



ERA CoBioTech

BIO TECH RESEARCH AND INNOVATION HACK 2021

Final seminar of the cofunded projects of ERA CoBioTech



Project name: Membrane Modulation for Bioprocess
Enhancement

Project acronym: MeMBrane

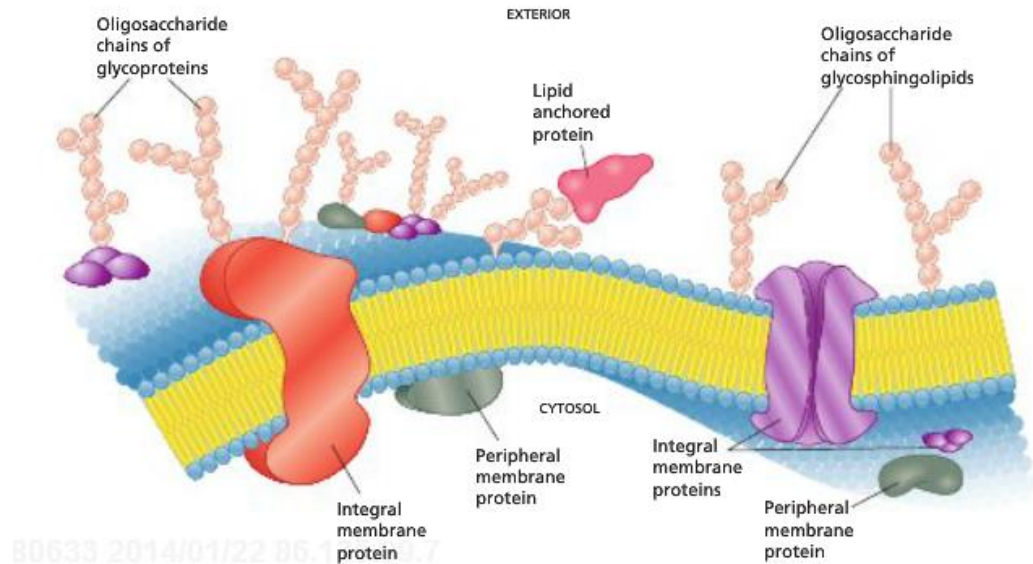
Name: Dr Alan Goddard



This project has received funding from the European Union's Horizon
2020 research and innovation programme under grant 722361

28.09.2021

“MeMBrane will create optimized high-yield microbial cell factories that perform effectively in commercial biotechnological processes in a profitable and sustainable way. To achieve this, significant advances in the understanding of how yeast and bacteria tune their cell membranes under different process stresses will be applied to design genetically and metabolically modified strains.”



80633 2014/01/22 06.1 1.7

- Total project budget: €2.4M
- Project start and end date: May 2018 (in some places) – December 2021 (in some places!)



- Aston University, UK:
 - *Dr Alan Goddard, Dr Alice Rothnie, Prof. Roslyn Bill, Prof. Corinne Spickett, Prof. Andrew Pitt, Dr Sarah Routledge, John Linney, Dr Joyce Bennett*



- University of York, UK:
 - *Dr. Gavin Thomas, Dr Vicky Springthorpe, Dr Sandy MacDonald*



- Forschungszentrum Jülich, Germany:
 - *Dr Stephan Noack, Dr Jan Marienhagen, Andrea Grego, Api Tharmasothirajan*



- Consejo Superior de Investigaciones Científicas (CSIC), Spain:
 - *Prof. Amparo M. Querol, Dr José Guillamón, Dr Eladio Barrio, Dr Javi Alonso del Real, Maria Lairon Perez*



- University of Groningen, Netherlands:
 - *Prof. Siewert-Jan Marrink, Dr Josef Melcr*



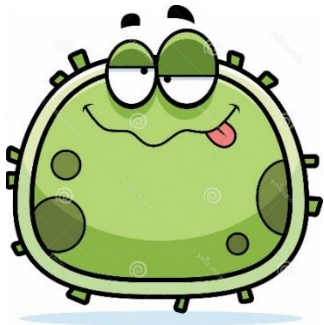
- Remembrane, Italy
 - *Dr Alex Chatgialloglu*
- Nova-Institute, Germany
 - *Niels de Beus, Francesco Longhini*
- Lallemand
 - *Dr Jose Heras*
- Pakmaya
 - *Mustafa Turker*
- Advisory Board
 - *Prof. Peter Henderson, Dr Harald Pichler, Dr Gerd Seibold, Dr Tim Davies, Dr Irina Borodina*



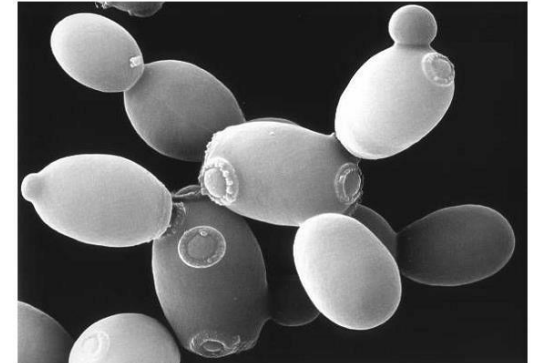
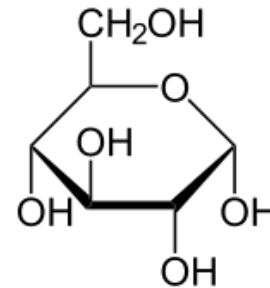
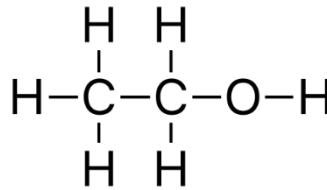
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● Project objectives

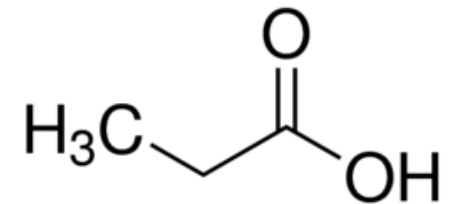
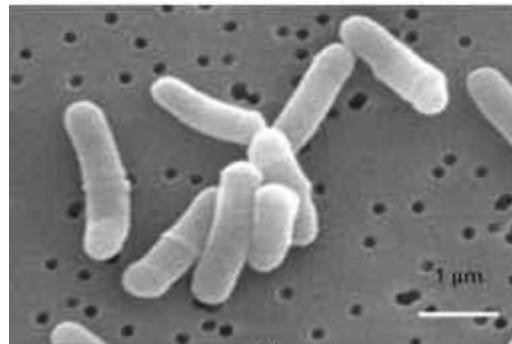
- Develop strong collaborations between leading academic research groups and industry to commercialise bioprocesses
- Overcome toxicity challenges in existing bioprocesses by engineering cellular membrane composition
- Achieve more sustainable, competitive and eco-efficient fermentative processes
- Achieve improved yield per mass unit biomass-input compared to current processes allowing validation of TRL 5



- Lallemand, Spain:
 - Mr José María Heras

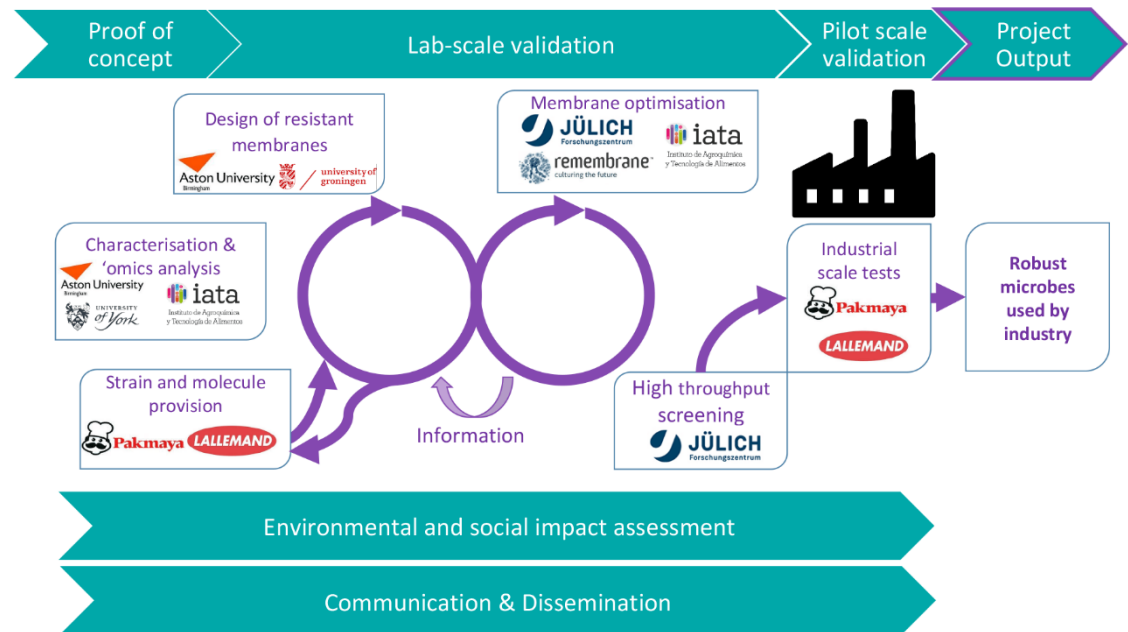


- Pakmaya, Turkey:
 - Dr Mustafa Turker

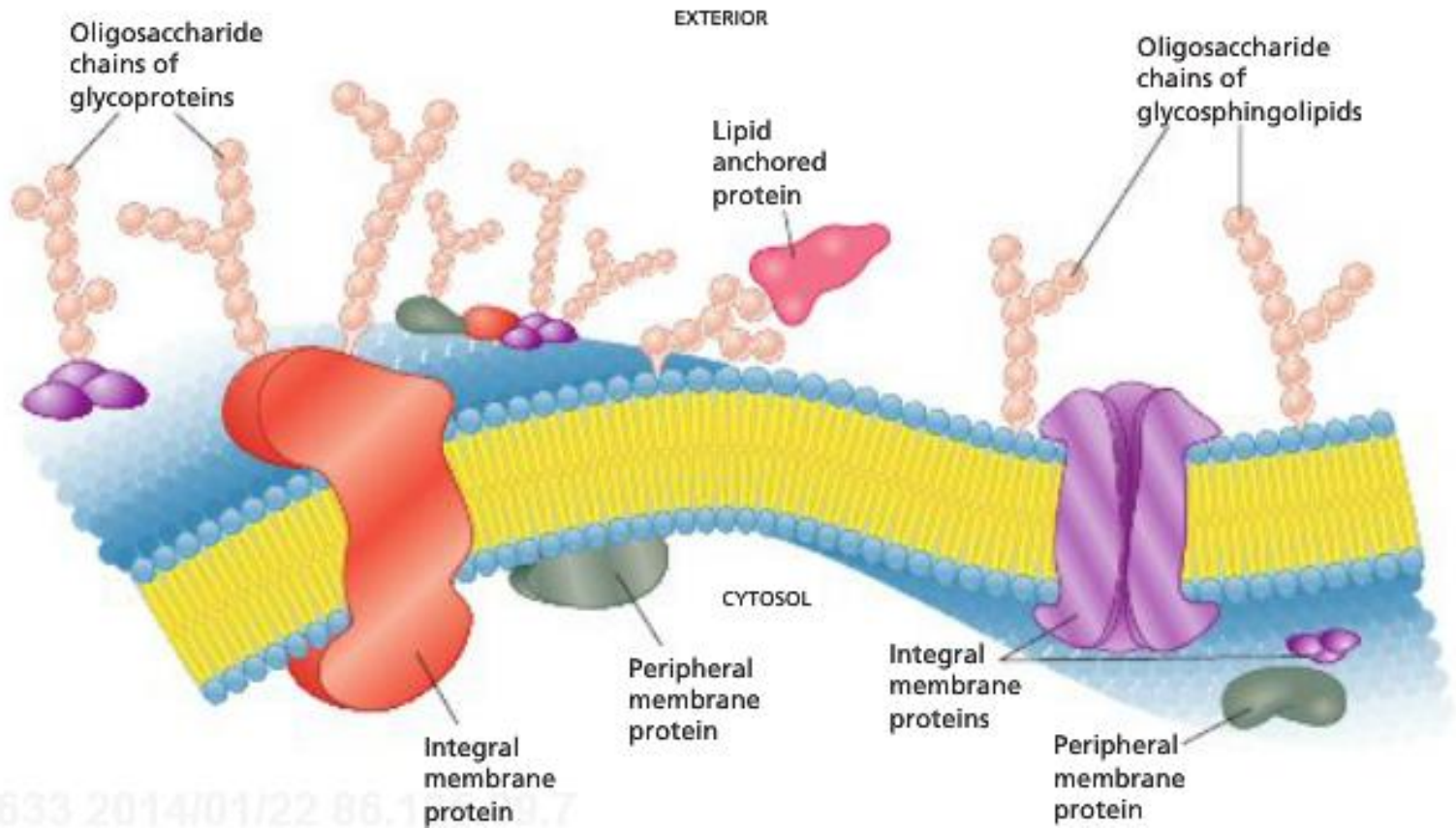


m WPs:

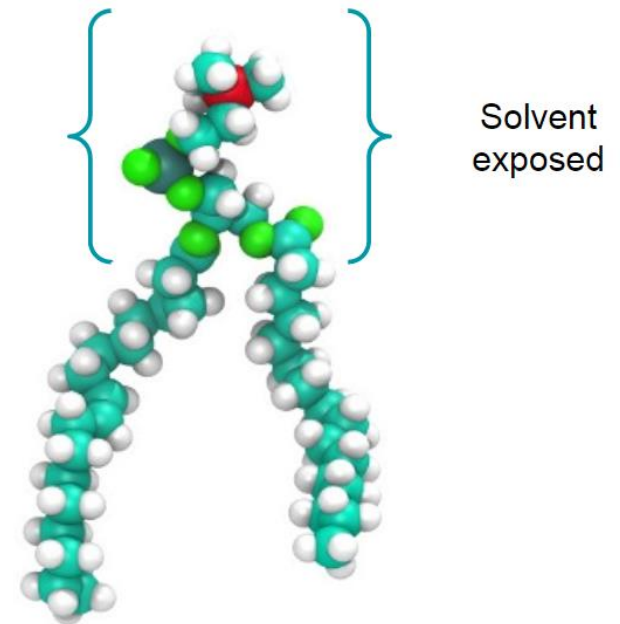
1. – omics.
2. *In vitro / in silico* analysis.
3. Membrane engineering.
4. HTS.
5. Life Cycle Analysis.
6. Communication.
7. Project Management.

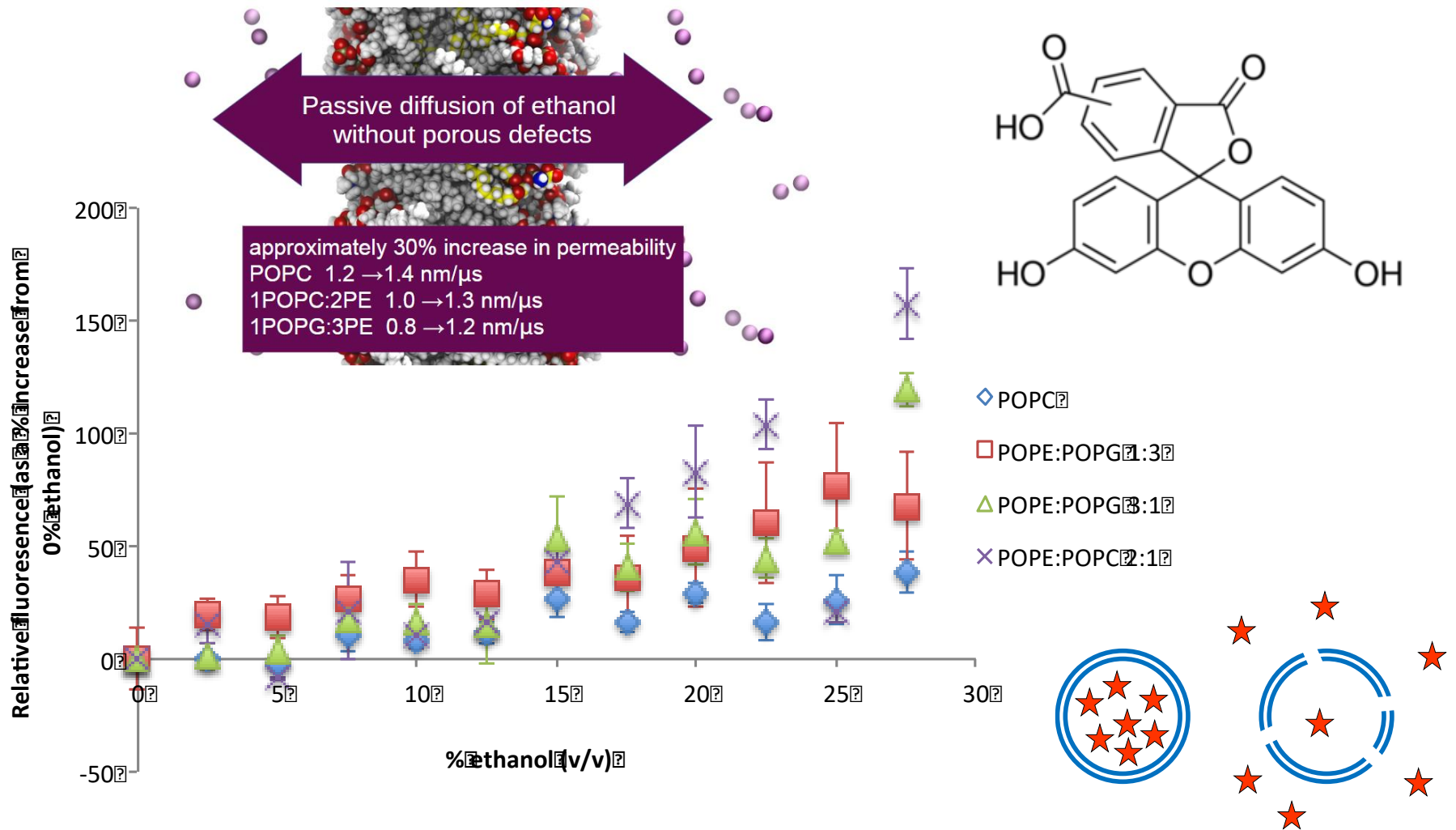


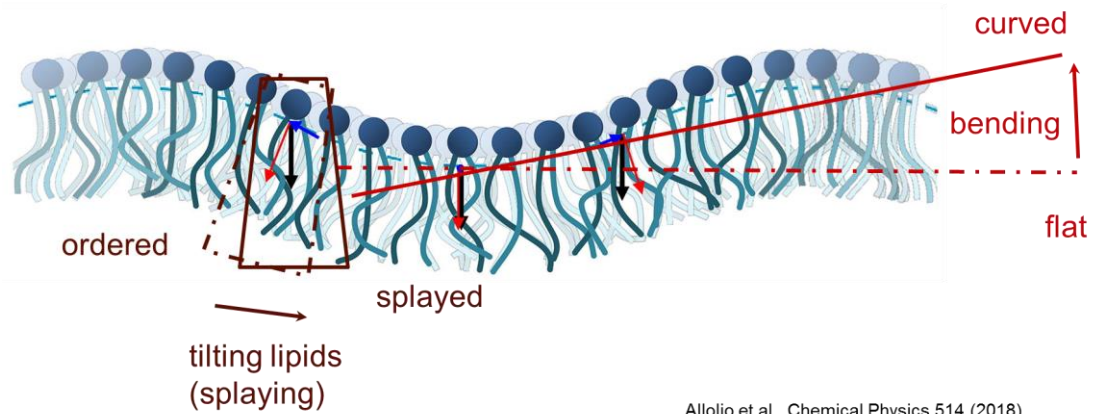
Lipids and Membranes



- Effect of climate change is significant on the wine industry.
- Generally leads to increased ABV%.
- Used a combination of molecular dynamics and “wet” experiments.
- Mainly focussed on phospholipids.





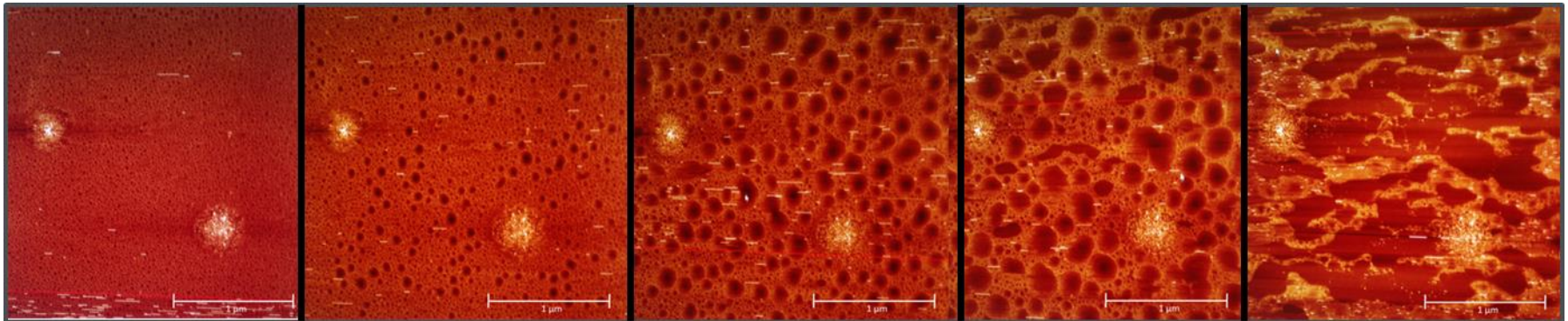


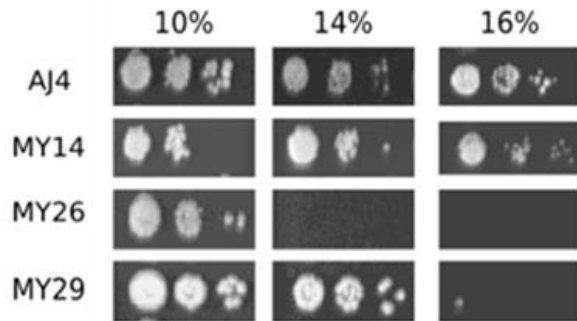
Allolio et al., Chemical Physics 514 (2018)

0 h

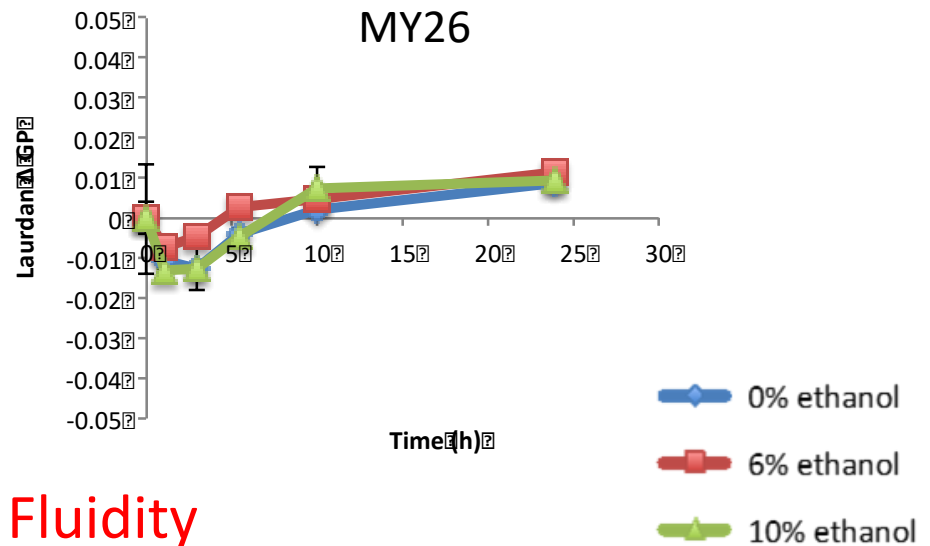
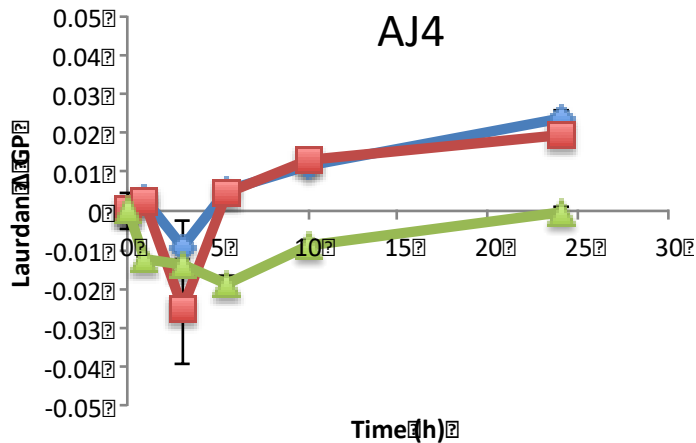
0.2 h

2 h





- Tolerant strains increase their membrane fluidity more during growth in high EtOH.



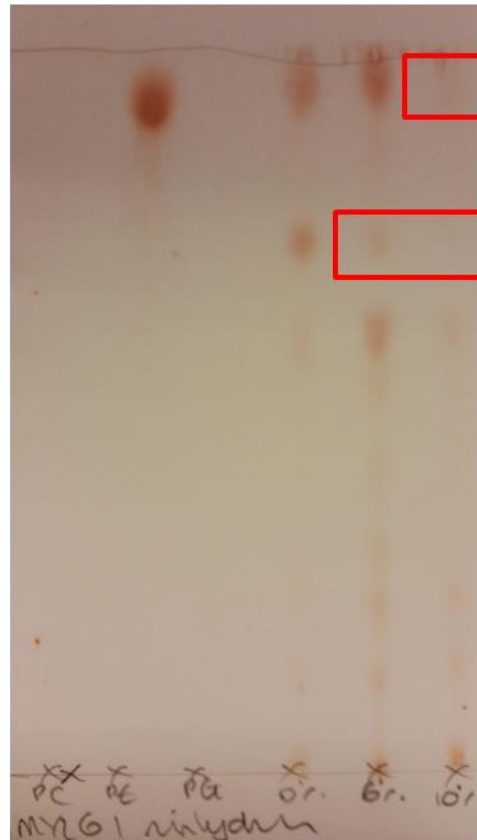
GP ↓ = ↑ Fluidity

AJ4



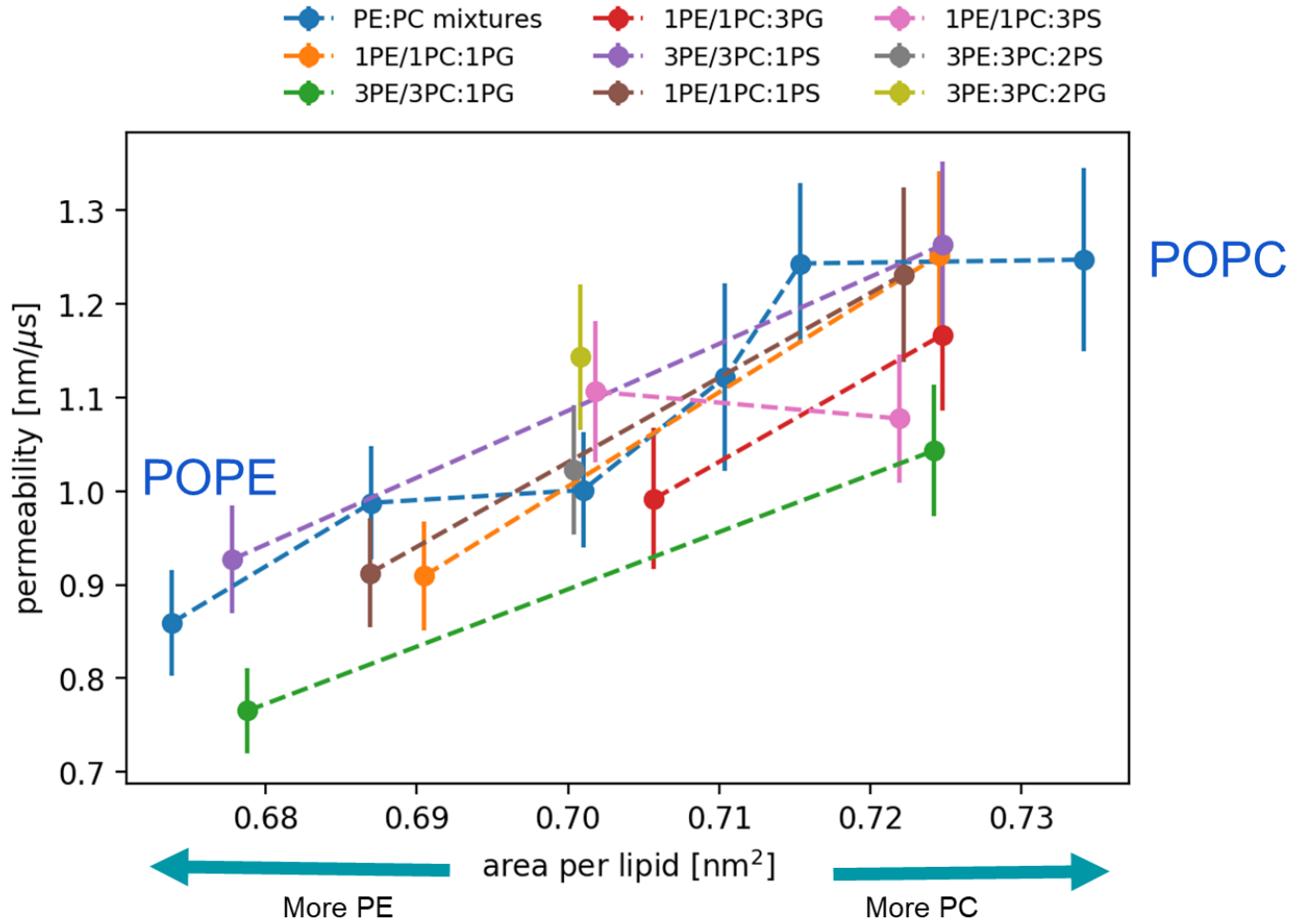
PC PE PG 0% 6% 10%
ethanol

MY26



PC PE PG 0% 6% 10%
ethanol

- Ninhydrin stains free amino groups.
- Decrease in PE with EtOH?

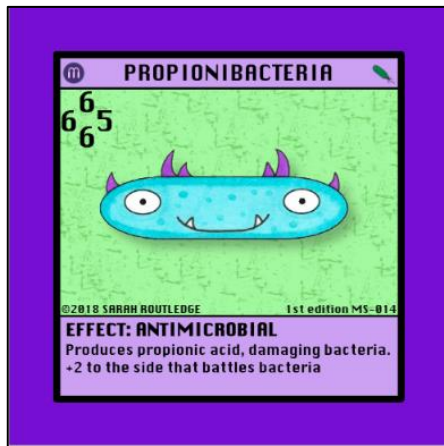


- Molecular dynamics shows that:

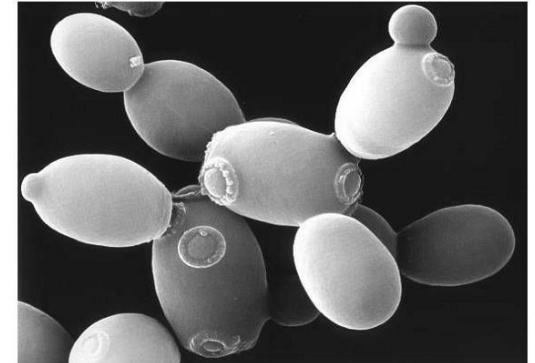
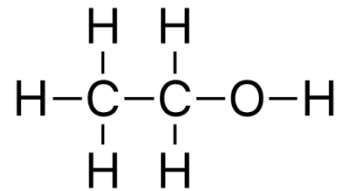
In total,
PE decreases
permeability, adsorption of ethanol,
fluidity of phospholipid membranes
and their area per lipid

- PE goes down with increasing EtOH.
- Are cells actually trying to become more fluid?
- Links to laurdan data.

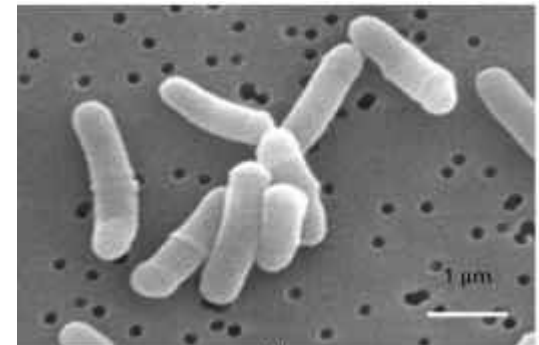
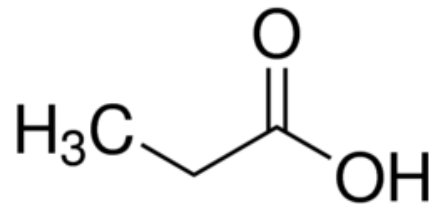
- Website.
- MicroStrike card game.
- Photography competition.
- SuperYeast citizen science project.
- Futurum article.
- Song and video.



- Lallemand, Spain:
 - Hybrid strains will be tested at industrial scale.



- Pakmaya, Turkey:
 - Optimised fermentation currently being scaled.



- *“MeMBrane will create optimized high-yield microbial cell factories that perform effectively in commercial biotechnological processes in a profitable and sustainable way. To achieve this, significant advances in the understanding of how yeast and bacteria tune their cell membranes under different process stresses will be applied to design genetically and metabolically modified strains.”*
- In depth analysis of membrane response to stress.
- Generation and analysis of strains that are more robust.
- Scale up of these strains.
- Potential follow up projects through PhDs and MSCA programmes.

- Lairón-Peris, M., Castiglioni, G.L., Routledge, S.J., Alonso-del-Real, J., Linney, J.A., Pitt, A.R., Melcr, J., Goddard, A.D., Barrio, E. and Querol, A (2021) Adaptive response to wine selective pressures shapes the genome of a *Saccharomyces* interspecies hybrid. *Microbial Genomics*. 7 (8), 000628.
- Lairón-Peris, M., Routledge, S.J., Linney, J.A., Alonso-del-Real, J., Spickett, C.M., Pitt, A.R., Guillamon, J.M., Barrio, E., Goddard, A.D.* and Querol, A.* (2021) Analysis of lipid composition reveals mechanisms of ethanol tolerance in the model yeast *Saccharomyces cerevisiae*. *Applied and Environmental Microbiology* 87 (12), e00440-21.

- New consortium that worked really well together.
- Many challenges, mostly due to the pandemic.
- Would have been great to physically meet more often!



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- www.MeMBrane.org.uk



Addressing the global need for sustainable bio-based products by engineering cell factories tolerant to product toxicity.

