Transition State Dynamics of Bacterial Methylthioadenosine Nucleosidases

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Two homologous bacterial enzymes, \textit{Escheria coli} 5'-methylthioadenosine/S-adenosylhomocysteine nucleosidase (EcMTAN) and \textit{Vibrio cholerae} MTAN (VcMTAN), that catalyze the conversion of methylthioadenosine (MTA) to methylthioribose and adenine and S-adenosylhomocysteine (SAH) to S-ribosylhomocysteine (SRH) and adenine. Despite their structural similarities, especially at the active site, the two enzymes have different affinities for the same transition state inhibitor, 5'-butylthio-DADMe-immucillin-A (BuT-DADMe-ImmA)—EcMTAN binds BuT-DADMe-ImmA more tightly than VcMTAN by a factor of approximately $10^3$. Molecular dynamics (MD) simulations suggest that dynamic elements contribute to the tight binding of the transition state analogue BuT-DADMe-ImmA, and thus the transition state of EcMTAN.