Course mechanics

Evolutionary Genetics (GENOME 453)

MWF 11:30-12:20 am, S110 Foege
Instructor: Dr. Mary Kuhner
Office: S420C Foege
Hours: TBA, or by appointment
Phone: (206) 543-8751
Email: mkkuhner@uw.edu
Web: http://courses.washington.edu/gs453/

Lecture slides will be on the web page, usually by the morning of the lecture.

Textbook

- No textbook for this course

- Three possibly useful books:
  - Felsenstein, *Theoretical Evolutionary Genetics,* free on the web at http://evolution.gs.washington.edu/pgbook/pgbook.html
  - Hartl and Clark, *Principles of Population Genetics*
  - Graur and Li, *Fundamentals of Molecular Evolution*

- The syllabus lists possible readings from these books (mainly Felsenstein) for students who want additional readings; they are not required

Homework

- 9 assignments
- Handed out Friday, due following Friday
- Lowest of 9 will be dropped
- Worth 1/3 of course grade
- If you don't do the homework, you will probably fail the exams
- You may work together, but be sure you individually know how to solve the problems

Exams

- Midterm and non-comprehensive final count 1/3 each
- Closed book and notes; equation sheet will be provided
- Calculators strongly encouraged
- Homework and practice problems are the best exam prep

Office Hours

- Wednesday after class? Friday before class?
- (Most HW due dates are on Fridays)
- Additional times by appointment

Course Plan

- First half: evolutionary forces
  - Inheritance
  - Mutation
  - Natural selection
  - Genetic drift
  - Population structure
- Second half: forces in action
  - Evolution of novelty
  - Sex, sexual selection, sexual competition
  - Selfish DNA
  - Genome evolution
  - Speciation
  - Evolution and public health
  - Phylogenetics

This lecture

- Why evolution is cool
- Why superficial appeals to evolution are bad
- Brief review of meiosis
- Brief review of probability

Why evolution is cool

- Gets away from purely descriptive view of biology
- Allows "Why?" as question (rare in science!)
- Full of paradoxes, puzzles, surprising results
- Practical importance:
  - Evolution of drug and pesticide resistance
  - Evolution of new pathogens (e.g. bird flu, Ebola virus)
  - Understanding humans through understanding other systems
  - Predicting effects of human policies
  - Evolution of somatic cells into cancer

Don't be superficial

- Off-the-cuff "evolutionary" explanations are popular
- If you can't validate it, it's just a story
- Organisms are complex and what seems plausible to us is often wildly wrong

Don't be superficial

"Africans are lactose-intolerant because milk spoils so quickly in a hot environment that it's better not to drink it, so there was natural selection against milk-drinking."

Don't be superficial

"Africans are lactose-intolerant because milk spoils so quickly in a hot environment that it's better not to drink it, so there was natural selection against milk-drinking."

- What is the ancestral state of lactose tolerance versus intolerance?
- How is tolerance/intolerance distributed worldwide?
- Does lactose intolerance effectively discourage milk drinking?
- Historically, is milk drinking the main form of milk consumption?

Be particularly skeptical of unsupported theories if they involve race or gender!

Don't be superficial

How to validate an evolutionary hypothesis:

- Show that it works out mathematically
- Make predictions based on the hypothesis and test them
  - A hypothesis that makes no predictions is no good
- Collect many cases in which it seems to have happened
- Acid test: watch it happen in a fast-evolving system
- Look for other, competing explanations

Practice problem

"British moths became darker-colored after the Industrial Revolution because of natural selection for better ability to hide on soot-stained tree trunks."

- Think of at least three ways to test this story
- Points to consider:
  - Historical confirmation
  - Experimental confirmation
  - Alternative hypotheses

Images by Olaf Leillinger

Evolutionary puzzles: two examples

- Cystic fibrosis gene (CFTR)
- Mitochondrial genome (mtDNA)

Cystic fibrosis gene (CFTR)

- Classically regarded as a recessive lethal
- Homozygotes have a severe disease
  - CFTR regulates ion balance across the cell membrane
  - Without it, lung mucus becomes too thick
  - Homozygotes are vulnerable to lung infections
  - Prior to modern treatment, most died before adulthood
- Most frequent genetic disease in Caucasians
- Carrier frequency 1 in 20
- Dozens of mutations known

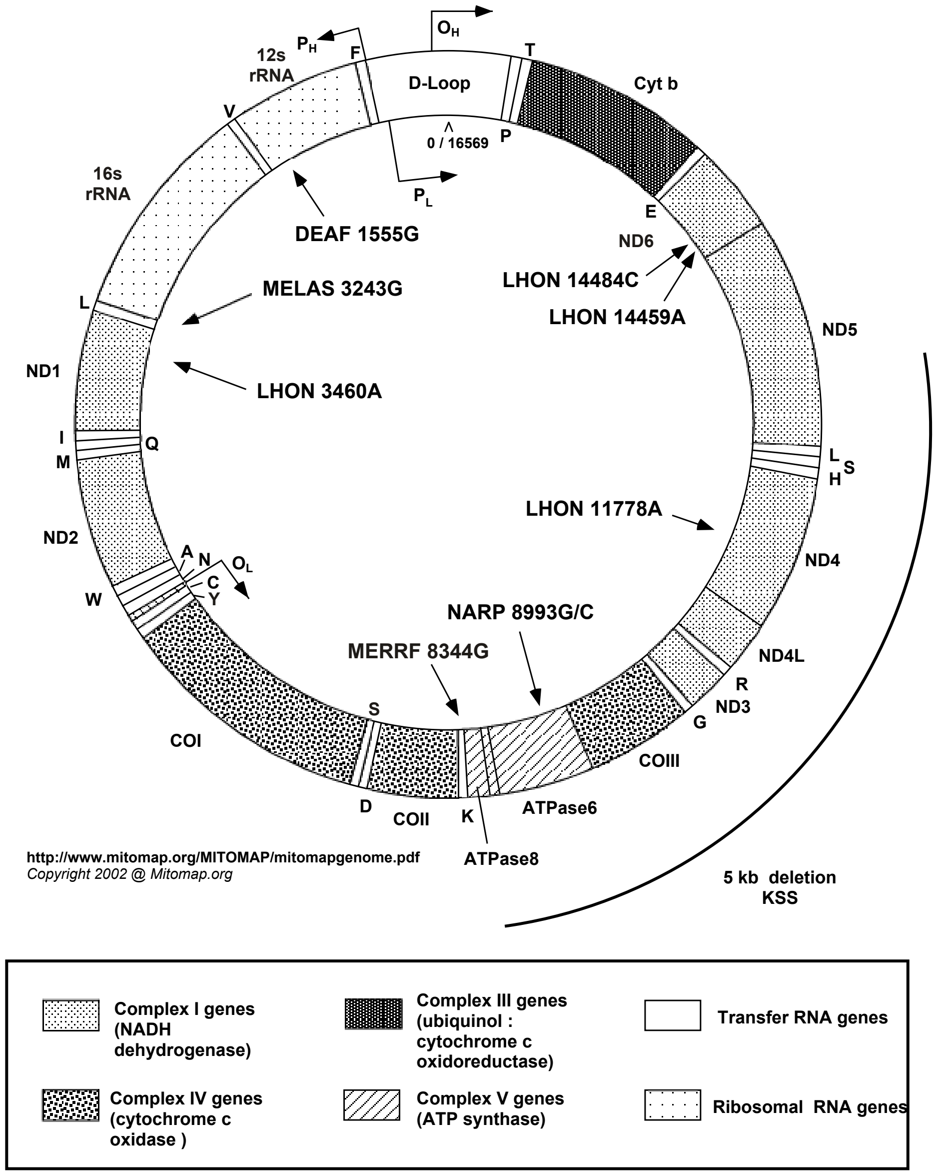
Cystic fibrosis gene

Questions raised by this gene:

- Why is a deadly disease so common?
  - Genetic drift/founder effect?
  - Heterozygote advantage?
  - Hitchhiking? (Is it linked to something good?)
- How will modern medicine change the allele frequency? (Are we all going to have CF eventually?)

Mitochondrial genome

- 60 kb circular genome
- Genes:
  - Protein-coding genes involved in mitochondrial function
  - tRNA genes
  - "Control" or "D-loop" region apparently contains no genes
- Found in almost all eukaryotes; essential in most
- Believed to be a captured bacterial cell
- In vertebrates, believed to be inherited only maternally



O_H
P_H
F
12s rRNA
D-Loop
T
Cyt b
0 / 16569
P
P_L
V
16s rRNA
DEAF 1555G
E
ND6
LHON 14484C
LHON 14459A
MELAS 3243G
L
ND1
LHON 3460A
ND5
I
Q
M
L
S
H
LHON 11778A
ND2
ND4
A
N
O_L
C
Y
W
NARP 8993G/C
MERRF 8344G
ND4L
R
ND3
G
S
COI
COIII
D
COII
K
ATPase6
ATPase8
http://www.mitomap.org/MITOMAP/mitomapgenome.pdf
Copyright 2002 @ Mitomap.org
5 kb deletion
KSS
Complex I genes (NADH dehydrogenase)
Complex III genes (ubiquinol : cytochrome c oxidoreductase)
Transfer RNA genes
Complex IV genes (cytochrome c oxidase)
Complex V genes (ATP synthase)
Ribosomal RNA genes

Mitochondrial genome

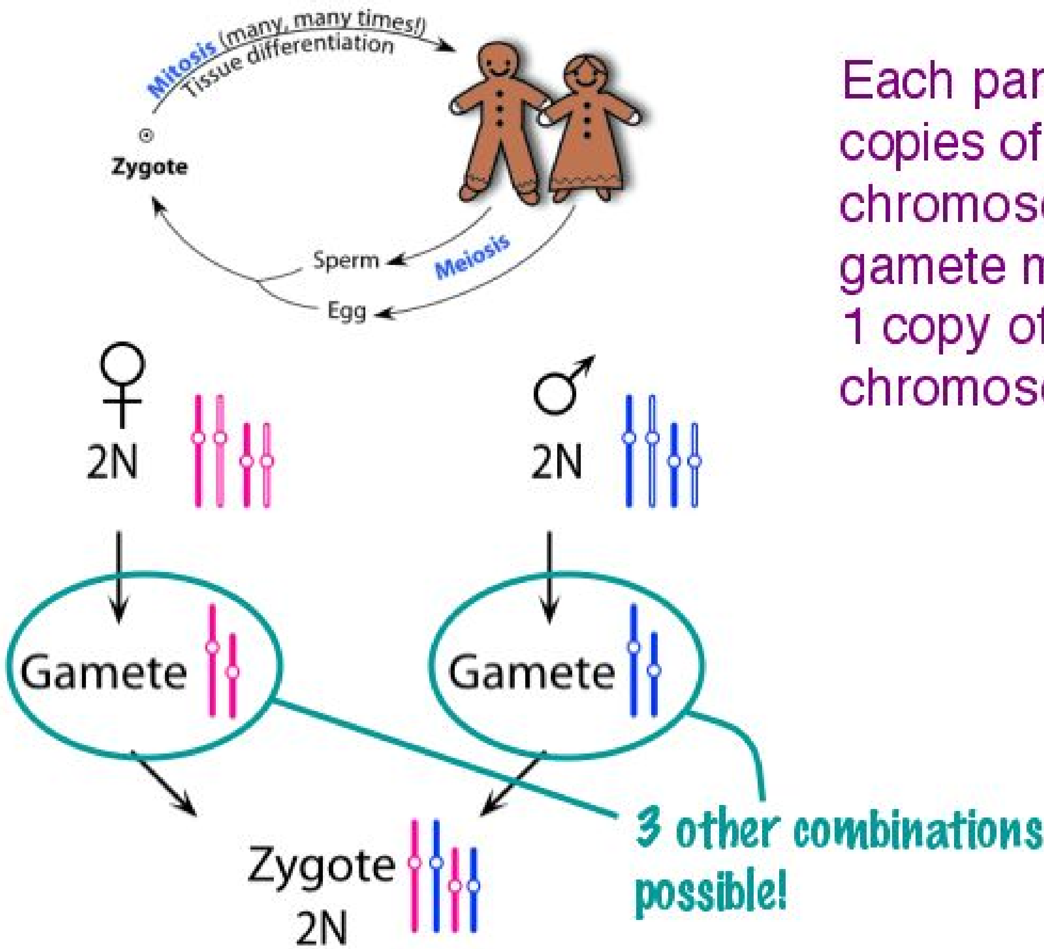
- Questions raised by this genome:
  - Why do we think it's an enslaved bacterium? How could that have happened?
  - What does it reveal about past population history? Can we discover past human history by tracing mtDNA lineages?
  - Is it really only inherited from the mother? Why?
  - Does the lack of recombination endanger it?
  - Is there genetic conflict between the nuclear and mitochondrial genomes? (How does the nucleus prevent a slave revolt?)
  - When were mitochondria enslaved? Did *Giardia* lose mitochondria or never have them?

Review of meiosis

Several aspects will be important:

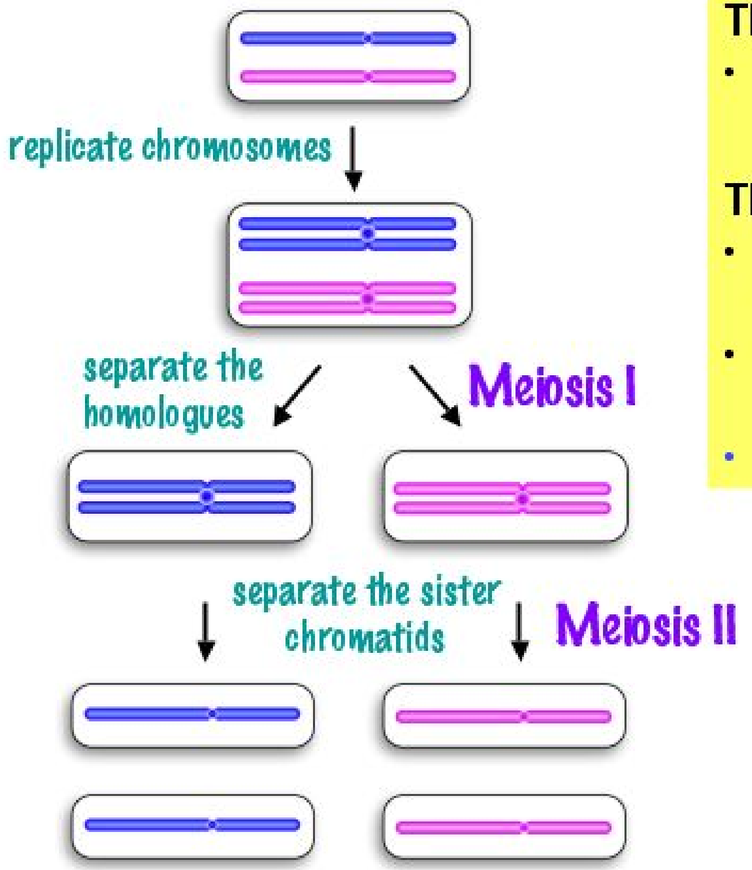
- Mendelian segregation
  - Basis for most genetic predictions
  - Subverted by genes with meiotic drive ("selfish genes")
- Recombination
  - Allows genes to have independent fates
  - Fundamental to "mystery of sex"
- Chromosomal rearrangement
  - Changes in chromosome structure can disrupt meiosis
  - Critical in some forms of speciation
- Please make sure you're comfortable with meiosis

Meiosis—to halve the ploidy for gametes



Each parent has 2 copies of every chromosome… but each gamete must have only 1 copy of each chromosome

Overview of meiosis

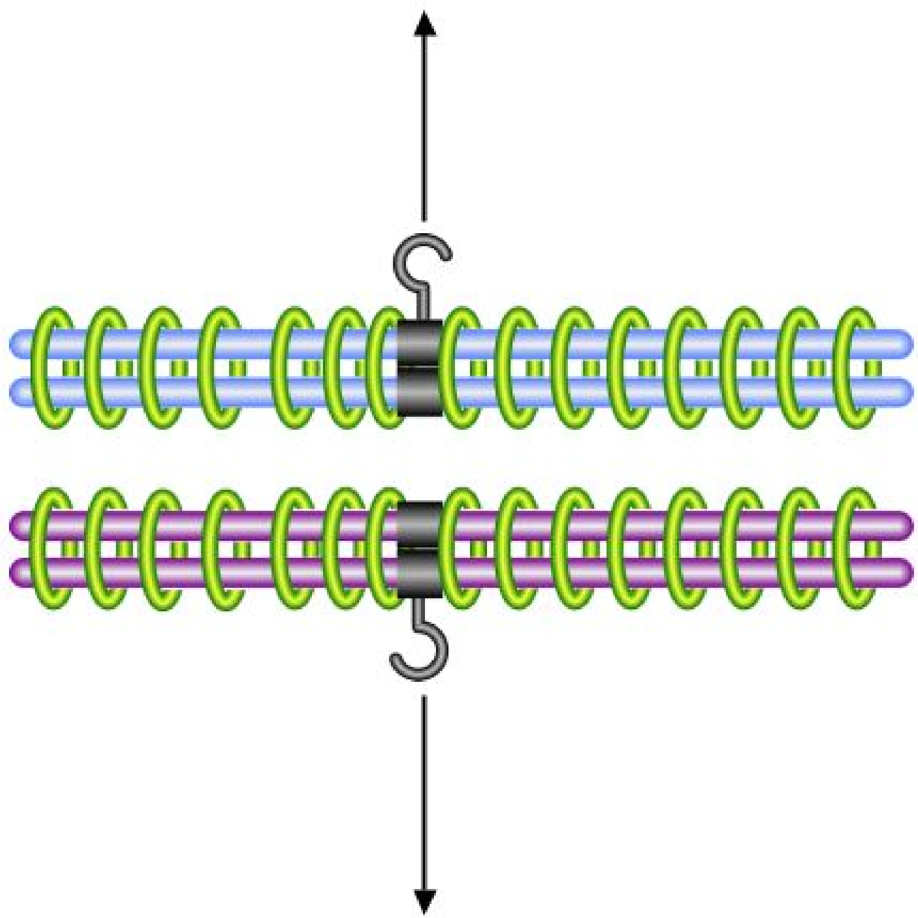


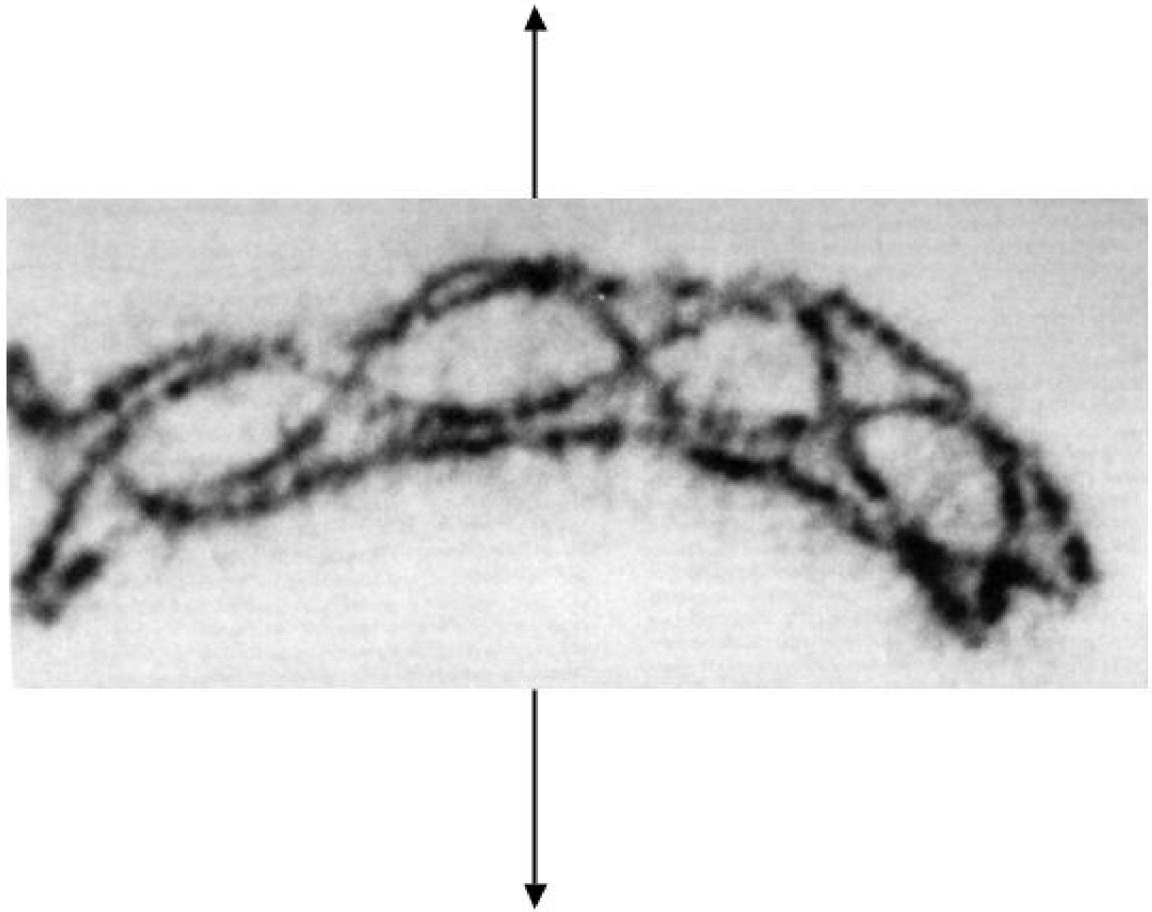
The problem:

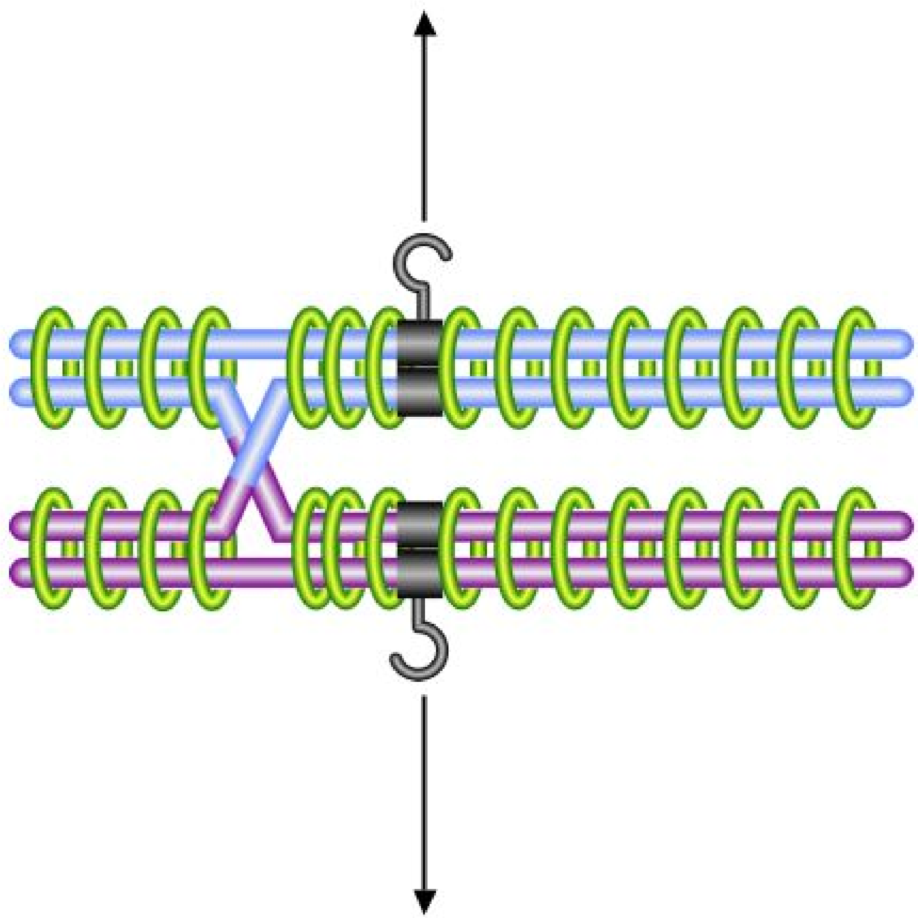
- ensuring that homologues are partitioned to separate gametes

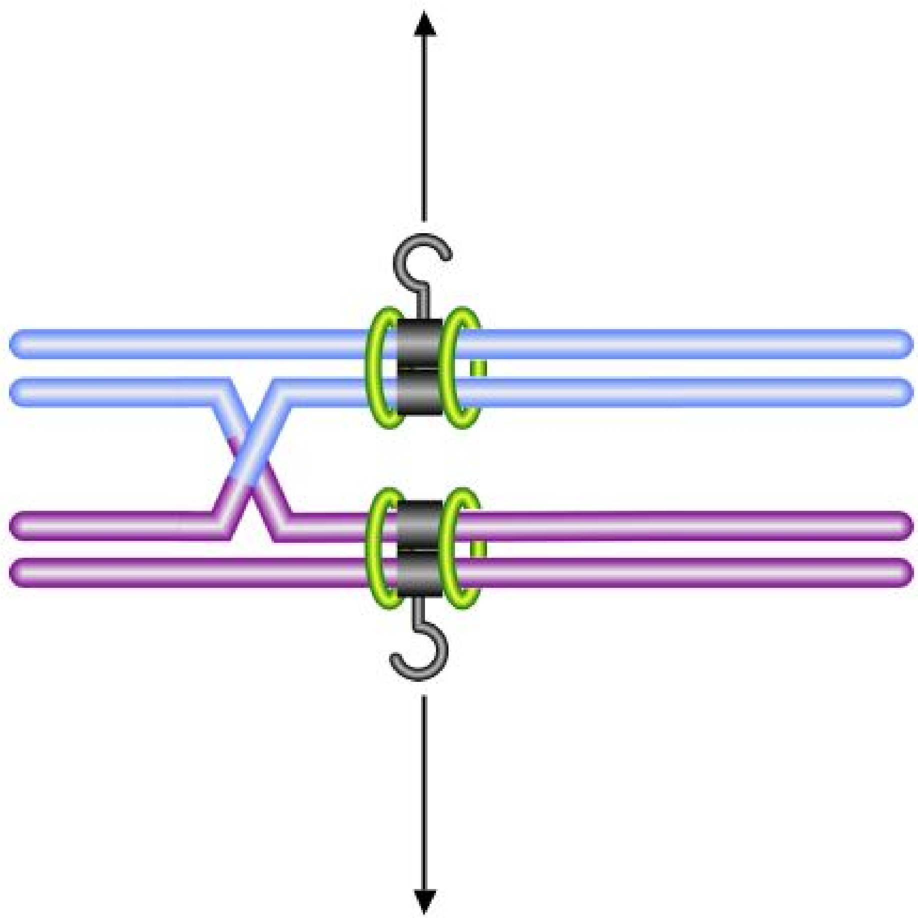
The solution:

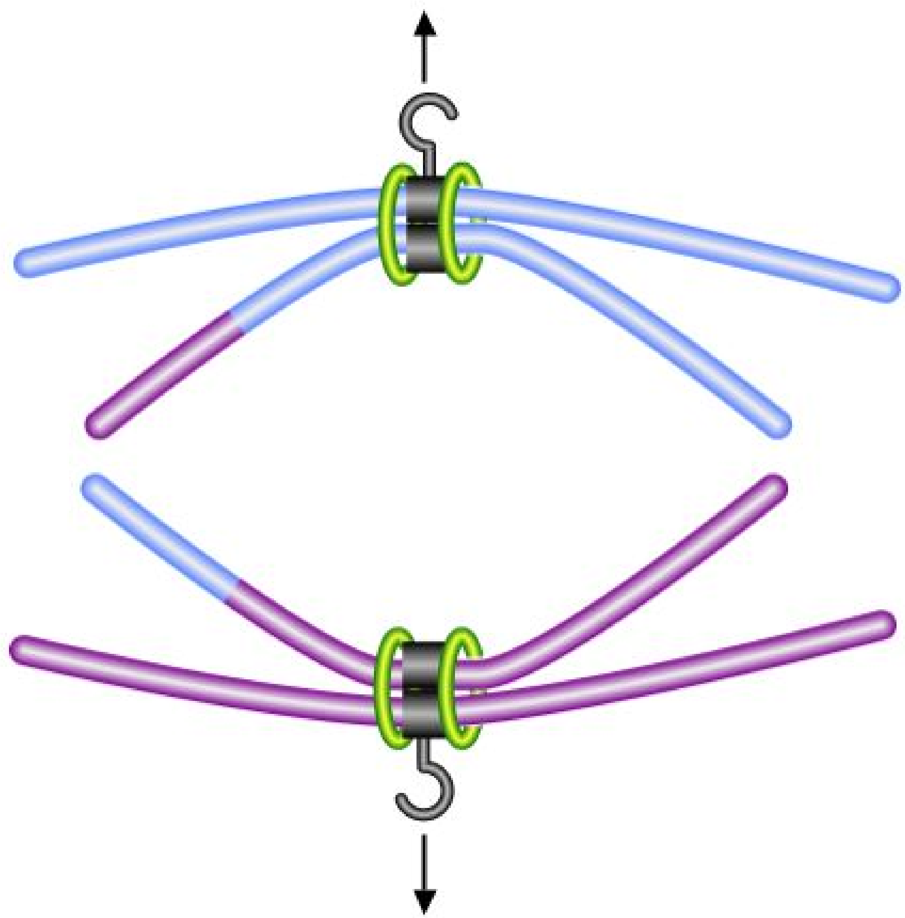
- Hold homologous chromosomes together by **some means**
- target homologues to opposite poles…
- **then** separate the homologues











Practice problem

An individual has two copies of chromosome 6, with alleles of various genes as shown:

```
-------A-----b-----CEN-----C-----D------
-------a-----B-----CEN-----c-----d------
```

We sample gametes (eggs or sperm) from this individual and find one with the following chromosome 6:

```
-------A-----B-----CEN-----C-----D------
```

- What is the minimum number of recombination events to explain this gamete?
- Sketch metaphase of meiosis I showing a set of recombinations that could have produced this gamete.

Practice problem

- What is the minimum number of recombination events to explain this gamete? 2
- Sketch metaphase of meiosis I showing a set of recombinations that could have produced this gamete.

```
----A----b----CEN----C----D----     ----A----b----CEN----C----D----
----A----b----CEN----C----D----     ----A----b----CEN----C----D----
      X     X                   OR          X          X
----a----B----CEN----c----d----     ----a----B----CEN----c----d----
----a----B----CEN----c----d----     ----a----B----CEN----c----d----
```

If this problem troubles you, please review meiosis.

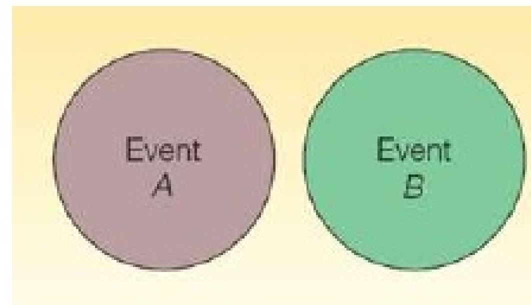
LO4 Calculate probabilities using rules of addition.

Rules of Addition for Computing Probabilities

Rules of Addition

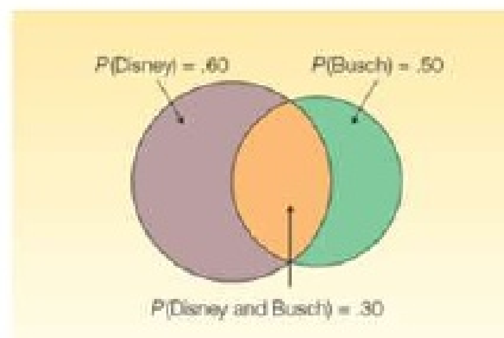
- Special Rule of Addition - If two events *A* and *B* are mutually exclusive, the probability of one *or* the other event's occurring equals the sum of their probabilities.

  P(A or B) = P(A) + P(B)



- The General Rule of Addition - If A and B are two events that are not mutually exclusive, then P(A or B) is given by the following formula:

  P(A or B) = P(A) + P(B) - P(A and B)



Probability of mutually exclusive events

- If two events are mutually exclusive:
  - A sperm either carries B or b but not both
  - In a race with many runners, Sue might win, or Tom might win, but they can't both win

- The probability that one of the two will happen is the sum of the individual probabilities

Probability of mutually exclusive events

- A sperm either carries B or b but not both
  - If the sperm carries B 50% of the time and b 50% of the time, it carries either B or b 100% of the time
- In a race with many runners, Sue might win, or Tom might win, but they can't both win
  - If Sue has a 20% chance to win and Tom has a 15% chance to win, there's a 35% chance that one of them will win

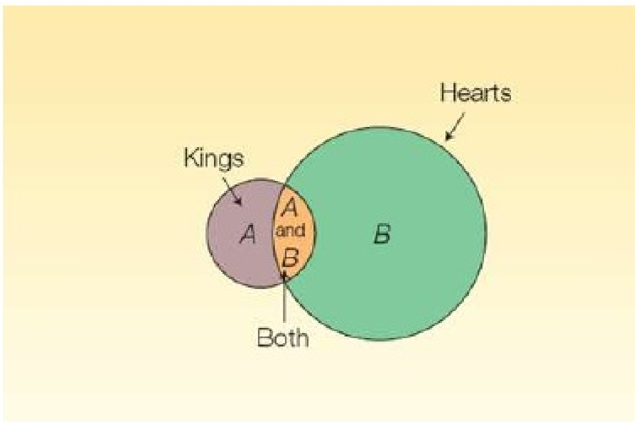
Probability of mutually exclusive events

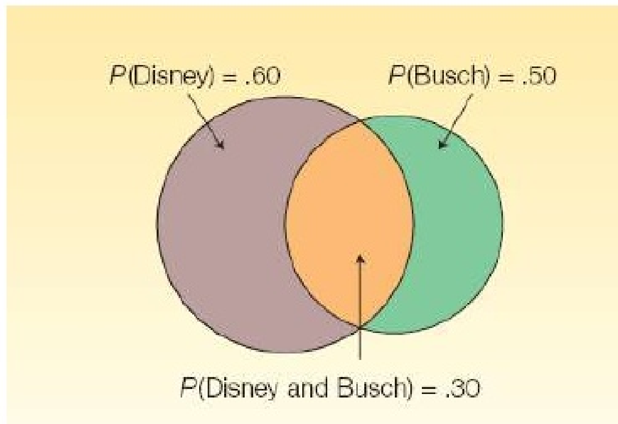
Things to watch out for:

- Doesn't work if events not mutually exclusive
- ...What if Sue and Tom can tie for first?
- If you have listed ALL possible events, total probability should be 1 (100%)
- Probabilities are never greater than 1 or less than 0
- Scientists tend to use percentages (70% chance of winning) and fractions (probability 0.7 of winning) interchangeably–don't get confused!

Joint Probability – Venn Diagram

JOINT PROBABILITY A probability that measures the likelihood two or more events will happen concurrently.





Probability of independent events

- If two events are independent (unrelated)
- The probability that both will happen is the *product* of the two probabilities

Probability of independent events

- If two events are independent (unrelated)
  - A sperm carries B and an egg carries b
  - Sue wins the sprint and Tom wins the marathon
- The probability that both will happen is the *product* of the two probabilities

Probability of independent events

- A sperm carries B and an egg carries b
  - Sperm has B 50% and egg has b 10%; joint probability is 5%
- Sue wins the sprint and Tom wins the marathon
  - Sue wins 90% and Tom wins 75%; joint probability is 67.5%

Probability of independent events

- Doesn't work if the events are not really independent
- ...What if Sue and Tom are part of a team and the whole team is disqualified?
- Be sure to consider all ways you could get your outcome
- Probabilities are STILL never greater than 1 or less than 0

Practice problem on probabilities

- At a chess tournament:
  - Mary plays Chouchanik; Mary has a 30% chance to win
  - Naomi plays Bada; Naomi has a 60% chance to win
  - Each game also has a 10% chance to be a draw (tie)
  - If Mary and Naomi both win, Mary ties for first
  - If Mary wins and Naomi and Bada draw, Mary ties for first

- What is the probability that Mary ties for first?

Practice problem on probabilities

- Assuming the two games are independent:
  - Mary wins 0.3 * Naomi wins 0.6 $= 0.18$
  - Mary wins 0.3 * Naomi draws 0.1 $= 0.03$
  - Total chance that Mary ties for first: $0.18 + 0.03 = 21\%$
- (Unfortunately for me Naomi lost)

Reality checks!

- Mary wins 30%, Naomi wins 60% (in separate games)
- Mary's chance of tying for first can't be greater than 30% (her chance of winning her game)
- Are the games really independent? Could the outcome of one game influence the other?

One-minute responses

- Tear off a half-sheet of paper
- Write one line about the lecture:
  - Was anything unclear?
  - Did anything work particularly well?
  - What could be better?
- Leave at the back on your way out