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Ligand-Binding and Conformational Thermodynamics of Tryptophanyl-Trna Synthetase (Trprs). M. Kapustina, C.W. Carter, Jr., Dept. of Biochemistry & Biophysics, Univ. of North Carolina, Chapel Hill, NC, 27599-7260.

TrpRS recognizes tryptophan, catalyzing its reactions with ATP and tRNA^{Trp}. During catalysis, it successively assumes an open state and two distinct closed conformations, termed "pre-TS" and "products", with different relative domain orientations [1]. Thermodynamic forces producing conformational transitions in response to ligand binding are crucial to enzyme function. Molecular dynamics (MD) simulations and free energy calculations with explicit/implicit solvent [2] can provide theoretical estimates of intrinsic protein stabilities. Simulations were performed with three liganded/unliganded conformations of both the TrpRS monomer and dimer. The estimated dimerization free energy corresponds to that estimated from buried surface area. Unrestrained MD simulations reveal that the pre-TS state has reduced stability, relative to the other two states, and crystallographic conformations of pre-TS states without bound ATP convert rapidly to the open conformation. We also used essential dynamics analysis to determine the individual residue behavior during the reaction. Supported by NIGMS 48519

1. Retailleau et al (2003) J. Mol. Biol., 325:39-63.
2. Vorobjev, Almagro, & Hermans (1998) PROTEINS: Struct. Func. Gen. 32:399-413.