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Quantum refinement used for time-resolved crystallography

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In standard crystallographic refinement of proteins, the experimental data are normally not enough to unambiguously decide the positions of all atoms. Therefore, the crystallographic data are supplemented by a set of empirical restraints that ensure that bond lengths and angles make chemical sense. To obtain more accurate results, we have suggested that this potential can be replaced by more accurate quantum-mechanical (QM) calculations for a small, but interesting part of the protein, giving the method of quantum refinement.1 Our group has shown that quantum refinement can locally improve crystal structures,2 decide protonation state of metal-bound ligands,3–6 oxidation state of metal sites,7,8 detect photoreduction of metal ions7,9 and solve scientific problems regarding what is really is seen in crystal structures.9–11 Several other groups have implemented this and similar approaches.12 We investigate how quantum refinement can be used for time-resolved crystallography. In time-resolved crystallography, the obtained electron-density maps will typically involve a mixture of several states (unreacted state, intermediates and products). Therefore, the structures will heavily depend on the empirical potential and the expectations of the crystallographer. The QM calculations will give more accurate results, especially if there are intermediates with unusual (e.g. twisted) structures or if metal sites are involved (which are hard to describe with general restraints). Moreover, we will couple the structural interpretations with expectations from kinetic models of the studied reaction. I will present some preliminary applications on cytochrome c oxidase, xylose isomerase and bacteriorhodopsin.

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