

De novo drug development is expensive and prone to high failure rates in commercialization.

An interpretation of predictions can be obtained by computing feature-wise importance scores [1-2], that quantifies the contribution of each feature to the predicted score for the pair.

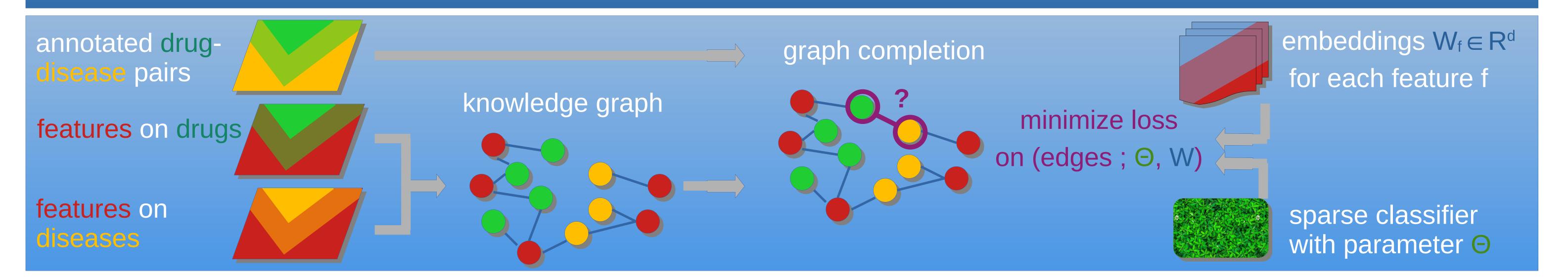
Drug repurposing screens documented molecules to therapeutic ("positive") drug-disease new uncover associations from unknown pairs (>90% of all pairs).

We design an algorithm to predict positive drug-disease pairs using information on drugs and diseases ("features").

**Research gap:** post hoc approaches for feature importance attribution might lead to unreliable results [3-4].

**Objective:** can we build a (drug repurposing) recommender system with embedded feature importance scores?

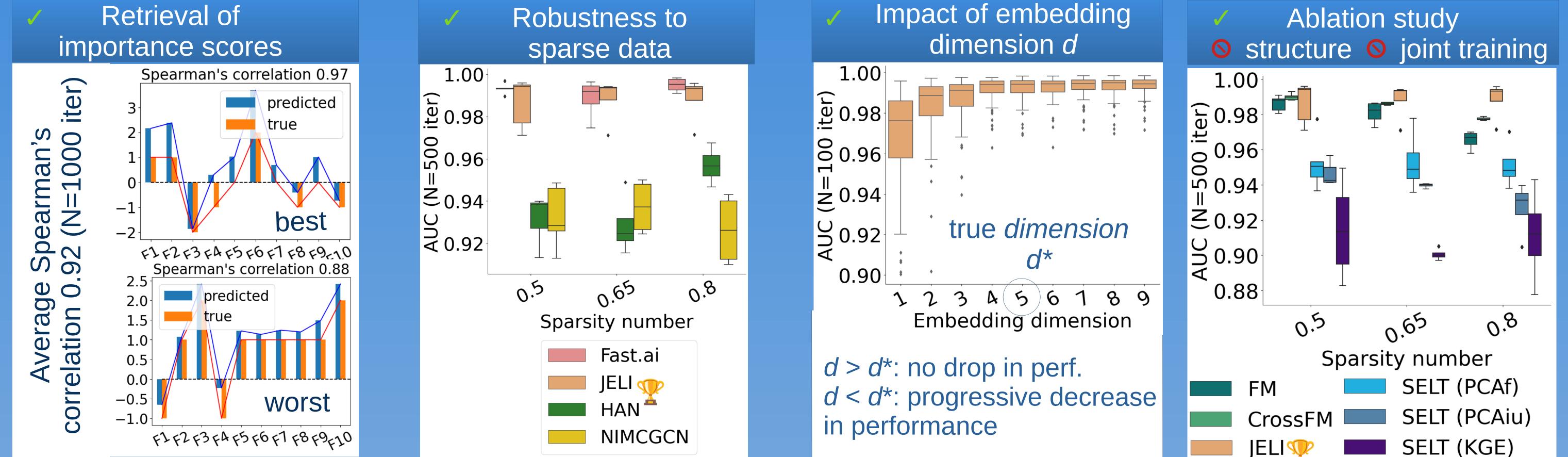
## Our contribution – Joint Embedding Learning-classifier for improved Interpretability (JELI)

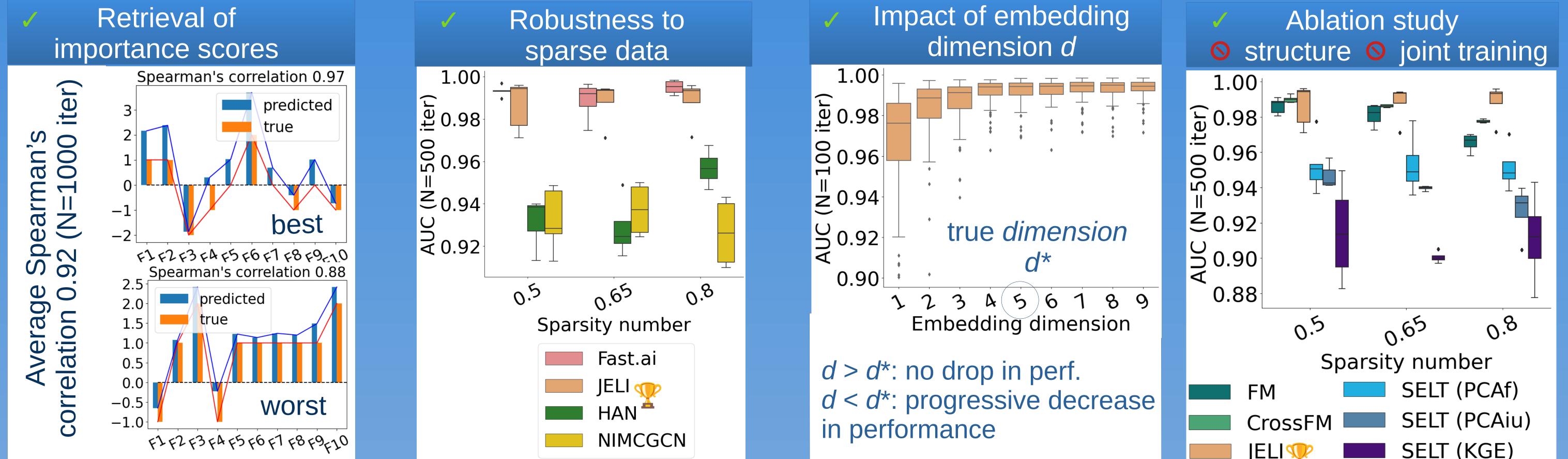


## Results with JELI – Interpretability, robustness, performance in classification

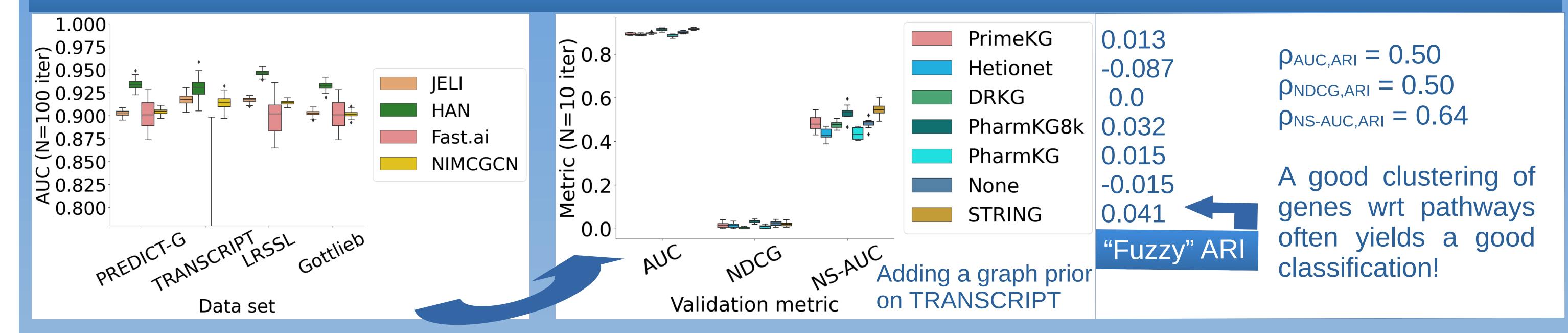
JELI can predict a score and compute an embedding for a *new* drug-disease pair, along with feature-wise importance scores.

**Synthetic data sets** – randomly generated embeddings giving ground truth importance scores and item-user associations





**Drug repurposing** – classification performance and consistency between gene embedding clusters and Hallmark pathways



JELI flexibly encodes a graph-based regularization constraint on drugs and diseases for drug repurposing. Notably: **2.** JELI can be readily applied for any recommendation task. **1.** JELI explicitly infers feature importance scores

[1] Lundberg and Lee. Advances in neural information processing systems, 30, 2017.

[2] Ribeiro, Singh and Guestrin. SIGKDD international conference on knowledge discovery and data mining, 1135–1144, 2016.

[3] Fokkema, de Heide and van Erven. Journal of Machine Learning Research, 24(360):1-37, 2023.

[4] Swamy, Radmehr, Krco, ..., and Käser. International Conference on Educational Data Mining, 2022.











