Case Study: New Path Molecular Research (NPM)
https://www.newpathmolecular.com/

New Path Molecular Research (NPM) and Vapourtec have collaborated on a number of projects during the last two years. NPM's innovative approach of using technology and automation to solve difficult problems in chemical synthesis fits very well with Vapourtec's desire to supply automated flow chemistry solutions into the fine chemical industries. Projects where Vapourtec and NPM have collaborated range from reactions using organometallic reagents to automated continuous flow peptide synthesis.

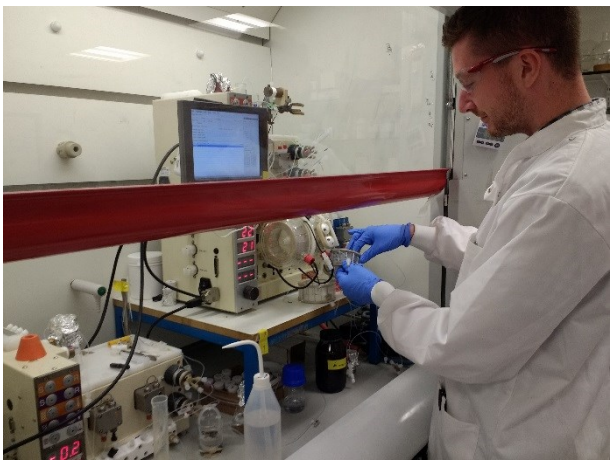
The Company
Located in the heart of the Cambridge Biotech hub, NPM was established in January 2015 out of the academic group at the University of Cambridge, led by Prof. Steven Ley. Driven by the desire to utilise the automated techniques pioneered over the past 15 years by the Ley research group to tackle difficult synthesis problems, often ones that cannot be solved using traditional methods, Prof. Ley founded the organisation with Dr Elizabeth Farrant as CEO and Dr Nikzad Nikbin as CTO.

NPM undertakes research collaborations. All research that the organisation undertakes is funded by collaboration and consultancy fees. NPM's Customers are a diverse range of organisations, from large pharmaceutical conglomerates to virtual biotechs, with no laboratory resources of their own. Projects come from pharmaceutical, animal health and agri-chemical companies. These organisations turn to NPM to draw on their flow chemistry expertise to solve their chemical synthesis challenges.

NPM has a team of 9, 7 of whom are directly involved in technical work in the lab. The team at NPM include some of the UK's most experienced flow chemists. They use their experience to select which reactions are likely to benefit and which ones are not likely to benefit from flow chemistry, as well as the practical considerations for producing the idea and putting it into practise:

"There are problems that are generally based on energy and mass transfer, these can be difficult to perform in batch mode. You can get two kinds of benefits from transferring them to flow.
One - process intensification. You can perform that reaction safer or cheaper or, more efficiently. Two - New Reactivity. There are some reactions that you can only, exclusively get that sort of reactivity in flow because the precise control of the time, the temperature, and mass and heat transfer that you have in flow. Essentially, it's impossible to get that sort of reactivity in batch." Nikzad Nikbin, CTO

The Approach



Clients come to New Path Molecular with a challenge. NPM then undertakes lab based research using a range of automated chemistry techniques and in-house equipment. The aim is to deliver problem-solving in their processes and giving the client back procedures, methods, techniques, and technologies that the client can use internally.

Typically, there are two different types of projects:

Using flow chemistry to scale up the reaction successfully

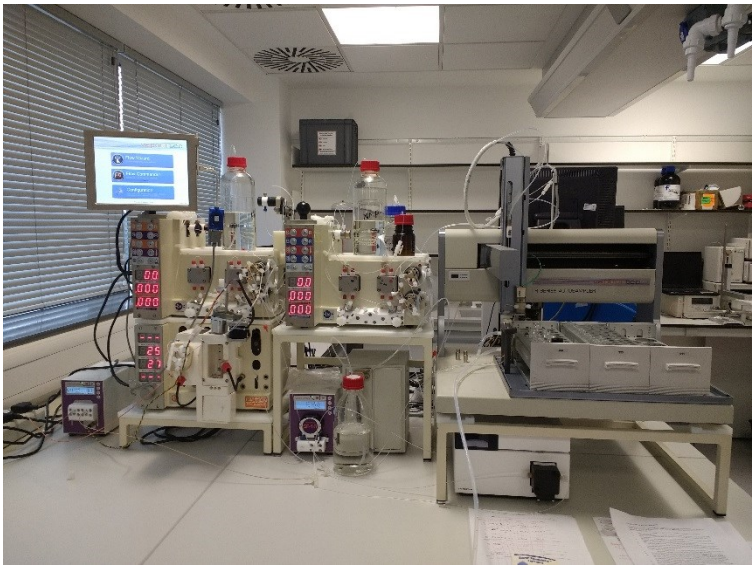
Some organisations have a molecule in really advanced stages. Their challenge is difficulty scaling up to produce their products at large scale. Flow chemistry can be used to solve that problem.

Using flow chemistry and automation to develop new compounds

Some organisations want to make molecules that, for one reason or another, are either very difficult or very time consuming to make in batch. They want to explore using flow chemistry, and particularly the automation aspect of flow chemistry, to develop new compounds on a small scale. Success would mean making the particular target compound that they set out to make, and also making various analogues of that compound in shorter periods compared to traditional batch methods. This is often achieved using automated continuous flow techniques.

One example project is with the Albemarle Corporation, a global specialty chemicals company with leading positions in lithium, bromine and catalysts used in petroleum refining.

Albemarle's aim is to develop the market for their highly concentrated lithium-based reagents. Typically, chemists use 1.6, or, in some cases, 2.5 molar butyllithium. Albemarle can supply 5, 7, and even 9 molar butyllithium in hexanes. They suggest that by using flow chemistry techniques to utilise these concentrated reagents, then enhanced reaction conditions will result from the reduced hexanes concentration within the reaction solution. NPM have been exploring the use of concentrated solutions of butyllithium and have provided data that supports this.



Flow Chemistry Systems
NPM uses predominantly Vapourtec systems for their flow chemistry work. All units are fully utilised and most of their work is based on a 4-pump system:

- 4 Vapourtec R-Series systems
- 1 Vapourtec E-Series system
- 1 x Vapourtec peptide synthesiser, on-loan as part of a collaboration
- UV-150 Photochemical Reactor
- Occasionally additional photochemistry and electrochemistry units borrowed from Vapourtec for specific collaborations

Collaboration with Vapourtec
The working relationship between the two companies is very collaborative, with NPM working with Vapourtec on a regular basis, asking questions about compatibility of different materials and reactions.

Peptide synthesis is one area of specific collaboration between the two organisations. NPM started with a particular problem, using resins in solid-phase synthesis. They approached Vapourtec for support, coincidentally at a time when Vapourtec was investigating technology for peptide synthesis in flow, and developing a novel type of reactor which could solve New Path Molecular particular problem. This development has enabled NPM to make peptides faster and more efficiently than by using conventional techniques, but also in larger scale as well:

"It will enable us to make molecules which are not possible to be made using commercially-available technology for peptide synthesis." Nikzad Nikbin, CTO

Vapourtec works closely with NPM to maintain the flow chemistry platforms, which is critical because the systems at NPM are fully deployed, and probably used more frequently than any other company in the UK.

Vapourtec has also been involved in supporting knowledge transfer to NPM's clients:

"A lot of times, for example in a recent collaboration, the collaborating company were interested in a particular technology in flow, namely electrochemistry, and we knew Vapourtec had expertise in that. Vapourtec actually helped us to transfer that sort of knowledge to the collaborating company. Also, another example would be photochemistry., We were aware that Vapourtec had developed this new technology and they actually, very generously, helped us to effectively transfer that sort of knowledge to the customer." Nikzad Nikbin, CTO

"We are chemists and we're not engineers. Whereas Duncan and his colleagues at Vapourtec are actually excellent engineers, and we really benefit from their engineering expertise because, the way we do chemistry, it does rely on high quality engineering to make it work." Elizabeth Farrant, CEO

"Over the years, out of all commercial flow chemistry units that I've used, definitely Vapourtec is my favourite. I think I'm known for that." Nikzad Nikbin, CTO

The future of Flow chemistry

Nikzad and Elizabeth were both happy to share their thoughts on the future of flow chemistry, with vision of growth and collaborative knowledge share:

"*More and more people are actually becoming familiar with flow chemistry. And I think the main reason for that is the availability of user-friendly commercially available units like Vapourtec. Because, if you go back to, say, 2003, 2004, it was a big barrier between the chemists and putting the devices together to start a flow chemistry project. So, I think that's the main reason that more and more people are using flow nowadays. When more people use it, they produce more and more knowledge that allow other people to use it. And a lot of different groups, both commercial and academics, have shown that a lot of types of chemistries can benefit from transferring to flow. We've seen that over the last few years flow chemistry actually has become more and more popular. So, I think this is a trend that will only continue the next few years*." *Nikzad Nikbin, CTO*

"I think the other thing that I've observed is that flow chemistry has always been talked about as a very good method for production of active pharmaceutical ingredients. For some time they have actually been putting together API production processes using flow chemistry, but increasingly now there are published examples of that coming through. Both GSK and Eli Lily, for example, have flow chemistry production processes now. I think that's really demonstrating the benefits of continuous processes when making pharmaceutically active molecules. And it's being actively encouraged by regulatory authorities, such as the FDA, as a very beneficial way of producing medicine." Elizabeth Farrant, CEO