BioNanoProbe

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We propose to construct a hard X-ray Bionanoprobe (BNP) at the Advanced Photon Source (APS) at Argonne National Laboratory for imaging of trace elements with a spatial resolution of better than 20 nanometers, and the ability to detect as few as 20 metal atoms in thin sections. This tool would be applicable both for bio-nanotechnology and for biomedical research.

The Specific Aims of this proposal are:

1. To build the Bionanoprobe instrument as a hard X-ray BNP with optimized optics. This instrument would be capable of microscopy, micro-spectroscopy and spectro-microscopy techniques (μ-XANES) and tomography, with an emphasis on X-ray fluorescence analysis of trace elemental content in biological samples.
2. To develop a complete toolbox of software data analysis utensils
3. To develop a database of collected data—cellular/tissue elemental maps of native specimens or samples treated with bio-nanovectors, and make it available to scientific community.

This instrument, once developed, will be used for i) high resolution 2D and 3D imaging of cellular elemental content under different experimental or environmental conditions; ii) high resolution 2D and 3D imaging of the intracellular distribution of bio-nanovectors with identifiable elemental content (elements heavier than Si); iii) 2D and 3D elemental mapping of cellular contents/cell "smears" and isolated hydrated subcellular structures thicker than one micron, engaged in interactions with one another and/or bio-nanovectors of characteristic elemental composition; iv) high resolution 2D and 3D elemental mapping of combinations of bio-nanovectors used to characterize molecular intracellular interactions (bio-nanovectors used as probes for cellular molecular studies). The significance of these types of investigations for the development of both bio-nanotechnology and "basic science" cellular and molecular biology is immense. Bio-nanotechnology requires thorough nanoparticle investigation at the intracellular level; while cellular molecular biology requires new tools (which bio-nanovectors may become) for the characterization of multi-molecular complexes that are too complex for standard methods of detection and monitoring. The completion of this project will permit not only studies associated with nanovectors in cellular systems, which is the primary focus of our group, but also open the door to faster determination of the role of the distribution of various elements in cells and subcellular compartments of tissues affected by neurodegenerative and other severe diseases, and the significance of different metal ion concentrations in the etiology of infectious diseases.

Visible light and optical fluorescence microscopy, electron microscopy, X-ray diffraction, two-photon excitation microscopy, secondary ion mass spectrometry, scanning electrochemical microscopy, and atomic force microscopy are all very important tools of bio-nanotechnology. Nevertheless, the wider community that will be using the BNP believes that the construction of this instrument will provide a critically important tool with the unique capacity for high sensitivity-high spatial resolution elemental detection and quantification. The Advanced Photon Source (APS) at Argonne National Laboratory is the only source of hard x-rays in the Western hemisphere that provides sufficient flux of coherent x-rays photons to achieve the high sensitivity that the hard X-ray BNP requires. We therefore propose to build the BNP at the APS. In addition, the Center for Nanoscale Materials (CNM) at Argonne National Laboratory has constructed a next-generation hard X-ray microscope instrument. The hard X-ray Nanoprobe provides the technology and staff expertise needed for imaging at the spatial resolution scale proposed here with the required sensitivity. This system is currently being commissioned, with an initial spatial resolution of 30 nm having been demonstrated. This system is designed primarily for applications in materials sciences, and will not have the necessary peripheral equipment needed for work with frozen hydrated biological samples. Only 25% of available beamtime will be open to general APS users, the channel through which biology users could apply for beamtime. At the same time, the development of the BNP will be significantly facilitated and expedited by the R&D invested in developing CNM's Hard X-ray Nanoprobe. Based on the initial commissioning results from that system, we are confident that the performance of the BNP will meet or exceed its specifications.