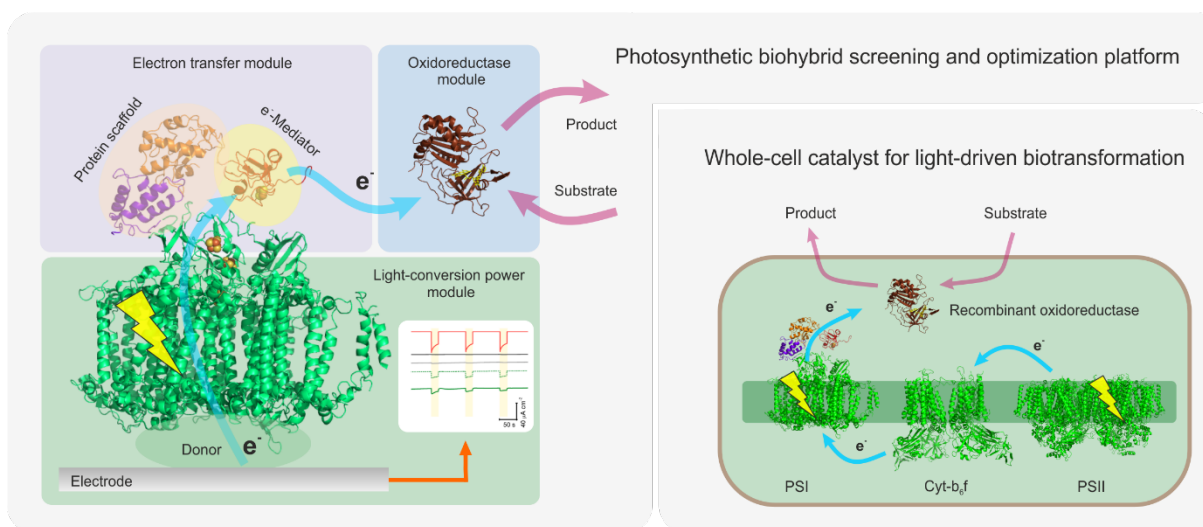


Marc Nowaczyk: Light-driven redox biotransformation with recombinant cyanobacteria

The process of oxygenic photosynthesis leads to the formation of redox equivalents, which can be used to drive whole-cell biotransformations. In this concept, recombinant oxidoreductases are coupled to photosynthetic electron transport for light-driven conversion of externally supplied substrates, with water as the primary electron donor. We have shown in a pilot study that overexpression of an ene-reductase from *Bacillus subtilis* in *Synechocystis* sp. PCC 6803 leads to high conversion rates and product titers. Further investigations revealed that this system is limited by electron supply due to the strong artificial electron sink, which can be optimized by streamlining of the electron transfer. Additionally, we have developed a universal screening platform based on isolated proteins and protein complexes to mimic and optimize electron transfer, which was also successfully tested as light-driven NADPH recycling systems to fuel double-bond or ketone reductases in vitro. Moreover, the IM7/E7 protein scaffold system was established to fuse components of the chain for confined electron transfer. These tools are now available to further facilitate the development of light-driven redox biotransformations in vitro or in vivo.



- Königer K, Gómez Baraibar Á, Mügge C, Paul CE, Hollmann F, Nowaczyk MM, Kourist R. 2016. Recombinant Cyanobacteria for the Asymmetric Reduction of C=C Bonds Fueled by the Biocatalytic Oxidation of Water *Angew Chem Int Ed* 55:5582-5585
- Assil-Companiononi L, Büchenschütz HC, Solymosi D, Dyczmons-Nowaczyk NG, Bauer KKF, Wallner S, Macheroux P, Allahverdiyeva Y, Nowaczyk MM, Kourist R. 2020. Engineering of NADPH Supply Boosts Photosynthesis-Driven Biotransformations *ACS catalysis* 10, 11864-11877
- Zhao F, Wang P, Ruff A, Hartmann V, Zacarias S, Pereira IC, Nowaczyk MM, Rögner M, Conzuelo F, Schuhmann W. 2019. A photosystem I monolayer with anisotropic electron flow enables Z-scheme like photosynthetic water splitting *Energy Environ Sci* 12:3133-3143
- Hartmann V, Harris D, Bobrowski T, Ruff A, Frank A, Pomorski TG, Rögner M, Schuhmann W, Adir N, Nowaczyk MM. 2020. Improved quantum efficiency in an engineered light harvesting/photosystem II super-complex for high current density biophotoanodes. *J. Mater. Chem. A* 8,14463-14471
- Wang P, Zhao F, Frank A, Zeria S, Lielpetere A, Ruff A, Nowaczyk MM, Schuhmann W, Conzuelo F. 2021. Rational design of a photosystem I photoanode for the fabrication of biophotovoltaic devices. *Adv Energy Mater* 2102858
- Sokol KP, Robinson WE, Warnan J, Kornienko N, Nowaczyk MM, Ruff A, Zhang JZ, Reisner E. 2018. Bias-free photoelectrochemical water splitting with photosystem II on a dye-sensitized photoanode wired to hydrogenase *Nature Energy* 3:944-951
- Böhmer S, Königer K, Gómez-Baraibar Á, Bojarra S, Mügge C, Schmidt S, Nowaczyk MM, Kourist R. 2017. Enzymatic Oxyfunctionalization Driven by Photosynthetic Water-Splitting in the Cyanobacterium *Synechocystis* sp. PCC 6803 *Catalysts* 7:240
- Baikie TK, Wey LT, Lawrence JM, Medipally H, Reisner E, Nowaczyk MM, Friend RH, Howe CJ, Schnedermann C, Rao A, Zhang JZ. 2023. Photosynthesis re-wired on the pico-second timescale. *Nature* 615, 836-840
- Medipally H, Guarneri A, Pospisil L, Franssen MCR, van Berkel WJH, Paul CE, Nowaczyk MM. 2023. Light-Driven NADPH Cofactor Recycling by Photosystem I for Biocatalytic Reactions. *ChemCatChem*, 15, e20230082
- Medipally H, Mann M, Kötting C, van Berkel WJH, Nowaczyk MM. 2023. A Clickable Photosystem I, Ferredoxin, and Ferredoxin NADP⁺ Reductase Fusion System for Light-Driven NADPH Regeneration. *ChemBioChem* 24, e202300025