Effect of Surface Roughness on Aggregation of Polypeptide Chains: A Monte Carlo Study

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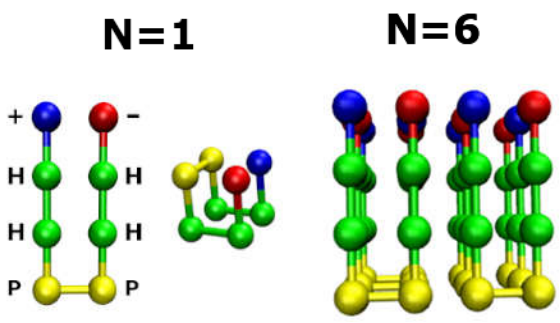
Introduction

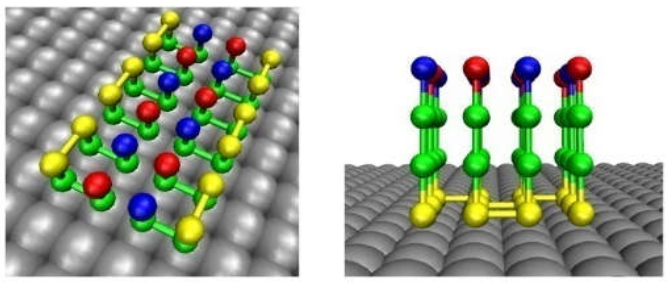
The self-assembly of amyloidogenic peptides and proteins into fibrillar structures has been intensively studied for several decades, because it seems to be associated with a number of neurodegenerative diseases, such as Alzheimer's and Parkinson's disease. Therefore, understanding the molecular mechanisms of this phenomenon is important for identifying an effective therapy for the corresponding diseases. Protein aggregation in living organisms very often takes place on surfaces like membranes and the impact of a surface on this process depends not only on the surface chemistry but also on its topology. Our goal was to develop a simple lattice model for studying the role of surface roughness in the aggregation kinetics of polypeptide chains and the morphology of aggregates. We showed that, consistent with the experiment, an increase in roughness slows down the fibril formation, and this process becomes inhibited at a very highly level of roughness. We predicted a subtle catalytic effect that a slightly rough surface promotes the self-assembly of polypeptide chains but does not delay it. This effect occurs when the interaction between the surface and polypeptide chains is moderate and can be explained by taking into account the competition between energy and entropy factors.

Materials and Methods

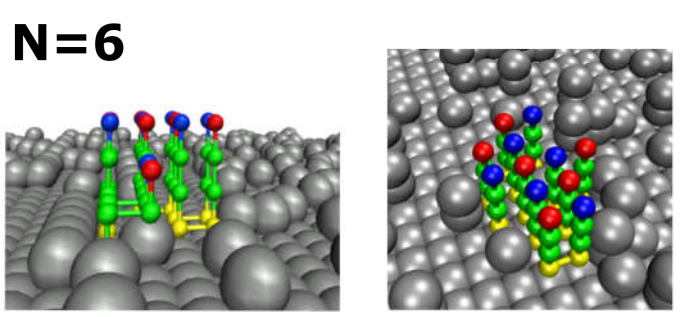
Lattice Model in Bulk



Lattice Model of Smooth Surfaces

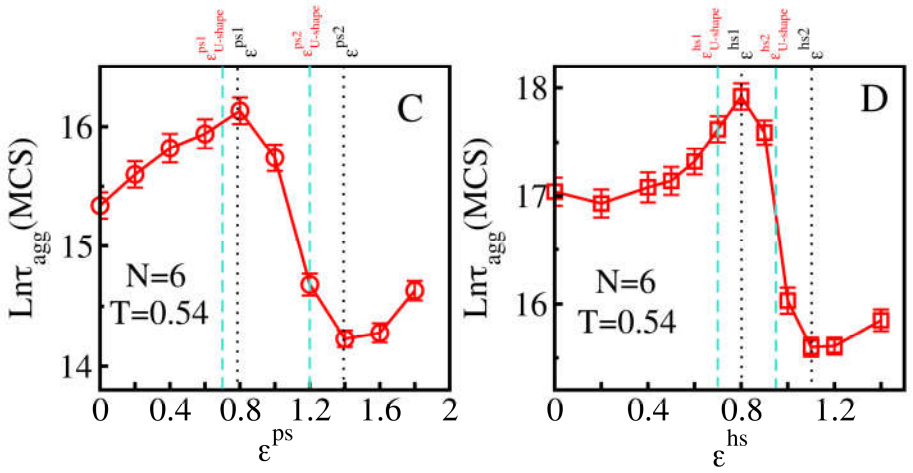


Lattice Model of Rough Surfaces

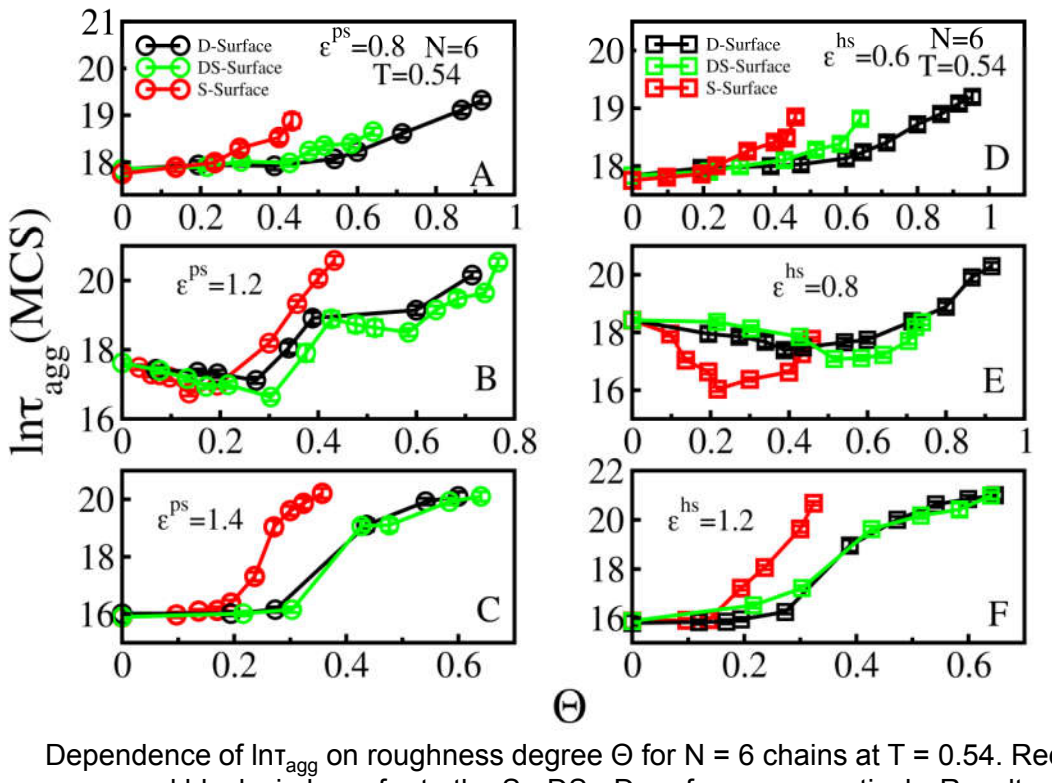


$$E = \sum_{l=1}^{N}\sum_{i<j}^{M} e_{sl(i)sl(j)}\delta(r_{ij}-a) + \sum_{m<l}^{N}\sum_{i,j}^{M} e_{sl(i)sm(j)}\delta(r_{ij}-a) + \sum_{m=}^{N}\sum_{i=1}^{M}\sum_{k=1}^{Ns} e^{vs}{}_{k,sm(i)}\delta(r_{ik}-a)$$

Results

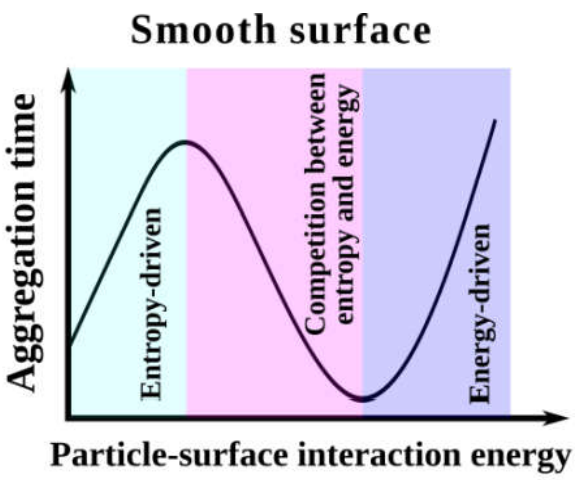


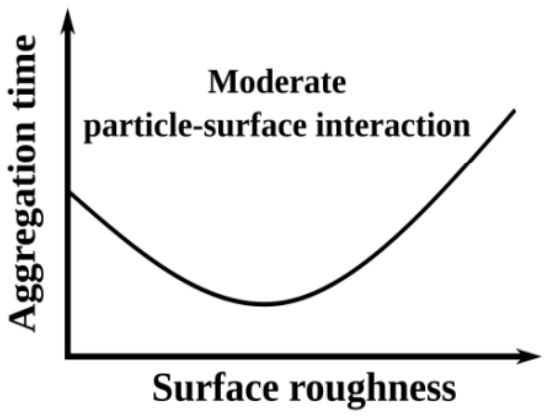
Dependence of ln τ_{agg} on the interaction of the systems consisting of N = 6 polypeptide chains for hydrophilic (**C**) and hydrophobic (**D**) smooth surfaces

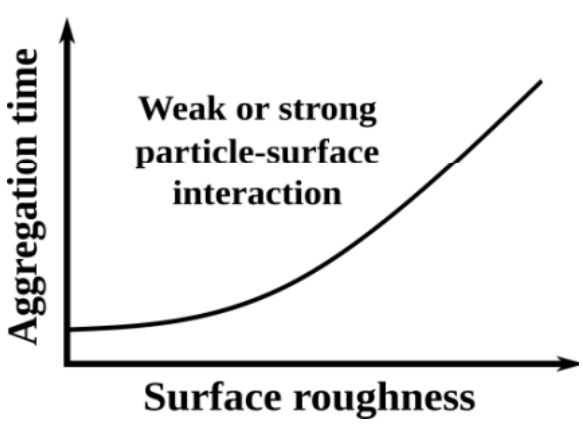


Dependence of $\ln\tau_{agg}$ on roughness degree Θ for N = 6 chains at T = 0.54. Red, green and black circles refer to the S-, DS-, D-surfaces, respectively. Results are shown for the weakly ε^{ps} = 0.8 (**A**), medium ε^{ps} = 1.2 (**B**), strongly ε^{ps} = 1.4 (**C**) absorbing hydrophilic surfaces, as well as for weak ε^{hs} = 0.6 (**D**), medium ε^{hs} = 0.8 (**E**) and strong ε^{hs} = 1.2. (**F**) regimes of attractive hydrophobic surfaces

Conclusions







References

Co, N.T.; Li, M.S. Effect of Surface Roughness on Aggregation of Polypeptide Chains: A Monte Carlo Study. *Biomolecules* **2021**

Li, M.S.; Klimov, D.K.; Straub, J.E.; Thirumalai, D. Probing the mechanisms of fibril formation using lattice models. *J. Chem. Phys.* **2008**, *129*, 17510