Predicting the Flexibility and Rigidity of Proteins: Geometry, Combinatorics, Conjectures, and Algorithms.

Walter Whiteley
Department of Mathematics and Statistics
York University

Abstract

The rigidity and flexibility of proteins is critical to what they do in the body, and how drugs can change this. Both too rigid and too flexibly proteins are the source of diseases in humans and predicting flexibility from a 3-D structural file is an important challenge. We present one computational approach, currently implemented at flexweb.asu.edu, based on the geometric, combinatorial and algorithmic theory of framework rigidity.

We introduce the general problems and methods of rigidity through plane frameworks, with examples and models. We describe the long-standing unsolved problems for frameworks in 3-space as well as the newer solved theory of body hinge structures (also with models). Recent work has refined these spatial theories for proteins through a pair of Molecular Conjectures that provide a basis for fast combinatorial algorithms for this special class of structures. We describe the steps current programs for proteins, from extracting a constraint graph from the geometry and biochemistry of the protein, through the application of these combinatorial rigidity algorithms to predictions of the "snap shot" rigidity and flexibility of a protein. We also describe some extensions to predictions of dynamic paths and other problems.