

Dynamic theory of protein crystallization

Jindrich Hasek¹

¹*Institute Of Biotechnology, Academy Of Sciences Of The CR, Vestec, Czech Republic*
E-mail: hasekj@seznam.cz

Diffraction quality of protein crystals depends on periodicity of its molecular skeleton. Inspection of PDB shows that only 20 % of crystal mass is enough to form a rigid skeleton of protein molecules responsible for diffraction. Protein crystals remind high-tech modern buildings relying on the framed skeleton strong in tension and compression. Therefore, the development of tools enforcing protein molecules to adhere each other in the required unique way is important.

Dynamic theory of protein crystallization (DTPC) describes mechanisms of crystallization process. It is about competition among alternative protein-protein adhesion-modes (PPAM). Crystallographer controls formation of temporary molecular adducts in crystallization solution and manipulates with intermolecular adhesion-modes. Success of crystallization is considered as result of competition between adhesion-modes between all components of crystallization solution. The criterion for success is a rigid and regular protein skeleton in permanent equilibrium with solution in crystal.

Principle of a single dominating adhesion-mode (PSDAM) is the key requirement for diffraction quality as it enforces strict periodicity of crystal. It should be respected in any crystallization method. It is a basis for the controlled design of the protein crystal architecture.

Large surface of proteins offers variety of adhesion-modes. Dominating adhesion-mode is combined with other crystallographically compatible adhesion-modes to form solid state. Any molecule deposited in crystallographically incompatible adhesion-mode induces deformation of periodicity and brings danger of spreading the error destroying diffraction ability of the crystal.

Crystallographer has several rational ways how suppress improper deposition of molecules leading to "amorphous" precipitant. The first option is an application of protein-surface active molecules (PSAM) [1].

These molecules with specific protein-sticky properties form temporary adducts possessing different adhesion-modes than the original protein. In practice PSAM work mostly as a suppressors of specific adhesion-modes (protein-surface shielding agents PSSA), but sometimes also as the adhesion supporting agents.

Crystallographer controlling architecture of the protein crystal via manipulating with adhesion forces in solution or by mutations of protein surface should set crystallization conditions to enhance the affinity of the dominating adhesion-mode and/or to suppress probability of all the crystallographically incompatible adhesion-modes.

Conclusions of dynamic theory agree with large-scale tests of crystallization screens performed in several laboratories. New proposals for former protein crystallization methods and screens following from PTPC and PSDAM will be summarized separately for:

1. crystallization controlled by chemical composition of solution,
2. choice of mutation sites in crystallization based on chemical or bio-chemical engineering of the target protein (lysine methylation, entropy reduction),
3. choice of homologs for crystallization screening.

DTPC, PSDAM and PSAM presented here offer more meaningful interpretation of empirically derived rules for protein crystallization. Understanding the adhesion modes brings better control over crystal growth and resolves many otherwise enigmatic phenomena met in practice.

Supported by BIOCEV-CZ.1.05-1.1.00-02.0109, RVO86652036

[1] Hašek, J. (2011) Z.Kristallogr. 28, 475-480; Hašek, J. et al (2006) Z.Kristallogr. 23, 613-619; Hašek, J. et al, (2011) J.Synchr.Radiation 18, 50-52.

Keywords: [dynamic theory of crystallization](#), [protein-surface active compounds](#), [protein-crystal architecture](#)