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BDamage: Quantifying radiation damage in MX structures

M. Gerstel[1], C. Deane[2], E. Garman[1]

[1]University of Oxford, Department of Biochemistry, Oxford, United Kingdom, [2]University of Oxford, Department of Statistics, Oxford, United Kingdom

Radiation damage is a limiting factor in macromolecular X-ray crystallography diffraction experiments. Global damage leads to a unit cell size increase and non-isomorphism, and to a loss of long range crystal order which is visible in the decay of the diffraction pattern and loss of high resolution information during data collection. Specific damage causes detectable changes at particularly susceptible sites in the protein structure [1,2], such as the reduction of metallo-centres, elongation and subsequent breaking of disulphide bonds and decarboxylation of aspartate and glutamate residues. Between and within these groups the decay does not happen uniformly at equal rates throughout the protein, leading to preferential specific damage. Specific damage can result in misleading biological conclusions on protein mechanism and function being drawn. We have defined a new atom-specific metric, BDamage, which facilitates the identification of protein regions susceptible to specific radiation damage as well as the quantification of the susceptibility, allowing further investigations into preferential specific damage. BDamage has been validated using a paired set of low-dose/high-dose protein structures [3]. Results show that BDamage successfully separates susceptible residues from stable parts of the protein. A non-redundant subset of previously refined structures submitted to the PDB was then analyzed for indications of specific radiation damage. BDamage indicates that the distribution of specific damage is independent of secondary protein structure or disulphide bond configuration, but shows a correlation with solvent accessibility. Results indicate a possible use of BDamage as a quality control metric for structure submission. Further research into an alternative quantification of real-space specific radiation damage, using the decay of electron density over multiple datasets, is outlined.

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