Positive Geometry of Enzymatic Quantum Tunneling in Alcohol Dehydrogenase

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A novel mathematical formalism is proposed that applies the apparatus of positive geometry (canonical forms, twisted cohomology, tropicalization) to the description of hydride quantum tunneling in the enzymatic catalysis of alcohol dehydrogenase (ADH). It is demonstrated that the instanton action for tunneling through the potential energy surface (PES) barrier of hydride transfer possesses the structure of a twisted period in the sense of Picard–Lefschetz theory, and that the tunneling-corrected enzymatic reaction rate can be expressed as the canonical form of the corresponding positive geometry on a semi-algebraic subvariety of configuration space. Three theorems are proved: (1) on the existence of a positive geometry for one-dimensional polynomial barriers of the Eckart–Morse type; (2) on the tropical convergence of the canonical form to the WKB tunneling amplitude in the limit $\hbar \to 0$; (3) on the resurgent structure of the trans-series for the enzymatic rate, wherein the transition from the perturbative sector (classical transition state theory) to the nonperturbative sector (tunneling) is described via Stokes phenomena on Lefschetz thimbles. Numerical calculations for hydride transfer in ADH with barrier parameters $V_0 = 18.4$ kcal/mol, width $a = 0.8$ Å, and donor–acceptor distance DAD = 3.2 Ådemonstrate that the tropical approximation of the canonical form reproduces the instanton tunneling rate with an error of less than 0.03%. The relationship between the boundary structure of canonical forms and physical singularities (kinetic isotope effects, the Klinman temperature transition at $T \sim 30$ °C) is discussed.