GENETICS · STUDY GUIDE

Exam 2 Study Guide

This guide covers chapters 3 and 4. Chapter 3 asks what happens when the sex of a parent, or of a child, changes the outcome of a cross. Chapter 4 asks what happens when two genes share a chromosome, and how often they get split apart tells you how far apart they sit. Work one chapter at a time. Read what to know, copy the formula table by hand, and try each worked example with the steps covered. Then take the ten item self-test. The cram sheet at the end pulls every rule and formula together.

WHAT THIS GUIDE COVERS

- Chapter 3 · sex determination, X linked and Y linked patterns, X inactivation, sex influenced and sex limited traits, mitochondria, maternal effect and imprinting.
- Chapter 4 · linkage phase, crossing over, recombination frequency and map units, chi square for linkage, three point crosses, interference, mapping functions, LOD scores and markers.

CHAPTER 3

Sex Linkage and Extranuclear Inheritance

What to know

Sex can be set by chromosomes, by ploidy or by the environment. In XX/XY systems, such as mammals and fruit flies, the male is the heterogametic sex, so the father's sperm decides the sex of each child. In XX/XO systems, such as grasshoppers, males have one X and no partner. In ZZ/ZW systems, such as birds and butterflies, the female is heterogametic, so the egg decides. In bees, wasps and ants, fertilized eggs become diploid females and unfertilized eggs become haploid males. This is **haplodiploidy**. Many turtles and all crocodilians use the incubation temperature instead.

In mammals the Y decides. The Y gene **SRY** encodes an HMG box transcription factor that switches on *SOX9* in the early gonad, and the gonad becomes a testis. A 45,X person develops as a female (Turner syndrome) and a 47,XXY person as a male (Klinefelter syndrome). XX males usually carry SRY moved onto an X. In fruit flies, the Y does not decide. Sex follows the **X:A ratio**: 1.0 or more is female, 0.5 or less is male. The fly Y is needed only for male fertility.

The X and Y share short **pseudoautosomal regions** at their tips. They pair and cross over there in male meiosis, so genes such as *SHOX* are inherited as if they were autosomal.

A male is **hemizygous** for X linked genes, so whatever his one X carries is expressed. That is why reciprocal crosses give different results. Morgan crossed a white eyed female with a red eyed male and saw crisscross inheritance: all sons white eyed, all daughters red eyed. Bridges traced the rare exceptions to nondisjunction and so tied genes to visible chromosomes.

In an **X linked recessive** pedigree, many more males than females are affected. There is no father to son transmission, every daughter of an affected man is a carrier, and the trait often skips through a carrier daughter to a grandson. If the allele frequency is q, affected males occur at q and affected females at q^2. An **X linked dominant** trait passes from an affected father to all daughters and no sons. A Y linked trait passes from father to every son.

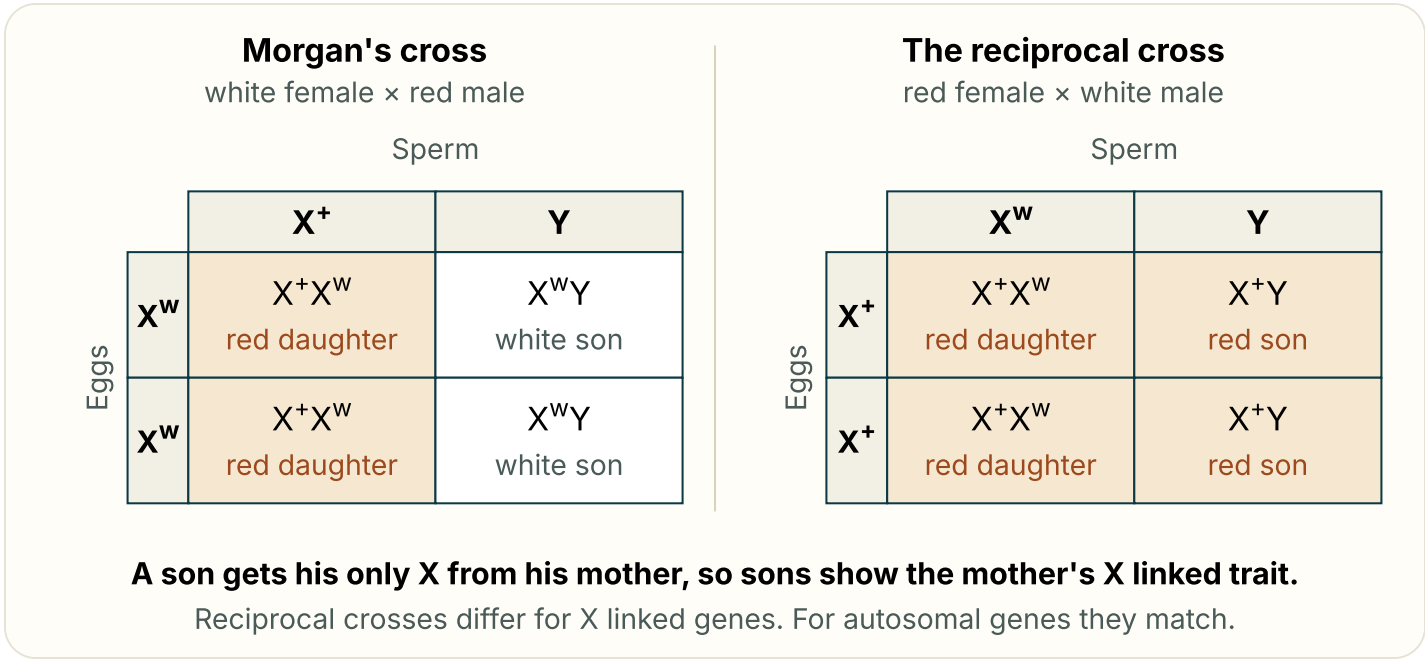
Dosage compensation evens out X gene output. Female mammals silence one X, fruit fly males double the output of their one X, and worm hermaphrodites halve both. In mammals, **XIST** RNA coats the future inactive X in cis and recruits repressive marks such as H3K27 methylation. The choice is random in each cell of the embryo and then inherited by every daughter cell, so every female is a mosaic. The number of Barr bodies is the number of X chromosomes minus one. About 15 percent of human X genes escape, which is why 45,X and 47,XXY still have effects. Calico cats show the mosaic. Skewed inactivation can make a carrier a manifesting heterozygote.

Sex influenced and **sex limited** traits are autosomal. In a sex influenced trait the heterozygote differs by sex: *Hh* rams are horned and *Hh* ewes are not. In a sex limited trait one phenotype shows in only one sex, as with milk yield or cock feathering. Father to son passage and F_2 ratios of 3:1 in one sex and 1:3 in the other separate them from X linkage.

Human mtDNA is a 16,569 base pair circle with 37 genes: 13 polypeptides, 22 tRNAs and 2 rRNAs. It passes from the mother to all her children, and a father passes it to none. **Heteroplasmy**, the bottleneck and the threshold effect make mitochondrial disease variable, even among siblings. A **maternal effect** is different. It is an ordinary nuclear gene, but the mother's genotype sets the child's phenotype, as in snail coiling, so the Mendelian ratio shows up one generation late. In **genomic imprinting**, one parental copy is silenced by germ line methylation. Loss of paternal 15q11 to q13 causes Prader Willi syndrome, and loss of maternal *UBE3A* causes Angelman syndrome.

LOCK THESE IN

- Mammals: the Y (SRY) makes males. Flies: the X:A ratio decides. Birds: ZW is female.
- No father to son transmission is the hallmark of X linkage. Male to male transmission rules it out.
- Every daughter of an affected man is a carrier of an X linked recessive allele.
- X linked recessive: males at q, females at q^2.
- Barr bodies = number of X chromosomes − 1.
- Sex influenced and sex limited traits are autosomal.
- mtDNA: mother to all children, father to none. 37 genes on 16,569 bp.
- Maternal effect: a snail's phenotype shows its mother's genotype, and its genotype shows its offspring's phenotype.



Crisscross inheritance. Fathers pass their X to every daughter and their Y to every son. That is why the two reciprocal crosses give different children.

Patterns, ratios and formulas

Item	Rule or formula	Use
Drosophila sex	X:A ≥ 1.0 female; ≤ 0.5 male; between is intersex	XXY fly is a fertile female; XO is a sterile male
Morgan cross A	red female × white male: F_1 all red; F_2 3 red : 1 white, all whites male	X linked recessive
Morgan cross B	white female × red male: F_1 red daughters, white sons; F_2 1 : 1 : 1 : 1	crisscross inheritance
Frequency of affected	males = q; females = q^2	X linked recessive
Carrier mother × normal father	sons 1/2 affected; daughters 1/2 carriers	X linked recessive risk
Affected father	all daughters carriers (recessive) or affected (dominant); no sons	X linked
Barr bodies	number of X − 1	47,XXY has 1; 45,X has 0
Sex influenced F_2	3 : 1 in one sex, 1 : 3 in the other	horns in sheep
Haplodiploid sisters	share 3/4 of genes by descent	versus 1/2 in diploids
Snail coiling	phenotype follows the mother's genotype	ratios appear a generation late
Imprinted gene, paternal expression	carrier father: 1/2 children affected; carrier mother: 0	parent of origin effect

Worked examples

WORKED EXAMPLE 1 · RISK THROUGH A CARRIER MOTHER

A woman's maternal uncle has hemophilia B. Her mother, her grandparents and she herself are unaffected, and so is her partner. (a) What is the chance the woman is a carrier? (b) What is the chance her first child is an affected son?

STEP 1 · THE GRANDMOTHER

The uncle's X came from his unaffected mother, so the grandmother is a carrier. Assume no new mutation.

STEP 2 · THE MOTHER

She got one of the grandmother's two X chromosomes, so P(carrier) = 1/2.

STEP 3 · THE WOMAN

She is a carrier only if her mother is and she got the mutant X: 1/2 × 1/2 = **1/4**.

STEP 4 · THE CHILD

If she is a carrier, a child is a son 1/2 of the time and a son gets the mutant X 1/2 of the time. So 1/4 × 1/2 × 1/2 = **1/16**.

KEEP THE QUESTIONS APART

If you already know the child is a son, drop the 1/2 for sex: 1/4 × 1/2 = 1/8. Read whether the question gives the sex.

WORKED EXAMPLE 2 · A CARRIER MOTHER AND A NORMAL FATHER

A woman who carries red green color blindness (X^CX^c) has children with a man with normal vision (X^CY). Predict the children by sex.

STEP 1 · GAMETES

Mother: 1/2 X^C, 1/2 X^c. Father: 1/2 X^C, 1/2 Y.

STEP 2 · DAUGHTERS

They get X^C from the father. So 1/2 X^CX^C and 1/2 X^CX^c. All have normal vision, and half are carriers.

STEP 3 · SONS

They get Y from the father. So 1/2 X^CY (normal) and 1/2 X^cY (color blind).

STEP 4 · ALL CHILDREN

Color blind sons are 1/2 of sons and 1/2 of births are sons: **1/4 of all children**.

WORKED EXAMPLE 3 · A SEX INFLUENCED CROSS

In a sheep breed, *H* (horns) is dominant in males and recessive in females. A *Hh* ram is mated with *hh* ewes. What fraction of rams, of ewes, and of all lambs will be horned?

STEP 1 · THE CROSS

Hh × *hh* gives 1/2 *Hh* and 1/2 *hh* in each sex, because the gene is autosomal.

STEP 2 · RAMS

Hh rams are horned, so **1/2 of rams** are horned.

STEP 3 · EWES

Hh ewes are hornless and so are *hh* ewes, so **no ewes** are horned.

STEP 4 · ALL LAMBS

With equal sexes: 1/2 × 1/2 + 1/2 × 0 = **1/4**.

SPOT IT

A horned father with horned sons is father to son passage, which an X linked gene could not give.

WORKED EXAMPLE 4 · MATERNAL EFFECT IN SNAILS

A *dd* female snail is crossed with a *DD* male. *D* (dextral, right coiling) is dominant. The F_1 are selfed, and then each F_2 snail is selfed. Predict the coiling at each step.

STEP 1 · THE F_1

All are *Dd*, but their mother is *dd*, so **all are sinistral**.

STEP 2 · THE F_2

Genotypes are 1 *DD* : 2 *Dd* : 1 *dd*. Their mother (an F_1) is *Dd*, so **all are dextral**.

STEP 3 · THE F_2 BROODS

DD and *Dd* mothers give dextral broods. *dd* mothers give sinistral broods. So **3/4 of broods are dextral and 1/4 sinistral**.

COMPARE

Maternal inheritance of mtDNA follows the egg's organelles. A maternal effect follows the mother's nuclear genes. Only the second gives a delayed 3:1.

TRAPS PEOPLE FALL INTO

- **Thinking two X chromosomes make a female in humans.** The Y decides in mammals. An XXY person is male. In flies it is the reverse, and XXY is female.
- **Calling ZW birds male.** In ZZ/ZW species the female is heterogametic.
- **Expecting an affected father to pass an X linked trait to sons.** He gives sons his Y.
- **Mixing joint and conditional risk.** "An affected son" among all births is half of "affected, given a son."
- **Calling a sex limited trait X linked.** Bulls pass milk yield genes to daughters. The genes are autosomal.
- **Confusing maternal effect with maternal inheritance.** One is a nuclear gene acting through the egg. The other is organelle DNA.
- **Flipping imprinting words.** Say paternally expressed or maternally expressed to stay clear.

- **Assuming one X inactive means no effect of extra X chromosomes.** About 15 percent of genes escape, including pseudoautosomal genes like *SHOX*.

Chapter 3 self-test · ten items

1. In birds, which parent's gamete decides the sex of the chick?

A. The father's sperm, since males are ZW

B. Neither, since nest heat sets the sex

C. The father's sperm, since males are XY

D. The mother's egg, since females are ZW

D. The mother's egg, since females are ZW. Birds use ZZ/ZW. The female is heterogametic and makes Z and W eggs, so the egg decides.

2. A fruit fly is XXY with two sets of autosomes. What is its sex?

A. A fertile female

B. An intersex adult fly

C. A sterile male

D. A fertile male

A. A fertile female. The X:A ratio is 2/2 = 1.0, which gives a female. In flies the Y does not make a male.

3. Which finding in a pedigree rules out X linked inheritance?

A. An affected grandson born to a carrier daughter of the eldest son

B. Many more affected males than affected females in the family

C. An affected father with an affected son by an unaffected mother

D. All daughters of one affected man are carriers of the allele

C. An affected father with an affected son by an unaffected mother. A father gives his son a Y, not an X. Male to male transmission therefore excludes X linkage. The other three fit an X linked recessive pattern.

4. An X linked recessive allele affects 1 in 50 males. About how often should it affect females?

A. 1 in 50
B. 1 in 2,500
C. 1 in 100
D. 1 in 1,250

B. 1 in 2,500. Males show it at q = 1/50. Females need two copies, at q^2 = 1/2,500.

5. How many Barr bodies are in the cells of a 48,XXXY person?

A. Two
B. None
C. Three
D. One

A. Two. Cells keep one X active and silence the rest. Three X chromosomes minus one gives two.

6. Why is a calico cat nearly always female?

A. Males inactivate their only X in half of their cells
B. The coat color gene is sex limited and sits on an autosome
C. The orange allele sits on the Y and is lost in females
D. Orange and black patches need two different X chromosomes

D. Orange and black patches need two different X chromosomes. The *Orange* gene is X linked. Patches come from random X inactivation in an $X^{O}X^{o}$ female. A rare male calico is usually XXY.

7. A woman has a heteroplasmic mtDNA mutation. Her children differ widely in how affected they are. Which idea best explains this?

A. Paternal mtDNA diluting the mutation

B. Crossing over between mtDNA molecules

C. The bottleneck during egg formation

D. Random X inactivation in each child

C. The bottleneck during egg formation. Only a small sample of mtDNA molecules fills each egg, so eggs can differ greatly in mutant load. mtDNA does not recombine, and sperm mitochondria are destroyed.

8. A gene is expressed only from the paternal copy. A woman passes a loss of function allele to her son. What happens?

A. The son is affected, since one bad copy is enough

B. The son is unaffected, since the maternal copy is silent

C. The son is affected only if he is also XXY

D. The son has a one half chance of being affected by it

B. The son is unaffected, since the maternal copy is silent. The copy from his mother is silenced in him. He can still pass it on, and his children who get it will be affected because it will then be paternal.

9. The same 15q11 to q13 deletion causes Angelman syndrome when it is inherited from which parent?

A. The father

B. Either one

C. The mother

D. Neither one

C. The mother. Angelman syndrome is loss of the maternal contribution, mainly maternal *UBE3A*. Loss of the paternal region causes Prader Willi syndrome.

10. In *Hh* × *Hh* sheep, what fraction of ewes are horned?

A 1/4

B 1/2

C 3/4

D 0

A. 1/4. Only *HH* ewes are horned, which is 1/4. Rams show the mirror image, 3/4 horned.

Read the full chapter: Chapter 3 · Sex Linkage and Extranuclear Inheritance

CHAPTER 4

Linkage and Genetic Mapping

What to know

Genes near each other on one chromosome are **linked** and tend to travel together. All genes linked to one another form a **linkage group**, and a well mapped species has one per chromosome. Fruit flies have four and humans have 23.

A double heterozygote has a **linkage phase**. In **coupling** (cis), written *AB*/*ab*, the dominant alleles share one homolog. In **repulsion** (trans), written *Ab*/*aB*, each homolog carries one dominant allele. The phase decides which gametes are parental. Writing *AaBb* says nothing about phase.

Crossing over happens in prophase I, after replication, between nonsister chromatids. It begins with Spo11 double strand breaks and shows as **chiasmata**. Each homolog pair needs at least one crossover to segregate well. One crossover affects two of the four chromatids, so a meiosis with a crossover in an interval gives only half recombinant products. That is why RF tops out at 50 percent.

Recombination frequency is recombinants divided by total. One percent equals one map unit, or one **centimorgan**. Genes 50 or more map units apart look unlinked even if they are syntenic. RF

underestimates long distances, because double crossovers look parental. Build maps from short intervals and add them.

To test for linkage, run chi square against 1:1:1:1 in a testcross. Four classes give df 3 and a critical value of 7.815. If you reject, the two big classes are the parentals and they tell you the phase.

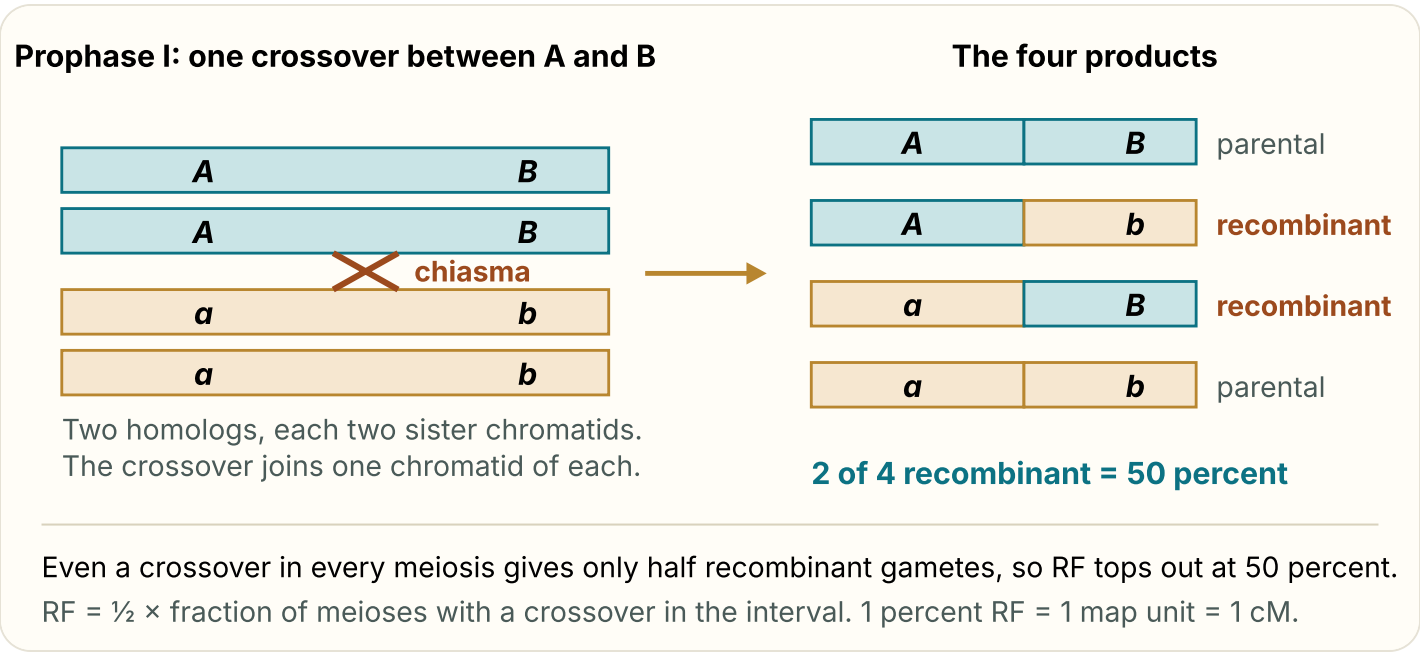
A **three point testcross** gives eight classes. The two largest are parental, the two smallest are double crossovers. The gene that differs between a parental class and its matching double crossover class is the **middle gene**. Each interval distance is its single crossovers plus the double crossovers, over the total. The outside distance is the sum of the two intervals.

Expected double crossovers equal the product of the two interval frequencies times the total. The **coefficient of coincidence** is observed over expected, and **interference** is 1 minus that. Interference is usually positive: one crossover discourages another nearby. **Mapping functions** correct RF for hidden crossovers. Haldane's assumes no interference. Kosambi's allows for it and corrects less.

Map units measure crossover frequency, not base pairs. In humans 1 cM averages about 1 Mb, but hotspots (many marked by PRDM9), cold regions near centromeres and the longer female map all shift it. Gene order on genetic and physical maps matches. In human families, the **LOD score** weighs the odds of linkage at θ against no linkage. Scores add across families. LOD 3 or more supports linkage and −2 or less excludes it. Markers went from RFLPs to microsatellites to SNPs, and linkage disequilibrium lets GWAS scan whole populations.

LOCK THESE IN

- Find the phase first. The two largest classes are the parentals.
- RF = recombinants ÷ total. 1% = 1 map unit = 1 cM. RF never passes 50%.
- One crossover in 30% of meioses gives RF = 0.30 × 0.5 = 15%.
- The middle gene is the one that differs between a parental and its double crossover.
- Add the double crossovers to both intervals.
- c.o.c. = observed DCO ÷ expected DCO. I = 1 − c.o.c.
- Haldane: d = −½ ln(1 − 2r). Kosambi: d = ¼ ln[(1 + 2r) ÷ (1 − 2r)].
- LOD ≥ 3 supports linkage. LOD ≤ −2 excludes it. LOD scores add across families.



Why recombination frequency stops at 50 percent. A crossover involves only two of the four chromatids. Half of the products stay parental no matter what.

Formulas for mapping

Quantity	Formula	Note
Recombination frequency	RF = recombinants ÷ total	1% = 1 map unit = 1 cM
RF from chiasma frequency	RF = ½ × fraction of meioses with a crossover in the interval	one crossover hits two of four chromatids
Expected gametes, two genes d cM apart	each recombinant = d/2 %; each parental = (100 − d)/2 %	phase decides which pair is parental
Interval distance, three point	(singles in that interval + DCOs) ÷ total	DCOs count in both intervals
Outside distance	interval I + interval II	direct count is lower by 2 × DCO frequency
Expected DCO	$RF_{I} \times RF_{II} \times$ total	assumes independence
Coefficient of coincidence	observed DCO ÷ expected DCO	usually below 1
Interference	I = 1 − c.o.c.	positive means fewer DCOs than expected
Haldane	$d = -\frac{1}{2} \ln(1 - 2r)$	d in Morgans; no interference
Kosambi	$d = \frac{1}{4} \ln[(1 + 2r) \div (1 - 2r)]$	allows interference
LOD, phase known	$\log_{10}[\theta^{R}(1 - \theta)^{NR} \div 0.5^{R + NR}]$	best θ = R ÷ total
Chi square for linkage	$\Sigma(O - E)^2 \div E$ against 1:1:1:1	df 3, critical 7.815

Worked examples

WORKED EXAMPLE 1 · A TESTCROSS IN REPULSION

A true breeding *AAbb* plant is crossed with an *aaBB* plant. The F_1 is testcrossed to *aabb*, giving 800 offspring. The genes are 16 map units apart. How many of each class do you expect?

STEP 1 · FIND THE PHASE

The F_1 got *Ab* from one parent and *aB* from the other. It is *Ab*/*aB*, in repulsion.

STEP 2 · NAME THE CLASSES

Parentals are *Ab* and *aB*. Recombinants are *AB* and *ab*.

STEP 3 · SPLIT THE PERCENTS

Recombinants total 16%, so 8% each. Parentals share 84%, so 42% each.

STEP 4 · MULTIPLY BY 800

Ab and *aB*: 0.42 × 800 = **336 each**. *AB* and *ab*: 0.08 × 800 = **64 each**. Check: 336 + 336 + 64 + 64 = 800.

WORKED EXAMPLE 2 · A THREE POINT CROSS FROM START TO FINISH

A female heterozygous for *x*, *y* and *z* is crossed to an *x y z*/*x y z* male. The 2,000 offspring, written in alphabetical order, are: *x* + *z* 758; + *y* + 754; *x y z* 146; + + + 142; + + *z* 96; *x y* + 92; *x* + + 6; + *y z* 6. Find the order, the distances and the interference.

STEP 1 · PARENTALS AND DOUBLES

Largest: *x* + *z* and + *y* +. Smallest: *x* + + and + *y z*.

STEP 2 · THE MIDDLE GENE

Compare *x* + *z* with *x* + +. Only *z* differs, so *z* is in the middle. The order is *x*, *z*, *y*.

STEP 3 · ASSIGN THE SINGLES

In true order the parentals are *x z* + and + + *y*. A crossover between *x* and *z* gives *x* + *y* and + *z* +, which are the 92 and 96 classes. A crossover between *z* and *y* gives *x z y* and + + +, the 146 and 142 classes.

STEP 4 · INTERVAL X TO Z

(92 + 96 + 6 + 6) ÷ 2,000 = 200 ÷ 2,000 = **10.0 cM**.

STEP 5 · INTERVAL Z TO Y

(146 + 142 + 6 + 6) ÷ 2,000 = 300 ÷ 2,000 = **15.0 cM**.

STEP 6 · OUTSIDE

10.0 + 15.0 = **25.0 cM**. A direct count of *x* to *y* recombinants gives (92 + 96 + 146 + 142) ÷ 2,000 = 23.8 cM. The gap, 1.2, is 2 × 12/2,000.

STEP 7 · INTERFERENCE

Expected DCO = 0.100 × 0.150 × 2,000 = 30. Observed = 12. c.o.c. = 12 ÷ 30 = **0.40**, so I = **0.60**.

WORKED EXAMPLE 3 · A LOD SCORE

A family with an autosomal dominant condition gives 10 informative, phase known meioses. Two are recombinant between the condition and a marker. Find the LOD score at θ = 0.2.

STEP 1 · LINKED LIKELIHOOD

$L(0.2) = 0.2^2 \times 0.8^8 = 0.04 \times 0.1678 = 0.006711$.

STEP 2 · UNLINKED LIKELIHOOD

$L(0.5) = 0.5^{10} = 0.0009766$.

STEP 3 · ODDS

$0.006711 \div 0.0009766 = 6.87$.

STEP 4 · LOG

$LOD = \log_{10} 6.87 =$ **0.84**.

WHAT IT MEANS

This is the peak, since 2/10 = 0.2 is the best θ. It is far short of 3. Three more families like this one would sum to about 3.35, which would cross the bar.

WORKED EXAMPLE 4 · TWO MAPPING FUNCTIONS

Two genes show 20 percent recombination. Estimate the map distance with Haldane's and with Kosambi's function.

STEP 1 · HALDANE

$1 - 2r = 1 - 0.40 = 0.60$. $\ln 0.60 = -0.511$. $d = -\frac{1}{2} \times (-0.511) = 0.255$ Morgans, or **25.5 cM**.

STEP 2 · KOSAMBI

$(1 + 0.40) \div (1 - 0.40) = 1.40 \div 0.60 = 2.333$. $\ln 2.333 = 0.847$. $d = \frac{1}{4} \times 0.847 = 0.212$ Morgans, or **21.2 cM**.

STEP 3 · COMPARE

Both are larger than 20, because double crossovers hid some recombination. Kosambi corrects less, because it assumes interference already removed some doubles.

TRAPS PEOPLE FALL INTO

- **Assuming coupling.** Let the two largest classes tell you the phase. In repulsion, *AB* and *ab* are the recombinants.
- **Forgetting the factor of one half.** A chiasma in 30% of meioses gives 15% recombinants, not 30%.
- **Leaving DCOs out of an interval.** Double crossovers are recombinant in both intervals.
- **Adding RFs over long spans without care.** Direct long distance RF misses doubles. Sum short intervals.
- **Mixing counts and frequencies in c.o.c.** Use counts for both, or frequencies for both.

- **Reading RF near 50% as "different chromosomes."** The genes may be far apart on one chromosome.
- **Treating map units as base pairs.** Hotspots, centromeres and sex all change the conversion.
- **Stopping at a LOD of 2.** You need 3 or more. Add more families.

Chapter 4 self-test · ten items

1. A dihybrid testcross gives 43% *Ab*, 43% *aB*, 7% *AB* and 7% *ab*. What was the phase of the dihybrid?

A. Complete linkage in coupling

B. Repulsion, *Ab*/*aB*

C. Unlinked, on two chromosomes

D. Coupling, *AB*/*ab*

B. Repulsion, *Ab*/*aB*. The large classes are the parentals, and they are *Ab* and *aB*. The genes are 14 map units apart.

2. In that same cross, how far apart are the genes?

A. 43 map units

B. 7 map units

C. 86 map units

D. 14 map units

D. 14 map units. RF = 7% + 7% = 14%, which is 14 map units.

3. Why can recombination frequency never be more than 50 percent?

A. One crossover recombines only two of the four chromatids

B. Every chromosome pair is limited to one single crossover each

C. Crossing over happens before DNA replication begins

D. Interference blocks all crossovers past 50 map units

A. One crossover recombines only two of the four chromatids. Crossing over happens at the four strand stage. Even very frequent crossing over leaves odd and even numbers of exchanges equally likely, so recombinants approach half.

4. A testcross of a dihybrid gives 300 offspring with $\chi^2 = 17.5$ against 1:1:1:1. What do you conclude?

A. Fail to reject, so the genes are on two chromosomes

B. Reject independent assortment, so the genes are linked

C. Reject, but only at df 1 with a critical value of 3.841

D. Fail to reject, since the value is below 3 × 7.815

B. Reject independent assortment, so the genes are linked. Four classes give df 3 and a critical value of 7.815. Since 17.5 is far higher, the deviation is not chance, which points to linkage.

5. In a three point cross the parentals are *a* + + and + *b c*, and the doubles are *a b* + and + + *c*. Which gene is in the middle?

A. Cannot tell

B. *c*

C. *b*

D. *a*

C. *b*. Compare *a* + + with *a b* +. Only the *b* gene differs, so *b* sits between *a* and *c*.

6. Two intervals are 0.20 and 0.10. Among 1,000 offspring, 14 double crossovers are seen. What is the interference?

A 0.14

B 0.02

C 0.70

D 0.30

D. 0.30. Expected = 0.20 × 0.10 × 1,000 = 20. c.o.c. = 14 ÷ 20 = 0.70, so I = 1 − 0.70 = 0.30.

7. What does a coefficient of coincidence of 1 mean?

A Crossovers in the two intervals are independent

B The two genes are on different chromosomes

C No double crossovers at all occurred in the cross

D Every crossover blocked a second crossover

A. Crossovers in the two intervals are independent. c.o.c. = 1 means observed doubles equal the expected product, so interference is zero.

8. Which statement about Haldane's mapping function is true?

A It is valid only for genes that are over 50 cM apart

B It assumes strong interference over short distances

C It always gives a map distance smaller than the RF

D It assumes crossovers fall at random, with no interference

D. It assumes crossovers fall at random, with no interference. Haldane uses a Poisson model of random crossovers. Kosambi is the one that allows interference. Both give distances at least as large as r.

9. Two families give LOD scores of 1.8 and 1.5 at θ = 0.1. What is the combined evidence?

A. LOD 1.65, the mean of the two

B. They cannot be combined at all

C. LOD 3.3, enough to accept linkage

D. LOD 2.7, the product of the two

C. LOD 3.3, enough to accept linkage. LOD scores from independent families add at the same θ. 1.8 + 1.5 = 3.3, which passes the threshold of 3.

10. Why can a SNP that does not cause a disease still flag it in a GWAS?

A. It changes the recombination rate near the disease gene

B. It sits in linkage disequilibrium with a nearby causal variant

C. It is typed only in families with many informative meioses

D. It always lies inside the coding region of the gene

B. It sits in linkage disequilibrium with a nearby causal variant. Nearby alleles stay associated for many generations. A marker SNP can travel with the causal variant on a shared haplotype.

Read the full chapter: Chapter 4 · Linkage and Genetic Mapping

ONE PAGE

Cram sheet

Everything from chapters 3 and 4 in one place. Cover the right column and see if you can rebuild each row.

Chapter 3 rules

Topic	Rule
Heterogametic sex	XY male in mammals and flies; ZW female in birds; haploid male in bees
Mammal sex	SRY on the Y turns on *SOX9*: testis. 45,X female; 47,XXY male
Fly sex	X:A ratio. 1.0 female, 0.5 male. XXY female, XO sterile male
X linked recessive	mostly males; no father to son; daughters of affected men are carriers; males q, females q^2
X linked dominant	affected father to all daughters, no sons; females about twice as often
Y linked	father to every son, never daughters
Dosage compensation	mammals silence one X; flies double male X; worms halve both
X inactivation	XIST in cis; random, clonal; Barr bodies = X − 1; about 15% escape
Sex influenced	autosomal; heterozygote differs by sex; F_2 3:1 versus 1:3
Sex limited	autosomal; shows in one sex only
mtDNA	16,569 bp; 37 genes (13 proteins, 22 tRNA, 2 rRNA); maternal; heteroplasmy, bottleneck, threshold
Maternal effect	mother's nuclear genotype sets phenotype; ratio one generation late
Imprinting	germ line methylation; paternal 15q loss: Prader Willi; maternal loss: Angelman

Chapter 4 formulas

Name	Formula	Note
Recombination frequency	recombinants ÷ total	1% = 1 cM; max 50%
From chiasmata	½ × fraction of meioses with a crossover	factor of one half
Three point interval	(singles + DCOs) ÷ total	add DCOs to both
Expected DCO	$RF_I \times RF_{II} \times$ total	
c.o.c. and I	obs ÷ exp; I = 1 − c.o.c.	positive I is usual
Haldane	$d = -\frac{1}{2} \ln(1 - 2r)$	no interference
Kosambi	$d = \frac{1}{4} \ln[(1 + 2r)/(1 - 2r)]$	with interference
LOD	$\log_{10}[L(\theta) \div L(0.5)]$	≥ 3 linked; ≤ −2 excluded; scores add
Chi square, linkage test	against 1:1:1:1	df 3; critical 7.815

Steps for a three point cross

Step	What to do
1	Pair the eight classes as reciprocals.
2	Largest pair: parentals. Smallest pair: doubles.
3	Find the gene that differs between a parental and its matching double. That is the middle gene.
4	Rewrite classes in true order and sort the singles into the two intervals.
5	Each interval: singles plus doubles, over total. Outside: the sum.
6	Expected doubles, c.o.c. and interference.

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