Improving the Growth of Biomacromolecular Crystals for Neutrons and X-rays

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The bottleneck in biomacromolecular crystallography still remains the growth of single crystals with good crystal quality and size. Whereas development of third generation synchrotron sources has allowed X-ray protein structures to be solved from crystals of a few 10^{-4} mm^3, a major hurdle to neutron protein crystallography is that unusually large crystals (~1mm^3) are required to compensate for the weak flux of available neutron beams [1].

We have invented a novel method for the crystallization of proteins allowing alteration and optimisation of the conditions in order to get crystals that are appropriate for X-ray and neutron diffraction analysis. We propose a rational physico-chemical approach of crystallization based on knowledge of the phase-diagram [2]. We have constructed a device, which enables the phase diagram to be investigated, the nucleation and crystal growth of biological macromolecules to be controlled, and the solubility of seeded H/D-labelled biological macromolecule crystals to be manipulated. This semi-automated crystallization tool is also intended for *in situ* observation by optical microscopy and allows sequential image acquisition, processing and storage. We report here our first experimental results obtained with “real” protein systems.

[1] Myles D.A.A., Bon C., Langan P., Cipriani F., Castagna J.C., Lehmann M.S., Wilkinson C., *Physica B,* 1998, **241-243**, 1122. [2] Budayova-Spano M., Lafont S., Astier J.P., Ebel C., Veesler S., *J. Cryst. Growth*, 2000, **217**, 311.

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