DNA structure

DNA structure shows a variety of forms, both double-stranded and single-stranded. The mechanical properties of DNA, which are directly related to its structure, are a significant problem for cells. Every process which binds or reads DNA is able to use or modify the mechanical properties of DNA for purposes of recognition, packaging and modification. The extreme length (a chromosome may contain a 10 cm long DNA strand), relative rigidity and helical structure of DNA has led to the evolution of histones and of enzymes such as topoisomerases and helicases to manage a cell's DNA. The properties of DNA are closely related to its molecular structure and sequence, particularly the weakness of the hydrogen bonds and electronic interactions that hold strands of DNA together compared to the strength of the bonds within each strand.

Experimental techniques which can directly measure the mechanical properties of DNA are relatively new, and high-resolution visualization in solution is often difficult. Nevertheless, scientists have uncovered large amount of data on the mechanical properties of this polymer, and the implications of DNA's mechanical properties on cellular processes is a topic of active current research.

It is important to note the DNA found in many cells can be macroscopic in length - a few centimetres long for each human chromosome. Consequently, cells must compact or "package" DNA to carry it within them. In eukaryotes this is carried by spool-like proteins known as histones, around which DNA winds. It is the further compaction of this DNA-protein complex which produces the well known mitotic eukaryotic chromosomes.

Structure determination

DNA structures can be determined using either nuclear magnetic resonance spectroscopy or X-ray crystallography. The first published reports of A-DNA X-ray diffraction patterns--and also B-DNA—employed analyses based on Patterson transforms that provided only a limited amount of structural information for oriented fibers of DNA isolated from calf thymus.[1] [2] An alternate analysis was then proposed by Wilkins et al. in 1953 for B-DNA X-ray diffraction/scattering patterns of hydrated, bacterial oriented DNA fibers and trout sperm heads in terms of squares of Bessel functions.[3] Although the `B-DNA form' is most common under the conditions found in cells,[4] it is not a well-defined conformation but a family or fuzzy set of DNA-conformations that occur at the high hydration levels present in a wide variety of living cells.[5] Their corresponding X-ray diffraction & scattering patterns are characteristic of molecular paracrystals with a significant degree of disorder (>20%)[6] [7] , and concomitantly the structure is not tractable using only the standard analysis.

On the other hand, the standard analysis, involving only Fourier transforms of Bessel functions[8] and DNA molecular models, is still routinely employed for the analysis of A-DNA and Z-DNA X-ray diffraction patterns.[9]

Base pair geometry

The geometry of a base pair can be characterised by 6 coordinates: rise, twist, slide, shift, tilt, and roll. These values precisely define the location and orientation in space of each base pair in a DNA molecule relative to its predecessor along the axis of the helix. Together, they characterise the helical structure of the molecule. In regions of a DNA molecule where the normal structure is disrupted these values are used to describe the disruption.

For each base pair, considered relative to its predecessor[10] [11] [12] :

Shear

Buckle

Stretch

Propeller twist

Rotation of one base with respect to the other in the same base pair.

Stagger

Opening

Shift

displacement along an axis in the base-pair plane perpendicular to the first, directed from the minor to the major groove.

Tilt

rotation around this axis.

Slide

displacement along an axis in the plane of the base pair directed from one strand to the other.

Roll

rotation around this axis.

Rise

displacement along the helix axis.

Twist

rotation around the helix axis.

x-displacement

y-displacement

inclination

tip

pitch

the number of base pairs per complete turn of the helix

Rise and twist determine the handedness and pitch of the helix. The other coordinates, by contrast, can be zero. Slide and shift are typically small in B-DNA, but are substantial in A- and Z-DNA. Roll and tilt make successive base pairs less parallel, and are typically small. A diagram [13] of these coordinates can be found in 3DNA [14] website.

Note that "tilt" has often been used differently in the scientific literature, referring to the deviation of the first, inter-strand base-pair axis from perpendicularity to the helix axis. This

corresponds to slide between a succession of base pairs, and in helix-based coordinates is properly termed "inclination".

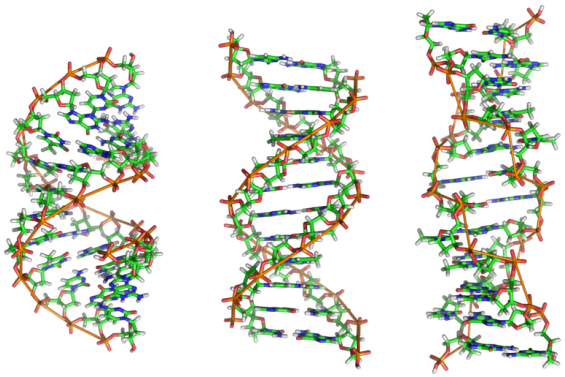
DNA helix geometries

Three DNA conformations are believed to be found in nature, A-DNA, B-DNA, and Z-DNA. The "B" form described by James D. Watson and Francis Crick is believed to predominate in cells[15] . It is 23.7 Å wide and extends 34 Å per 10 bp of sequence. The double helix makes one complete turn about its axis every 10.4-10.5 base pairs in solution. This frequency of twist (known as the helical *pitch*) depends largely on stacking forces that each base exerts on its neighbours in the chain.

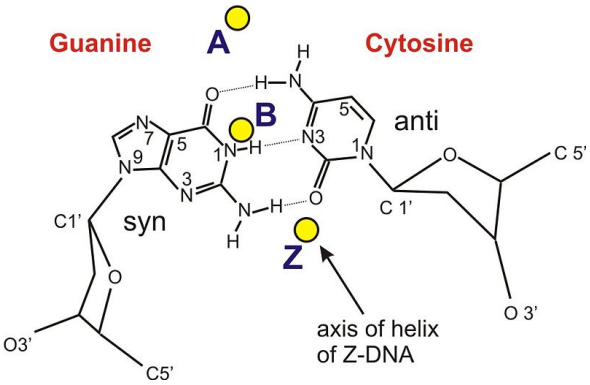
Other conformations are possible; A-DNA, B-DNA, C-DNA, D-DNA[16] , E-DNA[17] , L-DNA(enantiomeric form of D-DNA)[16] , P-DNA[18] , S-DNA, Z-DNA, etc. have been described so far.[19] In fact, only the letters F, Q, U, V, and Y are now available to describe any new DNA structure that may appear in the future.[20] [21] However, most of these forms have been created synthetically and have not been observed in naturally occurring biological systems. Also note the triple-stranded DNA possibility.

A-and Z-DNA

A-DNA and Z-DNA differ significantly in their geometry and dimensions to B-DNA, although still form helical structures. The A form appears likely to occur only in dehydrated samples of DNA, such as those used in crystallographic experiments, and possibly in hybrid pairings of DNA and RNA strands. Segments of DNA that cells have methylated for regulatory purposes may adopt the Z geometry, in which the strands turn about the helical axis the opposite way to A-DNA and B-DNA. There is also evidence of protein-DNA complexes forming Z-DNA structures.



The structures of A-, B-, and Z-DNA.



The helix axis of A-, B-, and Z-DNA.

Geometry attribute	A-DNA	B-DNA	Z-DNA
Helix sense	right-handed	right-handed	left-handed
Repeating unit	1 bp	1 bp	2 bp
Rotation/bp	33.6°	35.9°	60°/2bp
Mean bp/turn	10.7	10.0	12
Inclination of bp to axis	+19°	-1.2°	-9°
Rise/bp along axis	2.3 Å	3.32 Å	3.8 Å

Pitch/turn of helix	24.6 Å	33.2 Å	45.6 Å
Mean propeller twist	+18°	+16°	0°
Glycosyl angle	anti	anti	**C**: anti, **G**: syn
Sugar pucker	C3'-endo	C2'-endo	**C**: C2'-endo, **G**: C2'-exo
Diameter	25.5 Å	23.7 Å	18.4 Å

Supercoiled DNA

The B form of the DNA helix twists 360° per 10.4-10.5 bp in the absence of torsional strain. But many molecular biological processes can induce torsional strain. A DNA segment with excess or insufficient helical twisting is referred to, respectively, as positively or negatively "supercoiled". DNA *in vivo* is typically negatively supercoiled, which facilitates the unwinding (melting) of the double-helix required for RNA transcription.

Non-helical forms

Other non-double helical forms of DNA have been described, for example side-by-side (SBS) and triple helical configurations. Single stranded DNA may exist *in statu nascendi* or as thermally induced despiralized DNA.

DNA bending

DNA is a relatively rigid polymer, typically modelled as a worm-like chain. It has three significant degrees of freedom; bending, twisting and compression, each of which cause particular limitations on what is possible with DNA within a cell. Twisting/torsional stiffness is important for the circularisation of DNA and the orientation of DNA bound proteins relative to each other and bending/axial stiffness is important for DNA wrapping and circularisation and protein interactions. Compression/extension is relatively unimportant in the absence of high tension.

Persistence length/Axial stiffness

Example sequences and their persistence lengths (B DNA)

Sequence	Persistence Length /base pairs
Random	154±10
$(\mathbf{CA})_{\text{repeat}}$	133±10
$(\mathbf{CAG})_{\text{repeat}}$	124±10
$(\mathbf{TATA})_{\text{repeat}}$	137±10

DNA in solution does not take a rigid structure but is continually changing conformation due to thermal vibration and collisions with water molecules, which makes classical measures of rigidity impossible. Hence, the bending stiffness of DNA is measured by the persistence length, defined as:

> "The length of DNA over which the time-averaged orientation of the polymer becomes uncorrelated by a factor of *e*."

This value may be directly measured using an atomic force microscope to directly image DNA molecules of various lengths. In aqueous solution the average persistence length is 46-50 nm or 140-150 base pairs (the diameter of DNA is 2 nm), although can vary significantly. This makes DNA a moderately stiff molecule.

The persistence length of a section of DNA is somewhat dependent on its sequence, and this can cause significant variation. The variation is largely due to base stacking energies and the residues which extend into the minor and major grooves.

Models for DNA bending

Stacking stability of base steps (B DNA)

Step	Stacking ΔG /kcal mol^{-1}
T A	-0.19
T G or **C A**	-0.55
C G	-0.91
A G or **C T**	-1.06
A A or **T T**	-1.11
A T	-1.34
G A or **T C**	-1.43
C C or **G G**	-1.44
A C or **G T**	-1.81
G C	-2.17

The entropic flexibility of DNA is remarkably consistent with standard polymer physics models such as the *Kratky-Porod* worm-like chain model. Consistent with the worm-like chain model is the observation that bending DNA is also described by Hooke's law at very small (sub-piconewton) forces. However for DNA segments less than the persistence length, the bending force is approximately constant and behaviour deviates from the worm-like chain predictions.

This effect results in unusual ease in circularising small DNA molecules and a higher probability of finding highly bent sections of DNA.

Bending preference

DNA molecules often have a preferred direction to bend, ie. anisotropic bending. This is, again, due to the properties of the bases which make up the DNA sequence - a random sequence will have no preferred bend direction, i.e. isotropic bending.

Preferred DNA bend direction is determined by the stability of stacking each base on top of the next. If unstable base stacking steps are always found on one side of the DNA helix then the DNA will preferentially bend away from that direction. As bend angle increases then steric hindrances and ability to roll the residues relative to each other also play a role, especially in the minor groove. **A** and **T** residues will be preferentially be found in the minor

grooves on the inside of bends. This effect is particularly seen in DNA-protein binding where tight DNA bending is induced, such as in nucleosome particles. See base step distortions above.

DNA molecules with exceptional bending preference can become intrinsically bent. This was first observed in trypanosomatid kinetoplast DNA. Typical sequences which cause this contain stretches of 4-6 **T** and **A** residues separated by **G** and **C** rich sections which keep the A and T residues in phase with the minor groove on one side of the molecule. For example:

```
 |                 |                   |                   |
                  |                 |
G A T T C C C A A A A A T G T C A A A A A A T A G G C A A A A A A T G C
 C A A A A A A T C C C A A A C
```

The intrinsically bent structure is induced by the 'propeller twist' of base pairs relative to each other allowing unusual bifurcated Hydrogen-bonds between base steps. At higher temperatures this structure, and so the intrinsic bend, is lost.

All DNA which bends anisotropically has, on average, a longer persistence length and greater axial stiffness. This increased rigidity is required to prevent random bending which would make the molecule act isotropically.

DNA circularisation

DNA circularisation depends on both the axial (bending) stiffness and torsional (rotational) stiffness of the molecule. For a DNA molecule to successfully circularise it must be long enough to easily bend into the full circle and must have the correct number of bases so the ends are in the correct rotation to allow bonding to occur. The optimum length for circularisation of DNA is around 400 base pairs (136 nm), with an integral number of turns of the DNA helix, i.e. multiples of 10.4 base pairs. Having a non integral number of turns presents a significant energy barrier for circularisation, for example a 10.4 x 30 = 312 base pair molecule will circularise hundreds of times faster than 10.4 x 30.5 ≈ 317 base pair molecule.

DNA stretching

Longer stretches of DNA are entropically elastic under tension. When DNA is in solution, it undergoes continuous structural variations due to the energy available in the solvent. This is due to the thermal vibration of the molecule combined with continual collisions with water molecules. For entropic reasons, more compact relaxed states are thermally accessible than stretched out states, and so DNA molecules are almost universally found in a tangled relaxed layouts. For this reason, a single molecule of DNA will stretch under a force, straightening it out. Using optical tweezers, the entropic stretching behavior of DNA has been studied and analyzed from a polymer physics perspective, and it has been found that DNA behaves largely like the *Kratky-Porod* worm-like chain model under physiologically accessible energy scales.

Under sufficient tension and positive torque, DNA is thought to undergo a phase transition with the bases splaying outwards and the phosphates moving to the middle. This proposed structure for overstretched DNA has been called "P-form DNA," in honor of Linus Pauling who originally presented it as a possible structure of DNA[18]

The mechanical properties DNA under compression have not been characterized due to experimental difficulties in preventing the polymer from bending under the compressive force.

DNA melting

Melting stability of base steps (B DNA)

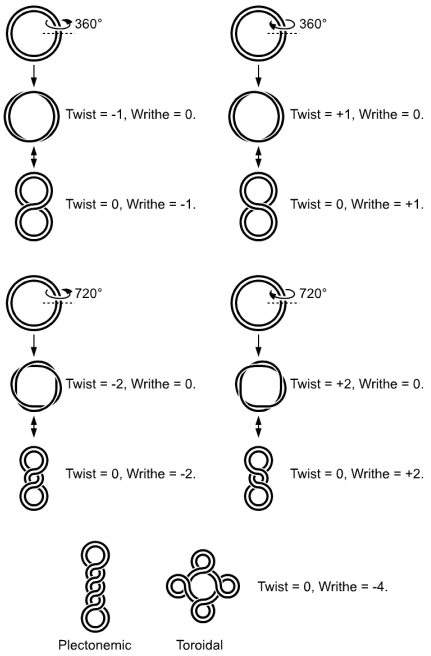
Step	Melting ΔG /Kcal mol^{-1}
T A	-0.12
T G or **C A**	-0.78
C G	-1.44
A G or **C T**	-1.29
A A or **T T**	-1.04
A T	-1.27
G A or **T C**	-1.66
C C or **G G**	-1.97
A C or **G T**	-2.04
G C	-2.70

DNA melting is the process by which the interactions between the strands of the double helix are broken, separating the two strands of DNA. These bonds are weak, easily separated by gentle heating, enzymes, or physical force. DNA melting preferentially occurs at certain points in the DNA.[22] **T** and **A** rich sequences are more easily melted than **C** and **G** rich regions. Particular base steps are also susceptible to DNA melting, particularly **T A** and **T G** base steps.[23] These mechanical features are reflected by the use of sequences such as **TATAA** at the start of many genes to assist RNA polymerase in melting the DNA for transcription.

Strand separation by gentle heating, as used in PCR, is simple providing the molecules have fewer than about 10,000 base pairs (10 kilobase pairs, or 10 kbp). The intertwining of the DNA strands makes long segments difficult to separate. The cell avoids this problem by allowing its DNA-melting enzymes (helicases) to work concurrently with topoisomerases, which can chemically cleave the phosphate backbone of one of the strands so that it can swivel around the other. Helicases unwind the strands to facilitate the advance of sequence-reading enzymes such as DNA polymerase.

DNA topology

Within the cell most DNA is topologically restricted. DNA is typically found in closed loops (such as plasmids in prokaryotes) which are topologically closed, or as very long molecules whose diffusion coefficients produce effectively topologically closed domains. Linear sections of DNA are also commonly bound to proteins or physical structures (such as membranes) to form closed topological loops.



Supercoiled structure of circular DNA molecules with low writhe. Note that the helical nature of the DNA duplex is omitted for clarity.

Francis Crick was one of the first to propose the importance of linking numbers when considering DNA supercoils. In a paper published in 1976, Crick outlined the problem as follows:

> In considering supercoils formed by closed double-stranded molecules of DNA certain mathematical concepts, such as the linking number and the twist, are needed. The meaning of these for a closed ribbon is explained and also that of the writhing number of a closed curve. Some simple examples are given, some of which may be relevant to the structure of chromatin.[24]

Analysis of DNA topology uses three values:

L = linking number - the number of times one DNA strand wraps around the other. It is an integer for a closed loop and constant for a closed topological domain.

T = twist - total number of turns in the double stranded DNA helix. This will normally try to be equal to the number turns a DNA molecule will make while free in solution, ie. number of bases/10.4.

W = writhe - number of turns of the double stranded DNA helix around the superhelical axis

$$L = T + W \text{ and } \Delta L = \Delta T + \Delta W$$

Any change of T in a closed topological domain must be balanced by a change in W, and vice versa. This results in higher order structure of DNA. A circular DNA molecule with a writhe of 0 will be circular. If the twist of this molecule is subsequently increased or decreased by supercoiling then the writhe will be appropriately altered, making the molecule undergo plectonemic or toroidal superhelical coiling.

When the ends of a piece of double stranded helical DNA are joined so that it forms a circle the strands are topologically knotted. This means the single strands cannot be separated any process that does not involve breaking a strand (such as heating). The task of un-knotting topologically linked strands of DNA falls to enzymes known as topoisomerases. These enzymes are dedicated to un-knotting circular DNA by cleaving one or both strands so that another double or single stranded segment can pass through. This un-knotting is required for the replication of circular DNA and various types of recombination in linear DNA which have similar topological constraints.

The linking number paradox

For many years, the origin of residual supercoiling in eukaryotic genomes remained unclear. This topological puzzle was referred to by some as the "linking number paradox".[25] However, when experimentally determined structures of the nucleosome displayed an overtwisted left-handed wrap of DNA around the histone octamer[26] [27] , this "paradox" was solved.

See also

- DNA nanotechnology
- Molecular models of DNA

References

[1] Franklin, R.E. and Gosling, R.G. received 6 March 1953. *Acta Cryst.* (1953). **6**, 673: The Structure of Sodium Thymonucleate Fibres I. The Influence of Water Content.; also *Acta Cryst.* **6**, 678: The Structure of Sodium Thymonucleate Fibres II. The Cylindrically Symmetrical Patterson Function.

[2] Franklin, Rosalind (1953). " Molecular Configuration in Sodium Thymonucleate. Franklin R. and Gosling R.G (http://www.nature.com/nature/dna50/franklingosling.pdf)" (PDF). *Nature* **171**: 740–741. doi: 10.1038/171740a0 (http://dx.doi.org/10.1038/171740a0). PMID 13054694. .

[3] Wilkins M.H.F., A.R. Stokes A.R. & Wilson, H.R. (1953). " Molecular Structure of Deoxypentose Nucleic Acids (http://www.nature.com/nature/dna50/wilkins.pdf)" (PDF). *Nature* **171**: 738–740. doi: 10.1038/171738a0 (http://dx.doi.org/10.1038/171738a0). PMID 13054693. .

[4] Leslie AG, Arnott S, Chandrasekaran R, Ratliff RL (1980). "Polymorphism of DNA double helices". *J. Mol. Biol.* **143** (1): 49–72. doi: 10.1016/0022-2836(80)90124-2 (http://dx.doi.org/10.1016/0022-2836(80)90124-2). PMID 7441761.

[5] Baianu, I.C. (1980). "Structural Order and Partial Disorder in Biological systems". *Bull. Math. Biol.* **42** (4): 464–468. doi: 10.1016/0022-2836(80)90124-2 (http://dx.doi.org/10.1016/0022-2836(80)90124-2).

[6] Hosemann R., Bagchi R.N., *Direct analysis of diffraction by matter*, North-Holland Publs., Amsterdam – New York, 1962

[7] Baianu I.C., X-ray scattering by partially disordered membrane systems, *Acta Cryst. A*, **34** (1978), 751–753.

[8] Bessel functions and diffraction by helical structures (http://planetphysics.org/encyclopedia/BesselFunctionsAndTheirApplicationsToDiffractionByHelicalStructures.html)

[9] X-Ray Diffraction Patterns of Double-Helical Deoxyribonucleic Acid (DNA) Crystals (http://planetphysics.org/encyclopedia/BesselFunctionsApplicationsToDiffractionByHelicalStructures.html)

[10] Dickerson RE (1989). "Definitions and nomenclature of nucleic acid structure components". *Nucleic Acids Res* **17** (5): 1797–1803. doi: 10.1093/nar/17.5.1797 (http://dx.doi.org/10.1093/nar/17.5.1797). PMID 2928107.

[11] Lu XJ, Olson WK (1999). "Resolving the discrepancies among nucleic acid conformational analyses". *J Mol Biol* **285** (4): 1563–1575. doi: 10.1006/jmbi.1998.2390 (http://dx.doi.org/10.1006/jmbi.1998.2390). PMID 9917397.

[12] Olson WK, Bansal M, Burley SK, Dickerson RE, Gerstein M, Harvey SC, Heinemann U, Lu XJ, Neidle S, Shakked Z, Sklenar H, Suzuki M, Tung CS, Westhof E, Wolberger C, Berman HM (2001). "A standard reference frame for the description of nucleic acid base-pair geometry". *J Mol Biol* **313** (1): 229–237. doi: 10.1006/jmbi.2001.4987 (http://dx.doi.org/10.1006/jmbi.2001.4987). PMID 11601858.

[13] http://rutchem.rutgers.edu/~xiangjun/3DNA/images/bp_step_hel.gif

[14] http://rutchem.rutgers.edu/~xiangjun/3DNA/examples.html

[15] Richmond, et al. (2003). "The structure of DNA in the nucleosome core". *Nature* **423**: 145–150. doi: 10.1038/nature01595 (http://dx.doi.org/10.1038/nature01595). PMID 12736678.

[16] Hayashi G, Hagihara M, Nakatani K (2005). "Application of L-DNA as a molecular tag". *Nucleic Acids Symp Ser (Oxf)* **49**: 261-262. PMID 17150733.

[17] Vargason JM, Eichman BF, Ho PS (2000). "The extended and eccentric E-DNA structure induced by cytosine methylation or bromination". *Nature Structural Biology* **7**: 758–761. doi: 10.1038/78985 (http://dx.doi.org/10.1038/78985).

[18] Allemand, et al. (1998). "Stretched and overwound DNA forms a Pauling-like structure with exposed bases". *PNAS* **24**: 14152–14157. doi: 10.1073/pnas.95.24.14152 (http://dx.doi.org/10.1073/pnas.95.24.14152).

PMID 9826669.
[19] List of 55 fiber structures (http://rutchem.rutgers.edu/~xiangjun/3DNA/misc/fiber_model.txt)
[20] Bansal M (2003). "DNA structure: Revisiting the Watson-Crick double helix". *Current Science* **85** (11): 1556-1563.
[21] Ghosh A, Bansal M (2003). "A glossary of DNA structures from A to Z". *Acta Cryst* **D59**: 620-626. doi: 10.1107/S0907444903003251 (http://dx.doi.org/10.1107/S0907444903003251).
[22] Breslauer KJ, Frank R, Blöcker H, Marky LA (1986). "Predicting DNA duplex stability from the base sequence". *PNAS* **83** (11): 3746-3750. PMID 3459152.
[23] Richard Owczarzy (2008-08-28). "DNA melting temperature - How to calculate it?" (http://www.owczarzy.net/tm.htm). *High-throughput DNA biophysics*. owczarzy.net. . Retrieved on 2008-10-02.
[24] Crick FH (1976). "Linking numbers and nucleosomes". *Proc Natl Acad Sci USA* **73** (8): 2639–43. doi: 10.1073/pnas.73.8.2639 (http://dx.doi.org/10.1073/pnas.73.8.2639). PMID 1066673.
[25] Prunell A (1998). "A topological approach to nucleosome structure and dynamics: the linking number paradox and other issues". *Biophys J* **74** (5): 2531–2544. PMID 9591679.
[26] Luger K, Mader AW, Richmond RK, Sargent DF, Richmond TJ (1997). "Crystal structure of the nucleosome core particle at 2.8 A resolution". *Nature* **389** (6648): 251-260. doi: 10.1038/38444 (http://dx.doi.org/10.1038/38444). PMID 9305837.
[27] Davey CA, Sargent DF, Luger K, Maeder AW, Richmond TJ (2002). "Solvent mediated interactions in the structure of the nucleosome core particle at 1.9 Å resolution". *Journal of Molecular Biology* **319** (5): 1097-1113. doi: 10.1016/S0022-2836(02)00386-8 (http://dx.doi.org/10.1016/S0022-2836(02)00386-8). PMID 12079350.

External links

- MDDNA: Structural Bioinformatics of DNA (http://humphry.chem.wesleyan.edu:8080/MDDNA/)
- 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.

Article Sources and Contributors

DNA structure *Source*: http://en.wikipedia.org/w/index.php?oldid=291765597 *Contributors*: Andreww, Antandrus, Bci2, CDN99, Chodges, DVD R W, DabMachine, Dysmorodrepanis, Forluvoft, Gene Nygaard, Hannes Röst, Harold f, Joel7687, Josq, Luuva, Maikfr, Mr.Z-man, MrHaiku, Nasz, Patrick0Moran, Rajan.kartik, Reinyday, Rich Farmbrough, Thorwald, TimVickers, Tomgally, Wknight94, Yahel Guhan, Zephyris, 21 anonymous edits

Image Sources, Licenses and Contributors

License

Version 1.2, November 2002

0.PREAMBLE

The purpose of this License is to make a manual, textbook, or other functional and useful document "free" in the sense of freedom: to assure everyone the effective freedom to copy and redistribute it, with or without modifying it, either commercially or noncommercially. Secondarily, this License preserves for the author and publisher a way to get credit for their work, while not being considered responsible for modifications made by others.
This License is a kind of "copyleft", which means that derivative works of the document must themselves be free in the same sense. It complements the GNU General Public License, which is a copyleft license designed for free software.
We have designed this License in order to use it for manuals for free software, because free software needs free documentation: a free program should come with manuals providing the same freedoms that the software does. But this License is not limited to software manuals; it can be used for any textual work, regardless of subject matter or whether it is published as a printed book. We recommend this License principally for works whose purpose is instruction or reference.

1.APPLICABILITY AND DEFINITIONS

This License applies to any manual or other work, in any medium, that contains a notice placed by the copyright holder saying it can be distributed under the terms of this License. Such a notice grants a world-wide, royalty-free license, unlimited in duration, to use that work under the conditions stated herein. The "Document", below, refers to any such manual or work. Any member of the public is a licensee, and is addressed as "you". You accept the license if you copy, modify or distribute the work in a way requiring permission under copyright law.
A "Modified Version" of the Document means any work containing the Document or a portion of it, either copied verbatim, or with modifications and/or translated into another language.
A "Secondary Section" is a named appendix or a front-matter section of the Document that deals exclusively with the relationship of the publishers or authors of the Document to the Document's overall subject (or to related matters) and contains nothing that could fall directly within that overall subject. (Thus, if the Document is in part a textbook of mathematics, a Secondary Section may not explain any mathematics.) The relationship could be a matter of historical connection with the subject or with related matters, or of legal, commercial, philosophical, ethical or political position regarding them.
The "Invariant Sections" are certain Secondary Sections whose titles are designated, as being those of Invariant Sections, in the notice that says that the Document is released under this License. If a section does not fit the above definition of Secondary then it is not allowed to be designated as Invariant. The Document may contain zero Invariant Sections. If the Document does not identify any Invariant Sections then there are none.
The "Cover Texts" are certain short passages of text that are listed, as Front-Cover Texts or Back-Cover Texts, in the notice that says that the Document is released under this License. A Front-Cover Text may be at most 5 words, and a Back-Cover Text may be at most 25 words.
A "Transparent" copy of the Document means a machine-readable copy, represented in a format whose specification is available to the general public, that is suitable for revising the document straightforwardly with generic text editors or (for images composed of pixels) generic paint programs or (for drawings) some widely available drawing editor, and that is suitable for input to text formatters or for automatic translation to a variety of formats suitable for input to text formatters. A copy made in an otherwise Transparent file format whose markup, or absence of markup, has been arranged to thwart or discourage subsequent modification by readers is not Transparent. An image format is not Transparent if used for any substantial amount of text. A copy that is not "Transparent" is called "Opaque".
Examples of suitable formats for Transparent copies include plain ASCII without markup, Texinfo input format, LaTeX input format, SGML or XML using a publicly available DTD, and standard-conforming simple HTML, PostScript or PDF designed for human modification. Examples of transparent image formats include PNG, XCF and JPG. Opaque formats include proprietary formats that can be read and edited only by proprietary word processors, SGML or XML for which the DTD and/or processing tools are not generally available, and the machine-generated HTML, PostScript or PDF produced by some word processors for output purposes only.
The "Title Page" means, for a printed book, the title page itself, plus such following pages as are needed to hold, legibly, the material this License requires to appear in the title page. For works in formats which do not have any title page as such, "Title Page" means the text near the most prominent appearance of the work's title, preceding the beginning of the body of the text.
A section "Entitled XYZ" means a named subunit of the Document whose title either is precisely XYZ or contains XYZ in parentheses following text that translates XYZ in another language. (Here XYZ stands for a specific section name mentioned below, such as "Acknowledgements", "Dedications", "Endorsements", or "History".) To "Preserve the Title" of such a section when you modify the Document means that it remains a section "Entitled XYZ" according to this definition.
The Document may include Warranty Disclaimers next to the notice which states that this License applies to the Document. These Warranty Disclaimers are considered to be included by reference in this License, but only as regards disclaiming warranties: any other implication that these Warranty Disclaimers may have is void and has no effect on the meaning of this License.

2.VERBATIM COPYING

You may copy and distribute the Document in any medium, either commercially or noncommercially, provided that this License, the copyright notices, and the license notice saying this License applies to the Document are reproduced in all copies, and that you add no other conditions whatsoever to those of this License. You may not use technical measures to obstruct or control the reading or further copying of the copies you make or distribute. However, you may accept compensation in exchange for copies. If you distribute a large enough number of copies you must also follow the conditions in section 3.
You may also lend copies, under the same conditions stated above, and you may publicly display copies.

3.COPYING IN QUANTITY

If you publish printed copies (or copies in media that commonly have printed covers) of the Document, numbering more than 100, and the Document's license notice requires Cover Texts, you must enclose the copies in covers that carry, clearly and legibly, all these Cover Texts: Front-Cover Texts on the front cover, and Back-Cover Texts on the back cover. Both covers must also clearly and legibly identify you as the publisher of these copies. The front cover must present the full title with all words of the title equally prominent and visible. You may add other material on the covers in addition. Copying with changes limited to the covers, as long as they preserve the title of the Document and satisfy these conditions, can be treated as verbatim copying in other respects.
If the required texts for either cover are too voluminous to fit legibly, you should put the first ones listed (as many as fit reasonably) on the actual cover, and continue the rest onto adjacent pages.
If you publish or distribute Opaque copies of the Document numbering more than 100, you must either include a machine-readable Transparent copy along with each Opaque copy, or state in or with each Opaque copy a computer-network location from which the general network-using public has access to download using public-standard network protocols a complete Transparent copy of the Document, free of added material. If you use the latter option, you must take reasonably prudent steps, when you begin distribution of Opaque copies in quantity, to ensure that this Transparent copy will remain thus accessible at the stated location until at least one year after the last time you distribute an Opaque copy (directly or through your agents or retailers) of that edition to the public.
It is requested, but not required, that you contact the authors of the Document well before redistributing any large number of copies, to give them a chance to provide you with an updated version of the Document.

4.MODIFICATIONS

You may copy and distribute a Modified Version of the Document under the conditions of sections 2 and 3 above, provided that you release the Modified Version under precisely this License, with the Modified Version filling the role of the Document, thus licensing distribution and modification of the Modified Version to whoever possesses a copy of it. In addition, you must do these things in the Modified Version:

1. Use in the Title Page (and on the covers, if any) a title distinct from that of the Document, and from those of previous versions (which should, if there were any, be listed in the History section of the Document). You may use the same title as a previous version if the original publisher of that version gives permission.
2. List on the Title Page, as authors, one or more persons or entities responsible for authorship of the modifications in the Modified Version, together with at least five of the principal authors of the Document (all of its principal authors, if it has fewer than five), unless they release you from this requirement.
3. State on the Title page the name of the publisher of the Modified Version, as the publisher.
4. Preserve all the copyright notices of the Document.
5. Add an appropriate copyright notice for your modifications adjacent to the other copyright notices.

6. Include, immediately after the copyright notices, a license notice giving the public permission to use the Modified Version under the terms of this License, in the form shown in the Addendum below.
7. Preserve in that license notice the full lists of Invariant Sections and required Cover Texts given in the Document's license notice.
8. Include an unaltered copy of this License.
9. Preserve the section Entitled "History", Preserve its Title, and add to it an item stating at least the title, year, new authors, and publisher of the Modified Version as given on the Title Page. If there is no section Entitled "History" in the Document, create one stating the title, year, authors, and publisher of the Document as given on its Title Page, then add an item describing the Modified Version as stated in the previous sentence.
10. Preserve the network location, if any, given in the Document for public access to a Transparent copy of the Document, and likewise the network locations given in the Document for previous versions it was based on. These may be placed in the "History" section. You may omit a network location for a work that was published at least four years before the Document itself, or if the original publisher of the version it refers to gives permission.
11. For any section Entitled "Acknowledgements" or "Dedications", Preserve the Title of the section, and preserve in the section all the substance and tone of each of the contributor acknowledgements and/or dedications given therein.
12. Preserve all the Invariant Sections of the Document, unaltered in their text and in their titles. Section numbers or the equivalent are not considered part of the section titles.
13. Delete any section Entitled "Endorsements". Such a section may not be included in the Modified Version.
14. Do not retitle any existing section to be Entitled "Endorsements" or to conflict in title with any Invariant Section.
15. Preserve any Warranty Disclaimers.

If the Modified Version includes new front-matter sections or appendices that qualify as Secondary Sections and contain no material copied from the Document, you may at your option designate some or all of these sections as invariant. To do this, add their titles to the list of Invariant Sections in the Modified Version's license notice. These titles must be distinct from any other section titles.

You may add a section Entitled "Endorsements", provided it contains nothing but endorsements of your Modified Version by various parties--for example, statements of peer review or that the text has been approved by an organization as the authoritative definition of a standard.

You may add a passage of up to five words as a Front-Cover Text, and a passage of up to 25 words as a Back-Cover Text, to the end of the list of Cover Texts in the Modified Version. Only one passage of Front-Cover Text and one of Back-Cover Text may be added by (or through arrangements made by) any one entity. If the Document already includes a cover text for the same cover, previously added by you or by arrangement made by the same entity you are acting on behalf of, you may not add another; but you may replace the old one, on explicit permission from the previous publisher that added the old one.

The author(s) and publisher(s) of the Document do not by this License give permission to use their names for publicity for or to assert or imply endorsement of any Modified Version.

5.COMBINING DOCUMENTS

You may combine the Document with other documents released under this License, under the terms defined in section 4 above for modified versions, provided that you include in the combination all of the Invariant Sections of all of the original documents, unmodified, and list them all as Invariant Sections of your combined work in its license notice, and that you preserve all their Warranty Disclaimers.

The combined work need only contain one copy of this License, and multiple identical Invariant Sections may be replaced with a single copy. If there are multiple Invariant Sections with the same name but different contents, make the title of each such section unique by adding at the end of it, in parentheses, the name of the original author or publisher of that section if known, or else a unique number. Make the same adjustment to the section titles in the list of Invariant Sections in the license notice of the combined work.

In the combination, you must combine any sections Entitled "History" in the various original documents, forming one section Entitled "History"; likewise combine any sections Entitled "Acknowledgements", and any sections Entitled "Dedications". You must delete all sections Entitled "Endorsements."

6.COLLECTIONS OF DOCUMENTS

You may make a collection consisting of the Document and other documents released under this License, and replace the individual copies of this License in the various documents with a single copy that is included in the collection, provided that you follow the rules of this License for verbatim copying of each of the documents in all other respects.

You may extract a single document from such a collection, and distribute it individually under this License, provided you insert a copy of this License into the extracted document, and follow this License in all other respects regarding verbatim copying of that document.

7.AGGREGATION WITH INDEPENDENT WORKS

A compilation of the Document or its derivatives with other separate and independent documents or works, in or on a volume of a storage or distribution medium, is called an "aggregate" if the copyright resulting from the compilation is not used to limit the legal rights of the compilation's users beyond what the individual works permit. When the Document is included in an aggregate, this License does not apply to the other works in the aggregate which are not themselves derivative works of the Document.

If the Cover Text requirement of section 3 is applicable to these copies of the Document, then if the Document is less than one half of the entire aggregate, the Document's Cover Texts may be placed on covers that bracket the Document within the aggregate, or the electronic equivalent of covers if the Document is in electronic form. Otherwise they must appear on printed covers that bracket the whole aggregate.

8.TRANSLATION

Translation is considered a kind of modification, so you may distribute translations of the Document under the terms of section 4. Replacing Invariant Sections with translations requires special permission from their copyright holders, but you may include translations of some or all Invariant Sections in addition to the original versions of these Invariant Sections. You may include a translation of this License, and all the license notices in the Document, and any Warranty Disclaimers, provided that you also include the original English version of this License and the original versions of those notices and disclaimers. In case of a disagreement between the translation and the original version of this License or a notice or disclaimer, the original version will prevail.

If a section in the Document is Entitled "Acknowledgements", "Dedications", or "History", the requirement (section 4) to Preserve its Title (section 1) will typically require changing the actual title.

9.TERMINATION

You may not copy, modify, sublicense, or distribute the Document except as expressly provided for under this License. Any other attempt to copy, modify, sublicense or distribute the Document is void, and will automatically terminate your rights under this License. However, parties who have received copies, or rights, from you under this License will not have their licenses terminated so long as such parties remain in full compliance.

10.FUTURE REVISIONS OF THIS LICENSE

The Free Software Foundation may publish new, revised versions of the GNU Free Documentation License from time to time. Such new versions will be similar in spirit to the present version, but may differ in detail to address new problems or concerns. See http://www.gnu.org/copyleft/.

Each version of the License is given a distinguishing version number. If the Document specifies that a particular numbered version of this License "or any later version" applies to it, you have the option of following the terms and conditions either of that specified version or of any later version that has been published (not as a draft) by the Free Software Foundation. If the Document does not specify a version number of this License, you may choose any version ever published (not as a draft) by the Free Software Foundation.

How to use this License for your documents

To use this License in a document you have written, include a copy of the License in the document and put the following copyright and license notices just after the title page:

> Copyright (c) YEAR YOUR NAME.
>
> Permission is granted to copy, distribute and/or modify this document
>
> under the terms of the GNU Free Documentation License, Version 1.2
>
> or any later version published by the Free Software Foundation;
>
> with no Invariant Sections, no Front-Cover Texts, and no Back-Cover Texts.
>
> A copy of the license is included in the section entitled "GNU
>
> Free Documentation License".

If you have Invariant Sections, Front-Cover Texts and Back-Cover Texts, replace the "with...Texts." line with this:

> with the Invariant Sections being LIST THEIR TITLES, with the
>
> Front-Cover Texts being LIST, and with the Back-Cover Texts being LIST.

If you have Invariant Sections without Cover Texts, or some other combination of the three, merge those two alternatives to suit the situation.

If your document contains nontrivial examples of program code, we recommend releasing these examples in parallel under your choice of free software license, such as the GNU General Public License, to permit their use in free software.