D-Retro Inverso (DRI) Amylin and the Stability of Amylin Fibrils

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1 Supplementary Tables

Supplementary Table 1: Twist angle for L-amylin and DRI-amylin.

	β1–Pr1 (°)		β1–Pr2 (°)	
	L-amylin	DRI-amylin	L-amylin	DRI-amylin
Run-1	-12.8 ± 2.9	10.7 ± 2.5	-5.0 ± 3.8	15.5 ± 2.4
Run-2	-23.7 ± 5.4	9.3 ± 2.7	-16.8 ± 2.9	12.5 ± 3.4
Run-3	-16.1 ± 2.6	15.7 ± 2.8	-15.9 ± 2.9	13.1 ± 2.6
Avg.	-17.5 (6.0)	11.9 (3.8)	-12.6 (6.3)	13.7 (3.1)
	β2–Pr1 (°)		β2–Pr2 (°)	
	L-amylin	DRI-amylin	L-amylin	DRI-amylin
Run-1	-3.9 ± 1.9	7.7 ± 2.0	-3.2 ± 1.9	6.4 ± 2.2
Run-2	-2.7 ± 2.1	4.4 ± 2.0	-3.2 ± 2.2	4.1 ± 1.9
Run-3	-2.2 ± 2.4	9.5 ± 2.0	-4.5 ± 3.5	13.4 ± 2.5
Avg.	-2.9 (2.3)	7.2 (2.9)	-3.6 (2.7)	8.0 (4.5)

Supplementary Table 2: Face to face contact distances of CC–interface double layers of L-amylin and DRI-amylin.

	L-amylin			DRI-amylin		
	Pr1-Lr2/Pr2-Lr2	Pr1-Lr3/Pr2-Lr3	Pr1-Lr4/Pr2-Lr4	Pr1-Lr2/Pr2-Lr2	Pr1-Lr3/Pr2-Lr3	Pr1-Lr4/Pr2-Lr4
L27–G33	7.5 (0.3)	7.7 (0.3)	7.7 (0.4)	8.8 (1.9)	8.2 (1.2)	8.0 (0.6)
S29–N31	6.5 (0.4)	6.8 (0.3)	7.2 (0.3)	8.3 (1.7)	7.4 (0.9)	7.0 (0.5)
N31–S29	6.6 (0.4)	6.9 (0.3)	7.4 (0.3)	8.2 (1.3)	7.4 (0.7)	6.8 (0.3)
G33–L27	7.9 (0.5)	8.0 (0.6)	8.3 (0.7)	8.9 (0.9)	8.4 (0.6)	8.4 (0.7)

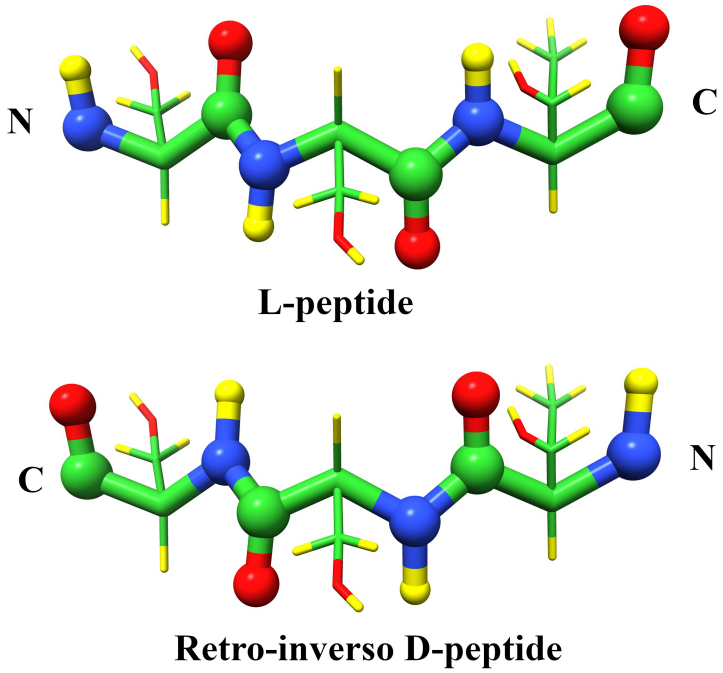
Values are shown after excluding the first and the last layers from each of the protofibril.

Supplementary Table 3: Structural changes in L-amylin (L), DRI-amylin (DRI) and Hybrid Amylin models in terms of average root-mean-square deviation (Å), average Radius of Gyration (Å) and average solvent-accessible-surface-area (Å^2).

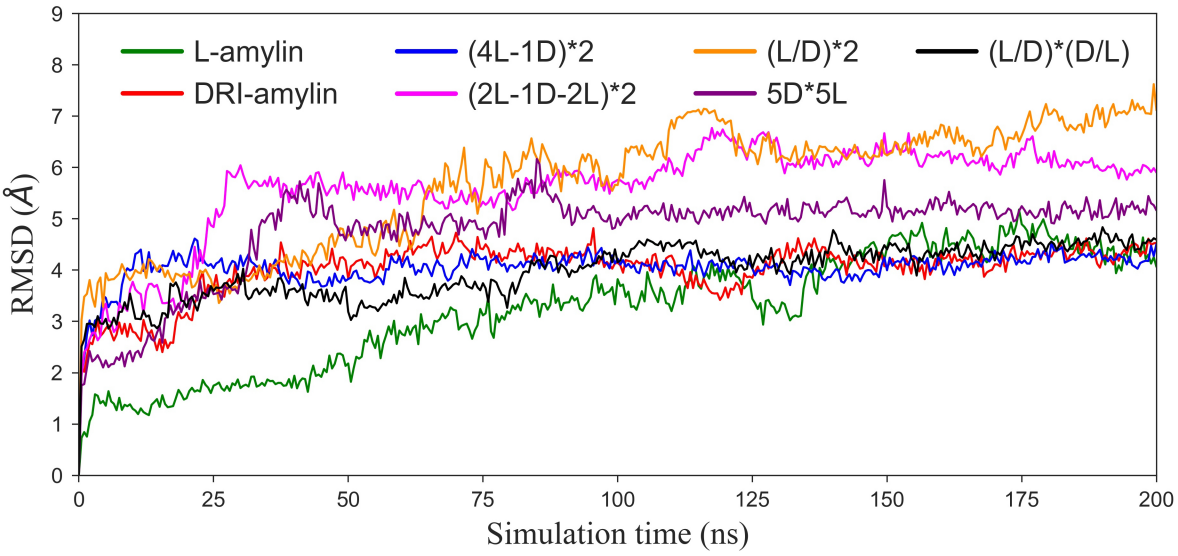
		L	DRI	(4L-1D)*2	(2L-1D-2L)*2	(L/D)*2	5D*5L	(L/D)*(D/L)
RMSD	Run-1	2.2 ± 0.1	3.5 ± 0.2	4.1 ± 0.2	4.2 ± 0.3	6.6 ± 0.3	3.3 ± 0.1	4.4 ± 0.2
	Run-2	4.2 ± 0.5	3.3 ± 0.2	3.8 ± 0.2	6.2 ± 0.2	4.1 ± 0.2	5.2 ± 0.1	4.0 ± 0.5
	Run-3	2.6 ± 0.3	4.2 ± 0.2	3.1 ± 0.2	4.7 ± 0.2	4.7 ± 0.3	2.8 ± 0.4	4.4 ± 0.2
	Avg.	3.0 (0.9)	3.7 (0.4)	3.7 (0.5)	5.0 (0.9)	5.1 (1.1)	3.8 (1.1)	4.3 (0.4)
Rg	Run-1	22.0 ± 0.2	22.4 ± 0.1	23.2 ± 0.2	22.2 ± 0.2	22.0 ± 0.3	22.4 ± 0.1	22.3 ± 0.3
	Run-2	22.8 ± 0.3	22.0 ± 0.1	22.4 ± 0.2	21.8 ± 0.2	22.4 ± 0.3	22.8 ± 0.2	21.6 ± 0.2
	Run-3	22.3 ± 0.2	22.3 ± 0.2	22.6 ± 0.1	22.9 ± 0.2	21.4± 0.4	22.8 ± 0.1	22.3 ± 0.2
	Avg.	22.4 (0.4)	22.2 (0.2)	22.7 (0.4)	22.3 (0.5)	21.9 (0.5)	22.7 (0.2)	22.1 (0.4)
SASA	Run-1	16469 ± 347	18180 ± 520	18389 ± 236	17594 ± 503	20285 ± 613	17176 ± 353	19158 ± 604
	Run-2	18283 ± 515	17257 ± 383	17551 ± 382	18197 ± 477	19019 ± 538	18263 ± 373	17410 ± 595
	Run-3	17413 ± 407	17724 ± 437	17132 ± 410	18110 ± 404	18213 ± 797	16844 ± 313	18544 ± 590
	Avg.	17388 (856)	17720 (587)	17691 (629)	17967 (534)	19172 (1077)	17428 (699)	18371 (938)

RMSD values are with respect to the start configuration and calculated over the last 80 *ns*. Only backbone atoms are considered, and the first seven residues of the flexible N-terminus not taken into account.

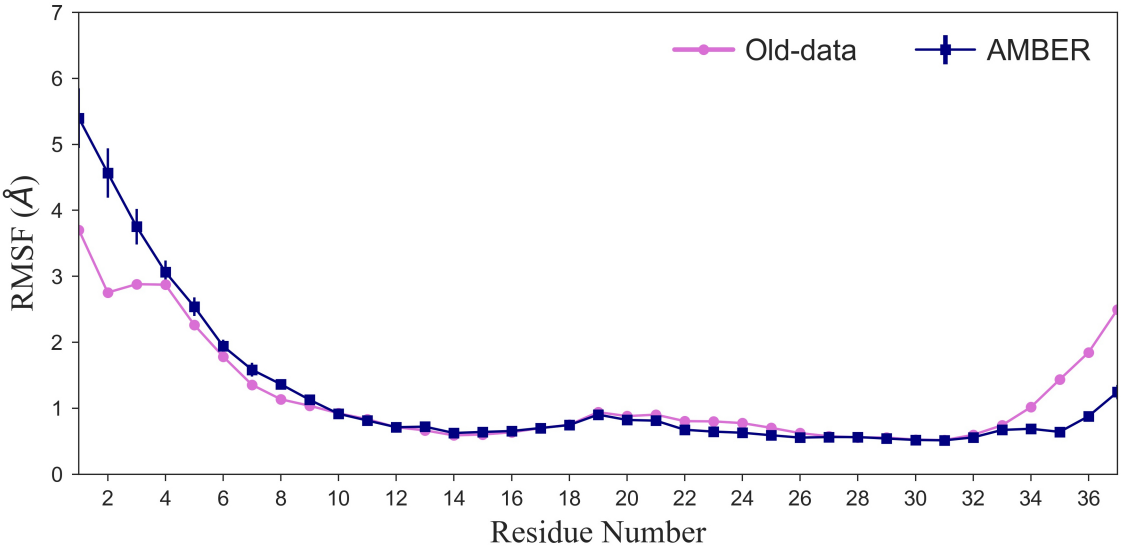
2 Supplementary Figures



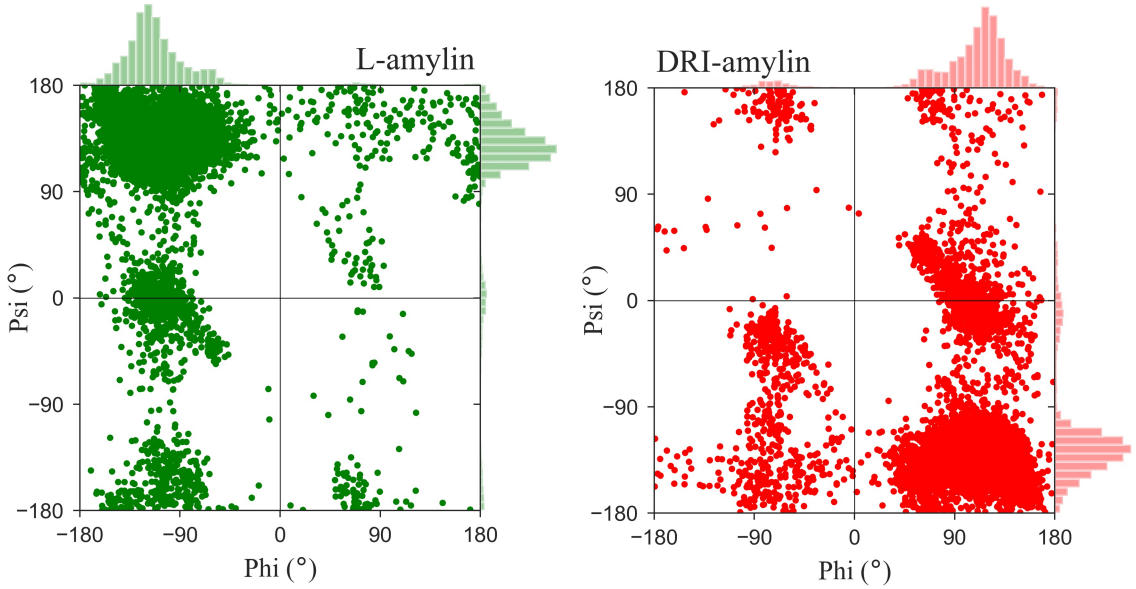
Supplementary Figure 1: Backbone switching to convert L–peptide into its retro-inverso DRI form made of D–amino acids. The backbone atoms are shown as spheres using the color code: N-blue, HN-yellow, C-green and O-red.



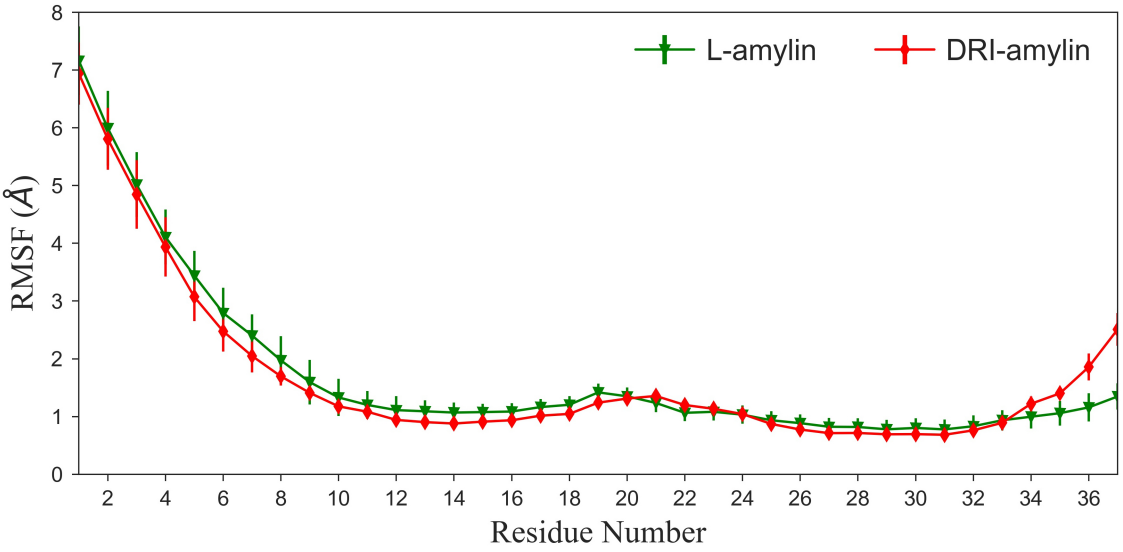
Supplementary Figure 2: Time evolution of root-mean-square deviation (RMSD) of L-amylin, DRI-amylin and L & DRI mixtures. RMSD values are calculated with respect to the starting configuration considering only backbone atoms. Due to higher fluctuation of first 7 residues, they were ignored while calculation of RMSD. Time evolution of RMSD is only shown for the trajectories with the highest fluctuations for the various amylin assemblies.



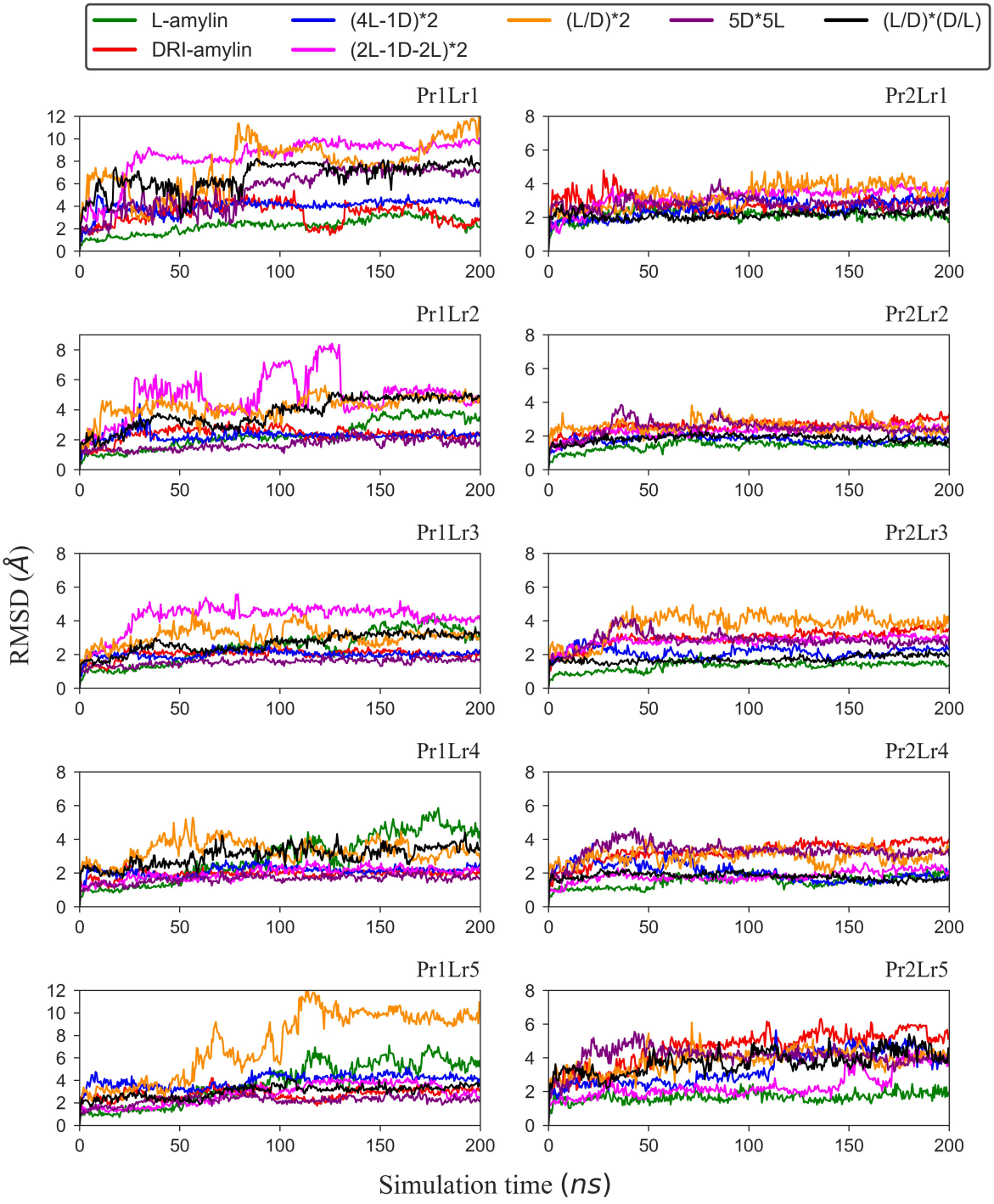
Supplementary Figure 3: Comparison of Root-mean-square fluctuation (RMSF) of the Cα atoms for AMBER force-field with Bernhardt *et. al* (2013). Values are averaged over all monomers and the three trajectories.



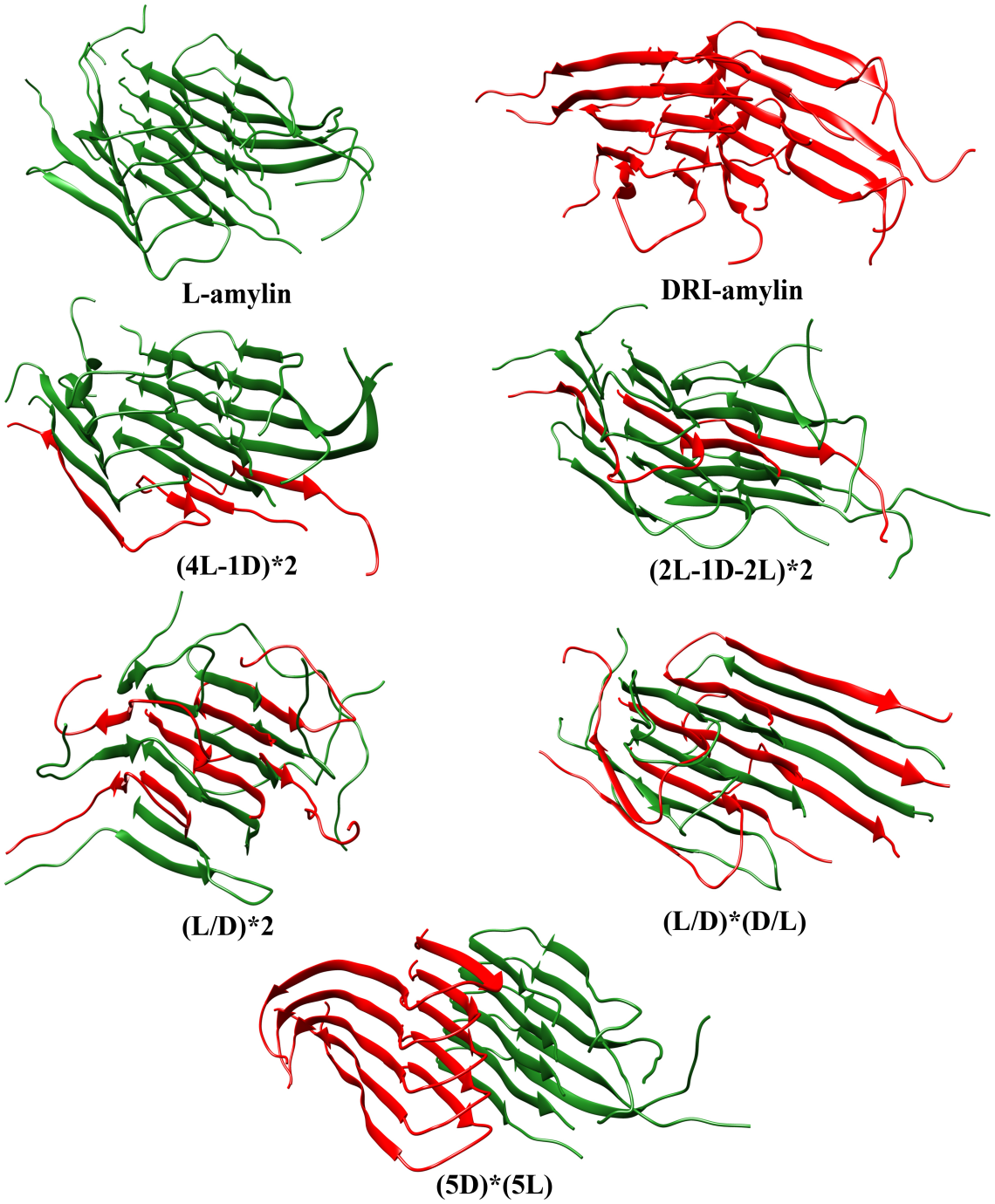
Supplementary Figure 4: Ramachandran plot for L-amylin and DRI-amylin.



Supplementary Figure 5: Root-mean-square fluctuation (RMSF) of the Cα atoms for L-amylin and DRI-amylin. Values are averaged over all monomers and the three trajectories.



Supplementary Figure 6: Time evolution of root-mean-square deviation (RMSD) of individual monomers of L-amylin, DRI-amylin and L & DRI mixtures. RMSD values are calculated with respect to the starting configuration considering only backbone atoms. Due to higher fluctuation of first 7 residues, they were ignored while calculation of RMSD. Time evolution of RMSD is only shown for the trajectories with the highest fluctuations for the various amylin assemblies.



Supplementary Figure 7: Representative conformations of L-amylin, DRI-amylin and L & DRI mixtures after 200 ns simulation.