Docket #: S20-207

ComBind: Enhanced Protein-Ligand Structure and Affinity Prediction Platform

Researchers at Stanford have developed ComBind, a computational platform that improves prediction of how drug molecules bind to their protein targets by combining structural modeling with readily available binding data from other molecules.

Current drug design relies heavily on predicting where and how tightly potential medicines will bind to disease-related proteins. Existing computational methods fall into two categories: physics-based approaches that use 3D protein structures but often predict incorrectly, and ligand-based methods that use data from similar molecules but cannot predict binding for substantially different compounds. Both approaches face significant accuracy challenges, with physics-based methods correctly predicting binding less than half the time and ligand-based methods failing for molecules substantially different from training data.

Stanford's ComBind platform addresses this challenge by integrating both approaches through a novel statistical framework. The system uses lists of molecules known to bind the same protein target and leverages the principle that different molecules often bind proteins in similar ways. This combination of structural and binding data improves prediction accuracy compared to conventional single-approach methods.

The technology outperforms state-of-the-art methods across all major drug target families, correctly predicting binding poses 57% of the time compared to 44% for conventional approaches, a 30% improvement. For virtual screening of drug candidates, ComBind achieves up to 50% better performance than standard methods when discovering novel drug types.

Stage of Development
Proof of concept with extensive validation across 248 protein-ligand complexes and 102 diverse targets

Applications

- Drug discovery and virtual screening campaigns
- Personalized medicine development
- Protein-ligand interaction prediction for biological research
- Agricultural biotechnology and crop protection development

Advantages

- 30% more accurate binding pose predictions than current methods
- Up to 50% better virtual screening performance for novel drug discovery
- Uses readily available ligand binding data without needing structural information for helper compounds
- Applicable across all major drug target families
- Improves performance even with minimal helper molecule data

Publications

- Paggi, J. M., Belk, J. A., Hollingsworth, S. A., Villanueva, N., Powers, A. S., Clark, M. J., Chemparathy, A. G., Tynan, J. E., Lau, T. K., Sunahara, R. K., & Dror, R. O. (2021). Leveraging nonstructural data to predict structures and affinities of protein–ligand complexes. Proceedings of the National Academy of Sciences, 118(51), e2112621118.

Patents

- Published Application: WO2021243097
- Published Application: 20230245713
- Issued: 12,633,373 (USA)

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