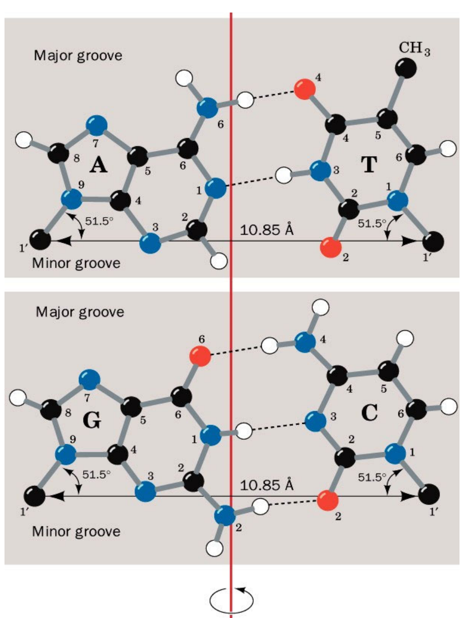
Outline: Chapter 24, Part I

1. Review: nucleic acid structure
2. DNA topology: physical properties of DNA in living cells (Ch 24.2)
3. Chromosome structure (Ch 24.3)

Review: nucleic acid structure



H-bond donors and acceptors

AT and GC base pairs are "isosteric"

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DNA is a very large macromolecule

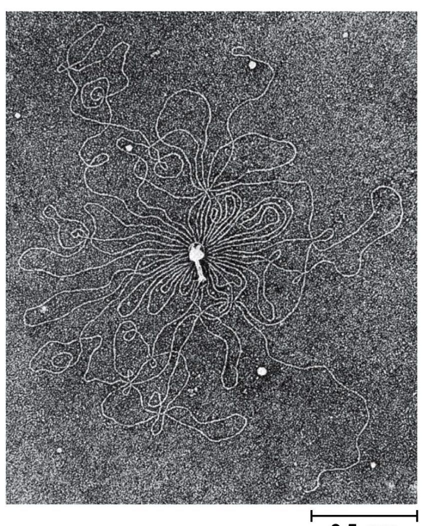

Figure 24-1
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T2 phage DNA from phage particle: A space problem!

Humans even worse:
2 m DNA packed into
5 μm nucleus

How does it all fit?

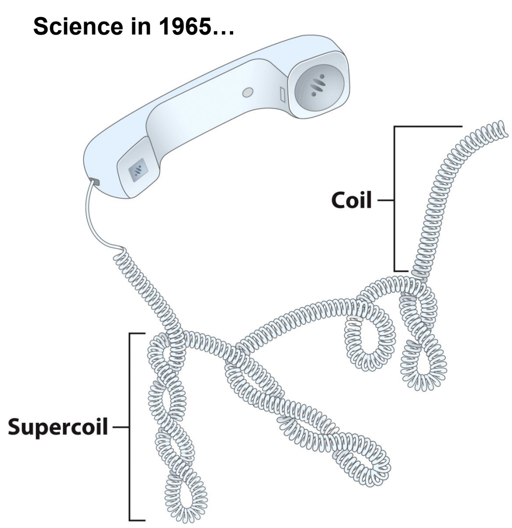
DNA supercoiling

DNA structure: opposing demands
- Compact
- Dynamic/Accessible

Supercoiling is the key
- Supercoiling allows for these two demands to be satisfied simultaneously

Supercoiling is a physical property of DNA-
- EVEN in vitro!

Supercoiling: coils of coils



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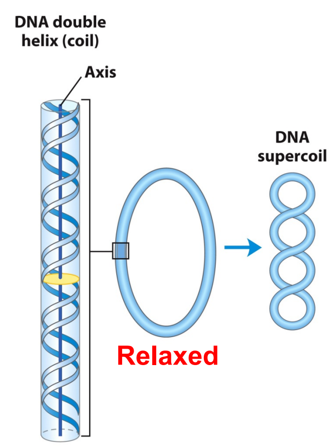

Figure 24-10
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Supercoiling is a manifestation of strain

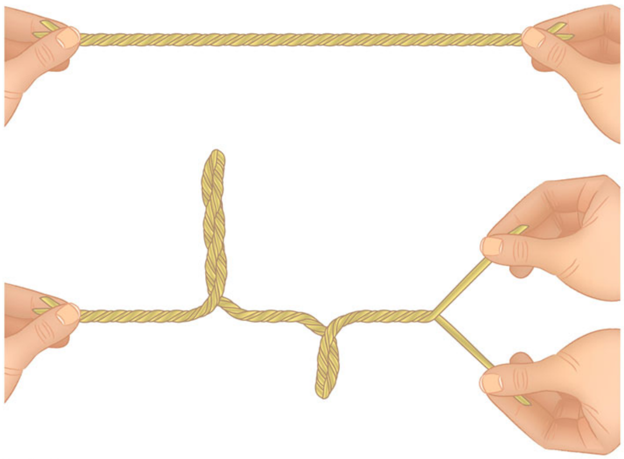
Figure 24-11a
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How to relieve strain?

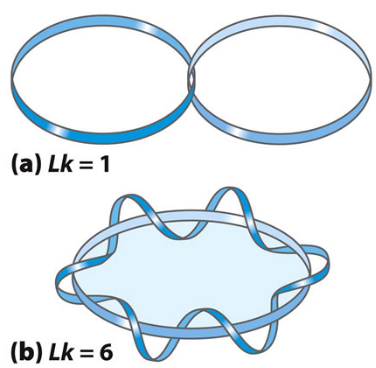
Supercoiling described by DNA Topology

Mathematical descriptions of coiled structures: Lk = Tw + Wr

Key parameter: Linking number (Lk, L, α)
Linking number:
Number of times one strand wraps around the other

Approximation that works for relaxed DNA:

bp / #bp per turn= Lk



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Supercoiling described by DNA Topology

Lk can be used to determine superhelical density (σ) relative to relaxed state:

$$\sigma = \frac{\Delta Lk}{Lk_0}$$

difference in number of turns- supercoiled vs relaxed
$Lk - Lk_0$

If σ is negative: "negative supercoil"= underwound

If σ is positive: "positive supercoil" = overwound

If break either strand: supercoiling gone, Lk is undefined

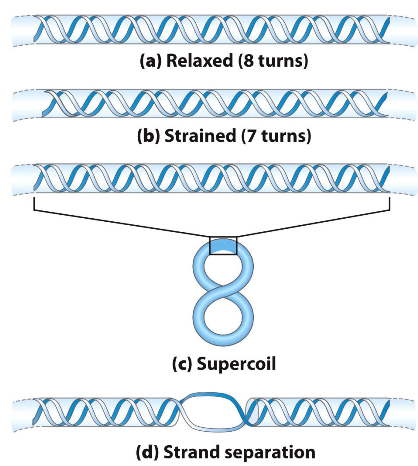
Biological importance of DNA topology

Fact: most cellular DNA is net negatively supercoiled
σ = -0.05 to -0.07

Does not look like (d) in cell.

But- Strand separation is easier:

Why is this important??



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Biological processes affect DNA topology

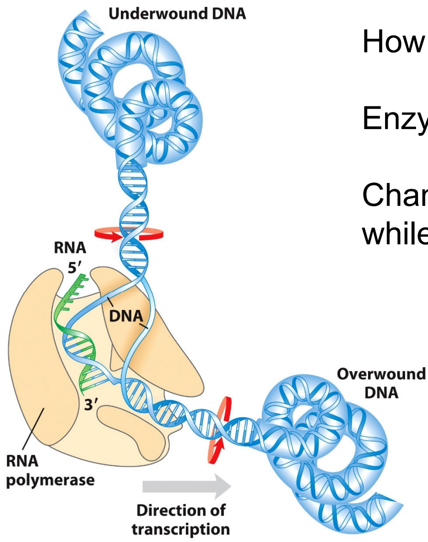

Figure 24-11b
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How do cells control topology?

Enzymes called Topoisomerases

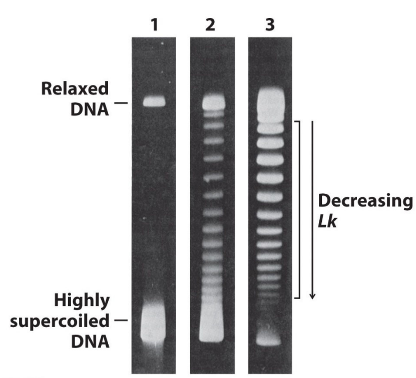
Change Lk by breaking strands while holding on to ends

Topoisomerases

Two types:

- Type I- change Lk in increments of 1 (break one strand)

- Type II- change Lk in increments of 2 (break both strands)



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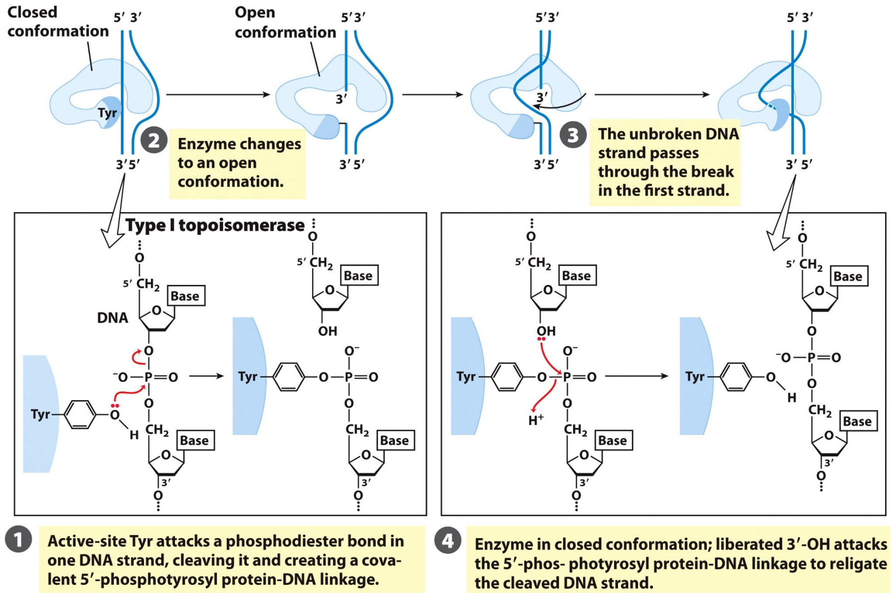
Treat supercoiled DNA with Topoisomerase I (lanes 2 and 3)- Relaxes DNA

Mechanism of bacterial topoisomerase I



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Topoisomerases have specific functions

***E. coli*:**

Type I:

relax DNA (remove supercoils- Lk → Lk_0)

Type II (DNA gyrase):

introduce negative supercoils (decrease Lk)
requires ATP

Eukaryotic cells:

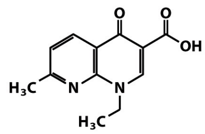
Type I:

same reactions as *E.coli*

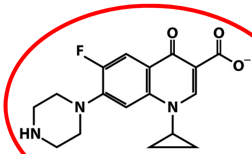
Type II:

relax supercoil or introduce positive supercoil
can NOT introduce negative supercoil!

Inhibitors of topoisomerases: Antibacterial activity

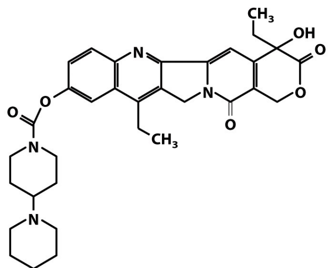


Nalidixic acid

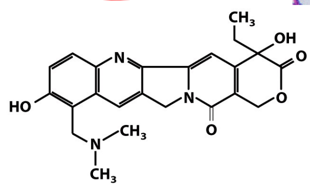


Ciprofloxacin

Bacillus anthracis



Irinotecan



Topotecan

Box 24-1 part 1
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WorldNetDaily- Oct. 24, 2001
"BIOLOGICAL WAR-FEAR
Saved from anthrax, sick from Cipro?"
Side effects could hit runners, coffee-drinkers, kids, elderly hardest

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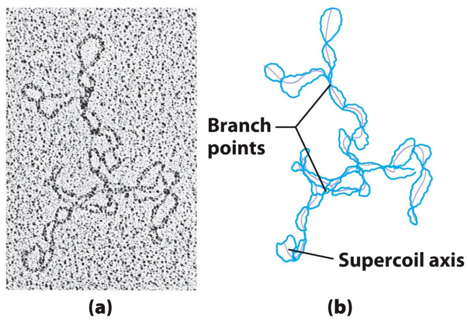
Chromosome Structure

How does supercoiling satisfy our 2 demands?
1) Dynamic/Accessible- negative supercoiling
2) Compact- solenoidal supercoiling (vs plectonemic)



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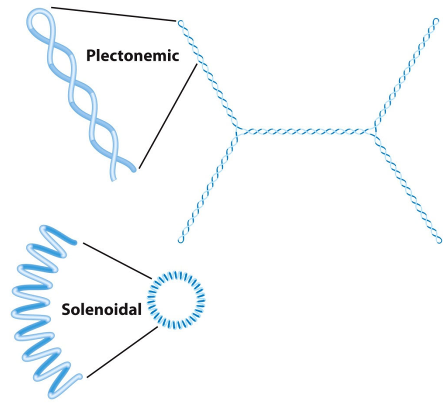

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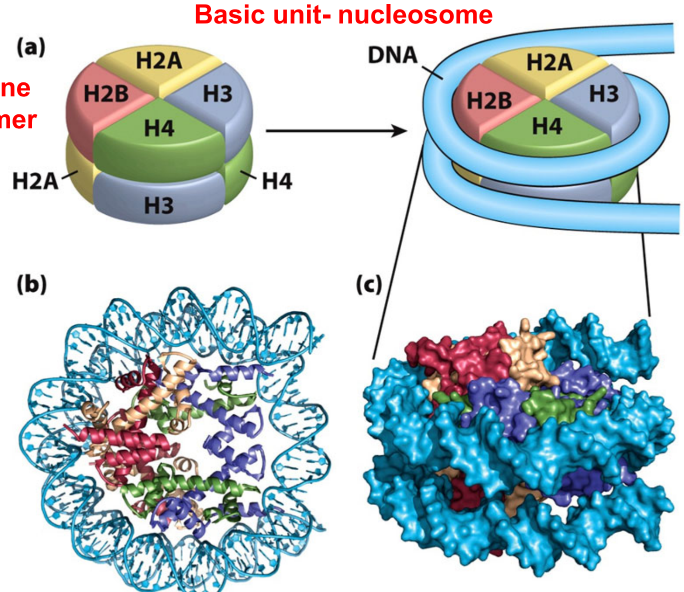
Eukaryotic chromosome structure: chromatin

Basic unit- nucleosome

Histone octamer



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How is net negative supercoiling achieved in eukaryotes?

Nucleosomes are packed into higher order structures

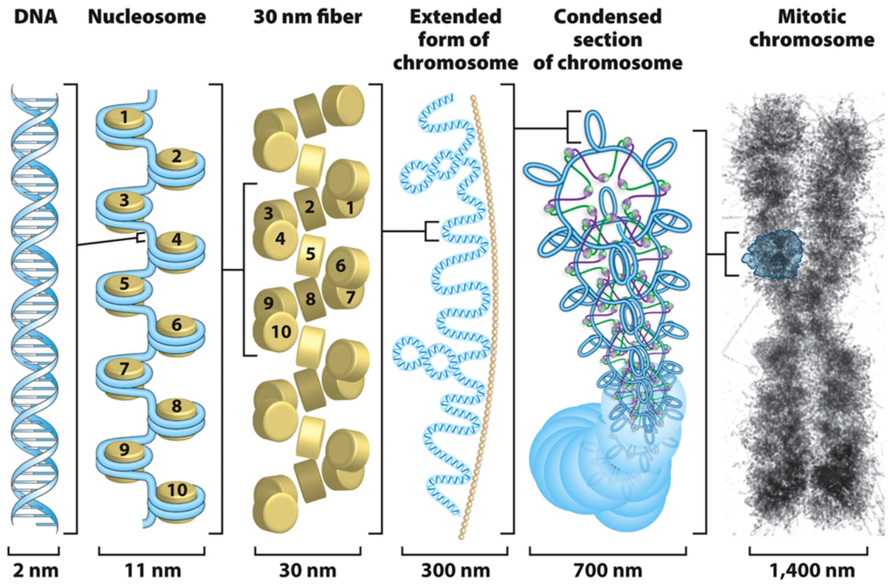

Figure 24-31
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Histone tails are involved in communication

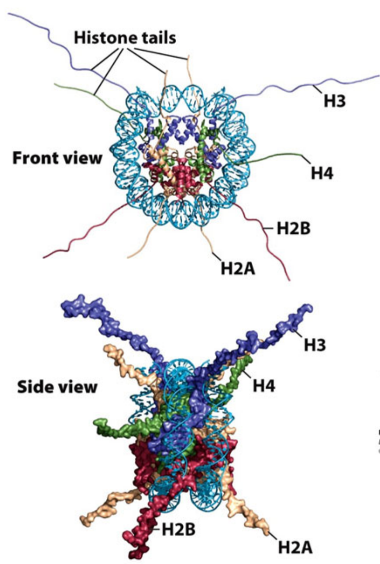

Figure 24-26d
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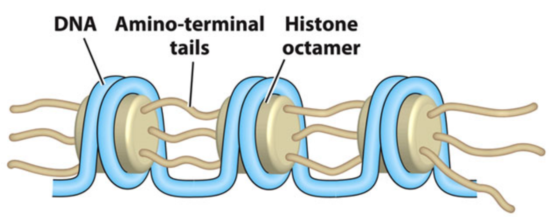

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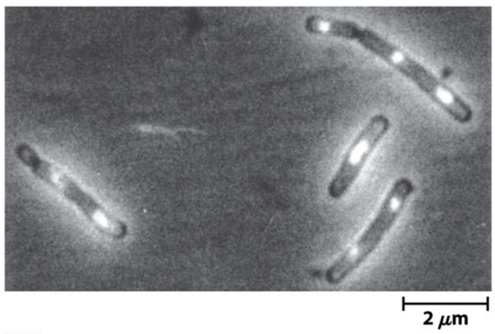
Bacterial chromosome structure: nucleoid

Bacteria do NOT have chromatin:
- But still compacted and organized
- Histone-like proteins exist- but dynamic structures



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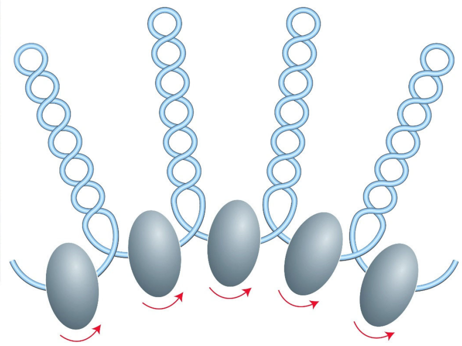

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Summary

DNA topology: physical properties of DNA
- Chromosomal DNA is negatively supercoiled (Compact and Dynamic/Accessible)
- Topoisomerases change Lk → affect supercoiling

Chromosome structure
- Biological DNA is highly structured
- Eukaryotes: histones organize DNA, nucleosome structure causes overall negative supercoiling
- Bacteria: DNA is organized differently, but still creates compact and topologically constrained systems