

## Biology by Design: From Directed Evolution to Autonomous Experimentation



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Synthetic biology aims to apply engineering principles to design novel or improved biological systems for a wide range of biotechnological and biomedical applications. However, due to the complexity of biology, it remains an overwhelming challenge to rationally design biological systems with desired features. In this talk, I will reflect my over three-decades of academic journey to tackle this challenge and highlight the paradigm shift from directed evolution to autonomous experimentation. Specifically, I will discuss a few representative case studies, including: (a) design and evolutionary engineering of artificial photoenzymes with new-to-nature reactivity for asymmetric synthesis; (b) development of new artificial intelligence (AI) models for enzyme property prediction, enzyme engineering, and metabolic engineering; and (c) design of an AI-powered self-driving biofoundry for protein engineering, pathway engineering, and retabolic engineering. I envision a future where autonomous experimentation, enabled by seamless integration of synthetic biology, AI, and biofoundry/robotics, accelerates basic and applied biological research for bioeconomy.