NEXTALIS: CRYSTALLISATION METHODOLOGIOES FOR NEUTRONS, SYNCHROTRONS, AND FELS

Leading beneficiary: ILL

Partners: ILL, ESRF, Douglas instruments, CFEL, Imperial College

Estimated budget (in person months, other direct cost) and tentative distribution per partner

ILL: 72 ESRF: 36, DI: 36, CFEL: 36, IC: 36

Abstract of your innovative activity:

Protein crystallography with neutrons faces a special challenge – that of securing suitably sized deuterated crystals. Crucial developments for deuteration have occurred over the recent past such that the crystal volumes needed are now a tenth of the what was required previously. At the time of the deuteration development, which has impacted so strongly on all areas of neutron structural biology, it seemed absurd to have to make the case that the cost of a single instrument's beamtime over just *one month* easily justifies making every reasonable investment in sample preparation; it turned out to be very difficult to win the case for deuteration, and it took a long time. For neutron crystallography the impact has been very strong but it has also been clear for some time that in order to get the best out of instruments such as D19 and LADI-III, a clear effort must be made for large crystal growth. There is no empirical reason why small crystals cannot be made to grow larger – it is simply a matter of spreading the net of conditions wide enough. Indeed the X-ray community were in rather the same situation themselves before the advent of robotic technologies some 15-20 years ago. Their projects, rather like the neutron ones of today, were powered by students and postdocs painstakingly setting up conditions manually over years. Now protein goes to robots that rapidly screen hundreds of conditions while research staff continue with other tasks – occasionally checking crystallisation from their desktop computers. An equivalent strategy for large crystal growth is possible but it requires development and a reasonable level of commitment by the institutes involved. A decisive effort in this area for neutrons will impact on ILL, ISIS, FRM-II, ESS.

Paradoxically, the X-ray world now faces a inverse problem. The power of synchrotron sources and in particular that of FELS (eg LCLS at Stanford) now means that X-ray crystallographers need large supplies of crystals that can be made consistently *small*. Despite small crystals being the early-day scourge of macromolecular crystallography, it turns out to be remarkably difficult to obtain small crystals in large quantities and the X-ray scientists now, for completely orthogonal reasons, face crystallogenesis problems that require many of the same sorts of development needed by the neutron crystallographers. FEL scientists at the LSLS, for example, need similar quantities of crystals by volume as the largest neutron crystals.

This JRA will bring together five partners that between them cover neutrons, SR, FELs, a company that deals with crystallisation robotics, and a world-renowned expert in crystallisation at Imperial College. Tasks will be arranged with the goals that are focused on automated approaches for both large crystal growth and batched nano-crystal growth.