Computer modelling of enzyme-catalysed reactions has advanced significantly and has the potential to complement and add a new dimension to experimental investigations. Molecular simulations can provide atomic-level insight into reaction mechanisms, and analyse the contributions of effects such as protein dynamics and quantum mechanical tunnelling. Calculations can analyse crucial species such as transition states and reaction intermediates, and identify specific interactions that stabilize them in enzymes. Combined quantum mechanics/molecular mechanics (QM/MM) methods are a good approach to modelling enzyme reactions, and can now be performed with high levels of QM theory. Recent examples include: modelling the mechanism of covalent intermediate formation for the natural substrate in wild-type hen egg white lysozyme; prediction of an unusual mechanism involving arginine as an acid in citrate synthase; and drug metabolism mechanisms in human cytochromes P450. QM/MM modelling has identified the productive mode of inhibitor binding of drug candidates in fatty acid amide hydrolase: multi-level modelling was found to be important to study conformational effects in this enzyme. Detailed comparison with experimental results is important in testing and validating computational methods, for example kinetic isotope effects, activation barriers for chemical steps, predictions of (e.g. stereo-) specificity, the effects of mutations, and spectra. In turn, calculations allow molecular-level interpretation of experimental data, and can suggest new experiments.