

## Supplementary Information

### “Self-repairing” nanoshell for cell protection

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## Experimental Section

**Cell culture.** *Saccharomyces cerevisiae*, purchased from China Center of Industrial Culture Collection, were picked from a yeast-extract-peptone-dextrose (YPD) broth agar plate and cultivated in the YPD broth in a shaking incubator at 30°C for 12h. *Synechococcus* cells, stain 7942, purchased from Freshwater Algae Culture Collection at the Institute of Hydrobiology, were cultivated in culture flasks with BG11 medium at 22-24°C, and subjected to illumination by fluorescent lamps of 1000 Lx and transferred into fresh media on a half-monthly basis.

**Preparation for biohybrid solution.** The synthesis of 2-3 nm Au nanoparticles was performed via reduction of Chloroauric acid. To summarize,  $2.5 \times 10^{-4}$  M chloroauric acid and trisodium citrate were mixed in a flask, followed by the addition of 0.1M sodium borohydride. The colloid was preserved at room temperature. 0.15 g L-cysteine powder was added to 90 ml Au colloid under continuously stirring condition. Biohybrid nanoparticles were collected by centrifugation (10000 rpm, 50 min). The resulting biohybrid aggregations were freeze-dried in vacuum overnight to obtain power for characterizations. For preparation of Au@PAH (poly allyamine hydrochloride) and Au@PLL (polyL-lysine) aggregates, the 0.025g PAH and PLL were added to 15mL Au solution, respectively. For synthesis of Au@L-lysine and Au@glutathione biohybrid solutions, 90 ml Au colloid was added into lysine solution and glutathione solution, respectively.

**Cell encapsulation.** Cells were harvested by centrifugation at 5000 rpm for 20 min and washed with aqueous PBS solution to get rid of excessive medium. Then the cells were immersed in the biohybrid solution and gently mixed at room temperature for 30 min. After mixing step, the cells were collected by centrifugation (4000 rpm, 15 min) and re-dispersed in medium and incubated under ambient conditions. For encapsulation of yeast cells within PAH/PSS@Au shell, PAH and PSS were dissolved in PBS solution. The cells were immersed in the PAH and PSS solution and incubated for 15 min, respectively. Subsequently, the coated cells were introduced into 15 mL Au colloid for half an hour. For the synthesis of yeast@PDADMA(poly(diallyldimethylammonium chloride))/PSS(polystyrene sulfonate)@SiO<sub>2</sub>, yeast cells were alternately added in the PDADMA solution (5mg/ml) and the PSS solution (5mg/ml) for 5 min for each step. Then, the coated-cells were placed in the 50mM silicic acid solution. For the preparation of L-cysteine coated cells, yeast cells are added into L-cysteine solution (0.05g L-cysteine in 30ml PBS) under ambient conditions.

**Characterization.** SEM, EDX and TEM studies were conducted with S-4800 (HITACHI, Japan) and JEM2100F (JEOL, Japan), respectively. The samples were first collected by centrifugation and washed with distilled water for three times. The biological samples were dropped onto specimen stage and dried. The ultrathin section samples were fixed with glutaraldehyde, OsO<sub>4</sub>, and dehydrated in acetone. They were embedded in Epon 812/ Araldite M resin. Thin sections (ca. 100nm) were cut by using ULTRACUT UCT ultramicrotome (Leica, Germany) and characterized

by TEM (Tecnai, Netherlands). Zeta potentials were measured by the electrophoretic mobility of particles/cells in an electric field (Ankersmid, Netherlands). Samples were diluted with PBS solution. The morphologies of cells were characterized by Optical microscopy (OM) (Fluorescence microscope (Olympus, Japan) in an optical-light mode). The FTIR was performed with a Bruker Vertex 80V FT-IR spectrometer. X-ray Photoelectron Spectroscopy (XPS) was obtained with VG Multilab 2000, USA. UV-vis spectrum was carried out with UV-2550 Shimadzu, Japan.

**The UVC-radiation experiment of native yeast cells, yeast@biohybrid shell.** Yeast cells were picked from YPD medium and washed with sterilized PBS solution, followed by re-dispersing into PBS solution. Yeast solution was divided into two parts: one part was used to prepare sample of yeast@biohybrid shell and the other part was the sample of native yeast cells. Samples of yeast@biohybrid shell were added into fresh YPD medium and PBS solution (as the normal solution without medium), respectively. Samples of native yeast were also added into fresh YPD medium and PBS solution, respectively. Each sample was cultivated in fresh medium under 15-W ultraviolet light. The activity of yeast cells was taken by plate count method. Samples were taken from the solution and diluted with sterilized water until the number of colonies on plates was between 30-300. The activity of yeast cells was taken by counting the number of colonies on each plate. In order to mitigate the effect of biological variability, three technical replicates were performed for each experiment. Each biological replicate was treated independently with the same procedure.

**The UVC-radiation experiment of yeast cells within silica.** Samples of yeast cells within silica were washed and re-dispersed in PBS solution. Subsequently they were exposed under ultraviolet light and tested by plate count method.

**Cell division characterization.** The mother cells were collected in the stationary phases and then transferred into fresh media and cultivated in a shaking incubator at 30°C under ambient conditions. Samples of were characterized by SEM every 2 hours after inoculation while samples of cyanobacteria were observed every 3 days.

**The test of cell growing before and after encapsulation.** Both of yeast cells and encapsulated yeast cells were cultivated in 50ml fresh YPD media and the activities of cells were measured every 2 hours at 600 nm by UV-visible spectroscopy.

**Yeast cells on biohybrid aggregations-coated surfaces and mixed in biohybrid solution.** Biohybrid aggregations-coated surfaces were prepared by a spin-coated method. The silicon substrates were firstly washed by methylbenzene, acetone, a mixture of concentrated sulfuric acid

and hydrogen peroxide and water, dried by nitrogen. Subsequently, a drop of biohybrid precursors are added onto silicon substrate and uniformly coated on silicon surface by spin coater. Biohybrid solution is prepared by adding biohybrid precursors into 10ml PBS solution. Yeast cells were harvested by centrifugation at 4000 rpm for 20 min and washed with aqueous PBS solution. The precipitates were re-dispersed into 1ml PBS solution and divided into same two parts. One part was dropped onto biohybrid aggregation coated-surfaces and the other part was mixed with biohybrid solution. Samples were observed by SEM techniques.

**Relative concentrations of lyticase in biohybrids.** 0.1 ml diluted lyticase was added into biohybrid solution. The concentrations of residual lyticase were tested by standard Bradford protein assay every one hour.

**Cell-lysis tests.** A single colony of yeast cells were picked up from YPD broth agar plate and cultured in a shaking incubator at 30°C. Both the native and encapsulated cells were collected and washed with 0.85% NaCl solution. The stock solution was prepared by dissolving lyticase powder (~3.8mg,  $\geq 2,000$  units/mg protein, from *Arthrobacter luteus*) in a mixture of glycerol and TRIS-EDTA (TE) buffer solution (pH 7.5). The 10  $\mu$ L of the stock solution was added to the mixture of cells (2mL) and kept in a shaking incubator at 37 °C. The activities of cells were measured at 600 nm by UV-visible spectroscopy. The morphologies of cells were characterized by optical microscopy (Fluorescence microscope (Olympus, Japan) in an optical-light mode).

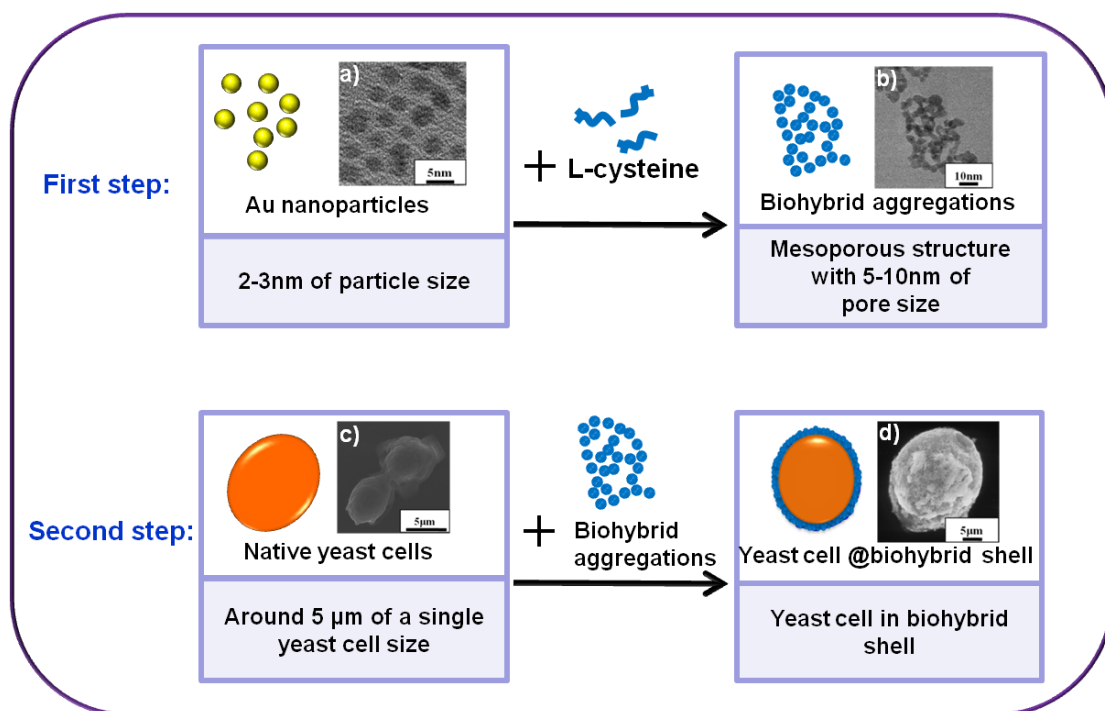
**High light, acid-base change experiment and UVC radiation of cyanobacteria experiment.** Experiments were carried out by Oxygen Lab (Hansatech, UK) that both of the encapsulated cells and native cells were monitored by measuring the rate of oxygen production. For high light experiment, both of encapsulated cyanobacteria and the native cyanobacteria were kept under illumination by fluorescent lamps of 2000 Lx. The data of oxygen production were obtained from Rate Measurement Window which is automatically generated by the Get Rate function. To test the viability of cyanobacteria in different pH value solutions, samples were treated for 1 hour in solutions with different value. For UVC radiation testing, each sample of cyanobacteria without capping was exposure under 70-W UVC ultraviolet light and the data for the activity was obtained by using Oxygen Lab.

**Supplementary Table S1** Relative concentrations of lyticase in the presence of biohybrid aggregations.

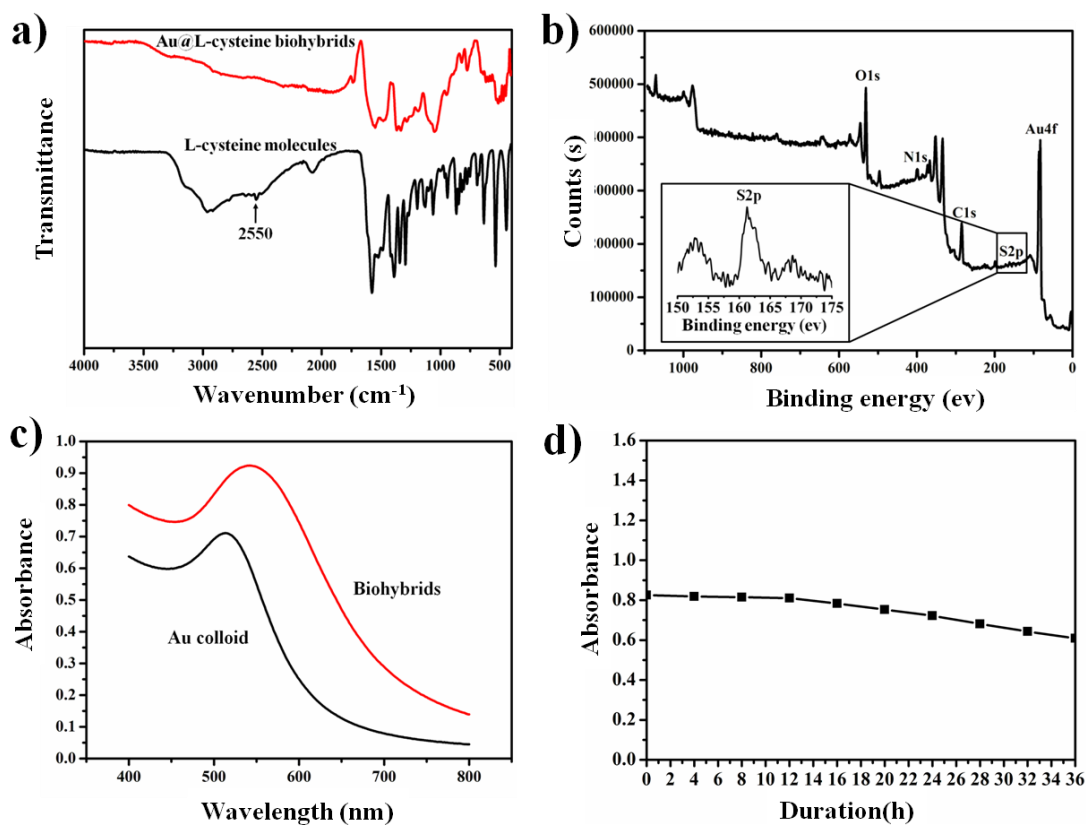
Time	0h	1h	2h	3h
Relative concentration	100%	76%	58%	56%

**Supplementary Table S2** Zeta potentials of native yeast cells, native cyanobacteria, biohybrids, yeast@biohybrid shell and cyanobacteria@biohybrid shell.

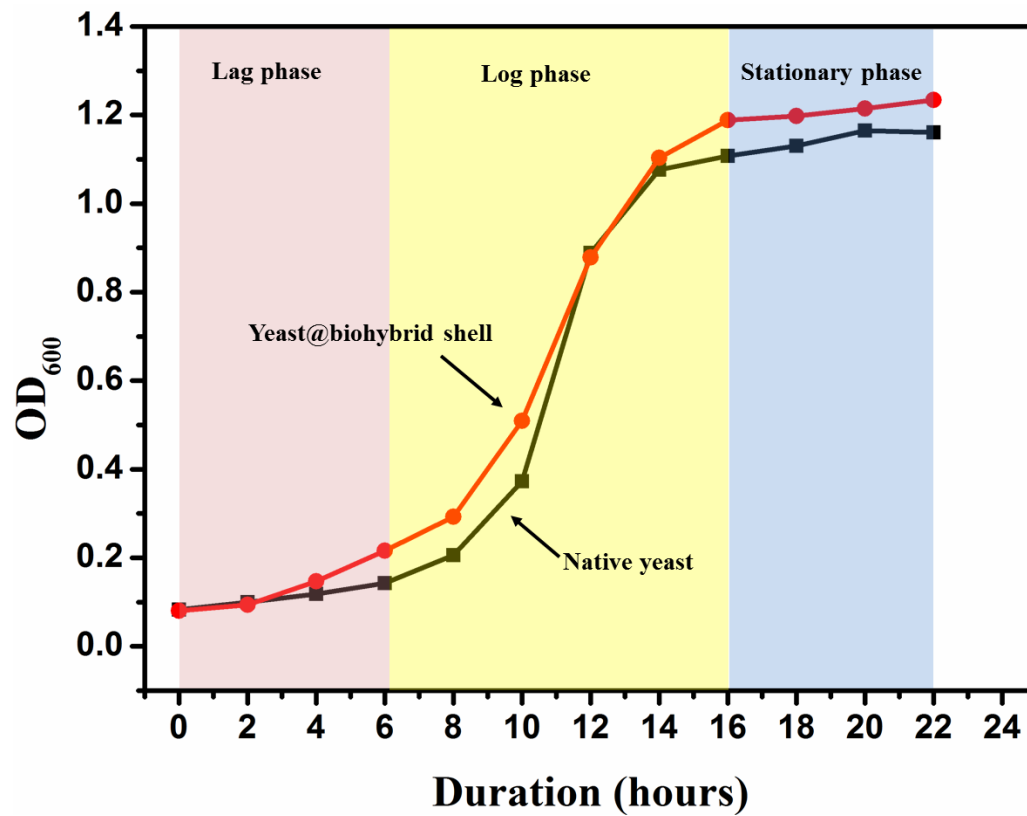
Sample	Yeast cells	Cyanobacteria	Biohybrids	Yeast@biohybrid shell	Cyanobacteria@biohy brid shell
Zeta potential	-17.1 ±1.2mV	-14.2±0.8 mV	-19.3±0.7mV	-18.5 ±1.5 mV	-16.4±1.4 mV



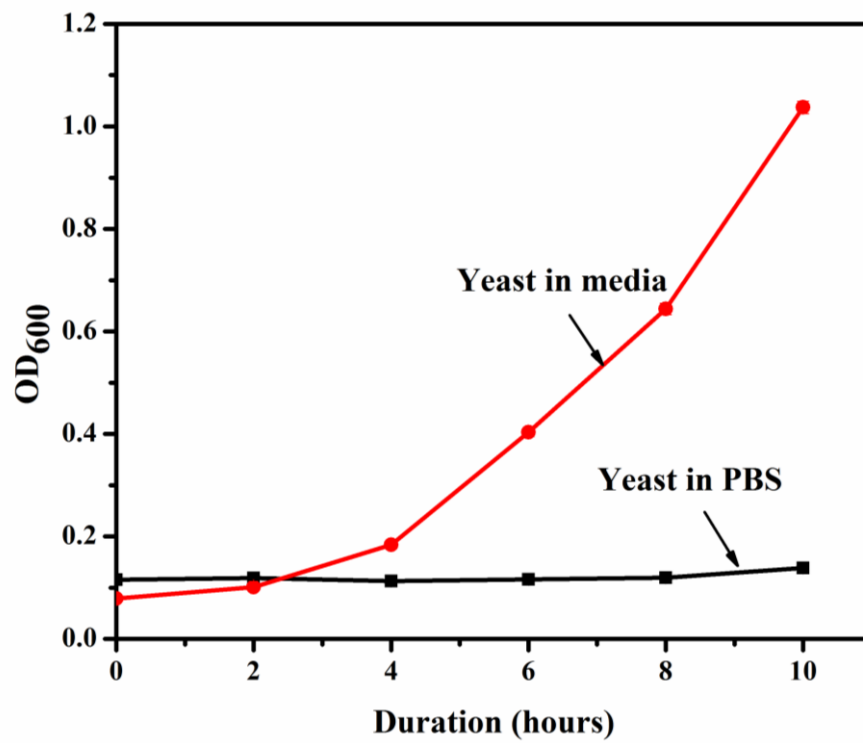
**Supplementary Figure S1** Schematic illustrating formation of biohybrid shell on yeast cell surface. Procedures for biohybrid shells encapsulation of individual yeast cells: a) TEM micrograph of monodispersed crystalline Au nanoparticles; b) TEM micrograph of biohybrid aggregations; c) SEM micrograph of native yeast cells; d) SEM micrograph of yeast cell@biohybrid shell.



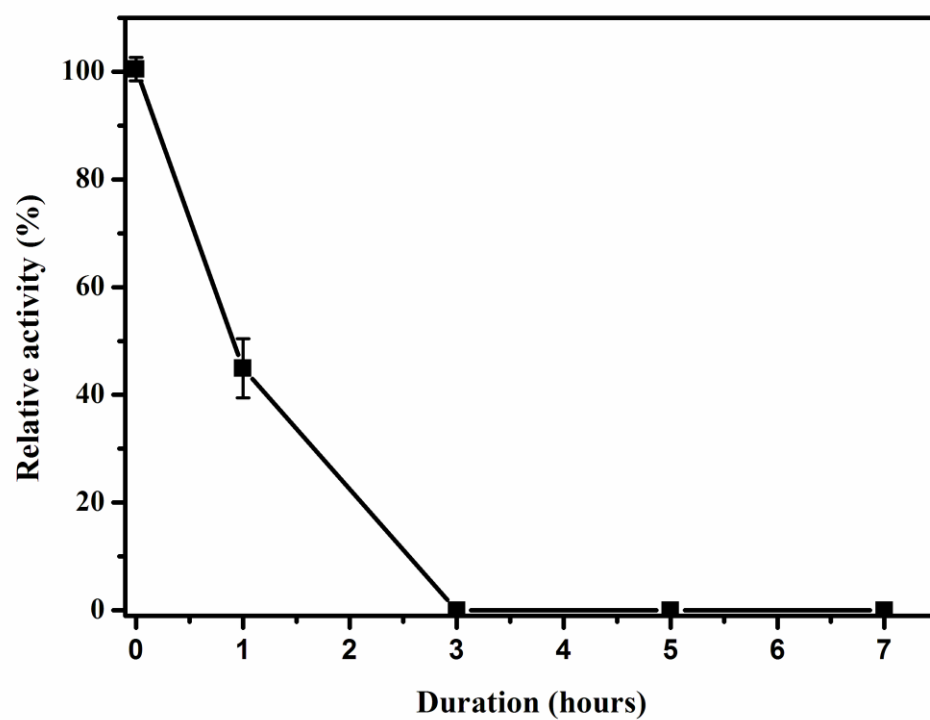
**Supplementary Figure S2** a) FTIR spectra of biohybrids (top) and L-cysteine (bottom; b) XPS spectrum of biohybrids and the narrow scan of S 2p (inset) with a binding energy of 162 eV; c) UV-vis spectra of Au colloid (bottom) and biohybrids (top) and d) the stability of biohybrids.



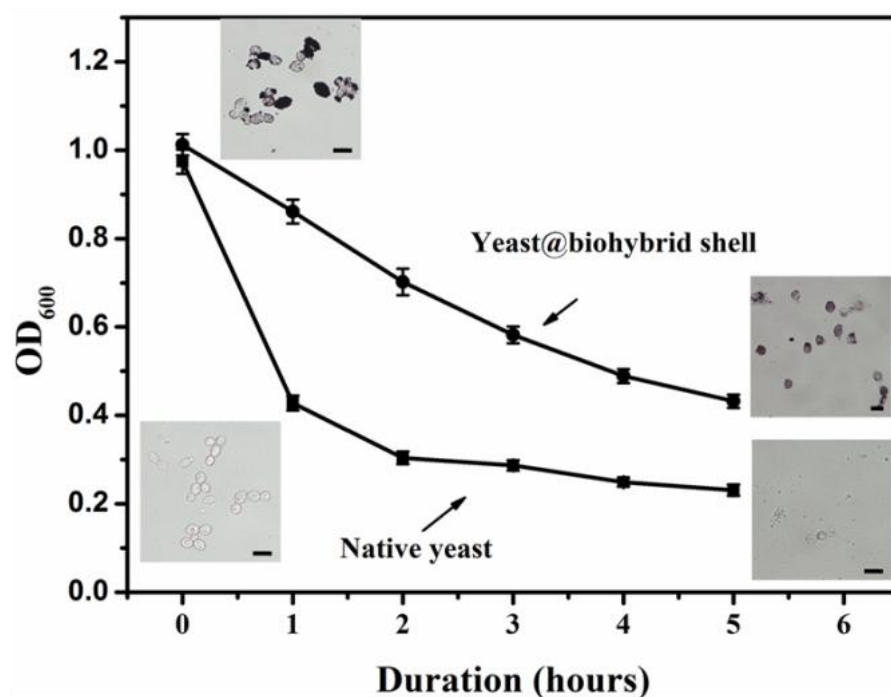
**Supplementary Figure S3** Growth curve of yeast@biohybrid shell (red) and native yeast cells (black). Three phases of cell growth are distinguished by shadows.



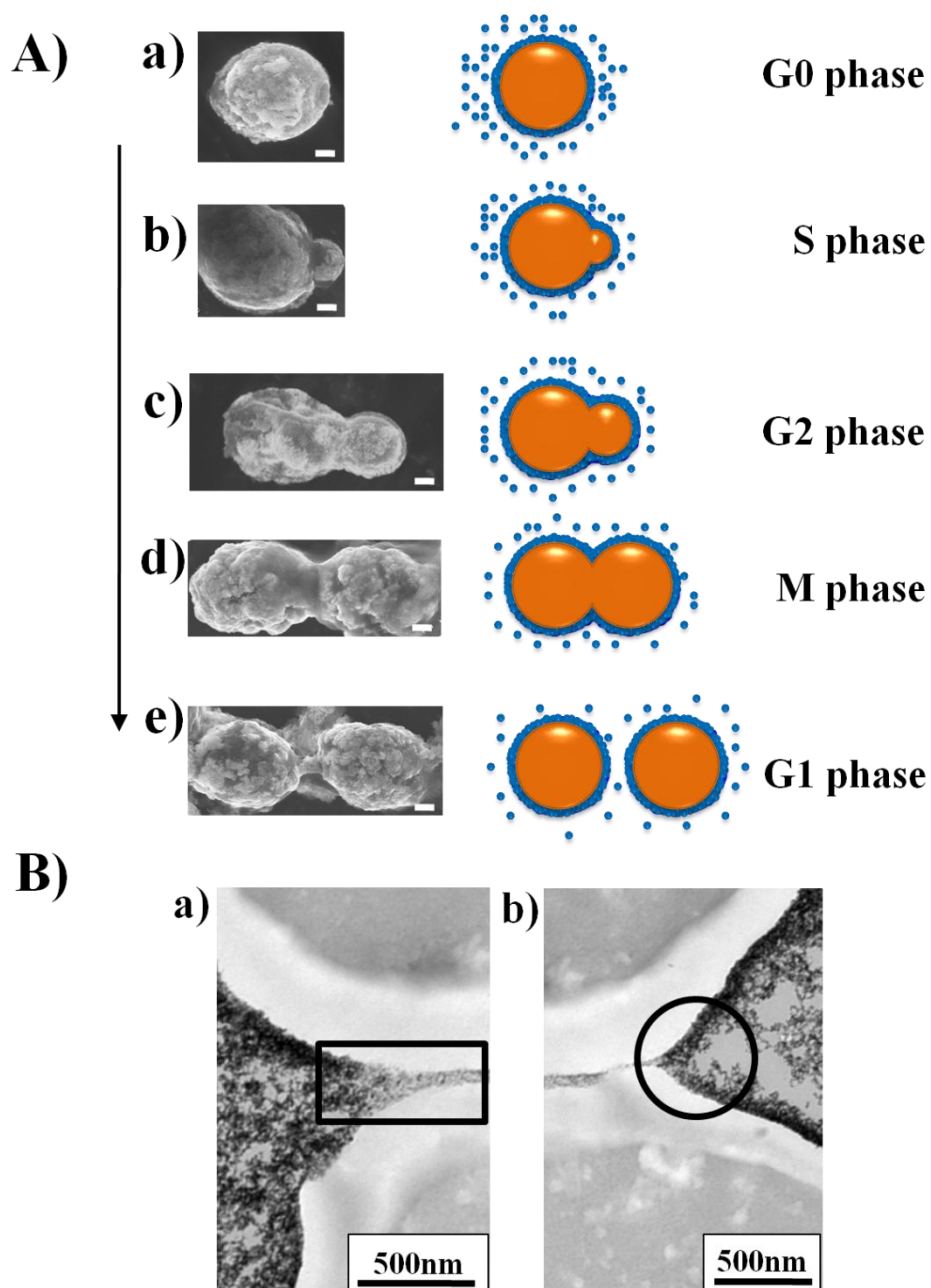
**Supplementary Figure S4** Growth curve of native yeast cells in fresh media (red) to keep their ability to proliferate and in PBS (black) to retard their proliferation.



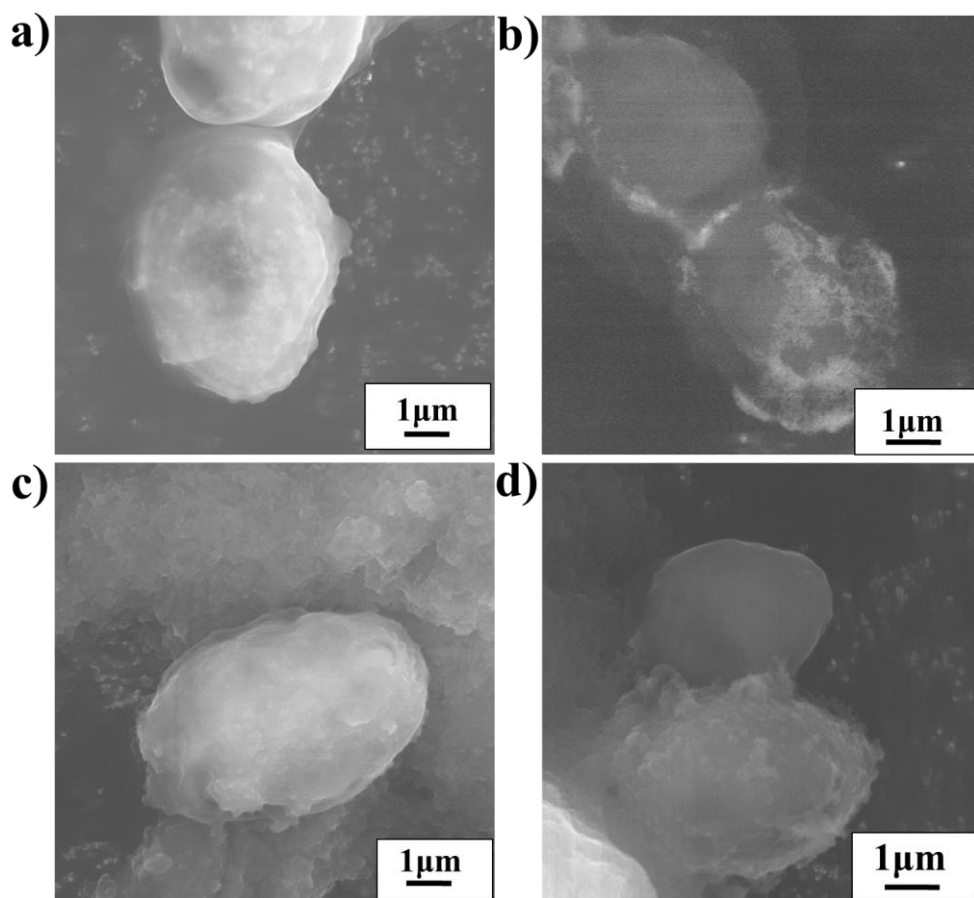
**Supplementary Figure S5** Relative activities by yeast cells within silica under UVC radiation.



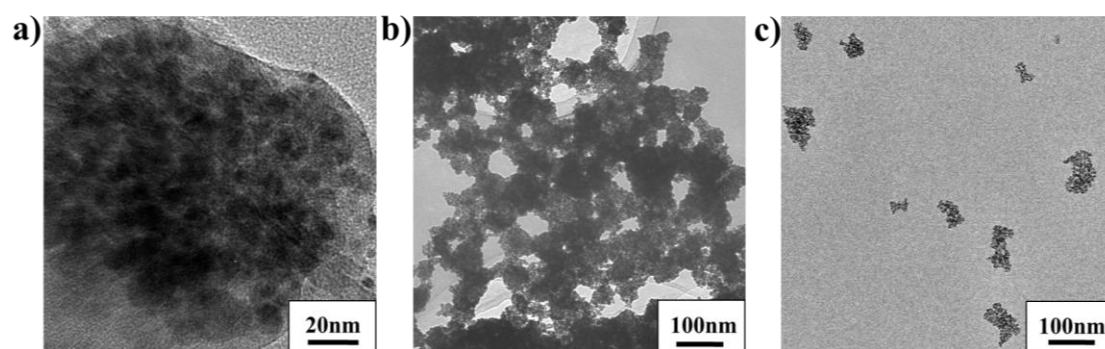
**Supplementary Figure S6** Relative activities by yeast@biohybrid shell (square) and native yeast (circle) in the presence of lyticase (Insets are the corresponding optical images on 0 hour and 5 hour. Scale bar: 8μm).



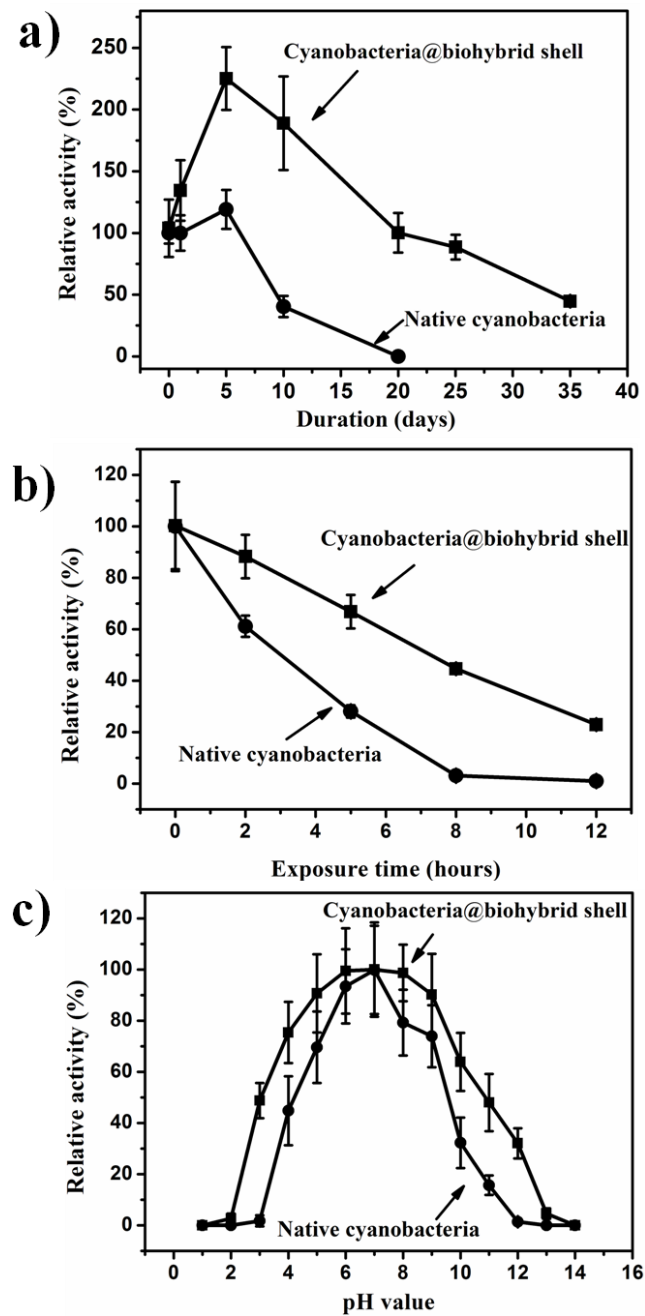
**Supplementary Figure S7** A) Process of self-encapsulating biohybrid nanoshell in yeast cell division. Left line: SEM micrographs. (Scale bar: 1 $\mu$ m) Right line: corresponding schemes (blue spheres represent biohybrid aggregations); B) TEM micrographs of encapsulated yeast cells on both sides during yeast cell division. Biohybrid aggregations are densely packed on a) interfaces between the mother cell and the daughter cell (square) once the bud begins to leave the mother cell and b) cell surface (circle).



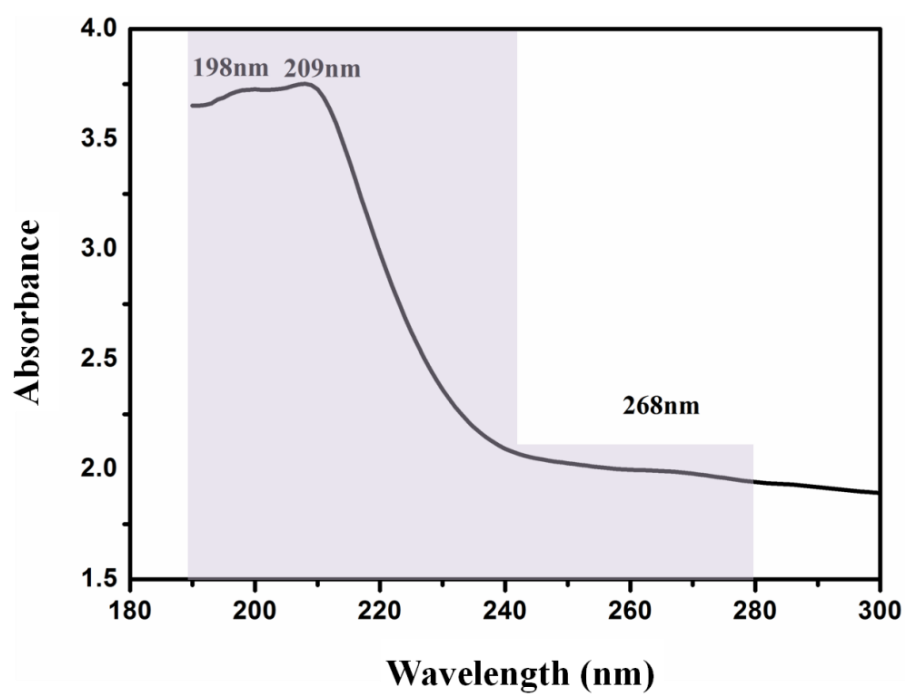
**Supplementary Figure S8** SEM micrographs of a) and b) yeast cell@PAH/PSS@Au shell, and c) and d) yeast cell@PDADMA/PSS@SiO<sub>2</sub> shell, a) and c) before cell division, and b) and d) after cell division.



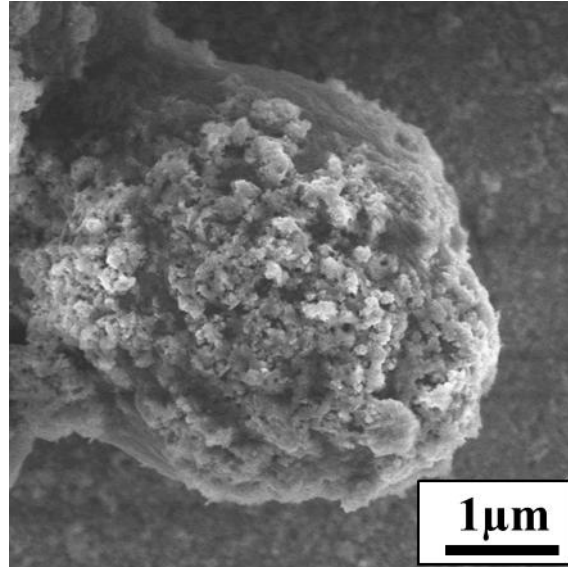
**Supplementary Figure S9** TEM micrographs of a) Au@PAH aggregations; b) Au@PLL aggregations and c) Au@L-cysteine biohybrids.



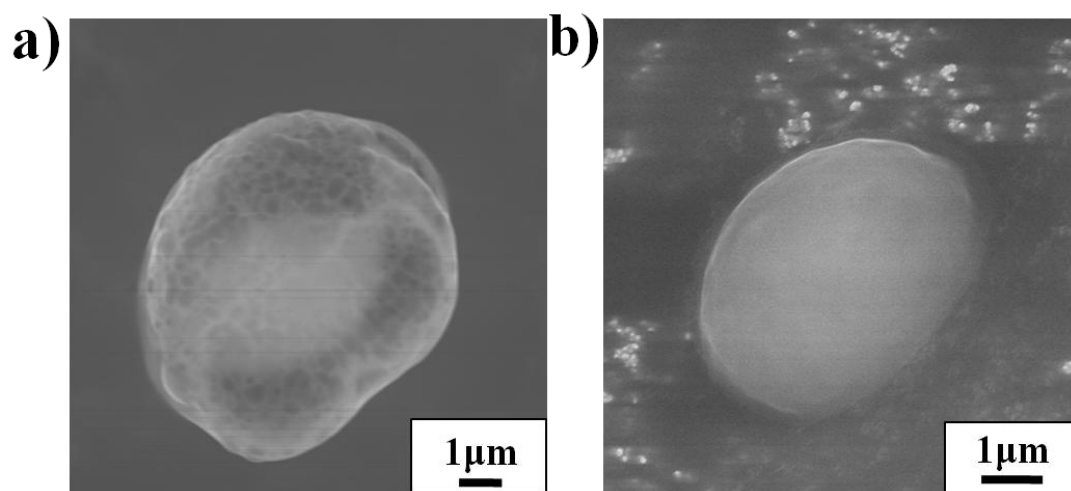
**Supplementary Figure S10** Cyanobacteria protection and surface functionalization tested by oxygen production. Data are presented as the relative oxygen production of encapsulated cyanobacteria (square) in comparison with native cyanobacteria (circle) exposed under a) high light, b) strong UVC radiation and c) in different pH value of micro-environments.



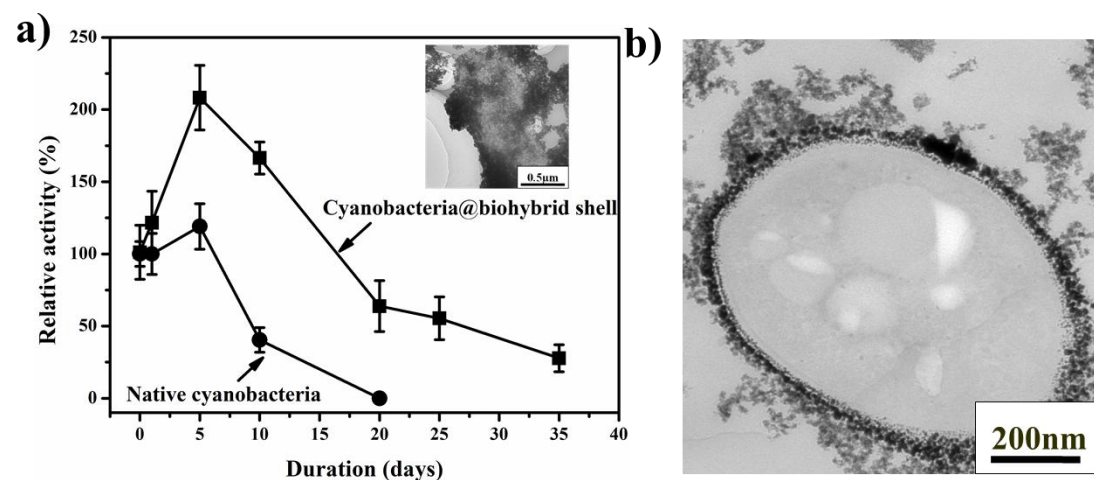
**Supplementary Figure S11** UV-visible spectrum of biohybrid sol in the wavelength range of 190-280 nm. Strong absorption in the wavelength of 190-240 nm and weak absorption in the wavelength of 240-280 nm are shown in the shadow areas.



**Supplementary Figure S12** SEM micrograph of yeast cell in biohybrid solution without shaking after 10 hours.



**Supplementary Figure S13** SEM micrographs of a) yeast cell@cysteine shell and b) native yeast cells.



**Supplementary Figure S14** Bioactive molecules in biohybrid shell can be available to other amino acids and peptides: a) TEM micrograph of cyanobacteria in Au/Lysine biohybrid shells (inset) and the relative oxygen production of encapsulated cyanobacteria (square) and native cells (circle) under high light; b) microtome-sliced TEM micrograph of cyanobacteria in Au/glutathione biohybrid shell.