Bio-Math Strategies
(sample for Chapter 3)

This document is an instructor's guide and resource for the Bio-Math Explorations in ICB. The following characteristics of each BME are summarized below the title.

Goal: why this BME is useful for understanding the biological information.

Prerequisites: what mathematical skills students need to be able to understand the BME.

Difficulty Level: On a scale from 1 to 5, how difficult this BME is expected to be for most students (1 = very easy, 2 = fairly easy, 3 = moderate, 4 = fairly difficult, and 5 = very difficult). Because students may find BME's more or less difficult for different reasons, some justification for the difficulty level is provided.

Special Features: Many BME's are linked with Excel files. Some BME's reference interactive web pages. These supplementary resources that allow students to experiment with the data and concepts explained in the BME.

Stages: Instructors may wish to cover less than the entire BME, due to time constraints or difficulty that builds over the course of the BME. Stages help the instructor find appropriate stopping places within each BME.

Following this summary information are solutions to BME IQ's, in addition to supplementary figures and text to help instructors explain the concepts in the BME and the BME IQ's.

BME 3.1: A Mathematical Model of Cell Growth

Goal: Understand and interpret the distribution of cell volumes in Figure 3.1 to discover an important fact about *E. coli* cell growth.

Prerequisites: Basic arithmetic, proportion, area of a triangle.

Difficulty Level: 2 (application of basic math concepts to building a mathematical model, application and interpretation of the new concept of a frequency function)

Special Features: Excel implementation allows students to experiment with the model.

Stages: (1) Understanding the frequency function, (2) Building a mathematical model that matches experimental data, (3) Applying the model to infer that growth rate depends on volume.

*Supplementary information and solutions to BME Integrating Questions*:

A histogram for these same data might look like this:

Cell Volume Distribution
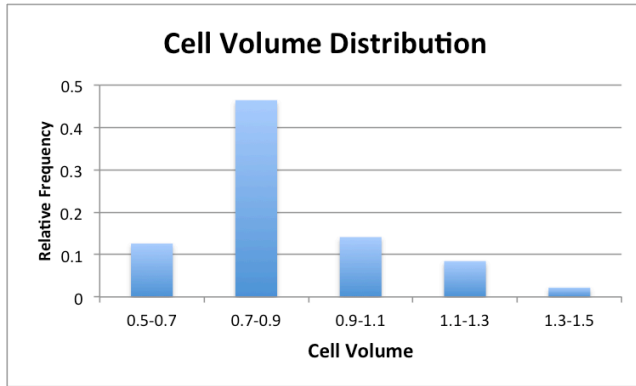
In a histogram, the proportion of cells in one of the chosen volume ranges is easy to determine by simply reading the height of the bar. For example, in this histogram, you can see that about 12% of the cells are between 0.5 and 0.67 µm³.

BME IQ 3.1a: The triangles needed to compute the proportions are shown below. Because these three ranges cover nearly the entire range of volumes, the proportions should add to nearly 1. In any frequency function, the area under the curve over the entire range of values on the horizontal axis should always be 1, because the area represents cumulative proportion.

A = ½*0.2*2.75 = 0.275

A = ½*0.3*2.75 = 0.4125

A = ½*0.5*0.6 = 0.15
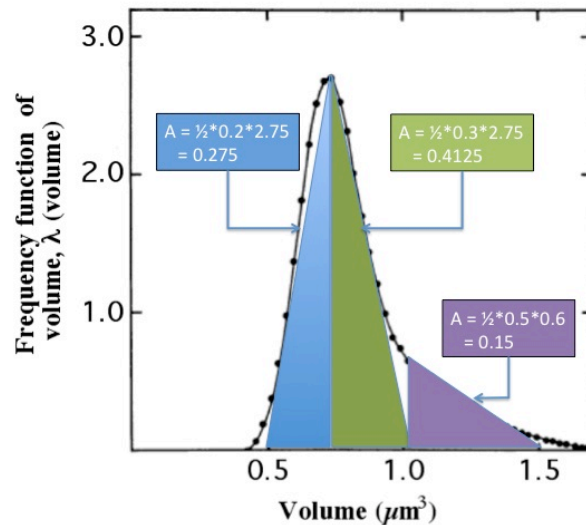
BME IQ 3.1b: A histogram is easier to read, but the person who makes the histogram makes all the choices of how to display the data. In a frequency function, the reader can calculate the percentage of cells in any range of volumes. For example, using the method described in the BME, the reader can compute the proportion of cells between 0.5 and 0.7, as shown here, or in the smaller interval between 0.5 and 0.6, or the even smaller interval between 0.5 and 0.55. So the frequency function is more powerful, but calculating areas is tedious, and the histogram saves the reader from doing this work.

BME IQ 3.1c: The curve produced by the model, shown below, is close to the same shape as the curve in Figure 3.1. The minor differences are caused by primarily by the fact that the model is discrete, rather than continuous, so there are "jumps" in values that the actual volumes do not exhibit.
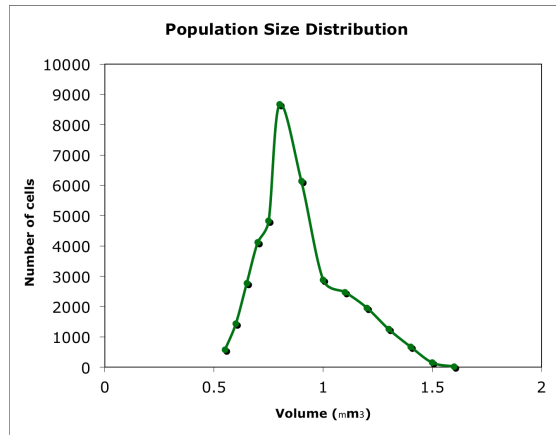
BME IQ 3.1d: Growth rates are a constant 0.024 μm^3 per minute for cell volumes up to 0.8 μm^3. This translates to $0.024/6 = 0.004$ μm^3 per 10 second time step. If cells are uniformly spread across the various volumes in an interval, then 0.004 divided by the size of the interval will be the proportion of cells that grow out of the interval. This explains how the proportions in line 6 of the spreadsheet are calculated. As the volume increases from 0.8 μm^3, the growth rates increase to 0.03, for one interval, then to 0.06 (nearly triple the rate of 0.024 for the smallest volumes) for volumes between 1.0 and 1.6 μm^3.

The cell division rates follow a similar pattern, but the peak in growth rate occurs just before the peak in the cell division rate. Specifically, the proportion of cells in each category that divide is 0 until the cells reach 1.1 μm^3, at which point the proportion gradually increases up to 0.5.

BME IQ 3.1e: Changing the growth rate to a constant 0.04 μm^3 across all volume categories produces a very different shape distribution curve. The new curve, with the original in light grey, is shown below.
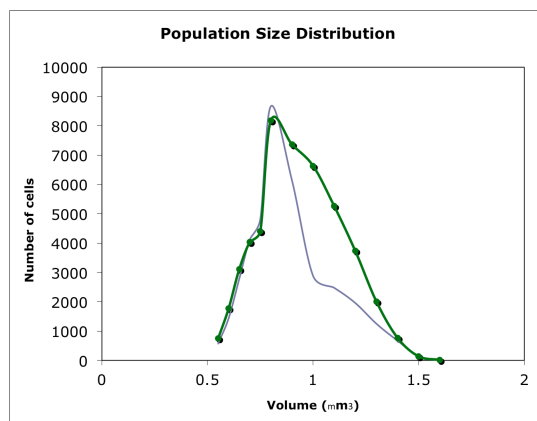
BME 3.2: How much variation is there in random mating outcomes?

    Goal: Understand the random variation in genetic data, illustrating the importance of Mendel's choice to isolate one trait at a time, and count large samples of peas.

    Prerequisites: Read and interpret a histogram, change values in a spreadsheet.

    Difficulty Level: 1 (enter values in spreadsheet and describe what you observe, no calculations, no new concepts, no dependence on previous concepts)

    Special Features: Excel simulation allows students to experiment with random mating of heterozygotes.

   *Stages*: This BME is short and consists of only one stage.

Supplementary information and solutions to BME Integrating Questions:

There will typically be more yellow than green peas in this simulation, because the probability that a pea has at least one dominant allele is 0.75, and therefore each pea is much more likely to be yellow than it is to be green. Because ¾ of the peas are expected to be yellow, and ¼ are expected to be green, the average yellow:green ratio should be about 3, but the average varies wildly for small number of peas. For example, when there are 19 peas, don't be surprised if you see yellow:green ratios as small as 0.9 (9 yellow and 10 green) or as large as 8.5 (18 yellow and 2 green) or even 19 (19 yellow and 1 green).

BME IQ 3.2a: A typical histogram resulting from counting the smallest number of peas (19) from a plant in Table 3.4 is shown here. The smaller numbers of peas tend to have histograms that are fairly flat and spread out over a large number of values on the horizontal axis.

Histogram of observed yellow:green ratios in 1000 trials
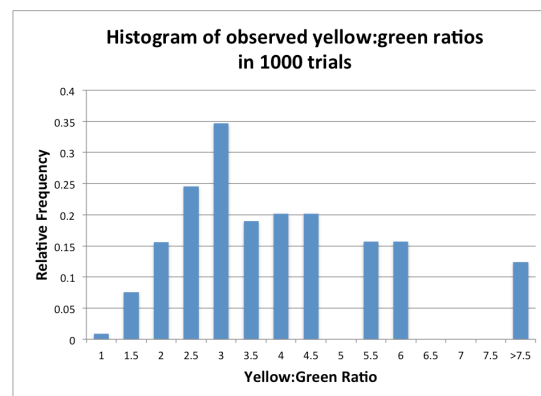
Typical histograms resulting from counting the largest number of peas (97) from a plant in Table 3.4, and from the total number of peas (478) is shown below. The larger numbers of peas tend to produce histograms that are narrower and more peaked near the expected yellow:green ratio of 3.
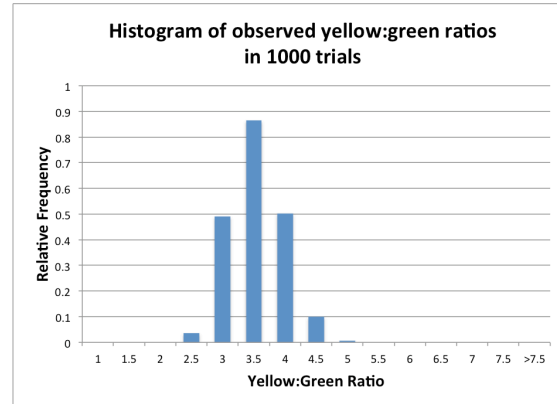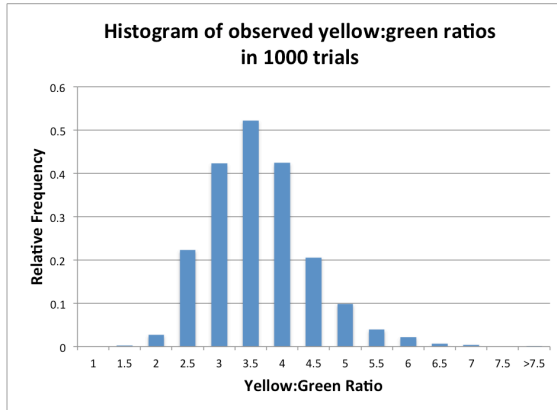
BME 3.3: What are the chances?

Goal: Learn the basic rules for when you can add and multiply probabilities to find the probability of particular genotypes and derive the 3:1 expected phenotype ratio. The rules explained in this BME will be used again in the text, in particular in BME 3.4 and BME 6.3.

Prerequisites: Basic arithmetic, and understanding of genetics terms and concepts.

Difficulty Level: 3 (the calculations are simple, but the concepts of independent and mutually exclusive events are somewhat sophisticated, and some IQ's require combinations of new rules explained in this BME)

Special Features: This BME is self-contained and requires only pencil-and-paper calculations.

Stages: (1) Finding the probability of a particular mating outcome, which requires the multiplication rule for independent events, (2) Finding the probability of a set of mating outcomes (such as those which lead to expression of the dominant trait, or those that imply heterozygosity or homozygosity), which requires the addition rule for mutually exclusive events.

Supplementary information and solutions to BME Integrating Questions:

Students often confuse the concepts of independence and mutually exclusive because the common language of both terms sound like the events "have nothing to do with each other." To help clarify the difference, it may be useful to point out that mutually exclusive events are as far from independent as you can get. If A and B are mutually exclusive, then knowing that event A has occurred means that event B is **impossible**. But for A and B to be independent, knowing that event A has occurred

should have no effect on the occurrence of event B. But making another event impossible is certainly a huge effect! Almost all genetics probability problems deal with independent events, because they are considering different alleles that are assumed to assort independently. However, many problems consider situations that are not mutually exclusive, such as the event of getting a Y from the pollen or a Y from the egg.

BME IQ 3.3a: P(yy) = ½ x ½ = ¼. P(Yy) = ½ x ½ = ¼. P(yY) = ½ x ½ = ¼.

BME IQ 3.3b: The probability of flipping heads on both the nickel and the dime is the probability of flipping heads on the nickel, multiplied by the probability of flipping heads on the dime. That is, P(HH) = ½ x ½ = ¼. The nickel represents the pollen, the dime represents the egg, and flipping the coin represents choosing an allele with a 50-50 chance of getting either one. For example, flipping heads can represent getting the Y allele.

BME IQ 3.3c: P(homozygous) = P(YY) + P(yy) = ¼ + ¼ = ½. P(heterozygous) = P(Yy) + P(yY) = ¼ + ¼ = ½. Homozygosity is analogous to flipping the same way on both coins (either both heads or both tails). Heterozygosity is analogous to flipping opposite faces on the two coins.

BME IQ 3.3d: P(yellow) = P(YY) + P(Yy) + P(yY) = ¼ + ¼ + ¼ = ¾. Even though you want the probability of getting Y from the pollen or Y from the egg, you cannot just add these two probabilities because these are not mutually exclusive events (it is possible to get Y from the pollen <u>and</u> Y from the egg). Also, the sum of these probabilities is 1, which means that the outcome is certain. The analogous outcome with coins is that you flip at least one heads when you flip both a nickel and a dime.

BME IQ 3.3e: For an F_3 pea to be heterozygous, it must be a heterozygous outcome from the self-fertilization of a heterozygous parent in the F_2 generation. This is a combination of an event in the F_2 generation *and* the F_3 generation. Since half of the F_2 peas are heterozygous, the probability in the F_2 generation is ½. The probability that the F2 heterozygote produced a heterozygous offspring in the F_3 generation is also ½. Therefore, the probability that a randomly chosen pea in the F3 generation is heterozygous is ½ x ½ = ¼. These peas are 6 of the 12 yellow peas in the rightmost block of peas in Figure 3.15.

BME IQ 3.3f: There are two mutually exclusive ways for an F_3 pea to be yy. One is that the F_2 parent is yy, in which case the F_3 offspring is guaranteed to be yy. Therefore the probability of this way of being yy in the F_3 generation is ½ x 1 = ½. The other way is that the F_2 parent is heterozygous, in which case the F_3 offspring is yy with probability ¼. Therefore, the probability of this way of being yy in the F_3 generation is ½ x ¼ = 1/8. Adding the probabilities of these two mutually exclusive events gives the desired probability: ½ + 1/8 = 3/8. In Figure 3.15, you can see that 3 out of 8 columns, or 3/8 of the F_3 peas, are true-breeding green peas.

BME 3.4: How many genotypes and phenotypes are there?

> *Goal*: Develop formulas for counting the number of genotypes and phenotypes in a Punnett square using the multiplication principle, rather than drawing the square and counting the boxes with each genotype and phenotype.
>
> *Prerequisites*: Multiplication principle from BME 1.1, multiplication rule for probability from BME 3.3.
>
> *Difficulty Level:* 1 (stage 1) – 3 (stage 3)
>
> *Special Features*: This BME is self-contained and requires only pencil-and-paper calculations.
>
> *Stages*: (1) Calculate the size of a Punnett square, (2) Calculate the number of possible progeny genotypes, (3) Calculate the number of possible progeny phenotypes, and find their relative frequencies to derive the famous 9:3:3:1 ratio, and extend this result to a trihybrid cross.

Supplementary information and solutions to BME Integrating Questions:

These formulas are an alternative way to discover the 9:3:3:1 ratio of phenotypes in a dihybrid cross, with the advantage that they immediately extend to the trihybrid cross, or even a cross of parents that are heterozygous at 7 traits.

BME IQ 3.4a: Considering a third trait to be the height, in which tall is dominant, each gamete can be one of 8 genotypes: YST, YSt, YsT, Yst, yST, ySt, ysT, yst. To calculate this number using the multiplication principle, note that each trait can be one of two alleles, so you can multiply the possibilities for each trait in turn: 2 x 2 x 2 = 2^3 = 8.

BME IQ 3.4b: When the parents are heterozygous for 7 traits, the multiplication principle says there are 2 x 2 x 2 x 2 x 2 x 2 x 2 = 2^7 = 128 possible genotypes for each gamete. In general, when the parents are heterozygous for n traits, there are 2^n possible genotypes for each gamete.

BME IQ 3.4c: There are 8 x 8 = 64 boxes in the Punnett square when the parents are heterozygous for 3 traits. For 7 traits, the number is 128 x 128 = 16,384. In general, for n traits, there are 2^n x 2^n = 2^{2n} = 4^n boxes in the Punnett square.

BME IQ 3.4d: YYSS, YYSs, YYss, YySS, YySs, Yyss, yySS, yySs, yyss.

BME IQ 3.4e: In a trihybrid cross, there are 3 x 3 x 3 = 3^3 = 27 possible progeny genotypes. They are:

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YYSSTT, YYSSTt, YYSStt,
YYSsTT, YYSsTt, YYSstt,
YYssTT, YYssTt, YYsstt,
YySSTT, YySSTt, YySStt,
YySsTT, YySsTt, YySstt,
YyssTT, YyssTt, Yysstt,
yySSTT, yySSTt, yySStt,
yySsTT, yySsTt, yySstt,
yyssTT, yyssTt, yysstt
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BME 3.4f: In a trihybrid cross, there are 2 x 2 x 2 = 2^3 = 8 possible progeny phenotypes. Three of them are dominant for two traits (*e.g.,* seed color and seed form, seed color and stem height, seed form and stem height). Three of them are dominant for one of the three traits (*e.g.,* seed color only, seed form only, and stem height only).

BME 3.4g: The probability that a pea is dominant for all three traits is ¾ x ¾ x ¾ = 27/64. There is only one such phenotype. The probability that a pea is dominant for exactly two of the three traits is ¾ x ¾ x ¼ = 9/64. There are three phenotypes like this (see BME 3.4f). The probability that a pea is dominant for exactly one of the three traits is ¾ x ¼ x ¼ = 3/64. There are three phenotypes like this (see BME 3.4f). Finally, the probability that a pea is recessive for all three traits is ¼ x ¼ x ¼ = 1/64. Therefore, the set of ratios for the 8 different phenotypes is: 27:9:9:9:3:3:3:1.

BME 3.4h: When the parents are heterozygous for 7 traits, the multiplication principle says there are 2^7 = 128 possible progeny phenotypes. In general, when the parents are heterozygous for *n* traits, there are 2^n possible progeny phenotypes.