AANSS2022

ANBUG-AINSE Neutron Scattering Symposium

9th – 11th November2022

Plenary & Keynote Speakers

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Plenary Speaker

Marianna Yanez Arteta
AstraZeneca

Lipid Nanoparticles for mRNA delivery: Using Neutron Scattering for Successful Redesign

The use of messenger RNA (mRNA) as a therapeutic treatment to produce a deficient protein in situ became a reality in 2020: 2 mRNA-based vaccines against SARS-CoV-2, produced by Pfizer/BioNTech and Moderna, received emergency authorization by multiple regulatory agencies around the world. The technology that made this possible was a lipid nanoparticle (LNP) used as a delivery vehicle that was originally designed for small interference RNA. These LNPs are mainly composed by a cationic ionizable lipid, which is responsible of encapsulating and facilitating release into the cell cytosol, and helper lipids to provide stability to the particle such as cholesterol, a phospholipid and a poly(ethylene glycol) lipid. Despite the great advances in LNP development, there are still challenges to overcome relating to their efficacy, which is typically in the single digit percentage, as well as ensuring their safety.

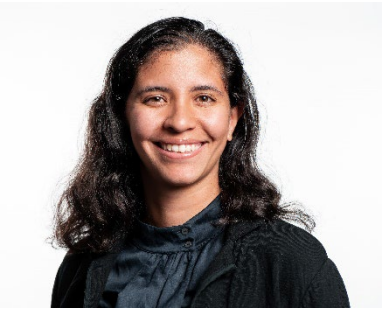
Our work shows how a fruitful collaboration between industry, academia and neutron research facilities helped us to elucidate the structure of mRNA-containing LNPs in order to guide their rational design towards an improvement in their efficacy. We have found that both cholesterol and the phospholipid DSPC are enriched at the LNP surface, giving them a core-shell profile. These results allowed us to variate the LNP size and surface composition in order to increase intracellular protein production of up to 50-folds for certain LNPs in 2 different types of clinically relevant cells, human adipocytes and hepatocytes. This improvement is most likely related to the ability of LNPs to fuse with early endosome membranes[1].

Additionally, we have used neutron scattering to investigate the fate of mRNA-containing LNPs in the presence of proteins[2] and also to characterize LNPs containing non-steroidal anti-inflammatory drugs (NSAIDs)[3]. The fundamental understanding gained from probing the structure of mRNA-containing LNPs with techniques as neutron scattering provides insight into the mechanisms leading to LNP effectivity and will improve the possibility of success of mRNA therapies.

Bio

Marianna Yanez Arteta, Ph.D., is an Associate Director at the Advanced Drug Delivery division within Pharmaceutical Sciences in AstraZeneca. She did her PhD at Lund University, where she employed neutron reflectometry to understand the interactions between polymers and surfactants at interfaces. Thereafter, she was a postdoctoral research at AstraZeneca where she brought small angle neutron scattering expertise to investigate the structure of lipid nanoparticles for mRNA delivery.

In her current position she leads the team developing new modalities pharmaceutics in pre-clinical and early clinical phases, including mRNA, antisense oligonucleotides and peptides. As part of her role, she has guided the development of nanomedicines for complex therapeutics from the understanding of the molecular interactions in the formulation.



Plenary Speaker

Valeska Ting
University of Bristol

Insights into hydrogen storage in porous materials from neutron scattering

High surface area nanoporous materials such as porous carbon nanomaterials, zeolites and metal-organic framework materials are exceptionally suited for applications in gas separation and storage. Their nanoscale and macroscopic structures can be tuned to allow exceptionally high densities of gas within their pores, which can lead to exciting possibilities for energy storage, both by physical adsorption of alternative fuel gases such as hydrogen. It can be, however, extremely challenging to characterise and study interactions of H2 with nanoporous host materials due to hydrogen's low of electron density (which makes it difficult to detect in the presence of heavier elements using X-ray techniques).
Accordingly, we confined hydrogen in a range of nanoporous solids and used a combination of neutron scattering techniques under low temperatures (down to 10 K) and high pressures (up to 2 kbar) to elucidate the phase, interactions and behaviours of hydrogen inside porous materials with different pore sizes and geometries.
Here we will present results from various studies, highlighting different approaches for extracting key information from a range of hydrogen-containing materials. These include parametric studies and combinations of techniques including neutron scattering under static and dynamic conditions, gas sorption, molecular modelling and properties measurements under coupled extremes of low temperature and high pressures.
These results indicated the presence of molecular hydrogen arrangements with densities greater than that of solid hydrogen at its triple point, as well as the stabilisation of unusual configurations of hydrogen under a variety of temperature and pressure conditions. Such studies can produce surprising and useful insights into the effect of nanoconfinement on the atomic arrangement and properties of hydrogen under extreme environmental conditions, paving the way for developing new materials that will result in highly dense hydrogen phases for sustainable energy applications.

Bio

Prof Valeska Ting (CEng, FIOM3) is a Professor of Smart Nanomaterials at the University of Bristol. She leads a team of researchers developing nanoporous materials for sustainable applications including hydrogen storage, holds an EPSRC Research Fellowship and is a member of the Strategic Advisory Committee for the EPSRC-led cross-research council Energy theme. Notable awards include the 2013 Sir Frederick Warner medal, the UK's Parliamentary and Scientific Committee's SET for Britain Gold Medal for Engineering, and Westminster Medal in 2013, and being named one of the Top 50 Women in Engineering in 2020.

Keynote Speaker

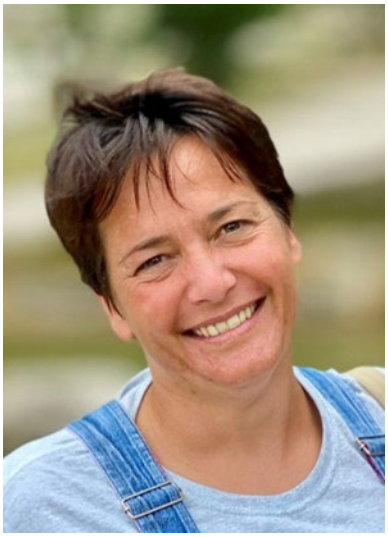
Anne Martel
Institut Laue-Langevin

BioSANS for membrane proteins

In the methodological landscape accessible to structural biology, SAS is a low resolution technique to study biomolecules in solution. Compare to X-ray scattering (SAXS), SANS focuses on molecular complexes, including protein-lipids or protein-detergent, using specific deuteration and contrast variation. Indeed, membrane proteins are notoriously difficult to express, purify and crystallize, and SANS can be a valuable complement to other techniques such as CryoEM, HD-exchange mass spectrometry... Last technical improvements on ILL/D22, in therm of instrumentation and sample environment, combine with the availability of new amphiphilic environments, to enable progress in this field. A few examples will be used to show the new possibilities opened by these technical improvements. Taken together, these examples show that biological structures are more dynamics and less symmetric than usually extrapolated from X-ray crystallography.

Bio

I studied cell and molecular biology at Grenoble University and Ecole Normale Superieure of Lyon. I did my PhD at European Synchrotron Radiation Facility (Grenoble) between 2005 and 2008, about silk protein aggregation process. Then I was appointed Beamline scientist on the BioSAXS instrument BL4-2, at stanford synchrotron radiation laboratory, in 2009, before coming back to France for a post-doc at the Institute of structural biology and Grenoble university. Since 2010, I am instrument co-responsible on D22, a SANS instrument of ILL, where I support the biologist users.



Keynote Speaker

Jeremy Lakey
Newcastle University

Defining the binding site for an antibiotic protein toxin using mutants and neutrons

Colicins, a class of antibacterial proteins secreted by *Escherichia coli*, kill closely related competing strains. Their lethal function relies on the, surprising, ability of these large toxins to cross the Gram-negative outer membrane (OM), an asymmetric lipid bilayer comprising an inner leaflet of phospholipid and an outer leaflet of lipopolysaccharide (LPS), which normally excludes molecules larger than 600 da. All colicins interact with specific outer membrane protein receptors but colicin N (ColN) initiates its toxic activity by also attaching to the core oligosaccharide of LPS. We have identified an exposed loop region which is critical for ColN toxicity. Using neutron reflectometry and *in vitro* models of the OM, we show that the inner core oligosaccharide of LPS must be exposed for colicin N to bind. Since such exposure naturally occurs next to the outer membrane protein receptor for colicin N (OmpF), the combined results suggest how this unusual LPS-binding region may guide the initial steps of ColN import

Bio

Jeremy Lakey is Professor of Structural Biochemistry, in the Medical School at Newcastle University (UK). His group use a range of physico chemical techniques to examine proteins in solution and in membranes. This led to work on various biotherapeutics such as antibodies and vaccines,. but the main academic driver has been the Gram negative bacterial outer membrane. First working with Stephen Holt when at ISIS and later with Luke Clifton they have developed and used in vitro models of the OM to understand antibiotic action.

Keynote Speaker

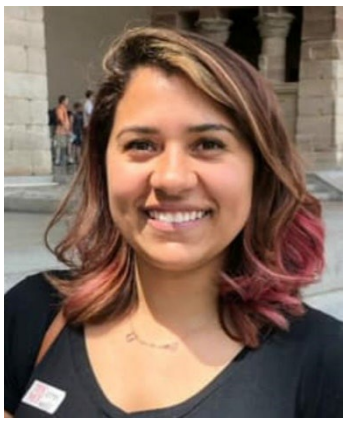
Carla Raymond
Macquarie Univeristy

Neutron Imaging and the Heritage Sector: Attitudes, Concerns, and Applications.

Neutron CT (NCT) is an area of huge potential in the study of cultural heritage materials, and has already had many successful applications over the past ~25 years since the development of the technique. Despite the success of NCT in heritage studies, there is a substantial disparity between publications utilising NCT in comparison to the more routine method of X-ray CT (XCT). This presentation investigates possible reasons for the disparity by directly conversing with the heritage community to understands their attitudes, concerns, and queries about NCT. Analyses and examination of the results helped to identifying areas of interest to the potential users, and areas for improvement that in turn could greatly increase use of NCT in the heritage sector. This work also showcases NCT applications through case studies of ancient objects to demonstrate the complementary and contrasting nature of NCT to XCT.

Bio

Ms Carla Raymond is a recently submitted PhD student from Macquarie University, who has been working with DINGO and the medical imaging beamline (IMBL) at the Australian Synchrotron since 2016. Over the past 6 years, Carla has had the opportunity and privilege to work on several projects involving to concrete core research, palaeontology with her supervisor Dr Bevitt, but most predominantly cultural heritage and archaeological science projects. Carla completed her MRes in 2017, which focussed on using neutron CT (NCT) and X-ray CT (XCT) to non-destructively study the contents and manufacture of an ancient Egyptian cat mummy (Raymond et al. 2019). Her PhD research conducted further research using NCT for cultural heritage analyses and investigated the attitudes and concerns of the heritage sector toward nuclear analysis techniques for heritage studies.



Keynote Speaker

Xiaolin Wang
University of Wollongong

The grand design of new class of materials and physical properties.

The discovery of new materials with superior performance will promote the rapid development of science and technology and will change and improve our daily lives. However, discovering new materials and properties is challenging due to their complexity in both materials chemistry and physics. How many of them are still waiting for us to explore and discover? What are they? How do we know or design them? These are the ultimate questions and goals of the grand design of new materials and properties. In this talk, I will summarize the conventional methods used in material design and introduce new strategies for the grand design of new materials and properties. I will discuss how to design new materials and properties based on new electronic states, new band structures, new states of matter etc. I will present some of the novel materials and properties we have designed for both solids and liquids, including new quantum materials with unique charge and spin attributes for novel electronics, spintronics, topological electronics, and dissipationless transport.

Bio

Distinguished Professor Wang Xiaolin is Director of Institute for Superconducting and Electronic Materials at the University of Wollongong and Node Director and theme leader of the Australian Research Council (ARC) Centre of Excellence for Future Low Energy Electronic Technologies. He received his PhD from the University of Wollongong in 2000. Prof Wang pioneered several ground-breaking studies in superconductors, topological insulators, spintronic materials, liquid metals, thermoelectric materials, wettability, and materials design. He invented a new class of materials, spin-gapless semiconductors, that have been regarded as a new quantum matter, offering a unique platform for next-generation low-energy spintronics and electronics. Prof Wang is committed to fostering and training the next generation of researchers and leaders. Prof Wang's significant contribution to the Australian research on materials science and condensed matter physics has led him to several Australian Research Council fellowships, including QEII Fellowship and Professorial Future Fellowship. Many of his important works were published in Nature Review Physics, Nature Materials, PNAS, Physical Review Letters, Nature Communications, Science Advances, etc., with 19000+ citations and an H index of 68.

Keynote Speaker

Colette Boskovic
University of Melbourne

Inelastic Neutron Scattering for Elucidation of Lanthanoid Single-Molecule Magnet Properties

Single-molecule magnets (SMMs) are molecular species that exhibit slow magnetic relaxation and magnetisation quantum tunnelling due to intrinsic molecular properties. The best performing examples are based on lanthanoid(III) ions. Possible future applications include serving as molecular components for high density data storage, qubits in quantum computers and molecular spintronics devices.
The design of SMMs for future applications relies on understanding key structure-property relationships. Determination of the molecular origin of the anisotropy barrier to slow relaxation and the relaxation mechanisms requires elucidation of the electronic structure of the lanthanoid(III) ion. Work in our group over the last ten years in collaboration with Richard Mole has focused on combining inelastic neutron scattering with other experimental techniques and electronic structure calculations to characterise crystal field splitting and exchange coupling in lanthanoid SMMs and analogues.1–6 Our work has highlighted the value of INS for this purpose and provided key insights into the role of exchange coupling in modifying SMM behaviour.

Bio

Colette graduated from the University of Melbourne with BSc(Hons) and PhD degrees in chemistry. After postdoctoral stints at Indiana University, USA, and the University of Berne, Switzerland, she returned to the School of Chemistry, University of Melbourne as a Lecturer, where she is now a full Professor. Her research interests lie in the areas of molecular magnetism, redox-active ligands and rare earth chemistry

Colette was awarded the 2004 Selby Research Award from the University of Melbourne, the 2013 Alan Sargeson Lectureship from the Royal Australian Chemical Institute (RACI) Inorganic Chemistry Division and the 2014 Dean's Award for Excellence in Research (Teaching and Research) from the Faculty of Science, University of Melbourne. She received an ARC Future fellowship in 2019.

Colette was elected a Fellow of the RACI in 2020 and she is presently the Chair-Elect of the RACI Inorganic Chemistry Division Committee. She is also the AINSE Councillor for the University of Melbourne. She is a member of the International Advisory Boards for the International Conference on Molecule-based Magnets (ICMM), Asian Conference on Molecular Magnetism (ACMM), the Asian Conference on Coordination Chemistry (ACCC) and the 11th International Conference on f Elements (ICFE-11).

Keynote Speaker Update

Ania Paradowska
ANSTO

Update on the progress of ACNS Industrial Liaison Office and future opportunities

Bio

Prof Anna Paradowska current role is to establish and lead the Industrial Liaison Office at the Australian Centre for Neutron Scattering. Her role is to promote the use of the Australian Centre for Neutron Scattering facilities for applied industrial research and to manage technology transfer. Her goal is to build long term collaboration and partnerships with universities, other research organisations, businesses and industries to support Australian and global industry.

Anna is also co-responsible for the KOWARI Strain Scanner. The main focus of her research activities is in residual-stress analysis using neutron and synchrotron X-ray diffraction with the goal of relating them to manufacturing procedures and integrity requirements for various types of engineering components. Additionally she has a strong interest in neutron in-situ study of thermo-mechanical properties of engineering materials and engineering application of imaging diffraction techniques.

Before joining the former Bragg Institute Prof Paradowska was working at ISIS at Rutherford Appleton Laboratory, UK. She was an Instrument Scientist on the materials and engineering beamline called ENGIN-X. Anna did her PhD at the Department of Mechanical Engineering at Monash University, Australia. Her thesis research focused on the investigation of residual stress in welds using neutron and synchrotron diffraction. Before that, she did her MSc degree at the Wroclaw University of Technology, Poland, where she specialized in Materials Technology and Monitoring Systems.

Anna has published a book on the residual stress measurements and has co-authored two book chapters, as well as published over 100 peer-reviewed journals and conference papers.

Keynote Speaker Update

Alison Edwards
ANSTO

KOALA decommissioned October 2022: what has been achieved? and what remains to be done KOALA2 implementation underway

Bio

Dr Alison Edwards is a specialist in structural chemistry and chemical crystallography who pushes the limits of technical feasibility and applies critical analysis to extract structures from the data measured to advance our fundamental knowledge of the structure of chemical compounds – not all of which are new! Neutron single crystal chemical crystallography presents a rich largely untapped vein which, due to the renaissance in Laue diffraction methods (employing the un-monochromated beam), can now be tapped. The Laue neutron diffractometer Koala , at ANSTO, has brought chemical crystallography within the scope of neutron diffraction studies and is leading to significant insights into materials of interest across a broad range of chemical sub-disciplines.

Alison has been mentored by colleagues of distinction in crystallography, including during her Ph.D. studies with Dr Bernard Hoskins at the University of Melbourne and then as a post-doctoral researcher with Prof. Keith Prout in the Chemical Crystallography Laboratory at the University of Oxford, where she was a core member of the team who pioneered the application of the combination of solid-state NMR and X-ray crystallography to characterise a range of structural dynamics occurring in the crystalline state. Now approaching 30 years experience as a chemical crystallographer, Alison is delighted to discover recurring themes in unexpected places and hopes to continue to contribute to the understanding of chemistry through crystallography.