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Scanning Compton X-ray Microscopy

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X-ray microscopes have the potential to bridge the imaging capabilities of super-resolution optical microscopy and cryo-electron microscopy, due to their penetration power and short wavelength. In practice, the resolution and sensitivity of current X-ray imaging techniques at synchrotron light sources are limited by radiation damage, especially for biological systems. Here, we present a novel X-ray microscope which optimizes the quantity and utility of the scattered photons by the sample in order to minimize the dose on the sample for a given resolution. Our microscope, which uses coherently and incoherently (Compton) scattered photons, minimizes the dose per imaging signal at 64 keV for biological samples to deliver three orders of magnitude less dose than current coherent X-ray imaging techniques. The microscope can be implemented at future high-energy and brightness storage rings to retrieve images of unsectioned and unlabeled cells in their native conditions. The results here presented are discussed in detail in Ref. [1].

X-rays with their short wavelength and penetration power offer a unique opportunity to image soft tissue in their natural state, such as whole cells, at few nanometers resolutions in all three dimensions. The three different types of X-ray interactions with matter (photoabsorption, coherent scattering, and incoherent scattering) lead to different imaging modalities with their corresponding associated doses per unit of contrast. Soft X-ray microscopy techniques at the "water-window" (between 284-534 eV) exploit the photoabsorption contrast between oxygen and carbon. They can obtain resolutions approaching 30 nm at tolerable doses. Nevertheless, in order to improve the resolution for this energy range it is required to increase the numerical aperture of the objective lens of such microscopes, which reduces the depth-of-focus to less than 1 μm, i.e. thinner than most cells.

Higher spatial resolution, depth of focus, and penetration can be reached at higher photon energies. The brilliance of third generation synchrotron sources which enabled soft X-ray microscopy has also enabled the development of coherent X-ray imaging techniques at energies beyond 10 keV, such as in-line holography, Zernike microscopy, coherent diffraction imaging or ptychography. Coherent imaging techniques exploit the elastic or coherent interaction between the X-rays and the sample. Although this interaction does not transfer energy to the sample, this process does not occur without a proportional number of incident photons being absorbed. This deposited energy or dose leads to structural changes in the sample which impair the achievable resolution. Current coherent X-ray imaging techniques operate near this resolution limit, which has been theoretically computed in Ref. [2] and extended to account for the sampling of smaller features embedded in larger object [3].

As the photon energy of the X-rays increases the ratio between the portions of coherent scattered photons vs. the photoabsorbed ones increases, being the optimal imaging energy between 20-40 keV, depending on the sample size. Nevertheless, at energies above 30 keV the dominant interaction for soft

tissue is Compton or incoherent scattering. Here we present a dose-optimization study for hard X-rays to image cells and soft tissue, including all the interactions. For this study, we optimize all the scattered photons (Compton and coherently scattered) by a standard protein model $H_{50}C_{30}N_9O_{10}S_1$ with a density of $\rho = 1.35$ g/cm^3 [2] as function of the imaging dose. Specifically, we compute the expected contrast as a function of the energy and imaging fluence for this protein embedded in water. From this study we conclude that the optimal imaging energy, independent of the volume of the protein embedded in water, is 64 keV. As the majority of the scattered photons at this energy are produced by Compton interaction, we propose a novel scanning Compton X-ray microscope (SCXM) which scans the sample recording all the scattered photons by the sample.

In order to validate these calculations we have performed several simulations. Specifically, we have simulated the aforementioned protein embedded in 5×5×5 μm^3 water volume and we have computed the required dose to image this protein as function of its size for SCXM at 64 keV and Coherent diffraction imaging (CDI) at 10 keV [3]. The results of this calculation are summarized in Fig. 1. It can be observed that the achievable resolution by SCXM is around 30 nm while for CDI is around 100 nm. The dose to image 30 nm biomolecule features for SCXM is 3.6×10^9 Gy while for CDI is 1.2×10^{12} Gy, almost three orders of magnitude difference.

Given the potential of SCXM, we present a concept design for this microscope to be implemented at high-energy and brilliance storage rings. The concept design is depicted in Fig. 2. As it is an incoherent scanning technique the resolution is determined by the focal spot. In order to obtain an efficient nanometer focus at high energies we propose to use multilayer Laue lenses. Given the bandwidth of these lenses we propose to combine them with an X-ray achromat composed of compound refractive lenses to use the whole undulator bandwidth and increase the scanning speed. As Compton scattering is distributed around the 4π solid angle our detector covers all the solid angle space except the incoming and outgoing direct beam. Finally, in order to reduce the background and avoid vacuum environments for the sample and detector we propose to use a beampipe, which encloses the focused beam.

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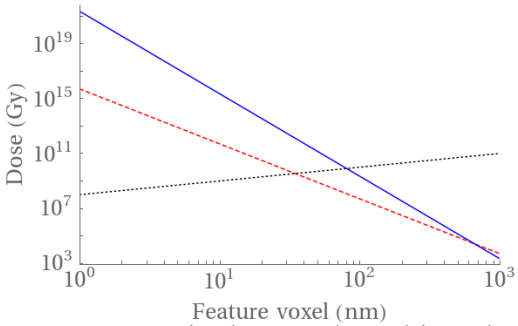

Figure. 1. Dose required to resolve a biomolecule voxel embedded in a 5 μm water cell as a function of voxel size for SCXM at 64 keV (red-dashed line) and CDI (blue-continuous line) at 10 keV. The black-dotted line represents the maximum tolerable dose [2].

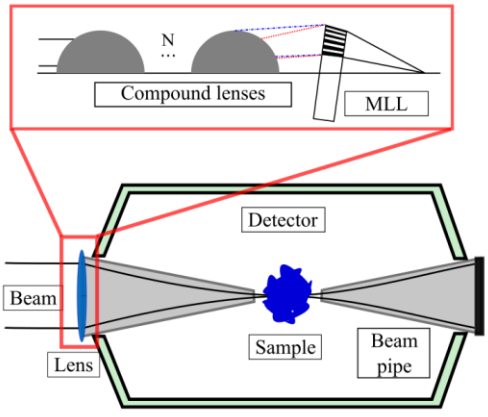

Figure. 2. Concept design of SCXM with a detail of the proposed MLL-achromat.

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