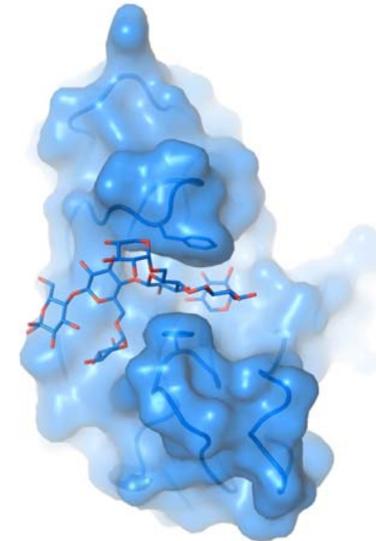
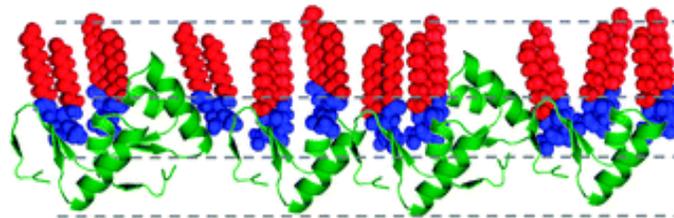
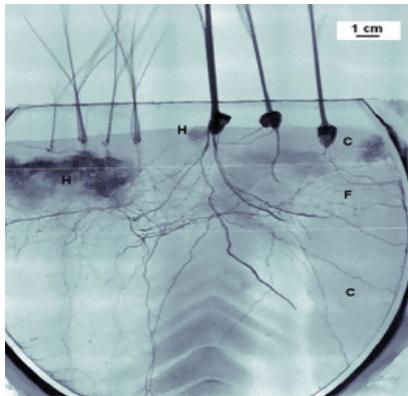


Life science research using neutrons



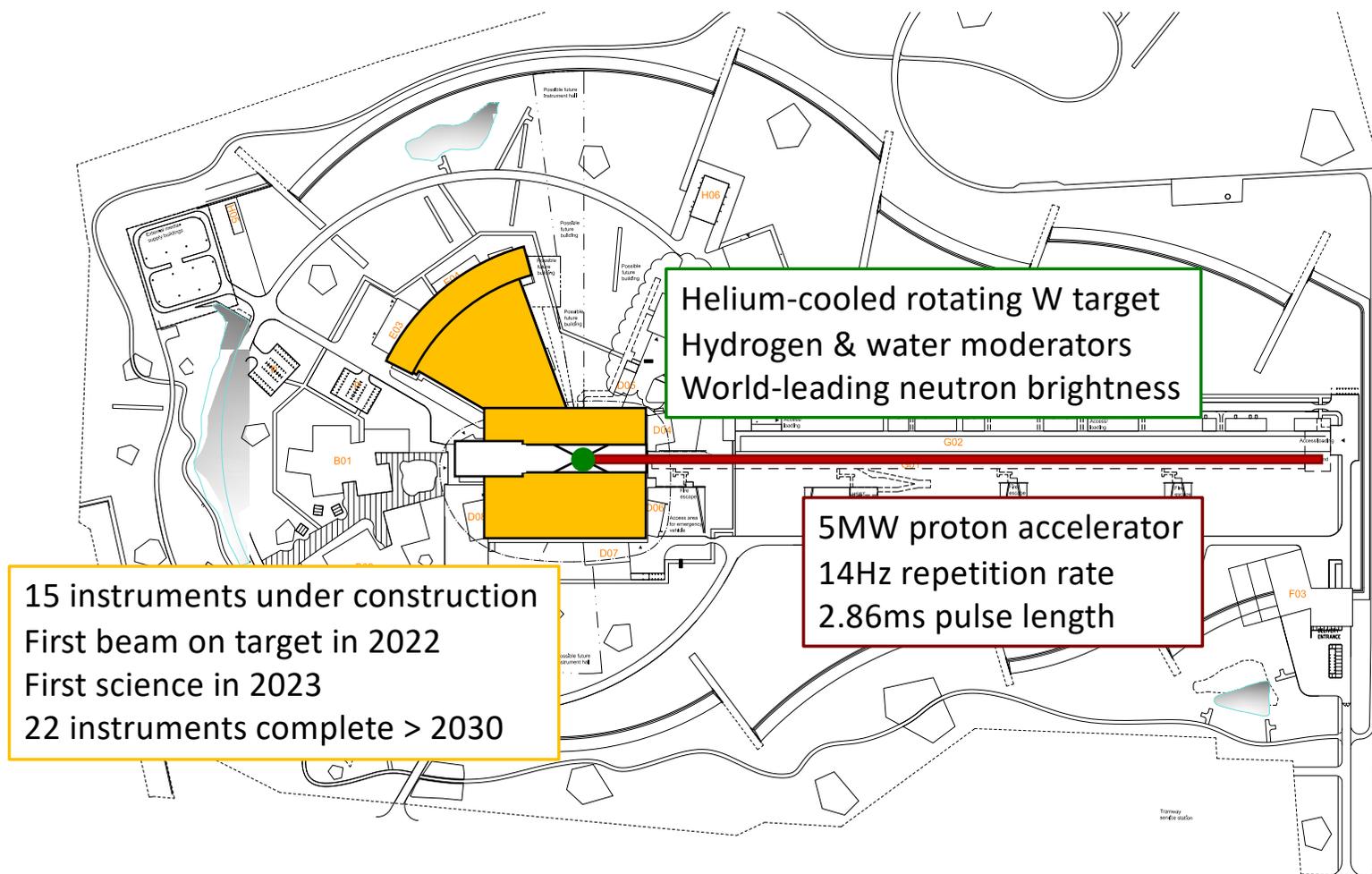
Dr. Zoë Fisher
Scientific Activities Division, European Spallation Source ERIC
Adjunct Snr Lecturer, Biology Department, Lund University



Outline

- (Brief) ESS overview: status & progress
- Properties of neutrons
- Isotope labeling & biological materials
- Neutron scattering techniques relevant to life science research (NPX, SANS, NR, Imaging)
- Conclusions

ESS: The Next-Generation Neutron Source



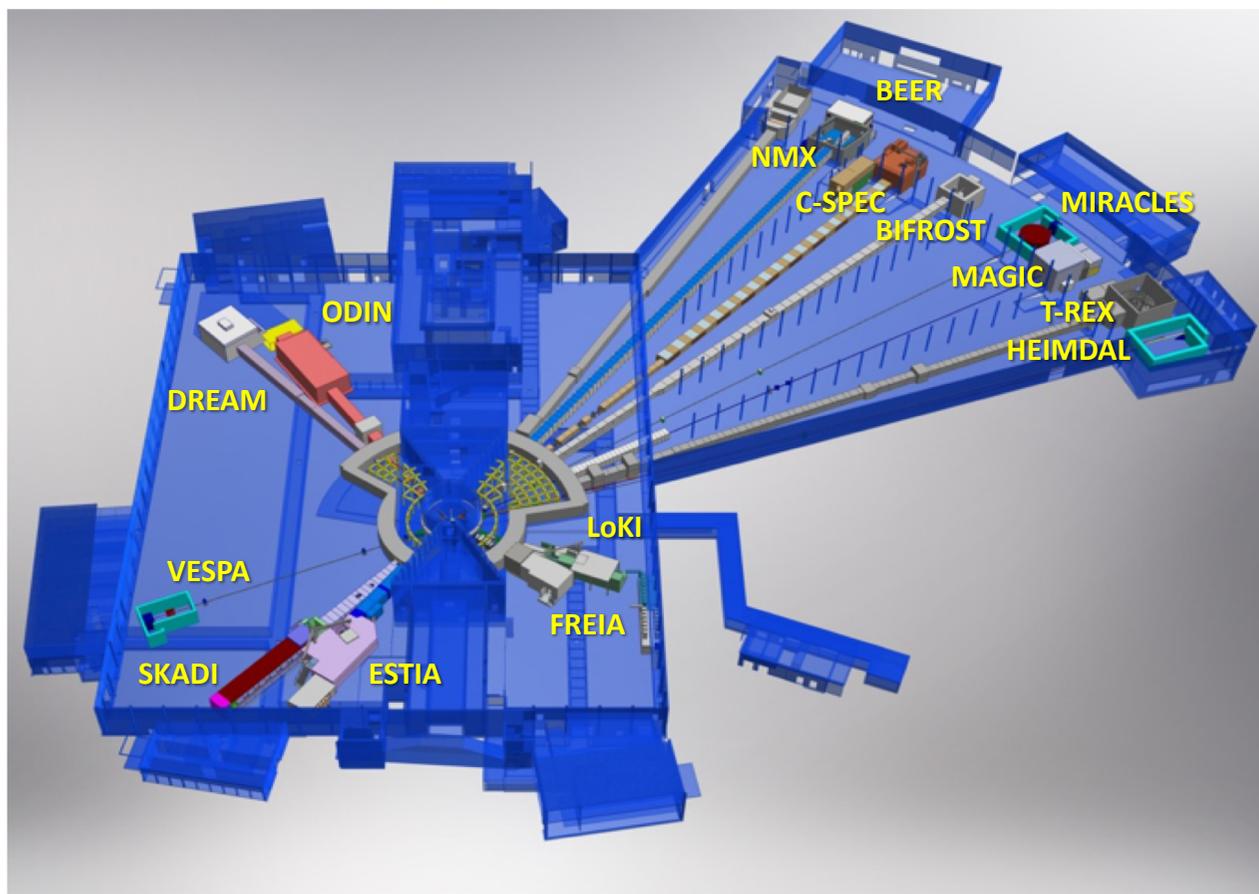
Construction progress: taken November 2020



<https://europeanspallationsource.se/site-weekly-updates>

Initial ESS instrument suite (15) is designed to make a wide and complementary range of neutron energies available to the neutron research community.

- LoKI**—Small-Angle Neutron Scattering 🌿🧪🔬
- NMX**—Macromolecular Diffraction 🌿
- ODIN**—Imaging 🌿🧪🔬
- BEER**—Materials and Engineering Diffraction
- ESTIA**—Reflectometry 🌿🧪🔬
- DREAM**—Powder Diffraction
- C-SPEC**—Direct Geometry Spectroscopy 🌿🧪
- SKADI**—Small-Angle Neutron Scattering 🧪🔬
- BIFROST**—Indirect Geometry Spectroscopy
- FREIA**—Horizontal Reflectometry 🌿🧪🔬
- HEIMDAL**—Powder Diffraction
- MAGiC**—Single Crystal Diffraction
- MIRACLES**—Backscattering Spectroscopy
- T-REX**—Time-of-Flight Spectroscopy
- VESPA**—Vibrational Spectroscopy



DEMAX offers 3 pillars of support



LUND UNIVERSITY



ESS Deuteration and Macromolecular Crystallization (DEMAX) Platform

Chemical Deuteration

- Organic & enzymatic synthesis of "small" molecules
- Separate, analyze a range of molecules
- Biomass-derived lipid extraction, analysis and purification
- *Future: optimize large scale separation/purification of lipids from biomass*

Biological Deuteration

- Deuterated biomass production (algae, bacteria, yeast)
- Protein & plasmid DNA production
- Biophysical characterization (DLS, Nanotemper, purity)
- D incorporation with ESI-MS
- *Future: optimization of fermenters for large scale yeast/bacteria cultures*

Macromolecular Crystallization

- High- and low-throughput screening
- Large volume crystallization
- Optimization (seeding, fine-screening, temperature)
- X-ray testing 100 K @ BioMAX (BAG with LP3)
- Support for xtal mounting & H/D exchange for RT measurements

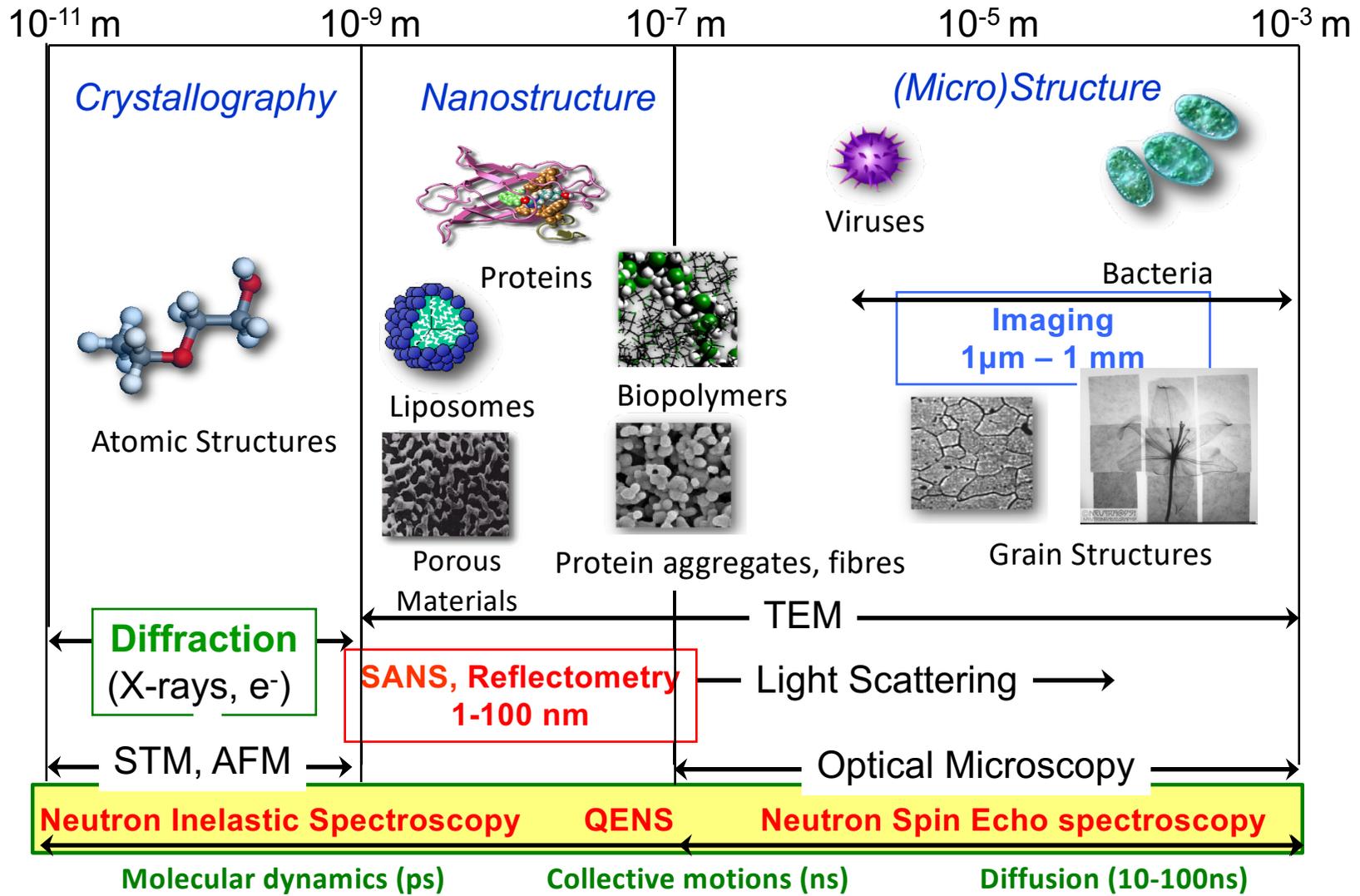


0.5 FTE
(LU)

Properties of the neutron

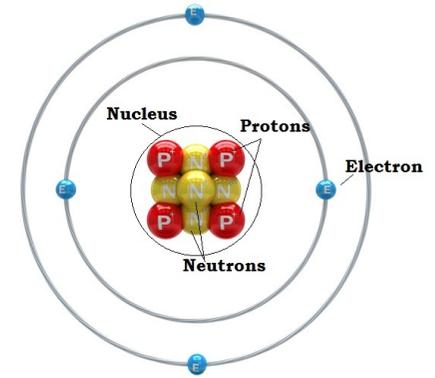
- Neutrons can be produced in a large range of energies (wavelengths) appropriate to study inter-atomic distances & molecular motions in most materials
- They interact weakly and penetrate into bulk materials
- Neutrons at thermal energies are non-damaging (*biological samples*)
- Sensitive to isotopes of the same element (^1H vs ^2H)
- Complementary to other techniques *NMR, MX, EM, AFM, DLS*

Length & Time Scales probed by neutrons

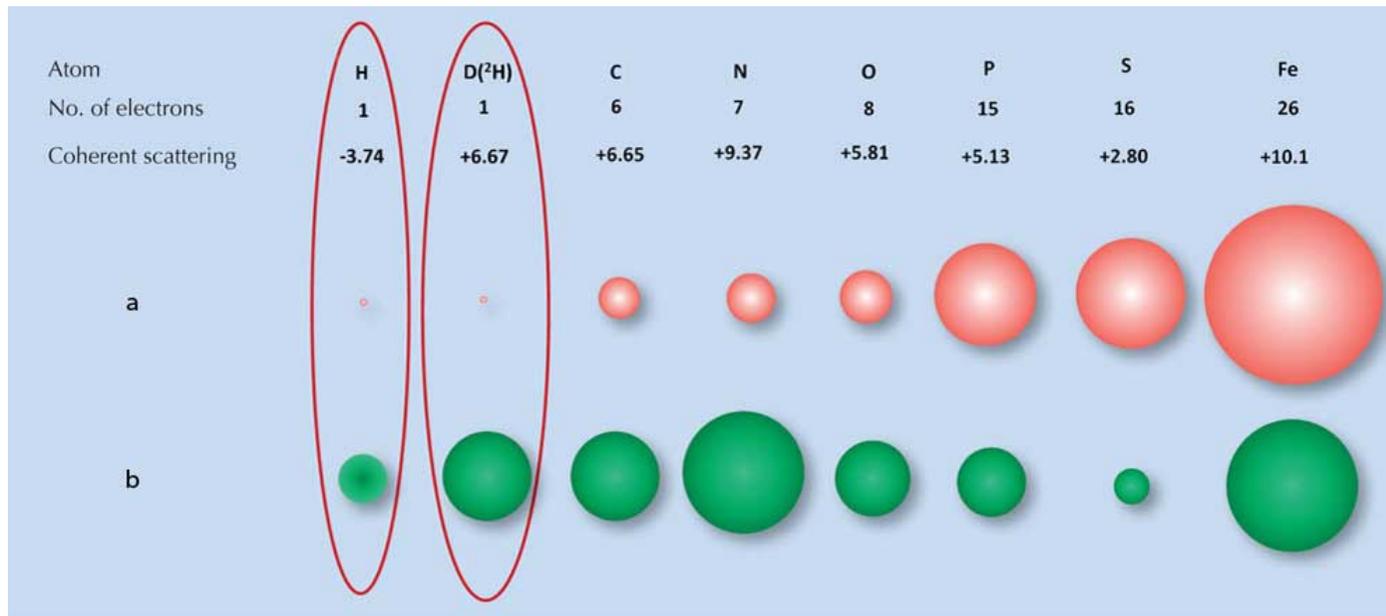


Neutron scattering properties

- Magnitude of scattering by X-rays depends on atomic Z no.
- Neutrons scatter from nuclei and magnitude is independent of Z no.



They can distinguish between different isotopes of the same element, very sensitive to $^1\text{H}/^2\text{H}$ (D)



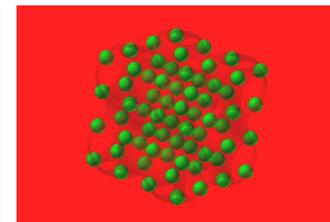
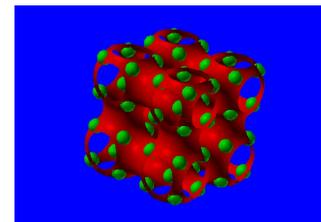
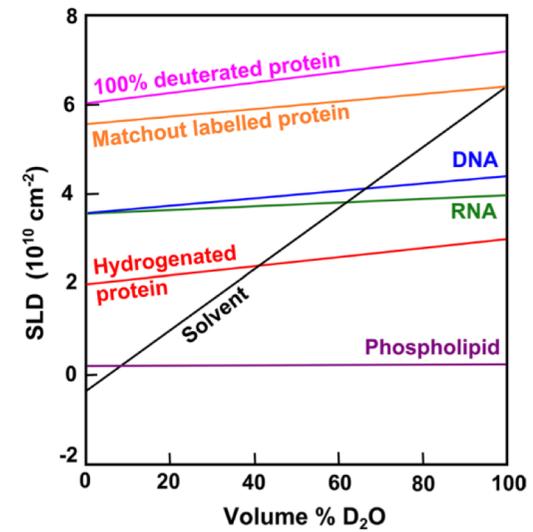
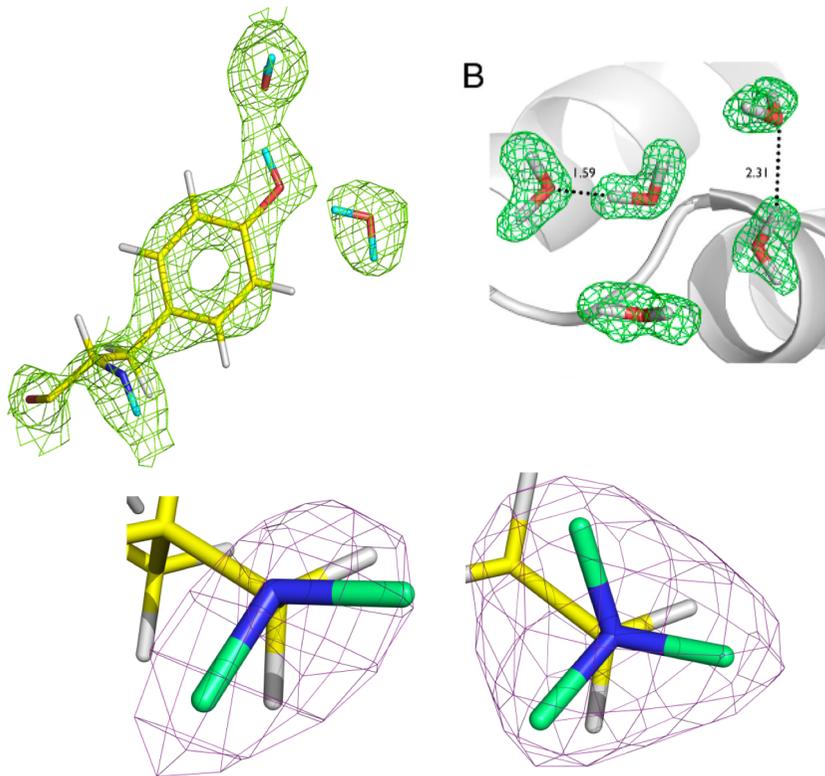
- ^1H have negative scattering & high background
- ^2H (D) has positive scattering & low background

Beneficial to “deuterate” samples. Can be partial, full (per)deuterated vs. H/D exchanged.

Purpose of deuteration depends on technique

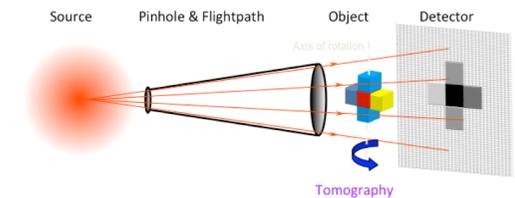
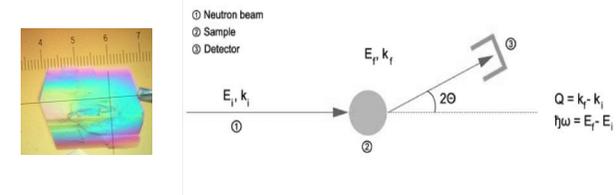
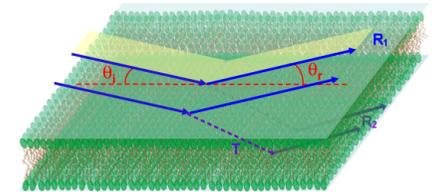
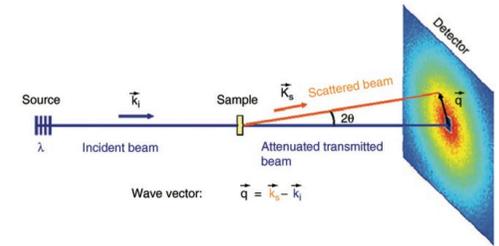
Determine position of **hydrogen** atoms in macromolecular structures

Neutrons enable **contrast variation** through selective deuteration of materials (SANS, NR, Imaging):



Life science using neutrons as a tool

- **SANS:** Low resolution (1-1000 nm) solution studies of large and dynamic complexes eg. protein: protein complex
- **NR:** Measure changes in surfaces (0.2 – 100 nm) e.g thickness or smoothness of lipid bilayer (cell membranes), membrane proteins in bilayers
- **NPX:** Atomic resolution (\AA) crystal structures of macromolecules eg. protein or DNA
- **Imaging:** with neutrons gives contrast that lets us “see” special features that are not possible with optical or X-ray techniques.



Current developments and challenges

- Use of neutrons for biological systems is increasing
- Biomedical problems often very complex and require many techniques and samples can be «precious»
- Deuterium labeling and sample preparation not always simple and also requires specialist facilities/expertise
- Current trend is for neutron facilities to provide more on-site laboratories, support, expertise in the form of scientific partnerships & collaborations

Contact & more information

- General info about ESS science & instruments:

<https://europeanspallationsource.se/science-instruments>

- Information about DEMAX labs, access, proposals:

Contact: Zoë Fisher zoe.fisher@ess.eu

<https://europeanspallationsource.se/science-support-systems/demax>

- Science Focus Team for Life Science and Soft Matter

Contact: Esko Oksanen esko.oksanen@ess.eu