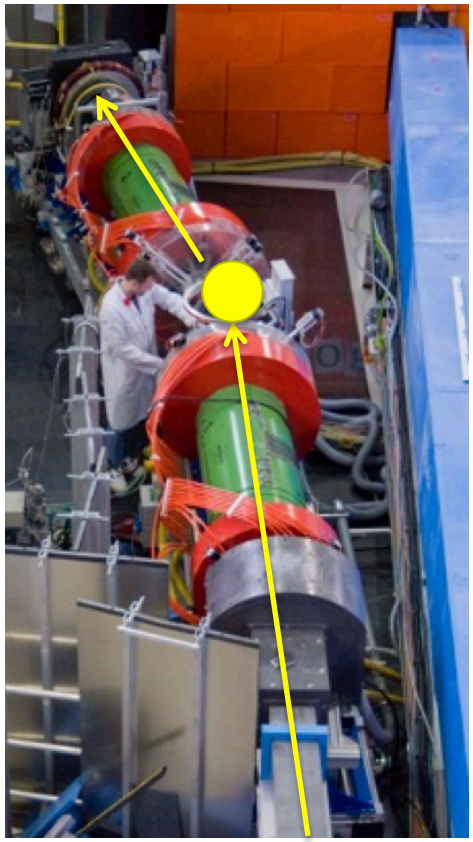
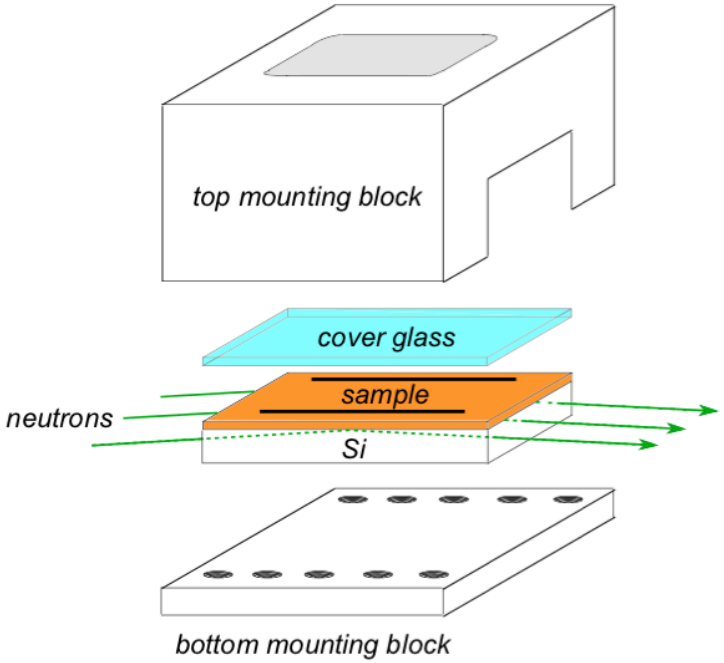
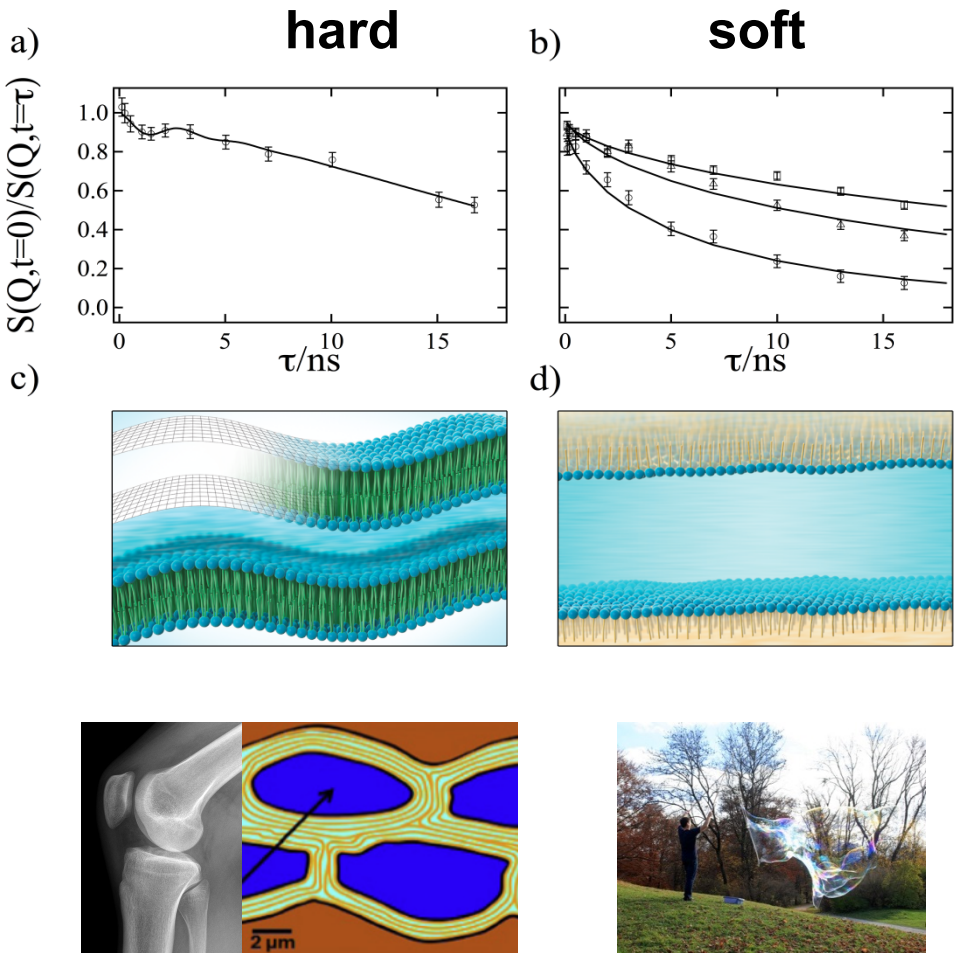
GINSES: Setup and Geometry





- Experiments performed at MLZ, Garching, Germany and SNS, Oak Ridge, USA
- Sample submerged in D_2O, 35°C

Comparison with soft membranes

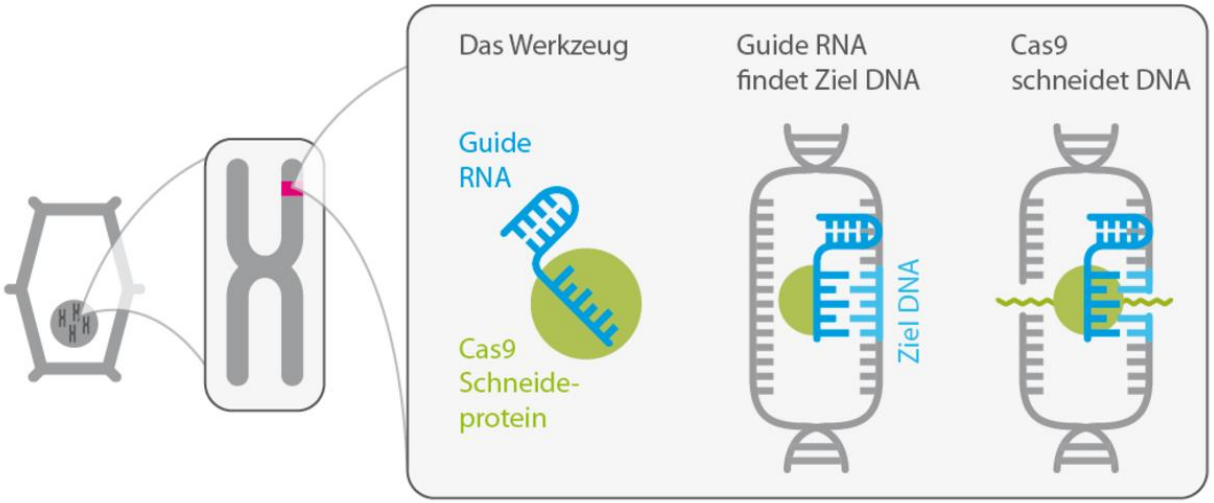


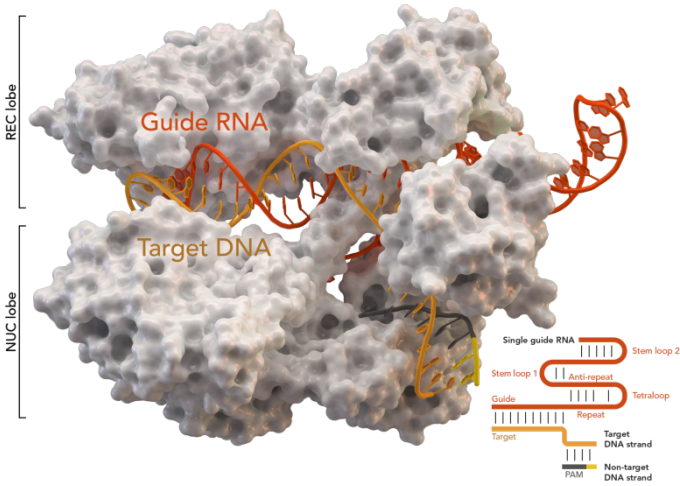
- Surface modes exist only for stiff membranes
- These undulations allow for long membranes lifetimes
- difference between cartilage and soap bubbles

Jaksch, S.; Frielinghaus, H. et al. Nanoscale rheology at solid-complex fluid interfaces, submitted (2016)

What moves biology forward at the moment:

- System biology: Understanding the interplay between proteins, RNA, etc. and Regulatory mechanisms in the cell and between cells.
- Using the knowledge of structural biology to change these processes
- Gene editing using CRISPR-Cas9





Our competition in Structural Biology in the next 5-10 years

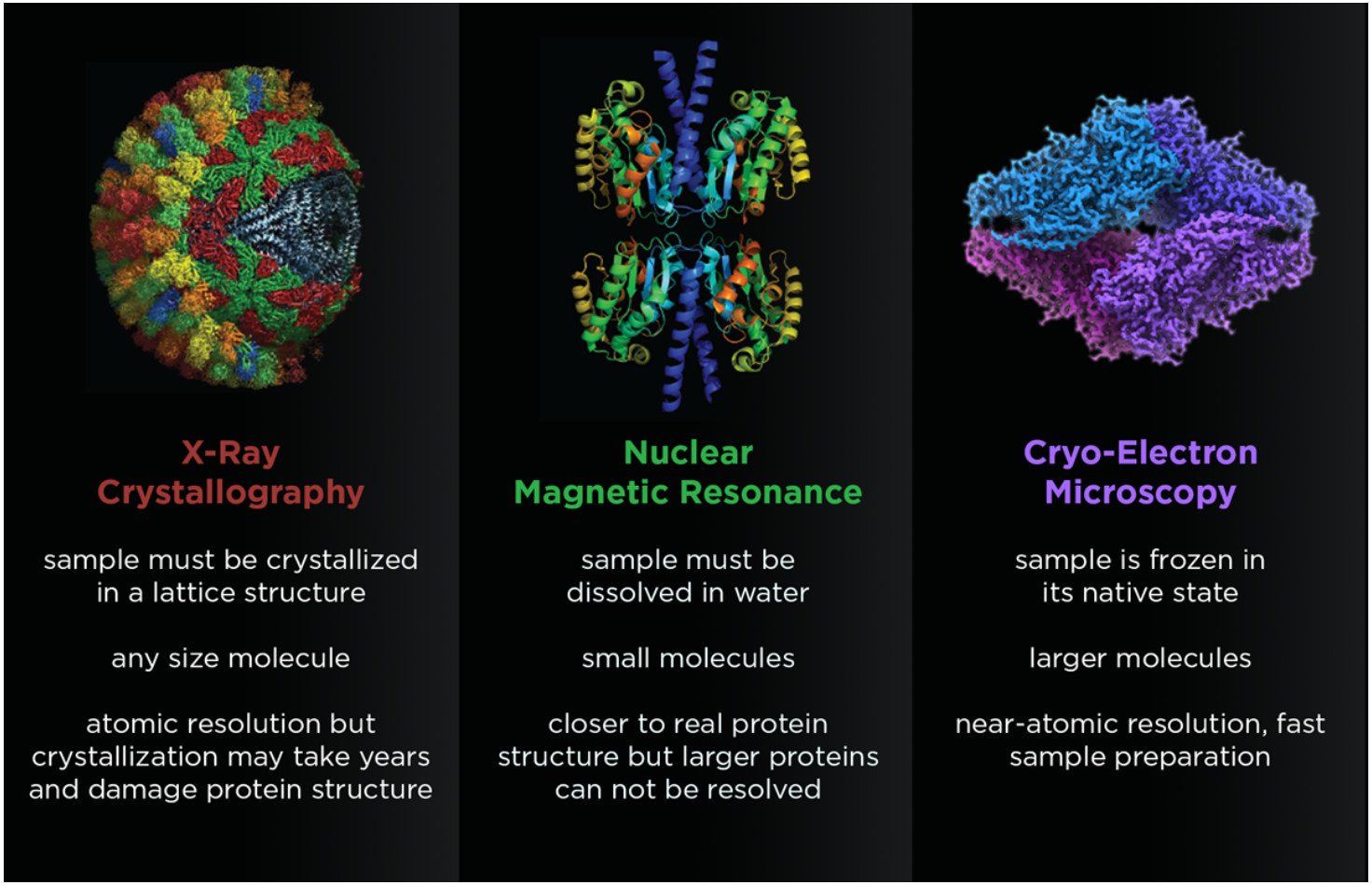
Tobias E. Schrader

Overview over structural biology techniques

- Cryo-EM
- X-ray Crystallography
- NMR (liquid phase)
- Solid State NMR
- Solution SANS/SAXS
- X-ray FEL
- Ultra high resolution Mass Spectrometry
- Electron diffraction
- Neutron Protein Crystallography

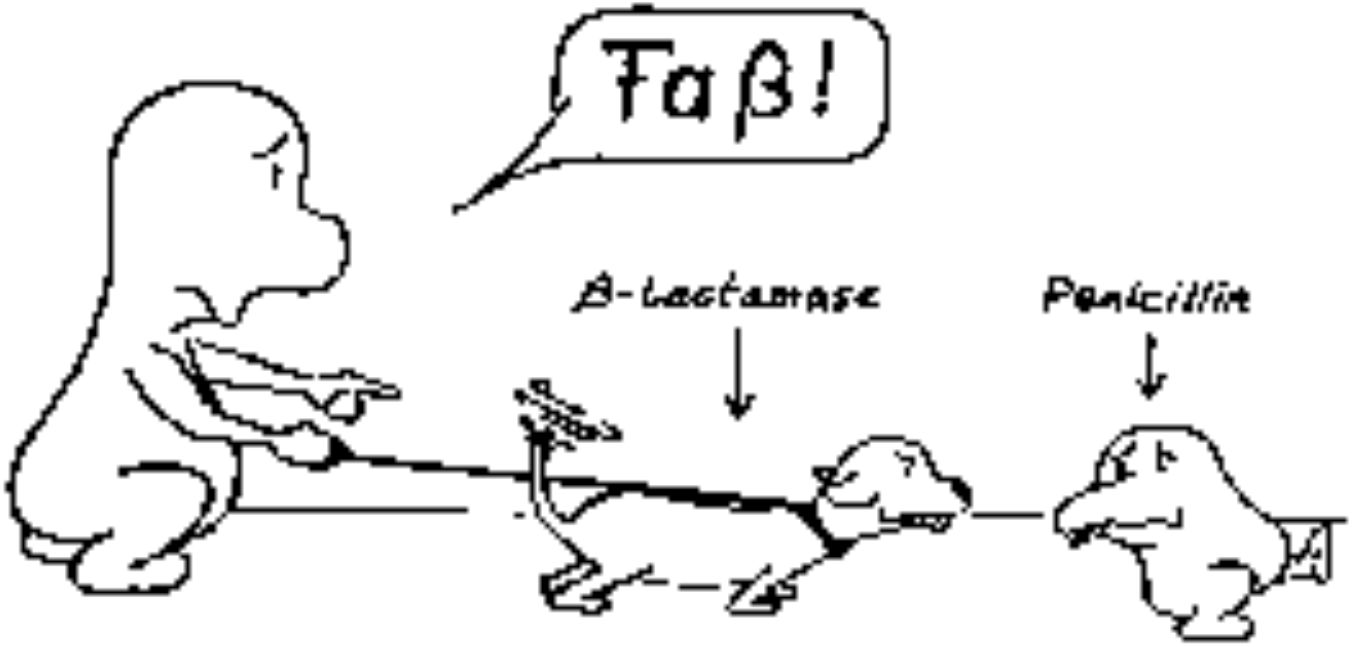
Only the red labelled methods can see the hydrogen atoms directly!

Methods in Structural Biology

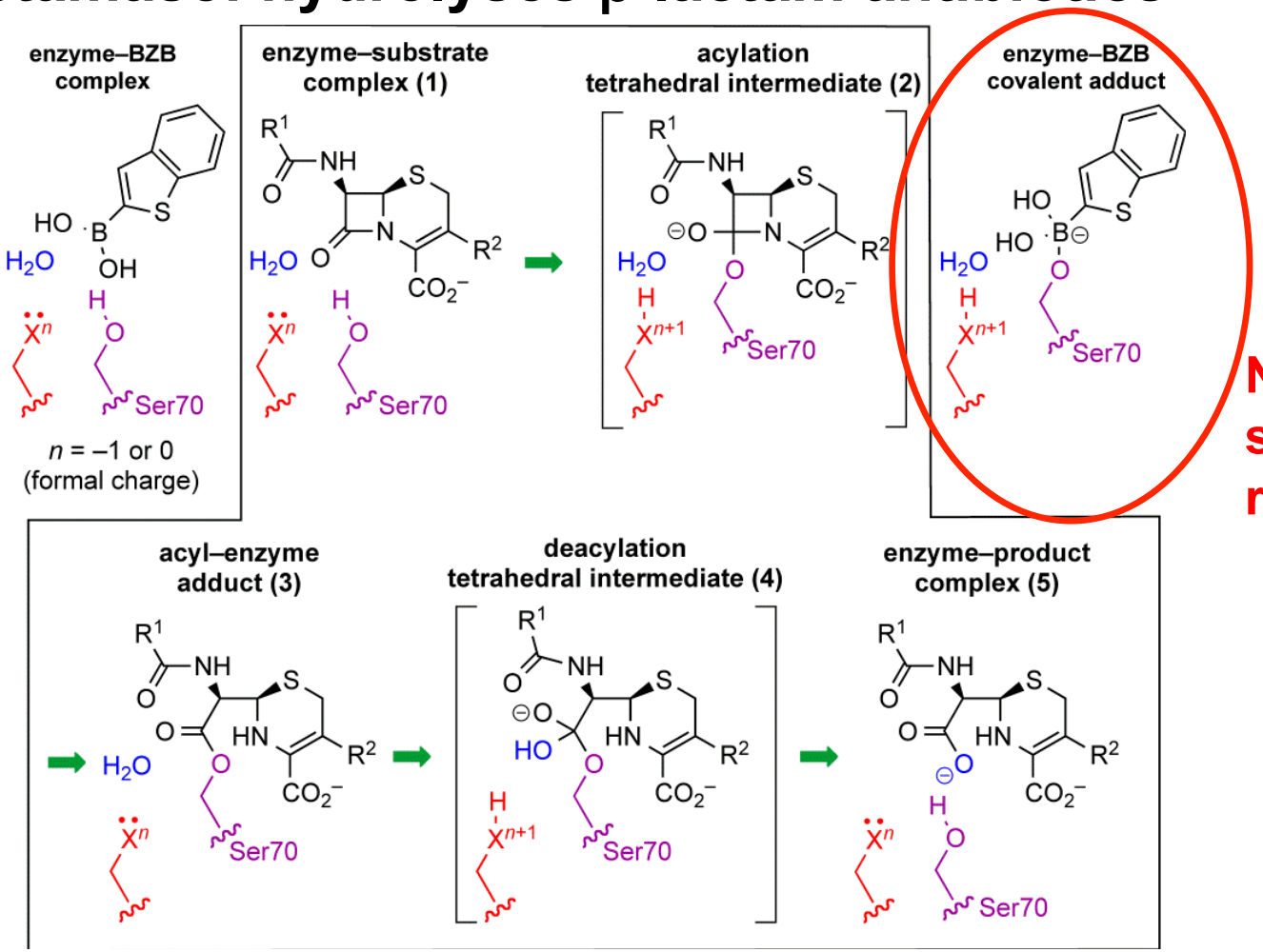


Application example of neutron protein crystallography: Protonation state of amino acid residues

The protein β-lactamase



β-lactamase: hydrolyses β-lactam antibiotics

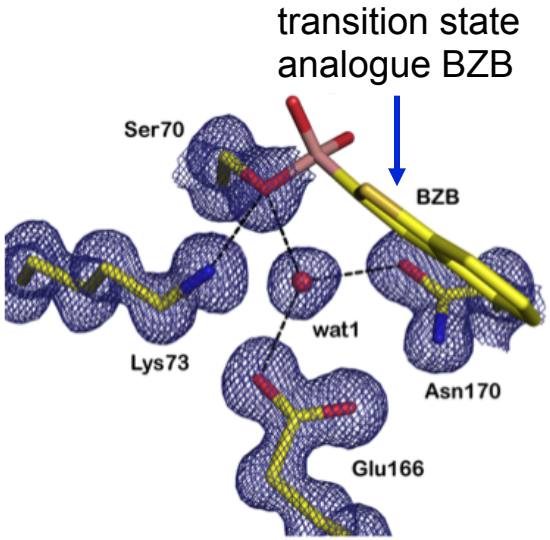


Neutron structure recorded

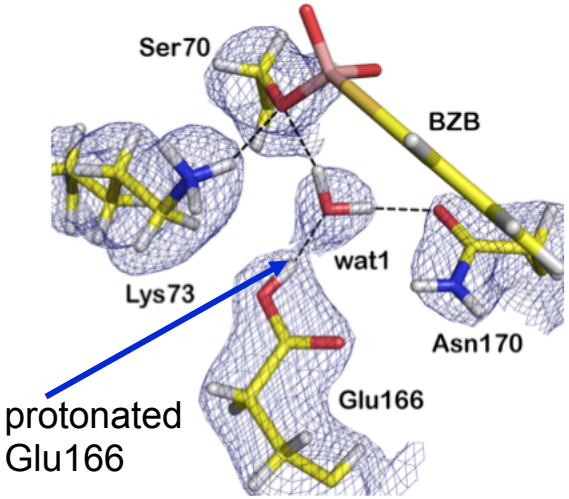
The catalytic cycle of a class A β-lactamase illustrated for a cephalosporin substrate (inside box) and the mode of inhibition by BZB (outside box). The general base employed is not necessarily the same for acylation and deacylation. The overall reaction pathway for β-lactam hydrolysis of a cephalosporin-like substrate by the class A β-lactamase enzymes.

Figures from: Tomanicek et al., doi: 10.1074/jbc.M112.436238

Catalytic Proton Network of the Toho-1 β-Lactamase



electron density map

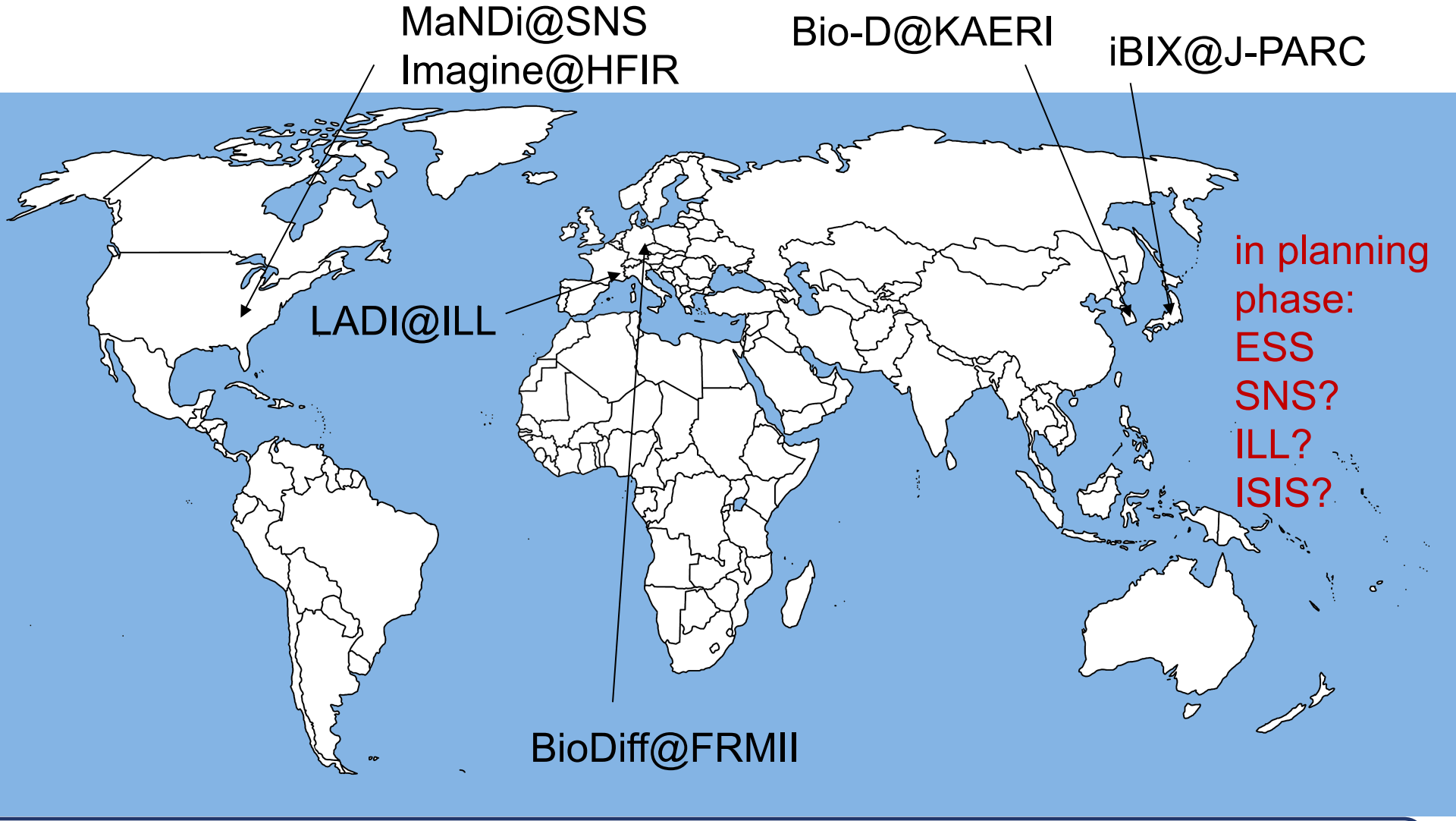


nuclear density map from BioDiff

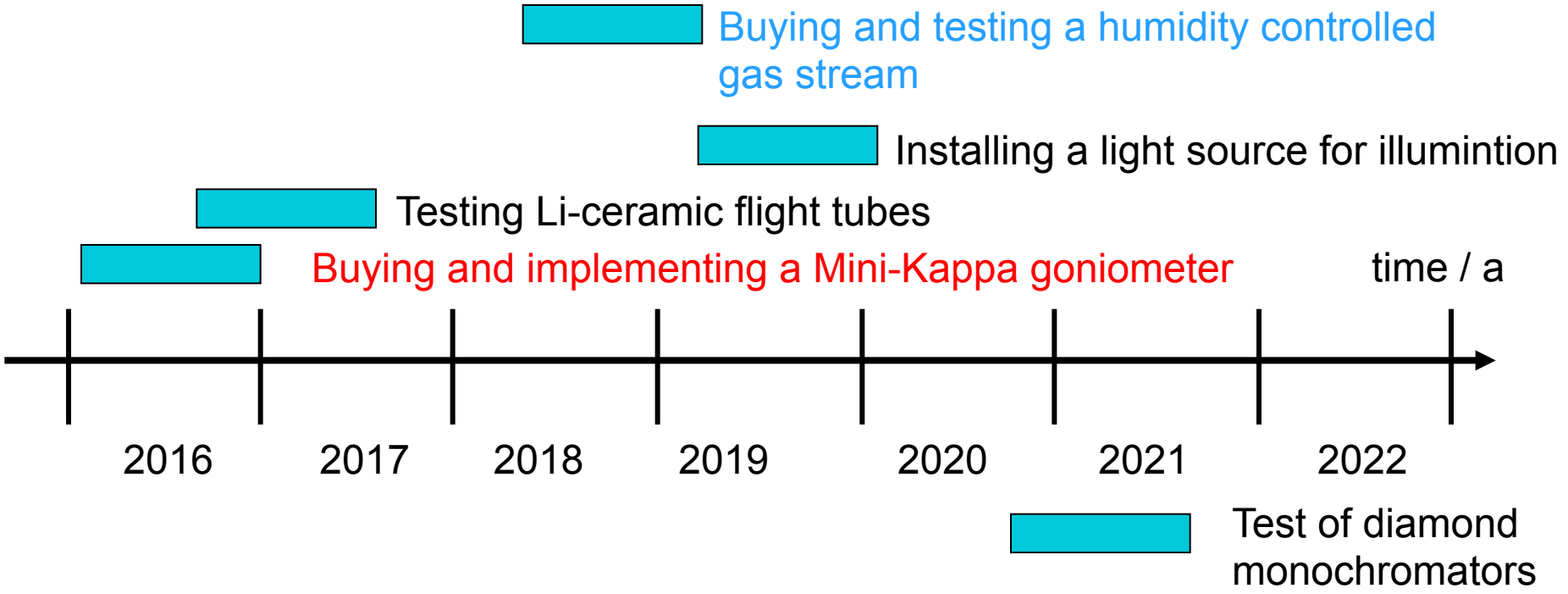
Glu166 acts as the general base during the catalytic action of the enzyme.

Stephen J. Tomanicek, Robert F. Standaert, Kevin L. Weiss,
Andreas Ostermann, Tobias E. Schrader, Joseph D. Ng, and Leighton Coates
J. Biol. Chem. 2013, 288:4715-4722

World map of neutron diffractometers optimized for protein crystals



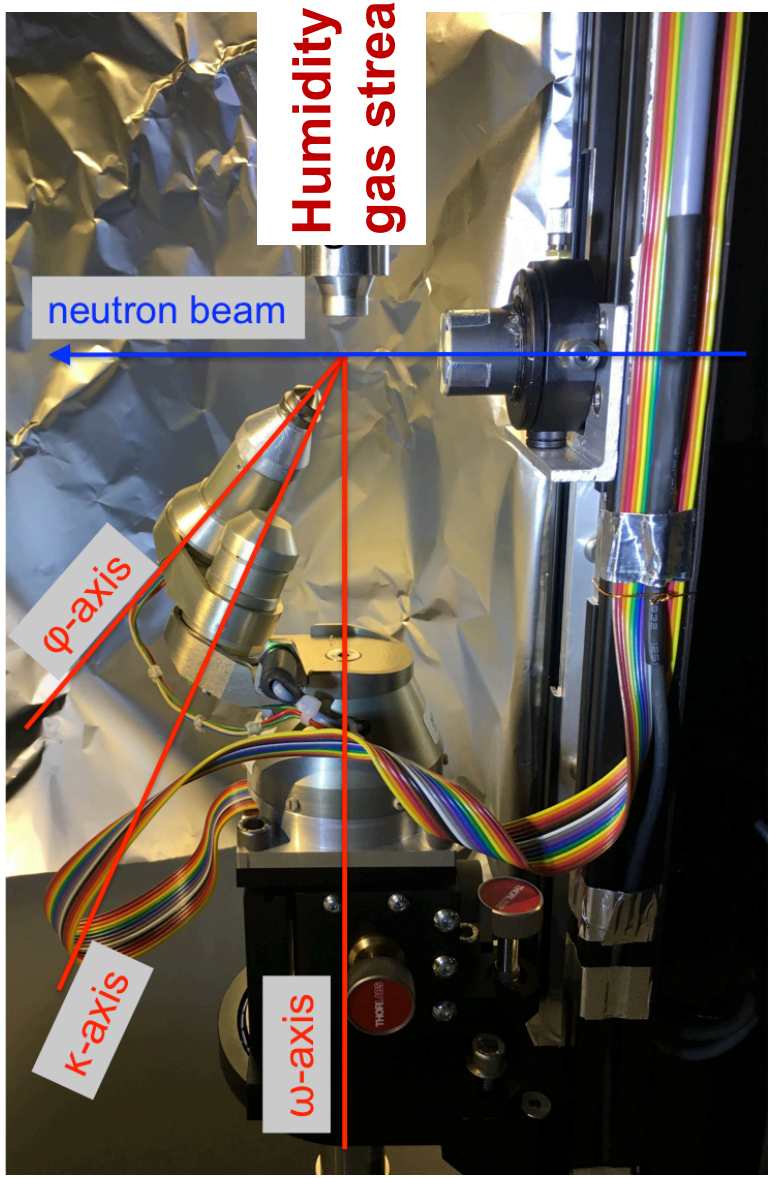
The Instrument Development Programme: Time Schedule



Possible PhD project together with Andreas Stadler, investment costs of ca. 30 k€.

New **BioDiff Upgrade:**

mini-kappa-goniometer
with humidity gas stream

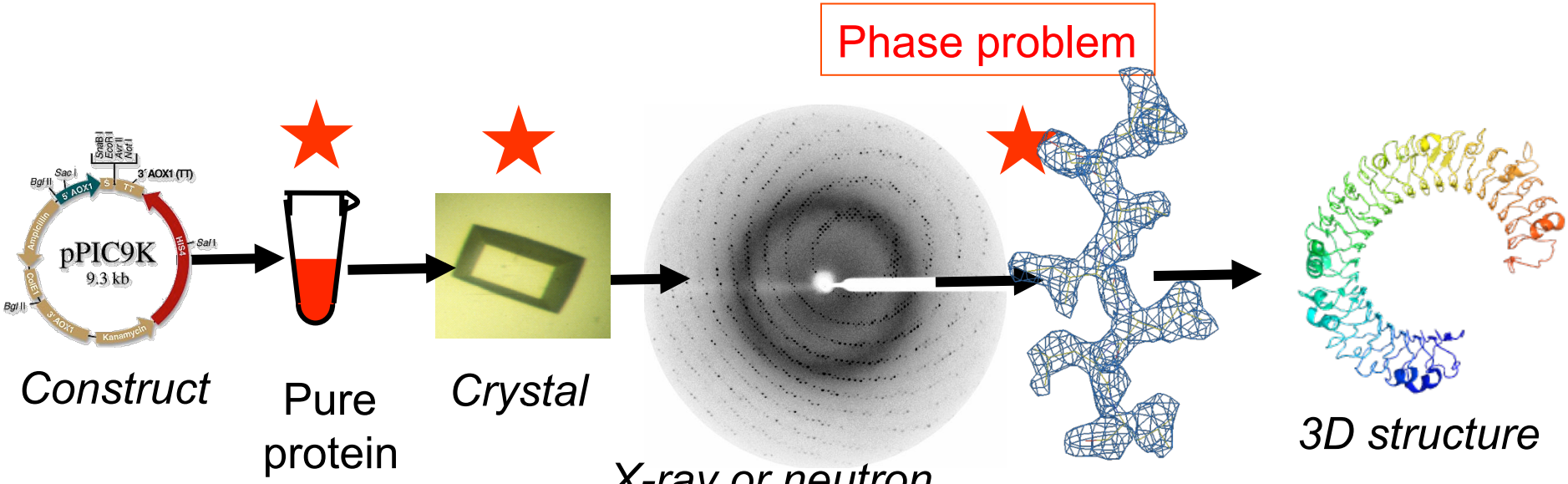


➡ Measurements possible at 4°C

↷ no need for a capillary

➡ hydration dehydration studies to optimize the resolution of the data set

Crystallography: Expand along the value chain…

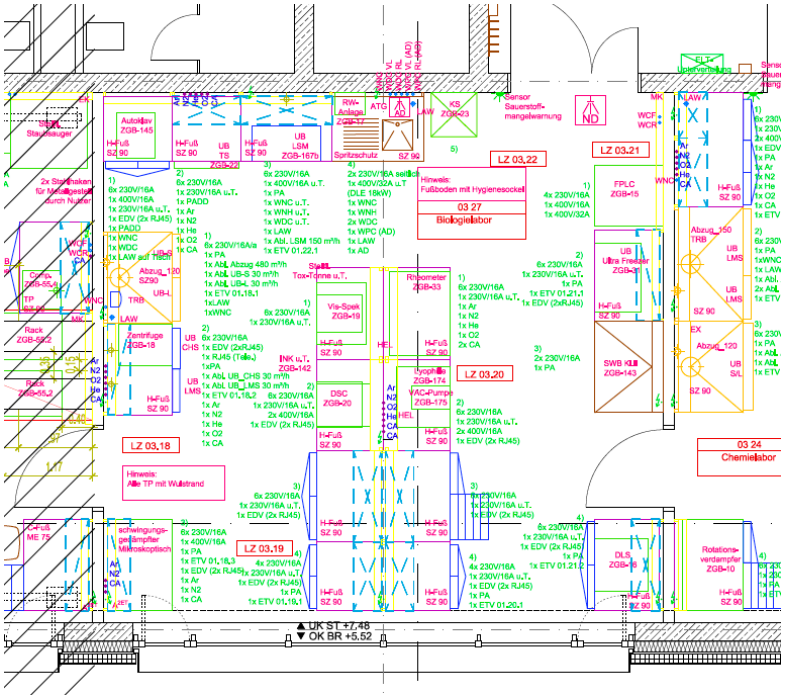


- Get earlier access to the user
- Pursue one‘s own research ideas
- Create more value to the user

My running projects

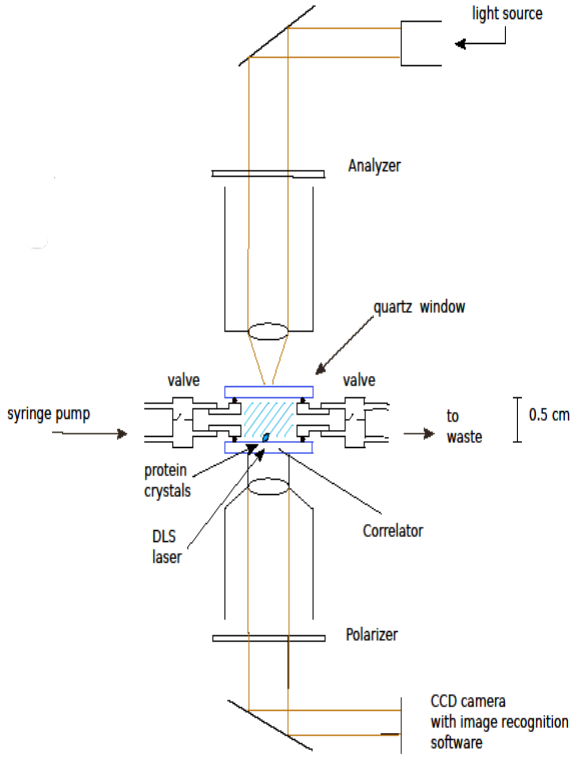
- Biology lab in the new building:

S1 grade lab: Setting up a protein production facility.



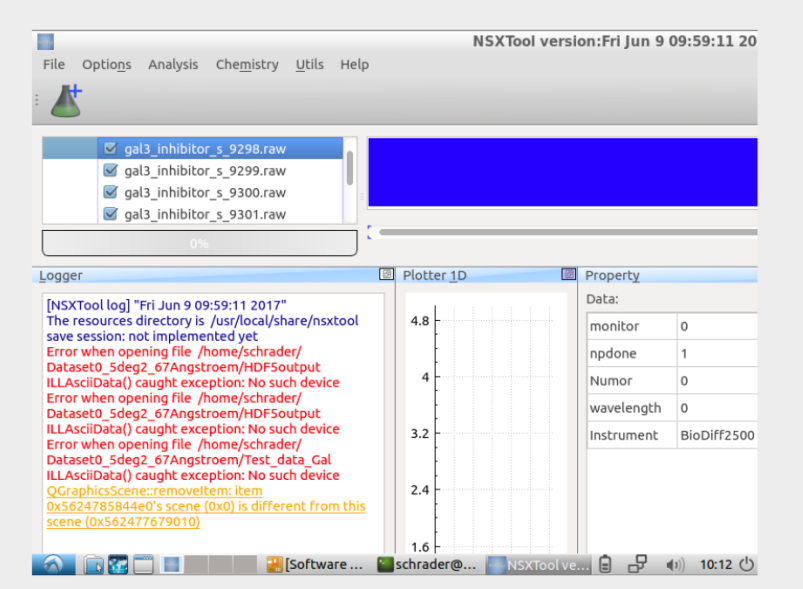
Technician: Kerstin Koch

- SINE2020 Project (Marialucia Longo) on large protein crystal growth: Test model system Streptavidin/Biotin; building a crystal growth apparatus



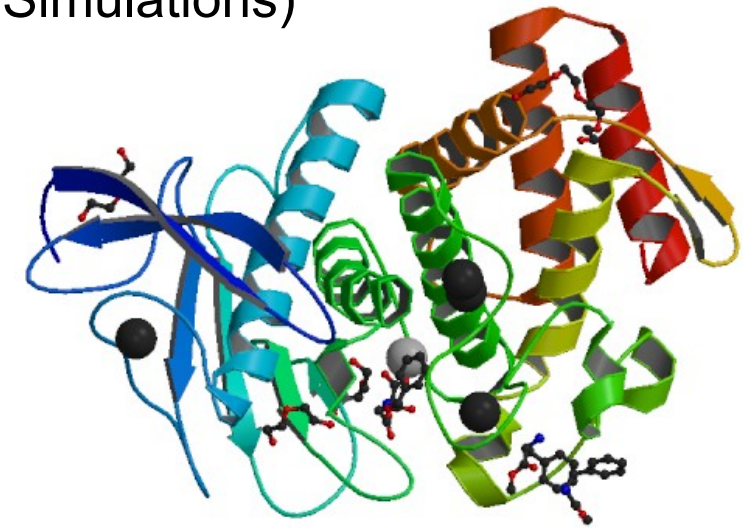
My running projects II

- Data reduction software writing with Jonathan Fisher from the Scientific computing group.



Optimize r-factors, get the best resolution and completeness out of one crystal

- DFG SP 1934 on the role of PEG and site directed mutagenesis in protein crystallization: PhD students Phillip Nowotny, Johannes Hermann (MD-Simulations)



NMR binding studies together with Ralf Biehl and Margarita Kruteva