



Welcome to the first edition of the Dial-a-Molecule network newsletter. The bulletins will contain updates on the network activities and announce events and opportunities that are of interest to the members. The newsletter will appear every month and you can use it to announce meetings, events and other news items to the network members so please send a message to the network coordinator, Bogdan Ibanescu.

What is Dial-a-Molecule?

Dial-a-Molecule is a Grand Challenge Network funded by EPSRC to promote research aimed at step change in our ability to deliver molecules quickly and efficiently: **How can we make molecules in days not years?**

Tackling this challenge will require collaboration between many areas of science, engineering and mathematics. The network aims to actively engage scientists across a wide range of disciplines in the pursuit of next-generation (and beyond) advances in the delivery of molecules 'to order' while addressing the environmental footprint associated with molecular synthesis. The network aims to form new research communities directed at Dial-a-Molecule extending beyond chemistry and chemical engineering and which involve academia, industry and users and will encourage and facilitate grant application in these areas.

The challenges have been grouped into four main themes:

- ✓ **Synthetic route selection** reflects the need to be able to reliably predict the outcome of reactions on specific molecules under particular conditions, and to thus be able to work out the best sequence of reactions to accomplish the desired synthesis.
- ✓ **Lab of the future** acknowledges that the way we carry out reactions has to change to provide the control and information needed, as well as to allow efficient sequencing of transformations.
- ✓ **A step change in molecular synthesis** looks at the reactions and strategies used in synthesis.
- ✓ **Catalytic paradigms for 100% efficient synthesis** highlights the crucial role which catalysis must play.

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The **Focusing our efforts** advisory group has a predominantly industrial representation and it guides priorities in developing the roadmap to maximise early stage (commercial) return. It also facilitates the crucial two-way flow of information between academia and industry. Users and manufacturers of molecules as well as companies involved in the supply of equipment and software to facilitate synthesis should be interested.

Dial-a-Molecule Network Launch Meeting



On 20th October 2010 the “Dial-a-Molecule” Network Grand Challenge was launched in Birmingham at the ICC, jointly with “Directed Assembly of Extended Structures with Targeted Properties” Network Grand Challenges. The meeting included compelling key note addresses from Prof. Steve Ley (University of Cambridge) and Prof. Matt Rosseinsky (University of Liverpool) and group discussion session to allow the delegates to help shape the key issues that the Grand Challenge networks will focus on and to take ownership of, or to join, the important challenge areas for them or their organisations. The event was attended by over 200 delegates from chemistry, chemical engineering, material sciences as well as industrial delegates from companies such as AstraZeneca, Novartis, Pfizer, Syngenta, Unilever and GlaxoSmithKline.

The scene for the development of the two networks was set in the opening presentation by Andrew Bourne, Head of Physical Sciences at the EPSRC. This was followed by an introduction of the two networks from the two principal investigators, Richard Whitby (for Dial-a-Molecule) and Paul Raithby (for Directed Assembly). David Hollinshead (AstraZeneca) and Neil Feeder (Pfizer) highlighted the importance of the networks to the UK industry.

The meeting included two plenary presentations. The first was given by Prof. Steve Ley FRS (Cambridge) and highlighted the benefits of “flow chemistry” and its importance in synthetic application. The second plenary was from Prof. Matthew Rosseinsky FRS (Liverpool) who developed the self-assembly theme and showed the importance of understanding the correlation between structure, property and function at the supramolecular level.

An important part of the meeting were the question-and-answer sessions followed by break-out sessions targeted at gaining community’s input into the next developments of the network. Many useful ideas were generated and willing volunteers were nominated for the workshops and “sandpits” that are being planned.

Focus areas for Dial-a-Molecule

Following the launch meeting we received a lot of comments concerning all of the theme areas of the network. We are glad to present you below a short summary of the topics proposed to be discussed within the Dial-a-Molecule at future meetings. This is only a draft list and we are eager to find which areas you consider of great interest. All your opinions and ideas are welcomed. Please feel free to send all your comments to the network coordinator, Bogdan Ibanescu (see first page for contact details). Alternatively you can post them on the discussion board.

A. Building for the future: Towards complete collection of reaction data. (*Lab of the future*)

There were many comments from all theme areas at the launch meeting on how important it will be to garner information on all reactions carried out, not just the 'best' ones, but to include 'failures'. Also much better quality and extent of information than typically provided in a publication is needed if we are to make synthesis more predictable.

What is needed to make the use of ELN's compelling in academia? How can we ensure that information stored in ELN's etc is useful and accessible? How might we enhance the equipment we use for synthesis to ease collection of complete reaction data?

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.

B. Reaction Informatics. Prediction of reaction outcomes from data. (*Synthetic route selection*)

Perhaps the key requirement for 'Dial-a-Molecule' is to be able to predict the outcome of unknown reactions under particular conditions. Multi-step synthesis could then be designed (either by chemists or computers) and executed 'first time'.

How can we better use known reaction data to predict the likely success of novel transformations, and the 'best' conditions/reagents to use? What is the role of computer based mining of past data? How can we determine the optimum synthetic route under various constraints? Can such computation be used as a tool to suggest new transformations that would have a big impact?

C. Real-time reaction analysis. (*Lab of the future*).

The ability to identify and quantify in real time the components of a reaction mixture is crucial to rapid automated reaction optimisation. How might we achieve this, particularly at a cost that allows incorporation in routine workflow? Integration of analytical techniques, and powerful software is probably needed, but perhaps entirely new analytical methods will provide a solution. What is the potential for miniaturisation of analytical tools?

D. Changing the technology of synthesis. (*Lab of the future*)

Can we (and should we) aim to make a step change in the way synthesis is performed in research laboratories? How can we move the technology of synthesis forward and what are the drivers for doing it? Some suggestions include flow chemistry, automated linked reactors for sequential steps, lab-on-a-chip, reagentless ways of getting energy into reactions (photochemistry, sonochemistry, electrochemistry, microwave chemistry).

E. Building complete reaction models. (*Cuts across all themes*)

A constant complaint, and severe barrier to 'Dial-a-Molecule' is that reactions which work well on one molecule can fail (or need re-optimising) for a very similar one. Could we use efficient high-throughput study of a transformation (perhaps combined with calculations) to build a reaction model so that subsequently the optimum conditions and outcome with any set of substrates can be predicted? How many such 'understood' reactions would be needed to allow predictable synthesis of a substantial part of chemical space?

F. 1000 Click Reactions. (*Step change in molecular synthesis*)

The concept of Click chemistry was introduced by K. Barry Sharpless in 2001 to describe chemistry designed to make molecules quickly and reliably by joining small units together. The fact that azide-alkyne addition has come to be called 'the click reaction' is an indication of how difficult it has been to develop such robust reactions. How can we invent ultra-robust reactions which work

well with a wide range of substrates? What would a minimal set of such reactions be to allow us to complete a substantial proportion of synthesis?

G. Building creative links between computation and synthesis. In silico Design and Discovery.

Can we use computation to inspire new reactions, transformations, synthetic strategies? Can theoretical methods and spin-off from 'computer designed synthesis' programs be useful? How could understanding and predicting the potential energy landscape of reactions allow us to predict synthetic routes?

H. Inventing reactions which make a difference. (*Step change in molecular synthesis*)

Which approach is best in identifying new transformations (or existing ones which need to be drastically improved) that would make the biggest contribution to 'Dial-a-Molecule'? Suggestions include brainstorming meetings, cloud sourcing, computational techniques to suggest likely target transformations.

Another aspect could be an emphasis on reactions designed for sequencing (e.g. which produce no by-products to interfere with subsequent reactions – reagentless or with benign reagents).

I. The Chemical Biology Solution (*Step change in molecular synthesis / New paradigms in catalysis*)

What is the potential of biosynthesis? It does not seem to have fulfilled the promise so far, but have the tremendous recent advances in genetics and chemical biology been focussed on synthesis yet? Could CHELLS (Chemical cells) become the 'laboratories of the future'? Where on the roadmap can 'Dial-a-Molecule' place such ideas and can we identify near-term opportunities for step-change?

We need to build a wide ranging network to promote the use of tools developed in molecular biology/synthetic biology to tackle the problem of molecular synthesis.

J. Increasing catalyst efficiency and economics

Several issues have been identified as holding catalysis back such as high catalyst loadings, lack of understanding of catalyst decomposition/deactivation pathways, poor understanding of the bond forming processes, lack of scalability (or understanding of scalability). Some of the suggested solutions include moving away from common transition metals to less precious metals, reinvigoration of heterogeneous catalysis, directed serendipity, better interactions with chemical engineers to understand scaling issues with catalysts and automated computational methods for catalyst design.

K. New catalytic reactions.

Chemistry needs to move away from petrochemicals and embrace different feedstocks as to increase scope of transformations. Potential areas include biomimetic catalysis to drive selective functionalisation (eg for site-selective C-H activation), 'total functionalisation' of simple feedstock molecules, multiple integrated chemocatalytic steps (more than one transformation per pot), CO₂/CH bond activation.

L. New paradigms for synthesis / Complexity made simple.

Changing synthesis design paradigm from "What bond can we make?" to "What bond should we make?" i.e. which approach simplifies synthesis the most. Holistic strategies for synthesis – getting away from the disconnection approach.

M. Plug & play / Ball & Stick molecular synthesis.

Develop standard modules or plug&play building blocks allowing the systematic synthesis of a wide range of molecules in a way analogous to building a molecular model ('molecular engineering'). Is there a (small) set of such modules which would allow us to make most molecules? Can the concept be extended to include typical processes such as mixing, reaction, separation, etc.