

Material on Exam 1

Complementation

If the two genes are the same, there is no complementation

If the two genes are different (they are at different loci), there is complementation

Both genes must be recessive

Chi-squared test

$$\chi^2 = \sum_{\text{all classes}} \frac{(O - E)^2}{E}$$

degrees of freedom = # classes - 1

Mapping

$$\text{map distance} = 100 \cdot \frac{\text{crossover gametes}}{\text{total gametes}}$$

Three-Factor Crosses

1. Group recombinant classes into reciprocal pairs.
2. The most frequent pair is the parental class.
3. Derive the gene order from the least frequent pair.
4. For three genes X, Y, Z: frequency(XZ) = frequency(XY) + frequency(YZ) + frequency(double crossovers)

Tetrad Analysis

diploid with 2 copies of each chromosome

PD, T, NPD

For tightly linked genes: distance = $100 \cdot \frac{T}{2\Sigma}$

For linked genes: distance = $100 \cdot \frac{T + 6NPD}{2\Sigma}$ (that is, PD >> NPD)

If PD : T : NPD = 1 : 4 : 1, genes are unlinked

Total crossovers = 4 NPD

3 of 1 and 1 of another is always a tetratype

Phage

Phages are sort of single-stranded

Back to distance = $\frac{\text{recombinants}}{\text{total}} \cdot 100$

Don't forget to think about invisible double null mutants (multiply by 2)

And DNA synthesis runs from 5' to 3' (and that is also how the final mRNA would read).

Cotransduction frequency = $\frac{\# \text{ showing trait}}{\text{total}}$ (expressed as a percentage)

remember that # showing trait is number showing trait linked to Tn5

Material on Exam 2

For the tRNA^{ser} mutation:

	Wildtype	Mutant
DNA template	5 T C G 3	5 T A G 3
DNA antisense	3 A G C 5	3 A T C 5
mRNA	5 U C G 3	5 U A G 3
tRNA^{ser}	3 A G C 5	3 A U C 5

Mutation type	Phenotype	D/R	Cis/Trans
repressor ⁻	constitutive	recessive	trans-acting
activator ⁻	uninducible	recessive	trans-acting
operator ⁻	constitutive	dominant	cis-acting
promoter ⁻	uninducible	recessive	cis-acting
repressor ^{-d}	constitutive	dominant	trans-acting
activator ^s			
repressor ^s	uninducible	dominant	trans-acting
activator ^{-d}			

epistatic to = regulated by

For regulation problems, draw it one way, then reverse the two genes and try to get the same result

As far as I'm concerned, Hfr is totally counterintuitive: genes that the ori_t points to are transferred late and inefficiently, whereas genes that are behind the ori_t are transferred early and efficiently. Whatever.

Material on Exam 3

Transgenes: add genes by pronuclear injection, random insertion

Knockouts: subtract gene, gene targeting, specific insertion with replacement

C57/BL6 pronucleus → BALBc blastocysts → chimera

mate male chimera with BALBc female

genotype black progeny for heterozygotes → mate heterozygotes

Population genetics

$$p = f(A) = f(A/A) + 1/2(A/a)$$

$$q = f(a) = f(a/a) + 1/2(A/a)$$

$$p + q = 1$$

for the next generation, $p^2 + 2pq + q^2 = 1$, and $f(A/A) = p^2$, $f(a/a) = q^2$, $f(A/a) = 2pq$

When mixing of gametes occurs at random, allele frequencies do not change generationally

For HWE, $p^2 + 2pq + q^2 = p + q = 1$

random mating, no new mutations, no selection, no genetic drift, no migration

Mutation and Selection

$$\Delta q_{\text{mut}} = \mu f(A) = \mu p \approx \mu$$

S = selective disadvantage [1-S = fitness]

for recessive disease, $q = \sqrt{\frac{\mu}{S}}$ because $\mu = Sq^2$

for dominant disease, $\mu = Sq$, so $q = \frac{\mu}{S}$

for balanced polymorphism, h (heterozygote advantage) = Sq , so $q = \frac{h}{S}$

Inbreeding Effects

F = likelihood of homozygosity by descent

for brother-sister matings, $F = \frac{1}{4}$

for first cousin matings, $F = \frac{1}{16}$

$p(\text{affected because of first cousin mating}) = F q$ f(first cousin marriages)

genetic load: lethal equivalents per haploid

Genetic Linkage Analysis

θ = hypothetical recombination frequency

$$LOD_{\theta} = \log_{10} \frac{p(\text{data arose if loci linked})}{p(\text{data arose if loci unlinked})}$$

P if linked at $\theta = \frac{1}{2}(P \text{ if phase 1}) + \frac{1}{2}(P \text{ if phase 2})$

P if phase 1 = $[0.5(\text{nonrecombination})]^n \text{ meioses} + [0.5(\text{recombination})]^n \text{ meioses}$

P if unlinked = $\frac{1}{4}^n$ informative meioses

Σ LODs... want score >3.0

Material covered in the last weeks of the class

allelic heterogeneity: multiple alleles in one gene contribute to a disease

non-allelic heterogeneity: multiple genes implicated

r = coefficient of relationship (likelihood two people share a gene by descent)

parent-child: 0.50; brother-sister: 0.50; aunt-niece: 0.25; first cousins: 0.125

concordant sib-pair analysis: find identity by descent for concordant sibs, then chi-squared test

M1 vs M2 nondisjunction: centromere-linked marker (AB in this case)

Proper disjunction A or B

M1 nondisjunction A and B

M2 nondisjunction AA or BB

Post-zygotic will never find 3 different alleles

$p(\text{incorporating uncorrected mismatched base}) = 10^{-10}$ per base pair per replication

HNPCC: inherit one mutation in gene which contributes to mismatch repair (MLH1, PMS2, etc)

mutator phenotype: SSR instability, mutations like crazy

Disease	MZ	DZ	interpretation
Huntington's	100	50	autosomal dominant
sickle cell	100	25	autosomal recessive
measles	97	94	environmental
diabetes	30	6	environment + ~1 gene
heart disease	46	12	environment + ~1 gene