DNA AND CHROMOSOMES

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1. The Building Blocks of DNA

- DNA has three types of chemical component:
  - **Phosphate**
  - a sugar called **deoxyribose**, and
  - four nitrogenous bases:
    - Adenine (A)
    - Guanine (G)
    - Cytosine (C)
    - Thymine (T).
  - Two of the bases, adenine and guanine, have a double-ring structure characteristic of a type of chemical called a **purine**. The other two bases, cytosine and thymine, have a single-ring structure of a type called a **pyrimidine**.

- The chemical components of DNA are arranged into groups called **nucleotides**, each composed of a phosphate group, a deoxyribose sugar molecule, and any one of the four bases.
2. The four nucleotides

Chemical structure of the four nucleotides (two with purine bases and two with pyrimidine bases) that are the fundamental building blocks of DNA. The sugar is called deoxyribose because it is a variation of a common sugar, ribose, which has one more oxygen atom.
3. The double helix

- DNA is composed of two side-by-side chains ("strands") of nucleotides twisted into the shape of a double helix. The two nucleotide strands are held together by weak associations between the bases of each strand, forming a structure like a spiral staircase.

- In three dimensions, the bases form rather flat structures, and these flat bases partly stack on top of one another in the twisted structure of the double helix. This stacking of bases adds tremendously to the stability of the molecule by excluding water molecules from the spaces between the base pairs.
4. Strand polarity

The arrangement of the components of DNA. A segment of the double helix has been unwound to show the structures more clearly. The diagram shows the sugar-phosphate backbone and the hydrogen bonding of bases in the center of the molecule.

The sugar-phosphate bonds are called phosphodiester bonds. The carbons of the sugar groups are numbered 1’ through 5’ (next slide). One part of the phosphodiester bond is between the phosphate and the 5’ carbon of deoxyribose, and the other is between the phosphate and the 3’ carbon of deoxyribose. Thus, each sugar-phosphate backbone is said to have a 5’-to-3’ polarity, and understanding this polarity is essential in understanding DNA properties. In the double-stranded DNA molecule, the two backbones are in opposite, or antiparallel, orientation. One strand is oriented 5’→3’; the other strand, though 5’→3’, runs in the opposite direction, or, looked at another way, is 3’→5’
5. Base pairing

The bases of DNA interact according to a very straightforward rule, namely, that there are only two types of base pairs: \( A\cdot T \) and \( G\cdot C \). The bases in these two base pairs are said to be complementary. This means that at any "step" of the stair like double-stranded DNA molecule, the only base-to-base associations that can exist between the two strands without substantially distorting the double-stranded DNA molecule are \( A\cdot T \) and \( G\cdot C \).

Note that because the \( G\cdot C \) pair has three hydrogen bonds, whereas the \( A\cdot T \) pair has only two, one would predict that DNA containing many \( G\cdot C \) pairs would be more stable than DNA containing many \( A\cdot T \) pairs. In fact, this prediction is confirmed. Heat causes the two strands of the DNA double helix to separate (a process called DNA melting or DNA denaturation); it can be shown that DNAs with higher G+C content require higher temperatures to melt them.
6. DNA forms giant molecules

- Although hydrogen bonds are individually weak, the two strands of the DNA molecule are held together in a relatively stable manner because there are enormous numbers of these bonds. It is important that the strands be associated through such weak interactions, since they have to be separated during DNA replication and during transcription into RNA.

- The sugar-phosphate backbone, being connected by covalent bonds, is also stable; bacterial DNA form a single giant molecule; in eukaryotes, each chromosome is composed by a single giant molecule of DNA.
7. How much DNA per genome?

- Almost all cells of all organisms contain at least **one copy of the entire genome** of the species (most cells are diploid, i.e. they contain two copies).
- Genome sizes are measured in units of thousands of nucleotide pairs (called kilobases, kb) or millions of nucleotide pairs (megabases, mb), or sometimes in picograms (10^{-12} gr).
- In general, the total amount of chromosomal DNA in different animals and plants does not vary in a consistent manner with the apparent complexity of the organisms.
- Yeasts, fruit flies, chickens, and humans have successively larger amounts of DNA in their haploid chromosome sets, in keeping with what we perceive to be the increasing complexity of these organisms. Yet the vertebrates with the greatest amount of DNA per cell are amphibians, which are surely less complex than humans in their structure and behavior.
8. Genome sizes

Amount of DNA in the genomes of various organisms
9. Length of a DNA molecule

The single chromosome of *Escherichia coli* is about 1.3 mm of DNA. To enable a macromolecule this large to fit within the bacterium, histone-like proteins bind to the DNA, segregating the DNA molecule into around 50 chromosomal domains and making it more compact. Then an enzyme called DNA gyrase supercoils each domain around itself forming a compacted, supercoiled mass of DNA approximately 0.2 µm in diameter, called nucleoid.
The nucleoid is one long, single molecule of double stranded, helical, supercoiled DNA. In most bacteria, the two ends of the double-stranded DNA covalently bond together to form both a physical and genetic circle.

The chromosome is generally around 1000 µm long and frequently contains as many as 3500 genes. *E. coli*, that is 2-3 µm in length has a chromosome approximately 1400 µm long.
11. Eukaryotic Nuclear Genomes

- A human cell contains about 2 meters of DNA, packed into 46 chromosomes, all inside a nucleus only 6 µm in diameter.
- Thus, in order to pack the DNA into the nucleus, there must be several levels of coiling and supercoiling.

These levels of DNA structure cannot be resolved by the optical microscope, under which interphase nuclei stained with DNA-specific dyes appears composed of a dense, dark-staining material called **heterochromatin**, and is scattered throughout the nucleus, and a very light-staining flocculent material which fills the rest of the nucleus, called **euchromatin**.
It is thought that most part of each chromosome in an interphase nucleus (chromatine) has the form of the “30 nm fiber”.

The figure on the left shows the tangled chromatin fibers obtained after disrupting a nucleus. Shearing forces can be used to further uncoil and stretch these fibers and the beaded filaments appear. The strands between the beads are segments of double stranded DNA (right panel).
13. The 30 nm fibre

Different levels of chromosome uncoiling. The bottom of the figure shows the DNA helix (which is DNA stripped of its histones). In the normal, unstripped chromosome, the double stranded DNA is wrapped around sets of 8 macromolecules of histones (proteins) to form a 10 nm filament. These sets of histones are separated by spacer regions of 4 nm DNA filament. They are the 10 nm nucleoprotein fibrils or "beads on a string" seen in electron micrographs which are called nucleosomes. The next level of coiling produces the 30 nm nucleoprotein fibers.
14. Compacting DNA into eukaryotic chromosomes

Stuffing the long strands of chromosomal DNA into a eukaryotic nucleus requires that the DNA be compacted in length approximately 10,000 to 50,000-fold. Cells achieve this task while still maintaining the chromosomes in a form that allows regulatory proteins to access DNA to turn on (or off) specific genes or to duplicate the chromosome (replication).

Model for chromosome structure. On the left is shown tight coiling, representing metaphase: here the loops are so densely packed that only their tips are visible. At the free ends, a solenoid is shown uncoiled to give an approximation of relative scale. On the right is shown a relaxed supercoil, as at interphase.
15. Compacting factors