

## Matched Molecular Pair and Activity Cliffs: the Next Dimension

Written by Tim Cheeseright

Monday, 24 March 2014 15:29 - Last Updated Wednesday, 30 August 2017 15:40

---

Tim Cheeseright gave this presentation at the International Symposium on Compound Design Technologies held in Tokyo and Osaka, Japan on 19 and 20 March 2014.

### Abstract

Matched Molecular Pair (MMP) analysis has become popular as a data driven idea generator for lead optimisation. Existing SAR data is mined for single point changes in structure and their effects on activity: changes that consistently have little effect on activity indicate potential bioisosteric replacements. An adjunct to this approach is to examine the existing SAR on a project to find 'activity cliffs', regions where large changes in activity are observed for relatively small changes in structure. However, these methods almost exclusively rely on studying the 2D structures of the molecules concerned rather than the 3D conformation that is involved in binding.

In this paper we will present our research into using 3D methods to detect and interpret activity cliffs. We will show that considering the shape and especially the electrostatic environment around a pair of molecules results in a richer more informed view of the factors causing changes in activity and a hypothesis driven understanding of existing SAR.

You can download this presentation as a [PDF](#).