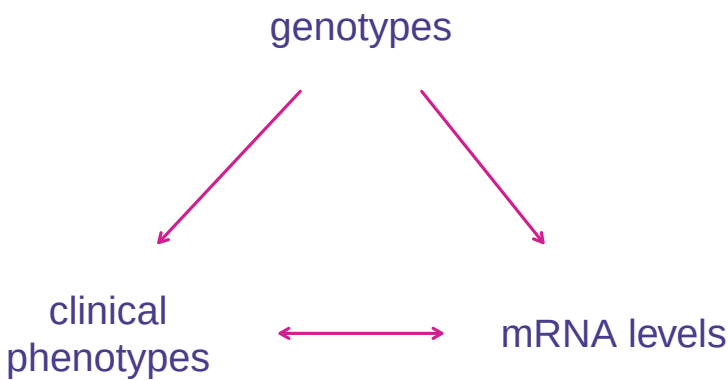
Identifying sample mix-ups in eQTL data

Karl Broman

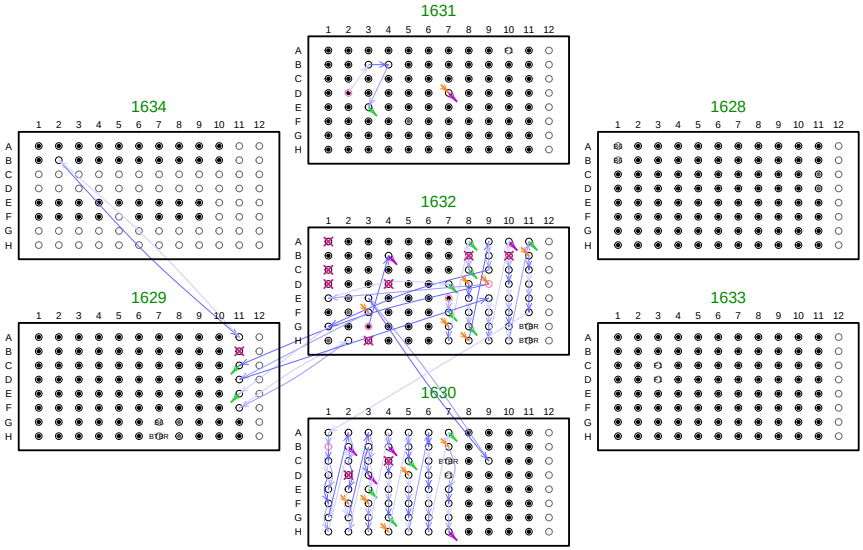
Biostatistics & Medical Informatics, Univ. Wisconsin–Madison

kbroman.org
github.com/kbroman
@kwbroman
Slides: kbroman.org/Talk_OSGA2021

Associations in systems genetics

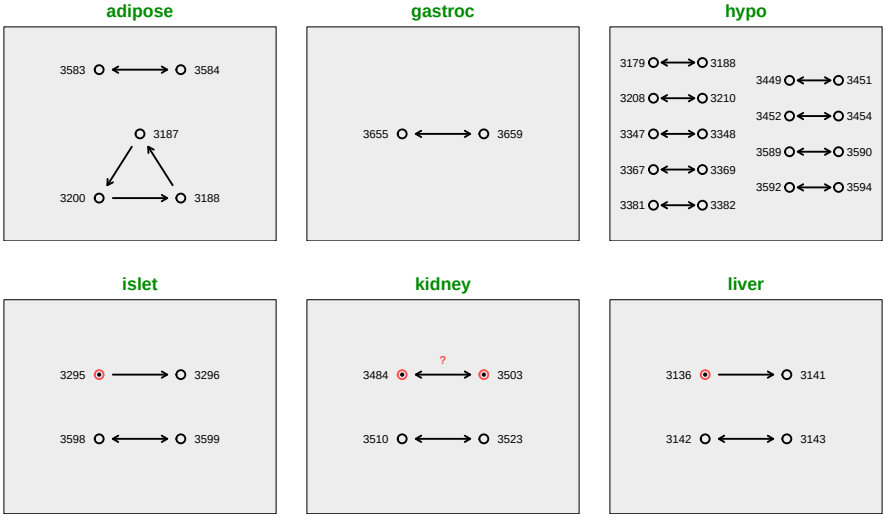


Sample mix-ups



Broman et al. (2015) doi:10.1534/g3.115.019778

More sample mix-ups



Broman et al. (2015) doi:10.1534/g3.115.019778

Westra et al. (2011)

Table 2. *Cis*-eQTL mapping and sample mix-up identification results

Stud	Population	Sample-size	Initial *cis*-eQTLs	Mix-ups detected[a] *n* (%)	Sample-size after correction *n* (%)	*cis*-eQTLs after correction *n* (%)
Choy *et al.* (2008)	CHB+JP	87	138	20 (23)	79 (90)	418 (+203)
	CE	84	558		NA	NA
	YR	85	274	2 (2)	83 (97)	287 (+5)
Stranger *et al.* (2007)	CHB+JP	90	1511		NA	NA
	CE	90	903		NA	NA
	YR	90	663	1 (1)	89 (99)	667 (+1)
Zhang *et al.* (2009)	CE	87	2581		NA	NA
	YR	89	1454	2 (2)	89 (100)	1635 (+12)
Webster *et al.* (2009)	Brai	36	1284	16 (4)	356 (98)	1367 (+6)
Heinzen *et al.* (2008)	Brai	93	349		NA	NA
	PBMC	80	297		NA	NA

Westra et al. (2011) doi:10.1093/bioinformatics/btr323

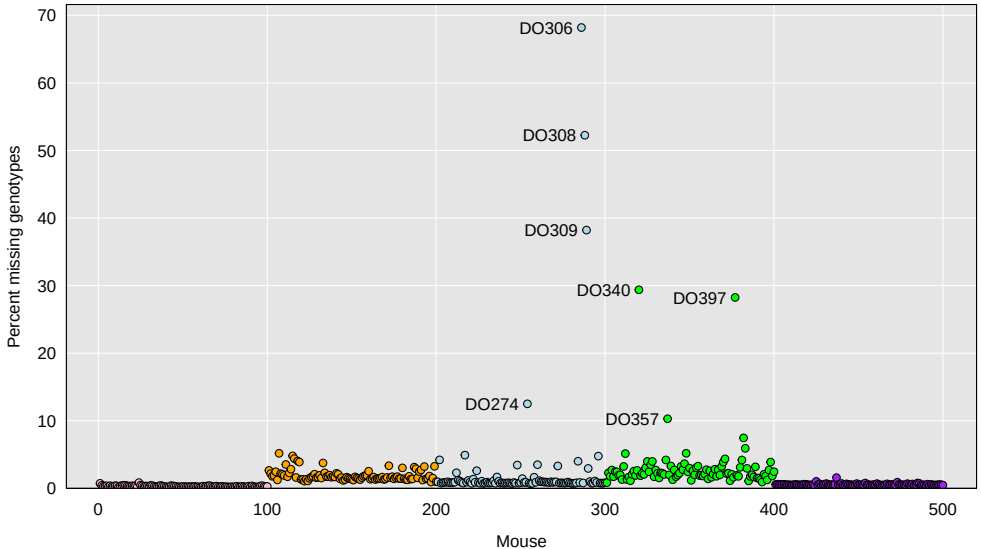
Outline

- Sample duplicates
- Sex verification
- Sample mix-ups:
  - mRNA $\leftrightarrow$ protein
  - mRNA $\leftrightarrow$ DNA
  - protein $\leftrightarrow$ DNA

But first

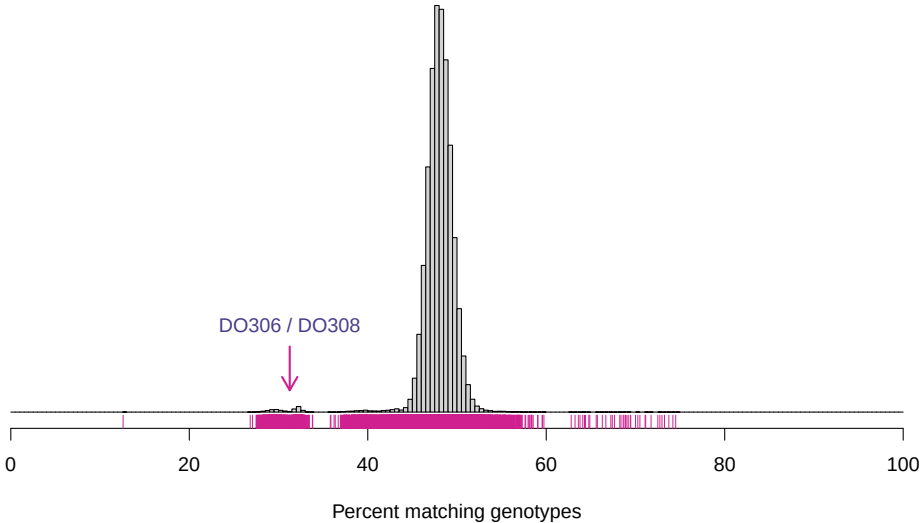
Missing Data

Percent missing genotypes

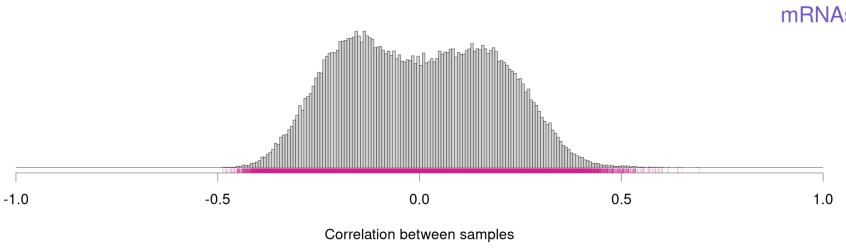


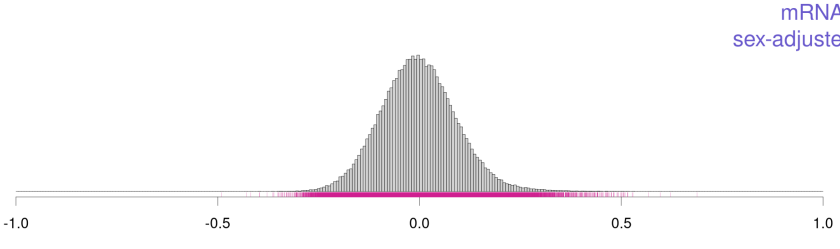
Sample duplicates

Percent matching genotypes

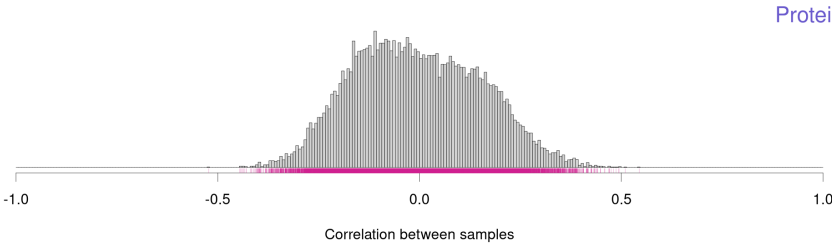


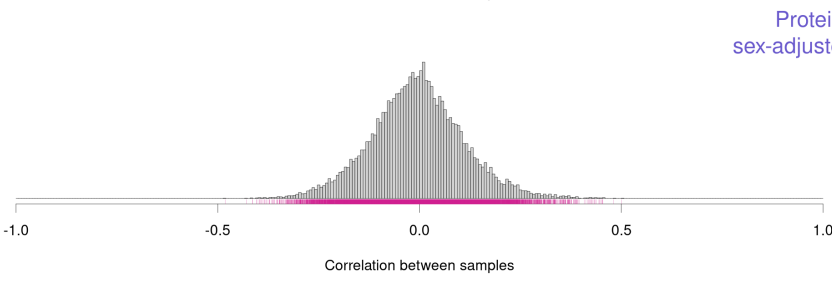
Correlation between mRNA samples





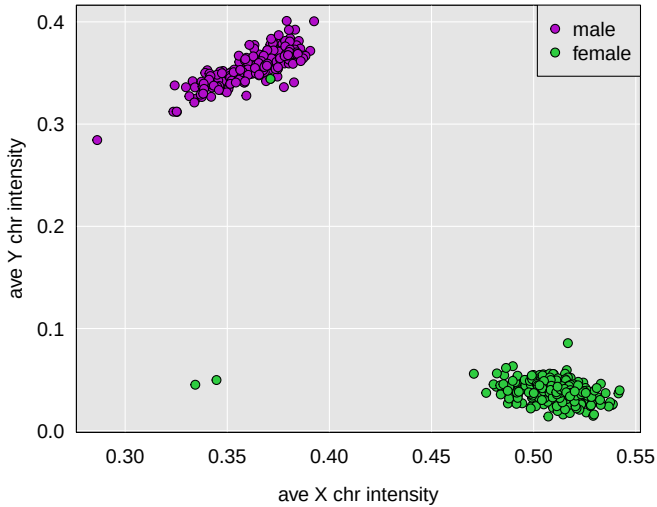
Correlation between protein samples



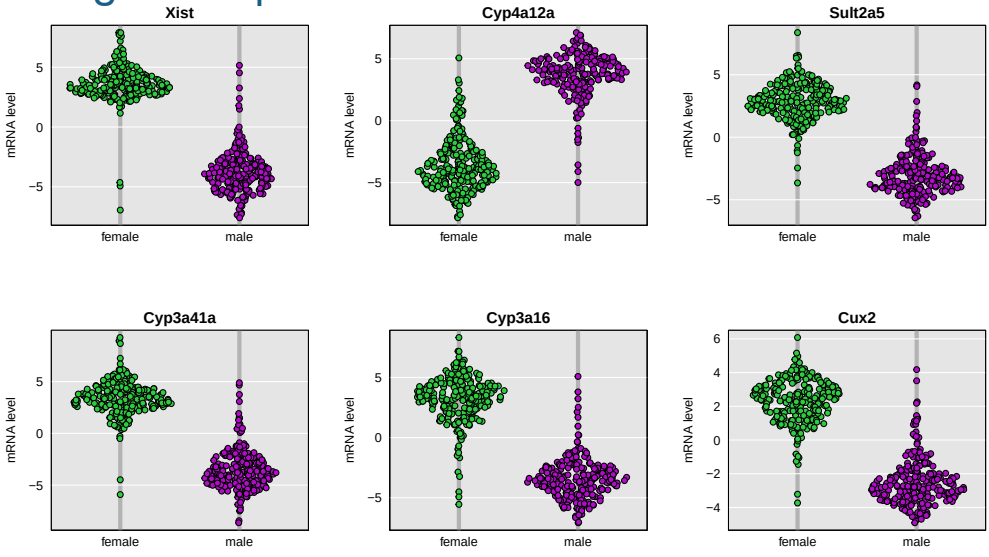


Sex verification

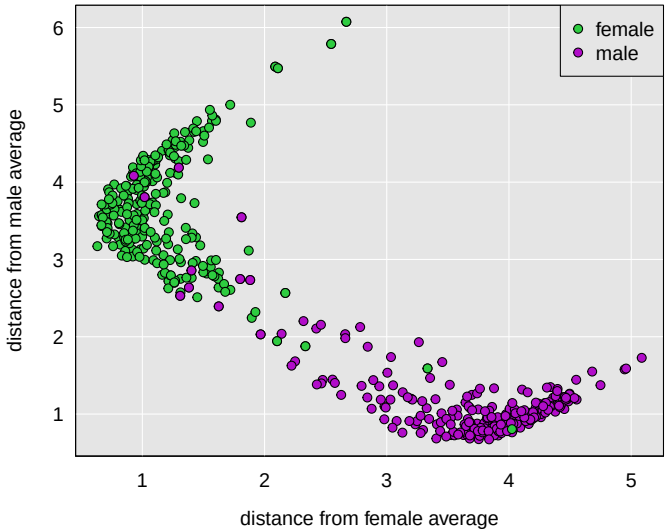
X and Y genotype dosage



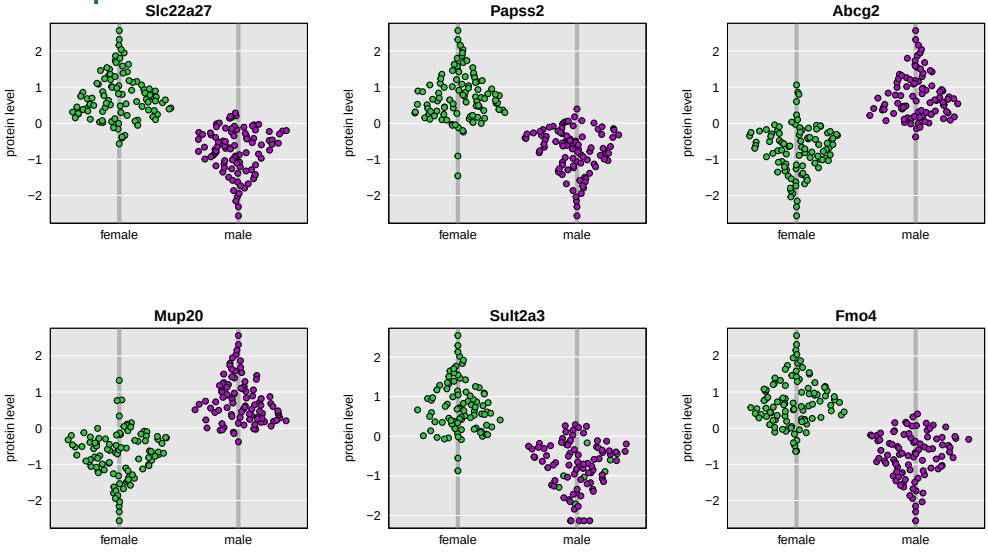
Sex and gene expression



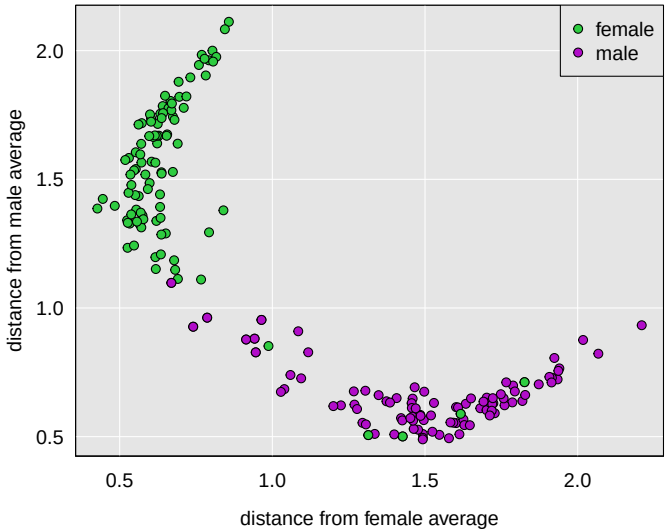
Sex and gene expression



Sex and proteins



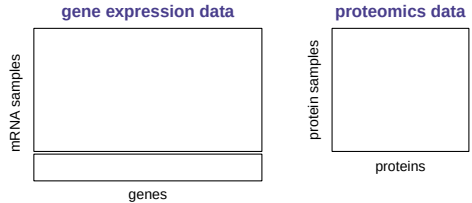
Sex and proteins



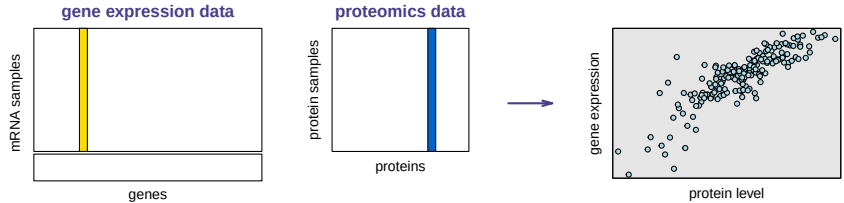
Sample mix-ups

mRNA $\leftrightarrow$ protein

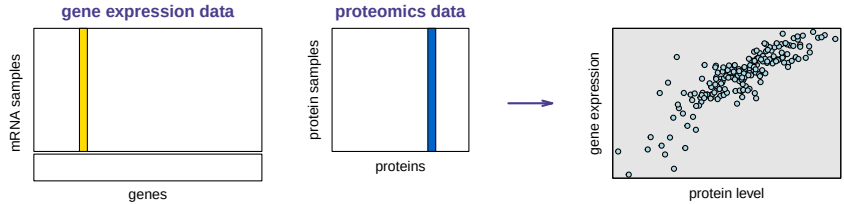
mRNA ↔ protein method



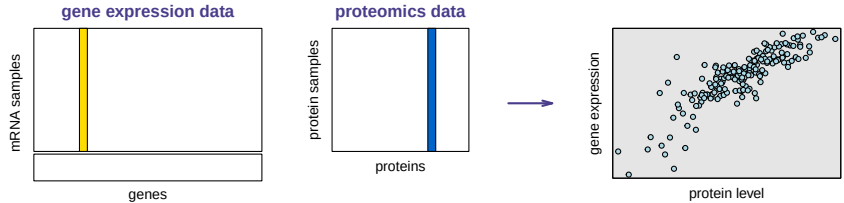
mRNA ↔ protein method



mRNA ↔ protein method

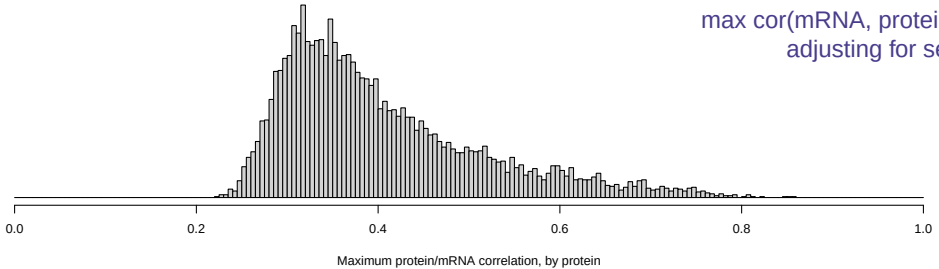


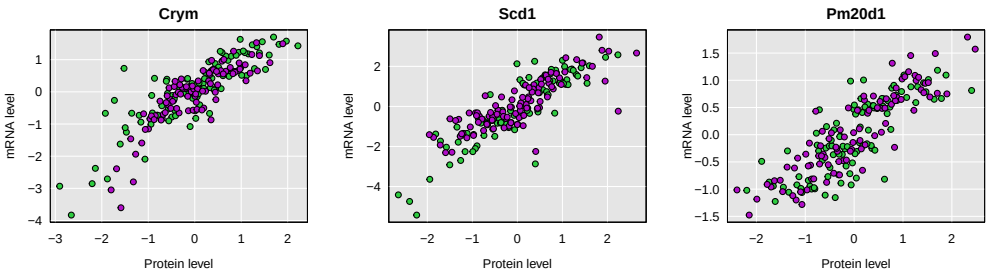
mRNA ↔ protein method



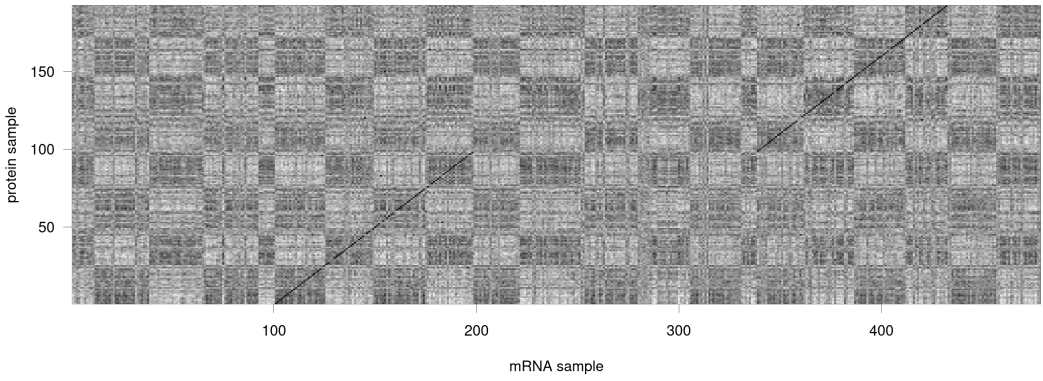
mRNA ↔ protein correlations

max cor(mRNA, protein)
adjusting for sex

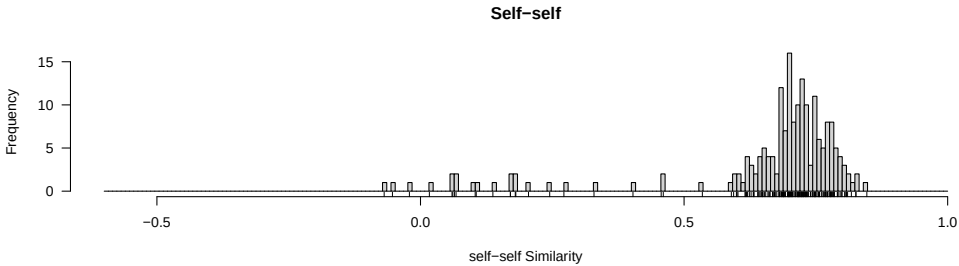




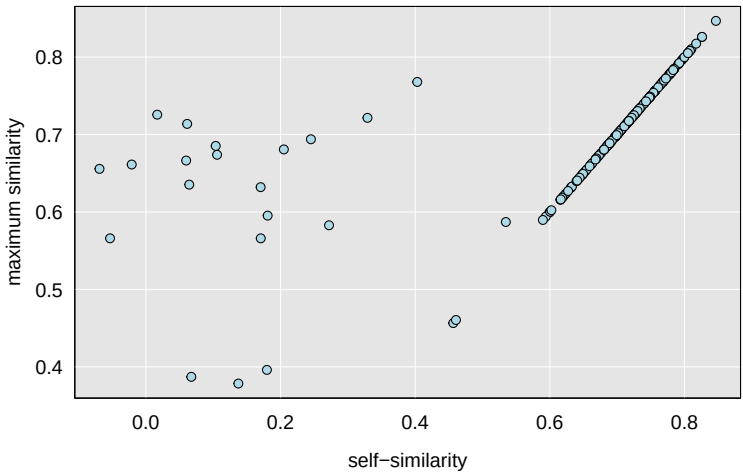
mRNA ↔ protein similarity matrix



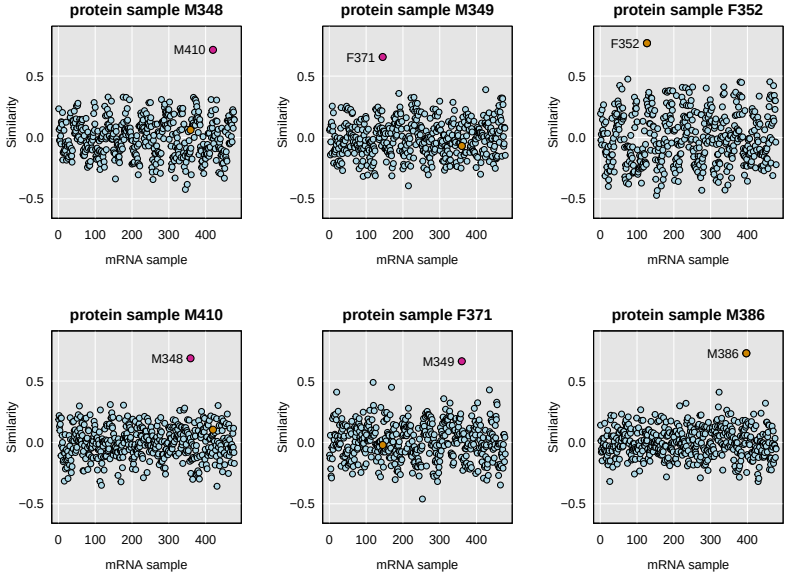
mRNA ↔ protein similarities



mRNA ↔ protein: closest vs self



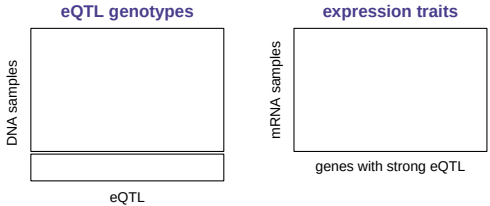
mRNA ↔ protein: selected samples



Sample mix-ups

DNA $\leftrightarrow$ mRNA

DNA ↔ mRNA method



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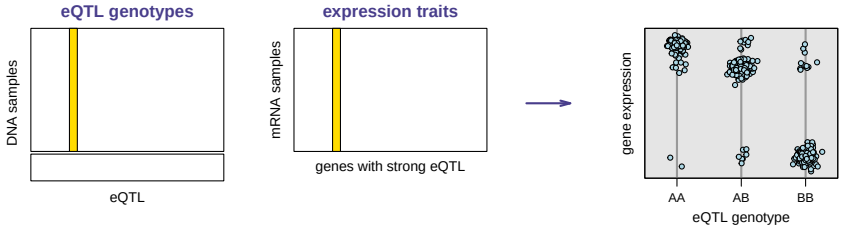

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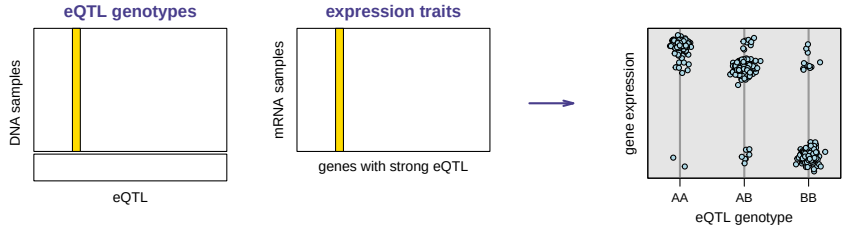

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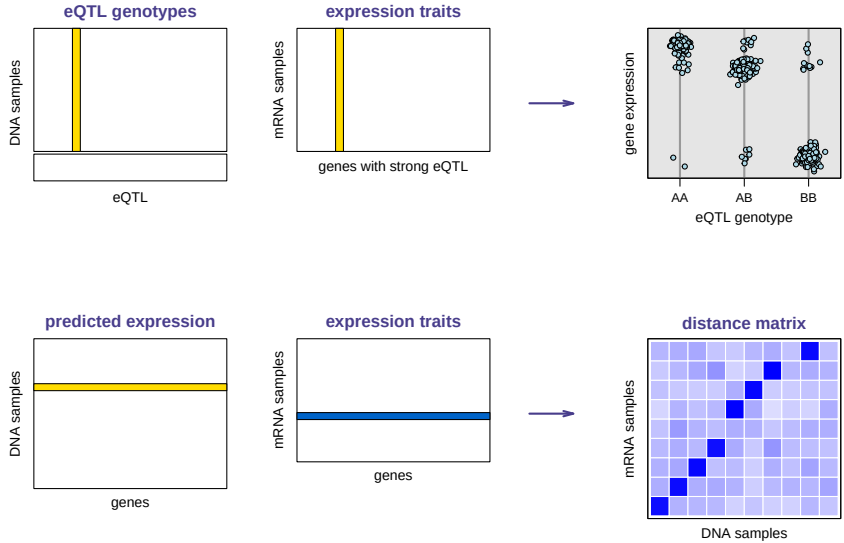
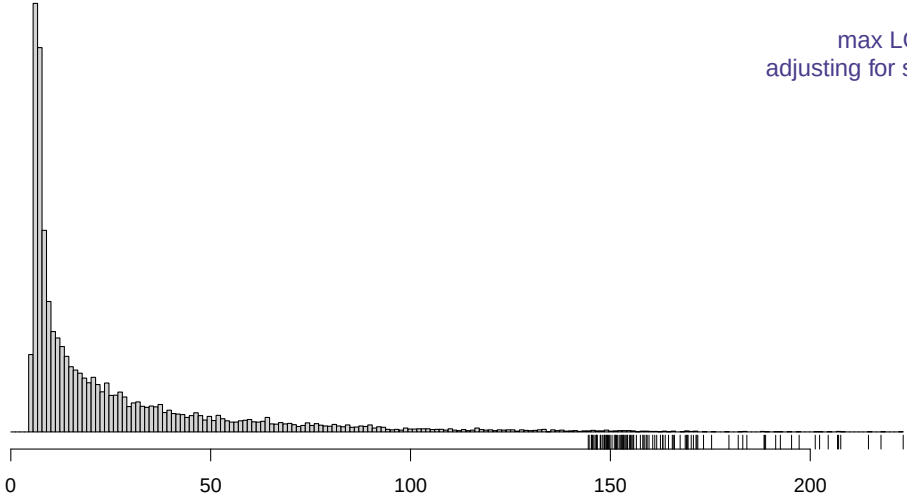
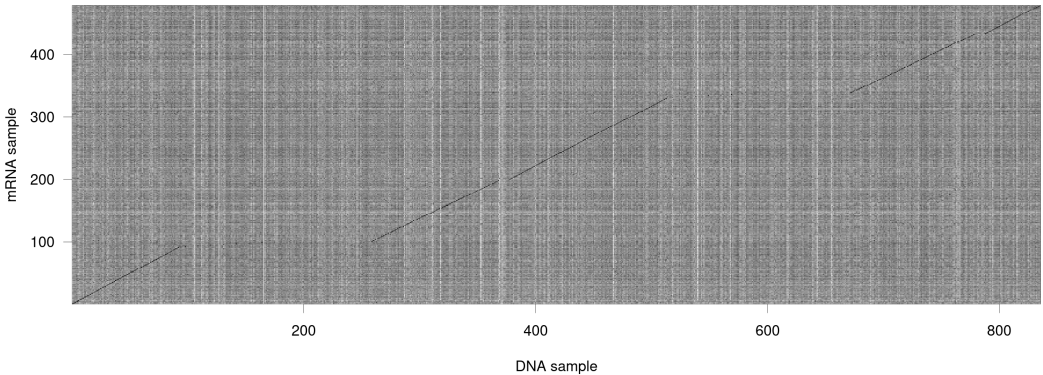


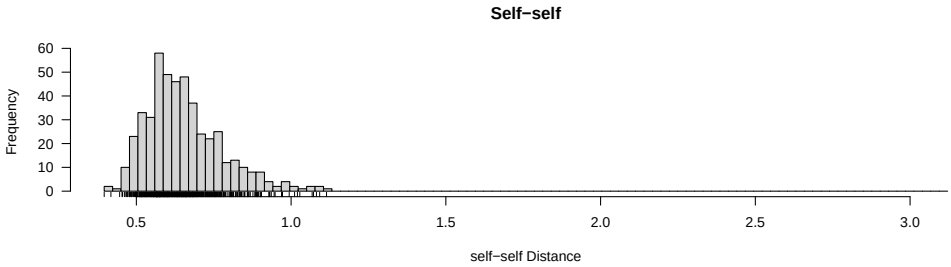
DNA ↔ mRNA LOD scores



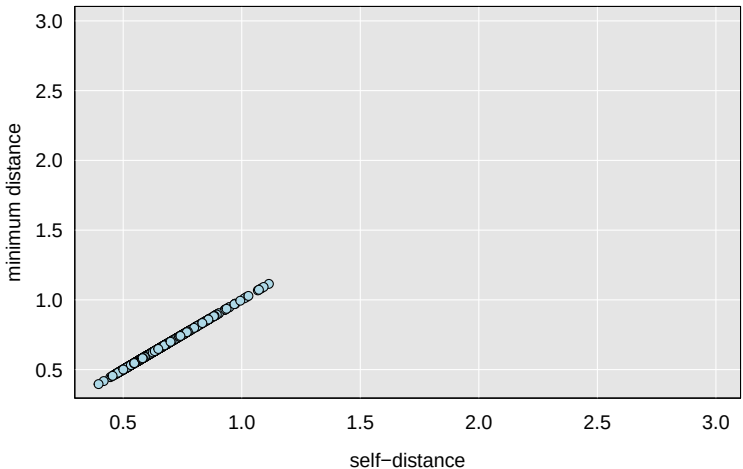
DNA ↔ mRNA distance matrix



DNA ↔ mRNA distances



DNA $\leftrightarrow$ mRNA: closest vs self



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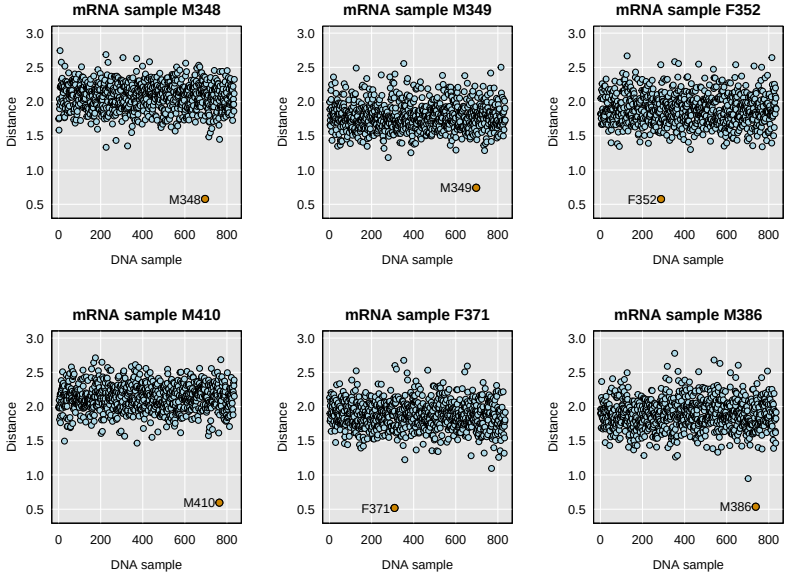

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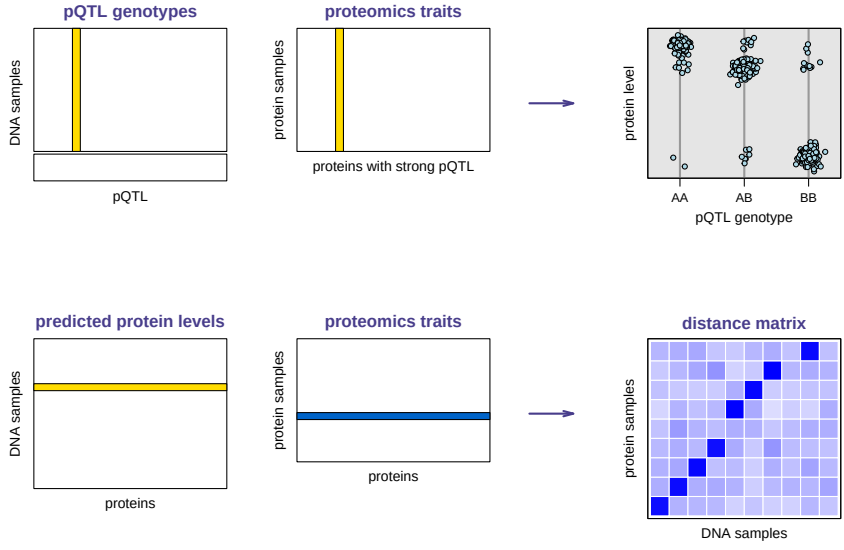
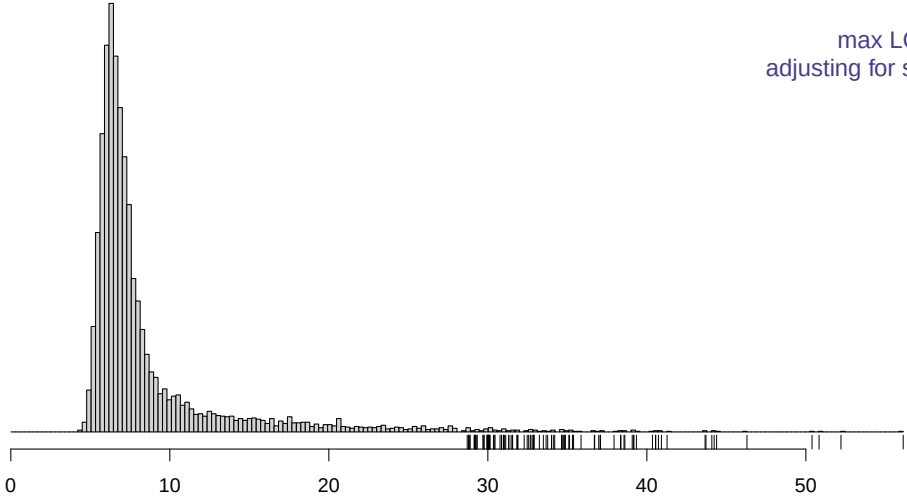
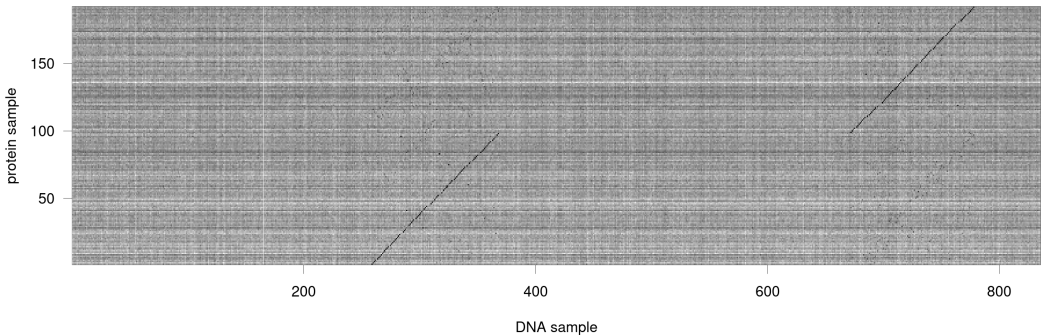


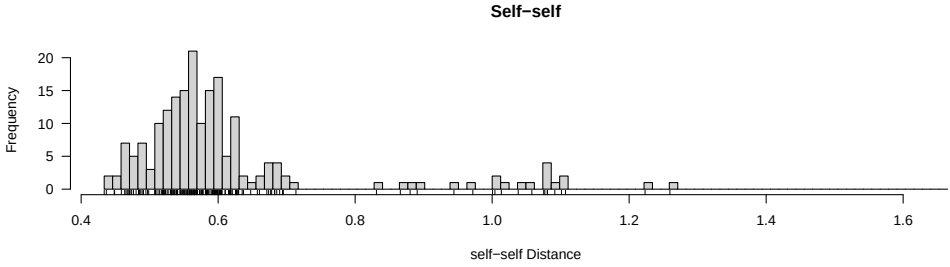
DNA ↔ protein correlations



DNA ↔ protein distance matrix



DNA ↔ protein distances



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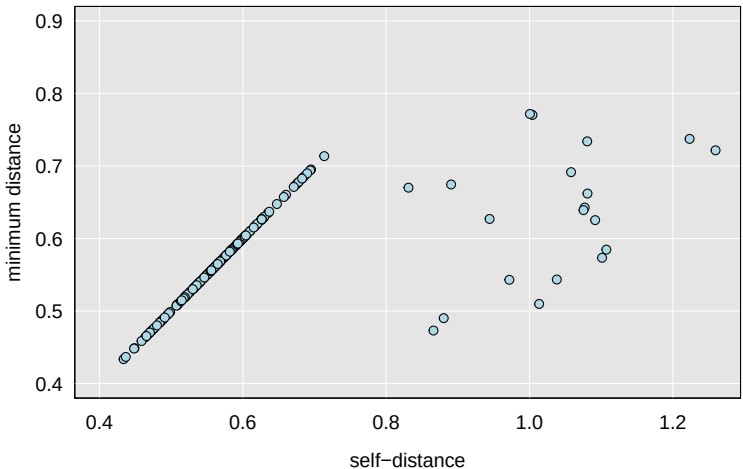
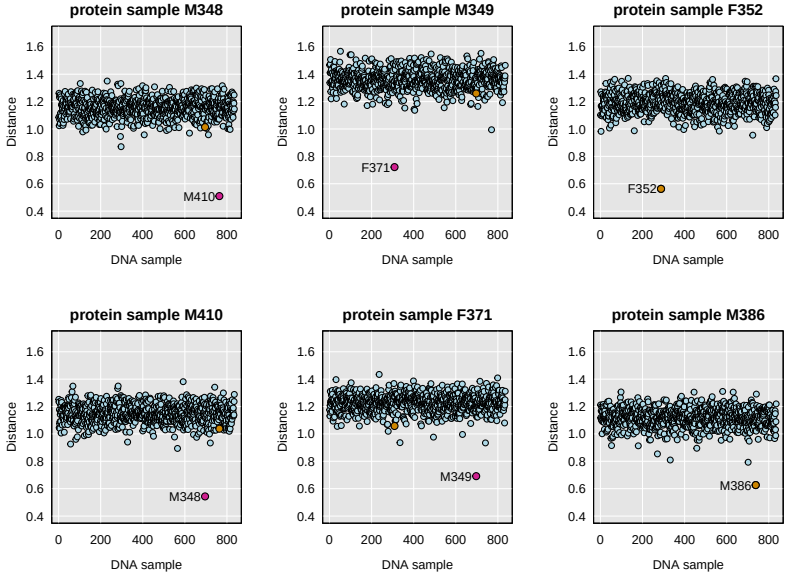
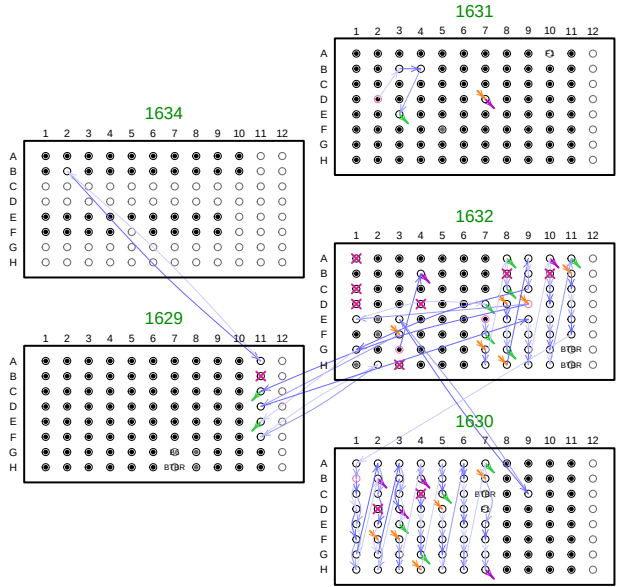


DNA ↔ protein: selected samples



Summary

- This shouldn't happen.
- But if it does, you should find it.
- If two data sets have rows that correspond, you should check that they do correspond.



References

- Westra et al. (2011) MixupMapper: correcting sample mix-ups in genome-wide datasets increases power to detect small genetic effects. Bioinformatics 15:2104–2111 doi:10.1093/bioinformatics/btr323
- Lynch et al (2012) Calling sample mix-ups in cancer population studies. PLOS One 7:e41815 doi:10.1371/journal.pone.0041815
- Broman et al. (2015) Identification and correction of sample mix-ups in expression genetic data: A case study. G3 (Bethesda) 5:2177–2186 doi:10.1534/g3.115.019778
- Broman et al. (2019) Cleaning genotype data from Diversity Outbred mice. G3 (Bethesda) 9:1571–1579 doi:10.1534/g3.119.400165

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github.com/kbroman

@kwbroman