and indicate the expected slope, 0.0064. These likewise pass excellently through their respective points in every case, notwithstanding the diverse conditions and times of observation.

But, even though the foregoing value for an "optimal" rate of starvation is actually witnessed in practice—we must avoid the conclusion that starvation would necessarily continue indefinitely in this way. Indeed, as it will appear in a subsequent paper, the "linear" phase in such experiments discloses merely a temporary, though an admirably close approach to what are fundamentally "ideal" conditions of starvation for the individual subject and for the kinetic system his organism represents. The true nature of the starvation curve is decidedly more complex, and will be described elsewhere.

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## On the Motion of Growth. VI. Energetics of Bacterial Growth and Heat Production.

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In several previous communications[1-5] we have outlined a concept in which the phenomena of growth and metabolism are viewed as separate forms of a single underlying mode of motion. A scaffolding is thus provided by which each of these major processes may be studied more directively. But our descriptions up to this point have been restricted to the special case of human growth and metabolism, and it is therefore proposed, since the methods and the theory are sufficiently general, to consider an example of the cognate phenomena in a population of unicellular organisms. In order, however, to apply the present theory, it is essential that we possess simultaneous information upon the two chief processes in action, namely, growth and coincidental heat production. Such data, for our purposes, need to be more than ordinarily accurate, else analysis is labor in vain. Considering the difficulties at hand, there is small wonder that suitable observations are few; indeed, in the bacteriological field there are no data which are more worthy of attention and study than those reported within the past few years by

[1-5] Wetzel, N. C., PROC. SOC. EXP. BIOL. AND MED., 1932, **30**, 224, 227, 233, 354, 358.

Bayne-Jones and Rhees.[6] We shall employ the data on growth and simultaneous heat production as recorded for their experiment 2 in order to illustrate the general method of application of our own results.

*The Growth Curves.*

The equations of motion are essentially the same as those already given in the case of human growth, save for the fact that the right hand side of,

$$\lambda\frac{d^2q}{dt^2} + \rho\frac{dq}{dt} + \frac{q}{\kappa} = E \qquad (12)$$

namely, the "applied force" representing $(E_s—E_c)$, the difference between the potential of energy at the source and cell respectively, is sufficiently constant to be treated so in this as well as in all other examples of bacterial growth which we have thus far investigated. But, in view of the fact that the descriminant,

$$\left[\left(\frac{\rho}{\lambda}\right)^2 - \frac{4}{\lambda\kappa}\right] < 0 \qquad (13)$$

in these instances, the solution of (12) may take the form,

$$q = E\kappa + K\epsilon^{-\alpha t}\sin(\beta t + \theta) \qquad (14)$$

$\alpha$ representing the real, $\beta$ the imaginary part of the roots of (12); $K$ and $\theta$ being arbitrary for integration.

From the latter equation we should expect the curves of bacterial growth to exhibit real oscillatory deflections that are dampened by the factor $\alpha$ which, like $\beta$ contains the fundamental constants of growth and metabolism, $\lambda$, $\rho$, and $\kappa$, implicitly. Applying (14) to the data mentioned, we get, by methods later to be described:[7]

$E\kappa = 10.734$ $\qquad K = —5.94405$
$\alpha = 0.6544$ $\qquad \theta = 0.302346$
$\beta = 0.187$

when $q$ is transformed to the Briggsian base. The curve of (14) computed with the aid of the foregoing values is illustrated in Figure 1. The numerical results are arranged in Table I. Graphical adjustment is obviously satisfactory, and shows, contrary to the general opinion frequently expressed, that the algebraic representation of bacterial growth during all of the well-known phases of reduplication is quite within the range of analysis.

[6] Bayne-Jones, S., and Rhees, Henrietta, *J. Bact.*, 1929, **17**, 123.

[7] Wetzel, N. C., to be published.

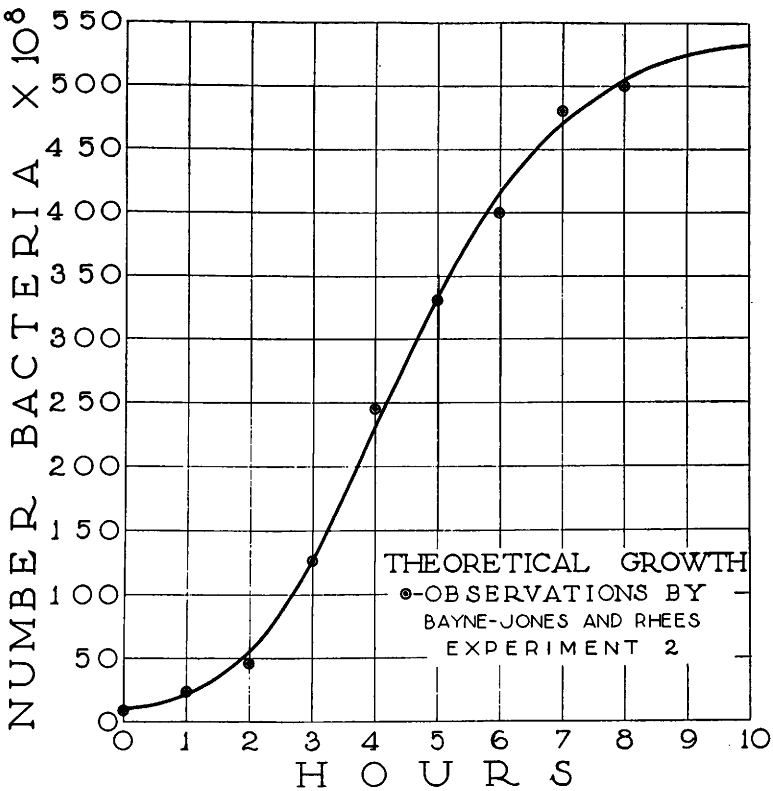


FIG. 1.

The smooth curve computed by means of equation (14) traces the theoretical course of growth in the culture observed by Bayne-Jones and Rhees,[6] and meets the data satisfactorily.

TABLE I.

A Comparison of the Theoretical and Observed Values for Cell Number and Total Heat Production in Experiment (2) of Bayne-Jones and Rhees.

| Age of Culture | Number of Bacteria $(z)$ | | Total Heat, $\mathfrak{T}_p$ | |
|---|---|---|---|---|
| | Observed | Calculated from Equation (14) | Observed | Calculated from Equation (17) |
| *hrs.* | $\times 10^8$ | $\times 10^8$ | *gm. cal.* | *gm. cal.* |
| 0 | 8.5 | 9.2 | —— | —— |
| 1 | 20.5 | 19.4 | 1.19 | —— |
| 2 | 45.4 | 53.4 | 8.95 | 9.52 |
| 3 | 126.0 | 126.0 | 16.30 | 15.10 |
| 4 | 245.0 | 229.0 | 20.90 | 21.27 |
| 5 | 330.0 | 332.0 | 25.90 | 26.58 |
| 6 | 400.0 | 415.0 | 31.00 | 31.56 |
| 7 | 480.0 | 470.0 | 36.10 | 36.10 |
| 8 | 500.0 | 505.0 | 40.50 | 40.54 |
| 9 | —— | 524.0 | 45.20 | 45.05 |
| 10 | —— | 533.0 | 49.90 | 49.91 |

*Heat Production.*

As before[8] we turn to,

$$\rho\left(\frac{dq}{dt}\right)^2 + E_c\frac{dq}{dt} + A' = U \qquad (15)$$

for the theoretical course of unit rate of heat production. Since, however, we have found that $E_c$ is small as compared with $\rho$ in the present case, equation (15) may be reduced to,

$$\rho\left(\frac{dq}{dt}\right)^2 + A' = U_a \qquad (16)$$

from which the unit rate of heat production, $U_a$ is now composed simply of heat dissipated and heat returned from maintenance.

The evaluation of $\rho$ and $A'$ could easily be completed were it possible reasonably to approximate the correct values of $U_a$ (gm. cal./cell/hr.) from the original observations which happen, however, to have been made in such a manner that total cumulative heat, and not rate of heat production was measured in the calorimeter. Hence, to make comparisons most satisfactory, we need here to rearrange and to proceed somewhat differently with (16). The foregoing equation is therefore multiplied by $z$ (cell number) as given in terms of $t$ with the aid of (14), remembering that $z = \epsilon^q$, and integrated once with respect to the independent variable. The result symbolically,

$$\rho\int z\left(\frac{dq}{dt}\right)^2 dt + A'\int z\,dt = \mathfrak{U}_\rho + C_o \qquad (17)$$

must, unfortunately, be partly expressed in series form, at least six terms of which will be required for computing $\mathfrak{U}_\rho$, the total heat produced by $z$ organisms up to and including time $t$. With the integrals in (17) evaluated and with $\mathfrak{U}_\rho$ given directly by the data, we are finally able to solve a set of equations of this type simultaneously for $\rho$, $A'$, and $C_o$. We have thus found,

$\rho = 0.0007652 \times 10^{-6}$
$A' = 0.00009 \times 10^{-6}$ gm. cal./cell/hr.
$C_o = -25.7$, the constant of integration

The details of the foregoing procedures, as illustrated in another example of similar nature, are being published elsewhere.[9]

By resubstituting the results just given into (17), hourly theoretical values for total cumulative heat, $\mathfrak{U}_\rho$, have been computed*

[8] Wetzel, N. C., PROC. SOC. EXP. BIOL. AND MED., 1932, **30**, 233.

* With the aid of the corresponding values of $\left(\frac{dq}{dt}\right)$ as obtained from the first derivative of (14).

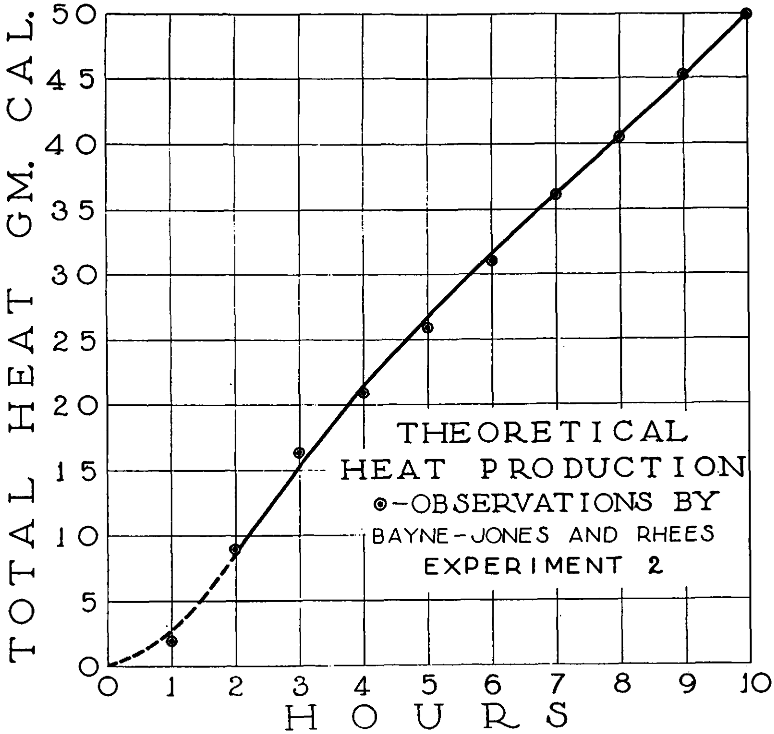


FIG. 2.

The theoretical course of heat production in the same experiment as in Fig. 1. The smooth portion of the curve has been computed from the integral of (17); the earlier portion by mechanical means from the curve of (16).

and are given in Table I. They trace the curve in Fig. 2. The correspondence is about all that could be expected in view of both experimental as well as analytical difficulties necessarily encountered. Consequently, it is worth emphasizing that the theoretical relations (15) and (16) which are thus seen to redescribe the course of bacterial heat production, just as they have succeeded in doing this for the human case, are actually part and parcel of the fundamental equations of growth set forth in this series of papers. No full discussion can be entered into here, although it is evident that the implications of these results are sufficient to warrant the application of present methods to further observations of a similar nature. In fact, as we shall later show,[9, 10] there is no other method, once $\rho$ has been determined, by which the unit *rate* of heat production can be as accurately computed for any and all phases of growth as by equation (15) or even (16). Such information is vitally

[9] Wetzel, N. C., to be published.

[10] Wetzel, N. C., to be published.

important to studies of bacterial growth and metabolism, but beyond this, there is at present, no other way by which the numerical values of the fundamental growth constants, λ, ρ, and κ can be determined, and consequently, no other means of approach to a further study of their ultimate physical and physiological properties.

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## Influence of Raw and Whole Dried Liver on Food Consumption and Utilization.*

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In experiments described by Smith[1] it was shown that liver tissue extracted with alcohol until fat-free has a biological value inferior to that of whole liver, as shown by a subnormal growth rate. In the present experiments an attempt was made to gain information as to the manner in which whole liver exerts its favorable influence. A combination of the efficiency quotient method of Palmer and Kennedy[2] and the paired-feeding method used by Mitchell and Carman[3] was used. Male albino rats on a complete diet containing 20% extracted liver,[1] supplemented by 0.5 gm. of dried whole liver or 1.5 gm. of raw liver daily, and whose food intake was limited to that of control animals, grew at a faster rate and had lower efficiency quotients than did the controls. Animals receiving the supplements

TABLE I.

| Exp. No. | Liver Supplement | Prelim. Period 21 days | | Exp. Period 40 days | | | | Remarks |
|---|---|---|---|---|---|---|---|---|
| | | Food | E.Q. | Wt. Start | Gain Wt. | E.Q. | Food | |
| | | gm. | | gm. | gm. | | gm. | |
| 1 | — | 126 | 4.66 | 74 | 100 | 2.53 | 314 | Control |
| | Whole | 105 | 4.42 | 73 | 115 | 2.10 | 314 | Limited |
| | ” | 118 | 4.63 | 80 | 146 | 1.82 | 416 | Unrestricted |
| 2 | — | 171 | 4.38 | 101 | 123 | 2.25 | 449 | Control |
| | Ext'd | 111 | 4.33 | 76 | 120 | 2.69 | 439 | Limited |
| | ” | 120 | 4.33 | 88 | 139 | 2.10 | 459 | Unrestricted |

* This work was in part supported by a grant from the National Live Stock and Meat Board.

1 Smith, H. G., PROC. SOC. EXP. BIOL. AND MED., 1931, **28**, 597; 1932, **29**, 669.

2 Palmer, L. S., and Kennedy, C., *J. Biol. Chem.*, 1931, **90**, 545.

3 Mitchell, H. H., and Carman, C. G., *J. Biol. Chem.*, 1926, **68**, 165.