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Chemosensation: Tasting with the Tail

Dispatch

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Animals employ multiple mechanisms to detect the presence and location of environmental stimuli. Recent work suggests that Caenorhabditis elegans uses chemosensory information provided by spatially distinct sensilla to generate a sensory map of its environment and to avoid noxious compounds.

Animals encounter a dizzying array of sensory cues in their environment. An organism must be able, not only to detect these cues, but to also deduce the source and location of the signals relative to itself, so that it can successfully find prey or potential mates and avoid predators and toxins. Generally speaking, for a particular sensory modality, animals tend to use similar strategies to locate a signal. For instance, mechanical stimuli are sensed by mechanoreceptors present at multiple locations in the body. Mechanoreceptors responsive to pressure and touch are distributed throughout our skin, and are present on the antenna, abdomen, legs and wings of insects [1]. Similarly, the lateral line sense organs of fish consist of mechanoreceptors distributed over the surface of their bodies [2]. The broad spatial distribution of these sensory organs allows animals to rapidly determine the location of the stimulus in their environment. The location of a stimulus can also be detected by spatially separated bilateral sense organs, such as ears. In auditory localization, the levels and timing of sounds arriving at each ear are compared to precisely deduce the source of the signal, a strategy used extremely effectively by animals such as barn owls, much to the disadvantage of their prey [3].

In olfaction and gustation, however, chemical cues are generally sensed by a single sense organ — nose or mouth — or multiple sense organs which are located too closely to allow for efficient spatial resolution. In these cases, organisms have been shown to use temporal integration mechanisms to detect and orient along the gradient of a chemical signal [4,5]. In this mechanism, changes in the concentration of the cue are compared as a function of time to alter the direction of movement. Although chemosensory organs have also been shown to be present in multiple locations in animals such as *Drosophila* [6], their role in chemosensory information processing has been relatively unclear. Interestingly, in a paper published recently in *Current Biology*, Hilliard *et al.* [7] show that, in addition to using temporal integration strategies to detect attractive chemicals, the nematode *Caenorhabditis elegans* uses chemosensory information provided by spatially distinct chemosensors to locate and avoid noxious chemicals.

C. elegans exhibits robust responses towards many distinct chemicals, a necessity for these soil-dwelling animals to successfully navigate their aroma-rich environment [8]. Worms respond to an attractive chemical by integrating changes in concentration as a function of time to move up a gradient [5]. Noxious chemical and mechanical stimuli are avoided by rapid reversals followed by forward movement in a different direction [9–11]. From anatomical and structural considerations, *C. elegans* is believed to sense its chemical environment using about 32 sensory neurons (of a total of 302 neurons in its nervous system) [12,13]. Twelve pairs of these sensory neurons are present in each of the bilateral amphid organs of the head, and two pairs in each of the bilateral phasmid sensory organs of the tail. Although the functions of the amphid sensory neurons have been defined and shown to mediate attractive and avoidance responses to multiple chemicals [8], the sensory functions of the tail phasmid organs — if any — have been a long-standing mystery.

Hilliard *et al.* [7] have now shown that the phasmid neurons PHA and PHB in the *C. elegans* tail play a role in modulating avoidance responses to repellents. To demonstrate this, the authors devised a rapid method by which to measure acute avoidance — the 'drop test'. A drop of the water-soluble repellent is placed near the tail of an animal that is moving forward and allowed to cover the animal by capillary action, such that both the amphid and phasmid sensory neurons are simultaneously stimulated. If the drop is perceived as a repellent, the animal exhibits an immediate — within 1–4 seconds — reversal in its direction of movement.

SDS, for example, is a known repellent for *C. elegans* [14], and worms exhibit a robust avoidance response to SDS in the drop test. This behavior is largely directed by the ASH amphid sensory neurons, as killing the ASH neurons dramatically reduces the reversal responses of animals to SDS in this test. Surprisingly, Hilliard *et al.* [7] found that killing the PHA and PHB phasmid neurons alleviated the avoidance defects of ASH-killed animals (Figure 1). Thus, while killing the PHA and PHB neurons alone did not affect avoidance behaviors, animals lacking the ASH, PHA and PHB neurons avoided SDS nearly as well as wild-type animals.

These results lead to two conclusions. First, they suggest that, in the absence of ASH, PHA and PHB function, an as yet unidentified, secondary SDS-sensing pathway (denoted by X in Figure 1) is revealed, restoring the ability of these animals to avoid SDS. Second, upon simultaneous stimulation of the amphid and phasmid neurons by SDS, the avoidance response driven by the ASH (and/or X) is negatively modulated by the PHA and PHB phasmid neurons. Under these conditions, the reversal response mediated by the ASH neurons overrides the PHA/PHB-mediated inhibitory inputs.

Hilliard *et al.* [7] further demonstrated this by spatially and temporally separating the stimuli encountered by the amphid and phasmids. In these experiments, stimulation of the amphids, but not the phasmids, led to a more robust avoidance response, consistent with

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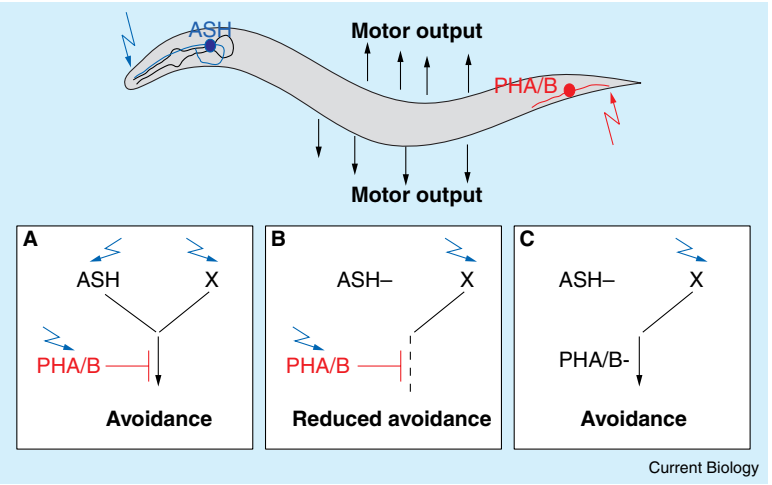

Figure 1. Proposed model for avoidance of SDS by spatially separated chemosensors shown at the top.

(A) Upon stimulation of both the amphid and phasmid neurons by SDS in the drop test (see text), the ASH-mediated inputs override the PHA/PHB-mediated antagonistic inputs to promote avoidance behavior. X denotes a secondary SDS-sensory input. (B) In ASH-killed animals, PHA/PHB-mediated negative modulation inhibits avoidance responses. (C) In the absence of both ASH and PHA/PHB inputs, X-mediated inputs restore avoidance.

the PHA/PHB neurons mediating antagonistic inputs into the avoidance behavior. Taken together, these results indicate that the decision to reverse in response to a repellent, as well as the duration of the reversal, incorporates inputs from the head as well as the tail sense organs.

How are these antagonistic sensory inputs integrated? Luckily, the circuit required for forward and backward movement has been well mapped by a combination of laser-killing and genetic experiments [15]. In response to posterior sensory stimulation, the AVB and PVC command interneurons mediate forward movement, while in response to anterior stimulation, the AVA, AVE and AVD command interneurons mediate backward movement by activating different subsets of motor neurons and muscles. This circuit functions in a distributed manner to regulate the duration spent in the forward versus the backward moving state [16]. Sensory inputs alter the time spent in each of these states, resulting in a net forward or backward movement.

ASH directly synapses onto these command interneurons [17], and is believed to drive backward movement in response to sensory stimulation of the amphid. Interestingly, PHB also synapses directly onto the locomotory circuit (PHA synapses primarily onto PHB) [17]. This leads to the speculation that, in response to simultaneous stimulation of the amphid and phasmid by a repellent, the PHA/PHB neurons act directly to modulate the functions of the locomotory circuit, such that the time spent reversing direction is decreased, allowing the animals to rapidly move forward again in a new direction.

What is the advantage of this mechanism? Spatially separated sensors allow animals to rapidly deduce the location of stimuli in the environment, similar to the mechanisms used in mechanosensation and proprioception. A spatial comparison mechanism is particularly advantageous for the urgent avoidance of noxious stimuli, as this bypasses the time-consuming temporal integration tasks that must be carried out by a single localized sense organ in order to locate the source of the stimulus. After all, when encountering a life-threatening toxin, time is a relative luxury. An organism must change its direction immediately, or risk severe consequences. Moreover, unlike attraction, avoidance does not require directed movement along a specific trajectory. Instead, the principal requirement is to reverse and alter movement towards any other direction. Consequently, it is advantageous to respond to attractive and repellent chemicals via distinct mechanisms. Thus, *C. elegans* appears to use multiple strategies in order to maximize its efficiency of response to environmental chemical cues.

These findings raise a number of questions. Is the mechanism described generally applicable to the avoidance of additional repellents? In related work, the authors have described the identification of several new compounds perceived as repellents by *C. elegans* (M. Hilliard, personal communication). Interestingly, these compounds are also perceived as toxic and bitter by other animals, and include poisons such as plant alkaloids. Do the phasmids respond to these chemicals as well? If so, do they employ signal transduction molecules similar to those used by the amphid neurons, or do they use broadly tuned molecules incapable of distinguishing among different repellents? How are the signals from the phasmid neurons integrated to modulate the functions of the locomotory circuit, and are these responses altered by experience? Finally, do other organisms also integrate information from spatially separated chemosensors to modulate behavioral responses, and is this mechanism limited to the avoidance of toxins? Maybe the tail will tell.

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