Supervised Learning: Classification, Part II

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Batch Effects

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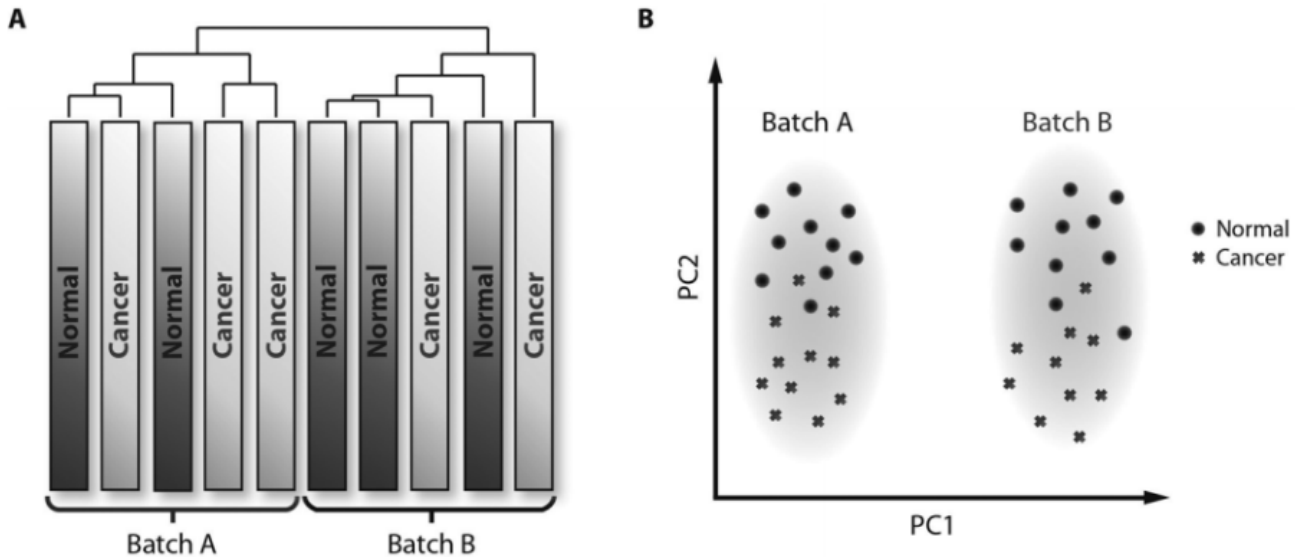
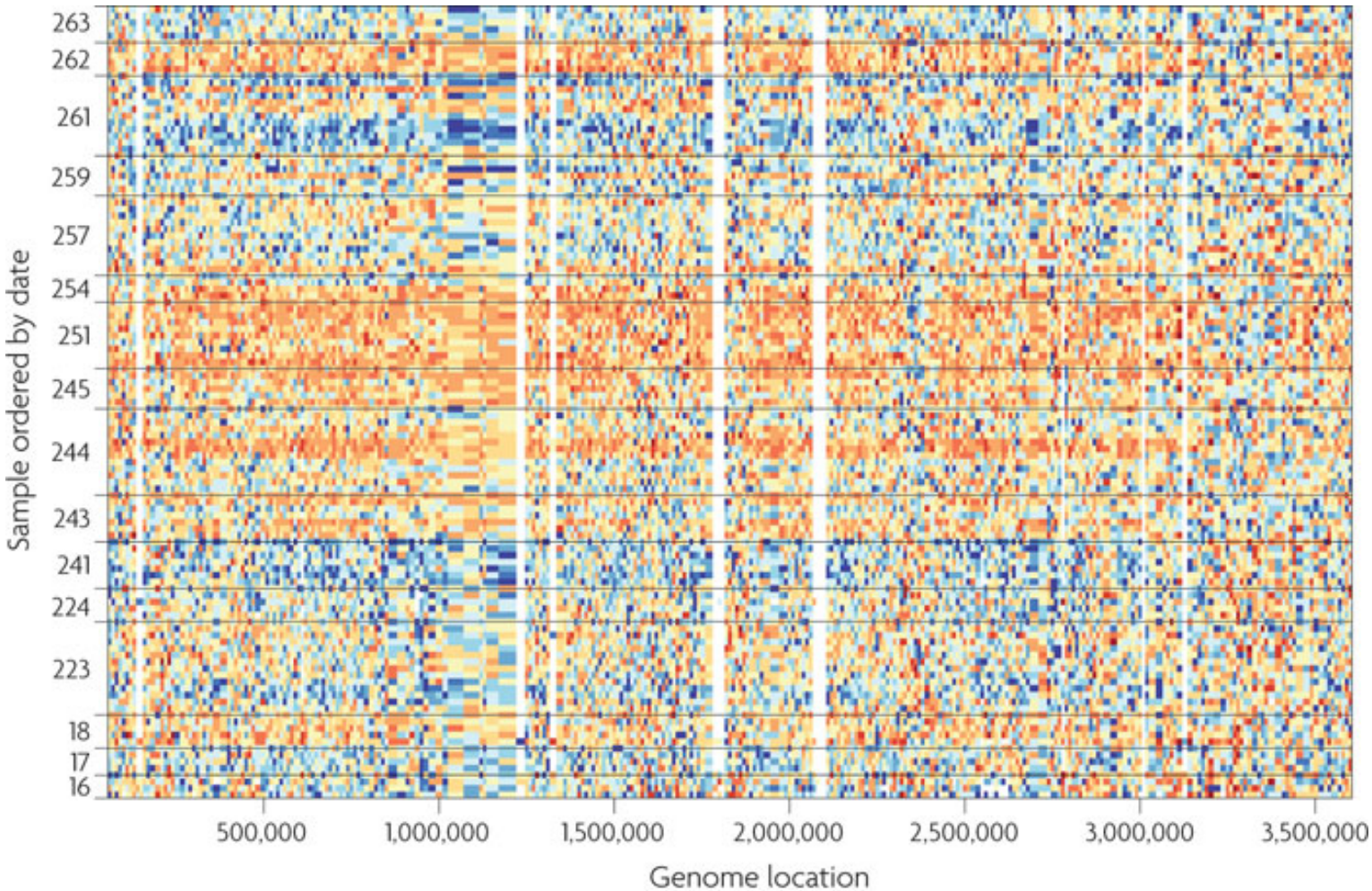
- Batch effects can make your data nonsense...

Batch Effects



Batch Effects in Practice



Nature Reviews | Genetics

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Batch effects are almost inevitable. But you can do your best to design an experiment and analyze the data in such a way that batch effects do not compromise the results obtained.

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- Controversy over the best classifier for this task:
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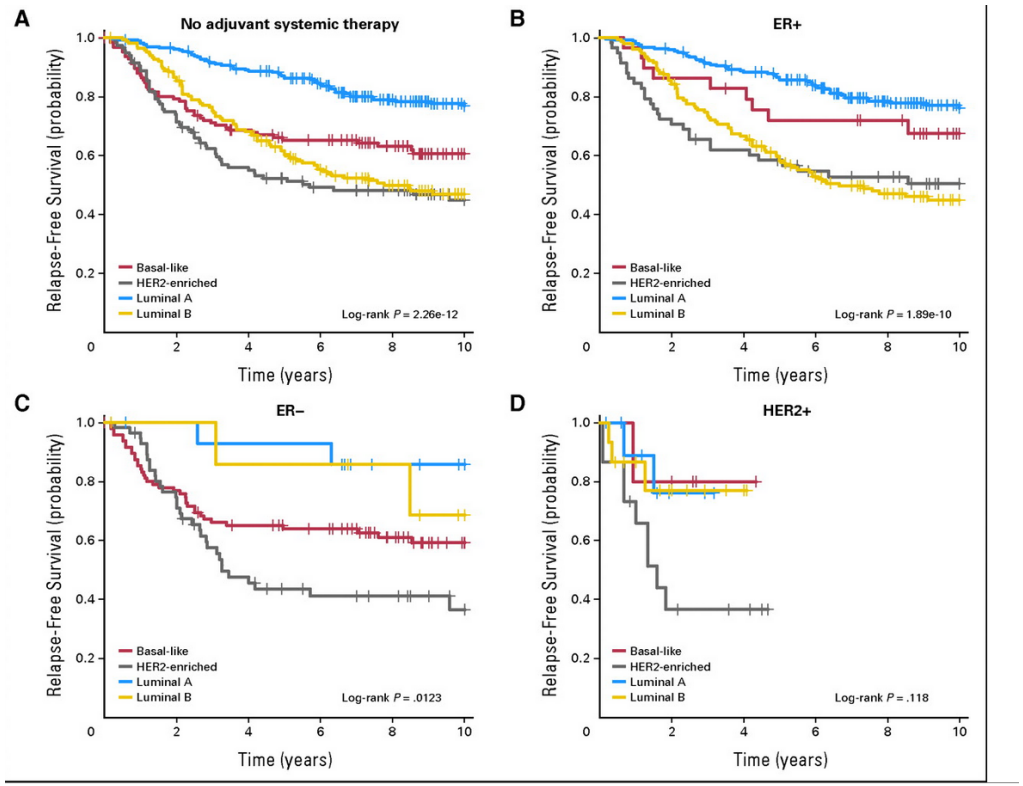
  - More recent proposal involving three genes.
- Moving target: nobody knows the "true" subtype!
- Prat et al., Breast Cancer Res Treat, 2012

Why Do We Care About Subtypes?



Citation: Parker et al, Journal of Clinical Oncology, 2009

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- Great enthusiasm in the popular press and general public.
- Plans were made to begin marketing a test based on the reported diagnostic.

Not So Fast!!

- Independent researchers took a look at the data, which was publicly available, and discovered:
  - inadvertent changes in protocol mid-experiment: i.e. major batch effects.
  - problems with instrument calibration.
  - difference in processing between tumor and normal samples.

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  - problems with instrument calibration.
  - difference in processing between tumor and normal samples.
- In summary: the observed differences between cancer and normal proteomic patterns were attributable to "artifacts of sample processing, not the underlying biology of cancer."

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- This research was hailed as a major breakthrough in cancer treatment, and researchers from all over the world tried to use these sorts of techniques in their own labs.

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- A shocking paper published by Baggerly and Coombes in Annals of Applied Statistics, detailing all of the errors made: "One theme that emerges is that the most common errors are simple (e.g., row or column offsets); conversely, it is our experience that the most simple errors are common."

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- Need to have clearly documented code that contains all steps of the analysis, from start to finish. You must be able to share this code with independent researchers, and you must be confident that your code is correct. If not, then your work isn't ready for prime time.

The Stakes are High!

At Duke:

- Dozens of papers retracted;
- Careers and reputations ruined;
- Patients endangered through unethical clinical trials.

Plus, a 60 Minutes special feature and an Institute of Medicine Committee!!!