ENGINEERING DYNAMIC PROTEIN TUNNELS

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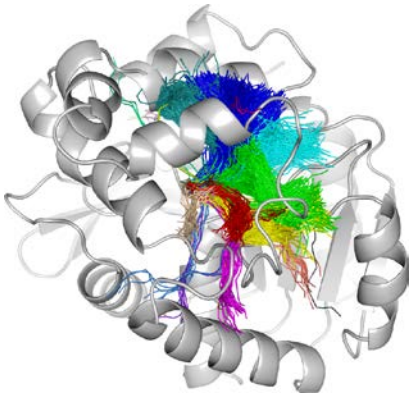
Protein structures contain a complex system of voids, making up specific features - clefts, pockets, cavities, channels and tunnels. These features are essential for the migration of solvents, ions and small molecules through the protein structure and represent the natural hot spots for protein engineering. This migration is often controlled by highly dynamical structures called molecular gates. In this lecture, I will present: (i) examples of protein families possessing tunnels[1] and gates[2], (ii) software tools[3] available for detection and analysis of molecular tunnels and gates, and (iii) success stories from engineering protein tunnels for improved catalytic activity[4], enantioselectivity[5] and stability[6]. I will demonstrate applicability of the software tools HOTSPOT WIZARD[7] and CAVER[8] for analysis and design of dynamic access pathways[9], and will advocate the design of tunnels and gates as a powerful strategy for construction of enzymes with novel catalytic properties.



Visualization of dynamic tunnels in enzyme haloalkane dehalogenase.

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