

A Comprehensive Bending Classification of Nucleic Acid Duplex Structures

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Introduction

The textbook picture of the DNA double helix structure has a straight helical axis. In most biological contexts, however, DNA or RNA duplexes exhibit slight or marked deviations from this ideal geometry. The most obvious effect is seen in a bent helical axis. **Helical axis bending** may be either due to **internal factors**, like *specific sequence elements*, *intra-strand crosslinking*, and *asymmetric charge neutralization*, or **external factors** including *drugs or other small-molecule ligands*, *proteins*, and *crystal packing*.

A bent helical axis can exhibit an abrupt change in its direction, a **kink**, or a smooth change that can be described by a **curved line**.

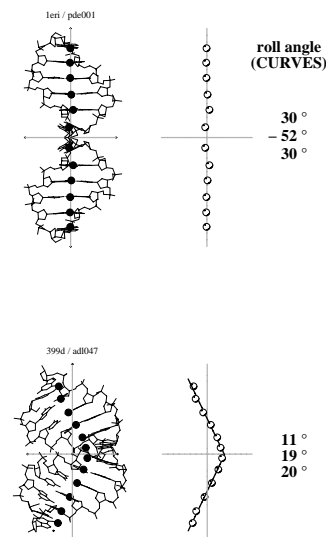
Helical axis bending should be reflected in unusual values of local base step parameters, like roll and tilt, for example. However, the deviations for different base pair steps may also cancel each other and thus finally lead to a straight helical axis. Moreover, bending may be either due to a significant change in only one base step or due to small or large changes in several steps. Therefore, a thorough **bending analysis** has to take into account both the **local and global point of view**.

We have developed a uniform approach for the bending analysis of nucleic acid double helix structures that provides information on both local and global geometry parameters. The results obtained for individual structures have been used to generate a comprehensive bending classification in terms of shape of the helical axis and extent of bending.

Methods

The results presented include tables for the base step parameters rise, shift, slide, twist, roll, tilt, and for selected backbone torsion angles, and plots of the base step parameters as well as of the minor and major groove widths. Moreover, full outputs of the programs CURVES (2) and FREEHELIX (3) are available. Three orthogonal views of the nucleic acid duplex including the CURVES helical axis are shown. The orientation of the duplex structures is not just taken from the original structure file. Rather, the coordinate axes are aligned to the principle axes of inertia of the global helix axis. These representations show the bending features of the helices at the first glance. The helical axis is fitted to a straight line, a circular line (arc), a single-kink line and a double-kink line. By means of a goodness-of-fit criterion the most appropriate model can be selected. In this way the global geometry properties are quantitatively described. Finally, the results obtained for each single structure are used to generate a comprehensive bending classification either in terms of the shape of helical axis or extent of bending. In the latter case a generalized bending measure **M** is defined. It corresponds to the *kink angle* for a *single-kink* helical axis and to either the *sum of kink angles* or the *largest kink angle* in the *double-kink* case. From *circular line* structures for which a single-kink line has an almost equal goodness of fit an empirical relationship between the radius of curvature and the *kink angle* has been derived: $kink\ angle = 465.4272 / (radius\ of\ curvature^{0.82575})$. In this way, also the bending of circular line structures can be measured, at least approximately, by means of a kink angle. Note, however, that this relationship works only for the data set used here.

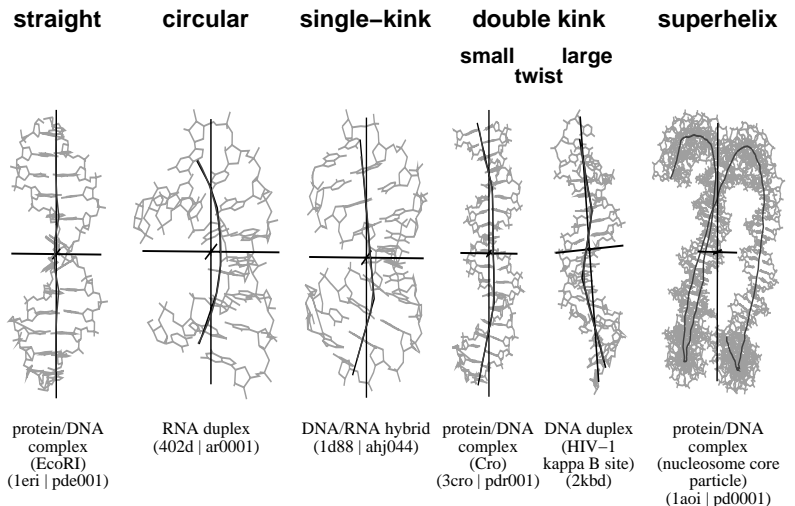
Global vs. Local Bending Analysis



It is often assumed that helical axis kinking in a global sense is due to a local roll angle of $> 20^\circ$ (3,4). The following two examples show that this is not correct in all cases. The DNA part of the ECO RI endonuclease/DNA complex (1eri) has an overall straight helical axis even though there are two local roll angles of 30° . Their effect is obviously cancelled by the roll angle of -52° for the base step in between. On the other hand, the most strongly bent free DNA duplex (399d) has only roll angles up to 20° . Nevertheless, in many cases a unusual local roll leads indeed to a global kink in the helical axis.

Classification

The following types of helical axis bending types occur in currently known nucleic acid structures:



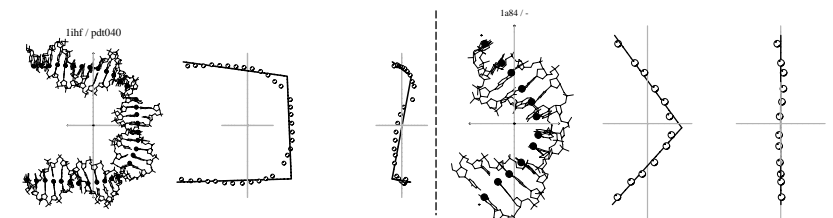
Among the more than 850 structures only 13 have a goodness-of-fit value larger than 2. Even most of these structures, like the integration host factor (PDB code: 1ihf), for example, can at least roughly be described by one of the models. The only exception is the DNA part of the nucleosome core particle with a superhelical axis (1aoi, 1ezq, 1dnn).

Using the geometrical parameters of the fitted models (radius of curvature, kink angle, twist angle) we have generated a comprehensive bending classification of nucleic acid duplex structures in terms of the geometrical shape of the helical axis and of the extent of bending.

Among the 40 most strongly bent structures with kink angles larger than 45° at a single kink point are almost exclusively nucleic-acid protein complexes, the most prominent example being the integration host factor (1ihf) with a kink angle of 92° . On the other hand, there are also nucleic acid-protein complexes with a straight helical axis, like the DNA/Eco RI endonuclease complex (1eri). Large kink angles do also occur for structures with intra-strand crosslinks (1a84: 78°). With a kink angle of 52° the most strongly bent free nucleic acid is an A-DNA with some B-DNA features (399d).

The currently known free B-DNA structures cover a range of kink angles between 0 and 37° (1d8x: 36° , 1cfl: 37°), whereas the corresponding range for A-DNA is between 0° and 53° (399d: 52° , 2d47: 53°).

In double-kink structures the twist angle between end segments and shows no correlation with the length of the central segment.



Availability

The results are accessible on the web as part of the IMB Jena Image Library of Macromolecules (<http://www.imb-jena.de/IMAGE.html>) (1). The database is updated on a regular basis and currently includes about 850 nucleic acid double helix structures (free or bound to drugs or proteins) with at least 6 consecutive base pairs available from the Protein Data Bank (PDB) and the Nucleic Acid Database (NDB).

References

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