

****Metal Nanoparticle-Based Strategy for Enhanced Contrast in XRF Imaging****

Friday 10 October 2025 12:00 (30 minutes)

X-ray fluorescence (XRF) imaging is a powerful technique for mapping elemental distributions, particularly metals, in biological tissues [1]. However, its broader application is constrained by the scarcity of effective contrast agents. To address this limitation, we developed a novel strategy that uses an approach to trigger site-specific growth of metal nanoparticles (NPs) *in situ*, enhancing spatial resolution in biological XRF imaging [2].

This synthesis strategy achieves three key advances:

(1) Biomarker-specific signal localization; (2) Significantly enhanced image contrast; (3) Compatibility with complex cellular architectures.

By employing this strategy, we anticipate notable improvements in image contrast and specificity, which may substantially broaden the utility of XRF imaging in biomedical research.

Central to our method is the use of catalytic or bio-orthogonal reactions to selectively deposit nanoparticles at molecular targets of interest. This enables highly sensitive detection of low-abundance biomarkers through amplified XRF signals. Furthermore, the modular design of the precursor probes allows for adaptation to various biological contexts, ranging from fixed tissue sections to live cell imaging. We will demonstrate the efficacy of this approach in model systems including mammalian cells and murine cancer tissues, showcasing its potential for applications in neurobiology, metallomics, and diagnostic pathology.

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Session Classification: Poster Presentation - DESY Foyer (Building 5)

Track Classification: MIN Life Science