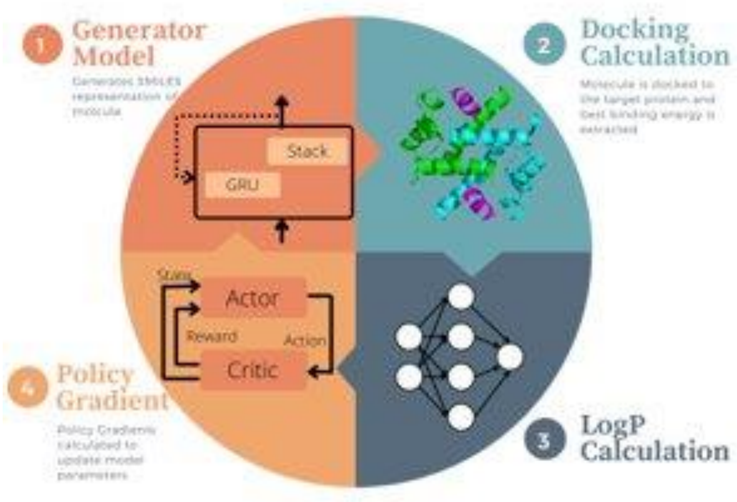
INTERNATIONAL INSTITUTE OF INFORMATION TECHNOLOGY
HYDERABAD
R&D SHOWCASE 2021
Technology, Social Impact

DockingRL: A Reinforcement Learning Guided Method to Generate Molecules that Dock Well to Drug Targets

ABSTRACT

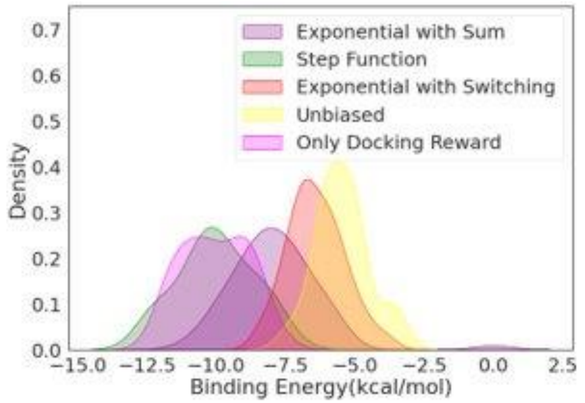
Drug discovery is an important problem that is quite time consuming and requires extensively combing through existing datasets to identify possible hits. In this study we pro-pose a computational strategy for de novo design of drug molecules that dock strongly to target proteins. This approach combines a generative model along with the binding affinity computed through docking which finds the orientation of the molecule when it binds to a target. The generative model uses a stack-augmented recurrent neural network (RNN) which is first trained separately to generate valid drug like molecules in the form of simplified molecular-input line-entry system(SMILES) strings and is then biased using reinforcement learning during which it is rewarded for molecules that bind strongly to the given target and penalized for drugs that do not. We present the application of this approach on generating drug molecules that bind to SARS-CoV-2 main protease M_{pro} an important target for COVID-19.

METHOD

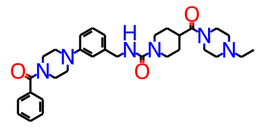


We experiment with multiple reward functions for docking scores and LogP along with optimizing for single and multiple objectives with different strategies.
Docking scores must be as negative as possible and LogP in the range 2 and 5 for drug like molecules

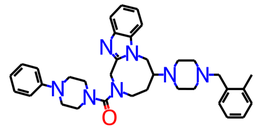
Experiments and Results



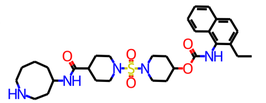
Some of the best generated molecules



Binding Affinity: -8.37
LogP: 2.37



Binding Affinity: -8.16
LogP: 4.02



Binding Affinity: -8.45
LogP: 4.67

Authors: Manan Goel, Shampa Raghunathan, Siddhartha Laghavarapu, U Deva Priyakumar

Research Center Name: CCNSB