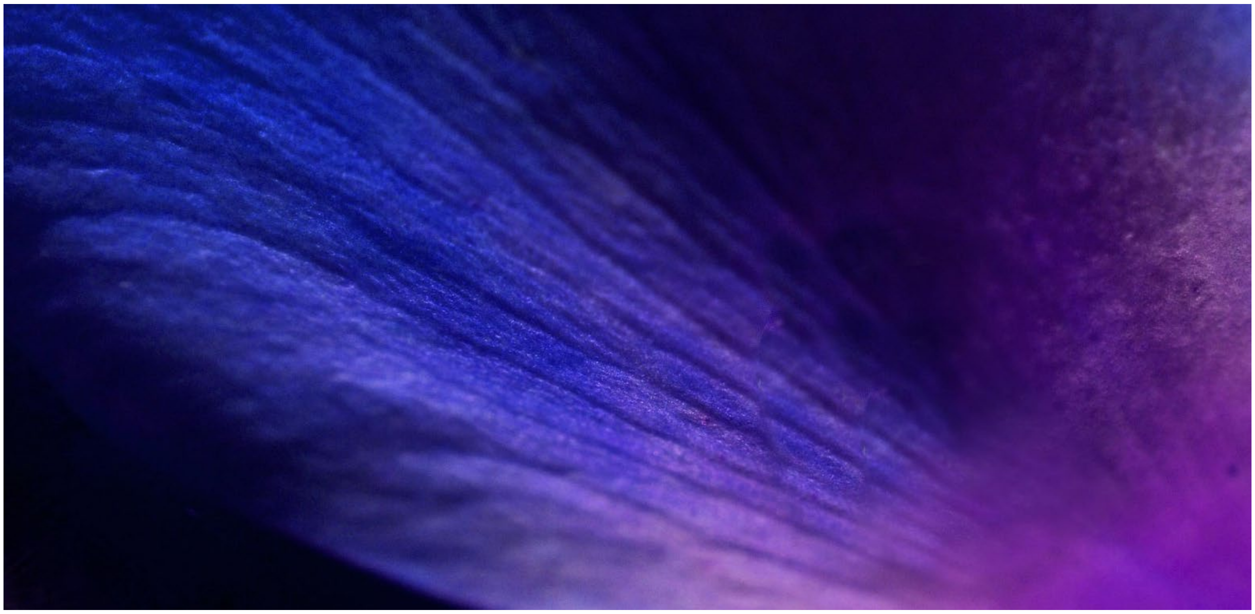

Cracking the Olfactory Code

By bioscentric | Biology

The sense of smell, or olfaction, is an extremely sophisticated molecular sensor. However, our understanding of how it works is limited. Olfaction's impact is widespread throughout diverse aspects of human biology – it is heavily implicated in memory, emotions are communicated through odor, and we use it to discriminate attractive and repulsive substances.

A recent (yet controversial) study estimated humans can distinguish between trillions of different odors. Even if that is a very generous estimate, the biological machinery required to achieve such a level of discrimination must be very complex. Your nose contains ~400 different olfactory receptors that bind all odorant molecules. Our ability to discern more than 400 odors excludes the possibility that each receptor corresponds to a single odorant. Many experts believe that odor perception is achieved through a combinatorial code. That is, each chemical can bind many receptors and each receptor can bind many chemicals. Upon entering the nose, each odorant becomes represented by a receptor activation pattern and is transmitted deeper into the brain where it eventually transforms into perception.

For vision and hearing, we can interpret how the spectrum of inputs are perceived by an individual. The wavelength of light determines the color that we see and the frequency of a sound wave the pitch that we hear. For olfaction, we are unable to predict smell from the chemical structure of an odor. This is largely because the vast majority (~86%)

of human olfactory receptors are ‘orphan’ – no odorants that bind these receptors have been identified. Without a comprehensive collection of binding data, our ability to model the ‘olfactory code’ is limited. In addition, the link between chemical structure and odor is difficult to map without large enough interaction maps to understand the relevant features of a chemical.

Recent work on the forefront of synthetic biology is changing this. Research led by Ph.D candidate Eric Jones and Dr. Rishi Jajoo of Sriram Kosuri’s lab at UCLA has demonstrated the ability to screen large groups of olfactory receptors against large panels of chemicals in a high-throughput format. In the paper, they screen thousands of receptor-chemical pairs in a cost-effective and low-labor format and elucidate many novel interactions. They claim the technology can relatively easily be scaled up to screen all human receptors against even larger chemical libraries.

Reverse engineering smells is challenging, but having a quantitative map of odorant-receptor binding patterns would change that . If an odor is just the combination of receptors it activates, then one could recreate any fragrance by mimicking its activation pattern. Interestingly, olfactory receptor genes are highly subject to variation between populations, there is an estimated 30% difference between what any two individuals can smell. Mapping population level differences will identify regional preferences and the ability to craft more targeted fragrances. Inversely, if one knew the activation pattern of undesirable odors, they could develop methods to block the activation of these receptors and disable our ability to smell such odors.

The work being described in the article by Jones et al holds out the possibility for transforming the way scents are composed as it allows for more precise and efficient targeting of receptors. One can imagine that rather than a palette of some 5,000 widely used aromachemicals and plant extracts, perfumers and flavorists of the near future will work with a much more restricted number of higher performing ingredients for more precisely targeted effects. This could drastically change the way perfumers think about fragrance construction and composition, as well as how fragrance houses operate their logistics and supply chains. The resource footprint can get smaller, formulas more compact, but the experience and evoked sensations much heightened.

The sense of smell is often overlooked and underappreciated, however it is quite possibly our most sophisticated sense and our ability to fully understand it will unlock future opportunities to synthetically modulate it. Putting high throughput biological tools at the center of the scent making process can have powerful ripple effects throughout the industry. We look forward to exploring some of these implications in future posts.

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