

Peer Review

Review of: "Strategies for Robust, Accurate, and Generalisable Benchmarking of Drug Discovery Platforms"

Wentao Dai¹

1. Fudan University, China

The manuscript entitled "Strategies for Robust, Accurate, and Generalisable Benchmarking of Drug Discovery Platforms," including the CANDO platform and the compbench benchmarking protocol, is commendable and has the potential to contribute to the field of drug discovery. Below are some suggestions and questions that I hope the authors will find constructive for further enhancing the manuscript.

1. Data Set Expansion: It would be interesting to explore the possibility of incorporating FDA-approved drugs and drugs in clinical phases I to III into the data set. By applying a weighted approach to these categories, you could potentially enhance the representativeness of the data set and improve the predictive performance of CANDO. Could you elaborate on the feasibility and potential impact of such an expansion?
2. Comparison with Other Algorithms: To further validate the effectiveness of compbench, it would be beneficial to include additional drug repositioning algorithms for comparison. This would not only demonstrate the value of compbench but also provide a more comprehensive view of its performance relative to other methods.
3. Detailed Design and Discussion: The following topics could benefit from more detailed design considerations and discussion:
 - Assisting in New Indications: How does CANDO assist in the decision-making process for expanding drug indications, especially the application of specific examples or case studies?
 - Drug Combination Efficacy Prediction: Is CANDO capable of predicting the efficacy of drug combinations, particularly in scenarios involving drug resistance? If so, how does it handle the

complexity of drug interactions?

- Integration of Additional Databases: Could the integration of databases such as CCLE and compound perturbation transcriptomic data enhance the capabilities of CANDO? What are the potential benefits and challenges of incorporating such data?

I believe that addressing these points will strengthen the manuscript and provide a more comprehensive understanding of the CANDO platform and the compbench protocol. Thank you for considering these suggestions.

Declarations

Potential competing interests: No potential competing interests to declare.