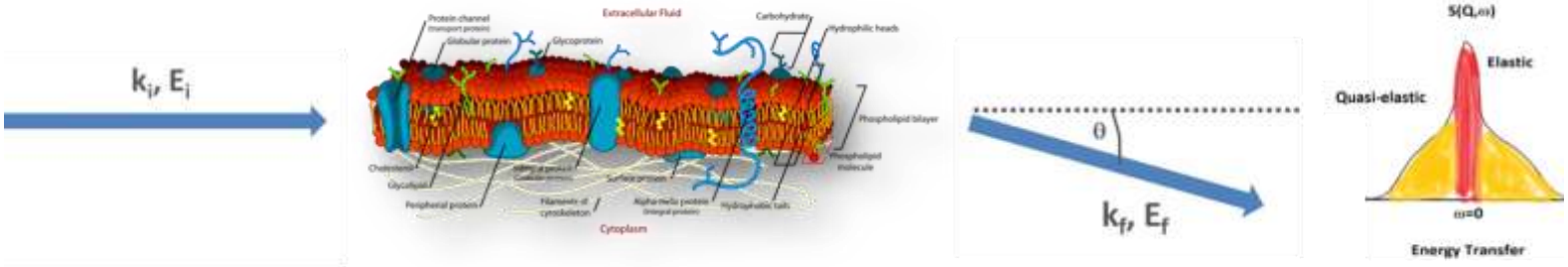
Dynamics of biomolecules from lipids to proteins



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Outline

Why do we need to study nanoscale motions in biomolecules
What is **quasi-elastic neutron scattering**
What information do **neutrons** give us
What **instruments** are available
Examples

Take home messages

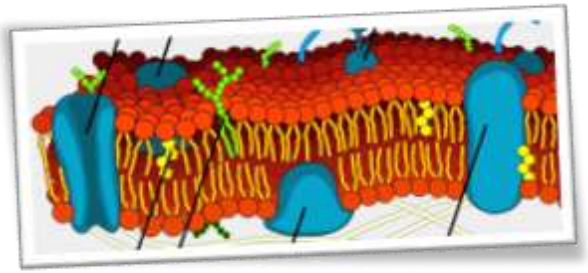
1. **Dynamics** provide insights into relevant biomolecules
2. **Instruments** available to probe different motions
3. **Complementary** to structural characterisation
4. Neutrons provide **unique** information

Importance of Dynamics for Biomolecules

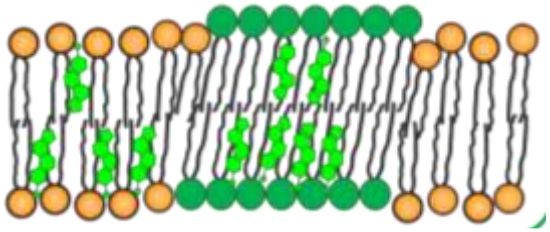
Function and Transport

- Enzymatic activity (internal motions, solvent dynamics)
- Ligand-binding and recognition (protein flexibility)
- Transport and permeability of lipids (dynamics of lipids and drugs)
- Lipid-protein, protein-protein interactions (membrane fluidity)
- Evolutionary understanding (protein folding and unfolding)
- Characteristics of extremophiles (protein flexibility, concentration dependence, and P and T dependence)
- Stability and endurance (rigidity)
- Drug delivery vectors (lipid dynamics)
- Diseases - cancer, Alzheimer's (lipid, protein and solvent dynamics)
- Cryopreservation (protein and solvent dynamics)
- …

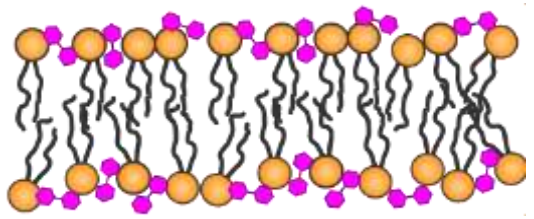
Protein-Protein and Protein-Membrane Interactions



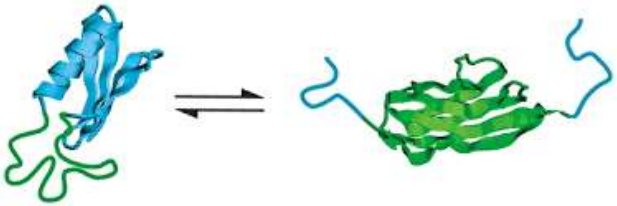
Lipids as model membranes



Effect of small molecules (drugs, carbohydrates ...)

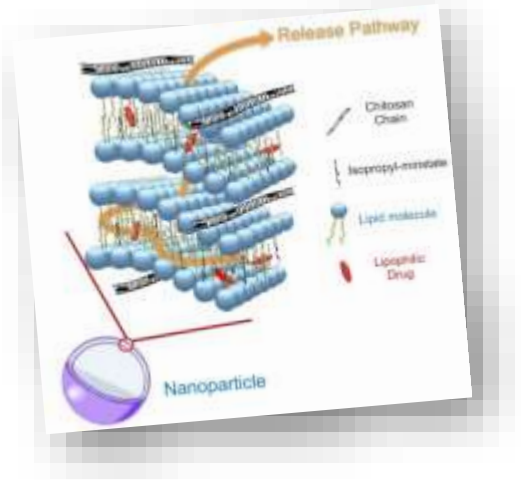


Protein folding/unfolding



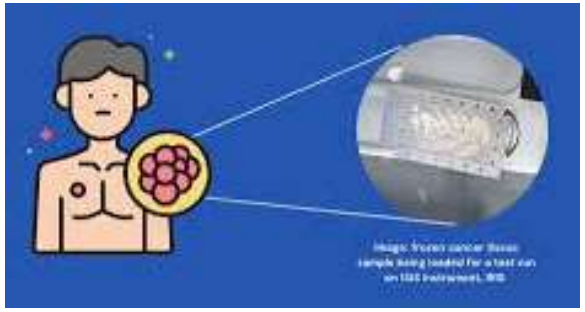
Fluidity
Permeability
Flexibility

Design of drug delivery vectors

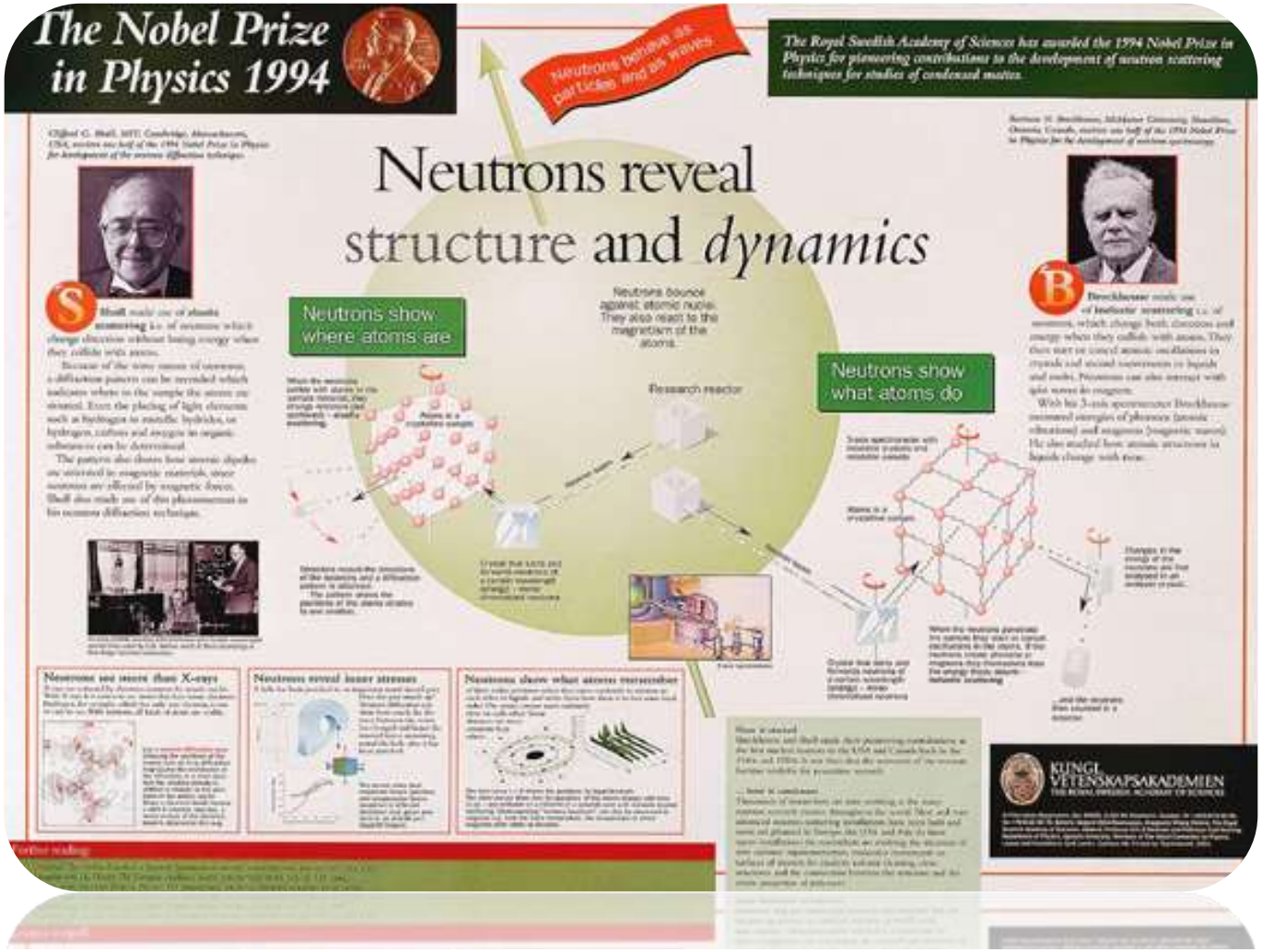


Understanding extremophiles

Cancer drug design



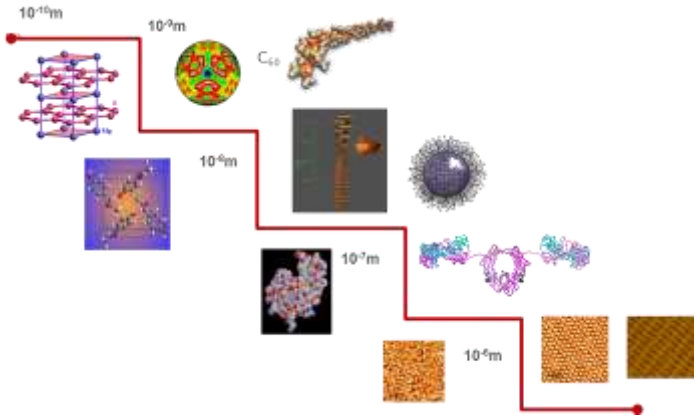
Neutrons for Studying Motions

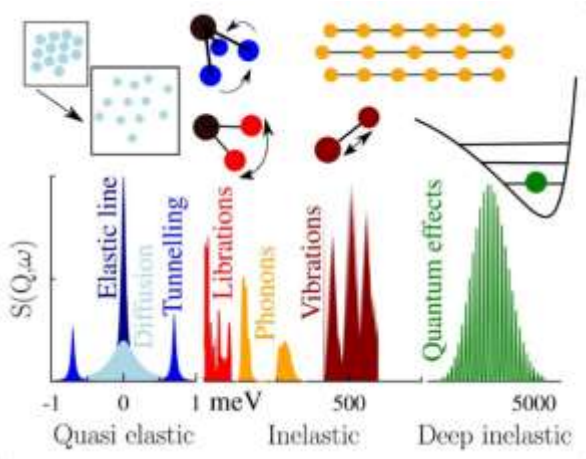


Neutrons tell us where atoms are and what atoms do

Neutron Properties

1. Neutron wavelengths are of the same order as atomic spacings - **structural information** from Å to mm with structural precision to 10^{-15}m.





2. Neutron energies are of the same order as molecular modes – **dynamical information** from fs to ms and with spatial info (vibrations, diffusive motions).

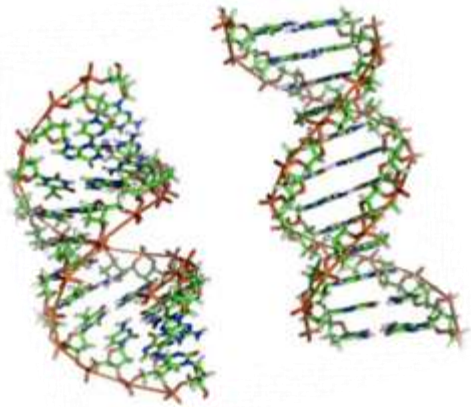
Complementary to many other techniques:

- X-rays
- Raman, IR
- Dynamic Light Scattering
- Photon Correlation Spectroscopy
- NMR
- MD simulations

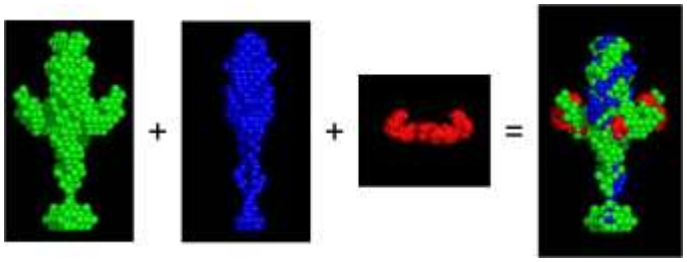
Neutron Properties

3. Neutrons are **neutral** – highly penetrating, non-destructive.

4. Neutrons interact with nuclei – **sensitive** to light atoms, particularly ^{1}**H**, allows exploitation of isotopic variation (**H/D**).



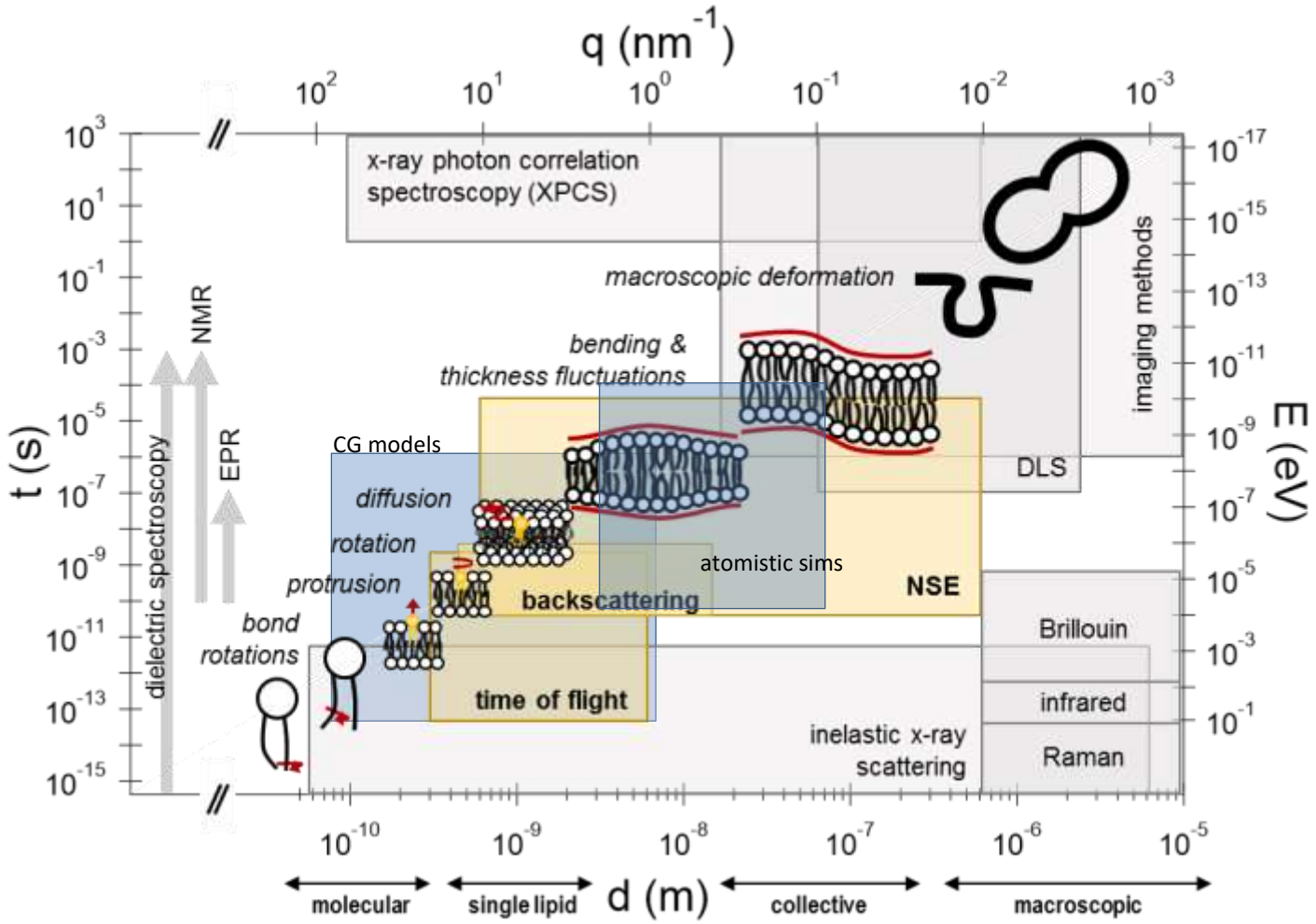
5. Neutrons have a **magnetic** moment– provides extra contrast and signal separation techniques.



Unfortunately there are some **impracticalities**:

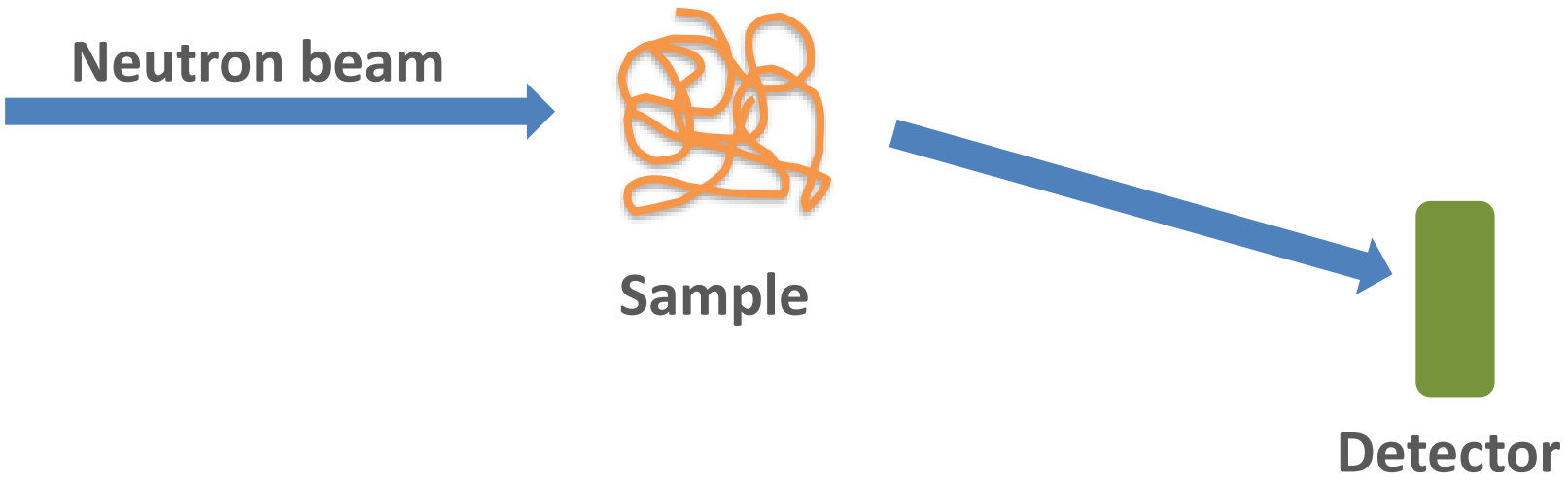
- neutrons are scarce and not available in your lab
- sample mass in some cases is large
- deuteration (isotopic substitution) is not always straight forward

Dynamical Modes for Lipid Membranes



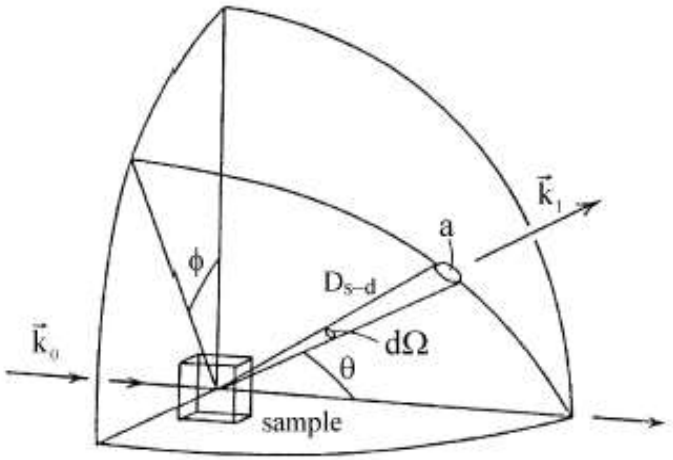
Thanks to L. Kelly & M.Nagao (NCNR)

Neutron Scattering



- Source of neutron **radiation** on a sample
- An interesting sample
- Particles are scattered by the sample – this depends on the **interaction potential** between the two
- A neutron detector measures the **distribution** of radiation scattered
- A description of the measured signal in terms of the physics in the sample

The Scattering Function, $S(Q,\omega)$



$$\frac{d^2\sigma}{d\Omega d\omega} \propto \frac{k_f}{k_i}\frac{\sigma}{4\pi}S(\boldsymbol{Q},\omega)$$

The **scattering function, $S(\boldsymbol{Q},\omega)$** contains all the physics of the system (in space and time) and depends only on the system.

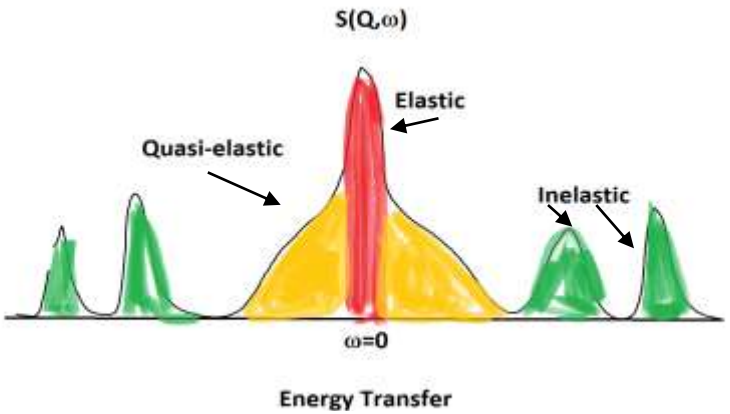
If your detector can analyse the energy of the neutrons, then the **double differential cross-section** can be defined as

$$\frac{d^2\sigma}{d\Omega dE} = \frac{number\ of\ particles\ scattered\ per\ s\ into\ a\ solid\ angle\ d\Omega\ with\ final\ energies\ between\ E_f\ and (E_f + dE_f)}{I_0 d\Omega dE_f}$$

The Scattering Function, $S(Q,\omega)$

Information on dynamics

$$S(\boldsymbol{Q},\omega) = S(\boldsymbol{Q},\omega)_{\text{elastic}} + \boxed{S(\boldsymbol{Q},\omega)_{\text{inelastic}} + S(\boldsymbol{Q},\omega)_{\text{quasi-elastic}}}$$



Elastic scattering – no energy exchange $\hbar\omega=0$. Ideally it is a δ function, in reality it is the resolution.

Quasi-elastic scattering (QENS)– a **small** energy exchange $\hbar\omega\neq0\approx$neV or few meV . Processes with a distribution of energies.

Inelastic scattering (INS) – energy exchange $\hbar\omega\neq0$. Processes of discrete energy steps, quantised (vibrations or excitations).

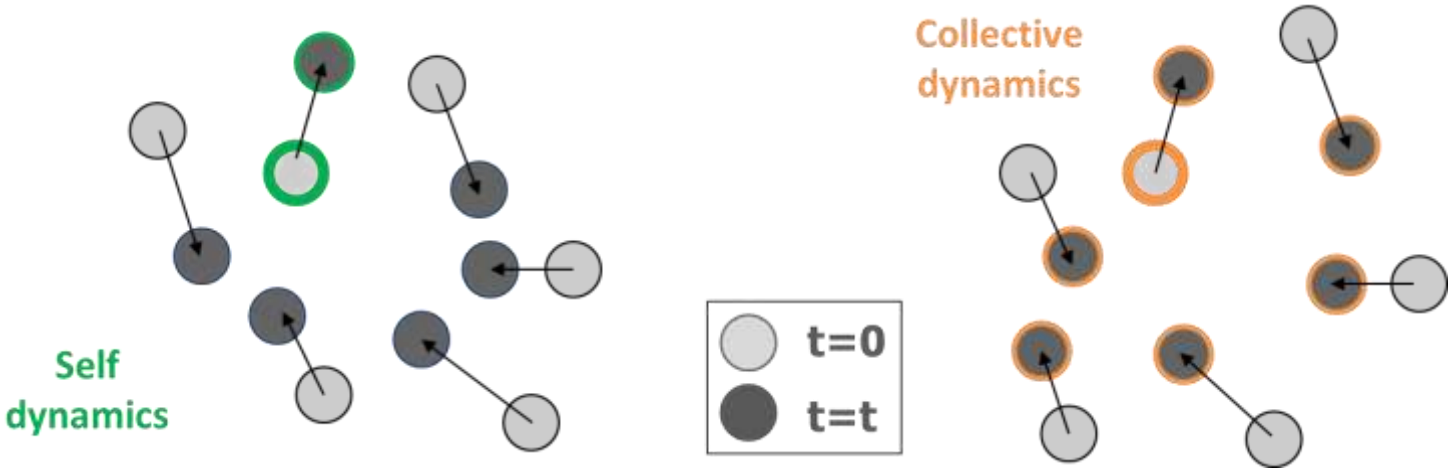
Scattering Function- Correlations

In the experiment we measure the total $S(\boldsymbol{Q},\omega)$ and that each term, coherent and incoherent is weighted by its respective cross-section σ

$$S(\boldsymbol{Q},\omega) = S_{\mathrm{inc}}(\boldsymbol{Q},\omega) + S_{\mathrm{coh}}(\boldsymbol{Q},\omega)$$

$$S_{\mathrm{inc}}(\boldsymbol{Q},\omega) = \frac{1}{2\pi}\int_{-\infty}^{+\infty}\sum_{i}\langle \exp(-i\boldsymbol{Q}\cdot\boldsymbol{R}_i(0))\exp(-i\boldsymbol{Q}\cdot\boldsymbol{R}_i(t))\rangle \exp(-iwt)\,dt$$

$$S_{\mathrm{coh}}(\boldsymbol{Q},\omega) = \frac{1}{2\pi}\int_{-\infty}^{+\infty}\sum_{i,j}\langle \exp(-i\boldsymbol{Q}\cdot\boldsymbol{R}_i(0))\exp(-i\boldsymbol{Q}\cdot\boldsymbol{R}_j(t))\rangle \exp(-iwt)\,dt$$



Dynamic Structure Factor, $S(Q,\omega)$

Incoherent scattering …

… describes dynamics of **individual** particles

… molecular and single amphiphilic molecule

… rotations, *trans-gauche* conformational transitions, diffusion

… main association of QENS technique (ps, ns)

… relies on large incoh x-section of H*

Coherent scattering…

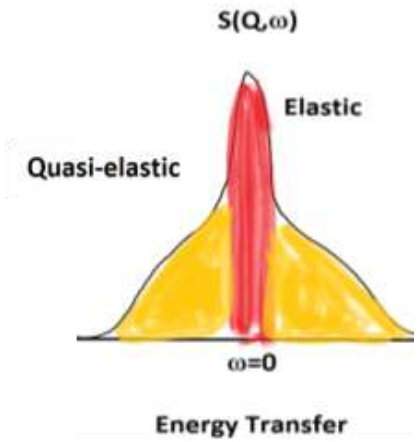
… describes **collective** dynamics of nuclei

… describes correlations between nuclei

… bending and thickness fluctuations

… strongly related to structure*

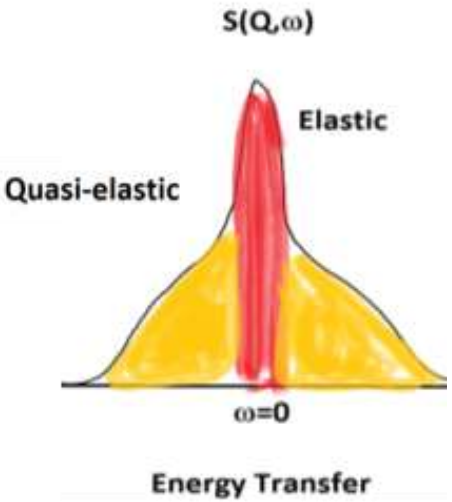
… main association with NSE technique (ns)



* Measurable is a function of **Q** and if coherent is considerable % of total signal need to pay attention to elastic structure factor S(**Q**)

Self-dynamics - Incoherent

Self-dynamics Incoherent QENS



We measure **the self correlation function**, ie. how particles move as a function of time. This corresponds to the incoherent signal which we can write as:

$$S_{\text{inc}}(\boldsymbol{Q},\omega) = S_{\text{vib}}(\boldsymbol{Q},\omega) \otimes S_{\text{rot}}(\boldsymbol{Q},\omega) \otimes S_{\text{trans}}(\boldsymbol{Q},\omega)$$

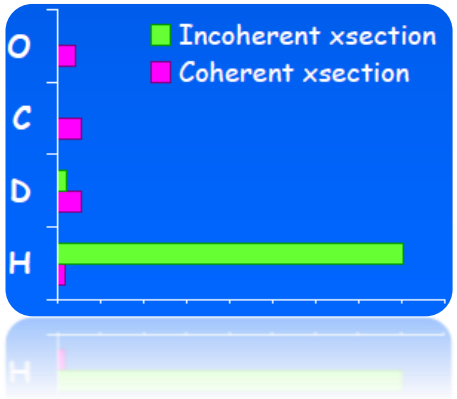
$$I_{\text{self}}(\boldsymbol{Q},t) = I_{\text{vib}}(\boldsymbol{Q},t) \times I_{\text{rot}}(\boldsymbol{Q},t) \times I_{\text{trans}}(\boldsymbol{Q},t)$$

It is a **convolution of components** which for simplicity are assumed **independent** motions. Note that in the time domain we multiply the terms (easier!)

Can't forget the instrumental resolution:

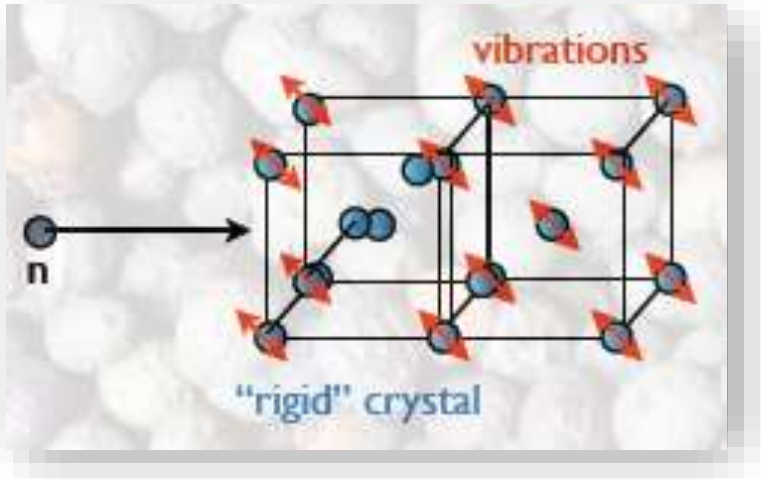
$$S'(Q,\omega) = S(Q,\omega) \otimes R(Q,\omega)$$

QENS relies on the large incoherent xsection of hydrogen.



Vibrations: Debye-Waller factor

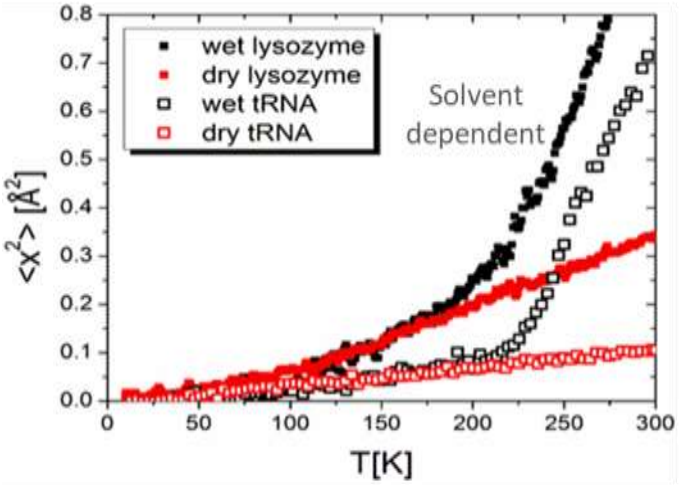
Nuclei (even in a rigid crystal) are **not stationary**, causing a decrease in the intensity of a diffracted beam (remember Bragg's law) because waves are not so well in phase. In addition, this smearing is a function of temperature. Assuming that **vibrations** are **harmonic** and **isotropic.**



$$DWF = \langle \exp(i\boldsymbol{Q}\cdot\boldsymbol{u})\rangle = \exp(-\langle(\boldsymbol{Q}\cdot\boldsymbol{u})^2\rangle) = \frac{1}{3}\exp\left(Q^2\langle u^2(T)\rangle\right)$$

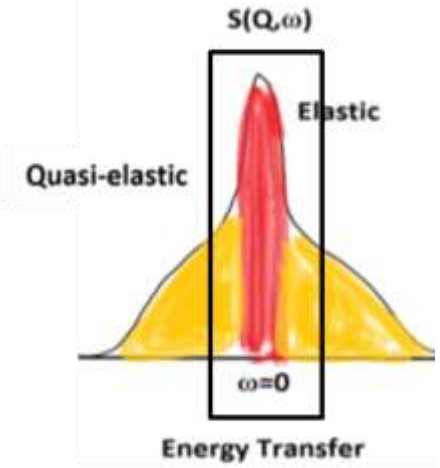
Mean-square displacement of atoms, $\langle u^2 \rangle$, is measured as a function of temperature.

We can obtain an **effective force constant** –measure of **flexibility**



Roh et al, *Phys Rev Letters* (2005)

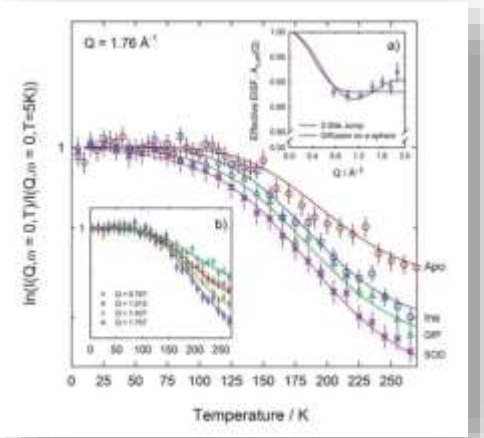
Fixed Energy Window Scans



Case of ***S(Q, ω ≈ 0):*** Elastic Fixed Window Scans

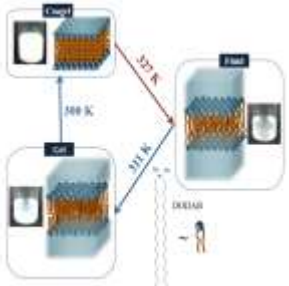
Measure the elastic intensity as a function of temperature (resembles a DSC scan).

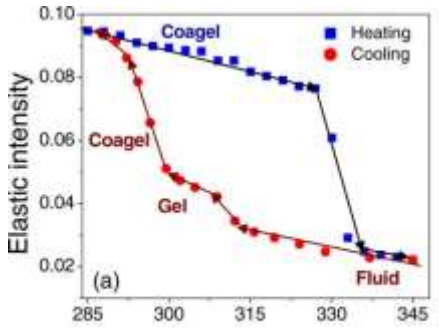
Used to calculate **<u^2>** using Gaussian approximation.



$$\frac{S^{inc}(Q,\omega=0,T)}{S^{inc}(Q,\omega=0,T\approx 0)} \propto \exp\left(-\frac{1}{3}Q^2\langle r^2\rangle\right) \quad \text{for} \quad Q^2\langle r^2\rangle \leq 1$$

However, also good for locating **transitions**, at what temperatures do the **dynamics enter the time window,** and comparative studies (parametric).



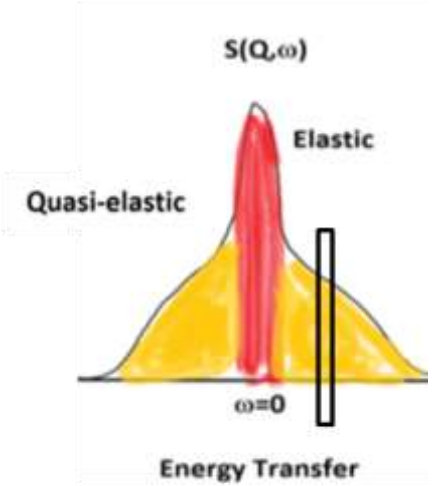


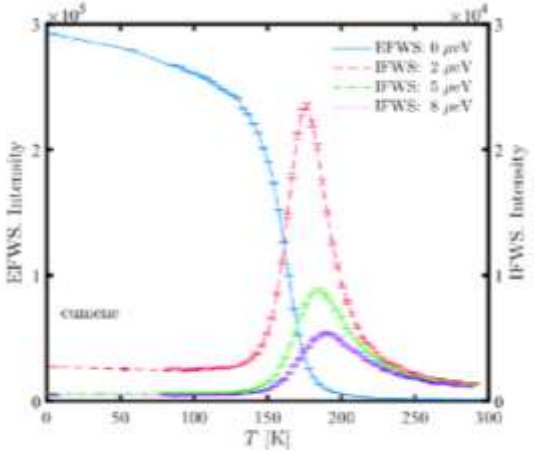
Dubey, VGS et al, Scientific Reports (2018)

Fixed Energy Window Scans

Case of ***S(Q, $\omega \approx$ offset):*** Inelastic Fixed Window Scans

If transitions are not so clear or **if difficult to gauge timescale,** measure 'inelastic' intensity as a function of temperature. Slightly different measurement in reactor and spallation instruments.

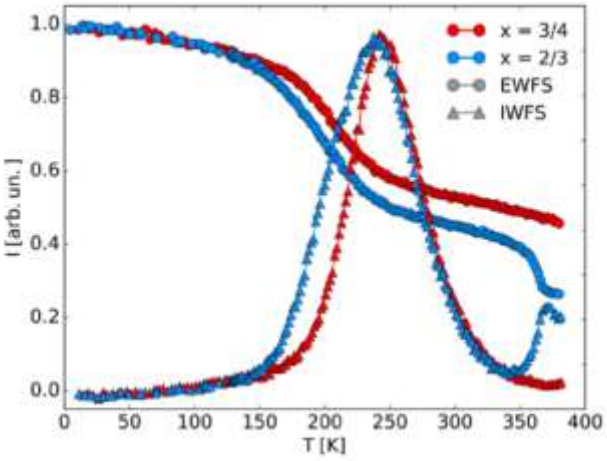




Hansen et al, PRB, 2017

Different offsets correspond to different timescales

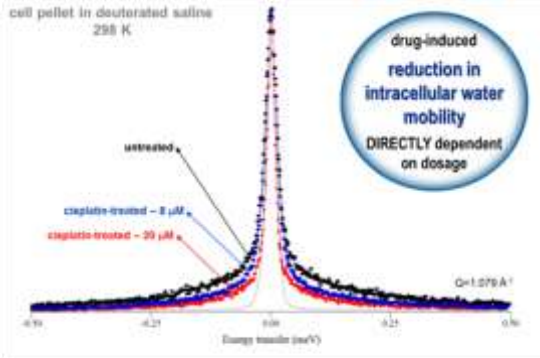
Peak shape and changes with Q provide additional information



Burankova et al, JPhysChemC, 2017

Diffusion

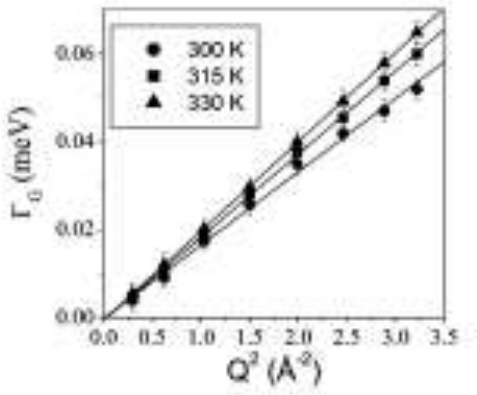
$$S_{\mathrm{inc}}(\boldsymbol{Q},\omega) = S_{\mathrm{vib}}(\boldsymbol{Q},\omega) \otimes S_{\mathrm{rot}}(\boldsymbol{Q},\omega) \otimes S_{\mathrm{trans}}(\boldsymbol{Q},\omega)$$



Batista de Carvalho et al, *Phys Chem Chem Phys* 19, 2017

QENS spectra describe by Lorentzians assigned to given diffusion model.

E.g. Fick's Law with Γ, the **half width at half maximum** is = DQ^2. Diffusion coefficient follows Arrhenius Law: $D \approx \exp(-Ea/kT)$.



- Diffusion coefficients of different motions
- Activation energies
- Lengths: confinement/jump
- Residence times (jumps)
- Geometry EISF …

More models including rotations

$$S_{\mathrm{inc}}(\boldsymbol{Q},\omega) = S_{\mathrm{vib}}(\boldsymbol{Q},\omega) \otimes S_{\mathrm{rot}}(\boldsymbol{Q},\omega) \otimes S_{\mathrm{trans}}(\boldsymbol{Q},\omega)$$

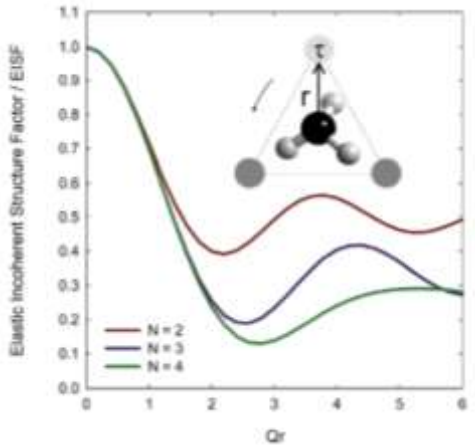
Elastic stationary part, EISF — **Quasi-elastic decaying part**

$$S_{\mathrm{inc}}(\boldsymbol{Q},\omega) = \exp(-Q^2\langle u^2\rangle)[A_0(\boldsymbol{Q})\delta(\omega) + \left(1 - A_0(\boldsymbol{Q})\right) L(\boldsymbol{Q},\omega)]$$

Localised motions including rotations give to a Q-independent line-width and a stationary part called the **Elastic Incoherent Structure Factor (EISF) -**fraction of elastic contribution. Gives information on the **geometry** of the motion/rotation.

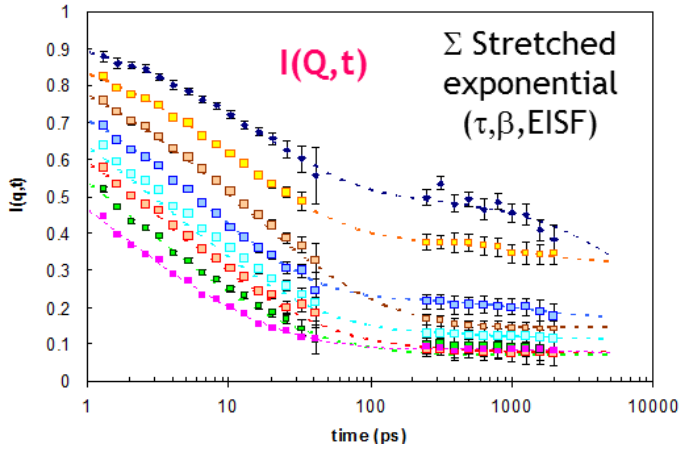
$$EISF = \frac{S_{inc}^{el}(\boldsymbol{Q})}{S_{inc}^{el}(\boldsymbol{Q}) + S_{inc}^{qel}(\boldsymbol{Q})}$$

- Jumps between 2, 3, … *n* sites
- Rotational diffusion on a circle
- Diffusion on a sphere
- Diffusion inside a sphere, cylinder…



or characteristic relaxation

$I_{self}(\boldsymbol{Q},t)$ = stretched exponential



Data is Fourier Transformed if necessary

Fit with one or more exponentials (typically stretched)

Each one assigned to a specific dynamical mode

$$\frac{I(\boldsymbol{Q},t)}{I(\boldsymbol{Q},0)} = Aexp\left[-\left(\frac{t}{\tau_{KWW}}\right)^{\beta}\right] = \int_{-\infty}^{+\infty} f(\ln\tau)\exp\left(-\frac{t}{\tau}\right)d(\ln\tau)$$

or related to dynamical variables

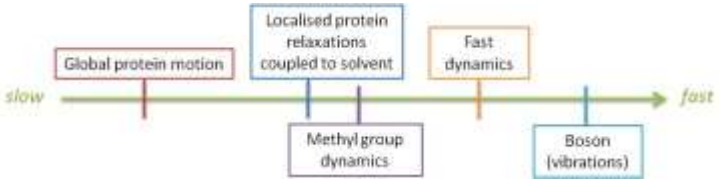
$$\frac{I(\boldsymbol{Q},t)}{I(\boldsymbol{Q},0)} = exp\left[-(\Gamma t)^{2/3}\right]$$

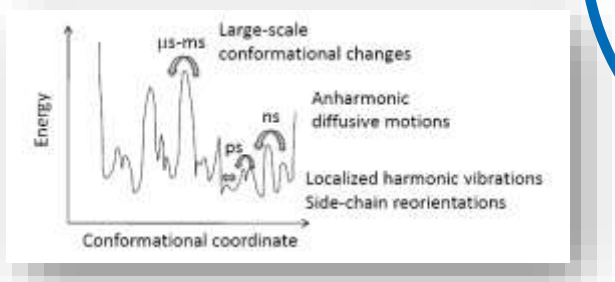
- Relaxation times
- Measure of heterogeneity
- Fraction moving
- Geometry
- Span of motion

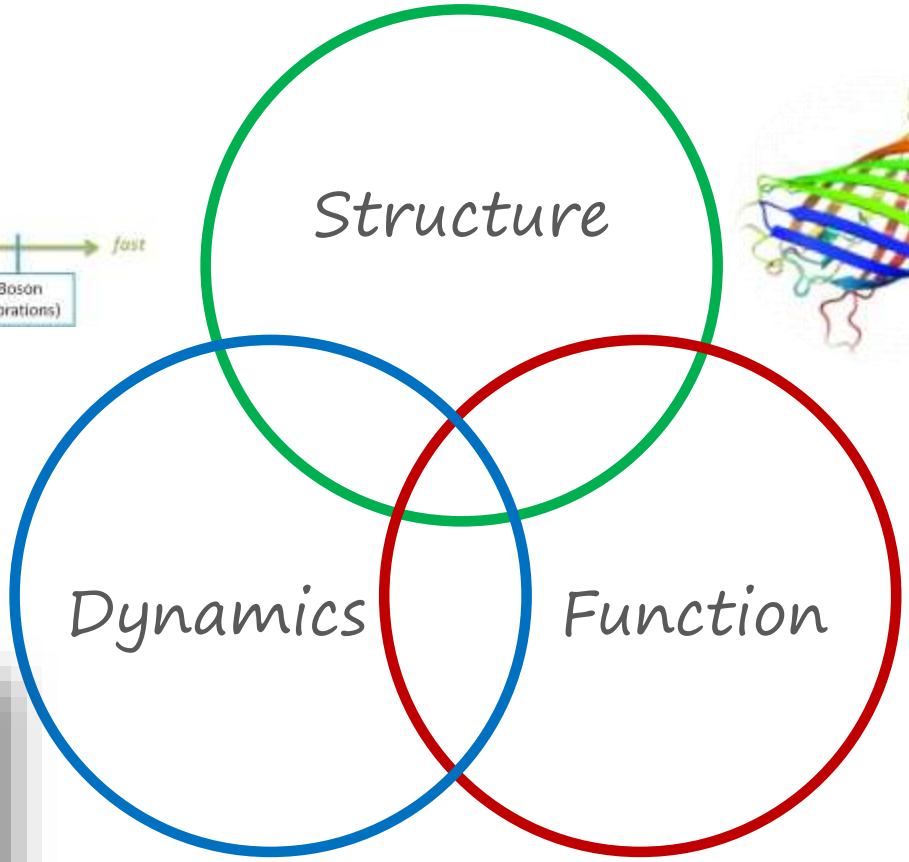
1. Protein Dynamics

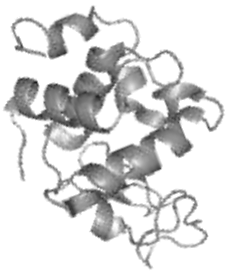
"The protein molecule model resulting from the X-ray crystallographic observations is a platonic protein, well removed in its perfection from the kicking and screaming stochastic molecule that we infer must exist in solution."

Gregorio Weber
(1916-1997)

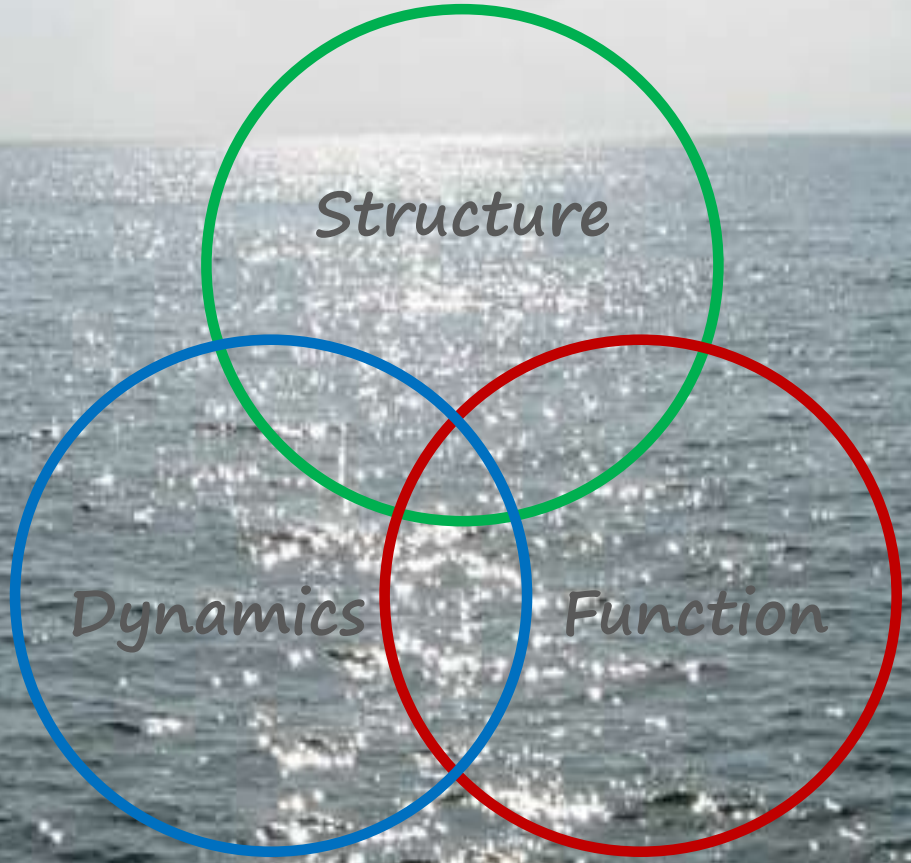




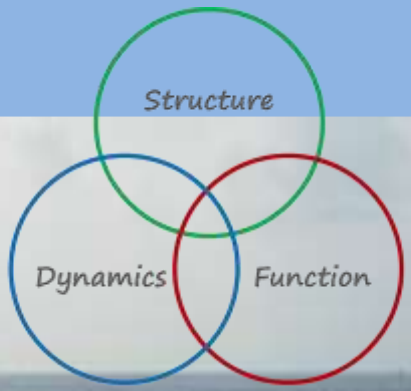




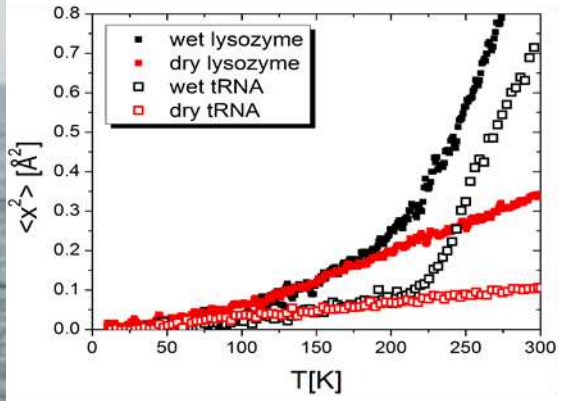
plus the Role of the Solvent



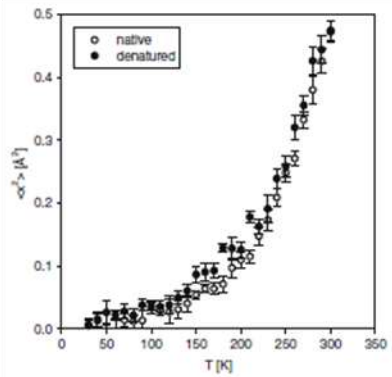
plus the Role of the Solvent



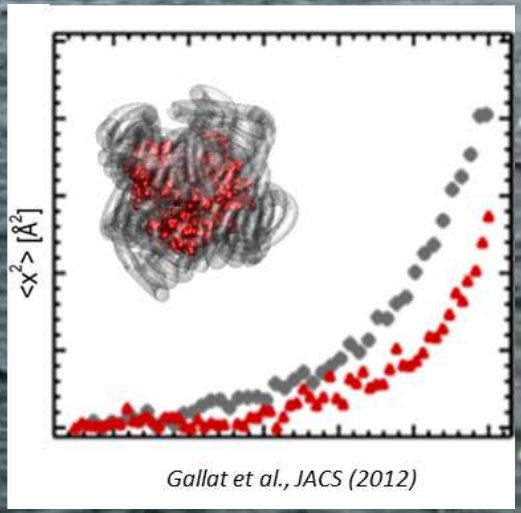
The dynamical transition



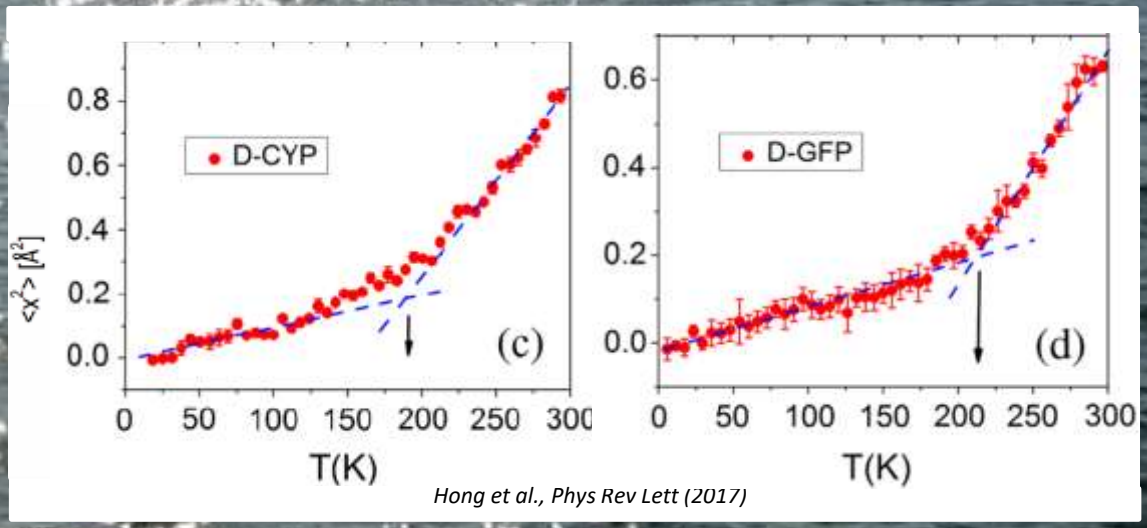
Caliskan et al, JACS (2006)



Mamontov et al, JBioPhys (2010)



Gallat et al., JACS (2012)



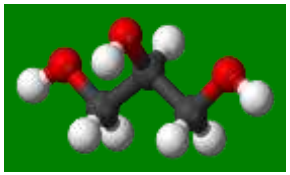
Hong et al., Phys Rev Lett (2017)

Solvent and Bio/Cryopreservation

Trehalose

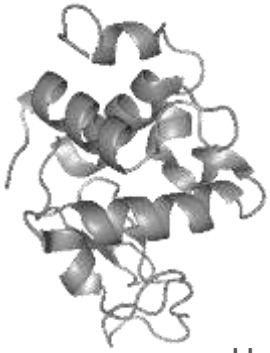
Tg ≈ 390K
10^{15} mPa.s
Fragile

Glycerol

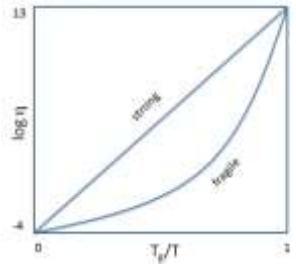


Tg ≈ 190K
1200 mPa.s
Strong

- What is the best solvent?
- Understanding stabilization mechanism
- Roles of viscosity, packing and fragility



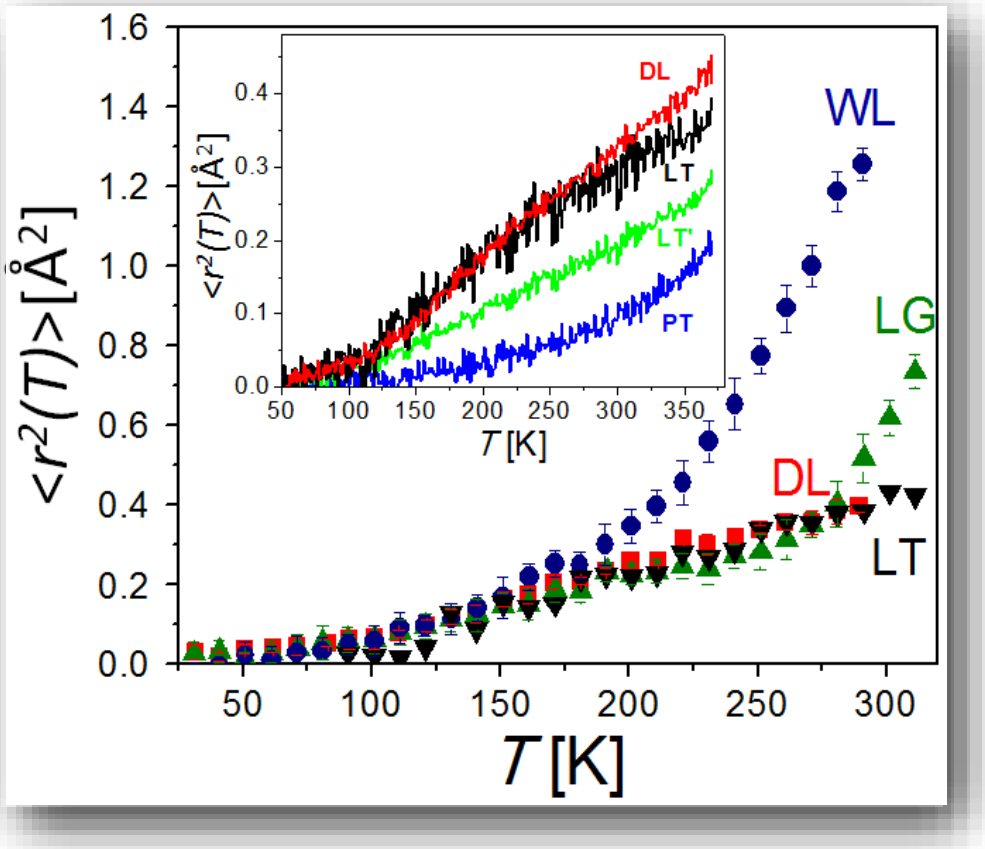
Lysozyme



Water
1 mPa.s

- Hydrated powders 1:1
- d-solvents
- HFBS backscattering (0.1-4ns) @ NIST
- Disk Chopper Spectrometer (0.01-50ps)

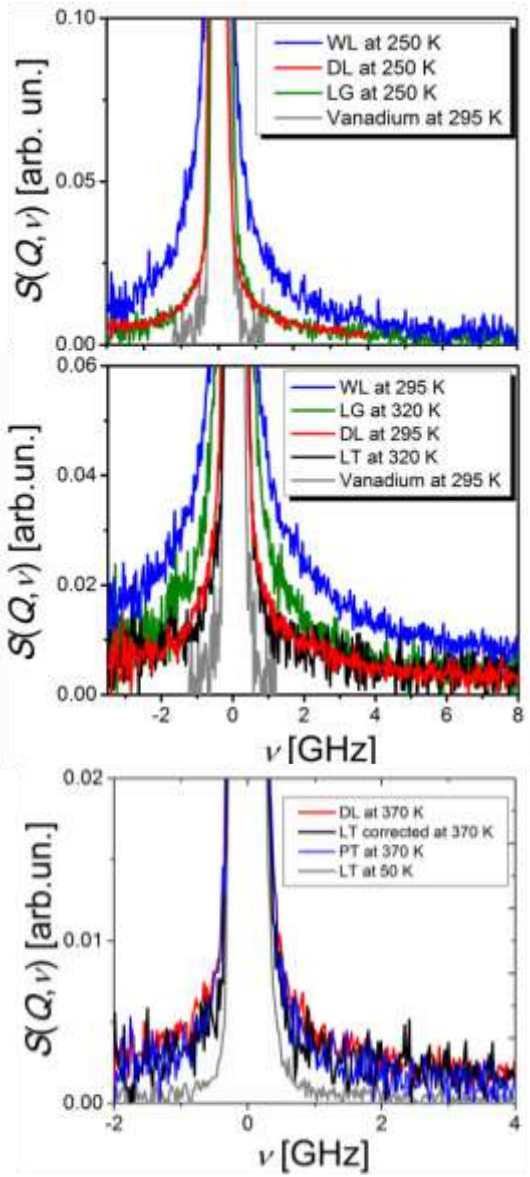
Mean-squared displacements



- CH_3 transition at 100K
- dynamical transition at ~200K for hydrated Lyz (WL)
- dynamical transition at ~270K for Lyz in glycerol (LG)
- no transition for Lyz in trehalose (LT)
- lower mobility in LT vs. dry Lyz (DL)

$$\langle r^2(T)\rangle = -3Q^{-2} \ln[I_{el}(Q,T)/I_{el}(Q,10K)]$$

Nanosecond dynamics



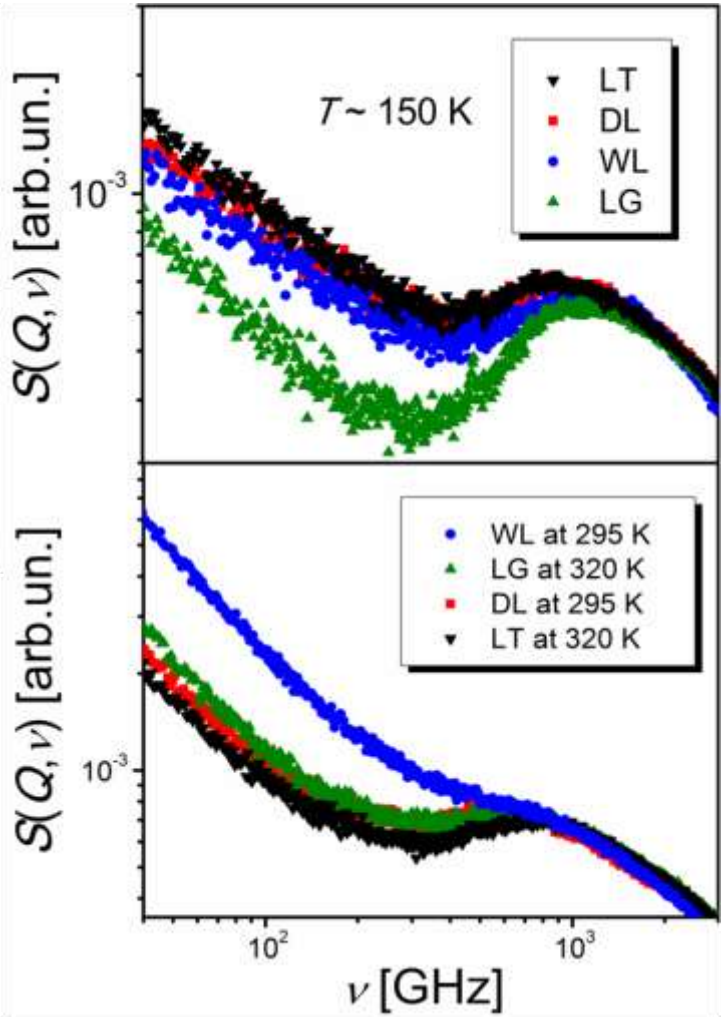
- Localised motions in DL and LG, unaffected by solvent
- water allows further flexibility

- at RT increased mobility in DL, LT
- LG increased flexibility, 50K above Td
- water strongest, 100K above Td

- Localised motions in DL out of energy window
- QENS broadening in LT < in DL

Picosecond dynamics

Increasing T



- Fast conformational transitions and Boson peak at 1THz
- DL and LT have highest mobility
- LG has strongly suppressed dynamics

- WL shows strongest dynamics
- LG slightly enhanced than LT
- LT weaker than DL even at lower T

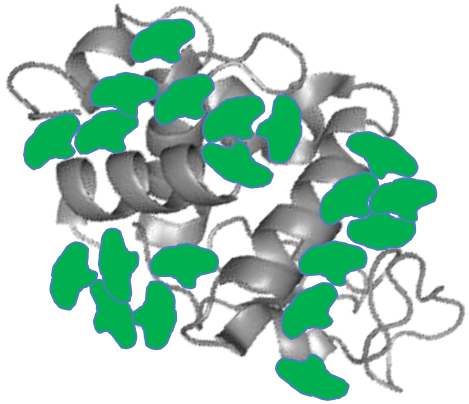
Emerging picture for low temperatures

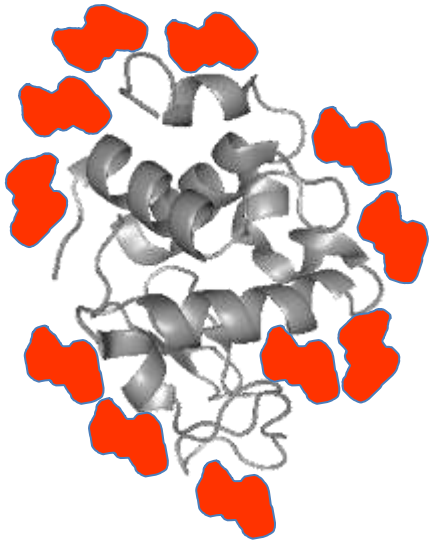
• Small glycerol molecules form rigid-well packed structures with weak fluctuations; can interact very efficiently with protein surface

• Reduced cage sizes – also for water

• Strong glass

• Higher viscosity compared to water



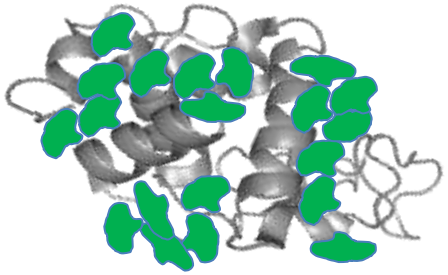


• Larger cages and less efficiently packed; poor interaction with protein

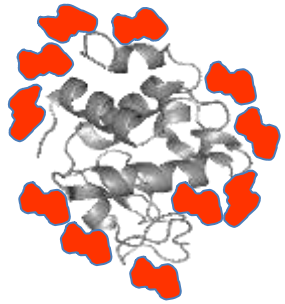
• Trehalose fast conformational fluctutations

• Trehalose softens dynamics

Emerging picture for high temperatures

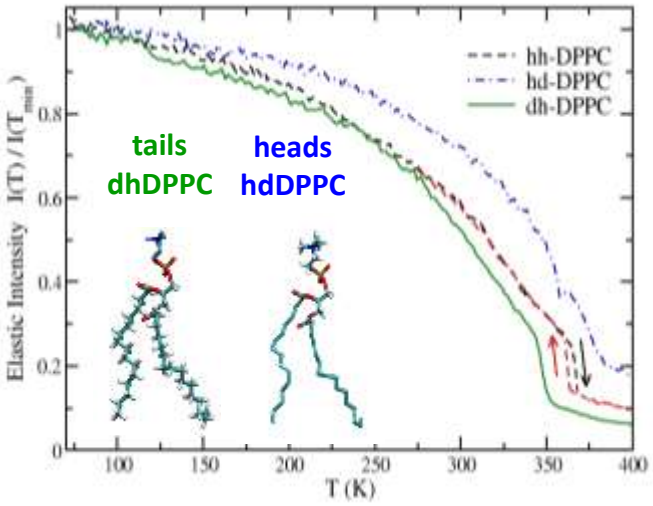


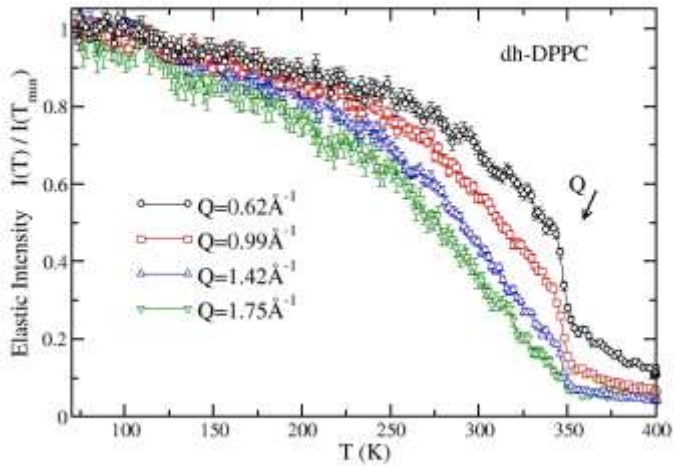
- Viscosity and high Tg of trehalose controls dynamics
- Water and glycerol are above Tg thus promote dynamics
- Above RT, trehalose suppresses onset of denaturation and unfolding, due to its high Tg
- Suggests that trehalose forms of a glassy ‘crust’ surrounding protein
- Similar observation as for lipids vesicles

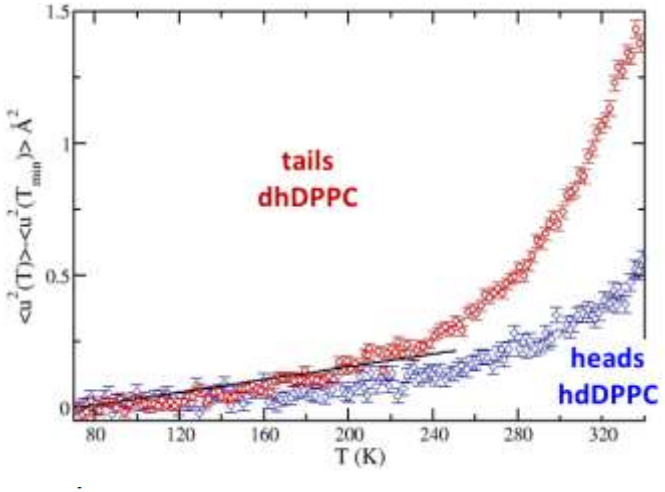


- For low temperatures, ie. for cryopreservation, glycerol is the best choice
- At RT and above, for biopreservation and stability, trehalose is the best choice
- Complex interplay between packing and fragility

2. Molecular View of Lipid Melting



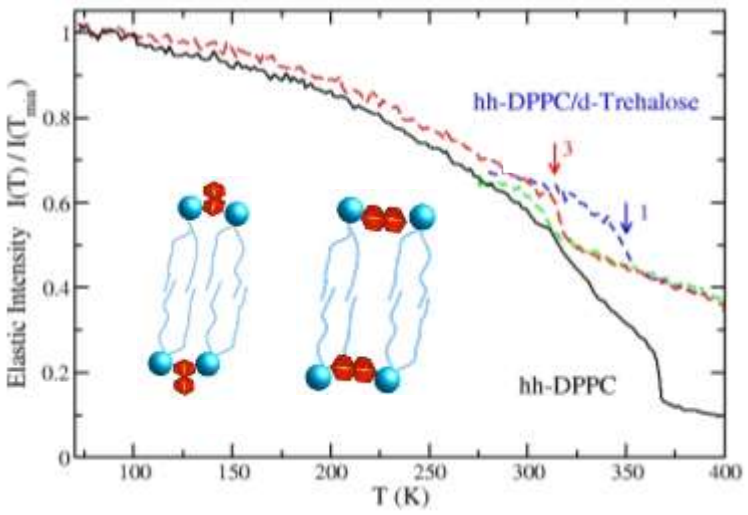


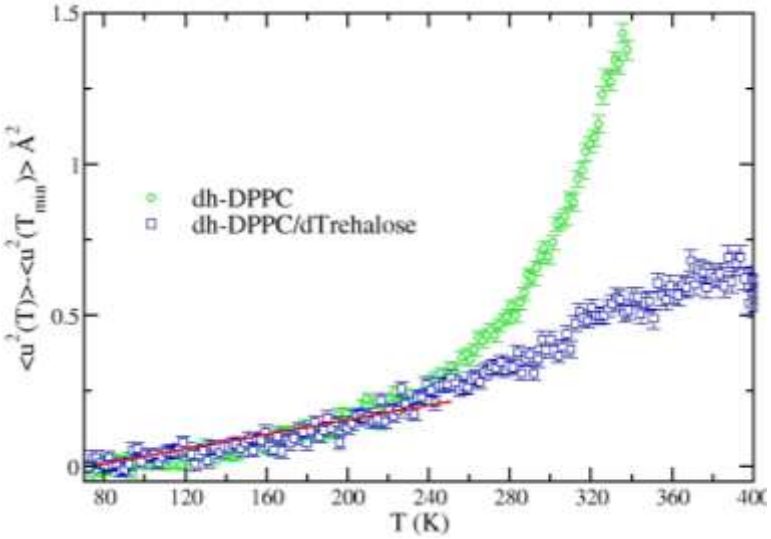


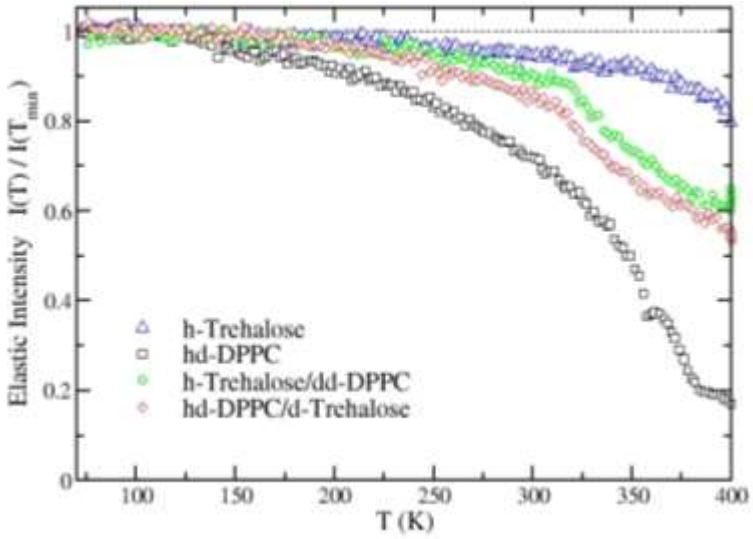
Sample	DSC	QENS
Protonated lipid (hh-DPPC)	378 K	363–367 K
Heads deuterated lipid (dh-DPPC)	366 K	—
Tails deuterated lipid (hd-DPPC)	367 K	348 K

- Tails responsible for T_m
- Heads less mobile than tails
- Spatial dependence of tail melting

Incorporation of trehalose







- Trehalose decreases T_m
- Partial incorporation, then full
- Strong association to heads
- Significant decrease in mobility

Quantifying Mobility

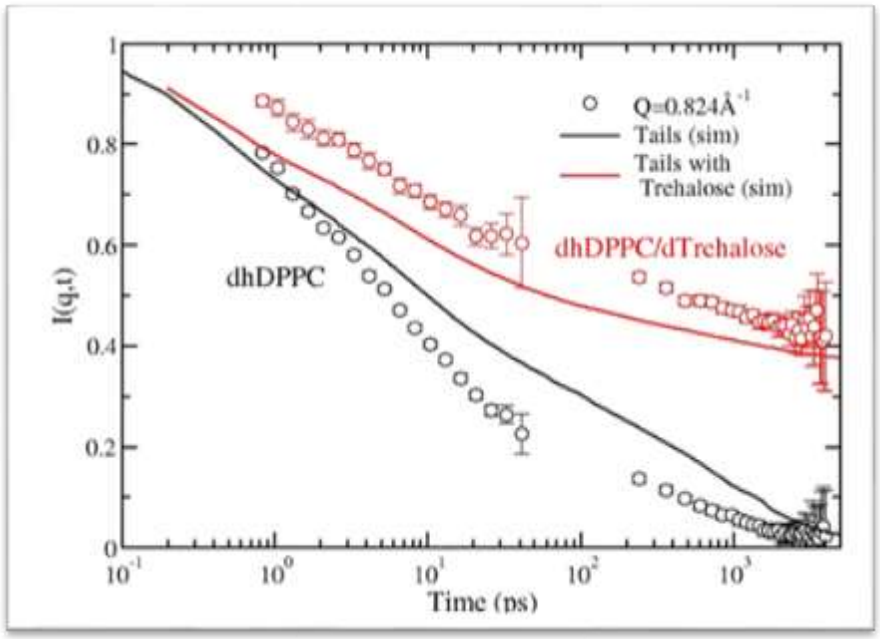


TABLE 3 Parameters of best fit for the model of diffusion inside a sphere using a sum of spheres distributed linearly along the lipidic tails (n = 2, 3, . . ., 16)

	Temperature (K)	R_{min} (Å)	R_{max} (Å)
Experiments	310	0.14 ± 0.05	3.20 ± 0.09
	330	0.47 ± 0.12	5.59 ± 0.24
	350	0.79 ± 0.03	5.85 ± 0.16
	370	0.86 ± 0.08	6.19 ± 0.45
	395	1.15 ± 0.07	6.44 ± 0.37
	308*	0.18 ± 0.08	2.75 ± 0.10
	333*	0.72 ± 0.09	4.44 ± 0.20
	370†	1.3	4.2
	390†	1.6	4.7
Simulations	310	0.45 ± 0.02	3.79 ± 0.07
	330	0.54 ± 0.06	3.91 ± 0.17
	350	0.71 ± 0.05	3.83 ± 0.08
	370	0.66 ± 0.07	4.56 ± 0.23
	395	0.77 ± 0.11	4.86 ± 0.23

Results from literature QENS studies probing alkyl tail mobility are also shown.
*Oriented multilayers of fully protonated DPPC with 12 wt % water. Data from König et al. (10).
†Dicopper alkanoate complexes with deuterated terminal methyl groups (R_{max} corresponds to n = 15). Data from Carpentier et al. (43).

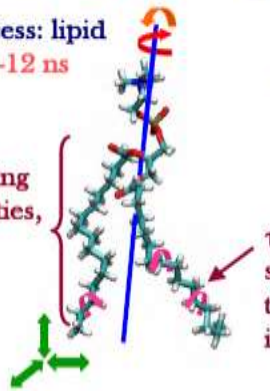
Fast process: trans/gauche isomerization 7-45 ps

Slow process: lipid rotation 2-12 ns

$$I(q,t) = A\,KWW_1\,KWW_2$$

$$KWW_i = E_i + (1-E_i)\exp\left[\left(-t/\tau_i\right)^{\beta_i}\right]$$

- τ: characteristic time
- β: distribution of times
- E: motion in restricted geometry



If varying mobilities, β < 1

τ: typical time scale for trans/gauche isomerization

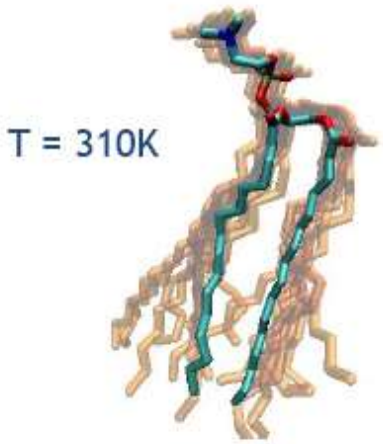
Molecular simulations are in good agreement over all lengths and times

Diffusion in a sphere where r varies linearly with tail position

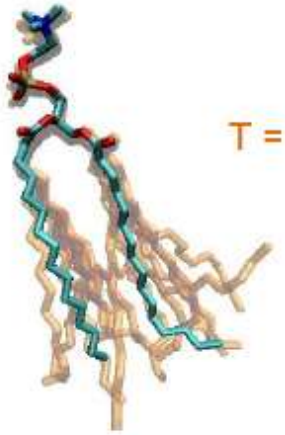
$$A(Q) = \frac{1}{N}\sum_{n=2}^{N}\left[\frac{3j_1(QR_n)}{QR_n}\right]^2$$

$$R_n = \frac{n-2}{N-2}\left[R_S - R_2\right] + R_2$$

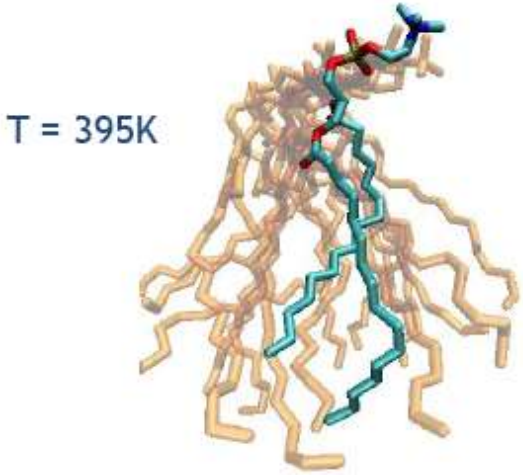
Picture of Interaction with Trehalose

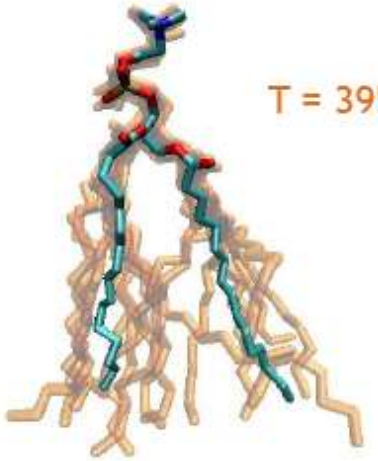


Pure DPPC



DPPC/Trehalose





- Trehalose decelerates fast conformational transitions along all tail bonds
- Rotations or any slower motions are significantly suppressed
- Spatial extent is significantly decreased

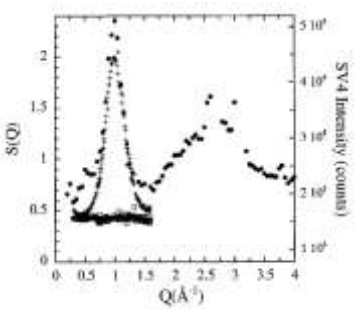
Collective dynamics - coherent

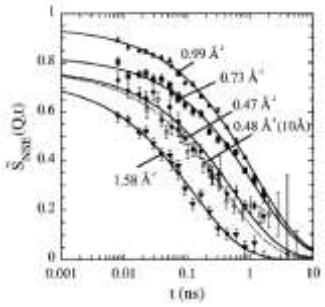
Collective Dynamics – Coherent QENS

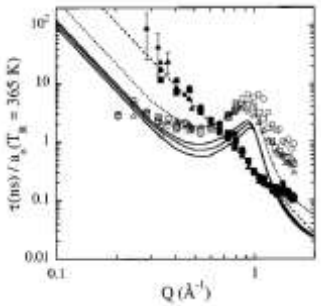
Let's consider the **coherent part of the correlation function**. Interpretation is trickier and you need to take into account the **structure factor**, ***S*(*Q*)**, ie. how atoms are distributed in space. Typically longer times and measurements in real time (not energy).

$$I_{\text{coll}}(Q,t) \approx I_{\text{self}}(Q,t)\left(\frac{Q}{\sqrt{S(Q)}},t\right)$$

$$\tau_{\text{coll}}(Q,T) \approx a(T)\tau_{\text{self}}(Q,T)S(Q)^{1/\beta}$$





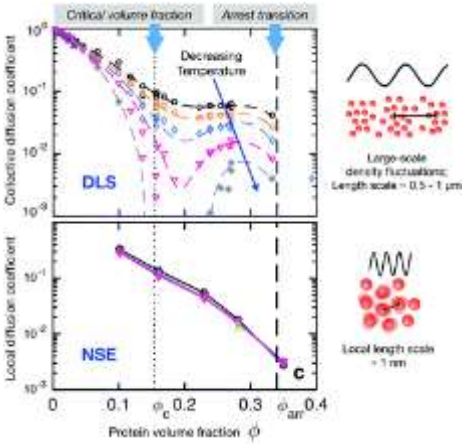


Farago et al, PRE, (2002)

Assignment of normal modes of proteins in solution

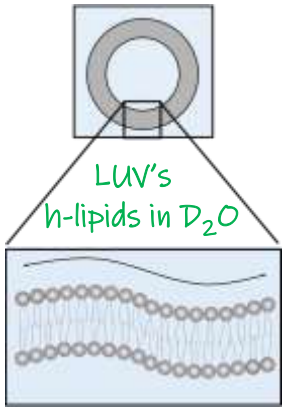
Bu et al, PNAS (2005)

Collective diffusion of proteins in solution



Stradner and Schurtenberger, Soft Matter (2019)

3. Bending Elasticity in Model Membranes



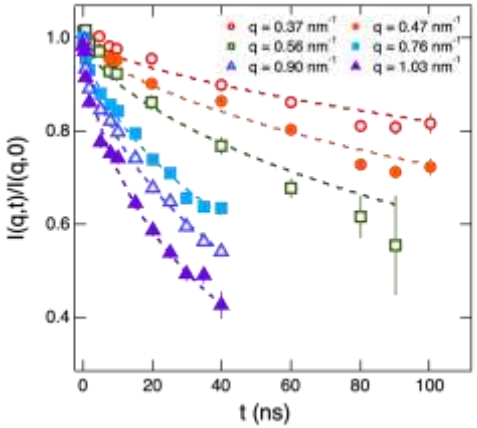
Zilman-Granek theory (*PRL* 77, 4788, 1996)

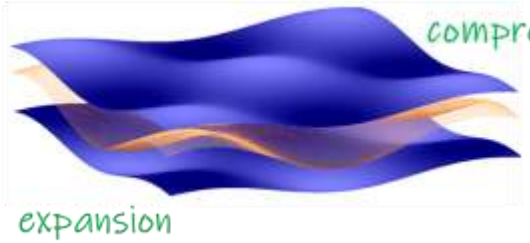
$$\frac{I(q,t)}{I(q,0)} = \exp\left[-(\Gamma t)^{2/3}\right]$$ ... measured by NSE

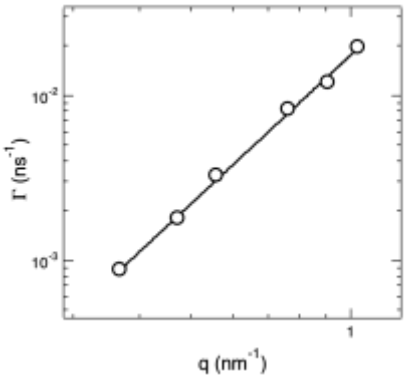
$$\Gamma_{bend} = 0.025\sqrt{\frac{k_BT}{\kappa}\frac{k_BT}{\eta}}q^3$$ Bending modulus, Solvent viscosity

$\tilde{\kappa} = \kappa + d^2 k_A$ Effective bending modulus, Compressibility modulus

Watson and Brown, *Biophys. J.*, 98 (2010).







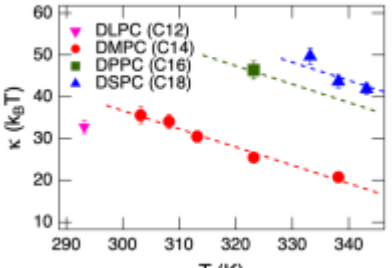
Zilman-Granek theory is for a homogeneous thin sheet

In fact, dissipation of stored energy through solvent and membrane

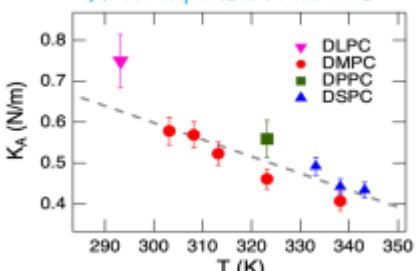
Additional motion controlled by K_A and both solvent and membrane viscosities

$$K_A = \frac{\beta\kappa}{h_C^2}$$ Monolayer constant

ß = 12 fully couple (like a slab)
ß = 48 fully uncoupled (each leaflet can slide past each other)
ß = 24 polymer brush model for lipids

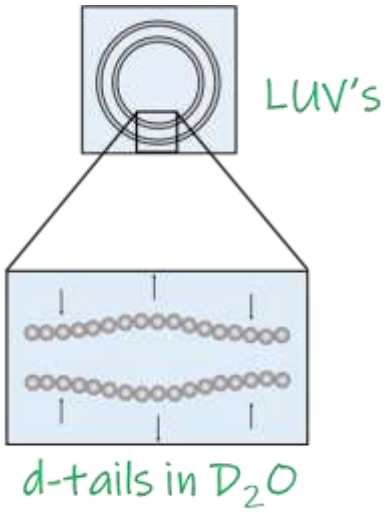


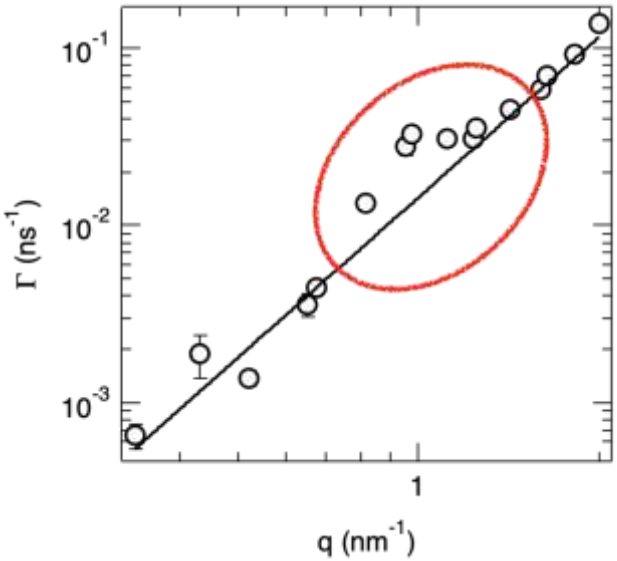
Area expansion modulus

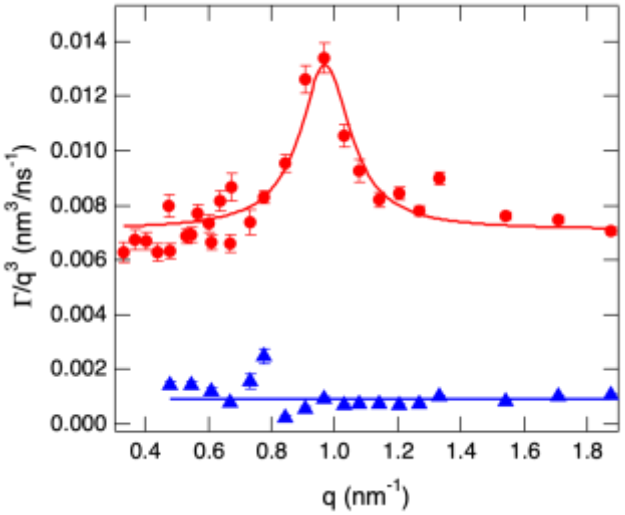


Courtesy of M. Nagao

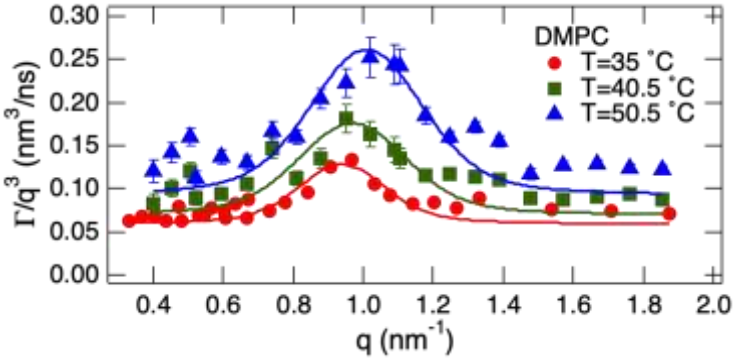
Bilayer thickness fluctuations

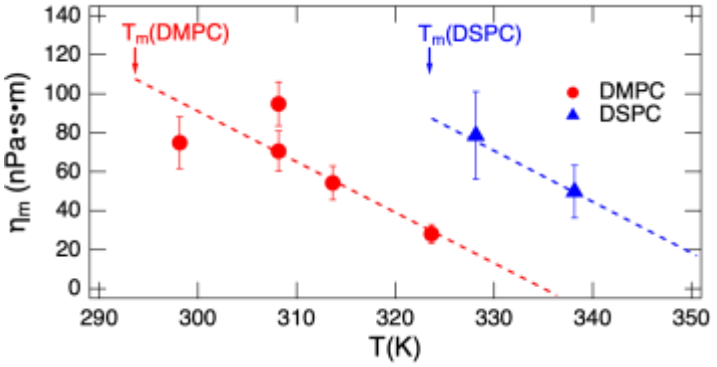






Excess dynamics observed at bilayer thickness only visible in fluid phase + estimation of the membrane viscosity





Nagao, *Phys. Rev. E* **80**, 031606 (2009).; Nagao *et al.*, *Soft Matter* **7**, 6598 (2011); Woodka *et al.*, *Phys. Rev. Lett*. **109**, 058102 (2012); Nagao *et al.*, *J Phys Chem Lett* **8**, 4679 (2017).

$$\frac{\Gamma}{q^3} = 0.0069\sqrt{\frac{k_BT}{\kappa}}\frac{k_BT}{\eta} + \frac{K_A k_B T}{\eta_m q_0^3 k_B T + 4\eta_m q_0 K_A A_L (q-q_0)^2}$$

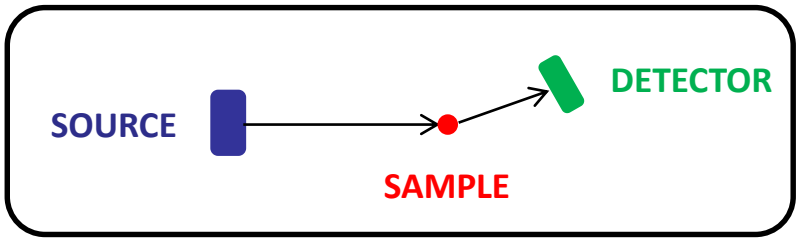
Courtesy of M. Nagao

Instruments

Neutron Spectrometers

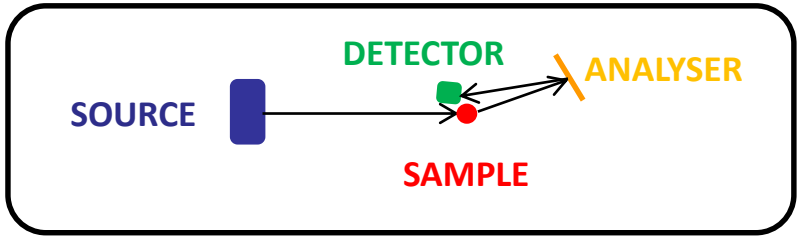
Frequency domain S(Q,ω)

Direct geometry



- Lower energy resolution
- Larger ΔE and Q range
- Flexible in choosing Q-E space
- Repetition Rate Multiplication
- picosecond motions (diffusion, rotations, trans-gauche conformations)
- Self-correlation function (H)
- IN5, LET, CNCS …

Indirect geometry or Backscattering

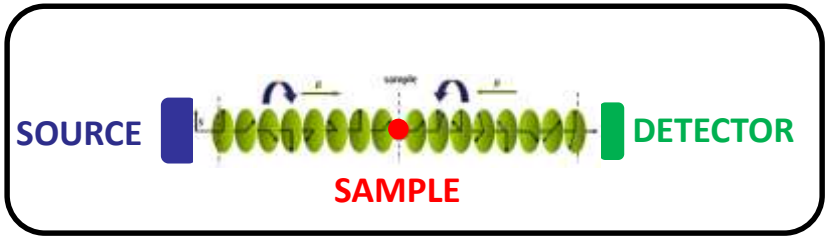


- Higher energy resolution
- Smaller DE and Q range
- Fixed Q-E space
- Picosecond-nanosecond (diffusion, rotations, trans-gauche conformations)
- Self-correlation function (H)
- DNA, IRIS, IN16B, HFBS

Neutron Spectrometers

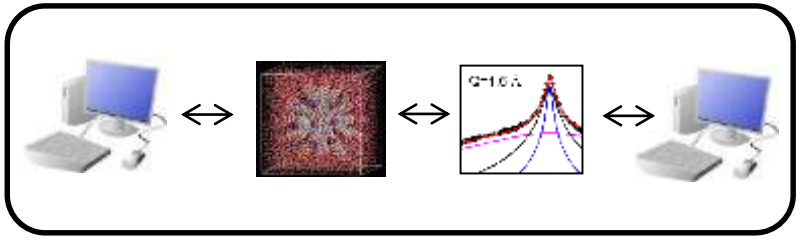
Time domain I(Q,t)

Neutron Spin Echo



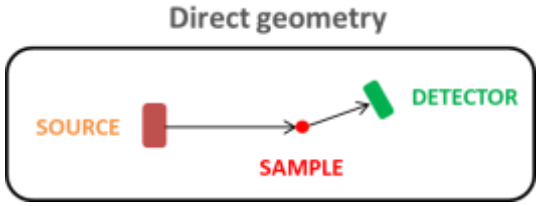
- Highest energy resolution
- Typically lower Q range
- Nanosecond (normal modes, bending elasticity, fluctuations)
- Collective dynamics (H/D)
- IN15, NIST-NSE

Molecular Dynamics Simulations



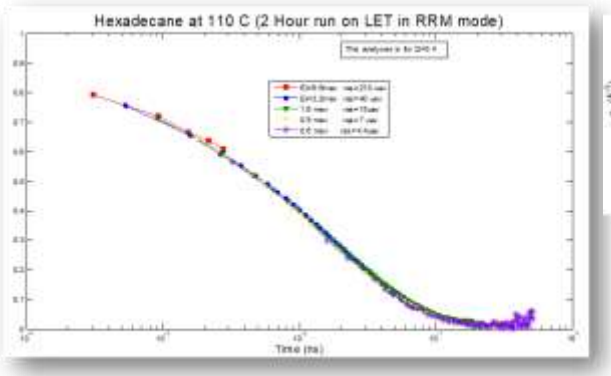
- Flexible parameter space
- Large parameter space
- Need to optimize and choose FF
- Directly comparable with neutron data

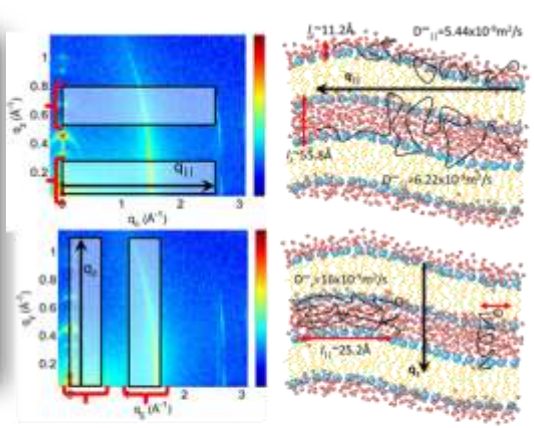
Time-of-flight Spectrometers



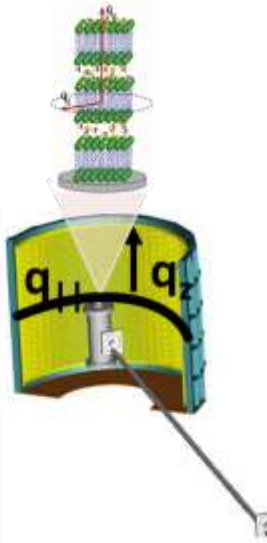
LET on ISIS

- Resolution 10-100ueV, but flexible Q and E range.
- Measure picosecond motions and fast collective modes
- Good choice for QENS over a broad range, especially making use of rep-rate multiplication
- Position sensitive detectors enable 2D studies
- Recently advances with polarisation analysis enables separation of coherent/incoherent scattering



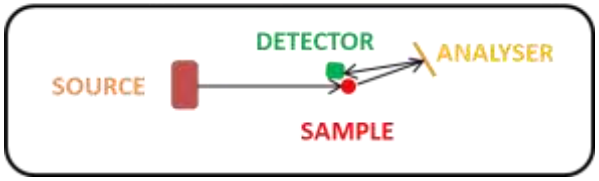


Toppozini, VGS et al, Soft Matter (2015)



Backscattering Spectrometers

Indirect geometry or Backscattering

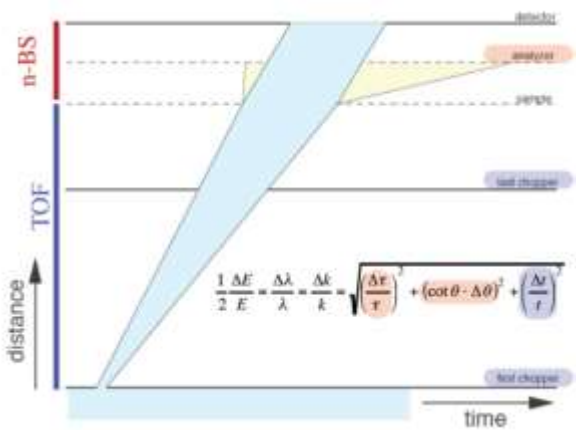


$$n\lambda = 2d\sin\theta$$

$$\frac{1}{2}\frac{\Delta E}{E} = \frac{\Delta\lambda}{\lambda} \sim \frac{\delta d}{d} + \cot(\theta)\delta\theta$$

- Energy resolution (ueV) selected by analyser crystals. Changing crystal changes δE, ΔE and ΔQ.
- Measure pico-nanosecond motions.
- Reactor ~ 0.9u eV, limited energy range, fixed Q-range.
- Spallation ~3-20ueV, broader/flexible ΔE but similar Q range
- Good choice for elastic fixed window scans and QENS

HFBS @ NIST

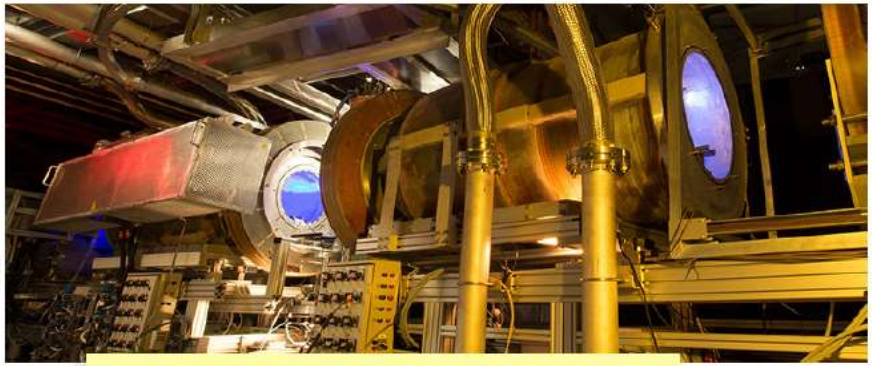


BASIS @ SNS

Neutron Spin-Echo

- NSE uses the neutron's **spin polarisation** to encode the difference in energies between incident and scattered beams. Very high energy resolution.
- Neutron perform **Larmor precessions** in two antiparallel magnetic fields, before and after the sample, resulting in polarization of the neutrons.
- Precession angles are equal and opposite and the difference is analysed at the detector. Small energy transfers lead to a change in the precession angle and thus a decrease in measured polarization.

$$I_{\mathrm{NSE}}(Q,t) = \frac{I_{\mathrm{coh}}(Q,t) - \frac{1}{3}I_{\mathrm{inc}}(Q,t)}{I_{\mathrm{coh}}(Q,0) - \frac{1}{3}I_{\mathrm{inc}}(Q,0)}$$



Today's IN15: measures up to 1 µs

- NSE is the neutron spectroscopy with highest energy resolution
- Time covered is 1ps < t < 1us (equivalent to neV resolution)
- Momentum transfer range is 0.002 < Q < 4Ang^{-1}
- Best signal is at the structural peaks and is very complementary to e.g. SANS

Outline

Why do we need to study nanoscale motions in biomolecules
What is **quasi-elastic neutron scattering**
What information do **neutrons** give us
What **instruments** are available
Examples throughout

Take home messages

1. **Dynamics** provide insights into relevant biomolecules
2. **Instruments** available to probe different motions
3. **Complementary** to structural characterisation
4. Neutrons provide **unique** information