Protein crystallization in a new meso oscillatory flow reactor

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Protein crystallization is best known for its use in protein three-dimensional (3D) structure determination by X-ray diffraction. On the other hand, little systematic know-how exists for protein crystallization as a process step [1]. However, protein crystallization offers great potential to be used for separation and formulation applications on an industrial scale [1,2]. Purification of proteins via crystallization may offer significant cost reductions compared to conventional downstream processing techniques such as chromatography. Moreover, protein crystals have a longer storage life and greater purity compared to the dissolved form.

Protein crystallization as a process step requires rapid and quantitative crystallization. However, most of the studies in protein crystallization had been focused on producing high quality crystals obtained by slow crystallization from small volumes under static conditions. But, crystallization under static conditions is often diffusion-limited, leading to rather long process durations and/or low yields. Hence, protein crystallization under flow conditions has attracted attention with the capability to improve the convective protein transport, reducing the crystallization time and improving yield.

In this work, we propose to investigate protein crystallization in a new meso oscillatory flow reactor (OFR) based on Reis work [3]. It consists of a glass jacketed tube provided with smooth periodic cavities (SPC). The reactor has an approximate volume of 4.5 mL and is operated under oscillatory flow mixing, controlled by the oscillation frequency and amplitude. Representative experiments can be performed in the mesoreactor and provide important information for industrial-scale crystallization, since only small amounts of protein are often available and hence experimentation on the liter scale is ruled out. The work will first be focused on the study of favourable crystallization conditions for a model protein, lysozyme. Afterwards, it will include the assessment of the effects of the degree of agitation on lysozyme crystallization. The mesoreactor performance will be compared with conventional systems, namely stirred tanks, for lysozyme crystallization studies reported in the literature.

References:

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