



News and opinions

Nanoparticles power yeast chemical factories

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The production of chemicals by microorganisms like yeast can be boosted using light-harvesting semiconducting nanoparticles, according to new research [Guo et al., *Science* **362** (2018) 813, <https://doi.org/10.1126/science.aat9777>].

The yeast, *Saccharomyces cerevisiae*, is biomanufacturing workhorse because of its ability to proliferate rapidly and convert renewable carbon sources into high-value chemicals. Integrating such natural systems with the light-harvesting properties of inorganic semiconducting materials introduces a new dimension into the process.

“We show that semiconductor nanoparticles can be synthesized independently and subsequently assembled onto the surface of genetically engineered yeast cells to produce high-value chemical compounds,” says first author of the study, Junling Guo of the Wyss Institute for Biologically Inspired Engineering.

Along with colleagues from the Departments of Chemistry and Chemical Biology, Systems Biology, and John A. Paulson School of Engineering and Applied Science at Harvard, the researchers fabricated inorganic-organic biohybrids from genetically modified yeast cells encrusted with photosensitive InP nanoparticles (Fig. 1).

“We functionalized the surface of InP nanoparticles with polyphenol moieties,” explains Guo. “This polyphenol-based functionalization layer facilitates an interfacial interaction between nanoparticles and cells, driving the assembly and inter-locking of nanoparticles on the cell surface.”

When light is shone on the biohybrid systems, photogenerated electrons are produced in the InP nanoparticles, which are in turn harvested by the yeast. The yeast cells use the photoexcited electrons to drive the regeneration of NADPH, a reduced form of nicotinamide adenine dinucleotide phosphate. NADPH is produced during the first stage of photosynthesis and helps fuel subsequent reactions. In this system, NADPH is essential for the biosynthesis of shikimic acid, a precursor of aromatic amino acids, the building blocks of proteins and other useful chemicals.

“The external electrons generated from assembled nanoparticles provide alternative energy sources to diverse metabolic pathways,” explains Guo. “[This] is the first time that the photoexcited electron generation capacity of semiconductor nanoparticles has been integrated with microbial synthetic biology, providing rational design of biological pathways for biosynthesis of more complicated fine chemicals,” he claims.

InP nanoparticles absorb a large portion of the solar spectrum efficiently, are stable to oxygen, and biocompatible, making them

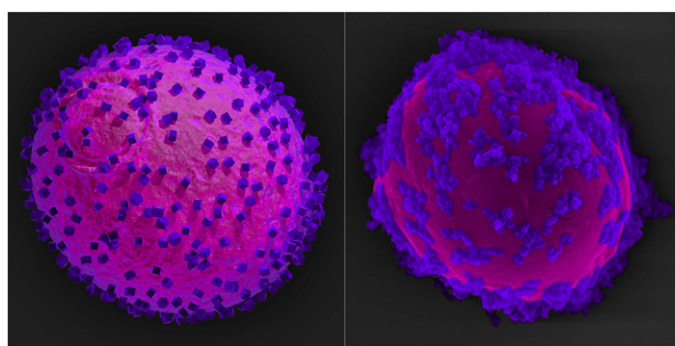


Fig. 1. Left: The researchers' model of a yeast cell (magenta) with semiconductor nanoparticles (purple) attached to its surface. Right: Scanning electron microscopy image of the actual biohybrid system. The semiconductor nanoparticles capture electrons from light and transfer them to the cell where they drive the shikimic acid metabolic pathway. [Credit: Wyss Institute at Harvard University and Dr. Junling Guo.]

ideal for the purpose. Moreover, biohybrids based on different nanoparticles with magnetic, semiconducting, or photo-responsive properties could be easily fabricated to produce a range of chemicals.

“The modularity of this biohybrid platform enables a mix-and-match approach, compatible with existing workhorse cellular chassis and a wide range of nanoparticle-cell combinations,” says Guo. “Our modular biohybrid platforms are likely to enable efficient and economical biochemical reactions of valuable chemicals.”

Ultimately, the approach could boost the production efficiency of alkaloid natural products, as well as other drugs and nutraceuticals, from yeast using alternative and sustainable energy sources.

“This idea of harnessing and combining the reaction pathways in whole organisms with the exceptional ability of semiconducting nanomaterials to harvest solar energy is quite powerful and will fundamentally change the way we think about the chemical and pharmaceutical industry,” comments Peidong Yang, co-director of the Kavli Energy Nanoscience Institute at the University of California, Berkeley.

Recently, Yang and his colleagues used a combination of photo-sensitized bacteria with *Escherichia coli* to fix carbon dioxide using

sunlight and produce a drug intermediate for the antimalarial agent artemisinin [Liu et al., *Nano Lett.* **15** (2015) 3634].

“I am glad to see another example of a photosensitized semiconductor biohybrid for light-driven chemical production of the drug precursor shikimic acid,” he told *Nano Today*.

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Nanoparticles focus new light on catalysis

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Researchers at Stanford University have observed light-driven chemical reactions taking place on a single metallic nanoparticle catalyst [Vadai et al., *Nature Communications* **9** (2018) 4658, <https://doi.org/10.1038/s41467-018-07108-x>].

Metallic nanoparticles are emerging as a new class of plasmonic photocatalysts because they have a particularly strong response to illumination. Led by Jennifer A. Dionne, the researchers focused their attention on a combination of gold nanodiscs (100 nm in diameter) and palladium nanocubes (with side lengths of 30 nm). The gold discs act as antennas to focus and intensify incident light onto the palladium nanoparticles, which catalyze the reaction. In this case, a simple hydrogenation reaction during which hydrogen atoms diffuse out of the palladium nanoparticles, transforming the material from a hydrogen-rich β -phase to a hydrogen-poor α -phase (Fig. 1).

“We were able to observe this chemical change upon illumination on a single nanoparticle, which is an important achievement,” says first author of the study Michal Vadai. “Only single particle measurements allow one to understand whether specific site on a nanoparticle is more favorable for the reaction.”

The researchers used an environmental transmission electron microscope (ETEM) with an external light source to follow the catalytic reactions directly. Image contrast between the α - and β -phases enables the appearance of the phase transition to be clearly observed. This direct imaging is backed up by the detection of

changes to the diffraction pattern and electron energy loss (EEL) signal as hydrogen is desorbed from the palladium nanocubes. The setup enabled the first experimental observations in real time of a light-activated reaction on a nanoparticle catalyst at nanoscale resolution.

“Real time observation of chemical reactions on a single particle allows one to understand the effect of light on different reactions steps,” points out Vadai.

Optical excitation enhances the overall reaction kinetics by a factor of ~ 10 , but the researchers’ findings indicate that plasmons affect individual reaction steps differently. In this reaction, when there is no illumination, nucleation initiates randomly at any corner of the palladium nanocubes. But under illumination when plasmons are generated, reactions are more likely to take place at corners closest to ‘hot-spots’ where light is most concentrated. Plasmons can also potentially open up new reaction paths as well, such as along the edges of the catalyst nanocubes.

“From a technological and experimental point of view, [our work] presents a new concept for studying plasmonic photocatalysts,” says Vadai. “No other approach currently has these capabilities at such high spatial resolution.”

Differences in nanoparticle type, size, or shape can affect catalytic activity, so the ability to observe what happens on an individual particle is very helpful to understanding the process, explains Vadai.

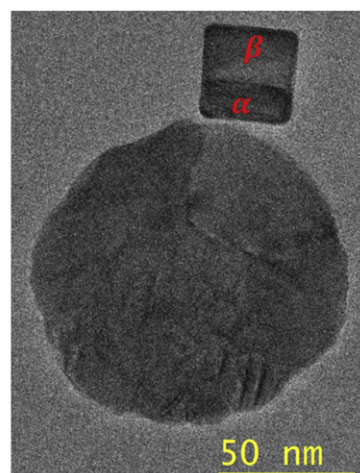
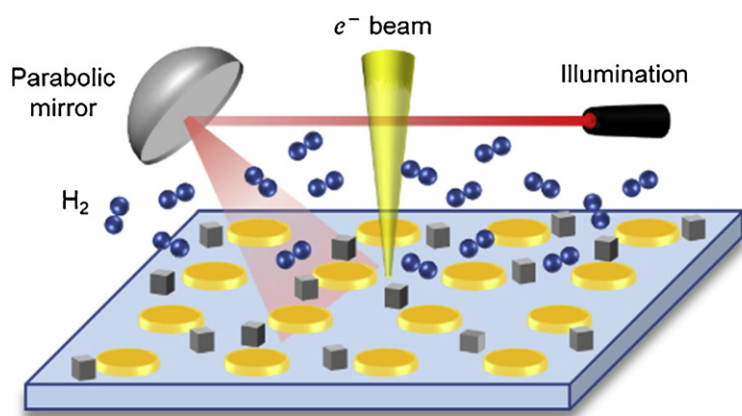


Fig. 1. (a) Schematic of light-coupled TEM. (b) TEM image of Au-Pd antenna reactor system showing the beta to alpha phase transition. [Credit: Jennifer Dionne's group.]