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Insect Olfaction: Deciphering System for Chemical Messages

Receptor cells beneath a porous cuticle are highly sensitive and specific to odor molecules.

D. Schneider

The term stimuli, as applied to living organisms, may be thought of as those influences that originate in the interior or exterior environment which elicit a biological reaction. Chemical stimuli, broadly considered, are those chemical influences to which at least one organism reacts. If we confine our consideration to animals, we find that there are two fundamentally different chemosensory mechanisms.

General chemosensitivity is a slow response which usually extends to the body surface and some inner organs of the body after exposure to a relatively high concentration of harmful chemicals. In most cases, this system is protective and serves to counteract the destructive effects of irritating substances.

Receptor sensitivity is a faster response. In this case the receptor cells or their dendritic endings are excited by a relatively narrow spectrum of adequate compounds to which the cell is specific. As a rule, these cells are moderately, or in some cases extremely, sensitive. Out of the receptor response, a nervous message is formed which travels by way of the afferent nerve fibers to the central nervous system. As in all receptor systems, basically similar receptor systems are found in related groups of organisms; however, some striking similarities have developed in nonrelated species as the result of functional adaptations to the environment. Such a receptor system comprises and limits the chemical world in which an organism lives. These worlds differ for different organisms owing to qualitative and quantitative differences in their chemosensory systems.

Taste and Olfaction

The transfer of chemical information requires a chemical source, a medium of transfer (air or water), and a receptor. We here distinguish olfaction from taste for man and the other vertebrates (*1*). Olfactory stimuli elicit a response in the nasal receptors; taste stimuli elicit response in the taste cells of the mouth cavity and, as in some fish and amphibia, also in the moist skin of the body surface.

The transfer medium of the taste stimulus is always water. The qualitative range of stimuli to which a taste cell responds is narrow, and the number of taste qualities is small. In man we recognize four tastes: sweet, sour, bitter, and salty. In the lower vertebrates, the number of different taste qualities may be greater.

The qualitative range of odor stimuli in most organisms is very great. No satisfactory psychophysical or physiological system of classifying odor qualities has been developed. The classical question here is how the sense of smell differentiates among a very large number of odorants (*2*).

Are there in the chemoreceptor systems of invertebrates modalities analogous to those in the olfactory and taste systems of vertebrates? Yes, at least in insects. Behavior tests associated with the localizations of gross anatomical features have suggested the presence of such capacities. Local electrophysiological recordings from the sense organs of insects revealed that the analogy with the vertebrate system is rather close. Taste stimuli in insects are waterborne compounds of a limited range of qualities, some of which are the same as the taste stimulants found in vertebrates. Olfactory stimuli in insects are either air- or waterborne compounds, often very different from one another chemically. As in the vertebrate, taste and olfactory receptors in the insect are anatomically distinct. Taste organs consist of innervated cuticular bristles, hairs, or pegs with an open tip; olfactory organs are of four types as described below. In order to elicit a reaction, the taste cells of insects require stimulating molecules in much higher concentration than do odor receptors.

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Insect Olfaction

Insects represent good subjects for the study of the transfer of olfactory sense information in general and highly specialized communication by means of species- or group-specific chemical releasers, pheromones in particular (*3*). Insects respond to the odors of their surroundings and are especially sensitive to biologically meaningful chemical signals, such as food, prey, and a mate. The system of pheromones is highly developed among the social insects. The life of colonies of ants, bees, and termites is to a large extent regulated by chemical signs such as the scent of the trail, assembly, alarm, avoidance, and attraction (*4*).

The world of specific odors is not easily accessible to the investigator, because he can neither detect all of them nor can he immediately understand their meaning. Nonsocial insects have fewer pheromones; however, most of them seem to have at least sex-attracting substances produced by one or both sexes.

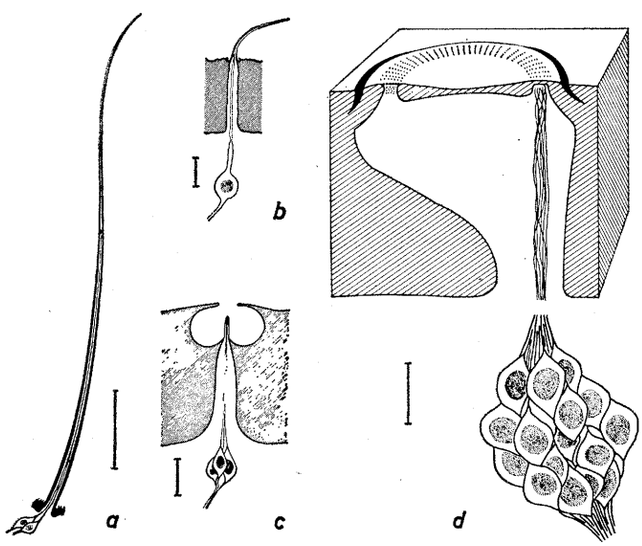
Insects appear to be well suited to research in the field of odor reception for a number of reasons. They are a model system with receptors that are readily accessible and morphologically well understood. Finally, insects possess many specialized food or pheromone receptors with cells of identical reactivity and extreme sensitivity that are ideally suited to an investigation of the chemoreceptor mechanism or, in other words, to a study of the question: What causes a substance to smell? This question apparently cannot be answered by psychophysical or behavioral methods. We need information on the odor spectrum of individual receptor cells in order to understand the basis of chemoreception. Odor discrimination is the next problem which might be attacked by a comparison of primary responses with the reaction of secondary integrative nerve elements. Such an approach is difficult. None of the theories of olfaction proposed thus far is more than a sometimes intelligent, speculative game (*2*). The history of our advanced understanding of vision should teach us that the combined efforts of investigators in biochemistry, biophysics, neurophysiology, and psychophysics are necessary for our understanding of the mechanism of olfaction.

Receptor Structure

External sense organs of insects are called sensilla. A sensillum is a specialized piece of cuticle with a minimum of three cells. Two of the cells are always formative, secreting the cuticle of this area, for example, a hair and its socket. The third cell is a sensory neuron or primary receptor cell. All these cells belong to the epidermis, having descended from one mother cell by differential cell division (*5*). Each olfactory receptor cell sends its neurite (axon) (0.1 to 0.2 μ in diameter) directly to that part of the brain which responds to olfactory stimulation (deutocerebrum).

Among the many differently shaped cuticular parts of the antennal sense organs of insects, we found, during localized electrophysiological recordings, four morphological types of olfactory organs (Fig. 1) (*6*): (i) sensilla trichodea, long, thick-walled hairs or pegs found, for example, in moths; (ii) sensilla basiconica, shorter, thin-walled hairs or pegs found in many insects; (iii) sensilla placodea, plate organs found in the bee and other Hymenoptera; (iv) sensilla coeloconica, pit pegs found in Lepidoptera, Hymenoptera, and many other orders of insects. Sensilla of types (i), (ii), and (iv) may have between one and several receptor cells; sensilla of type (iii) have between 10 and 30 cells in the bee.

The common feature of sensilla of types (i), (ii), and (iii) is a pore-tubule system which connects the outside medium with the hair lumen and the receptor dendrite (*7*). Sensilla



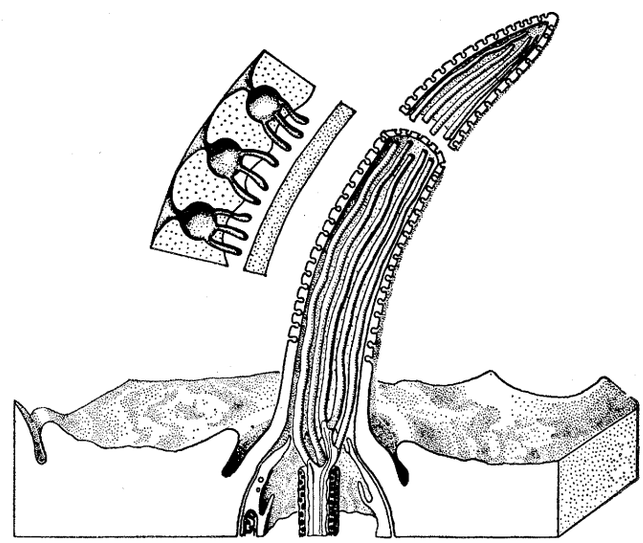


Fig. 1 (left). Examples of the four types of sensilla involved in insect olfaction: *a*. sensillum trichodeum (giant silkmoth, *Antheraea pernyi*); *b*, sensillum basiconicum (carrion beetle, *Necrophorus vespillio*); *c*, sensillum coeloconicum (migratory locust, *Locusta migratoria*); *d*, sensillum placodeum (honeybee, *Apis mellifica*). A sensillum is by definition a piece of the cuticle with formative and receptor cells. Only receptor cells are shown here. The distal cell endings (dendrites) either reach into the hair (*a–c*) or into a furrow of the cuticle plate (*d*). The scale indicates 50 μ in *a* and 5 μ in *b*, *c*, and *d*. Smaller details (for example, pores, dendrites, axons, and thin cuticular parts) are not drawn to scale. [From (*6*)] Fig. 2 (right). Fine structure of a thin-walled olfactory hair (sensillum basiconicum) of a carrion beetle *Necrophorus*. The cuticle of the hair is penetrated by many pores. This pore system is shown enlarged in the inset. Each pore is continuous with cuticular tubules reaching to the neighborhood of the branched dendrites. The dendrites are bathed by a fluid. The pore-tubule system is open to the outside. Hair diameter is 1 μ; tubule width is 100 angstroms. [Courtesy of Dr. K. D. Ernst]

coeloconica are differently constructed and not yet fully understood (*8*). The sensilla coeloconica, which will probably comprise several morphological subtypes, have receptor cells sensitive to either odor (including CO_2), or temperature, or humidity, or a combination of these. It follows from this that receptor cells which serve different sensory modalities may be attached to the same cuticular apparatus. But also the odor receptors, which are united in a given sensillum, frequently do not respond to identical odor spectra and thus serve different sensory qualities.

The pore-tubule system is shown schematically in Fig. 2. The outer part of the cuticle is penetrated by a pore which may open to a spherical "kettle." From this point several tubules penetrate the inner parts of the cuticle and reach into the hair lumen nearly as far as the cell membrane of the dendrite. These tubules are part of the cuticle and not, as suggested by several authors (*9*), neurofilaments or outgrowths of the dendrite which were thought to extend from the surface of the receptor cell to the outer medium. The tubules are clearly part of the cuticle, because they are fully present before the dendrite invades the hair lumen during morphogenesis. Furthermore, these tubules may have an outer diameter of only 100 angstroms and a wall thickness of 30 angstroms, which does not correspond to a tubular, cellular outgrowth with a unit-cell membrane of standard dimension. The innermost end of the cuticular tubules is clogged by material which looks different from that of the tubular wall.

The pore-tubule system is open to the outside in a basiconic sensillum; electron micrographs of sensilla bathed in oxidized hemolymph of the insect or colloidal silver (Protargol) indicate that these materials penetrate to the inner part of the tubule (Fig. 3) (*10*). This canal system presumably leads the odor molecules from the outside to the fluid-filled hair lumen and eventually to the dendritic membrane. Should this interpretation be correct, it would constitute another analogy to the nasal mucosa of vertebrates where odor particles must migrate through the mucus in order to reach the olfactory hair (*6, 10*).

Olfactory cells of insects, and perhaps all receptor cells of insects, have a ciliary body (*6, 9, 10*). The outermost part of the dendrite or the bundle of dendrites of the odor receptor contains only neurotubules and small vesicles but lacks all other normal cell organelles. The inner dendrite, proximal to the ciliary apparatus, has the usual cell inventory of membrane systems.

The fluid bathing the distal dendrite may be of great importance for the receptor process in a manner analogous to the nasal mucus of the vertebrate (*11*). This fluid, which has been called sensillum liquor (*10*), is probably mainly the secretory product of the formative cells.

The olfactory sensilla of insects, as described here, are located primarily on the antennae or feelers (*12*). Antennae have quite varied shapes. They are sometimes very short with only a few sense organs, as in some larvae. In other cases they are threadlike and elongated as in the cockroach, shorter but densely packed with sensilla as in bee, or even leaf-shaped with a feathery structure as in many moths. We found on the antenna not only olfactory organs but also receptors for taste, temperature, humidity, and mechanical stimulation. However, the odor receptors make up the bulk of the sense organs on the antennae. The branched part of the giant antenna of the male polyphemus moth (*Telea polyphemus*) bears more than 60,000 sensilla with 150,000 receptor cells (*13*). Approximately 60 to 70 percent of these cells are specialized receptors for the sex-attractant of the female, 20 percent respond to other odorants, and the rest serve other sensory modalities (*14*). The much less highly developed an-

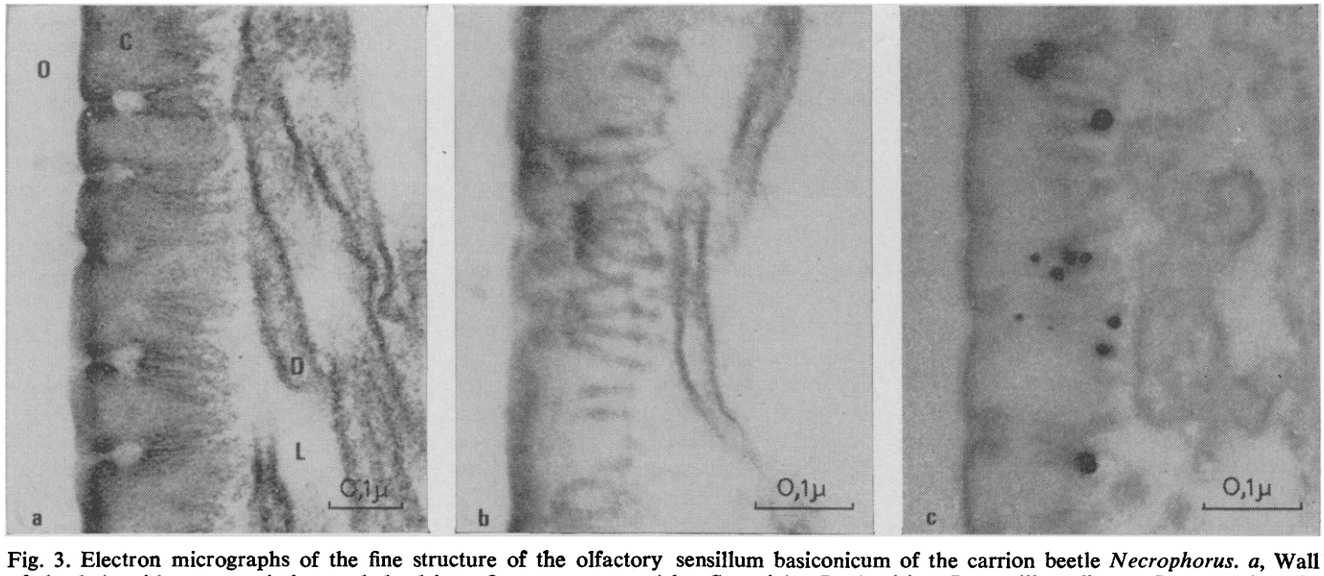


Fig. 3. Electron micrographs of the fine structure of the olfactory sensillum basiconicum of the carrion beetle *Necrophorus*. *a*, Wall of the hair with pores, tubules, and dendrites. *O* represents outside; *C*, cuticle; *D*, dendrite; *L*, sensillum liquor. In preparing the electron micrographs, we used OsO_4-fixation; the specimens were stained with lead citrate and uranyl acetate; specimens were imbedded in methacrylate. *b*, Same position as in *a*; the whole antenna, before fixation, was bathed in oxidized hemolymph of the beetle, which penetrated into the pores and tubules. Fixation and staining were the same as in *a*. Specimens were imbedded in Durcupan-ACM. *c*, Same position as in *a*. The whole antenna, before fixation, was bathed in Protargol solution (colloidal silver with minimum grain size of 50 angstroms). The silver is found inside the pores and tubules which are thus shown to be open to the outside. Some silver grains have assembled to form larger pellets in the tubules. Fixed and imbedded as in *b*, no staining. [Courtesy of Dr. K. D. Ernst]

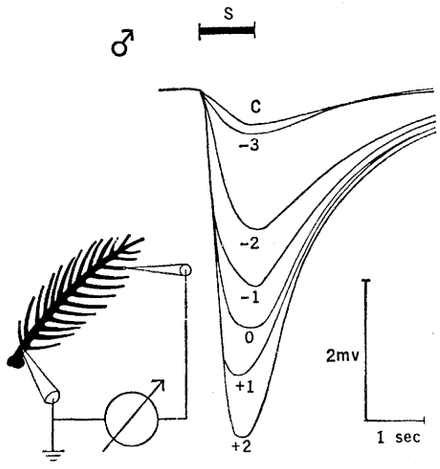


Fig. 4. Recordings of slow, electrical odor responses from the isolated antenna of the male silkmoth (*Bombyx*). Recording scheme is shown at the left. The antenna is stimulated by air puffs passing over the odor source, which is filter paper contaminated with the sex-attractant of the female moth. The attractant is bombykol (10-trans-12-cis-hexadecadien-1-ol) (*28*). The amount of bombykol on the odor sources is indicated for each recording (log values in μg). *C* represents control stimulus with air alone; *S*, stimulus duration. [From Boeckh *et al.* (*17*)]

tenna of the female polyphemus has none of the long sensory hairs with receptors for sex odor, but the antenna has a somewhat larger number of general odor receptors, including presumably receptors for the odor of the leaves on which the eggs are laid. None of the female moths in all the species we tested had any receptors for the sex-attractant which they produce. This situation, however, may be unique to moths. In the American cockroach (*Periplaneta americana*), both sexes produce the sex-attractant. However, it is uncertain whether both sexes have the corresponding receptors, because the pure pheromone is not yet available for electrophysiological tests (*15*). In the queen butterfly (*Danaus glippus*), both sexes respond to the sexual pheromone (an aphrodisiac) which is produced in the abdominal hair pencils of the male (*16*). In the honeybee, the queen produces the "queen substance" which lures the drones during the mating flight. This substance is also effective upon the olfactory receptors of the queen and worker bees. Outside the hive, the queen substance initiates the formation of clusters during swarming; inside the hive it prevents workers from raising new queens (*4, 17, 18*).

Not only is detailed knowledge of the fine structure of the olfactory sensilla necessary for a critical evaluation of the olfactory function. Also needed is precise information on the gross anatomy of the antenna, the types of sensilla, and their dimensions. In our attempts to estimate the hit-number of molecules (number of odor particles from the air to which the olfactory system responds) of the sex-attractant threshold of the silkworm moth (*Bombyx mori*), we used the following figures: the number of receptors for sex odor on the antenna, the area of the hair surface, the number and dimensions of the olfactory pores, and the area of the leaflike feather antenna (*17*). These antennae are effective molecular sieves. Tests with radioactive bombykol, the sex-attractant of *Bombyx*, demonstrated that more than 25 percent of the odor particles from the air streaming through the antenna are adsorbed (*19*). Some particles are certainly lost as carriers of olfactory information because they hit the wrong places. Only a comparatively small fraction of the total number of molecules streaming through the antenna will directly enter a pore. But the molecules adsorbed between pores may eventually enter also, owing to a theoretically possible surface diffusion in the uppermost epicuticle (*20*).

Basic Phenomena of Receptor Function

As with other receptors, we expected the olfactory cell of the insect to exhibit two types of electrical responses: a slow, local receptor or generator potential and traveling nerve impulses of the all-or-none type (in which the nerve fiber gives either maximum response or no response). Both responses have frequently been observed during recordings from individual antennal sensilla of the four types listed above. Recordings of the overall slow responses of whole antennae are the simplest available test of olfactory function in insects. This slow reaction has been called the electroantennogram (EAG) (*21*) and is composed of the receptor potentials elicited simultaneously in many olfactory sense cells. Electroantennograms are very useful for the study of antennae which have many identically reacting olfactory cells specialized for the detection of food or pheromones (Fig. 4) (*21, 22*). However, EAG's give a complex picture with antennae stimulated by odorants of a more general nature, because several types of olfactory cells which do not react identically may respond to the stimulus (*21*).

Recordings from single sensilla give some insight into the function of the olfactory receptor cell. With these small cells, only extracellular recordings have thus far been possible. However, this may be fortunate, because with one penetration of the cuticle at the base of the sensillum, one can record the impulses of several of the receptor cells of this organ simultaneously (Fig. 5). Impulse amplitudes, for the most part, are sufficiently different to permit a judgment on which cell is which. Slow receptor potentials of single sensilla are in most cases meaningful only with one cell or a number of cells which react identically.

The slow electrical response recorded from an olfactory sensillum may have two polarities, depending on the stimulus. Parallel with a stimulus-induced relative negativity of the recording electrode, we observed in a given cell the elicitation of impulses. However, when the slow potential showed a reversed polarity, the impulses were inhibited (Fig. 5) (*14, 17, 23–25*).

Whereas a correct judgment of the membrane potential of the receptor cell is not possible with extracellular recordings, these observations nevertheless can be interpreted on the basis of our knowledge of synaptic functions (*17, 24*). The most plausible interpretation of these slow electrical reactions of dendrites in the olfactory cells is that the negative potential is a membrane depolarization and the positive potential is a hyper- or repolarization. In the central nerve cells, synaptic membrane areas are either inhibitory or excitatory in nature. Synapses are highly specialized chemoreceptors in which the type of membrane and not the stimulus determines de- or hyperpolarization effects. With the olfactory cell of the insect, we lack any direct information on the membrane properties.

The response of most cells to an approximately rectangular stimulus shows an initial peak which levels off to a plateau. Such responses, which are neither phasic nor strictly tonic, are called phasic-tonic and are typical for the majority of animal receptors. Only in a few cases did we observe purely phasic cells; these cells showed the ini-

tial transient volley for only 20 to 50 milliseconds and no response for the rest of the stimulation. Peak frequencies of phasic or phasic-tonic cells may be as high as 500 impulses per second or more.

Many of the receptors showed a rather constant rate of impulses without any stimulus. Whether this resting signal rate is a truly spontaneous phenomenon is an open question. The resting frequency, however, is useful in a determination of the inhibitory effect of some odorants upon a given cell.

Intensity Range and Thresholds

The EAG curve for the intensity response of the *Bombyx* antenna has been rechecked with tritiated bombykol and improved stimulation methods, thus avoiding the adaptation of the receptors (Fig. 6). The EAG curve differs from the usual S-shaped receptor curves in not having an upper plateau of saturation (*26, 26a*). In its steeply rising middle part, the response grows proportional to the logarithm of the odor intensity. The slowly rising lower part of the curve is the threshold range.

Behavior experiments indicate that the lowest cellular threshold as "seen" from the brain may be even lower. Threshold and receptor range are best known in the silkmoth *Bombyx*. A very exact judgment of the stimulus intensities is now possible by the use of tritiated bombykol (*19*). Whereas the electrically determined EAG threshold is below 10^6 bombykol molecules per cubic centimeter of air, behavior reactions of *Bombyx* males are significant with air currents of 60 centimeters per second containing 10^4 bombykol molecules per cubic centimeter and a stimulation time of 2 seconds. These values are to some extent reduced by a longer stimulus time and the higher velocity of the air stream; this partly explains why the values differ from earlier ones (*17, 22*).

Using these figures, one can calculate how many molecules will hit the surface of a sex-attractant receptor hair of *Bombyx* or the "surface" of all the pore openings in the hair cuticle. Adsorption measurements of tritiated bombykol on the whole antenna give, as thresholds for EAG and behavior, 3×10^5 and 1.4×10^4 molecules, respectively. The antenna has approximately 10,000 receptor hairs for sex odor innervated by 1 or 2 receptor cells. At the behavior threshold, each hair receives a maximum of one molecule on the average during the 2-second stimulus.

These figures, which differ somewhat from earlier estimates before the tritiated attractant was available (*17, 22*), do not permit us to designate the individual receptor cell as a one molecule-hit (one quantum) detector. However, the one-hit function for single pores is significant. Electrophysiological threshold data, which are available for a number of specialized receptors, indicate that some receptors approach the sensitivity of the *Bombyx*, whereas others are less sensitive (*2, 17*).

Many odor receptors in insects which do not seem to respond in a specialized manner to biologically important odorants, such as food or pheromones, have much higher thresholds. [The CO_2-receptor in the honeybee holds the (biologically meaningful) record for low sensitivity with an electrophysiological threshold of 10^{15} molecules per cubic centimeter of air (*25*).] With the exception of the receptor cell for CO_2, all insect receptors respond to a spectrum of compounds. With the specialized cells, as for example the food or sex-odor receptors, one or a few compounds were more effective in eliciting a response than others. In order to elicit an electrical threshold response, the honeybee receptor specialized for the female pheromone (queen substance is 9-oxodecenoic acid) requires 10^8 molecules per cubic centimeter of air; however, 10^{12} molecules of caproic acid elicit the same effect (*17*). We have no satisfactory explanation for this discrepancy in the molecular requirement for the same biological reaction; in other words, the high specificity of a cell to a pheromone is not understood in principle.

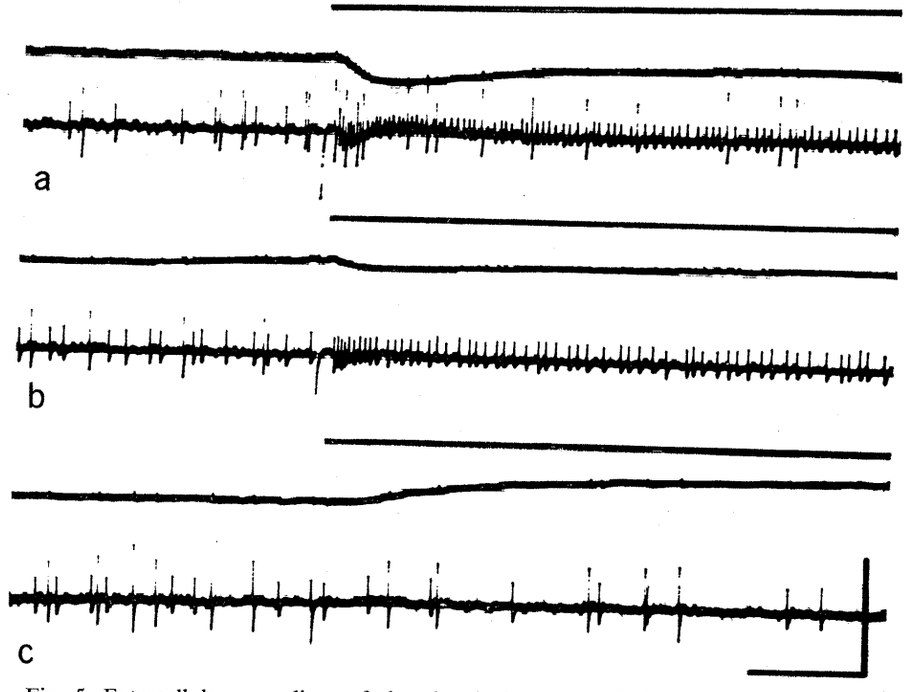


Fig. 5. Extracellular recordings of the electrical activity of the receptor cells in the antenna of male silkmoth (*Antheraea pernyi*): sensillum basiconicum with three olfactory cells tapped by the microelectrode as revealed by three different amplitudes of the nerve impulses (*a–c*). For each of the three recordings there is shown at the top the stimulus marker (black bar); in the middle the d-c recording with low amplification; and on the bottom the a-c recording. Calibration at *c*: time, 0.1 second and amplitude, 0.5 millivolt (a-c) or 5.0 millivolts (d-c) (*26*). *a*, Stimulus geraniol: three cells are spontaneously active. One (small impulses) is excited to the maximum, another cell (medium impulse size) remains indifferent to stimulus, and the third cell (big impulses) is slightly excited. The sum of the d-c receptor potentials is a relative negativity of the outside (recording) electrode at the hair base (the reference electrode is located in the blood space). *b*, Stimulus phenylethyl acetate; one cell is again excited, and the two others are inhibited; the d-c response is a very weak negative wave. *c*, Stimulus oil of clove: all three cells are weakly inhibited, and the d-c potential becomes slowly positive [note the long latency of the inhibition (*24*)]. [Modified from D. Schneider, *Jahrbuch der Max-Planck-Gesellschaft* (*26*)]

Odor Discrimination

One of the most striking capabilities of olfactory systems is their power to discriminate among a large number of odors. This number is especially great in humans and probably in other vertebrates. Many insects also possess this capability, as is apparent from studies on the honeybee (*27*). While it is reasonable to assume that odor discrimination is a task fulfilled by the central nervous system, it is logical to assume that the peripheral receptor cells must, insofar as the spectra of their odor reactions are concerned, supply a basis for the operation of the central nervous system. This problem has frequently been incorporated into more or less speculative theories which assume the presence of a certain number of types of odor receptors in the human nasal mucosa.

Is it possible to say anything about this problem on the basis of our recordings of receptor cells in insects? Yes, but the answer is not as yet conclusive. The situation with the specialized cells is understood in principle. There are, for example, on the antenna of the male honeybee (drone) many thousands of odor receptor cells, some of which are specialized for the queen substance and some of which are specialized for the pheromone of the Nasanov gland. Except for these two cells (of a type which we have called odor specialists) and a few more that one is inclined to predict in the bee, the bulk of the odor receptors in the antennae of the drone and worker bee seem to show a striking spectral variability from cell to cell (*25*). Our conclusion thus far is that the number of types of odor receptors that the central nervous system uses for the discrimination of odors is much greater than expected. In the bee and one species of moth, out of up to 100 individual receptor cells of certain sensillum types tested with an arbitrarily chosen set of odorants, very few had similar, and none had identical, reaction spectra (*14, 25*).

Receptors of this sort which have constant but highly individual reaction spectra, have been called odor generalists. In principle, the odor generalists may constitute an ideal peripheral substratum by which the central nervous system solves the odor problem. There are many of these cells, most of which signal spontaneously. Each (or a great number of them) has developed its private spectrum of reactions as a result of responding to a given compound in an excitatory or inhibitory manner, or not responding at all. The spectra of the cells do overlap considerably. It seems likely that nerve cells of the lobe of the brain where the receptor axons terminate, or cells of higher order, could, by "knowing" the capability of each of the peripheral cells, decipher the complex odor messages from the flux of signals (plus or minus or zero) that pass to them through the fine axons of the antennal nerve.

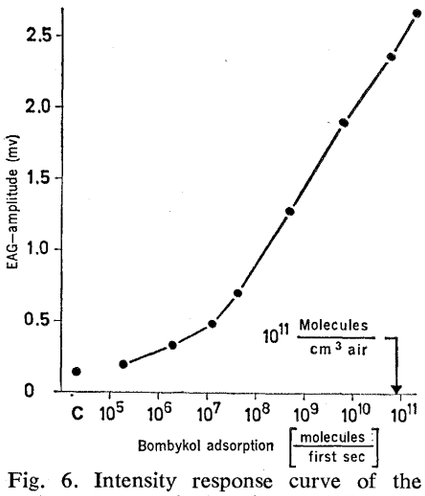


Fig. 6. Intensity response curve of the male antenna of the silkmoth *Bombyx* EAG amplitudes (ordinate) as a function of stimulation with the synthetic sex-attractant bombykol (abscissa). On the abscissa are numbers of odor molecules adsorbed on the whole antenna during the first second of stimulation. The stimulating air current contains 10^{11} molecules of bombykol per cubic centimeter of air at the point marked by the arrow. [Courtesy of Dr. K. E. Kaissling]

Summary

Insects are excellent subjects for the study of the function of olfactory receptors. Four types of sensilla on the antennae are innervated by olfactory receptor cells. Three sensilla, the cuticular hairs, pegs, and plates, show an ultrastructural pore-tubule system which penetrates the cuticle. The pores open to the outside and are proximally continuous with fine tubules. It is proposed that odor molecules penetrate the cuticle by way of the pore-tubule system, thus reaching the hair-fluid (sensillum liquor) which bathes the dendritic endings of the receptor cells. The neurofilaments which were thought by other authors to be dendritic extensions contacting the air in the pores, are the pore-tubules of the cuticle. The fourth type of olfactory sensilla (the pit peg) is differently constructed.

Many olfactory cells of insects are specialized for the detection of food, prey, or pheromones (compounds which send out a specific signal). The spectra of odorants to which single cells react can be determined with localized electrophysiological recordings of nerve impulses. Precise measurements of the threshold for the male silkworm moth were accomplished by use of the tritiated sex-attractant, bombykol; air currents of 60 centimeters per second and 2 seconds in duration containing 10^4 bombykol molecules per cubic centimeter elicited significant behavior reactions.

With extracellular recordings of bioelectrical responses, two opposite polarities were found in many of the receptor cells. Excitatory odor stimuli elicit a dendritic depolarization (receptor potential) followed by nerve impulses. Inhibitory odor stimuli hyperpolarize the same cell and depress the impulses. The system of specialized odor receptor cells (odor specialists) may be accompanied by the odor generalists. The latter receptors have spectra of odor reactions with high but overlapping variability from cell to cell. It is possible that these generalists are the peripheral substratum for discrimination, a task fulfilled by the brain.

References and Notes

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26a. Recent (unpublished) behavior and electrophysiological experiments which were performed in my laboratory have proved that the bombykol receptor cell reacts to the lowest possible stimulus for a chemoreceptor, namely one single molecule. In the behavior experiments (Dr. K. E. Kaissling), 22 percent *Bombyx* males reacted when less than 10^3 bombykol molecules were adsorbed per antenna. Using adequate mathematical treatment (Poisson-distribution) one can calculate that one molecule-hit suffices to elicit a single-cell response. Electrophysiological recordings (Dr. E. Priesner) from bombykol receptor cells gave corresponding results: Single nerve impulses which are fired by the receptor cell can be correlated to single molecule hits.
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Support of Scientific Research and Education in Our Universities

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No doubt at any moment in time there are people who feel that that particular moment is critical. I say this in apology because I do feel that now is a critical time for the support of science. It seems to me that we are approaching a major decision point on how we will support science in the United States, and specifically on how we will support scientific research and education in universities. If the nation is to reach this decision wisely, it surely needs the most thoughtful inputs possible from the people most involved—the scientific teachers and research scholars. It seems to me therefore of great importance that university scientists think through the problem as clearly as we can, and that, when we have some sense of vision and need, we present our conclusions with vigor and persuasiveness. What I wish to do is outline some aspects of the problem, give some tentative suggestions of things for us to do, and, in general, attempt to initiate what I think is a most necessary and important discussion.

I thought of saying, but hesitated to say, that we had reached the end of an era. On the other hand, I have no such hesitancy in saying that some 20 years ago the United States, and especially its federal government, did embark on what has been a new era in the support of universities and in the relationships between universities and the federal government. I speak, of course, of the decision to support basic research and graduate training in universities by utilizing funds from agencies of the federal government.

It is not characteristic of the United States to make its major decisions in one swoop. Rather, we are inclined to embark on a new line of effort or a new policy by making numerous smaller decisions, all of which then add up to a grand and important total. I think this is a good description of what has happened in the relationships between the universities and the federal government. In a relatively brief period between, roughly, 1946 and the early 1950's we made a set of decisions of major importance—or, more correctly, we put in motion a set of actions which have become translated into major decisions. Let me try to put down what I think were the key things that were done during these important years.

1) We reached a national decision that there should be federal support of higher education, especially at the level of graduate training and research.

2) We decided that the universities would have a central role for the nation in the conduct of basic research in science and engineering.

3) We decided that support for higher education and basic research at universities would be accomplished through a multiplicity of federal agencies, including mission-oriented agencies, such as the Department of Defense and the National Institutes of Health, and agencies more directly charged with support of education and basic research, such as the National Science Foundation and the Office of Education.

These decisions did not come into being fullblown, but the results have been as important to the country as if

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