SCIENCE & ENGINEERING SOUTH

Establishing Innovation at the Centre Of Drug Delivery

Trailblazing work at a London research centre is aiding development of new drug therapies that are not just more effective at preventing and treating diseases but also faster and more affordable to manufacture.

Hosted at UCL in collaboration with Imperial College London, the Engineering and Physical Sciences Research Council (EPSRC) Centre for Innovative Manufacturing in Emergent Macromolecular Therapies (CIM in EMTs) has a clear mission: to deliver a step-change in the competitiveness of the UK's biopharmaceuticals sector, generating opportunities for industrial growth as well as improved healthcare.

For example, the work of Professor Paul Dalby's team – harnessing the resources of the London Centre for Nanotechnology (LCN), another UCL/Imperial joint venture – is producing vital insights that could boost the safety and effectiveness of drugs targeting a whole range of conditions, from cancer to rheumatoid arthritis.

Better, Quicker, Cheaper

Biopharmaceuticals (drugs and vaccines derived from biological sources rather than synthesised chemically) are making an increasingly crucial contribution to healthcare across the globe. Many are based on natural proteins consisting of complex molecules made up from hundreds or thousands of atoms – and it is these 'macromolecules', whose properties can offer huge potential to underpin innovative advanced therapies, that form the focus of the CIM in EMTs.

> *"The ability to predict what additives will be able to limit protein aggregation potentially means a more reliable, more cost-effective route to delivering innovative biological therapies."*
>
> *Professor Paul Dalby, Associate Director, CIM in EMTs*

Working with 26 core partners from industry as well as 22 collaborating universities in the UK and overseas, the Centre addresses two key questions:

- equips experts to delve deeper into the past and safeguard it more effectively
- enables the public to connect with their heritage in new ways
- provides industry with opportunities to develop innovative solutions to meet future needs.

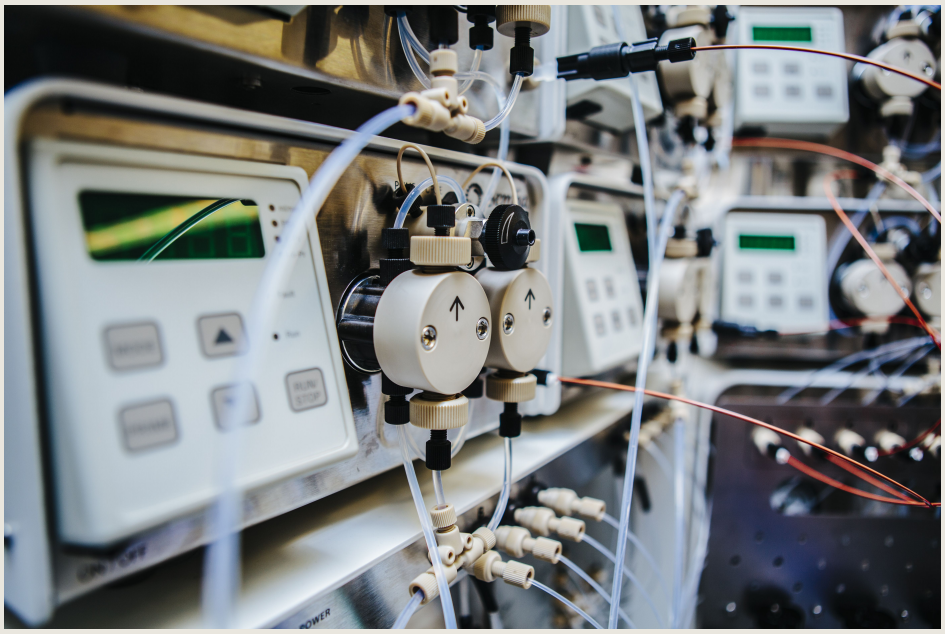
Established in 2011 and also incorporating a Centre for Doctoral Training to help drive forward fundamental research, the CIM in EMTs provides the crucial combination of stable long-term funding

and operational flexibility essential to securing progress in these spheres, weaving together a broad sweep of disciplines from biological science, physics and chemistry to engineering and the social sciences.

“Our purpose is to change the way that biomolecules with therapeutic potential are developed for manufacture by industry and for delivery to patients”, says Professor Nigel Titchener-Hooker, the Centre’s Director. “Co-created by business, we’re ideally placed to maximise the impact of our cutting-edge research because we tackle problems defined for us by the biopharmaceuticals sector itself.”

Penetrating The Secrets Of Proteins

One key challenge facing the sector is ensuring that protein-based drugs and vaccines stay stable while kept in storage, which can be for up to 2 years. “Proteins tend to clump together or ‘aggregate’,” explains Paul Dalby, Professor of Biochemical Engineering and Biotechnology at UCL and Associate Director of the CIM in EMTs. “For instance, aggregation of



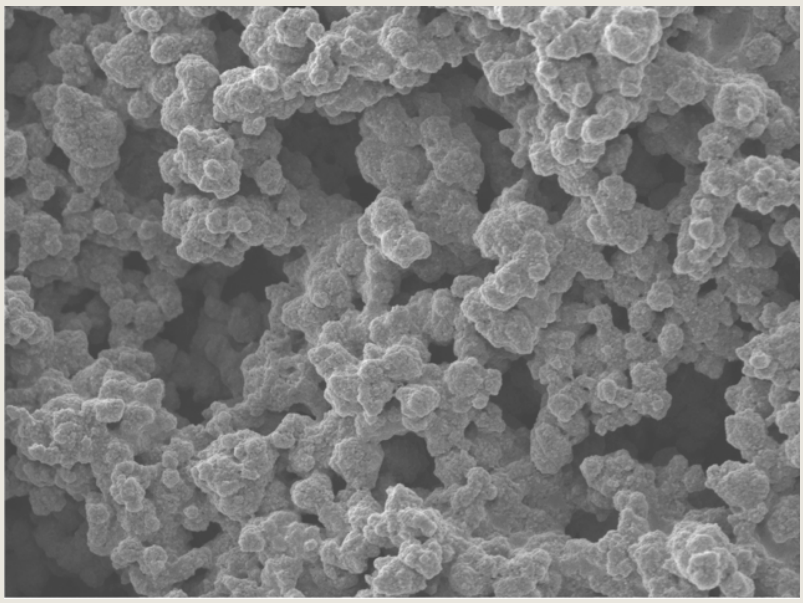
proteins that occur naturally in the body can trigger or exacerbate conditions such as Alzheimer’s and Parkinson’s Disease.

“In protein-based drugs and vaccines, aggregation can significantly compromise the formulation. Under some circumstances, formulations may even become ineffectual or unsafe to use and may require disposal – which obviously represents both a waste of resources and an unwanted cost – while a significant impact of poor formulations is the need to reinvest time and effort to find a better one. This delays time to market and can cause loss of revenue, especially if competitors come to market.”

To tackle the problem, Dalby and his team mapped in unprecedented detail the influence of environmental

conditions on the structure of, and the rate of aggregation in, antibody fragments used in protein-based therapies, before computationally modelling the features of protein structure that lead to aggregation and predicting chemical additives likely to suppress it. Professor Dalby is very

clear about the significance of this breakthrough: “The ability to predict what additives will be able to limit protein aggregation potentially means a more reliable, more cost-effective route to delivering innovative therapies”.



This research, for which funding from the EPSRC Centre was supplemented by support from the Biotechnology and Biological Sciences Research Council (BBSRC) and materials provided by biopharmaceutical multinational UCB Pharma, harnessed a wide range of capabilities and facilities:

- The team made extensive use of the LCN, which offers a phenomenal array of equipment and expertise for modelling, design, fabrication and characterisation at the scale of atoms and molecules. In particular, they utilised the LCN’s specialist clean rooms and developed cutting-edge metrology equipment to measure protein aggregation.
- For the computational modelling element of the work, the team developed a specific way of combining and using multiple commercial software packages that is suitable for replication by the biopharmaceuticals industry. Some of this work was undertaken using UCL’s High Performance Computing (HPC) platform Legion.
- Some of the physical experiments were performed at the European Synchrotron Radiation Facility (ESRF) in Grenoble, France – a joint research facility supported by 21 countries including the UK

“Now the aim is to prove the robustness of the methods we’ve developed, roll them out to include more types of protein and then carry out further validation work,” says Paul Dalby. “We hope to see our findings begin to be taken up by the biopharmaceuticals industry within the next 3-5 years.”

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National Impacts, Global Implications

Research like this has obvious benefits in supporting and strengthening the UK industry as it strives to expand its markets and extend its reach in every corner of the world. In the final analysis, the Centre’s mission has both a healthcare and an economic dimension, which fundamentally reinforce one another.

“We don’t just measure success in terms of cutting the

costs of drug manufacture and supply," comments Andrew Davidson, the Centre's National Outreach Manager. "We're also helping UK firms to enhance their global position while ensuring NHS budgets can go further in meeting rapidly rising demand for healthcare and for new life-changing therapies."

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