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Supporting Information

Bacteria-activated photodynamic nanosystem based on polyelectrolyte-coated silica nanoparticles

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Computer simulation

Computer simulation was conducted with GROMACS4.6.4 package.[1] We used CHARMM force field for lipids and TIP3P water model in our simulations.[2,3] The initial bacterial membrane model (pre-equilibrated) was constructed by the CHARMM-GUI membrane Builder.[4] Two types of phospholipids, palmitoyloleoylphosphatidylethanolamine (POPE) and palmitoyloleoylphosphatidylglycerol (POPG), were used in our simulation. The POPE and POPG are representative lipids that are commonly found in bacterial membrane. Following previous studies, the number of POPE and POPG are 258 and 86, respectively. The molar mixture ratio of 3:1 of POPE-POPG lipids is biological relevant and the lipopolysaccharides were omitted for simplicity.[5] For SiO_2 NPs, the particles used in our experiment have diameters around 70 nm, which is reasonably modelled as a slab surface with size of about 9.869 nm × 9.869 nm (the cross-section of simulation box in the *x-y* plane). The amorphous silica surface model developed by K. Schulten *et al*. was used,[6] which was parameterized based on the macroscopic wetting properties and was compatible with CHARMM and TIP3P. The atomic charges of Si and O atoms are 1.0 |e| and -0.5 |e|, recpectively, which can well reproduce the water contact angle observed experimentally.[7] The SiO_2 slab has a thickness of 2.7 nm. Following their study, the silica atoms were restrained to their original position by applying a harmonic force with a force constant of 1 kcal/mol/Å to keep the amorphous SiO_2 slab rigid. The topology of PAH was calculated using the R. E. D. server and adjusted to be in CHARMM format.[8] One PAH chain contains ten (allylamine hydrochloride) units (a decamer) with amidogens from three of them are protonated. Thirty decamers have been added to the water slab between bacteria and SiO_2 NPs surface. Periodic boundary conditions were applied in all directions of the simulation box. Constant temperature (at 300 K) was maintained by the velocity-rescale thermostat with a coupling coefficient of τ_T = 0.1 ps.[40] The *z* direction of the water box (normal direction of membrane and SiO_2 slab) is coupled at constant pressure at 1 bar by the Berendsen scheme with a coupling coefficient of τ_P = 1 ps. The Particle Mesh Ewald (PME) method was used to treat the long-range electrostatic interactions,[9] whereas the van der Waals interactions were handled with a cutoff distance of 1.2 nm. The bond length involving hydrogen atoms were constrained with LINCS algorithm.[10]

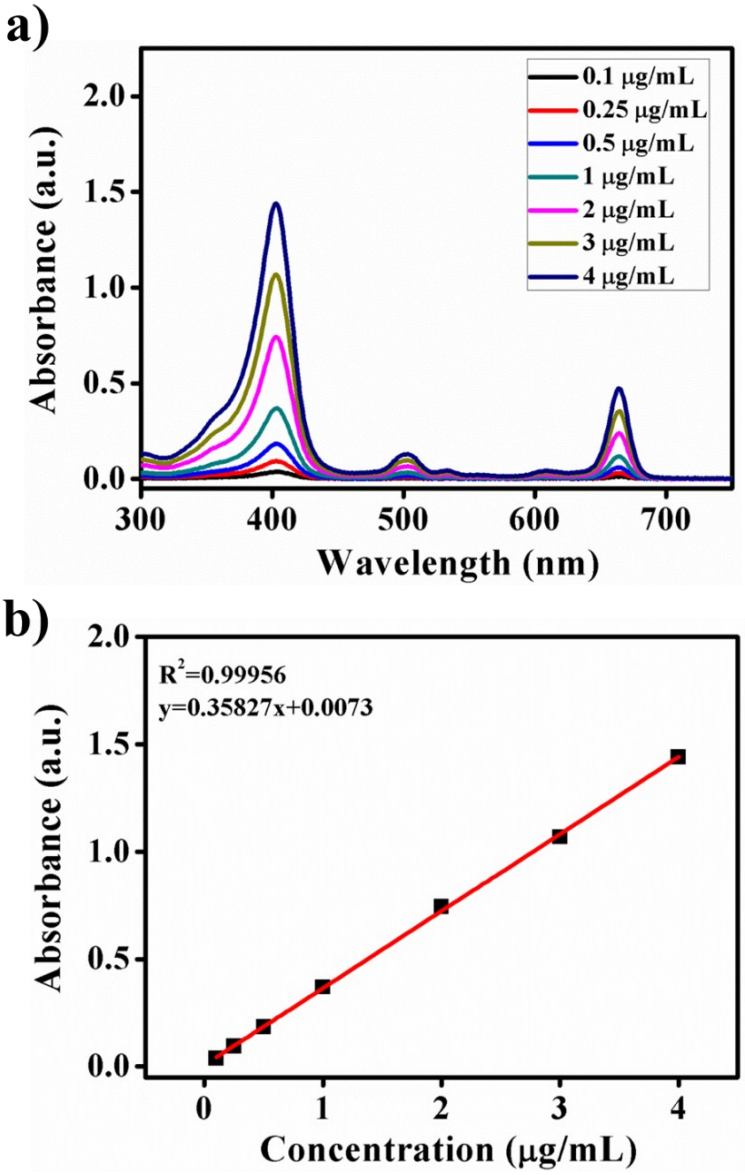

Fig. S1 a) Absorption spectra of Ce6 with different concentrations ranged from 0.1 to 4 μg/mL. b) The linear calibration curve between Ce6 concentration and its absorbance.

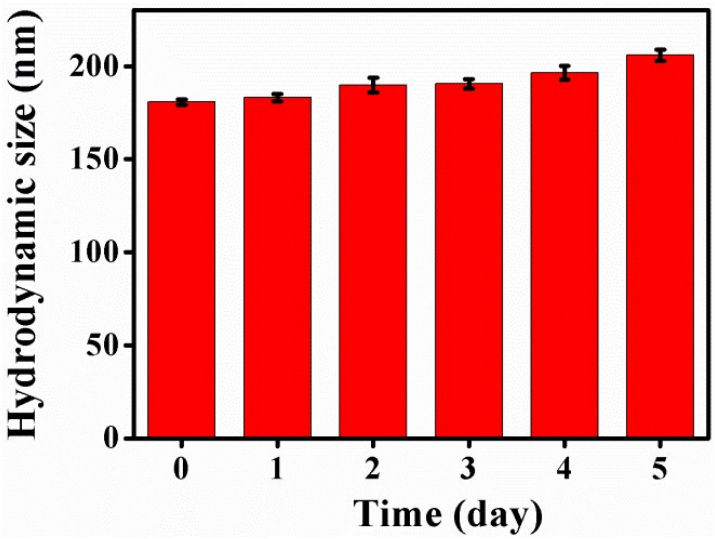

Fig. S2 Hydrodynamic diameters of the SiO_2/PAH-Ce6 nanosystem in PBS during 5 days storage.

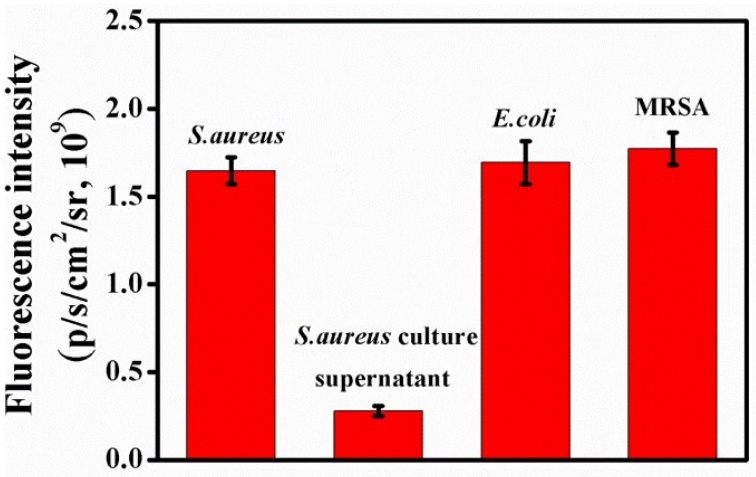

Fig. S3 The corresponding fluorescence intensities of the images shown in Figure 3a.

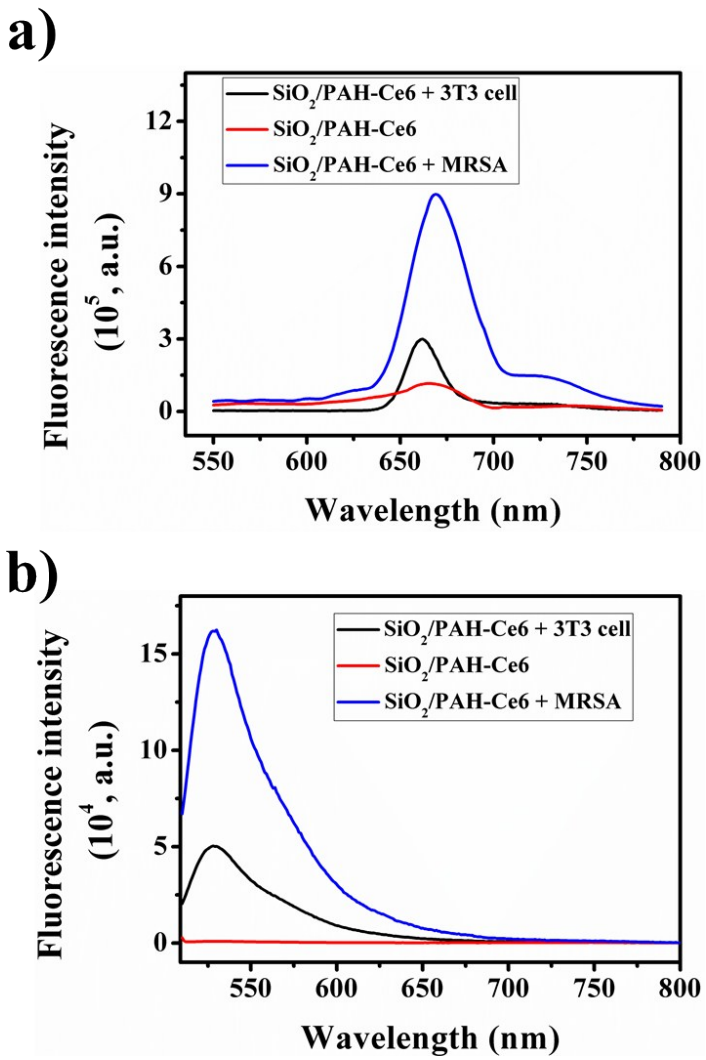

Fig. S4 The comparison of the fluorescence (a) and $^1O_2$ generation (b) of the SiO_2/PAH-Ce6 nanosystem before and after incubation with normal mammalian cells (NIH-3T3, 10^6) and MRSA (10^7 CFU), respectively. 10 μM of SOSG was used to quantify the level of $^1O_2$ generated. In the experiments, SiO_2/PAH-Ce6 conjugated with 166 μg/mL of Ce6 was used, but the final concentration of Ce6 in the mixtures was fixed at 3.3 μg/mL.

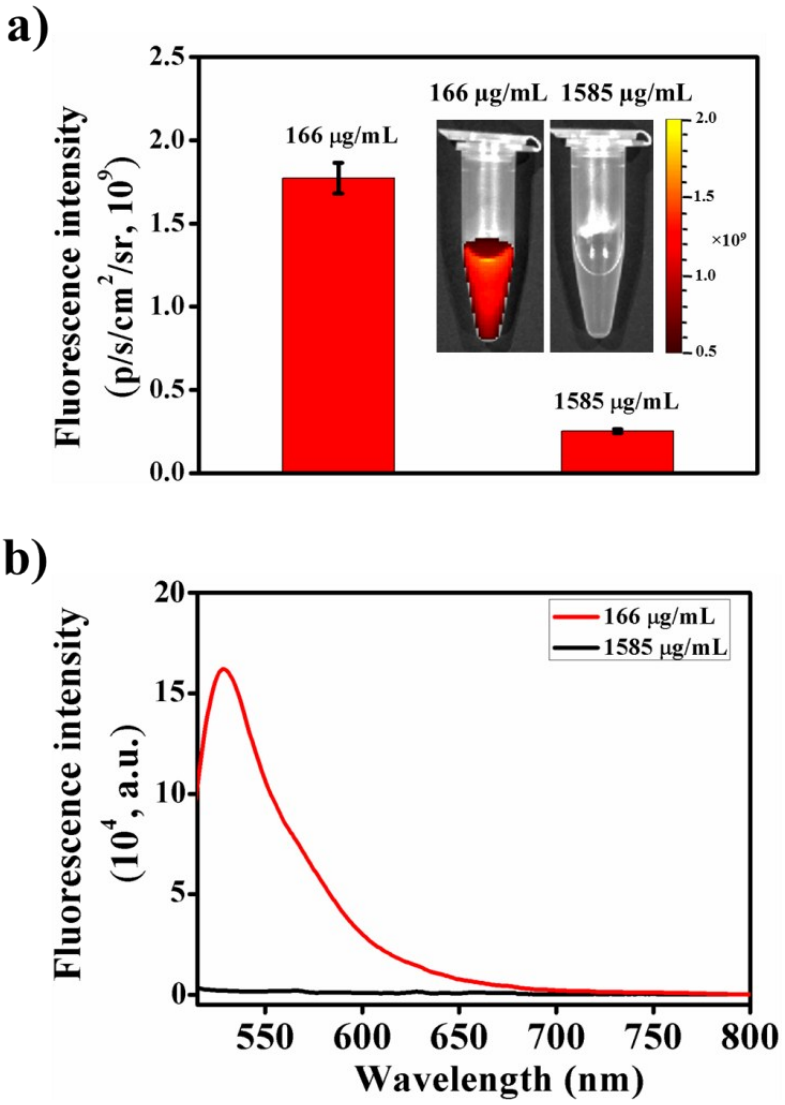

Fig. S5 Evaluation of the effect of loaded Ce6 concentration in the SiO_2/PAH-Ce6 nanosystem on the bacteria-activated fluorescence (a) and $^1O_2$ generation (b). 10^7 CFU *S. aureus* was used to activate the SiO_2/PAH-Ce6 nanosystem, and 10 μM of SOSG was used to quantify the level of $^1O_2$ generated. In the experiments, SiO_2/PAH-Ce6 conjugated with two different concentrations of Ce6 (166 and 1585 μg/mL) were used, but the final concentrations of Ce6 in the mixtures were all fixed at 3.3 μg/mL.

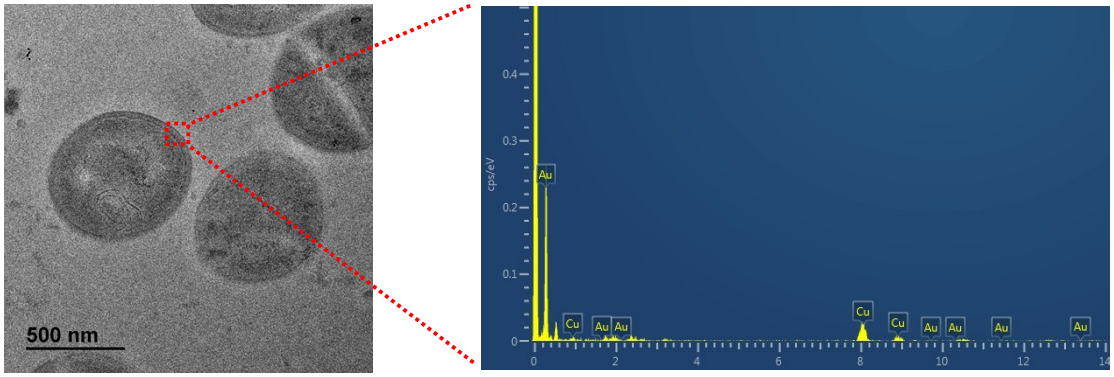

Fig. S6 Representative TEM image and corresponding EDX spectrum of MRSA cell without SiO_2/PAH-Ce6-AuNCs nanoparticles adherence. After incubation with the SiO_2/PAH-Ce6-AuNCs nanosystem for 4 h, MRSA cells (10^7 CFU) was purified by low-speed centrifugation (4000 rpm), dehydrated, and applied for TEM observation and EDX scan. In the experiments, SiO_2/PAH-Ce6-AuNCs conjugated with 166 μg/mL of Ce6 was used, but the final concentration of Ce6 in the mixtures was fixed at 3.3 μg/mL.

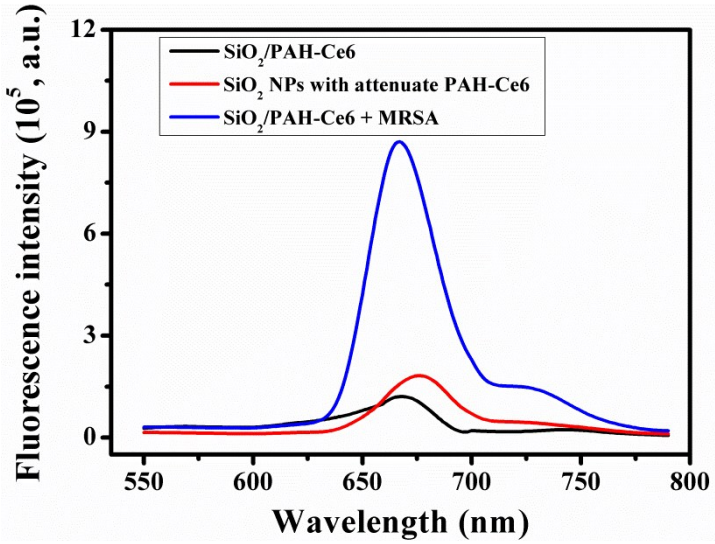

Fig. S7 The comparison of the fluorescence of the SiO_2/PAH-Ce6, the SiO_2 NPs with attenuate PAH-Ce6, and the SiO_2/PAH-Ce6 solutions upon MRSA (10^7 CFU) activation. In the experiments, SiO_2/PAH-Ce6 conjugated with 166 μg/mL of Ce6 was used, but the final concentration of Ce6 in the solutions was fixed at 3.3 μg/mL.

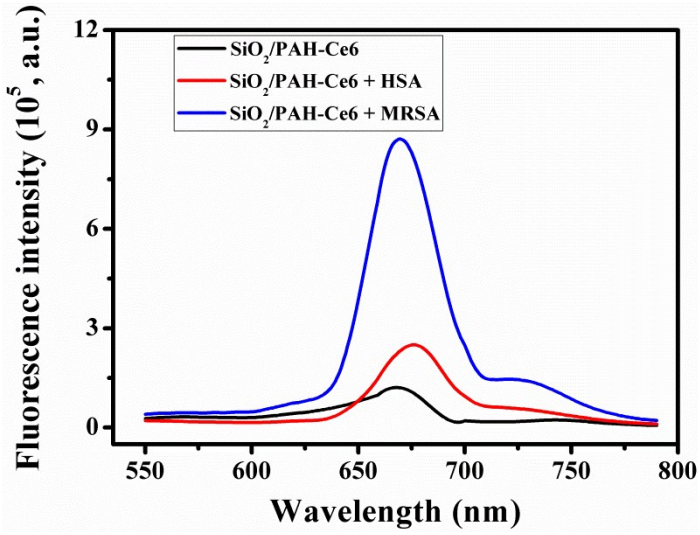

Fig. S8 The comparison of the fluorescence of the SiO_2/PAH-Ce6 nanosystem before and after incubation with human serum albumin (HSA, 10% in PBS) and MRSA (10^7 CFU), respectively. In the experiments, SiO_2/PAH-Ce6 conjugated with 166 μg/mL of Ce6 was used, but the final concentration of Ce6 in the mixtures was fixed at 3.3 μg/mL.

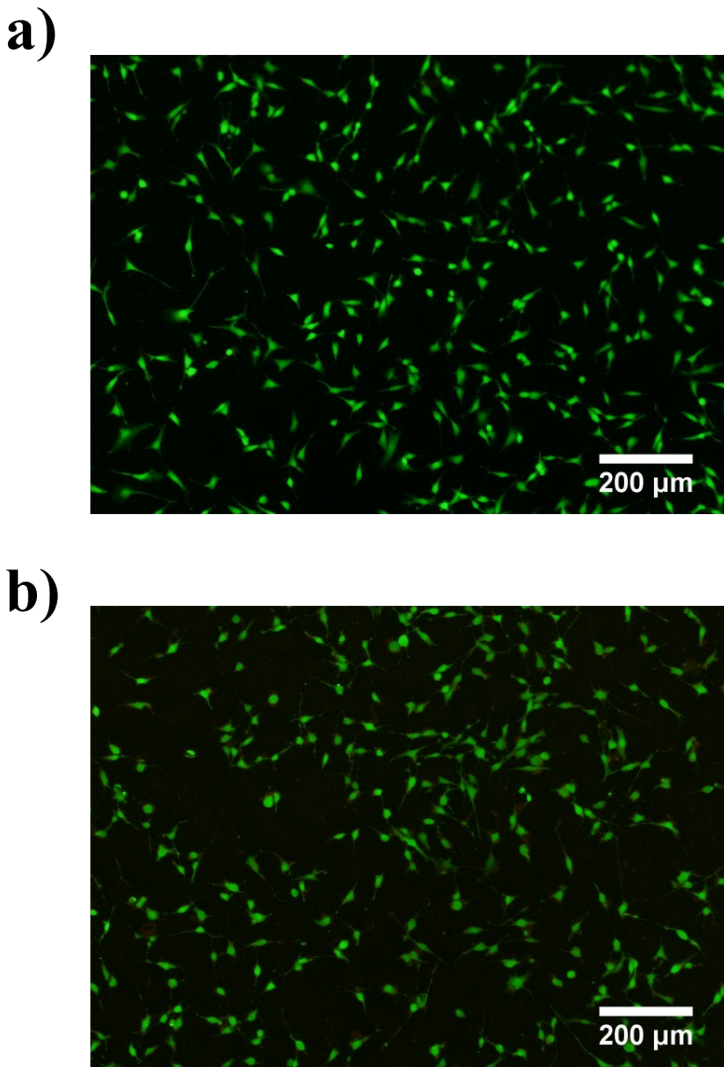

Fig. S9 The live/dead staining images for NIH-3T3 cells before (a) and after incubation with SiO2/PAH-Ce6 nanosystem and laser (660 nm, 0.8 W/cm^2) irradiation for 10 min (b). In the experiments, SiO_2/PAH-Ce6 conjugated with 166 μg/mL of Ce6 was used, but the final concentration of Ce6 in the mixtures was fixed at 3.3 μg/mL.

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