Binding of odorants to metal ions in receptor is key to sense of smell

Years ago, Yale University's Robert H. Crabtree speculated that the stench of ligands that bind strongly to metal ions might mean that olfactory receptors are metalloproteins. Now, chemists at the University of Illinois, Urbana-Champaign, have seized on that idea as a central motif in a proposed mechanism underlying the sense of smell [Proc. Natl. Acad. Sci. USA, published online, http://www.pnas.org/cgi/doi/10.1073/pnas.262792899]. Professors Kenneth S. Suslick and Zaida A. Luthey-Schulten and grad student Jiangyun Wang analyzed genome data for olfactory receptors, which are transmembrane proteins with seven characteristic \( \alpha \)-helices spanning the cell membrane. They identified in 75% of the receptors a common metal-binding site on a loop that sticks out from the membrane. The chemists synthesized a five-residue peptide analog of that binding site and found the peptide binds \( \text{Zn}^{2+} \) and \( \text{Cu}^{2+} \) strongly, curling into a helix. This conformational change, they propose, is part of a "shuttlecock" mechanism for conveying information across the cell membrane. Upon binding a metal ion, they suggest, the receptor shifts from a structure like that shown on the left to the one shown at right. Binding of an odorant to the metal triggers further events that the brain interprets as smell.