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Protein Crystallography as a Source of Data on Protein Quaternary Structures

Evgeny Krissinel, Kim Henrick

European Bioinformatics Institute, Hinxton, United Kingdom. E-mail: keb@ebi.ac.uk

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Protein Quaternary Structures (PQS) represent assemblies of protein chains, which are stable in a particular environment. Biological function of many proteins is closely associated with the ability to aggregation or changing the oligomeric state in general. Therefore, PQS are often viewed as Biological Units. Knowing PQS may help to better understand the role of a particular protein in the machinery of life.

Experimental means of PQS identification are very limited. Usually, only assembly composition and size are detectable. On the other hand, theoretical predictions require a reliable docking solution, which is yet to be achieved at affordable computation cost.

At the same time, experiments on X-ray diffraction on protein crystals provide ready docking solutions. It is reasonable to expect that protein assemblies serve as construction blocks during crystallisation, therefore PQS might be recovered from protein crystallography data. Given that about 80% of Protein Data Bank (PDB) entries have been obtained by means of protein crystallography, this unlocks a wealth of biologically important information. However, recovering PQS from crystals is not a straightforward procedure, because, generally, there is no link between PQS and assigned asymmetric units (ASU) or unit cells in PDB.

In this presentation, we outline a procedure for calculating PQS from crystal descriptions given in PDB entries. The procedure is based on exhaustive exploration of crystal contacts and assembly stability analysis in terms of chemical thermodynamics. Our approach also allows one to predict the probable dissociation patterns of protein assemblies. We discuss the role of entropy in PQS formation, which leads to the conclusion that biological significance of protein interfaces cannot be inferred solely from interface properties, and, as a consequence, it cannot be detached from the context of PQS.

The method achieves 89% correct predictions on the benchmark of 218 PDB entries with experimentally verified oligomeric states, published in Ref. [1]. This is higher than in previous attempts (cf. [1,2]), based on different scorings of individual interfaces. Comparison with manual annotation in PDB entries (for most of which no experimental evidence is provided) indicates 80% agreement.

The developed software has been made available for public use as an interactive web-server PISA (Protein Interfaces, Surfaces and Assemblies) at
http://www.ebi.ac.uk/msd-srv/prot_int/pistart.html.

The server comprises a database of precalculated interfaces, surfaces and assemblies for all PDB entries, and allows for analysis of uploaded protein structures. The server provides a wealth of details on interface and PQS properties, developed visualisation options and a facility for database searches for similar structures and interfaces in the whole PDB. The tool may be useful in PQS-related studies, crystal engineering, structure solution, choice of ASU and other related tasks and studies.

[1] Ponstingl, H.; Kabir, T.; Thornton, J. *J. Appl. Cryst.* 36 (2003) 1116.
[2] Henrick, K.; Thornton, J. *Thrends Biochem. Sci.*, 23 (1998) 358.

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Automated structure determination with PHENIX

P.D. Adams

Lawrence Berkeley Laboratory BLDG 64R0121, 1 Cyclotron Road CA 94611 USA, E-mail: PDAdams@lbl.gov

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A new software system called PHENIX (*P*ython-based *H*ierarchical *EN*vironment for *I*ntegrated *X*tallography) has been developed for the automation of crystallographic structure solution [1, 2]. This provides algorithms to go from reduced intensity data to a refined molecular model, and facilitates structure solution for both the novice and expert crystallographer. The user interfaces to PHENIX, the automation features, and the underlying algorithms will be presented along with recent advances in infrastructure and algorithms.

[1] Adams P. D., Grosse-Kunstleve R. W., Hung L.-W., Ioerger T. R., McCoy A. J., Moriarty N. W., Read R. J., Sacchettini J. C., Sauter N. K. and Terwilliger T. C. (2002). *Acta Cryst*. D58, 1948-1954.
[2] Adams P.D., Gopal K., Grosse-Kunstleve R.W., Hung L.-W., Ioerger T.R., McCoy A.J., Moriarty N.W., Pai R.K., Read R.J., Romo T.D., Sacchettini J.C., Sauter N.K., Storoni L.C. and Terwilliger T.C. (2004). *J. Synchrotron Rad.* 11, 53-55.