SHEDDING SYNCHROTRON LIGHT ON MERCURY TOXICITY

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Mercury is among the most problematic toxicants to which human populations are exposed. The nature and the extent of mercury toxicity depend largely on its molecular form. Neurotoxic methylmercury (CH_3Hg^+) compounds are particularly insidious due to the latency in the onset of toxic symptoms. Low level but widespread human exposure to methylmercury occurs through consumption of fish and shellfish. The WHO has estimated that over one billion people worldwide depend on fish for daily nutrition and thus may be at higher risk. Despite public health concerns, relatively little is known about the biochemical mechanisms underlying the neurotoxicity of methylmercury.

To some extent, this gap in our knowledge is caused by a lack of techniques suitable to probe chemical form of mercury as well as its localization directly *in situ*. Two synchrotron-based methods offer great possibilities in this respect. Synchrotron X-ray absorption spectroscopy (XAS) can reveal chemical speciation of the elements of interest in intact biological tissues whereas synchrotron X-ray fluorescence imaging (XFI) can directly visualize distributions of these elements down to the cellular and even subcellular levels (Figure 1).

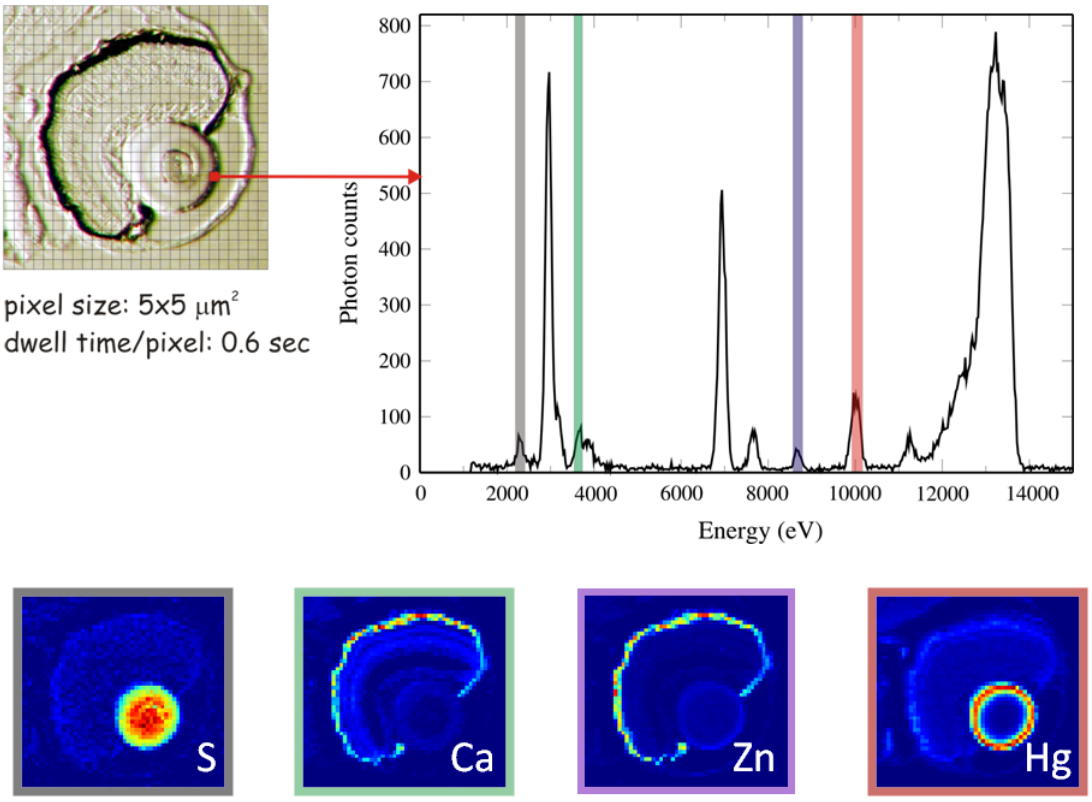

Figure 1: Principles of X-ray fluorescence imaging. The elemental distribution images (*lower panel*) are built by raster scanning a specimen, here, a 6 micron-thick section of a zebrafish larval eye (*upper panel, left*), in the synchrotron micro-beam and collecting the excited X-ray fluorescence signal (*upper panel, right*) from each irradiated spot. Maps are then obtained by filtering from each spectrum the X-ray fluorescence signal at the energies specific for the respective element.

To understand the molecular pathways by which mercury affects the function of the targeted organ, we have combined the zebrafish model system with synchrotron techniques. By taking advantage of the remarkably high elemental specificity and spatial resolution of XFI, we have revealed specific accumulation of methylmercury in the eye tissue (lens epithelium / fibers and retina) [1]-[3]. Recently, by taking advantage of a sub-micron X-ray beam spot size offered by the 2-ID-D beamline at the Advanced Photon Source (Argonne, USA), we have been able to pinpoint an exact cellular localization of methylmercury within the retina and other target organs.

In addition, using the same approach, we have also investigated the efficacy of two mercury chelators, meso-2,3-dimercaptosuccinic acid (DMSA) and alpha-lipoic acid (ALA), in treating mercury intoxication in developing zebrafish larvae following their acute exposures to organic and inorganic mercury toxicants.

This presentation will showcase some of the recent studies into the toxicology of mercury using synchrotron techniques. A main focus will be on the tissue and cell specific accumulation of different mercury compounds in developing vertebrates, with a special emphasis on mercury uptake by sensory organs. The efficacy of the studied chelators in reducing mercury burdens will also be highlighted.

In addition, I will briefly introduce the BioXAS Facility, a currently constructed suite of three beamlines at the Canadian Light Source, which has been specifically tailored for biological and health-related studies of metals in living systems using XAS and XFI.

References

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