Towards bio-inspired underwater adhesives: barnacle cement protein 19 structural ensembles via molecular modelling

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Barnacles are marine organisms with a remarkable ability to stick to almost any surface underwater. This, however, causes serious fouling problems in the marine industry, increasing fuel and maintenance costs. However, this extremely strong adhesion is also a source of inspiration. Producing synthetically in the lab a biobased, biocompatible underwater adhesive with equal, or superior, but also tunable characteristics, is highly fascinating but also holds high technological potential.

In nature, barnacle adhesion is through a protein-mediated process in which barnacle cement protein 19 (Cp19k) plays a key role. Central to the adhesion response are the structure and its changes of this intrinsically disordered protein, yet limited knowledge exists on the structural characteristics.

We have used molecular modelling, especially metadynamics enhanced sampling together with AlphaFold 3 (AF3) predictions combined with comparison to experimental Raman and CD spectroscopy characterization, as well as optical microscopy to examine Cp19k structural ensemble. We report that Cp19k adopts a coil structure that contains some β-sheets and helices but also that salt drives local structural ordering. Secondary structure and radius of gyration analysis on the ensemble are consistent with experiments and give insights on the phase separation behavior of the protein which is a critical step for material development. We pinpoint the changes to the amino acid sequence level, directly linking molecular detail to macroscopic material behavior. From a methodological perspective, the study offers a critical evaluation of AF3 vs advanced molecular modelling approach demonstrating that AF3 significantly overestimates the structural order in Cp19k. We discuss the origins of this based on the architecture and training data of the AF3 and similar algorithms. From a material design perspective, our results establish a mechanistic basis for the rational design of protein inspired adhesives with tunable desired material properties.

Keywords:

barnacles, adhesion, protein-based materials, metadynamics, structural ensemble, β-sheets, AlphaFold3

References:

[1] E. Mantzari, D. Tolmachev, and M. Sammalkorpi, Identifying the conformational landscape of barnacle cement protein 19 via metadynamics, to be submitted (2026).