ALADIN: A New Approach for Drug–Target Interaction Prediction

Krisztian Buza[a], Ladislav Peška[b]

[a] Knowledge Discovery and Machine Learning, Rheinische Friedrich-Wilhelms-Universität Bonn, Germany, buza@cs.uni-bonn.de

[b] Faculty of Mathematics and Physics, Charles University, Prague, Czech Republic, peska@ksi.mff.cuni.cz

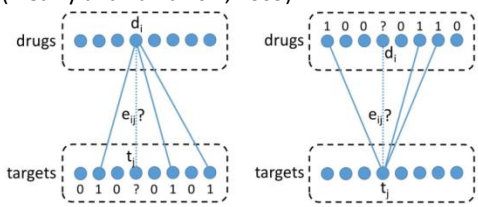
Supplementary material: http://www.biointelligence.hu/dti

1 Motivation

- Understand the pharmacology of drugs better
- Prediction of adverse effects
- Drug repurposing: use of an existing medicine to treat a disease that has not been treated with that drug yet (e.g. sildenafil)
- drug discovery is expensive and needs long time: up to $1.8 billion, 10+ years (Morgan, 2011)
- relation to recommender systems (Peska, 2017)

2 BLM: Bipartite Local Model

(Bleakly and Yamanishi, 2009)



3 Our approach: Advanced Local Drug–Target Interaction Prediction (ALADIN)

- ALADIN is based on BLM
- Local model: EC*k*NN – nearest neighbor regression with hubness-aware error correction (Buza et al., 2015)
- *Weighted Profile* approach for "new" drugs/targets
- Enhanced representation of drugs and targets in a multi-modal similarity space
- Projection-based ensemble

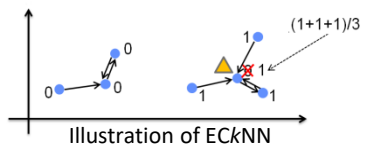
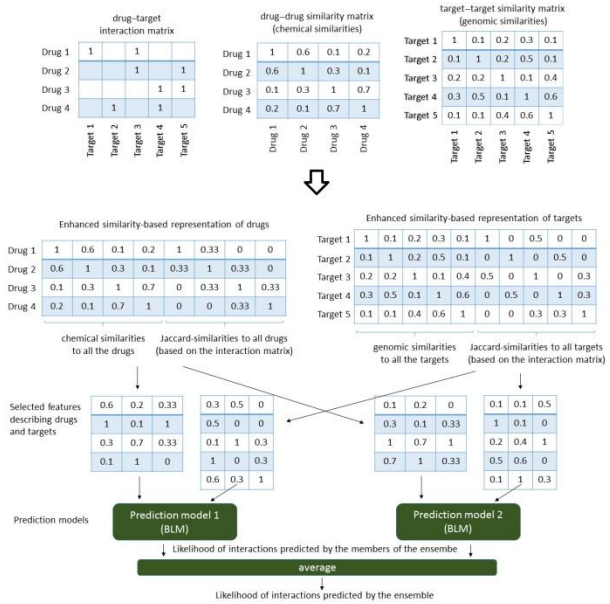


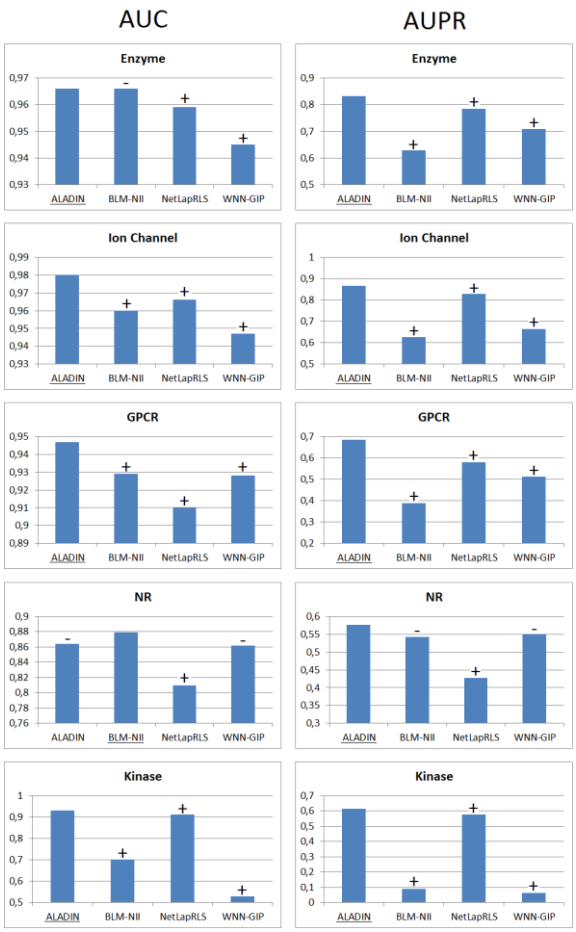
Illustration of EC*k*NN



Overview of the ALADIN approach

4 Experimental Evaluation

- Data: publicly available real-world drug-target interaction datasets: Enzyme, Ion Channel, G-protein coupled receptors (GPCR), Nuclear Receptors (NR), and Kinase
- Experimental protocol: 5x5 fold cross-validation
- Evaluation metrics:
  Area under the ROC curve (AUC)
  Area under Precision-Recall Curve (AUPR)
  Statistical significance tests (t-test, p=0.01), denoted as +/-
- Baselines:
  BLM-NII: bipartite local models with „neighbor-based interaction-profile inferring"
  NepLapRLS: „net Laplacian regularized least squares"
  WNN-GIP: combination of weighted nearest neighbor and Gaussian interaction profile kernels
- Hyperparameters of ALADIN and the baselines were learned with grid search on the training data



References

Bleakley, Yamanishi Supervised prediction of drug–target interactions using bipartite local models. Bioinformatics 25(18), 2397–2403 (2009)

Buza et al.: Nearest neighbor regression in the presence of bad hubs. Knowledge-Based Systems 86, 250–260 (2015)

Morgan et al.: The cost of drug development: a systematic review. Health Policy 100.1 4-17 (2011)

Peska et al.: Drug-target interaction prediction: A Bayesian ranking approach, Comp. Methods and Programs in Biomedicine 152, 15-21 (2017)