

Salvaging an eQTL project

Identifying and correcting sample mix-ups

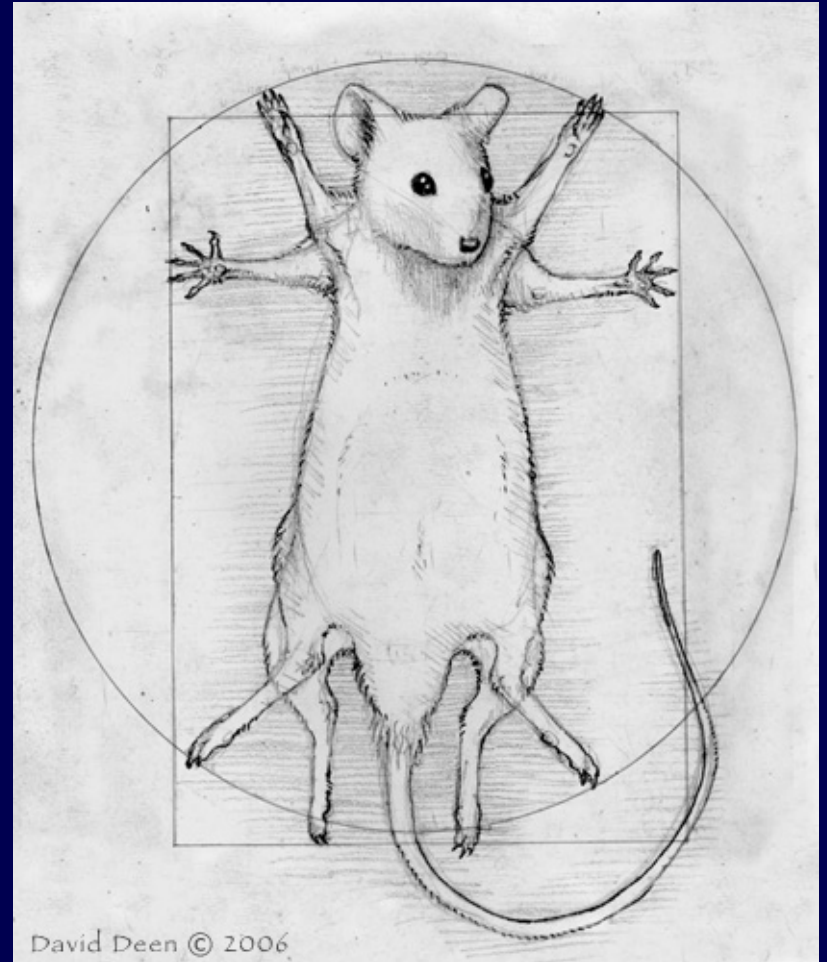
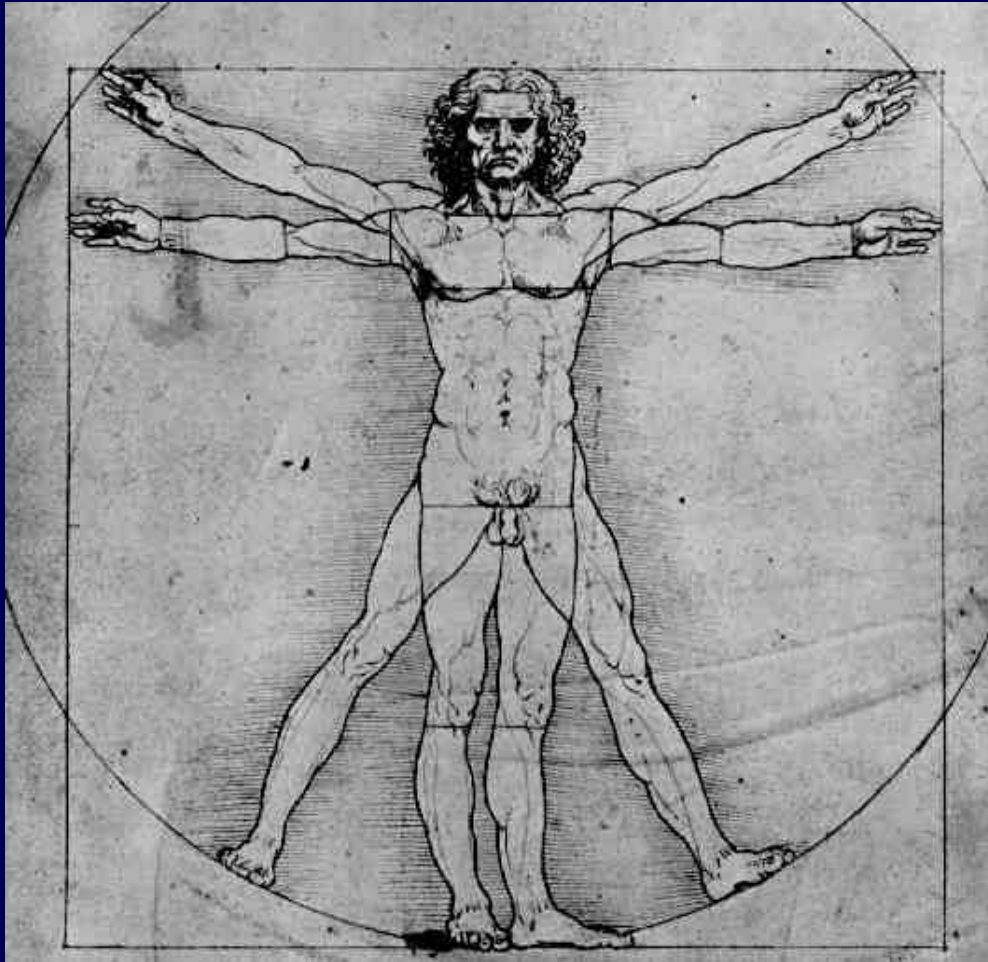
Karl W Broman

Department of Biostatistics & Medical Informatics
University of Wisconsin – Madison

www.biostat.wisc.edu/~kbroman

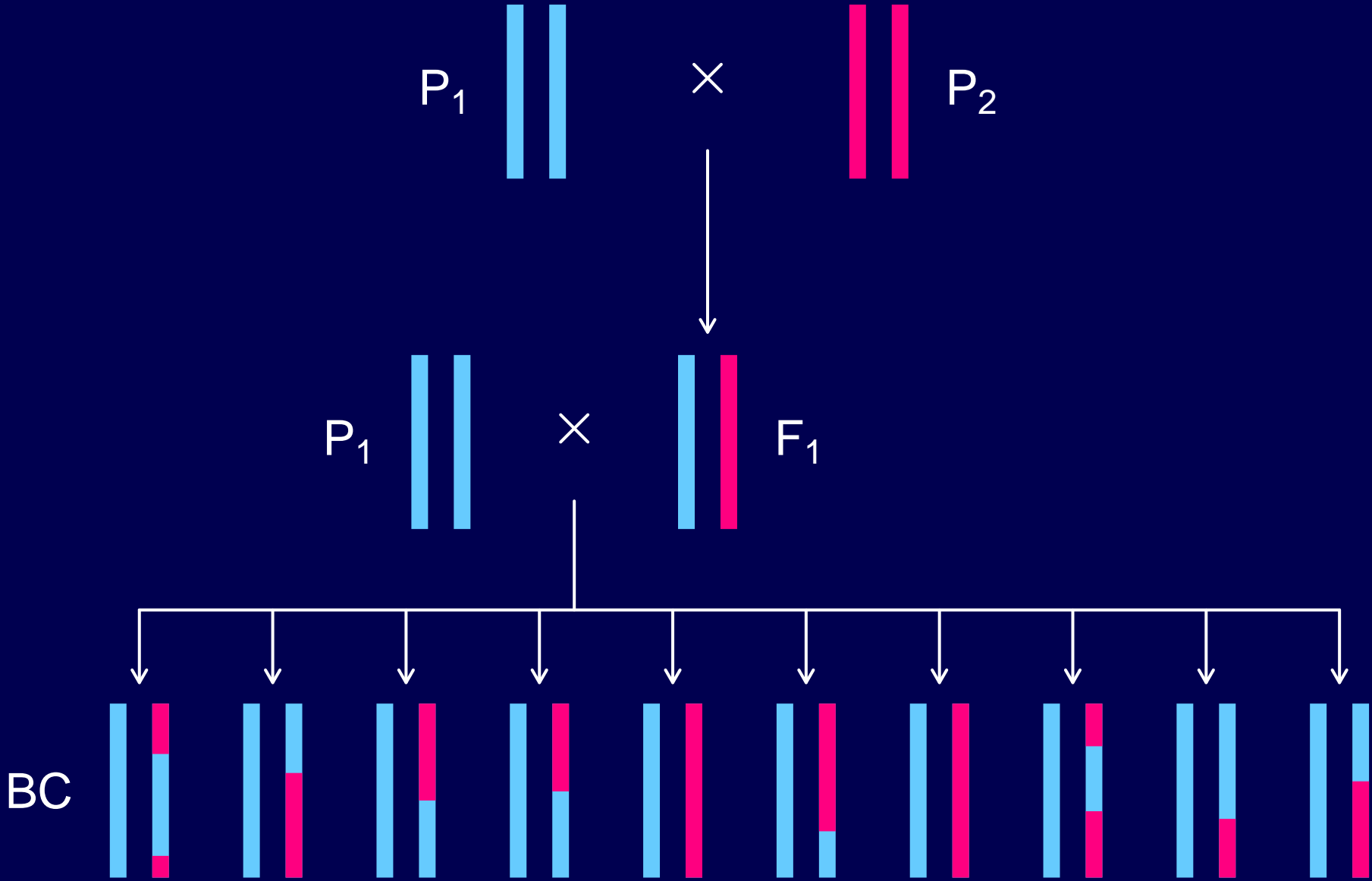


Human vs mouse

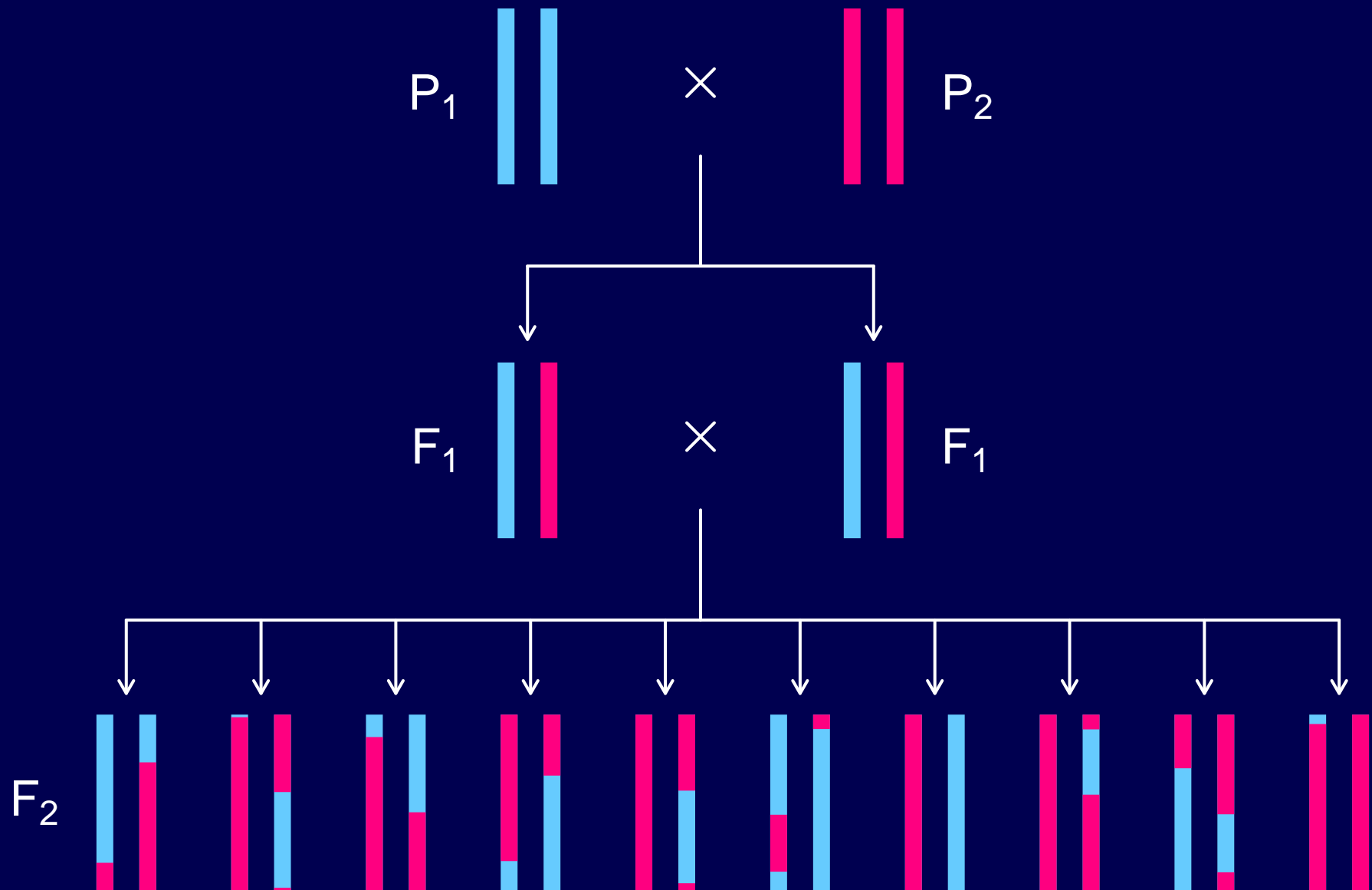


www.daviddeen.com

Backcross



Intercross



Attie project

~500 B6 × BTBR intercross mice, all ob/ob

Genotypes at 2057 SNPs (Affymetrix arrays)

Gene expression in six tissues (Agilent arrays)

- adipose
- gastrocnemius muscle
- hypothalamus
- pancreatic islets
- kidney
- liver

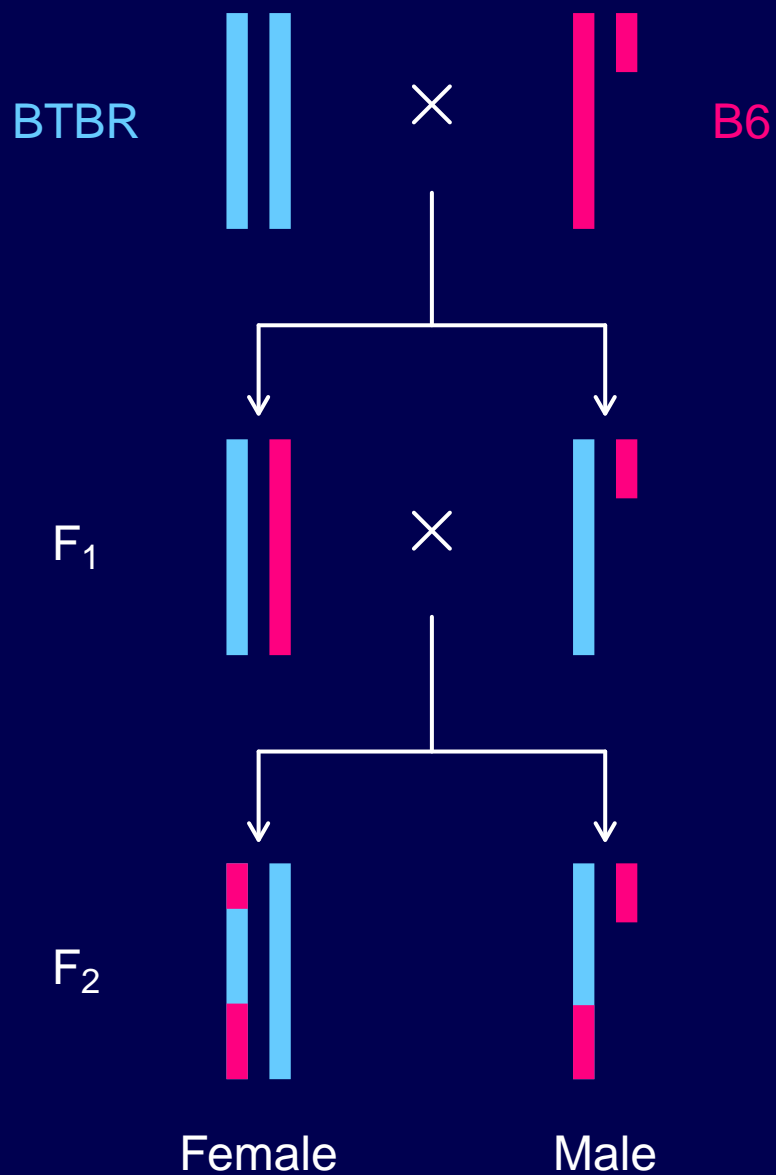
Numerous clinical phenotypes

(e.g., body weight, insulin and glucose levels)

Considerable brain power

Alan Attie, Karl Broman, Aimee Teo Broman, Danielle Greenawalt, Mark Keller, Christina Kendzierski, Amit Kulkarni, Eric Schadt, Brian Yandell, . . .

Sex and the X chr



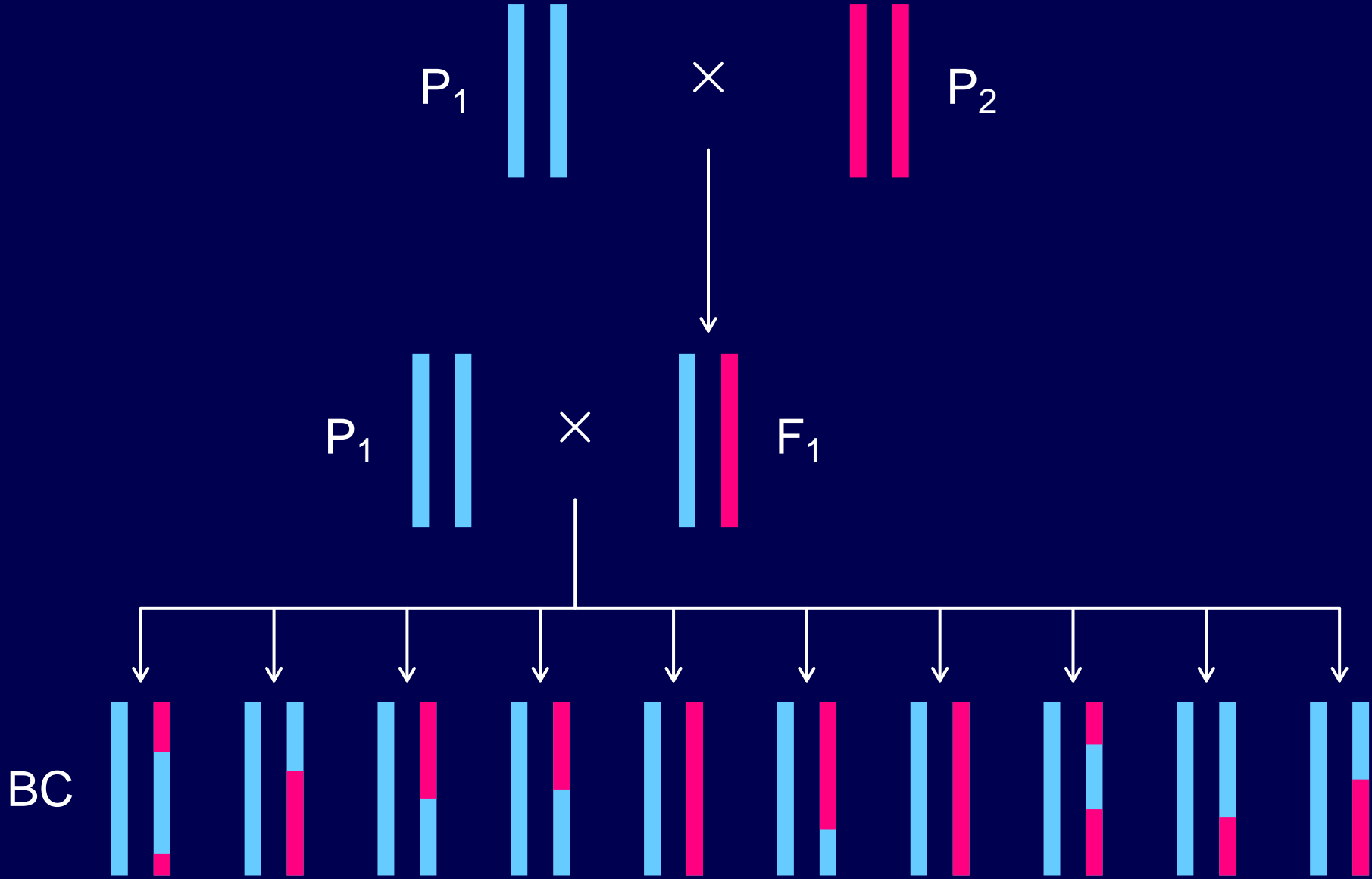
F₂ females: R/R or B/R

F₂ males: hemizygous B or R

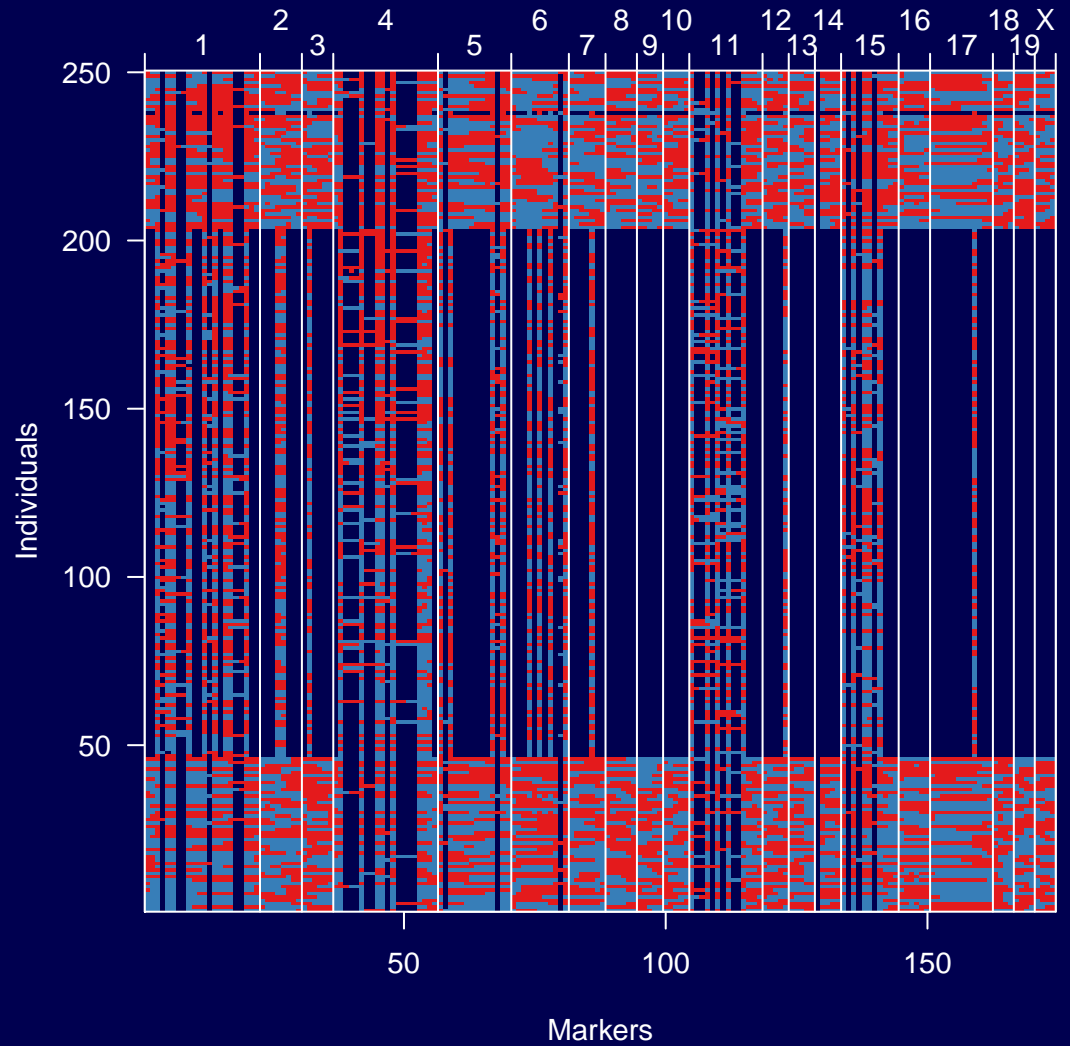
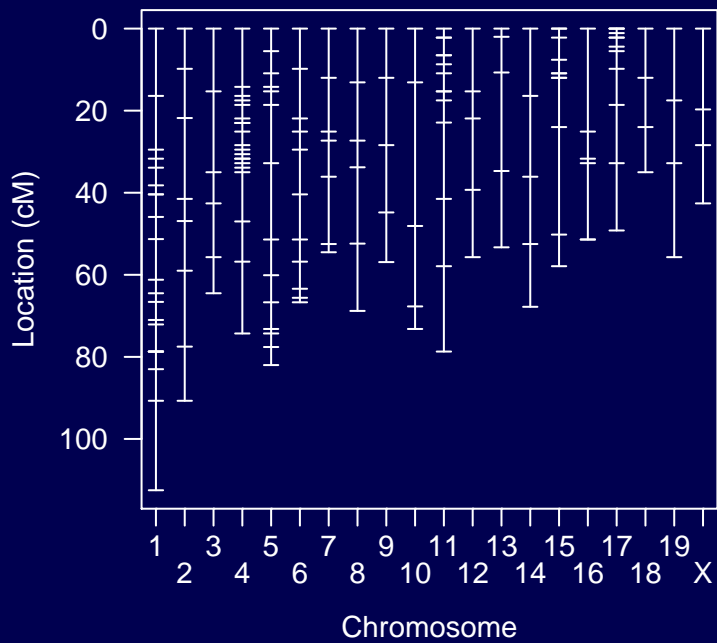
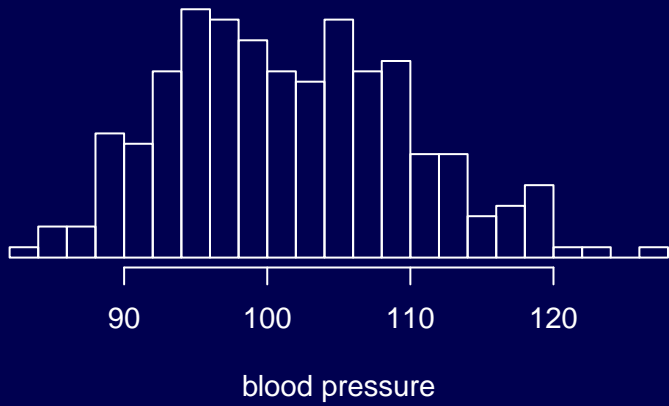
Genotype mix-ups



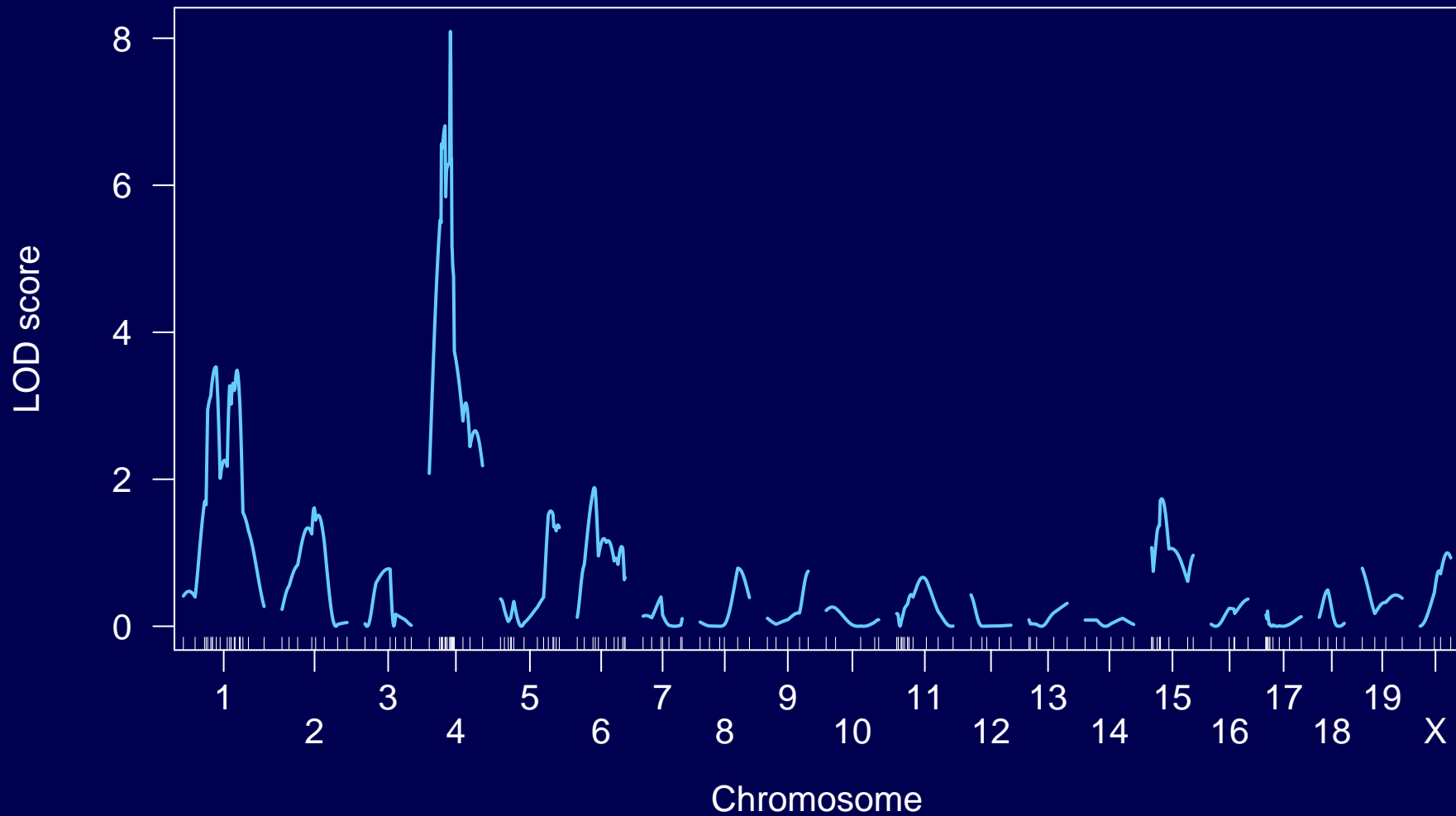
Backcross



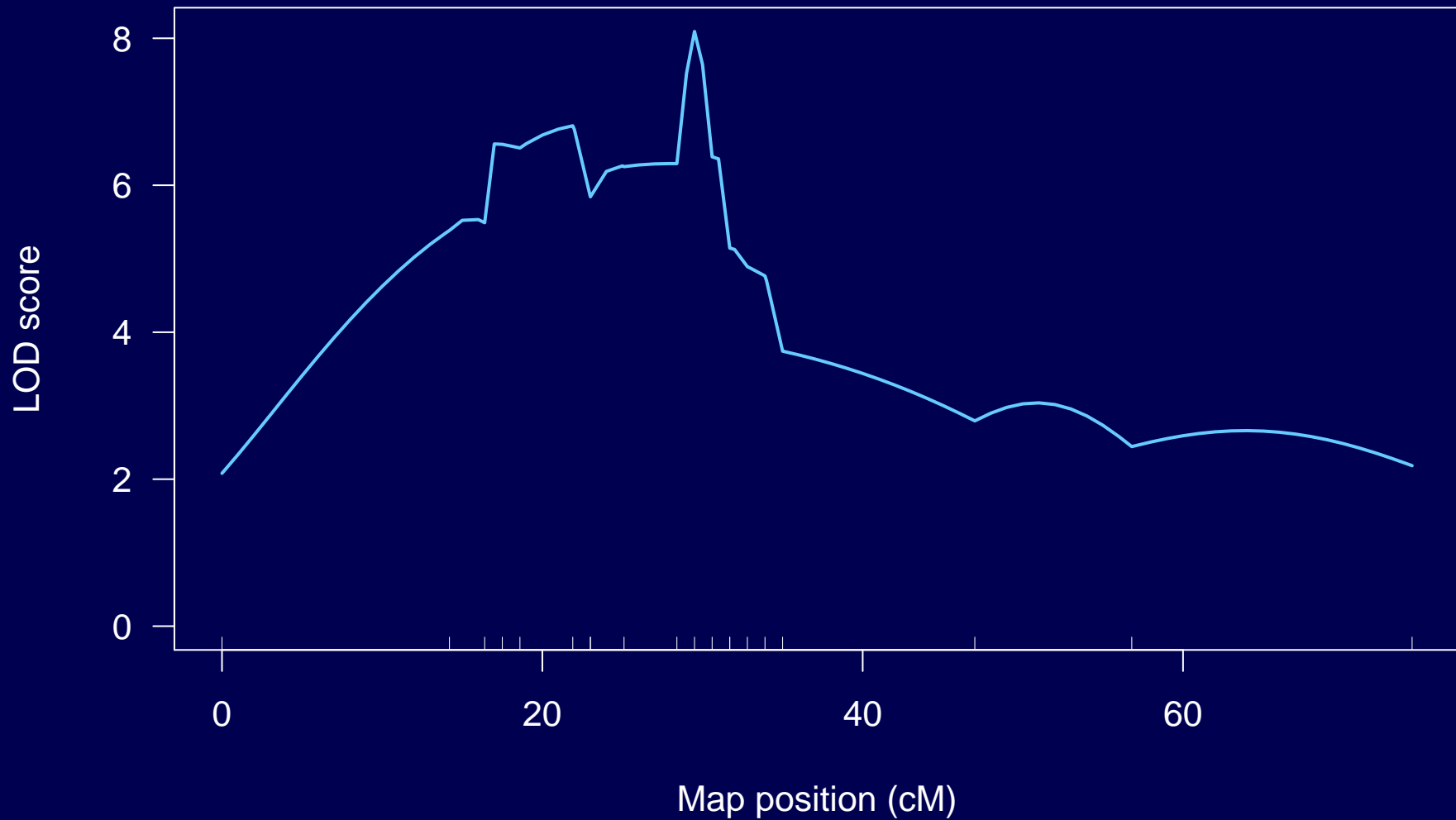
Data



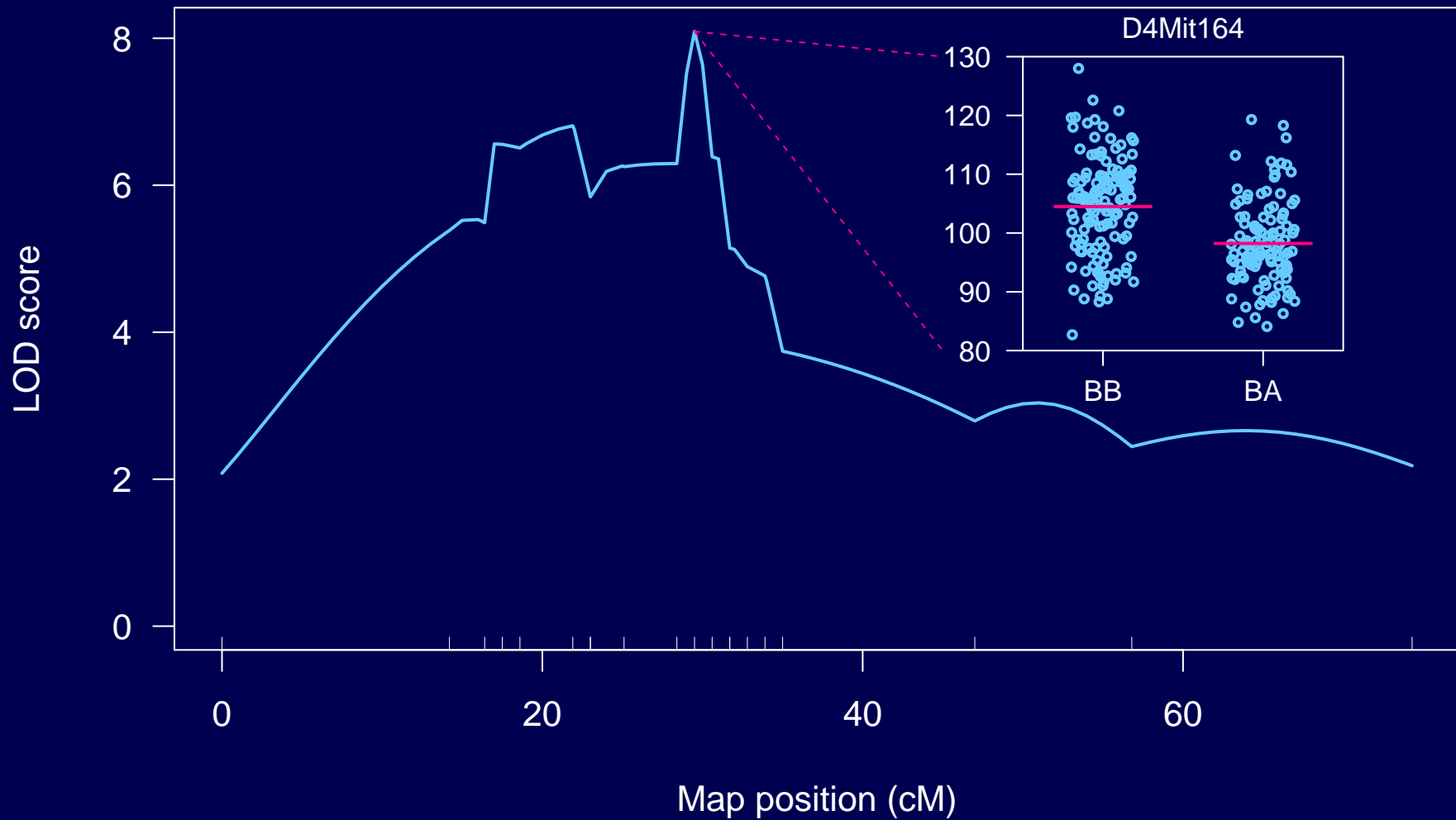
LOD curves



LOD curves



LOD curves



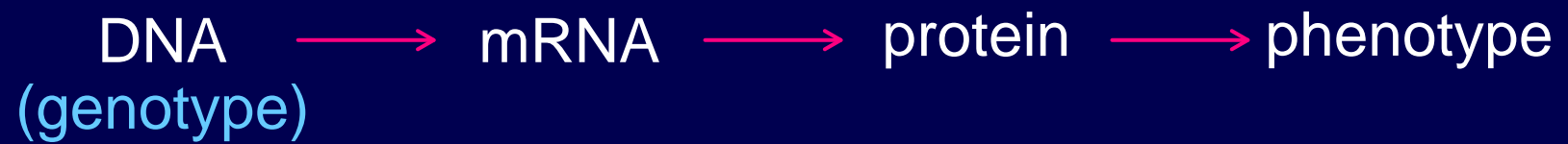
G to P

DNA
(genotype)

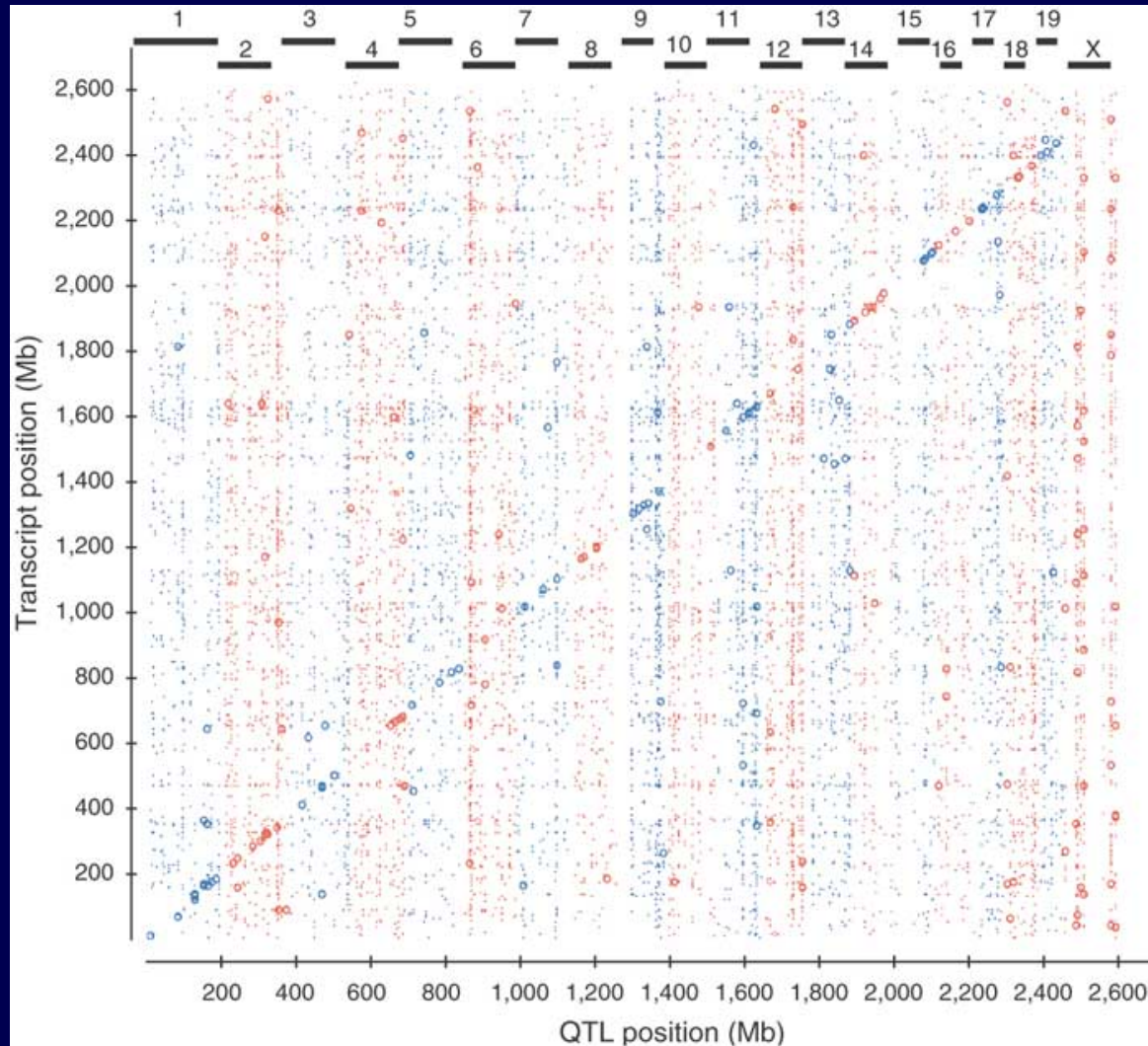


phenotype

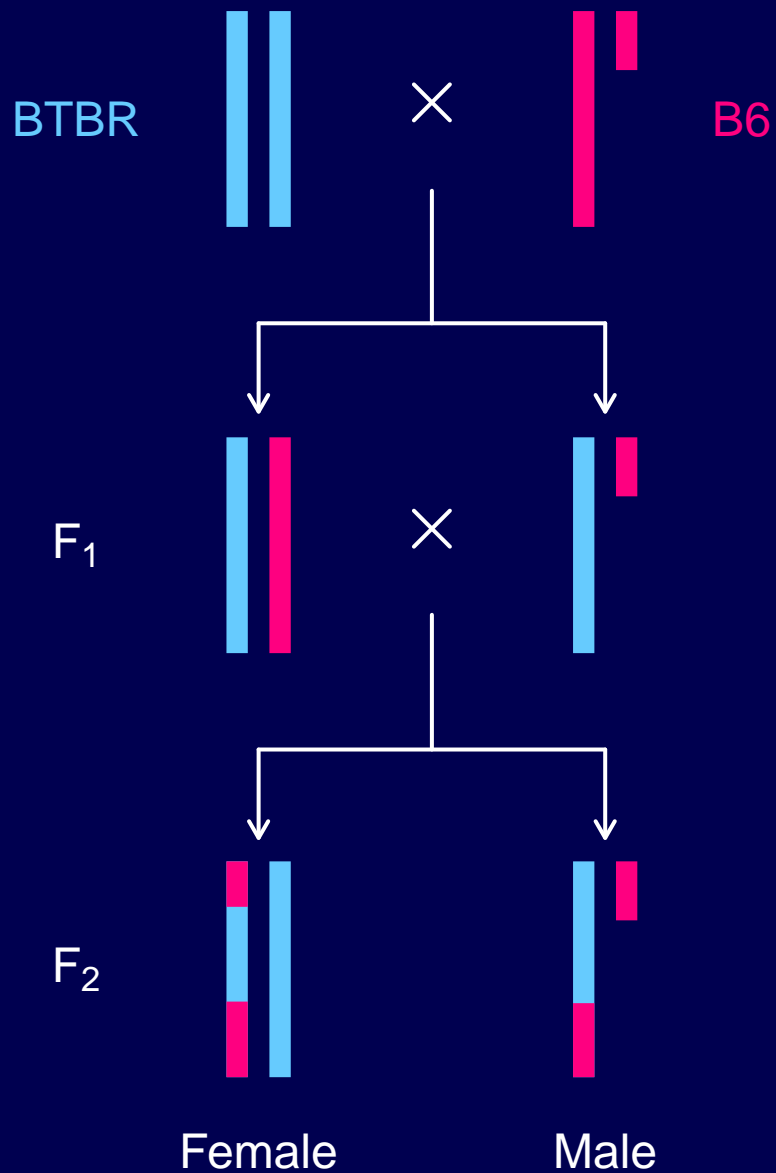
G to P



cis/trans plot



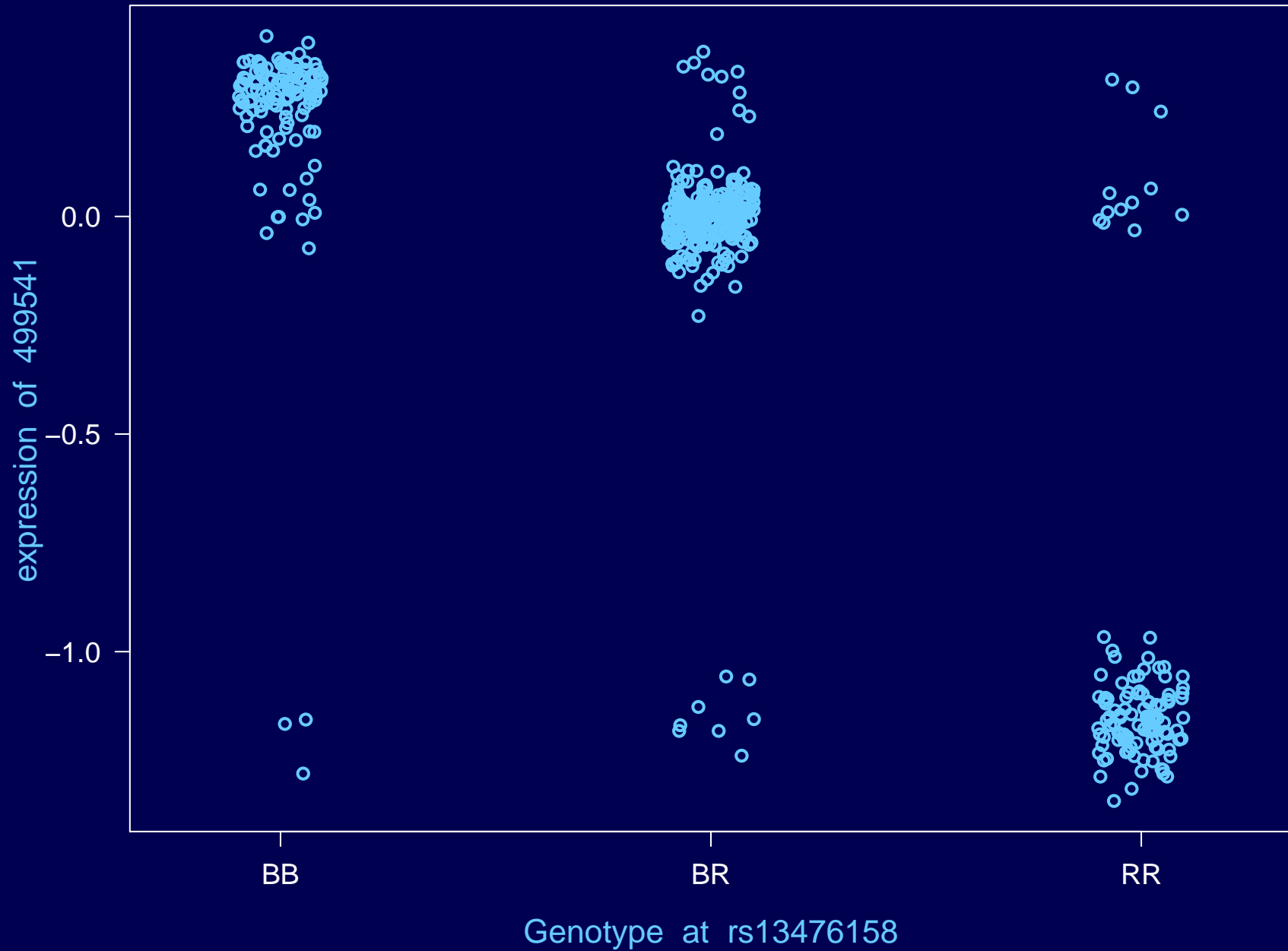
Sex and the X chr



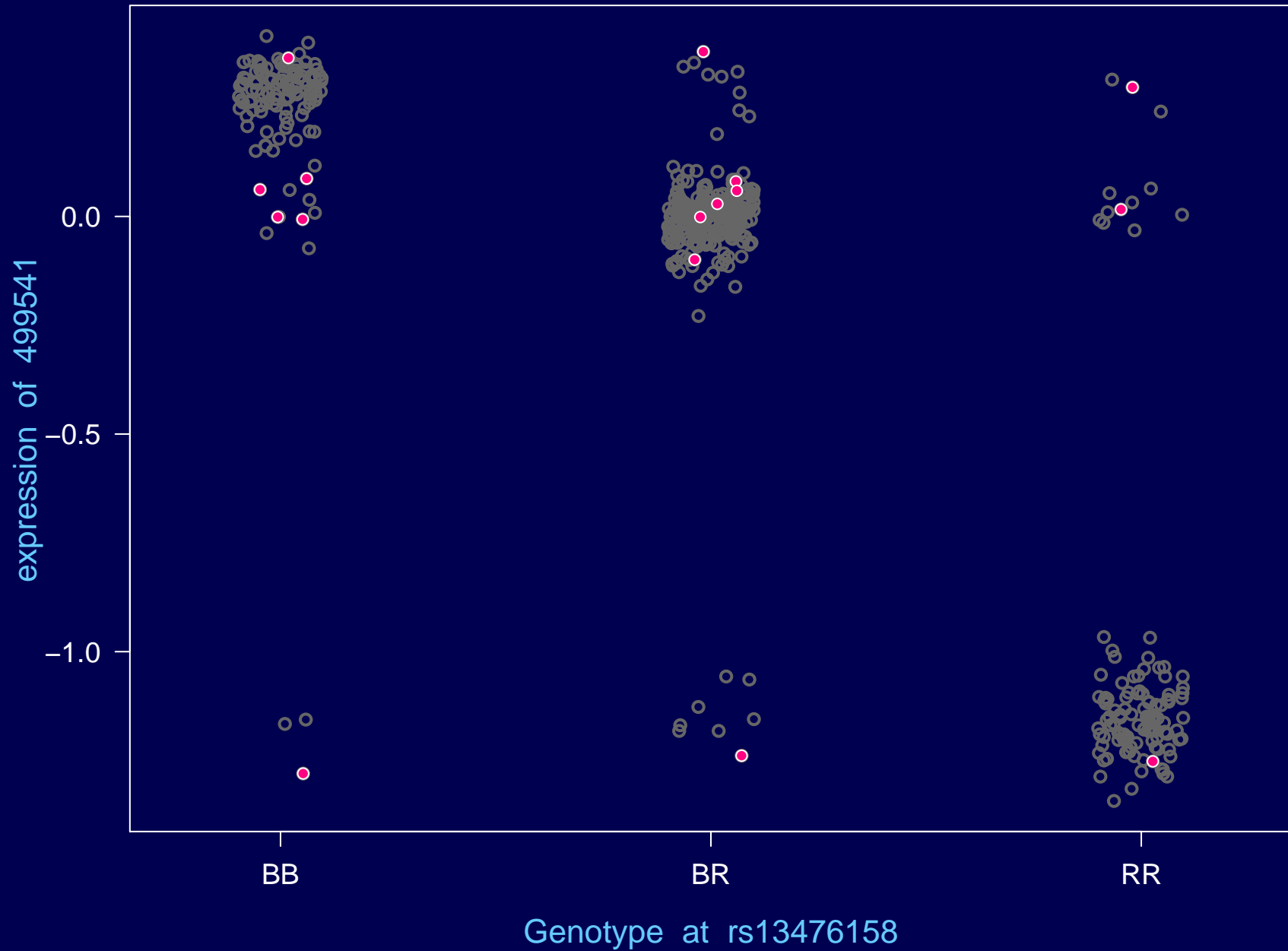
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F₂ males: hemizygous B or R

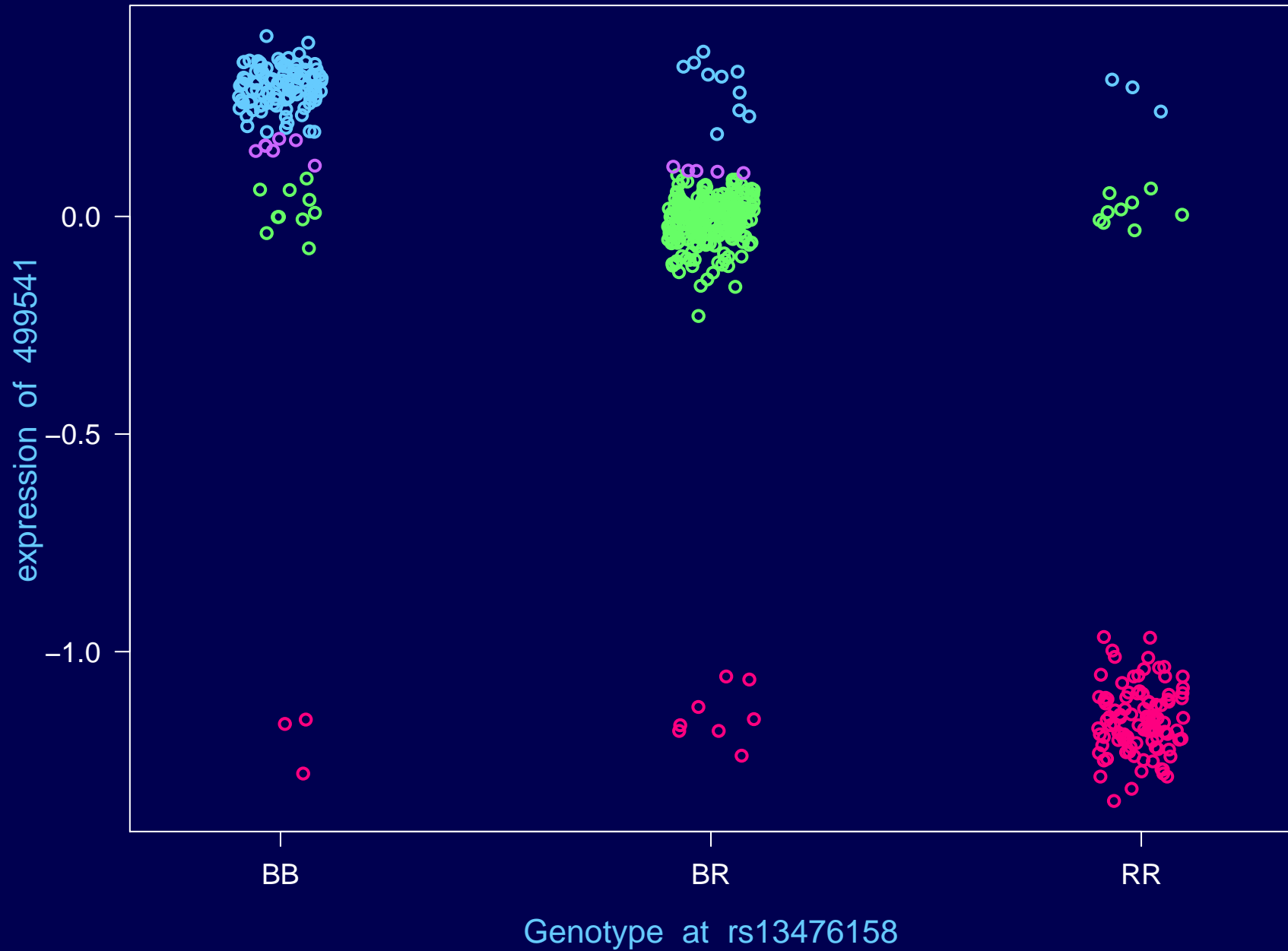
E vs G



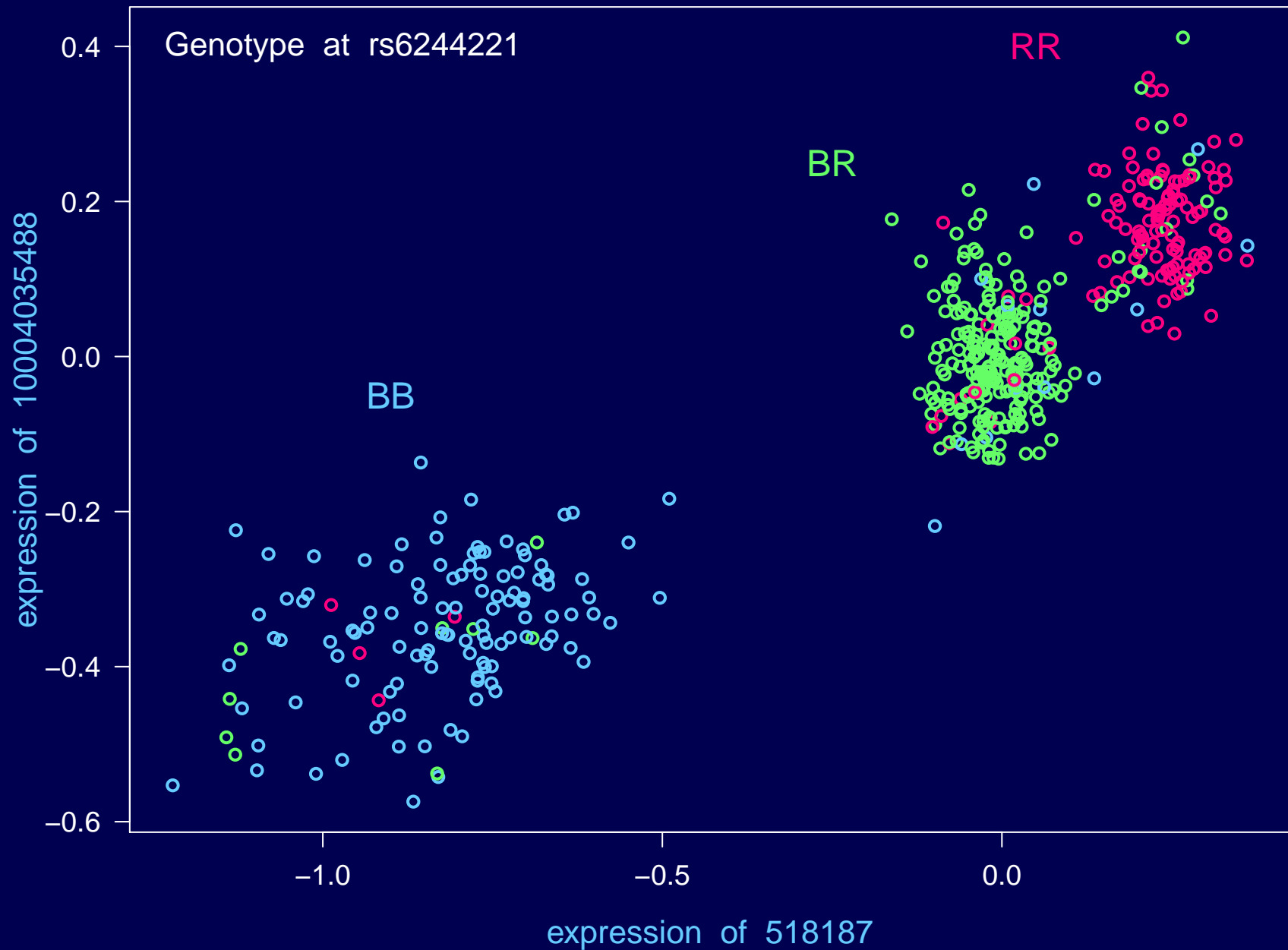
E vs G



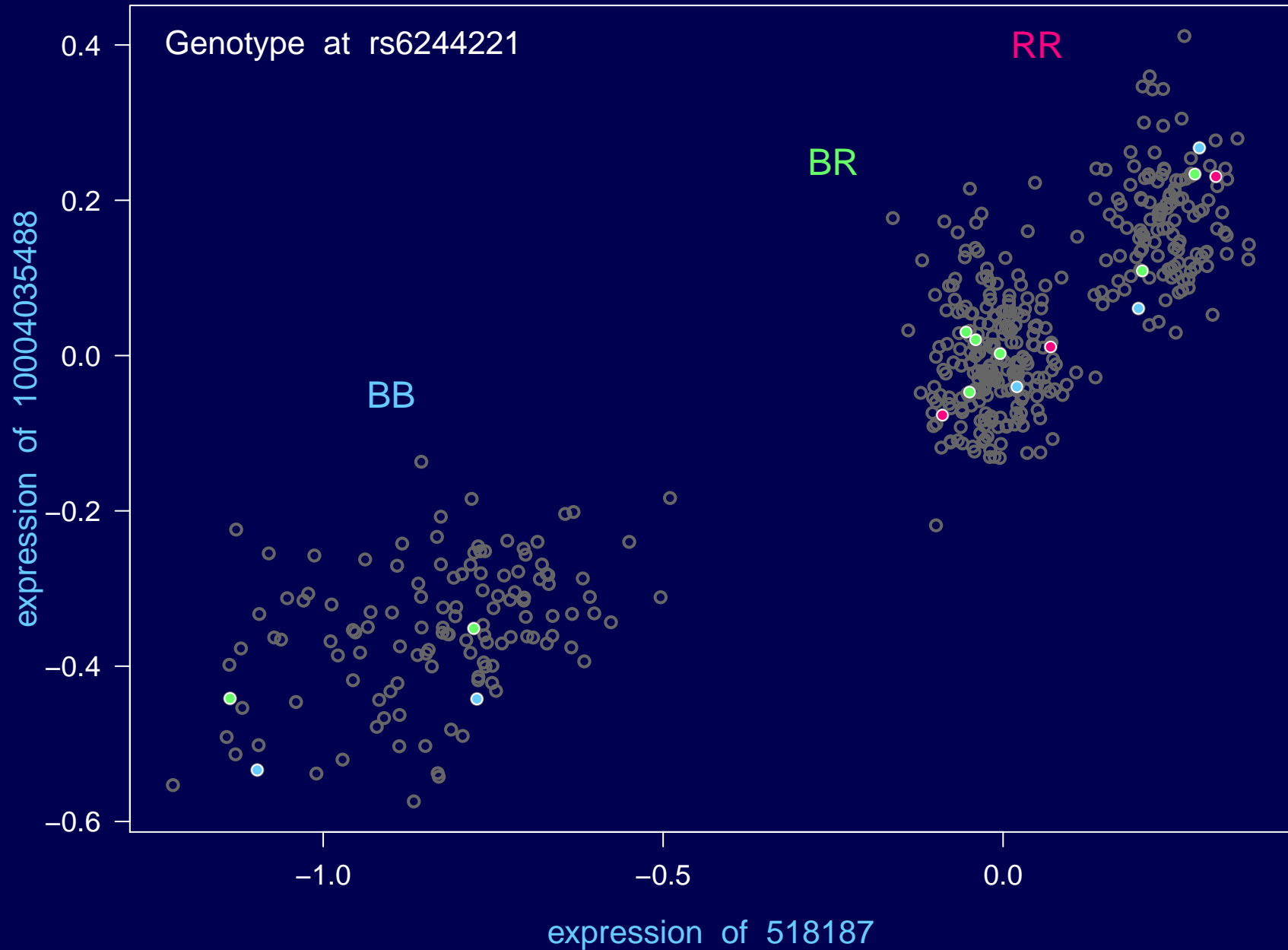
kNN classifier



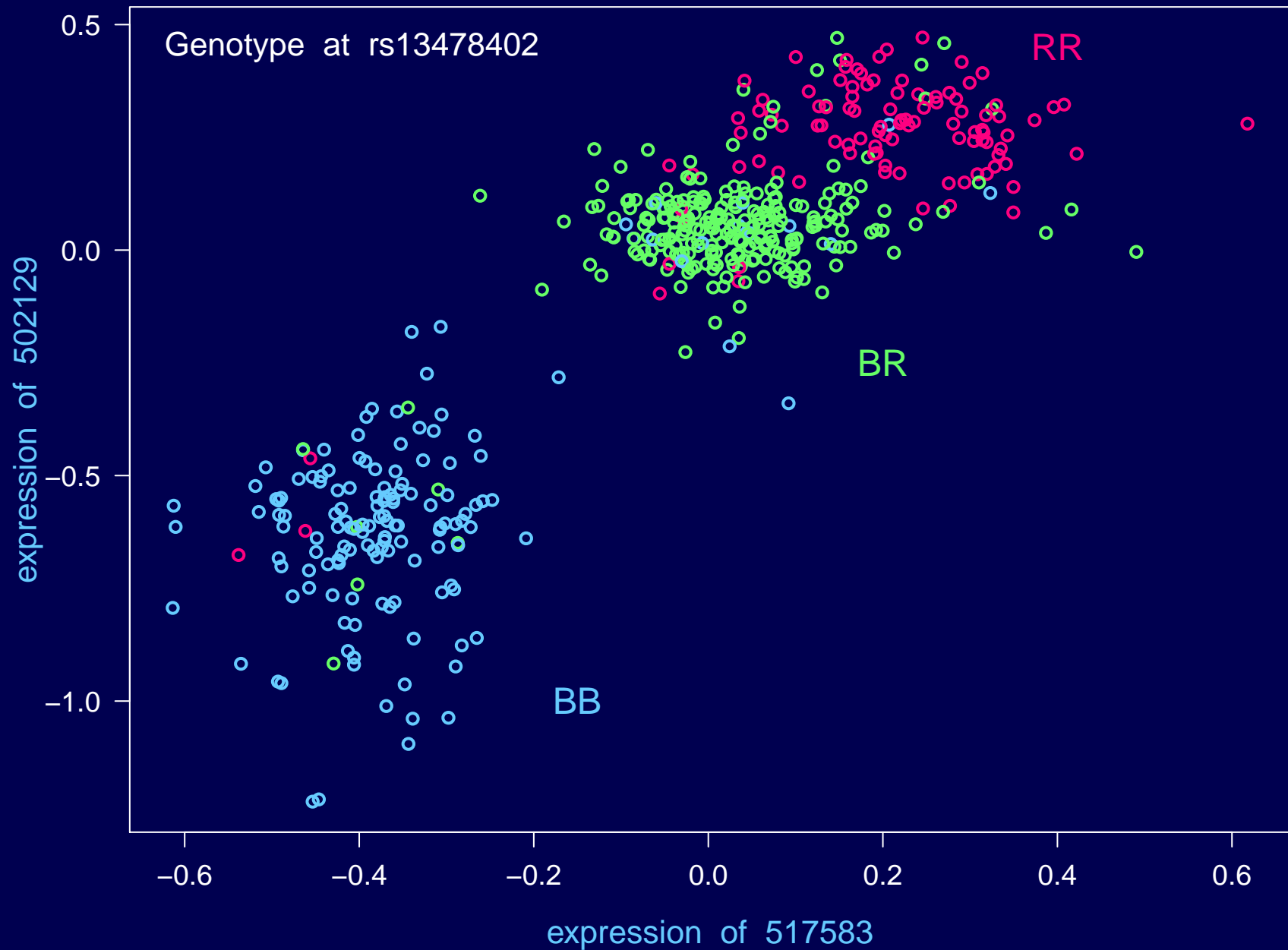
E vs G



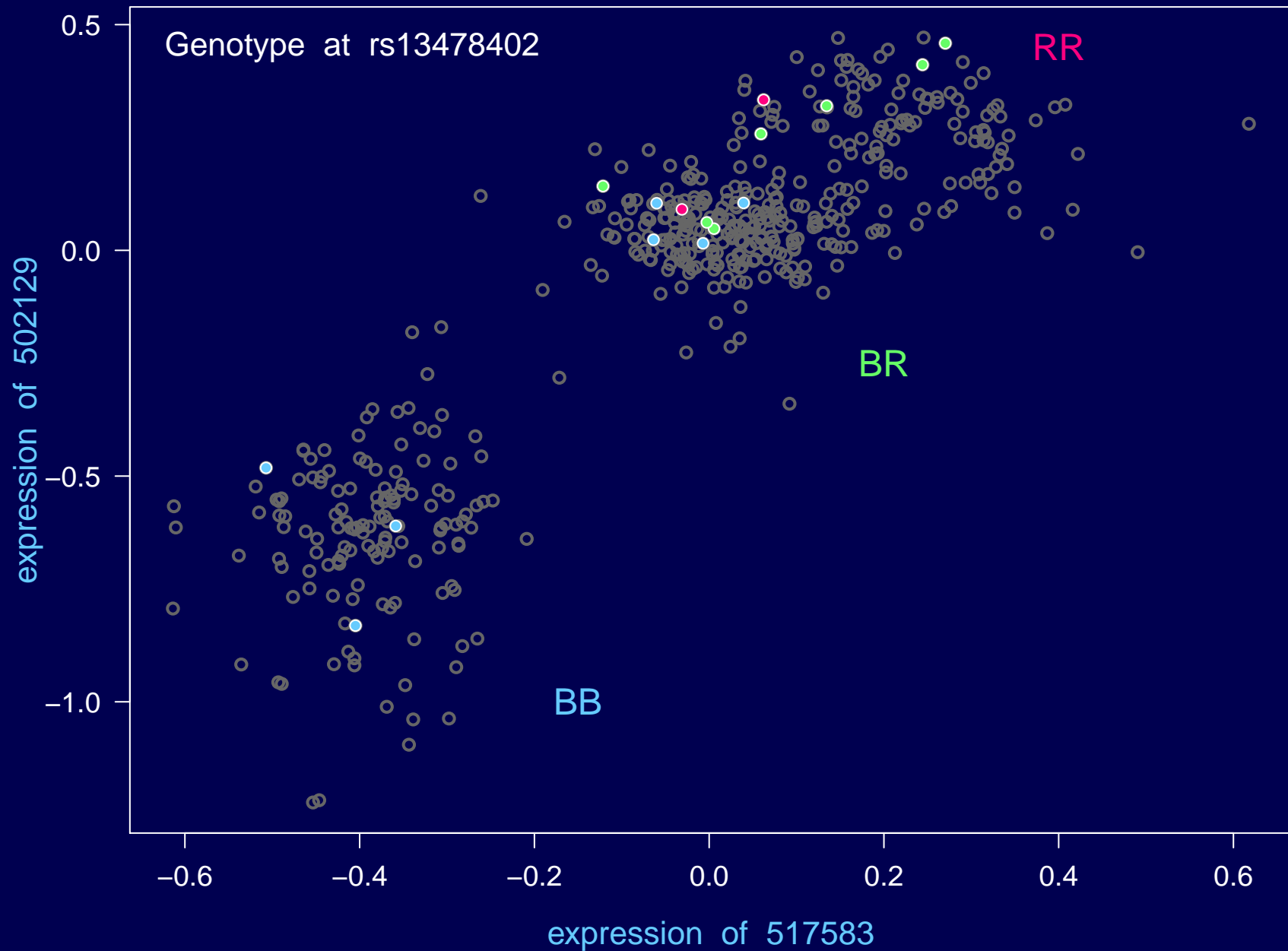
E vs G



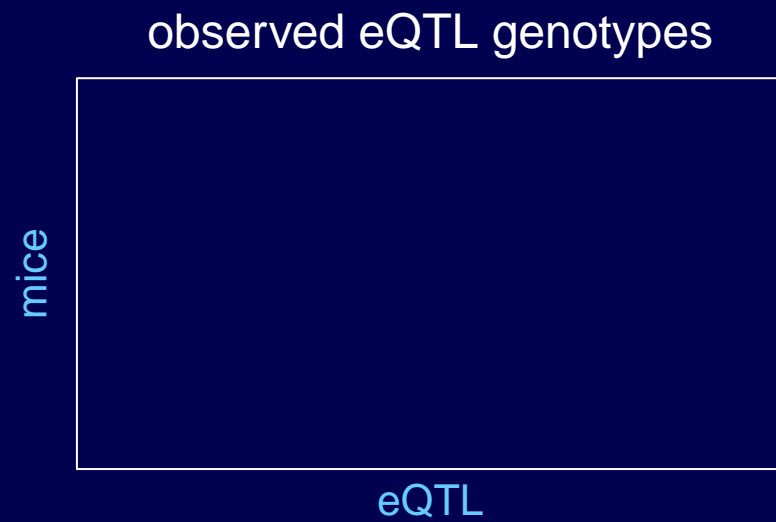
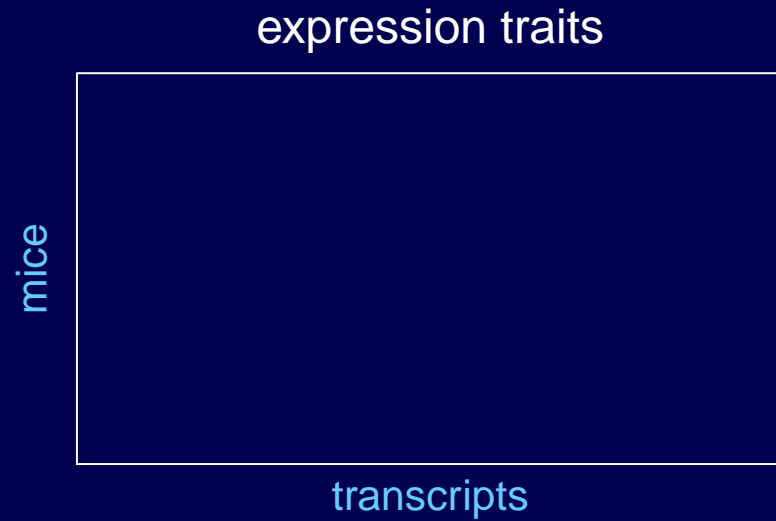
E vs G



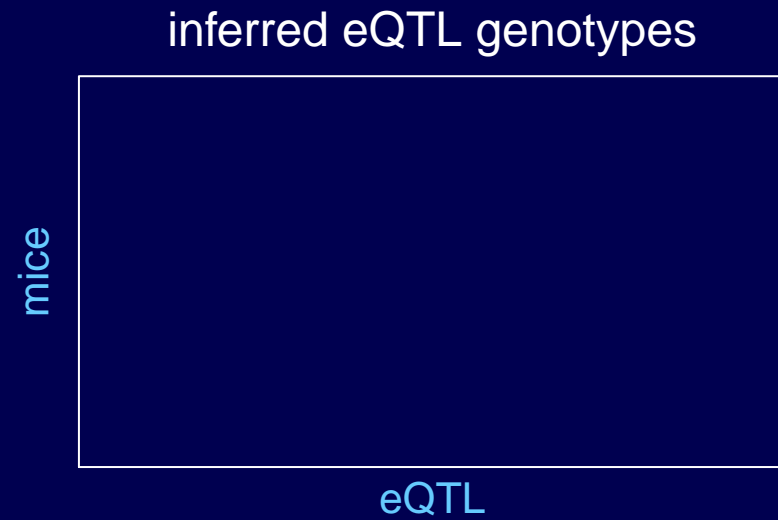
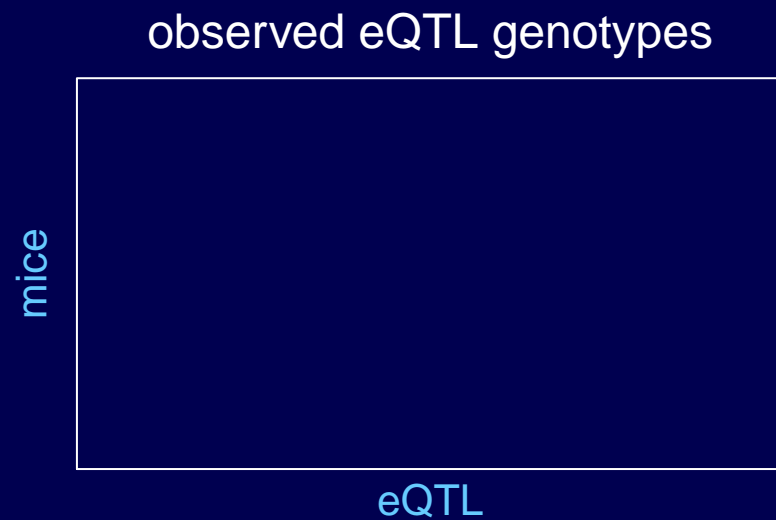
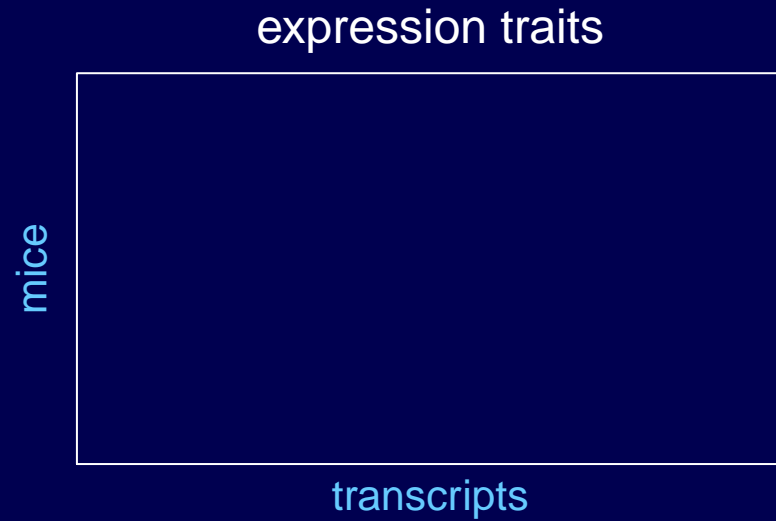
E vs G



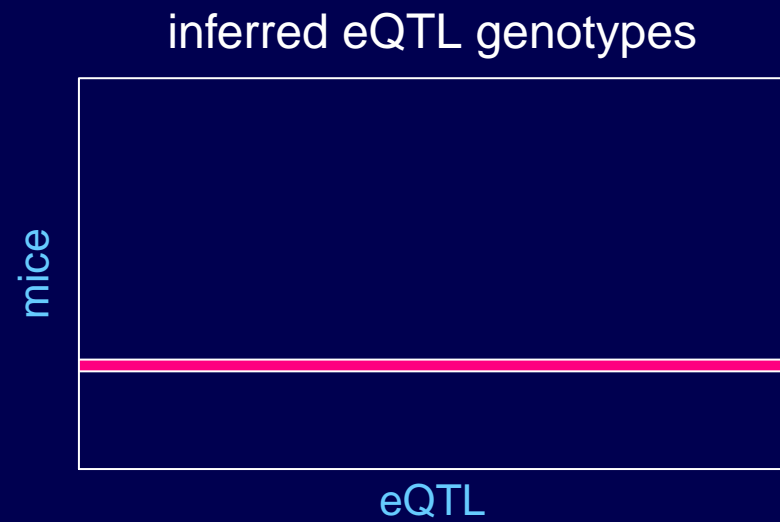
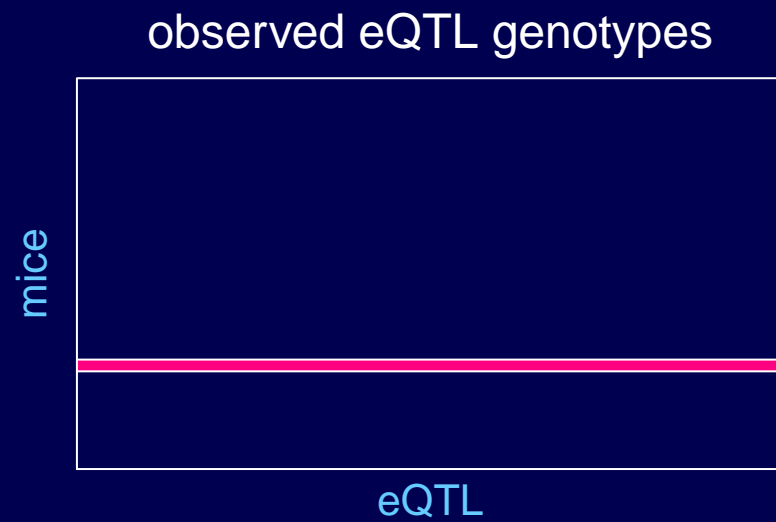
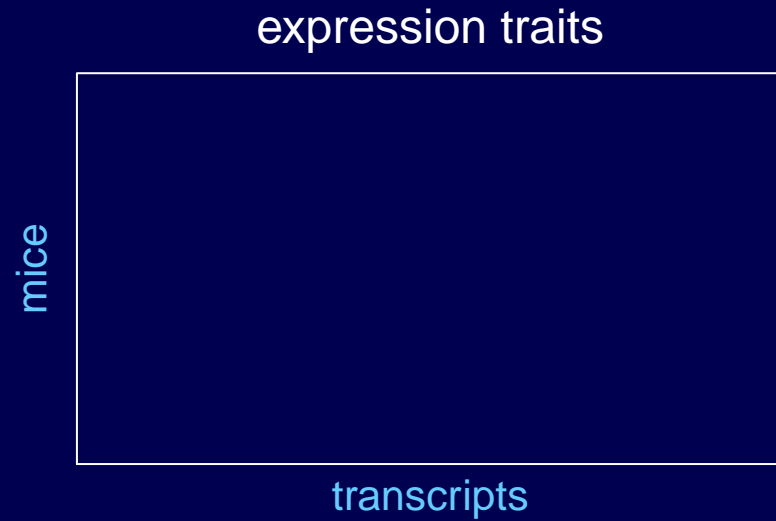
Basic scheme



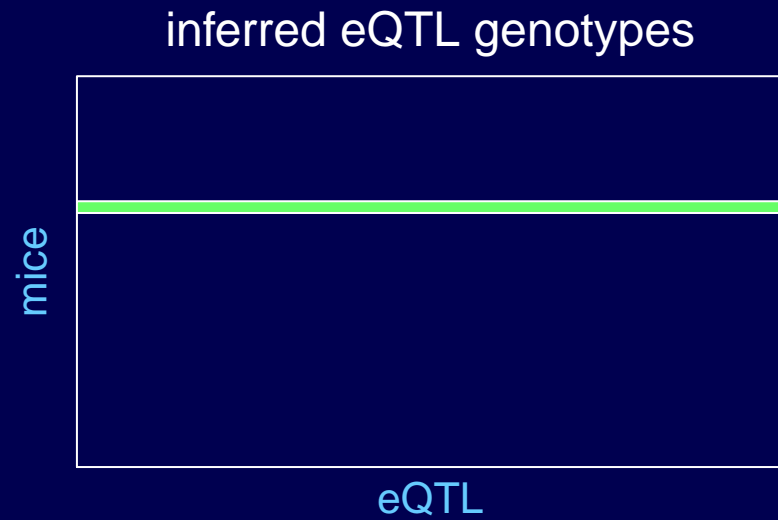
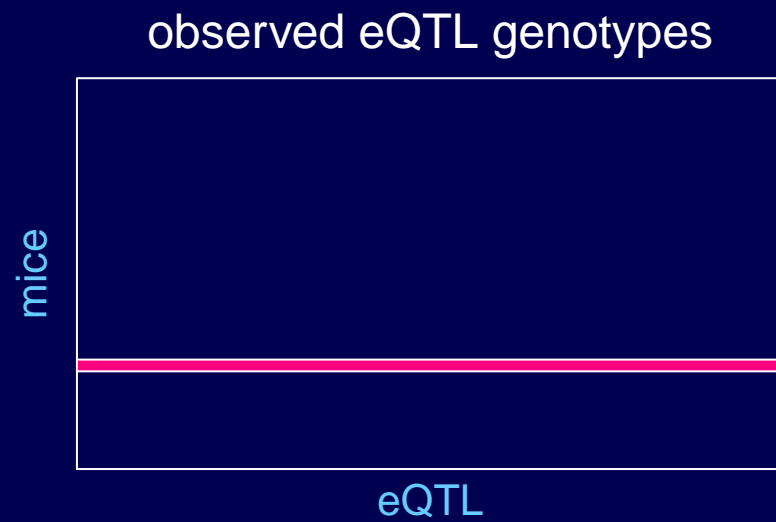
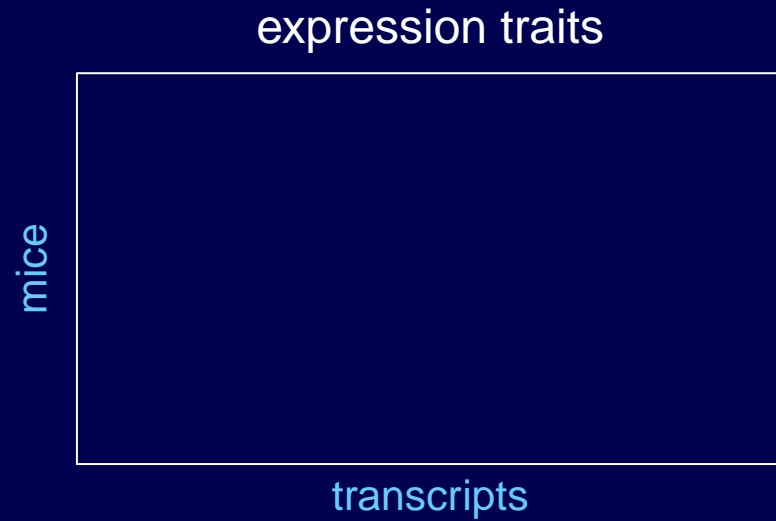
Basic scheme



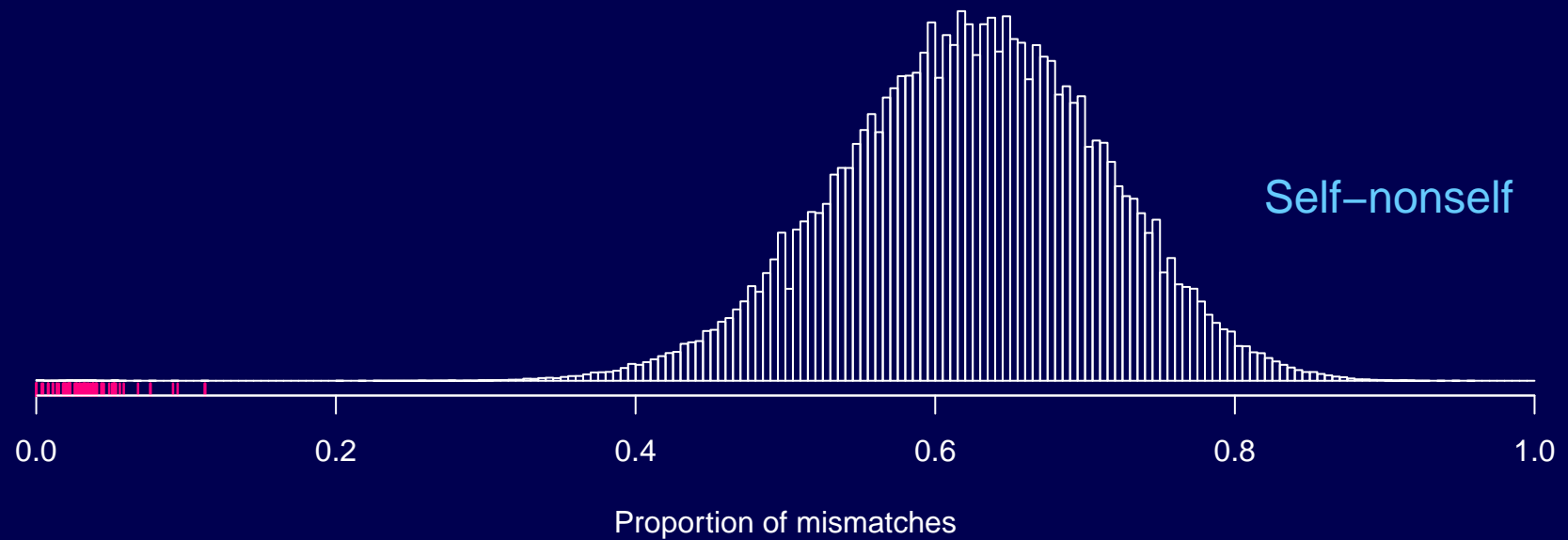
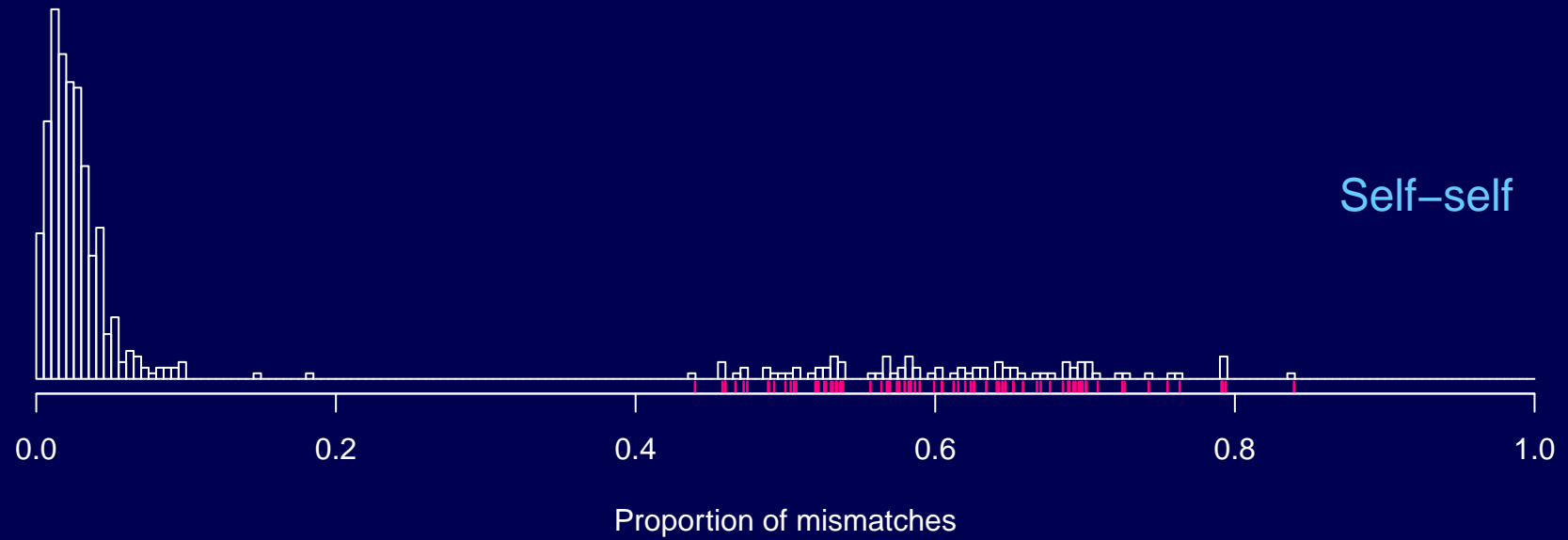
Basic scheme



Basic scheme

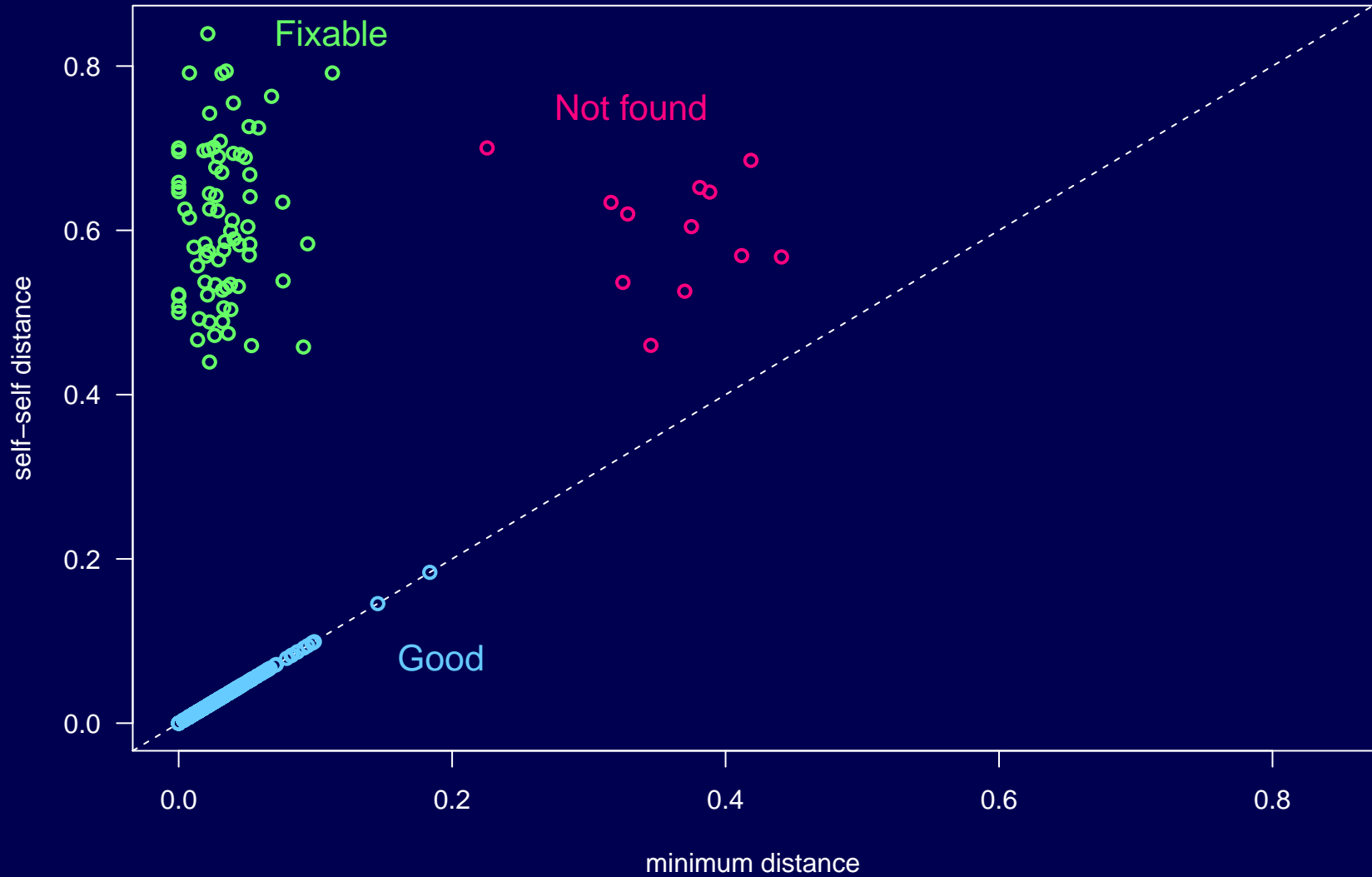


Prop'n mismatches



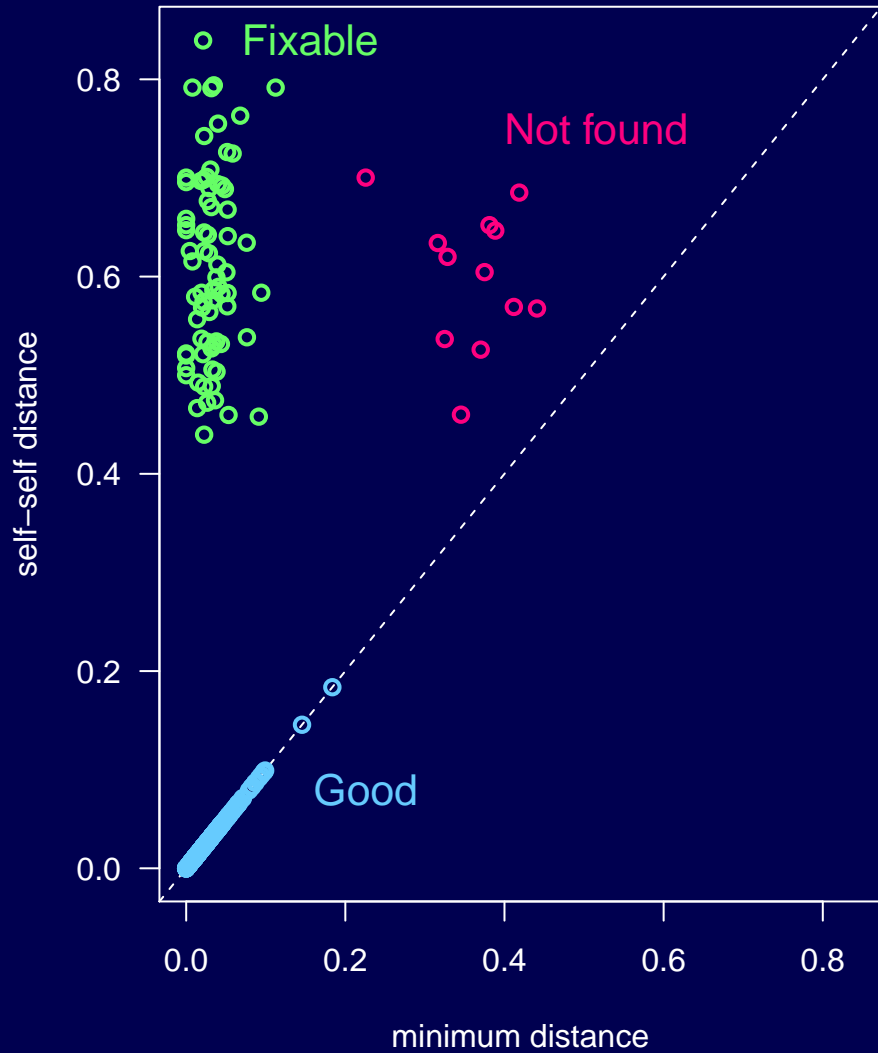
Decisions

Self vs best

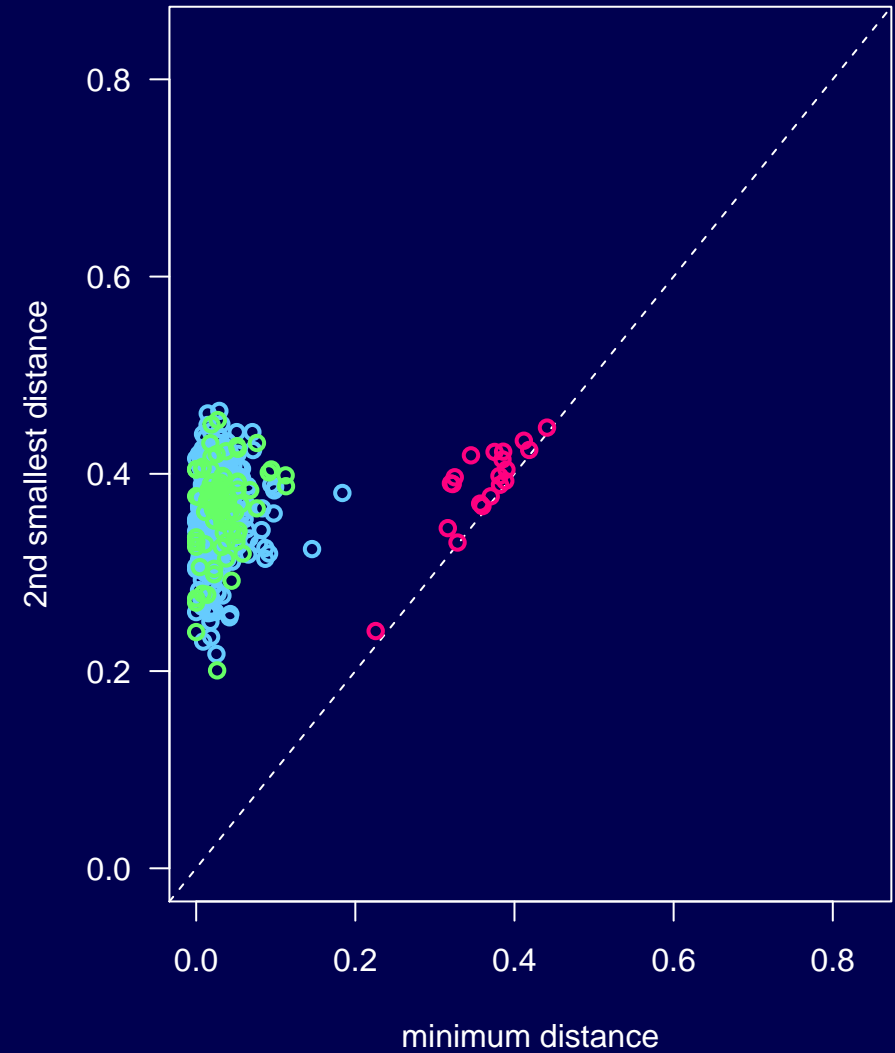


Decisions

Self vs best



Next-best vs best

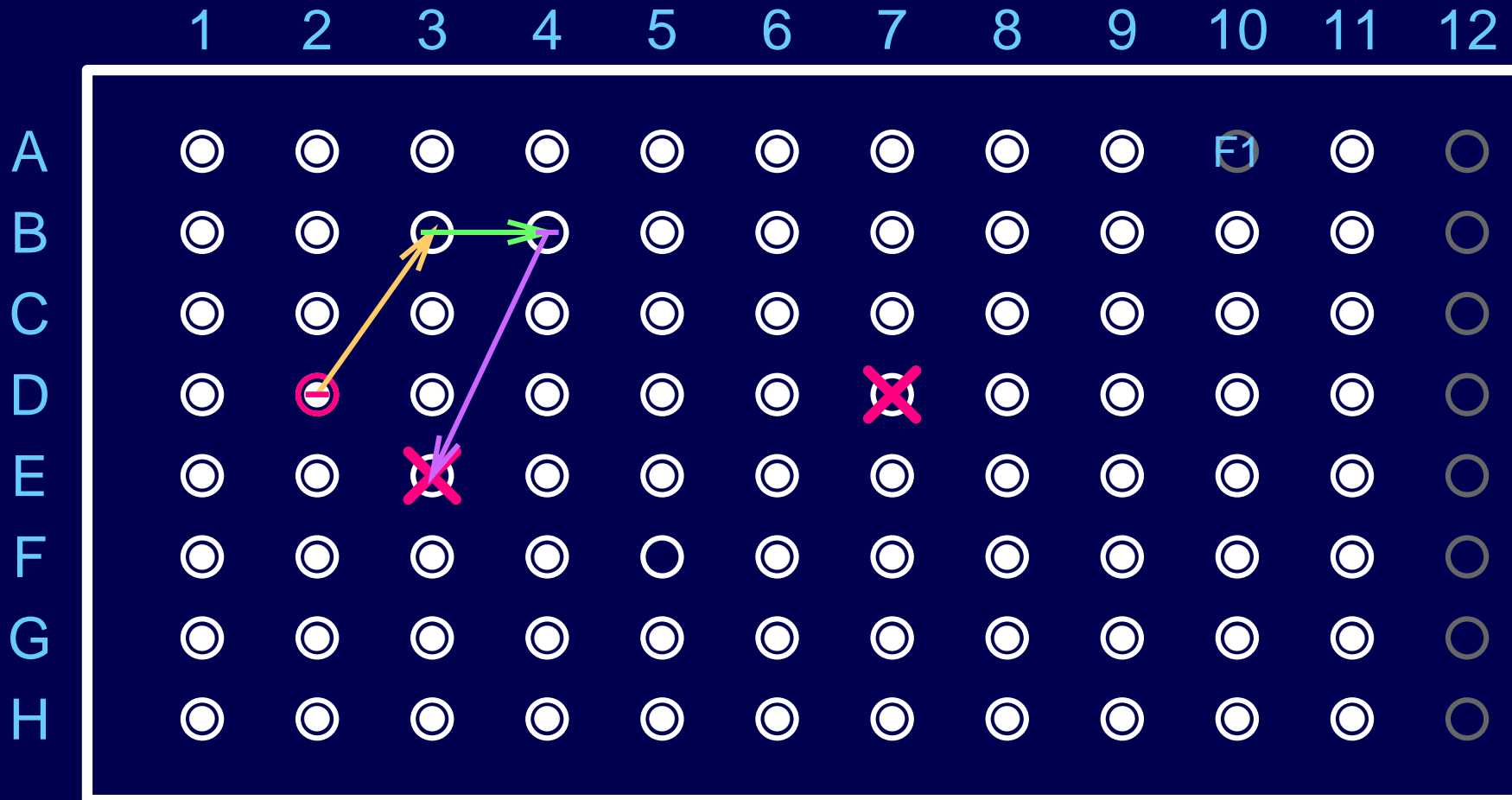


Genotype mix-ups



Plate 1631

1631



Plates 1632 and 1630

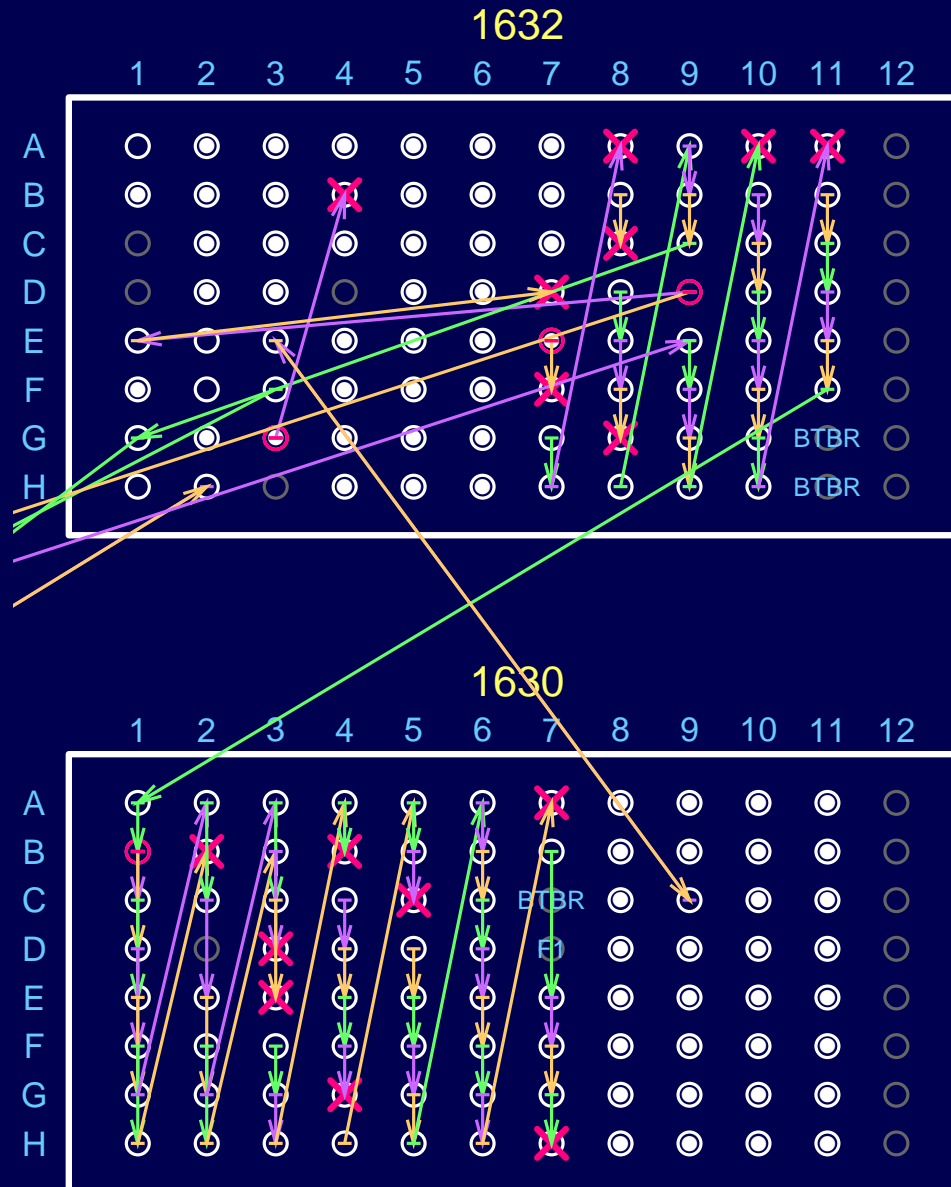
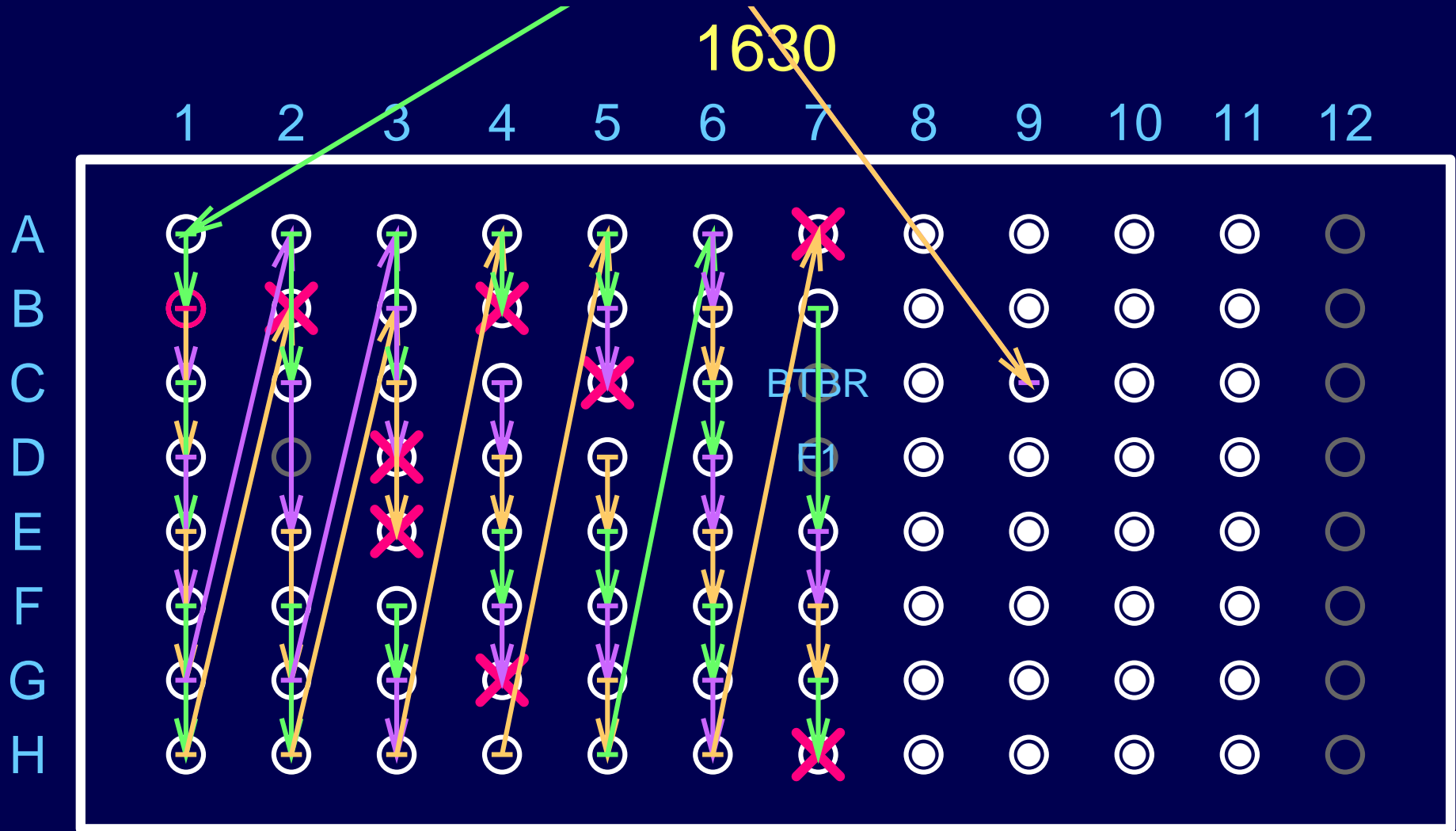


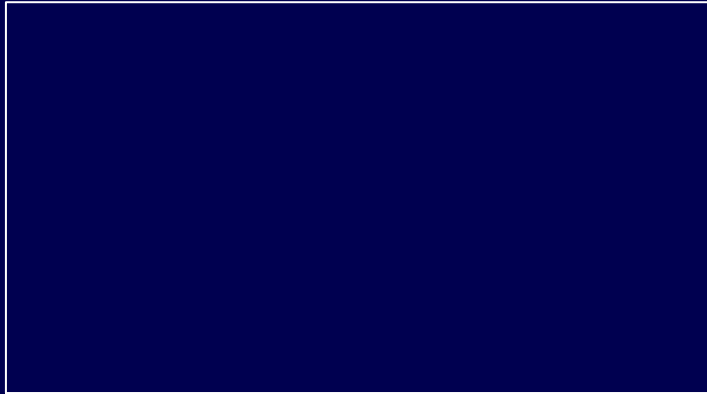
Plate 1630



E vs E

expression in islet

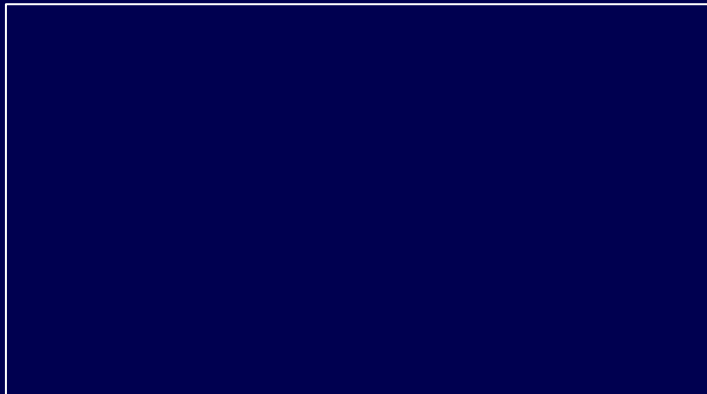
mice



transcripts

expression in liver

mice

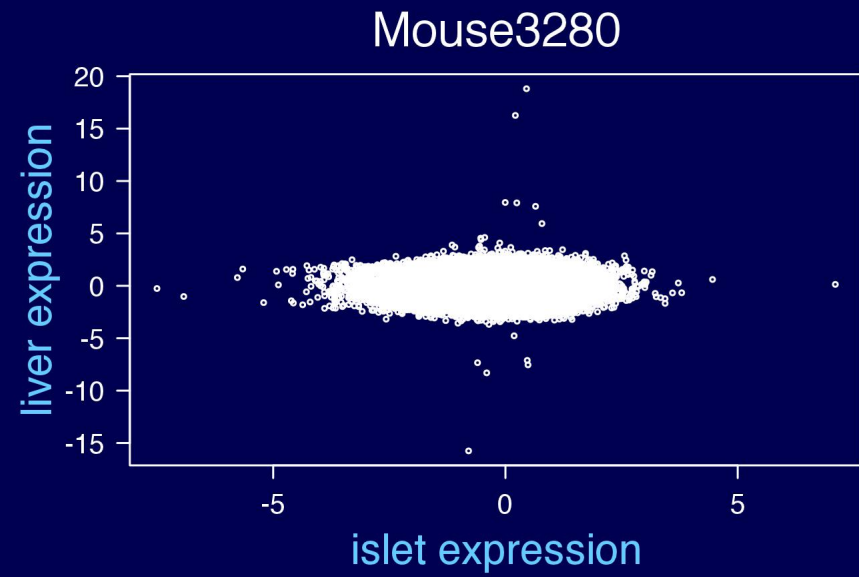


transcripts

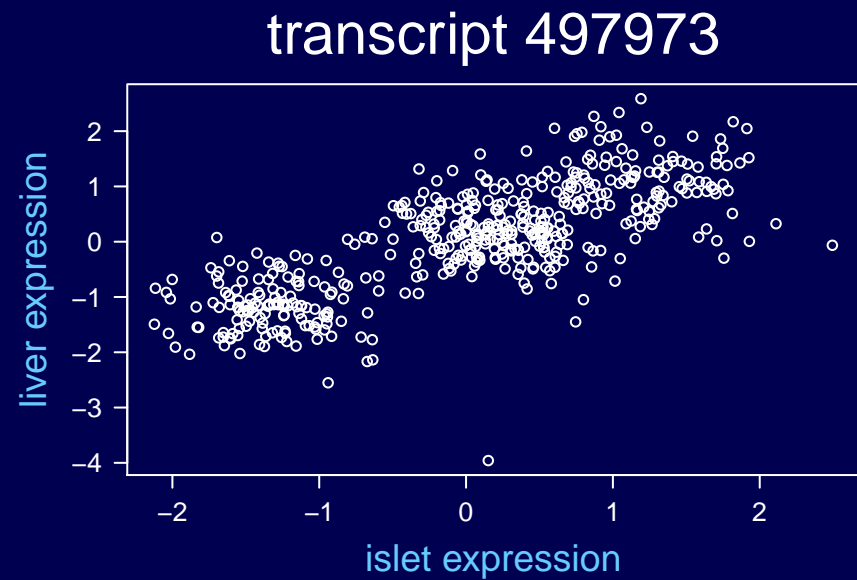
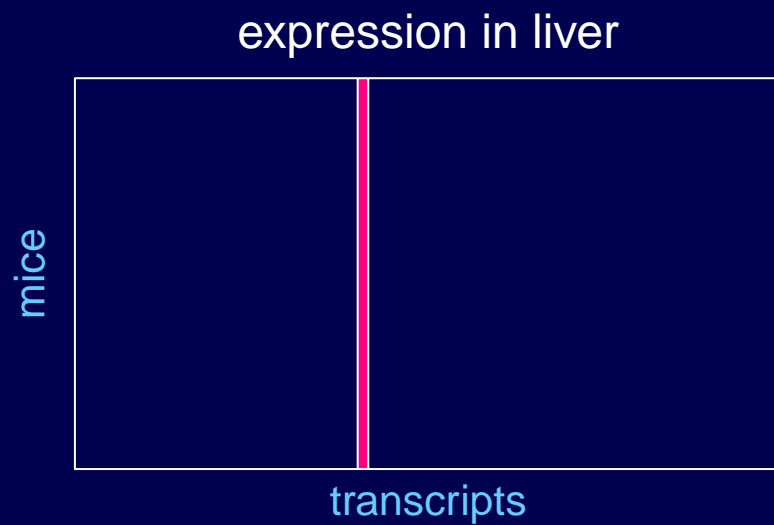
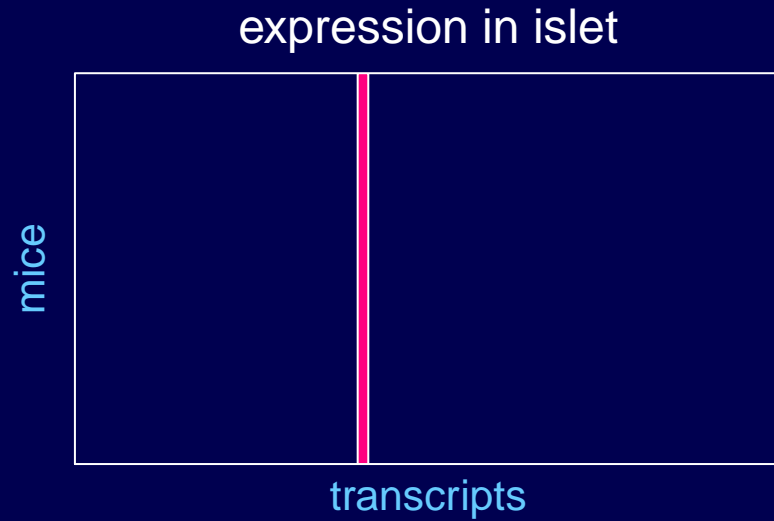
E vs E



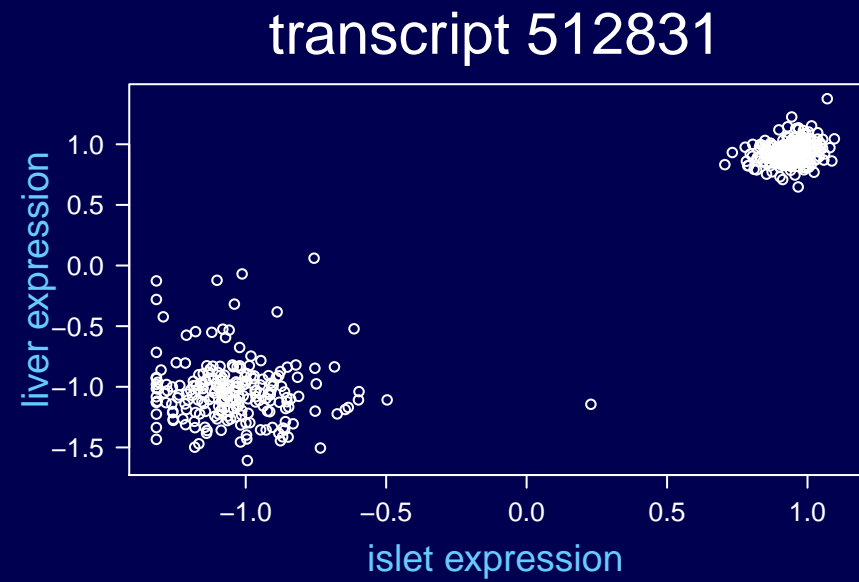
E vs E



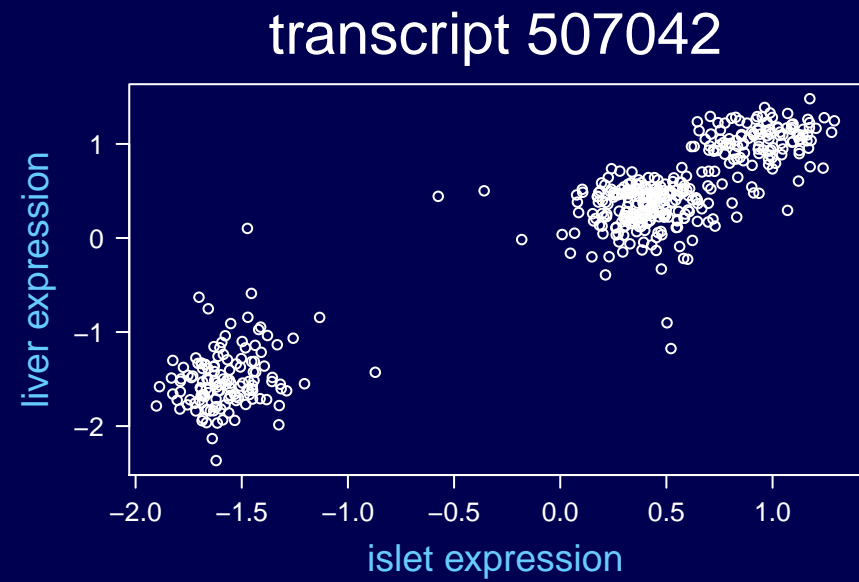
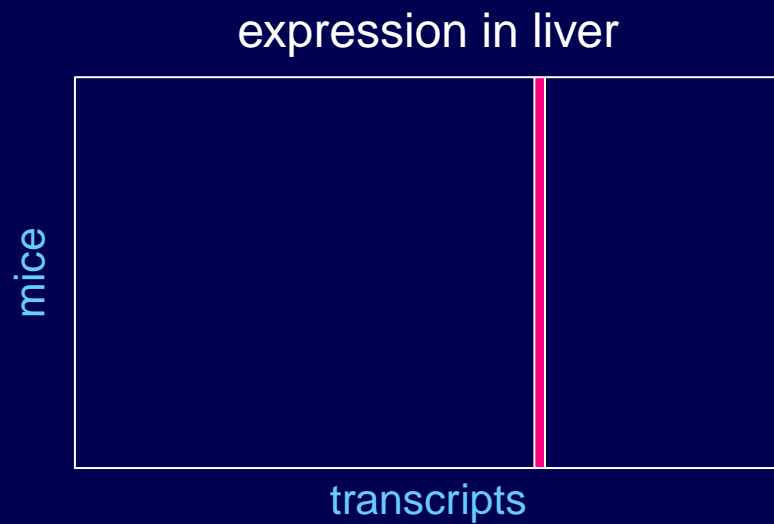
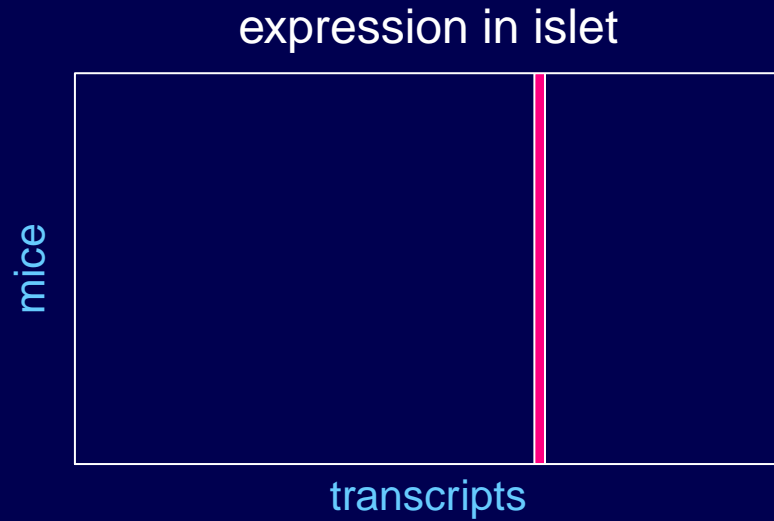
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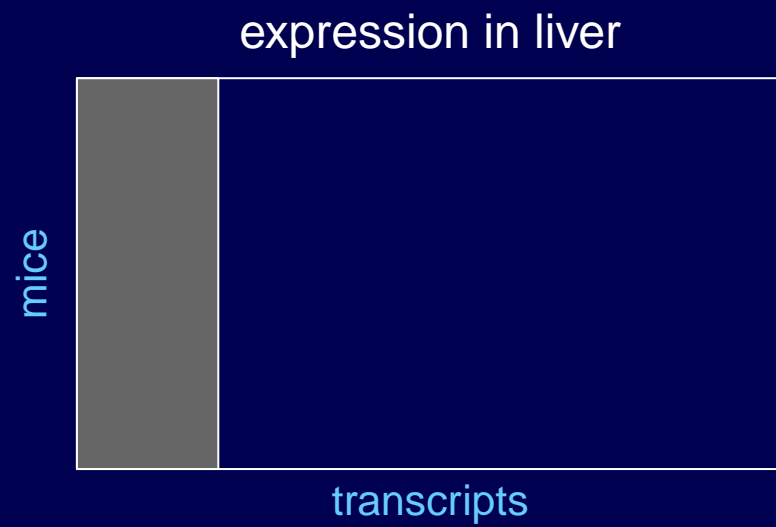
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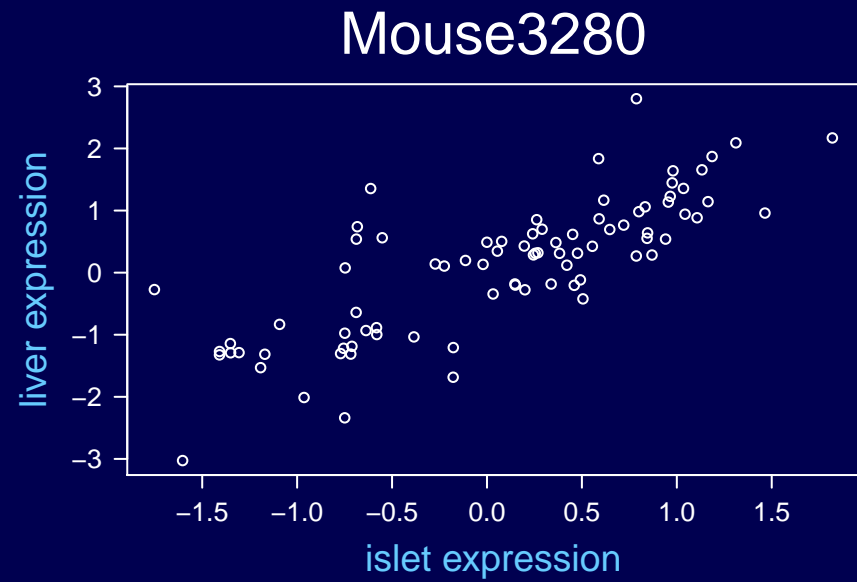
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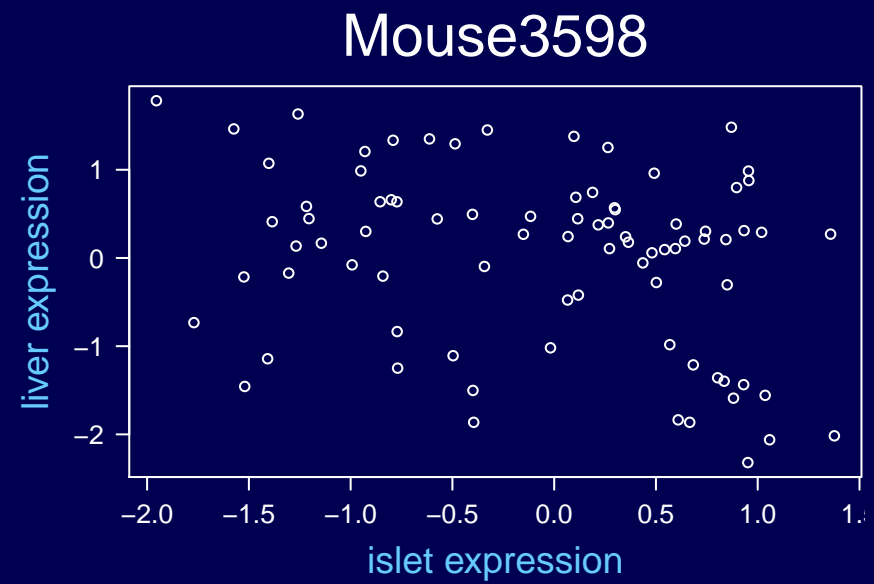
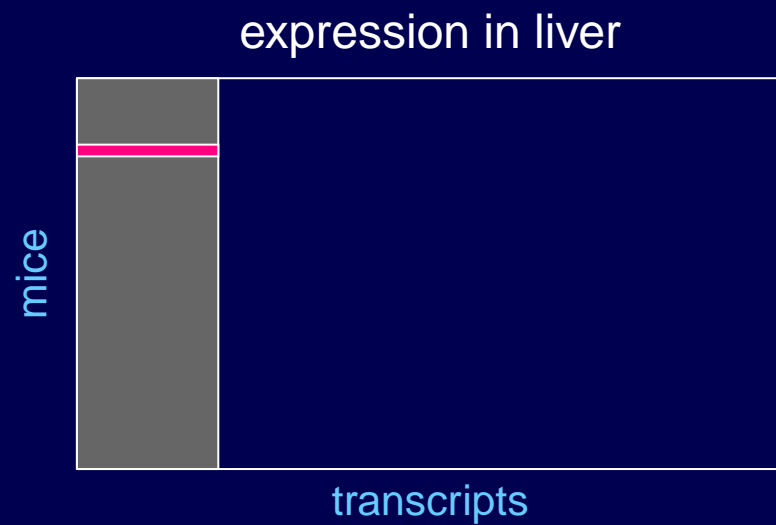
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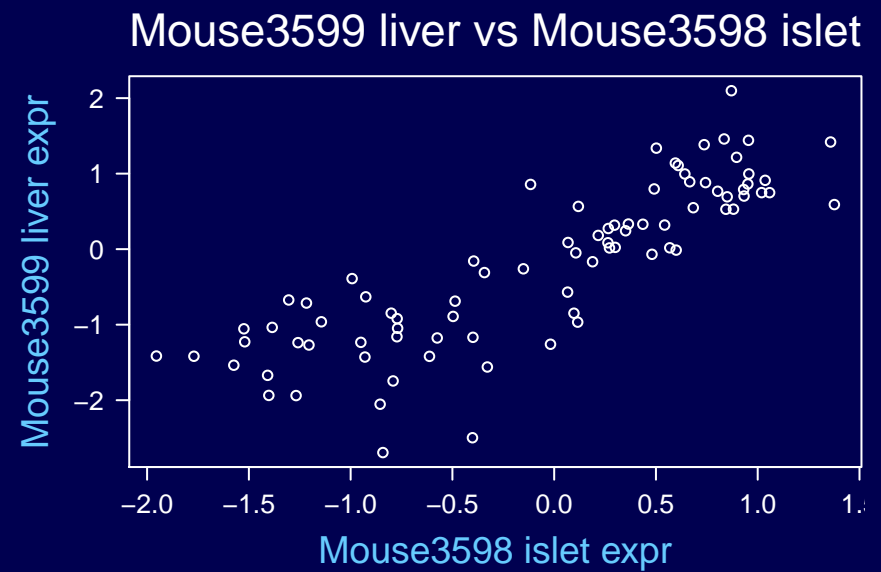
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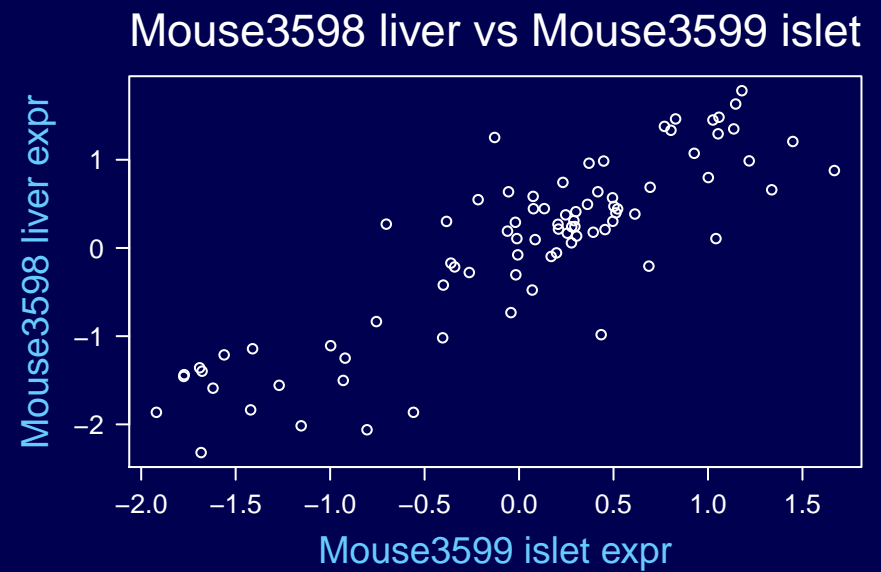
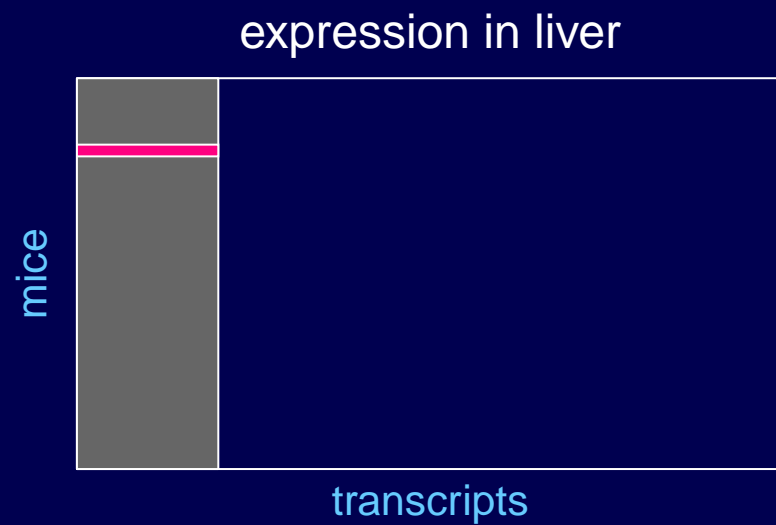
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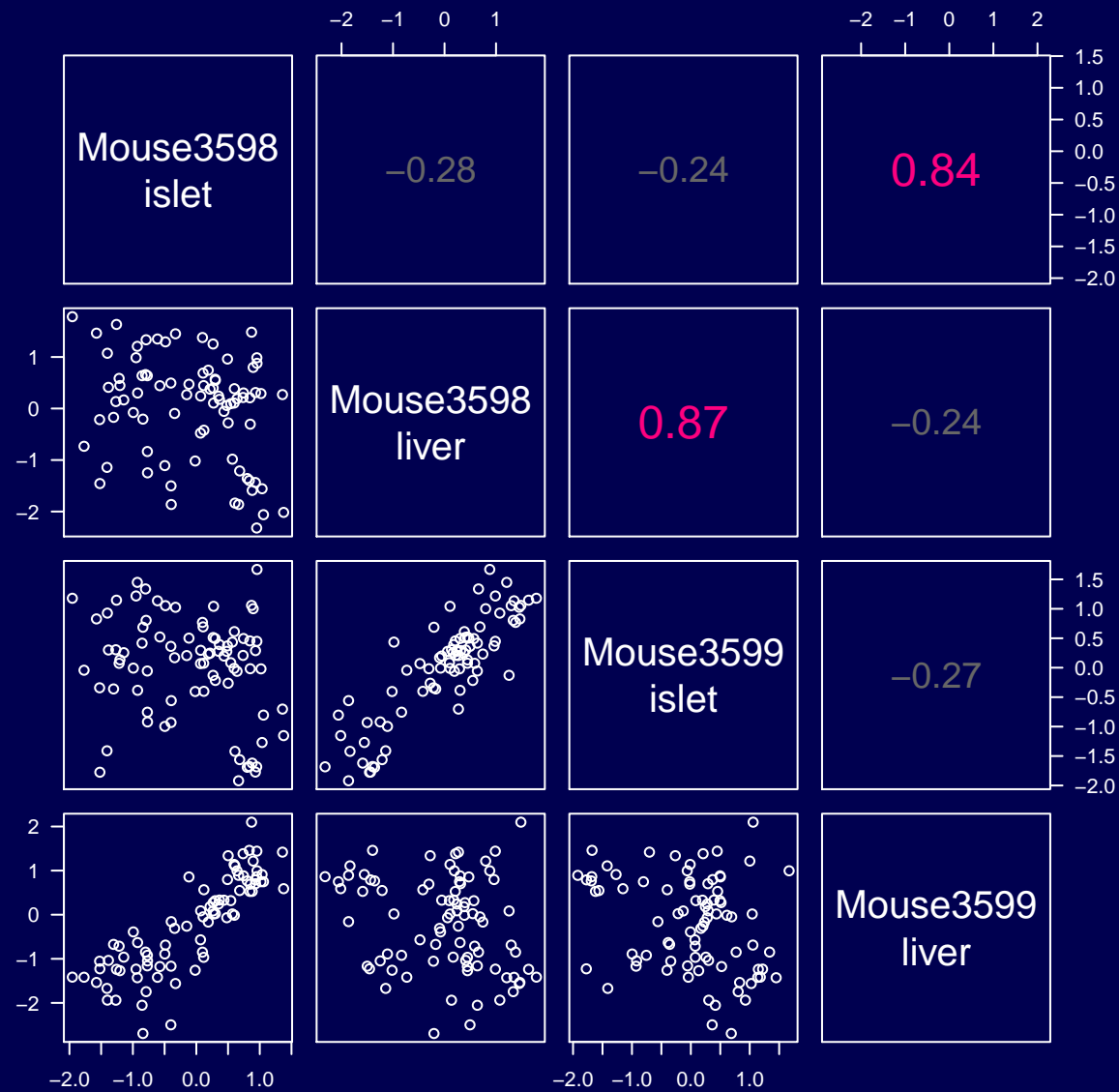
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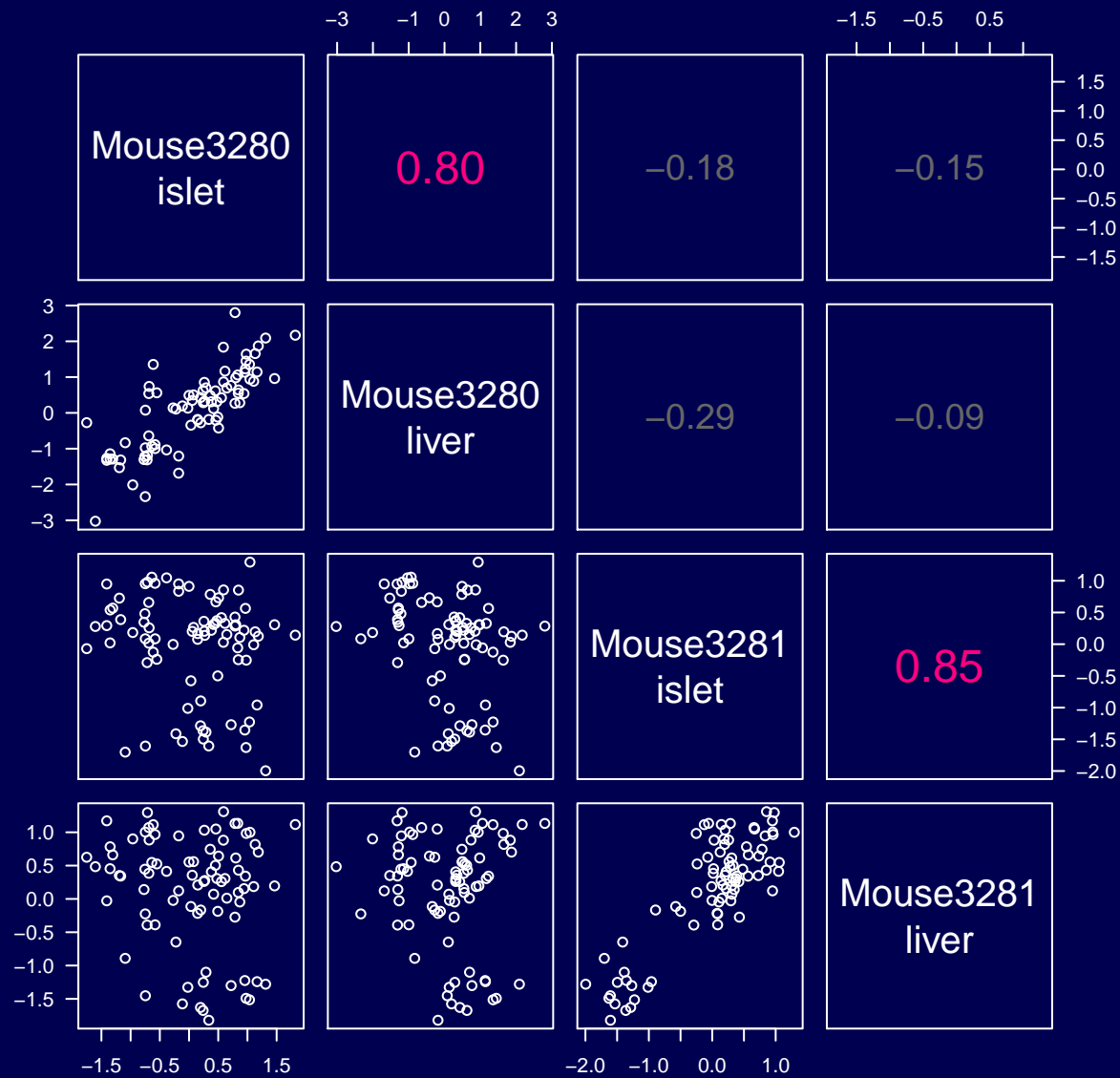
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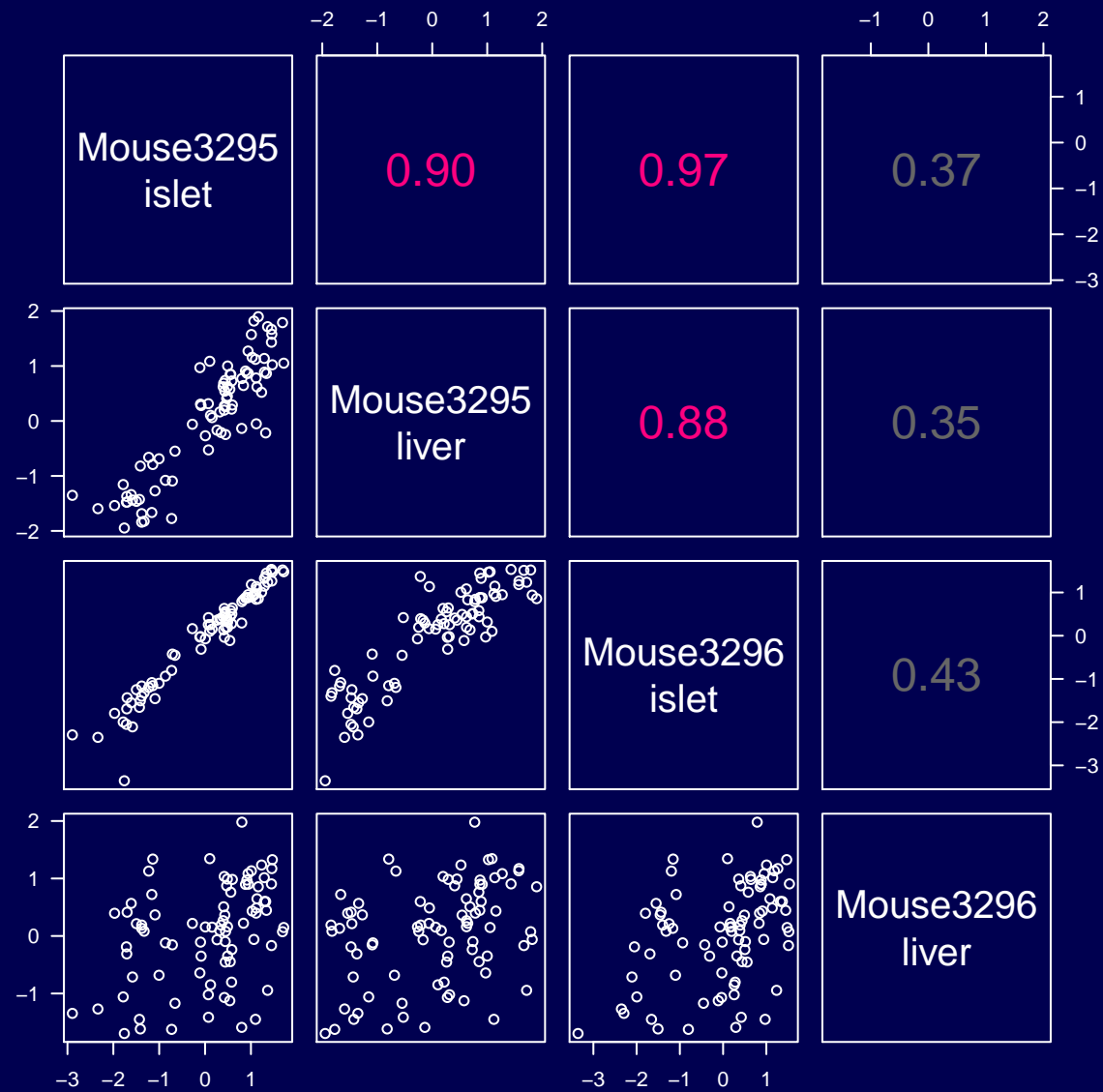
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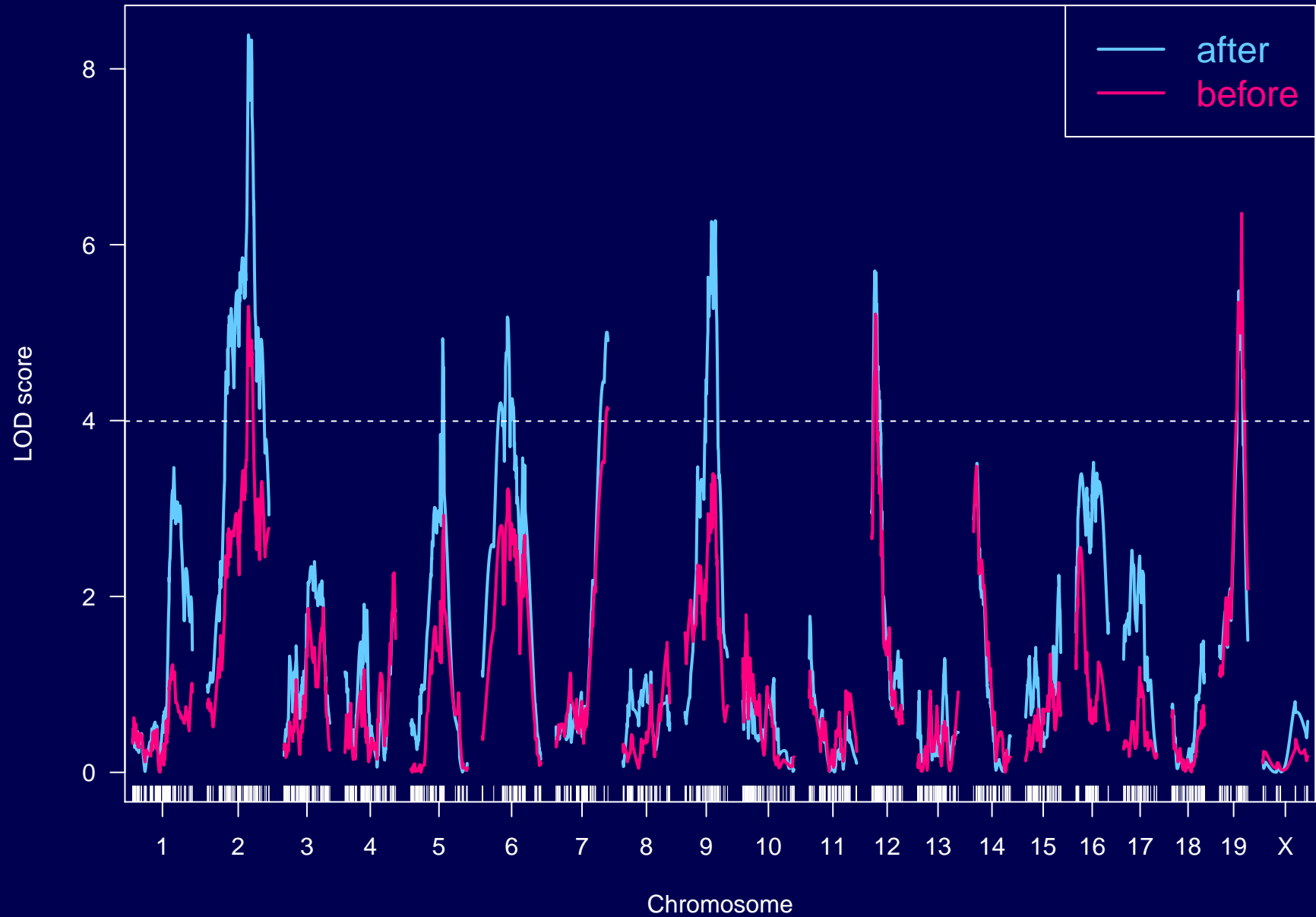
E vs E



E vs E



Insulin QTL



Summary

- Sample mix-ups happen
- With eQTL data, we can both identify and correct mix-ups
- There is great value in having expression on multiple tissues
- The general idea here has wide application for high-throughput data
- Very similar to [MixupMapper](#) (Westra et al., *Bioinformatics* 27:2104–2111, 2011)
 - Multiple tissues
 - Direct tissue-tissue comparisons
 - Predict genotype rather than expression phenotype

Acknowledgments

Alan Attie
Mark Keller

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Brian Yandell

Statistics and Horticulture, UW–Madison

Christina Kendzierski
Aimee Teo Broman

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Eric Schadt

Pacific Biosciences of California

Danielle Greenawalt
Amit Kulkarni

Merck & Co., Inc.

Śaunak Sen

UCSF

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