STUDIES ON THE THEORY OF CONTINUOUS PROBABILITIES, WITH SPECIAL REFERENCE TO ITS BEARING ON NATURAL PHENOMENA OF A PROGRESSIVE NATURE

By A. G. McKENDRICK, M.B., Ch.B., F.R.S.E., Major, Indian Medical Service.

[Received January 17th, 1914.—Read February 12th, 1914.]

THE accompanying analysis had its origin in the following problem :—

An intimate mixture of leucocytes and micro-organisms in a medium of serum is prepared and kept at the heat of the blood. Collisions occur between the two types of cells, with subsequent inclusion of micro-organisms into the substance of the leucocytes. These two stages constitute the phenomenon of phagocytosis. The process may be stopped at any moment, and a specimen preparation obtained, which, after suitable treatment by staining fluids, renders it possible for a complete record to be made of the distribution amongst the leucocytes of such micro-organisms as have been ingested. It is required to find the mathematical law which governs such distributions.

1. If ϕ be the probability that an individual will be affected in a particular manner in an event, then, amongst v_0 individuals which are simultaneously submitted to the event, ϕv_0 will be affected. The system of individuals will, after such an event, comprise two groups, ϕv_0 which have been affected and $v_0 - \phi v_0$ which have not been affected. Thus, ϕv_0 measures the decrease in the unaffected class. If we consider an event as occupying an interval of time Δt, and that the events follow each other in succession without intermission, then

$$\frac{\Delta v_0}{\Delta t} = -\phi v_0. \tag{1}$$

If we further consider that these decrements take place continuously from moment to moment, *i.e.*, if v_0 is a continuous function of the time, then

$$\frac{dv_0}{dt} = -\phi v_0. \tag{2}$$

Taking into consideration the condition that individuals may be affected once, twice, three times, ..., x times, then for each class of individuals above the zero class there is an increase due to incomers from the preceding class, and a decrease due to outgoers from the class under consideration. These are proportional to ϕ and to the numbers of individuals in the respective classes. Consequently

$$\frac{dv_x}{dt} = (v_{x-1} - v_x)\phi, \tag{3}$$

an equation in v, continuous as regards t, but not as regards x; for, from the very nature of the problem, the happenings x are positive integral numbers.

Combining equations (2) and (3) we have

$$\frac{dv_x}{dv_0} = \frac{v_{x-1} - v_x}{-v_0},$$

$$\frac{1}{v_0}\frac{dv_x}{dv_0} - \frac{v_x}{v_0^2} = -\frac{v_{x-1}}{v_0^2},$$

$$\frac{d}{dv_0}\left(\frac{v_x}{v_0}\right) = -\frac{v_{x-1}}{v_0^2},$$

$$\frac{v_x}{v_0} = C_x - \int \frac{v_{x-1}}{v_0^2}\,dv_0 = C_x + \int \frac{v_{x-1}}{v_0}\,d\log\frac{a_0}{v_0},$$

where $v_0 = a_0$, when $t = 0$.

Let $\log \frac{a_0}{v_0} = m$, then for $x = 1$, we have

$$\frac{v_1}{v_0} = C_1 + m = \frac{a_1}{a_0} + m,$$

where $v_1 = a_1$, when $t = 0$.

Similarly for $x = 2$,

$$\frac{v_2}{v_0} = \frac{a_2}{a_0} + \frac{a_1}{a_0}m + \frac{m^2}{2!},$$

and generally

$$\frac{v_x}{v_0} = \frac{a_x}{a_0} + \frac{a_{x-1}}{a_0}m + \frac{a_{x-2}}{a_0}\frac{m^2}{2!} + \ldots + \frac{a_1}{a_0}\frac{m^{x-1}}{(x-1)!} + \frac{m^x}{x!}. \tag{4}$$

2. As v_x denotes the number of individuals in the x-th class, the mean class among the total individuals is

$$\sum_{0}^{x=\infty} x v_x \div \sum_{0}^{x=\infty} v_x.$$

The numerator is

$$v_0 \left\{ \begin{array}{l} \frac{a_1}{a_0}+m \\ +2\left(\frac{a_2}{a_0}+\frac{a_1}{a_0}m+\frac{m^2}{2!}\right) \\ +3\left(\frac{a_3}{a_0}+\frac{a_2}{a_0}m+\frac{a_1}{a_0}\frac{m^2}{2!}+\frac{m^3}{3!}\right) \\ \vdots \\ +x\left(\frac{a_x}{a_0}+\frac{a_{x-1}}{a_0}m+\ldots+\frac{a_1}{a_0}\frac{m^{x-1}}{(x-1)!}+\frac{m^x}{x!}\right) \end{array} \right.$$

$$= v_0 \left\{ \begin{array}{l} m\left(1+m+\frac{m^2}{2!}+\ldots+\frac{m^x}{(x-1)!}\right) \\ +\frac{a_1}{a_0}\left(1+2m+3\frac{m^2}{2!}+\ldots+x\frac{m^{x-1}}{(x-1)!}\right) \\ +\frac{a_2}{a_0}\left(2+3m+4\frac{m^2}{2!}+\ldots+x\frac{m^{x-2}}{(x-2)!}\right) \\ \vdots \\ +\frac{a_x}{a_0}x. \end{array} \right.$$

When x is very large, we have in the limit

$$v_0 \left\{ me^m+\frac{a_1}{a_0}e^m(1+m)+\frac{a_2}{a_0}e^m(2+m)+\ldots+\frac{a_r}{a_0}e^m(r+m)\ \ldots \right\}$$

$$= v_0 \left\{ me^m\left(1+\frac{a_1}{a_0}+\frac{a_2}{a_0}+\ldots+\frac{a_r}{a_0}+\ldots\right) \right.$$
$$\left. +e^m\left(\frac{a_1}{a_0}+2\frac{a_2}{a_0}+\ldots+\frac{ra_r}{a_0}+\ldots\right)\right\}$$

$$= m(a_0+a_1+a_2+\ldots)+(a_1+2a_2+3a_3+\ldots).$$

The denominator when similarly treated becomes

$$v_0 e^m\left(1+\frac{a_1}{a_0}+\frac{a_2}{a_0}+\ldots+\frac{a_r}{a_0}+\ldots\right) = a_0+a_1+a_2+\ldots+a_r+\ldots,$$

as it should be, since the total number of individuals is unchanged.

Thus the mean class is

$$m+\left(\sum_{0}^{x=\infty} x a_x \div \sum_{0}^{x=\infty} a_x\right),$$

or if μ_t denote the mean at the time t,

$$\mu_t-\mu_0 = m.$$

Equation (4) may be now written in terms of the mean,

$$v_x = e^{-(\mu_t-\mu_0)}\left\{a_x+a_{x-1}(\mu_t-\mu_0)+a_{x-2}\frac{(\mu_t-\mu_0)^2}{2!}+\ldots\right.$$
$$\left.+a_1\frac{(\mu_t-\mu_0)^{x-1}}{(x-1)!}+a_0\frac{(\mu_t-\mu_0)^x}{x!}\right\}. \quad (5)$$

From equation (2) we have $\dfrac{dm}{dt} = \phi$;

therefore $$\mu_t-\mu_0 = \int_0^t \phi dt.$$

Thus the complete solution is

$$v_x = e^{-\int_0^t \phi dt}\left\{a_x+a_{x-1}\int_0^t \phi dt+a_{x-2}\frac{\left[\int_0^t \phi dt\right]^2}{2!}+\ldots\right.$$
$$\left.+a_1\frac{\left[\int_0^t \phi dt\right]^{x-1}}{(x-1)!}+a_0\frac{\left[\int_0^t \phi dt\right]^x}{x!}\right\}. \quad (6)$$

Note.—The square of the "standard deviation," *i.e.*,

$$\sum_{0}^{x=\infty} (\mu_t-x)^2 v_x \div \sum_{0}^{x=\infty} v_x,$$

becomes $$e^{\mu_0}\left\{m+\mu_0+\frac{a_1+4a_2+9a_3+\ldots}{a_0+a_1+a_2+\ldots}\right\},$$

which, when $\mu_0 = 0$, is equal to m.

3. In the particular case of the phagocytic experiment the following conditions occur :—

(*a*) All leucocytes are initially empty, *i.e.*

$$\sum_{0}^{x=\infty} a_x = a_0 \quad \text{and} \quad \mu_0 = 0.$$

(*b*) The probability ψ is an unknown function of the time. It is dependent on a diminishing concentration of micro-organisms, on a diminishing concentration of specific accelerating substances in the serum, and on the temperature. The distribution is thus defined by equation (4) in terms of v_0, as

$$v_x = v_0 \frac{\left(\log \frac{a_0}{v_0}\right)^x}{x!},$$

or, by equation (5), in terms of the mean, as

$$v_x = a_0 e^{-\mu_t} \frac{(\mu_t)^x}{x!}.$$

In the following table are shown results observed by various workers, and figures calculated by equation (4) from observed values of v_0 and a_0.

$v_x \rightarrow$	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.
$x = 0$	19	(19)	99	(99)	41	(41)	620	(620)	632	(632)
1	59	57·89	227	206·8	126	119·1	282	296·3	282	290
2	98	88·2	208	216·1	154	173·1	79	70·8	65	66·5
3	88	89·7	134	150·5	164	167·7	16	11·29	16	10·1
4	65	68·24	78	78·63	121	121·8	2	1·349	4	1·1
5	37	41·58	34	32·85	62	70·8	1	0·131	1	0·10
6	17	21·12	9	11·44	36	34·3				
7	8	9·192	7	3·415	35	14·2				
8	5	3·501	3	0·8921	5	5·17				
9	2	1·185	0		2	1·67				
10	1	0·361	0		3	0·48				
11	0		0		1					
12	1		1							
Mean	3·005	3·04702	2·0825	2·0832	3·040	2·9065	0·50	0·47804	0·48	0·45887
S.D.	1·777	1·7455	1·4134	1·443	1·8927	1·747	0·74	0·7757	0·74	0·6893

4. As an example of a complete solution in the form of equation (6) the distribution of collisions amongst a_0 molecules of a gas occurring subsequent to an arbitrary point of time $t = 0$ is denoted by the equation

$$\frac{dv_x}{dt} = (v_{x-1} - v_x)\, a_0 \psi,$$

where ψ is constant. The solution by equation (6) is

$$v_x = a_0 e^{-\psi a_0 t} \frac{(\psi a_0 t)^x}{x!}.$$

5. Returning to equation (4): in cases where

$$\sum_{0}^{x=\infty} a_x = a_0 \quad (i.e., \ \mu_0 = 0),$$

let us ascertain the maximum value of v. This will be the x-th term if, of

$$\frac{m^{x-1}}{(x-1)!}, \quad \frac{m^x}{x!}, \quad \frac{m^{x+1}}{(x+1)!}$$

the middle term be the greatest, or if, of

$$x(x+1), \quad (x+1)\,m, \quad m^2$$

the middle term be the greatest.

Thus,

$$x < m < x+1,$$

or x must be the greatest integer not exceeding m. Proceeding to the limit where a_0 is indefinitely large, and the number of classes is indefinitely large, we may put $x\tau = n$, where τ is a fixed small quantity. Thus, in the limit n may be regarded as increasing continuously from class to class, while x increases by successive steps of unity. The mean, for the continuous curve whose ordinates are v_x and abscissæ x, will be at $n = x\tau = m\tau$. The *mode* occurs when $n = (m-f)\tau$, where f is a fraction less than unity. Thus n is equal to $m\tau$ in the limit for the *mode* as for the mean.

The form of the curve in the limit may be approximated to, by the aid of Stirling's formula,

$$v_x = \frac{a_0 e^{-m} m^x}{x!} = \frac{a_0 e^{-m} m^x}{\sqrt{2\pi}\, e^{-x} x^{x+\frac{1}{2}}},$$

at the mean, where $x = m$, $\quad v_m = \dfrac{a_0}{\sqrt{2\pi m}}$,

and at a neighbouring point where $x = m+r$,

$$v_{m+r} = \frac{a_0 e^{-m} m^{m+r}}{\sqrt{2\pi}\, e^{-(m+r)} (m+r)^{m+r+\frac{1}{2}}}.$$

Now $\quad \log\left(1+\dfrac{r}{m}\right)^{m+r+\frac{1}{2}} = (m+r+\tfrac{1}{2})\left(\dfrac{r}{m} - \dfrac{r^2}{2m^2} + \dfrac{r^3}{3m^3} - \dots\right)$

$$= \left(1+\frac{2r+1}{2m}\right)\left(r - \frac{r^2}{2m} + \frac{r^3}{3m^2} - \dots\right)$$

$$= r + \frac{r^2+r}{2m} - \frac{2r^3+3r^2}{12m^2} + \dots.$$

Thus
$$v_{m+r} = \frac{a_0}{\sqrt{2\pi m}} e^{-(r^2+r)/2m + (2r^3+3r^2)/12m^2 - \dots},$$

and if r be large, though small as compared with m,

$$v_{m+r} = \frac{a_0}{\sqrt{2\pi m}} e^{-r^2/2m}. \tag{7}$$

6. In three dimensions equation (3) has the form

$$\frac{dv_{x,y,z}}{dt} = (v_{x-1,y,z} - v_{x,y,z})\phi_1 + (v_{x,y-1,z} - v_{x,y,z})\phi_2 + (v_{x,y,z-1} - v_{x,y,z})\phi_3.$$

Consequently when $\phi_1 = \phi_2 = \phi_3$, we have

$$\frac{dv_{x,y,z}}{dv_{0,0,0}} = \frac{v_{x-1,y,z} + v_{x,y-1,z} + v_{x,y,z-1} - 3v_{x,y,z}}{-3v_{0,0,0}},$$

which, when $\mu_0 = 0$, has for solution

$$v_{x,y,z} = \frac{v_{0,0,0}\left(\frac{m}{3}\right)^{x+y+z}}{x!\,y!\,z!}. \tag{8}$$

7. The theory which has so far been developed refers to cases of an *irreversible* nature, in which the only limitation to ϕ is that it is not a function of x. This restriction may now be removed, and equation (3) may be written

$$\frac{dv_x}{dt} = (f_{x-1}v_{x-1} - f_x v_x)\phi, \tag{9}$$

where f_x is a function of x.

Consequently $\quad \dfrac{dv_0}{dt} = -f_0 v_0 \phi \quad$ or $\quad \dfrac{dm}{dt} = f_0 \phi,$

where
$$m = \log \frac{a_0}{v_0}.$$

Thus
$$\frac{dv_x}{dm} + \frac{f_x}{f_0} v_x = \frac{f_{x-1}}{f_0} v_{x-1},$$

whence
$$v_x = e^{-(f_x/f_0)m}\left[\int \frac{f_{x-1}}{f_0} v_{x-1} e^{(f_x/f_0)m}\, dm + C_x\right].$$

When $x = 1$, $\quad v_1 = e^{-(f_1/f_0)m}\left[\int v_0 e^{(f_1/f_0)m}\,dm + C_1\right];$

but $v_0 = a_0 e^{-m}$, hence

$$v_1 = e^{-(f_1/f_0)m}\left[\frac{a_0 e^{(f_1/f_0-1)m}}{\frac{f_1-f_0}{f_0}} + C_1\right] = \frac{a_0 f_0 e^{-m}}{f_1-f_0} + C_1 e^{-(f_1/f_0)m}.$$

In cases where $\mu_0 = 0$, *i.e.*, $a_r = 0$ for all values of r other than $r = 0$,

$$C_1 = -\frac{a_0 f_0}{f_1-f_0}.$$

Consequently

$$v_1 = v_0 \frac{f_0}{f_1-f_0}\left(1 - \frac{a_0}{v_0} e^{-(f_1/f_0)m}\right) = v_0 \frac{f_0}{f_1-f_0}\left(1 - e^{(1-f_1/f_0)m}\right).$$

Similarly,

$$v_2 = v_0 \frac{f_0}{(f_1-f_0)}\frac{f_1}{(f_2-f_0)}\left[1 - \frac{f_2-f_0}{f_2-f_1} e^{(1-f_1/f_0)m} + \frac{f_1-f_0}{f_2-f_1} e^{(1-f_2/f_0)m}\right].$$

In the case where f_x is a linear function of x, we have, for $f_x = b + cx$,

$$v_1 = v_0 \frac{b}{c}\left(1 - e^{-c/b\,.\,m}\right),$$

$$v_2 = v_0 \frac{b}{c}\left(\frac{b}{c}+1\right)\frac{\left(1 - e^{-c/b\,.\,m}\right)^2}{2!},$$

$$\ldots \quad \ldots \quad \ldots \quad \ldots \quad \ldots$$

$$v_x = v_0 \frac{b}{c}\left(\frac{b}{c}+1\right)\ldots\left(\frac{b}{c}+x-1\right)\frac{\left(1 - e^{-c/b\,.\,m}\right)^x}{x!}. \tag{10}$$

The mean grade is

$$\sum_0^{x=\infty} x v_x \div \sum_0^{x=\infty} v_x = \frac{b}{c}\left(e^{c/b\,.\,m} - 1\right) = \mu.$$

The square of the standard deviation is

$$\sum_0^{x=\infty} (\mu - x)^2 v_x \div \sum_0^{x=\infty} v_x = \sum_0^{x=\infty} \frac{x^2 v_x}{a_0} - \mu^2 = e^{c/b\,.\,m}\mu = \nu.$$

Hence in terms of these moments

$$v_x = a_0 \frac{b}{c}\left(\frac{b}{c}+1\right)\ldots\left(\frac{b}{c}+x-1\right)\frac{\left(1-\frac{\mu}{\nu}\right)^x}{x!}\left(\frac{\mu}{\nu}\right)^{b/c}. \tag{11}$$

For $f_x = b-cx$, we have similarly

$$v_x = v_0 \frac{b}{c}\left(\frac{b}{c}-1\right)\ldots\left(\frac{b}{c}-x+1\right)\frac{(e^{c/b.m}-1)^x}{x!}, \tag{12}$$

$$\mu = \frac{b}{c}(1-e^{c/b.m}),$$

$$\nu = e^{-(c/b)m}\mu,$$

$$v_x = a_0 \frac{b}{c}\left(\frac{b}{c}-1\right)\ldots\left(\frac{b}{c}-x+1\right)\frac{\left(\frac{\mu}{\nu}-1\right)^x}{x!}\left(\frac{\nu}{\mu}\right)^{b/c}. \tag{13}$$

8. Let us now consider cases in which the phenomenon is of a *reversible* nature, and let us confine ourselves to particular cases in which ϕ is independent of x. Equation (3) takes the form (in one dimension)

$$\frac{dv_x}{dt} = (v_{x-1}-2v_x+v_{x+1})\,\phi. \tag{14}$$

In order to include cases in which ϕ is a function of the time, let us write t for $\int \phi\, dt$.

By Maclaurin's series we have

$$v_x = (v_x)_0 + \left(\frac{dv_x}{dt}\right)_0 t + \left(\frac{d^2v_x}{dt^2}\right)_0 \frac{t^2}{2!} + \ldots.$$

If when $t=0$, $v_r = a_r$, then for $x = 0$,

$$(v_0)_0 = a_0,$$

$$\left(\frac{dv_0}{dt}\right)_0 = a_{-1}-2a_0+a_1,$$

$$\left(\frac{d^2v_0}{dt^2}\right)_0 = a_{-2}-4a_{-1}+6a_0-4a_1+a_2,$$

$$\ldots \quad \ldots \quad \ldots \quad \ldots \quad \ldots$$

$$\left(\frac{d^nv_0}{dt^n}\right)_0 = a_{-n}-2na_{-n+1}+\frac{2n(2n-1)}{2!}a_{-n+2}-\ldots$$

$$+\frac{2n(2n-1)}{2!}a_{n-2}-2na_{n-1}+a_n.$$

Similarly for $x = 1$,

$$(v_1)_0 = a_1,$$

$$\left(\frac{dv_1}{dt}\right)_0 = a_0 - 2a_1 + a_2,$$

$$\left(\frac{d^2v_1}{dt^2}\right)_0 = a_{-1} - 4a_0 + 6a_1 - 4a_2 + a_3,$$

and so on.

In the case of an *instantaneous point source* a_0 at $x = 0$, when $t = 0$, all terms except those in a_0 disappear; and the derivatives in Maclaurin's series for v_0 are equal to a_0 multiplied by the coefficients of the middle terms of binomials of the type $(\alpha - \beta)^{2n}$ (*i.e.* the n-th terms), whilst for $v_{\pm 1}$ the coefficients are those of the $(n \mp 1)$-th terms of the same expansion, and for $v_{\pm x}$ they are those of the $(n \mp x)$-th terms.

Consequently

$$v_x = a_0 \sum_0^{n=\infty} (-)^{n+x} \frac{2n(2n-1)\dots[2n-(n-x)+1]\,t^n}{(n-x)!\,n!}$$

$$= a_0 \sum_0^{n=\infty} (-)^{n+x} \frac{2n!\,t^n}{(n-x)!\,n!\,(n+x)!}. \tag{15}$$

The distribution is obviously a symmetrical one. The mean grade is at $x = 0$.

The square of the standard deviation

$$\nu = \sum_0^{x=\infty} (\mu - x)^2 \nu_x \div \sum_0^{x=\infty} v_x = 2t,$$

where

$$t = \int \phi\, dt.$$

9. Cases in which the number of classes is limited are found in the laws governing chemical reactions. Thus, confining ourselves to monomolecular reactions, we have

(*a*) For an irreversible reaction in which the number of classes is two,

$$\frac{dv_0}{dt} = -\phi v_0, \quad \frac{dv_1}{dt} = \phi v_0,$$

which, when $v_0 = a_0$ and $v_1 = 0$, when $t = 0$ gives

$$\frac{dv_1}{dt} = \phi(a_0 - v_1).$$

(*b*) For an irreversible reaction in which the number of classes is three or more we have

$$\frac{dv_0}{dt} = -\phi_0 v_0,$$

$$\frac{dv_1}{dt} = \phi_0 v_0 - \phi_1 v_1,$$

$$\dots \quad \dots \quad \dots$$

$$\frac{dv_x}{dt} = \phi_{x-1} v_{x-1} - \phi_x v_x,$$

$$\frac{dv_{x+1}}{dt} = \phi_x v_x.$$

(*c*) For a reversible reaction in which the number of classes is two,

$$\frac{dv_0}{dt} = -\frac{dv_1}{dt} = -\phi_0 v_0 + \phi_1 v_1,$$

or for three classes,

$$\frac{dv_0}{dt} = -\phi_0 v_0 + \phi_1 v_1,$$

$$\frac{dv_1}{dt} = \phi_0 v_0 - \phi_1 v_1 - \phi_2 v_1 + \phi_3 v_2,$$

$$\frac{dv_2}{dt} = \phi_2 v_1 - \phi_3 v_2.$$

In the theory of the spread of epidemics by contagion similar cases occur. For instance, where there is no recovery, we have for distribution according to multiplicity of infections,

$$\frac{dv_x}{dt} = (v_{x-1} - v_x)\,\phi \sum_{1}^{x=\infty} v_x,$$

where a_1 cannot be less than unity; and in cases where the community may be divided into three classes, v_0 not yet infected, v_1 affected, v_2 dead or immune, we have

$$\frac{dv_0}{dt} = -\phi v_0 v_1,$$

$$\frac{dv_1}{dt} = \phi v_0 v_1 - \psi v_1,$$

$$\frac{dv_2}{dt} = \psi v_1.$$

10. Cases in which v_x is a continuous function of x. The differences Δx between successive classes have been, in the cases considered in paragraphs 1 to 8, equal to unity. Let us now apply the same reasoning to cases in which Δx may be made as small as we please.

11. *Irreversible Phenomena.*—The flux over a face $x-\frac{1}{2}\Delta x$ of a parallelepipedon Δx, Δy, Δz, whose centre is at x, is proportional to $v_{x-\Delta x}\Delta y\Delta z$, and that over the face $x+\frac{1}{2}\Delta x$ to $-v_x\Delta y\Delta z$. Consequently the excess of influx over efflux in the parallelepipedon is, in this dimension equal to $-\phi\ \frac{\partial v_x}{\partial x}\,dx\,dy\,dz$, as Δx, Δy, Δz tend to zero, if ϕ be independent of x, y, z. But this excess can also be considered as the rate of increase in the contents of the parallelepipedon, *i.e.*, by $\frac{\partial q}{dt}$, or by the rate of increase in concentration, *i.e.* by $\frac{\partial v}{\partial t}\,dx\,dy\,dz$.

Hence equation (3) has the form

$$\frac{\partial v}{\partial t} = -\phi\frac{\partial v}{\partial x}, \tag{16}$$

whence

$$v = f(x-\phi t).$$

Thus, for any constant value of $(x-\phi t)$, v is constant, that is to say, equation (16) expresses a translation along the x axis.

12. *Reversible Phenomena.*—In this case the flux over the face $x-\frac{1}{2}\Delta x$ is proportional to $\frac{v_{x-\Delta x}-v_x}{\Delta x}\Delta y\Delta z$, and that over the face $x+\frac{1}{2}\Delta x$ to $-\frac{v_x-v_{x+\Delta x}}{\Delta x}\Delta y\Delta z$. Thus, if ϕ be independent of x, and identical in the positive and negative directions, the excess of influx over efflux, as Δx, Δy, Δz tend to zero, tends to

$$\left(\frac{\partial v_{x+\frac{1}{2}dx}}{\partial x} - \frac{\partial v_{x-\frac{1}{2}dx}}{\partial x}\right) dy\,dz,$$

which is equal to

$$\frac{\partial^2 v}{\partial x^2}\,dx\,dy\,dz.$$

But, as before, this, with similar terms in y and z, measures the rate of increase in concentration of the parallelepipedon, *i.e.* $\frac{\partial v}{\partial t}\,dx\,dy\,dz$. Hence

$$\frac{\partial v}{\partial t} = \phi_x \frac{\partial^2 v}{\partial x^2} + \phi_y \frac{\partial^2 v}{\partial y^2} + \phi_z \frac{d^2 v}{\partial z^2}. \tag{17}$$

If ϕ_x, ϕ_y and ϕ_z be equal, that is to say, if there is *randomness* in direction as well as in sense, the equation is that of *Fourier*. For an instantaneous point source of value Q at $x = y = z = 0$ the solution is

$$v = \frac{Q}{8\,(\pi\phi t)^{\frac{3}{2}}}\, e^{-(x^2+y^2+z^2)\,4\phi t}. \tag{18}$$

This is the *error function of Gauss* in three dimensions, and is the logical outcome of equation (1) for cases of random reversible progressions, from a point source at the origin, in which v is a continuous function of t, x, y, and z.

13. *Incomplete Reversibility.*—Certain cases occur in which ϕ' in the positive sense is not equal to ϕ in the negative sense. If we divide the greater, say ϕ', into two quantities ϕ and ψ (*i.e.* $\psi = \phi' - \phi$), we may consider the phenomenon as the resultant of two progressions, one of them reversible and proportional to ϕ, the other irreversible and proportional to ψ.

Thus, combining equations (16) and (17), we have in one dimension

$$\frac{\partial v}{\partial t} = \phi \frac{\partial^2 v}{\partial x^2} - \psi \frac{\partial v}{\partial x}. \tag{19}$$

The solution of which for an instantaneous point source at the origin, is

$$v = \frac{Q}{2\sqrt{\pi\phi t}}\, e^{-(x-\psi t)^2\,4\phi t}. \tag{20}$$

14. When ϕ is a function of x, the flux over the face $x - \frac{1}{2}\Delta x$ is

$$\phi_{x-\frac{1}{2}\Delta x} \frac{v_{x-\Delta x} - v_x}{\Delta x} \Delta y\, \Delta z,$$

that over the face $x + \frac{1}{2}\Delta x$ is

$$-\phi_{x+\frac{1}{2}\Delta x} \frac{v_x - v_{x+\Delta x}}{\Delta x} \Delta y\, \Delta z.$$

Hence the excess of influx over efflux, as Δx, Δy, Δz tend to zero, is

$$-\phi_{x-\frac{1}{2}dx} \frac{\partial v_{x-\frac{1}{2}dx}}{\partial x}\, dy\, dz + \phi_{x+\frac{1}{2}dx} \frac{\partial v_{x+\frac{1}{2}dx}}{\partial x}\, dy\, dz,$$

which is equal to $\left(\phi_x \frac{\partial^2 v}{\partial x^2} + \frac{\partial \phi_x}{\partial x}\frac{\partial v}{\partial x}\right) dx\, dy\, dz.$

Hence, as before, $\frac{\partial v}{\partial t} = \phi_x \frac{\partial^2 v}{\partial x^2} + \frac{\partial \phi_x}{\partial x}\frac{\partial v}{\partial x} = \frac{\partial}{\partial x}\phi_x \frac{\partial v}{\partial x}.$ (21)

If $\phi_x = \kappa x^2$, we have

$$\frac{\partial v}{\partial t} = \kappa\left(x^2 \frac{\partial^2 v}{\partial x^2} + 2x\frac{\partial v}{\partial x}\right) = \kappa x\left(x\frac{\partial^2 v}{\partial x^2} + \frac{\partial v}{\partial x}\right) + \kappa x \frac{\partial v}{\partial x}$$

$$= \kappa x \frac{\partial}{\partial x} x \frac{\partial v}{\partial x} + \kappa x \frac{\partial v}{\partial x} = \kappa \frac{\partial^2 v}{\partial \log x^2} + \kappa \frac{\partial v}{\partial \log x};$$

hence $$v = \frac{Q}{2\sqrt{\pi\kappa t}} e^{-(\log x/x_0 + \kappa t)^2/4\kappa t}.$$

15. A modification which is of peculiar interest to statisticians occurs in what I may call the *target distribution*. It may be obtained as follows, taking the type of phenomena dealt with in paragraph 13 as an example. Consider a case of random diffusion in three dimensions, combined with translation along the z axis.

$$\frac{\partial v}{\partial t} = \phi\left(\frac{\partial^2 v}{\partial x^2} + \frac{\partial^2 v}{\partial y^2} + \frac{\partial^2 v}{\partial z^2}\right) - \psi \frac{\partial v}{\partial z}.$$

The solution for an instantaneous point source Q at the origin is

$$v = \frac{Q}{8(\pi\phi t)^{\frac{3}{2}}} e^{-[x^2+y^2+(z-\psi t)^2]/4\phi t}.$$

Let a target be introduced in the plane $z = a$, which records the position of particles in transit, but does not interfere with their progress. Writing l^2 for $x^2+y^2+a^2$, and integrating according to the time, we have

$$A = \int_0^\infty v\,dt = \frac{Qe^{\psi a/2\phi}}{8(\pi\phi)^{\frac{3}{2}}}\int_0^\infty e^{-l^2/4\phi t - \psi^2 t/4\phi}\frac{dt}{t^{\frac{3}{2}}},$$

putting $$s = \frac{1}{\sqrt{t}},$$

$$A = \frac{Qe^{\psi a/2\phi}}{8(\pi\phi)^{\frac{3}{2}}}\int_0^\infty e^{-l^2 s^2/4\phi - \psi^2/4\phi s^2} ds = \frac{Qe^{\psi/2\phi\,(a-\sqrt{x^2+y^2+a^2})}}{4\pi\phi\sqrt{x^2+y^2+a^2}}. \quad (22)$$

On integrating again according to x and y, from $-\infty$ to $+\infty$, using polar coordinates, we have

$$B = \int_{-\infty}^{\infty}\int_{-\infty}^{\infty} A\,dx\,dy = \frac{Qe^{\psi a/2\phi}}{4\pi\phi}\int_0^{\infty}\int_0^{2\pi}\frac{e^{-\psi/2\phi\sqrt{r^2+a^2}}}{\sqrt{r^2+a^2}}\,r\,dr\,d\theta$$

$$= \frac{Qe^{\psi a/2\phi}}{2\phi}\int_0^{\infty}\frac{e^{-\psi/2\phi\sqrt{r^2+a^2}}}{\sqrt{r^2+a^2}}\,r\,dr.$$

Putting

$$s^2 = r^2+a^2,$$

$$B = \frac{Qe^{\psi a/2\phi}}{2\phi}\int_a^{\infty} e^{-\psi s/2\phi}\,ds = \frac{Q}{\psi}.$$

Now A represents the length of time during which any point whose coordinates are x and y has been occupied by particles in transit across the plane $z=a$. It is thus directly proportional to the number of individuals which have crossed, and inversely to the time occupied in their transit. It will be noted that in the differential equation the translation due to the factor $-\psi\frac{\partial v}{\partial z}$ does not deviate from the direction *z plus*, and that, since by hypothesis ϕ is random in direction and sense at any moment of time, momentum is excluded; thus, any lengthening of individual occupation due to obliquity of transit is equally probable at any point in the plane $z = a$.

Hence if $w_{x,y}$ represent the number of transits at any point x, y in the plane $z = a$,

$$w_{x,y} = A\psi = \frac{Q\psi}{4\pi\phi}\frac{e^{\psi/2\phi(a-\sqrt{x^2+y^2+a^2})}}{\sqrt{x^2+y^2+a^2}}, \tag{23}$$

and the total number of transits is

$$B\psi = Q.$$

The approximation of the *target distribution* expressed by equation (23) to the error function, when ψ is great as compared with ϕ, and x^2+y^2 is less than a^2, may be shown as follows:—

$$w = \frac{Q\psi}{4\pi\phi}\frac{e^{\psi/2\phi(a-\sqrt{r^2+a^2})}}{\sqrt{r^2+a^2}}$$

$$= \frac{Q\psi}{4\pi\phi a}e^{\psi a/2\phi(1-\sqrt{1+r^2/a^2})-\frac{1}{2}\log(1+r^2/a^2)}$$

$$= \frac{Q\psi}{4\pi\phi a}e^{\psi a/2\phi(-r^2/2a^2+r^4/8a^4-r^6/16a^6+\dots)-(r^2/2a^2-r^4/4a^4+r^6/6a^6-\dots)}$$

$$= \frac{Q\psi}{4\pi\phi a}e^{-\psi r^2/4\phi a}\left[(1+2\phi/\psi a)-r^2/4a^2(1+4\phi/\psi a)+r^4/8a^4(1+16\phi/3\psi a)-\dots\right].$$

16. In conclusion, I trust that I have in these notes directed attention to methods of attack which will be of service in the solution of problems chiefly of a biological nature. Statisticians have not, I think, recognized the applicability of Fourier's theorem to many of the problems in the investigation of which they are engaged. If diffusion be considered as progression, random in sense and direction, and uniform as regards time, its applicability is apparent. For instance, the broad lines of mosquito distribution may be resolved into a problem of "sources," and, if destructive methods be employed, it may take the form of a problem of "sources" and "sinks." The range of applicability is further extended when the dimensions are not those of space, but of degree of certain characteristics. In paragraphs 13 and 15 I have broken ground for further investigation into the processes of *Evolution;* for evolution, with its accompanying degeneration, is in its essence a phenomenon of incomplete reversibility according to a number of characteristics. A collection of fossils is a target distribution, though of a much more complicated nature than the simple case I have instanced. The target may be considered as a fixed degree in the development of some characteristic z; the target distribution will classify this selected population according to degree of characteristics x and y. Some of the population $(z = a)$ will be early comers and some late comers, and, according as they come early or late, so will they tend to take up different positions according to the characteristics x and y.