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BioBots: Light-controlled microtools for biological applications

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Technological developments in micro- and nanofabrication have enabled the development of microscopic "tools" or "robots" that can perform a variety of tasks at the microscale. Such microtools are either autonomous or precisely controlled using e.g. chemical reactions, magnetic fields, temperature changes or focused light beams.

Microtools fabricated using two-photon polymerization and manipulated using focused laser light have already been successfully applied in e.g. surface probing [1], material transport [2], localized heating and mixing in microfluidic channels [3] or indirect cell manipulation [4] in water or simple aqueous solutions. We believe there is a need for such microtools to perform different functions in biologically relevant media in order to expand their usefulness for biomedical applications [5]. However, optical manipulation in biological media is a challenging task, due to the optical properties of biological samples and to the presence of chemical interactions between the microtools and various chemical compounds present in such environments.

Our aim is to develop a toolbox of BioBots, light-controlled microtools that can be manipulated in biological media, such as mucus, saliva or serum. Each microtool design is user-driven and tailored to specific microscale tasks. Depending on the number of spherical trapping handles, the 3D-printed microtools can be manipulated in 3D (1 or 2 handles) or with 6 degrees of freedom (3+ handles). The minimum feature size for our 3D-printed tools using two-photon polymerization is of approximately 200 nm, in good agreement with literature. Figures 1 and 2 show examples of light-controlled microtools developed in our lab. To enable such microtools to perform well in biological media, we are combining two approaches: tailoring the properties of the light employed for trapping, and tailoring the surface properties of the microtools.

Real-time optical manipulation in turbid media requires dynamic wavefront correction [6]. We employ several different algorithms to generate phase patterns that can be implemented on a spatial light modulator (SLM) to correct for light scattering in turbid media and thus improve focusing. An example of such a phase correction pattern is shown in Figure 3.

To minimize chemical interactions between the microtools and their environment, we functionalize the surface with compounds that either confer them "stealth" properties (e.g. PEG) or compounds with different charges (e.g. sugars or aminoacids). We use optical tweezers to characterize the interactions between coated particles and biological samples and between coated particles and model cell membranes. A schematic representation of the experimental setup for characterizing the interactions between model membranes and coated particles is shown in Figure 4.

This work contributes to the optimization of drug delivery systems with mucus-penetrating properties for improved bioavailability of peptide drugs upon oral administration.

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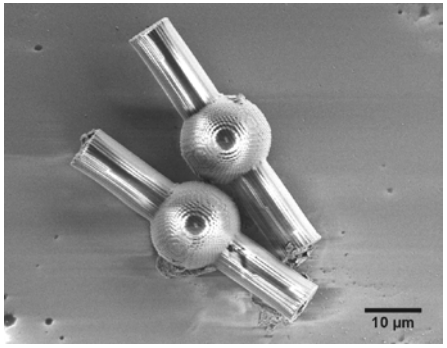

Figure 1. SEM image of a 3D-printed microtool with a single trapping handle allowing 3D optical manipulation.

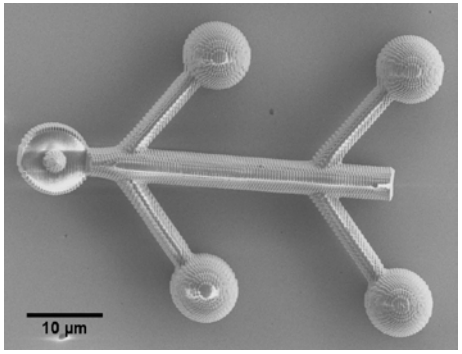

Figure 2. SEM of a disk-tip microrobot with 4 trapping handles allowing optical manipulation with 6 degrees of freedom.

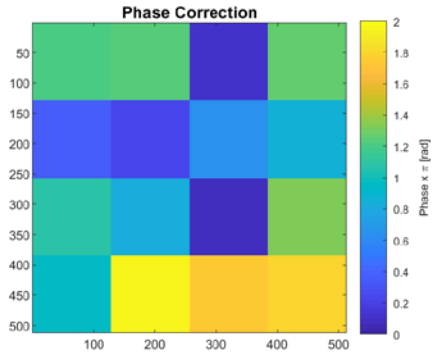

Figure 3. Arbitrary example of phase correction pattern implemented on the SLM to correct light scattering in turbid media and improve focusing.

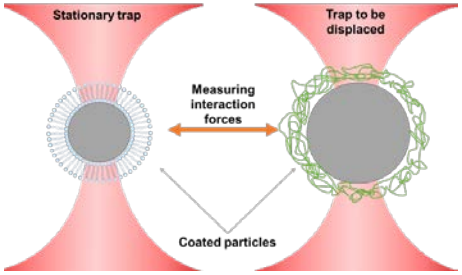

Figure 4. Schematic representation of how a dual optical trap system can be applied for measuring interaction forces between coated microparticles.