that can be infected by mechanical inoculation and that has a short incubation period. When such an indexing plant is used, both growth status and environment control (*5, 6*) are very important.

In late 1954 at the Plant Industry Station, Beltsville, Md., a systematic procedure was developed for finding an indexing host employing several methods of transmission including dodder, grafting, insect and mechanical methods and involving the sweetpotato and its relatives.

This report gives the results obtained by using a modification of the Yarwood (*7*) method of mechanical transmission, employing the freshly cut edges of leaf and necrotic root tissue. It singles out Scarlett O'Hara morning glory (*Ipomoea* sp., *8*) as a remarkably good indicator or indexing host.

The pot-label techniques of mechanical inoculation—of rubbing infected tissue between two pot labels and involving an exposure of 3 to 5 seconds—failed. However, the squeezing action of a flat-tipped tweezers forces virus extract out onto the wounded, buffer-carborundum-coated leaf surface, exposing the virus but a fraction of a second before it can enter leaf tissue. This morning glory is a rapid grower and may unfold as many as one leaf each day. Symptoms begin to show on the younger leaves, usually well above the point of inoculation. The incubation period is extremely short, ranging from 7 to 15 days, 8 to 11 days being most common. Among the numerous varieties and species under test, the only clearcut symptom picture was obtained on Scarlett O'Hara morning glory when the inoculum source was sweetpotato leaves with purple rings (induced by scion grafting) and roots containing necrotic tissue. The first symptom is a vein-banding mottle, and often the leaves are reduced in size and take on a variable chlorotic aspect (Fig. 1). Most infected plants are dwarfed somewhat but produce blossoms and apparently virus-free seed. During the past 7 months many experiments have been conducted successfully using this technique.

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8. Scarlett O'Hara morning glory is an *Ipomoea* hybrid (*I. bona-nox* L. × *I. hederacea* Jacq.) with two distinctive leaf shapes: (i) hastate or long shield shaped and (ii) 3-lobed or maple leaf shaped. The leaf shapes come true from seed but are usually mixed when common seed sources are used. Taxonomists now commonly employ *Calonyction aculeatum* L. House for *I. bona-nox*.

14 September 1955

Microfoundations

I would like to suggest the term *microfoundation* to complete the spectrum whose other end is occupied by the Ford Foundation. According to a recent editorial [*Science* **122**, 1253 (1955)] the small foundation is typified by an endowment of $2 million and so really belongs toward the middle of the spectrum. The Holter Research Foundation is a microfoundation operating on the income of an endowment of well under $50,000. It is an operating microfoundation with one full-time physicist, one full-time unpaid biophysicist, and one part-time unpaid technician.

The small foundation undoubtedly produces more per dollar per man-hour than the large foundations, because of greater ease of administration and simpler public relations problems. I do not know whether this condition can be extrapolated to the microfoundation.

The microfoundation is not blessed with any committees whatever, and every man-hour, outside of janitoring, can be used for the drawing board or the soldering iron. We at Holter stick the invoices in a drawer, and if the funds get low we wait until the next month's budget before purchasing anything more. Our results, although not spectacular, have adequately justified our existence through various original contributions in the fields of physics, medicine, and education. We may or may not be typical of microfoundations. The productivity unit is, of course, hard to define, particularly when quality is involved. Using publications by professional journals, for lack of any better criterion, as an index of at least passable quality, it might be interesting to find which size foundation produces the most results per dollar, per man, per year.

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Board of Trustees, Holter Research Foundation, Helena, Montana

13 January 1956

Mean Rate of Change and a Graphic Method for Its Evaluation

Given a set of data represented by n points P_i (x_i, y_i) on ordinary rectangular graph paper, with the x_i not necessarily regularly spaced, the determination of the mean rate of change of the dependent variable y is often a problem of practical importance (*1*). Merely taking an arithmetical average of the $n-1$ slopes $m_i = \left(\frac{y_{i+1}-y_i}{x_{i+1}-x_i}\right)$ of the segments joining successive points is not very satisfactory, since the presence of two points with almost equal abscissas but widely separated ordinates would lead to a numerically large slope (for example, P_1P_3, Fig. 1) and excessively distort the final average. This difficulty can be eliminated by using a weighted average, taking the difference in x-coordinates $x_{i+1}-x_i$ as the weight w_i to multiply each slope m_i. However, this results in telescoping sums, and the final formula would depend on only the first and last of the observed data (which are generally more subject to experimental errors than intermediate determinations):

$$\frac{\Sigma w_i m_i}{\Sigma w_i} = \frac{\Sigma(y_{i+1}-y_i)}{\Sigma(x_{i+1}-x_i)} = \frac{y_n - y_1}{x_n - x_1}$$

In an effort to develop a formula more representative of the entire series of values, the following plan proved to be the most effective. Consider joining on the graph pairs of points P_i and P_j in all possible ways and assigning to each slope

$$m_{ij}\left(=\frac{y_j - y_i}{x_j - x_i}\right), \text{ the weight } w_{ij} \text{ equal}$$

to the difference $x_j - x_i$ between the corresponding abscissas. The weighted average

$$\frac{\Sigma w_{ij} m_{ij}}{\Sigma w_{ij}} \ (1 \leq i < j \leq n)$$

of the slopes of *all* of these segments provides the following formula, which is easily derived algebraically (*2*).

Mean rate of change (m.r.c.) =

$$\frac{\Sigma(2i-n-1)y_i}{\Sigma(2i-n-1)x_i} \ (i = 1, 2, \ldots, n) \quad (1)$$

For example, with $n = 6$, m.r.c. =

$$\frac{-5y_1 - 3y_2 - y_3 + y_4 + 3y_5 + 5y_6}{-5x_1 - 3x_2 - x_3 + x_4 + 3x_5 + 5x_6}$$

It has been found advantageous to renumber the subscripts so that they will be centered about zero. Thus, for $n = 5$, the points may be thought of as P_{-2} (x_{-2}, y_{-2}), P_{-1}, P_0, P_1, P_2; for $n = 6$, the subscripts may be relabeled to read P_{-5} (x_{-5}, y_{-5}), P_{-3}, P_{-1}, P_1, P_3, P_5. In general, when n is odd, let $n = 2m + 1$, and then $h = -m, -m+1, \ldots, -1, 0, 1, \ldots, m$. When n is even, let $h = -n+1, -n+3, \ldots, -1, 1, 3, \ldots, n-1$.

With this change made, formula 1 takes the following more convenient form:

$$\text{m.r.c.} = \frac{\Sigma h y_h}{\Sigma h x_h} \quad (2)$$

For example, with five points, designated as in the preceding paragraph, the mean rate of change will become (*3*)

$$\frac{-2y_{-2}-y_{-1}+y_1+2y_2}{-2x_{-2}-x_{-1}+x_1+2x_2}$$

and for $n=6$, the value will equal

$$\frac{-5y_{-5}-3y_{-3}-y_{-1}+y_1+3y_3+5y_5}{-5x_{-5}-3x_{-3}-x_{-1}+x_1+3x_3+5x_5}$$

Formula 2 lends itself readily to arithmetical calculation, with or without a computing machine. The symmetry in the x's and y's should simplify the numerical evaluation. However, an interesting mechanical interpretation of this formula leads to a graphic method for determining the mean rate of change, along the same lines as a method recently described for mean values (*4*). Assume that the P_h's have been renumbered as described in a foregoing paragraph. Now assign to each point P_h a mass equal to the absolute or numerical value of the coefficient h corresponding to that point. Let C be the center of gravity of all the weighted points with positive coefficient h, and C' the centroid of the weighted points with negative h. Then it can be shown that the slope of the line $C'C$ joining the two centroids equals the mean rate of change for the n points (*2*).

Method (Fig. 1). Starting with the series of charted data, label the points according to the arrangement shown earlier (that is, with the h subscripts). Take the first two points with subscripts greater than zero, P_1 and P_2 or P_1 and P_3 as the case may be, and join them with a straight line. On this line, locate Q, the centroid of the first two weighted points (*5*), and mark the sum of the subscripts near Q. Next, draw the segment between Q and the next of the P's and locate the centroid of the end-points at R. Proceed until the last point toward the right has been included, thus arriving at C. Similarly start with the points having negative subscripts and work toward the left, determining Q', R', . . . , and finally C'. Last, join C' and C, obtaining the desired slope. (Actually, it is not necessary to label the points on the graph. It suffices to mark down merely the integers representing the respective weights, as is shown in parentheses in Fig. 1.)

If the numerical value for the mean rate of change is required, it may be obtained from the coordinates of any two points D and E on this line, preferably far apart for greater accuracy, and with conveniently selected x-coordinates for ease of division

$$\left(\text{m.r.c.} = \frac{y_e - y_d}{x_e - x_d}\right)$$

Special cases (Fig. 2). In certain instances, the graphic procedure assumes a particularly simple form. (i) With four points the mid-point of P_1P_3 is marked, and the outer segment is again bisected, providing C; similarly for C'. (ii) With five points, the only necessary step is to trisect P_1P_2 and $P_{-1}P_{-2}$, as is shown. (iii) With seven points, C is to be found at the mid-point of QP_3; similarly for C'.

It is to be noted that, even though the

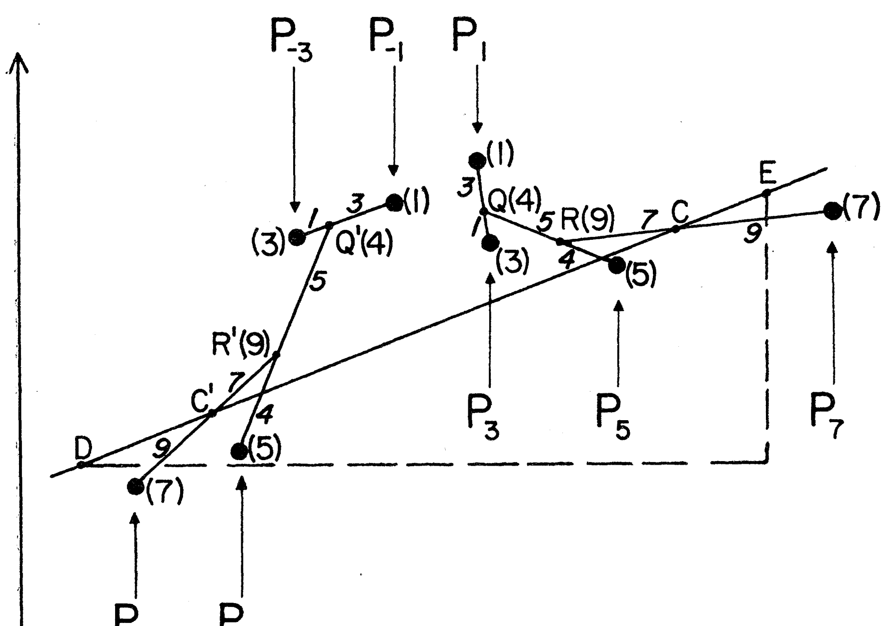

Fig. 1. Mean rate of change, graphical method. Numbers in italics represent division of the segments into proportional parts.

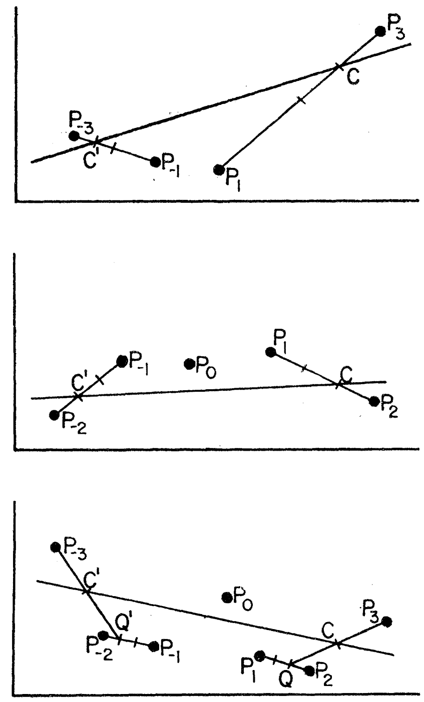

Fig. 2. Graphical determination of mean rate of change, special cases. (Top) Four points; (Middle) five points; (Bottom) seven points.

subscripts are arranged uniformly, it has not been anywhere assumed that the x's are equally spaced on the graph. When, however, the x values *are* equally spaced, the interesting result has been proved (*2*) that the slope then provided by formula 1 or formula 2 or by the graphic method is the same as the slope of the line best fitting the points according to the criterion of least squares. This leads to a new graphic method (*2*) for drawing the line of best fit. Furthermore, if the number of points is odd, the successive centroids will advance uniformly to the right (*6*), eliminating entirely the need to divide any segments into proportional parts.

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1. From the Ophthalmology Research Laboratory (I. H. Leopold, director), Albert Einstein Medical Center, Northern Division. This work was supported by a grant from the Weinstock Fund.
2. S. I. Askovitz, *J. Appl. Physiol.* 8, 347 (1955).
3. The absence of the middle point P_0 in the final formula for an odd number of points is a curious anomaly commonly found in other statistical procedures. For example, in determining the best line of fit according to the least-squares criterion, if the number of points is odd and the abscissas equally spaced, the centermost value does not enter into calculating the slope of the line. In the case of the mean-rate-of-change formula, the deletion of the central point from the series of data will alter the coefficients, so that its presence generally does exert an indirect effect on the value of the fraction.

4. S. I. Askovitz, *Science* 121, 212 (1955).
5. The centroid of two weighted points divides the segment joining the points in proportion to their masses and lies nearer to the "heavier" point. The division of the segment can generally be estimated with a ruler quite readily; or more exact methods may be used, to be found in any textbook on plane geometry.
6. The centroids have been proved to lie on ordinates spaced $\frac{2}{3}s$ apart from each other, where s is the uniform interval between the original x's.

26 September 1955

Interaction Product of Glycine and Dextrose Toxic to Phytophthora fragariae

Because of difficulties in isolating and culturing *Phytophthora fragariae* Hickman, the causal organism of red stele of strawberry, studies were made on the cause of its failure to develop on many media. It was found that potato agar supports growth although potato-dextrose agar does not, so it was concluded that dextrose in some manner was responsible for the lack of growth.

The effect of dextrose in oatmeal and bean agars, the only media reported which satisfactorily support growth of the fungus (*1*), was tested. When oatmeal and Difco lima-bean agars containing 0.1, 0.5, 2.0, and 10.0 percent dextrose were inoculated with *P. fragariae,* growth was retarded in the 0.5-percent dextrose media and completely inhibited in the 2.0- and 10.0-percent dextrose media. Maltose and lactose had the same effect, but the fungus was able to grow in culture media containing up to 20.0 percent sucrose.

These results indicated that inhibition occurred only when reducing sugars were used. The following nine reducing carbohydrates—arabinose, xylose, galactose, levulose, mannose, cellobiose, lactose, maltose, melibiose—and the following 15 nonreducing carbohydrates—sucrose, raffinose, trehalose, melezitose, adonitol, dulcitol, glycerol, inositol, mannitol, sorbitol, corn starch, dextrin, inulin, salicin, and soluble starch—were added to potato agar at a 2.0 percent concentration before autoclaving. *P. fragariae* did not grow on media containing any of the reducing carbohydrates, but did grow in the presence of each of the nonreducing carbohydrates with the exception of glycerol. However, the autoclaved glycerol-potato agar medium gave a positive Benedict test. *P. infestans* grew on oatmeal agar containing 2 percent dextrose, mannose, or galactose, but did not grow when 2 percent maltose, arabinose, levulose, or xylose was added to oatmeal agar.

If dextrose is sterilized by filtration in a Seitz filter or in the autoclave at 20-lb pressure for 20 minutes and then added to sterilized potato or oatmeal agar, *P. fragariae* grows on the media even if they contain as much as 12 percent dextrose. This proves that preheated or unheated dextrose is not in itself responsible for the inhibition.

However, if autoclaved potato agar containing 4 percent dextrose is added to autoclaved oatmeal (or potato) agar in equal proportion, the mixture will not support development of the pathogen.

Although it has been shown (*2*) that glucose reacts with amino acids and thiamine (which is required for the growth of certain species of *Phytophthora, 3*) and thus could make them unavailable, the presence of dextrose would not account for the afore-mentioned result unless dilution by 50 percent of an essential substance causes the inhibition of growth. It can be assumed that the oatmeal agar in the mixture provides the necessary amino acids and vitamins. It seemed more feasible to postulate that a toxic or fungistatic substance was formed through the interaction of the dextrose with constituents of the media during autoclaving. It was known that autoclaved glucose in the presence of phosphate gives considerable conversion to ketoses (*4*).

Proof of the production of a toxic or fungistatic substance through the interaction of an amino acid and a reducing carbohydrate was obtained when it was found that *P. fragariae* would not grow on media to which had been added an autoclaved mixture of glycine and dextrose, but that it would grow on media containing these constituents if they were autoclaved separately before being added. Glycine (0.024 g) and dextrose (2 g) were autoclaved separately and together in 0.5 ml of water and were added to 100 ml of oatmeal agar. When glycine and dextrose were autoclaved together, a browning reaction occurred (*2*).

P. cactorum, P. cambivora, P. cinnamomi, P. megasperma, and *P. parasitica,* which are able to grow on autoclaved media containing 2 percent reducing carbohydrate, were also sensitive to the product of interaction of autoclaved dextrose and glycine. They showed a range of sensitivity, but none were as sensitive as any of the *P. fragariae races* used. However, a species of *Phytophthora* (*5*) that causes loganberry root rot showed the same amount of sensitivity as *P. fragariae.*

Dilution of the glycine-dextrose mixture before autoclaving had a marked effect on the production of toxin. In 10 ml of water, 0.14 g of glycine was required with 2 g of dextrose, whereas if no water was added, only 0.01 g of glycine was required with 2 g of dextrose to produce sufficient toxin to inhibit growth of *P. fragariae*. No toxicity to *P. fragariae* was obtained when sucrose was substituted for dextrose.

When *dl*-alanine, *l*-(-)-leucine, and Bacto asparagine were autoclaved with dextrose, a substance that was toxic to *P. fragariae* was produced. However, the same amount of *l*-cystine and dextrose autoclaved together was nontoxic to *P. fragariae.*

The browning reaction (*2*) occurred when dextrose was autoclaved with glycine, alanine, leucine, and asparagine, but only to a very slight degree when cystine was used. It has been observed that when dextrose is autoclaved with oatmeal, potato, and lima-bean agars, the media become slightly brownish and thus a similar reaction probably occurs.

Because not all the reducing carbohydrates inhibited the growth of *P. infestans,* either different toxins or amounts of toxins are produced. The sensitivity of *Phytophthora* spp. and strains to the product of interaction of glycine and dextrose will aid in showing their relationship (*6*).

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Mathematics deals exclusively with the relations of concepts to each other without consideration of their relation to experience.—Albert Einstein.