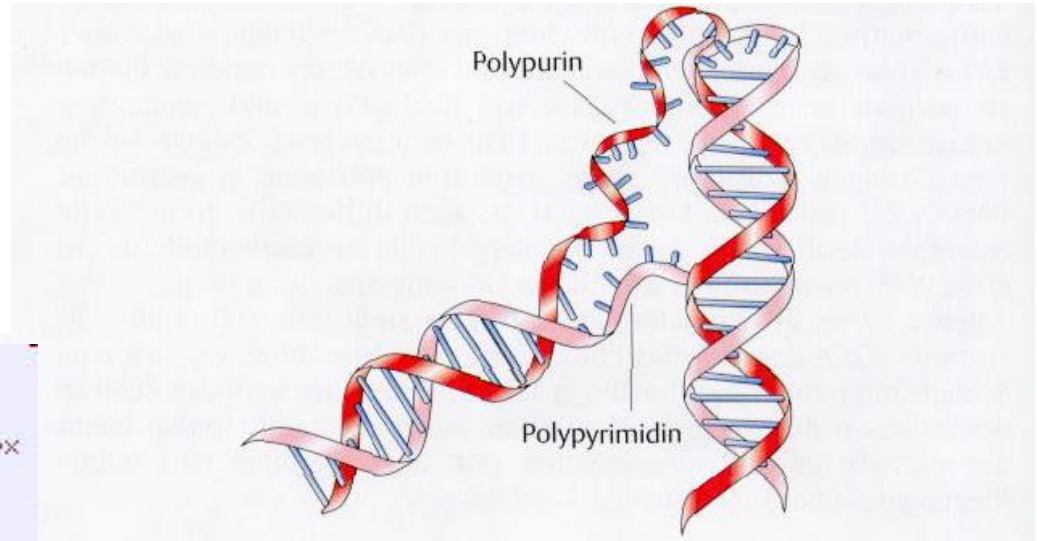


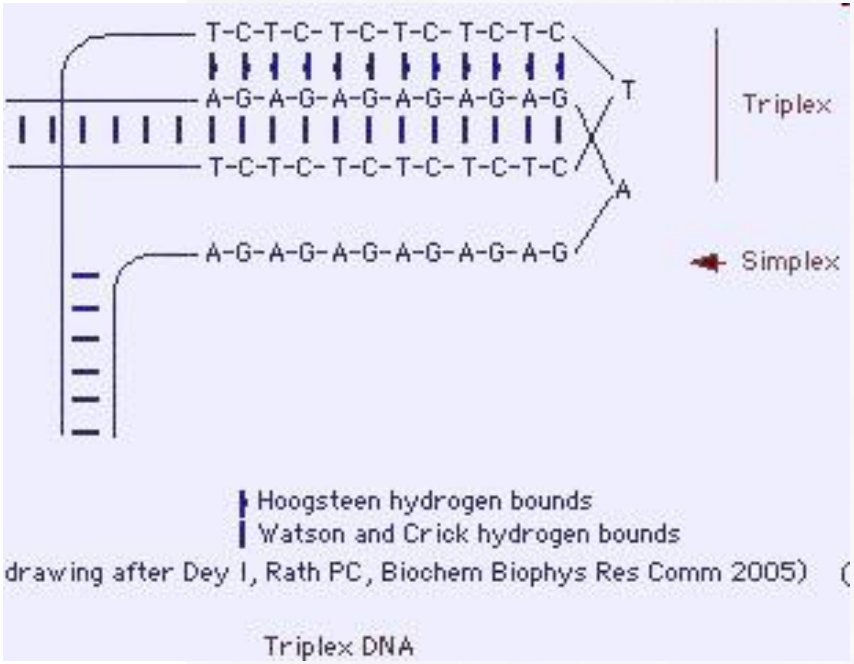
Nature Reviews Genetics 13, 770-780 (November 2012) doi:10.1038/nrg3296

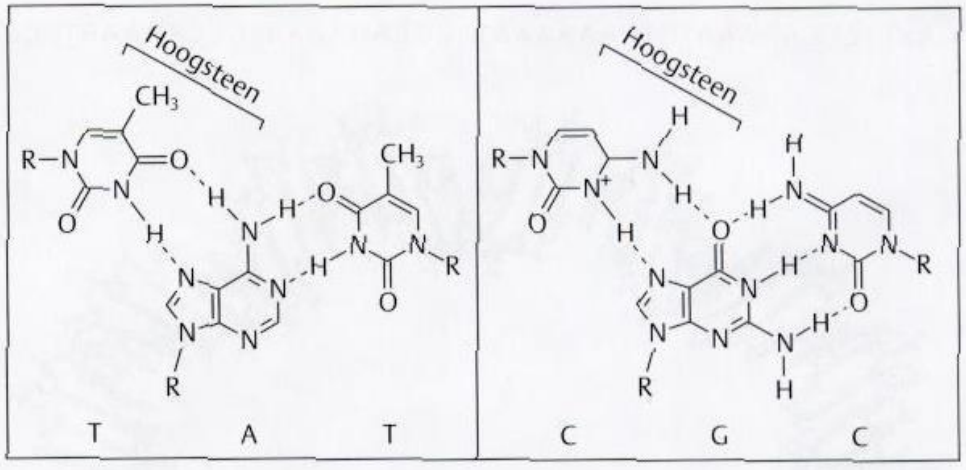
Triple Helix DNA



Model of an intramolecular triplex helix. Partial separation of a polypurine strand from a polypyrimidine strand: the polypyrimidine strand folds back and is taken up by the major groove where Hoogsteen pairings with the purine are formed. Low pH values promote the rearrangement as protonated cytosine is able to form a Hoogsteen base pairing.







http://atlasgeneticsoncology.org/Educ/Images/H-DNAE.jpg

Z-DNA

In contrast to standard B-form DNA (B-DNA), Z-DNA is a left-handed helix[128] (see the figure, part a). Z-DNA motifs (that is, sequences that form Z-DNA in vitro) are tracts of alternating purines and pyrimidines, which occur about once every 3,000 bp in metazoans[129]. Negative supercoiling stabilizes the formation of Z-DNA under physiological salt conditions[130], and it is hypothesized that Z-DNA relieves transcription-induced torsional stress[131]. Z-DNA motifs are tightly associated with transcriptional start sites in eukaryotic genomes[132], and these motifs can also cause genome instability, although the type of damage they cause varies from prokaryotes (dinucleotide insertions and deletions) to eukaryotes (double-strand breaks resulting in larger deletions)[120, 121, 133, 134].

Cruciform structures

Negative supercoiling can also cause B-DNA to adopt a four-armed, cruciform secondary structure that resembles a Holliday junction[135] (see the figure, part b). These structures require ≥6-nucleotide inverted repeats (cruciform motif) to form, and such motifs are located near replication origins, breakpoint junctions and promoters in diverse organisms[136, 137]. In metazoans, cruciform motifs are enriched near sites of gross chromosomal rearrangements[138], and deletions and translocations occur more frequently in vivo at sites of cruciform motifs than in B-DNA[139, 140, 141]. However, cruciforms might also serve positive roles (for example, stabilizing the human Y chromosome (reviewed in Ref. 134)).

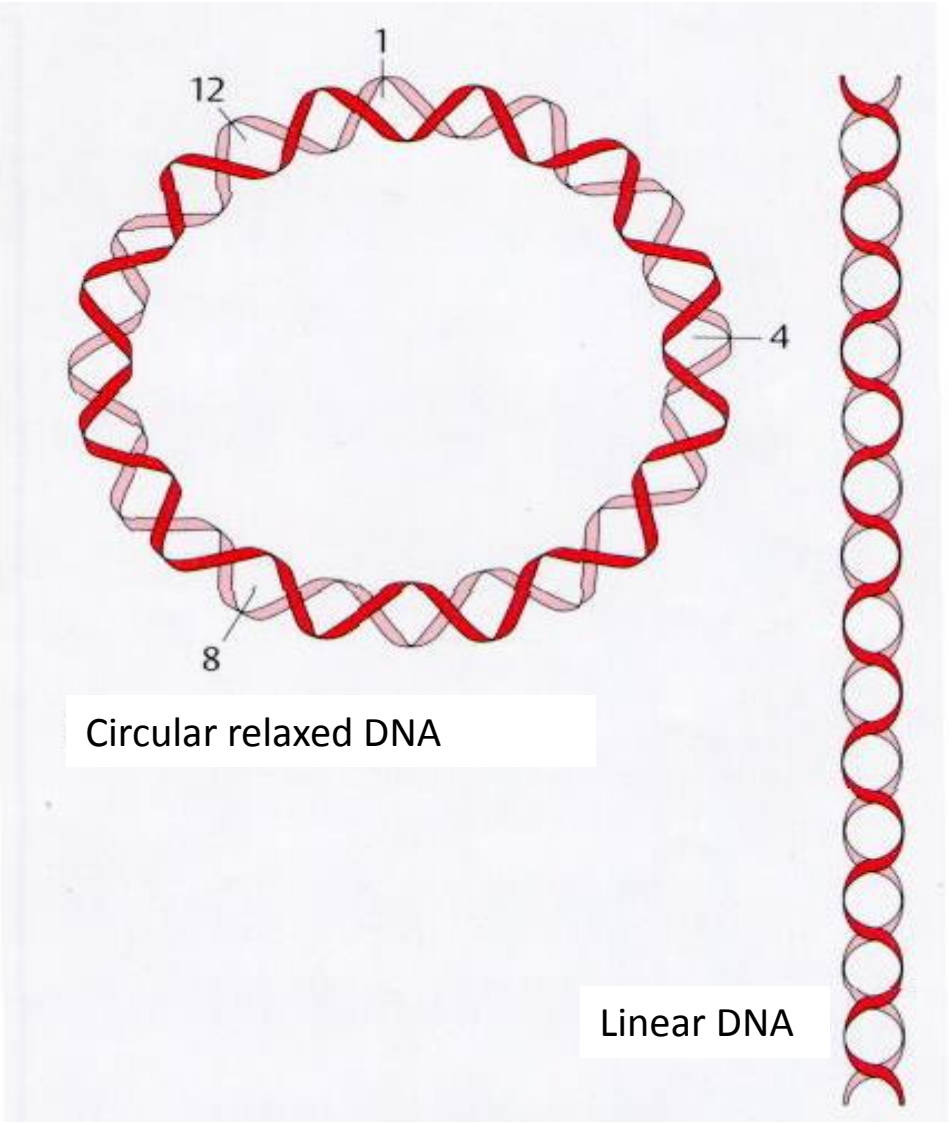
Triplex DNA

Three-stranded triplex DNA occurs when single-stranded DNA forms Hoogsteen hydrogen bonds in the major groove of purine-rich double-stranded B-DNA[142] (see the figure, part c). Triplexes in which the third strand is antiparallel to the DNA duplex can form at physiological pH, and these structures are stabilized by negative supercoiling[142]. Sequences capable of forming triplexes are common in eukaryotes but much rarer in prokaryotes[143]. In mammals, triplex-forming motifs are enriched in the introns of a variety of essential genes, including those involved in development and signalling[144]. Additionally, triplexes are hypothesized to cause genomic instability by causing double-strand breaks that result in translocations[145]. However, the formation of a triplex structure in a trinucleotide repeat sequence (for example, (CAG)n) can prevent the expansion of the repeat[138, 139]; repeat expansion is related to human genetic disorders[146, 147].

Circular and linear DNA.

The complementary strains of the linear, but not of the circular, DNA can be separated by melting. The linkage number of the relaxed circular DNA corresponds to the number of helical twists.

Lk = Tw = 12



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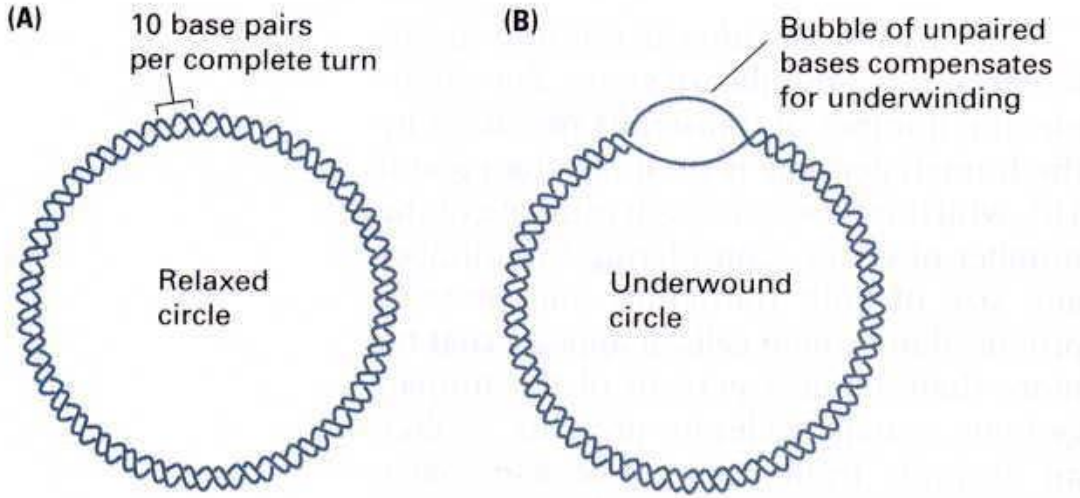


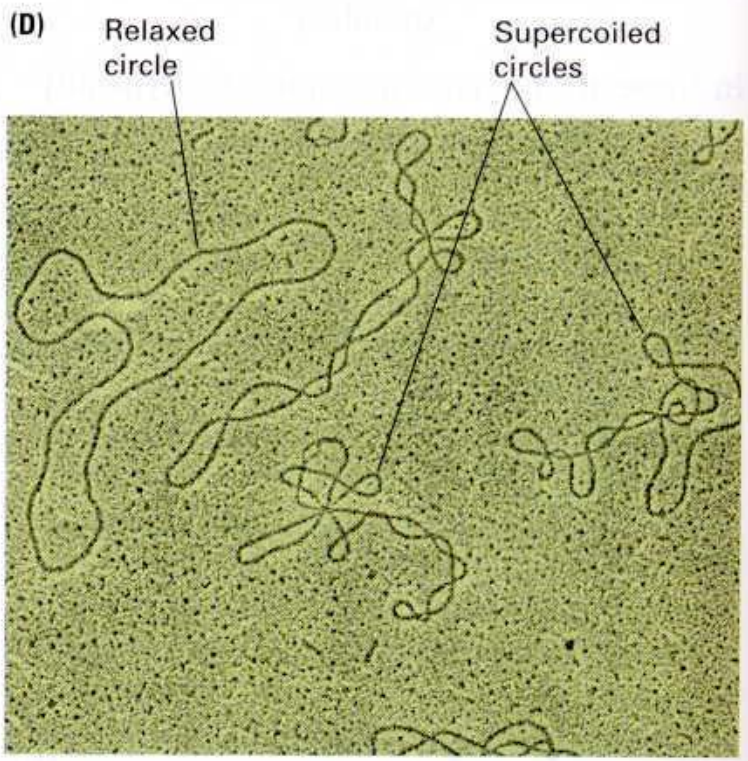
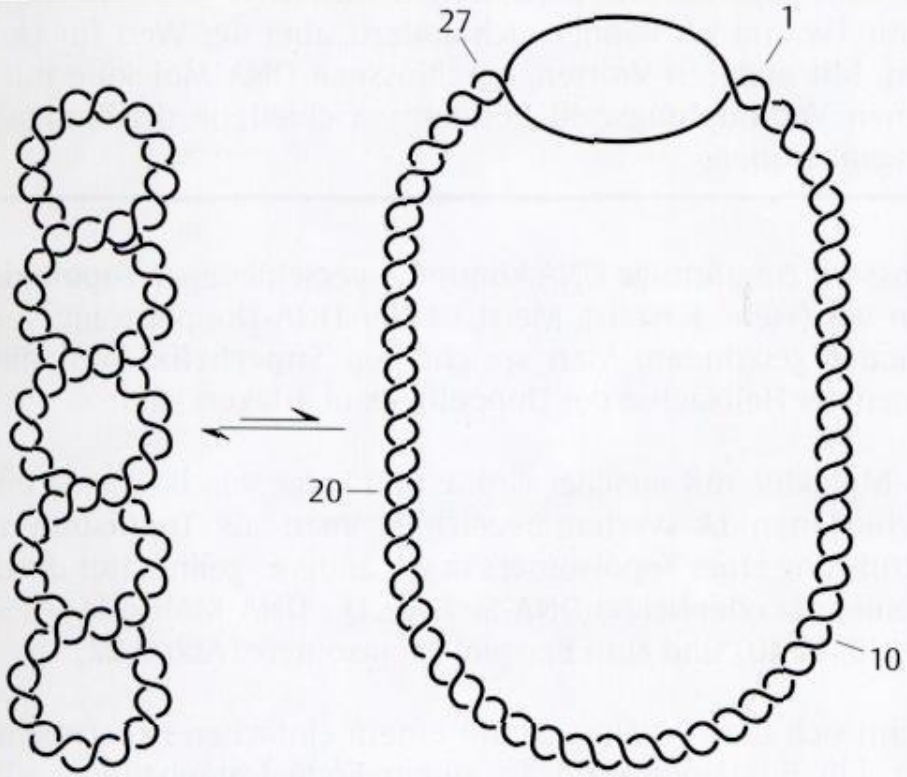


Figure 8.2 Different states of a covalent circle. (A) A nonsupercoiled (relaxed) covalent circle with 36 helical turns. (B) An underwound covalent circle with only 32 helical turns. (C) The molecule in part B, but with four twists to eliminate the underwinding. (D) Electron micrograph showing nicked circular and supercoiled DNA of phage PM2. Note that no bases are unpaired in part C. In solution, parts B and C would be in equilibrium. [Electron micrograph courtesy of K. G. Murti.]

Taken from: Daniel L. Hartl & Elizabeth W. Jones, Genetics: Analysis of Genes and Genomes, 6th Edition, Jones and Bartlett Publishers



Topology of underwound DNA.
Linkage number values with and without underwinding

	left	right
Basenpaare	310	310
Lk	27	27
Tw	31	27
Wr	−4	0

Lk: Linkage number
Tw: Twist
Wr: Writhe

DNA Topology:

A more detailed description of topology starts with the definition of the term „linking number“ (Lk). Concerning relaxed DNA, the linkage number is equivalent to the number of helical twists (Tw). Based on the following formula, „Lk“ can be determined easily:

Lk = N / 10,5

N: Total number of base pairs of a given DNA
10,5: number of base pairs per helical twist

In natural DNA rings the number of helical twists is mostly lower than in relaxed DNA molecules. Theoretically, the consequence can be as shown in Fig. 2.21: the unwound region is located as a single strand bubble somewhere in the molecule. Effectively, the pitch of the double helix in the DNA ring remains almost unchanged. Instead, the underwindings cause supercoils of the helical axis. Superhelical DNA has a three-dimensional conformation. Thus, a decrease in the number of helical twists is compensated by supercoils of the helical axis (writhe).

This relationship can be quantitatively drafted in a very simple way: **Lk = Tw + Wr**

Thus, Lk indicates the frequency of DNA strand cross overs.
Lk represents a topological property of closed DNA molecules: the values for Tw and Wr can vary, but Lk remains the same. In other words, closed DNA molecules with a given linking number can have various three-dimensional forms.

Topologie der DNA

Eine genauere Beschreibung der Topologie beginnt mit der Definition des Begriffs **Verknüpfungszahl Lk** *(linking number)*. Bei entspannter DNA (Abb. 2.**20**) entspricht die Verknüpfungszahl der Anzahl der Helixwindungen **Tw** *(twists)*, also der Häufigkeit, mit der die beiden Stränge der Doppelhelix gewunden sind. Aus den Kennzahlen der B-Form der DNA (Tab. 2.**1**) läßt sich der Wert leicht angeben:

$$Lk = \frac{N}{10,5}$$

N: Gesamtzahl der Basenpaare einer gegebenen DNA
10,5: Zahl der Basenpaare pro Helixwindung

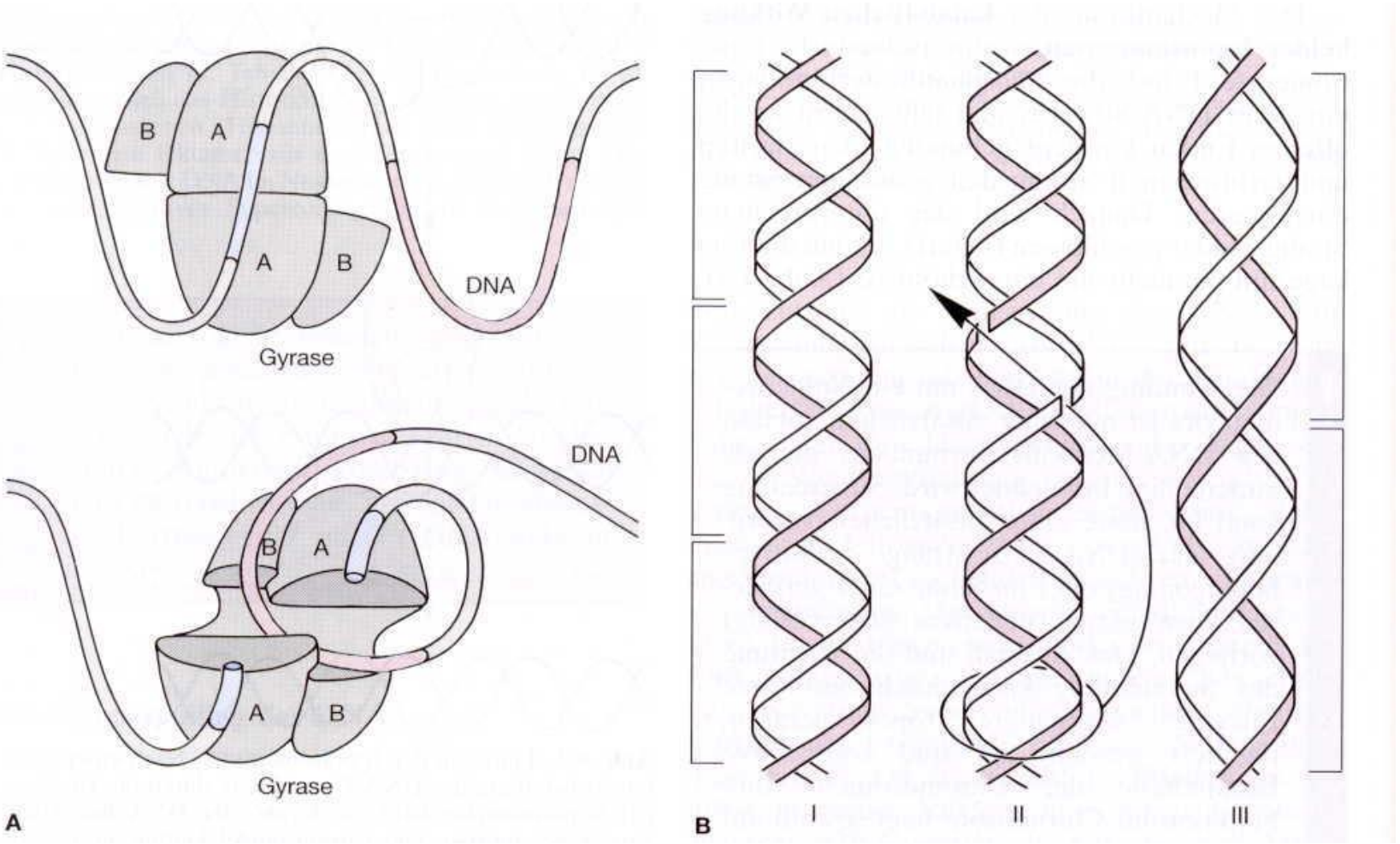
In natürlichen DNA-Ringen ist die Zahl der helikalen Windungen fast immer niedriger als in entspannten DNA-Molekülen. Theoretisch kann sich das so auswirken, wie im rechten Teil der Abb. 2.**21** gezeigt: Der entwundene Bereich liegt als einzelsträngige Blase an einer Stelle im Molekül. Tatsächlich ist aber die Ganghöhe der Doppelhelix im DNA-Ring wenig verändert. Statt dessen wirken sich die Unterwindungen in Form von Überdrehungen *(supercoils)* der Helixachse aus (Abb. 2.**21** links). Diese superhelikale DNA kann nicht mehr auf einer Ebene liegend dargestellt werden, weil sie eine dreidimensionale Konformation hat. Eine Abnahme in der Zahl der Helixwindungen Tw *(twists)* wird also durch Überdrehungen der Helixachse **Wr** *(writhe)* ausgeglichen.

Die Beziehungen zwischen den Windungen der Stränge in der Doppelhelix und den Überdrehungen der Helixachse kann man quantitativ in einer einfachen Weise formulieren:

$$Lk = Tw + Wr$$

Die Verknüpfungszahl Lk in dieser erweiterten Form gibt also die Häufigkeit an, mit der sich die Stränge der DNA überkreuzen.

Lk ist eine topologische Eigenart geschlossener DNA-Moleküle: Die Werte für Tw und Wr können sich ändern, aber der Wert für Lk bleibt erhalten. Mit anderen Worten, geschlossene DNA-Moleküle mit einer gegebenen Verknüpfungszahl können verschiedene dreidimensionale Formen einnehmen.



The function of topoisomerase II (gyrase). **A** Subunit A of topoisomerase II cuts the DNA double strand and separates the cutting sites from each other. After the intact double helix has passed the open DNA site, the severed strand is re-joined. **B** Consequences on DNA level. A negative supercoiling can be created by topoisomerase II (steps I to III).

Quelle???

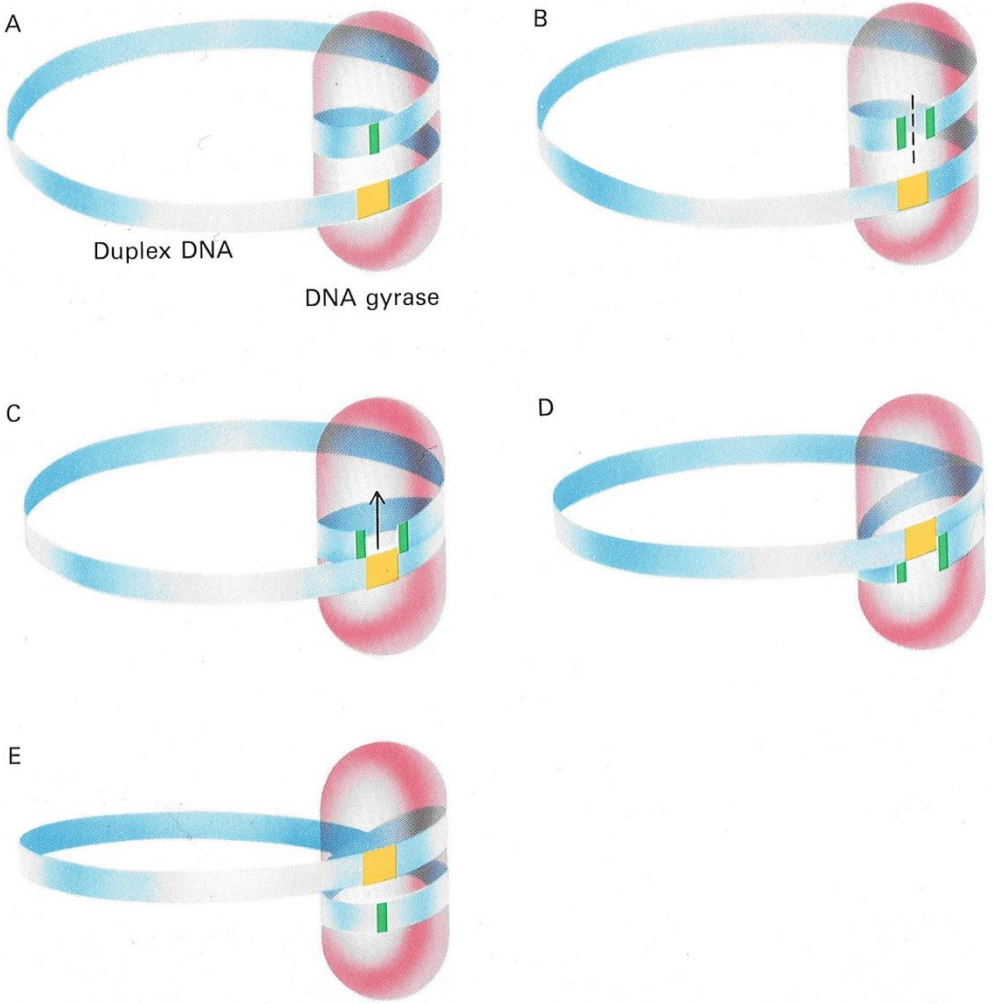


Figure 27-25
Topoisomerases catalyze changes in the linking number of DNA. DNA gyrase cleaves both strands of DNA, and passes a segment of double-helical DNA through this break. The severed strands are then rejoined. [After J. C. Wang. DNA topoisomerases. Copyright © 1982 by Scientific American, Inc. All rights reserved.]

Taken from: L. Stryer; Biochemistry, 3rd Edition; W.H. Freeman and Company / New York

Useful genome sizes

Phylum	Species	Genome (bp)
Algae	*Pyrenomas salina*	6.6×10^5
Mycoplasma	*M. pneumoniae*	1.0×10^6
Bacterium	*E. coli*	4.2×10^6
Yeast	*S. cerevisiae*	1.3×10^7
Slime mold	*D. discoideum*	5.4×10^7
Nematode	*C. elegans*	8.0×10^7
Insect	*D. melanogaster*	1.8×10^8
Bird	*G. domesticus*	1.2×10^9
Amphibian	*X. laevis*	3.1×10^9
Mammal	*H. sapiens*	3.3×10^9

Figure 4.8 The genome sizes of some common experimental organisms.

Taken from: B. Lewin, Essential Genes, Pearson Education International

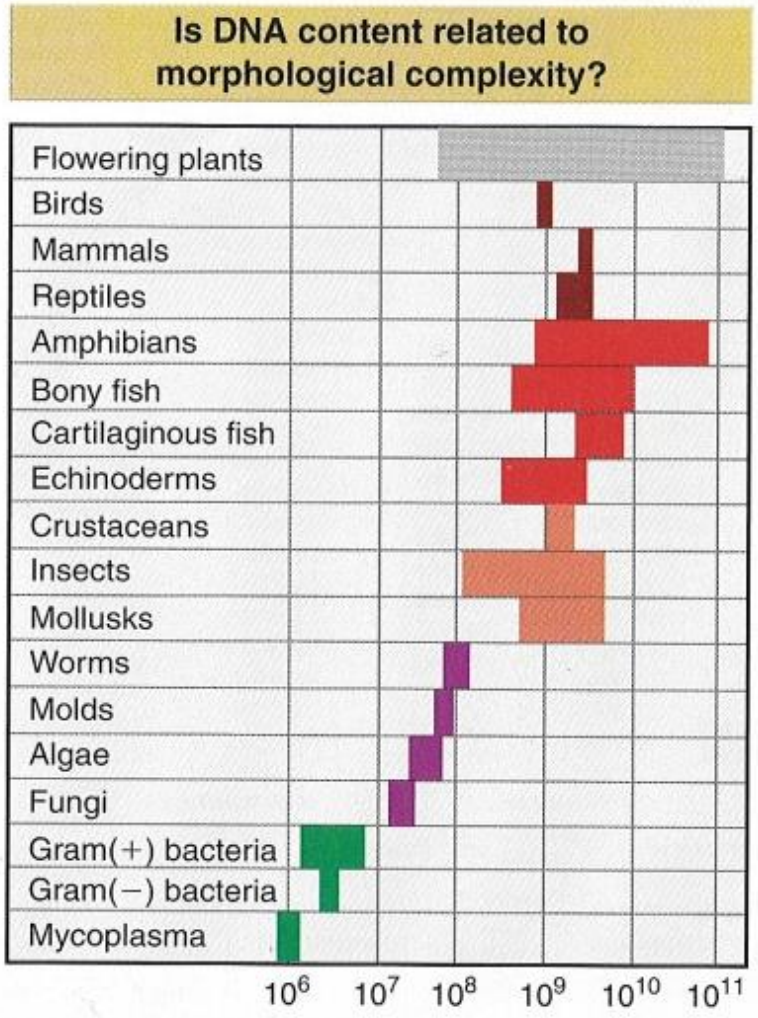


Figure 4.6 DNA content of the haploid genome increases with morphological complexity of lower eukaryotes, but varies extensively within some groups of higher eukaryotes.

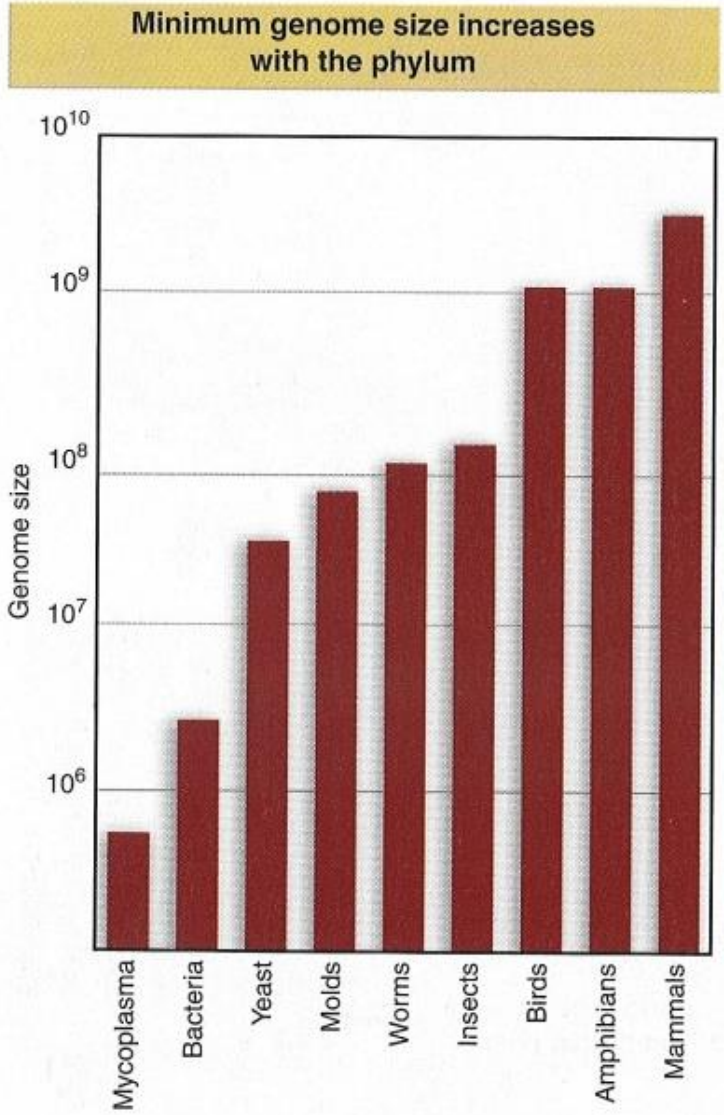


Figure 4.7 The minimum genome size found in each group increases from prokaryotes to mammals.

Taken from: B. Lewin, Essential Genes, Pearson Education International

Genomes vary greatly in size

Genome	Gene Number	Base Pairs
Organisms		
Plants	<50,000	$<10^{11}$
Mammals	30,000	$\sim 3 \times 10^{9}$
Worms	14,000	$\sim 10^{8}$
Flies	12,000	1.6×10^{8}
Fungi	6,000	1.3×10^{7}
Bacteria	2-4,000	$<10^{7}$
Mycoplasma	500	$<10^{6}$
ds DNA Viruses		
Vaccinia	<300	187,000
Papova (SV_{40})	~6	5,226
Phage T4	~200	165,000
ss DNA Viruses		
Parvovirus	5	5,000
Phage fX174	11	5,387
ds RNA Viruses		
Reovirus	22	23,000
ss RNA Viruses		
Coronavirus	7	20,000
Influenza	12	13,500
TMV	4	6,400
Phage MS2	4	3,569
STNV	1	1,300
Viroids		
PSTV RNA	0	359

Figure 1.32 The amount of nucleic acid in genomes varies over an enormous range.

Taken from: B. Lewin, Essential Genes, Pearson Education International

Some bacterial and viral genomes

	Length (µm)	Basepairs (bp)	Number of Genes
Simian Virus 40 (SV40, animal virus)	1,8	5243	6
Bacteriophage **M13** (double stranded, replicative form)	2,2	6407	10
Bacteriophage **Lambda**	16,5	48502	ca. 50
Bacteriophage **T4**	ca. 60	ca. 166000	> 100
Escherichia coli	ca. 1300	ca. 4720000	> 3000

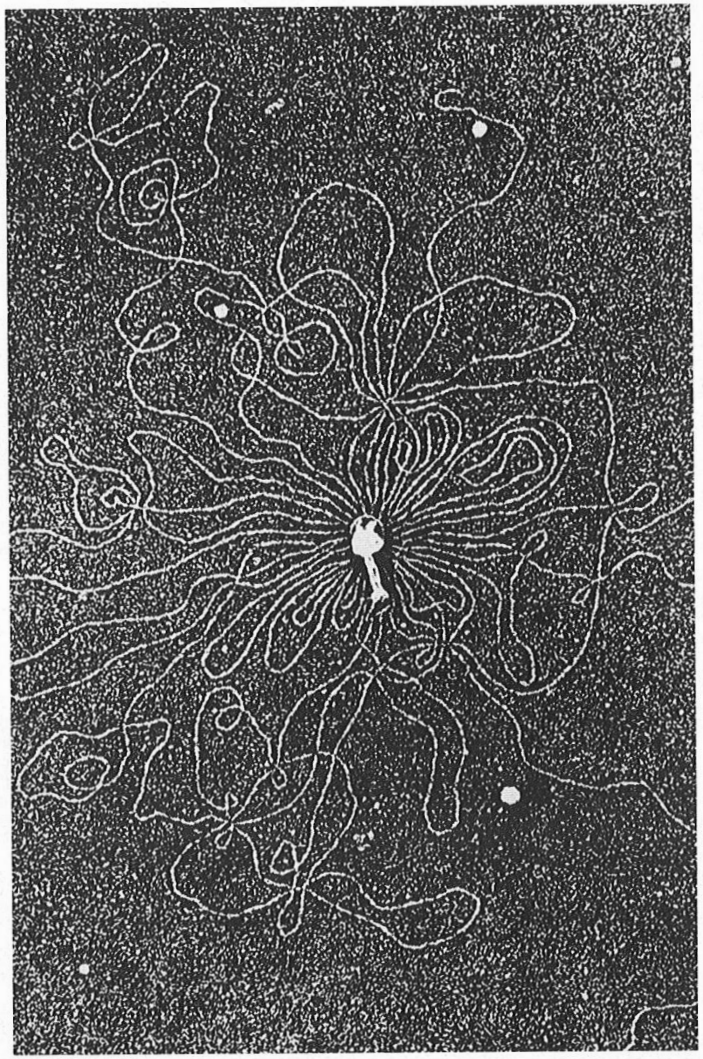


FIGURE 12–2 Electron micrograph of bacteriophage T2, which has had its DNA released by osmotic shock. The chromosome is 52 μm long.

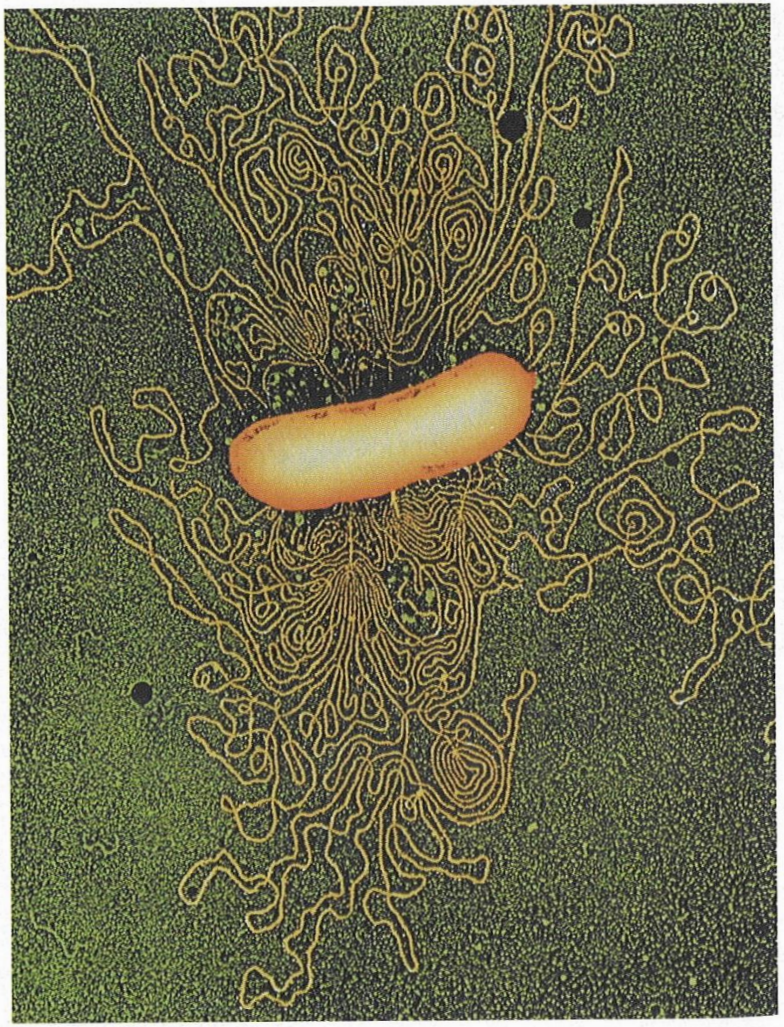
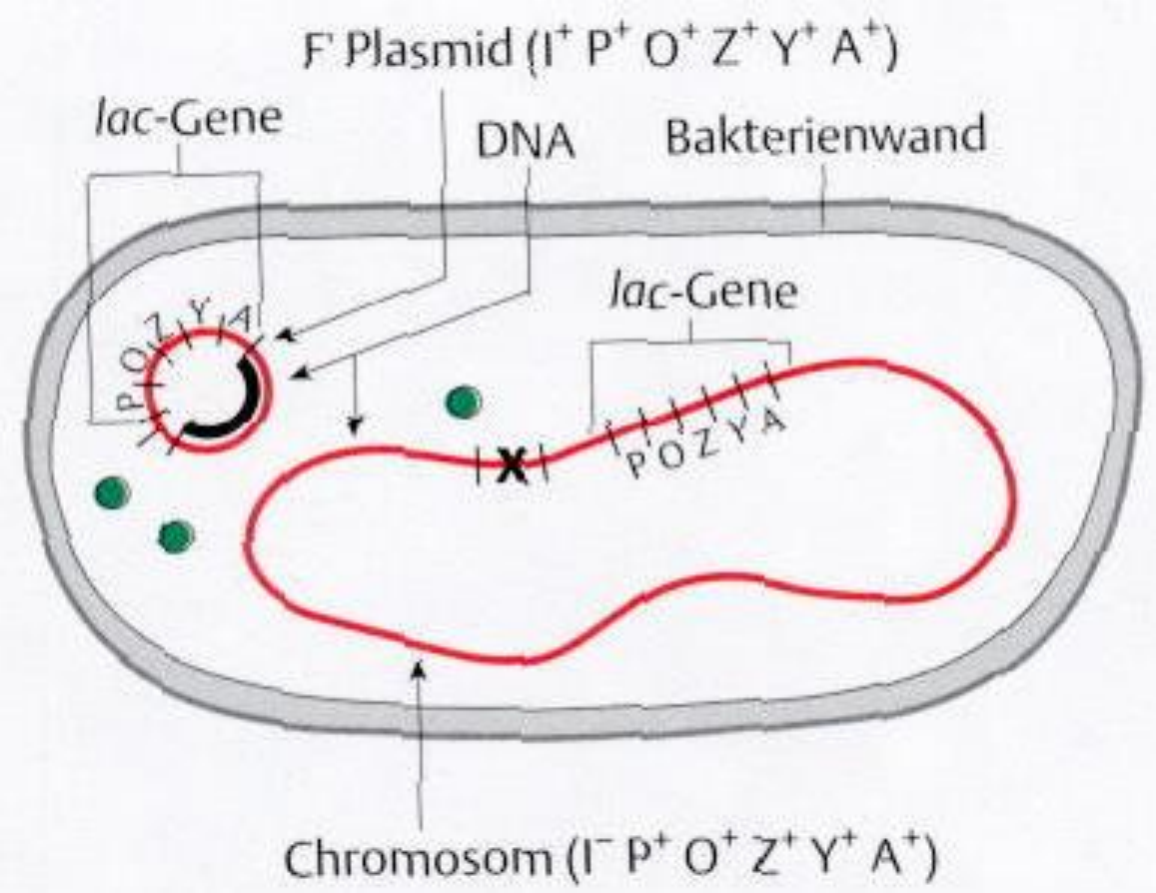


FIGURE 12–3 Electron micrograph of the bacterium *Escherichia coli*, which has had its DNA released by osmotic shock. The chromosome is 1200 μm long.

Taken from: W.S. Klug, M. R. Cummings, C.A. Spencer, M.A. Palladino; Concepts of Genetics, 9th Edition; Pearson Benjamin Cummings



Merodiploid cell (type $I^-/F'I^+$). *lacI* gene is drawn too big in proportion to the rest of the chromosome. In fact it´s just 0,15% of the *E.coli* chromosome. Wild type *lacI* gene produces an active repressor (green dots), which is free in the cell and can thus dock to the chromosomal *lac* operator as well as to the plasmid *lac* operator.

Taken from: R. Knippers; Molekulare Genetik; Thieme

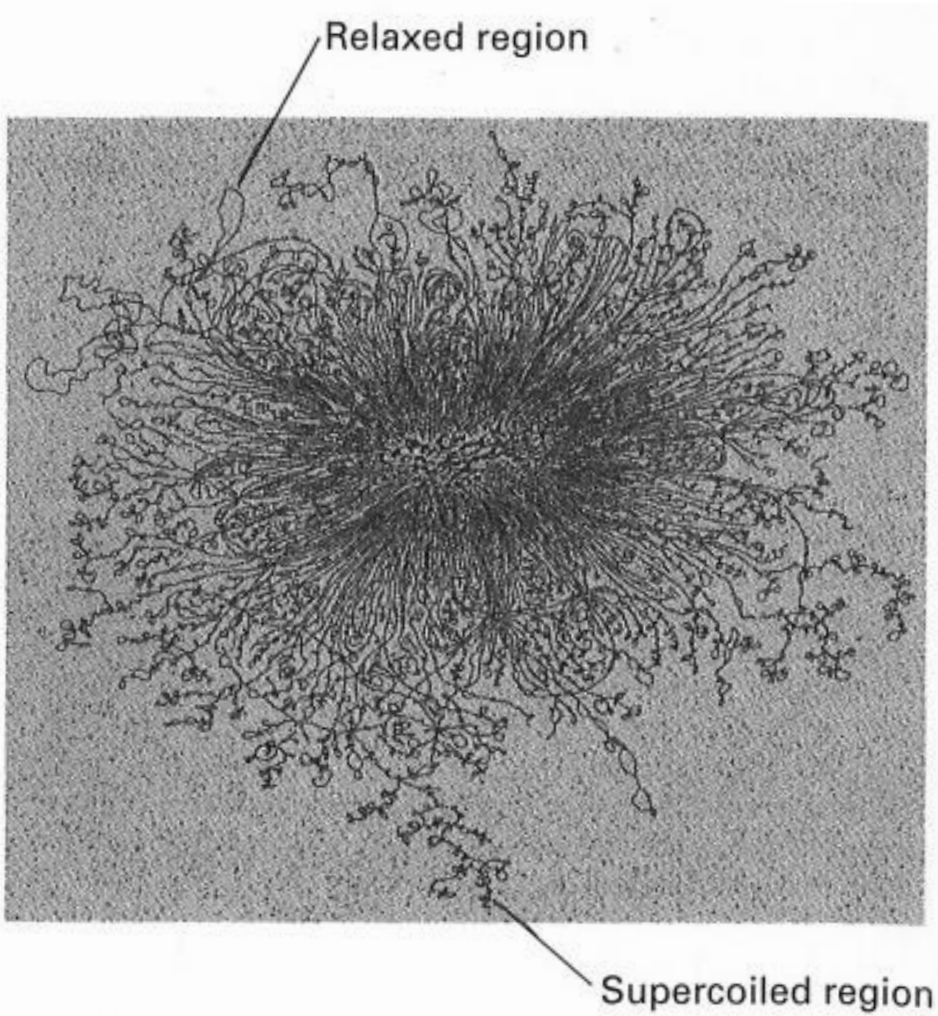


Figure 7.4 Electron micrograph of an *E. coli* chromosome, showing the multiple loops emerging from a central region. [Courtesy of Ruth Kavenoff.]

Taken from: Daniel L. Hartl & Elizabeth W. Jones, Genetics: Analysis of Genes and Genomes, 6th Edition, Jones and Bartlett Publishers

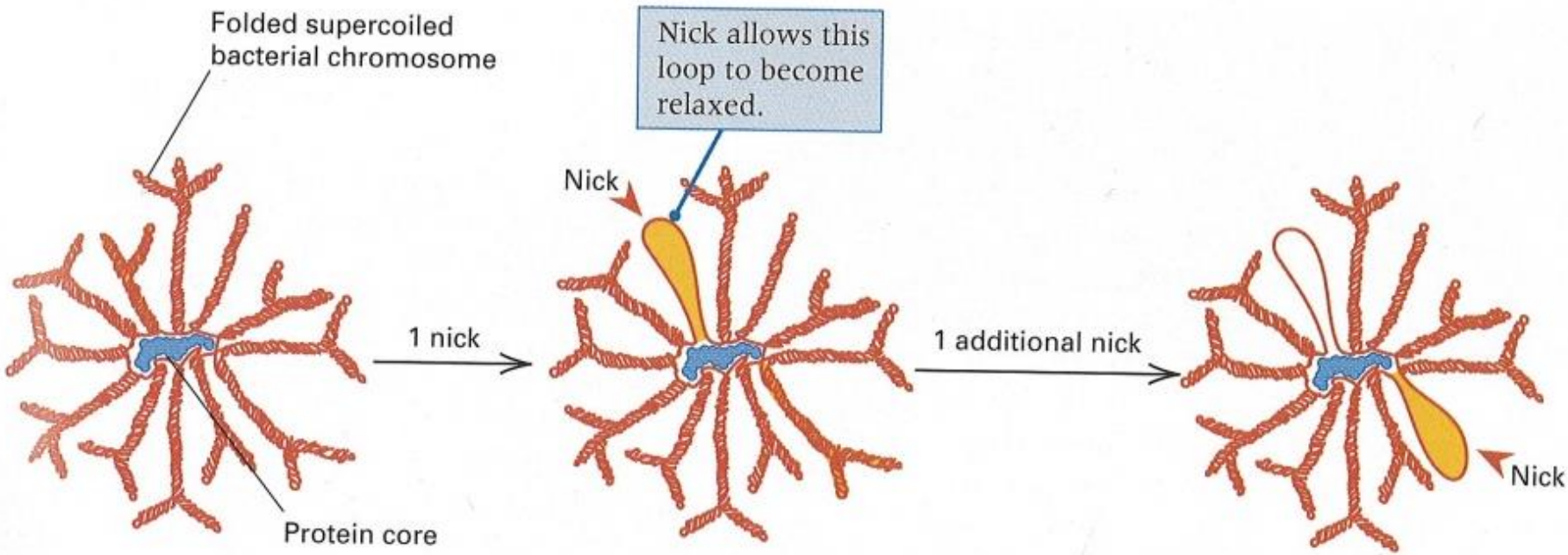


Figure 7.5 Schematic drawing of the folded supercoiled *E. coli* chromosome, showing 11 of the 40 to 50 loops attached to a protein core (blue shaded area) and the opening of loops by nicks.

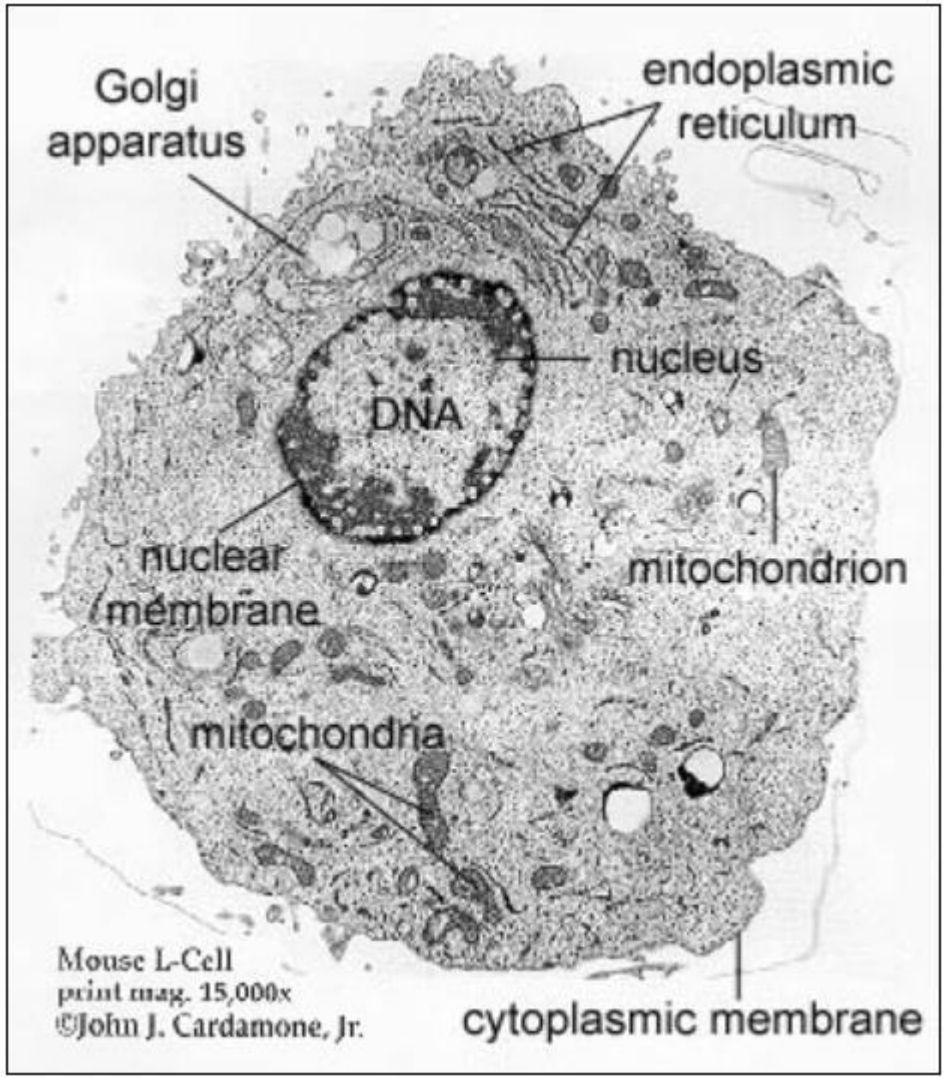
Taken from: Daniel L. Hartl & Elizabeth W. Jones, Genetics: Analysis of Genes and Genomes, 6th Edition, Jones and Bartlett Publishers

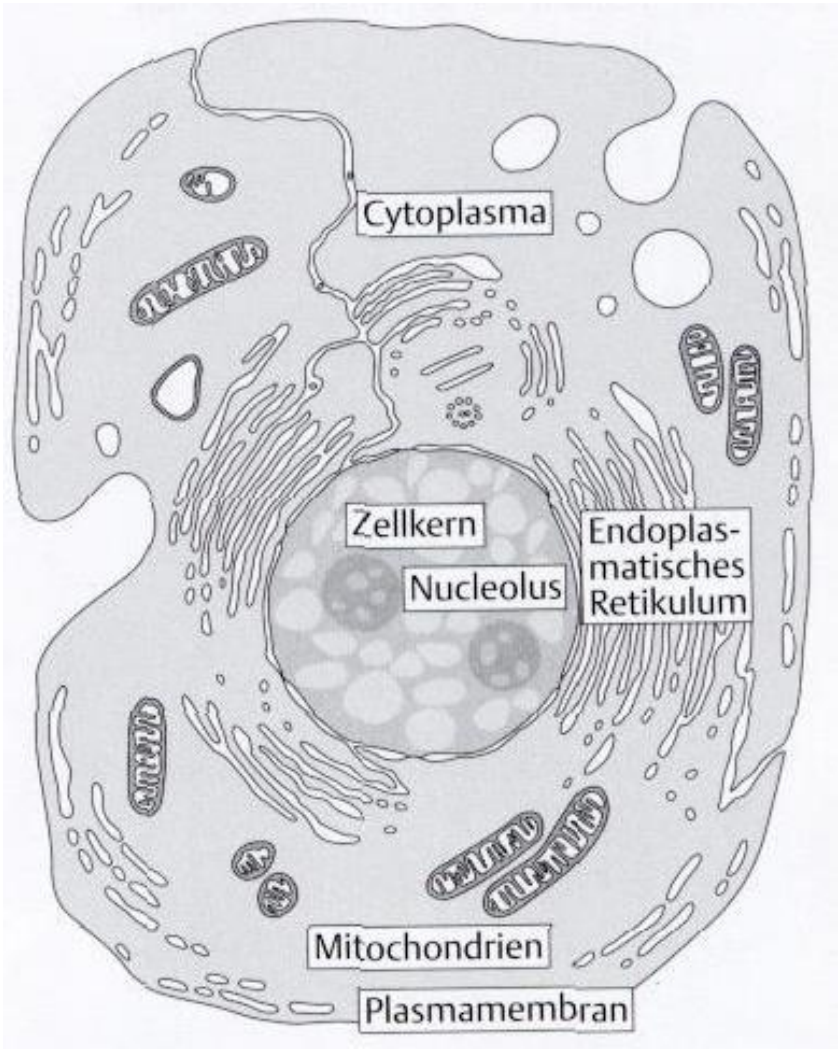
TABLE 5.3 Chromosome Numbers of Eukaryotic Cells

Organism	Genome size (Mb)[a]	Chromosome number[a]
Yeast (*Saccharomyces cerevisiae*)	12	16
Slime mold (*Dictyostelium*)	70	7
Arabidopsis thaliana	125	5
Corn	5000	10
Onion	15,000	8
Lily	50,000	12
Nematode (*Caenorhabditis elegans*)	97	6
Fruit fly (*Drosophila*)	180	4
Toad (*Xenopus laevis*)	3000	18
Lungfish	50,000	17
Chicken	1200	39
Mouse	3000	20
Cow	3000	30
Dog	3000	39
Human	3000	23

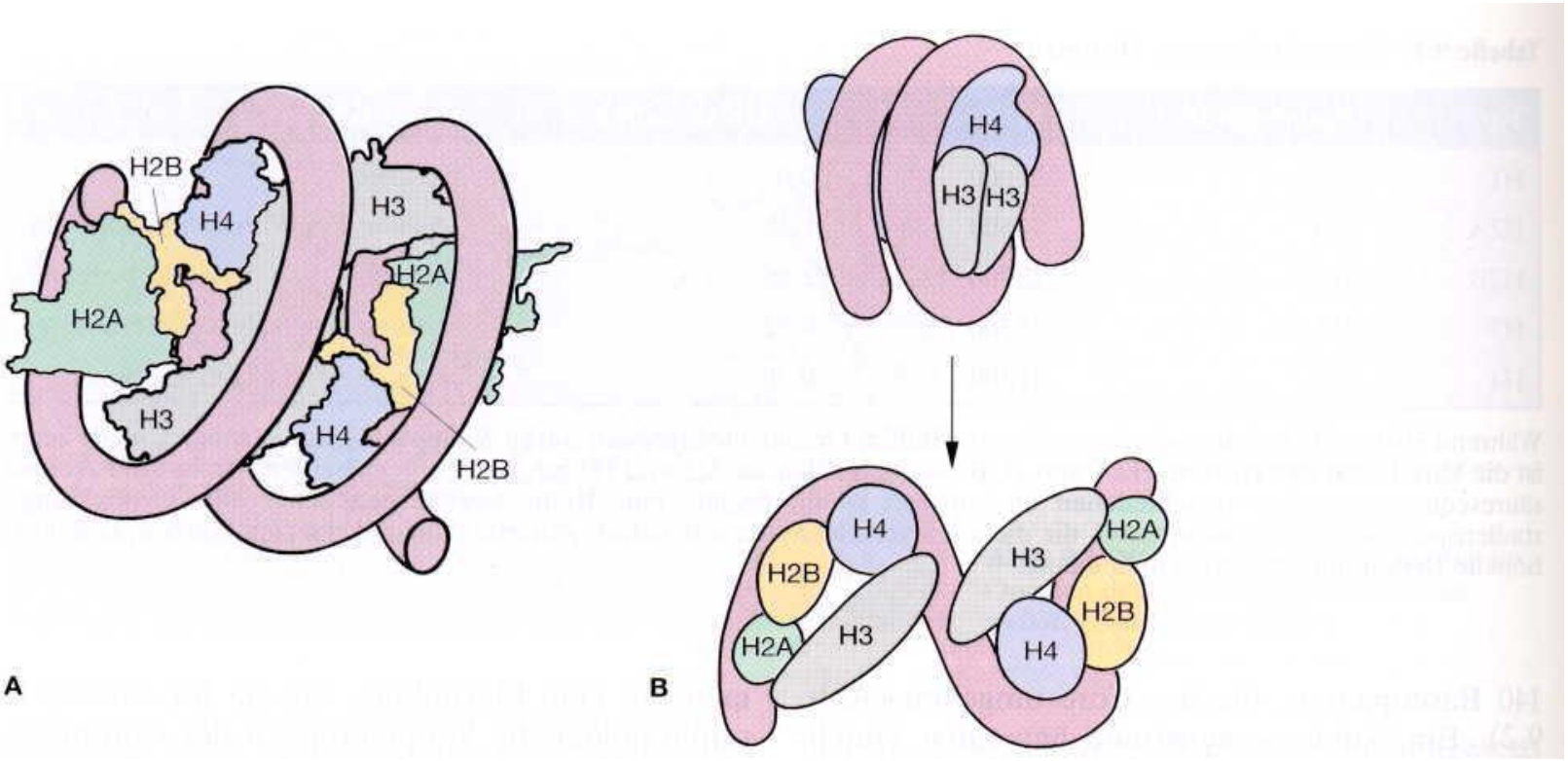
[a] Both genome size and chromosome number are for haploid cells.
Mb = millions of base pairs.

Taken from: G.M. Cooper, R.E. Hausman; THE CELL A Molecular Approach, 4th Edition; ASM Press





http://faculty.ccbcmd.edu/~gkaiser/SoftChalk%20BIOL%20230/Prokaryotic%20Cell%20Anatomy/proeu/proeu/proeu_print.html



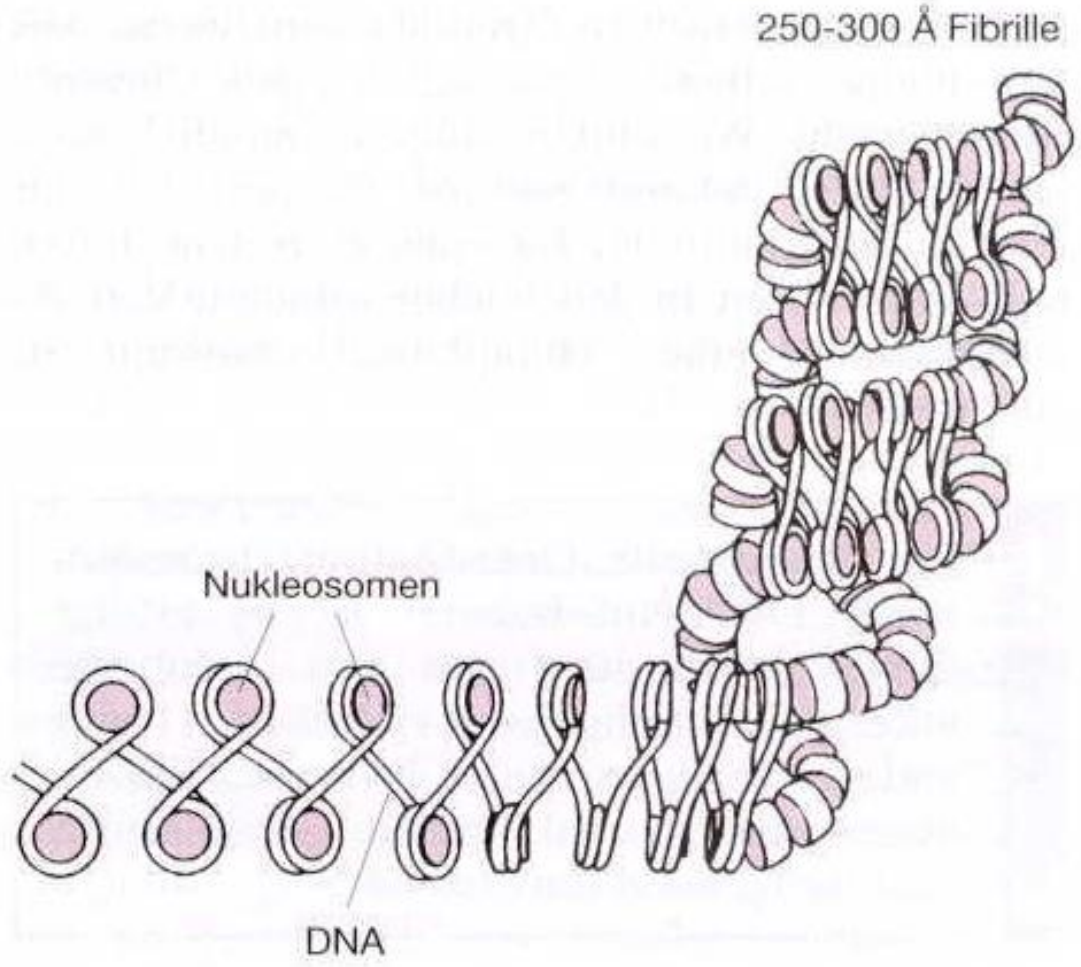
Structure of a nucleosome. A A single nucleosome with DNA: The DNA double helix winds twice around the protein core. The 8 different histone molecules are indicated (see Table 9.1). The histone core builds a symmetrical structure (an octamer made of 2 tetramers). The linkage number of DNA in the nucleosome is decreased causing a negative supercoiling. **B** Hypothetical model of nucleosomal structure during transcription. RNA polymerase cannot pass an intact nucleosome but demands a (at least partial) disintegration of the nucleosome. One of the models proposed assumes that the nucleosome disintegrates for a short time during transcription into two tetramers. A (Kornberg and Klug, 1981; B Prior et al. 1983)

Type	Amino acids	M_r	Lys/Arg ratio	Remarks
H1	215	21000	20,0	Variable
H2A	129	14500	1,25	Lysin rich, variability limited
H2B	125	13700	2,5	Lysin rich, variability limited
H3	135	15300	0,72	Arginine rich, very conserved
H4	102	11200	0,79	Arginine rich, very conserved

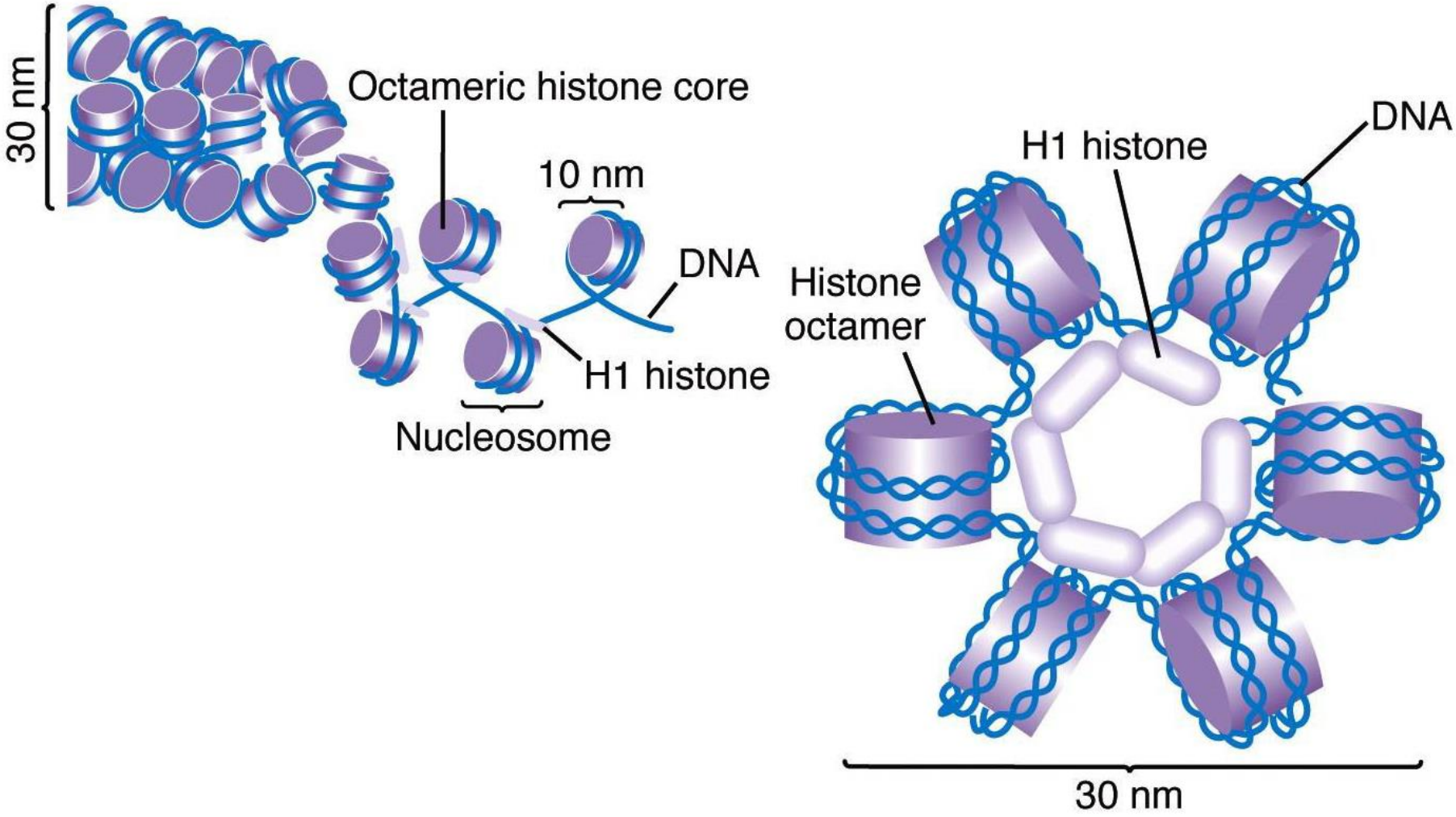
Quelle???

Nucleosomes in oocyte chromatin of *Pleurodeles waltlii* (from Scheer 1987)

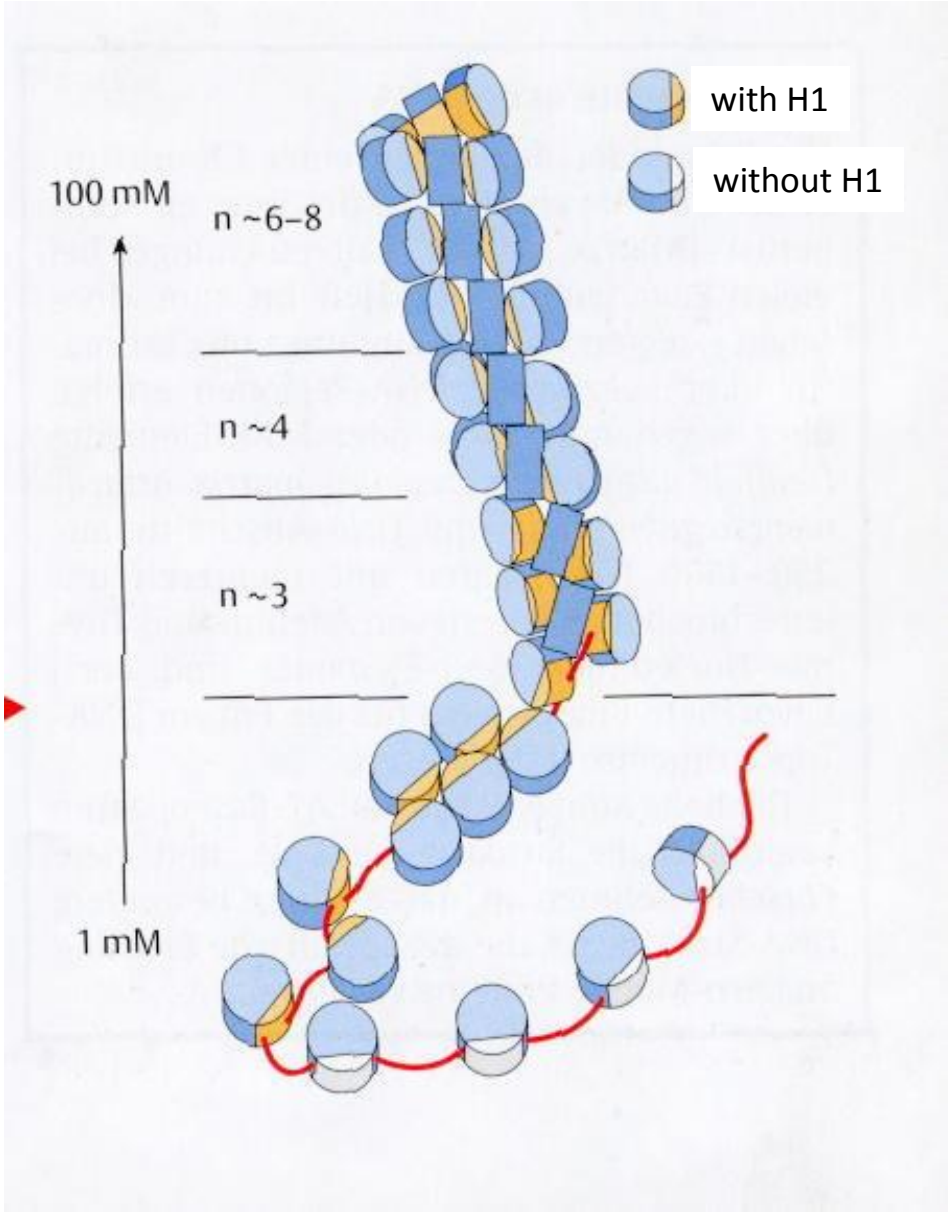
Quelle???



Model of a chromatid after partial unfolding of the nucleosome chain to the 300 Å fibril. Histone H1 molecules, connecting consecutive nucleosomes, are not shown. (according to Klug from Darnell et al. 1990)



https://beyondthedish.files.wordpress.com/2014/09/dna-solenoids.jpg


with H1
without H1
100 mM
n ~6–8
n ~4
n ~3
1 mM

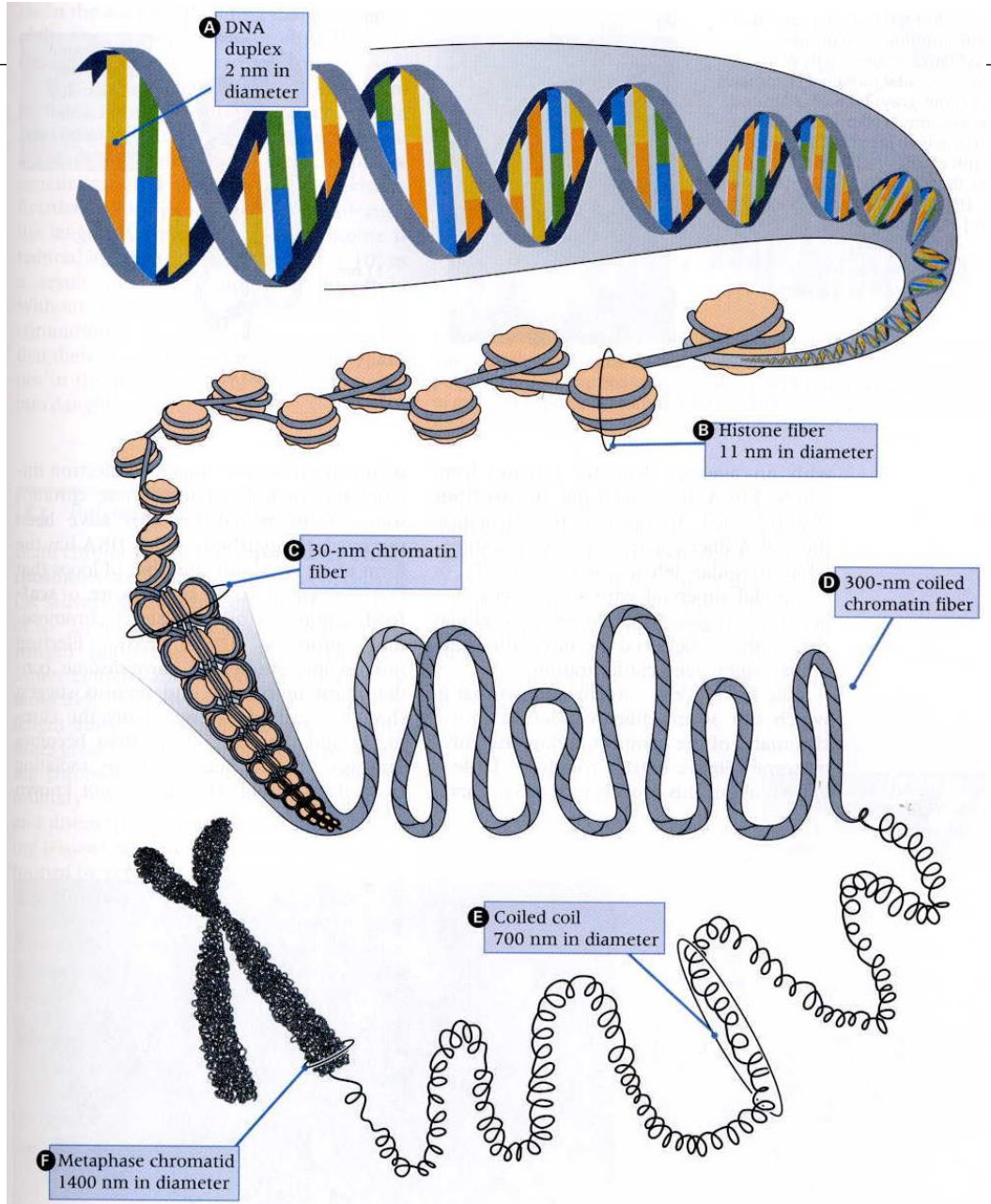
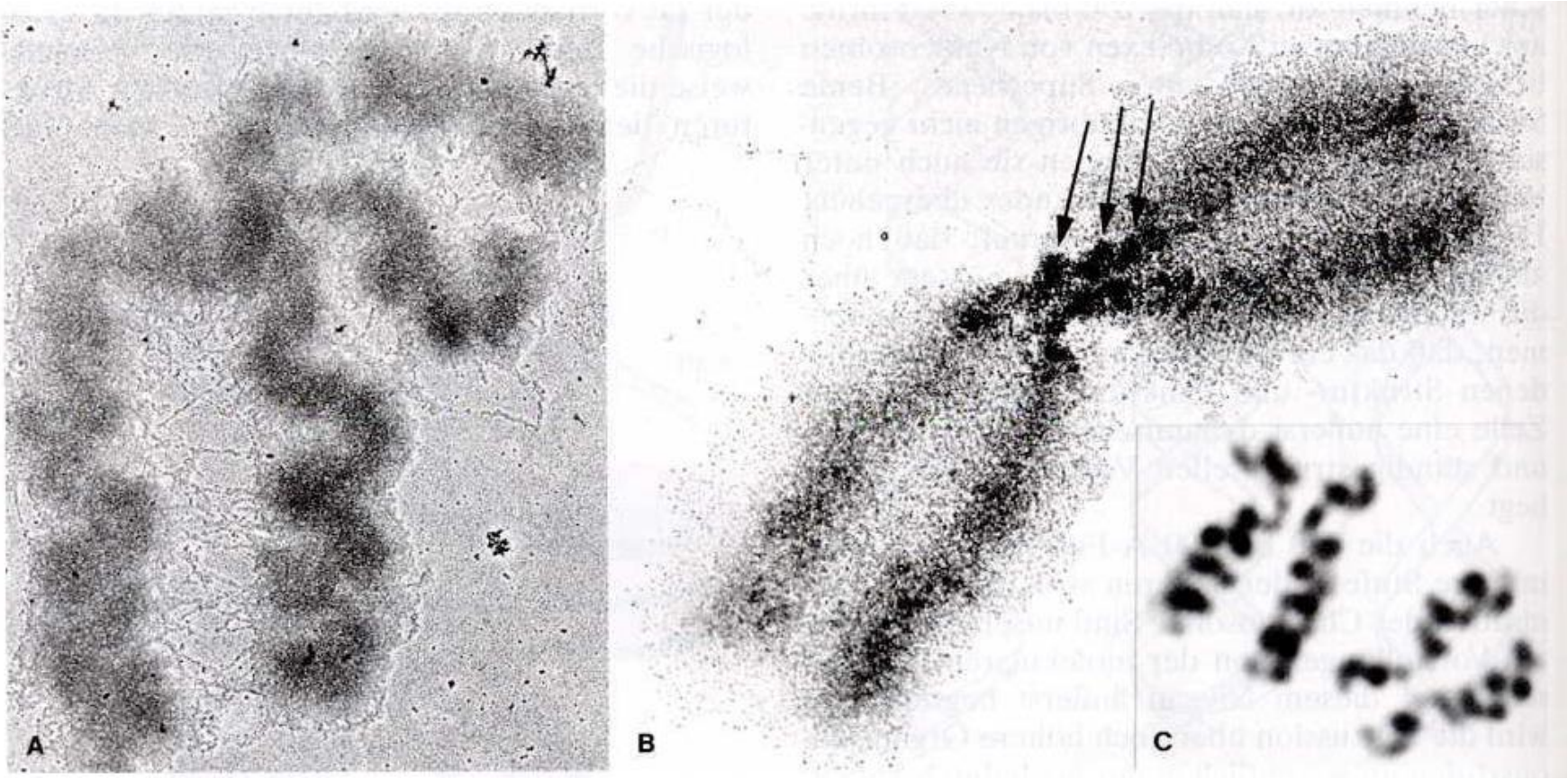


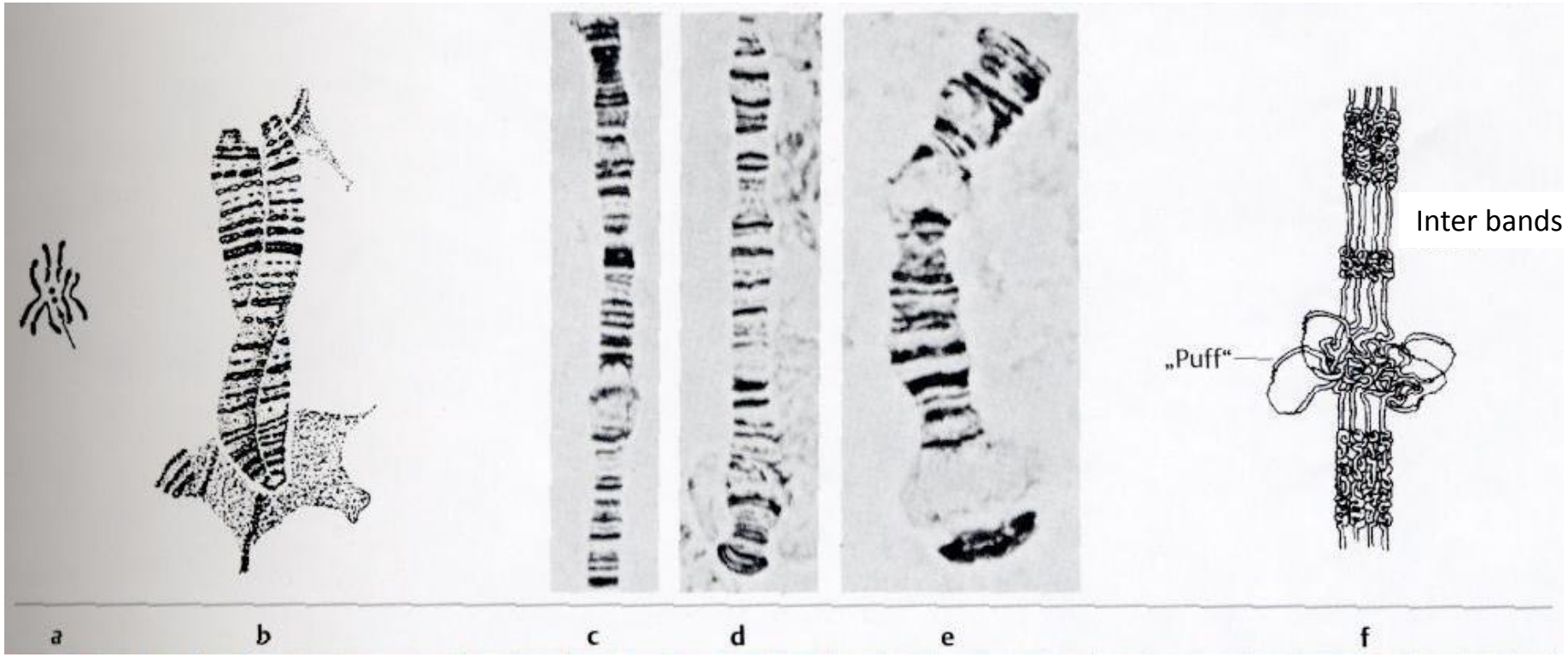
Figure 8.9 Various stages in the condensation of DNA (A) and chromatin (B through E) in forming a metaphase chromosome (F). The dimensions indicate known sizes of intermediates, but the detailed structures are hypothetical.

Taken from: Daniel L. Hartl & Elizabeth W. Jones, Genetics: Analysis of Genes and Genomes, 6th Edition, Jones and Bartlett Publishers



Structure of metaphase chromosomes.
A Submetacentric human chromosome from a cell line (COLO-320). The chromatid coils in the electron micrograph are easily visible. **B** Electron micrograph of a submetacentric chromosome from a mouse cell line (L929). Due to a special pre-treatment the coils in the centromere region are particularly clear. **C** The helical/spiral chromatid structure of human metaphase chromosomes (COLO-320) can be seen in a light microscope. (**A** and **C**: Rattner & Lin 1987a; **B** Rattner & Lin 1987b)

Giant Chromosomes



Amplified chromosomes present at specific stages of organisms (e.g. larvae of Insects

12.10.2015