A brief guide to multiple testing and FDR

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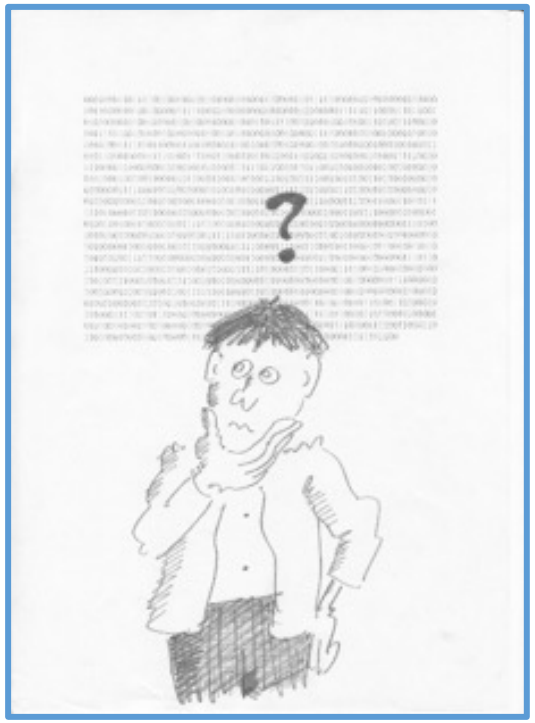
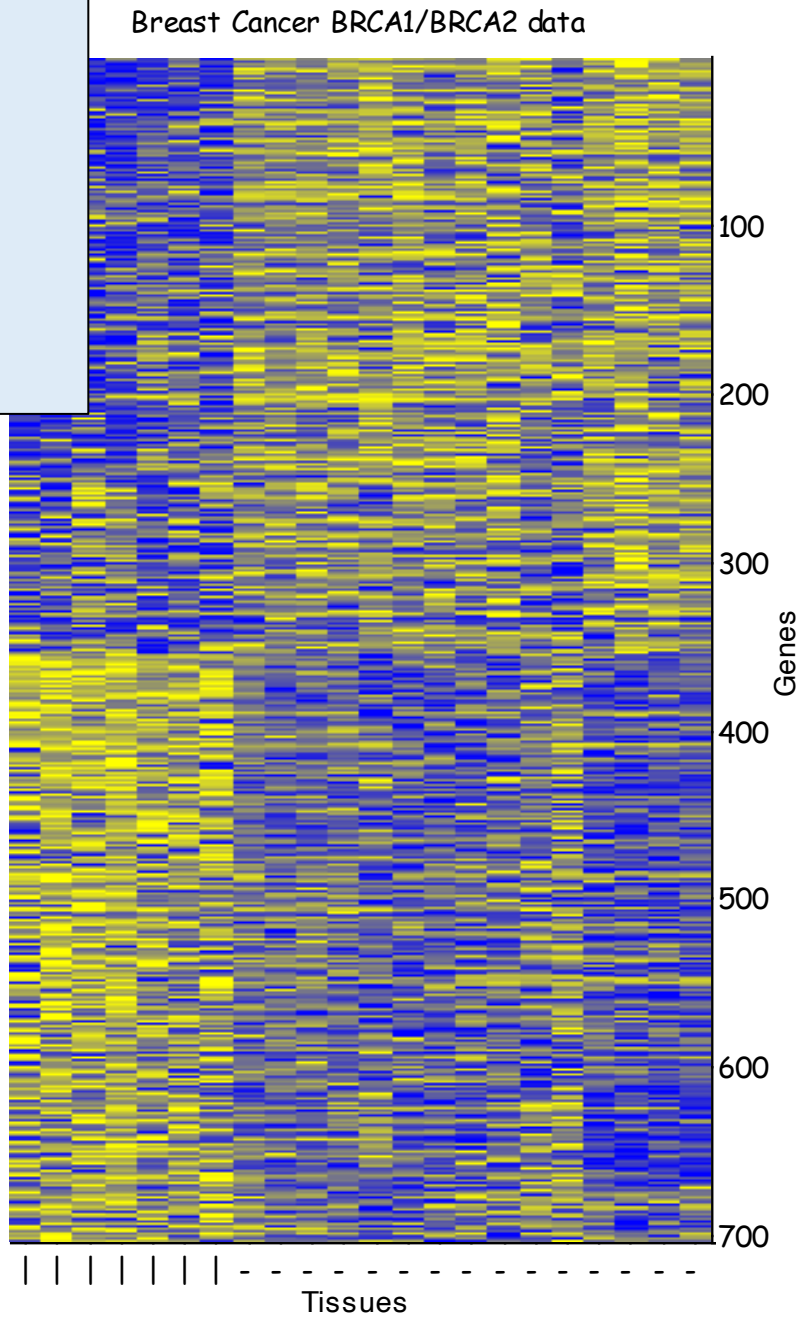
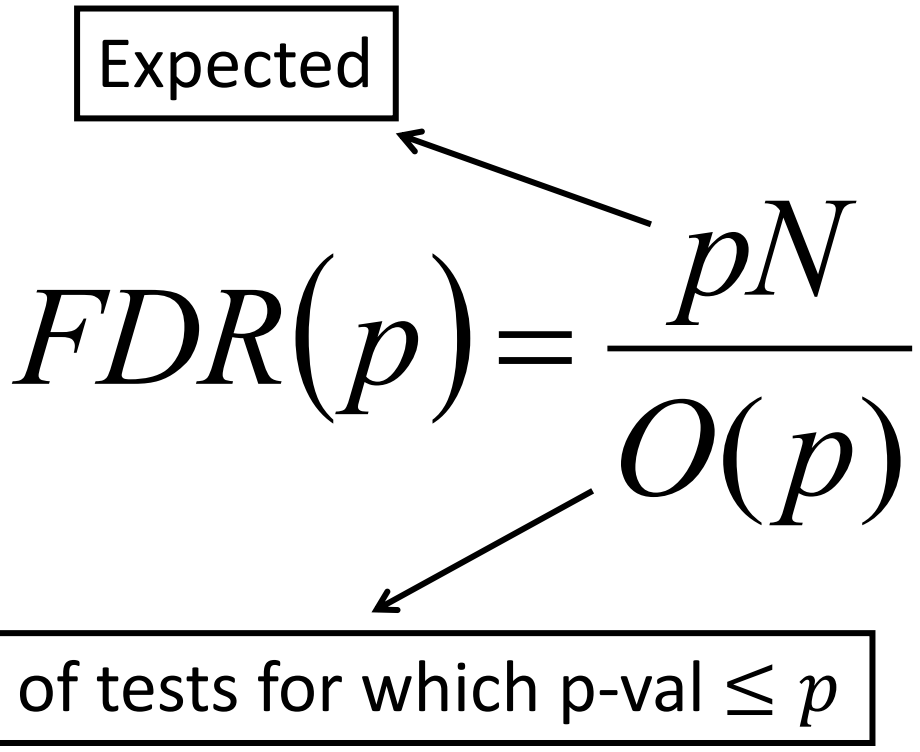




False Discovery Rate (FDR)

What fraction of the observed discoveries (e.g DE) is explained by what is expected at random (under a null-model)?



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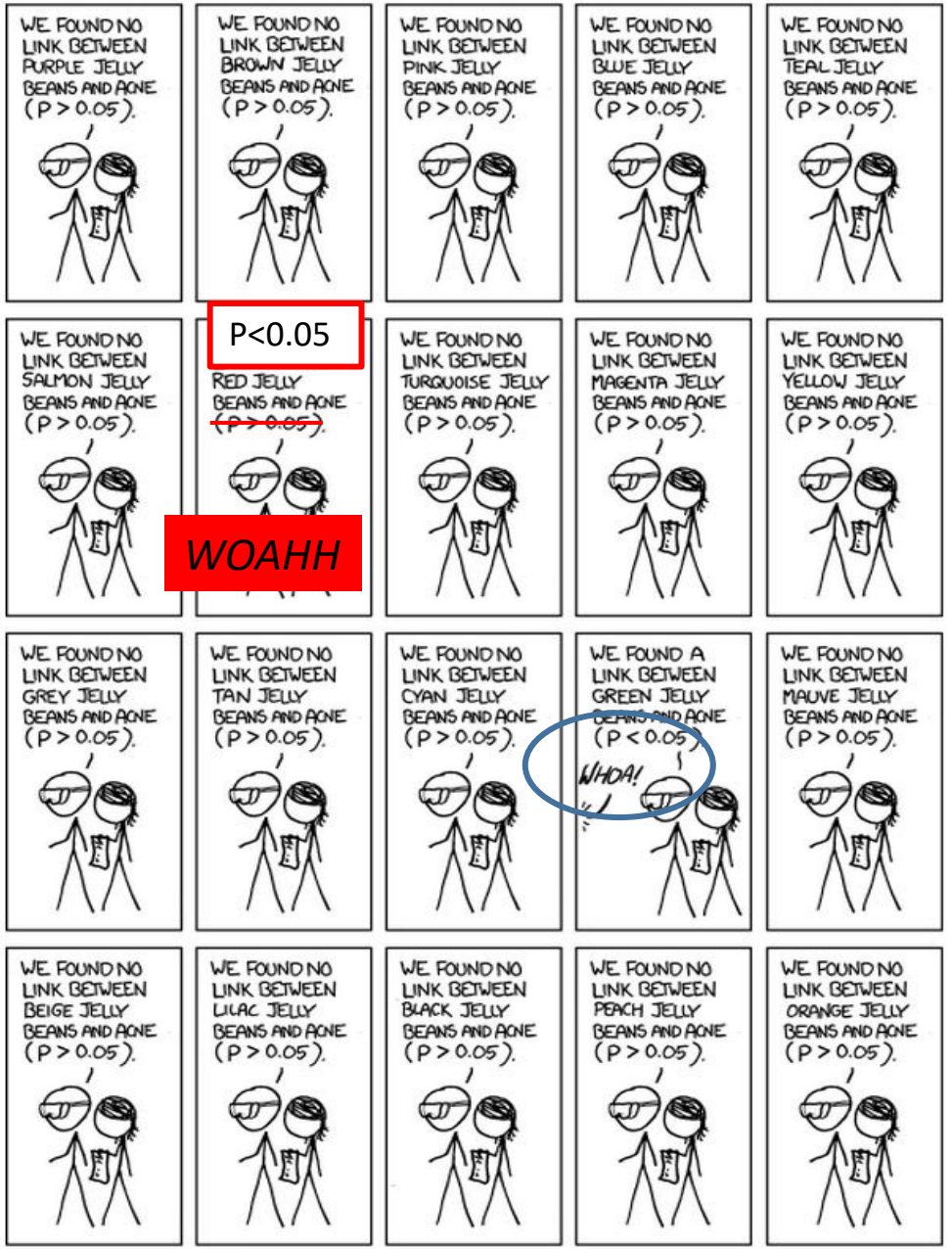
More events

What if two colors were linked at 0.05? Three?



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FDR at any i

$$FDR(p) = \frac{pN}{O(p)}$$

$$FDR(i) = \frac{p(i)N}{i}$$

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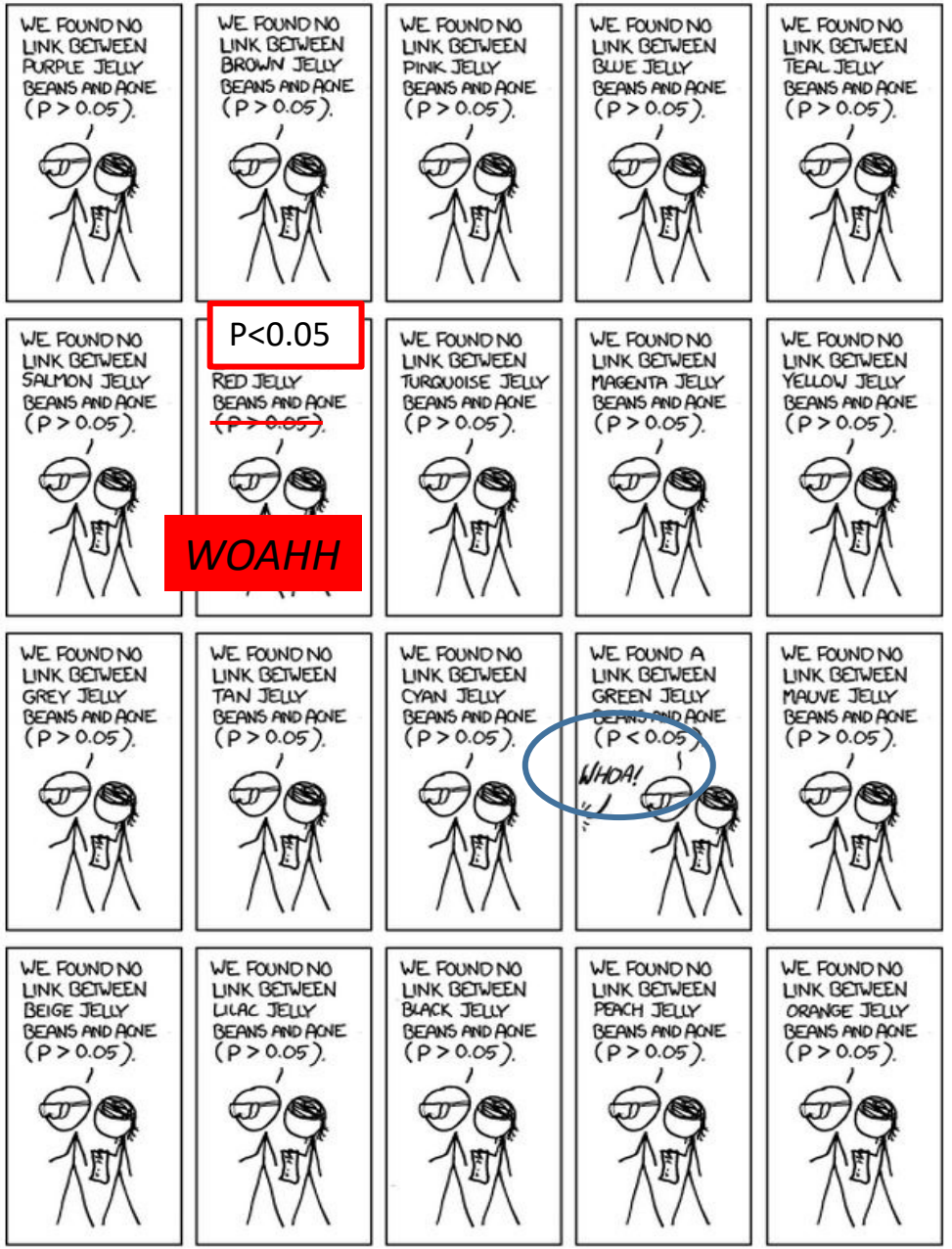
More events

$$FDR(2) = ?$$



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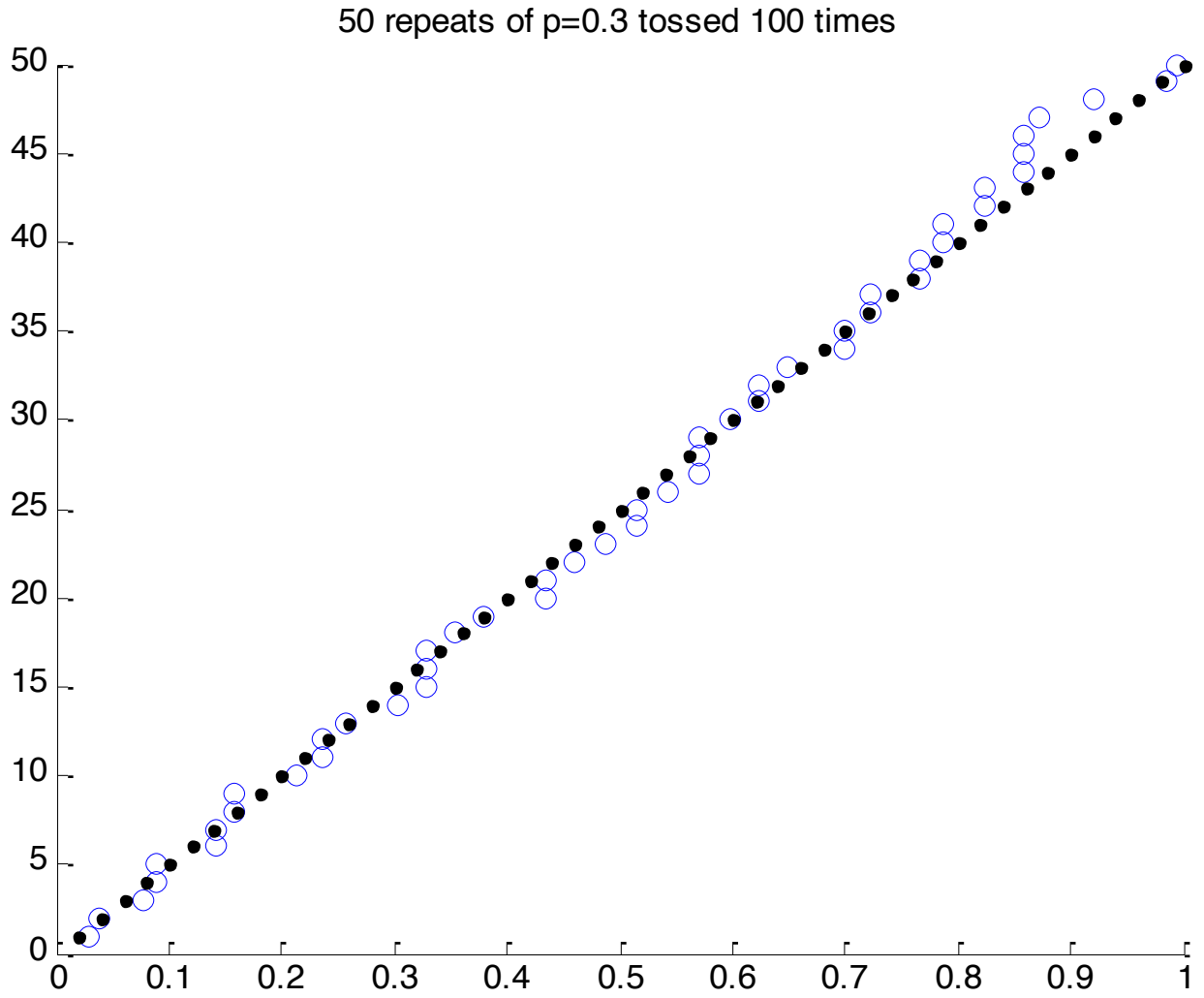
Distribution of p-values under the null model

- Generating data using a coin with $\boldsymbol{p = 0.3}$
- under a null model of $\boldsymbol{p = 0.3}$



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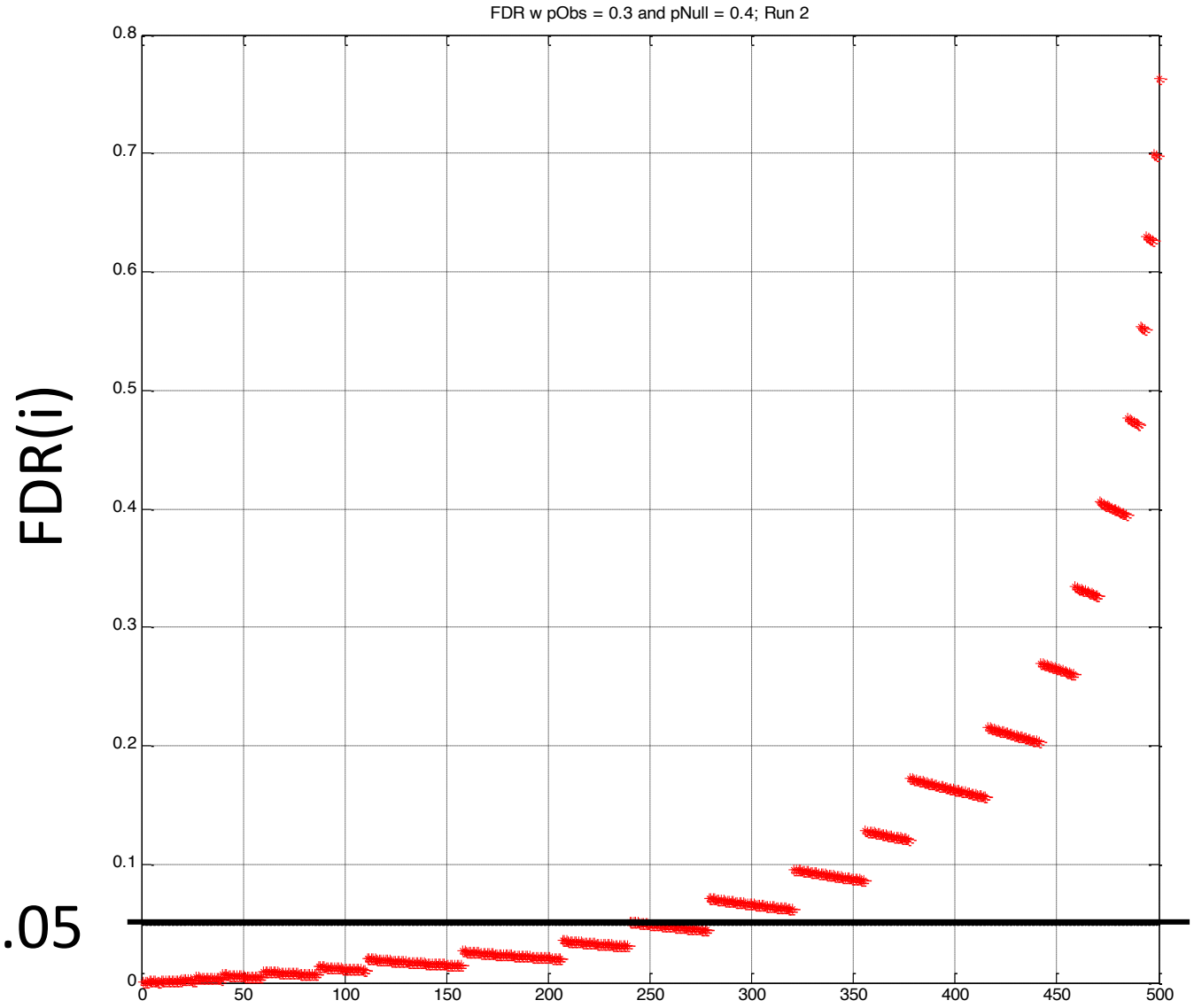
FDR

- Generating data using a coin with $\boldsymbol{p = 0.3}$
- under a null model of $\boldsymbol{p = 0.4}$



$$FDR(i) = p(i) \cdot N / i$$

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A more adequate correction

$$\mathrm{RobFDR}(i) = \min_{j \geq i} \left(\frac{p(j) \cdot N}{j} \right)$$

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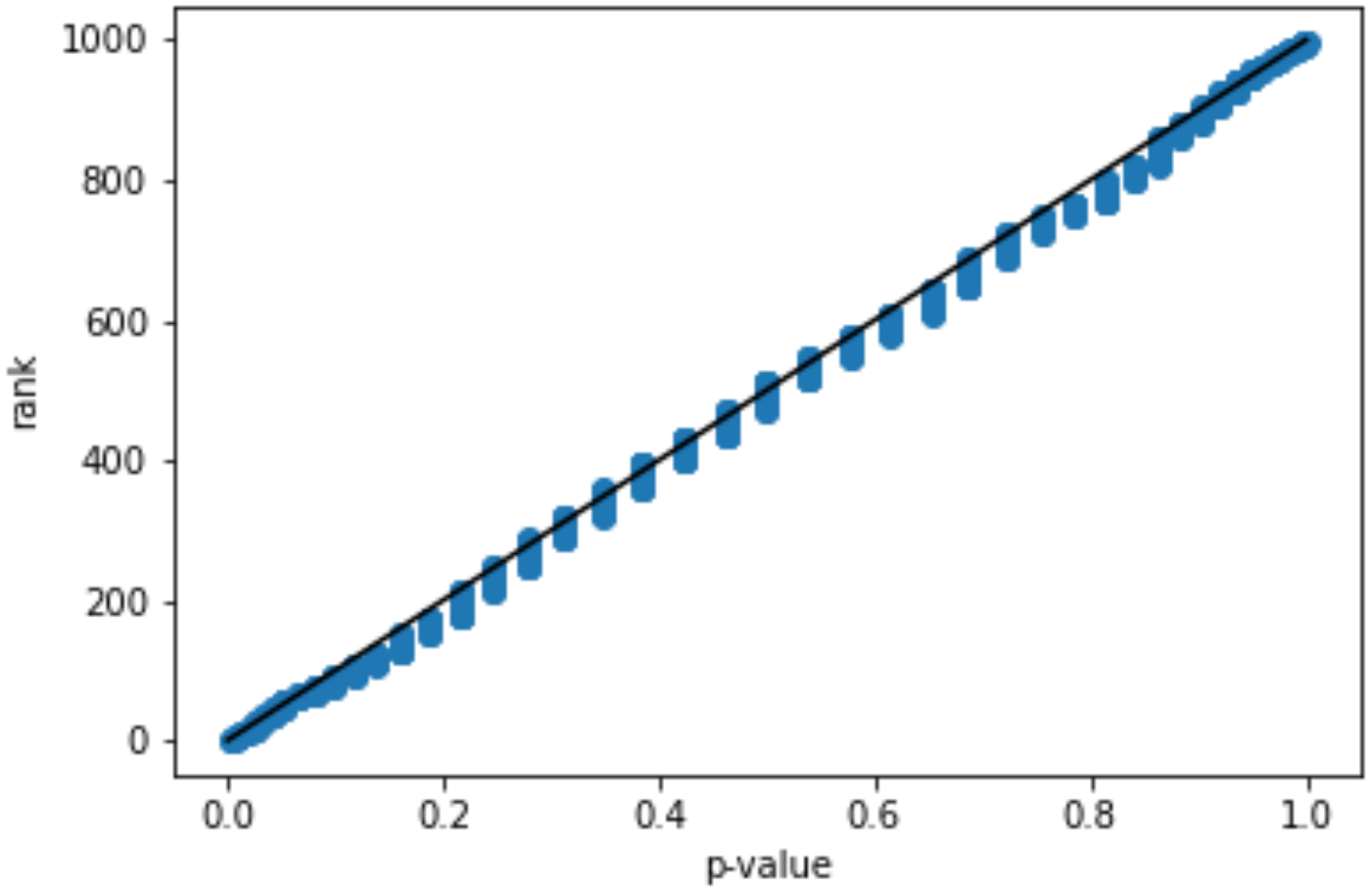
WRS FDR: A ~N(0,1) and B ~ N(0,1), n= 20,20



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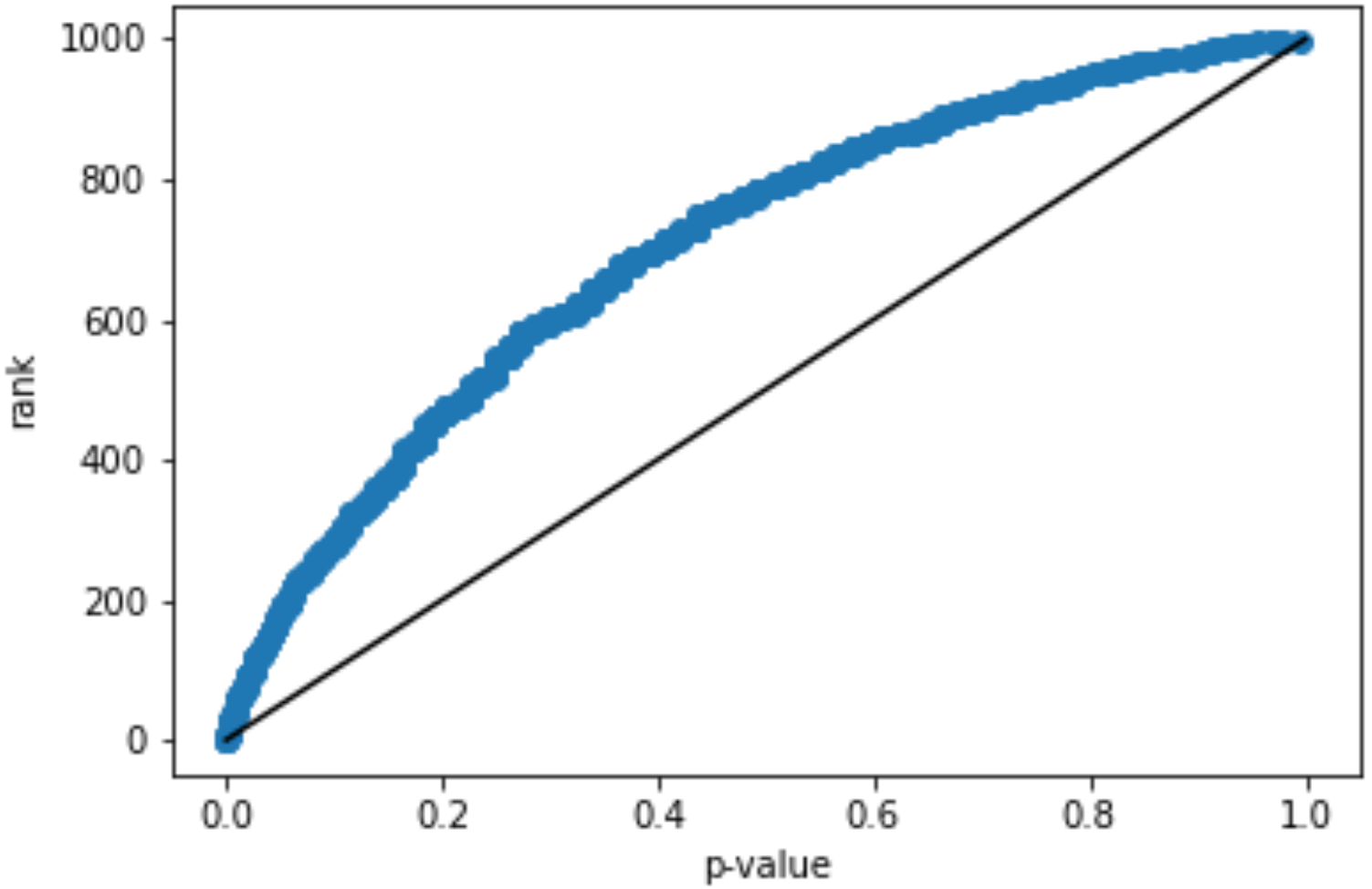
WRS FDR: A ~N(0,1) and B ~ N(0.25,1), n= 20,20



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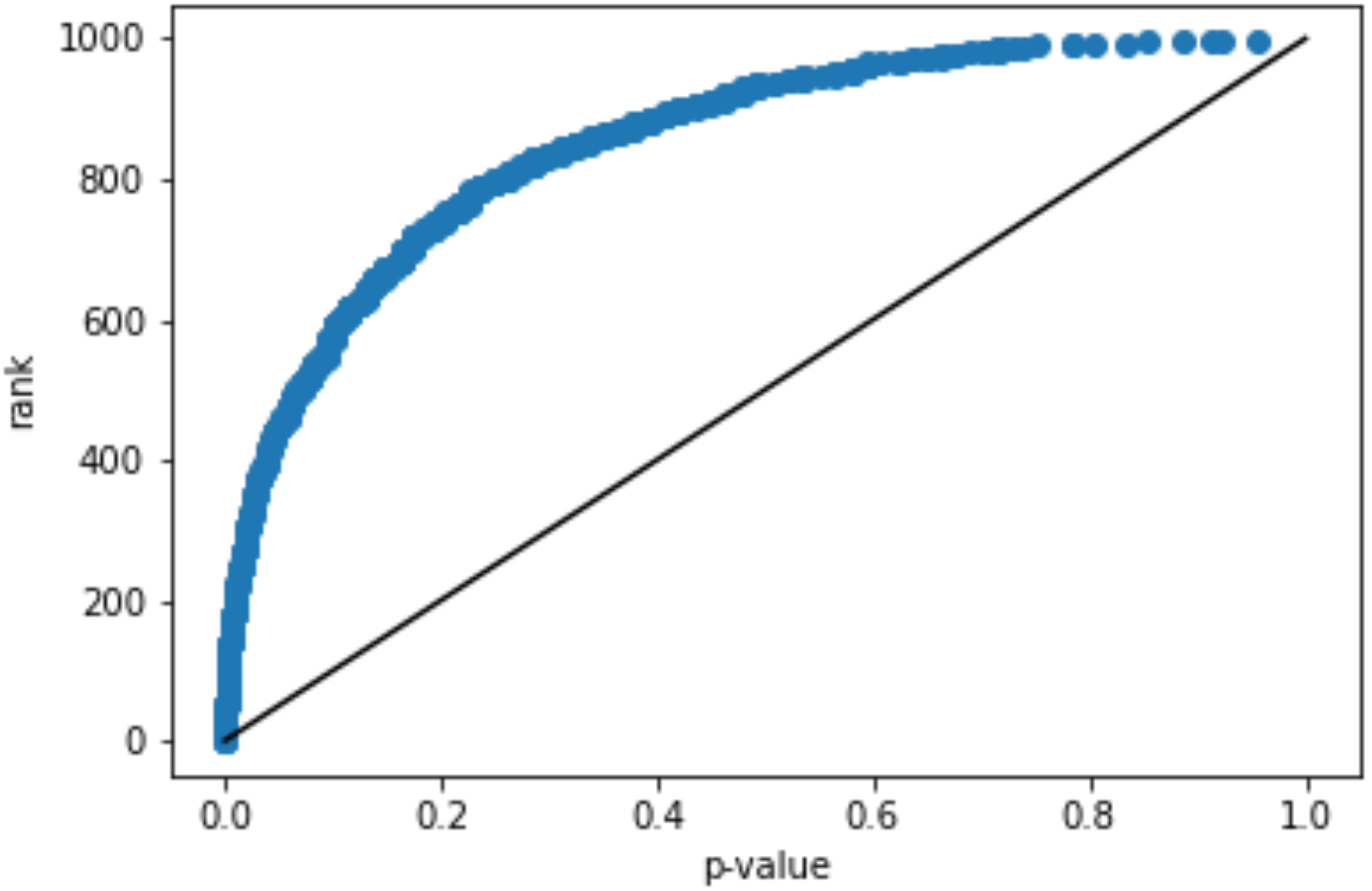
WRS FDR: A ~N(0,1) and B ~ N(?,1), n= 20,20



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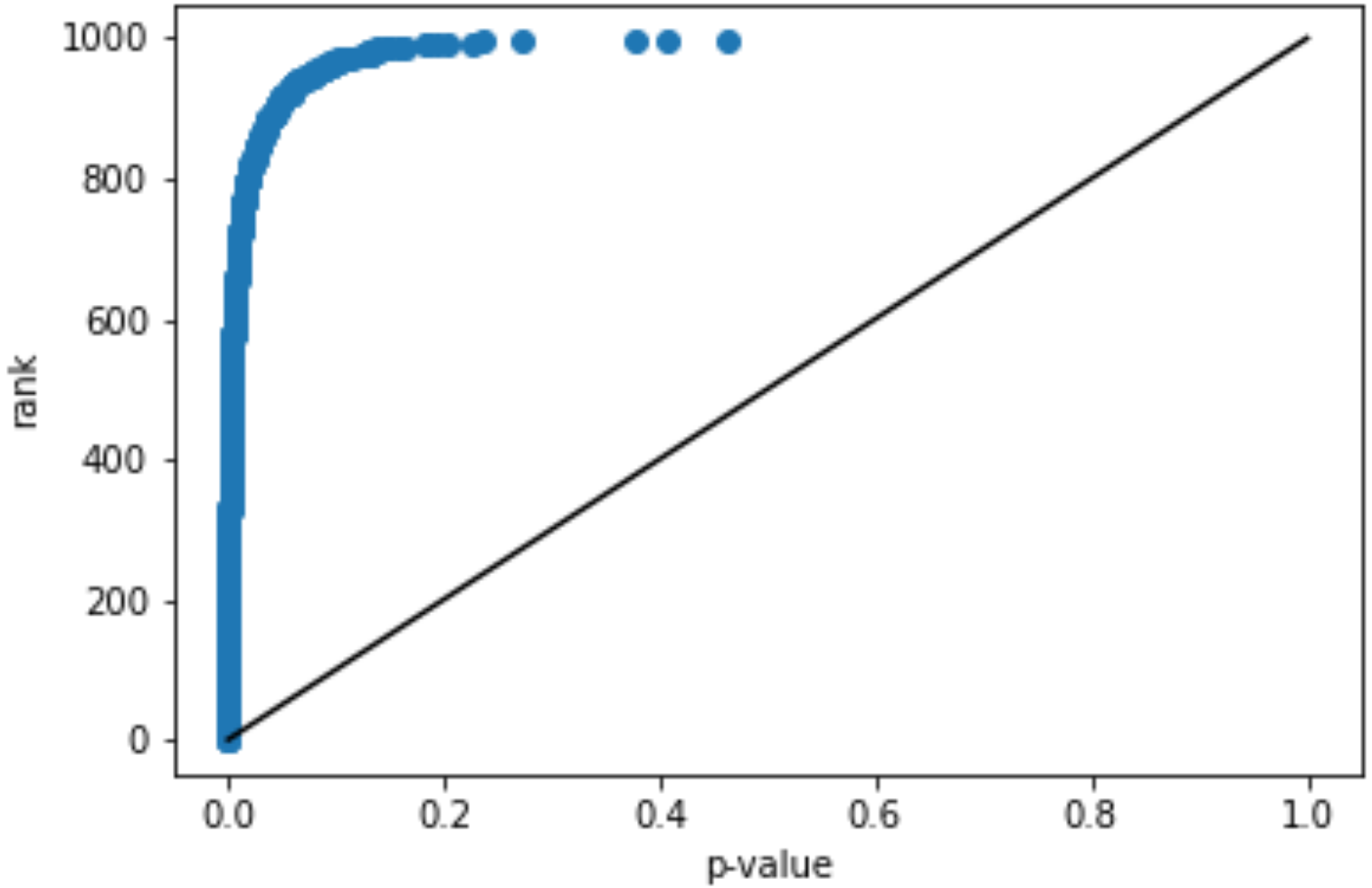
WRS FDR: A ~N(0,1) and B ~ N(1,1), n= 20,20



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FDR – the procedure

Yoav Benjamini and Yosef Hochberg 1995

- Assume that we performed N measurements (comparisons, observations etc)
- Rank the computed significance of the findings: $p(1) \leq p(2) \leq p(3) \leq p(4) \leq \ldots. \leq p(N\text{-}1) \leq p(N)$
- Under the null model, the expected number of observations with p-value better than p(i) is $p(i) \cdot N$
- The false discovery rate at i is therefore:

$$\mathrm{RobFDR}(i) = \min_{j \geq i} \left(\frac{p(j) \cdot N}{j} \right)$$

- A corrected hypothesis testing in this case would be to find the max i that satisfies $\mathrm{FDR}(i) \leq \tau$, where τ (e.g 0.05) is the required false discovery rate.

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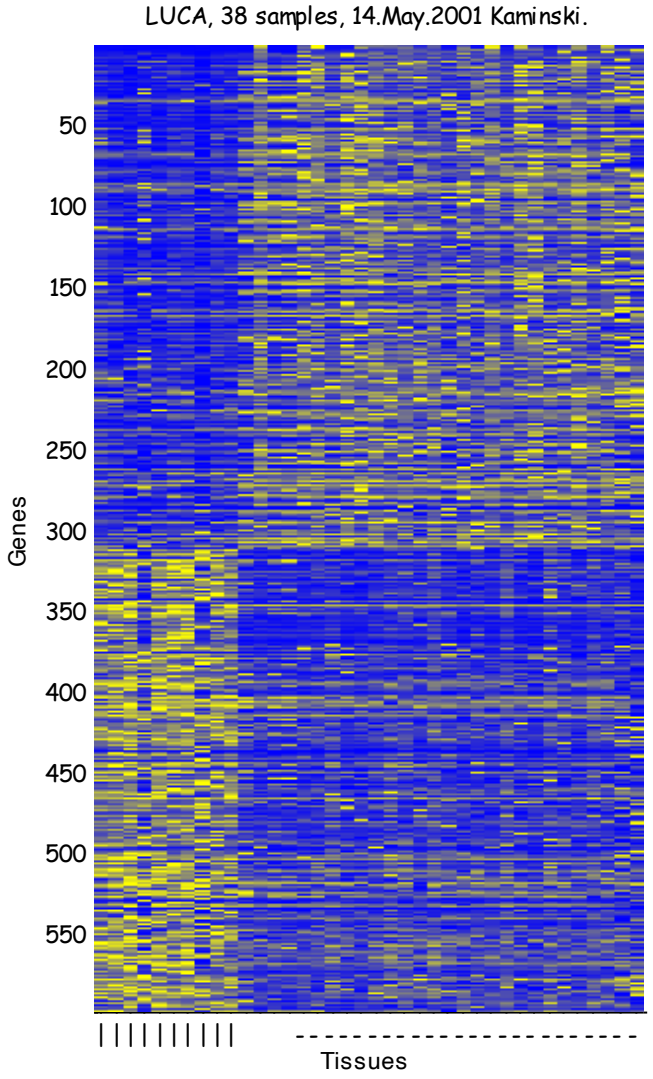
In the context of DGE …



We observed (say) 200 genes at FDR=0.05, using a WRS test

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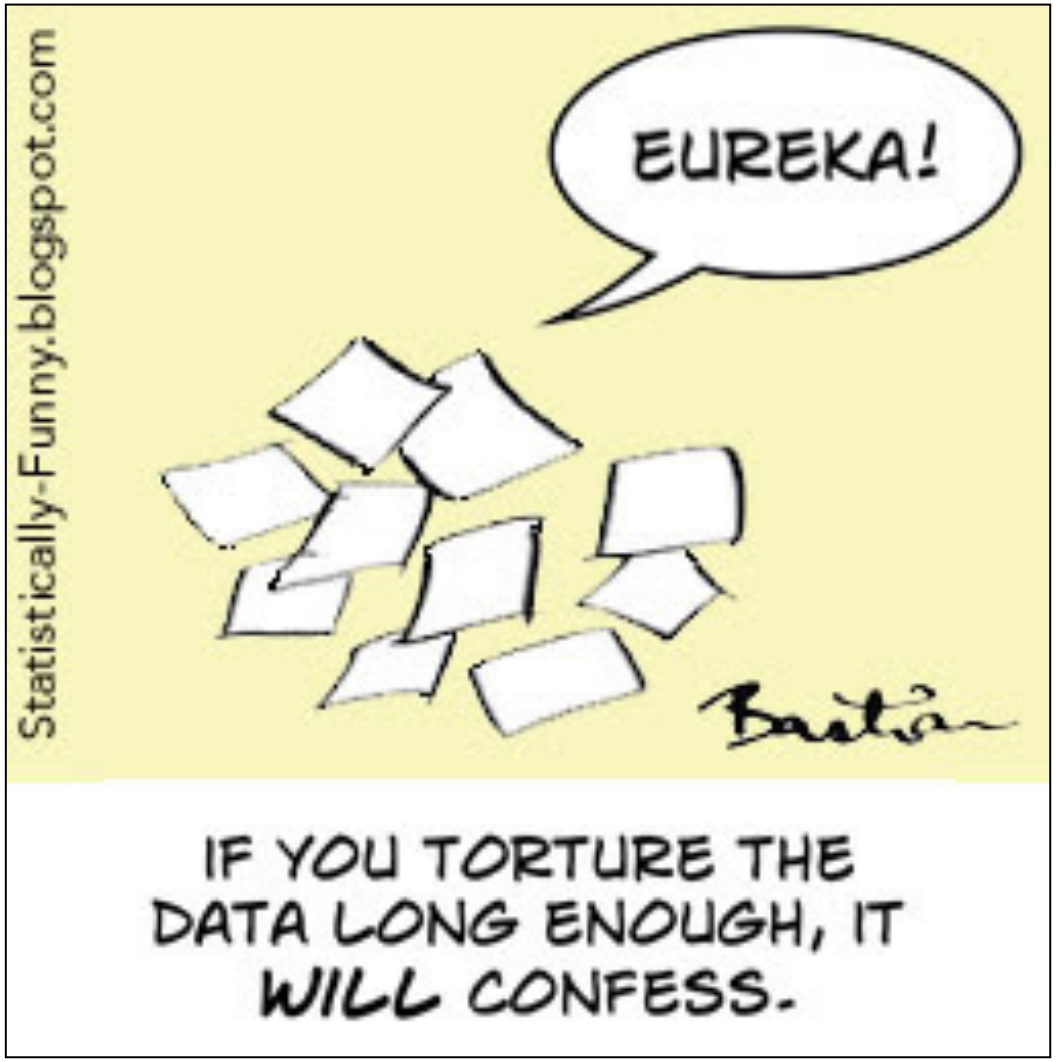
Multiple testing and FDR

- Greater data volumes require more careful inferential statistics approaches.
- Approaches to addressing multiple testing:
  - Bonferroni correction
  - Report FDR results
  - Simulations under a null



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