PiSQRD: a novel variational scheme to identify dynamical domains in proteins

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Motivation

The problem of describing the internal dynamics of proteins in terms of the relative movement of few quasi-rigid domains has several important ramifications. The latter range from the quantitative rationalization of the structure-> function relationship to the improvement of the computational effieciency of the sampling of the conformational space accessible to the protein.

Methods

A novel variational scheme [1] is presented, which identifies an optimal partitioning of a protein's structure exploiting information about its large-scale collective fluctuations. These modes of fluctuation are derived from atomistic molecular dynamics simulations or coarse-grained elastic network models. No contiguity in sequence or space of the amino acids taking part to the rigid domains is enforced. This overcomes limitations related to considering domains consituted of uninterrupted stretches of the primary sequence.

Results

By applying the decomposition scheme to several biomolecules of high biological interest, such as Adenylate Kinase or HIV-1 protease and other members of the hydrolase superfamily, the identification of dynamical domains is shown to provide valuable insight into the functionality of proteins and especially enzymes. The method not only has a physically appealing and transparent formulation, but is also apt for efficient computational implementation. The decomposition algorithm is made freely available to the academic community in the form of a web server [2].

Availability

http://pisqrd.escience-lab.org/

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