# Numerical Study of the Unilamellar Vesicle Structure via SANS on the Base of the SFF Model

**E.V. Zemlyanaya**
*Laboratory of Information Technology, JINR*
**M.A. Kiselev**
*Frank Laboratory of Neutron Physics, JINR*
**V.K. Aswal**
*Solid State Physics Division, Bhabha Atomic Research Centre, Trombay, Mumbai 400 085, India*
**R.H.H. Neubert**
*Institute of Pharmaceutical Technology and Biopharmacy, Martin-Luther-University, Halle (Saale) D-06120, Germany*

Investigation of model stratum corneum (MSC) lipid structure is a subject of interest in pharmacology and dermatopharmacy as a background for the formulation of new enhancer of drug penetration through human stratum corneum [1]. A determination of the internal lipid membrane structure is far beyond the resolution of light microscopy or light scattering. Neutron scattering (SANS) in the range of wavelength 1–10 Å provides better spatial resolution of an internal structure on the scale of Ångströms. It allows to determine the internal membrane structure with reasonable accuracy. Membrane thickness, thickness of polar head groups, thickness of methyl and methylene groups, surface area per lipid molecules, thickness of hydrophilic and hydrophobic membrane regions can be calculated from scattering experiment.

Small-angle neutron scattering (SANS) is the best method to study a membrane structure of the highly diluted unilamellar or oligolamellar vesicular systems. In the case of MSC, the SANS technique can be applied for systems where the possibility to prepare highly oriented planar multilamellar systems is limited, or as the complementary method.

The separated form factors model (SFF) was developed to describe the unilamellar vesicles structure with diameter $\geq 500$Å [2]. This approach allows a simulation of $\rho(x)$, the scattering length density of neutrons across the bilayer, by any integrable function.

The application of fluctuated membrane model in the framework of the SFF approach shows that the scattering density from $D_2O$ distribution function inside of hydrophilic region dominates under that from polar head groups [3]. Hence, one can expect that the linear function $\rho(x)$ of the neutron scattering length density across membrane in the hydrophilic region can provide realistic and simple approximation of the lipid membrane structure. Numerical study of the DMPC vesicles structure in assumption of linear water distribution has been done in [4, 5].

In [6], for the simulation the internal structure of unilamellar vesicles, the hydrophilic-hydrophobic (HH) approximation is applied. In this case, only two fit parameters (thickness of membrane and thickness of hydrophobic region) are needed to simulate $\rho(x)$ function. This approach sufficiently improves the fitting convergence relative to the more complex models of $\rho(x)$ function.

The parameters of the polydispersed unilamellar vesicle population were analyzed for three different types of membranes. The neutron scattering length density across the membrane is simulated on the base of the SFF model with the HH approximation of water distribution.

Parameters of the DMPC vesicle population (average radius, polydispersity, membrane thickness, thickness of hydrophobic part) were restored only from the SANS spectra, without additional experimental methods (light scattering, diffraction, etc.). Additionally, in the case of known molecular volume, the number of water molecules per one lipid molecule in the membrane bilayer and area per one lipid molecule can be calculated. Fitting results of the SANS experimental data obtained at the SANS-1 PSI spectrometer (Villigen, Switzerland), are shown at the Fig. 1.

The developed method of the one-component membrane structure analysis was applied to study the mixed polydispersed vesicular systems: binary system *DMPC/Ceramide 3* and quaternary system *Ceramide 6/Cholesterol/Palmitic acid/Cholesterol Sulfate*. The SANS experiment for the investigation of MSC membrane structure was carried out at the Budapest Neutron Scattering Center (Hungary). Fitting results for the quarternary vesicular system are demonstrated at Fig. 2.

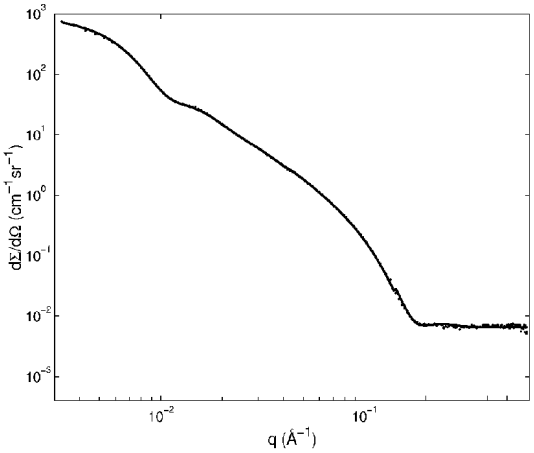


Fig. 1: SANS-I PSI spectrometer (Villigen). Experimental and fitting curves for DMPC vesicles at $T = 30^\circ$ C. 1% DMPC concentration in $D_2O$

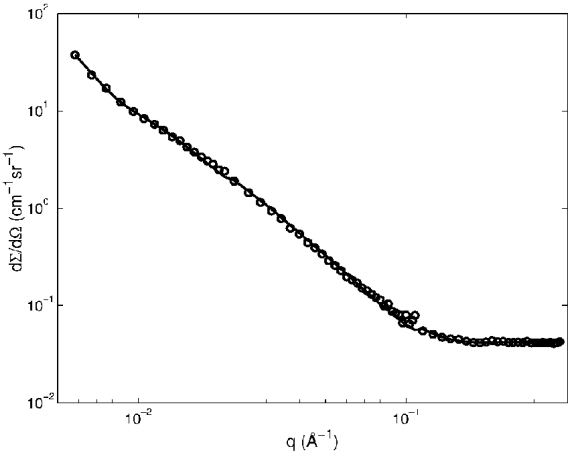


Fig. 2: "Yellow Submarine" SANS spectrometer (Budapest). Experimental and fitting curves for the quarternary system at $T = 30^\circ$ C. 0.5% of the lipid concentration in $D_2O$. Component ratio of Ceramide 6/Cholesterol/Palmitic acid/ Cholesterol Sulfate is 55/20/15/10 (w/w)

Membrane thickness 48Å and hydrophobic thickness 29Å obtained from SANS for the quaternary system are in good agreement with values 45.6Å and 28Å evaluated from the neutron diffraction experiment in [7].

In the recent paper [8], the developed approach has been applied to analyse the structure and properties of the polydispersed DMPC vesicles population in three phases: gel, ripple, and liquid. Dependence of the DMPC membrane thickness on temperature was restored from the SANS experiment on the basis the SFF-HH model. It was demonstrated that DMPC membrane thickness in liquid phase ($T = 30^\circ$ C) depends on the membrane curvature.

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