

Abstract for an Invited Paper  
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**High Pressure Cryocooling of Protein Crystals: The Enigma of Water<sup>1</sup>**

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A novel high-pressure cryocooling technique for preparation biological samples for x-ray analysis is described. The method, high-pressure cryocooling, involves cooling samples to cryogenic temperatures (e.g., 100 K) in high-pressure Helium gas (up to 200 MPa). It bears both similarities and differences to high-pressure cooling methods that have been used to prepare samples for electron microscopy, and has been especially useful for cryocooling of macromolecular crystals for x-ray diffraction. Examples will be given where the method has been effective in providing high quality crystallographic data for difficult samples, such as cases where ligands needed to be stabilized in binding sites to be visualized, or where very high resolution data were required. The talk concludes with a discussion of data obtained by high-pressure cryocooling that pertains to two of the most important problems in modern science: the enigma of water and how water affects the activity of proteins.

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