BE566

DNA Structure and Function

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1.*Introduction.* From the Watson-Crick double helix to the human genome sequence and beyond. Variety of structures of DNA and RNA. Variety of images of structures. DNA and RNA as micro-objects. RNAi revolution.

2.*Major structures of DNA and RNA.* Chemical structure of DNA and RNA. Sugar conformation. Conformations of nucleoside. B-DNA. X-ray diffraction from DNA. Alternative DNA duplex structures: A, B', Z. Structure of duplex RNA. Structure of single-stranded RNA. Polarity of strands. Parallel duplex. Pyrimidine-purine-pyrimidine and pyrimidine- purine-purine triplexes. Quadruplexes. Spontaneous and induced DNA bending.

3. *Methods to study structure of DNA and RNA.* Their advantages and disadvantages. Finding molecular structure as an ill-posed mathematical problem. Direct and indirect methods. X-ray analysis of fibers and crystals. Electron microscopy. Cryo-electron microscopy. Atomic force microscopy. Optical methods (absorption spectroscopy, circular dichroism, fluorecence, etc.). Fluorescence and its role in biotechnology. Fluorescence Resonance Energy Transfer (FRET). Mass spectrometry. Role of theory. Gel electrophoresis. Chemical, photochemical and enzymatic probing of structures of DNA and RNA.

4 . *Global changes of DNA structure.* DNA melting on heating and other changes of ambient conditions. Factors determining stability of the DNA double helix. Stability constant. Thermodynamics of DNA melting. DNA melting parameters. Kinetic effects in DNA melting. Lifetime of the DNA duplex state. Other global transitions (B-B', B-A, B-Z).

5. *DNA as a macromolecule*. Random walks. The freely jointed chain (FJC) model and its analogy with the random walk. Kuhn statistical length. The worm-like chain (WLC) model. Persistence length. The mean square end-to-end distance for FJC and WLC models. Random coil. Single DNA molecule under the external force. Reptation. Why DNA molecules of different lengths are separated by gel electrophoresis. Pulse-field gel electrophoresis.

6. *DNA topology.* Two levels of DNA topology. Difference between topology and geometry. Knots and links. Topological invariants. The Alexander polynomial as a topology invariant for knots. Examples. Linking number. Writhing and twisting. DNA supercoiling. Superhelix energy. Topoisomers. Structure of supercoiled DNA. Separation of DNA topoisomers by gel electrophoresis.

7. *Structural changes in DNA induced by negative supercoiling*. DNA unusual structures. D-loops. Cruciforms. The Z form. The H form. Two classes of H-DNA. Two isomeric forms of H-DNA. Two-dimensional gel electrophoresis. Detection of structural changes in supercoiled DNA by 2D gel electrophoresis. Thermodynamic treatment of the B-U transition between B-DNA and an unusual structure (U).

8. *Major tools in DNA and RNA research*. DNA cutting. DNA mapping. DNA sequencing. Sanger method. Genome sequencing. PCR (polymerase chain reaction). Hybridization. Molecular beacons. Real time PCR. DNA microarrays and DNA chips.

9. *Biological significance of nucleic acid structures.* Replication and transcription. Telomeres and telomerase. Bent DNA and its role in transcription. Role of DNA topology in replication and transcription. Topoisomerases.

10. *Postgenome challenges.* Antisense and antigene strategies of modulation of gene activity. The RNAi pathway. SNP (single-nucleotide polymorphism). Pathogen detection based on nucleic acids.

Textbooks:

Richard R. Sinden "DNA Structure and Function" Academic Press, 1994.

Andrew D. Bates and Anthony Maxwell "DNA Topology" Oxford University Press, 2005

Maxim D. Frank-Kamenetskii "Unraveling DNA" Addison -Wesley,1997. Available online