Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.


# Supporting Information: Modulation of A$\beta$ 16-22 Aggregation by Glucose

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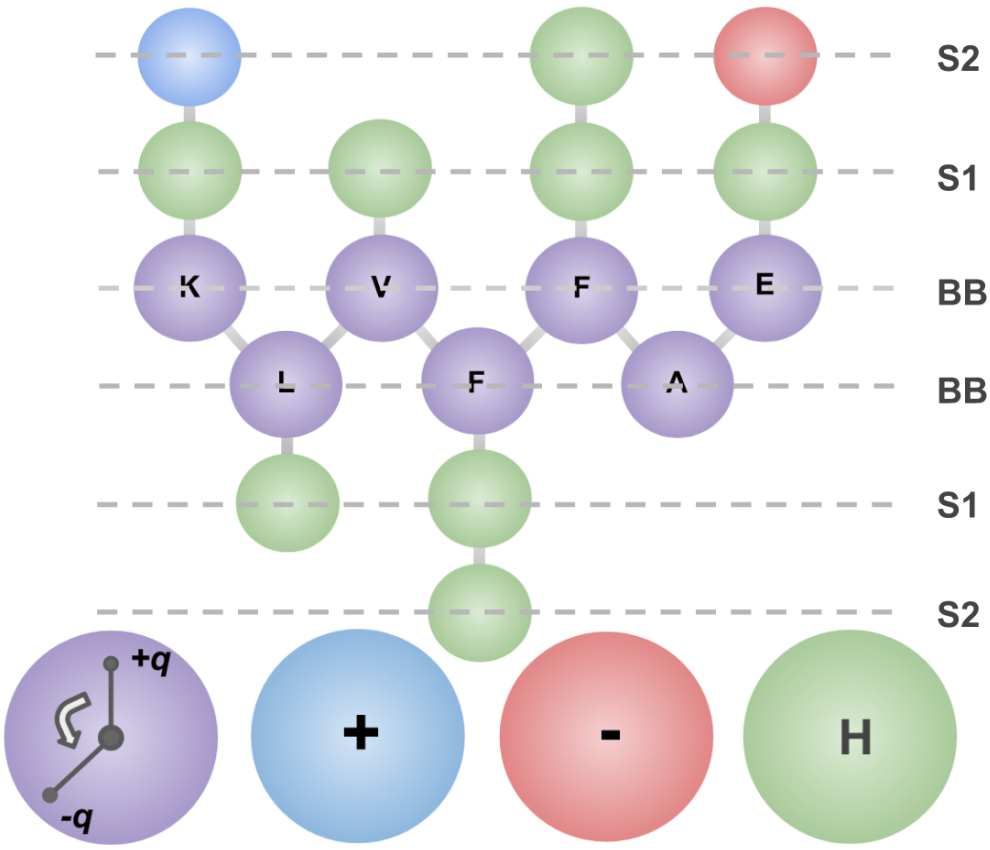


Figure S1: Schematic geometries of coarse-grained amino-acids. Reproduced from Sahoo *et al.*[1] with permission from the PCCP Owner Societies.

| Residue | Bead name | Bead type |
|---|---|---|
| K, lysine | BB* | PP5* |
| | S1 | C3 |
| | S2 | Qd |
| L, leucine | BB* | PP5* |
| | S1 | C1 |
| V, valine | BB* | PP5* |
| | S1 | C1 |
| F, phenylalanine | BB* | PP5* |
| | S1 | C3 |
| | S2 | C3 |
| A, alanine | BB* | PP5* |
| E, glutamate | BB* | PP5* |
| | S1 | C3 |
| | S2 | Qa |
| Glucose | B1* | PP1* |
| | B2* | PP4* |
| | B3* | PP4* |
| PW, MARTINI polarizable solvent | W* | POL* |

Table S1: Type of coarse-grained beads present in the A$\beta$ fragment $K_{16}LVFFAE_{22}$, glucose molecule and the MARTINI polarizable solvent model. Polarized beads are indicated with an asterisk (*); these beads contain internal dummies of equal and opposite charges. BB beads have dummies of type D2 and charge $\pm 0.34$,[2] beads present in glucose have dummies of type D1 and charge $\pm 0.19$ (parameterized to match the dipole moment of glucose molecule) and W beads have dummies of type D and charge $\pm 0.46$.[3]

| Bead type | PP5 | PP4 | PP1 | Qd | Qa | C3 | C1 | POL |
|---|---|---|---|---|---|---|---|---|
| PP5 | $5.02^a$ | $5.02^a$ | $5.02^a$ | $5.32^a$ | $5.32^a$ | 2.70 | 2.00 | $4.74^a$ |
| PP4 | $5.02^a$ | $4.42^a$ | $3.92^a$ | $5.32^a$ | $5.32^a$ | 2.70 | 2.00 | $4.17^a$ |
| PP1 | $5.02^a$ | $3.92^a$ | $3.92^a$ | $5.32^a$ | $5.32^a$ | 3.50 | 2.70 | $3.69^a$ |
| Qd | $5.32^a$ | $5.32^a$ | $5.32^a$ | 3.50 | 4.00 | 2.70 | 2.30 | 5.00 |
| Qa | $5.32^a$ | $5.32^a$ | $5.32^a$ | 4.00 | 3.50 | 2.70 | 2.30 | 5.00 |
| C3 | 2.70 | 2.70 | 3.50 | 2.70 | 2.70 | 3.50 | 3.50 | 2.57 |
| C1 | 2.00 | 2.00 | 2.70 | 2.30 | 2.30 | 3.50 | 3.50 | $1.00^a$ |
| POL | $4.74^a$ | $4.17^a$ | $3.69^a$ | 5.00 | 5.00 | 2.57 | $1.00^a$ | 4.00 |

Table S2: Non-bonded Lennard-Jones well depths ($\epsilon$, in units of kJ/mol) for the main-bead (i.e., not dummy charge) types used to model glucose, A$\beta$, and solvent molecules. The van der Waals interaction diameter, ($\sigma$), for main-bead interactions is 0.47 nm. Values marked with the superscript, $a$, were reparameterized by Sahoo *et. al.* for WEPPROM.[4] Unmarked interactions are borrowed directly from MARTINI.[5] Dummy charges with bead type D, which interact at $\epsilon = 0\ kJ/mol$ and $\sigma = 0\ nm^3$ with each other, and all other bead types except D1 and D2. Interactions of dummy charges with bead type D1 and D2 have a small repulsive core expressed by the Lennard-Jones repulsive term $C12 = 4.5355 \times 10^{-10}\ kJ\ nm^{12}/mol$, and an attractive term $C6 = 0\ kJ\ nm^6/mol$.[2,6] D2 dummy charges interact with each other through LJ-repulsive term $C12 = 4.5355 \times 10^{-09}\ kJ\ nm^{12}/mol$, and an attractive term $C6 = 0\ kJ\ nm^6/mol$ while they interact with all other beads through repulsive term $C12 = 4.5355 \times 10^{-10}\ kJ\ nm^{12}/mol$, and an attractive term $C6 = 0\ kJ\ nm^6/mol$. Interactions of D1 dummy charges are similar to D2 dummy charges.

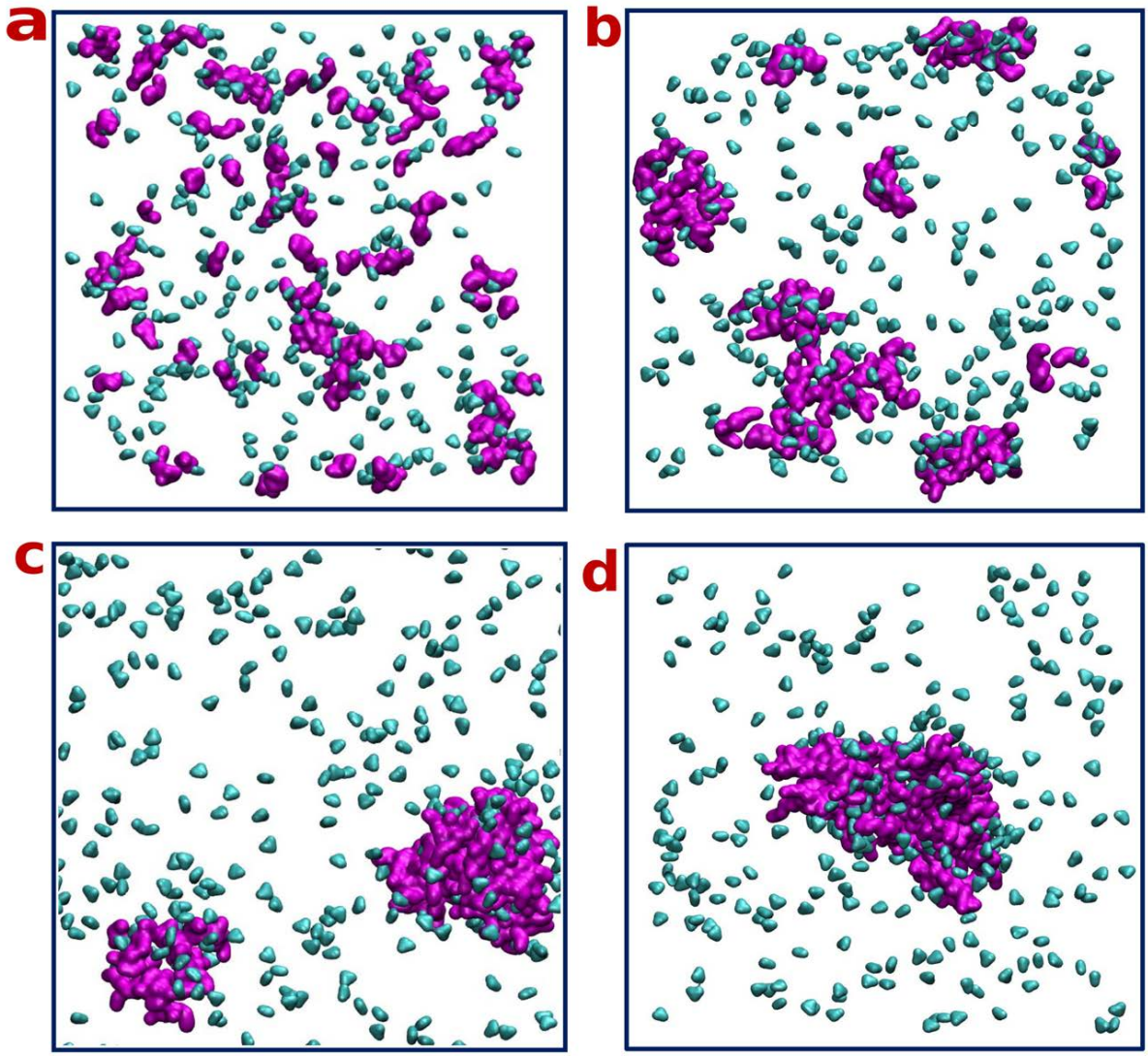


Figure S2: Snapshots from the peptide aggregation trajectory at 0 ns (a), 50 ns (b), 100 ns (c), and 1000 ns (d) for 1.55% glucose (w/v). Glucose molecules are depicted as cyan triangles, while A$\beta$ backbone beads are depicted as magenta surfaces. Solvent particles, side chain beads, and dummy particles are hidden for clarity.

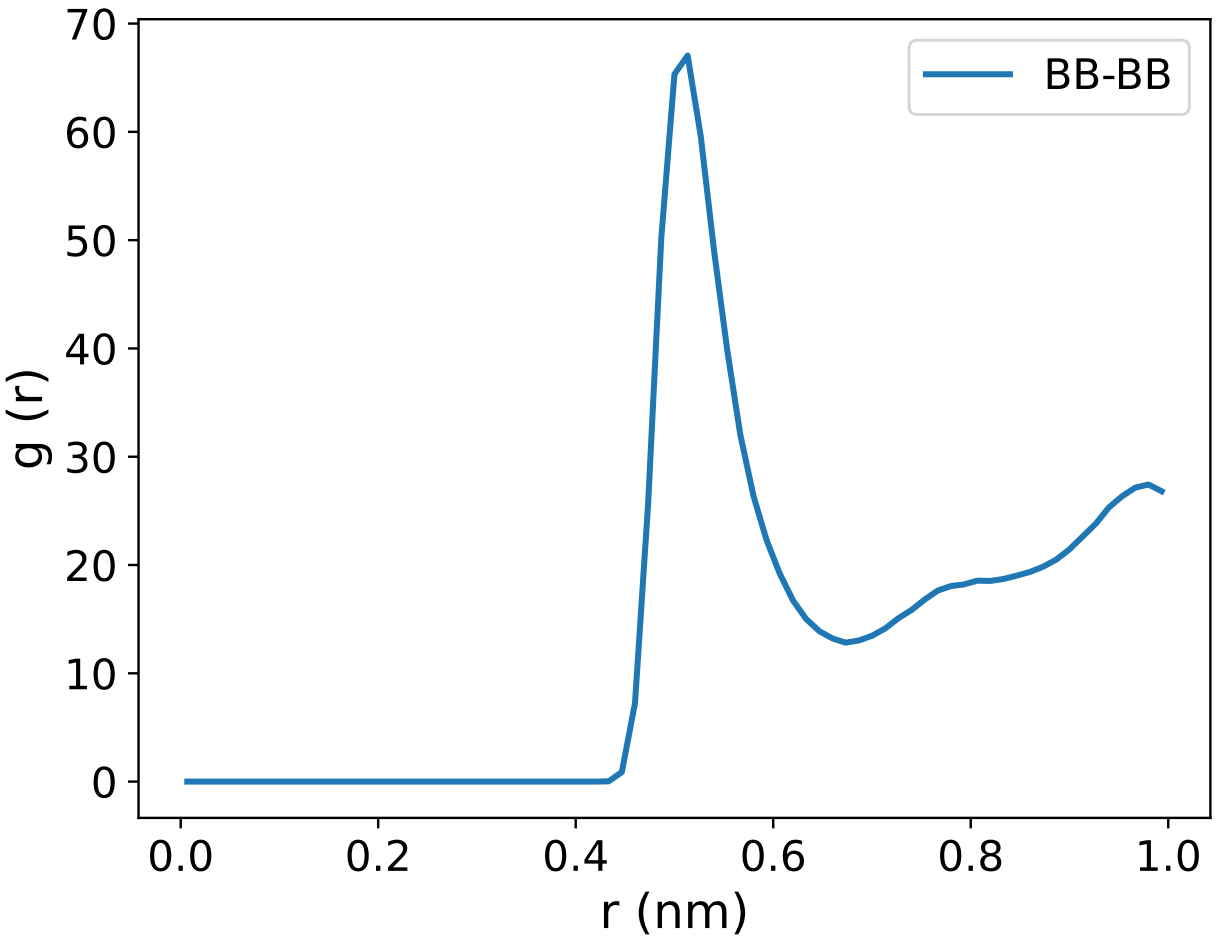


Figure S3: Radial distribution function between the backbone beads (BB) of different peptides.

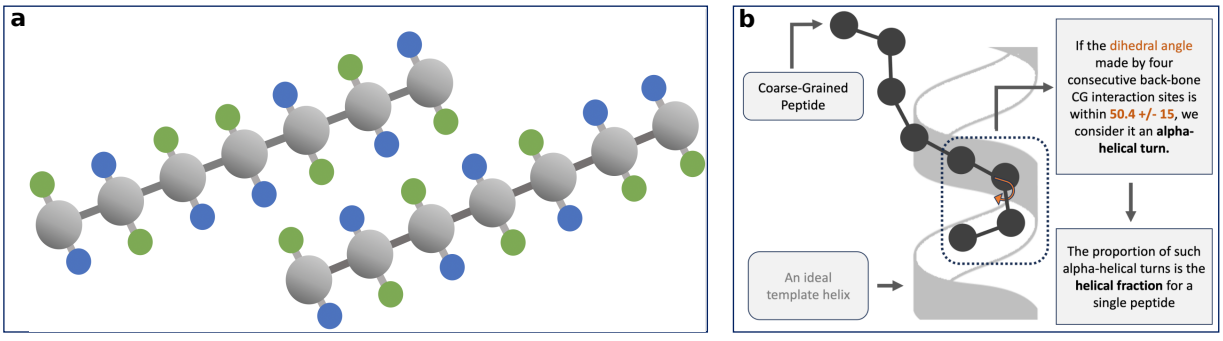


Figure S4: (a) Metric for determining peptides in a $\beta$-sheet aggregate. Reproduced from Sahoo et al.[1] with permission from the PCCP Owner Societies. (b) Criteria for determining the $\alpha$-helical fraction of a single peptide.

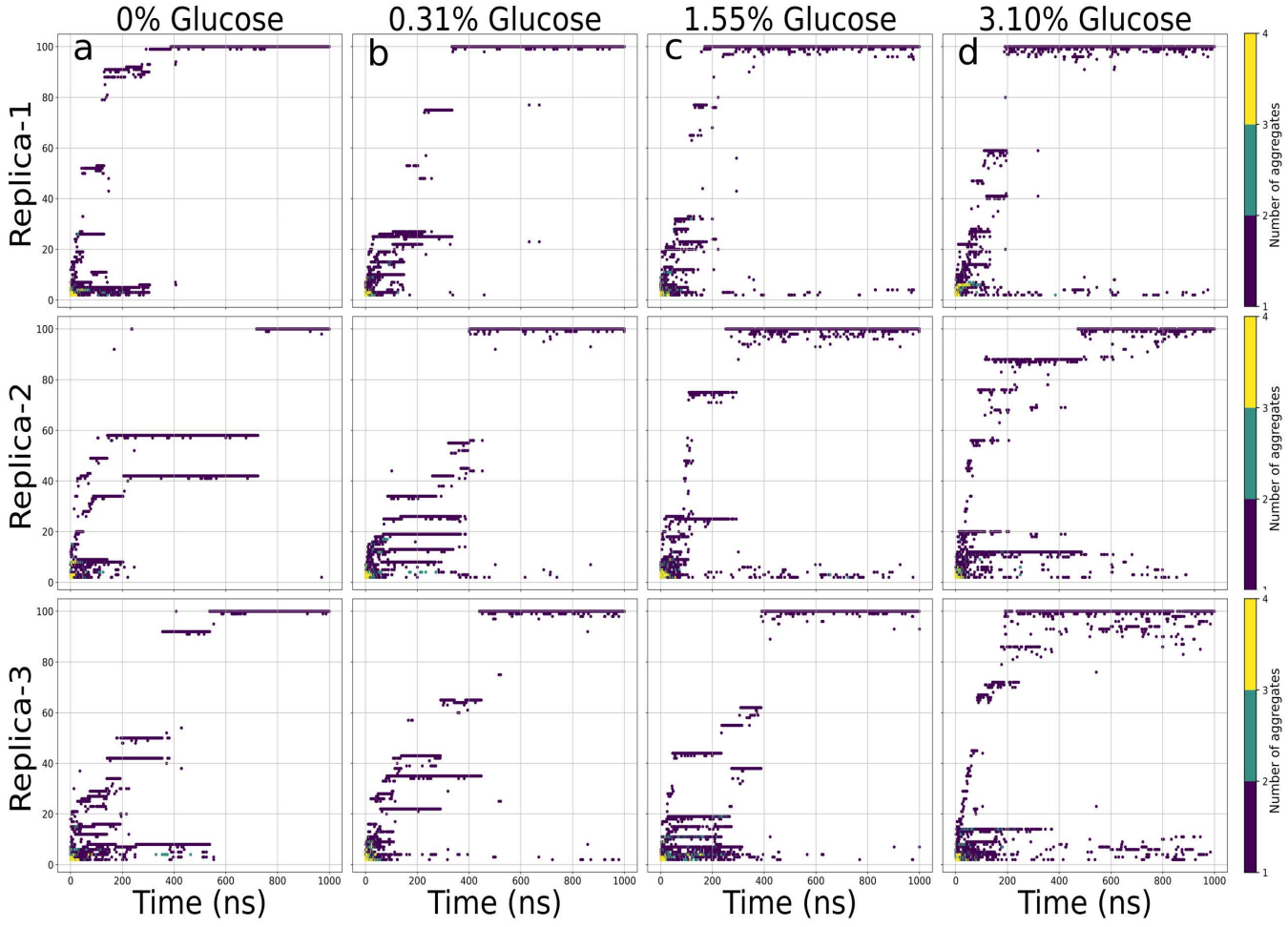


Figure S5: Evolution of size of peptide aggregates with 0% (a), 0.31% (b), 1.55% (c), and 3.10% (d) Glucose (w/v) for the three independent replica simulations.

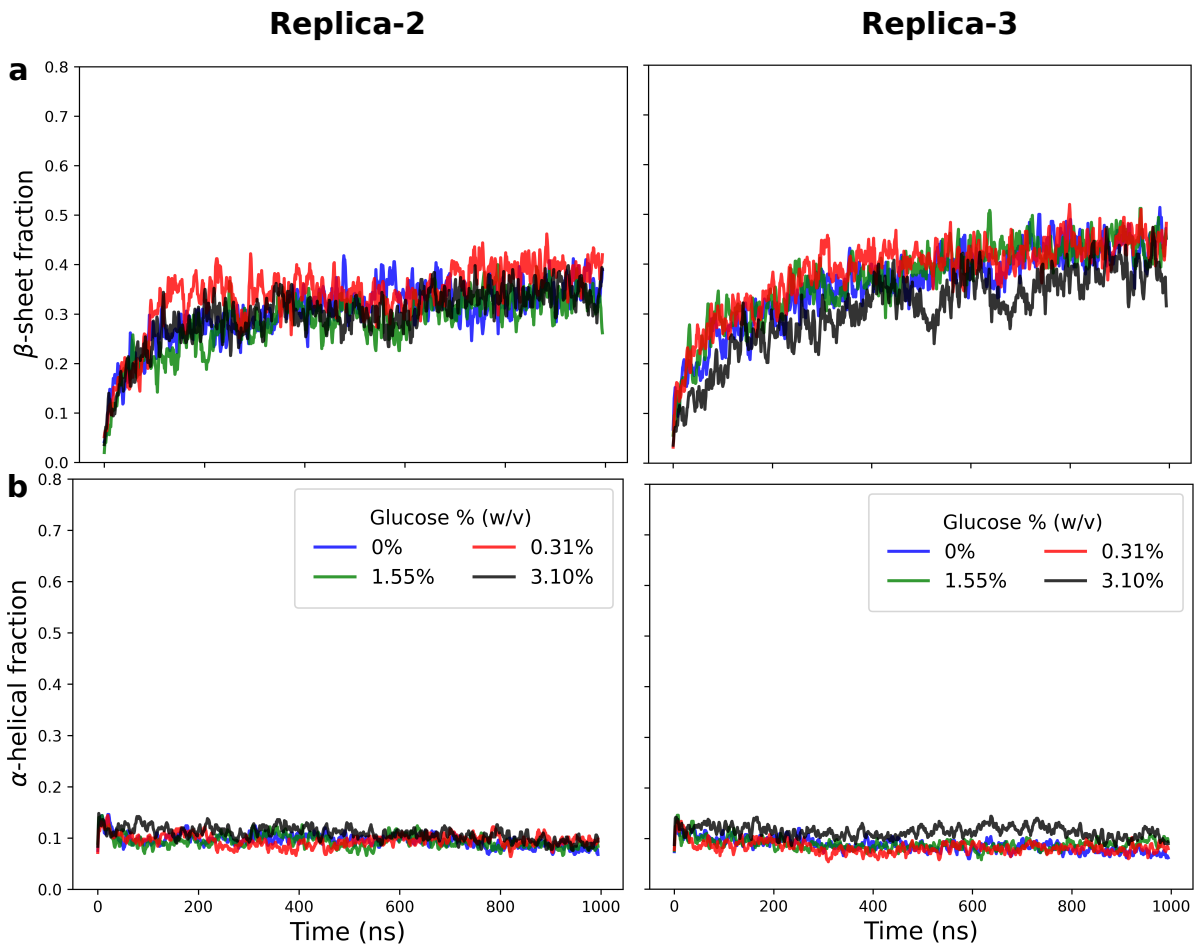


Figure S6: Time evolution of $\beta$-sheet (a), and $\alpha$-helical (b) fractions present in A$\beta$ aggregates for all glucose concentrations for the replica simulations.

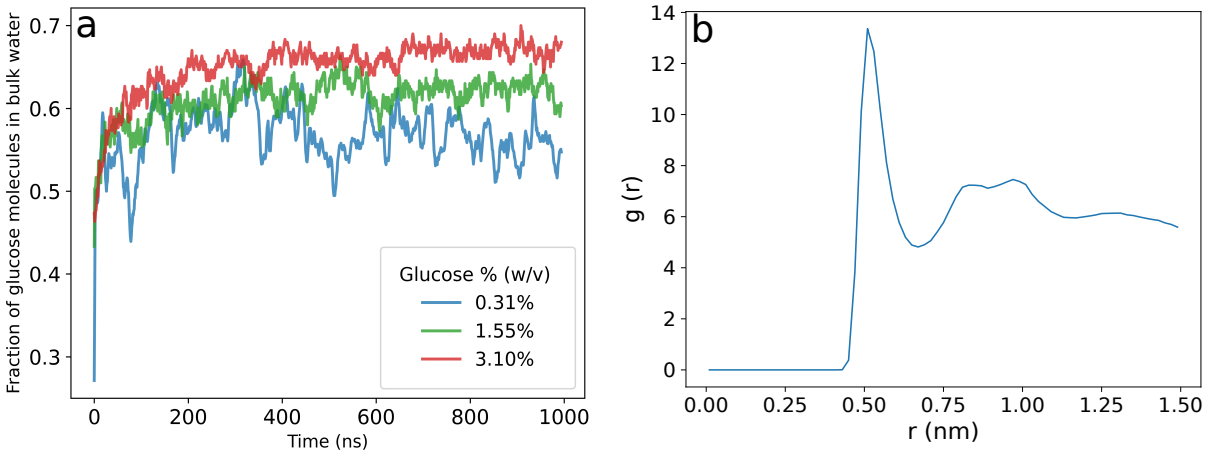


Figure S7: Time evolution of the fraction of glucose molecules present in bulk water for various % compositions of glucose molecules (a). Data are the mean over the three replicas. Bulk water is defined as the region beyond a distance of 12Å from the peptide backbone (BB) beads. This distance cutoff is determined from the second minima of radial distribution function between the peptide backbone beads and the CG interaction sites of the glucose molecule (b).

# References


(1) Sahoo, A.; Matysiak, S. Effects of applied surface-tension on membrane-assisted A$\beta$ aggregation. *Phys. Chem. Chem. Phys.* **2021**, *23*, 20627–20633.

(2) Ganesan, S. J.; Matysiak, S. Role of Backbone Dipole Interactions in the Formation of Secondary and Supersecondary Structures of Proteins. *J. Chem. Theory Comput.* **2014**, *10*, 2569–2576.

(3) Yesylevskyy, S.; Schäfer, L.; Sengupta, D.; SJ, M. Polarizable water model for the coarse-grained MARTINI force field. *PLoS Comput. Biol.* **2010**, *6*, 1–17.

(4) Sahoo, A.; Xu, H.; Matysiak, S. Pathways of amyloid-beta absorption and aggregation in a membranous environment. *Phys. Chem. Chem. Phys.* **2019**, *21*, 8559–8568.

(5) de Jong, D. H.; Singh, G.; Bennett, W. F. D.; Arnarez, C.; Wassenaar, T. A.; Schäfer, L. V.; Periole, X.; Tieleman, D. P.; Marrink, S. J. Improved Parameters for the Martini Coarse-Grained Protein Force Field. *J. Chem. Theory Comput.* **2013**, *9*, 687–697.

(6) Ganesan, S. J.; Xu, H.; Matysiak, S. Effect of lipid head group interactions on membrane properties and membrane-induced cationic $\beta$-hairpin folding. *Phys. Chem. Chem. Phys.* **2016**, *18*, 17836–17850.