A **Fast and Scalable** Joint Estimator for Integrating **Additional Knowledge** in Learning Multiple Related Sparse Gaussian Graphical Models

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http://jointggm.org/

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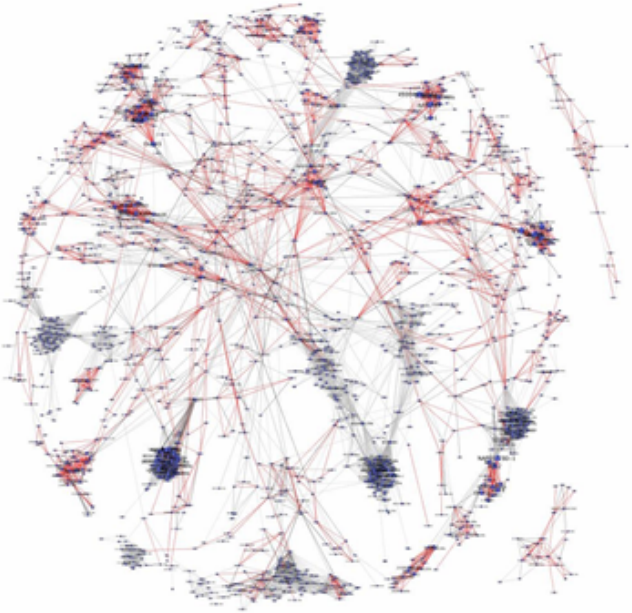
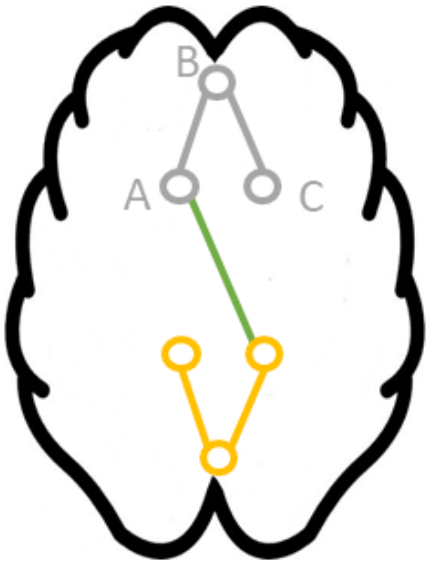
Motivation: Entity Graph

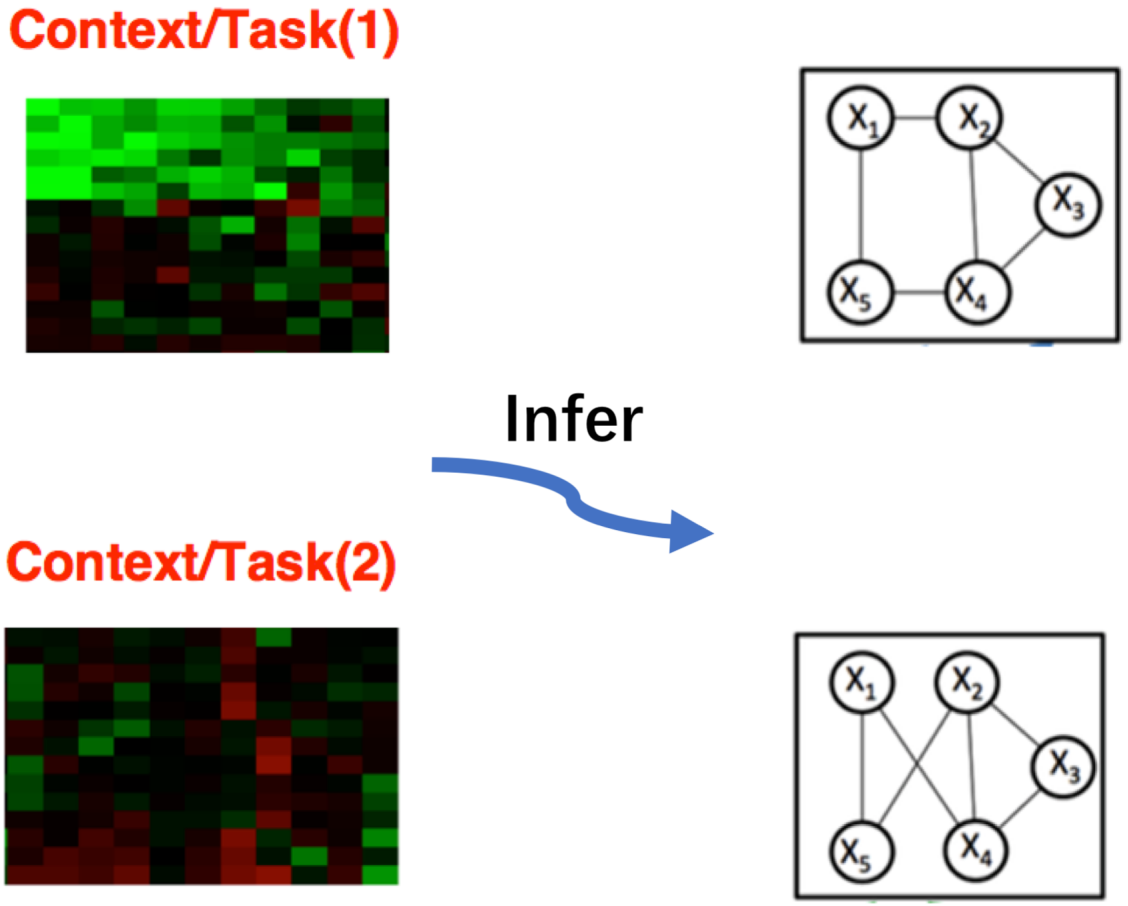




- Many applications need to know interactions among entities:
  - Gene Interactions
  - Brain connectivity
- Why to study the entity graph
  - Understanding
  - Diagnosis, e.g., marker
  - Treatment, e.g., drug development.

Motivation: Learning Multiple Related Graphs from Heterogeneous Samples about Multiple Contexts

- Multiple Datasets $\mathbf{X}^{(1)}, \ldots \mathbf{X}^{(K)} \rightarrow$ Multiple Graphs $G^{(1)}, \ldots, G^{(K)}$.



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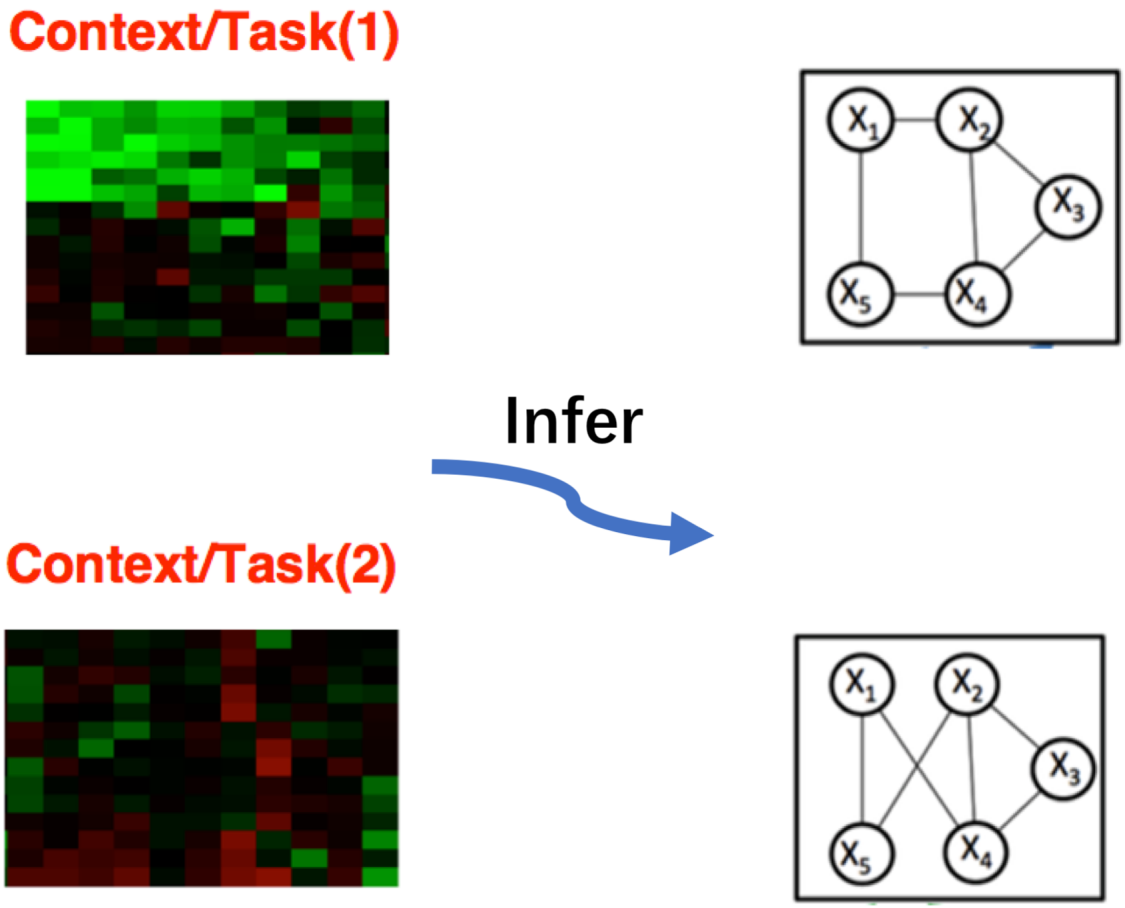

- e.g., Brain Connectomes from heterogeneous fMRI images
- e.g., Genetic Networks from heterogeneous RNA samples

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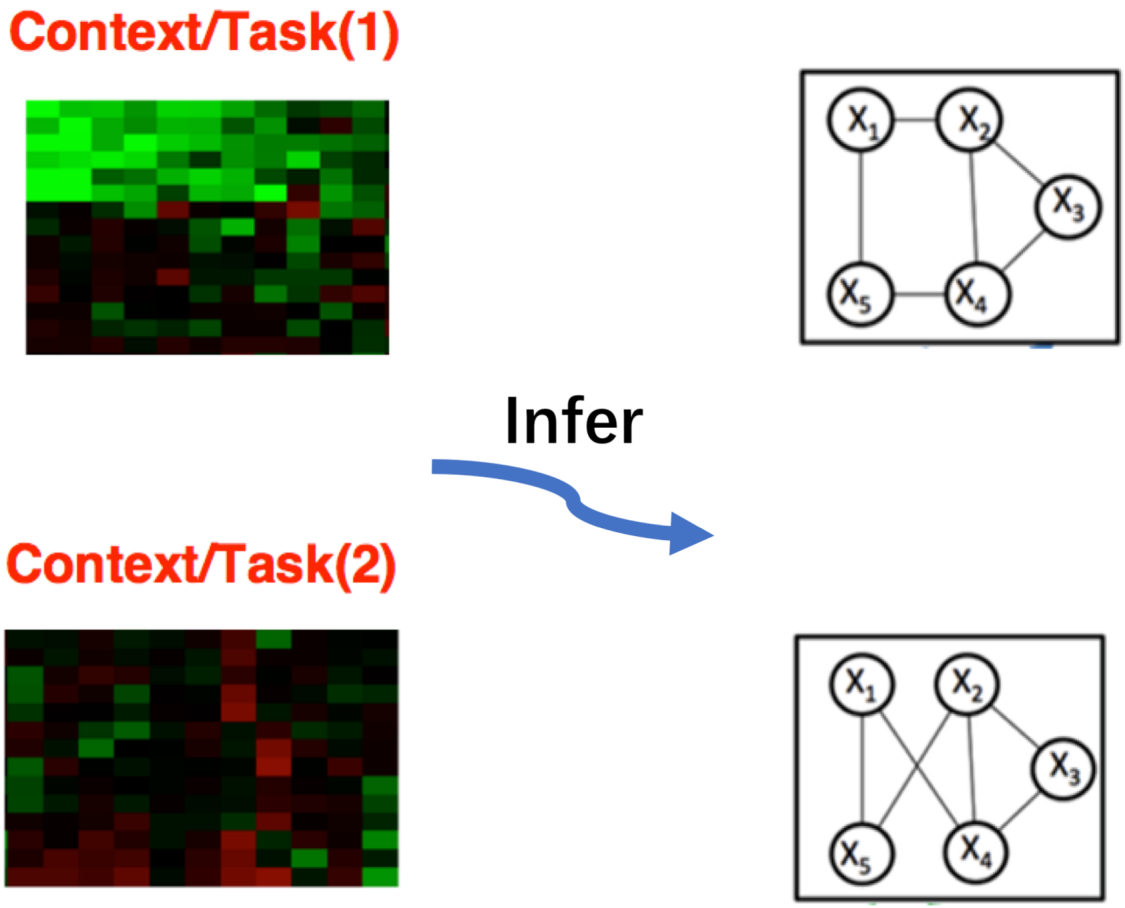
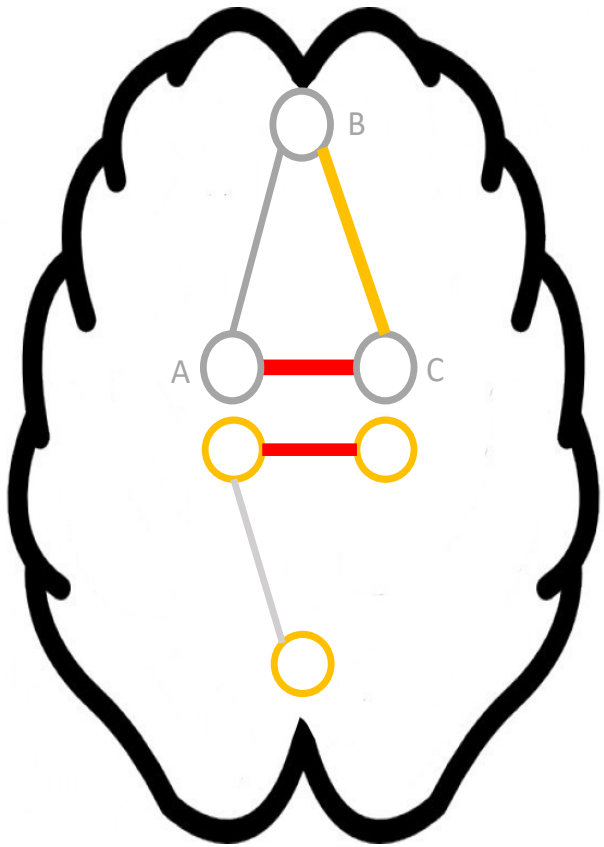


- Current Approch: Multi-sGGMs $\Rightarrow$
  Multi-task sparse Gaussian Graphical Models

Limitation I: Missing Known Knowledge

- No clear ways to consider Known Additional Knowledge in multi-sGGMs.
- However, in real-world applications, plenty of known information. (e.g., red edges in the figures.)



Spatial Knowledge

Limitation II: Slow computation and Not scalable

- K: number of tasks
  p: number of features

Method	Time Complexity	Bottleneck
W-SIMULE[1]	$O(K^4 p^5)$	LP with Kp variables
JGL[2]	$O(T \times Kp^3)$	SVD

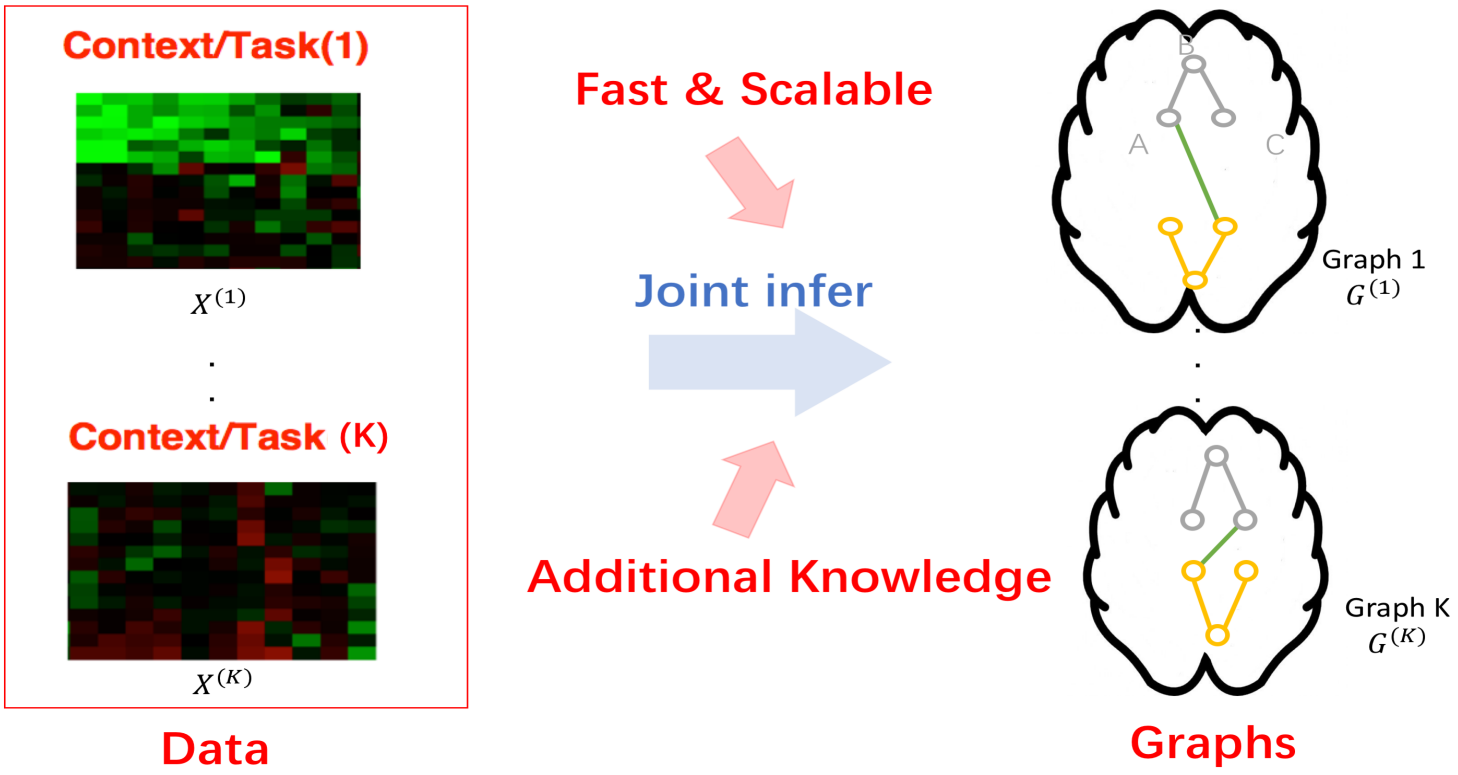
e.g., $K = 91$ and $p = 30$K

- W-SIMULE (Constrained ℓ_1 minimization based): 6 trillion years
- JGL (MLE): 3.5 days / iter

[1] [Singh et al.(2017)Singh, Wang, and Qi]
[2] [Danaher et al.(2013)Danaher, Wang, and Witten]

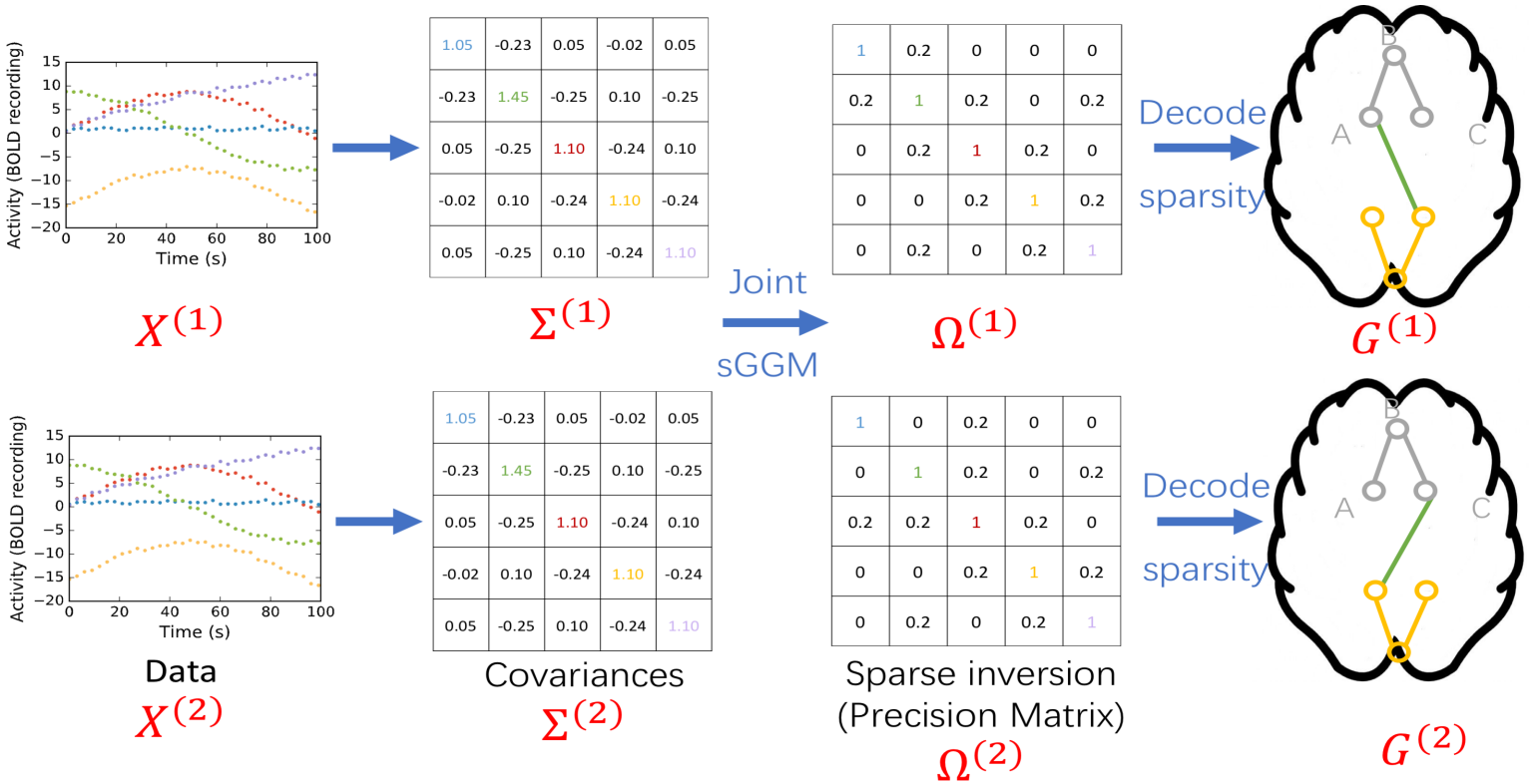
Summary of contributions: Integrating Additional Knowledge in Scalable Learning of multi-sGGMs

- Our focus: How to estimate multiple graphs $G^{(1)}, \ldots, G^{(K)}$ from heterogeneous data $\mathbf{X}^{(1)}, \ldots \mathbf{X}^{(K)}$ and integrate additional knowledge.



Notations: Multi-sGGMs

- A pipeline to infer Graph from heterogeneous datasets $\mathbf{X}^{(1)}, \ldots \mathbf{X}^{(K)}$[3].



[3] X^{tot}: the concatenation of $(X^{(1)}, X^{(2)}, \ldots, X^{(K)})$.
Σ^{tot}: the concatenation of $(\Sigma^{(1)}, \Sigma^{(2)}, \ldots, \Sigma^{(K)})$.
Ω^{tot}: the concatenation of $(\Omega^{(1)}, \Omega^{(2)}, \ldots, \Omega^{(K)})$.

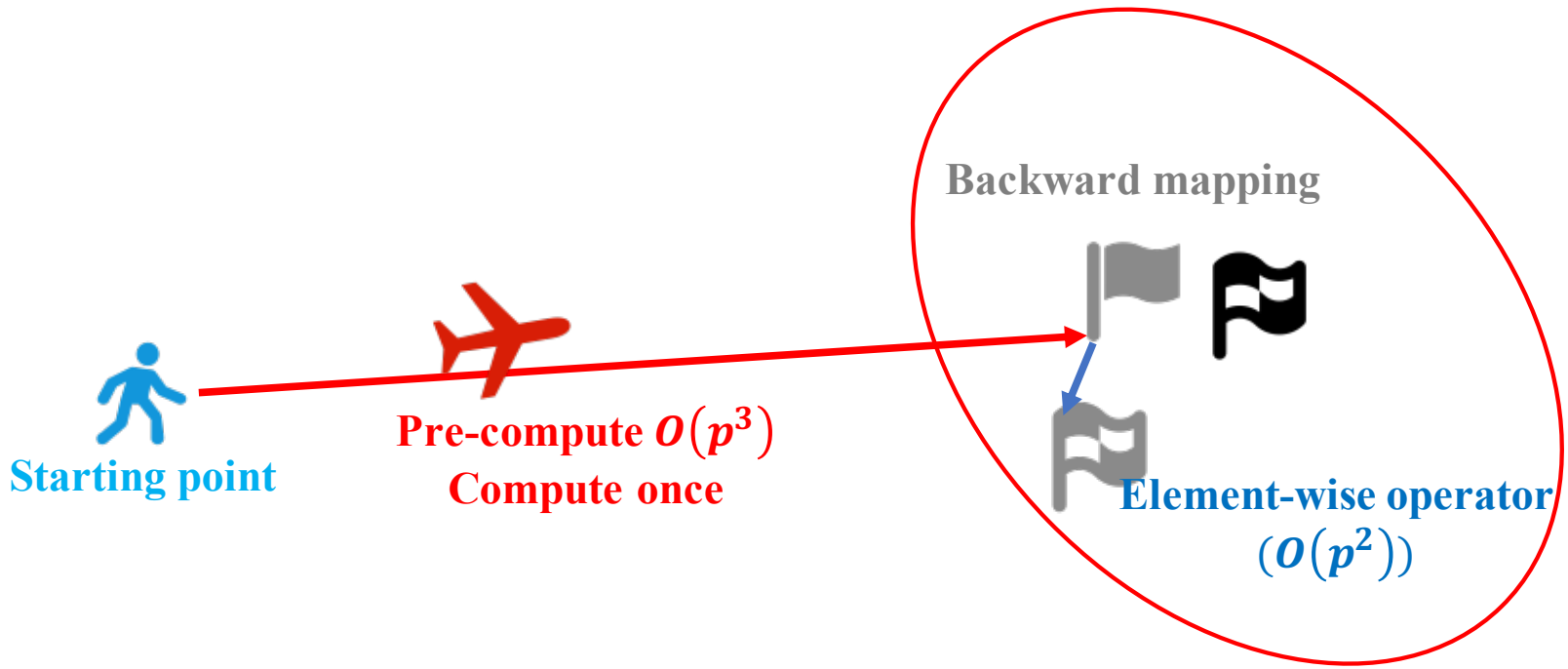
Notations

$X^{(i)}$	i-th Data matrix.
$\Sigma^{(i)}$	i-th Covariance matrix.
$\Omega^{(i)}$	i-th Inverse of covariance matrix (precision matrix).
p	The total number of feature variables.
n_{tot}	The total number of samples.
X^{tot}	the concatenation of all Data matrices.
Σ^{tot}	the concatenation of all Covariance matrices.
Ω^{tot}	the concatenation of all Inverse of covariance matrices (precision matrices).
W_I^{tot}	$(W_I^{(1)}, W_I^{(2)}, \ldots, W_I^{(K)})$
W_S^{tot}	$(W_S, W_S, \ldots, W_S)$

Solution to Limitation II: Elementary Estimator for sGGM

Elementary Estimator

$$\begin{aligned} &\underset{\theta}{\operatorname{argmin}} \mathcal{R}(\theta) \\ &\text{Subject to: } \mathcal{R}^*(\theta - \mathcal{B}^*(\widehat{\phi})) \leq \lambda_n \end{aligned} \tag{1.1}$$



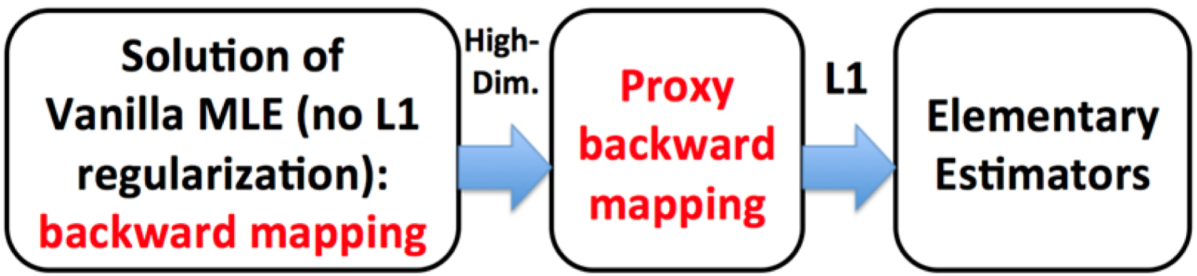
Background: Elementary Estimator

- The canonical parameter θ of an exponential family distribution can be learned through EE:

Elementary Estimator

$$\begin{aligned} &\underset{\theta}{\operatorname{argmin}} \mathcal{R}(\theta) \\ &\text{Subject to: } \mathcal{R}^*(\theta - \mathcal{B}^*(\widehat{\phi})) \leq \lambda_n \end{aligned} \tag{1.2}$$

- $\mathcal{B}(\widehat{\phi})$ denotes the backward mapping (i.e., vanilla MLE solution);
- For high-dimensional situations, vanilla MLE solutions are mostly not available. Therefore, we choose Proxy backward mapping $\mathcal{B}^*(\widehat{\phi})$.



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- For example, for sGGM:

EE	$\mathcal{R}(\cdot)$	θ	$\mathcal{B}^*$	$\mathcal{R}^*$
EE-sGGM	$\|\cdot\|_1$	Ω	$[T_v(\widehat{\Sigma})]^{-1}$	$\|\cdot\|_\infty$

Elementary Estimator for sGGM

$$\begin{aligned} &\underset{\Omega}{\operatorname{argmin}} ||\Omega||_1 \\ &\text{Subject to: } ||\Omega - [T_v(\widehat{\Sigma})]^{-1}||_\infty \leq \lambda_n \end{aligned} \tag{1.4}$$

single-sGGM Method	Time Complexity	Note
GLasso[4]	$O(p^3)$	Not a closed-form solution
EE-sGGM[5]	$O(p^2)$	entry-wise closed-form sharp convergence rate

multi-sGGM Method	Time Complexity	Notes
W-SIMULE[6]	$O(K^4 p^5)$	LP with Kp variables
JGL[7]	$O(T \times Kp^3)$	SVD
Proposed method	$O(K^4 p^2)$	entry-wise fast sharp convergence rate

[4] [Friedman et al.(2008)Friedman, Hastie, and Tibshirani]
[5] [Yang et al.(2014)Yang, Lozano, and Ravikumar]
[6] [Singh et al.(2017)Singh, Wang, and Qi]
[7] [Danaher et al.(2013)Danaher, Wang, and Witten]

Solution to Limitation I: Using Knowledge as Weight in Regularization (KW-norm)

EE	$\mathcal{R}(\cdot)$	θ	$\mathcal{B}^*$	$\mathcal{R}^*$
JEEK		Ω^{tot}	$inv[T_v(\widehat{\Sigma}^{tot})]$	

- Integrating additional knowledge through a novel regularization function $\mathcal{R}(\cdot)$

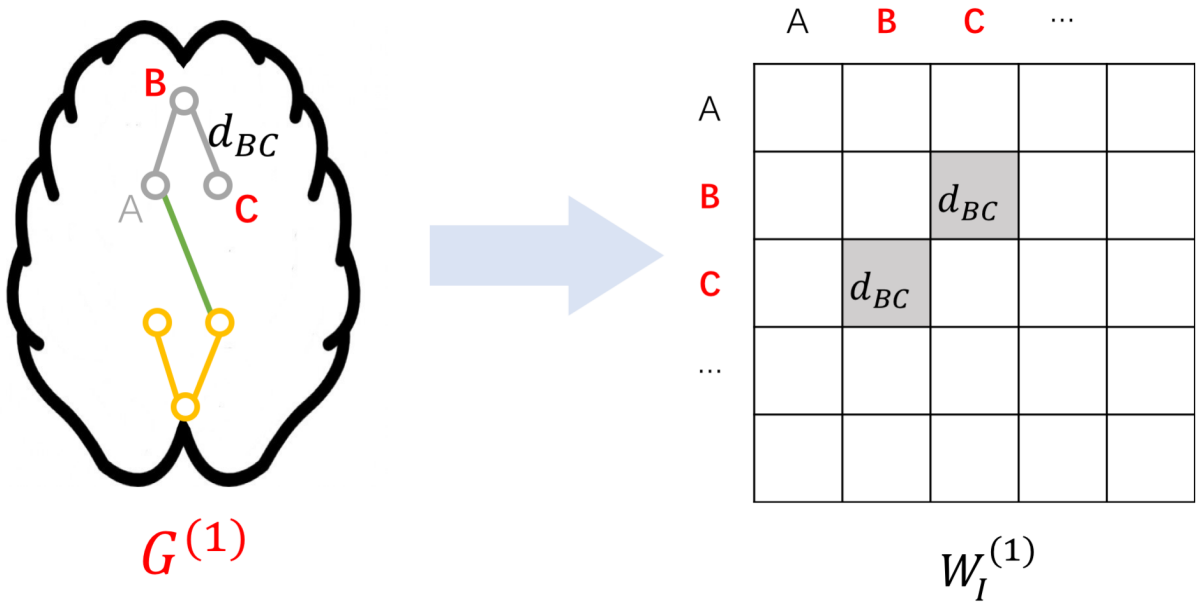
KW-norm

$$\mathcal{R}(\Omega^{tot}) = ||W_I^{tot} \circ \Omega_I^{tot}||_1 + ||W_S^{tot} \circ \Omega_S^{tot}||_1 \quad (2.1)$$

- W_I^{tot}: weights describing knowledge of each individual graph.
- W_S^{tot}: weights describing knowledge of the shared graph.
- No need to design knowledge-specific optimization
- KW-norm is flexible.

Example I: KW-norm representing the edge-level knowledge

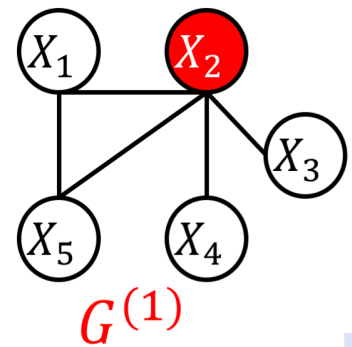
- e.g., Spatial distance among brain regions;



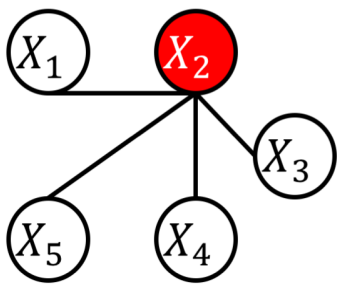
- Examples of adding more types of konwledge in Section S:5.

Example II: KW-norm describing the node-level knowledge

- e.g., X_2 is a known hub node;



$G^{(1)}$



$G^{(2)}$

	1	2	3	4	5
1		$1/\gamma$	1	1	1
2	$1/\gamma$		$1/\gamma$	$1/\gamma$	$1/\gamma$
3	1	$1/\gamma$		1	1
4	1	$1/\gamma$	1		1
5	1	$1/\gamma$	1	1	

W_s

Proposed Method: Joint Elementary Estimator incorporating additional Knowledge (JEEK)

EE	$\mathcal{R}(\cdot)$	θ	$\mathcal{B}^*$	$\mathcal{R}^*$
EE-sGGM	$\|\|\cdot\|\|_1$	Ω	$[T_v(\widehat{\Sigma})]^{-1}$	$\|\|\cdot\|\|_\infty$
JEEK	kw-norm	Ω^{tot}	$inv[T_v(\widehat{\Sigma}^{tot})]$	kw-dual

JEEK

$$\underset{\Omega_I^{tot},\Omega_S^{tot}}{\operatorname{argmin}} ||W_I^{tot} \circ \Omega_I^{tot}||_1 + ||W_S^{tot} \circ \Omega_S^{tot}||$$

$$\begin{aligned} \text{Subject to: } & ||(1 \oslash W_I^{tot}) \circ (\Omega^{tot} - inv(T_v(\widehat{\Sigma}^{tot})))||_\infty \leq \lambda_n \\ & ||(1 \oslash W_S^{tot}) \circ (\Omega^{tot} - inv(T_v(\widehat{\Sigma}^{tot})))||_\infty \leq \lambda_n \\ & \Omega^{tot} = \Omega_S^{tot} + \Omega_I^{tot} \end{aligned} \tag{2.2}$$

[8] Where $\oslash$ represents element wise division $[A \oslash B]_{ij} = A_{ij}/B_{ij}$.

Proposed method: JEEK – Solution

- Fast and Scalable solution[9] – p^2 small linear programming subproblems:

$$\begin{aligned} &\underset{a_i,b}{\operatorname{argmin}} \sum_i |w_i a_i| + K|w_s b| \\ &\text{Subject to: } |a_i + b - c_i| \leq \lambda_n \min(w_i, w_s), \\ &i = 1, \ldots, K \end{aligned} \tag{2.3}$$

[9] $a_i := \Omega_I^{(i)}{}_{j,k}$ (the $\{j,k\}$-th entry of $\Omega^{(i)}$)
$b := \Omega_{S\,j,k}$
$c_i = [T_v(\widehat{\Sigma}^{(i)})]^{-1}_{j,k}$.
$W^{(i)}_{j,k} = w_i$ and $W^{S}_{j,k} = w_s$.

Why JEEK is better

- Rich and flexible for integrating additional knowledge
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- Parallelizable optimization with small sub-problems. Faster than the previous studies:

Method	Time Complexity	Additional Knowledge
JEEK	$O(K^4p^2)$ ($\Rightarrow$ $O(K^4)$ if parallelizing completely)	YES
W-SIMULE	$O(K^4p^5)$	YES
JGL	$O(T \times Kp^3)$	NO

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- Theoretical guaranteed

Theoretical Results

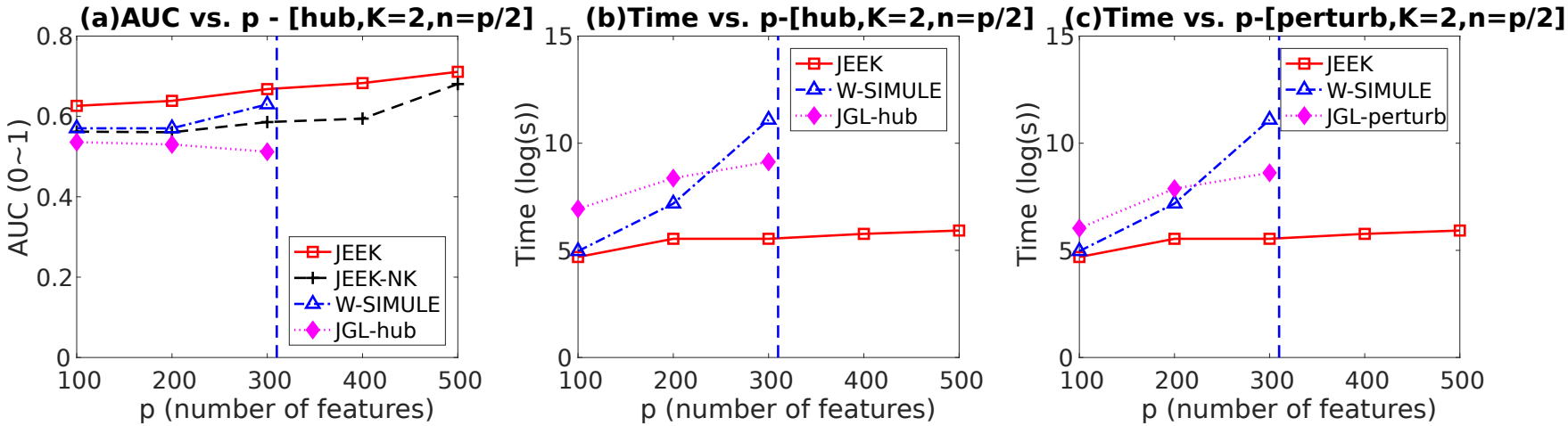
- Error bound: $||\widehat{\Omega}^{tot} - \Omega^{tot*}||$
- Sharp convergence rate as the state-of-art

$$
\begin{aligned}
&||\widehat{\Omega}^{tot} - \Omega^{tot*}||_F \leq 4\sqrt{k_i + k_s}\lambda_n \\
&\max(||(1 \oslash W_I^{tot}) \circ (\widehat{\Omega}^{tot} - \Omega^{tot*})||_\infty, ||(1 \oslash W_S^{tot}) \circ (\widehat{\Omega}^{tot} - \Omega^{tot*}||_\infty) \leq 2\lambda_n \\
&||(1 \oslash W_I^{tot}) \circ (\widehat{\Omega}_I^{tot} - \Omega_I^{tot*})||_1 + ||(1 \oslash W_S^{tot}) \circ (\widehat{\Omega}_S^{tot} - \Omega_S^{tot*})||_1 \leq 8(k_i + k_s)\lambda_n
\end{aligned} \tag{3.1}
$$

Where a, c, κ_1 and κ_2 are constants

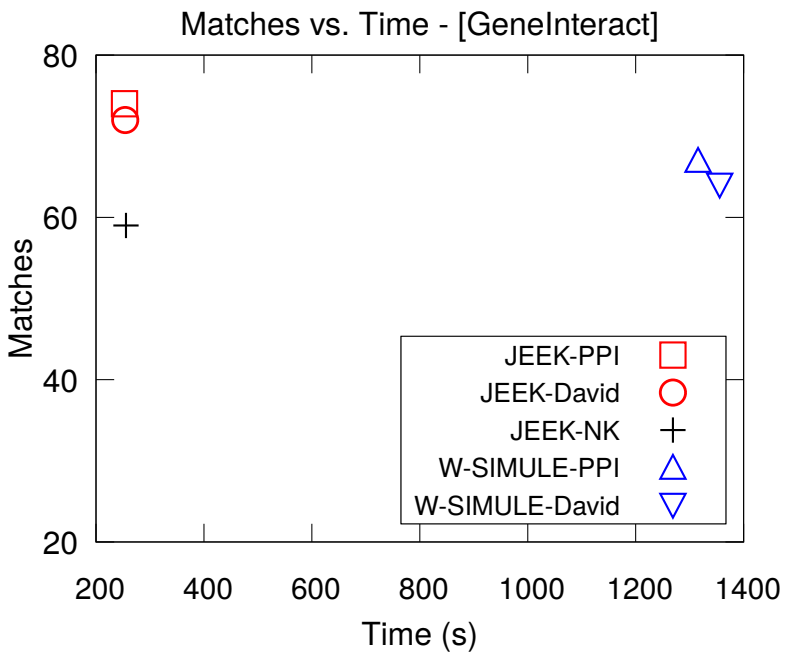
$$
\begin{aligned}
&||\widehat{\Omega}^{tot} - \Omega^{tot*}||_F \\
&\qquad \leq \frac{16\kappa_1 a \max_{j,k}(W_I^{tot}{}_{j,k}, W_S^{tot}{}_{j,k})}{\kappa_2} \sqrt{\frac{(k_i + k_s)\log(Kp)}{n_{tot}}}
\end{aligned} \tag{3.2}
$$

Empirical Results on Multiple Synthetic Datasets

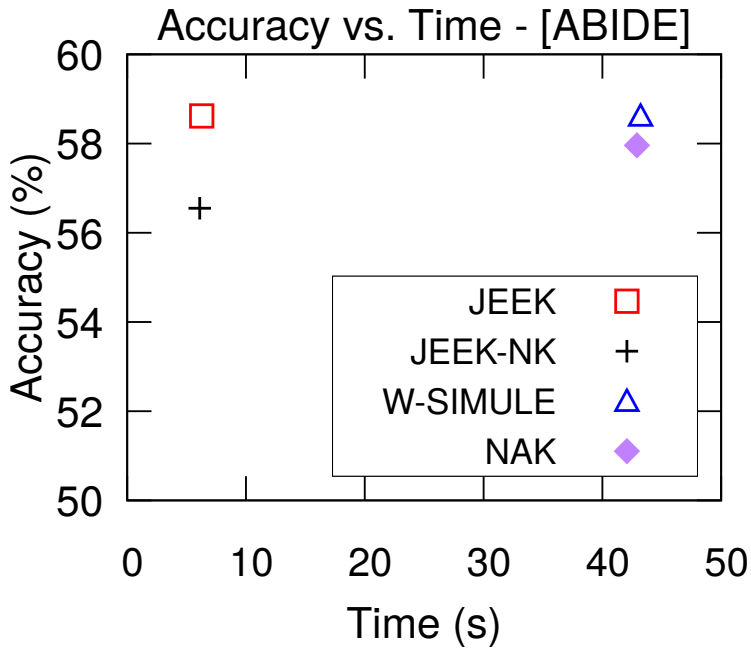


- JEEK outperforms the speed of the state-of arts significantly faster ($\sim 5000\times$ improvement);
- JEEK obtains better AUC as the state-of-the-art;
- JEEK obtains better AUC than JEEK-NK (no additional knowledge).

Empirical Results on Two Real-world Datasets



(a)



(b)

- (a). On real-world gene expression data about leukemia cells vs. normal blood cells. Used multiple types of additional knowledge;
- (b). On real-world Brain fMRI dataset: ABIDE. Using LDA as a downstream classification for evaluating JEEK vs. baselines.

R Package Publicly Available !!!

- The project website: `http://jointggm.org/`
- R package "jeek":
  - `install.packages("jeek")`
  - `library("jeek")`
  - `demo(jeek)`
- See Poster 133
- Acknowledgement: NSF CAREER award No. 1453580

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