

Data thinning to overcome double dipping

Anna Neufeld
Final Exam
May 9, 2023

What is double dipping?

Classical statistical methods assume that we only ever test pre-specified hypotheses about pre-specified models.

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In reality, we explore our data, fit several models, evaluate these models, select our favorite model, then test hypotheses about this model.

Double Dipping: Using the same data for two tasks, such as:

1. Generating and testing a null hypothesis.
2. Fitting and evaluating a model.

Approach 1: develop specialized procedures that account for double dipping

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Project 1

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Tree-Values: Selective Inference for Regression Trees

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R package and tutorials: <https://anna-neufeld.github.io/treevalues/>

Approach 2: avoid double dipping entirely via sample splitting

	Feature 1	Feature 2
Obs. 1	12	6
Obs. 2	31	8
Obs. 3	11	31
Obs. 4	22	34

Approach 2: avoid double dipping entirely via sample splitting

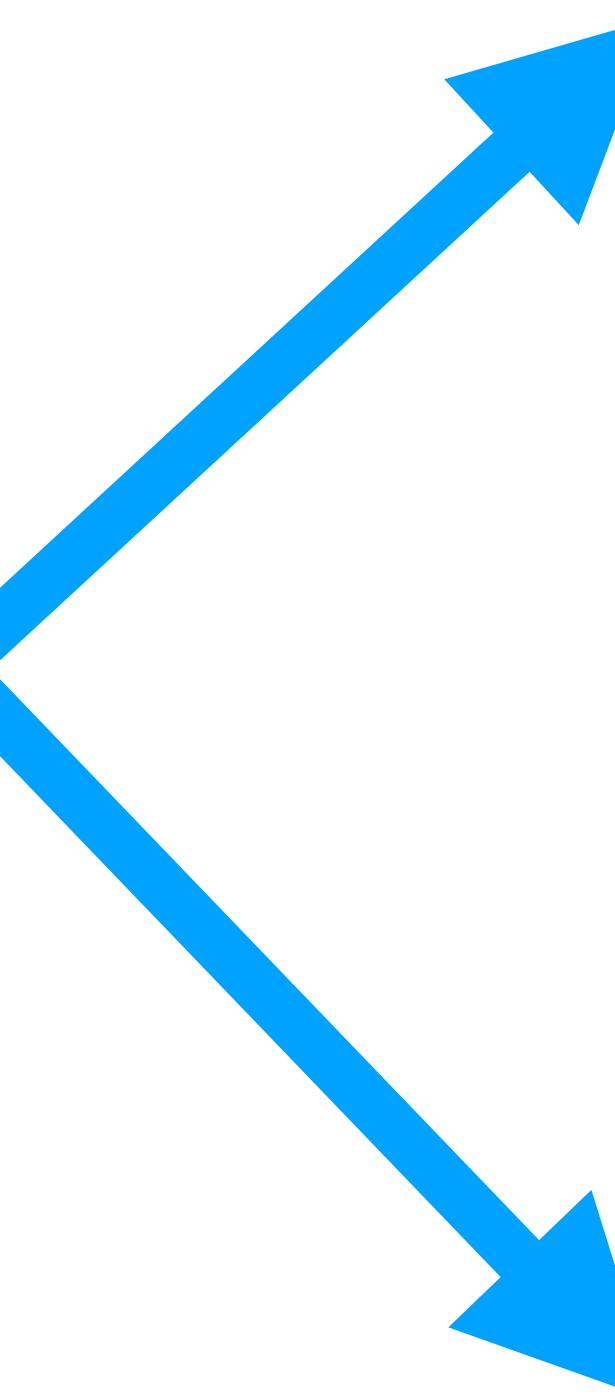
	Feature 1	Feature 2
Obs. 1	12	6
Obs. 2	31	8
Obs. 3	11	31
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Train

	Feature 1	Feature 2
Obs. 1	12	6
Obs. 2	31	8

Test

	Feature 1	Feature 2
Obs. 3	11	31
Obs. 4	22	34



Approach 2: avoid double dipping entirely via sample splitting

	Feature 1	Feature 2
Obs. 1	12	6
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Train

	Feature 1	Feature 2
Obs. 1	12	6
Obs. 2	31	8

Select hypothesis.

Test

	Feature 1	Feature 2
Obs. 3	11	31
Obs. 4	22	34

Approach 2: avoid double dipping entirely via sample splitting

	Feature 1	Feature 2
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Train

	Feature 1	Feature 2
Obs. 1	12	6
Obs. 2	31	8

Select hypothesis.

Test

	Feature 1	Feature 2
Obs. 3	11	31
Obs. 4	22	34

Test hypothesis.

Approach 2: avoid double dipping entirely via sample splitting

	Feature 1	Feature 2
Obs. 1	12	6
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Train

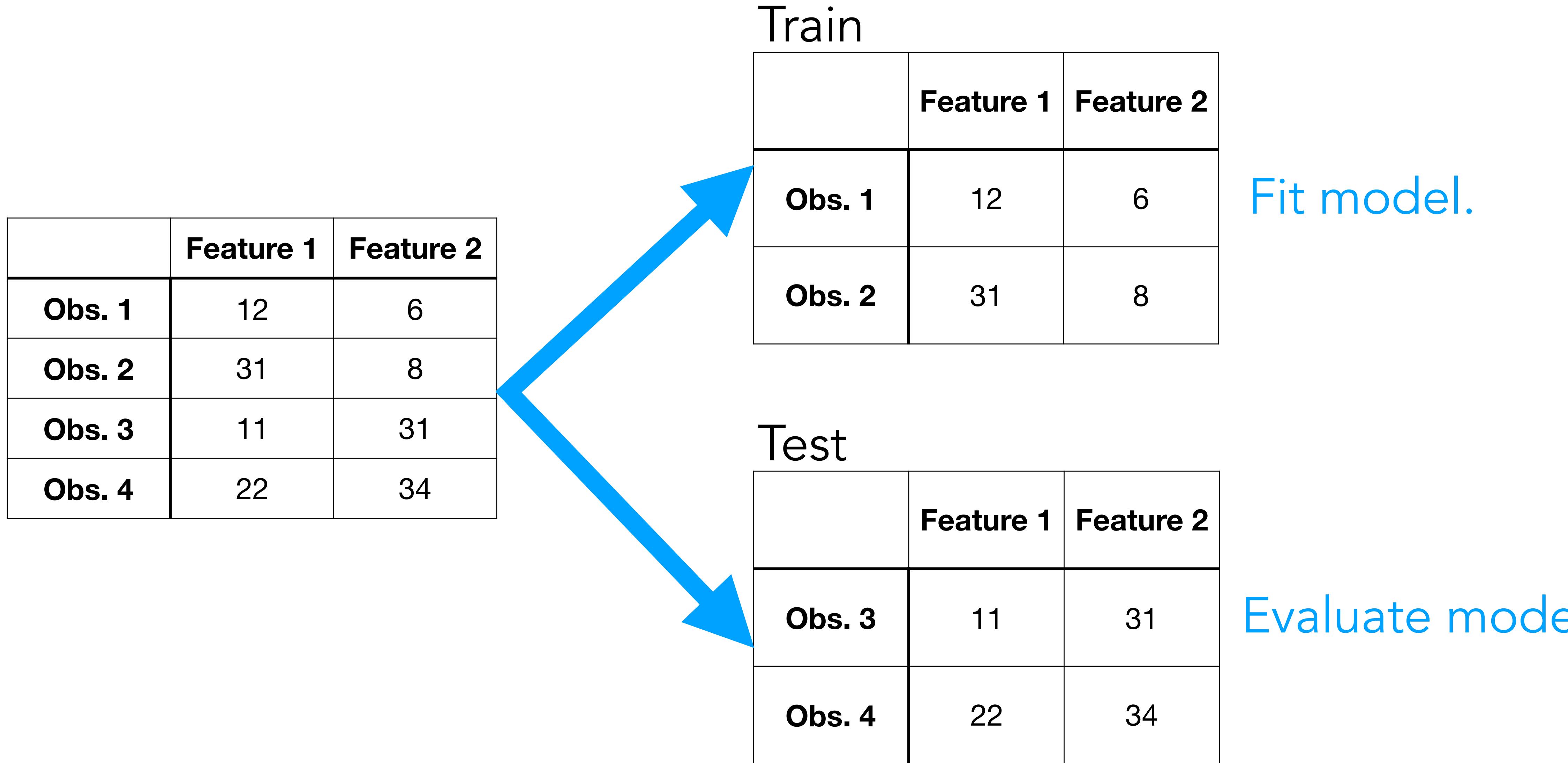
	Feature 1	Feature 2
Obs. 1	12	6
Obs. 2	31	8

Fit model.

Test

	Feature 1	Feature 2
Obs. 3	11	31
Obs. 4	22	34

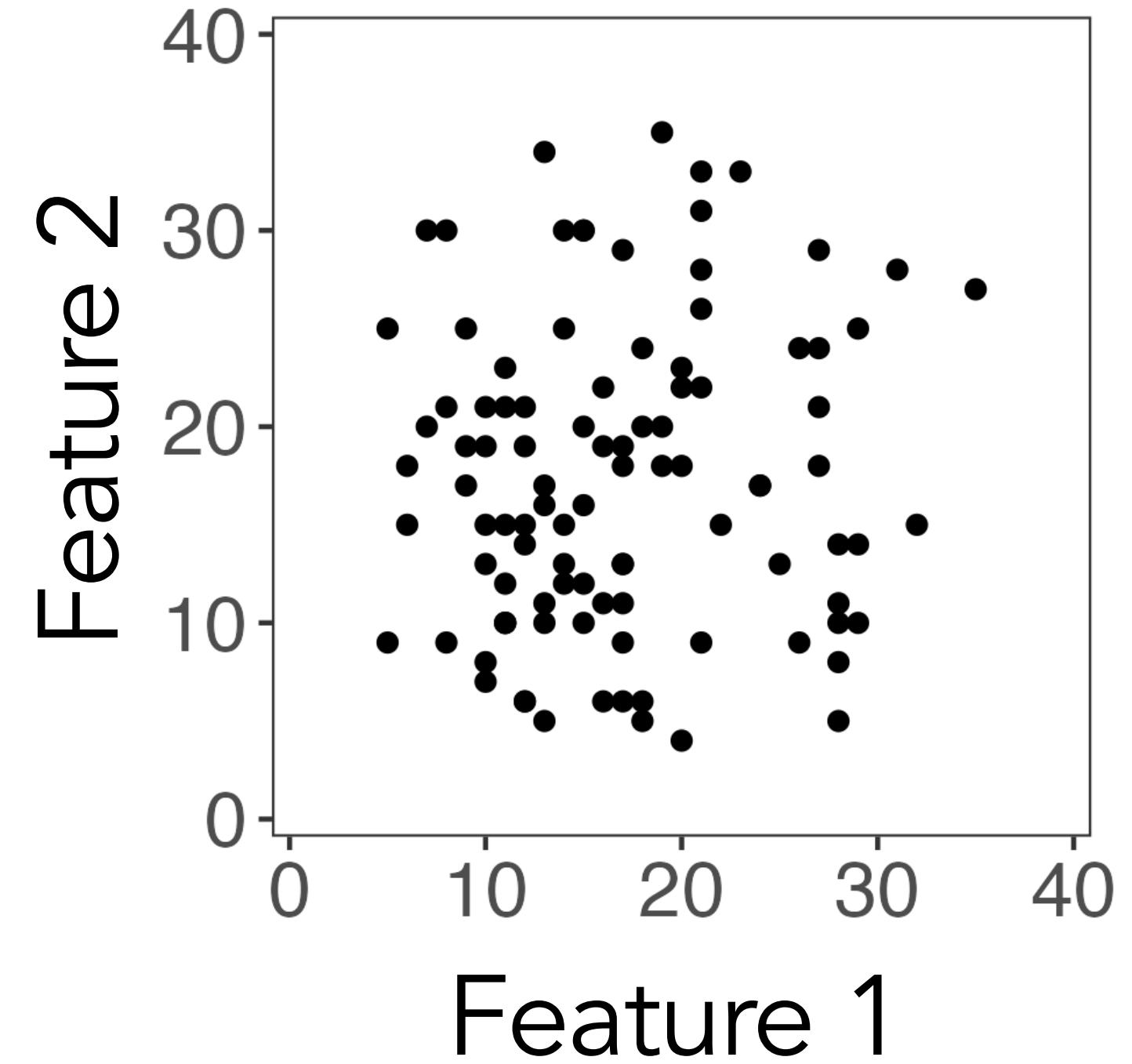
Approach 2: avoid double dipping entirely via sample splitting



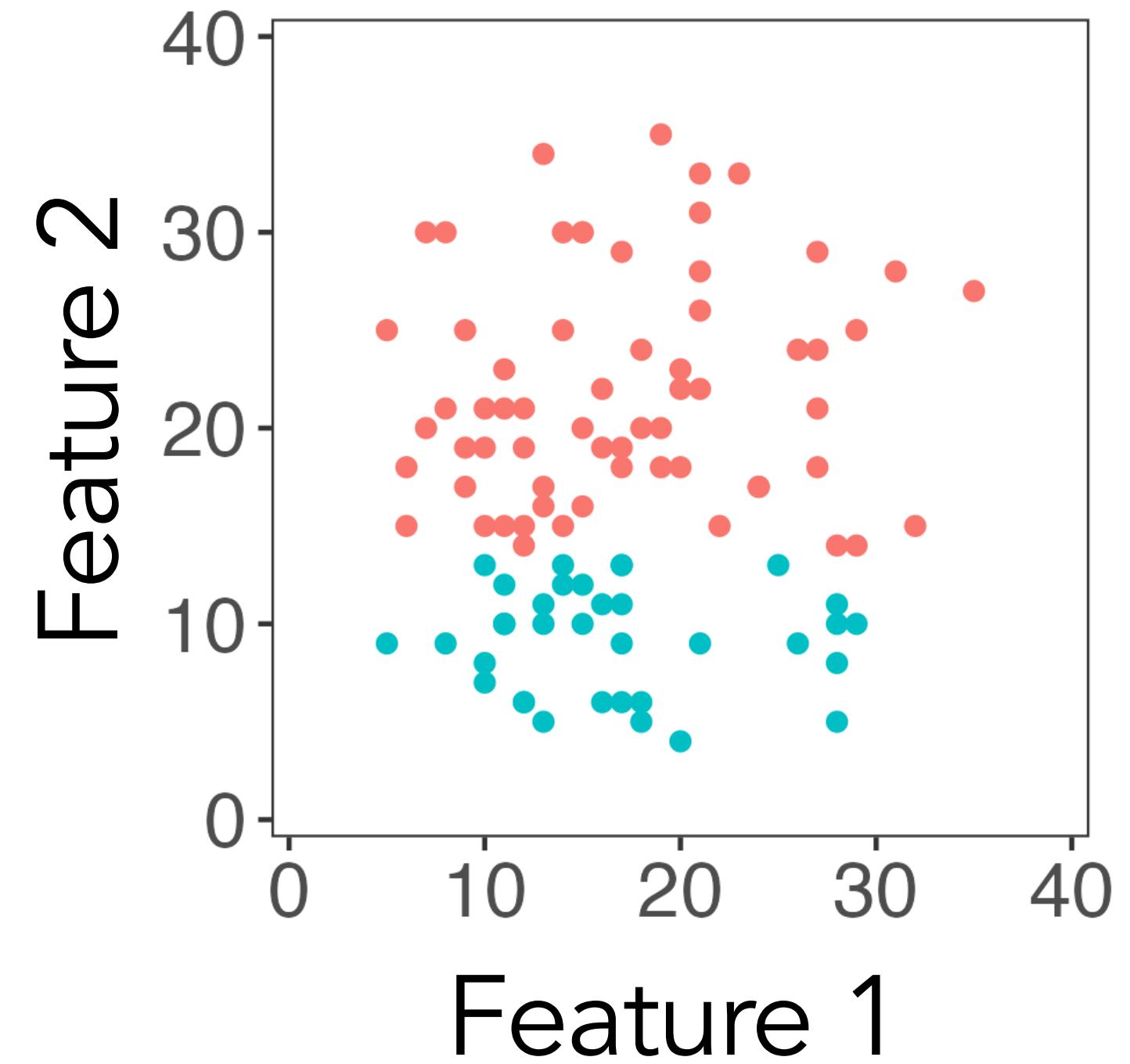
Outline

- 1. Motivation: settings where sample splitting doesn't work**
2. Poisson thinning
3. Data thinning
4. Application to single-cell RNA sequencing data
5. Ongoing work

Example 1: using the same data to generate and test a hypothesis

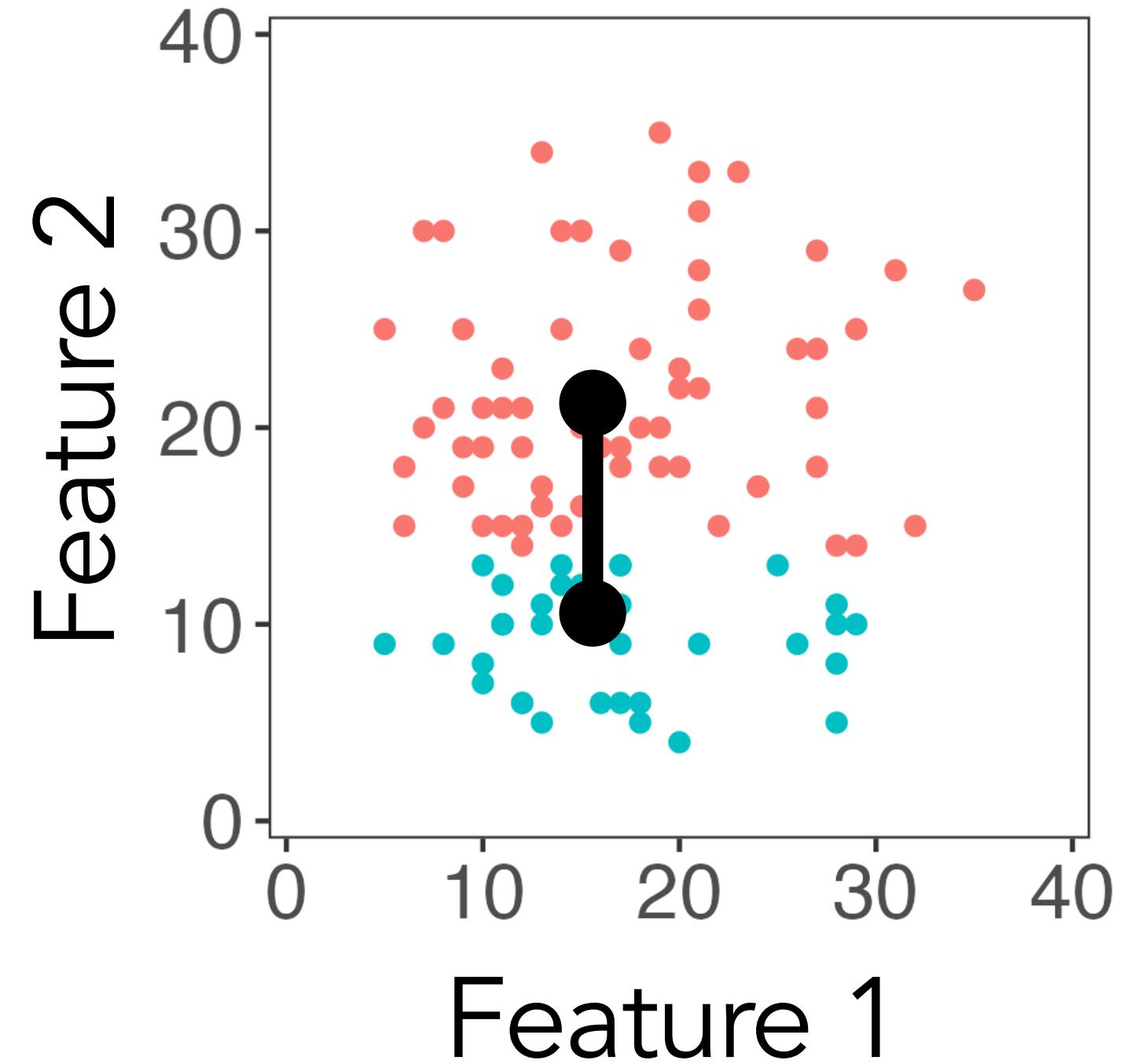


Example 1: using the same data to generate and test a hypothesis



Step 1: cluster the observations.

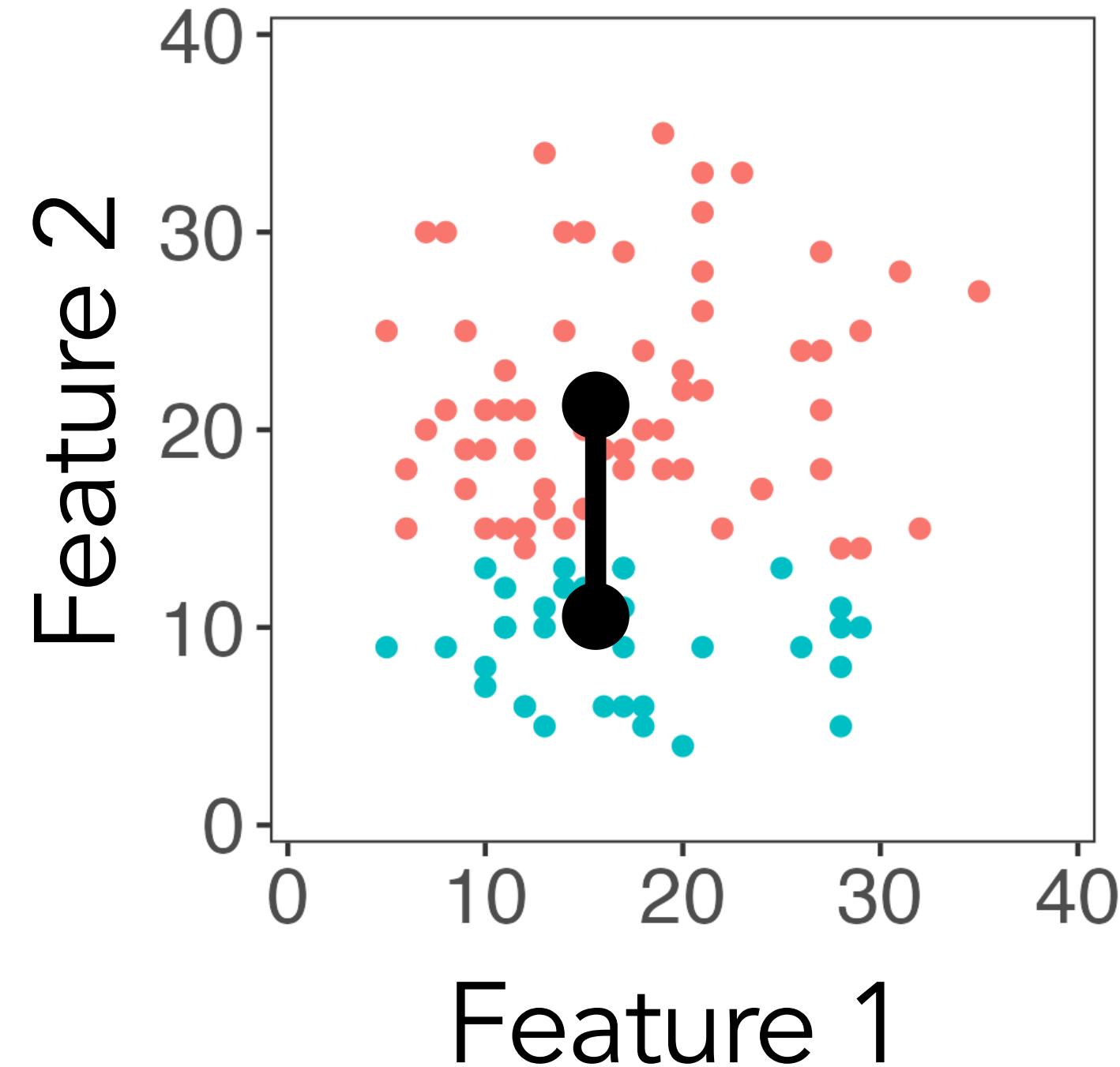
Example 1: using the same data to generate and test a hypothesis



Step 1: cluster the observations.

Generate H_0 : "the expected value of Feature 2 is the same between red observations and the blue observations."

Example 1: using the same data to generate and test a hypothesis



Step 1: cluster the observations.

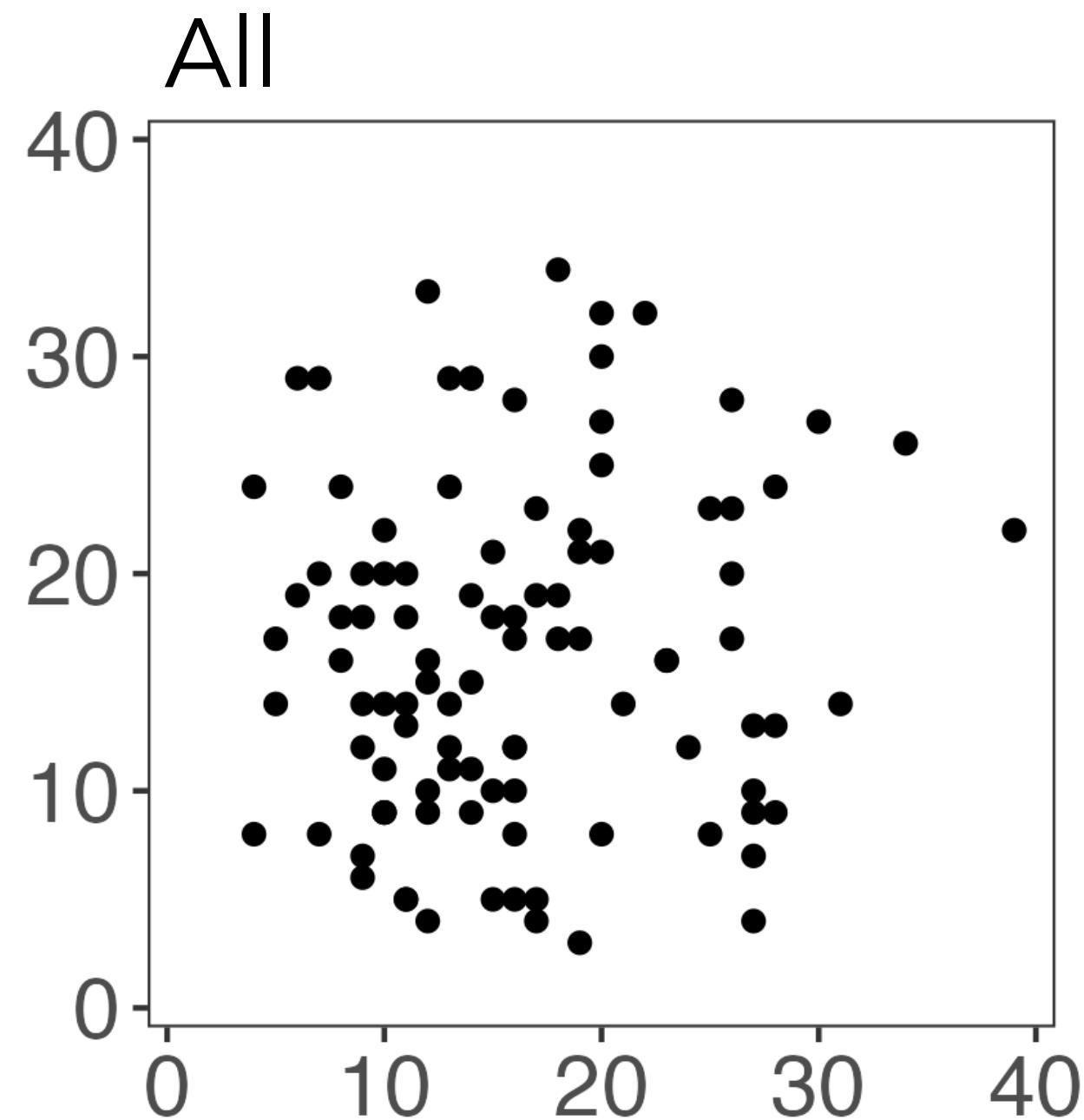
Generate H_0 : "the expected value of Feature 2 is the same between red observations and the blue observations."

$$p < 10^{-10}$$

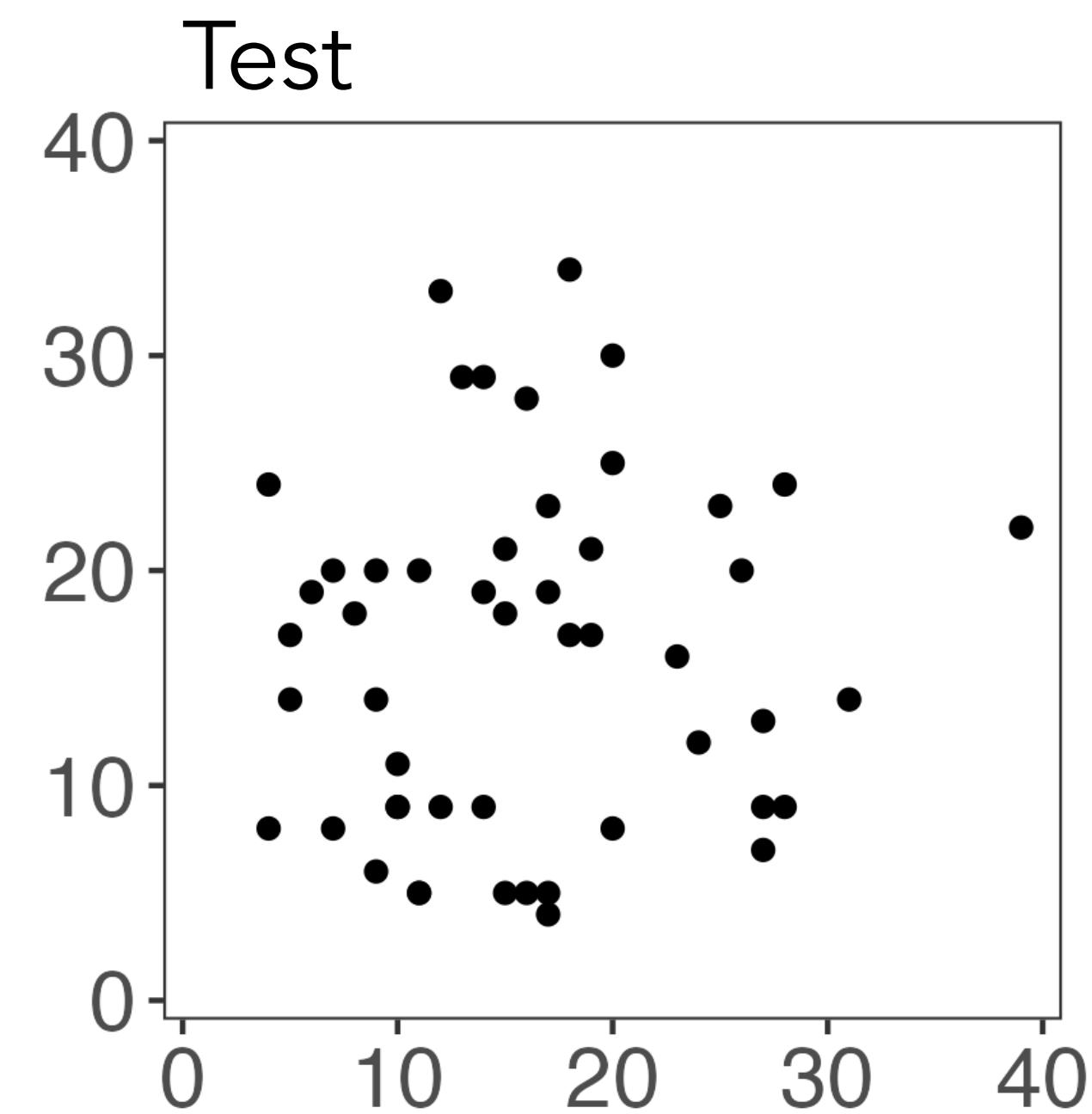
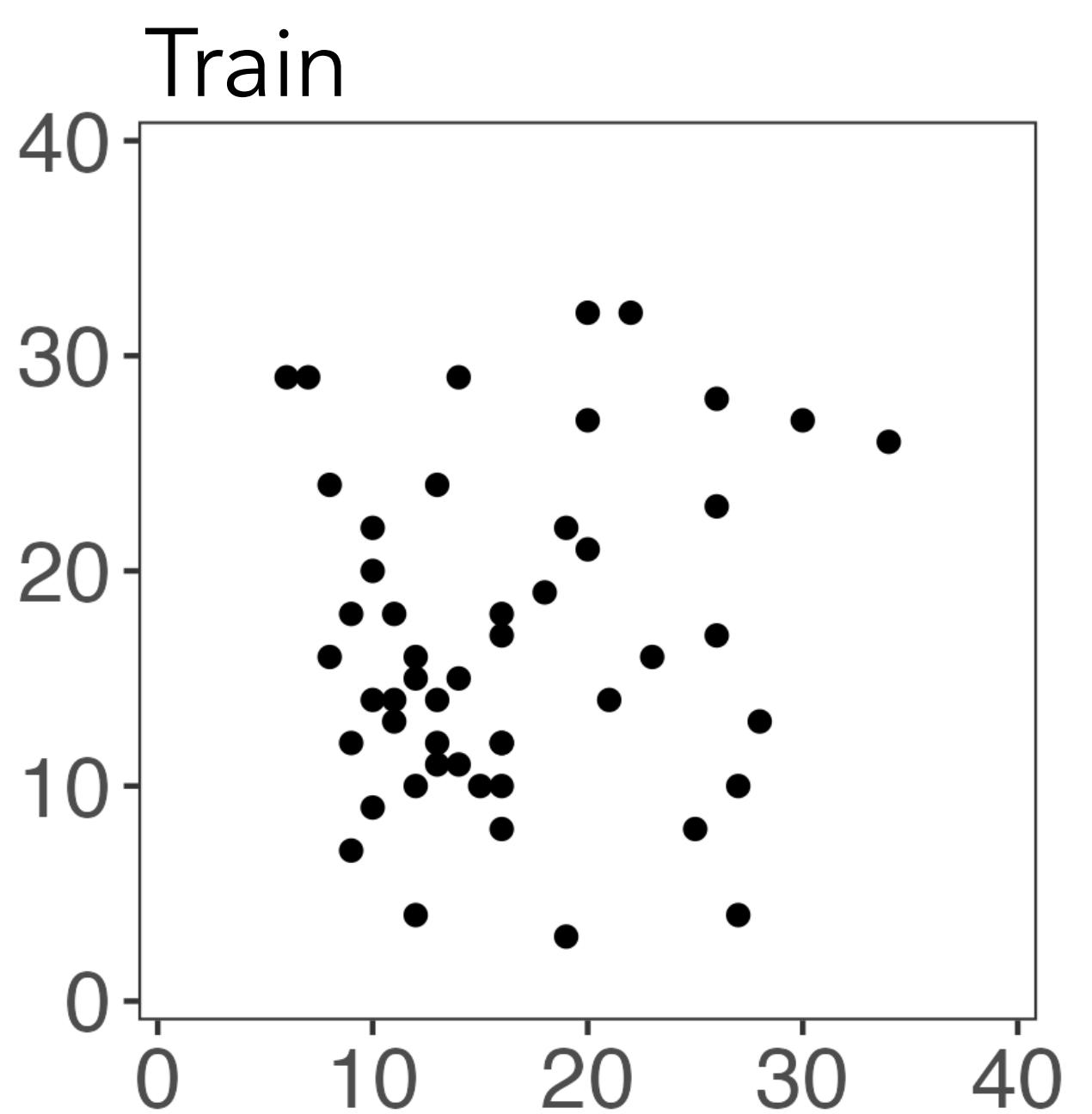
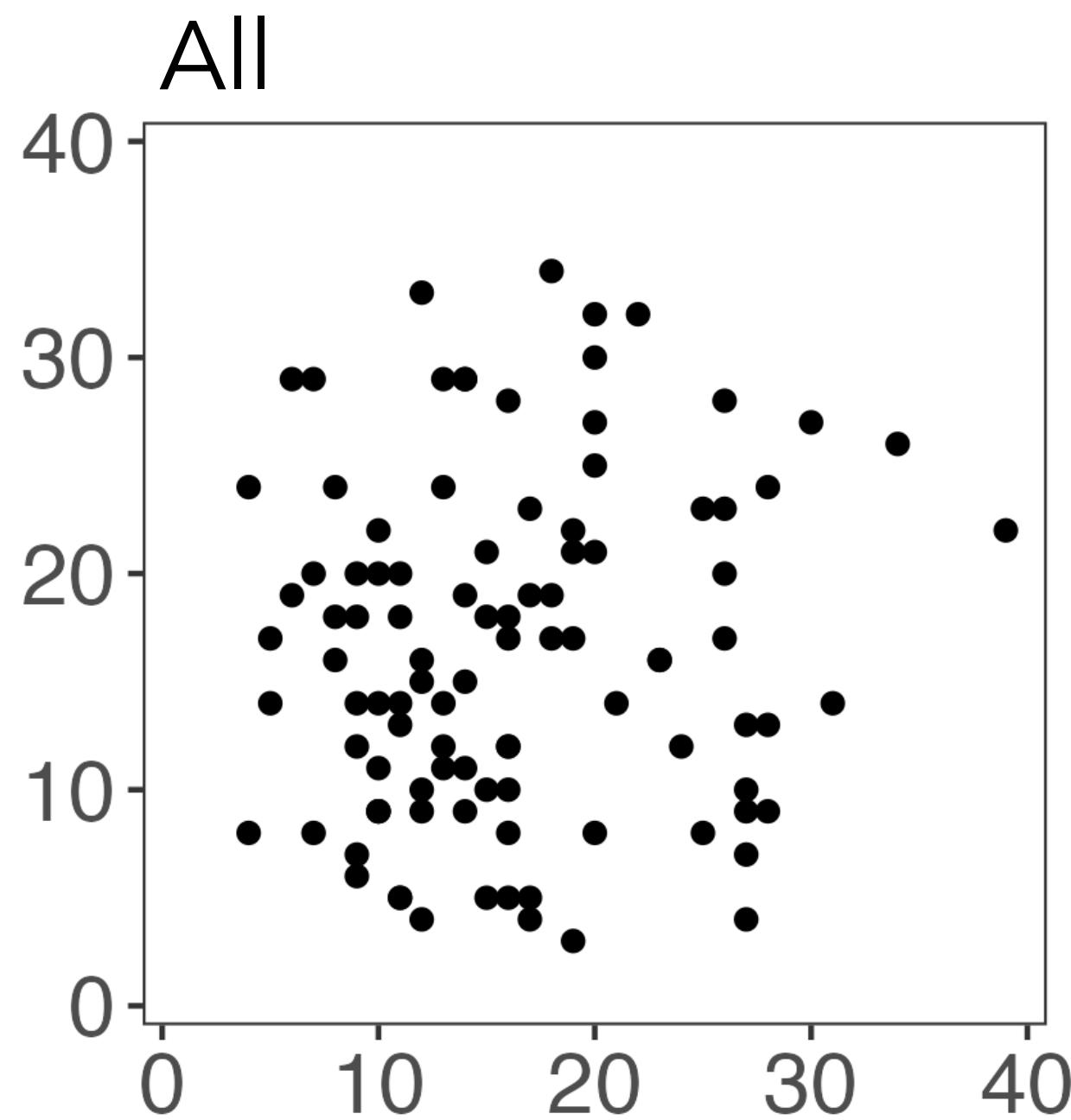


Step 2: test H_0 with a t-test.

Sample splitting cannot be used for example 1

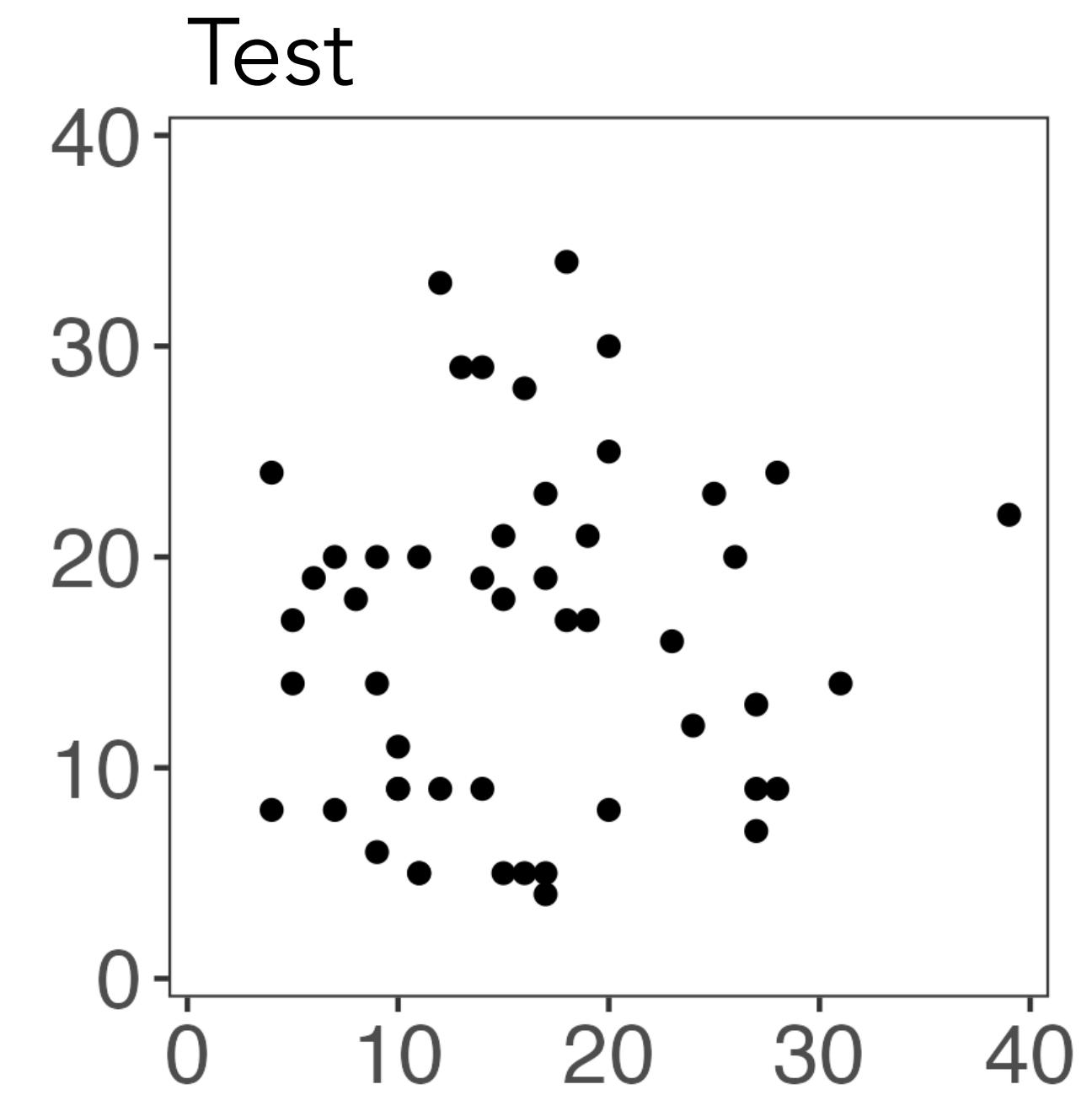
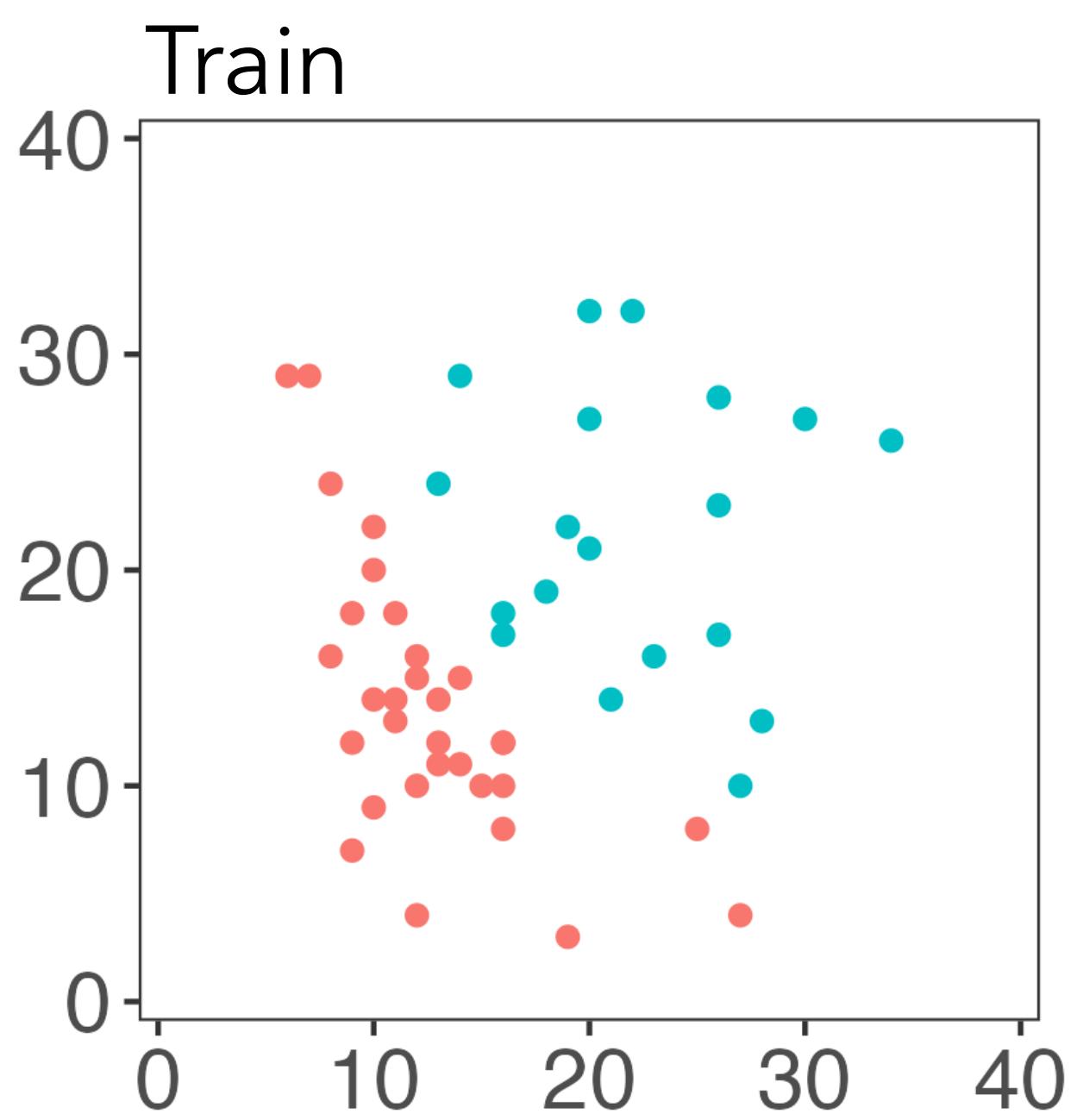
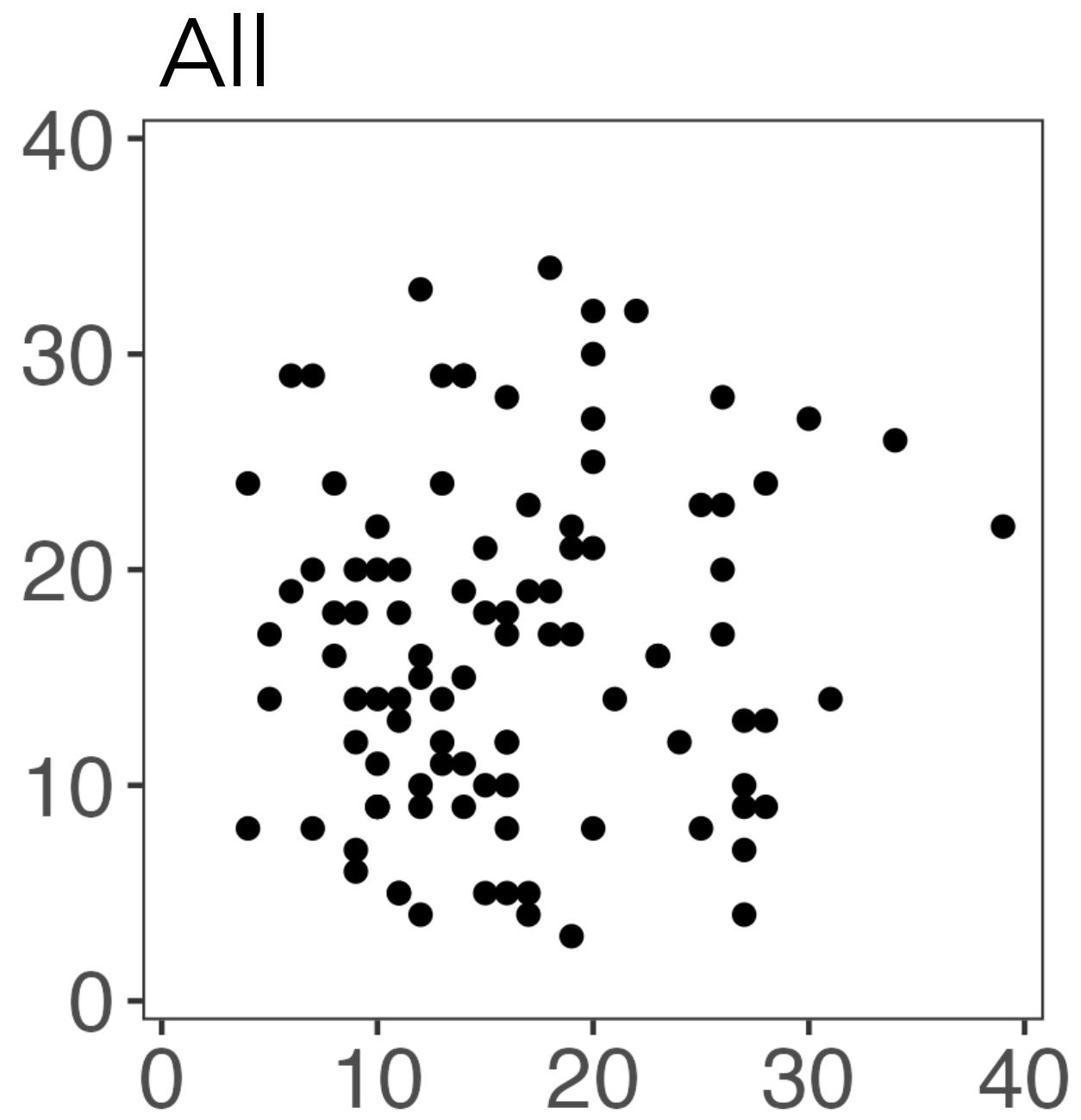


Sample splitting cannot be used for example 1



Step 1: split
observations into
train/test.

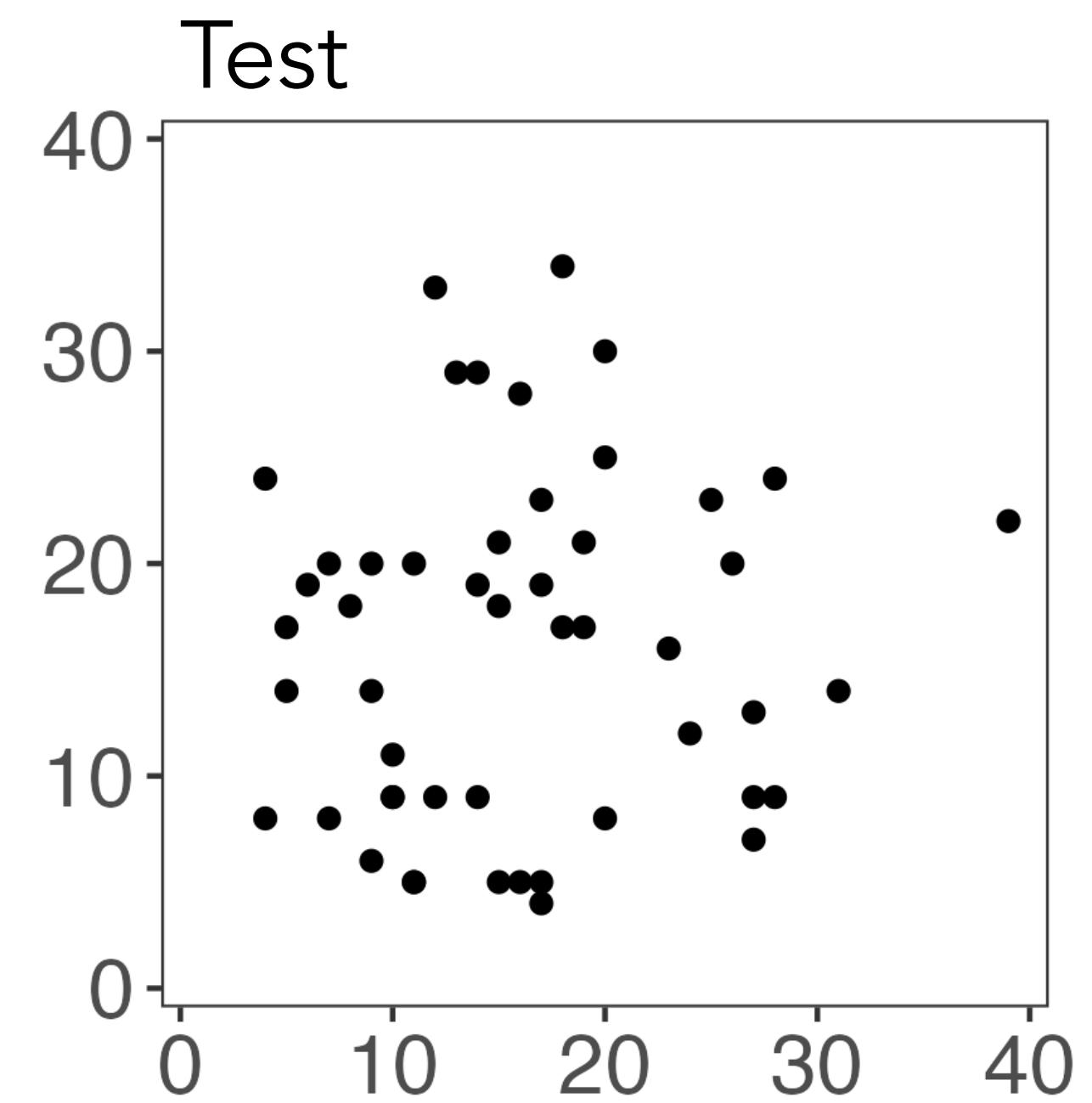
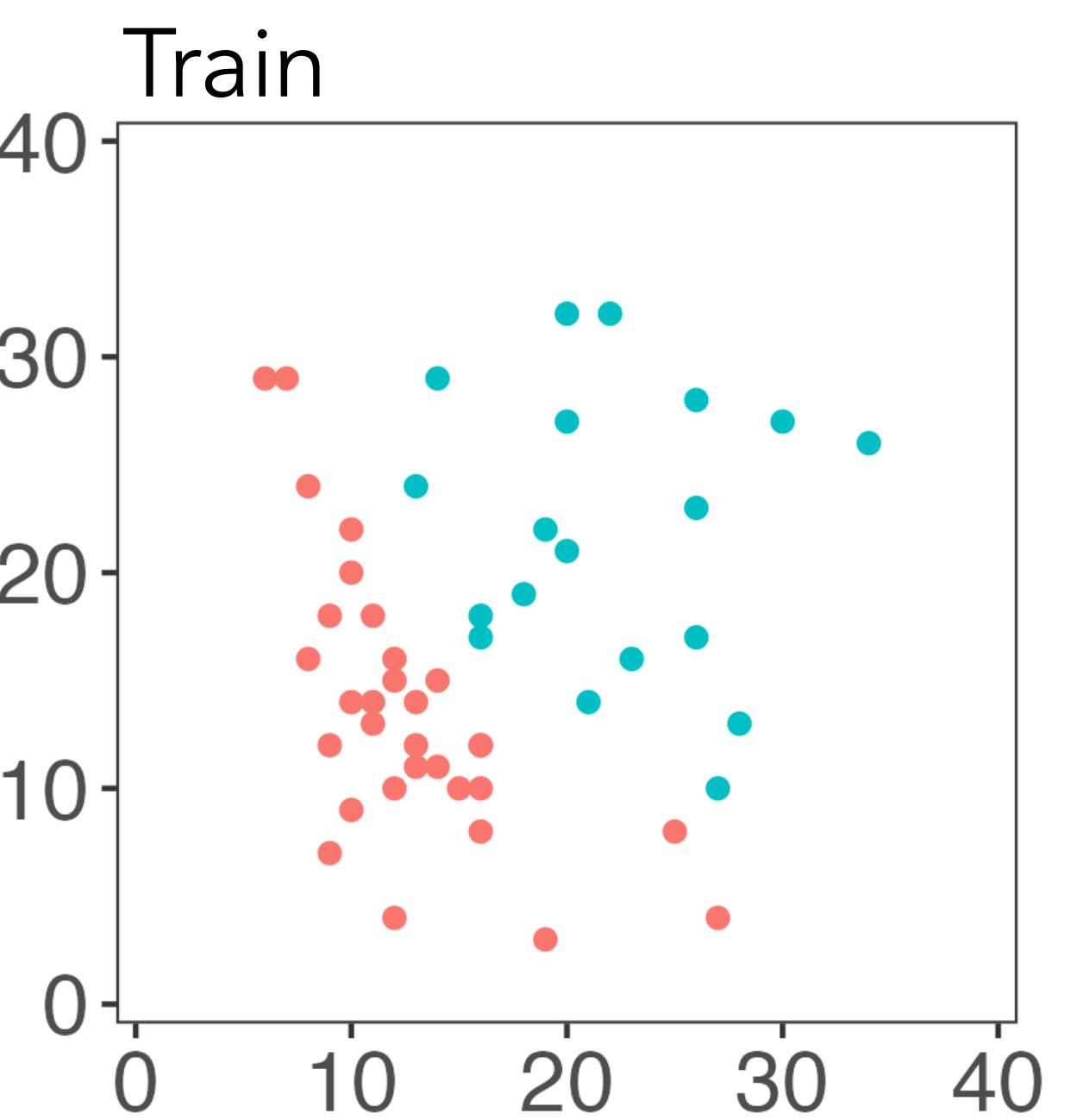
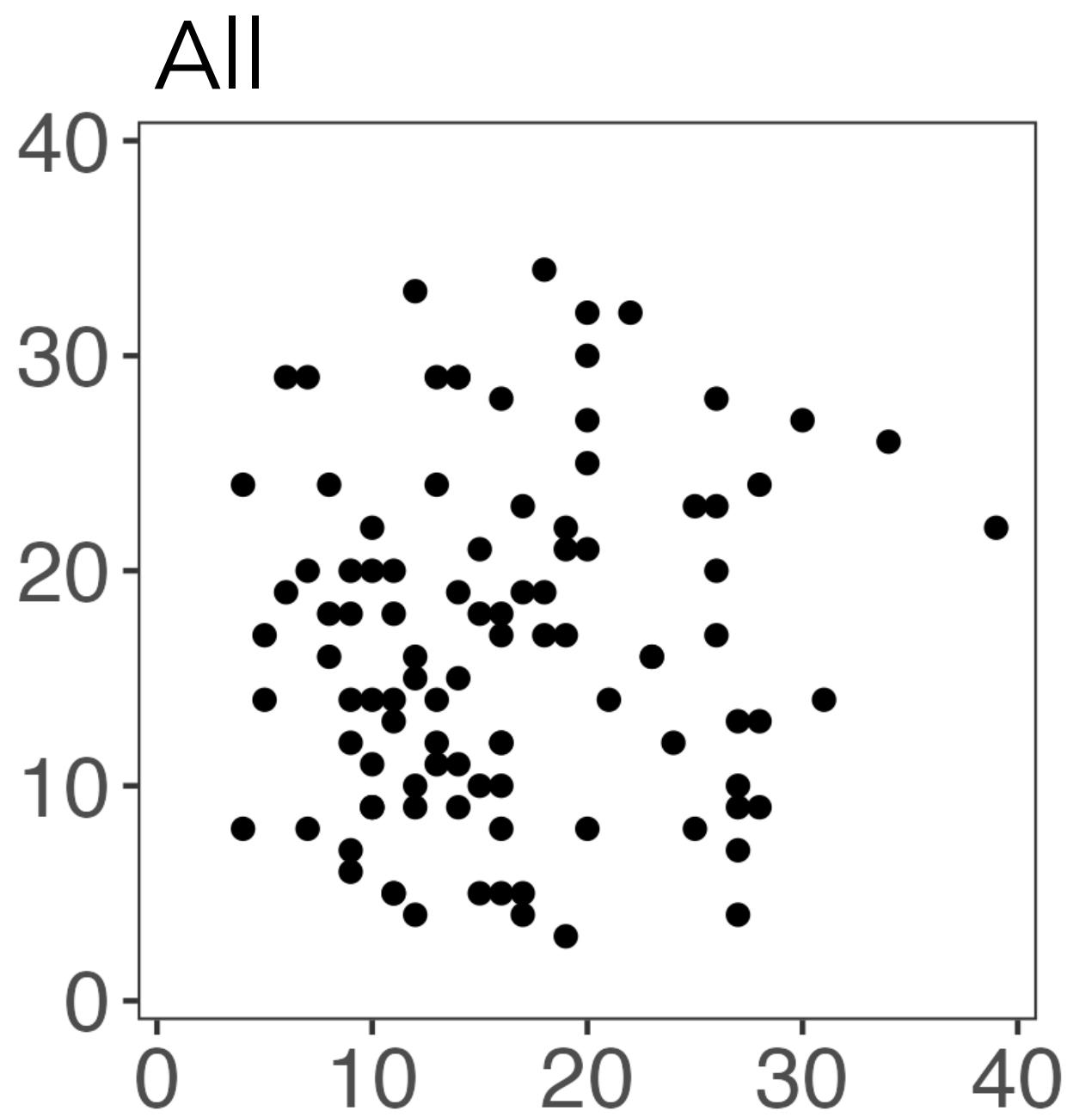
Sample splitting cannot be used for example 1



Step 1: split
observations into
train/test.

Step 2: cluster
the training set.

Sample splitting cannot be used for example 1

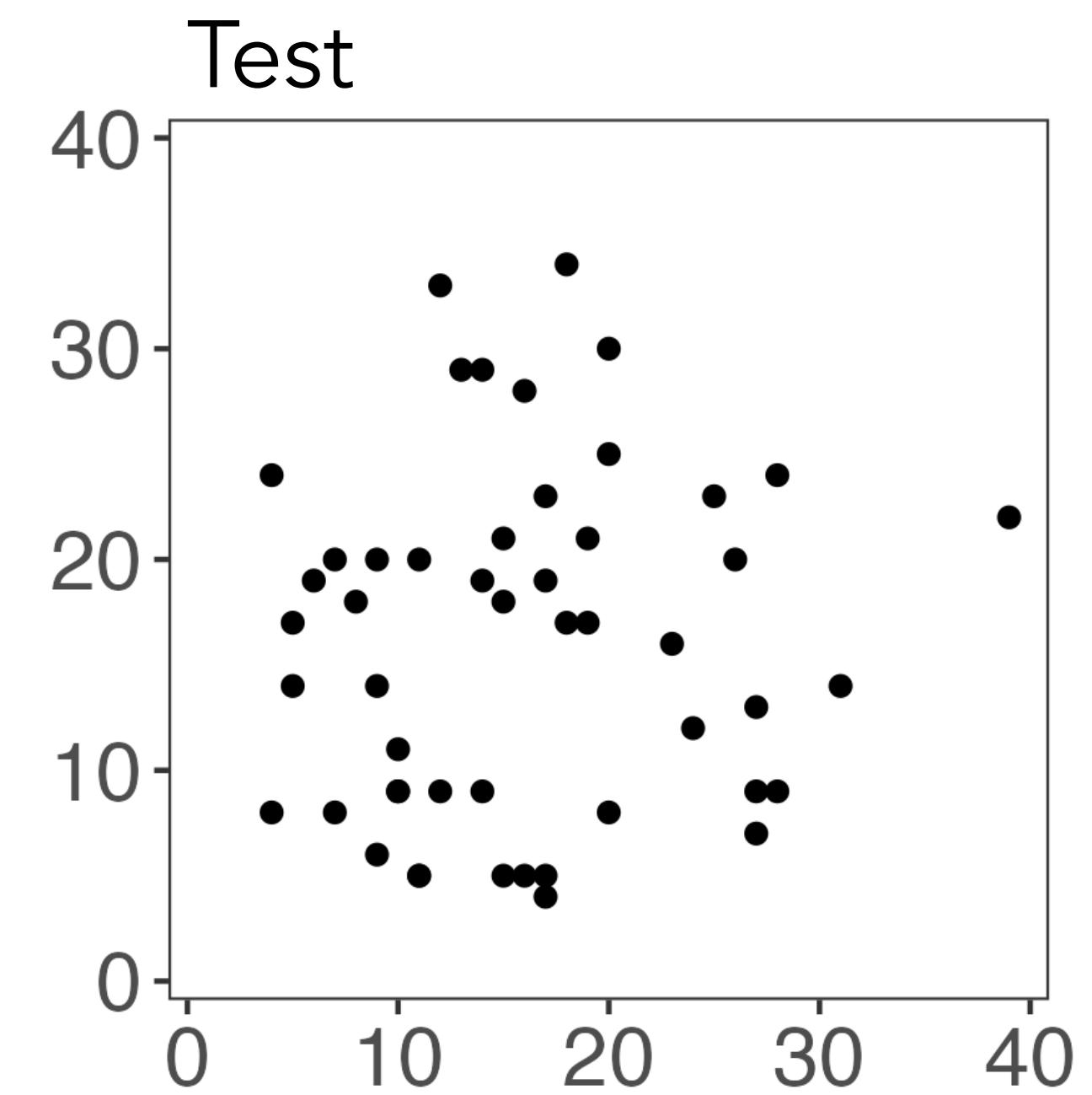
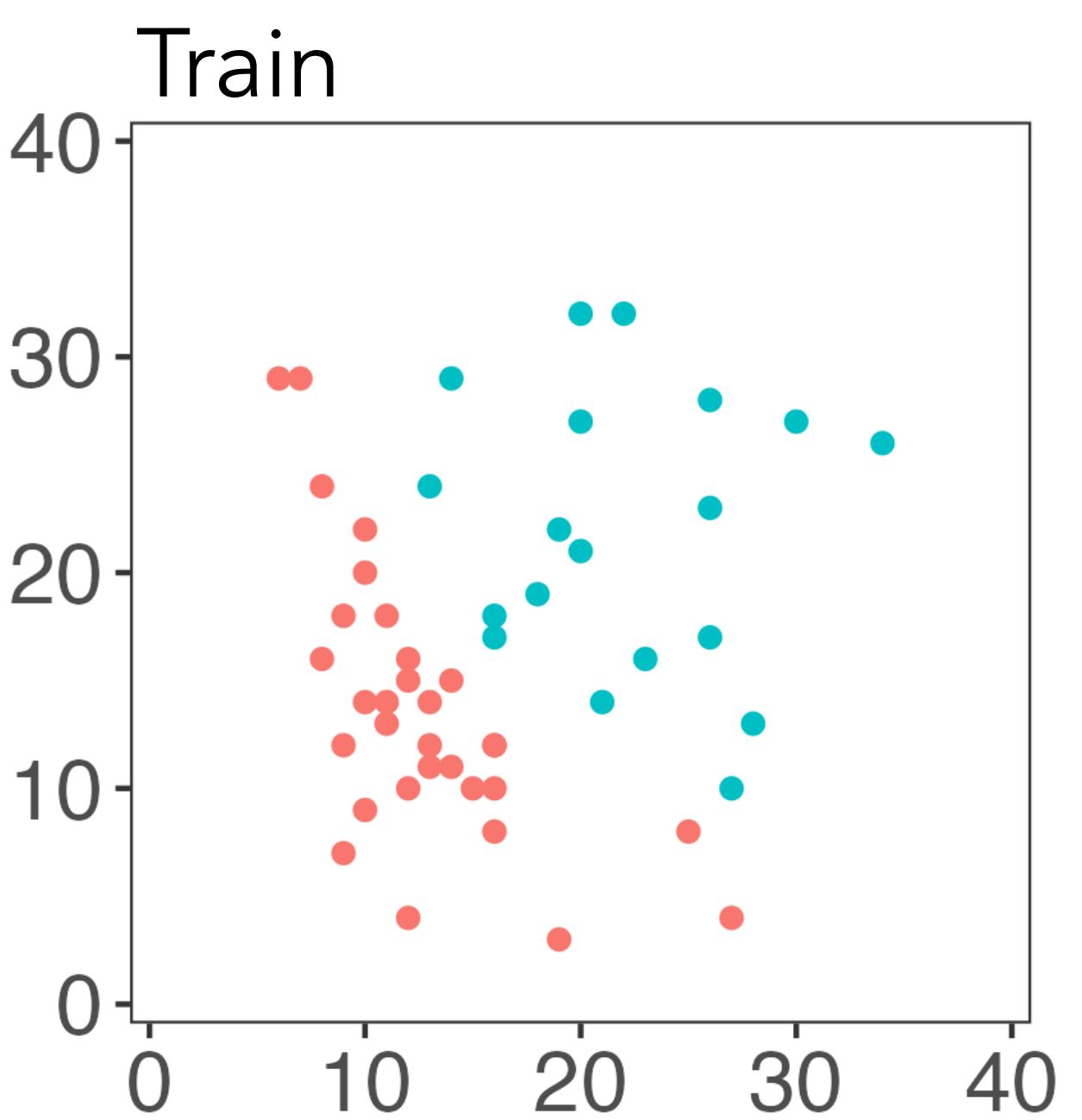
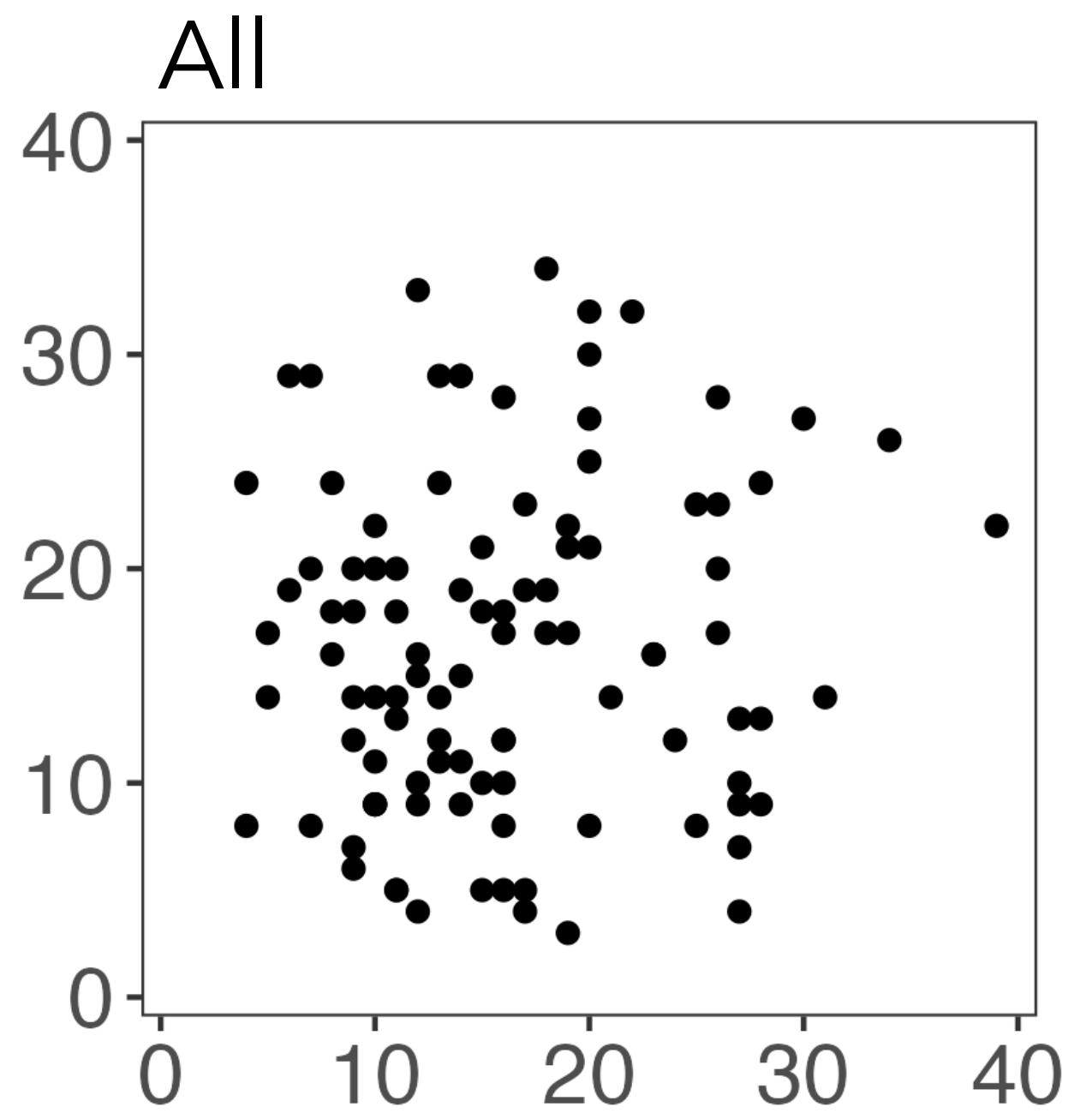


Step 1: split observations into train/test.

Step 2: cluster the training set.

Step 3: test for difference in means using test set.

Sample splitting cannot be used for example 1



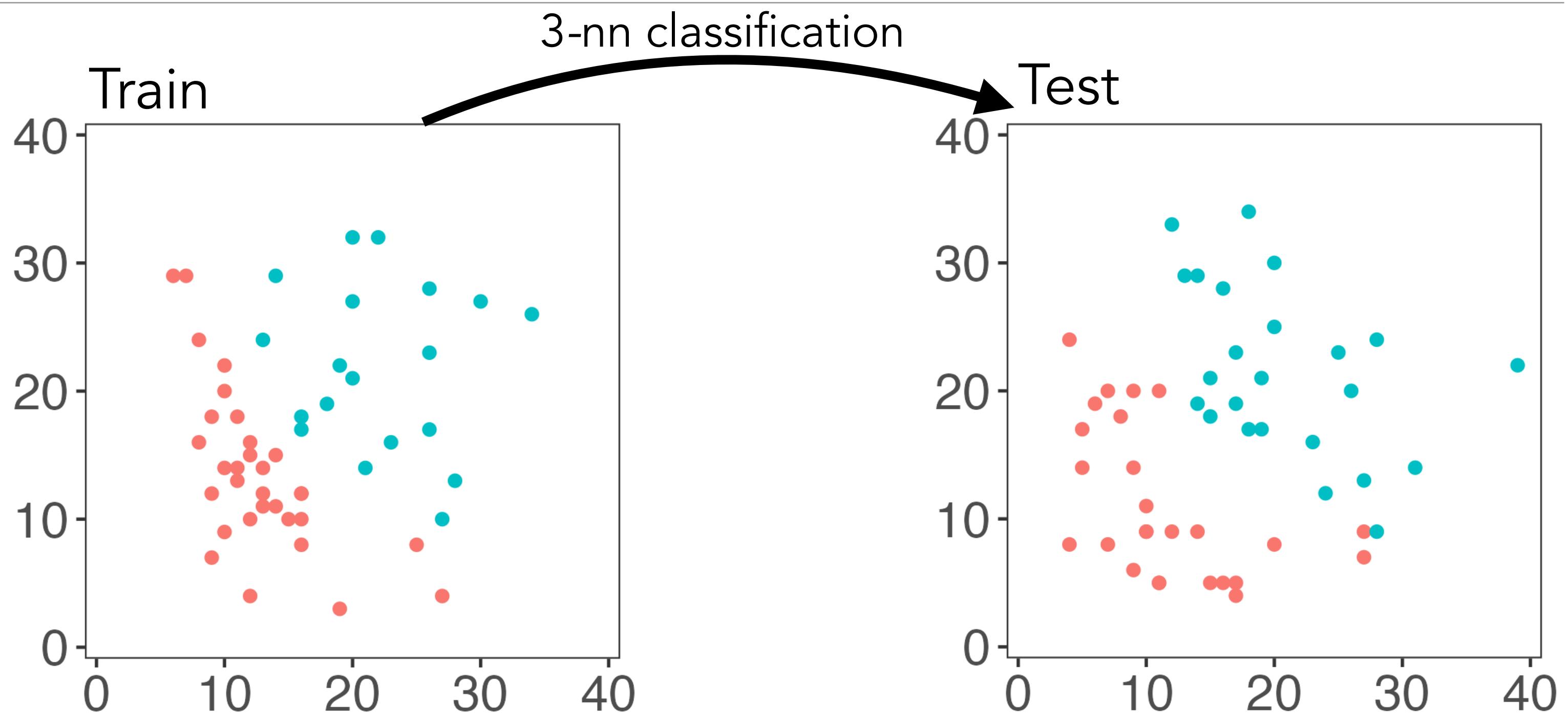
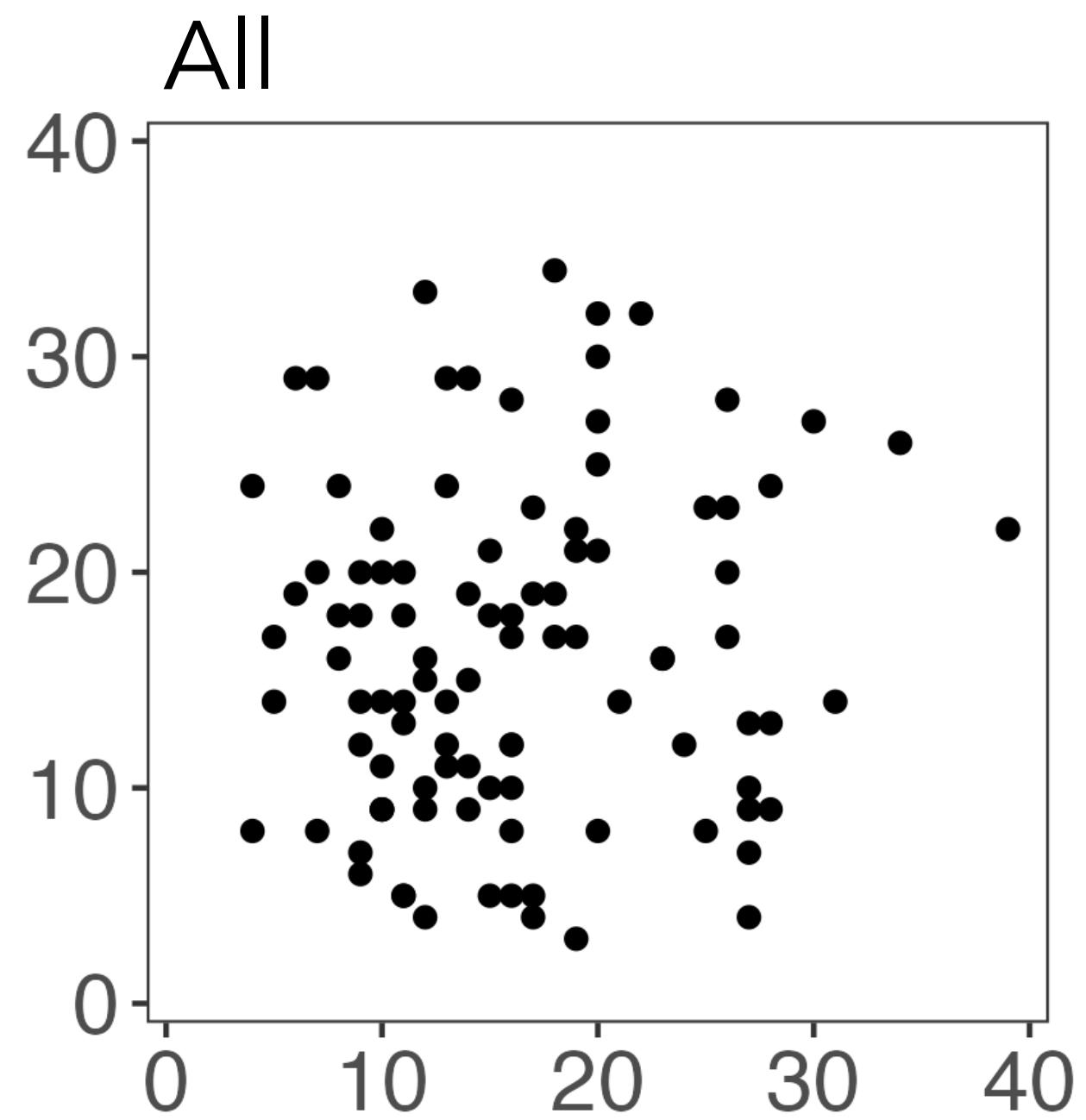
Step 1: split observations into train/test.

Step 2: cluster the training set.

Step 2.5: assign labels to observations in test set.

Step 3: test for difference in means using test set.

Sample splitting cannot be used for example 1



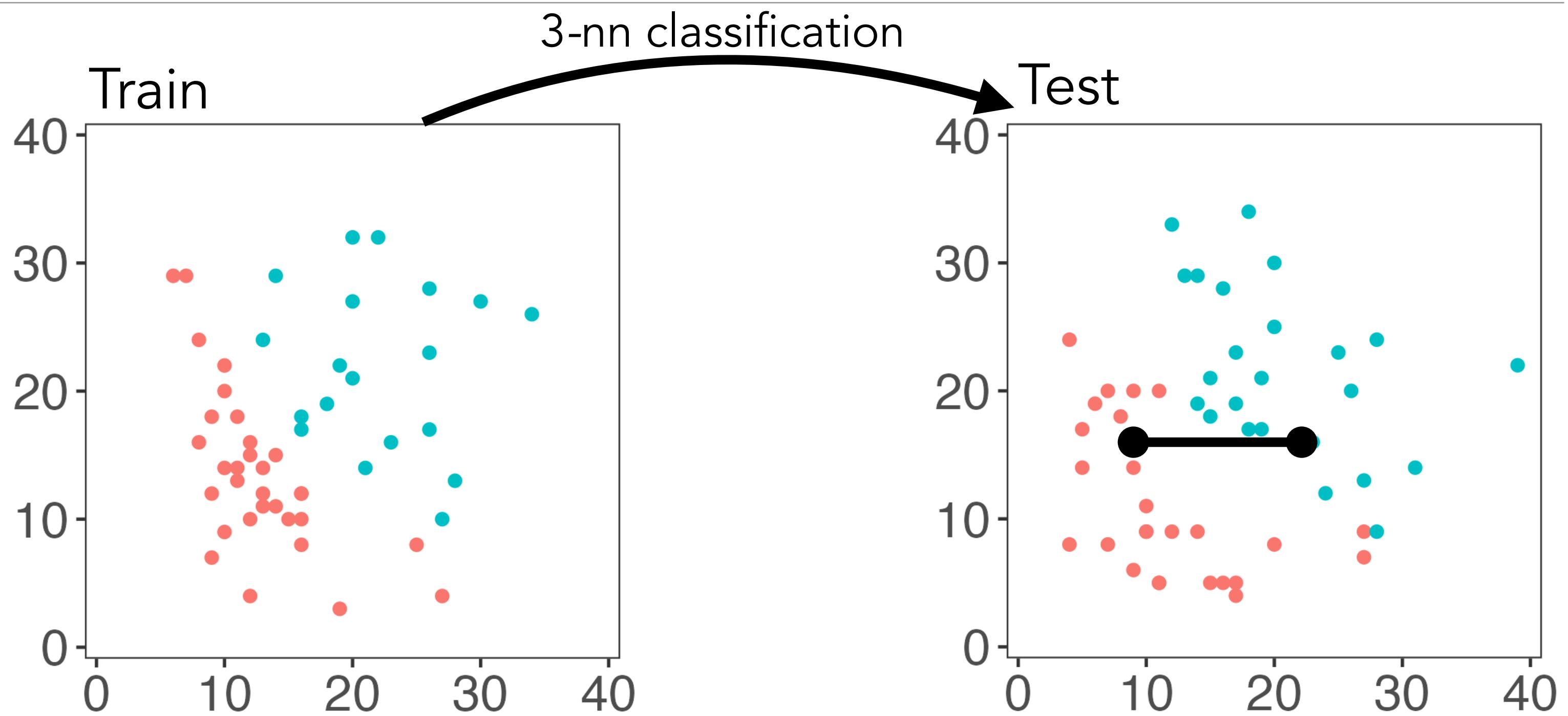
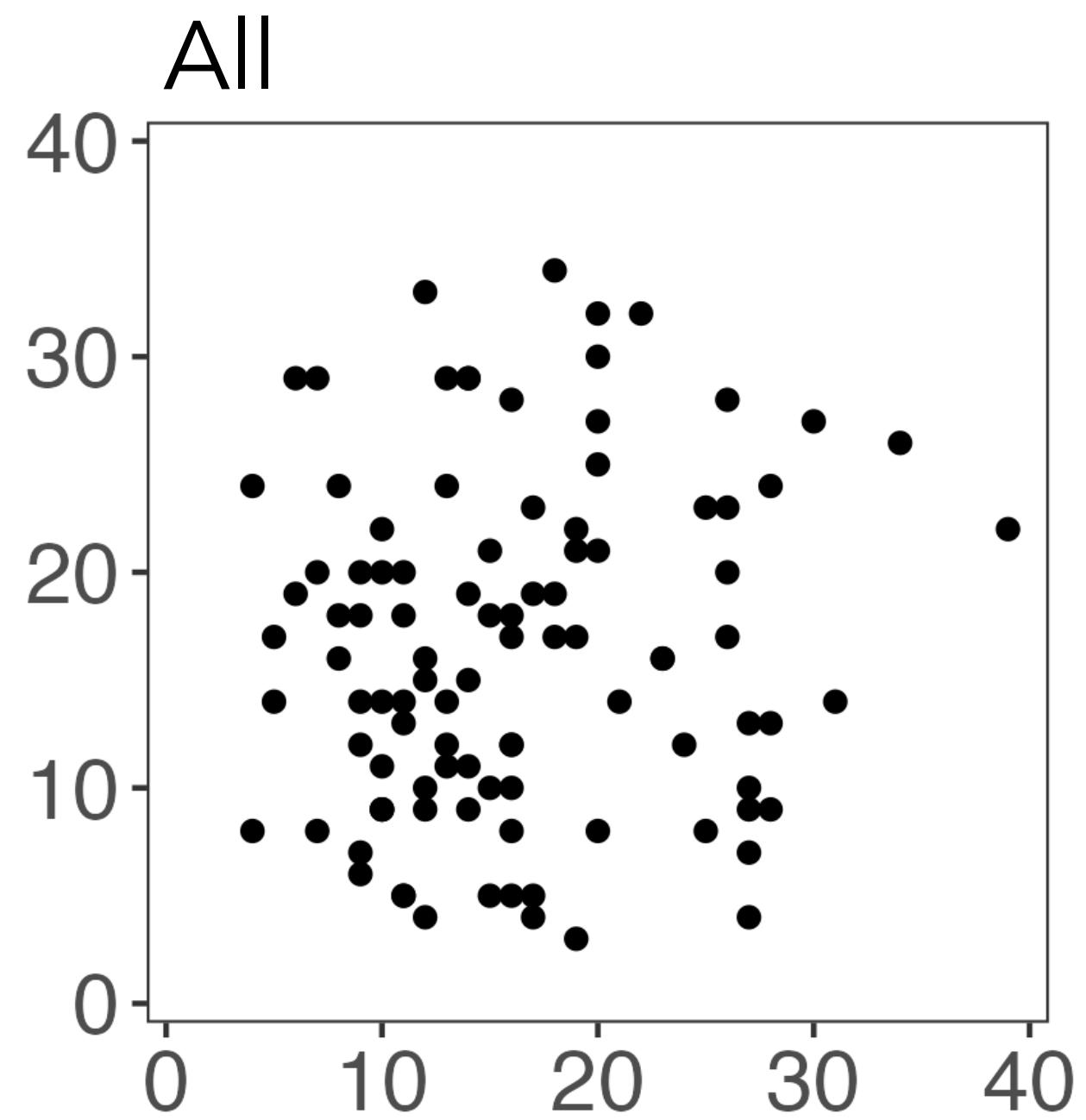
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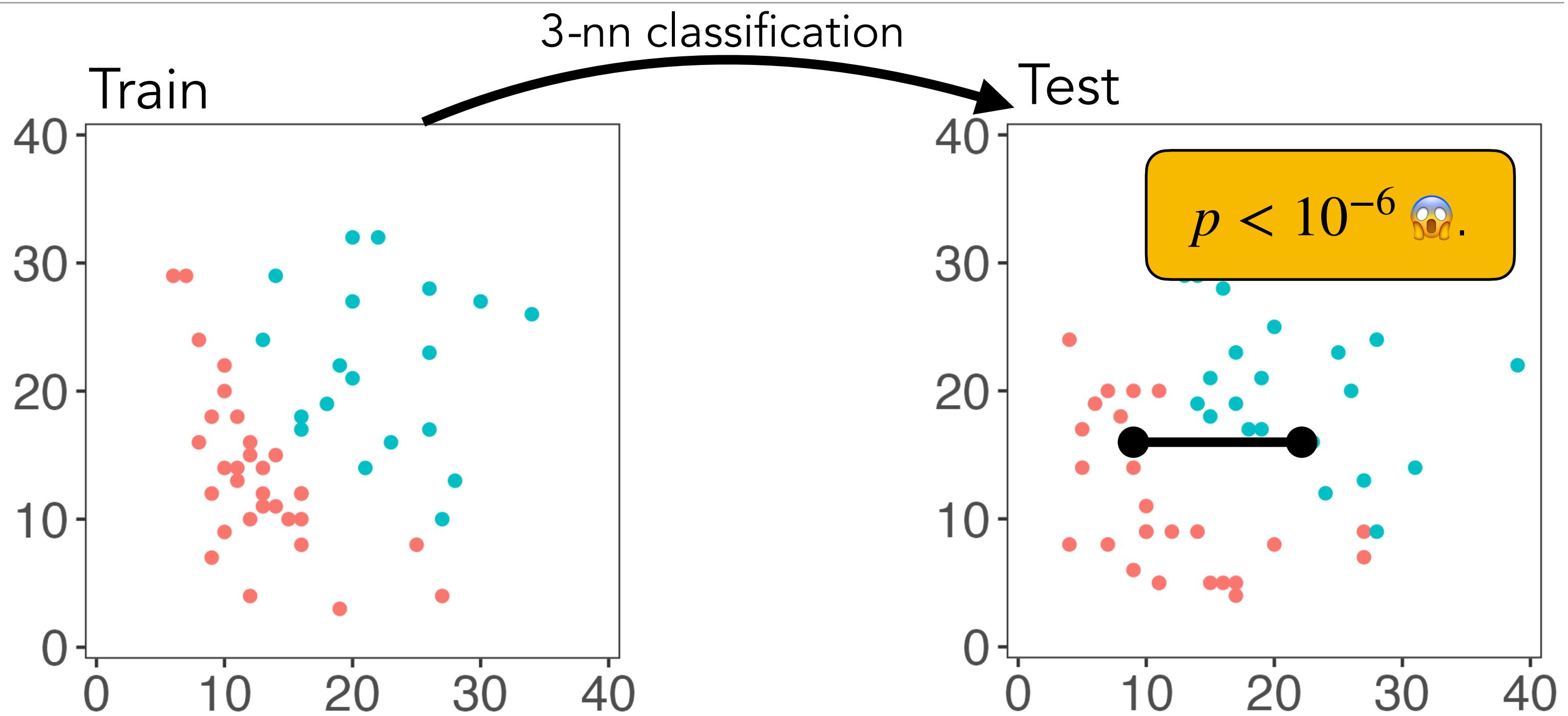
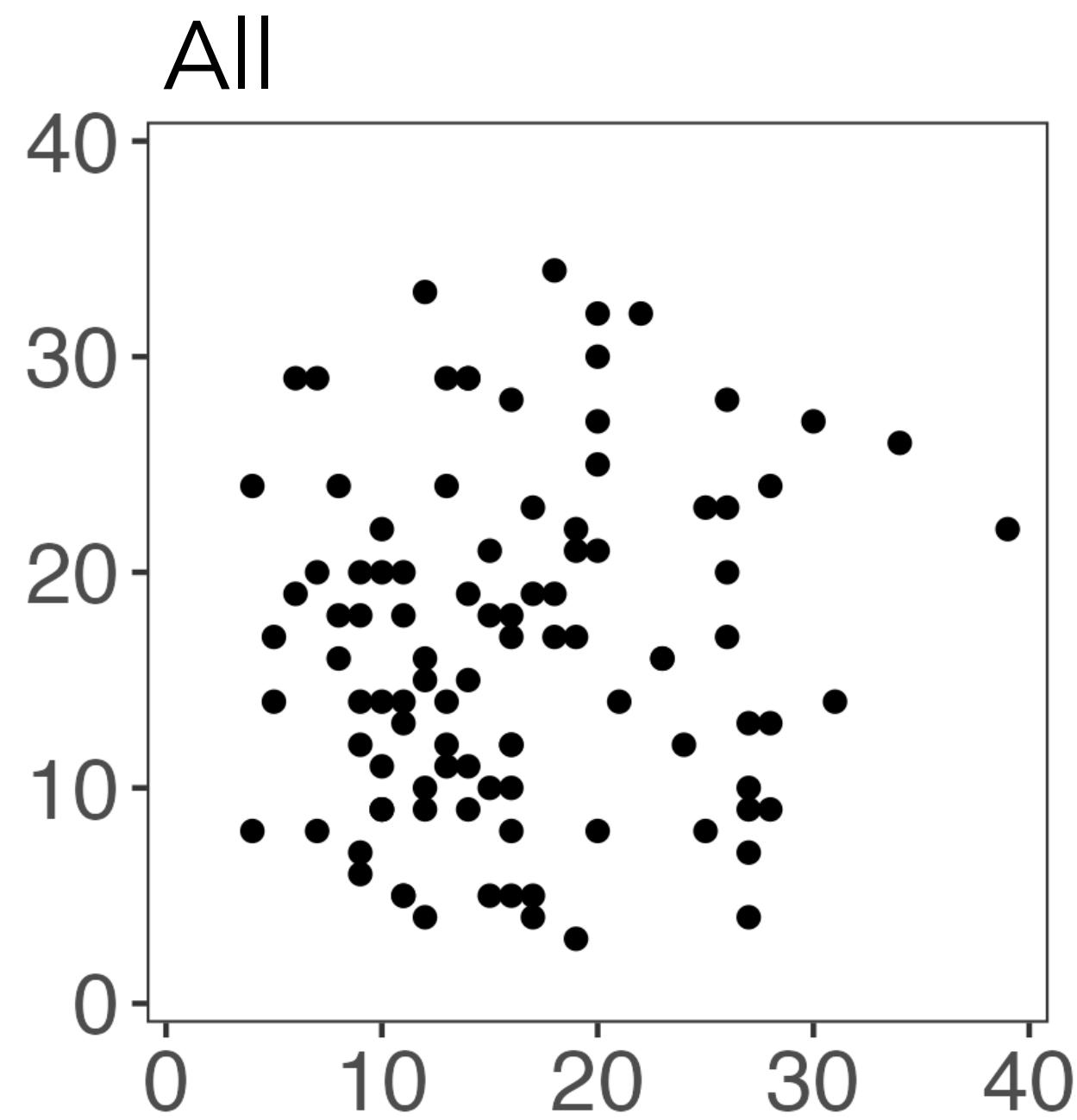
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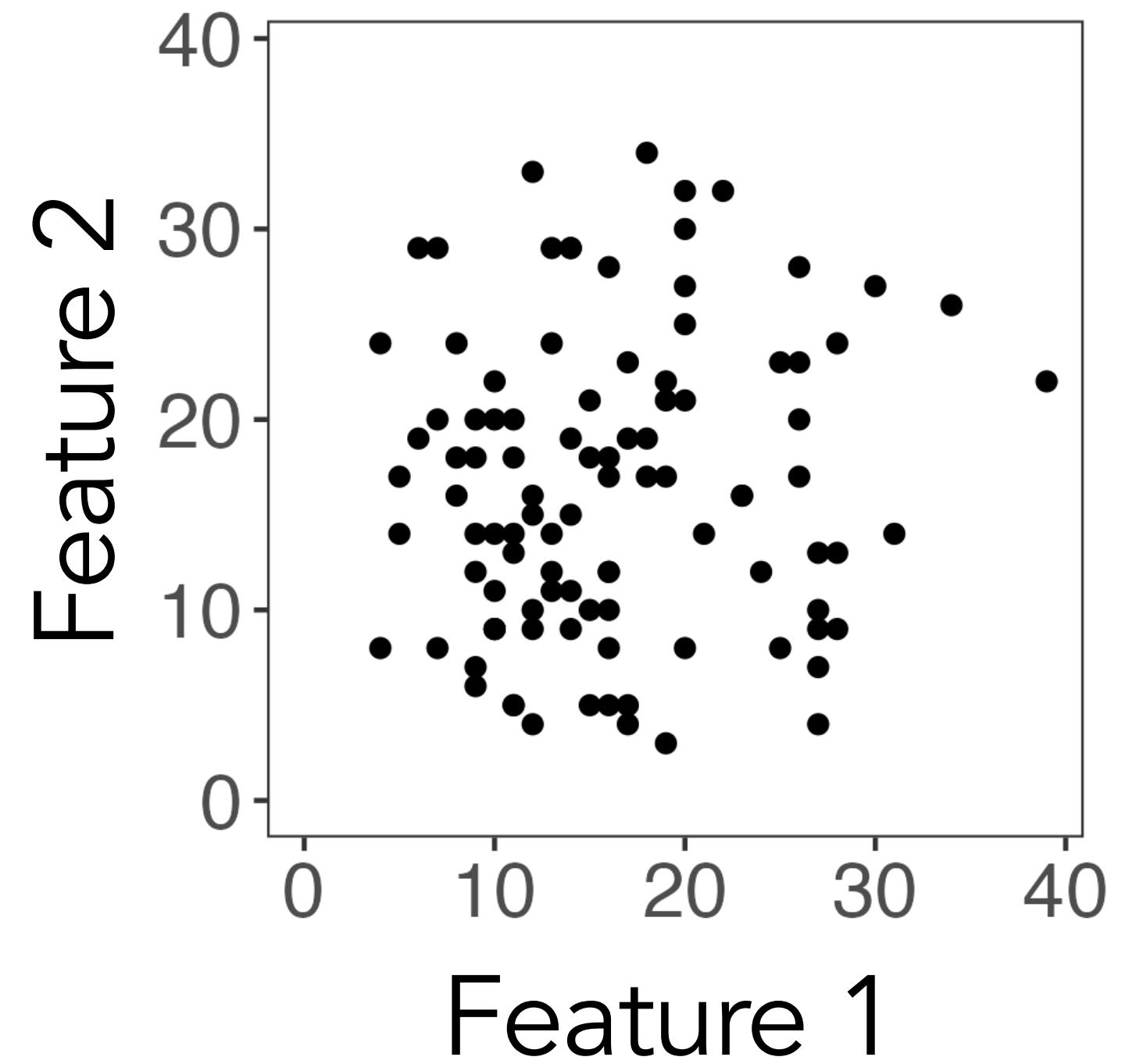
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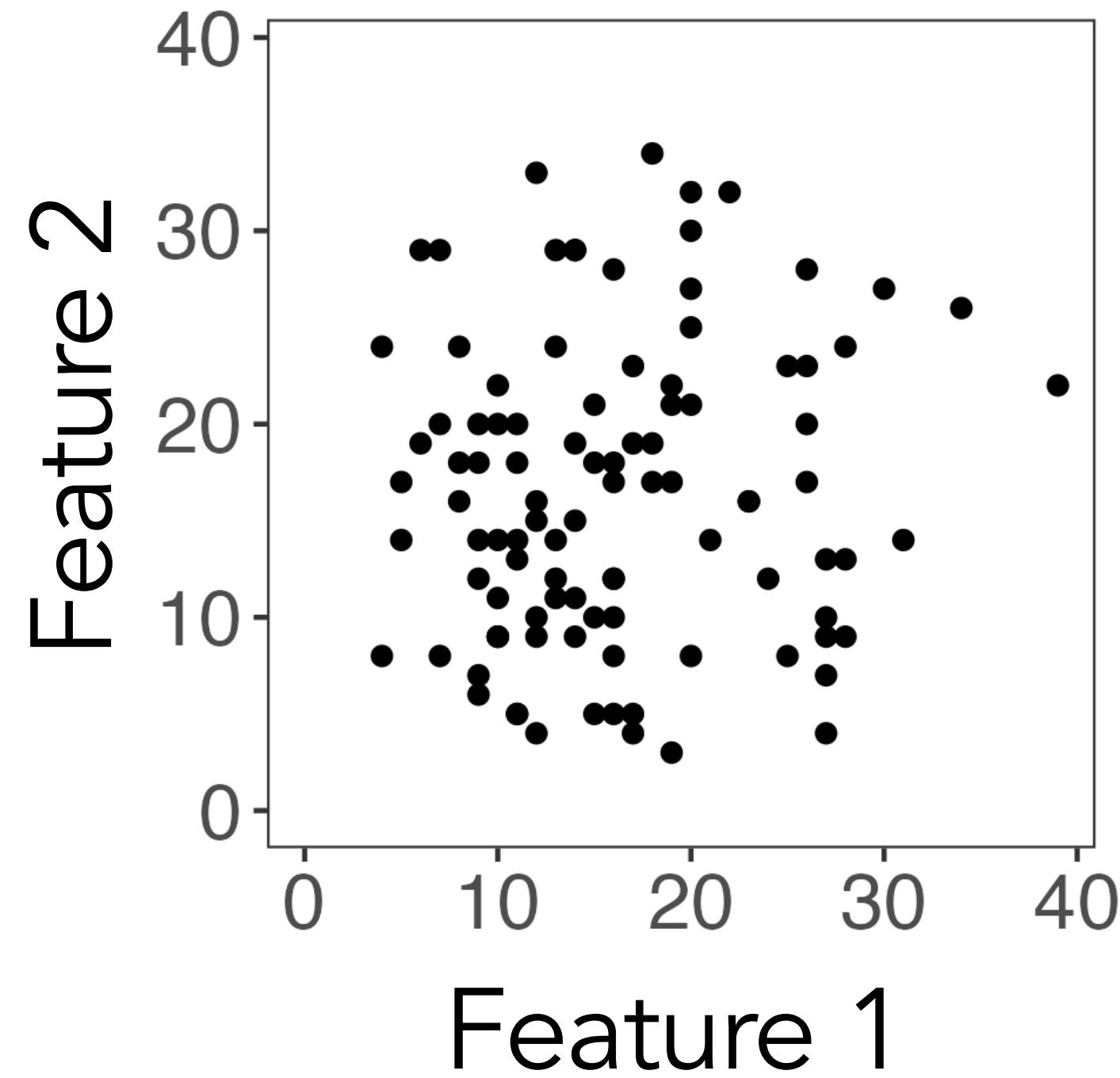
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Step 3: test for difference in means using test set.

Example 2: using the same data to fit and evaluate a model

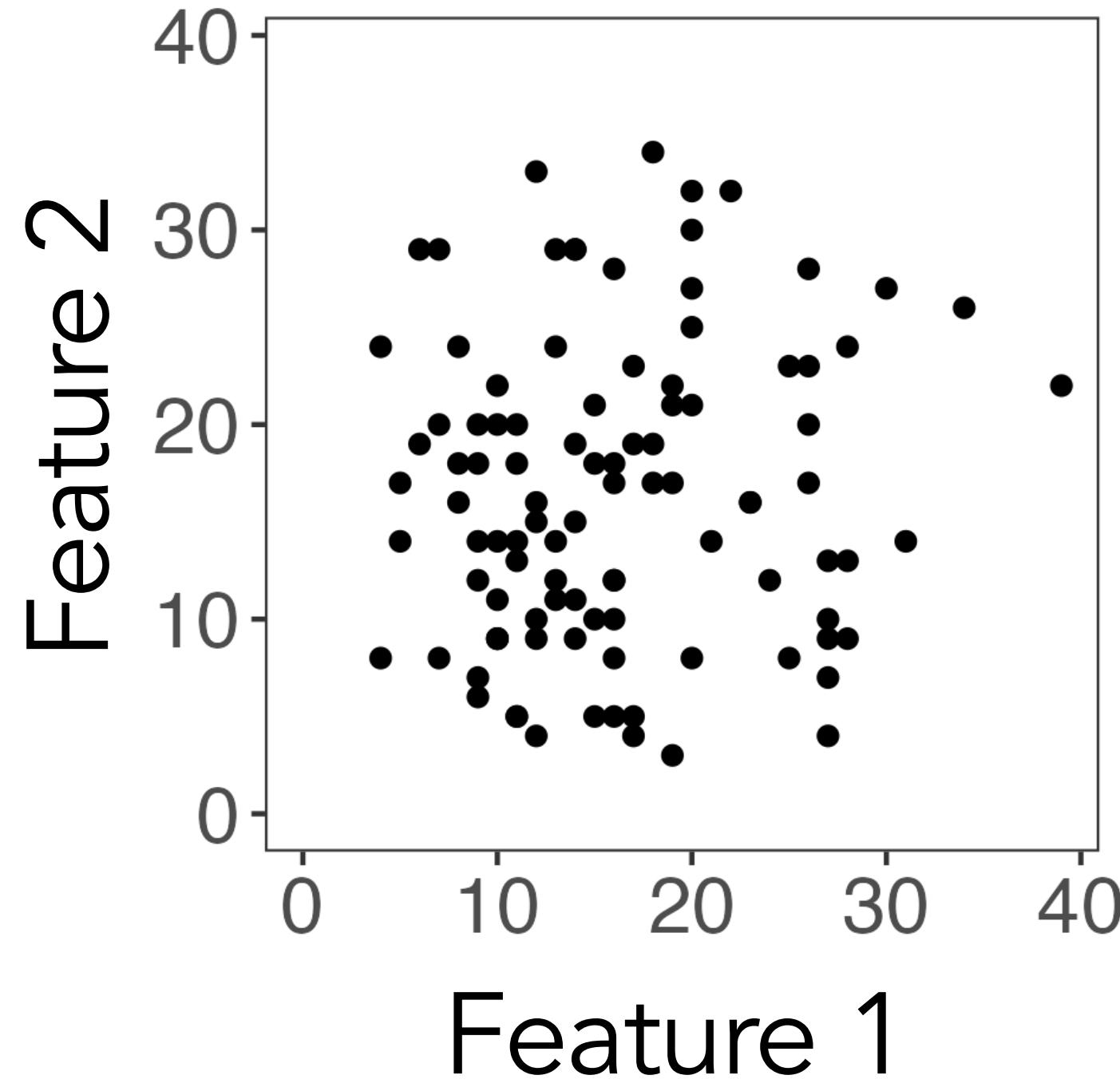


Example 2: using the same data to fit and evaluate a model



Goal: how many clusters are in this data?

Example 2: using the same data to fit and evaluate a model



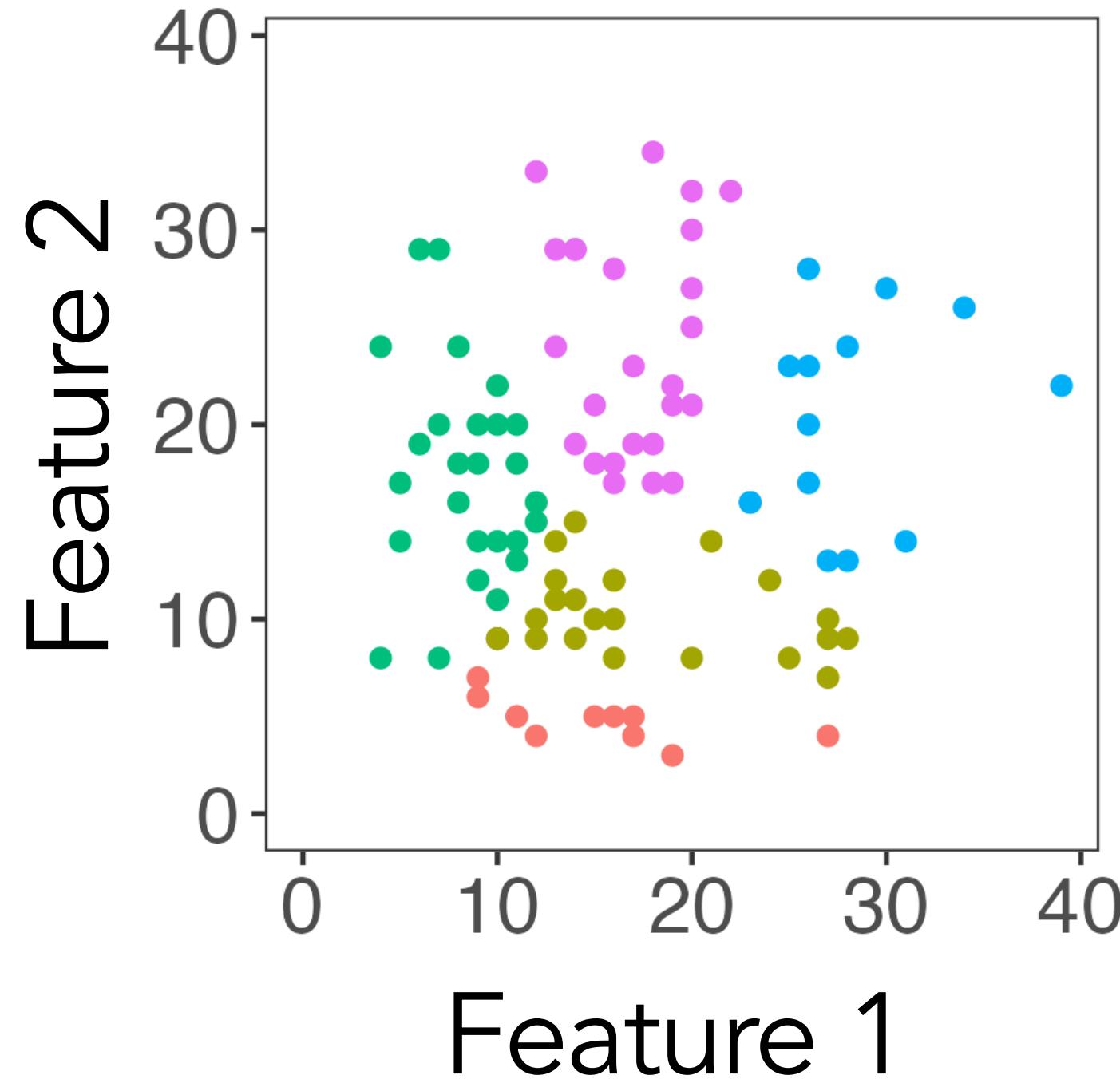
Goal: how many clusters are in this data?

For several values of k :

Step 1: fit a model with k clusters.

Step 2: evaluate model using a loss function.

Example 2: using the same data to fit and evaluate a model



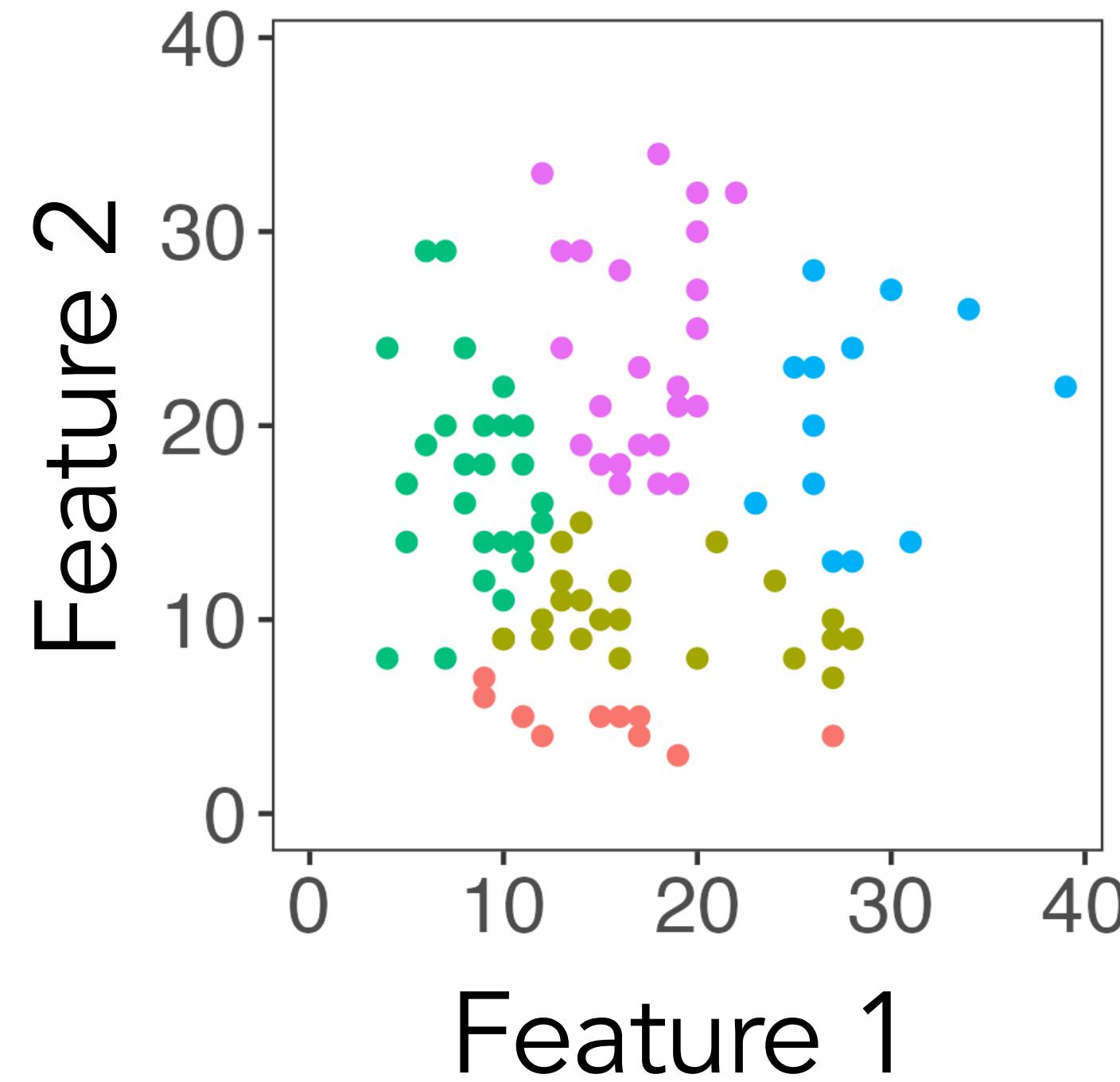
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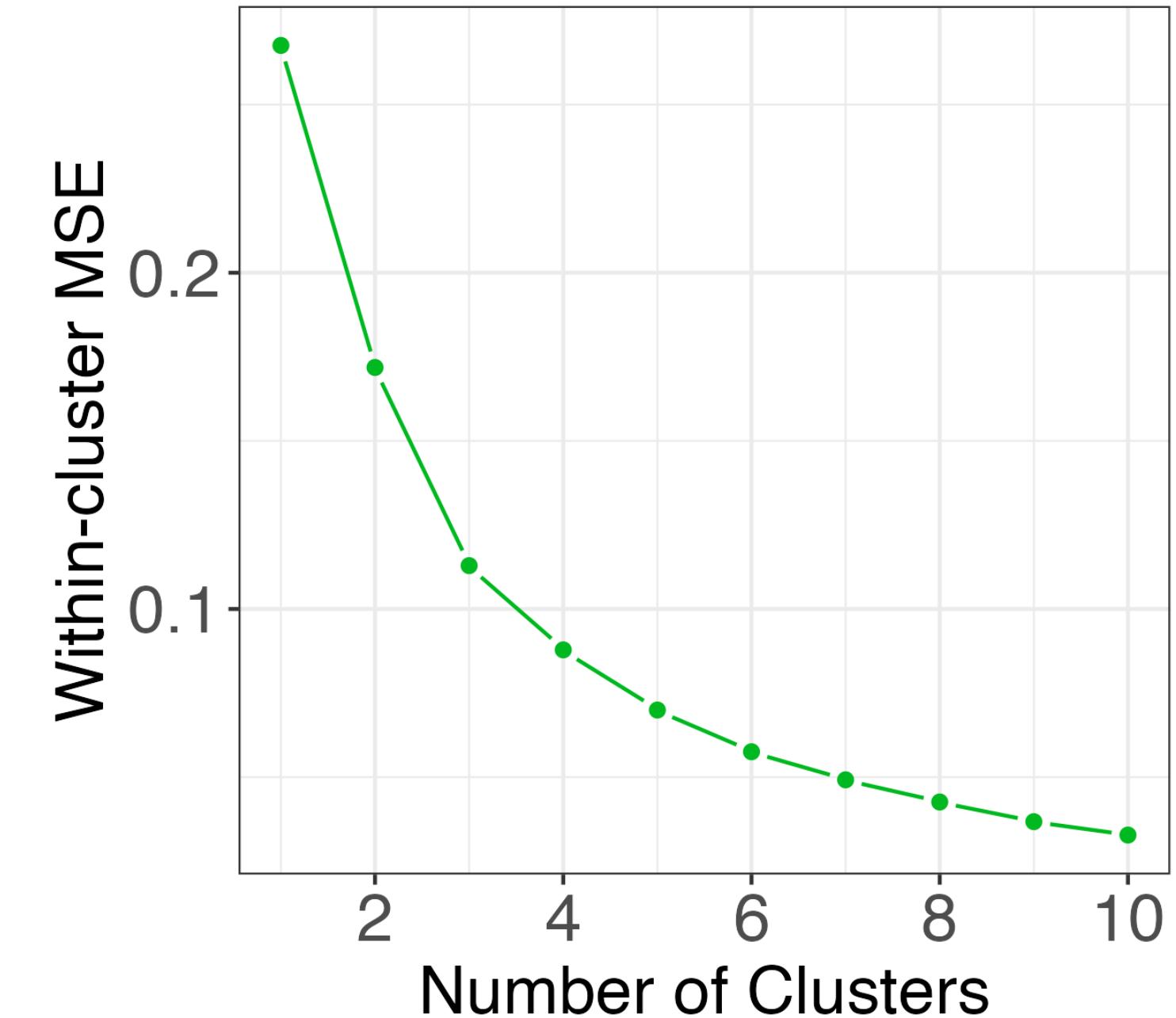


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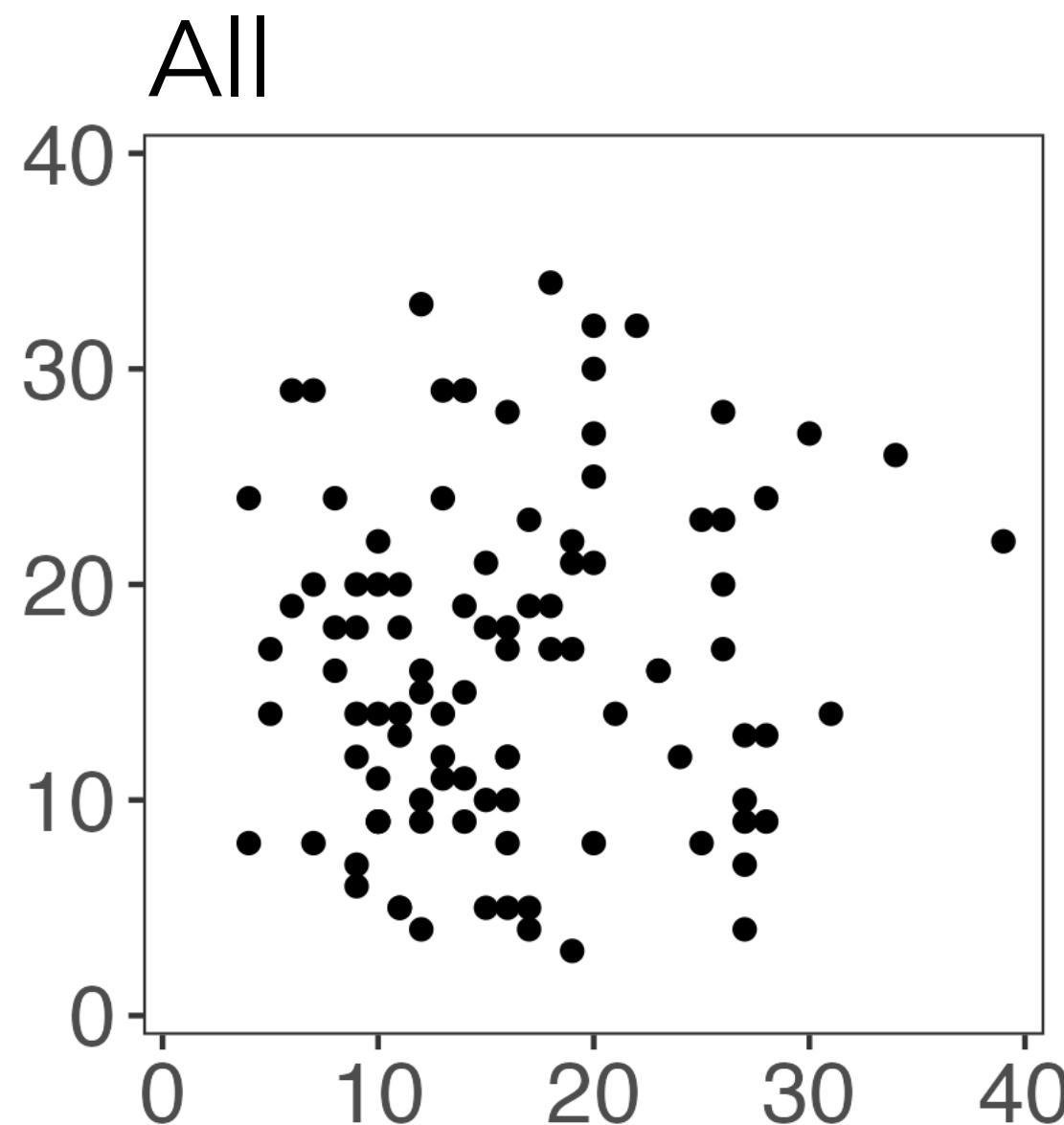
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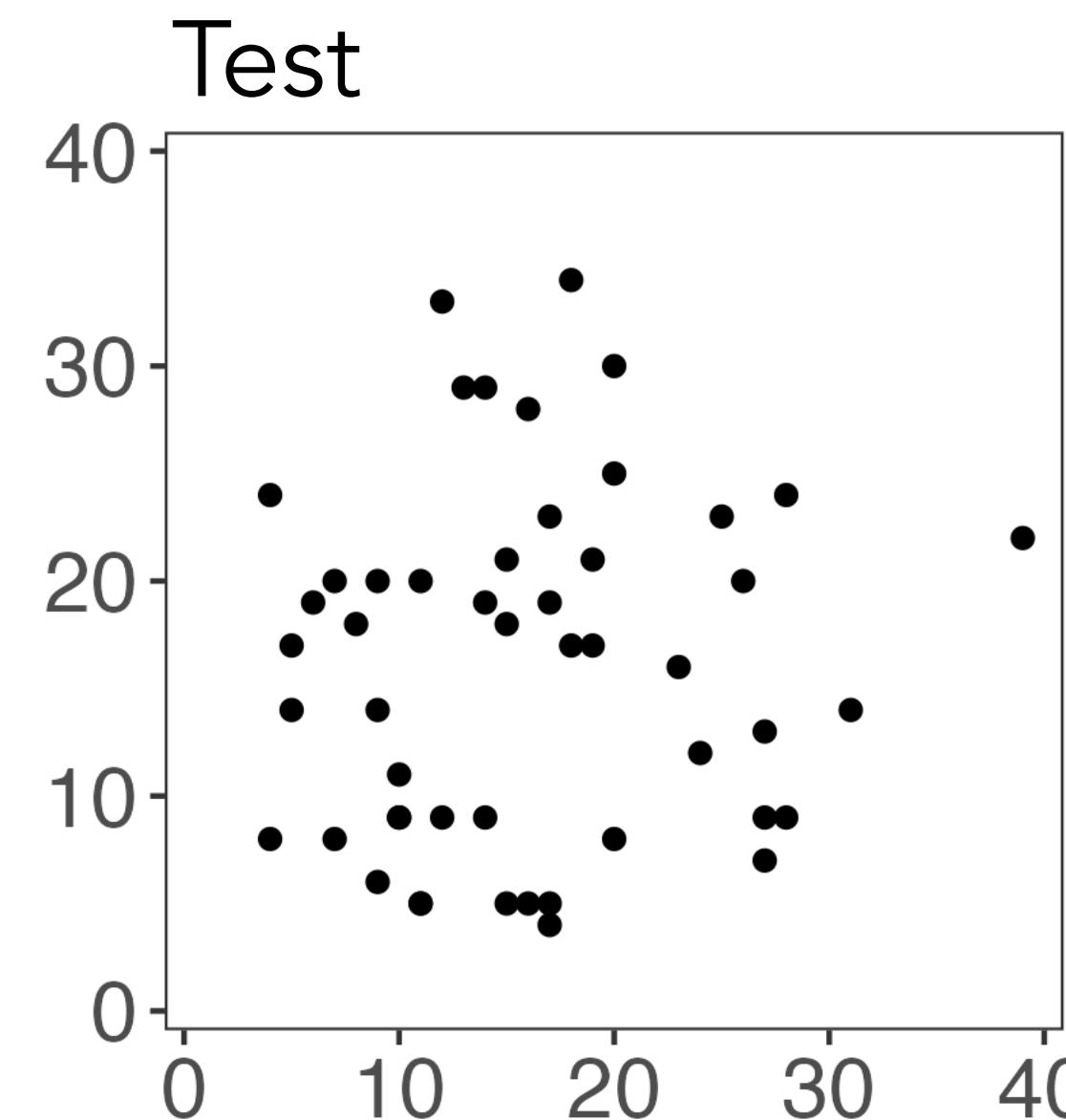
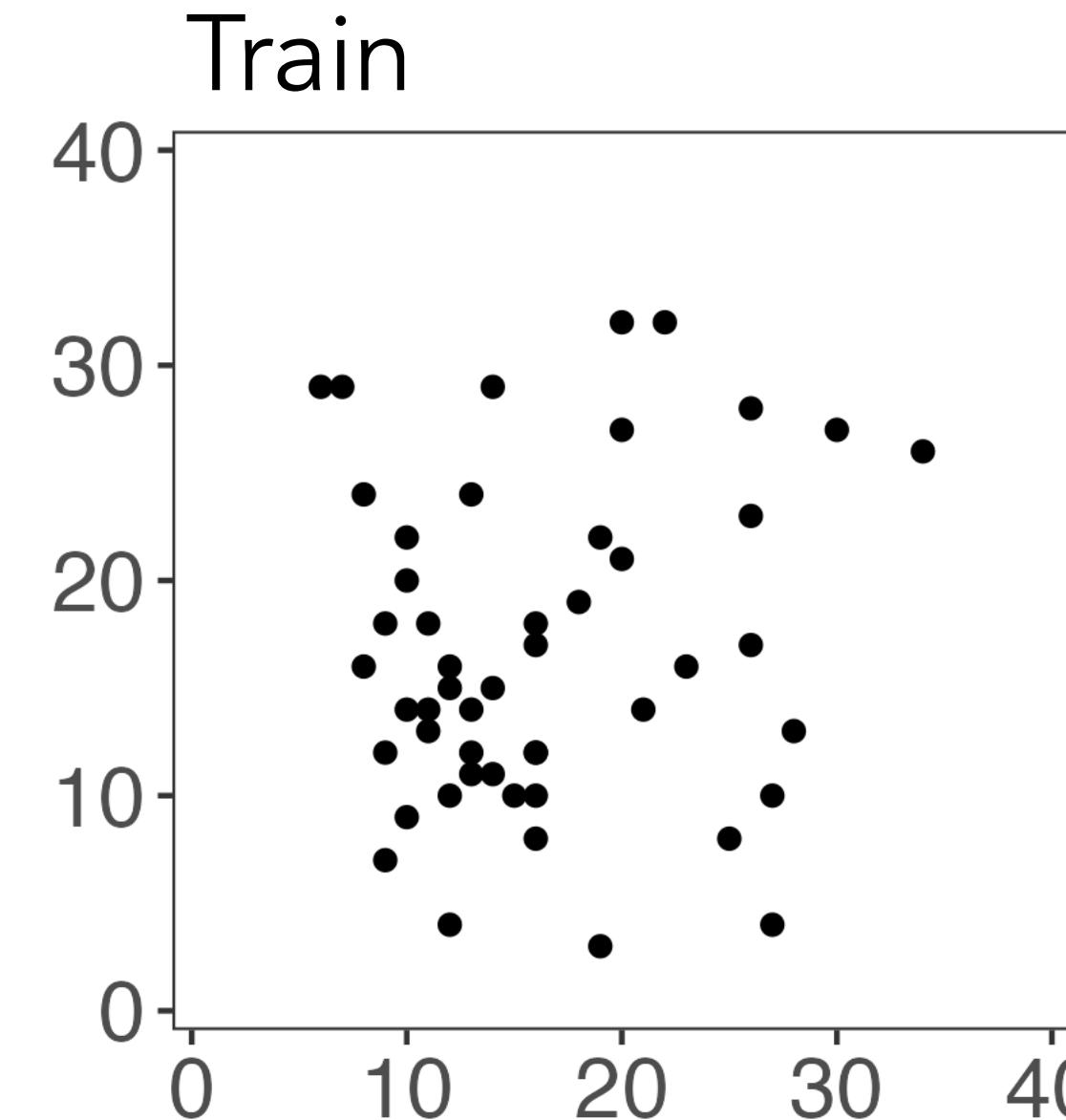
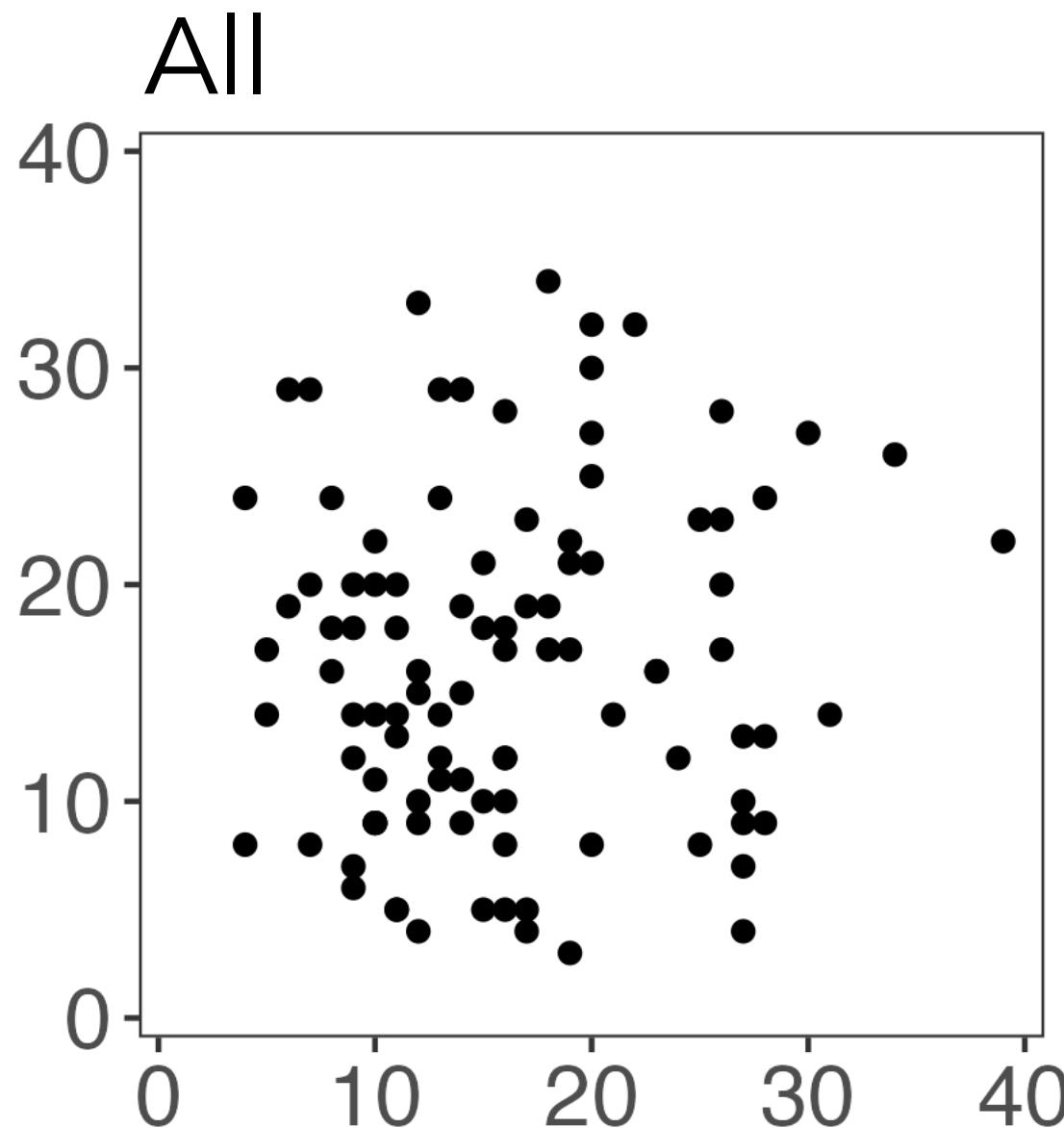
Step 2: evaluate model using a loss function.



Sample splitting cannot be used for example 2

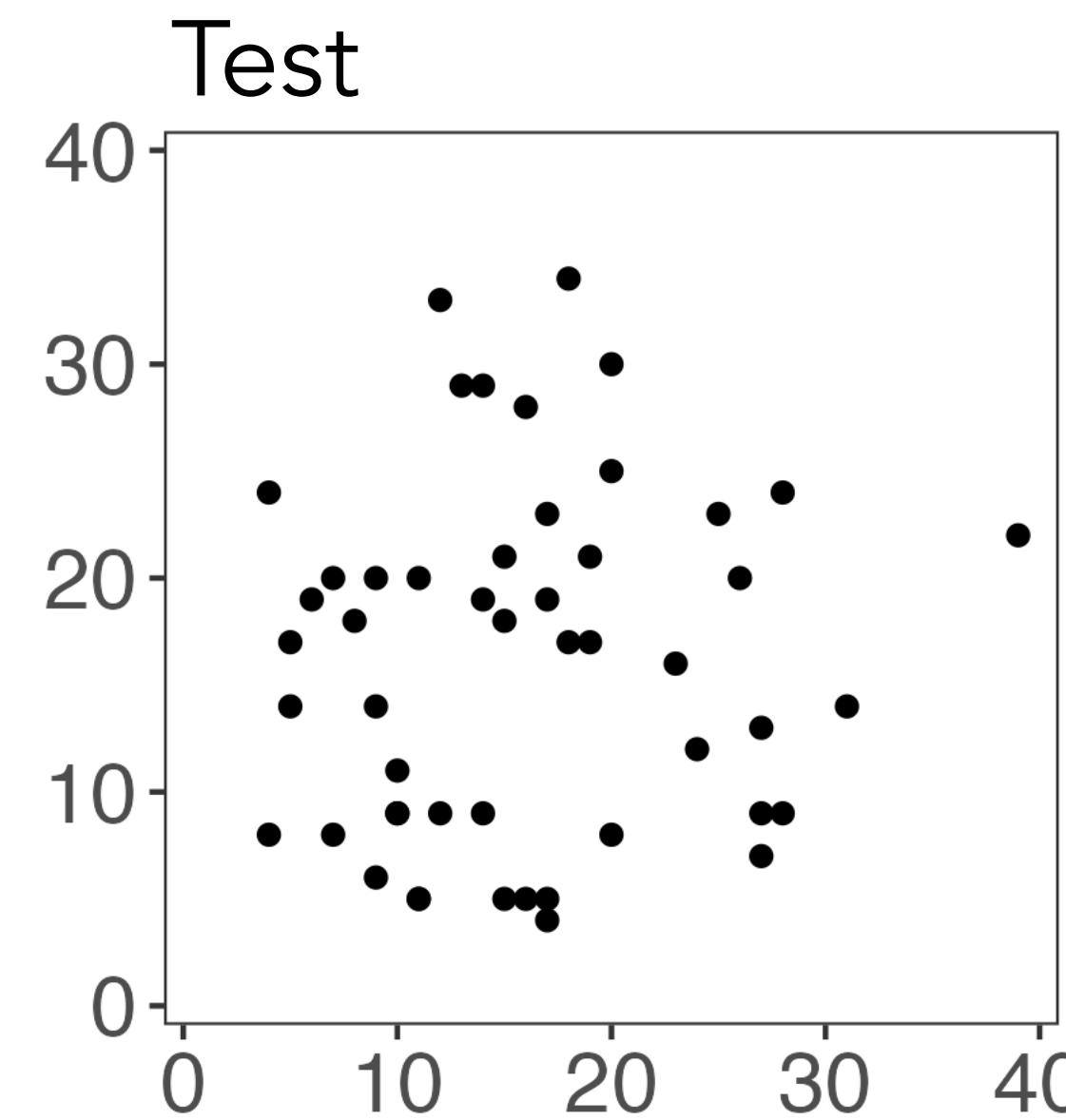
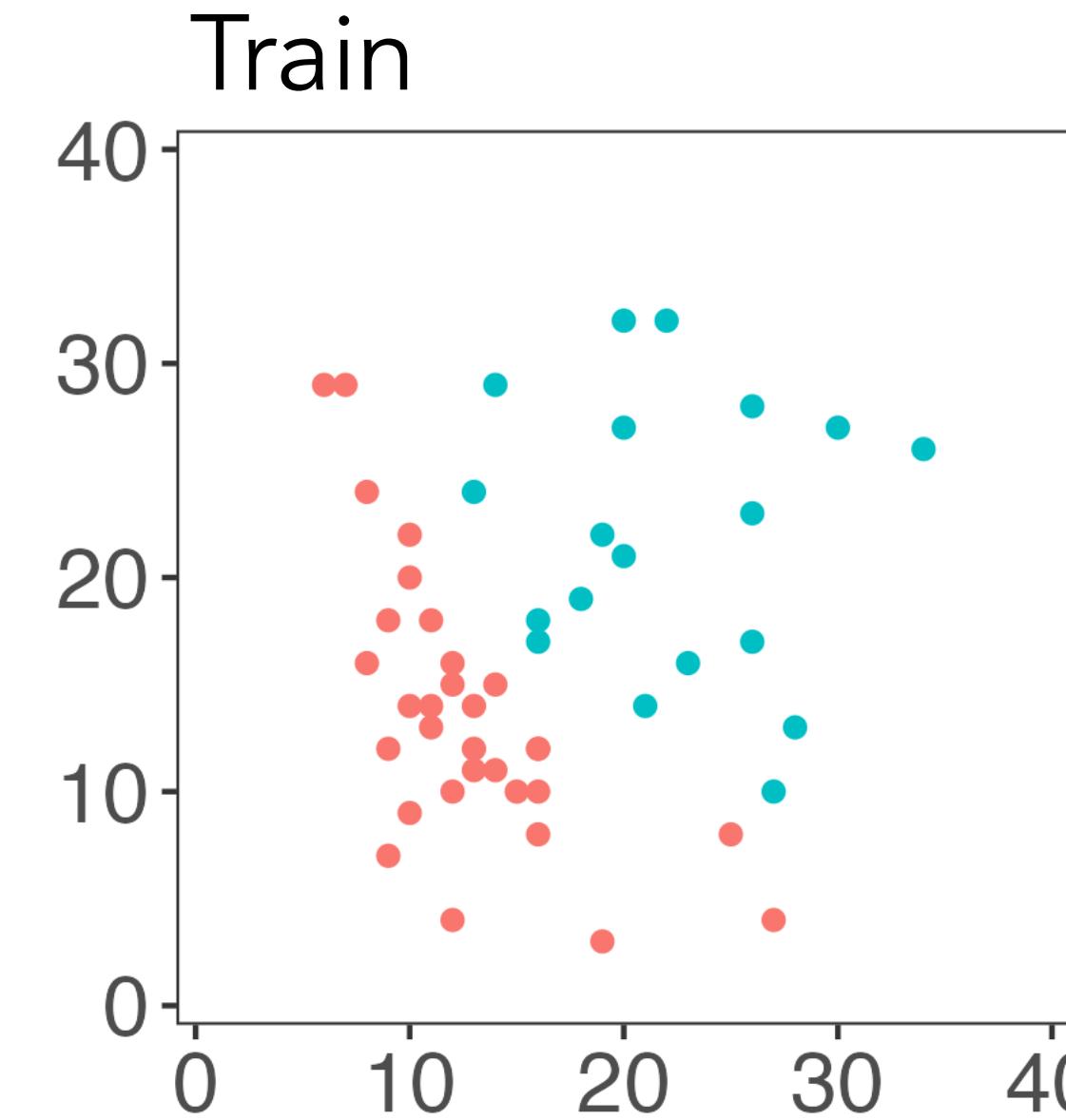
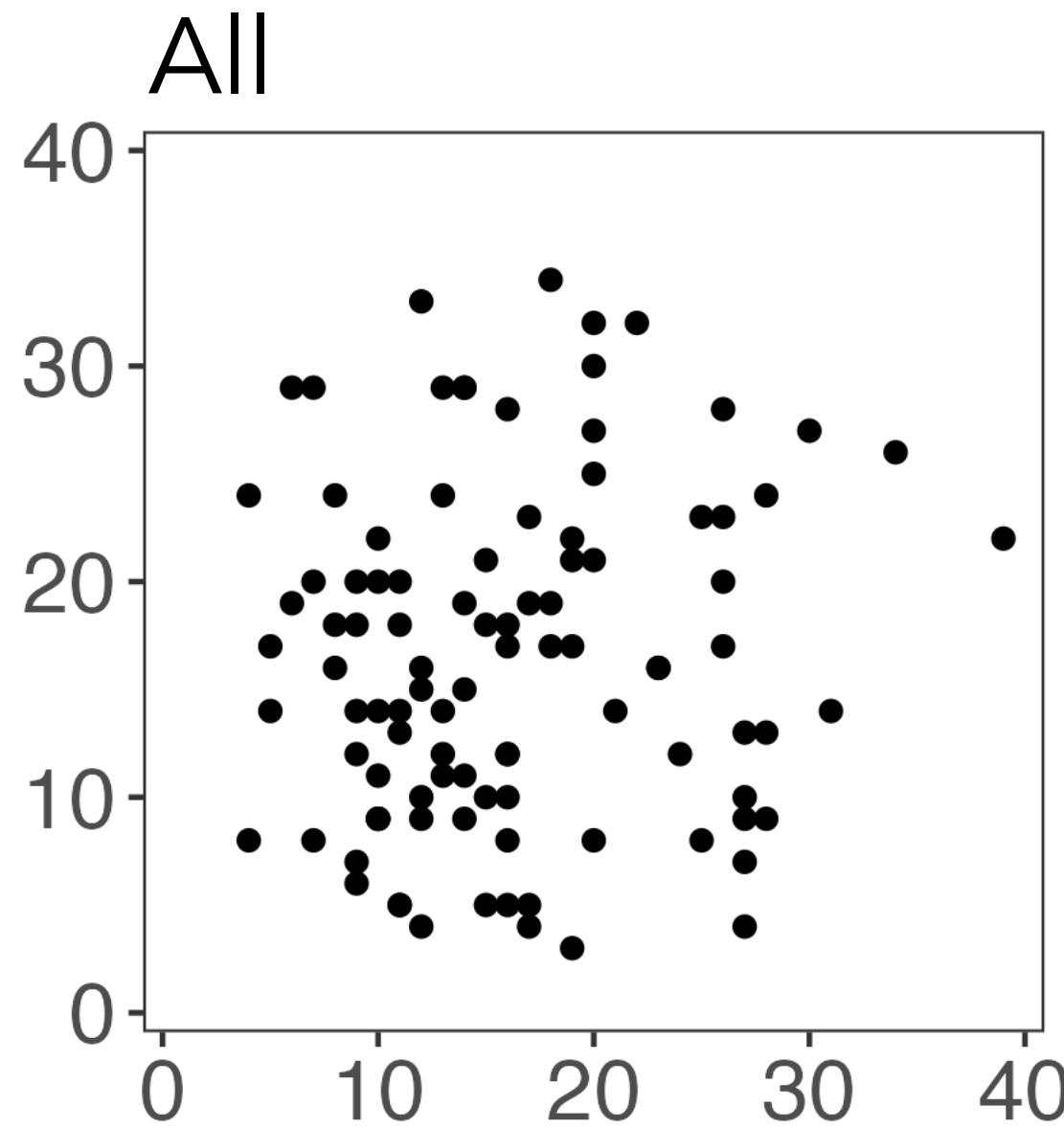


Sample splitting cannot be used for example 2



Step 1: split
observations
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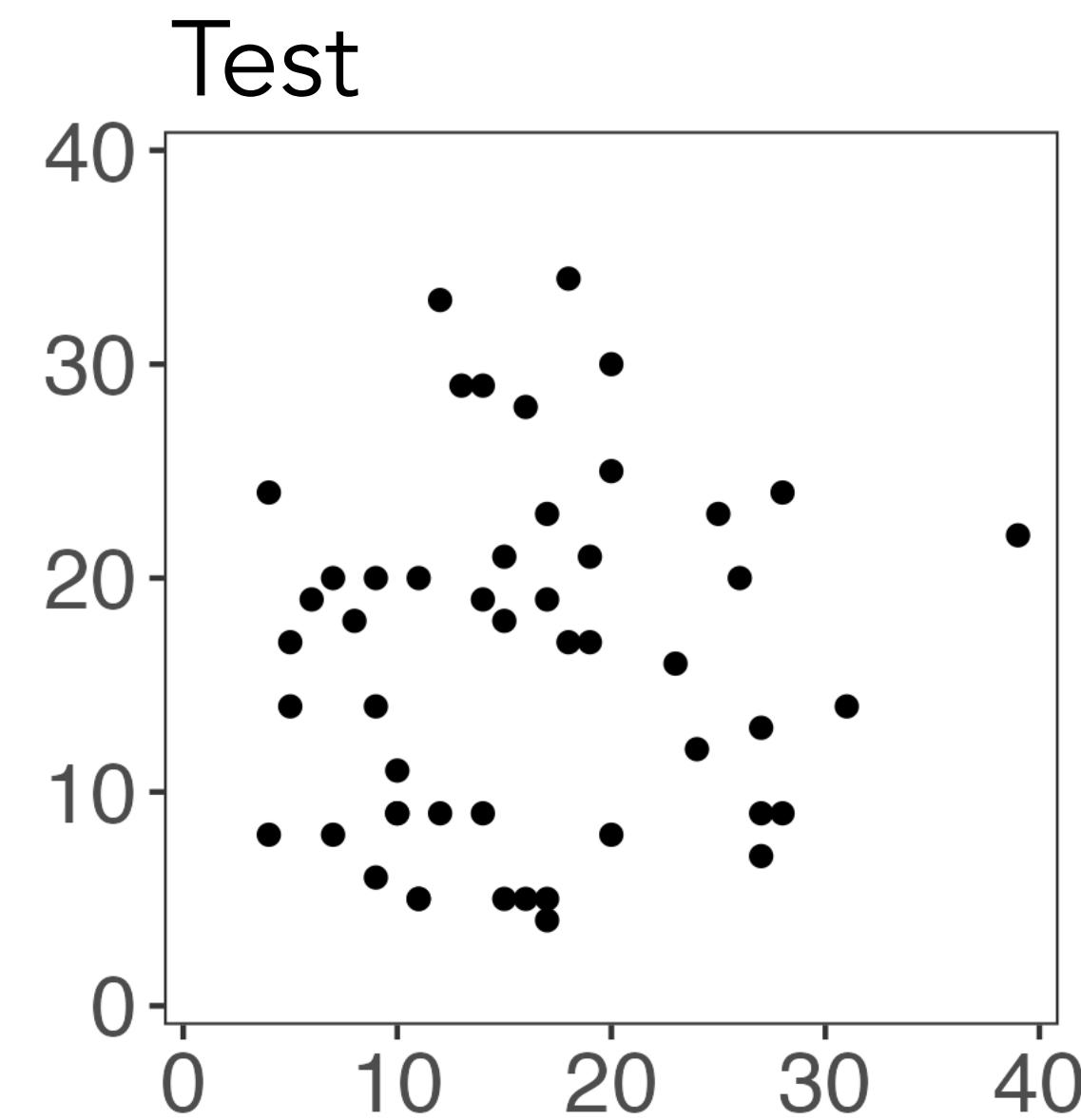
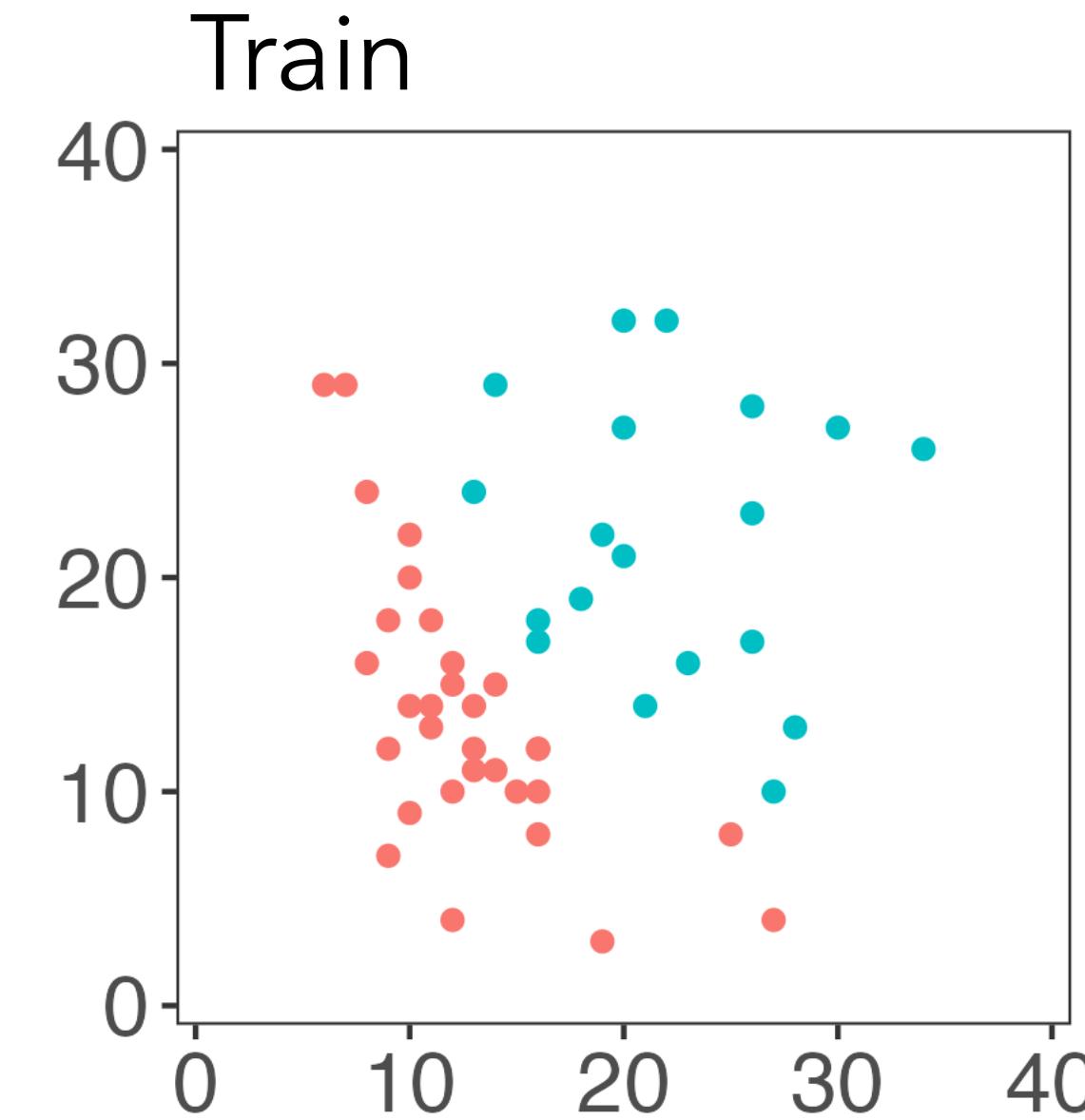
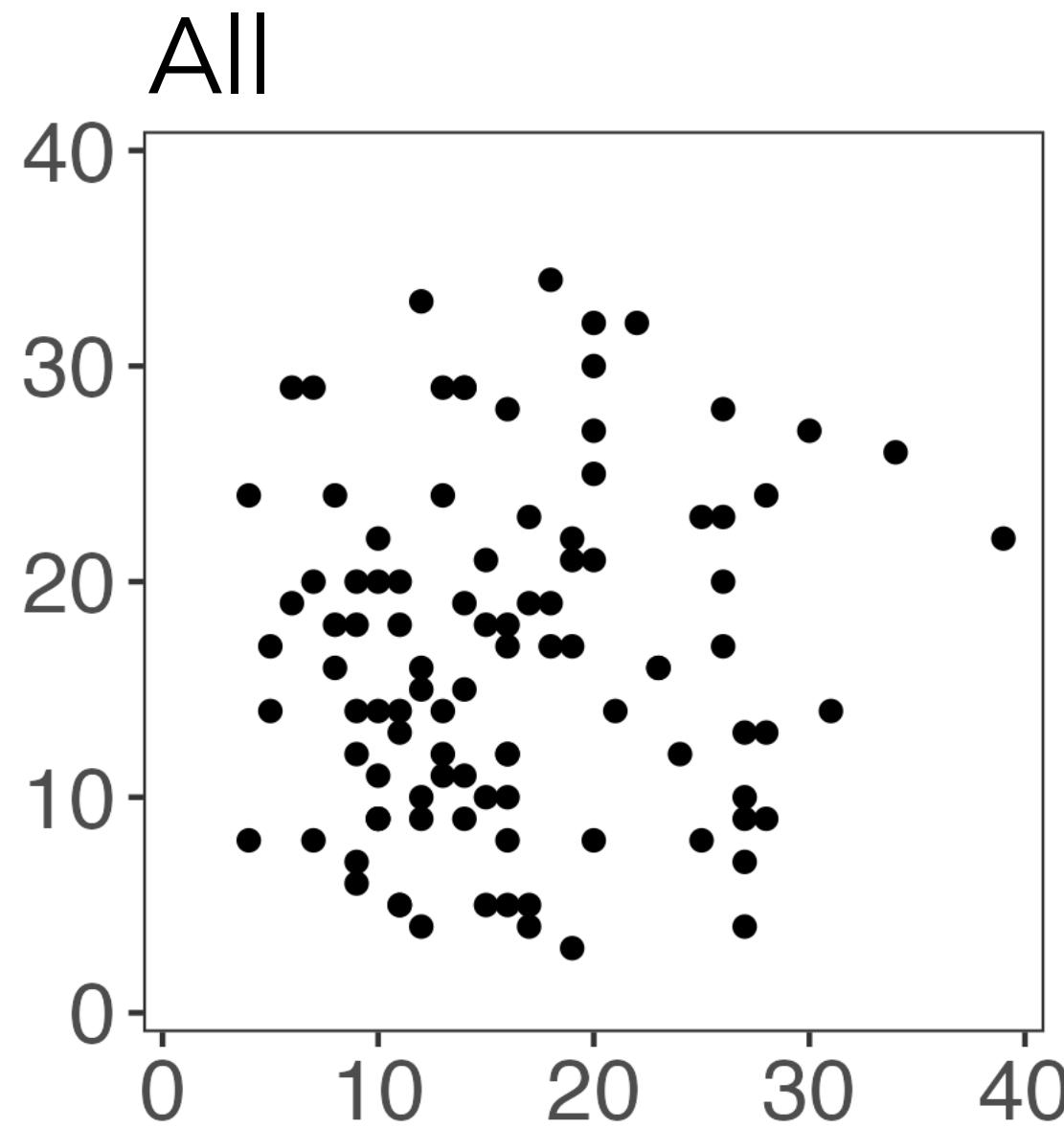
Sample splitting cannot be used for example 2



Step 1: split observations into train/test.

Step 2: cluster the training set.

Sample splitting cannot be used for example 2

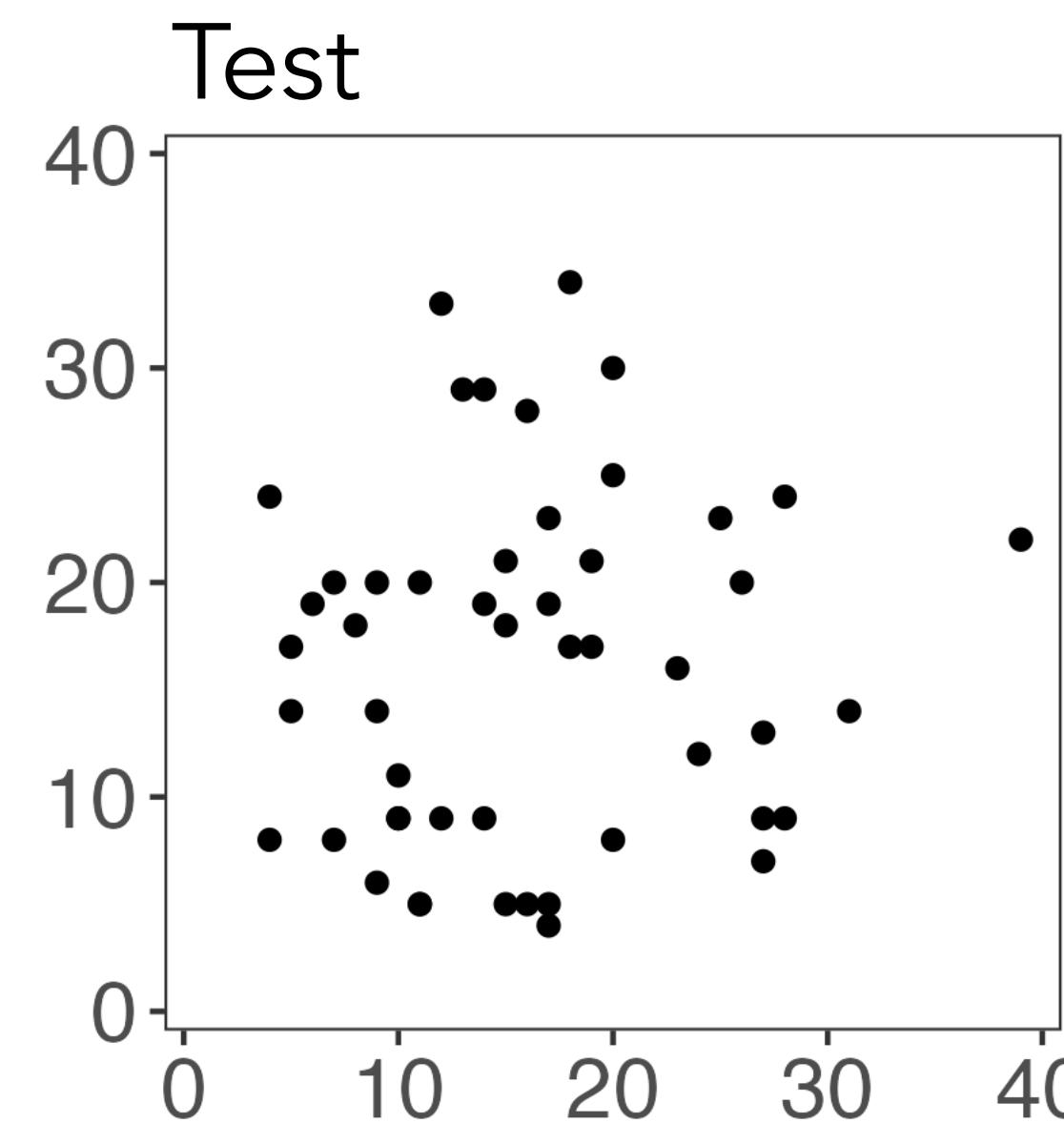
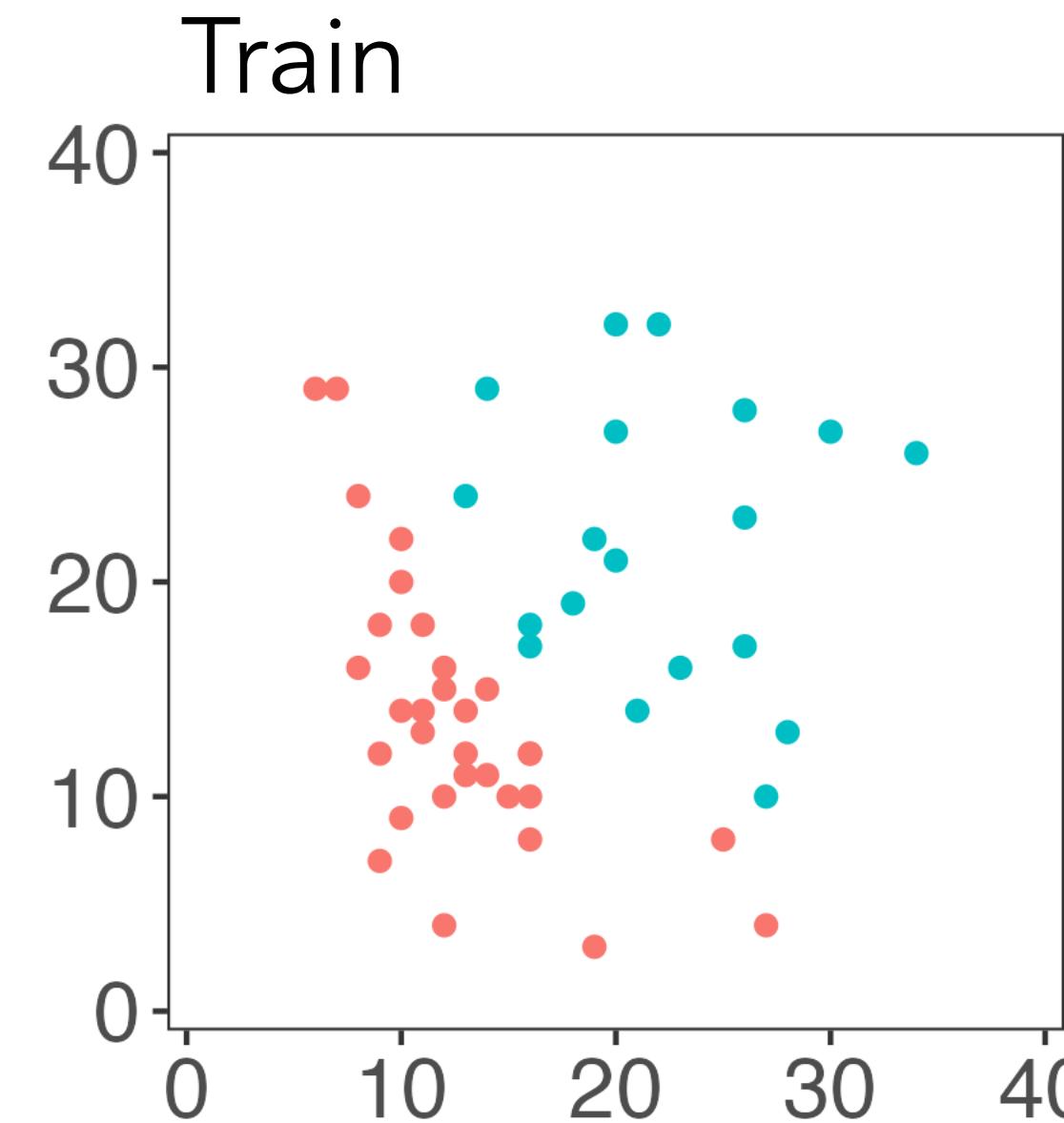
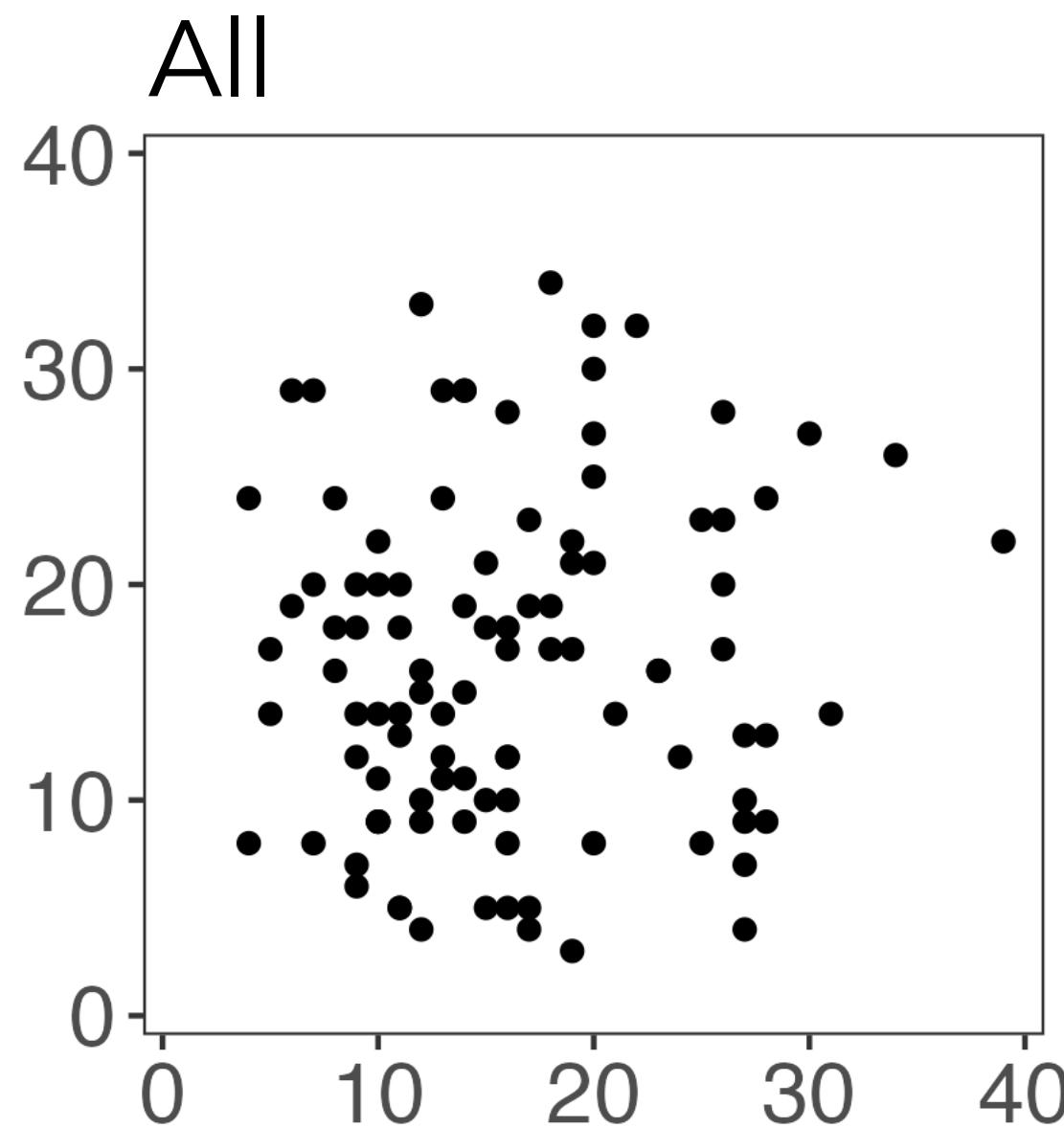


Step 1: split observations into train/test.

Step 2: cluster the training set.

Step 3: evaluate clusters using test set.

Sample splitting cannot be used for example 2



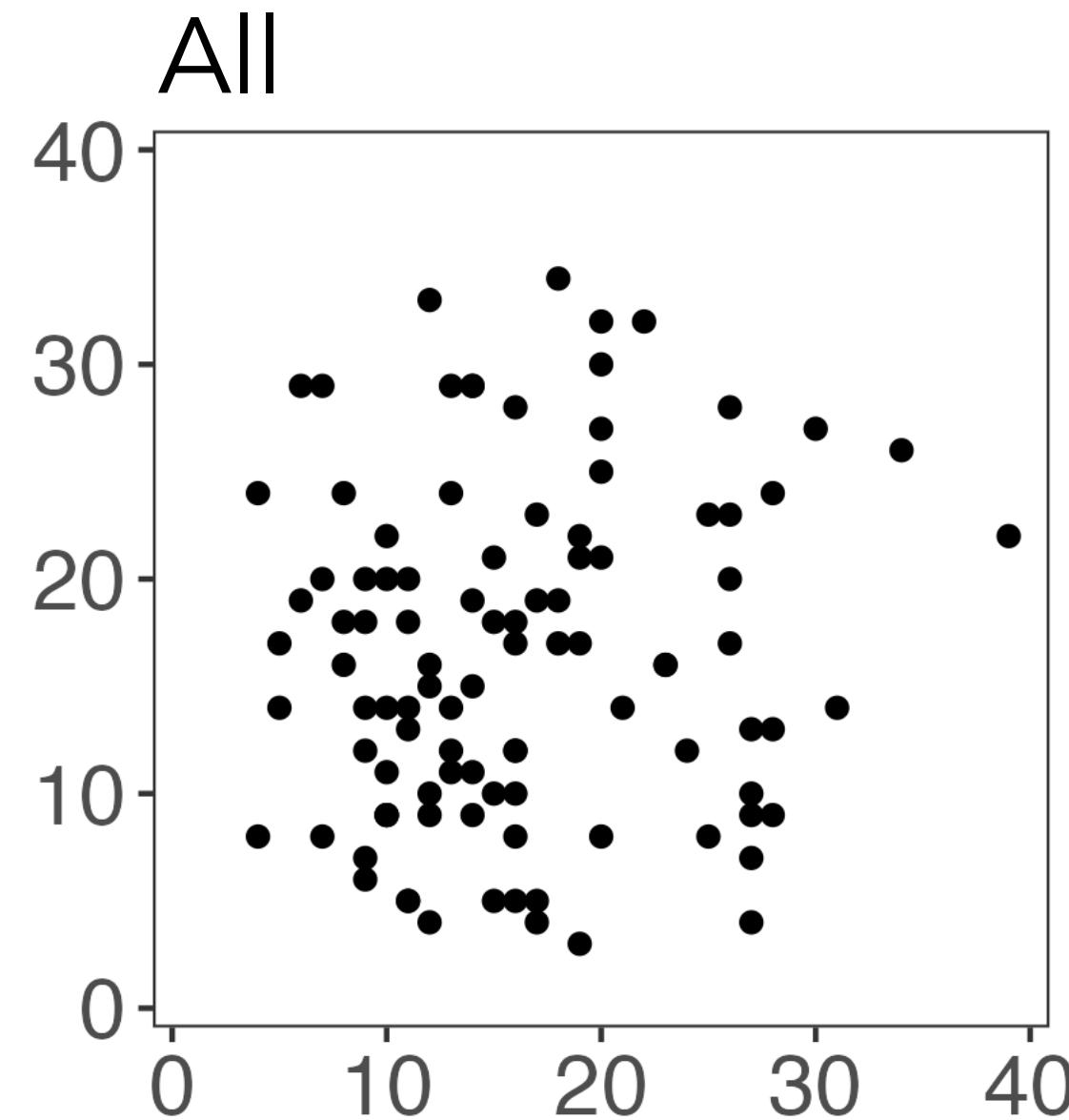
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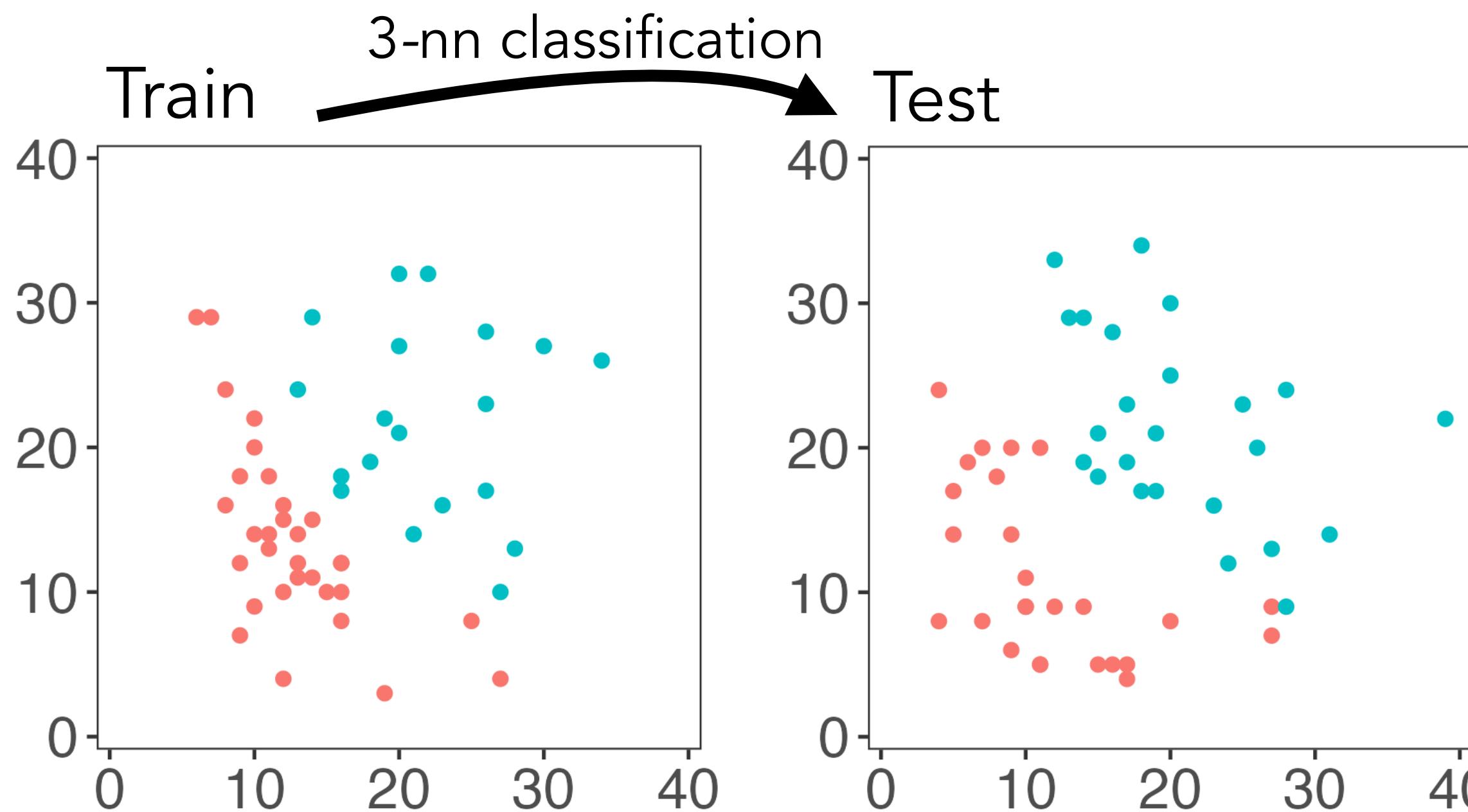
Step 2.5: assign labels to observations in test set.

Step 3: evaluate clusters using test set.

Sample splitting cannot be used for example 2



Step 1: split observations into train/test.

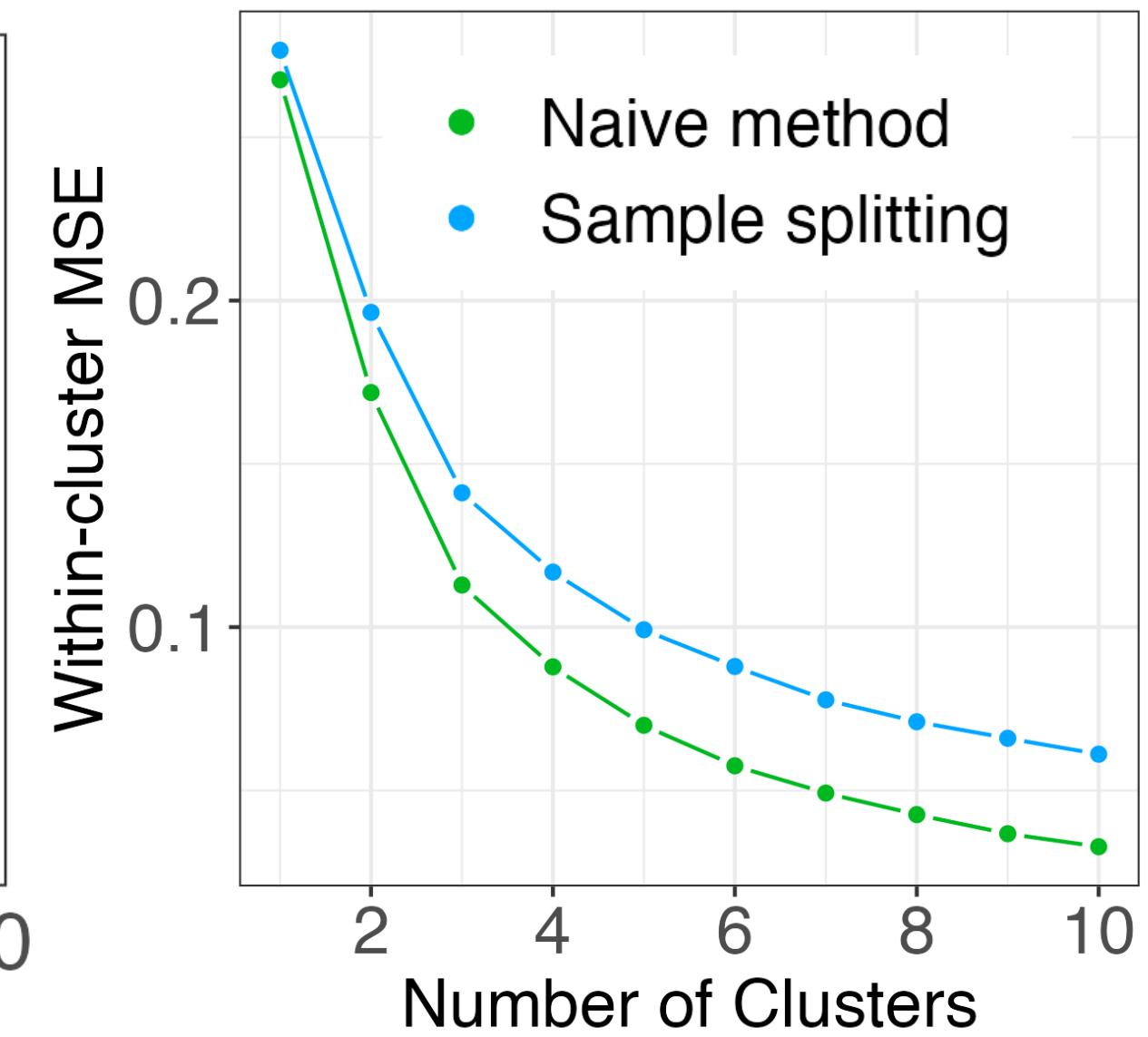
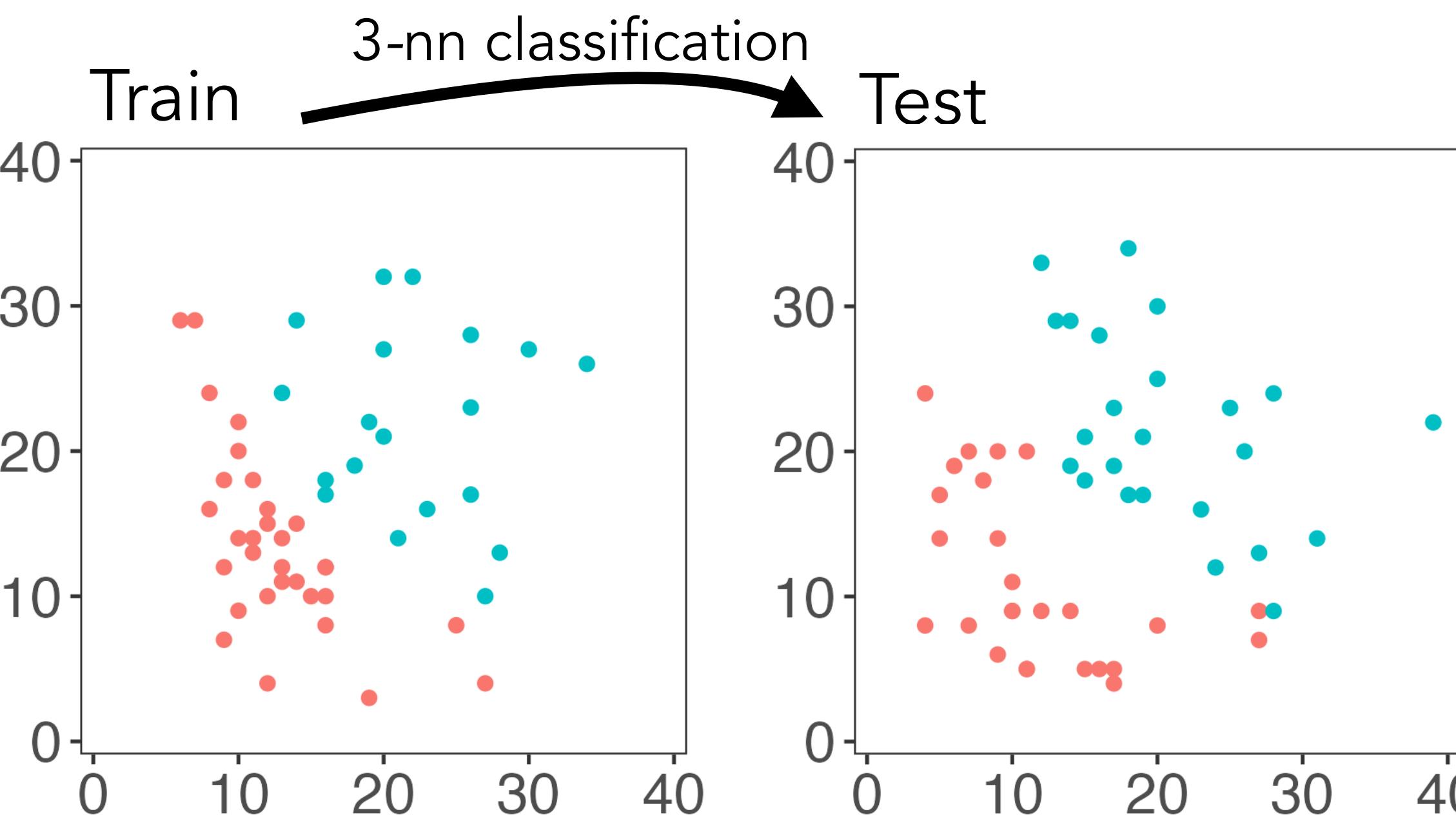
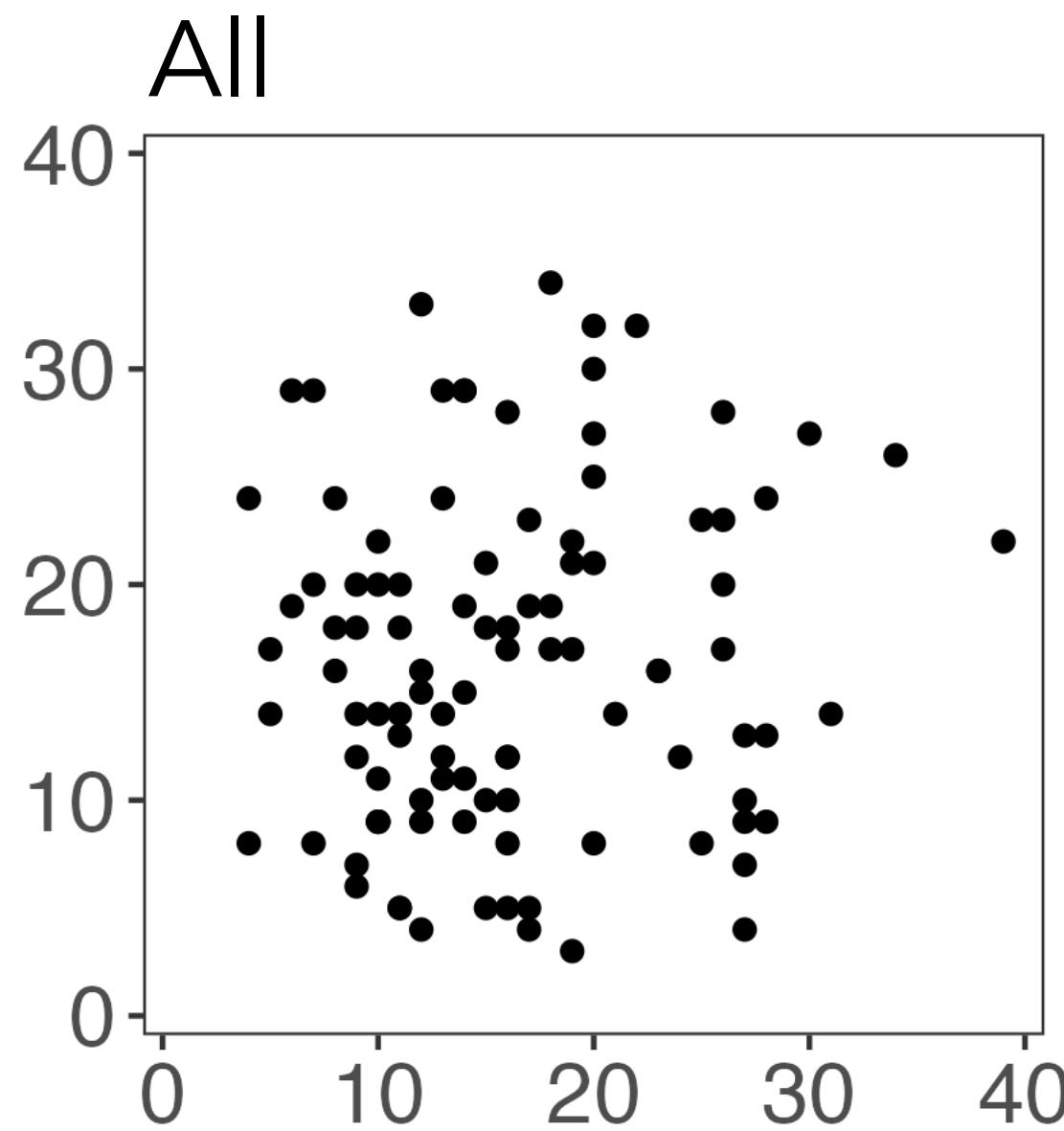


Step 2: cluster the training set.

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Sample splitting cannot be used for example 2



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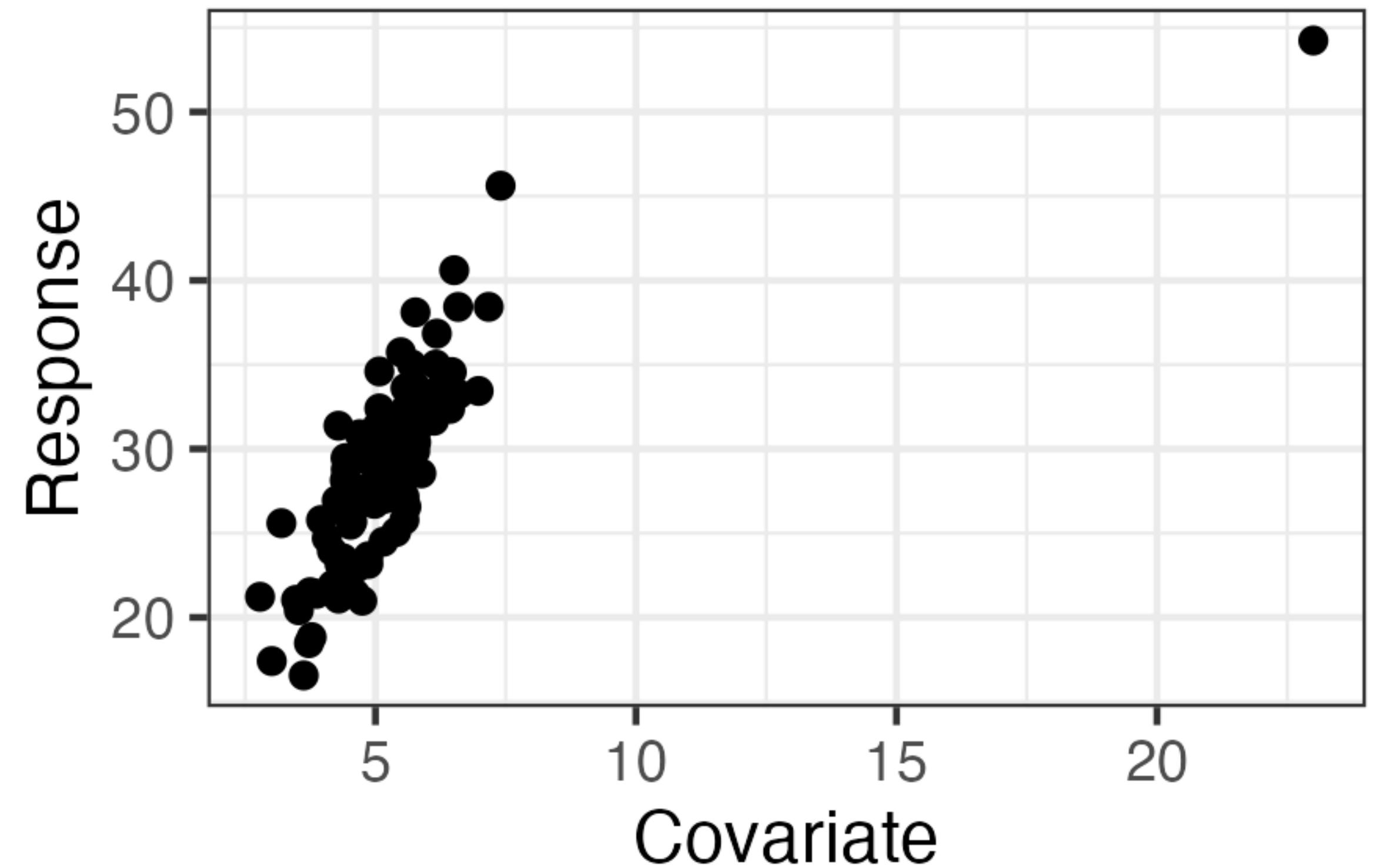
Step 3: evaluate clusters using test set.

Other situations in which sample splitting is not a good option

1. Fixed-X regression settings.

2. Non-IID data.

3. Data with outliers or influential points.



Outline

1. Motivation: settings where sample splitting doesn't work
2. **Poisson thinning**
3. Data thinning
4. Application to single-cell RNA sequencing data
5. Ongoing work

Poisson thinning

X

	Feature 1	Feature 2
Obs. 1	18	6
Obs. 2	31	8
Obs. 3	11	31
Obs. 4	22	34

Poisson thinning

X

	Feature 1	Feature 2
Obs. 1	18	6
Obs. 2	31	8
Obs. 3	11	31
Obs. 4	22	34

$X^{(1)}$

	Feature 1	Feature 2
Obs. 1	14	1
Obs. 2	10	6
Obs. 3	5	17
Obs. 4	6	25

$X^{(2)}$

	Feature 1	Feature 2
Obs. 1	4	5
Obs. 2	21	2
Obs. 3	6	14
Obs. 4	16	9

Poisson thinning

X

	Feature 1	Feature 2
Obs. 1	18	6
Obs. 2	31	8
Obs. 3	11	31
Obs. 4	22	34

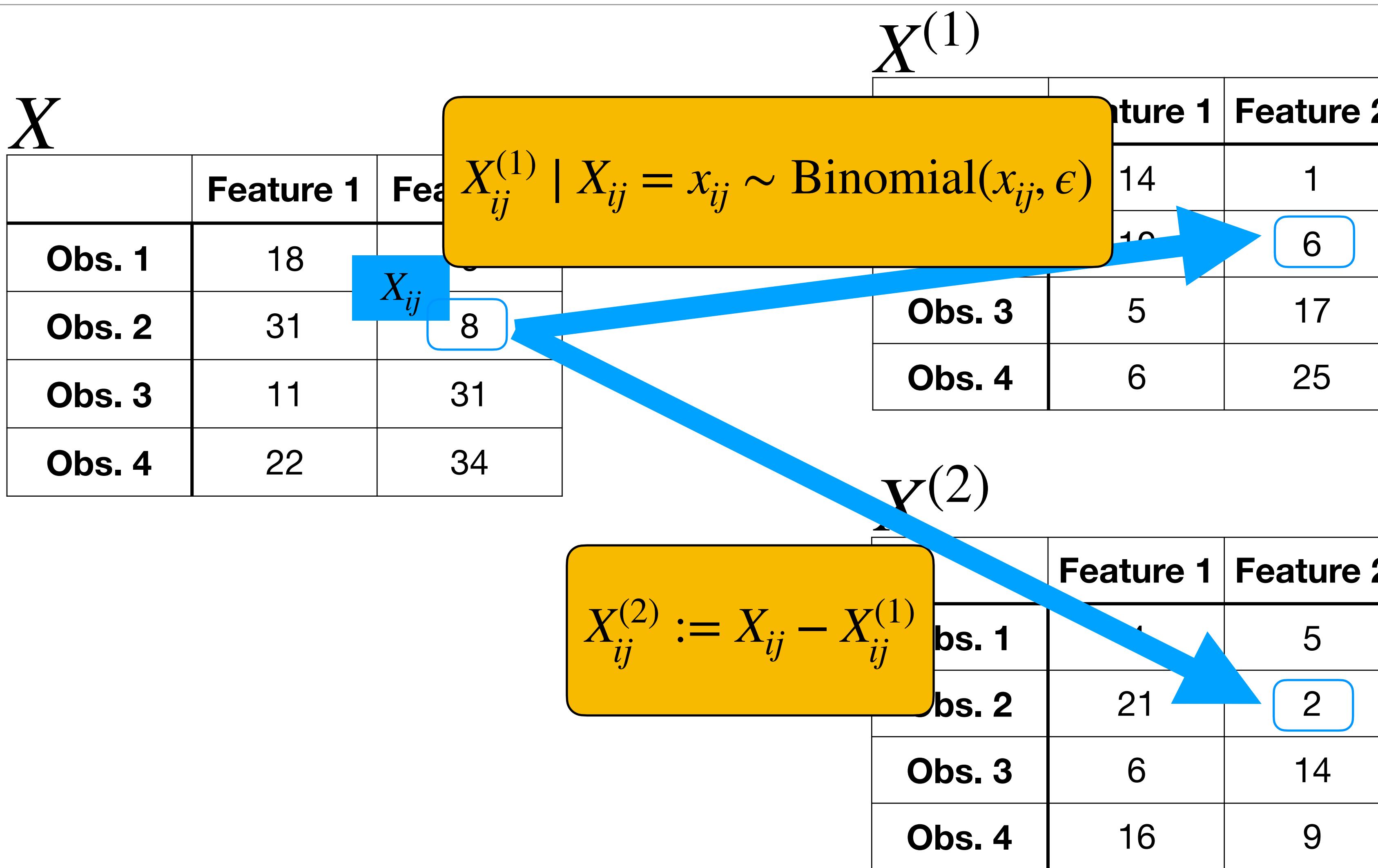
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Poisson thinning



Poisson thinning

X			$X^{(1)}$	$X^{(2)}$
	Feature 1	Feature 2		
Obs. 1	18	X_{ij}	$X_{ij}^{(1)} \mid X_{ij} = x_{ij} \sim \text{Binomial}(x_{ij}, \epsilon)$	14
Obs. 2	31	8		10
Obs. 3	11	31		5
Obs. 4	22	34		25

If $X_{ij} \sim \text{Poisson}(\Lambda_{ij})$, then:

1. $X_{ij}^{(1)} \sim \text{Poisson}(\epsilon \Lambda_{ij})$
2. $X_{ij}^{(2)} \sim \text{Poisson}((1 - \epsilon) \Lambda_{ij})$
3. $X_{ij}^{(1)} \perp\!\!\!\perp X_{ij}^{(2)}$

	$X^{(1)}$	$X^{(2)}$
	Feature 1	Feature 2
Obs. 1	14	5
Obs. 2	21	2
Obs. 3	6	14
Obs. 4	16	9

A very well-known result.

Poisson thinning

X

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	Feature 1	Feature 2
Obs. 1	18	14
Obs. 2	31	10
Obs. 3	11	5
Obs. 4	22	6
	31	17
	6	25

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$X^{(1)}$

$X_{ij}^{(1)} \mid X_{ij} = x_{ij} \sim \text{Binomial}(x_{ij}, \epsilon)$

X_{ij}

8

Select hypothesis.

$X^{(2)}$

$X_{ij}^{(2)} := X_{ij} - X_{ij}^{(1)}$

	Feature 1	Feature 2
Obs. 1	1	5
Obs. 2	21	2
Obs. 3	6	14
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A very well-known result.

Poisson thinning

X

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$X^{(1)}$

Select hypothesis.

X_{ij}

8

$X^{(2)}$

$X_{ij}^{(2)} := X_{ij} - X_{ij}^{(1)}$

	Feature 1	Feature 2
Obs. 1	1	5
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Test hypothesis.

A very well-known result.

Poisson thinning

	$X^{(1)}$	
	Feature 1	Feature 2
Obs. 1	18	14
Obs. 2	31	10
Obs. 3	11	5
Obs. 4	22	6

X

	Feature 1	Feature 2
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X_{ij}

$X_{ij}^{(1)} \mid X_{ij} = x_{ij} \sim \text{Binomial}(x_{ij}, \epsilon)$

Fit model.

If $X_{ij} \sim \text{Poisson}(\Lambda_{ij})$, then:

1. $X_{ij}^{(1)} \sim \text{Poisson}(\epsilon \Lambda_{ij})$
2. $X_{ij}^{(2)} \sim \text{Poisson}((1 - \epsilon) \Lambda_{ij})$
3. $X_{ij}^{(1)} \perp\!\!\!\perp X_{ij}^{(2)}$

	Feature 1	Feature 2
Obs. 1	4	5
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$X^{(2)}$

$X_{ij}^{(2)} := X_{ij} - X_{ij}^{(1)}$

A very well-known result.

Poisson thinning

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Obs. 1	18	14
Obs. 2	31	10
Obs. 3	11	5
Obs. 4	22	6

X_{ij}

$X_{ij}^{(1)} \mid X_{ij} = x_{ij} \sim \text{Binomial}(x_{ij}, \epsilon)$

Fit model.

$X^{(2)}$

	Feature 1	Feature 2
Obs. 1	1	5
Obs. 2	21	2
Obs. 3	6	14
Obs. 4	16	9

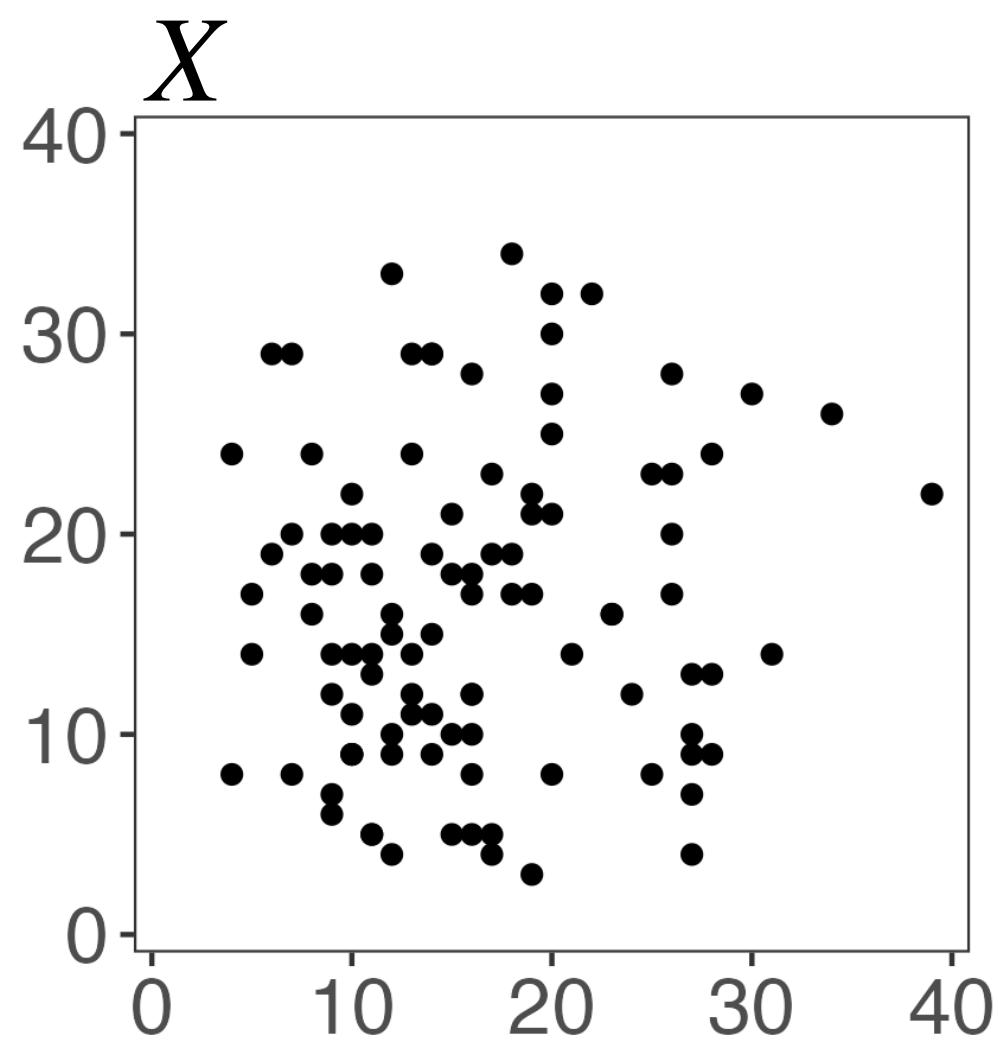
Evaluate model.

If $X_{ij} \sim \text{Poisson}(\Lambda_{ij})$, then:

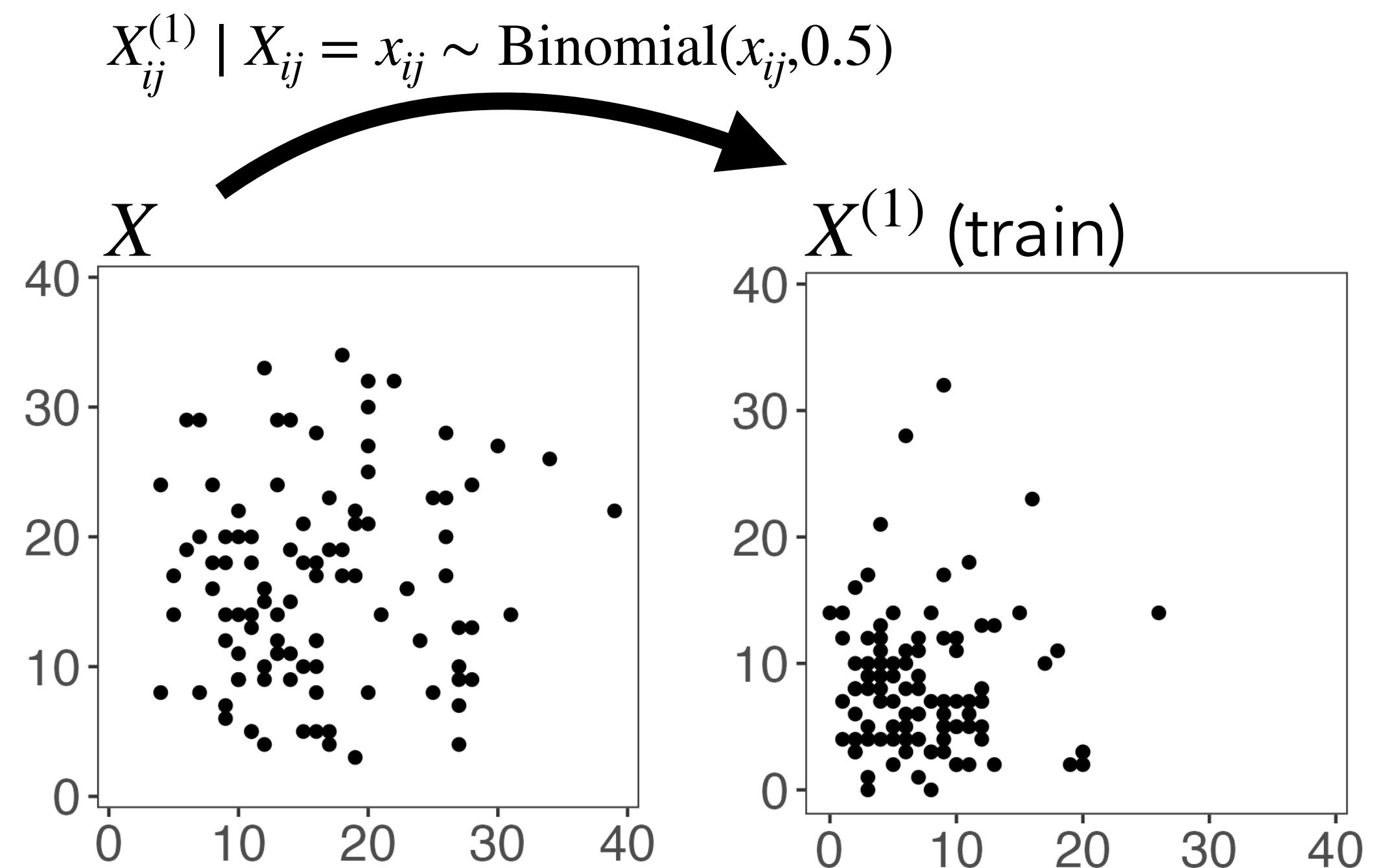
1. $X_{ij}^{(1)} \sim \text{Poisson}(\epsilon \Lambda_{ij})$
2. $X_{ij}^{(2)} \sim \text{Poisson}((1 - \epsilon) \Lambda_{ij})$
3. $X_{ij}^{(1)} \perp\!\!\!\perp X_{ij}^{(2)}$

A very well-known result.

Thinning avoids the pitfall of sample splitting on our motivating examples

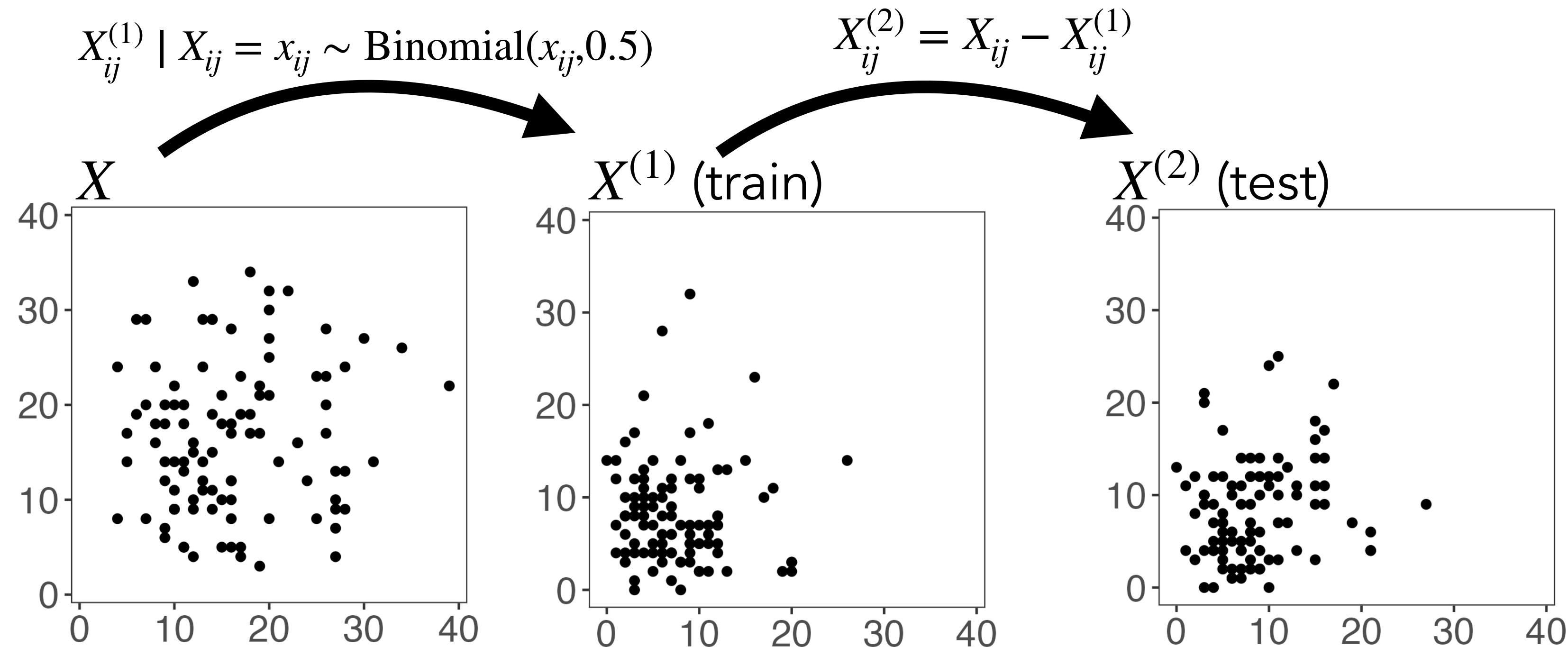


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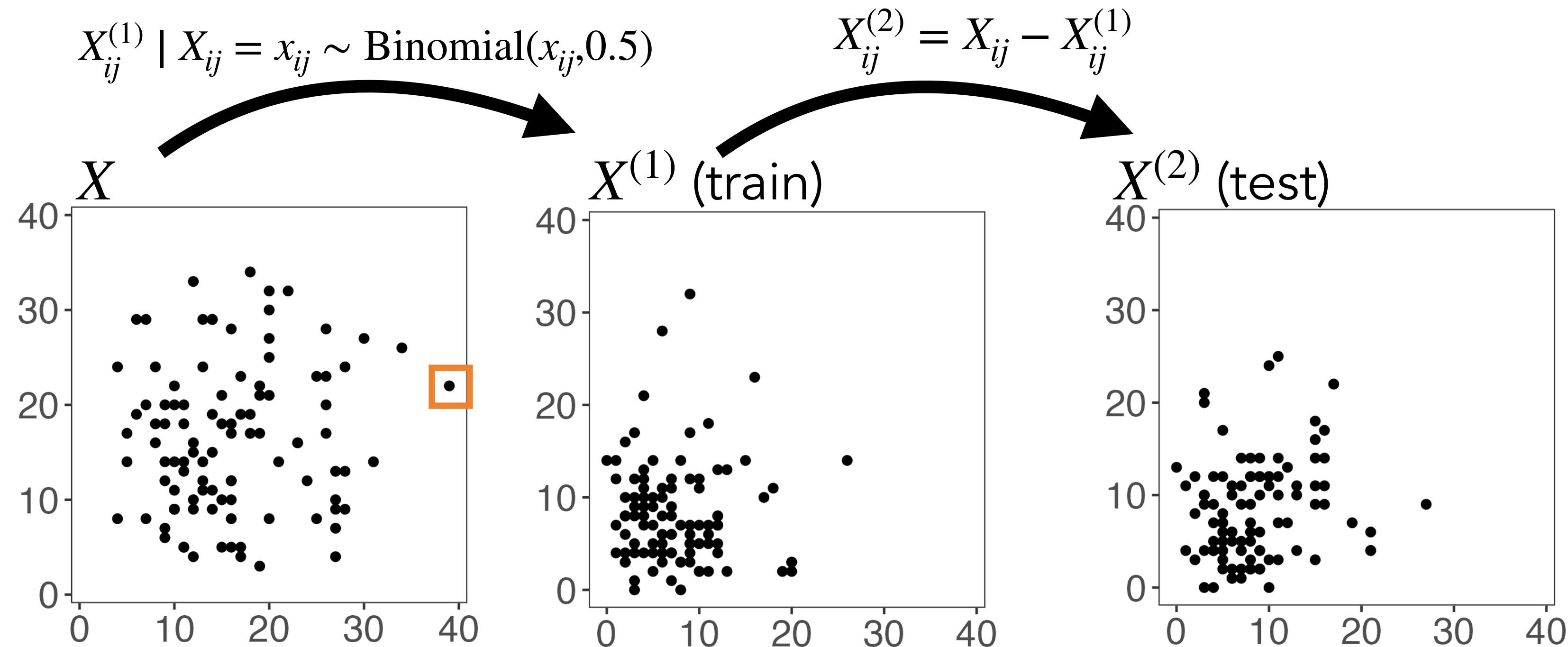
Step 1: thin observations into train/test.

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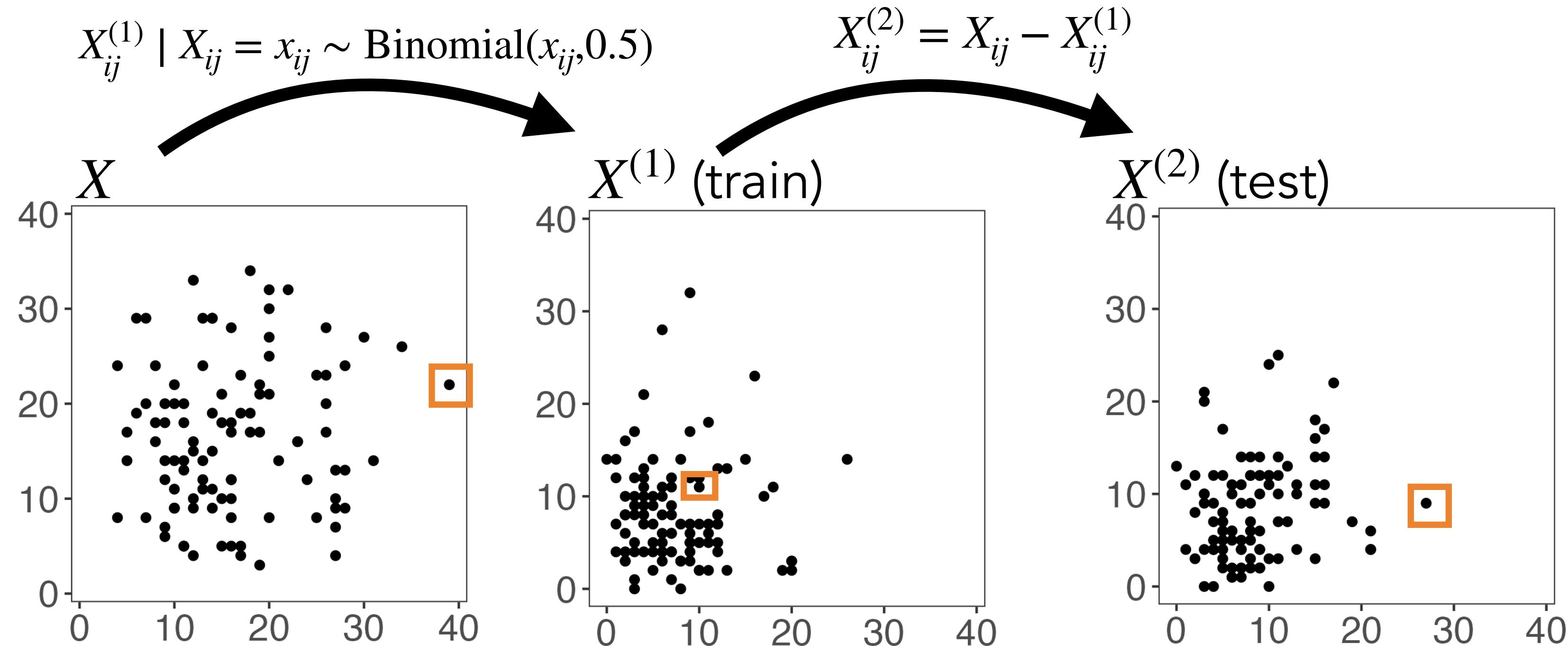
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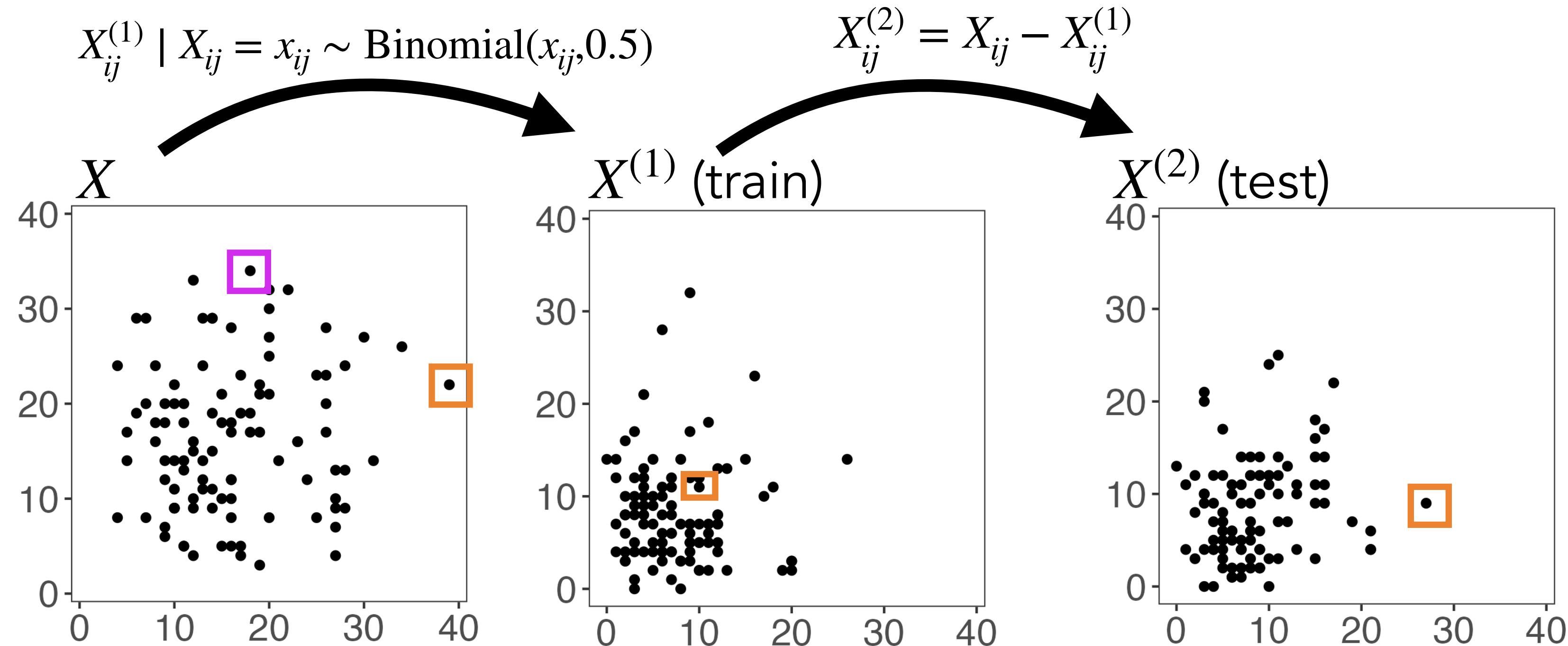
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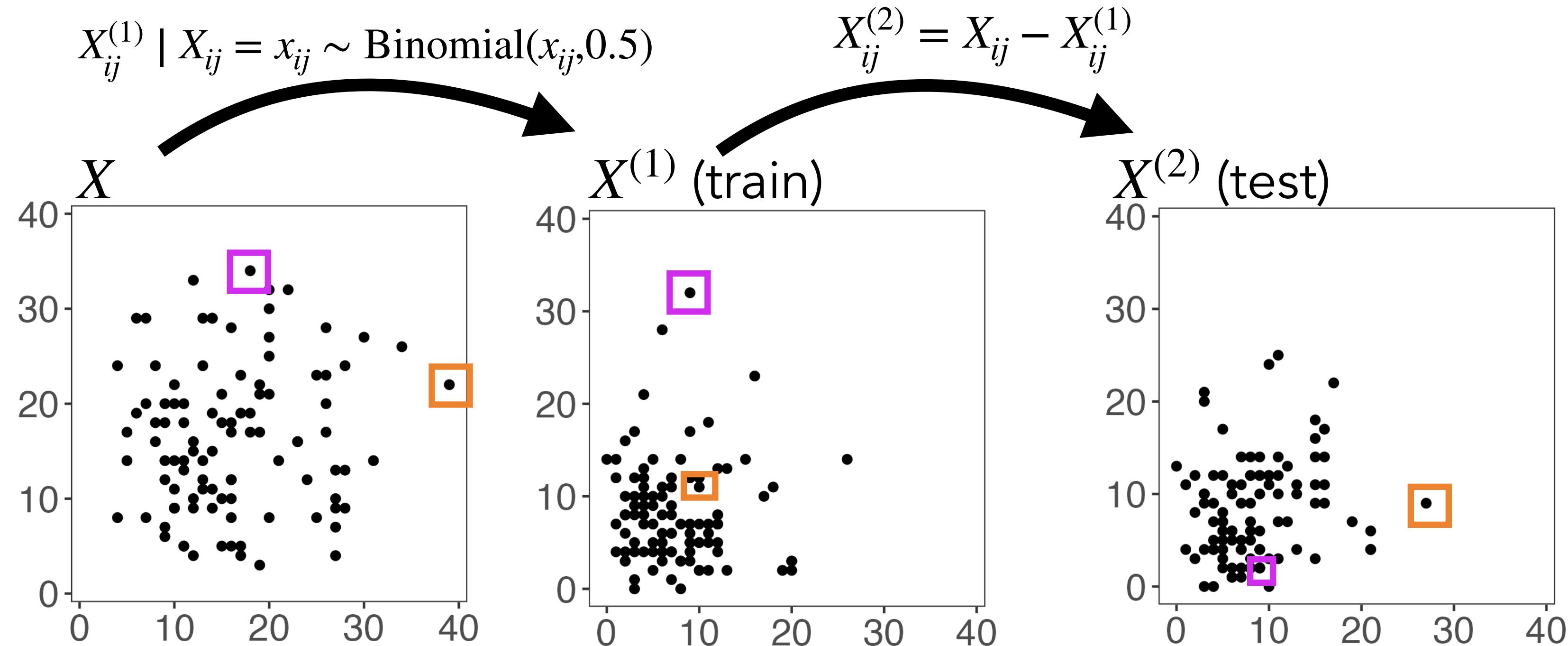
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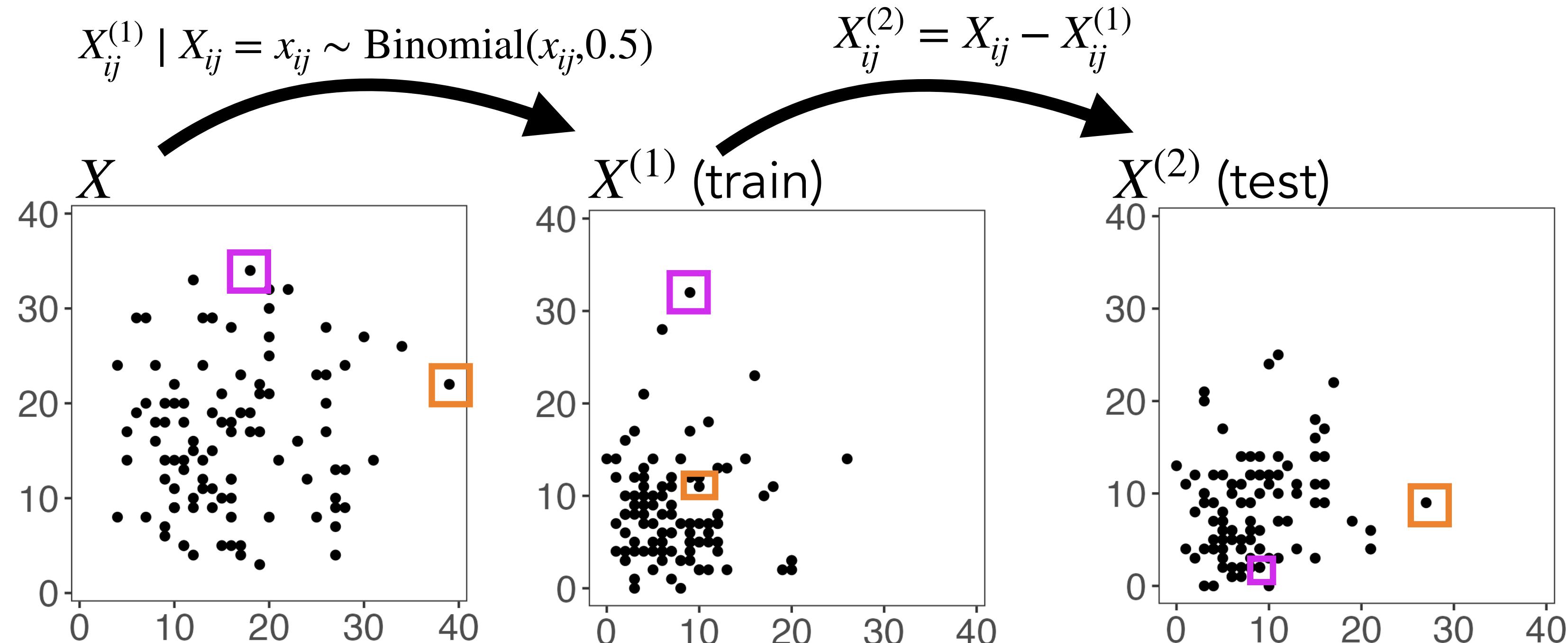
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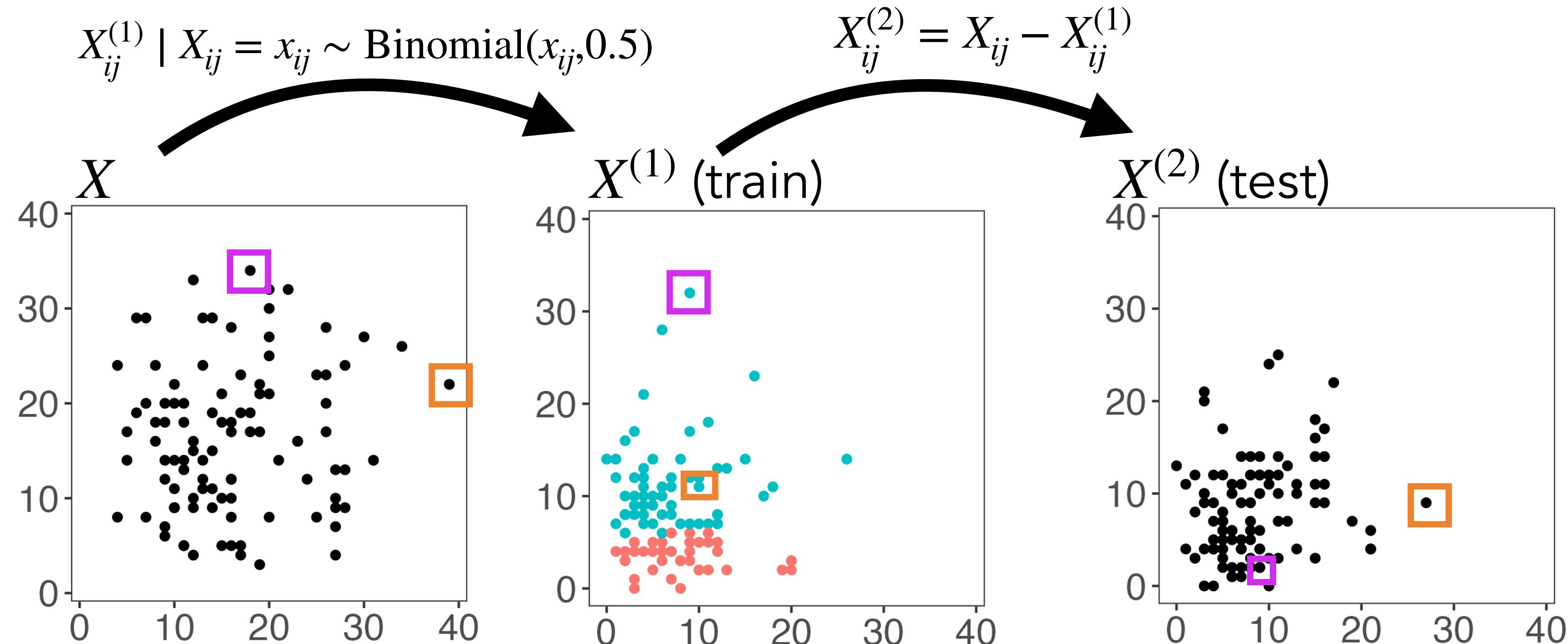
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Step 1: thin observations into train/test.

Step 2: cluster the training set.

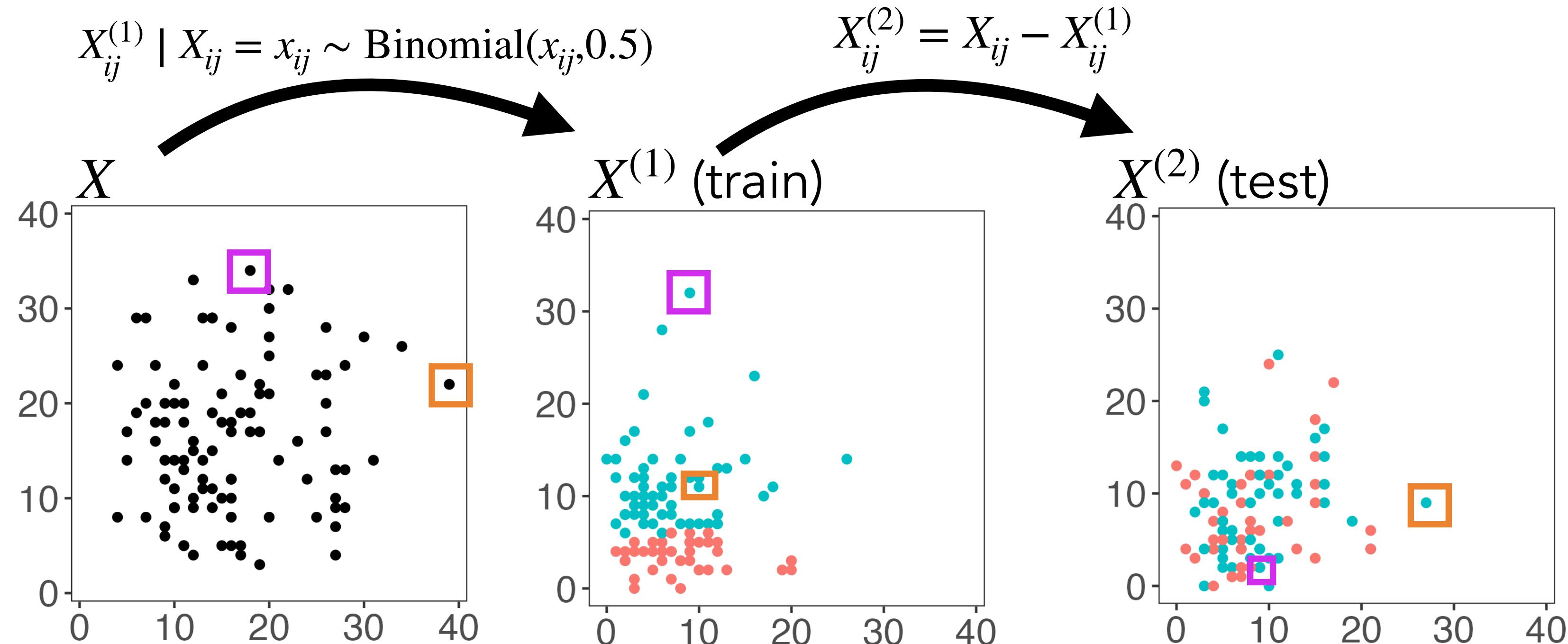
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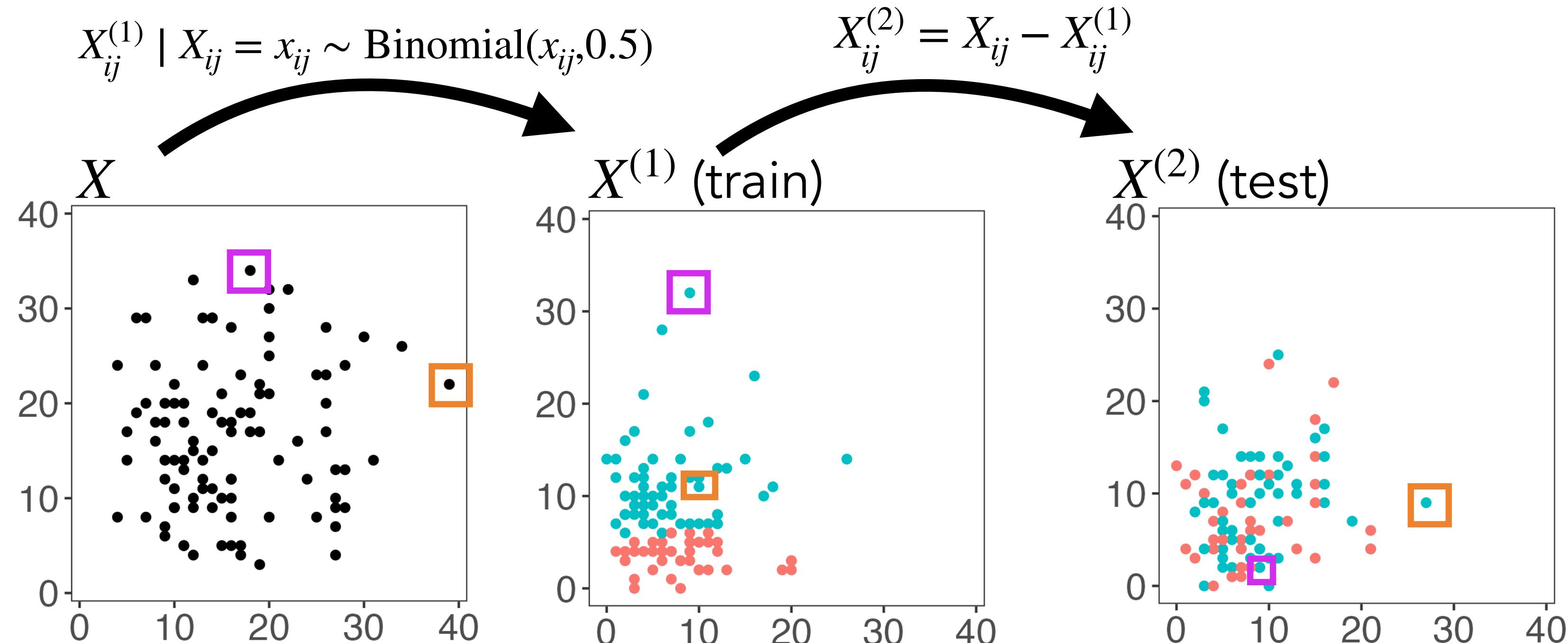
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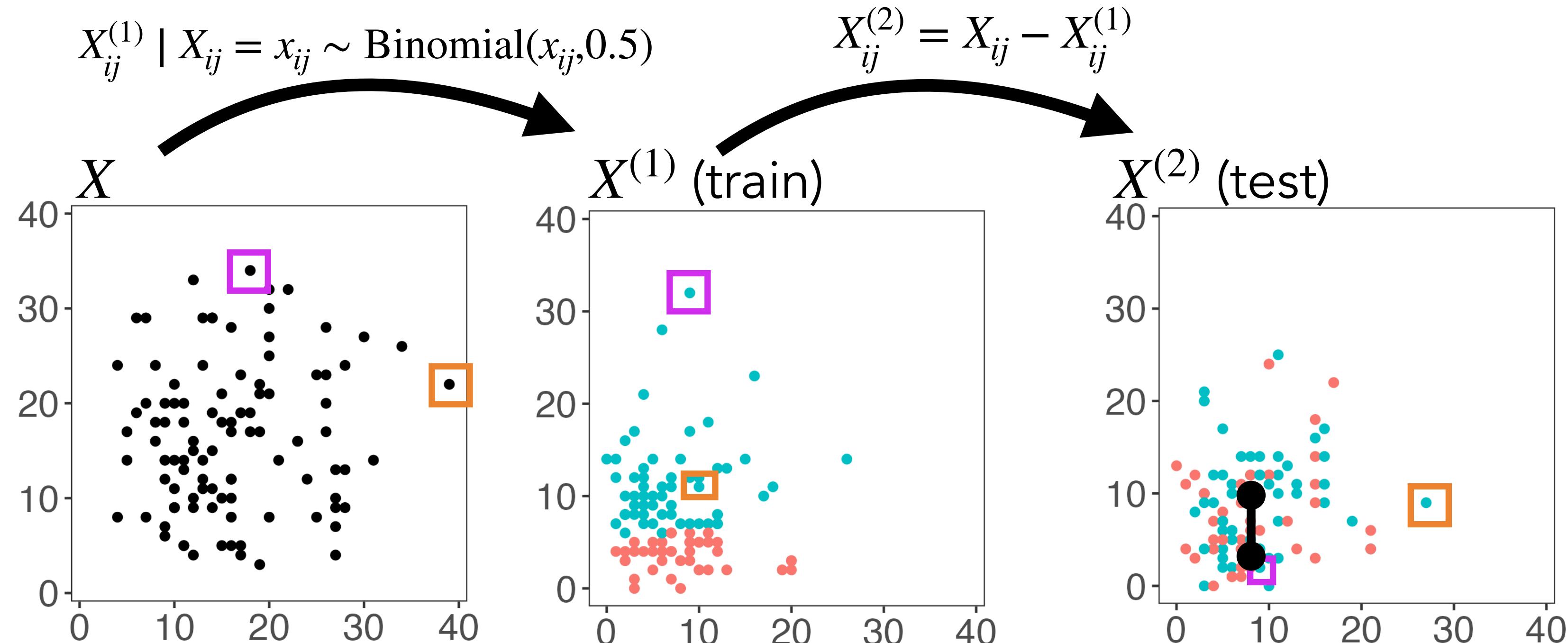


Step 1: thin observations into train/test.

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Step 3: test for difference in means or evaluate clusters on test set.

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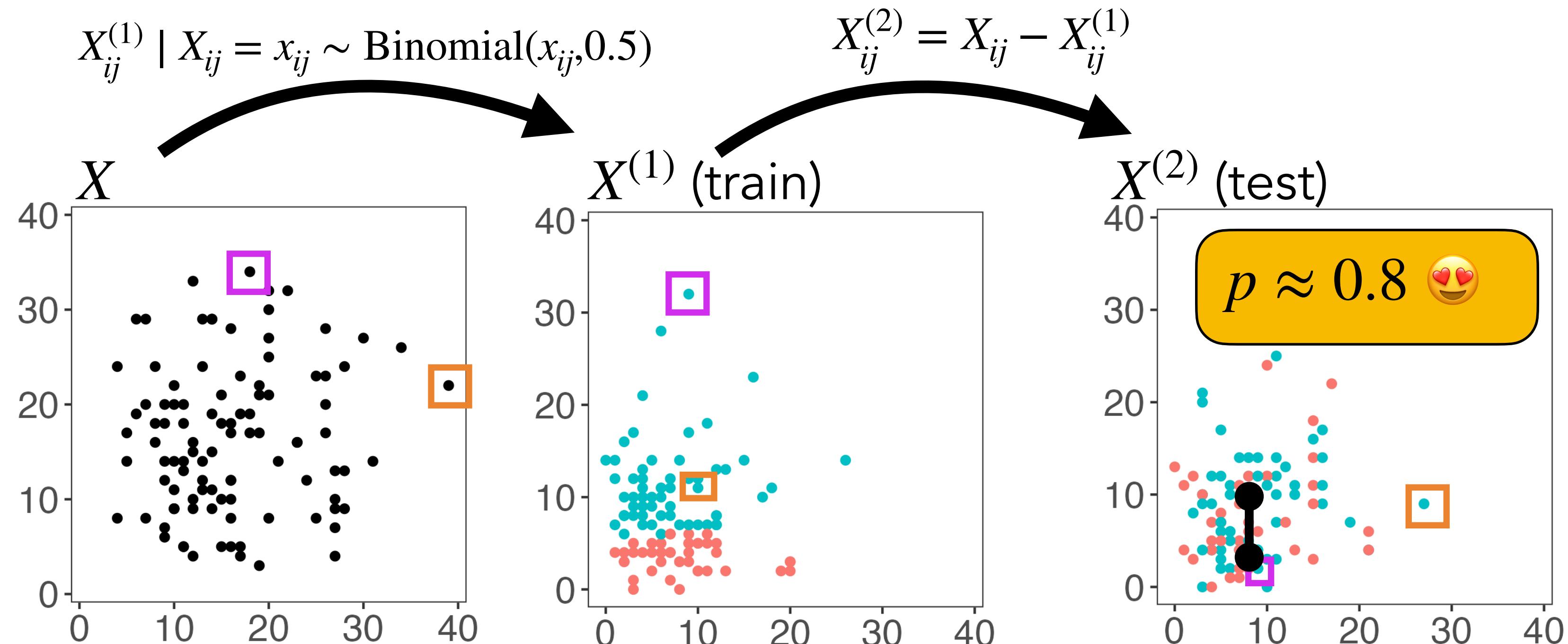


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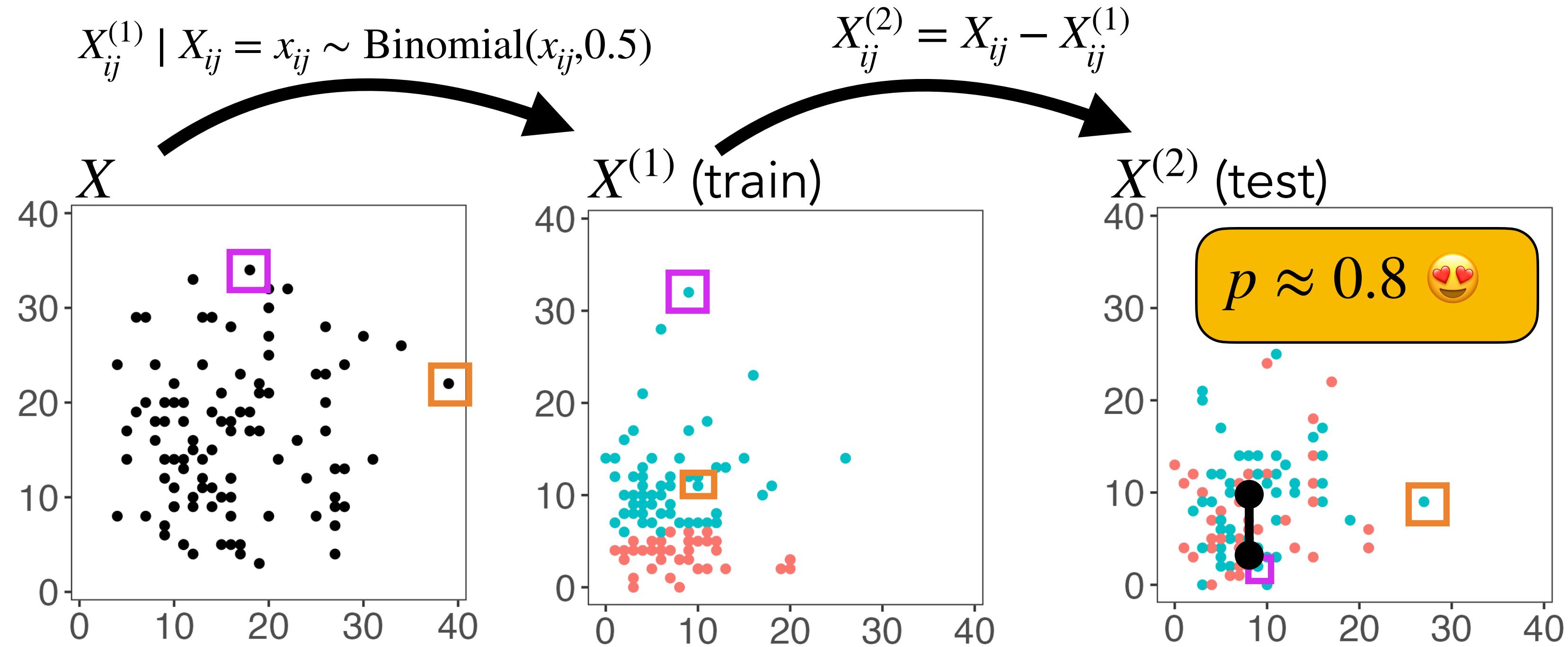


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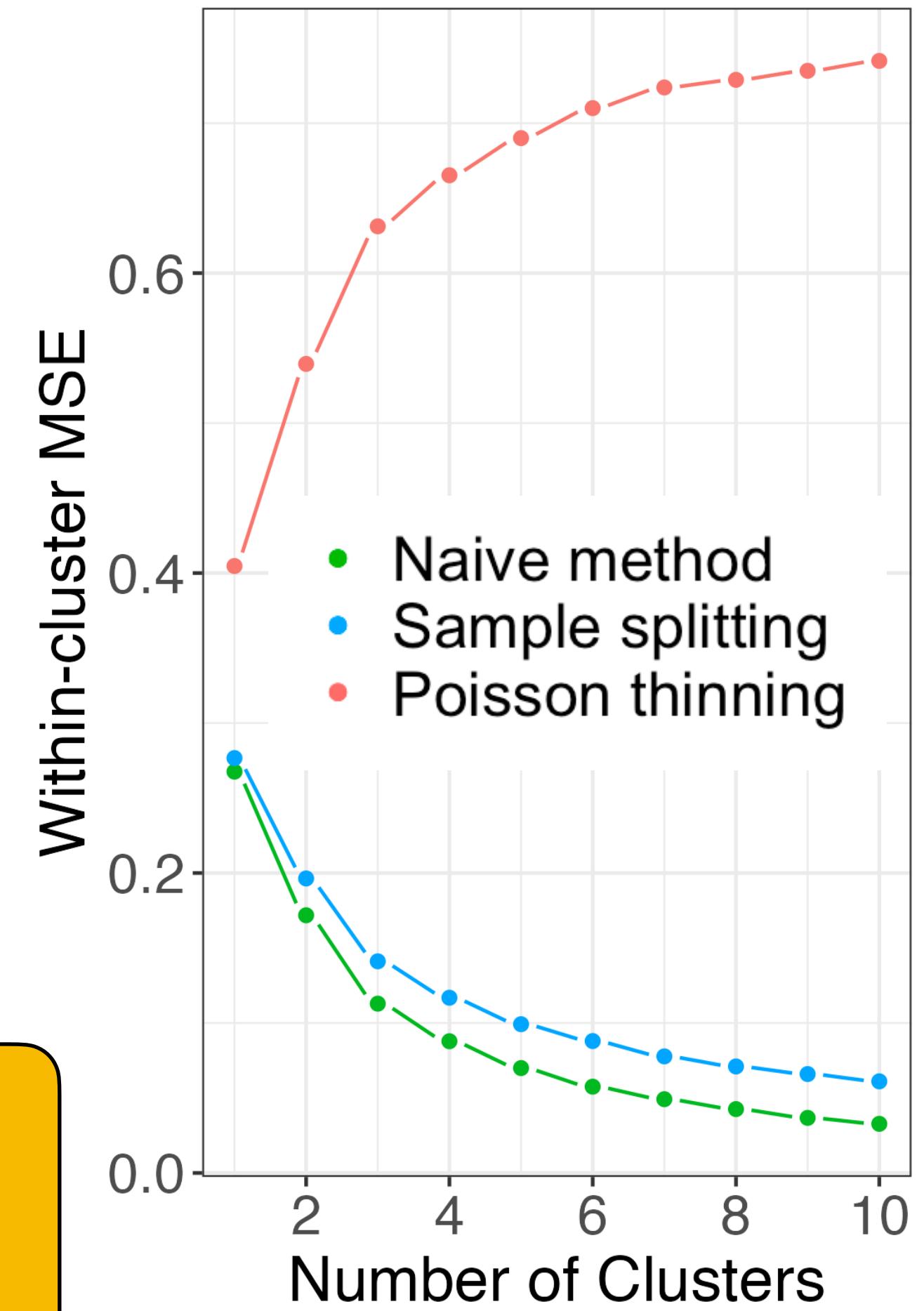
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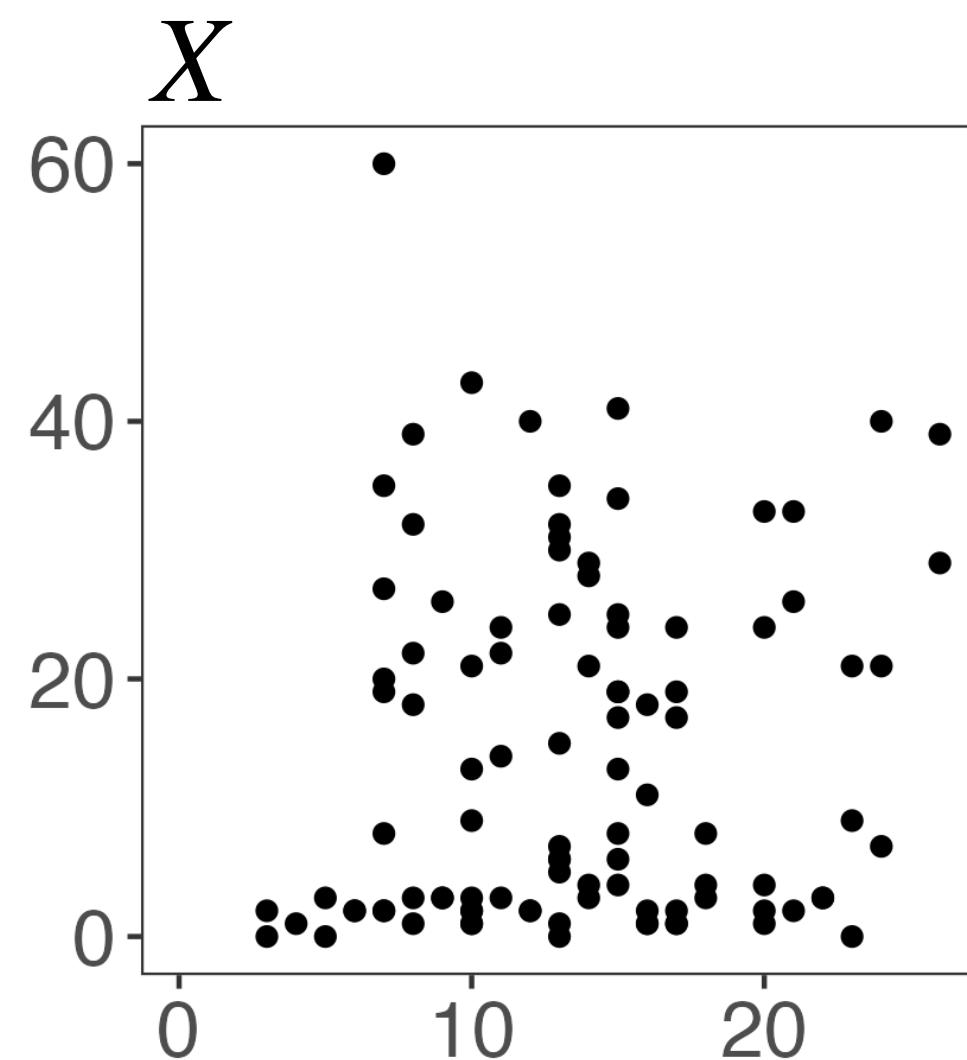
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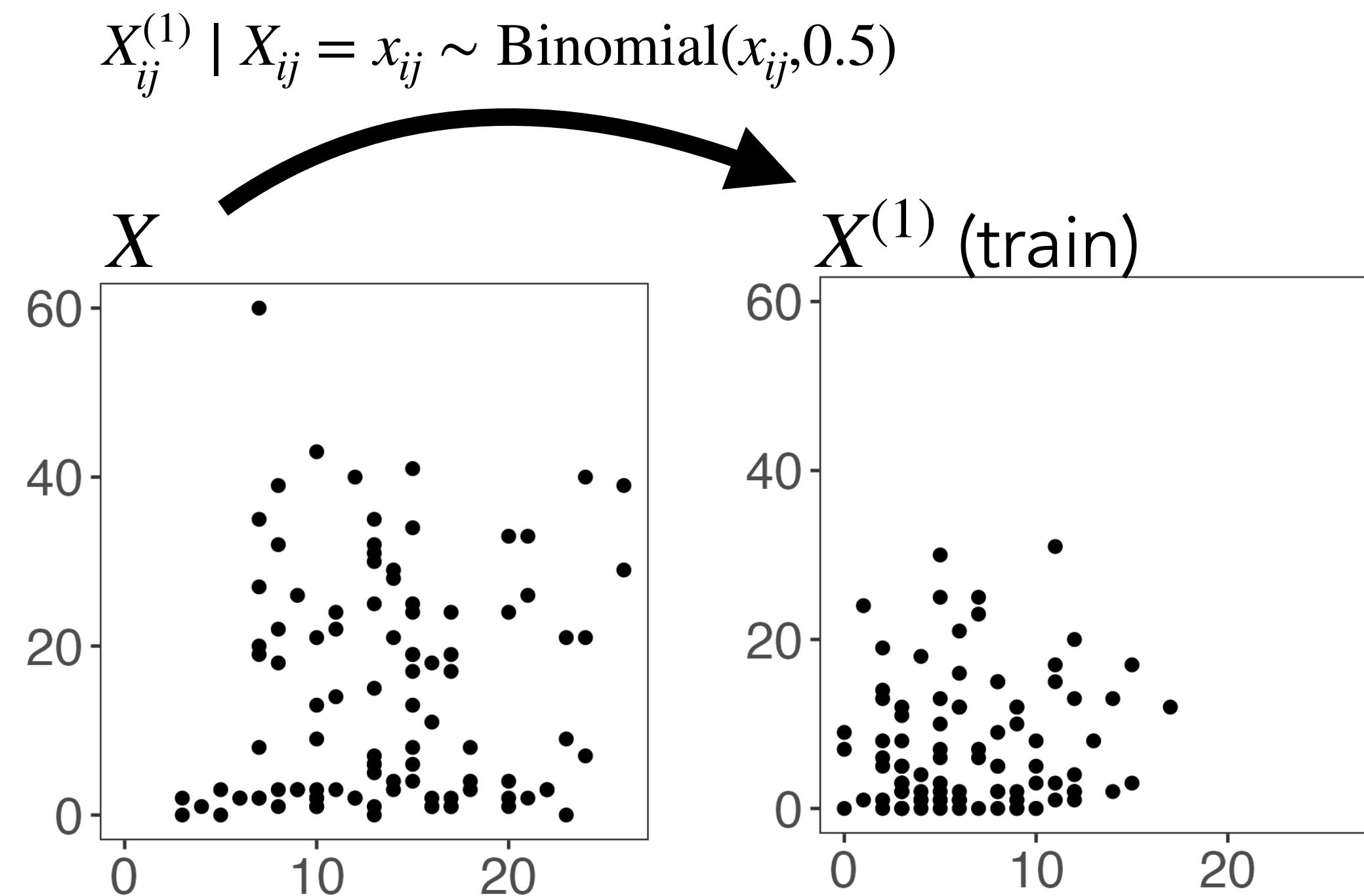


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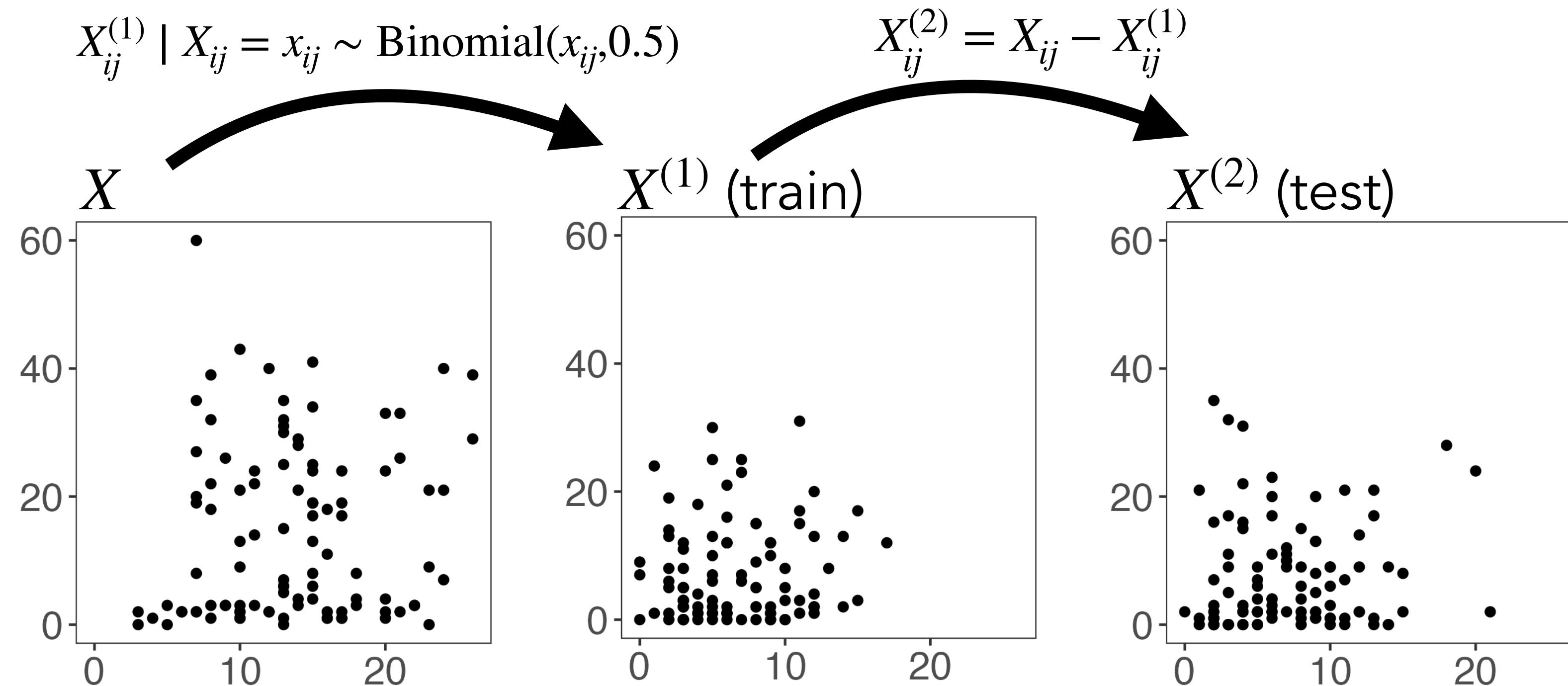
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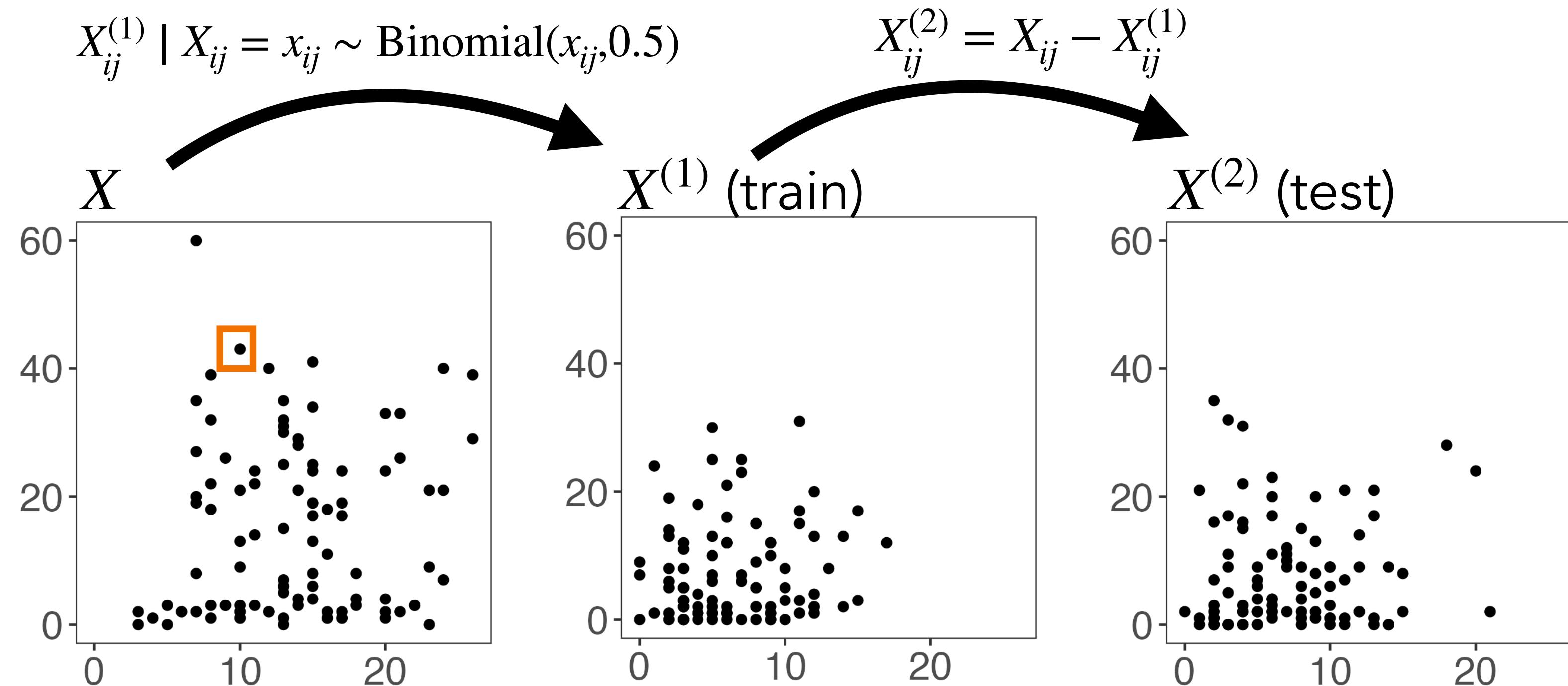
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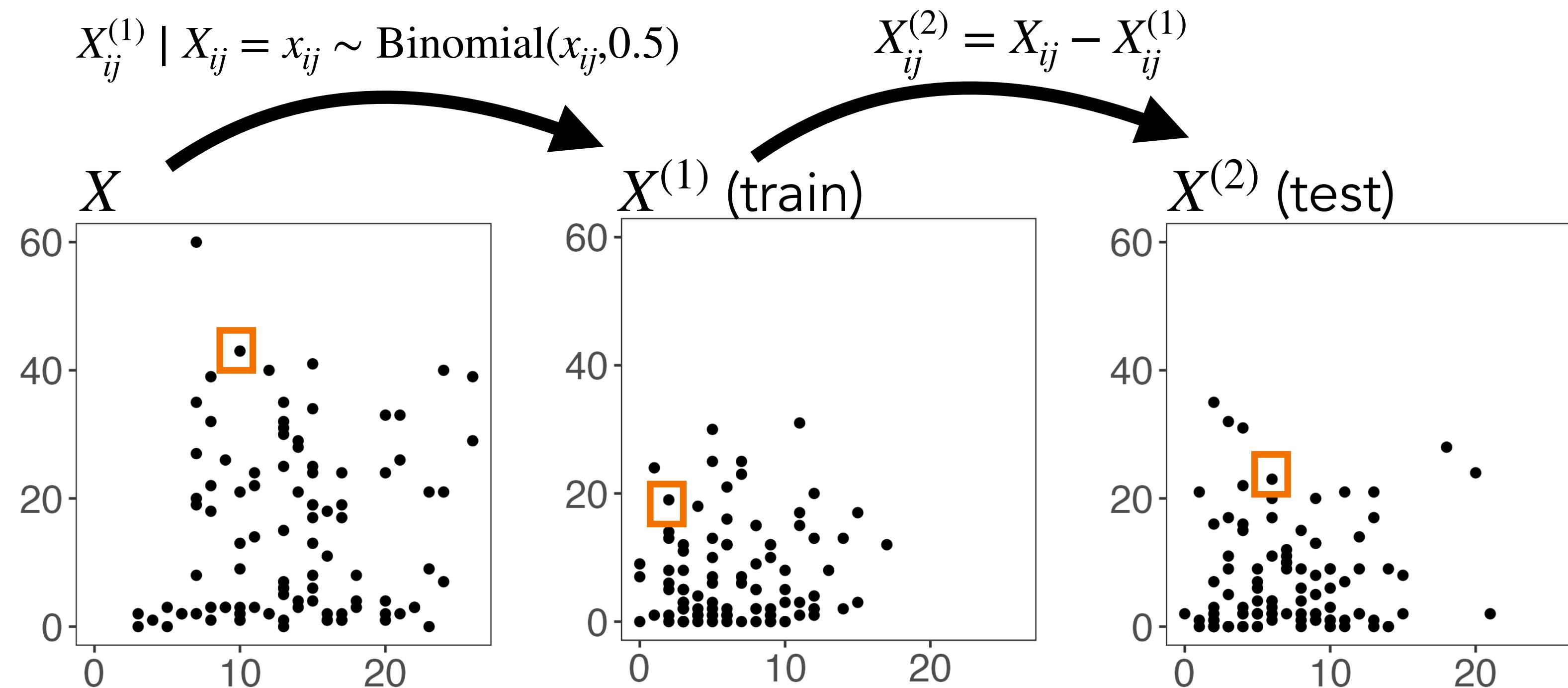
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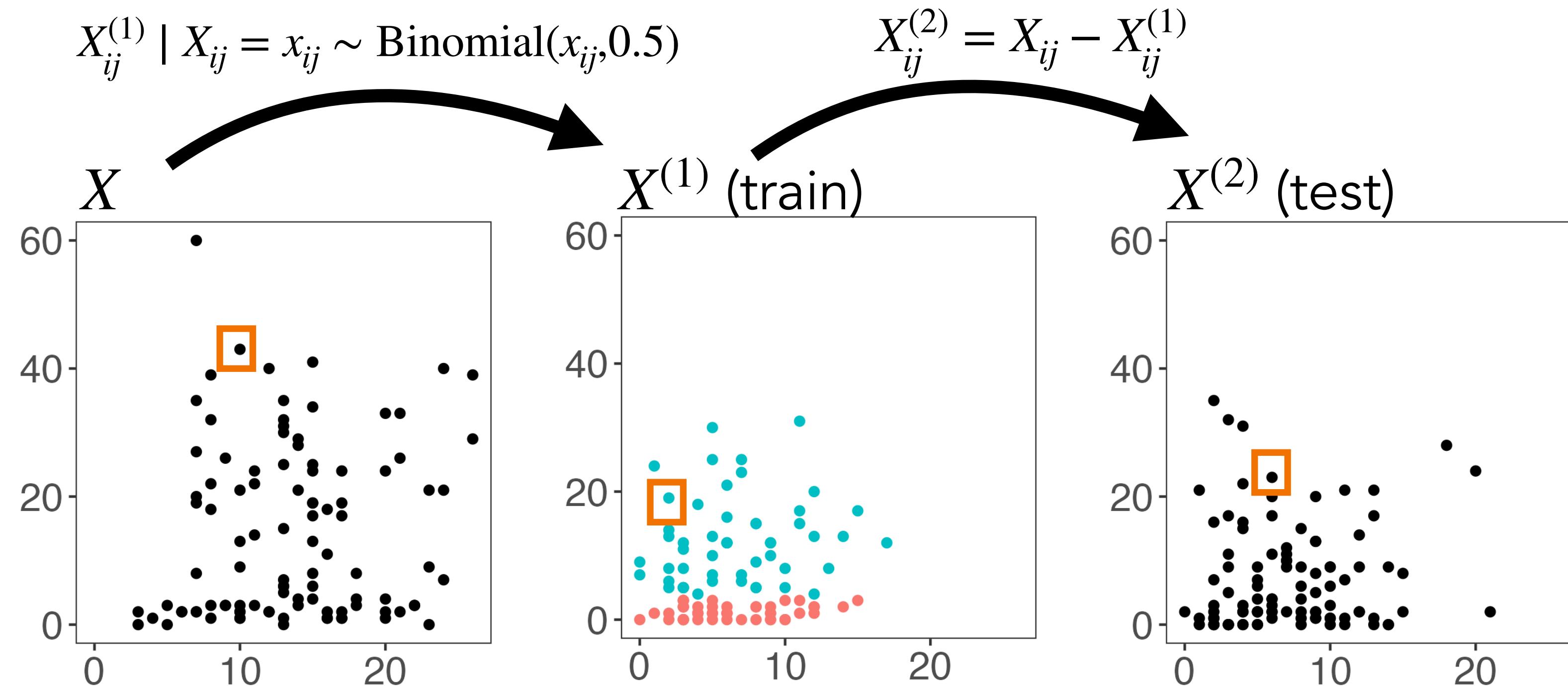
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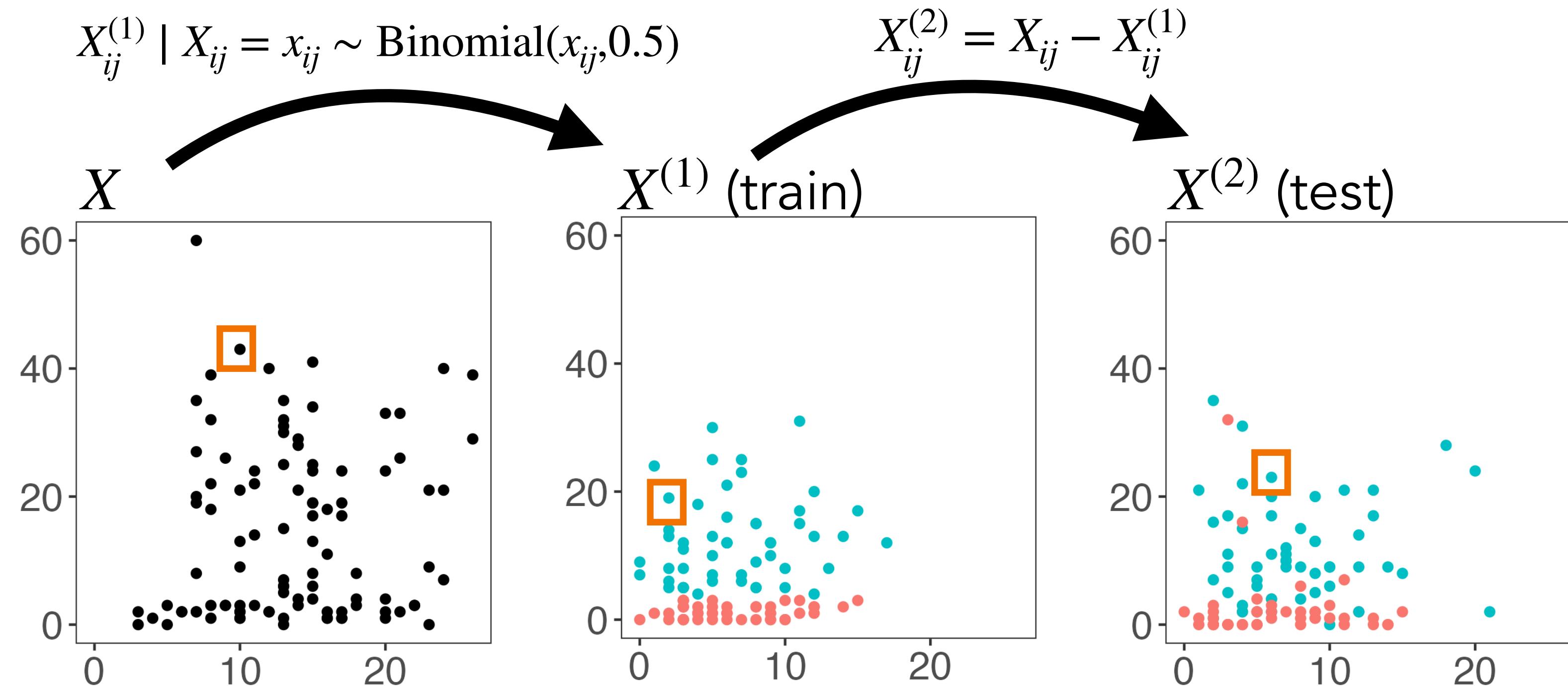
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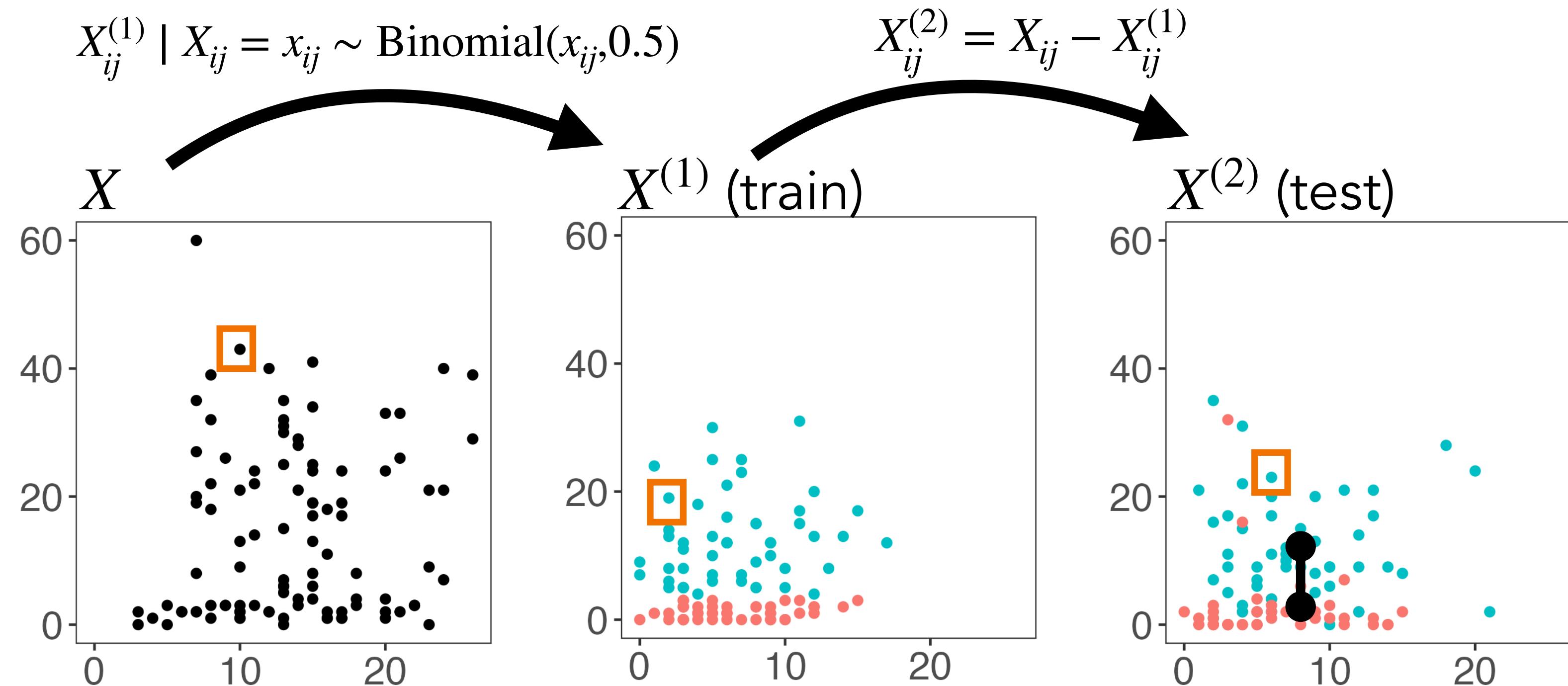
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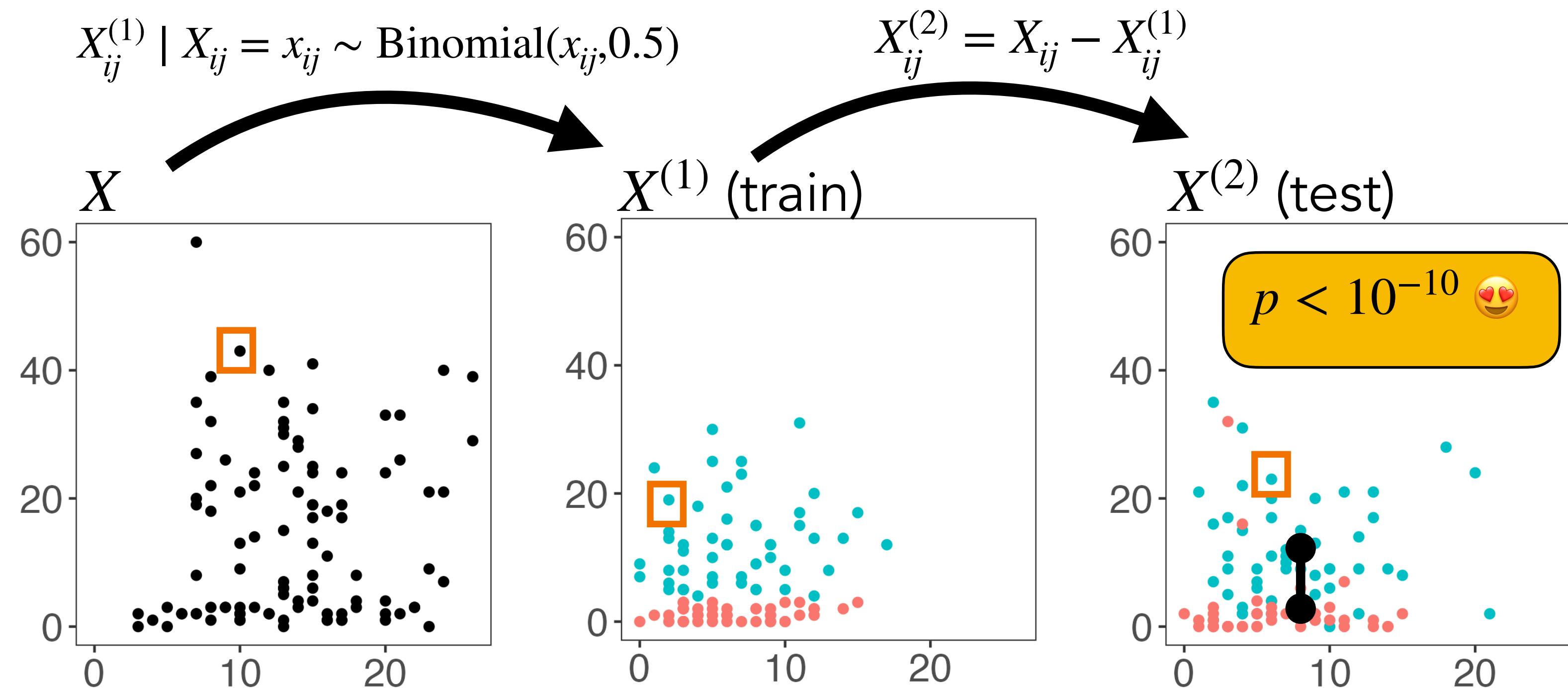
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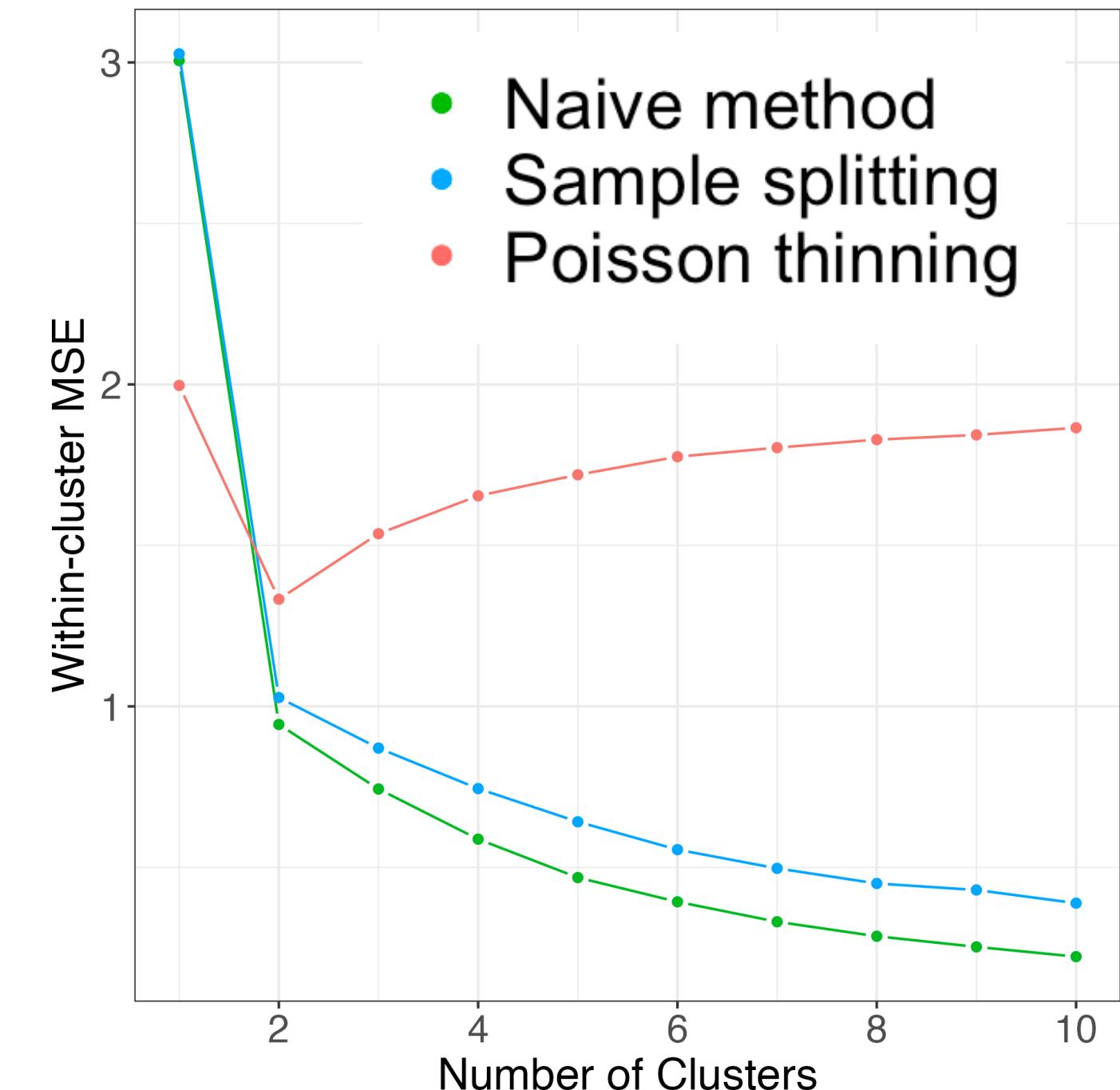
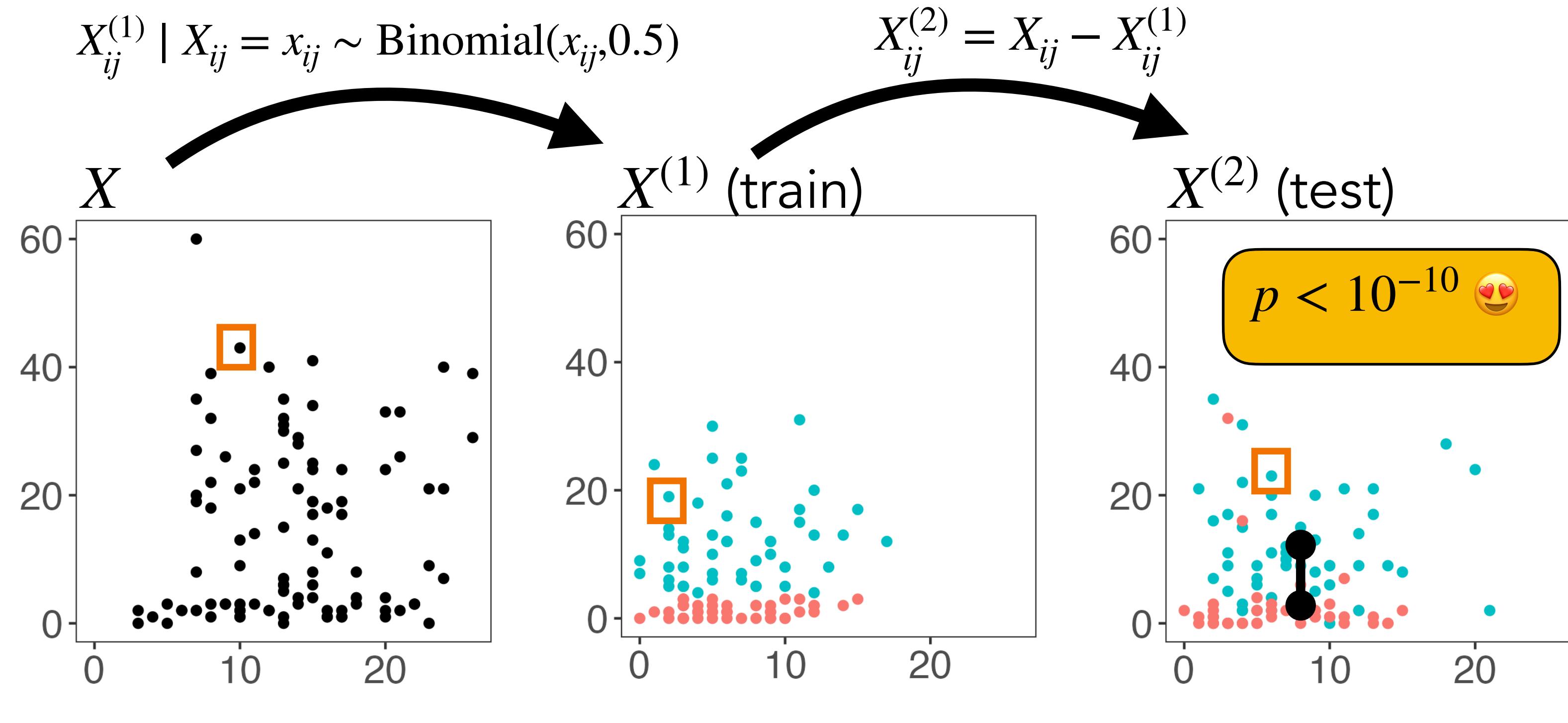
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Poisson thinning is useful in the analysis of single-cell RNA sequencing data

Lähnemann et al. *Genome Biology* (2020) 21:31
<https://doi.org/10.1186/s13059-020-1926-6>

Genome Biology

REVIEW

Open Access

Eleven grand challenges in single-cell data science



David Lähnemann^{1,2,3}, Johannes Köster^{1,4}, Ewa Szczurek⁵, Davis J. McCarthy^{6,7}, Stephanie C. Hicks⁸, Mark D. Robinson⁹ Catalina A. Vallejos^{10,11}, Kieran R. Campbell^{12,13,14}, Niko Beerenwinkel^{15,16}, Ahmed Mahfouz^{17,18}, Luca Pinello^{19,20,21}, Pavel Skums²², Alexandros Stamatakis^{23,24}, Camille Stephan-Otto Attolini²⁵, Samuel Aparicio^{13,26}, Jasmijn Baaijens²⁷, Marleen Balvert^{27,28}, Buys de Barbanson^{29,30,31}, Antonio Cappuccio³², Giacomo Corleone³³, Bas E. Dutilh^{28,34}, Maria Florescu^{29,30,31}, Victor Guriev³⁵, Rens Holmer³⁶, Katharina Jahn^{15,16}, Thamar Jessurun Lobo³⁵, Emma M. Keizer³⁷, Tzu-Hao Kuo³, Tobias Marschall⁴⁷, Jeroen de Ridder²⁹, Fabian J. Theis⁵⁴, H Sohrab P. Shah⁵⁹

Status

Currently, the vast majority of differential expression detection methods assume that the groups of cells to be compared are known in advance (e.g., experimental conditions or cell types). However, current analysis pipelines typically rely on clustering or cell type assignment to identify such groups, before downstream differential analysis is performed, without propagating the uncertainty in these assignments or accounting for the double use of data (clustering, differential testing between clusters).

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Project 2

Biostatistics (2022) **00**, 00, pp. 1–18
<https://doi.org/10.1093/biostatistics/kxac047>

C

Inference after latent variable estimation for single-cell RNA sequencing data

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Department of Biomedical Engineering, Johns Hopkins University, Baltimore, MD 21218, USA and
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DANIELA WITTEN

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Biostatistics, University of Washington, Seattle, WA 98195, USA

R package and tutorials:
<https://anna-neufeld.github.io/countspl/>

But generalizations of Poisson thinning are needed

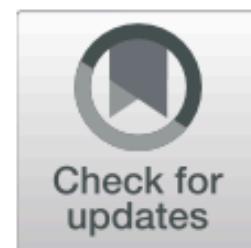
Choudhary and Satija *Genome Biology* (2022) 23:27
<https://doi.org/10.1186/s13059-021-02584-9>

Genome Biology

RESEARCH

Open Access

Comparison and evaluation of statistical error models for scRNA-seq



Saket Choudhary¹ and Rahul Satija^{1,2*} 

Results: Here, we analyze 59 scRNA-seq datasets that span a wide range of technologies, systems, and sequencing depths in order to evaluate the performance of different error models. We find that while a Poisson error model appears appropriate for sparse datasets, we observe clear evidence of overdispersion for genes with sufficient sequencing depth in all biological systems, necessitating the use of a negative binomial model. Moreover, we find that the degree of overdispersion varies widely across datasets, systems, and gene abundances, and argues for a data-driven approach for parameter estimation.

Outline

1. Motivation: settings where sample splitting doesn't work
2. Poisson thinning
3. **Data thinning**
4. Application to single-cell RNA sequencing data
5. Ongoing work

What did we like about Poisson thinning?

We split a single observation X into $X^{(1)}$ and $X^{(2)}$ such that:

- (1) $X^{(1)}$ and $X^{(2)}$ have the same distribution as X , up to a parameter scaling.
- (2) $X^{(1)} \perp\!\!\!\perp X^{(2)}$.

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Can we achieve these same properties when X is not Poisson?

Data thinning

Goal: split a single observation X into $X^{(1)}$ and $X^{(2)}$ such that:

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J. Appl. Prob. 33, 664–677 (1996)
Printed in Israel
© Applied Probability Trust 1996

**TIME SERIES MODELS WITH UNIVARIATE MARGINS
IN THE CONVOLUTION-CLOSED INFINITELY DIVISIBLE CLASS**

HARRY JOE,* *University of British Columbia*

Convolution-closed distributions

A family of distributions F_λ is “convolution-closed” in parameter λ if

- $X' \sim F_{\lambda_1}$
- $X'' \sim F_{\lambda_2}$
- $X' \perp\!\!\!\perp X''$

together imply that

$$X' + X'' \sim F_{\lambda_1 + \lambda_2}.$$

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together imply that

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Distribution	Convolution-closed in:
$X \sim \text{Poisson}(\lambda)$	λ
$X \sim N(\mu, \sigma^2)$	(μ, σ^2)
$X \sim \text{NegativeBinomial}(\mu, b)$	(μ, b)
$X \sim \text{Gamma}(\alpha, \beta)$	α , if β is fixed
$X \sim \text{Binomial}(r, p)$	r , if p is fixed
$X \sim N_k(\mu, \Sigma)$.	(μ, Σ) .
$X \sim \text{Multinomial}_k(r, p)$	r , if p is fixed
$X \sim \text{Wishart}_p(n, \Sigma)$	n , if p and Σ are fixed.

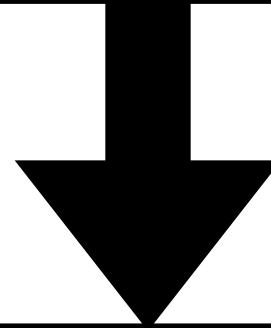
Data thinning for convolution-closed distributions

Data thinning for convolution-closed distributions

We observe realization x from $X \sim F_\lambda$.

Data thinning for convolution-closed distributions

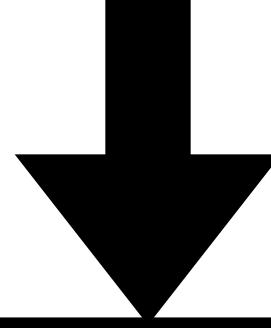
We know x could have arisen as $x' + x''$, where
 $X' \sim F_{\epsilon\lambda}$, $X'' \sim F_{(1-\epsilon)\lambda}$, $X' \perp\!\!\!\perp X''$.



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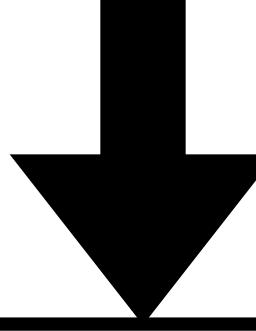


If we had observed x' and x'' , we would have satisfied our goal of data thinning!

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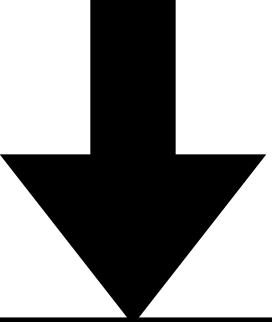
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Can we work backwards to recover x' and x'' ?

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Let $G_{\epsilon,x}$ be the conditional distribution of $X' | X = x$.

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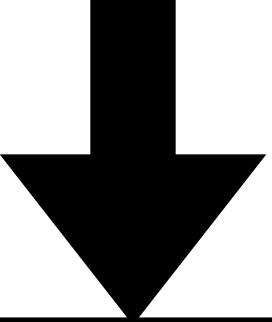
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Draw $X^{(1)}$ from $G_{\epsilon,x}$. Let $X^{(2)} := X - X^{(1)}$.

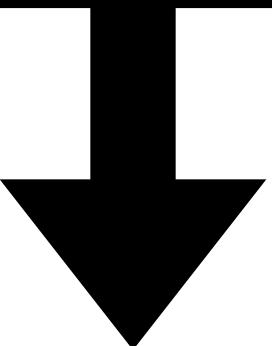
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Theorem:

$X^{(1)} \sim F_{\epsilon\lambda}$, $X^{(2)} \sim F_{(1-\epsilon)\lambda}$, $X^{(1)} \perp\!\!\!\perp X^{(2)}$.

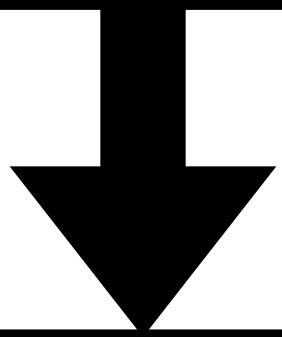
Data thinning for the Poisson distribution

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We observe realization x from $X \sim \text{Poisson}(\lambda)$.

Data thinning for the Poisson distribution

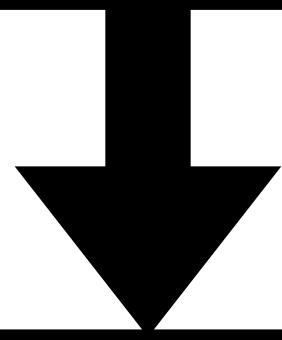
We know x could have arisen as $x' + x''$, where
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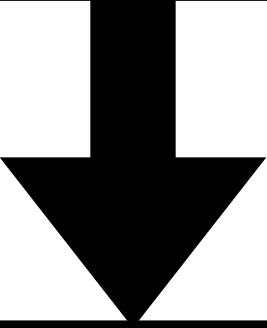


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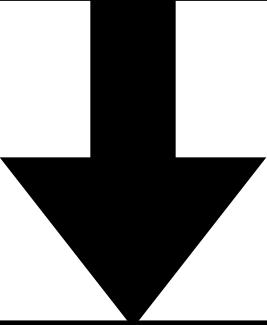
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Data thinning for the Poisson distribution

We know x could have arisen as $x' + x''$, where $X' \sim \text{Pois}(\epsilon\lambda)$, $X'' \sim \text{Pois}((1 - \epsilon)\lambda)$, $X' \perp\!\!\!\perp X''$.



We observe realization x from $X \sim \text{Poisson}(\lambda)$.

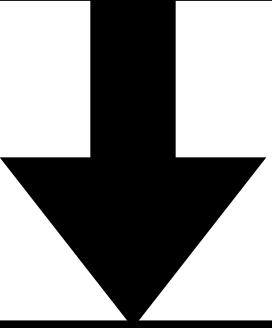
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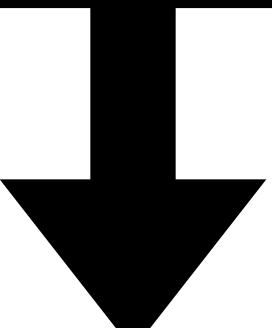
The conditional distribution of $X' | X = x$ is Binomial(x, ϵ).

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We observe realization x from $X \sim \text{Poisson}(\lambda)$.



Draw $X^{(1)}$ from $\text{Binomial}(x, \epsilon)$. Let $X^{(2)} := X - X^{(1)}$.

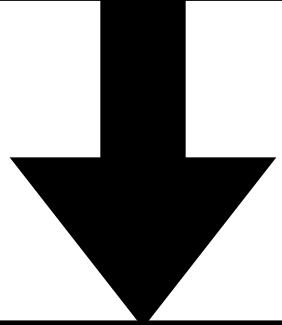
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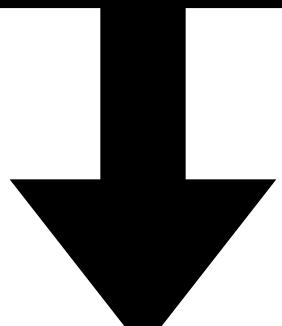
The conditional distribution of $X' | X = x$ is $\text{Binomial}(x, \epsilon)$.

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Can we work backwards to recover x' and x'' ?

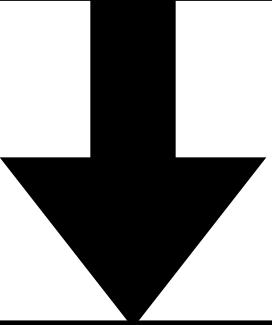
The conditional distribution of $X' | X = x$ is $\text{Binomial}(x, \epsilon)$.

Theorem:

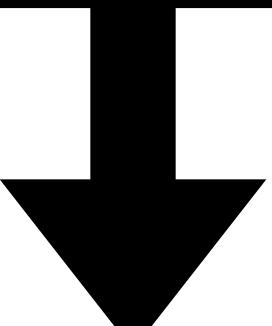
$X^{(1)} \sim \text{Pois}(\epsilon\lambda)$, $X^{(2)} \sim \text{Pois}((1 - \epsilon)\lambda)$, $X^{(1)} \perp\!\!\!\perp X^{(2)}$.

Data thinning for the Poisson distribution

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We observe realization x from $X \sim \text{Poisson}(\lambda)$.



Draw $X^{(1)}$ from $\text{Binomial}(x, \epsilon)$. Let $X^{(2)} := X - X^{(1)}$.

Theorem:

$X^{(1)} \sim \text{Pois}(\epsilon\lambda)$, $X^{(2)} \sim \text{Pois}((1 - \epsilon)\lambda)$, $X^{(1)} \perp\!\!\!\perp X^{(2)}$.

If we had observed x' and x'' , we would have satisfied our goal of data thinning!

Can we work backwards to recover x' and x'' ?

The conditional distribution of $X' | X = x$ is $\text{Binomial}(x, \epsilon)$.

We have recovered Poisson thinning!

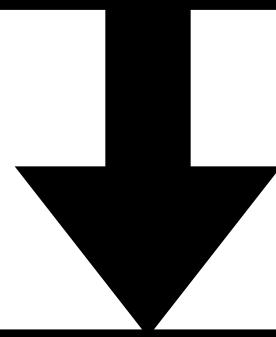
Data thinning for the Gaussian distribution

Data thinning for the Gaussian distribution

We observe realization x from $X \sim N(\mu, \sigma^2)$.

Data thinning for the Gaussian distribution

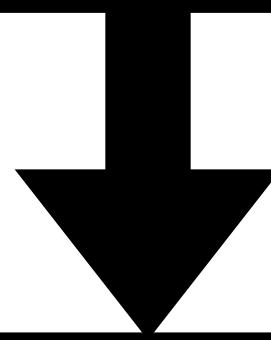
We know x could have arisen as $x' + x''$, where
 $X' \sim N(\epsilon\mu, \epsilon\sigma^2)$, $X'' \sim N((1 - \epsilon)\mu, (1 - \epsilon)\sigma^2)$, $X' \perp\!\!\!\perp X''$.



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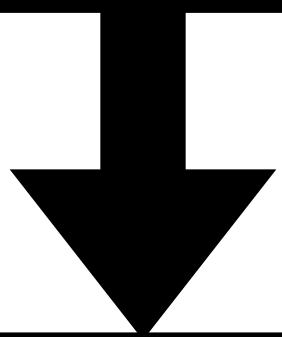


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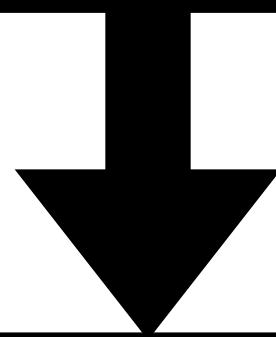
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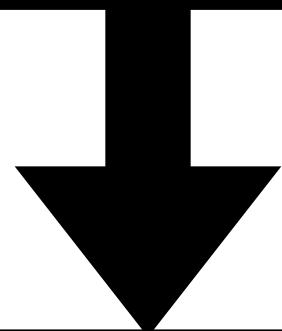
If we had observed x' and x'' , we would have satisfied our goal of data thinning!

Can we work backwards to recover x' and x'' ?

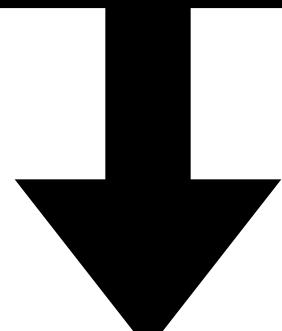
The conditional distribution of $X' | X = x$ is $N(\epsilon x, \epsilon(1 - \epsilon)\sigma^2)$.

Data thinning for the Gaussian distribution

We know x could have arisen as $x' + x''$, where $X' \sim N(\epsilon\mu, \epsilon\sigma^2)$, $X'' \sim N((1 - \epsilon)\mu, (1 - \epsilon)\sigma^2)$, $X' \perp\!\!\!\perp X''$.



We observe realization x from $X \sim N(\mu, \sigma^2)$.



Draw $X^{(1)}$ from $N(\epsilon x, \epsilon(1 - \epsilon)\sigma^2)$.
Let $X^{(2)} := X - X^{(1)}$.

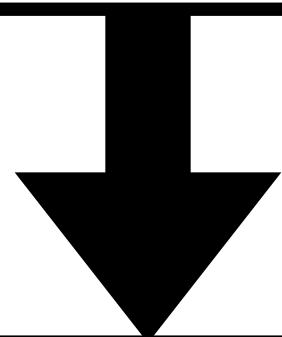
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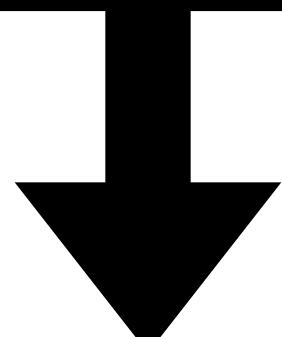
The conditional distribution of $X' | X = x$ is $N(\epsilon x, \epsilon(1 - \epsilon)\sigma^2)$.

Data thinning for the Gaussian distribution

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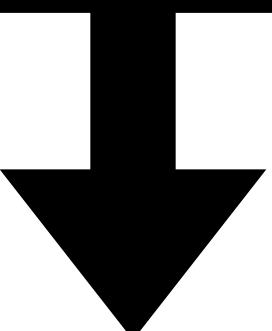
The conditional distribution of $X' | X = x$ is $N(\epsilon x, \epsilon(1 - \epsilon)\sigma^2)$.

Theorem:

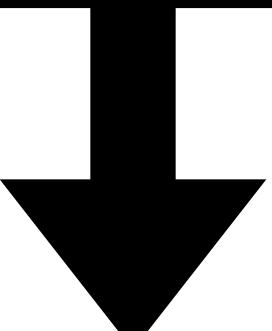
$X^{(1)} \sim N(\epsilon\mu, \epsilon\sigma^2)$, $X^{(2)} \sim N((1 - \epsilon)\mu, (1 - \epsilon)\sigma^2)$, $X^{(1)} \perp\!\!\!\perp X^{(2)}$.

Data thinning for the Gaussian distribution

We know x could have arisen as $x' + x''$, where $X' \sim N(\epsilon\mu, \epsilon\sigma^2)$, $X'' \sim N((1 - \epsilon)\mu, (1 - \epsilon)\sigma^2)$, $X' \perp\!\!\!\perp X''$.



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$X^{(1)} \sim N(\epsilon\mu, \epsilon\sigma^2)$, $X^{(2)} \sim N((1 - \epsilon)\mu, (1 - \epsilon)\sigma^2)$, $X^{(1)} \perp\!\!\!\perp X^{(2)}$.

This is (similar to) a well-known result!

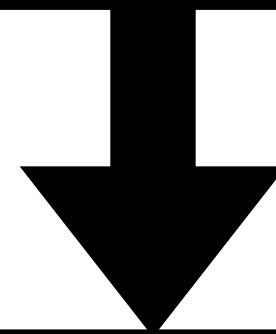
Data thinning recipe for the negative binomial distribution

Data thinning recipe for the negative binomial distribution

We observe realization x from $X \sim \text{NB}(\mu, b)$.

Data thinning recipe for the negative binomial distribution

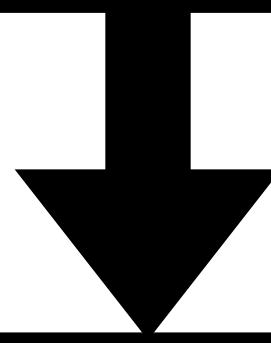
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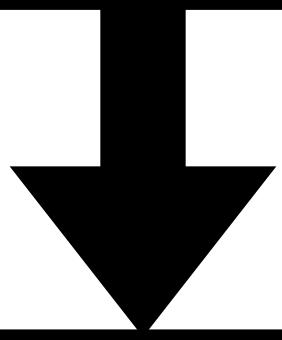


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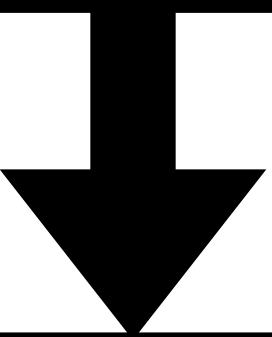
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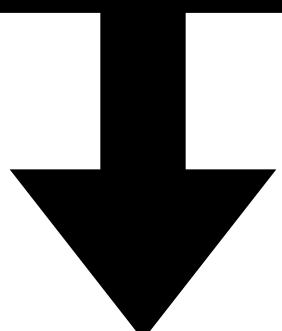
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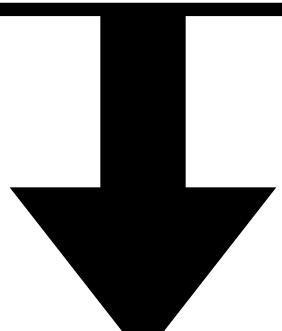
The conditional distribution of $X' | X = x$ is BetaBinomial($x, \epsilon b, (1 - \epsilon)b$).

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We observe realization x from $X \sim \text{NB}(\mu, b)$.



Draw $X^{(1)}$ from BetaBinomial($x, \epsilon b, (1 - \epsilon)b$).
Let $X^{(2)} := X - X^{(1)}$.

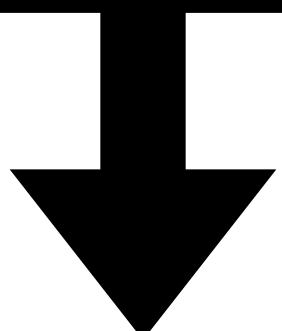
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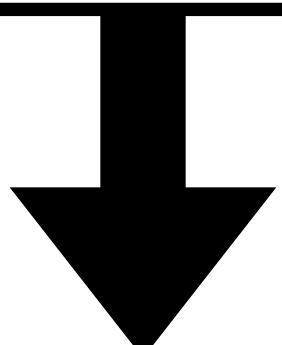
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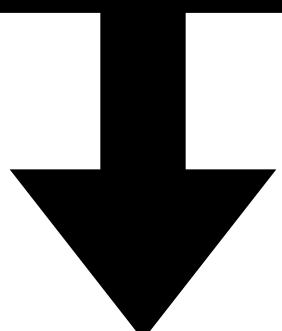
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Theorem:

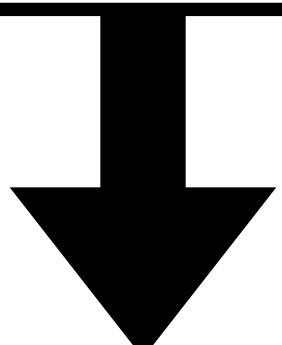
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This is a new result!

For many common distributions, the distribution $G_{\epsilon,x}$ has a simple form

Distribution of X :

Draw $X^{(1)} \mid X = x$ from
 $G_{\epsilon,x}$, where $G_{\epsilon,x}$ is:

Poisson(λ)

Binomial(x, ϵ)

Distribution of $X^{(1)}$:

Poisson($\epsilon\lambda$)

Distribution of $X^{(2)}$,

where $X^{(2)} = X - X^{(1)}$:

Poisson($(1 - \epsilon)\lambda$)

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Distribution of X :	Draw $X^{(1)} X = x$ from $G_{\epsilon,x}$, where $G_{\epsilon,x}$ is:	Distribution of $X^{(1)}$:	Distribution of $X^{(2)}$, where $X^{(2)} = X - X^{(1)}$:
Poisson(λ)	Binomial(x, ϵ)	Poisson($\epsilon\lambda$)	Poisson($(1 - \epsilon)\lambda$)

Related work on Poisson thinning:

- Sarkar and Stephens, 2021, Nature Genetics.
- Chen et al., 2021, arXiv:2108.03336
- Leiner et al., 2021, arXiv:2112.11079.
- Neufeld et al., 2022, Biostatistics.
- Oliveira, Lei, and Tibshirani, 2022, arXiv:2212.01943.

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Poisson(λ)	Binomial(x, ϵ)	Poisson($\epsilon\lambda$)	Poisson($(1 - \epsilon)\lambda$)
$N(\mu, \sigma^2)$	$N(\epsilon x, \epsilon(1 - \epsilon)\sigma^2)$	$N(\epsilon\mu, \epsilon\sigma^2)$	$N((1 - \epsilon)\mu, (1 - \epsilon)\sigma^2)$

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Related work on Gaussian thinning:

- Tian and Taylor, 2018, Annals of Statistics.
- Tian, 2020, Annals of Statistics.
- Rasines and Young, 2022, Biometrika.
- Leiner et al., 2022, arXiv:2112.11079.
- Oliveira, Lei, and Tibshirani, 2022, arXiv:2111.09447.

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Poisson(λ)	Binomial(x, ϵ)	Poisson($\epsilon\lambda$)	Poisson($(1 - \epsilon)\lambda$)
$N(\mu, \sigma^2)$	$N(\epsilon x, \epsilon(1 - \epsilon)\sigma^2)$	$N(\epsilon\mu, \epsilon\sigma^2)$	$N((1 - \epsilon)\mu, (1 - \epsilon)\sigma^2)$
NegativeBinomial(μ, b)	BetaBinomial($x, \epsilon b, (1 - \epsilon)b$).	NegativeBinomial($\epsilon\mu, \epsilon b$)	NegativeBinomial($(1 - \epsilon)\mu, (1 - \epsilon)b$)

For many common distributions, the distribution $G_{\epsilon,x}$ has a simple form

Distribution of X :	Draw $X^{(1)} \mid X = x$ from $G_{\epsilon,x}$, where $G_{\epsilon,x}$ is:	Distribution of $X^{(1)}$:	Distribution of $X^{(2)}$, where $X^{(2)} = X - X^{(1)}$:
Poisson(λ)	Binomial(x, ϵ)	Poisson($\epsilon\lambda$)	Poisson($(1 - \epsilon)\lambda$)
$N(\mu, \sigma^2)$	$N(\epsilon x, \epsilon(1 - \epsilon)\sigma^2)$	$N(\epsilon\mu, \epsilon\sigma^2)$	$N((1 - \epsilon)\mu, (1 - \epsilon)\sigma^2)$
NegativeBinomial(μ, b)	BetaBinomial($x, \epsilon b, (1 - \epsilon)b$).	NegativeBinomial($\epsilon\mu, \epsilon b$)	NegativeBinomial($(1 - \epsilon)\mu, (1 - \epsilon)b$)
Binomial(r, p)	Hypergeometric($\epsilon r, (1 - \epsilon)r, x$).	Binomial($\epsilon r, p$)	Binomial($(1 - \epsilon)r, p$)
Gamma(α, β)	$x \cdot \text{Beta}(\epsilon\alpha, (1 - \epsilon)\alpha)$.	Gamma($\epsilon\alpha, \beta$)	Gamma($(1 - \epsilon)\alpha, \beta$)
Exponential(λ)	$x \cdot \text{Beta}(\epsilon, (1 - \epsilon))$.	Gamma(ϵ, λ)	Gamma($(1 - \epsilon), \lambda$)
$N_k(\mu, \Sigma)$	$N(\epsilon x, \epsilon(1 - \epsilon)\Sigma)$.	$N_k(\epsilon\mu, \epsilon\Sigma)$	$N_k((1 - \epsilon)\mu, (1 - \epsilon)\Sigma)$
Multinomial $_k(r, p)$	MultivarHypergeom($x_1, \dots, x_K, \epsilon r$)	Multinom $_k(\epsilon r, p)$	Multinomial $_k((1 - \epsilon)r, p)$
Wishart $_p(n, \Sigma)$.	$x^{1/2} Z x^{1/2}$, where . $Z \sim \text{MatrixBeta}_p(\epsilon n/2, (1 - \epsilon)n/2)$	Wishart $_p(\epsilon n, \Sigma)$	Wishart $_p((1 - \epsilon)n, \Sigma)$

What if we get a nuisance parameter wrong?

Negative binomial thinning algorithm

Suppose $X \sim \text{NegBin}(\mu, b)$.

Draw

$X^{(1)} \sim \text{BetaBinomial}(x, \epsilon b, (1 - \epsilon)b)$,

$X^{(2)} = X - X^{(1)}$, then:

- 1) $X^{(1)} \sim \text{NegBin}(\epsilon\mu, \epsilon b)$.
- 2) $X^{(2)} \sim \text{NegBin}((1 - \epsilon)\mu, (1 - \epsilon)b)$
- 3) $X^{(1)} \perp\!\!\!\perp X^{(2)}$.

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Draw

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- 1) $X^{(1)} \sim \text{NegBin}(\epsilon \mu, \epsilon b)$.
- 2) $X^{(2)} \sim \text{NegBin}((1 - \epsilon) \mu, (1 - \epsilon) b)$
- 3) $X^{(1)} \perp\!\!\!\perp X^{(2)}$.

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Suppose $X \sim \text{NegBin}(\mu, b)$.

Draw

$X^{(1)} \sim \text{BetaBinomial}(x, \epsilon \tilde{b}, (1 - \epsilon) \tilde{b})$,

$X^{(2)} = X - X^{(1)}$, then:

1) $\cancel{X^{(1)} \sim \text{NegBin}(c\mu, cb)}$.

2) $\cancel{X^{(2)} \sim \text{NegBin}((1 - c)\mu, (1 - c)b)}$

3) $\cancel{X^{(1)} \perp\!\!\!\perp X^{(2)}}$.

What if we get a nuisance parameter wrong?

Negative binomial thinning algorithm

Suppose $X \sim \text{NegBin}(\mu, b)$.

Draw

$X^{(1)} \sim \text{BetaBinomial}(x, \epsilon \tilde{b}, (1 - \epsilon) \tilde{b})$,

$X^{(2)} = X - X^{(1)}$, then:

$$1) E[X^{(1)}] = \epsilon \mu.$$

$$2) E[X^{(2)}] = (1 - \epsilon) \mu$$

$$3) \text{Cov}(X^{(1)}, X^{(2)}) = \epsilon(1 - \epsilon) \frac{\mu^2}{b} \left(1 - \frac{b + 1}{\tilde{b} + 1}\right).$$

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Negative binomial thinning algorithm

Suppose $X \sim \text{NegBin}(\mu, b)$.

Draw

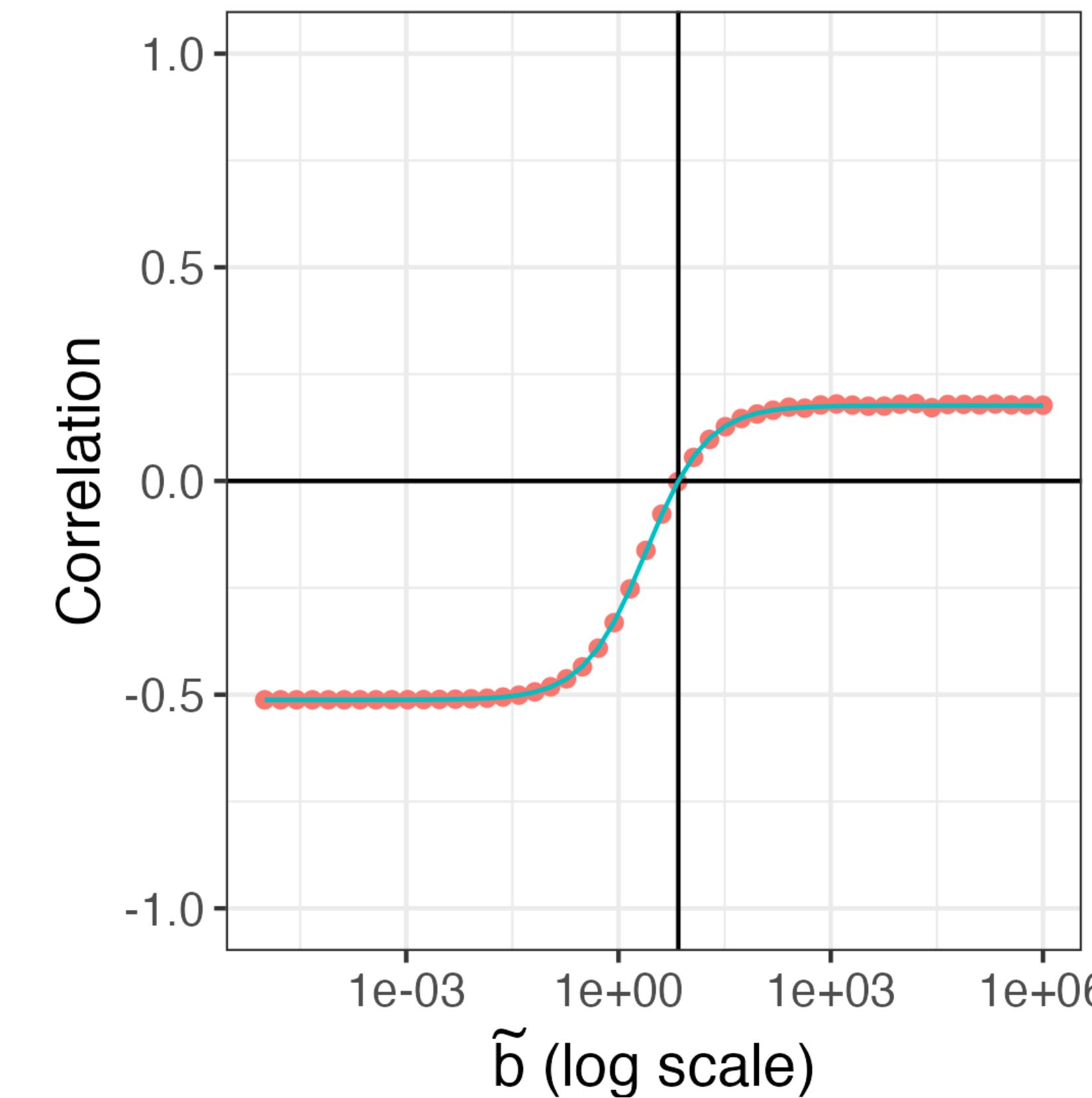
$X^{(1)} \sim \text{BetaBinomial}(x, \epsilon \tilde{b}, (1 - \epsilon) \tilde{b})$,

$X^{(2)} = X - X^{(1)}$, then:

1) $E[X^{(1)}] = \epsilon \mu$.

2) $E[X^{(2)}] = (1 - \epsilon) \mu$

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What if we get a nuisance parameter wrong?

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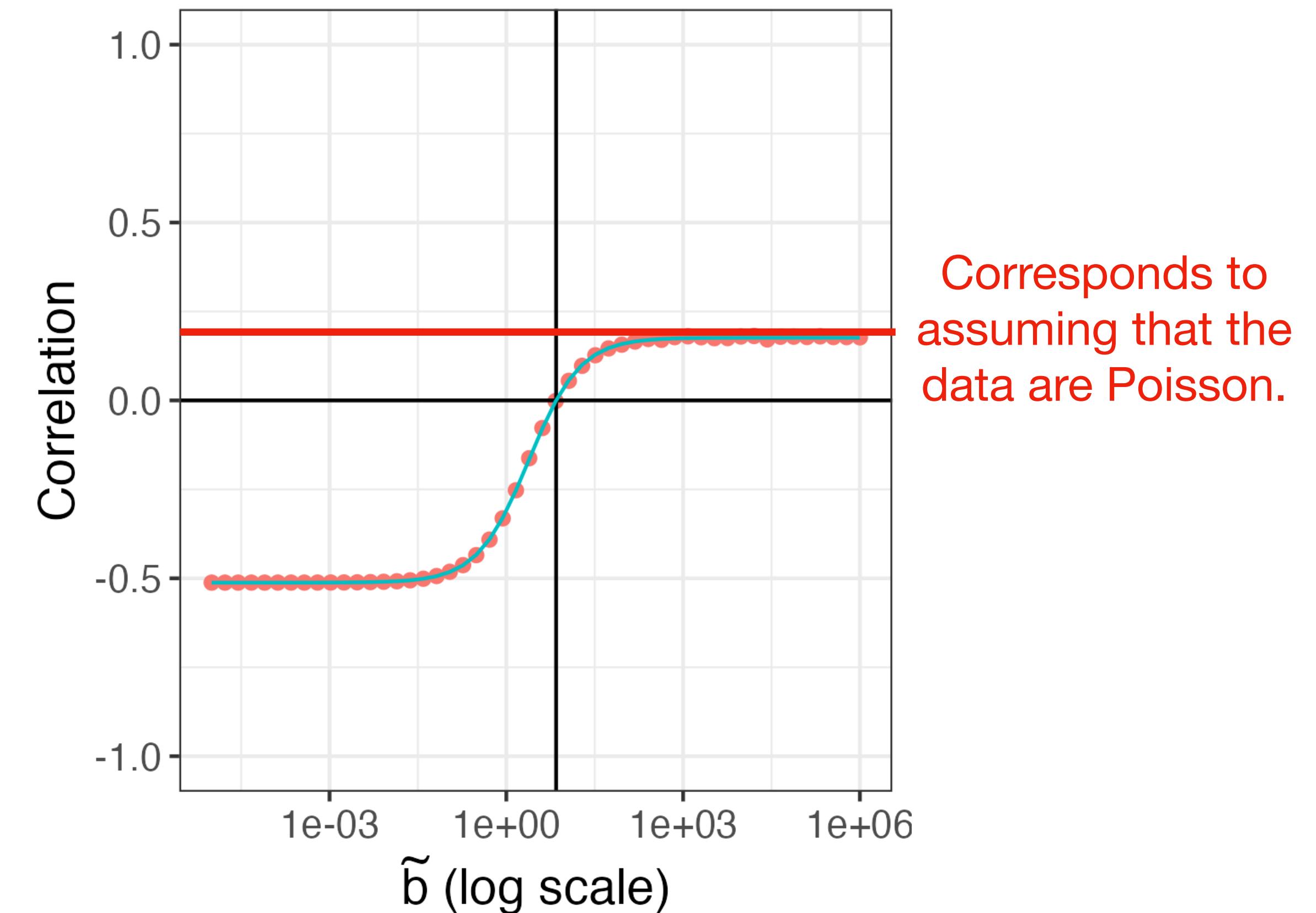
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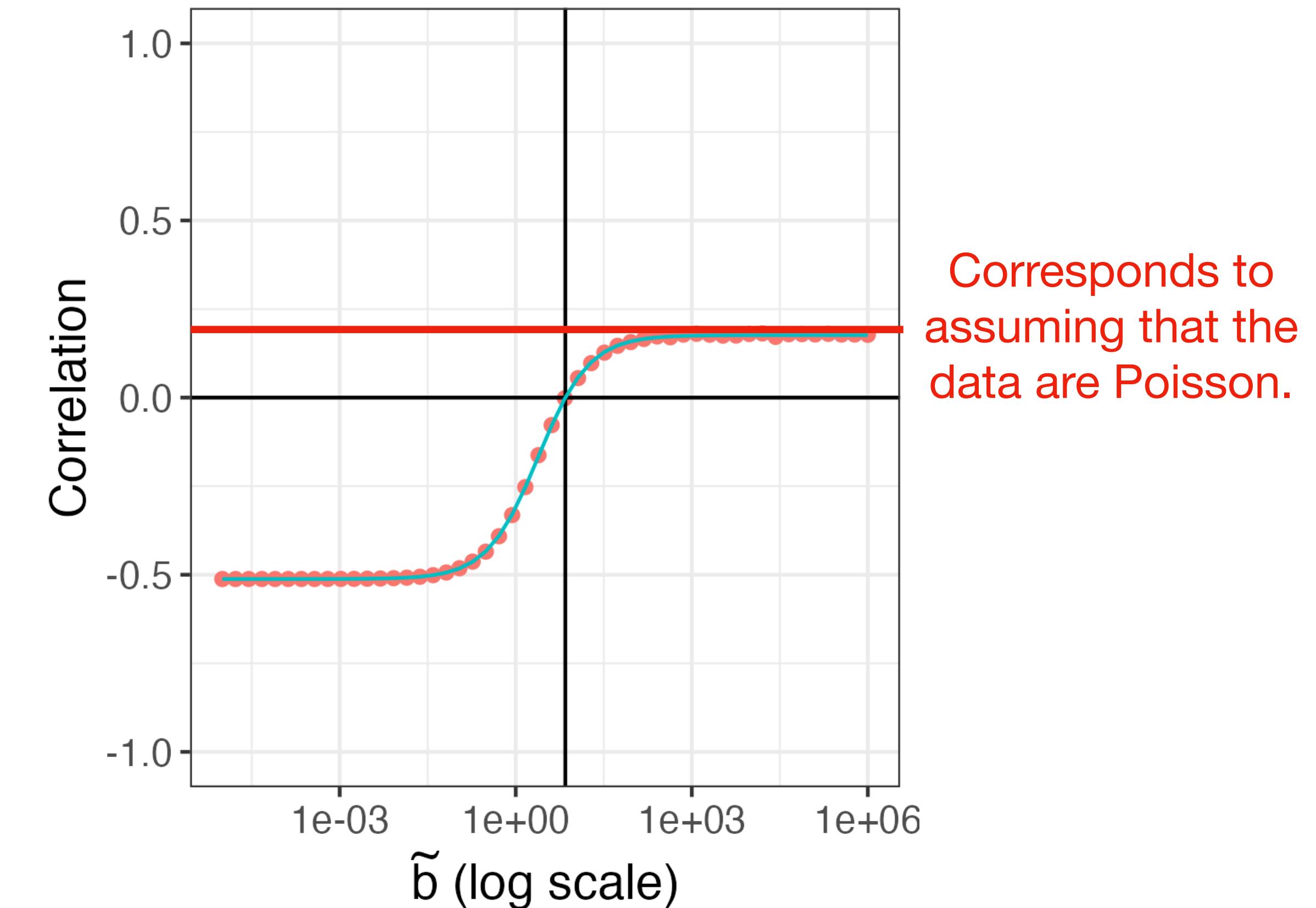
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Similar results can be derived for other decompositions.

The parameter ϵ governs an information tradeoff

Gaussian thinning algorithm

Suppose $X \sim N(\mu, \sigma^2)$.

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$X^{(1)} \sim N(\epsilon x, \epsilon(1 - \epsilon)\sigma^2)$ and

$X^{(2)} = X - X^{(1)}$.

Then:

$$1) \quad X^{(1)} \sim N(\epsilon\mu, \epsilon\sigma^2)$$

$$2) \quad X^{(2)} \sim N((1 - \epsilon)\mu, (1 - \epsilon)\sigma^2)$$

$$3) \quad X^{(1)} \perp\!\!\!\perp X^{(2)}.$$

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Theorem: If we data thin with parameter ϵ , the Fisher information in X about μ is divided between $X^{(1)}$ and $X^{(2)}$ with proportions ϵ and $1 - \epsilon$.

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- (1) Each $X^{(m)}$ has the same distribution as X , up to a parameter scaling.
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Our recipe extends naturally to splitting into M>2 folds

Distribution of X	Draw $(X^{(1)}, \dots, X^{(M)}) \mid X = x$ from:	Distribution of $X^{(m)}$
Poisson(λ)	Multinomial($x, \epsilon_1, \dots, \epsilon_M$)	Poisson($\epsilon_m \lambda$)

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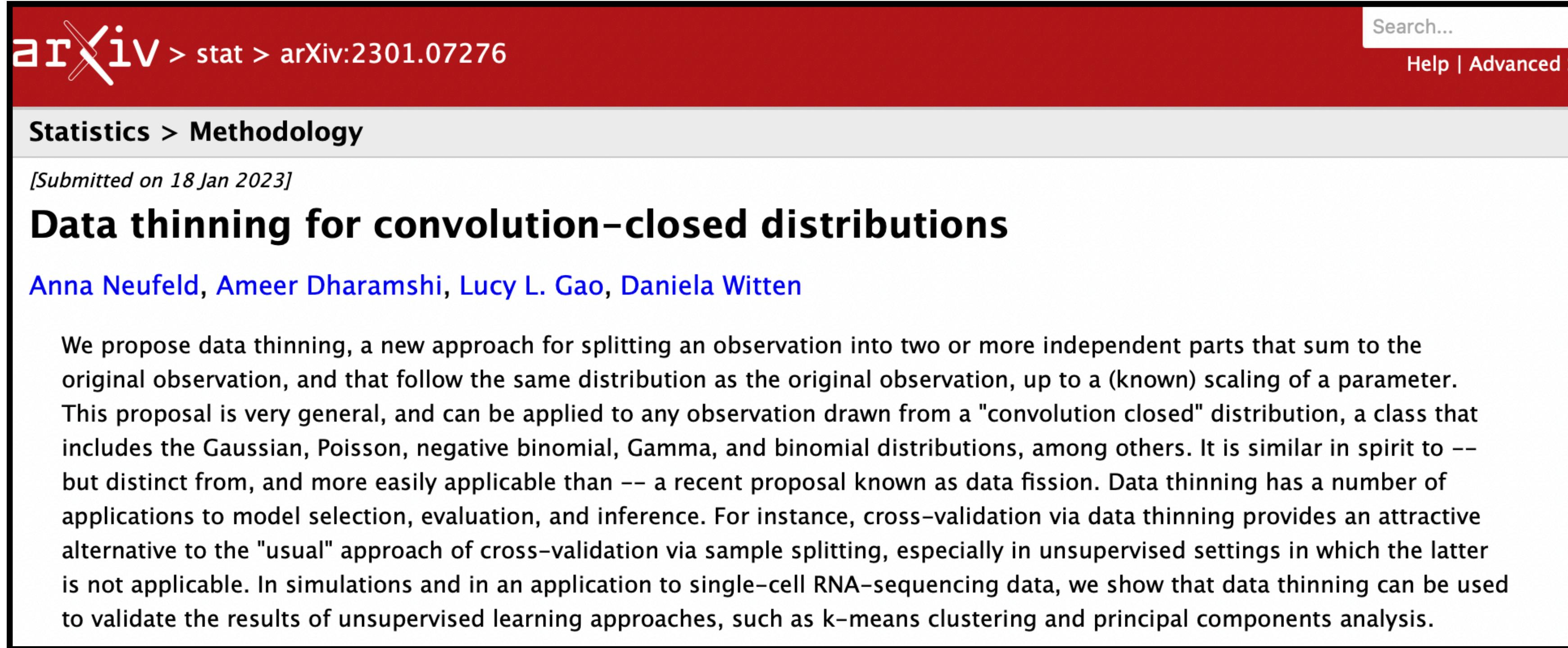
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Gamma(α, β)	$x \cdot \text{Dirichlet}(\epsilon_1 \alpha, \dots, \epsilon_M \alpha)$	Gamma($\epsilon_m \alpha, \beta$)
Exponential(λ)	$x \cdot \text{Dirichlet}(\epsilon_1, \dots, \epsilon_M)$	Gamma(ϵ_m, λ)
Binomial(r, p)	MultivariateHypergeometric($\epsilon_1 r, \dots, \epsilon_M r, x$).	Binomial($\epsilon_m r, p$)

Data thinning is a simple alternative to sample splitting that can be used in a variety of settings

Project 3



The image shows a screenshot of an arXiv preprint page. The header is red with the arXiv logo and navigation links. The title is "Data thinning for convolution-closed distributions" by Anna Neufeld, Ameer Dharamshi, Lucy L. Gao, Daniela Witten. The abstract discusses data thinning as a new approach for splitting observations into independent parts that sum to the original, applicable to convolution-closed distributions like Gaussian, Poisson, and binomial. It compares this to data fission and provides applications in model selection, cross-validation, and unsupervised learning.

arXiv > stat > arXiv:2301.07276

Search... Help | Advanced

Statistics > Methodology

[Submitted on 18 Jan 2023]

Data thinning for convolution-closed distributions

Anna Neufeld, Ameer Dharamshi, Lucy L. Gao, Daniela Witten

We propose data thinning, a new approach for splitting an observation into two or more independent parts that sum to the original observation, and that follow the same distribution as the original observation, up to a (known) scaling of a parameter. This proposal is very general, and can be applied to any observation drawn from a "convolution closed" distribution, a class that includes the Gaussian, Poisson, negative binomial, Gamma, and binomial distributions, among others. It is similar in spirit to -- but distinct from, and more easily applicable than -- a recent proposal known as data fission. Data thinning has a number of applications to model selection, evaluation, and inference. For instance, cross-validation via data thinning provides an attractive alternative to the "usual" approach of cross-validation via sample splitting, especially in unsupervised settings in which the latter is not applicable. In simulations and in an application to single-cell RNA-sequencing data, we show that data thinning can be used to validate the results of unsupervised learning approaches, such as k-means clustering and principal components analysis.

R package and tutorials: <https://anna-neufeld.github.io/datathin/>

Outline

1. Motivation: settings where sample splitting doesn't work
2. Poisson thinning
3. Data thinning
4. **Application to single-cell RNA sequencing data**
5. Ongoing work

How can we validate the results of clustering?

RESEARCH ARTICLE

HUMAN GENOMICS

A human cell atlas of fetal gene expression

Junyue Cao^{1*}, Diana R. O'Day², Hannah A. Pliner³, Paul D. Kingsley⁴, Mei Deng², Riza M. Daza¹, Michael A. Zager^{3,5}, Kimberly A. Aldinger^{2,6}, Ronnie Blecher-Gonen¹, Fan Zhang⁷, Malte Spielmann^{8,9}, James Palis⁴, Dan Doherty^{2,3,6}, Frank J. Steemers⁷, Ian A. Glass^{2,3,6}, Cole Trapnell^{1,3,10†}, Jay Shendure^{1,3,10,11†}

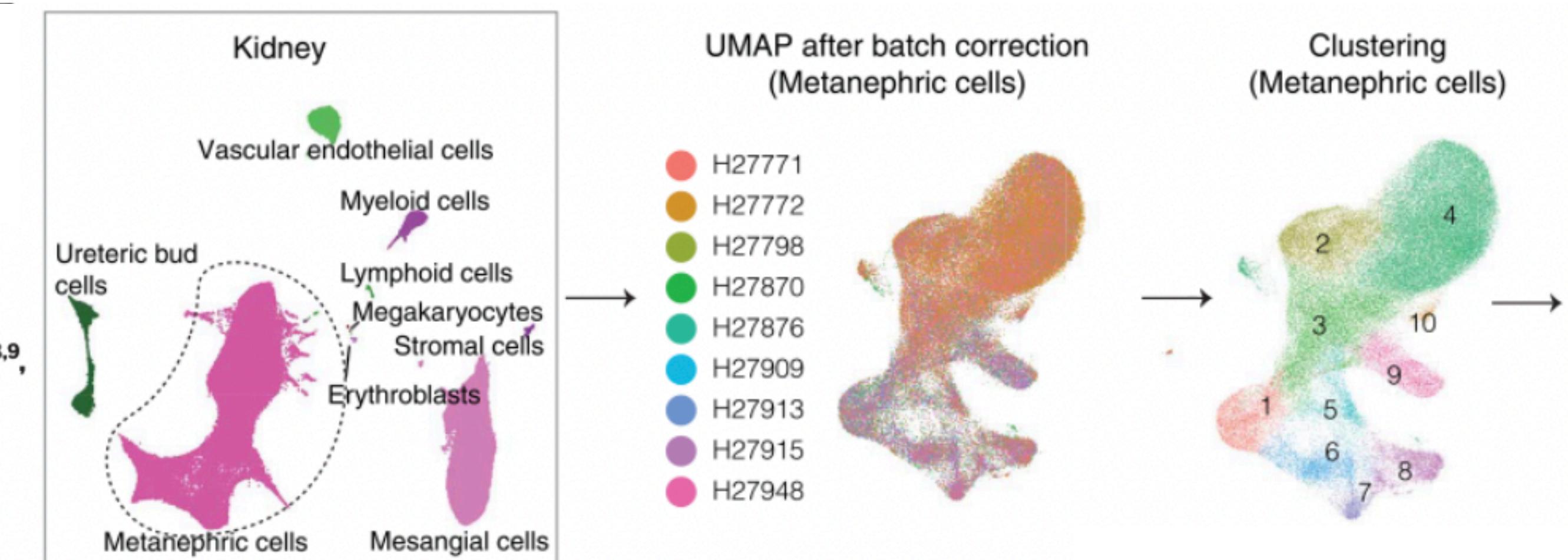
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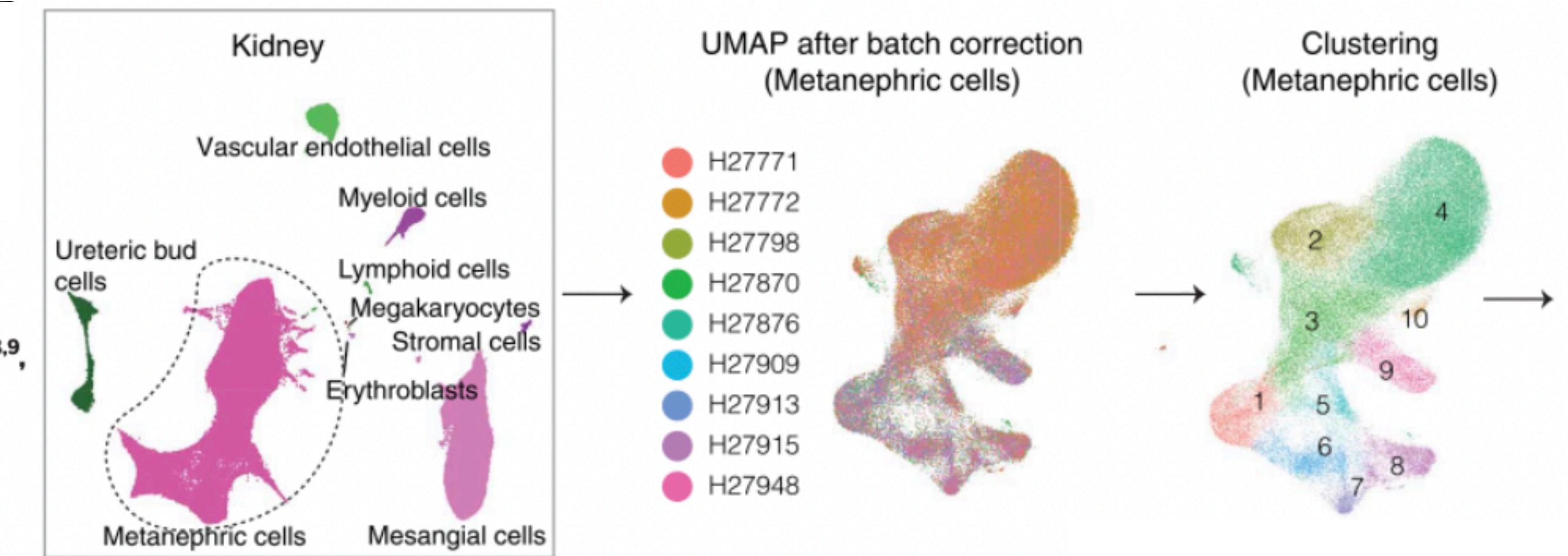
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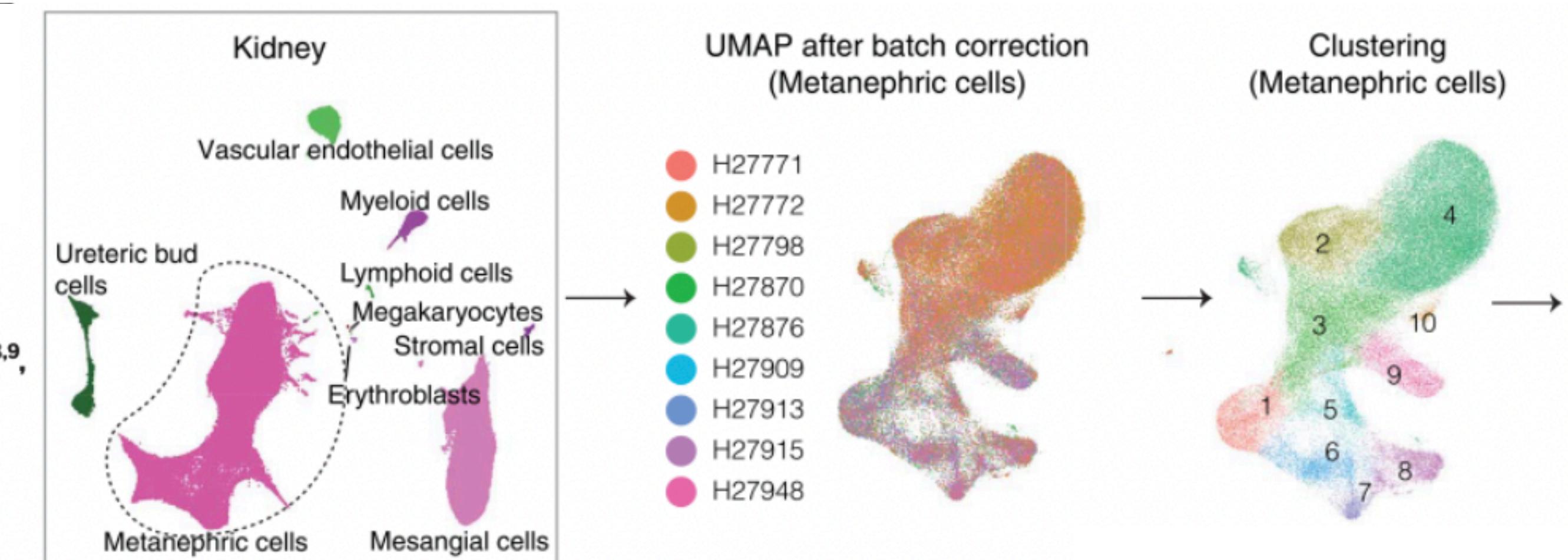
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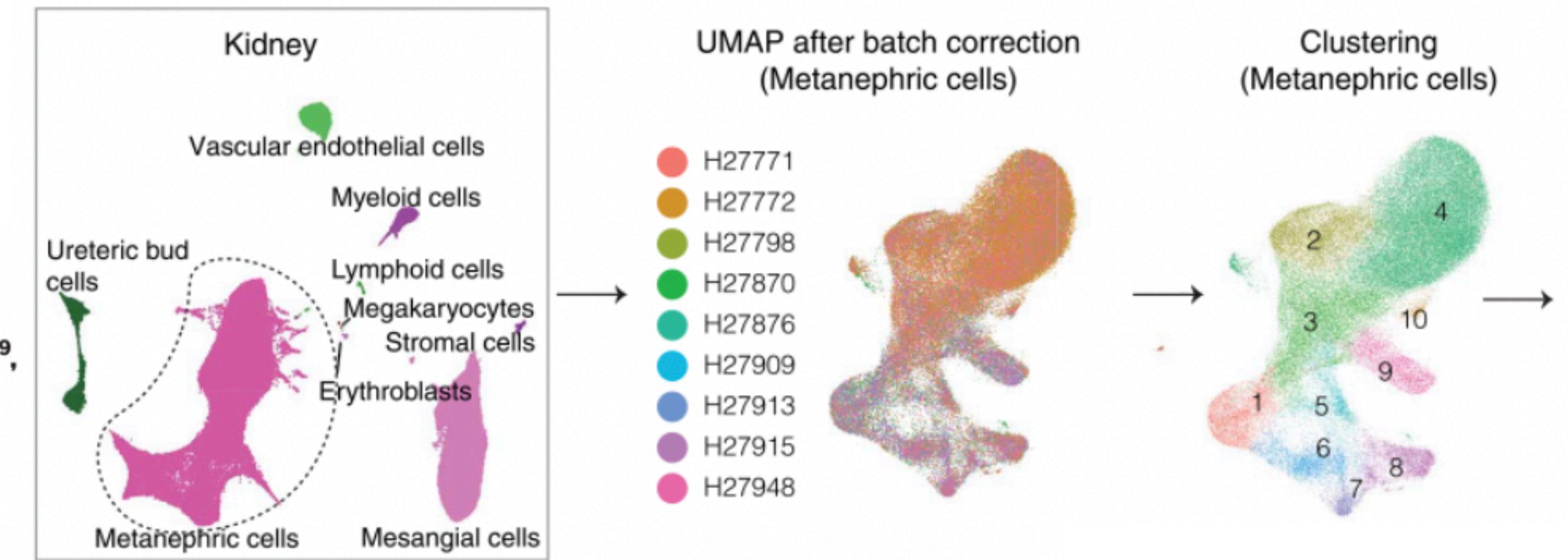
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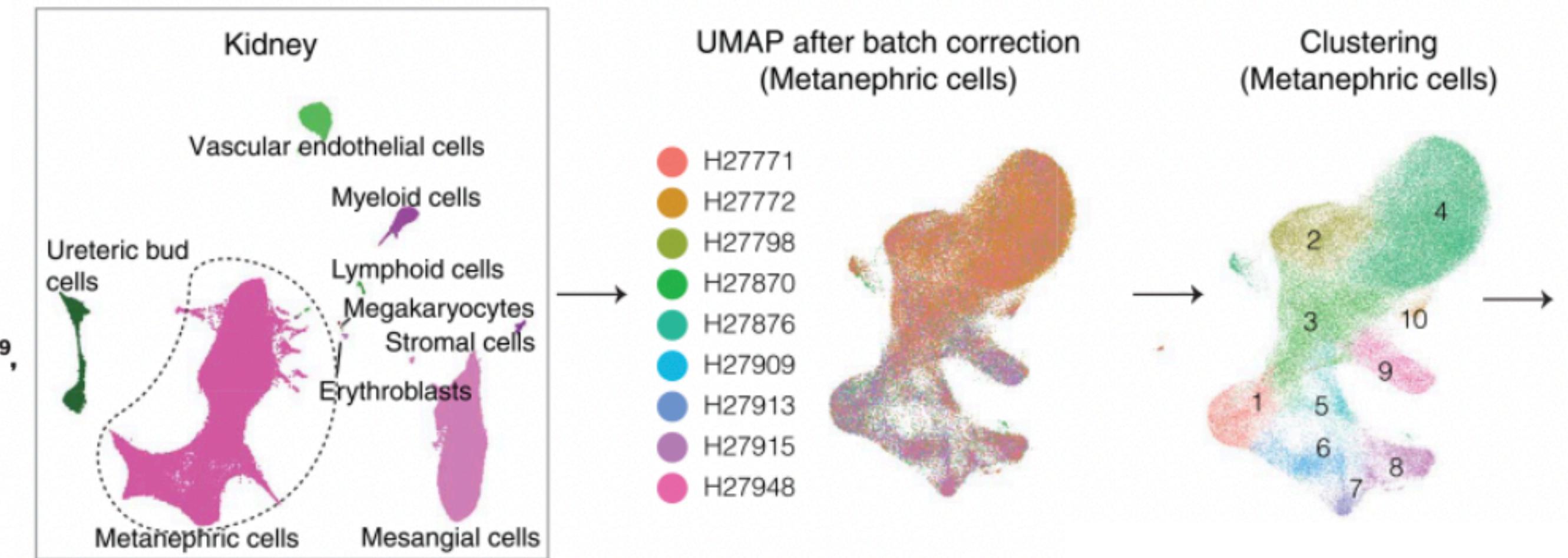
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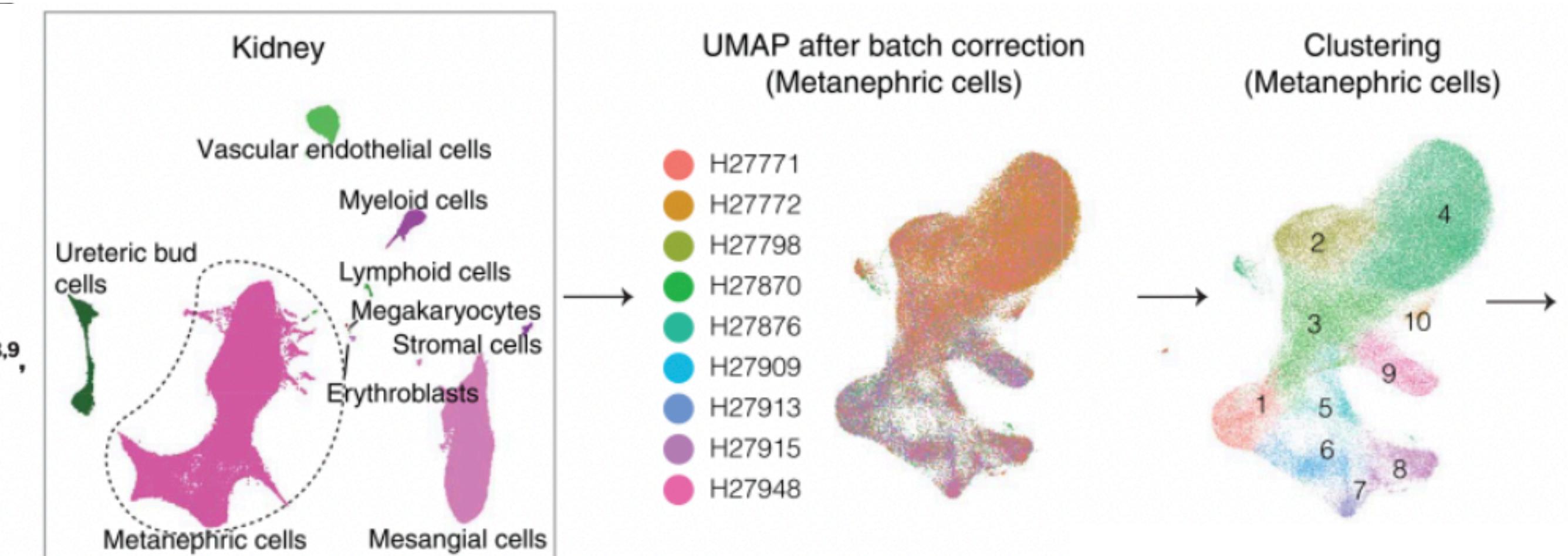
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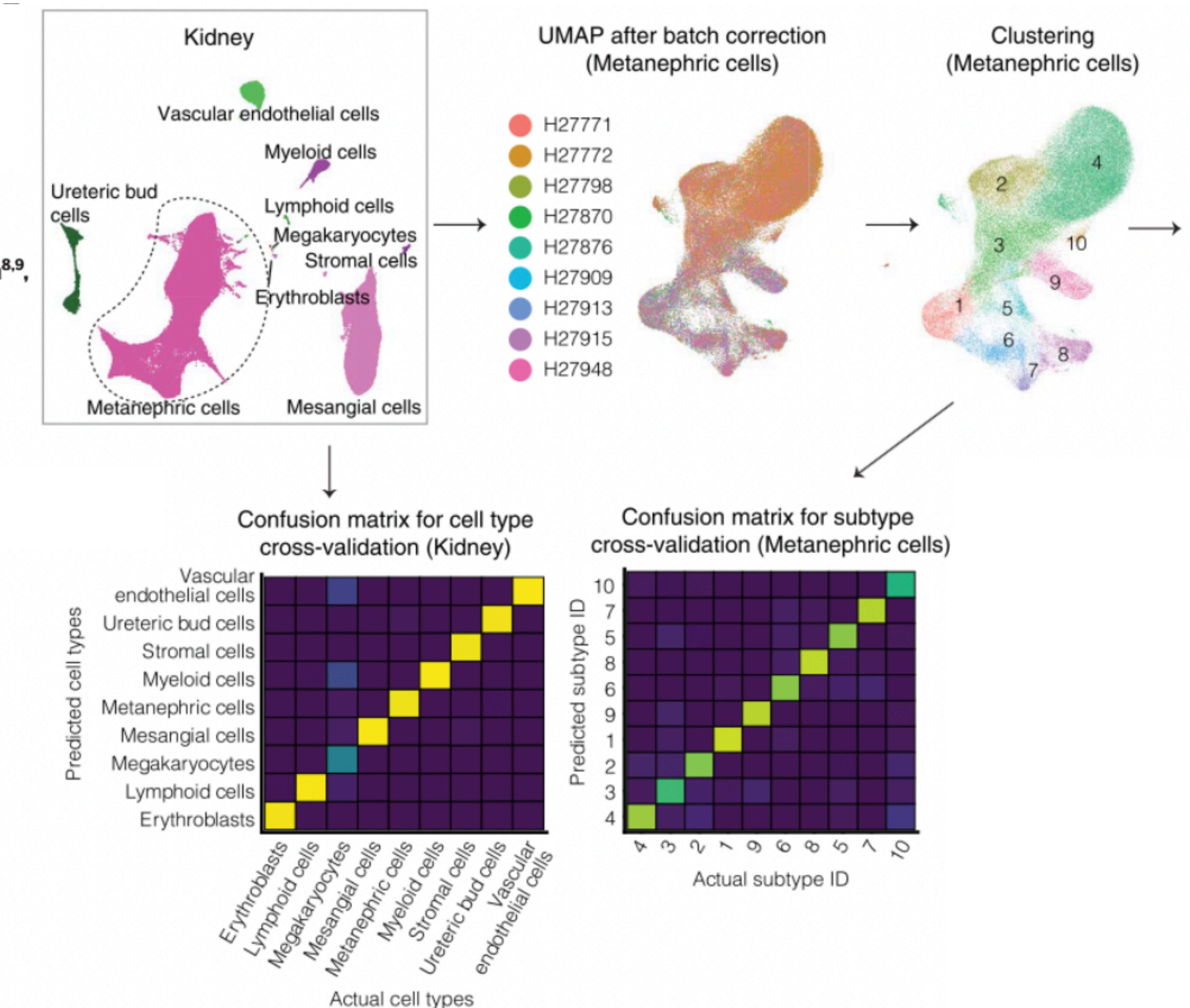
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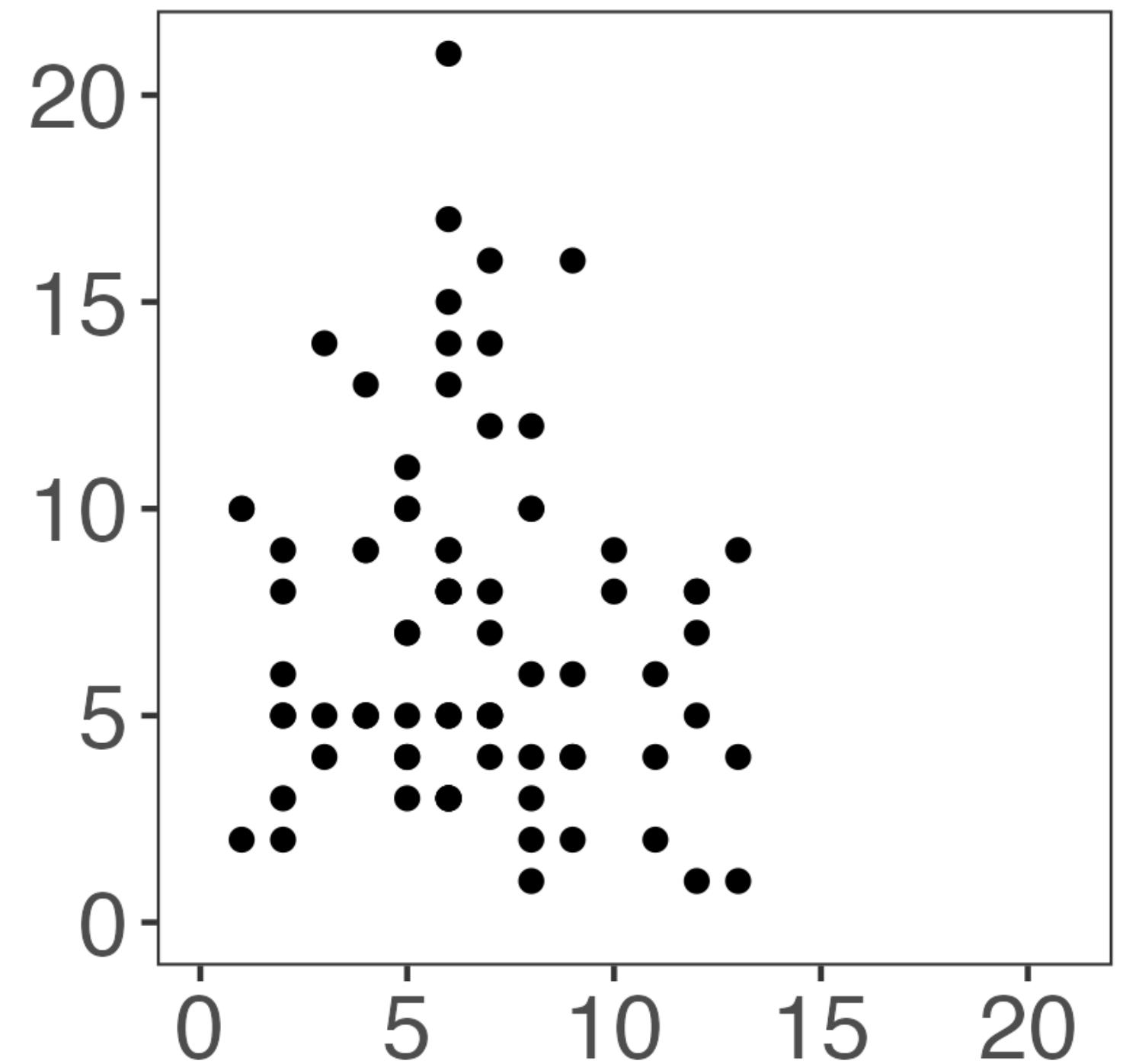
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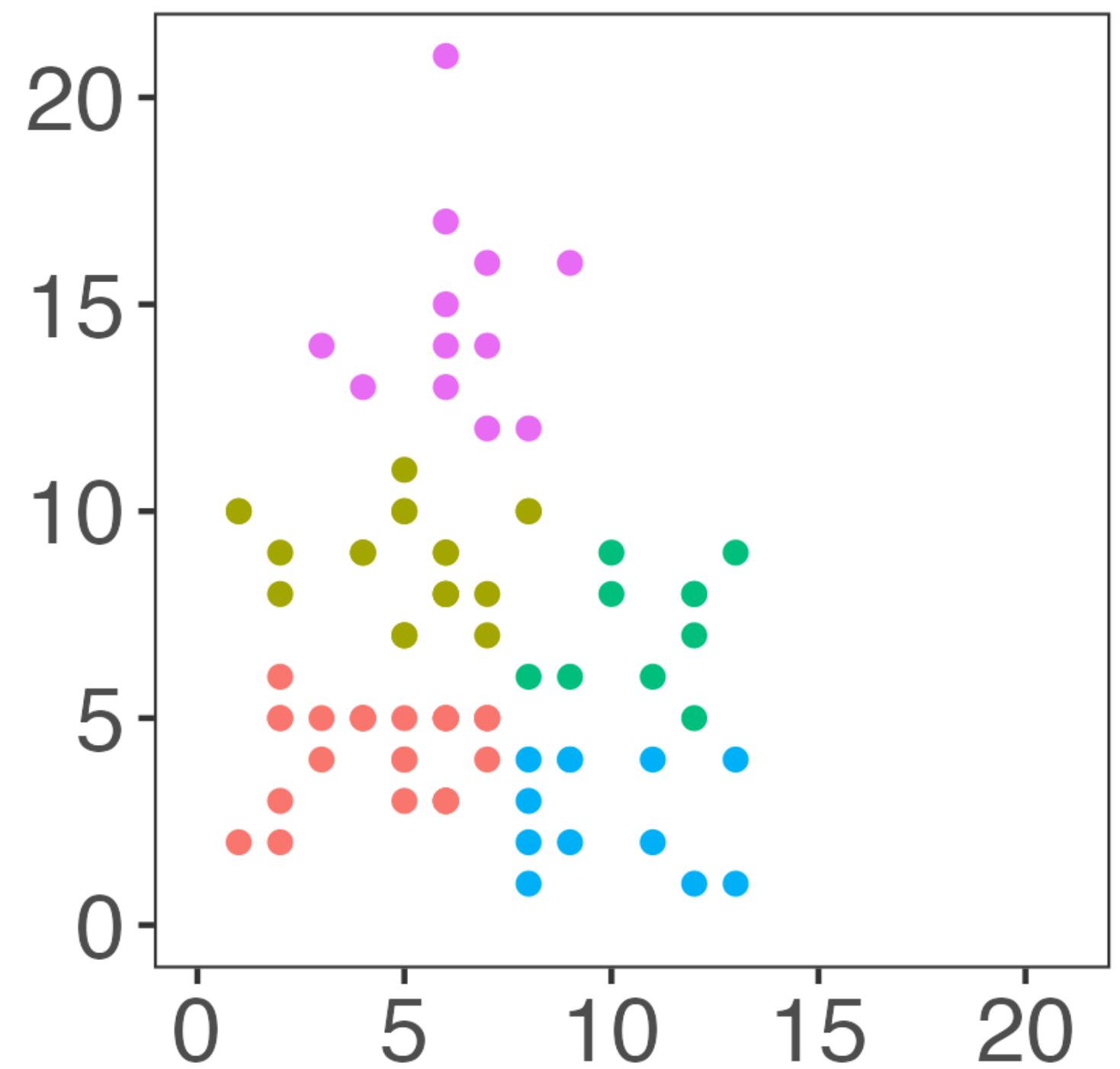
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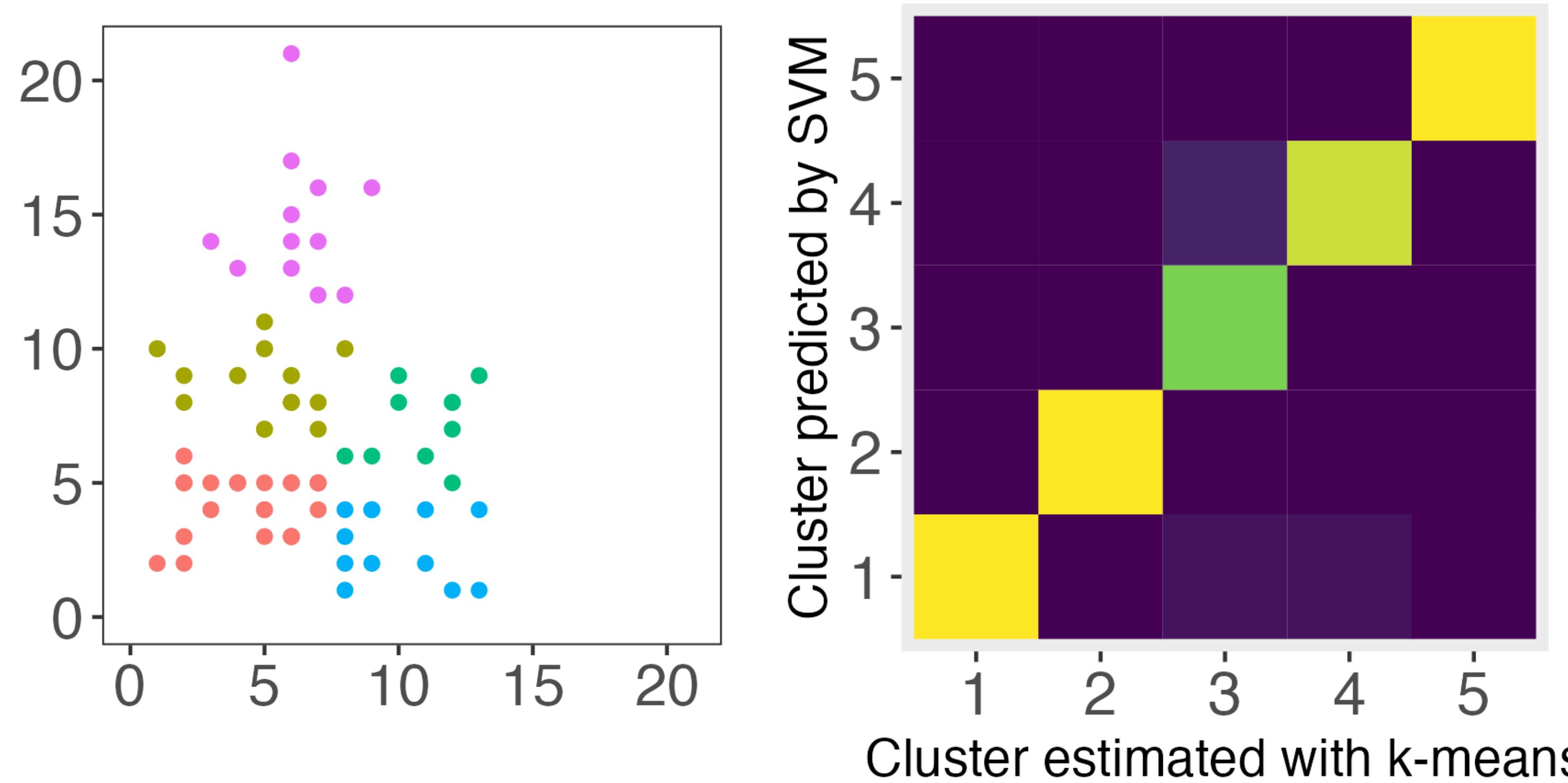
This cross validation procedure double dips



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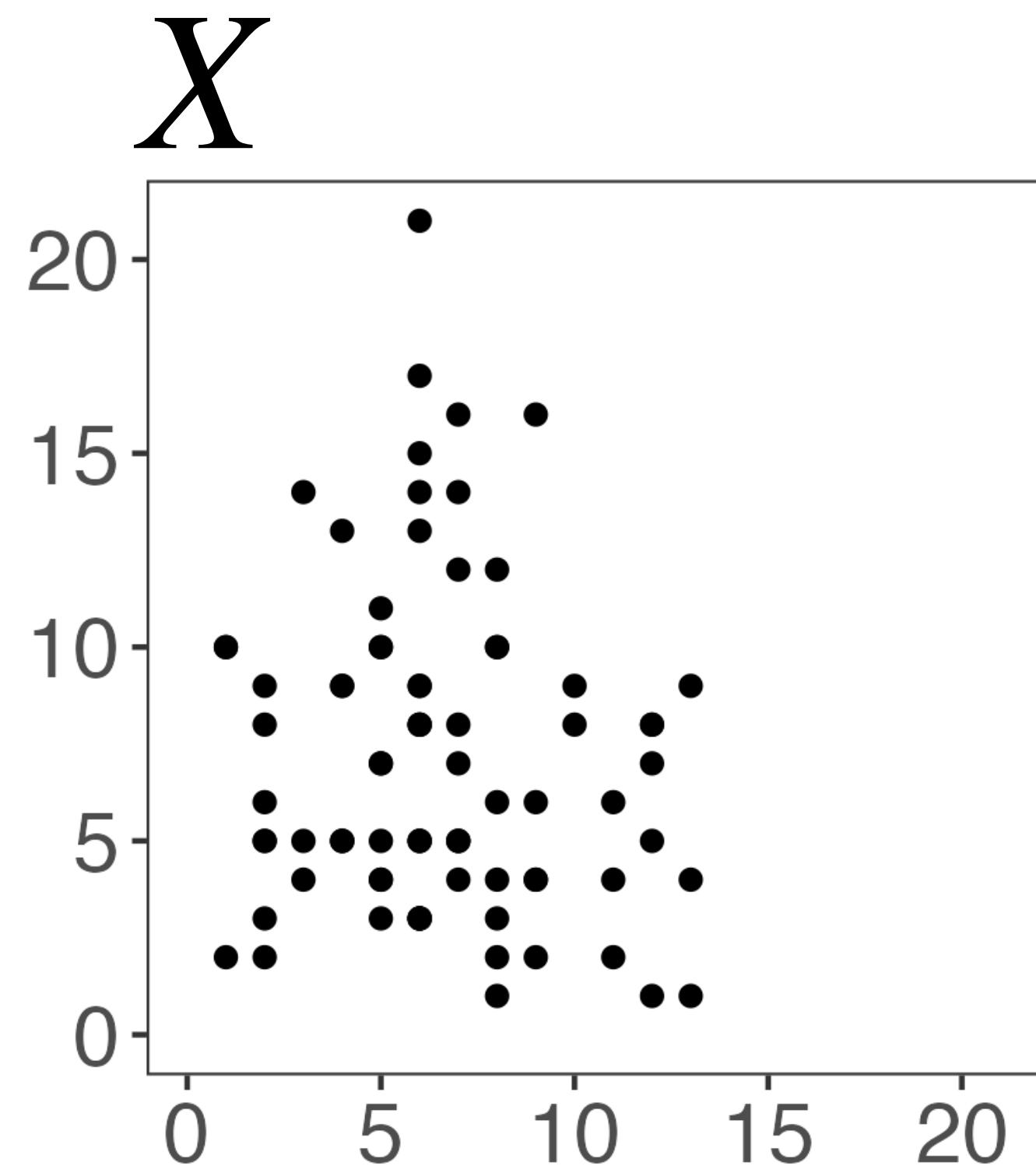


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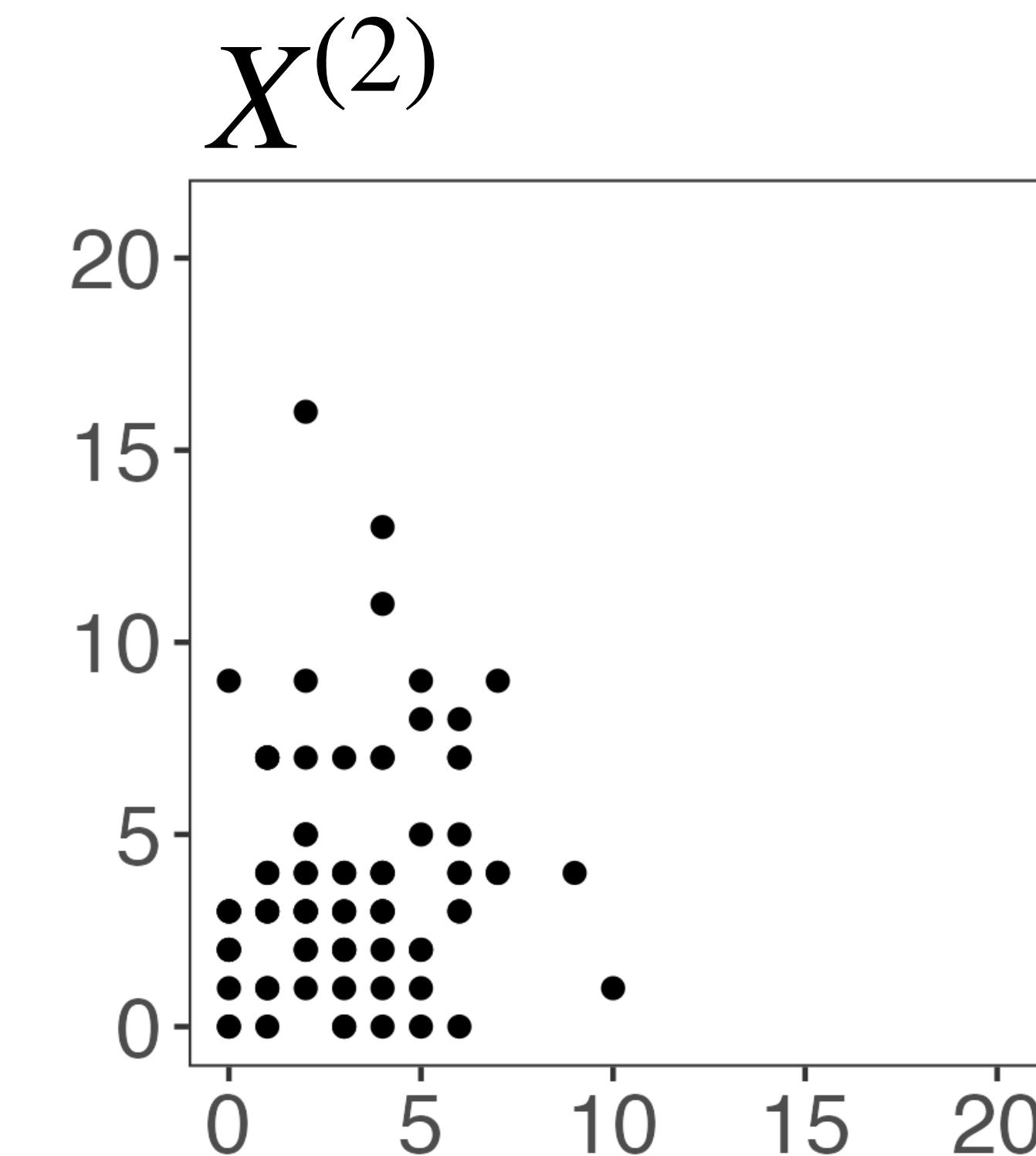
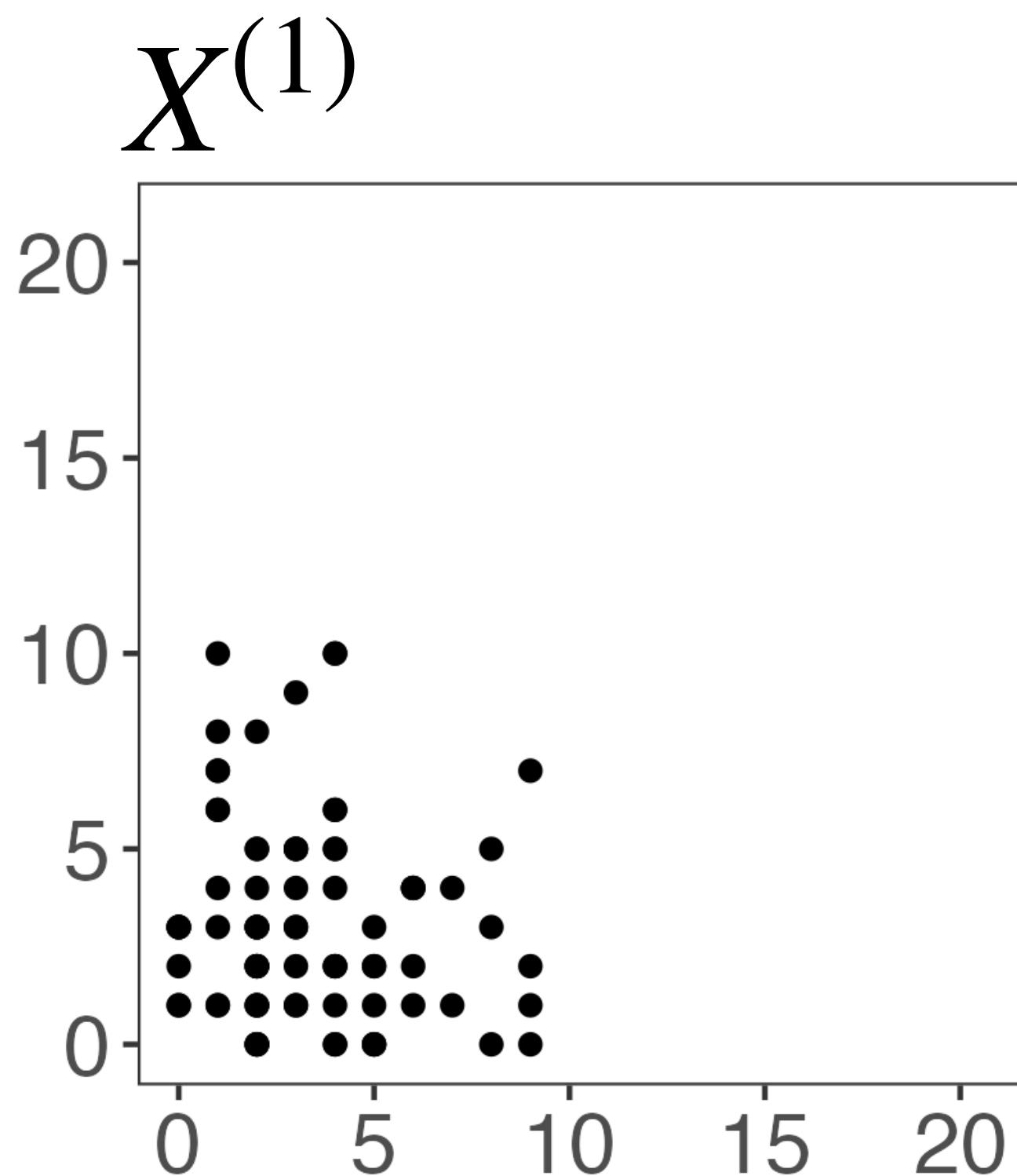
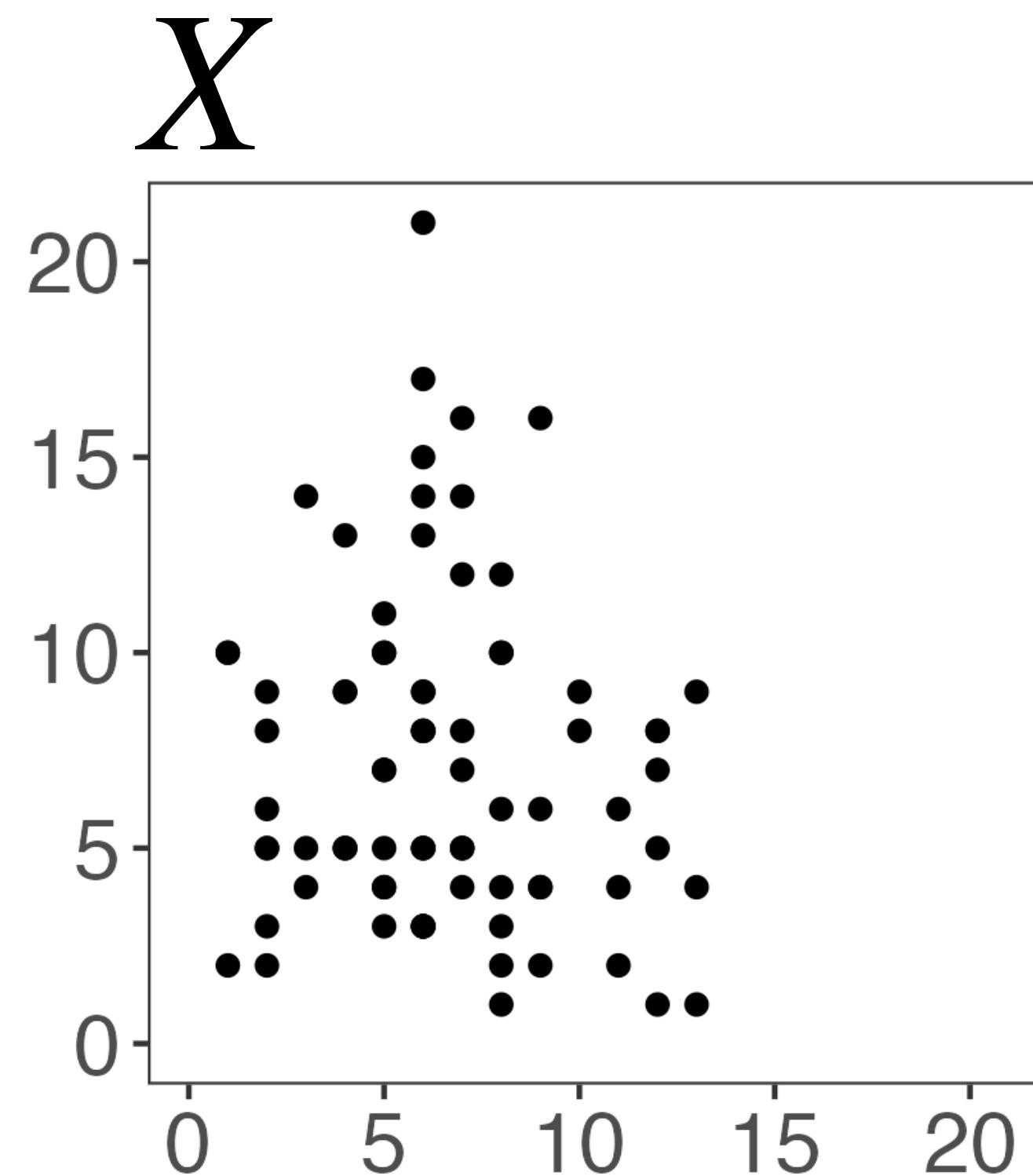


SVM gets 96% accuracy on test set, despite the fact that clusters are not "real".

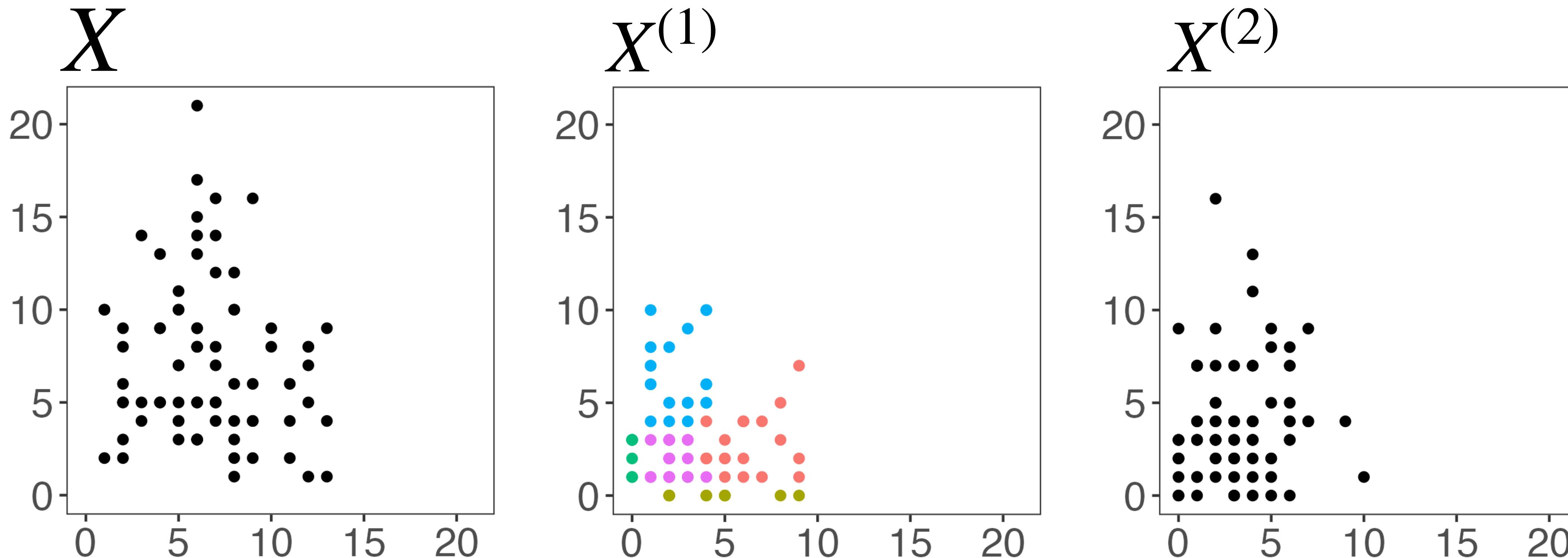
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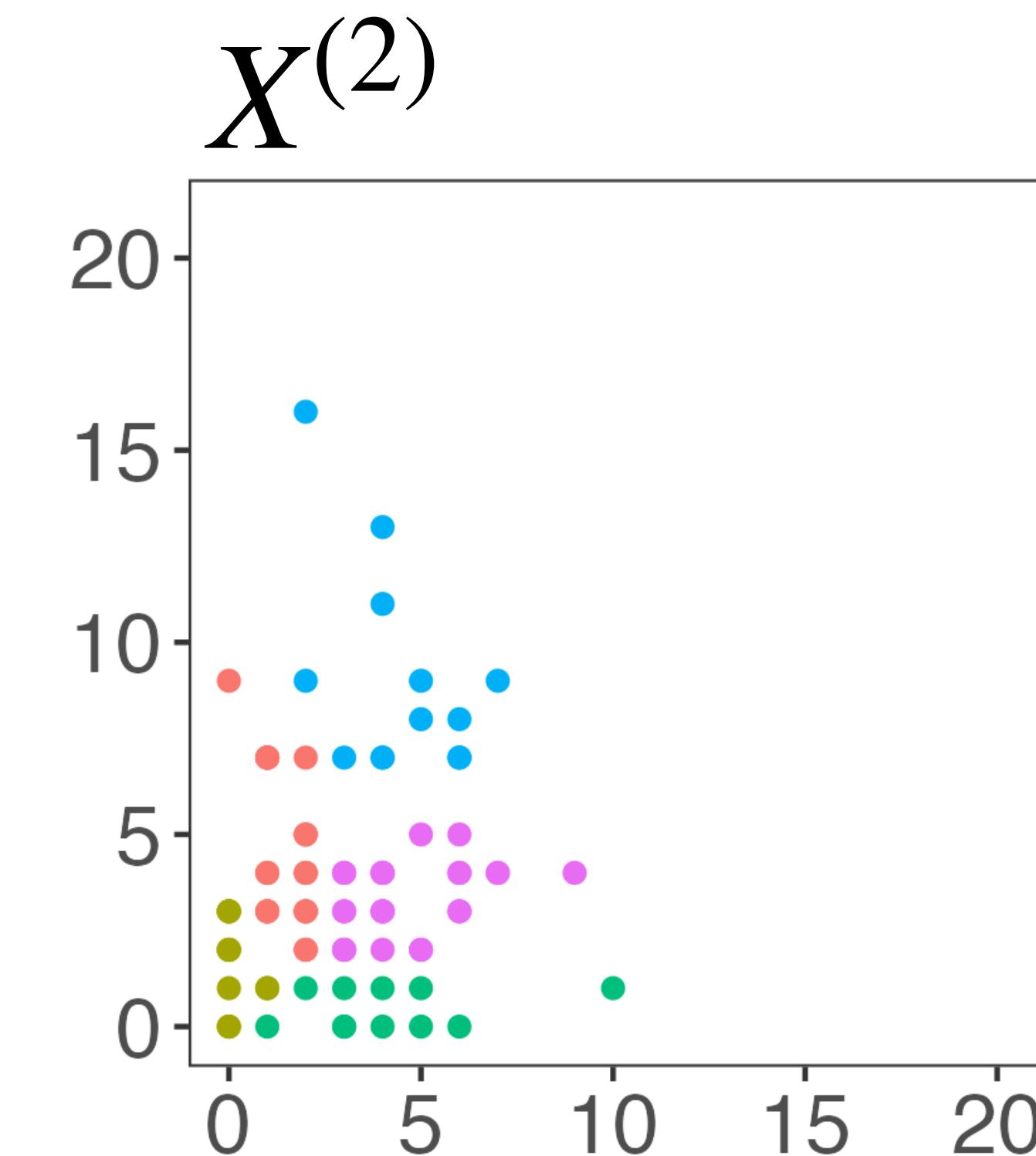
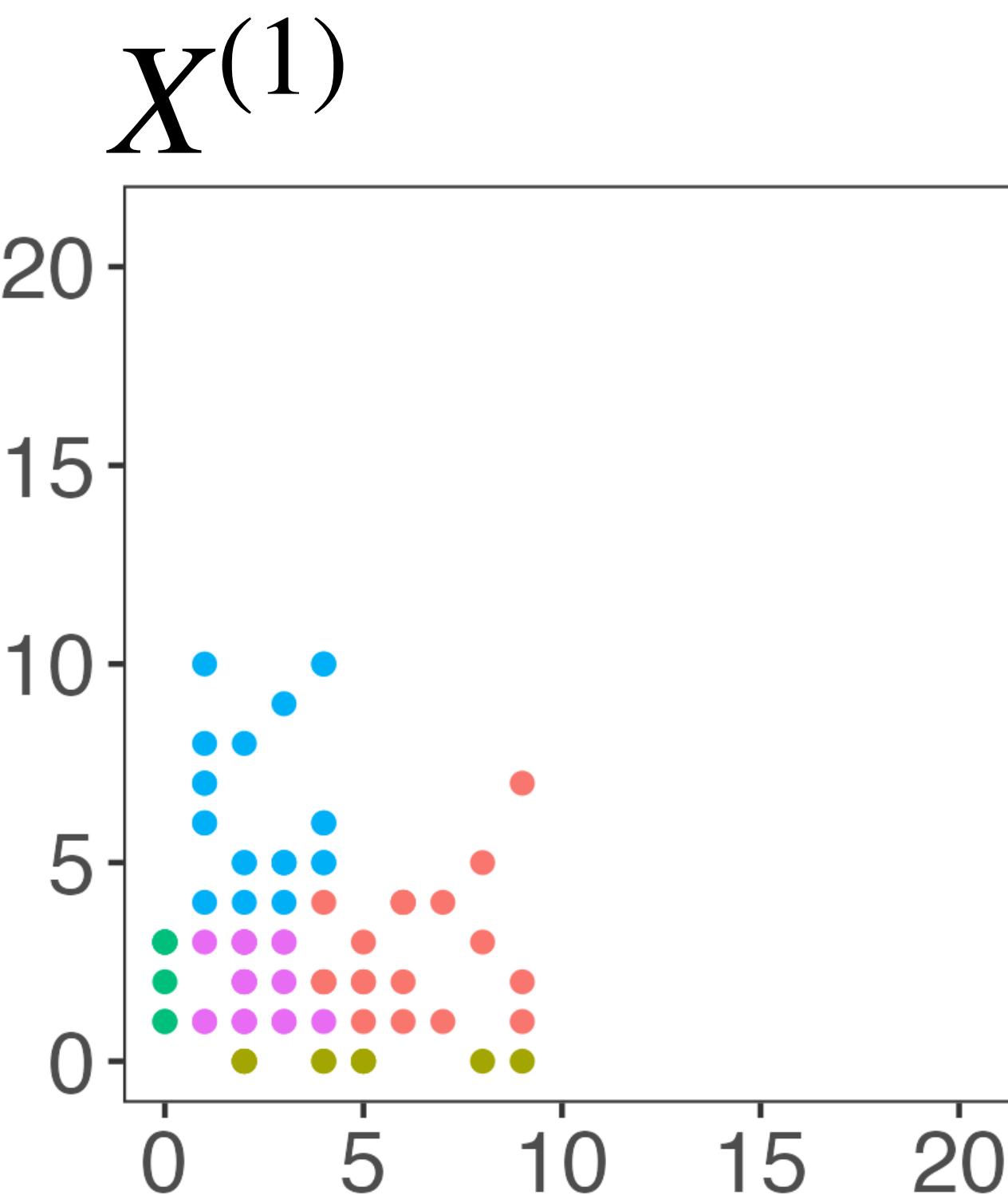
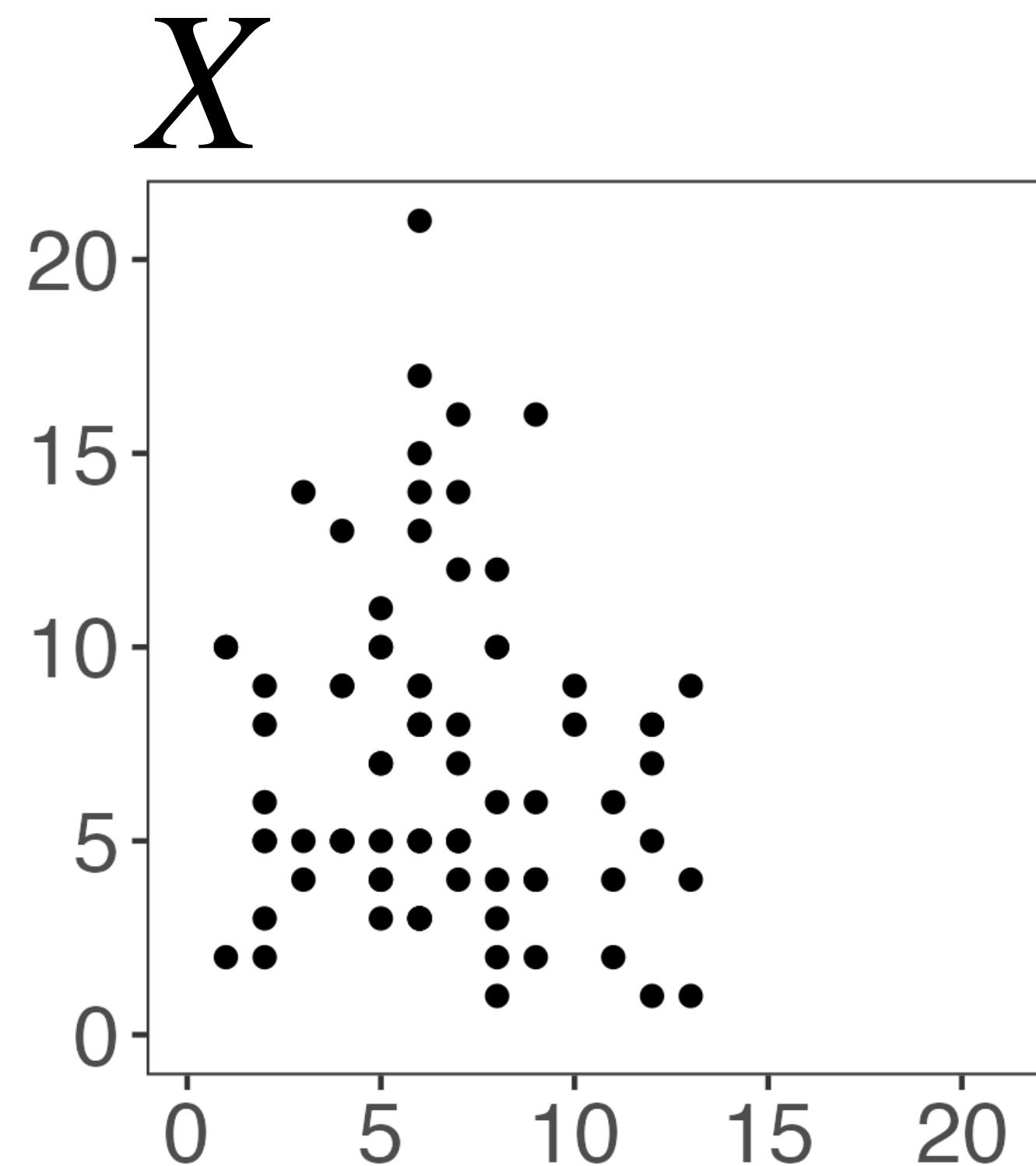
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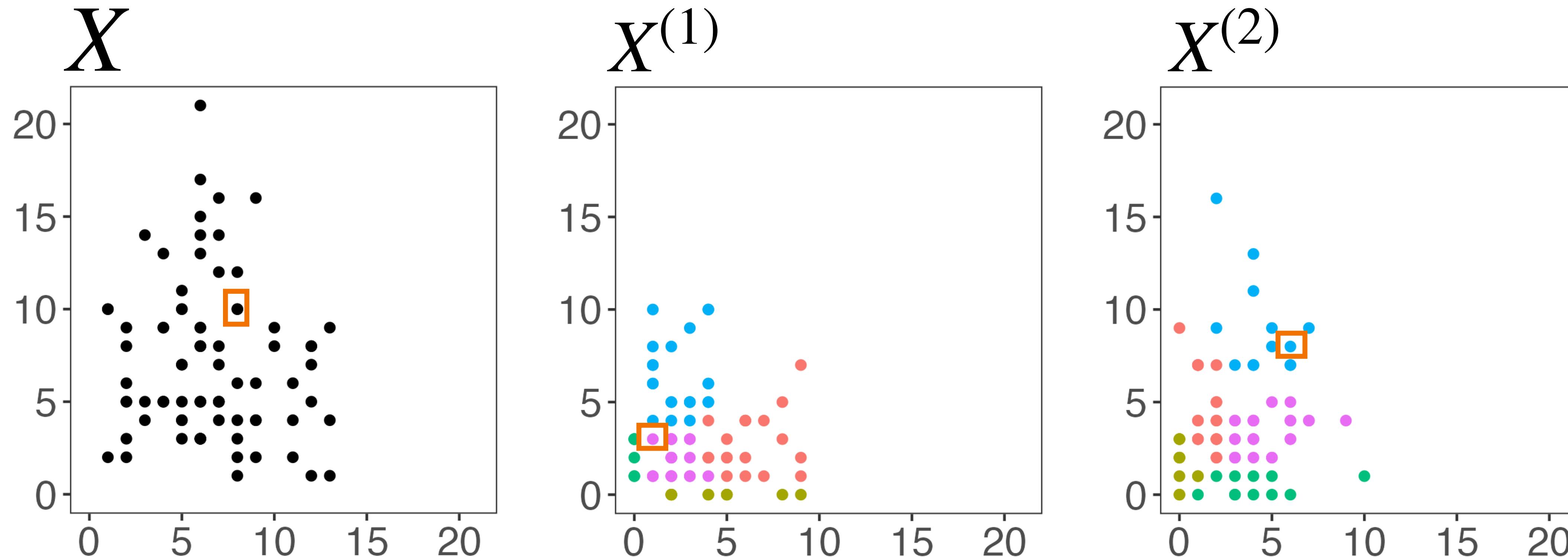
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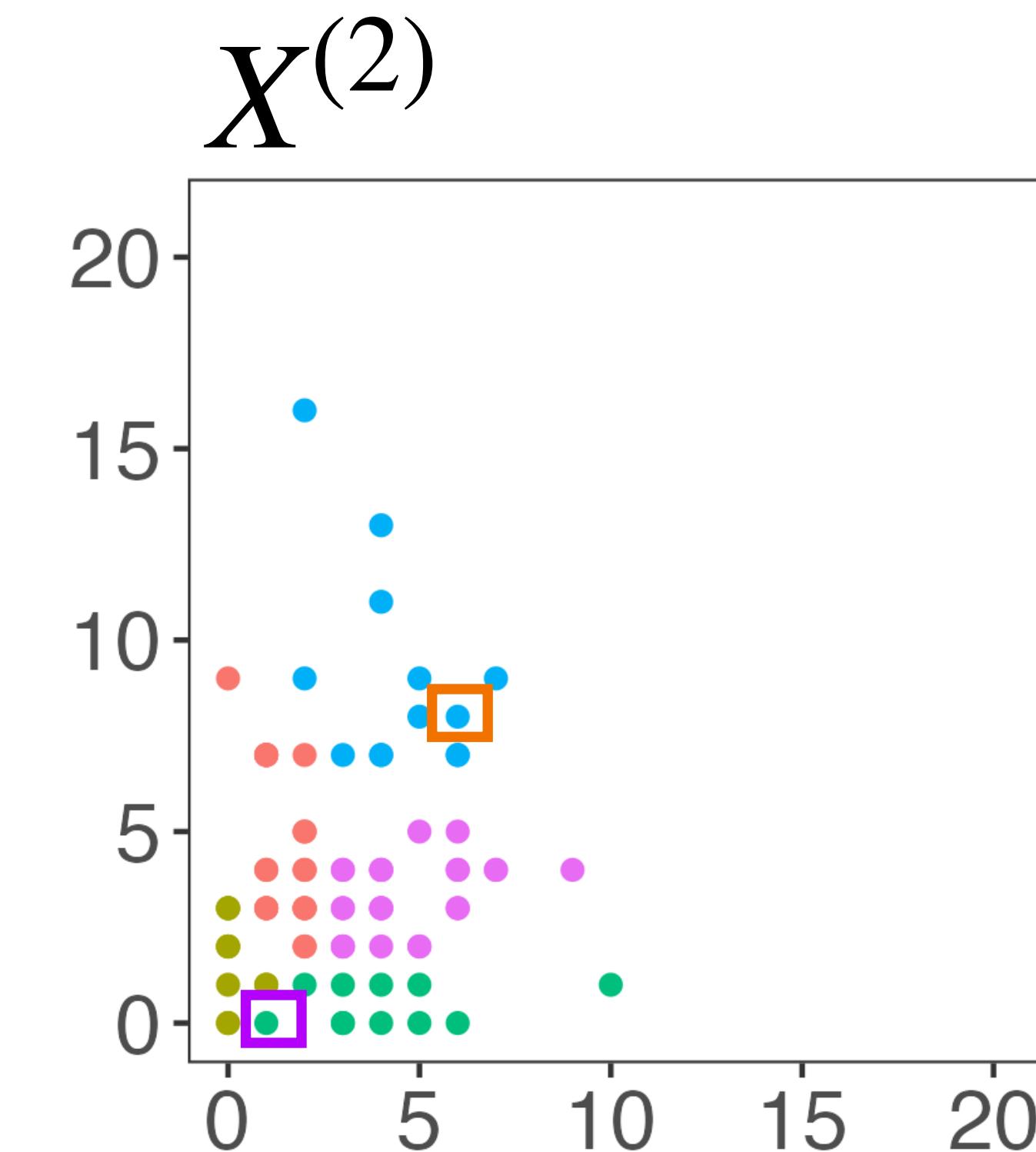
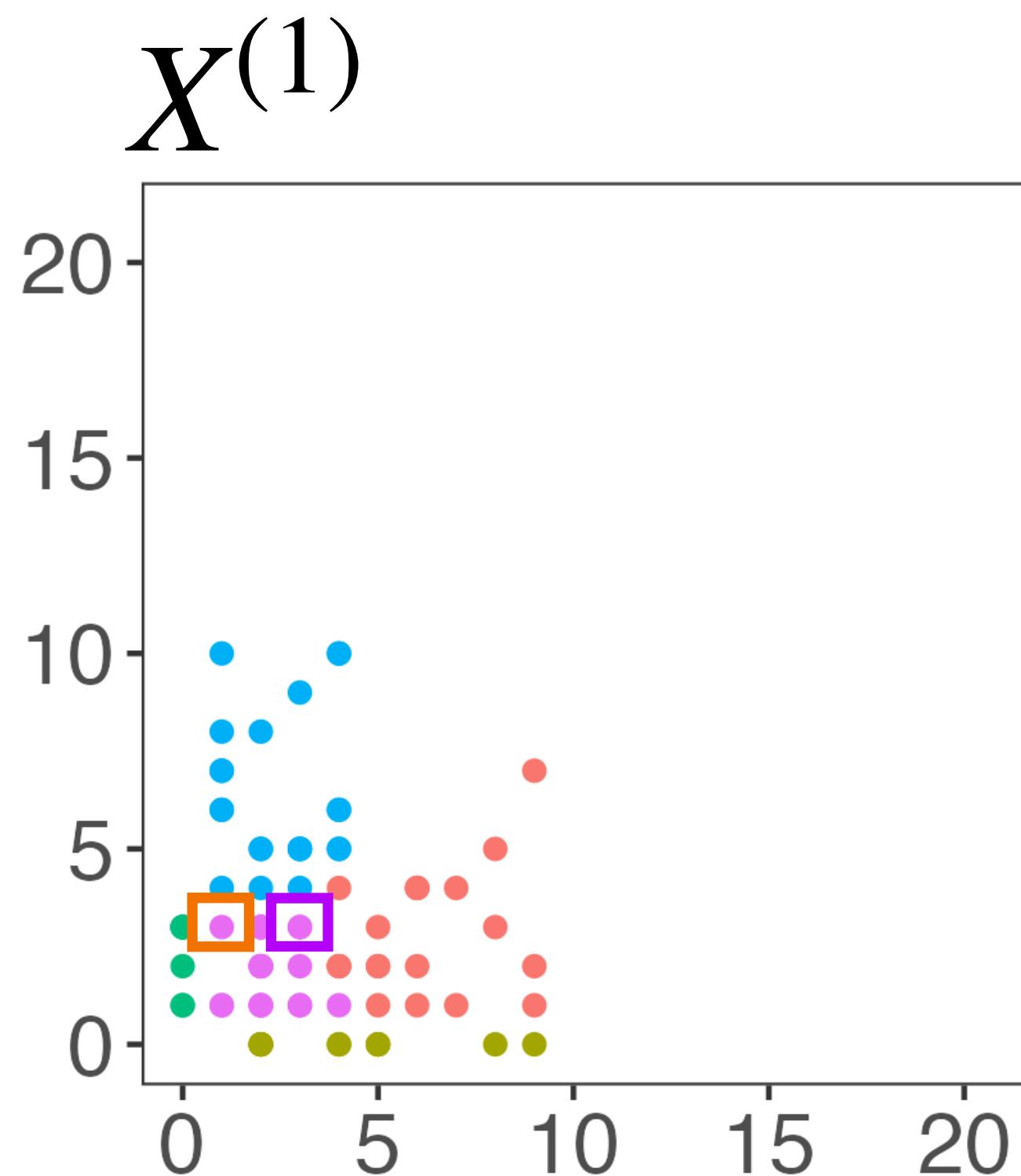
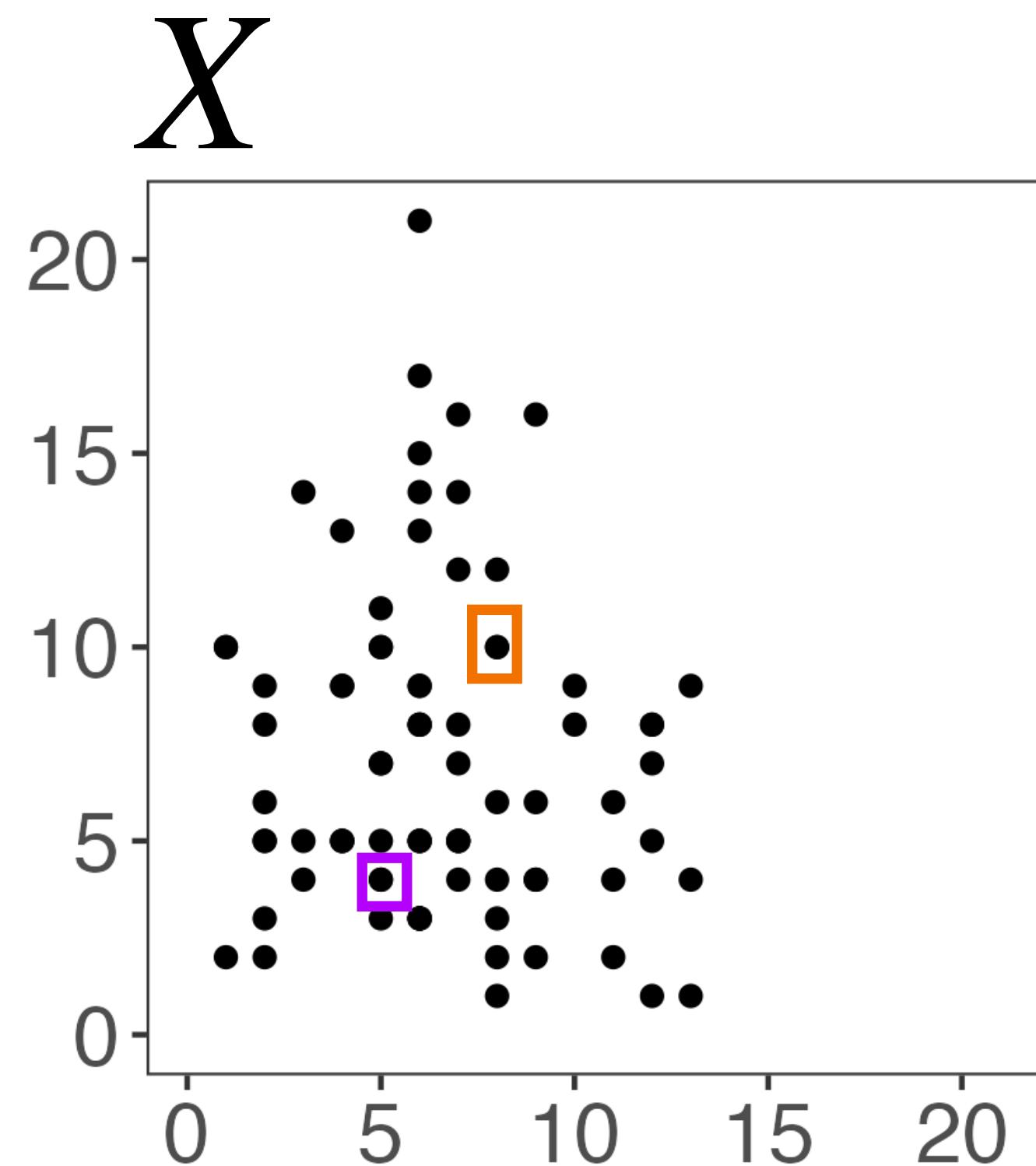
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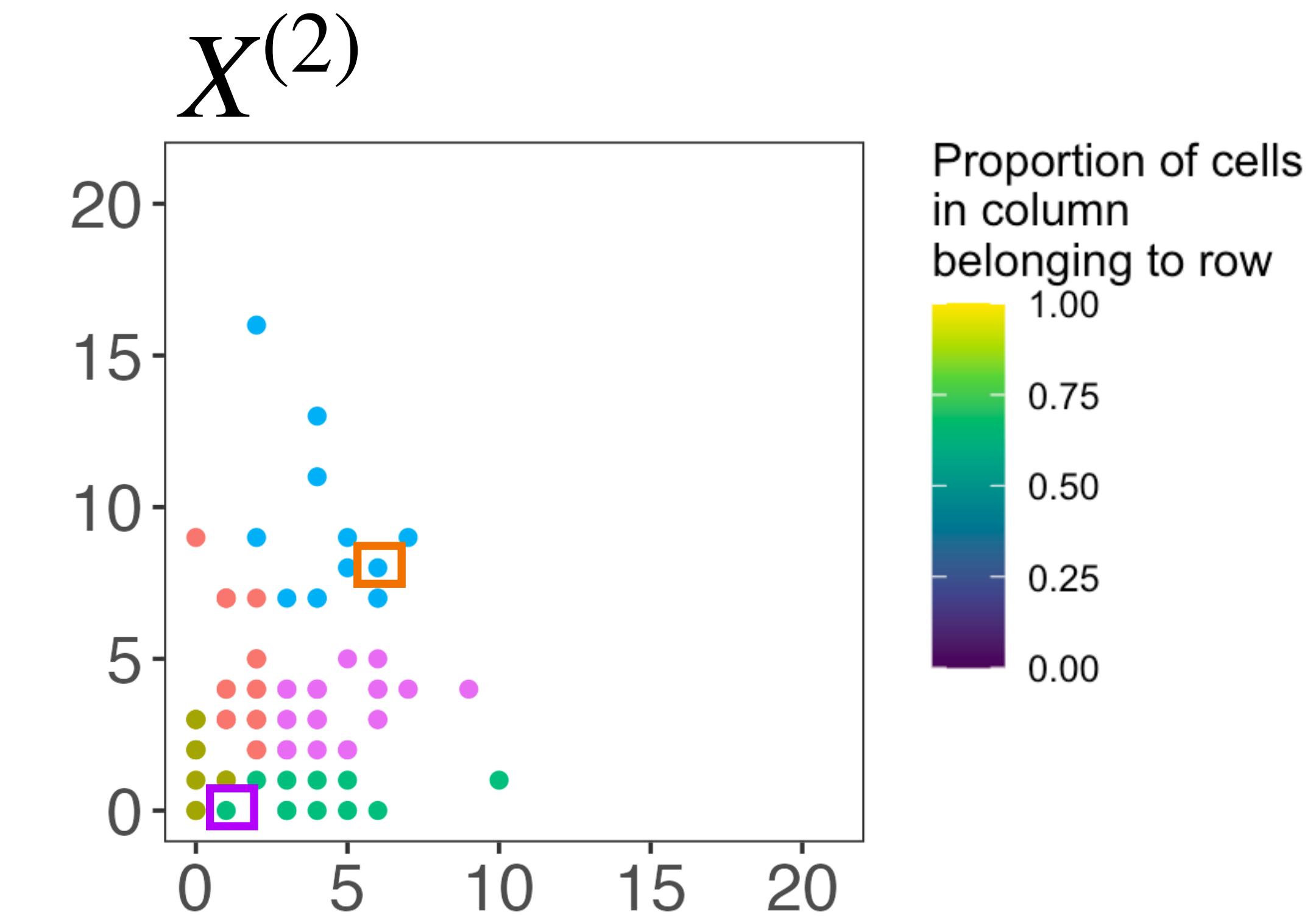
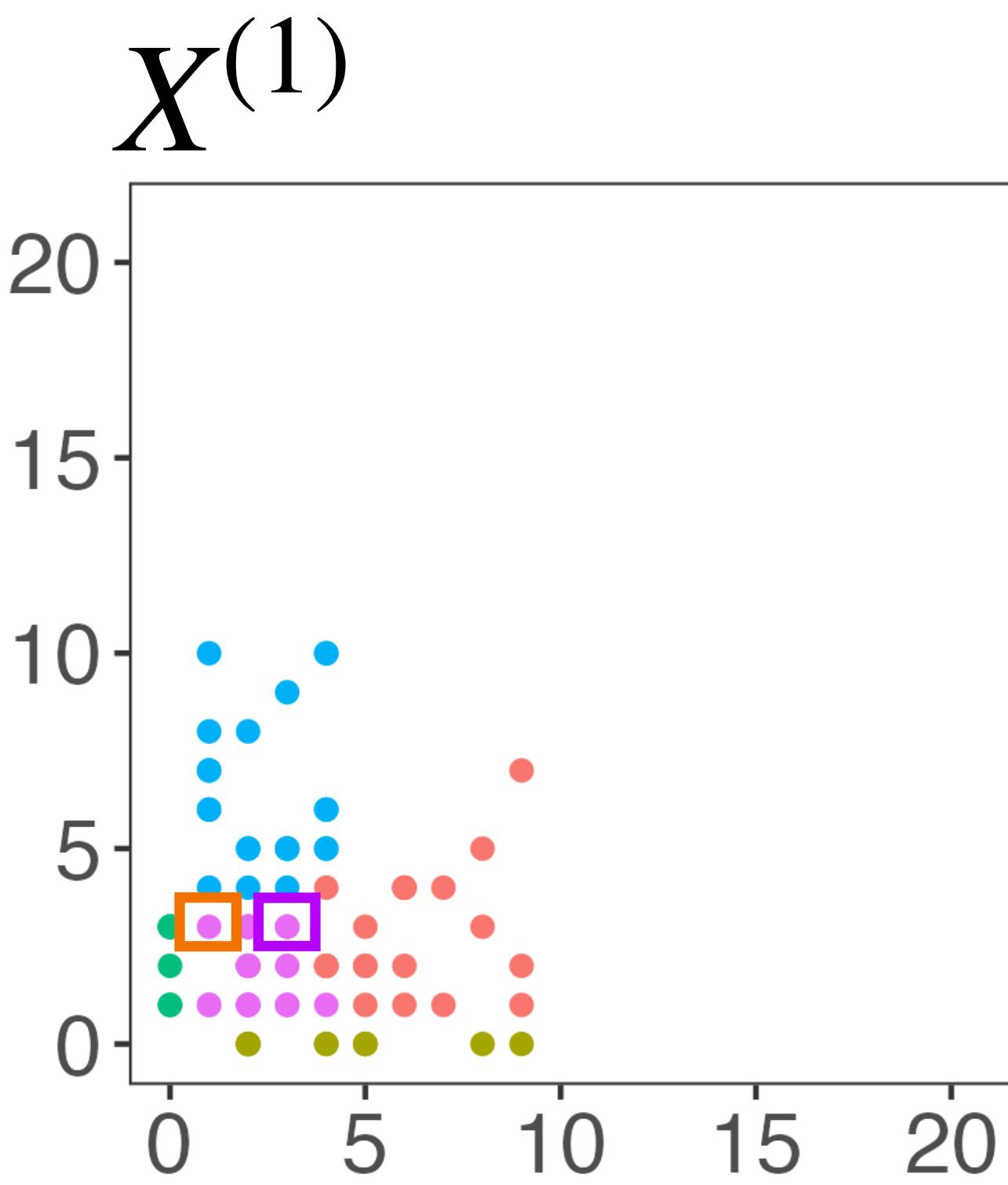
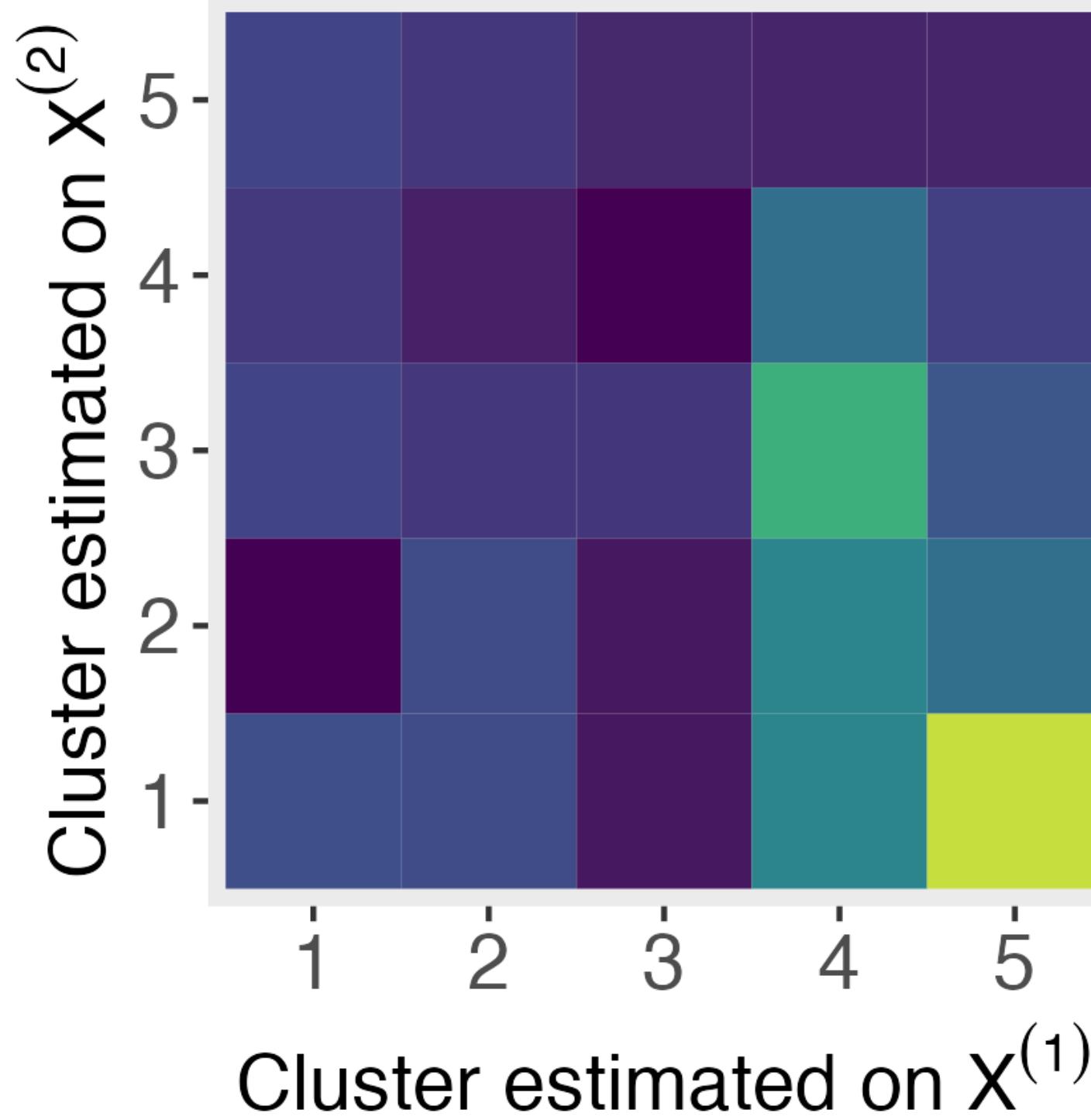
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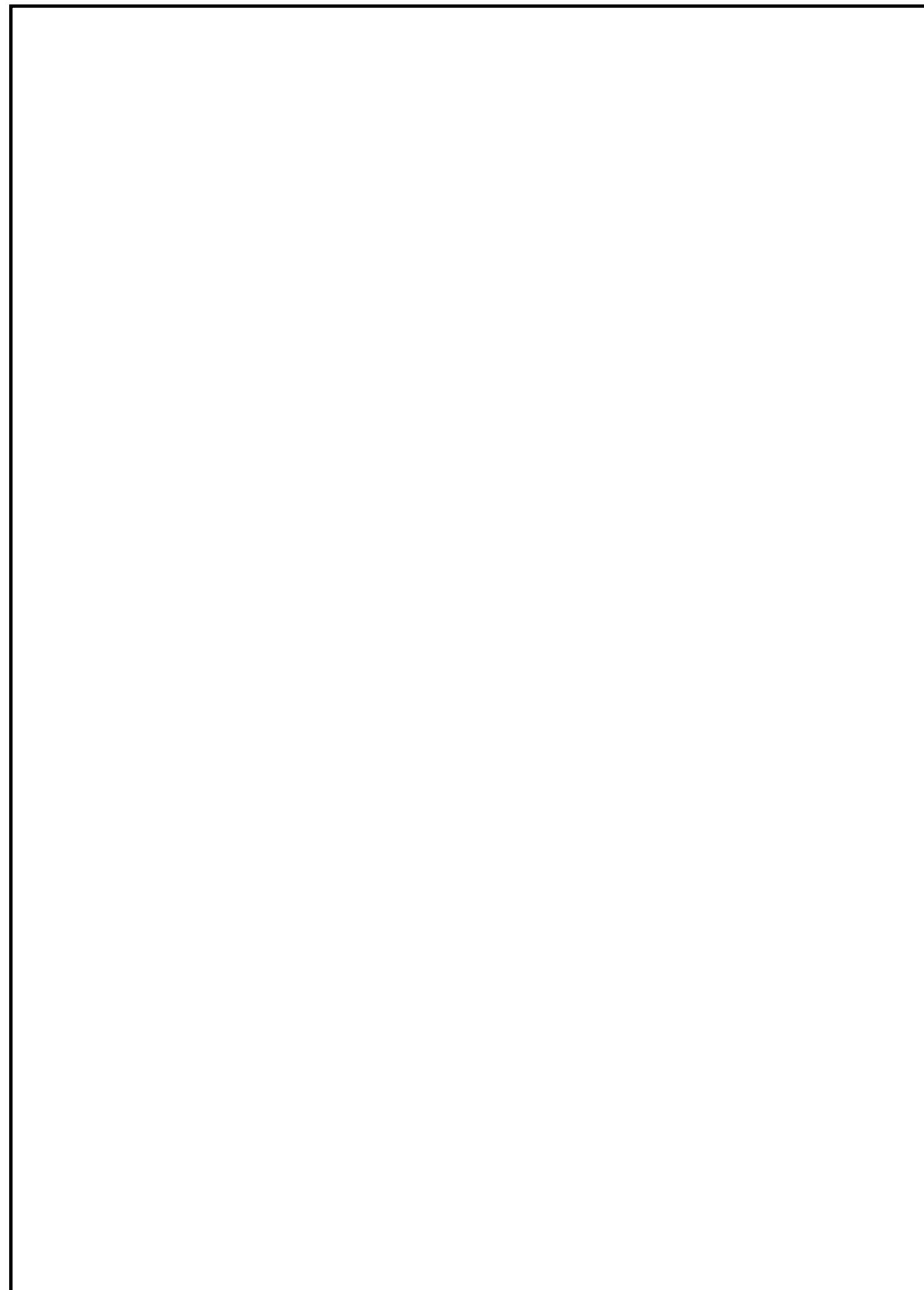


Adjusted Rand Index ≈ 0.01

Re-analysis of Kidney cell data from fetal cell atlas

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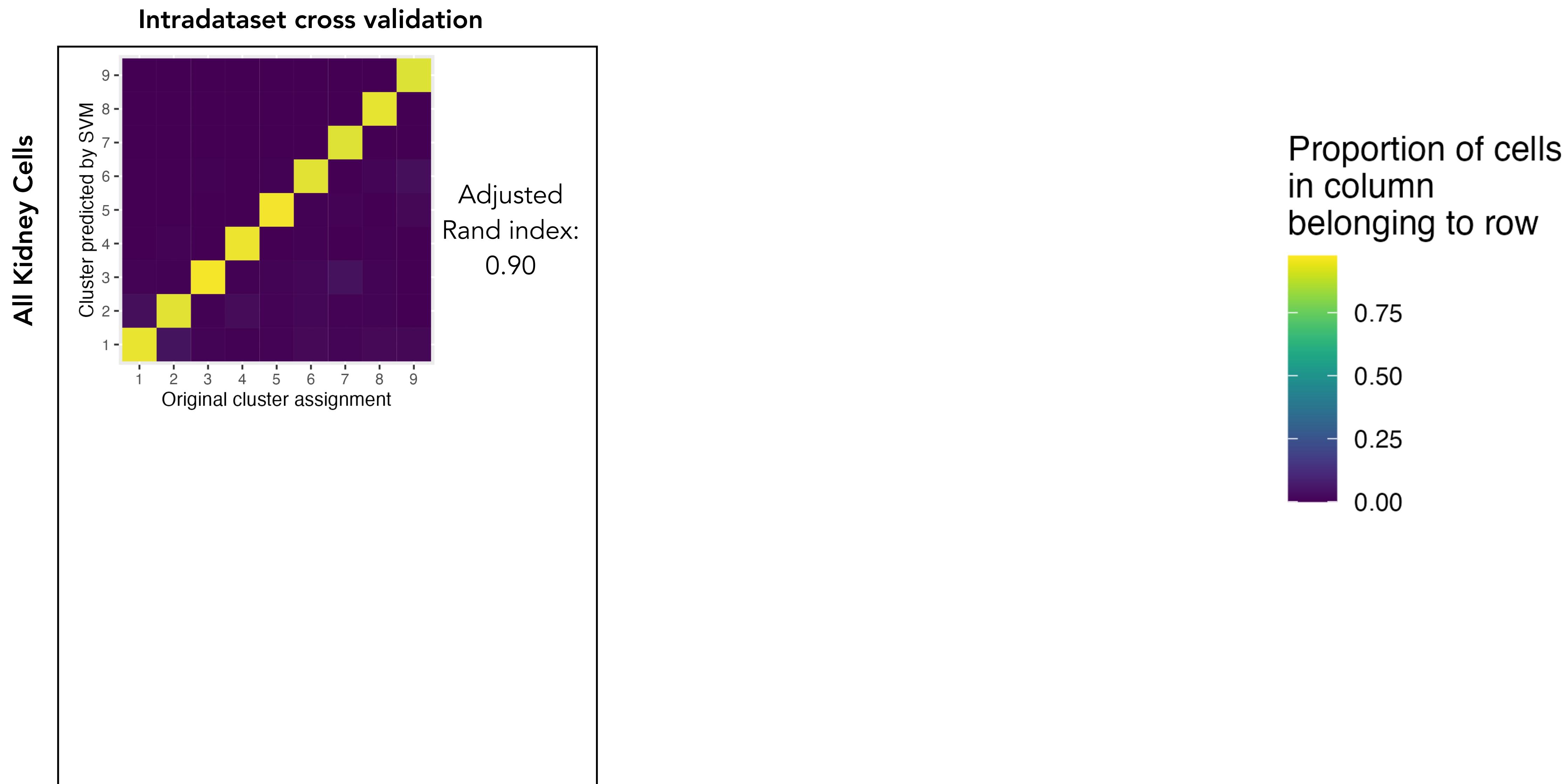
Intradataset cross validation



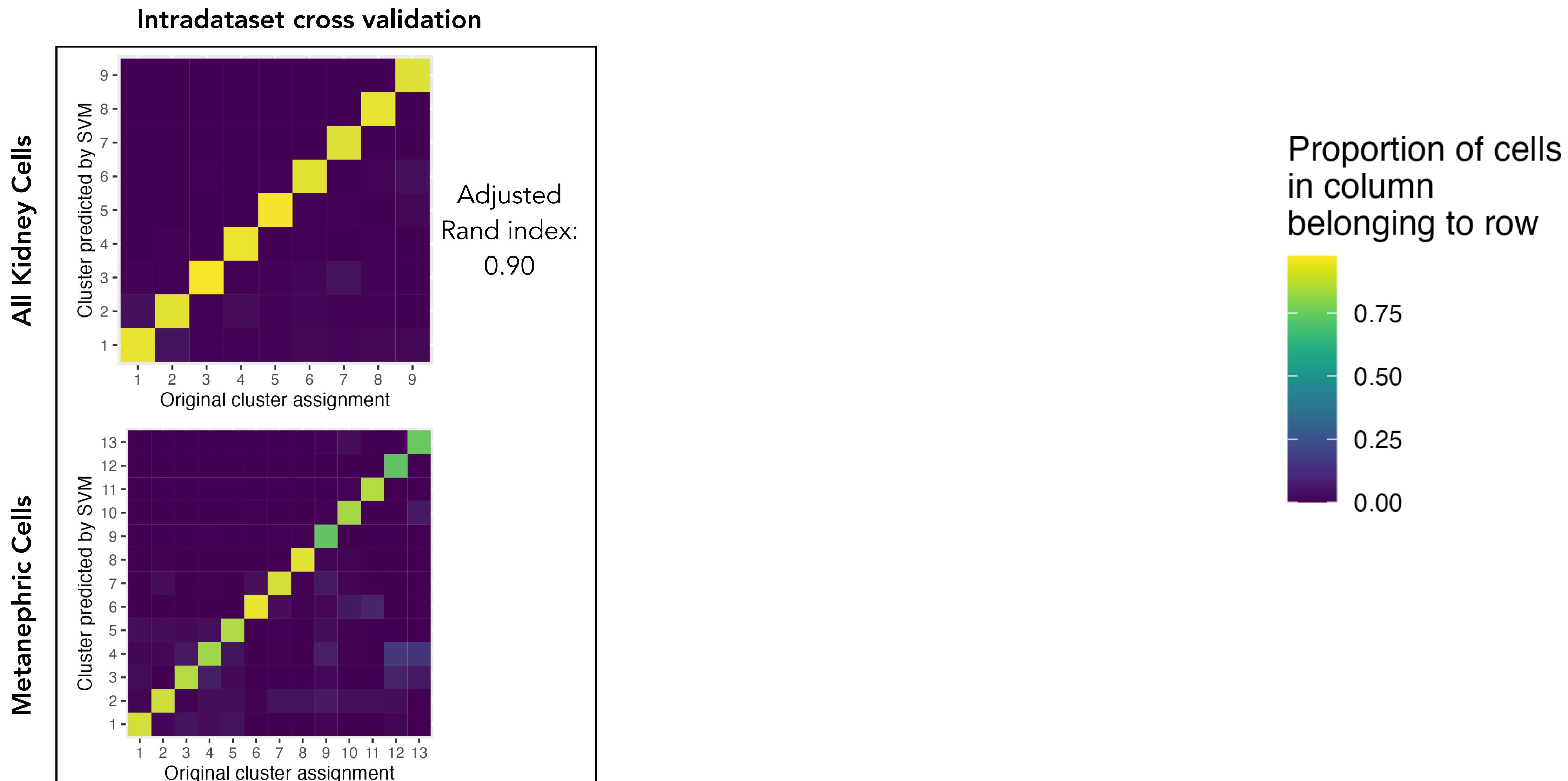
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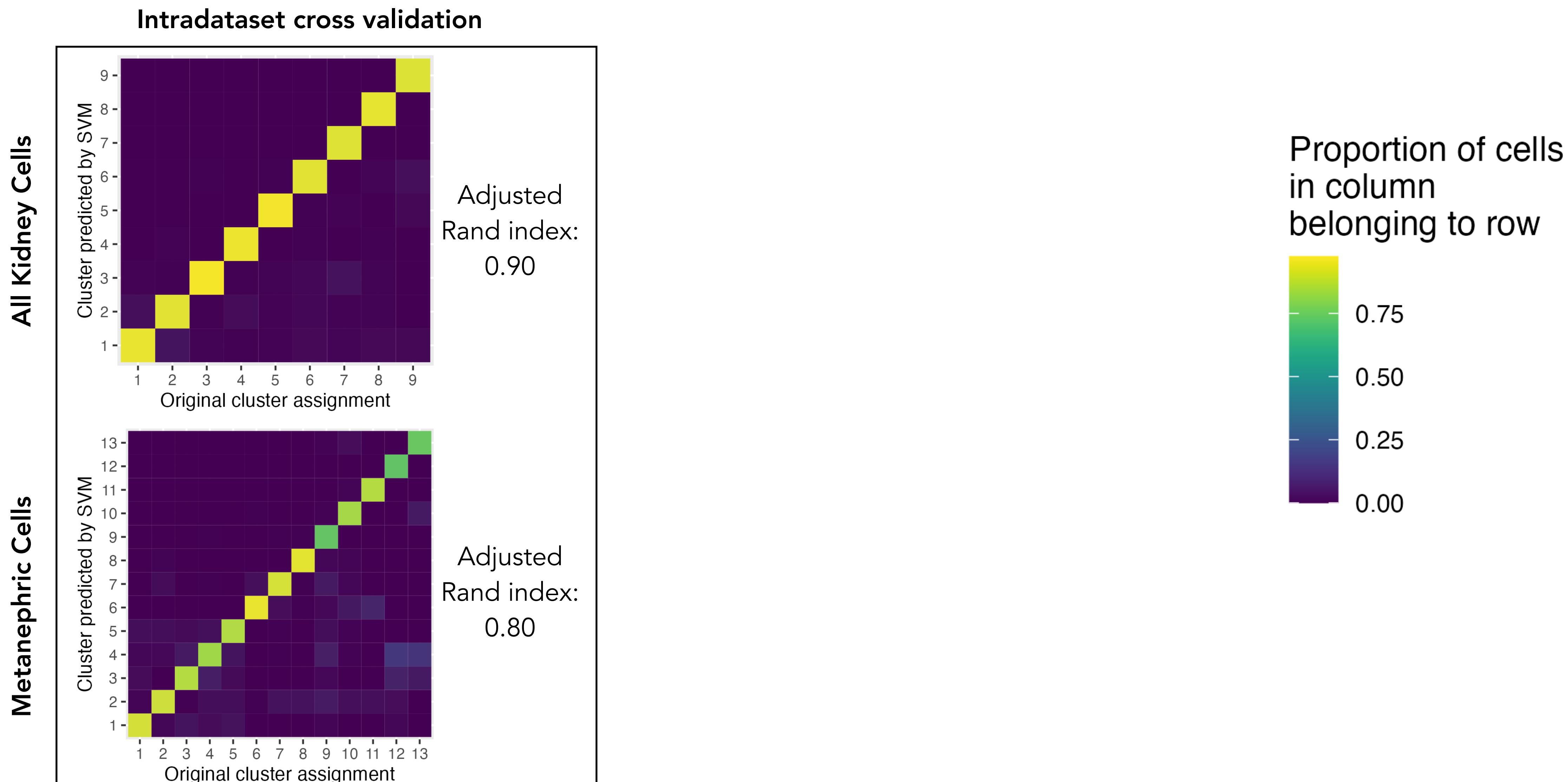
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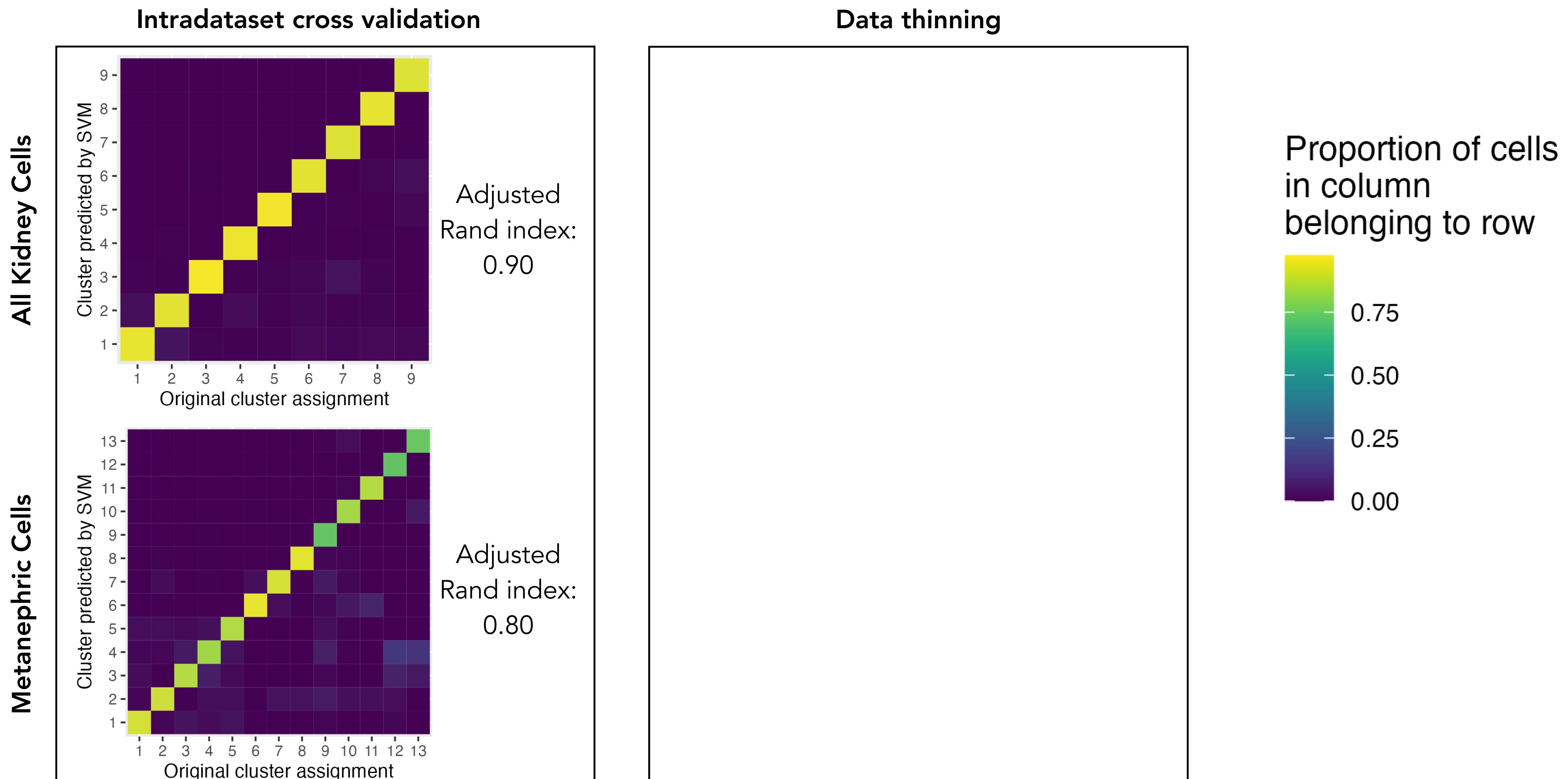
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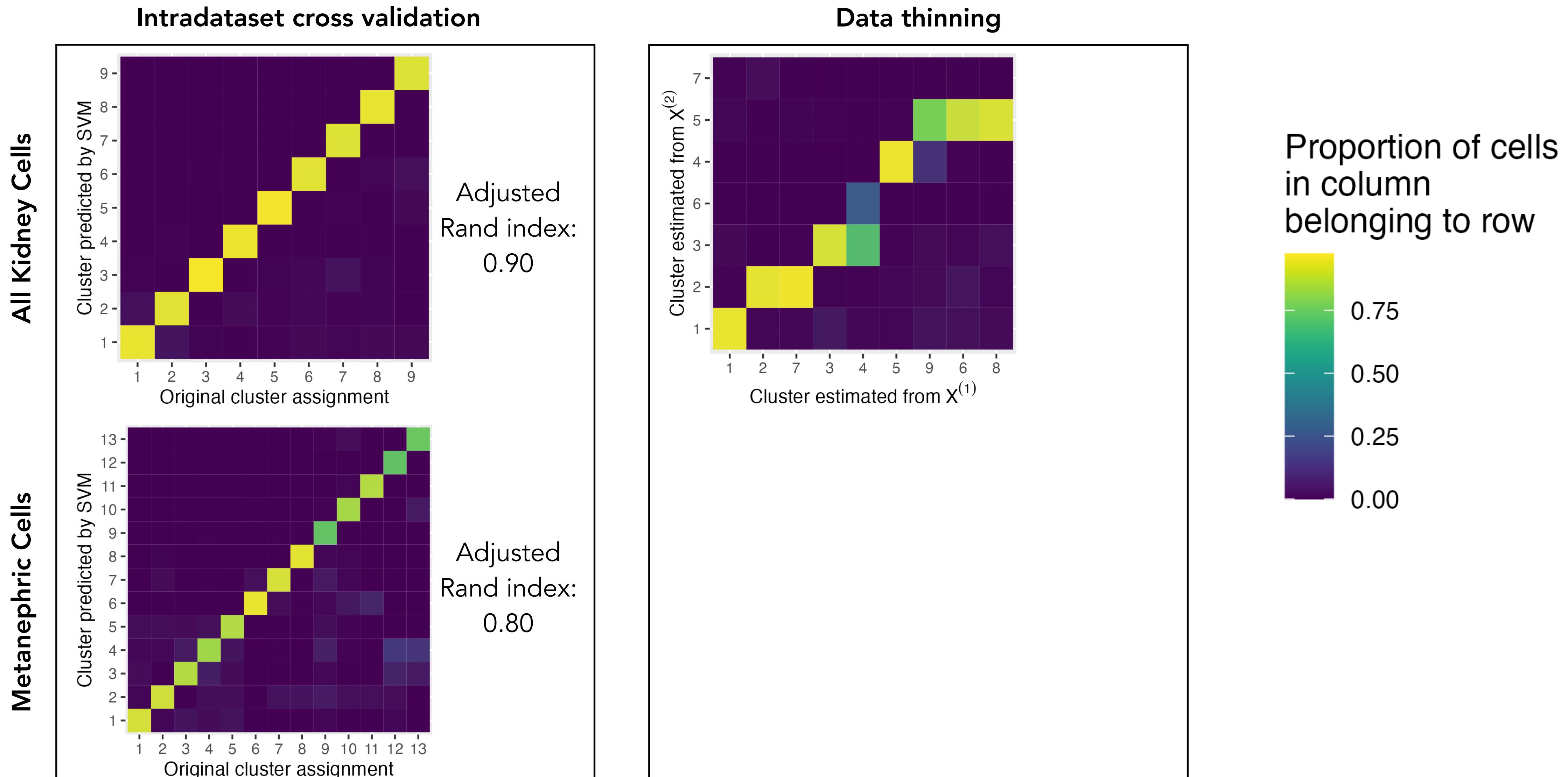
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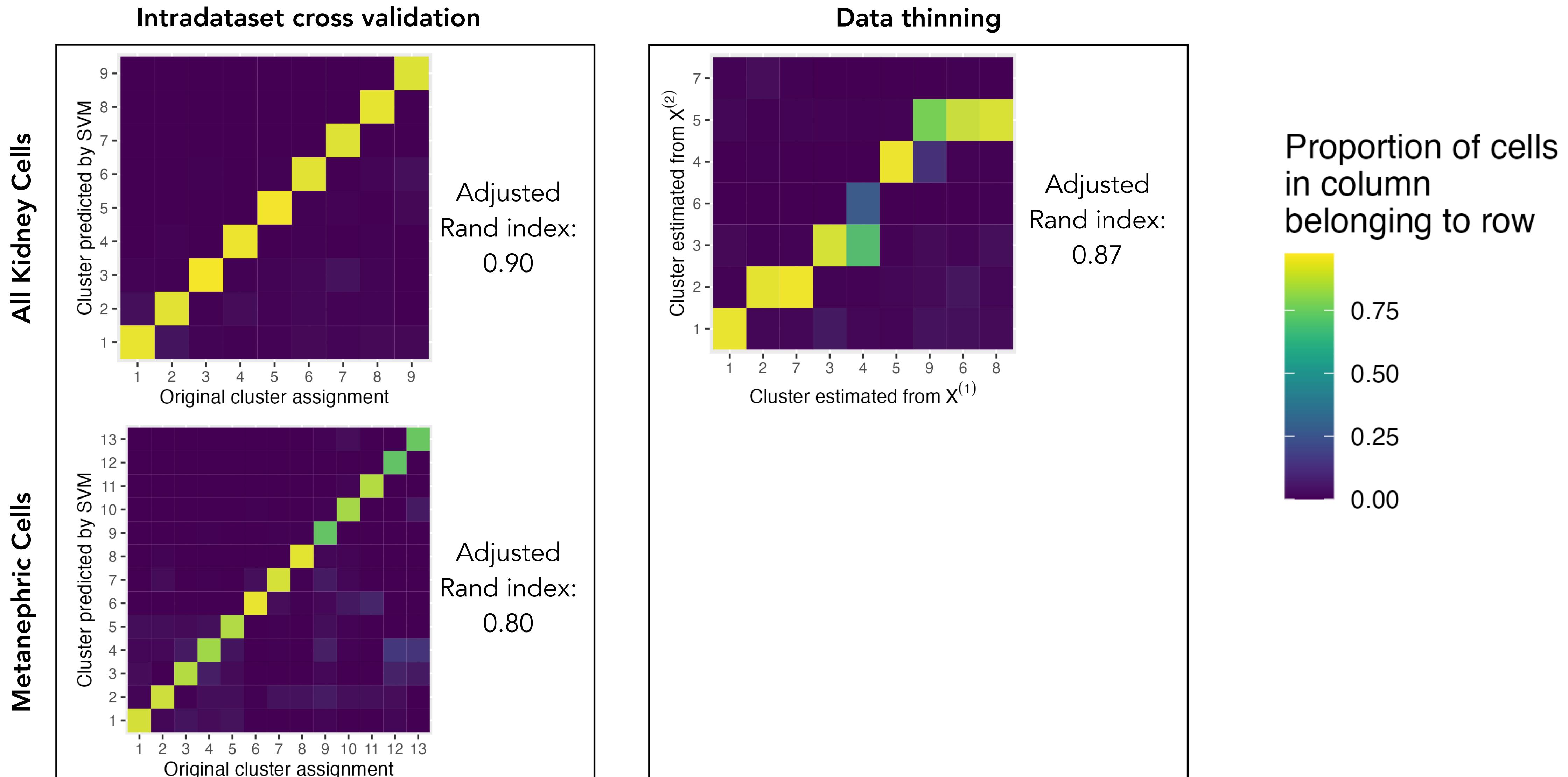
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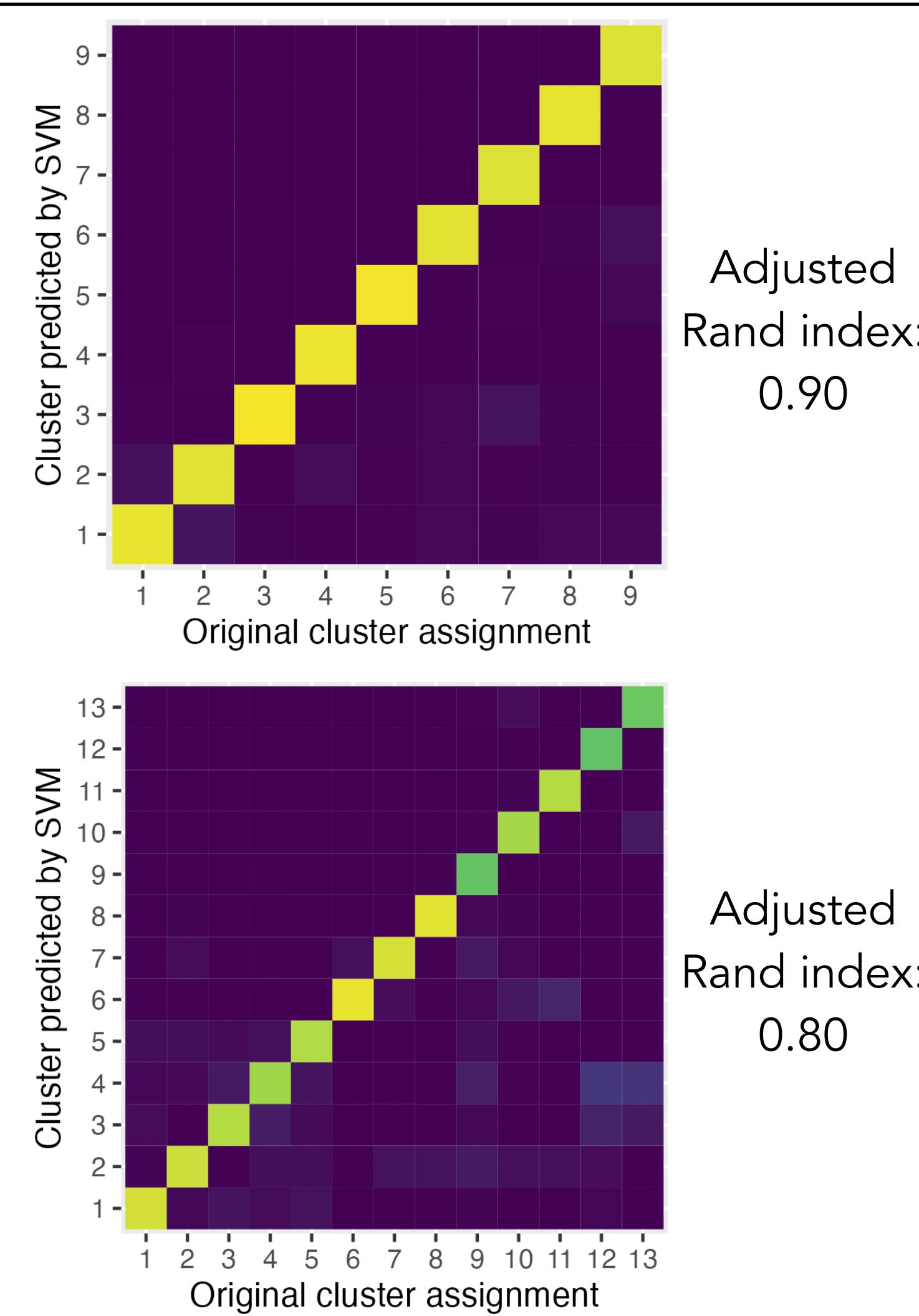
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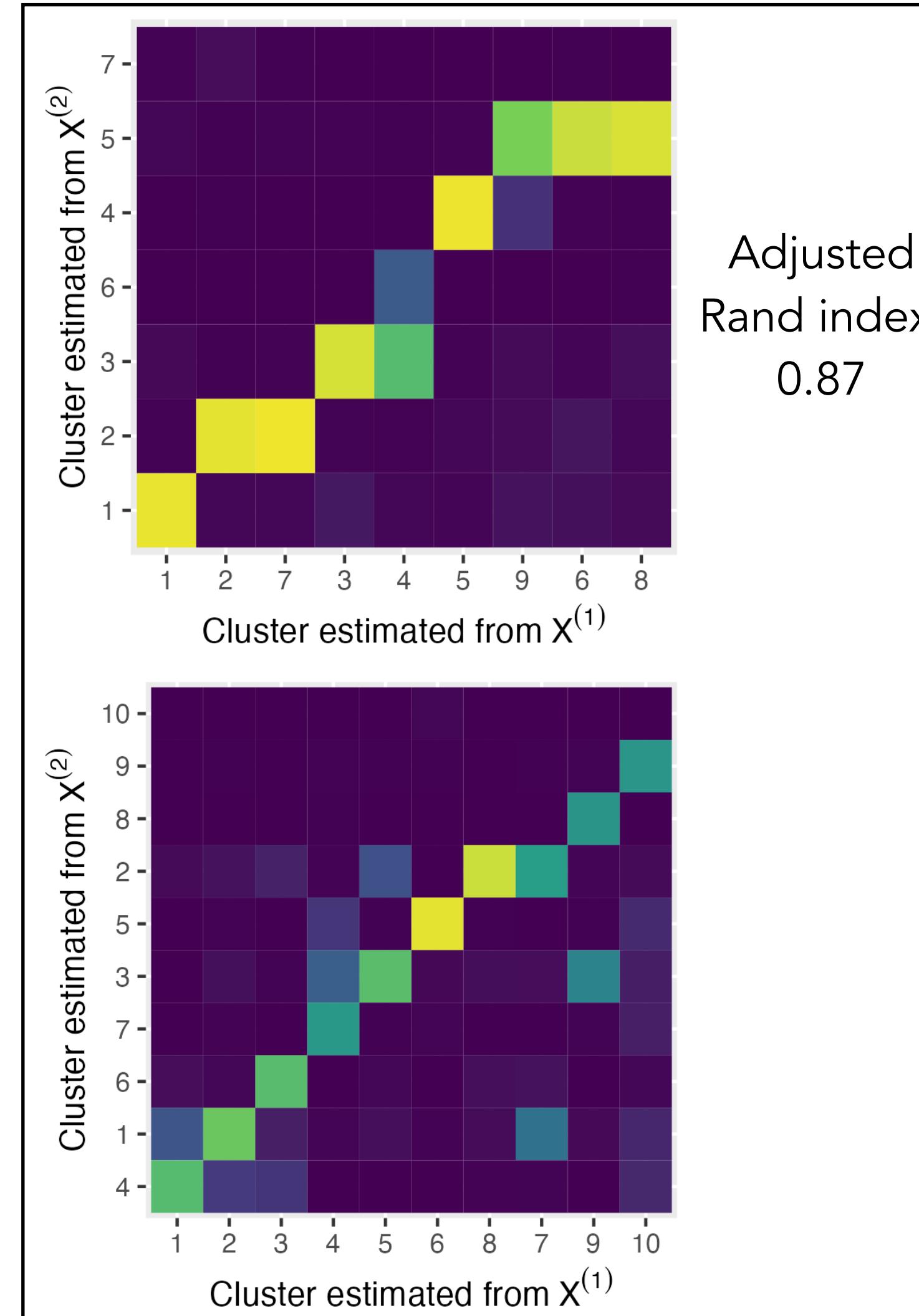
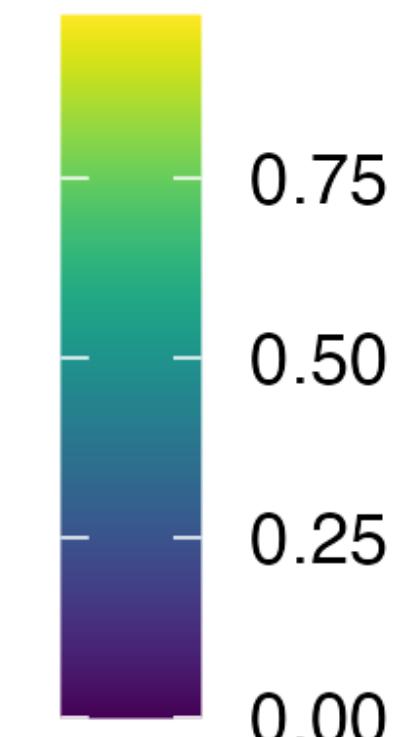
Intradataset cross validation

All Kidney Cells



Data thinning

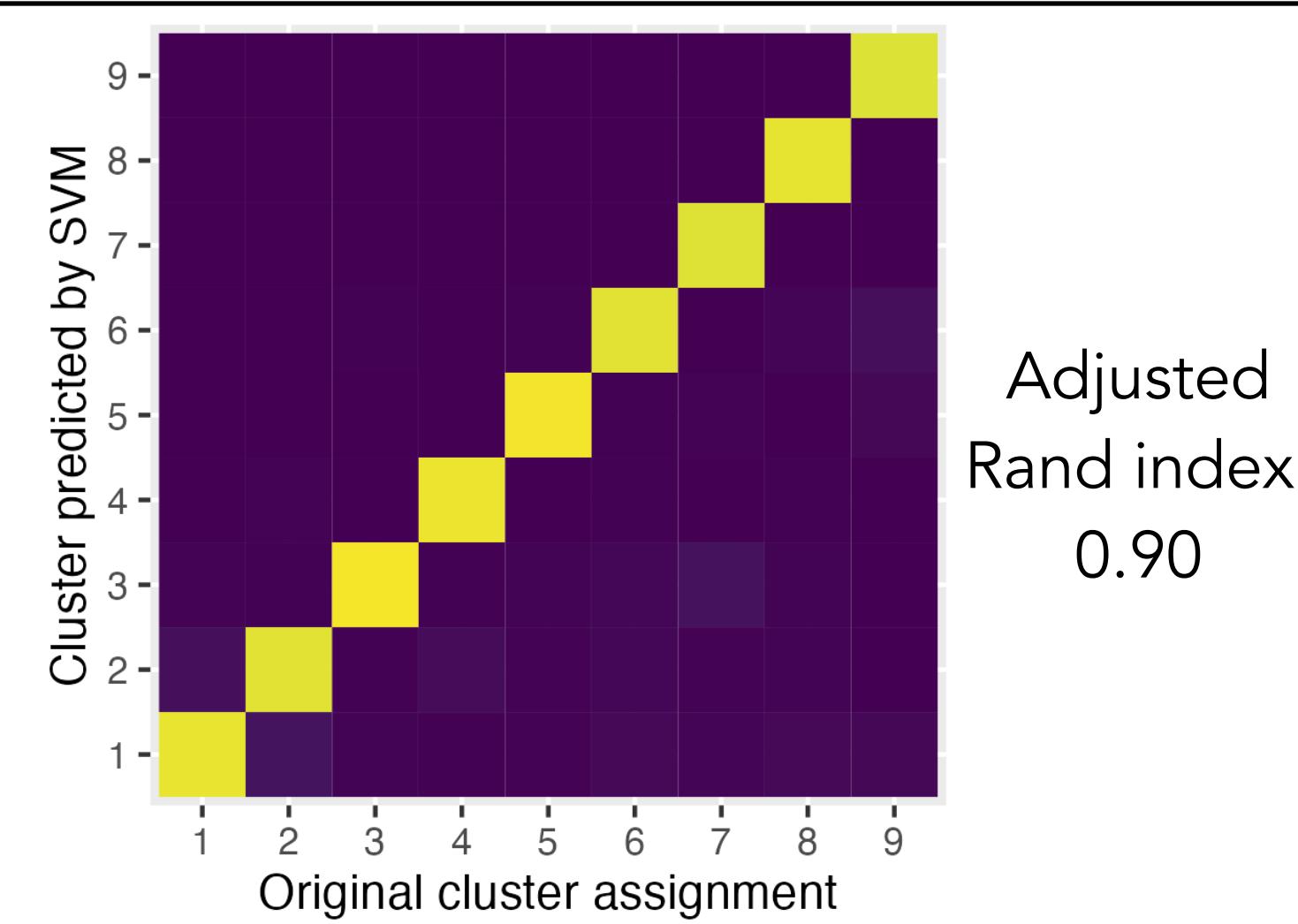
Proportion of cells
in column
belonging to row



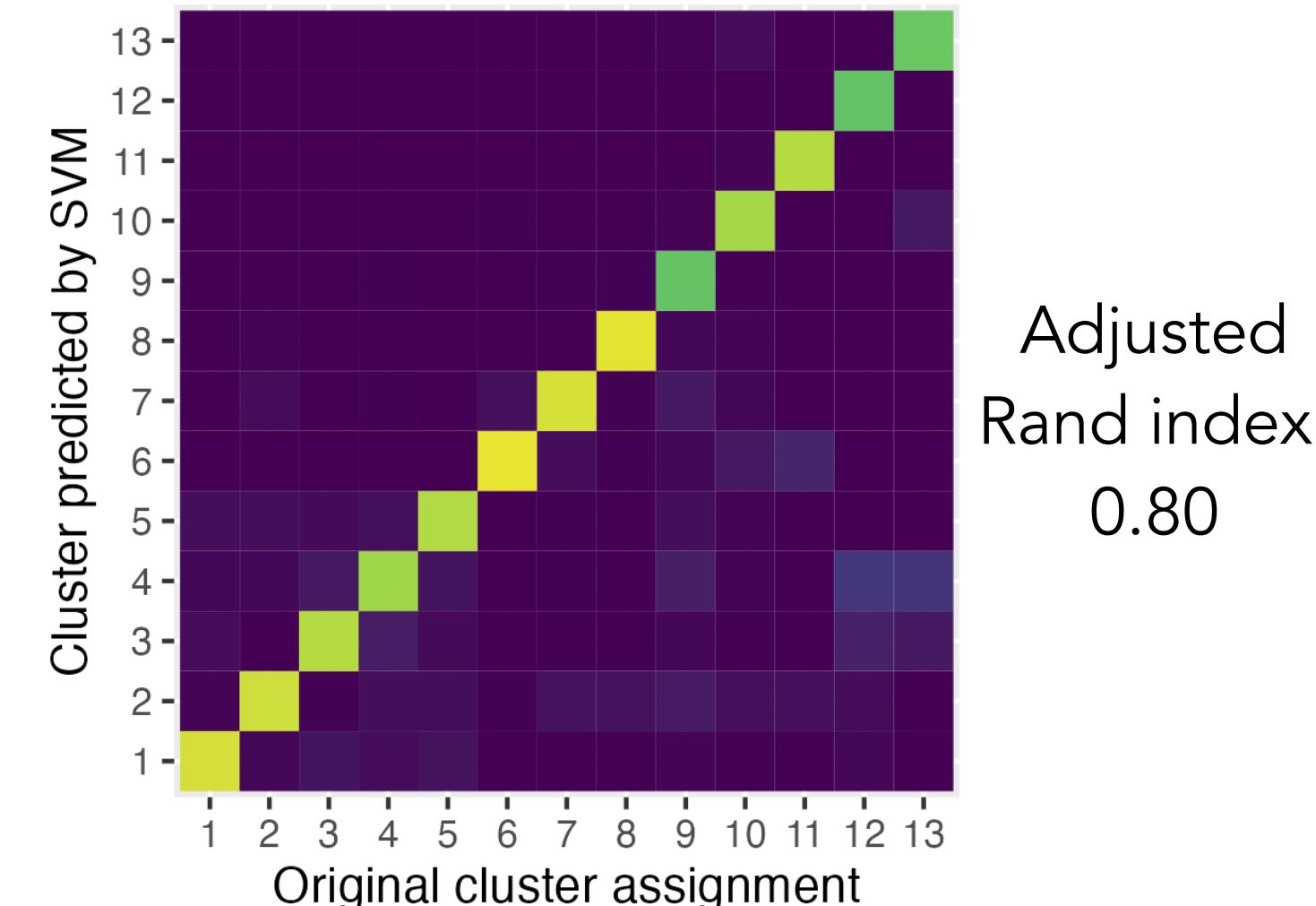
Re-analysis of Kidney cell data from fetal cell atlas

Intradataset cross validation

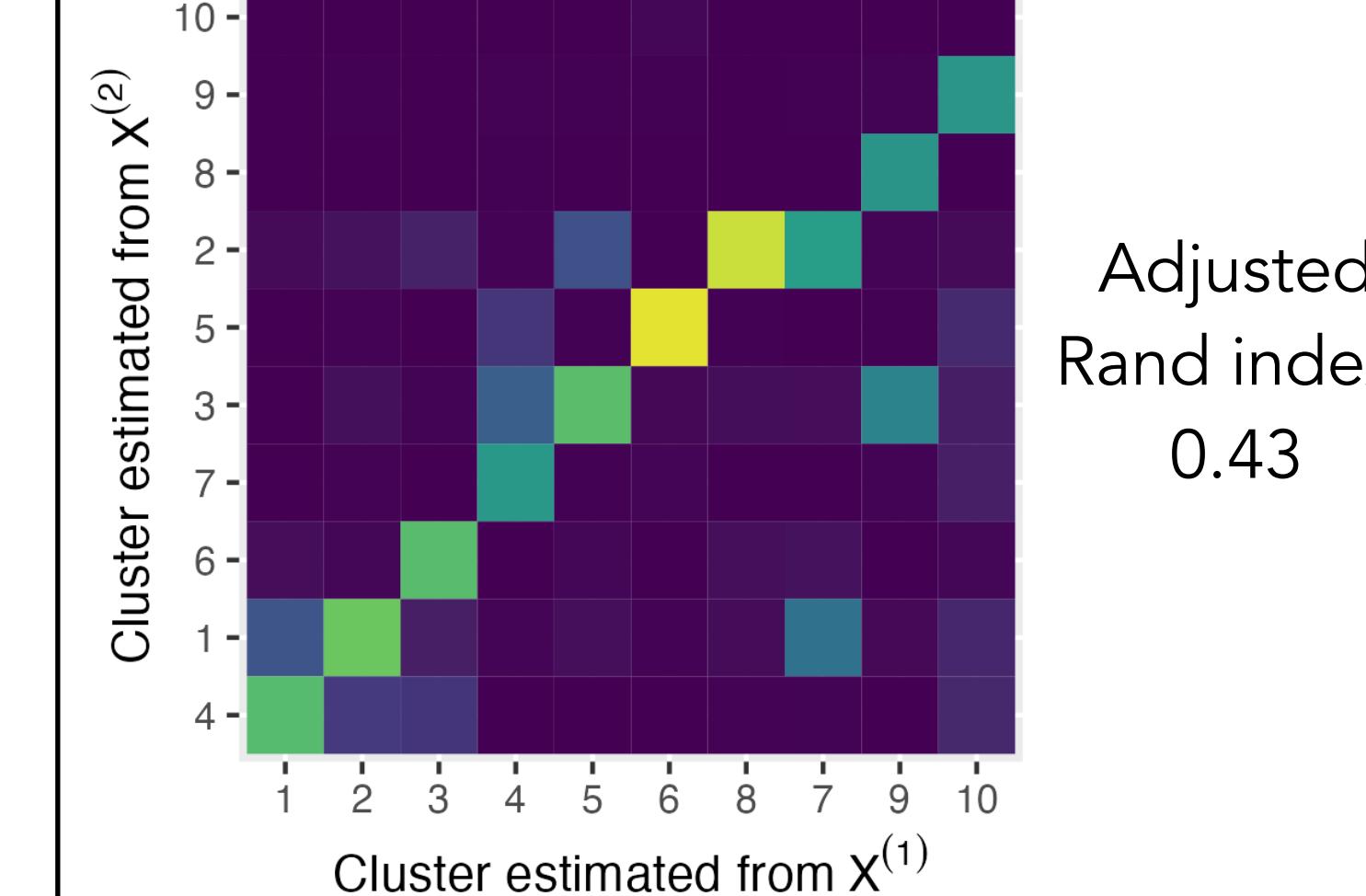
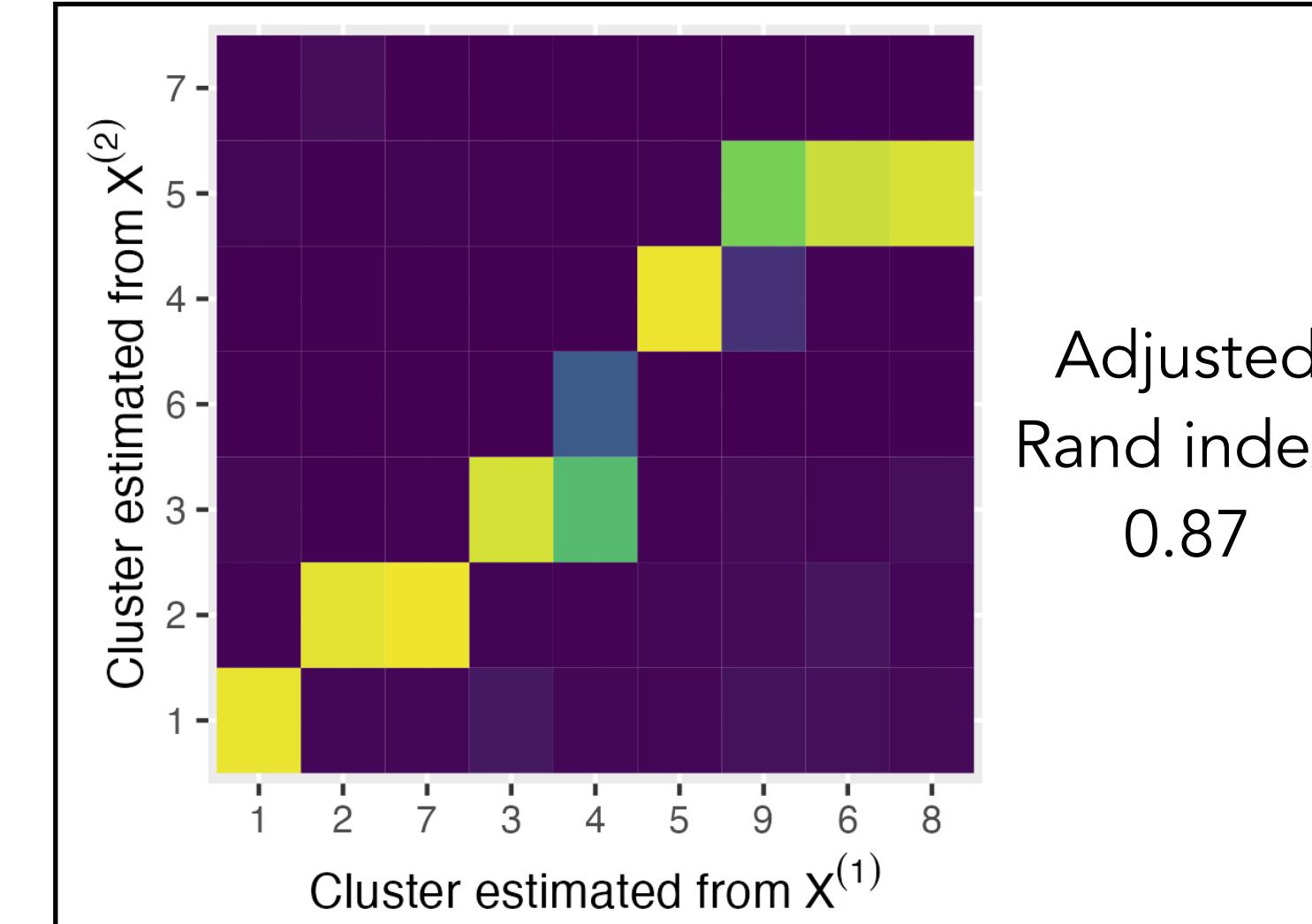
All Kidney Cells



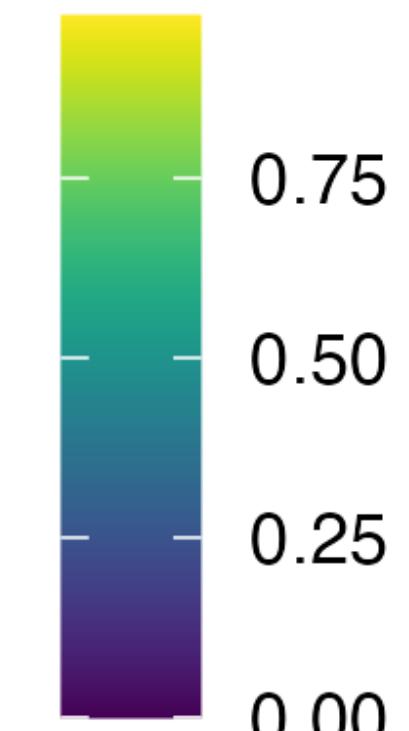
Metanephric Cells



Data thinning



Proportion of cells
in column
belonging to row



Negative binomial data thinning is useful in the analysis of single-cell RNA sequencing data

Project 4

Negative binomial count splitting
for single cell RNA sequencing data

Anna Neufeld, Lucy Gao, Josh Popp, Alexis Battle, Daniela Witten

Arxiv preprint will be posted soon!

Outline

1. Motivation: settings where sample splitting doesn't work
2. Poisson thinning
3. Data thinning
4. Application to single-cell RNA sequencing data
5. **Ongoing work**

Three ways to avoid double dipping

1. Specialized methods, such as selective inference.
2. Sample splitting.
3. Data thinning.

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Limited to convolution-closed distributions?

Revisiting the goals of data thinning

Goal: split a single observation X into $X^{(1)}$ and $X^{(2)}$ such that:

- (1) $X^{(1)}$ and $X^{(2)}$ have the same distribution as X , up to a parameter scaling.
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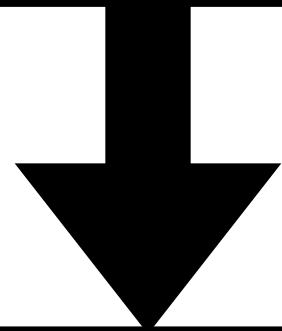
Generalized thinning with non-additive decompositions

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We observe realization x from $X \sim P_\theta$.

Generalized thinning with non-additive decompositions

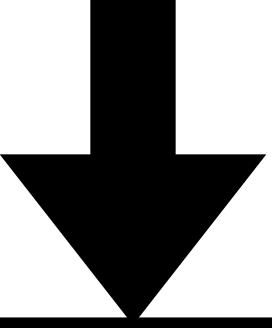
We know x could have arisen as $T(x', x'')$, where
 $X' \sim Q_\theta^1$, $X'' \sim Q_\theta^2$, $X' \perp\!\!\!\perp X''$.



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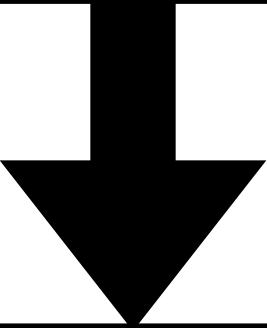


Can we work backwards to recover
 x' and x'' ?

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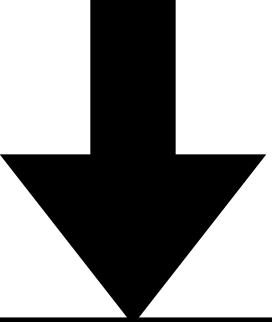
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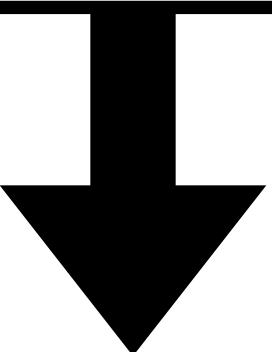
Let $G_{x,\theta}$ be the conditional distribution of
 $(X', X'') \mid X = x$.

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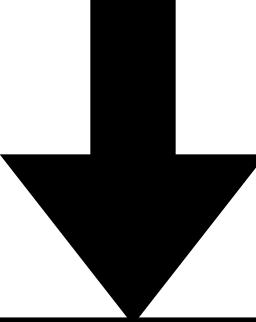
Draw $(X^{(1)}, X^{(2)})$ from $G_{x,\theta}$.

Can we work backwards to recover x' and x'' ?

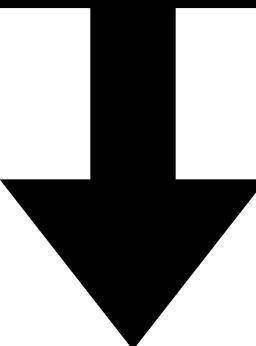
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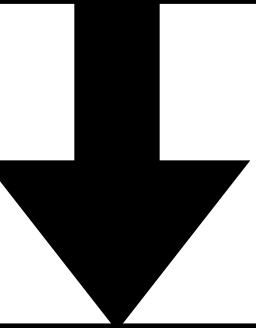
Let $G_{x,\theta}$ be the conditional distribution of $(X', X'') \mid X = x$.

Theorem:

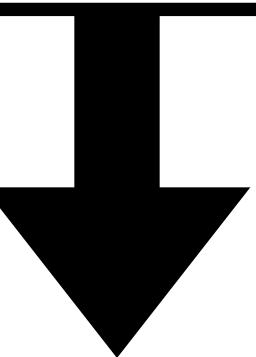
$$X^{(1)} \sim Q_\theta^1, \quad X^{(2)} \sim Q_\theta^2, \quad X^{(1)} \perp\!\!\!\perp X^{(2)}.$$

Generalized thinning with non-additive decompositions

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Theorem:

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Can we work backwards to recover x' and x'' ?

Let $G_{x,\theta}$ be the conditional distribution of $(X', X'') \mid X = x$.

Key idea: If $X = T(X', X'')$ is sufficient for θ in the joint of (X', X'') , then $G_{x,\theta}$ does not depend on θ .

The list of distributions we can thin is extensive

Family	Distribution P_θ , where $X \sim P_\theta$.	Distribution $Q_\theta^{(k)}$ where $X^{(k)} \stackrel{ind.}{\sim} Q_\theta^{(k)}$.	Sufficient statistic T (sufficient for θ)
Natural exponential family (in parameter θ)	$N(\theta, \sigma^2)$	$N(\epsilon_k \theta, \epsilon_k \sigma^2)$	
	Poisson(θ)	Poisson($\epsilon_k \theta$)	
	NegBin(r, θ)	NegBin($\epsilon_k r, \theta$)	
	Binomial(r, θ)	Binomial($\epsilon_k r, \theta$)	$\sum_{k=1}^K X^{(k)}$
	Gamma(α, θ)	Gamma($\epsilon_k \alpha, \theta$)	
	$N_p(\boldsymbol{\theta}, \Sigma)$	$N_p(\epsilon_k \boldsymbol{\theta}, \epsilon_k \Sigma)$	
	Multinomial $_p(r, \boldsymbol{\theta})$	Multinomial $_p(\epsilon_k r, \boldsymbol{\theta})$	
General exponential family (in parameter θ)	Gamma($K/2, \theta$)	$N(0, \frac{1}{2\theta})$	$\sum_{k=1}^K (X^{(k)})^2$
	Gamma(K, θ)	Weibull($\theta^{-\frac{1}{\nu}}, \nu$)	$\sum_{k=1}^K (X^{(k)})^\nu$
	Beta(θ, β)	Beta($\frac{1}{K}\theta + \frac{k-1}{K}, \frac{1}{K}\beta$)	$(\prod_{k=1}^K X^{(k)})^{1/K}$
	Beta(α, θ)	Beta($\frac{1}{K}\alpha, \frac{1}{K}\theta + \frac{k-1}{K}$)	$(\prod_{k=1}^K (1 - X^{(k)}))^{1/K}$
	Gamma(θ, β)	Gamma($\frac{1}{K}\theta + \frac{k-1}{K}, \frac{1}{K}\beta$)	$(\prod_{k=1}^K X^{(k)})^{1/K}$
Truncated support family	Weibull(θ, ν)	Gamma($\frac{1}{K}, \theta^{-\nu}$)	$(\sum_{k=1}^K X^{(k)})^{1/\nu}$
	Pareto(ν, θ)	Gamma($\frac{1}{K}, \theta$)	$\nu \times \text{Exp}(\sum_{k=1}^K X^{(k)})$
	$N(0, \theta)$	Gamma($\frac{1}{2K}, \frac{1}{2\theta}$)	$X^2 = \sum_{k=1}^K X^{(k)}$
Non-parametric	$N_K(\theta_1 \mathbf{1}_K, \theta_2 I_K)$	$N(\theta_1, \theta_2)$	sample mean and variance
	Unif($0, \theta$)	$\theta \cdot \text{Beta}(\frac{1}{K}, 1)$	$\max(X^{(1)}, \dots, X^{(K)})$
	$\theta \cdot \text{Beta}(\alpha, 1)$	$\theta \cdot \text{Beta}(\frac{\alpha}{K}, 1)$	$\min(X^{(1)}, \dots, X^{(K)})$
	F^n	F^{n_k}	$\text{sort}(X^{(1)}, \dots, X^{(K)})$

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We are working on additional extensions to Project 3

The image shows a screenshot of an arXiv preprint page. The header is red with the arXiv logo and navigation links. The main content area has a light gray background. It displays the category 'Statistics > Methodology', the submission date '[Submitted on 22 Mar 2023]', the title 'Generalized Data Thinning Using Sufficient Statistics', and the authors' names in blue.

arXiv > stat > arXiv:2303.12931

Search...
Help | Advanced

Statistics > Methodology

[Submitted on 22 Mar 2023]

Generalized Data Thinning Using Sufficient Statistics

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Acknowledgements



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Acknowledgements



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Questions?
