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Cryogenic X-ray Diffraction Microscopy with Hard X-rays for Biological Samples. Enju Lima[a], Lutz Wiegart[b], Petra Pernot[b], Malcolm Howells[b,c], Federico Zontone[b], Anders Madsen[b]. *[a]NSLS 2, Brookhaven National Laboratory, Upton NY 11973-5000, USA. [b]European Synchrotron Radiation Facility, BP 220 F-38043 Grenoble, France. [c]Advanced Light Source, Lawrence Berkeley Laboratory, Berkeley, CA 94720, USA.*
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Biological imaging is a challenging field since a high resolution is needed to probe the fine structures of the sample while the sample preparation and the radiation dose needed for a particular imaging method can both lead to structural damage and artifacts. Recently, x-ray diffraction microscopy (XDM) has emerged as a strong candidate for biological imaging since one can benefit from the high penetration power of x-rays to probe thick samples and reach resolutions beyond those currently available through x-ray optics. These advantages make XDM suitable for high-resolution, non-destructive imaging of a-few-micron-thick samples, such as a whole-cell or sub-cellular organelles. Previous work has shown the feasibility of biological XDM by imaging intact a yeast cell, bacteria, and a human chromosome in the dehydrated state [1,2,3]. However, to fully benefit from XDM in biological imaging, samples need to be imaged in the frozen-hydrated state to remove artifacts due to dehydration and to reduce the radiation damage effect. Yet the necessary sample handling can be challenging due to the delicate nature of biological samples. Hard XDM allows a non-vacuum imaging environment using a cryogenic jet of nitrogen gas to protect the sample from crystalline ice formation. This system facilitates easy sample mounting and monitoring, so that the risk of sample contamination can be significantly reduced. This paper will present recent work on the imaging of frozen-hydrated *Deinococcus Radiodurans* bacteria by hard x-ray diffraction microscopy using a non-vacuum cryogenic sample environment.

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