

Fig. 1. Schematic representation of a cross section of bladder wall with vertical lines denoting the mucosal and serosal surfaces, respectively.

mogenized in 10 percent trichloroacetic acid to extract the lactate from the tissue. The concentration of C^{14} -labeled lactate in tissue water (3) can thus be obtained. From the concentration of C^{14} -labeled lactate within the membrane water and its rate of appearance in the serosal bathing medium, k_2 can likewise be directly evaluated. By substituting values for K_{trans} and k_2 into Eq. 4, k_1 may then be calculated. Because of the relatively low permeability of the membrane to lactate, C_o will remain so much larger than C_i during an experiment that back diffusion may be ignored. The values for k_1 and k_2 may, of course, be evaluated as readily in the opposite direction.

Table 1 shows the values obtained for k_1 and k_2 when measurement was made from mucosal to serosal sides in nine 30-minute periods in three experiments, and from serosal to mucosal surface in twenty 30-minute periods in eight experiments. In every period, k_2 was found to be significantly larger than k_1 . Note that any C^{14} -labeled lactate from the medium adherent to the mucosal surface

Table 1. Mean values for permeability coefficients for C^{14} -labeled lactate through the isolated toad bladder. All values are means plus or minus the standard error of the mean and are expressed as cm/sec $\times 10^{-7}$. The figures in parentheses give the number of 30 minute periods upon which each value is based.

k_1	k_2	K_{trans}
A. C^{14} -labeled lactate placed on serosal side initially		
5.11 ± 0.59 (22)	94.4 ± 17 (20)	4.62 ± 0.47 (22)
B. C^{14} -labeled lactate placed on mucosal side initially		
4.86 ± 0.67 (9)	$95. \pm 20$ (9)	4.65 ± 0.62 (9)

of the bladder will be measured as tissue lactate and tend to make k_2 falsely too low while medium C^{14} -labeled lactate adherent to the serosal surface will result in underestimation of k_1 . In spite of this expected limitation in the experimental procedure, satisfactory agreement was found for the values of k_1 and k_2 , respectively, when measurement was made in the two directions. This difference in permeability of the two surfaces of the isolated toad bladder is sufficient to account for the observed asymmetrical distribution of lactate about this membrane.

Since all permeability measurements were made across the short-circuited membrane (4)—that is, with no electrical or chemical gradients across the membrane except those of the added radioactive isotopes—the expectation for passive ion movement through the membrane is an equal permeability coefficient as measured in the two directions across the membrane. The mean values and standard errors of the mean shown in Table 1 for lactate for K_{trans} , k_1 , and k_2 indicate no significant differences in permeability whether the values were obtained during measurements of mucosal to serosal or serosal to mucosal flux. Considering that the measurements in the two opposing directions were of necessity done on different membranes, the agreement is surprisingly good. Thus the passive nature of the lactate movement (simple diffusion) through this membrane is demonstrated.

The permeability coefficients are expressed in centimeters per second instead of square centimeters per second as is customary. This is necessary because the thickness of the diffusion barriers is as yet unknown. We do not know whether the difference between k_1 and k_2 is attributable to a difference in structure of the opposite surfaces of the membrane, to a difference in thickness of diffusion barriers of similar structure, or even to a difference in effective surface area of the two faces of the bladder. This limitation does not affect the relative functional magnitude of k_1 and k_2 , which is what has been measured simultaneously in the same membrane.

By analogy with lactate, it is suggested that the main barrier to passive diffusion of sodium is also at the mucosal surface. Such a situation would necessitate that at least part of the active sodium transport mechanism (moving sodium from the mucosal to serosal side) be located on the mucosal surface and function to admit sodium into the mucosal cells at a rate more rapid than can be accounted for by passive diffusion alone (5).

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References and Notes

1. A. Leaf, "Résumés," 3rd Intern. Congr. Biochem., Brussels, Aug. 1955; A. Leaf, J. Anderson, L. B. Page, Jr., *J. Gen. Physiol.*, in press.
2. T. H. Wilson, *Biochem. J.* 56, 521 (1954).
3. Chromatographic separation on paper of the tissue extract and of the medium at the termination of an experiment using a solvent system of ether, acetic acid, and water in the ratio of 13:3:1 revealed a single peak of radioactivity having an R_f characteristic of lactate. This confirms the assumption that all the tissue and medium activity was in fact lactate.
4. H. H. Ussing and K. Zerahn, *Acta Physiol. Scand.* 23, 110 (1951).
5. This work was supported by grants from the John A. Hartford Foundation and the National Institutes of Health (grant H-2822).

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Ability of Bats to Discriminate Echoes from Louder Noise

The dependence of bats upon echolocation suggests a vulnerability to interference by loud noises. Yet hundreds fly together in the darkness of caves, and artificial jamming sounds have remarkably little effect in the laboratory (1). Continuous thermal or "white" noise covering the entire frequency range of the orientation sounds of the long-eared bat *Plecotus (Corynorhinus) rafinesquii* does increase slightly the figure for minimum detectable size of wire obstacles. This finding permits measurements of the bat's ability to discriminate echoes from noise (2).

Across the central part of a 32- by 12- by 8-ft room, 28 vertical wires were arranged in four staggered rows, so that a bat had to fly a zigzag course to dodge the wires at more than the chance level of about 40 percent misses. With the more skillful individual *Plecotus*, the smallest size wire detectable in the quiet was one of diameter between 0.2 and 0.5 mm, well below the wavelengths of the bats' orientation sounds (8 to 14 mm). Thermal noise was generated by two banks of 35 electrostatic loud-speakers, which faced the array of wires from opposite ends of the room. In almost the whole space where wires were detected and dodged, the over-all sound-pressure level was between 80 and 90 db above the standard reference level of 0.0002 dyne/cm², and even at the lowest points it exceeded 70 db. The spectrum level of the noise varied no more than ± 5 db from 15 to 55 kcy/sec, but fell off sharply beyond these limits; thus, the noise level per cycle of band width was usually more than 34 db and always exceeded 24 db. Figure 1 includes all data for the five individual *Plecotus* whose flight was most consistent during 5 days when they were at the peak of their flying skill and avoided 1- to 1.5-mm wires in 80 to 100 percent of the flights, in quiet and in noise. In the control tests,

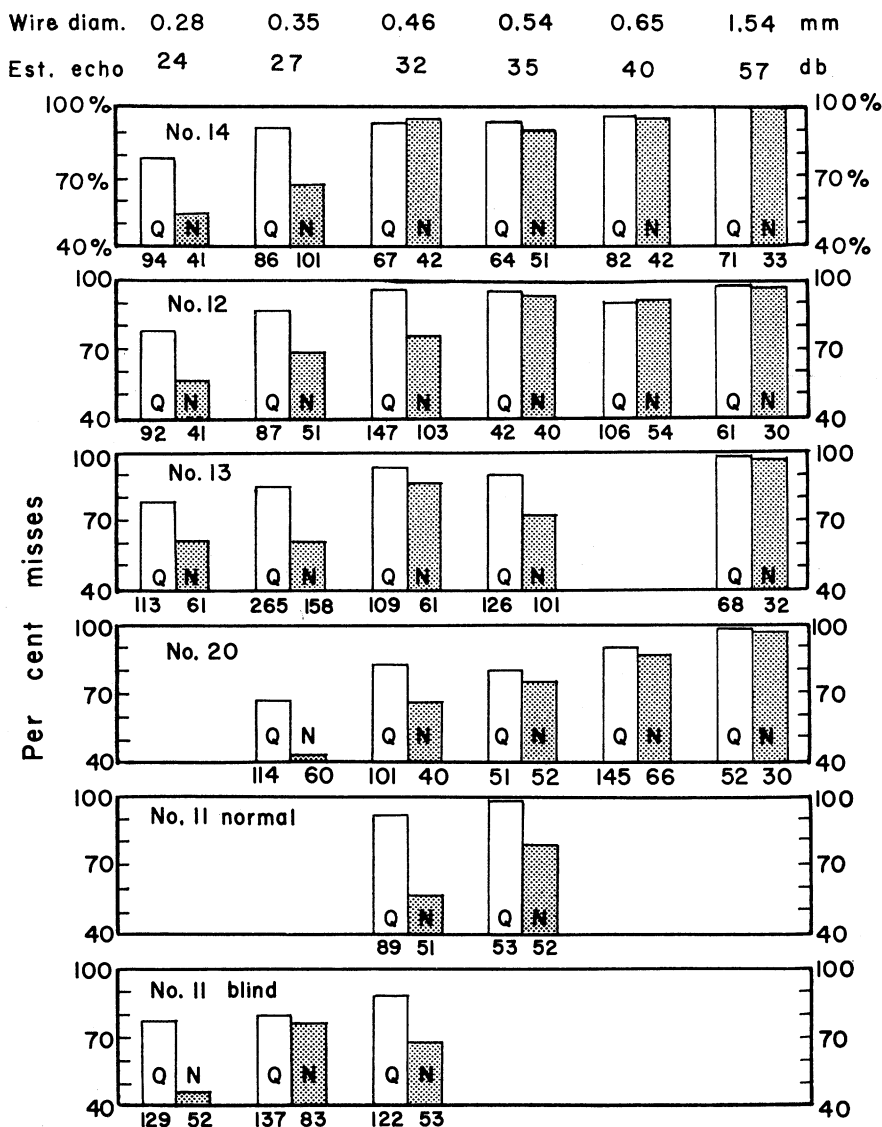


Fig. 1. Obstacle avoidance scores of *Plecotus rafinesquii* flying through an array of vertical wires, in quiet and in thermal noise, as a function of the diameter of the wires. Each bar graph shows the percentage of misses for a single bat during the period when it was at its maximum level of flying skill, for flights in the quiet (Q) and for those in the noise (N). The number of trials in each series is listed below each bar. The estimated echo levels are given in decibels above 0.0002 dyne/cm².

consisting of about equal numbers of flights in the quiet before and after introduction of the noise, these bats showed no appreciable deterioration of performance due to fatigue or other factors. All these bats flew skillfully in the noise, landed normally, and were difficult to capture with a net.

In each of the 1- to 2-msec pulses of sound used by these bats, the frequency drops from 40 to 25 kcy/sec—that is, by about 125 cy/sec from one wave to the next. Sound spectrographs showed that throughout each pulse the energy was spread over a band width of at least 5 kcy/sec, or 37 db above 1 cy. A listening system tuned to a single pass band narrower than this would simply exclude part of the signal. Spectrographs of

pulses emitted in the noise showed that, at 8 cm from the bat's mouth, the spectrum level of the outgoing sound was within ± 10 db of the level of noise in the same frequency band.

The echo levels included in Fig. 1 were calculated, by methods described elsewhere (1), on the assumption that echoes were not heard above the noise until the bat was 10 cm from the wires and that the emitted signal was at the highest level observed in the noise (about 80 db) rather than at the average level (65 db) observed in the quiet. It is unlikely that these bats had learned the position of the wires, because of the large number of wires and because, in the noise, the smaller-size wires were avoided at little better than the chance

level, although their positions should have been no more difficult to remember than those of the larger-size wires. If the wires were detected by listening not to echoes but to variations in the noise field itself, interference with sound emission should have had less effect in the noise than in the quiet. But application of ventilated paper muzzles similar to those used by Dijkgraaf (3) reduced obstacle avoidance to the chance level in both noise and quiet, with large obstacles and small. Only one or a few pulses could have been emitted while the *Plecotus* were within 10 cm of the wires, and at greater distances echoes would be still fainter. The 0.54-mm wire, which was dodged quite successfully by all five bats, returned echoes of 35 db, or 36 db below the noise in a 5-kcy/sec band, while the 0.35-mm wire, which bat No. 11 dodged rather well after being blinded, provided echoes 43 db below the level of the noise.

It seems conservative to conclude that these bats can hear echoes that are at least 35 db below the level of the noise and that this ability must involve selective recognition of some property of the echoes not shared by the random noise. The pulsed nature of the echoes might be one such property, but thermal noise switched on and off with a 50-percent duty cycle at rates up to 1000 per second was, if anything, less effective in jamming *Plecotus* than continuous noise. The large ears may render the hearing of this species highly directional, but wires were often dodged skillfully when they were directly (within $\pm 10^\circ$) in line with one of the loud-speakers. The frequency sweep within each pulse, or the time relations between emission of a pulse and arrival of echoes from objects at close range, may aid in this impressive auditory discrimination. In any event, a bat brain weighing less than 1 gram contains highly effective data-processing mechanisms which can act upon information contained in one or a few echoes having no more than 1/2000 of the noise energy simultaneously present in the same frequency band.

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References and Notes

1. D. R. Griffin, *Listening in the Dark* (Yale Univ. Press, New Haven, Conn., 1958).
2. These experiments were made possible by a contract between the Office of Naval Research (Biology Branch) and Harvard University. Reproduction in whole or in part for any purpose of the United States Government is authorized. An important part of the work was carried out at the Woods Hole Oceanographic Institution, where we were able to use a sound spectrograph through the kindness of J. B. Hersey. We are also grateful to the General Radio Company, Cambridge, Mass., for permission to analyze

tape recordings of the thermal noise with a harmonic analyzer, and to F. V. Hunt and S. S. Stevens of Harvard University and J. L. Stewart of the U.S. Naval Electronics Laboratory, San Diego Calif., for helpful discussions of these experiments.

3. S. Dijkgraaf, *Experientia* 2, 438 (1946).

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Effects of Methimazole on Thyroid and Live Weights of Cattle

Interest in the potential usage of different goitrogenic agents, especially thiouracil, in livestock and poultry production is manifest in the large number of investigations that have been made during the past 15 years, many of which are cited by Sykes *et al.* (1). Most investigators have studied the use of thiouracil in reducing basal metabolic rate in animals for purposes of either stimulating fattening in meat-producing animals or bringing about a more efficient over-all usage of the respective rations fed. Although some success has been achieved with thiouracil in reducing metabolic rate in animals (2), nevertheless other, unfavorable features have been noted in connection with its administration, such as its unpalatability and its tendency to slow rates of growth; hence, no general use of goitrogens in animal feeding has thus far been made. The objectives of the investigation described in this report were to determine the amount of a potent synthetic goitrogen, methimazole (1-methyl-2-mercaptoimidazole, or Tap-

azole) (3) necessary to bring about enlargement of the thyroid in cattle and to observe the influences of methimazole upon appetite, live-weight gains, and efficiency of feed utilization when it was fed to growing and fattening beef animals.

Thirty steers, weighing about 975 pounds each, were divided into six groups and full-fed a mixture of corn, hay, and protein supplement containing stilbestrol, a growth-promoting substance for beef cattle reported earlier (4). The rations were alike except for the amounts of methimazole added to the respective rations. Groups 1a and 1b received no methimazole, whereas groups 2, 3, 4, and 5 received rations that contained methimazole in the following percentages: 0.0017, 0.0035, 0.0052, and 0.0070, respectively. These levels corresponded to 200, 400, 600, and 800 mg per animal per day. The feeding experiment was carried out during the late fall and early winter season, during which the temperature was below freezing much of the time.

The results are presented in Table 1. Thyroid weights were rather variable within groups, but on the average they increased with each level of methimazole fed, the highest level producing thyroids approximately four times the size of those in the control cattle. The increased weights of the thyroids of the cattle in this study suggest that the levels of methimazole fed were sufficiently high to inhibit thyroxin secretion. The improvement noted in over-all feed utilization might be explained on the basis of a low-

ered thyroxin secretion and thus a lowered metabolic rate, whereby a higher percentage of the ration was converted into cattle live-weight gains. Live-weight gains were excellent in the cattle receiving methimazole, and in all cases these gains exceeded the gains made by the control animals. The maximum stimulation in gain by lots was 22 percent, and the average stimulation amounted to 11 percent. No depression in appetite accompanied the feeding of methimazole; rather, the cattle receiving the goitrogen consumed an average of 3 percent more feed than the control cattle. Over-all feed utilization was increased by the methimazole as much as 13 percent, with an average increase of 7 percent. The quality of meat produced by the inclusion of methimazole in the ration was indistinguishable from the quality of meat of the control cattle on the basis of federal grades and dressing percentages.

It was interesting to note that methimazole did not depress appetite, whereas thiouracil usually inhibits appetite and results in lowered rates of growth in almost all species of animals. This apparent discrepancy in the action of these two goitrogens is believed to be due to the unpalatableness of the thiouracil or to its greater toxicity at equivalent dosage levels. In earlier cattle experiments in this laboratory (5) it was impossible to feed sufficiently high levels of thiouracil to depress thyroid activity appreciably without at the same time decreasing feed consumption and rate of live-weight gain.

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Table 1. Results of adding methimazole to the ration of cattle in a 79-day experiment.

Item	Methimazole added				
	Lot 1 None	Lot 2 0.0017%	Lot 3 0.0035%	Lot 4 0.0052%	Lot 5 0.0070%
Av. initial wt. of cattle (lb)	976	977	981	976	985
Av. final wt. of cattle (lb)	1209	1245	1226	1258	1222
Av. daily gain (lb)	3.0 ± 0.1*	3.4 ± 0.2	3.1 ± 0.1	3.6 ± 0.1	3.1 ± 0.2
<i>Av. daily ration</i>					
Cracked corn (lb)	17.7	19.1	18.1	19.0	18.0
Alfalfa hay (lb)	6.0	6.0	6.0	6.0	6.0
Supplement (lb)	1.0	1.0	1.0	1.0	1.0
Total (lb)	24.7	26.1	25.1	26.0	25.0
Feed/100-lb gain (lb)	837	770	804	726	831
Dressing percentage	59.8	58.1	59.5	59.5	60.0
<i>Federal carcass grade</i>					
Choice	4	3	2	1	2
Good	6	2	3	4	3
Av. wt. of cattle thyroid (g)	29 ± 3	35 ± 5	65 ± 10	70 ± 8	123 ± 18

* Standard error of mean.

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References and Notes

1. J. F. Sykes *et al.*, *Natl. Acad. Sci.—Natl. Research Council Publ. No. 266* (1953), p. 1.
2. H. Singh and C. S. Shaffner, *Poultry Sci.* 29, 575 (1950).
3. This report is journal paper No. J-3330, Iowa Agricultural and Home Economics Experiment Station, Ames, Project No. 869, Acknowledgment is made of assistance by E. A. Kline in collecting thyroids and data at time of slaughter of the cattle. Methimazole was supplied by the Eli Lilly Co., Indianapolis, Ind.
4. W. Burroughs *et al.*, *Science* 120, 66 (1954).
5. W. Burroughs *et al.*, *Iowa Agr. Expt. Sta. Animal Husbandry Leaflet No. 218* (1957), p. 1; A. Raun, E. Cheng, W. Burroughs, *J. Animal Sci.* 16, 1062 (1957).

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Electron Microscopy of the Anaplasma Body: Ultrathin Sections of Bovine Erythrocytes

Anaplasmosis is an infectious disease of cattle. However, it has been recognized in another species (ovine) on one occasion in the United States (1). The acute or peracute form of the disease is