Supporting Information for

Absolute Free Energy of Binding Calculations for Macrophage Migration Inhibitory Factor in Complex with a Drug-like Inhibitor

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Figure S1. Atom Labelling for MIF180.

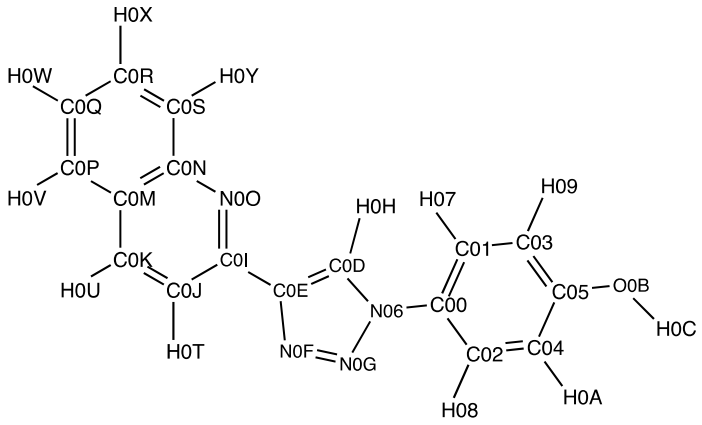


Figure S2. Histograms of the Hydrogen Bond Distances with Neutral N-terminal Proline: a) 1-r(OO); b) 2-r(NN); c) 3-r(NN); d) 4-r(NN); e) 5-r(NO).

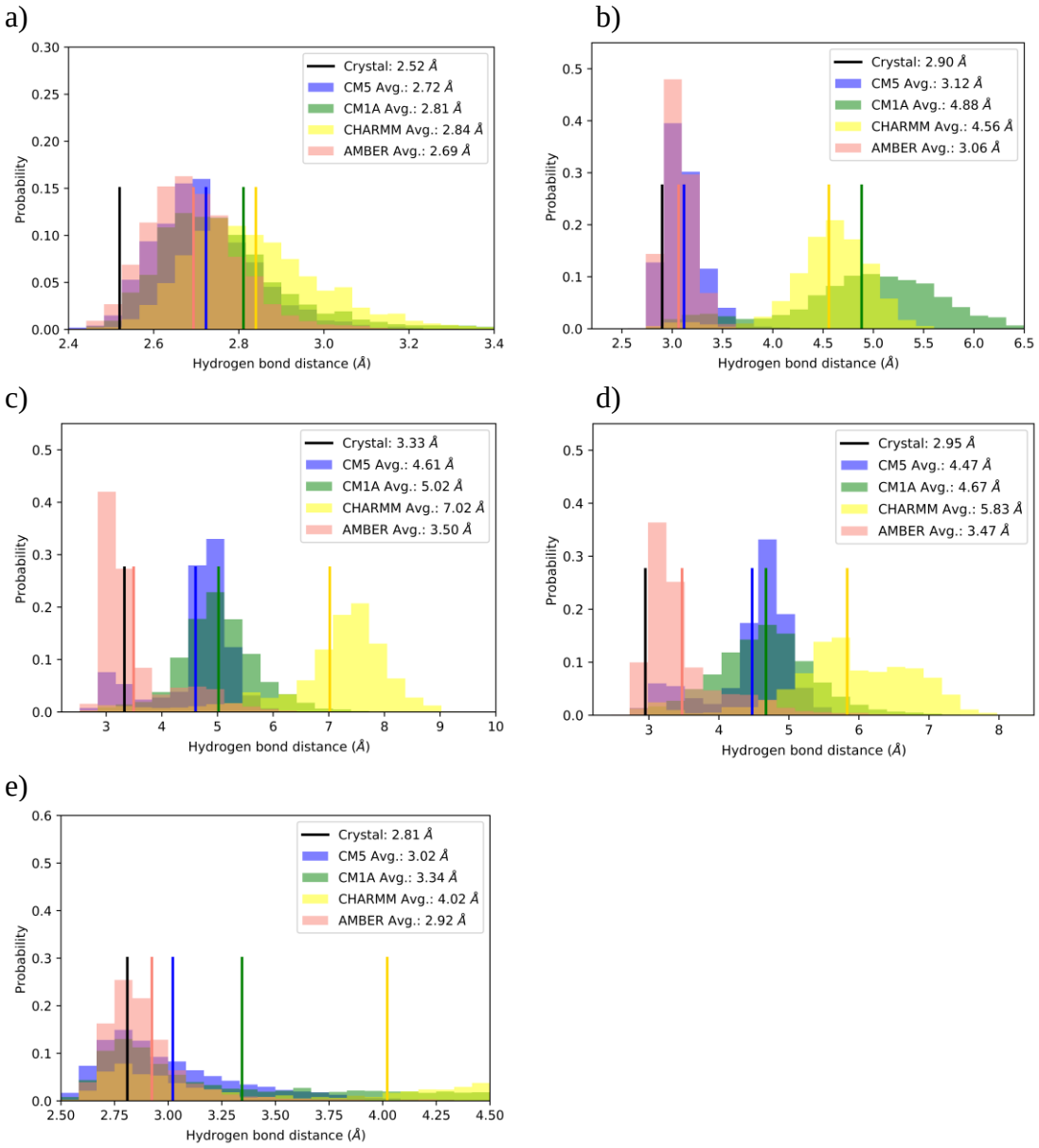


Figure S3: Histograms of the Hydrogen Bond Distances with Protonated N-terminal Proline: a) 1-r(OO); b) 2-r(NN); c) 3-r(NN); d) 4-r(NN); e) 5-r(NO).

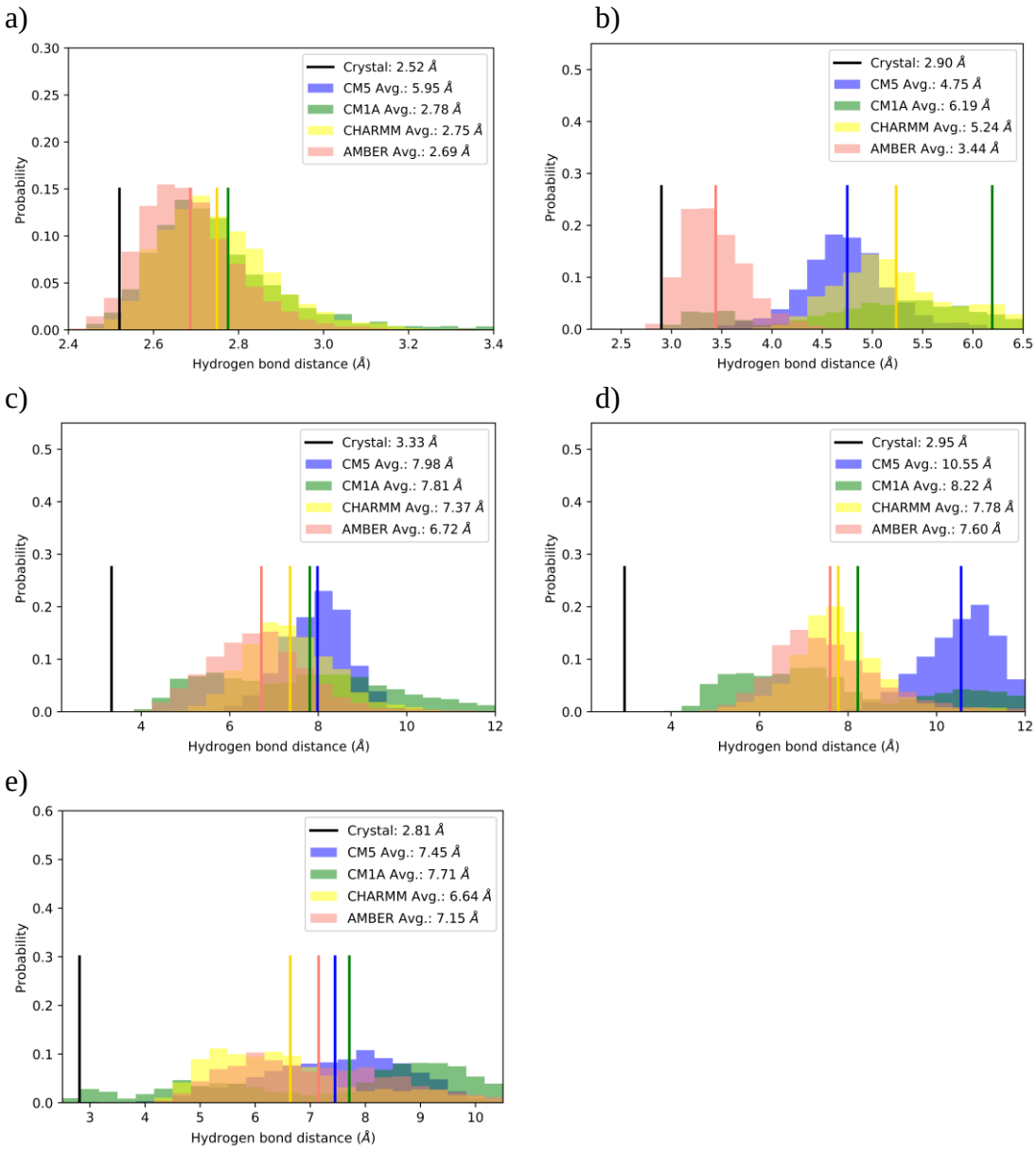


Figure S4: Bound State Free Energy Evolution for All LJ Windows (320 M/240 M).

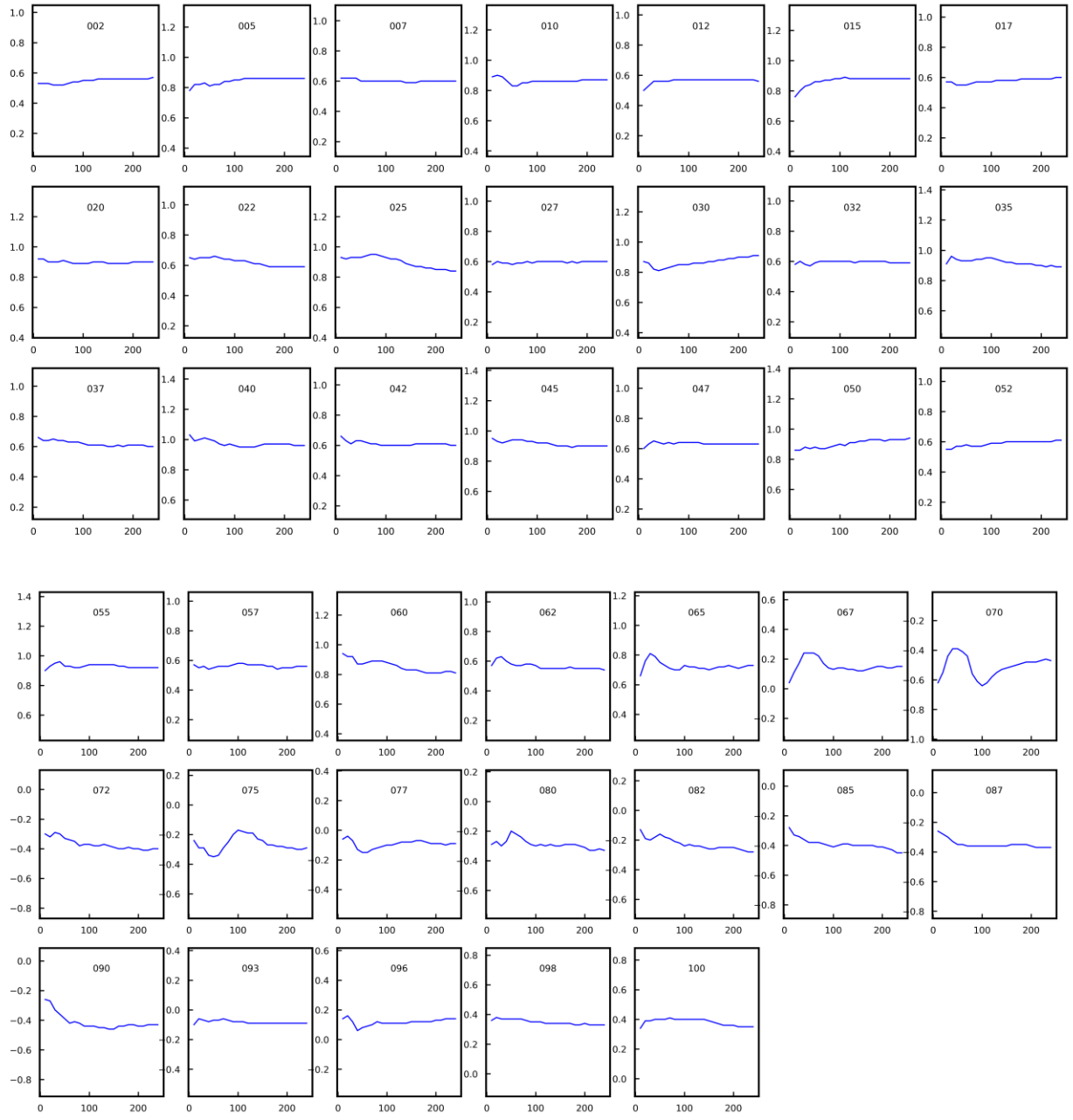
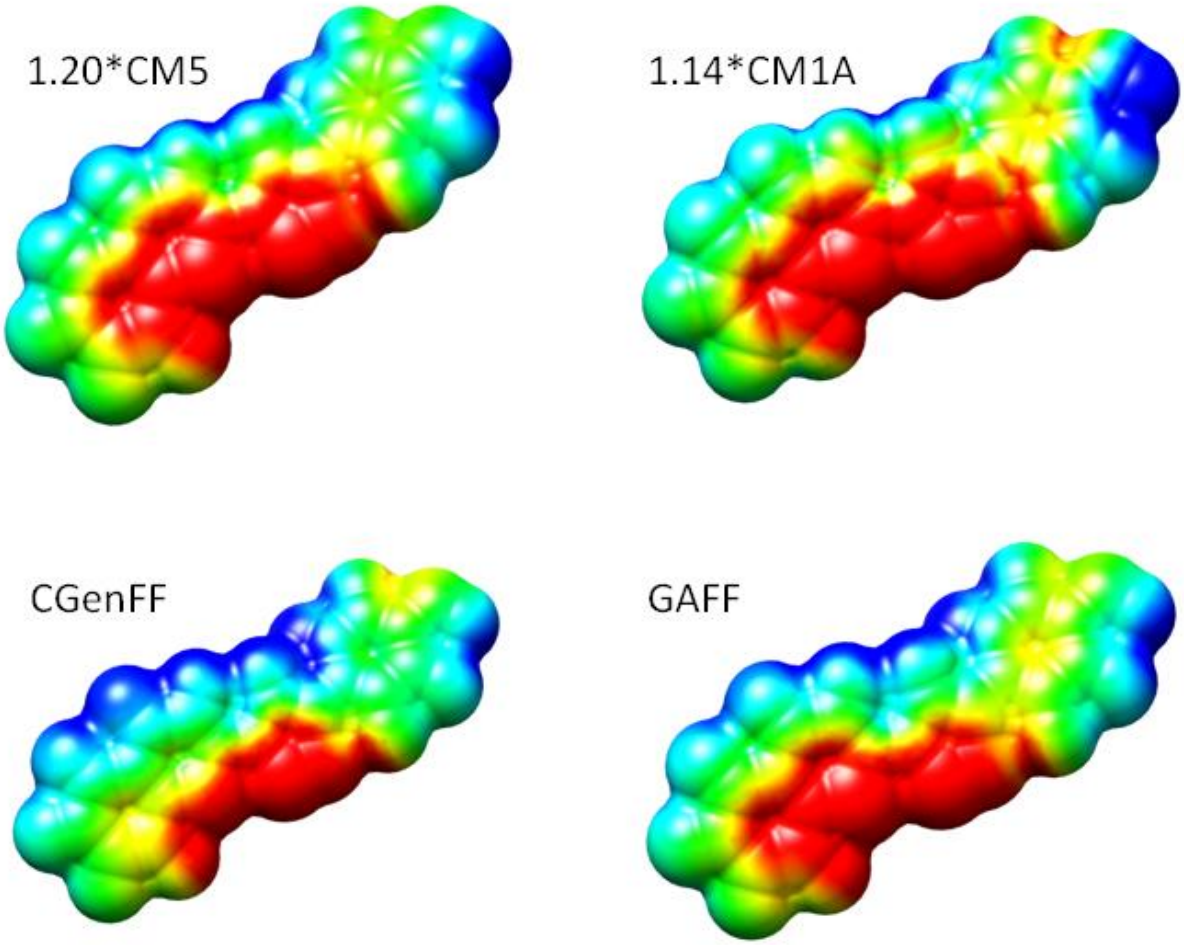


Figure S5. Electrostatic Potentials for MIF180 in The Four Force Fields used.



Tables S1. Charge Comparison with Four Small Molecule Force Fields.

Atom number	Atom Name	1.20*CM5	1.14*CM1A	CGenFF	GAFF
1	C00	0.112	0.060	0.087	-0.026
2	C01	-0.108	-0.094	-0.113	-0.090
3	C02	-0.108	-0.094	-0.113	-0.090
4	C03	-0.131	-0.204	-0.112	-0.174
5	C04	-0.131	-0.204	-0.112	-0.174
6	C05	0.109	0.156	0.108	0.129
7	N06	-0.181	-0.293	0.499	0.117
8	H07	0.139	0.173	0.115	0.154
9	H08	0.139	0.173	0.115	0.154
10	H09	0.139	0.171	0.115	0.151
11	H0A	0.139	0.171	0.115	0.151
12	O0B	-0.496	-0.504	-0.530	-0.491
13	H0C	0.439	0.439	0.420	0.424
14	C0D	0.032	-0.065	-0.443	-0.160
15	C0E	0.118	-0.106	0.095	0.185
16	N0F	-0.248	-0.113	-0.408	-0.338
17	N0G	-0.110	0.092	-0.332	-0.158
18	H0H	0.165	0.220	0.259	0.208
19	C0I	0.165	0.157	0.519	0.419
20	C0J	-0.122	-0.199	-0.119	-0.219
21	C0K	-0.087	-0.082	-0.110	-0.086
22	C0M	-0.019	-0.086	-0.004	-0.148
23	C0N	0.141	0.064	0.345	0.404
24	N0O	-0.418	-0.248	-0.625	-0.676

25	C0P	-0.117	-0.129	-0.113	-0.109
26	C0Q	-0.123	-0.139	-0.116	-0.129
27	C0R	-0.117	-0.136	-0.113	-0.123
28	C0S	-0.101	-0.115	-0.119	-0.168
29	H0T	0.130	0.160	0.115	0.165
30	H0U	0.132	0.151	0.115	0.141
31	H0V	0.122	0.145	0.115	0.135
32	H0W	0.130	0.156	0.115	0.135
33	H0X	0.133	0.159	0.115	0.135
34	H0Y	0.134	0.168	0.115	0.147
Net Charge	/	0.00	0.00	0.00	0.00

Tables S2. Average Hydrogen Bond Distances with Protonated N-terminal Proline (Å).

	Crystal	OPLS/ CM5	OPLS/ CM1A	CHARMM/ CGenFF	AMBER/ GAFF
1-r(OO)	2.52	5.95	2.78	2.75	2.69
2-r(NN)	2.90	4.75	6.19	5.24	3.44
3-r(NN)	3.33	7.98	7.81	7.37	6.72
4-r(NN)	2.95	10.55	8.22	7.78	7.60
5-r(NO)	2.81	7.45	7.71	6.64	7.15