

## Supporting Information

### **Multifunctional all hydrogel-based smart dressing system fabricated by a self-healing cross-linking strategy for real-time monitoring of wound temperature, strain and on-demand drug delivery**

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### **EXPERIMENTAL SECTION**

#### **Materials.**

Acrylylchloride (98%, Tokyo Kasei Kogyo Company, Japan), glycinamide hydrochloride (98%, Energy chemical, China), potassium persulfate (KPS, Energy chemical, China), N,N,N',N'-tetramethylethylenediamine (TMEDA, Energy chemical, China), *N,N'*-bis (acryloyl)cystamine (Bis, Energy chemical, China), methanol (Sinopharm Chemical Reagent limited corporation, china), ethyl alcohol (Sinopharm Chemical Reagent limited corporation, china), ether (Sinopharm Chemical Reagent limited corporation, china), sodium hydroxide (Sinopharm Chemical Reagent limited corporation, china), hydrochloric acid (Sinopharm Chemical Reagent limited corporation, china), gold acid chloride trihydrate (98%, Energy chemical, China), Cetrimonium bromide (99%, Shanghai Aladdin Bio-Chem Technology Co., Ltd., China), Silver nitrate (Shanghai Aladdin Bio-Chem Technology Co., Ltd., China), ascorbic acid (Shanghai Aladdin Bio-Chem Technology Co., Ltd., China), silver nanowire silver nanowire (5mg/ml, Jiangsu Xianfeng Nano Material Technology Co., Ltd., China), Cefazolin Sodium (99%, Energy chemical, China), Sodium chloride

(Sinopharm Chemical Reagent limited corporation, china), Yeast extract (Energy chemical, China), Casein Tryptone (Energy chemical, China), Bacto-Agar (Energy chemical, China) were used without further purification. All other chemicals and solvent are analytical reagents. Corresponding molds are customized at Guanghui Plexiglass Factory.

### **Characterization.**

**Nuclear magnetic resonance (NMR) and IR spectroscopy.** All NMR spectra were obtained using either a Bruker HW600 MHz spectrometer (AVANCE AV-600) and recorded in CDCl<sub>3</sub> (internal reference 7.26 ppm).

**UV/Vis spectroscopy.** The transmittance curves of the hydrogels were built by turbidity measurement to collect the transmittance at 700 nm with a scanning rate of 0.1°C min<sup>-1</sup> from 15 to 55 °C using a Shimadzu UV-2700 spectrophotometer equipped with a PTC-348WI temperature controller (±0.1°C). The UV absorption spectra of Au nanorods, Ag nanowires, hydrogel films and drug content were measured by a Shimadzu UV-2700 spectrophotometer at room temperature. In order to directly observe the drug release performance of the gel over time, we tested the UV absorption curves of different concentrations of cefazolin sodium (**Figure S7A**). The absorbance of Cefazolin Sodium at 272nm is fitted with the concentration of Cefazolin Sodium to obtain the calibration curve formula of Cefazolin Sodium:  $y=0.013x+0.012$ , where  $y$  represents the absorbance and  $x$  represents the concentration (**Figure S7B**). The absorbance is converted into concentration through the calibration curve, so as to calculate the release efficiency.

**Scanning electron microscope (SEM) analysis.** The morphology of the hydrogels at different temperature was observed by a FEI inspect F50 scanning electron microscope at accelerated electron energy of 5.0 kV. The hydrogel specimens at different temperature were flash frozen in liquid nitrogen for 5 min and immediately lyophilized for 48 hours to remove water. The cross-sections of the specimens were coated with gold by a sputter coater for 20 seconds before measurement.

**Differential Scanning Calorimetry (DSC).** The phase transition of hydrogels was investigated by differential scanning calorimetry using a DSC Q200 from TA instrument. Hydrogels at preparation state (ca. 80 mg), equilibrated with a reference filled with the same quantity of pure water, were submitted to temperature cycles between 20 and 60°C under nitrogen atmosphere. The heating and cooling rates were fixed at 2°C min<sup>-1</sup>.

**Dynamic mechanical analysis (DMA).** The storage moduli and loss moduli of the hydrogel samples (cylinders, 10 mm in diameter and 4 mm in height) were measured on a NETZSCH Dynamic Mechanical Analyzer at the constant frequency of 10 rad/s and 1% of strain, the time sweep tests were performed at 37°C.

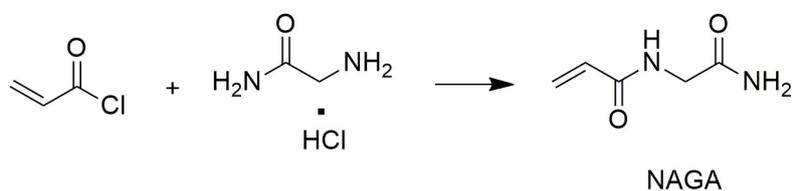
**Measurement of mechanical properties.** All mechanical properties of the hydrogels were tested on MTS Exceed E42 electronic universal testing machine equipped with pneumatic clamps (DQB203B) at room temperature. In this study, all the samples were fully equilibrated in deionized water before test. For tensile test, hydrogels with a

thickness of 0.5 mm were cut into rectangle (40 mm in length and 10 mm in width). The rate of extension was fixed at 50 mm min<sup>-1</sup> for tensile test and loading-unloading test. The cylinder-shaped hydrogels (10 mm in diameter and 10 mm in height) was used for compression test and the crosshead speed was set at 10 mm min<sup>-1</sup>.

**Light-to-heat conversion temperature.** The gel film was excited by 808nm near-infrared light, and a thermal imager (SMART SENSOR ST9450) was used to record the changes in the surface temperature of the hydrogels. At the same time, a thermal imager (SMART SENSOR ST9450) was used to take thermal imaging pictures at different times.

**Sensing measurements.** The tensile and compressive behaviors of the sensor were investigated using a Microforce Tester (Instron 5943). A digital source meter Keithley 4200-SCS was used to collect the electrical response of the sensors. To demonstrate the capability of our sensors for monitoring the force of the wound, the sensor is attached to the arm to record the electrical signal changes of the patient's movements such as raising the arm, lowering the arm, making a fist to relax, and scratching the wound.

#### Synthesis of Monomer NAGA.



**N-(2-amino-2-oxoethyl) acrylamide (NAGA).** The synthetic procedures is similar to that of the reference [1]. Glycinamide hydrochloride (3.15 g, 28.5 mmol), potassium carbonate (5.9 g, 42.75) 25 mL cold deionized water, and 10 mL cold diethyl ether were added into a 100 mL reaction flask, which was placed in an ice bath. Subsequently, a

solution of acryloyl chloride (3.1 g, 34.2 mmol) in 15 mL diethyl ether was added dropwise under stirring at 0 °C for about one hour. Then the mixture was further stirred for 5 hours at room temperature. After that, 6 mol L<sup>-1</sup> HCl was added into the solution to adjust pH to 2. Next, the mixture was washed three times with 100 mL of diethyl ether to remove the organic phase and the remaining diethyl ether was evaporated under vacuum. Again, the pH of the solution was adjusted to neutral with the 2 mol L<sup>-1</sup> NaOH, and the mixture was freeze-dried. The raw product was washed three times with 100 mL of ethanol/methanol mixture (4/1, V/V). Then the ethanol and methanol were removed by rotary evaporation and the mixture left was recrystallized at 0 °C to obtain the resultant NAGA which was dried in vacuo as a white solid (2.26 g, Yield: 62%). IR spectrum of NAGA in Figure S1a displays its feature bands:  $\nu = 3389\text{ cm}^{-1}$  (m, NH),  $3314\text{ cm}^{-1}$  (s, NH),  $3191\text{ cm}^{-1}$  (m, NH),  $1662\text{ cm}^{-1}$  (vs, C=O),  $1626\text{ cm}^{-1}$  (vs, C=O),  $1556\text{ cm}^{-1}$  (vs, NH). <sup>1</sup>H NMR (600 MHz, DMSO)  $\delta$  8.30 (s, 1H), 7.38 (s, 1H), 7.06 (s, 1H), 6.31 (m, J = 17.1, 10.2 Hz, 1H), 6.09 (m, J = 17.1, 2.1 Hz, 1H), 5.60 (m, J = 10.2, 2.1 Hz, 1H), 3.72 (d, J = 5.8 Hz, 2H).

#### **Preparation of the PNAGA/AgNW hydrogel**

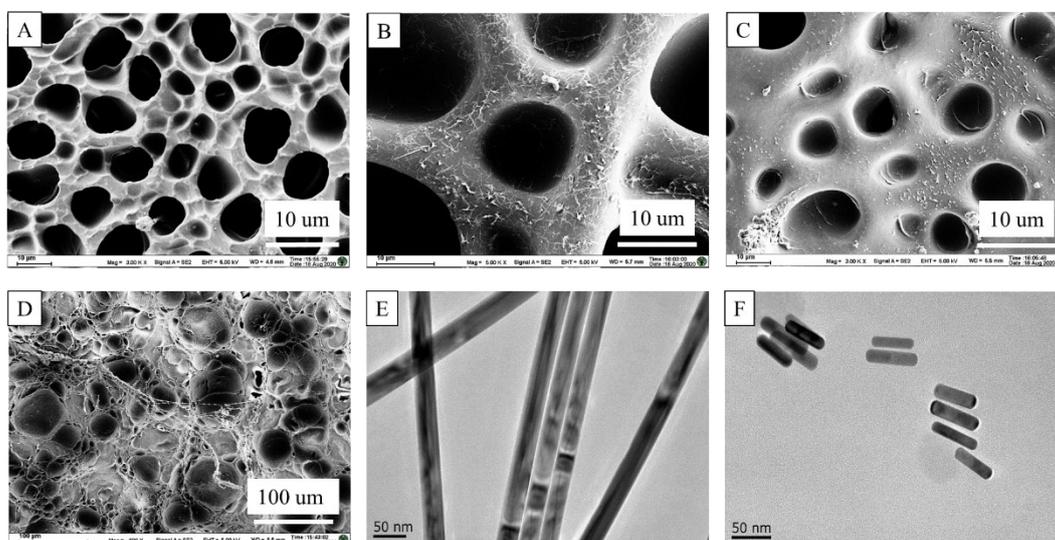
NAGA (0.2g, 1.56mmol), Bis (0.5mg, 0.0023mmol) was dissolved in AgNW aqueous solution (750uL,10mg/ml), which was sonicated for 10 minutes to make it completely dissolved. The mixture was deoxygenated under N<sub>2</sub> atmosphere for 2h, then 5mg KPS and 5uL TMEDA was added, and the reaction was closed for 24h to obtain PNAGA/AgNW hydrogel. The PNAGA/AgNW hydrogel was placed in pure water for 24h and repeated three times to remove the unpolymerized monomer, APS and TEMED.

#### **Preparation of the PNAGA/AuNPs hydrogel**

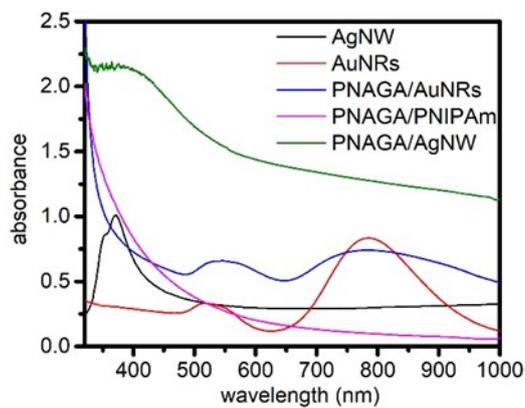
NAGA (0.2g, 1.56 mmol), Bis (0.5mg, 0.0032mmol) was dissolved in AuNRs aqueous solution (750uL,1mg/ml), which was sonicated for 10 minutes to make it completely dissolved. The mixture was deoxygenated under N<sub>2</sub> atmosphere for 2h, then 5mg KPS and 5uL TMEDA was added, and the reaction was closed for 24h to obtain PNAGA/ AuNPs hydrogel. The PNAGA/ AuNPs hydrogel was placed in pure water for 24h and repeated three times to remove the unpolymerized monomer, APS and TEMED.

### Preparation of the PNAGA/PNIPAm hydrogel

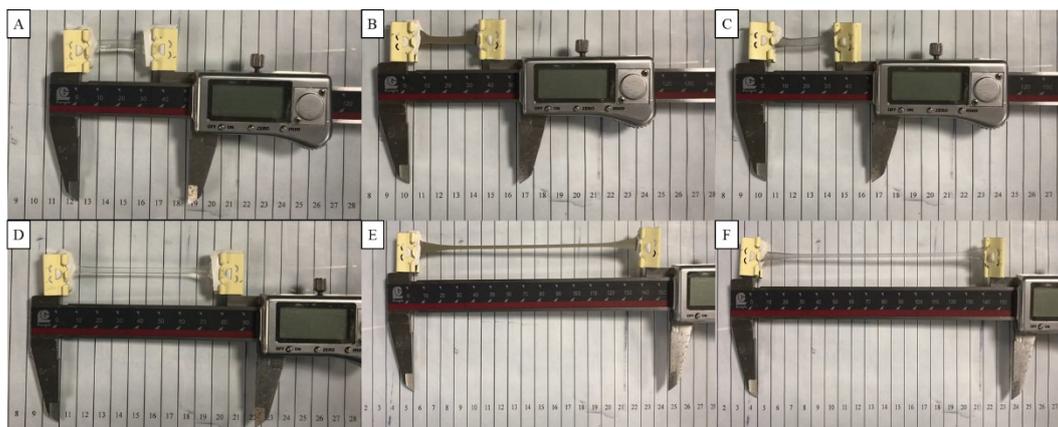
NAGA (0.2g, 1.56mmol), Bis (0.5mg, 0.0032mmol) was dissolved in 750uL H<sub>2</sub>O, which was sonicated for 10 minutes to make it completely dissolved. The mixture was deoxygenated under N<sub>2</sub> atmosphere for 2h, then 5mg KPS and 5uL TMEDA was added, and the reaction was closed for 24h to obtain PNAGA hydrogel. The PNAGA hydrogel was swelled in the NIPAm aqueous solution (0.08g/ml) for 24 hours, and then 5mg KPS and 5uL TMEDA were added for polymerization. The PNAGA/PNIPAm hydrogel was obtained by repeating the swelling and polymerization three times. The PNAGA/PNIPAm hydrogel was placed in pure water for 24h and repeated three times to remove the unpolymerized monomer, APS and TEMED.



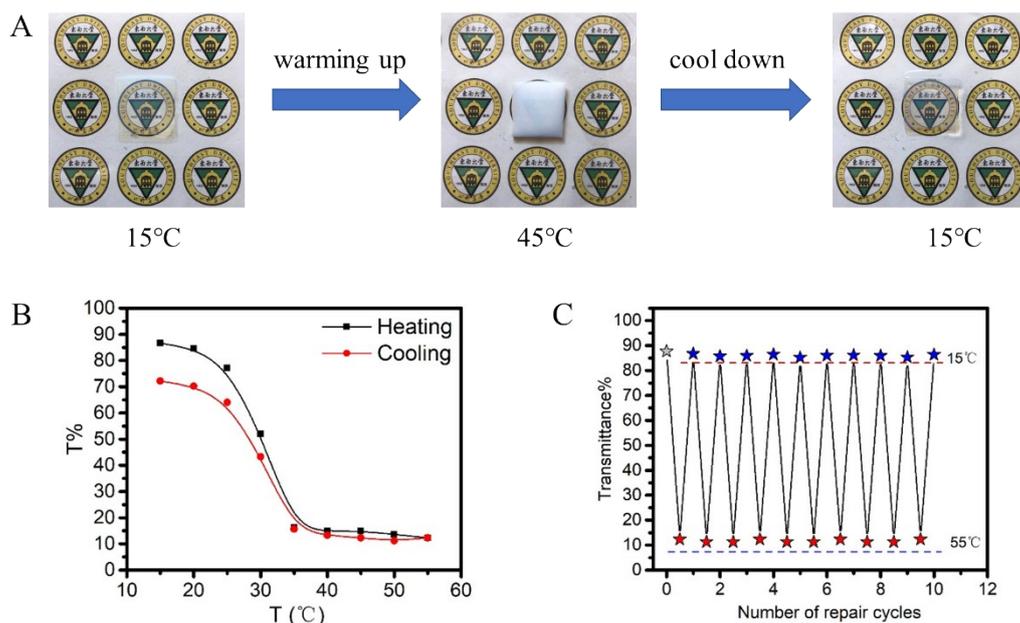
**Figure. S1.** SEM images of (A) PNAGA, (B) PNAGA/AgNW, (C) PNAGA/AuNRs, (D) PNAGA/PNIPAm. TEM images of (E) AuNRs (scale: 50 nm), (F) AgNW (scale: 50 nm).



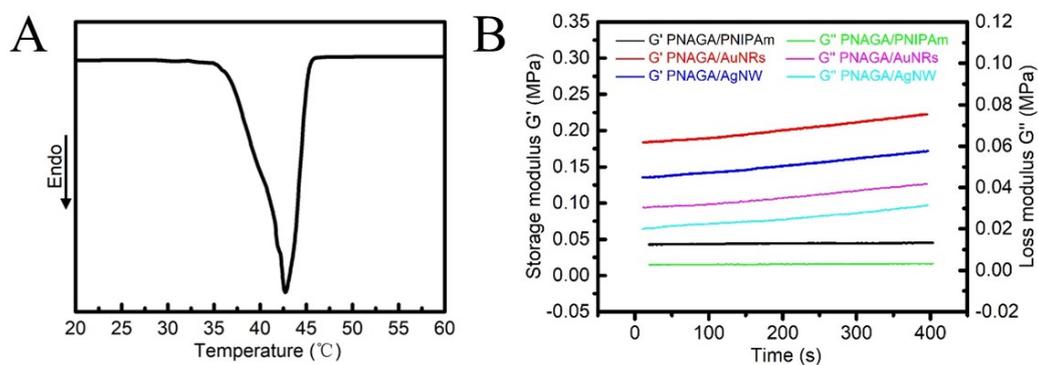
**Figure. S2.** UV absorption spectrum.



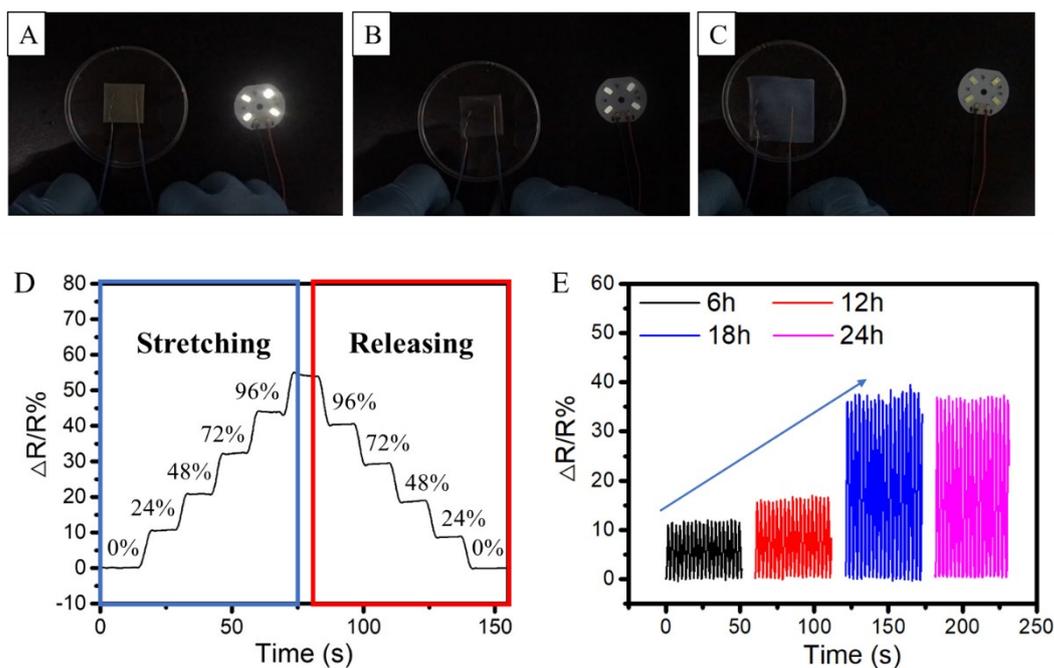
**Figure. S3.** Photographs of PNAGA/PNIPAm hydrogel showing their ability to withstand elongation (A and D); Photographs of PNAGA/AgNW hydrogel showing their ability to withstand elongation (B and E); Photographs of PNAGA/AuNRs hydrogel showing their ability to withstand elongation (C and F).



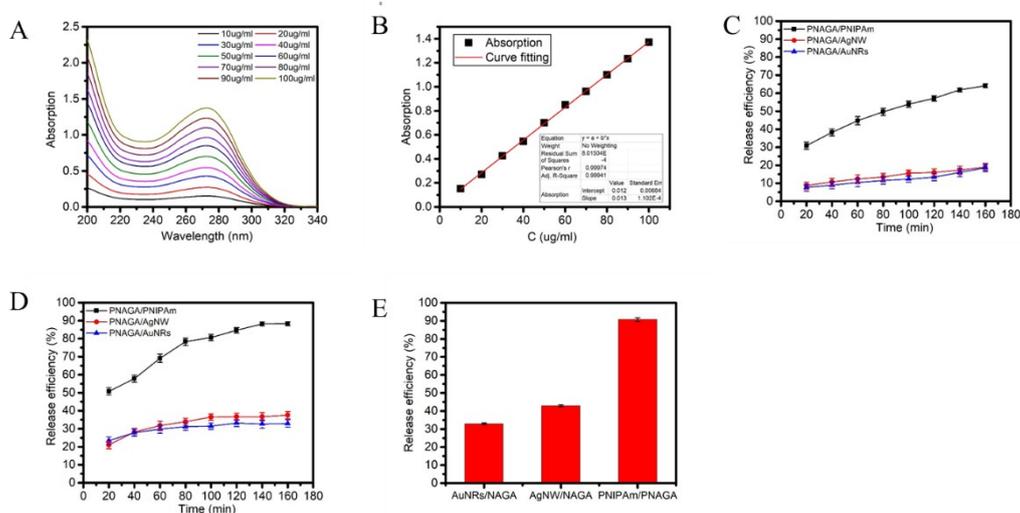
**Figure. S4.** (A) Photograph of the reversible optical behavior of PNAGA/PNIPAm thermosensitive hydrogel films. (B) Transmittance curves of PNAGA/PNIPAm hydrogel for heating and cooling at different temperatures (15-55°C) at 700 nm. (C) Transmittance of PNAGA/PNIPAm hydrogel repeated heating and cooling cycles for 10 times at 700nm, 15 °C and 55 °C.



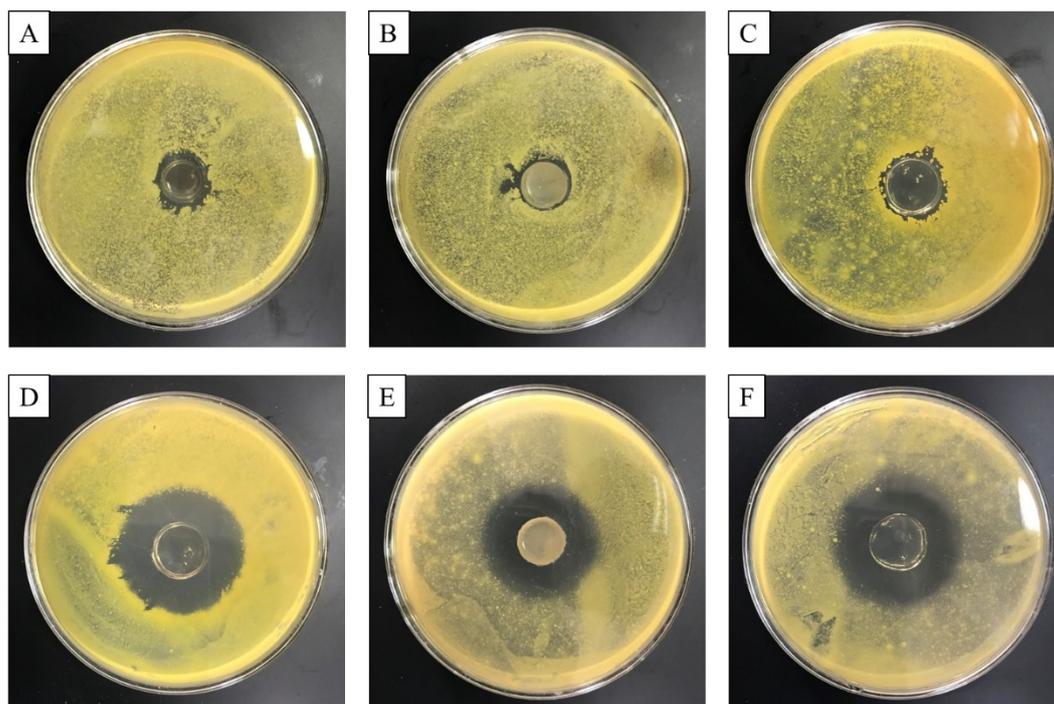
**Figure. S5.** (A) DSC curves of PNAGA/PNIPAm hydrogels. (B) The Storage modulus ( $G'$ ) and Loss modulus ( $G''$ ) of PNAGA/AuNRs, PNAGA/PNIPAm and PNAGA/AgNW hydrogels.



**Figure. S6.** The photos of PNAGA/AgNW (A), AuNPs/PNAGA (B) and PNAGA/PNIPAm (C) hydrogels lighting up the bulb under the conditions of 3V 2A. (D) Instantaneous resistance variation during stretching and releasing. (E) Long-term electrical durability of the sensor as a function of storage days.



**Figure. S7.** (A) UV absorption curves of different concentrations of Cefazolin Sodium. (B) Calibration curve of Cefazolin Sodium. Drug release efficiencies of different gel components (AuNPs/PNAGA, PNAGA/PNIPAm and PNAGA/AgNW hydrogels) at 25°C (C) and 40°C (D). (E) The final release efficiency of the AuNPs/PNAGA, PNAGA/PNIPAm and PNAGA/AgNW hydrogels were converted by the calibration curve of Cefazolin Sodium at 40°C.



**Figure. S8.** Inhibition zone of undrug-loaded of (A) AuNPs/PNAGA hydrogel, (B) PNAGA/AgNW hydrogel and (C) PNAGA/PNIPAm hydrogel. Inhibition zone of the drug-loaded (D) AuNPs/PNAGA hydrogel, (E) PNAGA/AgNW hydrogel and (F) PNAGA/PNIPAm hydrogel.

## References:

- [1] S. Ge, J. Li, J. Geng, S. Liu, H. Xu, Z. Gu, Adjustable dual temperature-sensitive hydrogel based on a self-assembly cross-linking strategy with highly stretchable and healable properties, *Materials Horizons* 8(4) (2021) 1189-1198.