The Impact of Collective Molecular Dynamics on Physiological and Biological Functionalities of Artificial and Biological Membranes

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Biological Physics is…

“the study of biological phenomena using physical methods and concepts ... the primary goal ... is to advance the understanding of biological structure and function by application of the principles of physical science”

“... a distinctively biophysical approach at all levels of biological organization will be considered, as will both experimental and theoretical studies”

Although living systems obey the laws of physics and chemistry, the notion of function or purpose differentiates biology from other natural sciences” (Hartwell et al.)
Hard- and Soft-Matter

missing or not well developed periodic structure (BZ concept)

high ‘intrinsic’ background because of mix of coherent and incoherent scattering and diffusion and different molecular components

‘multi-scale’: relevant dynamics in a large range of length and time scales
The Cell Membrane

Applications:

Bioengineering: Tailor membranes with specific properties

Understanding of physiological and biological functionalities: Drug transport

Membrane is the primary site of (inter)action
Membrane Dynamics

H. Heller, München, Germany

Study structure and dynamics on a molecular scale
“Broadband” Neutron Spectroscopy

Inelastic neutron scattering gives wave vector resolved access to dynamics

excitations \leftrightarrow \text{specific motions}

relaxations
Mesoscopic Membrane Fluctuations

Dispersion relation

\[ \tau^{-1} (\text{ns}^{-1}) \]

\( q (\text{Å}^{-1}) \)

Contains ‘dynamic’ information

q-dependence of excitation frequencies and relaxation rates

'Phonons in membranes'

Thermal membrane fluctuations

Elementary excitations

- Propagating
- Oscillating Mode
- Relaxating

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Membrane Dynamics

Local modes in bilayers

- Incoherent inelastic neutron scattering
- NMR
- Dielectric spectroscopy

Collective excitations

Correlated molecular motions might be responsible for ‘functionalities’ of the membrane and structural changes
Collective Excitations in model membranes

The ‘Neutron Window’

DMPC –d54

$2\AA < 2\pi/q_\parallel < 5000\AA$ & $1\text{ps} < \tau < 1\mu\text{s}$

Neutron-Spin-Echo-Spectrometer

Oscillation & Relaxation

Propagation

Relaxation

Triple-Axis-Spectrometer

Backscattering-Spectrometer

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Stacked Planar Membranes

Sample Preparation

Surfactant & Organic Solvent

Solid supported, highly oriented membrane stacks

Solvent Evaporation

several 1000 bilayers per Si-wafer, mosaicity ~ 0.5°

„Sandwich-sample“ with 500 mg of deuterated DMPC

“Humidity Chamber”
Scattering from aligned phases

Highly oriented solid supported membranes

Si-wafer

Isotropic solution “powder”
Membrane Permeability and Stiffness

Membrane Elasticity

Membrane Permeability

Cholesterol

Ethanol

Understanding and Controlling the Microscopic and Mesoscopic Properties of Membranes
Membrane Permeability

Neutron Three-Axes to measure the short wavelength fluctuations

Dispersion relation as found in ideal liquids as liquid argon or liquid helium

→ **Acyl-Chains behave “Quasi Liquid”**
Effect of Drug Enhancers: DMPC/Ethanol

**Drug Enhancer:** Facilitates the transport of molecules through the membrane

**Ethanol** (polar)  
**DMPC**  
**MD Simulation**

Enhanced Chain Fluctuations: **Phonon Assisted Diffusion**
Membrane Elasticity

Neutron Spin-Echo to measure long wavelength undulations

Rheinstädter, Häussler, Salditt, PRL 97, 048103 (2006)
Schäfer, Salditt, Rheinstädter, PRE, in press.
Membrane Elasticity

Mesoscopic membrane fluctuations

\[
K = \left( \frac{\kappa}{d} \right) \left[ \frac{J}{m} \right]
\]

Bending modulus

\[
B = -d \left( \frac{\partial \Pi}{\partial d} \right) \left[ \frac{J}{m^3} \right]
\]

Compressional modulus

\[
H = \int dV \left\{ B \left( \frac{\partial u}{\partial z} \right)^2 + K[\nabla^2 u]^2 \right\}
\]

timescales \quad 1ns = \frac{4.14}{1 \mu eV}
**Undulation Dispersion Relations**

Fit to smectic hydrodynamic theory

\[
\tau^{-1}(q_{\parallel}) = \frac{\kappa/d}{\eta_3} q_{\parallel}^2 \left(\frac{q_{\parallel}}{\pi/(\Lambda D)} + \frac{\pi/(\Lambda D)}{q_{\parallel}^2 + \frac{1}{\mu \eta_3} (\pi D)^2}\right)
\]

\(\kappa = 14.5 \ k_B T\)
\(\eta_3 = 0.016 \ \text{Pa} \cdot \text{s}\)
\(\Lambda = 10.3 \ \text{Å}\)
\(B = 1.08 \times 10^7 \ \text{J/m}^3\)

**Dynamics of solid supported bilayers**

Undulations


Relaxation

Romanov and Ul’yanov, PRE 66, 061701 (2002)

Surface mode?

Softening close to \(T_c\)

Effect of Cholesterol

DMPC

DMPC/40% Cholesterol

Quantify dynamics on different length scales

non polar

mesoscopic

microscopic

<5%

40%

MD simulations, Heller et al.

‘stiffens’
suppressed

T=30 °C

T=20 °C (Lβ)

T=23 °C (Lo)

T=30 °C (Lo)

neutron counts

neutron counts

\( q_t = 0.002 \text{ Å}^{-1} \)

\( q_t = 0.019 \text{ Å}^{-1} \)

\( q_t = 0.024 \text{ Å}^{-1} \)

\( q_t = 0.029 \text{ Å}^{-1} \)

\( q_t = 0.039 \text{ Å}^{-1} \)
Hard- and Soft-Matter

missing or not well developed **structure** (BZ concept)

Biophysics

Biology

Soft-Matter

‘membrane spectroscopy’:
- **combine** instruments and techniques to maximize length and time scales
- **overlap** between instruments
- **optimize** instruments (divergences, resolution)

**versatile instruments:**

Flux is not everything:
- tunable q-ω resolution
- tunable divergences/collimation

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Membrane Spectroscopy
ALV Dynamic Light Scattering System

ALV Compact Goniometer System, ALV/LSE-5004 Multiple Tau Digital Real Time Correlator, and Cuvette Rotation Unit

Laser

Intensity Monitor

Correlator & PC

Photon Counter

Fiber Optic

2θ Arm

Sample Cell

Beam Shutter

Optics

Correlator & PC

Photon Counter

Fiber Optic

2θ Arm

Sample Cell

Beam Shutter

Optics

PCS of Oriented Membranes

Solid Supported

Freestanding

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Dynamic Light Scattering – Scattering Geometry

Detector Position
Specular Reflection

2θ Scan in Reciprocal Space

Membrane Sample

Incident Laser Beam

Inelastically Scattered Laser Light

$q$ Scan in Reciprocal Space
Free standing ‘painted’ membrane

Damped Propagating Mode

Relaxating Mode

$\mathbf{q}_|| = 0.003 \text{ Å}^{-1}$

$\Delta \omega = \frac{2\pi}{\tau}$
Protein Dynamics

Bacteriorhodopsin in Purple Membrane

Sample: Dieter Oesterhelt, MPI Munich

Acoustic phonon spectrum

Karin Schmalzl, Dieter Strauch, ILL+U Regensburg

Data+Theory

Challenge: Study Dynamics of Proteins embedded in Membranes
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