carbohydrate recognition domains, locating both sugar binding sites face to face. Sequence evidence suggests other tandem-repeat galectins have the same arrangement. We show that the galectin domain binds carbohydrates containing lactose and N-acetyl-lactosamine units, and we present structures of the galectin domain with lactose, N-acetyl-lactosamine, 3-aminopropyl-lacto-N-neotetraose, and 2-aminoethyl-tri(N-acetyl-lactosamine), confirming the domain as a bona fide galectin domain.

Bacteriophages are the most numerous organisms in the biosphere. In spite of their biological significance and the spectrum of potential applications, little high-resolution structural detail is available on their receptor-binding fibres. We present the crystal structure of the receptor-binding tip of the bacteriophage T4 long tail fibre, which is highly homologous to the tip of the bacteriophage lambda side tail fibres. This structure reveals an unusual elongated six-stranded anti-parallel beta-strand needle domain containing seven iron ions coordinated by histidine residues arranged co-linearly along the core of the biological unit. At the end of the tip, the three chains intertwine forming a broader head domain, which contains the putative receptor interaction site. The structure reveals a previously unknown beta-structured fibrous fold, provides insights into the remarkable stability of the fibre, and suggests a framework for mutations to expand or modulate receptor-binding specificity.

Keywords: host cell attachment, beta-structure, tandem-repeat galectin

MS.29.3

Acta Cryst. (2011) A**67,** C76

The cell fusion proteins of the "FF" family are homologous to class II viral fusion proteins

Félix A. Rey,[a] Jimena Perez-Vargas[a], Thomas Krey,[a] Benjamin Podbilewicz,[b] *[a]Institut Pasteur, CNRS URA 3015, Unité de Virologie Structurale, 75015, Paris, (France). [b]Department of Biology, Technion - Israel Institute of Technology, Haifa, 32000, (Israel).* E-mail: rey@pasteur.fr

Structural studies of viral membrane fusion proteins have provided key information to understand the process of virus-cell membrane fusion, which is important during virus entry. Similar principles were inferred from structural studies of SNARE proteins, responsible for fusion of intracellular vesicles with their target membranes within the cell. No data are currently available on cellular fusion proteins responsible for cell-cell fusion, a process that is of high relevance during developmental biology and organogenesis.

We report here the crystal structure of a cell fusion protein from the nematode *C. elegans*, termed "Eff-1", where it plays a key role during organogenesis. This protein is the prototype of the "Fusion Family" (FF) of proteins recently described. The structure provides unanticipated evolutionary links with the class II viral fusion proteins observed in regular enveloped viruses. Eff-1 folds as three beta-sheet-rich domains, assembled as a trimer organized as in the post-fusion structures of the alphaviruses and flaviviruses envelope proteins. This type of fusion proteins had so far been observed only in regular envelope viruses, where they make an icosahedral coat completely enclosing the viral membrane in their pre-fusion form. This presentation will describe the structure and provide a model for its putative mechanism of action.

Keywords: cell-cell fusion, developmental biology, structural biology, class II viral fusion proteins

MS.29.4

Acta Cryst. (2011) A**67,** C76

Structural basis for the inhibition of apoptosis by Epstein-Barr virus BHRF1

Marc Kvansakul,[a,b] Andrew H Wei,[b] Jamie I Fletcher,[b] Simon N Willis,[b] Lin Chen,[b] Andrew W Roberts,[b] David CS Huang,[b] Peter M Colman,[b] *[a]La Trobe Institute of Molecular Sciences, La Trobe University, Melbourne, Victoria, (Australia). [b]The Walter & Eliza Hall Institute of Medical Research, Parkville, Victoria, (Australia).* E-mail: m.kvansakul@latrobe.edu.au.

Viruses must evade host apoptotic defences to ensure their own survival. Despite the complexity of mammalian cell death processes, viruses have evolved successful mechanisms for subverting the apoptotic machinery, including homologs of the mammalian pro-survival protein Bcl-2. The ubiquitous Epstein-Barr virus (EBV), a member of the gamma-herpesviruses, infects the epithelium of the oropharynx and resting B cells. Acute infection manifests as infectious mononucleosis or glandular fever, whereas chronic EBV-associated transformation is associated with Burkitt's lymphoma, Hodgkin's disease and nasopharyngeal carcinoma. EBV BHRF1 is a sequence, structural and functional homologue of Bcl-2, however its mechanism of action remained unclear. Previous structural studies indicated that BHRF1 lacks an accessible BH3 binding groove, and shows only weak affinity for BH3 ligands. We show that BHRF1 is a potent inhibitor of apoptosis, and confers chemoresistance in mouse lymphoma models similar to mammalian Bcl-2. Next, we determined the crystal structures of BHRF1 in complex with Bim and Bak BH3 peptides and show that in contrast to previous predictions, BHRF1 interacts with these proteins in a manner similar to its mammalian counterparts. Structure-based mutagenesis enabled us to address the molecular mechanisms underlying BHRF1 activity. We demonstrate that BHRF1 can prevent Bak activation by direct interaction, but prevents Bax activation indirectly by sequestering the BH3-only proteins Bim, Puma and tBid. Unlike mammalian pro-survival proteins, BHRF1 does not interact with the selective/sensitizer BH3-only proteins. These studies indicate that BHRF1 might be targeted by small molecule mimetics of BH3-only proteins.

[1] M. Kvansakul, A.H. Wei, J.I. Fletcher, S.N. Willis, A.W. Roberts, D.C. Huang, P.M. Colman, *PLoS Pathogens* **2010,** *6(12):*e1001236.

Keywords: viral, cancer

MS.29.5

Acta Cryst. (2011) A**67,** C76-C77

Crystal structure of the N-terminal domain of HIV-1 capsid in complex with an assembly- inhibiting nanobody

LuisCastillo,[a] JonasHelma,[b]PabloGuardado,[c]UlrichRothbauer,[b]Felix Rey,[c] Heirich Leonhardt,[b] Hans-Georg Kräusslich,[a] *[a]Department of Infectious Diseases, Virology, Universitätsklinikum, Heidelberg, (Germany). [b]Biozentrum, Ludwig Maximilians Universität, München, (Germany). [c]Unité de Virologie Structurale, Institut Pasteur, Paris, (France).* E-mail: luis.castillo@med.uni-heidelberg.de

HIV-1 maturation from a non-infectious into an infectious agent is accompanied by morphological changes in its capsid shell, which undergoes a protease-mediated conversion from a spherical into a conical shape; therefore capsid assembly is a target for development of antiviral drugs. Here we report the crystal structure at 2.0 Å resolution of the N-terminal domain of HIV-1 capsid in complex with a nanobody capable of inhibiting mature and immature particles in vitro.

The structure reveals that the nanobody binds a hydrophobic helix through its CDR1 and CDR3 loops, abolishing a well characterized interaction between the capsid N- and C- terminal domains. Interestingly, the interaction forms a hydrogen bond network with capsid residue N73, which is associated with host antiviral restriction. Structural alignments of this complex with high resolution crystal structures of pentameric and hexameric capsid building blocks suggests that upon binding, the nanobody sterically prevents the incorporation of either pentamers or hexamer to the mature capsid lattice.

Keywords: HIV-1, capsid, assembly

MS.30.1

Acta Cryst. (2011) A**67,** C77

Modeling diffuse scattering using evolutionary algorithms and super computing

Tara Michels-Clark,[a,c] Michal Chodkiewicz,[b] Christina Hoffmann,[c] Jürg Hauser,[d] Anthony Linden,[b] Vickie Lynch,[c] Thomas Weber,[e] Hans-Beat Bürgi,[b,d] [a]*University of Tennessee, (USA).* [b]*University of Zürich, (Switzerland).* [c]*Oak Ridge National Laboratory, Oak Ridge, TN, (USA).* [d]*University of Bern, (Switzerland).* [e]*ETH Zürich, (Switzerland).* E-mail: tmichels-clark@ion.chem.utk.edu

Materials possessing disorder within their crystalline structure often exhibit unusual and potentially useful properties. An elucidation of the local structure, rather than the average structure, is crucial to understanding the behavior of such materials. Disorder manifests itself as diffuse scattering in a diffraction experiment, but the measurement and interpretation of diffuse scattering is far from routine. It requires high-performance computing for carrying out Monte Carlo and Differential Evolution (DE) modeling techniques, high-flux radiation sources and user-friendly modeling software. With the capabilities at ORNL of high performance computing and the advent of the new $1.4bn Spallation Neutron Source, we are now exquisitely positioned to quantitatively model the disorder leading to diffuse scattering. An international collaboration was formed between the Universities of Zürich and Bern, the ETH Zürich and the Oak Ridge National Laboratory to develop a new general methodology for modeling diffuse scattering, including the Zürich Oak Ridge Disorder Simulation (ZODS) software, which will be discussed in another contribution.

Our first test case is tris(bicylco[2.1.1]hexeno)benzene, which exhibits hexagonal symmetry and one-dimensional streaks of diffuse scattering along the hexagonal axis. Layers of coplanar molecules are stacked in a disordered way along the *c*-axis. A four-layer model was initially developed to model the diffuse intensity of fourteen streaks of reciprocal lattice with four probabilistic stacking parameters [1]. These parameters have been optimized with a DE algorithm and parallel computing. Nearly noise free diffraction data were generated using 1280 clones of the best individual after 287 generations of DE refinement. Refinement of the probabilistic parameters against these reference data with a genetic algorithm, a swarm calculation and differential evolution are similarly efficient.

Our second test case is $NaLaF_4$, a member of a family of rare earth-doped (Er^{3+}, Yb^{3+}) sodium lanthanide tetra fluorides, which show occupational and displacive disorder reflected in distinct planes (2-D) of diffuse X-ray scattering. These materials are efficient up-conversion phosphors [2-4]. The average crystal structure alone does not allow a complete understanding of the physical properties. Site selective spectroscopic studies could only incompletely ascribe the high efficiency of the light emission to the presence in the crystal structure of multiple optical sites [5]. Specifically, we are reporting on our recently collected neutron data for $NaLaF_4$. Such data will allow us to better model the positions and site occupancies of the Na and F atoms than is possible in an X-ray experiment since the relative scattering lengths of Na, La and F for neutrons differ much less than for X-rays. From this data we plan to develop a fully quantitative model; the development and results of this model will be presented.

[1] H.B. Bürgi, M. Hostettler, H. Birkedal, D. Schwarzenbach, *Z. Kristallogr.* **2005**, *220*, 1066-1075. [2] T. Kano, H. Yamamoto, Y. Otomo, *J. Electrochem. Soc.:Solid State Science and Technology* **1972,** *119*, 1561-1564. [3] J.F. Suyver, J. Grimm, K.W. Kraemer, H.U. Guedel, *J. Lumin.* **2005**, *114*, 53-59. [4] A. Sarakovskis, J. Grube, A. Mishnev, M. Springis, *Opt. Mat.* **2009,** *31*, 1517-1534. [5] A. Aebischer, M. Hostettler, J. Hauser, K. Krämer, T Weber, H.U. Güdel, H.B. Bürgi, *Angew. Chem. Int. Ed.* **2006,** *45*, 2802-2806.

Keywords: diffuse scattering, differential evolution, disorder

MS.30.2

Acta Cryst. (2011) A**67,** C77

Diffuse Scattering from Stacking Faults: Scaling of Pair Correlation Function

Dhananjai Pandey[a], Pratyush Tiwary,[b] [a]*School of Materials Science and Technology, Institute of Technology, Banaras Hindu Univ (India).* [b] *Department of Applied Physics and Materials Science, California Institute of Technology (USA).* E-mail:dpandey_bhu@yahoo.co.in

Stacking faults are ubiquitous in several close-packed metals and alloys as also in polytypic compounds like SiC and ZnS where one of the atoms sit approximately on close–packed positions. These faults may result as an accident during growth (so-called growth faults), by plastic deformation (the deformation faults) and during structural phase transition (such as layer displacement faults) involving restacking of the closed-packed layers. The distribution of stacking faults introduced during crystal growth or plastic deformation is random whereas it is non-random for those introduced during restacking transitions. Theory of x-ray diffraction from randomly and non-randomly faulted crystals has been developed several decades ago. In recent years, Monte-Carlo techniques have also been employed to calculate the diffuse scattered intensity. In all these techniques (analytical or Monte Carlo), one first calculates the relevant pair correlation functions P(m), Q(m) and R(m) corresponding to A-A/B-B/C-C, A-B/B-C/ C-A and A-C/C-B/B-A type pairs of layers separated by 'm' intervening layer spacings. The fourier transform of these pair correlation functions yields the scattered intensity distribution along various reciprocal lattice rows. Conversely, the pair correlation function can be directly obtained from inverse fourier transform of the observed scattered intensity [1]. The purpose of this talk is to show a very special property of the pair correlation functions, and that is, their scaling property. It will be shown that the P(m)/Q(m)/R(m) for different values of fault probabilities when plotted against a scaled variable m/ξ (ξ is the correlation length corresponding to the values of P(m), Q(m) and R(m) tending towards 1/3) collapse into a master curve [2-3]. This collapse is also observed in the time domain (t) for the late stages of restacking transitions [4]. The scaling behavior of the pair correlation functions implies a power law dependence of ξ on fault probability or time; the exponent for the latter belongs to a universal class. This scaling property can be conveniently used for calculating the scattered intensity distribution.

[1] E. Estevez-Rams, J. Martinez, A. Penton-Madrigal, R. Lora-Serrano, *Phys. Rev. B* **2001,** *63,* 054109(1-10). [2] P. Tiwary, D. Pandey, *Acta Cryst.* **2007,** *A63,* 481-482. [3] P. Tiwary, D. Pandey, *Acta Cryst.* **2007,** *A63,* 289-296. [4] S.P. Shreshtha, D. Pandey, *Proc. R. Soc. London Ser. A* **1997,** *453,* 1311-1330.

Keywords: scaling, diffuse scattering , stacking faults