

# Presentation

## Investigation of the Protein Dynamics near Cell Death

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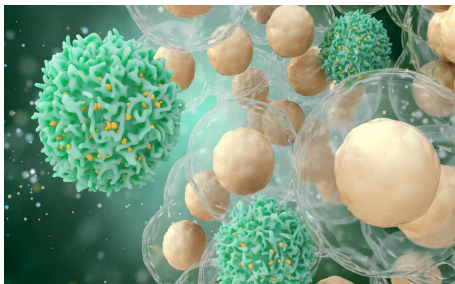
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# Introduction: Life at extreme conditions

- During evolution: Life has adapted to extreme conditions (e.g. glacial waters, deep-sea vents)
- Mechanism of how extremophilic bacteria can thrive under extreme conditions largely uncharacterized  
⇒ but understanding is fundamental for theoretical and applicative/biotechnological prospective
- All cellular components affected by stress ⇒ Focus on proteins: Most abundant and less stable macromolecules in the cytoplasm



# Goal of the Project

- Proteins unfold at high temperatures
  - Proteins live in crowded system
  - Unfolding of proteins can affect the complex network
- ⇒ **Goal:** Investigate dynamical properties of the proteins in the cytoplasm of different types of bacteria to understand the connection between the unfolding and the cell death

# Neutron Scattering

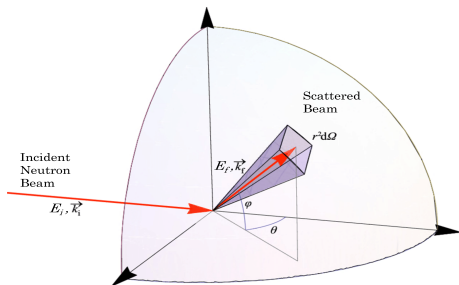
Neutron Scattering = experimental technique for studying sample structure and dynamics by analyzing the scattering beam of neutrons

- Neutrons are characterized by their energy and momentum

$$E = \hbar\omega \quad p = mv = \hbar k$$

- Thermal neutron wavelengths ( $\text{\AA}$ ) and energies ( $\text{meV}$ ) correspond to interatomic distances and energy of thermal excitations
- Important isotope effects, e.g.  $H$  (hydrogen),  $^2H$  (deuterium)

Experiment geometry:



# Neutron Scattering

- Neutrons are scattered by nuclei in the sample exchanging momentum and energy (or only momentum)

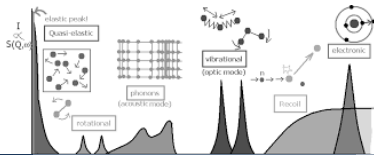
$$\Delta E = \hbar(E_f - E_i) \quad \Delta p = \hbar(k_f - k_i) = \hbar q$$

Elastic:  
 $\Delta E = 0$

Inelastic:  
 $\Delta E \neq 0$

Quasi-elastic:  
 $\Delta E < 1\mu eV$

- Scattering intensity measured as a function of  $q$  and  $E$ .
- Contains information on sample dynamics via spatio temporal Fourier transform to the positions of the sample scattering nuclei as a function of time
- Diffusive modes acting at different time-scales contribute to intensity of  $S(q, E)$



# Python Code for QENS data

Development of a Python code to fit and analyze **Quasi-Elastic Neutron Scattering** data

- i Reads and fits  $S(E)$  for all  $q$  values with a model of choice
- ii Extracts parameters of interest from the fittings, e.g. FWHM and plots as functions of  $q$
- iii Fitting of certain parameters to get further information on dynamical profile

# Analysis of QENS of the P.Arcticus

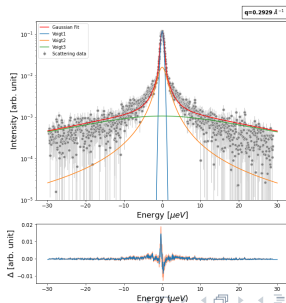
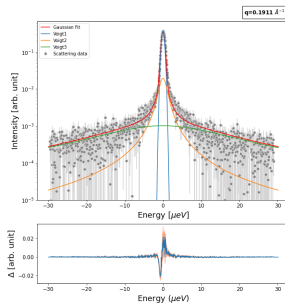
Application of the code for analysis of Psychrobacter Arcticus (Cell death temperature  $T_{CD} = 295.15K$ ):

- 1 Model for the scattering function:

$$S_{\text{exp}}(q, E) = R(E) \otimes [S_{AP}(q, E) + \alpha S_{D2O}(q, E)]$$

Model chosen for representing the average protein in the sample:

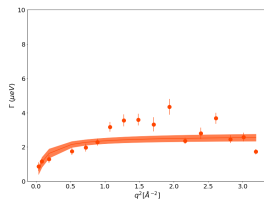
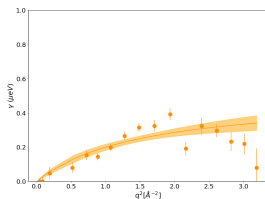
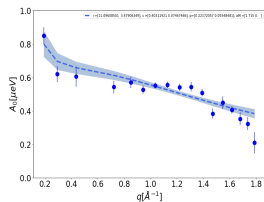
$$S_{AP}(q, E) = I(q) \{L_{\gamma}(E) \otimes [A_0 \delta(E) + (1 - A_0)L_{\Gamma}(E)]\}$$





# Analysis of QENS of the P.Arcticus

- ② Get parameters such as  $\gamma(q)$ ,  $\Gamma(q)$ ,  $A_0(q)$ :

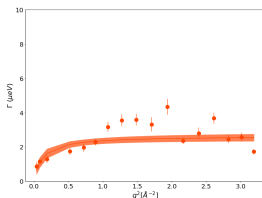
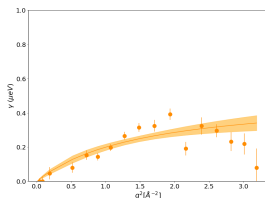
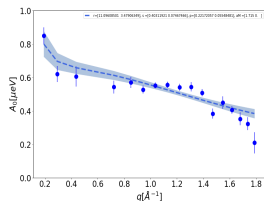


Lorentzian widths  $\gamma$  and  $\Gamma$  can be modelled with the jump diffusion model

$$\gamma(q, T) = \frac{q^2 D_\gamma(T)}{1 + q^2 D_\gamma(T) \tau_\gamma(T)} \quad \Gamma(q, T) = \frac{q^2 D_\Gamma(T)}{1 + q^2 D_\Gamma(T) \tau_\Gamma(T)}$$

# Analysis of QENS of the P.Arcticus

- 2 Get parameters such as  $\gamma(q)$ ,  $\Gamma(q)$ ,  $A_0(q)$ :



Lorentzian widths  $\gamma$  and  $\Gamma$  can be modelled with the jump diffusion model

$$\gamma(q, T) = \frac{q^2 D_\gamma(T)}{1 + q^2 D_\gamma(T) \tau_\gamma(T)} \quad \Gamma(q, T) = \frac{q^2 D_\Gamma(T)}{1 + q^2 D_\Gamma(T) \tau_\Gamma(T)}$$

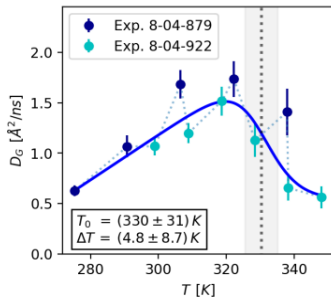
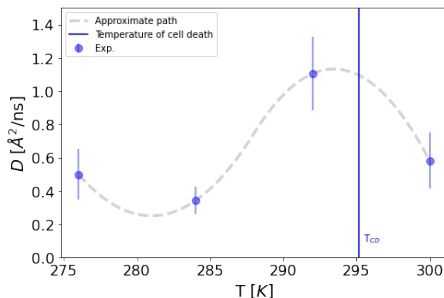
- 3 Apply fit to all measurements in temperature to get diffusion coefficients  $D_\gamma(T)$  and  $D_\Gamma(T)$

# Analysis of QENS of the P.Arcticus

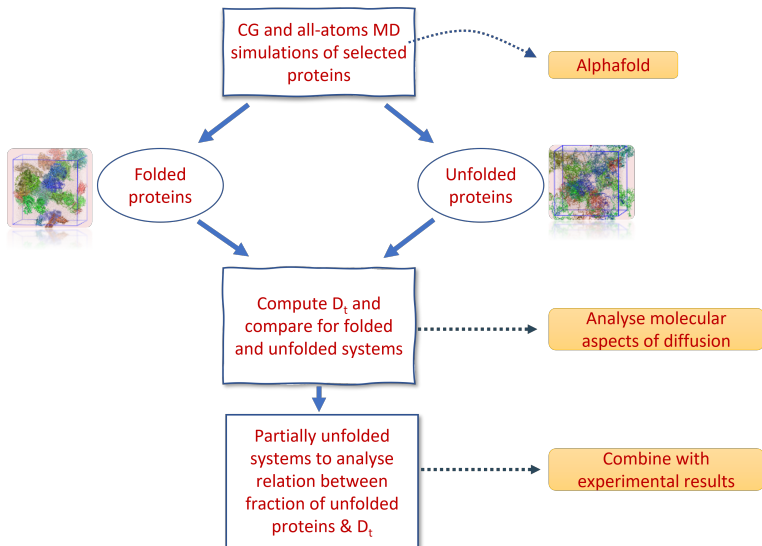
## Results

- Increase of global diffusion at low temperatures and drastic decrease after  $T = 292K$  shortly before cell death
- Around cell-death important reduction of the average motion of an entire protein

## Comparison with E.Coli (Mesophile):



# Outlook: Molecular Dynamics simulations



# Analysis of EINS data with Python

Analysis of **Elastic Incoherent Neutron Scattering** of the P.Arcticus, E.coli, A. Aeolicus

- For small  $q$ -values using the Gaussian Approximation the scattering function can be modelled as

$$S(q, E \approx 0) = \exp\left(-\frac{1}{6}\langle u^2 \rangle q^2\right)$$

where  $\langle u^2 \rangle$  is the atomic mean square displacement (MSD)

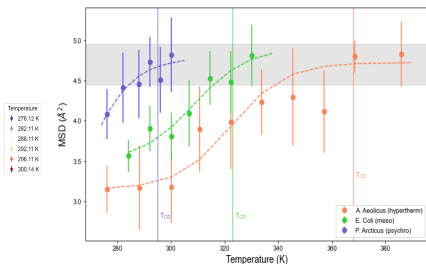
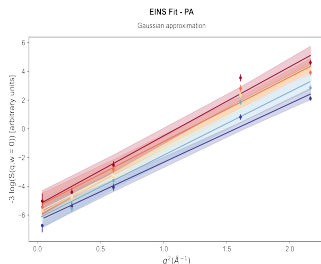
- Reformulation gives a linear form of the logarithmic scattering function

$$-6 \log(S(q, E \approx 0)) = \langle u^2 \rangle q^2$$

- Fit of logarithmic scattering function to get MSD values

# Analysis of EINS data with Python

- MSD values plotted together as functions of temperature



## Results:

- Common threshold and trend of the MSDs
- Reminiscent of the Lindemann criterion for solid melting, that has been verified also for powder systems
- Other Model by Hennig confirms same trend

$$-6 \log(S(q, \Delta E)) = b + \langle u^2 \rangle q^2 + cq^4$$

# Lectures at University of Perugia

Participation at Lectures in Physics at UniPG:

- Effective Field Theory I,II,III
- Nanosystems I,II,III (Exam)
- Teaching and Learning Physics (Exam)

# Neutron Scattering School

## Participation at the 24th JCNS Laboratory Course

- Week 1: Lectures in Neutron scattering and applications + Exercise sessions
- Week 2: Visit of the Heinz Maier-Leibnitz Zentrum MLZ



# Outlook

- Complete analysis of P. Arcticus, by taking further measurements at ILL and by performing all-atoms & CG MD simulations
  - ⇒ Proposal sent, preparation of protein sets for simulations started
  - ⇒ Reveal if there exists a set of protein that triggers arrest of the dynamics and analyse molecular aspects
  - ⇒ Hypertermophile
- Complement MSD data of EINS with data of molecular dynamics simulations
  - ⇒ Paper writing

# Summary





## Lectures:

- Effective Field Theory I,II,III
- Nanosystems I,II,III (Exam)
- Teaching and Learning Physics (Exam)





## Neutron Scattering School: 24th JCNS Laboratory Course

- Week 1: Lectures in Neutron scattering and applications + Exercise sessions
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