Kernelized Rank Learning for Personalized Drug Recommendation

Xiao He[1,2,*], Lukas Folkman[1,2,*], Karsten Borgwardt[1,2]

[1] Machine Learning & Computational Biology Lab, Department of Biosystems Science and Engineering, ETH Zurich; [2]Swiss Institute of Bioinformatics.

* These authors contributed equally to this work.

1 Introduction

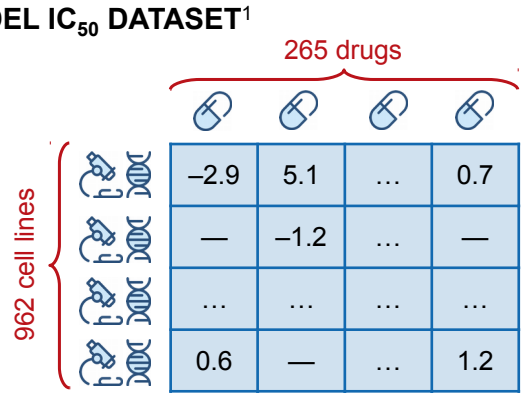
Large-scale screens of cancer cell lines against libraries of pharmacological compounds are being performed to enhance our ability to recommend therapies given the molecular profile of the tumor. These comprehensive screens differ from the clinical setting in which:

- biobanks contain patient's responses to very few drugs,
- drugs are recommended based on expert judgment, and
- selecting the most promising therapy is more important than predicting the sensitivity to all potential drugs.

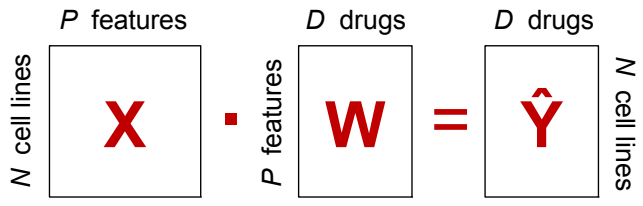
Current regression models for drug sensitivity prediction fail to account for these properties.

2 Methods

MODEL IC_{50} DATASET[1]



MACHINE LEARNING PERSPECTIVE



RANKING WITH DISCOUNTED CUMULATIVE GAIN

$$\mathrm{DCG@}k(\hat{y}, y) = \sum_{i=1}^{d} \delta(\mathrm{rank}(\hat{y}_i) \leq k) \frac{2^{y_i} - 1}{\log_2(1 + \mathrm{rank}(\hat{y}_i))}$$

where $\hat{y}$ is the predicted ranking vector, y is the true response vector, k is an evaluation hyper-parameter, $\delta(z) = 1$ if z is true and 0 otherwise, and $\mathrm{rank}(\hat{y}_i)$ returns the rank of $\hat{y}_i$ in $\hat{y}$, i.e. $\mathrm{rank}(\max(\hat{y}_i)) = 1$.

KERNELIZED RANK LEARNING (KRL)

- KRL is based on the idea of optimizing a convex upper bound of the normalized DCG (NDCG) loss[2]:

$$\ell_{\mathrm{NDCG@}k}(\hat{y}, y) = \max_{\pi}(c^T \hat{y}[\pi] - a[\pi]^T b) - c^T \hat{y} + a^T b$$

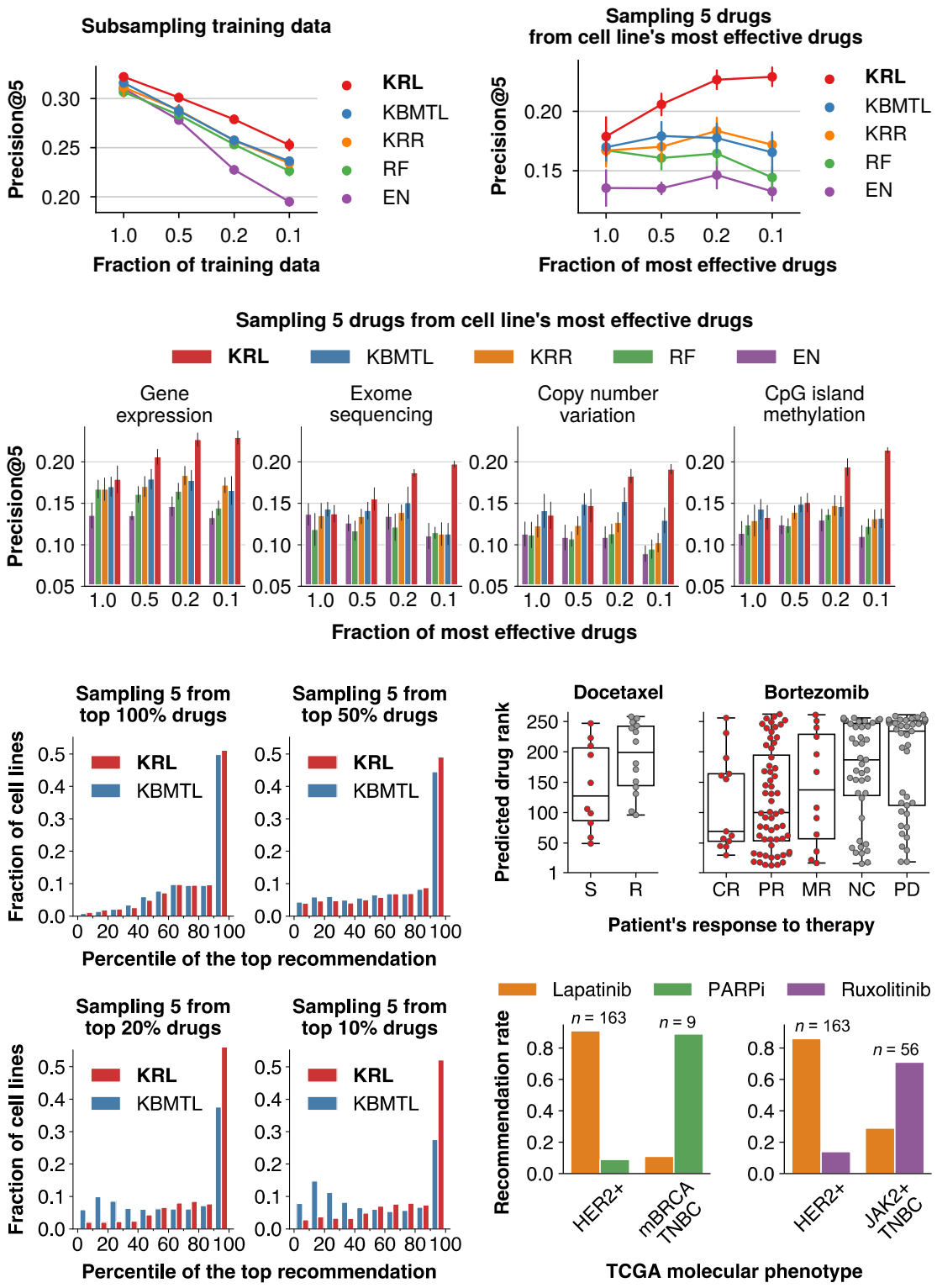
where π is a permutation,
$a_i = \frac{\delta(i \leq k)}{\log_2(i+1)}$, $b_i = 2^{y_i} - 1$, and $c_i = (i+1)^{-0.25}$.

- The kernelized objective function is optimized using the Bundle Method for regularized Risk Minimization[3]:

$$\min_{\beta} \sum_{i}^{n} \ell_{\mathrm{NDCG@}k}(K_i\beta, Y_i) + \lambda \mathrm{trace}(\beta^T K \beta)$$

where K is a kernel matrix on X, $\beta \in \mathbb{R}^{n \times d}$ such that $W = X^T\beta$, Y is the true drug response matrix, and λ is a regularization hyper-parameter.

3 Results



KRL: Kernelized Rank Learning (our method), KBMTL: Kernelized Bayesian Multi-Task Learning[4], KRR: Kernelized Ridge Regression, RF: Random Forest, EN: Elastic Net

4 Conclusion

- We phrased personalized drug recommendation as a ranking problem.
- KRL outperforms state-of-the-art predictors in simulated, clinically-relevant, scenarios.
- We showed its applicability using two clinical-trial datasets[5] and TCGA breast cancer cohort.
- You can read our paper in *Bioinformatics* (2018) **34**(16): 2808–2816.
- KRL's code is available at `https://github.com/BorgwardtLab/Kernelized-Rank-Learning`.

5 References

1. Iorio *et al*. (2016). *Cell*, **166**(3), 740–754.
2. Weimer *et al*. (2007). *NIPS* **20**, 1593–1600.
3. Teo *et al*. (2010). *Journal of Machine Learning Research*, **11**, 311–365.
4. Gönen & Margolin (2014). *Bioinformatics*, **30**(17), i556–i563.
5. Geeleher *et al*. (2014) *Genome Biology*, **15**, R47.