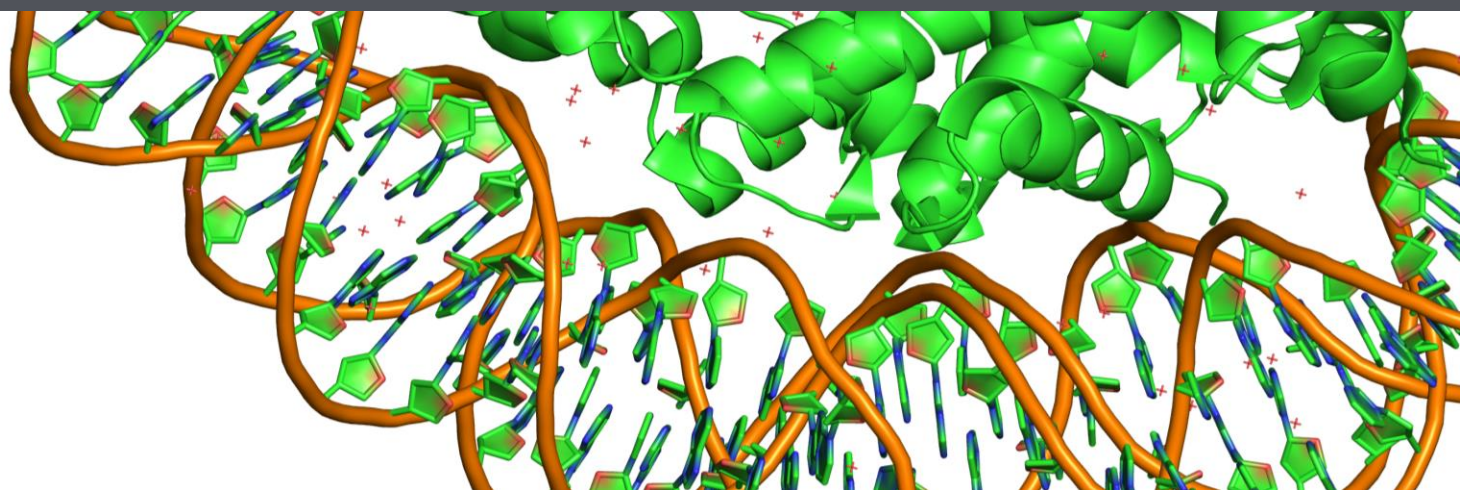


CRYSTALLOGRAPHY OF NUCLEIC ACIDS



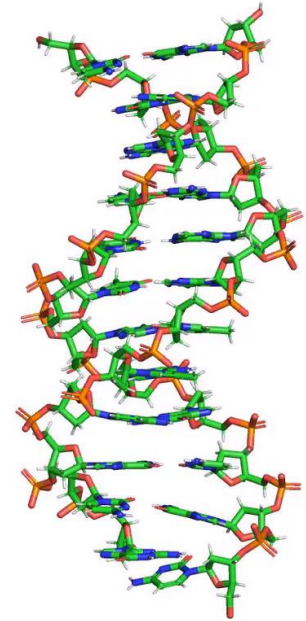
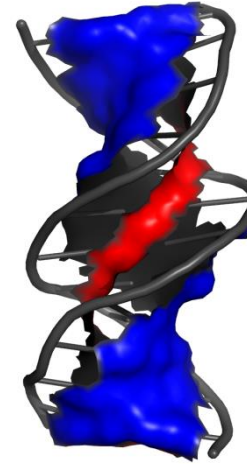
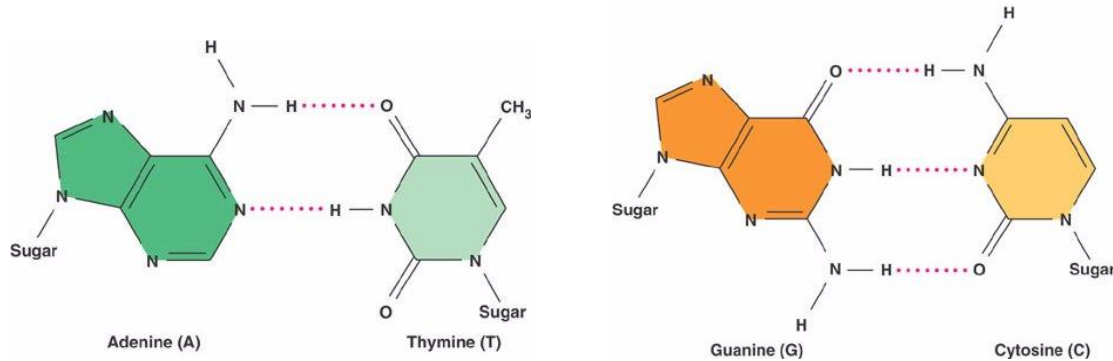
Dr James Hall
James.hall@reading.ac.uk
CCP4 Workshop 2022

OUTLINE

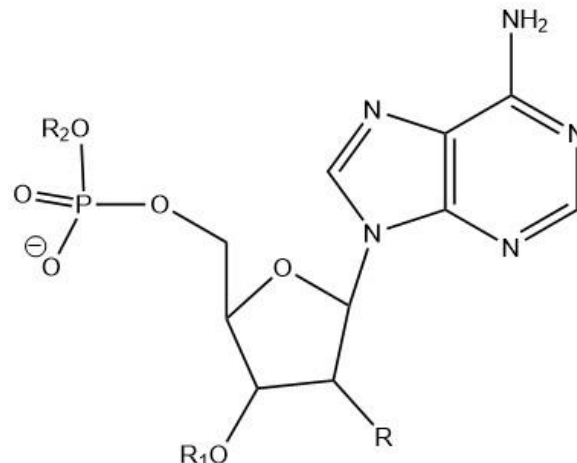
- 1) Introduction to nucleic acid structure
- 2) Comparison with protein crystallography - similarities, differences and opportunities
- 3) Useful tools...
- 4) Questions?

NUCLEIC ACID STRUCTURE

- Complementary base pairs form DNA ladder:



- Sequence written as base code: GCTTAAGAGGGCTCTGAGGA.....

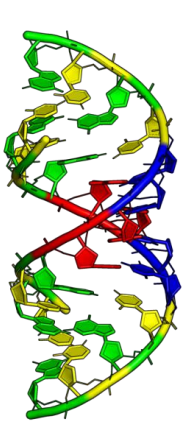


DNA – R = H

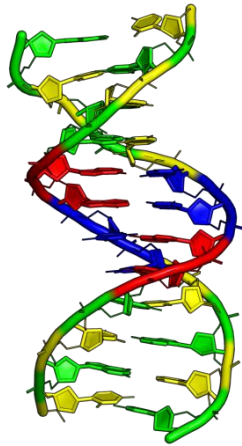
RNA – R = OH

NUCLEIC ACID STRUCTURE

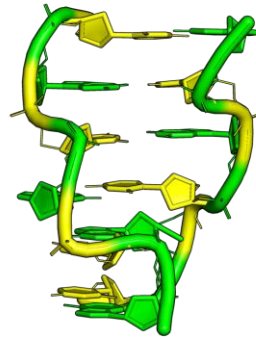
- However, nucleic acids are far more complex than this.....



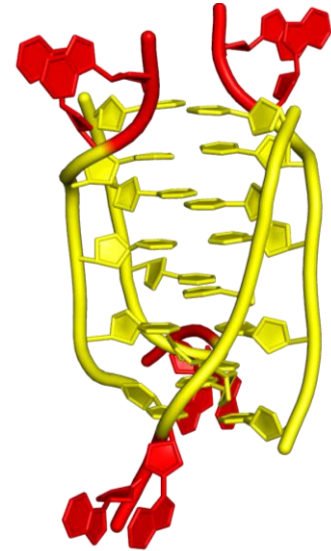
A-DNA
(Low humidity)



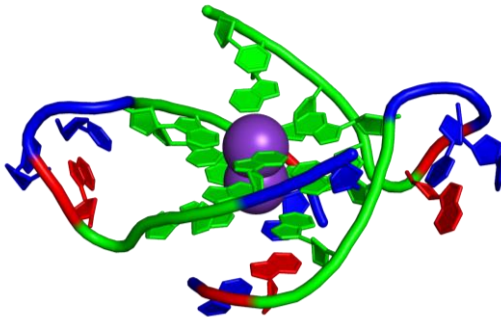
B-DNA
(Sequence)



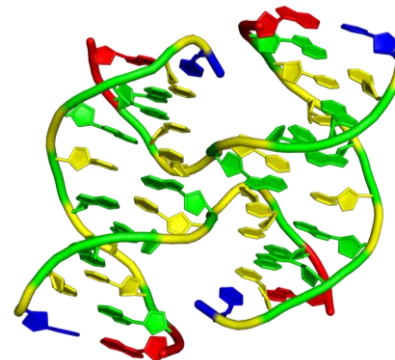
Z-DNA
(Left-handed, GC-
repeats)



I-motif
(C rich, H⁺
preferred)



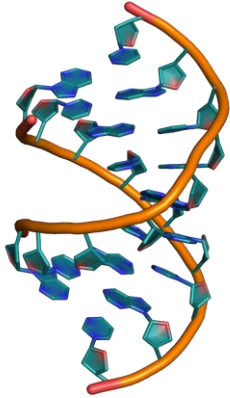
Quadruplex
(G rich, K⁺ preferred)



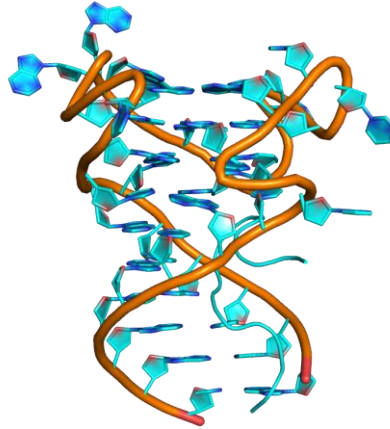
Holliday Junction
(Group 2 metals, sequence)

NUCLEIC ACID STRUCTURE

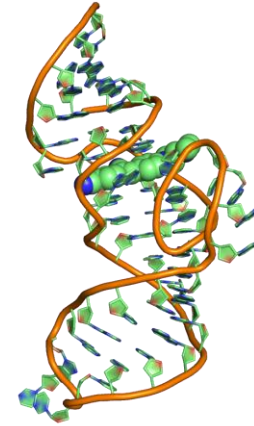
- RNA can be far more complex than DNA.....



A-RNA



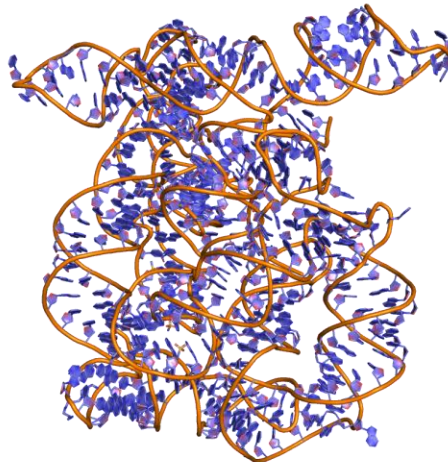
RNA Quadruplex



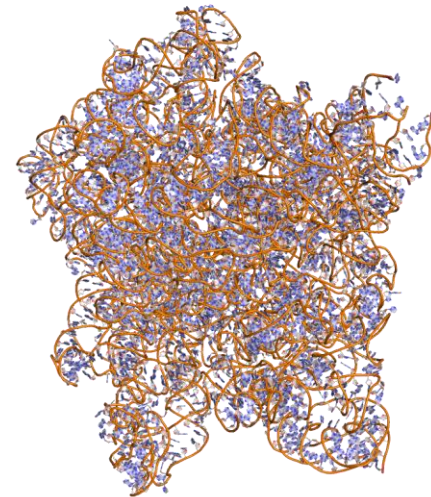
Aptamer



tRNA



Ribosyme



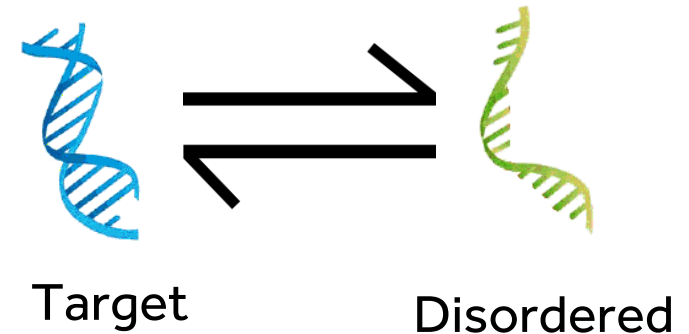
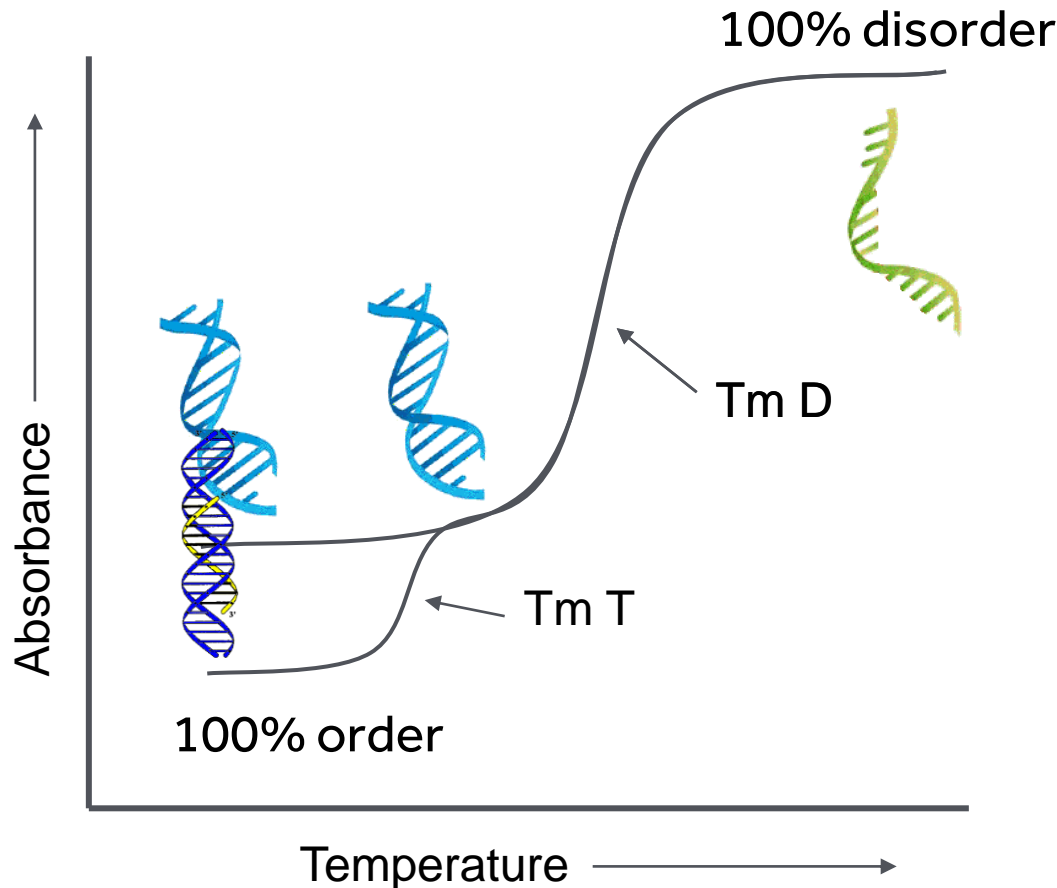
Ribosome subunit

STRUCTURAL VARIATION

- What causes this structural variation?
- Sequence – yes and no....
- Environment – yes and no.....
- Answer – both play a role. Understanding this can help with obtaining hits...
- **Nucleic acid structure is less dependent on sequence than proteins**

NUCLEIC ACID STRUCTURE

- Nucleic acid structures often exist in equilibrium....understanding this can help with crystallization



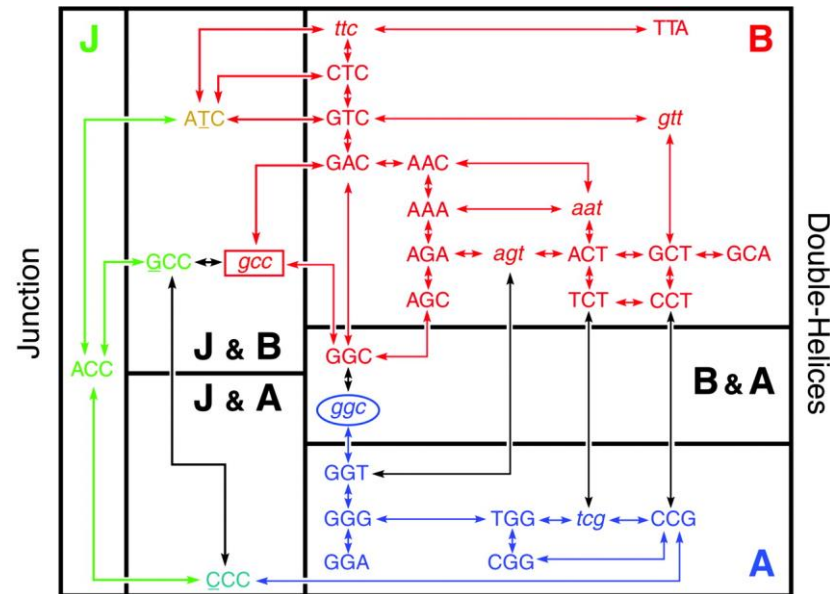
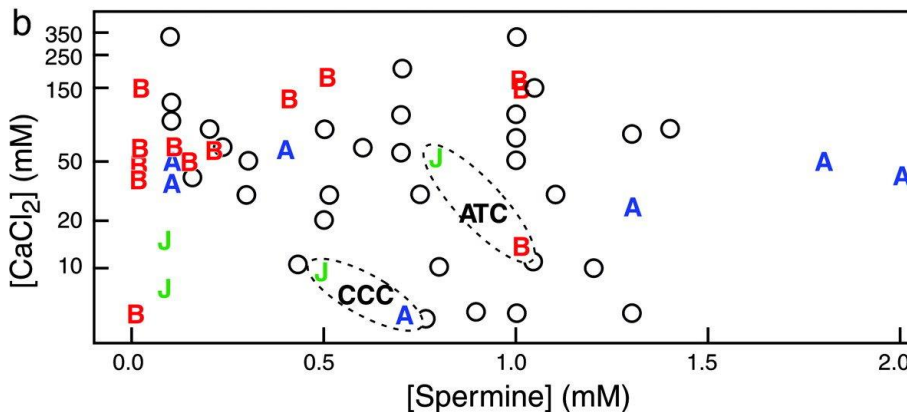
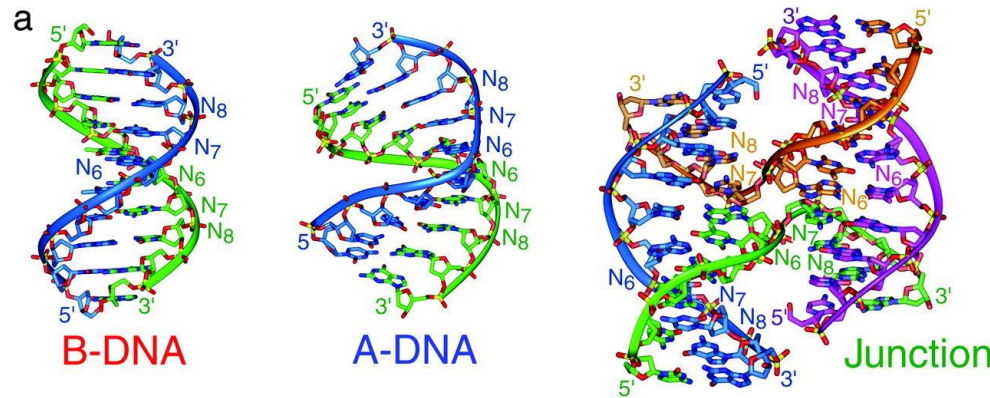
Large sequences –
regions of disorder

Small sequences –
Ordered or denatured

Melting temperature - T_m = 50% order/disorder

NUCLEIC ACID STRUCTURE

- Structure of small nucleic acids (<50 bases) is highly dependent on environment and sequence....challenging when it comes to structure solution!



d(CCnnnN₆N₇N₈GG) e.g. ATC = CCGATATCGG

Hayes, F.A. *et al. Proc Natl. Acad. Sci. USA.* 102 (20), 7157-7162, **2005.**

CHARACTERISATION

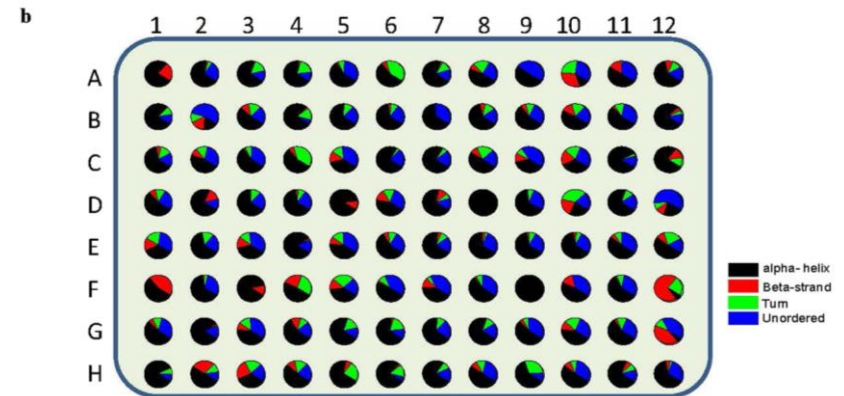
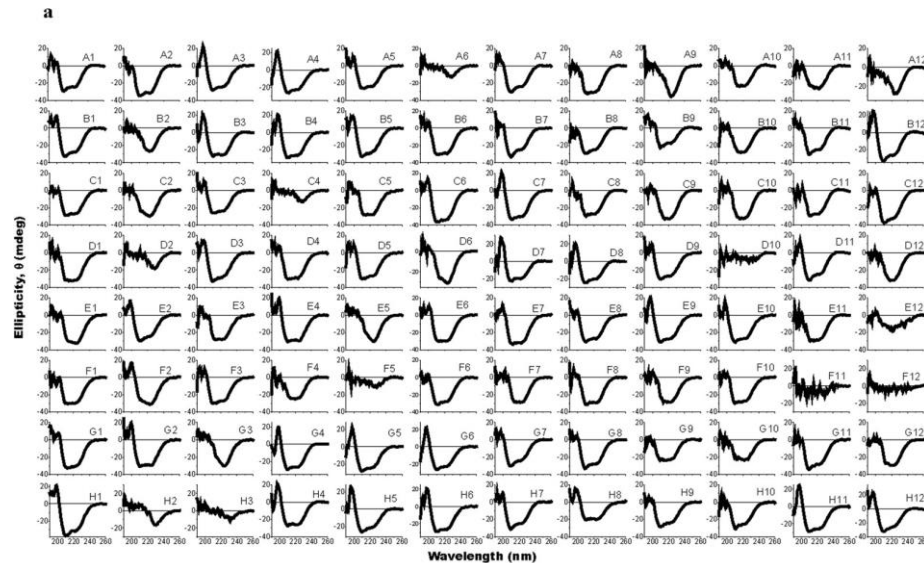
- UV/visible spectroscopy – characterise the stability of your system in your conditions
- Will give you T_m , not structure
- Easy to do:
 1. Add enough nucleic acid to a cuvette so absorption 0.1-1
 2. Measure UV spectrum at lowest temperature (5-20°C)
 3. Increase temperature 1-5°C
 4. Measure again
 5. Repeat until 90°C

Will take approx. 2h. May save you months of failed experiments and help to identify crystallization temperature

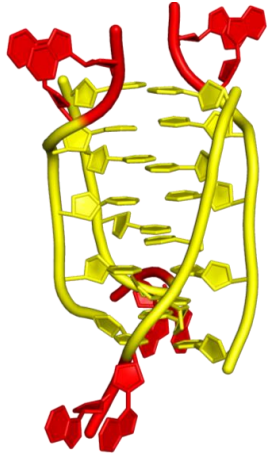
CHARACTERISATION

- Circular dichroism – characterise the structure of your system in crystallization conditions
- Will give you structural information (very low resolution!)

Will take approx. 8h on B23 using multi-well plate (longer at home). May save you months of failed experiments

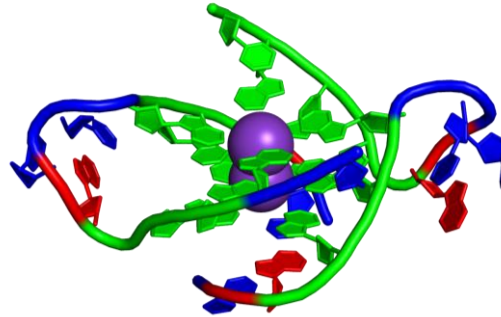


CHARACTERISATION



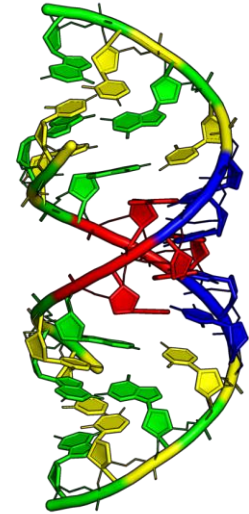
I-motif
(C rich, H⁺
preferred)

Ions/salts far less
important



Quadruplex
(G rich, K⁺ preferred)

pH far less important



A-DNA
(Low humidity)

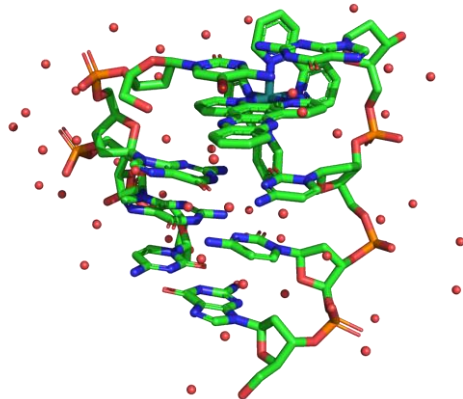
pH and ions/salts far
less important

**Knowledge of sequence behaviour/preferences is essential prior to
crystallization**

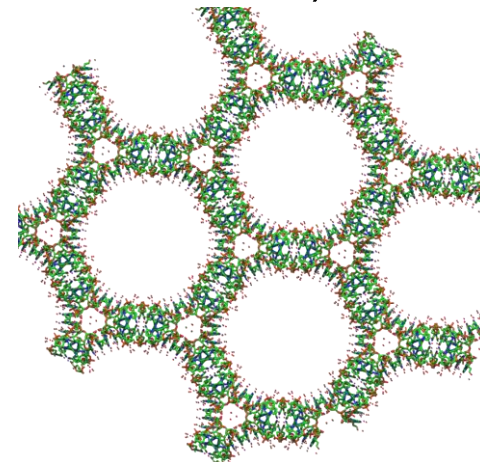
COMPARISON WITH PROTEIN CRYSTALLOGRAPHY

Length of sequence

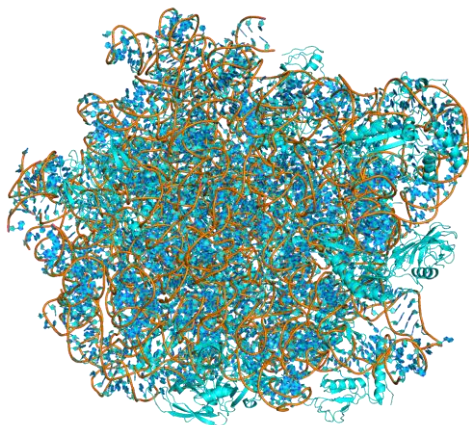
- A few bases.....(1-3 kDa..ca. 300 Da per base, DNA or RNA)



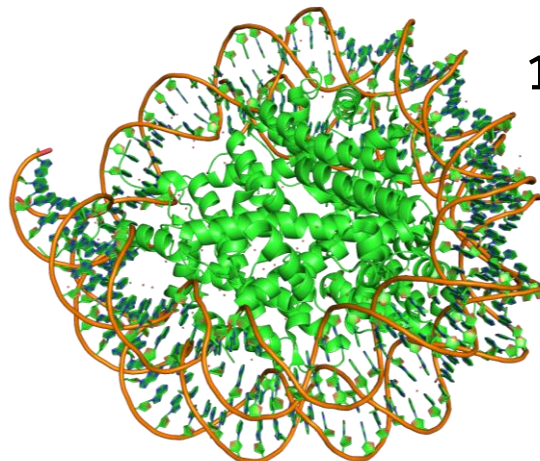
2x 4 base strands
1x Ligand
Waters + cations
5LFW
 $P6_4 2 2$
67.34, 67.34, 35.79



Large extended structures (RNA, DNA origami or DNA/RNA-Protein)



2923 bases RNA
1.36 MDa
4WCE
 $P6_5 2 2_1$
279.76, 279.76,
872.73



146 base pairs DNA
198.9 kDa
1P3K
 $P2_1 2_1 2_1$
104.99, 109.68,
180.72

COMPARISON WITH PROTEIN CRYSTALLOGRAPHY

- Crystallization methods – very similar!
- Sitting drop/hanging drop vapour diffusion is commonly used
- Nucleic acid-specific screens:

Hampton research – **Natrix**

Molecular Dimensions – Helix, MIDASplus

Salt and precipitant concentration are the most important to screen
pH less so unless system is pH responsive

nucleic acid structural stability is VERY sensitive to concentration and
type of salt, as nucleic acids are polyanionic

2-methyl-2,4-pentanediol (MPD, Hexylene glycol) precipitant of choice,
although this is system specific...MPD is a cryo protectant

Anecdotal – small nucleic acids don't seem to like PEG....

COMPARISON WITH PROTEIN CRYSTALLOGRAPHY

- Data collection – also very similar to protein crystallography, except:

Nucleic acids are far more resistant to radiation damage than proteins

Outcome of using model protein-DNA complex over a dose range 2.07-44.63 MGy

“At low doses the protein was observed to be susceptible to radiation damage while the DNA was far more resistant, damage only being observed at significantly higher doses.”

For nucleic acid-only crystals, significantly higher dose can be used with less risk of damage.....

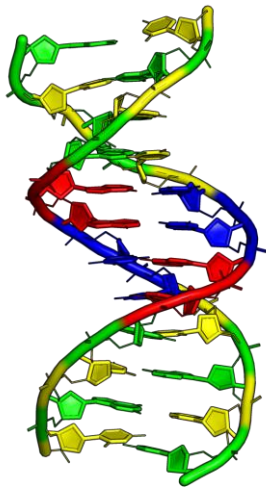
Site-specific damage manifests primarily to the phosphate groups

Bury, C. *et al. J. Synchrotron. Rad.* 22, 213-224, **2015**.

Bugris, V. *et al. J. Synchrotron Rad.* 26, 998-1009, **2019**.

COMPARISON WITH PROTEIN CRYSTALLOGRAPHY

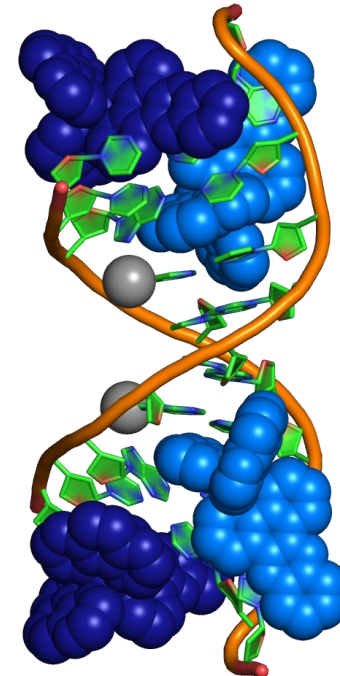
- Structure solution – same options (MAD/SAD, MR.....etc), different challenges
- For small nucleic acids, molecular replacement can be challenging, particularly if ligands are involved:



B-DNA

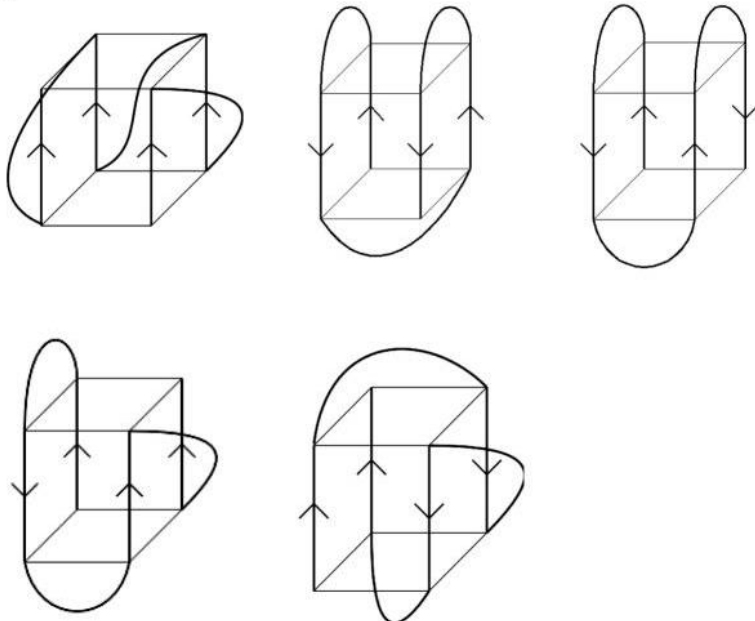


Add ligand....



COMPARISON WITH PROTEIN CRYSTALLOGRAPHY

- Structure solution – same options (MAD/SAD, MR.....etc), different challenges
- Flexibility in DNA and RNA is in the phosphate backbone.....
- Base pairs are less flexible but also have less scattering than phosphate groups
- Topological flexibility of sequence also a serious issue:



G-rich RNA and DNA can form quadruplexes

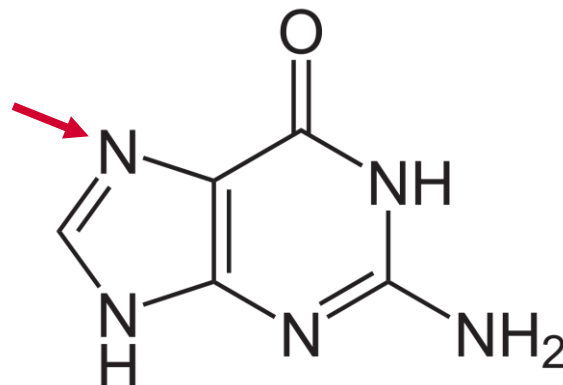
Left are five possible topologies.....there are over 20 theoretical possibilities, not all of which have been structurally characterised

Burge, S. *et al. Nucleic Acids Res.* 34 (19), 5402-5415, **2006.**

COMPARISON WITH PROTEIN CRYSTALLOGRAPHY

- Opportunity – SAD/MAD (radiation resistant so multiple datasets rarely a problem)
- Large nucleic acids (NAs) expressed and extracted – difficult to incorporate modifications
- If your sequence contains guanine.....get soaking!

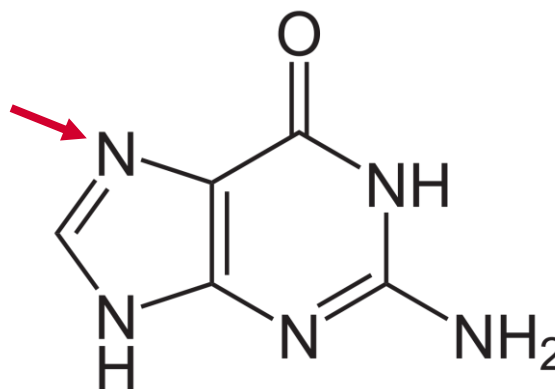
N7 – excellent group to coordinate metal centres



COMPARISON WITH PROTEIN CRYSTALLOGRAPHY

- Opportunity – SAD/MAD (radiation resistant so multiple datasets rarely a problem)
- If your sequence contains guanine.....get soaking!

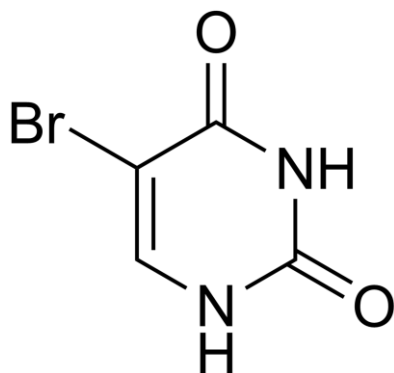
N7 – excellent group to coordinate metal centres



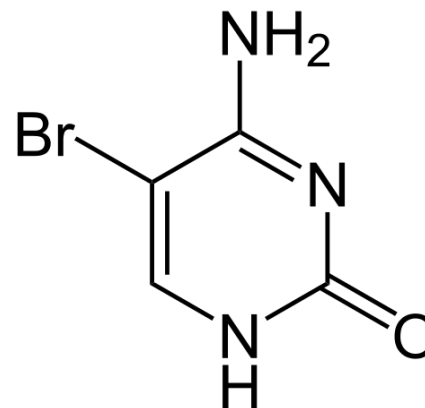
- Elements with atomic number higher than Ca²⁺ can work well
- Examples include:
- Sr²⁺, Ba²⁺ (this is excellent), Mn²⁺, Co²⁺, Ni²⁺, Zn²⁺ - avoid Fe²⁺ and Cu²⁺
Cis-platin will bind at N7 but low solubility can be challenging
- Natrix screen already contains some of the above ions for this reason!

COMPARISON WITH PROTEIN CRYSTALLOGRAPHY

- Opportunity – SAD/MAD (radiation resistant so multiple datasets rarely a problem)
- Large nucleic acids (NAs) expressed and extracted – difficult to incorporate modifications
- Small NAs (up to 100 bases) are normally purchased:
- Merck, Eurogentec, ATDBio – all good suppliers (HPLC purification essential!)



5-Br-U (replaces U/T)



5-Br-C (replaces C)

USEFUL TOOLS - ATDBIO

- <https://atdbio.com/tools/oligo-calculator> - calculate expected stability of duplex (underestimates for small oligos), mass, sequence composition etc



Sequence Input

Sequence

ATGCATGCATGCATGC

Salt concentration (mM)

100

Oligo concentration (μM)

1

DNA or RNA

DNA

Calculate Properties

Sequence Information

Type	DNA
Sequence	ATG CAT GCA TGC ATG C
Length	16 bases
GC content	50%
Chemical formula	C ₁₅₆ H ₁₉₇ N ₆₀ O ₉₄ P ₁₅
Molecular weight	4881.2

Thermodynamic properties of duplex formation ^

T_m (bc model)	52.1 °C
T_m (nn model)	55.3 °C
ΔH^\ominus	-121.2 kcal mol ⁻¹
ΔS^\ominus	-322.4 cal K ⁻¹ mol ⁻¹
ΔG^\ominus	-21.3 kcal mol ⁻¹

UV properties ^

E_{260} (ss DNA; bc model)	154.8 × 10 ³ M ⁻¹ cm ⁻¹
E_{260} (ss DNA; nn model)	152.0 × 10 ³ M ⁻¹ cm ⁻¹
E_{260} (ds DNA; bc model)	256.0 × 10 ³ M ⁻¹ cm ⁻¹
E_{260} (ds DNA; nn model)	251.1 × 10 ³ M ⁻¹ cm ⁻¹

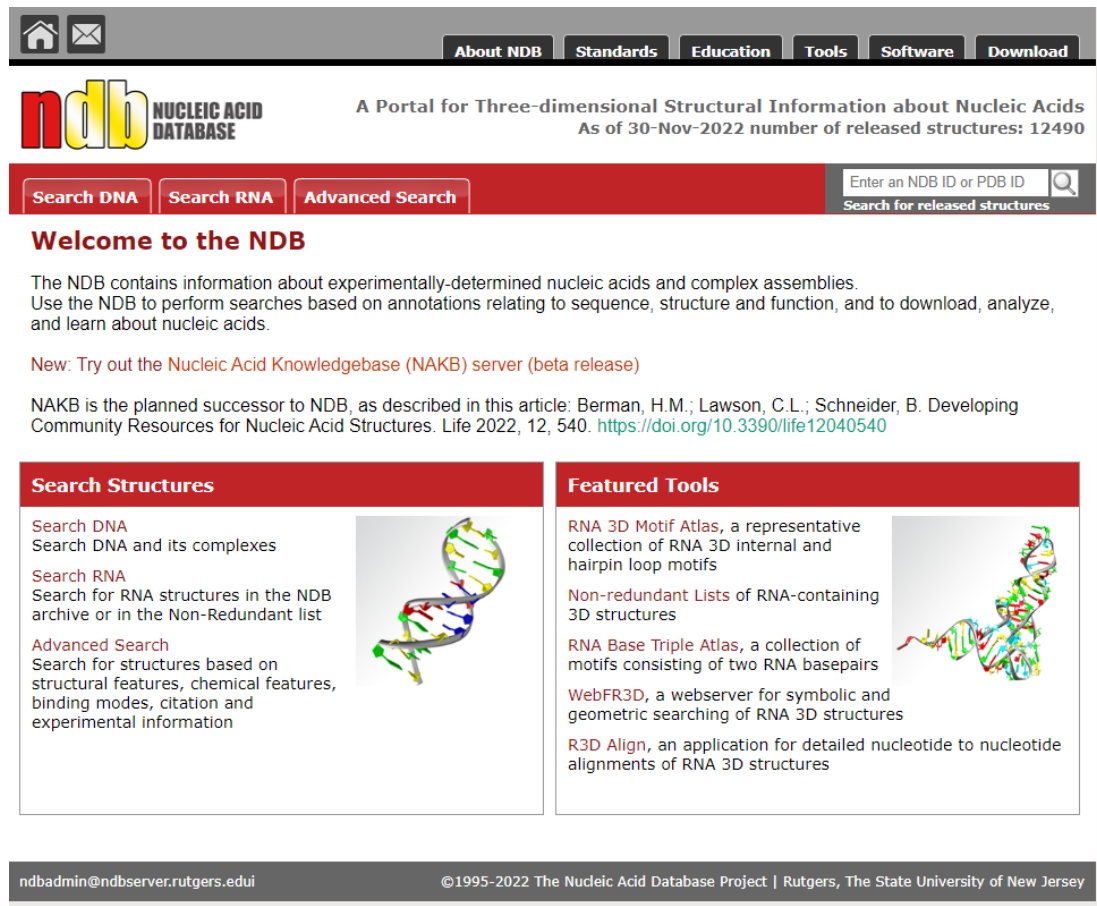
USEFUL TOOLS - NDB

- Nucleic Acid Database - <http://ndbserver.rutgers.edu/>

Soon to be replaced by Nucleic Acid Knowledgebase -

<https://beta.nakb.org/>

The PDB for nucleic acids



The screenshot shows the NDB website interface. At the top, there is a navigation bar with links: Home, About NDB, Standards, Education, Tools, Software, and Download. Below this is the NDB logo and the text "A Portal for Three-dimensional Structural Information about Nucleic Acids". A search bar is present with the text "Enter an NDB ID or PDB ID" and a search button. Below the search bar, there are three buttons: "Search DNA", "Search RNA", and "Advanced Search". The main content area starts with a "Welcome to the NDB" section, followed by a paragraph describing the database and its purpose. Below this, there is a "New: Try out the Nucleic Acid Knowledgebase (NAKB) server (beta release)" section. The bottom of the page features two columns: "Search Structures" and "Featured Tools". The "Search Structures" column lists "Search DNA", "Search RNA", and "Advanced Search" with brief descriptions. The "Featured Tools" column lists "RNA 3D Motif Atlas", "Non-redundant Lists of RNA-containing 3D structures", "RNA Base Triple Atlas", "WebFR3D", and "R3D Align" with brief descriptions. A footer at the bottom contains the email address "ndbadmin@ndbserver.rutgers.edu" and the copyright notice "©1995-2022 The Nucleic Acid Database Project | Rutgers, The State University of New Jersey".

Welcome to the NDB

The NDB contains information about experimentally-determined nucleic acids and complex assemblies. Use the NDB to perform searches based on annotations relating to sequence, structure and function, and to download, analyze, and learn about nucleic acids.

New: Try out the Nucleic Acid Knowledgebase (NAKB) server (beta release)

NAKB is the planned successor to NDB, as described in this article: Berman, H.M.; Lawson, C.L.; Schneider, B. Developing Community Resources for Nucleic Acid Structures. Life 2022, 12, 540. <https://doi.org/10.3390/life12040540>

Search Structures

Search DNA
Search DNA and its complexes

Search RNA
Search for RNA structures in the NDB archive or in the Non-Redundant list

Advanced Search
Search for structures based on structural features, chemical features, binding modes, citation and experimental information

Featured Tools

RNA 3D Motif Atlas, a representative collection of RNA 3D internal and hairpin loop motifs

Non-redundant Lists of RNA-containing 3D structures

RNA Base Triple Atlas, a collection of motifs consisting of two RNA basepairs

WebFR3D, a webserver for symbolic and geometric searching of RNA 3D structures

R3D Align, an application for detailed nucleotide to nucleotide alignments of RNA 3D structures

ndbadmin@ndbserver.rutgers.edu ©1995-2022 The Nucleic Acid Database Project | Rutgers, The State University of New Jersey

USEFUL TOOLS - NDB



A Portal for Three-dimensional Structural Information about Nucleic Acids
As of 30-Nov-2022 number of released structures: 12490

DNA Search Options:

Polymer

☒ All

☐ DNA Only

☐ Protein DNA Complexes

☐ Drug DNA Complexes

☐ Hybrids and Chimera

☐ Peptide Nucleic Acid / Mimetics

Protein Function

☒ All

☐ Enzymes

☐ Structural

☐ Regulatory

Structural Features

☒ All

☐ Single Stranded

☐ A DNA

☐ B DNA

☐ Z DNA

☐ Other Double Helical Structures

☐ Triple helices

☐ Quadruple helices

Experimental Method

☒ All

☐ XRAY

☐ NMR

Text Search

Filter results by text search

Use this option to narrow your results down considerably (>50% reduction) using any word seen in the results page. Eg. Any author name found in the right side

Polymer Type: **All** + Protein Function: **All** + Structural Features: **All** + Experimental Method: **All**

Results: 8575 [Download results as an excel file](#) [Gallery view](#)

NDB ID: 7VRU
PDB ID: 7VRU
Release: 2022-11-30



Title: **Crystal structure of PacII_M1M2S-DNA-SAH complex**


Classification: TRANSFERASE/DNA

Authors: Zhu, J., Gao, Y., Wang, Y., Zhan, Q., Feng, H., Luo, X., Li, P., Liu, S., Hou, H., Gao, P.

Citation: Molecular insights into DNA recognition and methylation by non-canonical type I restriction-modification systems. Nat Commun 13 pp.6391 - 6391 2022

Experiment: X-RAY DIFFRACTION Resolution:2.4Å R work:0.189 R free:0.234

NDB ID: 7V54
PDB ID: 7V54
Release: 2022-11-30



Title: **Crystal structure of PacII_M1M2S-DNA(m6A)-SAH complex**

Classification: TRANSFERASE/DNA

Authors: Zhu, J., Gao, Y., Wang, Y., Zhan, Q., Feng, H., Luo, X., Li, P., Liu, S., Hou, H., Gao, P.

Citation: Molecular insights into DNA recognition and methylation by non-canonical type I restriction-modification systems. Nat Commun 13 pp.6391 - 6391 2022

Experiment: X-RAY DIFFRACTION Resolution:2.55Å R work:0.18 R free:0.236

NDB ID: 7ZKL
PDB ID: 7ZKL
Release: 2022-11-30



Title: **X-ray structure of the complex between human alpha thrombin and a pseudo-cyclic thrombin binding aptamer (TBA-NNp/DDp) - Crystal form alpha**

Classification: HYDROLASE

Authors: Troisi, R., Riccardi, C., Perez de Carvasal, K., Smietana, M., Morvan, F., Del Vecchio, P., Montesarchio, D., Sica, F.

Citation: A terminal functionalization strategy reveals unusual binding abilities of anti-thrombin anticoagulant aptamers To Be Published pp. - 0

Experiment: X-RAY DIFFRACTION Resolution:3.18Å R work:0.19 R free:0.231

NDB ID: 7ZKM
PDB ID: 7ZKM
Release: 2022-11-30



Title: **X-ray structure of the complex between human alpha thrombin and a pseudo-cyclic thrombin binding aptamer (TBA-NNp/DDp) - Crystal form beta**

Classification: HYDROLASE

Authors: Troisi, R., Riccardi, C., Perez de Carvasal, K., Smietana, M., Morvan, F., Del Vecchio, P., Montesarchio, D., Sica, F.

Citation: A terminal functionalization strategy reveals unusual binding abilities of anti-thrombin anticoagulant aptamers To Be Published pp. - 0

Experiment: X-RAY DIFFRACTION Resolution:2.0Å R work:0.226 R free:0.252

Experimental Details

AND Space Group:

Unit Cell Dimensions:

AND Alpha = ° AND Beta = ° AND Gamma = °

AND a = Å AND b = Å AND c = Å

AND Resolution better than: Å AND R-factor better than:

Citation Information

NDB ID PDB ID AND Author

AND Publication Year: AND Released Since:

RNA 3D Interactions

AND Base Pair Interaction: ?

AND Base Phosphate Interaction: ?

AND Base Stack Interaction: ?

Relative Frequency of various RNA 3D Interactions: ?

AND Base Pair Interaction with relative frequency: >=

AND Base Phosphate Interaction with relative frequency: >=

AND Base Stack Interaction with relative frequency: >=

RNA 3D Motifs ?

AND Internal Loop Motif

AND Hairpin Loop Motif

Representative RNA 3D Structure Sets ?

AND Resolution cutoff:

Sequence

AND Nucleic Acid Sequence Pattern:

AND Oligonucleotide Sequence Length between and

USEFUL TOOLS - NDB

Search DNA

Search RNA

Advanced Search

Enter an NDB ID or PDB ID

Search for released structures

NDB ID: 7SM4 PDB ID: 7SM4 [↗](#) NAKB(beta): 7SM4 [↗](#)

Title:

[T:HG2+/AG+;T--PH 10.5] METAL-MEDIATED DNA BASE PAIR IN TENSEGRITY TRIANGLE IN AG+ AND HG2+ SOLUTION

Molecular Description:

Deposited:

2021-10-25

Released:

2022-11-23

Structural Keywords:

B DOUBLE HELIX

Nucleic Acid Sequence:

Click to show/hide 4 nucleic acid sequences

Protein Sequence:

No Protein Sequence Found

Primary Citation:

Lu, B., Ohayon, Y.P., Sha, R., Woloszyn, K., Rothschild, L., Wind, S., Hendrickson, W., Mao, C., Seeman, N.C., Vecchioni, S.

Crystallographic pH Titration of Silver and Mercury Mediated DNA Base Pairs

To Be Published, , pp. - , 0.

Experimental Information:

X-RAY DIFFRACTION

Space Group:

H 3

Cell Constants:

a = 106.313 b = 106.313 c = 92.616 (Ångstroms)

α = 90.0 β = 90.0 γ = 120.0 (degrees)

Refinement:

The structure was refined using the PHENIX program. The R value is 0.2293 for 2562 reflections in the resolution range 41.22 to 4.01 Ångstroms with Fobs > 1.92 sigma(Fobs) and with I > 0.0 sigma(I)

Download Data:

Asymmetric Unit coordinates (pdb format, Unix compressed(.gz))

Asymmetric Unit coordinates (cif format, Unix compressed(.gz))

Biological Assembly coordinates (pdb format) 1

Structure Factors (cif format)

XML | Complete with coordinates (xml format, GNU compressed(.gz))

XML | Coordinates only (xml format, GNU compressed(.gz))

XML | Header only (xml format, GNU compressed(.gz))

Structural Features

RNAML

Base Pair Hydrogen Bonding Classification

Nucleic Acid Backbone Torsions

Base Pair Morphology Parameters

Base Pair Morphology Step Parameters

Conformer Analysis (DNATCO)

Biological Assembly 1

RNA View

More Images...

ndbadmin@ndbserver.rutgers.edu

©1995-2022 The Nucleic Acid Database Project | Rutgers, The State University of New Jersey

Search DNA

Search RNA

Advanced Search

Enter an NDB ID or PDB ID

Search for released structures

NDB ID: 7SM4 PDB ID: 7SM4 [↗](#)

Base Pair Morphology Step Parameters

CSV Format

Model Number	Step Number	Step Name	CHIT	Slide	Rise	TR	Roll	Twist	X-Displacement	Y-Displacement	Helical Rise
1	1	AA_DA2D03-DC13DT14_CC	0.53	-0.68	3.282	-9.987	16.033	37.91	-2.519	-1.718	2.6
1	4	AA_DA3D06-DC10DT11_CC	0.093	-1.718	3.021	-13.522	7.391	23.039	-5.109	-2.968	2.026
1	12	AA_DA18DC17-DG6DT7_DD	0.174	-1.768	3.701	7.598	-4.758	28.972	-2.247	1.48	3.857
1	14	AA_DA18DT19-DA4DT5_DD	0.195	-1.004	3.227	-1.13	-0.411	34.319	-1.637	-0.504	3.23
1	3	AA_DC4DA5-DT11DG12_CC	-0.65	0.092	2.922	-0.9	7.58	46.75	-0.438	0.744	2.914
1	6	AA_DC7DC8-DG8DT9_CC	-0.422	-0.947	3.454	2.999	-9.039	44.226	-0.359	0.838	3.537
1	7	AA_DC8DT9-DA7DG6_BC	-2.48	-0.519	3.79	-2.801	-8.392	21.565	0.277	4.855	3.993
1	13	AA_DC17DA18-DT5DG6_DD	-0.124	0.026	3.129	1.841	-8.259	39.416	0.727	0.363	3.083
1	16	AA_DC20DA21-DT2DG3_DD	-0.347	-0.667	3.714	1.858	18.361	30.898	-3.178	0.936	3.302
1	2	AA_DG3DC4-DG12DC13_CC	-0.561	-1.621	3.086	-4.509	-2.851	27.059	-2.717	0.095	3.285
1	5	AA_DG6DC7-DG9DC19_CC	0.319	-2.014	3.219	-6.217	-0.835	27.379	-3.958	-2.096	3.13
1	10	AA_DG14DG15-DC1DC2_BB	0.05	0.728	3.573	-7.91	6.808	44.357	0.276	-0.837	3.582
1	11	AA_DG15DA16-DT7DC1_DD	-1.716	-0.707	2.824	-21.113	-13.851	21.619	1.466	-1.023	3.23
1	8	AA_DT9DG10-DC6DA7_BB	0.183	-0.53	3.298	-1.724	10.051	28.384	-3.034	-0.698	2.928
1	9	AA_DT13DG14-DC2DA3_BB	-0.81	2.594	3.369	-6.563	-6.241	48.597	3.568	0.482	3.112
1	15	AA_DT19DC20-DC3DA4_DD	0.464	0.115	3.14	7.038	-11.159	41.283	1.215	0.038	3.047

<http://web.x3dna.org/>

Home or other PDB ID

SUBMIT

Click the Summary/Torsions/Similar... tabs for more details.

Center view on ☒ step or ☐ molecule.

Show reference ☒ AA00 and contacts ☐

Summary

Torsions

Similar

Settings

Browse

Download

[T:HG2+/AG+;T--PH 10.5] Metal-mediated DNA base pair in tensegrity triangle in Ag+ and Hg2+ solution

Results of the assignment of 38 detected steps in 1 model(s), can be also downloaded as [csv](#) or [json](#) file.

Found 17/21/0 steps in 0.0/0.5-1.0/1.0+ Å Cartesian rmsd from reference. Average conval 17, percentile 10.

Click a row in table or a step in JSmol for analysis of results.

Click column headers to sort data

Step name	CANSA	NIC	conval	rmsd
7sm4_A_DA1_DA2	NAN	NANT	0	0.16
7sm4_A_DA2_DA3	NAN	NANT	0	0.66
7sm4_A_DA3_DA4	NAN	NANT	0	0.13
7sm4_A_DA4_DA5	NAN	NANT	0	0.71
7sm4_A_DA5_DA6	BBB	BB00	69	0.26
7sm4_A_DA6_DA7	BBB	BB01	65	0.28
7sm4_A_DA7_DA8	NAN	NANT	0	0.41
7sm4_A_DA8_DA9	NAN	NANT	0	0.13
7sm4_A_DA9_DA10	NAN	NANT	0	0.66
7sm4_A_DA10_DA11	NAN	NANT	0	0.72
7sm4_A_DA11_DA12	NAN	NANT	0	0.78
7sm4_A_DA12_DA13	NAN	NANT	0	0.81
7sm4_A_DA13_DA14	NAN	NANT	0	0.71
7sm4_A_DA14_DA15	NAN	NANT	0	0.41
7sm4_A_DA15_DA16	NAN	NANT	0	0.38
7sm4_A_DA16_DA17	BBB	BB00	60	0.27
7sm4_A_DA17_DA18	B12	BB04	60	0.23
7sm4_A_DA18_DA19	mB	BB10	44	0.40
7sm4_A_DA19_DA20	NAN	NANT	0	0.74
7sm4_A_DA20_DA21	NAN	NANT	0	0.72
7sm4_B_DC1_DC2	NAN	NANT	0	0.18
7sm4_B_DC2_DC3	B12	BB04	10	0.40

JSmol

See the JSmol wiki for description of applet controls.

©1995-2022 The Nucleic Acid Database Project | Rutgers, The State University of New Jersey

<https://dnatco.datmos.org/>

USEFUL TOOLS

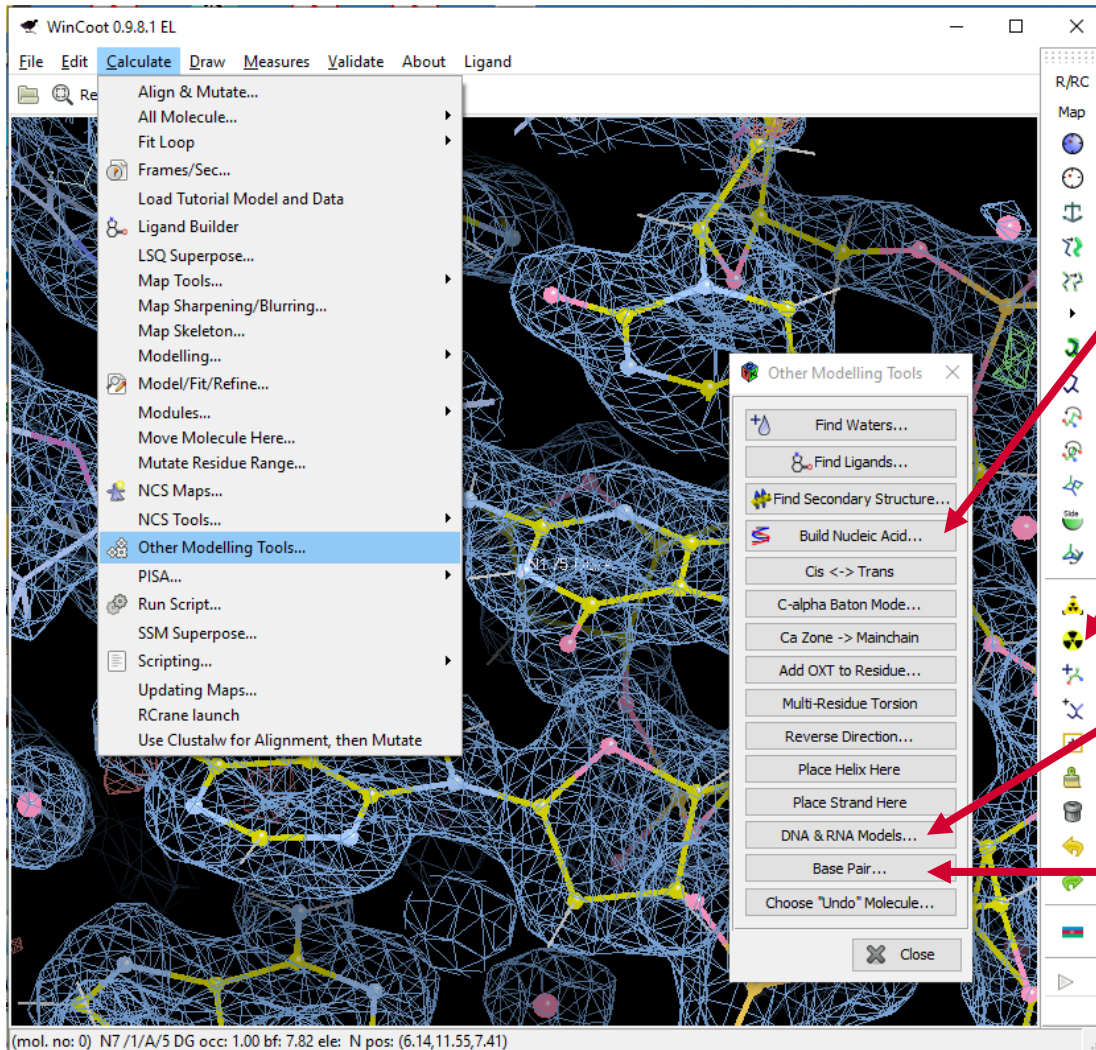
Within CCP4 – model building of nucleic acids

- Arp/wARP (web service also available)
 - Builds AND refines using electron density
 - Relatively slow (compared to Nautilus) but refines, builds protein, solvent and can assign ligands
-
- Nautilus
 - Builds from electron density
 - VERY quick!
-
- Both require electron density and can use a starting model as a start point

USEFUL TOOLS

Within CCP4 – manual editing of nucleic acid structures

- Coot - I assume needs no introduction...



Try to build NA in density automatically

Substitute base type (mutate)

Generate idealised RNA/DNA strands for manual fitting

Generate the complementary base to complete a base pair

SUMMARY

- Understanding your nucleic acid system BEFORE crystallization can save you a lot of time and help you to select more likely growth conditions
- Careful soaking or incorporation of modified bases may help with structure solution – MR is very challenging with NAs and prediction of structure is far less certain
- Thanks to the developers for all their tools and guidance over the years – NA crystallography has become much more straightforward in the last decade thanks to their input and efforts!
- Any questions?