Day 2
Genetic Maps and Recombination

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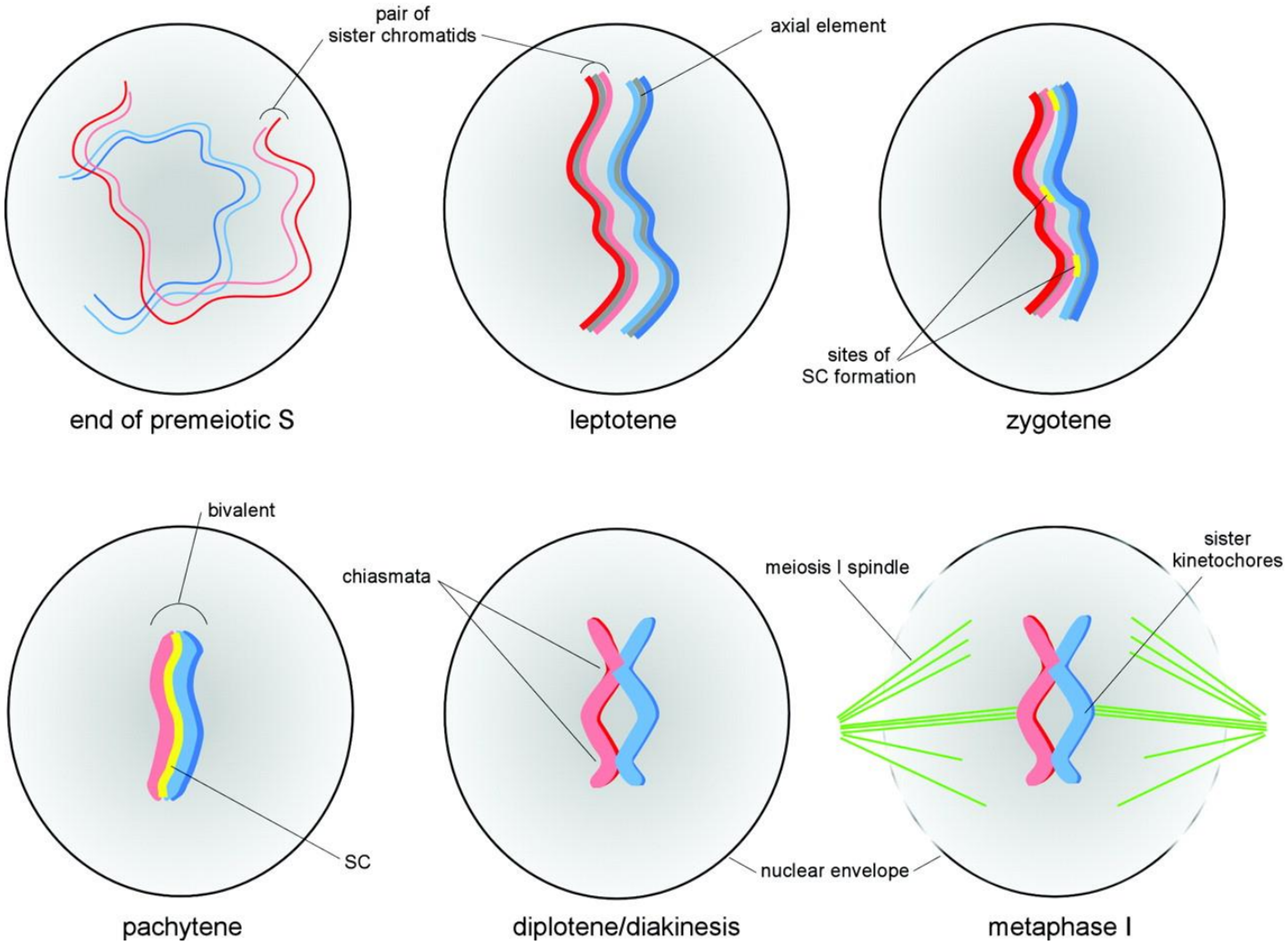
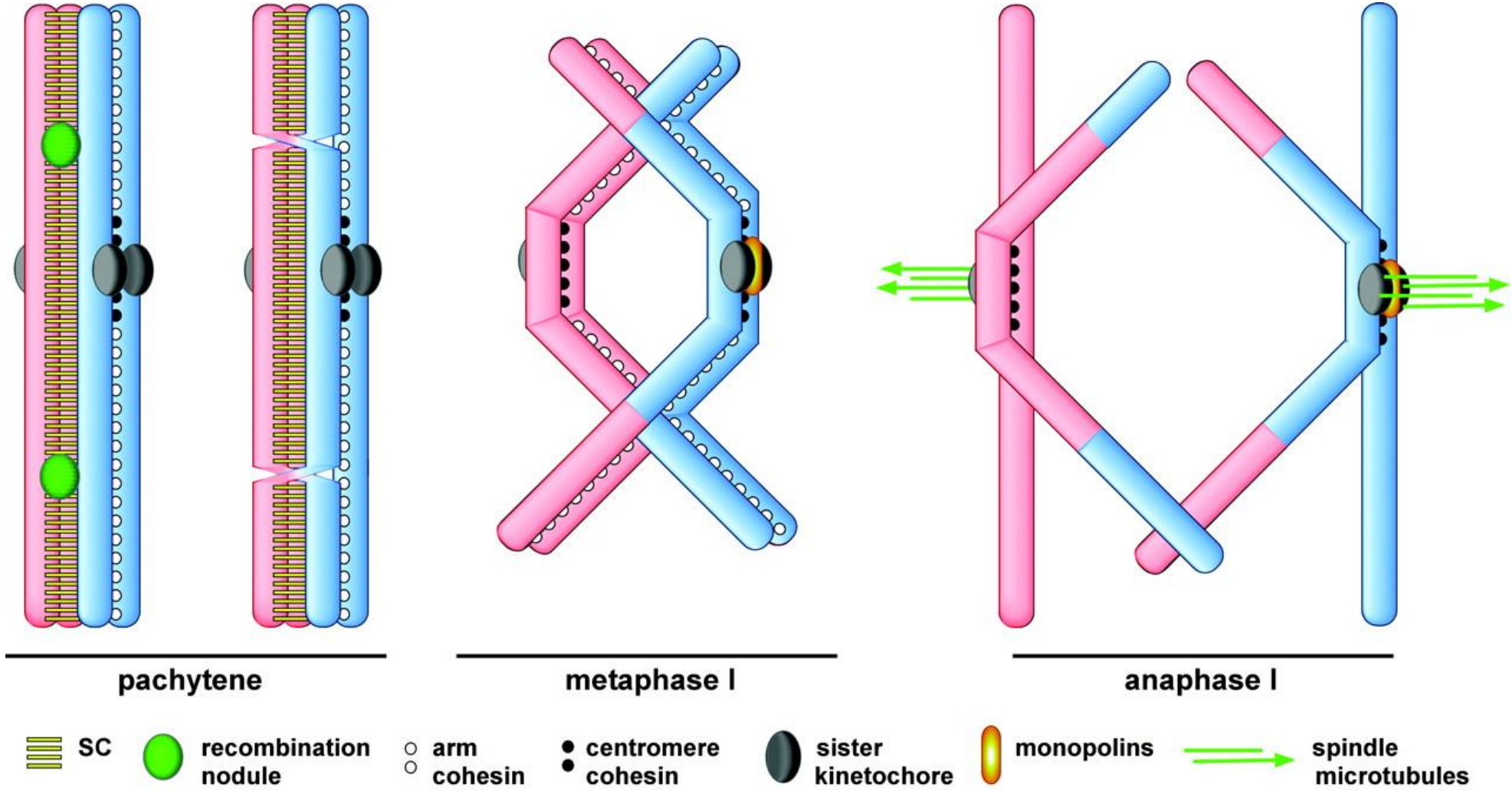
Meiosis Review



Source: Page and Hawley (2003)

Meiosis Review



Source: Page and Hawley (2003)

Genetic Map Development

- Morgan observed “linked” traits working on fruit flies
  - Developed pearls on a string hypothesis for genes
  - Used recombination and crossing over as an explanation

- Sturtevant developed the first linkage map
  - A student in Morgan’s lab
  - Map used recombination rate as a mapping unit
    - Rate is not additive, and they acknowledged this
  - Also documented the occurrence of crossover interference

Genetic Mapping Functions

- Haldane developed the first genetic mapping function
  - Converts recombination rate to an additive mapping unit
    - Expected number of recombinations
  - One Morgan means one expected recombination
  - Doesn’t account for crossover interference

- Kosambi first incorporated interference in a mapping function
  - Fits fly data very well
    - Different levels of interference in other species
  - Many subsequent mapping functions developed

Simple Modeling of Recombination

- Randomly choose a starting chromosome
- Determine if crossover occurs between 1st and 2nd locus
  - Convert genetic distance to recombination rate
- Repeat process for all intervals between loci
- Doesn’t model crossover interference
  - Consistent with Haldane mapping function
- Easy to implement but very slow computation

Count-Location Model

- More complex implementation but faster computation
  - Sample number of chiasmata from Poisson distribution (rate = 2M)
    - Thin by half to account for the 4 chromatids (tetrad)
  - Sample positions of crossovers from uniform distribution (0-M)
  - Randomly pick a starting chromosome and resolve crossovers

- Does not model crossover interference
  - Consistent with Haldane mapping function

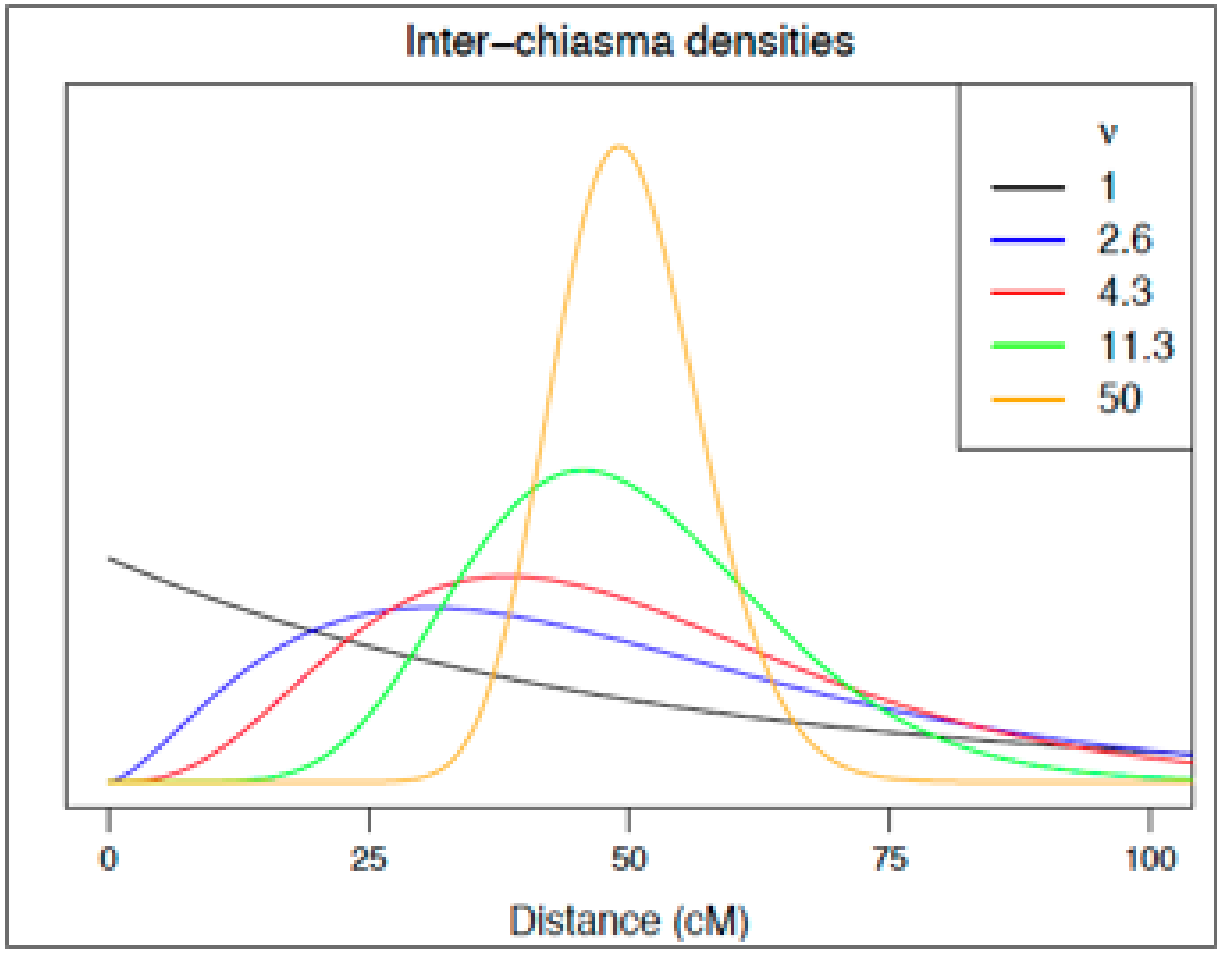
- Original AlphaSimR model

Gamma Model

- Positions of chiasmata sampled using a gamma distribution
  - Shape = v, rate = 2v
- Incorporates crossover interference (v)
  - Able to approximate many mapping functions
- Can incorporate species specific crossover interference
  - The value v can be estimated from real data

Interference in Gamma Model

- Crossover interference parameter (ν)
  - Haldane: ν = 1
  - Kosambi: ν ≈ 2.6
  - Humans: ν = 4.3
  - Mice: ν = 11.3



Source: Karl Broman

Gamma “Sprinkling” Model

- Models two pathways for recombination
  - Type I, no crossover interference
  - Type II, crossover interference

- Involves sampling from two separate gamma distributions
  - Parameter controlling the proportion from each pathway

- Current AlphaSimR model
  - Default set to v=2.6 and no type I crossovers (~Kosambi)

AlphaSimR Demonstration