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Editorial: Mixtures & modulations: responses to odorant chemicals in humans and other animals

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Editorial on the Research Topic
Mixtures & modulations: responses to odorant chemicals in humans and other animals

Odorant processing by the olfactory system is a complex and fascinating process that still poses many challenges. One reason is that the sense of smell is unique and distinct from other sensory systems. First the nature of the signal itself is challenging. Contrarily to light or sound that possess measurable physical properties as frequency or duration, odorants can be composed of one to hundreds of molecules with different volatile properties. These molecules may or may not be individually odorous and their combination is not predictable. In addition, unlike other sensory systems, from the olfactory epithelium to central olfactory regions, the olfactory system does not have a clear-cut spatial organization or topographic map, hence the challenge of neuroscientists is to find the code, the organization that relates molecules to percepts (Murthy, 2011; Uchida et al., 2014; Kurian et al., 2021). In this regard, one strategy employed to decipher odorant coding is breaking down olfactory stimulations into their component parts by using monomolecular odorants. However, not so surprisingly, psychophysical experiments, behavioral testing and brain activity recordings in both humans and animals have demonstrated that processing of odorant mixtures is very far from processing the sum of its parts (Xu et al., 2020).

Finally, starting from the olfactory bulb, odorant processing is strongly influenced by the predicted value of the odorant, i.e. by the experience of the animal, and also by other sensory traits of the stimulus or the source of the stimulus. Hence, despite significant efforts to understand the sense of smell, the mechanisms of odorant perception remain elusive and we are far from understanding what makes a chemical smell in a particular way and how this relates to molecules and mixtures.

This Research Topic is composed of 2 original research articles, 1 conceptual analysis and 1 review, which tackle these questions from diverse angles and open new challenging perspectives.

As the number of odorous molecule is uncountable, modelling efforts using artificial intelligence and machine learning, have been conducted, to establish the unique link between chemical features of molecules and psychophysical perception of the odorant. Still, the prediction of the perception of chemical molecules remains unattainable. In their highly thoughtful review article Barwich and Lloyd claim that the current models, which rely exclusively on chemical properties and miss the biological complexity of odorant-receptor interaction, target the wrong question and could be misleading for a comprehensive understanding of odor coding and perception.

As an illustration of the claim of Barwich and Lloyd and based on their pivotal former study showing complex receptor modulation at the level of peripheral olfactory sensory receptors (Xu et al., 2020), Xu et al. challenge the current understanding that we have of olfactory coding. Indeed, if a specific odorant receptor can exhibit opposing activity when its ligand is associated in a mixture with other odorants, this raises questions about the coding mechanisms in the central olfactory system. Xu et al. proposes the compelling hypothesis that the quest for the olfactory code may be vain and that new methods should be used such as medicinal chemistry to advance our understanding this problem.

Li et al. went deeper into the complexity of mixtures by pointing the trigeminal content of odorants. In natural environments, odorants are not only complexes mixtures of molecules with subtle interactions, but also they are very likely to stimulate the trigeminal nerve, which carries somatosensory perception, in the nasal epithelium. Even though the trigeminal sense is under looked in physiological studies, olfaction and trigeminal stimulation are fully interdependent. Does trigeminal stimulation influence odorant mixture perception? Li et al. question the role of trigeminal stimulation in overshadowing the effect of one odorant by the other in binary mixtures.

Finally, Vandroux et al. examined interactions between sex pheromones and plant volatiles in moths. In these insects, finding a mate relies on the female's release of sex pheromones and detections of this signals by males who have to navigate through a complex olfactory environment. Previous studies have shown that the interactions between sex pheromones and plant volatiles can occur in the peripheral olfactory system of moths at the level of the olfactory receptor neurons, implying that the olfactory receptor neurons that detect sex pheromones would also be able to detect certain volatile plant compounds. Vandroux et al. obtained unexpected results that appear to be in discrepancy with the dogma that each olfactory receptor neurons expresses only one type of olfactory receptor.

In conclusion, the articles published in this Research Topic although enlightening, reveal the thickness of shadows we yet have to explore in our journey to understand the perception of fragrant mixtures. So while your brain is silently processing the pleasant flavor coming out of the warm coffee cup you just pull yourself, ride your glasses, and walk with us though them, in order to catch up with your nose!

Author contributions

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

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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.

Publisher's note

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