All-Atom and Coarse-Grained Molecular Dynamics Simulations of a Membrane Protein Stabilizing Polymer

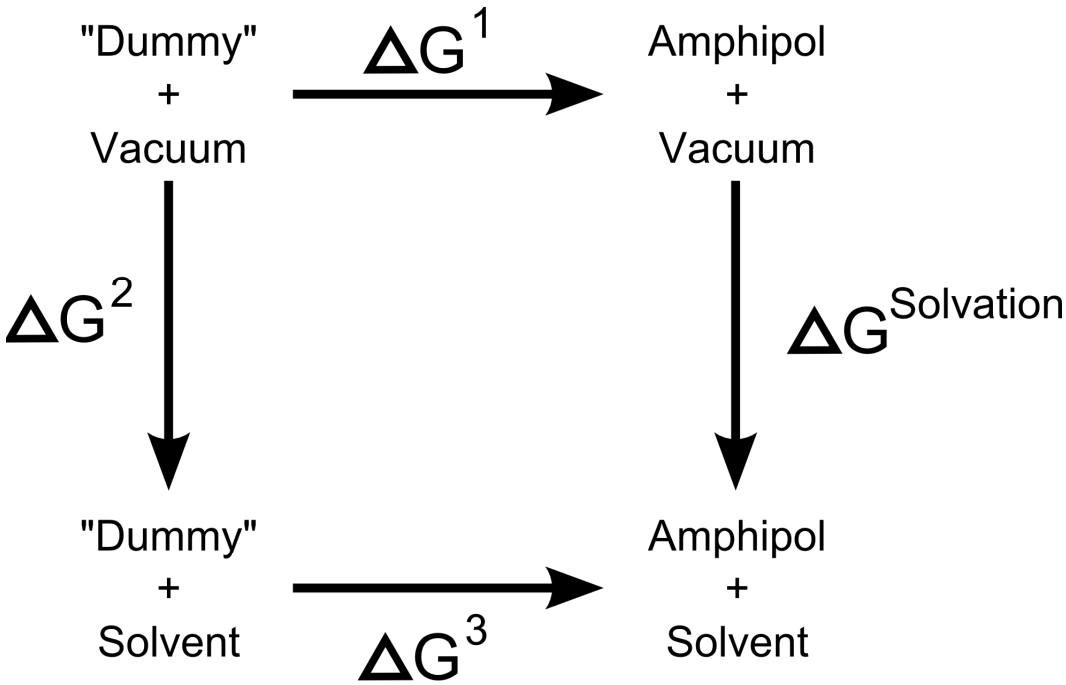
Jason D. Perlmutter[1], William J. Drasler[1], Wangshen Xie[2], Jean-Luc Popot[3], and Jonathan N. Sachs[1]

[1]Department of Biomedical Engineering, University of Minnesota, Minneapolis, Minnesota 55455

[2]Department of Chemistry, University of Minnesota, Minneapolis, Minnesota 55455

[3]CNRS/Université Paris-7 UMR 7099, Institut de Biologie Physico-Chimique, F-75005 Paris, France

Figure S1 – Thermodynamic cycle used for calculating ΔG_O and ΔG_W. The "Dummy" particle has no interaction with its environment. For the purposes of this calculation, Amphipol means a single unit containing either an isopropylamine or octylamine graft.



$$\Delta G^{1} + \Delta G^{Solvation} = \Delta G^{2} + \Delta G^{3}$$

$$\Delta G^{Solvation} = \Delta G^{2} + \Delta G^{3} - \Delta G^{1}$$

$$\Delta G^{Solvation} = \Delta G^{3} - \Delta G^{1}$$

Figure S2 – Bonded parameters (bond lengths, angles, and dihedrals) from the AAMD simulations with different grafting sequences (Random = Black, Homogeneous = Gray, Block = Dashed).

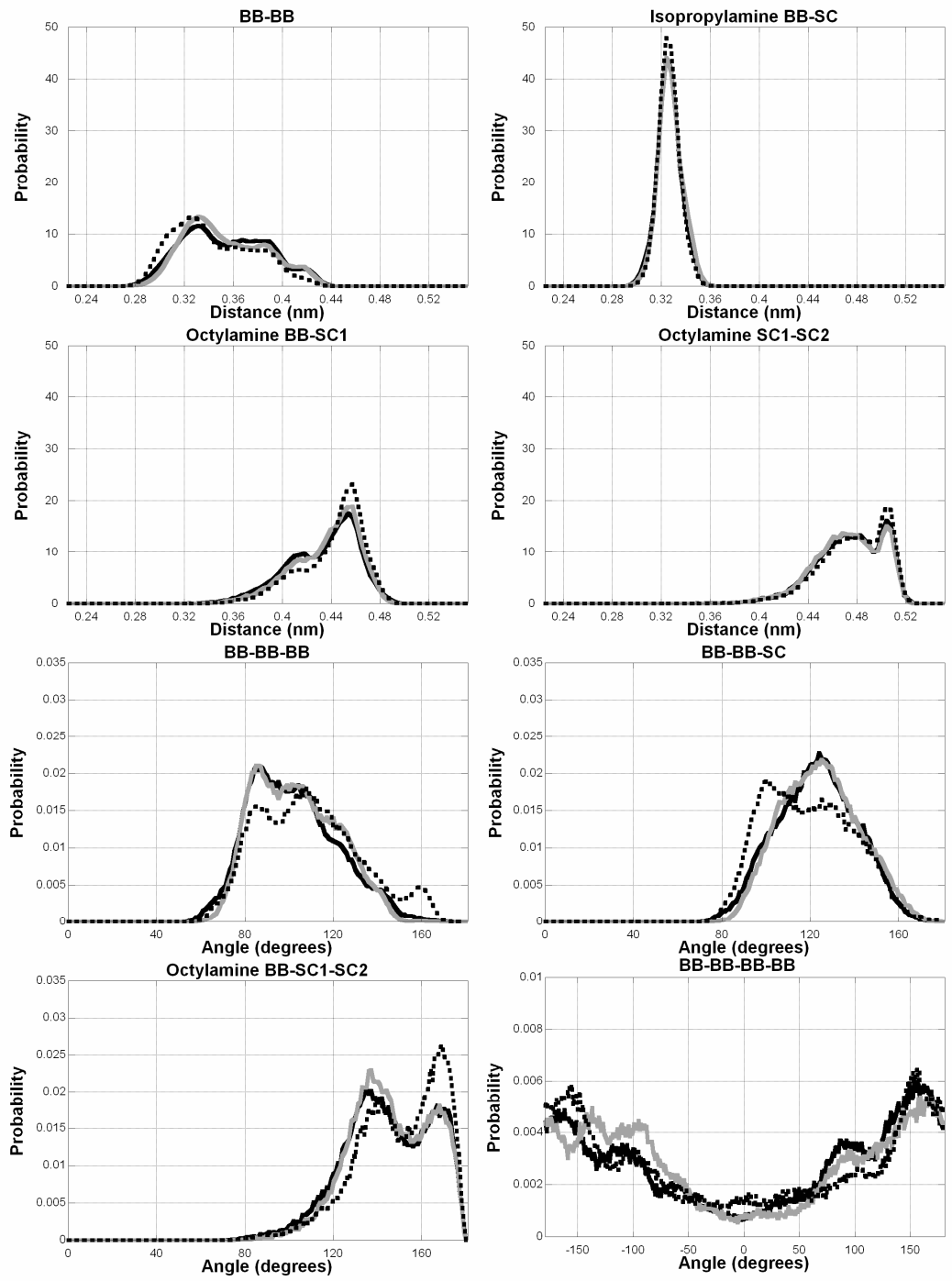


Figure S3 – Bonded parameters (bond lengths, angles, and dihedrals) from AAMD simulations of different structures. Four chains of an 89-mer (A8-35) = black, one chain of an 89-mer = gray, one chain of a 6-mer = dashed.

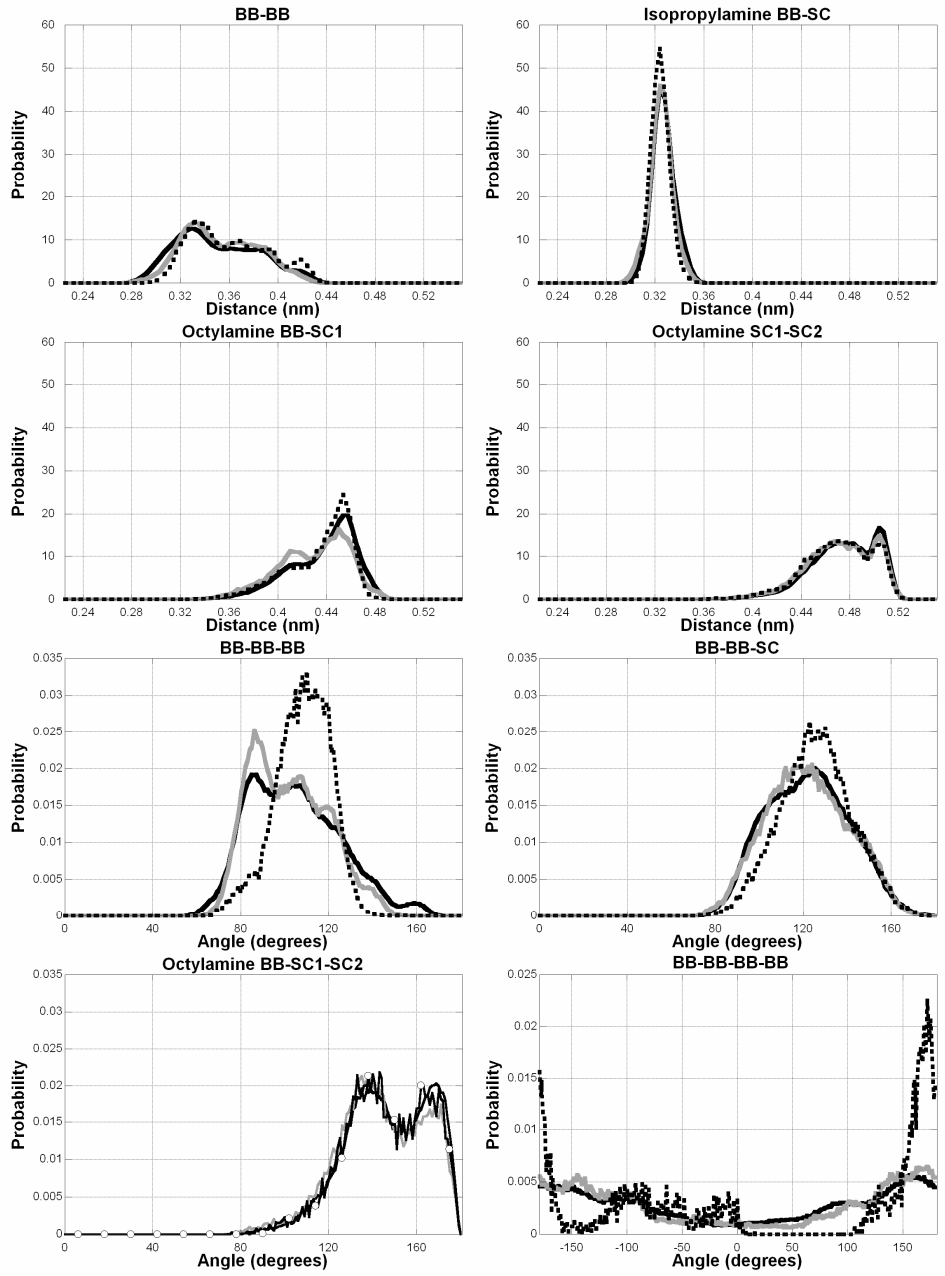


Figure S4 – A) Calculating the distance between the center of mass of the atoms mapped to the octylamine SC1 and SC2 in the AAMD simulations, reveals a multi-modal distribution. We hypothesized that this could be related to the two possible dihedral states of the central 4 carbons overlapping between the CGMD beads. When the distribution is separated based on the central dihedral angle, the gauche states are clearly at a lower distance than the trans states. However, within the states that have a trans dihedral, there is still an apparent bi-modal distribution.

B) When three separate dihedrals are considered, it is clear that each dihedral angle affects the distance. Interestingly, even within the cases where all three dihedrals are trans, the distance distribution is not uni-modal. This example demonstrates that the underlying chemistry which determines the structure of these molecules is more complex than can be easily captured in a CGMD model.

Further, it is well known that the frequency of the gauche dihedral in hydrocarbon chains is dependent on the environment. Thus the parametrization of this distance may be dependent upon the environment, and the general applicability of the CGMD parameters is uncertain. Though we note that Figure S3 suggests that this length distribution is consistent between multiple environments.

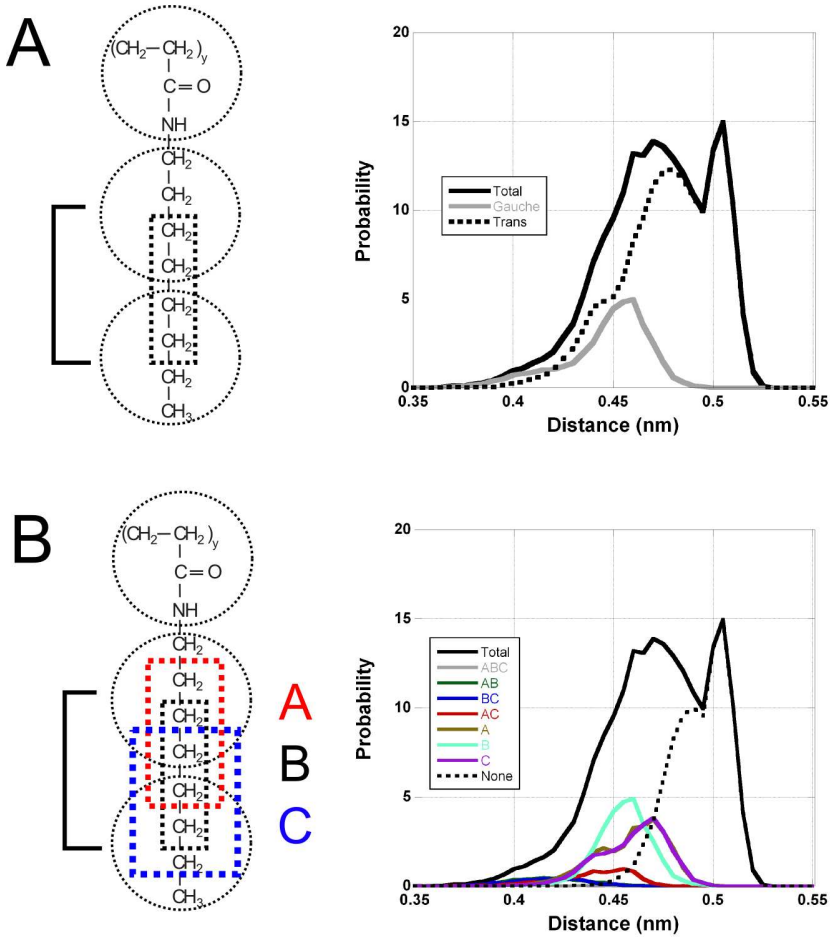


Figure S5 – In our current parametrization, backbone-backbone bonds are treated equivalently, independent of whether that backbone is ungrafted or grafted with octylamine or isopropylamine. This is the same strategy as was used for proteins. However, the multi-modal distribution of the BB-BB lengths calculated from the AAMD simulations suggests that the different grafts might have different BB bonding distances. In that case, separate CGMD bond parameters would improve fitting and only slightly increase the model complexity.

Here we present the distribution of distances from the AAMD simulation of the Random sequence separated based on BB grafting type. It is clear that this distance is not clearly differentiated by grafting type, and thus the model can not be improved by separate BB-BB parameters.

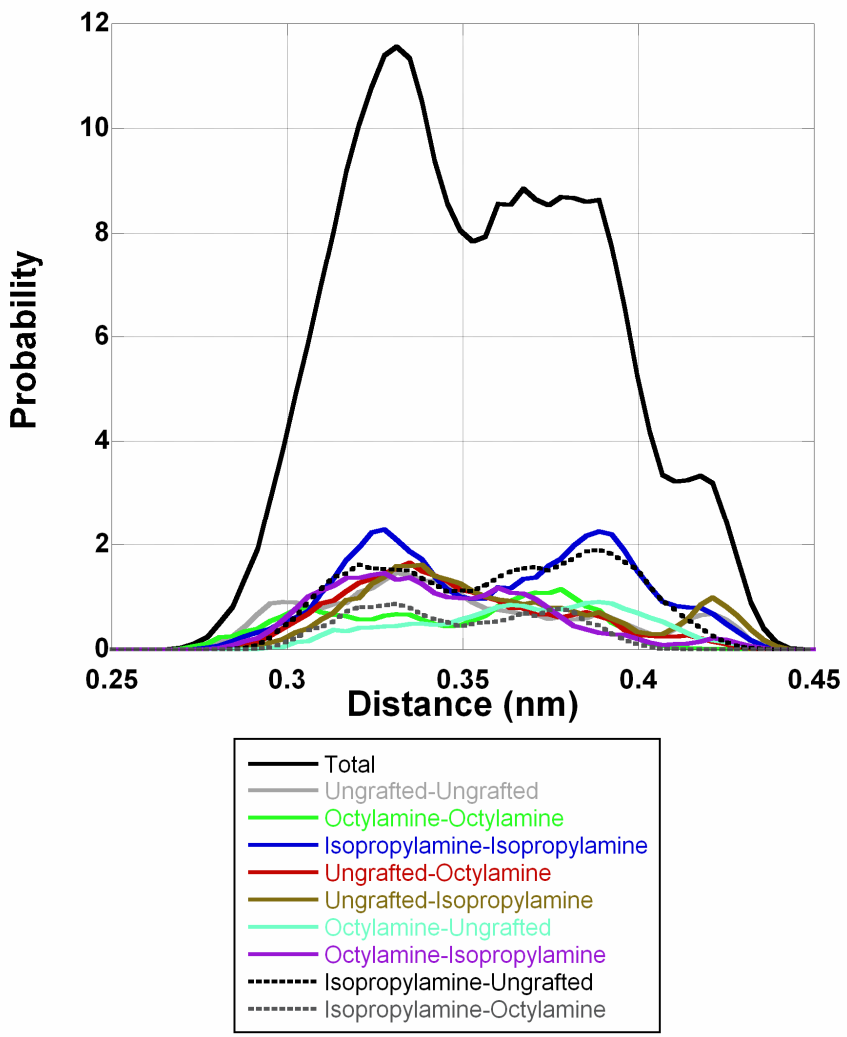


Figure S6 –Reverse Coarse-Grained RMSD. (Total=Black, Backbone=Gray, Octyl Side chain=Gray Circle, Isopropyl Side chain= Black Triangle).

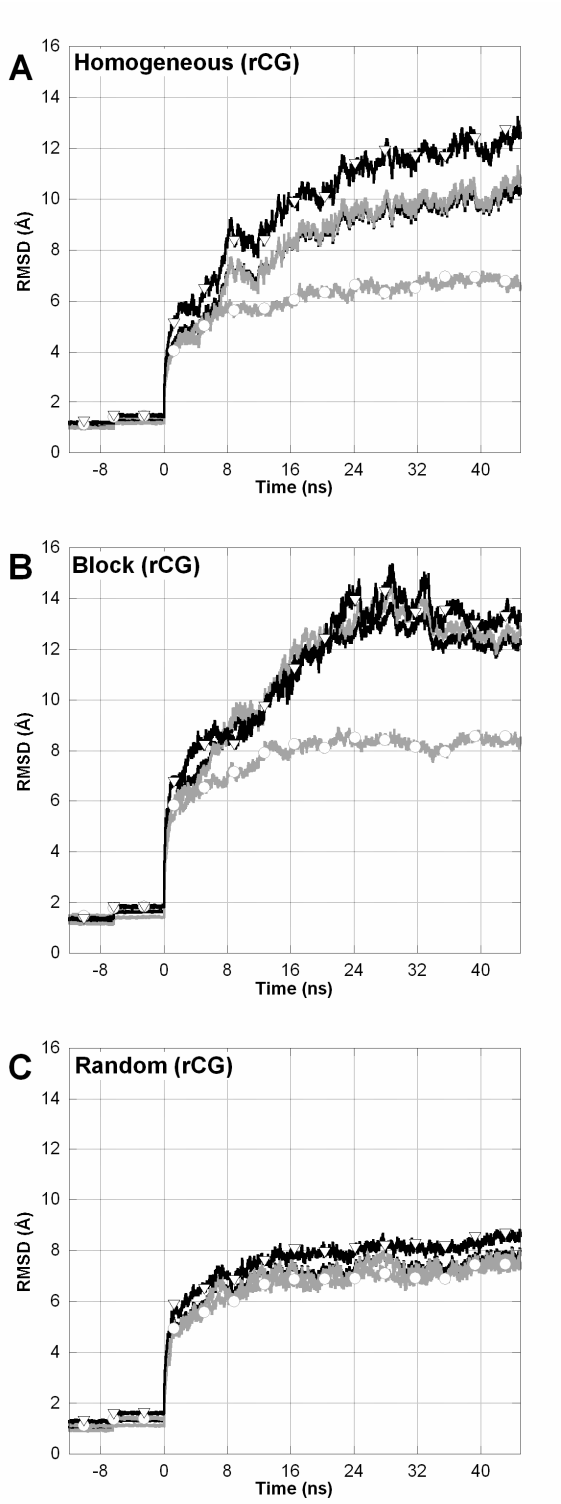
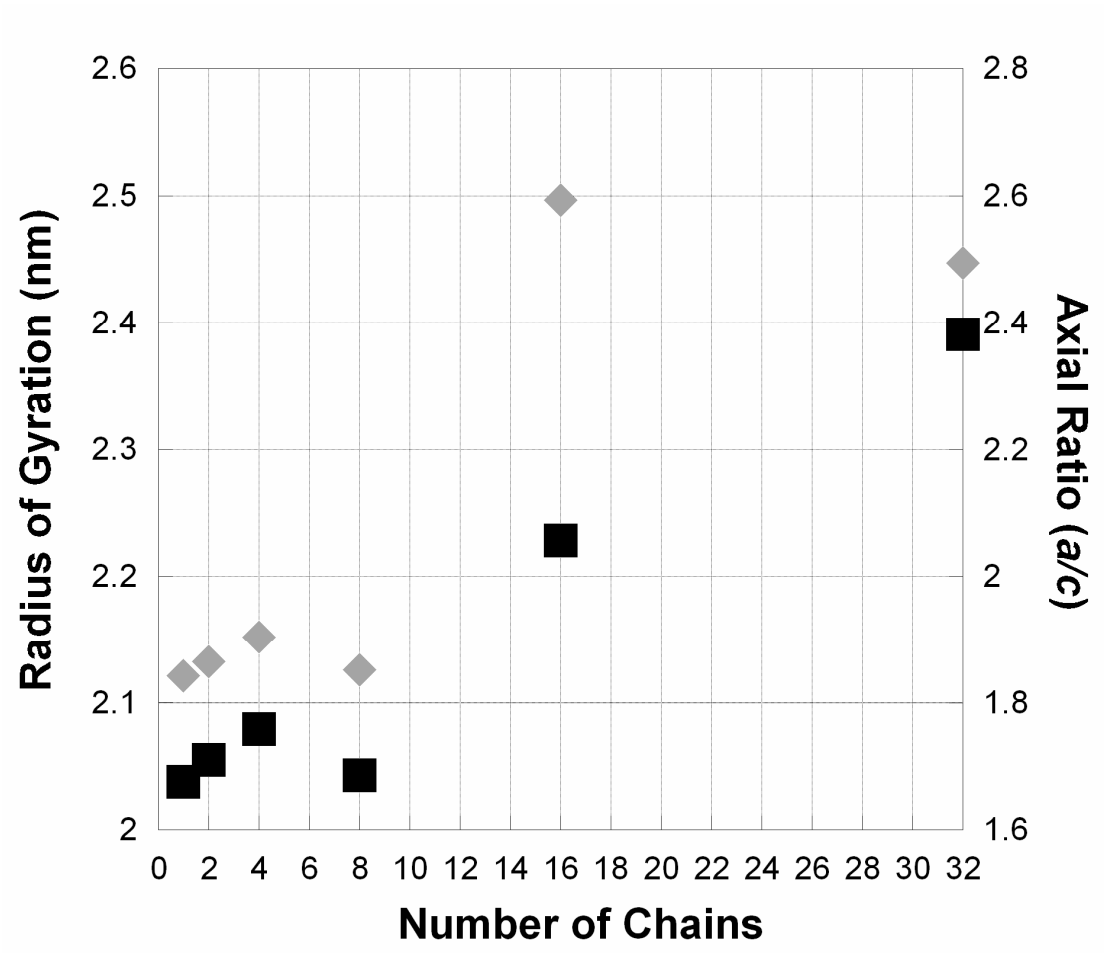



Figure S7 – A series of CGMD simulation were run to determine the effect of polymer chain length on particle properties. For each simulation, the total number of units, grafting ratio, and amount of water was conserved, but the number of chains was altered to either 1, 2, 8, 16, or 32 chains, from the original simulations which contained 4 chains. The results below suggest that particles containing either 1 chain (four times as long as the original simulation, 2 chains (each twice as long as the original simulations), or 8 chains (each half as long as the original simulations) are very similar to the original simulations, in terms of their radius of gyration (gray diamonds) and axial ratio (black squares). However, particles composed of many (i.e. 16 or 32) short chains show deviations in shape. Further, a simulation containing 64 very short chained polymers did not form a single particle over the 4 microsecond simulation, suggesting a dependence of aggregation number on chain length.