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Do rodents smell with sound?

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ABSTRACT

Chemosensation via olfaction is a critical process underlying social interactions in many different species. Past studies of olfaction in mammals often have focused on its mechanisms in isolation from other systems, limiting the generalizability of findings from olfactory research to perceptual processes in other modalities. Studies of chemical communication, in particular, have progressed independently of research on vocal behavior and acoustic communication. Those bioacousticians who have considered how sound production and reception might interact with olfaction often portray odors as cues to the kinds of vocalizations that might be functionally useful. In the olfaction literature, vocalizations are rarely mentioned. Here, we propose that ultrasonic vocalizations may affect what rodents smell by altering the deposition of inhaled particles and that rodents coordinate active sniffing with sound production specifically to enhance reception of pheromones. In this scenario, rodent vocalizations may contribute to a unique mode of active olfactory sensing, in addition to whatever roles they serve as social signals. Consideration of this hypothesis highlights the perceptual advantages that parallel coordination of multiple sensorimotor processes may provide to individuals exploring novel situations and environments, especially those involving dynamic social interactions.

Sensory processing in most species involves selective sampling of internal and external inputs through dynamic movements of end organs. Integrating across successive samples makes perception possible, guiding ongoing actions that lead to further selective sampling. Information seeking actions create stable states of perception-action coupling that drive much of the structure observed in both behavior and its neural correlates (Ahissar and Assa, 2016; Gibson, 1979; Warren, 2006). Following from Gibson's (1979) astute observation that, "We must perceive in order to move, but we must also move in order to perceive," one might add that we must select in order to perceive.

In most sensory modalities, this selection process is somewhat hidden. An individual might orient their head in the direction of a salient event or reach out their hand to pick up an interesting object, but the selective processes that initiated these overt actions (auditory and visual novelty detection and spatial localization) are not directly observable. There are some species, however, that behave in ways that more directly reveal their sensory sampling strategies. For instance, echolocating bats and dolphins (e.g., Simmons et al., 2014), and electrolocating fish (e.g., Carlson et al., 2019; Pedraja et al., 2020), reveal aspects of their sampling efforts through the timing and directionality of the fields they produce. Studies of animals that produce overt indications of sampling strategies can potentially clarify general principles of selective attention and perception-action coupling (Crimaldi et al., 2022; Jacobs, 2023; Roitblat et al., 1990; Schroeder et al., 2010; Wachowiak, 2011).

The most extensive studies of sensory sampling to date have been conducted with rodents[2] (e.g., Deschênes et al., 2012), and humans (e.g., Driver, 2001; S. C.-H. Yang et al., 2016). Initial interest in psychological experiments with rodents stemmed from the ease with which their actions could be manipulated and measured in behavioral tests (Hunter, 1935; Husband, 1929; Small, 1900). Their value as models of sensory processing was recognized later, primarily through studies of somatosensation (e.g., Gustafson and Felbain-Keramidas, 1977), and olfaction (e.g., Eayrs and Moulton, 1960). Rodents are particularly useful for investigations of perception-action coupling because of how they engage multiple sensory modalities during exploratory actions. Specifically, rodents show phasic relationships between sniffing, head movements, and whisking (Deschênes et al., 2012; Findley et al., 2021; Ranade et al., 2013; Welker, 1964), suggestive of highly orchestrated

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[2] Throughout this paper, the term "rodents" refers primarily to various species and strains of mice and rats.

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neural interactions across visual, tactile, olfactory, and motor systems (Courtiol and Wilson, 2017; Kay, 2005; Kepecs et al., 2006, 2007), all of which can be related to selective sampling of odorants and inspection of surfaces within the surrounding environment (Kleinfeld et al., 2023; Schroeder et al., 2010). Coordination between whisking, head movements, and sniffing is not obligatory, because these actions can occur alone and in patterns that are temporally decoupled (Fonio et al., 2015; Laplagne and Elías Costa, 2016). Understanding how the synchronization of sensorimotor processes in rodents facilitates or accommodates situation-specific sampling of inputs can potentially provide new insights into the exploratory, information-seeking, and communicative actions of many different species.

The sensations that rodents generate from actively whisking and sniffing provide complementary percepts relevant for finding food, forming social relationships, avoiding predators, and navigating. Olfactory processing, in particular, enables rodents to monitor territorial boundaries, recognize familiar individuals, detect potential predators, and assess the reproductive status of potential mates (Egnor and Seagraves, 2016; Jacobs, 2023; Stevenson, 2010). Studies of rodent olfaction have provided insights into general principles of sensory encoding (Mainen, 2006; Wesson et al., 2008), selective attention during exploration (Carlson et al., 2018; Ranade et al., 2013), the neural representation of stimuli (Leon and Johnson, 2003; Schaefer and Margrie, 2007), and memory formation (Aqrabawi and Kim, 2020; Eichenbaum, 1998), and have direct implications for human health, as shared molecular and neural pathways underlie olfaction across mammals (Lyons-Warren et al., 2021; Möhrle et al., 2020).

For rodents, olfaction involves active sampling of odorants via sniffs, as well as parallel processing of pheromones - biochemicals that are crucial for various social and reproductive behaviors. Although sniffing might seem like a less selective sensory sampling mechanism than environmental inspection via echolocation or visual saccades, sniffs enable rodents to modulate the duration, timing, location, and intensity of sampled olfactory inputs and are critical to olfactory perception (Kepecs et al., 2006; Mainland and Sobel, 2006; Wachowiak, 2011). How sniffing contributes to pheromonal processing in mammals remains unclear. Some researchers suggest that physical contact is necessary for pheromones to be sensed or completely processed (Cheetham et al., 2007; Luo et al., 2003). Additionally, most mammals have a duct between the mouth and nose through which they can sample pheromones without inhaling them. The only known way that rats and mice sample pheromones, however, is through their nostrils, suggesting that they might rely less on physical contact or ingestion than do other mammals.

Here, we review behavioral, neural, and physical evidence suggesting that rodents may have evolved a novel mechanism for selectively sampling pheromones through sniffs. The proposed mechanism involves acoustically manipulating pheromonal molecules in ways that affect how and where pheromones are deposited within the nasal cavity. In this way, rodents can potentially shift between sniffs that facilitate detection and discrimination of one class of odorants, and sniffs that facilitate the reception of pheromones. We first review the role that sniffs play in olfactory perception more generally before considering the roles they may play in pheromonal processing. Then, we present evidence from physical experiments and simulation studies showing that ultrasonic sound waves are well suited for manipulating nanoparticles. Finally, we review behavioral and neural findings suggesting that rodents can potentially enhance their reception of pheromones by using ultrasound to redistribute these organic compounds prior to inhalation. Ultimately, understanding how rodents combine and coordinate vocal actions with chemoreception may shed light on the origins of perception-action coupling and can clarify how mechanisms of selective attention contribute to social interactions.

1. Sniffs as snapshots

Smelling is a combination of chemoreception, perception, and recognition. Stimuli for the sense of smell include a wide range of chemical compounds, each with its own molecular signature. After inhalation, chemical particles can either pass through the nasal cavities and down into the lungs or may be deposited along the inner surfaces of the nose. Deposited chemicals may then bind to specialized receptor cells, initiating various signaling cascades that generate nerve impulses. In rodents, there are two main regions within the nasal cavities where such receptors are concentrated (Fig. 1), with millions present in the olfactory epithelium and vomeronasal organ (VNO). The diversity of olfactory receptors enables rodents and other mammals to detect and discriminate a vast array of different chemicals. Many receptors in the VNO are specialized for detecting pheromones (Døving and Trotier, 1998; Jacobs, 2023; Keverne, 1999).

Sniffing can occur reflexively during investigatory behavior (Ferdenzi et al., 2015; Mainland and Sobel, 2006; Schoenfeld and Cleland, 2006), and in response to the expectation of a reward (Deschênes et al., 2012). Sniffing also can be deliberately controlled (Bensafi et al., 2004; Deschênes et al., 2012), as when someone asks you to smell milk that has gone bad. In rodents, sniffing typically occurs in repetitive bouts, with the rate of sniffs varying depending on the context (Wachowiak, 2011; Welker, 1964; Wesson et al., 2009; Youngentob et al., 1987). During exploration, rodents position their heads strategically while sniffing (e.g., by rearing), thereby actively sampling the spatial distribution of airborne particles. Olfaction via sniffing is a closed-loop process (Ahissar and Assa, 2016) in that the detection of odors can trigger sniffing and sniffing can lead to the detection of odors. Rodents rapidly adjust the duration and intensity of their sniffs based on their recognition of smells and perception of odorant concentration, which may lead to olfactory constancy and/or reduced sensory adaptation (Mainland and Sobel, 2006).

The act of sniffing may enhance olfactory sensitivity and discrimination, as it facilitates the sampling of a larger number of odorants present in the environment (Courtiol et al., 2014). Sniff rate may modulate airflow to match the specific absorption rate of certain odorants (Mainland and Sobel, 2006; Schoenfeld and Cleland, 2006), thereby facilitating the perception of odorants. The possibility that sniffs modulate how odorants are processed is referred to as the sorption or zonation hypothesis (Wachowiak, 2011). Whether such flow-modulated optimization of reception actually happens, however, remains unclear (Coppola, 2022). Variations in sniff duration, rate, and intensity influence where and when odorants are deposited within the nasal cavities (Oka et al., 2009; Schoenfeld and Cleland, 2006; G. C. Yang et al., 2007; Zhao et al., 2006). Consequently, by adjusting sniffs in real-time, based

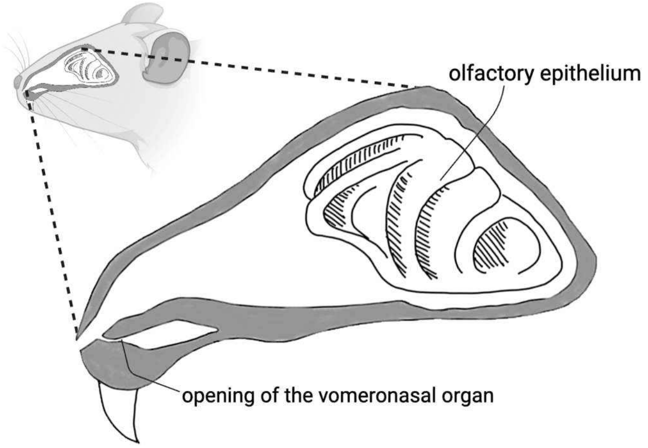

Fig. 1. *Regions in the Rodent's Nasal Cavities Where Airborne Particles are Collected, Note.* Microscopic openings near a rodent's nostrils lead to small, mucus filled tubes that deliver fluid-entrapped particles to receptors within the vomeronasal organ, while airborne particles are directly deposited onto the olfactory epithelium as air passes over this region.

on recently detected odorants or on learned associations, rodents may selectively refine olfactory percepts based on their current circumstances and informational needs.

Sniffs determine not only when and how airborne particles register at olfactory receptors, but also the responses of tactile receptors to airflow within nasal cavities. These somatosensory responses to airflow turn out to be critical for olfactory perception. When airflow is absent, individuals are less likely to report detecting any odor (Kepecs et al., 2007; Youngentob et al., 1987), and when air puffs occur in the absence of odorant reception, individuals are more likely to perceive illusory odors (Gottfried, 2006). Somatosensation of moving air within the nose thus appears to be both necessary and sufficient for smell percepts to form.

The increased airflow associated with sniffs can also increase the number of odorant molecules that bind to olfactory receptors. Repetitive nostril movements in rodents can entrain surrounding air movements, creating currents toward the nose that further expand the sampling range (Kepecs et al., 2006). Often, sniffing is necessary for odorants to even reach the olfactory epithelium, the regions in the nasal cavity where most olfactory receptor cells are located (Fig. 1). Thus, sniffs play a key role in initiating the neural signals involved in olfaction.

Many past discussions of olfaction describe olfactory transduction at receptors in the epithelium as the starting point for smell percepts. Given that most olfactory transduction (at least in exploratory contexts) will occur only after a sniff, this portrayal would only be accurate in cases where initial detection of an odor was incidental to a rodent's ongoing actions. When rodents are actively sampling odors, the starting points for percepts are the actions individuals make in seeking out odorants rather than the transduction of successfully obtained samples. In other words, when rodents detect novelty, feel uncertainty, or experience curiosity about their current context, they often sniff to actively explore and refine their perception of the surrounding smellscape, attempting to fill gaps in their knowledge rather than simply waiting for receptor activation to trigger olfactory processing.

Olfactory processing likely benefits from temporal linkages between sniffs and other ongoing motor and neural activity (Kepecs et al., 2007; Rosero and Aylwin, 2011; Schoenfeld and Cleland, 2006; Wachowiak, 2011; Wesson et al., 2008, 2009). For instance, rhythmic patterns of sniffing are often synchronized with whisking movements and hippocampal theta rhythms (Kepecs et al., 2007; Ranade et al., 2013). Additionally, detection of airflow in nasal cavities (i.e., somatosensation) generates theta waves in olfactory cortex (Kepecs et al., 2006), which may further facilitate multimodal synchronization of neural activity. It remains unclear what exactly the benefits of crossmodal coupling are, but one possibility is that synchronization of the olfactomotor system with other information seeking actions (e.g., whisking and visual inspection) facilitates multimodal integration of inputs within a common temporal (Kepecs et al., 2006; Komisaruk, 1970), or spatial framework (Jacobs, 2012). Every individual sniff performed by a rodent provides a stroboscopic sample of transduced odorants - an odor snapshot tagged to a specific time and place (Crimaldi et al., 2022) - somewhat like the echoic returns produced by a single cry from a bat echolocating while in flight. Sniffing is not merely a mechanical vacuuming process. Sniffing is a sampling effort intertwined with ongoing neural interactions within and outside of the olfactory system, influencing the timing and synchronization of activity in brain regions that contribute to the perceptually distinctive qualities of smell (Sharma et al., 2019).

In summary, sensorimotor control of sniffing plays a key role in olfaction. Sniffing involves coordinated motor actions driven by multiple sensory inputs and internal states. Rodents vary sniffing patterns based on the characteristics of detected odors, adjusting the frequency, duration, and intensity of inhalations to optimize scent detection and discrimination. Olfactory information is combined with somatosensation, allowing for more rich and comprehensive perception of the environment that enables rodents to make informed decisions while exploring, foraging, navigating, socializing, or avoiding potential threats (Deschênes et al., 2012; Findley et al., 2021; Jacobs, 2012; Schroeder et al., 2010).

2. Mechanisms for sampling pheromones

Rodent olfaction requires parallel processing across multiple sensory subsystems. Many studies of olfaction focus on describing mechanisms of chemoreception in the olfactory epithelium and/or in the VNO. These two subsystems are functionally, structurally, and spatially divergent, containing different receptor cell types, different mechanisms for collecting airborne particles, and projecting to different brain regions. Vomeronasal processing enables rodents to identify the species, gender, and identity of other animals from pheromones (Brennan, 2001; Brennan and Kendrick, 2006; Tirindelli, 2021; Wyatt, 2010), suggesting that the VNO provides information analogous to that used for face or voice recognition in humans.

While all mammals use sniffs to sample airborne particles, some mammals have evolved other sampling mechanisms more specifically linked to sensing pheromones. For instance, flehmen is an action that several mammals (e.g., goats, sheep, and lions) perform with their heads and mouths when collecting chemical samples associated with the reproductive status of conspecifics (e.g., from urine or genital secretions).[3] During flehmen, an individual typically adopts a stereotyped head posture, curls its upper lip, and moves its tongue along the roof of its mouth. These actions are thought to promote transfer of pheromones from the mouth to the VNO. Males flehmen after smelling the anogenital area or fresh urine of a female. Females also perform flehmen responses when investigating the urine of other females, but less frequently than is seen in males (Hart, 1983; Ladewig and Hart, 1980). Flehmen frequency also varies with seasonal fluctuations in hormones (Hart, 1983). Although this mode of pheromone sampling is most prevalent during sexual interactions, it also occurs in all-male groups and when females are investigating fluids produced during birth. Flehmen appears to be an analogue of sniffing directed specifically at enhancing chemosensation of pheromones within the VNO (Hart, 1983; Petrulis et al., 1999). Generally, the flehmen response is preceded by an olfactory investigation (Hart, 1983), suggesting that detection of specific odorants triggers the response. The specific role the flehmen response plays in olfactory perception is not entirely clear, but it is presumed to supplement or refine the information that animals might gain through sniffing alone.

Rodents release pheromones into the environment in much the same way as other mammals - through gland secretions and urine - and for many of the same reasons, including marking territories and communicating with conspecifics in reproductive contexts. As one might expect, sniffing features prominently when rodents are investigating fresh urine and the reproductive status of individuals they encounter (Hurst, 2009). Rats and mice do not show a flehmen response and do not appear to transmit pheromones to the VNO through their mouths (Hamacher et al., 2024; Hart, 1983). The fact that rodents do not flehmen suggests three possible scenarios: (1) mammals that flehmen have enhanced pheromonal reception relative to rodents; (2) the specific anatomical features of rodents' nasal cavities in some way achieves similar outcomes as a flehmen response with respect to pheromone collection and deposition; or (3) rodents have evolved alternative mechanisms for enhancing pheromone reception. Here, we evaluate the third possibility.

If rodents have evolved an alternative mechanism for increasing the amount or quality of pheromones that reach the VNO, then it is likely that they would engage this mechanism in contexts where flehmen is prevalent in other mammals, namely during social interactions with conspecifics and during the inspection of excreted fluids. Additionally, this mechanism would likely be triggered by the detection of specific

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[3] Some dogs chatter their teeth when inspecting urine from a conspecific; whether this reaction contributes functionally to processing of pheromones is unclear.

odorants produced by conspecifics (Ben-Shaul et al., 2010; Brennan, 2001; Tirindelli et al., 2009), or by stimuli that have become associated with such odors (Brennan, 2001; Brennan and Kendrick, 2006; Tirindelli, 2021), and thus should be linked with sniffing. In short, if rodents have any means of selectively increasing their ability to transduce pheromones (i.e., if their olfactomotor systems can "fixate" in ways that increase or refine the activation of pheromonal receptors), then rodents should engage these mechanisms in situations where obtaining the information available from pheromones is most functionally relevant. Rodents reliably produce ultrasonic vocalizations (USVs) when encountering conspecifics (Knutson et al., 2002; Okanoya and Screven, 2018), and when inspecting urine (Musolf et al., 2010; Roullet et al., 2011), thereby fulfilling all these criteria.

Observational studies of rats and mice implanted with pressure sensors revealed that rodents vocalized most often when they were actively sniffing, producing ultrasonic chirps (~50 kHz) at specific phases of the sniff cycle (Sirotin et al., 2014). Specifically, USVs were initiated immediately after inhalation and ended prior to the subsequent sniff (i.e., leading to alternating sniffs and USVs). In this way, the sniff cycle naturally segments sound production into bouts of discrete calls and the rate of sniffing determines the rate of calling. Both sniffing and vocal production in rodents often occur at theta frequencies (~5–10 Hz) (Kepecs et al., 2006; Perrodin et al., 2023; Vanderwolf and Szechtman, 1987). USV production does not appear to be a byproduct of sniffing, because rodents produce many sniffs with comparable pressure changes without producing any USVs (Sirotin et al., 2014).

The functional significance of tight coupling between vocal production and sniffing in rodents remains unclear. These interlocking processes could arise due to evolutionary constraints on the development of orofacial motor programs (Schoenfeld and Cleland, 2006; Sirotin et al., 2014). There might also be reproductive advantages to rapidly communicating information that is being obtained or sought, with respiratory and sniffing patterns simply constraining how rapidly that information can be transmitted. Given that activity and arousal levels strongly affect respiratory patterns, linking USV production rate to sniff rate might also provide listening conspecifics with indictors of a sniffing rodent's current physiological state (Sirotin et al., 2014). In all these scenarios, interleaved sniffing and vocalizing enables rodents to both collect information about conspecifics (through sniffs) and to provide information to conspecifics (through USVs) in parallel. Because rodents often produce 50 kHz vocalizations during social interactions (or in reaction to discovering urine), the transmitted information is thought mainly to facilitate reproductive behavior (Egnor and Seagraves, 2016; Willadsen et al., 2014), and/or to indicate that the vocalizer is in a positive state (Brudzynski, 2007, 2021; Burgdorf and Moskal, 2010).

Conspecifics hearing a sniffing rodent vocalize can gain behaviorally relevant information about the vocalizer. Importantly, predators with the capacity to hear ultrasound can also potentially benefit from this information, at a high cost to the vocalizer. The fact that 50 kHz vocalizations provide information about the vocalizer does not imply that this is their primary function (Blumberg, 1992; Blumberg and Alberts, 1992). In principle, these vocalizations could be inadvertent, like grunts (Blumberg and Alberts, 1992), or might provide the vocalizer with information about its environment, as occurs during echolocation (Gleason et al., 2023; Simmons et al., 2014). In the context of exploratory sniffing, a third possibility is that production of USVs may facilitate or enhance a rodent's ability to smell. In this scenario, 50 kHz vocalizations are tightly linked to sniffing because, like sniffing, they increase an individual's ability to selectively sample air-borne molecules, particularly pheromones.

How might ultrasonic vocalizations enhance olfaction? Sniffing increases the intake of molecules, thereby increasing opportunities for receptors to bind to those molecules. This allows for more effective and selective sampling of the molecules present at a particular location. Sniffing also imposes a rhythmic temporal pattern onto collected samples that can potentially affect how receptor activation influences neural processing (Courtiol et al., 2011; Schoenfeld and Cleland, 2006; Wesson et al., 2008), thereby increasing sensitivity to odors (Kepecs et al., 2007; Mainland and Sobel, 2006). When a rodent sniffs, the functional outcome is a boost to chemoreception beyond some modal baseline, much like visual fixations can selectively enhance the perception of elements within a visual scene. If *vocal sniffs* (Sirotin et al., 2014) are advantageous for olfaction, then presumably this is because they in some way further enhance reception or processing of biologically-relevant molecules. We hypothesize that the ultrasonic vibrations produced by vocalizing rodents cause small airborne particles to collide and stick together, a process called agglomeration. Agglomeration can lead to the formation of larger clusters of particles, thereby altering the size distribution of particles in the air. As discussed below, the size of inhaled particles affects where in a rodent's nasal cavities those particles will come to rest. By changing the size distribution of incoming particles, a rodent could potentially shift the location(s) where the particles settle, thereby selectively boosting registration of those particles at specific locations within the nasal cavities (Fig. 2). Hereafter, we refer to this hypothesis as the Ultrasonic Sieving (US) hypothesis. According to this hypothesis, rodents produce USVs to selectively enhance or modulate chemoreception of a subset of incoming molecules, specifically pheromones. In the following sections, we evaluate more closely the possibility that USV production enhances rodents' olfactory processing of pheromones.

3. Evaluating the ultrasonic sieving hypothesis

Pheromonal reception is an important aspect of rodents' daily lives. There is clear behavioral evidence that rodents are motivated to sample pheromones both directly from other individuals and indirectly from environmental sources such as urine (Baum, 2012; Bigiani et al., 2005; Johnston, 2003; Tirindelli et al., 2009). The main issues that need to be considered when comparing the US hypothesis to other proposed explanations for USV production in association with sniffing are: (1) Do USVs physically affect behaviorally-relevant organic molecules inhaled during sniffs? (2) Are any USV-related changes to such molecules conducive to enhanced chemoreception within a rodent's nasal cavities? and (3) Are rodents' actions during vocal sniffs consistent with active sensory processing? In the following, we review available evidence relevant to answering each of these questions, highlighting gaps in current knowledge that need to be filled to definitively test this hypothesis.

3.1. How ultrasonic vibrations affect airborne particles

When a rodent produces a USV, the resulting oscillations will necessarily affect the movements of any airborne nanoparticles around the rodent's head. This outcome is guaranteed by the physics of sound wave propagation in air (Nummela and Thewissen, 2008). A key assumption underlying the US hypothesis is that the USV-associated vibrations of airborne molecules around a rodent's nose will lead to interactions between those molecules that will change their configurations and distribution. Studies of particle agglomeration in non-biological contexts provide direct evidence of such effects (Čereška et al., 2016; T. L. Hoffmann and Koopmann, 1996; Khmelyov et al., 2023; Lilliehorn et al., 2005; Liu et al., 2009; Riera et al., 2006; Wang and Hu, 2015).

The mechanisms through which airborne, ultrasonic vibrations can cause tiny particles to agglomerate have been studied most extensively in filtration systems (Eggersdorfer and Pratsinis, 2014; Trujillo et al., 2014). For example, 50 kHz signals have been used to remove fine droplets from air (Wang and Hu, 2015), and 24 kHz signals have been used to agglomerate sand dust particles between 3–10 micrometers in diameter (Čereška et al., 2016). In the fields of sonochemistry and vibroengineering, the process of agglomerating particles by subjecting

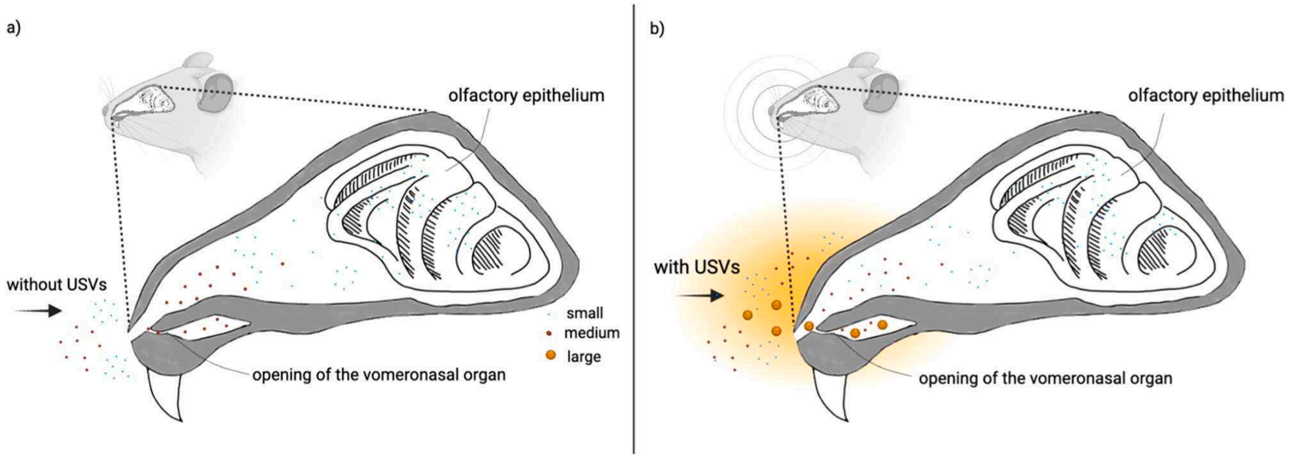

Fig. 2. *Hypothesized Effect of Ultrasonic Vocalizations on Airborne Particles, Note.* (a) A typical sniff produced without any vocalization will deposit airborne particles in different locations within a rodent's nasal cavity depending on the sizes of those particles. (b) The ultrasonic sieving hypothesis proposes that when a rodent produces an ultrasonic vocalization immediately prior to sniffing, this causes nanoparticles near the rodent's nostrils to agglomerate into larger particle clusters, thereby increasing the probability that those larger clusters of particles will be deposited near the opening of the vomeronasal organ.

them to ultrasound is called acoustic agglomeration (Song et al., 1994; Zhang et al., 2020; Zhou et al., 2016). Various theoretical models and simulations suggest that sound can promote agglomeration of small particles through multiple mechanisms, including collisions, dynamic flow interactions (e.g., when a particle is sucked into the wake of a nearby moving particle), and interacting molecular forces (Bantz et al., 2014; Eggersdorfer and Pratsinis, 2014; Khmelyov et al., 2023; Vollath, 2023). Experimental studies have shown that as the frequency of vibration increases, the agglomerating effects on particles smaller than one micrometer increase (Liu et al., 2009), and that higher amplitude vibrations lead to more agglomeration (Gallego-Juárez et al., 1999).

Past studies of acoustic agglomeration have focused on understanding how sound aggregates inorganic particles and on identifying how sonic and ultrasonic agglomeration can be used to remove pollutants from exhaust gases. While it is likely that organic molecules suspended in air are affected by sound fields in similar ways, such phenomena have so far been understudied. Experiments that examine the effects of ultrasonification on gaseous and fluid mixtures that a rodent might inhale during a sniff are needed to identify which particles are most likely to become agglomerated in the presence or absence of sound waves. For the purposes of this paper, we assume that at least some organic molecules will agglomerate when exposed to ultrasound in the same manner as inorganic molecules and leave this as an untested prediction of the US hypothesis.

USVs produced by rodents could potentially cause nearby nanoparticles to agglomerate while having no effect at all on olfactory processes. Agglomeration would not determine which airborne particles are available for detection and should not affect the number or density of particles within the volume of air available for sampling. The main difference between a sample of organic molecules that has been agglomerated versus one that has not is that the distribution of particle sizes changes. There are no existing measures of the distribution of particle sizes within samples of air near a urine deposit or near a rodents' genitals, head, or skin. There are, however, measures of the sizes of volatile odorant molecules and various pheromones that are present within and around such sources of organic compounds.

The behaviorally-relevant molecules that a sniffing rodent is likely to inhale are structurally diverse, but universally miniscule. On average, odorants are smaller than pheromones, though the distribution of sizes is overlapping and continuous. The larger pheromones include complex molecules like proteins and peptides. These molecules (e.g., major urinary proteins) have molecular weights of ~18–20 kDa (Liberles, 2014), corresponding to a radius on the order of two nanometers. Experimental and computational studies of particle deposition within the nasal cavities of rodents (Dong et al., 2018, 2022; Kelly et al., 2001; Shang et al., 2015), and humans (Tian et al., 2019), indicate that particle size strongly affects where particles are deposited within nasal cavities during inhalation. Simulations of the deposition of nanoparticles in the nasal cavities of rodents show complex, size-dependent variations in deposition patterns (Dong et al., 2022; Jiang and Zhao, 2010; Tian et al., 2019). For example, particles 2 nm or smaller (which would include all odorant and pheromone molecules) were less likely than 10 nm particles to reach receptors in the olfactory epithelium. Simulations of nanoparticle deposition also revealed that increasing flow rate increased the efficiency with which nanoparticles of a subset of sizes were captured within olfactory regions (Dong et al., 2018; Tian et al., 2019). The effect was most pronounced for particle sizes larger than any isolated pheromone molecules or other odorants. These findings suggest that if USVs agglomerate behaviorally-relevant airborne molecules, then this effect may be most advantageous when the resulting agglomerations fall within a restricted range of sizes.

There are significant gaps in what is currently known about the biophysics of chemoreception via inhalation in any mammal, largely due to methodological constraints. Increasing interest in nanotechnologies and the health effects of inhaled nanoparticles are rapidly removing many of these constraints, however. The US hypothesis makes several novel predictions about what happens during a vocal sniff that are not made by any alternative hypotheses, including: (1) self-generated ultrasonic sound fields around a rodent's head will rapidly change the distribution of particle sizes present; (2) the particles affected will include behaviorally-relevant molecules, such as pheromones and possibly other odorants, that rodents are sampling; (3) acoustic agglomeration will affect the distribution of particle sizes in ways that modify where behaviorally-relevant particles are deposited within a rodent's nasal cavities; and (4) the agglomeration-related changes in particle deposition within nasal cavities will increase the number of behaviorally-relevant particles that are sensed in specific regions.

Predicting what will happen to nanoparticles positioned near an ultrasonic source is nontrivial. Such predictions are further complicated when the source is moving (as rodents typically are when sniffing), and when the distribution and heterogeneity of particles within inhalation range is not well described. Detailed measurements of the acoustic field surrounding a vocalizing rodent's head are unavailable. Properties of ultrasonic fields surrounding the heads of bats (Jakobsen et al., 2013), and dolphins (Au et al., 1986, 1999), have been measured and modeled, however. In both groups, projected ultrasonic sound waves are highly directional, with most energy focused in a narrow beam aligned in the direction the animal is facing. USV production by rodents typically occurs close to at least one solid boundary, which will influence the properties of the acoustic fields generated and which could affect how nanoparticles agglomerate. Because USVs are rhythmically produced, the associated acoustic fields will be analogous to a strobing light, which is also the case for echolocating bats and dolphins. Given that bats vocalize at similar frequencies for comparable durations in air, acoustic radiation from their heads approximates how air likely vibrates around the head of a vocalizing rodent. Bat vocalizations have evolved in ways that increase their effective propagation over long distances, however, whereas rodent behavior and habitats suggest that their vocalizations are not propagating as far. For example, rodents often vocalize with their mouths closed or barely open and with their head close to the genitals or body of another animal, positions that are likely to reduce the range of sound transmission.

Describing the acoustic field around a vocalizing rodent's head is technically challenging, especially in the regions near a rodent's nose that would be relevant in relation to inhalation. Introduction of recording devices at such close ranges could potentially change the form and effects of the emitted field. However, knowing the nature of the ultrasonic field around a rodent's head is particularly relevant to assessing whether a primary function of USVs is to redistribute to-be-inhaled particles, because the acoustic fields that are maximally useful for communicating with conspecifics should differ significantly from those that are best suited for agglomerating nanoparticles prior to inhalation. Vocalizations that evolved to enhance chemoreception should be conducive to vibrating near-nose air in ways that promote particle agglomeration, as opposed to reliably propagating to conspecifics that are out of visual range.

The predictions summarized above do not specify which particles inhaled by rodents are most likely to be affected by ultrasonification. The fact that not all sniffs are vocal sniffs implies that if rodents are using USVs to enhance olfaction, then they are doing so selectively. The following sections provide evidence suggesting that USVs may selectively enhance the collection and processing of pheromones.

3.2. *Dispersion, collection, and processing of odorants and pheromones*

Part of the challenge of olfaction is that there are many particles that an animal might inhale that are either functionally irrelevant or deleterious. Sniffing is not simply an act of particle collection. It is the biological equivalent of separating the wheat from the chaff. Collecting, detecting, and decoding chemical signals from conspecifics is especially crucial for communication and environmental responses, particularly in contexts such as mate selection and territorial interactions, driving the evolution of mechanisms that can enhance pheromonal reception (e.g., flehmen), including in the glands that secrete pheromones.

Glands that release pheromones in rodents are found near the genitals, behind the eyes, in the skin, and near the mammary glands. Sniffs directed toward these regions (or their fluid products) can be viewed as selective attempts by individuals to collect and sense pheromones. Pheromones are often categorized based on their volatility – how likely a substance is to vaporize – which is correlated with their size (i.e., smaller molecules tend to be more volatile). Some of the largest, non-volatile pheromones are thought to only be transferred through direct nose-to-gland contact (He et al., 2010; Luo et al., 2003), or nose-to-urine contact (Cheetham et al., 2007). However, vaporization is not the only way that organic molecules can become airborne (e.g., consider sneeze-launched ejecta), and the specific biophysical mechanisms that enable rodents to sample pheromones have yet to be identified.

Pheromone-rich urine provides critical information about reproductive status, genetic compatibility, and social hierarchy between rodents (Francia et al., 2014; Keverne, 1999; Tirindelli, 2021). As urine evaporates, volatile components are released into the air, initiating the dissemination of pheromone cues within the surrounding environment (He et al., 2010). Aerosolization mechanisms may also contribute to the spread of pheromones from urine (Beynon and Hurst, 2003). These aerosols, consisting of minuscule liquid droplets carrying pheromones, may become suspended in the air, allowing for increased persistence of pheromone concentration due to the slow diffusion of aerosols (Jami et al., 2020). Airborne pheromones will be more dispersed than pheromones located near glands or in fluids released by those glands, leading to large variations in the concentration of organic molecules available for sampling.

Sniffing rodents collect series of air and possibly fluid samples by creating suction at locations where pheromones or other relevant odors may be present. Rodents have evolved elaborate convolutions within their nostrils and nasal cavities that likely facilitate filtration of biologically irrelevant particles (Dong et al., 2022)(Fig. 3). As noted earlier, the two major classes of inputs transduced by olfactory receptors – general odorants and pheromones – are processed in spatially segregated regions of the nasal cavities (Breer et al., 2006; Mori and Sakano, 2021) (Fig. 1). The entryways to the VNO consist of two tiny openings positioned laterally within pit-like depressions on the floor of the nasal cavity near the nostrils (Hamacher et al., 2024)(Fig. 3). Most olfactory receptors line the olfactory epithelium at the opposite corner of a rodent's nasal cavities, making up the main olfactory system (Halpern, 1987; Keverne, 1999; Tirindelli et al., 2009).

The mechanisms for transmitting particles to receptors within these two catty-cornered regions differ significantly. The VNO appears to convey solubilized molecules to receptors via two, thin, mucus-filled tubes that operate in ways loosely analogous to the digestive systems of conjoined earthworms (Hamacher et al., 2024; Meredith, 1994; Torres et al., 2023). Reception along the olfactory epithelium involves processes more akin to how a sundew entraps prey (Morrison and Costanzo, 1992). Transfer of particles from the microscopic entrances to the vomeronasal ducts to receptors within the VNO involves repetitive dilation and constriction of blood vessels, and/or surrounding muscles, leading to suctioning of fluid (Hamacher et al., 2024; Iwanaga and Nio-Kobayashi, 2020; Meredith et al., 1980; Yoles-Frenkel et al., 2017). Consequently, particles that settle within fluid-filled pits on the floor of a rodent's nasal cavities close to the nostrils are more likely to be suctioned into and transduced by the VNO (Breipohl et al., 1979; Hamacher et al., 2024; Naguro and Breipohl, 1982; Stowers and Spehr, 2015), and particles swept along airborne into the upper reaches of the nasal cavities are more likely to be transduced by the olfactory epithelium (Figs. 2 and 3).

According to the US hypothesis, the proportion of pheromones

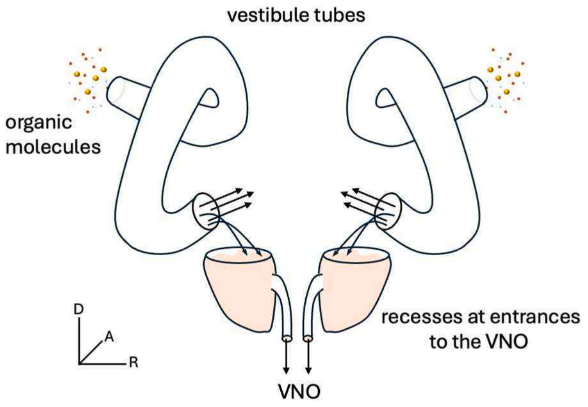

Fig. 3. *Schematic of the Nasal Vestibule in Relation to the Vomeronasal Duct Openings, Note.* Particles entering a rodent's nostrils travel through a looping path within the nasal vestibule before emerging into the nasal cavity. Once particles enter the nasal cavity, they may continue travelling airborne or may be deposited on the floor of the cavity. The suction produced by pumping mechanisms in the VNO pulls in fluid located within small recesses near the entrances to the nasal cavity, such that only a subset of inhaled particles will be sensed by this organ. Structural properties of this schematic were constructed based on anatomical studies of rats (Dong et al., 2022; Hamacher et al., 2024).

deposited near VNO entrances will increase when rodents agglomerate inhaled pheromones using USVs. Larger particles are generally less likely to be deposited within the upper regions of the nasal cavities (Schroeter et al., 2012). Any process that redistributes the sizes of incoming nanoparticles thus can potentially affect which receptors bind to inhaled particles. Organic molecules will be solubilized before becoming bound to receptors in both the olfactory epithelium and in the VNO. Furthermore, the kinds of odorants processed by the VNO and olfactory epithelium overlap in that some receptors in the olfactory epithelium can detect peptides and some receptors within the VNO can detect volatiles (Liberles, 2014; Spehr et al., 2006). A shift in the distribution of receptor activation would not preclude processing of pheromones by the olfactory epithelium, but could affect how olfactory inputs are perceived and interpreted. By analogy, redirecting one's gaze can shift reception of light by rods and cones in the retinal periphery to reception by densely packed cones in the fovea, thereby increasing resolution of colors.

The dendritic terminals of receptor neurons within the VNO form knobs with a few hundred microvilli immersed in the mucus of the cavity (Tirindelli, 2021). The microvilli project into the VNO lumen and are believed to be the subcellular sites of VNO receptor cells that interact with incoming VNO-targeted pheromones (Baxi et al., 2006; Estes, 1972; Menco et al., 2001). At the apical half of the VNO, neurons express the V1R family of receptors, while the basal half expresses V2R receptors, indicating specializations for detecting different types of pheromones (Trinh and Storm, 2004). V1R receptors respond to volatile molecules and steroids, in contrast to V2R receptors, which differentiate peptides and proteins (Dulac and Torello, 2003; Tirindelli, 2021; Touhara and Vosshall, 2009). Reception of pheromones within the VNO triggers neural responses that influence mate selection, territorial marking, and alterations in reproductive and social interactions (He et al., 2010; Liberles, 2014; Shorey, 2013).

VNO anatomy, coupled with the specificity of the receptors it houses, equips the VNO with sensitive pheromonal detection and discrimination abilities, facilitating the transmission of messages that encompass crucial information about an individual's reproductive status, genetic compatibility, and social hierarchy (Francia et al., 2014). Pheromonal activation of VNO neurons is highly specific since their receptors are not activated by additional ligands even at high concentrations (Leinders-Zufall et al., 2000). Such specializations are only functionally relevant, however, if there is adequate deposition of pheromones at highly localized regions within a rodent's nasal cavities (i.e., near the openings to the VNO).

Vomeronasal receptors project to the accessory olfactory bulb, which relays information to amygdalar and hypothalamic nuclei (Stowers and Logan, 2010). Unlike activity in the main olfactory bulb, firing patterns within the accessory olfactory bulb do not appear to entrain to the sniffing cycle (Tsitoura et al., 2020). These firing patterns are also unlikely to entrain to pumping rhythms within the VNO. There is not yet evidence of any functional coupling of pumping mechanisms with sniffs, vocal sniffs, or production of USVs. Nevertheless, there are multiple sites of convergence between the main olfactory system and the vomeronasal system that could mediate coordinated interactions between these systems (Baum and Larriva-Sahd, 2014). Furthermore, single neurons that encode both sound and smell have been identified in regions known to be major drivers of motivation (Varga and Wesson, 2013; Wesson, 2020; Wesson and Wilson, 2010, 2011), which could further facilitate the coordination of ultrasound production with olfactory processes and pheromonal reception.

The advantages that rodents could gain from adaptations that enhance pheromonal reception are clear. For one, the VNO plays a key role in facilitating precise mate selection, allowing rodents to discern subtle variations in pheromonal cues related to genetic compatibility and reproductive fitness (Goldey and van Anders, 2015; Witt and Wozniak, 2006). By increasing or refining the inputs processed by the VNO, rodents may better find potential mates or detect threats, thereby enhancing their reproductive success. Another way rodents could benefit from selective boosting of VNO reception is through territorial marking, a common behavior among rodents. The VNO is instrumental in decoding and responding to pheromonal signals associated with territorial boundaries (Arakawa et al., 2008; Isogai et al., 2011), and selective enhancement of VNO processing would allow for more effective marking and interpretation of these chemical cues, reducing the likelihood of territorial disputes. Increasing pheromonal transduction by the VNO may also enable rodents to make rapid adjustments to alterations in their environment (e.g., variations in population density, habitat availability, or shifts in the overall ecological landscape). Because the VNO plays such an important role in rodents' social interactions, adaptations that enhance processing within the VNO could greatly improve rodents' evolutionary success and ecological adaptability by increasing their capacity to navigate complex social dynamics, reproduce, and respond adaptively to environmental challenges.

The proportion of investigatory sniffs during physical social interactions that are vocal sniffs has not been closely monitored, but the tendency of rodents to produce USVs when their nostrils are close to a conspecifics' glands or urine is well known (John et al., 2023; Sangiamo et al., 2020; Wesson, 2013). In fact, presenting urine so reliably evokes USVs that this technique is often used to collect recordings of USVs from lone rodents (e.g., Chabout et al., 2015; F. Hoffmann et al., 2009). The US hypothesis predicts that rodents will predominantly produce vocal sniffs when they have either detected cues predictive of the presence of pheromones (i.e., after smelling associated odorants), or are directly engaged in attempts to collect information from detected pheromones (e.g., when closely interacting with a conspecific). The following section considers more closely whether past behavioral observations support these predictions.

3.3. *Ultrasound production and concomitant behavior*

Interest in the vocal behaviors of rodents has increased dramatically over the last fifty years, largely because of their increasing importance as animal models of various disorders (reviewed by Caruso et al., 2020; Schwarting, 2023; Yao et al., 2023). Consequently, sophisticated technologies are now available not only for rapidly and objectively characterizing the sounds rodents make (de Chaumont et al., 2021; e.g., Fonseca et al., 2021; Goussha et al., 2022; Stoumpou et al., 2023), but also for correlating the vocalizations of individuals with actions performed in a broad array of social contexts (e.g., Heckman et al., 2017; Sangiamo et al., 2020), and for relating sound production and perception to neural activity. Most of this work focuses on vocalizations produced by laboratory animals, with only a few studies characterizing the vocal behavior of rodents in more naturalistic settings (Briggs and Kalcounis-Rueppell, 2011; Chen et al., 2023; Musolf et al., 2010). Several authors have recently reviewed findings from studies of USVs in rodents (e.g., Brudzynski, 2021; Fernández-Vargas et al., 2022; Heckman et al., 2016; Premoli et al., 2023; Simola and Granon, 2019), and no attempt will be made here to replicate those efforts. There is wide consensus among researchers studying rodent vocalizations that USVs are primarily communicative signals that rodents use during social interactions and/or to express emotional states. Most papers that note alternative possibilities (e.g., that USVs are produced as a byproduct of other mechanisms or might be used as echolocation) often do so briefly and mainly to discount those alternatives.

The current paper focuses on a subset of USVs – those containing the highest frequencies – that are known to be phase-locked with sniffing in rats and mice (sometimes referred to as 50 kHz USVs). These higher-frequency USVs are associated with courtship in mice (e.g., Matsumoto and Okanoya, 2016; White et al., 1998; Zala et al., 2020), and with positive affective states in rats (e.g., Burgdorf and Moskal, 2010; Knutson et al., 2002; Yuki and Okanoya, 2014). Other USVs that have not been linked to sniffing behavior, such as the USVs produced by pups when separated from their mothers (Heckman et al., 2017), or by adults in reaction to the detection of predators (Blanchard et al., 1990), are not directly addressed or explained by the US hypothesis.

Correlations between USV production and a broad range of social and asocial contexts have been reported (Chabout et al., 2015; Hurley and Kalcounis-Rueppell, 2018; Sangiamo et al., 2020; M. R. Warren et al., 2020). There are some discrepancies across reports, however, regarding when males versus females vocalize and with respect to the influences that USVs have on social interactions between rodents. For instance, early reports suggested that male mice use USVs to gain reproductive access to females (Holy and Guo, 2005). These functions were inferred from observations of male mice producing USVs in the presence of females (or when exposed to urine from females). The rate and types of USVs that mice produce vary as a function of the context and sex of the vocalizer (e.g., Marconi et al., 2020; Zala et al., 2020), consistent with the idea that these vocalizations are serving a social function.

Observations of mice vocalizing in the wild (Hammerschmidt et al., 2012; Petric and Kalcounis-Rueppell, 2013), and continuously over multiple days (Ey et al., 2020), painted a somewhat different picture, however. Female and male mice were found to vocalize at comparable rates and in similar contexts, producing acoustically comparable USVs (Petric and Kalcounis-Rueppell, 2013). Only female-to-female vocal interactions exceeded what would be expected based on vocalization rates when mice were alone (i.e., USVs did not increase during social encounters). These findings are not what one would expect if USVs are primarily courtship signals that male mice use to entice females: males courting females should vocalize more when with females than when alone and should use USVs that are in some way distinctive from those used by females interacting with females. Observations of correlations between USV production and social contexts cannot definitively establish how mice are using USVs, even in situations where those correlations are consistent between laboratory and field studies. Mismatches in observed correlations across laboratories, methodological approaches, and contexts further weakens the functional inferences one can draw from such correlational studies.

Experimental studies of USV production and reception in rodents potentially could allow researchers to form more firm conclusions about how rodents use USVs. For example, playbacks of USVs can potentially provide evidence that USVs produced by male rats attract conspecifics (Seffer et al., 2014; Willadsen et al., 2014; Wöhr and Schwarting, 2007). Playback experiments have produced mixed results, however (Snoeren and Ågmo, 2014). Removing a rat's ability to vocalize might decrease their capacity to interact socially (e.g., Asaba et al., 2017; Musolf et al., 2010), but there is also compelling evidence that devocalized rats are as socially capable as intact rats (Ågmo and Snoeren, 2015; Kisko et al., 2015; Thomas et al., 1981; White et al., 1991). Devocalized rats also show typical exploratory behavior in novel social and asocial contexts (Heinla et al., 2021). Such evidence suggests that if USVs play an important social function for rodents, then there must be alternative communication channels that rapidly compensate for an individual's inability to vocalize.

Overall, the roles that various USVs play in rodents' social lives remain mysterious. Importantly, if rodents' use USVs to socially communicate, this in no way precludes the possibility that a primary function of at least some USVs is to enhance olfactory reception. Many bird and insect species use wing coloration and complex wing movements to communicate socially relevant information, including their reproductive fitness, but this does not prevent them from using their wings to fly.

A basic underlying premise of the US hypothesis is that high-frequency USVs can enhance a rodent's olfactory reception of pheromones, communicative chemical signals well established as critical mediators of social interactions. In this respect, the US hypothesis is fully consistent with USV production being associated with contexts where the collection of social information is adaptive. This hypothesis is also consistent with devocalization having minimal effects on social interactions, because removing USVs would not prevent rodents from detecting or processing pheromones. From the perspective of the US hypothesis, removing a rodent's ability to produce USVs is analogous to making a human nearsighted – individuals with moderately degraded sensory resolution should exhibit few social impairments compared to individuals who have lost the ability to vocally communicate critical social information.

Some researchers hypothesize that rodents produce USVs in reaction to shifts in emotional states (e.g., Blanchard et al., 1993; Brudzynski, 2021; Knutson et al., 2002; Okabe and Kanno, 2023), with the higher frequency, 50 kHz USVs being indicative of a pleasurable (appetitive) state. The underlying function of USVs in this scenario is to modify the conditions that led to the state or to make it known to others. Some researchers have drawn comparisons between 50 kHz vocalizations and laughter in humans because of associations between these vocalizations and tactile stimulation (Hinchcliffe et al., 2020; Panksepp and Burgdorf, 2003), and because of their occurrence during juvenile play behavior (e.g., Burke et al., 2017). Often, the USVs were found to occur before a positive event, however, suggesting they signaled when a vocalizer anticipated a rewarding stimulus (Burgdorf et al., 2000; Burke et al., 2021). Rats produce USVs as an unconditioned response to various drugs (e.g., cocaine, amphetamines, and apomorphine[4]) and as conditioned responses to contexts associated with rewards (Ahrens et al., 2009; Sangarapillai et al., 2021; Simola and Costa, 2018; Tripi et al., 2017).

Individual variations in the propensities of rodents to produce USVs in reaction to cocaine have been linked to differences in learning profiles (Meyer and Tripi, 2018), suggesting that unconditioned vocal reactions to drugs may reveal subjective differences in cocaine-induced pleasure that map onto more global variations in emotional reactions to unconditioned stimuli. Interestingly, the rats that produced the most USVs in reaction to cocaine were more likely to be "sign-trackers," meaning that they were disproportionately attentive to external stimuli during Pavlovian conditioning (see also Sangarapillai et al., 2021). The adaptive advantage of externally revealing internal feelings of pleasure or the anticipation of pleasure is non-obvious, but some have suggested that evoking positive feelings in potential listeners (through emotional contagion) might be beneficial (Hernandez-Lallement et al., 2022; Saito et al., 2016).

Although most past research has focused on the potential communicative value of USVs, a few studies have examined their use in more asocial contexts, such as during exploration of a new environment. While mice generate more USVs during social interactions, they also commonly produce them when alone and exploring (Chabout et al., 2012; Mun et al., 2015; Scattoni et al., 2008). Notably, mice produced more USVs when exploring a novel environment than when exploring a familiar environment (Mun et al., 2015). Mice often were walking or rearing when they produced USVs while exploring. This association between USV production and locomotion is also present in rats (Alves et al., 2016). Blumberg (1992) argued that links between walking and USV production occur because USVs are a biomechanical byproduct of respiration during locomotion. 50 kHz USV production is synchronized with stepping, consistent with this possibility (Laplagne and Elías Costa, 2016). However, rats often start vocalizing before initiating the first step, showing that a physical impact is not necessary for USV production (Alves et al., 2016; Laplagne and Elías Costa, 2016).

When rats walk faster, they produce USVs at a faster rate, probably because USV emission is tightly linked to the respiratory cycle (Boulanger-Bertolus and Mouly, 2021). In the one study showing that rats synchronize locomotion and USV production, researchers described the rats as engaging in exploratory behavior (in both social and asocial

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[4] Apomorphine also increases sniffing in rats and abnormal responses to olfactory stimuli (Vanderwolf and Szechtman, 1987); whether these drug-induced increases in USV and sniff production are temporally coordinated has yet to be investigated.

contexts), alternating between progressing and lingering (Laplagne and Elías Costa, 2016). During both phases, rats produced USVs, though at a somewhat higher rate when locomoting. These recent studies establish that: (1) rodents produce USVs during exploration; (2) they vocalize in ways that are precisely timed relative to their locomotion during exploration; and (3) they vocalize when both moving and stationary, but at a faster rate when moving.

Interestingly, the acoustic form of USVs appears to be correlated with a rat's speed of locomotion and/or gait (Laplagne and Elías Costa, 2016). Specifically, rats were more likely to produce USVs with nonlinear features when locomoting at high speeds. Researchers have classified high-frequency USVs into different types (e.g., "flat" and "trill") based on their frequency-modulation profiles (e.g., Coffey et al., 2019; Sangiamo et al., 2020; Wright et al., 2010). Variations in USV features produced by mice are correlated with specific types of actions during social interactions (e.g., chasing vs. being chased, Sangiamo et al., 2020), further suggesting that what rodents do while vocalizing may affect USV properties. Such variations could indicate social communication and/or constraints on sound production related to a vocalizer's head position, respiration, and laryngeal movements (Riede, 2013). The US hypothesis makes no specific predictions about how the modulation of ultrasonic frequencies might affect nearby nanoparticles and thus does not explain why some USVs are more frequency modulated than others.[5]

Individual rats and mice can differ substantially with respect to the diversity, rate, and number of USVs they produce (e.g., Ahrens et al., 2013; Laplagne and Elías Costa, 2016; Sundarakrishnan and Clarke, 2022). Such individual differences are commonly attributed to variations in the behavior or emotional state of the vocalizer (e.g., Sangiamo et al., 2020). The US hypothesis similarly assumes that individuals will vary their production of 50 kHz USVs based on their tendency to be bold and exploratory (Frynta et al., 2024; Žampachová et al., 2017), and on the specific interactions they engage in that might lead them to seek out information available from pheromones. Consistent with this assumption, removal of the VNO dramatically decreases USV production in social contexts (Bean, 1982; Johnston, 1992).

Generally, the US hypothesis predicts tight coupling between 50 kHz USV production and sniffing, such that individual- and context-dependent variations in sniffing (e.g., Wesson, 2013) should be linked to variations in USV production. Sniffing is closely associated with locomotion during exploration and with rearing (Kuga et al., 2019), consistent with behavioral correlates of USV production in asocial contexts (Heinla et al., 2021). Sniffing is also a prominent feature of rodent social interactions (e.g., Nadler et al., 2004). Concurrent measures of USV production and sniffing show that these two processes are tightly linked in rats and mice (John et al., 2023; Sirotin et al., 2014). Rats typically produce USVs during fast sniffing with emission being restricted to specific phases of a sniff cycle (Sirotin et al., 2014). Within social contexts, combined sniffing and USV production occurs most often when rats are less than five centimeters apart, specifically when they are nose-to-nose or nose-to-tail (John et al., 2023). These close-proximity interactions correspond to situations in which rodents are thought to sample pheromones by direct contact (Luo et al., 2003).

Overall, the US hypothesis is consistent with the diversity of contexts within which male and female rodents produce USVs, the minimal behavioral effects of devocalization on social interactions, rodents' use of USVs during exploratory actions – especially when they are alone, and the tight coupling between sniffing, USV production, and locomotion. Current behavioral data are insufficient to evaluate whether USVs affect what rodents smell, but they can at least clarify relationships between exploration, sniffing, and USV production. Carefully designed experiments are needed to determine whether USV emissions influence what happens in a rodent's nose and brain during olfactory reception, perception, and exploration.

4. Conclusions, limitations, and future directions

Rodents, particularly rats and mice, are generalists that show exquisite adaptations for exploring and exploiting a wide variety of habitats, including those constructed by humans. They engage multiple modes of active sensing when navigating both space and social scenarios. They whisk, scan, and sniff, rapidly and selectively differentiating the novel from the familiar. In parallel with these investigatory actions, they produce a variety of ultrasonic vocalizations. Researchers have debated the functions of rodent USVs since their first discovery and much remains unclear about their costs and benefits. Based on the evidence summarized above, we hypothesize that rodents have evolved a unique way of using sound to selectively amplify their reception of pheromones. This mode of active sensing would complement rodents' already formidable arsenal of information seeking strategies.

Researchers around the world are increasingly relying on rodent models of human psychological disorders, with USV production widely regarded as an index of social behavior and communication, stress and anxiety, and the rewarding or aversive consequences of drugs of abuse. Consequently, understanding how USV production in rodents relates to active sensing can have important implications for interpreting rodent behavior, as well as for developing treatments of multiple psychological disorders. For example, numerous studies have linked the effects of drug administration and neurostimulation to rodents' production of USVs. None have monitored sniffing behavior in parallel. It thus remains possible that increases in USVs in these experiments are concomitant with motivational shifts toward information seeking. In other words, if drugs increase a rodent's motivation to smell its surroundings, then this could lead to increases in USVs regardless of whether USVs serve to communicate information about the rat's emotional state. By analogy, cocaine can lead to increased arousal and alertness in human users, as well as increased exploratory actions, which may lead to an increase in rapid eye movements (as well as euphoria). In this case, the cocaine user's darting eyes are not expressing their subjective feelings of euphoria, even if their eye movements are highly correlated with those feelings. Similarly, USV production by rodents in past experiments involving drug effects may be less about expressing emotions and more about information seeking.

No experiments explicitly testing the predictions of the US hypothesis have been conducted to date. Most of the evidence consistent with this hypothesis was found serendipitously in studies designed to establish the social communicative functions of USVs. The hypothesis does not account for the wide variety of 50 kHz USVs produced by rats and mice or for the production of lower-frequency USVs in response to predator scents (e.g., Blanchard et al., 1990). In its current form, the US hypothesis does not specify how olfactory percepts generated by vocal sniffs will differ from those triggered by regular sniffs, or which particles will be most affected by USVs. Pheromone collection by other mammals often involves oral sampling, and transmission of non-volatile pheromones in rodents seems to require direct physical contact, suggesting that rodents may nasally suction fluids containing pheromones directly from glands during close social interactions. If non-volatile pheromones are never airborne while being inhaled, then it is unclear whether ultrasound would affect how those pheromones are deposited within a rodent's nasal cavities.

The US hypothesis leads to several testable predictions about the nature of acoustic, neural, and behavioral phenomena associated with vocal sniffs. In the domain of acoustics, the hypothesis predicts that 50 kHz USVs will agglomerate organic molecules in ways that change the distribution of particle sizes entering a rodent's nasal cavities and that the acoustic fields generated by rodents producing vocal sniffs will

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[5] Recent technologies for manipulating particles include the use of dynamic sound fields (Andrade et al., 2016), as would be generated by rapid frequency modulation, so in principle "trills" might affect the movements of organic molecules in ways that are functionally distinctive from "flat" USVs.

be focused near the nostrils. Neurally, the US hypothesis predicts that variations in neural activity driven by receptors within the VNO will be correlated with USV production, that initiation of VNO pumping will be correlated with vocal sniffing, and that patterns of VNO receptor activation in devocalized rodents will differ from what is seen in intact rodents in contexts where the rodents are inhaling pheromones. In relation to behavior, the US hypothesis predicts that psychophysical tests of thresholds for recognizing individuals from their pheromones would reveal that devocalizing rats raises their thresholds for recognition (i.e., more sniffs or higher concentrations would be required before the sniffer recognizes a familiar individual), that individual variations in sniffing and exploratory behavior would be correlated with individual differences in USV production, and that vocal sniffs would be more prevalent in contexts where rodents are likely to be seeking information about conspecifics. Through future experiments, interactions between vocalization and olfaction in rodents can be systematically assessed and the multimodal processes that rodents use to interrogate the world around them can be more fully revealed.

Just as echolocating dolphins and bats externalize their auditory attentional efforts by broadcasting ultrasonic waves out into the world, vocalizing rodents may reveal their olfactory interests through vocal sniffs. Because sniffs intuitively seem less motorically and cognitively sophisticated than whisks, saccades, or vocal shifts in sonar signals, researchers have been slow to recognize that smelling may involve active sensory sampling akin to what occurs during touching, seeing, and listening (Wachowiak, 2011; S. C.-H. Yang et al., 2016). If rodents are sonically sorting scents, however, then the relative sophistication of olfactory sampling relative to other sensory systems may need to be re-assessed. Either way, the close neural and behavioral coordination of sniffs, vocalization, whisking, and locomotion during exploratory investigations begs for an explanation of how and why rodents evolved such interleaved processes of information seeking, as well as what perceptual advantages such parallel orchestration of multiple sensorimotor processing provides.

Understanding how rodents coordinate olfaction in the context of multiple parallel sensory inputs can potentially provide new insights into how mammalian brains construct representations through selective sampling and cross-modal integration of sensorimotor inputs (Jacobs, 2012, 2023). Studies of rodent olfaction are clarifying not only how olfactory processes work, but also how basic mechanisms of sensory integration and learning operate (Crimaldi et al., 2022; Schroeder et al., 2010; Wachowiak, 2011). Scientists are investigating how experience shapes the neural representation of new odors (Coppola and Reisert, 2023; Wilson et al., 2006), how rodents distinguish between and generalize across similar odors (Kouremenou et al., 2020; Uchida and Mainen, 2003), and how they encode and recall sensory episodes (K. S. Carlson et al., 2018; Shakhawat et al., 2014; Sheridan et al., 2024). Olfaction in rodents rarely happens in isolation, but instead is integrated with visual, auditory, and tactile inputs to provide a multimodal view of ongoing events (Lipton et al., 1999; McRae et al., 2023; Pardasani et al., 2021). In social contexts, rodents perform a variety of odor-specific actions, including reactions to odors indicative of specific individuals or sexes (Johnston, 2003). Rodents rapidly learn to associate specific odors with positive or negative outcomes, enabling researchers to test basic principles of learning (e.g., Davis, 2004; Wilson and Stevenson, 2003), decision-making (reviewed by Mori and Sakano, 2021), and emotional processes (Kontaris et al., 2020; Sterley and Bains, 2021; Sullivan et al., 2015).

Collectively, past studies have revealed the flexibility with which rodents can adapt to changing environments, offering valuable insights into how mammalian perceptual and cognitive processes function. One might question whether knowing why rodents squeak at smelly excretions is of any practical or psychological relevance. Although we cannot know in advance which clues will be the ones that unlock the mysteries of how human perception and cognition work, there is mounting evidence that respiratory processes, and olfaction in particular, may provide a foundation for understanding how integrated memory, perception, emotion, and action systems initially emerged (Jacobs, 2021, 2023).

Author note

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References

Ågmo, A., Snoeren, E.M.S., 2015. Silent or vocalizing rats copulate in a similar manner. PLOS ONE *10* (12), e0144164. https://doi.org/10.1371/journal.pone.0144164.

Ahissar, E., Assa, E., 2016. Perception as a closed-loop convergence process. eLife *5*, e12830. https://doi.org/10.7554/eLife.12830.

Ahrens, A.M., Ma, S.T., Maier, E.Y., Duvauchelle, C.L., Schallert, T., 2009. Repeated intravenous amphetamine exposure: Rapid and persistent sensitization of 50-kHz ultrasonic trill calls in rats. Behav. Brain Res. *197* (1), 205–209. https://doi.org/10.1016/j.bbr.2008.08.037.

Ahrens, A.M., Nobile, C.W., Page, L.E., Maier, E.Y., Duvauchelle, C.L., Schallert, T., 2013. Individual differences in the conditioned and unconditioned rat 50-kHz ultrasonic vocalizations elicited by repeated amphetamine exposure. Psychopharmacology *229* (4), 687–700. https://doi.org/10.1007/s00213-013-3130-9.

Alves, J.A., Boerner, B.C., Laplagne, D.A., 2016. Flexible coupling of respiration and vocalizations with locomotion and head movements in the freely behaving rat. Neural Plast. *2016*, e4065073. https://doi.org/10.1155/2016/4065073.

Andrade, M.A.B., Skotis, G.D., Ritchie, S., Cumming, D.R.S., Riehle, M.O., Bernassau, A. L., 2016. Contactless acoustic manipulation and sorting of particles by dynamic acoustic fields (IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control). IEEE Trans. Ultrason., Ferroelectr., Freq. Control *63* (10), 1593–1600. https://doi.org/10.1109/TUFFC.2016.2608759.

Aqrabawi, A.J., Kim, J.C., 2020. Olfactory memory representations are stored in the anterior olfactory nucleus. Nat. Commun. *11* (1), 1246. https://doi.org/10.1038/s41467-020-15032-2.

Arakawa, H., Blanchard, D.C., Arakawa, K., Dunlap, C., Blanchard, R.J., 2008. Scent marking behavior as an odorant communication in mice. Neurosci. Biobehav. Rev. *32* (7), 1236–1248. https://doi.org/10.1016/j.neubiorev.2008.05.012.

Asaba, A., Osakada, T., Touhara, K., Kato, M., Mogi, K., Kikusui, T., 2017. Male mice ultrasonic vocalizations enhance female sexual approach and hypothalamic kisspeptin neuron activity. Horm. Behav. *94*, 53–60. https://doi.org/10.1016/j.yhbeh.2017.06.006.

Au, W.W.L., Kastelein, R.A., Rippe, T., Schooneman, N.M., 1999. Transmission beam pattern and echolocation signals of a harbor porpoise (*Phocoena phocoena*). J. Acoust. Soc. Am. *106* (6), 3699–3705. https://doi.org/10.1121/1.428221.

Au, W.W.L., Moore, P.W.B., Pawloski, D., 1986. Echolocation transmitting beam of the Atlantic bottlenose dolphin. J. Acoust. Soc. Am. *80* (2), 688–691. https://doi.org/10.1121/1.394012.

Bantz, C., Koshkina, O., Lang, T., Galla, H.-J., Kirkpatrick, C.J., Stauber, R.H., Maskos, M., 2014. The surface properties of nanoparticles determine the agglomeration state and the size of the particles under physiological conditions. Beilstein J. Nanotechnol. *5* (1)), 1774–1786. https://doi.org/10.3762/bjnano.5.188.

Baum, M., 2012. Contribution of pheromones processed by the main olfactory system to mate recognition in female mammals. Front. Neuroanat. *6*, 20 https://www.frontiersin.org/articles/10.3389/fnana.2012.00020.

Baum, M., Larriva-Sahd, J.A., 2014. Interactions between the mammalian main and accessory olfactory systems. Front. Neuroanat. *8*, 45. https://doi.org/10.3389/fnana.2014.00045.

Baxi, K.N., Dorries, K.M., Eisthen, H.L., 2006. Is the vomeronasal system really specialized for detecting pheromones? Trends Neurosci. *29* (1), 1–7. https://doi.org/10.1016/j.tins.2005.10.002.

Bean, N.J., 1982. Olfactory and vomeronasal mediation of ultrasonic vocalizations in male mice. Physiol. Behav. *28* (1), 31–37. https://doi.org/10.1016/0031-9384(82)90097-X.

Bensafi, M., Zelano, C., Johnson, B., Mainland, J., Khan, R., Sobel, N., 2004. Olfaction: From sniff to percept. In: Gazzaniga, M. (Ed.), The cognitive neurosciences. MIT Press, pp. 259–280 https://psycnet.apa.org/record/2005-01373-022.

Ben-Shaul, Y., Katz, L.C., Mooney, R., Dulac, C., 2010. In vivo vomeronasal stimulation reveals sensory encoding of conspecific and allospecific cues by the mouse accessory olfactory bulb. Proc. Natl. Acad. Sci. *107* (11), 5172–5177. https://doi.org/10.1073/pnas.0915147107.

Beynon, R.J., Hurst, J.L., 2003. Multiple roles of major urinary proteins in the house mouse, *Mus domesticus*. Biochem. Soc. Trans. *31* (1), 142–146. https://doi.org/10.1042/bst0310142.

Bigiani, A., Mucignat-Caretta, C., Montani, G., Tirindelli, R., 2005. Pheromone reception in mammals. Reviews of Physiology, Biochemistry and Pharmacology. Springer, pp. 1–35. https://doi.org/10.1007/s10254-004-0038-0.

Blanchard, R.J., Blanchard, D.C., Rodgers, J., Weiss, S.M., 1990. The characterization and modelling of antipredator defensive behavior. Neurosci. Biobehav. Rev. *14* (4), 463–472. https://doi.org/10.1016/S0149-7634(05)80069-7.

Blanchard, R.J., Yudko, E.B., Blanchard, D.C., Taukulis, H.K., 1993. High-frequency (35–70 kHz) ultrasonic vocalizations in rats confronted with anesthetized conspecifics: Effects of gepirone, ethanol, and diazepam. Pharmacol. Biochem. Behav. *44* (2), 313–319. https://doi.org/10.1016/0091-3057(93)90467-8.

Blumberg, M.S., 1992. Rodent ultrasonic short calls: Locomotion, biomechanics, and communication. J. Comp. Psychol. *106* (4), 360–365. https://doi.org/10.1037/0735-7036.106.4.360.

Blumberg, M.S., Alberts, J.R., 1992. Functions and effects in animal communication: Reactions to Guilford and Dawkins. Anim. Behav. *44* (2), 382–383. https://doi.org/10.1016/0003-3472(92)90044-A.

Boulanger-Bertolus, J., Mouly, A.-M., 2021. Ultrasonic vocalizations emission across development in rats: Coordination with respiration and impact on brain neural dynamics. Brain Sci. *11* (5), 616. https://doi.org/10.3390/brainsci11050616.

Breer, H., Fleischer, J., Strotmann, J., 2006. The sense of smell: Multiple olfactory subsystems. Cell. Mol. Life Sci. CMLS *63* (13), 1465–1475. https://doi.org/10.1007/s00018-006-6108-5.

Breipohl, W., Bhatnagar, K.P., Mendoza, A., 1979. Fine structure of the receptor-free epithelium in the vomeronasal organ of the rat. Cell Tissue Res. *200* (3), 383–395. https://doi.org/10.1007/BF00234850.

Brennan, P.A., 2001. The vomeronasal system. Cell. Mol. Life Sci. CMLS *58* (4), 546–555. https://doi.org/10.1007/PL00000880.

Brennan, P.A., Kendrick, K.M., 2006. Mammalian social odours: Attraction and individual recognition. Philos. Trans. R. Soc. B: Biol. Sci. *361* (1476), 2061–2078. https://doi.org/10.1098/rstb.2006.1931.

Briggs, J.R., Kalcounis-Rueppell, M.C., 2011. Similar acoustic structure and behavioural context of vocalizations produced by male and female California mice in the wild. Anim. Behav. *82* (6), 1263–1273. https://doi.org/10.1016/j.anbehav.2011.09.003.

Brudzynski, S.M., 2007. Ultrasonic calls of rats as indicator variables of negative or positive states: Acetylcholine–dopamine interaction and acoustic coding. Behav. Brain Res. *182* (2), 261–273. https://doi.org/10.1016/j.bbr.2007.03.004.

Brudzynski, S.M., 2021. Biological functions of rat ultrasonic vocalizations, arousal mechanisms, and call initiation. Brain Sci. *11* (5), 605. https://doi.org/10.3390/brainsci11050605.

Burgdorf, J., Knutson, B., Panksepp, J., 2000. Anticipation of rewarding electrical brain stimulation evokes ultrasonic vocalization in rats. Behav. Neurosci. *114* (2), 320–327. https://doi.org/10.1037/0735-7044.114.2.320.

Burgdorf, J., Moskal, J.R., 2010. Frequency modulated 50 kHz ultrasonic vocalizations reflect a positive emotional state in the rat: Neural substrates and therapeutic implications. In: Brudzynski, S.M. (Ed.), Handbook of Behavioral Neuroscience, Vol. 19. Elsevier, pp. 209–214. https://doi.org/10.1016/B978-0-12-374593-4.0021-8.

Burke, C.J., Kisko, T.M., Swiftwolfe, H., Pellis, S.M., Euston, D.R., 2017. Specific 50-kHz vocalizations are tightly linked to particular types of behavior in juvenile rats anticipating play. PLOS ONE *12* (5), e0175841. https://doi.org/10.1371/journal.pone.0175841.

Burke, C.J., Markovina, M., Pellis, S.M., Euston, D.R., 2021. Rat 50 kHz trill calls are tied to the expectation of social interaction. Brain Sci. *11* (9), 1142. https://doi.org/10.3390/brainsci11091142.

Carlson, K.S., Gadziola, M.A., Dauster, E.S., Wesson, D.W., 2018. Selective attention controls olfactory decisions and the neural encoding of odors. Curr. Biol. *28* (14), 2195–2205.e4. https://doi.org/10.1016/j.cub.2018.05.011.

Caruso, A., Ricceri, L., Scattoni, M.L., 2020. Ultrasonic vocalizations as a fundamental tool for early and adult behavioral phenotyping of Autism Spectrum Disorder rodent models. Neurosci. Biobehav. Rev. *116*, 31–43. https://doi.org/10.1016/j.neubiorev.2020.06.011.

Čereška, A., Tetsmann, I., Maskeliūnas, R., Grinbergienė, I., Paškevičius, P., 2016. Investigation of effect of acoustic field to coagulation of particles in air flow. *International*. J. Vibroengineering *18*, 2004–2015. https://doi.org/10.21595/jve.2016.16983.

Chabout, J., Sarkar, A., Dunson, D.B., Jarvis, E.D., 2015. Male mice song syntax depends on social contexts and influences female preferences. Front. Behav. Neurosci. *9*, 76.

Chabout, J., Serreau, P., Ey, E., Bellier, L., Aubin, T., Bourgeron, T., Granon, S., 2012. Adult male mice emit context-specific ultrasonic vocalizations that are modulated by prior isolation or group rearing environment. PLOS ONE *7* (1), e29401. https://doi.org/10.1371/journal.pone.0029401.

de Chaumont, F., Lemière, N., Coqueran, S., Bourgeron, T., Ey, E., 2021. LMT USV Toolbox, a novel methodological approach to place mouse ultrasonic vocalizations in their behavioral contexts—A study in female and male C57BL/6J mice and in Shank3 mutant females. Front. Behav. Neurosci. *15*, 735920. https://doi.org/10.3389/fnbeh.2021.735920.

Cheetham, S.A., Thom, M.D., Jury, F., Ollier, W.E.R., Beynon, R.J., Hurst, J.L., 2007. The genetic basis of individual-recognition signals in the mouse. Curr. Biol. 17 (*20*), 1771–1777. https://doi.org/10.1016/j.cub.2007.10.007.

Chen, Y., Xiang, Z., Su, Q., Qin, J., Liu, Q., 2023. Vocal signals with different social or non-social contexts in two wild rodent species (*Mus caroli* and *Rattus losea*). Anim. Cogn. *26* (3), 963–972. https://doi.org/10.1007/s10071-023-01745-6.

Coffey, K.R., Marx, R.E., Neumaier, J.F., 2019. DeepSqueak: A deep learning-based system for detection and analysis of ultrasonic vocalizations. Neuropsychopharmacology *44* (5), 859–868. https://doi.org/10.1038/s41386-018-0303-6.

Coppola, D.M., 2022. The sorption/chromatography hypothesis of olfactory discrimination: The rise, fall, and rebirth of a Phoenix. BioEssays *44* (3), 2100263. https://doi.org/10.1002/bies.202100263.

Coppola, D.M., Reisert, J., 2023. The role of the stimulus in olfactory plasticity. Brain Sci. *13* (11), 1553. https://doi.org/10.3390/brainsci13111553.

Courtiol, E., Hegoburu, C., Litaudon, P., Garcia, S., Fourcaud-Trocmé, N., Buonviso, N., 2011. Individual and synergistic effects of sniffing frequency and flow rate on olfactory bulb activity. J. Neurophysiol. *106* (6), 2813–2824. https://doi.org/10.1152/jn.00672.2011.

Courtiol, E., Lefèvre, L., Garcia, S., Thévenet, M., Messaoudi, B., Buonviso, N., 2014. Sniff adjustment in an odor discrimination task in the rat: Analytical or synthetic strategy? Front. Behav. Neurosci. *8*, 145. https://doi.org/10.3389/fnbeh.2014.00145.

Courtiol, E., Wilson, D.A., 2017. The olfactory mosaic: Bringing an olfactory network together for odor perception. Perception *46* (3–4), 320–332. https://doi.org/10.1177/0301006616663216.

Crimaldi, J., Lei, H., Schaefer, A., Schmuker, M., Smith, B.H., True, A.C., Verhagen, J.V., Victor, J.D., 2022. Active sensing in a dynamic olfactory world. J. Comput. Neurosci. *50* (1), 1–6. https://doi.org/10.1007/s10827-021-00798-1.

Davis, R.L., 2004. Olfactory learning. Neuron *44* (1), 31–48. https://doi.org/10.1016/j.neuron.2004.09.008.

Deschênes, M., Moore, J., Kleinfeld, D., 2012. Sniffing and whisking in rodents. Curr. Opin. Neurobiol. *22* (2), 243–250. https://doi.org/10.1016/j.conb.2011.11.013.

Dong, J., Shang, Y., Tian, L., Inthavong, K., Tu, J., 2018. Detailed deposition analysis of inertial and diffusive particles in a rat nasal passage. Inhal. Toxicol. *30* (1), 29–39. https://doi.org/10.1080/08958378.2018.1439549.

Dong, J., Shang, Y., Tian, L., Tu, J., 2022. Uniqueness of inspiratory airflow patterns in a realistic rat nasal cavity. Comput. Biol. Med. *141*, 105129. https://doi.org/10.1016/j.compbiomed.2021.105129.

Døving, K.B., Trotier, D., 1998. Structure and function of the vomeronasal organ. J. Exp. Biol. *201* (21), 2913–2925. https://doi.org/10.1242/jeb.201.21.2913.

Driver, J., 2001. A selective review of selective attention research from the past century. Br. J. Psychol. *92* (1), 53–78. https://doi.org/10.1348/000712601162103.

Dulac, C., Torello, A.T., 2003. Molecular detection of pheromone signals in mammals: From genes to behaviour. Nat. Rev. Neurosci. *4* (7), 551–562. https://doi.org/10.1038/nrn1140.

Eayrs, J.T., Moulton, D.G., 1960. Studies in olfactory acuity. I: Measurement of olfactory thresholds in the rat. Q. J. Exp. Psychol. *12* (2), 90–98. https://doi.org/10.1080/17470216008416708.

Eggersdorfer, M.L., Pratsinis, S.E., 2014. Agglomerates and aggregates of nanoparticles made in the gas phase. Adv. Powder Technol. *25* (1), 71–90. https://doi.org/10.1016/j.apt.2013.10.010.

Egnor, S.R., Seagraves, K.M., 2016. The contribution of ultrasonic vocalizations to mouse courtship. Curr. Opin. Neurobiol. *38*, 1–5. https://doi.org/10.1016/j.conb.2015.12.009.

Eichenbaum, H., 1998. Using olfaction to study memory. Ann. N. Y. Acad. Sci. *855* (1), 657–669. https://doi.org/10.1111/j.1749-6632.1998.tb10642.x.

Estes, R.D., 1972. The role of the vomeronasal organ in mammalian reproduction. Mammalia *36* (3), 315–341. https://doi.org/10.1515/mamm.1972.36.3.315.

Ey, E., Chaumont, F. de, & Bourgeron, T. (2020). Spontaneous social communication in laboratory mice—Placing ultrasonic vocalizations in their behavioral context. *bioRxiv*, 2020–07. https://doi.org/10.1101/2020.07.09.195362.

Ferdenzi, C., Fournel, A., Thévenet, M., Coppin, G., Bensafi, M., 2015. Viewing olfactory affective responses through the sniff prism: Effect of perceptual dimensions and age on olfactomotor responses to odors. Front. Psychol. *6*, 1776. https://doi.org/10.3389/fpsyg.2015.01776.

Fernández-Vargas, M., Riede, T., Pasch, B., 2022. Mechanisms and constraints underlying acoustic variation in rodents. Anim. Behav. *184*, 135–147. https://doi.org/10.1016/j.anbehav.2021.07.011.

Findley, T.M., Wyrick, D.G., Cramer, J.L., Brown, M.A., Holcomb, B., Attey, R., Yeh, D., Monasevitch, E., Nouboussi, N., Cullen, I., Songco, J.O., King, J.F., Ahmadian, Y., Smear, M.C., 2021. Sniff-synchronized, gradient-guided olfactory search by freely moving mice. eLife *10*, e58523. https://doi.org/10.7554/eLife.58523.

Fonio, E., Gordon, G., Barak, N., Winetraub, Y., Oram, T.B., Haidarliu, S., Kimchi, T., Ahissar, E., 2015. Coordination of sniffing and whisking depends on the mode of interaction with the environment. Isr. J. Ecol. Evol. *61* (2), 95–105. https://doi.org/10.1080/15659801.2015.1124656.

Fonseca, A.H., Santana, G.M., Bosque Ortiz, G.M., Bampi, S., Dietrich, M.O., 2021. Analysis of ultrasonic vocalizations from mice using computer vision and machine learning. eLife *10*, e59161. https://doi.org/10.7554/eLife.59161.

Francia, S., Pifferi, S., Menini, A., Tirindelli, R., 2014. Vomeronasal receptors and signal transduction in the vomeronasal organ of mammals. In: Mucignat-Caretta, C. (Ed.), Neurobiology of Chemical Communication. CRC Press/Taylor & Francis http://www.ncbi.nlm.nih.gov/books/NBK200993/.

Frynta, D., Tomanová, L., Holubová, K., Vobrubová, B., Štolhoferová, I., Rudolfová, V., 2024. Structural consistency of exploratory behaviour of sub-adult and adult spiny mice (*Acomys cahirinus*) in seven different tests. Behav. Process. *216*, 105003. https://doi.org/10.1016/j.beproc.2024.105003.

Gallego-Juárez, J.A., Riera-Franco De Sarabia, E., RodrÍguez-Corral, G., Hoffmann, T.L., Gálvez-Moraleda, J.C., RodrÍguez-Maroto, J.J., Gómez-Moreno, F.J., Bahillo-Ruiz, A., MartÍn-Espigares, M., Acha, M., 1999. Application of acoustic agglomeration to reduce fine particle emissions from coal combustion plants. Environ. Sci. Technol. *33* (21), 3843–3849. https://doi.org/10.1021/es990002n.

Gibson, J.J., 1979. The ecological approach to visual perception. Houghton Mifflin.

Gleason, M.E., Eddington, V.M., Kloepper, L.N., 2023. Acoustic behavior in the northern short-tailed shrew (*Blarina brevicauda*): Ultrasonic click production in a novel environment. J. Acoust. Soc. Am. *154* (1), 411–417. https://doi.org/10.1121/10.0020071.

Goldey, K.L., van Anders, S.M., 2015. Sexual modulation of testosterone: Insights for humans from across species. Adapt. Hum. Behav. Physiol. *1* (2), 93–123. https://doi.org/10.1007/s40750-014-0005-1.

Gottfried, J.A., 2006. Smell: Central nervous processing. Adv. Oto-Rhino-Laryngol. *63*, 44–69. https://doi.org/10.1159/000093750.

Goussha, Y., Bar, K., Netser, S., Cohen, L., Hel-Or, Y., Wagner, S., 2022. HybridMouse: A hybrid convolutional-recurrent neural network-based model for identification of mouse ultrasonic vocalizations. Front. Behav. Neurosci. *15*, 810590.

Gustafson, J.W., Felbain-Keramidas, S.L., 1977. Behavioral and neural approaches to the function of the mystacial vibrissae. Psychol. Bull. *84* (3), 477–488. https://doi.org/10.1037/0033-2909.84.3.477.

Halpern, M., 1987. The organization and function of the vomeronasal system. Annu. Rev. Neurosci. *10* (1), 325–362. https://doi.org/10.1146/annurev.ne.10.030187.001545.

Hamacher, C., Degen, R., Franke, M., Switacz, V.K., Fleck, D., Katreddi, R.R., Hernandez-Clavijo, A., Strauch, M., Horio, N., Hachgenei, E., Spehr, J., Liberles, S.D., Merhof, D., Forni, P.E., Zimmer-Bensch, G., Ben-Shaul, Y., Spehr, M., 2024. A revised conceptual framework for mouse vomeronasal pumping and stimulus sampling. Curr. Biol. *34* (6), 1206–1221. https://doi.org/10.1016/j.cub.2024.01.036.

Hammerschmidt, K., Radyushkin, K., Ehrenreich, H., Fischer, J., 2012. The structure and usage of female and male mouse ultrasonic vocalizations reveal only minor differences. PLOS ONE *7* (7), e41133. https://doi.org/10.1371/journal.pone.0041133.

Hart, B.L., 1983. Flehmen behavior and vomeronasal organ function. In: Müller-Schwarze, D., Silverstein, R.M. (Eds.), Chemical Signals in Vertebrates 3. Springer US, pp. 87–103. https://doi.org/10.1007/978-1-4757-9652-0_5.

He, J., Ma, L., Kim, S., Schwartz, J., Santilli, M., Wood, C., Durnin, M.H., Yu, C.R., 2010. Distinct signals conveyed by pheromone concentrations to the mouse vomeronasal organ. J. Neurosci. *30* (22), 7473–7483. https://doi.org/10.1523/JNEUROSCI.0825-10.2010.

Heckman, J.J., McGuinness, B., Celikel, T., Englitz, B., 2016. Determinants of the mouse ultrasonic vocal structure and repertoire. Neurosci. Biobehav. Rev. *65*, 313–325. https://doi.org/10.1016/j.neubiorev.2016.03.029.

Heckman, J.J., Proville, R., Heckman, G.J., Azarfar, A., Celikel, T., Englitz, B., 2017. High-precision spatial localization of mouse vocalizations during social interaction. Sci. Rep. *7* (1), 3017. https://doi.org/10.1038/s41598-017-02954-z.

Heinla, I., Chu, X., Ågmo, A., Snoeren, E., 2021. Rat ultrasonic vocalizations and novelty-induced social and non-social investigation behavior in a seminatural environment. Physiol. Behav. *237*, 113450. https://doi.org/10.1016/j.physbeh.2021.113450.

Hernandez-Lallement, J., Gómez-Sotres, P., Carrillo, M., 2022. Towards a unified theory of emotional contagion in rodents—A meta-analysis. Neurosci. Biobehav. Rev. *132*, 1229–1248. https://doi.org/10.1016/j.neubiorev.2020.09.010.

Hinchcliffe, J.K., Mendl, M., Robinson, E.S.J., 2020. Rat 50 kHz calls reflect graded tickling-induced positive emotion. Curr. Biol. *30* (18), R1034–R1035. https://doi.org/10.1016/j.cub.2020.08.038.

Hoffmann, T.L., Koopmann, G.H., 1996. Visualization of acoustic particle interaction and agglomeration: Theory and experiments. J. Acoust. Soc. Am. *99* (4), 2130–2141. https://doi.org/10.1121/1.415400.

Hoffmann, F., Musolf, K., Penn, D.J., 2009. Freezing urine reduces its efficacy for eliciting ultrasonic vocalizations from male mice. Physiol. Behav. *96* (4), 602–605. https://doi.org/10.1016/j.physbeh.2008.12.014.

Holy, T.E., Guo, Z., 2005. Ultrasonic songs of male mice. PLOS Biol. *3* (12), e386. https://doi.org/10.1371/journal.pbio.0030386.

Hunter, W.S., 1935. Conditioning and maze learning in the rat. J. Comp. Psychol. *19* (3), 417–424. https://doi.org/10.1037/h0059874.

Hurley, L.M., Kalcounis-Rueppell, M.C., 2018. State and context in vocal communication of rodents. In: Dent, M.L., Fay, R.R., Popper, A.N. (Eds.), Rodent Bioacoustics. Springer International Publishing, pp. 191–221. https://doi.org/10.1007/978-3-319-92495-3_8.

Hurst, J.L., 2009. Female recognition and assessment of males through scent. Behav. Brain Res. *200* (2), 295–303. https://doi.org/10.1016/j.bbr.2008.12.020.

Husband, R.W., 1929. A comparison of human adults and white rats in maze learning. J. Comp. Psychol. *9* (6), 361–377. https://doi.org/10.1037/h0074679.

Isogai, Y., Si, S., Pont-Lezica, L., Tan, T., Kapoor, V., Murthy, V.N., Dulac, C., 2011. Molecular organization of vomeronasal chemoreception. Nature *478* (7368), 241–245. https://doi.org/10.1038/nature10437.

Iwanaga, T., Nio-Kobayashi, J., 2020. Unique blood vasculature and innervation in the cavernous tissue of murine vomeronasal organs. Biomed. Res. *41* (5), 243–251.

Jacobs, L.F., 2012. From chemotaxis to the cognitive map: The function of olfaction. Proc. Natl. Acad. Sci. *109* (supplement_1), 10693–10700. https://doi.org/10.1073/pnas.1201880109.

Jacobs, L.F., 2021. How the evolution of air breathing shaped hippocampal function. Philos. Trans. R. Soc. B: Biol. Sci. *377* (1844), 20200532. https://doi.org/10.1098/rstb.2020.0532.

Jacobs, L.F., 2023. The PROUST hypothesis: the embodiment of olfactory cognition. Anim. Cogn. *26* (1), 59–72. https://doi.org/10.1007/s10071-022-01734-1.

Jakobsen, L., Brinkløv, S., Surlykke, A., 2013. Intensity and directionality of bat echolocation signals. Front. Physiol. *4* https://www.frontiersin.org/articles/10.3389/fphys.2013.00089.

Jiang, J., Zhao, K., 2010. Airflow and nanoparticle deposition in rat nose under various breathing and sniffing conditions—A computational evaluation of the unsteady and turbulent effect. J. Aerosol Sci. *41* (11), 1030–1043. https://doi.org/10.1016/j.jaerosci.2010.06.005.

John, S.R., Tiwari, R., Goussha, Y., Amar, R., Bizer, A., Netser, S., Wagner, S., 2023. Simultaneous recording of ultrasonic vocalizations and sniffing from socially interacting individual rats using a miniature microphone. Cell Rep. Methods *3* (11), 100638. https://doi.org/10.1016/j.crmeth.2023.100638.

Johnston, R.E., 1992. Vomeronasal and/or olfactory mediation of ultrasonic calling and scent marking by female golden hamsters. Physiol. Behav. *51* (3), 437–448. https://doi.org/10.1016/0031-9384(92)90163-V.

Johnston, R.E., 2003. Chemical communication in rodents: From pheromones to individual recognition. J. Mammal. *84* (4), 1141–1162. https://doi.org/10.1644/BLe-010.

Kay, L.M., 2005. Theta oscillations and sensorimotor performance. Proc. Natl. Acad. Sci. *102* (10), 3863–3868. https://doi.org/10.1073/pnas.0407920102.

Kelly, J.T., Bobbitt, C.M., Asgharian, B., 2001. In vivo measurement of fine and coarse aerosol deposition in the nasal airways of female Long-Evans rats. Toxicol. Sci. *64* (2), 253–258. https://doi.org/10.1093/toxsci/64.2.253.

Kepecs, A., Uchida, N., Mainen, Z.F., 2006. The sniff as a unit of olfactory processing. Chem. Senses *31* (2), 167–179. https://doi.org/10.1093/chemse/bjj016.

Kepecs, A., Uchida, N., Mainen, Z.F., 2007. Rapid and precise control of sniffing during olfactory discrimination in rats. J. Neurophysiol. *98* (1), 205–213. https://doi.org/10.1152/jn.00071.2007.

Keverne, E.B., 1999. The vomeronasal organ. Science *286* (5440), 716–720. https://doi.org/10.1126/science.286.5440.716.

Khmelyov, V.N., Golykh, R.N., Nesterov, V.A., Shalunov, A.V., 2023. Numerical model of ultrasonic agglomeration of submicron particles in resonant gas gaps. J. Eng. Phys. Thermophys. *96* (1), 255–265. https://doi.org/10.1007/s10891-023-02682-4.

Kisko, T.M., Himmler, B.T., Himmler, S.M., Euston, D.R., Pellis, S.M., 2015. Are 50-kHz calls used as play signals in the playful interactions of rats? II. Evidence from the effects of devocalization. Behav. Process. *111*, 25–33. https://doi.org/10.1016/j.beproc.2014.11.011.

Kleinfeld, D., Deschênes, M., Economo, M.N., Elbaz, M., Golomb, D., Liao, S.-M., O'Connor, D.H., Wang, F., 2023. Low- and high-level coordination of orofacial motor actions. Curr. Opin. Neurobiol. *83*, 102784. https://doi.org/10.1016/j.conb.2023.102784.

Knutson, B., Burgdorf, J., Panksepp, J., 2002. Ultrasonic vocalizations as indices of affective states in rats. Psychol. Bull. *128* (6), 961–977. https://doi.org/10.1037/0033-2909.128.6.961.

Komisaruk, B.R., 1970. Synchrony between limbic system theta activity and rhythmical behavior in rats. J. Comp. Physiol. Psychol. *70* (3, Pt.1), 482–492. https://doi.org/10.1037/h0028709.

Kontaris, I., East, B.S., Wilson, D.A., 2020. Behavioral and neurobiological convergence of odor, mood and emotion: a review. Front. Behav. Neurosci. *14*, *35*. 〈https://www.frontiersin.org/articles/10.3389/fnbeh.2020.00035〉.

Kouremenou, I., Piper, M., Zalucki, O., 2020. Adult neurogenesis in the olfactory system: improving performance for difficult discrimination tasks? BioEssays *42* (10), 2000065. https://doi.org/10.1002/bies.202000065.

Kuga, N., Nakayama, R., Shikano, Y., Nishimura, Y., Okonogi, T., Ikegaya, Y., Sasaki, T., 2019. Sniffing behaviour-related changes in cardiac and cortical activity in rats. J. Physiol. *597* (21), 5295–5306. https://doi.org/10.1113/JP278500.

Ladewig, J., Hart, B.L., 1980. Flehmen and vomeronasal organ function in male goats. Physiol. Behav. *24* (6), 1067–1071. https://doi.org/10.1016/0031-9384(80)90049-9.

Laplagne, D.A., Elías Costa, M., 2016. Rats synchronize locomotion with ultrasonic vocalizations at the subsecond time scale. Front. Behav. Neurosci. *10*, 184.

Leinders-Zufall, T., Lane, A.P., Puche, A.C., Ma, W., Novotny, M.V., Shipley, M.T., Zufall, F., 2000. Ultrasensitive pheromone detection by mammalian vomeronasal neurons. Nature *405* (6788), 792–796. https://doi.org/10.1038/35015572.

Leon, M., Johnson, B.A., 2003. Olfactory coding in the mammalian olfactory bulb. Brain Res. Rev. *42* (1), 23–32. https://doi.org/10.1016/S0165-0173(03)00142-5.

Liberles, S.D., 2014. Mammalian pheromones. Annu. Rev. Physiol. *76* (1), 151–175. https://doi.org/10.1146/annurev-physiol-021113-170334.

Lilliehorn, T., Simu, U., Nilsson, M., Almqvist, M., Stepinski, T., Laurell, T., Nilsson, J., Johansson, S., 2005. Trapping of microparticles in the near field of an ultrasonic transducer. Ultrasonics *43* (5), 293–303. https://doi.org/10.1016/j.ultras.2004.11.001.

Lipton, P.A., Alvarez, P., Eichenbaum, H., 1999. Crossmodal associative memory representations in rodent orbitofrontal cortex. Neuron *22* (2), 349–359. https://doi.org/10.1016/S0896-6273(00)81095-8.

Liu, J., Zhang, G., Zhou, J., Wang, J., Zhao, W., Cen, K., 2009. Experimental study of acoustic agglomeration of coal-fired fly ash particles at low frequencies. Powder Technol. *193* (1), 20–25. https://doi.org/10.1016/j.powtec.2009.02.002.

Luo, M., Fee, M.S., Katz, L.C., 2003. Encoding pheromonal signals in the accessory olfactory bulb of behaving mice. Science *299* (5610), 1196–1201. https://doi.org/10.1126/science.1082133.

Lyons-Warren, A.M., Herman, I., Hunt, P.J., Arenkiel, B.R., 2021. A systematic-review of olfactory deficits in neurodevelopmental disorders: from mouse to human. Neurosci. Biobehav. Rev. *125*, 110–121. https://doi.org/10.1016/j.neubiorev.2021.02.024.

Mainen, Z.F., 2006. Behavioral analysis of olfactory coding and computation in rodents. Curr. Opin. Neurobiol. *16* (4), 429–434. https://doi.org/10.1016/j.conb.2006.06.003.

Mainland, J., Sobel, N., 2006. The sniff is part of the olfactory percept. Chem. Senses *31* (2), 181–196. https://doi.org/10.1093/chemse/bjj012.

Marconi, M.A., Nicolakis, D., Abbasi, R., Penn, D.J., Zala, S.M., 2020. Ultrasonic courtship vocalizations of male house mice contain distinct individual signatures. Anim. Behav. *169*, 169–197. https://doi.org/10.1016/j.anbehav.2020.09.006.

Matsumoto, Y.K., Okanoya, K., 2016. Phase-specific vocalizations of male mice at the initial encounter during the courtship sequence. PLOS ONE *11* (2), e0147102. https://doi.org/10.1371/journal.pone.0147102.

McRae, B.R., Andreu, V., Marlin, B.J., 2023. Integration of olfactory and auditory cues eliciting parental behavior. J. Neuroendocrinol. *35* (7), e13307. https://doi.org/10.1111/jne.13307.

Menco, B.Ph.M., Carr, V.Mc.M., Ezeh, P.I., Liman, E.R., Yankova, M.P., 2001. Ultrastructural localization of G-proteins and the channel protein TRP2 to microvilli of rat vomeronasal receptor cells. J. Comp. Neurol. *438* (4), 468–489. https://doi.org/10.1002/cne.1329.

Meredith, M., 1994. Chronic recording of vomeronasal pump activation in awake behaving hamsters. Physiol. Behav. *56* (2), 345–354. https://doi.org/10.1016/0031-9384(94)90205-4.

Meredith, M., Marques, D.M., O'Connell, R.J., Stern, F.L., 1980. Vomeronasal pump: significance for male hamster sexual behavior. Science *207* (4436), 1224–1226. https://doi.org/10.1126/science.7355286.

Meyer, P.J., Tripi, J.A., 2018. Sign-tracking, response inhibition, and drug-induced vocalizations. In: Tomie, A., Morrow, J. (Eds.), Sign-tracking and drug addiction. University of Michigan Press.

Möhrle, D., Fernández, M., Peñagarikano, O., Frick, A., Allman, B., Schmid, S., 2020. What we can learn from a genetic rodent model about autism. Neurosci. Biobehav. Rev. *109*, 29–53. https://doi.org/10.1016/j.neubiorev.2019.12.015.

Mori, K., Sakano, H., 2021. Olfactory circuitry and behavioral decisions. Annu. Rev. Physiol. *83* (1), 231–256. https://doi.org/10.1146/annurev-physiol-031820-092824.

Morrison, E.E., Costanzo, R.M., 1992. Morphology of olfactory epithelium in humans and other vertebrates. Microsc. Res. Tech. *23* (1), 49–61. https://doi.org/10.1002/jemt.1070230105.

Mun, H.-S., Lipina, T.V., Roder, J.C., 2015. Ultrasonic vocalizations in mice during exploratory behavior are context-dependent. Front. Behav. Neurosci. *9*, 316.

Musolf, K., Hoffmann, F., Penn, D.J., 2010. Ultrasonic courtship vocalizations in wild house mice, *Mus musculus musculus*. Anim. Behav. *79* (3), 757–764. https://doi.org/10.1016/j.anbehav.2009.12.034.

Nadler, J.J., Moy, S.S., Dold, G., Simmons, N., Perez, A., Young, N.B., Barbaro, R.P., Piven, J., Magnuson, T.R., Crawley, J.N., 2004. Automated apparatus for quantitation of social approach behaviors in mice. Genes, Brain Behav. *3* (5), 303–314. https://doi.org/10.1111/j.1601-183X.2004.00071.x.

Naguro, T., Breipohl, W., 1982. The vomeronasal epithelia of NMRI mouse. Cell Tissue Res. *227* (3), 519–534. https://doi.org/10.1007/BF00204782.

Nummela, S., Thewissen, J., 2008. The physics of sound in air and water. In: Thewissen, J., Nummela, S. (Eds.), Evolution on the threshold. University of California Press, pp. 175–181.

Oka, Y., Takai, Y., Touhara, K., 2009. Nasal airflow rate affects the sensitivity and pattern of glomerular odorant responses in the mouse olfactory bulb. J. Neurosci. *29* (39), 12070–12078. https://doi.org/10.1523/JNEUROSCI.1415-09.2009.

Okabe, S., Kanno, K., 2023. Acoustic properties and biological significance of ultrasonic vocalizations in rodents: Emotional expressions. In: Seki, Y. (Ed.), Acoustic Communication in Animals: From Insect Wingbeats to Human Music (Bioacoustics Series Vol.1). Springer Nature, pp. 153–173. https://doi.org/10.1007/978-981-99-0831-8_10.

Okanoya, K., Screven, L.A., 2018. Rodent vocalizations: Adaptations to physical, social, and sexual factors. In: Dent, M.L., Fay, R.R., Popper, A.N. (Eds.), Rodent bioacoustics. Springer International Publishing, pp. 13–41. https://doi.org/10.1007/978-3-319-92495-3_2.

Panksepp, J., Burgdorf, J., 2003. Laughing" rats and the evolutionary antecedents of human joy? Physiol. Behav. *79* (3), 533–547. https://doi.org/10.1016/S0031-9384(03)00159-8.

Pardasani, M., Marathe, S.D., Purnapatre, M.M., Dalvi, U., Abraham, N.M., 2021. Multimodal learning of pheromone locations. FASEB J. *35* (9), e21836. https://doi.org/10.1096/fj.202100167R.

Pedraja, F., Hofmann, V., Goulet, J., Engelmann, J., 2020. Task-related sensorimotor adjustments increase the sensory range in electrolocation. J. Neurosci. *40* (5), 1097–1109. https://doi.org/10.1523/JNEUROSCI.1024-19.2019.

Perrodin, C., Verzat, C., Bendor, D., 2023. Courtship behaviour reveals temporal regularity is a critical social cue in mouse communication. eLife *12*, RP86464. https://doi.org/10.7554/eLife.86464.

Petric, R., Kalcounis-Rueppell, M.C., 2013. Female and male adult brush mice (*Peromyscus boylii*) use ultrasonic vocalizations in the wild. Behaviour *150* (14), 1747–1766. https://doi.org/10.1163/1568539X-00003118.

Petrulis, A., Peng, M., Johnston, R.E., 1999. Effects of vomeronasal organ removal on individual odor discrimination, sex-odor preference, and scent marking by female hamsters. Physiol. Behav. *66* (1), 73–83. https://doi.org/10.1016/S0031-9384(98)00259-5.

Premoli, M., Pietropaolo, S., Wöhr, M., Simola, N., Bonini, S.A., 2023. Mouse and rat ultrasonic vocalizations in neuroscience and neuropharmacology: state of the art and future applications. Eur. J. Neurosci. *57* (12), 2062–2096. https://doi.org/10.1111/ejn.15957.

Ranade, S., Hangya, B., Kepecs, A., 2013. Multiple modes of phase locking between sniffing and whisking during active exploration. J. Neurosci. *33* (19), 8250–8256. https://doi.org/10.1523/JNEUROSCI.3874-12.2013.

Riede, T., 2013. Stereotypic laryngeal and respiratory motor patterns generate different call types in rat ultrasound vocalization. J. Exp. Zool. Part A: Ecol. Genet. Physiol. *319* (4), 213–224. https://doi.org/10.1002/jez.1785.

Riera, E., Gallego-Juárez, J.A., Mason, T.J., 2006. Airborne ultrasound for the precipitation of smokes and powders and the destruction of foams. Ultrason. Sonochem. *13* (2), 107–116. https://doi.org/10.1016/j.ultsonch.2005.04.001.

Roitblat, H.L., Penner, R.H., Nachtigall, P.E., 1990. Matching-to-sample by an echolocating dolphin (*Tursiops truncatus*). J. Exp. Psychol.: Anim. Behav. Process. *16* (1), 85–95. https://doi.org/10.1037/0097-7403.16.1.85.

Rosero, M.A., Aylwin, M.L., 2011. Sniffing shapes the dynamics of olfactory bulb gamma oscillations in awake behaving rats. Eur. J. Neurosci. *34* (5), 787–799. https://doi.org/10.1111/j.1460-9568.2011.07800.x.

Roullet, F.I., Wöhr, M., Crawley, J.N., 2011. Female urine-induced male mice ultrasonic vocalizations, but not scent-marking, is modulated by social experience. Behav. Brain Res. *216* (1), 19–28. https://doi.org/10.1016/j.bbr.2010.06.004.

Saito, Y., Yuki, S., Seki, Y., Kagawa, H., Okanoya, K., 2016. Cognitive bias in rats evoked by ultrasonic vocalizations suggests emotional contagion. Behav. Process. *132*, 5–11. https://doi.org/10.1016/j.beproc.2016.08.005.

Sangarapillai, N., Ellenberger, M., Wöhr, M., Schwarting, R.K.W., 2021. Ultrasonic vocalizations and individual differences in rats performing a Pavlovian conditioned approach task. Behav. Brain Res. *398*, 112926. https://doi.org/10.1016/j.bbr.2020.112926.

Sangiamo, D.T., Warren, M.R., Neunuebel, J.P., 2020. Ultrasonic signals associated with different types of social behavior of mice. Article 3. Nat. Neurosci. *23* (3). https://doi.org/10.1038/s41593-020-0584-z.

Scattoni, M.L., Gandhy, S.U., Ricceri, L., Crawley, J.N., 2008. Unusual repertoire of vocalizations in the BTBR T+tf/J mouse model of autism. PLOS ONE *3* (8), e3067. https://doi.org/10.1371/journal.pone.0003067.

Schaefer, A.T., Margrie, T.W., 2007. Spatiotemporal representations in the olfactory system. Trends Neurosci. *30* (3), 92–100. https://doi.org/10.1016/j.tins.2007.01.001.

Schoenfeld, T.A., Cleland, T.A., 2006. Anatomical contributions to odorant sampling and representation in rodents: Zoning in on sniffing behavior. Chem. Senses *31* (2), 131–144. https://doi.org/10.1093/chemse/bjj015.

Schroeder, C.E., Wilson, D.A., Radman, T., Scharfman, H., Lakatos, P., 2010. Dynamics of active sensing and perceptual selection. Curr. Opin. Neurobiol. *20* (2), 172–176. https://doi.org/10.1016/j.conb.2010.02.010.

Schroeter, J.D., Kimbell, J.S., Asgharian, B., Tewksbury, E.W., Singal, M., 2012. Computational fluid dynamics simulations of submicrometer and micrometer particle deposition in the nasal passages of a Sprague-Dawley rat. J. Aerosol Sci. *43* (1), 31–44. https://doi.org/10.1016/j.jaerosci.2011.08.008.

Schwarting, R.K.W., 2023. Behavioral analysis in laboratory rats: challenges and usefulness of 50-kHz ultrasonic vocalizations. Neurosci. Biobehav. Rev. *152*, 105260. https://doi.org/10.1016/j.neubiorev.2023.105260.

Seffer, D., Schwarting, R.K.W., Wöhr, M., 2014. Pro-social ultrasonic communication in rats: insights from playback studies. J. Neurosci. Methods *234*, 73–81. https://doi.org/10.1016/j.jneumeth.2014.01.023.

Shakhawat, A.M., Gheidi, A., Hou, Q., Dhillon, S.K., Marrone, D.F., Harley, C.W., Yuan, Q., 2014. Visualizing the engram: Learning stabilizes odor representations in the olfactory network. J. Neurosci. *34* (46), 15394–15401. https://doi.org/10.1523/JNEUROSCI.3396-14.2014.

Shang, Y., Dong, J., Inthavong, K., Tu, J., 2015. Comparative numerical modeling of inhaled micron-sized particle deposition in human and rat nasal cavities. Inhal. Toxicol. *27* (13), 694–705. https://doi.org/10.3109/08958378.2015.1088600.

Sharma, A., Kumar, R., Aier, I., Semwal, R., Tyagi, P., Varadwaj, P., 2019. Sense of smell: Structural, functional, mechanistic advancements and challenges in human olfactory research. Curr. Neuropharmacol. *17* (9), 891–911. https://doi.org/10.2174/1570159X17666181206095626.

Sheridan, C.L., Lang, S., Knappenberger, M., Albers, C., Loper, R., Tillett, B., Sanchez, J., Wilcox, A., Harrison, T., Panoz-Brown, D., Crystal, J.D., 2024. Replay of incidentally encoded episodic memories in the rat. Curr. Biol. *34* (3), 641–647. https://doi.org/10.1016/j.cub.2023.12.043.

Shorey, H.H., 2013. Animal communication by pheromones. Academic Press.

Simmons, J.A., Houser, D., Kloepper, L., 2014. Localization and classification of targets by echolocating bats and dolphins. In: Surlykke, A., Nachtigall, P.E., Fay, R.R., Popper, A.N. (Eds.), Biosonar. Springer, pp. 169–193. https://doi.org/10.1007/978-1-4614-9146-0_6.

Simola, N., Costa, G., 2018. Emission of categorized 50-kHz ultrasonic vocalizations in rats repeatedly treated with amphetamine or apomorphine: possible relevance to drug-induced modifications in the emotional state. Behav. Brain Res. *347*, 88–98. https://doi.org/10.1016/j.bbr.2018.02.041.

Simola, N., Granon, S., 2019. Ultrasonic vocalizations as a tool in studying emotional states in rodent models of social behavior and brain disease. Neuropharmacology *159*, 107420. https://doi.org/10.1016/j.neuropharm.2018.11.008.

Sirotin, Y.B., Costa, M.E., Laplagne, D.A., 2014. Rodent ultrasonic vocalizations are bound to active sniffing behavior. Front. Behav. Neurosci. *8*, 399. https://doi.org/10.3389/fnbeh.2014.00399.

Small, W.S., 1900. An experimental study of the mental processes of the rat. Am. J. Psychol. *11* (2), 133–165. https://doi.org/10.2307/1412267.

Snoeren, E.M.S., Ågmo, A., 2014. The incentive value of males' 50-kHz ultrasonic vocalizations for female rats (*Rattus norvegicus*). J. Comp. Psychol. *128* (1), 40–55. https://doi.org/10.1037/a0033204.

Song, L., Koopmann, G.H., Hoffmann, T.L., 1994. An improved theoretical model of acoustic agglomeration. J. Vib. Acoust. *116* (2), 208–214. https://doi.org/10.1115/1.2930414.

Spehr, M., Spehr, J., Ukhanov, K., Kelliher, K.R., Leinders-Zufall, T., Zufall, F., 2006. Parallel processing of social signals by the mammalian main and accessory olfactory systems. Cell. Mol. Life Sci. CMLS *63* (13), 1476–1484. https://doi.org/10.1007/s00018-006-6109-4.

Sterley, T.-L., Bains, J.S., 2021. Social communication of affective states. Curr. Opin. Neurobiol. *68*, 44–51. https://doi.org/10.1016/j.conb.2020.12.007.

Stevenson, R.J., 2010. An initial evaluation of the functions of human olfaction. Chem. Senses *35* (1), 3–20. https://doi.org/10.1093/chemse/bjp083.

Stoumpou, V., Vargas, C.D.M., Schade, P.F., Boyd, J.L., Giannakopoulos, T., Jarvis, E.D., 2023. Analysis of Mouse Vocal Communication (AMVOC): a deep, unsupervised method for rapid detection, analysis and classification of ultrasonic vocalisations. Bioacoustics *32* (2), 199–229. https://doi.org/10.1080/09524622.2022.2099973.

Stowers, L., Logan, D.W., 2010. Sexual dimorphism in olfactory signaling. Curr. Opin. Neurobiol. *20* (6), 770–775. https://doi.org/10.1016/j.conb.2010.08.015.

Stowers, L., Spehr, M., 2015. The vomeronasal organ. Handbook of Olfaction and Gustation. John Wiley & Sons, Ltd, pp. 1113–1132. https://doi.org/10.1002/9781118971758.ch51.

Sullivan, R.M., Wilson, D.A., Ravel, N., Mouly, A.-M., 2015. Olfactory memory networks: from emotional learning to social behaviors. Front. Behav. Neurosci. *9*, 36. ⟨https://www.frontiersin.org/articles/10.3389/fnbeh.2015.00036⟩.

Sundarakrishnan, A., Clarke, P.B.S., 2022. Stable long-term individual differences in 50-kHz vocalization rate and call subtype prevalence in adult male rats: comparisons with sucrose preference. PLOS ONE *17* (10), e0276743. https://doi.org/10.1371/journal.pone.0276743.

Thomas, D.A., Talalas, L., Barfield, R.J., 1981. Effect of devocalization of the male on mating behavior in rats. J. Comp. Physiol. Psychol. *95* (4), 630–637. https://doi.org/10.1037/h0077803.

Tian, L., Shang, Y., Chen, R., Bai, R., Chen, C., Inthavong, K., Tu, J., 2019. Correlation of regional deposition dosage for inhaled nanoparticles in human and rat olfactory. Part. Fibre Toxicol. *16* (1), 6. https://doi.org/10.1186/s12989-019-0290-8.

Tirindelli, R., 2021. Coding of pheromones by vomeronasal receptors. Cell Tissue Res. *383* (1), 367–386. https://doi.org/10.1007/s00441-020-03376-6.

Tirindelli, R., Dibattista, M., Pifferi, S., Menini, A., 2009. From pheromones to behavior. Physiol. Rev. *89* (3), 921–956. https://doi.org/10.1152/physrev.00037.2008.

Torres, M.V., Ortiz-Leal, I., Sanchez-Quinteiro, P., 2023. Pheromone sensing in mammals: a review of the vomeronasal system. Anatomia *2* (4), 346–413.

Touhara, K., Vosshall, L.B., 2009. Sensing odorants and pheromones with chemosensory receptors. Annu. Rev. Physiol. *71* (1), 307–332. https://doi.org/10.1146/annurev.physiol.010908.163209.

Trinh, K., Storm, D.R., 2004. Detection of odorants through the main olfactory epithelium and vomeronasal organ of mice. discussion S224-241 Nutr. Rev. *62* (11 Pt 2)), S189–192. https://doi.org/10.1111/j.1753-4887.2004.tb00098.x.

Tripi, J.A., Dent, M.L., Meyer, P.J., 2017. Individual differences in food cue responsivity are associated with acute and repeated cocaine-induced vocalizations, but not cue-induced vocalizations. Psychopharmacology *234* (3), 437–446. https://doi.org/10.1007/s00213-016-4476-6.

Trujillo, F.J., Juliano, P., Barbosa-Cánovas, G., Knoerzer, K., 2014. Separation of suspensions and emulsions via ultrasonic standing waves – A review. Ultrason. Sonochem. *21* (6), 2151–2164. https://doi.org/10.1016/j.ultsonch.2014.02.016.

Tsitoura, C., Malinowski, S.T., Mohrhardt, J., Degen, R., DiBenedictis, B.T., Gao, Y., Watznauer, K., Gerhold, K., Nagel, M., Weber, M., Rothermel, M., Hanganu-Opatz, I. L., Ben-Shaul, Y., Davison, I.G., Spehr, M., 2020. Synchronous infra-slow oscillations organize ensembles of accessory olfactory bulb projection neurons into distinct microcircuits. J. Neurosci. *40* (21), 4203–4218. https://doi.org/10.1523/JNEUROSCI.2925-19.2020.

Uchida, N., Mainen, Z.F., 2003. Speed and accuracy of olfactory discrimination in the rat. Nat. Neurosci. *6* (11), 1224–1229. https://doi.org/10.1038/nn1142.

Vanderwolf, C.H., Szechtman, H., 1987. Electrophysiological correlates of stereotyped sniffing in rats injected with apomorphine. Pharmacol. Biochem. Behav. *26* (2), 299–304. https://doi.org/10.1016/0091-3057(87)90122-5.

Varga, A.G., Wesson, D.W., 2013. Distributed auditory sensory input within the mouse olfactory cortex. Eur. J. Neurosci. *37* (4), 564–571. https://doi.org/10.1111/ejn.12063.

Carlson, B.A., Sisneros, J.A., Popper, A.N., Fay, R.R. (Eds.), 2019. Electroreception: Fundamental insights from comparative approaches, Vol. 70. Springer International Publishing, pp. 2195–2205. https://doi.org/10.1007/978-3-030-29105-1.

Vollath, D., 2023. Agglomeration and aggregation of nanoparticles. Nanoarchitectonics *4*, 45–57. https://doi.org/10.37256/nat.4220233222.

Wachowiak, M., 2011. All in a sniff: Olfaction as a model for active sensing. Neuron *71* (6), 962–973. https://doi.org/10.1016/j.neuron.2011.08.030.

Wang, Y., Hu, J., 2015. Ultrasonic removal of coarse and fine droplets in air. Sep. Purif. Technol. *153*, 156–161. https://doi.org/10.1016/j.seppur.2015.09.002.

Warren, W.H., 2006. The dynamics of perception and action. Psychol. Rev. *113* (2), 358–389. https://doi.org/10.1037/0033-295X.113.2.358.

Warren, M.R., Clein, R.S., Spurrier, M.S., Roth, E.D., Neunuebel, J.P., 2020. Ultrashort-range, high-frequency communication by female mice shapes social interactions. Sci. Rep. *10* (1), 2637. https://doi.org/10.1038/s41598-020-59418-0.

Welker, W.I., 1964. Analysis of sniffing of the albino rat. Behaviour *22* (3–4), 223–244. https://doi.org/10.1163/156853964X00030.

Wesson, D.W., 2013. Sniffing behavior communicates social hierarchy. Curr. Biol. *23* (7), 575–580. https://doi.org/10.1016/j.cub.2013.02.012.

Wesson, D.W., 2020. The tubular striatum. J. Neurosci. *40* (39), 7379–7386. https://doi.org/10.1523/JNEUROSCI.1109-20.2020.

Wesson, D.W., Carey, R.M., Verhagen, J.V., Wachowiak, M., 2008. Rapid encoding and perception of novel odors in the rat. PLOS Biol. *6* (4), e82. https://doi.org/10.1371/journal.pbio.0060082.

Wesson, D.W., Verhagen, J.V., Wachowiak, M., 2009. Why sniff fast? The relationship between sniff frequency, odor discrimination, and receptor neuron activation in the rat. J. Neurophysiol. *101* (2), 1089–1102. https://doi.org/10.1152/jn.90981.2008.

Wesson, D.W., Wilson, D.A., 2010. Smelling sounds: Olfactory–auditory sensory convergence in the olfactory tubercle. J. Neurosci. *30* (8), 3013–3021. https://doi.org/10.1523/JNEUROSCI.6003-09.2010.

Wesson, D.W., Wilson, D.A., 2011. Sniffing out the contributions of the olfactory tubercle to the sense of smell: Hedonics, sensory integration, and more? Neurosci. Biobehav. Rev. *35* (3), 655–668. https://doi.org/10.1016/j.neubiorev.2010.08.004.

White, N.R., Colona, L.C., Barfield, R.J., 1991. Sensory cues that elicit ultrasonic vocalizations in female rats (*Rattus norvegicus*). Behav. Neural Biol. *55* (2), 154–165. https://doi.org/10.1016/0163-1047(91)80136-3.

White, N.R., Prasad, M., Barfield, R.J., Nyby, J.G., 1998. 40- and 70-kHz vocalizations of mice (*Mus musculus*) during copulation. Physiol. Behav. *63* (4), 467–473. https://doi.org/10.1016/S0031-9384(97)00484-8.

Willadsen, M., Seffer, D., Schwarting, R.K.W., Wöhr, M., 2014. Rodent ultrasonic communication: male prosocial 50-kHz ultrasonic vocalizations elicit social approach behavior in female rats (*Rattus norvegicus*). J. Comp. Psychol. *128* (1), 56–64. https://doi.org/10.1037/a0034778.

Wilson, D.A., Kadohisa, M., Fletcher, M.L., 2006. Cortical contributions to olfaction: plasticity and perception. Semin. Cell Dev. Biol. *17* (4), 462–470. https://doi.org/10.1016/j.semcdb.2006.04.008.

Wilson, D.A., Stevenson, R.J., 2003. Olfactory perceptual learning: the critical role of memory in odor discrimination. Neurosci. Biobehav. Rev. *27* (4), 307–328. https://doi.org/10.1016/S0149-7634(03)00050-2.

Witt, M., Wozniak, W., 2006. Structure and function of the vomeronasal organ. Adv. Oto-Rhino-Laryngol. *63*, 70–83. https://doi.org/10.1159/000093751.

Wöhr, M., Schwarting, R.K.W., 2007. Ultrasonic communication in rats: can playback of 50-kHz calls induce approach behavior? PLOS ONE *2* (12), e1365. https://doi.org/10.1371/journal.pone.0001365.

Wright, J.M., Gourdon, J.C., Clarke, P.B.S., 2010. Identification of multiple call categories within the rich repertoire of adult rat 50-kHz ultrasonic vocalizations: effects of amphetamine and social context. Psychopharmacology *211* (1), 1–13. https://doi.org/10.1007/s00213-010-1859-y.

Wyatt, T.D., 2010. Pheromones and signature mixtures: defining species-wide signals and variable cues for identity in both invertebrates and vertebrates. J. Comp. Physiol. A *196* (10), 685–700. https://doi.org/10.1007/s00359-010-0564-y.

Yang, G.C., Scherer, P.W., Zhao, K., Mozell, M.M., 2007. Numerical modeling of odorant uptake in the rat nasal cavity. Chem. Senses *32* (3), 273–284. https://doi.org/10.1093/chemse/bjl056.

Yang, S.C.-H., Wolpert, D.M., Lengyel, M., 2016. Theoretical perspectives on active sensing. Curr. Opin. Behav. Sci. *11*, 100–108. https://doi.org/10.1016/j.cobeha.2016.06.009.

Yao, K., Bergamasco, M., Scattoni, M.L., Vogel, A.P., 2023. A review of ultrasonic vocalizations in mice and how they relate to human speech. J. Acoust. Soc. Am. *154* (2), 650–660. https://doi.org/10.1121/10.0020544.

Yoles-Frenkel, M., Cohen, O., Bansal, R., Horesh, N., Ben-Shaul, Y., 2017. In vivo stimulus presentation to the mouse vomeronasal system: surgery, experiment, setup, and software. J. Neurosci. Methods *285*, 19–32. https://doi.org/10.1016/j.jneumeth.2017.05.001.

Youngentob, S.L., Mozell, M.M., Sheehe, P.R., Hornung, D.E., 1987. A quantitative analysis of sniffing strategies in rats performing odor detection tasks. Physiol. Behav. *41* (1), 59–69. https://doi.org/10.1016/0031-9384(87)90131-4.

Yuki, S., Okanoya, K., 2014. Behavioral correlates of 50-kHz ultrasonic vocalizations in rats: progressive operant discrimination learning reduces frequency modulation and increases overall amplitude. Anim. Behav. Cogn. *1*, 452–463. https://doi.org/10.12966/abc.11.03.2014.

Zala, S.M., Nicolakis, D., Marconi, M.A., Noll, A., Ruf, T., Balazs, P., Penn, D.J., 2020. Primed to vocalize: Wild-derived male house mice increase vocalization rate and diversity after a previous encounter with a female. PLOS ONE *15* (12), e0242959. https://doi.org/10.1371/journal.pone.0242959.

Žampachová, B., Kaftanová, B., Šimánková, H., Landová, E., Frynta, D., 2017. Consistent individual differences in standard exploration tasks in the black rat (Rattus rattus). J. Comp. Psychol. *131* (2), 150–162. https://doi.org/10.1037/com0000070.

Zhang, G., Ma, Z., Shen, J., Zhang, K., Wang, J., Chi, Z., 2020. Experimental study on eliminating fire smokes using acoustic agglomeration technology. J. Hazard. Mater. *382*, 121089. https://doi.org/10.1016/j.jhazmat.2019.121089.

Zhao, K., Dalton, P., Yang, G.C., Scherer, P.W., 2006. Numerical modeling of turbulent and laminar airflow and odorant transport during sniffing in the human and rat nose. Chem. Senses *31* (2), 107–118. https://doi.org/10.1093/chemse/bjj008.

Zhou, D., Luo, Z., Jiang, J., Chen, H., Lu, M., Fang, M., 2016. Experimental study on improving the efficiency of dust removers by using acoustic agglomeration as pretreatment. Powder Technol. *289*, 52–59. https://doi.org/10.1016/j.powtec.2015.11.009.