[L10] Artificially-intelligent drug design

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In the midst of the 4th industrial revolution, there is much excitement about the potential of artificial intelligence (AI) to further pharmaceutical research and development. How might we define intelligent behaviour in the context of drug discovery? Essentially, an intelligent agent – man or machine – demonstrates an ability to solve problems, to learn from experience, and to deal with new situations. With regard to these three central criteria, certain machine learning modalities, specifically autonomous adaptive systems, may be considered instances of domain-specific AI. To date, several such systems have been designed and developed to rationalize and articulate next steps in compound selection, synthesis, and testing. We will showcase some of our activities in this area, with an emphasis on combinations of computational approaches to macromolecular target prediction and *de novo* molecular design, and their combination with chemical synthesis for the discovery of innovative bioactive ligand structures. In this context, the umbrella term 'constructive learning' describes an entire class of problem–solving techniques, including generative deep networks, for which the ultimate learning goal is not necessarily to find the optimal model for the training data but rather to identify new instances (*e.g.*, molecules) from within the applicability domain of the model which are likely to exhibit the desired properties. We trained recurrent deep neural networks to capture the constitution of a large set of known bioactive compounds represented as SMILES strings. By transfer learning, this general model was fine-tuned on nuclear receptor modulation. We synthesized the top-ranking compounds designed by the generative model. The majority of these computer-generated compounds revealed nanomolar to low-micromolar receptor modulatory activity in cell–based assays. Apparently, the computational model intrinsically captured relevant chemical and biological knowledge without the need for explicit synthesis rules. We will further showcase molecular feature extraction by cascaded networks and convolutional nets, together with practical applications.

Bibliography:

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