THE KINETICS OF STARVATION.

II. THE LOSS OF WEIGHT IN PIGEONS SUBSISTING ON WATER ALONE.

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In a previous paper, it was shown that the single cycle symmetrical form of the autocatalytic law could not by itself be made to represent the changes of weight during the entire course of starvation in pigeons suffering from partial inanition. By the addition of two autocatalytic curves, however, a procedure which recognized the cyclical nature of the process, it was found that very good agreement between theoretical and observed losses in weight could be obtained. Consequently, it was suggested that the course of starvation is governed by the rate of destruction of body protein and that it is modified by the amount and by the rate of destruction of reserve tissues. Plausible as this conclusion is, it could not be applied to the phenomena of complete inanition without experimental verification. The present paper, accordingly, deals with the application of the earlier principles to the problem of pure starvation.

THEORY.

At the outset it may be stated that the following analysis is only incidentally concerned with fitting a curve to the loss of weight observed in partial and in complete inanition. Strictly curve-fitting enterprises have been previously attempted. The primary object

has been to present a function which will not only have the power of
meeting the observational results, but which, when completely
analyzed, will also convey an impression as to the nature of the funda-
mental reactions participating in the process and will finally afford
some quantitative measure of these reactions. These postulates are
satisfied by a suitable application of the law of autocatalysis.  

Only a short time ago, in further studies of the population problem,
Pearl \(^5\) derived a general equation for the mathematical expression of
this law free from the restrictions of the single cycle form. This equa-
tion may be written:

\[
y = \frac{k}{1 + me^F(t)}
\]

in which \(y\) represents the increments on the ordinate, \(k\) the asymptote
of the curve, and \(F(t)\), some undefined function of time expanded by
means of Taylor's theorem into an infinite series so that

\[
me^F(t) = e^{ad} + a^2t^2 + a^3t^3 + \ldots + a^n t^n
\]

the factor \(m\) being equal to \(e^b\). In this form the expression provides
for any number of cycles which may be either symmetrical or asym-
metrical in nature. The labor of fitting this curve to cases where the
changes in adjacent cycles are nearly symmetrical is reduced by
using a simpler form substantially like that employed in the previous
communication:\(^4\)

\[
y = d + \frac{k}{1 + me^{awt}}
\]

in which \(d\) is the upper asymptote of the earlier cycle and \(awt\) gives
the rate of change in the epoch under consideration. Henceforth,
the discussion is limited to the general relation represented by equa-
tion (1).

If then, the whole course of partial starvation can be denoted by
the addition of two symmetrical autocatalytic curves, it should like-

\(^5\) Lotka, A. J., Elements of physical biology, Baltimore, 1925, 76. (This
author recalls the suggestion of W. Ostwald as to the preference for the above
term which is free from the chemical implication of autocatalysis.)

\(^6\) Pearl, R., Studies in human biology, Baltimore, 1924.
wise conform to the general modification. As a matter of fact, the necessary constants for equation (1) were calculated from the data on partial inanition previously reported, as well as from the more recent data on several groups of birds which received nothing but water. The resultant curves gave a most remarkable fit to the observed values of weight loss, considering the fact that over thirty observations are represented by a five constant equation. Only curves of total starvation are shown in Fig. 1 since the results of partial inanition were for all purposes the same as before.

Although equation (1) is a purely mathematical relation which defines a curve so closely approximating the curve of weight loss observed in fasting pigeons during complete as well as during partial inanition, it is desirable to have such a relation denote something more definite from the standpoint of the physiology and the physical chemistry of the process. It must be clear that as long as an equation contains a term such as Taylor’s series this object will not be easily attained. As it stands the above expression has far more to commend it than the several types of merely empirical relations, such as the conic sections or the inverse logarithmic equations that have been proposed to meet the requirements of the starvation curves in different animals. Equation (1) does express the kinetic relationships of a definite type of chemical reactions and it makes provisions for the cyclical character of certain processes the extent of which is limited by the value of \( k \). The difficulty in employing this expression, however, lies in the fact that the coefficients of time in the exponential expansion do not easily lend themselves to interpretation in terms of physicochemical conceptions. There is, moreover, the difficulty of clearly differentiating between the successive cycles or phases as regards the rate of decomposition during the course of the process, a matter of considerable importance in the problem under discussion.

For these reasons it has seemed more appropriate to express the exponential function directly in terms of the constants of the participating reactions. It has been shown that the entire process can be

7 The chief objection to these functions is that the weight diminishes indefinitely as \( t \) increases. The equation suggested by Morgulis (p. 89) when rearranged becomes the familiar monomolecular law of chemical change.
represented completely by an equation which may be written in the form

\[ y = \frac{A}{1 + e^{-k(t-h)}} + \frac{B}{1 + e^{-k'(t-h)}} \]  

(3)

in which the constants have the same significance as previously described. Letting

\[ Z = A + B \]
\[ P = 1 + e^{-k(t-h)} \]
\[ Q = 1 + e^{-k'(t-h)} \]

the exponential factor in the denominator of (1) may be easily transformed by making the proper substitutions leading to the result

\[ m e^{\phi(t)} = \frac{Q \left( \frac{Z}{B} (P - 1) + 1 \right) - P}{Q \left( \frac{Z}{B} - 1 \right) + P} = \theta. \]  

(4)

The equation giving the loss of weight during the entire course of starvation then becomes

\[ y = \frac{Z}{1 + \theta} \]  

(5)

in which \( y \) represents tissue loss in gm. or in percentage units, \( Z \) the maximum loss attainable, and \( \theta \) the function of time determined from (4). Similarly, it is evident that the actual weight curve is given by

\[ M_t = \frac{M_0 \left[ \theta + (1 - \alpha) \right]}{1 + \theta} \]  

(6)

in which \( M_0 \) and \( M_t \) are the weights at the beginning of the starvation period and at time \( t \) respectively, and \( \alpha \) is the fraction of tissue destroyed, namely, \( \frac{Z}{M_0} \).

Such a transformation, evidently, overcomes the difficulties to which reference has been made. It must be noted, however, that this
procedure is valid only when the successive cycles are symmetrical or nearly so. Should marked asymmetry develop in any cycle the

TABLE I.

Showing the Observed Weight Loss Compared to the Loss Calculated by Means of Equation (5) and the Corresponding Values of the Exponential Function in Equations (1) and (4).

<table>
<thead>
<tr>
<th>Time (days)</th>
<th>( \sum \Delta \theta )</th>
<th>( \Delta \theta )</th>
<th>Weight loss (gm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Calculated</td>
</tr>
<tr>
<td>0</td>
<td>14.880</td>
<td>11.300</td>
<td>24.9</td>
</tr>
<tr>
<td>1</td>
<td>9.900</td>
<td>7.900</td>
<td>33.8</td>
</tr>
<tr>
<td>2</td>
<td>6.680</td>
<td>5.580</td>
<td>43.9</td>
</tr>
<tr>
<td>3</td>
<td>4.400</td>
<td>4.060</td>
<td>55.2</td>
</tr>
<tr>
<td>4</td>
<td>3.300</td>
<td>3.020</td>
<td>65.0</td>
</tr>
<tr>
<td>5</td>
<td>2.700</td>
<td>2.420</td>
<td>76.5</td>
</tr>
<tr>
<td>6</td>
<td>2.100</td>
<td>1.900</td>
<td>86.0</td>
</tr>
<tr>
<td>7</td>
<td>1.700</td>
<td>1.570</td>
<td>95.0</td>
</tr>
<tr>
<td>8</td>
<td>1.430</td>
<td>1.320</td>
<td>101.0</td>
</tr>
<tr>
<td>9</td>
<td>1.200</td>
<td>1.200</td>
<td>109.0</td>
</tr>
<tr>
<td>10</td>
<td>1.050</td>
<td>1.030</td>
<td>114.0</td>
</tr>
<tr>
<td>11</td>
<td>0.914</td>
<td>0.940</td>
<td>121.1</td>
</tr>
<tr>
<td>12</td>
<td>0.795</td>
<td>0.830</td>
<td>128.2</td>
</tr>
<tr>
<td>13</td>
<td>0.705</td>
<td>0.730</td>
<td>134.5</td>
</tr>
<tr>
<td>14</td>
<td>0.619</td>
<td>0.650</td>
<td>142.0</td>
</tr>
<tr>
<td>15</td>
<td>0.539</td>
<td>0.564</td>
<td>151.5</td>
</tr>
<tr>
<td>16</td>
<td>0.464</td>
<td>0.466</td>
<td>160.2</td>
</tr>
<tr>
<td>17</td>
<td>0.399</td>
<td>0.385</td>
<td>168.8</td>
</tr>
<tr>
<td>18</td>
<td>0.333</td>
<td>0.316</td>
<td>176.5</td>
</tr>
<tr>
<td>19</td>
<td>0.280</td>
<td>0.255</td>
<td>185.1</td>
</tr>
<tr>
<td>20</td>
<td>0.223</td>
<td>0.199</td>
<td>189.8</td>
</tr>
<tr>
<td>21</td>
<td>0.183</td>
<td>0.170</td>
<td>200.0</td>
</tr>
<tr>
<td>22</td>
<td>0.135</td>
<td>0.109</td>
<td>202.1</td>
</tr>
<tr>
<td>23</td>
<td>0.100</td>
<td>0.099</td>
<td>206.1</td>
</tr>
<tr>
<td>24</td>
<td>0.067</td>
<td>0.076</td>
<td>210.8</td>
</tr>
<tr>
<td>25</td>
<td>0.033</td>
<td>0.057</td>
<td>213.0</td>
</tr>
<tr>
<td>26</td>
<td>0.026</td>
<td>0.042</td>
<td>215.8</td>
</tr>
<tr>
<td>27</td>
<td>0.016</td>
<td>0.032</td>
<td>218.0</td>
</tr>
<tr>
<td>28</td>
<td>0.010</td>
<td>0.024</td>
<td>216.9</td>
</tr>
<tr>
<td>29</td>
<td>0.007</td>
<td>0.018</td>
<td>219.0</td>
</tr>
<tr>
<td>30</td>
<td>0.003</td>
<td>0.002</td>
<td>221.0</td>
</tr>
</tbody>
</table>

general form (1) alone would meet the requirements. Any cyclical and nearly symmetrical function of the foregoing type can then be
analyzed either by means of the identical relations (3) and (2) or by
means of the $\theta$ transformation and (5). The latter method has
the additional advantage of combining the summations necessary for
the former procedures into a single expression similar in form to the
general law.

Owing to the nature of the present problem certain further restric-
tions must be imposed on both equations (4) and (5). In the first
place, all negative values of time are immediately eliminated since the
onset of starvation must necessarily coincide with the point $t = 0$
on the $x$ axis. Again, it can be seen from inspection of the elements in
equation (4) that as $t$ increases, $P$ as well as $Q$ must diminish, remain
positive, and approach $+1$ as a limit. The ratio $\frac{Z}{B}$ is likewise
restricted to positive values greater than 1, otherwise the amount of
tissue decomposed would be greater than the amount initially avail-
able. Under these conditions $\theta$ remains positive and approaches 0
while $y$ approaches the upper asymptote $Z$. For diminishing values of
$t$, on the other hand, the curves of $P$, $Q$, and $\theta$ ascend hyperbolically,
intercepting the $y$ axis well above 0. The solution for $y$ at this point,
accordingly, gives a result that cannot be interpreted as tissue loss.
It could, perhaps, be taken to indicate the potential instability of the
system near this parameter immediately prior to a displacement of
equilibrium. Nevertheless, any increment in $y$ however small must
require a correspondingly small but definite interval of time for the
change. Thus, the limitation of $t$ to positive values greater than 0
enables equation (5) to describe the changes in mass with a precision
that can hardly be due to chance alone.

RESULTS.

1. Experimental.—The loss of weight observed in one of the groups
of twenty pigeons which received nothing but water is recorded in
the last column of Table I and is charted by small circles along Curve
1 in Fig. 1, the curve itself passing through the points calculated by
means of equation (5), the values of which are set up in the fourth
column of the table. Curve 2 is plotted from another group of twenty

\footnote{Lotka, Chapter XXII.}
birds which were also on water alone, merely to demonstrate the identity of the processes and to present another instance of the singular agreement between observed and theoretical results. To date, the curves of about 100 birds thus treated have been studied and have been found to be similar in all essential respects to those of Fig. 1. For the present, the group represented in the table and by Curve 1 is selected for discussion. The remainder, including those of Curve 2, have been treated somewhat differently in order to study the effect of various feedings preliminary to starvation. These data have not yet been completely analyzed.

![Graph](https://example.com/graph.png)

Fig. 1. Two curves showing the loss of weight in pigeons on water alone. The curves themselves pass through the points calculated by means of equation (5). The small dots represent the experimentally observed loss of weight. Curve 1 corresponds to the data in the table.

The mean weight of the selected group on the initial day of the experiment was $429 \pm 2.88$ gm. Particular care was taken to choose individual pigeons which were as nearly alike in respect to weight as possible, so that the active masses undergoing change might likewise be more comparable. Consequently, the standard deviation of the group was only $19.1 \pm 2.02$ gm. In order to give still greater reliability to the final results the number of birds placed in a single group was relatively large, in this particular instance twenty, and in no case below fifteen. The probable error of the mean, therefore, during the
entire experiment fluctuated closely about a value of 1 per cent of the mean. The weights were recorded to the nearest gm. at 24 hour intervals. The average weight of the group was taken as the weighted mean of those pigeons still alive on any particular day.

The maximum relative loss observed on the 40th and final day of the experiment was 53.4 per cent. The mean duration of life was found to be $25.2 \pm .908$ days. The former value, however, appears to be somewhat higher than a critical analysis of the data would war-

![Figure 2](image.png)

**Fig. 2.** The variation of the exponential factor with time. The plotted points are the values of $\theta$ in Table I, the curve representing the values of $me^{F(\theta)}$.

rant, due to the fact that two birds survived as long as the 34th and 40th days respectively. Since the curve rapidly becomes asymptotic to its limiting value in the final stages, the geometric mean between the average loss on the 25th and 40th days was taken as a first approximation to the most probable figure for the maximum relative weight loss, namely $51.5 \pm .613$ per cent, precisely the loss observed on the 30th day of starvation which itself is close to the geometric mean between the average and final lethal day.

2. Computation of Results.—If the curve of the function $me^{F(\theta)}$,
in which $F(t)$ is expanded by Taylor's theorem, be regarded as the more exact representation of this function it is of interest to note in Fig. 2 how closely the values of $\theta$ approximate the curve. The greatest deviations occur in the region where the slope is the steepest and have, accordingly, little effect on the corresponding values of $\gamma$.

The constants for this curve were computed by Pearl's method for the coordinate points:

\[
\begin{align*}
    t_1 &= 1 & y_1 &= 20 \\
    t_2 &= 9 & y_2 &= 100 \\
    t_3 &= 17 & y_3 &= 159 \\
    t_4 &= 25 & y_4 &= 213 \\
    t_5 &= 33 & y_5 &= 222 \\
\end{align*}
\]

and were found to be:

\[
\begin{align*}
    \beta_1 &= -2.1138 & a_0 &= 2.3126 \\
    \beta_2 &= 3.2384 & a_1 &= -0.41366 \\
    \beta_3 &= -5.4767 & a_2 &= 0.024157 \\
\end{align*}
\]

The whole equation then became:

\[
\gamma = \frac{222}{1 + e^{-2.3126 - 0.41366t + 0.024157t^2 - 0.00068393t^3}}
\]

The constants for equation (3) were calculated by Robertson's method. They are:

\[
\begin{align*}
    k_1 &= 5.58 & t_1 &= .128 \text{ mos.} & A &= 100 & Z &= 222 \\
    k_2 &= 3.80 & t_2 &= .575 & B &= 122 & Z &= 1.86 \\
\end{align*}
\]

Values of $\theta$ for each day were then determined directly from equation (4). Finally, the theoretical weight loss, $\gamma$, was calculated by means of equation (5). Experience has shown that the adjustment of the two cycles can be made almost as closely by inspection of the curves plotted from the experimental data as by the method of least squares, a process involving an undue amount of time and labor.

Thus, the evidence submitted in the present study would tend to show that the fundamental kinetic relations governing the processes

\[\text{Robertson, T. B., The chemical basis of growth and senescence, Monographs on experimental biology, Philadelphia and London, 1923.}\]
of complete and partial starvation are essentially alike. This evidence, in both its experimental and mathematical aspects is wholly in accord with the results of the earliest investigations into this problem made nearly a century ago by Chossat,\textsuperscript{10} who observed that the changes in mass are by no means uniform throughout the period of tissue destruction.

SUMMARY AND CONCLUSIONS.

1. The loss of weight in pigeons subjected to prolonged starvation on water alone may be accurately represented by an appropriate form of the law of autocatalysis.

2. This function, within proper limitations, gives a definite indication as to the nature and character of the fundamental reactions involved. In addition, it provides quantitative measures of the relative progress and importance of these reactions.

3. Analytically, the process of starvation consists of two nearly symmetrical cycles, corresponding chemically to the destruction of the carbohydrate-fat reserves and to the decomposition of body protein.

4. A suitable transformation overcoming certain difficulties inherent in the general form of the law is discussed and applied to the data reported.