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Unraveling How CYP450 Channel Drives Stepwise Translocation and Optimal Binding of Prostaglandin H_2 for Cyclization

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Enzymes are dynamical systems that perform homeostatic abilities, in precise control of their local environment through inter-conversions of chemical and mechanical energy and self-regulating feedback connections organized hierarchically across many scales of states. They can carry out effective rate accelerations by virtue of their ability to utilize substrate-channeling forces to act as a mechanochemical valve. Such a channeling process is treated quantitatively using the key aspects of the free energy landscape; the balance between substrate positioning and conformational changes reflects the severe geometric and electronic requirements for the relatively tight transition state. The observed k_{cat}/K_M of about 10^6 M^{-1} s^{-1} for PGH_2 cyclization has been revealed to be brought about by bringing together two properly oriented reactants of substrate and enzyme regarding the magnitude significance of the contribution from outer- and inner-binding stereopopulation along the free-energy channeling pathway and thus shapes the cascade cyclization route, enforcing precise spatial and temporal control. The apparent constant k_{cat} of many P450 reactions involving the heme catalytic cycle, which is often on the order of 10^1−10^2 s^{-1} and is usually attributed to compound 0 to compound I formation, may be in large part a consequence of channeling conformation changes toward the rate-limiting state that is made possible by preorganizing the proximal hydrogen-bonding pattern of the amide groups to the cysteine sulfur, and to the push−pull modulation of the relevant heme axial ligation and activation. We published the work in *ACS Catal.* **2018**, *8 (3)*, 2534-2545 " Substrate Channeling of Prostaglandin H_2 on the Stereochemical Control of a Cascade Cyclization Route." **doi:** 10.1021/acscatal.7b03687.

References

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Dr. Yang's research has concentrated on the fundamental understanding of structure-function-dynamics in complex systems, encompasses the characterization of fundamental structural function relationship in the enzymes processes, interactions at interfaces and sites, the structure and dynamics of carrier transport and signal transduction. Current interest has focused on the hybrid approaches utilizing SAXS with high-resolution MD simulation techniques, but also with biochemical, biophysical, and numerical programming methods by a series of breakthrough experiments with the synchrotron/neutron beamline (BL23A1 at NSRRC/ QUOKKA at ANSTO) and developed computational techniques for solving the inverse mapping problems of X-ray/neutron scattering.

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2004 Ph.D., National Sun Yat-Sen University
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Experiences
Associate Professor, Department of Chemistry, Fu Jen Catholic University (2012/02 – 2019/01)
Assistant Professor, Department of Chemistry, Fu Jen Catholic University (2006/08 – 2011/01)
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Secretary-general, 1st, Taiwan Theoretical and Computational Molecular Sciences Association (2013/8–2017/07)
2006 Postdoctoral Research Fellow, The Ohio State University
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Awards
Ministry of Science and Technology, Ta-You Wu Memorial Award, Taiwan (2016).
Fu Jen Catholic University, Outstanding Research Award, Taiwan (2015).
The 62nd SPSJ "Asia Excellence Award", Japan (2013)
Science Editor's Choice, Science **2011**, *333*, 500.
International Young Polymer Scientist **2008** the 42nd World Polymer Congress (Macro 2008)