Meeting a 100-year-old challenge could lead the way to digital aromas

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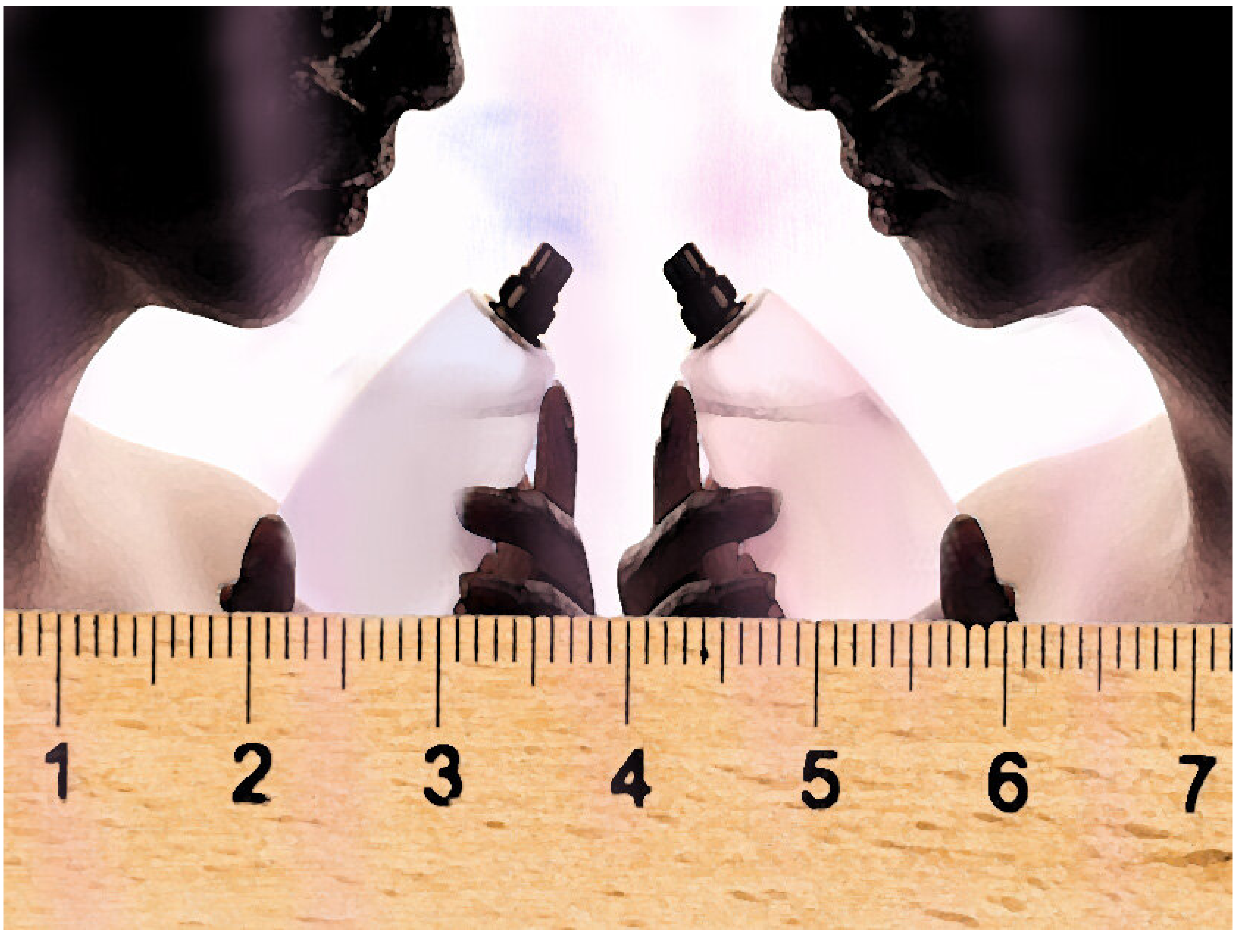

Smells may be measured by their distance from one another. Credit: Weizmann Institute of Science

Fragrances—promising mystery and intrigue—are blended by master perfumers, their recipes kept secret. In a new study on the sense of smell, Weizmann Institute of Science researchers have managed to strip much of the mystery from even complex blends of odorants, not by uncovering their secret ingredients, but by recording and mapping how they are perceived. The scientists can now predict how any complex odorant will smell from its molecular structure alone. This study may not only revolutionize the world of perfumery, but eventually lead to the ability to digitize and reproduce smells on command. A proposed framework for odors, created by neurobiologists, computer scientists, and a master perfumer and funded by a European Commission initiative called Future and Emerging Technologies (FET) Open, was published in *Nature*.

"The challenge of plotting smells in an organized and logical manner was first proposed by Alexander Graham Bell over 100 years ago," says Prof. Noam Sobel of the Weizmann Institute's Department of Neurobiology. Bell threw down the gauntlet, saying: "We have very many different kinds of smells, all the way from the odor of violets and roses up to asafoetida. But until you can measure their likenesses and differences you can have no science of odor." His challenge remained unmet—until now.

This century-old challenge highlighted the difficulty in fitting odors into a logical system, as there are millions of odor receptors in our noses, with hundreds of subtypes, each shaped to detect particular molecular features. Our brains potentially perceive millions of smells in which these single molecules are mixed and blended at varying intensities; thus, mapping this information has been a challenge. But the study by Prof. Sobel and his team, led by graduate student Aharon Ravia and Dr. Kobi Snitz, found that there is an underlying order to odors. They reached this conclusion by adopting Bell's concept—namely, to describe not the smells themselves, but rather the relationships between smells as they are perceived.

In the initial experiment, the researchers created 14 aromatic blends, each comprising about 10 molecular components, and presented them two at a time to nearly 200 volunteers. The participants rated the pairs of smells on how similar they seemed, ranking them on a scale ranging from 'identical' to 'extremely different.' By the end of the experiment, each volunteer had evaluated 95 pairs.

To translate the resulting database of thousands of perceptual similarity ratings into a useful layout, the team refined a physicochemical measure they had previously developed. In this calculation, each odorant was represented by a single vector that combines 21 physical measures (polarity, molecular weight, etc.). To compare two odorants, each represented by a vector, the scientists measured the angle between the vectors to reflect the perceptual similarity between them. Pairs of odorants with a short angle distance between them were predicted to be similar, and those with high angle distance were predicted to be different.

To test this model, the team first applied it to data collected by other researchers, primarily a large study in odor discrimination by Caroline Bushdid and colleagues in the lab of Prof. Leslie Vosshall at the Rockefeller University in New York. The Weizmann team found that their model and measurements accurately predicted the Bushdid results: Odorants with low angle distance between them were difficult to discriminate; those with high angle distance were simple. Encouraged by the model's accuracy in predicting data collected by others, the Sobel group continued to test for themselves.

The team concocted new scents and invited a fresh group of volunteers to smell them, again using their method to predict how this set of participants would rate the pairs—at first 14 new blends and then, in the next experiment, 100 blends. The model performed exceptionally well. In fact, the results were in the same ballpark as those for color perception—sensory information that is grounded in well-defined parameters. This was particularly surprising considering that every person likely has a unique complement of smell receptor subtypes, which can vary by as much as 30% across individuals.

Because the 'smell map,' or metric, predicts the similarity of any two odorants, it can also be used to predict how an odorant will ultimately smell. For example, any novel odorant that is within 0.05 radians (a unit of measurement for angles) or less from the odor of banana will smell exactly like banana. As the novel odorant gains distance from banana, it will smell banana-ish, and beyond a certain distance, it will stop resembling banana.

The Sobel lab is now developing a web-based tool. These techniques not only predict how a novel odorant will smell, but can also synthesize odorants by design. For example, one can take any perfume with a known set of ingredients and, using the map and metric, generate a new perfume with no components in common with the original perfume, but with exactly the same smell. Such creations in color vision—namely, non-overlapping spectral compositions that generate the same perceived color—are called color metamers, and the Sobel team has produced olfactory metamers.

The findings are a significant step toward realizing a vision of study coauthor Prof. David Harel of the Weizmann Institute's Department of Computer Science and Applied Mathematics, who also serves as Vice President of the Israel Academy of Sciences and Humanities: Enabling computers to digitize and reproduce smells. In addition to being able to add realistic flower or sea aromas to vacation pictures on social media, giving computers the ability to interpret odors in the way that humans do could have an impact on environmental monitoring and the biomedical and food industries, to name a few. Still, master perfumer Christophe Laudamiel, who is also a co-author of the study, remarks that he is not concerned for his profession just yet.

Prof. Sobel says, "One-hundred years ago, Alexander Graham Bell posed a challenge. We have now answered it: The distance between rose and violet is 0.202 radians (they are remotely similar), the distance between violet and asafoetida is 0.5 radians (they are very different), and the difference between rose and asafoetida is 0.565 radians (they are even more different). We have converted odor percepts into numbers, and this should indeed advance the science of odor."

More information: Aharon Ravia et al. A measure of smell enables the creation of olfactory metamers, *Nature* (2020). DOI: 10.1038/s41586-020-2891-7

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