Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Table 1SI: Main H-bonding interactions and their average distances (and standard deviation measured in Å) in each protein – ligand complex along 10 ns molecular dynamics trajectories.

Systems	CDK2/ligand							p38/ligand				AuroraA/ligand		
Compound[a]	Glu81=O	Leu83-N	Leu83=O	Lys33-NH_3	Asp86=OD*	Asp86-N	Gln131=O	Glu71=OE*	Thr106-OH	Asp168-N	Met109-N	Ala212-N	Lys161-NH_3	Pro213
1 (1aq1+)	2.86±0.13	2.80±0.11	-	-	3.36±0.84	-	2.91±0.40	3.24±0.70	-	3.12±0.23	3.14±0.17	3.30±0.20	-	-
2 (1e1x)	2.89±0.16	3.45±0.24	2.87±0.15	-	-	-	-	-	-	2.98±0.17	3.07±0.15	3.38±0.21	2.82±0.29	-
3 (1h1s)	2.79±0.13	3.60±0.21	2.96±0.17	-	-	3.58±0.76	-	3.04±0.25	-	-	3.18±0.17	3.32±0.20	-	-
4 (1h1p)	2.79±0.13	3.29±0.28	3.06±0.35	-	-	-	-	-	3.07±0.19	2.95±0.20	3.21±0.22	3.32±0.20	4.08±0.82	-
5 (1ogu)	2.8±0.11	3.44±0.27	2.87±0.15	-	3.04±0.79	-	-	-	-	3.02±0.22	3.10±0.17	3.38±0.20	3.22±0.57	-
6 (1pkd+)	2.89±0.13	3.03±0.18	-	-	-	-	2.84±0.19	-	3.21±0.24	3.21±0.26	3.04±0.14	3.23±0.18	-	-
7 (1pxj)	3.40±0.31	-	-	2.98±0.17	-	-	-	-	-	-	3.07±0.16	3.32±0.20	-	-
8 (1pxl)	-	2.95±0.13	2.96±0.17	2.99±0.18	-	-	-	-	3.30±0.31	3.20±0.28	3.06±0.15	3.39±0.22	3.11±0.27	-
9 (1pxm)	-	3.48±0.46	2.82±0.12	-	2.63±0.14	-	-	3.08±0.24	3.00±0.17	2.96±0.17	3.17±0.16	3.35±0.21	-	-
10 (1pxn)	-	3.03±0.14	2.94±0.16	3.03±0.2	3.4±0.98	-	-	3.94±1.00	-	2.95±0.15	3.14±0.16	3.24±0.20	4.20±1.14	-
11 (1pxp)	-	2.92±0.11	2.94±0.16	2.97±0.16	-	-	-	3.19±0.32	-	2.93±0.16	3.21±0.18	3.36±0.23	3.53±0.63	-
12 (2a4l)	-	3.61±0.21	2.84±0.13	-	-	-	-	-	3.24±0.26	3.02±0.17	3.01±0.13	-	-	3.29±0.50
13 (2exm)	2.80±0.12	3.43±0.22	-	3.09±0.21	-	-	-	-	3.00±0.16	2.99±0.18	3.22±0.21			
14 (2fvd)	2.89±0.14	3.89±0.22	2.84±0.13	-	-	3.58±0.65	-							
15 (2x1n)	-	3.16±0.18	2.83±0.12	-	-	-	-							

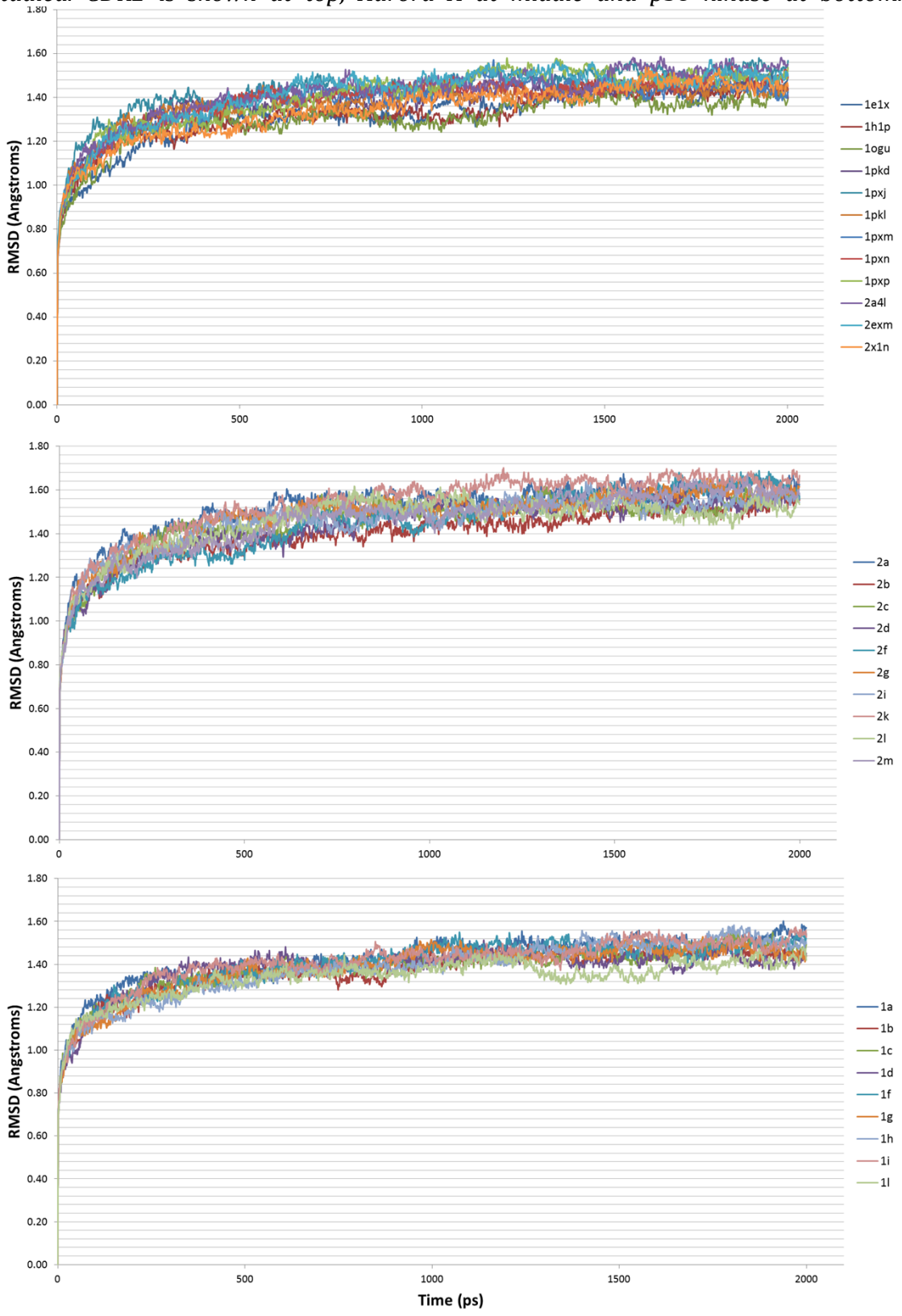
a p38 and Aurora A ligands were numbered in the same order as they appeared in the reference article, except that we use numbers instead of letters. The codes in parenthesis correspond to the ligands interacting with CDK2 and the numbering of compounds was also conserved.

Table 2SI: Specific interactions and their occurrence (expressed as %) in each protein – ligand complex along 2ns molecular dynamics trajectories.

Systems	CDK2/ligand							p38/ligand				AuroraA/ligand		
Compound[a]	Glu81=O	Leu83-N	Leu83=O	Lys33-NH_3	Asp86=OD	Asp86-N	Gln131=O	Glu71=OE*	Thr106-OH	Asp168-N	Met109-N	Ala212-N	Lys161-NH_3	Pro213
1 (1aq1+)	100%	98%	-	-	57%	-	96%	63%	-	74%	79%	98%	-	-
2 (1e1x)	91%	96%	87%	-	-	-	-	-	-	80%	81%	64%	80%	-
3 (1h1s)	100%	81%	99%	-	-	65%	-	75%	-	-	77%	70%	-	-
4 (1h1p)	100%	98%	86%	-	-	-	-	-	52%	80%	71%	73%	46%	-
5 (1ogu)	65%	88%	100%	-	88%	-	-	-	-	80%	79%	64%	72%	-
6 (1pkd+)	100%	89%	-	-	-	-	87%	-	39%	69%	82%	86%	-	-
7 (1pxj)	95%	-	-	99%	-	-	-	-	-	-	80%	70%	-	-
8 (1pxl)	-	99%	100%	94%	-	-	-	-	35%	69%	82%	62%	78%	-
9 (1pxm)	-	80%	99%	-	98%	-	-	66%	66%	82%	78%	69%	-	-
10 (1pxn)	-	99%	97%	58%	61%	-	-	57%	-	83%	74%	84%	47%	-
11 (1pxp)	-	99%	100%	96%	-	-	-	38%	-	81%	80%	69%	78%	-
12 (2a4l)	-	92%	100%	-	-	-	-	-	35%	77%	83%	-	-	56%
13 (2exm)	100%	97%	-	77%	-	-	-	-	61%	81%	70%			
14 (2fvd)	82%	58%	100%	-	-	55%	-							
15 (2x1n)	-	98%	100%	-	-	-	-							

a p38 and Aurora A ligands were numbered in the same order as they appeared in the reference article, except that we use numbers instead of letters. The codes in parenthesis correspond to the ligands interacting with CDK2 and the numbering of compounds was also conserved.

Figure 1SI. Plots of RMSD (Angstroms) values against simulation time (picoseconds). Data correspond to equilibration molecular dynamics of compounds on the series studied. CDK2 is shown at top, Aurora A at middle and p38 kinase at bottom.



Code 1SI. Example of an ISF (Interaction Specification Format) file used for the analysis of all compounds bound to CDK2. Atom numbering corresponds to crystal PDB ID 1H1S.

```
alias atom1 A:1298:N3
alias atom2 A:1298:N9
alias atom3 A:1298:N2

#hbond
distance: @0.5
4864
#H:N9
A:81:O

distance: @0.5
atom1
A:83:H
```