Solved Bi 110 assignment ✔

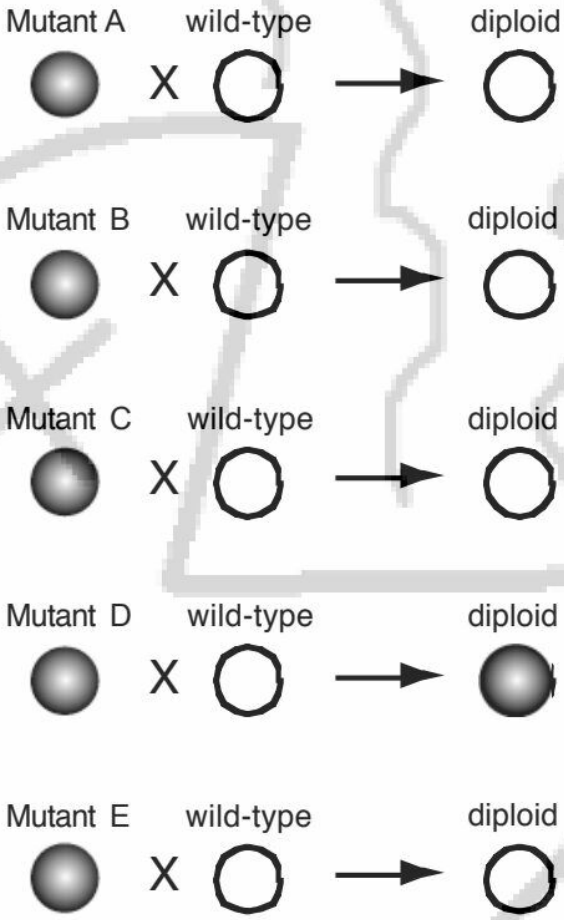
Totoz Collection

THE COPPERBELT UNIVERSITY

Bi111 Assignment 1

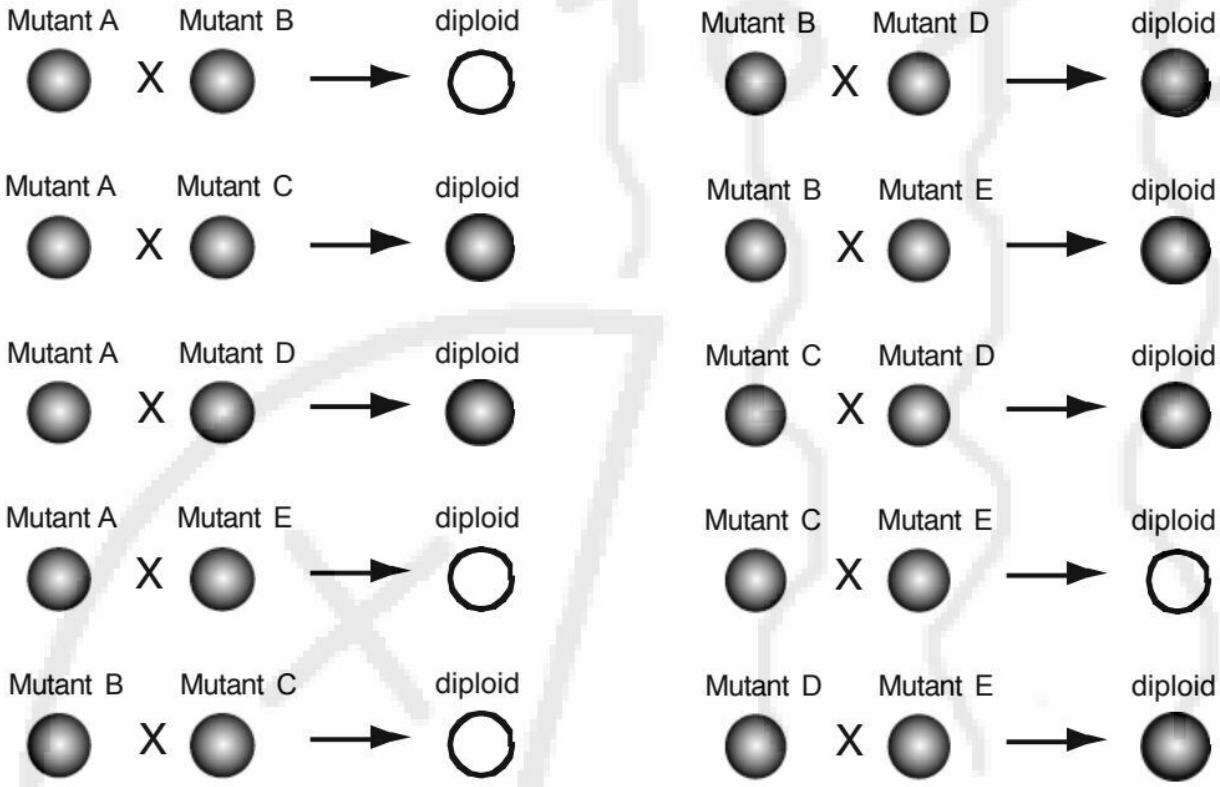
Due before 16hrs on Tuesday, January 30, 2024.

1. Mr. Chimweka, the laboratory Assistant, put aside a set of five yeast mutants. These mutants appear to form dark red colonies and not the usual white colonies of wild-type yeast. Mr. Chimweka later crossed each of the mutants to a wild-type haploid strain and obtain he the results shown below:



(a) What do these results tell you about each of the mutants?

(b) Mr. Chimweka later crossd every haploid mutant strain to a different haploid mutant of the opposite mating type. Help Mr. Chimweka deduce as much as possible about which mutations lie in the same gene. Help him by clearly stating any remaining ambiguities and suggest some general ways that the ambiguities might be resolved.


Mutant A
Mutant B
diploid
Mutant A
Mutant C
diploid
Mutant A
Mutant D
diploid
Mutant A
Mutant E
diploid
Mutant B
Mutant C
diploid
Mutant B
Mutant D
diploid
Mutant B
Mutant E
diploid
Mutant C
Mutant D
diploid
Mutant C
Mutant E
diploid
Mutant D
Mutant E
diploid

2. In this question we will consider the interaction of selection and inbreeding in determining the incidence of autosomal recessive diseases. Consider a gene in which recessive mutations occur at a rate of 10^{-5}. Assume a selective disadvantage S of 0.4 in homozygotes for the recessive allele.

In answering the various parts of this question, show your calculations (unless none are required), and state any additional simplifying assumptions that you employ.

(a) Calculate q, the frequency of the recessive allele. Also calculate the incidence of the disease. Assume random mating.

(b) Now assume that, for thousands of generations, 10% of all children have been products of first-cousin matings (the remaining 90% being products of random matings). Calculate the steady-state value of q. Also calculate the incidence of the disease at steady state. (Hint: first modify the equation $\Delta q_{sel} = - Sq^2$ [from lecture 26] to reflect inbreeding's effects on the incidence of homozygotes for the recessive allele.)

(c) Now assume that the population described in part **(b)** suddenly and completely ceases all inbreeding. Calculate the incidence of disease in the first generation conceived with no inbreeding.

(d) Would q be expected to rise, fall, or remain unchanged during the first 10 generations after the cessation of inbreeding described in part **(c)**? Briefly justify your answer. (No calculations needed.) What numerical value would q approach after thousands of generations with no inbreeding?

Further Reading:
Genetics: Analysis and Principles, Robert Booker
Principles of Genetics, Gardner
Human Genetics concepts and application, Ricki Lewis
Genetics: A Molecular Approach,T. A. Brown
Concept of Genetics, Klug
Genetics: A conceptual Approach, Pierce
An introduction to Genetic Analysis, Griffiths
Theory and Problems of Genetics, Stansfield.
Genetics: Analysis of Genes and Genomes , Hartl and Rubolo

QUESTION 1

a) Crossing each yeast haploid mutant to wild-type will help you to determine if the mutant is recessive or dominant to wild-type. If the diploid is wild-type phenotype, then the mutation is recessive to wild-type. If the diploid is mutant phenotype, then the mutation is dominant to wild-type. Therefore from results depicted, mutants A, B, C and E are recessive to wild-type while the mutant D is dominant to wild-type.

b) These crosses are termed to be complementation tests as they are aiding us to know whether the two mutants crossed have mutations in the same gene or in different genes. Mutations that fail to restore normal function when combined (resulting in offspring displaying a mutant phenotype) are considered to belong to the same complementation group, indicating that they are located within the same gene.Based on non-complementation of the recessive mutations, we can conclude the following

- ✓ mutations B and E form a complementation group and are mutations in same gene (gene 1).
- ✓ mutants A and C form a second complementation group and are mutations in the second gene (gene 2).
- ✓ We are unable to determine whether mutant 4 represents a mutation in a new gene or a mutation in one of the other two genes because it is a dominant mutation.

The first ambiguity is whether mutant 4 has a mutation in gene 1 or 2, or whether it represents a unique gene. To determine this, you would cross mutant 4 to one mutant from each of the two complementation groups, generating a diploid. You would then generate spores and look at the segregation pattern of the white/red phenotypes in the resulting haploids. If any of the haploids form white wild-type colonies, then gene 4 is not likely to be in the same gene as the mutant it was crossed with because a crossover is likely to have occurred.

QUESTION 2

a) Given μ and S we can calculate q using the equation;

$$q = \sqrt{\frac{\mu}{s}}$$

$$q = \sqrt{\frac{10^{-5}}{0.4}}$$

$$\mathbf{q = 0.005}$$

The incidence of the disease in the population would be;

$$q^2 = (0.005)^2$$

$$\mathbf{q^2 = 2.5 \times 10^{-5}}$$

therefore, one in forty thousand people would be affected by the disease.

b) At steady state, $\Delta q = 0$, and $\Delta q_{sel} = \Delta q_{mut}$.

Let us call the number of affected people n_h^{total} , which is the sum of homozygotes arising from inbreeding and from random mating. The number of homozygotes arising from inbreeding are described by the equation:

$$n_h^{inbreeding} = Fq$$

where **q** is the allele frequency and **F** is the inbreeding coefficient. The number of homozygotes arising from random mating is described by the familiar random equation:

$$n_h^{random} = q^2$$

Adding the respective weights, as random mating corresponds to 90% and cousin marriage corresponds to 10% of the mating, we get a final equation of:

$$n_h^{total} = \frac{90\%}{100\%}(n_h^{random}) + \frac{10\%}{100\%}(n_h^{inbreeding})$$

$$n_h^{total} = 0.9n_h^{random} + 0.1n_h^{inbreeding}$$

$$n_h^{total} = 0.9q^2 + 0.1Fq$$

We plug this modified in the n_h^{total} , into the Δq_{sel} equation to get

$$\Delta q = -S(0.9q^2 + 0.1Fq)$$

Setting this equal to $\Delta q_{mut} = \mu = 10^{-5}$ and plugging in values for F and S, we get a final equation:

$$\Delta q = \Delta q_{mut} - \Delta q_{sel} = \mu - S(0.9q^2 + 0.1Fq) = 0$$

$$10^{-5} - 0.4[0.9q^2 + 0.1(^1/_{16})q] = 0$$

$$10^{-5} - 0.36q^2 - 0.0025q = 0$$

$$-0.36q^2 - 0.0025q + 10^{-5} = 0$$

$$q = \frac{-b \pm \sqrt{b^2 - 4ac}}{2a}$$

$$q = \frac{-(-0.0025) \pm \sqrt{(-0.0025)^2 - 4(-0.36)(10^{-5})}}{2(-0.36)}$$

$$q = \frac{0.0025 \pm \sqrt{0.00002065}}{-0.72}$$

$$q = \frac{0.0025 \pm 0.004544227}{-0.72}$$

$$\mathbf{q = 0.002839} \quad \text{or} \quad \mathbf{q = -0.009784}$$

As we cannot have negative allele frequencies, final answer is q = 0.00284.

To find the incidence of the disease, we plug in our q value into

$$n_h^{total} = 0.9q^2 + 0.1Fq$$

$$n_h^{total} = 0.9(0.0028)^2 + 0.1(^1/_{16})(0.00284)$$

$$n_h^{total} = 0.000025009 = \mathbf{2.5 \times 10^{-5}}$$

This is the same number obtained due to random mating

c) The allele frequency can be calculated by

$$q_{new} = q_{old} + \Delta q \approx q, \text{ after one generation}$$
$$\Delta q = -Sq^2 + \mu = -0.4q^2 + 10^{-5}$$

Assuming that our inbred population was at steady-state, we can use a q = 0.00284 , giving us

$$\Delta q = -0.4(0.00284)^2 + 10^{-5} = 6.77 \times\times 10^{-6}$$

$$q_{new} = 0.00284 + 6.77 \times 10^{-6} = 0.00285$$

$$q_{new}^2 = (0.00285)^2 = 8.104 \times 10^{-6}$$

Incidence of disease right after cessation of inbreeding is approximately one in 125,000. This is much lower than at Hardy-Weinberg equilibrium.

d) The allele frequency would be expected to rise after cessation of inbreeding until q=0.005. This is due to the fact that the mutation rate is creating more alleles than are being selected out in the population. The allele frequency, q, approaches 0.005 as time approaches infinity.