A novel indicator for distinguishing biologically relevant interfaces from crystal contacts

Schaerer MA[1], Gruetter MG[2], Capitani G[1]

Motivation

Protein crystals contain two different kinds of interfaces: biologically relevant ones, found in oligomeric proteins and in protein-protein complexes, and non-specific ones, that correspond to crystal lattice contacts. Since structural biologists often tackle molecular objects of considerable complexity, distinguishing biological contacts from crystal contacts can be a non-trivial task. Computational approaches aimed at assigning a given interface as either “biological” or as “crystal contact” are therefore helpful in avoiding wrong interpretations of macromolecular structures and in guiding subsequent biochemical experiments (e.g. mutational studies on the interface assigned as “biological”).

Methods

We present a new indicator, called CRK, which we devised to differentiate biologically relevant interfaces from non-specific ones. CRK carries out the following steps on a protein-protein interface to be analyzed: 1) obtain a set of homologues to the sequences of the proteins that constitute the interface 2) retrieve the corresponding coding sequences and align them based on a multiple alignment of the protein sequences 3) carry out a residue-by-residue Ka/Ks ratio (omega) calculation on the aligned coding sequences 4) partition interface residues into a rim and a core set 5) analyze the omega values of the residues belonging to the two sets to assign the interface as biological or as crystal contact.

Results

CRK was evaluated on different datasets, which are composed of biologically relevant contacts, non-specific ones or of both types. The indicator proved to effectively distinguish the two types of interfaces, with an overall accuracy rate of 88%. CRK is based on different principles compared to current tools for inferring the biological relevance of interfaces, so it is optimally suited for use in combination with them. Moreover, CRK can be employed for validating structures of oligomeric proteins and of protein complexes.

Contact e-mail

guido.capitani@psi.ch

[1] Biomolecular Research, Paul Scherrer Institute, Villigen, CH [2] Institute of Biochemistry, University of Zurich, CH