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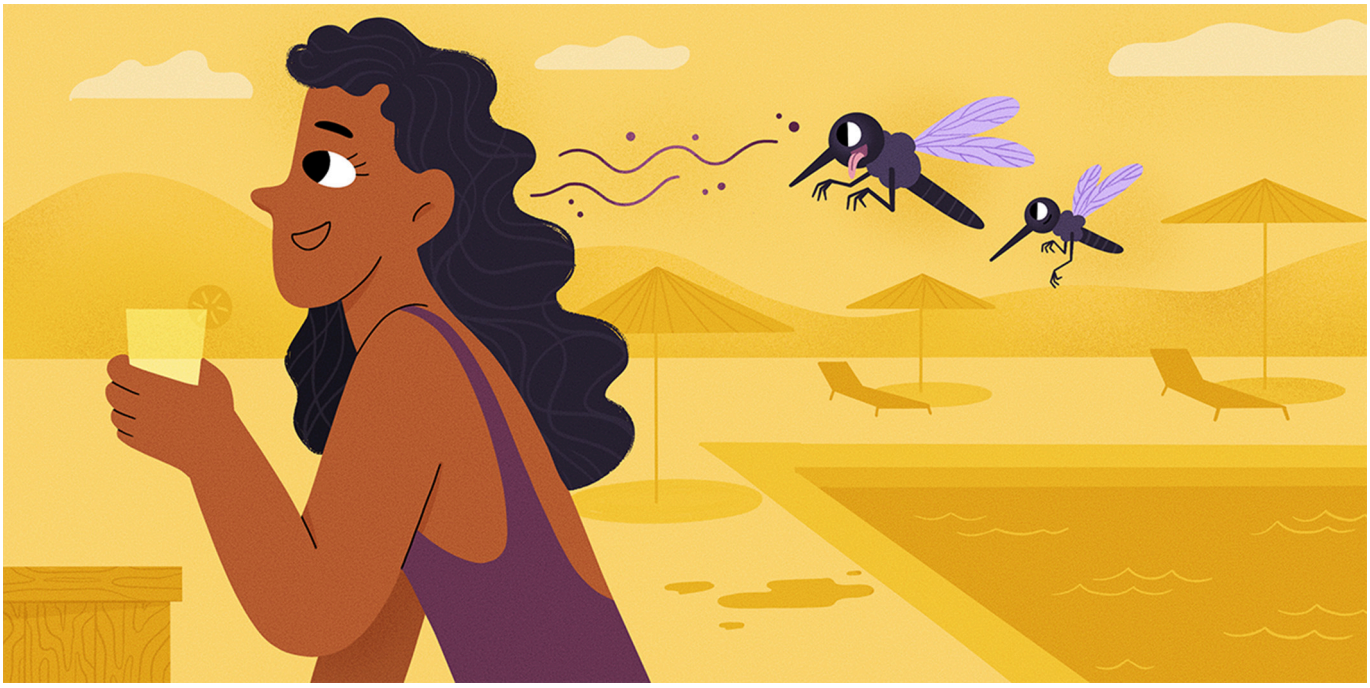

A MOSQUITO'S SENSE OF SMELL: WHAT IS THE BUZZ ALL ABOUT?

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YOUNG REVIEWERS:


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AGE: 12


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If it feels like you attract mosquitoes, you are on to something. Females of most mosquito species need to consume blood to produce eggs, and they use specialized senses to scope out their next snack. The saliva they leave behind after "taking a bite" can cause anything from a little itching to painful bumps and a fever. These thirsty insects use their ability to detect carbon dioxide, odor molecules, and heat to find food. In this article, we discuss the basics of smell in mosquitoes: how they smell, what their "nose" looks like, and how they specifically detect humans like you. There is more to mosquitoes than buzzing and bites! A better understanding of how mosquitoes detect odors and find prey may be the key to protecting against the diseases they cause.

THE BASICS

Have you ever gotten out of the pool only to smack mosquitoes off your skin every few seconds? Do you end your summers with

mosquito bites dotting your legs? If it feels like mosquitoes are picking on you, you are not the only one. Females of most mosquito species need to consume blood to produce eggs, and they use specialized senses to scope out their next snack. The saliva they leave behind after "taking a bite" can cause anything from a little itching to painful bumps and a fever. Though there probably is not any *one* reason you attract all the buzz, there are a few factors that can make you particularly appealing.

Mosquitoes use lots of cues when tracking down their meals, like body heat and levels of carbon dioxide (CO_2), which tell them that there is a breathing animal nearby. Mosquitos can sense CO_2 from almost 30 feet away! When they find a potential target, mosquitos approach using their sense of smell, following a delicious odor until they get very close [1]. Then, they switch to sensing heat, to scope out the perfect biting area, and land on your skin. How do mosquitoes actually sniff you out? And—considering there are 3,559 species of mosquitoes in the world—why do all of them seem to want to bite certain people more than others [1]?

HOW DO MOSQUITOES SMELL THINGS?

OLFACTION

The ability to detect odor molecules in the air. Also known as the sense of smell. In humans, the organ of olfaction is the nose.

Let us first focus on the basic biology of **olfaction**, or sense of smell, which is a complex and finely tuned system. Olfaction detects molecules that float into your nose, or around the antennae of mosquitoes. One smell, like the smell of chocolate or freshly cut grass, is made of hundreds of different odor molecules detected together. Maybe you have smelled a perfume and caught a whiff of vanilla, or a hint of lemon. Think of this like a beautiful piece of music. Our ears mix the notes of a chord together to produce one sound, and our noses mix many molecules to form a specific smell.

OLFACTORY SENSORY NEURONS (OSNS)

Cells that detect and transmit information about odors from the olfactory organs to the brain.

Each of the many types of odor molecules is detected by a specific **olfactory sensory neuron** (OSN) in the nose. OSNs and odor molecules work a bit like locks and keys. Each key opens a specific lock, just like each odor molecule is detected by a specific OSN. Some mosquitoes have over 80 different types of OSNs, but this number does not quite measure up to the 350 types of OSNs found in your nose [2, 3]!

OSNs tell the brain which odor molecules have been detected. Since each OSN detects one specific molecule, and smells are made of hundreds of different molecules, the information sent to the brain is like a list of individual odor molecules. The brain must read the list and understand which smell it corresponds to. This is called the olfactory code, and it is almost infinite. It is like writing: we only have 26 letters in the English language, but we have thousands of words. Similarly, we have 350 types of OSNs, but we can recognize thousands of different

smells—some even claim that we can identify more than a trillion [2, 3]!

WHAT DOES THE NOSE OF A MOSQUITO LOOK LIKE?

Insects like mosquitoes do not have noses like humans do. Instead, they have multiple olfactory organs that stick out from the body, each acting as a small nose. You probably already know what these organs look like. On adult mosquitoes, they are the antennae, the proboscis (the mouth part that sticks out to poke you) and the maxillary palps (the little claws around the face) (Figure 1) [1]. Mosquitoes have tiny sensory bristles on their antennae. You may have seen these furry hairs in close-up photos of insects. All these organs are covered with OSNs, which allow mosquitoes to detect odor molecules floating nearby.

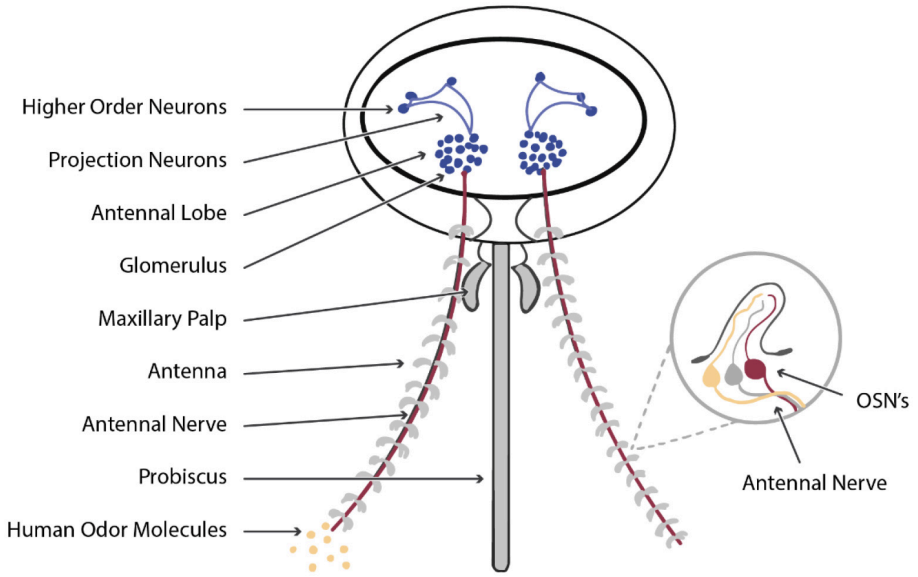

Figure 1

Figure 1

The mosquito olfactory system, as if we were looking down at a mosquito's head from above. OSNs (see expanded view in circle) on the mosquito's antennae, proboscis, and maxillary palps detect various odor molecules, including CO_2. The antennal nerve, which is made of OSN axons, relays odor information from the mosquito's body to the antennal lobe of the mosquito's brain, where the glomeruli are located.

GLOMERULUS (PLURAL GLOMERULI)

In the insect olfactory system, a spherical cluster of nerve endings located inside the brain's antennal lobe.

AXON

The long extension of a neuron, with which it connects and sends information to neighboring neurons.

HOW DO THESE SMELLS "LOOK" IN THE MOSQUITO BRAIN?

Now that you know how mosquitoes pick up smells from the environment, let us discuss how smells "look" in their brains. When an OSN detects an odor molecule, it reports it to the brain, by sending a signal to a structure called a **glomerulus**, found at the front of an insect's brain in a region called the antennal lobe (Figure 1). Glomeruli are circular clumps of brain cell endings, where the arms of OSNs, called the **axons**, contact the arms of other brain cells (Figure 2). You can imagine glomeruli as the places where brain cells "shake hands" and relay information about smells.

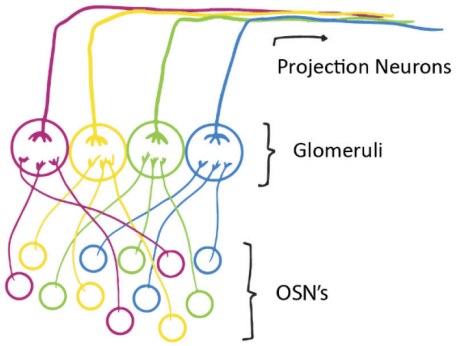

Figure 2

The axons of OSNs meet the axons of other brain cells in brain structures called glomeruli. Each OSN detects just one type of odor molecule, which are indicated by different colors in the figure. The axons of OSNs detecting the same odor molecule come together into the same glomerulus. Signals from the glomeruli are then sent along the projection neurons to deeper brain regions.

PROJECTION NEURONS

Neurons whose axons extend from the glomeruli to deeper regions of the mosquito's brain, like the lateral horn and mushroom body.

LATERAL HORN

A higher-order processing center in the insect brain that projection neurons connect to.

MUSHROOM BODY

A pair of mushroom-shaped processing centers in the insect brain, composed of many densely packed neurons. Projection neurons project here and to the lateral horn.

When contacting the glomeruli, OSNs are very organized: all OSNs detecting a specific type of odor molecule send their endings to the same glomerulus (Figure 2). This means that glomeruli combine information coming from many different OSNs in various parts of the mosquito's olfactory organs. Scientists call these glomeruli an odor map because each glomerulus relays the presence of a specific odor molecule [1, 4]. In glomeruli, the cells that "shake hands" with OSNs then relay smell information from the antennal lobe to deeper parts of the mosquito's brain, hence their name: **projection neurons** (Figure 1).

Research is lacking on the next stage of smell detection in the mosquito brain, the higher-order neurons. Fortunately, much more research has been done on a related insect: the fruit fly. The last common ancestor of fruit flies and mosquitoes lived 260 million years ago, but their brains are very similar. In flies, projection neurons target regions called the **lateral horn** and **mushroom body**. Scientists believe that these regions are similar in the mosquito brain...and also in humans [1, 5]! Just like flies and mosquitoes, your OSNs send their arms to glomeruli, which form an odor map in your brain [3]. We may look nothing like mosquitos and be separated by over 800 million years of evolution, but the basic biology of our sensory organs is amazingly similar.

HOW DO MOSQUITOES KNOW WHO THEY SHOULD BITE?

You now understand how mosquitoes—and humans—smell. So, what about our original question—how do mosquitoes know they should bite *you*? Recent research suggests mosquitoes have OSNs on their antennae that specifically detect humans, allowing them to detect odor molecules from our sweat [6]. To test this theory, researchers removed antennae from a group of mosquitoes. These antennae-less mosquitoes tracked down future meals through CO_2 and heat detection. However, they struggled to detect humans [6]. The

particular human odor molecule they no longer detected was **lactic acid**—a molecule secreted by the skin when we sweat.

LACTIC ACID

An odor molecule produced by the body when it is low in the oxygen it needs to convert sugar into energy, which happens when we exercise. Lactic acid appears in sweat.

The OSN that helps mosquitoes detect lactic acid is called Ir8a. When researchers "knocked out" this OSN, they found that mosquitoes were not as attracted to humans—they went after humans only about half as often [6]! This means that people with higher levels of lactic acid on their skin probably smell tastier to mosquitoes. Lactic acid is a byproduct of a process that your cells use to produce energy when you exercise or do sports. So, people who have recently exercised therefore have more lactic acid on them, which means they are also likely to make for a tastier mosquito snack.

WHAT NEXT?

Lactic acid is the key mosquito-attracting ingredient of human body smell. But we do not know all the other complex smells that might make humans especially irresistible to mosquitoes. The good news here is that the question is still open to exploration—and *you* could become the scientist who finds the answer! If you succeed, you could even create the perfect mosquito trap and end all the buzzing and itching. More importantly, many illnesses, like malaria, Zika, and dengue fever, are carried by mosquitoes. Figuring out how to get infected mosquitoes to stop biting humans and transmitting illnesses has serious positive implications for human lives.

We can not guarantee a bug-free summer, but sprays that disguise your human smell can help. It is helpful to replace your human smell with something mosquitoes do not enjoy, like eucalyptus. Showering right after exercise is important too, since exercise causes your muscles to release the lactic acid that mosquitoes sniff out. If all else fails, hug a bite-free buddy. Maybe some of their mosquito-repelling skin chemicals will rub off on you!

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CONFLICT OF INTEREST: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

YOUNG REVIEWERS

DHANVI, AGE: 12
I love to read and hang out with my friends outside. I will read almost anything I can get my hands on. And to read articles on science is amazing because I can learn things and read at the same time!

SHIVASAI, AGE: 10
I am a 5th grader and my favorite subjects are math and science. My favorite book series is Harry Potter and I like to watch Duck Tales. Some of my hobbies include sketching and playing table tennis.

SPANDANA, AGE: 11
Spandana is a elementary school student who loves science. She also loves to draw, paint, and read. She just started learning the flute!

SRAVYA, AGE: 14

Sravya is a high school student who loves STEM. She has many hobbies such as playing the piano and basketball. Her favorite subject at school is biology.

YAJURVI, AGE: 12

Hey, my name is Yajurvi! I am a 7th grader in VA. I like reading books and hanging out with my friends in my free time. I listen to music (mostly K-Pop) 24/7 and I also like singing.

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