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model.it: building three dimensional DNA models from sequence data

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Abstract

Summary: A WWW server is described for creating 3D models of canonical or bent DNA starting from sequence data. Predicted DNA trajectory is first computed based on a choice of di- and tri-nucleotide models (M.G.Munteanu et al., Trends Biochem. Sci. 23, 341–347, 1998); an atomic model is then constructed and optionally energyminimized with constrained molecular dynamics. The data are presented as a standard PDB file, directly viewable on the user's PC using any molecule manipulation program. Availability: The model.it server is freely available at http://www.icgeb.trieste.it/dna/

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Supplementary information: A series of help files is available at the above address.

Visualization of DNA 3D structure is essential for designing and interpreting molecular biology experiments. Several PC programs are available for modelling canonical and curved DNA (Bansal et al., 1995; Dlakic and Harrington, 1998; Jursa, 1994; Shpigelman et al., 1993; Tung and Carter, 1994), but very often these programs are built for a specific computer platform and use custom user interfaces that may be too complex for an intermittent user. Moreover, PC programs have difficulties in building curved DNA models, as the construction of a sugar phosphate backbone requires compute-intensive molecular mechanics calculations. The model.it server was designed to provide 3D models of DNA in response to DNA sequence queries. The results are presented as a standard PDB file that can be viewed directly using any of the widely available molecule manipulation programs such as Swiss PDB viewer (Guex et al., 1999) or Rasmol (Sayle and Milner-White, 1995). The server's help files contain instructions for installing these programs.

The *model.it* server was written using 'NAB'—a high level molecule manipulation language (Macke and Case, 1998). The construction is based on canonical A- and B-DNA basepairs with idealized geometries. The molecule

building process is performed in a local coordinate system based on transformations defined by the Cambridge convention (Dickerson, 1989). The first basepair is placed at the origin of a Cartesian coordinate system and then each following basepair is rotated (roll, tilt and twist rotations) and translated (rise is 3.4 Å for B- and 2.8 Å for A-DNA, respectively) with respect to the previous one. The server provides a choice of dinucleotide (Bolshoy et al., 1991; Olson et al., 1993; Ulyanov and James, 1995) and trinucleotide (Brukner et al., 1995) parameter sets for building curved DNA. Coordinates of the sugar-phosphate backbone are optionally optimized with constrained molecular dynamics using energy parameters from the AMBER package (Case et al., 1997). At present, the server can produce models of 700 bp in length, but models longer than 50 bp will not be optimized. Modelling of canonical, straight B or A DNA structures proceeds in a similar way, but without the need for backbone geometry optimization.

Naturally, modelling of DNA based on idealized or statistically derived geometry parameters is a rough approximation that does not take into account interactions with proteins or with the medium. While these models may not be highly accurate in terms of atomic detail, the gross spatial orientation of motifs with respect to each other is still a useful piece of information for designing or explaining experimental data. Since the DNA segments in question are often too long for current methods of structure determination, structure prediction can be particularly useful in this sense. Moreover, location of bends in DNA sequences can be predicted with reasonable accuracy, thus the orientation of motifs with respect to adjacent curved elements can also be studied. For example, it is an intriguing question whether or not such features can remain conserved in functionally equivalent sequences that have little sequence homology. Figure 1 shows a non-redundant set of Zea mays promoter regions chosen from the Eukaryotic Promoter Database (Perier et al., 1999) as an example. Their predicted conformations show that the corresponding DNA segments are all curved to the same extent and 11 out of 14 are bent in the same direction.

(a)				-
(u)	EP07003	1	ACAAATCCAAAAAAATTTATATGACATCTCACCTATTTAAATA CGCCCAAATCACT 56	
	EP16002	1	AACATTCCAAAACCCATCGATCHTCTATAAATGCCTAGCTCCCACATATGAACTACT 56	
	EP58009	1	CTCTCCTGT TRAGCACACAA TTTTCCTTTGT TCTCCAATCGTGTATCCATC 56	
	EP58013	1	AGTCATGCACCATCCCATCCG CLCACATCCACTATAATGCATATTGGCTCATGCA 56	
	EP58008	1	TG CGGACAACACCTGACCATTCATCTCACATCCCATTTTAGCTCTCTCATTCTCT 56	
	EP41001	1	AGATAAGGACCCCATCCCCGGCCACGCTATTTACCCAGGTGCCCCCCCC	
	EP35018	1	AGATGACCT CTATCCAAACCCAACTGTATAAAAG CAGCTGCTGTGTTCTGTTAT 56	
	EP11004	1	CCACCGCATCCACCTACGAGCACCTGCCCGTCTATTATTGCTCCCTCTCCCGTC 56	
	EP14012	1	CTACTGCCCTCCCCCCCCCCCCCCCCCCCCCCCCCCCCC	
	EP15001	1	CCAACCTTAAACACTCCCGCTCTTGCGCCATTATATATCACACCGTCGTCCATCCG 56	
	EP11006	1	TCCTCCTTTAGAGCTACCACTATATAAATCAGGCCTCATTTTCTCGCTCCTCACAG 56	
	EP14013	1	CCCTCGTAGACTAGACTCTAGACCACTATATACAGTACTCTCCCCCTTTTCTT 56	
	EP29016	1	CCCCCCACCCACCCCCCCCCCCCCCCCCCCCCCCCCCC	
	EP14014	1	GANTOTTOTGCACGCCCCATCTCCTCAATAAAACCTCCTCGGCTCCTCCAGTGTCC 56	
	EP07003	57	ACTTAATCCATCHCCCATAATCCTT 81	
	EP16002	57	CTCTATCATCATCCACACACACA 81	
	EP58009	57	CTATAATATTTTCAGCAATCACAAA 81	
	EP58013	57	TCCCTAATGGTGCTTCTTTACTGTT 81	
	EP58008	57	AGTCTCACCCTGACTATTTAGGTCT 81	
	EP41001	57	ACTCCACCAGCGCCATOTATACCAA 81	
	EP35018	57	GACACAGECATCHCACGCATACTGC 81	
	EP11004	57	CCAGAGAAACCCTCCCTCCTCCCC 81	
	EP14012	57	GCCCCGTCACATCCATCCACC 81	
	EP15001	57	AACTCCAGCAGCAGCTAAAGAAGCA 81	
	EP11006	57	CTCCTCCCTTTCCATCCCTTGC 81	
	EP14013	57	CCTCACCAACTTCTCATCAGCC 81	
	EP29016	57	ATCGACGAGAGAGCGAGCGCGATGG 81	
	EP14014	57	CTCGTCTCTCGCCTGPGARAAAAA 81	

(b)

ĺ	EP07003	10000000000000000	EP11004	20000000000000000000000000000000000000
	EP16002	2002020202020		00000000000000000000000000000000000000
	EP58009	202020202020000000000000000000000000000	EP15001	NON 2000000000
	EP58013	200000000000000000000000000000000000000	EP11006	200000000000000
	EP58008	200000000000000	EP14013	2000000000000000
	EP41001	000000000000000000000000000000000000000	EP29016	30000000000000000C
	EP35018	1000100000000000	EP14014	200000000000000000000000000000000000000

(c)

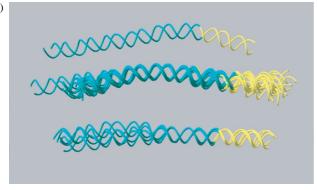


Fig. 1. (a) Alignment of 14 Zea mays promoter regions from EPD database. Transcription origin is marked with a red letter. (b) Predicted conformation based on the consensus parameter set (see Ref. Munteanu *et al.*, 1998, for details). Transcribed part is shown in yellow. (c) Superposition reveals three conformation groups.

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