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Interplay of Crystal Structures and Computational Methods in the Design of Bioactive Molecules. Olaf Wiest, Difei Wang, Patrick Laine, Marco Jonas, Mickael Pauvert, Dept. of Chemistry & Biochemistry, Univ. of Notre Dame, Notre Dame IN 46556 USA.

The rapidly increasing availability of crystal structures for both bio-macromolecules and small molecules can be exploited using the methods of Computer Aided Molecular Design (CAMD), which can in turn be validated using x-ray crystallography. The strengths and weaknesses of the two approaches are often complementary and will be discussed in two case studies. The first is the elucidation of the mechanism of histone deacetylase (HDAC1) and the design of new inhibitors based on the crystal structure of an enzyme-small molecule complex of a histone deacetylase-like protein (HDLP). In the second example, different approaches to the structure-based design of artificial enzymes for the recognition and repair of cyclobutane pyrimidine dimers (CPD) will be discussed.