Molecular biology and bacterial genetics

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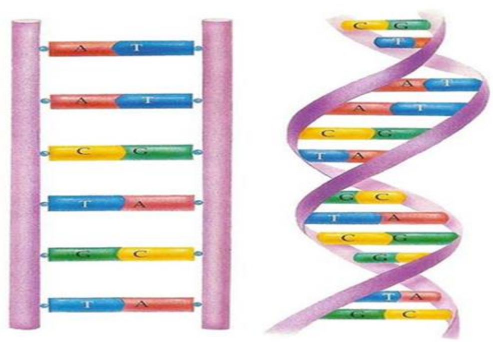

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2020-2019

3-The Tertiary Structure of DNA

Packing DNA in to small Spaces

The packaging of tremendous amounts of genetic information in to the small volume of the cell has been called the ultimate storage problem. Consider the chromosome of the bacterium E.coli, a single molecule of DNA with approximately 4.64 million base pairs. Stretched out straight, this DNA would be about 1000 times as long as the cell within which it resides .

Human cells contains 6 billion base pairs of DNA, which would measure some 1.8 meters stretched end to end. Even DNA in the smallest human chromosomes would stretch 14,000 times the length of the nucleus . clearly , DNA molecules must be tightly packed to fit into such small spaces.

Supercoiling

One type of DNA tertiary structure is supercoiling, which occurs when the DNA helix is subjected to strain by being overwound or underwound. The lowest energy state for B-DNA is when it has approximately 10 bp per turn of its helix. In this relaxed state, a stretch of 100 bp of DNA would assume about 10 complete turns. If energy is used to add or remove any turns by rotating one strand around the other, strain is placed on the molecule, causing the helix to supercoil, or twist, on itself.

Supercoiling is a natural consequences of the over rotating or under rotating of the helix; it occurs only when the molecule is placed under strain. Molecules that are overrotated exhibits positive supercoiling. underrotated molecules exhibits negative supercoiling , in which the direction of the supercoil is opposite that of the right- handed coil of the DNA helix.(figure 1).

Most DNA found in cells is negatively supercoiled, which has two advantages for the cell. First, supercoiling makes the separation of the two strands of DNA easier during replication and transcription. Negatively supercoiled DNA is underrotated; so separation of the two strands during replication and transcription is more rapid and requires less energy. Second, supercoiled DNA can be packed into a smaller space because it occupies less volume than relaxed DNA.

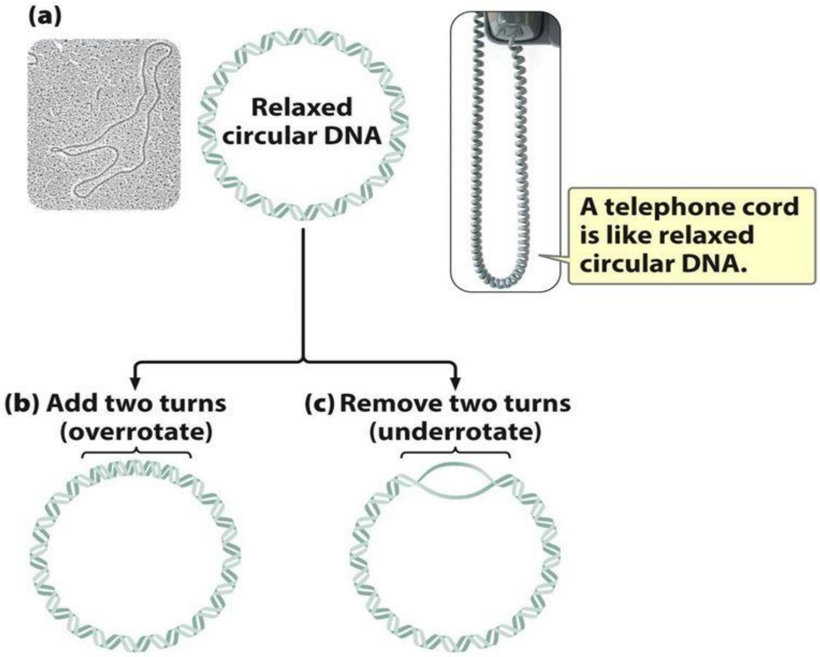

Figure 11.2 part 1
Genetics: A Conceptual Approach, Fifth Edition
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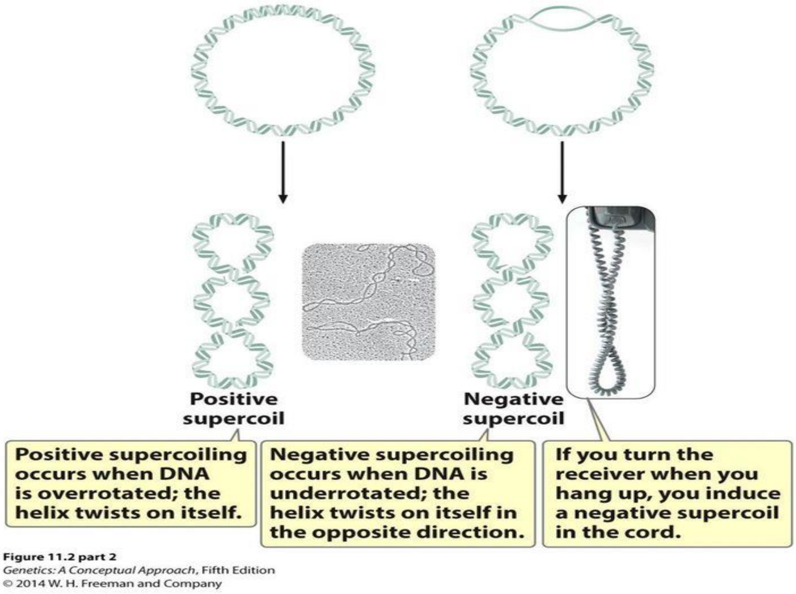

Figure1: supercoiled DNA is overwound or underwound, causing it to twist on itself.

The bacterial chromosomes

Most bacterial genomes consist of a single , circular DNA molecule, although linear DNA molecules have been found in a few species. In circular bacterial chromosomes, the DNA does not exist in an open relaxed circular; the 3 million to 4 million base pairs of DNA found in a typical bacterial genome would be much too large to fit into a bacterial cell when a bacterial cell is viewed with the electron microscope, its DNA frequently appears as a distinct clump , the nucleoid, which is confined to a definite region of the cytoplasm. If a bacterial cell is broken open gently its DNA spills out in a series of twisted loops. The ends of the loops are most likely held in place by proteins.(figure 2). Many bacteria contain additional DNA in the form of small circular molecules called plasmids, which replicate independently of the chromosome. Chromosomal DNA exists in the form of very long molecules, which must be tightly packed to fit into the small confines of a cell.

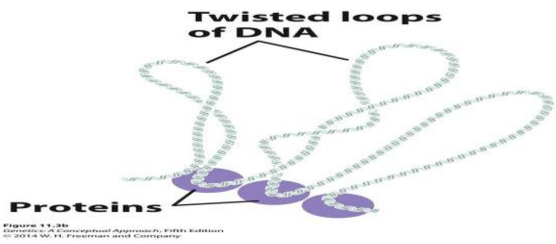

Figure 2:bacterial DNA is highly folded into a series of twisted loops

The eukaryotic chromosomes

Each eukaryotic chromosome consist of a single, extremely long molecule of DNA. For all of this DNA to fit in to the nucleus, tremendous packing and folding are required, the extent of which must change through time. The chromosomes are in an elongated, although the DNA of interphase chromosomes is less tightly packed than DNA in mitotic chromosomes , it is still highly condenses, its just less condensed. In the course of cell cycle, the level of DNA packaging changes- chromosomes progress from a highly packed state to a state of extreme condensation . DNA packaging also changes locally **in replication and transcription, when the two nucleotide strands must unwind** so that the particular base sequences are exposed. Thus packaging of eukaryotic DNA is not static but changes regularly in response to cellular processes.

Chromatin structure

Chromatin is a mass of genetic material composed of DNA and proteins that condense to form chromosomes during eukaryotic cell division. Chromatin is located in the nucleus of our cells.

The primary function of chromatin is to compress the DNA into a compact unit that will be less voluminous and can fit within the nucleus. Chromatin consists of complexes of small proteins known as histones (two copies each of H2A, H2B, H3, and H4) and DNA.

histones have a positively charged amino acids that give them a net positive charge. The positive charges attract the negative charges on the phosphates of DNA and holds the DNA in contact with the histones.

Histones help to organize DNA into structures called nucleosomes by providing a base on which the DNA can be wrapped around. A nucleosome consists of a DNA sequence of about 150 base pairs that is wrapped around a set of eight histones called an octamer. The nucleosome is further folded to produce a chromatin fiber. Chromatin fibers are coiled and condensed to form chromosomes.(figure3). Chromatin makes it possible for a number of cell processes to occur including DNA replication, transcription, DNA repair, genetic recombination, and cell division. (figure 3) (figure 4).

Euchromatin and Heterochromatin

Chromatin within a cell may be compacted to varying degrees depending on a cell's stage in the cell cycle. In the nucleus, chromatin exists as euchromatin or heterochromatin. During interphase of the cycle, the cell is not dividing but undergoing a period of growth. Most of the chromatin is in a less compact form known as euchromatin. More of the DNA is exposed in euchromatin allowing replication and DNA transcription to take place. During transcription, the DNA double helix unwinds and opens to allow the genes coding for proteins to be copied. DNA replication and transcription are needed for the cell to synthesize DNA, proteins, and organelles in preparation for cell division (mitosis or meiosis). A small percentage of chromatin exists as heterochromatin during interphase.

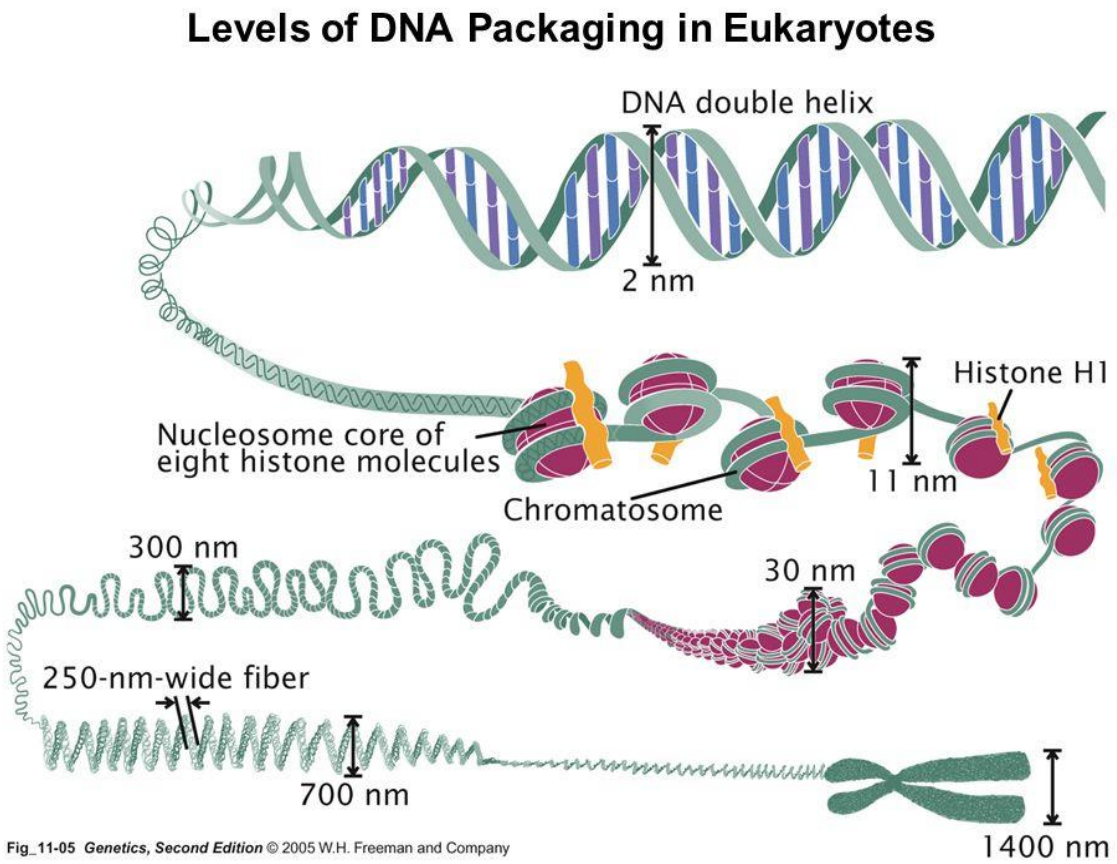

Figure 3:chromatin folded in chromosomes

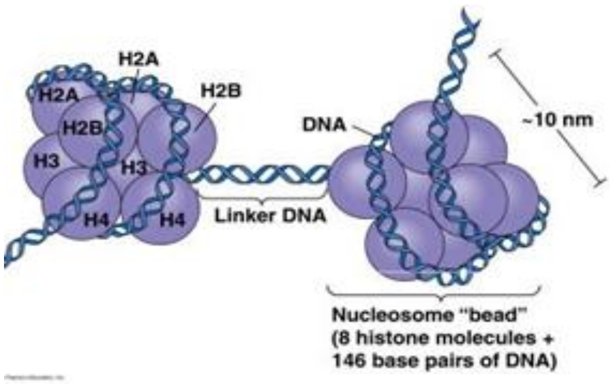

figure 4: Nucleosomes and histones, the basic unit in the folding of eukaryotic DNA is the nucleosome as shown here. A nucleosome is composed of eight histones comprising a core and one separate histone (H1) at the site where the wrapped DNA diverges.

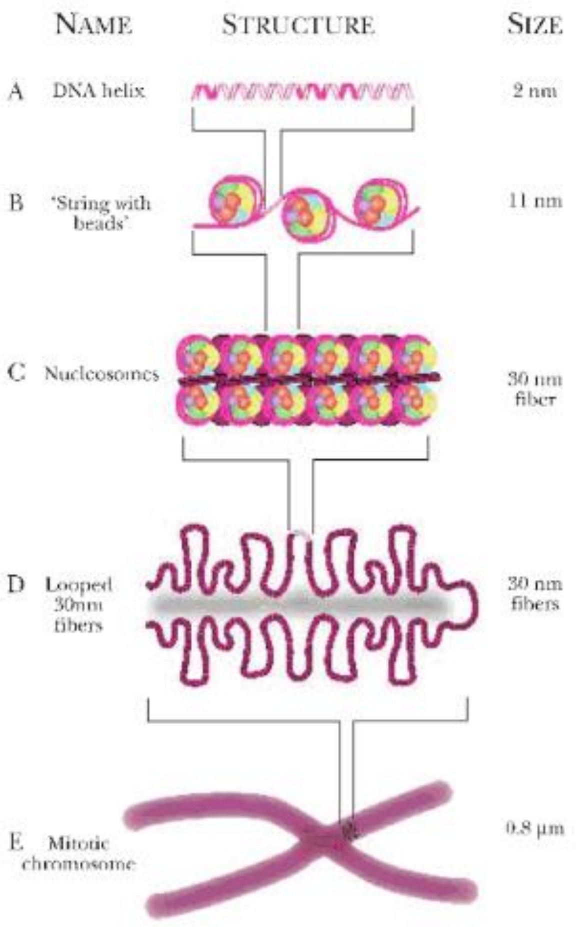

FIGURE 4.27 Summary of the Folding of DNA in Eukaryotic Chromosomes

The DNA helix (A) is wrapped around (B) eight histones (the core). The linker DNA regions unite the nucleosomes to give a "string with beads." This in turn is coiled helically (C) (not clearly indicated) to form a 30 nm fiber. The 30 nm fibers are further folded by looping and attachment to a protein scaffold. Finally, during mitosis the DNA is folded yet again to yield very thick chromosomes.

DNA methylation

The primary structure of DNA can be modified in various ways. These modifications are important in the expression of the genetic material, as we will see in the chapters to come. One such modification is DNA methylation, in which methyl groups (-CH3) are added (by specific enzymes)to certain positions on the nucleotide bases. In bacteria: adenine and cytosine are commonly methylated, whereas in eukaryotes, cytosine is the most commonly methylated base. Bacterial DNA is frequently methylated to distinguish it from foreign, unmethylated DNA that may be introduced by viruses; bacteria use proteins called restriction enzymes to cut up any unmethylated.

In eukaryotic DNA cytosine bases are often methylated to form 5-methylcytosine. Methylation is often related to gene expression.