Drug Recommendation toward Safe Polypharmacy

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2. The Proposed Method

3. Experiments

Drug-drug Interaction

1. DDIs: Drug-drug interactions

The pharmacological effects of a drug are altered by actions of another drug
Leading to unpredictable consequences.

2. ADRs: Adverse drug reactions

Undesired or harmful reactions due to drug administration.

A recent thread is dedicated **to understanding the interaction patterns among high-order DDIs**, and how such patterns can relate to induced ADRs.

Two problems

1. To-avoid Drug Recommendation:

Given the multiple drugs in a prescription that have been taken simultaneously, **recommend a short of ranked list of drugs** that should be avoided taking together with the prescription in order to avoid a particular ADR.

2. Safe Drug Recommendation

Given the multiple drugs in a prescription that have been taken simultaneously, **recommend a short ranked list of safe drugs** that, if token together with the prescription, are not likely to induce a particular ADR.

Notations

a drug

a prescription

$$
\begin{array}{c|ccccccc|l}
 & d_1 & d_2 & d_3 & \cdots & d_j & \cdots & d_n & \\
\hline
\boldsymbol{a}_1 & 1 & 0 & 1 & \dots & 1 & \dots & 0 & y_1 = 1 / -1 \\
\boldsymbol{a}_2 & 0 & 1 & 1 & \dots & 0 & \dots & 1 & y_2 \\
\dots & \dots & \dots & \dots & \dots & 0 & \dots & 1 & \dots \\
\boldsymbol{a}_i & 1 & 0 & 1 & \dots & 1 & \dots & 0 & y_i \\
\dots & 0 & 1 & 1 & \dots & 0 & \dots & 1 & \dots \\
\boldsymbol{a}_m & 1 & 1 & 1 & \dots & 0 & \dots & 0 & y_m \\
\end{array}
$$

$A \in R^{m \times n}$ $\quad$ $A \approx \tilde{A}$

A^+ prescriptions known to induce ADRs

A^- prescriptions known not to induce ADRs

Two Methods

1. SLIM (Sparse Linear Method)

Motivation: A matrix decomposition method that decomposes to obtain a sparse matrix of W that can be used for feature selection and compression of the data.

$$\tilde{A} = \mathrm{AW}$$

2. LogR (Logistic Regression)

Motivation: binary classification

SLIM:

SLIM learns **a sparse coefficient matrix** for the items in the system solely from user purchase/rating profiles by solving a regularized optimization problem.

$$\tilde{a}_{ij} = \boldsymbol{a}_i \boldsymbol{w}_j^{\mathsf{T}}$$

$\tilde{a}_{ij}$ is the estimated score of d_j in $\boldsymbol{a}_i$ $\boldsymbol{a}_i \cup \{d_j\}$.

$$\tilde{A} = \mathrm{AW}$$

$\boldsymbol{w}_j^{\mathsf{T}}$ is a spare column vector of aggregation coefficients

the sparse coefficient matrix

$$W = [\boldsymbol{w}_1^{\mathsf{T}}, \boldsymbol{w}_2^{\mathsf{T}}, \cdots, \boldsymbol{w}_n^{\mathsf{T}}]$$

Control the value of W

$$\min_{W} \quad \mathrm{SLIM}(A; W, \alpha, \lambda) = \frac{1}{2}\|A - AW\|_F^2 + \frac{\alpha}{2}\|W\|_F^2 + \lambda\|W\|_{\ell_1}$$

$$\text{subject to} \quad W \geq 0, \mathrm{diag}(W) = 0,$$

$$\boxed{\tilde{A} = \mathrm{AW}}$$

Control the sparsity of W

LogR

the probability of a prescription ai inducing the ADR is modeled as follows

$$p(y_i|\boldsymbol{a}_i;\boldsymbol{x},c) = (1+\exp(-y_i(\boldsymbol{a}_i\boldsymbol{x}^\top + c)))^{-1}$$

Where $\boldsymbol{x}^\top$ and c are the parameters. To learn the parameters, LogR solves the following optimization problem,

$$\min_{\boldsymbol{x},c} \quad \mathrm{LogR}(\boldsymbol{y}|A;\boldsymbol{x},c,\beta,\gamma)$$

$$= \sum_{i=1}^{m} \log\{1+\exp[-y_i(\boldsymbol{a}_i\boldsymbol{x}^\top + c)]\} + \frac{\beta}{2}\|\boldsymbol{x}\|_2^2 + \gamma\|\boldsymbol{x}\|_1$$

where $\boldsymbol{y} = [y_1; y_2; \cdots, y_m]$, $\|\boldsymbol{x}\|_1 = \sum_{i=1}^{n} |x_i|$, and $\|\boldsymbol{x}\|_2^2 = \sum_{i=1}^{n} {x_i}^2$.

outline

SlimLogR

SlimLogR learns the SLIM and LogR components jointly through solving the following optimization problem

$$
\begin{aligned}
\min_{W^+, W^-, \boldsymbol{x}, c} \quad & \mathtt{SLIM}(A^+; W+, \alpha, \lambda) + \mathtt{SLIM}(A^-; W^-, \alpha, \lambda) \\
& \omega\{\mathtt{LogR}(\boldsymbol{y}^+ | \tilde{A}^+ \circ \boxed{M^+}; \boldsymbol{x}, c, \beta, \gamma) + \\
& \quad \mathtt{LogR}(\boldsymbol{y}^- | \tilde{A}^- \circ \boxed{M^-}; \boldsymbol{x}, c, \beta, \gamma)\} \\
\text{subject to} \quad & \tilde{A}^+ = A^+ W^+, \tilde{A}^- = A^- W^-, \\
& W^+ \geq 0, W^- \geq 0, \mathrm{diag}(W^+) = 0, \mathrm{diag}(W^-) = 0
\end{aligned}
$$

$M = \mathbf{1}$ → $\mathtt{SlimLogR_{in}}$

$M = \mathbb{I}(A)$ → $\mathtt{SlimLogR_{ex}}$

where $\mathbb{I}$ is an indicator function $((I)(x) = 0$ if $x = 0$, 1 otherwise$)$

Training SlimLogR

$$\min_{W^+, W^-, \boldsymbol{x},\, c} \quad \mathtt{SLIM}(A^+; W+, \alpha, \lambda) + \mathtt{SLIM}(A^-; W^-, \alpha, \lambda)$$

$$\omega\{\mathsf{LogR}(\boldsymbol{y}^+ | \tilde{A}^+ \circ M^+; \boldsymbol{x}, c, \beta, \gamma) + \mathsf{LogR}(\boldsymbol{y}^- | \tilde{A}^- \circ M^-; \boldsymbol{x}, c, \beta, \gamma)\}$$

$$\text{subject to} \quad \tilde{A}^+ = A^+ W^+, \tilde{A}^- = A^- W^-,$$

$$W^+ \geq 0, W^- \geq 0, \mathrm{diag}(W^+) = 0, \mathrm{diag}(W^-) = 0$$

$$\min_{W^+, W^-, Z^+, Z^-, \boldsymbol{x},\, c} \quad L(W^+, W^-, Z^+, Z^-, \boldsymbol{x}, c, \boldsymbol{u}^+, \boldsymbol{u}^-, \rho^+, \rho^-) =$$

$$\mathtt{SLIM}(A^+; W+, \alpha, \lambda) + \mathtt{SLIM}(A^-; W^-, \alpha, \lambda)$$

$$\omega\{\mathsf{LogR}(\boldsymbol{y}^+ | \tilde{B}^+ \circ M^+; \boldsymbol{x}, c, \beta, \gamma) + \mathsf{LogR}(\boldsymbol{y}^- | \tilde{B}^- \circ M^-; \boldsymbol{x}, c, \beta, \gamma)\}$$

$$\boldsymbol{u}^{+\mathsf{T}} \boldsymbol{v}^+ + \frac{\rho^+}{2} \|\boldsymbol{v}^+\|_2^2 + \boldsymbol{u}^{-\mathsf{T}} \boldsymbol{v}^- + \frac{\rho^-}{2} \|\boldsymbol{v}^-\|_2^2,$$

$$\text{subject to} \quad \tilde{B}^+ = A^+ Z^+, \tilde{B}^- = A^- Z^-,$$

$$\boldsymbol{v}^+ = \mathrm{vec}(W^+) - \mathrm{vec}(Z^+), \boldsymbol{v}^- = \mathrm{vec}(W^-) - \mathrm{vec}(Z^-),$$

$$W^+ = Z^+, W^- = Z^-, W^+ \geq 0, W^- \geq 0,$$

$$\mathrm{diag}(W^+) = 0, \mathrm{diag}(W^-) = 0,$$

Training SlimLogR

$$
\begin{aligned}
\min_{W^+, W^-, Z^+, Z^-, \boldsymbol{x}, c} \quad & L(W^+, W^-, Z^+, Z^-, \boldsymbol{x}, c, \boldsymbol{u}^+, \boldsymbol{u}^-, \rho^+, \rho^-) = \\
& \mathtt{SLIM}(A^+; W+, \alpha, \lambda) + \mathtt{SLIM}(A^-; W^-, \alpha, \lambda) \\
& \omega\{\mathtt{LogR}(\boldsymbol{y}^+ | \tilde{B}^+ \circ M^+; \boldsymbol{x}, c, \beta, \gamma) + \\
& \quad \mathtt{LogR}(\boldsymbol{y}^- | \tilde{B}^- \circ M^-; \boldsymbol{x}, c, \beta, \gamma)\} \\
& \boldsymbol{u}^{+\mathsf{T}} \boldsymbol{v}^+ + \frac{\rho^+}{2} \|\boldsymbol{v}^+\|_2^2 + \boldsymbol{u}^{-\mathsf{T}} \boldsymbol{v}^- + \frac{\rho^-}{2} \|\boldsymbol{v}^-\|_2^2, \\
\text{subject to} \quad & \tilde{B}^+ = A^+ Z^+, \tilde{B}^- = A^- Z^-, \\
& \boldsymbol{v}^+ = \mathrm{vec}(W^+) - \mathrm{vec}(Z^+), \boldsymbol{v}^- = \mathrm{vec}(W^-) - \mathrm{vec}(Z^-), \\
& W^+ = Z^+, W^- = Z^-, W^+ \geq 0, W^- \geq 0, \\
& \mathrm{diag}(W^+) = 0, \mathrm{diag}(W^-) = 0,
\end{aligned}
$$

Algorithm 1 Learning `SlimLogR`

function `SlimLogR`$(A, \omega, \alpha, \lambda, \beta, \gamma)$

- $\rho^+ = 10, \rho^- = 10, \boldsymbol{u}^+_{(0)} = \boldsymbol{0}, \boldsymbol{u}^-_{(0)} = \boldsymbol{0}, k = 0$
- $Z^+_{(0)} = W^+_{(0)}, Z^-_{(0)} = W^-_{(0)}$
- learn $W^+_{(0)}$ and $W^-_{(0)}$ from `SLIM` (Section 6.3)
- learn $\boldsymbol{x}_{(0)}$ and $c_{(0)}$ from `LogR` (Section 6.2)
- **while** not converge **do**
  - $\{W^+_{(k+1)}, W^-_{(k+1)}\} := \operatorname{argmin}_{W^+, W^-} L(W^+_{(k)}, W^-_{(k)}, Z^+_{(k)}, Z^-_{(k)}, \boldsymbol{x}_{(k)}, c_{(k)}, \boldsymbol{u}^+_{(k)}, \boldsymbol{u}^-_{(k)})$
  - $\{Z^+_{(k+1)}, Z^-_{(k+1)}\} := \operatorname{argmin}_{Z^+, Z^-} L(W^+_{(k+1)}, W^-_{(k+1)}, Z^+_{(k)}, Z^-_{(k)}, \boldsymbol{x}_{(k)}, c_{(k)}, \boldsymbol{u}^+_{(k)}, \boldsymbol{u}^-_{(k)})$
  - $\{\boldsymbol{x}_{(k+1)}, c_{(k+1)}\} := \operatorname{argmin}_{\boldsymbol{x}, c} L(W^+_{(k+1)}, W^-_{(k+1)}, Z^+_{(k+1)}, Z^-_{(k+1)}, \boldsymbol{x}_{(k)}, c_{(k)}, \boldsymbol{u}^+_{(k)}, \boldsymbol{u}^-_{(k)})$
  - $\boldsymbol{u}^+_{(k+1)} = \boldsymbol{u}^+_{(k)} + \rho^+(\mathrm{vec}(W^+_{(k+1)} - Z^+_{(k+1)})$
  - $\boldsymbol{u}^-_{(k+1)} = \boldsymbol{u}^-_{(k)} + \rho^+(\mathrm{vec}(W^-_{(k+1)} - Z^-_{(k+1)})$
  - $k = k + 1$
- **end while**
- **return** $W^+_{(k+1)}, W^-_{(k+1)}, Z^+_{(k+1)}, Z^-_{(k+1)}, \boldsymbol{x}_{(k+1)}$ and $c_{(k+1)}$

end function

Applying SlimLogR

- Step 1: use the learned SLIM component to recommend a list of potential to-avoid/safe drug candidates $\{d_{r_j}\}$;

the scores of being potential to-avoid drugs: $\tilde{\boldsymbol{a}}^+ = \boldsymbol{a}W^+$

the scores of being potential safe drugs: $\tilde{\boldsymbol{a}}^- = \boldsymbol{a}W^-$

- Step 2: for each recommended candidate d_{r_j}, combine it with $\boldsymbol{a}$ (i.e., $\boldsymbol{a} \cup \{d_{r_j}\}$) and use the learned LogR component to predict the ADR probability of the new prescription.

the ADR probabilities

$$p(y^+ | \boxed{\boldsymbol{f}_i(j)^+}; \boldsymbol{x}, c)$$
$$p(y^- | \boxed{\boldsymbol{f}_i(j)^-}; \boldsymbol{x}, c)$$

LogR$_b$

$$\boxed{\boldsymbol{r}_i(j)^+} = \boldsymbol{a}_i^+ \cup \{d_{r_j}^+\}$$
$$\boxed{\boldsymbol{r}_i(j)^-} = \boldsymbol{a}_i^- \cup \{d_{r_j}^-\}$$

$$\boxed{\boldsymbol{s}_i(j)^+} = \tilde{\boldsymbol{a}}^+$$
$$\boxed{\boldsymbol{s}_i(j)^-} = \tilde{\boldsymbol{a}}^-$$

LogR$_s$

Overview

$$\tilde{a}_{ij} = \boldsymbol{a}_i \boldsymbol{w}_j^{\mathsf{T}}$$

$$p(y_i|\boldsymbol{a}_i; \boldsymbol{x}, c) = (1 + \exp(-y_i(\boldsymbol{a}_i \boldsymbol{x}^{\mathsf{T}} + c)))^{-1}$$

SlimLogR$_{\mathrm{in}}$

$$\min_{W^+, W^-, \boldsymbol{x}, c} \ \mathrm{SLIM}(A^+; W+, \alpha, \lambda) + \mathrm{SLIM}(A^-; W^-, \alpha, \lambda)$$

$$\omega\{\mathrm{LogR}(\boldsymbol{y}^+|\tilde{A}^+ \circ \boxed{M^+}; \boldsymbol{x}, c, \beta, \gamma) +$$

$$\mathrm{LogR}(\boldsymbol{y}^-|\tilde{A}^- \circ M^-; \boldsymbol{x}, c, \beta, \gamma)\}$$

SlimLogR$_{\mathrm{ex}}$

subject to $\tilde{A}^+ = A^+W^+, \tilde{A}^- = A^-W^-,$

$W^+ \geq 0, W^- \geq 0, \mathrm{diag}(W^+) = 0, \mathrm{diag}(W^-) = 0$

the ADR probabilities

$$p(y^+|\boxed{f_i(j)^+}; \boldsymbol{x}, c)$$
$$p(y^-|\boxed{f_i(j)^-}; \boldsymbol{x}, c)$$

$$\boxed{r_i(j)^+} = \boldsymbol{a}_i^+ \cup \{d_{r_j}^+\} \qquad \boxed{s_i(j)^+} = \tilde{\boldsymbol{a}}^+$$

$$\boxed{r_i(j)^-} = \boldsymbol{a}_i^- \cup \{d_{r_j}^-\} \qquad \boxed{s_i(j)^-} = \tilde{\boldsymbol{a}}^-$$

LogR$_{\mathrm{b}}$ LogR$_{\mathrm{s}}$

A_{pool}	mdl	prd	rec$_t$	prec$_t$	acc$_t$
A_{FAERS}	SlimLogR$_{\mathrm{in}}$	LogR$_{\mathrm{s}}$	**0.2361**	**0.2361**	**0.2958**
		LogR$_{\mathrm{b}}$	**0.2361**	**0.2361**	**0.2958**
	SlimLogR$_{\mathrm{ex}}$	LogR$_{\mathrm{s}}$	0.2108	0.2108	0.2795
		LogR$_{\mathrm{b}}$	0.2108	0.2108	0.2795
	Rand	-	0.0060	0.0118	0.0238
	LogR	-	0.2082	0.2081	0.2430
	SLIM	-	0.2127	0.2126	0.2811
	SLIM+LogR	-	0.2127	0.2126	0.2813

outline

Experiments

Datasets:

dataset	stats	A^-		A^+	
		A^-_-	A^-_0	A^+_0	A^+_+
A_{FAERS}	$\#\{\boldsymbol{a}\}$	621,449	1,264	8,986	27,387
	$\#\{d\}$	1,209	417	881	1,201
	avgOrd	6.100	2.351	3.588	7.096
	avgFrq	1.761	225.317	13.730	1.402
	avgOR	-	0.546	16.343	-
A_*	$\#\{\boldsymbol{a}\}$	2,200	1,264	2,464	1,000
	$\#\{d\}$	562	417	692	679
	avgOrd	2.678	2.351	3.809	7.615
	avgFrq	42.082	225.317	20.565	5.520
	avgOR	-	0.546	31.998	-

Experiments

Table 3: Comparison based on the Best $\overline{\text{rec}_t}$ ($N = 5$)

A_{pool}	mdl	prd	$\overline{\text{rec}_t}$	$\overline{\text{prec}_t}$	$\overline{\text{acc}_t}$
A_{FAERS}	$\text{SlimLogR}_{\text{in}}$	LogR_s	**0.2361**	**0.2361**	**0.2958**
		LogR_b	**0.2361**	**0.2361**	**0.2958**
	$\text{SlimLogR}_{\text{ex}}$	LogR_s	0.2108	0.2108	0.2795
		LogR_b	0.2108	0.2108	0.2795
	Rand	-	0.0060	0.0118	0.0238
	LogR	-	0.2082	0.2081	0.2430
	SLIM	-	0.2127	0.2126	0.2811
	SLIM+LogR	-	0.2127	0.2126	0.2813
A_*	$\text{SlimLogR}_{\text{in}}$	LogR_s	**0.2618**	**0.2615**	**0.2815**
		LogR_b	**0.2618**	**0.2615**	**0.2815**
	$\text{SlimLogR}_{\text{ex}}$	LogR_s	0.2479	0.2479	0.2748
		LogR_b	0.2479	0.2479	0.2748
	Rand	-	0.0029	0.0059	0.0034
	LogR	-	0.1780	0.1781	0.1032
	SLIM	-	0.2469	0.2467	0.2754
	SLIM+LogR	-	0.2469	0.2467	0.2754

The column "mdl" corresponds to models. The column "prd" corresponds to prediction methods. The best $\overline{\text{rec}_t}$ is underlined. The best overall performance is **bold**.

Table 4: Comparison based on the Best $\overline{\text{prec}_t}$ ($N = 5$)

A_{pool}	mdl	prd	$\overline{\text{rec}_t}$	$\overline{\text{prec}_t}$	$\overline{\text{acc}_t}$
A_{FAERS}	$\text{SlimLogR}_{\text{in}}$	LogR_s	**0.2361**	**0.2361**	**0.2958**
		LogR_b	**0.2361**	**0.2361**	**0.2958**
	$\text{SlimLogR}_{\text{ex}}$	LogR_s	0.2108	0.2108	0.2795
		LogR_b	0.2108	0.2108	0.2795
	Rand	-	0.0060	0.0118	0.0238
	LogR	-	0.2082	0.2081	0.2430
	SLIM	-	0.2127	0.2128	0.2809
	SLIM+LogR	-	0.2127	0.2128	0.2811
A_*	$\text{SlimLogR}_{\text{in}}$	LogR_s	**0.2613**	**0.2615**	**0.2821**
		LogR_b	**0.2613**	**0.2615**	**0.2821**
	$\text{SlimLogR}_{\text{ex}}$	LogR_s	0.2477	0.2479	0.2759
		LogR_b	0.2477	0.2479	0.2759
	Rand	-	0.0029	0.0059	0.0034
	LogR	-	0.1780	0.1781	0.1032
	SLIM	-	0.2465	0.2467	0.2754
	SLIM+LogR	-	0.2465	0.2467	0.2754

The column "mdl" corresponds to models. The column "prd" corresponds to prediction methods. The best $\overline{\text{prec}_t}$ is underlined. The best overall performance is **bold**.

Table 5: Comparison based on the Best $\overline{\text{acc}_t}$ ($N = 5$)

A_{pool}	mdl	prd	$\overline{\text{rec}_t}$	$\overline{\text{prec}_t}$	$\overline{\text{acc}_t}$
A_{FAERS}	$\text{SlimLogR}_{\text{in}}$	LogR_s	**0.2355**	**0.2355**	**0.2969**
		LogR_b	**0.2355**	**0.2355**	**0.2969**
	$\text{SlimLogR}_{\text{ex}}$	LogR_s	0.2099	0.2099	0.2797
		LogR_b	0.2108	0.2108	0.2797
	Rand	-	0.0060	0.0118	0.0238
	LogR	-	0.2036	0.2039	0.2468
	SLIM	-	0.2019	0.2020	0.2830
	SLIM+LogR	-	0.2019	0.2020	0.2825
A_*	$\text{SlimLogR}_{\text{in}}$	LogR_s	**0.2589**	**0.2592**	**0.2832**
		LogR_b	**0.2589**	**0.2592**	**0.2832**
	$\text{SlimLogR}_{\text{ex}}$	LogR_s	0.2477	0.2479	0.2765
		LogR_b	0.2477	0.2479	0.2765
	Rand	-	0.0029	0.0059	0.0034
	LogR	-	0.1780	0.1781	0.1032
	SLIM	-	0.2434	0.2432	0.2776
	SLIM+LogR	-	0.2434	0.2432	0.2776

The column "mdl" corresponds to models. The column "prd" corresponds to prediction methods. The best $\overline{\text{acc}_t}$ is underlined. The best overall performance is **bold**.

Parameter Study

$$\begin{aligned}
\min_{W^+, W^-, \boldsymbol{x}, c} \quad & \mathsf{SLIM}(A^+; W+, \alpha, \lambda) + \mathsf{SLIM}(A^-; W^-, \boxed{\alpha}, \lambda) \\
& \boxed{\omega}\{\mathsf{LogR}(\boldsymbol{y}^+ | \tilde{A}^+ \circ M^+; \boldsymbol{x}, c, \beta, \gamma) + \\
& \quad \mathsf{LogR}(\boldsymbol{y}^- | \tilde{A}^- \circ M^-; \boldsymbol{x}, c, \beta, \gamma)\} \\
\text{subject to} \quad & \tilde{A}^+ = A^+ W^+, \tilde{A}^- = A^- W^-, \\
& W^+ \geq 0, W^- \geq 0, \operatorname{diag}(W^+) = 0, \operatorname{diag}(W^-) = 0
\end{aligned}$$

Table 6: $\overline{\texttt{rec}_\texttt{t}}$ **of** $\texttt{SlimLogR}_{\texttt{in}}$ **+**$\texttt{LogR}_\texttt{s}$ **(**$N = 5$**)**

$\omega \backslash \alpha$	100	50	20	10	5
20	0.2324	0.2344	0.2346	0.2349	0.2338
10	0.2315	0.2352	0.2349	0.2358	0.2344
5	0.2318	0.2355	**0.2361**	**0.2361**	0.2341
1	0.2315	0.2327	0.2321	0.2304	0.2290

A_{pool} is A_{FAERS}. The best performance is **bold**.

Table 7: $\overline{\texttt{prec}_\texttt{t}}$ **of** $\texttt{SlimLogR}_{\texttt{in}}$ **+**$\texttt{LogR}_\texttt{s}$ **(**$N = 5$**)**

$\omega \backslash \alpha$	100	50	20	10	5
20	0.2325	0.2343	0.2347	0.2349	0.2339
10	0.2315	0.2351	0.2351	0.2359	0.2345
5	0.2321	0.2355	**0.2361**	0.2359	0.2341
1	0.2315	0.2327	0.2321	0.2305	0.2290

A_{pool} is A_{FAERS}. The best performance is **bold**.

Table 8: $\overline{\texttt{acc}_\texttt{t}}$ **of** $\texttt{SlimLogR}_{\texttt{in}}$ **+**$\texttt{LogR}_\texttt{s}$ **(**$N = 5$**)**

$\omega \backslash \alpha$	100	50	20	10	5
20	0.2951	0.2919	0.2890	0.2895	0.2874
10	0.2943	0.2967	0.2938	0.2915	0.2891
5	0.2955	**0.2969**	0.2958	0.2951	0.2924
1	0.2938	0.2953	0.2936	0.2919	0.2893

A_{pool} is A_{FAERS}. The best performance is **bold**.

Top-N Performance

Table 9: Top-N Performance of $\texttt{SlimLogR}_{\texttt{in}}$ with $\texttt{LogR}_{\texttt{s}}$

N	A_{FAERS}			A_*		
	$\overline{\texttt{rec}_t}$	$\overline{\texttt{prec}_t}$	$\overline{\texttt{acc}_t}$	$\overline{\texttt{rec}_t}$	$\overline{\texttt{prec}_t}$	$\overline{\texttt{acc}_t}$
5	**0.2358**	**0.2359**	0.2915	**0.2613**	**0.2615**	0.2821
	0.2324	0.2325	**0.2929**	0.2589	0.2592	**0.2832**
10	**0.2497**	**0.2497**	0.3076	**0.3469**	**0.3467**	0.3419
	0.2467	0.2467	**0.3110**	0.3434	0.3432	**0.3439**
20	**0.2885**	**0.2887**	0.2762	**0.4403**	**0.4407**	0.4016
	0.2694	0.2695	**0.3289**	0.4265	0.4273	**0.4135**

Column of "N" represents the number of recommended drugs. Columns of "A_{FAERS}" and "A_*" represent that "A_{FAERS}" and "A_*" are used as A_{pool}, respectively. The **bold** performance is the best under the corresponding metrics in each column.