To explore drug space smarter: artificial intelligence in drug design for G protein-coupled receptors

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Propositions

1. The process of drug discovery can be seen as “looking for a needle in a haystack”, i.e. it is about searching the optimal molecules from a huge chemical space. (Polishchuk P.G. et al. 2013, doi: 10.1007/s10822-013-9672-4)

2. Artificial intelligence is defined as the simulation of human intelligence to make machines think like humans and mimic their actions such as learning, reasoning, perception, and problem solving. (Rajaram N.S. 1990, doi: 10.1016/0019-0578(90)90023-e)

3. Because of the huge data accumulation in the field of biomedicine, artificial intelligence has obtained extensive application scopes to develop more efficient methods for drug discovery. (Fleming N. et al. 2018, doi: 10.1007/s10822-013-9672-4)

4. G protein-coupled receptors play a crucial role in many biological processes and are involved in many diseases. Therefore, about 1/3 of all FDA approved drugs have a GPCRs as drug target. (Hauser A.S. et al. 2017, doi:10.1038/nrd.2017.178)

5. Although there are many differences between optimization and machine learning methods for *de novo* drug design, the better way to exploit them is cooperative rather than competitive. (Chapter 2)

6. An effective exploration strategy is a rewarding approach to help deep learning (DL) models improve the diversity of generated molecules. The idea from evolutionary algorithms is a promising exploration strategy to enhance the performance of these DL models. (Chapter 3 & 4)

7. The paradigm of “one drug, one target” has been shifted in drug discovery. Faced with multiple objectives Pareto optimization is an effective approach for deep learning models applied in polypharmacology. (Chapter 4)

8. Graph representation is much more suitable to deal with scaffold-constrained molecule generation compared with SMILES representation because of its natural data structure without any extra grammar. (Chapter 5)

9. The web-based graphic utility interface (GUI) is easily accessible for users to render complicated problems being simple and convenient. (Chapter 6)

10. Data and algorithm are the shoulders of giants, upon which I can see further in the field of science.

11. I have been tempted to give up again and again in trials and errors to know that persistence should be inexhaustible for scientific research.