INNOVATING CROSS-DOMAIN SOLUTIONS TO DETECT EMERGING BIOLOGICAL THREATS

Metadynamics Free Energy Analysis of High Temperature Degradation of Fentanyl

Bharat Poudel Oregon State University **Susan Rempe** Sandia National Laboratories **Jason Sammon** Sandia National Laboratories **Joshua Whiting** Sandia National Laboratories **Matthew Moorman** Sandia National Laboratories **Haley Bennett** Sandia National Laboratories **Juan Vanegas** Oregon State

While experimental studies have probed the thermal degradation of fentanyl, little theoretical work has been done to understand the mechanism. Here, we studied the thermal degradation pathways of fentanyl using extensive ab initio molecular dynamics simulations combined with enhanced sampling via multiple-walker metadynamics. We calculated the free energy profile for each bond suggested earlier as a potential degradation point to map the thermodynamic driving forces. We also estimated the forward attempt rate of each bond degradation reaction to gain information about degradation kinetics. This modeled degradation prediction was then compared to experimental data. Details of the modeling and comparisons of the experimental and theoretical results will be presented.

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