Use of NtC knowledge for nucleic acid structure refinement

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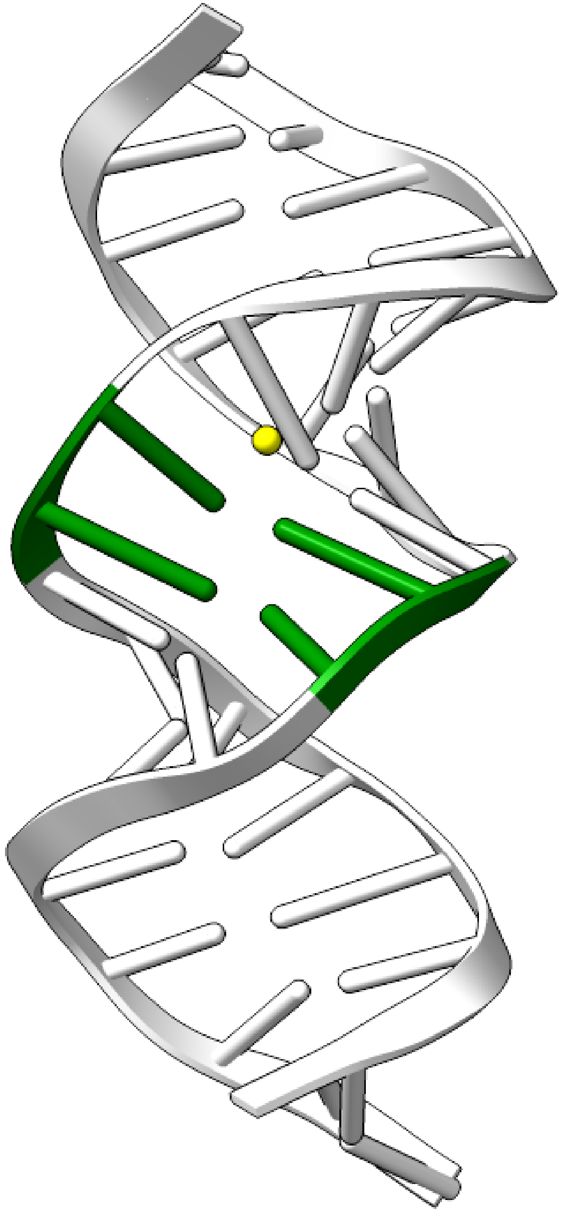
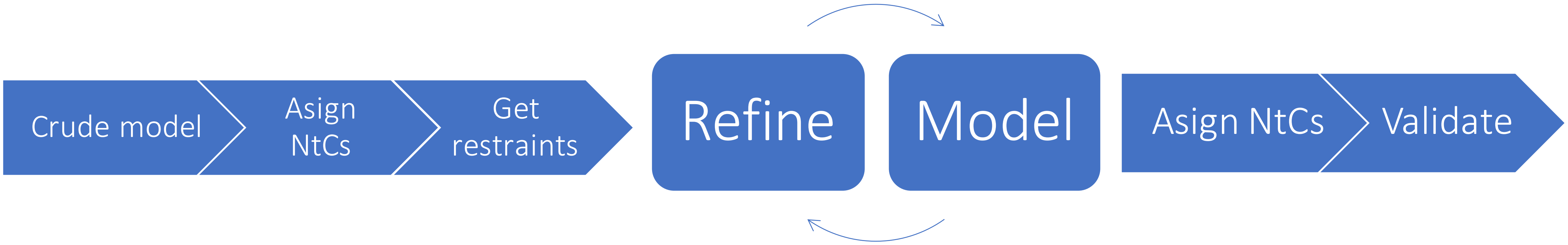
Refinement

- Restraints generated on the dnatco.datmos.org website (for Refmac and Phenix)
- NtC restraints greatly improved refinement procedure



Workflow – not yet automatic



Crude model

Asign NtCs

Get restraints

Refine

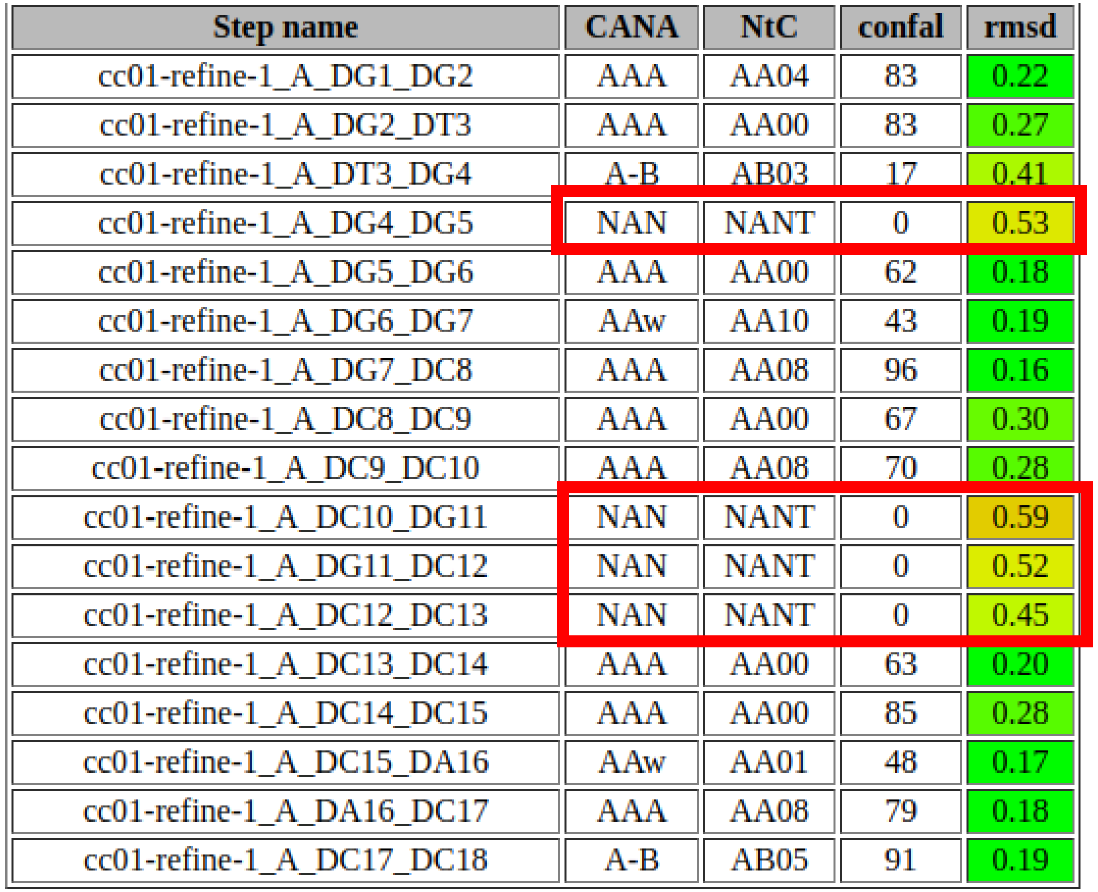
Model

Asign NtCs

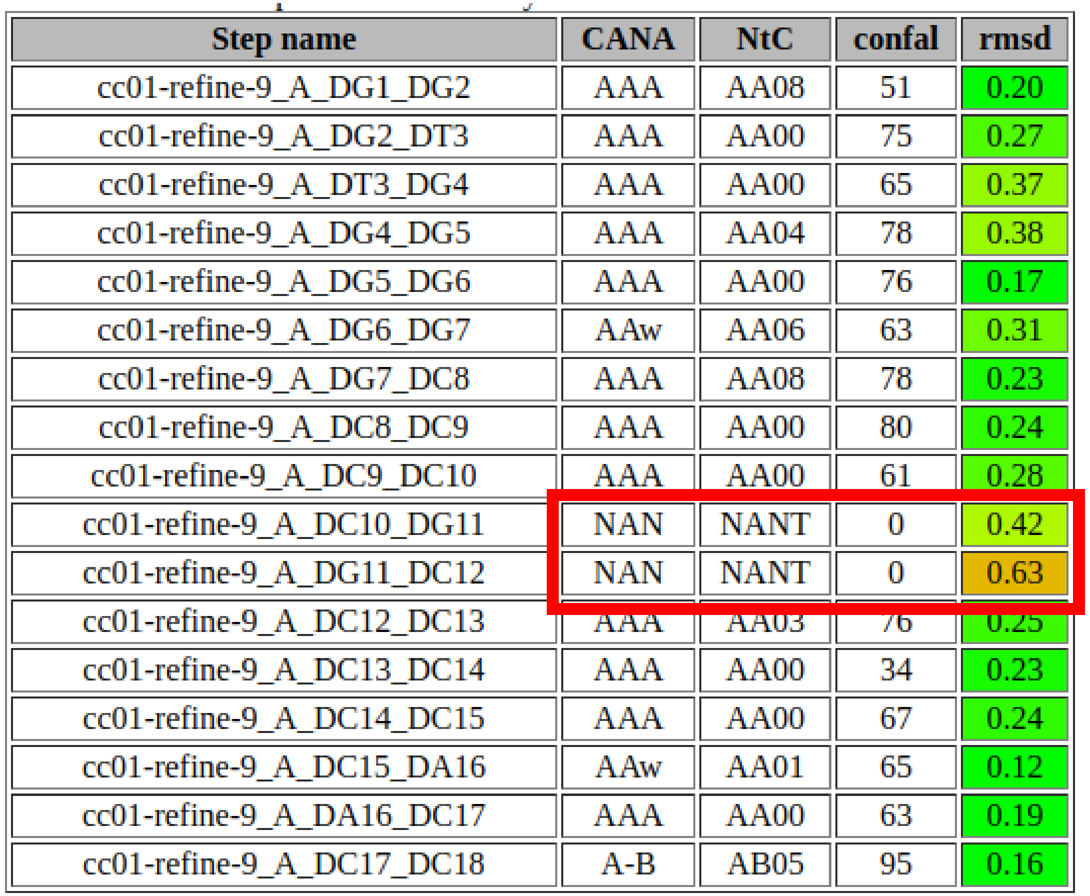
Validate

18mer DNA with CC mismatch

Resolution: 2.4 Å



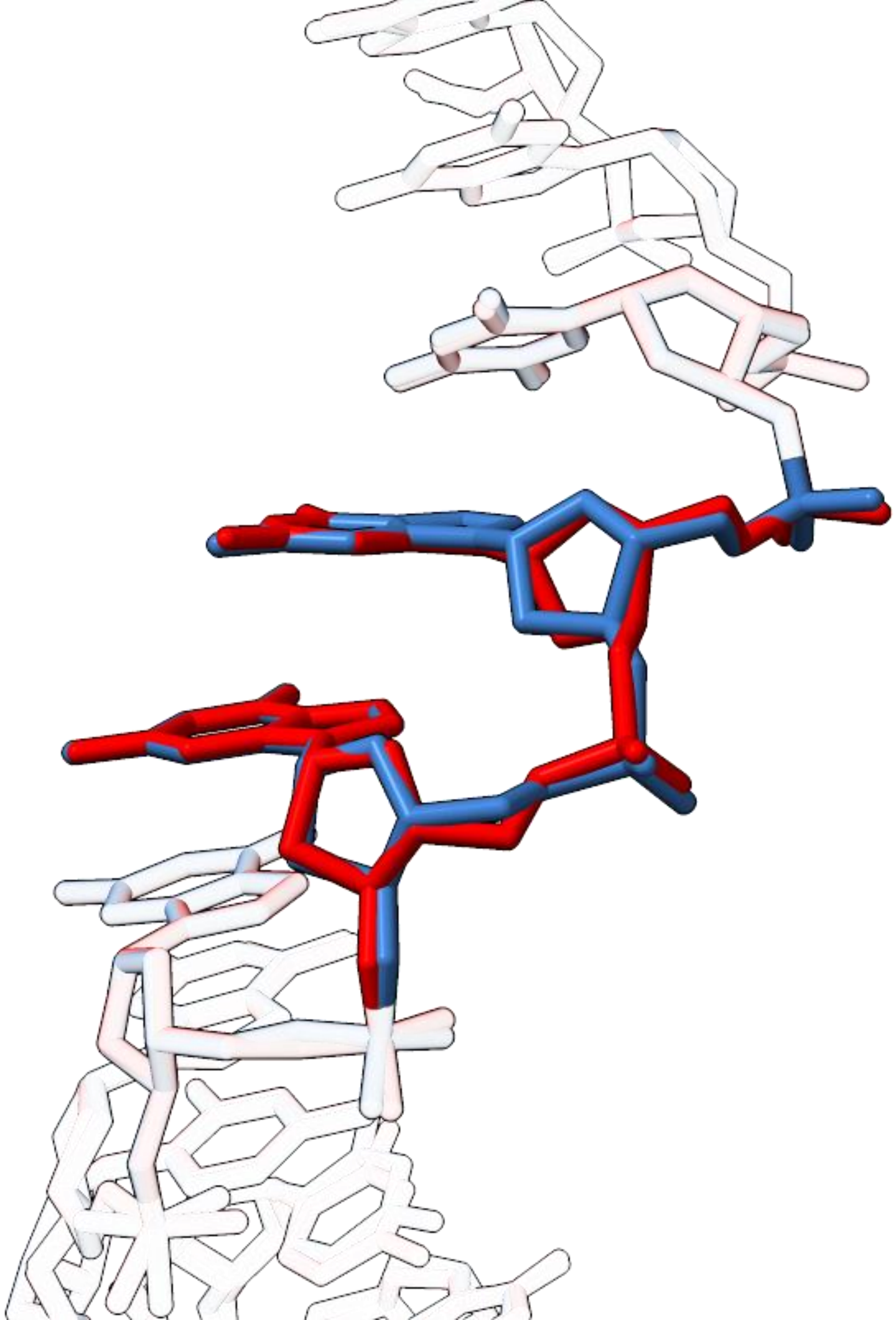
Step name	CANA	NtC	confal	rmsd
cc01-refine-1_A_DG1_DG2	AAA	AA04	83	0.22
cc01-refine-1_A_DG2_DT3	AAA	AA00	83	0.27
cc01-refine-1_A_DT3_DG4	A-B	AB03	17	0.41
cc01-refine-1_A_DG4_DG5	NAN	NANT	0	0.53
cc01-refine-1_A_DG5_DG6	AAA	AA00	62	0.18
cc01-refine-1_A_DG6_DG7	AAw	AA10	43	0.19
cc01-refine-1_A_DG7_DC8	AAA	AA08	96	0.16
cc01-refine-1_A_DC8_DC9	AAA	AA00	67	0.30
cc01-refine-1_A_DC9_DC10	AAA	AA08	70	0.28
cc01-refine-1_A_DC10_DG11	NAN	NANT	0	0.59
cc01-refine-1_A_DG11_DC12	NAN	NANT	0	0.52
cc01-refine-1_A_DC12_DC13	NAN	NANT	0	0.45
cc01-refine-1_A_DC13_DC14	AAA	AA00	63	0.20
cc01-refine-1_A_DC14_DC15	AAA	AA00	85	0.28
cc01-refine-1_A_DC15_DA16	AAw	AA01	48	0.17
cc01-refine-1_A_DA16_DC17	AAA	AA08	79	0.18
cc01-refine-1_A_DC17_DC18	A-B	AB05	91	0.19



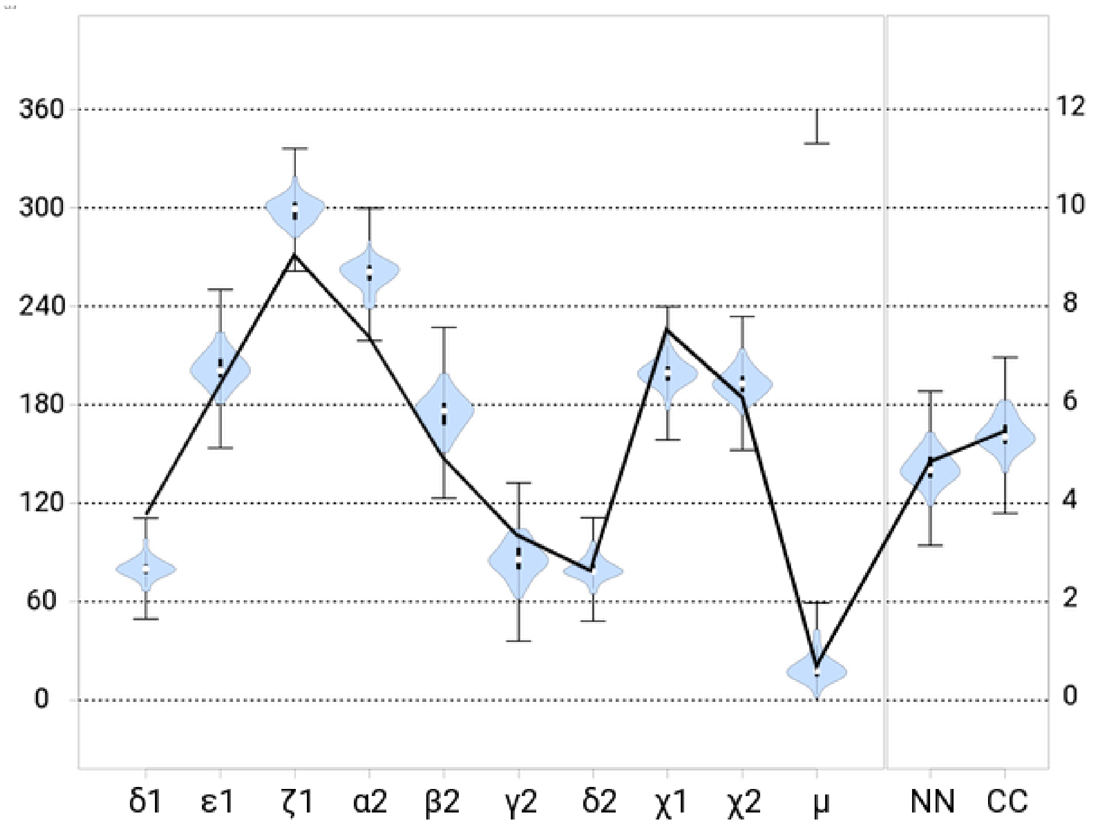
Step name	CANA	NtC	confal	rmsd
cc01-refine-9_A_DG1_DG2	AAA	AA08	51	0.20
cc01-refine-9_A_DG2_DT3	AAA	AA00	75	0.27
cc01-refine-9_A_DT3_DG4	AAA	AA00	65	0.37
cc01-refine-9_A_DG4_DG5	AAA	AA04	78	0.38
cc01-refine-9_A_DG5_DG6	AAA	AA00	76	0.17
cc01-refine-9_A_DG6_DG7	AAw	AA06	63	0.31
cc01-refine-9_A_DG7_DC8	AAA	AA08	78	0.23
cc01-refine-9_A_DC8_DC9	AAA	AA00	80	0.24
cc01-refine-9_A_DC9_DC10	AAA	AA00	61	0.28
cc01-refine-9_A_DC10_DG11	NAN	NANT	0	0.42
cc01-refine-9_A_DG11_DC12	NAN	NANT	0	0.63
cc01-refine-9_A_DC12_DC13	AAA	AA03	76	0.25
cc01-refine-9_A_DC13_DC14	AAA	AA00	34	0.23
cc01-refine-9_A_DC14_DC15	AAA	AA00	67	0.24
cc01-refine-9_A_DC15_DA16	AAw	AA01	65	0.12
cc01-refine-9_A_DA16_DC17	AAA	AA00	63	0.19
cc01-refine-9_A_DC17_DC18	A-B	AB05	95	0.16

Step 4-5

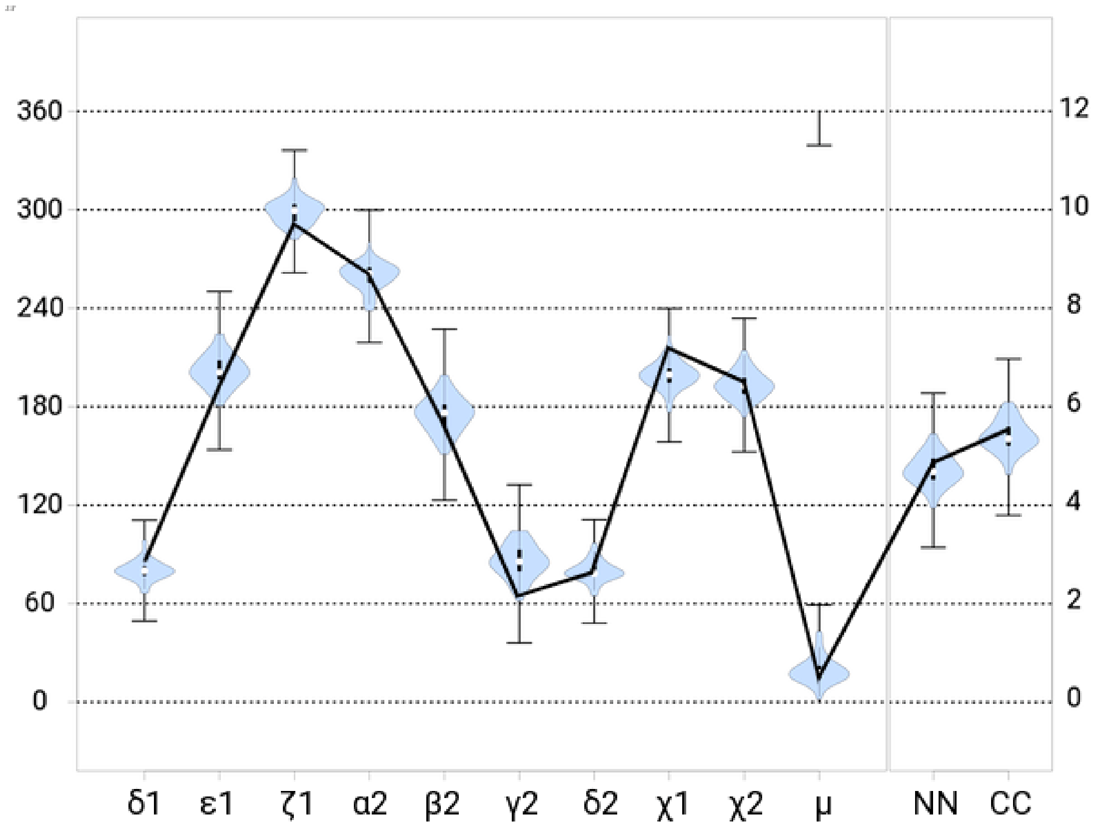
NANT -> AA04



Step 4-5 NANT -> AA04



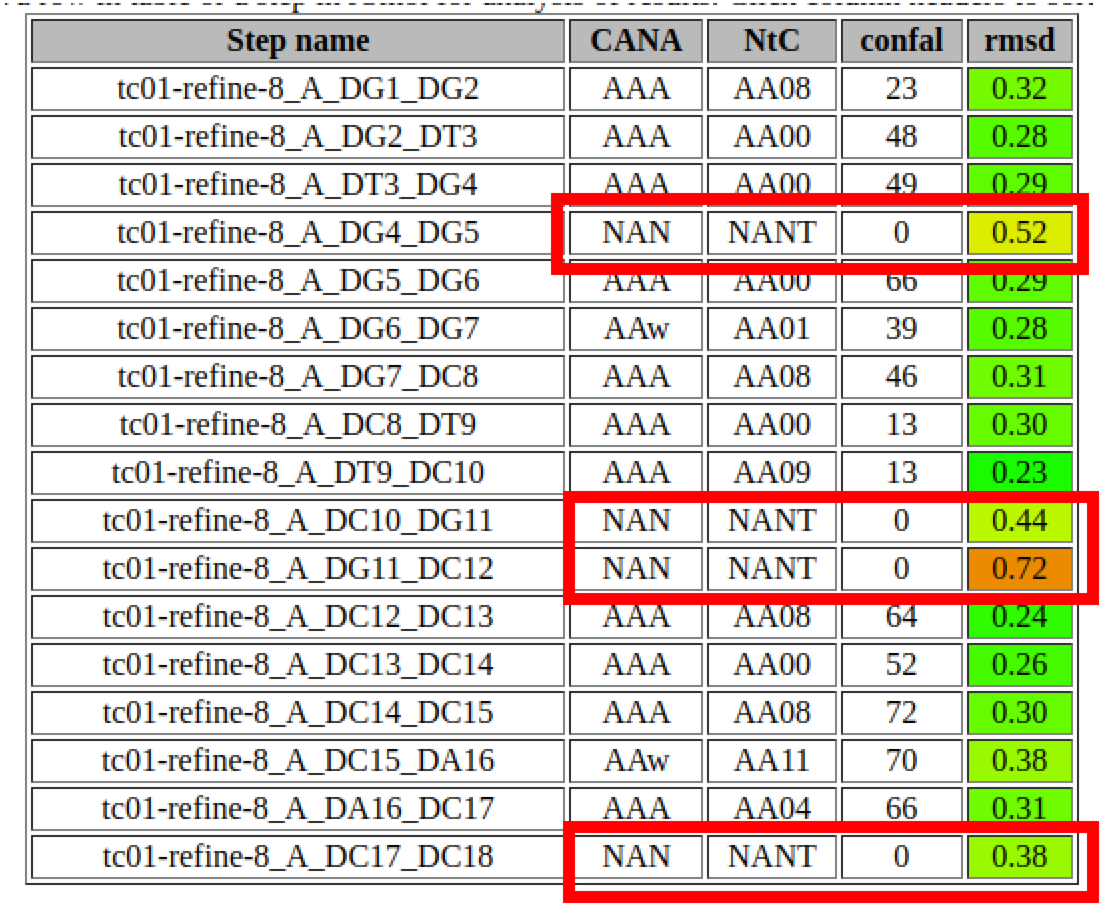
NAN/NANT	δ1	ε1	ζ1	α2	β2	γ2	δ2	χ1	χ2	μ	NN	CC
step_torsions	112.9	192.4	270.9	221.6	148.0	100.6	78.8	225.5	184.1	20.9	4.84	5.45
NtC_average	80.2	201.9	298.8	259.4	175.1	85.4	79.7	199.2	193.1	19.2	4.71	5.39
Δ torsions	32.7	-9.5	-27.9	-37.8	-27.1	15.2	-0.9	26.3	-9.0	1.7	0.13	0.06
torsion confals	1	84	8	2	29	62	100	15	80	99	97	99



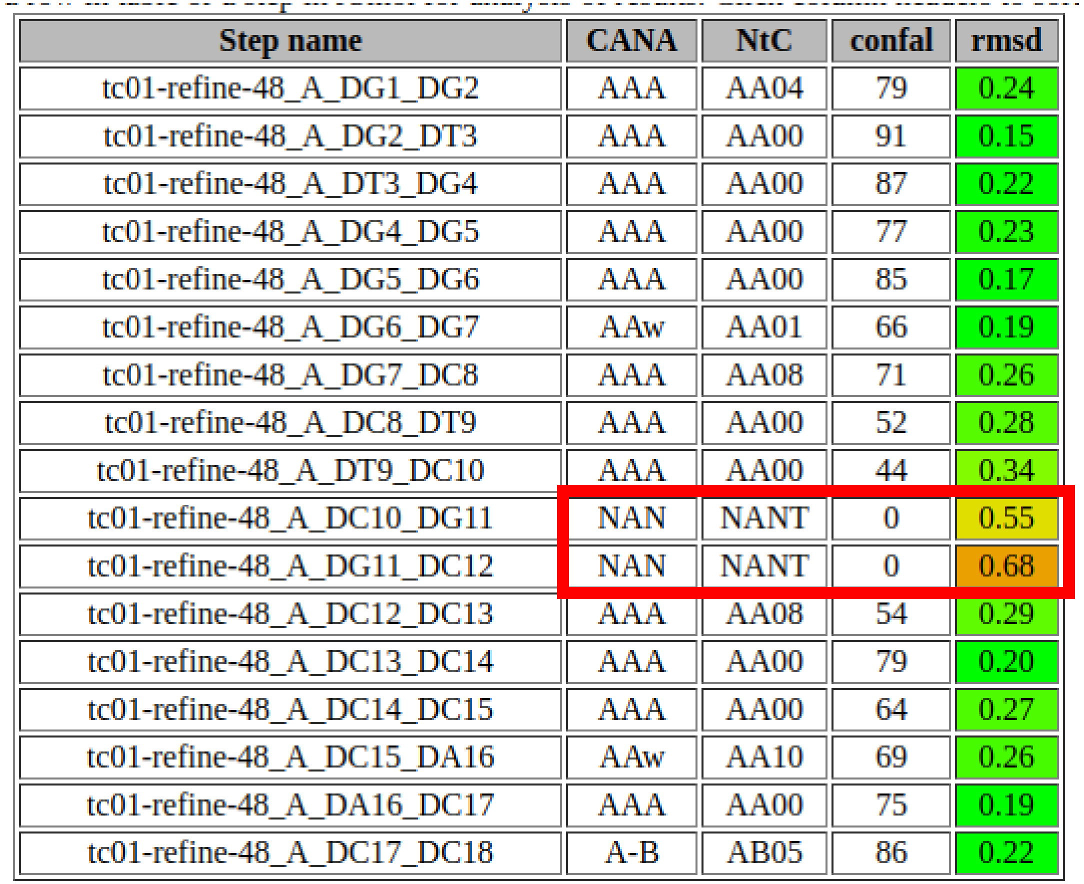
AAA/AA04	δ1	ε1	ζ1	α2	β2	γ2	δ2	χ1	χ2	μ	NN	CC
step_torsions	85.5	192.2	291.1	260.8	169.9	64.5	78.6	215.5	194.9	14.9	4.86	5.52
NtC_average	80.2	201.9	298.8	259.4	175.1	85.4	79.7	199.2	193.1	19.2	4.71	5.39
Δ torsions	5.3	-9.7	-7.7	1.4	-5.2	-20.9	-1.1	16.3	1.8	-4.3	0.15	0.13
torsion confals	87	83	82	100	96	40	100	48	99	95	96	97

18mer DNA with TC mismatch

Resolution: 2.75 Å



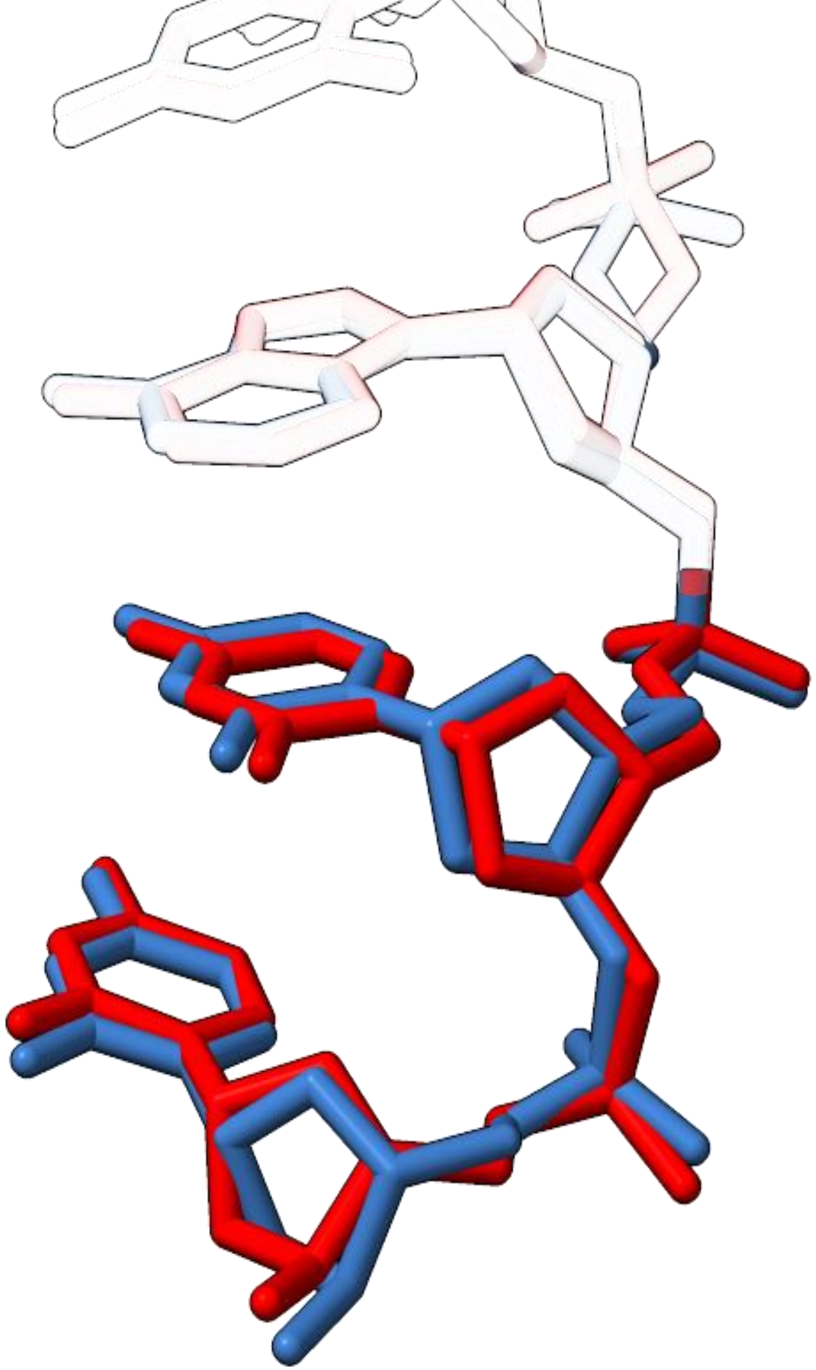
Step name	CANA	NtC	confal	rmsd
tc01-refine-8_A_DG1_DG2	AAA	AA08	23	0.32
tc01-refine-8_A_DG2_DT3	AAA	AA00	48	0.28
tc01-refine-8_A_DT3_DG4	AAA	AA00	49	0.29
tc01-refine-8_A_DG4_DG5	NAN	NANT	0	0.52
tc01-refine-8_A_DG5_DG6	AAA	AA00	66	0.29
tc01-refine-8_A_DG6_DG7	AAw	AA01	39	0.28
tc01-refine-8_A_DG7_DC8	AAA	AA08	46	0.31
tc01-refine-8_A_DC8_DT9	AAA	AA00	13	0.30
tc01-refine-8_A_DT9_DC10	AAA	AA09	13	0.23
tc01-refine-8_A_DC10_DG11	NAN	NANT	0	0.44
tc01-refine-8_A_DG11_DC12	NAN	NANT	0	0.72
tc01-refine-8_A_DC12_DC13	AAA	AA08	64	0.24
tc01-refine-8_A_DC13_DC14	AAA	AA00	52	0.26
tc01-refine-8_A_DC14_DC15	AAA	AA08	72	0.30
tc01-refine-8_A_DC15_DA16	AAw	AA11	70	0.38
tc01-refine-8_A_DA16_DC17	AAA	AA04	66	0.31
tc01-refine-8_A_DC17_DC18	NAN	NANT	0	0.38



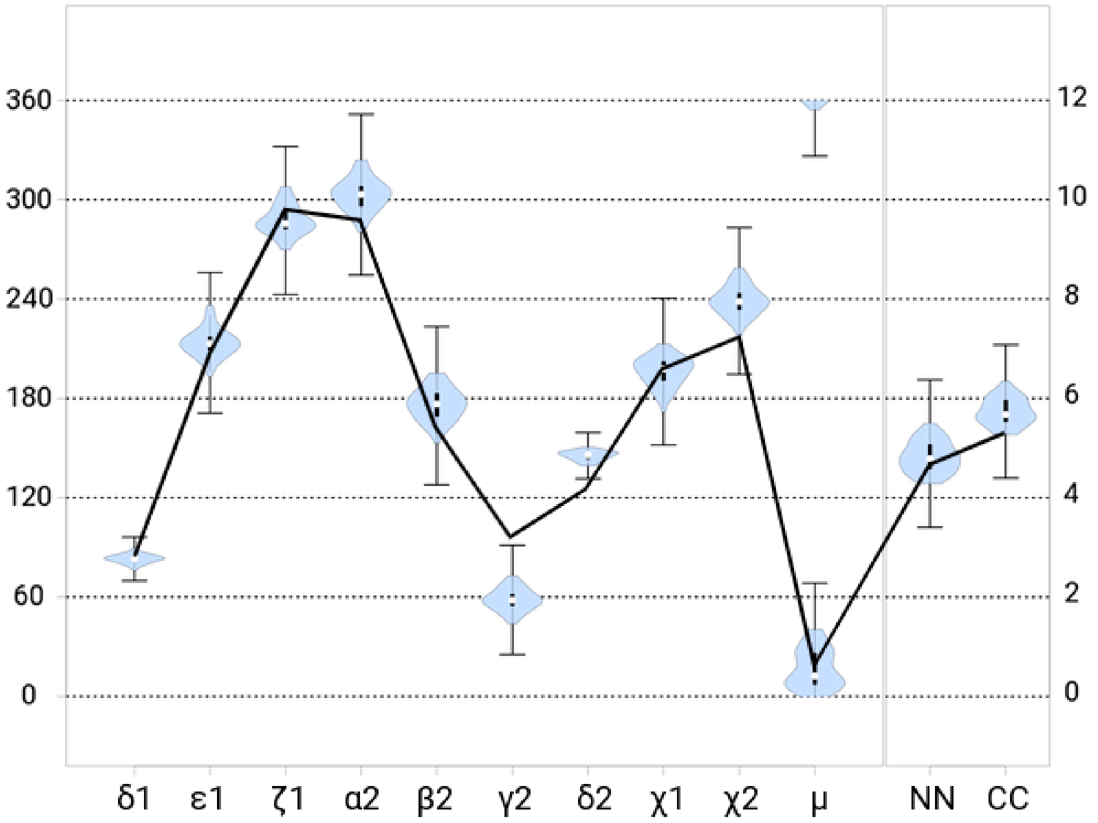
Step name	CANA	NtC	confal	rmsd
tc01-refine-48_A_DG1_DG2	AAA	AA04	79	0.24
tc01-refine-48_A_DG2_DT3	AAA	AA00	91	0.15
tc01-refine-48_A_DT3_DG4	AAA	AA00	87	0.22
tc01-refine-48_A_DG4_DG5	AAA	AA00	77	0.23
tc01-refine-48_A_DG5_DG6	AAA	AA00	85	0.17
tc01-refine-48_A_DG6_DG7	AAw	AA01	66	0.19
tc01-refine-48_A_DG7_DC8	AAA	AA08	71	0.26
tc01-refine-48_A_DC8_DT9	AAA	AA00	52	0.28
tc01-refine-48_A_DT9_DC10	AAA	AA00	44	0.34
tc01-refine-48_A_DC10_DG11	NAN	NANT	0	0.55
tc01-refine-48_A_DG11_DC12	NAN	NANT	0	0.68
tc01-refine-48_A_DC12_DC13	AAA	AA08	54	0.29
tc01-refine-48_A_DC13_DC14	AAA	AA00	79	0.20
tc01-refine-48_A_DC14_DC15	AAA	AA00	64	0.27
tc01-refine-48_A_DC15_DA16	AAw	AA10	69	0.26
tc01-refine-48_A_DA16_DC17	AAA	AA00	75	0.19
tc01-refine-48_A_DC17_DC18	A-B	AB05	86	0.22

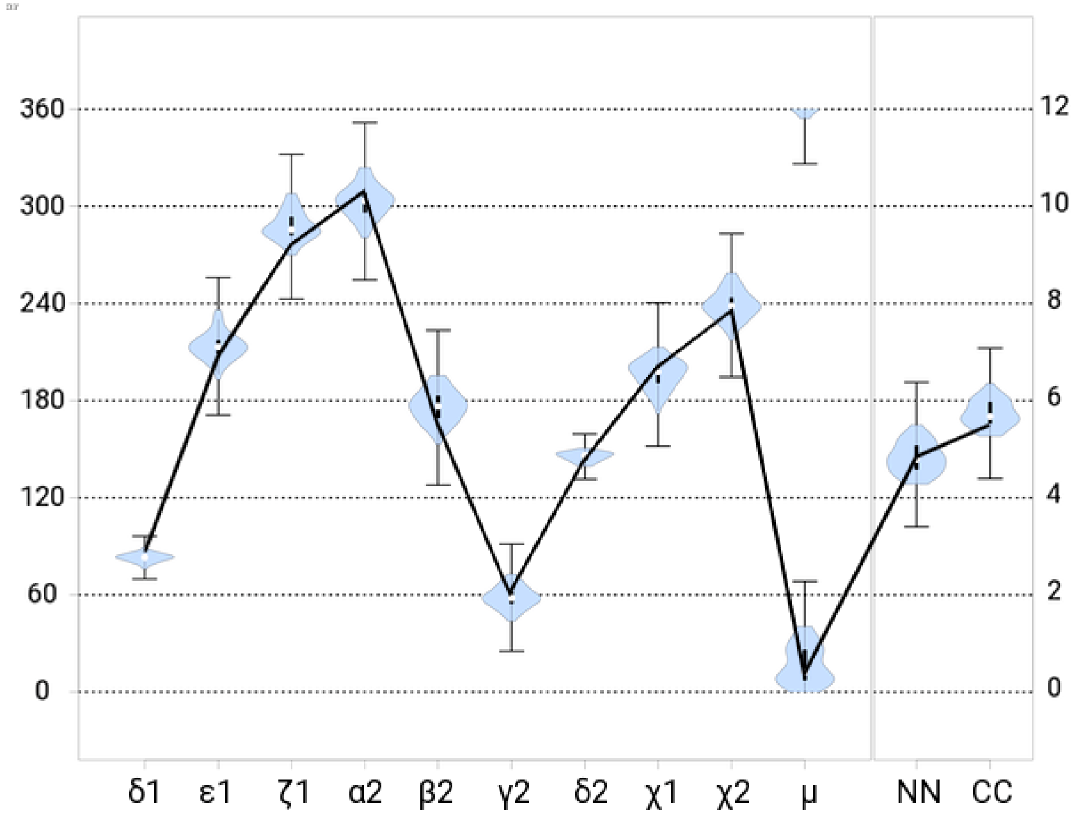
Step 17-18

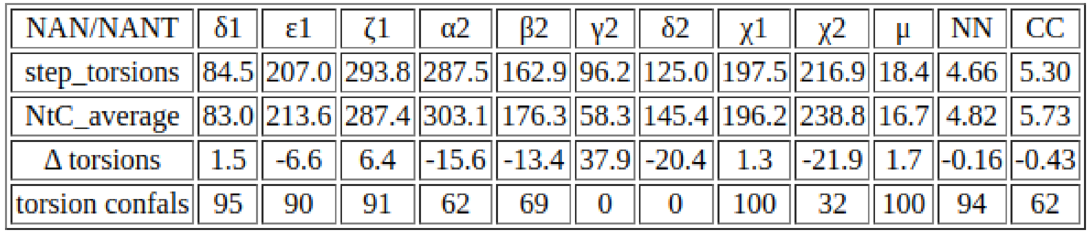
NANT -> AB05



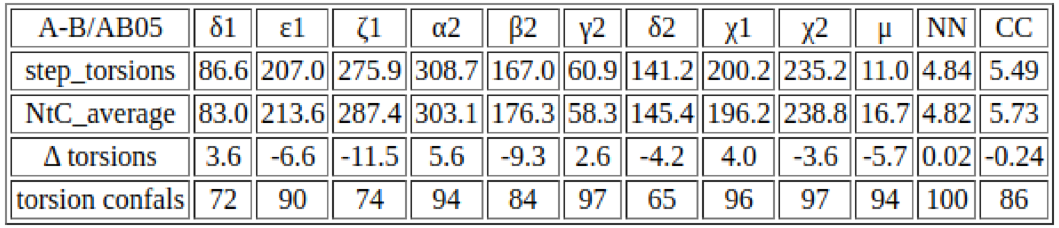
Step 17-18 NANT -> AB05





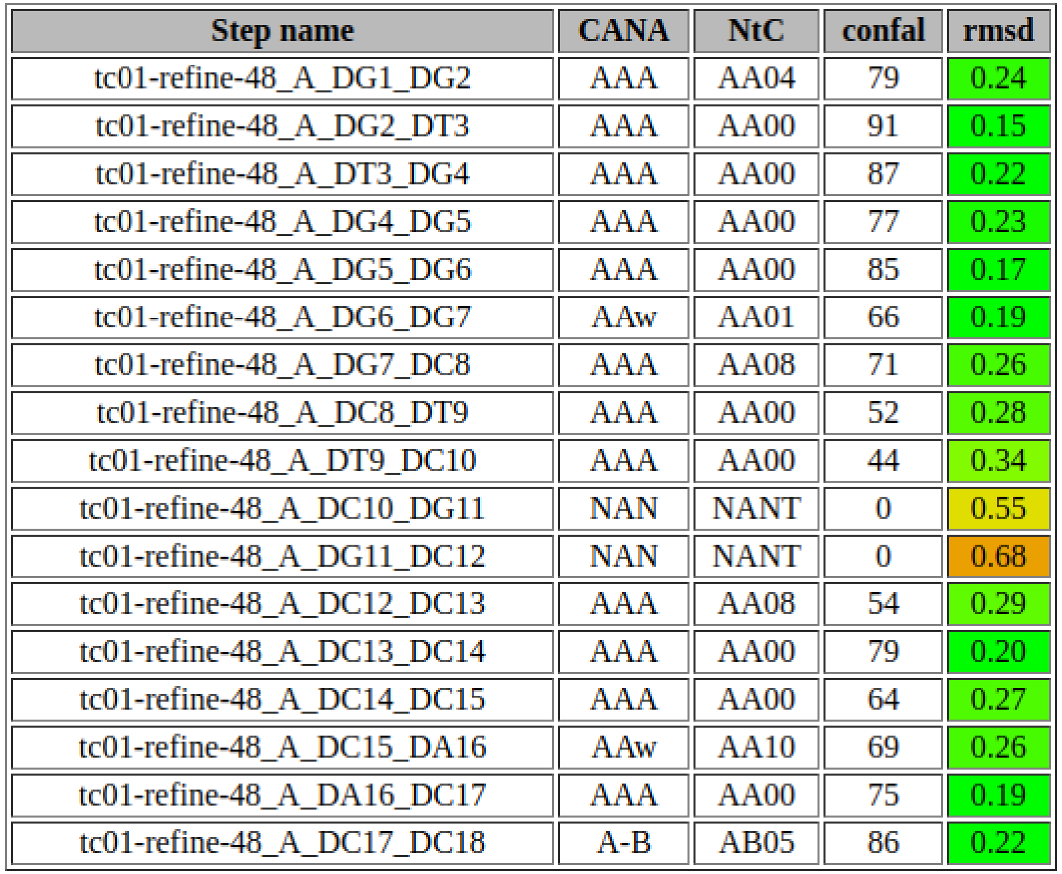


NAN/NANT	δ1	ε1	ζ1	α2	β2	γ2	δ2	χ1	χ2	μ	NN	CC
step_torsions	84.5	207.0	293.8	287.5	162.9	96.2	125.0	197.5	216.9	18.4	4.66	5.30
NtC_average	83.0	213.6	287.4	303.1	176.3	58.3	145.4	196.2	238.8	16.7	4.82	5.73
Δ torsions	1.5	-6.6	6.4	-15.6	-13.4	37.9	-20.4	1.3	-21.9	1.7	-0.16	-0.43
torsion confals	95	90	91	62	69	0	0	100	32	100	94	62



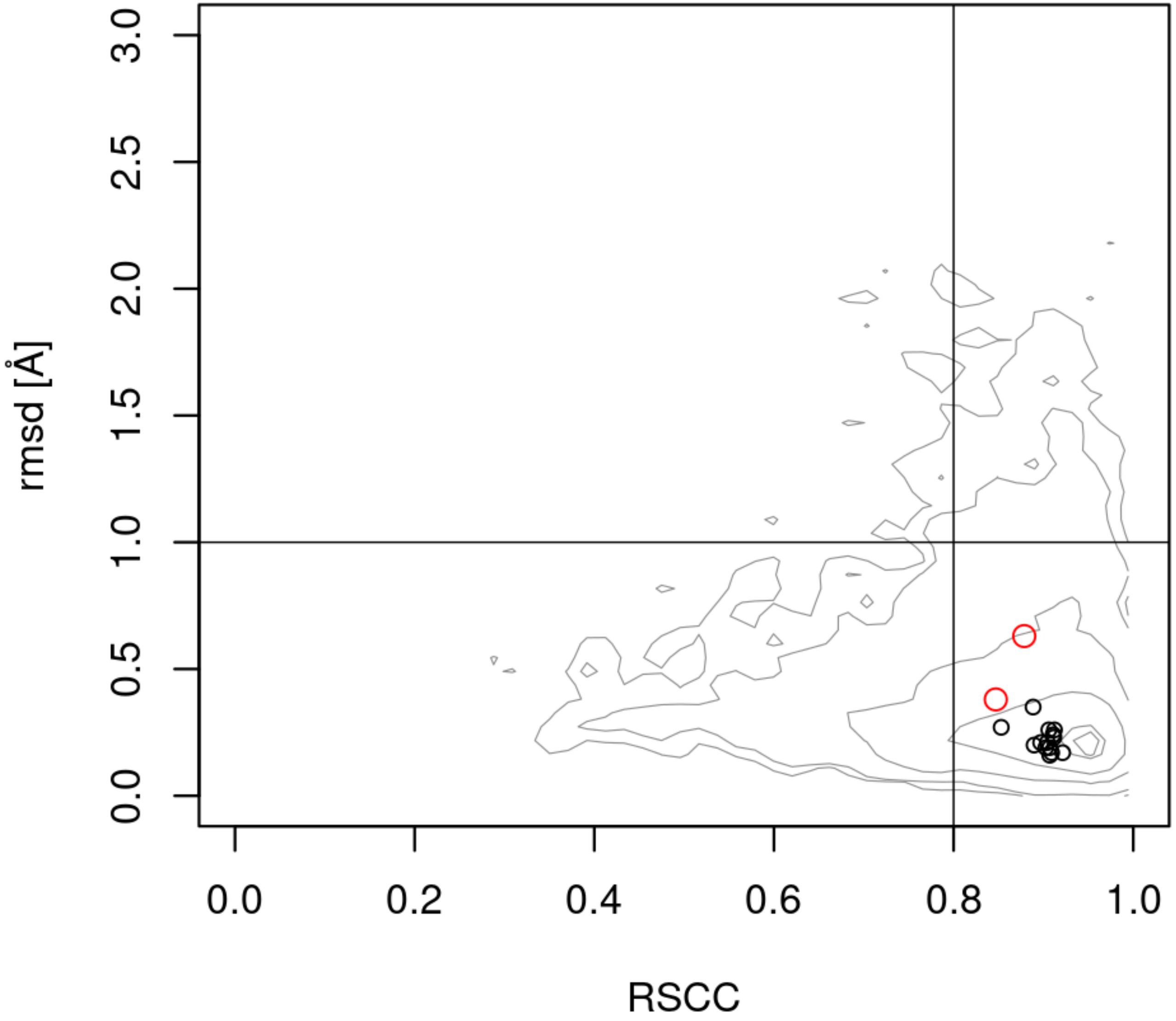
A-B/AB05	δ1	ε1	ζ1	α2	β2	γ2	δ2	χ1	χ2	μ	NN	CC
step_torsions	86.6	207.0	275.9	308.7	167.0	60.9	141.2	200.2	235.2	11.0	4.84	5.49
NtC_average	83.0	213.6	287.4	303.1	176.3	58.3	145.4	196.2	238.8	16.7	4.82	5.73
Δ torsions	3.6	-6.6	-11.5	5.6	-9.3	2.6	-4.2	4.0	-3.6	-5.7	0.02	-0.24
torsion confals	72	90	74	94	84	97	65	96	97	94	100	86

RSCC vs rmsd



Step name	CANA	NtC	confal	rmsd
tc01-refine-48_A_DG1_DG2	AAA	AA04	79	0.24
tc01-refine-48_A_DG2_DT3	AAA	AA00	91	0.15
tc01-refine-48_A_DT3_DG4	AAA	AA00	87	0.22
tc01-refine-48_A_DG4_DG5	AAA	AA00	77	0.23
tc01-refine-48_A_DG5_DG6	AAA	AA00	85	0.17
tc01-refine-48_A_DG6_DG7	AAw	AA01	66	0.19
tc01-refine-48_A_DG7_DC8	AAA	AA08	71	0.26
tc01-refine-48_A_DC8_DT9	AAA	AA00	52	0.28
tc01-refine-48_A_DT9_DC10	AAA	AA00	44	0.34
tc01-refine-48_A_DC10_DG11	NAN	NANT	0	0.55
tc01-refine-48_A_DG11_DC12	NAN	NANT	0	0.68
tc01-refine-48_A_DC12_DC13	AAA	AA08	54	0.29
tc01-refine-48_A_DC13_DC14	AAA	AA00	79	0.20
tc01-refine-48_A_DC14_DC15	AAA	AA00	64	0.27
tc01-refine-48_A_DC15_DA16	AAw	AA10	69	0.26
tc01-refine-48_A_DA16_DC17	AAA	AA00	75	0.19
tc01-refine-48_A_DC17_DC18	A-B	AB05	86	0.22

$$\mathrm{RSCC} = \frac{\sum(\rho_{obs} - \langle\rho_{obs}\rangle)(\rho_{calc} - \langle\rho_{calc}\rangle)}{\left[\sum(\rho_{obs} - \langle\rho_{obs}\rangle)^2 \sum(\rho_{calc} - \langle\rho_{calc}\rangle)^2\right]^{1/2}}$$



Summary

- NtC classes can efficiently guide the refinement process
- RSCC vs rmsd plot is a novel validation method

Acknowledgment

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