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Stochastic Analysis
of Multi-Compartment Systems

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Mathematics Research

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STOCHASTIC ANALYSIS OF MULTI-COMPARTMENT SYSTEMS

by

G. Marsaglia

Mathematical Note No. 313

Mathematics Research Laboratory

BOEING SCIENTIFIC RESEARCH LABORATORIES

July 1963

1. Introduction

This is a discussion of methods for describing, mathematically, flows between compartments in a multi-compartment system. We will give the conventional theory, based on the solution of a system of linear differential equations; we will also give a theory based on probability, viewing the system as a collection of "states" with a particle moving from state to state with certain probabilities, remaining in each state a random time with an exponential distribution. Finally, we will take still another approach, again based on probability theory, in which we consider the sojourn time of a particle, that is, the time it spends after leaving a given compartment before returning to that compartment. This last approach seems to be potentially the most useful, as it fits well the practical situation in which an experimenter is able to observe the disappearance of tracer amounts of a substance from only one of several biological "compartments". He is then interested in finding models consistent with his observed disappearance curve. In our parlance, we will look for models with a given sojourn time. The procedures for finding a class of models with a given sojourn time from, say, the first compartment, will be easier than those based on solving the system of linear differential equations, in addition, the methods will be more general, and apply to non-linear situations as well.

2. Multi-compartment systems viewed as a set of simultaneous linear differential equations

It is customary to express the amount of tracer in each of the

compartments of a multi-compartment system as the solution to a system of linear differential equations. We give a brief outline of a method for solving such systems, using matrix theory. Define the vector $\xi = (x_1(t), x_2(t), \dots, x_n(t))$. We want to solve

$$\dot{\xi} = \xi A, \quad \xi(0) = \xi_0,$$

where A is an $n \times n$ matrix of constants, and is diagonalizable; the dot means differentiation with respect to t . We express A in terms of its principal idempotents, $A = r_1 E_1 + \dots + r_m E_m$, with $r_1, \dots, r_m$ the distinct characteristic roots of A and $E_i = \prod_{j \neq i} \frac{(A - r_j I)}{r_i - r_j}$. Then

$$e^{tA} = e^{r_1 t} E_1 + e^{r_2 t} E_2 + \dots + e^{r_m t} E_m$$

and the solution to (1) is

$$\xi = \xi_0 (e^{r_1 t} E_1 + e^{r_2 t} E_2 + \dots + e^{r_m t} E_m).$$

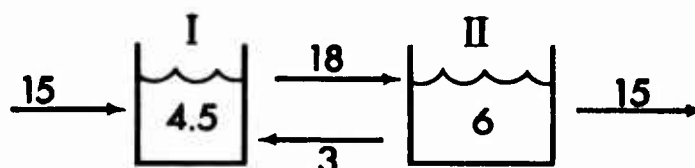
As examples, consider $m = 2$ and 3 . When A has two distinct roots, r_1, r_2 , we have

$$\xi = \xi_0 \left[\frac{A - r_2 I}{r_1 - r_2} e^{r_1 t} + \frac{A - r_1 I}{r_2 - r_1} e^{r_2 t} \right].$$

If A has distinct roots r_1, r_2, r_3 , then the solution to (1) is

$$\begin{aligned} \xi = \xi_0 \left[\frac{(A - r_2 I)(A - r_3 I)}{(r_1 - r_2)(r_1 - r_3)} e^{r_1 t} + \frac{(A - r_1 I)(A - r_3 I)}{(r_2 - r_1)(r_2 - r_3)} e^{r_2 t} \right. \\ \left. + \frac{(A - r_1 I)(A - r_2 I)}{(r_3 - r_1)(r_3 - r_2)} e^{r_3 t} \right]. \end{aligned}$$

For a numerical example, consider this system



If we introduce a trace amount in the first pool, what proportion of the tracer will be in the first and second pools at time t ? Let $x_1(t)$ and $x_2(t)$ be those proportions, so that $x_1(0) = 1$ and $x_2(0) = 0$. Then

$$\frac{dx_1(t)}{dt} = -4x_1(t) + \frac{1}{2}x_2$$

$$\frac{dx_2(t)}{dt} = 4x_1(t) - 3x_2(t).$$

In matrix form, if $A = \begin{pmatrix} -4 & 4 \\ \frac{1}{2} & -3 \end{pmatrix}$ and $\xi = (x_1(t), x_2(t))$, we have

$$\dot{\xi} = \xi A, \quad \xi_0 = (1, 0).$$

We need the roots of A ; they are found by solving

$$|A - \lambda I| = \begin{vmatrix} -4-\lambda & 4 \\ \frac{1}{2} & -3-\lambda \end{vmatrix} = (4 + \lambda)(3 + \lambda) - 2 = 0.$$

The roots are $r_1 = -5, r_2 = -2$. Hence the solution is

$$\xi = (1, 0) \frac{(A + 2I)}{-3} e^{-5t} + (1, 0) \frac{(A + 5I)}{3} e^{-2t}$$

or

$$\xi = \left(\frac{2}{3}, -\frac{4}{3}\right)e^{-6t} + \left(\frac{1}{3}, \frac{4}{3}\right)e^{-2t},$$

that is,

$$x_1(t) = \frac{2}{3}e^{-5t} + \frac{1}{3}e^{-2t}, \quad x_2(t) = -\frac{4}{3}e^{-5t} + \frac{4}{3}e^{-2t}.$$

3. Theory of a particle moving from state to state

We will give a brief development of the probability theory that describes the behavior of a particle which moves from compartment to compartment in a multi-compartment system. We assume that the time that the particle spends in the i^{th} compartment has an exponential distribution, say with density $a_i e^{-a_i x}$, and that the probability a particle leaving the i^{th} compartment will go to the j^{th} compartment is a constant, independent of time, say p_{ij} . Let $B(t) = (b_{ij}(t))$ be the transition matrix of the system, which is defined as follows: Suppose there are n compartments in the system. Then $B(t)$ is an $n \times n$ matrix whose elements, $b_{ij}(t)$, are functions of t ; they give the probability that a particle placed in the i^{th} compartment at time zero will be in the j^{th} compartment at time t . The key to the theory lies in the fact that the matrix function $B(t)$ satisfies $B(s+t) = B(s)B(t)$, and hence there is a constant matrix A such that $B(t) = e^{tA}$. The argument runs along these lines - to show, for example, that $B(9) = B(5)B(4)$, and in particular, say when $n = 3$, that

$$b_{23}(9) = b_{21}(5)b_{13}(4) + b_{22}(5)b_{23}(4) + b_{23}(5)b_{33}(4)$$

we note that $b_{23}(9)$ is the probability that a particle placed in

compartment II will be in compartment III after 9 time units, say hours. Now the only way that a particle can start in II and be in III after 9 hours, is at $t = 5$, to be in I and then go to II during the next four hours, or at $t = 5$, be in II and go to III in the next four hours, or at $t = 5$, be in III and also be in III after four more hours. Thus the relation we want is*

$$(1) \quad b_{23}(9) = b_{21}(5)b_{13}(4) + b_{22}(5)b_{23}(4) + b_{23}(5)b_{33}(4).$$

The same argument applies to any breakdown of a time interval into two parts, and hence the relation

$$(2) \quad B(s + t) = B(s)B(t),$$

which expresses all relations of the type (1) simultaneously, by way of matrix multiplication.

From (2), we see that for integers m , $B(m) = B(1)^m$, and that $B(\frac{1}{m}) = B(1)^{1/m}$. Hence for rational $r > 0$, $B(r) = B(1)^r$ and since the elements of B are continuous functions of t , we have $B(t) = B(1)^t$ for all $t \geq 0$. Writing $B(1) = e^A$, we get the basic formula for the transition matrix of the system:

$$B(t) = e^{tA},$$

where A is a matrix of constants whose elements we must find. We do this by studying the limiting behavior of $B(t)$ as $t \rightarrow 0$. Let the elements of A be a_{ij} . We have

$$(3) \quad B(t) = e^{tA} = I + tA + \dots$$

* In this argument, it is essential that the time in each compartment have the exponential distribution, in order that the future time in a compartment, given that a particle is in a compartment at time t , be independent of t . The exponential is the only distribution with this property.

When t is small, $b_{11} \approx e^{-a_1 t} \approx 1 - a_1 t$, while from (3), $b_{11}(t) \approx 1 + ta_{11}$. Thus

$$a_{11} = -a_1.$$

A similar argument will show that

$$a_{ij} = p_{ij}a_i,$$

with p_{ij} the probability that a particle leaving the i^{th} compartment will go to the j^{th} compartment. Thus

$$A = \begin{pmatrix} -a_1 & a_1 p_{12} & a_1 p_{13} & \dots & a_1 p_{1n} \\ a_2 p_{21} & -a_2 & a_2 p_{23} & \dots & a_2 p_{2n} \\ \vdots & \vdots & \vdots & \vdots & \vdots \\ a_n p_{n1} & a_n p_{n2} & a_n p_{n3} & \dots & -a_n \end{pmatrix}.$$

We summarize the theory in this form:

Theorem. If a particle moves from compartment to compartment in a system of n compartments, and if the time a particle spends in the i^{th} compartment has the exponential density, $a_i e^{-a_i x}$, and if p_{ij} is the probability a particle leaving the i^{th} compartment will enter the j^{th} compartment, then the matrix $B(t)$, whose elements $b_{ij}(t)$ give the probability that a particle starting in the i^{th} compartment will be in the j^{th} compartment at time t , satisfies

$$B(s + t) = B(s)B(t)$$

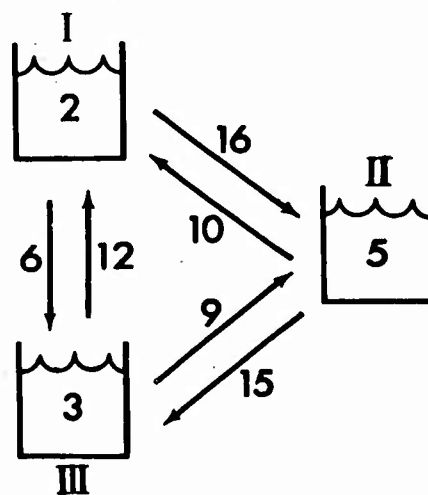
and hence

$$B(t) = e^{tA},$$

where

$$A = \begin{pmatrix} -a_1 & a_1 p_{12} & a_1 p_{13} & \dots & a_1 p_{1n} \\ a_2 p_{21} & -a_2 & a_2 p_{23} & \dots & a_2 p_{2n} \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ a_n p_{n1} & a_n p_{n2} & a_n p_{n3} & \dots & -a_n \end{pmatrix}.$$

As an example, consider this system.



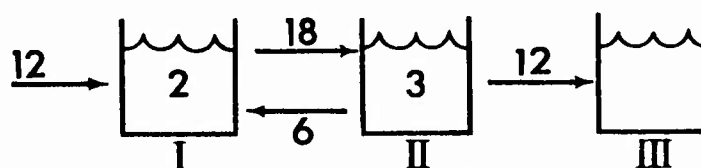
The density functions for the time a particle spends in I, II, and III are $11e^{-11t}$, $5e^{-5t}$, and $7e^{-7t}$. The probability that a particle leaving I will go to II is $p_{12} = \frac{16}{22}$, similarly, $p_{13} = \frac{6}{22}$, $p_{21} = \frac{10}{25}$, $p_{23} = \frac{15}{25}$,

$$p_{31} = \frac{12}{21}, \quad p_{32} = \frac{9}{21}. \quad \text{Thus}$$

$$A = \begin{pmatrix} -11 & 11(\frac{16}{22}) & 11(\frac{6}{22}) \\ 4(\frac{10}{25}) & -5 & 4(\frac{15}{25}) \\ 7(\frac{12}{21}) & 7(\frac{9}{21}) & -7 \end{pmatrix}$$

and the transition matrix of the system is $B(t) = e^{tA}$.

The above method may also be applied to systems with absorbing states, that is, compartments with flow in but no flow out. This is done by putting $a_i = 0$ for such states. For example, in this system,



we put $a_1 = 9, a_2 = 6, a_3 = 0, p_{12} = 1, p_{13} = 0, p_{21} = \frac{6}{18}, p_{23} = \frac{12}{18}$ and the transition matrix is $B(t) = e^{tA}$, where

$$A = \begin{pmatrix} -9 & 9 & 0 \\ 6(\frac{6}{18}) & -6 & 6(\frac{12}{18}) \\ 0 & 0 & 0 \end{pmatrix}.$$

There remains the problem of finding the matrix e^{tA} when the matrix A is given. This may be done, at least in the case when A is similar to a diagonal matrix, and most practical problems seem to fall in this category, as follows: Let the distinct characteristic roots of A be $r_1, r_2, \dots, r_m$. Let the principle idempotents of A be $E_1, E_2, \dots, E_m$, where

$$E_i = \prod_{j \neq i} \frac{(A - r_j I)}{r_i - r_j}.$$

Then

$$e^{tA} = e^{r_1 t} E_1 + e^{r_2 t} E_2 + \dots + e^{r_m t} E_m.$$

For example, when A has two distinct roots,

$$e^{tA} = \frac{(A - r_2 I)}{r_1 - r_2} e^{r_1 t} + \frac{(A - r_1 I)}{r_2 - r_1} e^{r_2 t}.$$

When A has three distinct roots,

$$e^{tA} = \frac{(A - r_2 I)(A - r_3 I)}{(r_1 - r_2)(r_1 - r_3)} e^{r_1 t} + \frac{(A - r_1 I)(A - r_3 I)}{(r_2 - r_1)(r_2 - r_3)} e^{r_2 t} + \frac{(A - r_1 I)(A - r_2 I)}{(r_3 - r_1)(r_3 - r_2)} e^{r_3 t}.$$

For a simple numerical example, let A be the matrix of the system given above,

$$A = \begin{pmatrix} -9 & 9 & 0 \\ 2 & -6 & 4 \\ 0 & 0 & 0 \end{pmatrix}.$$

The roots are found by solving

$$|A - \lambda I| = \begin{vmatrix} -9-\lambda & 9 & 0 \\ 2 & -6-\lambda & 0 \\ 0 & 0 & -\lambda \end{vmatrix} = -\lambda[(9 + \lambda)(6 + \lambda) - 18] = 0.$$

The roots are $r_1 = -3$, $r_2 = -12$, $r_3 = 0$.

Hence

$$E_1 = \frac{(A + 12I)(A - 0I)}{(-3 + 12)(-3 - 0)} = \begin{pmatrix} \frac{1}{3} & 1 & -\frac{4}{3} \\ \frac{2}{9} & \frac{2}{3} & -\frac{8}{9} \\ 0 & 0 & 0 \end{pmatrix}$$

$$E_2 = \frac{(A + 3I)(A - 0I)}{(-12 + 3)(-12 - 0)} = \begin{pmatrix} \frac{2}{3} & -1 & \frac{1}{4} \\ -\frac{2}{9} & \frac{1}{3} & -\frac{1}{9} \\ 0 & 0 & 0 \end{pmatrix}$$

$$E_3 = \frac{(A + 3I)(A + 12I)}{(0 + 3)(0 + 12)} = \begin{pmatrix} 0 & 0 & 1 \\ 0 & 0 & 1 \\ 0 & 0 & 1 \end{pmatrix}$$

and

$$e^{tA} = e^{-3t}E_1 + e^{-12t}E_2 + e^{0t}E_3.$$

If we write this as a single matrix, we have

$$B(t) = e^{tA} = \begin{pmatrix} \frac{1}{3}e^{-3t} + \frac{2}{3}e^{-12t} & e^{-3t} - e^{-12t} & 1 - \frac{4}{3}e^{-3t} + \frac{1}{3}e^{-12t} \\ \frac{2}{9}e^{-3t} - \frac{2}{9}e^{-12t} & \frac{2}{3}e^{-3t} + \frac{1}{3}e^{-12t} & 1 - \frac{8}{9}e^{-3t} - \frac{1}{9}e^{-12t} \\ 0 & 0 & 1 \end{pmatrix}.$$

Thus, the probability that a particle starting in II will be in I at time t is $\frac{2}{9}e^{-3t} - \frac{2}{9}e^{-12t}$. The probability it will be in III is $1 - \frac{8}{9}e^{-3t} - \frac{1}{9}e^{-12t}$. If a trace amount of substance is put into compartment I, then at time t , the proportion of that amount in compartments I, II,

and III will be

$$\frac{1}{3}e^{-3t} + \frac{2}{3}e^{-12t}, e^{-3t} - e^{-12t}, \text{ and } 1 - \frac{4}{3}e^{-3t} + \frac{1}{3}e^{-12t}.$$

4. Theory based on a particle's sojourn time

In this section we will develop a method for interpreting the disappearance of tracer amounts of a substance from a single compartment or pool. The method is different from those of Sections 2 and 3; it is more general, and easier to apply. The idea is roughly as follows: A radioactively labelled particle enters the compartment under investigation. It spends a random amount of time, presumably with an exponential distribution, in the main compartment. It then escapes from the main compartment, after which there are two possibilities - the particle does not return, or else it returns after some random time whose distribution we wish to find. We will call this the sojourn time of the particle. We consider how to relate the tracer disappearance curve to these two factors - the probability that a particle will not return, and the distribution of sojourn time for those particles that do return. Having the distribution of sojourn time, we will consider physical situations consistent with that distribution.

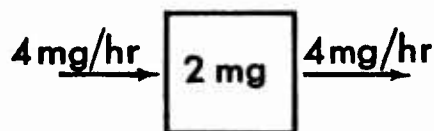
This is the situation: We add a unit amount of radioactive tracer to a compartment, and observe the amount still in the compartment, say $f(t)$, at times $t_1, t_2, \dots, t_n$. We assume that a radioactive particle spends a random amount of time in the compartment, and then escapes. Having escaped, with a certain probability it will not return, otherwise

it will return after a random sojourn time with density function $g(x)$. The relation between f and g is given by this rather formidable appearing integro-differential equation:

$$(4) \quad \frac{df(t)}{dt} = -hf(t) + h \int_0^t f(x)g(t-x)dx.$$

We will go through an example to show why (4) describes the situation and to show that the analysis of (4) is not as difficult as it first appears.

Suppose that we have a pool which contains 2 mg. of the substance in question. We use a radioactive isotope to label a tracer amount of the substance and inject it into the pool. We then observe the disappearance curve $f(t)$, the (relative) amount of tracer still present at time t . Suppose that the initial slope of the disappearance curve is -2 . This means that 4 mg. of the substance are leaving the pool each hour, and, presumably, 4 mg. are entering the pool each hour, on the assumption that we have a steady state:



Now if none of the radioactive particles were fed back to the main pool, the disappearance curve would satisfy

$$\frac{df(t)}{dt} = -2f(t)$$

and hence $f(t) = e^{-2t}$, since $f(0) = 1$. But suppose that there is a feedback mechanism which we characterize by a function $g(x)$. Then (4) becomes

$$(5) \quad \frac{df(t)}{dt} = -2f(t) + 2 \int_0^t f(t-x)g(x)dx,$$

the first term on the right indicating that tracer is lost from the pool at the rate of two times the amount present; the second, integral term, reflecting the cumulative feedback. To illustrate the feedback term, say when $t = 8$ hours, we have

$$\int_0^8 2f(x)g(8-x)dx = 2f(1)g(7) + 2f(2)g(6) + 2f(3)g(5) + \dots + 2f(7)g(1),$$

the terms on the right showing that at $t = 8$ hours, the feedback is made up of the amount received seven hours ago, $2f(1)$, times the proportion of that amount which is to be returned, $g(7)$, plus the amount received six hours ago, $2f(2)$, times the proportion of that amount which is to be returned, $g(6)$, etc.

Next, suppose that we have observed the disappearance curve $f(t)$ at enough time points to have determined that it has a particular functional form, say

$$f(t) = .6e^{-3t} + .4e^{-.5t}.$$

The initial slope of f is still -2 , but it became evident after a short time that the disappearance curve was not a single exponential, and hence that some of the tracer was being fed back. To find the distribution of sojourn time for particles returning to the compartment, we must solve (5) for $g(x)$. Now a little fiddling with equation (4) will

establish the following rule: If f is a linear combination of exponentials, then g is a linear combination of one fewer exponentials.

In our case, we assume that g has the form $g(x) = ce^{-bx}$, and try to solve (5). The procedure is elementary, we merely substitute ce^{-bx} for g and get conditions on c and b . We have

$$-1.8e^{-3t} - .2e^{-.5t} = -1.2e^{-3t} - .8e^{-.5t} + 2 \int_0^t (.6e^{-3x} + .4e^{-.5x}) ce^{-b(t-x)} dx.$$

Integrating and collecting terms, this reduces to

$$-.3e^{-3t} + .3e^{-.5t} = \frac{.6c}{b-3}(e^{-3t} - e^{-bt}) + \frac{.4c}{b-.5}(e^{-.5t} - e^{-bt}).$$

We thus need to have

$$\frac{.6}{b-3} + \frac{.4}{b-.5} = 0, \quad \text{or } b = 1.5,$$

and

$$\frac{.6c}{b-3} = -.3, \quad \frac{.4c}{b-.5} = .3, \quad \text{or } c = .75.$$

Thus our feedback mechanism is described by

$$g(x) = .75e^{-1.5x}, \quad x > 0.$$

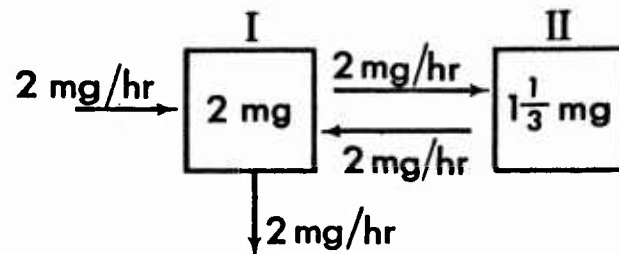
Notice that g is not a proper probability density function, since the area under g is .5, not 1:

$$\int_0^{\infty} g(x) dx = \int_0^{\infty} .75e^{-1.5x} dx = .75/1.5 = .5.$$

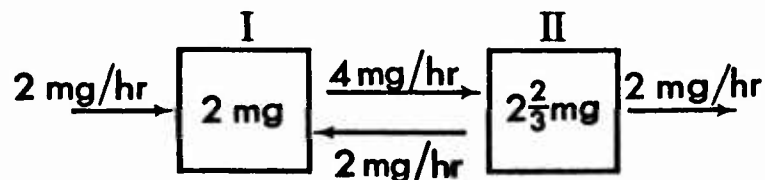
This means that only one-half of the particles escaping from the main compartment are being fed back; the other half do not return. Thus we

have the stochastic interpretation of this particular disappearance curve, $f(t) = .6e^{-3t} + .4e^{-.5t}$: A radioactive particle entering the main compartment spends a random time in that compartment, the distribution of that time is exponential with density function $2e^{-2t}$. After a particle escapes from the main compartment, with probability one-half it does not return, and with probability one-half it returns after a sojourn time with exponential density $1.5e^{-1.5x}$.

We now look for physical situations which can produce this sort of feedback; fifty percent not returned, fifty percent returned after a random delay with density $1.5e^{-1.5x}$. Unfortunately, and this is typical of actual problems of this type, there are very many plausible situations which will produce the required feedback and hence the given tracer disappearance curve. For example, this two-pool system would have tracer disappearance curve $f(t) = .6e^{-3t} + .4e^{-.5t}$;

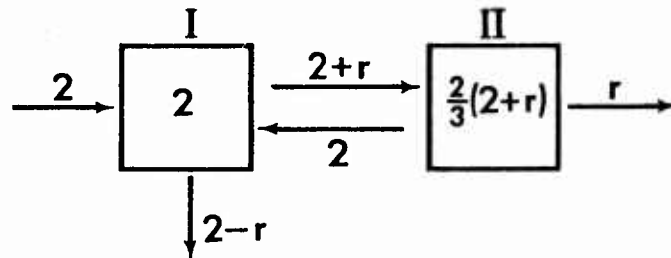


But this pool system would also have the same disappearance curve,



for it meets the feedback requirements - half of the particles leaving do not return and those that do return have a sojourn time with distribution $1.5e^{-1.5x}$.

We can assign, in fact, an infinite number of two-compartment systems which will have disappearance curve $.6e^{-3t} + .4e^{-.5t}$. For any assignment of r , $0 \leq r \leq 2$, this two-compartment system will have the required disappearance curve:



For if a particle leaves the main compartment, I, then with probability $\frac{2+r}{4}$ it will go to the second compartment, and once there it will return with probability $\frac{2}{2+r}$. The product of these is $\frac{2+r}{4} \cdot \frac{2}{2+r} = \frac{1}{2}$. Thus the probability that a particle will be fed back is one-half, and the random sojourn time has the exponential distribution $1.5e^{-1.5x}$, since the time a particle spends in II has that distribution.

5. Relations between the disappearance curve f , and the sojourn time, or feedback function, g

We have seen in the previous section that if $f(t)$ is the amount of tracer present in the main compartment at time t , then f satisfies

this differentio-integral equation:

$$\frac{df(t)}{dt} = -hf(t) + h \int_0^t f(x)g(t-x)dx,$$

where $g(x)$ is the feedback function which describes the probability distribution of the time that particles spend after leaving and before returning to the main compartment. The area under $g(x)$ gives the probability that a particle will be fed back, and when $g(x)$ is normalized by dividing by that probability, it gives the density function of the sojourn time.

In multiple pool systems with constant pool sizes and flows, the disappearance curve and feedback function will be linear combinations of exponential functions. We summarize here the formulas which give f in terms of g and vice versa when f is made up of two or three exponential components:

When f and g are related by

$$\frac{df(t)}{dt} = -hf(t) + h \int_0^t f(x)g(t-x)dx$$

and f is a linear combination of exponentials, then g will be a linear combination of one fewer exponentials. Relations between f and g in this case are as follows:

1. If $f(t) = p_1 e^{-a_1 t} + p_2 e^{-a_2 t}$, $f(0) = 1, f'(0) = -h$,
then $g(x) = ce^{-bx}$, where

$$b = a_1 + a_2 - h$$

$$c = -(h - a_1)(h - a_2)/h.$$

2. If $g(x) = ce^{-bx}$, then $f(t) = p_1 e^{-a_1 t} + p_2 e^{-a_2 t}$, where a_1 and a_2 are the two roots of the quadratic equation
- $$x^2 - (h + b)x + h(b - c) = 0$$

and p_1, p_2 are the solutions to the linear equations

$$p_1 + p_2 = 1$$

$$p_1 a_2 + p_2 a_1 = b.$$

An explicit formula for p_1 is $p_1 = (h - a_2)/(a_1 - a_2)$.

3. If $f(t) = p_1 e^{-a_1 t} + p_2 e^{-a_2 t} + p_3 e^{-a_3 t}$, $f(0) = 1, f'(0) = -h$, then $g(x) = c_1 e^{-b_1 x} + c_2 e^{-b_2 x}$, where b_1 and b_2 are the roots of the quadratic equation

$$x^2 - (a_1 + a_2 + a_3 - h)x + p_1 a_2 a_3 + p_2 a_1 a_3 + p_3 a_1 a_2 = 0$$

and c_1, c_2 satisfy the two linear equations

$$c_1 + c_2 = b_1 + b_2 - \frac{a_1 a_2 + a_1 a_3 + a_2 a_3 - b_1 b_2}{h}$$

$$b_2 c_1 + b_1 c_2 = b_1 b_2 - \frac{a_1 a_2 a_3}{h}.$$

4. If $g(x) = c_1 e^{-b_1 x} + c_2 e^{-b_2 x}$, then $f(t) = p_1 e^{-a_1 t} + p_2 e^{-a_2 t} + p_3 e^{-a_3 t}$, where a_1, a_2, a_3 are the roots of the cubic equation

$$x^3 - (b_1 + b_2 + h)x^2 + [b_1 b_2 + h(b_1 + b_2 - c_1 - c_2)]x - h(b_1 b_2 - c_1 b_2 - c_2 b_1) = 0$$

and p_1, p_2, p_3 are solutions to the three linear equations

$$p_1 + p_2 + p_3 = 1$$

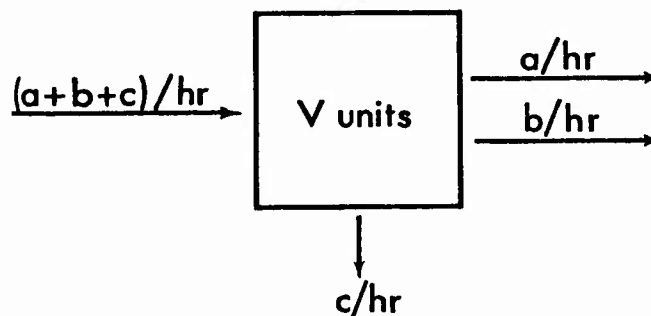
$$p_1 a_1 + p_2 a_2 + p_3 a_3 = h$$

$$p_1 a_2 a_3 + p_2 a_1 a_3 + p_3 a_1 a_2 = b_1 b_2.$$

6. Quick and easy solutions to two and three-compartment systems

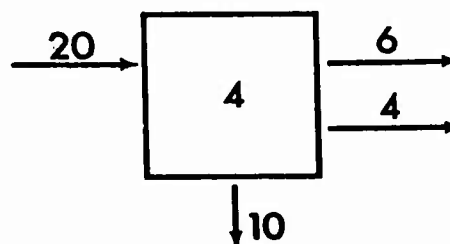
In this section we will show, by means of examples, how easy it is to determine the sojourn time of a particle which goes from compartment to compartment in a multiple pool system. We need this basic rule:

If a particle enters a compartment which has several possible exits, such as this:



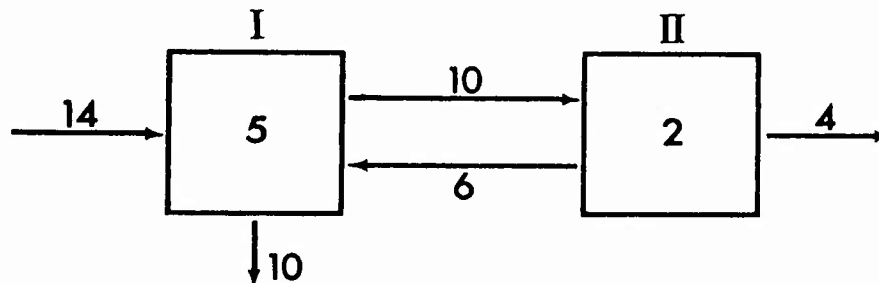
then the probability it will leave by the "a" exit is $\frac{a}{a+b+c}$, by the "b" exit, $\frac{b}{a+b+c}$, etc. Given that the particle leaves by the "a" exit, the time the particle spends in the compartment has the exponential distribution with mean $\frac{V}{a+b+c}$ and density function $\frac{a+b+c}{V} e^{-x(a+b+c)/V}$. Particles leaving by the "b" or "c" exit have the same distribution time in the compartment, that is, the distribution of the time that a particle spends in a compartment, given that it leaves by a particular exit, does not depend on the particular exit, but only on the volume and total flow out of the compartment.

For example, in this system



the probabilities a particle will leave by the "6", "4", or "10" exits, are $\frac{6}{20}$, $\frac{4}{20}$, and $\frac{10}{20}$, respectively, and particles leaving by any of these exits will have remained in the compartment a random time with mean $\frac{1}{5}$ and density function $5e^{-5x}$, since $\frac{6+4+10}{4} = 5$.

As an illustration of how to find tracer disappearance curves and sojourn times for a system, consider this two-pool system:



We ask such questions as: What is the sojourn time of particles leaving I? What proportion of the particles leaving I never return? What is the tracer disappearance curve from I?

First note that the probability a particle leaving I will go to II is $\frac{10}{10+10} = .5$. Once in II, the particle will be fed back to I with probability $\frac{6}{6+4} = .6$. Hence the probability that a particle leaving I will be fed back is the product of these, or $(.5)(.6) = .3$. Now for particles fed back, the distribution of sojourn time is $5e^{-5x}$, since flow out of II is five times the amount present. Thus the feedback mechanism is described by

$$g(x) = ce^{-bx} = .3(5e^{-5x}) = 1.5e^{-5x}.$$

Referring to Rule 2 in Section 5, we know that the disappearance curve will be

$$f(t) = p_1 e^{-a_1 t} + p_2 e^{-a_2 t}$$

where a_1, a_2 are the roots of

$$x^2 - (4 + 5)x + 4(5 - 1.5) = x^2 - 9x + 14 = 0$$

that is,

$$a_1 = 7, a_2 = 2.$$

Then

$$p_1 = \frac{4 - 2}{7 - 2} = .4$$

and hence

$$f(t) = .4e^{-7t} + .6e^{-2t}$$

is the disappearance curve of a unit amount of tracer placed in compartment I at $t = 0$.

Now consider another type of problem: Given that the tracer disappearance curve from a compartment is a particular function, say

$$f(t) = \frac{1}{4}e^{-3t} + \frac{3}{4}e^{-7t}, \quad f'(0) = -6,$$

construct pool systems with that disappearance function.

To do this, we find the sojourn function, $g(x) = ce^{-bx}$, where, according to Rule 1 of Section 5, $b = 3 + 7 - 6 = 4$, and

$$c = -\frac{(6-3)(6-7)}{6} = \frac{1}{2}. \quad \text{Thus}$$

$$g(x) = \frac{1}{2}e^{-6x} = \frac{1}{8}(4e^{-4x}), \quad x > 0.$$

Thus the area under $g(x)$ is $\frac{1}{8}$, and hence $\frac{7}{8}$ of the particles leaving the compartment do not return; of the $\frac{1}{8}$ that do return, the sojourn time has an exponential density, $4e^{-4x}$. There are, as usual, an infinite number of two-compartment systems with the given disappearance curve and sojourn function. For any choice of r in $0 \leq r < 5.25$, this system will be such a one:

