periment is to be used. If curves intersect, as is likely, neither his experimental design nor his analysis is powerful enough to depict "without loss of faithfulness . . . the essentials of the . . . *D,T,E* relationship." As a step in the direction of taking individual differences into account, it is a useful procedure when interpreted somewhat differently than Loewe suggests. His case for rejecting quantization as a matter of principle does not appear to be well founded.

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4. L. J. Cronbach, *Am. Psychologist* **12**, 671 (1957); C. Shagass and A. Kerenyi, *Can. Psychiat. J.* **3**, 101 (1958).
5. L. R. Tucker, "Determination of generalized learning curves by factor analysis," ONR Tech. Rept., Project NR150-088 (Educational Testing Service, Princeton, N.J., 1960); R. Weitzman, dissertation, Princeton University (1959).

27 January 1961

As is clearly stated in the introduction of my paper (*1*), the sole purpose was to examine the general question whether or not the task of quantifying the relation between dose (*D*) and effect (*E*)—which is appropriately solved by presenting the change in *E* with increasing *D* in a so-called "graded-response" *D,E* curve—can also be solved by presenting, in a so-called "quantal-response" curve, the change, with increasing *D*, of a third magnitude (called *T* in my paper, p_E in Cronbach and Gleser's), the percentage of test individuals attaining or exceeding a certain single preset *E* level (*2*). The question was answered—to the negative—by linking the three magnitudes concerned in a three-dimensional coordinate system with an *E* coordinate rising over a rectangular *D,T* plane, by then forming a *D,T,E* space surface under use of values freely chosen but compatible with experience, and by demonstrating that, since any quantal *D,T* curve lies in a horizontal, any graded *D,E* curve in a vertical plane, they intersect rectangularly "and never the twain shall coincide."

This simple demonstration of the nature of the relation between three basic magnitudes required no experiments, and in fact my paper contains no experimental data nor does it describe, prescribe, recommend, or touch any practical, technical, methodical, or procedural matter. From the fact that in Cronbach and Gleser's reply this model demonstration is called an "experiment" one may consider it possible that the authors have misunderstood the scope and essence of my article. It is food for such supposition that one encounters nowhere in their reply direct and specified objections against my completely theoretical demonstration or against conclusions drawn from it, or against both, but that instead their discussion begins with the extensive description of an "experiment" allegedly encountered in my paper ("Loewe then describes an experiment . . ."), the details of which then form the starting-points and targets of their objections. Even if it were appropriate to call my demonstration an experiment, the experiment described by Cronbach and Gleser is in many important respects unrelated to the object of my demonstration; it is *their* experiment, not mine.

It is true that my *D,T,E* model, by definition (and an extensive, unmistakable definition) is identical with what they call their D,E,p_E surface—which makes any objection to my "*T*" a mere quarrel about *names*. However, their experiment also deals with entirely new relations such as the enigmatic "p_E as a function of *E*." Most, and the most grave and intricate, objections are directed against the "single-dose experiment" character of "my" experiment. This obviously refers to the use of figures and curves obtained from single individual test objects rather than from groups of such. And indeed, actually all of the subsequent discussion of Cronbach and Gleser's reply is focused to the inadequacies, dangers, and fallacies of such "single-dose experiments." Now quite incidentally, although any such questions of experimental procedure are irrelevant in our analysis of basic relations, a technical subject was touched, quite at random, *once* in my article: by mentioning in reference to the *D,T* curves that the percentile distribution values are customarily (and, of course, necessarily) "derived from single-dose *group* experiments." And just as customarily in this statistically minded age the values for *D,E* curves come from single-dose *group* experiments. The authors' "anti-individual" campaign cannot possibly be due to misinterpreting "single-dose group" into its contrary; at any rate, such a campaign is directed to the wrong address, so much more so as in pharmacology intra-individual variation from one test to the other is a well-known, much discussed, and well-heeded phenomenon (see, for example, *3*). Unfortunately, both the constructive suggestion made by Cronbach and Gleser and their promise to contribute to future developments refer only to problems of individual variation, important in *their* experiment but irrelevant to my analysis of fundamentals and my two conclusions submitted: (i) that in the treatment of the problem in question, namely, how to obtain information on intensity of *E* as a function of *D*, the quantal-response *D,T* curve cannot replace the graded-response *D,E* curve, and (ii) that multiple *D,T* curves offer an important tool for statistically supporting and refining the graded-response information.

It is a distressing paradox that, in the summarizing sentence of Cronbach and Gleser's reply, this championing of mine for an appropriate application of quantal-response studies in graded-response investigations is called Loewe's "case for rejecting quantization as a matter of principle."

For those who still adhere to the belief that a quantal-response curve is equivalent to a graded-response curve in depicting the *D,E* relation, my image of the level path of the student of the former and the up-hill climb of that of the latter should perhaps be thrown into somewhat bolder relief: In college towns, such a strictly level promenade built halfway up along a hillside for the convenience of elderly scholars is often named "Philosophers' Lane"; should the meditating philosopher insist that in walking there he gained altitude, one would call that an illusion.

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References and Notes

1. S. Loewe, *Science* **130**, 692 (1959).
2. Using the name "*E*" for this third magnitude and calling the *D,T* (or D,p_E) curve a "*D,E* curve" goes beyond the franchise of christening; that this greatly misleading misnomer is so often used gave rise to the question underlying my previous paper.
3. W. Kalow, *Arch. exptl. Pathol. Pharmakol. Naunyn-Schmiedeberg's* **207**, 301 (1949); A. Giotti and F. Nardini, *Arch. intern. pharmacodynamie* **95**, 187 (1955); S. Loewe, *Arzneimittel-Forsch.* **9**, 449 (1959).

13 February 1961

Chromosomes of Lemurine Lemurs

Abstract. A wide variation in chromosome number and morphology was observed among different species and subspecies of lemurine lemurs. Comparative karyotype analysis indicates close phylogenic relationships and strongly suggests that chromosome structural rearrangements may have played an important role in the evolution of this group of primates.

The lemurs, a unique group of the most primitive primates, the Prosimiae, have survived millions of years. Their distribution has been limited to the island of Madagascar (the Malagasy Republic), and they are now threatened with extinction. Although the diversity of forms has been noted since before

Table 1. Mitotic chromosome numbers of lemurs. M, male; F, female.

Name of lemur	Animals studied (No.) M	Animals studied (No.) F	Diploid No. ($2n$)
Division I			
H. griseus olivaceus (grey gentle)		1	58
H. griseus griseus (grey gentle)	1	1	54
Division II			
L. mongoz (mongoose)	2	3	60
L. fulvus rufus (red-fronted)		2	60
L. fulvus albifrons (white-fronted)		1	60
L. catta (ring-tailed)	2		56
Division III			
L. sp. nov. (*6*) (brown)	1		52
L. fulvus fulvus (brown or fulvous)	1	1	48
L. variegatus (ruffed)	1		46
L. macaco (black)	1	1	44

Darwin's time, the cytology of this group was virtually unknown until recently, when a description of the chromosomes of the black lemur (*Lemur macaco*) was reported (*1*). In fact, only five other prosimian species have been examined cytologically (*1*).

We have made a study of the somatic chromosomes of a number of species and subspecies of lemurs, all belonging to the subfamily Lemurinae of the family Lemuridae. Skin biopsy specimens were obtained and sent to this laboratory, either directly from Madagascar or from New Haven, Connecticut, where some of the captive animals are kept (*2*). Chromosome analyses were made on cells grown in culture. The cell culture and cytological techniques employed were essentially the same as those for human materials and have been previously described (*3*).

The diploid chromosome numbers of the group of lemurs so far examined are listed in Table 1. Variations in both the number and morphology of the chromosomes exist within a single genus and even within hitherto recognized taxonomic species (*4*). The length of metaphase chromosomes varies from approximately 0.3 to 14 μ. The X chromosome is medium-sized and either rod-shaped (acrocentric) or J- or V-shaped (metacentric); the Y is invariably acrocentric and is the smallest in the complement. In some species (*Hapalemur griseus, Lemur variegatus,* and *L. macaco*) two distinct classes, macro- and microchromosomes, are present; in the other species there seems to be no discontinuity in the range of chromosome lengths. A cell from a male brown lemur (*L. fulvus fulvus*, $2n = 48$) is shown in Fig. 1, which shows variations in the size and shape of the chromosomes. In this species the X is an acrocentric macrachromosome, and the Y is the smallest element.

There is a direct relation between the total number of chromosomes and the number of acrocentric chromosomes. For example, in *L. mongoz* ($2n = 60$) all but two pairs of autosomes are acrocentrics, whereas in *L. macaco* ($2n = 44$) only ten pairs of autosomes are acrocentrics. In addition, detailed karyotypic comparisons of chromosome lengths, position of centromeres, secondary constructions, and other morphological features indicate similarities between certain chromosomes of different species or subspecies. The presence of these "marker" chromosomes suggests homology, thus denoting close interspecific relationships. In many instances, karyotypic differences between any two particular species can be interpreted as the result of one or more chromosome structural rearrangements such as reciprocal translocation and pericentric inversion. A Robertsonian-type of chromosome evolution (see *5*) has probably played a significant role in this group of primates. On the basis of these cytological findings, the lemurs examined to date may be subdivided into three tentative divisions (Table 1). Species within each division seem to be closely related, and stepwise interrelationships are easily traced. Nevertheless, interdivision resemblances are not uncommon. On the other hand, it should be pointed out that the lemurine lemurs as a group exhibit sufficient karyotypic differences from other prosimian primates studied to obscure the interfamily relationships (*7*).

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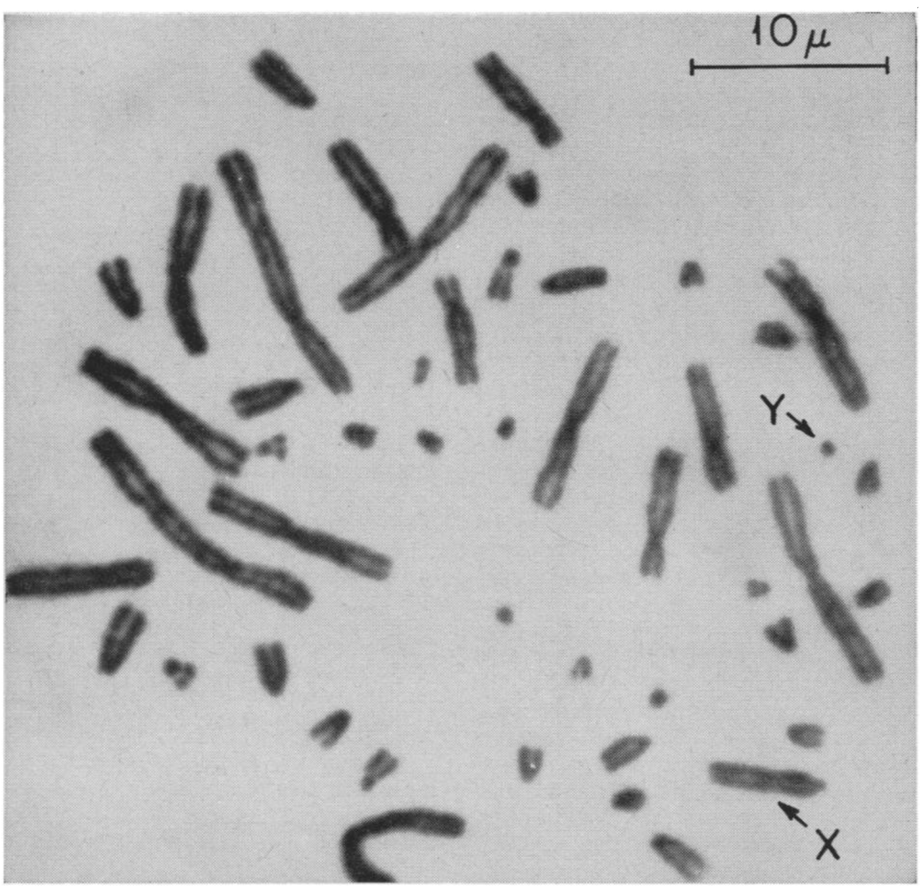

Fig. 1. A metaphase cell in culture from skin biopsy of *L. fulvus fulvus* male ($2n = 48$) showing variations in chromosome morphology. The sex chromosomes, X and Y, are labeled. An aceto-orcein stain was used in this air-dried permanent preparation.

References and Notes

1. E. H. Y. Chu and M. A Bender, *Science* 133, 1399 (1961).
2. The specimens were obtained through the support of a National Science Foundation grant, G-12331, to J. Buettner-Janusch, Yale University.
3. E. H. Y. Chu, J. Warkany, R. B. Rosenstein, *Lancet*, in press.
4. The classification used is that of W. Fiedler, *Primatologia* 1, 1 (1956).
5. M. J. D. White, *Animal Cytology and Evolution* (Cambridge Univ. Press, London, ed. 2, 1954).
6. The specimen, as yet unnamed, did not closely resemble any lemur described in the literature, although it had some features similar to the male *L. fulvus fulvus.* In view of its different chromosome number it can probably be considered a separate species.
7. A detailed cytological description of the lemurs and a proposed phylogeny is in preparation.

16 January 1961