Programme

9.00 – 9.45	**Registration** in Fitzwilliam College Auditorium. Refreshments served.
9.45 – 10.00	**Welcome** by the Organising Committee
10.00 – 10.30	**Opening Address** by the HoD, Prof. Nigel Slater
10.30 – 11.20	**Session 1**
10.30 – 10.55	Axel Zeitler - *Tetrahertz spectroscopy and imaging for chemical engineering applications*
10.55 – 11.20	Gabriele Kaminski Schierle - *In vivo studies of protein aggregation kinetics with multiparametric imaging*
11.20 – 11.40	**Coffee Break / Networking**
11.40 – 13.20	**Session 2**
11.40 – 12.05	Ian Wilson - *Soft solids are hard work*
12.05 – 12.30	Polina Yaseneva - *Sustainability of flow processes in pharmaceutical industry*
12.30 – 12.55	Goeff Moggridge - *An Improved Prosthetic Heart Valve*
12.55 – 13.20	Flash Poster Presentation
13.20 – 15.00	**Lunch Break with Poster Session / Networking**
15.00 – 16.15	**Session 3**
15.00 – 15.25	Silvia Gonzalez Calera - *Sooting tendency and Soot particles characterisation of liquid hydrocarbons in wick-fed diffusion flames*
15.25 – 15.50	Sabine Bahn - *Disease Biomarkers for Schizophrenia- from laboratory to patient bedside-*
15.50 – 16.15	David Fairen-Jimenez - *Adsorption Processes in Metal-Organic Frameworks*
16.15 – 17.00	**Plenary Talk:** Daan Frenkel – *Entropy and addressable self-assembly*
17.00 – 17.15	**Closing** of the Research Day by the Organising Committee / HoD
17.15 – 18.30	**Drinks Reception**

Abstracts

Axel Zeitler:

Terahertz spectroscopy and imaging for chemical engineering applications

Terahertz radiation has excellent potential to help with the understanding of fundamental and exciting new challenges at the interface between physics, materials chemistry and the life sciences but it is, as yet, largely unexplored. Radiation located in this range of the electromagnetic spectrum was very difficult to generate until quite recently. Since the 1990s new developments in semiconductor physics and femtosecond laser technology have made it possible to provide light at terahertz frequencies (a frequency of 1 THz equals a wavelength of 0.3 mm) in a relatively simple way.

Terahertz radiation has unique properties in that it easily penetrates through most polymeric materials and is therefore an exciting new tool to study such materials, which are often opaque at visible frequencies. As well as being a non-destructive probe of materials, in organic molecular crystals terahertz radiation has the important property that it interacts with vibrational modes that extend across large domains of a crystal lattice. This makes terahertz spectroscopy unique: even though it is possible to excite molecules using a variety of energies it is only through the careful selection of the low energy in the terahertz range that it is possible to selectively excite crystal lattice vibrations and study in a unique way the presence and nature of interactions between molecules.

Using terahertz spectroscopy it is possible to understand the physical characteristics of a wide variety of materials spanning the fields of pharmaceuticals, catalysis, biologicals, nanotechnology and non-destructive testing and I will present some examples of what we have studied in the recent past in our group at CEB.

Gabriele S Kaminski Schierle

In vivo studies of protein aggregation kinetics with multiparametric imaging

Misfolding and aggregation of peptides and proteins is a characteristic of many neurodegenerative disorders, including Parkinson's (PD) and Alzheimer's disease (AD). Their common feature is that normally unstructured and soluble proteins misfold and aggregate into insoluble amyloid fibrils, which make up the deposits in the brains of patients suffering from these devastating illnesses. A key requirement to gain insight into molecular mechanisms of disease and to progress in the search for therapeutic intervention is a capability to image the aggregation process and structure of ensuing fibrils *in situ*.

We have recently reported that amyloid proteins that are associated with protein misfolding diseases, including PD, AD and various other types of amyloidosis develop an intrinsic fluorescence in the visible range. The discovery of intrinsic amyloid fluorescence has enabled the process of amyloid formation from disease-relevant polypeptides to be monitored in a label-free manner and with high specificity. I will show here how specific and sensitive *in vivo* probes of amyloid structures can be developed using external fluorophores covalently attached to the amyloid backbone. Such external fluorophores can participate in Förster resonance energy transfer (FRET) with intrinsic energy states of amyloid

structures if present, providing a readout in the form of a reduced fluorescence lifetime of the external fluorophores.

I will provide an overview on the application of all-optical techniques to inform on the aggregation state of α-synuclein (relevant to PD), amyloid β and Tau (relevant to AD) *in vitro*, in live cells and model organisms.

Ian Wilson

Soft solids are hard work

Many conventional as well as newer advanced materials are soft solids. Their behaviour depends chiefly on the timescale of the deformation. The soft solids we are interested in are multiphase materials structured at the microscale, which is required for their product properties. In highly dense suspensions and bubbly liquids this gives rise to a rich variety of rheological behaviours and time dependencies. The complexity of these systems means that modelling must be accompanied by experimentation to determine the dominant physical phenomena. This talk will outline some of the challenges involved and progress made, illustrated with examples from food to pharma.

Polina Yaseneva

Sustainability of flow processes in pharmaceutical industry

It is a well-known fact that the pharmaceutical industry has the highest rate of generated waste per unit of produced drug and consequently produces considerable environmental impacts. In recent years external pressures from society, political agenda and tightening regulatory requirements forced the pharmaceutical industry to move towards developing more sustainable processes. However the question arises: how to assess sustainability? Published assessment methods to date include whole-route evaluation of process mass metrics, inclusion of safety and risk indicators into mass metrics analyses, and linking of streamlined LCA and PMI.

We are interested in metrics methods to support simultaneous development of chemistry and process options using technical, economic and environmental benchmarking on the basis of comprehensive LCA and simplified indicator methods. Such a methodology is required when new process options, such as flow processes applied to pharmaceutical syntheses.

The EU SYNFLOW project has the aim to develop more sustainable chemical processes based on novel catalytic and process technologies. Within the project we developed a three-step evaluation methodology, starting with material proxy indicator, then gate-to-gate process evaluation and finally a comprehensive LCA. In this case we are confident in representing the supply-chain issue dominating chemical routes selection at the early stage of process development, revealing problematic stages of a process using gate-to-gate flow-sheet analysis and, finally, revealing targets for optimisation of the overall process based on LCA and costing analysis. As a comparative benchmark we use the original batch process.

Geoff D. Moggridge,

An Improved Prosthetic Heart Valve

Diseased and dysfunctional heart valves are routinely repaired or replaced through surgical intervention. If damage is too severe to enable valve repair, the native valve is replaced by a prosthetic valve. Over 290,000 heart valve procedures are performed annually worldwide and that number is expected to triple to over 850,000 by 2050.

Commercially available heart valve prostheses are at present either mechanical or biological. Despite having excellent durability, current mechanical prostheses are prone to thromboembolic complications causing patients to require lifelong anti-coagulation therapy. Bioprosthetic tissue-based valves (usually porcine or bovine in origin) exhibit good hemodynamic performance; however they are prone to calcification and tissue failure.

Polymeric materials could offer the optimal compromise between the use of mechanical valves and natural tissues; but as yet no clinically acceptable such polymeric valve has been manufactured. Suitable polymers are typically isotropic and behave differently to natural healthy soft tissue, which includes fibrous reinforcement. In the natural valve leaflets collagen fibres are arranged with specific structure and orientation to reinforce the tissue and provide the requisite structural integrity, while allowing for very thin leaflets that produce minimal pressure gradient across the valve. The collagen fibres in the leaflet tissue optimally align themselves for fatigue strength. This results in material properties that are anisotropic in nature and a stress-strain relationship substantially different to that of isotropic polymeric materials. We are investigating self-assembling polymeric nano-composites, which mimic the anisotropic fibrous structure of natural tissues, as potential prosthetic heart valve materials; combining the durability of mechanical valves and the hemocompatibility and flexibility of natural tissue valves.

Silvia González Calera

Sooting tendency and Soot particles characterisation of liquid hydrocarbons in wick-fed diffusion flames

Commercial fuels are mixtures of hundreds of hydrocarbons. The complexity of petroleum-based fuels has prompted researchers to search for mixtures of limited number of components that represent the behaviour of real fuels. These surrogate fuels are used to facilitate the development of new combustion technologies and to generate insight and understanding of underlying fundamental processes. Differential mobility spectrometry (DMS) and high resolution electron microscopy (HR-TEM) were used to characterise soot particles generated at different heights in a laminar wick-fed diffusion flame for a variety of components found in surrogate fuels. The DMS is a fast particle analyser that enables the particle size distribution (PSD) to be measured in real-time, and was used to investigate the influence of the molecular structure of the fuel on the PSD. Image analysis of a “lattice-fringe” extracted from HR-TEM micrographs was used to study the morphology of the soot particles, fringe length, tortuosity and separation distance. HR-TEM image analysis algorithms used were developed and implemented using MATLAB.

Sabine Bahn

Disease Biomarkers for Schizophrenia- from laboratory to patient bedside-

Schizophrenia is a multifaceted neuropsychiatric disorder. Its onset is the result of complex interactions between genetic, developmental and environmental factors. It almost certainly presents a heterogeneous group of aetiologies which may not be reflected in the symptomatic/clinical presentation of patients. Therefore, a better molecular understanding of the disease onset and progression is urgently needed. Multi-omics profiling approaches can be employed to investigate large numbers of patient and control samples in a single experiment. These large scale experiments are required to identify disease intrinsic molecular signatures as well as patient subgroups with potentially distinct biochemical pathways underpinning their symptoms.

I will present results from our biomarker discovery studies. We have identified a number of highly significant peptides and proteins in serum that distinguish first-onset paranoid schizophrenia patients from healthy controls. Our findings suggest alterations in glucoregulatory, inflammatory and hormonal processes in drug-naïve patients with first-onset schizophrenia. Interestingly, we also identified disease-relevant metabolic and inflammatory changes in affected and unaffected siblings of schizophrenia patients and have preliminary evidence for the existence of schizophrenia sub-groups, based on the expression of serum proteins.

More recently, we identified a biomarker panel for schizophrenia based upon a meta-analysis of five schizophrenia cohorts and tested their predictive performance in psychiatric at-risk individuals before the onset of schizophrenia or psychosis.
Validation testing of the panel on first-onset schizophrenia patients gave an AUC of 0.97 for disease detection and a true positive rate of 89%. Analysis of a cohort from the US military, where blood was collected prior to disease onset of either schizophrenia or bipolar disorder, yielded an AUC of 0.90 and 0.53 respectively. The AUC was 0.82 for prediction of schizophrenia conversion in a cohort of prodromal/UHR individuals, which increased to 0.92 when CAARMS positive subscale scores were incorporated into the model.

David Fairen-Jimenez

Adsorption Processes in Metal-Organic Frameworks

Self-assembled functional materials have emerged as an extensive class of materials with an extraordinary degree of variability. On a fundamental level, self-assembled materials symbolise the beauty of chemical structures and the possibility of modifying their individual chemical and physical properties. In particular, metal-organic frameworks (MOFs), one of the most exciting developments in recent porous-materials science, have received great attention as an attractive way of combining structural diversity with multiple organic functionalities. MOFs are known for their extraordinary porosities, being able to reach apparent surface areas up to 8,000 m^2 per gram of material. The fundamental understanding of the specific properties of these systems presents a critical importance in the necessary shift from today's fossil-based energy economy to a more sustainable economy based on hydrogen and renewable energy, as well as medicine applications, where nanotechnology has a fundamental impact to revolutionise cancer diagnosis and therapy.

The fundamental understanding of the adsorption phenomena is crucial for the design of new porous materials and MOFs, and the study of their performance in industrial applications. In our research, we combine molecular computational techniques with a range of experimental techniques that include

gas adsorption, neutron and X-Ray diffraction and *in vitro* studies for drug delivery applications. This combination of techniques presents several benefits. Firstly, experimental characterisation is crucial for an application under realistic conditions. On the other hand, simulations provide a detailed picture on the molecular scale that is not easily accessible from experimental methods. This allows studying in detail how the structure influences the adsorption performance and therefore forms an essential part in the identification and design of promising materials.

Daan Frenkel

Entropy and addressable self-assembly

A holy grail of nano-technology is to create truly complex, multi-component structures by self-assembly.

Most self-assembly has focused on the creation of `structural complexity'. In my talk, I will discuss `Addressable Complexity': the creation of structures that contain hundreds or thousands of distinct building blocks that all have to find their place in a 3D structure.

Simulation and theory yield surprising insights that inform us how such structures can be made a reality.