PERSPECTIVE

The mosquito taste system and disease control

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Mosquitoes are a widely diverse group of organisms, comprising ∼3,500 species that live in an enormous range of habitats. Some species are vectors of diseases that afflict hundreds of millions of people each year. Although understanding of mosquito olfaction has progressed dramatically in recent years, mosquito taste remains greatly understudied. Since taste is essential to feeding, egg laying, and mating decisions in insects, improved understanding of taste in mosquitoes could provide new mechanistic insight into many aspects of their behavior. We provide a guide to current knowledge in the field, and we suggest a wealth of opportunities for research that are now enabled by recent scientific and technological advances. We also propose means by which taste might be exploited in new strategies for mosquito control, which may be urgently needed as the geographical ranges of vector species increase with climate change.

mosquito | vector biology | taste

Mosquitoes are remarkably diverse in terms of their morphology, the environments that they inhabit, the hosts upon which they feed, and the behaviors that they exhibit (Fig. 1). Mosquitoes have been on Earth for over 200 million years and comprise ∼3,500 species. They reside on six continents and in a wide range of habitats—in marshes, forests, deserts, Arctic regions, and urban centers.

Mosquitoes have an enormous ecological impact as pollinators, food sources, and vectors of pathogens that afflict wildlife. Males and females of most species feed on nectar and other plant juices, pollinating host plants. Mosquitoes also serve as food sources to a variety of predators, including birds, frogs, spiders, and lizards. Females of most species bite animals and draw blood, which provides nutrients essential for reproduction. Because of their need for blood, certain mosquitoes are vectors of pathogens causing animal diseases and have thereby had major impacts on species abundance and biodiversity. These mosquitoes have decimated a number of North American bird populations by transmitting West Nile virus, and they have driven certain native Hawaiian songbirds extinct via avian malaria (1–3). Mosquitoes also transmit pathogens that afflict livestock such as cows, sheep, and horses.

Mosquitoes are also vectors of pathogens causing human diseases. Although only a small fraction of mosquito species is anthropophilic and bites humans, they have an enormous impact on global health (Fig. 2). These species collectively spread diseases to hundreds of millions of people and kill nearly a million each year. These diseases include malaria, dengue fever, yellow fever, Zika fever, West Nile fever, and chikungunya. Because of the toll they take on human life, mosquitoes are often said to be the deadliest animals on Earth. Interest in mosquito vectors of disease pathogens is increasing as their geographic ranges expand due to climate change.

Mosquitoes have evolved sophisticated chemosensory systems to detect and identify chemical cues in their environments, including cues of the hosts they bite. Our understanding of mosquito olfaction has advanced a great deal in recent years (4–13), but mosquito taste remains greatly understudied. Taste is essential to feeding, mating, biting, and egg-laying decisions in insects (Fig. 3), and mosquitoes have evolved elaborate taste organs on their mouthparts and legs and internally. The molecular, cellular, and circuit mechanisms by which these organs signal taste cues remain a largely unexplored frontier. Progress in understanding mosquito taste could yield insight into

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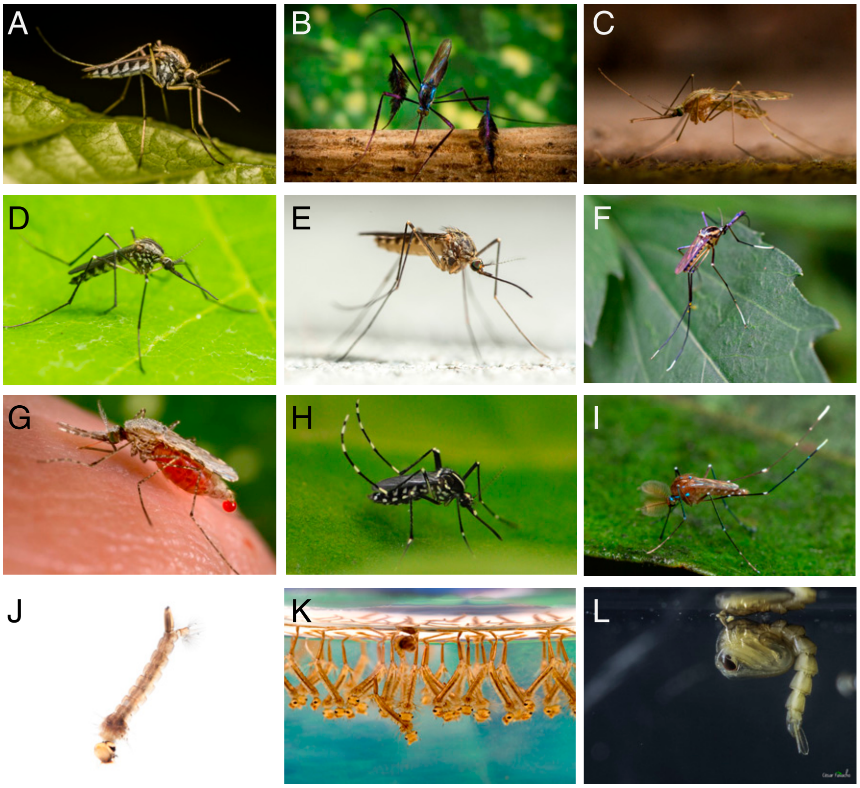

Fig. 1. **Mosquitoes. (*A*) *Aedes sticticus*; (*B*) *Sabethes cyaneus*; (*C*) *Anopheles maculipennis*; (*D*) *Toxorhynchites speciosus*; (*E*) *Culiseta glaphyroptera*; (*F*) *Toxorhynchites rutilus*; (*G*) *Anopheles stephensi*; (*H*) *Aedes albopictus*; (*I*) *Uranotaenia sapphirina*; (*J*) *Aedes* larva; (*K*) *Culex* larvae; and (*L*) *Aedes aegypti* pupa. Image credits: (*A, C, D, E,* and *J*) Anders Lindström (photographer); (*B, G,* and *K*) Centers for Disease Control and Prevention/James Gathany; (*F*) Ellen Honeycutt (photographer); (*H*) Ary Faraji (photographer); and (*I* and *L*) César Favacho (photographer).**

many aspects of their diverse behaviors and could provide new means of controlling both mosquitoes and the diseases they spread.

Taste Organs

Mosquito taste organs include the tarsal segments of the legs, the labellum and labrum of the mouthparts, and the cibarium, an internal organ (Fig. 4 *A*–*D*). The tarsi are the first taste organs to make contact with a potential food source, blood source, or oviposition site. The labellum lies at the distal tip of one of the mouthparts. The labrum, a distinct mouthpart, is shaped like a needle and serves as a conduit through which blood or food is ingested. Once ingested, the blood or food passes the cibarium on their transit to the midgut or crop, respectively.

These taste organs all contain sensory hairs called sensilla, which house gustatory receptor neurons. The sensilla fall into different morphological types. Trichoid sensilla extend outward from the surface of the tarsi and the labellum and typically have a single pore at the distal end of a blunt tip (Fig. 4*E*). Other sensilla lie at an acute angle to the apical and subapical surfaces of the labrum; they are commonly referred to as apical and subapical sensilla (Fig. 4*F*). Papilla sensilla are small and found on the cibarium (Fig. 4*G*).

Tarsi contain more trichoid sensilla on the forelegs and midlegs than the hindlegs in some species (14–16). Correspondingly, the forelegs and midlegs make more contact with substrates than do hindlegs. Interestingly, hindlegs are often suspended in air and move while the animal is on a surface, suggesting the possibility they may have additional sensory functions other than taste.

Sexual dimorphism is observed at many levels in the mosquito taste system. Among organs, the labrum is sharper in females, which use it to pierce skin. The presence or number of some types of taste sensilla is sexually dimorphic. For example, in the vector species *Aedes aegypti*, there are more tarsal sensilla in females than males, suggesting the possibility of a host-recognition function for the supernumerary sensilla in females (14, 16). In blood-feeding species, the apical and subapical sensilla of the labrum and the ventral papilla sensilla of the cibarium are present only in females. These sensilla are absent in both males and females of nonblood-feeding species, suggesting a role in blood sensing (17–21).

Other potential taste organs include the wing margin, the pharynx, and the ovipositor. These organs have been implicated in taste in *Drosophila* or other dipterans. Their roles in taste detection and in the behavior of mosquitoes present interesting directions for future research.

Taste Neurons

Taste sensilla house small numbers of gustatory neurons. Trichoid sensilla on the tarsi typically house up to five taste neurons; labellar trichoid sensilla and labral sensilla typically house up to four, and cibarial sensilla contain up to three (14, 15, 19, 22). The cell bodies of these neurons project dendrites toward the pore through which tastants enter (Fig. 4 *E*–*G*).

The sensitivities of taste neurons can be investigated by electrophysiological recording. An electrode containing a tastant solution is placed in contact with the tip of the sensillum (Fig. 5). The physiological responses elicited by the tastant are then

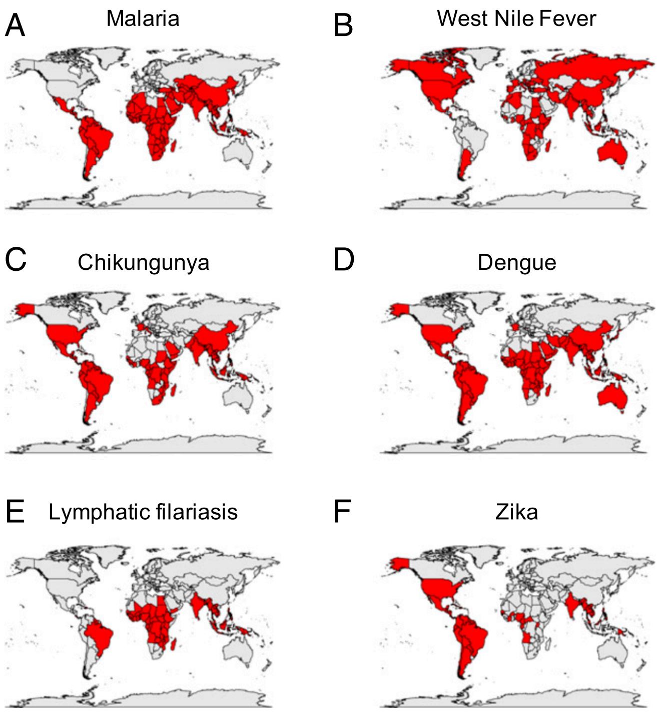

Fig. 2. **Global distribution of mosquito-borne diseases. World maps indicating prevalence of diseases caused by mosquito-borne pathogens. Red indicates countries with recent or current reports of disease presence. (*A*) Malaria. Data from ref. 108. (*B*) West Nile fever. Data from ref. 109. (*C*) Chikungunya. Data from ref. 110. (*D*) Dengue. Data from ref. 110. (*E*) Lymphatic filariasis. Data from ref. 108. (*F*) Zika. Data from ref. 108.**

measured by recording the amplitudes and frequencies of action potentials. Different neurons within the sensillum, often distinguishable by their different action potential amplitudes, respond to different tastants (23–28).

Neurons in the labellar sensilla respond to sugars, bitter compounds, salts, and amino acids (22–28). Recording from tarsal sensilla has been limited, but responses to sucrose, salt, and amino acids have been reported (22, 29). In a sensillum of the labrum, one neuron responded to salt, while another responded physiologically to adenosine triphosphate (ATP) (22, 30, 31). Interestingly, ATP induces engorgement (i.e., ingestion of a large volume), a response usually induced by blood but not by nectar (32).

Taste Receptors

Mosquito genomes contain a wide variety of candidate taste receptor genes, including members of the *Gr* (*Gustatory receptor*), *IR* (*Ionotropic receptor*), *Trp* (*Transient receptor potential*), and *Ppk* (*Pickpocket*) families (Fig. 6). There are large numbers of some of these genes. For example, there are 90 *Gr* genes in the malaria vector *Anopheles gambiae*; 107 in the Zika, dengue, and yellow fever vector *Ae. aegypti*; and 126 in *Culex quinquefasciatus*, which transmits Zika and West Nile viruses (33–35).

Expression of some of these genes shows organ specificity. Some *Gr* genes are expressed in the labellum but not the tarsi, whereas others are expressed in the tarsi but not the labellum (36). These differences invite questions about the roles of individual taste receptors and suggest different roles for these organs in taste. Intriguing questions about function are also posed by the differential expression of taste receptors in mosquitoes of different sex, developmental stage, or physiological state (e.g., after mating or a blood meal) (36–40).

Roles of the Taste System

Taste input modulates many behaviors in insects. Studies in mosquitoes have revealed roles for taste in driving or modulating several behaviors that are likely to contribute to survival and disease spread. These behaviors include feeding, biting, mating, and oviposition (Fig. 3).

Feeding. Feeding decisions are made after evaluating the benefits and risks of a potential food source. Taste provides a mechanism for evaluating the content of potential food sources. It allows detection of both nutritive and toxic compounds.

Adult mosquitoes feed on sugary substrates including plant nectar, honey dew, and plant sap. Nectar meals generally contain high concentrations of sugars. When mosquito taste organs are stimulated with sugars, the animal responds with proboscis movements and pharyngeal pumping, which result in ingestion (41–43). Behavioral responses depend on the identity of the sugar molecule (e.g., sucrose) as well as on the dose.

By contrast, bitter compounds and high concentrations of salts elicit aversive responses. Ammonium chloride or high concentrations of salts evoke rejection responses, such as proboscis withdrawal, and inhibit feeding behavior (23, 43–46). These responses may have evolved in part to prevent ingestion of harmful food sources.

The biting behavior that precedes blood feeding is also influenced by taste cues. *N*,*N*-Diethyl-*meta*-toluamide (DEET), a repellent that is a bitter tastant as well as an odorant, suppresses biting in part through taste organs (47). We note also a classical behavioral experiment with mosquitoes that had undergone surgical ablation of their antennae, which are the primary, although not the only, olfactory organs of the mosquito. These antennaless mosquitoes showed biting behavior upon contact with human skin, indicating that biting behavior is not driven exclusively by chemosensory input through the antenna (48).

Mating. Identification of a mating partner of the same species and subsequent mating behaviors are driven by taste detection of

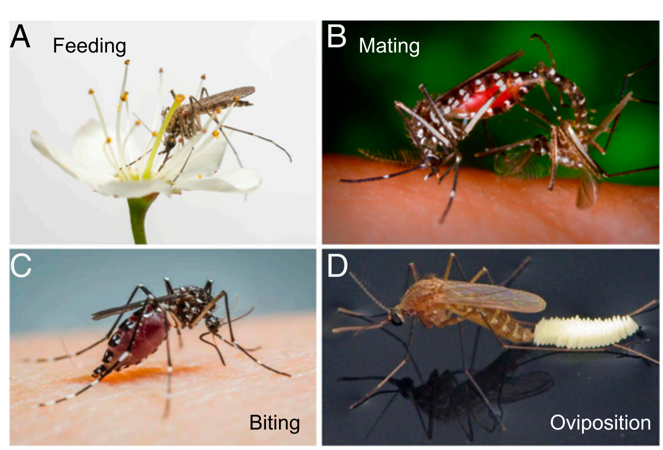

Fig. 3. **Mosquito behaviors. (*A*) *Aedes cantans* feeding on nectar. Image credit: Anders Lindström (photographer). (*B*) *Aedes albopictus* mating. Image credit: Centers for Disease Control and Prevention/James Gathany. (*C*) *Aedes albopictus* biting. Image credit: Centers for Disease Control and Prevention/Pablo Cabrera. (*D*) *Culex quinquefasciatus* ovipositing. Image credit: Sean McCann (photographer).**

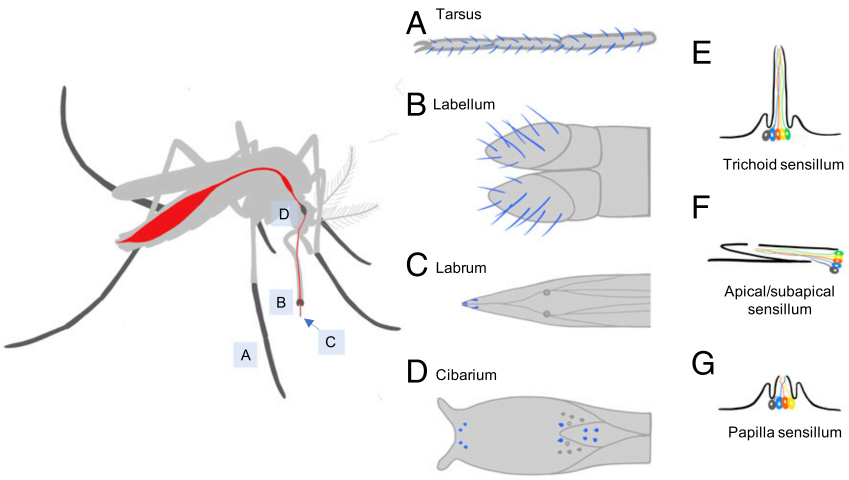

Fig. 4. **Anatomy of mosquito taste organs and sensilla. (*Left*) Illustration of mosquito with taste organs highlighted in dark gray. (*A–D*) Taste sensilla are depicted in blue: (*A*) tarsus (third to fifth segments), (*B*) labellum, (*C*) apical/subapical portion of labrum, and (*D*) cibarium. (*E–G*) Morphology of taste sensilla containing several gustatory receptor neurons (in color) and one mechanosensory neuron (in dark gray): (*E*) trichoid sensillum, (*F*) apical/subapical sensillum, and (*G*) papilla sensillum.**

nonvolatile pheromones in many insects. In a number of mosquito species, males have enlarged claws that they use to grasp females. In so doing, male legs make contact with females and may detect nonvolatile pheromones that induce male behavioral responses, including excitatory behavior and mating attempts (49–53).

The context of male–female contact varies dramatically among the many species of mosquitoes. In some species, an isolated male and an isolated female make contact and mate. In other species, the males form a flying swarm into which a female flies and mates with a male. Males of *Opifex fuscus* and *Deinocerites cancer* perform a behavior called "pupal attendance": an adult male contacts a female pupa with its tarsi, grabs it, and awaits her eclosion, upon which the male attempts to mate (52, 54). In some instances, males attempt to mate with recently discarded pupal cases (52). Little is known about the nonvolatile pheromones that are detected and their roles in driving mosquito mating behaviors.

Oviposition. The selection of a suitable site to lay eggs is critical to the survival of a mosquito species. After hatching from eggs, larvae and pupae develop at the oviposition site, so the presence of nutrition and the absence of predators are essential. Oviposition behavior of adult female mosquitoes varies across species. *Culex* species lay eggs directly on the surface of water, *Anopheline* species tend to hover over the surface of water and drop eggs onto it from the air, and *Aedine* species lay eggs on surfaces adjacent to water, often right above the waterline. Despite these differences, females of diverse species contact the substrate with taste organs before oviposition, consistent with a role for taste cues in oviposition site selection (55–57). We note that oviposition is also influenced by olfactory cues, and some cues may operate via both olfaction and taste.

What taste cues stimulate or deter oviposition? Salinity is one factor. Many species prefer to lay eggs in water with low salt concentrations (56, 58, 59). Other species are less discriminating and lay eggs in salt marshes or marine rock pools with much higher salt concentrations (60, 61). The ability to discriminate oviposition site salinity affects offspring fitness and survival and requires taste organs (56, 58, 59, 62).

Most mosquito larvae eat various plant materials and microorganisms. Correspondingly, a variety of chemical cues from plant and microbial sources stimulates oviposition through either taste, olfaction, or both (63). By contrast, cues associated with natural predators such as fish, dragonflies, and other insect predators deter oviposition (63–66).

Chemical cues from eggs, larvae, and pupae are a particularly intriguing factor. Many species such as *Ae. aegypti*, *Aedes albopictus*, *Cx. quinquefasciatus*, and *Ochlerotatus australis* prefer to oviposit in water with conspecific larvae and pupae or cues associated with them (63, 67–70). Some *Culex* species also prefer to oviposit in water containing a cue from conspecific egg rafts, Mosquito Oviposition Pheromone (71–73). Oviposition site attraction has been shown to be mediated at least in part by the olfactory system, but a role for taste has not yet been explored. In contrast to this preference for conspecific cues, adult *Toxorhynchites* females prefer to lay eggs in water containing cues of heterospecific larvae, which *Toxorhynchites* larvae eat (74).

The Larval Taste System

Not only do chemical cues of larval food sources stimulate oviposition by adult females, but they also stimulate feeding in

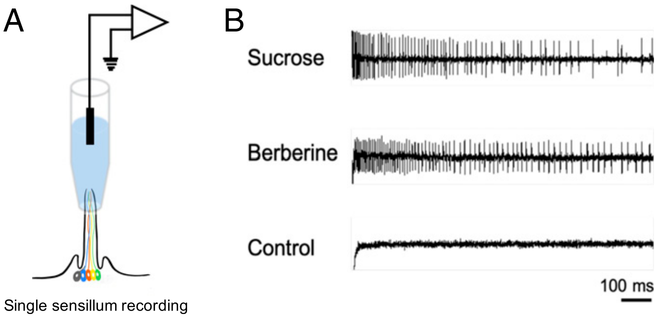

Fig. 5. **Electrophysiological recordings of taste sensilla. (*A*) Schematic of single-sensillum electrophysiological recording. An electrode containing a tastant solution is placed over the tip of a sensillum. The tastant enters the sensillum via a pore at the tip of the sensillum and activates taste neurons within. (*B*) Physiological recordings from *Aedes albopictus* labellar sensilla in response to sucrose (*Top*), berberine chloride (*Middle*; bitter compound), or control diluent tricholine citrate (*Bottom*).**

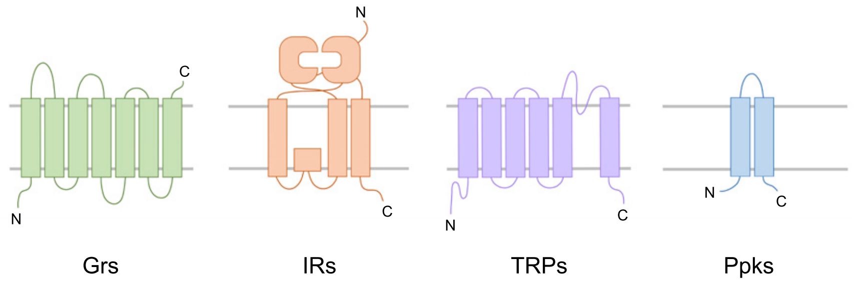

Fig. 6. Classes of taste receptors. Several classes of taste receptors are shown: Grs, IRs, TRPs, and Ppks, which are members of the degenerin/epithelial sodium channel family. Adapted from ref. 111, with permission from Elsevier.

larvae. Larvae feed on microorganisms, organic detritus, and even on live larvae of other mosquito species and carcasses of their own species (75). Both the rate and duration of feeding are increased by mixtures of nutrients such as yeast extract or nucleotides (75–79). Mixtures are more effective than individual nutrients in stimulating feeding and larval aggregation (75, 79). Some bitter compounds such as DEET and quinine elicit aversive or turning behaviors in larvae (80, 81).

Larvae have an antenna that contains a sensillum with the anatomical characteristics of a taste sensillum. It contains a pore at the tip and houses several neurons, each with dendrites that extend to the tip (82–84). There are also chemosensory sensilla on the larval maxillary palp and internally (15, 85). Multiple *IR* genes are expressed in the larval antenna, and one has been implicated in DEET response (80). The molecular basis of larval taste awaits exploration.

Opportunities for Future Directions

Mosquito taste offers a great variety of problems to solve and excellent opportunities to solve them. Questions lie at every level of biological organization, from molecular biology to ecology. Mosquitoes have had hundreds of millions of years to evolve sensitive and discriminating taste organs, but little is known about the receptors, neurons, and circuits that underlie mosquito taste. A particularly intriguing dimension is added by the large number of diverse mosquito species, each likely to have a taste system adapted to its own special needs.

Taste Cues. The first and most basic question is what tastants mosquitoes detect. The number of taste compounds that have been tested in physiological or behavioral assays is relatively small. Yet, *Drosophila* and other insects have been found to respond to an immense variety of tastants. These compounds extend far beyond common sugars, salts, and amino acids to include nucleic acids, polyamines, organic acids, and a vast panoply of structurally diverse bitter compounds (86, 87).

Taste compounds found on human and animal hosts are of particular interest. It seems plausible that taste cues could provide a checkpoint to confirm the suitability of a host for biting. Taste cues could also help guide the precise location of a site at which to bite. A great deal of chemical information is available to the mosquito on human and animal skin, including compounds synthesized by the hosts and by the microbes that inhabit their surfaces. It seems likely that the mosquito taste system uses this information. Salient compounds can be identified by behavioral testing in feeding, biting, or oviposition paradigms (Fig. 7). Alternatively, compounds can be tested in physiological assays (Fig. 5).

The ∼3,500 mosquito species collectively live in immensely diverse habitats such as Alpine meadows, tropical rainforests, and arid plateaus. They feed on different plants and different hosts that produce a wide variety of taste cues. It will be interesting to determine which taste responses have been conserved in evolution and which have evolved to serve the needs of individual species.

Taste Coding. What are the principles by which mosquitoes encode tastants? A great deal of insight can be obtained in straightforward fashion via electrophysiology. Available data are currently sparse: they are from few tastants, few neurons, and few species. Moreover, most sensilla that have been analyzed were not identified by name or position.

Recordings with relatively small panels of tastants should indicate how many distinct functional types of taste sensilla are in each organ. Testing with a modest number of tastants should reveal whether individual taste neurons of a particular class (e.g., bitter-sensing neurons) are narrowly tuned to a small fraction of bitter compounds or broadly tuned to many. Such studies should also show whether there are distinct classes of bitter neurons. If different bitter compounds elicit different responses from multiple bitter-sensing neurons, this organization would provide the basis of a combinatorial code of bitter taste. Such organization would endow the system with the capacity to discriminate among bitter compounds.

Testing different doses of tastants should illuminate how taste intensity is encoded. For example, different neurons may be specialized to report the concentration of a tastant over different concentration ranges. The intensity of some compounds, such as salt, might thereby be assessed more precisely than if it were represented by the activity of a single class of neuron.

The function of sex-specific sensilla is particularly interesting. For example, there are more tarsal sensilla in females than males in *Ae. aegypti* (14, 16). It will be interesting to determine if there are female-specific tarsal sensilla in these vector species that detect host tastants; alternatively, they might be specialized for identifying suitable oviposition sites. Similarly, sensilla unique to blood-feeding species may detect host cues or blood.

Taken together, this analysis should illuminate the neural basis of taste coding. It may reveal how the coding properties of the tarsi and labellum differ, which may provide insight into the functions of these organs in influencing mosquito behavior. The feasibility of elucidating principles of neural coding by taste organs via electrophysiology has been demonstrated in *Drosophila* (88–90).

At the molecular level, recent technological and intellectual advances provide new and exciting opportunities. Candidate taste receptors in several mosquito species have been identified, including over a hundred Grs and/or IRs for some species, and

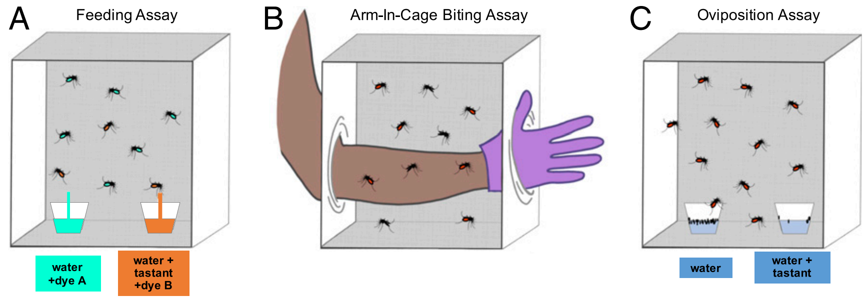

Fig. 7. Behavioral assays measuring taste-driven behaviors. (*A*) Feeding assay measures feeding preference by presenting mosquitoes with a choice of two feeding sites: one containing water and the other containing water with tastant. Each choice contains different fluorescent dyes used to visualize feeding choice. (*B*) Arm-in-cage biting assay measures percentage of female mosquitoes biting human arm treated with either solvent or tastant. (*C*) In an oviposition assay, blood-fed and egg-carrying female mosquitoes are presented with a choice of two oviposition sites: one containing water alone and the other containing water with tastant. Oviposition is measured as percentage of eggs laid in each site.

await functional analysis (33, 34, 80, 91–94). The molecular basis of taste coding is now accessible for genetic analysis via CRISPR-Cas9 gene editing technology. For example, if a species shows female-specific expression of a *Gr* gene in the labellum, one can mutate the gene and determine if it is required for responses to particular host or oviposition cues. There is now ample precedent for genetic analysis of sensory receptors in *Ae. aegypti* and *An. gambiae* (62, 95–97).

The expression of taste receptors can be analyzed at high resolution by using the promoters of receptor genes to drive reporter constructs. Gene editing also allows the use of genetically encoded Ca^{2+} or voltage indicators (9, 62, 98–100). Such indicators permit functional analysis of taste neurons such as those of the cibarium, which are less accessible to electrophysiological recording than those of the tarsi or labellum on account of their internal location. Similarly, the activity of higher-order neurons in taste circuits can be monitored using such indicators.

Taste Behaviors. Taste behavior can now be investigated at the molecular and cellular levels. Analysis of taste receptor mutants may identify not only ligands of the receptors but also their roles in driving feeding, biting, or oviposition behavior. Just as promoters of receptor genes may drive reporters, they may also drive effectors that silence or activate defined taste neurons. In this manner, one can identify and characterize neurons that stimulate or deter critical mosquito behaviors.

Mating behavior is particularly understudied in mosquitoes. Analysis of the taste system could identify pheromones and neurons that influence either male or female behavior. It will be interesting to determine whether taste plays a role in preventing interspecies mating. Understanding mechanisms that mosquitoes use to recognize each other could also have applications to mosquito control.

Taste circuits can also be investigated by expressing genetically encoded Ca^{2+} indicators or voltage indicators in higher-order neurons (9, 62, 98–100). While genetic manipulation of mosquitoes is less convenient than that of *Drosophila*, a variety of genetic tools used in *Drosophila* can in principle now be used in the mosquito. One question of particular interest is how taste cues from a host are processed and integrated with other host cues in the central nervous system to drive behaviors such as biting.

Another intriguing question is how taste reception and perception are influenced by the internal state of the mosquito. After a female mosquito bites, the need for a host is supplanted by the need for an oviposition site. Are there molecular or cellular changes in the physiology of individual taste neurons? Are there changes in the activity of higher-order neurons in the taste circuit?

In the long term, comparative studies could illuminate the mechanisms by which mosquito behaviors have evolved. For example, what molecular and cellular differences are there between the taste systems of mosquitoes that feed on animal hosts and those that feed exclusively on nectar? A related problem of interest is how the taste systems of mosquitoes that feed on humans differ from those that do not. Identifying differences between anthropophilic mosquitoes and zoophilic mosquitoes could suggest new targets useful in vector control.

Disease Control. Mosquitoes spread a multitude of diseases, including malaria, dengue, yellow fever, chikungunya, and Zika. As climate change expands the range of mosquito vectors, so too it will extend their devastating impact on health. New means of mosquito control will be sought with increasing urgency. Taste might be exploited in a variety of ways to manipulate mosquito behavior and prevent the spread of disease. Thus, new insight into basic mechanisms of taste may be invaluable. Moreover, prospects for translating discoveries into practical applications should improve rapidly with the accelerating development of technology for studying and manipulating mosquitoes.

Screening of tastant libraries may identify several kinds of compounds useful in mosquito control. Aversive compounds that act via taste could be useful when applied to skin surfaces or even clothing. Such aversive compounds could act in several ways. They could conceivably reduce the time a mosquito spends on a skin surface, the likelihood that a biting event is initiated, or the duration of a biting event. Tastants that activate bitter-sensing neurons may be particularly interesting to test in biting assays. In addition to compounds that act exclusively via taste, it may be possible to identify compounds like DEET that deter mosquitoes via taste as well as olfaction (47, 99, 101).

Taste compounds that activate feeding behaviors could also be useful. If applied to insecticide-treated bed nets, they may stimulate greater ingestion of insecticides and thus, increase lethality. Likewise, taste compounds that stimulate feeding could be added to attractive toxic sugar baits, which are commonly used in pest control.

Tastants that stimulate oviposition behavior could be deployed in oviposition traps that kill adult females or their progeny. There is precedent for the use of lethal oviposition traps in the control of *Ae. aegypti*, and the attractiveness of the traps is considered a critical parameter in their effectiveness (102). Accordingly, it seems plausible that the presence of positive oviposition cues could enhance the effectiveness of such traps and the success of this form of control.

In addition to tastants that activate aversion, feeding, or oviposition responses, another kind of compound could also be useful: molecules that inhibit or mask taste responses. A wide variety of compounds inhibits the activities of insect olfactory receptor neurons (99, 101, 103, 104), and it seems plausible that various compounds might inhibit taste neurons. Other compounds might act by masking the stimulatory effects of other tastants. Compounds that inhibit or mask taste responses might be used, for example, to inhibit biting behaviors elicited by taste cues on the skin.

Another interesting prospect for future research is the potential of nonvolatile pheromones for mosquito control. Pheromones, both volatile and nonvolatile, drive a variety of insect behaviors (105, 106). A wide variety of control strategies based on the deployment of pheromones has been used successfully to control agricultural pests. There are interactions between the responses elicited by pheromonal signals and those elicited by food sources (107). Further research is needed to determine whether nonvolatile mosquito pheromones, of negative or positive valence, might reduce the duration of landing on a surface or reduce the frequency of biting events.

If genetic modification of mosquitoes via gene drive or other systems becomes common practice, then the taste system may conceivably offer useful targets that could be manipulated. For example, if individual taste receptors influence the likelihood of biting a human vs. an animal host, then manipulation of genes encoding such receptors in mosquito populations might redirect biting from humans to animal hosts while avoiding strong selective pressure against the genetic modification. Analysis of Grs that are specific to females of anthropophilic species could identify interesting candidates for modification. Receptors that detect human host cues could be especially worthy of investigation. If genetic modification proves difficult, another option is to screen for compounds that manipulate such receptors.

In the long term, understanding of taste at the circuit level may allow additional vector control strategies. For example, one might envision the conditional activation of circuits that deter feeding or the inactivation of circuits that promote biting. In principle, such circuits could be manipulated chemically and/or genetically. Further research into the mechanisms of mosquito taste will allow assessment of the feasibility of such possibilities.

In summary, a great variety of interesting problems awaits investigation in the taste system of mosquitoes. Studies of this system may provide new insight into the biology of an intriguing and highly diverse group of insects. The results of such studies could also have applications to a global health challenge of enormous dimension.

Data Availability. There are no data underlying this work.

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