SSPC

Advances in Process Engineering - Part 1

Innovative process engineering makes manufacturing cost-effective, sustainable and responsive. SSPC teams work to develop fundamental scientific understanding underpinning process engineering applications to enable advances beyond the current state of the art. Our key research focus is on process intensification and continuous manufacturing including the development of modular manufacturing platforms. The advances in these areas are facilitated by multi-scale modelling of multiphase flows, materials and processes. This first part of our spotlight on process engineering shares some exciting recent breakthroughs.

Publications

Journal of Pharmaceutical Sciences targetted feature on co-processed active pharmaceutical ingredients (APIs). Highlighted research from a focussed workshop sponsored by the Food and Drug Administration (FDA) and the University of Maryland Centre for Excellence in Regulatory Science and Innovation (M-CERSI) co-chaired by **Associate Professor Steven Ferguson, University College Dublin.**

Dedicated Issue in Honor of Professor Vivek V. Ranade, **University of Limerick,** preface by Prof. Ashwin W. Patwardhan, *Industrial & Engineering Chemistry Research*.

Automated Repetitive Liquid Phase RNA Synthesis Enhanced by Membrane Separation


Ronan Kelly, PhD student
Associate Professor Steven Ferguson
University College Dublin

Development of a scalable manufacturing platform for oligonucleotide manufacturing could help provide a new technology for the synthesis on a tonne scale where current solid phase methods are limited to 15 kg batches. Our approach develops a liquid phase therapeutic oligonucleotide manufacturing platform to address scalability limitations with current solid phase synthesis technology. It is looking at the implementation of organic solvent nanofiltration (OSN) and ultrafiltration membranes (OSUF) for efficient intermediate separation which is currently a limitation for widespread adoption of liquid phase oligonucleotide synthesis (LPOS). Chemically stable and efficient commercially available membrane for intermediate separation are utilised and a one-pot synthesis strategy is implemented to telescope all reaction steps to reduce the number of separation steps from the current state-of-the-art of 2-4 down to a single step. This work is also of interest for the field of organic solvent nanofiltration (OSN) as a pharmaceutically relevant application for this emerging technology.

Multi-scale Simulations of Flow and Crystallisation

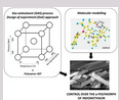

Prof. Patrick Frawley
Assoc. Prof. Orest Shardt
University of Limerick

Stephen O'Regan
PhD student

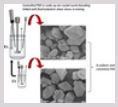
A better understanding of the conditions under which particle collisions occur will allow for a greater understanding of the extent of attrition in crystallisation processes. This project uses computational fluid dynamics simulations to help to identify the conditions under which particle collisions can be sufficiently suppressed. Simulating three-dimensional particle interactions, using inclined impinging jets, can be used to better understand large-scale crystallisation operations. The work will determine whether secondary nucleation is possible in the absence of particle collisions. It will also increase our understanding of how fundamental physicochemical materials and environmental interactions contribute to effective fluid dynamics inside industrial reactors. This increased understanding will also facilitate greater control of particle size distribution during crystallisation processes.

Publication highlights

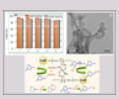
Formulation of ionic liquid APIs via spray drying processes to enable conversion into single and two-phase solid forms, **Tsolaki, E.| Stocker, M.W.| Healy, A.M.| Ferguson, S.**, *Int. J. Pharm.*, 2021, 603, 120669.



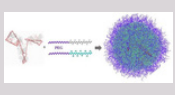
Controlling the Polymorphism of Indomethacin with Poloxamer 407 in a Gas Antisolvent Crystallization Process, **Cañellas, F.M.| Verma, V.**| Kujawski, J.| Geertman, R.| **Tajber, L.**| **Padrela, L.**, *ACS Omega*, 2022, 7, 48, 43945-43957.



Quantitative Link between Secondary Nucleation and Mixing Hydrodynamics in Batch Cooling Crystallization: A New Approach in Process Development, Yousuf, M.| Frawley, P.J., *Org. Process Res.* Dev., 2019, 23, 9, 2009-2019.



Applications of bio-resource based sustainable heterogeneous Pd-Nanocatalyst for Cross-Coupling and Michael addition reactions, Islam, M. D. | Sarkar, S.M. | Rahman, M.L. | Hasan, K. | **O' Reilly, E.J.,** *Chemical Engineering Journal*, 2024, Vol. 483, 149271.



Design rules for antibody delivery by self-assembled block-copolyelectrolyte nanocapsules, S. Javan Nikkhah | **P.A. Cazade** | **J.J. McManus** | **D. Thompson**, *Macromolecules*, 2022, 55, 2383-2397.

Optimal Control of mAb Glycosylation: model based regulation of glycosyltransferase expression


Dr Ioscani Jimenez Del Val
Dr Apostolos Tsopanoglou
University College Dublin

In the area of biotherapeutics manufacturing, the production of mAbs with consistent and less variable glycosylation profiles is of major importance. This is due to the fact that glycosylation is considered a key quality attribute and by finding ways to control and minimise variations in a consistent way, can provide industry a competitive advantage while also accelerating regulatory approval of new biopharmaceutical products.

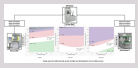
This research project aims to define a platform to study CHO cell glycosylation and identify further cell engineering strategies to optimise mAb production. It designs and constructs a synthetic gene circuit to tightly control and minimise variability in mAb galactosylation by supplementing culture media with and inducer molecule It also looks at optimising a metabolic engineering strategy to control galactosylation by feeding cells with a fluorinated analogue of galactose, needed after additionally looking to establish an in line soft sensor to monitor N-glycosylation.

Computational Studies on Processes in Turbulent Stirred Vessel

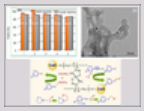
Prof. Harry Van den Akker
University of Limerick

Several computational studies are conducted to on the processes taking place in the turbulent flow in stirred vessels, such as solids suspension and mass transfer in aerated bioreactors, both at lab scale and and the industrial scale. The computational studies focus on turbulence modelling, numerical techniques, power draw, and two-phase flow features such as fluid-particle interaction, the just-suspended speed for solid particles, bubble sizes and their size distribution due to coalescence and break-up, gas hold-up, and mass transfer (oxygen, carbon dioxide). In addition, we are developing an innovative technique for modelling the sub-grid scale turbulence in large-eddy simulations.

Publication highlights



Two-fluid simulations of an aerated lab-scale bioreactor, **Roya Jamshidian** | James Scully | **Harry E.A. Van den Akker**, *Chemical Engineering Research and Design, 2023, Vol. 196, 254-275.*



Modelling the Compaction Step of a Platform Direct Compression Process. Peddapatla, R.V.G.; Slevin, C.; Sheridan, G.; Beirne, C.; Swaminathan, S.; Browning, I.; O'Reilly, C.; Worku, Z.A.; Egan, D.; Sheehan, S.; and **Crean, A.**, *Pharmaceutics 2022, 14, 695.*

Platform Modelling Approach to Support Tablet Development, Scale-up and Technology Transfer

Prof. Abina Crean, University College Cork, in collaboration with **Alkermes,** Ireland.

The project established a platform approach to inform the design of direct compression tablet formulations for future commercial products. A platform approach is the application of common processes that can be used to streamline development activities. The use of a platform approach during product development has the potential to decrease development time and cost, decrease time to market, and simplify scale up and process transfer.

Potential Spin-outs

Prof. Sarah Hudson, NanoComp
Developing a patented oral drug formulation platform that utilises simple and efficient manufacturing processes to change insoluble APIs into powder that is ready for tableting while adding superior dissolution and stability to the final form.

Associate Professor Luis Padrela, CM Nano
Commercialising patented technology for the continuous production & isolation of spray dried nanoparticles onto carrier particles to undergo direct compression.

Associate Professor Emmet O' Reilly, Chromwatch
Developing a unique Process Analytical Technology (PAT) tool capable of providing "contactless" scientific measurements. Designed for use in sterile environments such as biotherapeutic manufacturing it provides real time information facilitating reduced manufacturing times, improved process consistency and enhanced regulatory compliance.

Dr Michael Stocker, SEncIL
Commercialising a novel platform technology that enables the spray encapsulation of ionic liquids to enable formulation of poorly soluble active ingredients.

SSPC Expertise

Process Modelling

Prof. Damien Thompson, UL
Associate Prof. Sarah Guerin, UL
Prof. Michael Vynnycky, UL
Dr Ioscani Jimenez del Val, UCD
Dr Jessica Whelan, UCD
Associate Prof. Kevin Moroney, UL
Associate Prof. Doireann O'Kiely, UL
Dr Philip Donnellan, UCD

Multiphase/ continuous processes/ reactors

Prof. Vivek Ranade, UL
Associate Prof. Steven Ferguson, UCD
Prof. Gavin Walker, UL
Prof. Harry Van den Akker, UL
Prof. Pat Frawley, UL
Associate Prof. Luis Padrela, UL
Associate Prof. Emmet O' Reilly, UL
Associate Prof. Mattias Vandichel, UL

Formulation

Prof. Michael Zaworotko, UL
Associate Prof. Sarah Hudson, UL
Associate Prof. Orest Shardt, UL
Prof. Abina Crean, UCC
Dr Sonja Vucen, UCC
Prof. Anne Marie Healy, TCD
Prof. Lidia Tajber, TCD
Prof. Liz Topp, NIBRT
Dr Niall O'Reilly, SETU

Infrastructure

Next Generation Nanopharma Process Development Platform (NaPRO) at the University of Limerick


Assoc. Prof. Luis Padrela and **Prof. Vivek Ranade**'s NaPRO project establishes a unique state-of-the-art suite of facilities, which will allow to de-risk the scalability and manufacture of nano(bio)pharmaceuticals and facilitate the adaptation of these technologies to existing industrial facilities.

For more information on SSPC and the SSPC Process Engineering Community, please contact SSPC Industry Engagement Manager aisling.arthur@ul.ie