

# Life Science with neutrons at the European Spallation Source

MAXESS SmiLe

Medicon Village, Lund

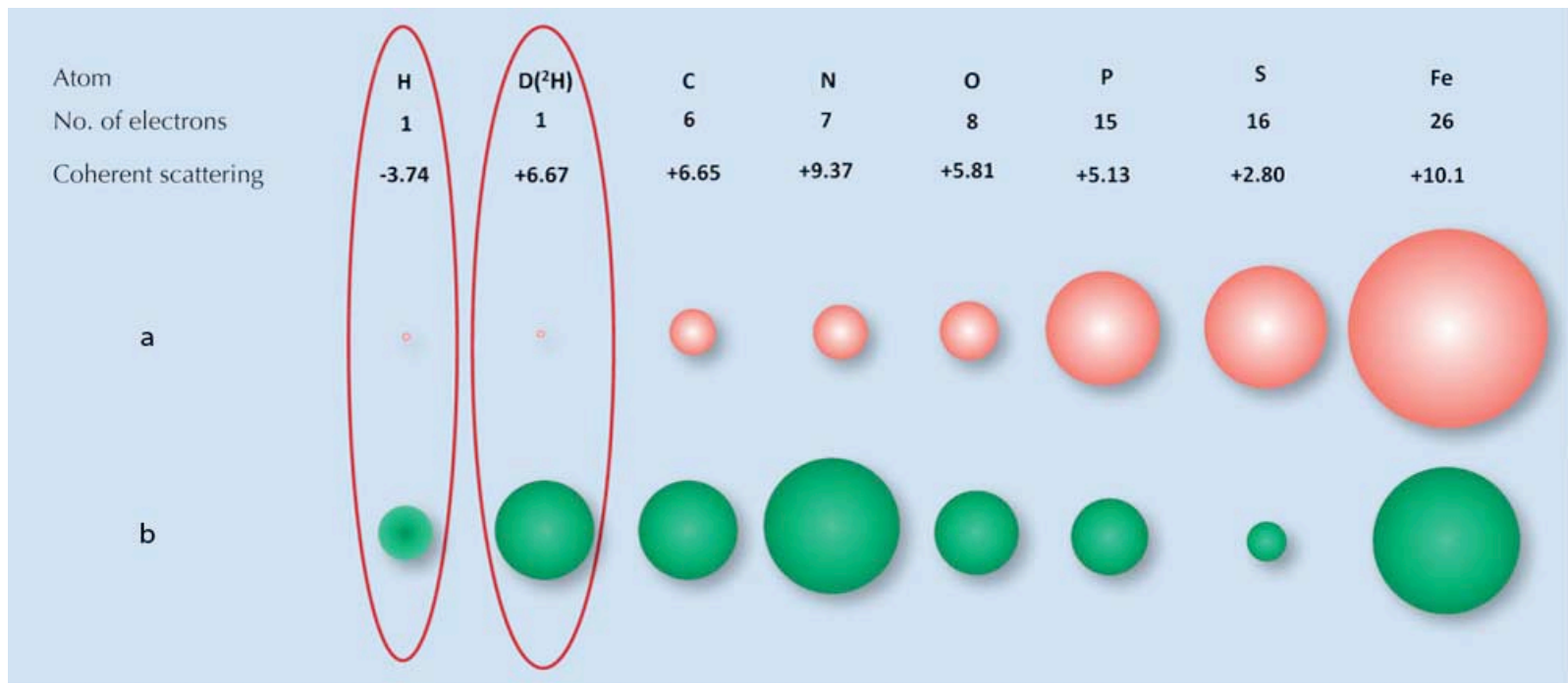
2023-05-09

**Esko Oksanen Instrument Scientist,**

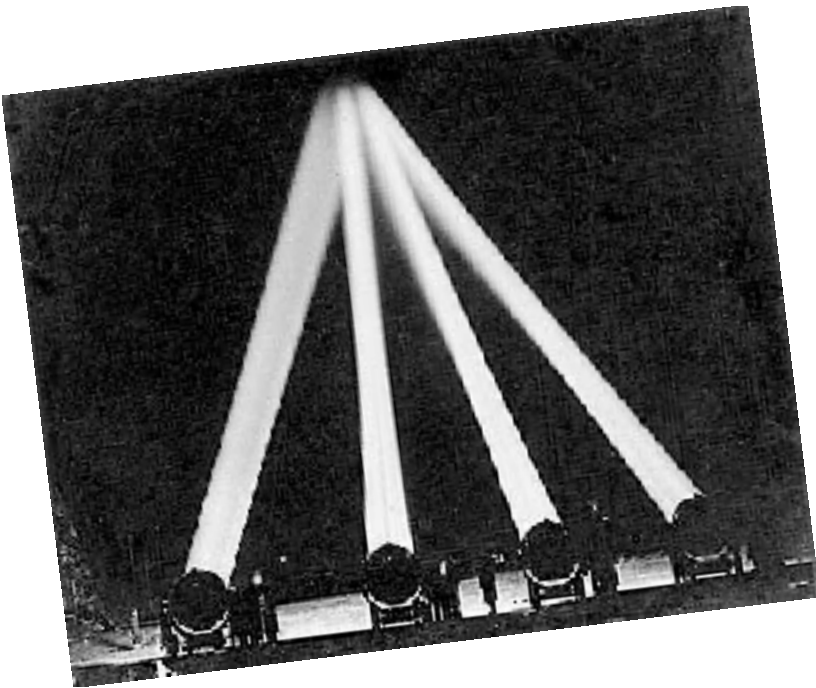
Macromolecular Crystallography

# Neutrons as a probe for condensed matter

- They have wavelengths similar to atomic distances
- They have a magnetic moment
- They are non-destructive
- They see a completely different contrast to x-rays → isotope contrast & labelling



# Neutron sources are weak!



X-rays

VS

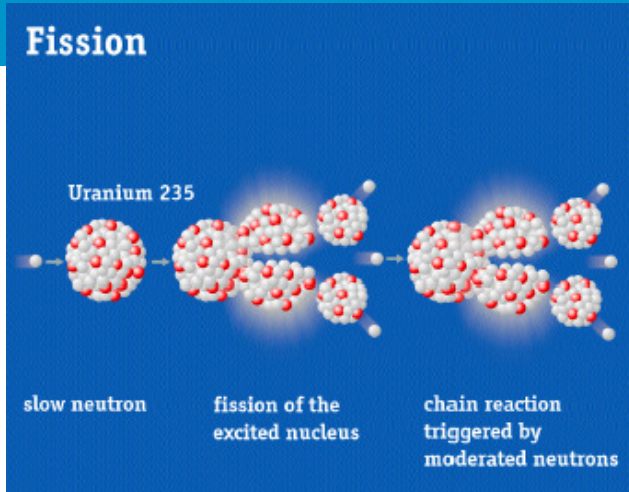


Neutrons

# How to produce neutron beams



ILL - France

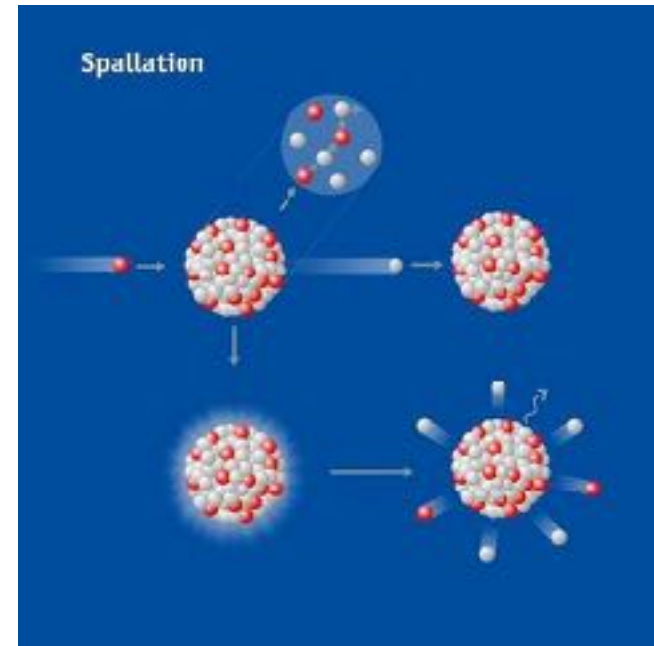


Typically continuous

**Fission: One neutron in, three neutrons out; Use a nuclear reactor**



**Spallation: Up to 30 neutrons per proton; Accelerator to propel proton onto target**

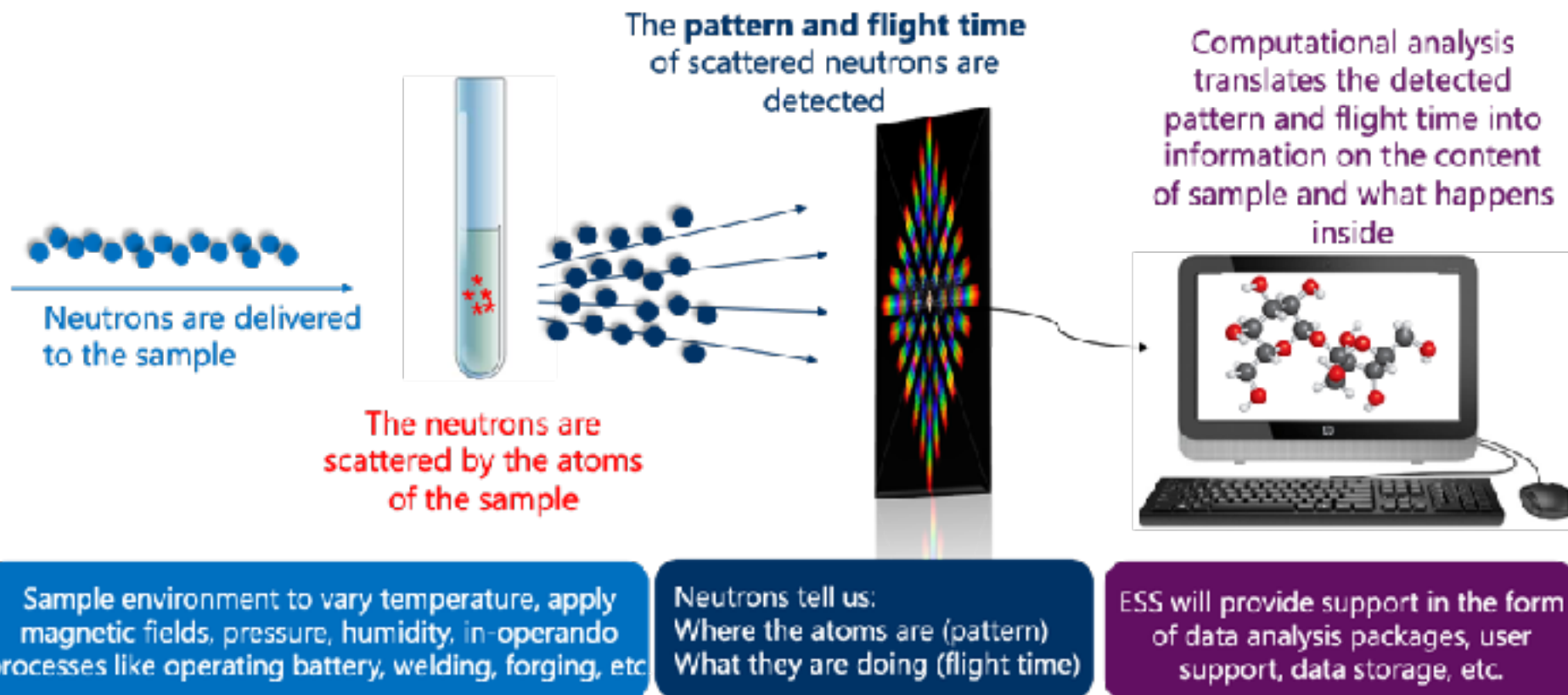


Typically pulsed



ESS-Sweden

# Neutron scattering simplified



# Why neutrons for biological structures?

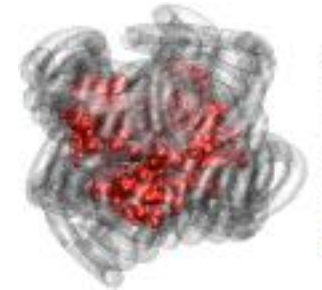
- We can see light atoms → hydrogen positions **Crystallography**
- We can use isotope labelling to create contrast → protein-protein complexes, membranes **Small angle scattering**
- We can observe dynamics with neutron energy changes → relating dynamics to function **Reflectometry**
- We can see through large objects → water transport **Inelastic scattering**
- We can see through large objects → water transport **Imaging**



**Small angle scattering**

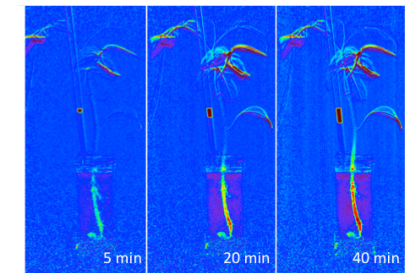


**Reflectometry**

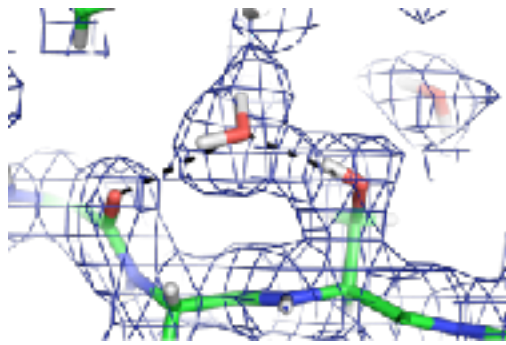


**Inelastic scattering**

**Imaging**



# Neutron Macromolecular Crystallography



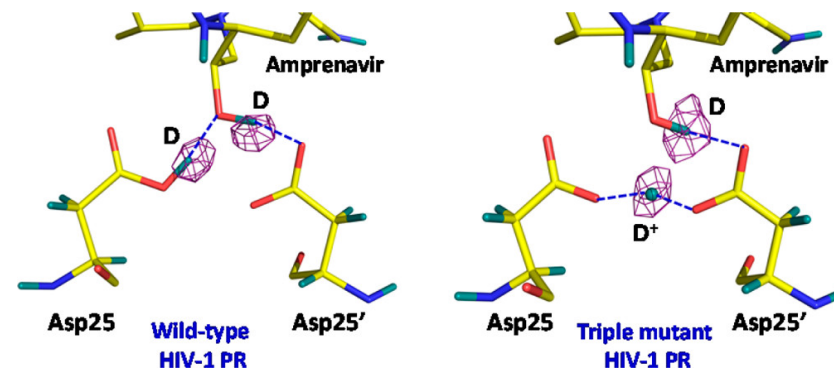
- ☺ Hydrogens are visible
- ☺ No radiation damage
- ☹ Large crystals needed
- ☹ Data collection takes weeks
- ☹ Few instruments available

Where are hydrogens important?

Enzyme mechanisms

Protein-ligand interactions

Proton transport across membranes

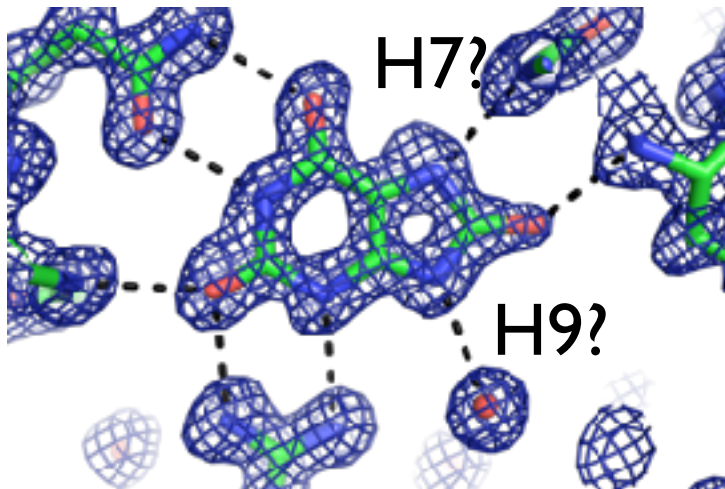


Gerlits et al., (2017) *J. Med. Chem.* **60**, p.2018

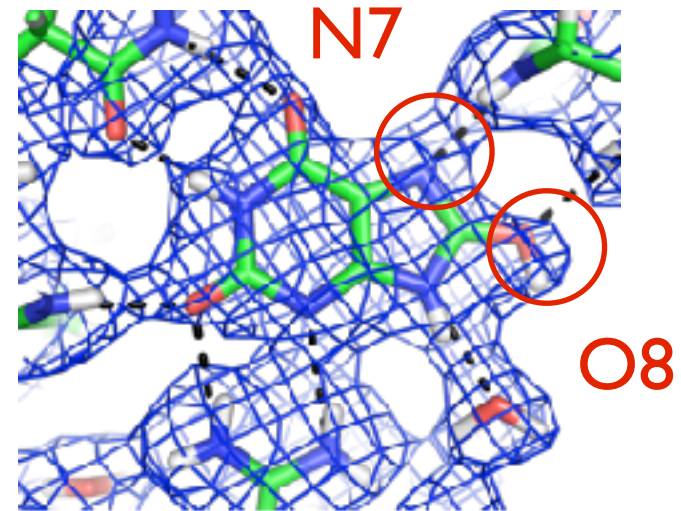
# Why is hydrogen interesting?

Enzyme mechanism

Urate oxidase



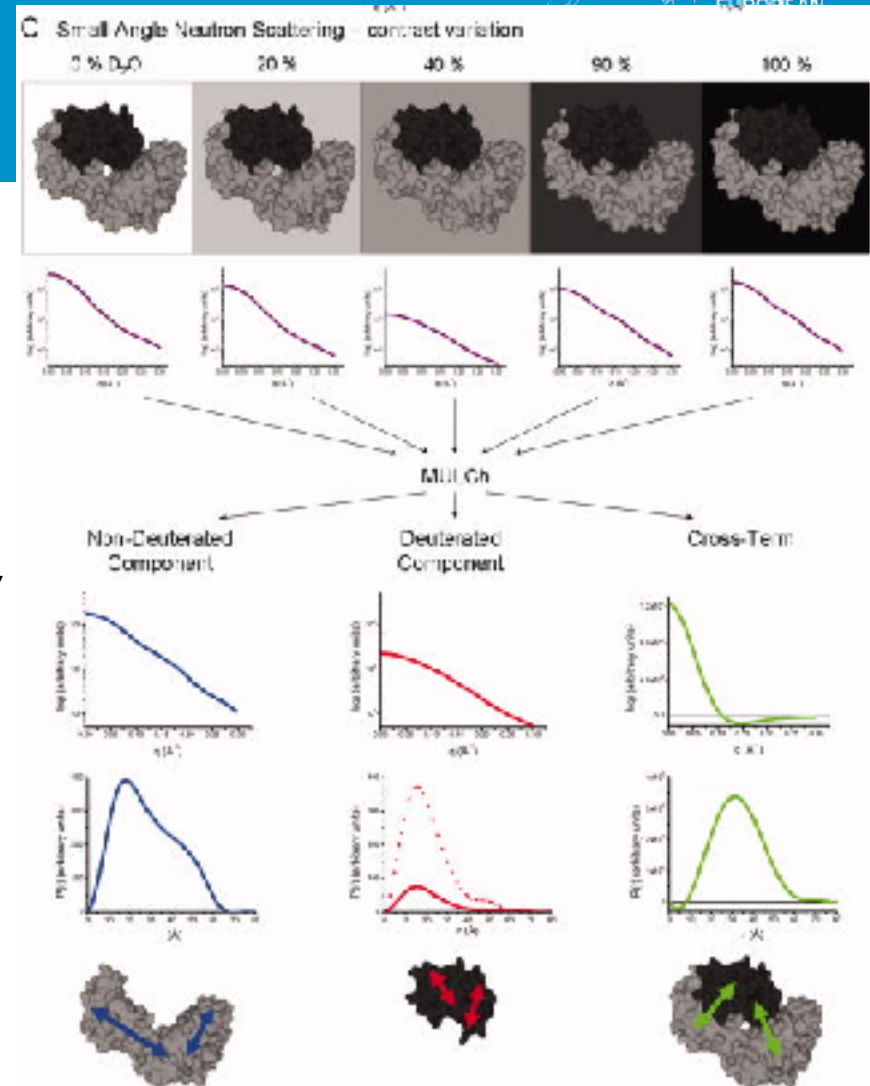
Mono- or dianion?



Unexpected enol form  
(8-hydroxyxanthine)

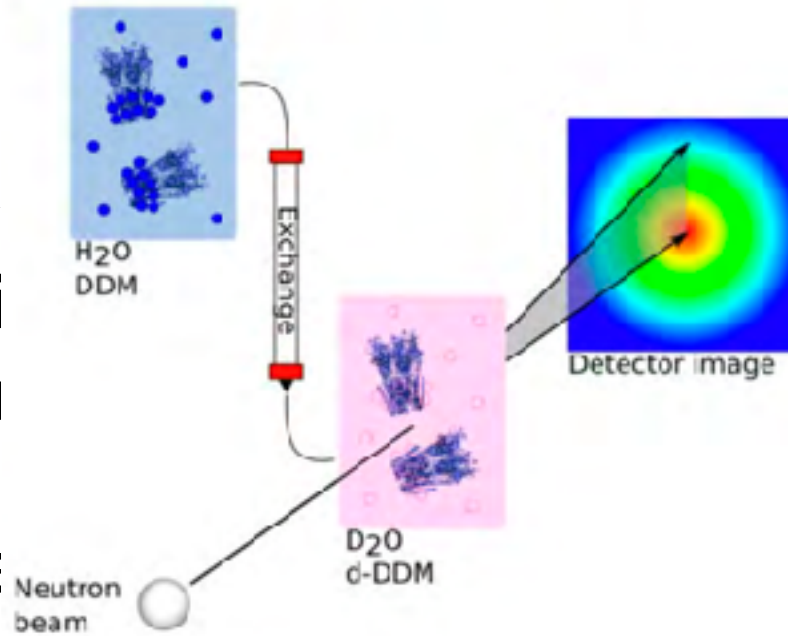
# Small Angle Neutron Scattering

- ☺ Solution structure
- ☺ Complexes resolved by contrast variation
- ☺ Membrane proteins can be studied with “invisible” micelles
- ☹ Requires D-labelling

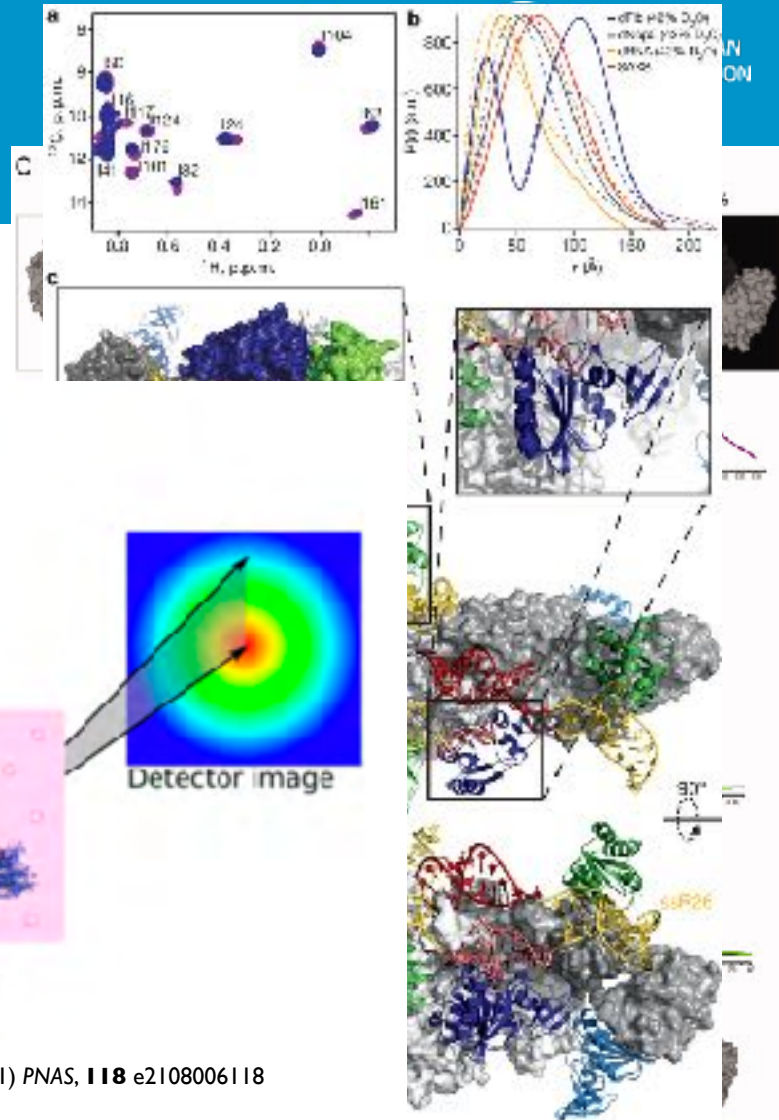


# Small Angle Neutron Scattering

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Lycksell et al. (2021) *PNAS*, **118** e2108006118

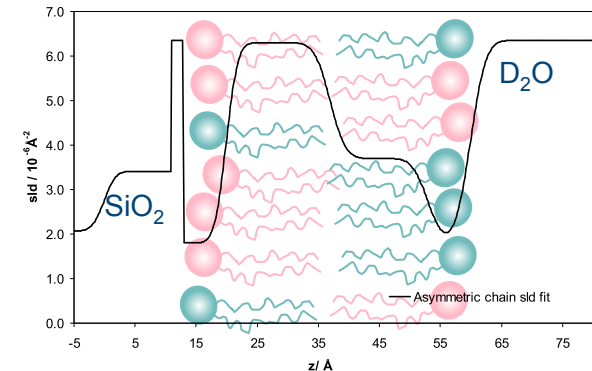
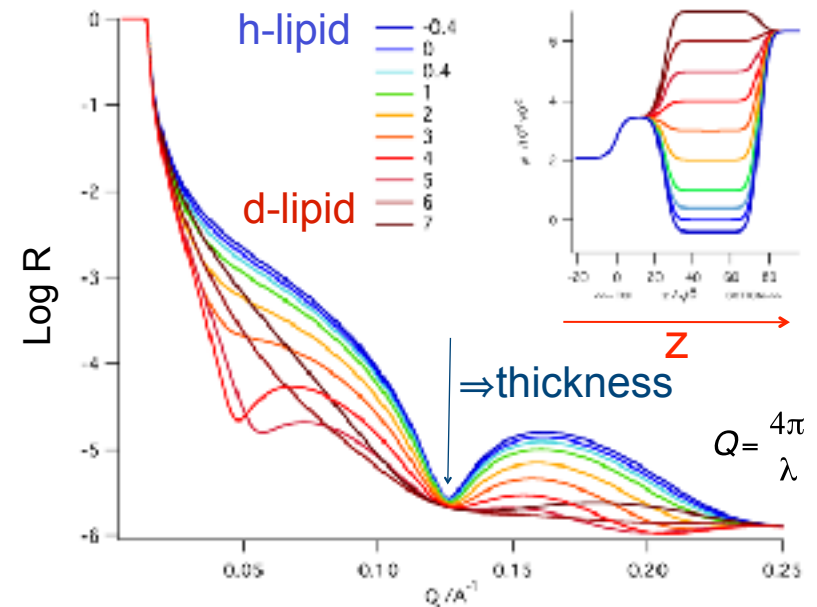


Lapinaite et al. (2013) *Nature*, **502** 519-523

Jacques, D.A., Trewhella, J. (2010) *Protein Science* **19** 642-657

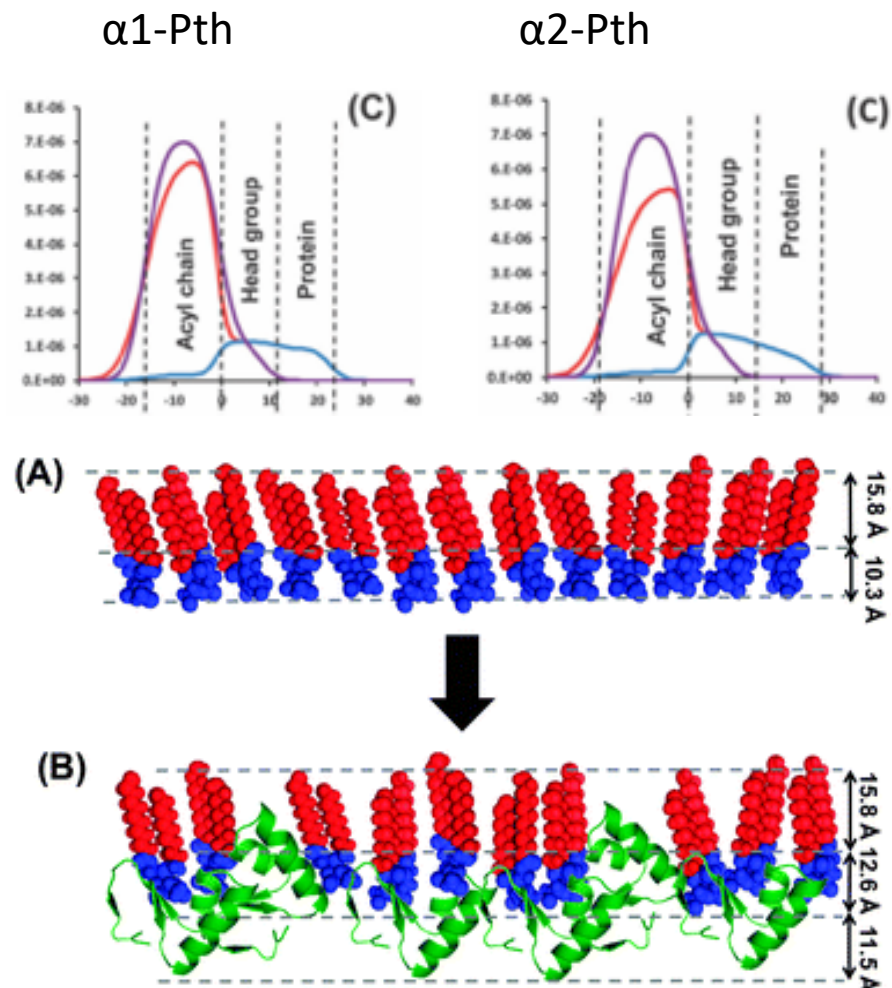
# Neutron Reflectometry

- ☺ Membrane composition at atomic resolution
- ☺ Can study surfaces in solution
- ☹ Deuterated compounds essential
- ☹ Information only along membrane normal



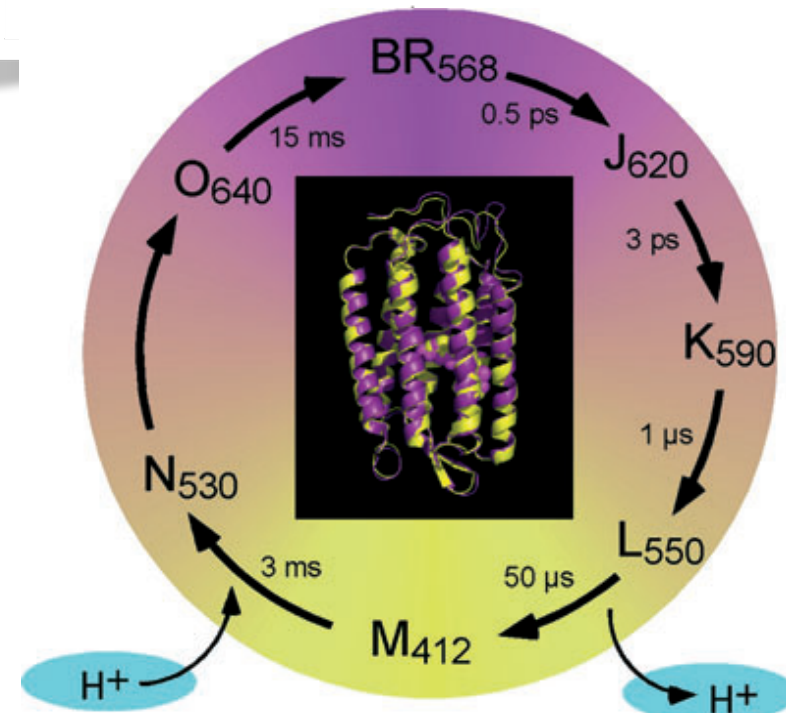
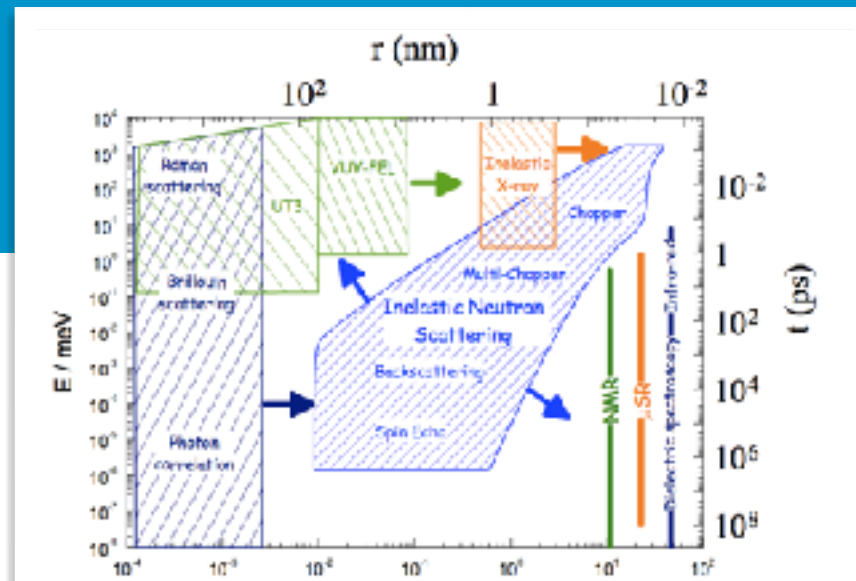
# Neutrons as a tool to "see" details of AMP penetration

- $\alpha 1$  and  $\alpha 2$ -purothionins (Pth) are produced by wheat in response to bacterial and fungal infections
- Both disrupted in-plane structure of phospholipid monolayers: by adsorbing as a single protein layer, penetrating the lipid, and actually removing lipid.
- $\alpha 2$  showed faster disruption and removed  $\sim 12\%$  of the lipids – the hydrophobicity of the peptide made a huge difference in efficacy.

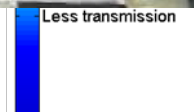
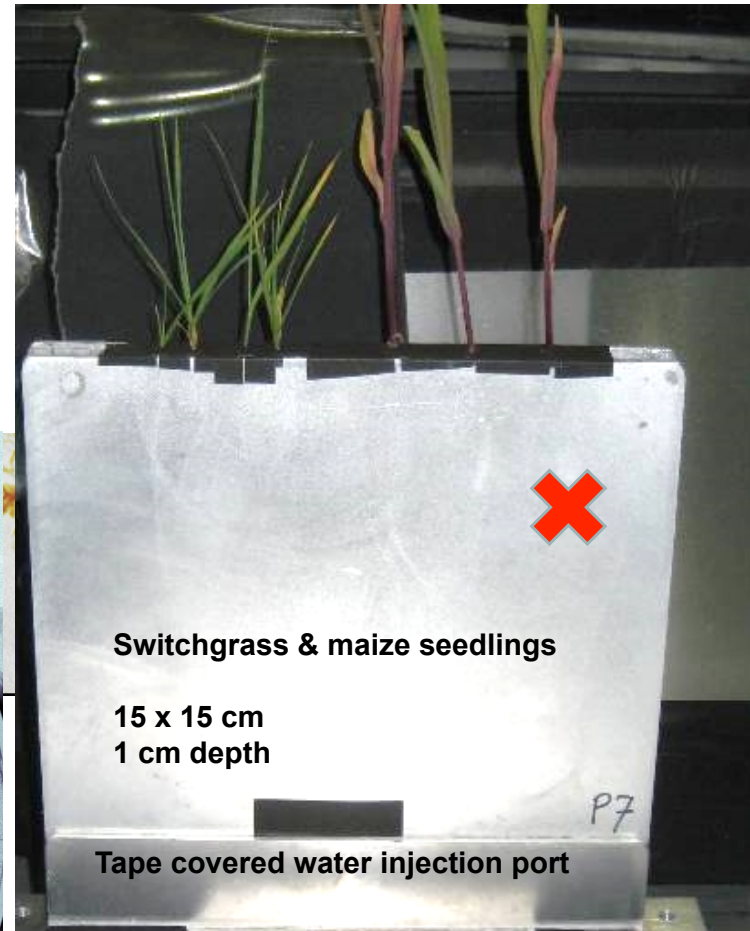
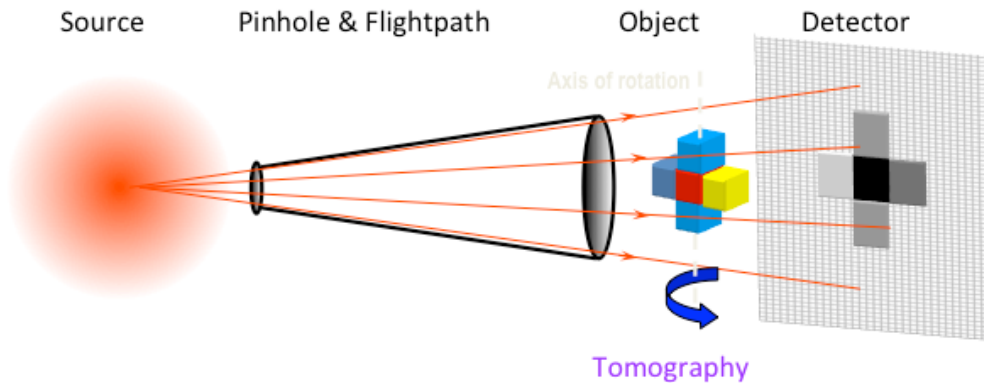


# Inelastic neutron scattering

- Dynamics information in time and length scales inaccessible by other techniques
- Directly comparable with MD simulations

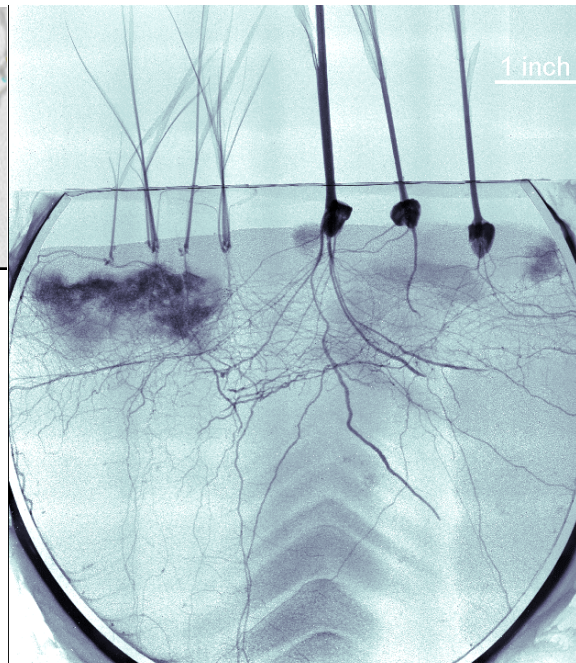


# Neutron imaging



J.M. Warren, ORNL

- We can see light elements → Water!
  - We can create contrast with  $D_2O$  → Water uptake
- approximate injection site



# A European Project

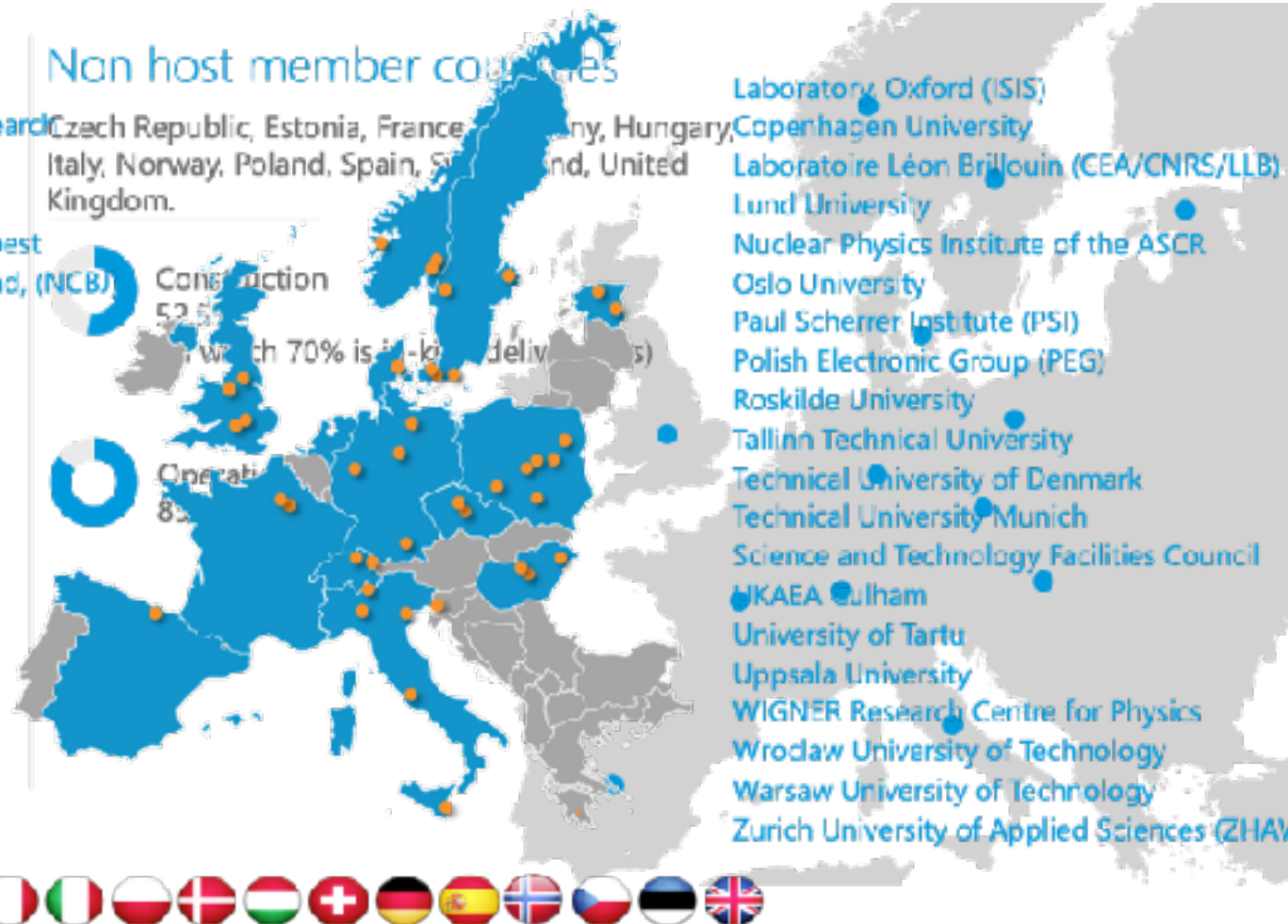
## How will it be built?

### Host countries

- Karlsruhe University
- Swedish Institute for Nuclear Research
- Bergen University
- CEA Saclay, Paris
- Centre for Energy Research, Budapest
- Centre for Nuclear Research, Poland, (NCB)
- CNR, Frascati
- CNRS Orsay, Paris
- Cockcroft Institute, Daresbury
- Elettra – Sincrotrone Trieste
- ESS Billings
- Forschungszentrum Jülich
- Helmholtz-Zentrum Geesthacht
- INFN, Krakow
- INFN, Catania
- INFN, Legnaro
- INFN, Milan
- Institute for Energy Research (IFE)
- Rutherford-Appleton

### Non host member countries

- Czech Republic, Estonia, France, Germany, Hungary, Italy, Norway, Poland, Spain, Sweden, Switzerland, United Kingdom.



# ESS Timeline



2009  
Decision to site  
ESS in Lund

2014  
Start of  
construction

2022  
Today

2026  
First science

2003  
Concept design  
of ESS presented

2012  
ESS design  
update phase  
complete

2019  
Start of initial  
operations phase

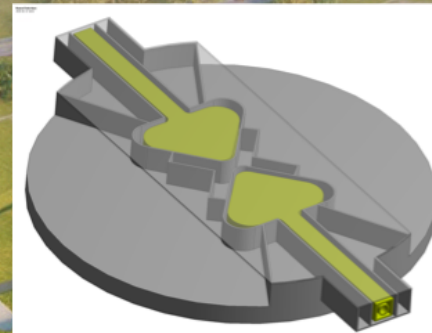
2025  
First neutrons

2027  
Construction  
phase completed

# ESS High Level Design

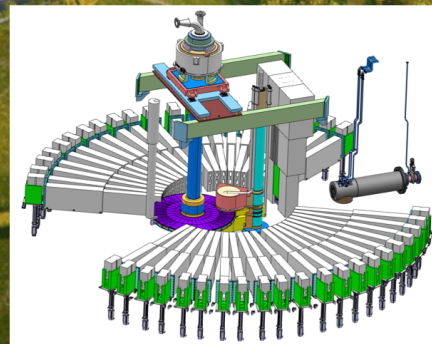


Flat moderator delivering smaller and brighter neutron beams

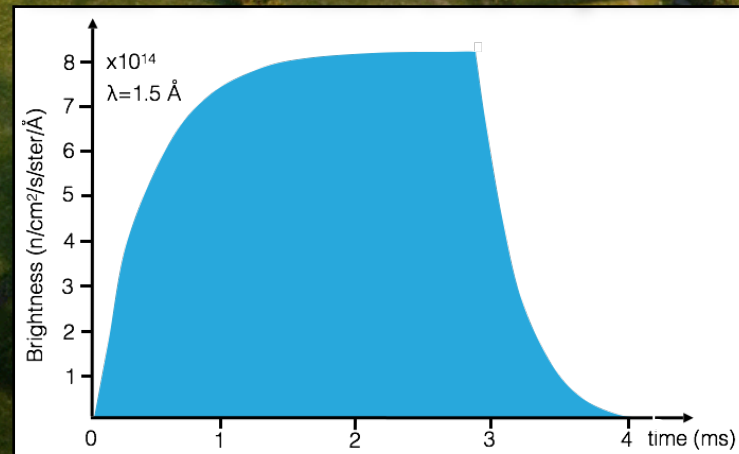


High Power Accelerator means more neutrons

High brightness and tuneable resolution makes new measurements possible



An Innovative Target Station that can host >30 instruments



# The world's brightest neutron source



## Target station

- Rotating tungsten wheel 2.5 m diameter
- He cooled
- Water (293 K) and liquid hydrogen (20 K) moderators

## 5 MW Linear proton accelerator (~600 m)

- 2.86 ms pulses **Long pulse**
- 2 GeV
- 62.5 mA
- 14 Hz
- Flexible design for future upgrades

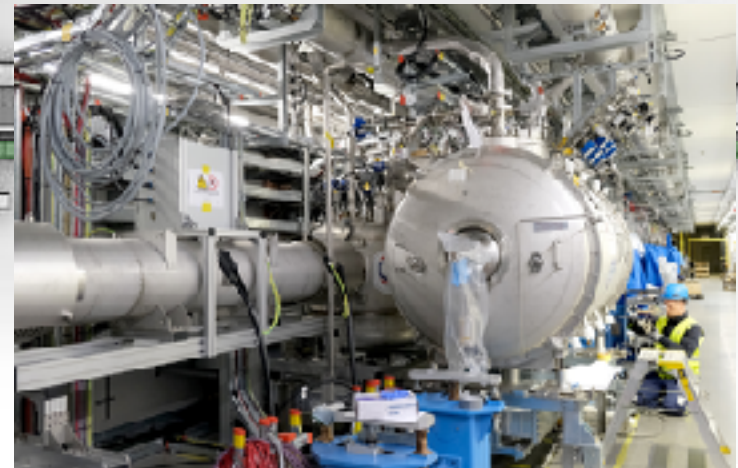
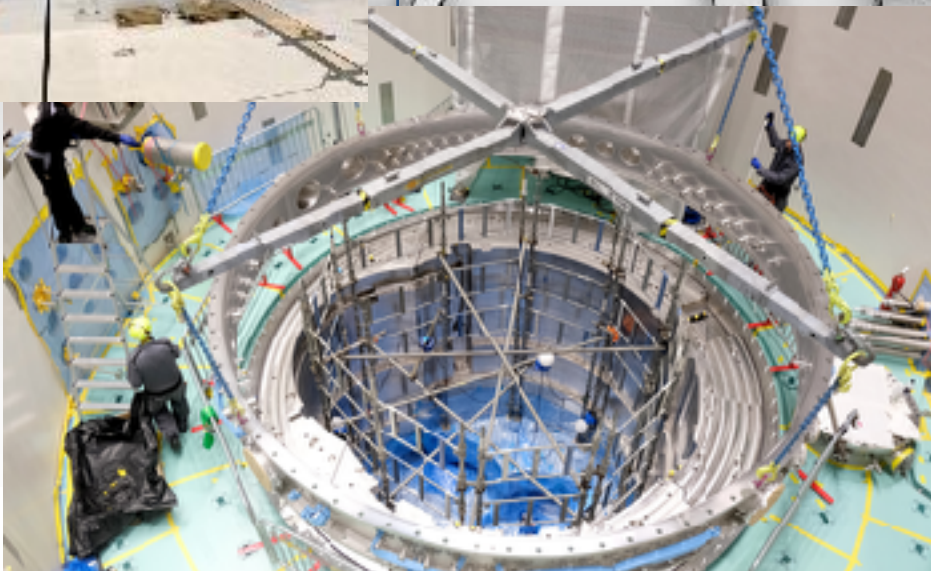
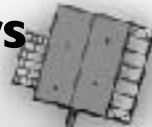
## High brilliance moderators



Hall 3

neutron guide hall

sp.  
Hall 2



# ESS Instrument suite



Crystallography

Imaging

Inelastic scattering

Helmholtz-Zentrum Geesthacht  
Zentrum für Material- und Küstenforschung

TUM  
Technische Universität München

DTU

ESS bilbao

LB

JÜLICH  
FORSCHUNGSZENTRUM

AARHUS UNIVERSITET

Small angle scattering

Science & Technology Facilities Council  
ISIS

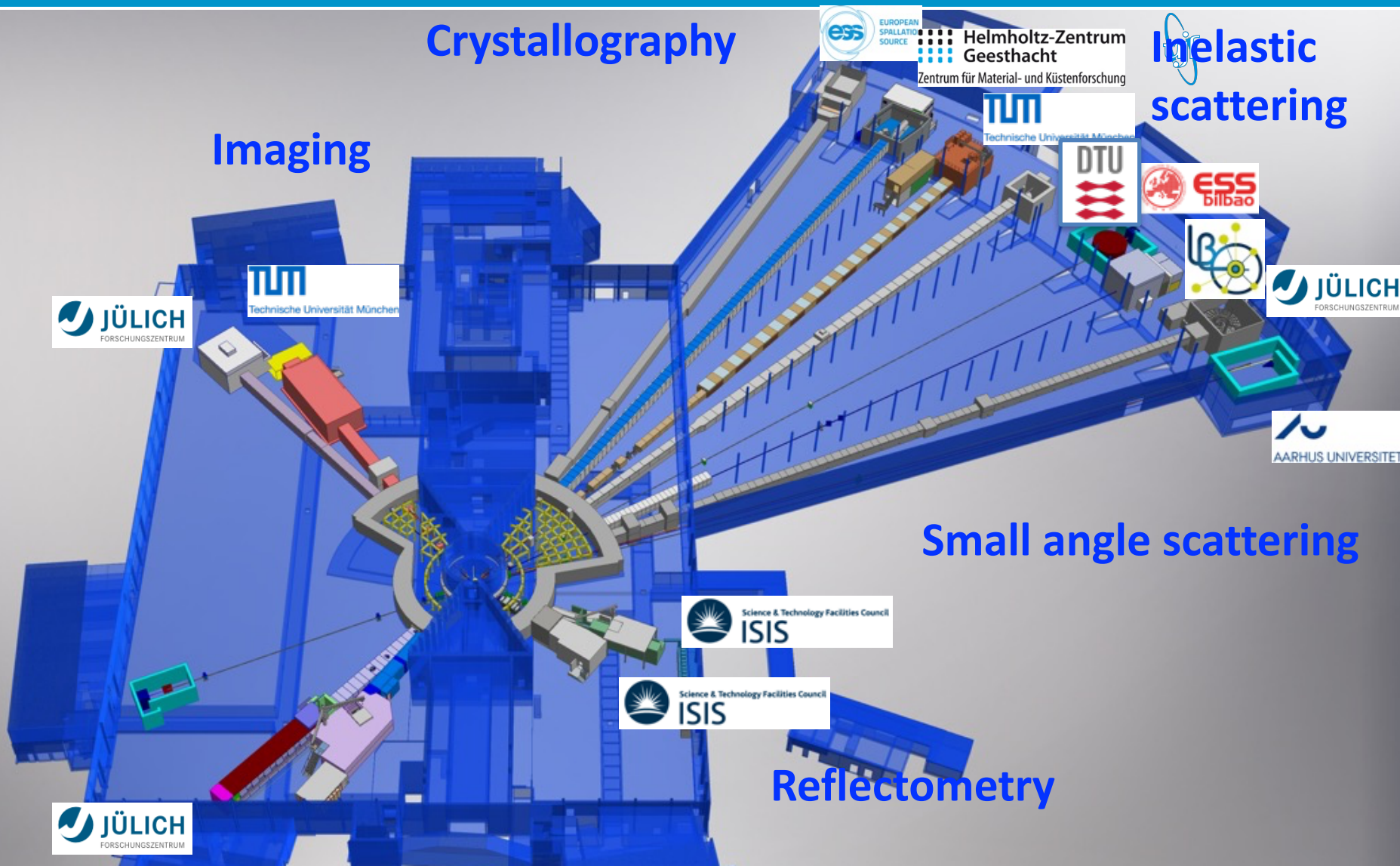
Science & Technology Facilities Council  
ISIS

Reflectometry

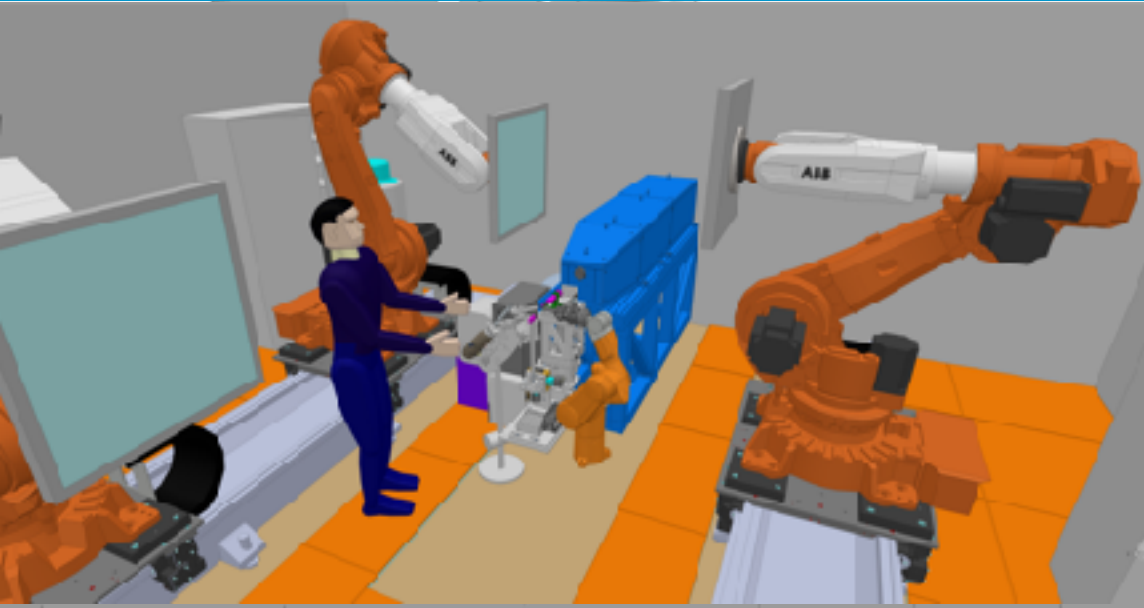
JÜLICH  
FORSCHUNGSZENTRUM

TUM  
Technische Universität München

JÜLICH  
FORSCHUNGSZENTRUM



# NMX – Macromolecular diffractometer at ESS

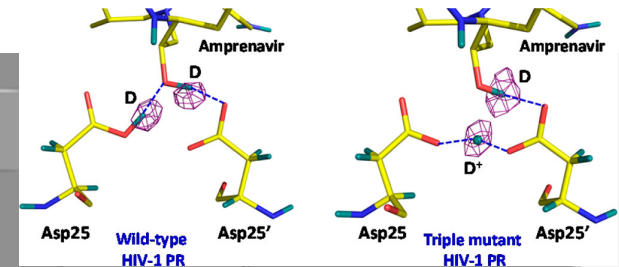


Where are hydrogens important?

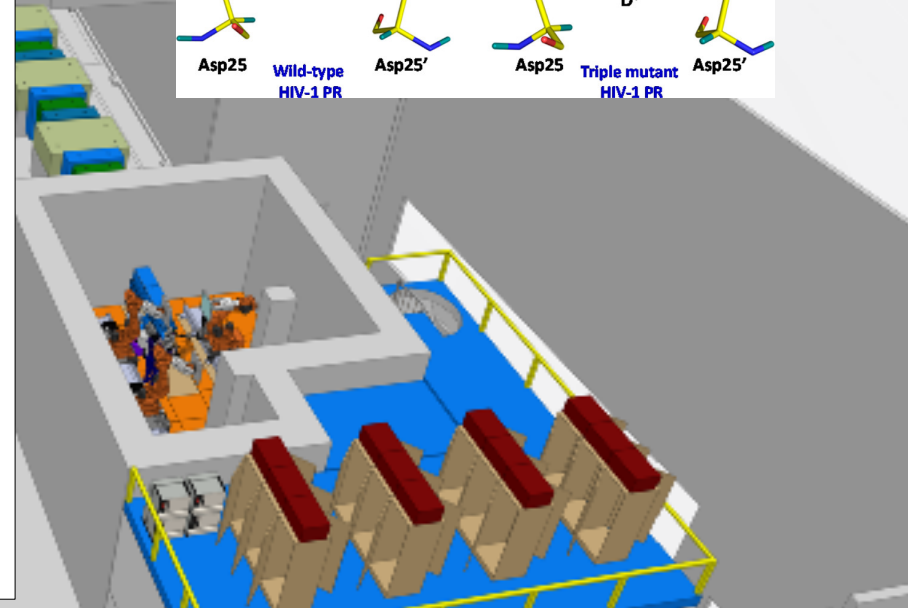
Enzyme mechanisms

Protein-ligand interactions

Proton transport across membranes



## Partners



# NMX – Macromolecular diffractometer at ESS



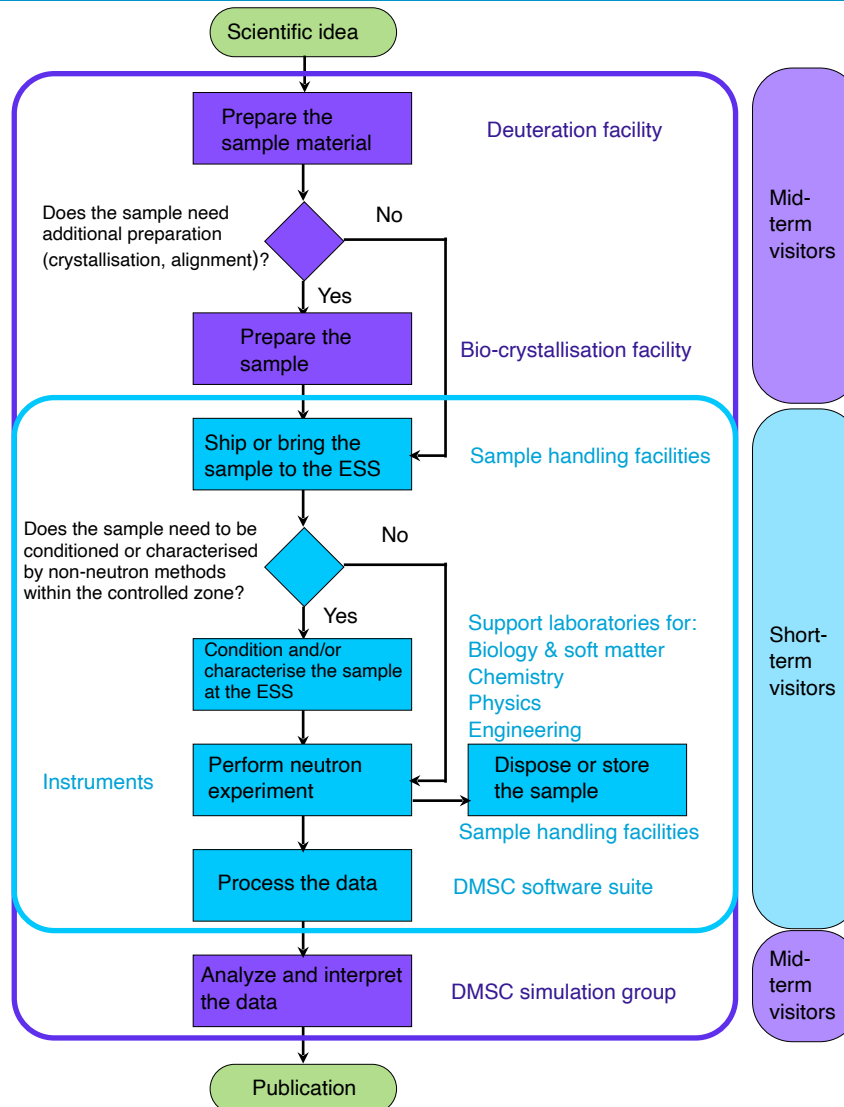
- LoKI will have high flux, wide simultaneous size range, and a large sample area.
- LoKI will enable the use of small beams, making scanning experiments & microfluidics routine.
- LoKI aims to provide the ability to perform “single-shot” kinetic measurements on sub-LoKI will have high flux, wide simultaneous size range, and a large sample area.



# LoKI Broad Band SANS



# Supporting facilities



DEMAX platform  
together with Lund  
University



LUND  
UNIVERSITY



Lund Protein-Production Platform

# Questions?

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