The efficacy of ligands, that is whether they stimulate, inhibit or have no effect on receptor activation, is an important parameter both for understanding drug action and for drug discovery. In this presentation, I shall describe some of our work on trying to understand the basis of agonist efficacy.

Agonist efficacy is defined using functional assays. Efficacy parameters that can be used include the maximal response to a ligand ($E_{\text{max}}$) and the extent to which the functional response curve is displaced from the binding curve ($K_i/EC_{50}$). These parameters may, in principle, be used to set up scales of efficacy for a receptor and a group of ligands.

We have been using the $[^{35}\text{S}]\text{GTP}\gamma\text{S}$ binding assay with the $D_2$ dopamine receptor as a means of profiling ligands in order to examine such scales of efficacy as well as examining the basic mechanisms underlying efficacy. In this presentation I shall discuss some of the following topics with regard to these assays:

- Which step is rate determining in the $[^{35}\text{S}]\text{GTP}\gamma\text{S}$ binding assay?
- How is agonist efficacy expressed in the $[^{35}\text{S}]\text{GTP}\gamma\text{S}$ binding assay?
- What does $[^{35}\text{S}]\text{GTP}\gamma\text{S}$ bind to and how reversible is this binding?