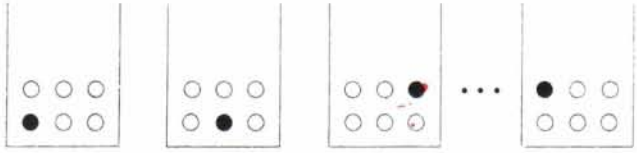
CHAPTER 8 Bad Odds: Poisson Distribution

8.A. RADIOACTIVE COUNTING

The origin of radioactivity and its interaction with matter is a topic for advanced quantum mechanics; for now, we are concerned with applications in which the number of radioactive counts serves as an indicator of the location and the concentration of a species of chemical or biological interest. The only facts required are (1) the probability, a, that any one nucleus will emit radiation during a given time interval of observation (say, one second) is very small compared to unity, and (2) for a sample containing a large number of radioactive nuclei, the observed average number of counts is proportional to time.

This situation is closely related to the bags and marbles problem we have previously solved, except that now the desired event (observing a radioactive decay) has a probability, $a \ll 1$, rather than the case of $a = (1/2)$ that led to Eq. 6-4. In other words, observation of radioactivity is like looking for a black marble in a bag containing nearly all white marbles: the



probability of finding the desired black marble (radioactive decay) in a given bag (nucleus) is much less than one, and one would like to know how many black marbles (decays) one is likely to find in examination of many bags (nuclei). From intuitive reasoning precisely analogous to that which led to Eq. 6-4, the solution is clearly

$$P_N(m) = \frac{N!}{m!\,(N-m)!}\,a^m b^{(N-m)} \tag{8-1}$$

where $P_N(m)$ is the probability of obtaining m black marbles in one draw from each of N bags, a is the probability that any single draw will yield a black marble, and b is the probability that any single draw will yield a white marble. In order to apply Eq. 8-1 to the radioactive counting problem (and others in this section), it will now be supposed that the probability of obtaining a black marble on a single draw (i.e., the probability that any one unstable nucleus will decay during the observation period) is small:

$$a \ll 1 \tag{8-2}$$

but the total number of draws (nuclei) is very large,

$$N \gg 1 \tag{8-3}$$

such that the average number of black marbles drawn in a given experiment is

$$aN = \bar{m} \tag{8-4}$$

where $\bar{m}$ ranges from zero to 1000 or more.

Solving Eq. 8-4 for $a = \bar{m}/N$ and substituting into Eq. 8-1

$$P_N(m) = \frac{N!}{m!\,(N-m)!}\left(\frac{\bar{m}}{N}\right)^m\left(1-\frac{\bar{m}}{N}\right)^{(N-m)} \tag{8-5}$$

where it has been recognized that

$$a + b = 1 \tag{8-6}$$

Equation 8-5 may now be rearranged more conveniently:

$$\begin{aligned} P_N(m) &= \frac{N!}{m!\,(N-m)!}\left(\frac{\bar{m}}{N}\right)^m\left(1-\frac{\bar{m}}{N}\right)^N\left(1-\frac{\bar{m}}{N}\right)^{(-m)} \\ &= \left(\frac{\bar{m}^m}{m!}\right)\left(1-\frac{\bar{m}}{N}\right)^N\left(\frac{N!}{(N-m)!\,N^m\left(1-\frac{\bar{m}}{N}\right)^m}\right) \\ &= A \cdot B \cdot C \end{aligned} \tag{8-7}$$

Letting N now approach infinity, the three factors of Eq. 8-7 reduce to:

$$\lim_{N\to\infty} A = \frac{\bar{m}^m}{m!} \tag{8-8a}$$

$$\lim_{N\to\infty} B = e^{-\bar{m}} \qquad \text{(definition of } e^x\text{)} \tag{8-8b}$$

and

$$\lim_{N\to\infty} C = 1 \qquad \text{(see Problems)} \tag{8-8c}$$

Equation 8-1, under the restrictions of 8-2 to 8-4 thus reduces to:

$$P_N(m) = \frac{\bar{m}^m}{m!} e^{-\bar{m}} \tag{8-9}$$

which is the celebrated Poisson distribution.

As a check on the derivation, we will evaluate the *average* number of successes, $<m>$ using the definition of an average of a discretely varying quantity (Eq. 6-38):

$$\bar{m} = <m> = \lim_{N\to\infty} \sum_{m=0}^{N} m \frac{\bar{m}^m}{m!} e^{-\bar{m}}$$

$$= e^{-\bar{m}} \lim_{N\to\infty} \left[0 + \frac{\bar{m}}{1!} + \frac{2\bar{m}^2}{2!} + \frac{3\bar{m}^3}{3!} + \cdots + \frac{N\bar{m}^N}{N!} \right]$$

$$= \bar{m}\, e^{-\bar{m}} \lim_{N\to\infty} \left[1 + \bar{m} + \frac{\bar{m}^2}{2!} + \cdots + \frac{\bar{m}^N}{N!} \right]$$

$$= \bar{m}\, e^{-\bar{m}} e^{\bar{m}}$$

$$\Rightarrow \quad \boxed{<m> = \bar{m} = Na} \tag{8-10}$$

in agreement with the intuitively derived Eq. 8-4. It is left as an exercise (see Problems) to show the principal useful property of the Poisson distribution:

$$(m - \bar{m})^2 = \boxed{<(m - <m>)^2> = \bar{m} = Na} \tag{8-11}$$

In other words, the result of many separate radioactive counting experiments will be to give an average result of $\bar{m} = Na$, with a root-mean-square deviation of $\pm\sqrt{\bar{m}} = \pm\sqrt{Na}$.

Just as the algebraic equation for an ellipse is complicated, while a

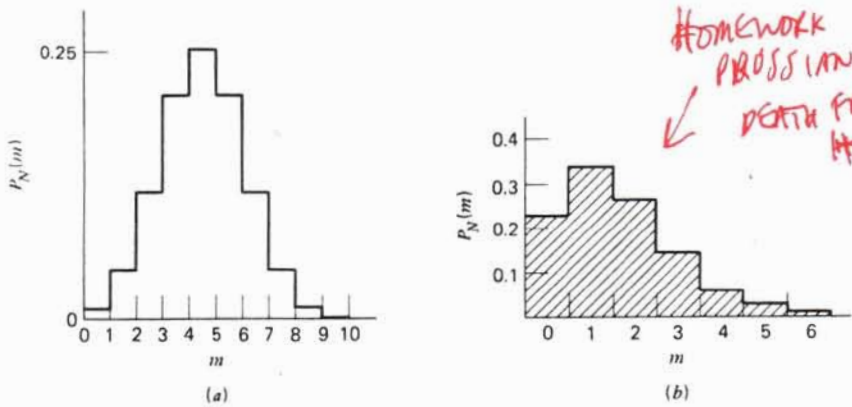


FIGURE 8-1. Two binomial distributions that approach the Gaussian and Poisson limits shown in Table 8-1. (*a*), $(0.5 + 0.5)^{10}$; (*b*), $(0.95 + 0.05)^{30}$. Note the skew in the right-hand plot.

Table 8-1. Illustration of the Common Origin of the Poisson and Normal (Gaussian) Distributions as Special Cases of the Binomial Distribution.*

BINOMIAL DISTRIBUTION

$$P_N(m) = \frac{N!}{m!\,(N-m)!}\,a^m b^{(N-m)}$$

$a = b = (1/2);\ N \to \infty$	$a \ll 1;\ N \to \infty$
NORMAL (GAUSSIAN) DISTRIBUTION	POISSON DISTRIBUTION
$P_N(m) = \sqrt{\frac{2}{\pi N}}\, e^{-2(m-\langle m\rangle)^2/N}$	$P_N(m) = \frac{\bar{m}^m}{m!}\, e^{-\bar{m}}$
$\langle m\rangle = Na = \frac{N}{2}$	$\bar{m} = Na$
and $\sqrt{\langle (m-\langle m\rangle)^2\rangle} = \sqrt{\frac{\langle m\rangle}{2}} = \sqrt{\frac{N}{4}}$	and $\sqrt{\langle (m-\bar{m})^2\rangle} = \sqrt{\bar{m}} = \sqrt{Na}$

* *Note that although the algebraic form of the Poisson is different from that of the Gaussian distribution, the principal property (the standard deviation from the average result) is similar in both cases.*

sketch is simple, the meaning of Equations 8-9 and 8-11 is most readily apparent from a graph (see Fig. 8-1). Table 8-1 summarizes the basic mathematics of this chapter.

As far as radioactive counting experiments are concerned, the most important result from the Poisson treatment is that if the average number of counts observed during a given observation period is $\bar{m}$, then in any particular observation period, the observed number of counts, m, will generally be within $\pm\sqrt{\bar{m}}$ of the average value, $\bar{m}$. Now since the number of counts increases as the length of the observation period ($\bar{m} \propto t$), while the imprecision in the measurement increases as $\sqrt{\bar{m}}$, it is necessary to count for *four* times as long in order to decrease the *fractional* error, $\Delta m/\bar{m} = \sqrt{1/\bar{m}}$, by a factor of *two*, as shown in Fig. 8-2.

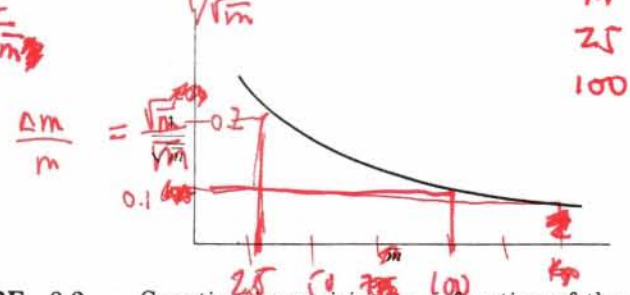


FIGURE 8-2. Counting imprecision as a function of the average number of counts.

EXAMPLE How many radioactive counts must be accumulated in order that the per cent error in the result be ±2%?

Solution: $\frac{\sqrt{\bar{m}}}{\bar{m}} = (1/\sqrt{\bar{m}}) = 0.02$
$\bar{m} = 2500$ counts, with imprecision of ±50 counts

Before proceeding to some applications, it is necessary to dispense with two practical difficulties connected with the counting process: background radiation (from cosmic rays, natural radioactivity of the surroundings) and the finite resolving time of the counter itself.

It would seem simple to find the *net* activity (observed counts per unit time)

$$A = \frac{\bar{m}}{t} \tag{8-12}$$

of a radioactive sample from the difference between the total (sample + background) activity, A_{total}, and the activity of the background (determined in the absence of the sample), $A_{\text{background}}$:

$$A = A_{\text{total}} - A_{\text{background}} \tag{8-13}$$

However, the *imprecision*,

$$\sigma = \frac{\sqrt{\bar{m}}}{\bar{m}} \tag{8-14}$$

in the sample activity is determined by the imprecision in both A_{total} and $A_{\text{background}}$, from the usual rule for the imprecision of a sum:

$$\sigma = \sqrt{\sigma_{\text{total}}^2 + \sigma_{\text{background}}^2} \tag{8-15}$$

$$= \sqrt{\frac{\bar{m}_{\text{total}}}{t_{\text{total}}^2} + \frac{\bar{m}_{\text{background}}}{t_{\text{background}}^2}} \tag{8-16}$$

$$\sigma = \sqrt{\frac{A_{\text{total}}}{t_{\text{total}}} + \frac{A_{\text{background}}}{t_{\text{background}}}} \tag{8-17}$$

If some of the available time is spent in counting the background ($t_{\text{background}}$) and the remainder is spent in counting the sample (t_{total}), then it may be shown that the time available should be divided according to

$$\frac{t_{\text{total}}}{t_{\text{background}}} = \sqrt{\frac{A_{\text{total}}}{A_{\text{background}}}} \tag{8-18}$$

Thus if the sample were nine times as active as the background, for example, then the sample should be counted for $\sqrt{9} = 3$ times as long.

EXAMPLE A sample (including background) has an activity of 900 counts per minute with a background activity of 225 counts per minute. How much time should be spent in counting the sample and in counting the background to achieve an imprecision of 2% in the net activity of the sample?

Solution The net activity of the sample is $900 - 225 = 675$ cpm. An imprecision of 2% in that number corresponds to $(0.02)675 = 14$ cpm. The time should be divided according to

$$\frac{t_{\text{total}}}{t_{\text{background}}} = \sqrt{\frac{900}{225}} = 2$$

or

$$t_{\text{total}} = 2\, t_{\text{background}}.$$

Substituting into Eq. 8-17

$$14^2 = \frac{900}{t_{\text{total}}} + \frac{225 \cdot 2}{t_{\text{total}}}$$

to give

$$t_{\text{total}} = 6.9 \text{ minutes}$$

and

$$t_{\text{background}} = 3.5 \text{ minutes}$$

For any radioactivity counter, there is a short period (100 μsec for geiger counters, less than 10 μsec for scintillation counters) following registry of a given count, during which the counter cannot record any further counts. If this period of insensitivity, or "dead time," is τ, and the observed number of counts per second is A_{obs}, then the total length of time that the counter is inoperative during one second is $A_{\text{obs}}\,\tau$. During that period, the number of counts that will be missed is $A \cdot A_{\text{obs}}\,\tau$, where A is the true number of counts per second from the sample. Thus

$$A = \text{observed counts} + \text{unobserved counts},$$

or

$$A = A_{\text{obs}} + A \cdot (A_{\text{obs}}\,\tau) \tag{8-19}$$

Solve for A:

and

$$A_1 = \frac{A_{\text{obs}}}{1 - A_{\text{obs}}\,\tau} \tag{8-20}$$

To determine the dead time, τ, of the counter, one need merely measure the count rate for three situations: sample #1 alone, sample #2 alone, and sample #1 and #2 together. The corrected (true) count rates for #1 and #2 alone must then sum to the combined corrected count rate for #1 and #2 together:

$$\frac{A_1}{1 - A_1\tau} + \frac{A_2}{1 - A_2\tau} = \frac{A_{(1 \text{ and } 2)}}{1 - A_{(1 \text{ and } 2)}\,\tau} \tag{8-21}$$

Since $\tau \ll 1$, and $\tau^2 \ll \tau$, Eq. 8-21 may be simplified to yield

$$\tau \approx \frac{A_1 + A_2 - A_{(1 \text{ and } 2)}}{2A_1A_2} \tag{8-22}$$

EXAMPLE A geiger counter gave a count rate of 1242 counts/sec for sample #1 alone, 1371 counts/sec for sample #2 alone, and 2209 counts/sec for samples #1 and #2 together. Calculate the dead time of the counter and the error introduced when it is not corrected for. Background is 3 counts/sec and is negligible.

Solution

$$\tau = \frac{1242 + 1371 - 2209}{2(1242)(1371)} = 1.19 \times 10^{-4} \text{ sec}$$

The true count rate for source #1 is given by

$$A_1 = \frac{A_{\text{obs}}}{1 - A_{\text{obs}}\,\tau} = \frac{1242}{1 - 1242(1.19 \times 10^{-4})}$$

$A_1 = 1460$ counts/sec, so that neglect of the correction for dead time leads to an error of about 15% in the counting rate

Isotopic Dilution and Tracer Methods

Modern medical diagnosis often relies in part on the determination of the *amount* of a particular metabolite in a particular body fluid or organ. However, while it is generally possible to isolate the desired substance in *high purity*, it is generally not possible to obtain *high yield*. The technique of isotopic dilution is a clever solution to this problem, and has led to the common use of radioisotopes in medicine (see examples).

In isotopic dilution, radiation *activity* (count *rate*) is used as a measure of the *concentration* of radioactive material per gram of substance. If a sample of some pure compound consisting of n_0 grams of activity, A_0 per gram, is mixed with an additional n_{unk} grams of the same inactive compound, then the count rate for the mixture will be "diluted" to the value,

$$A = A_0 \left[\frac{n_0}{n_0 + n_{unk}} \right] \tag{8-23}$$

just as the concentration of an ordinary chemical is decreased on dilution with solvent. The amount of the inactive compound may then be found by rearrangement of Eq. 8-23:

$$\boxed{n_{unk} = n_0 \left[\frac{A_0 - A}{A} \right]} \tag{8-24}$$

EXAMPLE *Calculation of Human Blood Volume*

a. *Labeling the plasma.* In this method, human serum albumin (a large protein, MW 68,000, normally present in human blood) is covalently iodinated with ^{131}I to some of the tyrosine residues at a position ortho to the hydroxyl group, prior to the test. Then 10cc of labeled albumin with activity of about 1 μCi/cc (1 Curie amounts to 3.7×10^{10} counts/sec) is injected into the elbow vein; it takes about ten minutes for the injected albumin to become equilibrated with the total blood volume. A blood sample of 3 cc is then withdrawn from the individual, and the radioactivity measured.

If the activity of the 3cc blood sample is 3287 counts/min, where the background count for 3cc of blood withdrawn from the same individual *before* the injection of labeled albumin is 175 counts/min, and the activity of the labeled albumin (3 cc) used for injection is 5702 counts/min at a dilution of 1:200 (to make the count rate more similar to that to be measured for the blood), then the plasma volume is simply

$$\text{Plasma volume} = \frac{200\,(5702 - 175) - (3287 - 175)}{(3287 - 175)}\,10 \text{ cc}$$

$$= 3550 \text{ cc} = 3.5 \text{ liter}$$

Finally, the relative volume of the blood cells themselves may be determined by centrifuging a blood sample and determining the packed cell volume. For the example given, the blood cell volume might be 2.8 liters, to give a total blood volume (plasma plus cells) of 6.3 liter.

b. *Labeling the red blood cells.* For this experiment, ^{51}Cr is incubated with the patient's own blood *in vitro*, until most of the CrO_4^- has become bound to the blood *cells*. Then a reducing agent is added (say, sodium ascorbate) to reduce any unreacted CrO_4^- to Cr^{+3}. The Cr^{+3} binds almost exclusively

to plasma proteins. Finally, following injection, equilibration, and extraction of blood as before, one can determine the count rate for the labeled blood before injection, the count rate for whole blood after injection, and the count rate for plasma (obtained by centrifugation) after injection, to find the volume of red blood cells.

Determination of blood volume is of most immediate use in deciding whether blood or plasma transfusions are required in cases of bleeding, burns, or surgical shock, and has been responsible for saving a great number of lives of accident victims.

For lean individuals, blood volume varies nearly in direct proportion to body weight, at about 80 cc/kg for males. When a person puts on weight, however, the ratio of blood volume to body weight drops, because fat tissue requires less associated volume of blood vessels. Women, on the average, have a blood volume about 20% less than men (about 65 cc/kg) because of their greater ratio of fat-to-lean tissue.

Although the *total* blood volume may change somewhat when the body malfunctions, a more sensitive diagnostic indicator is the *ratio* of red blood cell volume to total blood volume, the so-called hematocrit. In severe anemia, the hematocrit may fall from its normal value (40% for males, 36% for females) to as low as 15, due to a shortage of red blood cells. In contrast, excess red blood cells (an a hematocrit of up to 70%) result from continued exposure to high altitude or from a tumor of the blood cell-producing organs. Finally, since the kidneys are largely responsible for returning the blood volume to normal following a relatively sudden change (such as drinking a lot of water), measurement of blood volume as a function of time following a deliberate change in blood volume can provide a probe of renal (kidney) function. In all these cases, the radioisotope methods provide quick and accurate results for diagnosis.

BLOOD – CELLS PLASMA – CLOT SERUM

EXAMPLE *Thyroid Function*

Although the *physical* properties of (stable) ^{127}I and (radioactive) ^{131}I are different, their *chemical* properties are the same, so that ^{131}I provides a natural tracer for the metabolism of iodine and the iodinated compounds connected with thyroid function. The thyroid gland is unique in its capacity to selectively concentrate *and* retain iodide, for conversion to iodo-tyrosine and then thyronine.

a. *Iodide uptake.* Although the *total amount* of iodide in an individual is roughly constant, and also relatively unaffected by thyroid malfunction, the *rate of uptake* of iodide is a good diagnostic indicator of thyroid activity: the thyroid gland extracts from 0.5 to 6.8% of the circulating iodide pool per hour in a normal case, rising to 2.5 to 6.8% in hyperthyroidism, or 0 to 1.3% in myxedema. Uptake of ^{131}I is readily measured by counting the activity at a position on the patient's neck just above the thyroid, with calibration using the un-diluted ^{131}I sample at the same distance from the counter.