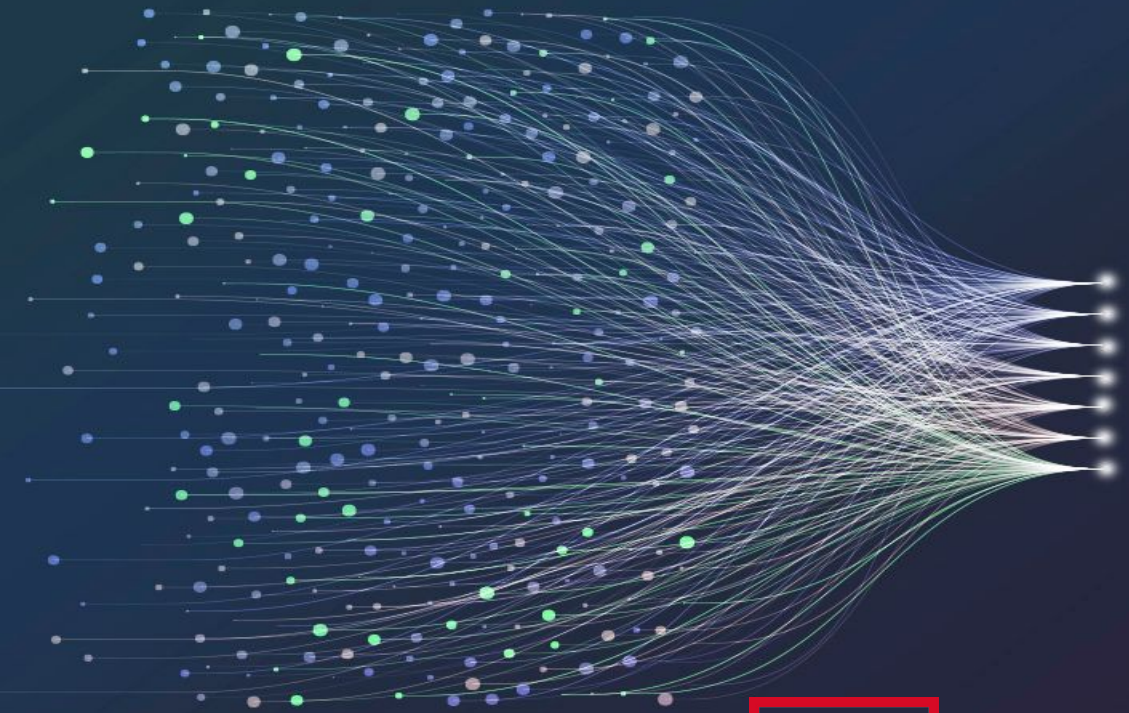
D3R Grand Challenge 4: How we did it.



Alejandro Varela Rial, Industrial PhD student at:

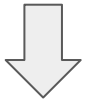
Acellera Labs & Computational Science Lab

upf. Universitat Pompeu Fabra Barcelona

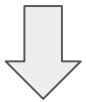
acellera®

Pose prediction challenge: Exploiting structural knowledge

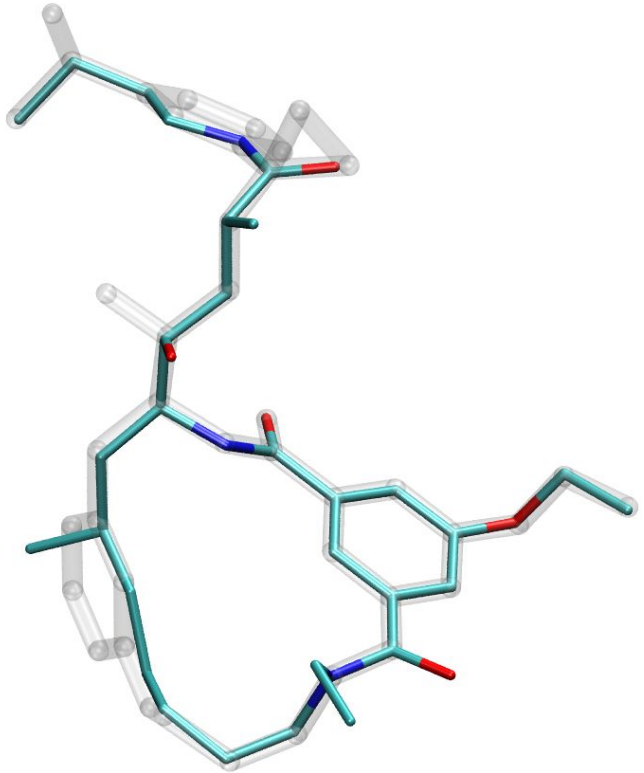
Search for homologs (BLAST)



SkeleDock (MCS like)

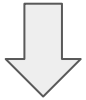


Optional refinement (MD/rDock)

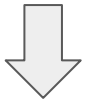


SkeleDock: How does it work?

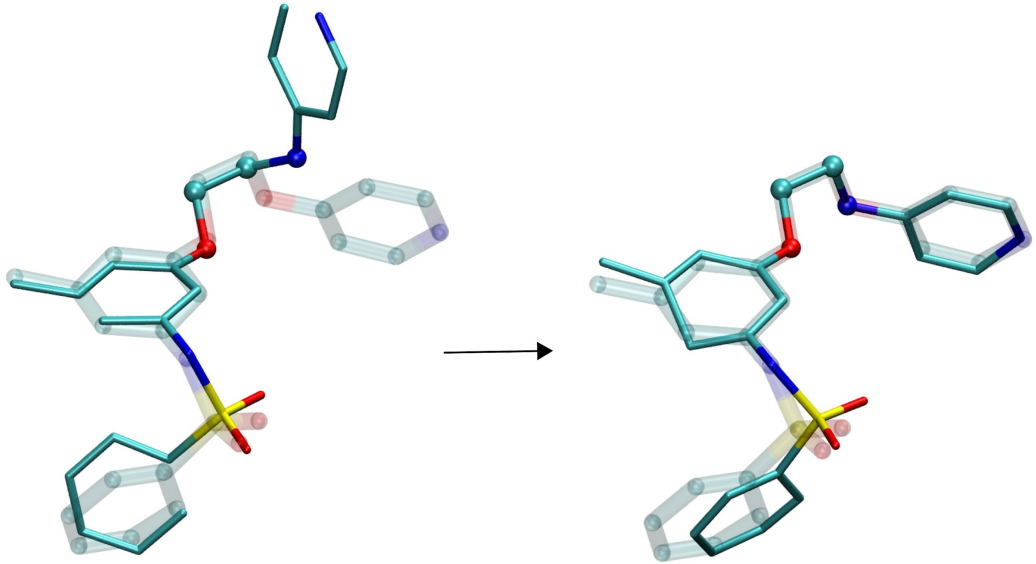
Graph comparison:
Template VS query molecule



Autocompletion step

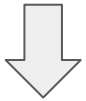


Tethering

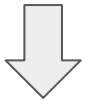


MD refinement step: Double purpose

SkeleDock



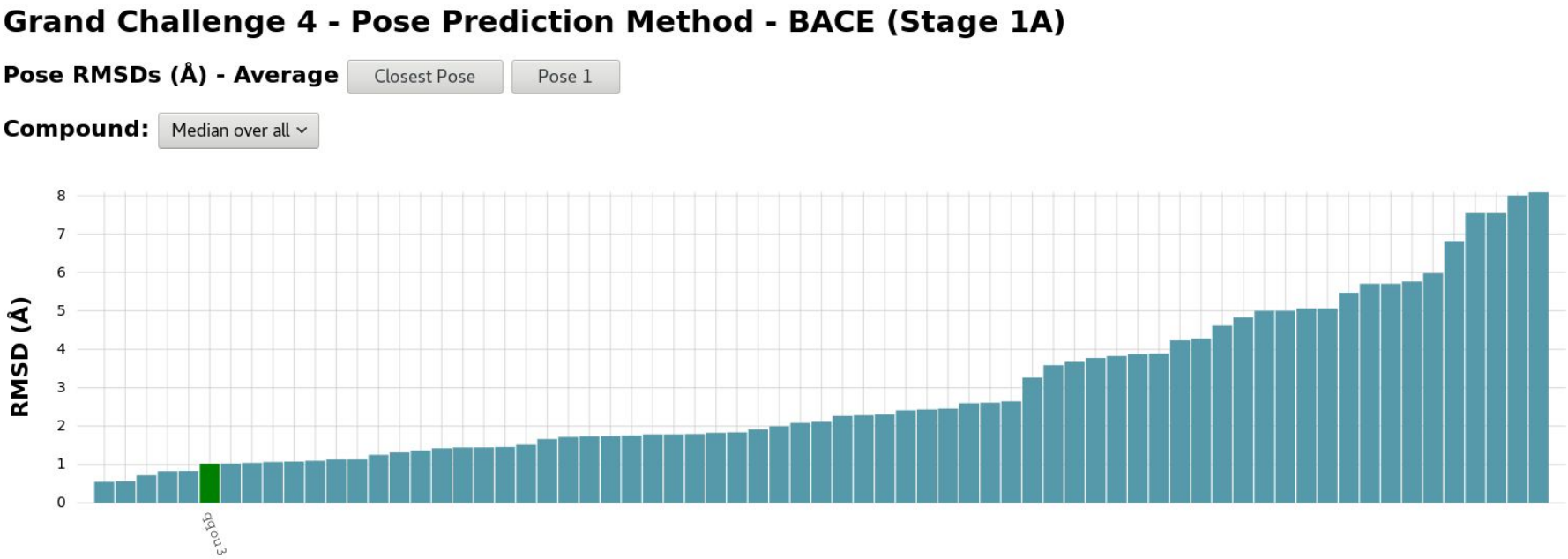
Minimization



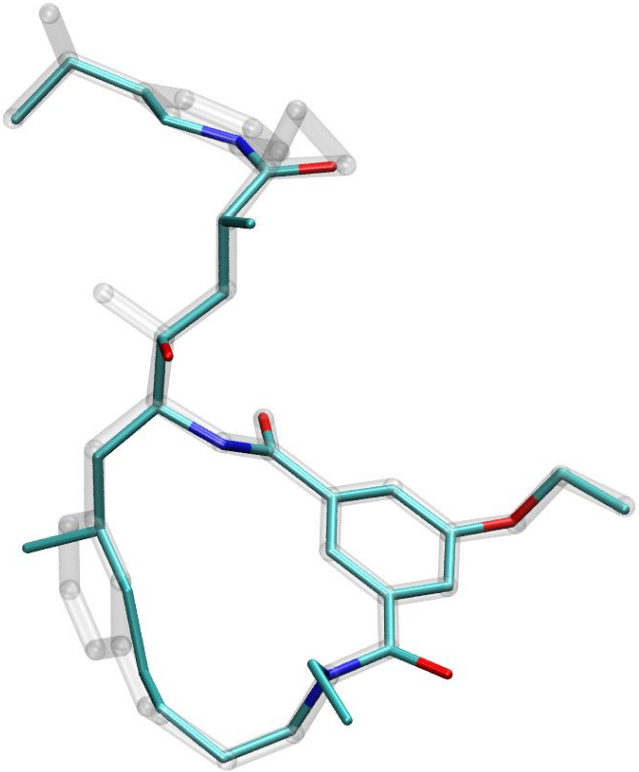
Equilibration (3 ns)

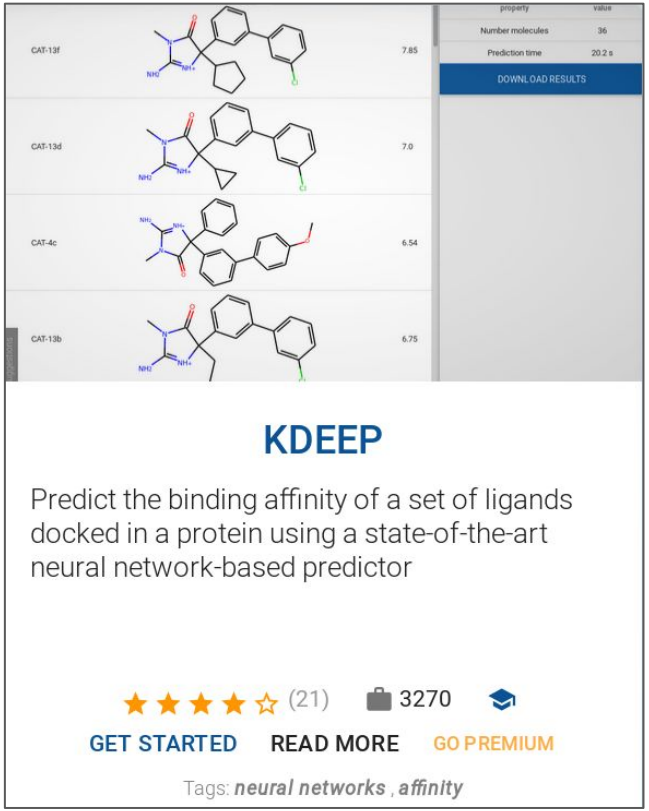
htmd + ACEMD™ MOLECULAR SIMULATIONS

Pose prediction: results



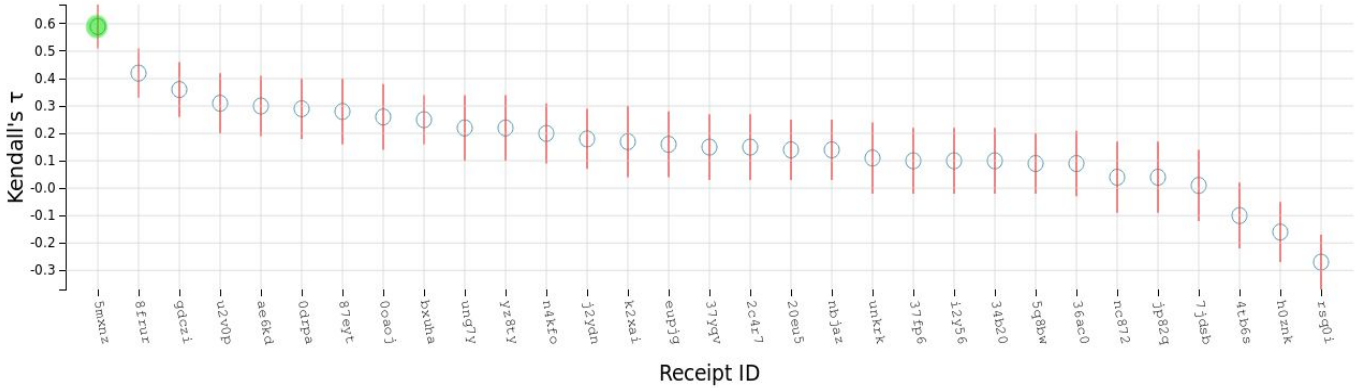
Affinity prediction challenges: SkeleDock & KDeep



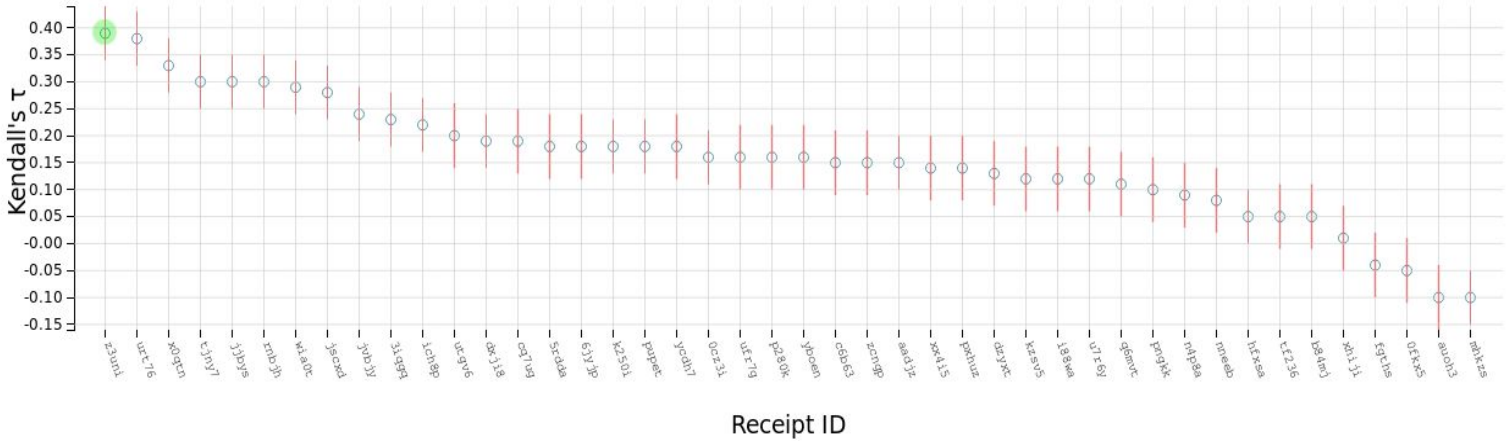


Affinity prediction results

Free Energy Prediction (n=34)



Ligand Scoring (n=154)



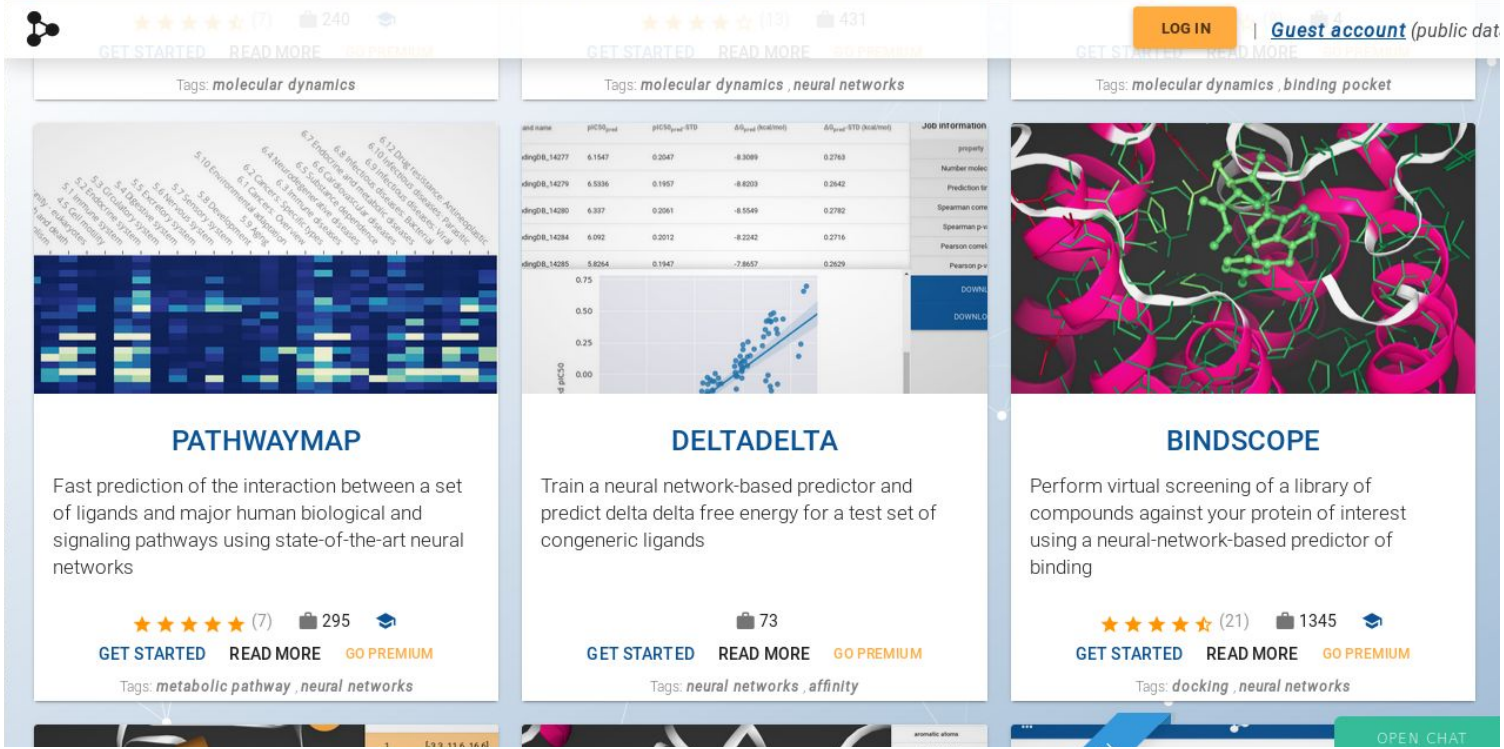
log P challenge, by Boris Sattarov

- EPI Kow dataset (from EPA's OPERA toolkit)
- After filtering, training set size was 12,746 compounds
- Features: (ECFP4 + Avalon1024 + MACCS keys), and 199 RDKit (MolWt, Chi's, ...)
- Extreme gradient boosting trees-based method
- 2nd out of 90 others in mean RMSE (0.39) and achieved mean 0.74 R^2

Usual problems:

- Converting between formats
- Assigning charges and partial charges
- Chemistry (in general)
- Manual supervision
- How to *systematically* use previous affinity knowledge

PlayMolecule: A repository of molecular applications



Thanks!

- To the D3R organizers
- To my colleagues at Acellera and the Computational Science Lab
- And… To this audience!