

MS02-01 | HOW NOT TO SHOOT YOURSELF INTO THE FOOT

Rupp, Bernhard (Medical University Innsbruck, Innsbruck, AUT)

Protein-ligand complexes are some of the most interesting structures studied by crystallography and often support hypotheses directly relevant to therapeutic drug discovery and human health. The atomic models are the result of the interpretation of reconstructed electron density, which for the ligands is often weak or spurious, and the interpretation thus subject to discussion: telling what is from what is not becomes non-trivial. Some of the often concurrent fundamental difficulties regarding binding sites are that (i) out of principle, binding sites are only asymptotically fully occupied; (ii) by design, binding sites will seek to capture anything that is even remotely similar to the desired ligand; (iii) ligands are often present in multiple or varying conformations; and (iv) ligands displace solvent that is often close in density to that of the purportedly bound molecules. Particularly the latter points, in combination with certain features of the implementation of bulk solvent corrections can lead to self-deception and non-parsimonious modelling of ligands.