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Quantitative cellular imaging of Soft X-Ray tomography

Soft X-ray tomography (SXT) reveals cellular structures based on the unique organic composition of each structure and, because of the short wavelengths of light used for imaging, achieves nano-scale spatial resolution. The absorption properties of these soft x-rays, which are in the so-called "water window"(284 eV , 4.4 nm to 543 eV, 2.3 nm), enable high contrast images because water doesn't absorb these x-rays while carbon and nitrogen in biological samples are highly absorbing. Since absorption adheres to the Beer-Lambert law, quantitative information about each cellular structure is generated yielding a unique linear absorption coefficient (LAC) value. Neither chemical fixation nor contrast enhancement agents are required, allowing specimen observation in the most native state. The penetration ability of these X-rays also enables tomographic imaging to visualize the entire cell rather than just a few thin sections. To do this we use a tapered capillary as sample holder, which enables full rotation angles to achieve three-dimensional isotropic resolution. SXT has been successfully applied to image a variety of cell types, including bacteria, yeast and mammalian cells. We extended the SXT observation modality by incorporating information from different contrast mechanisms, combining fluorescence and x-ray imaging to place molecular information on top of structural information. I will present several applications of these techniques, including examples of phenotypic consequences of genetic manipulations and a quantitative, 3D analysis of changes during cell differentiation and cancer.

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