

# Rethinking Evaluation for Multi- Label Drug-Drug Interaction Prediction

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# Problems & Ideas

- Problems of traditional multi-label DDI prediction task.
  - Selecting sub-labels relies on prior knowledge of which reactions will occur for a given drug pair, which is often unavailable in real-world applications.
  - Traditional settings produce homogeneous labels (either all 1 or all 0), ultimately simplifying the task to merely predicting whether a reaction occurs between two drugs, rather than specifying the exact side effects.
- Ideas
  - We have discussed the limitation of existing settings, and believe it is essential to predict multi-label DDIs within the original label space.
  - We propose a Label-aware tuning (LAT) strategy to overcome the new imbalance challenge caused by this new setting, which can be easily combined with existing methods.

# Main Contributions

- Contributions:
  - A novel multi-label representation for DDI side effect prediction which not only focuses on observed adverse reactions, but also considers various specific reaction types simultaneously.
  - A Label-aware tuning (LAT) method to alleviate imbalanced categories of DDI side effects and relieve the impact of unobserved DDIs.
  - Experimental results clearly show that LAT consistently and effectively improves many existing methods under the multi-label evaluation.

**Algorithm 1** Pseudo-code of LAT

**Input:** Training dataset  $\mathcal{D} = \{(x_i, y_i)\}_{i=1}^n$ , hyper-parameter  $\lambda_{ema}$ ,  $\lambda_{wei}$ , model  $\Theta$ , epoch  $E$ ,  $E_{wa}$

**Procedure:**

Initialize  $\bar{y} = \mathbf{y}$

$$p_i = \lambda_{wei} * \frac{\min_{j=1}^n \mathbb{I}(y_i^j=1)}{\sum_{j=1}^n \mathbb{I}(y_i^j=1)}$$

**for**  $e = 1$  **to**  $E$  **do**

    Get prediction score  $s = \Theta(x)$

$$L = - \sum_{j=1}^n \sum_{i=1}^m [p_i * \bar{y}_i^j \log(s_i^j) + (1 - \bar{y}_i^j) * \log(1 - s_i^j)]$$

**if**  $e > E_{wa}$  : **then**

$$\bar{y} = \bar{y} * \lambda_{ema} + (1 - \lambda_{ema}) * s$$

**end if**

    Update  $\Theta$  according to  $L$  by optimizer.

**end for**

Methods	AUROC	F1	$\lambda_{wei}$	$\lambda_{ema}$
MLP	87.81 ± 0.05	6.36 ± 0.82	–	–
+LAT	88.28 ± 0.07	26.83 ± 0.12	20	0.99
KGDDI	87.68 ± 0.07	4.72 ± 0.05	–	–
+LAT	88.06 ± 0.06	26.37 ± 0.28	20	0.99
SkipGNN	87.85 ± 0.03	3.61 ± 0.35	–	–
+LAT	88.08 ± 0.02	24.38 ± 0.13	50	0.999
Decagon	78.84 ± 0.29	1.98 ± 0.30	–	–
+LAT	78.51 ± 0.12	18.67 ± 0.22	10	0.999
SumGNN	82.27 ± 0.14	1.86 ± 0.27	–	–
+LAT	84.67 ± 0.10	24.17 ± 0.23	20	0.99