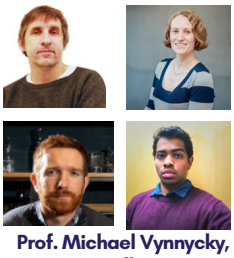
SSPC The Research Ireland Centre for Pharmaceuticals

Modelling Spotlight

Predictive computational modelling and design is a key accelerator of synthesis, formulation and process control in drug development and manufacturing in the biopharma sector. World-leading modelling experts in SSPC are creating blueprints for next-generation medicines and platforms that are more patient-centred and sustainable. The Centre plays a key role in development and exchange of research and talent at the industry-academic interface to ensure the Irish pharma sector has the digital skills needed to continue to grow and develop as a leader in drug development and manufacturing.

Development of a Modelling Framework for Polymorphism in Anti-Solvent Crystallisation



Prof. Michael Vynnycky, Associate Prof's Doireann O' Kiely, and Kevin Moroney, Dr Milton Assunção
University of Limerick

A team of researchers from the SSPC Modelling theme have joined forces with Varda Space Industries to advance mathematical modelling of crystallisation in microgravity. The aim of this project is to improve the understanding of the role that hydrodynamics, and specifically the effect of gravity, plays in polymorphic crystallisation. The team developed a novel mathematical model combining growth and nucleation mechanisms with hydrodynamic effects in order to predict crystal distributions during antisolvent polymorphic crystallisation. Gravity, supersaturation and antisolvent fraction interact nonlinearly, influencing both mass yield and polymorph ratios in a complex manner. For a fixed experimental timeframe, increased gravity leads to a higher mass yield, particularly at lower crystal nucleation rates. In further work, the team shed light on the dynamics of a growing, sedimenting particle, obtaining an accurate analytical solution for the particle's velocity and size which otherwise would have taken days to compute numerically.

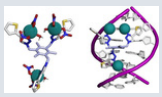
Analysis of a model for polymorphism in gravity-driven, antisolvent crystallization. Assunção, M., Moroney, K. M., O'Kiely, D., & Vynnycky, M. (2025) *SIAM Journal on Applied Mathematics. 85 (3) 1261-1286.*

Unlocking the Stability of Multi-Component Pharmaceutical Forms

Prof. Andrew Kellett, Prof. Damien Thompson, Dr Robert Fox, Dr Alex Gibney
Dublin City University

Co-crystals have enormous potential to improve and speed up the development of pharmaceutical solid forms, for example, improving solubility. The formation and stability of co-crystals are hard to predict, this project uses state-of-the-art computational modelling to explore the intermolecular interactions that hold these crystals together and to understand the factors governing co-crystal stability. The new understanding of stability was used to develop new tools for rapidly predicting the formation of co-crystals crystals and, in turn, key properties such as solubility.

Our work has identified key features that promote co-crystallisation and further identified adequate methods to carry out these calculations. This work will have impact on the formulation of drug substances so that the stability and solubility of co-crystal drugs might be improved. This work will also have an impact on anticancer agents informing the structural features binding the copper metal centre enabling more effective anticancer agents to be produced.



A click chemistry-based artificial metallo-nuclease. Gibney, A., de Paiva, R. E. F., Singh, V., **Fox, R., Thompson, D.**, Hennessy, J., **Kellett, A**. (2023). *Angewandte Chemie (International Ed. in English)*. 62, e202305759.

A computational Fluid Dynamics Study of Mass Transfer in a Large Scale Aerated Stirred Bioreactor

Prof. Harry Van den Akker
Dr Roya Jamshidian
University of Limerick

Computational Fluid Dynamics (CFD) is exploited to study mass transfer in a specific stirred aerated bioreactor used in a cell culture process. The focus is on which empirical correlations from the literature can best be used for calculating the volumetric mass transfer coefficient kLa on the basis of the spatially distributed and/or average energy dissipation rate obtained in CFD simulations. A set of CFD simulations was carried out using a two-fluid version of a finite volume-based code, ANSYS-Fluent, as well as an LBM-based code with Lagrangian bubble tracking, M- Star. While the former is a RANS-based code exploiting a two-equation turbulence model, the latter uses the Large-Eddy Simulation (LES) technique. Gassed power draw, air volume fraction, energy dissipation rate, and (kLa) are calculated in both codes and compared mutually as well as to experimentally measured data and analytical correlations available in the literature. The energy dissipation rate was underpredicted by Fluent, leading to lower breakup rates and an underprediction of kLa. The M-Star simulations also underpredict kLa although predicting much higher levels of energy dissipation. However, using a constant value for kL and just the volume-averaged a from Fluent or M- Star improved the results significantly, which then are in good agreement with the experimental kLa value.

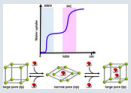
A computational fluid dynamics study of mass transfer in a large-scale aerated stirred bioreactor. **Jamshidian, R., Scully, J., Van den Akker, H.E.A.,** (2025). *Chemical Engineering Journal. 509, 160723.*

One step Further: A Flexible Metal-Organic Framework that Functions as a Dual-Purpose Water Vapor Sorbent



Prof. Mike Zaworotko
Assoc. Prof. Matthias Vandichel
Dr Sousa Javannikkhah
University of Limerick

This research is a recent example of the collaboration between the Zaworotko and Vandichel groups that has thus far resulted in 19 joint publications since 2020. In this work, reducing the energy footprint of water purification and dehumidification is addressed in a desiccant that has a flexible structure. The desiccant in question, [Zn3(OH)2(otca)2], is only the second that exhibits water induced transformations that involve water induced shrinkage and represents the first regeneration optimised sorbent (ROS) with two steps at RH ranges relevant for both atmospheric water harvesting and dehumidification. To evaluate and substantiate the mechanism of water sorption by [Zn3(OH)2(btca)2], density functional theory (DFT) calculations and grand canonical Monte Carlo (GCMC) simulations were conducted. These state-of-the-art modelling studies indicate that hydrogen bonding involving water molecules is what drives the unusual properties of this ROS material. For other joint studies, combinations of different modelling approaches (e.g., hybrid GCMC/MD) have also played a key role in revealing framework mobility during adsorption.



One Step Further: A Flexible Metal-Organic Framework that Functions as a Dual-Purpose Water Vapor Sorbent. Shabangu, S.M., Bezrukov, A.A., Eaby, A.C., Nikkhah, S.J., **Darwish, S.**, Nikolayenko, V.I., Sensharma, D., Wang, S.-Q., **Vandichel, M., Zaworotko, M.J.** (2025) *ACS Materials Letters*. 7 (2) 433-441.

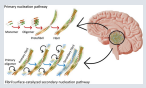
Meet the SSPC Researchers

Prof. Norma Bargary
Prof. Patrick Frawley
Assoc. Prof. Sarah Guerin
Assoc. Prof. Kevin Moroney
Prof. Stephen O'Brien
Assoc. Prof. Doireann O'Kiely
Dr Orest Shardt
Prof. Christophe Silien
Prof. Damien Thompson
Dr Davide Tiana
Prof. Harry Van den Akker
Assoc. Prof. Matthias Vandichel
Prof. Michael Vynnycky
Dr Javad Zeinali

Accelerated Alzheimer's Aβ-42 Secondary Nucleation Chronologically Visualized on Fibril Surfaces

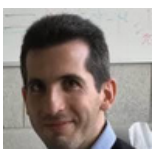

Prof. Damien Thompson
Assoc. Prof. Shayon Bhattacharya
University of Limerick

A longstanding joint modelling/experimental collaboration between the Modelling theme and researchers at EMPA, this research investigates how toxic amyloid oligomers, which are linked to Alzheimer's disease, form on the surfaces of amyloid fibrils through secondary nucleation mechanism. By combining nanoscale imaging with atom-scale modelling, we can track how these oligomers bind and proliferate at specific catalytic sites on fibril surfaces—from the initial stages all the way to the formation of mature structures. Collectively, the knowledge gained from this study may prove to be useful in identifying valid therapeutic targets and explaining how amyloids grow and spread in the AD brain. In particular, one of the key findings is the identification of a subpopulation of fibrils exhibiting heightened surface catalytic activity. These unique fibrils could offer new insights for slowing or preventing harmful aggregations associated with Alzheimer's. In this way, pioneering visual tools to understand these mechanisms not only enhances our grasp of Alzheimer's disease pathology but may also inspire new therapeutic strategies.



Accelerated Alzheimer's Aβ-42 secondary nucleation chronologically visualized on fibril surfaces. Nirmalraj, P. N., **Bhattacharya, S., & Thompson, D.** (2024) *Science Advances*. 10, eadp5059.

Enhancing Advanced Pharmaceutical Formulation Processing via Molecular Modelling

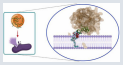




Assoc. Prof. Sarah Guerin
Dr Pierre Cazade, Niamh Hickey (PhD)
University of Limerick

This PhD project looks to advance the understanding of single-component crystalline materials (SCCMs) and, especially, multi-component crystalline materials (MCCMs) in order to enable improved orally delivered drug products. It aims to enable a disruptive change in manufacture of drug substances & drug products by developing new techniques to design and predict behaviour in silico in order to reduce trial-and-error experimentation. It looks at developing new transformative physical models for broad uptake in drug manufacture by modelling the interactions between excipients, excipients and active pharmaceutical ingredients (APIs) and the interaction in water and ethanol.

Further Publication Highlights

Molecular switching by proton-coupled electron transport drives giant negative differential resistance. Zhang, Q., Wang, Y., Nickle, C., Zhang, Z., Leoncini, A., Qi, D.C., Sotthewes, K., Borrini, A., Zandvliet, H. J. W., Del Barco, E., **Thompson, D.,** Christian A. Nijhuis. (2024), *Nature Communications*. 15, 8300.



Solid lipid nanoparticle formulation maximizes membrane-damaging efficiency of antimicrobial nisin Z peptide. Ratrey, P., Bhattacharya, S., Coffey, L., Thompson, D., Hudson, S,P., (2024), *Colloids and Surfaces. B, Biointerfaces*. 245, 114255.

Guest Molecule-Mediated Energy Harvesting in a Conformationally Sensitive Peptide-Metal Organic Framework. Chen, Y., **Guerin, S.,** Yuan, H., O'Donnell, J., Xue, B., **Cazade, P.**-A., Haq, E.U., Shimon, L.J.W., Rencus-Lazar, S., Tofail, S.A.M., Cao, Y., **Thompson, D.,** Yang, R., Gazit, E. (2022), *Journal of the American Chemical Society*. 144 (8).

Dynamic molecular switches with hysteretic negative differential conductance emulating synaptic behaviour. Wang, Y., Zhang, Q., Astier, H.P.A.G., Nickle, C., Soni, S., Alami, F.A., Borrini, A., Zhang, Z., Honnigfort, C., Braunschweig, B., Leoncini, A., Qi, D.-C., Han, Y., del Barco, E., **Thompson, D.**, Nijhuis, C.A. (2022), *Nature Materials*. 21, 1403-1411.