What to Do with Mistakes in the PDB: Resolving the Active Site of PYCR1

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The identification and characterization of ligand binding sites in proteins is a major strength of X-ray crystallography and a foundation of structure-based drug design. However, an alarming number of structures have appeared in the PDB and the peer-reviewed literature where the electron density features for ligands have been misinterpreted. These cases raise many questions for the macromolecular crystallography community. How do we alert the community to potentially mistaken structures? What is the burden of proof for labeling a ligand-binding site as "incorrect"? What should be done with the articles and the corresponding PDB entries? What are the roles of journals and the PDB in validating the modeling of ligands into electron density before deposition and publication, as well after a mistake has been found? Here I present a case study in which the electron density for the cofactor of pyrroline-5-carboxylate reductase was initially misinterpreted, leading to the incorrect identification of the active site. I will demonstrate one approach – perhaps the most elaborate, time-consuming, and costly approach - to dealing with a mistake in the protein crystallography literature.