

Office Hours

No rooms are available, sorry!

Friday 10:30-11:30 in Vista Cafe (just down the hall)

If you can't make this time and need help, please email or talk to me and we'll make an appointment.

One-minute responses

- Talk louder and use bigger fonts! (I'll try; remind me if I slip up.)
- Does a great-grandmother share identical mtDNA with all her descendants?
 - She will not share her mtDNA with her sons' children, only her daughters' children
 - Mutations can happen at each step
- Rusty on recombination

Basics of recombination

- Chromosomes duplicate (4 chromatids)
- Chromatids break and rejoin (recombination)
- Chromosomes segregate (meiosis I)
- Chromatids segregate (meiosis II)

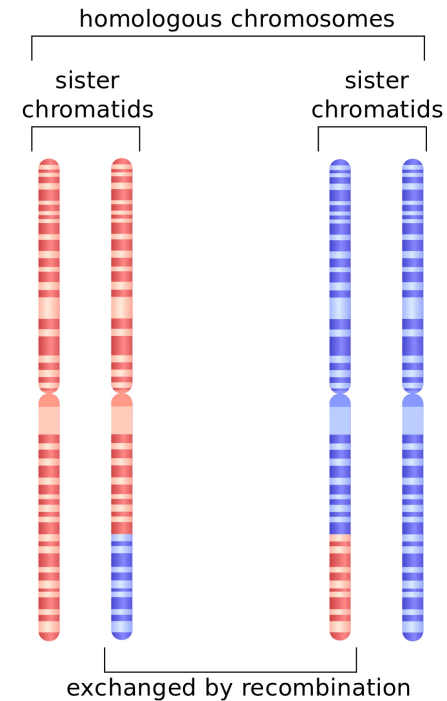


Image by Emw

Probability of mutually exclusive events

- If two events are mutually exclusive
- The probability that one of the two will happen is the *sum* of the individual probabilities

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?
 - If you have listed ALL possible events, total probability should be 1 (100%)
 - Probabilities are never greater than 1 or less than 0

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

- 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
 - Sperm has B 50% and egg has b 10%; joint probability is 5%
 - Sue wins 90% and Tom wins 75%; joint probability is 67.5%

Probability of independent events

- Things to watch out for:
 - 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?
 - Consider all ways you could get your outcome
 - Probabilities are STILL never greater than 1 or less than 0

Practice problem on probabilities

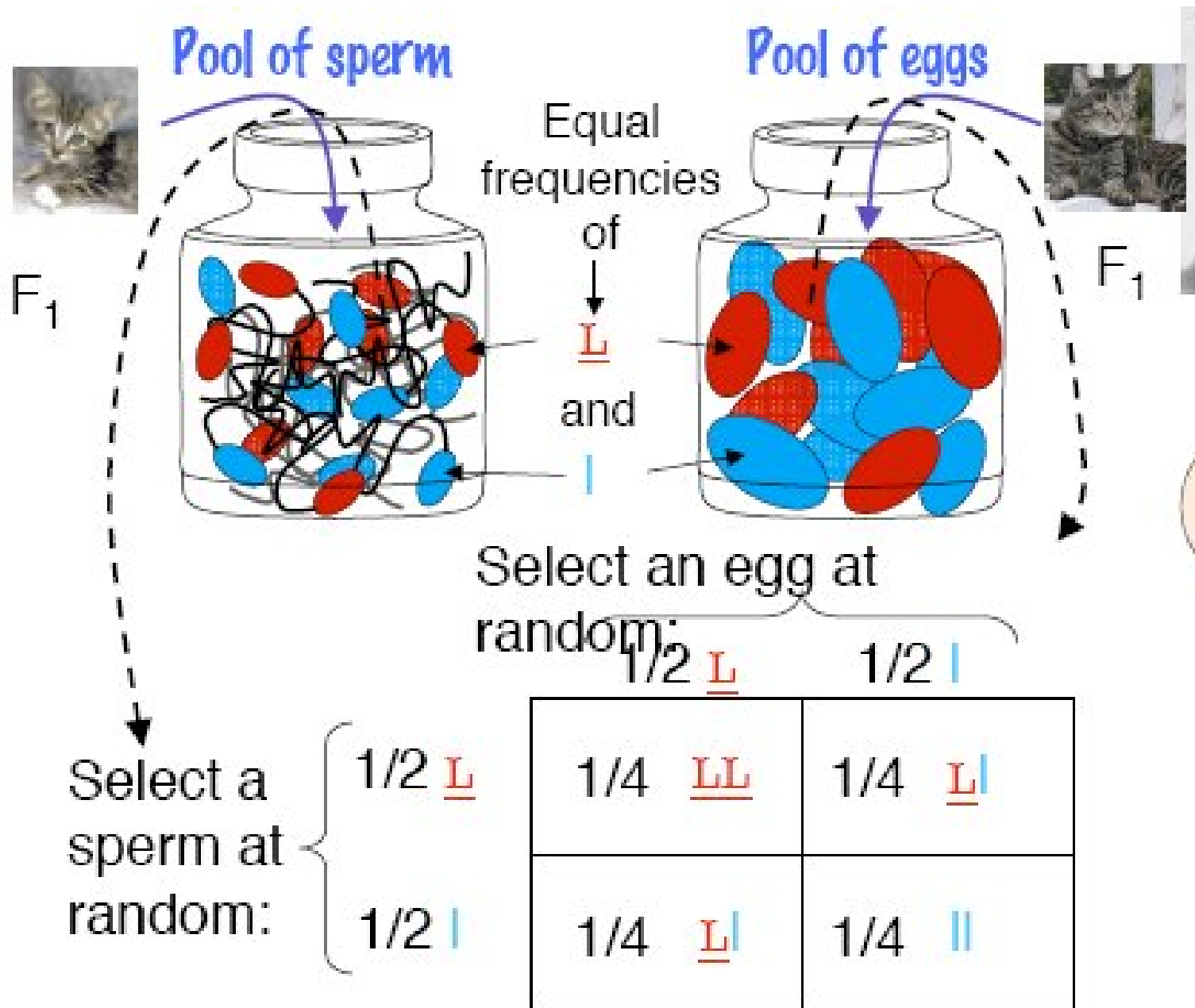
- At a chess tournament:
 - Mary plays Chouchanik; Mary has a 30% chance to win
 - Naomi plays Bada; Naomi has a 60% chance to win
 - Each game also has a 10% chance to be a draw (tie)
 - If Mary and Naomi both win, Mary ties for first
 - If Mary wins and Naomi and Bada draw, Mary ties for first
- What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

Practice problem on probabilities

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

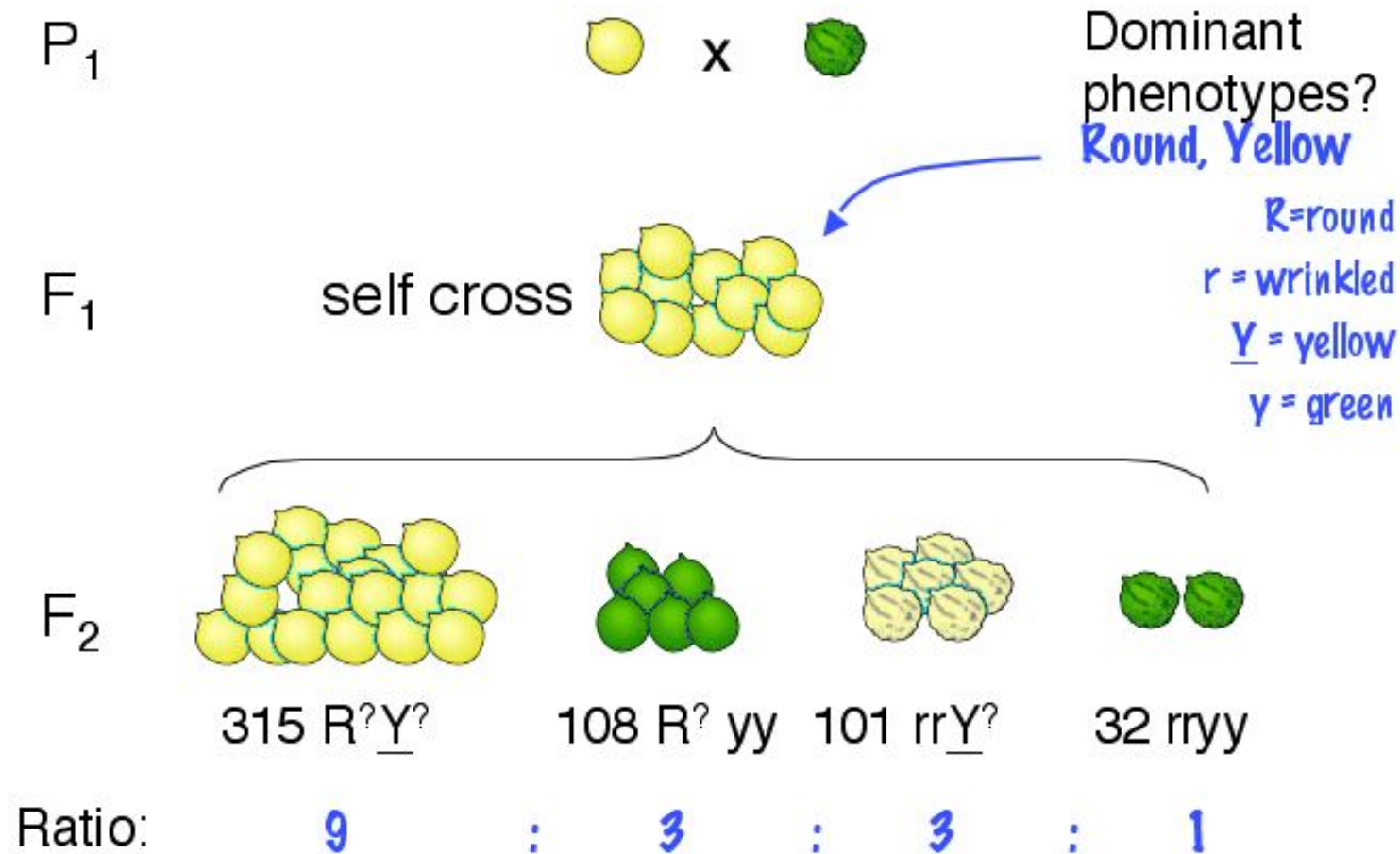
Mendel's Laws

- Law of Segregation
 - Each individual transmits one of its two copies at random
- Law of Independent Assortment
 - Transmission of each trait is independent of others



Independent Assortment

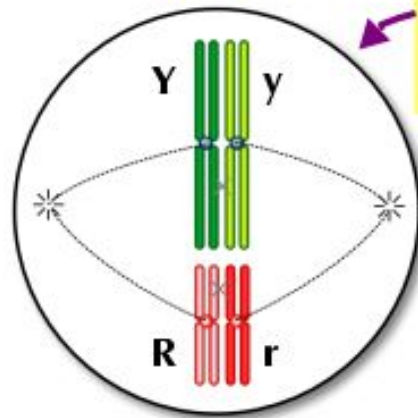
Inheritance of more than one trait in a cross



Chance, meiosis, and independent assortment

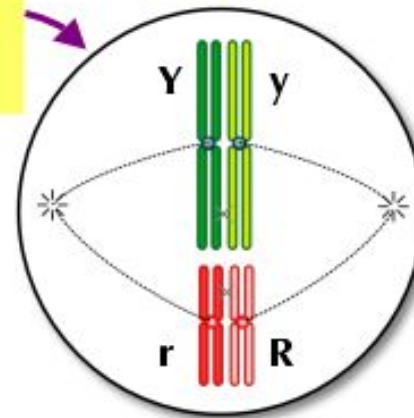
Genotype:

RrYy



equally
probable!

RrYy



Gamete
genotype:

RY

ry

rY

Ry

1/4 each

Mendel's Laws

Exceptions:

- Law of Segregation
 - (rare) meiotic drive
- Law of Independent Assortment
 - Linked traits (close together on same chromosome)
 - Traits controlled by the same gene
 - Traits controlled by interactions among genes

Hardy-Weinberg

What happens at the population level?



- Brachydactyly is a dominant genetic trait
- Many peoples' intuition is that it should increase in frequency
- Hardy and Weinberg independently showed why not

Hardy-Weinberg Law

- Allele frequencies p (chance of A) and q (chance of a)
- One generation of random mating
- Genotype frequencies will be p^2 , $2pq$, and q^2
- Allele frequencies will not change

Hardy-Weinberg Law

- Calculate the allele frequencies:

$$p = AA + 1/2 Aa$$

$$q = 1/2 Aa + aa$$

- So for 200 individuals: 83 AA, 62 Aa, 55 aa

$$p = 83/200 + 1/2 * 62/200 = 0.57$$

$$q = 1/2 * 62/200 + 55/200 = 0.43$$

- These are frequencies and should add up to 1

Hardy-Weinberg Law

$$AA = p^2$$

$$Aa = 2pq$$

$$aa = q^2$$

- Calculate the new genotype frequencies:

$$p^2 = 0.57^2 = 0.3249$$

$$2pq = 2 * 0.57 * 0.43 = 0.4902$$

$$q^2 = 0.43^2 = 0.1849$$

- These are also frequencies and should add up to 1

Did dominance matter?

$$p^2 = 0.57^2 = 0.3249$$

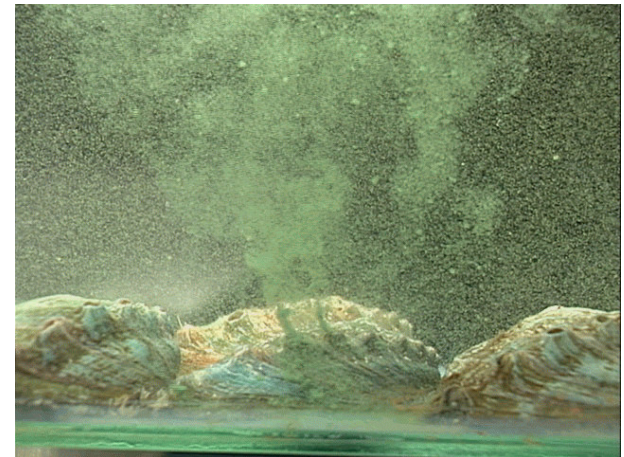
$$2pq = 2 * 0.57 * 0.43 = 0.4902$$

$$q^2 = 0.43^2 = 0.1849$$

- Starting frequency of A (dominant allele): 0.57
- Ending frequency of A: $0.3249 + 0.4902/2 = 0.57$
- Dominance doesn't matter at all here

Alternative way to look at H-W: Abalone

- It's hard to think about specific pairs of individuals mating (too many possibilities)
- Abalone simply dump eggs and sperm into the ocean and let them mix
- Draw a Punnet square using the allele frequencies



Hardy-Weinberg

- Three allele version:
 - Homozygotes are p^2 , q^2 , r^2
 - Heterozygotes are $2pq$, $2pr$, $2qr$
- This generalizes to any number of alleles

Hardy-Weinberg equilibrium

- A random mating, unperturbed population will tend to have genotypes in H-W proportions
- This state is called “Hardy-Weinberg equilibrium”
- A random mating population that is not in H-W equilibrium will tend to move there and stay there
- The allele frequencies do not change
- After H-W is reached, the genotype frequencies do not change either

Hardy-Weinberg

- Things that can disrupt H-W proportions:
 - Non-random mating
 - Population admixture
 - Selection
 - Genetic drift
 - Mutation (rarely)
 - Observational error
- Despite all this, most genes are very close to H-W

Practice problem 1

Are these genotypes in H-W proportions?

HH	36
Hh	48
hh	16
<hr/>	
Total	100

Practice problem 2

Are these genotypes in H-W proportions?

HH	75
Hh	10
hh	15
<hr/>	
Total	100

H-W test detects a problem

The experimenter presented us with this (is it H-W?):

aa 47%

ab 31%

bb 22%

H-W test detects a problem

The experimenter presented us with this:

aa 47%

ab 31%

bb 22%

On questioning, she admitted that she really observed this:

aa 450

ab 300

bb 210

test failed 40

H-W test detects a problem

On questioning, she admitted that she really observed this:

aa	450
ab	300
bb	210
test failed	40

There is an allele present which her test fails to detect:

aa + ac	450
ab	300
bb + bc	210
cc	40

and the results could be in H-W after all, with $p(a) = 0.5$, $p(b) = 0.3$ and $p(c) = 0.2$.

This is a common problem with electrophoretic or serological studies. The ABO blood groups behave this way.

Not enough information

Suppose we're given this:

brown eyes 80

blue eyes 20

- We happen to know that brown is dominant over blue
- Don't know allele frequencies
- Can assume H-W to calculate them

Not enough information

brown eyes 80

blue eyes 20

- **Impossible to test H-W if we assumed it**
- We need either:
 - Independent estimate of allele frequencies
 - Way to tell homozygous brown from heterozygous brown

Chi-square test

- Is a deviation from H-W due to chance?
- Chi-square (χ^2) test is appropriate
- For two alleles we have one degree of freedom
- **Test must be done on counts, not frequencies!**

Chi-square and degrees of freedom

- We make a certain number of observations of nature
- These can differ from expectations in a variety of ways
- The more we have to use our data to determine what we expect...
- ...the fewer resources are left to notice that it doesn't match
- Degrees of freedom are ways in which the data could differ from expectations

Chi-square test

- Start with number of observations
- Lose one degree of freedom for each estimated variable
- If degrees of freedom drop to 0, no tests are possible

Chi-square test

- To test H-W with three categories:
 - Start with three observations
 - Use one up to get totals
 - Use one up to get allele frequencies
 - Left with 1 df

Chi-square table

df	0.10	0.05	0.025	0.01	0.005
1	2.706	3.841	5.024	6.635	7.879
2	4.605	5.991	7.378	9.210	10.597
3	6.251	7.815	9.348	11.345	12.838

Chi-square test

$$\chi^2 = \sum \frac{(\text{observed} - \text{expected})^2}{\text{expected}}$$

Genotype	Observed	Expected	$(o - e)^2 / e$
HH	750	640	18.9
Hh	100	320	151.3
hh	150	40	302.5
			472.7

Compare this with the 95% critical value for 1 df (3.841) and there is no question we are not in H-W.

Why counts and not frequencies?

- Flip a coin 4 times—3 heads 1 tail
 - Is this surprising?
- Flip a coin 100 times—75 heads 25 tails
 - Is this surprising?
- Flip a coin an unknown number of times—75% heads
 - How can we tell if this is surprising?

Why do we care?

- H-W is what happens when nothing is happening
- Basis of all evolutionary calculations
- Deviation means something interesting is happening
- Many discoveries from failure to meet H-W:
 - Hidden alleles
 - Population admixture
 - Cryptic species
 - Lethal alleles
 - Mating preferences
 - Natural selection

Example: Dobzhansky and Levene 1948

- Two different gene orders on chromosome 3 in *D. pseudoobscura*
- Wild animals were caught and bred in a large “population cage”
- Not in H-W: too many heterozygotes were observed
- What are some possible explanations?

Example: Dobzhansky and Levene 1948

- Females were taken from the cage and their eggs genotyped
- Eggs were in H-W for the two gene orders
- Which explanations does this rule out?

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