

KEYNOTE LECTURE PRESENTATION

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# The tyranny of the use of homologous series of chemical odorants in olfactory research: does the olfactory system recognize molecules or odors?

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In some sense, the idea that the olfactory system is a chemical component analyzer can be traced to the hypothesis attributed to Titus Lucretius Carus in 50B.C. that human olfactory perception is directly linked to the general features of the shape of the molecules that “penetrare pute primordialis forma in naris hominum” (i.e. “work their way into the nostrils of men”). Consistent with this ancient hypothesis, for much of the last 200 years, the dominant experimental approach used to probe the functional organization of the olfactory system has involved the presentation of carefully selected homologous series of chemical compounds organized, for example, according to carbon chain length. In this presentation, data will be presented suggesting that, in fact, this may be entirely the wrong metric to use in understanding olfaction and olfactory perception. Based on an analysis of the organization of industry standard odor descriptors, we have proposed instead that the olfactory system might be organized to detect specific metabolic pathways, in effect already incorporating into its structure and circuitry a deep understanding of the metabolic world. As a test of this hypothesis, human psychophysical data will be presented suggesting that molecules derived from the same metabolic pathways are more likely to interfere perceptually than are molecules that are simply structurally similar. Preliminary data will also be presented suggesting that primary olfactory receptors themselves might be organized as metabolic pathway detectors, rather than as traditional detectors of molecular structure. Finally, evidence will be briefly presented that this “understanding” of the metabolic world might be built into the neural networks of the olfactory system itself. This proposal is based on the results of realistic model-based

efforts initially intended to better understand dynamic patterns of oscillatory behavior in the olfactory system. These modeling results will be presented in more detail in several posters being presented at the meeting itself. Accordingly, this presentation will provide a more general context for this work as well as the historical context for work to be presented by several other workshop participants.

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