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Molecular mechanics of mussel adhesion proteins

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ABSTRACT

Mussel foot protein (mfp), a natural glue produced by marine mussel, is an intriguing material because of its superior ability for adhesion in various environments. For example, a very small amount of this material is sufficient to affix a mussel to a substrate in water, providing structural support under extreme forces caused by the dynamic effects of waves. Towards a more complete understanding of its strength and underwater workability, it is necessary to understand the microscopic mechanisms by which the protein structure interacts with various substrates. However, none of the mussel proteins' structure is known, preventing us from directly using atomistic modeling to probe their structural and mechanical properties. Here we use an advanced molecular sampling technique to identify the molecular structures of two mussel foot proteins (mfp-3 and mfp-5) and use those structures to study their mechanics of adhesion, which is then incorporated into a continuum model. We calculate the adhesion energy of the mussel foot protein on a silica substrate, compute the adhesion strength based on results obtained from molecular modeling, and compare with experimental data. Our results show good agreement with experimental measurements, which validates the multiscale model. We find that the molecular structure of the folded mussel foot protein (ultimately defined by its genetic sequence) favors strong adhesion to substrates, where L-3, 4-dihydroxyphenylalanine (or DOPA) protein subunits work in a cooperative manner to enhance adhesion. Our experimental data suggests a peak attachment force of 0.4 ± 0.1 N, which compares favorably with the prediction from the multiscale model of $F_c = 0.21$–0.33 N. The principles learnt from those results could guide the fabrication of new interfacial materials (e.g. composites) to integrate organic with inorganic surfaces in an effective manner.

1. Introduction

The *Mytilidae* is generally known as the family of marine mussels, which are found world-wide in primarily cold sea water (Bayne, 1976). The animals are well known to attach themselves to substrate in water using a bundle of mussel threads (Lee et al., 2011), as shown in Fig. 1. Each thread grows from the muscular tissue ended by an adhesion plaque that adheres to the substrate (Lee et al., 2007a, 2006; Lin et al., 2007). Unlike other marine animals such as barnacles and oysters,

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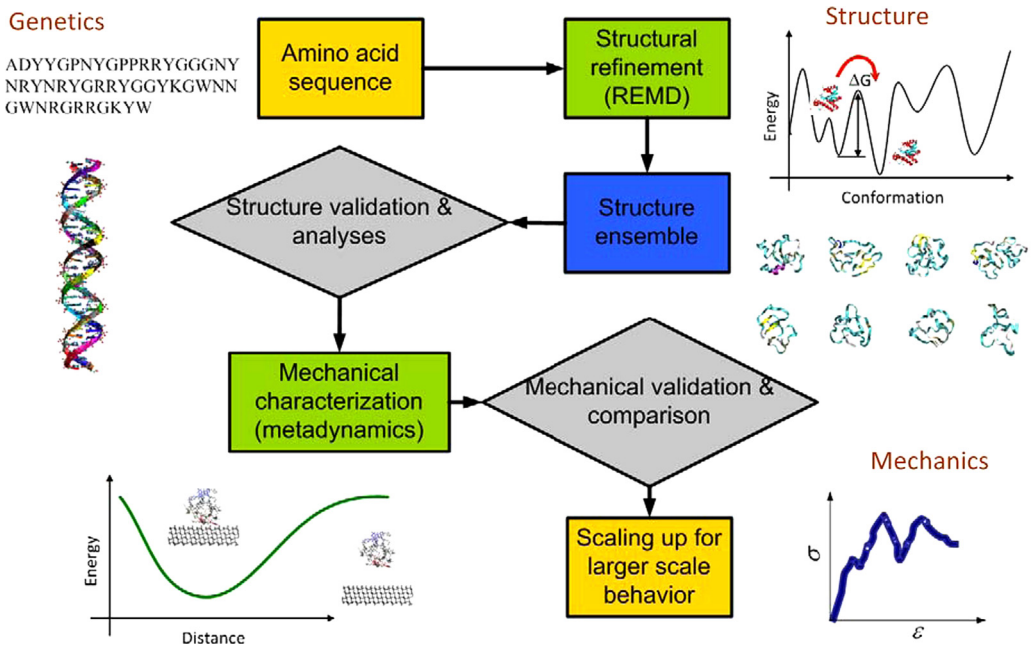

Fig. 1. Schematic of our process, and detailed methods used to link protein sequence with its corresponding molecular structure and mechanics. The method used here is a generic approach that can find many applications in other materials.

which completely fix their bodies or shells to the substrate with a relatively large contact area, mussels suspend and attach to the substrate with several mussel threads (Wiegemann, 2005). Mussels are commonly found attaching to shorelines and ships, subjecting them to mechanical forces caused by the irregular movements of waves (Qin and Buehler, 2013). Hence, the adhesion strength of the mussel thread is important for the animal to survive and thrive in this challenging environment.

It is understood that the strong adhesion of mussel thread relates to its peculiar molecular composition. Although the entire mussel thread contains roughly 25–30 different proteins, only 7–8 different proteins are present in the adhesion plaque (Lee et al., 2011). Six kinds of mussel foot proteins (mfps) make up the plaque, and they share similar characteristics with high concentrations of a specific molecule called L-3,4-dihydroxyphenylalanine, or DOPA. DOPA is derived from the naturally occurring amino acid tyrosine which is modified by the tyrosine hydroxylase enzyme (Silverman and Roberto, 2007). It has been found to have a strong affiliation with almost any type of material surface including Teflon, which was shown in various experimental studies and more recently in molecular modeling (Lee et al., 2007a; Qin and Buehler, 2012c). Many applications have been proposed for this natural molecule (Holten-Andersen et al., 2011; Lee et al., 2002, 2007a; Shao et al., 2009), for example to produce new types of super glues that resist forces of a thousand pounds per square inch, to generate coatings with strong adhesive properties, to incorporate them into soft materials to facilitate self-healing, as well as to improve clinical applications with biocompatibility, such as teeth and bone repair or tissue engineering. It is intriguing to ask how mussel foot proteins, which have widely different sequences, are folded to fully utilize DOPA for adhesion as a larger mechanical unit. This question is critical to fully understand the molecular mechanism of mussel adhesion.

Indeed, a multiscale model of mussel threads is needed to fully understand how adhesion acts synergistically with other material structures and components. This is a critical feature shared by many biomaterials and enables the material to integrate disparate advanced material properties via hierarchical structures. Prominent examples are silk, bone and intermediate filaments (Cranford et al., 2012; Qin and Buehler, 2012a; Qin et al., 2009; Sen and Buehler, 2011). Here, we focus on how the adhesion strength of a single DOPA protein molecule correlates with the molecular structures of mussel foot proteins, and how they combine with the geometry and structure of mussel adhesion plaques to define an impressive adhesion strength. By using multiscale modeling, we reveal the mechanism of synergistic mussel adhesion. Our work may provide a recipe to design the chemistry and structure of new materials towards the invention of improved adhesives.

In this study we apply replica exchange molecular dynamics (REMD) (Sugita and Okamoto, 1999) to predict the folded structures of mussel foot proteins. This technique combines molecular dynamics with the Monte-Carlo method to enable protein folding calculations. We use the structures obtained using REMD to investigate the mechanisms by which mussel foot proteins adheres to silica substrate, and characterize their adhesion properties. The procedure used in our study is summarized in Fig. 1. We utilize the understanding of single-molecule adhesion to predict the adhesion of the plaque surface on a substrate, which can be directly compared with experimental measurement. The results may provide guidance towards designing biocompatible interfacial materials in connecting organic materials to inorganic materials, which could