MEMORIAL UNIVERSITY

Newfoundland & Labrador, Canada

# Small Angle Neutron Scattering Studies on Polymeric Micelles and Lipids System

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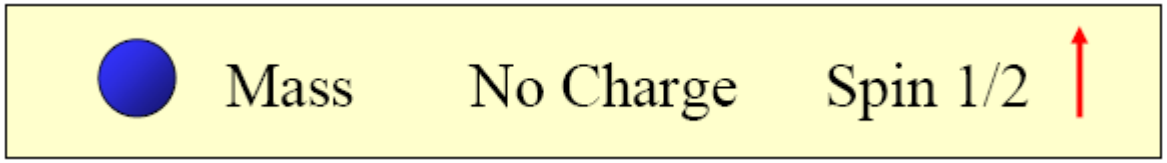
**Phy-6900, December 03, 2008**

# Outline

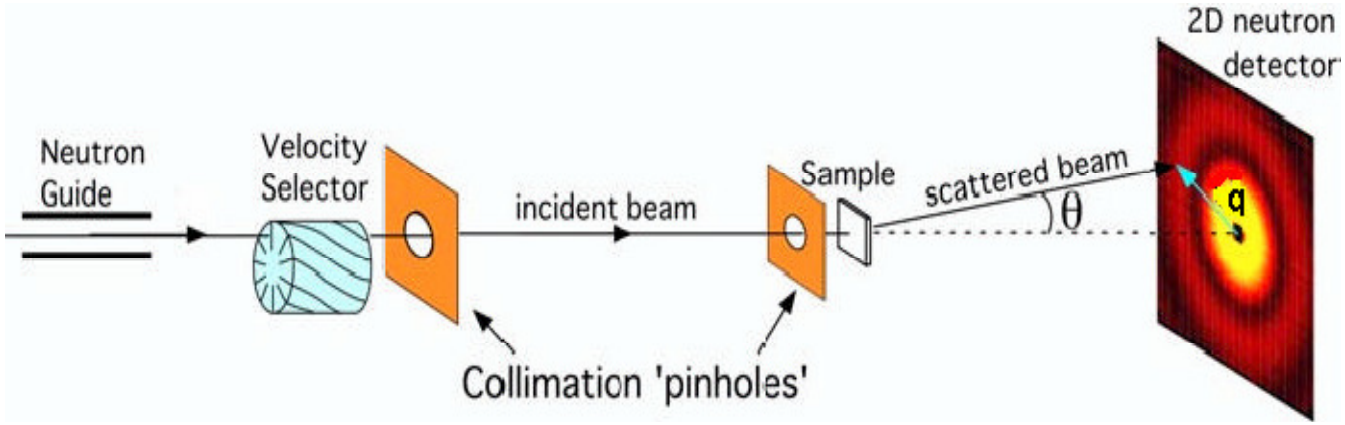
- Why Neutron?
- Instrumentation
- Scattering basics
- Contrast variation
- Time resolved SANS
- Experimental results
- Conclusion

# Why Neutrons?




- Non-destructive
- Highly penetrating
- Wavelength (~1A) in molecular dimensions, so small angle is required to probe large structure
- Energies (~meV) similar to molecular vibrations
- Isotopically variable scattering power: Deuterium and $D_2O$ can be used for labelling

# Instrument




$$q = |\vec{q}| = |\vec{k}_f - \vec{k}_i| = \frac{4\pi}{\lambda} Sin\,\theta$$

- Small Angle Neutron Scattering (SANS) probes structure on a scale *d* where

$$d \approx \frac{\lambda}{\theta}$$ *(wavelength)*

(scattering angle)

$$d = \frac{2\pi}{q}$$

- 0.5 nm < λ < 2 nm (cold neutrons)
- 0.1° < θ < 10° (small angles)
- 1 nm < *d* < *300 nm*

George D. Wignall, *Physical Properties of Polymers Handbook, Chapter 23,* Springer, 2007

# Scattering basics

- Macroscopic scattering cross section: Normalized by scattering volume

$$\frac{d\Sigma(\vec{q})}{d\Omega} = \frac{N}{V}\frac{d\sigma(\vec{q})}{d\Omega} = \frac{1}{V}\left|\int_V \rho(\vec{r})\exp(i\vec{q}.\vec{r})d\vec{r}\right|^2$$

where ρ(r ) is scattering length density, measure of the interaction of neutron wave with a given nucleus

$$\rho\ (\ \vec{r}\ )\ =\ \frac{\sum_j^n b_j}{V}$$

# Scattering basics

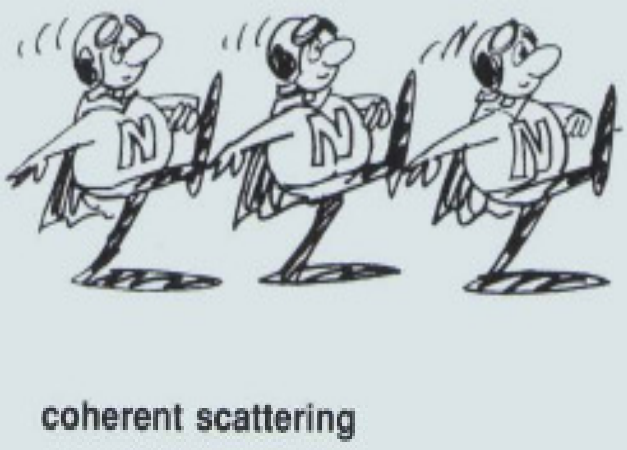
- Cross section for identical particles:

$$\frac{d\Sigma(Q)}{d\Omega} = \left(\frac{N_A}{V}\right)(\rho_A - \rho_B)^2 V_A{}^2 P(Q) S_I(Q)$$

cross section | number density | contrast factor | particle volume | form factor | structure factor

- Structure factor tells us about interactions between particles
- Form factor provides information about the structure of individual particles
- S(Q) is most often found from $\frac{I_{conc}}{I_{dil}}$
- Scattered Intensity: $I(Q) \propto \frac{d\Sigma(\vec{Q})}{d\Omega}$
- The position and height of peaks can tell us about the system

# Types of Scattering




Coherent scattering:

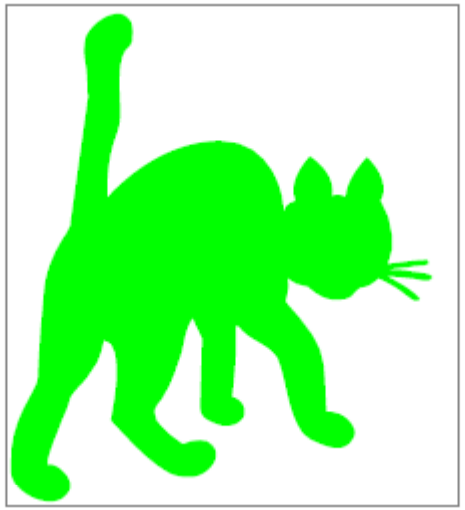
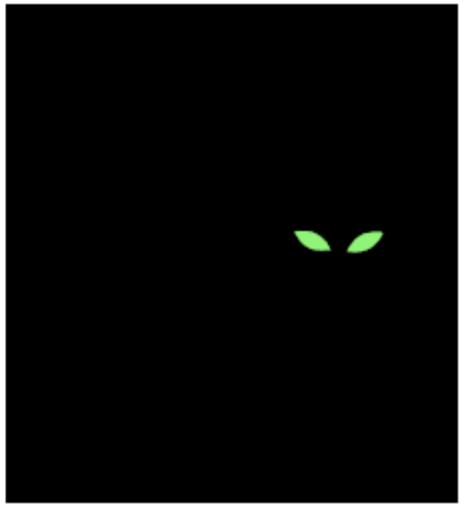
- Elastic-Equilibrium structure
- Inelastic-collective motions of the atoms


Incoherent scattering:

- Can tell us movement of one atom
- Is not Q-dependent and contributes only to the noise level, while absorption reduces the overall signal

Roger Pynn, Neutron Scattering- A primier, 1990

# Contrast Variation

- Very sensitive to hydrogen
- H and D are very different

Scattering lengths:

- $b_H$= -3.74 fermis (coherent), 25.18 fermis (incoherent)
- $b_D$= 6.67 fermis (coherent), 3.99 fermis (incoherent)

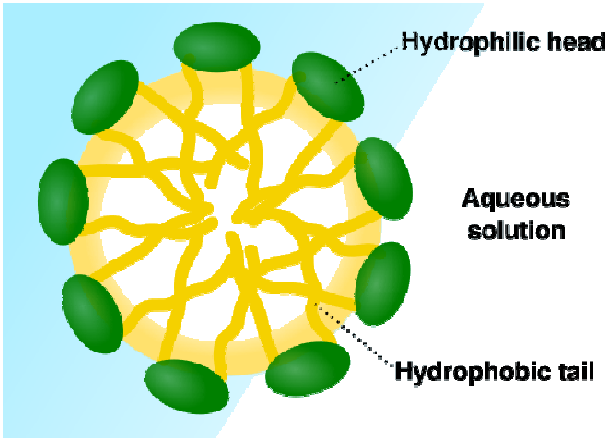
# Polymeric micelles

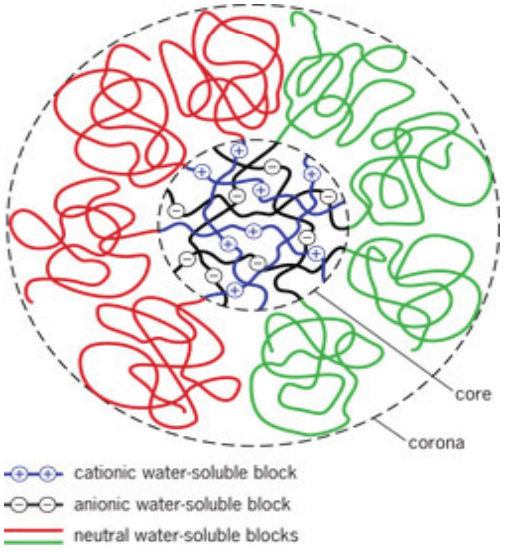
- Polymeric micelles are designed with a branched, hydrophobic interior (core) and hydrophilic exterior (shell) to maintain physical properties characteristic of conventional micelles.

- PEP-PEO micelles where PEP constituting the core and PEO constituting the corona (shell)

- Star polymer-macromolecules having small core of molecules with branches radiating from the core.

- SANS measurements reveal the structural behavior and prove as star polymers

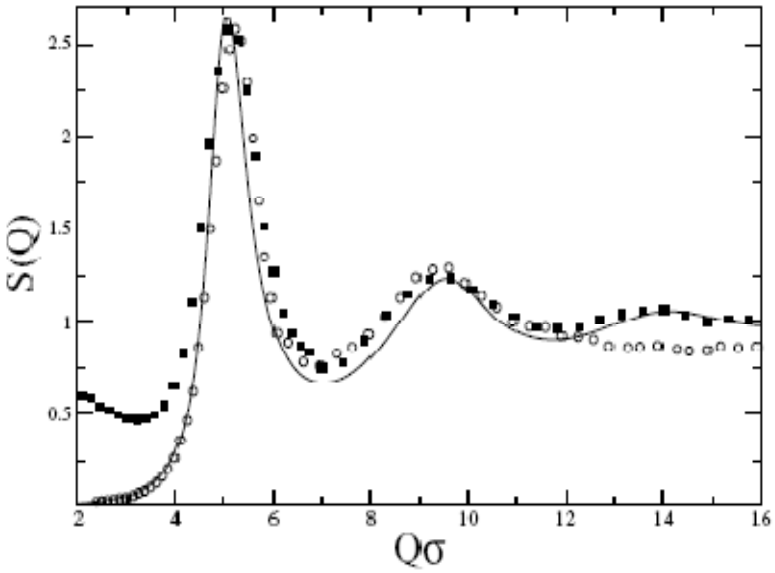



http://en.wikipedia.org/wiki/Micelle
http://www.pcc.wur.nl/UK/research/Strategic%20program%20colloids%20and%20interfaces

# Experimental Results: polymeric micelles I

- Features of the star S(Q) w. r. t. peak positions and heights are nearly same for 1st and 2nd peaks.
- 3rd peak only for micellar system as for PB star this peak is masked by blob scattering of the polymer arms.
- 3rd peak is correlated to the formation of a crystalline phase in micellar system above $\phi^*$.
- Some increase of micellar S(Q) at low Q indicating some excess scattering
- Might arise either from inherent mesoscopic heterogeneities or from weak attractive interactions due to the decreasing solvent quality with increasing molar fraction.

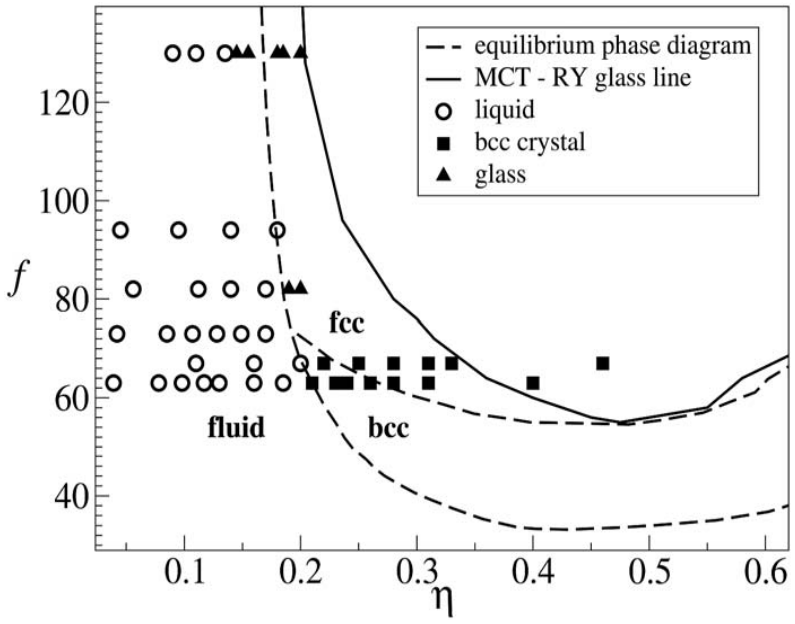



➢ $S(Q)$ for PEP-PEO micelles with $f$ =63 (■) compared to the 64 arm PB star (○) at $\phi/\phi^* \approx$ 1. Solid line: $S(Q)$ from theory

M. Laurati *et al.*, Phys. Rev. Lett. **94**, 195504 (2005)

# Experimental Results : polymeric micelles II

- Good agreement between theory and expt. for liquid-solid boundary for all f and η
- Liquid to bcc crystal transition is perfectly reproduced experimentally for f<70.
- Packing fraction for crystallization at η≈0.21




M. Laurati *et al.*, Physical Review E **76,** 041503, 2007

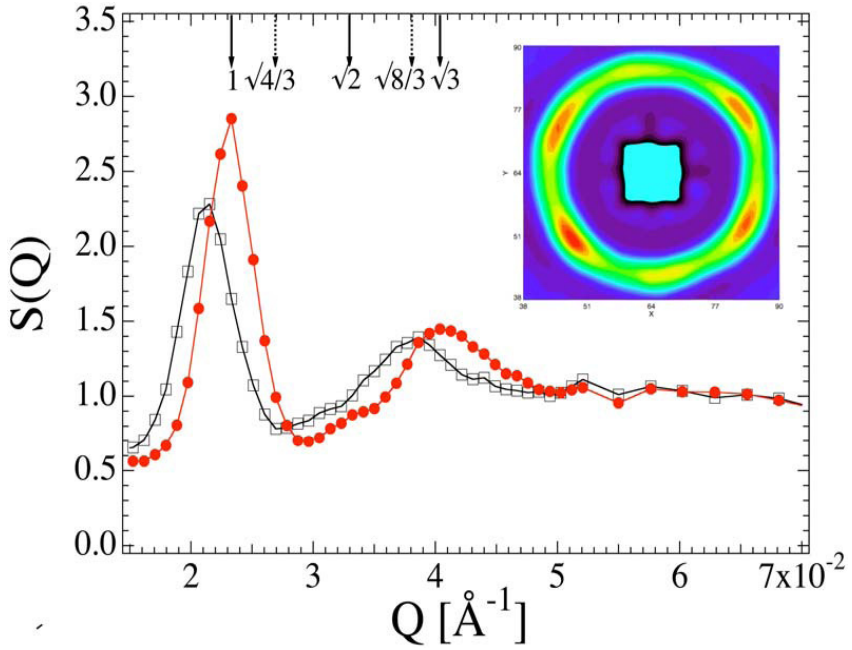
# Experimental Results : polymeric micelles III

- For the first peak of $S(Q)$ crossing $\phi^*$ *with f=67* is bigger than 2.8, minimum value for a freezing transition according to the *Hansen-Verlet* criterion.

- This implies the disordered phase as a glass.

- The peak is further growing with increasing $\phi$.

- for $\phi > \phi^*$ a third small peak is forming, and the position ratio between the three peaks is corresponding to a simple cubic (sc) or bcc lattice.

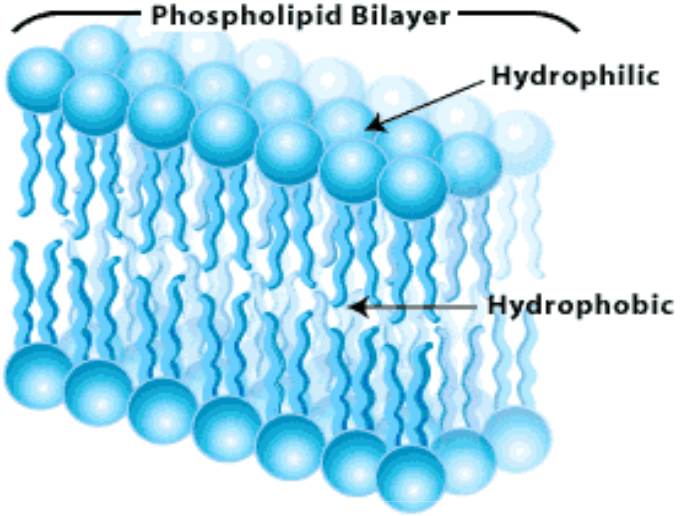


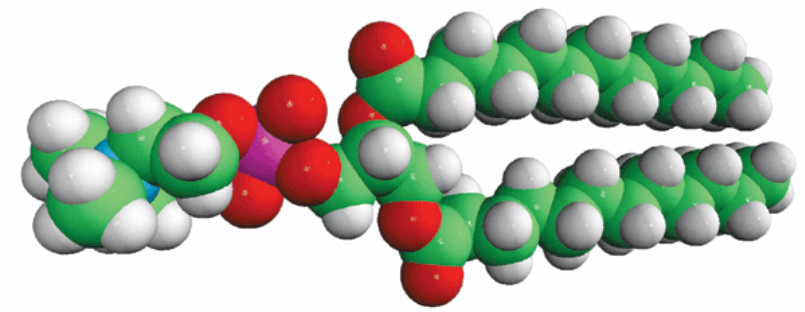

- Inset: 2-dimensional SANS detector picture of $f = 63$, $\phi = 0.16$ evidencing Bragg reflections.

M. Laurati *et al.*, Physical Review E **76,** 041503, 2007

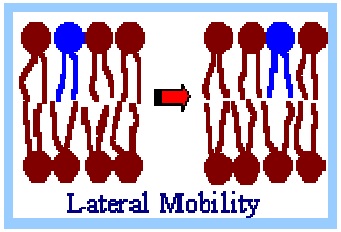
# Lipid bilayers: excellent for cell membrane

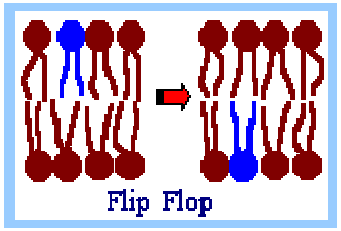
- Composed of lipid molecules: 4-5nm thick.
- Lipid molecules spontaneously form bilayer when hydrate
- **Phospholipid**: A hydrophilic polar **head group**
  Two Hydrophobic **acyl chains**
- Hydrophobic interaction is the driving force
- Tendency to close on themselves
- Extensive; upto millimetres



Avanti Polar Lipids (DMPC)




http://www.avantilipids.com/ProductStructures.asp?n=850345
http://www.rpi.edu/dept/bcbp/molbiochem/MBWeb/mb1/part2/lipid.htm

# Time resolved SANS

- Describe as sending the neutron beam into a sample and watching how it is temporarily broaden when reaching the detector after passing through the sample

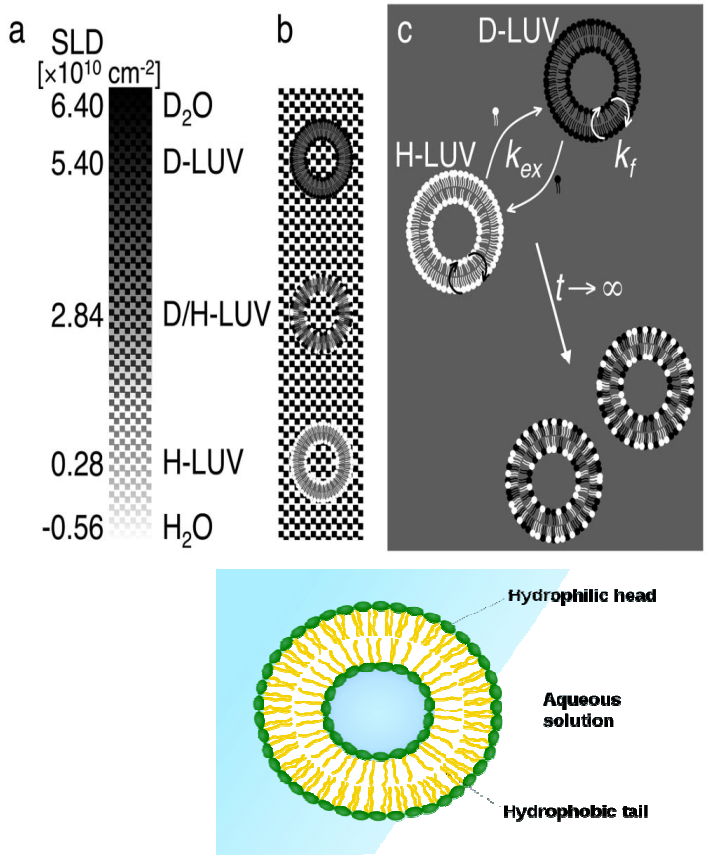
- Useful for kinetics studies because perturbations are inevitable in most experimental techniques

- If time scale is shorter - time slicing required

- With chopper at the source it is possible to get 50μs - 100ms time resolution.

# Experimental Result: Lipid kinetics I

- Principle of the detection of lipid kinetics by TR-SANS
- Here two LUV's, D/H-LUV exhibited little scattering, D/H-LUV is "invisible" for neutrons in this contrast-matching condition [Fig. (b)].
- Fig. (c) shows how the lipid exchange between D- and H-LUV reduces the difference in the SLD of LUV's from solvent (i.e., contrast) with time, this leads to a decrease in the scattering intensity.

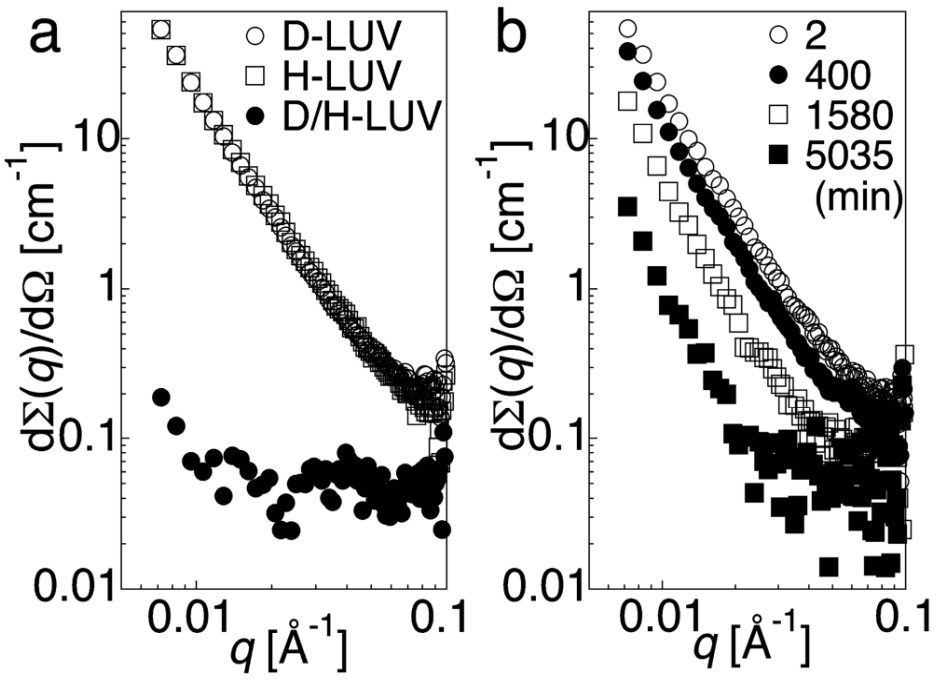



Minora Nakano *et al*., Phys. Rev. Lett. **98**, 238101 (2007)

# Experimental Results: Lipid kinetics II

- The scattering from the mixture of D-LUV and H-LUV faded over time indicating lipid exchange in the observable time scale.

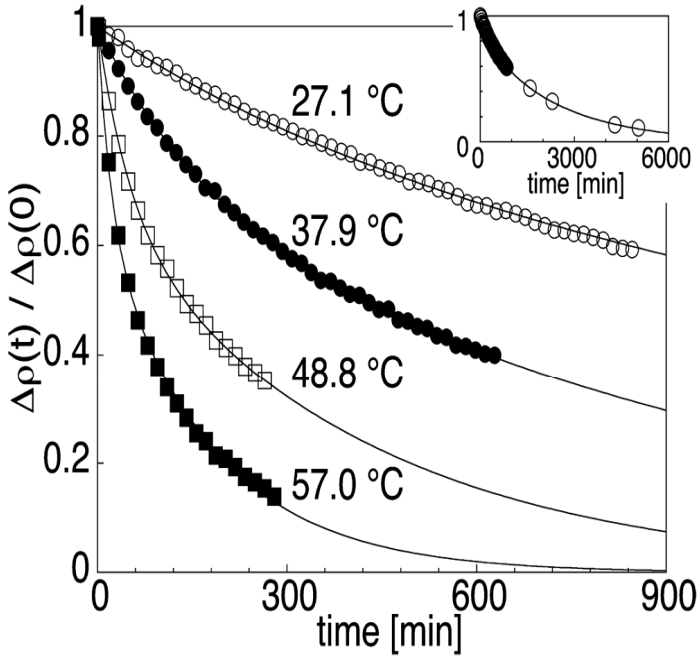
- SANS profile shows identical shape for all times indicating the shell construction of LUV is maintained during lipid exchange process.




Minora Nakano *et al*., Phys. Rev. Lett. **98**, 238101 (2007)

# Experimental Results : Lipid kinetics III

- Contrast decays of LUV's after mixing D- and H-LUV at four different temperatures.
- The contrast decays more sharply with the increase of temperature.
- Inset shows the contrast decay over a longer period at $27.1^0$C.

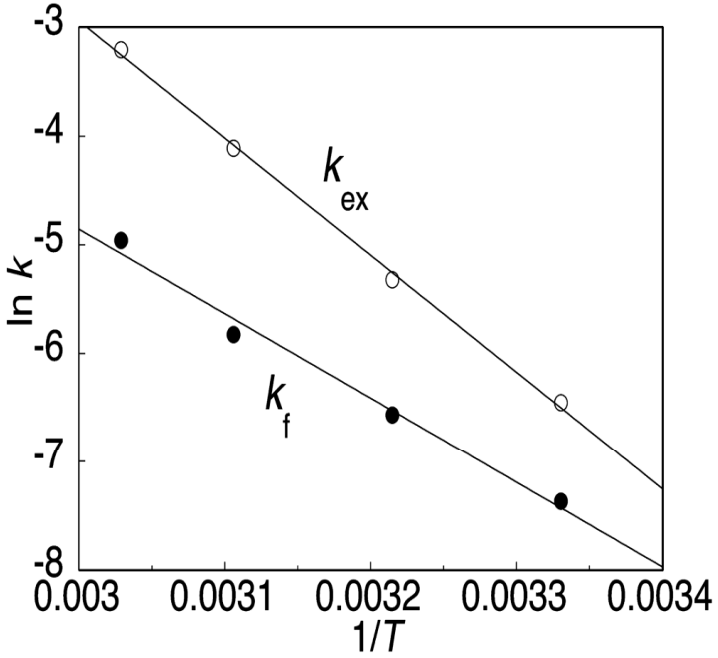



Minora Nakano *et al*., Phys. Rev. Lett. **98**, 238101 (2007)

# Experimental Results : Lipid kinetics IV

- The half-lives ($t_{1/2}$ =(ln2/$k$) of the lipid exchange at 50 and 30$^0$C were estimated at 0.67 and 5.4 h, respectively, which are close to or slightly smaller than those obtained using a radioisotope (0.74 and 9.6 h, respectively).

- Arrhenius plots of the obtained parameters exhibited a good linear relationship.




Arrhenius plots of the rates of intervesicular exchange ($k_{ex}$) and flip-flop ($k_f$).

Minora Nakano *et al.*, Phys. Rev. Lett. **98**, 238101 (2007)

# Drawbacks of SANS

- SANS is a routine technique available at neutron-scattering facilities associated with research nuclear reactors.
- No home version of this technique.
- Neutron sources are very expensive to build and to maintain.
- Another problem with this technique is that neutron flux is very low.
- The interaction of neutrons with matter is weak.

# Conclusion

- Small-angle neutron scattering (SANS) is a very popular method used by physicists, material scientists, chemists and biologists.
- SANS can determine structures, phase transitions, and morphology.
- Possible to do experiments in bulk systems
- TR-SANS is a new method to determine kinetics studies of lipid and polymeric micelles precisely.

**Thank you**

**Questions?**