Ed Champness, gave this presentation at the "Streamlining Drug Discovery" symposia held in Shanghai, China on 31 May 2018 and Tokyo, Japan on 5 June 2018.

Abstract

Compound design requires a combination of knowledge and expertise from different perspectives: Understanding of structure-activity relationships (SAR), based on data from previously studied compounds; expertise from diverse fields to define the multi-parameter optimisation (MPO) objectives of a project; and knowledge of synthetic strategies that may be applicable to create the next rounds of compounds for investigation. All of these forms of knowledge can be captured and applied computationally: Machine learning methods can generate quantitative structure-activity relationship (QSAR) models to predict the properties of novel, virtual compounds; MPO methods capture the desired property criteria for a successful compound for a specific project and rigorously prioritise ideas for consideration; and, optimisation strategies can be captured as structural transformations that reflect steps made in previous chemistry projects.

In this presentation, we will describe these methods and illustrate how they can be seamlessly combined to rigorously explore new, relevant compound ideas and prioritise those most likely to achieve a project objective. This approach can help to stimulate the search for new optimisation strategies and explore a much broader range of compounds than could be achieved based on a single chemist's or even a project team's experience. Example applications include the optimisation of compounds with a desired polypharmacology or selectivity profile and exploration of lead hopping strategies to overcome pharmacokinetic issues, while maintaining target potency.

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