Plasticity of base pairing observed in the A-form 18-mer DNA structures

Jakub Svoboda

Institute of Biotechnology, Czech Academy of Sciences

My goals

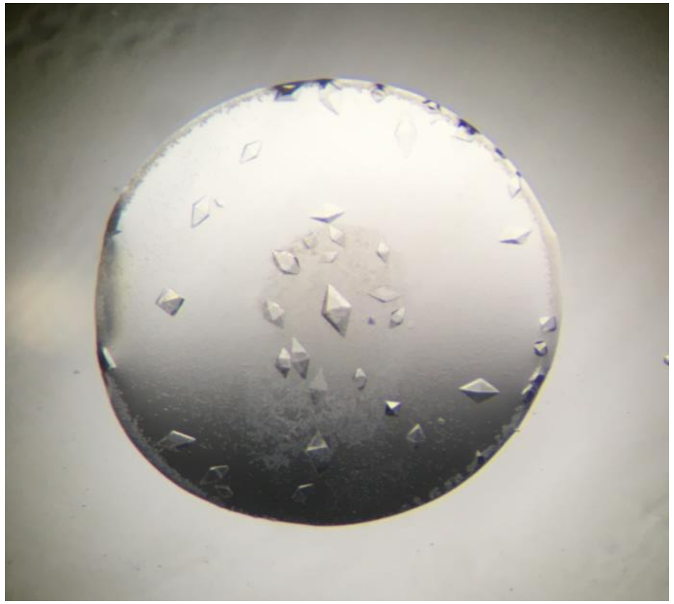
- Characterize geometry of various base pairs in crystal structures
- How base pairs affect local/global structural features
- Use of the NtCs (diNucleotide conformers)

Sequences

5'-GGTGGGGC**XY**GCCCCACC

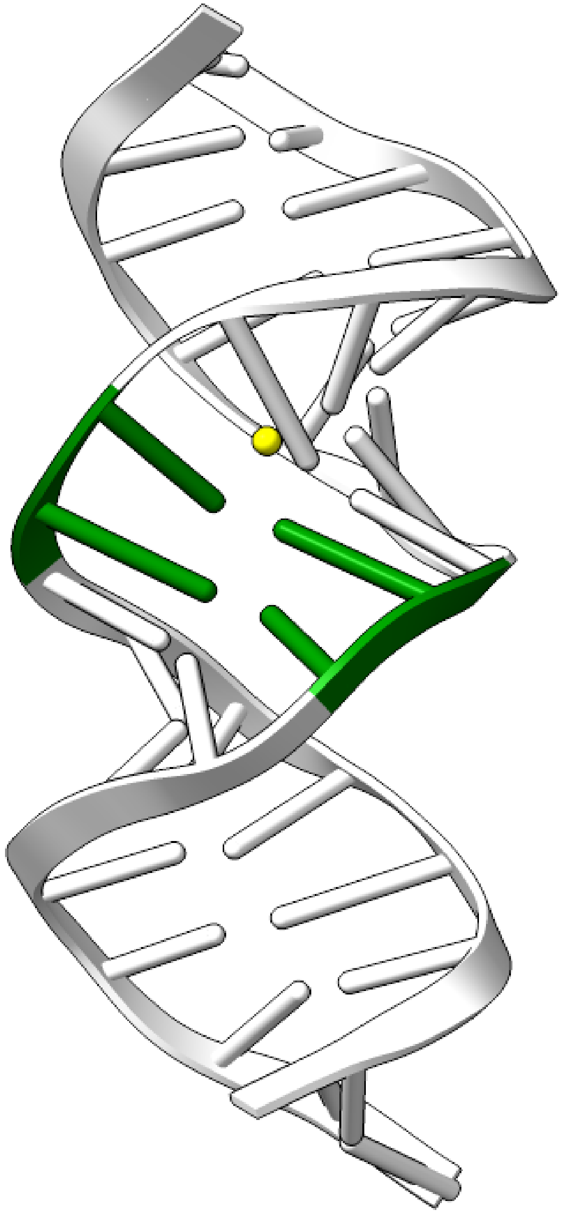
16 possibilities

AA	**AC**	**AG**	**AT**	**CA**	**CC**	**CG**	**CT**	**GA**	**GC**	**GG**	**GT**	**TA**	**TC**	**TG**	**TT**

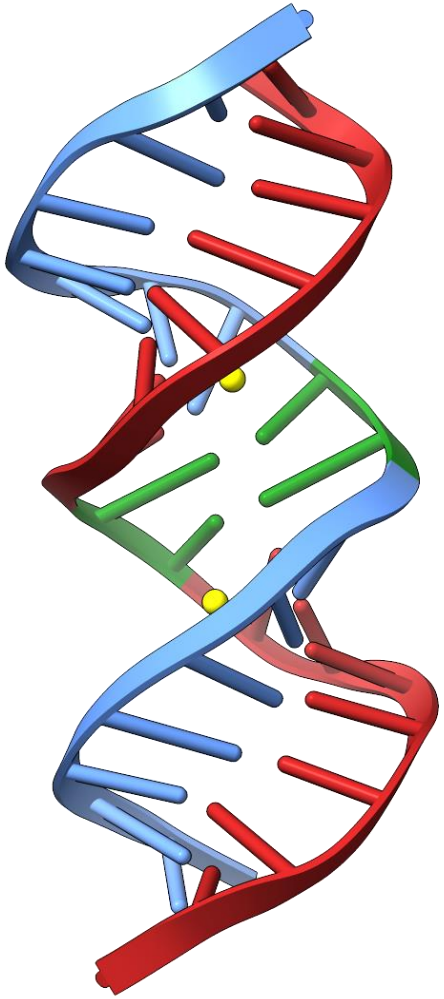


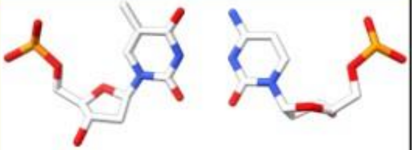
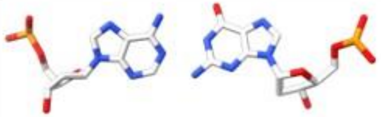
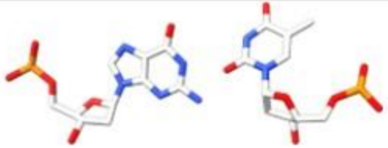
Refinement

- Restraints generated on the dnatco.datmos.org website
- NtC restraints greatly improved refinement procedure



X-ray structures - features



9th base → 10th base ↓	Adenine	Cytosine	Guanine	Thymine
Adenine				 20/1
Cytosine	 NA/NA	 NA/NA	 NA/NA	 18/1
Guanine	 8/1	 ?/?		
Thymine	 20/1		 ?/?	 16/1

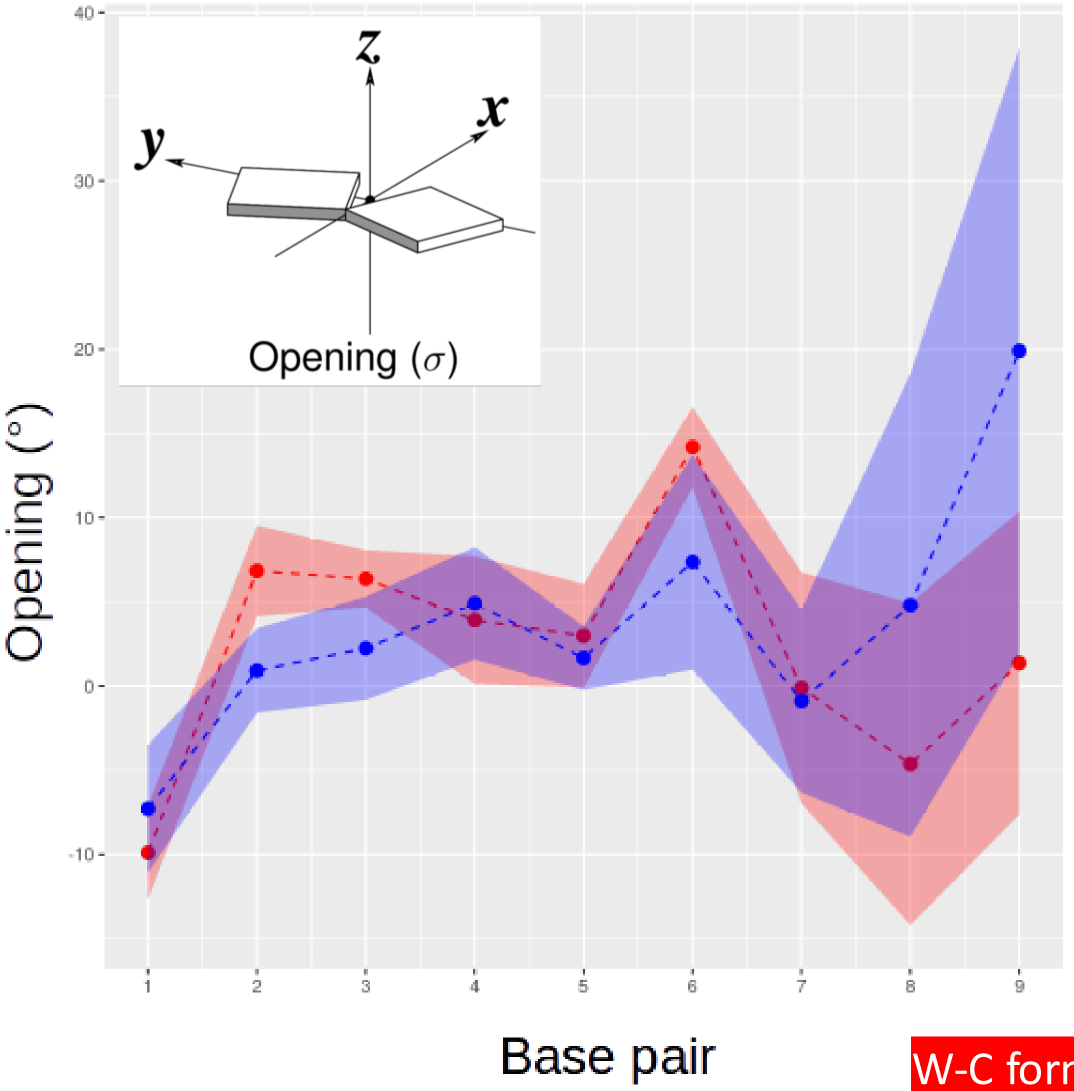
NtC (diNucleotide Conformer) assignment at dnatco.datmos.org

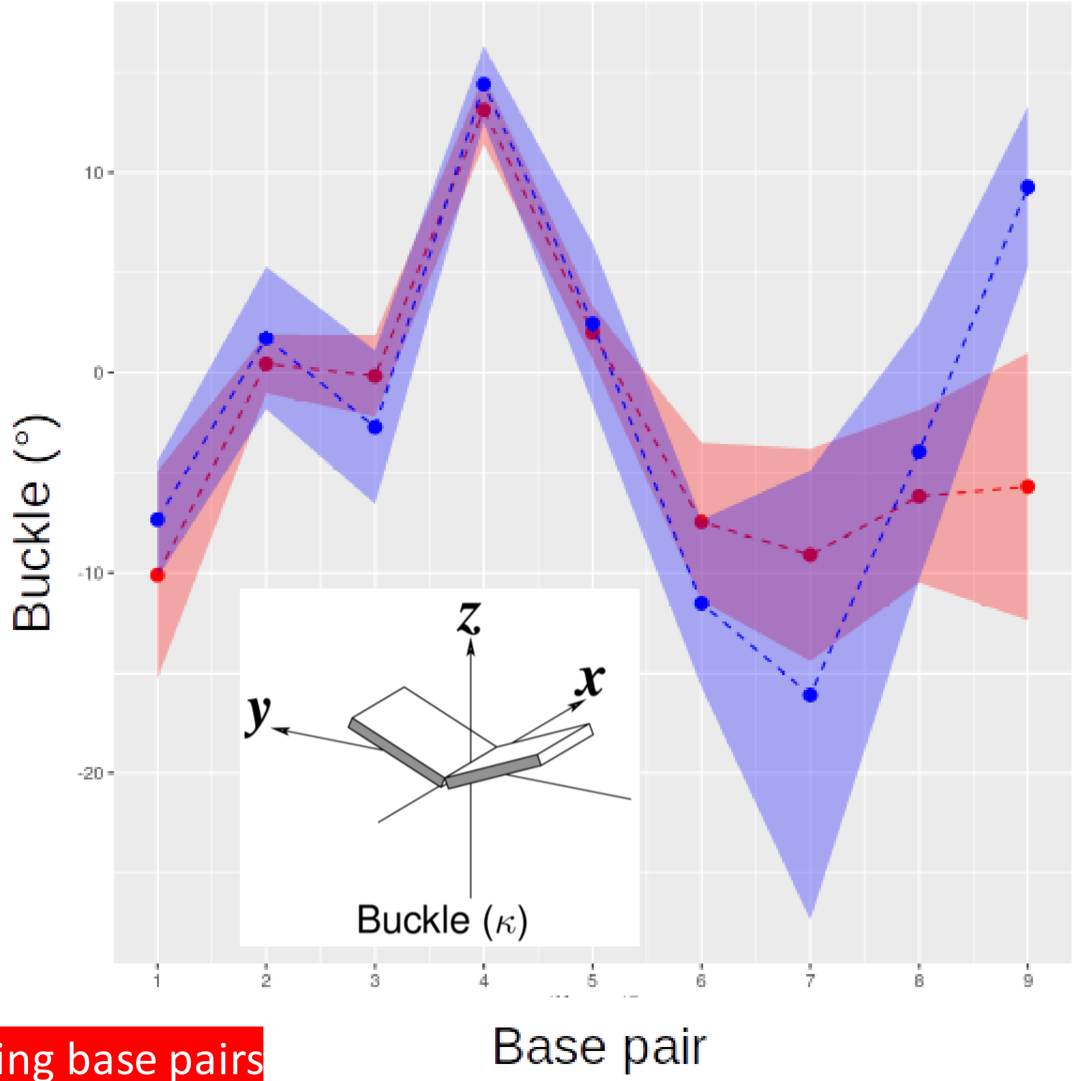
	AT	CG	GC	TA	CC	AC	GT	TC	AG	TT
A_DG_1_DG_2	AA04	AA04	AA04	AA00	AA00	AA04	AA04	AA04	AA04	AA08
A_DG_2_DT_3	AA00	AA00	AA00	AA00	AA00	AA00	AA00	AA00	AA00	AA00
A_DT_3_DG_4	AA00	AA00	AA00	AA00	AA08	AA00	AA00	AA00	AA00	AA08
A_DG_4_DG_5	AA00	AA00	AA00	AA01	AA04	AA00	AA00	AA00	AA00	AA04
A_DG_5_DG_6	AA00	AA00	AA00	AA08	AA00	AA00	AA00	AA00	AA00	AA00
A_DG_6_DG_7	AA01	AA01	AA01	AA06	AA01	AA01	AA01	AA01	AA01	AA10
A_DG_7_DC_8	AA08	AA08	AA08	NANT	AA08	AA08	NANT	AA08	NANT	AA08
A_DC_8_DX_9	AA00	AA11	AA00	AA08	AA00	AA00	AA00	AA00	AB01	AA00
A_DX_9_DY_10	AA03	AA08	AA08	NANT	AA00	AA00	AA00	AA00	NANT	AA08
A_DY_10_DG_11	NANT	AA00	AA00	AA00	NANT	AA06	AA06	NANT	NANT	NANT
A_DG_11_DC_12	AA01	AA10	AA10	AA08	NANT	AA11	AA11	NANT	NANT	NANT
A_DC_12_DC_13	AA08	AA08	AA08	AA00	AA08	AA08	AA08	AA08	AA08	BA08
A_DC_13_DC_14	AA00	AA00	AA00	AA03	AA00	AA00	AA00	AA00	AA00	AA00
A_DC_14_DC_15	AA00	AA00	AA00	AA08	AA00	AA00	AA00	AA00	AA00	AA08
A_DC_15_DA_16	AA10	AA10	AA10	AA06	AA01	AA10	AA10	AA10	AA10	AA06
A_DA_16_DC_17	AA00	AA00	AA00	AA08	AA00	AA00	AA00	AA00	AA00	AA08
A_DC_17_DC_18	AB05	AB05	AB05	NANT	AB05	AB05	AB05	AB05	AB05	AB05

NtC (diNucleotide Conformer) assignment at dnatco.datmos.org

	AT	CG	GC	TA	CC	AC	GT	TC	AG	TT
A_DG_7_DC_8	AA08	AA08	AA08	NANT	AA08	AA08	NANT	AA08	NANT	AA08
A_DC_8_DX_9	AA00	AA11	AA00	AA08	AA00	AA00	AA00	AA00	AB01	AA00
A_DX_9_DY_10	AA03	AA08	AA08	NANT	AA00	AA00	AA00	AA00	NANT	AA08
A_DY_10_DG_11	NANT	AA00	AA00	AA00	NANT	AA06	AA06	NANT	NANT	NANT
A_DG_11_DC_12	AA01	AA10	AA10	AA08	NANT	AA11	AA11	NANT	NANT	NANT

Base pair parameters

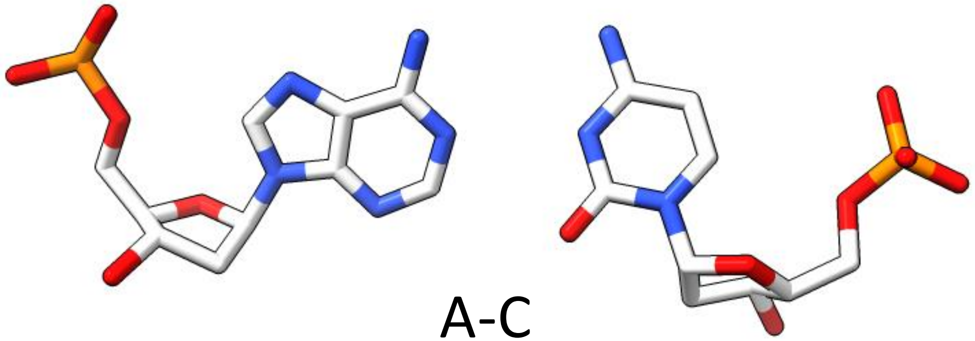




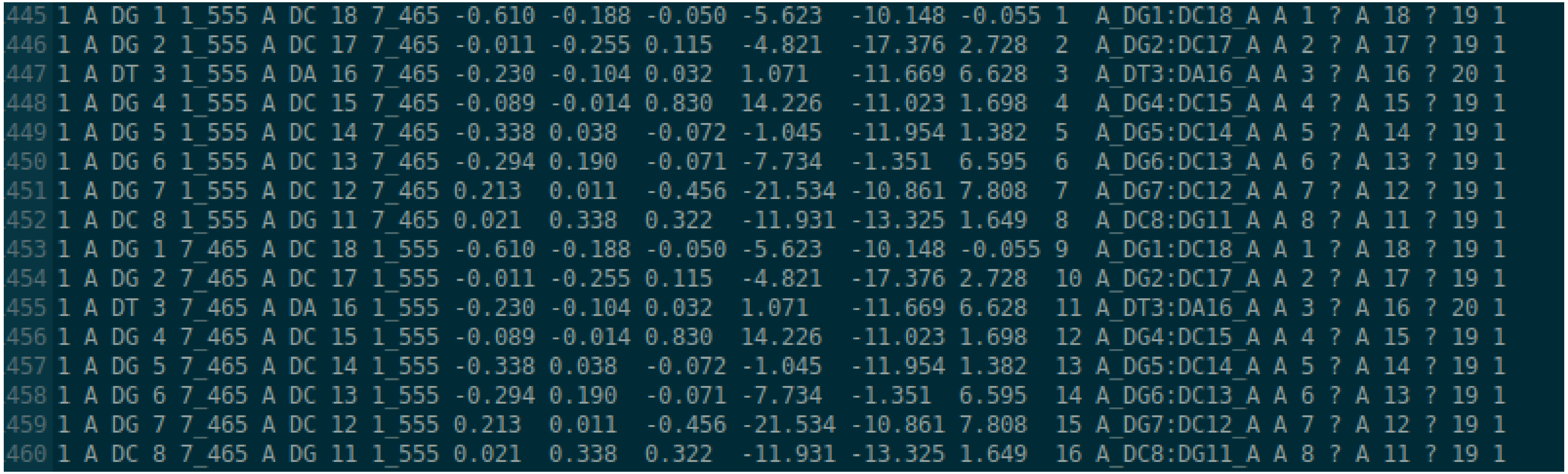
🟥 W-C forming base pairs

🟦 Non-W-C forming base pairs

Issues with BP and Step parameters



A-C



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1 A DG 1 1_555 A DC 18 7_465 -0.610 -0.188 -0.050 -5.623  -10.148 -0.055 1  A_DG1:DC18_A A 1 ? A 18 ? 19 1
1 A DG 2 1_555 A DC 17 7_465 -0.011 -0.255 0.115  -4.821  -17.376 2.728  2  A_DG2:DC17_A A 2 ? A 17 ? 19 1
1 A DT 3 1_555 A DA 16 7_465 -0.230 -0.104 0.032  1.071   -11.669 6.628  3  A_DT3:DA16_A A 3 ? A 16 ? 20 1
1 A DG 4 1_555 A DC 15 7_465 -0.089 -0.014 0.830  14.226  -11.023 1.698  4  A_DG4:DC15_A A 4 ? A 15 ? 19 1
1 A DG 5 1_555 A DC 14 7_465 -0.338 0.038  -0.072 -1.045  -11.954 1.382  5  A_DG5:DC14_A A 5 ? A 14 ? 19 1
1 A DG 6 1_555 A DC 13 7_465 -0.294 0.190  -0.071 -7.734  -1.351  6.595  6  A_DG6:DC13_A A 6 ? A 13 ? 19 1
1 A DG 7 1_555 A DC 12 7_465 0.213  0.011  -0.456 -21.534 -10.861 7.808  7  A_DG7:DC12_A A 7 ? A 12 ? 19 1
1 A DC 8 1_555 A DG 11 7_465 0.021  0.338  0.322  -11.931 -13.325 1.649  8  A_DC8:DG11_A A 8 ? A 11 ? 19 1
1 A DG 1 7_465 A DC 18 1_555 -0.610 -0.188 -0.050 -5.623  -10.148 -0.055 9  A_DG1:DC18_A A 1 ? A 18 ? 19 1
1 A DG 2 7_465 A DC 17 1_555 -0.011 -0.255 0.115  -4.821  -17.376 2.728  10 A_DG2:DC17_A A 2 ? A 17 ? 19 1
1 A DT 3 7_465 A DA 16 1_555 -0.230 -0.104 0.032  1.071   -11.669 6.628  11 A_DT3:DA16_A A 3 ? A 16 ? 20 1
1 A DG 4 7_465 A DC 15 1_555 -0.089 -0.014 0.830  14.226  -11.023 1.698  12 A_DG4:DC15_A A 4 ? A 15 ? 19 1
1 A DG 5 7_465 A DC 14 1_555 -0.338 0.038  -0.072 -1.045  -11.954 1.382  13 A_DG5:DC14_A A 5 ? A 14 ? 19 1
1 A DG 6 7_465 A DC 13 1_555 -0.294 0.190  -0.071 -7.734  -1.351  6.595  14 A_DG6:DC13_A A 6 ? A 13 ? 19 1
1 A DG 7 7_465 A DC 12 1_555 0.213  0.011  -0.456 -21.534 -10.861 7.808  15 A_DG7:DC12_A A 7 ? A 12 ? 19 1
1 A DC 8 7_465 A DG 11 1_555 0.021  0.338  0.322  -11.931 -13.325 1.649  16 A_DC8:DG11_A A 8 ? A 11 ? 19 1
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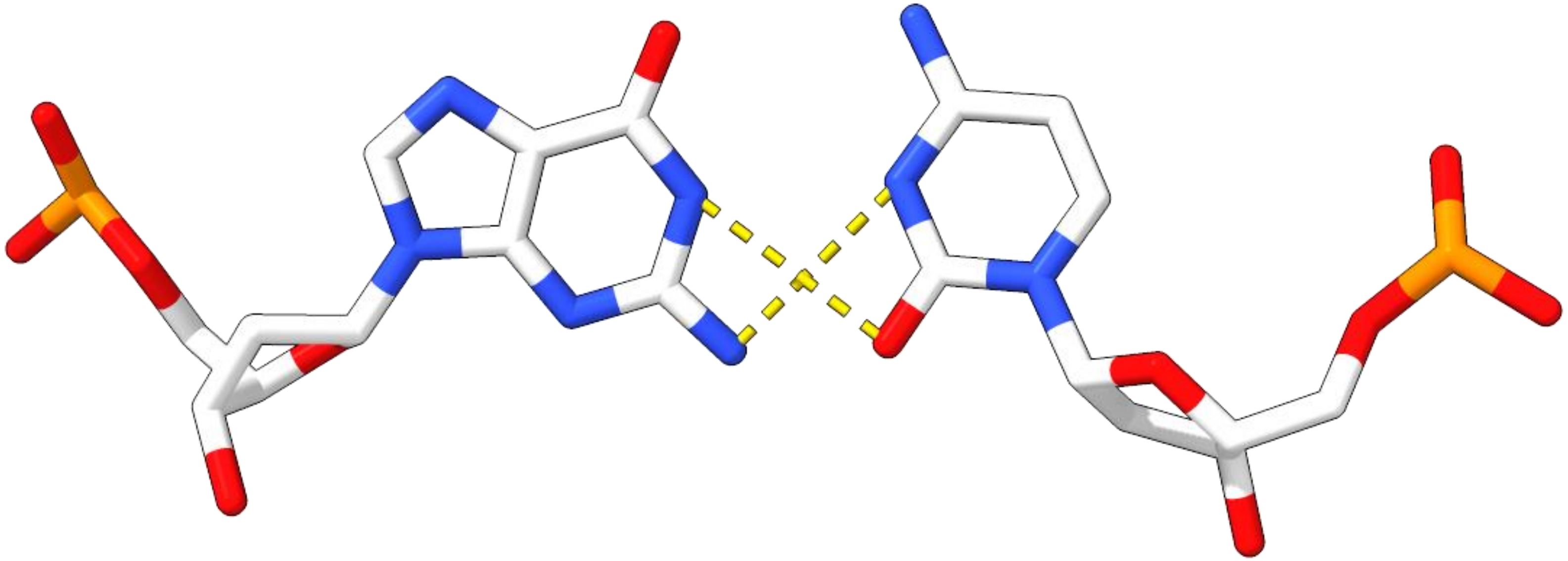
Base pair is not recognized → BP and Step parameters are not calculated

Analysis of mismatches across PDB unreliable: we discovered many mislabeled pairing patterns



PDBid: 5av9

Summary

- DNA backbone accommodates the changing central base pairs
- Structural imprint of the central dinucleotide is present but subtle
- NtC classes effortlessly annotate nucleic acid structures and help in the refinement process

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