tioned reinforcers, this result is contrary to all theories of conditioned reinforcers.

Other studies (*4*, *9*) have shown that stimuli associated with food strengthen performance during extinction. In this experiment, however, these stimuli eased the animal's transfer to another food site. The main difference in procedure is that an alternative key was present in the box. It may be that signals hastened the bird's transfer because the other key was available. Alternatively, the whir of the motors and associated stimuli may not, in fact, be conditioned reinforcers. To investigate these possibilities I repeated the experiment with only one key available during each session.

There were six daily pairs of sessions; the order of the sessions with and without conditioned reinforcers and the key to be used were decided randomly. Sessions began with 25 food deliveries on the VR10 schedule, after which the key no longer produced food. Sessions ended when 60 seconds had elapsed without a single response, a criterion chosen because it never occurred in a normal nonextinction session but was judged to be not so severe as to extinguish responses at the start of the next session.

If only one key was available, the bird generally took longer to reach the criterion of extinction when its pecks produced stimuli that had been associated with food than when they produced nothing (Fig. 1).

If an alternative feeding site is available, signals for food allow the dove to abandon the no-longer-profitable site more quickly. When no alternative site is present, the same signals keep the dove working on the only available site, despite its unprofitability. This being the case, how may one account for the more rapid switch seen in the presence of signals for food when an alternative key is available?

Foraging consists of a chain of responses, each leading to the next until the final act of consuming the food (*10*). Responses early in the chain are performed more often than responses late in the chain and are rewarded correspondingly less often. Estimates of the profitability of a patch are updated largely with the outcome of responses very late in the chain, rather than with every act in the chain. When no food is obtained because only early elements in the chain are completed, the profitability estimate drifts slowly down until the patch no longer fulfills the animal's expectations and is abandoned (*11*). But when the whole chain save the consumatory act is completed, the estimate of profitability is revised every time the consumatory act is reached but not performed. If the dove averages profitability over a short period of feeding, under the latter conditions its estimate of patch profitability will decline sharply.

Krebs *et al.* (*8*) have shown that the great tit (*Parus major*) efficiently gathers information about resource profitability. This report extends their findings to encompass a change in profitability during the feeding session. The signals that accompany food provide usable information (*2*) more rapidly than the nonarrival of both signals and food. They also interrupt the repeated pecking of the key and so provide both the information and opportunities needed for the bird to transfer its attention to the other key. In this way, signals for food during extinction allow the doves to obtain more food than simple extinction without signals (*12*).

Much recent work on foraging has stressed the qualitatively good fit between observed behavior and models of optimal behavior (*7*, *13*). Deviations from predicted results are usually seen in terms of the deficiencies of simple foraging models (*8*, *14*), rather than as reflections of the mathematical complexities of even simple models. Real psychological mechanisms must underlie real foraging behavior, but in very few cases (*15*) has understanding gone beyond the simple fact of near-optimal foraging to the mechanisms that govern the acquisition and use of information. I have demonstrated that one psychological mechanism, that of the conditioned reinforcer, may be used by the animal to aid its decision-making in a way that is counterintuitive; almost obtaining food is as important as actually obtaining it because both provide more information than does obtaining nothing at all.

JEREMY JON CHERFAS*
Department of Psychology,
University of Toronto,
Toronto, Ontario, Canada M5S 1A1

References and Notes

1. R. C. Bolles, *Theory of Motivation* (Harper & Row, New York, 1967); N. J. Mackintosh, *The Psychology of Animal Learning* (Academic Press, London, 1974).
2. E. Fantino, in *Handbook of Operant Behavior*, W. K. Honig and J. E. R. Staddon, Eds. (Prentice-Hall, Englewood Cliffs, N.J., 1977), p. 313.
3. J. M. Pearce and G. Hall [*J. Exp. Psychol. Anim. Behav. Process.* **4**, 356 (1978)] also reported decreased responding in the presence of conditioned reinforcers, but attributed it to overshadowing of the response by the conditioned reinforcers. Their experiment 4 shows the expected increase in responding with the Egger and Miller (*4*) paradigm.
4. M. D. Egger and N. E. Miller, *J. Exp. Psychol.* **64**, 97 (1962).
5. J. J. Cherfas (in preparation) gives details of the apparatus and procedures and results of the two-key experiments.
6. See J. A. Hogan and P. Rozin [*J. Exp. Anal. Behav.* **4**, 81 (1961)] and S. J. Shettleworth [*Anim. Learn. Behav.* **6**, 352 (1978)] for details of the wheels used to deliver food.
7. J. R. Krebs, in *Behavioural Ecology*, J. R. Krebs and N. B. Davies, Eds. (Blackwell, Oxford, 1978), p. 23.
8. ———, A. Kacelnik, P. Taylor, *Nature* (*London*) **275**, 27 (1978).
9. B. R. Bugelski, *J. Comp. Psychol.* **26**, 121 (1938); W. H. Melching, *J. Comp. Physiol. Psychol.* **47**, 370 (1954).
10. G. Collier, L. W. Kaufman, R. Kanarek, J. Fagen, *Carnivore* **1**, 34 (1978).
11. J. R. Krebs, J. Ryan, E. L. Charnov, *Anim. Behav.* **22**, 953 (1974).
12. Total pecks delivered to both keys for each food crumb actually obtained in choice trials were calculated. Birds pecked significantly less when empty food cups appeared during extinction of the VR10 key. In other words,the total feeding session was more profitable, in terms of pecks expended for each food item gained, when empty food cups provided the doves with information that the patch was exhausted.

Median pecks per food delivery in choice trials; N.S., not significant.

Bird	Condition		Statistics*		
	Empty cups	No cups	*T*	*N*	*P*
1	24.3	42.1	2	7	<.05
2	22.0	28.0	0	6	<.05
3	25.0	32.8	3	7	N.S.
4	24.0	30.6	2	7	<.05

*Wilcoxon matched-pairs signed-ranks test.

13. A. C. Kamil, *J. Comp. Physiol. Psychol.* **92**, 388 (1978); G. H. Pyke, H. R. Pulliam, E. L. Charnov, *Q. Rev. Biol.* **52**, 137 (1977).
14. M. L. Cody, *Theor. Popul. Biol.* **2**, 142 (1971); *Science* **183**, 1156 (1974); G. H. Pyke, *Anim. Behav.* **26**, 241 (1978).
15. S. E. G. Lea, *Anim. Behav.* **27**, 875 (1979); D. S. Olton, in *Cognitive Processes in Animal Behavior*, S. H. Hulse, H. Fowler, W. K. Honig, Eds. (Erlbaum, Hillsdale, N.J., 1978), p. 341.
16. I thank J. A. Hogan for financial support. A. Bouzas and K. Hollis criticized and encouraged.
* Present address: Department of Zoology, University of Oxford, Oxford, England OX1 3PS.
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Protein Secretion by the Pancreas

Isenman and Rothman report that ligation of the exocrine duct does not increase the concentration of amylase in pancreatic juice (*1*). In spite of studies demonstrating increased permeability of the entire network of exocrine ducts after the main duct is obstructed, they propose that their finding supports the view that diffusion (as opposed to exocytosis) is the chief mechanism directing secretion of protein into pancreatic juice. However, the entire exocrine duct system is permeable to large molecules even at low pressures (*2*), and excess fluid containing large amounts of pancreatic enzyme activity begins to leak from the confines of this system and, within 10 to 30 minutes of ligation of the main duct,

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to accumulate in interstitial fluid and in lymph (*3*, *4*). The finding reported by Isenman and Rothman was therefore, to a degree, predictable.

That the rate of protein secretion is determined by the rate at which secretion granules fuse with plasma membrane seems likely. Electron microscopic evidence indicates that ligation of the pancreatic duct has a direct and rapid effect on the secretory process itself (*5*). Thus the rough endoplasmic reticulum of almost all pancreatic acinar cells undergoes swelling and vesiculation within 1 hour of duct ligation. Some of these cells develop swelling of zymogen granules, and various mitochondrial abnormalities can also be observed.

In a note added in proof, Isenman and Rothman state that the concentration of amylase in stimulated pancreatic juice remains unchanged after ouabain-induced or hyponatremia-induced reduction in volume of pancreatic juice. This observation is in direct contrast to the results of an earlier study in which Diamox (2 acetylamino-1,3,4-thiadiazole-5-sulfonamide), an inhibitor of carbonic anhydrase, was used to reduce flow. Under these circumstances, the volume of pancreatic juice fell to half of control values while the concentration of amylase in this fluid increased almost 70 percent (*6*).

Isenman and Rothman's suggestion that a "diffusion-like process," rather than exocytosis, accounts for the secretion of enzyme molecules into pancreatic juice implies the presence of information which is, in fact, still lacking.

ALLAN E. DUMONT
Department of Surgery, New York University School of Medicine, New York 10016

References

1. L. D. Isenman and S. S. Rothman, *Science* **204**, 1212 (1979).
2. S. Godart, *Bibl. Anat.* **7**, 410 (1965).
3. A. E. Dumont, H. Doubilet, J. H. Mulholland, *Ann. Surg.* **152**, 403 (1960).
4. A. E. Dumont and A. B. Martelli, *ibid.* **168**, 302 (1968).
5. J. D. Zeligs, A. Janoff, A. E. Dumont, *Am. J. Pathol.* **80**, 203 (1975).
6. D. A. Dreiling, H. D. Janowitz, M. Halperm, *Gastroenterology* **29**, 262 (1955).

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The purpose of our discussion (*1*) was to propose a diffusion-based hypothesis as the simplest explanation for the movement of molecules across thin biological membranes; it is a hypothesis that is independent of popular, but not well-documented, beliefs about such processes.

We think that Dumont's statement that "the entire exocrine duct system is permeable to large molecules even at low pressures" is not justified by the evidence he offers in its support, which is that (i) the forced retrograde injection of two dyes resulted in the appearance of some dye in interstitial space (*2*, reference 2), and (ii) "duct ligation" led to an increase in the concentration of digestive enzyme in lymph and to some apparent tissue edema (*2*, references 3 and 4). In the cited articles, experiments are not described that directly measure the permeability of the duct system to digestive enzyme. They also do not contain evidence for the existence of paracellular shunts through which digestive enzymes can pass freely, and which reversibly open and close in response to small changes in transductal pressure. Although stated as fact, Dumont's assertions are hypotheses put forth to explain the cited observations, which, however, may be due to other causes. If he believes that enzyme found in lymph must come from duct contents because there is no other possible source, then we would point out that the basolateral membrane of the acinar cell is permeable to digestive enzyme (*3*). In the case of duct blockage, assuming continued protein synthesis, the equilibrium hypothesis predicts the increased enzyme concentration in interstitial fluid that he reports. Thus, the question is not whether duct ligation produces such an increase, but whether the increase is due to the movement of enzyme across the duct or out of the acinar cell itself.

We did consider the possibility that Dumont raises. If pressure caused reduced enzyme output, then enzyme output should remain unchanged when flow is decreased in ways that do not increase intraductal pressure. As we pointed out in our report, when fluid flow was reduced in two ways that do not increase intraductal pressure, our results were essentially the same; that is, enzyme output was inhibited to approximately the same quantitative extent [see (*4*) for a discussion of these and other similar experiments]. Thus, flow appears to be the independent variable that leads to a dependent reduction in enzyme output (presumably via a concentration-sensitive mechanism for digestive enzyme secretion) as we had proposed. This view is in fact reinforced by the experiments that Dumont cites (*2*, reference 6) in which another metabolic method used to reduce flow also led to a reduction in enzyme output—the increased concentration of enzyme that Dumont points to notwithstanding. This increase in concentration would also be expected if enzyme were not distributed across the secretory membrane at its equilibrium or maximum steady-state value prior to flow restriction.

As for pathological changes with duct ligation in situ, Dumont does not use the term in its usual sense [preventing outflow of fluid from the intestinal end of the main collecting duct or ducts], but rather to describe the passage of a ligature "around the entire pancreas . . . tied tightly midway long (sic) the pancreatic tail," apparently encircling blood vessels, nerves, ducts, and even acinar tissue in its noose (*2*, reference 5). In our in vitro studies the functional characteristics of the biological preparation were unaltered by 90 minutes of true duct blockage.

Dumont further says that it "seems likely" that secretion occurs by exocytosis, although he cites no experimental evidence. Given the broad acceptance of this hypothesis, there is little primary experimental evidence that exocytosis occurs at all in the pancreas, or accounts for the secretion of digestive enzyme under normal circumstances.

STEPHEN S. ROTHMAN
LOIS D. ISENMAN
JENNY J. L. HO
Department of Physiology, University of California, San Francisco, San Francisco 94143

References

1. L. D. Isenman and S. S. Rothman, *Science* **204**, 1212 (1979).
2. A. E. Dumont, *ibid.*, **209**, 1553 (1980).
3. L. D. Isenman and S. S. Rothman, *Proc. Natl. Acad. Sci. U.S.A.* **74**, 4068 (1977).
4. S. S. Rothman, *Am. J. Physiol.* **238**, G391 (1980).

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