BIS101 F2013 Lecture 4: Genetic Mapping

Reading for next time:

Include Section 3.4 of ch. 3

Notes/Questions?

Recombination

What does independent assortment mean physically ❓

Different chromosomes, or far enough apart that recombination breaks up any correlation. "independent" means no correlation.

Draw AB on two chromosomes. Can you tell me what gamete you get at B locus if I tell you at A locus ❓ (NO)

Draw on one chromosome close together. Now can you tell me ❓ (yes). These loci are linked.

Mendel got lucky or threw away data maybe. Things close together physically are called **linked**.

Biologists working on fruit flies began to discover that things weren't always 100% linked or totally independent. Some genes seemed to move together most but not all the time. This lead to discovery of recombination, and cytological mechanism of which was finally proven in corn.

Maps

Chapter illustrates with comparison of london subway maps the idea that there are two kinds of maps of interest to geneticists (define)

Physical map ❓

- measured in Kb or kilobase pairs (1000bp) or Mb (megabase 10^6 bp)

genetic map

- genetic map is a map of marker or gene order
- ❓ what's a marker?
- any change in DNA that can be assayed — SNP, CNV, etc. -- and give us genotype.
- can phenotype be used as a marker ❓ Sure! b/c it can give us a genotype.
- Fig. 4-13 is great stuff. You might see it again in the future

- not always bigger genetic = bigger physical. why❓
- draw Gore like genetic map

combine the two: if I know genetically my gene is between marker A and B, and I know where A and B are physically -- BAM! I found the piece of DNA where my gene of interest is!

Two-point crosses

Let class pick phenotypes dom/recess @ two genes. Use A1/A2 and B1/B2

I want to know whether they are linked. And if so how close?

Two inbred lines A1A1 B1B1 A2A2 B2B2. (save on board)

F1: A1/A2;B1/B2 (save on board)

Test cross ❓ with F1 (to what?) to A2/A2;B2/B2

Why do test cross❓ lets me figure out what gametes I got from parent.

With no linkage (draw), Mendel tells me I expect to get ❓ 1/4 each of (phenotypes):

- A1/A2;B1/B2 (A1-; B1-)
- A1/A2;B2/B2 (A1-; B2)
- A2/A2;B1/B2 (A2; B1-)
- A2/A2;B2/B2 (A2; B2)

What if they're right next to each other on same piece of DNA (draw, ask phenotypes) ❓ I might see: 1/2 of

- A1/A2;B1/B2 (dominant pheno @ both)
- A2/A2;B2/B2 (recessive pheno @ both)

Linked genes will usually not be so close that recombination impossible. % recombination tells you how close genes are.

Let's say instead these two genes are linked. Take my F1 above and testcross. Why testcross and not F1 self❓

Of 2839 offspring I see (phenotypes)

- 1339 (A1-; B1-)
- 1195 (A2A2; B2B2)
- 154 (A1-;B2B2)
- 151 (A2A2;B1-)

In a two point cross, we can see 2 equal classes (no recombination), 4 equal (free

recombination, no linkage), or 2 common classes at eq. freq. and 2 uncommon at eq. freq.

Common classers are **parental** Why ?> he common are (?) no-crossover or parental classes uncommon are crossover or recombinant classes calculate recombination we add and divide 305/2839 = 10.7% what about different F1 test cross: 1067 gH, 965 Gh, 146 GH, 157 gh which are parental? what's recombination freq. 12.9% about same. what's genotype of F1? G_h/g_H (explain line) what of previous F1? G_H/g_h

Three-point testcross

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why three? find order! w/ two only know distance
go back to Green Hairy, add SF (smelly fruit) locus
I make inbred lines, cross G, H, quiet with white, bald, Loud, make F1
what is the genotype of the F1? G/g; H/h; SF/sf (know phase? yes, know order?
no)
    test cross:  GsfH 580, gSFh 592,  Gsfh 45, gSFH 40, gsfh 89, GSFH 94, gsfH
3, GSFh 5
    can identify parentals as most common (GsfH gSFh)
    can identify double Xovers as least (gsfH, GSFh).
        double Xovers differ by one from parent (draw), so you automatically
know which is in the middle
        here? G so we know order, F1s were sf_G_H / SF_g_h
    now distances:
        if we ignore H, we can do same two-locus combo to find distance between
SF and G -> 13.2% recombo, 13.2 % (draw)
        now ignore SF and do G and H -> 6.4 % (draw)
In a simple world, we'd be done & freq. of double crossovers would be
    0.064 * 0.132 = 0.00845, and of 1448 gametes we expect ~12 double crossover
gametes
    we see 8?  what the heck?
    turns out crossing-over takes physical space, and you can't have two close
to each other.  so having one here makes the chance of having another lower
    we can calculate this chance as interference. simply 1-obs/exp, or in this
case 1-8/12 = 33%
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Linkage mapping higher % recombination = bigger distance apart (in general) can use this plus order from 3-point crosses to build genetic maps of where genes are in relation to each other limited search for candidates Interesting notes about recombination recombination varies along chromosome (draw maize) recombination hotspots (concentrated in few hundred bp)

Mechanism of crossing over

Holliday junction, DSB, heteroduplex, gene conversion.