

cell exhibit cytotoxicity for this cell but exhibit little or no cytotoxicity for cells from primary cultures of monkey kidney or heart tissue. On the other hand, antisera from inoculated chicks are cytotoxic both for the continuously propagating cell line and for cultured cells from tissues of these organs. Thus, the common antigen or antigens between the continuously propagating cell line and the cells derived from freshly extirpated organs of the monkey is revealed by the chick; the monkey, however, reveals the existence of another antigen in the continuously propagating heart cell that is not present in cells from freshly removed organs of the monkey.

The antiserum for the continuous monkey heart cell line is also highly cytotoxic for the following continuously propagating human cell lines derived from both normal and neoplastic sources: human carcinoma (HeLa, HEP-2, KB); human embryo [intestine (Henle)]; human marrow (Detroit 6); human conjunctiva and liver (Chang); human heart (Girardi).

The cytotoxic effect of both monkey and chick antiserum has also been demonstrated for trypsinized suspensions of cells from human tissues, both normal (tonsil, lung, kidney) and neoplastic (melanoma, Wilms' tumor); similar effects have been shown for suspensions of cells cultured from these tissues. Adsorption of antibody on monkey heart cell does not remove all of the cytotoxic antibody for human tonsil, and adsorption of the cytotoxic antibody upon suspensions of normal human tonsil, or monkey kidney, does not seem to remove the cytotoxic activity against the established monkey heart cell. Furthermore, studies of antibody-combining capacity, by cells and by cell extracts, also reveal the complexity of antigens involved.

It is apparent that considerably further study is required before any conclusions can be drawn. The purpose of this communication is to report a simple technique for measurement of cytotoxic antibody by means of which the relationship among continuously propagating cells may be investigated and, through this, the question of the use in man of vaccines prepared from such cells can be dealt with further.

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Rate as Response Probability in Discrimination Learning

It has been argued that rate of responding is the only appropriate datum to a formulation of behavioral change in terms of response probability (1). It has also been shown that, under certain restrictions, rate is mathematically equivalent to response probability (2). The experiments reported in this paper were designed to evaluate response rate as it corresponds to specific probabilistic predictions.

In discrimination, the organism comes to respond primarily to one set of stimuli (S) which are the occasion for reinforcement, or reward, and not to another set (S') for which responding is never reinforced. This study is concerned with the forms of S and S' response curves when the probabilities of sampling, or perceiving, stimulus elements in S and S' , θ_1 and θ_2 , respectively, vary from equality to a considerable inequality. Response frequency is known to be quite sensitive to differences in the manner of reinforcement. Consequently, two conditions of reinforcement known to produce marked differences in response rate were employed to determine the extent to which the forms of the curves predicted on the basis of stimulus control are distorted or overridden by the effects of such reinforcement contingencies.

From a discrimination model (3) developed from the Estes-Burke statistical learning theory (4), one predicts that the S and S' response curves approach their asymptotes monotonically when the sampling probabilities or θ values are equal. When θ_1 is larger than θ_2 , the S curve accelerates more rapidly than is the case in the equal θ condition, and the S' curve may increase to a "peak" before it declines to a lower asymptote.

In experimental groups I and III, θ values were contrived to be equal through the expedient of setting an equal number of experimentally manipulated stimulus elements in S and S' . In groups II and IV, six times as many elements were assigned to S' as to S ; hence, for these groups, $\theta_2 = \theta_1/6$. Five subjects were run individually in each of the four groups. The subject was required to pull a Lindsay manipulandum (5) for points on a counter as a series of patterns of lights were presented to him. Each pattern,

composed of subsets of ten jewel lights mounted in two rows of five lights each, was presented for 1 minute. The subject was instructed to try for a maximum score on the counter at the same time he was trying to determine the principal defining S patterns. The only other room illumination was supplied by a blue 7-watt bulb mounted above the counter: white noise was piped in through a speaker and headphones for masking purposes.

Groups I and II were placed on a 10/1 variable-ratio schedule of reinforcement—that is, subjects in these groups were awarded one point for every tenth response, on the average, made in the presence of S patterns. Figure 1 shows the mean frequency of response per stimulus pattern. In the second experiment, subjects in groups III and IV were placed on a 30-sec fixed-interval schedule of reinforcement—that is, they were awarded a point for the first response made after each 30 sec interval during S presentations. Only 25 S and 25 S' patterns were presented in these latter groups, as opposed to 30 S and 30 S' presentations in the ratio groups. As is shown in Fig. 2, the over-all mean response rates are considerably lower in the interval groups. This is in agreement with previous studies of the effects of schedules of reinforcement upon rate of response. It should be noted that, despite the large differences in rates obtained under the different schedules, the predicted ordinal positions of the curves are invariant and as predicted insofar as the more difficult discriminations are not far advanced. The S' curves under

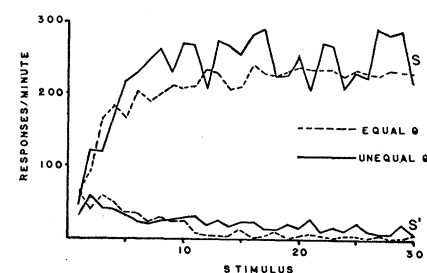


Fig. 1. Rates of responding in discrimination learning under a 10/1 variable ratio schedule of reinforcement.

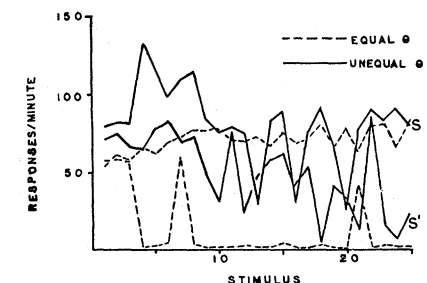


Fig. 2. Rates of responding in discrimination learning under a 30-sec fixed-interval schedule of reinforcement.

the unequal θ conditions are some distance from their asymptotes, but their relative positions are the same under both conditions of reinforcement.

Different schedules of reinforcement thus produce large differences in rate and temporal patterning of response. It seems safe to conclude, however, that despite these effects, rate of response is a sensitive datum for the evaluation of probabilistic predictions. This is of importance, for it makes possible direct extensions of current learning models to more general experimental conditions than have hitherto been employed.

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Food or Training in Paramecium?

From behavioral and biological studies of the protozoan *Paramecium aurelia*, we hope to get generalizable information about relations between intracellular dynamics and behavior.

In a series of experiments I have investigated a response by which food-deprived *P. aurelia* can be induced to cling to the sides of a clean and sterile platinum wire after having been exposed to the wire when it was baited with food. It has been suggested (1) that the organisms' approach to the clean wire after training is a response to bacterial material that was previously left in the culture and nothing more. This would seem to mean that exposure of paramecia to food with wire would not have any very different effect from exposure to food alone.

To test this notion, two experiments were performed to investigate the effects of various amounts of wire presentation (2). In one experiment, a microdrop of bacterial suspension (food) was introduced at the edge of a depression containing a "hungry" culture of paramecia, while the clean wire was simultaneously lowered into the middle of it. After 8 minutes, the wire was removed. Control cultures received the food but not the wire. After 30 minutes, the clean and sterile wire was introduced into both kinds of cultures. The experimental culture, which had had food and wire simultaneously, ringed the wire significantly more than did the controls ($p < 0.02$).

In another experiment, two wires were used, one 3 times the diameter of the

other. On the larger wire, 3 times as many wipes of bacteria were applied as on the smaller, but the smaller wire was immersed in the paramecium culture 3 times as often, with shorter time intervals between immersions. Total duration of training period, amount of food, and area of wire exposed were equated for both groups, but the time of exposure to wire was 3 times as long in one group as in the other. The cultures which had longer exposure gave the wire-clinging response on tests, while the large-wire, shorter-exposure group did not noticeably exceed zero. For the difference between the groups, p was less than 0.01.

In all experiments, "trained" cultures have been routinely stirred up by rotation of the slide before placement on the microscope stage for final tests. Yet, when the wire is lowered, paramecia come to it. The response, in a good culture, is a slow and direct swoop toward the wire, different from any other behavior we have observed.

A response of lying motionless at the bottom seems to be built into the organism. When isolations are being made with a micropipette, many paramecia settle motionless to the bottom of the depression when the pipette is reintroduced. In "training" experiments, this lying down usually appears by the fifth descent of the wire and can be elicited as readily by a clean wire as by one which is baited with food. The response of actually clinging to the side of a clean wire, or remaining motionless in a limited area, is quite unusual.

If modification of behavior is due to presence of carbon dioxide or of bacterial food, and only to this, then change in training schedules (3) or in life-history (4), or from light to darkness (5), with food reinforcement administered similarly throughout, should affect strength of response only to the extent of chance variability, but the differences were found to be highly significant statistically.

We have tried to repeat Jensen's experiment with paramecia in the following way. We used media and bacteria on which paramecia were being satisfactorily maintained at the time, since a strain of, say, *Aerobacter aerogenes* on which satisfactory cultures of *P. aurelia* have been bred for some time may suddenly become inadequate or even lethal (6). One drop of a suspension of bacteria in medium was added to a moderately food-deprived culture of paramecia such as we usually use in training experiments. To a matched culture, a drop of distilled water was added. A drop from each culture, was placed on a bacteriological slide, with a space of about 1 mm between the two drops. The two drops of paramecium culture were joined by drawing a narrow bridge of fluid between them. In one case, the bridge was drawn

from the clear to the bacteria-clouded drop. In the other case, the bridge was drawn in the opposite direction. Fluid from each drop diffused into the other, forming clearly discernible phases of bacterial dilution.

When the bridge was drawn from the clear drop to the cloudy one there were some 48 paramecia in each drop. As time passed, the feeding paramecia slowed down, but at no time were any entirely motionless. After 1 hour, there were 21 animals in the cloudy side; 74 in the originally clear side, which by now showed a large infusion of bacteria; and some three paramecia in the bridge between the drops. This difference, which is opposite to what Jensen found, is significant beyond the 0.001 level of confidence.

When the bridge was drawn from the cloudy drop to the clear one, 25 paramecia were in each drop, exactly as Jensen reported. Again, no animals were motionless, but activity decreased with feeding. At the end of 1 hour, there were 31 paramecia (one in fission) in the cloudy side and 19 in the originally clear side. This difference is not statistically significant. Other, previous efforts to repeat Jensen's experiment had also yielded differences either not significant or in the direction opposite to that of his report. No doubt this can be explained by differences in procedure or in the condition of paramecia or bacteria, or both, that were used.

Our results conform well with the known fact that sufficiently dilute acid such as carbon dioxide or acetic acid will induce congregation of paramecia, while higher concentrations will repel them (7), response being made to monovalent, but apparently not to divalent or trivalent, cations (8). A rich suspension of bacteria lowers pH. The paramecia probably collected in those areas which offered the most nearly optimal pH conditions, always near the bridge between the drops.

Of course, in Jensen's experiments, many thousand times as many bacteria were used as in our behavioral work. Such a large quantitative difference has qualitatively different effects. Introduction of distilled water into a culture also has effects. Even the addition of a very small amount of water (as from condensation) into a culture growing rapidly in a depression slide will delay fission for hours.

In Jensen's experiment No. 1, bacteria were apparently introduced into distilled water from a platinum wire. The location and number of bacteria found after introduction into clear water cannot be compared with the location and number of bacteria similarly introduced into a thick culture of actively moving and feeding paramecia; (the amount of steak found in a dish placed on the floor in an