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Bio-catalytic mesoporous Janus nano-motors powered by catalase enzyme

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ABSTRACT

Enzyme triggered bio-catalytic reactions convert chemical energy into mechanical force to power micro/nano-machines. Though there have been reports about enzymes powered micro/nano-motors, enzymatic Janus nano-motor smaller than 100 nm has not been reported yet. Here, we prepared an enzyme powered Janus nano-motor by half-capping a thin layer of silicon dioxide (4 nm SiO_2) onto a mesoporous silica nanoparticle (MSNP) of 90 nm, enabling asymmetry to the nano-architecture. The nano-motors are chemically powered by the decomposition of H_2O_2 triggered by the enzyme catalase located at one face of the nanoparticles. The self-propulsion is characterized by dynamic light scattering (DLS) and optical microscopy. The apparent diffusion coefficient was enhanced by 150% compared to their Brownian motion at low H_2O_2 concentration (*i.e.* below 3 wt%). Mesoporous nano-motors might serve as active drug delivery nano-systems in future biomedical applications such as intracellular drug delivery.

Since the pioneering work from Feringa and co-workers on the use of enzyme catalysis to power nanostructures,[1] the field has received increasing attention due to its potential as active drug carriers using biocompatible fuels.[2] Catalytic micro- and nano-devices are autonomous self-propelled particles with interesting capabilities in fields ranging from biosensing, cargo transport, crack repair and environmental fields.[3,4] After a steep development of catalytic micro- and nanomotors since a decade ago, some challenges have appeared such as the search of fuels (chemical substrate for triggering the propulsion) which are more bio-friendly than the typical hydrogen peroxide used for the propulsion of those tiny vehicles. In order to gain versatility in the fuel-catalyst couple, enzymes are presented as excellent alternatives. Feringa and co-workers demonstrated the tandem glucose oxidase and catalase which, upon addition of glucose to the media, generated oxygen bubbles that in turn propelled bundle of carbon nanotubes.[1] Mano and Heller powered a carbon fiber with glucose oxidase and bilirubin oxidase, which moved at the air-liquid interface.[5] Sanchez et al. coupled catalase to the inner wall of a microtubular structure, where oxygen bubbles generated and released from the interior of the tube pushed the micro-tube forward.[6]

In virtue of unique mesoporous structure, good biocompatibility, and easy surface functionalization properties, MSNPs have been regarded as ideal carrier for drug delivery,[7–9] and multifunctional MSNPs have been designed and studied as a useful theranostic platform.[10] For instance, MSNP were employed for targeted drug delivery both *in vitro* and *in vivo*. By combination with other theranostic techniques, such as photothermal therapy and photodynamic therapy, multifunctional theranostic platform based on MSNP have been developed as well.[7, 11]Therefore, the combination between mesoporous silica and enzyme-fuel provides a promising candidate for active nano-system for drug delivery. Our group recently reported the fabrication of enzyme based micro- and nanomotors using mesoporous silica micro- and nanoparticles as chassis.[12–14] There have been other reports using enzymes to power solid micro-size particles,[15,16] supramolecular stomatocytes,[17] as well as metallic nano-rods,[18] which successfully used biocompatible fuel to power the micro/nano-motors. However, the

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miniaturization of enzyme-nanomotors below 100 nm has not been achieved so far, which is an ideal size for nanoparticles to be used in drug delivery systems.

Hereby, we present the design and fabrication of a bio-catalytic Janus mesoporous silica nano-motor as shown in Fig. 1. We first prepared the MSNPs with an average diameter of 90 nm by sol-gel chemistry. Then, two-step surface chemistry process was carried out to modify external surface of the MSNPs with amine groups which were further converted to carboxylic groups (-COOH), noted as MSNP-COOH (See experimental details in the Supporting Information (SI)). A monolayer of MSNP-COOH was prepared before depositing the thin layer of SiO_2 to produce Janus structure by E-beam deposition. After releasing the Janus nanoparticles from the substrate, enzyme catalase was immobilized onto the uncovered surface of the Janus MSNP to produce the enzymatic mesoporous nano-motors. Up to our knowledge, this is the first report on the versatile use of Janus nano-motors with size smaller than 100 nm (and mesoporous in particular) for bio-catalytic propulsion, named as Janus mesoporous silica nano-motors (JMSNM). Considering the small size and drug loading capability, such mesoporous silica nano-motor will be able to serve as active drug delivery vehicles that are advantageous for future biomedical applications *in vitro* and *in vivo*.

In previous reports, it was claimed that enzyme driven MNM provide higher efficiency than Pt metal and could power micro/nano-motors at low H_2O_2 concentration.[6] Here, catalase was conjugated onto the JMNSPs to replace the Pt and acted as bio-catalyst to trigger decomposition of H_2O_2. The MSNPs were initially functionalized with carboxylic group (−COOH) by a two-step methods according to previous reports.[19] The functionalization process was traced by both FT-IR spectra and zeta-potential measurements. The new peak at 1520 cm^{-1} indicated successfully modifying MSNP with primary amine (-NH_2) (Fig. 2a). And then, 1726 cm^{-1} from −COOH groups and 1560 cm^{-1} from secondary amine (−NH-) in amide bond clearly evidenced the presence of −COOH. Initially, the zeta-potential value of bare MSNP was −36.3 ± 4.06 mV which was reversed into positive value of 38.8 ± 3.04 mV for MSNP-NH_2 due to protonation of −NH_2 in DI H_2O. Then, after converting -NH_2 into −COOH, zeta-potential value again changed into negative value of −48.4 ± 3.83 mV (Fig. 2b). In this study, MSNP with average diameter of 90 nm was chosen for catalase conjugation. A monolayer of the obtained MSNP-COOH was prepared on glass slide according to the method described earlier.[12,20] From Fig. 2c, a uniform monolayer of MSNP-COOH without any nanoparticle stacking was observed, suggesting that the surface functionalization process did not bring any unwanted aggregations.

In this particular strategy, a thin layer of the same material SiO_2 (4 nm) was deposited onto one side of the MSNP(90 nm)-COOH, producing Janus structure. From the TEM image, smooth silica coating layer indicated by red arrows on half side of the JMSNP(90 nm)-COOH@SiO_2(4 nm) is clearly observed. The silica coated side appears smoother edge than the non-coated side bearing nano-roughness given by the mesoporous structure of the MSNPs (Fig. 2d). Furthermore, after E-beam deposition, the −COOH groups would be completely capped at the silica coated side, while

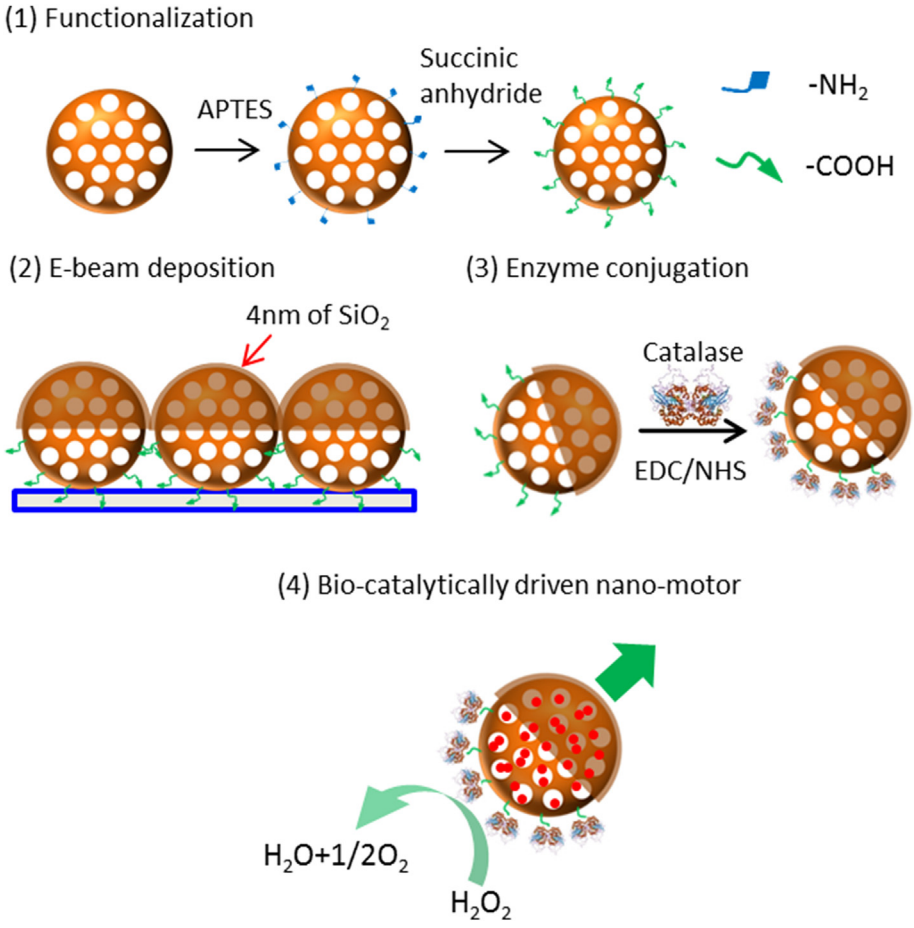

Fig. 1. Schematic illustration of fabrication of bio-catalytic Janus mesoporous silica nano-motors (JMSNM).