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Radiation damage in macromolecular crystallography: the current knowns and unknowns

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Much progress has been made over the last 15 years in characterising radiation damage (RD) to macromolecular crystals during 100 K X-ray diffraction experiments [1], and to a lesser extent, for those irradiated at room temperature (RT). Despite a now extensive body of literature on various aspects of RD in MX and SAXS (e.g. Special RD Issues of the Journal of Synchrotron Radiation in Nov 2002, May 2005, Jan 2007, March 2009, Jan 2013, March 2015, and Jan 2017), and new tools being developed to better characterise the effects, there are still a number of unanswered questions in our understanding of RD phenomena and in our knowledge of the pertinent radiation chemistry. Since these effects can not only prevent structure solution, but can also compromise the biological interpretation of structures, an awareness of the issue and of RD-induced artefacts is important for all structural biologists.

Systematic work on the topic has included attempts to identify suitable robust metrics for monitoring both global and specific damage, and establishing an appropriate quantity against which to plot these metrics: the most useful x-axis is absorbed dose rather than time, image number or photons per second. Dose cannot be directly measured but can be estimated (for example by the software program RADDOSE-3D [2]), from knowledge of the atomic contents and size of the crystal, and the X-ray beam properties (energy, flux, profile, size). This information allows the absorption coefficients to be calculated and the dose distributions for various experimental strategies to be compared, in order to optimise the use of the crystal volume and minimise inhomogeneous irradiation. In addition, comparisons can then more easily be made between experiments carried out by different researchers using a range of X-ray facilities.

RD related knowns and unknowns will be summarised, and some new approaches to electron density loss quantitation will be reported. In addition, we are working to improve dose estimations in RADDOSE-3D by explicitly taking into account both fluorescent X-ray escape and photoelectron escape from microcrystals [3], thus reducing the absorbed dose. Our model will allow the relative dose tolerances of micro and macro crystals to be estimated, which has implications for planning serial synchrotron crystallography experiments.

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