

Biochemistry IN PERSPECTIVE

Quantum Tunneling and Enzyme Catalysis

How does quantum mechanics explain the transfer of hydrogen during enzyme catalysis? Investigations with increasingly sophisticated technologies have revealed that transition state theory does not fully account for the catalytic power of the several enzymes thus far studied. It is now believed that when hydrogen is transferred in the form of hydrogen atoms ($H\cdot$), hydride ions ($H:^-$) or protons (H^+), a phenomenon called tunneling occurs. *Tunneling* is a quantum mechanical process in which a particle passes through an energy barrier instead of over it. *Quantum mechanics* is the science that deals with the properties of matter and electromagnetic radiation on the atomic and subatomic scales. One of the most remarkable contributions of quantum theory is particle-wave duality, the recognition that particles of matter have wavelike properties and radiation has particle-like properties. For example, light is composed of photons (packets of energy) that propagate through space as a wave. In the quantum world, a particle such as a proton can move through an energy barrier rather than over it, because it behaves like a wave. Such an event is forbidden in classical (Newtonian) physics.

Quantum tunneling is possible only for light particles such as electrons and hydrogen atoms because a particle's wavelength is inversely proportional to the square root of the particle's mass. According to quantum mechanical calculations, a proton can tunnel over a distance of 0.58 Å. Among the best-documented cases of hydrogen tunneling is the hydride transfer reaction catalyzed by dihydrofolate reductase (DHFR). DHFR, the enzyme that reduces 7,8-dihydrofolate to 5,6,7,8-tetrahydrofolate (the biologically active form of folic acid, see pp. 525–526), uses the coenzyme NADPH as a hydride donor. Compelling evidence indicates that vibrational energy resulting from protein conformation changes during the reaction reduces the tunneling distance, thereby compressing the activation barrier and increasing the probability of hydride transfer between NADPH and the substrate. The progress of a reaction *through* rather than *over* an energy barrier (therefore, requiring more kinetic energy) would lead to an acceleration of reaction rate comparable to that seen in many enzyme-catalyzed reactions. Macromolecular dynamics and its link to the phenomenon of quantum tunneling is an important area for future research and appears to provide an explanation for the high rates of enzymatic reactions.

QUESTION

Quantum tunneling appears to play a significant role in the facilitation of efficient enzyme catalysis, particularly in reactions involving small-species transfer (H^+ , $H:^-$, etc). Provide an energy diagram for a hypothetical reaction in the presence and absence of an enzyme that clearly illustrates the quantum tunneling process. [*Hint:* Refer to the progress of reaction diagram in Figure 6.1.]

SUMMARY: Conformational changes in enzymes that catalyze hydrogen transfers release vibrational energy that drives the tunneling of hydrogen through, rather than over, energy barriers.