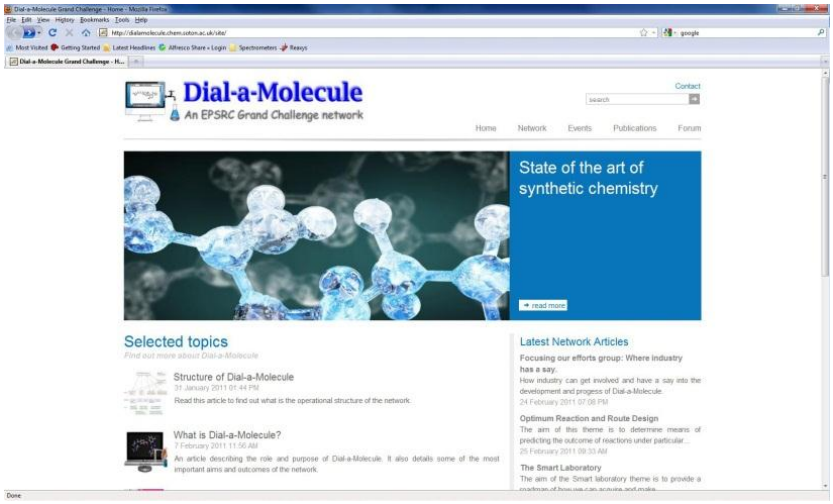
Welcome to the second edition of the Dial-a-Molecule network newsletter. We have the launch of our new improved website to announce, as well as the focus areas which will form the basis for future work in the network.

New website at www.dial-a-molecule.org

We have a new-look website based on an articles structure with the benefit that it is easy to provide comments and feedback on any of the pages. Hopefully you will find it more appealing and user-friendly. The new website can be expanded with various functionalities and, if you would like to have a feature added please let us know.



The new website contains a wealth of information concerning Dial-a-Molecule, ranging from a presentation of the network, its focus areas and themes, upcoming and past events and up to publications relating to the network. Registered members of the network have a special section (**Forum**) where they can share documents relevant to the network, participate in discussions, create wiki pages and maintain blogs. If you would like to have access to this area and join the discussion, please send an email to the network coordinator.

Focussing our efforts meeting in London

The **Focussing Our Efforts** Group has been established within the Grand Challenge to ensure that the outputs from Dial-a-Molecule are **industry relevant**, **academically challenging** and **fundable**. It is an outward advocate for chemistry and Dial-a-Molecule, with the specific aim to engage the community, including funders and political decision makers, as effectively as possible.

The current focus areas of the Grand Challenge will be reviewed by this group on **Monday 11th April (London)** and new areas of focus may be proposed. The strategy for industrial engagement will also be finalised.

Membership of the group is open to any industrialist who is passionate about this area and wants to see Dial-a-Molecule be as successful and impactful as possible.

If you would like to be involved with the Grand Challenge at this strategic level, then please contact Dr. Stephen Hillier (Chemistry Innovation) or Prof Richard Whitby (University of Southampton).

Next Steps meeting, London

On February 1st 25 people who had volunteered at some point to take a leading role in the network met to decide where the main focus areas should be. Although overshadowed by the Pfizer closure announcement, the meeting was a success and provided a list of potential areas. These have since been worked-up and are briefly described below. For more information on the themes please consult our website at www.dial-a-molecule.org. All are actively recruiting so if you are interested in them please get in touch with the champions or via the Web site.

Themes and Focus areas

Theme 1. Lab of the future and Synthetic route selection (Richard Whitby co-ordinating)

Joining in

If you'd like to get more closely involved, to influence the development of the roadmap or to work up a joint research proposal with other network members in a theme area, please register your interest on our website at www.dial-a-molecule.org or contact our network coordinator with your contact details.

This theme covers the use of new technology – both hardware and software – in synthesis. It tackles the problem of how we gather and use information on all reactions carried out to enable Dial-a-Molecule. Four focus areas have been identified in the theme.

Focus area 1: Optimum reaction and route design (ORRD) (Champions: Frank Langbein and Sophie Schirmer).

The aim of focus area is to determine means of predicting the outcome of reactions under particular conditions enabling both selection of the best reaction and optimum conditions. Making full use of past data on reaction outcomes is crucial, but theoretical methods will also be important. The theme also covers methods to optimise reactions as they are carried out, and to efficiently experimentally define the scope and robustness of reactions. The selection of the best synthetic route under various constraints (scale, cost, sustainability, time, and available equipment) is another strand of the focus area. In each case developing suitable models and performance measures that can be optimised under realistic constraints provides a unified approach.

Focus area 2: The Smart Laboratory (Champion: Richard Whitby).

At the Launch Meeting of Dial-a-Molecule an often-repeated theme was that a key enabling step would be to collect and make available information on all reactions carried out, including failed reactions. The necessity for more complete information was also identified as a contributory factor in the common difficulty to repeat, or at least to require substantial re-optimisation of, literature reactions. A **Smart Laboratory** should automatically collect and make available all such data, as well as enabling the precise repetition of reaction conditions. For the immediate future the promotion of e-lab note books in academia together with the infrastructure to allow sharing of the data produced is an important step towards Dial-a-Molecule. This focus area aims to promote development of the technologies outlined, as well as their widespread adoption in academia.

Focus area 3: Next generation reaction platforms (Champion: Harris Makatsoris).

Meeting the challenges set by Dial-a-Molecule requires a wide spread adoption of technology to allow for a step change in synthetic capability. The aim of this focus area is to look at the prospects for, and likely impact of, new technology for carrying out synthesis. It will also promote the design and adoption of such new technology. Equally important is to consider both near-term (what affordable changes would have the greatest impact) and longer term (e.g. fully automated general synthesis machines) developments that need to be incorporated in the Dial-a-Molecule roadmap.

Focus area 4: Rapid Complete Reaction Analysis. (Champion: vacant).

The capability to rapidly, ideally in real time, analyse the components in a reaction is critical to the achievement of Dial-a-Molecule, for example by enabling the auto-optimisation of reactions. It requires both dramatic reductions in size and cost of analytical / spectroscopic instruments, and huge advancement of the data analysis techniques used to obtain the required information. Volunteers needed!

Theme 2. A step change in molecular synthesis (David Harrowven co-ordinating)

How can we focus our efforts in inventing and developing new reactions and methods of organic synthesis to maximise the impact on the Dial-a-Molecule aims, as well as shorter term benefits to U.K. industry and other users of synthesis. Two complementary approaches have been initially identified.

Focus area 1: Stepwise perfection (1000 Click Reactions) (Champion: Andy Russell).

Conceivably, if we had enough reactions with close to 100% robustness and efficiency ('Click reactions'), we could sequence them to make any molecule of our choosing. The length of the synthetic route would be relatively unimportant. We are a long way from realising this ambition, as illustrated by the term 'click' coming to refer to a specific reaction. This focus area looks at how we can invent 'perfect' reactions, and to identify which ones are most needed to enable synthesis. Measures for quantifying general reaction robustness and efficiency will allow us set realistic targets to stretch the boundaries of current practicability.

Steering Group

PI: Prof. Richard Whitby
University of Southampton
rjw1@soton.ac.uk

Co-I: Prof. Steve Marsden
University of Leeds
S.P.Marsden@leeds.ac.uk

Prof. David Harrowven
University of Southampton

Dr. Mimi Hii
Imperial College London

Dr. Peter Murray-Rust
University of Cambridge

Dr. Harris Makatsoris
Brunel University

Dr. Stephen Hillier
CIKTN

Dr. David Fox
Pfizer

Prof. Asterios Gavriilidis
UCL

Prof. Joe Sweeney
University of Reading

Dr. David Hollinshead
AstraZeneca

Prof. Kevin Brooker-Milburn
University of Bristol

Network Coordinator

Dr. Bogdan Ibanescu
University of Southampton
B.C.Ibanescu@soton.ac.uk

Web: www.dial-a-molecule.org

Focus area 2: Holistic approach to molecular synthesis (Champion: Don Craig).

We want to move towards a change in thinking such that the goal is one-pot synthesis, of any target molecule. This requires a new holistic way of conceiving synthetic routes in which maximisation of complexity build-up and minimisation of steps is central. Existing retrosynthetic analysis is intrinsically step-intensive, because of the need for FGIs, and the implicit (because we have been taught that way) idea that usually only one C-C bond may be made at a time. The focus group aims are both development of the types of reactions with the desired properties, and methods for planning such synthesis.

Theme 3. Catalytic paradigms for 100% efficient synthesis (Steve Marsden co-ordinating)

Catalysis will undoubtedly underpin the successful attainment of the goals of Dial-a-Molecule. The development of truly sustainable syntheses (from the point of view of input/output) and the generation of complexity made simple (minimal manipulations; rapid evolution of complex polyfunctionals from simple unfunctionalised/monofunctional materials, etc) are at the heart of Dial-a-Molecule and all require the development of new catalytic paradigms. It is likely that most, if not all, new synthetic paradigms in the future will be based on efficient, selective, tunable and sustainable catalytic protocols. Three interconnected focus areas are envisaged to underpin this as outlined below.

Focus area 1: Engineering control through fundamental mechanistic understanding. (Champion: Joe Sweeney)

The notion underpinning this focus area is that to enable sustainable catalysis with a minimal footprint will require control of selectivity, reactivity and catalyst lifetime. To be truly useful, the design or choice of catalyst for a particular transformation ought to be predictable without recourse to extensive screening regimes. Without a fundamental insight into and understanding of the modes of reactivity (and decomposition) of catalysts and active intermediates on the catalytic cycle, this is unlikely to be achieved.

Focus area 2: Intervention-free synthesis by phase-distinct, multi-dimensional catalysis (Champion: Robin Bedford)

The ultimate goal of the focus area is to create integrated multi-catalytic systems that are capable of sequentially and controllably processing multiple synthetic operations in a mutually compatible manner to allow complex synthesis to occur with minimal external intervention. This focus area aims to develop innovative technologies that will underpin the next generations of synthesis with minimal intervention, which may be tagged “conveyor belt catalysis”.

Focus area 3: New reactivity: target-driven catalysis (Champion: Matt Cook).

This focus area aims to define, prioritise and address the key new reactivity principles that will be required to underpin the aims of Dial-a-Molecule. Particularly there is a recognition that most efforts in, for example, C-H activation are directed towards (hetero)aromatic functionalisation and that the overall range of transformations is limited. Additional consideration needs to be given to feedstocks.