Quantifying Cooperativity in Mutated Collagen

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ABSTRACT

Many biological systems can be considered coupled systems, arising from the interconnected structure of on (or more) molecular/protein components. An important characteristic of any such "built up" macromolecule is the need for synergistic behavior between the individual components. In nature, this behavior is evident, e.g., the double stranded constitution of DNA is a well-known fact; however, it is the highly cross-linked helical structure that shows potential as a structural material at a nanoscale. Similarly, in a synthetic environment cooperativity has been demonstrated in a small sample, i.e., polyelectrolytes and hydrogen graphene oxides. The integration of different components to functional materials requires an intimate knowledge of the mechanical cooperativity of the system. This cooperativity can be seen as the optimization of contact, adhesion and/or deformation. Mechanical cooperativity can be thought of as the equivalent behavior between components and the system. This concept is well understood; however, the difficulty arises in quantifying cooperativity. We have recently developed metrics based on the gyration tensor of individual molecules to explore the use of universal shape ratios to conclude whether the system is behaving as a cohesive unit. Cooperativity can then be objectively defined by invariants derived from the gyration tensor of each chain. These metrics include the slip (an indication of size), the differential anisotropy (shape configuration), and skewness (orientation of the pair). Here, we apply this framework to a simple tropocollagen molecule using full atomistic molecular dynamics. In a natural state, the triple helix is a highly cooperative macromolecule. By introducing known mutations (e.g., those that result in osteogenesis imperfecta) we track and quantify the change in cooperativity. We then link the change in cooperativity to known effects of mechanical behavior with severity of the mutation, inferring changes in mechanical stability with purely geometric measures. Such a molecular-shape-based analysis can potentially be adapted to assess the health and stability of other biological systems.