PROCESS ENHANCEMENT OF ENZYME-CATALYZED REACTIONS BASED ON MICRO- AND NANO-REACTORS

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Enzymes are the core catalysts for biomanufacturing. However, natural enzymes lack catalytic activity for unnatural substrates, have poor stability and low cofactor recycling efficiency. To enhance the efficiency of enzyme-catalyzed reactions, enzyme catalytic enhancement based on the nanoconfinement effect was proposed, and a multi-enzyme reactor based on nano-virus-like particles was constructed, which improved the cofactor NADPH recycling efficiency in the nanoreactor by up to 45-fold and reduced the NADPH consumption in the scaled-up reaction by an order of magnitude compared to the free enzyme system (Figure 1). The improved oxygen transfer efficiency using the confinement effect resulted in a 96-fold increase in the space-time yield of continuous-flow enzymatic synthesis of ursodeoxycholic acid compared to batch reactions, a 10-fold increase in the cycling efficiency of the cofactor NAD^+, a 7-fold reduction in enzyme consumption, and a substantial reduction in enzyme and cofactor costs. On this basis, we constructed a continuous-flow enzyme-catalyzed reaction system based on 3D microfluidic chips (Figure 2), realizing the precise synthesis of chiral molecules and scaling-up of reactions, and promoted the wider application of enzyme-catalyzed technology in biopharmaceutical field.

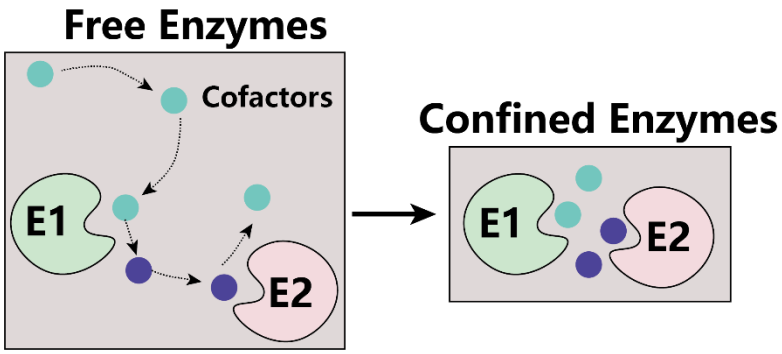

Figure 1–Confined enzymes in micro- and nanoreactors for enhanced cofactor recycling.

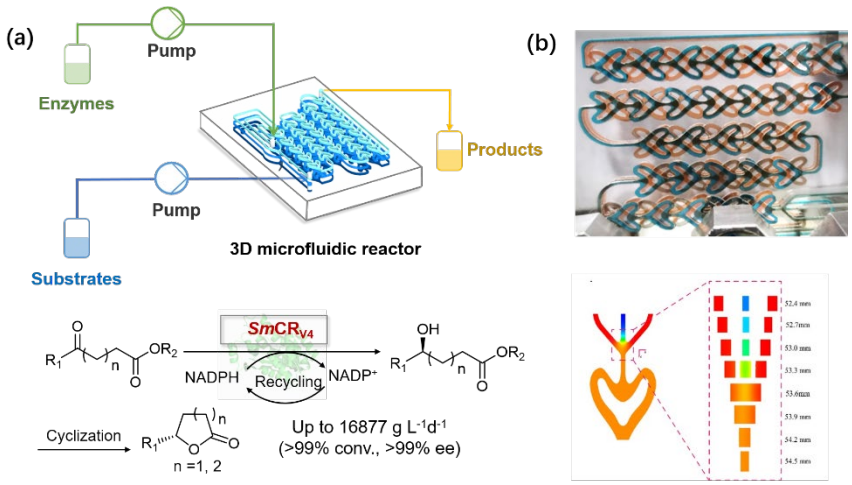

Figure 2–Continuous-flow synthesis of chiral lactones via 3D microfluidic reactors