SINGLE-MOLECULE CHEMISTRY OF CATALYSIS AND BIOENERGY CONVERSION

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Modern single-molecule imaging and manipulation methods have enabled new ways to probe molecules and chemical processes, providing unprecedented insights. One can visualize and manipulate individual cells, particles, molecules, and even individual molecules inside a single cell, with nanometer spatial resolution and under in situ or operando conditions. All these capabilities open huge opportunities to examine and dissect chemical processes that are intrinsically heterogeneous, where behaviors of the individual constituents differ or change as a function of space and/or time, or whose players reside at different locations and are required to coordinate their actions spatiotemporally for function.

My discussion here will showcase some advances in our laboratory in the development and application of such methods to study catalyst particles, synthetic polymers, and energy conversion processes in bacteria.

Catalysis on single particles

Solid-state particles, especially nanoparticles, are important catalysts for many chemical transformations and they can be made of a variety of materials. Understanding their structure-activity correlation has been a central research goal. For structure, electron microscopy methods have made it possible to visualize the structure of individual particles down to atomic resolution. However, for activity, they had been mainly studied at the ensemble level, obtaining averaged activity behaviors. Such ensemble activity studies are inherently insufficient due to the intrinsic structural heterogeneity of catalyst particles. Over the past two decades, our group has applied and developed single-molecule fluorescence-based methods to image catalytic reactions on single nanoparticles in real time with single-turnover temporal resolution and nanometer spatial resolution. We have discovered time-dependent activity fluctuations of single metal nanoparticles, manifesting the underlying dynamic surface structure (Fig. 1A) [1]. We have mapped catalytic activity on a single catalyst particle at nanometer resolution, directly visualizing the site/region-specific activity (Fig. 1B) [2][3], uncovering bimetallic enhancement within single bimetallic catalyst particles [4], and revealing the cooperative communication of reactions within and between single catalysts [5].

Combining single-molecule super-resolution reaction imaging with single-to-sub-particle photoelectrochemical measurements, we discovered the correlation between charge-carrier surface activity and local water oxidation performance on single particulate semiconductor photoanodes [6]. On single anisotropically shaped semiconductor particles, we discovered interfacet junction effects between adjoining facets [7]; such interfacet junction effects create broad surface band bending zones that can dictate the whole-particle' performance in photoelectrochemical water oxidation.

We further developed two methods to image nonfluorescent surface reactions on catalyst surfaces, named COMPEITS and adCOMPEITS [8,9]. These methods enabled quantitative imaging of molecular adsorption on particle surfaces, visualizing facet-dependent molecular adsorption on single particles [8], uncovering ligand adsorption cooperativity [10], and discovering long-range adsorption enhancement on metal-promoted semiconductor photocatalysts [9].

Outlook: Moving forward, an important direction is to understand quantitatively how real-time, spatially resolved activity of a catalyst particle is related to local molecular properties (such as adsorption affinity of reactants, intermediates, and products on particle surfaces) and local surface structures and chemical nature. Integrating many in situ and operando methods whose resolution spans different length and time scales would be a key to these endeavors.

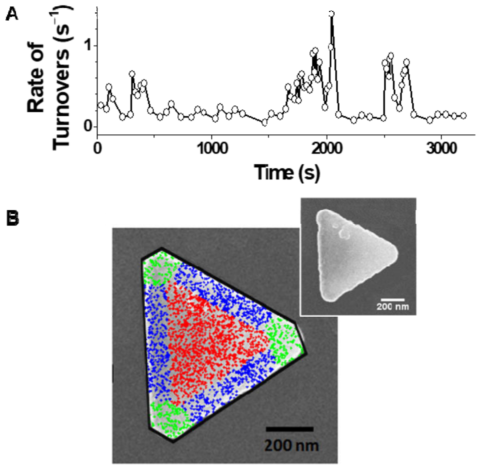

Fig. 1. (**A**) Rate of turnover of a single 6 nm Au nanoparticle in catalyzing a chemical reaction [1]. (B) Map of catalytic products on a single mesoporous silica coated Au nanoplate, where the individual products (dots) are color-coded based on their locations being in the corner (green), edge (blue), or top facet regions (red) [3]. Inset: corresponding scanning electron microscopy image of the Au nanoplate.

Single-chain polymerization dynamics

Polymerization reactions are another intrinsically heterogeneous process: individual polymers differ in length, and for copolymers, in composition and monomer arrangements. We have developed a magnetic tweezers-based method to enable following the growth of single-polymer chains in real time under living polymerization conditions (Fig. 2A) [11]. We discovered the stochastic formation and unraveling nonequilibrium conformational entanglements that play key roles in controlling the polymerization kinetics [11]. Such entanglements also play roles in conjugated polymers [12] and can be tuned by intermolecular forces such as H-bonds to alter polymerization kinetics [13]. The presence of an applied pulling force in magnetic tweezers can be utilized to interrogate the single-chain mechanics of an in-situ grown polymer, testing long-existing theory of polymer conformational mechanics [12] and uncovering new force-dependent mechanochemistry in polymerization reactions [14]. Moreover, we developed a single-molecule fluorescence-based approach, named CREATS, to enable imaging polymerization of a single chain at single-monomer resolution in real time, and, for copolymerization reactions, determining the microscopic sequences of individual copolymer chains and quantifying their sequence patterns (Fig. 2B) [15].

Outlook: The sequence of copolymers is known to dictate the large part of their properties. But the sequence-property correlations of synthetic copolymers are only known at the bulk level, in which individual copolymers differ greatly. Defining the sequence-property correlation of individual synthetic copolymer chains would be a key research area to grow.

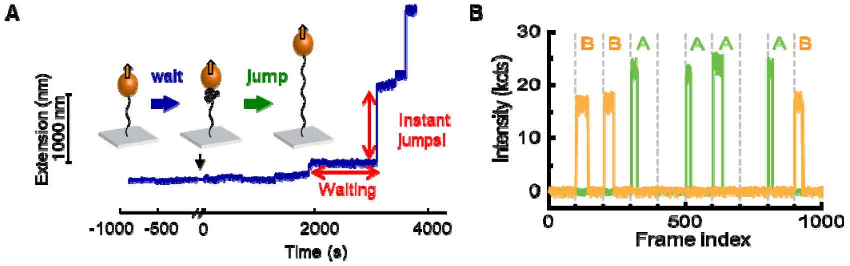

Fig. 2. (**A**) End-to-end extension vs. time trajectory of a single growing polymer under living polymerization conditions, with the inset cartoon illustrating the formation and unraveling of nonequilibrium conformational entanglements [11]. (B) Fluorescence intensity vs. time (in image frame index) showing the incorporation of monomer A (green) or monomer B (orange) at single-monomer resolution into a single molecular catalyst catalyzing the formation of a single copolymer chain [15].

Bacterial energy conversion

Recent advances have shown that microbes, such as bacteria, with their vast capabilities of mediating specific chemical transformations intracellularly, can be integrated with inorganic solids for energy conversion, including CO_2 fixation, electrosynthesis, and bioelectricity generation. Underlying all these energy applications are the spatiotemporal coordinations of proteins that often reside at different cellular compartments. We have been studying how single bacterial cells can uptake photogenerated electrons from semiconductors under light excitation to fuel bioplastic formation in the cell, and how each cell's capability in doing so is related to the cellular levels of electron-transfer proteins [16]. We have also uncovered how membrane electron transfer proteins in bacteria can spatially reorganize to coordinate spatiotemporally with partner proteins to mediate electron transfer across the cell envelop with extracellular redox pairs.

Outlook: Microbic cells are complex systems. Dissecting the cellular mechanism of co-actions of many individual proteins in accomplishing energy conversion will remain an important research area. Combining with synthetic biology to alter, tailor, or enhance overall cell performance in such energy conversion processes would be another important area.

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References

1 W. Xu, J. S. Kong, Y.-T. E. Yeh & P. Chen, *Nat. Mater.* **7**, 992 (2008).

2 X. Zhou, N. M. Andoy, G. Liu, E. Choudhary, K.-S. Han *et al.*, *Nat. Nanotechnol.* **7**, 237 (2012).

3 N. M. Andoy, X. Zhou, E. Choudhary, H. Shen, G. Liu *et al.*, *J. Am. Chem. Soc.* **135**, 1845 (2013).

4 G. Chen, N. Zou, B. Chen, J. Sambur, E. Choudhary *et al.*, *ACS Cent. Sci* **3**, 1189 (2017).

5 N. Zou, X. Zhou, G. Chen, N. M. Andoy, W. Jung *et al.*, *Nat. Chem.* **20**, 607 (2018).

6 J. B. Sambur, T.-Y. Chen, E. Choudhary, G. Chen, E. J. Nissen *et al.*, *Nature* **530**, 77 (2016).

7 X. Mao & P. Chen, *Nat. Mater.* **21**, 331 (2022).

8 X. Mao, C. Liu, M. Hesari, N. Zou & P. Chen, *Nat. Chem.* **11**, 687 (2019).

9 M. Zhao, W. Li, M. Yang, Z. Zhao, R. Ye *et al.*, *Nat. Catal.* **7**, 912 (2024).
10 R. Ye, M. Zhao, X. Mao, Z. Wang, D. A. Garzón *et al.*, *Nat. Commun.* **12**, 4287 (2021).
11 C. Liu, K. Kubo, E. Wang, K.-S. Han, F. Yang *et al.*, *Science* **358**, 352 (2017).
12 S. Baral, C. Liu, U. K. Chakraborty, K. Kubo, X. Mao *et al.*, *Chem* **7**, 2175 (2021).
13 S. Baral, C. Liu, X. Mao, G. W. Coates & P. Chen, *ACS Cent. Sci* **8**, 1116 (2022).
14 U. K. Chakraborty, M. Yang, S. Baral, C. Liu, A. Chen *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **122**, e2418844122 (2025).
15 R. Ye, X. Sun, X. Mao, F. S. Alfonso, S. Baral *et al.*, *Nat. Chem.* **16**, 210 (2024).
16 B. Fu, X. Mao, Y. Park, Z. Zhao, T. Yan *et al.*, *Nat. Chem.* **15**, 1400 (2023).