

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

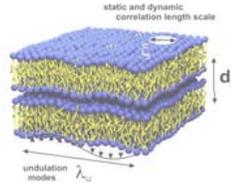
Maikel C. Rheinstädter  
Department of Physics and Astronomy  
University of Missouri – Columbia

*XPCS NSLS-II Workshop  
January 10-11, 2008  
Brookhaven National Laboratory*





# Biological Physics is...



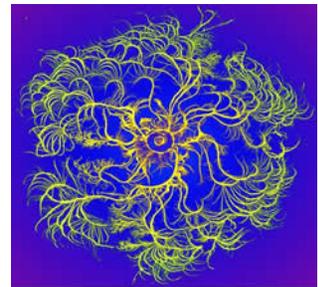
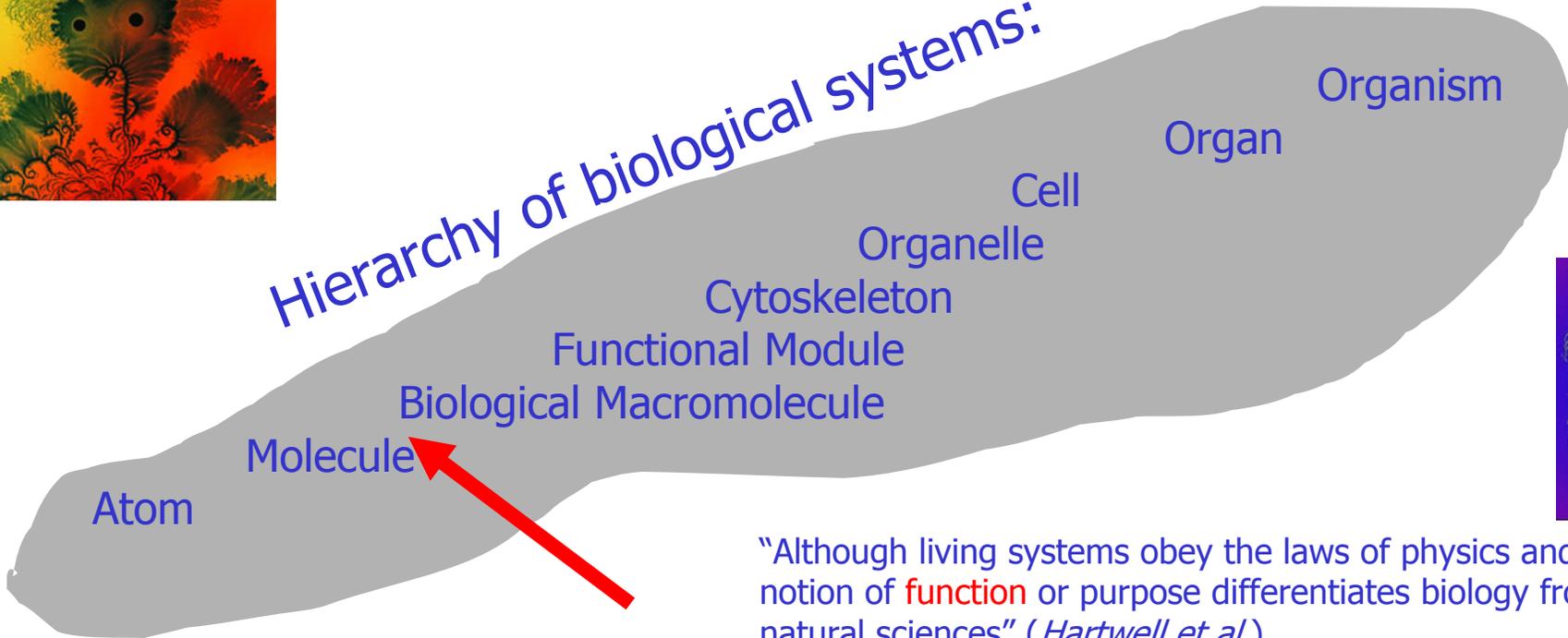
*Aims and Scope,  
European Biophysical  
Journal:*

"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"



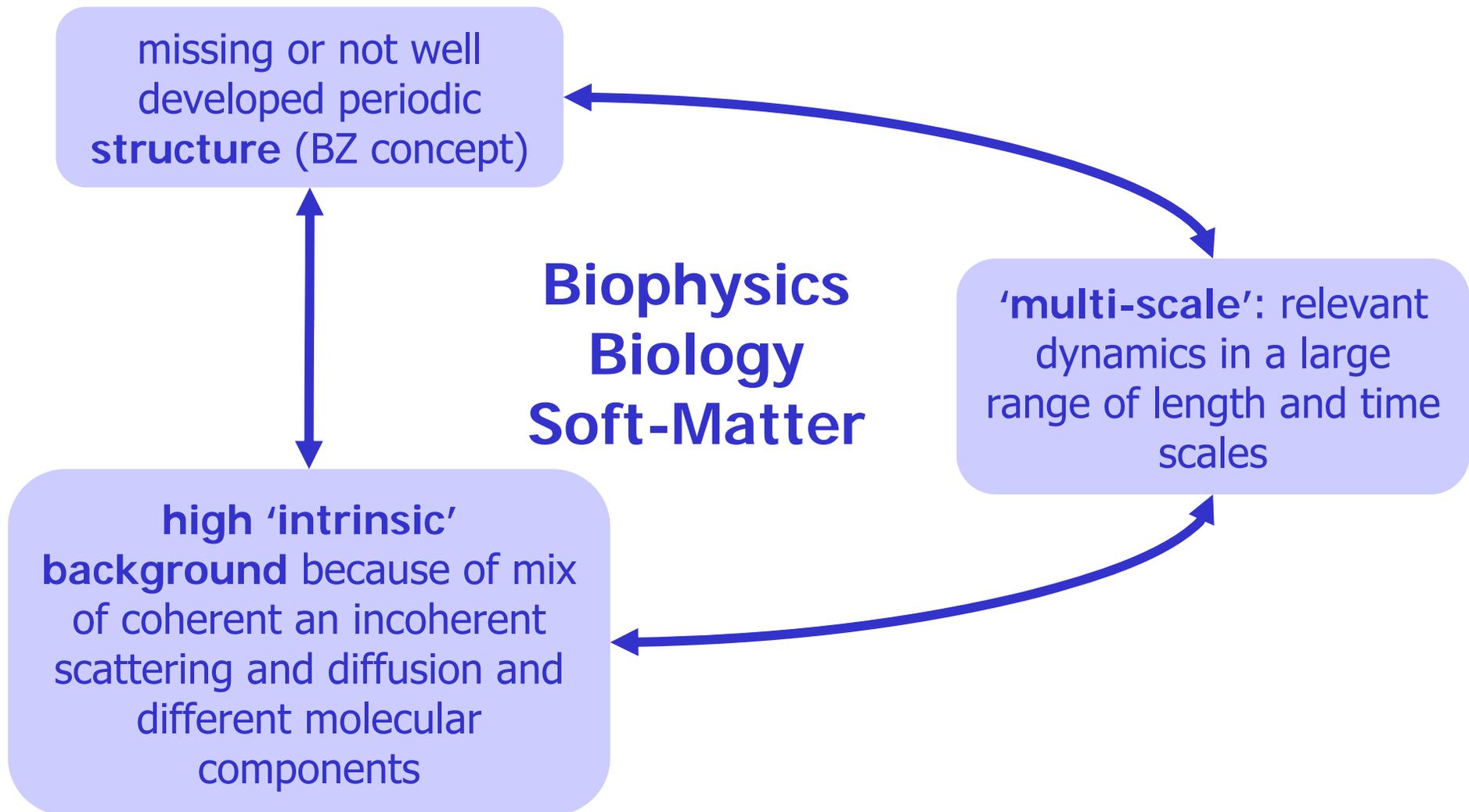
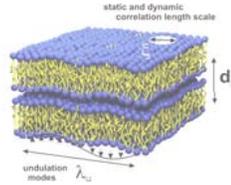
Hierarchy of biological systems:



"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.*)

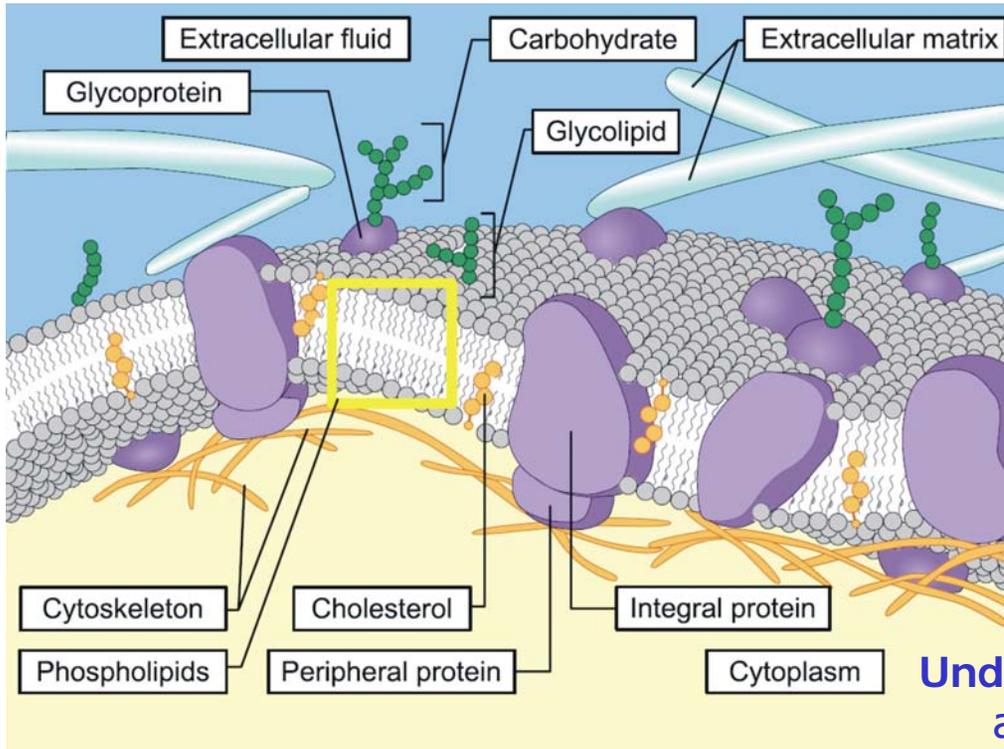
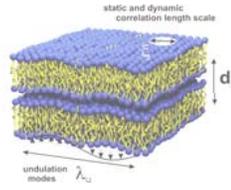


# Hard- and Soft-Matter



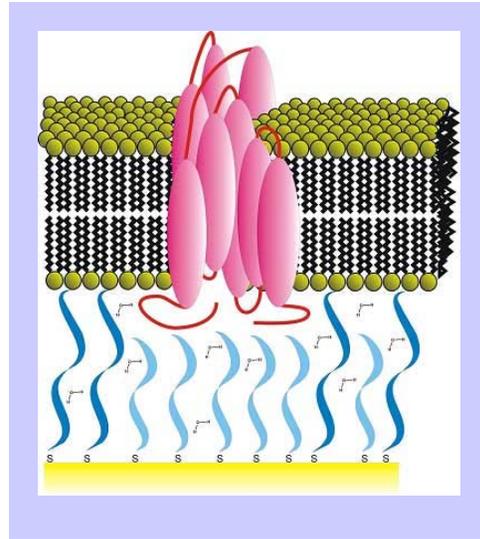


# The Cell Membrane

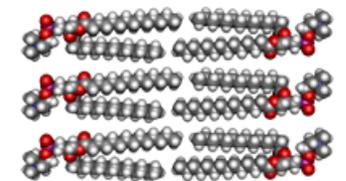
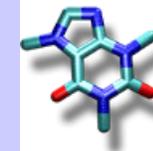


## Applications:

Bioengineering:  
Tailor membranes with  
specific properties



Understanding of physiological  
and biological functionalities:  
Drug transport

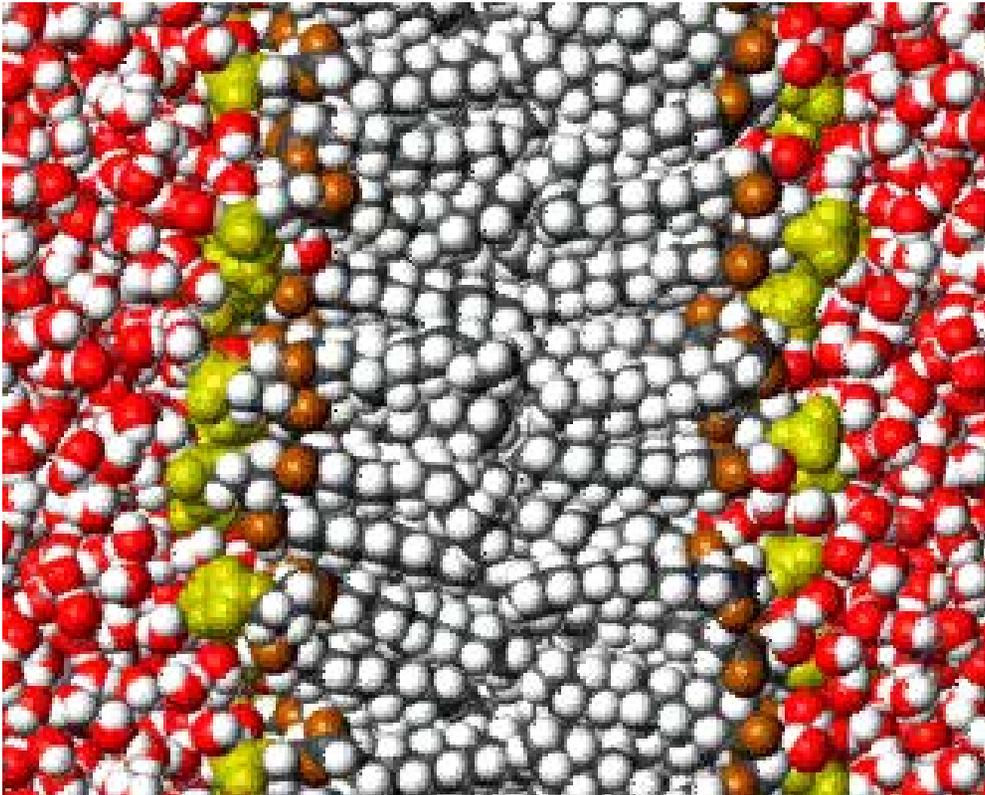
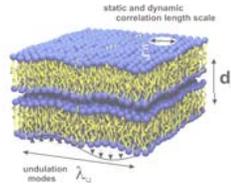


Membrane is the primary site of  
(inter)action

D. Neumann, Saarbrücken, Germany



# Membrane Dynamics

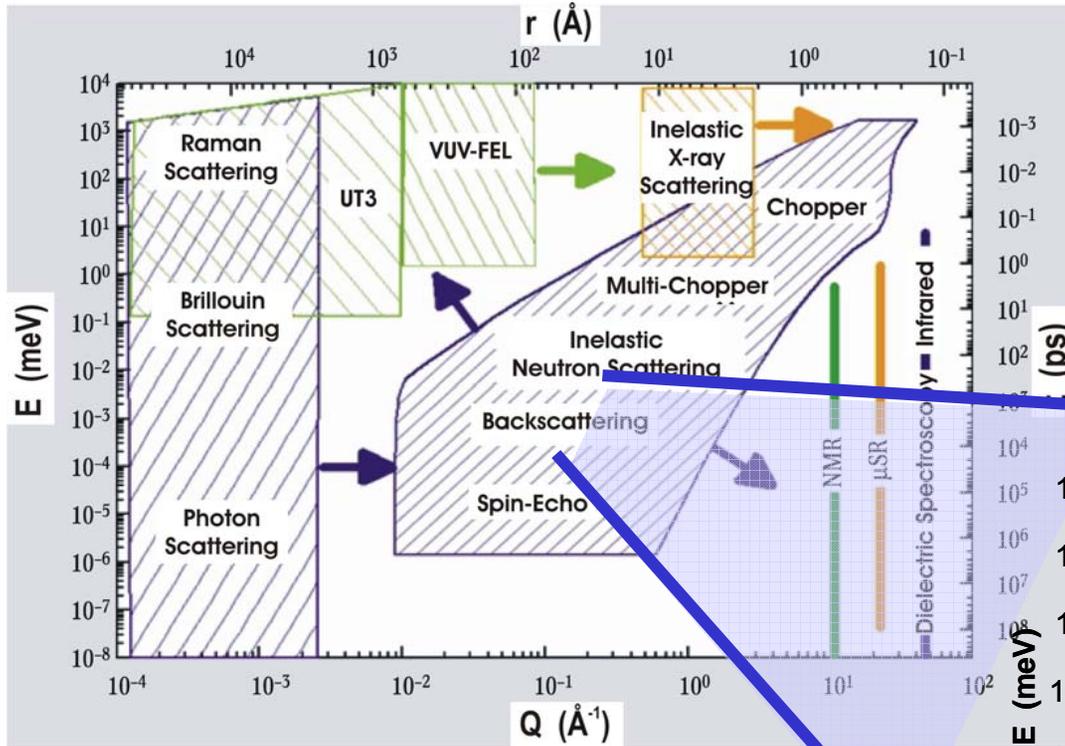
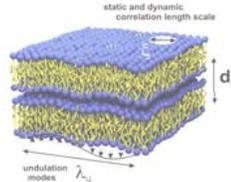


H.Heller, München, Germany

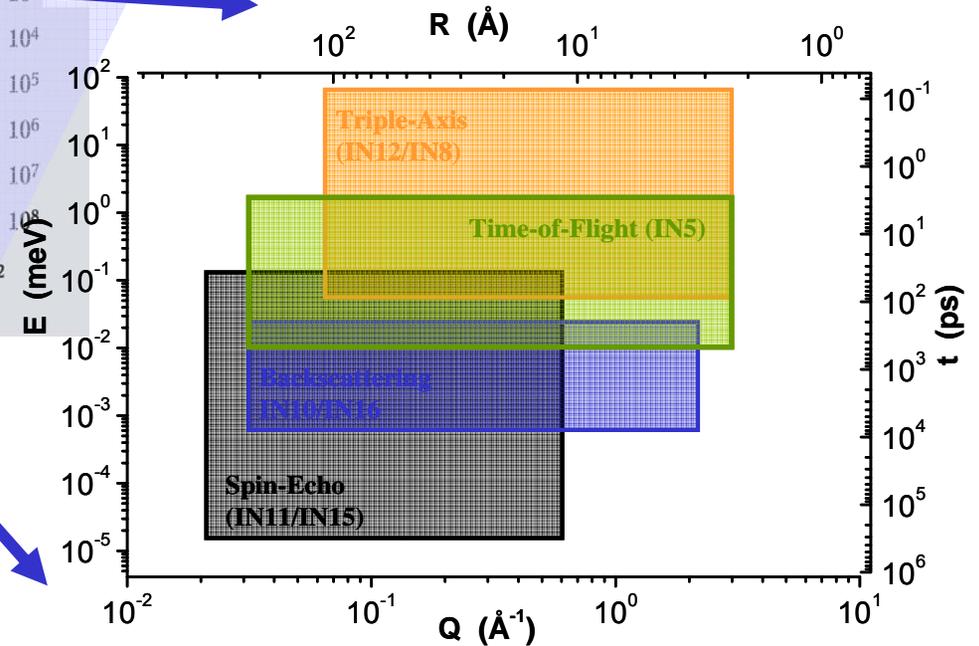
Study structure and dynamics on a  
molecular scale



# "Broadband" Neutron Spectroscopy



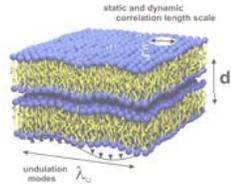
Inelastic neutron scattering gives wave vector resolved access to dynamics



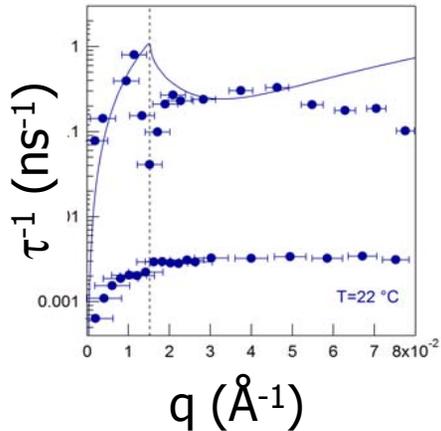
excitations ↔ specific motions  
relaxations



# Mesoscopic Membrane Fluctuations



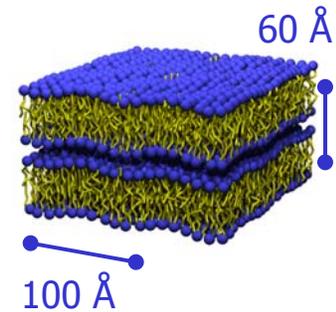
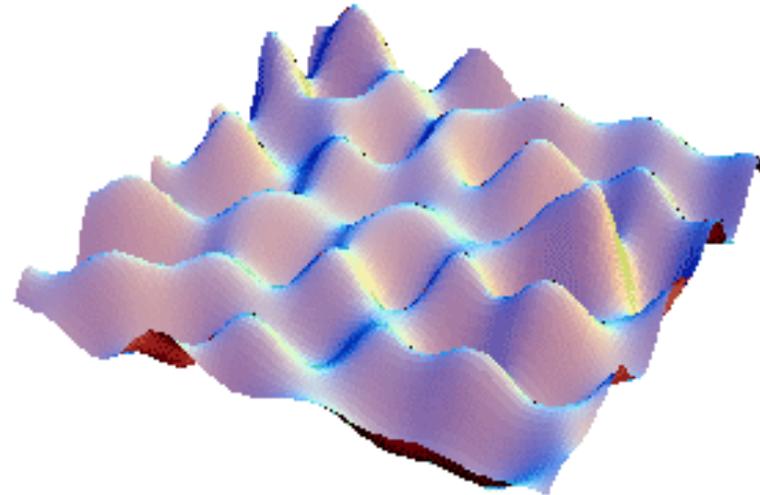
## Dispersion relation



Contains 'dynamic' information

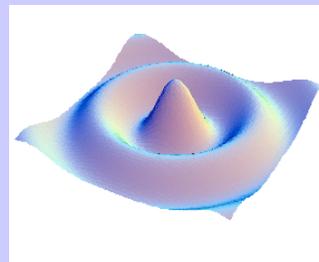
*'Phonons in membranes'*

q-dependence of excitation frequencies and relaxation rates



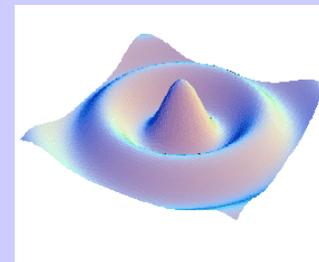
Thermal membrane fluctuations

Elementary excitations



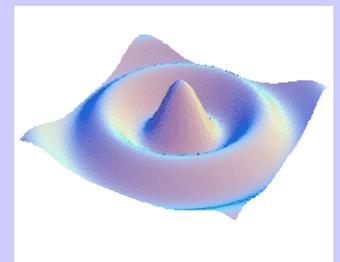
Propagating

+



Oscillating

+

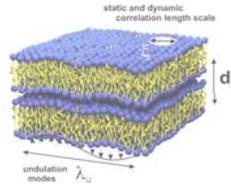


Relaxing

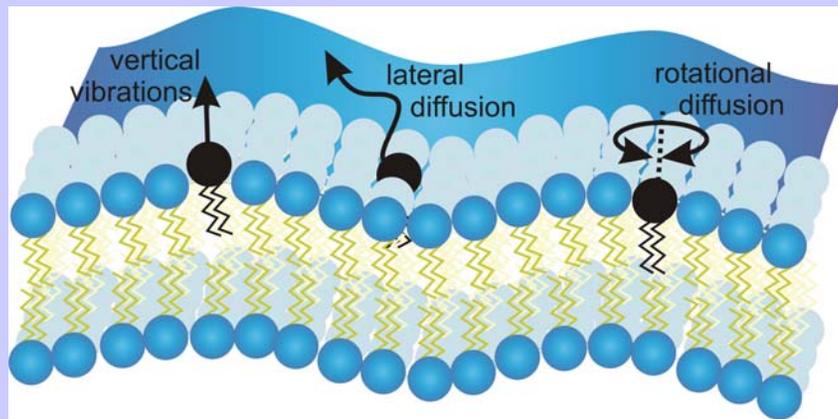
Mode



# Membrane Dynamics

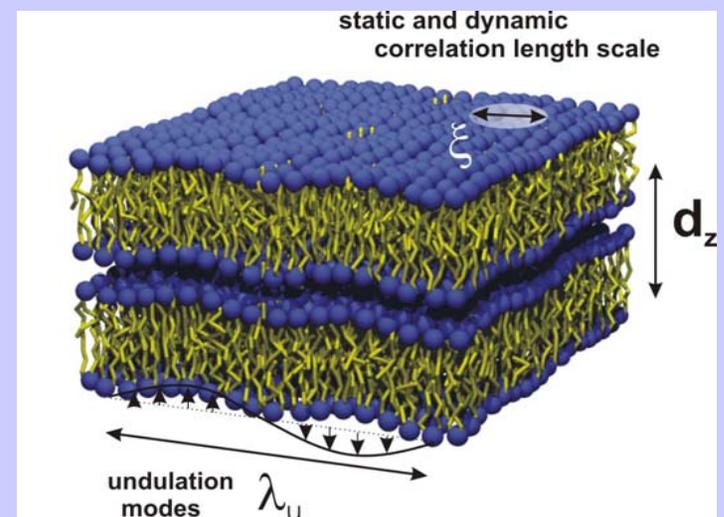


## Local modes in bilayers



- Incoherent inelastic neutron scattering
- NMR
- Dielectric spectroscopy

- Coherent in- and quasielastic neutron scattering
- Inelastic X-ray scattering
- Dynamic Light Scattering (PCS)
- XPCS

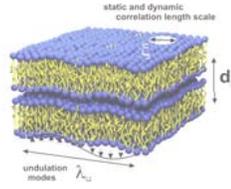


Collective excitations

Correlated molecular motions might be responsible for 'functionalities' of the membrane and structural changes



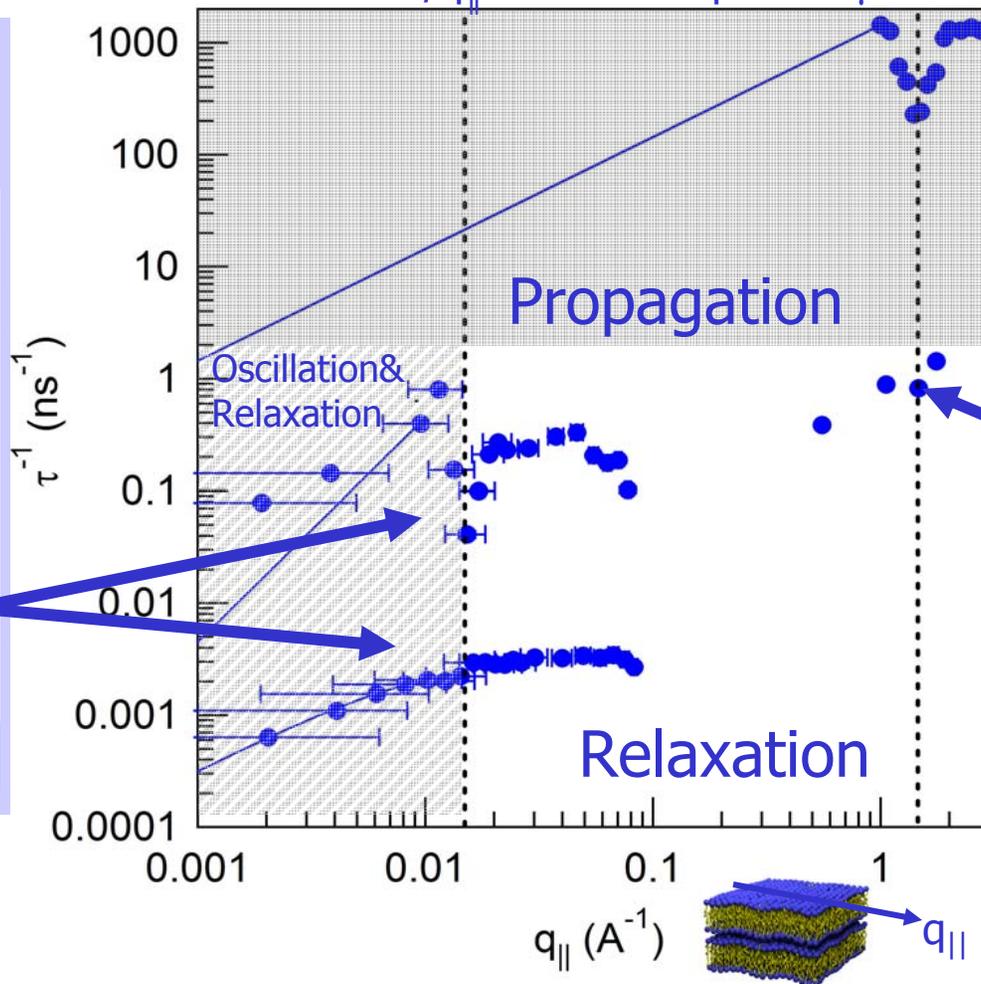
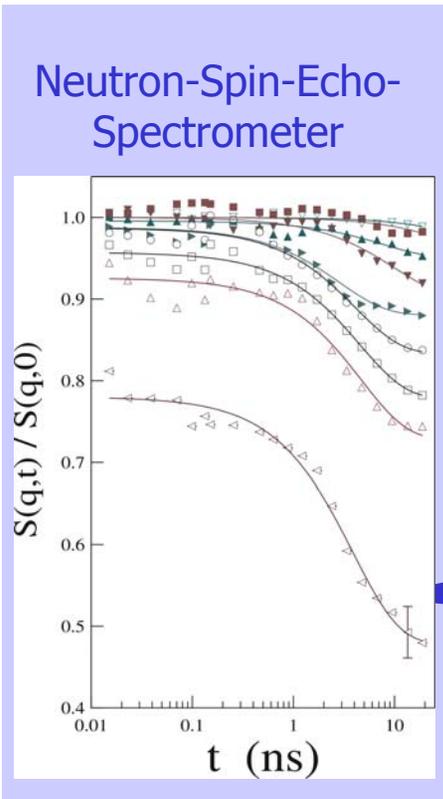
# Collective Excitations in model membranes



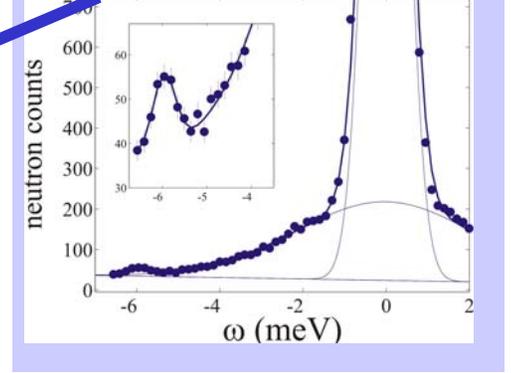
## The 'Neutron Window'

DMPC -d54

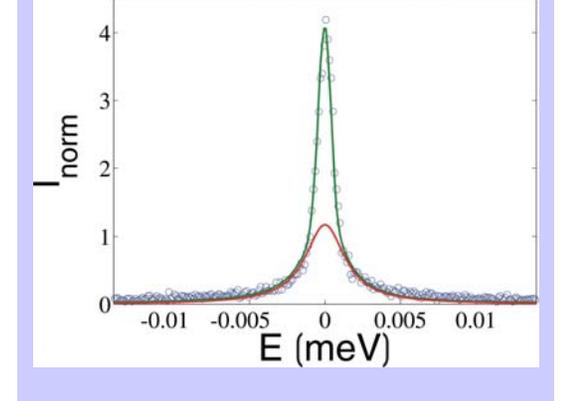
$$2\text{\AA} < 2\pi/q_{\parallel} < 5000\text{\AA} \quad \& \quad 1\text{ps} < \tau < 1\mu\text{s}$$



## Triple-Axis-Spectrometer

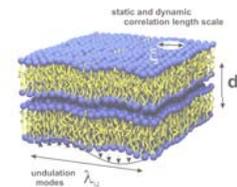


## Backscattering-Spectrometer

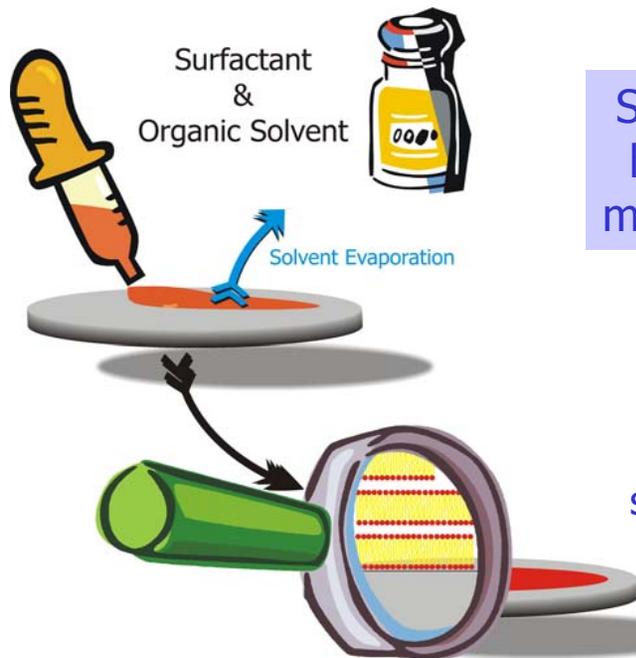




# Stacked Planar Membranes



## Sample Preparation



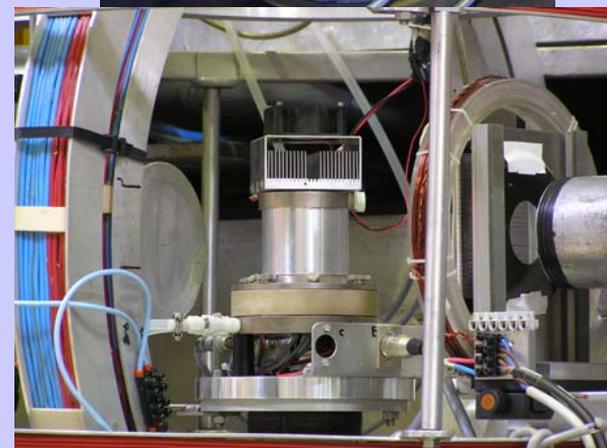
Solid supported,  
highly oriented  
membrane stacks

several 1000 bilayers  
per Si-wafer,  
mosaicity  $\sim 0.5^\circ$



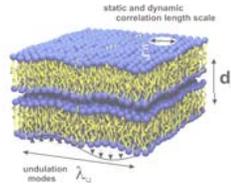
„Sandwich-sample“  
with 500 mg  
of deuterated DMPC

## “Humidity Chamber”



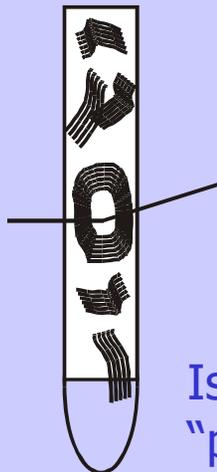
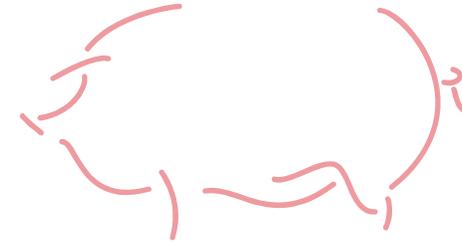
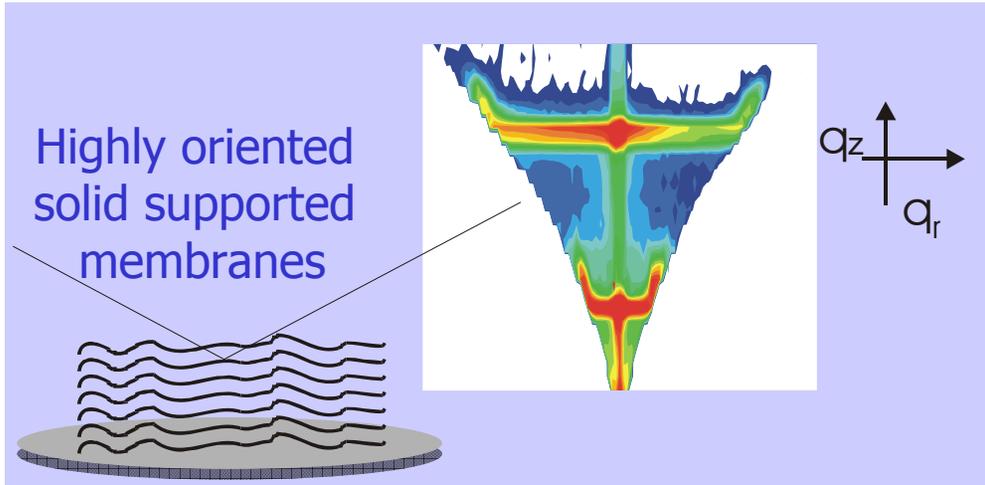


# Scattering from aligned phases

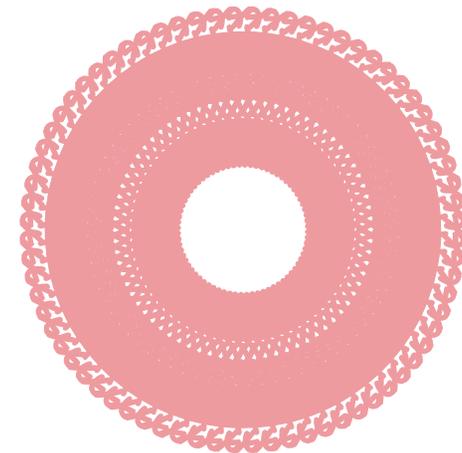
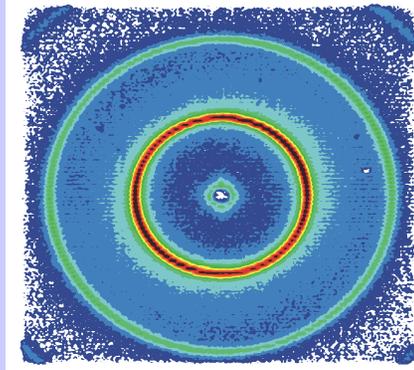


Highly oriented  
solid supported  
membranes

Si-wafer

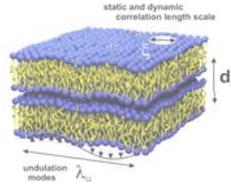


Isotropic solution  
"powder"



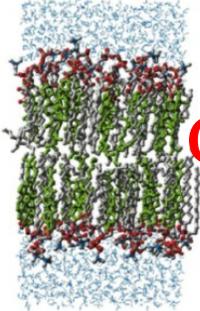
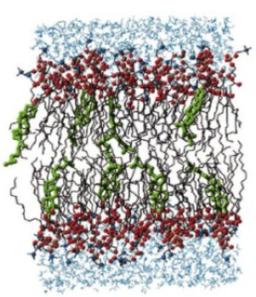


# Membrane Permeability and Stiffness



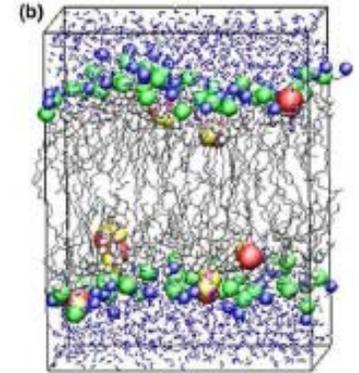
## Membrane Elasticity

## Membrane Permeability

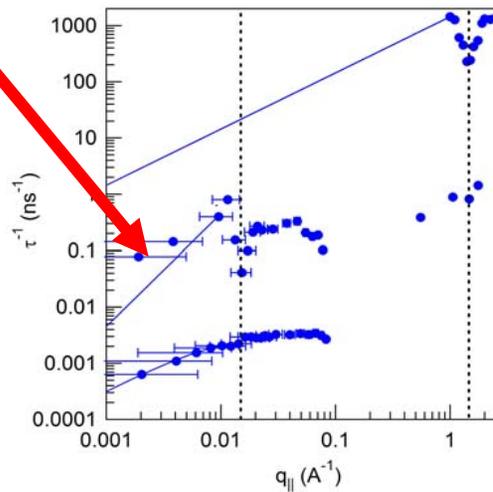


**Cholesterol**

**Ethanol**



Long wavelength dynamics

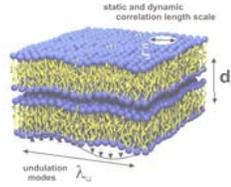


Short wavelength dynamics

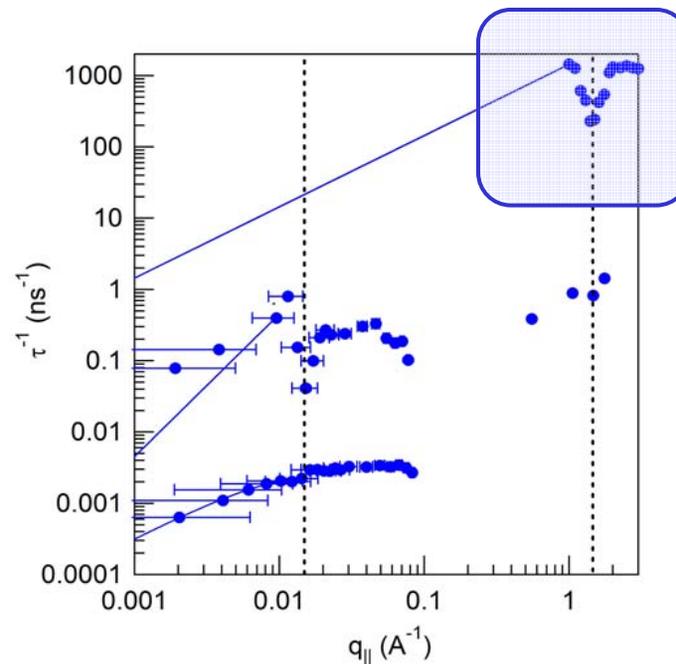
**Understanding and Controlling the Microscopic and Mesoscopic Properties of Membranes**



# Membrane Permeability



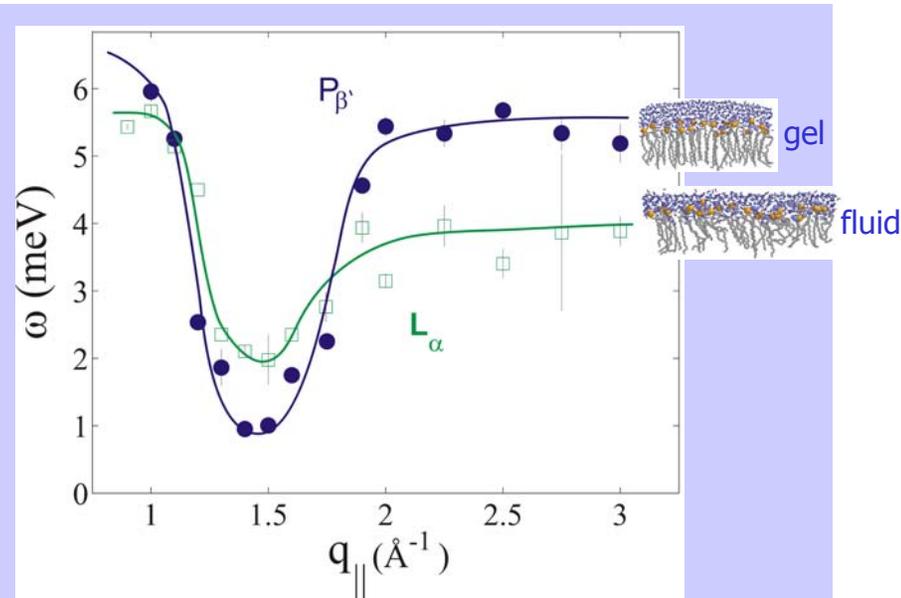
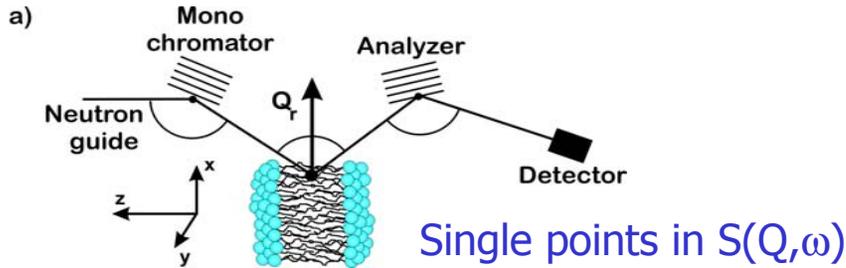
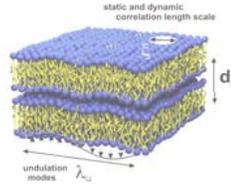
Neutron Three-Axes to measure the short wavelength fluctuations



Rheinstädter, Ollinger, Fragneto, Demmel, Salditt, PRL **93**, 108107 (2004).



# Short-Range Dispersion Relation on TAS

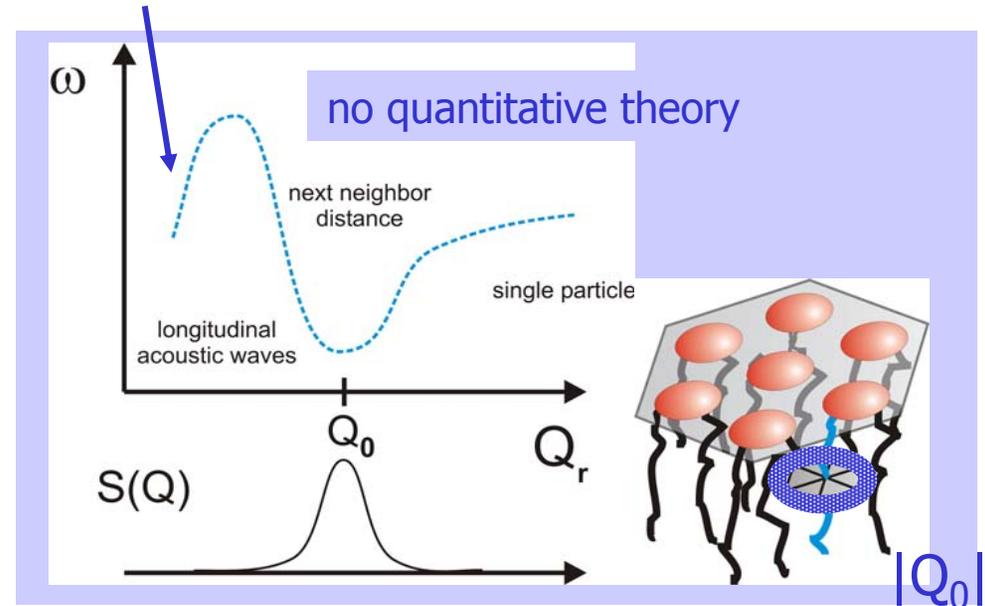


Rheinstädter *et al.*, PRL (2004)

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

→ **Acyl-Chains behave "Quasi Liquid"**

Low-Q range difficult to access for neutrons (and X-rays)

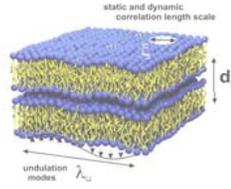


$2\pi/Q_0$  defines quasi „Brillouin-zone“

Directed transport?

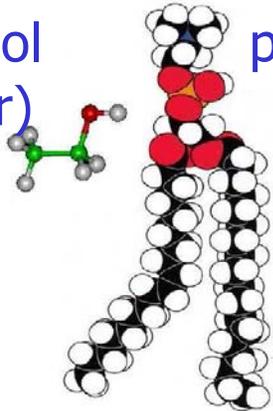


# Effect of Drug Enhancers: DMPC/Ethanol

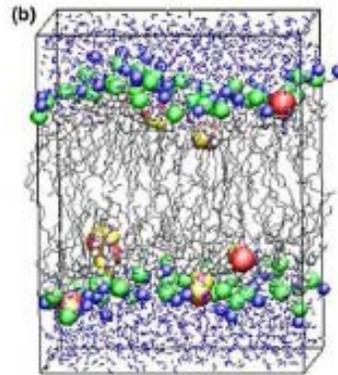


*Drug Enhancer: Facilitates the transport of molecules through the membrane*

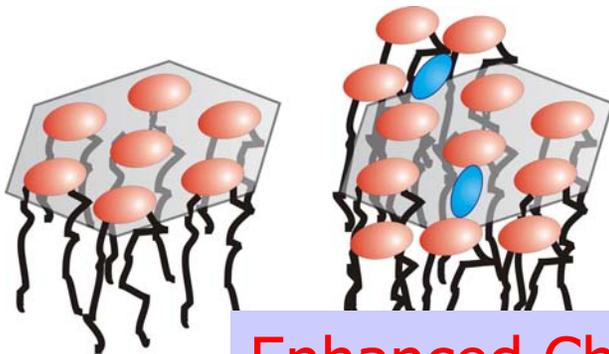
Ethanol (polar)      polar head group



DMPC

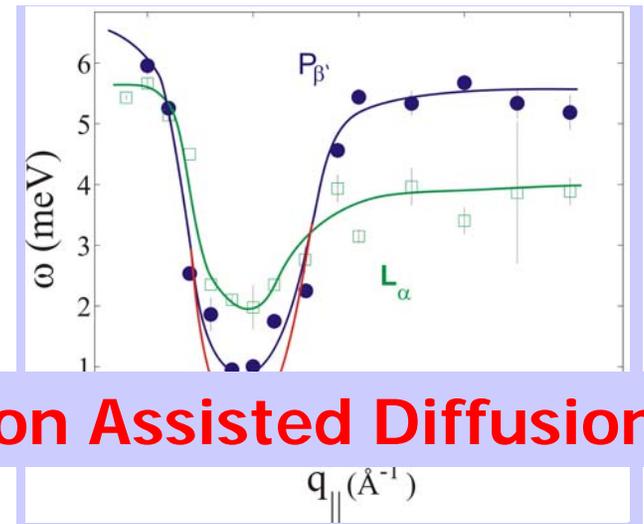
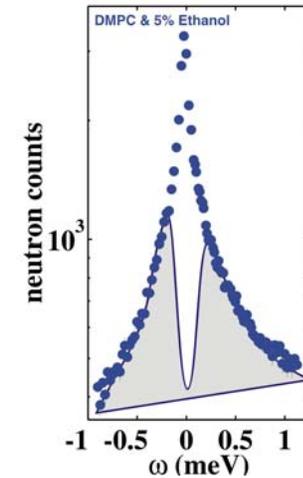
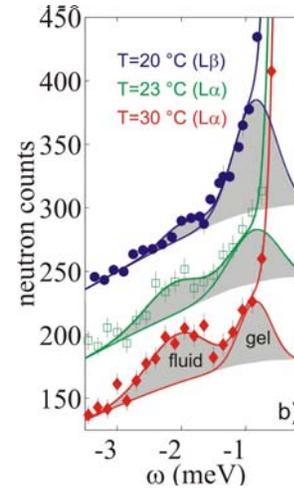


MD Simulation



DMPC

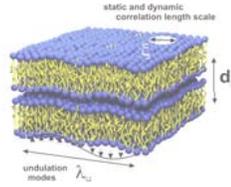
DMPC/5% Ethanol



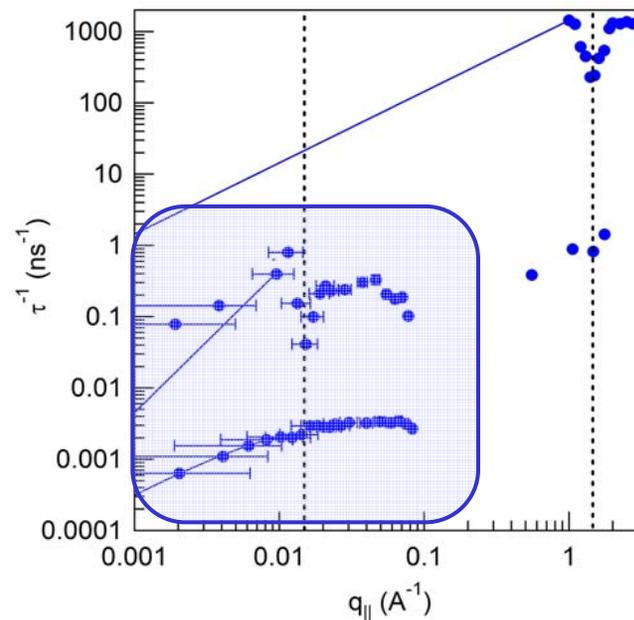
**Enhanced Chain Fluctuations: Phonon Assisted Diffusion**



# Membrane Elasticity



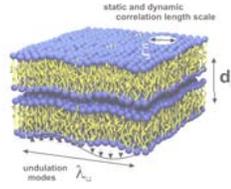
## Neutron Spin-Echo to measure long wavelength undulations



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



# Membrane Elasticity



Mesoscopic membrane fluctuations

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

Bending modulus

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

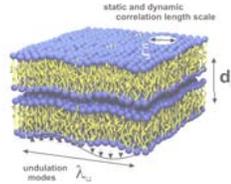
Compressional modulus

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

timescales  $1ns = \frac{4.14}{1\mu eV}$



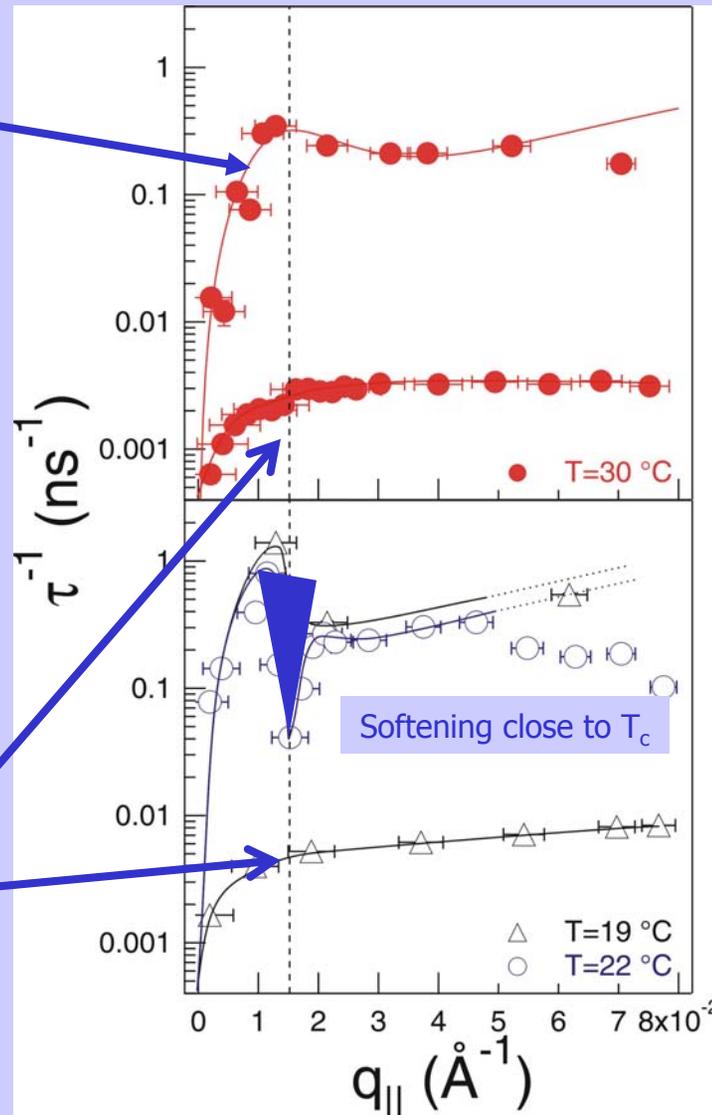
# Undulation Dispersion Relations



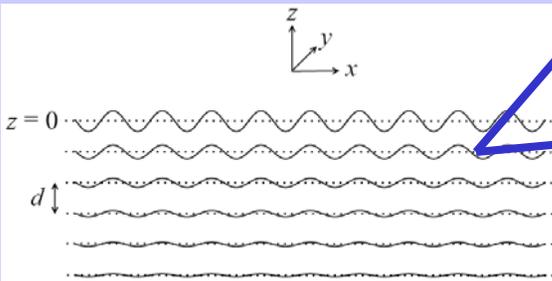
Fit to smectic hydrodynamic theory  
Ribotta, PRL 32, 6, (1974).

$$\tau^{-1}(q_{\parallel}) = \frac{\kappa/d}{\eta_3} q_{\parallel}^2 \frac{q_{\parallel}^4 + (\pi/(\Lambda D))^2}{q_{\parallel}^4 + \frac{1}{\mu\eta_3} (\pi D)^2}$$

$\kappa = 14.5 \text{ k}_B T$   
 $\eta_3 = 0.016 \text{ Pa} \cdot \text{s}$   
 $\Lambda = 10.3 \text{ \AA}$   
 $B = 1.08 \cdot 10^7 \text{ J/m}^3$



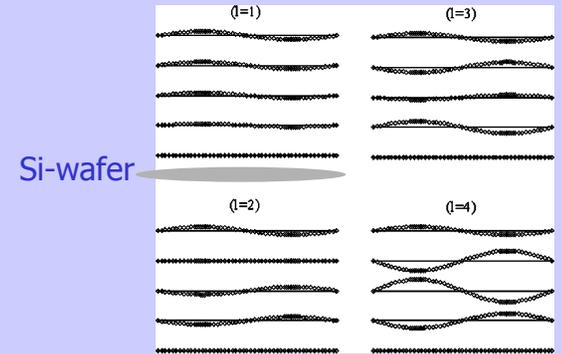
Surface mode ?



Bary-Soroker and Diamant,  
Europhys. Lett., 73, 871 (2006), March 15, 2006

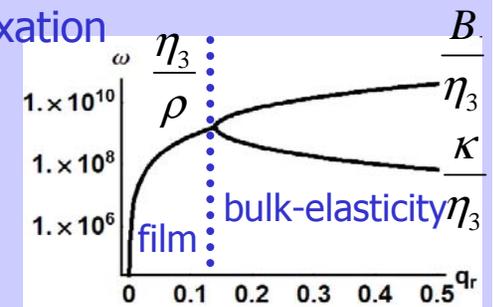
Dynamics of solid supported bilayers

Undulations



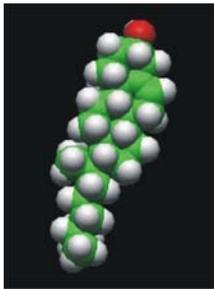
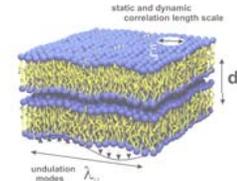
Romanov and Ul'yanov, PRE 66, 061701 (2002)

Relaxation

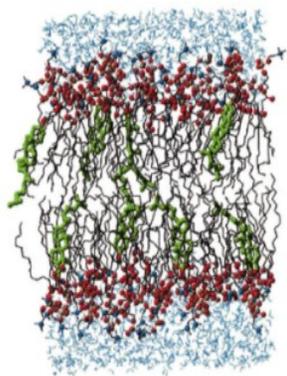




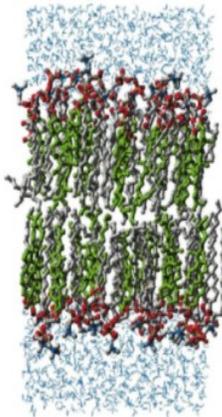
# Effect of Cholesterol



non polar

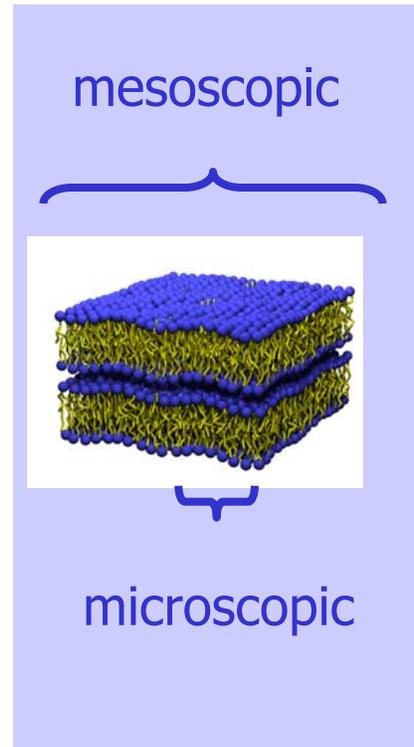


<5%



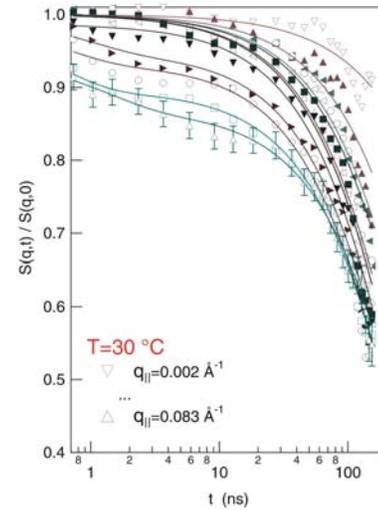
40%

MD simulations,  
Heller et al.

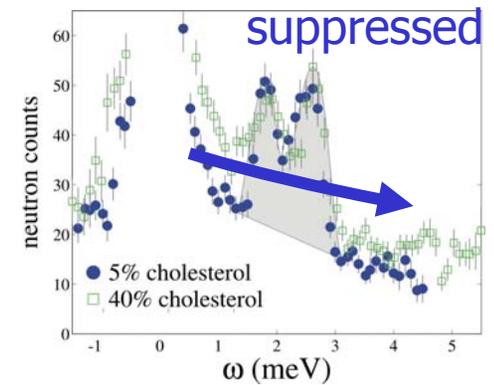
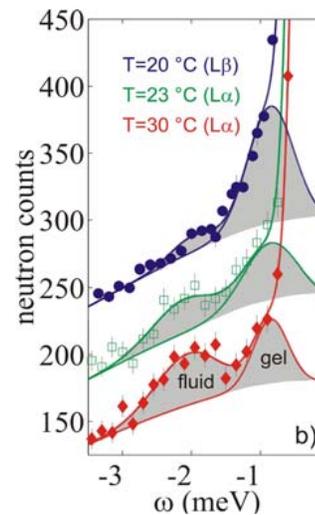
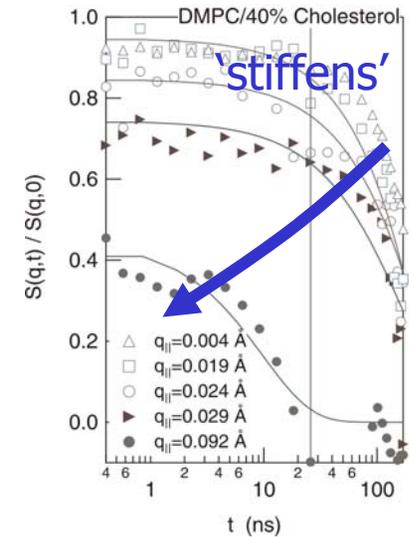


Quantify dynamics on different length scales

DMPC

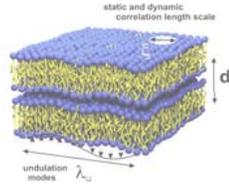


DMPC/40%Cholesterol





# 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)

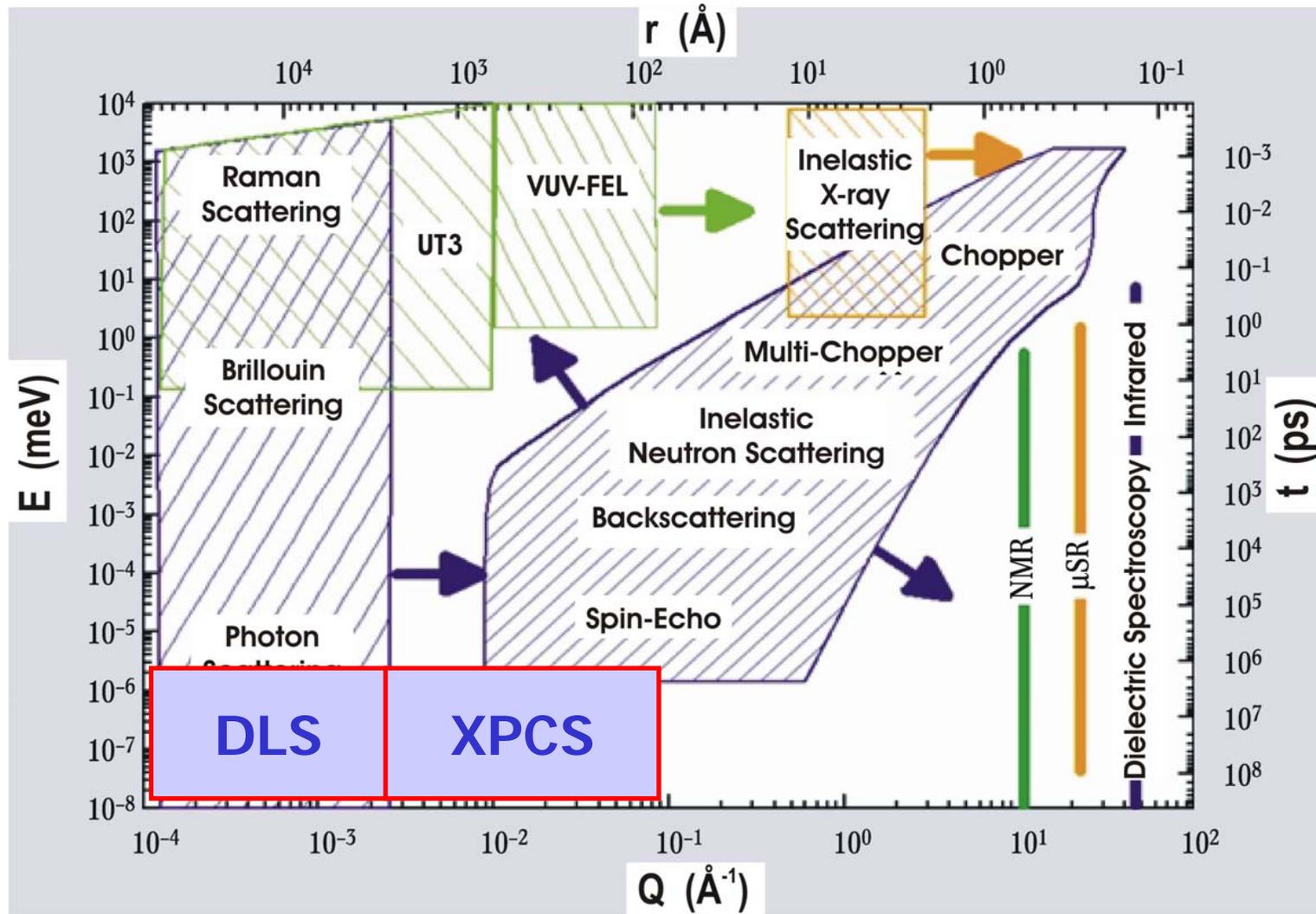
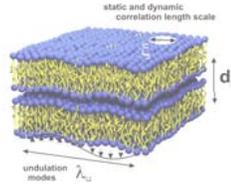
**versatile instruments:**

Flux is not everything:

- tunable  $q$ - $\omega$  resolution
- tunable divergences/collimation

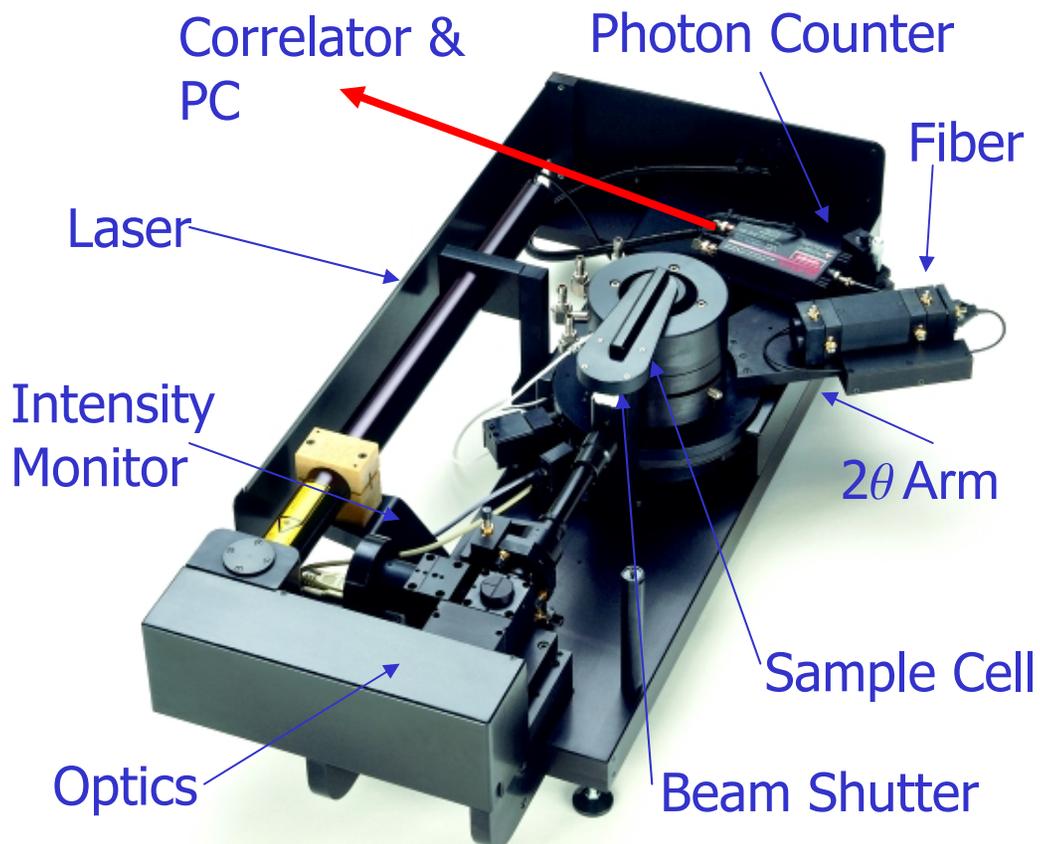
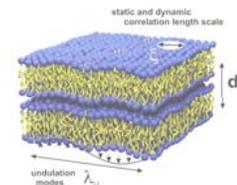


# Membrane Spectroscopy



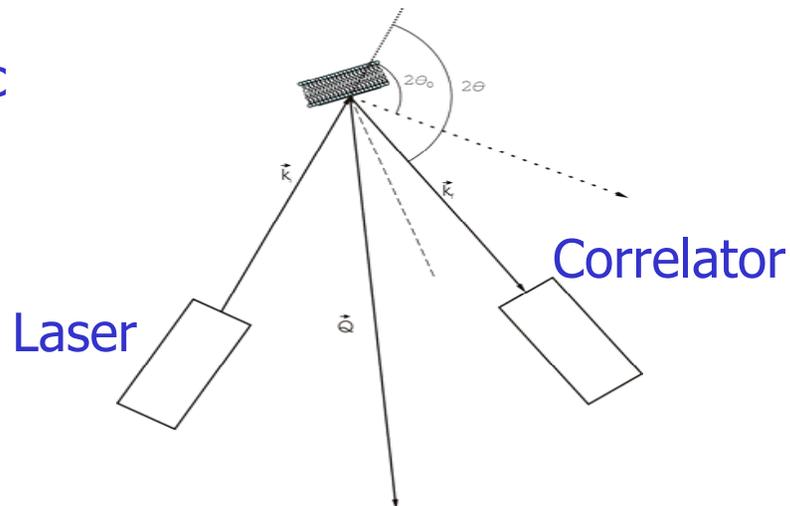


# ALV Dynamic Light Scattering System

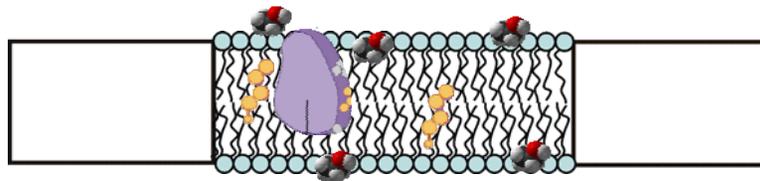


ALV Compact Goniometer System, ALV/LSE-5004 Multiple Tau Digital Real Time Correlator, and Cuvette Rotation Unit

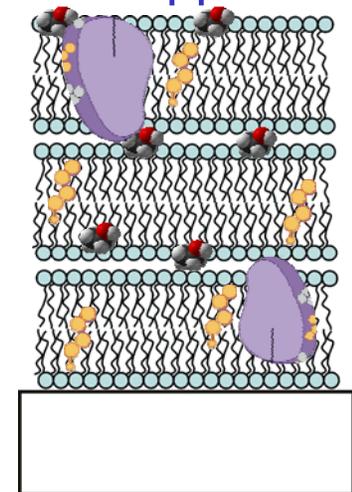
## PCS of Oriented Membranes



### Freestanding

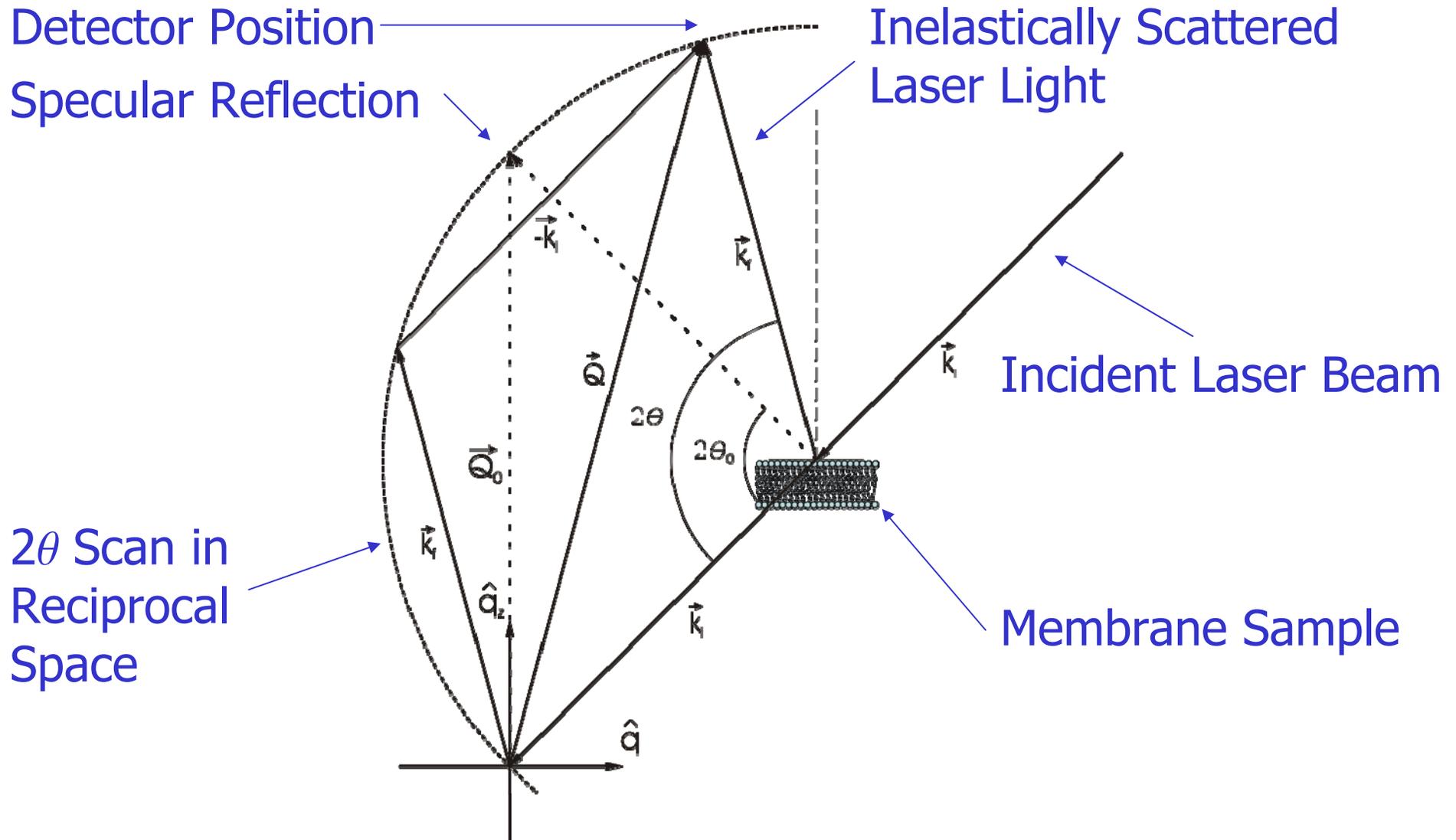
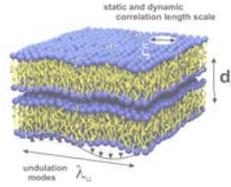


### Solid Supported



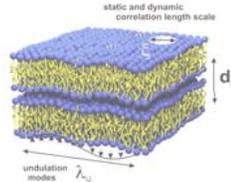


# Dynamic Light Scattering – Scattering Geometry

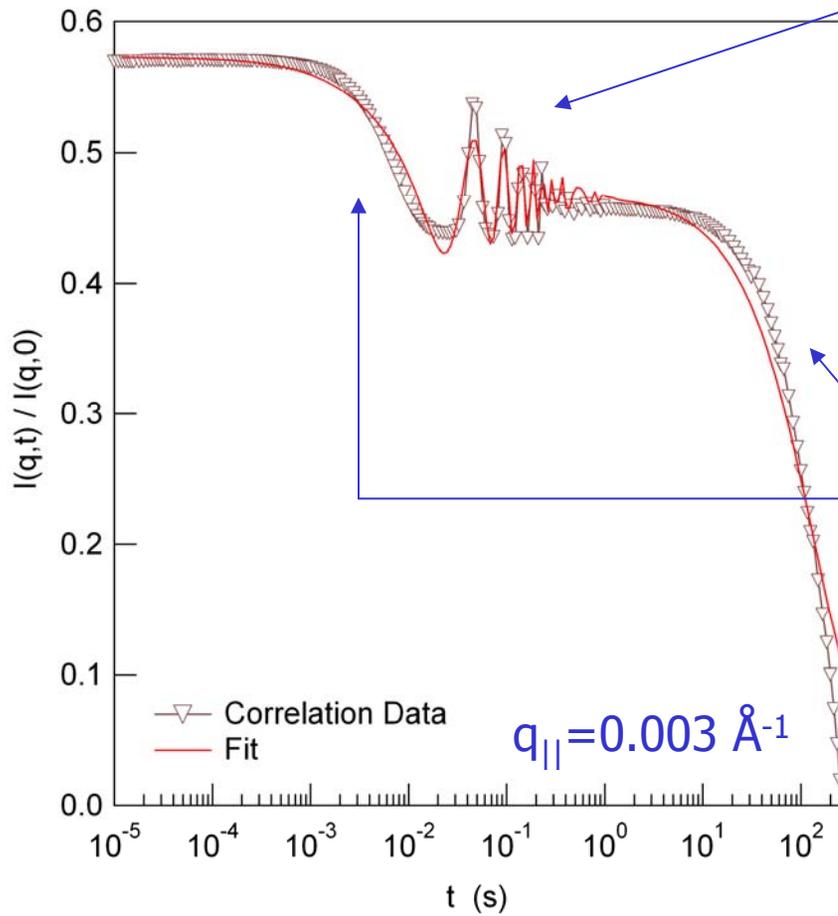




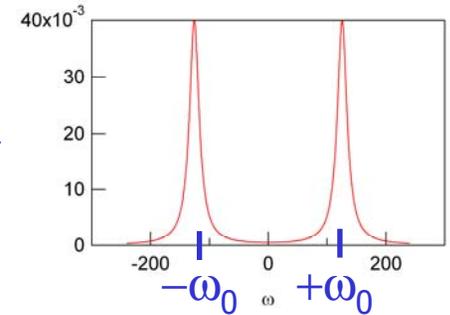
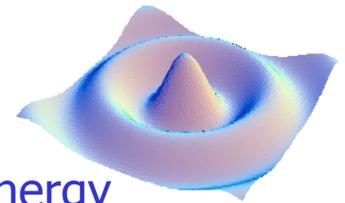
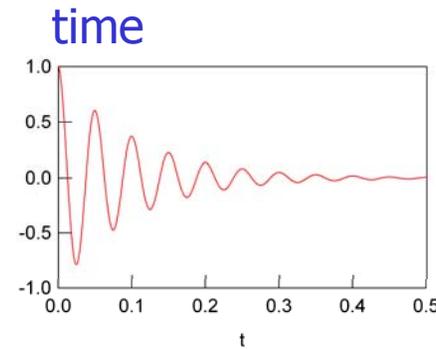
# Dynamic Light Scattering – Data & Analysis



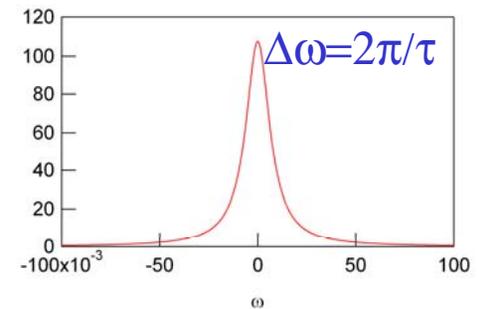
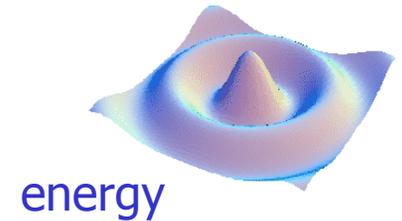
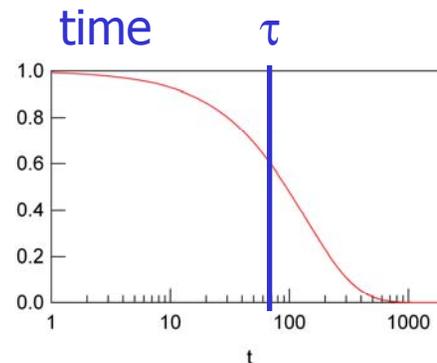
Free standing 'painted' membrane



Damped Propagating Mode



Relaxing Mode

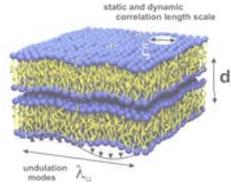


exponential

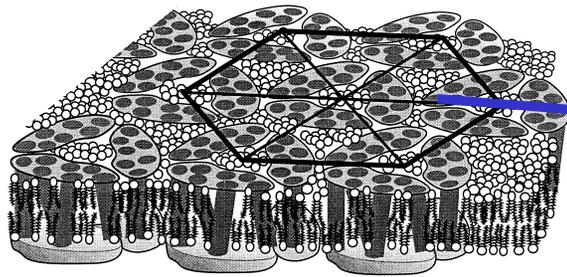
Lorentzian



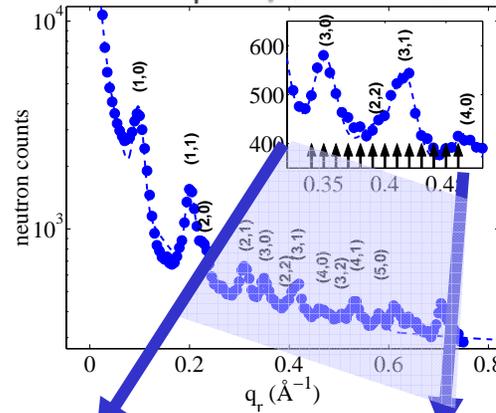
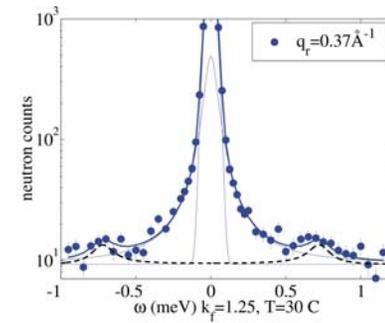
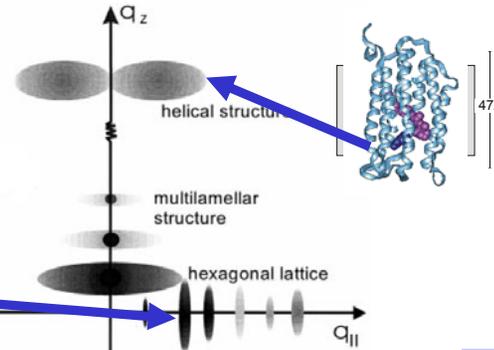
# Protein Dynamics



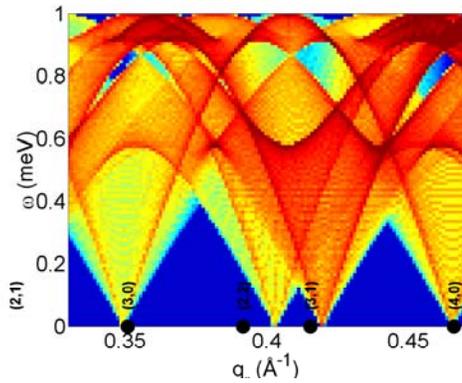
## Bacteriorhodopsin in Purple Membrane



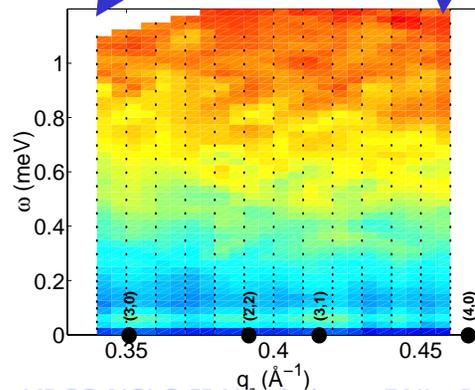
Sample: Dieter Oesterhelt, MPI Munich



## Acoustic phonon spectrum



Karin Schmalzl, Dieter Strauch, ILL+U Regensburg

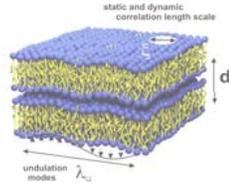


Data+Theory

Challenge: Study Dynamics of Proteins  
embedded in Membranes



# Thanks to



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- Klaus Kiefer, HMI
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- Dieter Strauch, Regensburg
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