Imaging and Reaction Dynamics in Model Membranes: Soft Nanoscience

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During the past few years, our lab has developed a wide range of methods for patterning lipid bilayers on solid supports [1]. These 2D fluids are interesting as a model for biological membranes, as a physical system with unusual properties, and as a step towards the creation of controlled interfaces between biological and non-biological surfaces. Methods have been developed for controlling the composition of patterned membrane corrals by variations on microcontact printing and microfluidics. Charged components can be moved around within these fluid surfaces by a form of 2D electrophoresis. Although this is a model membrane system, it provides an excellent platform for the development of advanced imaging and analysis methods, and components displayed in the supported bilayer model membrane can interact with and affect the function of native cell membranes.

The planar geometry of the supported bilayer systems is ideal for surface sensitive imaging methods. We have used imaging mass spectrometry and interferometry. Our lab has developed the application of the NanoSIMS50 (Cameca Instruments) to obtain *quantitative* composition information on membrane components with *sub-100 nm* lateral resolution and very high sensitivity [2]. By suitable calibration, high spatial resolution images can be converted into composition images with good precision. We have recently developed a novel membrane interferometer in which free standing membrane is assembled in close proximity to a flat Si mirror to exploit variable incidence angle fluorescence interference contrast microscopy to study *nm* scale conformational changes of membrane proteins in their native environment [3].

Synthetic or natural vesicles can be tethered to fluid bilayers by short complimentary DNA sequences. Once tethered, vesicles are laterally mobile in the plane of the supported bilayer. Arrays of corrals can be used to tether and sort vesicles displaying the complimentary sequence, and different vesicles can have different contents, lipid composition and/or membrane-associated proteins encoded by the corresponding oligonucleotide sequence. Because the vesicles are laterally mobile, individual vesicle-vesicle interactions, including vesicle fusion [5], mediated by different components on the vesicle surface or in solution, can be observed directly.

[1] "Micropattern Formation in Supported Phospholipid Membranes" J, T. Groves and S, G. Boxer, Accounts of Chemical Research, **35**, 149 (2002); "Model Membrane Systems and their Applications" Y-H. M. Chan and S. G Boxer, *Current Opinion in Chemical Biology,* **11**, 581 (2007).

[2] "Phase Separation of Lipid Membranes Analyzed with High-Resolution Secondary-Ion Mass Spectrometry", M. L. Kraft, P. K. Weber, M. L. Longo, I. D. Hutcheon, S. G. Boxer, *Science,* **313**, 1948-1951 (2006).

[3] "Variable Incidence Angle Fluorescence Interference Contrast Microscopy for z-Imaging Single Objects", C. M. Ajo-Franklin, P. V. Ganesan and S. G. Boxer, *Biophysical J.*, **89**, 2759-2769 (2005); "A membrane interferometer", P. Ganesan and S.G. Boxer, *in preparation*.

[5] "Kinetics of DNA-mediated docking reactions between vesicles tethered to supported lipid bilayers" Y-H. M. Chan, P. Lenz and S. G. Boxer, *PNAS,* **104**, 20189-20194 (2007); "Lipid-anchored DNA Mediates Vesicle Fusion as Observed by Lipid and Content Mixing, "Y-H. M. Chan, B. van Lengerich, S. G. Boxer, *in press.*