Supporting Information

Figure 1. Comparison of ^{1}H-^{15}N TROSY-HSQC spectra from uniformly $^{15}N/^{13}C$ labeled and perdeuterated, and ^{15}N-Phe or ^{15}N-Leu specifically labeled, fully protonated M.HhaI. The spectra from ^{15}N-Phe (green) and ^{15}N-Leu (red) specifically labeled protein samples are superimposed with the spectrum from uniformly labeled protein (black). Two peaks (boxed), one each for the two amino acid specifically labeled samples, are absent from the uniformly labeled protein.

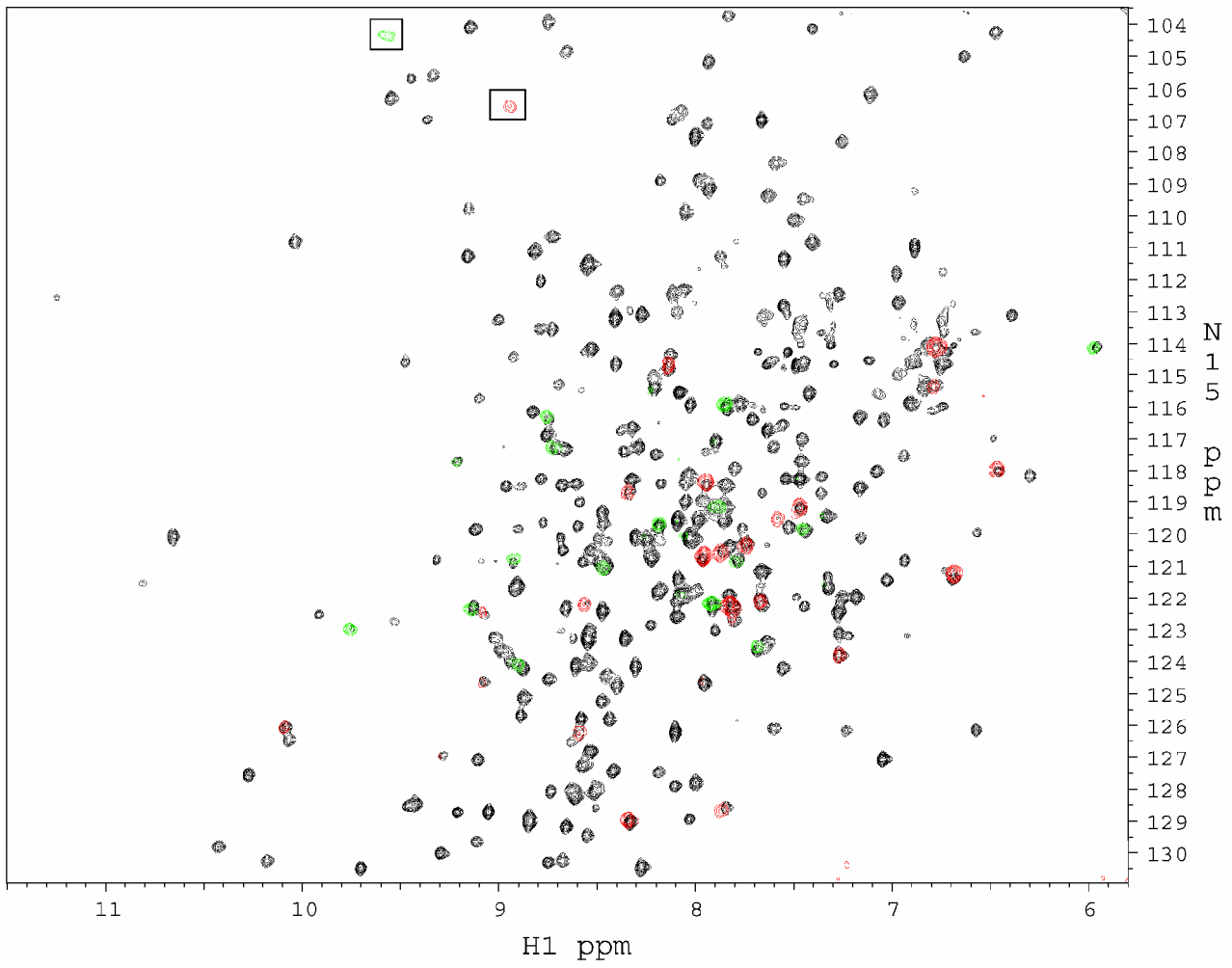

Table S.1 Measured and calculated dynamics parameters for M.HhaI.

Res	R_1	ΔR_1	R_2	ΔR_2	NOE	ΔNOE	S^2	ΔS^2	τ_e	$\Delta\tau_e$
10	0.720	0.034	25.37	1.26	0.730	0.050	0.924	0.032	78.0	179.5
11	0.576	0.026	29.26	0.69	0.860	0.050	0.894	0.028	8.8	14.2
20	0.619	0.063	26.71	2.91	0.900	0.050	0.898	0.065	55.7	289.1
22	0.833	0.063	26.71	2.92	0.680	0.050	0.918	0.032	1198.0	526.5
24	0.799	0.059	30.57	2.57	0.860	0.050	0.973	0.034	241.3	576.8
32	0.769	0.066	27.39	1.02	0.850	0.050	0.973	0.030	325.5	674.5
35	0.597	0.058	29.91	1.69	0.730	0.050	0.925	0.056	451.5	682.5
40	0.749	0.023	28.55	1.10	0.860	0.050	0.988	0.020	47.3	192.3
41	0.751	0.038	26.10	2.18	0.890	0.050	0.955	0.041	50.6	242.4
42	0.736	0.083	29.05	3.01	0.860	0.050	0.956	0.045	352.0	707.7
44	0.695	0.059	31.95	2.93	0.920	0.050	0.957	0.046	397.5	752.5
46	0.550	0.011	30.12	1.80	0.810	0.050	0.866	0.029	7.9	12.2
47	0.632	0.015	27.04	1.22	0.850	0.050	0.913	0.024	11.9	17.8
49	0.726	0.071	33.47	3.72	0.590	0.050	0.915	0.038	354.5	340.6
54	0.499	0.053	28.90	2.10	0.800	0.050	0.795	0.095	12.6	88.4
55	0.724	0.064	23.77	2.37	0.550	0.050	0.878	0.049	155.3	207.6
58	0.681	0.034	32.69	0.44	0.750	0.050	0.948	0.028	114.1	210.6
59	0.607	0.017	24.13	1.69	0.700	0.050	0.900	0.036	67.8	45.2
60	0.530	0.028	29.63	1.22	0.800	0.050	0.845	0.032	7.2	12.0
64	0.658	0.067	33.44	1.17	0.860	0.050	0.967	0.032	416.2	744.4
65	0.715	0.043	25.72	1.26	0.790	0.050	0.930	0.035	76.0	255.9
67	0.770	0.093	27.45	0.58	0.620	0.050	0.923	0.030	620.6	485.0
68	0.783	0.049	24.00	2.52	0.500	0.050	0.892	0.028	669.0	261.1
69	0.692	0.038	24.77	5.20	0.660	0.050	0.897	0.060	72.8	90.8
81	0.608	0.020	27.82	1.62	0.480	0.050	0.900	0.030	134.6	61.4
84	0.739	0.089	35.73	6.44	0.860	0.050	0.931	0.073	639.6	887.2
85	0.715	0.026	24.95	1.72	0.520	0.050	0.892	0.033	113.7	76.3
86	0.865	0.014	20.39	1.06	0.500	0.050	0.822	0.018	1053.8	178.0
87	1.052	0.050	23.72	0.69	0.420	0.050	0.767	0.024	1042.6	138.9
88	1.123	0.070	14.70	0.63	0.390	0.050	0.578	0.025	1246.1	135.6
90	1.088	0.023	18.78	0.77	0.270	0.050	0.665	0.019	982.1	91.7
91	0.998	0.071	18.40	0.53	0.450	0.050	0.724	0.028	1174.7	166.2
92	0.846	0.056	22.50	2.36	0.570	0.050	0.863	0.031	1069.1	271.6
93	0.773	0.073	26.48	4.94	0.650	0.050	0.921	0.042	764.4	579.5
99	0.793	0.098	32.43	0.98	0.370	0.050	0.870	0.034	483.1	262.2
100	0.626	0.092	42.07	5.41	0.680	0.050	0.875	0.148	273.8	435.1
102	0.575	0.086	34.73	1.59	0.600	0.050	0.891	0.052	222.2	335.2
103	0.589	0.064	38.40	5.66	0.740	0.050	0.910	0.077	425.9	710.1
124	0.720	0.064	26.27	0.00	0.510	0.050	0.908	0.028	242.9	213.5
125	0.715	0.106	29.82	6.12	0.280	0.050	0.843	0.054	335.9	246.7
126	0.684	0.022	30.73	4.27	0.860	0.050	0.971	0.039	42.4	190.9
127	0.807	0.069	27.19	2.94	0.830	0.050	0.947	0.032	1194.4	824.6
128	0.707	0.025	32.15	9.70	0.840	0.050	0.936	0.092	23.0	158.4
129	0.666	0.030	31.26	1.59	0.860	0.050	0.984	0.023	84.1	279.2
130	0.717	0.108	29.01	1.50	0.600	0.050	0.914	0.039	434.5	475.8
134	0.610	0.038	34.62	0.82	0.820	0.050	0.967	0.029	63.9	264.4
136	0.707	0.075	33.00	2.97	0.790	0.050	0.966	0.038	288.4	654.6
147	0.587	0.025	25.53	0.95	0.510	0.050	0.819	0.038	48.4	14.9
150	0.492	0.075	29.73	1.59	0.900	0.050	0.803	0.078	22.0	162.3
151	0.562	0.038	28.49	3.15	0.860	0.050	0.868	0.057	7.4	14.8
153	0.616	0.060	25.71	3.77	0.890	0.050	0.877	0.080	29.1	188.8
154	0.609	0.031	31.07	3.76	0.620	0.050	0.909	0.044	96.7	81.4
158	0.712	0.066	25.22	1.10	0.710	0.050	0.899	0.049	324.7	579.6
159	0.736	0.036	30.75	2.31	0.850	0.050	0.979	0.028	94.0	351.0
173	0.528	0.053	27.83	2.57	0.840	0.050	0.828	0.076	6.3	14.1
174	0.665	0.017	30.97	0.66	0.760	0.050	0.976	0.019	80.3	74.8

Res	R_1	ΔR_1	R_2	ΔR_2	NOE	ΔNOE	S^2	ΔS^2	τ_e	$\Delta\tau_e$
175	0.679	0.050	22.85	2.90	0.860	0.050	0.848	0.155	5.1	18.5
176	0.619	0.043	31.80	1.40	0.780	0.050	0.948	0.038	93.0	267.9
180	1.090	0.066	18.23	0.66	0.210	0.050	0.643	0.028	939.0	87.1
181	0.726	0.024	22.14	0.22	0.680	0.050	0.906	0.027	70.7	57.1
186	0.710	0.030	29.61	1.80	0.800	0.050	0.982	0.025	85.5	299.7
187	0.651	0.048	26.45	1.32	0.680	0.050	0.900	0.040	106.3	235.1
188	0.628	0.050	25.36	3.08	0.790	0.050	0.870	0.063	30.1	136.4
189	0.555	0.030	23.77	1.94	0.860	0.050	0.802	0.039	3.6	6.3
190	0.672	0.042	27.25	3.03	0.850	0.050	0.936	0.053	50.4	239.2
191	0.671	0.059	27.06	1.92	0.850	0.050	0.932	0.047	74.8	299.5
193	0.780	0.007	27.46	2.17	0.730	0.050	0.953	0.020	1051.2	539.0
194	0.633	0.021	31.63	2.14	0.770	0.050	0.955	0.030	45.1	131.5
196	0.603	0.033	29.44	1.49	0.860	0.050	0.925	0.034	11.3	24.5
199	0.661	0.033	28.29	0.58	0.800	0.050	0.946	0.025	38.6	92.1
200	0.758	0.012	27.91	1.05	0.860	0.050	0.990	0.018	28.2	86.0
202	0.639	0.015	27.61	1.71	0.610	0.050	0.900	0.031	71.8	46.4
203	0.710	0.086	27.81	1.95	0.810	0.050	0.966	0.037	411.0	757.2
206	0.654	0.054	24.03	1.74	0.780	0.050	0.860	0.050	23.8	81.0
207	0.659	0.059	27.74	1.47	0.860	0.050	0.915	0.059	301.0	667.5
211	0.704	0.037	31.54	1.75	0.580	0.050	0.931	0.027	286.3	243.8
212	0.594	0.030	24.87	1.57	0.790	0.050	0.840	0.066	11.5	20.4
215	0.682	0.117	24.72	2.72	0.340	0.050	0.839	0.051	232.1	228.4
217	0.652	0.034	21.05	0.14	0.530	0.050	0.855	0.028	60.4	35.1
219	0.754	0.083	26.95	1.76	0.570	0.050	0.918	0.031	435.8	385.4
220	0.729	0.070	24.00	0.07	0.570	0.050	0.883	0.036	176.0	249.2
221	0.684	0.018	20.67	1.08	0.210	0.050	0.765	0.040	79.4	34.1
223	0.712	0.007	27.40	0.48	0.860	0.050	0.969	0.013	24.7	34.7
226	0.651	0.028	31.47	3.60	0.900	0.050	0.973	0.031	65.3	219.9
228	0.646	0.042	26.72	1.23	0.860	0.050	0.922	0.036	11.3	23.1
229	0.591	0.072	17.60	2.97	0.280	0.050	0.779	0.071	87.1	61.9
231	0.461	0.022	27.67	3.55	0.860	0.050	0.749	0.067	2.4	3.7
232	0.527	0.049	30.42	4.40	0.790	0.050	0.833	0.101	7.7	13.4
234	0.704	0.033	21.91	2.01	0.540	0.050	0.831	0.050	53.3	28.5
235	0.706	0.043	26.96	1.64	0.700	0.050	0.938	0.029	164.7	235.6
236	0.803	0.064	29.81	3.44	0.730	0.050	0.943	0.032	975.5	726.4
246	0.657	0.071	31.67	3.70	0.730	0.050	0.912	0.085	201.4	448.0
248	0.723	0.070	33.65	0.10	0.770	0.050	0.971	0.031	320.1	665.3
250	0.820	0.038	28.97	2.09	0.670	0.050	0.935	0.022	993.0	481.6
251	0.610	0.049	30.62	1.56	0.660	0.050	0.918	0.035	113.6	195.0
253	0.758	0.067	26.20	2.12	0.860	0.050	0.955	0.041	139.8	452.5
256	0.876	0.096	20.76	1.99	0.580	0.050	0.840	0.041	1179.9	333.8
257	1.023	0.048	20.94	0.73	0.570	0.050	0.778	0.024	1440.8	260.4
259	0.442	0.034	27.69	3.77	0.570	0.050	0.847	0.049	63.1	52.1
263	0.653	0.038	30.21	3.18	0.630	0.050	0.918	0.051	188.0	256.2
264	0.698	0.069	20.16	2.65	0.660	0.050	0.851	0.059	114.5	181.4
266	0.613	0.053	27.31	1.07	0.860	0.050	0.900	0.044	34.8	196.0
267	0.564	0.028	29.24	3.50	0.700	0.050	0.856	0.048	25.9	26.9
268	0.706	0.077	27.87	1.51	0.400	0.050	0.878	0.034	291.0	225.9
269	0.586	0.068	29.55	0.81	0.860	0.050	0.903	0.059	74.3	325.6
271	0.503	0.035	36.46	1.59	0.790	0.050	0.838	0.043	7.2	12.2
272	0.607	0.058	39.66	4.31	0.480	0.050	0.870	0.050	258.3	288.7
281	0.655	0.048	28.81	1.48	0.740	0.050	0.939	0.036	131.9	295.7
283	0.631	0.040	28.97	4.06	0.860	0.050	0.930	0.055	37.9	184.4
285	0.718	0.041	29.42	2.07	0.710	0.050	0.948	0.036	116.6	271.3
287	0.699	0.024	29.69	1.40	0.880	0.050	0.985	0.023	40.0	132.0
288	0.839	0.075	26.69	2.64	0.860	0.050	0.942	0.032	1269.2	783.6
289	0.620	0.051	26.35	3.56	0.700	0.050	0.876	0.063	68.6	194.8
290	0.526	0.097	17.23	3.93	0.860	0.050	0.655	0.094	2.0	3.1
291	0.633	0.005	30.43	2.17	0.700	0.050	0.937	0.030	63.6	48.8
292	0.825	0.065	30.27	0.67	0.620	0.050	0.920	0.026	836.7	468.8

Res	R_1	ΔR_1	R_2	ΔR_2	NOE	ΔNOE	S^2	ΔS^2	τ_e	$\Delta\tau_e$
294	0.625	0.071	34.32	1.97	0.860	0.050	0.961	0.040	394.9	744.6
300	0.786	0.072	30.31	3.77	0.640	0.050	0.930	0.031	564.4	451.4
303	0.596	0.013	27.08	0.66	0.740	0.050	0.868	0.016	20.1	14.2
304	0.769	0.056	28.13	2.70	0.630	0.050	0.933	0.025	654.0	453.1
305	0.546	0.010	25.58	2.92	0.790	0.050	0.830	0.076	8.3	13.9
307	0.727	0.072	22.97	1.40	0.850	0.050	0.884	0.057	155.2	484.1
309	0.632	0.052	30.65	4.22	0.900	0.050	0.945	0.056	127.2	402.7
310	0.711	0.042	27.54	3.11	0.830	0.050	0.955	0.043	82.4	342.1
313	0.479	0.052	25.64	3.44	0.860	0.050	0.755	0.064	2.9	4.7
314	0.648	0.035	31.12	0.43	0.770	0.050	0.964	0.023	106.2	277.2
316	0.556	0.064	45.33	4.69	0.790	0.050	0.925	0.067	117.1	378.5
317	0.492	0.085	33.72	2.56	0.670	0.050	0.898	0.053	242.2	352.9
319	0.621	0.031	26.61	3.33	0.790	0.050	0.883	0.069	15.5	24.0
320	0.454	0.027	35.81	2.75	0.790	0.050	0.761	0.051	3.8	6.3
323	0.583	0.043	24.53	1.97	0.650	0.050	0.899	0.042	86.0	127.6
326	0.606	0.014	14.57	0.99	0.430	0.050	0.739	0.027	53.1	12.8

All experimental data were collected on a 600 MHz spectrometer. The measured data for each residue (Res) are listed as the longitudinal relaxation rate (R_1, sec^{-1}), transverse relaxation rate (R_2, sec^{-1}), and $\{^1H\}^{15}N$ NOE and their corresponding uncertainties from fitting, ΔR_1, ΔR_2, and ΔNOE. The data were fit with the model-free approach under the assumption of isotropic motions. The extracted parameters tabulated here are order parameters (S^2) and correlation times (τ_e, psec) for internal motions. The uncertainty in the NOE data was estimated from the spectrum noise level. The uncertainties in the S^2 and τ_e were estimated from 250 Monte Carlo simulations.