Biological Applications of Perturbed Angular Correlations of γ-Ray Spectroscopy

IS448: “Pb(II) and Hg(II) binding to de novo designed proteins studied by 204mPb- and 199mHg-Perturbed Angular Correlation of gamma rays (PAC) spectroscopy: clues to heavy metal toxicity”

Monika Stachura
University of Copenhagen

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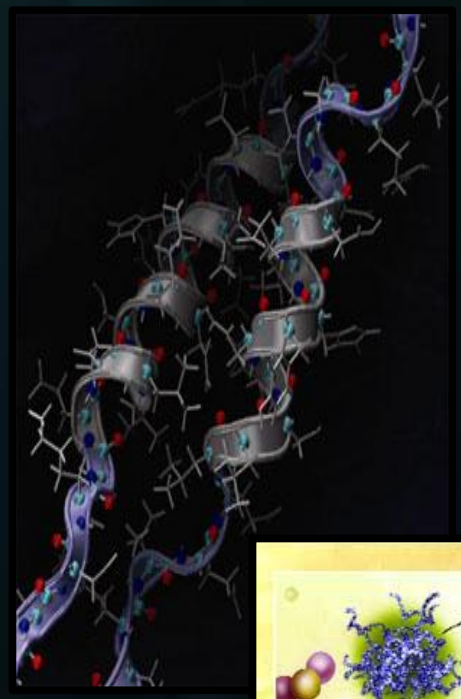
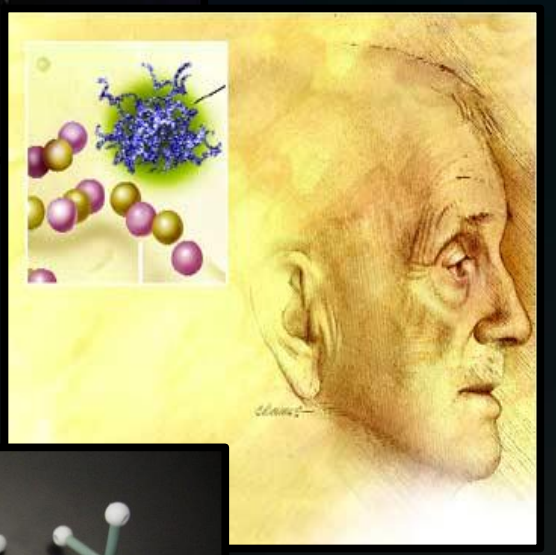
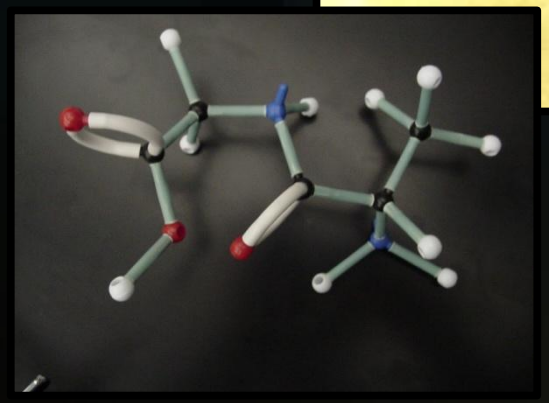






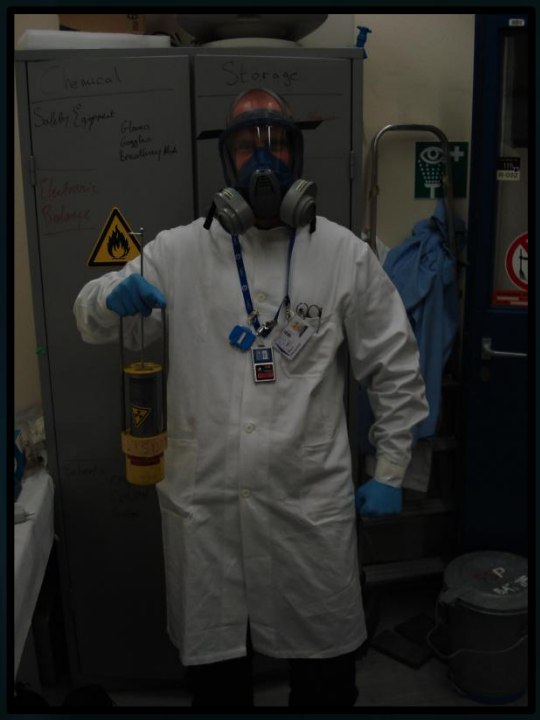
Group members

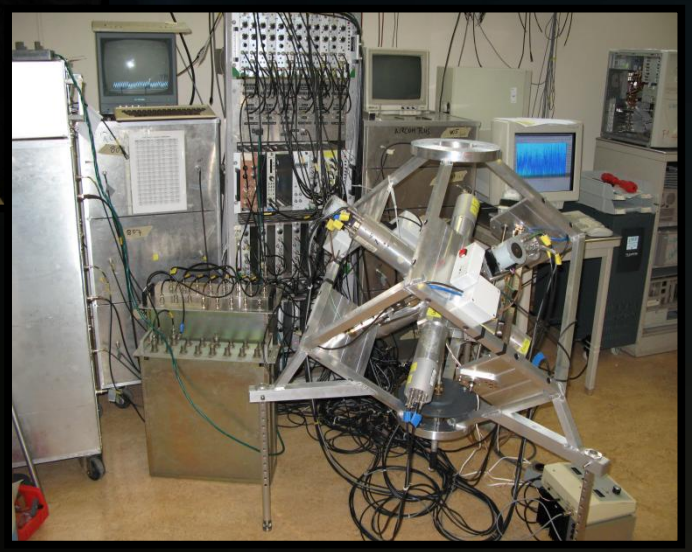
University of Copenhagen - LIFE

University of Copenhagen - Chemistry

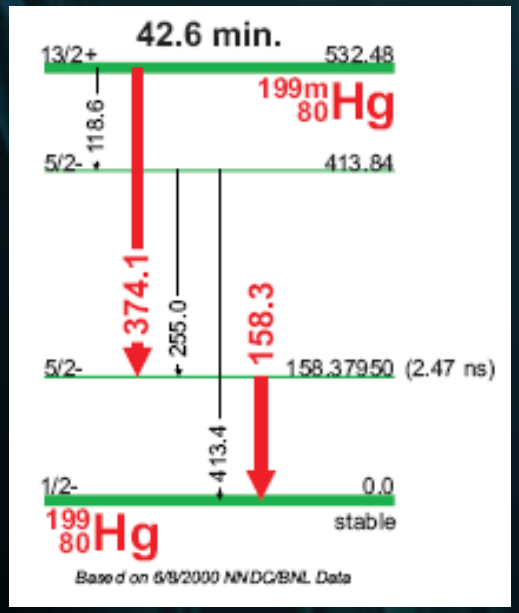
University of Michigan

A word about our work..





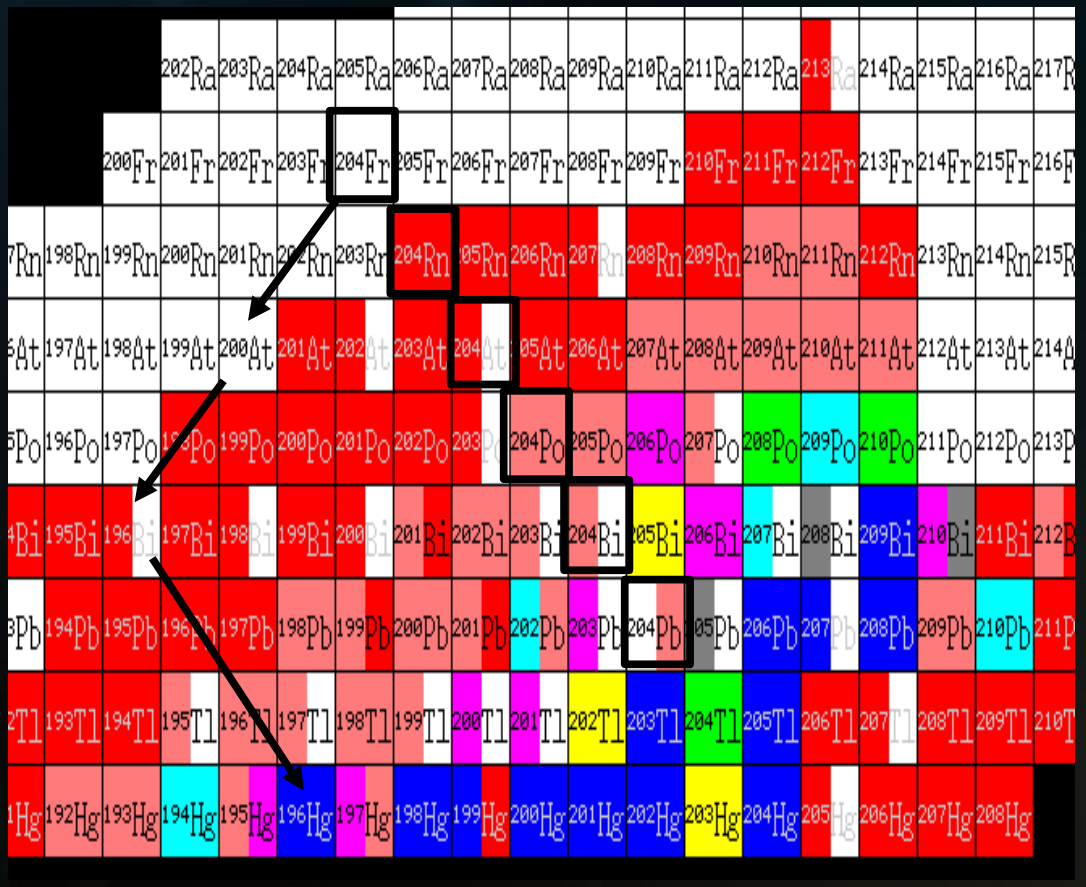
^{199m}Hg



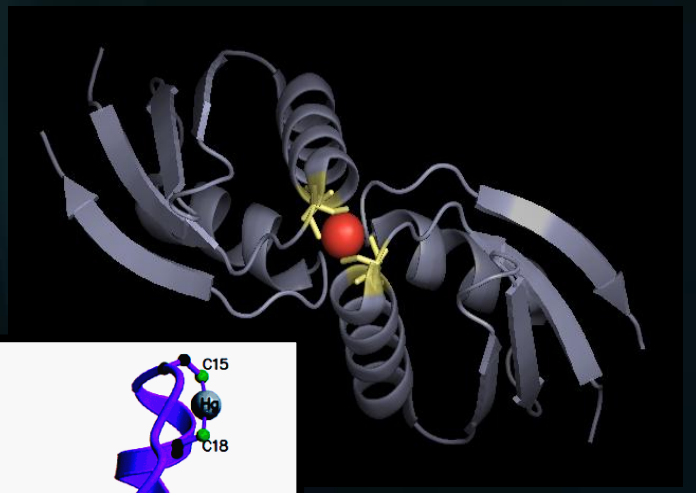
Half life: 42,6min
Decay propoerties: IT mode
γ-γ cascade: 374 keV
158 keV
Half-live of the intermediate state: 2.3 ns

^{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



HAH1

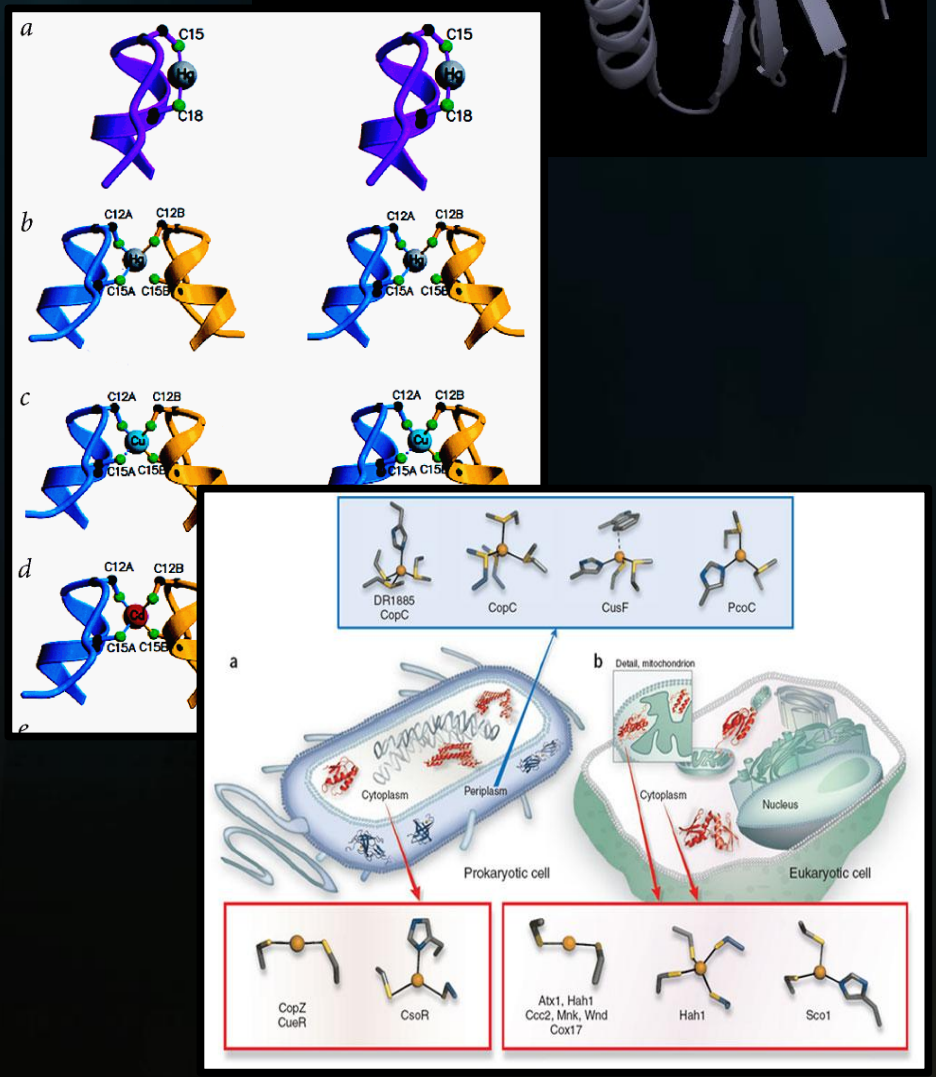


- Metallochaperone protein implicated in Cu(I) delivery to the Menkes and Wilson disease proteins
- metal binding domain characterized by a conserved MXCXXC motif in the connecting loop between the first β-sheet and the first α-helix

Crystal structure of HAH1 determined in the presence of Cu(I), Hg(II), and Cd(II) by O'Halloran et al. In 2000 (Nature, 2001)

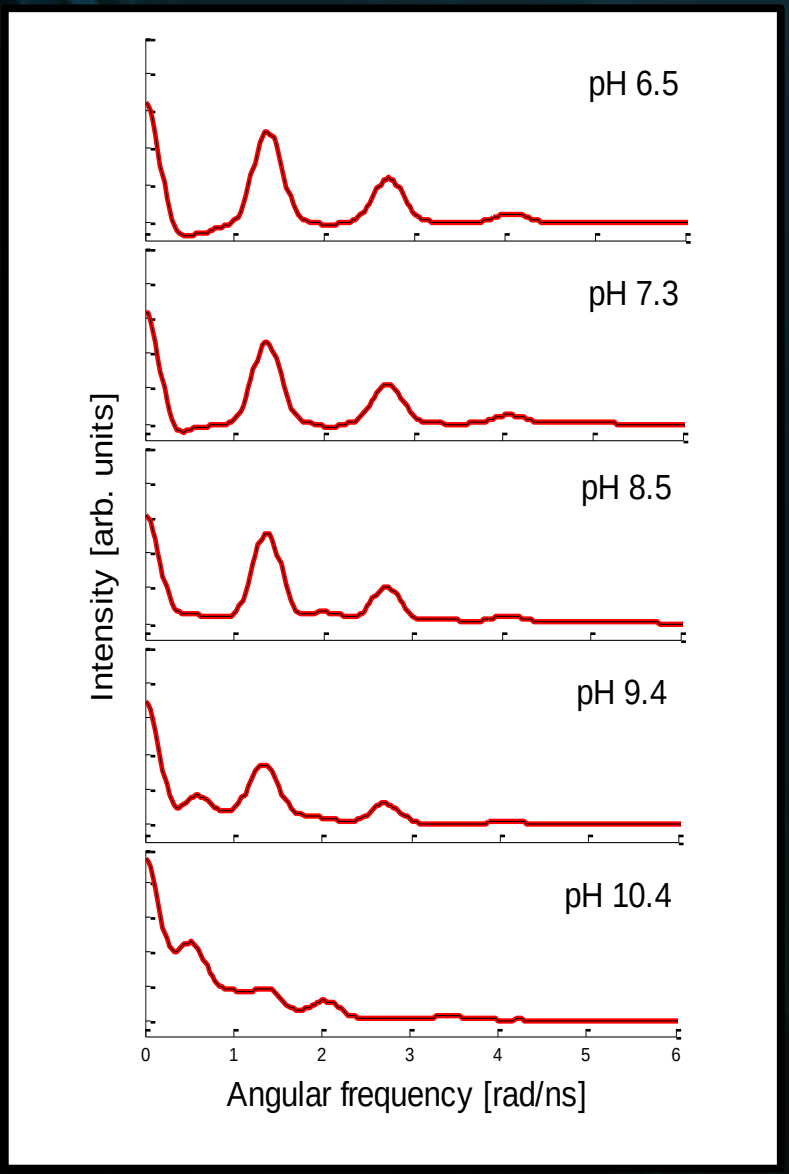
Atx1 - HAH1's counterpart in yeast

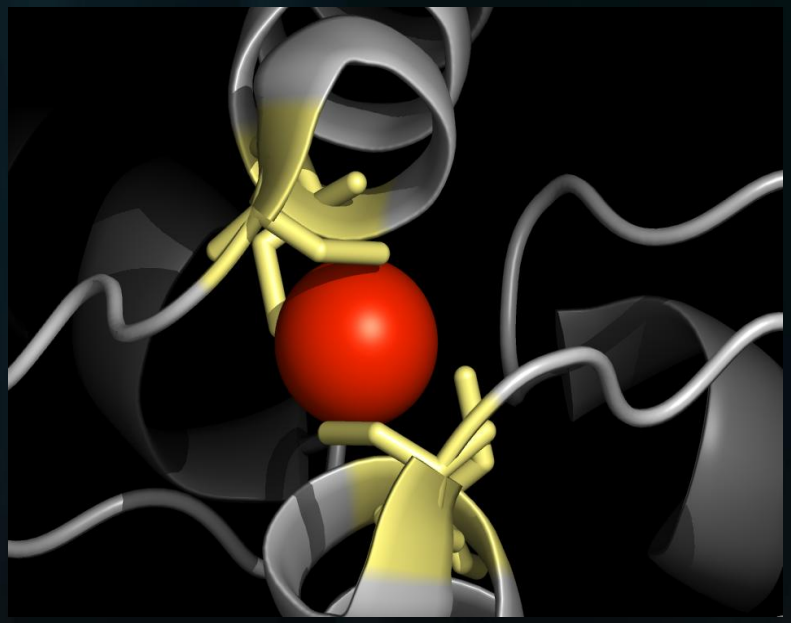
Ccc2 - the yeast homologue for Menkes and Wilson proteins

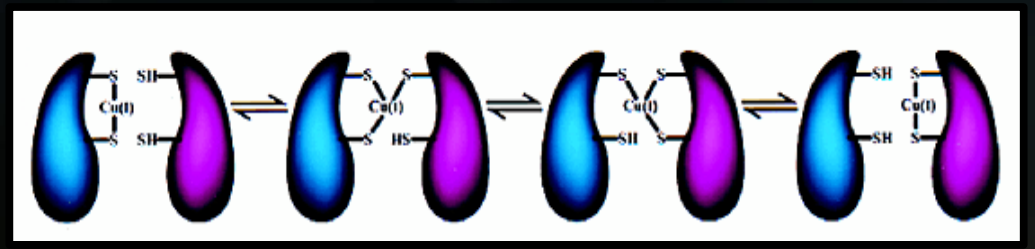


Wernimont AK et al. Nature Structural Biology 7, 766 - 771 (2000)

HAH1







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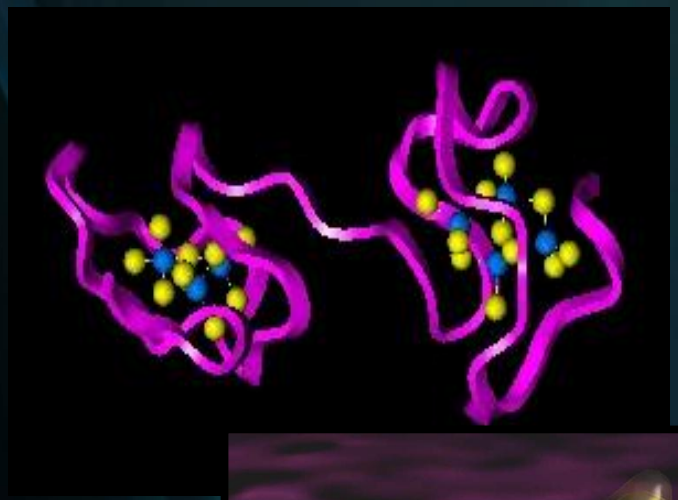
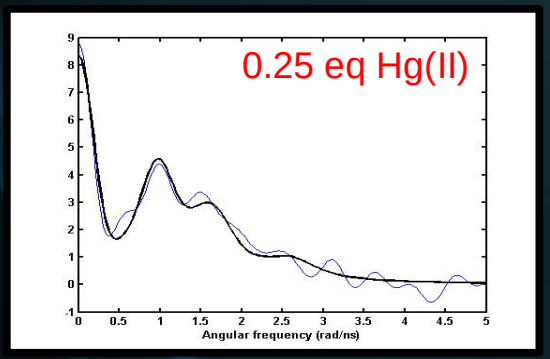
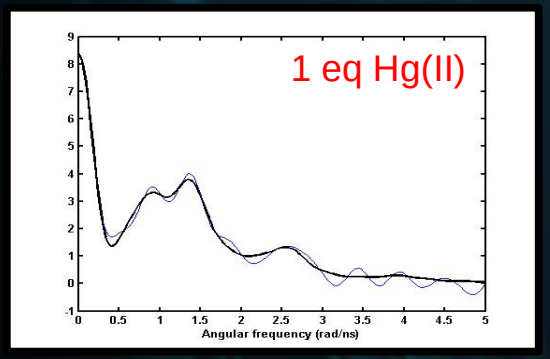
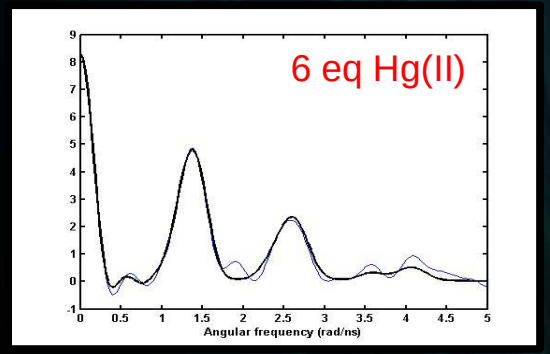


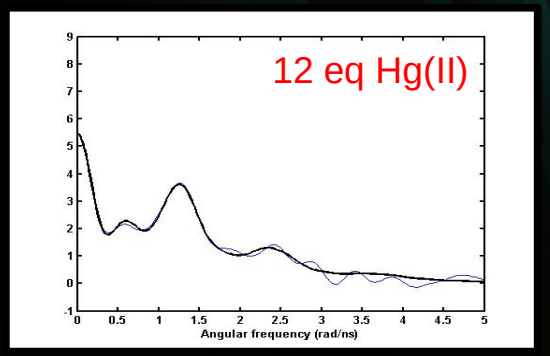
Metallothionein

- MTs are proteins of extremely high metal and sulfur content
- They play essential role in controlling the concentrations of the free ions of Cd and Zn and in neutralising the harmful influences of exposure to toxic elements such as Cd and Hg
- MT was discovered in 1957 and it is still the only biological compound known to naturally contain Cd. Nevertheless, Cd is only one of several optional metallic components in MT, the others are Zn and Cu
- MTs are most abundant in liver, kidneys and pancreas



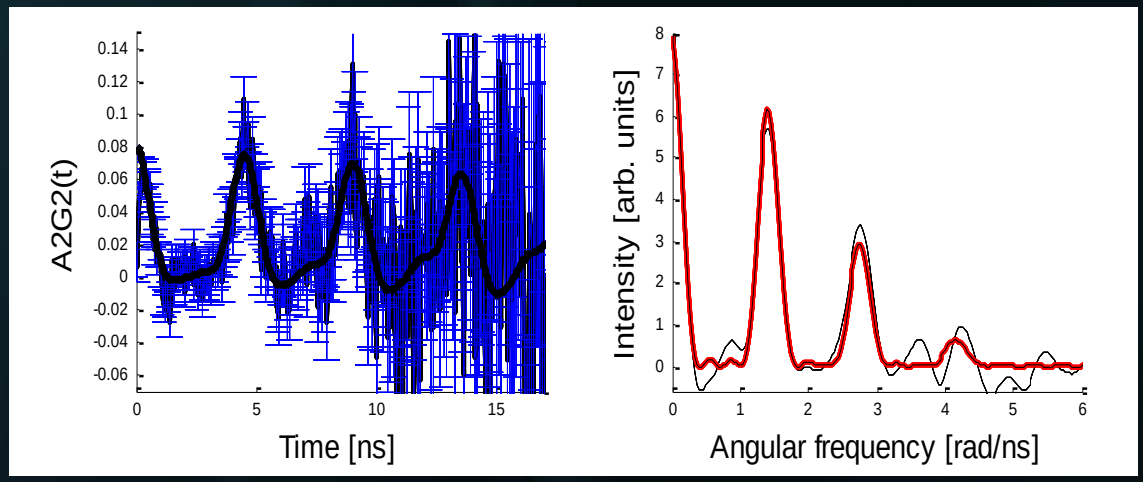




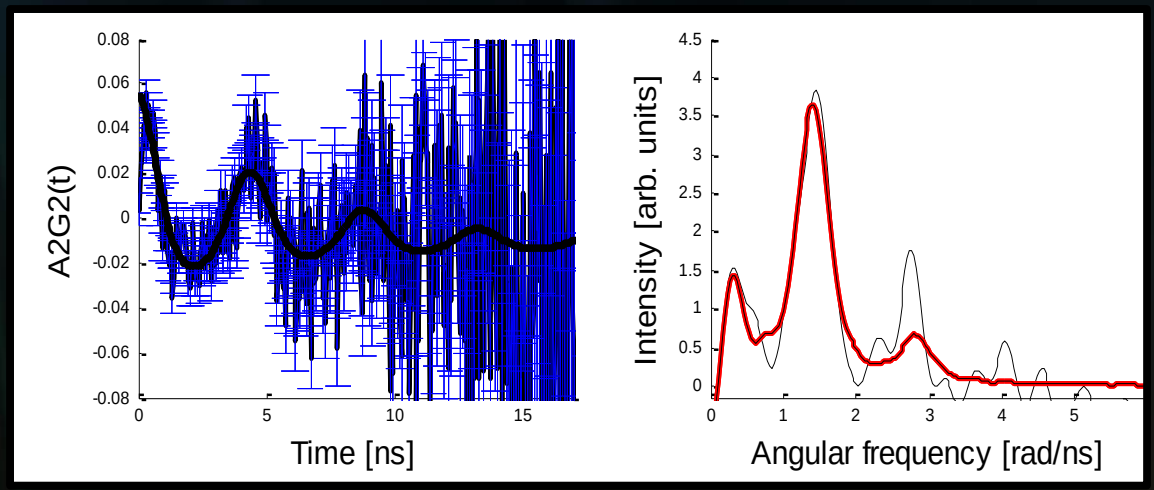


Metallothionein

In vivo experiments



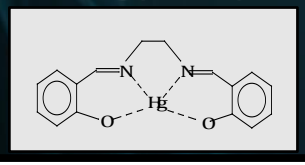
Whole plant with roots (only the collected Hg(II) and water added)

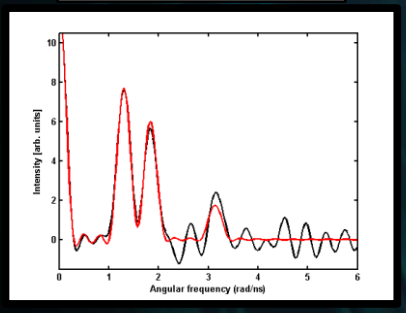


Only leaves (only the collected Hg(II) and water added)

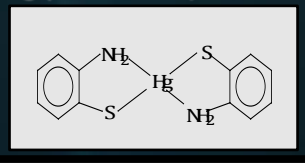
Model complexes

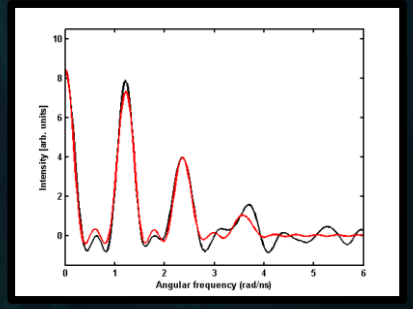
Hg(salen)



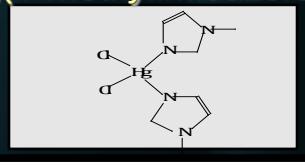


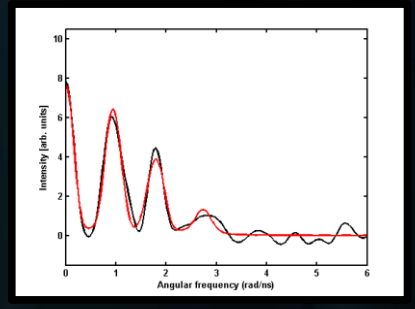
Hg(2-mercaptoanilin)2



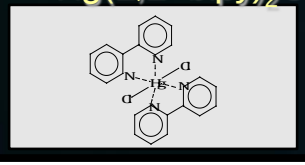


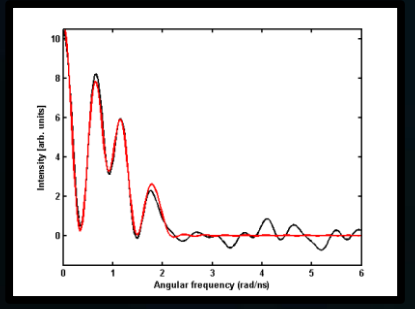
Hg(1-methylimidazole)$_2$Cl$_2$



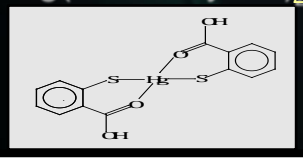


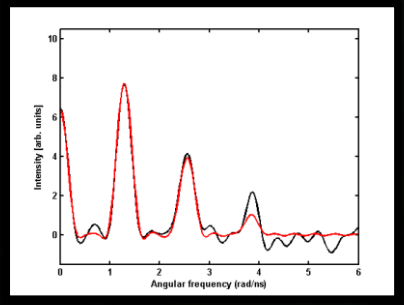
Hg(2,2'-bipy)$_2$Cl$_2$



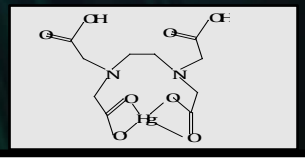


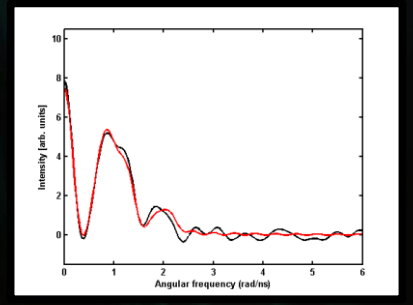
Hg(thiosalicylate)$_2$



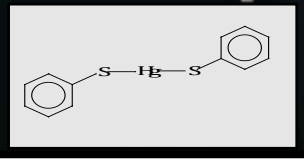


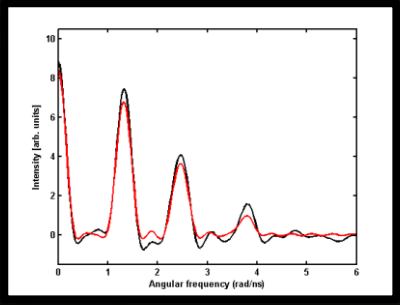
Hg(edta)



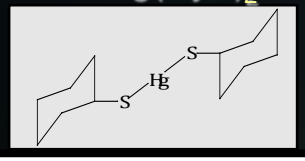


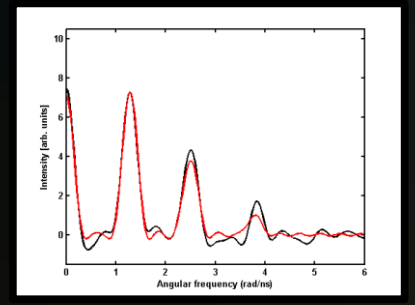
Hg(PhS)$_2$





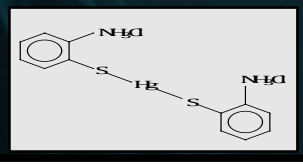
Hg(CyS)$_2$

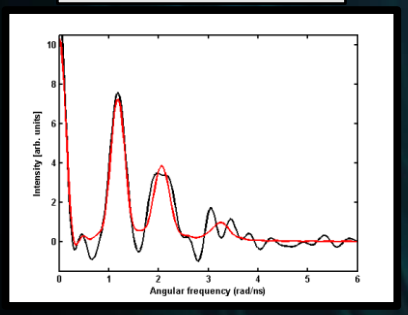




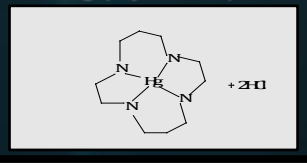
Model complexes

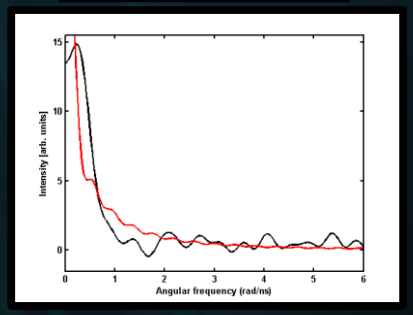
Hg(2-mercaptoanilin).2HCl



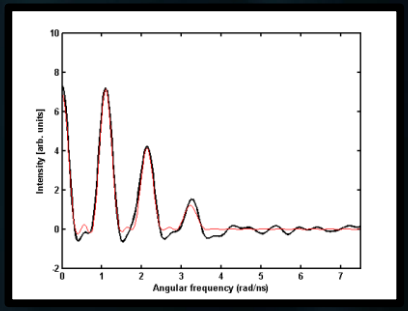


Hg(cyclam).2HCl

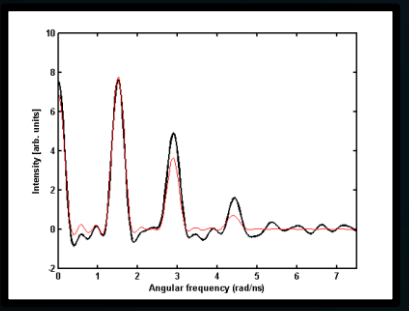




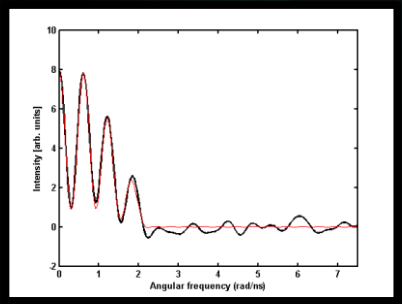
$Hg(benzoato)_2$



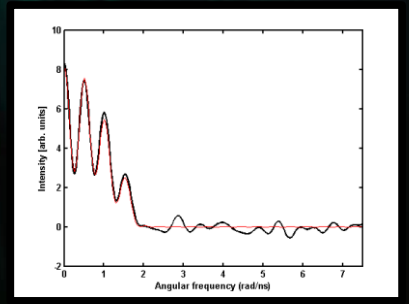
$Hg(benzamido)_2$



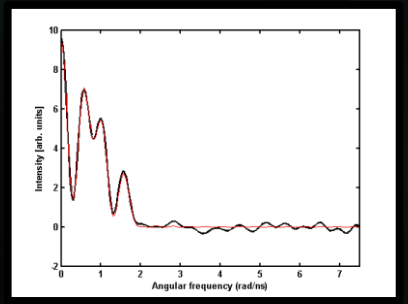
$Hg(Et_2NCS_2)_2$



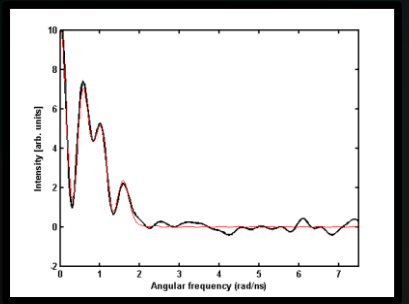
$rac\text{-}Hg(troegersbase)_2Br_2$



$(+)Hg(troegersbase)_2Br_2$



$(-)Hg(troegersbase)_2Br_2$



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- The ISOLDE collaboration
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And many more...

"Particles, particles, particles."

Thank you