making sense of smell

A NEW GENERATION OF RESEARCHERS FROM THE NATURAL SCIENCES TO HUMANITIES SHOWS SOME LOVE TO THE SENSE THAT HAS LONG BEEN OVERLOOKED

Tal Yehezkely (left) and Michal Andelman Gur (right) enjoy the sweet smell of research success. Andelman Gur is developing a way to use smell as a biomarker for Parkinson's disease, while Yehezkely explores how writers employ smell to communicate the struggle of outsiders.

By Alan Morantz
Photographs by Hadas Parush

Smell may be the most elusive of all senses, and the most intimate.

The sense of smell helps us identify odorants, but that's not all. Because smell and emotion are stored as a single memory, odours add an emotional dimension to events and influence our mood and thoughts. Yet, while scientists can tell us so much about the inner workings of hearing, vision, taste and touch, it is only in recent decades that smell has attracted the attention it deserves.

Modern-day interest can be traced to 1991, when molecular biologists Richard Axel and Linda Buck announced they had identified 18 of the genes that control odour receptors; the milestone showed young neuroscientists a pathway to a rich field of research. Advances in the natural sciences have inspired experts in the humanities to incorporate the study of smell into their own work.

We may still not know why a particular molecule smells the way it does; intriguingly, the chemical structure of a molecule says little about its odour. But we are learning more about the ways the olfactory system operates and its overall role.

Scientists, for example, have developed a molecular-level, three-dimensional model of how an odour molecule activates a human odorant receptor, a crucial step in understanding the sense of smell. Labs with expertise in organic chemistry, software engineering, machine learning and other disciplines are developing digital smell technology that may lead to devices that can help clinicians diagnose disease and allow users to sense and transmit odours via the internet.

The arts are also recognizing the value in engaging the sense of smell. A growing number of museums are creating "scentscapes" to provide visitors with a visceral experience. The most pungent of them all is Brunel's SS Great Britain, a museum in Bristol, England, that immerses visitors in the experience of travelling on a Victorian-era steamship with the help of odours that suggest smoky bacon, rum, urine, vomit and horse manure.

Clearly, for the sense of smell, everything is coming up roses, and that suits Michal Andelman Gur and Tal Yehezkely just fine. Andelman Gur, a former Azrieli Graduate Studies Fellow, is an MD and a PhD student and neurobiologist in the Weizmann Olfaction Research Group at the Weizmann Institute of Science. Yehezkely is a scholar of comparative literature and a current Azrieli Graduate

Studies Fellow pursuing research at the School of Cultural Studies at Tel Aviv University.

Both Andelman Gur and Yehezkely are making their names as up-and-coming smell investigators. Andelman Gur is developing a way to use the sense of smell and patterns of respiration as biomarkers for Parkinson's disease, a movement disorder of the nervous system. Yehezkely is using smell as a marker as well, though within the world of literature. She explores how writers use smell to communicate the struggle of outsiders, a sensitive theme often difficult to express.

Aperio editor Alan Morantz spoke with Andelman Gur and Yehezkely to explore why smell is now such an alluring topic of enquiry.

Alan Morantz: *Michal, you're trained as a medical doctor, and Tal, you're trained as a philosopher. How did you end up studying the science of smell or exploring its literary merits?*

Michal Andelman Gur: For me, smell and respiration are windows to the brain, and that's why I chose to study them. The sense of smell is the only sense with a direct pathway to the brain. It's closely linked to the brain centres of memory and emotions that are called the hippocampus and amygdala. And there's also evidence that respiratory patterns are closely linked with brain activity, something we call the "sniffing brain."

AM: *When did you first realize there was something about smell worth studying?*

MAG: I remember when I was in med school, we were taught about Parkinson's disease, that it's a movement disorder. But only afterwards, I heard that many years before the motor symptoms appear, patients lose their sense of smell. And I thought this was so strange, and it has something to do with the brain in a way that I didn't think of until that moment. That got me curious.

Because smell and emotion are stored as a single memory, odours add an emotional dimension to events and influence our mood and thoughts — and are a connection to our most ancient memories

AM: *Tal, what was the pathway to your research?*

Tal Yehezkely: Since I was a child, I was always interested in smells. Whenever I did field trips and hikes with my parents, they would always teach me to smell flowers and plants, just what you do with children when you take them to experience nature.

When I started my master's in philosophy and literature, I had to choose my subject. I was really surprised by how little attention was given to smell and how little importance was attributed to it in the study of philosophy, in the study of literature and in cultural studies. I couldn't understand why, but I also took this as a challenge. I saw a gap and wanted to see where it would take me, merging the aesthetic experience that I had as a child with the aesthetic experience I've learned to have as an adult — reading, going to museums, thinking critically.

AM: *Of all the human senses, smell is usually considered the most dispensable. For both of you, what does smell offer that other senses don't?*

MAG: I'm not so sure it is dispensable since the sense of smell is highly important in very basic human functions, such as eating and sexual activity.

I think what's interesting about the sense of smell is that it influences us in an unconscious manner. Even odours that are not consciously perceived can highly influence our behaviour. And I would also mention that people without a sense of smell, anosmic patients, have a lower life expectancy and higher rates of depression. So maybe we're not so focused on smell, but it does have some basic influence on our behaviour and our lives.

TY: From a literary point of view, reading descriptions of smell definitely makes the experience of reading very sensory and very real.

But the fact that smell is considered dispensable is interesting. Freud considered the repression of smell as the first and primary form of repression, which was the model for all other repressions to come. Kant was asked, in one of his lectures, what he thought was the most dispensable sense. And he said smell. Well, we can either take it for granted and say, Okay, smell is dispensable, or we can ask, Why would someone like Kant consider smell dispensable? And what does it say about our culture?

AM: *So what does it say about our culture that smell is repressed and considered dispensable?*

TY: Maybe that we prefer not to face certain aspects of our being. For example, the difficulty of being around other people or the extent to which our biology still has hold on us, which are all triggered by smell.

AM: *One of the unique aspects of the Azrieli Fellowship is that it provides a meeting ground for researchers from all scientific disciplines. When you get together and talk shop, what do you talk about?*

MAG: When we first met, I remember talking about the gap between how we look at the sense of smell in our lab and how it is written about in literature. When we consider smell perception, its primary axis is "pleasantness." It's surprising because even though there are about a thousand different receptor types in our nose and humans can detect and discriminate countless odorants, it's hard for them to name the odorant. However, they can quite easily say if the odour is pleasant or unpleasant. This is somehow in contradiction to the richness of words in literature, of the ways that are used to describe all kinds of odours.

TY: I have the privilege of not being confined to what is measurable through neuroscience. When I analyze olfactory expressions in texts, I can do so from various angles. I can consider the vast information that is transferred through smell — about people, materials and spaces. This is a privilege of comparative literature and philosophy that I definitely indulge in.

AM: *Smell interacts with the brain differently than other senses in that it goes directly through the limbic system. And in evolutionary terms, the olfactory receptor gene family is the largest in the mammal genome. There are plenty of reasons why smell should be a focus of research.*

"When we first met, we talked about the gap between how we look at the sense of smell in our lab and how it is written about in literature"

MAG: I completely agree with you. It seems that the entire olfactory system influences us much more than we would think. And really, the sense of smell of humans is incredible. We can detect just a tiny amount of odorants. My supervisor, Professor Noam Sobel, likes to give this example that humans can sense odorants that are in one drop of an entire Olympic swimming pool. So we are very good at that and we can discriminate between two odours very well. Another study of his shows that we can also track scent very well.

So we have all these olfactory capabilities. But we don't give them that much attention. And one of the reasons we believe this is the case is that unlike vision — which we're constantly aware of, since our eyes are wide open while we're awake — the sense of smell is interrupted. We can smell only when we inhale. When we exhale, we can't smell. So we have this interrupted flow of information and we think this may be one of the reasons why we don't sometimes focus on what we smell.

TY: Building on the fact that smell has such an influence on us, it goes directly to the brain from the limbic system. So it has such a strong connection to our strongest and our most ancient memories. It's not surprising that writers and thinkers would try to make sense of it.

AM: *Yet we spend $12 billion a year on synthetic fragrances. We seem to have a need to control what we smell, or at least to mask it.*

MAG: There is a lot of information on body odours. Humans can interact with each other using only their sense of smell — by sensing chemosignals that are produced by others. Chemosignals in humans are chemical cues, often found in sweat, tears or other bodily secretions, that can convey emotional states or influence social interactions. For example, chemosignals in sweat may communicate fear or stress, influencing others' emotional states, while compounds in tears have been shown to reduce sexual arousal in others. What happens when these chemo signals are somehow masked? How does it influence us?

Our desire to control what we smell isn't limited to adding external fragrances. We also adjust our breathing patterns internally to regulate the odours we perceive. There's an interesting response in humans known as the sniff response. It's a modulation of inhalation in response to unpleasant odours. For example, imagine yourself going near a garbage can and then holding your breath. We can learn a lot about not only smell but also health from this response. There's a modulated sniff response in autism and in all kinds of consciousness disorders. I also found it in Parkinson's disease. So the way we respond to unpleasant odours is very indicative and important for us to better understand human health.

TY: I can say from a literary standpoint that many times when writers want to depict a difficult situation, they use smells. You could see why people would want to mask smells because they convey a lot of information — sometimes too much information, things we don't want to think about or experience.

I can definitely see it in my own work. When we talk about social or political conflicts, smell is very present. And this presence is important to convey the difficulty, the concreteness of information that goes from one person to another. Smell is ephemeral, but there's also something very concrete about it. It shows us certain aspects of reality that we prefer to avoid, and that's not always easy to handle, but maybe it's worth a try. ▲●■

CAN A SNIFF BE A CLUE TO PARKINSON’S DISEASE?

One of the most frustrating aspects of Parkinson’s disease is that it operates in stealth mode. Parkinson’s is the second most common neurodegenerative disease after Alzheimer’s, affecting about 10 million people worldwide, yet it can lie hidden for years. By the time a diagnosis is made, usually on the basis of motor disturbances such as resting tremor or rigidity, more than 50 per cent of the brain cells in the substantia nigra — the part of the brain that controls movements — may no longer function.

A prompt diagnosis could dramatically improve outcomes, but isolating Parkinson’s from a host of other conditions has confounded medical researchers for decades. Symptoms such as irritability, fatigue and troubled sleep are hardly unique, while other symptoms, such as Parkinson-like movements, are also seen in some types of dementia and other disorders. Even when doctors make a clinical diagnosis of Parkinson’s, post-mortem analysis shows that they are correct in their assessment only 80 per cent of the time.

Considerable resources have been invested in a global race to identify a biomarker sufficiently specific and reliable to identify Parkinson’s early in its progression. A biomarker is a biological molecule found in blood, other body fluids or tissue that indicates the presence of disease. It often involves measuring samples from cerebrospinal fluid or serum to identify damaged proteins; other biomarker identification tools include genetic analysis or imaging to track changes in brain structure.

One promising biomarker for Parkinson’s is the presence of alpha-synuclein, the damaged protein associated with the disease, in cerebrospinal fluid. There is, however, the question of scalability; a spinal tap is required to extract a cerebrospinal sample, and the procedure is expensive and requires advanced technology.

Now, thanks to Michal Andelman Gur and her colleagues at the Weizmann Olfaction Research Institute, smell and respiration have emerged as less-invasive potential biomarkers for Parkinson’s.

There is good reason to pursue this line of research, given that olfactory decline is prevalent in up to 90 per cent of Parkinson’s patients. But simply measuring olfactory performance based on tasks such as the detection, discrimination and identification of smells will not necessarily isolate Parkinson’s, since there could be other causes of decline.

In a soon-to-be-published study, Andelman Gur and colleagues showed that Parkinson’s patients share a unique olfactory perceptual fingerprint (OPF). An OPF defines a person’s olfactory perception based on ratings such as odour pleasantness and intensity. Other studies have shown that OPFs can accurately distinguish patients with COVID-related olfactory dysfunction from healthy individuals. Using an OPF to identify Parkinson’s would be a game changer because of its ease of use.

Andelman Gur’s study involved 33 Parkinson’s patients, 28 non-Parkinson’s subjects with olfactory decline and 33 healthy subjects. All subjects completed an olfactory sniff jar test that involved sniffing and rating 10 different monomolecules such as isoamyl acetate, which has a strong banana scent. The study also measured sniff response, which is the modulation of respiration in response to odour. The sniff response can dramatically change in various health conditions, such as alteration of consciousness or autism, and may serve as an objective non-verbal test that is easy to administer.

Andelman Gur found that differences in olfactory perceptual ratings could reliably distinguish between those with Parkinson’s, those with olfactory decline brought about by other causes and the control group. Differences in sniff response were also noteworthy: in response to an unpleasant odorant, both healthy controls and the non-Parkinson’s olfactory-decline group reduced sniff duration, while the Parkinson’s subjects took longer sniffs.

Based on perceptual ratings and sniff responses, Andelman Gur was able to classify Parkinson’s disease with an 88 per cent accuracy rate. Even better, she was able to distinguish with an 89 per cent accuracy rate between subjects with Parkinson’s and non-Parkinson’s subjects with olfactory decline, finally managing to isolate the specific Parkinson’s disease-related olfactory impairment.

Respiration may also serve as a potential biomarker. In an earlier study, Andelman Gur tested the hypothesis that changes in breathing patterns could be an early sign of Parkinson’s. After all, parts of the brain that control breathing are among the first to suffer damage in Parkinson’s disease.

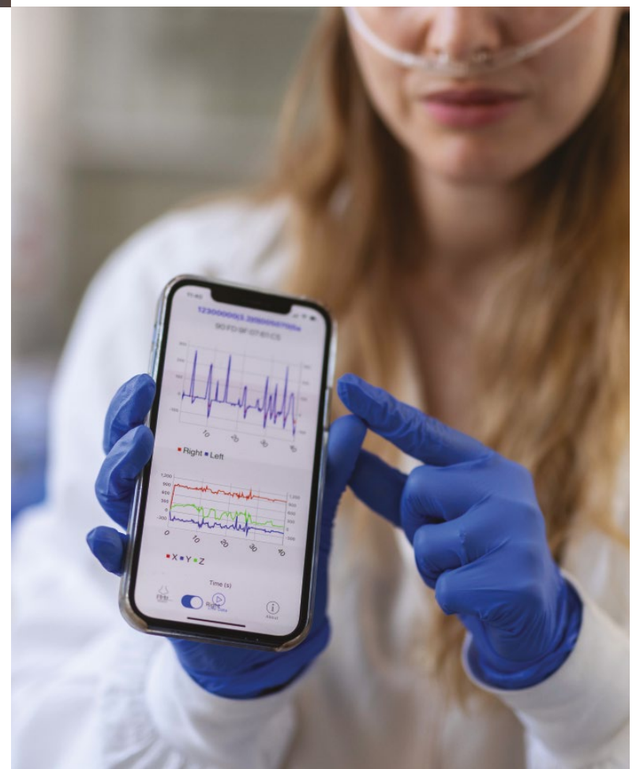
To investigate whether respiration could be harnessed as a biomarker, Andelman Gur conducted a study involving 28 individuals diagnosed with Parkinson’s disease and 33 healthy individuals who served as a control group. The study participants wore a small electronic device, dubbed the nasal holter, that was pasted to the nape of their neck. The device was designed by Noam Sobel, Andelman Gur’s PhD supervisor and the director of the Azrieli National Institute for Human Brain Imaging and Research, based at the Weizmann Institute of Science. It is outfitted with sensitive pressure sensors that can measure and record airflow patterns through the nose while subjects go about their daily activities.

The results were, in Andelman Gur’s words, “striking.” She found that people with Parkinson’s exhibited significantly different breathing patterns compared to the healthy control group. They took longer, steadier breaths, while those without the disease had a more dynamic breathing pattern with greater fluctuations in breath rate. She found that by analyzing just 30 minutes of recorded breathing data, she could identify Parkinson’s with an 87 per cent accuracy rate.

Andelman Gur’s leading research on Parkinson’s disease reflects her unique background: she is not only a neuroscientist but also a medical doctor. “Her MD background allows her to see through what is potentially important and meaningful in the study, and what aspects to push the hardest,” says Sobel.

If her study findings hold up, a biomarker based on smell or respiration would be much easier to scale than the existing alternatives, as these are affordable and non-invasive tools. And it may have diagnostic applications beyond Parkinson’s to general brain health.

“Imagine a simple, wearable device that could monitor your breathing and provide health care professionals with crucial information about your neurological health,” says Andelman Gur. “Such technology could revolutionize how we diagnose and treat Parkinson’s disease, potentially leading to earlier interventions and a better outcome for patients.” ▲●■



To investigate whether respiration could be harnessed as a biomarker, Andelman Gur had study participants wear a specially designed electronic device pasted to the nape of their neck (left). The device recorded airflow patterns through the nose while subjects went about their daily activities.

How to Read by Smell

Reading literature is a sensory experience. We read by sight on printed pages, by touch with Braille or by sound via digital media. For an even richer and more moving experience, Tal Yehezkely invites us to engage in "smell reading."

Reading with our noses sounds rather unpleasant. Smell is so . . . odorous. After all, smells usually carry negative connotations: you may read "something smells here" but really think "something smells bad." As Yehezkely herself points out, olfactory vocabulary is rather dull. In the Indo-European and Semitic languages in which she works as a scholar of comparative literature, there are few words to describe odours. The words that do exist either refer to the source of the odour (the smell of flowers or cinnamon) rather than the odour itself — or rely on other senses to do the heavy lifting (a sweet or sharp smell).

Smells "generate powerful emotions and therefore reach areas that are usually repressed. Depictions of smell allow us to reflect on these issues within the safe space of literature"

This limitation makes it a challenge for writers to describe a smell, says Yehezkely, but it also forces them to be creative and carve out new paths in language expression.

So what can we possibly gain by being mindful of how smells show up in literature?

A lot, says Yehezkely. The presence of smell within texts carries an important message. "Smell is such a crucial part of how we perceive others, how we perceive ourselves and how we perceive the difference between the self and the other," she says. "It also makes you very attuned to what's going on in the text, prompting you to put a lot of effort into imagining the smell and trying to identify it with something you already know." When you read with smell in mind, she says, "you merge your own world with the world of the literary work, and vice versa."

Yehezkely focuses on canonical works of Hebrew and Italian literature that relate to social and political conflicts. In her ultra-close reading, she searches for "meaningful smell moments" — passages where smells are significant to the narrative, to the reader's understanding of the text or to the general message conveyed. So far, she has analyzed nine such texts, investigating not only creative strategies used to incorporate smell into the narrative, but also what smell can reveal about relations between in-groups and outsiders. "What I discovered through my research," she says, "is that the presence of smell in these texts always ties political concepts with literary or poetic innovation."

Smell in literature can certainly pack a punch. Writings about smell in political and social contexts might be perceived as offensive by individuals or groups, if, for example, they refer to immigrants' or women's body odour. Smells can express stereotypes and racism in visceral ways, Yehezkely says. "But it can also generate powerful emotions and therefore reach areas that are usually repressed or that we just prefer not to discuss. Depictions of smell allow us to reflect on these issues within the safe space of literature."

Yehezkely points to a notable Israeli short story by A.B. Yehoshua, "Mul ha-ye'arot" ("Facing the Forests"), which employs smell to explore the charged relationship between Israelis and Palestinians. The story tells of a Palestinian, his daughter and a young Jewish forest firewatcher, who are the only people in an isolated stone house overlooking the forest. The story contains several references to smell: a faint smell of kerosene that triggers fear of a potential fire; the Palestinian girl's "womanly smell"; the alienating "foreign smell" the Palestinian and his daughter sense as the firewatcher approaches them.

Yehezkely says the story's smells conjure the tensions between ethnic belonging and alienation as well as sexual attraction and repulsion, and the ways in which these tensions become entangled in the Israeli–Palestinian political context. Smells, in this story, stress the problematic relationship between Israelis and Palestinians (characterized by denial, violence and miscommunication), but also suggests a potential — though radical — collaboration.

Galili Shahar, a professor of comparative literature at Tel Aviv University and one of Yehezkely's PhD supervisors, says Yehezkely's "groundbreaking enterprise" provides "a new mode of thinking about senses as literary organs, while analyzing their imprints in contemporary writing." Her approach "is of critical meaning today."

Yehezkely certainly sees herself as part of a new "scholarly olfactory wave." Asked how she views her future in the field, she says one option would be to delve more deeply into the field of olfactory art, comparing olfactory artworks in different media. Another possibility could be to harness literary big data to identify trends in the use of smell in literature.

Her favourite pastime, though, is being a smell evangelist. She likes to warn people that once they start thinking about smell in the books they read, they will notice smells everywhere. It all begins with learning to pay attention.

"I invite you to reflect not only on smells in literature but also on your own experience when you sense a smell that is foreign to you, or even disgusting. Take a step back and reflect on this experience. Ask yourself, 'In what way is it foreign to me? And how do I react to this foreignness?' I hope this pause will allow us to encounter others and differences with less violence and more tolerance — in literature and outside of it." ▲●■