

# **Phenomena of protein crystallization**

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In the first half of the 19th century, scientists had discovered that proteins can be crystallized. For the next hundred years, this process was mainly used for protein isolation and purification from natural substances. The first X-ray diffraction experiment on a protein crystal was performed in 1934. Twenty five years later, the first protein crystal structure was published. The development of macromolecular crystallography created a big need for good quality protein crystals.

Protein crystals possess unique properties. They are composed of protein macromolecules surrounded by a solvent (the solvent fraction is usually 50%, but varies from 20% up to 90%). Proteins crystallize only in chiral space groups with proper symmetry, with a fraction of highly symmetrical systems larger than that of small molecule crystals. Proteins preserve their biological activity in crystalline form. The number of interactions inside of protein molecules is a hundred times greater than the number of intermolecular contacts responsible for crystal assembly, which causes protein crystals to be very fragile.

The process of macromolecular crystallization is more complex in comparison with crystallization of small molecule compounds. During this process, protein structure, stability and activity have to be maintained. A number of physical, chemical and biochemical factors influence the protein crystallization process. There are many ways to achieve a supersaturated protein solution, depending on which protein crystallization techniques are utilized. For some of the techniques, it is possible to use robots to set up the crystallization. The currently used methods of protein crystallization are simple, reliable, and repeatable, which allow setting a hundred different conditions from a few milligrams of a protein sample.

Protein crystallization can be divided into two stages. The goal of the first stage is to establish initial crystallization conditions. During the second, the conditions are optimized to provide crystals of size and quality suitable for an x-ray diffraction experiment.

The knowledge about protein crystallization has greatly increased in the last few decades, but the very large number of factors responsible for that process and the variety of proteins make growing well diffracting protein crystals more of an art than a craft.