

Supporting information for:

Simulation Studies on the Lipid Interaction
and Conformation of Novel Drug Delivery
Pseudopeptidic Polymers

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Force Field Parametrisation

The force field work involved adding definitions of new fragments into the aminoacid.rtp (main definition of all charge/angle/torsion definitions), aminoacid.c.tdp, aminoacid.n.tdp and aminoacid.hdb files (C terminal, N terminal, or hydrogen number modification upon coupling to another unit) of GROMACS amino acid database.^{S1} The monomers parametrised using the amino acid database, and the monomer definitions were also added into the database along with the rules of modifying the C and N termini in order to bind monomers together. In this way, native GROMACS tools enabled the generation of the topology for any possible combination of monomers.

For new bonds/angles/torsions needing definitions in the monomers, the most suitable ones within the amino acid database were picked.^{S1} This includes giving the aromatic ring in isophthalamid the same parameters as those in phenylalanine side chain. The amide groups used the same parameters as those in amino acid backbone amide coupling.

The force fields for the monomer units, initial configurations of the monomers used to form polymers as well as other scripts mentioned in the main text can be found in the GitHub repository <https://github.com/hjuinj/Simulation-Scripts/tree/master/topology>.

RDFs and Implied Time-scale Analysis

References

- (S1) Oostenbrink, C.; Villa, A.; Mark, A. E.; Van Gunsteren, W. F. A Biomolecular Force Field Based on the Free Enthalpy of Hydration and Solvation: The GROMOS Force-Field Parameter Sets 53A5 and 53A6. *J. Comput. Chem.* **2004**, *25*, 1656–1676.

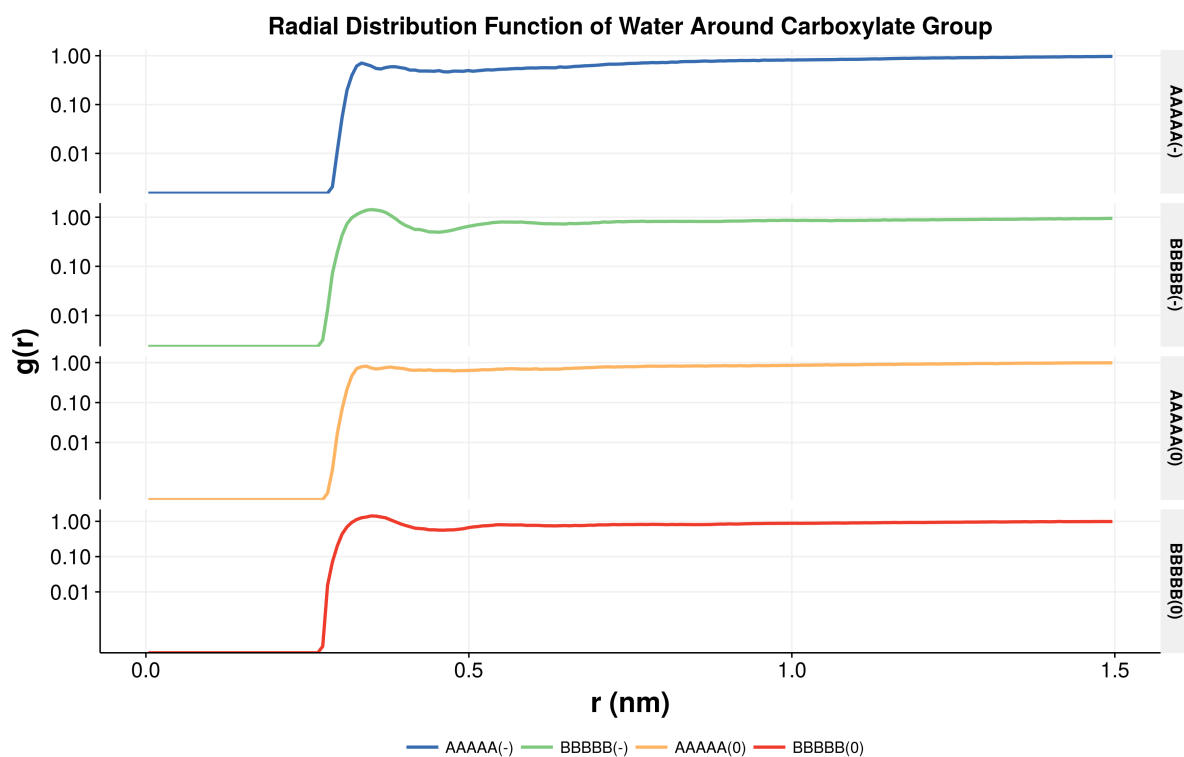


Figure S1: Radial distribution function $g(r)$ between carboxylate group (highlighted in Figure 2) carbon (either 'CO' or 'CN' carbon for type A and B monomer) and water. The RDFs for each polymer were obtained from averaging the results from 1.5×10^3 frames spanning 30 ns.

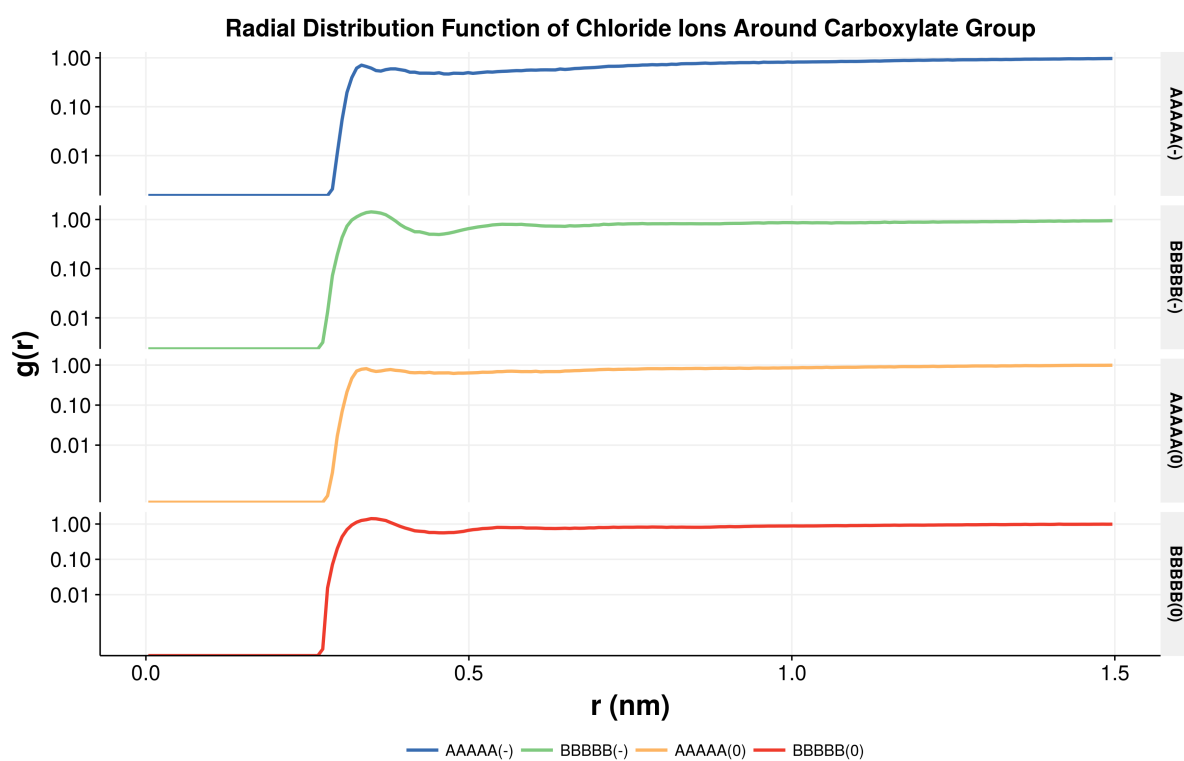


Figure S2: Radial distribution function $g(r)$ between carboxylate group (highlighted in Figure 2) carbon (either 'CO' or 'CN' carbon for type A and B monomer) and the Cl^- anions. The RDFs for each polymer were obtained from averaging the results from 1.5×10^3 frames spanning 30 ns.

Implied Time-scale Analysis for Top 20 Transition Matrix Eigenvalues

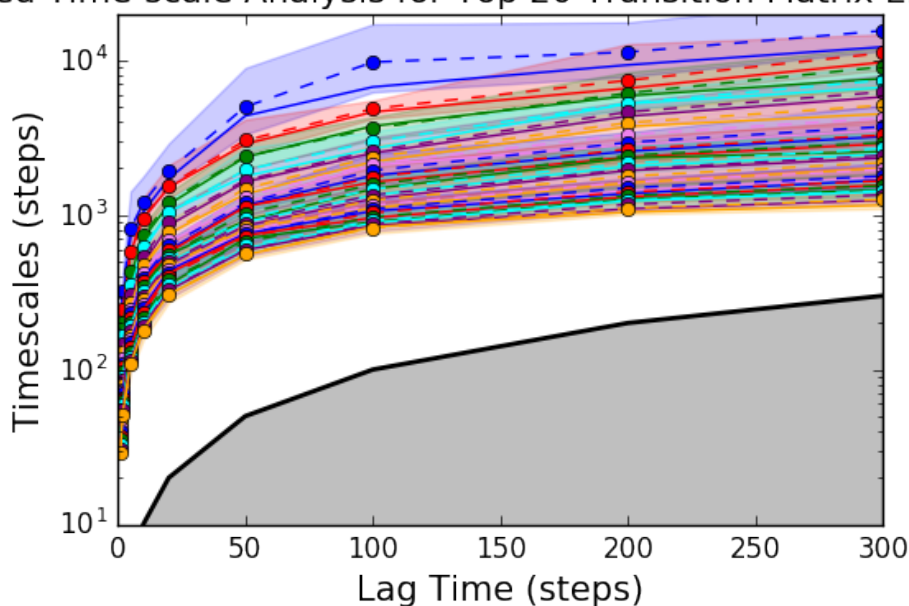


Figure S3: Implied time analysis for BBBB(-) on the 20 largest eigenvalues obtained from transition matrices. Each curve (dots of the same colour threaded by line) indicates the decay time-scale change obtained from the transition matrix at a given lag time. The shaded region around each curve indicates the Bayes estimated error. It can be observed that at lag times larger than 100 steps the decay time-scale becomes invariant to increasing lag time steps. The grey area is defined by lag time > time-scale, thus no reliable estimates on the conformation of the polymers can be made in this region.