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A competitive binding model predicts the response of mammalian olfactory receptors to mixtures VIJAY SINGH, University of Pennsylvania, NICOLLE MURPHY, JOEL MAINLAND, Monell chemical senses center, VIJAY BALASUBRAMANIAN, University of Pennsylvania — Most natural odors are complex mixtures of many odorants, but due to the large number of possible mixtures only a small fraction can be studied experimentally. To get a realistic understanding of the olfactory system we need methods to predict responses to complex mixtures from single odorant responses. Focusing on mammalian olfactory receptors (ORs in mouse and human), we propose a simple biophysical model for odor-receptor interactions where only one odor molecule can bind to a receptor at a time. The resulting competition for occupancy of the receptor accounts for the experimentally observed nonlinear mixture responses. We first fit a dose-response relationship to individual odor responses and then use those parameters in a competitive binding model to predict mixture responses. With no additional parameters, the model predicts responses of 15 (of 18 tested) receptors to within $10 - 30\%$ of the observed values, for mixtures with 2, 3 and 12 odorants chosen from a panel of 30. Extensions of our basic model with odorant interactions lead to additional nonlinearities observed in mixture response like suppression, cooperativity, and overshadowing. Our model provides a systematic framework for characterizing and parameterizing such mixing nonlinearities from mixture response data.

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