Annotation and validation of nucleic acid structures.

Increasing quality and interoperability of the data

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Computational Approaches to RNA Structure and Function

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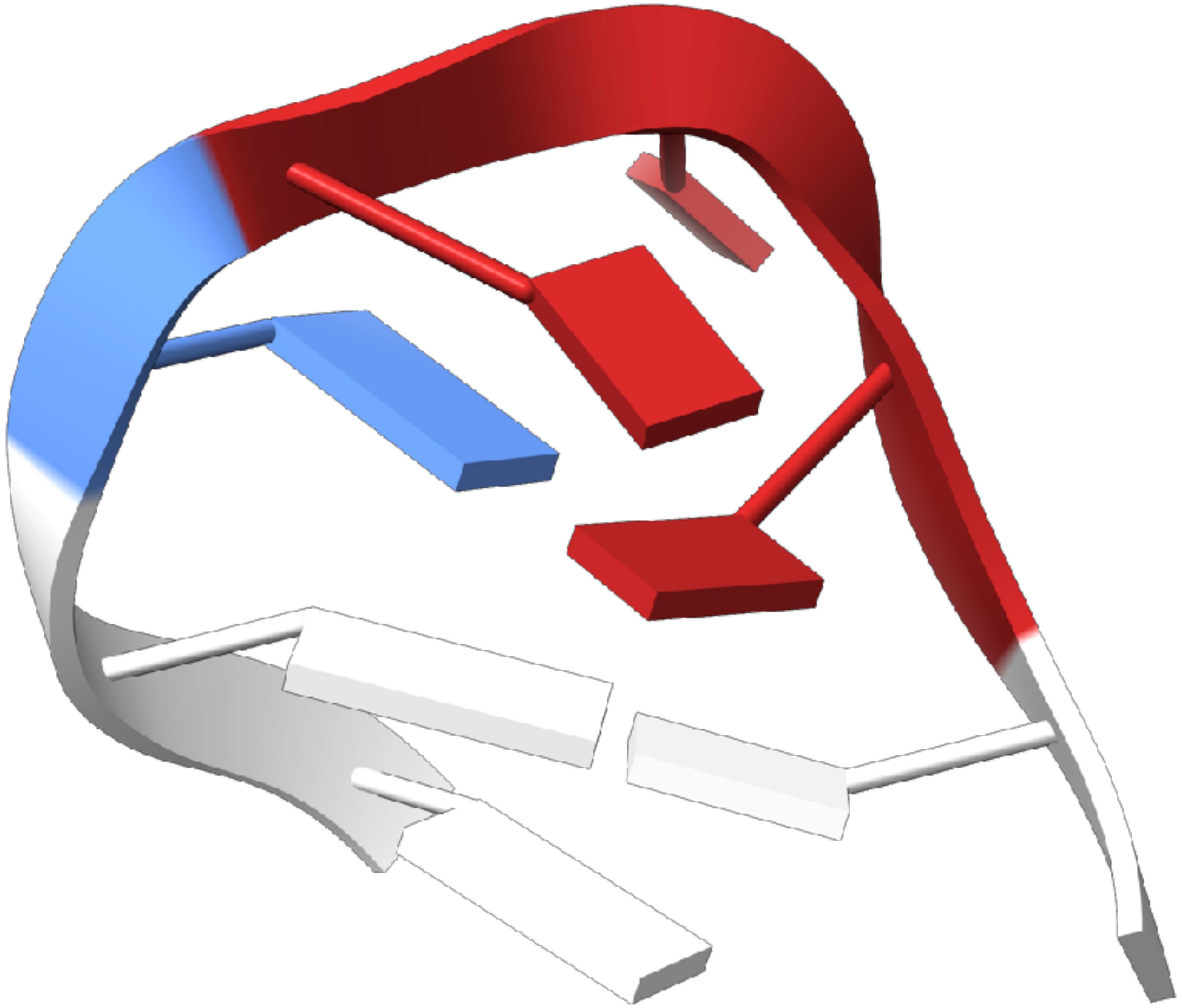
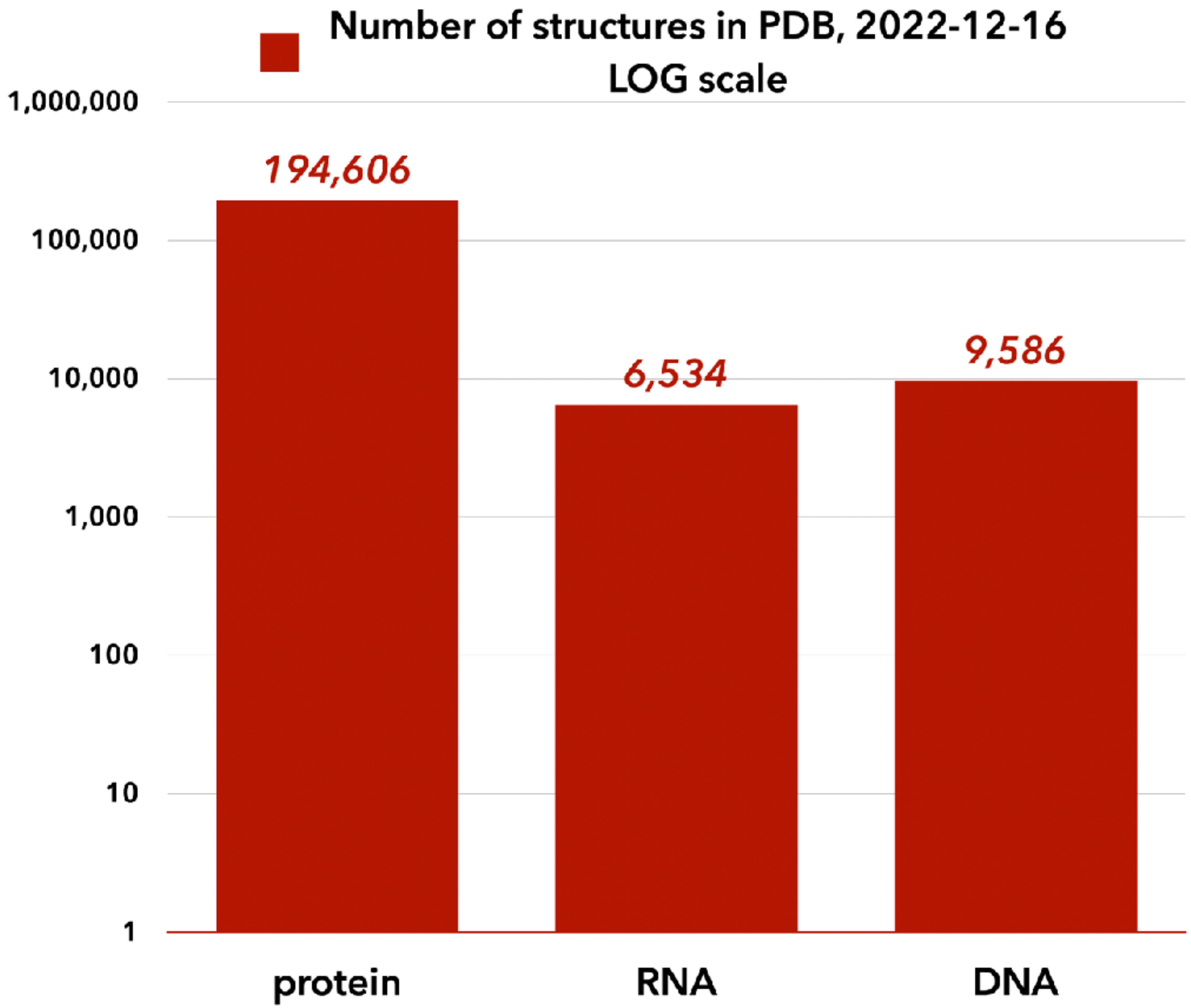
Why discuss the quality of structural data

- Public archive should be reliable source of ***validated*** information
    - PDB data are often used by non-experts
    - mmCIF does not capture all features of biomolecules

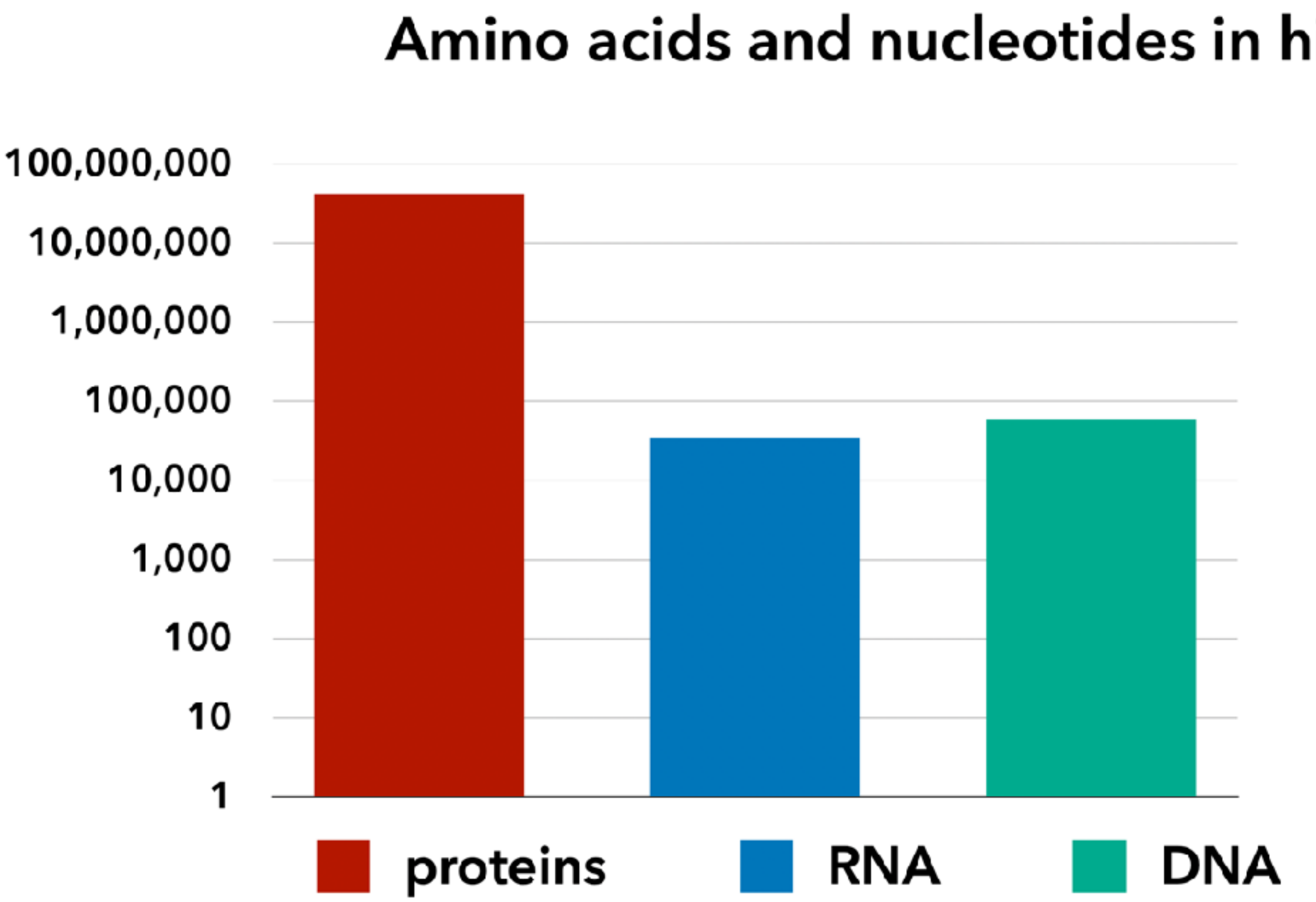
- Nucleic acids are of special concern …



PDB archive: 7.6% of NA structures

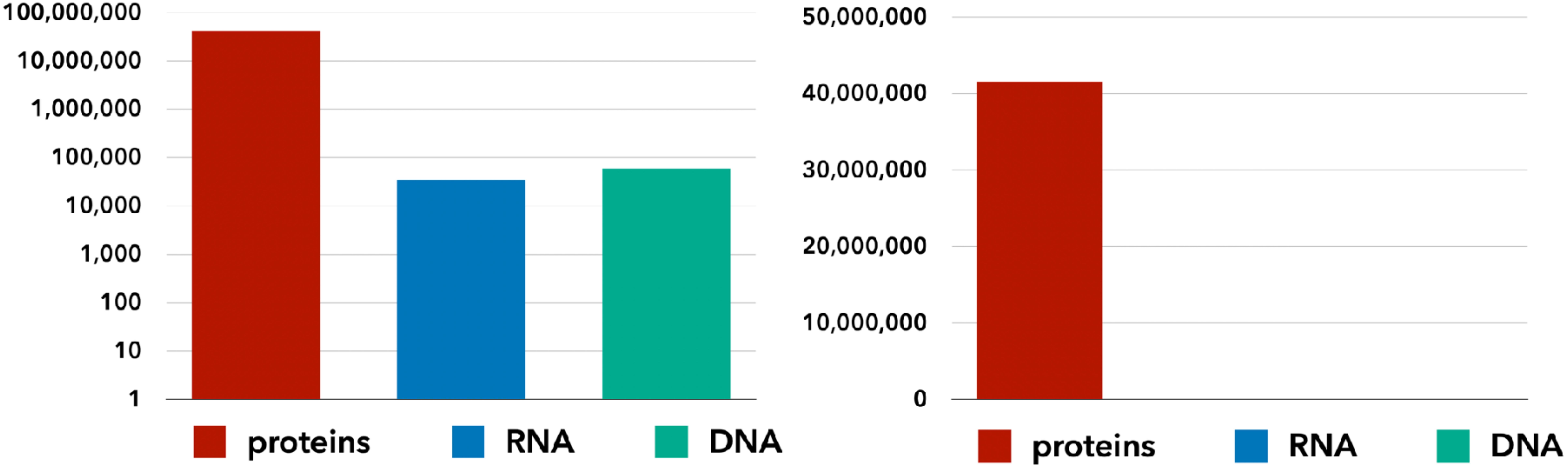


Small number of high quality NA models: need for sophisticated tools



Small number of high quality NA models: need for sophisticated tools

Amino acids and nucleotides in high-resolution structures (≤2.0 Å)

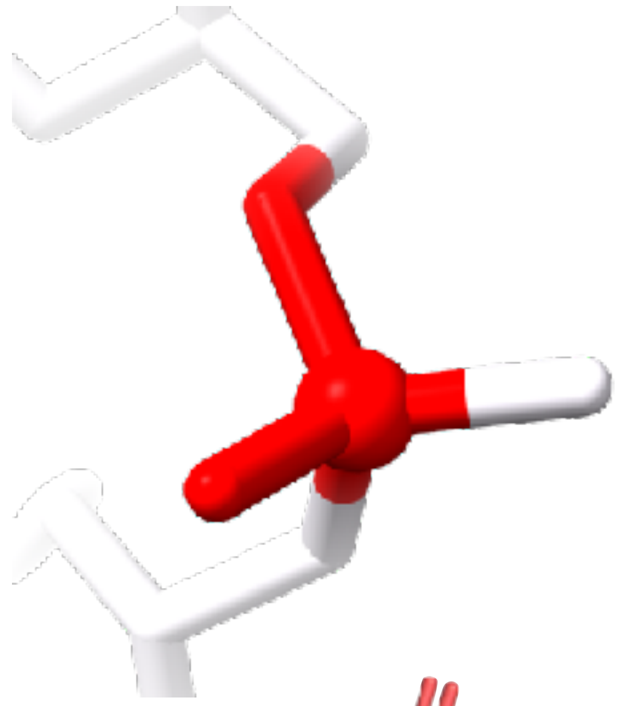


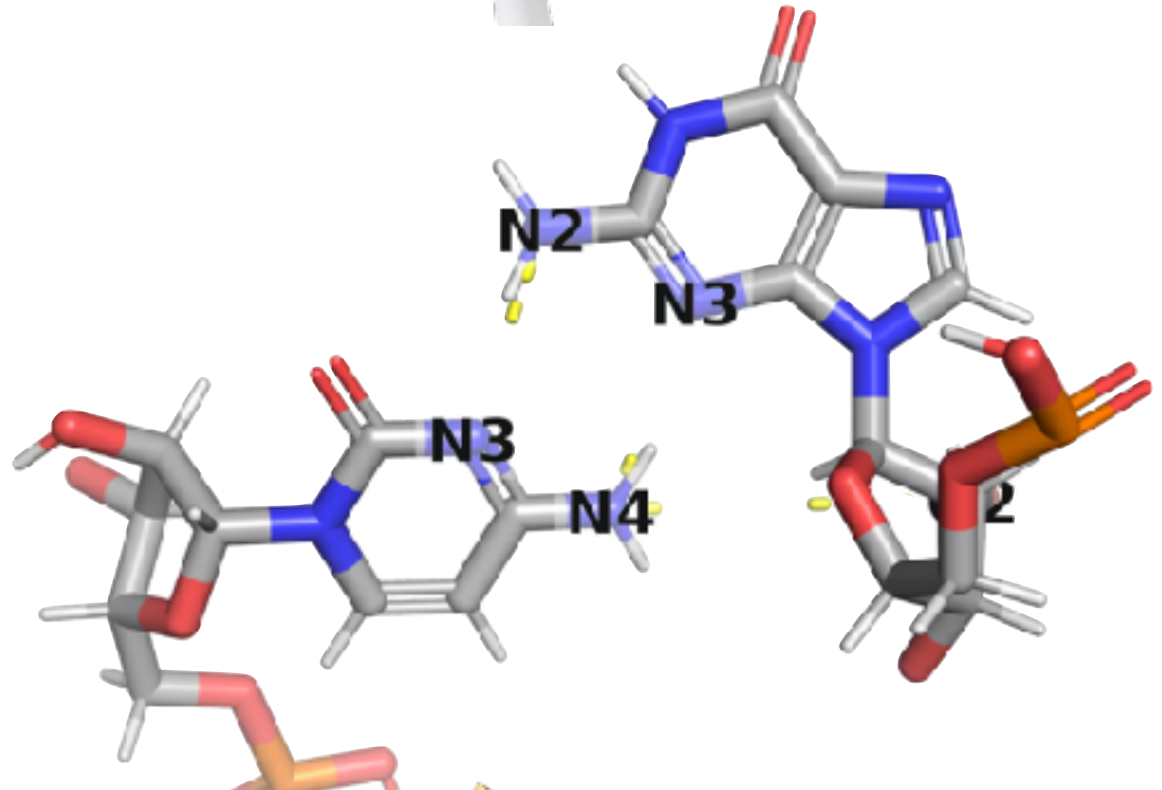
Three main sources of errors in NA structures

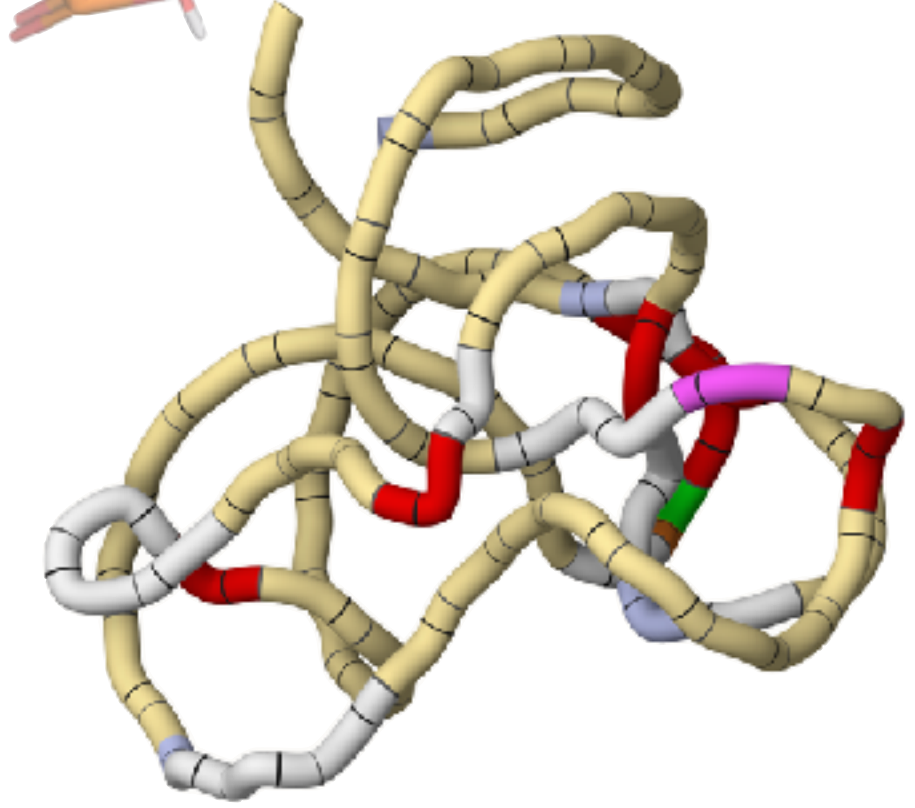
1. Valence geometry

2. Base pairing

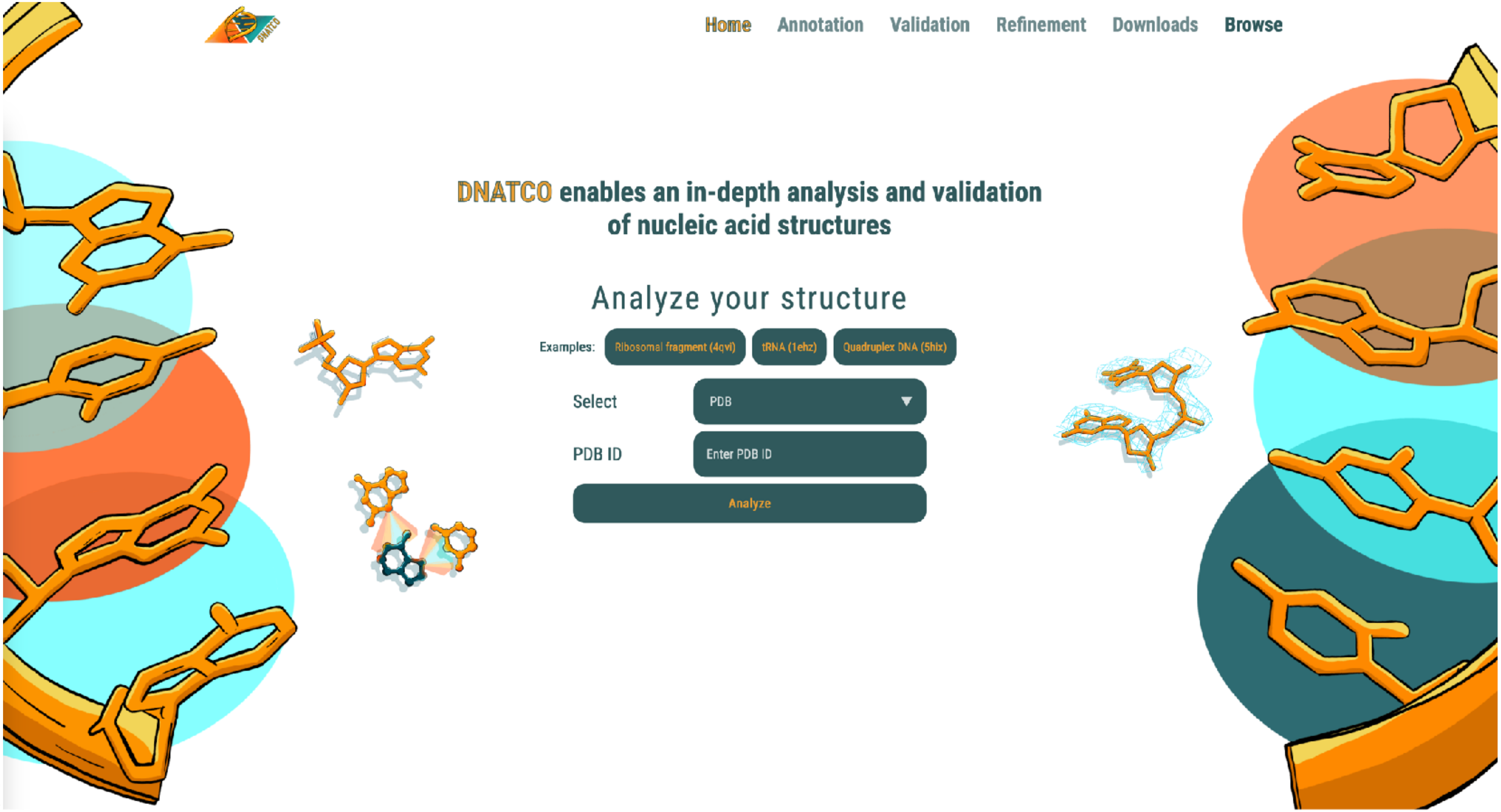
3. Backbone geometries







Remediation at *dnatco.datmos.org*

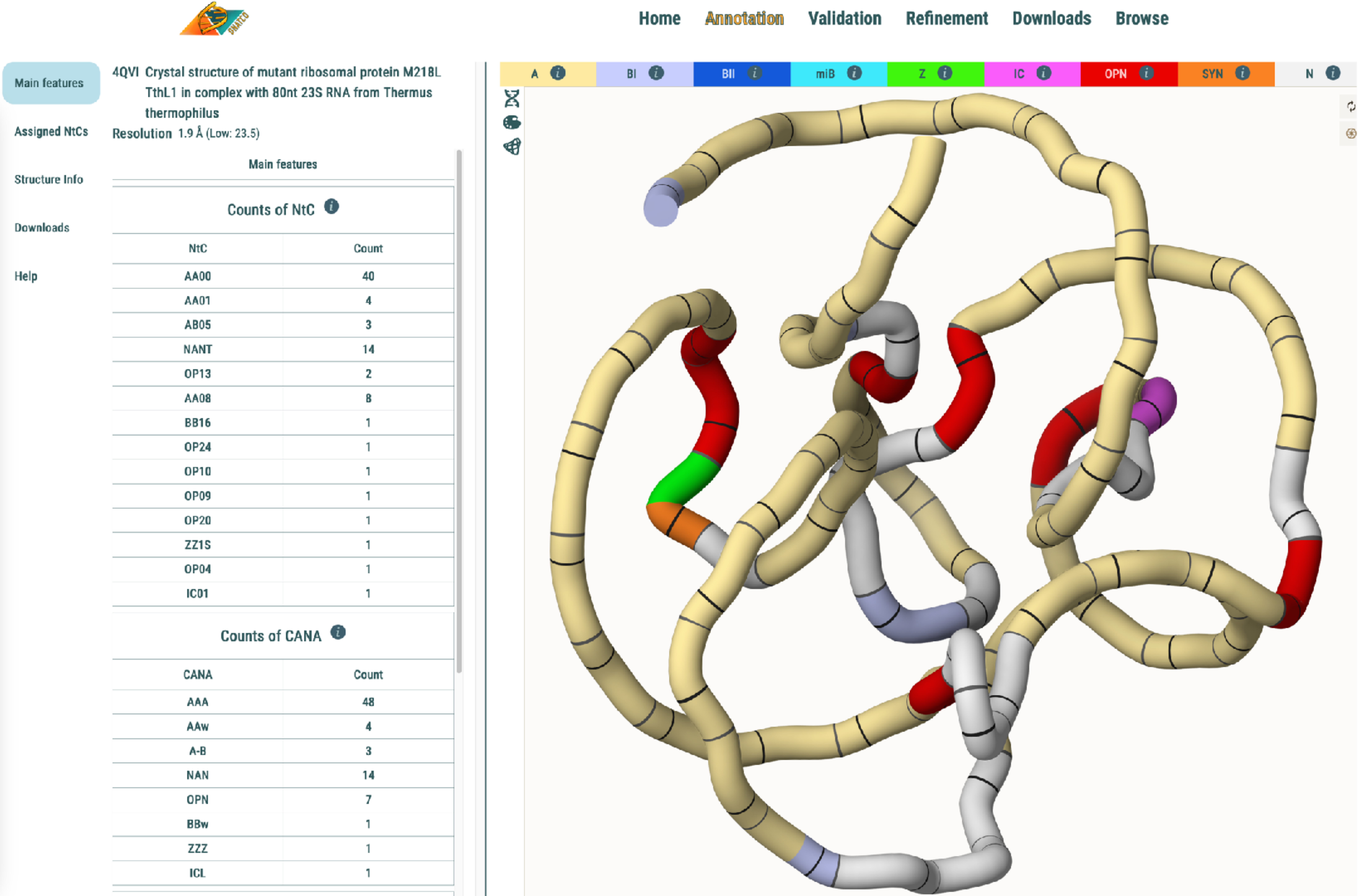


DNATCO enables an in-depth analysis and validation of nucleic acid structures

Analyze your structure

Select: PDB

PDB ID: Enter PDB ID



4QVI Crystal structure of mutant ribosomal protein M218L TthL1 in complex with 80nt 23S RNA from Thermus thermophilus

Resolution 1.9 Å (Low: 23.5)

Main features

Counts of NtC

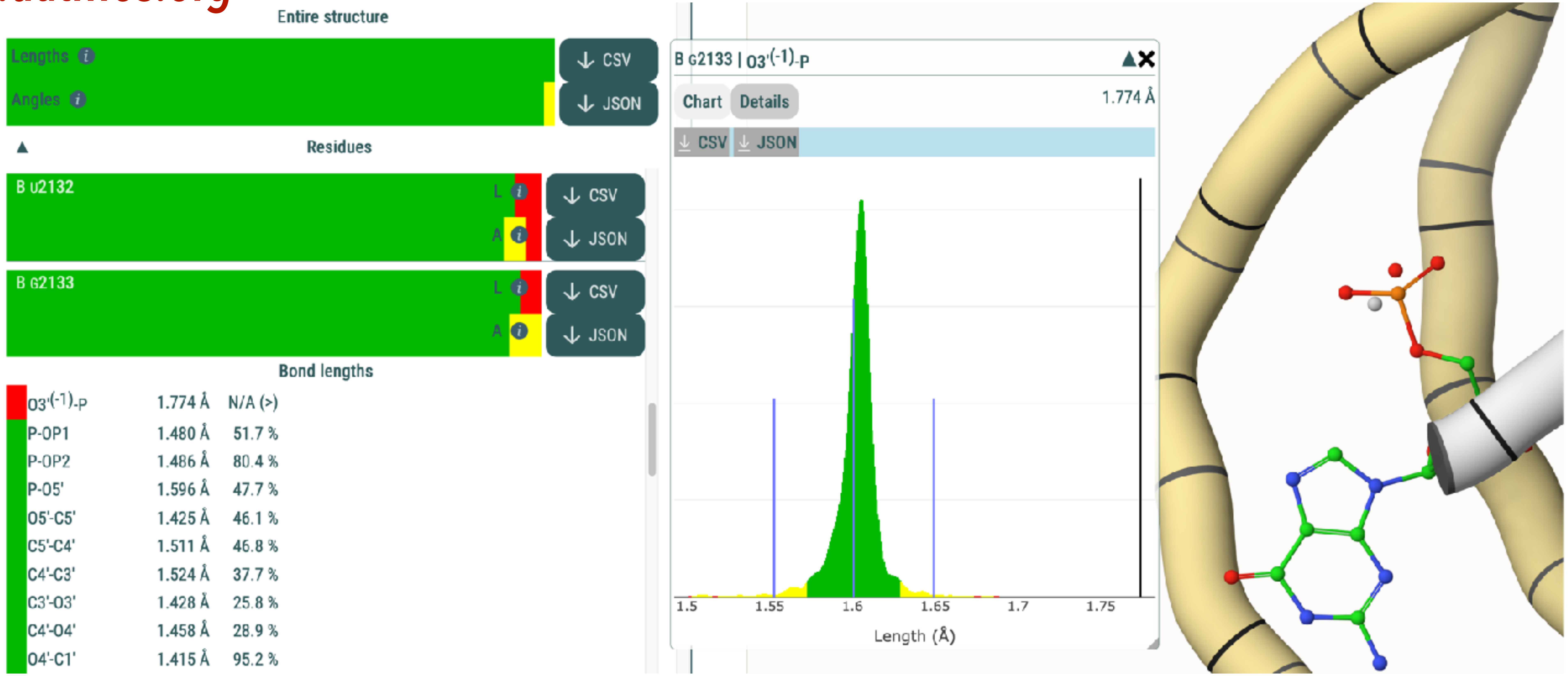
NtC	Count
AA00	40
AA01	4
AB05	3
NANT	14
OP13	2
AA08	8
BB16	1
OP24	1
OP10	1
OP09	1
OP20	1
ZZ1S	1
OP04	1
IC01	1

Counts of CANA

CANA	Count
AAA	48
AAw	4
A-B	3
NAN	14
OPN	7
BBw	1
ZZZ	1
ICL	1

1. Valence geometry

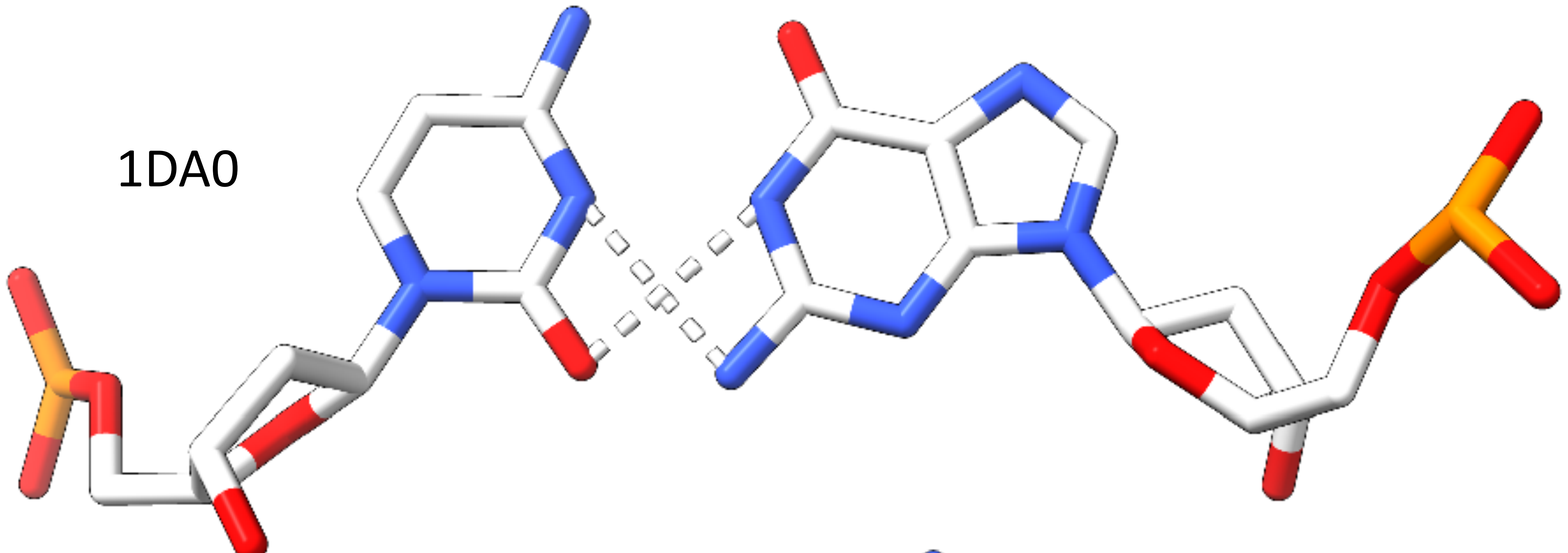
- Refinement programs use different restraints
- Validation by PDB and other tools is inconsistent and statistically naive
- NAVAL - an expert group to suggest clarification
    - results at ***dnatco.datmos.org***



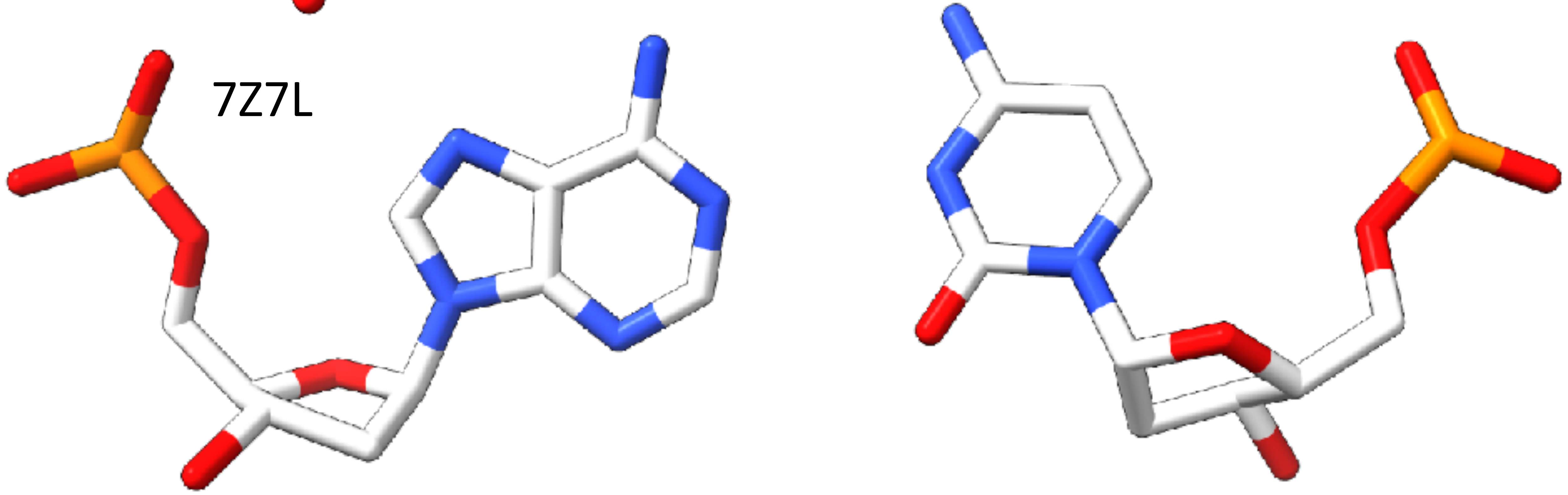
🟥	$O3'^{(-1)}$-P	1.774 Å	N/A (>)
🟩	P-OP1	1.480 Å	51.7 %
🟩	P-OP2	1.486 Å	80.4 %
🟩	P-O5'	1.596 Å	47.7 %
🟩	O5'-C5'	1.425 Å	46.1 %
🟩	C5'-C4'	1.511 Å	46.8 %
🟩	C4'-C3'	1.524 Å	37.7 %
🟩	C3'-O3'	1.428 Å	25.8 %
🟩	C4'-O4'	1.458 Å	28.9 %
🟩	O4'-C1'	1.415 Å	95.2 %

2. Base pairing classification is essential for prediction of RNA 2D and 3D

- The PDB archive is not reliable
- Available programs provide incomplete & conflicting results

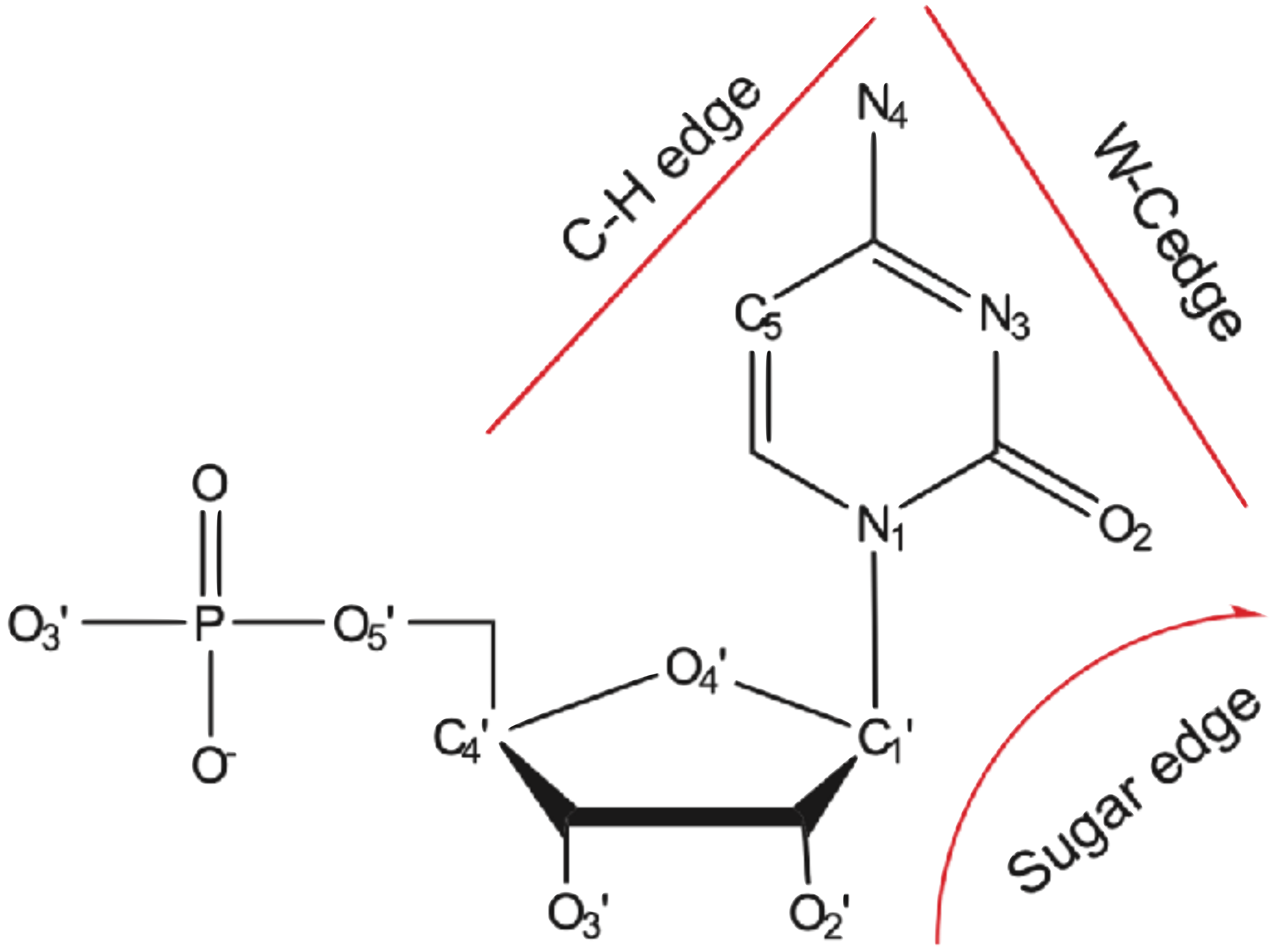


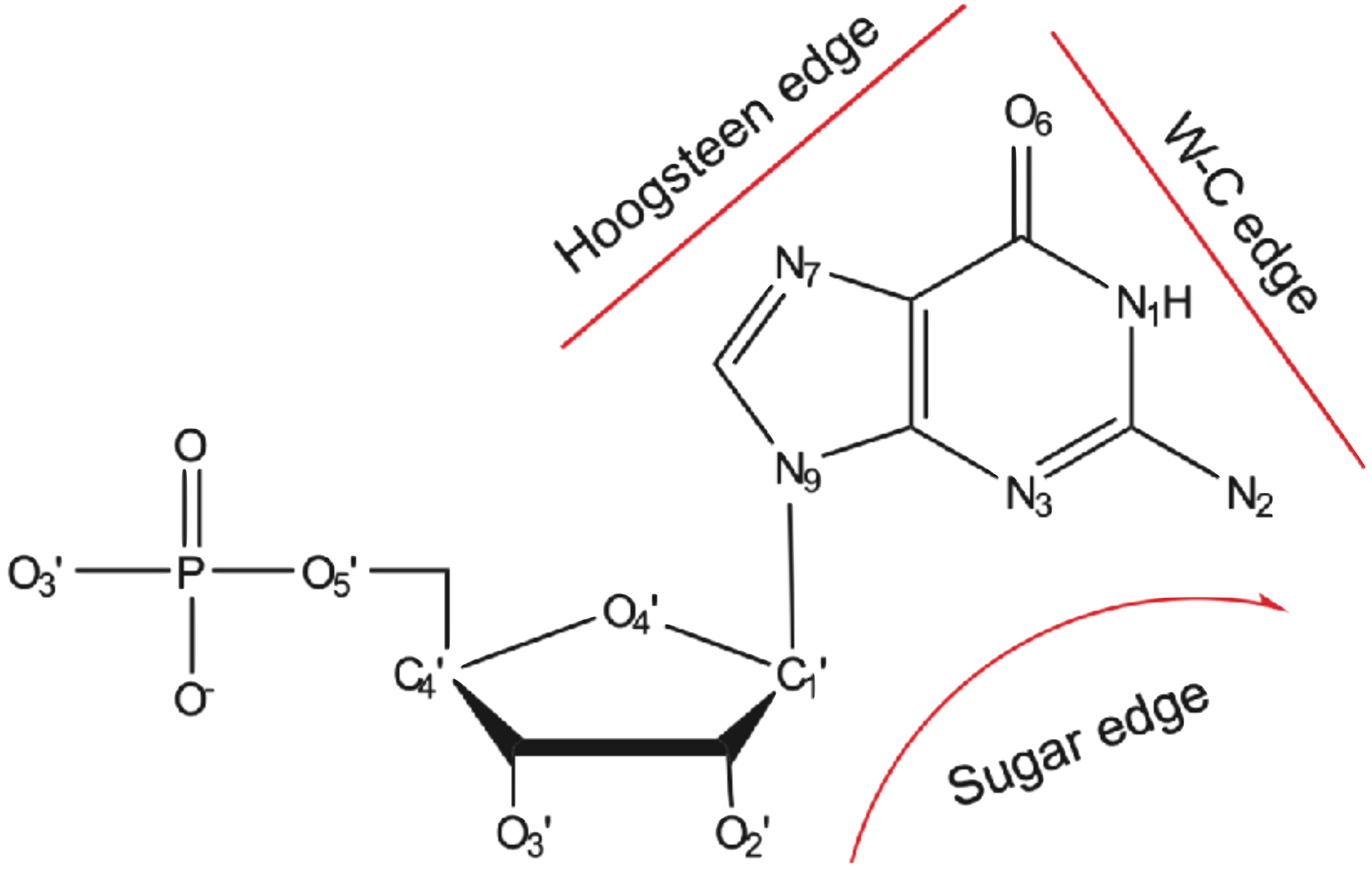
1DA0



7Z7L

2. New Base Pair assignment based on the Leontis-Westhof classes





2. New Base Pair assignment at *basepairs.datmos.org*

Home | cWW | cWWa | tWW | tWWa | cWH | tWH | cWS | **tWS** | cHH | tHH | cHS | tHS | cSS | tSS

A-A (39) | **A-C** (6) | **A-G** (632) | **A-U** (0) | **C-A** (27) | **C-C** (18) | **C-G** (35) | **C-U** (2) | **G-A** | **G-C** (11) | **G-G** | **G-U** (186) | **U-A** (79) | **U-C** (8)

U-G (30) | **U-U** (12)

6: trans Watson-Crick / Sugar

	A	G	C	U
A	**3ccq** 0-A**2018** · · · 0-A**1829** show statistics + exemplars	not defined	**3ccu** 0-C**1983** · · · 0-A**1981** show statistics + exemplars	**1s72** 0-U**779** · · · 0-A**776** show statistics + exemplars

● Basic ○ Parameter ranges ○ SQL

Data source

All Polar Contacts — Reference Set

○ RNA ○ DNA ● Both

Order by

Smallest Edge RMSD

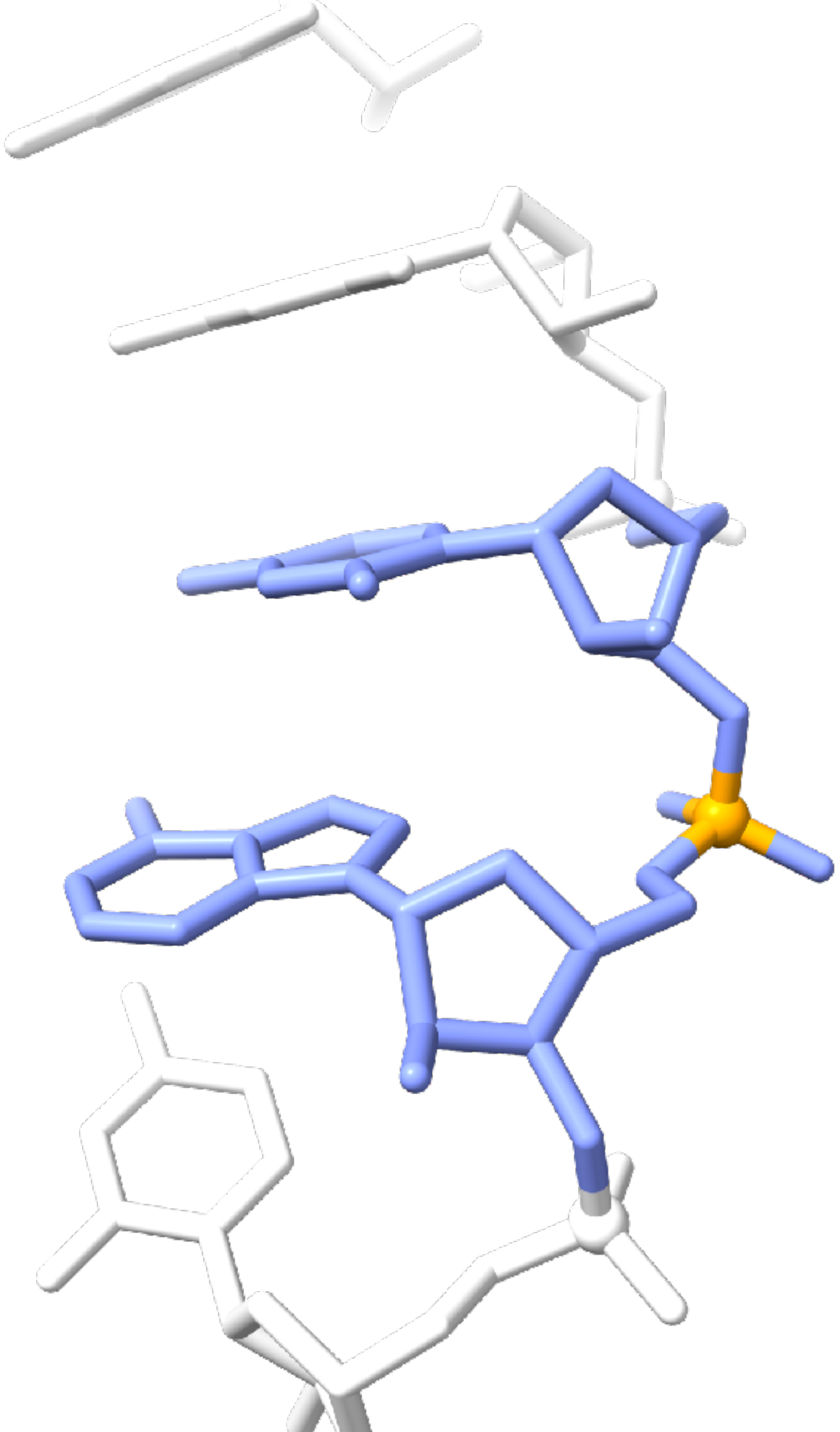
☐ Rotate images

Reference tWS C-G basepair

58462 × tWS-C-G from **3954** PDB structures

▽ expand plots ▽

3. The NA backbone geometry: often ignored … to the detriment of the field

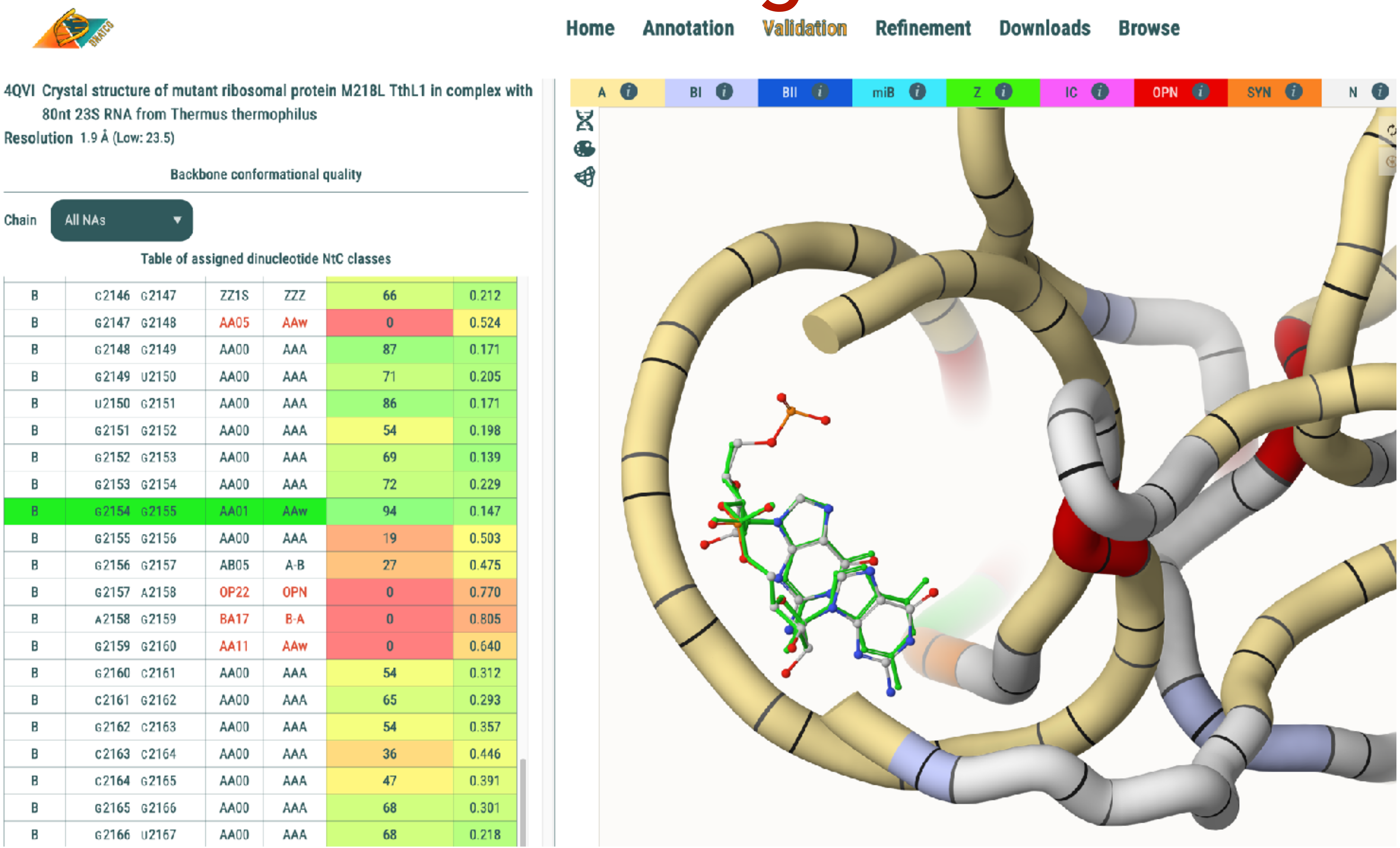


- NA backbone is conformationally complex:
  - the smallest unit for analysis is ***dinucleotide***
  - torsion angles correlate, 2- or 3-D correlations are misleading
- Complex analysis of the PDB data provided
  96 NtC classes

3. NtC: dinucleotide conformational classes

dnatco.datmos.org

- annotate, validate, and refine



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Resolution 1.9 Å (Low: 23.5)

Backbone conformational quality

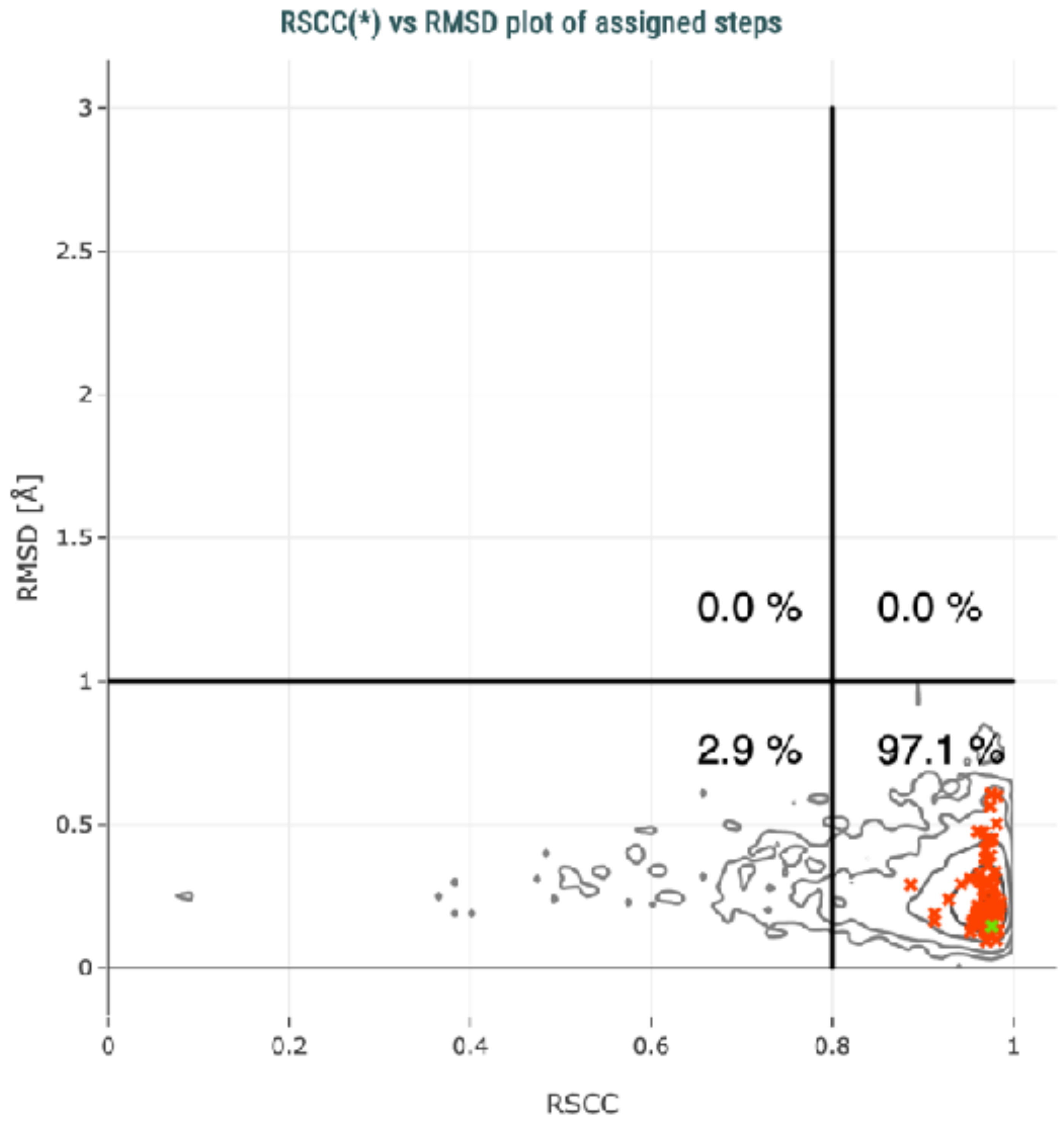
Chain All NAs

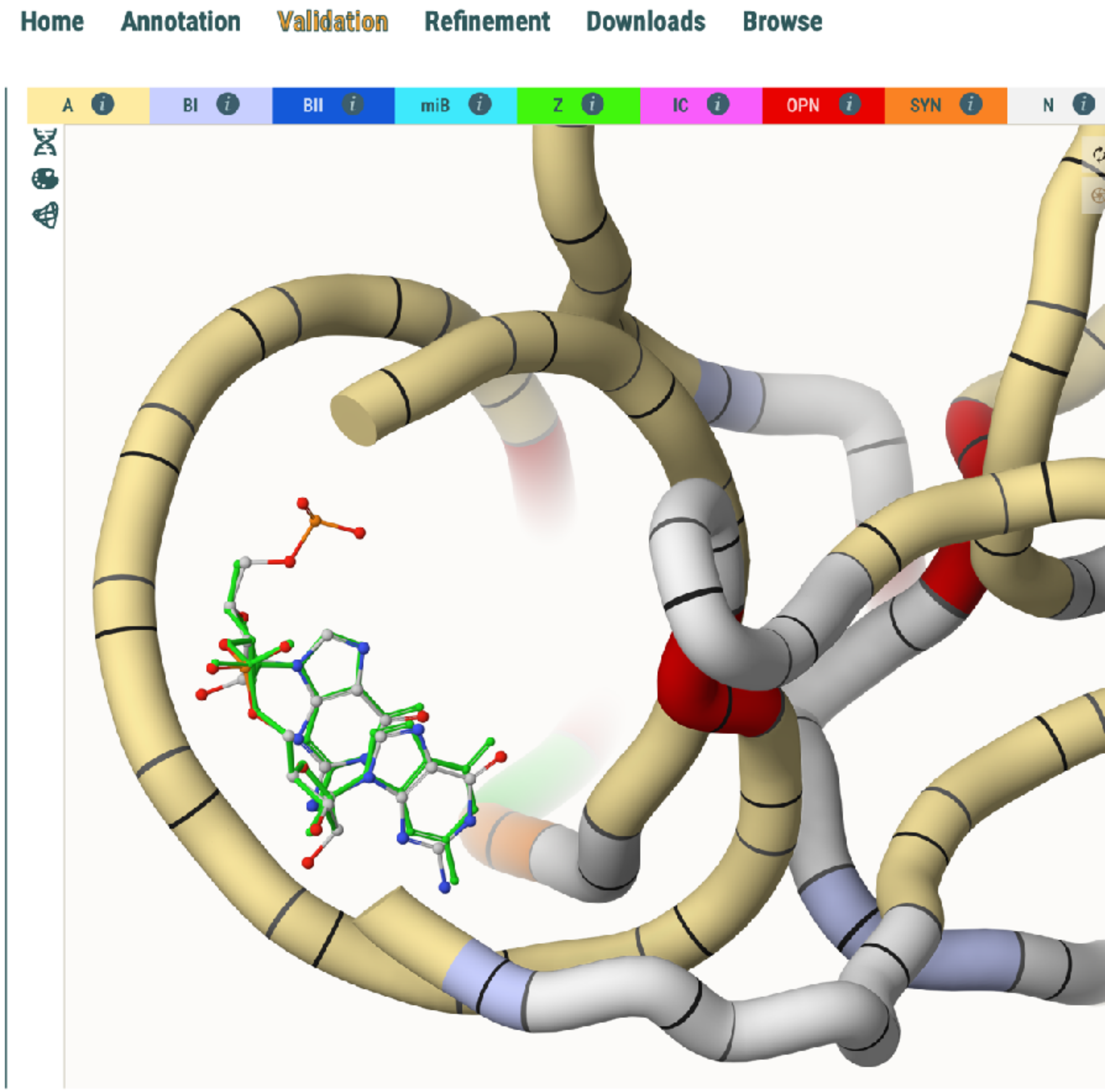
Table of assigned dinucleotide NtC classes

B	C2146 G2147	ZZ1S	ZZZ	66	0.212
B	G2147 G2148	AA05	AAw	0	0.524
B	G2148 G2149	AA00	AAA	87	0.171
B	G2149 U2150	AA00	AAA	71	0.205
B	U2150 G2151	AA00	AAA	86	0.171
B	G2151 G2152	AA00	AAA	54	0.198
B	G2152 G2153	AA00	AAA	69	0.139
B	G2153 G2154	AA00	AAA	72	0.229
B	G2154 G2155	AA01	AAw	94	0.147
B	G2155 G2156	AA00	AAA	19	0.503
B	G2156 G2157	AB05	A-B	27	0.475
B	G2157 A2158	OP22	OPN	0	0.770
B	A2158 G2159	BA17	B-A	0	0.805
B	G2159 G2160	AA11	AAw	0	0.640
B	G2160 C2161	AA00	AAA	54	0.312
B	C2161 G2162	AA00	AAA	65	0.293
B	G2162 C2163	AA00	AAA	54	0.357
B	C2163 C2164	AA00	AAA	36	0.446
B	C2164 G2165	AA00	AAA	47	0.391
B	G2165 G2166	AA00	AAA	68	0.301
B	G2166 U2167	AA00	AAA	68	0.218

3. New validation tool: rmsd/RSCC diagrams

- … fit between electron density (RSCC) & the closest NtC (rmsd)





Thank you for your time!

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