Matt presented this poster at ISSX in September 2010.

Abstract:

A number of methods have been developed for the prediction of regioselectivity of metabolism by the major drug metabolising isoforms of Cytochrome P450 [1,2,3]. However, while valuable, predicting the relative proportion of metabolite formation at different sites on a molecule is only a partial solution to designing more stable molecules. Valuable additional information comes from predicting a measure of the vulnerability of each site to metabolism. Such a measurement is the site lability, as calculated by StarDrop. This important factor in determining the overall rate of metabolism, when combined with other descriptors relating to substrate affinity, can provide good predictive models of in vitro metabolic rate which can, in turn, guide design of compounds with improved stability.

We will demonstrate this with a case study, targeting a fast follower for a compound that has problems with poor oral bioavailability and short and variable half-life in man.


A copy of this poster as available as a PDF.

Psychological research has demonstrated that reproducible biases affecting human decision-making, known as cognitive biases, threaten objectivity and balance in individual and team decision-making. Drug discovery leaders receive much conflicting advice on possible ways to improve productivity and restore the rate of successful drug launches; however with help to overcome these psychological barriers, better decision-making can enhance R&D performance [1].
We will discuss four of the common biases that have serious implications for decision-making in drug discovery (summarised below). We will suggest approaches for overcoming these, such as strategies adapted from evidence-based medicine and computational tools that seek to guide the decision-making process, encouraging objective consideration of all of the available information and explicit consideration of the impact of uncertainty in drug discovery.