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The Nose Knows

Froot Loops mascot Toucan Sam knew what he was talking about when he exhorted cereal lovers to “Follow your nose! It always knows!” But what Sam may not have realized is that all those circles, colored according to the fruit they were meant to represent, tasted exactly the same.

Associations between visual and olfactory sensations corresponding to fruits of different colors confound the perception of taste, which is closely tied to the sense of smell. “You think each color tastes different, but the flavor is identical,” said Anne-Marie Oswald, an assistant professor in the Department of Neuroscience at the University of Pittsburgh. “It’s the visual perception of the different colors that makes you think they should taste different.”

Oswald was one of four coordinators of “Deconstructing the Sense of Smell,” an eight-week program at UC Santa Barbara’s Kavli Institute for Theoretical Physics (KITP). An international team of experimental and theoretical neuroscientists from a variety of disciplines came together to discuss the chemical, molecular, cellular, circuit and systems mechanisms that underlie neural and behavioral responses to odors. Their goal: to explore organizing principles behind the sense of smell.

Smell has been the most difficult of the senses to describe in scientific terms because the olfactory system is highly complex. The system must rapidly detect, identify, categorize and prepare for memory storage myriad odorants that vary in molecular structure and concentration, all while taking other sensory perceptions into consideration.

Despite an extensive body of genetic and perceptual data, scientists face obstacles in quantifying the properties of odorant molecules that lead to the perception of smell. Because subjective language is used to describe smell, researchers are limited in their ability to develop cohesive and comprehensive theories for olfaction.

“Understanding smell is a subset of understanding how the brain perceives the sensory world around us,” said Sandeep Robert Datta, an assistant professor in the Department of Neurobiology at Harvard Medical School. He co-organized a weeklong olfaction conference during the KITP program. “I think one of the challenges is that our ability to generate data far outstrips our ability to understand it. One of the main products of this program has been getting all of us together in a room to think about how we might better understand the data we have.”

Olfactory processing is achieved by relatively few layers of neurons, with anatomical structures and physiological mechanisms that appear repeatedly in widely divergent species. Thus, a study of olfaction offers the promise of insight into a successful and perhaps optimal biological algorithm for processing complex information.

Driven by novel techniques, including next-generation sequencing, optogenetics and imaging/recordings in awake and behaving animals, there is explosive growth in experimental data that can newly inform theory. At the same time, a variety of proposed computational and theoretical models also can help to explain the data.

Most natural odors are mixtures of molecules, and there are hundreds of olfactory receptor types. In many animals, the olfactory sense is also used for tracking objects in turbulent environments, an issue that can benefit greatly from physical approaches. For humans, the sense of smell strongly contributes to our quality of life and is particularly vulnerable to aging and many neurodegenerative diseases.

“There is this need to understand how it works in terms of the pure science point of view,” said another program coordinator, Venkatesh Murthy, a professor of molecular and cellular biology at Harvard University. “But then more practically one might ask whether the sense of smell is related to human disease. There are epidemiological studies that say you are more likely to be depressed if you lose your sense of smell and that loss also may be a biomarker for neurodegenerative diseases.”

As Froot Loops so aptly demonstrate, the chemosensory processes of smell and taste are highly linked. Oswald illustrates this concept in some of her classes. She gives students grape-flavored candy and asks them to taste it while holding their noses. They taste only sweet. When the students let go of their noses, the grape flavor comes alive. “It’s like watching light bulbs go off when they realize on a visceral level this physical connection,” she said. “Smell has such quick links to our emotional processing.”

The goal of “Deconstructing the Sense of Smell” has been to help parse out the biological processes that power the sense of smell. The end result has been new collaborations between theorists and experimentalists and even among those in each group.

“Building on the strong tradition of fruitful collaborative interactions among scientists carrying out theoretical, experimental and computational research, we are confident this KITP program will help catalyze rapid progress in this field,” said KITP Deputy Director Greg Huber, a participant in the program.

Other coordinators of “Deconstructing the Sense of Smell” were Maxim Bazhenov, an associate professor in the Department of Cell Biology and Neuroscience at UC Riverside, and Alexei Koulakov, a professor at the Cold Spring Harbor Laboratory in New York.

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About UC Santa Barbara

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