Microcavity Supported Lipid Bilayers: Versatile microfluidic models for Biophysical studies of membrane proteins and lipids.



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A key prerequisite in an ideal supported lipid bilayer based cell membrane model is that the mobility of both the lipid matrix and its components are unhindered by the underlying support. This is not trivial and with the exception of liposomes, many of even the most advanced approaches, although accomplishing lipid mobility, fail to achieve complete mobility of reconstituted membrane proteins. Herein, we describe a versatile platform for study of membrane proteins by fluorescence and electrochemical techniques, see Figure, comprising lipid bilayers assembled over buffer-filled, arrays of microcavities spherical cap formed from microsphere template from polydimethoxysilane or gold. The platform is built into a simple flow through platform suitable for fluorescence correlation spectroscopy and electrochemistry/Raman spectroscopy when fabricated in gold.



As the bilayers are suspended over deep aqueous reservoirs, reconstituted membrane proteins experience an aqueous interface at both membrane interfaces and attain full lateral mobility. Their utility as supports for the study of membrane and peripheral proteins will be exemplified in three case studies with proteins of different dimensions in their extracellular and cytoplasmic domains reconstituted into DOPC lipid bilayers; transmembrane protein Glycophorin A, and Integrin allbB3 and cholera toxin. In the latter case the impact of lipid bilayer composition and asymmetry on toxin-recognition will be discussed. In all cases, the proteins exhibited 100% mobility with high lateral diffusion coefficients.

References:

- [1] Aqueous-filled polymer microcavity arrays: versatile & stable lipid bilayer platforms offering high lateral mobility to incorporated membrane proteins, Basit H, Gaul V, Maher S, Forster RJ, Keyes TE, Analyst. 2015, 140, 3012.
- [2] Microcavity Supported Lipid Bilayers; Evaluation of Drug-Lipid Membrane Interactions by Electrochemical Impedance, and Fluorescence Correlation Spectroscopy, Ramadurai S1, Sarangi NK1, Maher S, MacConnell N, Bond AM, McDaid D, Flynn D, Keyes TE.Langmuir. 2019, 35(24):8095-8109
- [3] Microcavity Supported Lipid Membranes: Versatile Platforms for Building Asymmetric lipid bilayers and for Protein Recognition:, Berselli, G Ramadurai S, Sarangi NK, Keyes TE, ACS Appl. Bio Mater. 2019, 2, 8, 3404-3417
- [4] Macromolecular inversion-driven polymer insertion into model lipid bilayer membranes, S. Ramadurai; A.Kohut; A. Voronov; N. Kumar Sarangi; O. Zholobko; V. Baulin, T.E. Keyes., J. Coll. Interface Sci, 2019 J Colloid Interface Sci. 2019 Apr 15;542:483-494

SHORT BIOGRAPHY

Tia's research interests lie in the field of molecular spectroscopy & photophysics and in supramolecular & interfacial chemistry. She currently leads a research team of 12 whose focus is on the applications of these fields to biological and biophysical problems, including cell imaging/environmental mapping, cell capture and microfluidic and plasmonic biomembrane mimetic systems. Tia is author/co-author of over 220 peerreviewed publications in international journals in these domains and she has supervised/co-supervised 28 PhDs to completion to date. Tia is a PI in the Irish Photonics Integration Centre, IPIC, and a funded investigator in CURAM, she is a member of the National Centre for Sensors Research and the Water institute at DCU and she directed the National Biophotonics and Imaging Platform at DCU from 2009 until 2014. Tia is a Fellow the Royal Society of Chemistry and a Fellow of the Institute of Chemistry of Ireland. For more information on Keyes research group activities please visit: https://sites.google.com/dcu.ie/keyes-research-group/home