I. Genes *al-1*, *cit-1* and *ilv-2* are all on chromosome 5 in *Neurospora crassa*. Results of a cross where all 3 genes were heterozygous in the diploid gave the following 100 linear asci: (for simplicity, the mutant alleles are shown as a, c and v respectively and the normal alleles as "+"). The numbers of each ascus type (A through I) recovered are shown below the "ascus".

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>G</th>
<th>H</th>
<th>I</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>c</td>
<td>v</td>
<td>a</td>
<td>c</td>
<td>v</td>
<td>a</td>
<td>c</td>
<td>v</td>
<td></td>
</tr>
<tr>
<td>a</td>
<td>c</td>
<td>v</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td>v</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>c</td>
<td>v</td>
<td></td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td>+</td>
<td>a</td>
<td>c</td>
<td>v</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>+</td>
<td>c</td>
<td>v</td>
<td>+</td>
<td>c</td>
<td>v</td>
<td>a</td>
<td>c</td>
<td>v</td>
<td>+</td>
</tr>
<tr>
<td>32</td>
<td>28</td>
<td>3</td>
<td>6</td>
<td>9</td>
<td>12</td>
<td>3</td>
<td>1</td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>

A) What were the genotypes of the two parents?
   a, c, v  X +, +, +

B) How far is each gene from the centromere?
   a: 2 cm   c: 6.5 cm   v: 20 cm

C) Which asci (A, B, C etc) are tetratype for:
   genes a and c?  C, D, I
   genes a and v?  C, D, E, F, G, H, I
   genes c and v?  C, E, F, G, H, I

D) Are there any NPD asci? If so, which one(s).  H for genes a&c

E) Draw a tetrad showing crossovers that could explain ascus H.
II. A series of bacteriophage T4 mutants that could not lyse *E. coli* were isolated. Electron examination of one set of 7 mutants revealed that each formed normal heads but did not assemble tails. All could be "rescued" after lysis by adding a "tail-mix" from a temperature sensitive strain. The 7 were tested in all possible pairwise combinations, by simultaneous infection of *E. coli*, cells which were then spread at $10^7$ per plate in top agar. Results of the pairwise mixtures (5 of each phage per bacterial cell) are shown in the table below, which gives the number of plaques per plate in the lawn, or "+" which indicates complete lysis of the lawn.

<table>
<thead>
<tr>
<th>Mutant</th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>T4</th>
<th>T5</th>
<th>T6</th>
<th>T7</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>3</td>
<td>+</td>
<td>4</td>
<td>3</td>
<td>15</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>T2</td>
<td>4</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>T3</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>T4</td>
<td>0</td>
<td>3</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T5</td>
<td>0</td>
<td>4</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T6</td>
<td>0</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5</td>
</tr>
</tbody>
</table>

A) Which T mutants are point mutations? 1, 2, 5, 7  Deletions 3, 4, 6

B) How many different tail genes are represented in the mutants? 3

C) Which mutations are in the same gene(s)? (1, 3, 4, 5) (2) (6, 7)

D) Is there any indication of recombination of any mutations in the same gene? Explain.
   Yes, T1 X T5 are point mutations in same gene and give more colonies than expect from reverions

E) As best as possible, make a map showing the combined information.
III. About 1 in 20 persons of European descent is heterozygous for cystic fibrosis \((Cf/cf)\) which is still a recessive lethal since homozygous individuals cannot reproduce.

A) Assuming random mating in this population, what frequency of affected \(cf/cf\) children is expected? \(\frac{1}{20} \times \frac{1}{20} \times \frac{1}{4} = \frac{1}{1600}\)

B. What are the frequencies of the \(Cf\) and \(cf\) alleles?

\[ F(cf) = \sqrt{\frac{1}{1600}} = \frac{1}{40} = 0.025 \] (close enough since "about" 1 in 20).

\[ F(Cf) = 1 - 0.025 = 0.975 \]

C) If the \(Cf\) to \(cf\) mutation rate is 100 per million gametes, is this a case where mutation is balanced by selection? Justify your answer.

no: \(\mu = \frac{100}{10^6} = 10^{-4}\); if so \(q^2\) would equal this or 1 in 10,000.

Actual \(q^2\) is 1/1,600

D) It has been speculated that heterozygotes had a selective advantage during times of plague. Assuming the gene frequencies haven’t changed significantly, calculate the selection coefficient \((t)\) against the homozygous \(Cf/Cf\) genotypes that would account for these allele frequencies. Show the formulas you use.

\[ p_{eq} = \frac{s}{s+t}; \ s \ is \ 1 \ and \ p \ is \ 0.975. \] Solving for \(t\) gives 0.026

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E) Now that plague has not been around for about 500 years, (say 25 generations), what forces, if any, are changing the equilibrium? How much has it changed so far (a numerical formula is enough!)

selection against recessive since no longer favor heterozygotes has removed \(cf\) alleles at \(25 = \frac{1}{q_0} - \frac{1}{0.025}\), but mutation has added them at \(p_0(0.9999)^{25}\).

F) Suppose two first cousins (1 set of common grandparents) marry.

a) Draw a path diagram that will allow you to calculate \(F\) for their child and use it to calculate \(F\).

\[ F = \left(\frac{1}{2}\right)^5 + \left(\frac{1}{2}\right)^5 = \frac{1}{16} \]

b) What is the probability they will have a child with cystic fibrosis?

\[ q^2 \ (\text{random}) + pqF \ (\text{inbreeding}) = \frac{1}{1600} + \frac{(0.975)(0.025)}{16} \]
IV. A maize plant (inbred P1) with yellow \((c1c1)\) kernels and homozygous for \(Ac\) 12 map units away is crossed to another yellow kernel plant (inbred P2) without \(Ac\), but which has \(Ds\) elements in the \(c\) locus \((c-m1/c-m1)\). Predict the phenotype of the F1 kernels and of the progeny of the F1 backcrossed to P2.

F1: All will have \(Ac\), causing \(Ds\) to come out of \(c-m1\) giving colored spots

Backcross progeny:

1/2 will have \(Ac\), so these will have colored spots; the 1/2 that do not should still be yellow.

V. A) What is the evidence that gene conversion is not the result of mutation?
- it does not happen in "selfs" and only the alleles that were present in the cross are recovered

B) What is the evidence that gene conversion and recombination are correlated?
- very closely linked flanking markers show recombination in 50% of cases where conversion is detected.

VI. When Curt Stern examined flies heterozygous as shown for linked recessive genes yellow \((y)\) and singed, \((sn)\)

he found some flies with a) twin yellow/singed spots, b) flies with singed spots and c) a few with just yellow spots. Explain how each class arises.

Twin spots are produced by mitotic crossing over (recombination) and chance segregation of the XO arms to the same pole.

a) crossover between centromere and \(y\)
b) crossover between \(y\) and \(sn\)
c) these suggest a DXO in both regions or perhaps conversion + mutation
VII. Chromosome 4 in Drosophila is tiny and has very few genes. Both monosomics and trisomics for chromosome 4 are viable and normal in phenotype if wild type alleles are present. A trisomy-4 male with normal phenotype but recessive "bent" alleles on 2 chromosome-4s (+, b, b) is crossed to a normal monosomy-4 female. (+) Predict the phenotypes and karyotypes in the progeny.

The male will produce gametes with 1 or 2 # 4 chromosomes in the frequency: 2/6 (b, +) : 2/6 (b) : 1/6 (+) : 1/6 (b, b)

Female

<table>
<thead>
<tr>
<th></th>
<th>1 (+)</th>
<th>2/12 b++</th>
<th>2/12b+</th>
<th>1/12++</th>
<th>1/12+bb</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (0)</td>
<td>2/12b+</td>
<td>2/12b</td>
<td>1/12+</td>
<td>1/12bb</td>
<td></td>
</tr>
</tbody>
</table>

Thus the answers are that 3/12 or 1/4 will have bent wing and that the ratio of monsomy4 : disomy4 : trisomy4 will be 3:6:3 (1:2:1)

VIII. Retinoblastoma (Rb) in humans for years was classified as a dominant mutation with about 90% penetrance. What is it in terms of molecular cytogenetics and how is the reduced penetrance explained?

Inherited retinoblastoma generally results from a deletion of the Rb tumor suppressor gene; a somatic mutation in the one remaining copy in developing retinal cells of these individuals will lead to cancer. The reduced penetrance reflects the possibility that in some individuals the somatic mutation will not occur during retina development.

IX. One of the accomplishments reported by the USDA Citrus Laboratory in Florida last year was "Produced several new tetraploid breeding parents". Speculate on the origin of these lines and their potential use.

They likely used colchicine to double chromosome numbers. The tetraploids could be crossed with diploids to create seedless triploid fruits. They also tend to have larger fruits which may be of value.
X. Crosses between two maize inbreds (Tom Thumb X Black Mexican) gave the following results for ear length: (Numbers were adjusted for simplicity.)

<table>
<thead>
<tr>
<th>Population</th>
<th>Average length (cm)</th>
<th>Variance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tom Thumb</td>
<td>6.5</td>
<td>0.6</td>
</tr>
<tr>
<td>Black Mexican</td>
<td>16.6</td>
<td>3.4</td>
</tr>
<tr>
<td>F1</td>
<td>12.1</td>
<td>2.0</td>
</tr>
<tr>
<td>F2</td>
<td>12.8</td>
<td>5.4</td>
</tr>
</tbody>
</table>

a) What are the values for Vt, Ve, & Vg?
Ve can be calculated from inbred parents and F1:average = 2
V_T is 5.4 from the F2 and V_g is V_T - V_e = 3.4
b) Calculate heritability. Is it H^2 or h^2? Explain

it is H^2 = 3.4/5.4 since all types of genetic variation is included in F2

c) How many genes contribute to ear length in this cross?
assuming parents are extremes, N = D^2/8Vg or (10.1)^2/27.2 = 3.75
d) How many phenotypic classes would be expected if Ve was 0?

if we take N = 4, there will be 2N + 1 classes or 9

X. About 0.3% of humans are homoplasmic for a very mild form of LHON caused by a mutation that substitutes an asn for asp in the mitochondrial NADH complex.
a) What are the allele and genotype frequencies for this trait?
This is a mitochondrial trait, so is either present or absent. Thus, the f(LHON) alleles and genotypes = 0.3; F(normal) = 99.7
b) If a eugenics movement decided to eliminate this form of LHON from the population, who would be denied reproduction? How many generations would be required for elimination? What would be the limiting factor in terms of population genetics?

Prevent affected females from mating, for just one generation in theory. However new mutations and segregation from heteroplasmic females would make it a fruitless effort.
XI. Two highly inbred "species" of cats differ by 3 chromosomal aberrations, namely a reciprocal translocation, a paracentric inversion and a pericentric inversion. Matings between the two species produce viable hybrids. A) Use labeled line drawings to show synaptic pairing for the involved chromosomes of the hybrids.

- [Image: paracentric inversion]
- [Image: pericentric inversion]
- [Image: translocation]

B) What factors determine the frequency of viable gametes for each of the aberrations?
   - translocation: alternate versus adjacent segregation
   - paracentric inversion: crossovers within the loop
   - pericentric inversion: crossover inside the loop

C) Predict the fraction of functional gametes for hybrid males and females.
   Each aberration can cause 50% loss of functional gametes (semisterile)
   males: 1 in 8
   females: bridges from pericentric shunted into polar bodies, so 1 in 4

D) One of the aberrations leads to "isochromosomes", in which both arms of a bi-armed chromosome have the same set of genes. Use your answer to part A to point out how this is most likely to occur.
   (XO near centromere in pericentric inversion)
XII. Recombinant Inbred (RI) populations are especially useful for mapping genes and QTLs since the same population can be used over and over. What fraction of the genes heterozygous in the F1 would still be heterozygous:

a) after 7 generations of selfing to produce a sorghum RI population?  
selfing eliminates 1/2 of the heterozygosity each generation, so $\left(\frac{1}{2}\right)^7$

b) after 7 generations of sib matings to produce a mouse RI population?  
sib matings, $F=1/4$ so $\left(\frac{3}{4}\right)^7$ of the original variation remains after 7 generations.

XIII Cancer eye in cattle is an autosomal recessive (ee) that is often not detected until after reproduction and may not show up in animals that get little sun exposure. If 4% of a cattle herd that has been maintained by random mating are affected:

a) What is the expected frequency of the E and e alleles in this population?  
$q = F(e) = \text{square root of } 0.04 = 0.2$, so $p = F(E) = 0.8$

b) What genotypic frequency is expected in this herd?  
$64EE : 32Ee : 4ee \ (p^2 + 2pq + q^2)$

c) Assume that a molecular tag now allows identification of the E and e alleles.  
Rancher 1 decides to have the animals tested and eliminate all those that are ee from his herd. What will the frequency of the alleles be in the next generation?  
He will have 64 EE and 32 Ee, so $p = (128 +32)/(2X96) = 0.833 \ (= 5/6)$ and $q=0.1667$

Rancher 2 decides to eliminate all Ee and ee males but feels he cannot afford to eliminate any females. What will be he effect of his selective breeding on the allele frequencies in the next generation?  
Female eggs 0.8 E | 0.2 e  
Male sperm 1 E 0.8EE | 0.2Ee  so $P = 0.9$ and $q = 0.1$

If the second rancher then returns to a random mating scheme, what will be the genetic makeup of the resulting herd?  
$81 \ EE : 18 \ Ee : 1 \ ee$
XIV. Make a drawing that explains how $h^2$ can be calculated based on the results of selection.

realized gain is a measure of $h^2$

XV. Which are more complex, immunoglobin light chain or heavy chain genes? Justify your answer.

Heavy, since they contain diversity (D) segments absent in Light chains and also have multiple C regions expressed during class-switching

XVI. The concordance for psoriasis in monozygotic twins is 65 to 70% compared to 15 to 20% in dizygotic twins. Streptococcal infection and stress have been implicated as factors. Certain HLA alleles are associated with increased risk, and in some pedigrees, genes for susceptibility have been mapped to different chromosomes. How will you respond when someone asks you if they are likely to have psoriasis?

Both genes (high concordance when gene are the same and mapping of multiple susceptibility loci) and environment play a role. If it is common in their family, they are at increased risk, but worrying won't help!