Batch effects and confounders

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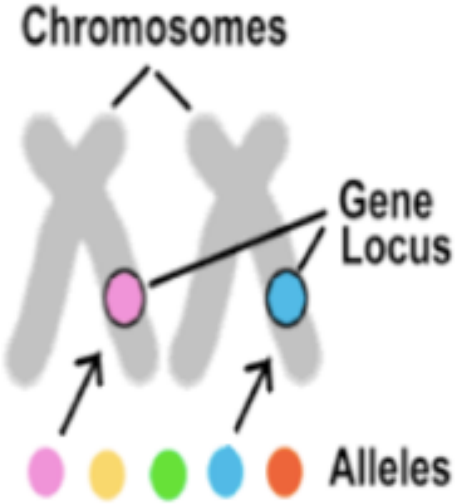
Sources of “batch” effects

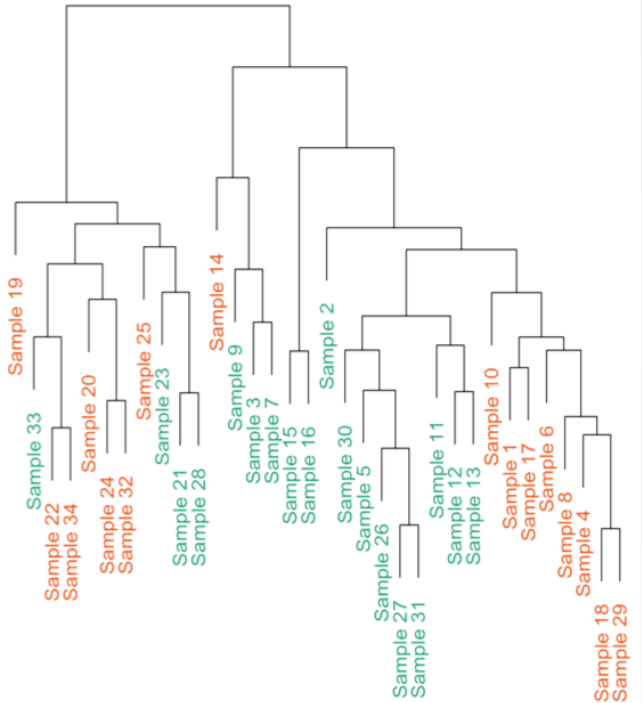
External Factors (like environment)



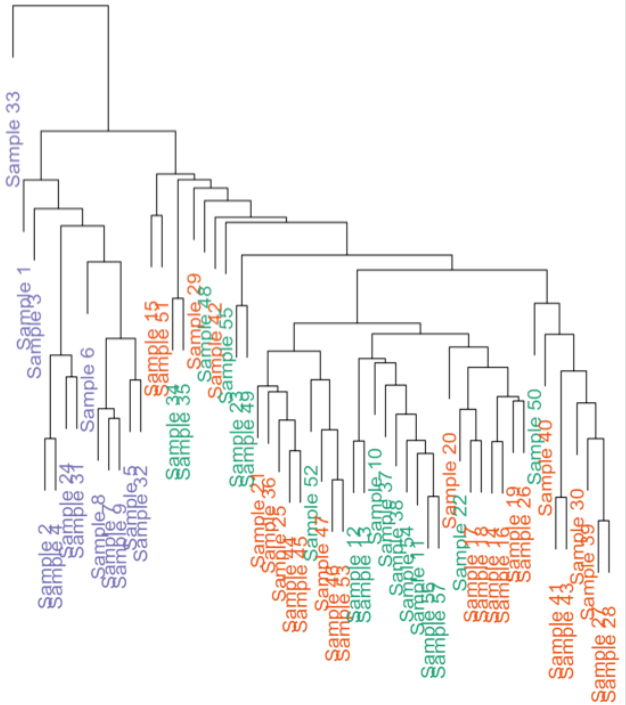
Genetics/Epigenetics

Technical Factors

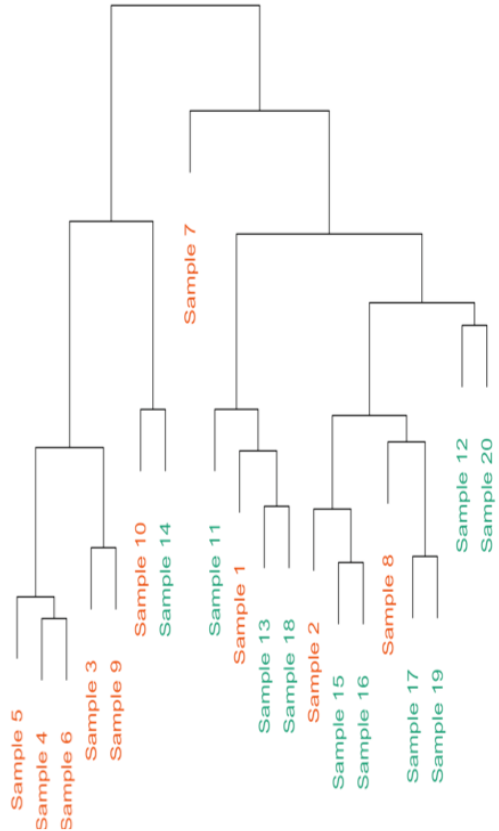
Color = Environment
(Idaghdour et al. 2008)



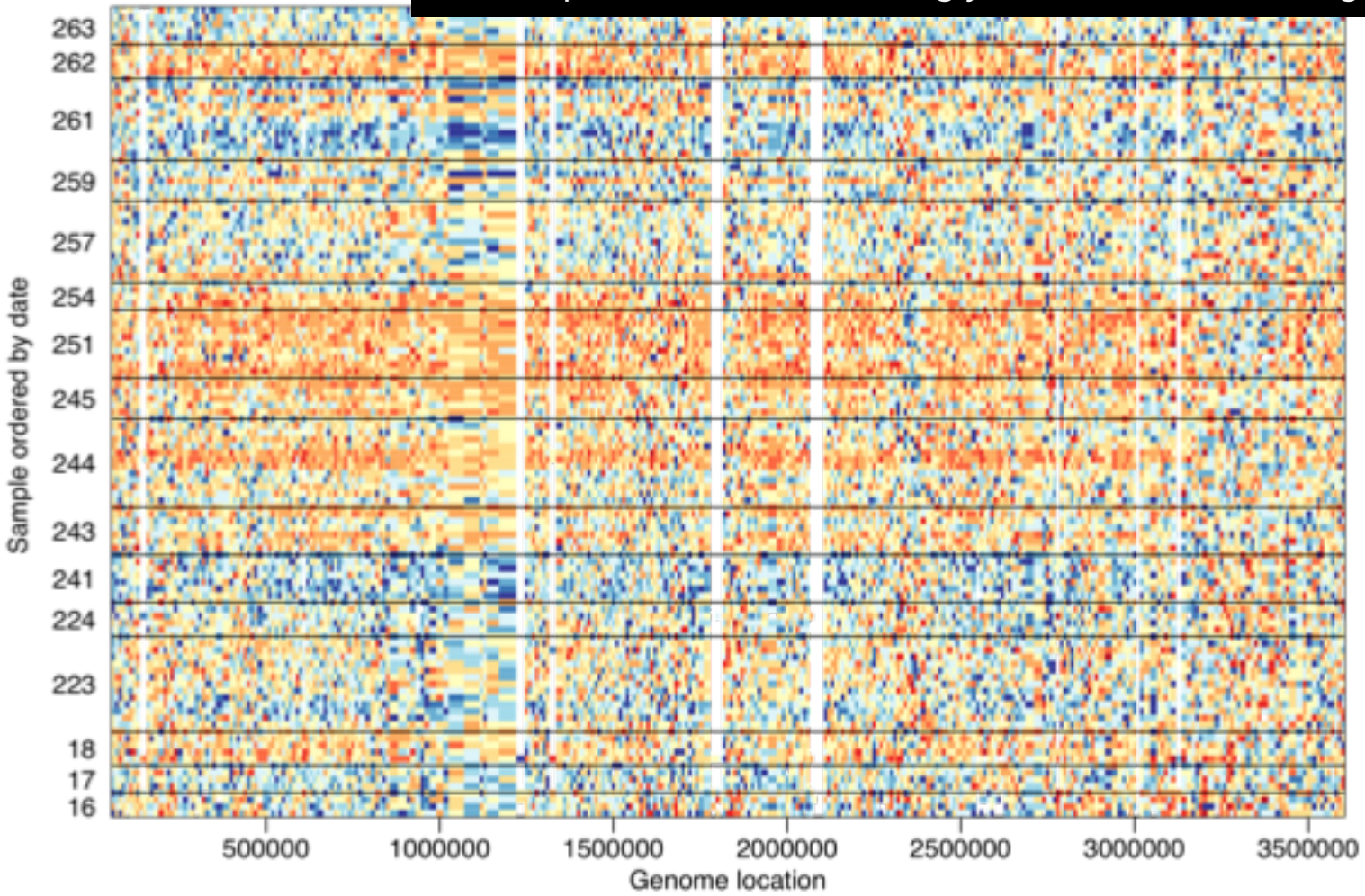
Color = Processing Year
(Cheung et al. 2008)



Color = Allele
(Brem et al. 2005)



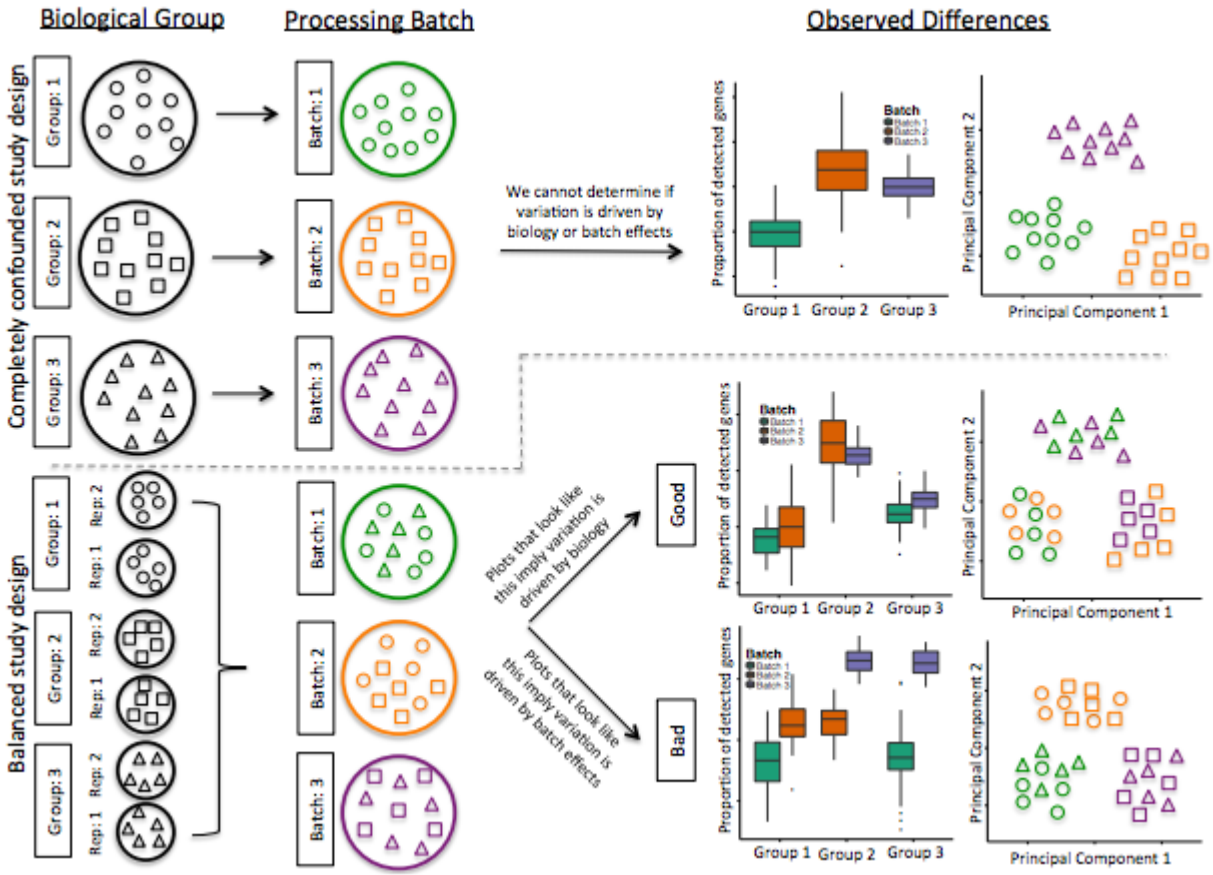
http://www.nature.com/nrg/journal/v11/n10/full/nrg2825.html



When can you remove batch effects?

When they don’t perfectly overlap with what you care about

http://biorxiv.org/content/biorxiv/early/2015/08/25/025528.full.pdf



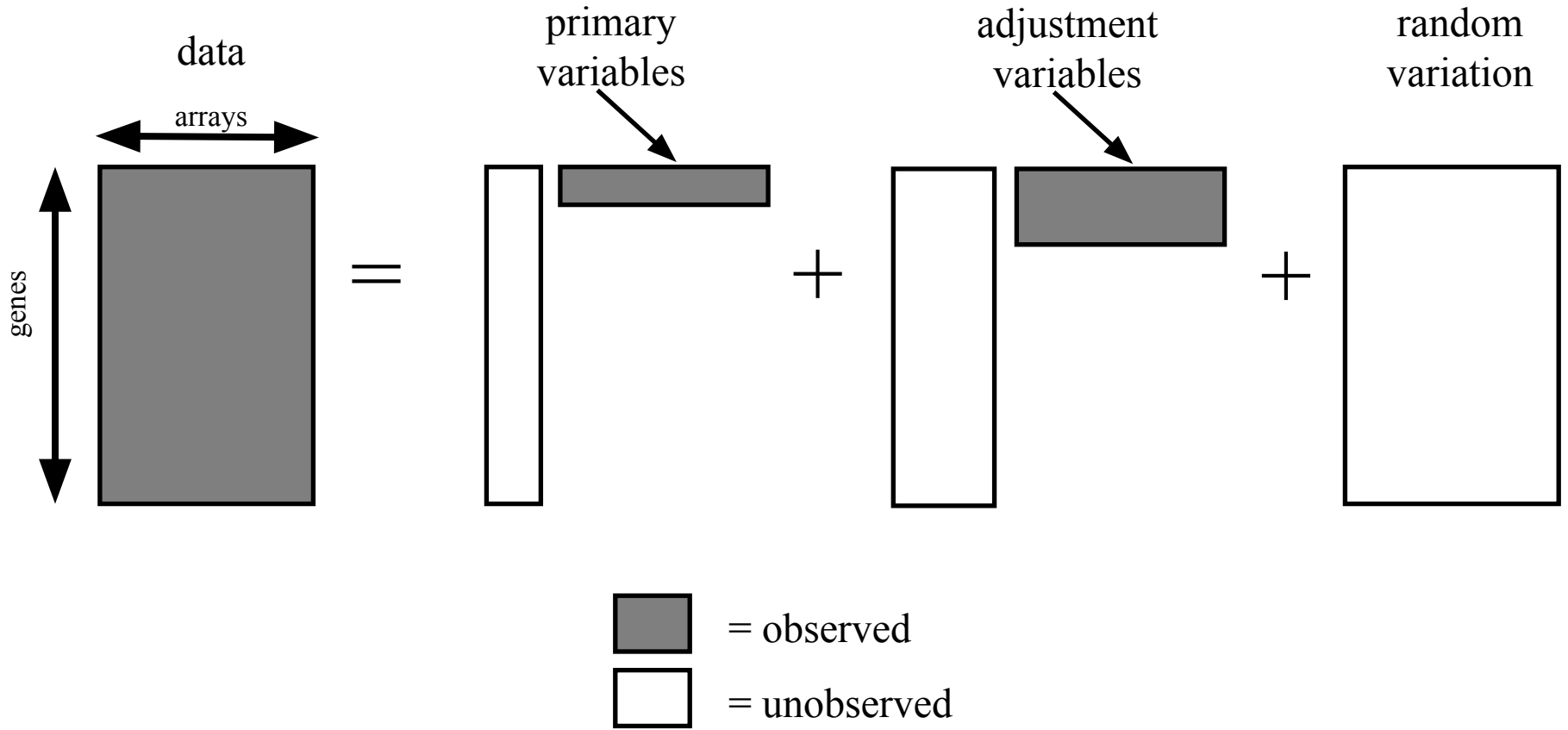
When “batch” is known

$$Y = b_0 + b_1 P + b_2 B + e$$

P = Phenotype you care about

B = Batch

Slide adapted from: John Storey



http://biostatistics.oxfordjournals.org/content/8/1/118.abstract

Adjusting batch effects in microarray expression data using empirical Bayes methods

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Abstract

Non-biological experimental variation or "batch effects" are commonly observed across multiple batches of microarray experiments, often rendering the task of combining data from these batches difficult. The ability to combine microarray data sets is advantageous to researchers to increase statistical power to detect biological phenomena from studies where logistical considerations restrict sample size or in studies that require the sequential hybridization of arrays. In general, it is inappropriate to combine data sets without adjusting for batch effects. Methods have been proposed to filter batch effects from data, but these are often complicated and require large batch sizes (> 25) to implement. Because the majority of microarray studies are conducted using much smaller sample sizes, existing methods are not sufficient. We propose parametric and non-parametric empirical Bayes frameworks for adjusting

Table of Contents

This Article

Biostat (2007) 8 (1): 118-127. doi: 10.1093/biostatistics/kxj037
First published online: April 21, 2006

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July 2015 16 (3)

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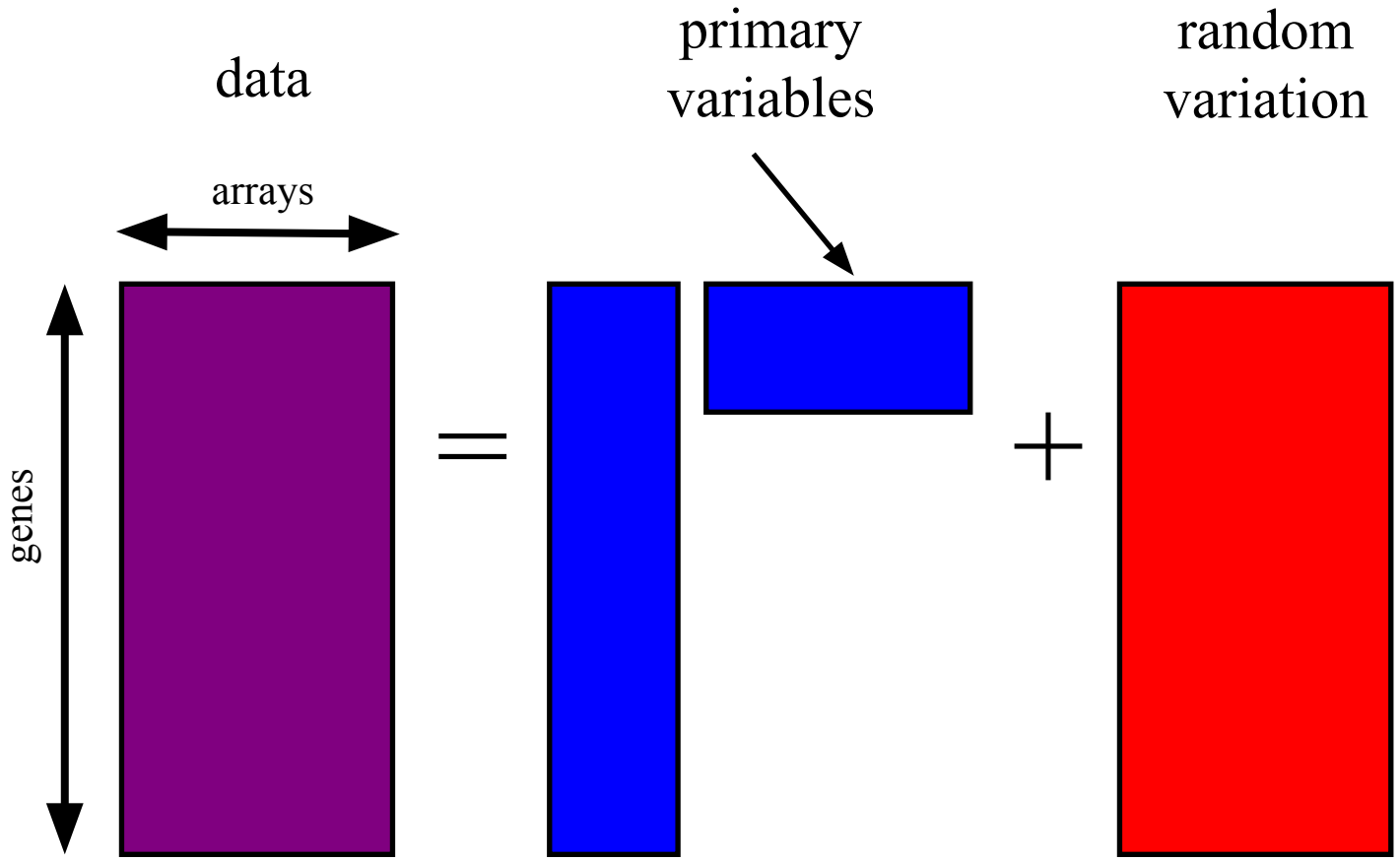
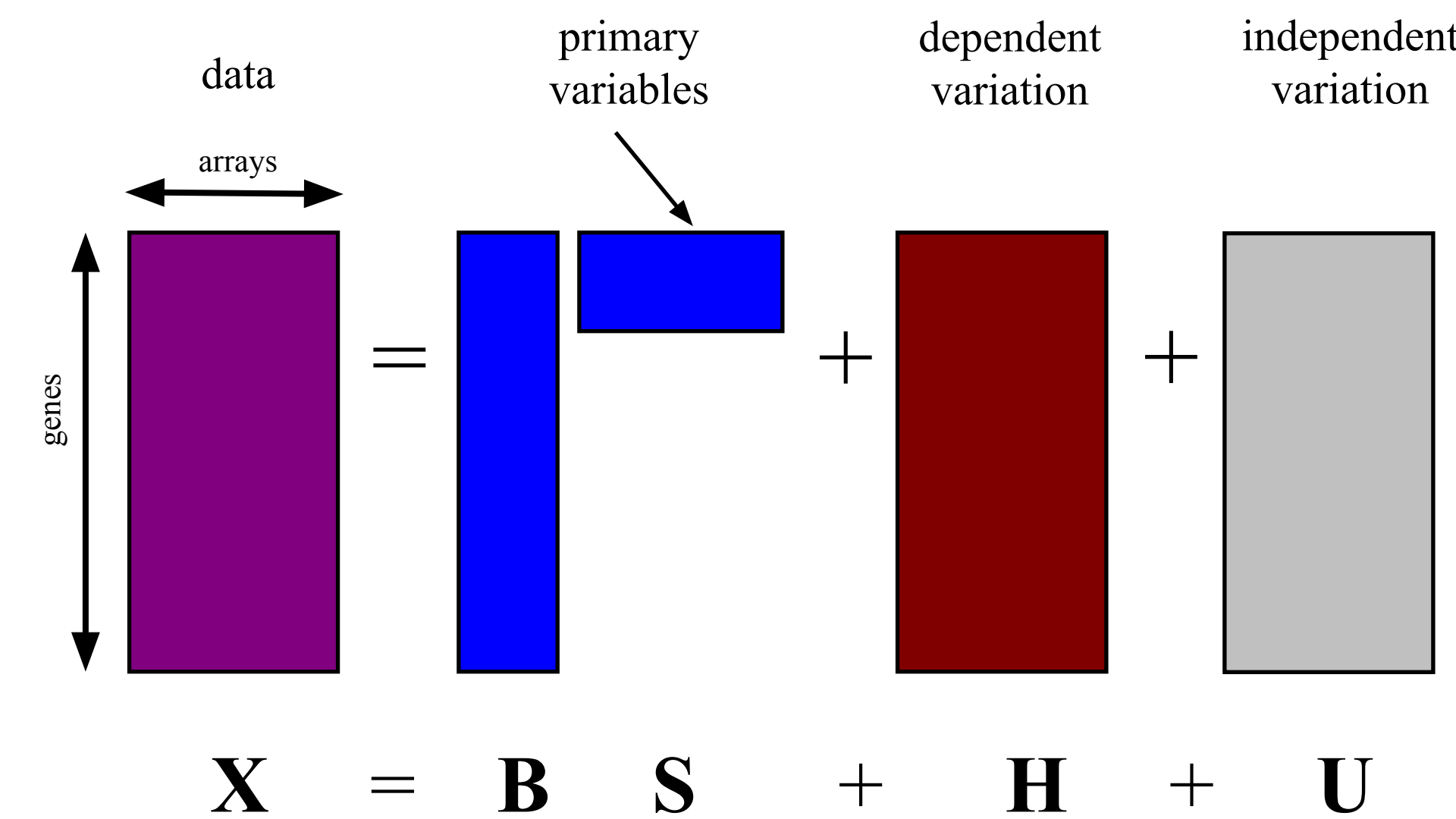
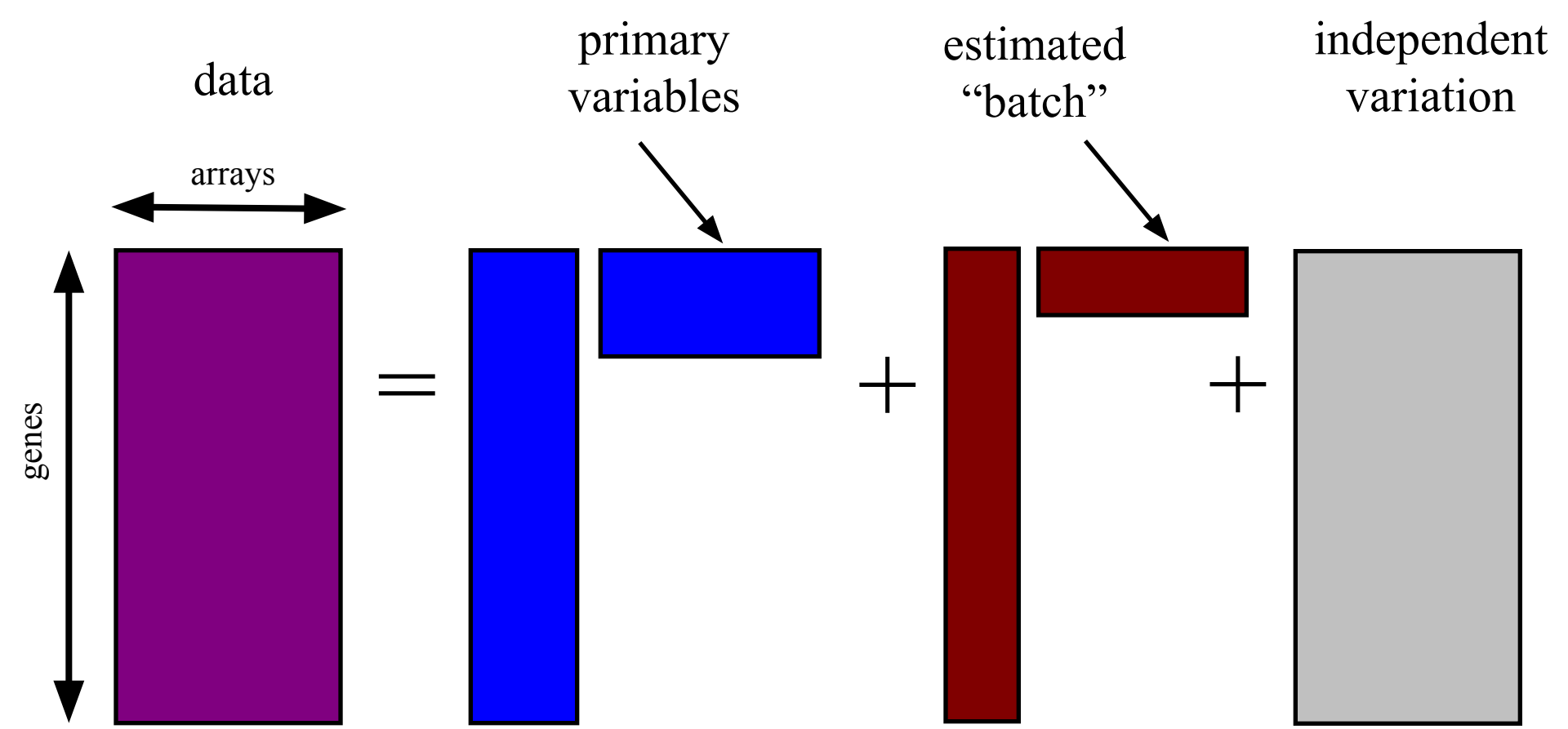
When “batch” is unknown



$$\mathbf{X} = \mathbf{B}\,\mathbf{S} + \mathbf{E}$$

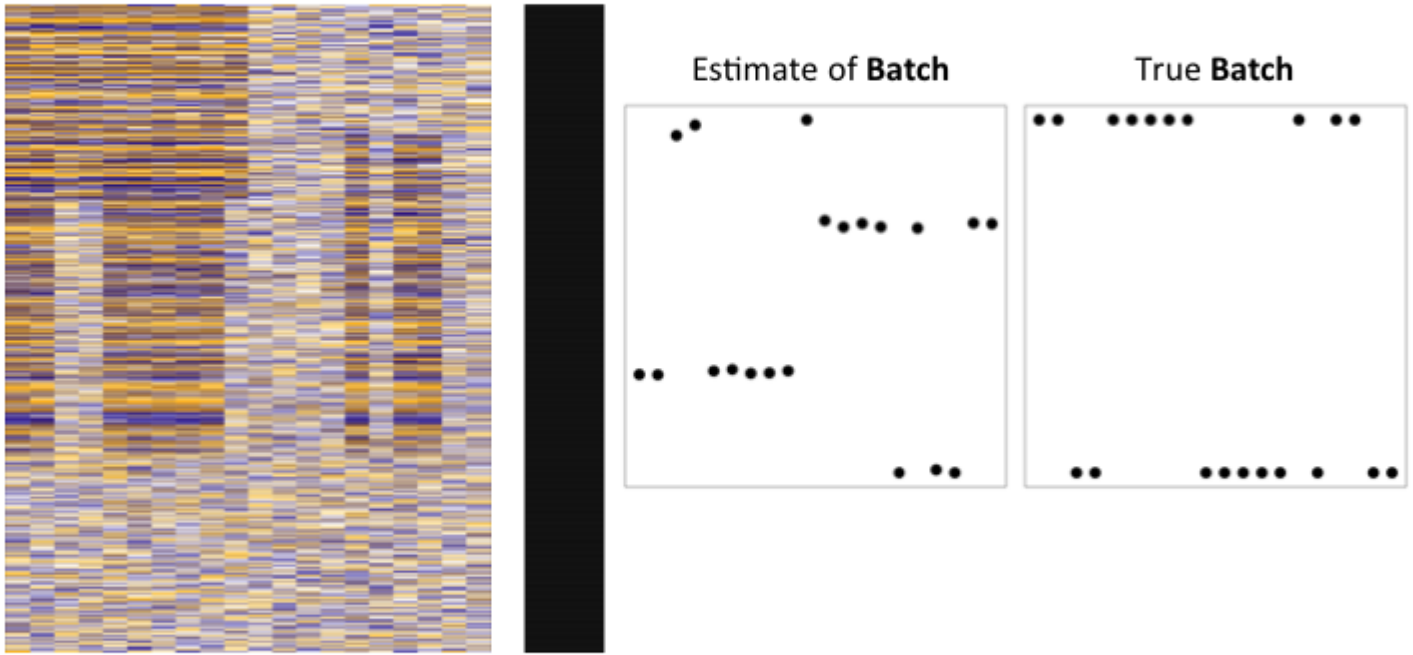

data
primary variables
dependent variation
independent variation
arrays
genes
X = B S + H + U



$$\mathbf{X} = \mathbf{B}\,\mathbf{S} + \mathbf{\Gamma}\,\mathbf{G} + \mathbf{U}$$

http://www.pnas.org/content/105/48/18718.full

Surrogate Variable Analysis



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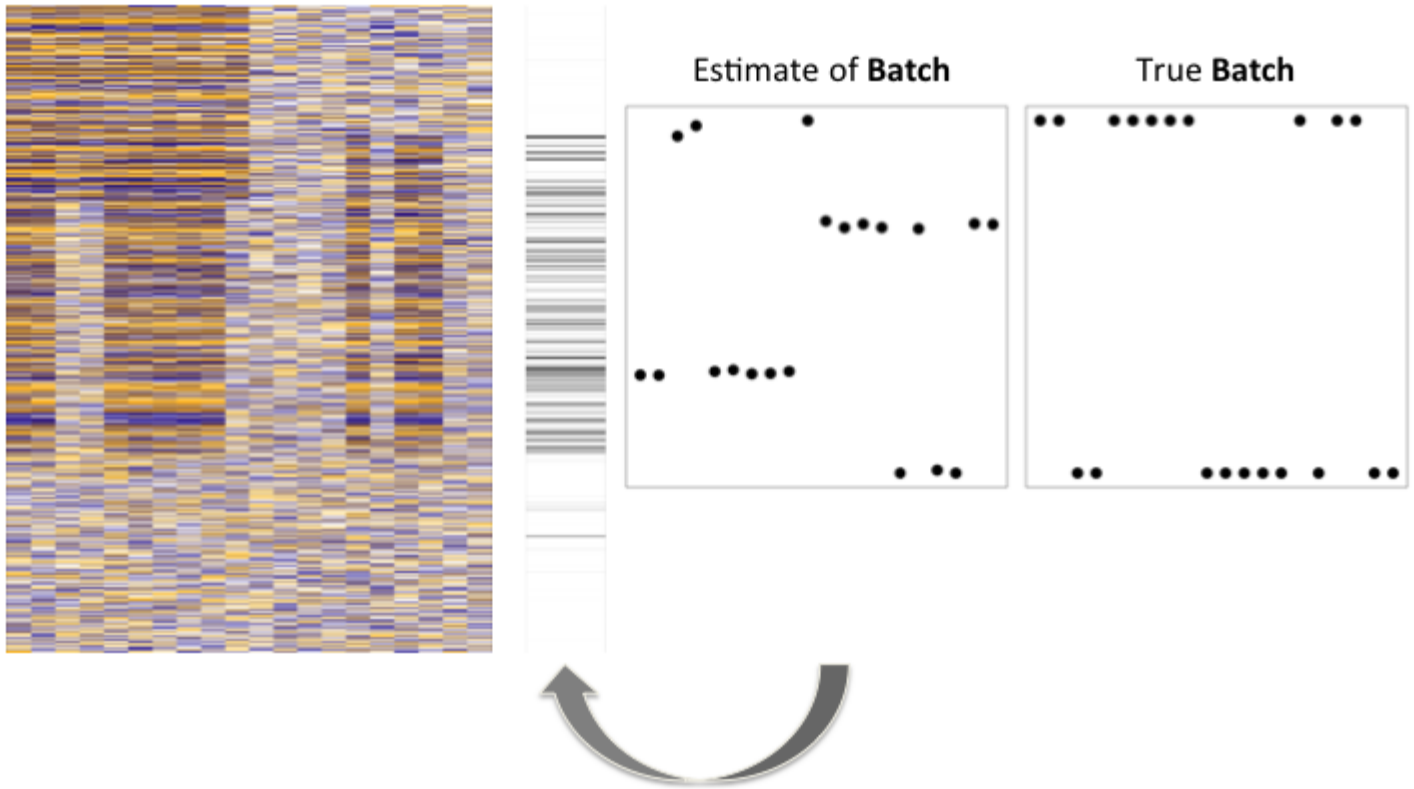
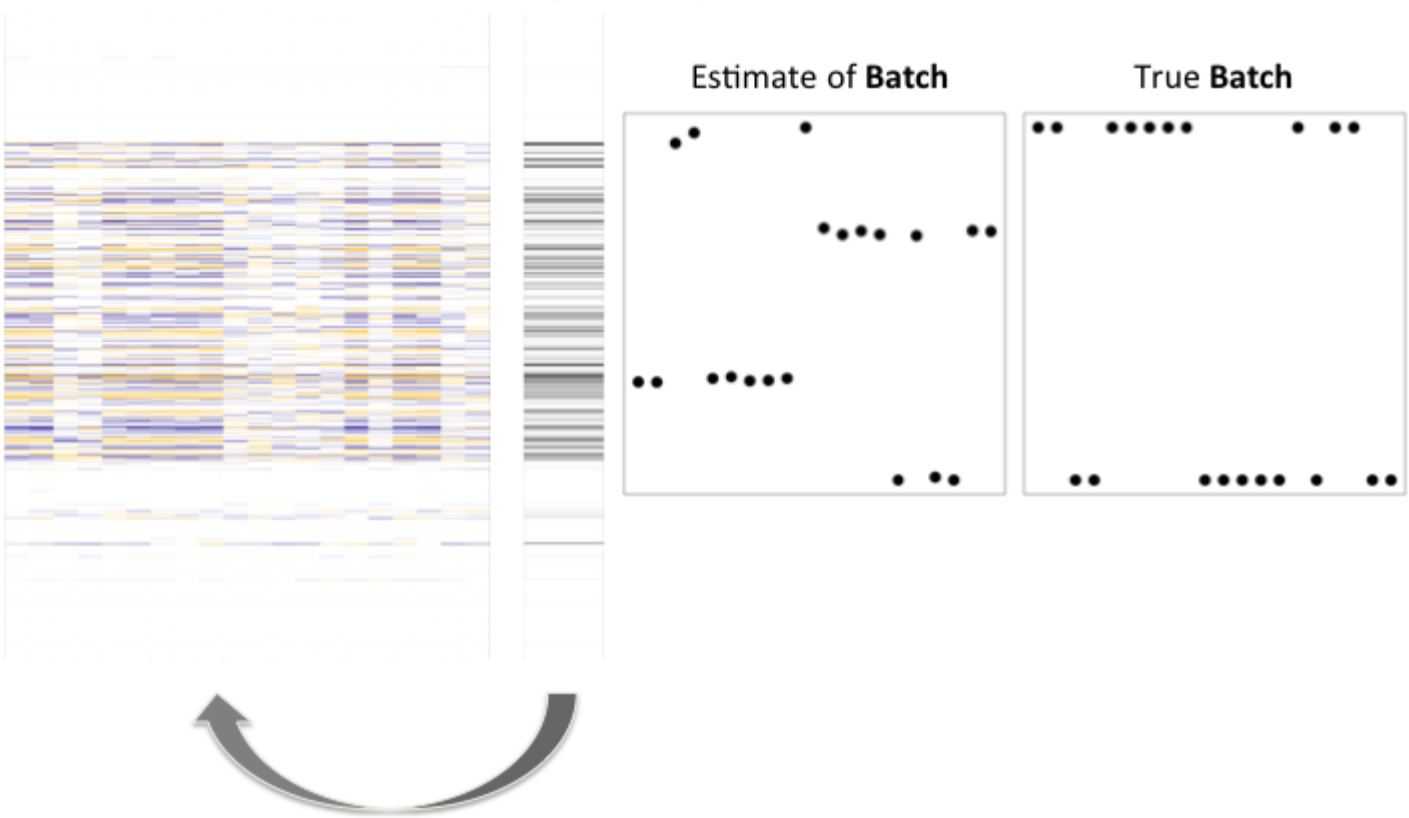
Surrogate Variable Analysis



http://www.pnas.org/content/105/48/18718.full

Surrogate Variable Analysis



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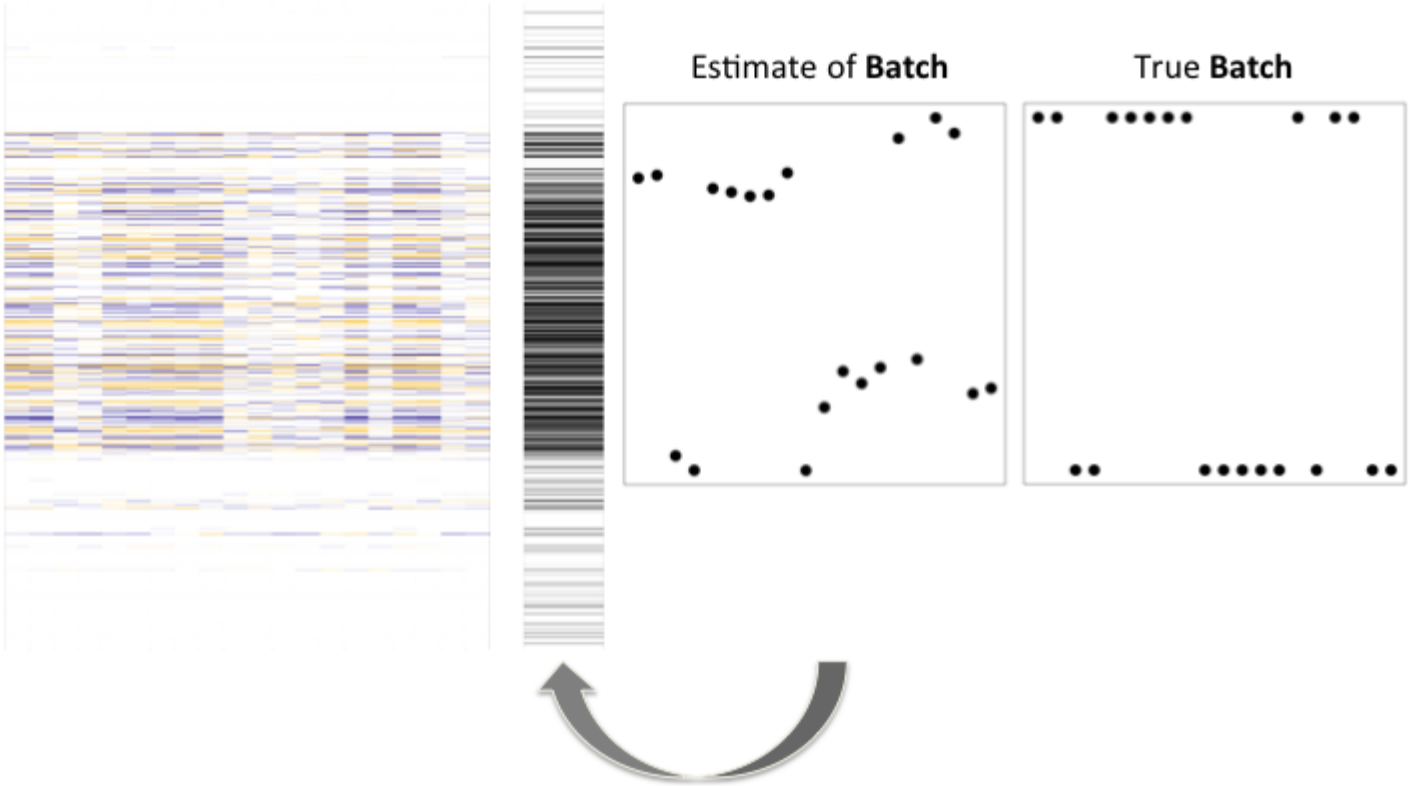
Surrogate Variable Analysis



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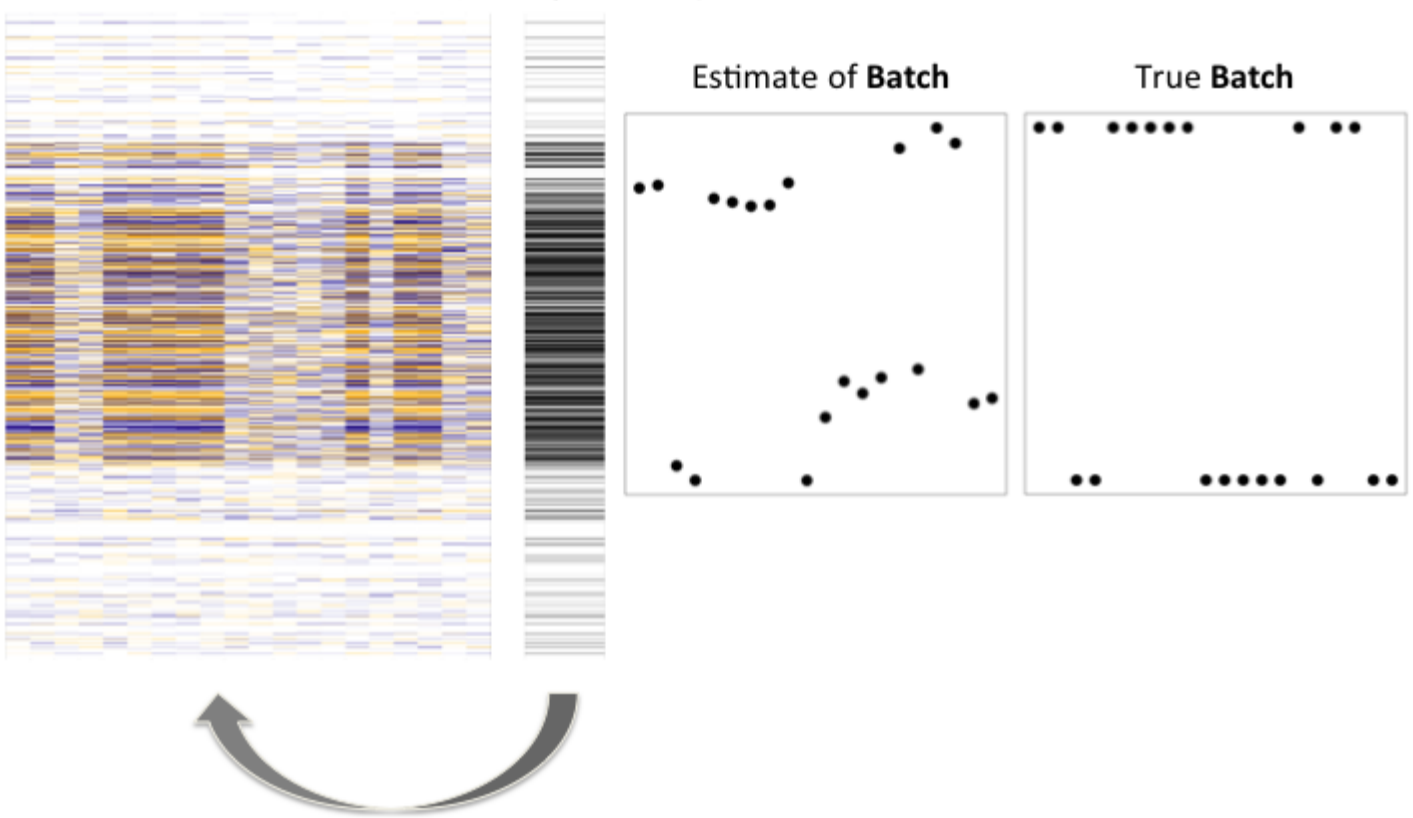

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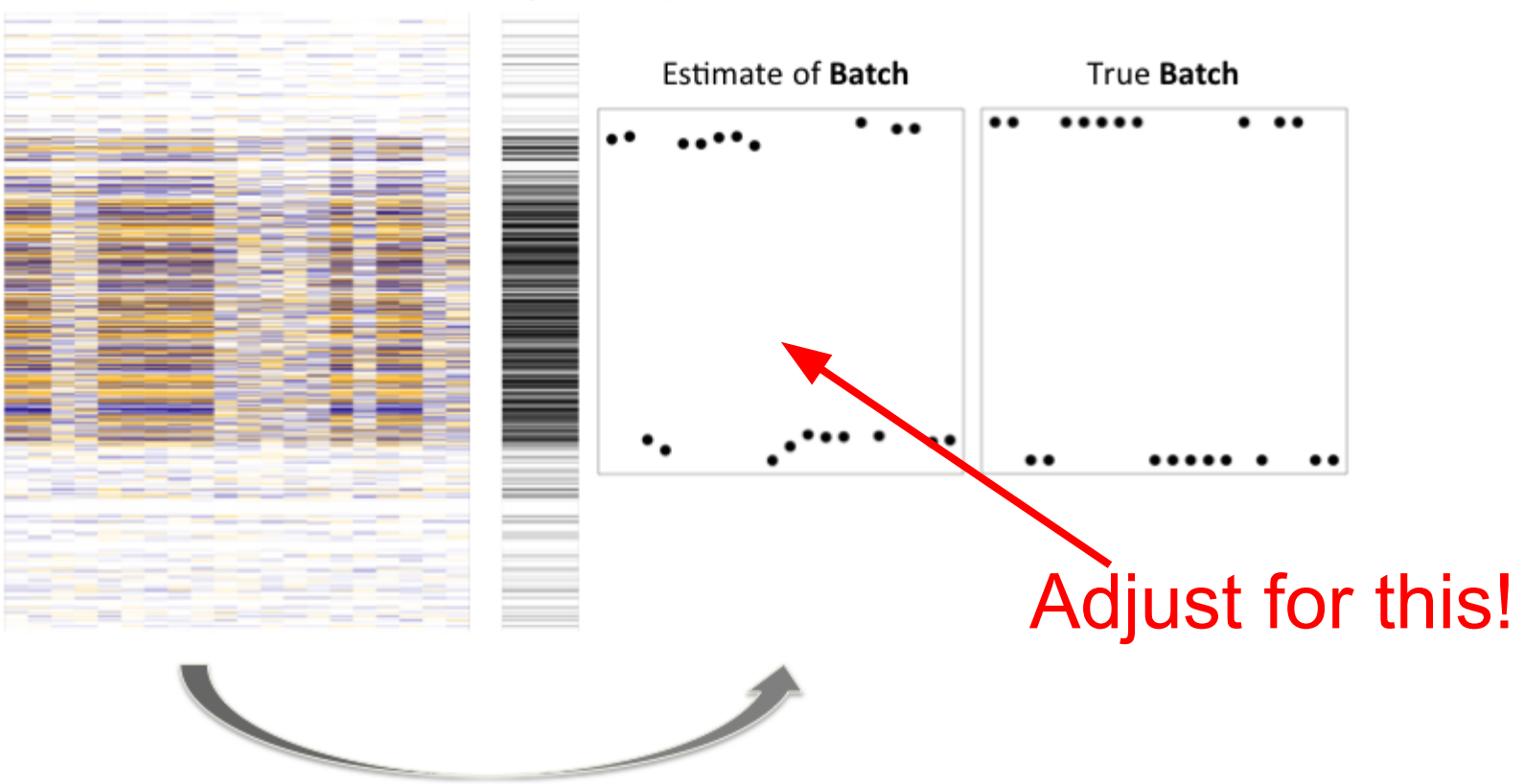
Surrogate Variable Analysis



Notes and further reading

- Introduction to batch effects
  - http://www.nature.com/nrg/journal/v11/n10/abs/nrg2825.html
- Introduction to batch effects with linear models
  - http://biostatistics.oxfordjournals.org/content/8/1/118.abstract
- Surrogate variable analysis
  - http://journals.plos.org/plosgenetics/article?id=10.1371/journal.pgen.0030161