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DeepLig: A de-novo Computational Drug Design Approach to Generate Multi-Targeted Drugs

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Abstract : Mono-targeted drugs can be of limited efficacy against complex diseases. Recently, multi-target drug design has been approached as a promising tool to fight against these challenging diseases. However, the scope of current computational approaches for multi-target drug design is limited. DeepLig presents a de-novo drug discovery platform that uses reinforcement learning to generate and optimize novel, potent, and multitargeted drug candidates against protein targets. DeepLig's model consists of two networks in interplay: a generative network and a predictive network. The generative network, a Stack- Augmented Recurrent Neural Network, utilizes a stack memory unit to remember and recognize molecular patterns when generating novel ligands from scratch. The generative network passes each newly created ligand to the predictive network, which then uses multiple Graph Attention Networks simultaneously to forecast the average binding affinity of the generated ligand towards multiple target proteins. With each iteration, given feedback from the predictive network, the generative network learns to optimize itself to create molecules with a higher average binding affinity towards multiple proteins. DeepLig was evaluated based on its ability to generate multi-target ligands against two distinct proteins, multi-target ligands against three distinct proteins, and multi-target ligands against two distinct binding pockets on the same protein. With each test case, DeepLig was able to create a library of valid, synthetically accessible, and novel molecules with optimal and equipotent binding energies. We propose that DeepLig provides an effective approach to design multi-targeted drug therapies that can potentially show higher success rates during in-vitro trials.

Keywords : drug design, multitargeticity, de-novo, reinforcement learning
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