Molecular models of DNA

Molecular models of DNA structures are representations of the molecular geometry and topology of Deoxyribonucleic acid (DNA) molecules using one of several means, such as: closely packed spheres (CPK models) made of plastic, metal wires for 'skeletal models', graphic computations and animations by computers, artistic rendering, and so on, with the aim of simplifying and presenting the essential, physical and chemical, properties of DNA molecular structures either in vivo or in vitro. Computer molecular models also allow animations and molecular dynamics simulations that are very important for understanding how DNA functions in vivo. Thus, an old standing dynamic problem is how DNA "self-replication" takes place in living cells that should involve transient uncoiling of supercoiled DNA fibers. Altough DNA consists of relatively rigid, very large elongated biopolymer molecules called "fibers" or chains (that are made of repeating nucleotide units of four basic types, attached to deoxyribose and phospate groups), its molecular stucture in vivo undergoes dynamic configuration changes that involve dynamically attached water molecules and ions. Supercoiling, packing with histones in chromosome structures, and other such supramolecular aspects also involve in vivo DNA topology which is even more complex than DNA molecular geometry, thus turning molecular modeling of DNA into an especially challenging problem for both molecular biologists and biotechnologists. Like other large molecules and biopolymers, DNA often exists in multiple stable geometries (that is, it exhibits conformational isomerism) and configurational, quantum states which are close to each other in energy on the potential energy surface of the DNA molecule. Such geometries can also be computed, at least in principle, by employing ab initio quantum chemistry methods that have high accuracy for small molecules. Such quantum geometries define an important class of *ab initio* molecular models of DNA whose exploration has barely started.

In an interesting twist of roles, the DNA molecule itself was proposed to be utilized for quantum computing. Both DNA nanostructures as well as DNA 'computing' biochips have been built (see biochip image at right).

The more advanced, computer-based molecular models of DNA involve molecular dynamics simulations as well as quantum mechanical computations of vibro-rotations, delocalized molecular orbitals (MOs), electric dipole moments, hydrogen-bonding, and so on.





Spinning DNA generic model.

Importance

From the very early stages of structural studies of DNA by X-ray diffraction and biochemical means, molecular models such as the Watson-Crick double-helix model were succesfully employed to solve the 'puzzle' of DNA structure, and also find how the latter relates to its key functions in living cells. The first high quality X-ray diffraction patterns of A-DNA were reported by Rosalind Franklin and Raymond Gosling in $1953^{[1]}$. The first calculations of the Fourier transform of an atomic helix were reported one year earlier by Cochran, Crick and Vand ^[2], and were followed in 1953 by the computation of the Fourier transform of a coiled-coil by Crick^[3]. The first reports of a double-helix molecular model of B-DNA structure were made by Watson and Crick in $1953^{[4]}$. Last-but-not-least, Maurice F. Wilkins, A. Stokes and H.R. Wilson, reported the first X-ray patterns of *in vivo* B-DNA in partially oriented salmon sperm heads ^[6]. The development of the first correct double-helix molecular model of DNA by Crick and Watson may not have

been possible without the biochemical evidence for the nucleotide base-pairing ([A---T]; [C---G]), or Chargaff's rules^{[7] [8] [9] [10] [11] [12]}.

Examples of DNA molecular models

Animated molecular models allow one to visually explore the three-dimensional (3D) structure of DNA. The first DNA model is a space-filling, or CPK, model of the DNA double-helix whereas the third is an animated wire, or skeletal type, molecular model of DNA. The last two DNA molecular models in this series depict quadruplex DNA ^[13] that may be involved in certain cancers^{[14] [15]}. The last figure on this panel is a molecular model of hydrogen bonds between water molecules in ice that are similar to those found in DNA.













• Spacefilling models or CPK models - a molecule is represented by overlapping spheres representing the atoms.



Images for DNA Structure Determination from X-Ray Patterns

The following images illustrate both the principles and the main steps involved in generating structural information from X-ray diffraction studies of oriented DNA fibers with the help of molecular models of DNA that are combined with crystallographic and mathematical analysis of the X-ray patterns. From left to right the gallery of images shows:

- First row:
- 1. Constructive X-ray interference, or diffraction, following Bragg's Law of X-ray "reflection by the crystal planes";
- 2. A comparison of A-DNA (crystalline) and highly hydrated B-DNA (paracrystalline) X-ray diffraction, and respectively, X-ray scattering patterns (courtesy of Dr. Herbert R. Wilson, FRS- see refs. list);
- 3. Purified DNA precipitated in a water jug;
- 4. The major steps involved in DNA structure determination by X-ray crystallography showing the important role played by molecular models of DNA structure in this iterative, structure--determination process;
 - Second row:
- 5. Photo of a modern X-ray diffractometer employed for recording X-ray patterns of DNA with major components: X-ray source, goniometer, sample holder, X-ray detector and/or plate holder;
- 6. Illustrated animation of an X-ray goniometer;
- 7. X-ray detector at the SLAC synchrotron facility;
- 8. Neutron scattering facility at ISIS in UK;
 - Third and fourth rows: Molecular models of DNA structure at various scales; figure #11 is an actual electron micrograph of a DNA fiber bundle, presumably of a single

bacterial chromosome loop.















Paracrystalline lattice models of B-DNA structures

A paracrystalline lattice, or paracrystal, is a molecular or atomic lattice with significant amounts (e.g., larger than a few percent) of partial disordering of molecular arranegements. Limiting cases of the paracrystal model are nanostructures, such as glasses, liquids, etc., that may possess only local ordering and no global order. Liquid crystals also have paracrystalline rather than crystalline structures.



Highly hydrated B-DNA occurs naturally in living cells in such a paracrystalline state, which is a dynamic one in spite of the relatively rigid DNA double-helix stabilized by parallel hydrogen bonds between the nucleotide base-pairs in the two complementary, helical DNA chains (see figures). For simplicity most DNA molecular models ommit both water and ions dynamically bound to B-DNA, and are thus less useful for understanding the dynamic behaviors of B-DNA *in vivo*. The physical and mathematical analysis of X-ray^[16] ^[17] and spectroscopic data for paracrystalline B-DNA is therefore much more complicated than that of crystalline, A-DNA X-ray diffraction patterns. The paracrystal model is also important for DNA technological applications such as DNA nanotechnology. Novel techniques that combine X-ray diffraction of DNA with X-ray microscopy in hydrated living cells are now also being developed (see, for example, "Application of X-ray microscopy in the analysis of living hydrated cells" ^[18].

Genomic and Biotechnology Applications of DNA molecular modeling

The following gallery of images illustrates various uses of DNA molecular modeling in Genomics and Biotechnology research applications from DNA repair to PCR and DNA nanostructures; each slide contains its own explanation and/or details. The first slide presents an overview of DNA applications, including DNA molecular models, with emphasis on Genomics and Biotechnology.

Gallery: DNA Molecular modeling applications







Databases for DNA molecular models and sequences

X-ray diffraction

- NDB ID: UD0017 Database ^[19]
- X-ray Atlas -database ^[20]
- PDB files of coordinates for nucleic acid structures from X-ray diffraction by NA (incl. DNA) crystals ^[21]
- Structure factors dowloadable files in CIF format ^[22]

Neutron scattering

- ISIS neutron source
- ISIS pulsed neutron source: A world centre for science with neutrons & muons at Harwell, near Oxford, UK. ^[23]

X-ray microscopy

• Application of X-ray microscopy in the analysis of living hydrated cells ^[24]

Electron microscopy

• DNA under electron microscope ^[25]

Atomic Force Microscopy (AFM)

Two-dimensional DNA junction arrays have been visualized by Atomic Force Microscopy $\rm (AFM)^{[26]}$. Other imaging resources for AFM/Scanning probe microscopy(SPM) can be freely accessed at:

- How SPM Works ^[27]
- SPM Image Gallery AFM STM SEM MFM NSOM and more. ^[28]

Gallery of AFM Images





Mass spectrometry--Maldi informatics



Spectroscopy

- Vibrational circular dichroism (VCD)
- FT-NMR^{[29] [30]}
 - NMR Atlas--database ^[31]
 - mmcif downloadable coordinate files of nucleic acids in solution from 2D-FT NMR data [32]
 - NMR constraints files for NAs in PDB format ^[33]
- NMR microscopy^[34]
- Microwave spectroscopy
- FT-IR
- FT-NIR^[35] [36] [37]
- Spectral, Hyperspectral, and Chemical imaging)^{[38] [39] [40] [41] [42] [43] [44]}.
- Raman spectroscopy/microscopy^[45] and CARS^[46].
 Fluorescence correlation spectroscopy^[47] ^[48] ^[49] ^[50] ^[51] ^[52] ^[53] ^[54], Fluorescence cross-correlation spectroscopy and FRET^[55] [56] [57].
- Confocal microscopy^[58]

Gallery: CARS (Raman spectroscopy), Fluorescence confocal microscopy, and Hyperspectral imaging









Genomic and structural databases

- CBS Genome Atlas Database ^[59] contains examples of base skews.^[60]
- The Z curve database of genomes a 3-dimensional visualization and analysis tool of genomes ^{[61][62]}.
- DNA and other nucleic acids' molecular models: Coordinate files of nucleic acids molecular structure models in PDB and CIF formats ^[63]

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See also

- DNA
- Molecular graphics
- DNA structure
- X-ray scattering
- Neutron scattering
- Crystallography
- Crystal lattices
- Paracrystalline lattices/Paracrystals
- 2D-FT NMRI and Spectroscopy
- NMR Spectroscopy
- Microwave spectroscopy
- Two-dimensional IR spectroscopy
- Spectral imaging
- Hyperspectral imaging
- Chemical imaging
- NMR microscopy
- VCD or Vibrational circular dichroism
- FRET and FCS- Fluorescence correlation spectroscopy
- Fluorescence cross-correlation spectroscopy (FCCS)
- Molecular structure
- Molecular geometry
- Molecular topology
- DNA topology
- Sirius visualization software
- Nanostructure
- DNA nanotechnology
- Imaging
- Atomic force microscopy
- X-ray microscopy
- Liquid crystal
- Glasses
- QMC@Home
- Sir Lawrence Bragg, FRS
- Sir John Randall
- James Watson
- Francis Crick
- Maurice Wilkins
- Herbert Wilson, FRS
- Alex Stokes

External links

- DNA the Double Helix Game (http://nobelprize.org/educational_games/medicine/ dna_double_helix/) From the official Nobel Prize web site
- MDDNA: Structural Bioinformatics of DNA (http://humphry.chem.wesleyan.edu:8080/ MDDNA/)
- Double Helix 1953–2003 (http://www.ncbe.reading.ac.uk/DNA50/) National Centre for Biotechnology Education
- DNA under electron microscope (http://www.fidelitysystems.com/Unlinked_DNA.html)
- Ascalaph DNA (http://www.agilemolecule.com/Ascalaph/Ascalaph_DNA.html) Commercial software for DNA modeling
- DNAlive: a web interface to compute DNA physical properties (http://mmb.pcb.ub.es/ DNAlive). Also allows cross-linking of the results with the UCSC Genome browser and DNA dynamics.
- DiProDB: Dinucleotide Property Database (http://diprodb.fli-leibniz.de). The database is designed to collect and analyse thermodynamic, structural and other dinucleotide properties.
- Further details of mathematical and molecular analysis of DNA structure based on X-ray data (http://planetphysics.org/encyclopedia/ BesselFunctionsApplicationsToDiffractionByHelicalStructures.html)
- Bessel functions corresponding to Fourier transforms of atomic or molecular helices. (http://planetphysics.org/?op=getobj&from=objects& name=BesselFunctionsAndTheirApplicationsToDiffractionByHelicalStructures)
- Application of X-ray microscopy in analysis of living hydrated cells (http://www.ncbi. nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract& list_uids=12379938)
- Characterization in nanotechnology some pdfs (http://nanocharacterization.sitesled. com/)
- overview of STM/AFM/SNOM principles with educative videos (http://www.ntmdt.ru/ SPM-Techniques/Principles/)
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- How SPM Works (http://www.parkafm.com/New_html/resources/01general.php)
- U.S. National DNA Day (http://www.genome.gov/10506367) watch videos and participate in real-time discussions with scientists.
- The Secret Life of DNA DNA Music compositions (http://www.tjmitchell.com/stuart/ dna.html)

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