Supplementary Table I. Utility of side chain repacking in clash minimization.

PDB ID	Size[1]	R^2	Initial Clash Score[3]	SCWRL	
				Final Clash Score[3]	Total Sim Time[4]
1CTX	71	2.80	16	12.7	0.74s
1PFC	111	3.13	20	19.8	1.3s
2ABX	148	2.50	17	13.3	2.1s
1PY4	388	2.90	13	12.4	11.6s
1MCW	430	3.50	14	16.8	6.6s
1CN1	474	3.20	15	14.6	7.4s
2ZIX	529	3.50	13	13.3	19.1s
1TMF	806	3.50	22	13.9	19.24s
1R24	846	3.10	13	14	111.3s
4GPD	1332	2.80	13	13	42.6s
1JKT	552	3.50	10	10.1	20.61s
1RYX	686	3.50	10	13.8	18.42s
2P6A	816	3.40	9	9.9	20.64s
1FN4	858	2.80	10	14	23.47s
1IGY	1294	3.20	9	11.9	34.16s
2LDX	1324	2.96	10	9.8	31.88s
1BVS	1464	3.00	9	10	43.48s
3HI8	1482	3.20	11	14.2	35.28s
1GFF	606	3.00	12	10.5	23.72s
2NN6	2176	3.35	10	11.3	84.39s

[1]Number of amino acids in the protein [2]Resolution of the crystal structure in angstroms [3]Normalized clash-score x 10^2, [4]Total user time taken to complete the simulations on a single processor. d - days; h - hours; m – minutes.

Supplementary Table II. Performance of Chiron compared to CHARMM for ten additional structures.

PDB ID	Size[1]	R[2]	Initial Clash Score[3]	Chiron			CG/MD		
				Final Clash Score[3]	D[4]	Total Time[5]	Final Clash Score[3]	D[4]	Total Time[5]
1JKT	552	3.50	10	1.92	0.22	32 m	1.85	0.13	1 m
1RYX	686	3.50	10	1.99	0.29	49 m	2.00	0.19	5 m
2P6A	816	3.40	9	1.95	0.39	1 h 32 m	1.97	0.17	6 m
1FN4	858	2.80	10	1.98	0.29	1 h 5 m	Not Converged		
1IGY	1294	3.20	9	1.99	0.29	1 h 35 m	1.75	0.10	12 m
2LDX	1324	2.96	10	1.97	0.48	2 h 30 m	1.87	0.21	23 m
1BVS	1464	3.00	9	1.99	0.23	1 h 38 m	1.85	0.14	25 m
3HI8	1482	3.20	11	1.97	0.30	1 h 44 m	1.10	0.45	7 h
1GFF	606	3.00	12	1.92	0.24	20 m	Not Converged		
2NN6	2176	3.35	10	1.99	0.28	1 h 41 m	1.99	0.18	58 m

[1]Number of amino acids in the protein [2]Resolution of the crystal structure in Å [3]Normalized clash-score x 10^2, [4]Cα RMSD in Å, [5]Total user time taken to complete the simulations on a single processor. d - days; h - hours; m – minutes.

Supplementary Table III. Backbone and all-atom RMSD of minimized structures compared to the input structures.

PDB ID	Size[1]	R[2]	Chiron			CG/MD			Rosetta		
			CA[3]	BB[4]	AA[5]	CA[3]	BB[4]	AA[5]	CA[3]	BB[4]	AA[5]
1CTX	71	2.80	0.48	0.50	1.04	0.41	0.45	0.80	1.35	1.32	1.88
1PFC	111	3.13	0.58	0.64	0.94	0.28	0.34	0.45	1.16	1.15	1.91
2ABX	148	2.50	0.49	0.58	1.03	0.50	0.65	1.06	2.79	2.80	3.13
1PY4	388	2.90	0.28	0.32	0.48	0.17	0.22	0.25	1.54	1.54	1.91
1MCW	430	3.50	0.51	0.59	0.84	0.29	0.35	0.42	1.47	1.48	1.78
1CN1	474	3.20	0.34	0.39	0.53	0.29	0.38	0.52	0.94	0.94	1.39
2ZIX	529	3.50	0.33	0.40	0.54	0.23	0.32	0.37	1.97	1.99	2.35
1TMF	806	3.50	0.34	0.40	0.55	Not Converged			2.35	2.36	2.65
1R24	846	3.10	0.28	0.34	0.43	0.18	0.23	0.25	1.19	1.20	1.51
4GPD	1332	2.80	0.31	0.36	0.49	Not Converged			1.20	1.20	1.57
1JKT	552	3.50	0.22	0.26	0.34	0.13	0.19	0.21			
1RYX	686	3.50	0.29	0.35	0.46	0.19	0.29	0.33			
2P6A	816	3.40	0.39	0.44	0.76	0.17	0.24	0.28			
1FN4	858	2.80	0.29	0.34	0.44	Not Converged					
1IGY	1294	3.20	0.29	0.33	0.44	0.10	0.15	0.16			
2LDX	1324	2.96	0.48	0.53	0.76	0.21	0.27	0.32			
1BVS	1464	3.00	0.23	0.28	0.35	0.14	0.22	0.22			
3HI8	1482	3.20	0.30	0.35	0.51	0.45	0.50	0.65			
1GFF	606	3.00	0.24	0.28	0.37	Not Converged					
2NN6	2176	3.35	0.28	0.32	0.45	0.18	0.23	0.26			

[1]Number of amino acids in the protein [2]Resolution of the crystal structure in Å, [3]Root Mean Squared Deviation (RMSD, in Å) of the minimized structure from the initial structure considering only the Cα atoms, [4]RMSD (in Å) considering only the backbone atoms (N, Cα, C, O) and [5]RMSD (in Å) considering all heavy atoms in the structures.

Supplementary Table IV. Number of unsatisfied hydrogen bonds before and after minimization for ten additional structures.

PDB ID	Size[1]	No. of Unsatisfied Hydrogen Bond Partners								
		Initial Structure			Chiron			CG/MD		
		BB[2]	SC[3]	Total[4]	BB[2]	SC[3]	Total[4]	BB[2]	SC[3]	Total[4]
1JKT	552	53	11	64	33	12	45	25	12	37
1RYX	686	118	23	141	85	20	105	60	24	84
2P6A	816	34	13	47	23	16	39	31	12	43
1FN4	858	69	38	107	62	39	101	Not Converged		
1IGY	1294	125	52	177	82	56	138	77	51	128
2LDX	1324	182	53	235	179	50	229	104	28	132
1BVS	1464	88	10	98	53	10	63	28	12	40
3HI8	1482	128	7	135	86	11	97	67	12	79
1GFF	606	44	22	66	37	16	53	Not Converged		
2NN6	2176	217	61	278	183	70	253	160	64	224

[1]Number of amino acids in the protein, Polar atoms belonging to the backbone[2] or side-chains[3] that do not form hydrogen bonds and belong to residues that are buried [4]total number of unsatisfied hydrogen bonding partners in the protein

Supplementary Table V. Side-chain geometry of input and minimized structures.

PDB ID	Size[1]	R[2]	Initial Z-score[3]	Chiron[4]	CG/MD[5]	Rosetta[6]
1CTX	71	2.80	2.79±1.54	1.79±1.27	1.34±0.92	0.46±0.62
1PFC	111	3.13	2.18±1.34	2.22±1.61	1.58±0.98	0.36±0.47
2ABX	148	2.50	2.33±1.35	1.83±1.48	1.37±1.12	0.58±0.67
1PY4	388	2.90	1.87±1.33	1.85±1.30	1.45±1.15	0.30±0.29
1MCW	430	3.50	2.31±1.48	2.19±1.38	1.49±1.11	0.34±0.37
1CN1	474	3.20	2.39±1.54	2.10±1.44	1.45±1.16	0.33±0.31
2ZIX	529	3.50	1.93±1.31	1.99±1.29	1.46±1.00	0.30±0.30
1TMF	806	3.50	2.13±1.33	1.96±1.36	Not Converged	0.30±0.31
1R24	846	3.10	1.84±1.31	1.88±1.40	1.52±1.18	0.33±0.36
4GPD	1332	2.80	2.02±1.39	2.00±1.40	Not Converged	0.30±0.34
1JKT	552	3.50	1.50±0.99	1.64±1.11	1.31±0.91	
1RYX	686	3.50	1.50±1.23	1.84±1.33	1.26±1.07	
2P6A	816	3.40	1.58±1.16	1.81±1.35	1.28±1.00	
1FN4	858	2.80	2.08±1.52	2.01±1.43	Not Converged	
1IGY	1294	3.20	1.29±0.97	1.76±1.39	1.26±0.98	
2LDX	1324	2.96	1.83±1.18	2.14±1.43	1.46±1.09	
1BVS	1464	3.00	1.99±1.43	1.88±1.36	1.56±1.27	
3HI8	1482	3.20	1.67±1.09	1.94±1.25	1.45±1.01	
1GFF	606	3.00	1.76±1.37	1.71±1.21	Not Converged	
2NN6	2176	3.35	1.42±1.06	1.80±1.26	1.33±1.03	

[1]Number of amino acids in the protein [2]Resolution of the crystal structure in Å, [3]Mean and standard deviation of Z-scores of all the side-chain χ angles of the initial structure, Mean and standard deviation of Z-scores of all the side-chain χ angles obtained after Chiron minimization[4], CG/MD[5] and Rosetta[6]

Supplementary Table VI. Performance of Chiron compared to Rosetta and CHARMM in minimizing homology models less than 250 residues long.

Uniprot ID	Size	Initial Clash Score[1]	Chiron			MM			Rosetta		
			Final Clash Score[1]	D^2	Total Time[3]	Final Clash Score[1]	D^2	Total Time[3]	Final Clash Score[1]	D^2	Total Time[3]
A0LLF4	154	15.4	1.60	0.54	6 m	1.23	0.70	5 m	1.53	1.45	3 h 34 m
A2BNX7	173	14.3	1.80	0.60	8 m	1.09	0.78	7 m	1.46	1.05	6 h 32 m
A3Q267	139	10.4	1.98	0.25	3 m	1.87	0.28	7 m	1.50	1.50	3 h 6 m
A5UF43	241	12.2	1.95	0.50	12 m	1.98	0.33	1 m	1.50	0.74	11 h 14 m
A6L8G0	186	10.2	1.92	0.33	4 m	Not Converged			1.46	1.34	5 h 45 m
B5XM21	183	10.8	1.82	0.49	8 m	1.96	0.36	1 m	1.62	1.76	7 h 42 m
P04521	224	13.9	1.94	0.46	10 m	1.94	0.30	1 m	1.52	2.19	7 h 35 m
P49048	235	18.7	1.84	0.60	12 m	Not Converged			1.72	1.51	10 h 14 m
P57358	217	13.2	1.76	0.57	10 m	1.90	0.45	11 m	1.81	1.57	8 h 22 m
Q03EE3	127	13.7	1.85	0.51	6 m	Not Converged			1.98	1.43	3 h 1 m
Q057J1	81	10.5	1.87	0.44	3 m	1.75	0.35	1 m	1.95	2.35	2 h 2 m
Q13823	57	13.8	1.89	0.58	2 m	1.70	0.34	1 m	1.56	1.28	49 m
Q1CV70	134	12.5	1.89	0.40	6 m	1.98	0.43	4 m	1.73	1.70	3 h 37 m
Q46CW8	236	10.7	1.97	0.25	8 m	1.94	0.22	1 m	1.49	1.01	6 h 54 m
Q5F479	158	10.8	1.90	0.50	8 m	1.37	0.71	5 m	1.95	1.42	3 h 59 m
Q5GT42	169	11.4	1.98	0.32	5 m	0.89	0.63	6 m	1.89	2.61	4 h 59 m
Q6FS76	189	13.5	1.97	0.58	11 m	1.15	0.71	8 m	1.73	1.79	6 h 3 m
Q6L2N4	232	11.7	1.97	0.30	6 m	1.93	0.34	1 m	1.63	1.37	10 h
Q7DJ53	127	13.3	1.78	0.49	7 m	0.58	0.63	3 m	1.27	1.07	3 h 41 m
Q7VA23	147	18.2	1.95	0.51	5 m	1.31	0.78	5 m	1.57	1.85	4 h 26 m
Q7Y175	85	10.1	1.99	0.27	1 m	1.93	0.28	1 m	1.20	1.05	1 h 42 m
Q8DQV2	98	10	1.92	0.56	3 m	1.98	0.33	1 m	1.37	0.83	2 h 20 m
Q8R1F1	134	10.6	1.84	0.50	6 m	1.59	0.61	4 m	1.68	1.36	2 h 57 m
Q8XJW2	118	16.4	1.90	0.34	2 m	1.96	0.38	1 m	1.70	1.23	2 h 44 m
Q9HLB6	211	12.3	1.68	0.54	9 m	1.93	0.41	9 m	1.87	1.00	6 h 45 m

[1]Normalized clash-score x 10^2, [2]Cα RMSD in Å, [3]Total user time taken to complete the simulations on a single processor. d - days; h - hours; m - minutes

Supplementary Table VII. Performance of Chiron compared to CHARMM in minimizing homology models larger than 250 residues.

Unitprot ID	Size	Initial Clash Score[1]	Chiron			MM		
			Final Clash Score[1]	D[2]	Total Time[3]	Final Clash Score[1]	D[2]	Total Time[3]
A1RNX8	323	16.5	1.98	0.46	16 m	Not Converged		
A3PJ80	409	15.9	1.75	0.55	21 m	1.99	0.43	33 m
A6LEJ3	687	14.7	1.88	0.44	41 m	Not Converged		
A9WVT5	369	17.2	1.98	0.48	19 m	Not Converged		
B0S0W3	415	12.4	1.96	0.53	22 m	Not Converged		
B4SKW0	708	17.8	1.99	0.49	45 m	1.99	0.38	7 m
B5E369	293	15.2	1.83	0.54	13 m	1.98	0.41	1 m
O64240	679	18.1	1.94	0.59	48 m	Not Converged		
O87627	428	14.3	1.95	0.48	24 m	Not Converged		
O94524	261	17.1	1.99	0.54	13 m	1.03	0.61	21 m
P08482	428	19.4	1.78	0.53	25 m	Not Converged		
P61194	264	13.1	1.93	0.51	16 m	1.23	0.67	14 m
P62222	354	13.3	1.92	0.32	14 m	1.96	0.33	1 m
P68580	537	12.1	1.99	0.29	34 m	Not Converged		
P97377	346	13.4	1.85	0.51	21 m	Not Converged		
Q0T5L2	417	13.9	1.97	0.53	22 m	1.99	0.41	1 m
Q2J771	320	17.8	1.98	0.54	15 m	1.32	0.68	23 m
Q47JA6	694	13.6	1.99	0.46	41 m	Not Converged		
Q4G073	390	12.4	1.9	0.51	20 m	1.87	0.33	1 m
Q54SV8	605	13.1	1.97	0.41	35 m	1.99	0.36	4 m
Q65GN4	343	26.6	1.99	0.57	18 m	Not Converged		
Q75W84	341	18.7	1.84	0.54	18 m	Not Converged		
Q92396	401	14.3	1.84	0.56	23 m	Not Converged		
Q9A3K4	686	15.8	1.99	0.44	43 m	Not Converged		
Q9S449	415	15.6	1.86	0.55	25 m	Not Converged		

[1]Normalized clash-score x 10^2, [2]Cα RMSD in Å, [3]Total user time taken to complete the simulations on a single processor. d - days; h - hours; m - minutes

Supplementary Table VIII. Performance of Chiron compared to Rosetta and CHARMM for CASP8 predictions

CASP Prediction[1]	Size[2]	D_{ori}[3]	PDB ID[4]	R[5]	Initial Clash Score[6]	Chiron		Rosetta		CG/MD	
						Final Clash Score[6]	D[7]	Final Clash Score[6]	D[7]	Final Clash Score[6]	D[7]
TR432TS083_2	130	1.2	3DAI	1.95	4.3	1.99	1.3	0.70	1.4	1.68	1.3
TR432TS083_3	130	1.6	3DAI	1.95	4.7	1.99	1.5	0.90	1.6	1.99	1.6
TR432TS208_1	130	2.4	3DAI	1.95	13.9	1.91	2.5	1.10	2.4	1.99	2.5
TR435TS208_1	137	1.2	3DB5	2.15	16.5	1.87	1.2	1.00	1.4	1.97	1.2
TR453TS208_2	87	1.7	3DED	2.14	13.2	1.88	1.7	0.70	1.9	1.70	1.7

[1]CASP8 Prediction, [2]Number of amino acids in the predicted structure, [3]Cα RMSD in Å of the prediction to the native state, [4]Native state PDB ID, [5]Resolution of the native state structure, [6]Normalized clash-score x 10^2, [7]Cα RMSD in Å of the minimized structure to the native state

Supplementary Table IX. Number of unsatisfied hydrogen bonds before and after minimization for CASP8 predictions.

	Crystal Structure			Prediction			Chiron			Rosetta			CG/MD		
CASP Prediction[1]	BB[2]	SC[3]	TL[4]	BB[2]	SC[3]	TL[4]	BB[2]	SC[3]	TL[4]	BB[2]	SC[3]	TL[4]	BB[2]	SC[3]	TL[4]
TR432TS083_2	1	1	2	2	2	4	0	2	2	1	2	3	1	2	3
TR432TS083_3	1	1	2	2	2	4	0	2	2	0	3	3	2	2	4
TR432TS208_1	1	1	2	2	3	5	3	5	8	1	2	3	2	5	7
TR435TS208_1	5	1	6	2	2	4	7	1	8	1	2	3	5	2	7
TR453TS208_2	2	1	2	2	0	2	2	0	2	3	0	3	1	0	1

[1]CASP8 prediction. [2]Number of unsatisfied backbone-backbone hydrogen bonds. [3]Number of unsatisfied sidechain-sidechain hydrogen bonds. [4]Total number of unsatisfied hydrogen bonds