

# **Uncertainty Quantification for Interpretable Machine Learning**

- For Trustworthy Discoveries & Decision-making**
- 

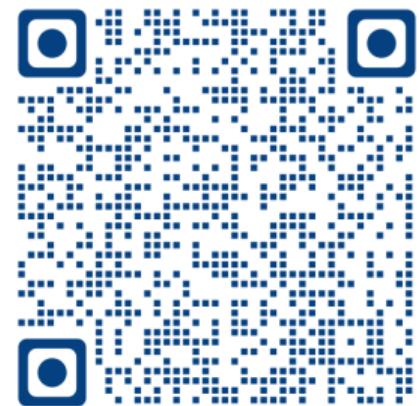
Lili Zheng

Department of Electrical and Computer Engineering, Rice University

1/19/2024

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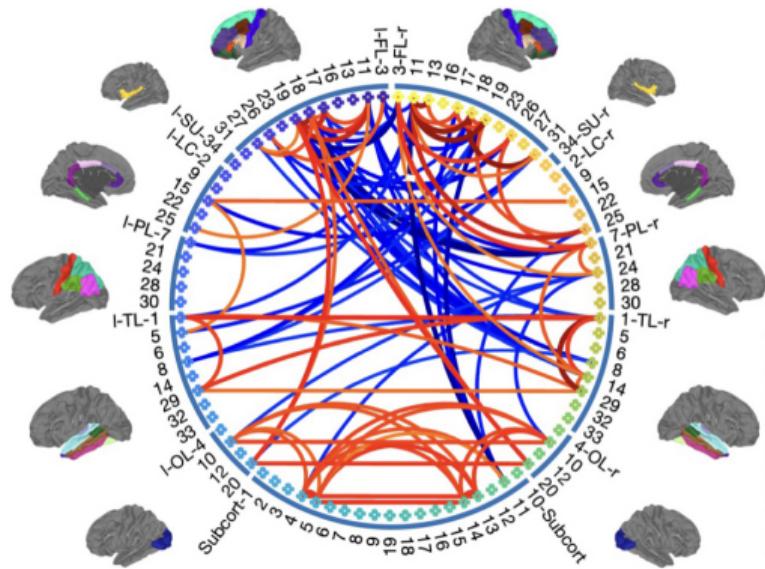
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(Graph) Learning
3. Uncertainty Quantification for Model-agnostic Machine  
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4. Other Works and Future Directions



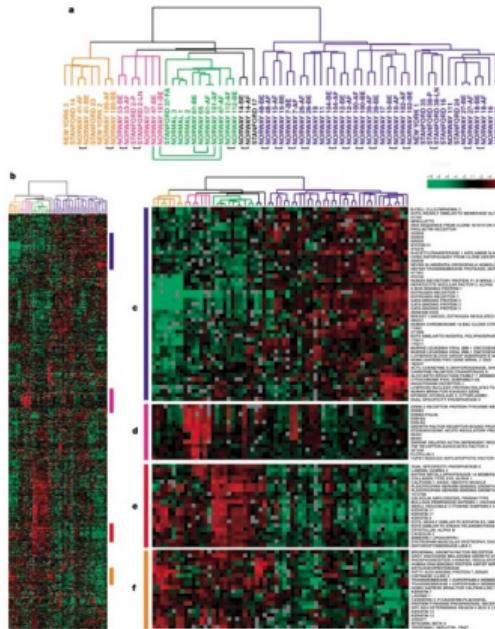
## Background

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# Machine Learning Propels Discoveries



Association between brain regions from fMRI data



Hierarchical clustering for tumor data  
(Perou et al., 2000)

# Machine Learning Propels Decision-making



Treatment in healthcare



Loan approval

Picture source: [https://www.aamc.org/news/electronic-health-records-what-will-it-take-make-them-work/](https://www.aamc.org/news/electronic-health-records-what-will-it-take-make-them-work;)

<https://auto.economictimes.indiatimes.com/news/auto-technology/us-lawmakers-raise-concerns-over-chinese-self-driving-testing-data-collection/105283633>

# Interpretable Machine Learning (IML)

## Interpretable Machine Learning

Generate human-understandable insights into **the data, the ML model, or the model output**

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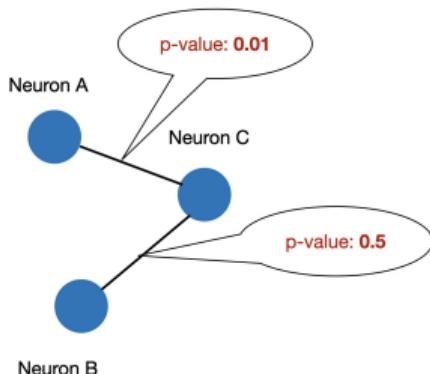
- **Insights into the data:** functional association between brain regions; which treatment is more effective?
  - **Insights into the model:** model-diagnostics; safety check
- ⇒ **scientific discoveries, decision-making**

Can we trust interpretable machine learning for discoveries and decision-making?

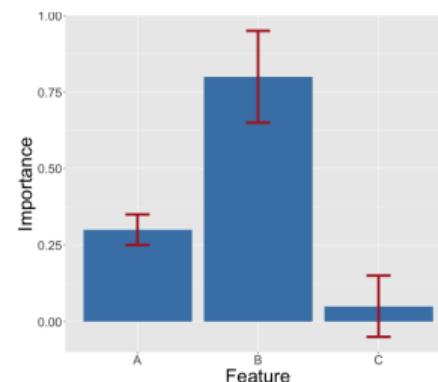
# Trust in IML?

## One Potential Solution

Provide **uncertainty quantification** (UQ) associated with machine learning interpretations!



p-values for  
detected  
association



Confidence  
intervals for  
feature  
importance

– draw conclusions/make decisions only based on *significant signals*.

# Uncertainty Quantification: Challenges in the Modern Era

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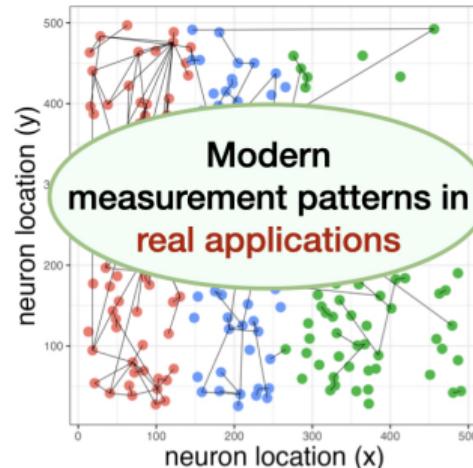
- Great tools in statistics & machine learning: selective inference, conformal inference, Bayesian inference...
- Numerous challenges from **large-scale, complex data and models!**

**Rigorous uncertainty quantification in practical and complex scenarios?**

# Uncertainty Quantification: Challenges in the Modern Era

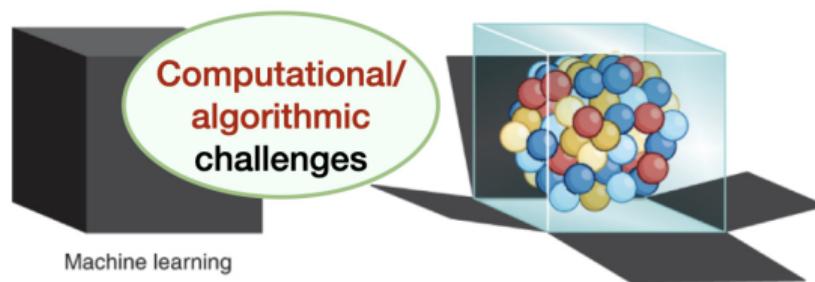
First part:

ML in science  
UQ for graph learning



Second part:

ML in the society  
UQ for model-  
agnostic ML  
interpretations

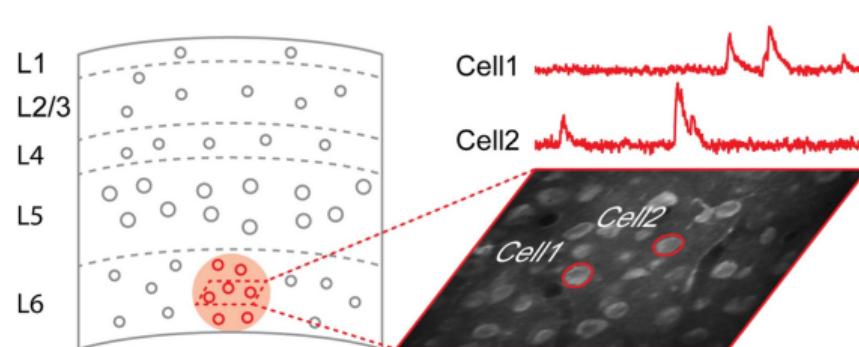


# **Uncertainty Quantification for Statistical Structure (Graph) Learning**

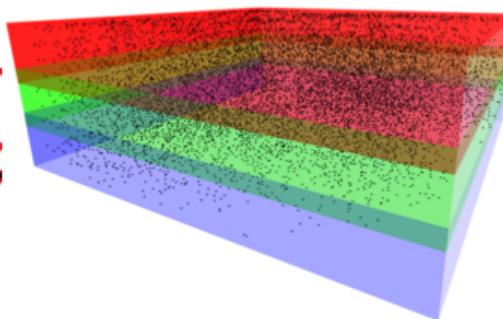
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# Challenges from Data: Erose Measurements

**Erose measurements:** irregular, highly uneven measurements over a large system



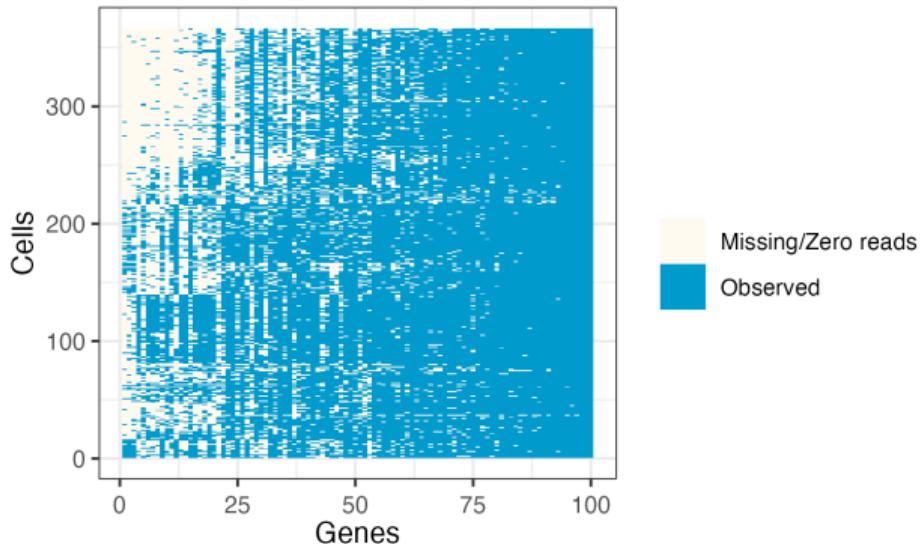
Calcium imaging data in neuroscience  
(Birkner et al., 2017)



Measurements in semi-overlapping cubes; also called graph quilting (Vinci et al., 2019)

## Challenges from Data: Erose Measurements

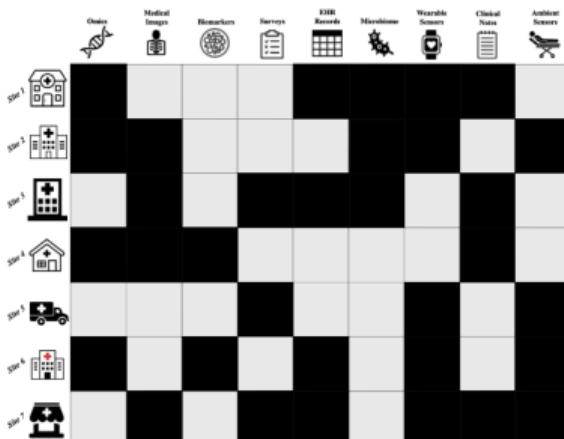
**Erose measurements:** irregular, highly uneven measurements over a large system



Single-cell RNA sequencing  
(Darmanis et al., 2015)

# Challenges from Data: Erose Measurements

**Erose measurements:** irregular, highly uneven measurements over a large system



**patchwork learning in healthcare**  
(Rajendran et al., 2023)

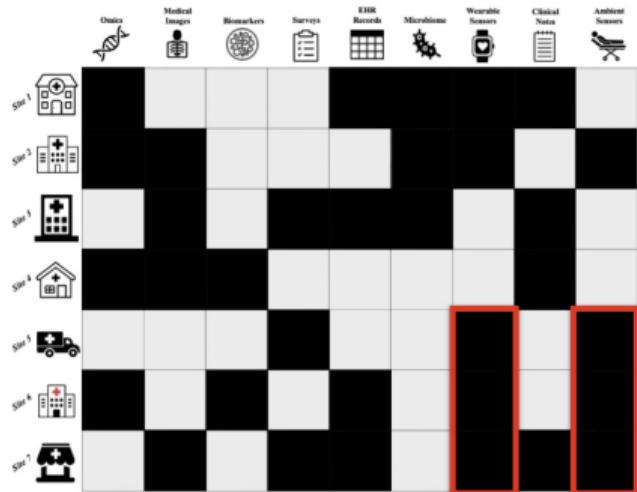
Table 1. Some examples of unequally spaced surveys.		
Country	Panel A: household surveys for monitoring poverty in developing countries <sup>a</sup>	
	Survey	Survey periods
Bolivia	Encuesta Integrada de Hogares (EIH)	Mar 89, Nov 89, Sept 90, Nov 91, Nov 92, July-Dec 93, July-Dec 94, June 95
Brazil	Pesquisa Nacional por Amostra de Domicílios (PNAD)	Annual surveys since 1971, but surveys not taken in census years 1980 and 1991
Chile	Caracterización Socioeconómica Nacional (CASEN)	1985, 87, 90, 92, 94, 96
Ethiopia	Welfare monitoring survey	1995, 97, 98
Ghana	Ghana living standards survey	1987, 88, 91, 98
Kenya	Welfare monitoring survey	1992, 94, 97
Kyrgyz Republic	Poverty monitoring survey	1993, 96, 96, 97, 98
Mexico	Encuesta nacional de Ingreso-Gasto de los hogares (ENIGH)	1984, 89, 92, 94, 96
Nigeria	National consumer survey	1980, 85, 92, 96
Panama	Encuesta de Hogares-Mano de Obra (EMO)	1979, 89, 91, 95, 96
Peru	Encuesta Nacional de Hogares Sobre Medición de Niveles de Vida (ENNIV)	1985, 90, 91, 94
Senegal	Enquête Démographique et de Santé	1986, 92, 97
Thailand	Thailand Socio-Economic Survey (SES)	1975, 81, 86, 88, 90, 92, 94, 96, 98

**unevenly spaced time series in econometrics** (Millimet and McDonough, 2017)

# Structure Learning from Erose Measurements?

## Common practices

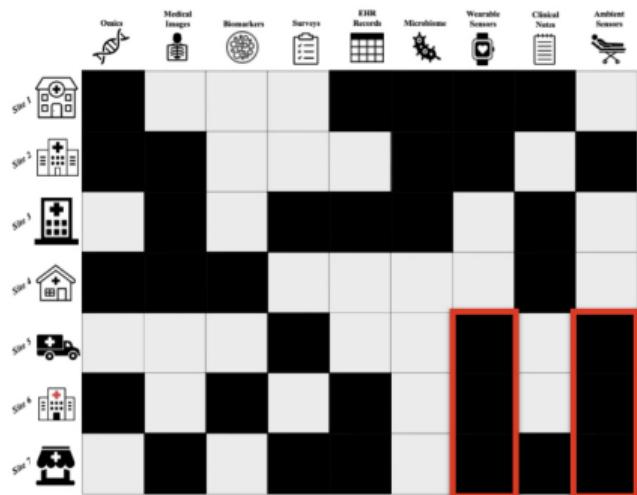
- Downsampling: focus on a complete block;
  - throw too much data away!



# Structure Learning from Erode Measurements?

## Common practices

- Downsampling: focus on a complete block;
  - throw too much data away!
- Ad-hoc imputation + downstream analysis;
  - low-rank completion methods?
    - provable mainly for random missingness
    - not low-rank?
    - extra uncertainty from imputation



Focus on graph learning from erode measurements in this talk

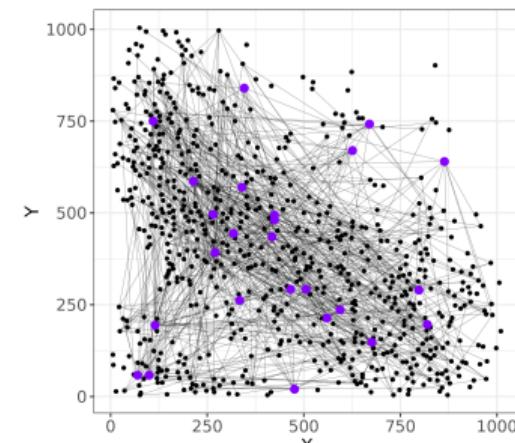
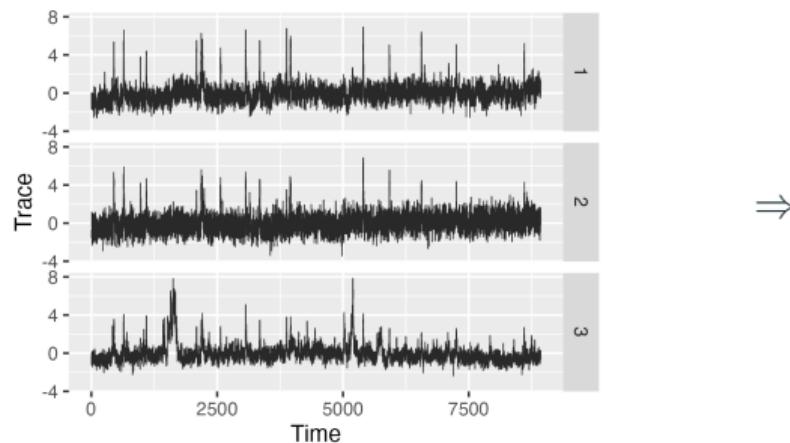
# Why Graph Learning?

## Graphical Model Structural Learning

Extract **conditional dependency** relationships:

An edge between node  $j$  and  $k \iff$  Observations for  $j$  and  $k$  are conditionally dependent given all other nodes.

**Functional Connectivity:** a graph between neurons that reflect their co-firing patterns



Many applications: gene co-expression networks, sensor networks, statistical physics, ...

# Gaussian Graphical Model Learning from Erose Measurements

---

- Focus on Gaussian graphical models in this talk

- Nodes:  $V = [p]$ ;
- $n$  samples of  $p$ -dimensional r.v.s:  
 $\mathbf{X}_1, \dots, \mathbf{X}_n \sim \mathcal{N}(0, \Theta^{*-1})$ ;
- $\Theta_{j,k}^* \neq 0 \Leftrightarrow j \not\perp\!\!\!\perp k \mid \text{all other nodes}$
- Edges:  
 $E = \{(j, k) : 1 \leq j, k \leq p, \Theta_{j,k}^* \neq 0\}$ ;
- **Goal:** identify non-zero entries in  
 $\Theta^*$

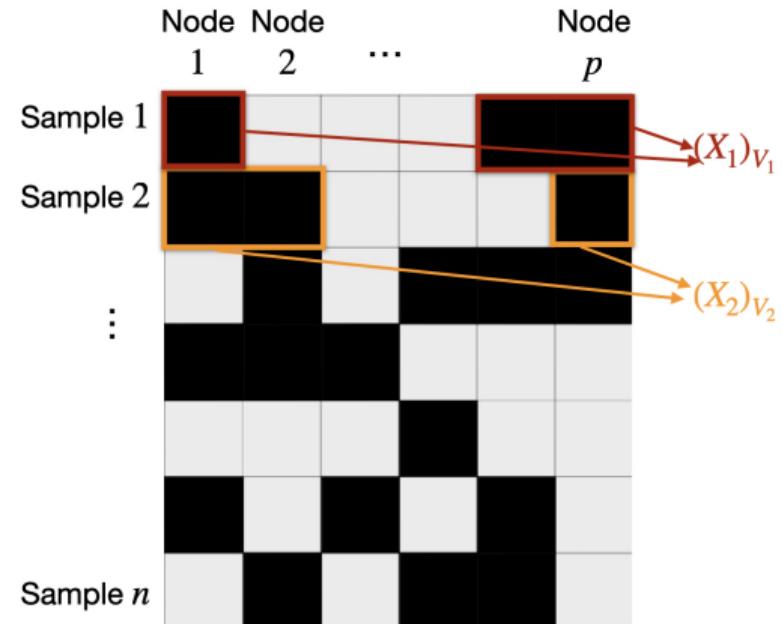
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- Erose measurements**

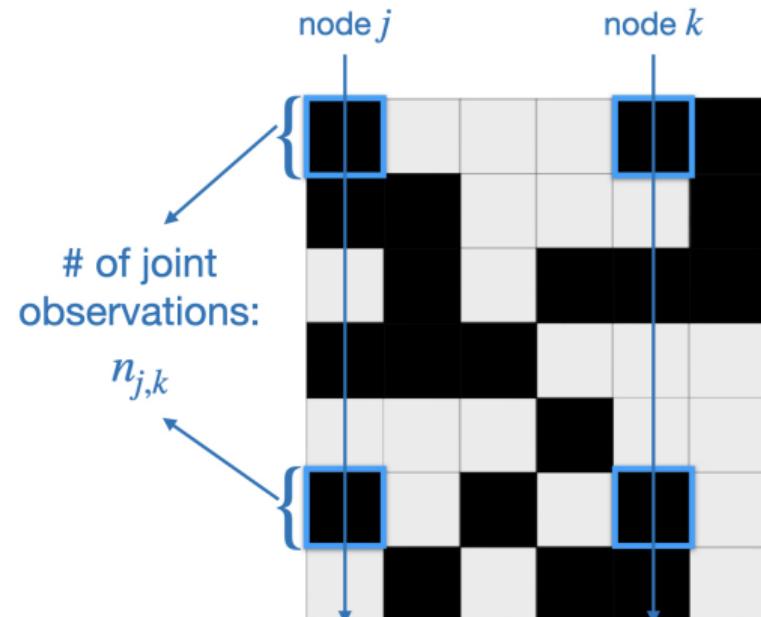
Observe  $(\mathbf{X}_i)_{V_i}, 1 \leq i \leq n; V_i \subset [p]$   
are irregular feature subsets,  
independent from  $\mathbf{X}_i$ .



# Gaussian Graphical Model Learning from Erose Measurements

- **Erose measurements**

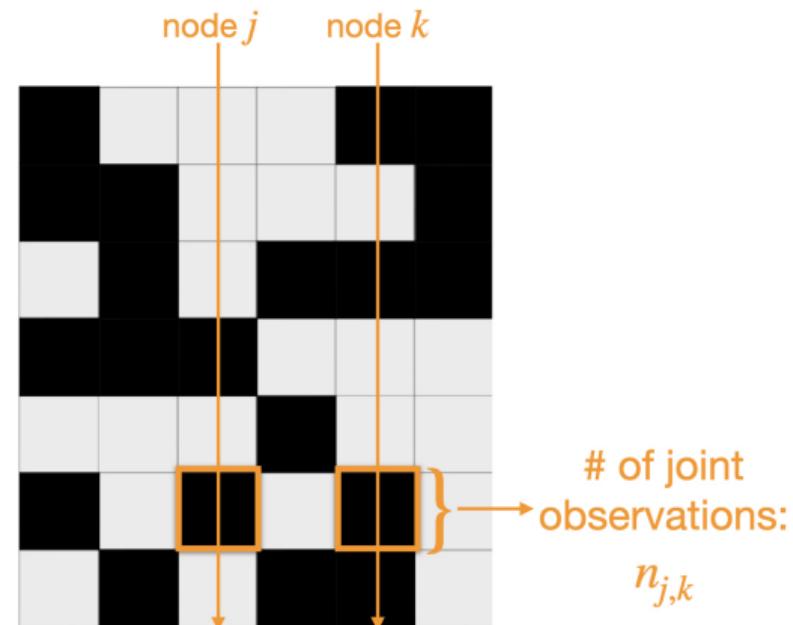
Even for assessing marginal dependency:  
joint sample sizes for node pairs  
 $\{n_{j,k} : 1 \leq j, k \leq p\}$  are **highly**  
different



# Gaussian Graphical Model Learning from Erose Measurements

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## Estimation

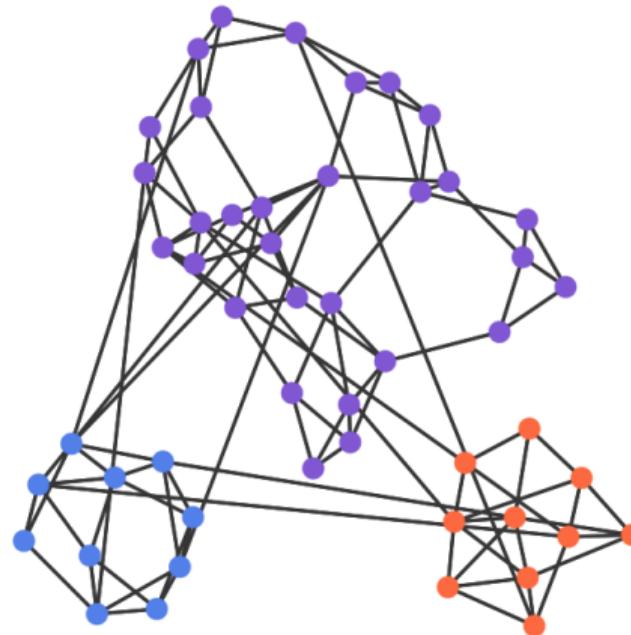
- Plug in covariance estimates into graphical Lasso (Kolar and Xing, 2012; Park et al., 2021)
- Most theory assumes missing with the **same/similar probability!**
- Existing characterization in minimum pairwise sample size  $\min_{j,k} n_{j,k}$
- **Limited insights for our setting**

## Inference

- Fully observed data
- **Missing independently with same probability**
- **Not applicable for our setting**

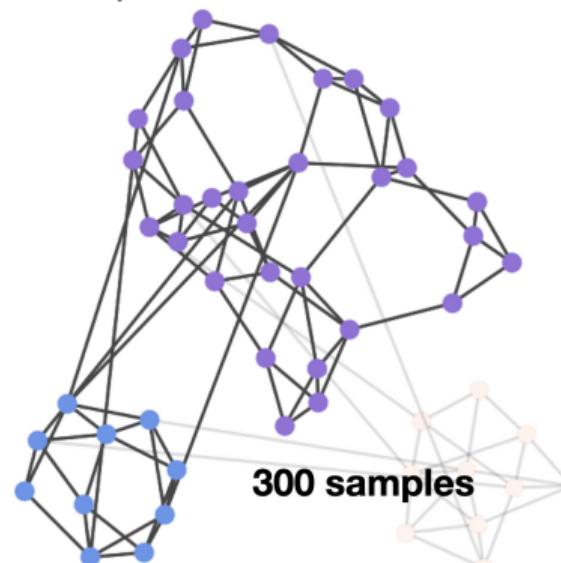
## Toy Example: UQ Promotes Reliable Graph Learning

- Toy example: irregular patchwise observations
- $p = 30 + 10 + 10 = 50$  nodes in total

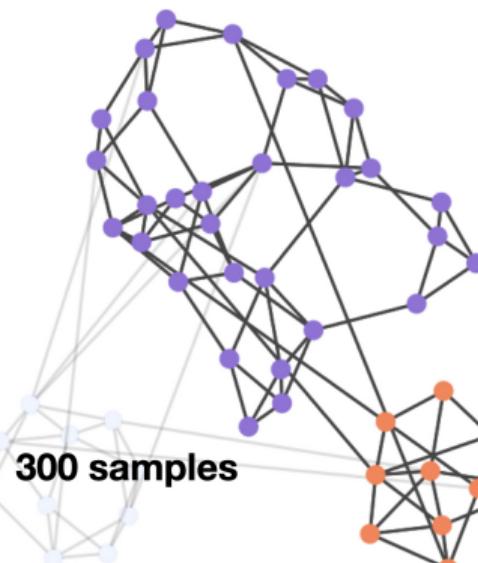


## Toy Example: UQ Promotes Reliable Graph Learning

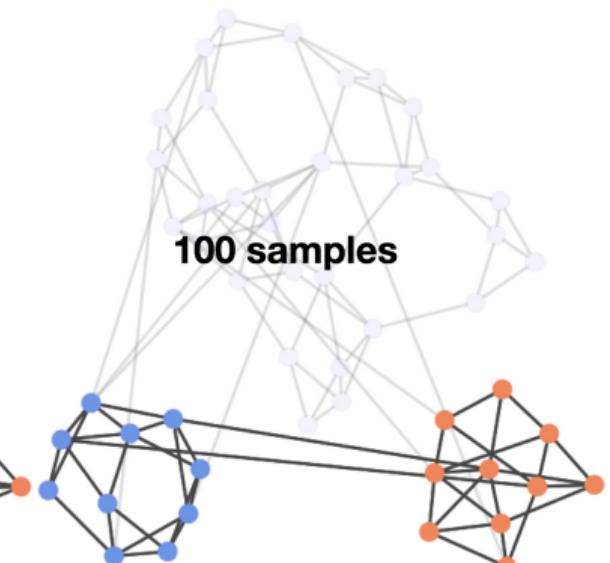
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Measurement 1



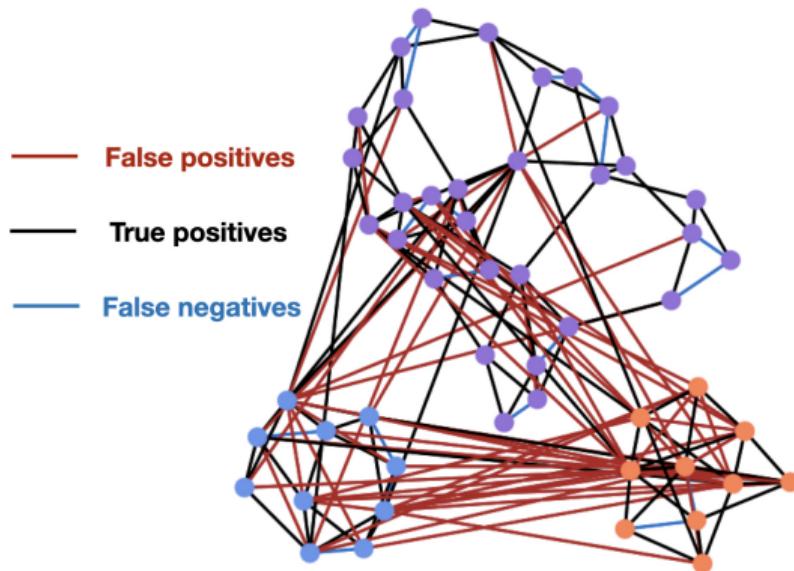
Measurement 2



Measurement 3

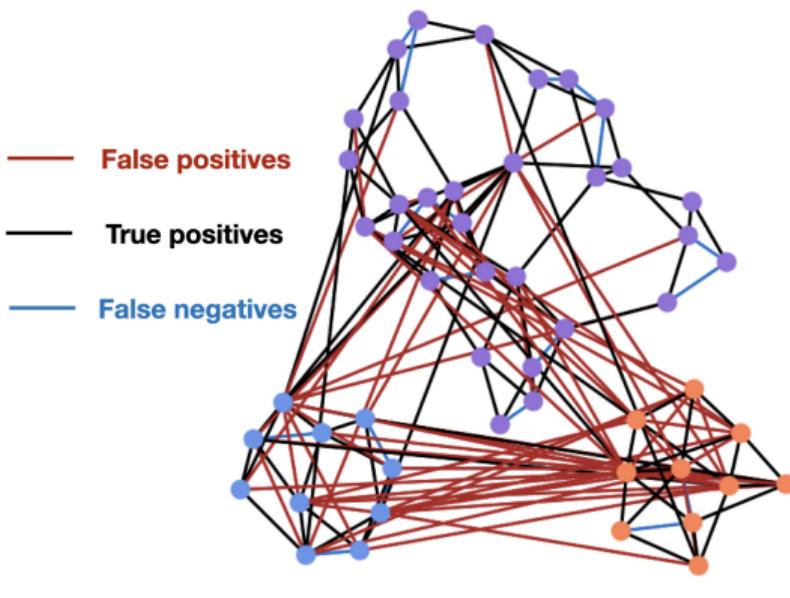
## Toy Example: UQ Promotes Reliable Graph Learning

- Plug-in estimate using graphical lasso

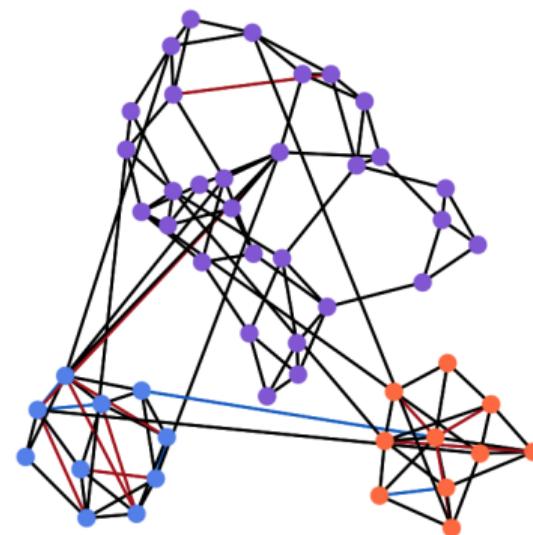


## Toy Example: UQ Promotes Reliable Graph Learning

- Plug-in estimate using graphical lasso



- We develop GI-JOE (**G**raph **I**nference when **J**oint **O**bservations are **E**rode) with FDR control



## **Problem Setup and Proposed Method**

## Recall: Model Setup

---

Gaussian graphical model:

- $p$ -dimensional  $\mathbf{X}_1, \dots, \mathbf{X}_n \sim \mathcal{N}(0, \Theta^{*-1})$ ;
- Nodes:  $V = [p]$ ;
- Edges:  $E = \{(j, k) : 1 \leq j, k \leq p, \Theta_{j,k}^* \neq 0\}$ ;

Observations

- $(\mathbf{X}_i)_{V_i}, 1 \leq i \leq n; V_i \subset [p]$  are irregular feature subsets independent from  $\mathbf{X}_i$
- Pairwise joint sample sizes  $\{n_{j,k} : 1 \leq j, k \leq p\}$  are highly different

## Recall: Model Setup

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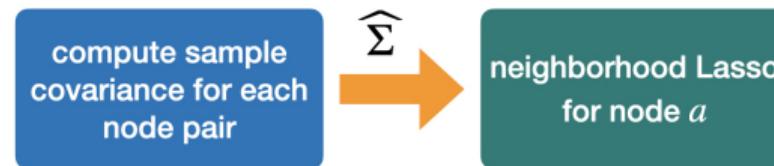
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**Edgewise-testing:**  $\mathcal{H}_0 : (a, b) \notin E$  for  $a, b \in [p]$  (**Whole graph testing later**)

## Edgewise Inference: Debiased Neighborhood Lasso

- Many existing methods are covariance-based.
- **Step 1:** Plug in pairwise sample covariance into neighborhood Lasso (Meinshausen and Bühlmann, 2006) and perform debiasing (Van de Geer et al., 2014):

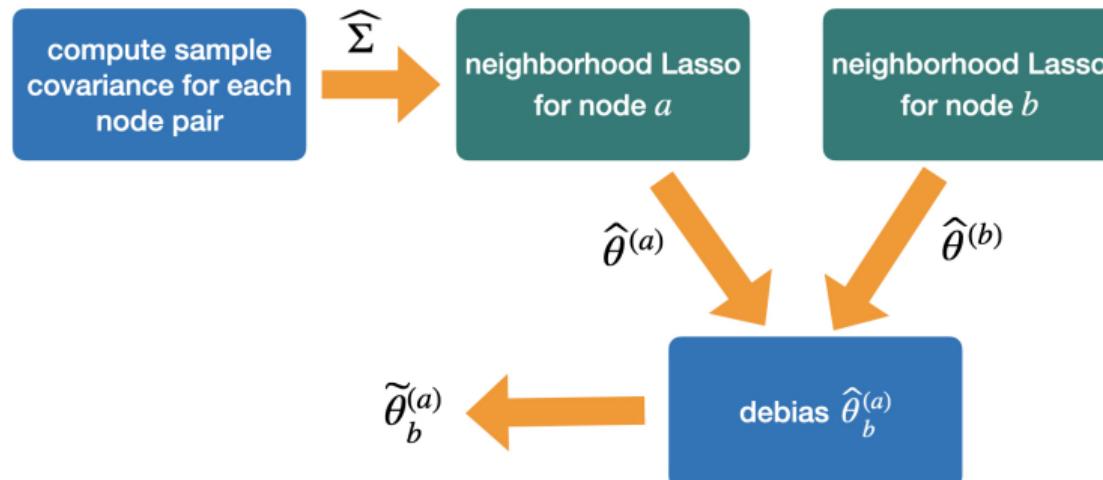


$$\hat{\theta}^{(a)} = \arg \min_{\theta \in \mathbb{R}^p, \theta_a=0} \frac{1}{2} \theta^\top \hat{\Sigma} \theta - \hat{\Sigma}_{a,:} \theta + \sum_{j=1}^p \lambda_j |\theta_j|,$$

$|\hat{\theta}_b^{(a)}|$  indicates edge strength of  $(a, b)$

## Edgewise Inference: Debiased Neighborhood Lasso

- **Step 1:** Plug in pairwise sample covariance into neighborhood Lasso (Meinshausen and Bühlmann, 2006) and perform debiasing (Van de Geer et al., 2014):



$|\tilde{\theta}_b^{(a)}|$  also indicates edge strength of  $(a, b)$

## Edgewise Inference: Debiased Neighborhood Lasso

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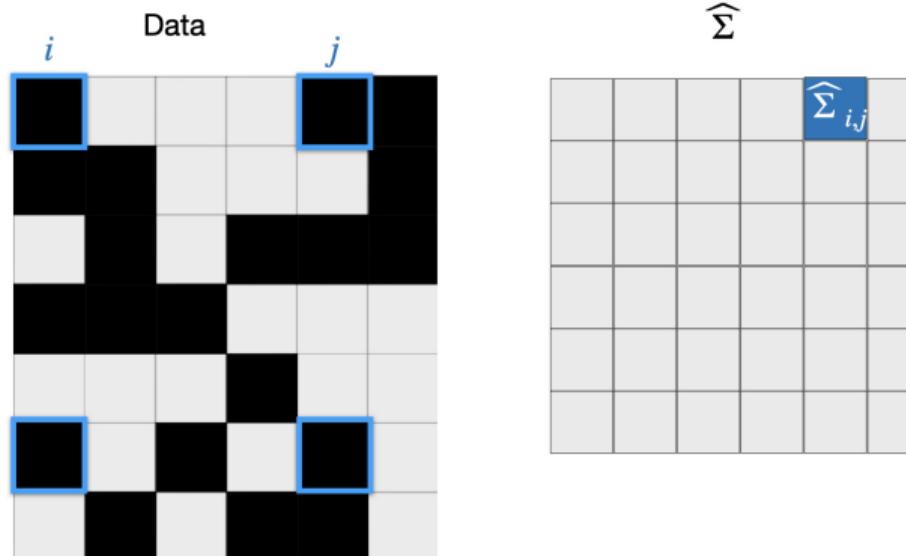
- **Step 2:** Normal approximation for  $\tilde{\theta}_b^{(a)}$  and variance estimation  
If fully observed with  $n$  samples:  $\text{var} \propto \frac{1}{n}$ .

**Challenge:**  $\hat{\Sigma}$  computed from irregular data patches!

# Edgewise Inference: Debiased Neighborhood Lasso

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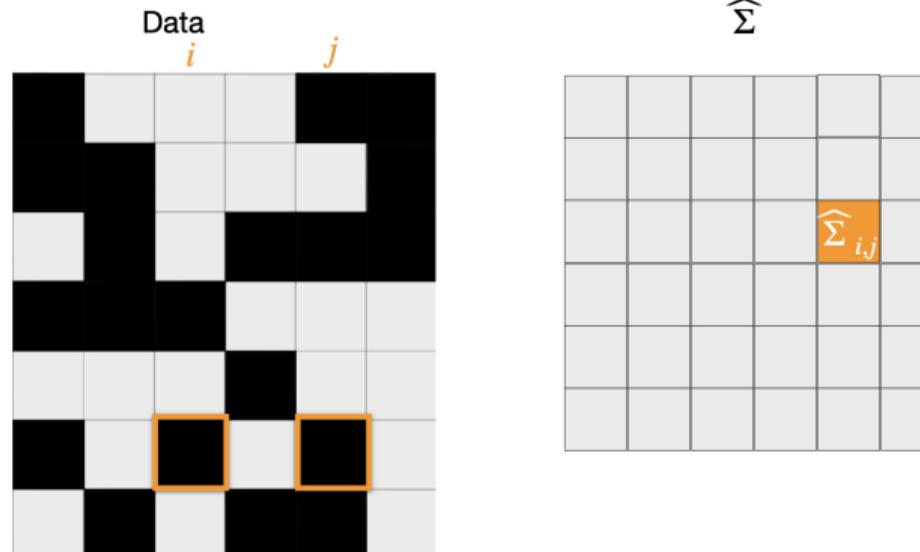
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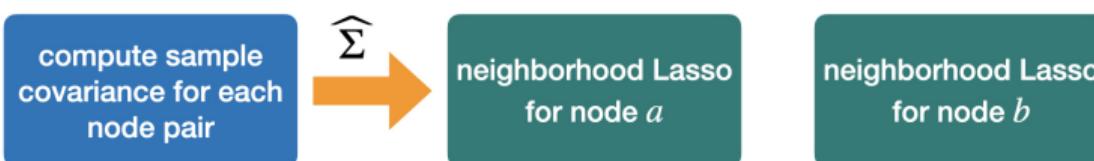


## Edgewise Inference: Debiased Neighborhood Lasso

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**Challenge:**  $\widehat{\Sigma}$  computed from irregular data patches!

All entries of  $\widehat{\Sigma}$  play a role: **from marginal to conditional dependency!**



# Characterization of Debiased Neighborhood Lasso

A Closer Look into  $\tilde{\theta}_b^{(a)}$

With appropriately chosen tuning parameters in the neighborhood Lasso,

$$\tilde{\theta}_b^{(a)} = -\frac{\Theta_{a,b}^*}{\Theta_{a,a}^*} + \text{mean-zero first order term} + \text{high-order residuals}$$

# Characterization of Debiased Neighborhood Lasso

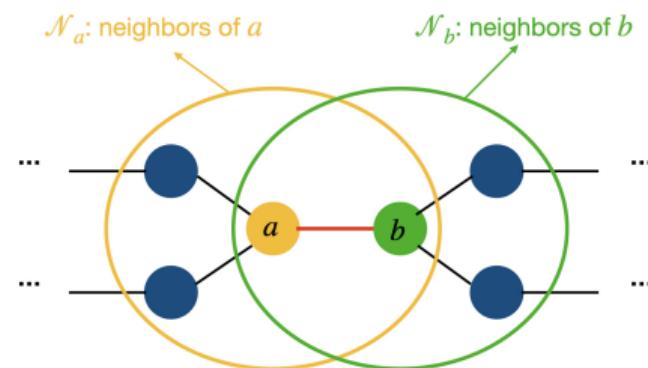
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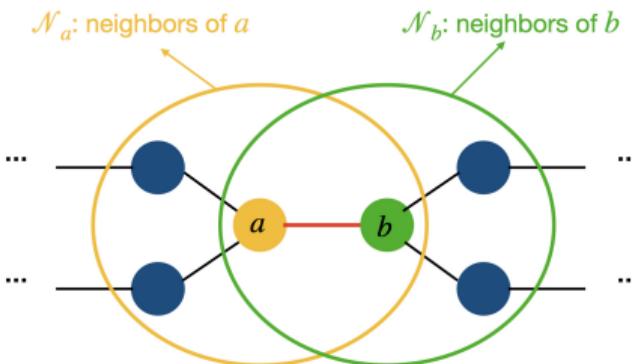
- mean-zero first-order term

$$\propto \sum_{j,k} (\hat{\Sigma}_{j,k} - \Sigma_{j,k}^*) \underbrace{\Theta_{a,j}^* \Theta_{b,k}^*}_{\text{weight of node pair } (j, k)}$$



- only involve neighbors of  $a$  and  $b$ !

# GI-JOE: Edge-wise Uncertainty Quantification

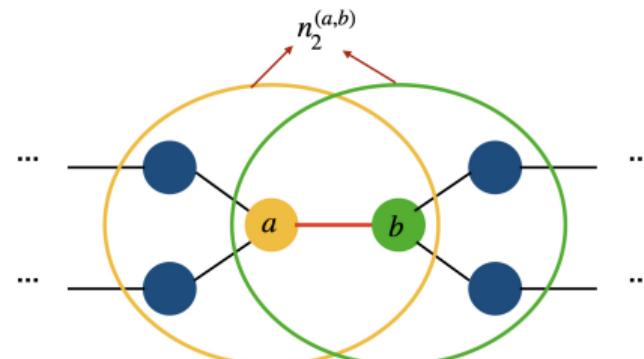
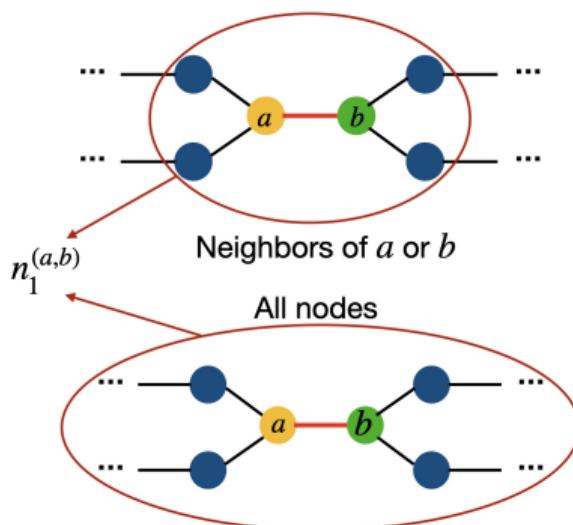


- **Step 2:** Estimate variance of first-order term
  - Variance contribution from each node pair  $(j, k)$ :  
 $\widehat{\theta}_j^{(a)}, \widehat{\theta}_k^{(b)}, 1/n_{j,k}$
  - Plus some edge-edge correlations
  - Obtain  $\widehat{\sigma}_n^2(a, b)$
- **Output:** Reject  $\mathcal{H}_0 : (a, b) \notin E$  if  
$$\frac{|\widehat{\theta}_b^{(a)}|}{\widehat{\sigma}_n(a, b)} > z_{\alpha}/2.$$

# **Edgewise Testing: Theoretical Guarantees**

## Assumption for Validity: Sufficient Local Sample Sizes

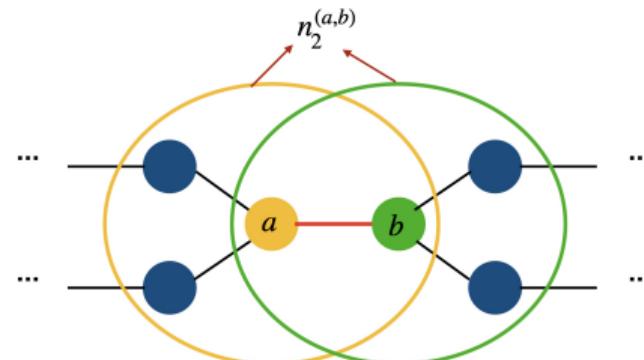
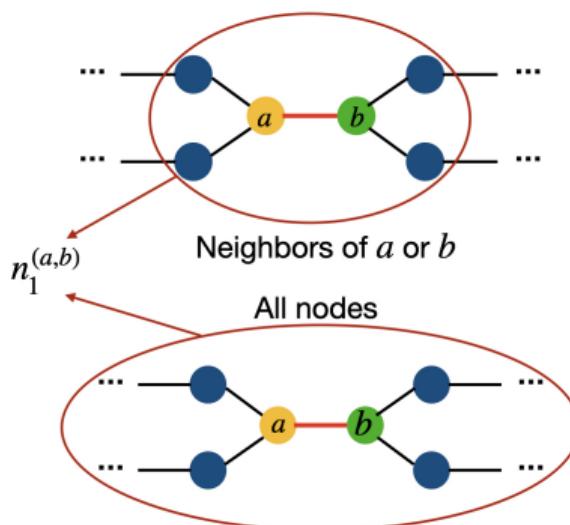
Minimum of the pairwise sample sizes  $\{n_{j,k}\}$  for  
 $\begin{cases} j \text{ is neighbor of } a \text{ or } b, k \text{ is any node: } n_1^{(a,b)} \\ j \text{ is neighbor of } a, k \text{ is neighbor of } b: n_2^{(a,b)} \end{cases}$



# Assumption for Validity: Sufficient Local Sample Sizes

## Main Assumption (Informal)

- A1. The local sample size  $n_1^{(a,b)}$  is sufficiently large, as a function of node degrees and dimensions.



## Statistical Validity of GI-JOE (Edge-wise Testing)

Main Theorem: Type I error and power (Informal)

Suppose Assumption A1 holds. For testing  $\mathcal{H}_0 : (a, b) \notin E$ :

1. GI-JOE (edgewise testing) has **asymptotically valid type I error control**;
2. The asymptotic power is an increasing function of  $|\Theta_{a,b}^*| \sqrt{n_2^{(a,b)}}$ .

- Same sample size  $n_{j,k} = n$  setting: **reduces to prior requirements**  $n \gg d^2 \log^2 p$
- **First theory that allows for general erose measurements:**
  - **arbitrary data-independent missing pattern!**
  - **localized** sample size requirement!

## Main Proof Idea for GI-JOE: Edge-wise Testing

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- Want to control **high-order terms** and **variance estimation errors**

## Main Proof Idea for GI-JOE: Edge-wise Testing

- Want to control **high-order terms** and **variance estimation errors**
- Want small **weighted errors** for neighborhood Lasso:  
 $\varepsilon^{(a)} = \hat{\theta}^{(a)} - \theta^{(a)*}$ ,  $\varepsilon^{(b)} = \hat{\theta}^{(b)} - \theta^{(b)*}$ , need to control

$$\left\langle \frac{1}{\sqrt{N}}, \varepsilon^{(a)} \varepsilon^{(b)\top} \right\rangle;$$

$$\left\langle \frac{1}{N}, \varepsilon^{(a)} \otimes \varepsilon^{(b)} \otimes \varepsilon^{(a)} \otimes \varepsilon^{(b)} \right\rangle.$$

- Under-measured nodes are weighted more.

## Main Proof Idea for GI-JOE: Edge-wise Testing

- Want to control **high-order terms** and **variance estimation errors**
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- Under-measured nodes are weighted more.

Node-wise  $\ell_1$  penalty:  $\lambda_j \asymp \sqrt{\frac{\log p}{\min_k n_{j,k}}}$   $\Rightarrow$  weighted error bounds.

# **GI-JOE: FDR control**

Whole graph testing with FDR control?

- Want: **95% of the selected edges are true positives**
- Take edgewise  $p$ -values; apply a variation of Benjamini-Hochberg's procedure
- **Valid for sparse graphs under mild sample size assumptions!**

# **Empirical Studies**

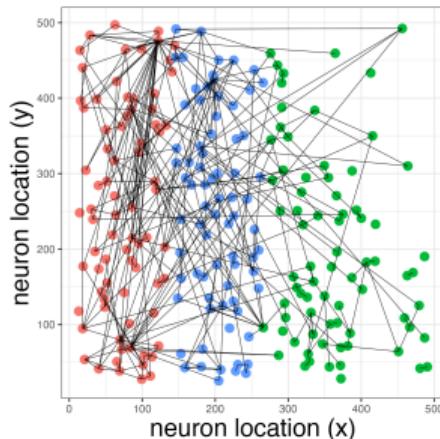
## Application to Neuronal Functional Data

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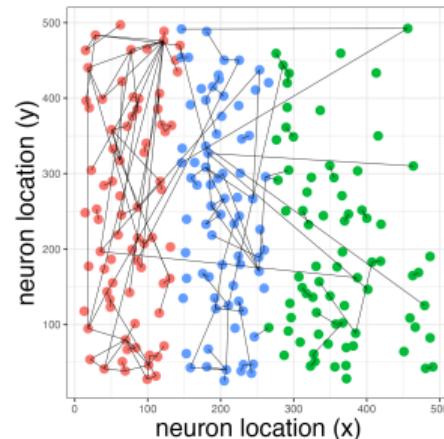
- Neuronal functional recordings of a mouse's visual cortex from Allen Brain Atlas
- Firing activities of  $p = 227$  neurons,  $n = 8931$  time points
- Goal: learn **functional connectivity amongst these neurons**
- Data is fully observed; we test how our method performs on **manually masked data**

# Application to Neuronal Functional Data

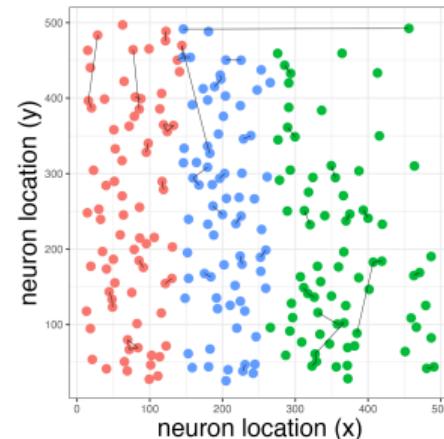
Manually mask functional data; three sets of neurons observed with high, median, and low probabilities.



FDR-selected graph with  
**full data (oracle)**



GI-JOE (FDR), applied to  
erase data



DB-Glasso with minimum  
sample size, applied to  
erase data

## Summary

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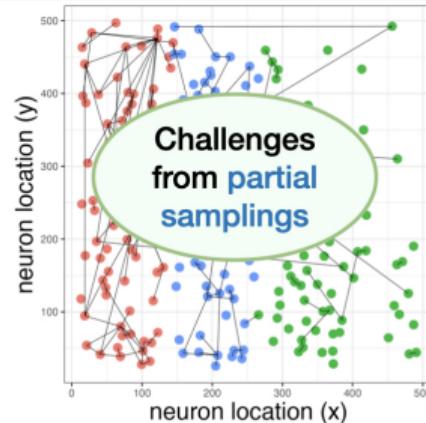
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- Erose measurements: challenge for reliable graph learning
- Edge-wise uncertainty hinges on neighbors; can be estimated by GI-JOE;
- Quantify different uncertainty levels over the graph with FDR control  $\Rightarrow$  Better graph selection with erose data!
- Future directions: more reliable **feature selection / causal structural learning** from erosely measured data under dependency?
- L. Zheng, G. I. Allen, “Graphical Model Inference with Erosely Measured Data”, *Journal of the American Statistical Association, Theory and Methods*, 2023.

# From Complex Data Collection to Complex Machine Learning Systems

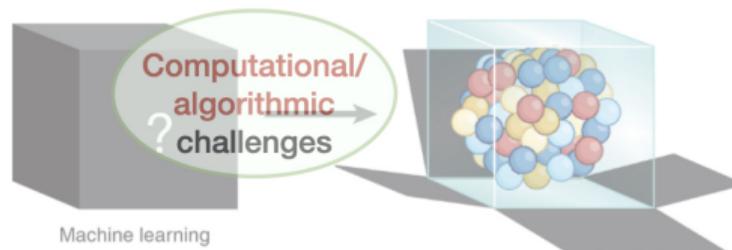
First part:

UQ for reliable  
scientific  
discoveries



Second part:

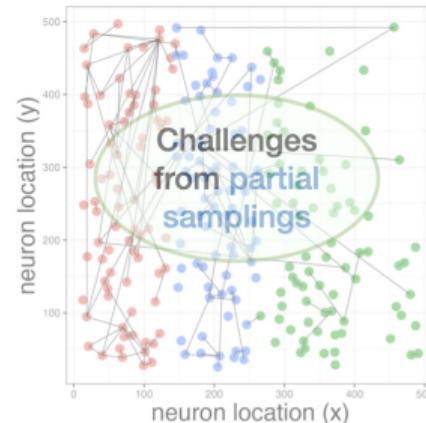
ML in the society  
UQ for model-  
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interpretations



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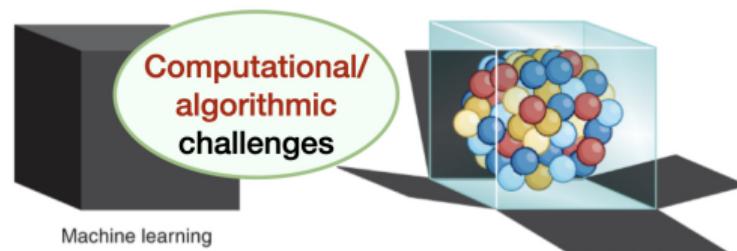
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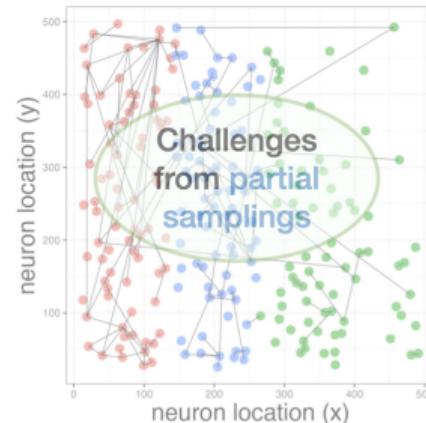
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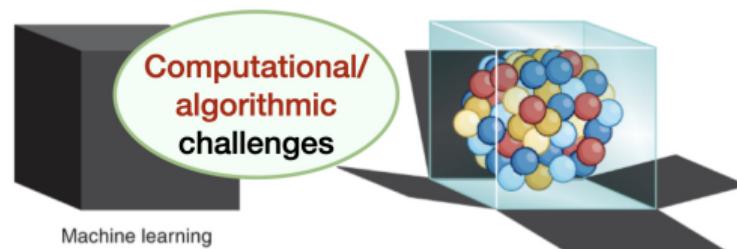
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# Uncertainty Quantification for Model-agnostic Machine Learning Interpretations

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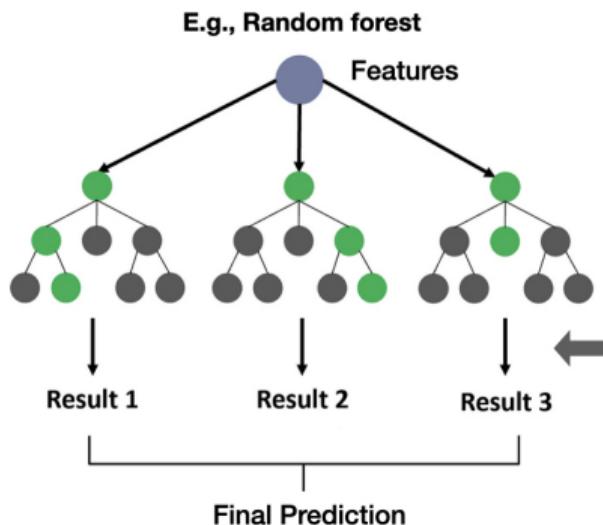
# Interpreting Black-box Machine Learning Models

Machine learning is widely applied in **high-stakes applications**:

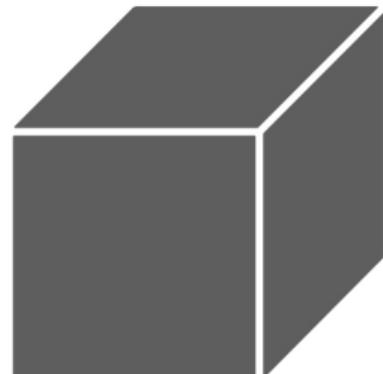


Can we trust machine learning? Make it interpretable!

# Interpreting Black-box Machine Learning Models



Blackbox ML model



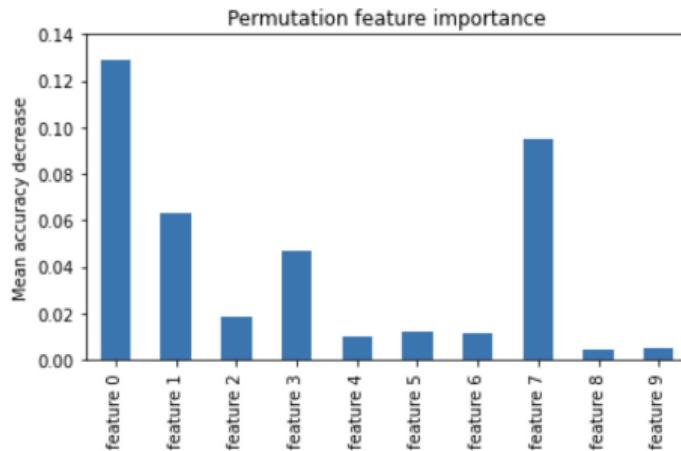
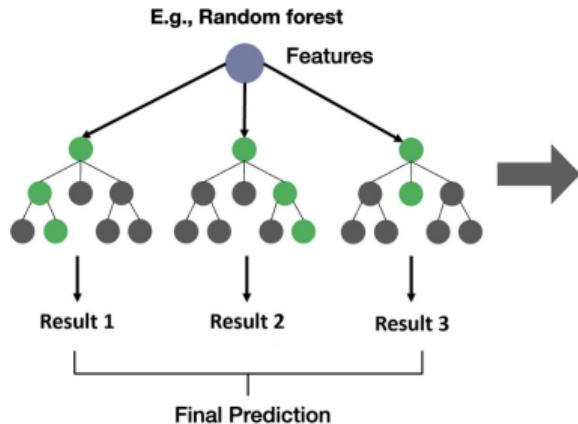
Predictions/Decisions



Why is this ML system rejecting my mortgage application?

# Feature Importance for Interpretable Machine Learning

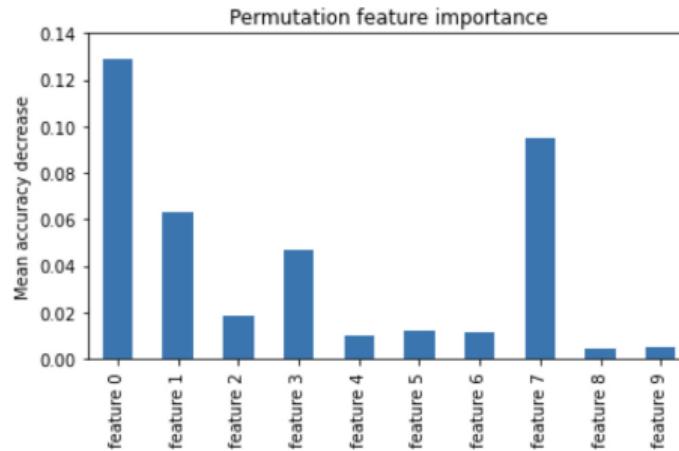
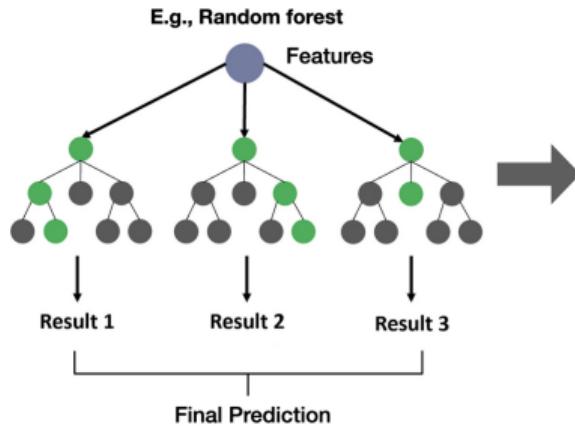
**Feature importance:** How does my model's prediction rely on each feature?



- Model-specific: defined for random forest, linear models, deep learning, etc.
- **Model-agnostic:** feature occlusion (Covert et al., 2021), permutation (König et al., 2021), Shapley values (Sundararajan and Najmi, 2020), etc.

# Feature Importance for Interpretable Machine Learning

**Feature importance:** How does my model's prediction rely on each feature?



Can we trust feature importance? Uncertainty quantification?

# Two Types of Feature Importance

---

## Population feature importance

- Assume a [data-generating model](#); infer about the population
- E.g., [Conditional independence test](#), knockoff
- ML models are only tools
- [Impossible without strong assumptions about the data or model](#) (Shah and Peters, 2020)!

# Two Types of Feature Importance

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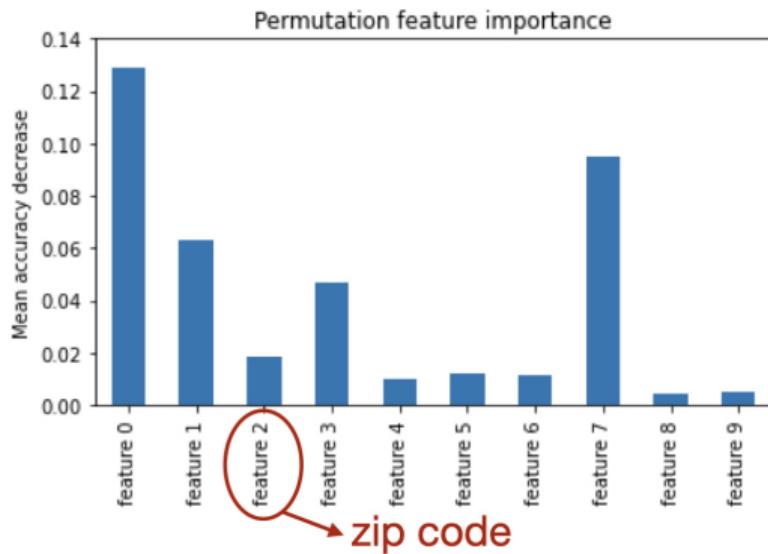
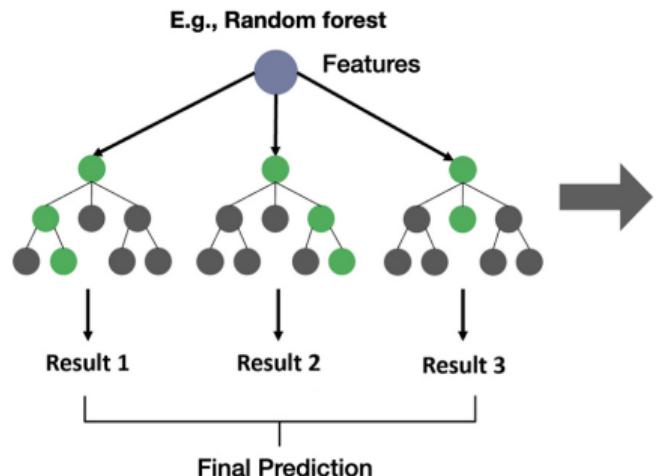
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## ML feature importance

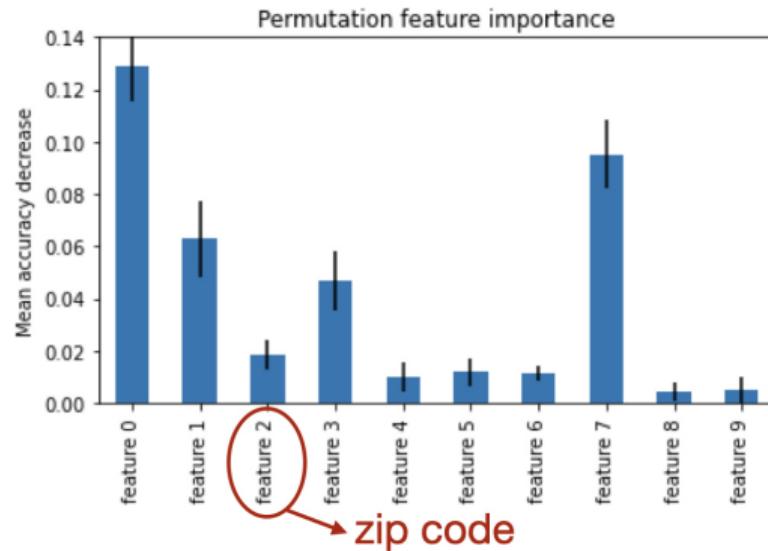
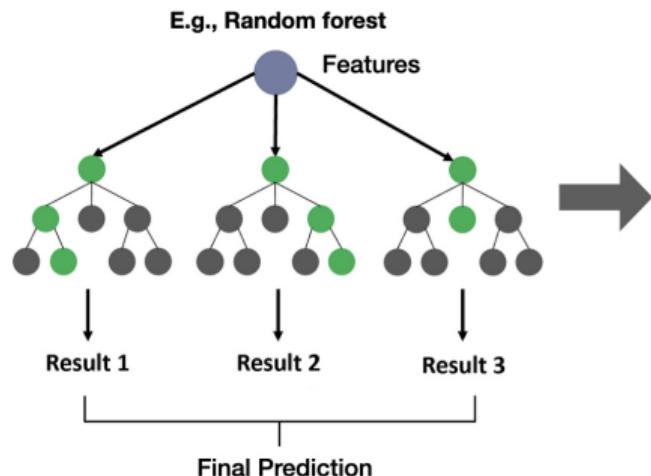
- Property of the **model**
- Which feature does my ML model rely on for decisions?
- Desired for **model diagnostics, auditing, and deployment**

# ML Feature Importance



- Example: mortgage decision unfair w.r.t. races
- Why? Model is race-blind
- Check feature importance: zip code is a proxy of race?

# ML Feature Importance



UQ for ML feature importance:

- **important societal consequences but understudied!**

## Population feature importance

- Inference for Lasso (Lee et al., 2016; Van de Geer et al., 2014)
- Conditional independence test for random forest (Chi et al., 2022)
- Model-agnostic methods: Floodgate (Zhang and Janson, 2020), GCM (Shah and Peters, 2020), VIMP (Williamson et al., 2021)

## ML feature importance

- Only a few works (Fisher et al., 2019; Lei et al., 2018; Rinaldo et al., 2019; Watson and Wright, 2021)
- Many are heuristic
- Most face computational challenges
- Efficient and rigorous UQ for ML feature importance?

## Prior Work: LOCO Inference

**Leave-One-Covariate-Out (LOCO) Inference**  
(Lei et al., 2018; Rinaldo et al., 2019):



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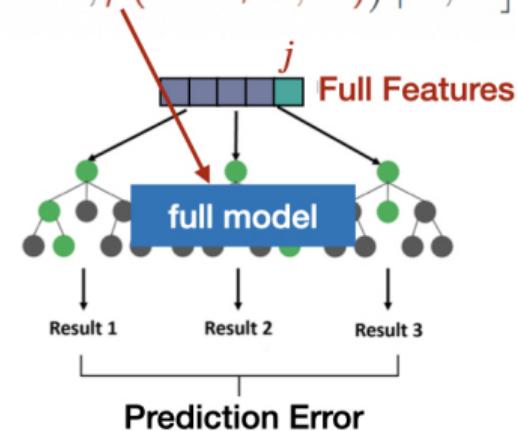


**Inference target:** Predictive power without feature  $j$  vs. with feature  $j$ .

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$$\Delta_j^*(\mathbf{X}, \mathbf{Y}) = \mathbb{E} [\text{Error}(Y^{\text{test}}, \mu_{-j}(X_{-j}^{\text{test}}; \mathbf{X}_{-j}, \mathbf{Y})) - \text{Error}(Y^{\text{test}}, \mu(X^{\text{test}}; \mathbf{X}, \mathbf{Y})) | \mathbf{X}, \mathbf{Y}]$$



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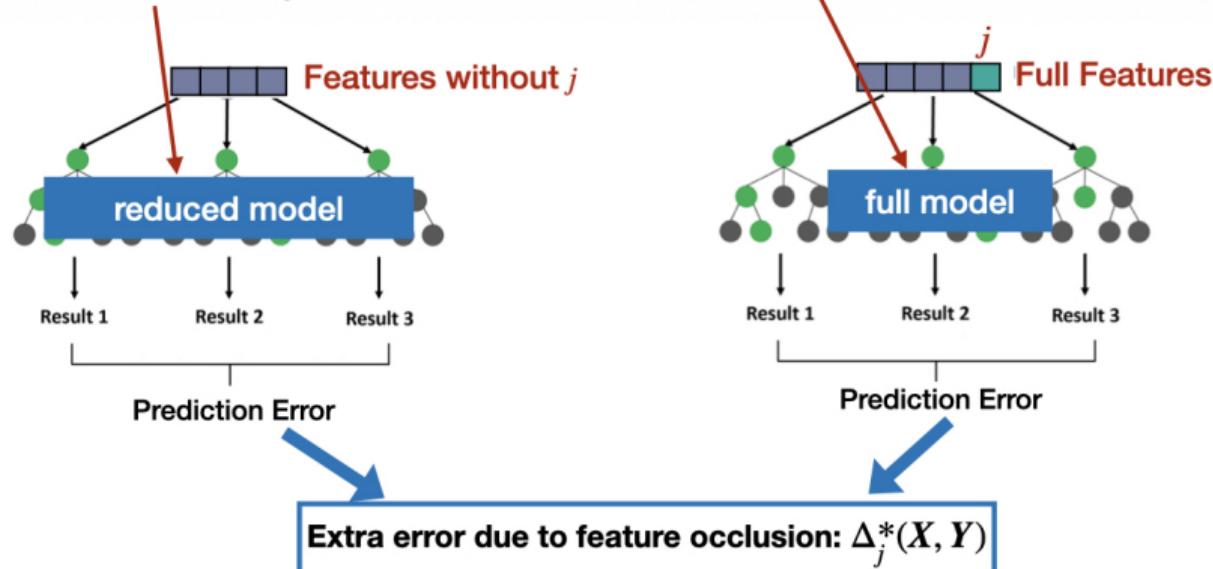
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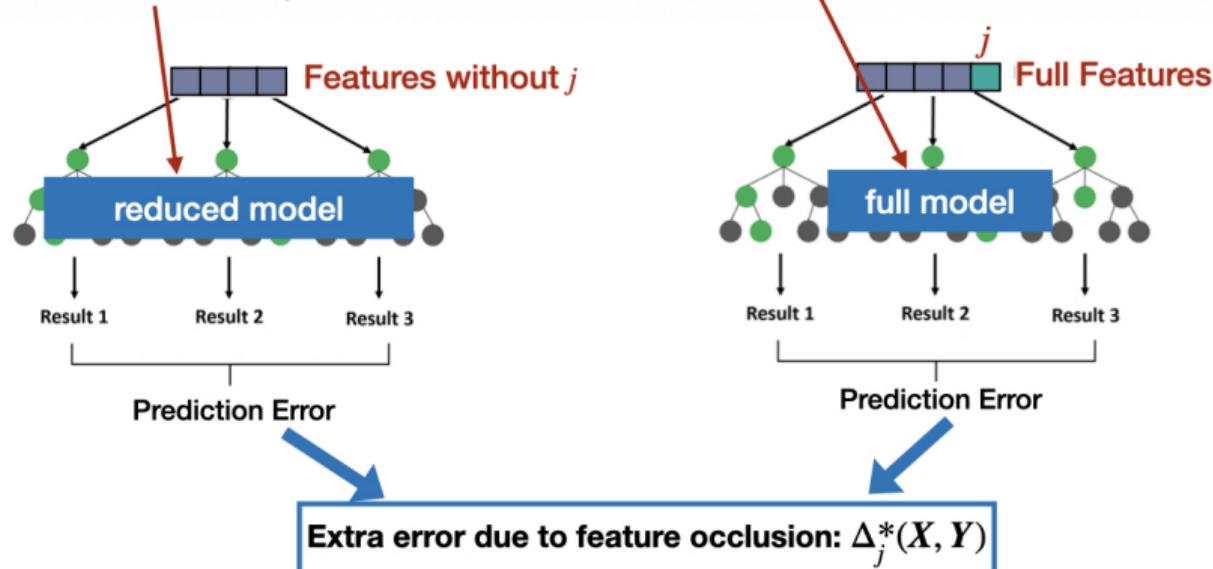
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Property of the current models; model-agnostic

### LOCO inference approach:

- Split data; fit full and reduced models to training data
- Feature occlusion scores on test data  $\Rightarrow$  confidence intervals

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#### Advantages

- Model-agnostic (applicability).
- Statistically valid without assuming data distribution/model choice.

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#### Challenges

- Data splitting loses statistical power;
- Interpretation is not for the full model & depends on random data splitting
- Model refitting for each feature: prohibitive computation after model training

### LOCO inference approach:

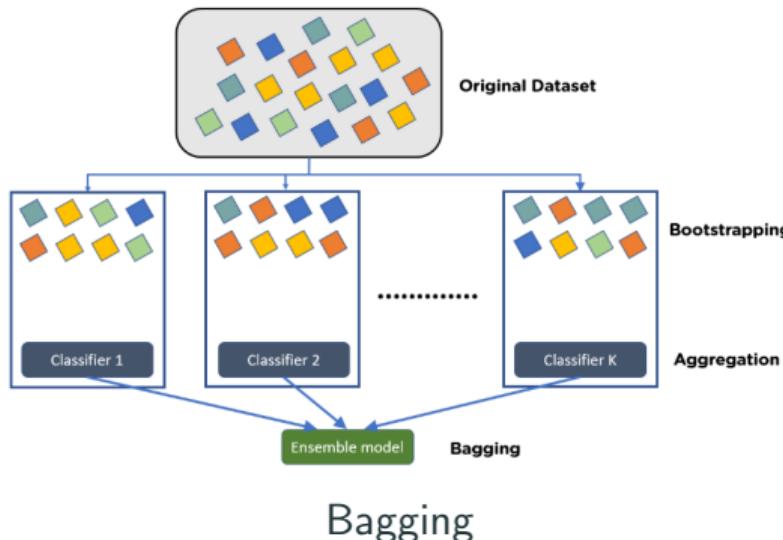
- Split data; fit full and reduced models to training data
- Feature occlusion scores on test data ⇒ confidence intervals

#### Our Goal

Can we utilize the general LOCO framework to perform ML feature importance inference, while [avoiding data splitting and model refitting](#)?

# **Our Approach: LOCO Inference for an Ensemble Framework**

# LOCO Inference for Ensemble Learning



Picture source: <https://www.simplilearn.com/tutorials/machine-learning-tutorial/bagging-in-machine-learning>

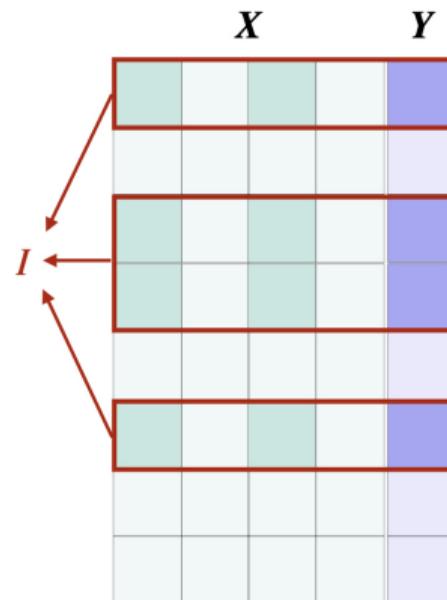
**Inspiration:** Jackknife+ After Bootstrap (Kim et al., 2020).

- Many ensemble methods are good predictors
- Conformal inference (Jackknife+) for bagging is **computationally free with no data-splitting!**

**Idea: Minipatch Ensembles.**

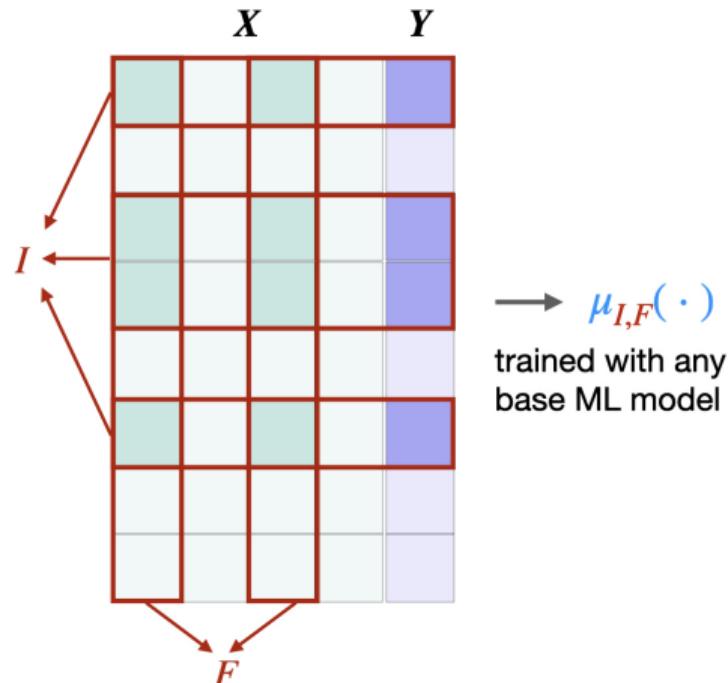
# Minipatch Ensemble Learning

**Minipatch ensembles:** like bagging, but double-subsampling for both observations and features (Yao and Allen, 2020).



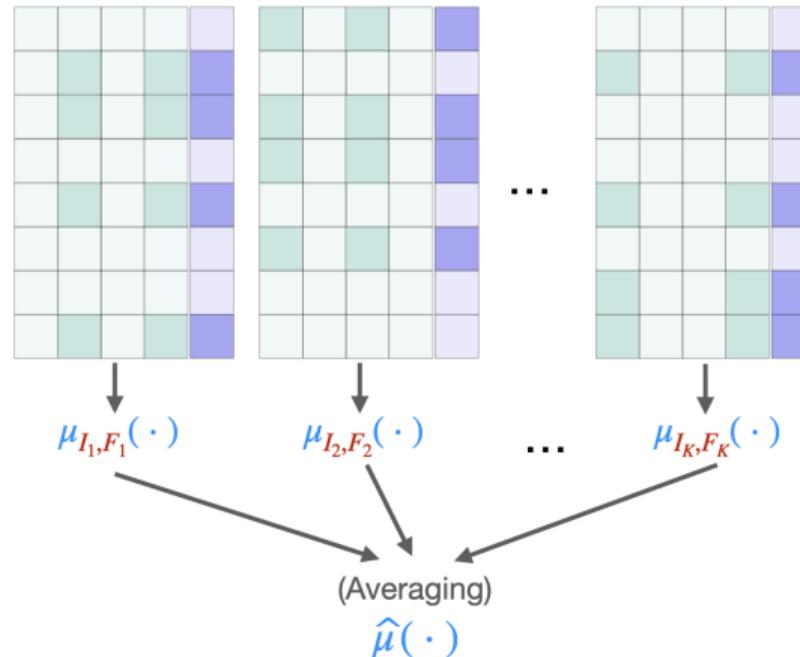
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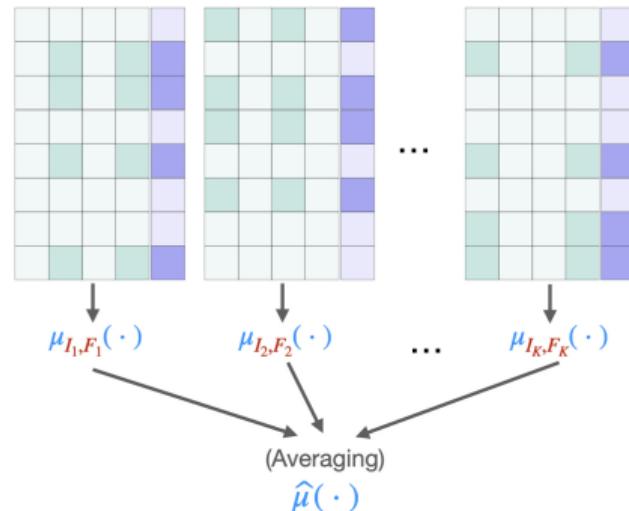


# Minipatch Ensemble Learning

**Inspiration:** Bagging; Random Forests (Louppe and Geurts, 2012); Stochastic Optimization & Dropout.

## Advantages:

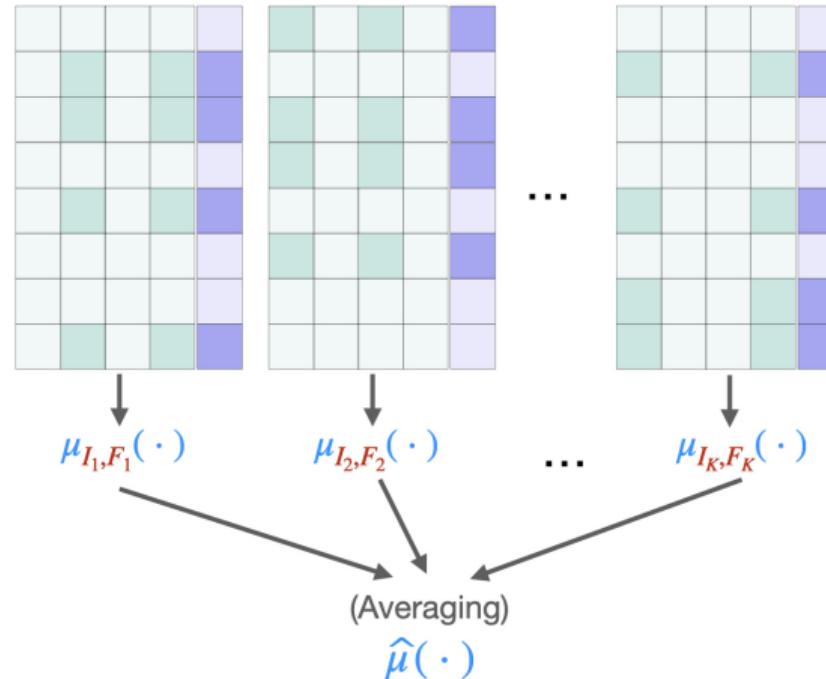
- Fast and easily parallelizable
- Ensemble diversity; **implicit regularization** (LeJeune et al., 2020; Yao et al., 2021)



**LOCO Inference for Minipatch Ensembles?**

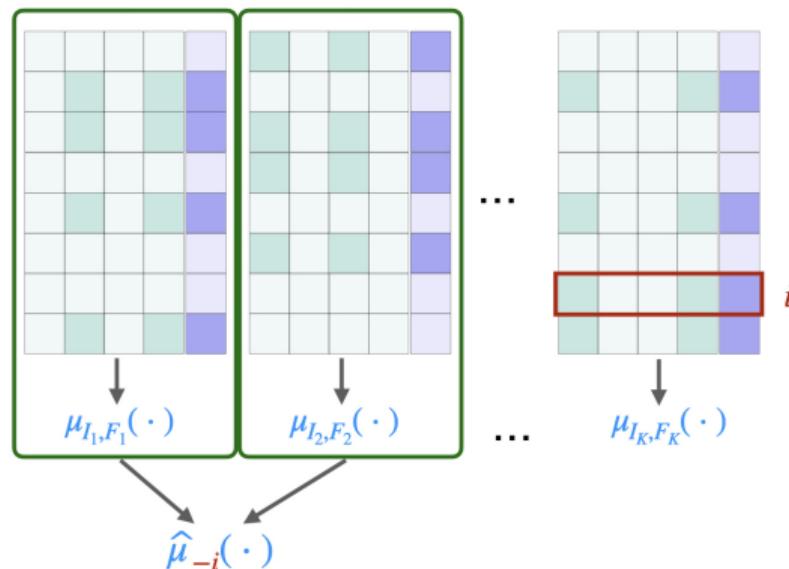
## Algorithm: LOCO for Minipatch

- Step 1. Fit minipatch learning predictor:  $\hat{\mu}$ .



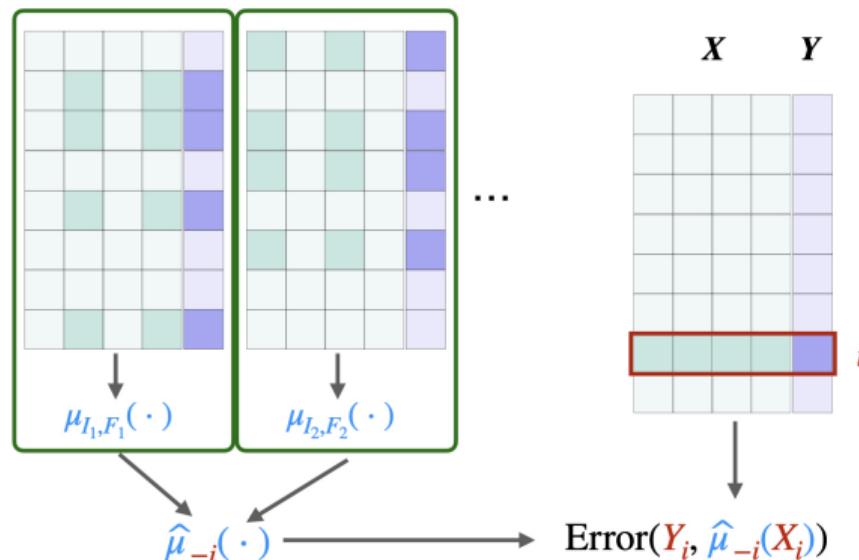
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- Step 2. LOO (leave-one-observation-out) predictor:  $\hat{\mu}_{-i}(X_i)$ .
  - Ensemble minipatches without observation  $i$ .
  - Compute test error on sample  $i$ .



## Algorithm: LOCO for Minipatch

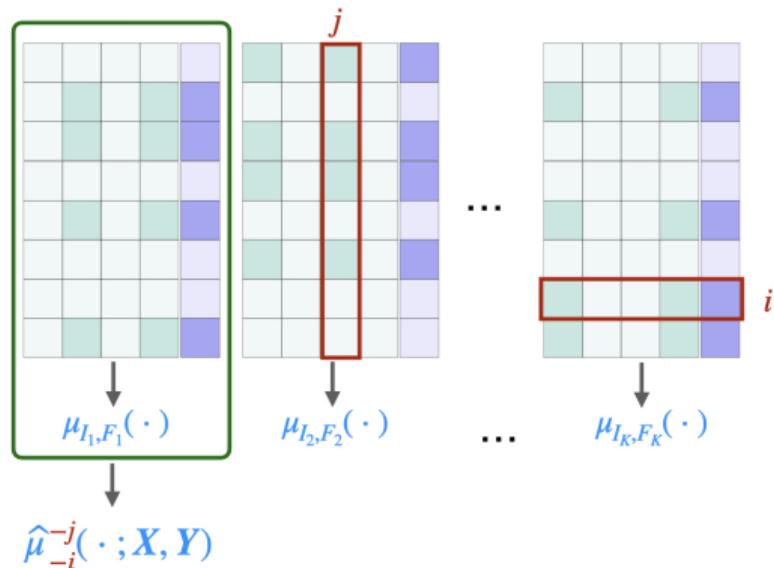
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No data-splitting!  
Simple model averaging;  
Free computationally!

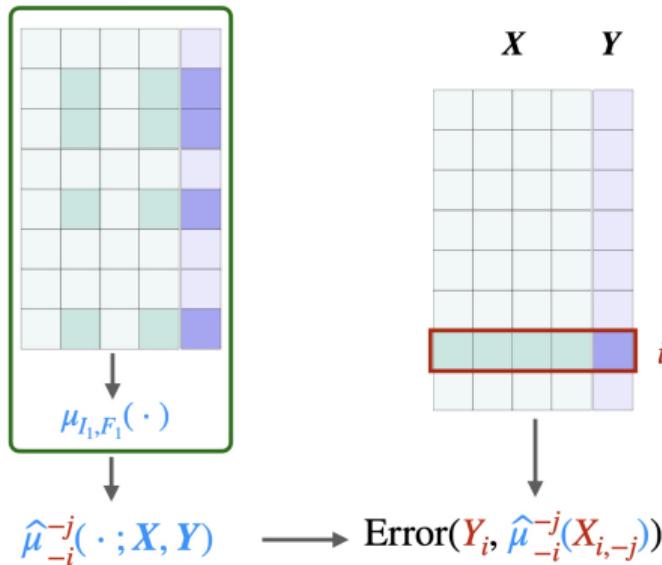
## Algorithm: LOCO for Minipatch

- **Step 3. LOCO-LOO predictor:**  $\hat{\mu}_{-i}^{-j}(X_i)$ .
  - Ensemble minipatches **without observation  $i$  and without feature  $j$ .**
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## Algorithm: LOCO for Minipatch

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Simple model averaging;  
Free computationally!

## Algorithm: LOCO for Minipatch

- **Step 4.** Compute feature occlusion score for observation  $1 \leq i \leq N$ :

$$\hat{\Delta}_j(X_i, Y_i) = \text{Error}(\textcolor{red}{Y_i}, \hat{\mu}_{-i}^{-j}(\textcolor{red}{X_i})) - \text{Error}(\textcolor{red}{Y_i}, \hat{\mu}_{-i}(\textcolor{red}{X_i})).$$

**Importance of feature  $j$  for predicting sample  $i$ .**

- **Step 5.** Construct asymptotically normal interval from  $\{\hat{\Delta}_j(X_i, Y_i)\}_{i=1}^N$ :

$$\hat{\mathbb{C}}_j = \left[ \bar{\Delta}_j - \frac{z_{\alpha/2} \hat{\sigma}_j}{\sqrt{N}}, \bar{\Delta}_j + \frac{z_{\alpha/2} \hat{\sigma}_j}{\sqrt{N}} \right],$$

$\bar{\Delta}_j$ : mean occlusion score,  $\hat{\sigma}_j$ : standard deviation.

## Algorithm: LOCO for Minipatch

### Full Algorithm

- **Step 1.** Fit minipatch learning predictor.
- **Step 2&3.** For each sample  $i$ , compute **LOO** and **LOCO-LOO** predictor by simple model averaging.
- **Step 4&5.** Construct the normal confidence interval.

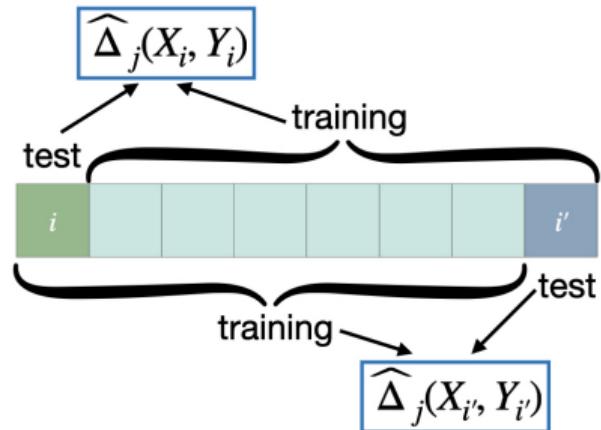
#### Algorithmic advantages

- **No model-refitting**  $\Rightarrow$  once predictive model is trained, confidence intervals are **computationally free!**
- **No data-splitting**  $\Rightarrow$  **powerful**; feature importance inference **for the current model at hand!**

# Theoretical Guarantees

Does LOCO-MP confidence interval have valid coverage?

- **Leave-one-observation-out instead of data-splitting**  $\Rightarrow$  dependency amongst  $\{\widehat{\Delta}_j(X_i, Y_i)\}_{i=1}^N$ !
- $\widehat{\Delta}_j(X_i, Y_i)$  and  $\widehat{\Delta}_j(X_{i'}, Y_{i'})$  switches  $i$  and  $i'$  for training and testing; **share  $N - 2$  training samples**.
- Central limit theorem not applicable!



## Theoretical Guarantees

---

- A1. Smoothness of  $\text{Error}()$ .
- A2. Minipatch predictors have bounded difference (automatically hold for classification).
- A3. Small MP:  $n = o(\sqrt{N})$
- A4. Large number of MPs:  $K \gg \frac{N}{\sigma_j^2}$

## Theoretical Guarantees

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- A1. Smoothness of Error().
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- A3. Small MP:  $n = o(\sqrt{N})$
- A4. Large number of MPs:  $K \gg \frac{N}{\sigma_j^2}$

### Theorem

Suppose samples  $(\mathbf{X}_i, Y_i)$  are i.i.d., and assumptions A1-A4 hold. Then

$$\lim_{N \rightarrow \infty} \mathbb{P}(\Delta_j^* \in \hat{\mathbb{C}}_j) = 1 - \alpha.$$

**Valid asymptotic coverage** under mild assumptions; applicable to **any data distributions and base ML models**.

## Theoretical Guarantees

---

- **Algorithmic stability:** prediction is stable against change in one training sample.
- Stability facilitates **statistical inference under dependency!** (Bayle et al., 2020)!

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- **Algorithmic stability:** prediction is stable against change in one training sample.
- Stability facilitates **statistical inference under dependency!** (Bayle et al., 2020)!
- Minipatch ensembles are **stable with any base model and any data distribution!**
- Independent interest: stability also helps with conformal inference, selective inference.

## Predictive inference is also free after training!

- Leave-one-observation-out residuals are free to compute
- Use quantiles of LOO residuals to construct distribution-free predictive intervals (**conformal inference**)
- Similar to Jackknife+ after bootstrap (Kim et al., 2020)

Simultaneous, immediate inference for both feature importance & prediction ⇒ convenient safety check for ML systems

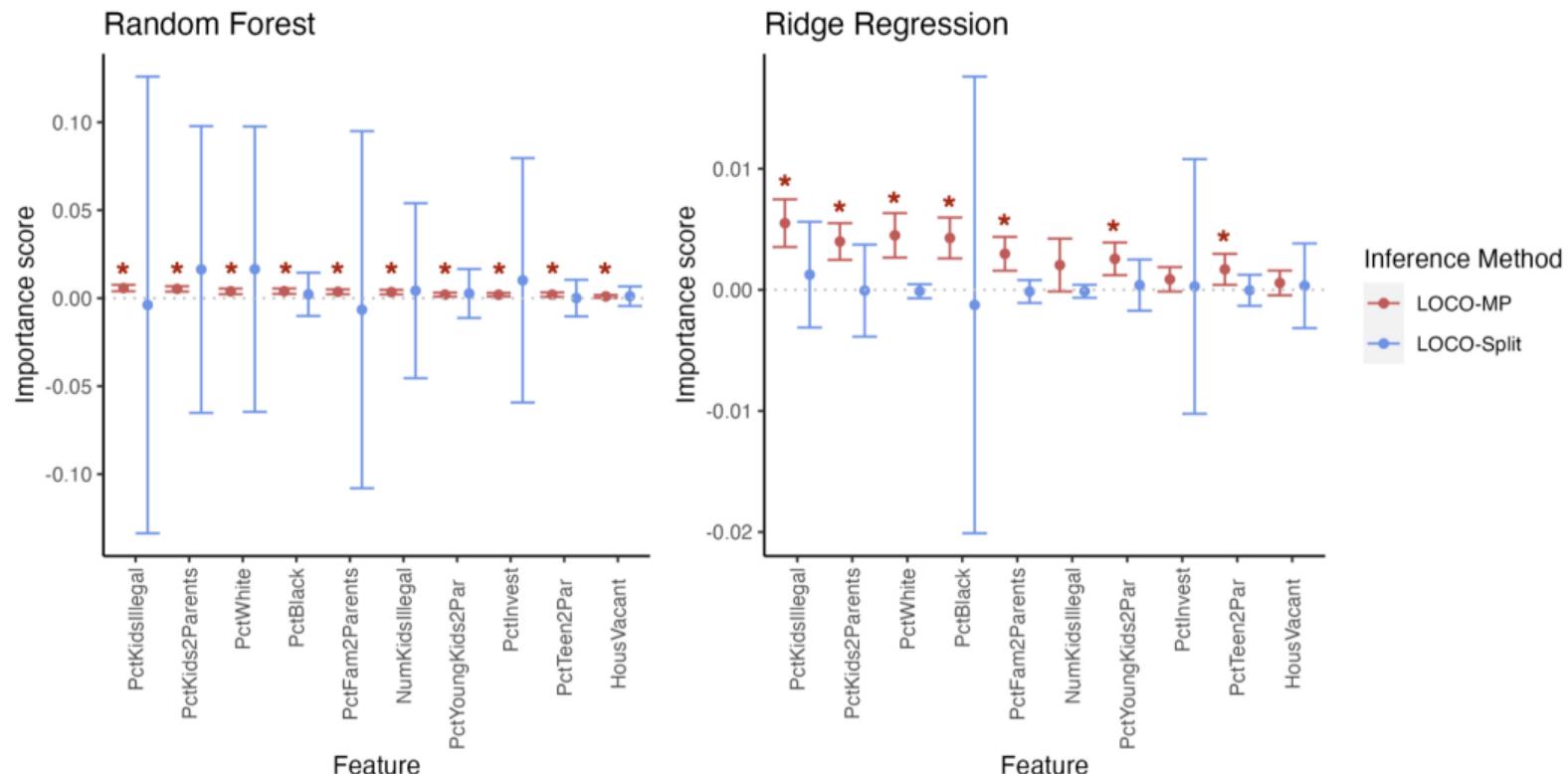
# **Empirical Studies**

## Real Data Example

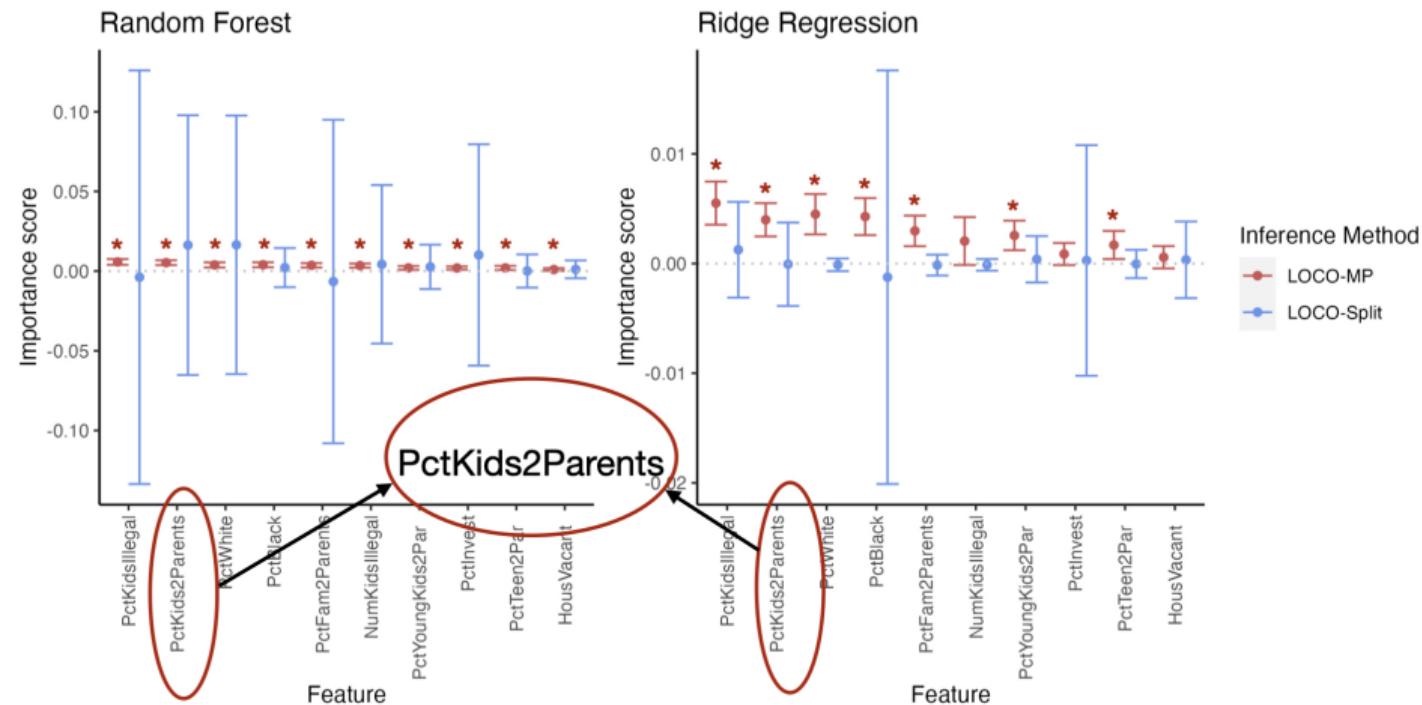
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- Communities and Crimes data (Redmond, 2009).
- 1994 observations, 122 features.
- Predict the **per capita violent crime rate** based on **community features**.

# Real Data Example



# Real Data Example



## Conclusion

---

- **Uncertainty quantification for ML feature importance for minipatch ensembles**

## Conclusion

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  - Free computationally (after minipatch learning).
  - Also (free) predictive intervals.
  - Statistically powerful; assumption-light.

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- **Going beyond model diagnostics: LOCO-MP for discovery?**
  - Relationship to population feature importance?
  - Correlated features?

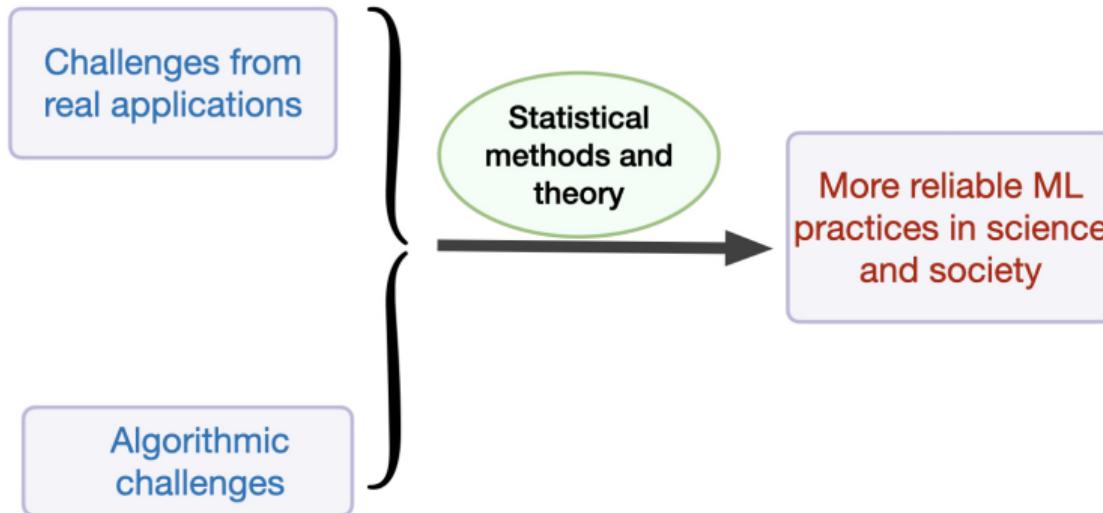
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- L. Gan\*, L. Zheng\*, G. I. Allen (\*: equal contribution), "Model-Agnostic Confidence Intervals for Feature Importance: A Fast and Powerful Approach Using Minipatch Ensembles",  
<https://arxiv.org/abs/2206.02088>.

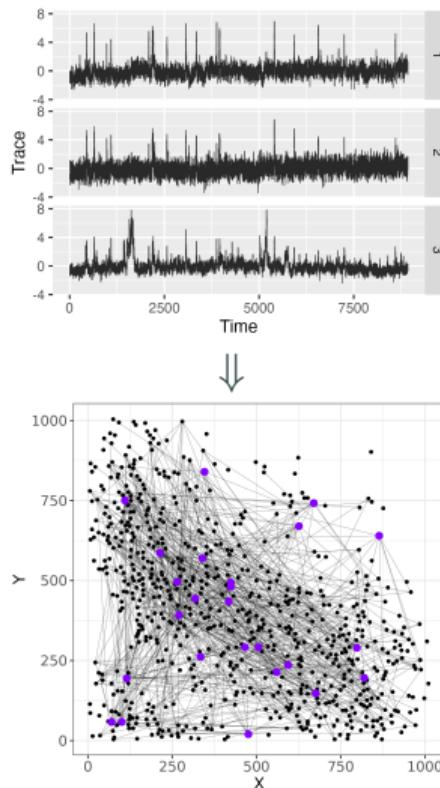
## **Other Works and Future Directions**

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# Research Theme



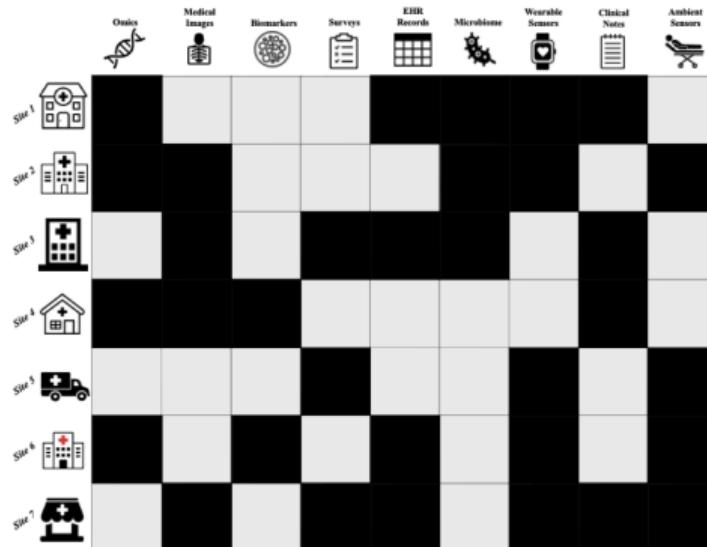
## Learning Functional Connectivity in Neuroscience



- Uncertainty quantification: GI-JOE
- Low-rank covariance completion for graph quilting  
A. Chang, **L. Zheng**, G. I. Allen,  
*under revision at JASA, Applications and Case Studies*
- Nonparanormal graph quilting  
*STAT, 2023.*

# Reliable Statistical Learning in Real Applications

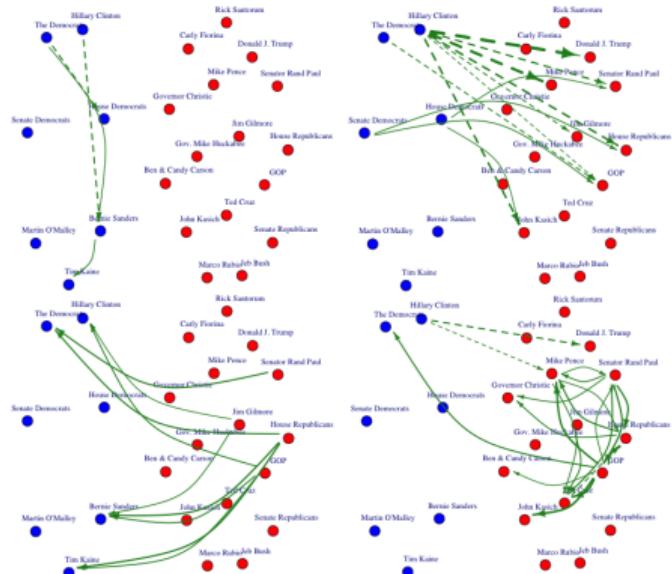
## Clustering for Patchwise Multi-modal Healthcare Data



- Provable spectral clustering for patchwork learning
- PCA for patchwork learning?

# Reliable Statistical Learning in Real Applications

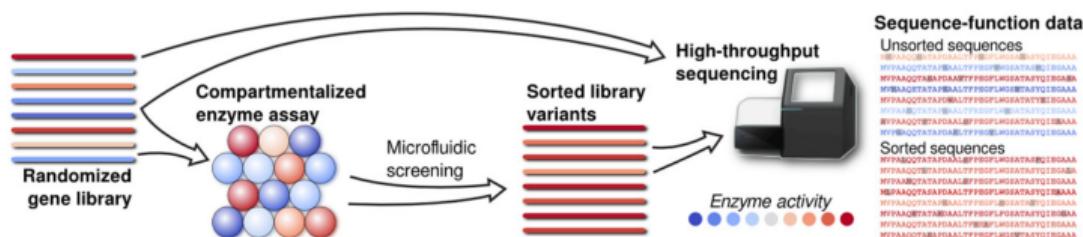
## Granger Causal Network on Social Media and Stock Market



- Hypothesis testing for Granger causal edges in linear AR( $p$ ) models  
**L. Zheng, G. Raskutti,**  
*Electronic Journal of Statistics, 2019*
- Context-dependent Granger causal network learning for mixed data types L.  
**Zheng, G. Raskutti, R. Willett, B. Mark**  
*Journal of Machine Learning Research, 2020*

# Reliable Statistical Learning in Real Applications

# Protein Engineering from Label-contaminated Data



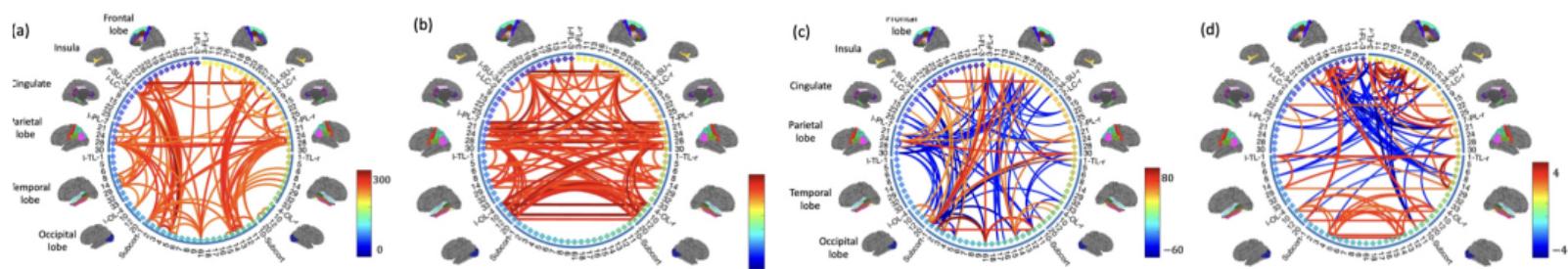
## High-dimensional classification with positive-unlabeled data

L. Zheng, G. Raskutti,

*under revision at Electronic Journal of Statistics*

# Reliable Statistical Learning in Real Applications

## Joint Analysis of Functional & Structural Brain Connectivity in Neuroimaging



Joint **Tensor PCA** for Multi-modal Populations of Networks

J. Liu, L. Zheng, Z. Zhang, G. I. Allen.

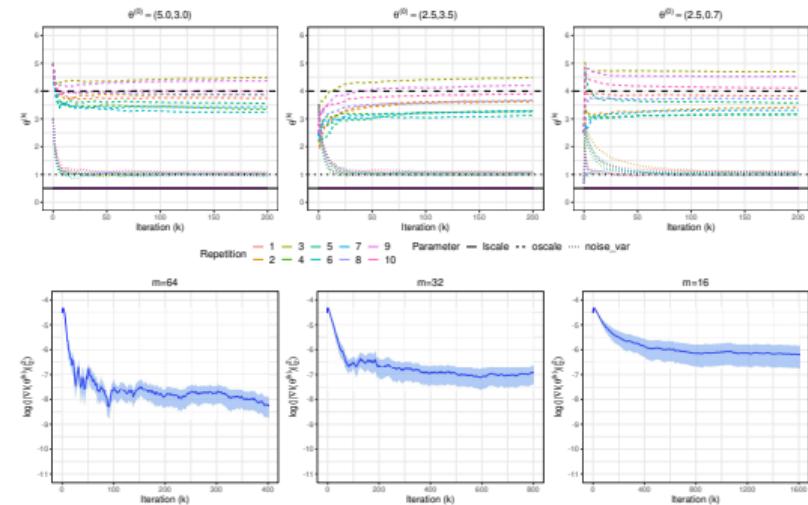
# Addressing Algorithmic Challenges for Large-scale Machine Learning

Subsampling helps both computationally and statistically

- LOCO-MP for free inference of ML interpretation
- **Provable Convergence: Stochastic Gradient Descent can Speed up Gaussian Processes!**

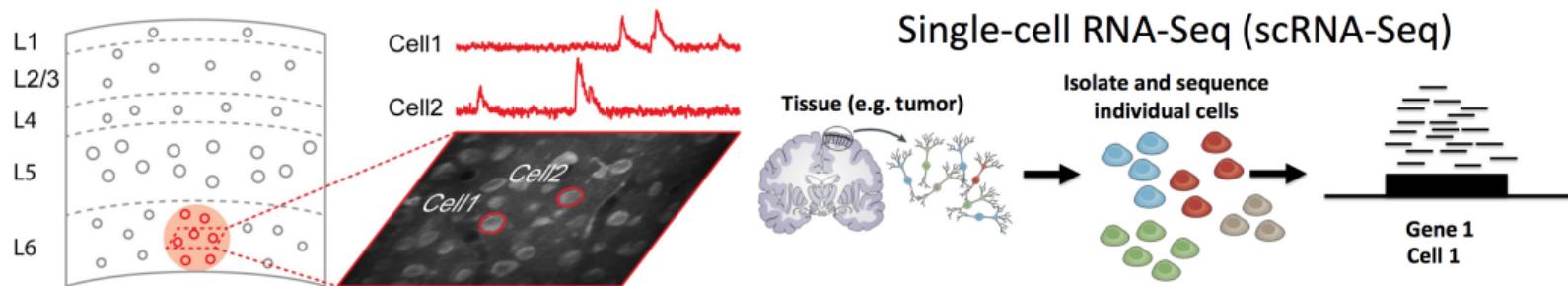
H. Chen, L. Zheng, R. Al Kontar, G. Raskutti

*Journal of Machine Learning Research, 2022*



# Future Directions

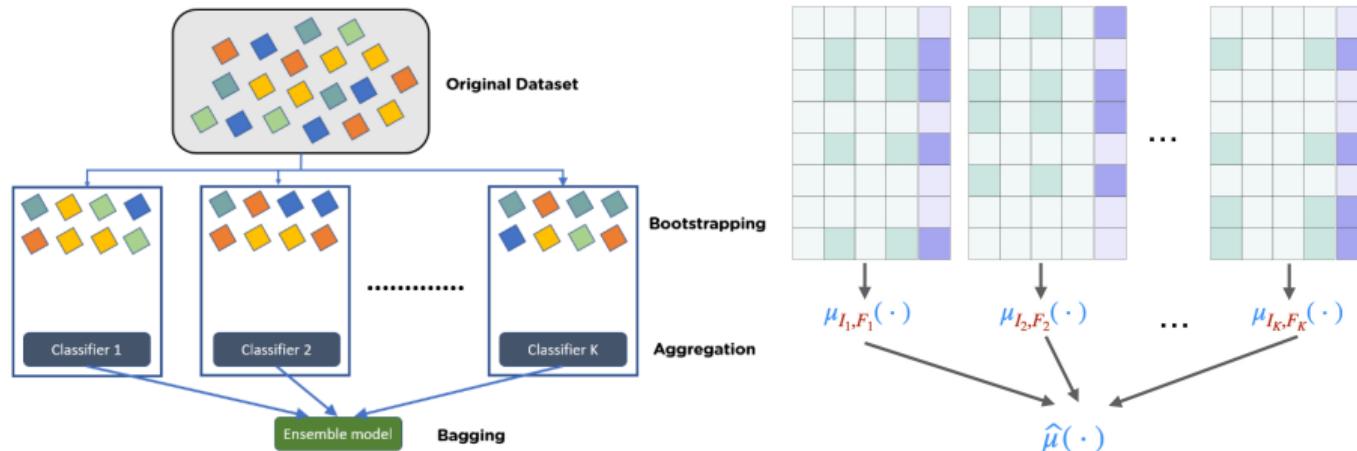
## Reliable statistical learning from messy biomedical data?



Picture source: <https://speakerdeck.com/stephaniehicks/welcome-to-the-world-of-single-cell-rna-sequencing?slide=3>

latent neurons; imputation for frequent dropouts

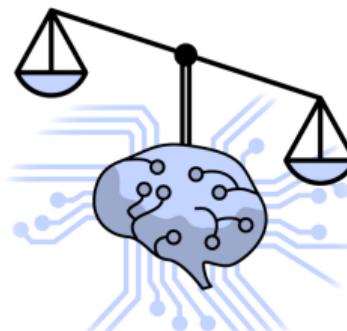
Exploit ensemble learning for statistical & computational advantages, and convenient uncertainty quantification?



## Fairness in machine learning interpretations?

ML interpretations can

- inherit bias from data
- only depict the majority group



Picture source:

<https://sitn.hms.harvard.edu/uncategorized/2020/fairness-machine-learning/>

# Acknowledgments

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## Coauthors

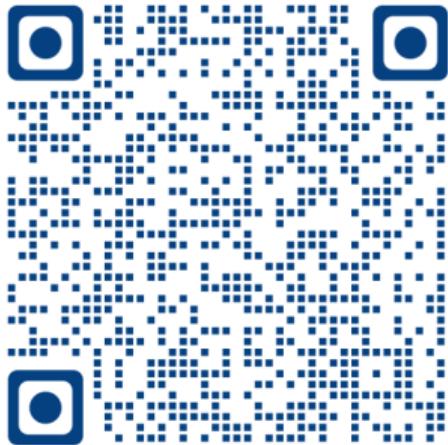


Luqin Gan



Genevera I. Allen

# Thank you!



# **Supplementary Details for GI-JOE**

## GI-JOE: Variance Computation

---

Variance for node pair  $(a, b)$  is estimated by:

$$\hat{\sigma}_n^2(a, b) = \sum_{j, k, j', k'} \frac{n_{j, k, j', k'}}{n_{j, k} n_{j', k'}} \hat{\Theta}_{j, b}^{(a)} \hat{\theta}_k^{(a)} \hat{\Theta}_{j', b}^{(a)} \hat{\theta}_{k'}^{(a)} (\hat{\Sigma}_{j, j'} \hat{\Sigma}_{k, k'} + \hat{\Sigma}_{j, k'} \hat{\Sigma}_{k, j'}).$$

$n_{j, k, j', k'}$  : number of joint measurements of quadruple  $(j, k, j', k')$ ;

$n_{j, k}$  : number of joint measurements of pair  $(j, k)$ ;

$n_{j', k'}$  : number of joint measurements of pair  $(j', k')$ ,

$$\hat{\sigma}_n^2(a, b) \propto (n_2^{(a, b)})^{-1}.$$

# GI-JOE: Assumptions for Valid Edgewise Testing

---

## Assumption

The local sample sizes  $n_1^{(a,b)}$ ,  $n_2^{(a,b)}$ , degrees of node  $a$ ,  $b$  ( $d_a$ ,  $d_b$ ), graph size  $p$  satisfy

$$n_1^{(a,b)} \gg (d_a + d_b)^2 (\log p)^2 \frac{n_2^{(a,b)}}{n_1^{(a,b)}},$$

$$n_1^{(a,b)} \gg (d_a + d_b)^2 \log p \left( \frac{n_2^{(a,b)}}{n_1^{(a,b)}} \right)^2.$$

## GI-JOE: Valid FDR Control (Informal)

Theorem: Valid FDR control (Informal)

Assume

1.  $n_1^{(a,b)}$  is sufficiently large for all  $(a, b)$  (**holds even if  $\max n_{j,k} \gg \min n_{j,k}$** );
2. Most edge pairs  $(a, b), (a', b')$  are only **weakly correlated** (satisfied by most sparse graphs).

The edge set selected by GI-JOE (FDR) has **asymptotically valid FDR control**.

## Assumption (Sample Size Condition)

For all node pairs  $(a, b) \in [p] \times [p]$ ,

$$n_1^{(a,b)} \gg C(d+1)^2(\log p)^5 \log \log p \left( \frac{n_2^{(a,b)}}{n_1^{(a,b)}} \right)^2, \quad n_2^{(a,b)} \geq C(d+1)^6(\log p)^6.$$

- Weaker assumption than  $p < n^C$  for  $C > 0$  in prior literature (Liu, 2013);
- Let  $g(d, p) = C(d+1)^2(\log p)^5 \log \log p$ , then this is implied by

$$n_{\min} \gg g(d, p), \quad \frac{n_{\min}}{g(d, p)} \gg \left( \frac{n_{\max}}{g(d, p)} \right)^{2/3}$$

## Assumption (Edge-edge correlations)

Total number of edge pairs:  $p^4$ .

- $\mathcal{A}_1$ : set of strongly correlated edge pairs;  $|\mathcal{A}_1| \leq Cp^2$
- $\mathcal{A}_2$ : set of moderately correlated edge pairs;  $|\mathcal{A}_2| \ll p^{4-\varepsilon}$  for a small constant  $\varepsilon > 0$ .
- In full observational setting, this is implied by (i) each node only has constant number of strongly connected neighbors; (ii)  $d \ll p^{1-c}$ ;
- Empirical evidence supports this assumption for general graph and measurement patterns.

## Proof Sketch for GI-JOE: Edgewise Testing

---

$$\tilde{\theta}_b^{(a)} = -\frac{\Theta_{a,b}^*}{\Theta_{a,a}^*} + \text{mean-zero first-order term} + \text{high-order residuals}$$

- Mean-zero first-order term  $\asymp \frac{1}{\sqrt{n_2^{(a,b)}}}$
- High-order residuals carefully controlled:  $\lesssim \frac{\log p}{n_1^{(a,b)}}$  (collects errors from neighborhood Lasso)
- Variance estimates depend on (i) neighborhood Lasso; (ii)  $\widehat{\Sigma}_{j,k} - \Sigma_{j,k}^*$  mainly for the  $j \in \mathcal{N}_a, k \in \mathcal{N}_b$ .

## Key Proof Tool for GI-JOE: FDR Control

### Key technical tool

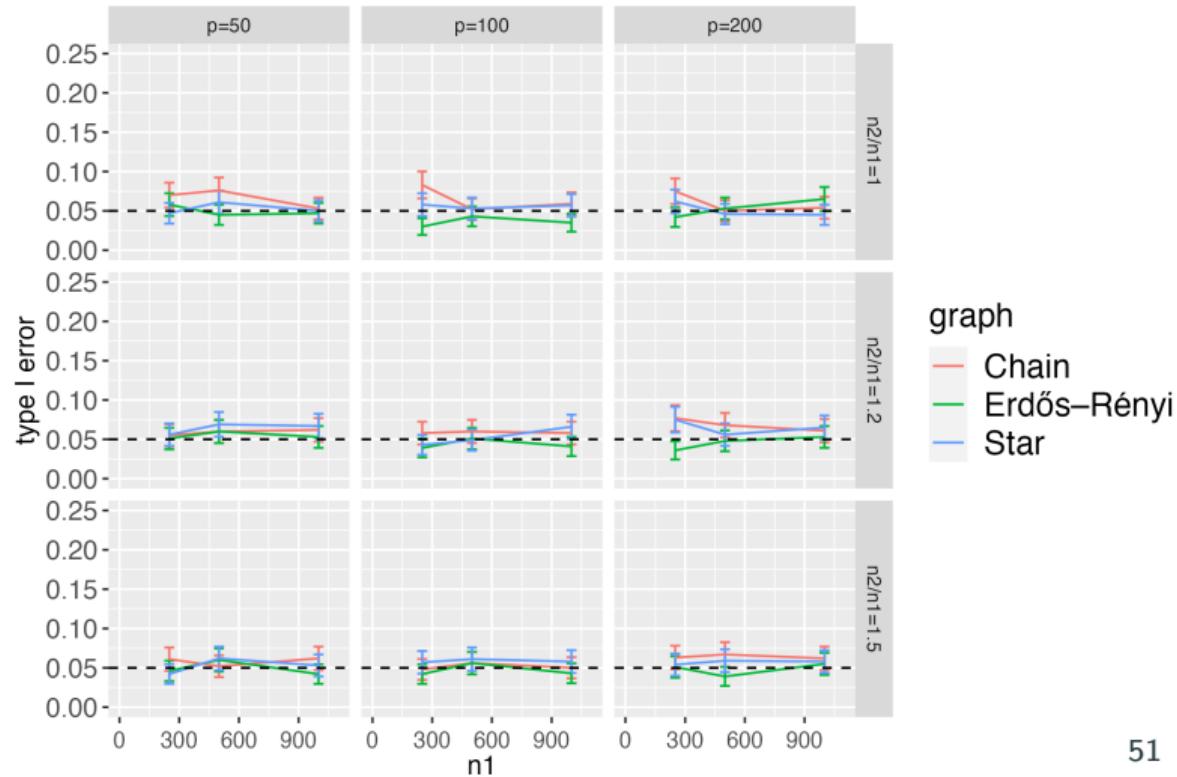
For each node pair, test statistics  $(\xi^{(a,b)}, \xi^{(a',b')})$  converge to a two-variate independent Gaussian distribution:

Let  $(Z_1, Z_2) \sim \mathcal{N}(0, I_2)$ , we have

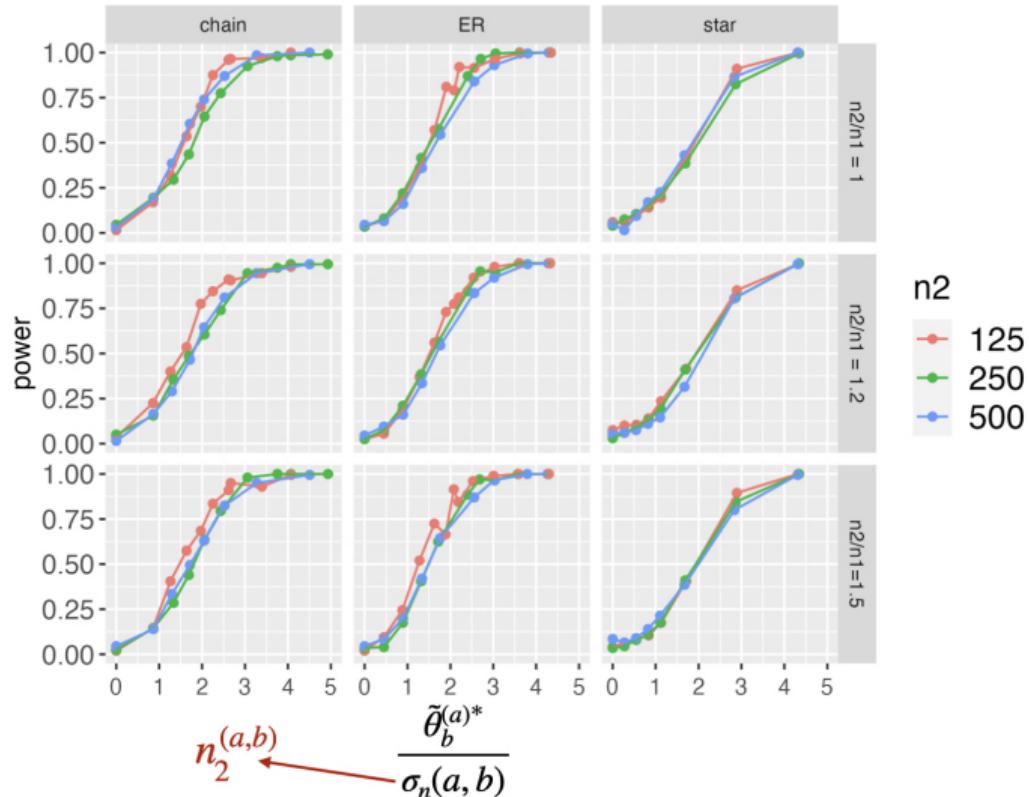
$$\begin{aligned} & \mathbb{P}(|\xi^{(a,b)}| > t_1, |\xi^{(a',b')}| > t_2) \\ & \leq \mathbb{P}(|Z_1| > t_1 - \varepsilon, |Z_2| > t_2 - \varepsilon) + C \exp\{-c\varepsilon\sqrt{n_2^{(a,b)}}\}. \end{aligned}$$

# GI-JOE Simulation: Edge-wise Testing

**Valid type I error** with  
differing pairwise sample  
sizes!



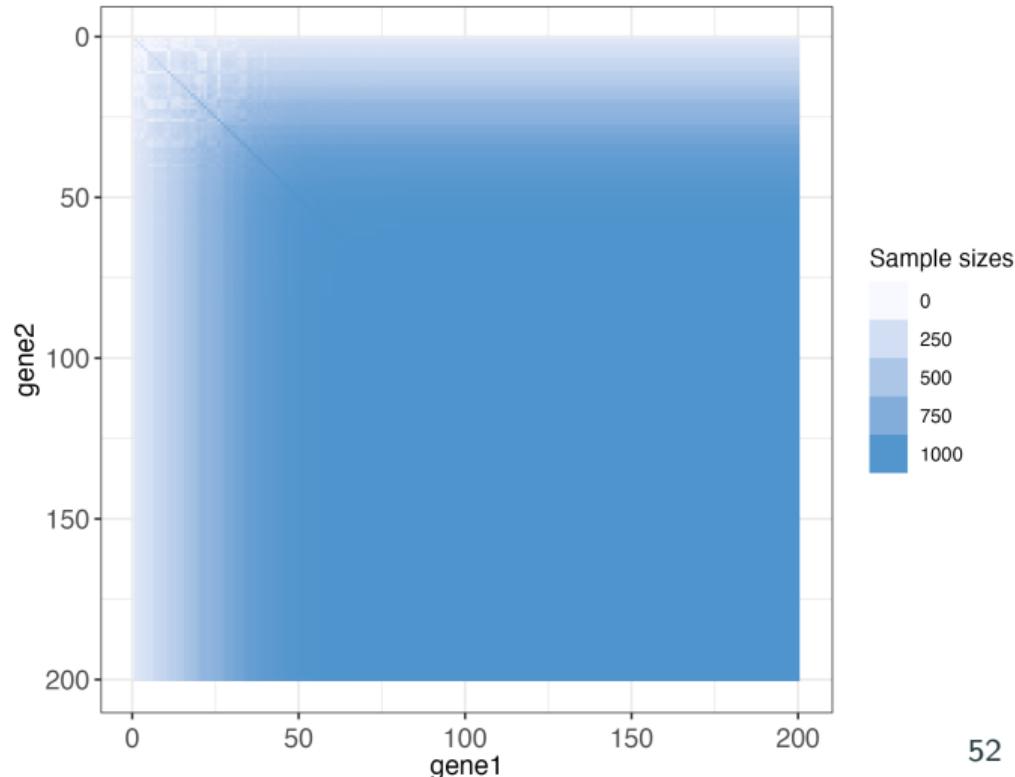
# GI-JOE Simulation: Edge-wise Testing



Power depends on signal  
strength & **localized**  
sample size  $n_2^{(a,b)}$

## Simulation: Graph Selection Comparison

- Simulate data from a **scale-free graph** with 200 nodes
- **Real measurement pattern** in a [real single-cell RNA sequencing](#) data set (Chu et al., 2016)

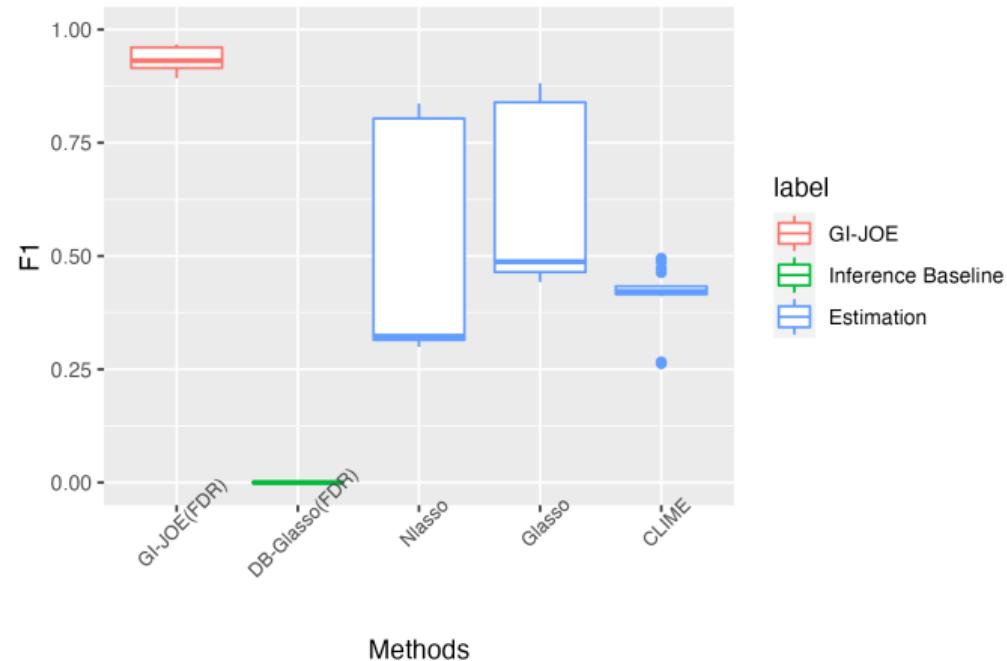


# Simulation: Graph Selection Comparison

F1-score:  $2/(TPR^{-1}+TDR^{-1})$ ;

**the higher the better**

- Our method GI-JOE with FDR control
- Baseline inference methods: Plug-in method with debiased graphical lasso, minimum sample size
- Estimation methods: graphical lasso, neighborhood lasso, CLIME



## Assumptions for Validity of LOCO-MP

---

- A1.  $\text{Error}()$  is Lipschitz continuous.
- A2. Bounded difference in MP predictions  $||\hat{\mu}_{I,F}(X) - \hat{\mu}_{I',F'}(X)|| \leq B$ .

## Assumptions for Validity of LOCO-MP

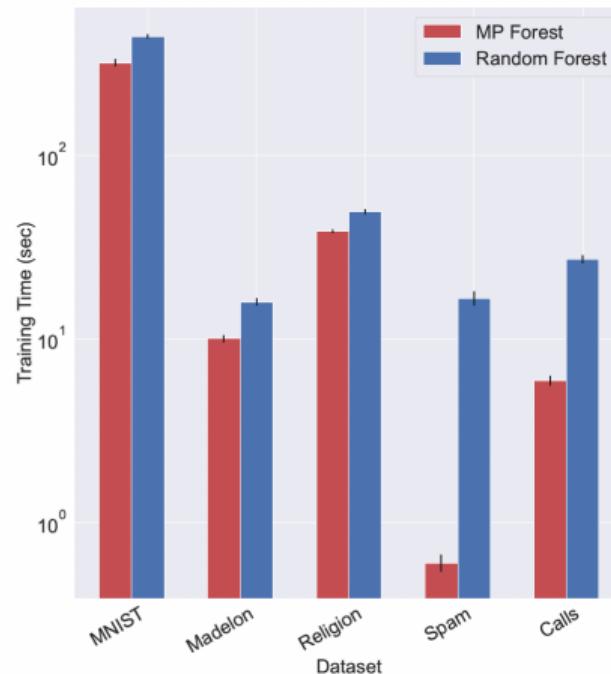
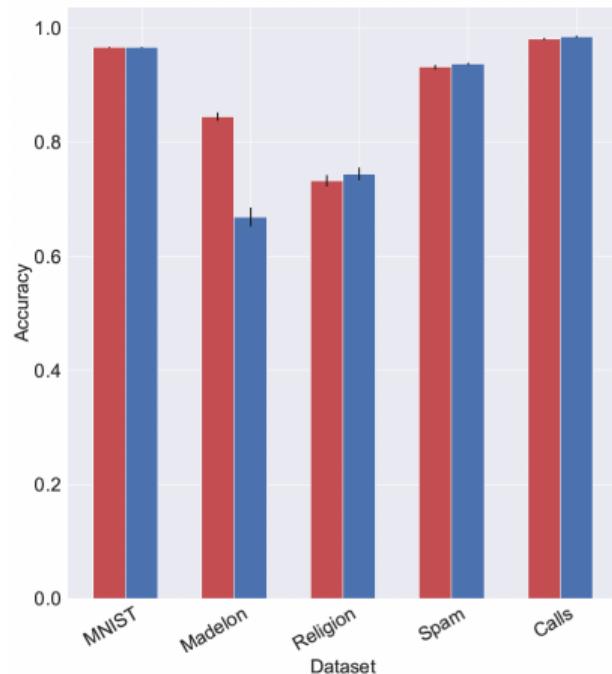
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- A1.  $\text{Error}()$  is Lipschitz continuous.
- A2. Bounded difference in MP predictions  $\|\hat{\mu}_{I,F}(X) - \hat{\mu}_{I',F'}(X)\| \leq B$ .  
*(automatically hold for classification)*
- A3. MP size:  $n = o\left(\frac{\sigma_j}{LB}\sqrt{N}\right)$ .
- A4.  $K \gg \left(\frac{L^2B^2N}{\sigma_j^2} + \frac{LB\sqrt{N}}{\sigma_j} + 1\right)\log(N)$ .

## **Supplementary Details for LOCO-MP**

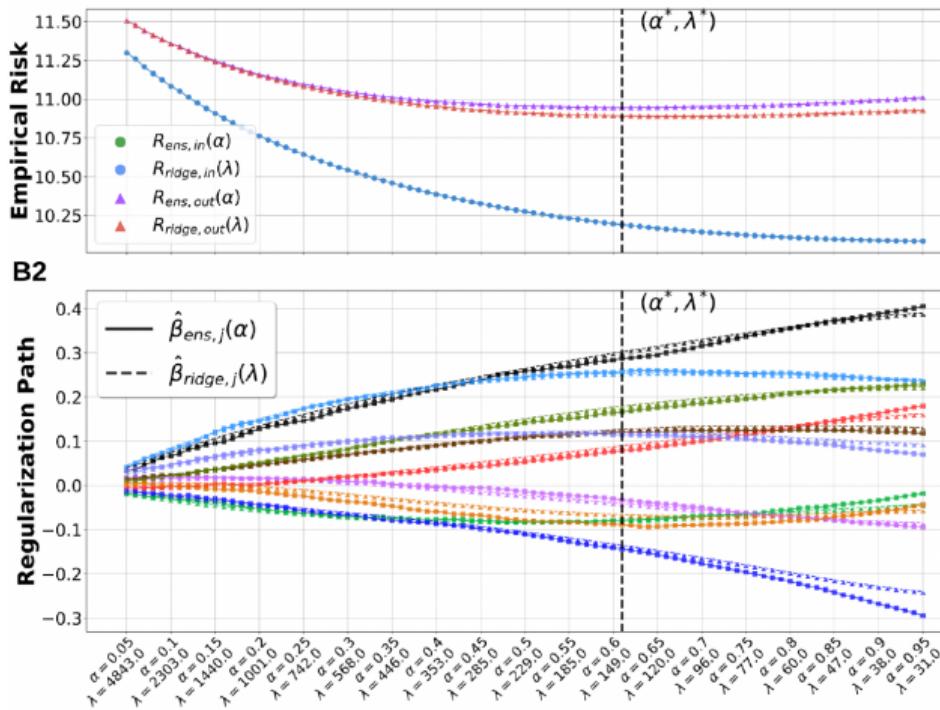
# What is the Minipatch Learning Predictor?

When base models are trees, Minipatch predictor is similar to random forest



# What is the Minipatch Learning Predictor?

When base models are linear regression, Minipatch predictor is equivalent to ridge regression (LeJeune et al., 2020; Yao et al., 2021)



## Minipatch Feature Importance vs. Population Feature Importance?

---

**Special Case: Linear Model.** For independent features,

- $\Delta_j^*$  concentrates around  $\tilde{\Delta}_j^*$ :  $\tilde{\Delta}_j^* \asymp 2\gamma \left( \beta_j^{*2} - \frac{\|\beta_{\setminus j}^*\|_2^2}{M-1} \right)$  (with  $\gamma = m/M$ ).
- Under assumptions on the minipatch size and number; valid coverage for  $\tilde{\Delta}_j^*$ .

## Minipatch Feature Importance vs. Population Feature Importance?

---

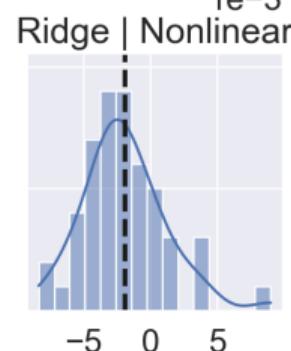
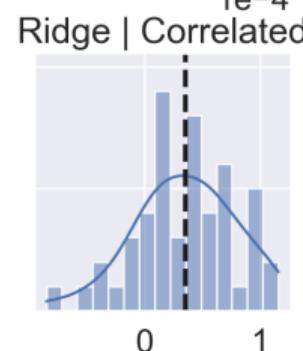
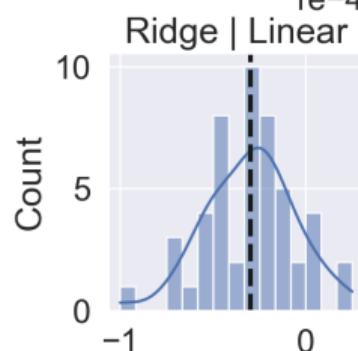
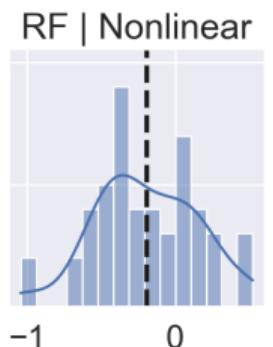
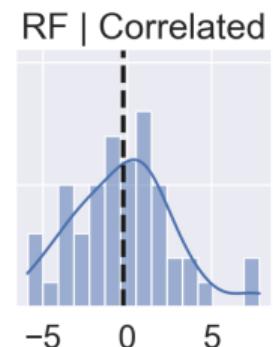
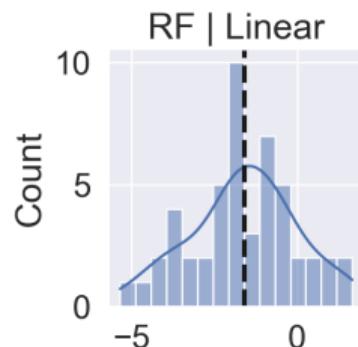
**Special Case: Linear Model.** For correlated features:

- When  $x_1$  and  $x_2$  have correlation  $\rho \rightarrow 1$ , we prove that  $\Delta_1^* \rightarrow \Delta_2^*$  and are a function of  $(\beta_1^* + \beta_2^*)^2$  for LOCO-MP.

As a comparison: original LOCO inference tends to miss correlated features.

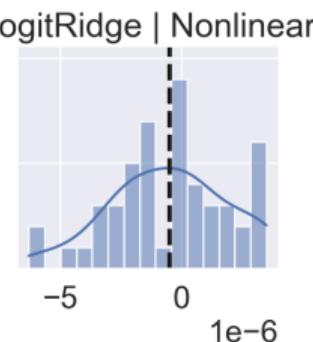
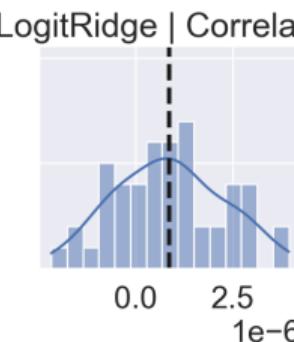
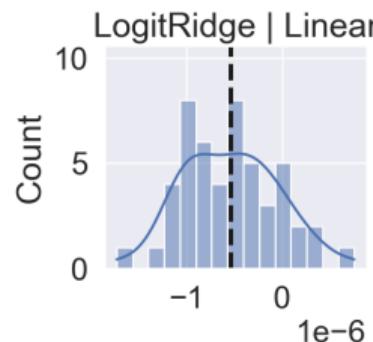
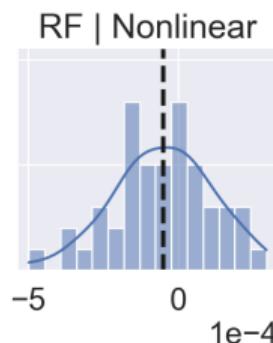
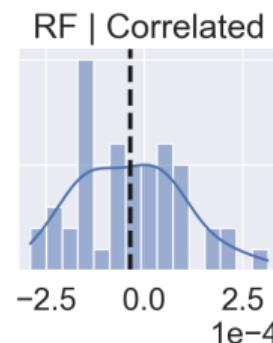
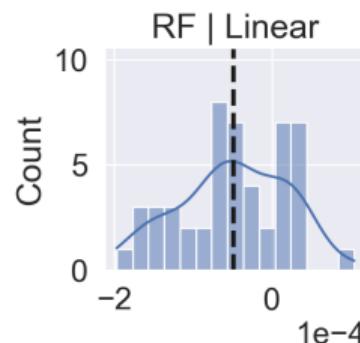
# Minipatch Feature Importance vs. Population Feature Importance?

Histograms of the inference target for a noise feature in the regression setting



# Minipatch Feature Importance vs. Population Feature Importance?

Histograms of the inference target for a noise feature in the classification setting



## LOCO-MP: Detailed Assumption for Valid Coverage

---

- A1.  $\text{Error}(Y, \hat{Y})$  is Lipschitz- $L$  w.r.t. the prediction  $\hat{Y}$ .
- A2. Bounded difference in MP predictions  $\|\hat{\mu}_{I,F}(X) - \hat{\mu}_{I',F'}(X)\| \leq B$ .  
*(automatically hold for classification)*
- A3. Minipatch size:  $n = o\left(\frac{\sigma_j}{LB} \sqrt{N}\right)$ .
- A4. Minipatch number:  $K \gg \left(\frac{L^2 B^2 N}{\sigma_j^2} + \frac{LB\sqrt{N}}{\sigma_j} + 1\right) \log(N)$ ,  $K \gg \frac{M}{m} \log M$ .

## LOCO-MP Simulations: Validate Coverage

---

Simulation Set-up:

- Vary  $N, M = 200$  (unless otherwise specified) & 10 true features.
- 3 Scenarios:
  1. Sparse Linear Regression (or Logistic Regression); iid features.
  2. Sparse Linear Regression (or Logistic Regression); correlated features.
    - Adjacent features have correlation 0.5.
  3. Sparse Non-linear Regression (or Logistic Regression); iid features.
    - Polynomial and MARS spline non-linearity.
- Minipatch LOCO (LOCO-MP) run with  $m = \sqrt{M}$  and  $n = \sqrt{N}$  and  $K = 10,000$ .

## LOCO-MP Simulations: Validate Coverage

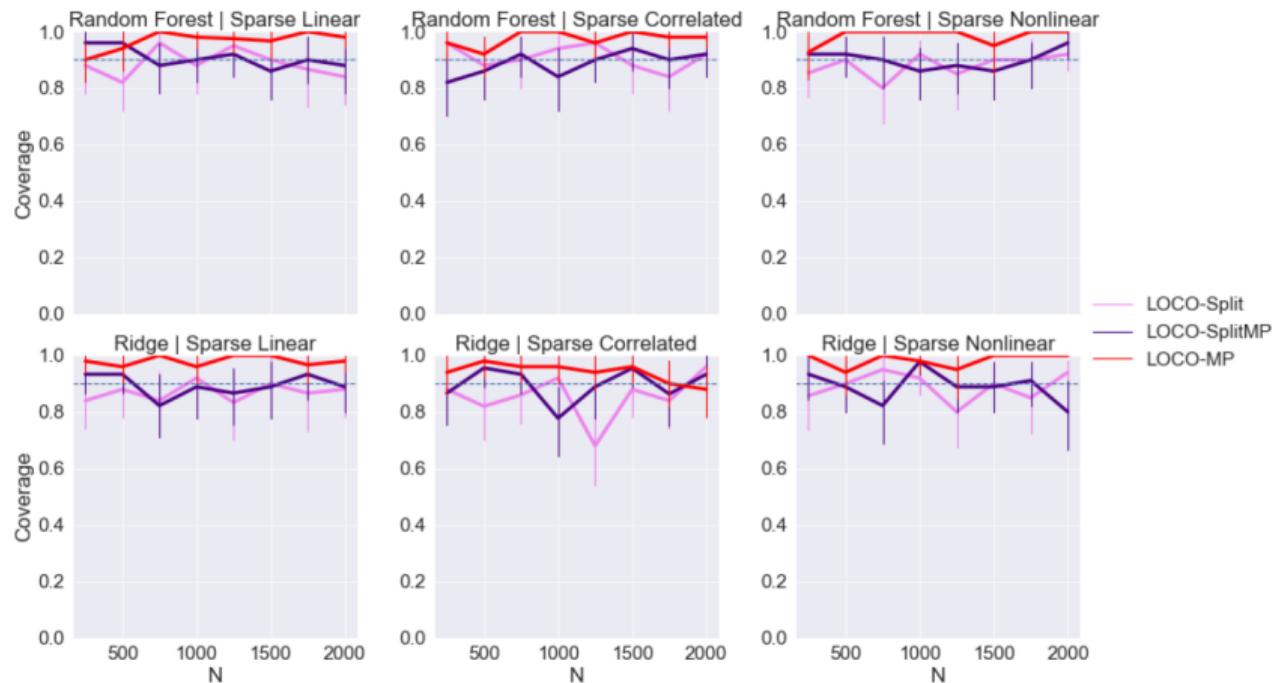
---

Simulation Set-up:

- $M = 200$ , varying  $N$ , 10 signal features
- Sparse linear & nonlinear (logistic) regression; i.i.d. or correlated features
- LOCO-MP with  $m = \sqrt{M}$ ,  $n = \sqrt{N}$ ,  $K = 10,000$

# LOCO-MP Simulations: Comparative Results

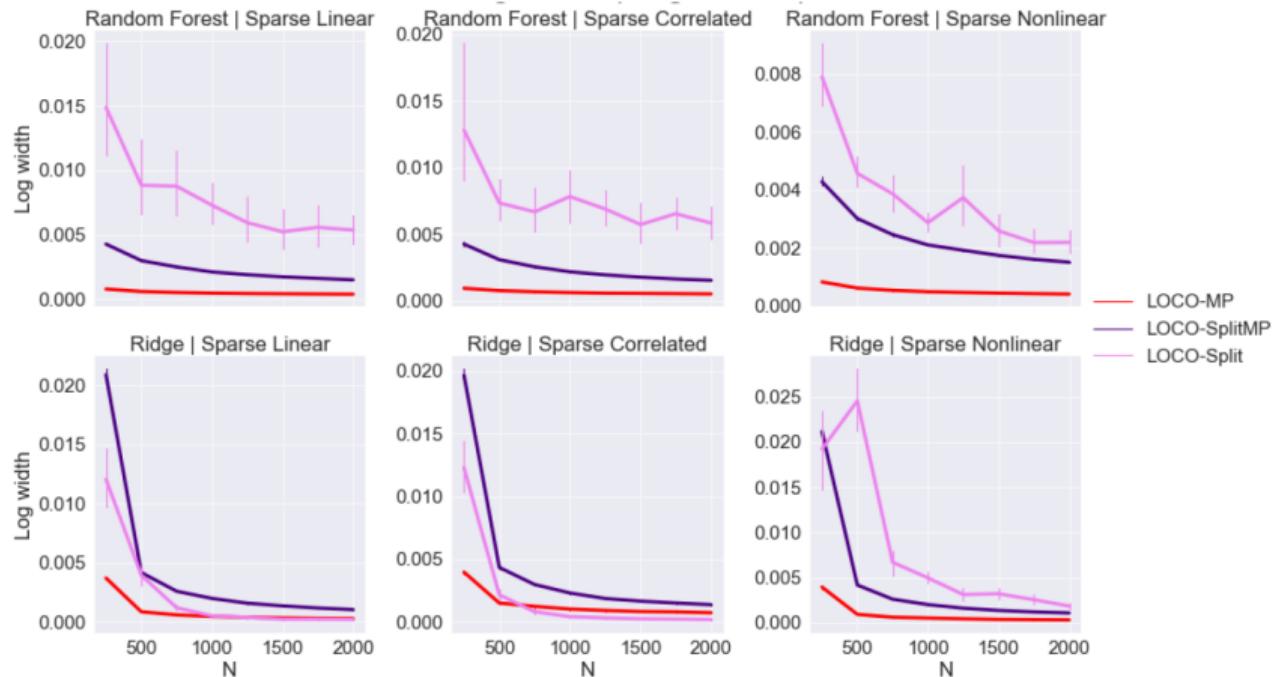
## Theory Validation: Coverage.



Coverage for regression simulations for a null feature.

# LOCO-MP Simulations: Comparative Results

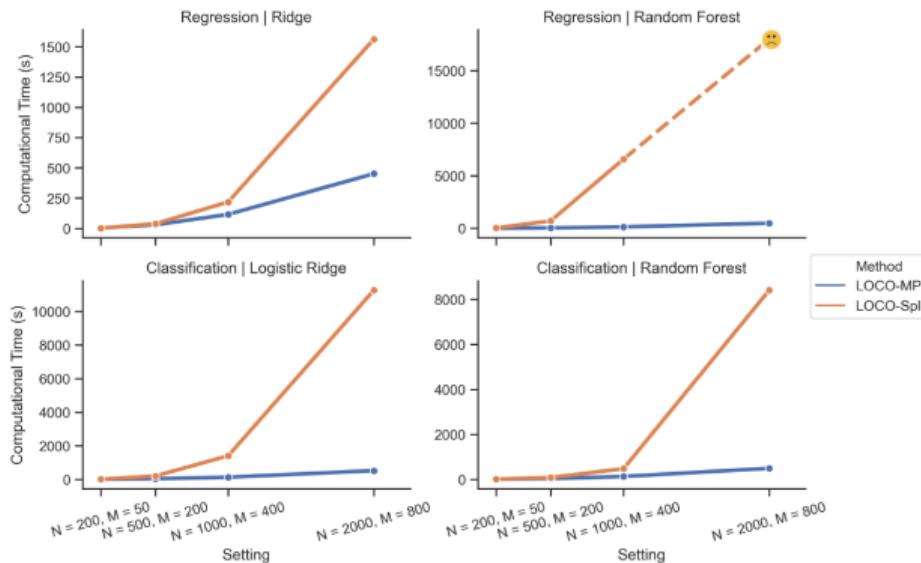
Interval Width:



Log interval width for regression simulations for a null feature.

# LOCO-MP Simulations: Comparative Results

## Computational Time:



Computational time for inference on all features in sparse linear regression and classification simulations.

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