Dial-a-Molecule

An EPSRC Grand Challenge Network

September 2015

Welcome to the September edition of the Dial-a-Molecule Newsletter. In this edition, we advertise the last meeting to be held this year and report on two which were held in September.

Dial-a-Molecule is also asking for your help – as the Network draws to a close we are interested in hearing about how being part of the Network has benefited you. Be it new collaborations that came about from Dial-a-Molecule meetings, funding awarded for research aligned with the Grand Challenge or how your research directions have been influenced by the Roadmap. Please get in touch if you feel you have anything relevant to tell us.

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Dial-a-Molecule EPSRC Grand Challenge

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The Grand Challenge is owned by the community and we value your input and feedback, so if there is anything you think the Network should support or get involved in, please get in touch

Smart Materials: Efficiency, Complexity and Design

University of Warwick, 21 October 2015

A meeting to bring synthetic and polymer chemists together

The UK is a global leader in polymer synthesis and academic activity in the area continues to deliver palpable economic advantage to society. Building on the advances delivered in the use of polymers in smart, functional materials will require a step-change in the synthetic chemistry which underpins the subject; only by ensuring access to new generations of functionalized, high-value monomers and delivering improved methods for polymerization will advances continue.

This meeting will consist of short presentations followed by facilitated round-table discussions which will be focused on identifying technology gaps and creating new collaborative frameworks.

Registration Details: The meeting is free to attend, but to facilitate with catering we ask you to register at the following **link**. Travel bursaries for Early Career Researchers are available and should be applied for upon registration.

Organising Committee: Prof. Joe Sweeney and Prof. Rachel O'Reilly

Confirmed Speakers:

Prof Cameron Alexander
University of Nottingham

Dr Francisco Fernandez-Trillo
University of Birmingham

Dr Matthew I. Gibson
University of Warwick

Dr Rachael Rowlands-Jones
Knowledge Transfer Network

Dr Helen Willcock
Loughborough University

Dial-a-Molecule Grand Challenge Institute

Community Consultation – Your Input is Needed

Rapid Reaction Analysis has been identified by the Dial-a-Molecule Grand Challenge as an area most in need of a **central facility**, due to the cost of equipment and instruments, and even more critically, the provision to provide training in the use and interpretation of data.

Such a facility would give access to state-pf the art **automated synthesis and analysis equipment**, **advanced data analysis**, **mining and management software** and **skilled staff**.

The proposed Grand Challenge Institute would be available to all UK Scientists across all sectors. To help shape the proposal and identify what is required we are asking for feedback form the community. Please take five minutes to fill in the survey at:

www.surveymonkey.com/r/DJSZNF3

The facility would aim to:

1. Provide *UK wide access* to facilities that are currently unavailable to the majority of chemists thus *accelerating discovery and manufacture*
2. Drive the *development* and *adoption* of equipment and software for *next generation synthesis*
3. Enable *research* for reaction scoping, robustness and predictability
4. Address the current skills gap and *improve the employability of graduates*.
5. Act as a *Hub*, liaising with existing centres

Workshop Report:

Design of Experiments: Undergraduate Lab Module Transfer Workshop

University of Leeds, 16 – 17 September 2015

The Dial-a-Molecule Grand Challenge Network has been particularly active in promoting the education and deployment of statistical methods in Chemistry Research. Previous events held under this sub-theme of the Network have indicated that although the tools and techniques are widely used in Industry, many academics have never exploited them (often because they were never made aware of them during their own training).

Realising the numerous advantages that training in statistical methods such as Design of Experiments (DoE) and Principle Component Analysis (PCA) would offer, Dial-a-Molecule has the vision that every chemistry graduate should have a grounding in the techniques, and an understanding of when to use them appropriately. To advance this vision, Dial-a-Molecule has awarded financial support to Dr Richard Bourne (University of Leeds) who has worked with Brian Taylor (AstraZeneca) to enable the development of an UG 'Design of Experiments' laboratory module. A proviso of the funding was that the output (i.e. the lab module) was made available to the chemistry departments across the UK, to incorporate into their own laboratory courses as seen fit.

The practical was first run at the University of Leeds during 2015, where both UG (3rd year) and CDT-masters students had the opportunity to take part. It involved carrying out a simple SNAr reaction using flow methodology, which allowed large amounts of data to be generated quickly. Overall, it was a great success, particularly among the students who provided very positive feedback and enjoyed carrying out Industrially relevant experiments. Importantly, the practical allowed them to see the value of DoE.

On September the 16th and 17th, Dial-a-Molecule provided partial support for a workshop to begin to roll out the practical to other departments across the UK. As a pilot 'train-the-trainer' event, two representatives from Cardiff University, The University of Strathclyde, The University of Nottingham and Loughborough University attended the workshop.

Day One began with the participants learning about designing and planning the lab module, and how it had been initially implemented at the University of Leeds. It also gave the attendees the chance to provide feedback on the barriers that would preclude its inclusion in other institutions, so that these can be addressed before it is rolled out on a larger scale.

After lunch, the participants split up into two groups and became students again, either donning lab coats to perform the lab practical or returning to the classroom to be given an "Introduction to DoE" tutorial. The roles were reversed on the morning of the second day so that participants had the opportunity to experience both the taught and hands-on elements of the course. The afternoon of Day two was devoted to analysing the results from the practical sessions, and getting an overview of how to use the Modde software package.

The feedback from participants was extremely positive and many could see how the practical could be used, or modified slightly to fit into their home institutions teaching program. The course developers are currently preparing a manuscript describing the lab module for publication in The Journal of Chemical Education, and hope to run further workshops like the one described above to enable the practical to be carried out at other institutions.

If you are interested in finding out more about the lab module, or if you want to incorporate into your own institution, please get in touch. Likewise, as the Dial-a-Molecule Network draws to a close we are seeking sponsorship to run future workshops – it you are interested, please get in touch!

We thank the University of Leeds (facilities and staff time), AstraZeneca (staff time) and Umetrics (loan of Modde software) for helping to run this workshop

Meeting Report:

Lead-Oriented Synthesis: Exploring Drug Relevant Chemical Diversity

GSK Stevenage. 25 September 2015

Lead-Oriented Synthesis: Exploring Drug-Relevant Chemical Diversity was a one-day meeting organized by the Dial-a-Molecule Grand Challenge Network, and held at GlaxoSmithKline's Stevenage site on September 25, 2015. The meeting attracted 92 registered

delegates, and featured **scientific talks** from academic and industrial leaders in the field. It also coincided with the launch of the open access software package **LLAMA** (Lead-Likeness And Molecule Analysis), developed at the University of Leeds.

Dr Ian Churcher (GSK) kicked off the meeting and set the scene for the remaining talks with a personal account of "*How Synthetic Chemistry Can Drive the Discovery of Drugs of the Future*", and concluding with the message that "synthesis is not a mature science and still needs to grow". This was followed by **Prof. Peter O'Brien** (University of York) who began his talk "*Exploring 3-D Pharmaceutical Space: Lead-oriented and Fragment-oriented Synthesis*" by introducing the growing interest in "moving away from flat-land", before discussing the progress his group has made in this area by utilizing organo-lithium chemistry.

After the lunch break, **Prof. Steve Marsden** (University of Leeds) spoke on "*Synthetic Strategies for the Efficient Exploration of Lead-Like Space*" and provided some recent examples from his group. **Dr Jason Kettle** (AstraZeneca) followed with "*Design and Exploitation of Novel Medicinal Chemistry Reagent Sets*", which explained some of the concepts used by industry to gain access to novel building blocks. The session was concluded with **Prof. David Spring** (University of Cambridge) who talked about "*Enriching Chemical Space to Drug Undruggable Targets*" and the work his group is carrying out with PPI's.

The day concluded with a Plenary Lecture from **Prof. Jeffrey Bode** (*ETHZ*) on "*Cross-Coupling 2.0*", where he gave an excellent account of both the SNAP and SLAP "Click" reagents developed in his group, and the KAT and KAHA ligation reactions they have developed to synthesize large peptides and proteins.

Alongside these excellent scientific presentations, the meeting involved also coincided with the launch of the **LLAMA** (Lead Likeness And Molecule Analysis), an open access, free to use tool which allows the lead-likeness of different molecular scaffolds to be evaluated and compared. The tool was developed at The University of Leeds as part of an EPSRC-funded collaboration with GSK. **Dr Richard Doveston** (*TU Eindhoven*) and **Prof Adam Nelson** (*University of Leeds*) gave a brief introduction to software and over the lunch and refreshment breaks delegates got the chance to try the software and assess the lead-likeness of their own molecules.

Overall, the meeting was a huge success and enjoyed by all. The quality of the chemistry that was spoken about, and demonstrated over the lunch breaks, was truly innovative and at the forefront of synthetic developments, really emphasizing the point made in the opening session that synthesis is not a mature science and still needs to grow.