Due to their large surface, the protein molecules can form several different protein-protein adducts in solution as a rule. When the probability of the “dominant protein-protein interaction” is several orders higher than the probability of any other protein-protein interaction, than the crystal grows with a small number of stacking faults. However, when the probability of some “incompatible protein-protein adhesion mode” increases (e.g. to 1 %), it leads to significant increase of stacking faults (seriously lowering diffraction quality of crystal), or to a crystallization failure. Special “additives” in crystallization solution suppress probability of the unwanted protein-protein adhesion modes, and increase thus a range of crystallizable proteins and also their diffraction quality. The theory of “Protein Surface Active Molecules” (PSAM) [1,2,3] clarifies why some additives work positively, other negatively, why combination of two positive ingredients can be negative, etc. The theory describing the protein crystallization as a regular deposition of short-life-time protein-PSAM complexes stresses the role of molecules exhibiting highly specific adhesion to the specific protein surface patches active in crystallization process. These “sticking molecules” mutate differently the kinetics of different protein-protein interactions driving the crystallization process. Proper choices of PSAM active in formation of “incompatible protein-protein interactions” eliminate deposition on the growing crystal surface in the unwanted adhesion modes. It can be decisive for success of protein crystallization in many cases. A combination of more “additives” in solution can act positively in synergy but also can lead to a complete failure depending on the specificity of the protein-adhesion properties. The positive effect appears only if the “additive(s)” form a unique (and structurally well-defined) semi-stable adduct with protein molecules in solution and when the adhesion force of the “additive(s)” is sufficiently low to allow it (them) to leave the protein surface in the course of crystallization. The concept of crystallization of “protein adducts” crumbled during their stacking into the crystal lattice may be more complicated for imaging, but it provides an explanation of many enigmatic crystallization phenomena, provides better control over the crystal quality and over preparation of different crystal forms. The crystallization kinetics of protein-PSAM adducts differ largely from the one of pure protein. Knowing the rules governing formation of protein-PSAM adducts and their adhesion properties, one can choose the optimal adhesion modes dominating the crystallization by a careful adjustment of the crystallization conditions. This way the PSAM are used (1) for increasing the number of crystallizable proteins, (2) for suppressing the competitive adhesion modes incompatible in a single crystal form (minimizing thus probability of the stacking faults which are the main source of lower quality of most protein crystals), (3) for selection of the optimal polymorph. It is important because the polymorph with lower water contents in crystal exhibits statistically much better diffraction quality then the other polymorphs. The project is supported by GA CR 310/09/1407 and MŠMT OPVK CZ.1.07/2.3.00/30.0029


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