DoGSite3 Scorer: Explainable Binding Site Druggability Predictions

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Abstract Text: The discovery of a new drug generally takes several years, incurs significant costs, and is never guaranteed to succeed. Due to these high stakes, reducing the failure probability for novel drug discovery projects is paramount. One crucial consideration, therefore, is the druggability of a given target. Given a protein binding site, druggability describes the likelihood that a small drug-like molecule can bind to this pocket and modulate the protein's activity. We developed a novel druggability prediction tool based on the pocket detection algorithm DoGSite3[1], which predicts the druggability of a pocket based on a set of physicochemical pocket descriptors. To alleviate the black-box characteristic of our gradient-boosting machine-learning model, we used Shapley Additive Explanations[2] to quantify the contributions of individual features to a prediction. Such explanations can then be used to identify how various properties influence druggability.

Bibliography :

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[2] Scott M. Lundberg, Su-In Lee; Adv. Neural. Inf. Process. Syst. 2017