whatever means has been in focus. A dramatic step forwards was due to Ada Yonath 1980 when she managed to get the first crystals of ribosomal subunits. Numerous improvements of methodology and crystals led to the first structural results 1998. Year 2000 high resolution structures of both subunits became available and the year after a medium resolution structure of the whole ribosome. This has made the whole field flourish both biochemically and structurally like for all fields where the central molecules have been clarified by crystallography.

KN-6

The European spallation source ESS. Colin Carlile (Lund/SE)
E-Mail: colin.carlile@esss.se

KN-7

From hot to cool and more for less: new developments for Structural Biology. Elspeth F.Garman, *Department of Biochemistry, University of Oxford, South Parks Road, OXFORD, OX1 3QU, U.K.*
E-mail: elspeth.garman@bioch.ox.ac.uk

Structural biology relies on X-ray crystallography to provide much of the three dimensional information on macromolecules that informs biological function. To enable problems not previously accessible to structure solution to be tackled, improved methods must be developed. A notable example of this has been the progress in finding protocols to cryocool protein crystals prior to 100K data collection to reduce the rate of radiation damage by around a factor of 70 compared to that at room temperature (RT): from hot to cool and more for less. Radiation damage to the sample is an inherent problem when utilising ionising X-radiation in macromolecular crystallography (MX), and it is now known that radiation damage can also be a limiting factor for MX at 100K [1]. Following our measurement of 30 MGy (1 Gy =1 J/kg energy absorbed) for the experimental dose limit for 100K [2] protein crystals, we tried to determine a limit for RT samples. The unexpected discovery of an RT inverse dose rate effect over a limited dose rate range [3] led us to search for RT scavengers [4], which in turn has elucidated the radiation chemistry induced in protein crystals when irradiated at 100K. Current ongoing methods investigations that will be described include studies of 100K and RT radiation damage in macromolecular crystals in order to inform both our understanding and putative mitigation strategies, and the trace elemental analysis of liquid and crystalline proteins using microPIXE (particle induced X-ray emission), allowing determination of their stoichiometric ratio to an accuracy of between 10 and 20% [5].

[1] Ravelli, R.B.G.; Garman E.F *Current Opinion of Structural Biology* 2006, 16, 624-629. [2] Southworth-Davies, R.J.; Medina, M.A.; Carmichael, I.; & Garman, E.F. *Structure* 2007, 15**,** 1341-1351. [3] Owen, R.L.; Rudiño-Piñera, E.; Garman, E.F. *Proc. Nat. Acad. Sci.* 2006, 103, 4912-4917. [4] Barker, A.I.; Southworth-Davies, R.J.; Paithankar, K.S.; Carmichael. I.; Garman, E.F. *Journal Sync Rad.* 2009**,** 16, 205-216. [5] Garman, E.F.; Grime, G. *Progress in Biophysics and Molecular Biology* 2005, 89/2, 173-205.

Keywords: macromolecular crystallography methods, radiation damage, PIXE.

KN-8

Single Crystal Diffraction Studies at Multimegabar Pressures. Malcolm McMahon, *SUPA, School of Physics & Astronomy, and Centre for Science at Extreme Conditions, The University of Edinburgh, UK.*
E-mail: mim@ph.ed.ac.uk

By the late 1990s, it was clear that the structural complexity induced in simple materials by compression was such that powder-diffraction methods were no longer able to solve complex structures being observed. While single-crystal techniques offer the ability to solve such structures, attaining the necessary high-quality samples at pressures above 20 GPa, perhaps after passing though one or more phase transitions, is extremely difficult. But the remarkable behaviour of the alkali metals Li and Na at extreme pressures, coupled with techniques developed at the SRS and ESRF synchrotrons, has enables us to push single-crystal techniques first to 100 GPa [1] and, most recently, to 145 GPa [2]. We have found previously unimagined structural complexity in both Na and Li [3], and have also been able to collect high-quality data from weakly scattering samples such oxygen [4] and nitrogen [5], including at both high- and low-temperature studies.
In this talk I will review both the new techniques, and the results we have obtained recently on these simple systems. I will also look to the future, and give some pointers as to the kind of crystallographic experiments that might be conducted on the next, "4th", generation of light sources.

[1] McMahon, M.I.; Gregoryanz, E.; Lundegaard, L.F.; Loa, I.; Guillaume, C.; Nelmes, R.J.; Kleppe, A.K.; Amboage, M.; Wilhelm, H.; Jephcoat, A.P.; *Proc. Nat. Acad. Sci.* 2007 104, 17297. [2] Lundegaard, L.F.; Gregoryanz, E.; McMahon, M.I.; Guillaume, C.; Loa, I.; Nelmes, R.J.; *Phys. Rev. B* 2007 79, 064105. [3] Gregoryanz, E.; Lundegaard, L.F.; McMahon, M.I; Guillaume, C.; Nelmes, R.J.; Mezouar, M.; *Science* 2008 320, 1054. [4] Lundegaard, L.F.; Guillaume, C.; McMahon, M.I.; Gregoryanz, E.; Merlini, M.; *J. Chem. Phys*. 2009 130, 164516. [5] Stinton, G.W.; Loa, I.; Lundegaard, L.F.; McMahon, M.I.; *J. Chem. Phys*. 2009 131, 104511.

Keywords: high-pressure crystallography, synchrotron radiation, crystal structure determination

KN-9

Symmetry breaking in complex molecular assemblies. Jürg Hulliger, *Department of Chemistry and Biochemistry, University of Berne, Switzerland*
E-mail: juerg.hulliger@iac.unibe.ch

A mechanism leading to effects of symmetry breaking in the solid state results from the fact that at the nutrient-crystal interface incoming building blocks interact under the influence of a lower symmetry [1] than in the bulk. In case the attachment state shows kinetic stability, symmetry breaking in particular growth sectors can occur. A process most investigated during the last ten years [2, 3] is 180° orientational disorder of incoming dipolar molecules. Because of selective recognition at growing surfaces, this kind of symmetry breaking can lead to polar property formation. The lecture is reviewing the field, including examples from supramolecular crystals, single component and solid solution molecular materials. Because of generality, the theory applies also to the formation of polar tissues [4].

[1] C. Gervais; J. Hulliger; *Cryst. Growth Design*, 2007, 7, 1925. [2] J. Hulliger; H. Bebie; S. Kluge; A. Quintel, *Chem. Mater.*, 2002, 14, 1523. [3] J. Hulliger, *Chem. Eur. J.*, 2002, 8, 4578. [4] J. Hulliger, *Biophys. J.*, 2003, 84, 3501.

Keywords: crystals, defects, symmetry

KN-10

The Crystallography of Piezoelectric Perovskites: Domains, Disorder and Disagreements.

Pam Thomas, *Department of Physics, University of Warwick, Coventry CV4 7AL, UK*
E-mail: p.a.thomas@warwick.ac.uk

Piezoelectric materials are of enormous importance for a wide range of technological applications from medical imaging to energy harvesting. The industry leader is currently the well-known perovskite solid-solution lead zirconate titanate, PbTixZr1-xO3 (PZT). However, environmental legislation dictates that technological materials should become lead-free in the coming decade – hence, there is an urgent need to find alternatives. To date, the majority of studies have focused on other perovskite solid solutions such as sodium bismuth titanate ($Na_{0.5}Bi_{0.5}TiO_3$, NBT[1]) complexed with barium titanate ($BaTiO_3$, BT) to form NBT-BT or potassium niobate ($KNbO_3$, KN) complexed with sodium niobate ($NaNbO_3$) to form KNN [2]. In making these solid solutions, researchers in lead-free materials are seeking to replicate a key feature of PZT, namely that the phase diagram possesses a special transition region at x=0.48 near to which the piezoelectric properties are massively enhanced. The boundary, which is nearly temperature independent (a technologically advantageous feature) marks a rather abrupt change in the long-range crystal structure, and is termed a morphotropic phase boundary (MPB) after Jaffe *et al* [3] in 1955. For many years, it was understood that this transition was from rhombohedral (R) symmetry on the Zr-rich side to tetragonal (T) symmetry on the right-hand side. The work of Noheda *et al* [4] invoked the presence of an interim monoclinic phase, which appeared neatly to resolve the questions around how a transition from space group *R3m* to *P4mm* could take place smoothly *via* an interim *Cm* subgroup. However, controversy continued, with some accepting the existence of the *Cm* phase, others still supposing a coexistence of *R* and *T* phases, but expressed as nanoscale domains visible only in TEM studies (the so-called adaptive phases model). Still others questioned the whole notion of an MPB at all, postulating that the local scale symmetry of the material was always monoclinic right across the phase diagram so that at on this length-scale, there was not a boundary at all.
In this lecture, I will review the controversies surrounding the study of this (apparently unique) phase boundary in PZT in the context of the last decade of research on lead-free alternatives materials, including our own work on members of the NBT and KNN families. Using the results of combined techniques to look at local structure (NMR and x-ray diffuse scattering), domain structure (optical and electron microscopies, high-resolution diffraction) and crystal structure (x-ray and neutron diffraction), I will discuss to what extent the properties of PZT have been successfully replicated in lead free materials to date and look at the role of the "MPB" in producing large piezoelectric effects – must we have it or can we manage without?

[1] Jaffe B., Roth R.S., Marzullo S., *J. Res. Natl. Bur. Stand.* 1955, 55, 239 [2] Noheda B., Cox D.E., Shirane G., Guo R., Jones B., Cross L.E., *Phys. Rev. B* 2000 63, 014103 [3] Jones G.O., Thomas P.A., *Acta Cryst.* 2002 B58(2), 168-178 [4] Baker D.W., Thomas P.A., Zhang N., Glazer A.M. *Appl. Phys. Lett.* 2009, 95, 091903

Keywords: piezoelectrics, lead-free materials, crystallography

KN-11

Structural studies of influenza polymerase: implications for the mechanism of cap-snatching, host adaption and anti-viral drug design.

Dr. Stephen Cusack, *EMBL Grenoble Outstation, European Molecular Biology Laboratory, 6 rue Jules Horowitz, BP181, 38042 Grenoble Cedex 9, France*
E-Mail:cusack@embl-grenoble.fr

Influenza virus polymerase transcribes and replicates the viral RNA genome within the context of a ribonucleoprotein complex that has been hitherto remarkably intractable to high resolution structural analysis. As a result many aspects of the detailed mechanism of action of the polymerase remain obscure, despite years of study. However in the last two years, crystal structures of independent domains covering roughly half of the heterotrimeric polymerase have been determined (1). These results will be reviewed with a particular focus on the mRNA cap-binding (2) and endonuclease domains (3), critical for the unique cap-snatching mechanism of influenza viral mRNA transcription. Implications for influenza polymerase assembly (4,5), transcription and host adaptation (5,6) will be discussed as well as the new impetus given to structure-based anti-influenza drug design targeting the polymerase. Finally, structural data will also be presented on the endonuclease domain of another family of cap-snatching viruses, the bunyaviruses.

[1] Towards an atomic resolution understanding of the influenza virus replication machinery. Ruigrok RW, Crépin T, Hart DJ, Cusack S. Curr Opin Struct Biol. 2010 Jan 8. [Epub].
[2] The structural basis for mRNA cap-binding by influenza virus polymerase subunit PB2. Delphine Guilligay, Franck Tarendeau, Patricia Resa-Infante, Rocío Coloma, Thibaut Crépin, Rob W. H. Ruigrok, Juan Ortin, Darren J. Hart and Stephen Cusack. *Nat Struct Mol Biol*. 2008, 15(5):500-6.
[3] The cap-snatching endonuclease of influenza virus polymerase resides in the PA subunit. Alexandre Dias, Denis Bouvier, Thibaut Crépin, Andrew A. McCarthy, Darren J. Hart, Florence Baudin, Stephen Cusack and Rob W. H. Ruigrok. *Nature* 2009 458(7240):914-8. Epub 2009 Feb 4.
[4] Nuclear import and assembly of the influenza A virus RNA polymerase studied in live cells by Fluorescence Cross Correlation Spectroscopy. Huet S, Avilov SV, Ferbitz L, Daigle N, Cusack S, Ellenberg J. J Virol. 2010 Feb;84(3):1254-64. Epub 2009 Nov 11.
[5] Structure and nuclear import function of the C-terminal domain of influenza virus polymerase PB2 subunit. Tarendeau F, Boudet J, Guilligay D, Mas PJ, Bougault CM, Boulo S, Baudin F, Ruigrok RW, Daigle N, Ellenberg J, Cusack S, Simorre JP, Hart DJ. *Nat Struct Mol Biol*. 2007, 14(3):229-33.
[6] Host determinant residue lysine 627 lies on the surface of a discrete, folded domain of influenza virus polymerase PB2 subunit. Franck Tarendeau, Thibaut Crépin, Delphine Guilligay, Rob W. H. Ruigrok, Stephen Cusack and Darren J. Hart. *PLoS Pathog*. 2008, 4(8):e1000136.