Appyling the Partitioning Principle to Genome Scans

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joint work with

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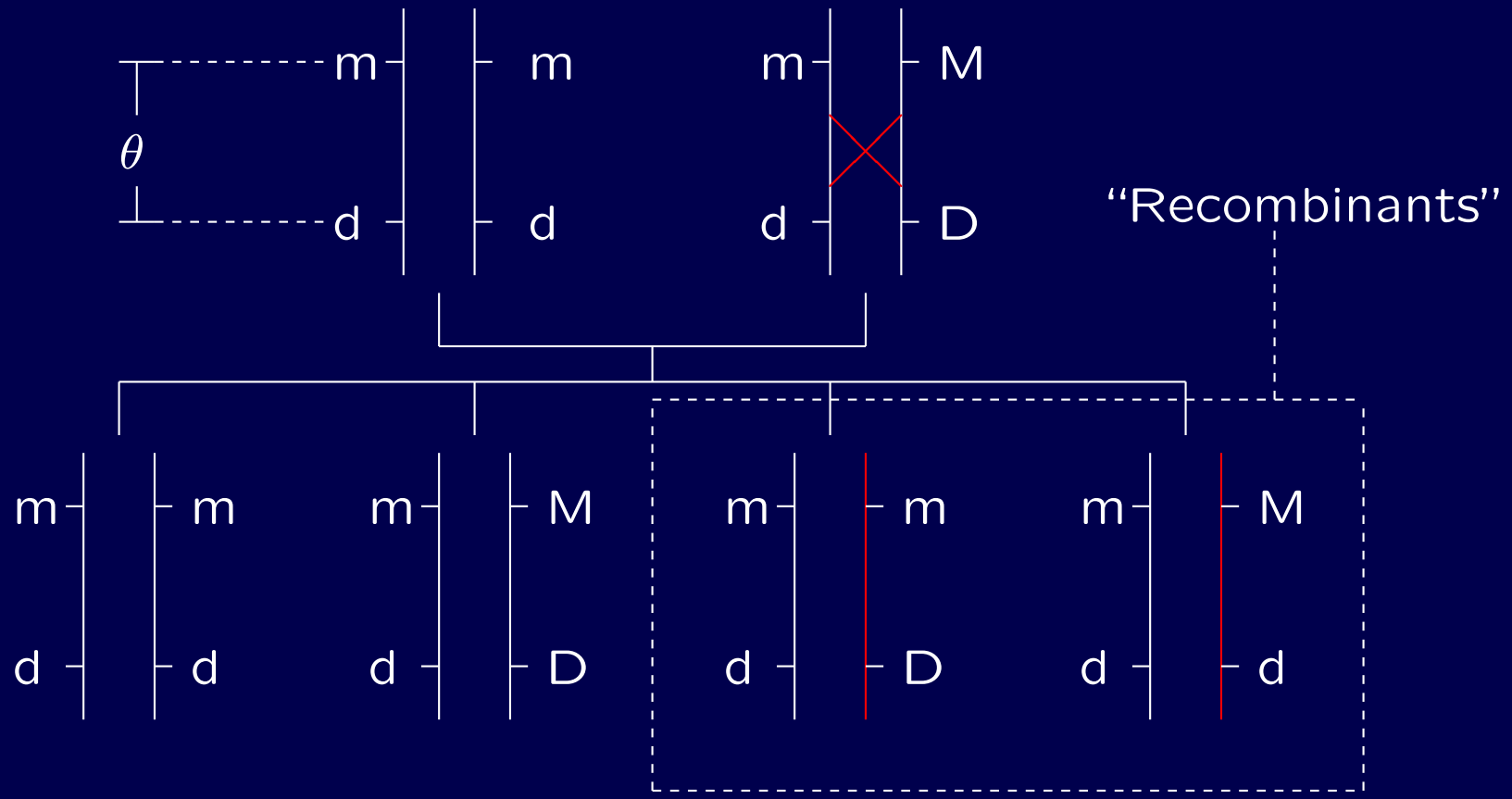
Genetic Recombination



Model for Simple Data Type

- Suppose one large nuclear family with k children.

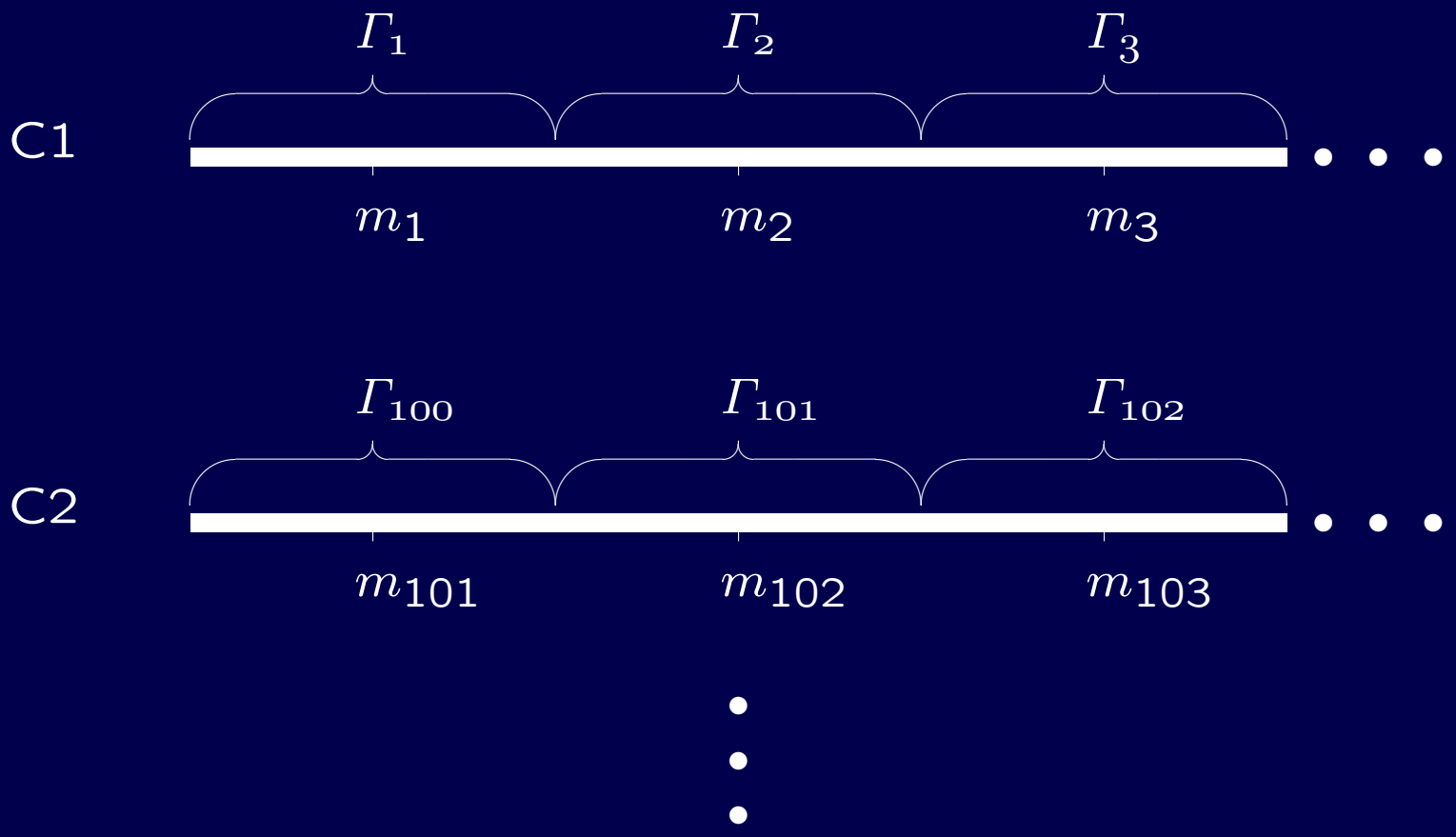
- For each marker m, define

$$R_m = \#\text{ of children in family who are recombinant w.r.t. marker } m.$$

- Then:

$$\begin{aligned} R_1 &\sim \textit{Binomial}(\theta_1, k) \\ &\vdots \quad\quad \vdots \\ R_{1000} &\sim \textit{Binomial}(\theta_{1000}, k) \end{aligned}$$

Partitioning the Parameter Space



Testing Every Possible Disease Locus

- Let γ denote the (unknown) locus of the disease gene.
- For $\gamma' \in \Gamma_i$,
  - $\gamma = \gamma' \iff \theta_i = \theta_i'$ for some θ_i'.
  - we test $H_{0\gamma'} : \gamma = \gamma'$ by testing

$$H_{0\theta_i'} : \theta_i \leq \theta_i' \text{ versus } H_{A\theta_i'} : \theta_i > \theta_i'$$

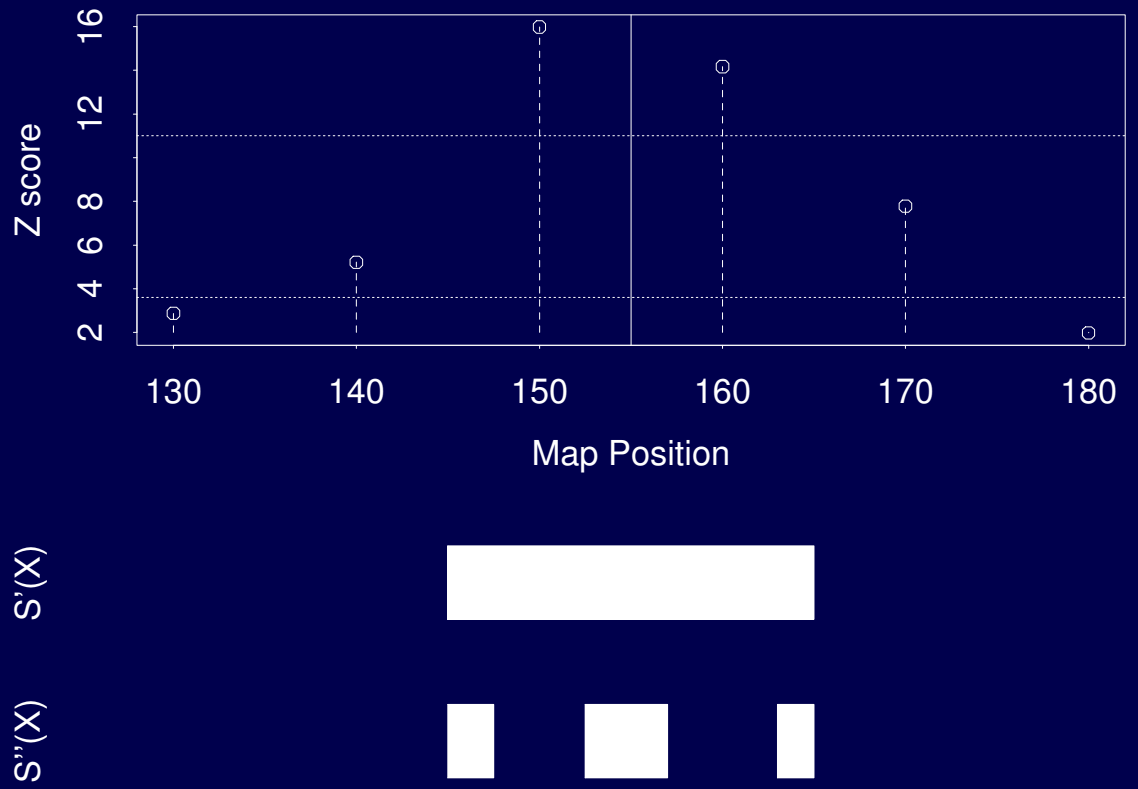
  - use R_i to test $H_{0\gamma'}$ at level α.
- Do this for every γ' on the genome.

Assembling the Confidence Set

- $S(R_1, \ldots, R_{1000}) = \{\gamma' : H_{0\gamma'}$ is accepted$\}$ is a $100(1-\alpha)\%$ confidence set for γ.

- No Multiplicity Adjustment ! (relevant multiplicity is number of disease genes, not number of markers or number of hypotheses).

Application to Simulated Data



To Learn More ...

- Lin, Rogers and Hsu (2001). A Confidence Set Approach for Finding Tightly Linked Genomic Regions. *American Journal of Human Genetics* **68**, 1219–1228.

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