

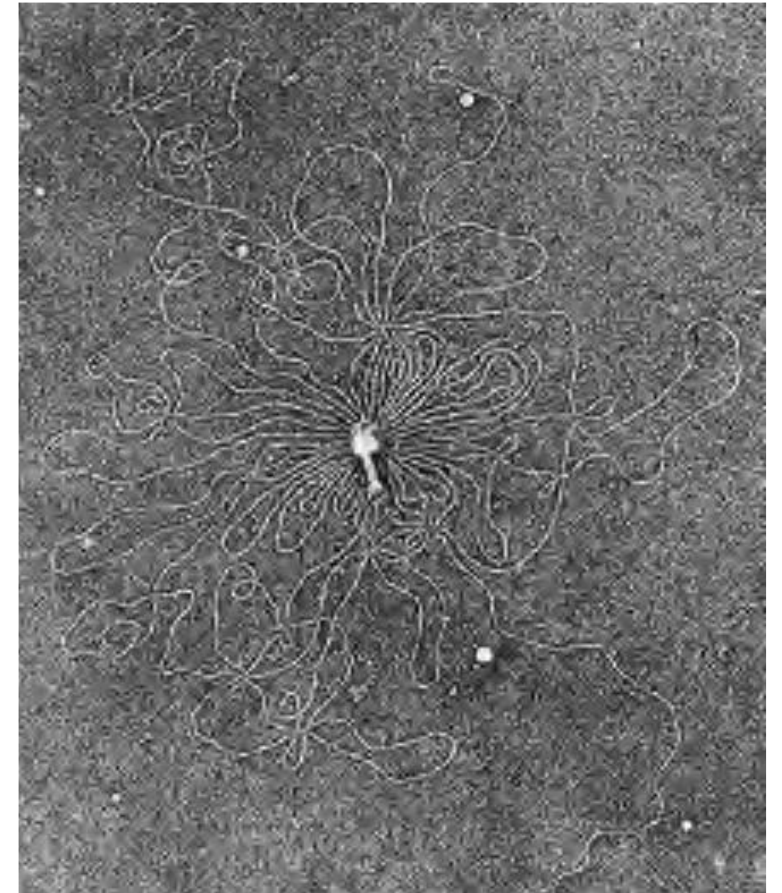
LECTURE 16

Chromosomal DNAs are often many orders of magnitude longer than the cells or viruses in which they are located.

A **gene** is all the DNA that encodes the primary sequence of some final gene product, which can be either a polypeptide or an RNA with a structural or catalytic function.

DNA also contains other segments or sequences that have a purely regulatory function.

Regulatory sequences provide signals that may denote the beginning or the end of genes, or influence the transcription of genes, or function as initiation points for replication or recombination



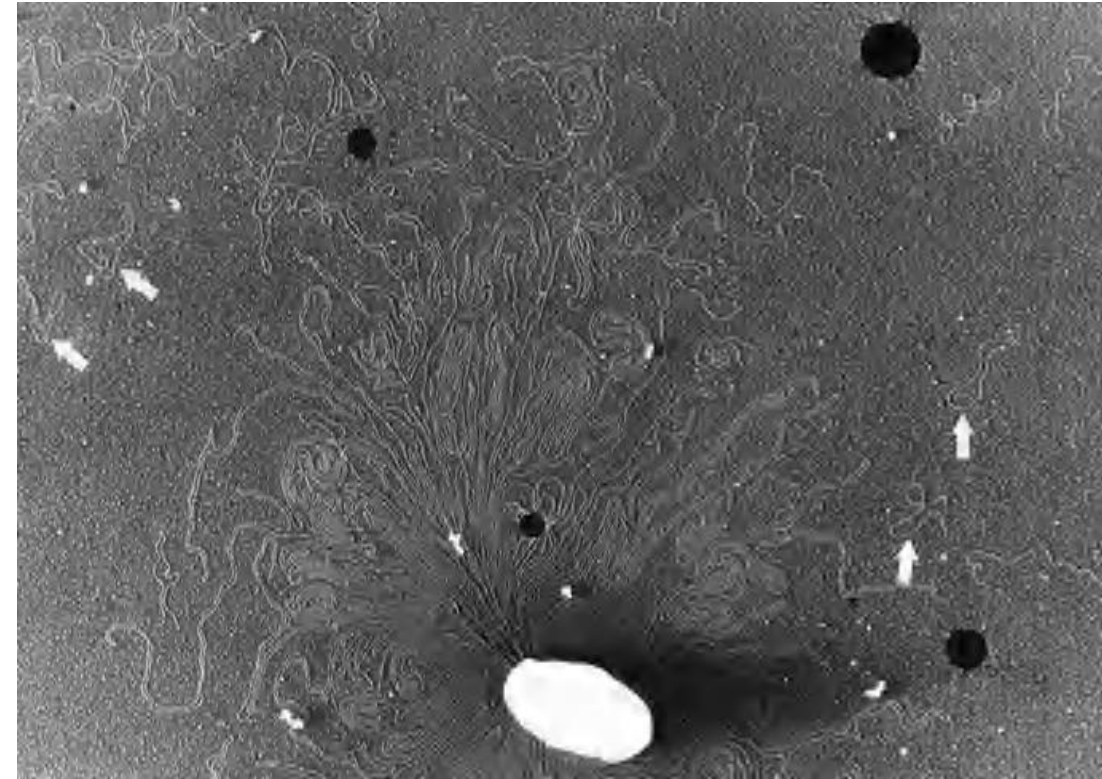
A single *E. coli* cell contains almost 100 times as much DNA as a bacteriophage particle.

The chromosome of an *E. coli* cell is a single doublestranded circular DNA molecule.

Its 4,639,675 bp have a contour length of about 1.7 mm, some 850 times the length of the *E. coli* cell.

In addition to the very large, circular DNA chromosome in their nucleoid, many bacteria contain one or more small circular DNA molecules that are free in the cytosol.

These extrachromosomal elements are called **plasmids**



In many cases plasmids confer no obvious advantage on their host, and their sole function seems to be self-propagation.

However, some plasmids carry genes that are useful to the host bacterium.

For example, some plasmid genes make a host bacterium resistant to antibacterial agents.

Nontranslated DNA segments in genes are called **intervening sequences** or **introns**, and the coding segments are called **exons**.

Commonly observed in eukaryotic genes. Few bacterial genes contain introns.

In most cases the function of introns is not clear. In total, only about 1.5% of human DNA is “coding” or exon DNA, carrying information for protein or RNA products.

highly repetitive sequences, are also referred to as **simple-sequence DNA** or **simple sequence repeats (SSR)**.

These short sequences, generally less than 10 bp long, are sometimes repeated millions of times per cell.

The simple-sequence DNA has also been called **satellite DNA**,

Eukaryotic chromosomes have two important special-function repetitive DNA sequences

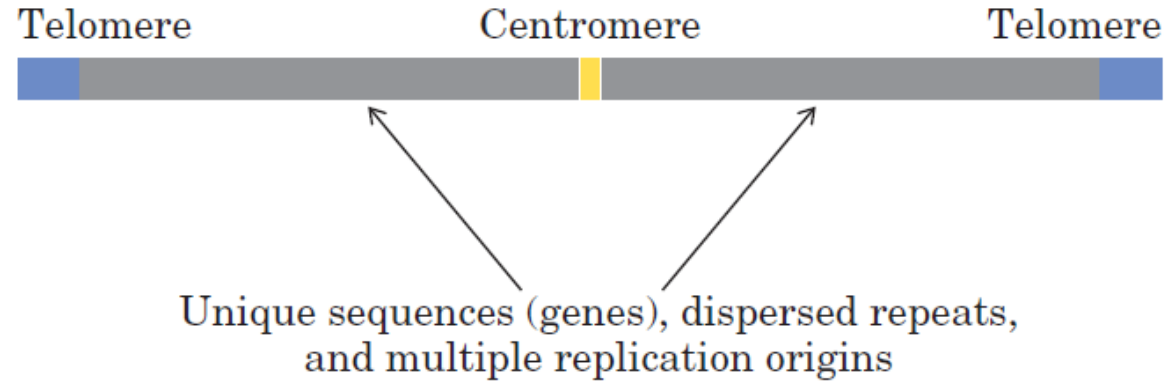


FIGURE 24–9 Important structural elements of a yeast chromosome.

The **centromere** is a sequence of DNA that functions during cell division as an attachment point for proteins that link the chromosome to the mitotic spindle.

This attachment is essential for the equal and orderly distribution of chromosome sets to daughter cells.

• **Telomeres** (Greek *telos*, “end”) are sequences at the ends of eukaryotic chromosomes that help stabilize the chromosome.

Telomeres end with multiple repeated sequences of the form

$$(5)(T_xG_y)_n$$

$$(3)(A_xC_y)_n$$

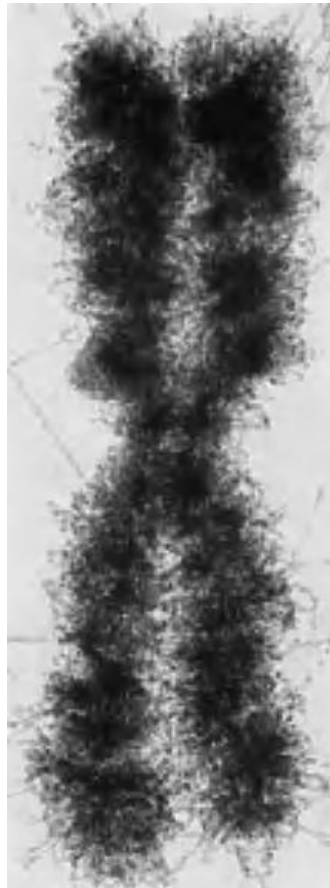
where x and y are generally between 1 and 4

The number of telomere repeats, n , is in the range of 20 to 100 for most single-celled eukaryotes and is generally more than 1,500 in mammals.

A dramatic illustration of the extraordinary degree of DNA compaction in our cells.

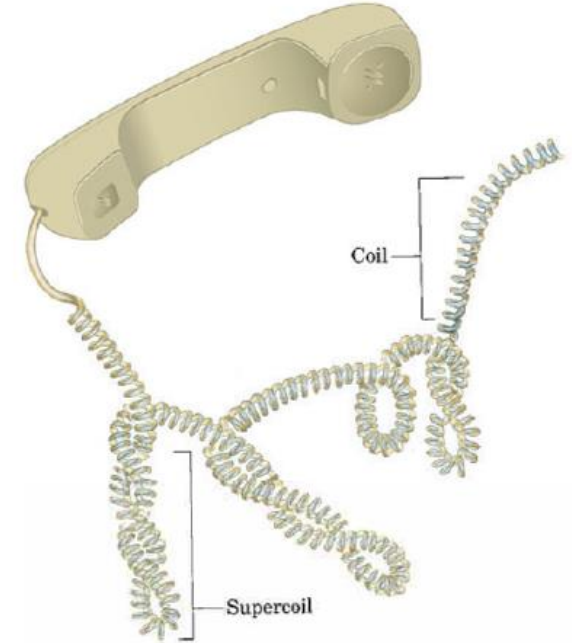
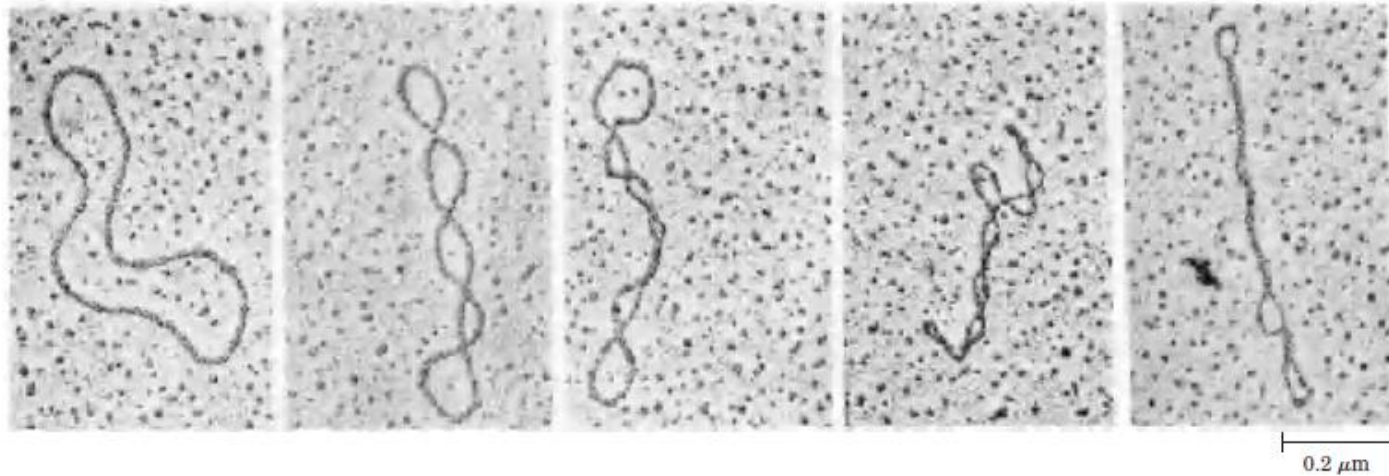
An adult human body contains approximately 10^{14} cells and thus a total DNA length of 2×10^{11} km.

Compare this with the circumference of the earth (4×10^4 km) or the distance between the earth and the sun (1.5×10^8 km)—



DNA Supercoiling

“Supercoiling” means the coiling of a coil



Supercoiling is an intrinsic property of DNA tertiary structure.
It occurs in all cellular DNAs and is highly regulated by each cell.

Regulates access to the genetic code

If the DNA of a closed-circular molecule conforms closely to the B-form structure, with one turn of the double helix per 10.5 bp, the DNA is relaxed rather than supercoiled

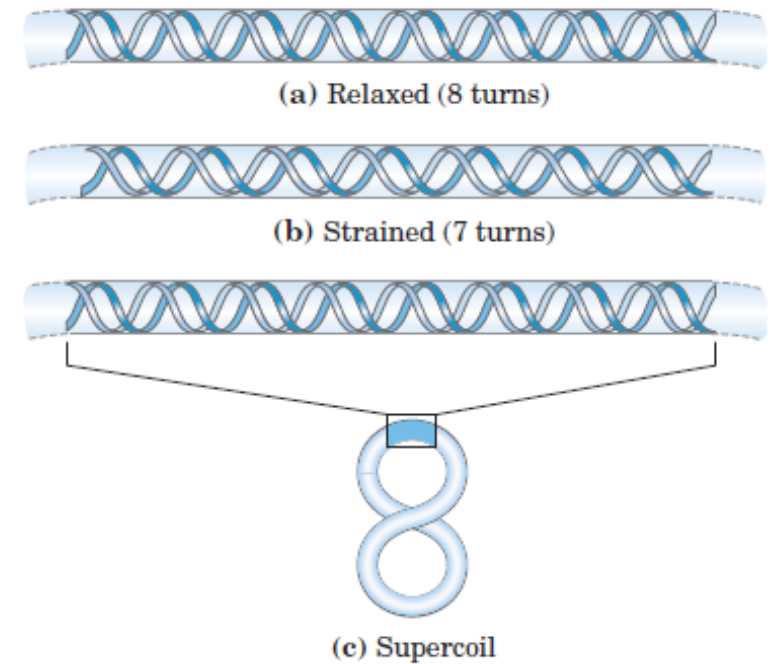
Supercoiling results when DNA is subject to some form of structural strain.

The strain is a result of **underwinding** of the DNA double helix. (overwinding also results in strain)

In other words, the DNA has *fewer* helical turns than would be expected for the B-form structure.

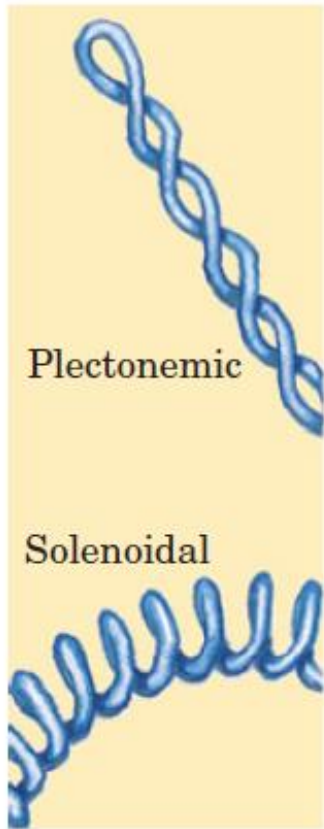
An under-wound DNA molecule (fewer turns than the relaxed state) is said to be negatively supercoiled.

An over-wound DNA molecule is said to be positively supercoiled

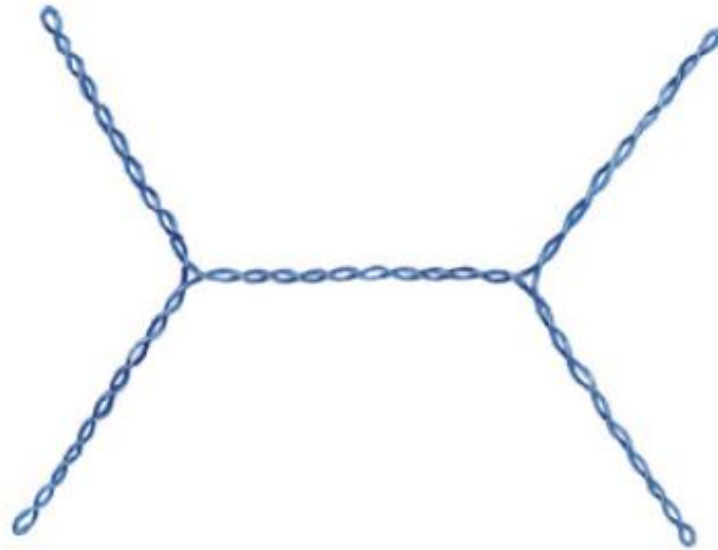


An 84 bp segment of a circular DNA in the relaxed state would contain eight double-helical turns

If one of these turns were removed, there would be 12.0 bp per turn, rather than the 10.5 found in B-DNA



(a)



(b)

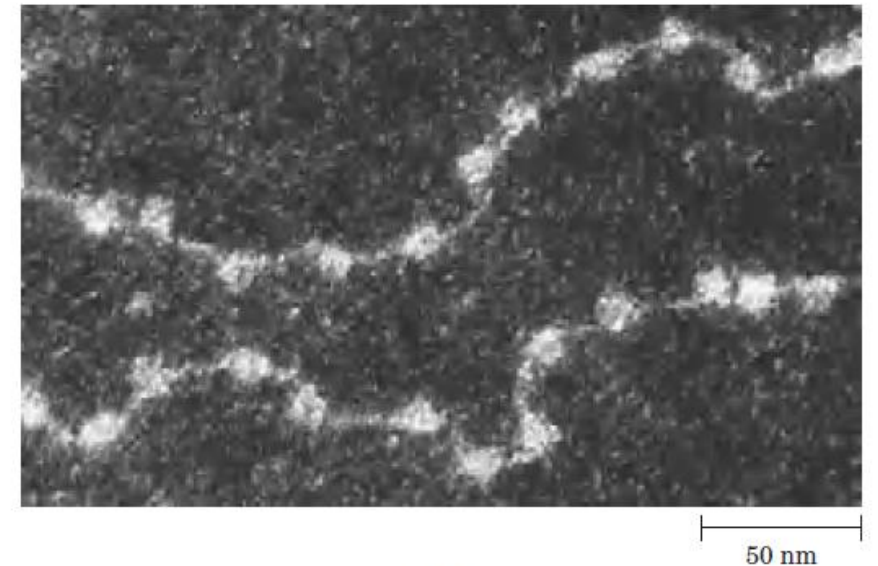
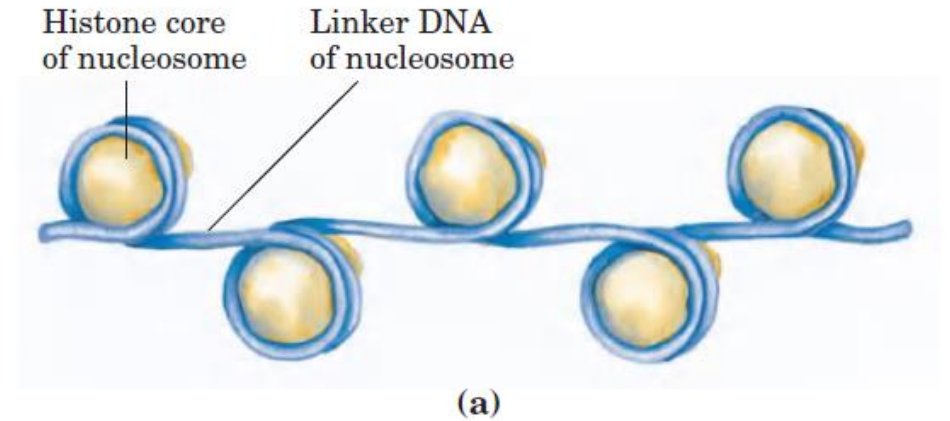
In prokaryotes, plectonemic supercoils are predominant, because of the circular chromosome and relatively small amount of genetic material. In eukaryotes, DNA supercoiling exists on many levels of both plectonemic and solenoidal supercoils, with the solenoidal supercoiling proving most effective in compacting the DNA.

Chromatin Consists of DNA and Proteins

Chromatin consists of fibers containing protein and DNA in approximately equal proportions (by mass)

The DNA in the chromatin is very tightly associated with proteins called **histones**, which package and order the DNA into structural units called **nucleosomes**

Also found in chromatin are many nonhistone proteins, some of which help maintain chromosome structure and others that regulate the expression of specific genes



Histones Are Small, Basic Proteins

Found in the chromatin of all eukaryotic cells, histones have molecular weights between 11,000 and 21,000 and are very rich in the basic amino acids arginine and lysine

All eukaryotic cells have five major classes of histones, differing in molecular weight and amino acid composition

Each type of histone is subject to enzymatic modification by methylation, acetylation, ADP-ribosylation, phosphorylation, glycosylation, sumoylation, or ubiquitination.

Such modifications affect the net electric charge, shape, and other properties of histones, as well as the structural and functional properties of the chromatin, and they play a role in the regulation of transcription.

Nucleosomes Are the Fundamental Organizational Units of Chromatin

The bead of each nucleosome contains eight histone molecules: two copies each of H2A, H2B, H3, and H4.

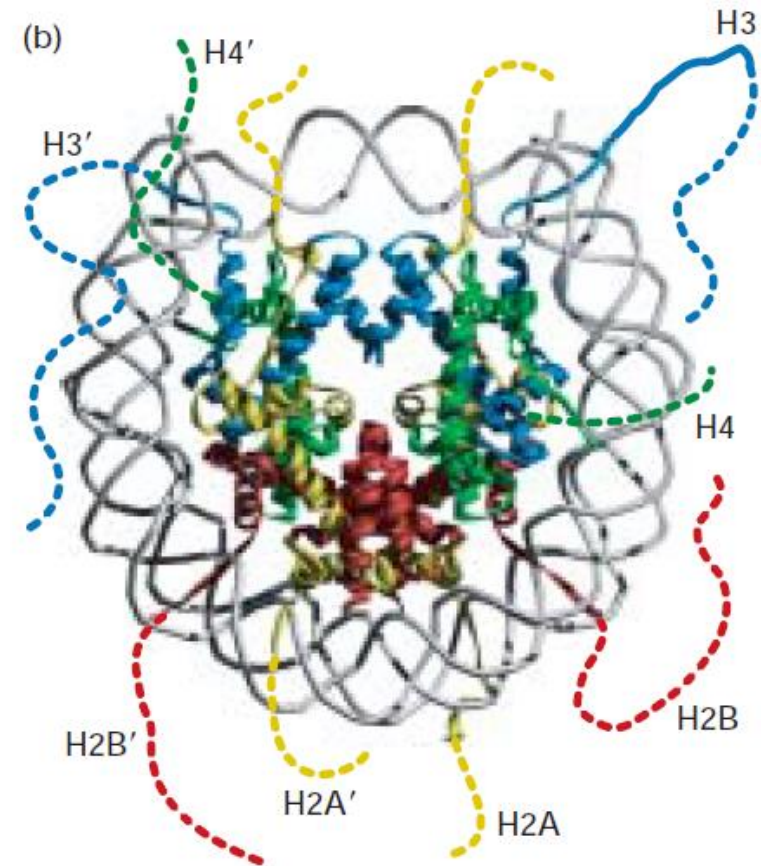
The spacing of the nucleosome beads provides a repeating unit typically of about 200 bp, of which 146 bp are bound tightly around the eight-part histone core and the remainder serve as **linker DNA** between nucleosome beads.

Histone cores do not bind randomly to DNA; rather, they tend to position themselves at certain locations. This positioning is not fully understood but in some cases seems to depend on a local abundance of AT base pairs in the DNA helix where it is in contact with the histones

Nucleosomes from all eukaryotes contain 146 base pairs of DNA wrapped slightly less than two turns around the protein core.

The length of the linker DNA is more variable among species, ranging from about 15 to 55 base pairs.

Each of the histone proteins making up the nucleosome core contains a flexible amino terminus of 11–37 residues extending from the fixed structure of the nucleosome; these termini are called *histone tails*.



Nucleosomes Are Packed into Successively Higher-Order Structures

Wrapping of DNA around a nucleosome core compacts the DNA length about sevenfold.

The overall compaction in a chromosome, however, is greater than 10,000-fold

2nd level – beaded string coils to form 30nm fibre

3rd level – forms looped domains attached to a scaffold of non-histone protein

4th level - ...

Bacterial DNA is compacted in a structure called the **nucleoid**, which can occupy a significant fraction of the cell volume

The DNA seems to be attached at one or more points to the inner surface of the plasma membrane.

Much less is known about the structure of the nucleoid than of eukaryotic chromatin, but a complex organization is slowly being revealed.

In *E. coli*, a scaffoldlike structure seems to organize the *circular* chromosome into a series of about 500 looped domains, each encompassing 10,000 bp on average

Histone like proteins are abundant in *E. coli*—the best characterized example is a two-subunit protein called HU (M_r 19,000)—but these proteins bind and dissociate within minutes, and no regular, stable DNA-histone structure has been found.

