Supplemental Material

3D Structural Diversity of 150 Protein Structures - Methods

In order to assess the degree of 3D structural diversity the volume of the CDK2 binding cavity was calculated. The volume of the active site cavity defined by a subset of 44 CDK2 residues[1] was computed using the Molcad program[2] with the "FAST CONNOLLY CHANNEL" option and a CONNOLLY PROBE_RADIUS of 2 Å.

Furthermore for five key residues the RMSD from the reference coordinates of the published structure with PDB code 2r3i[3] was determined. 2r3i was superimposed on the common reference structure 1b38 (PDB code) in the same fashion as described in "Protein Preparation" section of Part 1.

3D Structural Diversity of 150 Protein Structures – Figures and Table

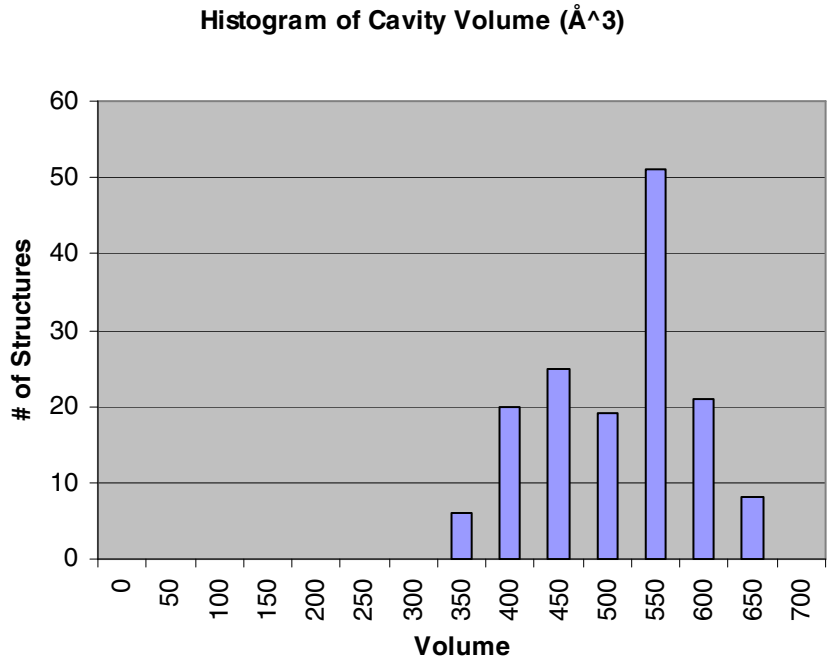
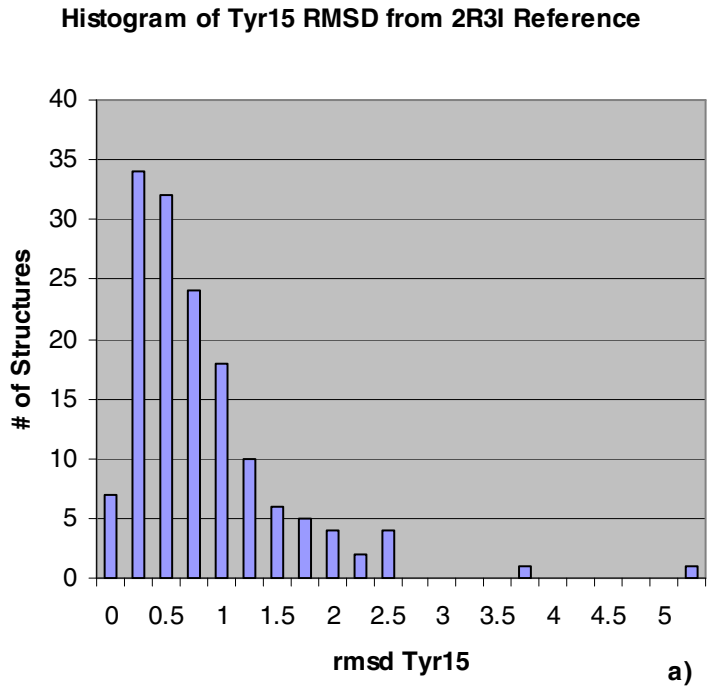
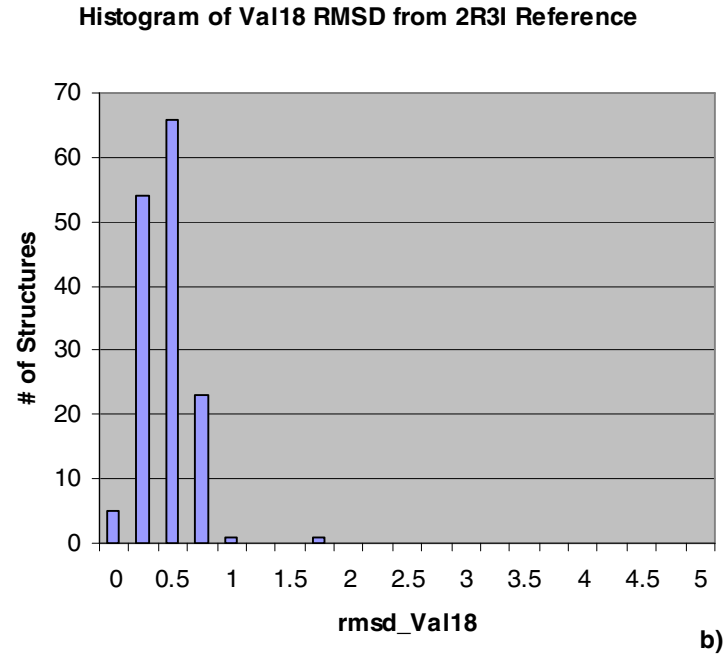


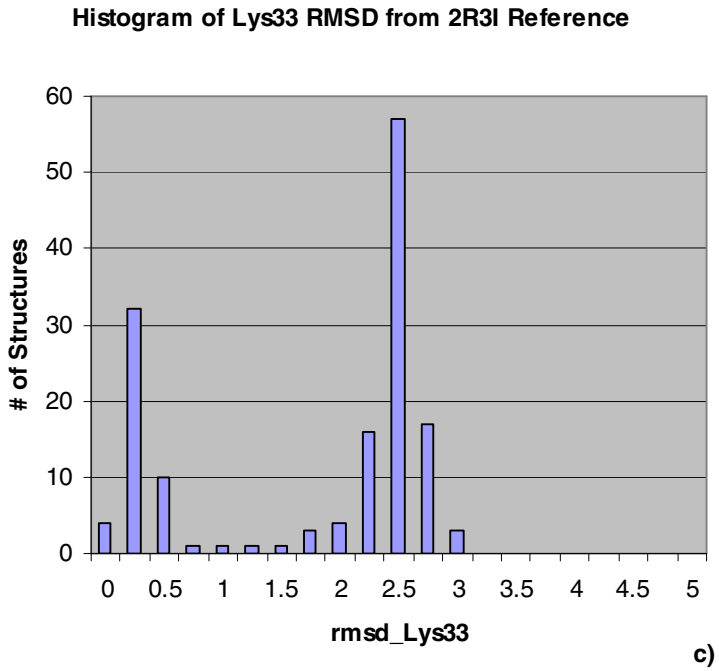
Figure 1. Centered histogram of the CDK2 ATP-site cavity volume.


Histogram of Tyr15 RMSD from 2R3I Reference
# of Structures
40
35
30
25
20
15
10
5
0
0 0.5 1 1.5 2 2.5 3 3.5 4 4.5 5
rmsd Tyr15

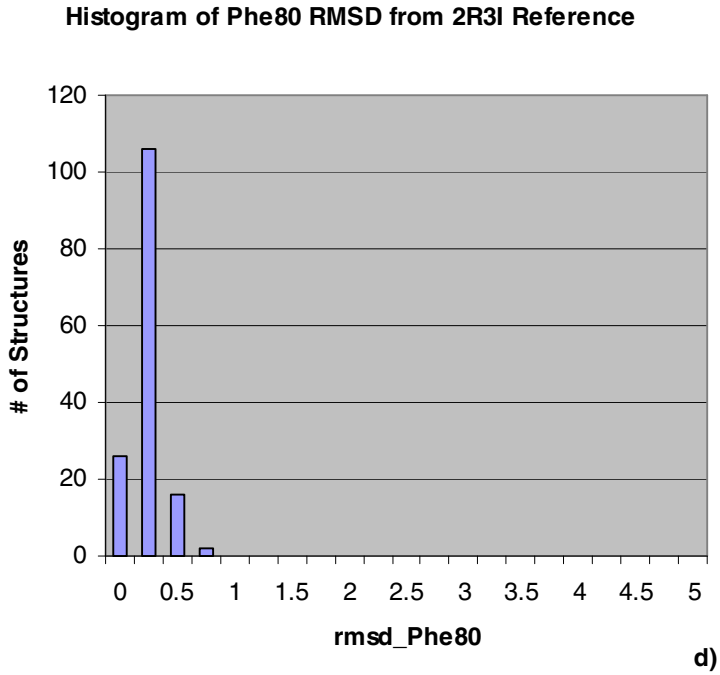
a)


Histogram of Val18 RMSD from 2R3I Reference
# of Structures
70
60
50
40
30
20
10
0
0 0.5 1 1.5 2 2.5 3 3.5 4 4.5 5
rmsd_Val18

b)


Histogram of Lys33 RMSD from 2R3I Reference
# of Structures
60
50
40
30
20
10
0
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
rmsd_Lys33

c)


Histogram of Phe80 RMSD from 2R3I Reference
# of Structures
120
100
80
60
40
20
0
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
rmsd_Phe80

d)

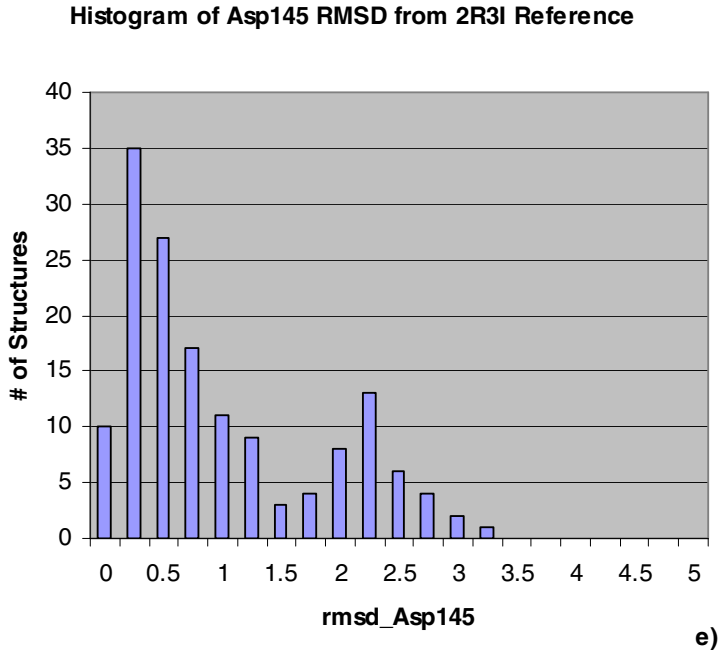


Figure 2. a)-e) RMSD from 2R3I reference crystal structure for five CDK2 active site residues.

Residue	*present in N structures*	*rmsd from 2R3I*	*rmsd_Mean*	*rmsd_StdDev*	*rmsd_Min*	*rmsd_Max*
Tyr 15	148	0.70	0.82	0.72	0.00	5.13
Val18	150	0.42	0.43	0.22	0.00	1.65
Lys 33	150	2.41	1.76	1.03	0.00	2.98
Phe 80	150	0.24	0.25	0.12	0.00	0.73
Asp 145	150	0.65	0.99	0.84	0.00	3.14

Table 1. RMSD from 2R3I reference crystal structure for five CDK2 active site residues.

References

1 CDK2 residues: 7, 8, 9, 10, 11, 12, 16, 17, 18, 19, 20, 21, 29, 30, 31, 32, 33, 64, 66, 78, 79, 80, 81, 82, 83, 84, 85, 86, 88, 89, 131, 132, 134, 135, 136, 142, 143, 144, 145 , 146, 147, 296, 298, 299

2 Sybyl 7.3, Tripos Inc., St. Louis, MO

3 Fischmann, T. O.; Hruza, A.; Duca, J. S.; Ramanathan, L.; Mayhood, T. et al. Structure-guided discovery of cyclin-dependent kinase inhibitors. *Biopolymers (Peptide Science)*, **2007** (in press).