Stable Polyglutamine Dimers Can Contain β-Hairpins with Interdigitated Side Chains—But Not α-Helices, β-Nanotubes, β-Pseudohelices, or Steric Zippers

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To assess when a given dimer replica lost its structure, we inspected all the 180 trajectories visually and calculated the center of mass distance (COMD) between the two monomers and the root mean squared deviation (RMSD) of all the backbone atoms as a function of time.

The β-sheet dimers were practically unaffected by a 100 ns simulation (Fig. S1). Similar behavior was observed for all the β-hairpin-containing dimers, as shown by the unchanging COMDs (Fig. S2) and small RMSDs (Fig. S3).

We found that an RMSD-limit of 0.25 nm described the disintegration of the structure well for all but the α-helical structures (Fig. S3). The α-helical monomers were able to roll on one another, which increased the RMSD, but did not qualitatively change the structure of the dimer, hence an RMSD-limit of 1.0 nm was found to be more appropriate; this was supplemented by a COMD-limit of 2.0 nm to pinpoint the events in which the two helices separated (Fig. S4). In addition to the α-helix dimers, the separation of peptides was only observed once, in a CHARMM27 replica of the β-nanotube dimer (Fig. S5).

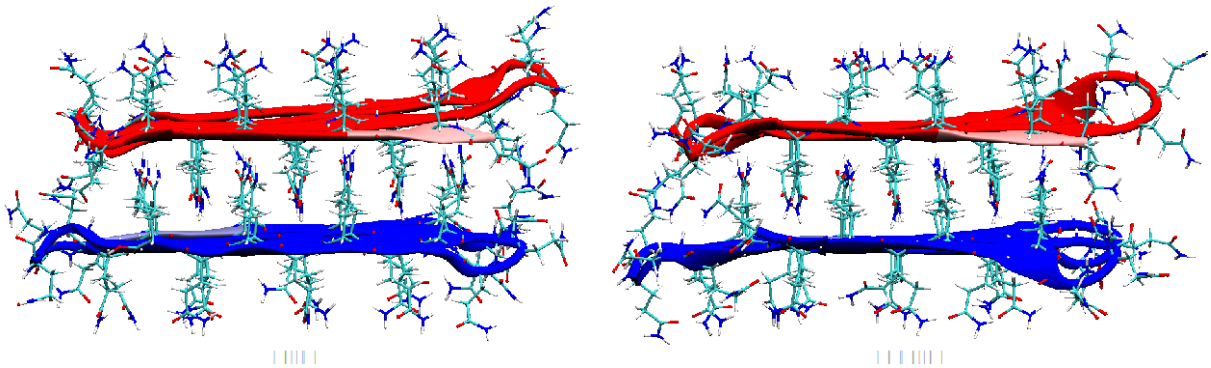

FIG. S1: In the β-sheet dimer the side chains of the monomers interdigitated. The resulting structure was thus stabilized by intra-peptide backbone–backbone hydrogen bonds in one direction and inter-peptide side chain–side chain interdigitation in the other. The same motif occurs in the β-sheetstack conformer. The structure was very stable, experiencing practically no changes in a 100 ns simulation.

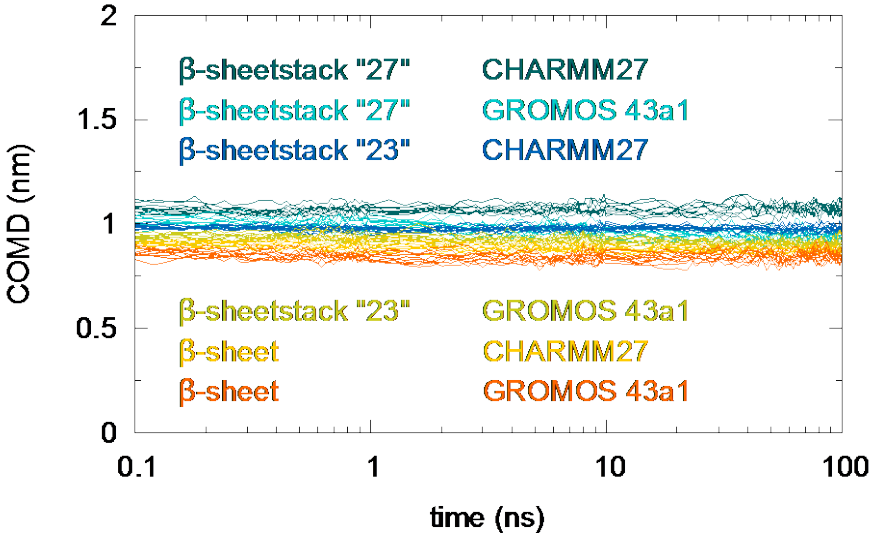

FIG. S2: The peptide–peptide center of mass distance (COMD) as a function of simulation time in the 60 simulations of β-hairpin-containing dimers. The numbers “23” and “27” refer to the two orientations of monomers for the β-sheetstack dimer, see Fig. 2.

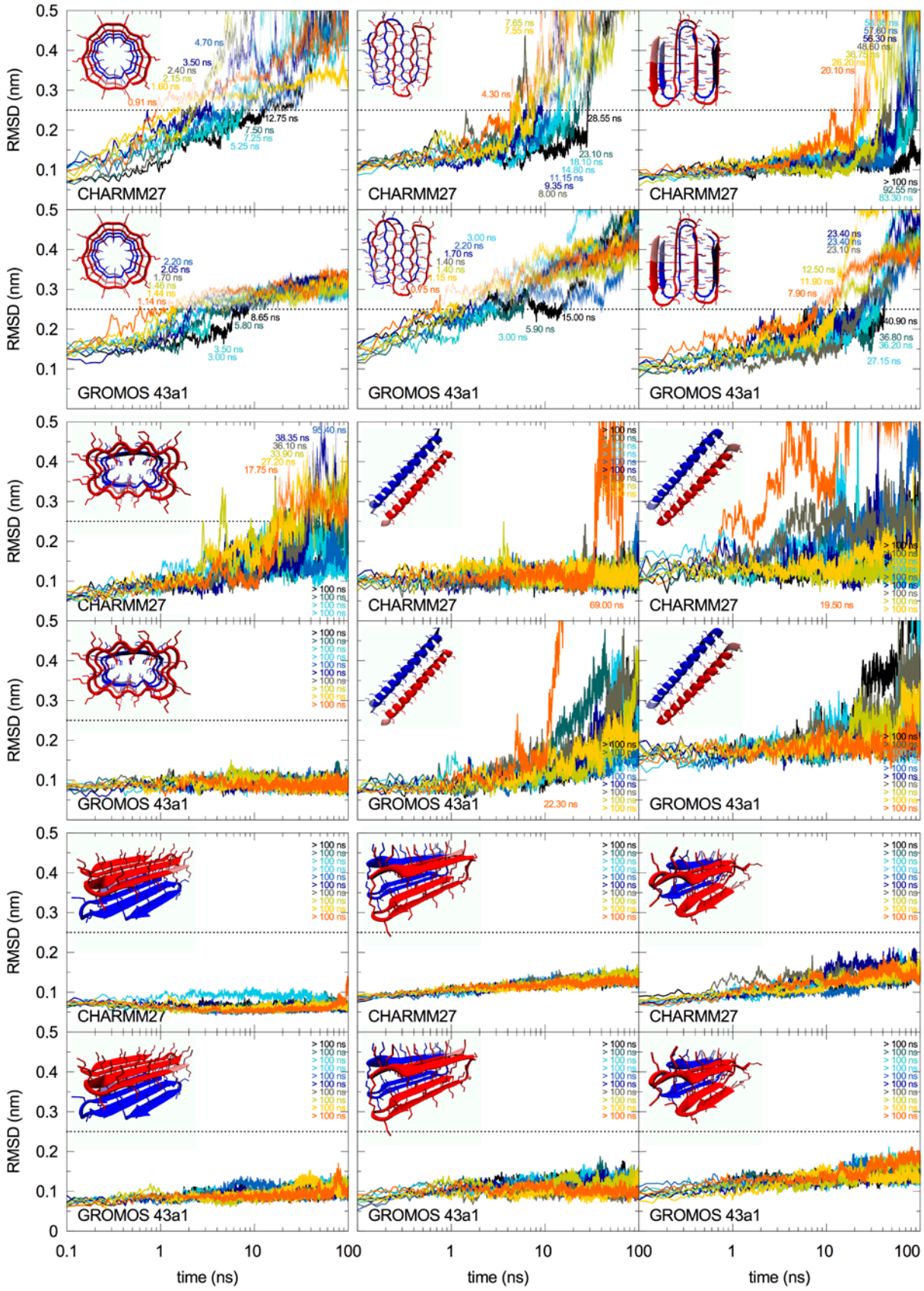

FIG. S3: The root mean squared deviation (RMSD) of backbone atoms for all the 180 simulations. The snapshots show the initial structures. The dotted line at 0.25 nm shows the limit beyond which the dimer was considered to have lost its initial structure. For α-helix dimers this limit was set to 1.0 nm. The colored numbers are the disintegration times of their respective replicas.

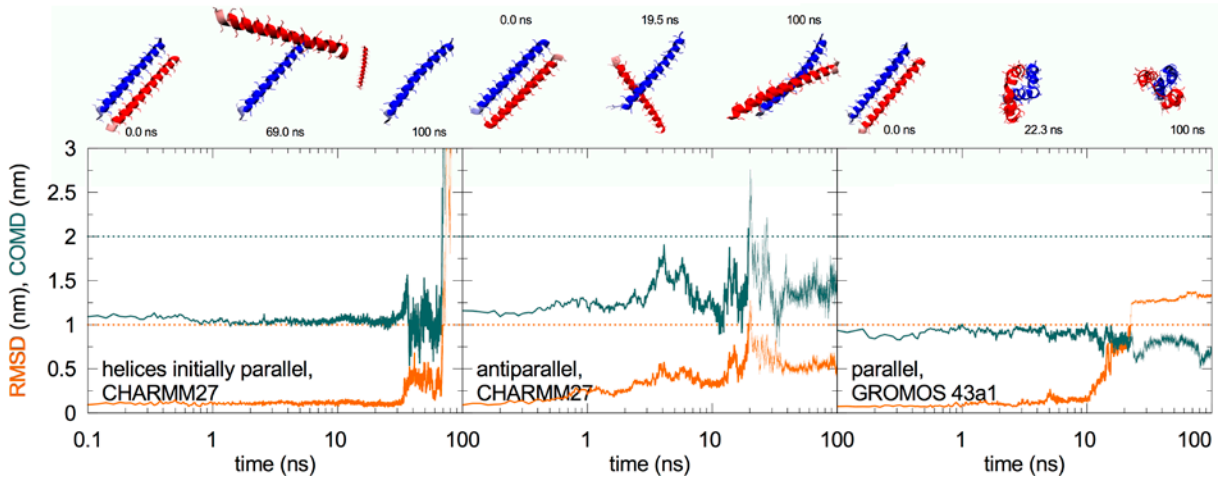

FIG. S4: The breaking events observed for α-helix dimers comprised two cases where the monomers separated while staying α-helical (left and middle panel) and one case where they collapsed while staying together (right).

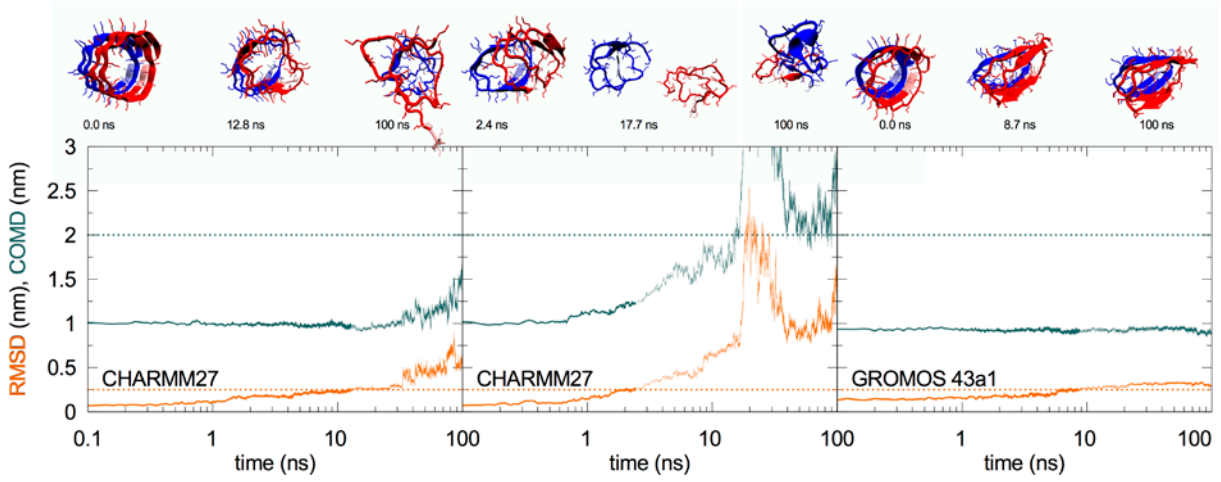

FIG. S5: Examples of breaking events observed for the β-nanotube dimers. With the CHARMM27 force field, the initial structure was always lost to a great extent, but the monomers stayed together (left panel) except for one replica, which after essentially unfolding at 2.4 ns also experienced separation of the peptides at 17.7 ns (middle). With GROMOS 43a1, the initial structure was typically lost by squeezing of the nanotube, leading to a configuration resembling the dry-core β-pseudohelix (right).