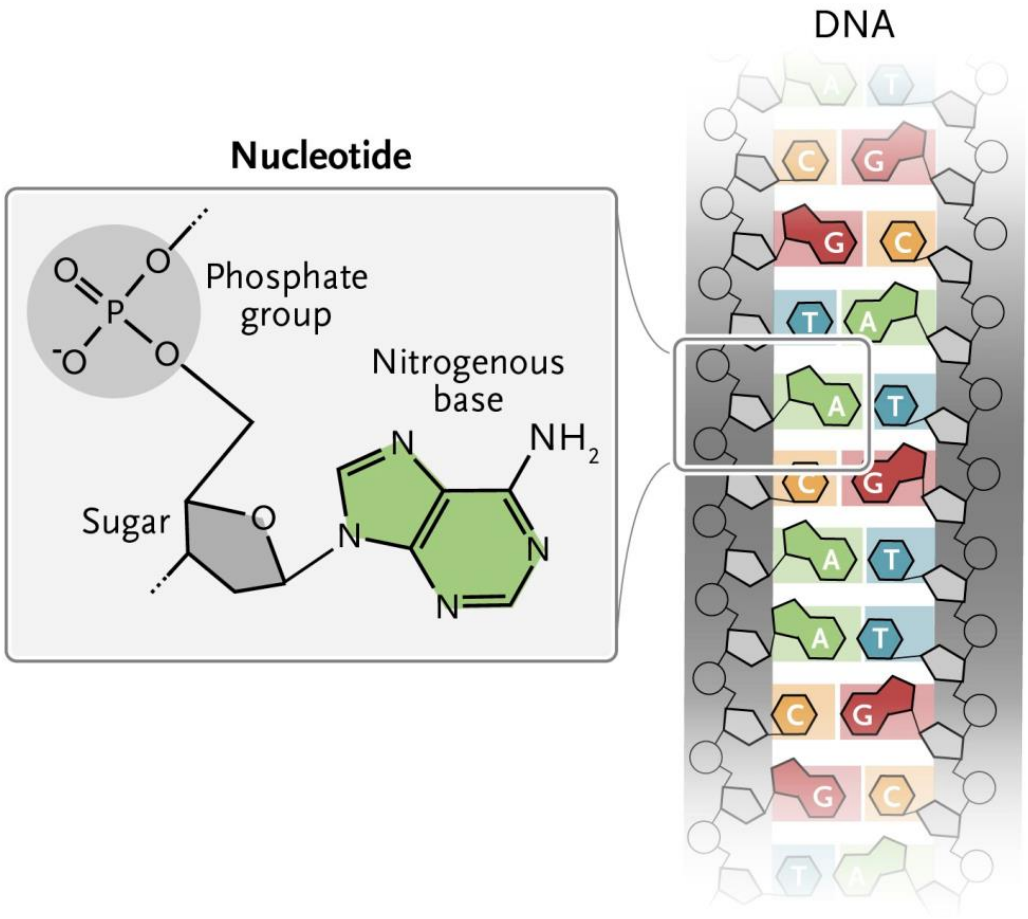
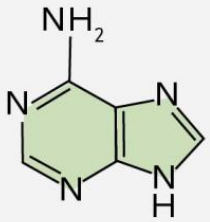
STRUCTURE OF DNA

THE DOUBLE HELIX

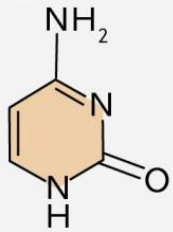


Nitrogenous bases

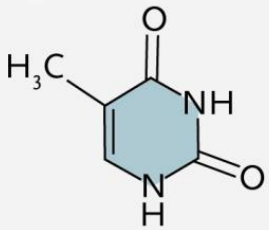
Adenine



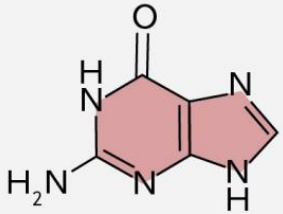
Cytosine



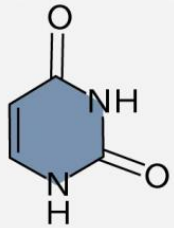
Thymine (DNA only)



Guanine



Uracil (RNA only)



Section 17.1: DNA

* Mendel discovered genetic traits but didn't know about DNA structure.

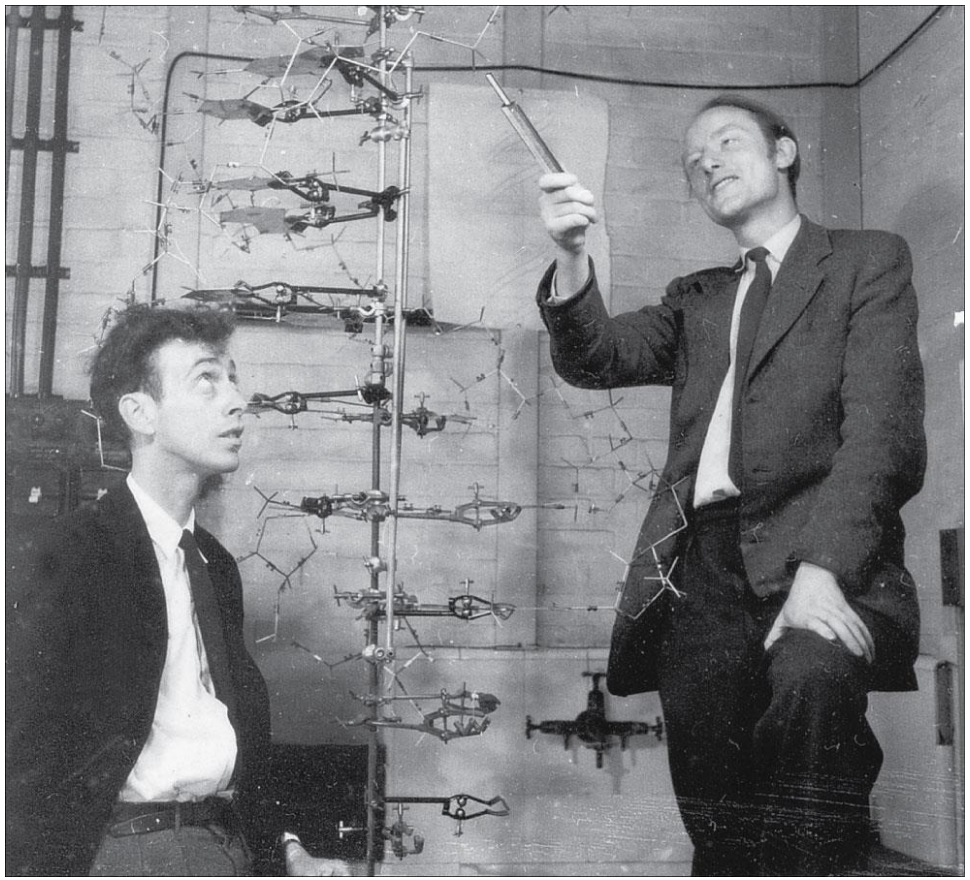


Figure 17.1 The First Complete Structural Model of DNA

- Chromosomes were also identified as the carriers of genetic information
- Deoxyribonucleic acid (DNA) was eventually recognized as the genetic information carrier
- DNA structure was elucidated in 1953 by James Watson and Francis Crick
  - **Molecular biology** emerged as a new science

Rosalind Franklin, 1920–1958

She has done the key expiriements that lead to discovery of DNA structure.

Maurice Wilkins, 1916–2004

Unnumbered 8 p288

Lehninger Principles of Biochemistry, Sixth Edition

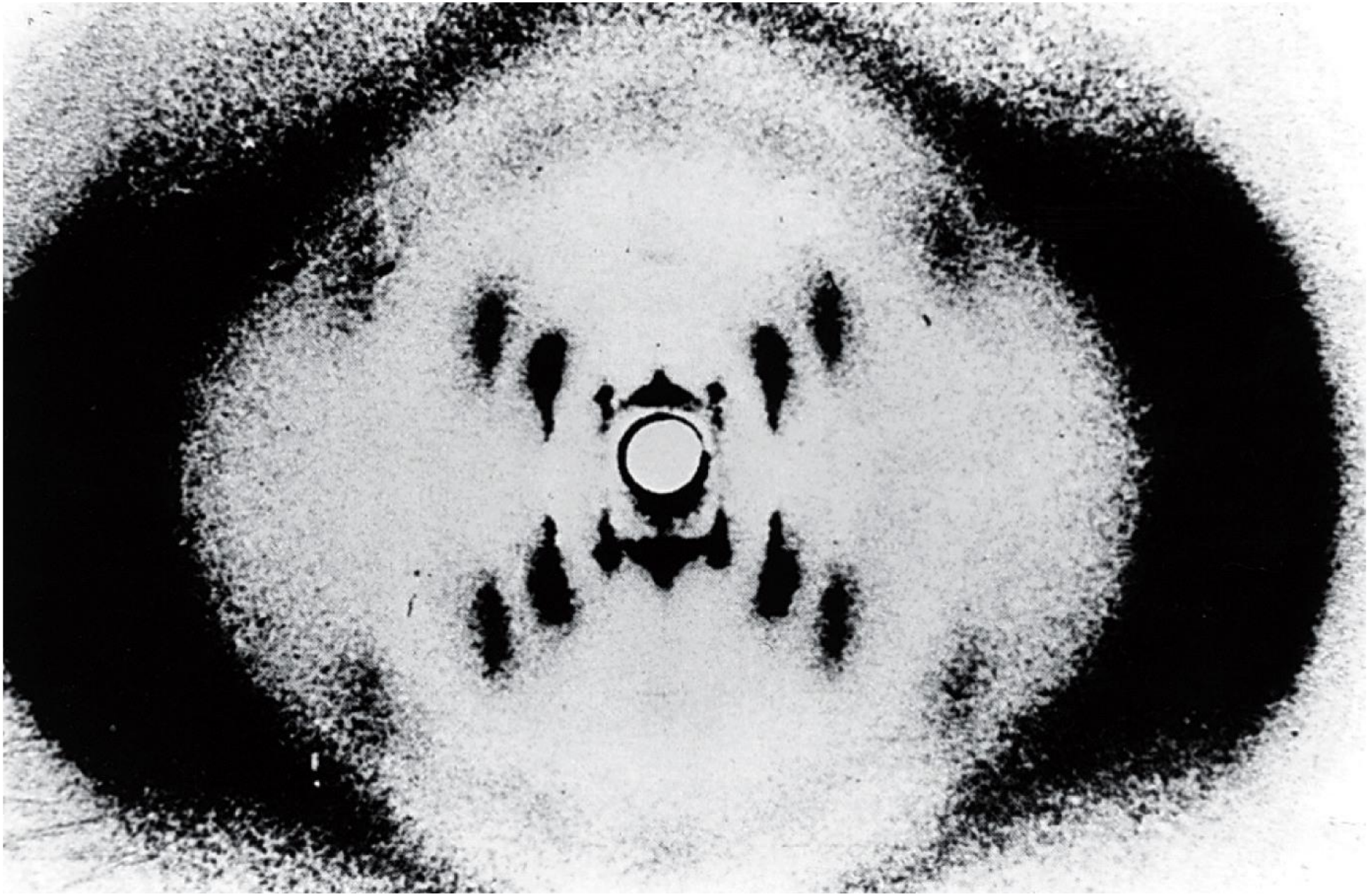


Figure 8-12
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X-ray Crystallography

- DNA is a relatively stable molecule with several noncovalent interactions adding to its stability

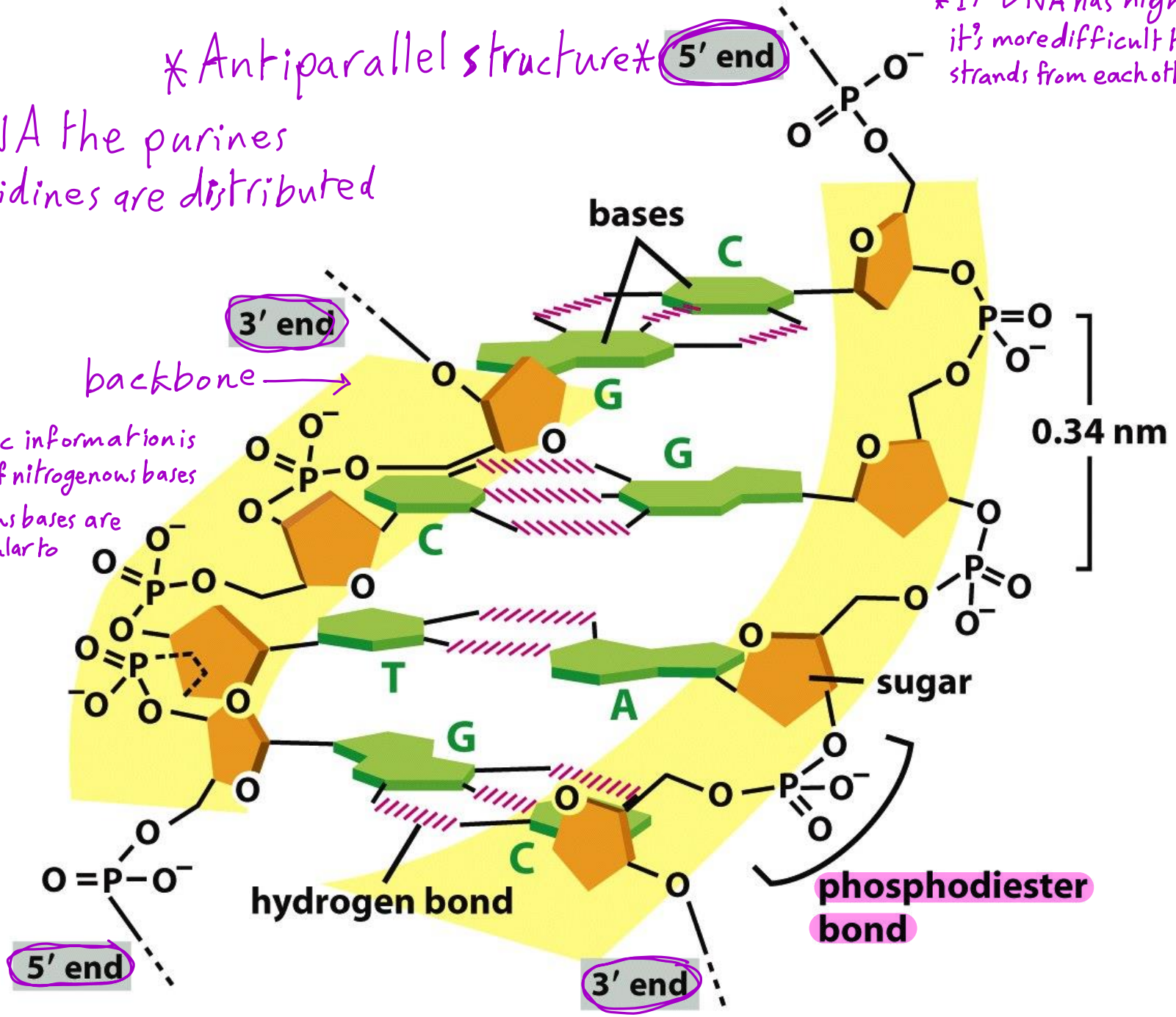
1. **Hydrophobic interactions**—internal base clustering
2. **Hydrogen bonds**—formation of preferred bonds: three between CG base pairs and two between AT base pairs
3. **Base stacking**—bases are nearly planar and stacked, allowing for weak van der Waals forces between the rings
4. **Hydration**—water interacts with the structure of DNA to stabilize structure
5. **Electrostatic interactions**—destabilization by negatively charged phosphates of sugar-phosphate backbone are minimized by the shielding effect of water on Mg^{2+}

They can propel each other.

* Antiparallel structure *

* If DNA has high C G content, it's more difficult to seperate the strands from each other.

* In DNA the purines & pyrimidines are distributed evenly.

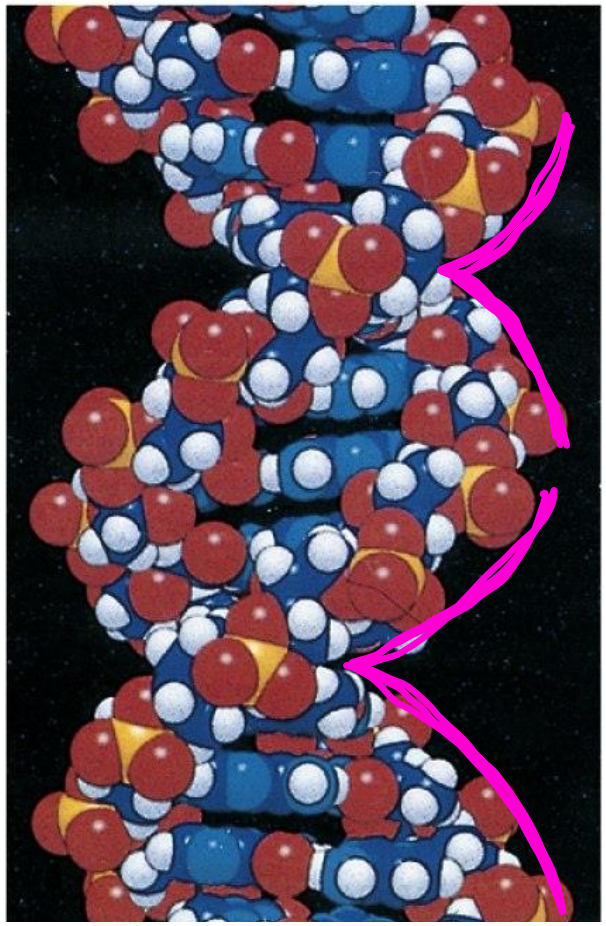


* The genetic information is the sequence of nitrogenous bases

* The nitrogenous bases are always perpindicular to the backbone

Figure 4-5b *Molecular Biology of the Cell* (© Garland Science 2008)

2 nm



minor groove

major groove

* These grooves play a major role in the action of many drugs

Many proteins involved in the process of DNA replication bind to this groove.

* other proteins help the very long bacteria DNA to fit inside the cell.

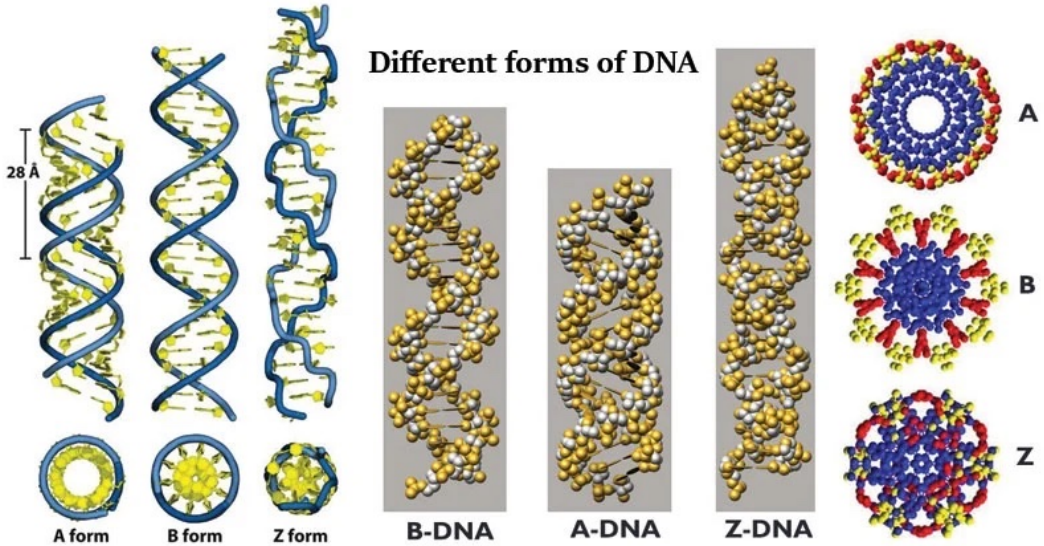


Figure 4-5a *Molecular Biol*

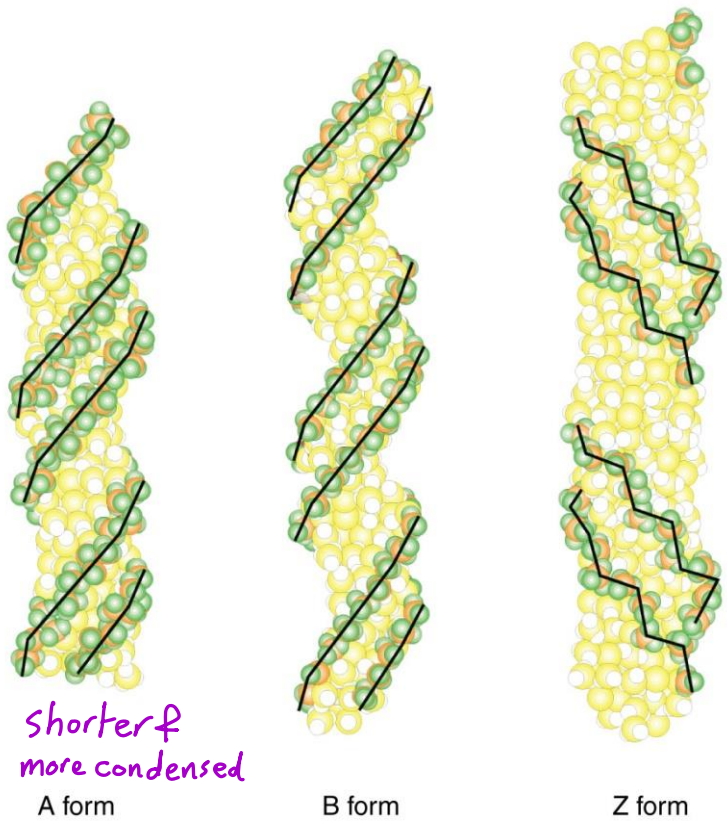
DNA Conformations

- The DNA double helix can ~~exit~~ exist in various forms
- In cells, double-stranded DNA generally adopts a conformation called B-DNA, whose helical structure repeats itself approximately every 10.5 bp as one looks along the double helix
- DNA can also adopt other helical conformations. For example, A-domain which has 11-bp per turn with the base pairs tilted relative to the DNA axis. Although A-DNA differs in several details from B-DNA, they are both right-handed helices

  ↳ Physiological form

  bio
- Z-DNA – an unusual form of DNA helix that spirals in the opposite direction, and is therefore left-handed. This conformation of DNA can form under special conditions *(in vitro)* in DNA strands with alternating G and C bases. Formation of Z-DNA is favored by a chemical modification of cytosine, methylation, and high salt concentrations

  ↳ Transient

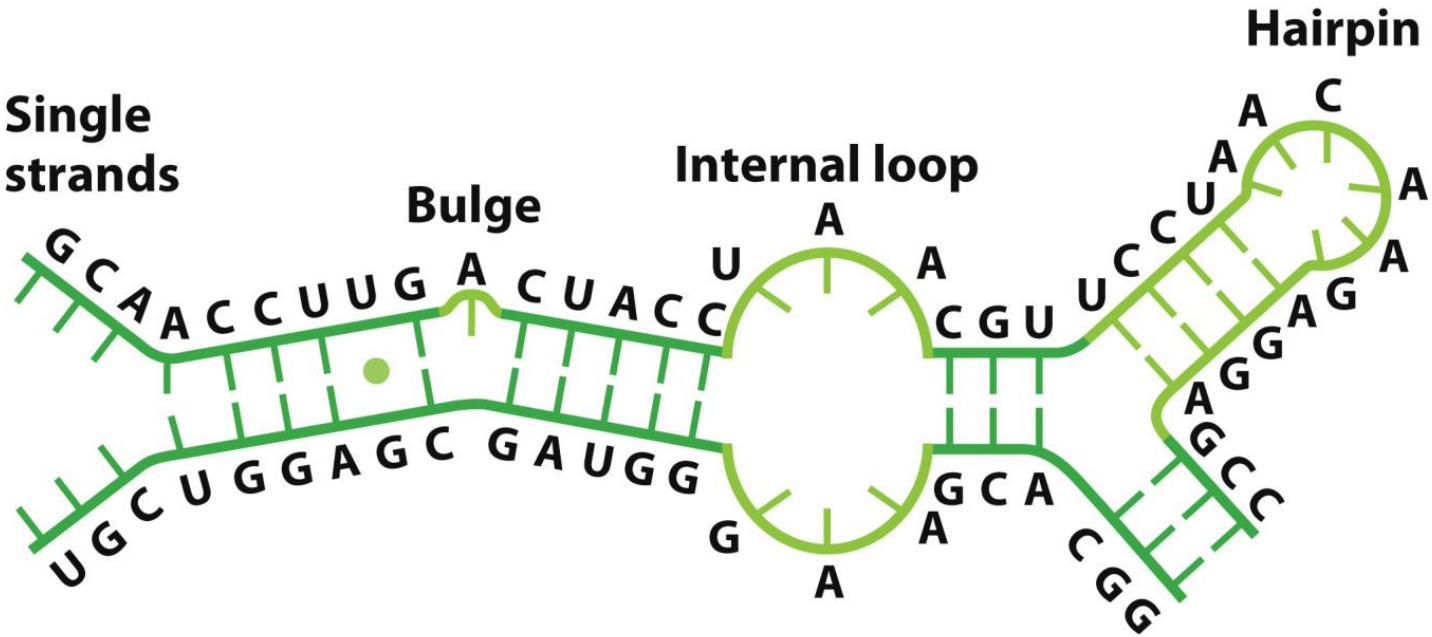


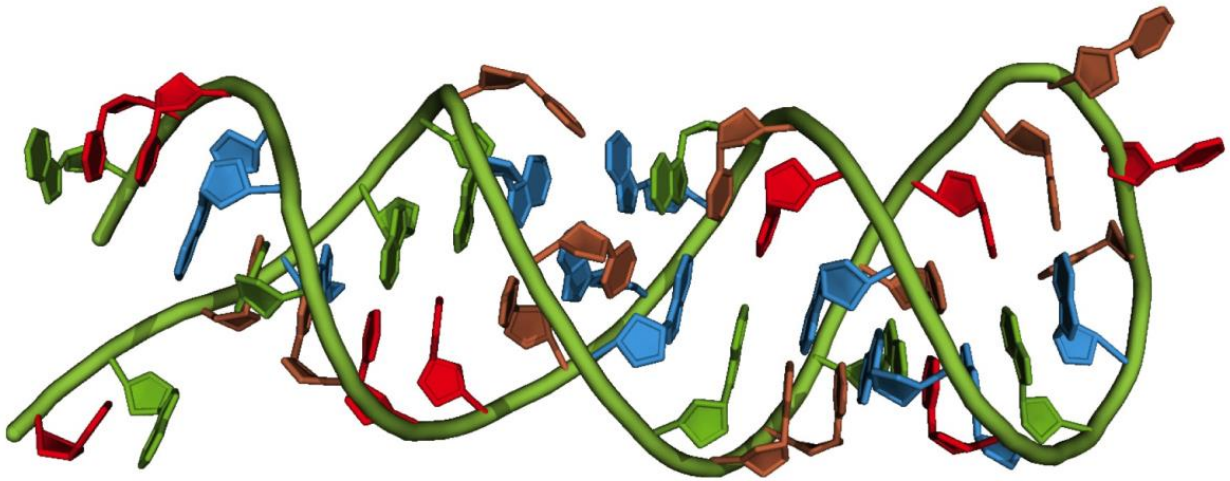
shorter & more condensed

Figure 17.10 A-DNA, B-DNA, and Z-DNA

DNA Structure: Variations on a Theme

- Watson and Crick's discovery is referred to as **B-DNA** (sodium salt)
- Another form is the **A-DNA**, which forms when RNA/DNA duplexes form
- **Z-DNA** (zigzag conformation) is left-handed DNA that can form as a result of torsion during transcription* * not important in the function of DNA, but you can see it in test tubes.





Hairpin double helix

(b)

Figure 8-23
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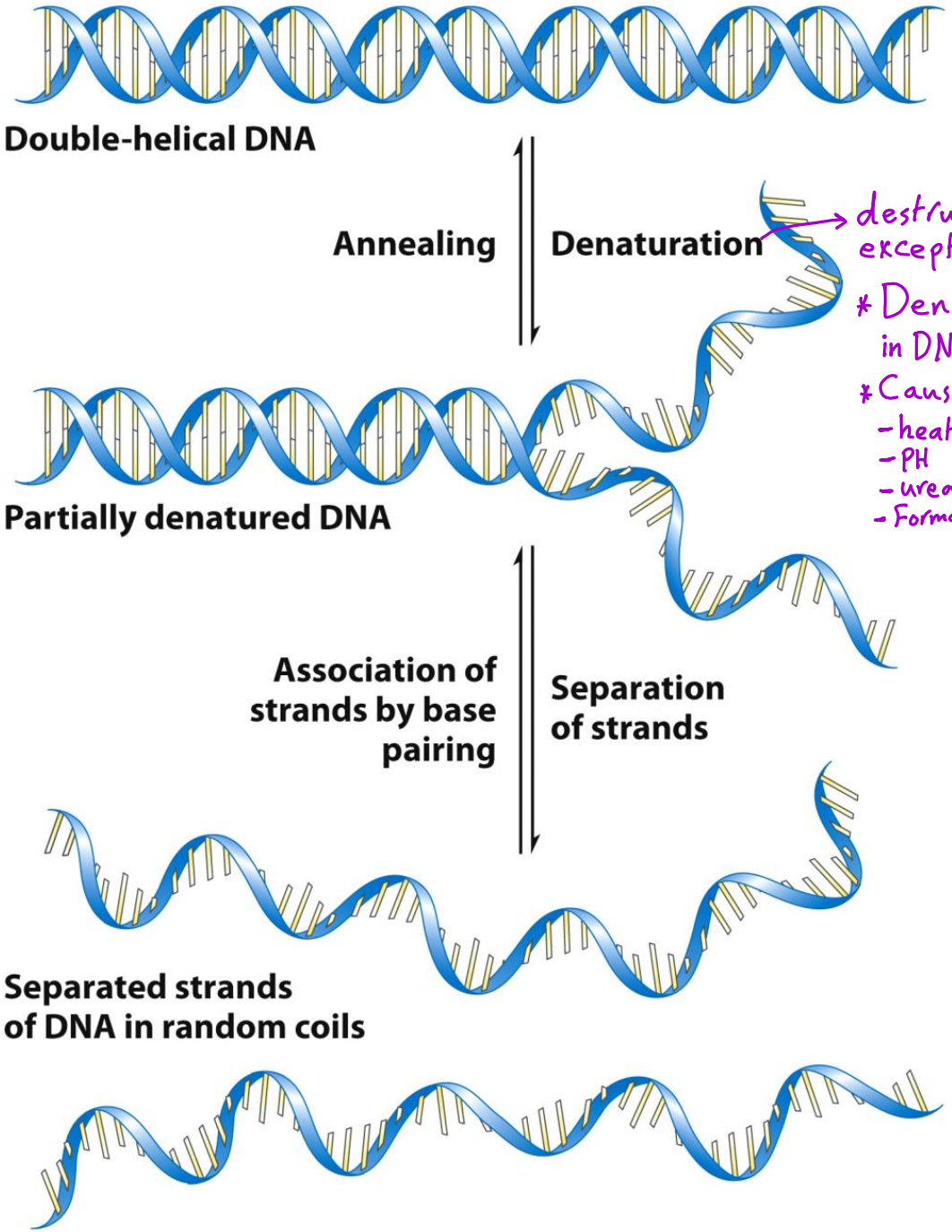

destruction of all bonds except the primary bonds.

* Denaturation is reversible in DNA & irreversible in Proteins.
* Causes of denaturation:-
  - heat
  - PH
  - urea
  - Formaldehyde

Figure 8-26
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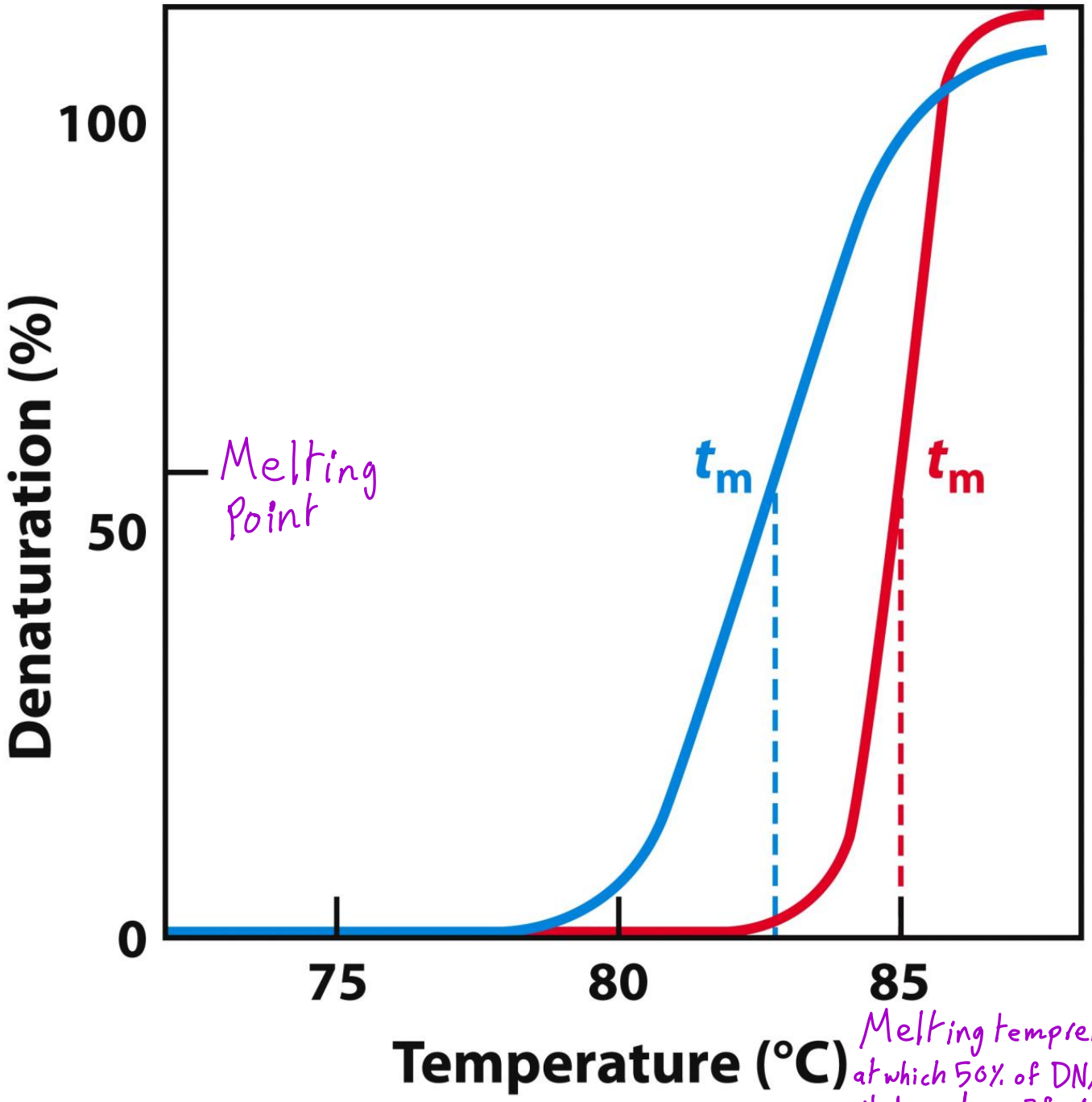

Melting tempreture: the tempreture at which 50% of DNA length is denatured, it depends on 3 factors:-
- PH - electrons present - type of base pairing

Figure 8-27a
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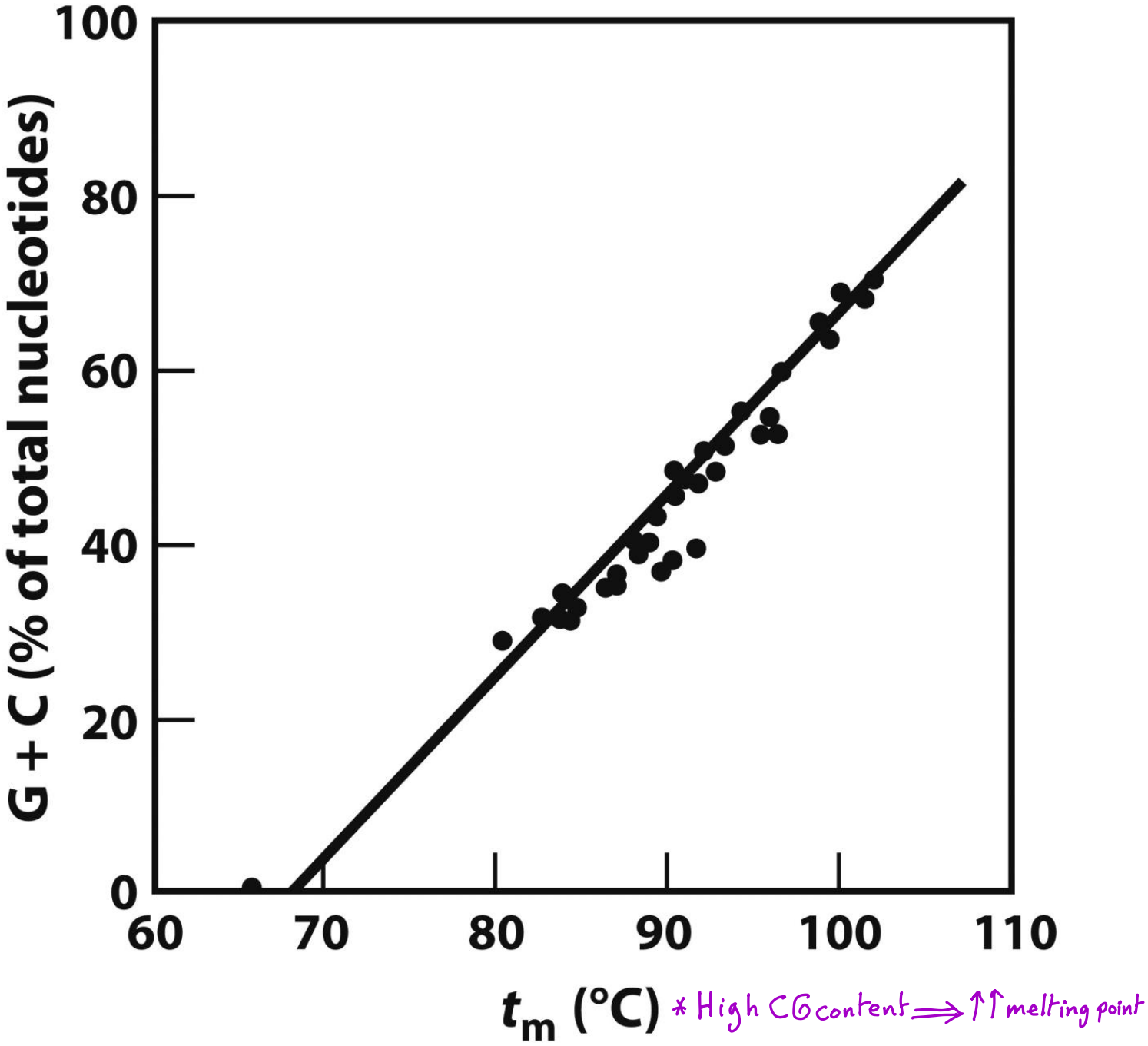

Figure 8-27b
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- **DNA Supercoiling**
  - Facilitates several biological processes: packaging of DNA, replication, and transcription
  - Linear and circular DNA can be in a relaxed or supercoiled shape

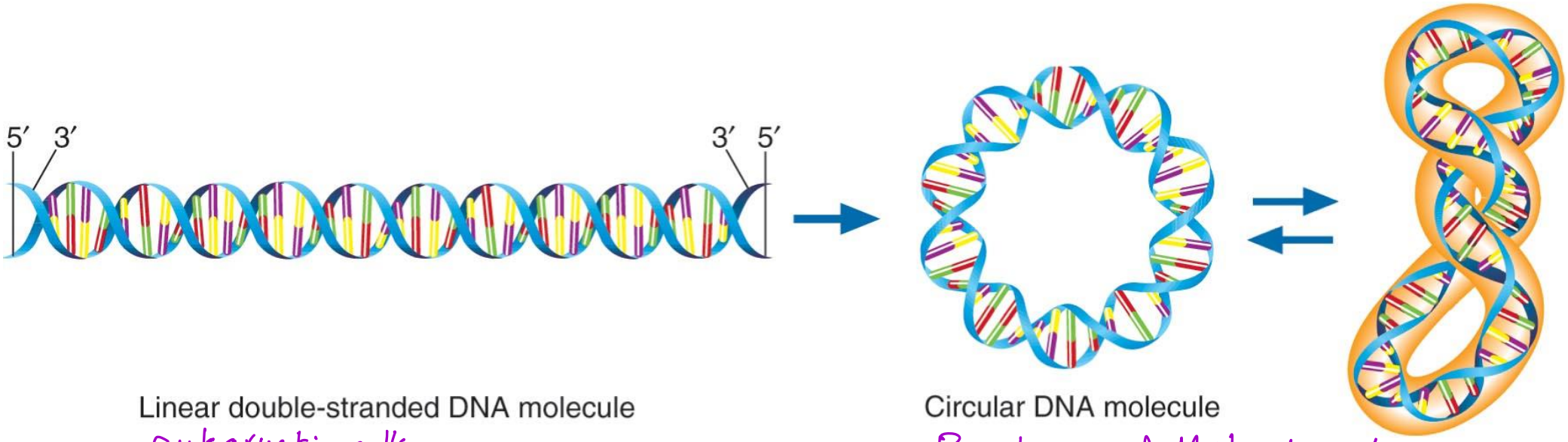
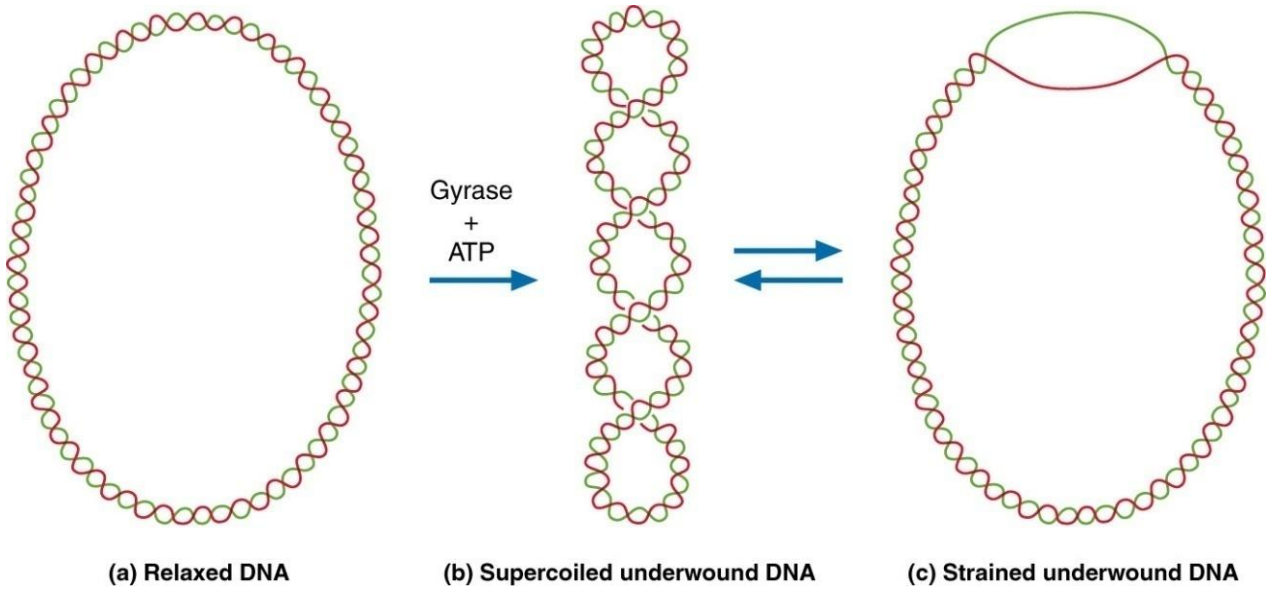


Figure 17.11 Linear and Circular DNA and DNA Winding

Figure 17.13 Effect of Strain on a Circular DNA Molecule



- This stored energy facilitates strand separation in replication and transcription

- Supercoiling that forms during strand separation can be relieved by a class of enzymes called **topoisomerases**
  - Make reversible cuts that allow the supercoiled segments to unwind

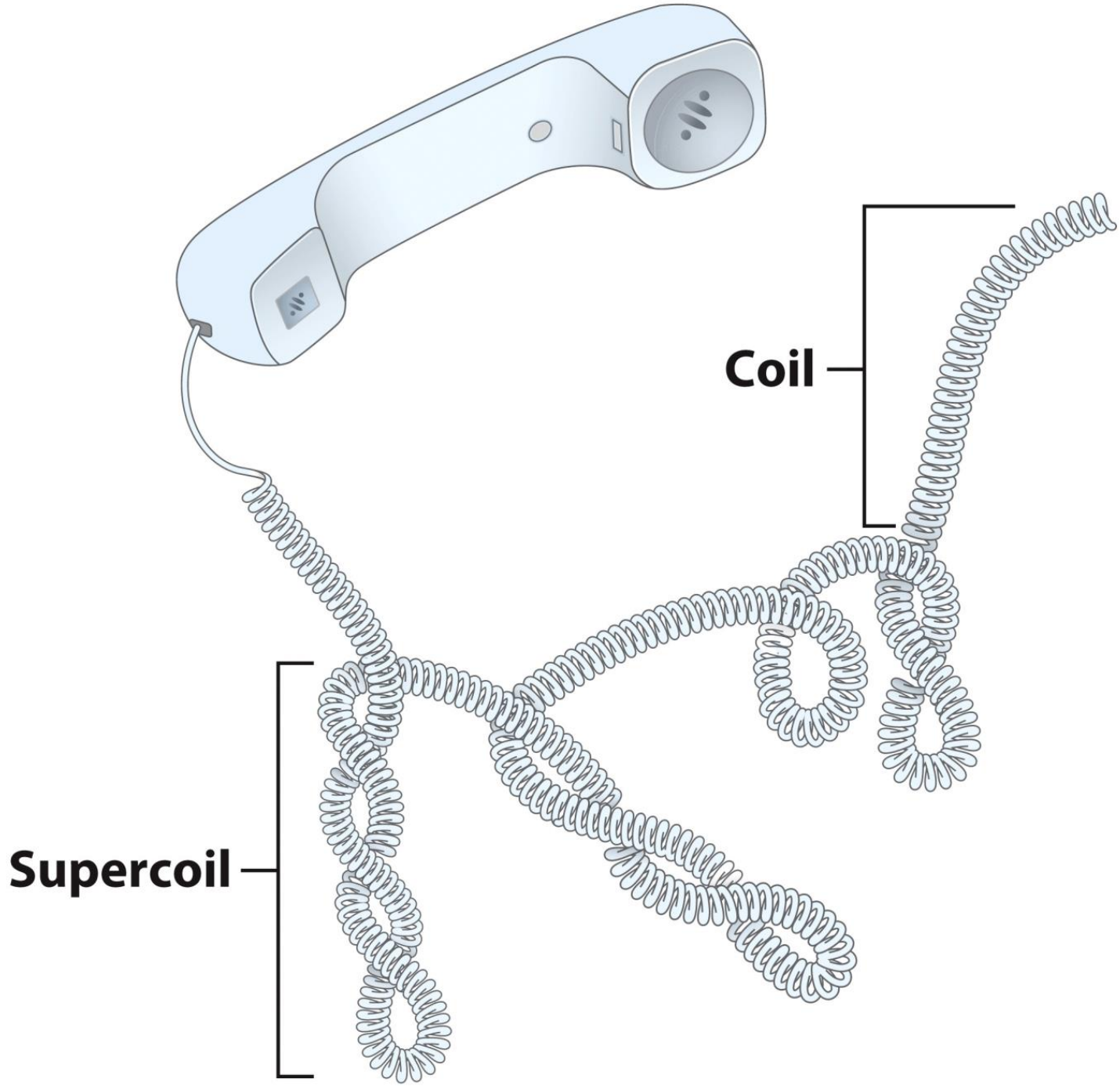


Figure 24-9
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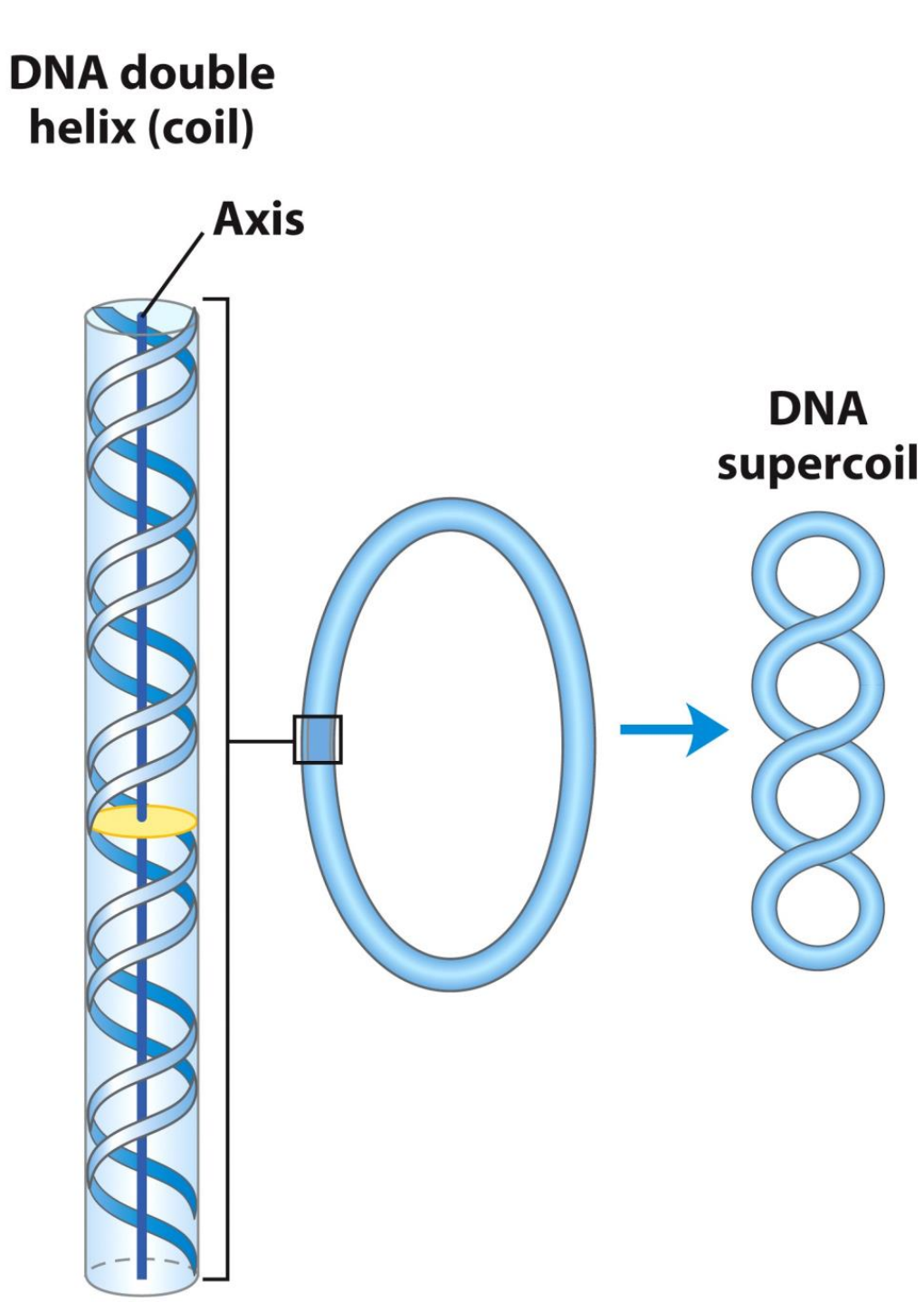

Figure 24-10
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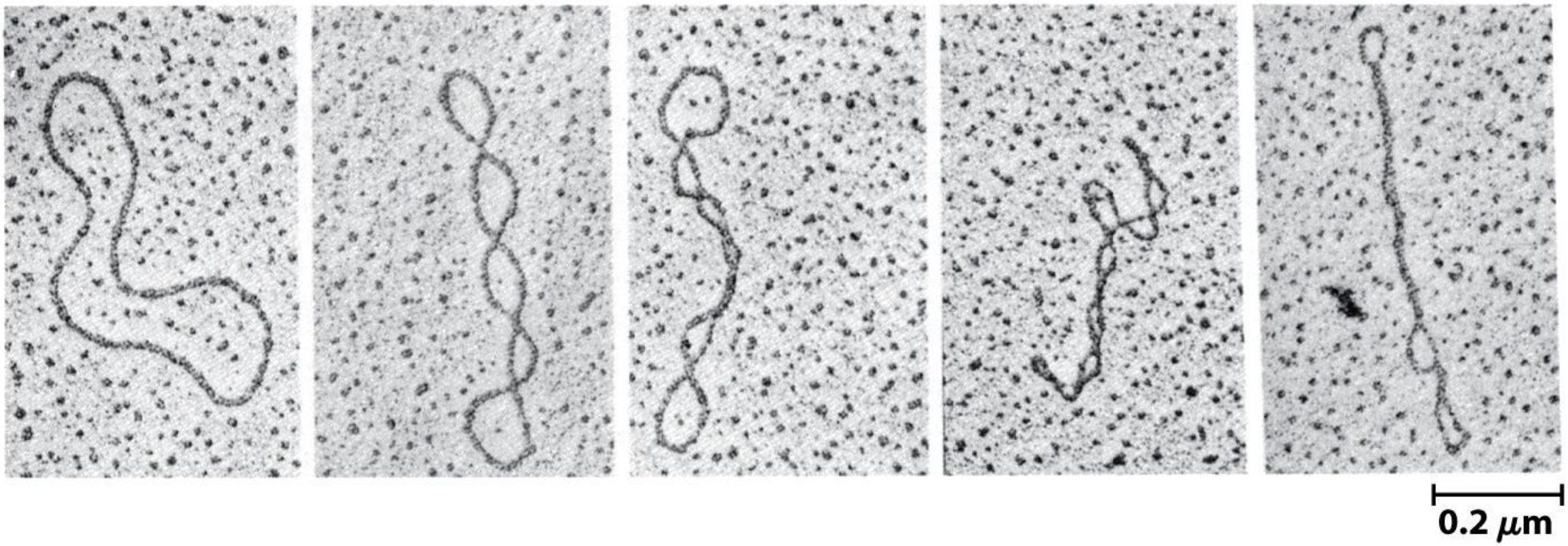

Figure 24-12
Lehninger Principles of Biochemistry, Sixth Edition

- Negative supercoiling – local unwinding of DNA (in a clockwise direction). Negative supercoils can be removed by unwinding one or more turns of DNA (which is equivalent to separating the strands).

- Positive supercoiling - an initial twisting of DNA in a counterclockwise direction. Positive supercoiling can also occur in linear fragments of DNA in which the ends are immobilized, and therefore are not free to rotate and release super-helical tension.

- Supercoiled DNA is under torsional strain (that is, there is tension in the molecule). If a nick or break is introduced into a supercoiled plasmid or chromosome, one end will swivel around the other to relax the supercoiling, and hence alleviate the strain on the DNA molecule

- Circular DNAs found in nature (e.g., mitochondrial, viral, bacterial) are invariably negatively supercoiled. Supercoiling is not restricted to small, circular DNAs but also occurs in linear, eukaryotic DNA

Type 1: cuts 1 strand of DNA

Type 2: cuts 2 strands of DNA

TOPOISOMERASES

help alleviate/relax the supercoils ← p8

highly expressed in cancer cells

ENZYMES THAT CAN RELAX SUPERCOILED DNA

Topoisomerase Inhibitors

- Important pharmaceutical agents for treating disease

- Antibiotics – coumarins, including novobiocin and courmermycin A1, are natural products derived from *Streptomyces* species. They inhibit ATP binding of the bacterial type II topoisomerases, DNA gyrase and topoisomerase IV (not often used for treating infections in humans)

- Quinolone antibiotics – inhibit bacterial DNA gyrase and topoisomerase IV. The broad-spectrum antibiotic ciprofloxacin (a fluoroquinolone) is one of the few antibiotics reliably effective in treating anthrax infections
  - ↳ produces spores
  - ↳ can be used as a bioweapon

- Important chemotherapeutic agents used in cancer treatment. Inhibitors of both type I and type II topoisomerases have been developed as an anticancer drugs

- Topoisomerases are generally present at elevated levels in tumor cells, and agents targeted to these enzymes are much more toxic to the tumors than to most other tissue types

- Camptothecin, isolated from a Chinese ornamental tree (tested clinically in the 1970s), is an inhibitor of eukaryotic type I topoisomerases. Camptothecin and related drugs trap the topoisomerase-DNA complex leading to DNA cleavage, and inhibition of religation

Some normal cells will also be affected.

- Doxorubicin (anthracycline) – type II topoisomerase inhibitor, effective against several kinds of human tumors