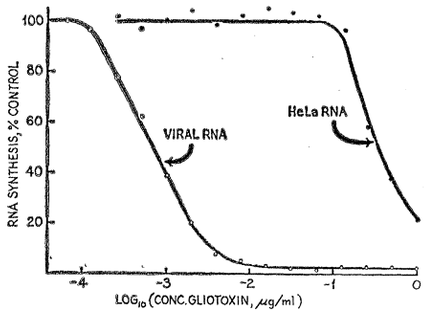

Fig. 3. Dose-response curves relating gliotoxin concentration with viral and cellular RNA synthesis. Poliovirus-infected HeLa cell suspensions were prepared as described for the control sample *Z* in the legend of Fig. 1, except that arginine, lysine, valine, and leucine were present in normal concentrations and no ^{14}C-labeled amino acids were added. The medium was also supplemented with calf serum (2.5 percent). Uninfected cell suspensions were prepared in this same medium, except that no actinomycin D was added. Infected cells were incubated with graded concentrations of gliotoxin for the period from 1 to 6 hours after infection. Uninfected cells were incubated with gliotoxin for 4 hours.

collected on Millipore filters. To measure viral RNA synthesis, cellular RNA synthesis was suppressed with actinomycin D (2.5 μg/ml). Viral protein synthesis is equated with the second phase of protein synthesis which begins approximately 3 hours after infection in poliovirus-infected cells (*6*) (Fig. 1A).

When gliotoxin (0.05 μg/ml) was added at the time of infection (Fig. 1), it completely suppressed viral RNA and protein synthesis. The action of gliotoxin is irreversible in that repeated washing of the infected cells 30 minutes after infection did not relieve the inhibition (Fig. 1B). This inhibition is not caused by extracellular inactivation of virus, nor can it be attributed to interference with virus adsorption or penetration into the cell, because, in the presence of gliotoxin, shutoff of cellular protein synthesis coded for by the viral genome (*6*) still occurs (Fig. 1A). Rather, gliotoxin seems to block directly and specifically the processes by which viral protein and RNA are made within the cell. However, these processes are interdependent (*7*); thus, it is possible that only one of them is sensitive to gliotoxin, since specific inhibition of either one early in the infection would result in the suppression of both.

Therefore, in a second experiment, we added gliotoxin 240 minutes after infection, at a time when viral RNA and protein are both present in considerable amounts and are synthesized at a linear rate (Fig. 1). Labeled amino acids were not added until 135 minutes after infection, when all cellular protein synthesis had ceased (Fig. 1A) and viral protein synthesis was about to begin. Thus, the observed protein synthesis (Fig. 2A) is entirely viral. Gliotoxin had no effect on viral protein synthesis for at least 30 minutes after its addition. In contrast to this, it caused an immediate and striking inhibition of viral RNA synthesis (Fig. 2B). We conclude that viral RNA synthesis is the prime target of inhibition by gliotoxin and that the progressive inhibition of viral protein synthesis observed 30 to 120 minutes after addition occurs as a consequence of the primary action.

To show the specific inhibition of viral RNA synthesis of gliotoxin (Fig. 3), we incubated infected and uninfected cells with graded concentrations of gliotoxin. RNA was determined by an automated paper disk method (*8*). Approximately 1000 times more gliotoxin is required to achieve a 50-percent inhibition of HeLa RNA synthesis than to produce a similar inhibition of viral RNA synthesis.

Thus, gliotoxin appears to block RNA-dependent synthesis of RNA in poliovirus-infected cells and to be without effect on cellular, DNA-dependent synthesis of RNA. Whether this interesting specificity—the reverse of that shown by actinomycin D—is the result of the topographical separation of the two sites of RNA synthesis (*7*, *10*) or of specificity at the molecular level remains to be determined. Our recent experiment favor the latter alternative.

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28 September 1967

Serial-Choice Reaction Time: Inadequacies of the Information Hypothesis

Abstract. *The results of an experiment on serial-choice reaction time, specifically designed as a critical test of the Information Hypothesis, lead to rejection of the hypothesis; information is found to be neither a necessary nor a sufficient condition to account for the data. Where previously information had been interpreted as a determinant of reaction time, it was usually confounded with the probability of nonrepetition of a signal. Thus, to the extent that this confounding is present in previous experiments, the inference attributing an increase in reaction time to an increase in information is logically invalid.*

Shortly after publication of Shannon's monograph (*1*), three reports (*2*) provided the basis for the Information Hypothesis in choice reaction time (RT). These studies provided compelling evidence that choice RT behaved as a linearly increasing function of transmitted information. During the following decade the Information Hypothesis served as the focal point for most studies of the problems of choice RT. As the results accumulated, it became increasingly evident that the scope of the Information Hypothesis was far more restricted than was originally thought; factors such as training, stimulus-response compatibility, coding, discriminability, and payoffs were all shown to be playing an important—often overriding—role in determining the characteristics of performance of RT tasks. Nevertheless a hard core of evidence remains, on the basis of which the Information Hypothesis is viable to this day. It is to that body of evidence and arguments that I address myself.

With rare exceptions it can be shown that, for a fixed number of signals, the

sequences of signals on which the evidence for the Information Hypothesis is based were constructed in such a way that stimulus information increased simultaneously with the probability of nonrepetitions (p_{nr}) (*3*). Logically, therefore, the observed increase in RT could just as well have been attributed to an increase in p_{nr} as to an increase in information. This confounding has more than merely formal interest, however, for it has recently been shown that under certain conditions the RT for repetitions is considerably faster than for nonrepetitions (*4*). The mean of the overall RT distribution is simply the sum of the means of the RT for repetitions and nonrepetitions, each weighted by its own probability of occurrence; therefore, an increase in p_{nr} has the effect of increasing the proportion of slower responses in the overall RT distribution, which in turn increases the mean of the overall distribution. In the light of these arguments I recently suggested (*4*) that a critical test of the Information Hypothesis could be performed by pitting information against p_{nr}.

This is easily accomplished by generating the signal sequences by means of symmetric transition matrices with equiprobable signals, where all the diagonal elements are equal and all the off-diagonal elements are also equal. For such matrices it can be shown that information is a nonmonotone function of p_{nr}, with a maximum (that is, information $= \log_2 K$) at $p_{nr} = (K - 1)/K$ (K being the number of signals). Information and p_{nr} will be positively correlated on one side of the maximum and negatively correlated on the other side. By restricting oneself to values of information in the range in which p_{nr} is a two-valued function of information, one can in addition obtain pairs of equi-information conditions having a high and a low value of p_{nr} within each pair. Table 1 lists the set of such four-choice sequences that I used.

The stimuli consisted of four neon lights mounted behind translucent disks on a Masonite board. The disks, 1.3 cm in diameter, were horizontally arranged, the two middle disks being slightly lower than the two outer ones. The two middle lights were separated by 1.3 cm; the lights of the left and right pairs, by 6.4 mm. A thin white vertical line served as a fixation line between the two middle lights; the bottom edge of each disk was underscored by a thin white line which made the alternatives always clear. The Masonite board was painted gray and placed 1.7 m in front of a seated subject, with the lights appoximately at eye level. The responses were made by depressing the appropriate one of four keys with the index or middle finger of the left or right hand: the extreme-left light was responded to by the left middle finger; the next light, by the left index finger; and so on. The keys required pressure between 140 and 170 g and 3-mm travel for activation.

Table 1. Conditions of the experiment: The information (H) and p_{nr} values for the eight equiprobable four-choice sequences that I used; $H = -\sum_j p_j \sum_i p(i/j) \log p(i/j)$

$$p_{nr} = \sum_j p_j \sum_{i \neq j} p(i/j)$$

There are three pairs of equi-information conditions, one condition that is unique by virtue of the fact that it corresponds to H_{max} (2.00 bits), and one unmatched high-p_{nr} condition at H = 1.93.

Information	p_{nr}	
	High	Low
1.59	1.00	0.39
1.73	0.97	.47
1.87	.92	.56
1.93	.88	
2.00	0.75	

Eight types of sequences, differing only in their transition probabilities (see Table 1) and with 300 trials per sequence, were used in the experiment. The signals were equiprobable in all sequences. Signals and responses were automatically presented and recorded; the time between a response and the next signal was 140 msec. Eight subjects participated in the experiment for 3 days each. The 1st day was used for training; on the 2nd and 3rd days each subject received all eight sequences in a latin square; during all 3 days the subjects were always informed of the precise stochastic properties of the sequence that they were about to receive.

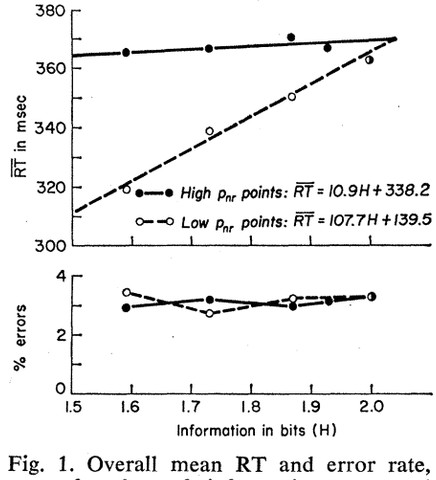

Fig. 1. Overall mean RT and error rate, as a function of information, averaged over all subjects and both days (*5*).

My results are based on an analysis of correct responses; errors, and responses that immediately followed errors, were excluded from the data. One of the necessary conditions that RT data must meet in order to confirm the Information Hypothesis unequivocally is that, all other things being equal (such as stimulus-response compatibility, training, discriminability, and error rate), equi-information conditions must produce equal overall mean RT's. This condition may be relaxed by formulating the hypothesis in a different form: given two sets of sequences spanning the same range in information, such that sequences are matched across sets to form equi-information pairs, the slope of the mean overall RT, against information, must be equal for both sets; that is, all other things being equal, equal increments in information produce equal increments in RT. Figure 1 illustrates the overall mean RT and error rate for sequences having high and low values of p_{nr}, averaged over subjects and days, as a function of information (*5*). The best-fitting straight line for the low-p_{nr} points has a slope of 107.7 msec per bit, with a statistically significant linear trend ($t_{(7)} = 5.7$, $P < .001$). The slope for the high-p_{nr} points is 10.7 msec per bit, with a statistically insignificant linear trend ($t_{(7)} = 0.8$, $.4 < P < .5$); that is, the slope for the high-p_{nr} points is not statistically different from a zero slope (*6*). When the RT's for repetitions and nonrepetitions are analyzed separately it appears that each is a linear function of the conditional probability of the signal. Thus the overall mean RT can be expressed as a parabolic function of p_{nr}, with the slope and intercept of the RT for repetitions and nonrepetitions as parameters.

In view of these arguments and experimental results the Information Hypothesis must be rejected as an erroneous and misleading interpretation of serial choice RT data (*7*).

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3. An important exception is Hyman's observation (*2*) that the only nonlinear variance in his data is completely accounted for by sequence containing no repetitions of the signal. This and his subsequent observations in this regard completely accord with my findings.
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5. The results for individual subjects show essentially the same patterns: in every instance the RT for the high-p_{nr} sequence is longer than for the low-p_{nr} sequence (matched on information).
6. The difference between the high- and low-p_{nr} points is, of course, highly significant ($t_{(7)} = 5.03$, $P < .001$).
7. At this point I estimate that results would be similar with considerably longer response-to-signal intervals (longer than 140 msec) if the stimulus-response relations were made less compatible than mine. Such findings would extend my conclusions, beyond serial tasks, to encompass discrete-choice RT tasks.

8. Research aided by the University of Michigan's Office of Research Administration. I thank J. Alford, H. Hamburger, and J. E. K. Smith for help and cooperation. This is a preliminary and partial report; the results emphasized are those bearing most directly on the Information Hypothesis. A more complete report will be published elsewhere.

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Baroreceptors in the Adrenal Gland

Abstract. *Afferent activity from dissected filaments of nerves to the adrenal gland was recorded. Firing rates of single fibers followed changes in systemic blood pressure. Chemically and mechanically induced changes in blood pressure were reflected by an appropriate directional change in unit activity.*

The existence of baroreceptors in the region of the carotid sinus and aortic arch has been well documented (*1*). There is also evidence that similar receptors are present in the pulmonary artery and in the heart (*2*). To our knowledge, baroreceptors in the smaller vessels of the arterial system have not been described. We now present neurophysiological evidence which suggests the existence of baroreceptors located in the vessels of the adrenal gland.

Experiments (24) with different nerve preparations were performed on six rabbits and two cats anesthetized with sodium pentobarbitone. Arterial blood pressure was recorded from polyethylene catheters in the cardiac end of the common carotid artery or the caudal portion of the abdominal aorta, or both.

We injected drugs into the jugular vein, recorded afferent nerve discharges with a negative-capacitance electrometer, and stored these records on magnetic tape. Single-fiber activity was converted into standard pulses by a discriminator and analyzed by a digital computer. Afferent discharge rate, blood pressure, electrocardiogram, and respirations were also recorded on a polygraph. The small nerves of the adrenal gland were located and isolated, and all branches which did not lead directly to the gland were cut. Recordings were taken from the peripheral portions of these nerves after their central connections were severed.

When a small filament was dissected from a nerve branch to the adrenal gland and placed on the recording electrode, spontaneous afferent discharges were observed frequently. Our study is only concerned with afferent firing related to changes in arterial blood pressure. As shown in the top line of Fig. 1, these units demonstrate some rhythmic activity with each pressure wave. After the epinephrine was injected (line 2), the discharge rate gradually increased, blood pressure increased, and rhythmical activity became more pronounced. After a maximum value was reached (line 3), the firing rate decreased and returned to that of the control (line 4). Firing rates closely paralleled the direction and magnitude of the changes in blood pressure.

In Fig. 2, results of experiments to determine the dependency of afferent firing rates on blood pressure levels are shown. The lower traces represent the number of spikes occurring each 0.1 second. This value, determined by the computer, is displayed on the polygraph record. The vertical axis represents firing frequency, and the horizontal axis represents time. Clamping the abdominal aorta proximal to the adrenal artery resulted in rapid cessation of firing of these fibers. Touch receptors, which responded to distension of the adrenal capsule, however, were readily excited during the brief

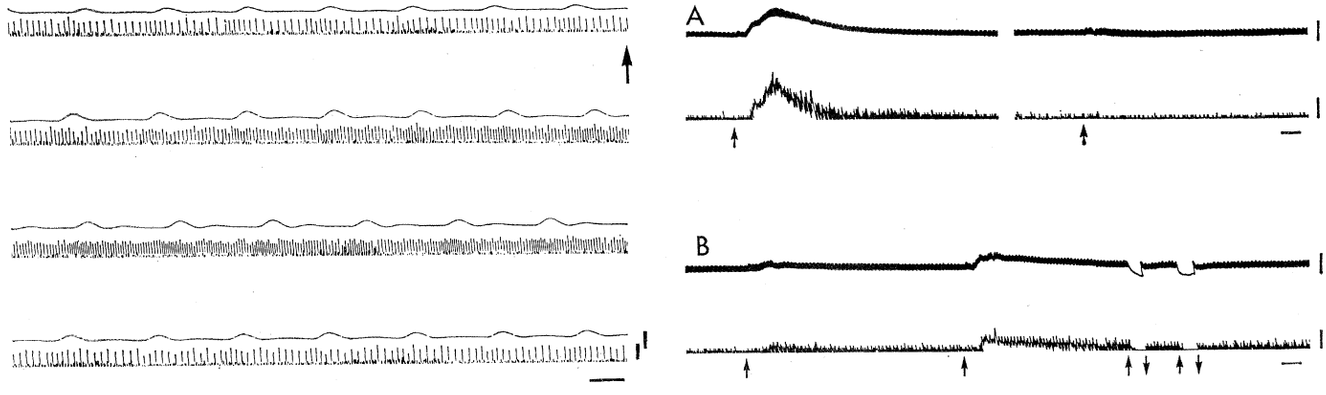

Fig. 1 (left). Effect of an intravenous injection of epinephrine (30 μg) on blood pressure (upper beam) and discharge rate of a single afferent fiber (lower beam) from the adrenal gland in rabbit. Calibrations: upper vertical bar, 0 to 100 mm-Hg; lower vertical bar, 1 mv; horizontal bar, 0.1 second. Fig. 2 (right). (A) Effect of 10 μg of epinephrine (left) and 100 μg of isoproternol (right) on blood pressure (upper trace) and firing rate (lower trace) of adrenal afferent. (B) Effect of 300 μg of metaraminol (left), 10 μg of norepinephrine (center), and repeated clamping of the abdominal aorta (right) on blood pressure and firing rate of adrenal afferent. Calibrations: vertical bars, 0 to 100 mm-Hg (blood pressure); spikes, 0.1 second (afferent discharge). Horizontal bars, 10 seconds.