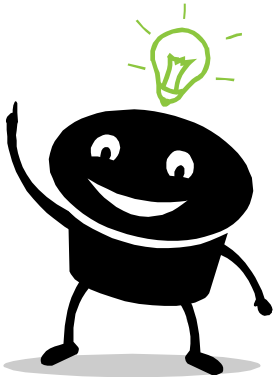
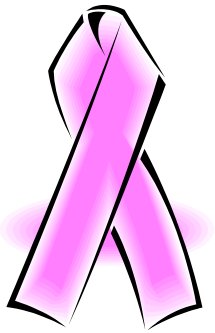
How to Write a Successful Neutron Proposal

Victoria Garcia Sakai

JSTS

sample



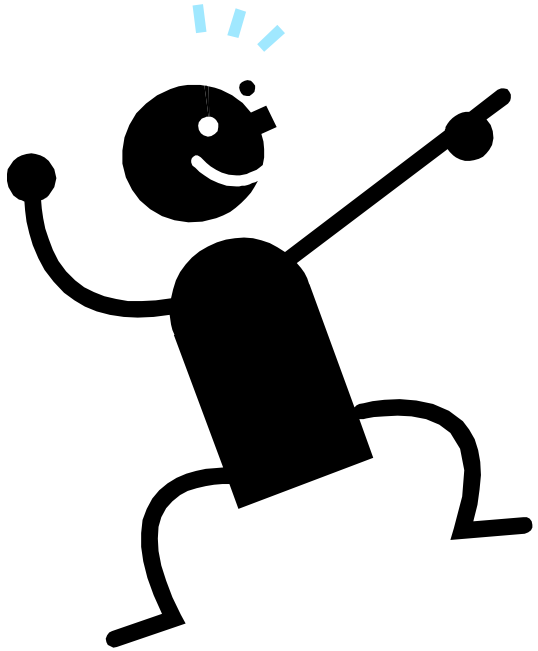


Idea & Research problem

Pre- characterisation

the unique information obtained from neutron experiments

Can ~~neutrons~~ help me?



Are you sure?

Can you obtain the information with a different technique?

Are you completely sure?

Before writing a proposal

- Literature review on similar experiments

Before writing a proposal

- Literature review on similar experiments
- Talk to colleagues

Before writing a proposal

- Literature review on similar experiments
- Talk to colleagues
- Research available instruments worldwide

Where should I go to get my neutrons?

Sources http://neutronsources.org/

Where should I go to get my neutrons?

- Where can I do the best science?
  - Instrument specs
  - Flux
  - Sample environment
  - Technical/user support
  - Laboratory space/facilities
  - PhD programmes
  - Software
- Proximity/ease of access
- Funding
- Personal connections/collaborations
- Food/Scenery

Before writing a proposal

- Literature review on similar experiments
- Talk to colleagues
- Research available instruments worldwide
- Contact instrument scientist and ask questions!
    - *instrument configuration*
    - *sample environment*
    - *time required*
    - *…*

Before writing a proposal

- Literature review on similar experiments
- Talk to colleagues
- Research available instruments worldwide
- Contact instrument scientist and ask questions!
    - *instrument configuration*
    - *sample environment*
    - *time required*
    - *…*
- Decide on proposal type

Access Types

- **Normal proposal rounds** – twice per year
- **Rapid access** – for urgent studies or ‘hot topics’, submit at any time
- **Xpress access**, including postal service
- **Industrial access** (collaborative or for cash)
- **Back door** – collaboration/tests with institute scientists
- **Programme access** – long time proposals

Before writing a proposal

- Literature review on similar experiments
- Talk to colleagues
- Research available instruments worldwide
- Contact instrument scientist and ask questions!
    - *instrument configuration*
    - *sample environment*
    - *time required*
    - *…*
- Decide on proposal type
- Preliminary sample characterisation?

Before writing a proposal

- Literature review on similar experiments
- Talk to colleagues
- Research available instruments worldwide
- Contact instrument scientist and ask questions!
    - *instrument configuration*
    - *sample environment*
    - *time required*
    - *…*
- Decide on proposal type
- Preliminary sample characterisation?
- How will neutrons answer my questions?

Before writing a proposal

- Contact instrument scientist and ask questions!
- Have I done preliminary characterisation?
- Will neutrons answer my questions?

the Proposal Process (in general)

- Two proposal calls per year
- Deadline is real!
- Technical reviews (by facility scientists) – feasibility, safety…
- Scientific Review
  - Classification is done by subject or technique
  - At least 2 reviewers per proposal by external experts
  - Panel meetings at facilities
  - Time recommended
- Final balance (eg. national funding)
- Letters sent out to PI's

Things to keep in mind…

Scientific reviewers are not always experts in your specialty since science at the facilities is so diverse. So, don't assume they know everything.

Most reviewers spend minutes per proposal! Many will not have time to read through the references!

So, you must get all relevant information in the proposal.

Make your point, clearly and succinctly.

Things to keep in mind…

Scientific reviewers are not always experts in your specialty since science at the facilities is so diverse. So, don't assume they know everything.

Most reviewers spend 5-8 minutes per proposal! Many will not have time to read through the references!

So, you must get all relevant information in the proposal.

Make your point, clearly and succinctly.

Proposal Ingredients (Part I)

- User/participant information
- Title and abstract
- Sample description
- Sample environment requirements
- Instrument specs requested and time
- Publications, student thesis, scientific area, grants, submission status, safety…

JCNS, Munich

Proposal No. : 8744
Proposer :
Affiliation :
Short Name :

Subject

Title	

Title

Scientifique area	Soft Condensed Matter
Grand Challenges	Soft Matter, Macromolecules, Complex fluids
Instrument	KWS-1

Instrument

Continuation of experiment No.	7211
Resubmission of proposal nr.	

Rapid Access only available for instruments KWS-2, PGAA and SPODI.
Each accepted Rapid Access proposal will receive up to a maximum of 12 hours of beamtime.

Rapid Access Proposal?	No
Internal beam time	No
Did you submit this proposal also to another facility?	No
Measuring time [days]	1

Time

Abstract (max 200 words)	

Abstract

Experimental team

Co-authors name, affiliation	
Local contact	

User info

Sample

Substance	deuterium oxide
Elemental formula	D2O
Sample type	liquid
sample size [mm] weight [mg]	1 (mm) thickness, 20 (g)
Number of samples	2
Availability of samples	2013-07-19
Space group	
unit cell parameters	

Sample info

Sample environment

No sample environment needed	Yes
Cryostat	
High temperature furnace	
Pressure cell	
Magnetic field	
other sample environment	shear cell (Anton Paar)
Temperature range	
Temperature stability	
Pressure range	
Magnetic field	

Sample environment info

Security aspects

Toxic	No
explosive	No
radioactive	No
Sample gets activated	No
activity after experiment [Bq / isotope]	
Other risks	

Miscellaneous

Sample preparation laboratory (neutron guide hall)	No
Typ of work, materials, equipment in use	
Special technical support	No
Details(e.g. own equipment, special configurations, mechanics, control, software)	

ISIS, UK

Science & Technology Facilities Council

ISIS

Experiment Proposal

Experiment Number: 920168

Principal investigator(*)	Dr V Garcia Sakai, STFC, United Kingdom	
Co-investigator		
Co-investigator		
Co-investigator		
Co-investigator		
Co-investigator		
Co-investigator		
Co-investigator		
Co-investigator		
Experiment Title		
Instrument	IRIS/ OSIRIS	Days Requested: 7
Access Route	Direct Access - Resubmission	Previous RB Number: -
Science Areas	Biology and Bio-materials	
Sponsored Grant	No	Sponsor: -
Grant Title	-	
Grant Number	-	
	Start Date: -	Finish Date: -
EU Access?		
Similar Submission?	No	

Abstract

Publications

User info

Title

Time & Instrument

Abstract

ISIS Sample record sheet

Principal contact	Dr V Garcia Sakai, Victoria.garcia-sakai@stfc.ac.uk, Tel: 00-44-1235-446703
Instrument	IRIS/ OSIRIS, 7 days, preferred contact is Garcia Sakai, V (Victoria.garcia-sakai@stfc.ac.uk)
Special requirements	-

SAMPLES

Material	protein
Formula	-
Forms	Solid
Volume	1 cc
Weight	-
Container / substrate	-
Storage requirements	-
Xtal details	

SAMPLE ENVIRONMENT

Equipment	CCR
Temperature range	10-330 K
Pressure range	-
Magnetic field range	-
Special equipment	-

SAFETY

Hazards	-
Hazard details	-
Sample sensitivity	-
Experimental hazards	-
Sample prep hazards	-
Equipment hazards	-
Prep lab needed	Yes
Special equip reqs	-
Sample will be	Removed By User

Sample info

Sample environment info

NCNR, USA

NIST Center for Neutron Research

Proposal for Neutron Beam Experiment

Submission ID:13104 Proposal Number: E23-19

Experiment Title

Title: Dynamics of phospholipid vesicles in the presence of bioprotectants

Title

Proposal Type: New Proposal

Time Received: 21-MAR-08 17:52

Scheduling

Desired Dates: 07-01-2008 to 12-31-2008

Impossible Dates:

Estimated Duration: 6 days

Time

Participants

User info

	Name	Address	Country	Telephone/e-mail
Principal Investigator	Garcia-Sakai, Victoria	Rutherford Appleton Laboratory ISIS Facility Chilton, Didcot Oxon, OX11 0QX	United Kingdom	000-000-0000 victoria.garcia-sakai@stfc.ac.uk
User 2	Nanda, Hirsh	National Institute of Standards and Technology NIST Center for Neutron Research 100 Bureau Drive, MS6102 Gaithersburg, MD 20899-6102	United States	hirsh.nanda@nist.gov

Instrument

Instrument Requested:	NG-5 -- NSE, Neutron spin echo spectrometer (CHRNS)
Suggested Local Contact:	Antonio Faraone
Instrument Resolution:	
Instrument Configuration:	Default instrument configuration

Instrument

Sample Description

	Sample 1
Name	DPPC/D2O/maltose
Chemical Formula	
Mass (grams)	
Form	Liquid

Sample info

Temperature Measurement Range (K)	300-330
Number of Runs	
Total Collection Time (hrs)	
Sample Availability	2008-03-01 00:00:00.0

	Sample 2
Name	DPPC/D2O/sucrose
Chemical Formula	
Mass (grams)	
Form	Liquid
Temperature Measurement Range (K)	300-330
Number of Runs	
Total Collection Time (hrs)	
Sample Availability	2008-03-01 00:00:00.0

Sample Environment

Sample Environment Equipment:

Sample environment info

Special Requirements

Please describe any non-routine needs for sample temperature, magnetic field, etc., or other ancillary equipment. Specify any equipment needed at NIST for sample loading, treatment, storage, etc. (inert atmosphere, refrigeration, dry box, etc.). Also describe any equipment you plan to bring to NIST.

Safety

Check *at least* one box that describes your sample

[X] No Hazards

[] Toxic [] Corrosive [] Radioactive [] Explosive [] Flammable

If there are any hazards associated with your proposed experiment, please indicate how any risks are to be handled.

Categorization

For reporting purposes, please categorize your proposal:

Research Area:	Biomolecular Science
Funding Agency:	NRC and STFC UK

Publications

Proposal Ingredients (Part II)

Two-page description of proposed research (incl. references)

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- Brief background, state the problem clearly and why the experiment is important, why it will make a difference – **Why should one care?**

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- Brief background, state the problem clearly and why the experiment is important, why it will make a difference – **Why should one care?**
- Clear justification of need for neutrons and particular instrument- **why do you need beamtime on X?**

Proposal Ingredients (Part II)

Two-page description of proposed research (incl. references)

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- Description of preliminary characterisation or work on the sample/system- **do you understand your sample?**

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- Evidence team's productivity and experience – **Will they publish in a timely manner?**

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- Description of data analysis/modelling – **What will you do with the data?**
- Evidence team's productivity and experience – **Will they publish in a timely manner?**
- **Be clear and specific – not vague and general!**
- **Think of yourself as a reviewer! What would annoy you?**

2-page case including references and figures/tables

FRM II
Forschungs-Neutronenquelle
Heinz Maier-Leibnitz

User Office
Lichtenbergstr. 1, 85748 Garching/ Germany
Tel.: +49.(0)89.10703/ 10794
Fax: +49.(0)89.10799
Email: userinfo@frm2.tum.de Web: user.frm2.tum.de

SUBMISSION OF A PROPOSAL

Experiment Title

Proposer

Name
Email
Affiliation
Co-Proposers

Scientific background and detailed description of the proposed experiment

Abstract (~100 words)

Introduction

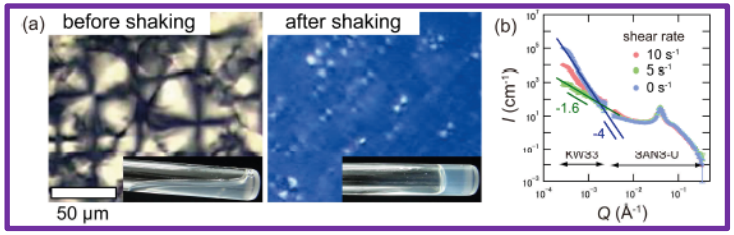
Reference

[1] K. Sadakane, A. Onuki, K. Nishida, S. Koizumi, and H. Seto, *Phys. Rev. Lett.*, **103**, 167803 (2009). [2] A. Onuki, *J. Chem. Phys.*, **128**, 224704 (2008).

Previous results

FRM II
Forschungs-Neutronenquelle
Heinz Maier-Leibnitz

User Office
Lichtenbergstr. 1, 85748 Garching/ Germany
Tel.: +49.(0)89.10703/ 10794
Fax: +49.(0)89.10799
Email: userinfo@frm2.tum.de Web: user.frm2.tum.de



Aim of proposed work

Proposed experiments

Here is our experimental plan:

1) Instrument: KWS1 with rheo-meter (Anton Paar)
2) Shear-rate: 0 s^{-1}, 0.1 s^{-1}, 1 s^{-1}, 3 s^{-1}, 5 s^{-1}, 7 s^{-1}, 10 s^{-1}, 50 s^{-1}, 100 s^{-1}, 1000 s^{-1}
3) The measured spatial domain: Q = 0.003 $Å^{-1}$ to 0.3 $Å^{-1}$
4) Sample: (i) D_2O / 3-methylpydine / $NaBPh_4$
   (ii) D_2O / $C_{14}E_5$
5) Temperature: 298 K

We assume that one measurement takes 45 minutes (15 minutes at high-Q and 45 minutes at low-Q region).Then, the total measurement time is estimated as
0.75 (hours) × 10 (shear rate) × 2 (samples) × 1 (temperature) = 15 (hours).
Additionally, we need 8 hours for setting rheo-meter and changing the detector length.
Threfore, we request 1 days beam-time.

Your publication record (give references to papers published in the last two years arising from experiments at FRM II instruments)

There is no paper arising from experiments at FRM II instruments.

2-page case including references and figures/tables

SANS Study

Proposers:

Introduction

Experiment

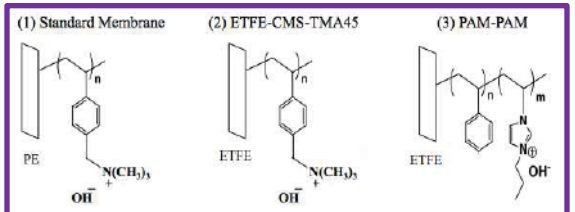


Figure 1. Molecular structure of the membranes used in this study.

Table 1. Characterization of the samples.

Sample	Grafting degree (%)	IEC (mmol/g)	σ (mS/cm²)	Density (Dry) (g/cm³)
(1)	103	1.8	15	1.02
(2)	45	1.2	30	1.56
(3)	80	2.0	10	1.47

2-page case including references and figures/tables

Changes in lipid dynamics induced by melittin absorption on membrane surfaces

The rise of infectious bacterial strains resistant to current antibiotic treatments is a growing concern universally. This has spurred an intensified interest both in the discovery and understanding of naturally occurring anti-microbial agents and the molecular mechanism by which they function. Most anti-microbial compounds associate with the cellular membrane and disrupt the delicate electro-chemical balance required for bacterial cellular life. One such naturally occurring molecule is melittin (MLT), found in the venom of honeybees. MLT posses many characteristics shared among known anti-microbial peptides. It is a single domain a-helix with a strong amphipathic quality (Fig. 1a). Structural studies from X-ray diffraction experiments [1] show partitioning into the lipid membrane of cells - intercalating with the headgroup region (Fig. 1b). Significant perturbations to the lipid chains are also observed: a thinning of the hydrocarbon region as well as a broadening of the terminal methyl distribution suggest an increase in chain disorder due to MLTs presence. At higher concentrations, MLT fully penetrates the membrane as self-assembled helical bundles that form large pores in the membrane, leading to cell death.

Detailed structural data from diffraction experiments has helped elucidate the function of MLT. However the mechanism for biological activity stems from the dynamics. We propose to use quasielastic neutron scattering (QENS) to characterize the changes in mobility of a model dioleoylphosphatidylcholine (DOPC) phospholipid membrane, in the presence of MLT. The protein:lipid system will be divided into three major components, the phospholipid headgroups, the lipid hydrocarbon tails and the MLT itself. Selective deuteration will allow us to follow the mobility of each of the three components separately. Regions of lipid that interact with MLT the most will be identified by comparison of dynamical changes with the pure DOPC bilayer measurements. Furthermore a study combining molecular dynamic (MD) simulations with neutron results on a similar system [2] suggests that regulating the mobility of phospholipid headgroups controls melting transitions. Measuring the effect on the membrane Tm provides another method for probing the balance between headgroup and chain interactions with MLT.

Previous QENS measurements of ordered lipid systems have used a combination of several dynamic models to describe motions in the ps to ns range of accessible time scales [1,3-4]. Given the sub ns dynamic range of the IRIS backscattering instrument our experiments will primarily be sensitive to methyl rotations, dihedral isomerization and localized diffusion (Fig. 2a). Despite the use of selective deuteration, the dynamical processes are still complex and may prove difficult to dissect into their individual contributions. Therefore, we will use an experimentally validated MD simulation [5] to provide a powerful method for aiding in the interpretation of QENS data, since there is total overlap in time and length scales accessed by both methods. Preliminary analysis of a DOPC/MLT simulation already provides some insights into potential perturbation in lipid dynamics caused by the peptide. Fig. 2b shows a snapshot of the simulation in which lipids within the vicinity of the protein are either highly kinked or extended. Furthermore the less mobile headgroups adjust their packing behavior around MLT. The results already suggest a possible framework for interpreting QENS data for this system.

We propose to perform experiments on the following samples:

(1) Fully hydrogenated DOPC [hh-DOPC]
(2) Fully hydrogenated DOPC with melittin [hh-DOPC+h-melittin]
(3) Hydrogenated head-group DOPC [hd-DOPC]
(4) Hydrogenated head-group DOPC with melittin [hd-DOPC+h-melittin]

The experiments proposed are presented in turn below:

(a) Elastic window scans (10-350K): elastic scans will give us a number of preliminary results. A comparison of the scans of the non-labeled lipid with and without MLT (samples 1,2), will show changes in Tm and in the dynamic regimes within the timescale of the IRIS spectrometer. Comparing head labeled with fully hydrogenated (signal dominated by tail protons) DOPC will indicate if the gel-to-fluid transition is characteristic to a specific part of the lipid (samples 1,3). Addition of the MLT to the labeled DOPC will show any differences in mobility in the presence of MLT that are specific to the individual components of the lipid (samples 2,4). Finally, mean-square displacement data for all samples will reveal changes in the mobility of all three components in the system (all samples). Elastic scans will require 3 days.

(b) Dynamic runs: we propose to measure the dynamics of each of samples 3-6 at two temperatures, below and above Tm. The measurements will allow analysis of the mobility of the DOPC head and tail groups quantitatively (samples 1,3), allowing for precise assessment of their response to the addition of MLT (samples 2,4). These experiments require 4 days (assuming 12hr per temperature run based on sample quantities).

The samples will consist of multilayers of DOPC and DOPC/MLT mixtures containing 1.5 mol % MLT per mol DOPC, plated onto a series of silicon wafers. Around 15 wafers are stacked in an aluminium slab-shaped cell with the face area of the same dimensions as the neutron beam. Such a cell has already been used for experiments on the backscattering spectrometer at the NIST Center for Neutron Research. The cell is contained in a humidity chamber and the samples are kept at 66 % r.h. with a $NaNO_2$ solution in D_2O. Use of D_2O allows minimization of incoherent scattering from the buffer and also from the exchangeable protons in the MLT. The concentration of MLT and the humidity is chosen to match the MD simulations and diffraction experiments.

We propose to use the IRIS spectrometer with the PG002 configuration at a resolution of 8.8 ueV (HWHM) and an energy range of 1.0 meV, giving us access to timescales between ca. 0.5-100 ps. The Q-range accessible is 0.3- 1.8 inv. Ang. These distances and times are directly comparable to the MD simulations. For the completion of the proposed work we are requesting a total of 7 days.

We note that this is a resubmission of RB 0720585 which was awarded 7days. Since then we have been trying to synthesize MLT and encountered some difficulties, thus we have not used our beamtime and we thought it would be better to resubmit. We now have a successful route for expressing MLT and will be ready to perform the experiment.

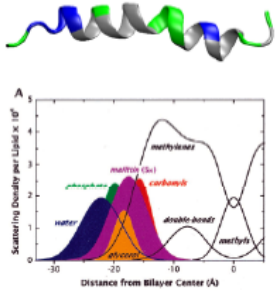


Figure 1: (a) The amphipathic MLT monomer is shown with polar residues in green, basic residues in blue and non-polar residues in grey. b) X-ray scattering length density profiles show MLT partitioning into the lipid headgroup region of a dioleoylphosphatidylcholine (DOPC) bilayer [1].

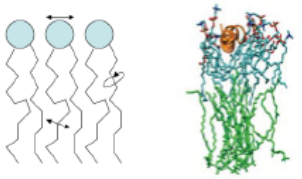


Figure 2: (a) A schematic of accessible motions on the sub ns time scale. Straight arrows represent localized mobility and circular arrows represent dihedral isomerization or terminal methyl rotation. (b) Snapshot of a DOPC/MLT MD simulation. Perturbation to lipid tail conformation and packing defects in lipid headgroups are evident.

References:

[1] K. Hristova et al, *Biophysical J.* **80** 801 (2001).
[2] M. Doxastakis et al, *Biophysical J.* **92** 147 (2007).
[3] S. König et al, *J. Phys II France* **2** 1589 (1992).
[4] S. König et al, *Biophysical J.* **68** 1871 (1995).
[5] R. W. Benz et al, *Biophysical J.* **91** 3617 (2006).

2-page case including references and figures/tables

(If you have been allocated beam time through proposals to the NCNR during the past three years, please list the instrument and resulting publications)

Local Polymer Dynamics in Polymer-C60 Mixtures J. M. Kropka, V. Garcia Sakai, and P. F. Green, Nanoletters (in press). Role of Hydration Water in Dynamics of Biological Macromolecules, A. P. Sokolov, J. H. Roh, V. García Sakai, and E. Mamontov, Chem. Phys. (in press). Dynamics of PEO in blends with PMMA: study of the effects of blend composition via quasi-elastic neutron scattering, V. García Sakai, J.K. Maranas, I. Peral, and J.R.D. Copley, Macromolecules (accepted). Direct Analysis of the Ion-Hopping Process Associated with the alpha-relaxation in Perfluorosulfonate Ionomers using Quasielastic Scattering, K. A. Page, J. K. Park, R. B. Moore, and V. Garcia Sakai, Macromolecules (submitted) Confinement Induces Both Higher Free Volume and Lower Molecular Mobility in Hydrogen Bonded Glass-Former, D. Kilburn, P. E. Sokol, V. García Sakai, and M. A. Alam, Applied Physics Letters (submitted) Role of Hydration Water in Dynamics of Biological Macromolecules, A. P. Sokolov, J. H. Roh, V. García Sakai, and E. Mamontov, Chem. Phys. (in press) Observation of a Dynamic Crossover in Water Confined in Double-Wall Carbon nanotubes, X.-Q. Chu, A. I. Kolesnikov, A. P. Moravsky, V. García Sakai, and S.-H. Chen, Phys. Rev. E (2008). Dynamics and Structure of Hydration Water on Rutile and Cassiterite Nano-powders Studied by Quasielastic Neutron Scattering and Molecular Dynamics Simulations, E. Mamontov, L. Vleck, D. J. Wesolowski, P. T. Cummings, W. Wang, L. M. Anovitz, J. Rosenqvist, C. M. Brown, and V. García Sakai, J. Phys. Chem. C, 111, 4328-4341 (2007). Microscopic Protein Diffusion at High Concentrations, S. Busch, W. Doster, S. Longeville, V. García Sakai, and T. Unruh, in Quasi-Elastic Neutron Scattering Conference 2006 (QENS 2006), edited by Paul E. Sokol, H. Kaiser, D. Baxter, R. Pynn, D. Bossev, and M. Leuschner (Mater. Res. Soc., Warrendale, PA, 2007), 107-114. Diffusion of Water in the Na0.3CoO2.1.4H2O Superconductor, V. García Sakai, E. Mamontov, J. W. Lynn, L. Viciu and R. J. Cava, Physical Review B, 75, 014505 (2007). A Molecular View of Melting in Anhydrous Phospholipidic Membranes M. Doxastakis, V. García Sakai, S. Ohtake, J. K. Maranas and J. J. de Pablo, Biophysical Journal, 92, 147-161 (2007). Local Dynamics of Syndiotactic Poly(methyl methacrylate) Using Molecular Dynamics Simulation, C. Chen, J. K. Maranas, and V. García Sakai, Macromolecules, 39, 9630-9640 (2006). The composition dependence of the segmental dynamics of poly(methyl methacrylate) in miscible blends with poly(ethylene oxide), J. Liu, V. García Sakai, J. K. Maranas and Z. Chowdhuri, Macromolecules, 39, 2866-2874 (2006). Local dynamics of syndiotactic poly(methyl methacrylate) using molecular dynamics simulation, C. Chen, J.K. Maranas, and V. Garcia Sakai, Macromolecules 39, 9630 (2006). Dynamic transition in tRNA is solvent induced, G. Caliskan, R. M. Briber, D. Thirumalai, V. García Sakai, S. A. Woodson, and A. P. Sokolov, Journal of American Chemical Society, 128, 32-33 (2006). Miscible Blend Dynamics and the Length Scale of Local Compositions, V. García Sakai, J. K. Maranas, Z. Chowdhuri, I. Peral, and J. R. D. Copley, J. Polym. Sci. Part B: Polym. Phys., 43, 2914 (2005).

Description of Proposed Research

(Please include scientific context; relevance of proposed experiment; preliminary work performed using neutron scattering and other techniques; details of proposed experimental approach; appropriate references.)

Background: The interactions of sugars with biological molecules have been investigated thoroughly in an effort to understand the preservation and stability of biomolecules. Biological systems such as proteins, vaccines or cells must often be stored for extended periods of time and this is done by lyophilisation in solutions of lyoprotectants, which results in products that are stable under ambient conditions.[1-3] Phospholipids are one of the major structural components of cell membranes and have been studied extensively, primarily as phospholipidic liposomes, which serve as a simple membrane model. The stabilization of these liposomes by lyophilisation has been studied to gain insight into their behaviour at low hydration [2,4-9] It is suggested that the stabilization by sugars is achieved by their ability to prevent the increase in the gel-to-fluid transition temperature Tm, associated with dehydration [5]. Sugars prevent the occurrence of a phase transition during hydration and dehydration [10] which is crucial, since this leads to leakage across the bilayer membrane [11].

Despite the many experimental and numerical studies on sugar bioprotection and stabilisation, the molecular mechanisms remain unclear. There are three proposed mechanisms: (a) formation of a glass that maintains the conformation of the membrane and prevents dehydration-induced stresses and fusion (vitrification) [1, 6-7], (b) preferential exclusion of the sugars cause an increase in the surface tension of water, allowing the free water to hydrate the biomolecule [12] and water replacement hypothesis [13] where the sugars directly hydrogen bond with the polar head groups of the lipids and compensate with the loss of hydrogen bonds upon dehydration.

In the recent years, computational [14-16] and experimental studies [17-19] have provided new insights into lipid-sugar interactions. Simulations suggest that the interactions occur along the surface of the membrane and that the sugar preferentially partitions to the headgroup region, where it increases the density. The area per headgroup is only slightly altered. In contrast, sugars induce significant changes to the dynamics. Lipid mobility is reduced considerably as a result of the sugar molecules binding to the lipids. In particular, rotational and translational modes of the membrane are slowed down which suggests that the sugar inhibits changes to the lateral organisation of the bilayer component. This is vital in preventing leakage. Such studies were performed at low hydration.

Amongst the common sugars, trehalose has superior preservative effects [2] and accumulates to high concentrations in many anhydrobiotic organisms. Other dissacharides, such as sucrose, which is found in high concentrations in plants and maltose, also reduce the Tm but are not as effective as biopreservatives [13,22]. Although the three sugars have the same chemical formula, they have different structures, which could account for their differing preservation effectiveness and could provide insight to lipid-sugar interactions.

We have recently carried out experiments using the neutron spin-echo spectrometer on fully hydrated unilamellar vesicles of 1,2-dipalmitoylphosphatidylcholine (DPPC) in D2O with and without trehalose at temperatures below and above the melting transition (Tm = 42C) of DPPC. The data was analyzed using the Zilman-Granek theory to obtain values of the bending modulus and look for changes in the bending elasticity of the vesicles. The results are shown in figure 1. At all temperatures measured, trehalose stiffens the bilayer suggesting strong interactions between trehalose and the lipid bilayer. Trehalose appears to broaden the melting transition although it does not change the Tm. This agrees with observations using differential scanning calorimetry [18].

Objective:
With the proposed experiment we aim to characterize the changes induced by sucrose and maltose on the bending elasticity of hydrated DPPC vesicles and compare the results with those for trehalose. NSE will give us bending modulus as a function of sugar. We aim to confirm a possible relationship between preservation effectiveness and lipid-sugar interactions in the bilayer. We will conduct measurements at temperatures below and above the Tm of DPPC, so as to characterize the changes in each of the lipid phases. In this experiment we will focus on hydrated bilayers; lower hydrations will be measured at a later stage.

Experimental details:
We plan to use 100nm diameter uninamellar vesicles prepared by the extrusion method which gives a narrow size distribution of vesicles and almost entirely unilamellar vesicles. We will measure DPPC/D2O/sugar solutions of a lipid concentration of 1% by weight, and lipid to sugar molar ratio of 1:5. We plan to measure a total of six temperatures per sample, each temperature

taking approximately 9hrs. Including time to measure the resolution, the solvent and four temperatures for the pure lipid solution, we estimate we will need 7 days of beamtime for the completion of the experiment.

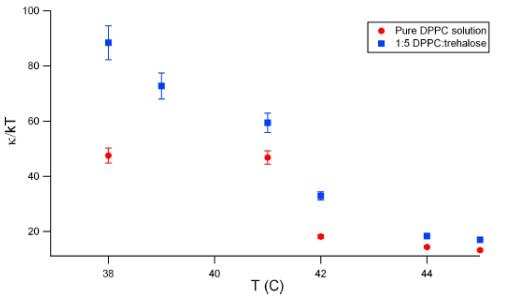


FIGURE 1. The effect of trehalose on the bending elasticity of DPPC unilamellar vesicles. The plot shows the temperature dependence of the bending modulus.

Do's and Don't's'

- ✓ Use all space allocated
- ✓ Add readable figures/graphs
- ✓ Justify need for neutrons
- ✓ Add references
- ✓ Check before submission

- ✗ Use miniture font
- ✗ Include if they do not add to proposal
- ✗ Use generic arguments
- ✗ Expect reviewer to read
- ✗ Make silly mistakes

Proposal Submission

- Online
- Read guidelines for given facility system
- Follow instructions carefully
- Meet the deadline (don’t play tricks!)

INSTITUT MAX VON LAUE - PAUL LANGEVIN (ILL)

Guidelines for the scientific background and detailed description of the proposed experiment

(For electronic proposal submission only)

Please remove this first page before creating your post-script file

The two pages of this form are to be filled in by all users or groups of users who apply for beamtime for experiments at the ILL via the Internet. Please print pages two and three of this document into a postscript file and attach it to your proposal on the **E**lectronic **P**roposal **S**ystem. This two-page description will be reduced by the system to a one-page, A4 format in black & white, and will be attached to your web proposal.

When preparing your description, please follow the instructions below:

- *Give a brief statement of the **background** and the general importance of the research.*
- *Give a clear account of the **aims of the proposed experiment** and a detailed description of the experiment; keep in mind that not all of the subcommittee members are experts in the field.*

Proposal Review Process

- Panel review
  - by technique or by science area
  - at least 2 reviewers per proposal
  - meeting at facility

@ the ILL, France

College 1	Applied materials science, instrumentation and techniques
College 2	Theory
College 3	Nuclear and Particle Physics
College 4	Magnetic excitations
College 5	Crystallography
College 6	Magnetism
College 7	Structure and dynamics of liquids and solids
College 8	Structure and dynamics of biological systems
College 9	Structure and dynamics of soft-condensed matter

@ SNS-HFIR, USA

Subcommittee 1	Engineering and Materials
Subcommittee 2	Imaging
Subcommittee 3	Triple Axis
Subcommittee 4	Time-of-flight
Subcommittee 5	Low Q reflectometry
Subcommittee 6	Low Q SANS
Subcommittee 7	Single crystal diffraction
Subcommittee 8	Powder drffraction
Subcommittee 9	Disordered Materials
Subcommittee 10	Low energy/Chemical spectroscopy

Proposal Review Process

- Proposal given a rating: eg. 1 to 5 (by 0.5), 1 to 10 (1)
- Typical marking definitions (NIST)

5 = E = Excellent proposal. Experiment must be carried out. Highest priority for beam time.

4 = VG = Very good proposal. Experiment is highly deserving of beam time. No reason to deny beam time except under conditions of unusually high demand.

3 = G = Good experiment. May receive beam time under normal circumstances, but may not, depending on demand

2 = F = Fair proposal. While scientific merit does not appear to be exceptionally high, the experiment may receive beam time if it is available, but will probably not receive time.

1 = P = Poor proposal. Scientific merit not convincingly documented. Beam time should not be allocated to the proposal.

Examples of Reviewer's Comments

ID# 6412 PI: Jones

The proposed measurements of moisture absorption in polymer thin films are **interesting** and of commercial interest. What is **unclear** from the proposal is **whether neutron reflectometry (NR) is sufficiently sensitive t**o the levels of absorption anticipated, since **no estimated values are given**. The investigators **should use complementary methods** (e.g., sensitive weighing of samples) to help eliminate ambiguities that undoubtedly arise in fitting data of this type.

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ID# 6420 PI: Striver

This proposal was **rather confusing** as to its **purpose and feasibility**. The first paragraph suggests an investigation of metal/polymer adhesion, but metals are not used in this study (?). From the proposal description, it seems instead that a silicon wafer coated with a polymer layer will serve as a reasonable model system, but **it's not clear what the study is attempting to determine**. **I could be misunderstanding** the experiment, but the proposal doesn't spell out the **objectives or methods** very clearly, unfortunately.

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ID# 6601 PI: Einstein

An **ingenious** set of experiments is proposed which could give very **nice results**, if contrast is sufficient and if the reaction front can be expected to remain roughly constant over the course of a measurement. The surface swelling of the film will be then be measured in deuterated solution and compared with the dry state. **If the experiment is successful, the results could lead to a major advance in the field.**

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ID# 6440 PI: Joker

The proposers **fail to delineate a specific set of measurements**. The scientific **objectives are equally unclear**. **No samples are on hand**.

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ID# 6440 PI: Joker

The proposers **fail to delineate a specific set of measurements**. The scientific **objectives are equally unclear**. **No samples are on hand**. Rating: P

Success …

… depends on many factors:

- Quality of proposal
- Days available
- Oversubscription
- Committee's feeling about high risk-high reward proposal versus unexciting but definite publication
- Mood, tiredness…
- Country balances
- …

Neutron Proposal Exercise

- In pairs/trios
- Use proposal template in your packs
- No printers
- One experiment
- Deadline is 5pm Tuesday 15th

- Panel meetings afternoon Wednesday 16th