

Effective photothermal ablation of biofilm by using pH-responsive AuNPs modified with mixed-charge zwitterion



Dengfeng Hu, Huan Li, Wenxi Lei, Xiaoli Fan, Qiao Jin, Kefeng Ren and Jian Ji*
MOE Key Laboratory of Macromolecular Synthesis and Functionalization, Department of Polymer Science and Engineering, Zhejiang University, Hangzhou 310027, China.

*Contact to: Ji Jian, email: jijian@zju.edu.cn, Tel/Fax: +86-571-87953729



Introduction

■ Biofilms which contribute to the persistent bacterial infections pose a serious threat to global public health, mainly due to their resistance to antibiotics and avoidance to innate immune attacks by phagocytes^[1].

■ Nanoparticles possess many novel properties after modification, which provides much possibility to kill and eliminate biofilm.

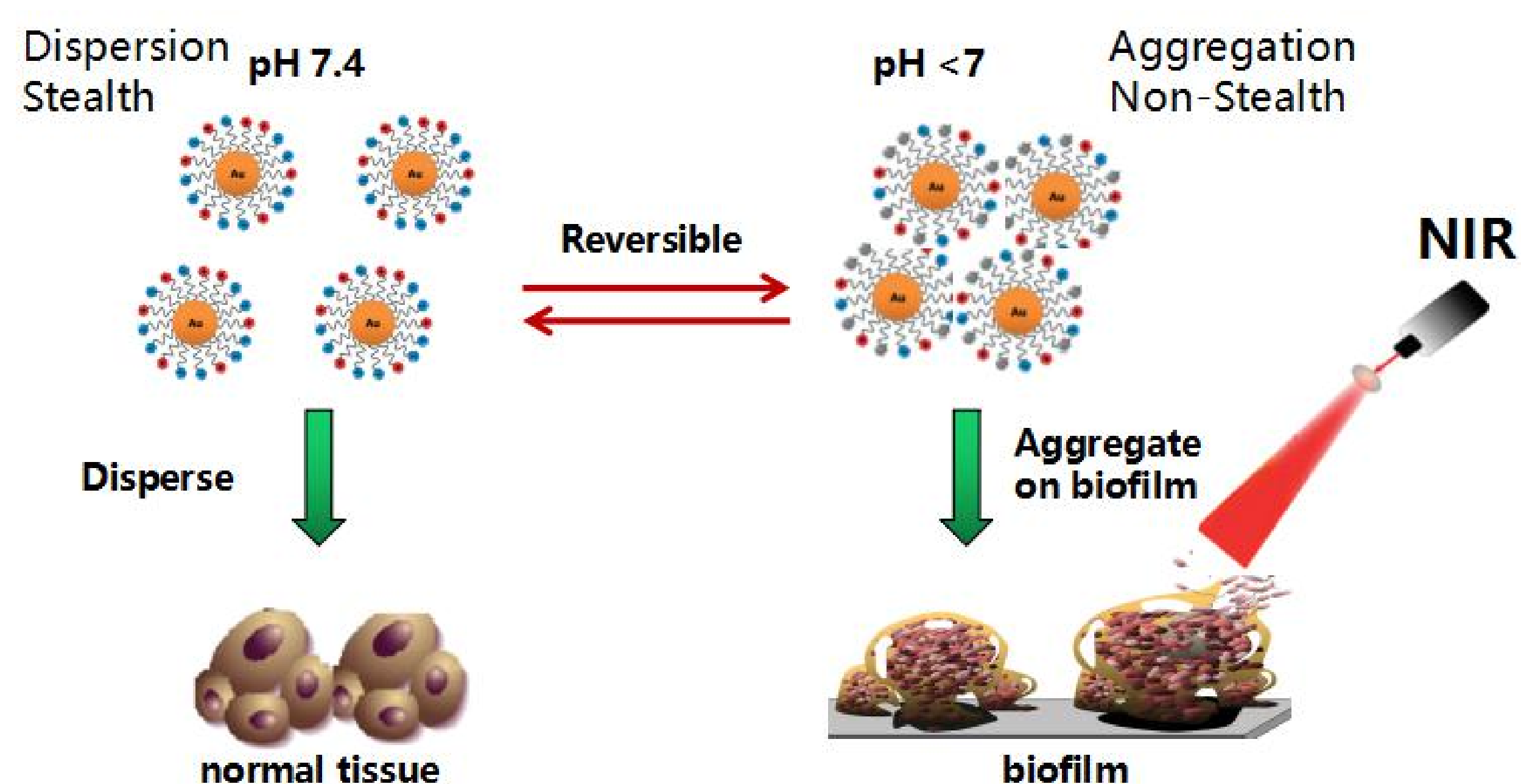
■ Photothermal therapy is a great approach which utilizes materials with high photothermal convert ratio under external light irradiation to realize therapeutic efficacy^[2]. As an excellent photothermal material, gold nanoparticles (AuNPs) have lots of beneficial applications.

■ However, how to achieve AuNPs stable dispersion in normal tissue but rapid aggregation in biofilm microenvironment is the key to achieve effective biofilm ablation but no harm to normal tissue.

■ After modification, mixed-charge zwitterion composed of weakly electrolytic negative ligand and strongly electrolytic positive ligand provides AuNPs with great pH sensibility^[3].

Objective

In this work, gold nanoparticles (AuNPs) were facilely prepared by surface modification with mixed-charge zwitterionic self-assembled monolayers, which can be stable at the pH of blood and normal tissues but aggregate instantly in response to the acidic extracellular pH of biofilms.



Scheme 1. Schematic illustration of biofilm ablation by pH-responsive AuNPs modified with mixed-charge zwitterion.

Results and Discussion

1. Preparation and characterization of pH-responsive zwitterionic AuNPs

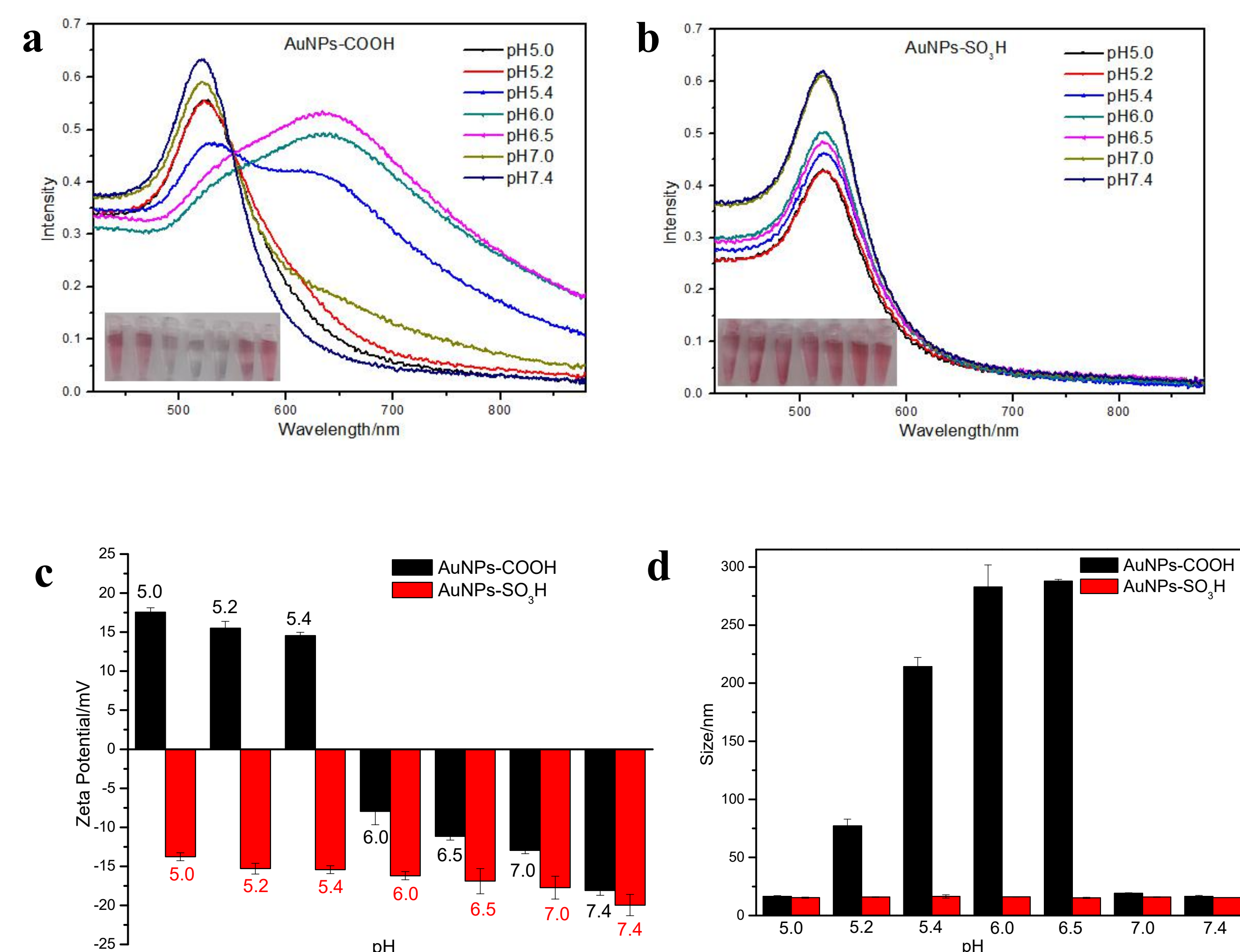


Figure 1. pH-responsivity of AuNPs-SO₃H and AuNPs-COOH in phosphate buffer (PB, 10 mM) solution at different pH values. (a,b)UV-vis spectra; (c)Zeta potential and (d) hydrodynamic size of nanoparticles.

2. Aggregation of AuNPs in biofilm

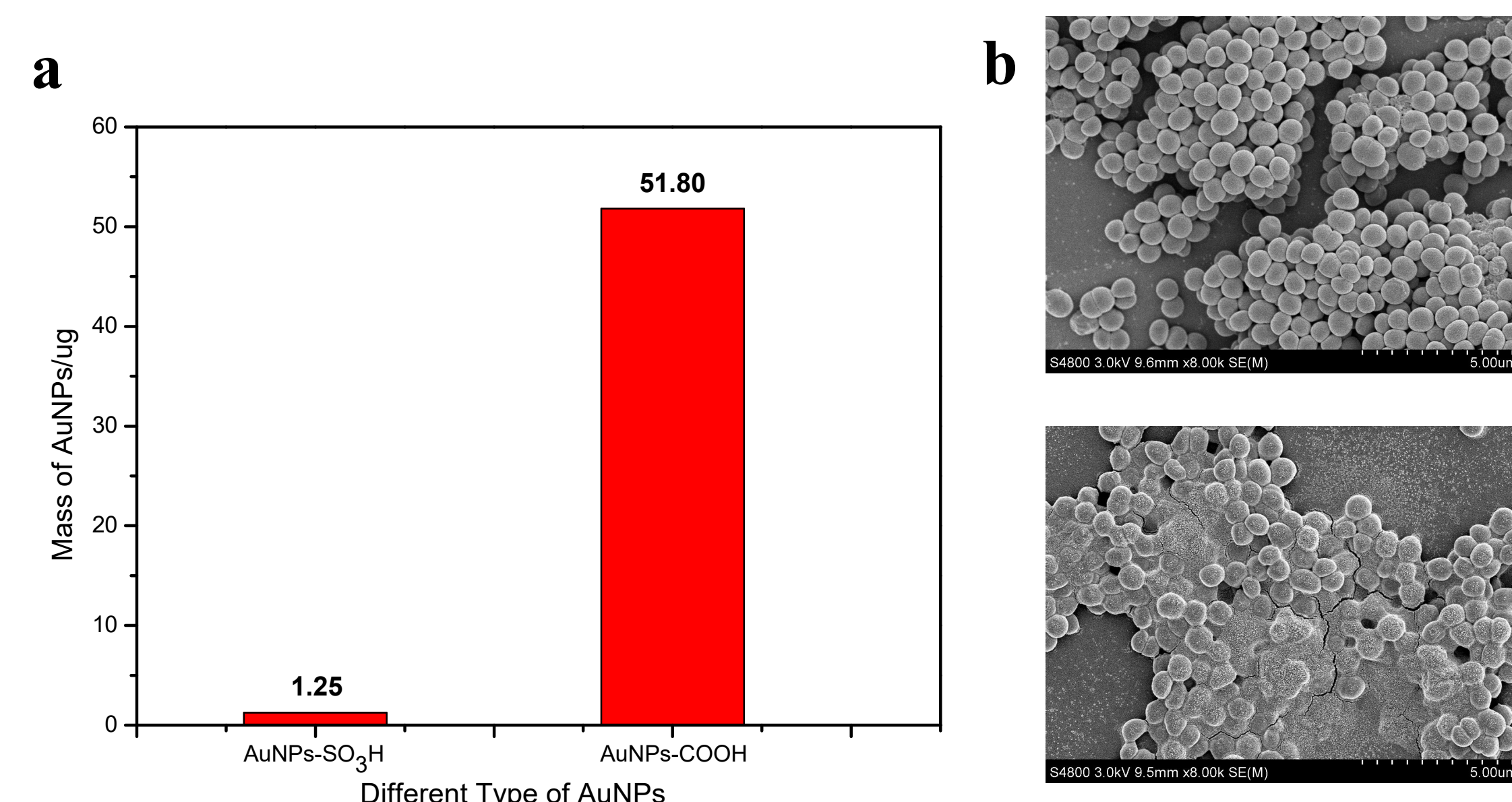


Figure 2. Aggregation of AuNPs in biofilm. (a) Mass of different type of AuNPs aggregated in biofilm measured by ICP-MS and (b) SEM of biofilm once added with different type of AuNPs.

3. Antibacterial effect of zwitterionic AuNPs under NIR light irradiation

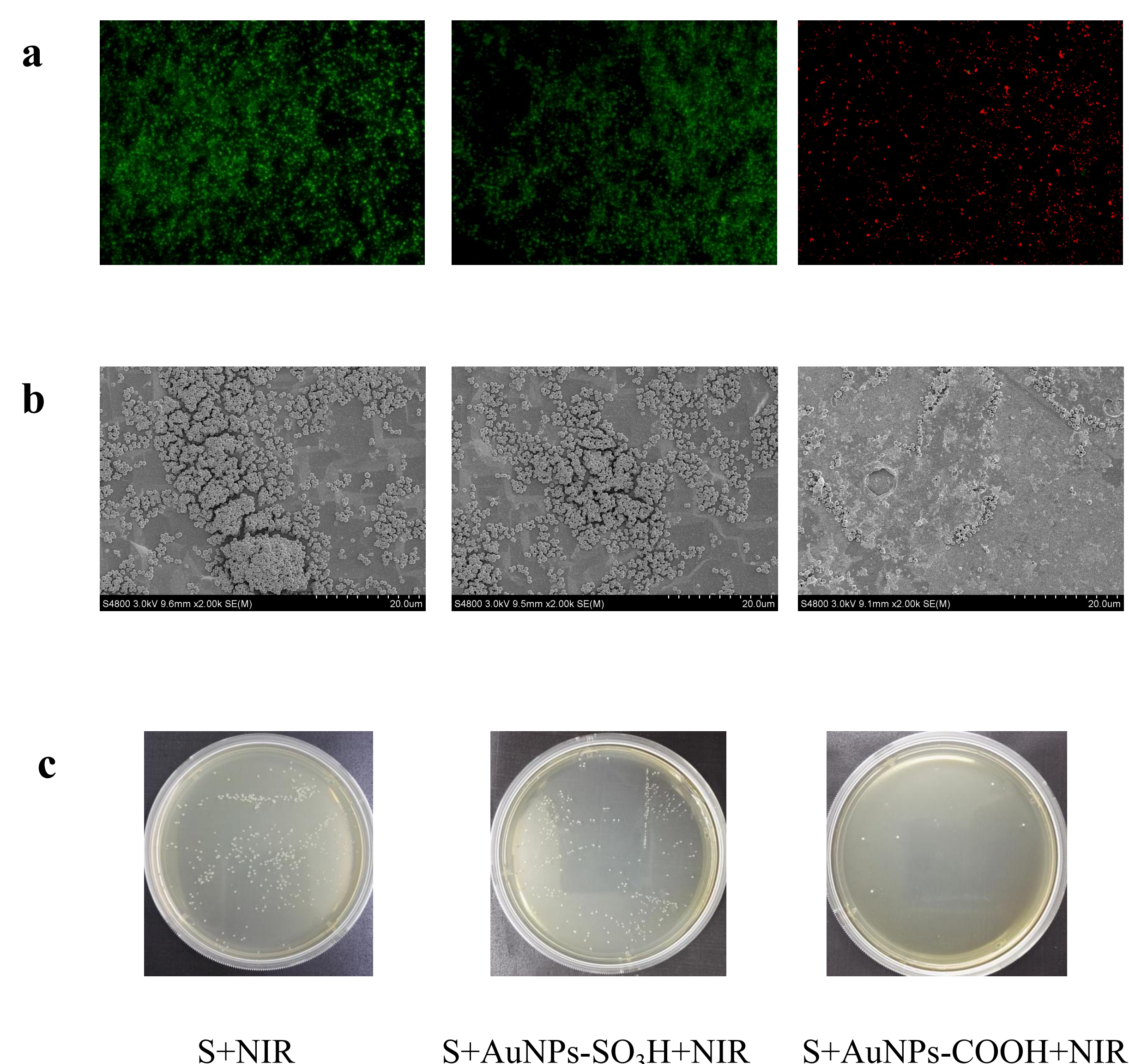


Figure 3. Antibacterial effect of only NIR, AuNPs-SO₃H with NIR and AuNPs-COOH with NIR by (a)Live/Dead dye assay (green represent live bacteria and red represent dead bacteria);(b)SEM and (c)cultivating in culture medium.

Conclusion

In summary, after modification with mixed-charge zwitterion composed of weakly electrolytic negative ligand and strongly electrolytic positive ligand, gold nanoparticles (AuNPs) have great pH responsiveness, which can disperse stably in normal tissue but aggregate rapidly in biofilm microenvironment and then show effective biofilm ablation under NIR light irradiation.

References

- [1]. Yuyun Zhao. et al., J. AM. CHEM. SOC. 2010,132, 12349–123569.
- [2]. Chun-Wen Hsiao. et al. Adv. Funct. Mater. 2015, 25, 721–728
- [3]. Xiangsheng Liu. et al. ACS Nano. 2013,7,6244-6257.