Random variation and the interpretation of biological response curves

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Biological processes frequently consist of a chain of successive reactions which may be represented as

$$a \longrightarrow b \longrightarrow c \longrightarrow d$$

$a, b, \ldots$ being products which in turn are the raw materials for the next. The amount of the final product d obtained per unit of time depends on the slowest reaction in this series. If this slowest process is $a \longrightarrow b$, and the concentration of product b can be increased, e.g. by accelerating this reaction, the rate of accumulation of d will be increased until some other link in the chain becomes limiting.

BLACKMAN (1905) formulated this idea with respect to assimilation in plants as follows: "When a process is conditioned as to its rapidity by a number of separate factors, the rate of the process is limited by the pace of the slowest factor."

If assimilation rate is assumed to be a linear function of the concentration of some factor, say a, the position is represented in FIG. 1.

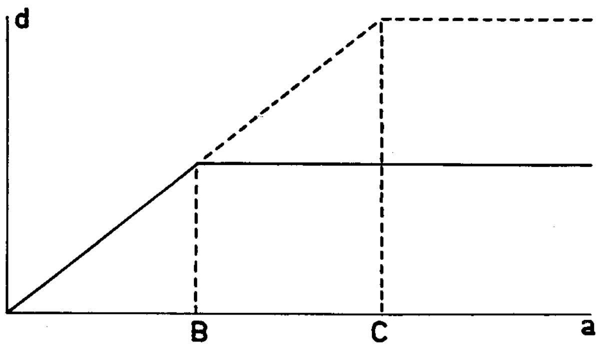

FIGURE 1
(Explanation in text)

Initially d increases proportionally with a until at B some other factor (b) becomes limiting so that further increase of a is without effect. If b is supplied abundantly, increase of a continues until C, where factor c, say, becomes limiting. The value of d at B may be called a *"ceiling"* value for the conditions prevailing.

In a similar way a response curve showing a maximum might be regarded as a composition of two lines. A temperature optimum curve could consist of an ascending and a descending branch, due to a factor a with a positive and a factor b with a

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negative temperature response (FIG. 2). Here *b* is a limiting factor after the point of intersection.

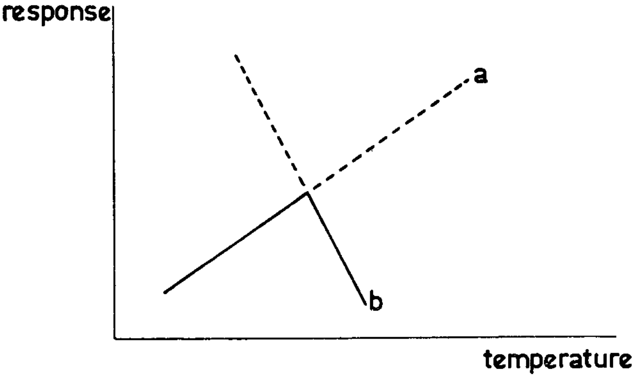

FIGURE 2
(Explanation in text)

A third case is met with in toxicology where the response curve could take the form as in FIG. 3, e.g. dosis against velocity of fatality. The dose A is called the treshhold value, that is, the value above which larger doses show some response and below which there is none.

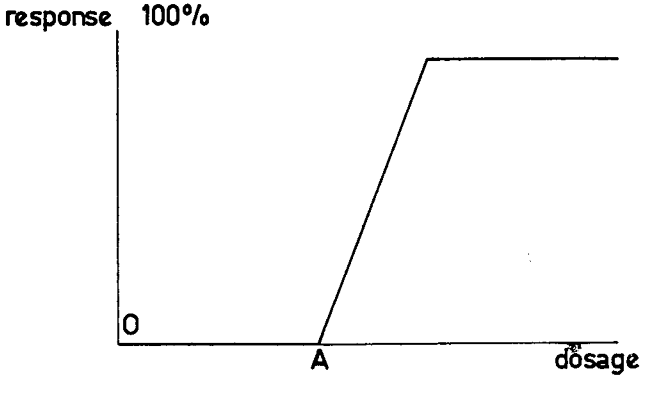

FIGURE 3
(Explanation in text)

Finally there is JUSTUS VON LIEBIG's Law of the Minimum (1862) which states that the yield of a crop in a given environmental state is determined by the concentration of one nutrient only, called the minimum factor.

When trying to confirm the above experimentally the expected straight lines and angles shown in the diagrams are rarely found. As a result Blackman's proposition as well as Liebig's Minimum Law has been seriously criticized. In the case of assimilation VAN DEN HONERT (1928), however, pointed out that the observed deviations were due to internal circumstances, e.g. that the chloroplasts in a plant are in different positions with respect to the light, the upper side receiving more light than the under side. When he used unicellular algae in a thin layer his results confirmed Blackman's rule.

In 1922 MITSCHERLICH proposed his "Wirkungsgesetz der Wachstumsfaktoren", in which the effect of a growth factor was taken to depend on the difference between the available amount and the amount necesssary to obtain the maximum yield, this condition leading to an exponential function instead of Liebig's straight lines.
However, it can easily be shown that if the response is a stochastic variable, smooth curves appear instead of straight lines in the case of the Law of the Minimum also. We shall consider two statistical models, namely first, that the response is a truncated normal variable with a fixed limit at a value t, the variable assuming the value t for all values of the normal variable exceeding t and, secondly, that the response is a truncated normal variable with a limit t that is itself a normal variable stochastically independent of the former. We want in these cases the mathematical expectation of the variable.

1. Let y be a stochastic variable which takes the value t with probability $P(\underline{\chi} > t)$ and has a probability density function

$\frac{e^{-\frac{x^2}{2}}}{\sqrt{2\pi}}$ for values $x < t$, then the expectation of $\underline{y}$ is:

$$E(\underline{y}) = \int_{-\infty}^{t} x \frac{e^{-\frac{x^2}{2}}}{\sqrt{2\pi}} dx + t\, P(\underline{\chi} > t) =$$

$$= \frac{e^{-\frac{x^2}{2}}}{\sqrt{2\pi}} \Bigg/_{-\infty}^{t} + t \,.\, P(\underline{\chi} > t) = - \frac{e^{-\frac{t^2}{2}}}{\sqrt{2\pi}} + t \,.\, P(\underline{\chi} > t)$$

a function which may be plotted from tables of the normal variable.

2. In this model the variable $\underline{y}$ takes the value $\underline{t}$ with probability $\underline{P}(\underline{x} > \underline{t})$, $\underline{t} \cong \mu + \sigma \underline{\chi}$ and $\underline{x} \cong \underline{\chi}$ stochastically independent,

and has a probability density $\frac{1}{\sqrt{2\pi}} e^{-\frac{x^2}{2}}$ if $\underline{x} \leqslant \underline{t}$.

We may write:
$E(\underline{y}) = E(\underline{x} \mid \underline{x} \leqslant \underline{t}) \,.\, P(\underline{x} \leqslant \underline{t}) + E(\underline{t} \mid \underline{x} > \underline{t}) \,.\, P(\underline{x} > \underline{t})$
which may be shown to be [1]:

$$E(\underline{y}) = \mu \,.\, P(\underline{\chi} > \frac{\mu}{\sqrt{1+\sigma^2}}) - \sqrt{1+\sigma^2} \,.\, \frac{e^{-\frac{\mu^2}{2(1+\sigma^2)}}}{\sqrt{2\pi}},$$

which again for given μ and σ may be plotted.

[1] A complete derivation will be published in a paper by JUSTESEN and KUIPER in the *Biom. Zeitschr.:* Eine Statistische Bemerkung über dass sogenannte Gesetz des Minimums.

As an example we consider the case of FIG. 3 with the lower limit fixed and the upper limit stochastic with $\sigma^2 = 3$. From the graph in FIG. 4 we see that the deviation from the straight line is more pronounced in the stochastic case. In fact, the larger σ^2 the more gradually the curve approaches the limiting value. The same principle can be applied for an optimum curve.

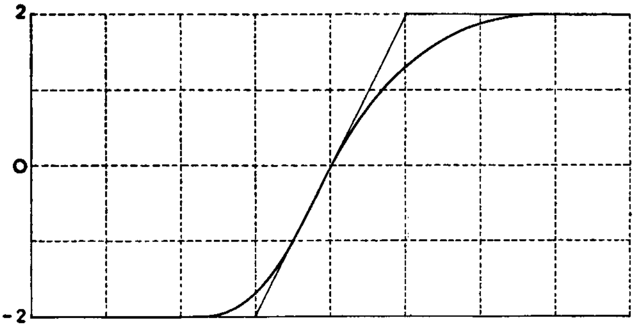

FIGURE 4
(Explanation in text)

It may be concluded then that the fact of nonlinear responses being observed in experiments is not a sufficient reason for rejecting the theory of a fundamental linear response law. On the other hand the experimental results will not in any way confirm those laws, unless straight lines can be obtained by reducing variation, due to internal or external circumstances.

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REFERENCES

BLACKMAN, F. F. 1905 Optima and Limiting Factors. *Ann. of Bot. 19,* p. 281.

LIEBIG, J. VON 1862 Die Chemie in ihre Anwendung auf Agrikultur und Physiologie. 7. Aufl., Braunschweig.

HONERT, T. H. VAN DEN 1928 Koolzuurassimilatie en beperkende factoren. Thesis, Utrecht.

MITSCHERLICH, E. A. 1922 Das Wirkungsgesetz der Wachstumsfaktoren. *Zeitschr. f. Pflanzenernährung und Düngung.* p. 49—95.