gests, in the absence of other explanations, the possibility of a cellular mechanism for the secretion of inert material.

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References and Notes

1. G. Hüfner, *Arch. Anat. u. Physiol. Physiol. Ab.* 54 (1892).
2. P. F. Scholander *et al., Biol. Bull.* 101, 178 (1951).
3. R. L. Saunders, *Can. J. Zool.* 31, 547 (1953).
4. P. F. Scholander and I. van Dam, *Biol. Bull.* 104, 75 (1953).
5. T. Schloesing and J. Richard, *Compt. Rend.* 122, 615 (1896); P. F. Scholander, *Biol. Bull.* 107, 260 (1954).
6. Contribution No. 816 from the Woods Hole Oceanographic Institution. This investigation was supported by a grant from the National Science Foundation. We are indebted to Peter I. Tack of Michigan State University for help in arrangements to get the whitefish and for determining the species. We were able to secure samples from live fishes as they were hauled aboard the boat through the courtesy of E. L. Hill of Grand Haven, Mich.
7. P. F. Scholander, *J. Biol. Chem.* 167, 235 (1947).
8. F. P. Chinard and T. Enns, *Am. J. Physiol.* 178, 203 (1954).
9. H. Koch, *Rev. questions sci.* (*Belg. France*) 26, 385 (1934).
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15 July 1955

New Scheme for Performance of Osmotic Work by Membranes

There is now a wealth of literature dealing with the fact that a variety of cell membranes are able to remove inorganic salts and other neutral organic molecules from dilute solutions and transport them through the membrane into more concentrated solutions (*1*). This "active transport" of molecules against a concentration gradient requires energy that is thought to be provided by the metabolic activity in the neighborhood of the membrane. Several proposals have been made regarding the mechanism of active transport (*2*), all of which are possible, but perhaps none of which is the simplest mechanism that could be described.

It is the purpose of this communication to suggest that in the simplest case, active transport can be performed by a single enzyme. This enzyme, which acts as a "carrier" of the transported species, is confined between two closely spaced semipermeable membranes and is engaged in the conversion of a substrate S into products P. Let us examine the state of affairs when a substrate diffuses into the enzyme "sandwich" from the left-hand side. Inside the membrane, the enzyme-substrate complex ES is formed and diffuses to the right, driven by its own concentration gradient. If the ES complex binds another ion or molecule, this species will be transported to the right as a "passenger." On the way over to the right side of the membrane, the ES complex is broken down, forming the products and the free enzyme E which we suppose for the moment can no longer bind the "passenger species" in question. Thus, the passenger species is continually being removed from the left and deposited on the right in the membrane. In the steady state, the back diffusion of the free passenger species is just balanced by the flux of ES (with bound passenger molecules) to the right.

If the kinetics can be adequately described by the Michaelis-Menton expression, we have (*3*):

$$S + E \underset{k_2}{\overset{k_1}{\rightleftarrows}} (ES) \xrightarrow{k_3} E + P$$

where S, E, and ES denote the molar concentration of the species. When a steady state has been attained, we have the following equations for the conservation of mass:

$$D_S(d^2S/dx^2) - k_1SE + k_2(ES) = 0 \quad (1)$$

$$D_{ES}[d^2(ES)/dx^2] + k_1SE - k_2(ES) - k_3(ES) = 0 \quad (2)$$

$$D_E(d^2E/dx^2) - k_1SE + k_2(ES) + k_3(ES) = 0 \quad (3)$$

where D_S, D_E and D_{ES} represent the diffusion constants of the species.

Although the following assumptions are probably not necessary for the operation of the transporting membrane, we make them in order to solve this set of equations easily: (i) k_2 is small and can be neglected; (ii) the concentration of free enzyme inside the membrane is not

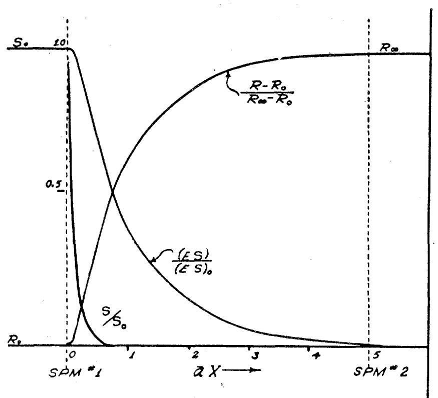

Fig. 1. Relative concentrations of the substrate S, the enzyme-substrate complex ES, and the transported passenger species R between two semipermeable membranes, *SPM#1* and *SPM#2*. These have been calculated from equations 4, 5, and 7, respectively, assuming $c/a = 10$.

appreciably affected by reaction with the substrate. This is comparable to the assumption of negligible atmosphere depletion in flame kinetics (*3*), a problem that has recently been solved by Smith (*4*). The solution to Eq. 1 becomes

$$S = S_0\exp(-cx)\,;\; c^2 = k_1E/D_S \quad (4)$$

Assuming that all the substrate that enters the membrane is converted to P, we have a solution to Eq. 2:

$$(ES) = D_Sc^2S_0/D_{ES}(c^2 - a^2) \cdot [c/a \cdot \exp(-ax) - \exp(-cx)]$$

$$(ES)_0 = D_Sc^2S_0/D_{ES}a(a + c)\,;\quad a^2 = k_3/D_{ES} \quad (5)$$

Referring to Fig. 1, we see that for all values of x there will be a flux of ES to the right. Likewise, there will be a continual return flux (from right to left) of the free enzyme E, although this is not evident under the assumption that E is constant.

In order that active transport occur, the passenger species, or those molecules that are transported against their gradient, must be bound more (or less) strongly to ES than they are to E. In the case where 1 mole of ES binds only 1 mole of a neutral passenger species R, we have:

$$D_R(d^2R/dx^2) + (KR/1 + KR) \cdot D_{ES}(d^2(ES)/dx^2) = 0 \quad (6)$$

where K is the equilibrium constant for the binding reaction. Solving Eq. 6 for the case of complete binding, $KR/(1 + KR) \cong 1$, we have

$$R - R_0 = D_{ES}/D_R \cdot [(ES)_0 - (ES)] \quad (7)$$

The maximal concentration achieved by the membrane would be

$$R_\infty - R_0 = D_{ES}/D_R \cdot (ES)_0$$

One can imagine many ways in which the binding characteristics of the enzyme-substrate complex might be different from that of the free enzyme. For instance, a slight change in the $p\mathrm{K_a}$ of titratable groups that are in the neutral pH region will cause a change in the gross charge of the enzyme. Since electroneutrality must prevail in the immediate neighborhood of the protein, this means that a different number of counter ions will accompany the enzyme-substrate complex than accompany the free enzyme. Such pK shifts have been observed (*5*).

The interpretation of active transport along these lines is attractive for the following reasons. (i) It is in terms of enzyme reactions that are better understood and are encountered elsewhere in biological systems. (ii) It avoids postulating extreme differences in oxidation-reduction potentials, differences in voltage, differences in catalytic surfaces, and so forth.

(iii) The coupling of the metabolic energy supply is explicit (the conversion of S to P). (iv) The specificity of ion transport can be interpreted in terms of the specific binding properties of the enzyme and/or enzyme-substrate complex.

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References and Notes

1. H. T. Ussing, in *Ion Transport across Membranes*, H. T. Clarke, Ed. (Academic Press, New York, 1954); W. Rummel, *Naturwissenschaften* 10, 277 (1953); T. Rosenberg and W. Wilbrandt, *Intern. Rev. Cytol.* 1, 65 (1952); J. F. Sutcliffe, *ibid.* 2, 179 (1952).
2. E. J. Conway, *Intern. Rev. Cytol.* 2, 419 (1952); R. J. Goldacre, *ibid.* 1, 135 (1952); J. Frank and J. E. Mayer, *Arch. Biochem.* 14, 297 (1947).
3. M. Polanyi, *Atomic Reactions* (William and Northgate, London, 1932); D. Garvin and G. B. Kistiakowsky, *J. Chem. Phys.* 20, 105 (1953).
4. F. T. Smith, *J. Chem. Phys.* 22, 1605 (1954).
5. M. Dixon, *Biochem. J.* 55, 161 (1953).

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8 August 1955

Rodenticidal Effect on Pine Mice of Endrin Used as a Ground Spray

For many years, poison baits have been the basis for control of mice in orchards. World War II stimulated research involving bioassays on toxicity of hundreds of potential bait type rodenticides (*1*). In orchard practice, zinc phosphide, with all its limitations, is still rated above the newer materials. However, the lack of effectiveness of zinc phosphide led Kalmbach (*2*) to anticipate its replacement by other more suitable rodenticides.

Experience has shown that the sublethal acceptance of poisonous bait by numerous mice, coupled with the high reproductive capacity of these animals, places the dependability of poisoned baits for orchard mouse control in great doubt. One large Virginia orchardist loses about 600 to 700 apple trees annually, even though he uses poisoned baits close to maximum advantage. Since numerous reasons exist for such failures (*3*), the need for more effective mouse control is evident.

Since 1949, a number of potential ground spray rodenticides have been tested in orchards of Virginia, including endrin, the coined name for an insecticide. Endrin has been 100-percent effective in each of the past 3 years as a pine mouse control.

In the experiments in apple orchards reported here, the chemicals were applied as a ground spray to heavily mouse-infested plots that contained 42 trees each. All replicated plots were six rows wide and seven tree spaces long, or about 1.2 acres per plot. Since the range of pine mouse colonies is reported to be about ¼ acre (*4*), test plots nearly 5 times the maximum colony area were selected. The six center trees in each such treated plot appeared to be well protected from mouse invasion by the sprayed strips of orchard 70 or more feet wide and occupied by two surrounding "guard rows" of trees. A uniform ground spray was applied to a continuous straight strip 11 feet wide on each side of each row of trees. Preferably the treated strip reached to the trunk. For large trees, only 11 feet inward from the limb ends could be covered. Because pine mouse activity was concentrated in the tree rows (*3*), alleys between rows were not sprayed. The spray coverage was usually about 65 percent of the total orchard floor.

Table 1 indicates that there was a rapid decline in mouse activity to near final levels in 6 days or less during 1954. For 1953, a period of 3 to 6 weeks was required for a similar action. Apparently the difference in response is associated with moisture differentials in soil and cover. In 1953, the spraying was done under extremely dry conditions, which continued for some time. In 1954, at the time of spraying and subsequently, the orchard floor litter was moist, and the surface soil moisture was near field capacity.

As is the case with numerous other recent organic pesticides except DDT, the effect of endrin ground sprays on human beings and wildlife has not been well evaluated. The evidence that exists indicates that the orchard use of endrin as described here causes little or no evident deleterious effect on men or game animals. In the fall of 1954, one orchardist with extensive fruit plantings sprayed with a gun about 1000 acres of apple orchard. Members of the spray crews felt no ill effects. Neither was there any apparent reduction in numbers of quail or deer. None of the pets that had free range of the orchard died. A dog that closely followed one workman during the spraying was not visibly injured. In another 6-acre orchard area that was treated with endrin, active rabbits were observed during the period when mouse activity declined to zero. No increased vulture activity following endrin application was observed.

Table 1. Decline in pine mouse activity following endrin ground sprays in apple orchards. Mouse activity before the spraying was considered to be 100 percent.

Chemical	Endrin per 42-tree plot (lb)	Post-treatment mouse activity (%)		
		After 3–7 days	After 21–25 days	After 43–51 days
Plots sprayed 26–29 Nov. 1954				
Controls		67	83	58
(3 plots)		55	73	73
		90	91	91
Emulsifiable	2.50	0	9	0
endrin	2.50	0	10	0
(3 plots)	2.50	0	0	0
Emulsifiable	3.25	0	8	0
endrin	3.25	0	0	0
(3 plots)	3.25	8	8	0
Wettable				
endrin	2.50	0	0	0
(2 plots)	2.50	27	0	0
Plots sprayed 13–18 Nov. 1953				
Emulsifiable	1.5		30	40
endrin	1.5		0	30
(4 plots)	1.5		33	42
	1.5		8	33
Emulsifiable	2.5		25	0
endrin	2.5		0	0
(4 plots)	2.5		25	0
	2.5		33	0

An indication of the relative safety in the use of endrin is its acceptance for the control of insects on food plants. A label has been issued by the U.S. Department of Agriculture for the use of endrin on cabbage plants. This material was accepted earlier for tobacco insect control. As presently used against rodents, endrin is not applied either to the tree or to its fruits. Moreover, the treatments have been fully effective only in the dormant season when surface contamination of fruits could not occur.

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References and Notes

1. E. R. Kalmbach, Natl. Research Council Insect Control Committee Rept. No. 172 (1945).
2. ———, in *U.S. Department of Agriculture Yearbook 1943–1947* (Government Printing Office, Washington, D.C., 1947), pp. 890–896.
3. F. Horsfall, Jr., *Virginia Agr. Expt. Sta. Bull. 465* (1953).
4. W. H. Burt, *Misc. Publ. Museum Zool. Univ. Mich. No. 45* (1940).

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Citation Indexes for Science

Eugene Garfield's article, "Citation indexes for science" [*Science* 122, 108 (1955)], is interesting beyond doubt. If we had in our library a citation index such as he proposes, I should use it to advantage.

Amid today's overwhelming difficulties in scientific communication, however, this index would solve too few problems to justify its surely great cost at this time.

Even though all the cited references in a given article were indexed, those ideas and key words not covered by the cited references would remain excluded, according to Garfield's system. The most