This poster by Matthew D Segall, Aishling Cooke, James Chisholm, Edmund Champness, Peter Hunt and Tamsin Mansley was presented at the ACS National Spring Meeting 2018 in New Orleans.

Abstract

Enumeration of a virtual library based on cores or scaffolds of interest helps to quickly explore potential substituents around hit or lead series and prioritise strategies that are most likely to yield high quality compounds. In this poster, we will describe a seamless workflow, beginning with a search of commercially available building blocks. These can then be ‘clipped’ to generate the corresponding R-groups for enumeration of virtual libraries, using a flexible and visual approach based on defining substitution points around a substructure search of the building blocks. This flexibility means that chemists are not restricted to a limited number of pre-defined patterns for reagent clipping and can adapt to many different reaction schemes, while the visual interface makes it intuitive and easy to use.

The resulting R-groups, corresponding to the available building blocks, can be incorporated into virtual libraries around scaffolds of interest. However, with an extensive list of R-groups, enumeration of a fully combinatorial library might generate a vast number of compounds, which may be too large to explore or even overwhelm the resources of a computer. Therefore, we will illustrate how the enumeration can be integrated with predictive modelling and multi-parameter optimisation, to prioritise and retain the compounds that are most likely to achieve the objectives of a project and avoid this ‘combinatorial explosion’. The resulting compounds and corresponding building blocks guide the synthesis of focused, high quality libraries targeting a project’s optimisation objectives.

A copy of Aishling’s poster is available to download here.