References and Notes

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20 May 1957

The deviations from the control group found by Albert Damon for a sample of 203 patients with chromophobe adenoma of the pituitary are smaller than those found by Mayr *et al.* in smaller Boston samples. They are, in Damon's sample, for group 0, + 9 percent among whites and + 16 percent among Negroes, and for group A, − 18 percent among whites and − 14 percent among Negroes (controls = 100 percent). Yet it is gratifying to learn that the direction of all of these deviations is exactly the same as that found in the Boston samples, even though in this rare disease it is difficult to obtain sufficiently large samples to substantiate the significance of the deviations statistically.

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Standard Human Beings versus Standard Values

A fact which is highly pertinent to the thinking of many scientists has received very little or no attention in the application of statistical methods to the study of human beings—namely, that the expected number of individuals in any standard group diminishes, and may diminish greatly, when a *series* of measures is applied. If one uses as standards (i) the medial 50 percent, (ii) the medial 95 percent, or (iii) the medial 99.8 percent, the fractions of a given group that remain after specific numbers of independent measures are shown in Table 1.

In our thinking, we often carry the concept of "standard" or "normal" individuals. If such a "standard individual" means one who is in the medial 50-percent range in every measurable way, then, making the simplifying assumption that only ten independent measurable items exist, we must arrive at the conclusion that only one person in 1024 is "standard." Seldom are there published data which are sufficiently detailed so that this idea can be applied. However, such data are to be found in an article entitled "Plasma lipids of normal men at different ages" (*1*).

There are 65 individuals for whom complete data are given with respect to seven items: (i) total lipid C, (ii) total lipid P, (iii) total lipid N, (iv) lipid amino N, (v) total cholesterol, (vi) free cholesterol, and (vii) esterified cholesterol, each present in 100 ml of plasma. Selection of the medial 50 percent of the individuals after each measurement yields the results given in Table 2. If the measures were independent ones (which they obviously are not), the number remaining in the medial group would have been two after five measures instead of after seven measures, as in this actual case. On the basis chosen, two individuals out of 65 turn out to be standard with respect to the seven somewhat related measures.

If we wish to think of a standard individual in terms of the medial 95 percent with respect to every measurement (making the assumption that there are only ten measurable items), we find that about six out of ten individuals are standard. If, however, we do not make this simplifying assumption and recognize that human beings are of such complexity that hundreds of relatively independent measures are possible (anatomical, histological, physiological, pharmacological, biochemical, psychological, and so on), we are faced with the fact that even in a large sample every individual may be nonstandard with respect to some of the measures in which we may choose to be interested, even at the 95-percent level under consideration. We certainly could not expect any randomly selected individual to be standard in terms of our initial definition.

If we choose to expand our concept of "standard individual" to include the medial 99.8 percent, we will be able to find a substantial number of individuals who are standard, even though many independent measures are made. Some have assumed that selection of 99.8 percent as the standard would result in the exclusion of only 200,000 individuals from a population of 100 million (roughly the adult population of the United States) (*2*). Actually, however, approximately this many are excluded by *each* successive measurement, so that on the basis of 100 measurements, about 18 million would be excluded. If we make the conservative assumption that only 100 measurable items exist for each individual human being, there is about one chance in five that a randomly selected individual will be nonstandard with respect to some of the items, even on the 99.8-percent basis. The use of the concept of a standard man (in contrast to the search for standard values) thus becomes difficult to justify on any definitive basis. If we expand our concept to encompass practically the whole of the population, then the usefulness of the standard vanishes.

Table 1. Results of successive independent measures.

Size of medial group (%)	No. of measures	Fraction of original group remaining in medial group
50	1	0.50
50	5	0.03
50	10	0.001
95	1	0.95
95	10	0.60
95	15	0.468
95	100	0.0059
99.8	1	0.998
99.8	10	0.98
99.8	100	0.82

There are many areas where the afore-mentioned ideas are applicable and where the concept of standard individuals is inherent, whether or not it is overtly expressed. The one which comes closest to the field of my professional competence is that of nutrition. The Food and Nutrition Board and the U.S. Food and Drug Administration have set up "Recommended daily allowances" and "Minimum daily requirements," respectively, for standard or normal human beings. At the present time, 12 items are included in these lists; as further information becomes available, these lists will be expanded. The "recommended allowances" are, in general, more generous than the "minimum daily requirements" and are designed to be "suitable for the maintenance of good nutrition in essentially the whole population."

The point which our data (*3*) emphasize is that, if the level for each nutrient is satisfactory for a specified percentage of the population, the levels *taken as a group* would be satisfactory for a smaller percentage. If 12 levels are individually satisfactory for 90 percent of the population, the 12 levels taken as a group (on the assumption that they are independent of one another) would be satisfactory for only about 28 percent of the population. These needs are not completely independent of one another; hence, the 28-percent figure is low by an unknown amount. As the number of items on the list increases, the discrepancy between the validity of the indi-

Table 2. Size of medial 50-percent group after successive measurements.

Number of measures	1	2	3	4	5	6	7
Individuals in medial group	33	21	14	10	8	3	2

vidual items and their validity as a group increases.

The principle which we have pointed out in connection with the nutritional example applies whenever the concept of standard or normal human beings is used. Does not a substantial amount of our scientific thinking involve this questionable concept?

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12 June 1957

Membrane Time Constant of Motoneurons

New information about motoneuron membranes has been obtained in recent experiments in which intracellular electrodes were used for both stimulation and recording at the motoneuron soma (*1–6*). Unexpectedly low membrane time-constant values have been inferred from the subthreshold transients of membrane potential observed when constant current was applied across the soma membrane (*2–4*). It is shown in this report, however, that these experimental transients are theoretically consistent with significantly larger membrane time-constant values, provided that the cablelike properties of dendrites are taken into account. This correction removes the apparent discrepancy (*3–5*) between the soma membrane time constant and the time constant of synaptic potential decay and thus removes the need for special explanations, such as a hypothetical prolongation of synaptic depolarizing activity (*4, 6*), or a prolongation of soma synaptic potential by electrotonic spread from a larger and slower synaptic potential postulated to occur in the dendrites (*5*).

The membrane time constant τ is defined as the product of passive membrane resistance and capacitance. The assumption (*2–4, 6*) that the experimentally observed membrane transients may be regarded as exponential curves having this time constant τ would be valid only if constant current were applied uniformly to the entire membrane surface. For the experiments in question, this could be true only for the hypothetical case of a *soma without dendrites.* The lower dashed curve in Fig. 1 illustrates the exponential time course of membrane potential change V, relative to its final steady value V_s for this hypothetical case.

Since the motoneurons are known to possess several large dendrites, a significant portion of the current applied to the soma must spread (electrotonically) along these several dendrites. This will change the time course of soma membrane potential. For example, as the size and number of dentrites is increased relative to soma size, there is a limiting case, *dendrites without soma.* This case is illustrated by the upper dashed curve in Fig. 1, on the assumption that these dendrites have the same membrane time constant τ and that they may be represented as cylinders of infinite length. This time course can be precisely expressed as

$$V/V_S = \operatorname{erf}\sqrt{t/\tau}$$

for the membrane potential at the point (soma) where constant current is applied across the membrane of each dendrite. It is the same as that obtained in the more familiar problem of electrotonic potential beneath an electrode ($x=0$), when constant current is applied between external electrodes placed far apart on a cylindrical axon (*7*). This curve is not a simple exponential: the time required to reach half of the steady value V_s is one-third of the time required in the lower dashed curve, while the time required to reach 90 percent of V_s is about three-fifths of that required in the lower dashed curve.

The middle curve in Fig. 1 corresponds to an intermediate relation between dendrites and soma (*8*). It has been assumed that soma and dendrite membranes have the same membrane time constant and that the membrane potential at any moment is uniform over the soma surface (*9*), up to and including the origins of the dendrites. The dendrites can be treated either as cylinders of infinite length or as structures which taper and branch exponentially.

This intermediate curve was calculated with a value of 5 for the ratio between the steady-state membrane current drawn by the dendrites and the steady-state current drawn by the soma membrane. This value is theoretically consistent with the specific example of a soma with six cylindrical dendrites (used in *1* and *6,* as well as in *3*), provided that a value of about 2000 ohm cm^2 is used for the membrane resistivity. Since this example probably underestimates the size and number of dendrites (*1*, p. 322), it is predicted that the time course of soma membrane potential change, when constant current is applied to the soma, will lie *between* the two upper curves in Fig. 1, for many motoneurons.

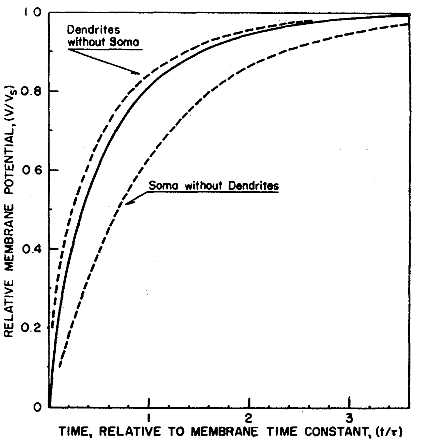

Fig. 1. Membrane potential transients at the neuron soma and origins of dendrites, when constant current is applied across the soma membrane.

On the basis of this theoretical prediction, the membrane time constant can be estimated as being the time required for the experimental transients to reach about 82 percent of the final steady value. Since, however, the experimental error permits exponential curves to be fitted to the experimental transients (*2–4*), it should be noted that the time constants of such curves can be expected to be smaller than the actual membrane time constant, by a factor of about 2. It appears, therefore, that these experimental transients do not conflict significantly with the earlier estimate (*10*), of about 4 msec for the membrane time constant of cat motoneurons, which was based on the decay time constant of synaptic potentials (*10*) and of monosynaptic facilitation (*11*).

This is consistent with the simple notion of synaptic potential decay as a purely passive process, having the same characteristics on both soma and dendrites (*12*).

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12. The opinions expressed in this note are my own, and are not to be construed as official or as reflecting the views of the U.S. Navy Department or the naval service at large.

31 May 1957