

An update and review of arthropod vector sensory systems: Potential targets for behavioural manipulation by parasites and other disease agents

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Abstract

For over a century, vector ecology has been a mainstay of vector-borne disease control. Much of this research has focused on the sensory ecology of blood-feeding arthropods (black flies, mosquitoes, ticks, etc.) with terrestrial vertebrate hosts. Of particular interest are the cues and sensory systems that drive host seeking and host feeding behaviours as they are critical for a vector to locate and feed from a host. An important yet overlooked component of arthropod vector ecology are the phenotypic changes observed in infected vectors that increase disease transmission. While our fundamental understanding of sensory mechanisms in disease vectors has drastically increased due to recent advances in genome engineering, for example, the advent of CRISPR-Cas9, and high-throughput “big data” approaches (genomics, proteomics, transcriptomics, etc.), we still do not know if and how parasites manipulate vector behaviour. Here, we review the latest research on arthropod vector sensory systems and propose key mechanisms that disease agents may alter to increase transmission.



1. Introduction

1.1 Vector ecology in the 21st century

Vector-borne diseases (see **Glossary**) like malaria, dengue fever, and West Nile Virus claim countless human and non-human animal lives every year. According to the World Health Organization¹, over 700,000 people are killed annually by disease-causing agents (primarily bacteria, protists, and viruses) vectored by **hematophagous** arthropods (black flies, fleas, mosquitoes, ticks, etc.) that transmit them from infected to uninfected individuals via blood meals ([Fig. 1](#)). Although, not all blood-feeding arthropods are known to transmit disease, notably lice and bed bugs, which typically live in close association with their hosts ([Lai et al., 2016](#)). These diseases play an important role in emerging infectious diseases worldwide ([Daszak et al., 2000](#)) and are responsible for large-scale population declines of wild animals around the globe ([LaDeau et al., 2007](#)). Indeed, reducing the negative impacts of vector-borne diseases poses a serious challenge for researchers and policy makers, especially under the increasing disruption of known

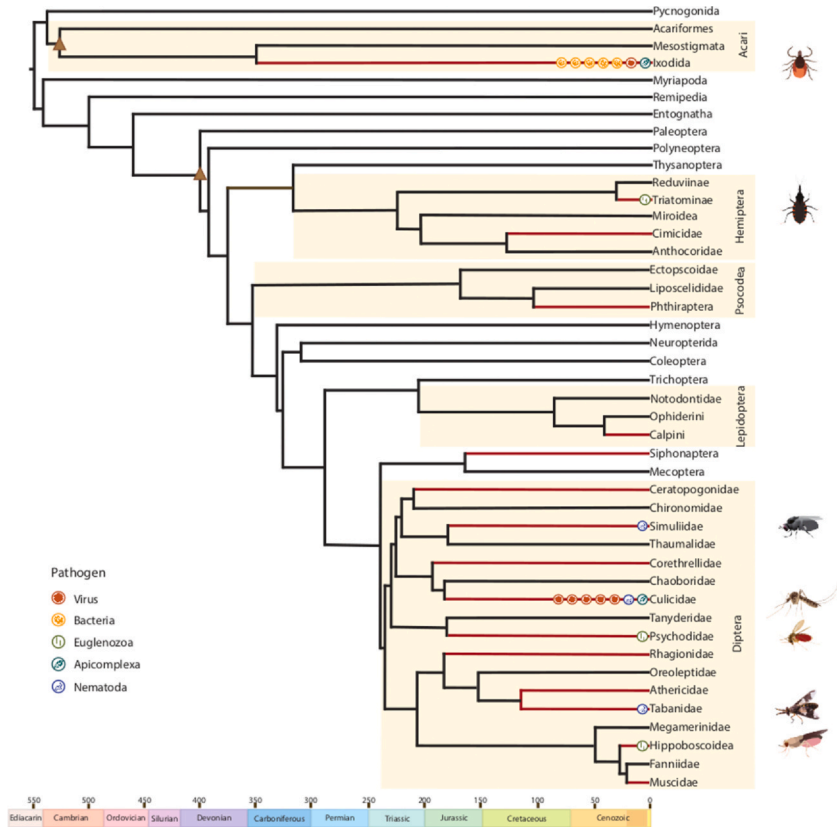


Fig. 1 Hematophagy (blood feeding) across Arthropoda. Branching corresponds to estimated divergence times (in millions of years), with divergence estimates of Arachnida and Hexapoda denoted by red triangles. Note that tips are not collapsed to the same phylogenetic resolutions. Red branches indicate blood feeders: Ixodida (ticks), Triatominae (kissing bugs), Cimicidae (bed bugs), Phthiraptera (lice), Calpini (vampire moths), Siphonaptera (fleas), and the dipteran families Ceratopogonidae (biting midges), Simuliidae (black flies and sand flies), Corethrellidae (frog biting midges), Culicidae (mosquitoes), Psychodidae (moth flies), Rhagionidae (snipe flies), Athericidae (watersnipe flies), Tabanidae (horse flies and deer flies), Muscidae (house flies), and the superfamily Hippoboscoidea, with the families Glossinidae (tsetse flies), Hippoboscidae (louse flies), Streblidae (bat flies), and Nycteriidae (bat flies) placed within. Coloured circles indicate disease agents vectored by arthropods. Multiple instances of the same color circle denote multiple disease agents in the same group. Phylogenetic relationships and molecular clock calibrations were adjusted according to the literature (Fontaine et al., 2011; Hwang and Weirauch, 2012; Johnson et al., 2018; Kawahara et al., 2019; Mans, 2011; Mans et al., 2013; Narayanan Kutty et al., 2018; Song et al., 2012; Van Dam et al., 2019; Wiegmann et al., 2011; Zheng et al., 2022).

vector-disease patterns caused by anthropogenic change (Carlson et al., 2023). Vector ecology has been one of the main research focuses of vector control for decades (Wilson et al., 2020), and while we have gained an appreciation for the main drivers governing global disease patterns (Doherty et al., 2021), there are still wide knowledge gaps in many systems. Thus, we are far from having a complete picture of vector-disease diversity (Swei et al., 2020). One of the prominent research efforts in vector ecology is to elucidate how vectors seek and feed on hosts, which is driven by sensory information integrated from external cues (vision, olfaction, taste, etc.) and internal states like hunger (Ignell et al., 2022) (Fig. 2). Within the past decade, advances in gene editing technologies, for example, **CRISPR-Cas9**, have rapidly expanded our capacity to test for the function of practically any gene (Wang and Doudna, 2023), including sensory receptors in vectors (Kistler et al., 2015) and **pathogenicity** of vector-borne diseases (Puschnik et al., 2017). Because of their importance to human health, most of these studies have focused on genetically modifying disease-vectoring mosquito species from the *Aedes* and *Anopheles* genera (Konopka et al., 2023). These technologies have allowed us to pinpoint fundamental aspects of sensory or neural pathways that modulate vector host seeking and host feeding behaviours (Raji et al., 2019; Ye et al., 2022).

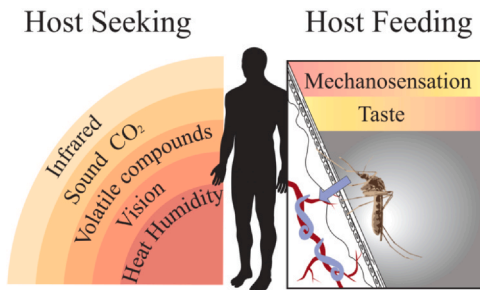


Fig. 2 Cues or stimuli driving host seeking and host feeding in vectors (pictured here, an *Anopheles* mosquito). Host seeking cues can vary from long-range infrared radiation to short-range heat and humidity signals emitted by a host (pictured here, a human). Host feeding cues include taste and touch (mechanosensation), and the internal mechanosensory cues that occur during a blood meal like abdominal distension (proprioception). Disease transmission can only happen during host feeding, when fluids are exchanged between the vector and the host (pictured here, the malaria parasite *Plasmodium* entering the host blood stream via mosquito saliva). Note that the combination of cues used to locate and feed on hosts can vary between vector species, and some cues may not be used at all.

1.2 Host manipulation in vectors

We now know that infected vectors can behave differently than their uninfected conspecifics, and several controlled observational studies and experimental studies have shown changes in host seeking or host feeding that increase the transmission of disease agents (Ignell et al., 2022; Javed et al., 2021; Stanczyk et al., 2017). These behavioural changes typically occur when the **parasite** reaches a particular developmental stage, suggesting potential **adaptive host manipulation** (Poulin, 1995; Vantaux et al., 2021). For example, mosquitoes (Culicidae; vectors of malaria, dengue fever, yellow fever, etc.) infected with *Plasmodium* sporozoites (infective stage) can take longer to probe during blood feeding, increasing the odds of transmission (Cornet et al., 2019). Ticks (Ixodida; vectors of Lyme disease, **babesiosis**, etc.) appear more capable of finding hosts when infected with *Borrelia burgdorferi*, the main bacterium that causes Lyme disease (Faulde and Robbins, 2008). Kissing bugs (Triatominae; vectors of Chagas disease) infected with the protist *Trypanosoma cruzi* (cause of Chagas disease) take less time to locate potential hosts and bite more frequently than uninfected controls (Botto-Mahan et al., 2006) (Fig. 3). Many more examples have been compiled in recent reviews (Ignell et al., 2022; Javed et al., 2021), and the behavioural changes that occur in vectors often appear to favour parasite transmission. As in other host-parasite systems (Poulin and Maure, 2015), most cases of host manipulation remain descriptive in nature, using natural infections and excluding any real test of mechanism. Another hurdle is distinguishing between adaptive manipulation and fortuitous side effects of infection, which is one of the greatest challenges in host manipulation research (Bhattarai et al., 2021; Poulin, 2010). Host immune reactions can mediate behaviours that just happen to favour parasites. For example, heat-killed bacteria and malarial-causing *Plasmodium yoelii* promote similar neurophysiological responses that increase protist transmission in *Anopheles* mosquitoes, putting into question the actual extent of host manipulation as opposed to isolated immune responses (Cator et al., 2013); other such examples exist in closely related host-parasite systems (Stanczyk et al., 2019). Although still an open question, the evidence accumulated to date suggests that some vector-borne diseases modulate vector behaviours to increase transmission, and here we offer likely pathways through which parasites can accomplish this.

Although vector behaviours are nearly always considered in epidemiological modelling (Cator et al., 2020), parasite-induced modification of

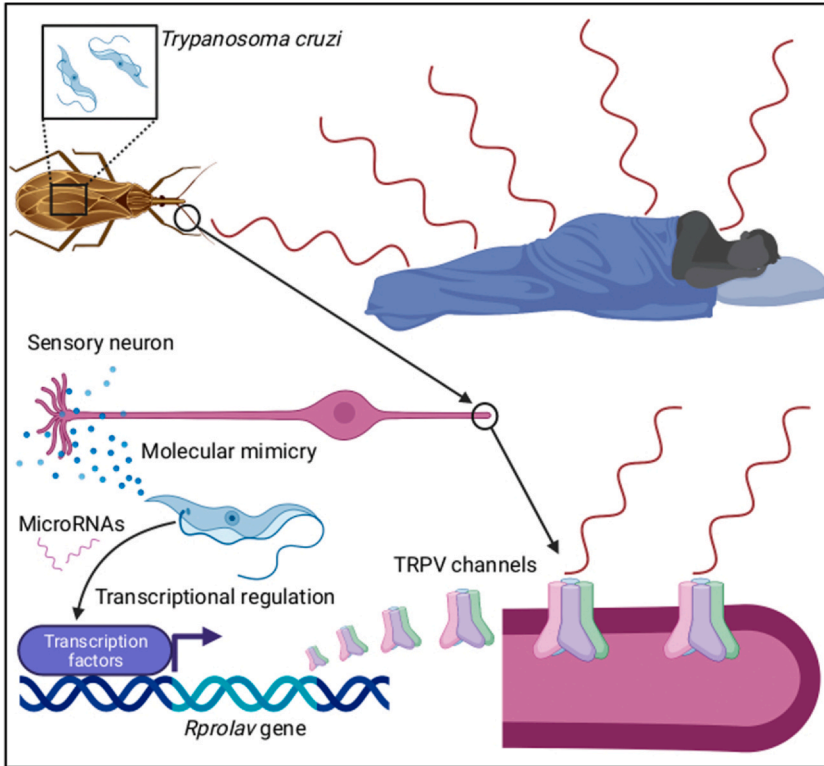


Fig. 3 Hypothetical mechanisms of host manipulation of the kissing bug *Rhodnius prolixus* by *Trypanosoma cruzi* (protist that causes Chagas disease). Kissing bugs detect infrared radiation emitted by mammals through TRPV channels (receptors) located on the dendrite (typically housed within sensilla in arthropods) in the antennae (Zermoglio et al., 2015). The transmissible stage of *T. cruzi* (metacyclic trypomastigotes) could increase the number of receptors through transcriptional regulation on the *Rprolav* gene, by means of small non-coding RNAs such as microRNAs or proteins that mimic transcription factors (protein mimicry). The parasite could also secrete molecules that mimic downstream neuronal activities governed by fast-acting neurotransmitters or slow-acting neuromodulators. One or multiple changes described here could increase the sensitivity of kissing bugs to infrared radiation or increase their general movement towards the source (here, a human), increasing the odds of parasite transmission. Created with BioRender.com.

vector traits are rarely included (Ignell et al., 2022). If these disease agents are indeed adapted to change vector phenotype to their advantage, it must somehow be manifest in the biology of the vector. While our understanding of vector sensory mechanisms has increased considerably within the past two decades (Baik and Carlson, 2020; Martin et al., 2011), we still

have little to no inkling as to how vector-borne diseases could modulate the behaviours of vectors (Ignell et al., 2022; Javed et al., 2021). This discrepancy highlights a critical knowledge gap in the ecology and evolution of vector-parasite interactions. Here, we review the latest scientific developments on vector sensory mechanisms across the known diversity of human and non-human disease vector systems (Fig. 1). Specifically, we discuss recent research on the mechanisms underpinning vector behaviours that may be modulated to increase disease transmission. We focus on the environmental cues that guide vectors to a potential host and the proximate cues that encourage a blood meal, when the odds of disease transmission are highest. Albeit rare, we also include any research that specifically tests for mechanisms underlying parasite-induced physiological states in the vector that might promote the spread of disease. Finally, we tie all this information together to propose key pathways that parasites may be adapted to exploit (see Fig. 3 for an example) and suggest future research directions to address these current important gaps in knowledge.



2. Host seeking versus host feeding

Disease transmission occurs when fluid is exchanged between a vector and its host (Shaw and Catteruccia, 2019), like when vector saliva containing infective stages of a disease agent enters the host blood stream (Fig. 2). To highlight this decisive moment in the life cycle of vectored parasites, we hereby distinguish between environmental signals and mechanisms that allow vectors to locate a host (host seeking) and proximate signals and mechanisms involved in probing, biting, or blood uptake by vectors (host feeding). The mechanisms reviewed here generally comprise entire **sensory systems** (receptor neurons, ganglia, and the brain) within arthropods and the molecules that control their activities (receptors, neurotransmitters, and neuromodulators) (Smarandache-Wellmann, 2016; Whittington and Mayer, 2011) (Fig. 3). Unless otherwise specified, “vectors” include infected and uninfected individuals in the arthropod taxa highlighted by icons in Fig. 1 (although we note that other blood-feeding taxa may also vector diseases yet undiscovered).

2.1 Host seeking mechanisms

Vectors are already highly specialised to locate and feed upon hosts (Ribeiro, 1995), owing to the fact that host blood is typically necessary for females to produce eggs. They have a multitude of receptors (Box 1)

Box 1 Sensory receptor gene families in arthropods.

There are many gene families in arthropod genomes that encode proteins or protein subunits mediating sensory transduction (Table 1). These are often multigene families with high rates of duplication, deletion, and sequence mutability across evolutionary time, allowing species with diverse ecological niches and life histories to sense the cues most important for them.

Table 1 (Box 1). Main gene receptor families in arthropod vectors with their sensory modalities.

Gene family	Sensory modality
Gustatory receptors (GRs)	Olfaction, taste
Ionotropic receptors (IRs)	Taste, olfaction, heat and humidity sensation
Odorant receptors (ORs)	Olfaction
Opsins	Vision
Pickpocket (PPK) channels	Taste, mechanosensation
Transient receptor potential (TRP) channels	Taste, mechanosensation, heat and humidity sensation

Gustatory receptors (GRs) are presumptive ligand-gated ion channels with uncertain stoichiometry. Despite the name, some GRs have also been implicated in the sensation of volatile cues, most notably carbon dioxide.

Ionotropic receptors (IRs) are variant ionotropic glutamate receptors, forming a family of ion channels that sense volatile olfactory cues, contact chemical cues, humidity, heat, as well as others. They appear to have evolved as sensory receptors in early protostomes, and many arthropod genomes contain hundreds of IR subunits. They are thought to be heteromeric proteins made up of subunits which can include broadly expressed co-receptors such as Ir8a, Ir25a, and Ir76b.

Odorant receptors (ORs) are heterotetrameric ligand-gated ion channels that are made up of a co-receptor subunit, Orco, and a ligand-specific ORx subunit. Upon ligand binding, the conformation of the channel shifts to allow ion flow.

Opsins are G-protein coupled receptors that are bound to light-absorbing chromophores. Distinct opsin and chromophore complexes are tuned to be maximally sensitive to specific wavelengths of light.

Pickpocket (PPK) channels are amiloride-sensitive degenerin epithelial sodium channels (DEG/eNaCs). In insects, they have been implicated as pheromone detectors (taste), as well as sensors of salt, osmotic pressure, and mechanical forces.

Transient Receptor Potential (TRP) channels are evolutionarily conserved cation channels that have been implicated in taste, heat and humidity, and mechanical sensation.

expressed in sensory neurons (Fig. 3), allowing them to detect and respond to diverse cues, including host visual cues and odours, carbon dioxide (CO₂), heat, sound, and moisture (van Breugel et al., 2015), which are critical to finding hosts and thus disease transmission. These cues are often perceived by vectors at various distances relative to a potential host; these distances can vary greatly between vector species (Fig. 2). To predict how parasites potentially manipulate vector host seeking, it is first necessary to have a solid understanding of the complex sensory systems involved.

2.2 Seeing

Vision is crucial for many vectors to navigate and locate potential hosts, therefore a direct parasite-induced alteration of visual acuity or preference could increase the odds of finding a host. At its most basic level, light can influence the overall activity of vectors by impacting **circadian rhythms** (Helfrich-Förster, 2020). Light sensing is especially important for vectors that concentrate host seeking efforts around specific times of day, for example, **crepuscular** species of mosquito. Common visual structures across all arthropods include **compound eyes** or **ocelli**, which possess photoreceptors that detect light (Bitsch and Bitsch, 2005). These receptors contain proteins, called opsins (Box 1), tuned to undergo **conformational changes** in response to specific wavelengths of light, thereby defining their visual spectrum (Barrozo et al., 2017; van der Kooi et al., 2021).

Light contrast is a primary stimulus for identifying host targets and is even seen in arthropods with relatively underdeveloped visual systems such as ticks (Leonovich, 2015). Negative **phototaxis** can occur when ticks detect shadows moving across their visual field, leading to a change in orientation towards that object or potential host (Leonovich, 2015). Generic visual identification of host targets is also seen in frog-biting midges (Corethrellidae; vectors of *Trypanosoma*), which can discern the outline of frogs to hone in on their location at closer ranges (da Silva and Breviglieri, 2021).

In more complex systems, individual photoreceptor classes can respond to different properties of light (wavelength, **polarisation**, etc.). The compound eyes in horse flies (Tabanidae; vectors of **equine infectious anemia**) are specialised to recognise different orientations of polarised light to distinguish hosts from background shades (Horváth et al., 2017). Depending on the different classes of photoreceptors (contained within “pale” or “yellow” ommatidia), this tuning either is or is not sensitive to polarisation (Meglič et al., 2019). Within the compound eyes of the *Aedes aegypti* mosquito, two highly related opsins (Op1 and Op2) were found, through targeted gene knockouts, to be integral to visual host attraction (Zhan et al., 2021). Mosquitoes can integrate visual information in tandem with other environmental cues such as heat and odour (Carnaghi et al., 2021; van Breugel et al., 2015). For instance, high-contrast visual and heat cues can be attractive to *Ae. aegypti*, but landing and aggregation only occur in the presence of CO₂ (Liu and Vosshall, 2019). For other vectors, however, vision may play little to no role in host seeking. In kissing bugs, there has been no evidence found so far that vision is an important factor when searching out hosts; they appear fully capable of locating hosts in the dark (Lazzari, 2021).

Little evidence exists on the modulation of vector visual systems by disease agents. For instance, the biting midge *Culicoides sonorensis* (Ceratopogonidae; vectors of **bluetongue disease**) appears to display aversion to the ultraviolet light emitted by traps when infected with Bluetongue virus, which were revealed to aggregate at very high levels in the ommatidia of infected midges (McDermott et al., 2015). Given the importance of light contrast for host seeking, perhaps a parasite-induced increase in sensitivity to contrast could mean a greater attraction to potential hosts. Any damage to the eyes or photoreceptors that decreases the ability of a vector to see contrast would likely not be advantageous to the parasite. Considering the universal nature of opsins within the animal kingdom (Terakita, 2005), any change in their numbers or sensitivity within the eyes of vectors may contribute to altering host seeking behaviours.

2.3 Hearing

True hearing, that is the conversion of sound-induced vibrations into electrical signals (a type of mechanosensation), evolved independently across several groups of insects and involves modified chordotonal organs (a type of stretch receptor) (Göpfert and Hennig, 2016). If infected vectors were more sensitive to frequencies emitted by their hosts, this

would increase their ability to locate hosts from sound alone. These sensory organs have been well studied in vectors such as mosquitoes. In dipterans, they are called the Johnston's organ and are found in the second antennal segment. They have an operational range of millimetres to metres and have been shown to respond to sound from up to 10 m away (Menda et al., 2019).

Growing evidence suggests that mosquitoes also use auditory cues to locate hosts (Steele and McDermott, 2022). It has been shown that male mosquitoes can use short-range auditory signals (based on the frequency of female flight tones) when searching for mates (Cator et al., 2009; Simões et al., 2016). Moreover, the range of frequencies within which mosquitoes hear can coincide almost perfectly with sound frequencies emitted by their host, suggesting a role for hearing in host seeking (Menda et al., 2019). In *An. gambiae* and *Ae. aegypti* mosquitoes, octopamine acts as an auditory modulator involved in the mechanical responses to sounds (Xu et al., 2022; Georgiades et al., 2023). Frog-biting midges are known to use host acoustic cues to locate anuran hosts by detecting their mating calls (de Silva et al., 2015). In ticks, which lack chordotonal organs, there is no evidence to suggest that they use auditory cues to seek hosts, although they may rely on mechanical vibrations during **questing** (Leal et al., 2020). Though studies are currently lacking, if parasites were adapted to modify hearing in vectors (in this case, dipterans such as midges and mosquitoes) to increase transmission, the underlying mechanisms would most likely implicate the stretch receptors located in the Johnston's organ.

2.4 Smelling

Much of what we know about olfaction in disease vectors comes from the large body of literature on mosquitoes. Olfaction is often considered a dominant cue for host seeking (Sumner and Cardé, 2022), since odours move by air convection and can thus travel much further away from the host (Sehdev et al., 2019). Because of their importance in host seeking, infected vectors may be more sensitive or attuned to certain olfactory cues produced by hosts. Olfactory cues include CO₂ and various **volatiles** emitted by a host (Fig. 2) that are detected by olfactory receptors expressed in olfactory sensory neurons (OSNs). These OSNs are housed in **sensilla** typically located on the antennae or other specialised sensory organs. The number and expression of these receptors can vary widely between species (Carey and Carlson, 2011). Vectors share both the ionotropic receptor (IR) and gustatory receptor (GR) families for olfaction (Vizueta Moraga et al., 2018), while the odorant

receptor (OR) family and the OR **co-receptor** (Orco) evolved shortly before the advent of terrestrial insects and are not found in non-insect vectors such as ticks (Brand et al., 2018) (Box 1). The ORs can play important roles in host preference through odour detection and integration of multiple sensory information, including host seeking and blood feeding (Jung et al., 2015; Ni et al., 2022). Receptors in this family also modulate repellency to synthetic compounds such as DEET (Xu et al., 2014).

In mosquitoes, CO₂ is the first olfactory cue that activates or primes sensory receptors and promotes positive **chemotaxis** in the direction of the host or a general increase in arousal (Sorrells et al., 2022). Depending on the species, the type of receptors can vary, but generally only three are known to be involved. For instance, GR1, GR2, and GR3 are found in *Ae. aegypti* and *Culex* spp., whereas the orthologs GR22, GR23, and GR24 are found in *Anopheles* spp. It has been shown, especially in *An. coluzzii*, that two of the receptors are necessary for CO₂ detection, while the third acts as a modulator (Liu et al., 2020). CO₂, as a by-product of **aerobic respiration**, is also an attractant in many other vectors including kissing bugs, tsetse flies, black flies, sand flies, ticks, and fleas (Indacochea et al., 2017; Jones, 2013), although the receptor(s) involved in its detection are generally unknown outside of well-studied mosquito taxa. However, CO₂ is not known to attract and may even repel vectors such as frog-biting midges, which feed on anurans with low metabolisms and are likely more dependent on acoustic and visual cues for host seeking (see previous sections). Similarly, the nature of attractive volatiles detected by IRs can depend on the type of host that vectors co-evolve with (Raji et al., 2019; Ye et al., 2022). For example, 1-octen-3-ol, an alcohol emitted by mammals, attracts *An. gambiae* and *Ae. aegypti* mosquitoes (primarily feed on mammalian hosts), but repels *Cx. quinquefasciatus* (primarily feeds on avian hosts) (Wolff and Riffell, 2018). In humans, *Ae. aegypti* mosquitoes react to specific volatiles such as carboxylic acids (via IRs) and aldehydes (via ORs) (De Obaldia et al., 2022; Zhao et al., 2022); differences in the amounts or the relative ratios of these cues can increase or decrease the attractiveness of a human host (De Obaldia et al., 2022; Giraldo et al., 2023), signalling a potential target mechanism for disease agents to exploit.

While the limited evidence that exists suggests that disease agents increase host seeking by modulating the attractiveness of host volatiles in vectors (Javed et al., 2021; Stanczyk et al., 2017; Vantaux et al., 2021), no study to our knowledge has identified any specific mechanism responsible for this increase in attractiveness. Disease agents may indirectly increase

attractiveness to hosts in vectors by altering the relative mixture of volatiles emitted by hosts (Díez-Fernández et al., 2020; Robinson et al., 2018; Zhang et al., 2022). In humans infected with *Plasmodium*, certain aldehydes were found to be produced in greater quantities than in uninfected individuals, which were detectable by *Anopheles* mosquitoes, effectively increasing the attractiveness of infected human skin odours in this vector (Robinson et al., 2018). Thus, depending on the vector and the importance of volatiles for host seeking, for example, high importance in mosquitoes, any change in the number, tuning, or sensitivity of receptors expressed in peripheral olfactory tissues could alter these behaviours.

2.5 Sensing temperature and humidity

Olfactory cues may guide vectors over longer ranges, but temperature and humidity gradients can alert vectors to a nearby host (Laursen et al., 2023; Zermoglio et al., 2017). Parasite-induced changes to these systems could therefore increase the ability of a vector to home in on its host at closer ranges. Among the three families of receptors (Box 1), the IRs have been found to be more ancestral than the GRs and ORs, and their functions are conserved across many taxa (Benton et al., 2009; Croset et al., 2010; Rytz et al., 2013). Consequently, they carry out a wide range of functions in addition to chemosensation (Box 1), including the detection of heat (thermosensation) and humidity (hygrosensation) (Benton et al., 2009; Enjin et al., 2016; Greppi et al., 2020; van Giesen and Garrity, 2017). Certain deeply conserved IRs are responsible for sensing humidity across most insect species, including mosquitoes (Enjin et al., 2016; Knecht et al., 2016). Because of the apparent dual role of some IRs, hygrosensation and thermosensation seem to function closely in parallel. Pioneering studies in *Drosophila* have shown that IR21a and IR25a mediate thermal preferences and hygrosensation (Budelli et al., 2019; Knecht et al., 2017; Ni et al., 2016). Several IRs, such as IR21a and IR93a, have been proven to be crucial for thermosensing in mosquitoes (Greppi et al., 2020). IR93a can also act as a humidity sensor and was shown to be necessary in maintaining attraction to human hosts and promoting consumption of warmed blood (Laursen et al., 2023); several IRs were found to have conserved thermosensory and hygrosensory functions in the sacculus of *Drosophila melanogaster*, although their exact function(s) depends on the combination of receptors involved (Knecht et al., 2016; Ni, 2021). In addition to the IR family, the TRP cation channel A1, or TRPA1, protein has been associated with thermosensation and host seeking in *An. stephensi* (Maekawa et al., 2011) and in controlling

avoidance of noxious temperatures in *Ae. aegypti* (Corfas and Vosshall, 2015). TRPs are highly conserved in animals and likely contribute to many sensory modalities (Fowler and Montell, 2013) (Box 1).

In other vectors such as kissing bugs and ticks, heat dispersed by hosts can also be used as a cue for host seeking (Ignell et al., 2022), and orthologs to the IRs mentioned above likely play a key role. For instance, kissing bugs use heat and humidity to locate hiding places and seek hosts, and the TRP channels *nanchung* and *waterwitch* likely mediate these behaviours (Latorre-Estivalis and Lorenzo, 2019). Heat cues can work in tandem with other cues to elicit host seeking in vectors. To illustrate, if CO₂ primes *Ae. aegypti* mosquitoes to seek hosts, the addition of proximal host heat cues will then initiate probing behaviours (Sorrells et al., 2022). IR21a, a cooling-activated receptor that mediates heat-avoidance in *Drosophila* (Ni et al., 2016), was found to drive heat seeking in *An. gambiae* (Greppi et al., 2020). Because of the ancestral nature of IRs (Croset et al., 2010), it is likely that this receptor was repurposed for host seeking in this vector, suggesting again that sensory circuits expressing members of this large gene family could be a prime target for manipulation by disease agents.

2.6 Infrared sensing

In addition to sensing temperature gradients as vectors approach very close by to potential hosts, some vectors have sensory organs that are sensitive to infrared radiation, enabling a longer-range mechanism for detecting heat in the environment that could be subjected to host manipulation. Unlike wavelengths in the visual spectrum, infrared radiation is not known to be detected by opsins in the visual system (Guignard et al., 2022). Temperature gradients caused by host-emitted heat are typically detectable within a few centimetres (Laursen et al., 2023), whereas host-emitted infrared gradients are in theory detectable for ranges of several centimetres up to several hundred metres (Catala, 2011) (Fig. 2). Ticks and kissing bugs are equipped with specialised sensory organs, for example, Haller's organ in ticks, to detect infrared radiation using the highly conserved TRP receptors (Barrozo et al., 2017) (Fig. 3). Multiple tick species utilise infrared-sensitive receptors on their **tarsi** and have demonstrated varying behavioural responses to infrared cues based on feeding state (Mitchell et al., 2017). While mosquitoes are not yet known to detect infrared wavelengths (Zermoglio et al., 2017), its use as a cue by other host-seeking arthropods begs the question of whether future work will find that infrared detection is indeed a component of the mosquito multisensory host seeking toolkit, and as such, a potential avenue of exploitation by disease agents.

2.7 Host feeding mechanisms

Once vectors effectively locate a suitable host through host seeking, they must then rely on proximate host cues for probing, biting, and blood feeding, all three of which are grouped under host feeding mechanisms. Like for host seeking, various sensory systems are involved in host feeding. Taste and mechanosensation underpin important host feeding behaviours such as the time spent probing and the length of blood meals (Ignell et al., 2022; Javed et al., 2021). Since disease transmission occurs during host feeding, there is indeed great potential for parasites to have adapted traits that increase host feeding behaviours to maximise transmission.

2.8 Tasting

In vectors, gustation or taste plays a critical role in host feeding (Ortega-Insaurralde and Barrozo, 2022). The behavioural response to taste cues governs the final decision about whether to feed or not, therefore any parasite-driven modulation of this system could determine if transmission is at all possible. Insect vectors have taste organs distributed throughout the body, including the margins of wings, the tarsi on the legs, and various mouthparts (King and Gunathunga, 2023). The **stylet** is usually responsible for piercing or cutting the skin and drawing blood in hematophagous insects (ticks use highly modified chelicerae and a barbed hypostome to cut through skin) (Krenn and Aspöck, 2012). Taste receptors, comprised primarily of GRs and IRs (Box 1), are expressed in gustatory receptor neurons housed in the gustatory organs with dendrites extending into hair-like sensilla. It is through these dendrites that the cells will make physical contact with a taste cue. Different tastes will elicit different responses in neurons depending on the receptors expressed on that cell. For example, in mosquitoes, taste can be used to sense cues both external (e.g., sweat) and internal (e.g., blood) during blood feeding. Taste is also used for non-blood-feeding behaviours, such as nectar ingestion by both male and female mosquitoes. Overall, taste allows the detection of both nutritive and toxic compounds; sugar and low salt are attractive while bitter compounds and high concentrations of salts elicit aversive responses (Baik and Carlson, 2020). A mixture of key plasma components such as adenosine triphosphate (ATP), sodium chloride (NaCl), and sodium bicarbonate (NaHCO₃) are crucial stimulants that trigger blood feeding. In *Ae. aegypti* mosquitoes, neurons in the stylet are the first to detect blood after a bite (Jové et al., 2020). Similarly, taste is known to modulate the feeding behaviours of

other arthropod vectors such as kissing bugs and ticks (Pontes et al., 2022; Soares et al., 2013).

When it comes to the perception of distinct taste cues found in blood, IR7a and IR7f have been identified as key receptors in the stylet of *Ae. aegypti* mosquitoes (Jové et al., 2020). Another study conducted in *An. coluzzii* mosquitoes confirmed that targeted gene knockout of IR76b, a broadly expressed IR co-receptor found in the neurons of the stylet, showed a robust reduction in blood feeding, pointing to a key mechanism underpinning this important behaviour (Ye et al., 2022). Thus, there are multiple plausible impacts on taste that could yield increases in disease transmission, for example, a downregulation of responses to bitter or other aversive cues or an increase in sensitivity to appetitive feeding cues could each hypothetically increase the rates of biting and feeding.

2.9 Mechanosensation

Mechanosensation involves the detection of physical forces on and within the body and is involved in senses such as hearing (see above), nociception (detection of painful forces), proprioception (sense of the body in space), and touch. The detection of these forces is carried out by a broad diversity of receptors that detect changes in membrane stretch and direct physical forces on the receptor (Box 1).

For arthropod vectors, mechanosensory cues may be important to initiate feeding. In *D. melanogaster*, channel like receptor 1 (TMC1) and the TRP channel, no mechanoreceptor potential C are necessary for evaluating the texture of foods (Sánchez-Alcañiz et al., 2017; Zhang et al., 2016; Zhou et al., 2019). These texture cues synergise with volatile and taste cues to mediate food acceptance or rejection (Oh et al., 2021). Here, a parasite may alter the degree to which a vector senses food texture, which can lead to an increase in probing or feeding time. In *Ae. aegypti* mosquitoes, a pair of mechanosensory campaniform sensilla are found near the tip of the labrum and mediate blood feeding (Jové et al., 2020; Jung et al., 2015). The mechanosensory cues from these sensilla are likely combined with volatile cues to enable the mosquito to find and ingest host blood (Jung et al., 2015). Additionally, during probing, the labrum-interacting protein of the saliva 2 secreted in the saliva of *Aedes* mosquitoes binds to labrum cuticular proteins, resulting in a morphological change that is most likely sensed by proprioceptive receptors (Arnoldi et al., 2022). In this study, experimental knockdown of this protein resulted in mosquitoes taking longer to feed to

engorgement and spending more time probing the skin, suggesting an important role of these proteins in blood feeding.

Mechanosensation is also an important cue in controlling food intake once feeding has begun. In *D. melanogaster*, the mechanoreceptor Piezo (from Greek, meaning “pressure”) detects gut distension and controls food intake (Eun Kim et al., 2012; Min et al., 2021). During feeding, activation of Piezo as the abdomen distends reduces appetite and food intake. Experimental knockout of this gene can result in gut bloating and increased food consumption. Likewise, in *Ae. aegypti* abdominal distension is proposed to act as the first mechanism to terminate feeding and suppress host seeking behaviour following engorgement from a blood meal, though the receptor mechanism is yet unknown (Klowden and Lea, 1979). Following this initial cue, further host seeking suppression is, in part, mediated by neuropeptide signalling detected by the NPY-like receptor 7 (NPYLR7) in the brain (Duvall et al., 2019). This signalling is triggered by the secretion of insulin-like peptides from the fat body during digestion of a blood meal. To increase the length of a blood meal and maximise disease transmission, these recently discovered mechanosensory mechanisms may be the target of parasite-induced alterations.



3. Vector sensory systems and manipulation by disease agents

The recent literature reviewed here strongly supports the idea that vector sensory systems are indeed multimodal or redundant (Fig. 4). When a vector senses its environment, each sensory system can respond to various cues (Fig. 2), and the right combination of cues triggers a synergistic response that drives host seeking and host feeding. The research on multimodal sensation in vectors has been largely conducted on mosquitoes (Carnaghi et al., 2021; Greppi et al., 2020; Laursen et al., 2023; Liu and Vosshall, 2019; McMeniman et al., 2014, Sorrells et al., 2022) (Fig. 4), however this is most likely a universal feature across vectors (Fig. 1), for example, frog-biting midges (da Silva and Breviglieri, 2021; de Silva et al., 2015), kissing bugs (Barrozo et al., 2017; Indacochea et al., 2017), and ticks (Leal et al., 2020; Leonovich, 2015).

Blood-feeding vectors (Fig. 1) have evolved highly specialised traits to seek and feed on hosts, and they are effectively stuck in the middle of an evolutionary arms race between the parasites they carry and the hosts that provide them with nutrients crucial to their reproductive success.

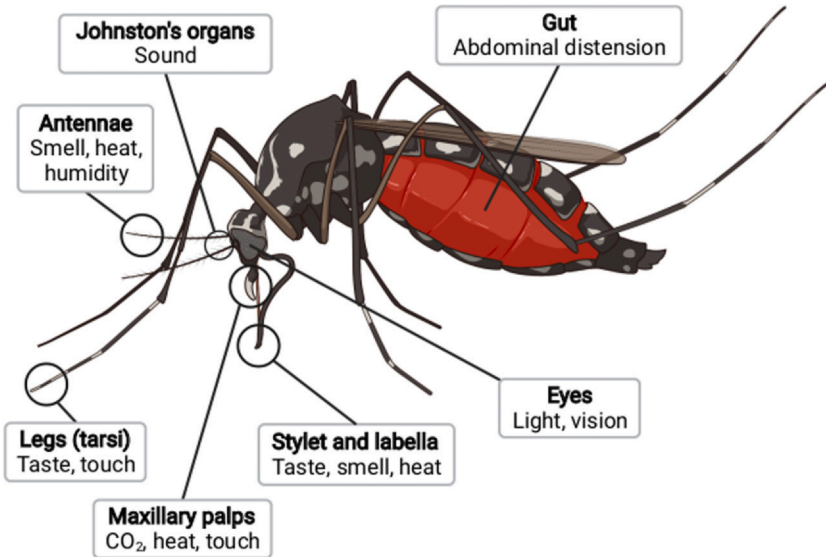


Fig. 4 Multimodal nature of sensory systems that are important for host seeking and host feeding in vectors, depicted here with the *Aedes aegypti* mosquito. The main cues are listed under each organ. These systems can integrate signals from a number of receptors (Box 1) that react to multiple cues, highlighting the redundancy of sensory mechanisms in vectors. Sensory organs and cues for *Ae. aegypti* are based on the recent literature (Jung et al., 2015; Matthews et al., 2016; van Breugel et al., 2015). Created with BioRender.com.

Consequently, vector-borne disease transmission may indeed promote the evolution of parasite-induced behavioural states favouring transmission (de Angeli Dutra et al., 2022). Highly conserved vector genes governing these behavioural states, for example, IRs, TRPs, and opsins (Croset et al., 2010; Fowler and Montell, 2013; Terakita, 2005), can be implicated in sensing multiple cues (Box 1); they also predate the evolution of vector-borne diseases such as malaria (Evans and Wellem, 2002). Parasites may have therefore evolved to exploit these already existing sensory systems to perhaps increase the sensitivity of vectors toward host cues, increase general vector activity, or decrease the responsiveness of vectors during a blood meal. Because of the highly conserved nature of vector genes involved in host seeking and host feeding, there may be convergence in the mechanisms used by distantly related groups of parasites to manipulate vector behaviour. Here, we highlight key sensory mechanisms involved in vector host seeking and host feeding and propose how parasites may adaptively manipulate these behaviours.

3.1 Candidate vector sensory mechanisms subject to manipulation

The TRP receptor family represents a generalised mechanism through which vectors can detect potential hosts (Barrozo et al., 2017; Fowler and Montell, 2013; Latorre-Estivalis and Lorenzo, 2019; Maekawa et al., 2011). The highly conserved nature of these sensory receptors and the existing mechanisms for its regulation (Mitchell et al., 2017; Risper et al., 2022) make them a reasonable target for parasites. Because olfaction plays such an important role for many vectors, namely mosquitoes (Sumner and Cardé, 2022), IRs, GRs, and ORs are also prime targets. Malaria-infected *An. gambiae* mosquitoes, harbouring transmissible sporozoites, showed general transcript upregulation in IRs, GRs, ORs, and TRPs, potentially increasing sensitivity to host olfactory cues and other synergistically operating sensory mechanisms (Carr et al., 2021). Indeed, because of the importance of IRs and TRPs across key sensory systems used by vectors to seek and feed on hosts (Box 1), these should be considered as prime suspects when it comes to vector manipulation. This does not undermine the importance of other receptor families (GRs, ORs, opsins, and PPK channels) (Matthews et al., 2016; Ni et al., 2022), because they likely play important roles in the multimodal responses (Fig. 4) that are required in a signal-rich environment (Fig. 2). The evolutionary ecology of the vector must be understood to determine the relative importance of each sensory system. For example, frog-biting midges that use host mating calls and vision to locate anuran hosts (da Silva and Breviglieri, 2021; de Silva et al., 2015) most likely rely more heavily on opsins, PPKs channels, and TRPs, whereas kissing bugs and ticks may rely mostly on TRPs for long-distance infrared sensing (Barrozo et al., 2017; Mitchell et al., 2017).

Because host seeking and blood feeding are suppressed after a blood meal (Klowden and Lea, 1979), receptors and signalling molecules that are differentially regulated pre- and post-feeding constitute potential candidates for vector manipulation. In *Ae. aegypti* mosquitoes, stretch receptors (mechanosensation) in the gut detect abdominal distention in the short term and long-term feeding suppression is mediated through neuropeptide signaling (Duvall et al., 2019; Klowden and Lea, 1979), which could be targeted by disease agents to modify the length of a blood meal or the tendency of a vector to seek hosts and feed again – both of which could increase likelihood of transmission. Perhaps the most fundamental determinant of general sensory activity are the daily biological rhythms attuned to sunlight, i.e., the circadian clock (Helfrich-Förster, 2020). This light-dependent cycle is tightly linked to photoreceptors and opsins located

in the eyes, therefore any targeted damage or alteration to this primary sense system could have profound impacts on overall vector activities and disease transmission. Ticks infected with the *Rickettsia* bacterium showed increased expression of genes modulating the circadian rhythm, which correlated with an increase in blood feeding, engorgement weight, and hastened feeding (Khanal et al., 2022). Indeed, there is growing concern that anthropogenic light sources may already be changing vector-borne disease dynamics (Coetzee et al., 2022) and the evolution of host-parasite interactions (Poulin, 2023).

Parasite-induced up- and downregulation of host genes are most likely behind the behavioural changes observed in infected vectors. Increasing the number of receptor proteins (Box 1) expressed in receptor neurons can increase the sensitivity toward specific cues that already elicit a strong attraction in vectors (see Carr et al., 2021), for example, alcohols, aldehydes, and carboxylic acids emitted by humans that are highly attractive to mosquitoes (De Obaldia et al., 2022; Wolff and Riffell, 2018; Zhao et al., 2022). In addition, changes in gene expression that regulate neuronal excitability could also render specific sensory neurons more or less sensitive reporters of the cues that they sense. Such changes could impact multiple sensory pathways simultaneously, increasing general attractiveness in hosts during host seeking. Moreover, parasite-driven alterations on the downstream biochemical pathways in sensory systems could effectively modify the amount of time that vectors spend performing specific behaviours. These could include direct up- or downregulation of fast-acting neurotransmitters, or indirect changes through the longer-lasting actions of neuromodulators, i.e., molecules including neuropeptides and hormones that regulate neurotransmitter activities. For instance, neuropeptide signalling has been shown to regulate blood feeding in *Ae. aegypti* mosquitoes (Duvall et al., 2019; Klowden and Lea, 1979), thereby changing the length of blood meals. Hormones such as dopamine and serotonin (both are also neurotransmitters) can affect host seeking in mosquitoes and increase the frequency of blood meals when transmissible stages of a disease agent (La Crosse virus or *P. yoelii*) are present, thus increasing the odds of disease transmission (Briggs et al., 2022; Yang et al., 2019). Though, how disease agents induce these changes in vector phenotype remains very much an open question.

3.2 Proximate mechanisms of vector manipulation

The crux of host manipulation research has been to identify the genes and gene products (manipulation factors) originating from the parasite that

induce the cascade of behavioural and morphological changes documented across many host–parasite systems (Poulin and Maure, 2015) (Fig. 3). Convincing evidence connecting a parasite gene(s) to host phenotypic change has been elusive (Hoover et al., 2011), even though we now have the tools (transcriptomics, proteomics, gene editing, etc.) to explore molecular candidates (Doherty and Matthews, 2022). For vector-borne disease ecology, even though a lot of work has been done to describe behavioural change (Javed et al., 2021), we have just begun to look at baseline differences between infected and uninfected vectors (Carr et al., 2021). The manipulation factors expressed by a parasite or disease agent could impact any number of systems, including gene expression, neuromodulation, and immunomodulation (Doherty and Matthews, 2022; Herbison, 2017). Recently, small non-coding RNAs secreted by parasites have been highlighted as candidate modulators in vector–disease interactions, with the potential to up- or downregulate important sensory pathways involved in vector host seeking and host feeding (Bensaoud et al., 2019). However, parasites may also directly secrete proteins that mimic important regulatory or sensory functions in hosts (Berger et al., 2021).

3.3 Interactions with vector microbiomes

Microbiomes, i.e., the microbial communities of bacteria, viruses, protists, and others living within an organism, can have profound impacts on the general health of vectors and vertebrate hosts, directly affecting their ability to harbour and transmit diseases (Ippolito et al., 2018; Videvall et al., 2021), and even modulating vector behaviour to some extent (Ezenwa et al., 2012). *Wolbachia* can mitigate viral transmission by suppressing the replication of human viruses within mosquito vectors (Johnson, 2015). Trypanosomes tend to establish and mature more successfully in young adult tsetse flies, which can be partly attributed to an immature or underdeveloped microflora within the midgut (Haines, 2013). Vector competence, or the ability of a vector to transmit a pathogen, may thus be heavily impacted by the composition of the microbiome (de Angeli Dutra et al., 2023). How these microbes affect vector manipulation by disease agents remains an open question. For instance, should there be a negative consequence to the microbiome after an infected blood meal is ingested by the arthropod, natural selection may favour an antagonistic response from those microbes present, which would play against the ability of disease agents to manipulate vectors.



4. Key questions and ways to address them

In this section, we highlight key research questions to help guide future research. We also propose some general methodologies that can be used to test them experimentally.

Question (1). What vector phenotypes are targeted by disease agents to increase their transmission between hosts, and how specific are parasite-induced phenotypic changes in altering vector sensory systems?

To test this, one would ideally be capable of experimentally infecting the arthropod vector in a laboratory to observe and quantify behavioural responses to specific cues that are emitted by hosts during host seeking. These behavioural assays could be conducted in a simple choice test with, for example, a Y-maze if testing for responses to specific odorant cues, which requires a constant, unidirectional air flow. More elaborate experiments could combine multiple cues to observe multimodal responses to various stimuli. Host feeding experiments would require a substrate that mimics the external surface of the vertebrate host to test for probing, biting, and feeding behaviours in response to various cues in isolation or combined.

Question (2). Do parasites modulate vector behaviours by increasing the sensitivity of receptor neurons through gene expression changes, or do they act downstream on biomolecular pathways involving the activity of neurotransmitters and neuromodulators, and do parasites interact with highly conserved and ancient vector genes that govern general biological activities such as the circadian rhythm?

Differences in gene expression in the parasite is highly contingent upon the development of the parasite, which likely determines when the manipulation factors are released into the vector. If there is indeed evidence of behavioural manipulation in the vector, collecting samples at multiple stages of infection or parasite development would allow researchers to test for differences in gene or protein expression by measuring total messenger RNA (transcriptomics) or individual protein counts (proteomics). This would allow us to track internal biomolecular changes and match these with quantifiable changes in behaviour, which could help determine candidate mechanisms that are differentially expressed between infected vectors and uninfected controls at key moments of parasite transmission. In addition, techniques to profile the activity of neurons, for example, electrophysiology or calcium imaging, could be used to discern whether the sensitivity of specific sets of vector sensory neurons is altered upon infection.

Question (3). What are the proximate mechanisms or manipulation factors encoded in the parasite genome that directly or indirectly cause vectors to behave in ways that increase disease transmission?

This would require mapping gene or protein expression through transcriptomics and proteomics (see previous question) and linking these to specific genes found in the parasite genome. Therefore, sequencing the genome of the parasite is also essential. To test for the function of the candidate mechanisms involved in host manipulation, gene knockout experiments using the CRISPR-Cas9 can be used by designing guide RNA to target a specific region of the parasite genome to remove a gene or genes of interest. Researchers would need to develop a specific protocol to inject CRISPR-Cas9 components in the parasite of their model system. Once successful, they can then test for differences in host manipulation abilities between knockout parasites and controls, allowing us to test the function of the targeted knockout gene.

Question (4). How have these host-parasite interactions evolved in other disease vector systems that have not been researched or have received far less attention than the heavily studied model systems such as the fruit fly and mosquitoes?

Researchers need to increase the current breadth of host-parasite model systems to have a better appreciation of the diversity of parasite life history strategies involved in vector-borne diseases. Unfortunately, this remains one of the greatest challenges for researchers in parasitology: creating new host-parasite model systems. Many rounds of trial and error, and a lot of patience, are required to bring natural systems into the laboratory. Some systems simply do not work well in artificial conditions; therefore, we may be somewhat limited in the diversity of parasites that can be tested in an experimental context. A lot of money and effort may be required to successfully establish a working and reliable model system.

Question (5). Since blood feeding evolved independently in several arthropod vectors, have the parasites that evolved with these independent taxa adapted host-specific alterations or do they show signs of convergence due to the conserved nature of sensory systems?

The more we collect genomes of different parasites and other disease-causing agents, and the more we identify genes involved in vector behavioural manipulation, the better we can answer this question. Comparative genomics thus becomes an essential tool to test for the evolution of parasite-mediated phenotypic change. This goes without saying: we need to have a strong foundation of knowledge of candidate genes and mechanisms from several species of parasite in order to compare them and look for differences or signs of convergence.



5. Conclusions and future directions

To account for the full nature and diversity of disease vectors and their role in emerging infectious diseases worldwide, and to better prepare for the inevitable impacts of large-scale anthropogenic change, we need to address the current large gaps of knowledge in basic vector ecology. This includes changes in host seeking and host feeding behaviours of vectors carrying disease agents, which may increase disease transmission between hosts. The advent of genome engineering has allowed researchers to identify key sensory mechanisms underpinning the behavioural ecology of vectors, but many questions remain unanswered (see previous section). We still have little evidence as to if and how parasites manipulate vectors to their advantage, yet these fundamental interactions are extremely important and cannot be ignored if we wish to predict future patterns in disease ecology. By reviewing recent studies in vector sensory ecology, we have identified some key potential mechanisms that could be the target of parasite-induced phenotypic change, namely the highly conserved IR and TRP gene families of receptors. However, studies explicitly testing for mechanistic change in infected vectors are sorely lacking, even though we now have the technologies to test them. There is also only a small number of model disease vector systems used in research. We rely heavily on the fruit fly and mosquitoes to address foundational questions in physiology and molecular biology, and rightly so, but our very narrow window into the diversity of vector ecology likely limits our predictive power when it comes to modelling complex sensory landscapes and vector behaviours under various scenarios. Nevertheless, with the tools readily available to us, we can now gain important ground into the hidden interactions between disease agents and their vector hosts. This opens a whole new field of research, and we are sure to uncover fascinating co-evolutionary adaptations driving vector-borne disease transmission.

Glossary

Adaptive host manipulation any parasite-induced phenotypic change of a host (typically behaviour or morphology) encoded in the parasite genome that increases parasite fitness, for example, increasing the likelihood of transmission or life cycle completion.

Aerobic respiration a chemical process of converting carbohydrates into energy that consumes oxygen, producing carbon dioxide.

Babesiosis a parasitic infection in red blood cells caused by members of the apicomplexan genus *Babesia*.

- Bluetongue disease** transmissible viral infection found mainly in ruminants.
- Chagas disease** transmissible disease caused by *Trypanosoma cruzi*.
- Chemotaxis** movement in response to a chemical stimulus, guided by a corresponding concentration gradient.
- Circadian rhythm** biological processes that follow an internal 24-hour cycle; these processes respond to light and darkness patterns.
- Compound eye** a type of visual organ found in arthropods that consists of numerous independent photoreceptors housed within distinct units called ommatidia.
- Conformational change** a change in the shape of a protein or macromolecule, usually related to a change in function.
- Co-receptor** a cell-surface receptor that acts in tandem with a primary receptor to elicit ligand-mediated biological responses.
- Crepuscular** occurring or active during twilight periods.
- CRISPR-Cas9** gene editing technology that cuts specific regions of DNA, allowing for the insertion or deletion of genetic material.
- Degenerin epithelial sodium channels** a class of ion channels from the degenerin/epithelial sodium channel gene family that are expressed in the epithelial tissues of animals.
- Equine infectious anemia** disease caused by a transmissible viral disease that only affects equids.
- Hematophagous** feeding on blood.
- Heteromeric** a protein complex consisting of non-identical subunits.
- Heterotetrameric** a protein complex consisting of four subunits, with at least one being non-identical to the others.
- Ocellus (plural ocelli)** eye consisting of a single lens, functions as a second visual system.
- Pathogenicity** the ability or extent to which an organism can cause disease.
- Parasite** an organism that lives on or within a host organism, negatively impacting its fitness; this definition includes disease-causing agents like pathogens.
- Phototaxis** movement in response to light, either towards (positive) or away from (negative) the source.
- Polarisation** light with electromagnetic vibrations which oscillate in only the direction perpendicular to its source.
- Questing** a position ticks hold while waiting for a host to pass by close enough for them to climb onto.
- Sensillum (plural sensilla)** a sensory receptor consisting of a modified cuticle or epidermis cell that is typically hair- or rod-shaped.
- Sensory system** a network of neurons and receptors that relay stimulus information to the nervous system.
- Stylet** a hollow, hardened protrusion of the labella using for piercing and feeding on liquids.
- Tarsi** the most distal segments of the legs used for surface contact.

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Author contributions

J-FD conceived the idea for the review in consultation with all other authors; J-FD led the writing with significant contributions to core review sections and figures from all other authors. All authors gave final approval for publication.

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Resources

<https://www.who.int/news-room/fact-sheets/detail/vector-borne-diseases>.

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