Gold nanorods as near infrared photothermal transducers for biomedical applications

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Introduction. Gold nanoparticles with unconventional shapes, such as gold nanorods exhibit intense localized plasmon resonances at frequencies in the near infrared (NIR),[1,2] which is the window of principal interest in biomedical optics where the penetration of light into the body is maximal. Upon excitation with radiation from a NIR laser, these plasmon resonances undergo excitation and relaxation through radiative and non radiative channels. These dynamics give rise to a wealth of physiochemical features such as e.g. 1) a very unique enhancement of the near field, 2) much better light scattering and photothermal transduction efficiency (by a few orders of magnitude), 3) exceptional optical flexibility (possibility to tune the plasmon resonances within a broad window), 4) much higher stability in the body and thresholds before photo / thermo bleaching, 5) and unparalleled possibility of conjugation with additional biochemical functionalities (e.g. vitamin derivatives, antibodies, etc. which may allow for active targeting).[3-5] Therefore these gold nanoparticles may become valuable contrast agents in a variety of diagnostic and therapeutic applications (e.g. optical and photoacoustic imaging, flow cytometry, welding, hyperthermia, photoporation, photoacoustic microsurgery, etc.).

Here we discuss our preliminary findings on the possibility to modulate various features of the gold nanorods (average size, shape and surface modification), in order to gain substantial control over the nano / bio and nano / opto interfaces. Moreover we show the efficiency of gold nanorods as photothermal transducers in a model biomedical application i.e. the NIR laser welding of connective tissues.

Synthesis and functionalization of gold nanorods. Aqueous solutions of gold nanorods are synthesised by reduction of chloroauric acid by ascorbic acid in the presence of silver nitrate, the surfactant cetrimonium bromide and a gold catalyst.[1] The accurate balance of all these reagents governs the average size and shape of the gold nanorods, in a way which is still poorly understood. In turn, the size and shape (length / diameter ratio) of the nanoparticles determines the optical response and functionality of the solution. We developed a new sustainable approach to tune the progress and rate of the reaction, which leads to a fine control over the average size and shape of the gold nanorods. Moreover we acquired flexible strategies to replace the primary stabilizer cetrimonium bromide by thiol modified compounds such as biopolymers and silicates (Figure 1) to improve the stability, biocompatibility, specificity, etc. of the nanoparticles.

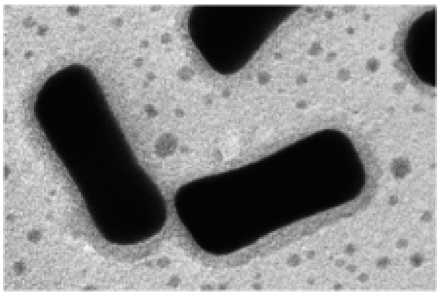

Figure 1: 180 × 120 nm^2 transmission electron micrograph of silica coated gold nanorods

Laser welding of lens capsule. As a model biomedical application, we combined a stain of gold nanorods and a pulse from a diode laser (810 nm) to mediate the welding of fragments of connective tissues,[6] which may be exploited to close surgical / accidental wounds wherever the use of stitches may prove undesirable.[7]

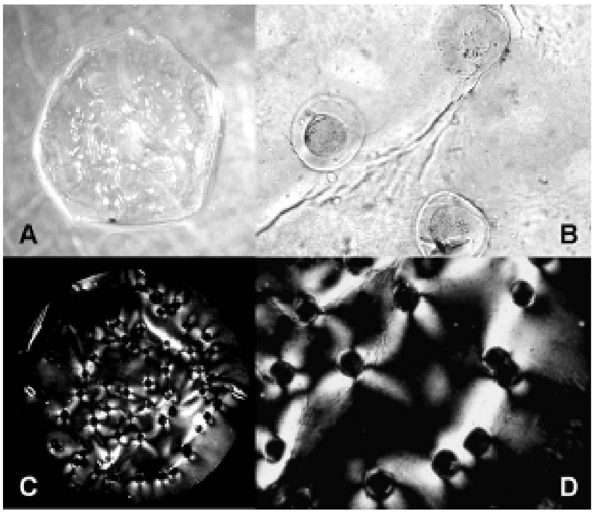

Figure 2: A and B conventional micrographs, C and D polarisation micrographs from welds of eye lens capsules. A ~ (1.1 × 1.1) cm^2; B ~ (0.18 × 0.14) cm^2; C ~ (0.7 × 0.7) cm^2; D ~ (0.3 × 0.2) cm^2.

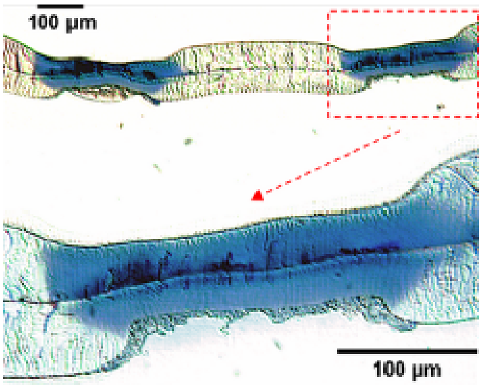

Figura 3: Histological section of a laser-welded sandwich of anterior lens capsules (Toluidine blue stain). The effects achieved are well reproducible from spot to spot.

We simulated heterotransplants of fragments of eye lens capsules from a porcine model (*ex vivo*), which may be exploited to assist the eye lens refilling for a surgical solution of the presbyopia (impossible by conventional suturing methods). A stain of gold nanorods was applied at the interface between capsular tissues from a donor eye and a recipient eye. Then by administration of single laser pulses of 40 ms and 100 – 140 Jcm^{-2}, we achieved the local denaturation of the endogenous collagen filaments, which resulted into very satisfactory welds. The numerical simulations and microscopical analysis of the welds (Figure 2) were consistent with temperatures above 50°C. The thermal damage was confined within 50 – 70 µm in a radial distance from the area under direct laser irradiation (Figure 3), which is very important to preserve the vision of a hypothetical patient.

The whole of our preliminary findings is very encouraging to develop functional synergies at the crossroads of nanomedicine and biomedical optics.

References

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