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Anesthetics lower T_c of a 2D miscibility critical point in the plasma membrane BENJAMIN MACHTA, Princeton Univ, ELLY GRAY, SARAH VEATCH, University of Michigan — Many small hydrophobic molecules induce general anesthesia. Their efficacy as anesthetics has been shown to correlate both with their hydrophobicity and with their potency in inhibiting certain ligand gated ion channels. I will first report on our experiments on the effects that these molecules have on the two-dimensional miscibility critical point observed in cell derived vesicles (GPMVs). We show that anesthetics depress the critical temperature (T_c) of these GPMVs but do not strongly affect the ratio of phases found below T_c. The magnitude of this affect is consistent across the n-alcohols only when their concentration is rescaled by the median anesthetic concentration (AC50) for tadpole anesthesia and at AC50 we see a 4K downward shift in T_c. I will next present a model in which anesthetics interfere with native allosteric regulation of ligand gated channels by the critical membrane, showing that our observed change in critical properties could lead to the previously observed changes in channel conductance without a direct interaction between anesthetic molecules and their target proteins. Finally, I will discuss ongoing experiments that will clarify the role of this membrane effect in mediating the organism level anesthetic response.

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