CBMNet

CROSSING BIOLOGICAL MEMBRANES NETWORK, A BBSRC NIBB

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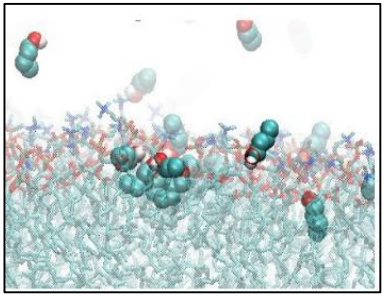
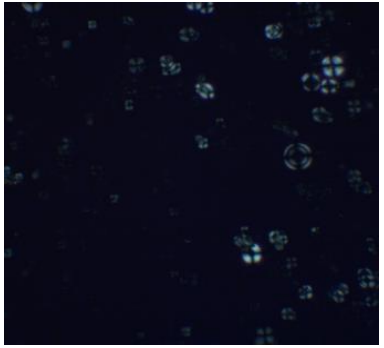
In vitro and *in silico* models of n-butanol-membrane interactions





The Challenge

Solventogenic Clostridia are used by Green Biologics to generate n-butanol from a variety of feed-stocks providing sugars for fermentation. However, n-butanol is expensive to purify from the fermentation broth. The cost of in-situ solvent removal is greatly decreased by fermenting at higher concentrations of n-butanol. However, n-butanol is toxic to Clostridia at concentrations above ~2%.

It has been recently demonstrated that this toxicity is likely due to damage to the cell plasma membrane. In addition, it has been previously shown that n-butanol interacts with lipid membranes, but we lack an understanding of the molecular mechanisms involved. Understanding this will enable the engineering of more resistant clostridia strains.

The Research

Dr Alan Goddard is a Lecturer at Aston University. The research in his laboratory focusses mainly on the lipid membrane that surrounds biological cells and the integral proteins residing within this. Dr Manuela Mura is a Senior Lecturer at the University of Lincoln. She uses classical molecular dynamics tools to study the interaction of molecules with modelled lipid bilayer membranes.

Green Biologics converts a wide range of sustainable feedstocks into high performance green chemicals. They combine advanced, high productivity fermentation utilising superior-performing Clostridium microbial biocatalysts to produce renewable n-butanol and acetone.

Dr Goddard and Dr Mura applied for a CBMNet Business Interaction Voucher with Green Biologics to further develop their collaborative partnership and produce preliminary data that could be built on in future funded projects. The project aimed to use a combination of *in vitro* and *in silico* approaches to probe the nature of the n-butanol-membrane interaction.

CBMNet Business Interaction Voucher

The Result

Dr Goddard's and Dr Mura's group obtained results demonstrating that n-butanol appears to intercalate into lipid bilayers in a lipid-dependent manner. In many ways n-butanol appears to act in a similar manner to a detergent but does not solubilise the membrane.

The combination of *in vitro* assays and *in silico* modelling provided a unique insight into the mechanisms of n-butanol-bilayer interactions. A better understanding of this, and the lipid-dependence of the interaction, paves the way for creation of more robust industrial strains.

The Future

The data generated in this project will feed into a future research council funding application to continue the collaboration with Green Biologics determining the precise nature of the n-butanol-membrane interaction in order to better understand how to engineer more resistant strains.

Dr Goddard and Dr Mura continue to collaborate on a number of related projects investigating the interaction of biomolecules with lipid bilayers.

"This project provided an excellent opportunity to become involved in an interdisciplinary project that has revealed new insights that would not have been accessible via a single technique".

Dr Alan Goddard
Aston University

"This project was a great opportunity to apply my expertise to an industrially-relevant project and helped build strong links between the new School of Maths and Physics and the School of Life Sciences".

Dr Manuela Mura
University of Lincoln

"GBL focusses on commercial research but fundamental understanding is needed to identify targets. This BIV allowed us to collaboratively apply expert knowledge to a new application. The outputs will lead to further research and ultimately better commercial strains".

Dr Tim Davies, Green Biologics

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Email: cbm@sheffield.ac.uk
Telephone: 0114 222 9766

Website: www.cbmnetnibb.net
Twitter: @CBMNet_NIBB