

D3R Grand Challenge 4: How we did it.



Alejandro Varela Rial, Industrial PhD student
at:

Acellera Labs & Computational Science Lab

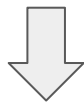


Universitat
Pompeu Fabra
Barcelona

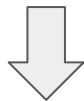


Pose prediction challenge: Exploiting structural knowledge

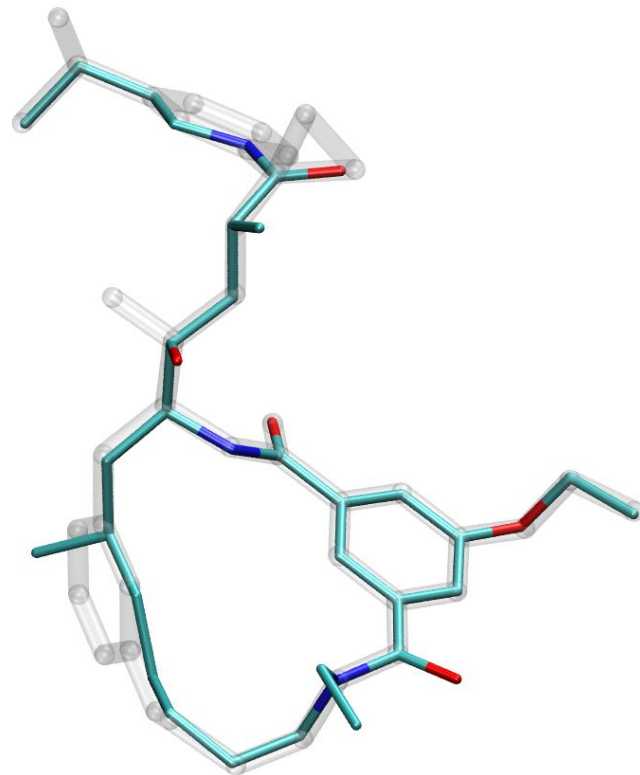
Search for homologs (BLAST)



SkeleDock (MCS like)

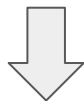


Optional refinement (MD/rDock)

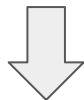


SkeleDock: How does it work?

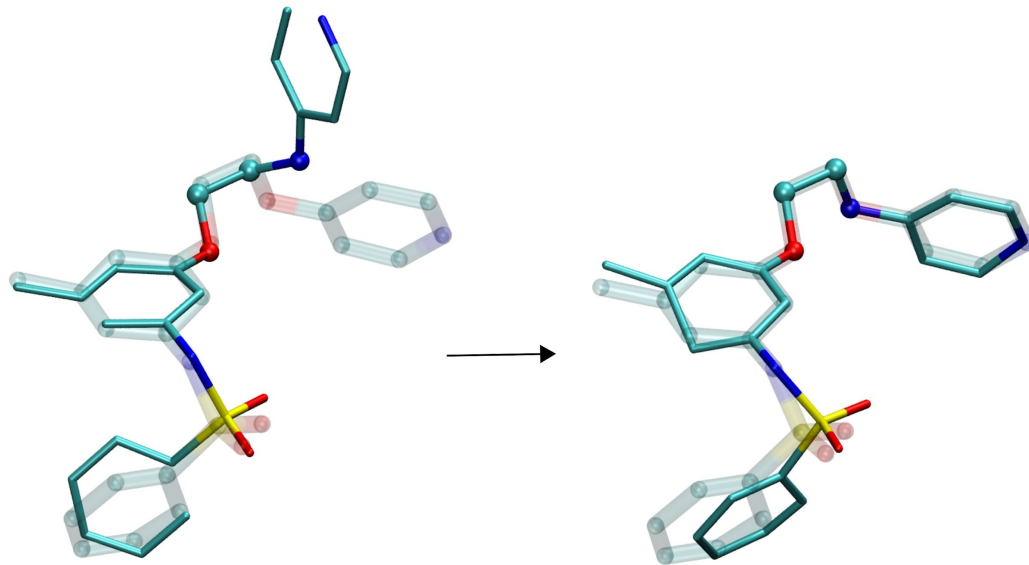
Graph comparison:
Template VS query molecule



Autocompletion step

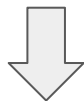


Tethering

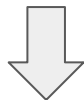


MD refinement step: Double purpose

SkeleDock



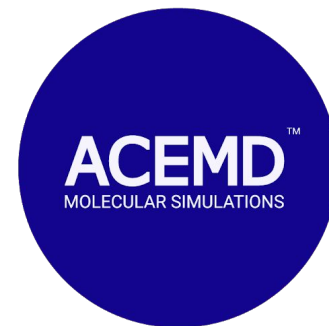
Minimization



Equilibration (3 ns)



+



Pose prediction: results

Grand Challenge 4 - Pose Prediction Method - BACE (Stage 1A)

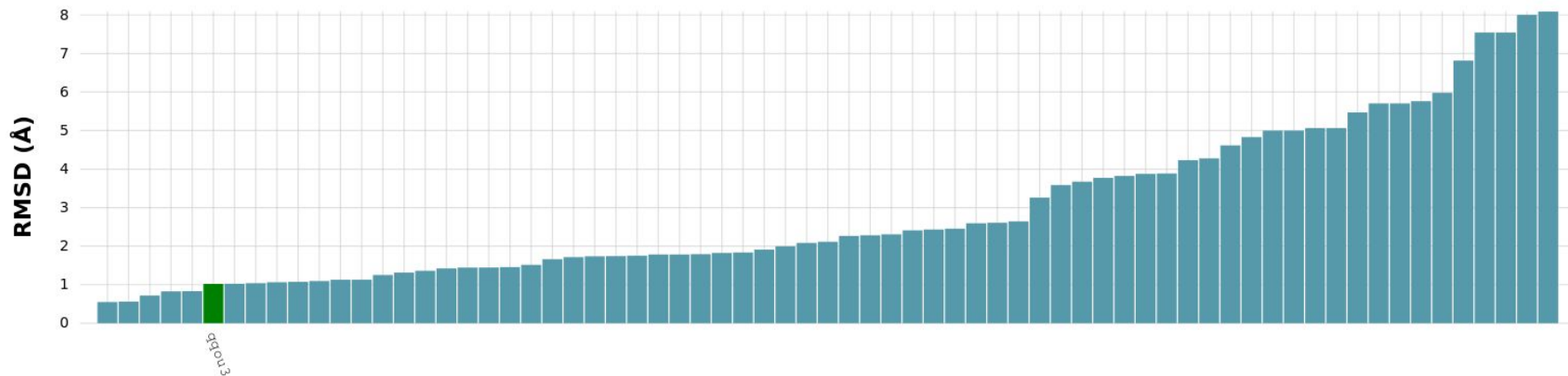
Pose RMSDs (Å) - Average

Closest Pose

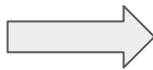
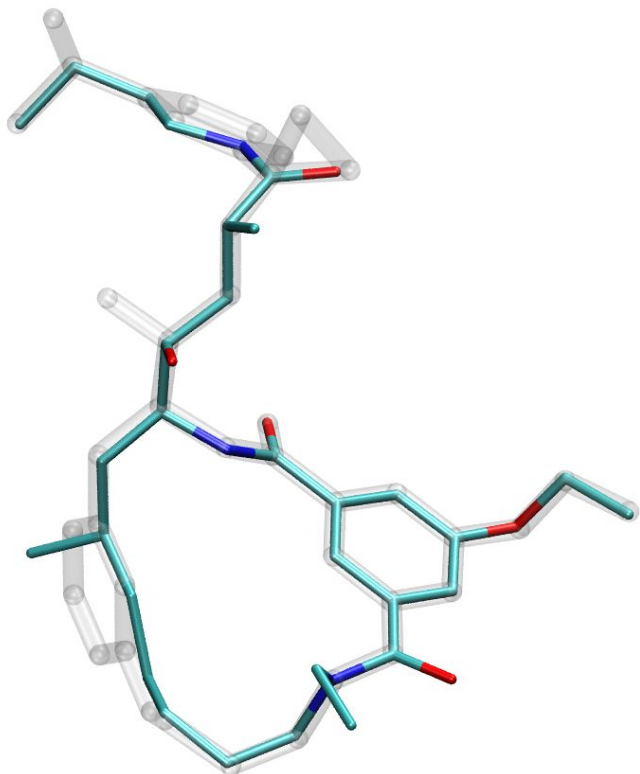
Pose 1

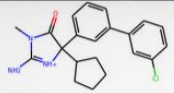
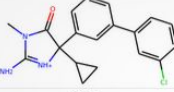
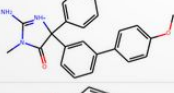
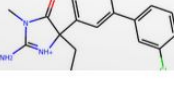
Compound:

Median over all ▾



Affinity prediction challenges: SkeleDock & KDeep



	property	value
	Number molecules	36
	Prediction time	20.2 s
DOWNLOAD RESULTS		
CAT-13f		7.85
CAT-13d		7.0
CAT-4c		6.54
CAT-13b		6.75

KDEEP

Predict the binding affinity of a set of ligands docked in a protein using a state-of-the-art neural network-based predictor

★★★★☆ (21)

3270



[GET STARTED](#)

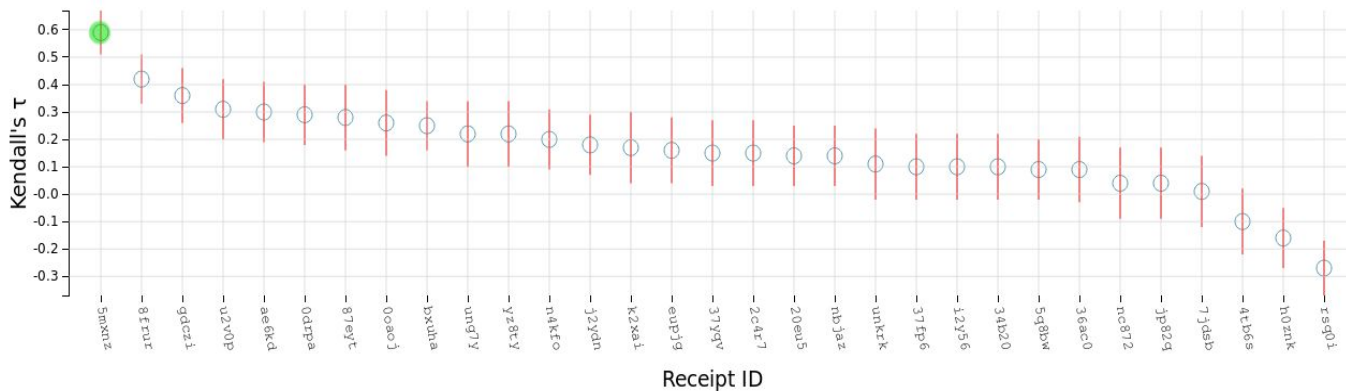
[READ MORE](#)

[GO PREMIUM](#)

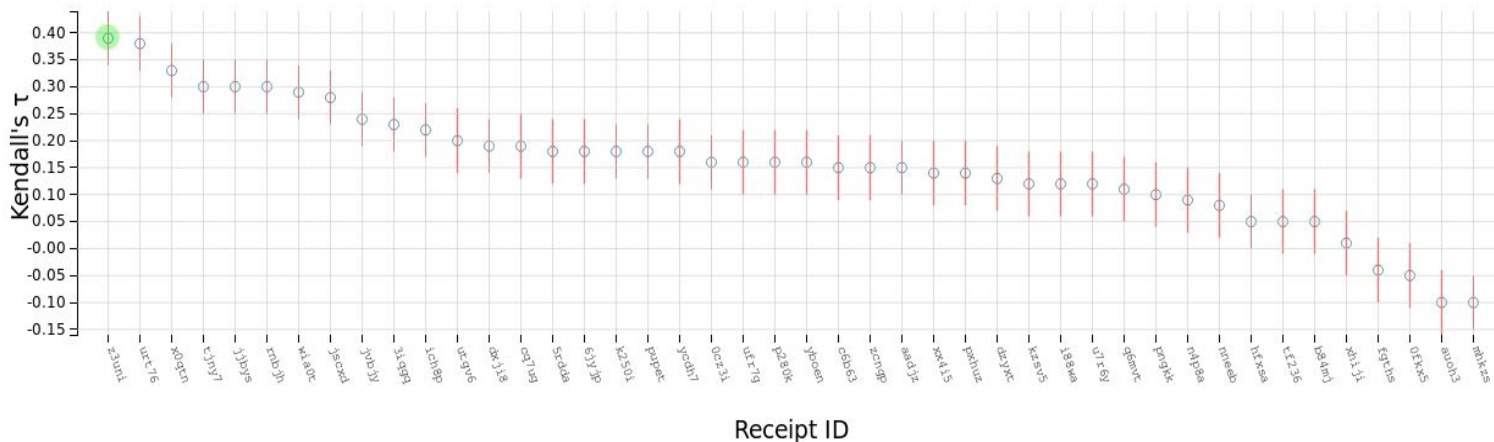
Tags: *neural networks*, *affinity*

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

The screenshot displays three application cards from the PlayMolecule repository. Each card includes a header with navigation links, a title, a description, a visual representation of the application's output or interface, and a footer with user ratings and tags.

PATHWAYMAP

Fast prediction of the interaction between a set of ligands and major human biological and signaling pathways using state-of-the-art neural networks

Tags: *metabolic pathway*, *neural networks*

DELTADELTA

Train a neural network-based predictor and predict delta delta free energy for a test set of congeneric ligands

Tags: *neural networks*, *affinity*

mol name	$\Delta G_{\text{bind}}^{\text{pred}}$	$\Delta G_{\text{bind}}^{\text{pred}} - \Delta G_{\text{bind}}^{\text{STD}}$	$\Delta G_{\text{bind}}^{\text{pred}} - \Delta G_{\text{bind}}^{\text{real}}(\text{meV})$	$\Delta G_{\text{bind}}^{\text{pred}} - \Delta G_{\text{bind}}^{\text{STD}} - \Delta G_{\text{bind}}^{\text{real}}(\text{meV})$
ding08_14277	6.1547	0.2047	-8.3069	0.2763
ding08_14279	6.5336	0.1957	-8.6203	0.2642
ding08_14280	6.337	0.2061	-8.5549	0.2762
ding08_14284	6.092	0.2012	-8.2242	0.2716
ding08_14285	5.6264	0.1947	-7.8657	0.2629

BINDSCOPE

Perform virtual screening of a library of compounds against your protein of interest using a neural-network-based predictor of binding

Tags: *docking*, *neural networks*

Thanks!

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