The Interactions of Biological Macromolecules with Metals Revealed by Neutron and X-ray Scattering Techniques

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Mercury (Hg) is a pervasive global pollutant which, as methylmercury, bioaccumulates in the food web and is highly toxic to humans and other organisms. Microbes have naturally evolved to deal with heavy metal toxicity resulting in elaborate heavy metal resistance mechanisms. Bacterial mercury resistance is mediated by the *mer* operon. It encodes specific genes that facilitate removal of toxic mercury species from the cell. X-ray and neutron scattering techniques combined with molecular dynamics simulations can provide unique insights into the interactions of mercury and other metals with proteins relevant to their function.

Expression of *mer* genes is mediated by MerR, a metal-responsive transcriptional regulator. We have used small-angle X-ray scattering (SAXS) and molecular dynamics (MD) simulations to describe changes in the conformation of MerR in response to Hg(II). Our results show that Hg(II) triggers a reconfiguration of the MerR dimer, from a compact state to a conformation revealing two distinct domains. Such a dramatic change in the MerR structure may be the driving force behind a reorientation of DNA recognition sites and ultimately result in initiation of transcription.

Reduction of Hg(II) to Hg(0) is catalyzed by mercuric reductase, MerA. We have combined homology modeling with SAXS/SANS and MD simulations to explore mercury handover between the MerA metallochaperone domains and its catalytic core.