Crystallographic and XAFS Studies of Copper Proteins

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Metalloproteins are an important class of proteins that perform a variety of fundamental biological processes and in doing so exploit the redox and ligand chemistry of biological metals. In order to understand how these metalloproteins utilize the chemistry of metals to perform a particular function, it is imperative to know the three-dimensional structure of these proteins, in general, and of the metal site, in particular, to a very high resolution. Perhaps nowhere in the determination of molecular structure is precision more at a premium than in the case of metalloproteins. A combined approach based on high resolution (~1.5Å) crystallographic studies and the very high resolution (~0.1Å) XAFS studies of the metal centre in aqueous/crystalline state is thus most powerful in elucidating mechanisms of metalloenzyme catalysis and regulation. We note that XAFS is also a diffraction technique but of electrons which are selectively generated from a single type of atoms using the x-ray absorption edge of the element. Here, we will concentrate on the combined use of XAFS and crystallography for two copper proteins, namely the blue copper containing nitrite reductase and bovine superoxide dismutase. Crystallographic data for nitrite reductase[1] have provided information about the mode of substrate binding, changes in the water structure, and a communication channel between the two types of copper while the XAFS data[2] have provided information suggesting that an ordered mechanism is operative in this enzyme. For superoxide dismutase, XAFS provides[3] evidence for cyclic oxidation/reduction of copper, key for substrate utilization; while our crystallographic data shows that reduced state is highly sensitive to the crystal form.[4] The complementary information provided by the two techniques has thus helped advance our current understanding of the biological mechanism operative in these two cases. We believe that it is only through the rigor of quality structural data that the chemistry of this class of proteins can be underpinned.

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[1]Dodd, F. E., Beeumen, J. V., Eady, R. R. & Hasnain, S. S. (1998; In press) JMB.
[2]Strange, R. W., Murphy, L. M., Dodd, F. E., Abraham, Z. H. L., Eady, R. R., Smith, B. E. & Hasnain, S. S. (to be submitted to JMB).
[3]Murphy, L. M., Strange, R. W. & Hasnain, S. S. (1997), Structure 5, 371.
[4]Hough, M. A. & Hasnain, S. S. (1998, submitted) Structure.