How to... enhance the success of protein crystallization

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Protein crystals play a pivotal role in facilitating rational drug design and other industrial applications. The past decade has seen momentous progress in the miniaturisation, automation and analysis of crystallization experiments. However, production of high quality crystals still presents a major barrier to structure determination; it is often the case that no crystals are formed at all or that clusters of useless crystals are obtained. There is no ‘magic bullet’ that will guarantee the yield of useful crystals, hence rational approaches leading to the development of new and improved technologies for attaining high quality crystals is of crucial importance to progress [1,2]. This talk will present strategies for increasing the chances of success and highlight a variety of practical methods that have led to successful crystallization when standard crystal growth procedures had failed. These methods involve active influence and control of the crystallization environment in order to lead crystal growth to the desired result [e.g. 3-6]. Many of the techniques can be automated and adapted to high throughput experiments and several have been patented and commercialised.

References

Keywords: proteins, crystallization, nucleation, protein crystallization

Toward the mitigation of growth rate dispersion through pretreatment of seed crystals

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Crystals grown under identical conditions are found to have different growth rates independent of size, which leads to an often undesired broadening of the particle size distribution. Multiple potential causes of this phenomenon, known as growth rate dispersion (GRD) in crystallization literature, have been identified and are used to model systems that exhibit this phenomenon. Namely, differences in the number and structure of dislocations in crystals, lattice strain, and surface roughness are plausible candidates for GRD[1]. Recently, a modeling approach was proposed for the observed GRD of β L-glutamic acid in water that takes into account both non-spherical particle shape and the non-static nature of a generic growth affecting property, both on the level of single crystals and that of particle ensemble; this model was successfully used to quantitatively describe multiple sets of experiments subjected to a range of operating conditions[2]. In that work, it was hypothesized that performing pretreatments like temperature cycling on seed crystals would lead to a reduction of GRD due to refacetting, or healing of the surface of crystals; however, the efficacy of these methods have not yet been studied in detail. Populations of β L-glutamic acid crystals subjected to temperature cycles (or not) are characterized in terms of particle size and shape distribution using an in-house built stereoscopic imaging setup and in terms of growth of single crystals using a hot-stage microscopy setup. A deeper insight on the effect of temperature cycling on the surface of the treated crystals will be provided by surface analysis using surface characterization methods. The studies performed on single crystals and particle ensemble along with surface characterization of these crystals pre- and post-temperature cycling will shed more light on the underlying consequences of GRD and will provide a framework to test the validity of the model that was developed previously to describe GRD.

References:

Keywords: crystallization, growth rate dispersion, seed crystal pretreatment, temperature cycling