Structural bioinformatics

VDNA: The virtual DNA plug-in for VMD

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Summary: The DNA inter base pair step parameters (Tilt, Roll, Twist, Shift, Slide, Rise) are a standard internal coordinate representation of DNA. In the absence of bend and shear, it is relatively easy to mentally visualize how Twist and Rise generate the familiar double helix. More complex structures do not readily yield to such intuition. For this reason, we developed a plug-in for VMD that accepts a set of mathematical expressions as input and generates a coarse-grained model of DNA as output. This feature of VDNA appears to provide a unique approach to DNA modeling. Predefined expressions include: linear, sheared, bent and circular DNA, and models of the nucleosome superhelix, chromatin, thermal motion and nucleosome unwrapping.

Availability: VDNA is pre-installed in VMD, http://www.ks.uiuc.edu/Research/vmd. Updates are at http://dna.ccs.tulane.edu.

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1 INTRODUCTION

The DNA inter base pair step parameters (Tilt, Roll, Twist, Shift, Slide, Rise) are widely employed to model the structure, energetics and dynamics of DNA. These parameters describe the relative rotations and translations along a length of DNA needed to move from one base pair to the next. The parameters are well defined (Dickerson, 1989), and there are a number of programs for extracting these parameters from a Cartesian coordinate representation of DNA or for assembling a model of DNA given a set of helical parameters (El Hassan and Calladine, 1995; Lavery and Sklenar, 1988; Lu and Olson, 2003; Macke and Case, 1998; Tung and Carter, 1994; Vlahovicic and Pongor, 2000). However, none of these enable the user to specify a set of mathematical functions for the helical parameters and rapidly visualize the corresponding 3D model. This is a major obstacle in development of an understanding of the energetics and dynamics of DNA. These parameters describe the bend, shear, Twist and Rise as a function of the variable $s$ which is the distance from the accumulation of bend, shear, Twist and Rise as a function of $s$. We emphasize that the helical parameter description is suitable for any fiber like chain of local directors can be embedded in the fiber. Thus, while VDNA is intended to represent DNA it is actually much more widely applicable. The complete set of helical parameters includes intra base pair parameters (Shear, Stretch, Stagger, Buckle, Propeller-Twist, Opening), which describe deformations of the base pairs. VDNA does not utilize these descriptors.

Here, let $\Omega = (\text{Tilt}, \text{Roll}, \text{Twist})$ and $\Gamma = (\text{Shift}, \text{Slide}, \text{Rise})$ represent the DNA helical parameters. In general $\Omega$ and $\Gamma$ are functions of $s$ and $t$ where $s$ represents the continuum limit of position measured in base pair steps along the DNA and $t$ represents time. To obtain a 3D representation of DNA as a space curve $\vec{r}$ with local directors $\hat{d}_i(s)$ requires integration of $\Omega(s,t)$ and $\Gamma(s,t)$ as a function of $s$ at time $t$. VDNA simply provides an interface for defining $\Omega(s,t)$ and $\Gamma(s,t)$, integrating the expressions and displaying results. In case $\Omega$ and $\Gamma$ are time dependent, VDNA automatically integrates $\Omega$ and $\Gamma$ from $s = 0$ to $s = \max S$ for each instance $t = 0$ to $\max T$ with a time step of $\Delta t$. The result is max $T + 1$ structures corresponding to $t = 0, 1, 2, \ldots, \max T$.

For the purposes of numerical integration VDNA utilizes El Hassan’s algorithm (El Hassan and Calladine, 1995). This algorithm has proven to be extremely fast and robust and ensures invariance to the direction of integration, i.e. integration from $s = 0$ to $s = \max S$ or $s = \max S$ to $0$ gives the same result. Note the sign of Shift and Tilt must be changed during a ‘reverse’ integration.

3 USAGE

The main VDNA panel, Figure 1, is generated by selecting ‘Extensions’ ± ‘Virtual DNA Viewer’ from the VMD pull-down menus. This panel provides text boxes for inputing the inter base pair step parameters with local directors and denoted $\hat{d}_i(s)$ are rotated (Tilt, Roll, Twist) and translated (Shift, Slide, Rise) to achieve the set of directors associated with the $(i\pm1)$-th base pair. The local bend is $\sqrt{\text{Roll}^2 + \text{Twist}^2}$ and local shear is $\sqrt{\text{Shift}^2 + \text{Slide}^2}$. In Cartesian coordinates, DNA is a space curve with centerline $\vec{c}_i(s)$ and directors $\hat{d}_i(s)$ that results from the accumulation of bend, shear, Twist and Rise as a function of $s$. VDNA will generate a total of $\max S$ (Dickerson, 1989), and there are a number of programs for extracting these parameters from a Cartesian coordinate representation of DNA or for assembling a model of DNA given a set of helical parameters (El Hassan and Calladine, 1995; Lavery and Sklenar, 1988; Lu and Olson, 2003; Macke and Case, 1998; Tung and Carter, 1994; Vlahovicic and Pongor, 2000). However, none of these enable the user to specify a set of mathematical functions for the helical parameters and rapidly visualize the corresponding 3D model. This is a major obstacle in development of an understanding of the complex relations between local and global structure. Only for the most most distributions of DNA helical parameters is it easy to mentally visualize the global structure of DNA. For this purpose, we have developed a plug-in for VMD (Humphrey et al., 1996) that allows users to generate models of dsDNA using arbitrarily complex mathematical expressions.

2 METHODS

The inter base pair step parameters are a local or internal coordinate representation of DNA that specify how a set of vectors attached to the $(i)$-th base pair and denoted $\hat{d}_i(s)$ are rotated (Tilt, Roll, Twist) and translated (Shift, Slide, Rise) to achieve the set of directors associated with the $(i\pm1)$-th base pair. The local bend is $\sqrt{\text{Roll}^2 + \text{Twist}^2}$ and local shear is $\sqrt{\text{Shift}^2 + \text{Slide}^2}$. In Cartesian coordinates, DNA is a space curve with centerline $\vec{c}_i(s)$ and directors $\hat{d}_i(s)$ that results from the accumulation of bend, shear, Twist and Rise as a function of $s$. VDNA will generate a total of $\max S$ structures. In all cases, the angular deformations are defined in degrees per base pair step, and the translations are given in angstrom per base pair step. Any string that forms a valid argument to the Tcl command ‘expr’ can be used in defining the helical parameter integrations. (Consult the examples or a Tcl language reference source for more details.) VDNA recognizes several defined variables: V1, V2, Nuc and Lk (SP) is predefined as $\pi$ to single precision). The procedures $\omega$ and $\gamma$ utilize whatever text is entered for these variables. Such variable substitution provides a convenient means of introducing arbitrarily complex expressions into more than one helical parameter statement simultaneously. The text box ‘Cores’ defines the procedure
VMD in which all max
the base pair at
'Make Molec' button, while the 'Draw It' button loads a graphics object into
be further manipulated, e.g. fit, as was done for thermal model in Figure 2.

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sequence-dependent values for the helical parameters, greater
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4 FUTURE PLANS AND CONCLUSION
Features to be included in future versions of VDNA include sequence-dependent values for the helical parameters, greater support for conversion between all atom models and helical parameter models using either 3DNA or Curves and the reading of helical parameters from file. Presently, the parameter file produced by VDNA can be used to create an all atom model with 3DNA.

Finally, VDNA includes a number of predefined examples from
which to choose, see Figure 2. Some examples are intended to
demonstrate geometric relations and to assist in developing
intuition rather than model biologic entities. These models are not
pictured, but include: straight, bent, sheared, polygonal, circular
and superhelical structures. Others are designed to be building
blocks for modeling biologically relevant structures, Figure 2, but
are not parameterized to represent specific biophysical entities. The
default model, Figure 1, demonstrates how to combine the generic,
predicted Shear Helix and Thermal models to accurately represent
a specific biological entity: a Shear Helix model of nucleosome
core particle (Bishop, 2008) with DNA linkers that exhibit average
shear. Users can also select from predefined expressions, draw coarse-grained
mathematical expressions. The default model, right, is a parameterization of
Fig. 1.

We have introduced a general purpose tool for creating fiber-
like models, four-atom-per-base-pair models and all atom models
of DNA from mathematical expressions. Predefined expressions are
provided as building blocks to investigate structural, thermal and
dynamical properties including: shear (Shift or Slide); non-uniform
Twist; a Torsion Helix and a Shear Helix (Bishop, 2008); linker
DNA in simple models of chromatin; thermal variations; and time
evolutions. VDNA is written entirely in tcl so it can be readily
modified by users with limited programming experience.

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