

Letters

Drug Tests: Integrity and Courage

The increasing concern with the investigation and development of new drugs leads me to record some of my own experiences.

I have been engaged in the investigation of new psychopharmaceuticals in double- and single-blind studies since 1954, working in various clinical programs and as an investigator for the National Institute of Mental Health. A pharmaceutical manufacturer who sponsors a study is obliged to report the findings, including toxicity, to the Food and Drug Administration. In 1965 I had occasion to ask if our Pontiac State Hospital study of Dornwal for Wallace and Tiernan in 1961 had been reported to the FDA. It had not. I wonder how often the pharmaceutical houses conducting new-drug investigations have failed to report the results of my own twenty or so studies to the FDA. Do other drug investigators know whether their studies are ever placed in the hands of the FDA? To resolve this doubt, I would suggest that each new-drug investigator be required to send a copy of his report directly to the FDA at the same time he reports to the sponsoring pharmaceutical house. The direct relationship thereby established between investigators and the FDA will be of mutual value.

Another, more difficult problem related to investigation also deserves comment. I received a letter from Sandoz Pharmaceuticals saying that all studies approved by them for investigation of LSD-25 and Psilocybin have been cancelled because of the publicity related to these drugs. It seems that we are in the grip of a national hysteria concerning LSD, as exemplified by the 30-year sentence of Timothy Leary, who has been convicted of bringing marihuana into the United States but who is better known for his public espousal of LSD and internal freedom. The merits of LSD as an adjunct to psychotherapy in character disorders remain to be clearly established but call for a carefully designed double-blind

study. Many types of neurophysiological and psychiatric investigation using LSD offer potential benefits. For Sandoz to be so timorous suggests the Cowardly Lion of Oz. Who is our Dorothy? the FDA? NIMH? the National Research Council? Who will assume the responsibility for the necessary investigative work with LSD?

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Molecular Biology and the Nature of Man

In his article on "The biological nature of man" (22 April, p. 472) G. G. Simpson seems unnecessarily cavalier in stating his opinion that "nothing that has so far been learned about DNA has helped significantly to understand the nature of man or of any other whole organism," especially if this statement is read in the context of page 495 of the same issue in which a book by Bruce Wallace is praised for presenting evolution in terms of molecular biology. Surely our understanding of whole organisms has been carried far beyond Simpson's statement that "Man is not *merely* an animal, that is, his essence is not simply in his shared animality." The essence of man and of other whole organisms may well be already available in terms of the molecular interaction between a fixed genome and a variable environment. The documentation in molecular terms of negative feedback on enzyme activity and repression and derepression of enzyme synthesis, dating from the earliest reports by Pardee and by Umbarger in 1956, clearly supplies a justification for a more positive statement than "In due course, molecular biology will undoubtedly become more firmly connected with the biology of whole organisms and with evolution . . ." While molecular biologists have never been noted for humility,

and although much remains to be learned, isn't the present-day impact of molecular biology precisely that it shows as never was possible before how the nature of man may indeed reside in the fact that he is a complicated feedback-operated machine that responds to its environment with a certain built-in indeterminacy? The operation of feedback principles can explain the whole basis of teleology. The natural selection of effective feedback controls can make any natural phenomenon look purposeful.

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Ages of Test Animals: A Formula

The discussion (Letters, 1 April) of N. O. Calloway's proposal (Letters, 31 Dec.) that the distribution of ages of biological test animals be chosen according to some exponential criterion stemmed from Calloway's having neglected to specify how the base age should be chosen. In suggesting that the age of the n th animal go as the n th power of the age of the first—that is, $A_n \sim (A_1)^n$ —Calloway of course assumed that all ages were understood to be measured in terms of some standard unit of time. The confusion resulting from the lack of an explicit unit for time still persists in the formulation offered in R. M. Levy's letter. ("Thus it is perfectly reasonable to start our clock at $t = 1$." One what?)

The correct formulation of Calloway's suggestion is as follows:

$$A_n = A_{std} (A_1/A_{std})^n,$$

where A_{std} is some standard age and A_1 is the age of the first member of the set. The set is a two-parameter one, which can easily be transformed into the form

$$A_n = A_{std} (A_{max}/A_{std})^{n/N},$$

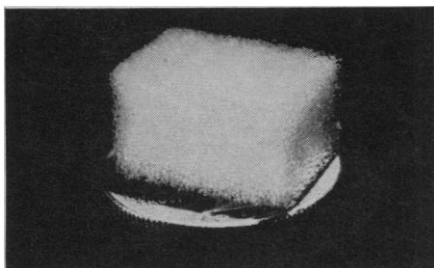
where A_{max} is the maximum age one wishes in the set and N the total number of ages to be represented. Noting, as G. G. Simpson does in his letter (1 April), that A_{max} forms a natural time scale for the ages of the animals in the set and putting

$$A_{max}/A_{std} = R,$$

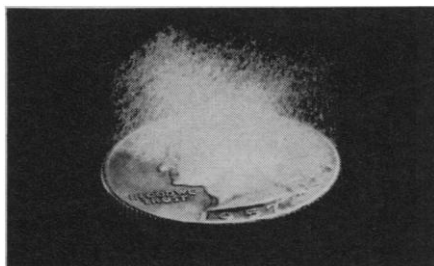
we have the two-parameter form

$$A_n = A_{max} R^{(n/N)-1}.$$

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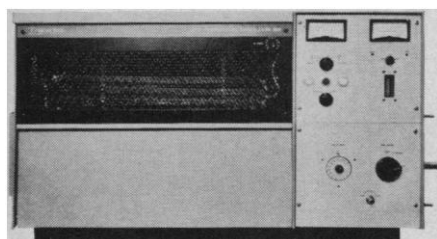


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(Simpson thinks $R = 100$ is a convenient choice.) The equation is, of course, the same as Calloway's, with the unit of time taken as $A_{\max}/R = A_{\text{std}}$. It can also be put into the familiar form

$$A_n = A_{\text{std}} e^{n\lambda},$$

with $\lambda = (\ln R)/N$. (With Simpson's choice of $R = 100$, $A_n = 0.01 A_{\max} e^{n\lambda}$, $\lambda = 4.605/N$.)

The following table shows the ages of the members of a set for which $A_{\max} = 70$ years, $R = 100$, and $N = 10$. (Note that the Calloway unit of time for this case is 0.70 year.)

n	A_n (yr)	n	A_n (yr)
1	1.10	6	11.0
2	1.75	7	17.5
3	2.80	8	28.0
4	4.40	9	44.0
5	7.00	10	70.0

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Computer-Time Allocation

In suggesting that a computation center, like a library, should provide its services free, Anthony Ralston (Letters, 29 April) has oversimplified a complex and increasingly important problem.

The demand for computing on any university campus is virtually unlimited if the service is free. When a university's computing power is multiplied by an order of magnitude, the new facilities are saturated within 2 or 3 years. Therefore, computing services must be allocated—the price mechanism being, of course, only one of several possible mechanisms. To simplify the problem, the “library” principle may be applied up to a limit: say everyone could be allowed \$100 worth of free service per year. Allocation would then limit only large users. Some such policies are already in effect on many campuses.

The real question about large users, however, is not whether the accounting should be done in dollars or hours but who should make the allocations. One alternative is to create a process on the campus for weighing the competing claims of quantum calculations for large molecules, research in artificial intelligence, statistical analysis of

the business cycle, and concordances of Goethe's works. Spare me from participation in that process!

A second alternative is to have the value of computing judged in relation to its value to the research projects it is supposed to serve—that is, as part of the regular foundation and government processes for making research grants. Chemical computing would then be evaluated by chemists, construction of concordances by humanists. There needs to be (and already is, of course) a substantial allocation for the development of computer science itself. This alternative is in the spirit of “program budgeting” or “cost-benefit analysis,” now popular in the federal government.

It may be objected that the problem of balancing the chemist against the humanist simply reappears at a higher level—at the level of the federal budget for NSF and the Humanities Foundation. So it does, but that is unavoidable, and it is better that we make use of existing arrangements for these political decisions than that every campus duplicate such arrangements.

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Safety: A Parallel

Many individuals who have been following the accounts in *Science* of the current controversy over automobile and traffic safety will, I believe, be interested in reading “Bursting boilers and the federal power,” by John G. Burke [*Technology and Culture* 7, No. 1, 1–23 (winter 1966)].

The story in a nutshell is this: “Marine boiler explosions . . . provoked a crisis in the safe application of steam power, which led to a marked change in American political attitudes. The change, however, was not abrupt but evolved between 1816 and 1852” and culminated in Congress passing “the first positive regulatory legislation and [creating] the first agency empowered to supervise and direct the internal affairs of a sector of private enterprise.”

I found Burke's detailed account of the story to be fascinating reading against the background of current events.

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