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pH-dependent conformational changes of diphtheria toxin adsorbed to lipid monolayers by neutron and X-ray reflection MICHAEL KENT, Sandia National Labs, HYUN YIM, Sandia National Labs, SUSHIL SATIJA, National Institute of Standards and Technology, IVAN KUZMENKO, Argonne National Labs — Several important bacterial toxins, such as diphtheria, tetanus, and botulinum, invade cells through a process of high affinity binding, internalization via endosome formation, and subsequent membrane penetration of the catalytic domain activated by a pH drop in the endosome. These toxins are composed of three domains: a binding domain, a translocation domain, and an enzyme. The translocation process is not well understood with regard to the detailed conformational changes that occur at each step, To address this, we performed neutron reflectivity measurements for diphtheria toxin bound to lipid monolayers as a function of pH. While the final membrane inserted conformation will not be reproduced with the present monolayer system, important insights can still be gained into several intermediate stages. In particular, we show that no adsorption occurs at pH = 7.6, but strong adsorption occurs over at a pH range from 6.5 to 6.0. Following binding, at least two stages of conformational change occur, as the thickness increases from pH 6.3 to 5.3 and then decreases from pH 5.3 to 4.5. In addition, the dimension of the adsorbed layer substantially exceeds that of the largest dimension in the crystal structure of monomeric diphtheria, suggesting that the toxin may be present as multimers.

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