BIS101 F2013 Lecture 1: Introduction

Welcome to BIS101! Go over syllabus and launch into first (easy) lecture.

Syllabus

On Smartsite, will be updated with lectures, homework, clarifications, new dates, etc.

- **Instructors**
    - **Ross-Ibarra**: evolutionary genetics of maize
    - contact info (email, website, twitter, office hours on board
    - TA introduction, contact info, office hours on board
    - no JRI office hours this week, start 9th (next Thursday)
- **Sections**
    - not required for lecture
    - required for some majors
    - take lecture with this section of the course (002)
- **Course objectives**
    - understand how we get from DNA to phenotype
    - how genes work at the molecular level
    - methods and concepts geneticists use to make conclusions
    - understand how to read genetics papers and evaluate research
    - So next time you hear "the gene for baldness has been discovered" or "scientists discover dark matter of the genome" or read your 23 and me medical profile you'll be better equipped to understand and interpret this information.
    - not interested in memorization
- **Text**
    - required, hard to do course without as ref.
    - 10th edition: John/Sue, Transposable elements, pop and quant gen
    - other editions OK, but don't have nifty new chapters
    - but on reserve
    - readings a good idea -- give background for lecture. you will be responsible for some material in book that is not covered in detail in lecture (e.g. mitosis/meiosis)
    - some book material can skip (e.g. the section on penguins in chapter 6 is really dumb)
- **Lectures**

- note lecture order is not same as book order!
- concepts not memorization (example of midterm Spring 2013 that I couldn't pass)
- my philosophy: appreciate genetics, know general concepts, can look rest up
- lecture will be on chalk board (I'm old school), welcome to record
- lecture notes will be on smartsite, but when i can get to it
- how many know github? welcome to edit/correct my notes!
- if not, but catch an error or can think of better way to explain something, please tell me!

- **Paper discussion**
  - How many have read a scientific paper from the primary research lit?
  - This is gonna be hard for many.
  - 70 minutes lecture, 5-10 minute break, 30 minutes on paper
  - how to read a paper: links on syllabus. don't treat like text. read AT LEAST twice. once get general idea, mark stuff you don't understand. then come back and work through parts you didn't get. don't assume authors are right. goal is to learn to evaluate their results and interpretation.
  - pdfs will be online in resources section of smartsite
  - I will post my annotated version of pdfs online.
- **Grading**
  - Curve based on current highest score. Should work out to be ~50% of class getting B or higher.
- **Exams**
  - i love takehomes. unfortunately...
  - in class, 1 page handwritten
  - let me know ahead of time if you need (and have documented) additional accomodations
- **Quizzes**
  - quiz every day! 5 questions, written by TAs.
  - collaborative -- 1 min. to work with neighbors to answer question
  - turn in your own; bring paper. write student ID. no credit if we don't know who you are
  - only ONE quiz each week will be graded
- **Homework**
  - not required, not graded. solution manual in library on reserve
  - good idea to do, can work through in office hours
- **Academic honesty**

- **Email Policy**

Reading

For Tuesday read ch. 3. Section 3.4 will is relevant for later lecture on quant gen.

Definitions

Lots of vocab today.

❓ Gene (draw example)

- funamental unit of heredity
- definition: a piece of DNA that encodes transcribed sequence and linked regulatory stuff
- regulatory elements. what about regulatory elements far away? (polydactyly example)
- show box/line drawing (make me explain if not clear!)

❓ Locus

- a particular region of DNA of interest
- from chromosome to bp

❓ Allele

- a particular variant at a locus
- examples -- 3 alleles at a gene
    - TE insertion
    - syn bp change
    - frameshift del 1bp
- my locus could be one bp, and have two alleles Adenine or Guanine

❓ Genotype

- alleles at a locus or loci of interest (including whole genome)

❓ Phenotype

- what something looks like (expression, morphology, enzyme atvitiy, behavior, etc.)
- form taken by a trait. e.g. if trait is height phenotype can be tall, short, 145cm, etc

❓ Omes: Genome, transcriptome, proteome, metabolome, etc.

- lots of bad omes: "connectome" -- map of synapses and neurons etc.

Organization & Ploidy

Organization

Genes not islands, but linked together along chromosomes

- point out "junk" DNA that we'll return to

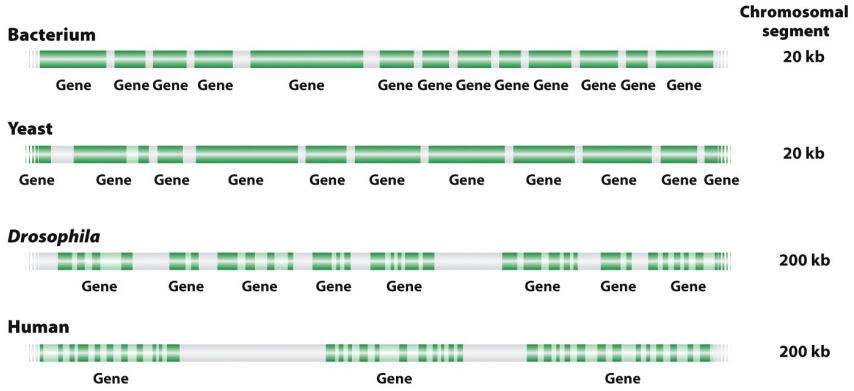

Figure 1-7
Introduction to Genetic Analysis, Tenth Edition
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We will discuss genome organziation more later, but

Genes in DNA -> wrapped around nucleosomes -> organized into chromatin -> chromosomes

Draw chromosome X, show centromere telomere

What does it mean to draw a chromosome like this?

Two identical copies of same chromosome, called **sister chromatids**

But we actually have two different copies of the chromsomes, one from each parent. **homologs** or **homologous chromosomes**

Why 2? Humans are diploid. Meaning ❓

❓ Haploid?

Genotypes and crosses

Crosses are fundamental to lots of genetic analysis, to understand gene action, segregation, dissect genotypes

Often consider **diploid** individuals (but **haploid** bacteria too)

- in diploids two alleles at a locus, written with abbreviations, not always one letter
    - A/a, Bg/Bg etc.

- ❓ define: **heterozygote**, **homozygote**
- **WT** weird term to mean the "normal" allele or phenotype
- origin of variation by mutation: ❓ what's a mutation?
    - any change to the DNA sequence
    - SNP
    - insertion or deletion
    - TE
    - chromosomal change
- **Dominance:** the phenotype of het == phenotype of one hom.
    - Big A ≠ dominant!
    - if we know phenotype, but not genotype, can draw e.g. A/-
    - Bob+/Bob+ == Bob+/Bob-, the gene is **haplosufficient**. If not, **haploinsufficient**.
    - **incomplete dominance** is phenotype is partial
    - **codominance** both alleles show up (we will come back to these)
- **testcross:** cross the dominant phenotype back to recessive homozygote **tester** to test it's genotype
- **backcross:** cross progeny back to parent (example of why plants rule: they don't let us do this in human genetics!)
- **monoybrid cross** cross two indidividuals that are each het for a single locus. dihybrid, trihybrid etc.

Introducing tb1

Teosinte branched 1 is a locus we'll hear about multiple times throughout the course as a good example system.

Also an example of confusing terminology. Here the **WT** is what corn looks like!

We'll define WT allele as tb1-M for maize, and the teosinte allele as tb1-T.

Draw phenotypes of all three genotypes.

❓ Is this dominant? Haplosufficient? : example of incomplete dominance

Mendel's first law

Mendel crossed some peas. Based on lots of careful examinations, lots of statistics, he figured out general rules of inhertiance. We'll see some exceptions, but by and large the dude was right.

❓ First law: equal segregation. Alleles at a locus segregate w/ equal probability. An A_1/A_2 individual will produce 50% A_1 and 50% A_2.

❓ What's the cellular basis for this?

Meiosis

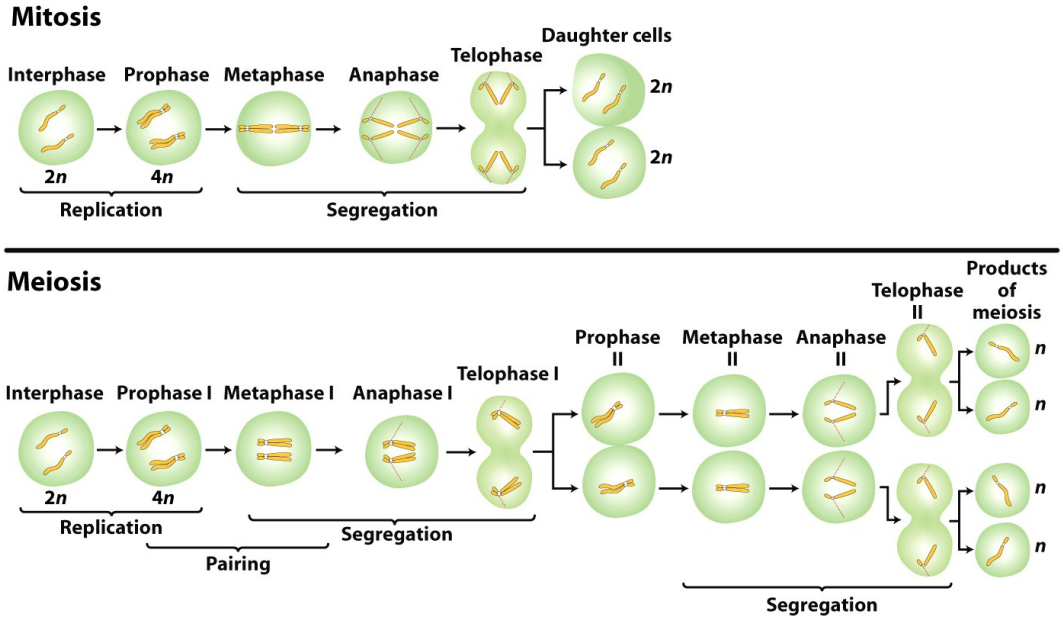

Figure 2-8
Introduction to Genetic Analysis, Tenth Edition

Draw
label loci A1, A2.

Different from mitosis (check out book for differences)

Cross two corn plants

tb1-M/tb1-M x tb1-T/tb1-T * label **parental**, **fileal** generation

* ? are all F1 alike? (yes, at this locus, what about others? unless we know it's inbred line, can't say)

Draw Punnett square for tb1, show phenotypes.

Note phenotype ratios ≠ genotype ratios!!

1:2:1 -> incomplete dominance.

what if tb1-M were dominant?

if tb1-M were recessive?

Redo for CENH3+. Explain recessive lethality. Do Cross. 3:1 dominance. 2:1 lethality!

Example problem:

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In the plant Arabidopsis thaliana, a geneticist is interested in the development
of trichomes (define). A large screen turns up two mutant plants (A and B) that
have no trichomes, and these mutants seem to be potentially useful in studying
trichome development. Each plant is crossed with wild type; in both cases, the
next generation (F1) had normal trichomes. When F1 plants were selfed, the
resulting F2's were as follows:
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Use H1 for WT allele and H2 mutant

Draw hairy WT, and glabrous normal. Show F1. Ask genotpye of F1. ❓ Don't know yet! What if mutant was heterozygous for a dominant mutation and both F1 got WT allele?

Show F2: F2 from mutant A: 602 normal; 198 no trichomes F2 from mutant B: 267 normal; 93 no trichomes.

What does this show❓ Dominance! 3:1 segregation - H1 is dominant to H2

What are genotypes of parents and F1?

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b. Under your explanation to part a, is it possible to confidently predict the
F1 from crossing the original mutant A with the original mutant B?
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Pedigrees

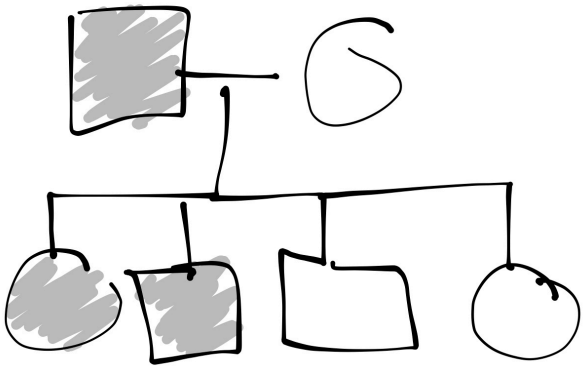
Draw pedigree, w/ male (square) female (circle), offspring.

Affected filled, unaffected empty.

Practice working with these, and calculating probabilities (we'll come back to prob next time).

Exploding ear disorder. Draw simple example: individual affected with WT parents. Ask what is probability that new ofspring would have disease❓ (1/4)

Ch.2 problem 43: Very rare Mendelian disease.



Likely to be dominant, or recessive? Dominant b/c for rece. mom would have to be het and dad homozygote for rare allele.

Other forms of inheritance:

sex linked

Notice reciprocity in crosses above. This doesn't always happen!

Above we have considered non-sex chromosomes, also called **autosomes**

humans have two sex chromosomes X and Y. 1 from each parent, but XX is female, XY male.

- some plants have sex chromosomes! (and sexually transmitted diseases!)
- instead of heterozygote or homozygote we say heterogametic or homogametic
- works same, but genes on X ≠ Y

Drosophila also have XY system

- Draw Punnet square for w+/w+ Drosophila female (red WT) x w male
- Compare to square for red w+ male x w/w/ female (if time permits)
- For both show color, sex of F1 and F2 products

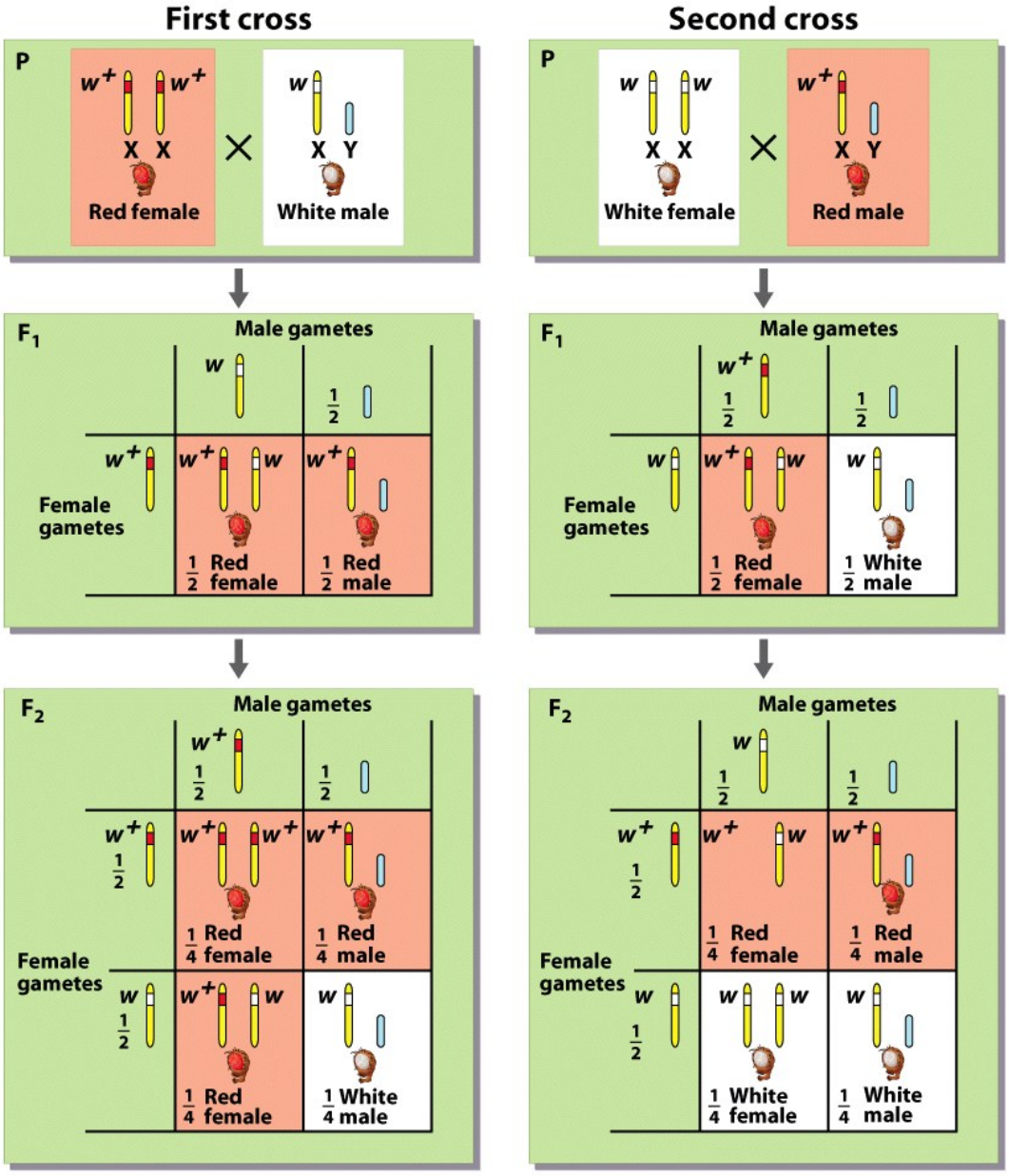


Figure 2-19
Introduction to Genetic Analysis, Tenth Edition

Reciprocal crosses not same for sex-linked traits

Not all F1 will be the same

Ratios not the same because gene is not present on both chromosomes.

organellar

Eukaryotes defined by presence of nucleus and organelles Some phenotypes defined by organellar (Mitochondria and chloroplast) genes.

Endosymbiosis first eukaryotes likely formed as infoldings -> nucleus

both mito and chloro originated as endosymbionts alpha-protobacteria or cyano taken up by archaea * ribulose-1,5-biphosphate caroxylase oxygenase (top left) * needed for photosynthesis, ~50% protein plants * made up of rbcL in chloroplast and rbcS subunit in nucleus

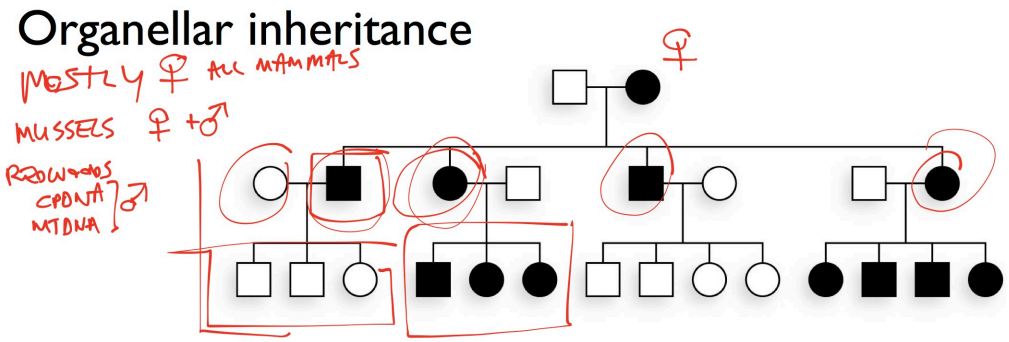
aquisition of mito due to respiration in increasingly oxygenated environ. as oxygen increased in atmosphere -> aerobic respiration a plus

some euks (giardia & some amoeba) have subsequently lost mito

some lineages took up cyanobacteria -> photosynthesize

There are some mitochondrial diseases (some deafness, muscle myopathy)

Mito in mammals -- always maternal



homoplasmy and **heteroplasmy** which helps explain incomplete penetrance

Not always maternal

- redwoods both mito and cp are male
- some pine trees, cpDNA male, mtDNA female
- mussels have double uniparental: F mito is maternal, M mito is paternal