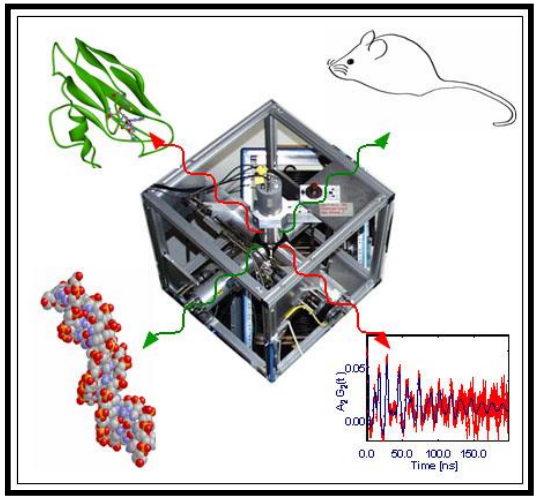
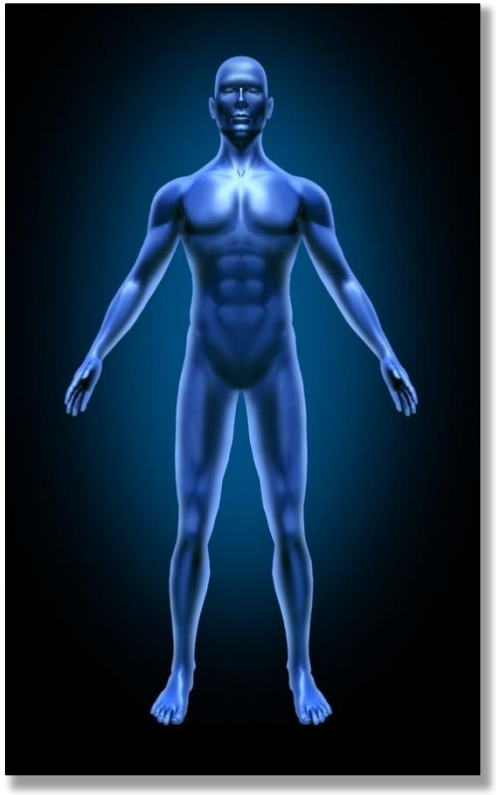
Cu(I), Ag(I), Cd(II), Hg(II), and Pb(II) binding to biomolecules studied by Perturbed Angular Correlation of γ-rays (PAC) spectroscopy (P-427)

L. Hemmingsen, P. W. Thulstrup (Univ. of Copenhagen, DK)
V. L. Pecoraro (Univ. of Michigan, USA)
A. Jancso (Univ. of Szeged, HU)
J. Müller (Westfalische Wilhelms Univ., DE)
K. Johnston, M. Stachura, J.G.M. Correia (CERN, CH)



Chem. Rev. **2004**, 104, 4027-4062

Metal ions in biological systems



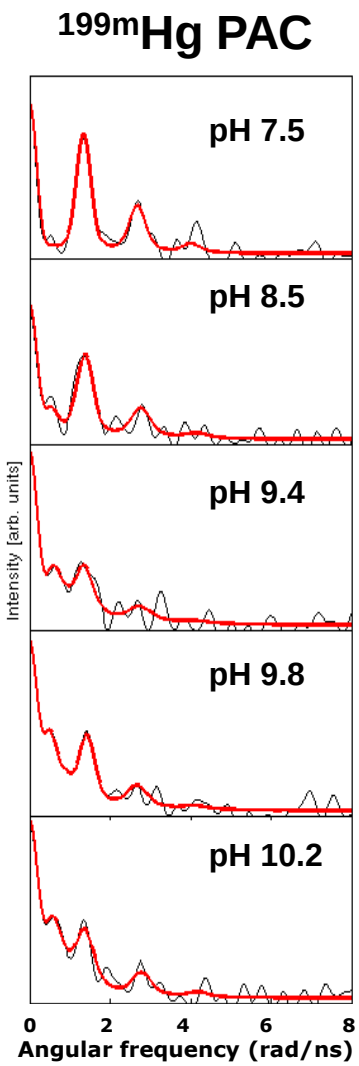
- Metal ions → essential components in protein structure and function
- Metal ions → used to control structure and function of synthetic molecules → tool in design of a desired function

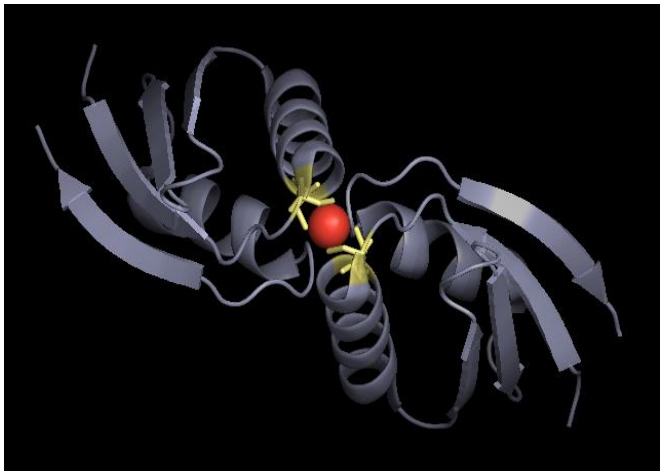
This project:

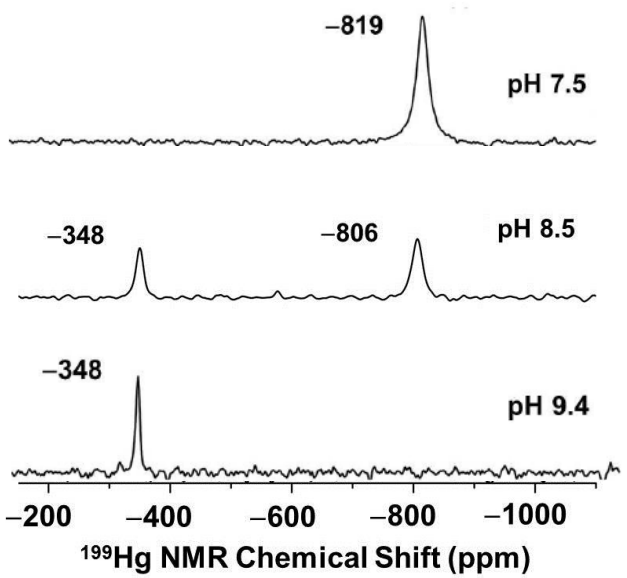
- Function of metal ions in natural systems
- Function of metal ions in synthetic molecules
- Metal-mediated DNA structures
- Toxic effect of some metal ions (Cd, Hg, Pb)

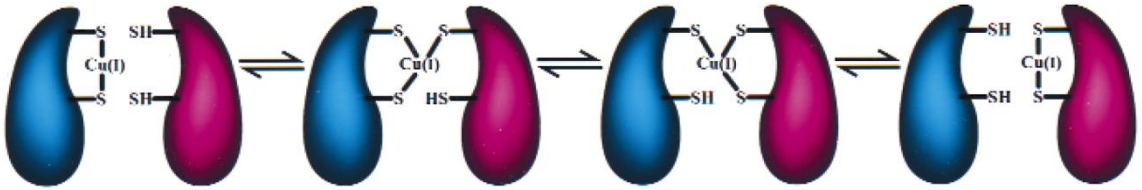
Metal ion transfer between proteins:

The Cu(I) binding protein HAH1 (^{199m}Hg-PAC)



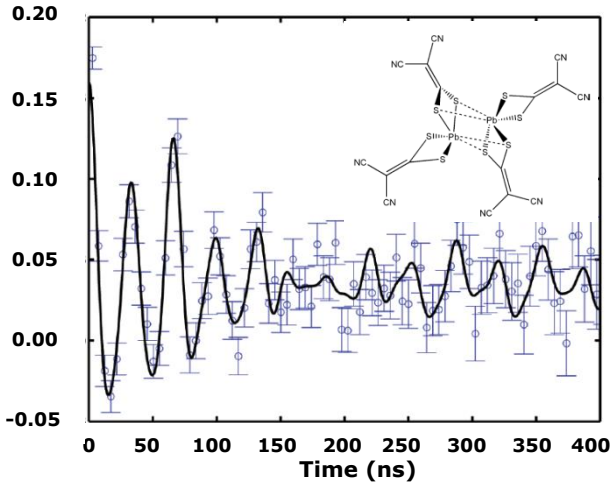


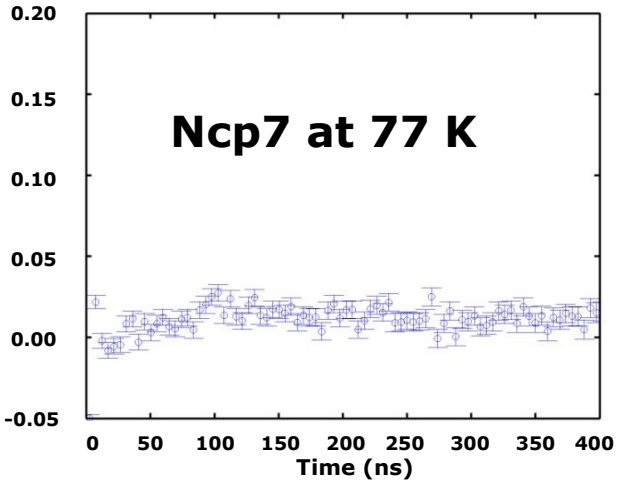


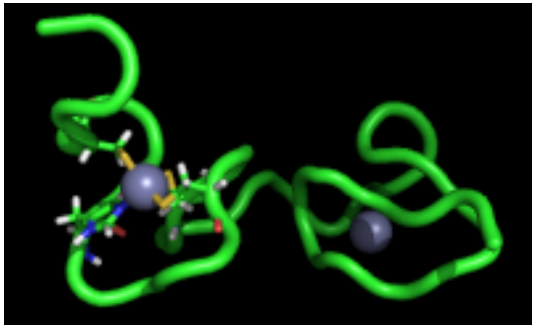


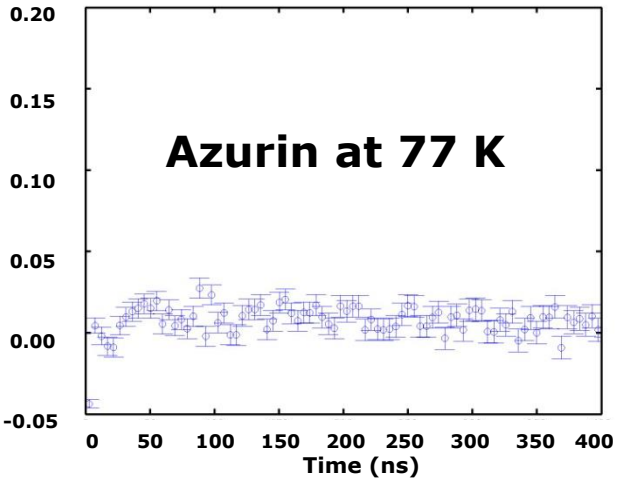
Wernimont et al. Nat. Struct. Biol., 2008, 102, 114
Luczkowski et al., Chem. Eur. J. 2013, 19, 9042

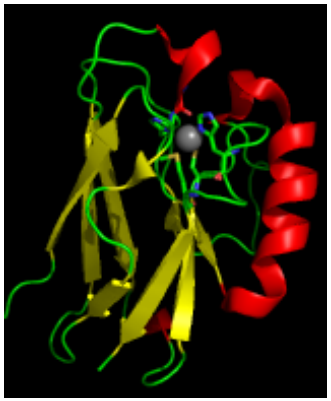
^{204m}Pb-PAC spetroscopy on proteins (lead toxicity)



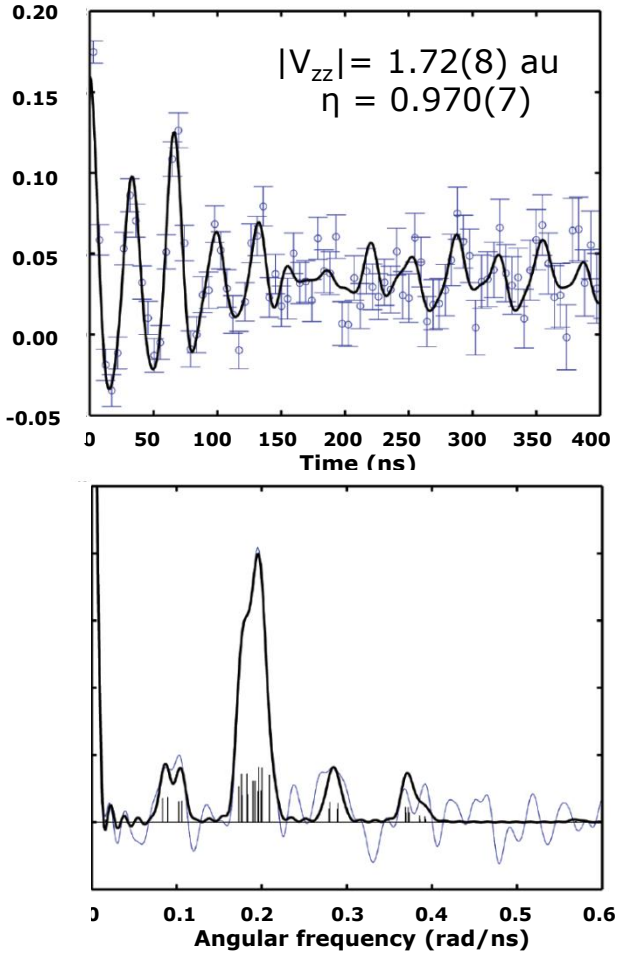








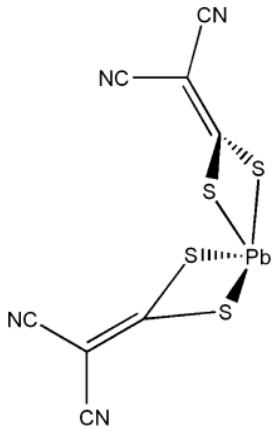
Lead toxicity: ^{204m}Pb-PAC spetroscopy on a molecular crystal

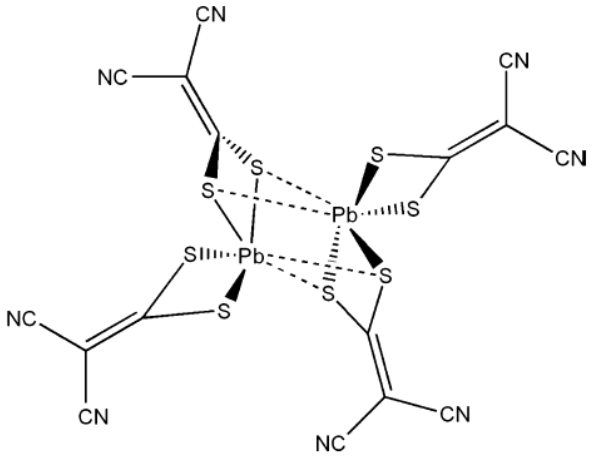


PW91/QZ4P, ZORA:

V_{zz} = 2.32 au
η = 0.59

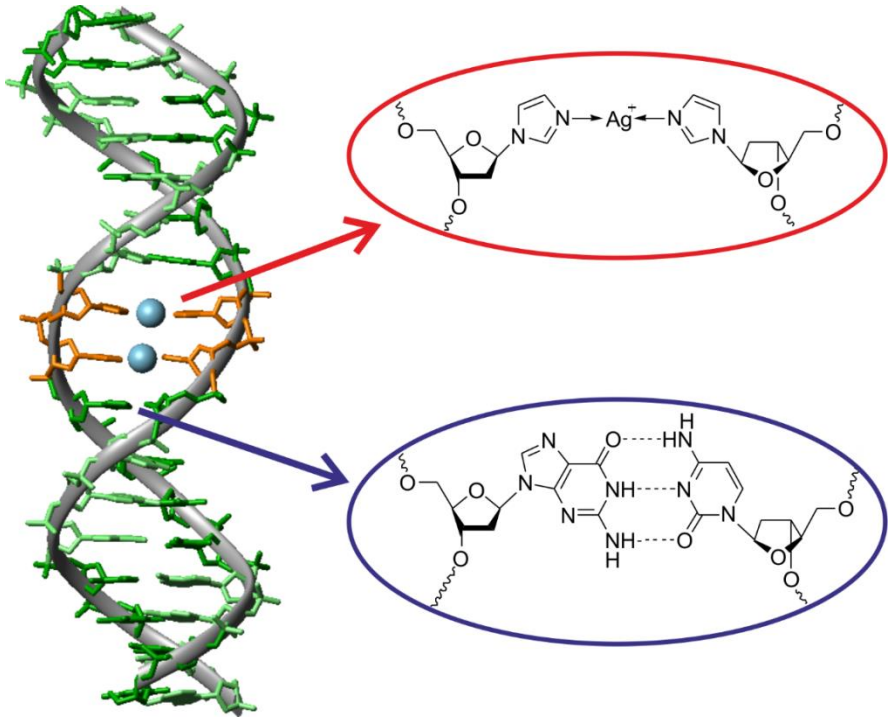
V_{zz} = 1.51 au
η = 0.77





Vibenholt J., Schau-Magnussen M., Stachura M., Thulstrup P.W., Arcisauskaite V., Bjerrum M.J., Hemmingsen L. Inorg. Chem. **2012**, 51,1992-1994

^{111}Ag-PAC: DNA duplex with two Ag(I)-mediated base pairs



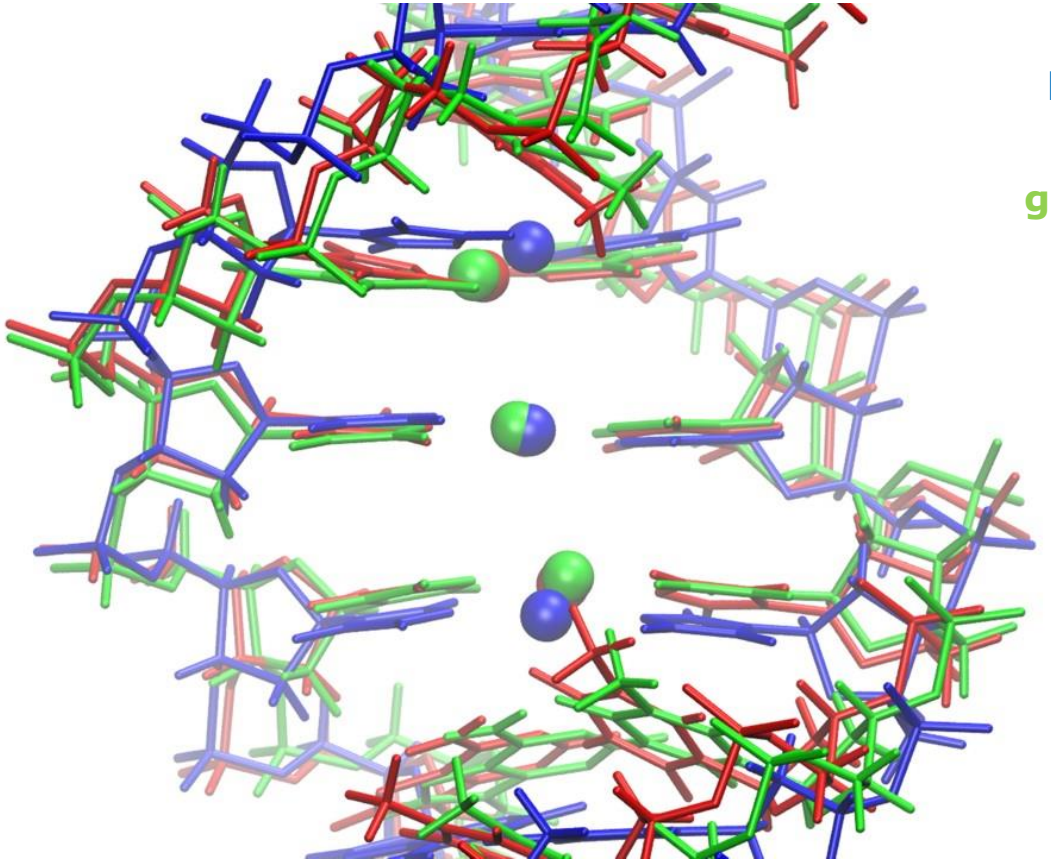
- Metal-modified nucleic acids
- Applications: nanoscale electronic architectures
- Structure of the local metal site: unknown
- Effect of multiple neighbouring metal ions: unknown

This project:

- Structure, electronic properties of the Ag(I) binding site: mono- and di-nuclear → differences, interaction
- Low Ag(I) concentration → high Ag(I) concentration
- Ag(I) vs Cd(II) binding (frozen solution)

Adapted from: S. Johannsen, N. Megger, D. Böhme, R.K.O. Siegel, J. Müller, Nat. Chem. 2010,2, 229-234

Comparison of experimental and computed structures



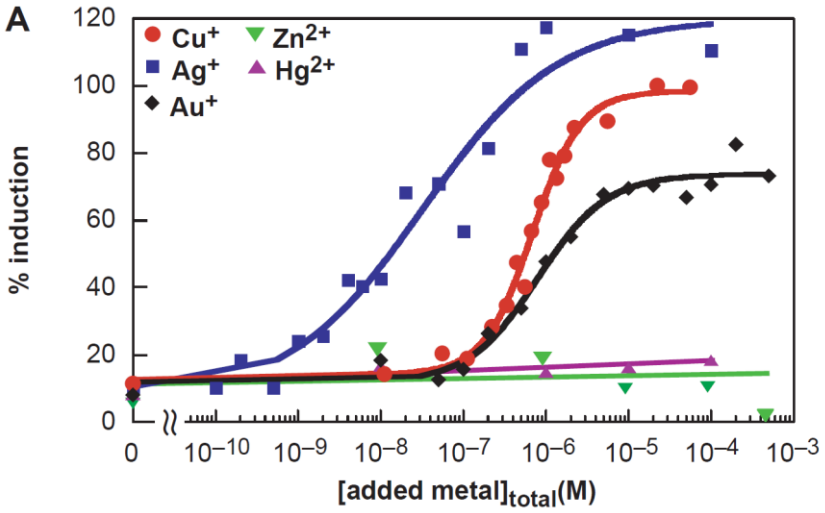
blue: experimental NMR structure
red: gas phase QM/MM structure
green: solvated QM/MM structure

Disagreement between experiments and calculations !

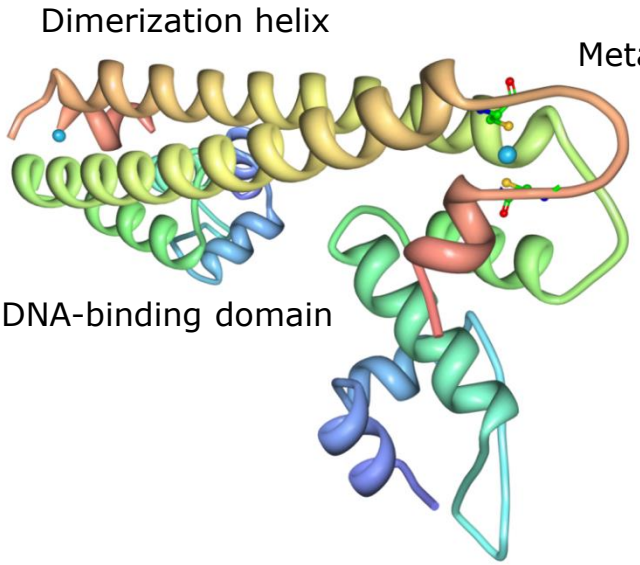
S. Kumbhar, S. Johannsen, R.K.O. Siegel, M.P. Waller, J. Müller, J. Inorg. Biochem. 2013, 127, 203-210

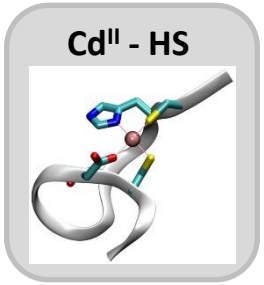
X-ray structure of the Cu^{I} form of *E. Coli* Cu-efflux regulator (CueR)

- M^{I} ions restricted to a linear coordination environment
- CueR: two Cys in the metal binding loop
- CueR responds to the monovalent group 11 metal ions (Cu^{I},Ag^{I},Au^{I}) but shows no activity in the presence of the divalent ion Hg^{II} or Zn^{II}.
- M^{I} sensing factor of CueR: unknown



Overall structure of the CueR dimer (PDB: 1Q05)





A. Changela, K. Chen, Y. Xue, J. Holschen, C.E. Outten, T.V. O'Halloran, A. Mondragón, Science 301, 1383-1387, 2003

Requested shifts

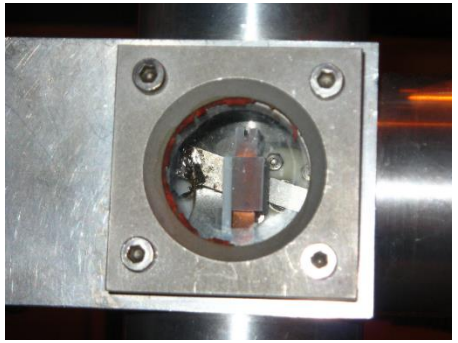
Isotope	Target	Ion Source	Yields [ion/μC]	Shifts
^{111m}Cd	Sn	HP (VADIS)	$2 \cdot 10^8$	6
^{111}Ag	UC_X	RILIS (Ag)	$5 \cdot 10^7$	6
^{199m}Hg	Pb	HP (VADIS)	$2 \cdot 10^8$	6
^{204m}Pb	UC_X	RILIS (Pb)	$2 \cdot 10^8$	3
^{61}Cu	ZrO_2	RILIS (Cu)	$1 \cdot 10^8$	0.5
^{68m}Cu*	UC_X	RILIS (Cu)	$1 \cdot 10^8$	0.5

* *Online experiment at VITO*

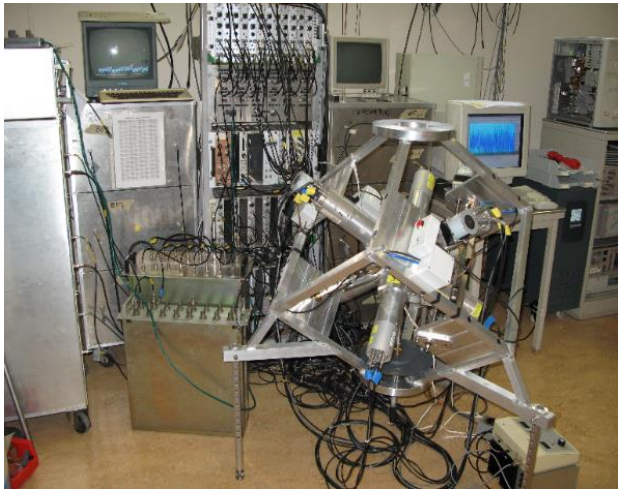
Total: 22 shifts / 2 years

PAC experiments

Collections into ice in the biophysics chamber attached to GLM:

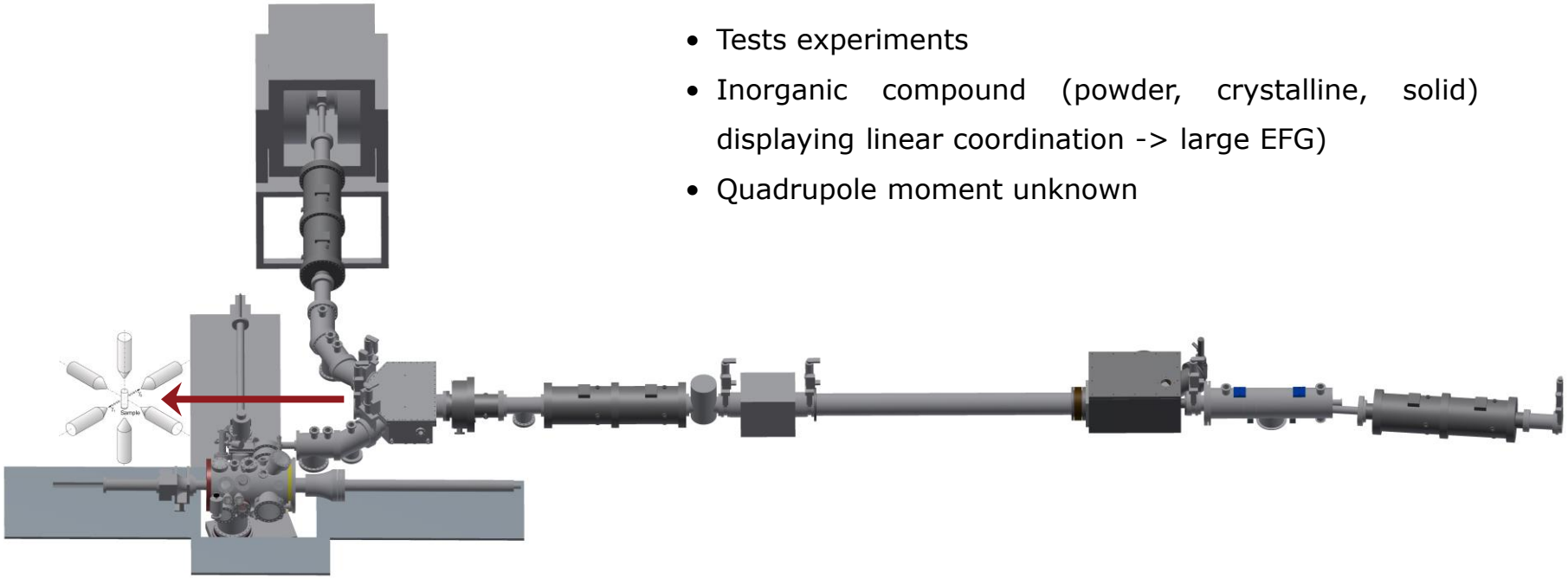


Offline sample preparation (chemistry lab) and measurements (solid state physics lab):



^{68m}Cu-PAC on VITO (online experiment)

β-NMR end-station



ASPIC end-station

- Tests experiments
- Inorganic compound (powder, crystalline, solid) displaying linear coordination -> large EFG)
- Quadrupole moment unknown

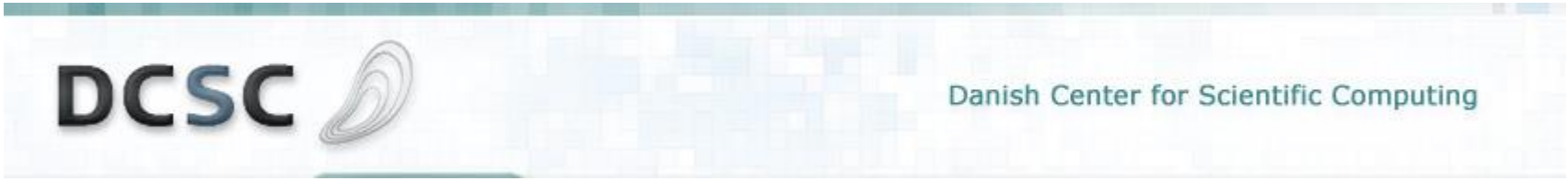
Funding


CERN

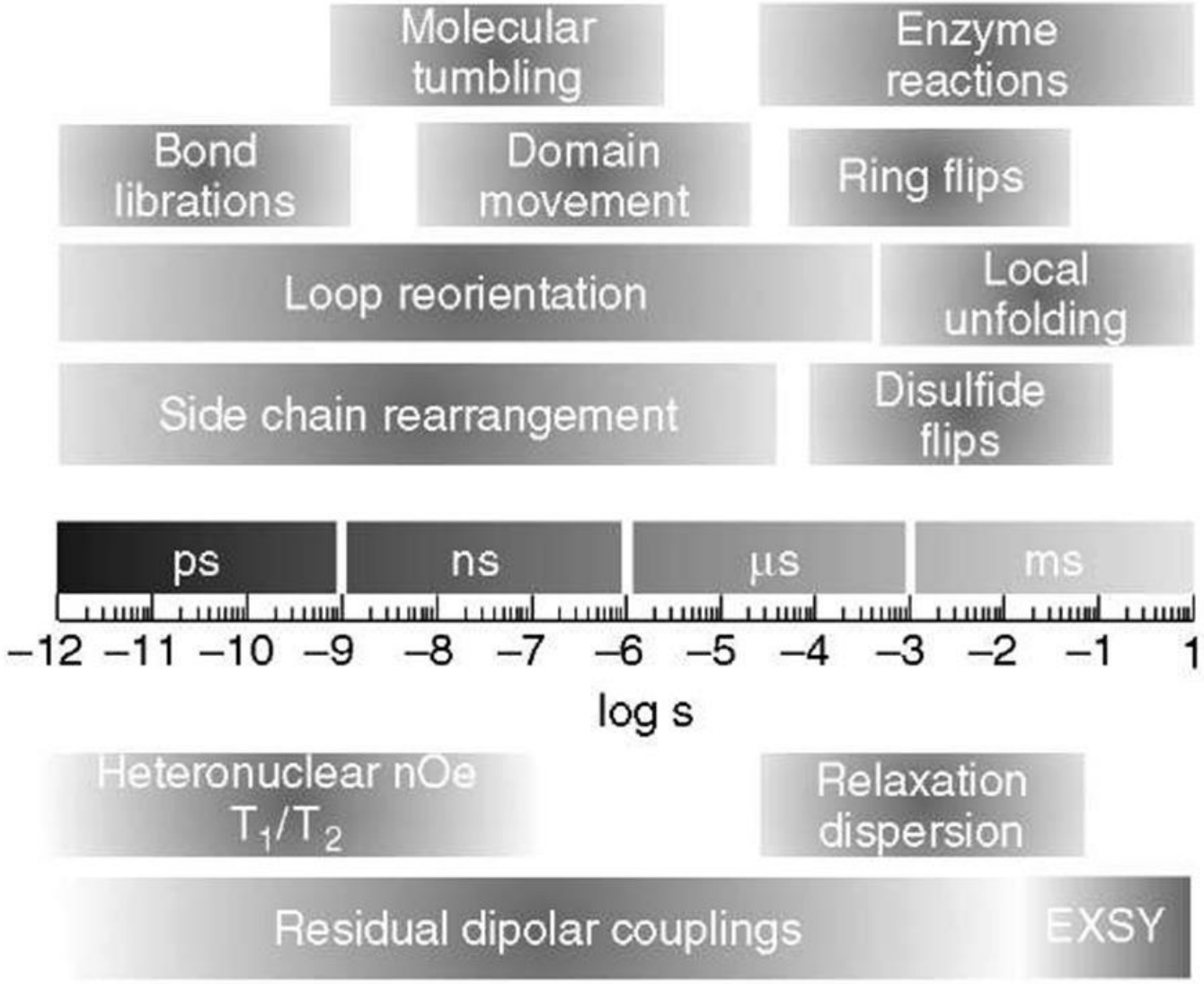

Bundesministerium
für Bildung
und Forschung


Danish Agency for Science
Technology and Innovation
Ministry of Science
Technology and Innovation

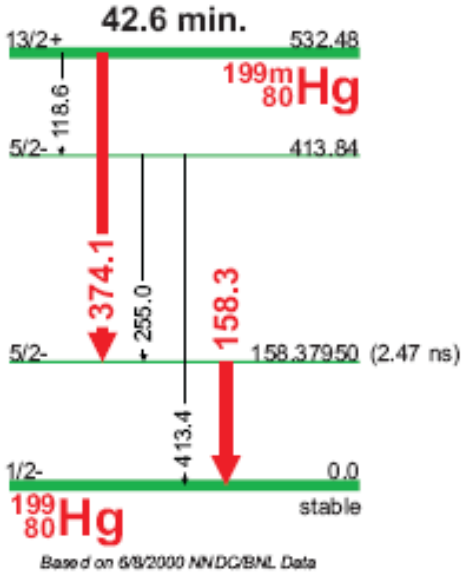

Liberté • Égalité • Fraternité
RÉPUBLIQUE FRANÇAISE
AMBASSADE DE FRANCE
AU DANEMARK


DCSC
Danish Center for Scientific Computing


VILLUM KANN RASMUSSEN FONDEN
& VELUX FONDEN


Molecular tumbling
Enzyme reactions
Bond librations
Domain movement
Ring flips
Loop reorientation
Local unfolding
Side chain rearrangement
Disulfide flips
ps
ns
µs
ms
–12 –11 –10 –9 –8 –7 –6 –5 –4 –3 –2 –1 1
log s
Heteronuclear nOe
T_1/T_2
Relaxation dispersion
Residual dipolar couplings
EXSY

^{199m}Hg



Half life: 42,6min
Decay propoerties: IT mode
γ-γ cascade: 374 keV
158 keV
Half-live of the intermediate state:
2.3 ns

^{204m}Pb

Half life: 67,2min
Decay propoerties: IT mode
γ-γ cascade: 912 keV
375 keV
Half-live of the intermediate state: 265 ns