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Developing plasmonic nanoparticles for application in stimulating ion channel activity in living cells

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Motivation

Gold nanoparticles (AuNP) are widely investigated for biomedical applications [1]. The most attention is paid to tailoring their surface with various chemical or biological agents, in order to achieve the stability of the AuNP in the biological liquids and their desired function. For most of the applications smaller NP size is desired because of a higher ability of penetration through the tissues and cell membranes.

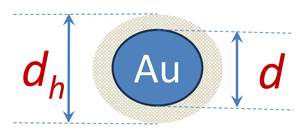
In our previous studies [2,3] we have established that fluctuations in intracellular calcium can modulate plasmonic AuNP-induced gating of BKCa channels in smooth muscle cells and neurons through an indirect mechanism, probably involving the interaction of localized surface plasmon resonance (**LSPR**) with calcium-permeable ion channels. Those previous results indicated that the effect may be enhanced by using AuNPs of smaller size. Although numerous various approaches to synthesis of AuNPs of different size have been reported in literature, hardly any of them was reaching sizes below 10 nm, especially when synthesized in water.

In this work we optimized the synthesis conditions for highly stable AuNP with localized surface plasmon resonance (LSPR). We sought to obtain NPs of the smallest size, preferably <10 nm, retaining their properties in biological buffer system for a time sufficient to study their effect on membrane ion channels and associated intracellular calcium signaling in isolated vascular smooth muscle cells and spinal ganglia neurons of the rat.

Experiment

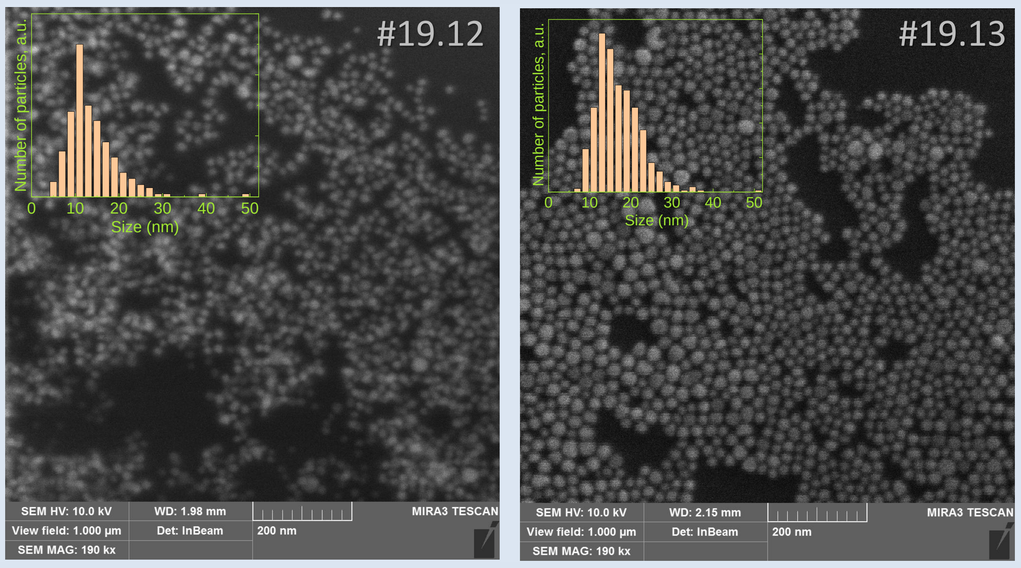
Series 19 was performed by mixing 100mL of DI water, 1mL of 1% solution of $HAuCl_4$ and 1% solution of sodium citrate(5-10mL). Series 11 was performed by adding to 150mL of DI water (t≈70˚C) 0,1ml of 2,5mM tannic acid, 1% solution of $HAuCl_4$ and different amounts of 2,2mM sodium citrate(from 1mL to 50mL) and mixing them on magnetic stirrer for 10 minutes. Series 12 was almost the same but we varied the quantity of tannic acid (from 0.05 mL to 5mL). Obtained solutions of both series we keep at dark place during 24 hours for stabilization of nanoparticles.

SEM – Scanning Electron Microscopy – used to determine the size of the inorganic (metallic) part of individual NPs *(**d**)*;
DLS – Dynamic Light Scattering – used to determine the hydrodynamic size of NPs *(d_h)* including ;
UV-vis – UV-visible optical absorption spectroscopy – used to determine the position of the **LSPR** band;

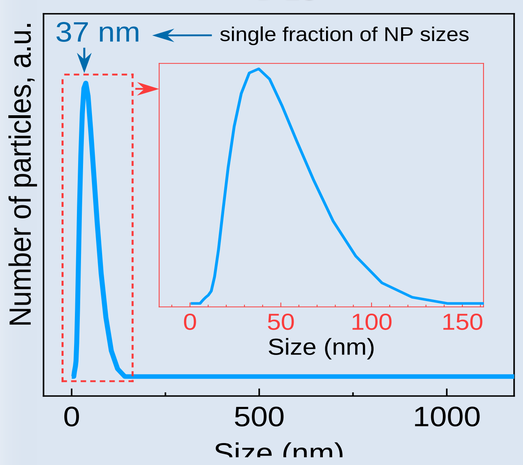


Results and discussion

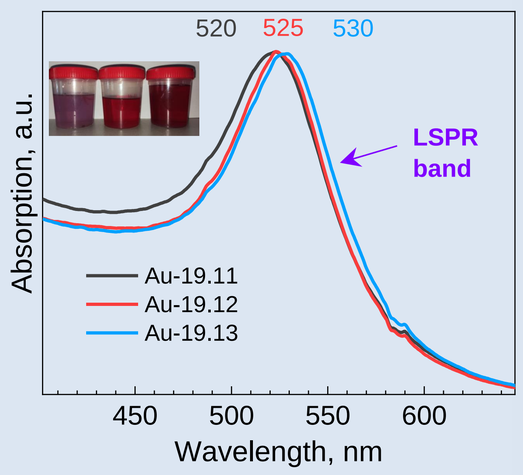
SEM



DLS

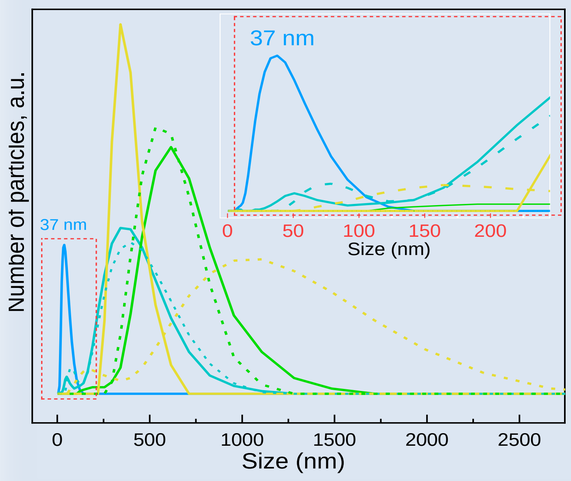


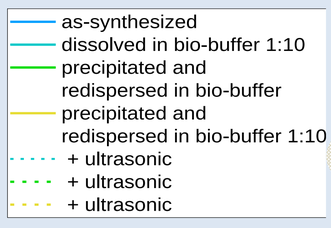
UV-vis

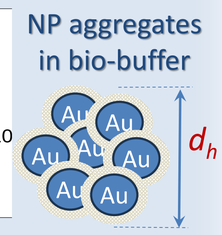


The mean NP size *(e.g.* #19.13) correlate in DLS and in SEM. Thus, the DLS measurements for other sample scan be considered as reliable.

Effect of bio-medium



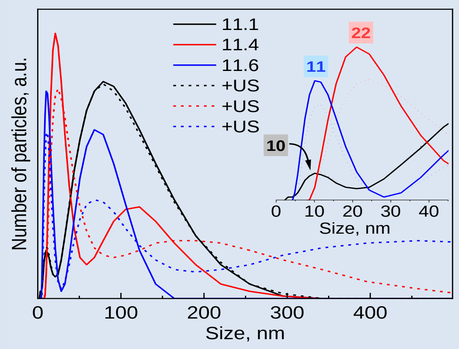


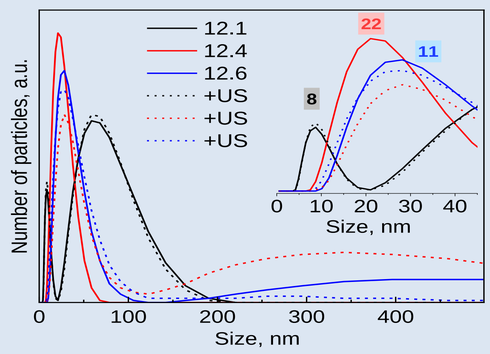


Dissolving of as-synthesized AuNPs in the bio-buffer leads to their partial aggregation (manifesting itself as additional band in DLS) which is less intense if AuNPs are not subject to removal of excess stabilizer by precipitation.

Treatment in the ultrasonic bath does not solve aggregates and even enhances aggregation for NPs without excess stabilizer.

Tuning AuNP size towards ≤10 nm





By tuning the amount of sodium citrate (in series 11) and tannic acid (in series 12) the size of AuNPs could be varied, with the targeted size <10 nm (8 nm in #12.1).

However, further experiments are needed to reduce NP aggregation both in the as-synthesized solution and in the bio-buffer.

Conclusion

The developed facile method of colloidal synthesis in aqueous solutions allows the AuNPs size to be tuned down to below 10 nm, but additional efforts need to be undertaken to improve NP stability against aggregation in bio-buffer, which becomes an issue for such small NPs.

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