LIGHT DIRECTED ASSEMBLY OF BUILDING BLOCKS WITH MICROSCALE CONTROL

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In this study, we demonstrated a high-throughput light-directed assembly as a printing technology by introducing gold nanorods to induce thermal convection flows that move microparticles and cell-laden hydrogel microparticles (diameter = 40 μm to several hundreds of micrometers) to specific light-guided locations, forming desired patterns.

Light-directed technologies, such as optical tweezers [1], optoelectronics tweezers [2], and fiber devices [3], offer precise control of the movement of nano/microscale objects to manipulate functional units. However, high laser intensities are usually required to generate sufficient optical forces to pattern the objects, which might damage micro-bio-objects, such as tissues. To enhance optical forces, researchers developed arrays of plasmonic nanoantennas [4], plasmonic nanostructures and electrokinetics [5] to convert light energy into local heat-generating convection flows for object assembly. Nevertheless, with plasmonic methods, arbitrary control over the configuration was not easily achieved because the assembled structures were predetermined by the patterned nanoarray. To date, a lack of light-directed manipulation technologies exists for the microscale, especially for bottom-up biofabrication using low-power lasers to effectively assemble micro-bio-objects with precise control.

Here, a novel high throughput light-directed assembly method on the microscale was investigated by suspending gold nanorods (GNRs), as photothermal transducers, in a fluidic medium to induce thermoplasmonic convections for the assembly of building blocks fabricated through microfluidics (Figure 1). Because significant local thermoplasmonic convections (Figure 2) were generated by precisely controlling the low-power infrared laser spot size and direction, effective building block assembly with high resolution enabled the desired patterns (Figure 3). By using an automatic motorized stage with optical source integration, the assemblies with desirable patterns were approached with programmable manner (Figure 4). This method was used as an advanced printing technology to form centimeter-scale functional units in ~10 min by integrating various hydrogel building blocks, which were fabricated using droplet-based microfluidics (Figure 5). To illustrate the application of light-directed assembly in bottom-up tissue engineering, we demonstrated that tissue patterns (scaffold-free) with high cell viability and proliferation after long-term culture can be assembled and printed using mesenchymal stem cell (MSC)-seeded microgel as building blocks to form bioinspired microtissues containing an extracellular matrix (ECM) surrounded by MSCs. Excellent cell viability and proliferation were characterized in these microtissues after the long-term culturing of the MSC seeded inside (Figure 6 & 7).

The presented high-throughput, bottom-up method of building block assembly through precise thermoplasmonic convective flow controls can revolutionize current biofabrication processes This method is suitable for biomedical engineering, including surgical operations and *in vivo* applications such as the elimination of a preshaping scaffold and prevention of contamination, as well as reagent delivery and precise cell deposition. With the capability of precisely controlled high-throughput building-block assembly, a broad array of applications is expected, ranging from 3-D bio-printing to regenerative medicine, tissue engineering, bottom-up manufacturing and biofabrication.

Word Count: 457

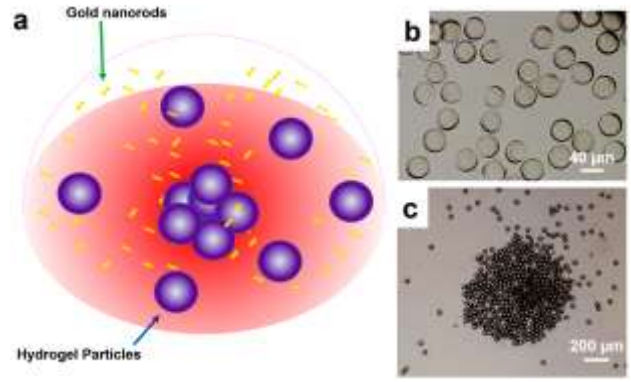

Figure 1. Principle of light assembly of microparticles through plasmonic nanoparticles (gold nanorods (GNRs))

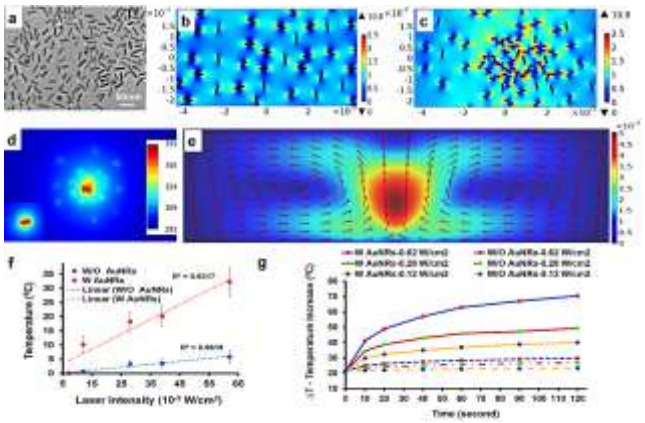

Figure 2. Gold nanorod (GNR) synthesis, simulation and characterization

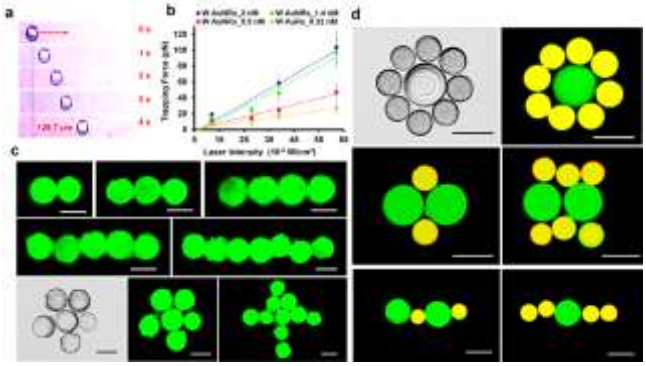

Figure 3. Spatial and temporal control of individual hydrogel microparticle

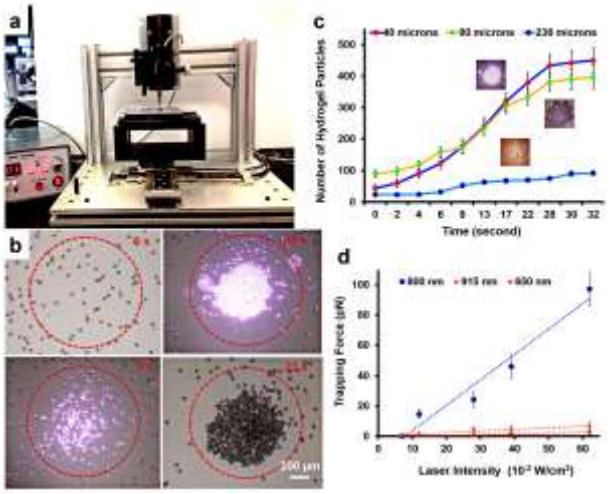

Figure 4. High-throughput light assembly of microparticles by controlling the laser equipped in an automatic stage

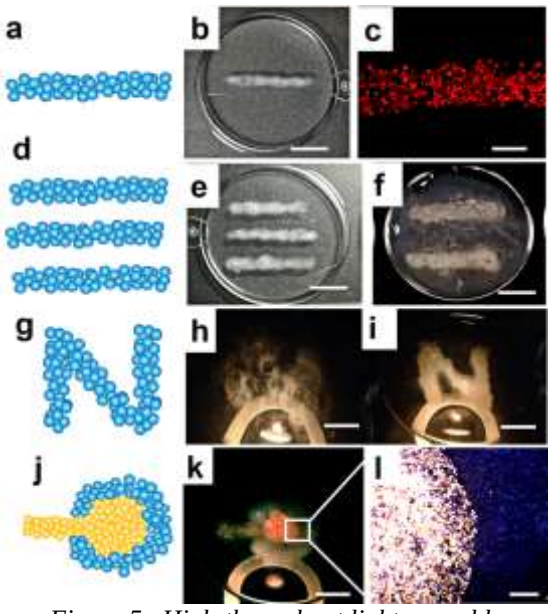

Figure 5. High-throughput light assembly

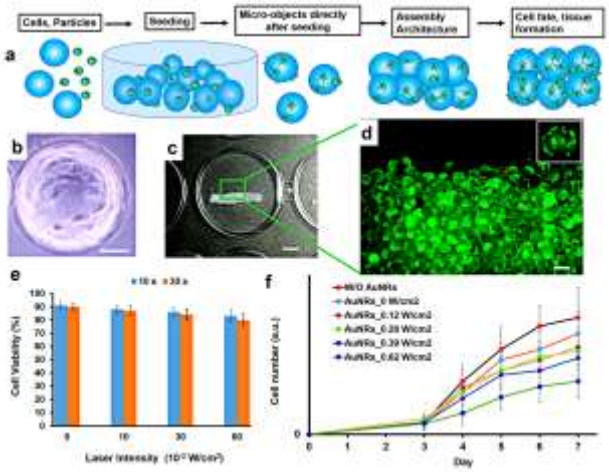

Figure 6. Hydrogel microparticle cell-laden assembly

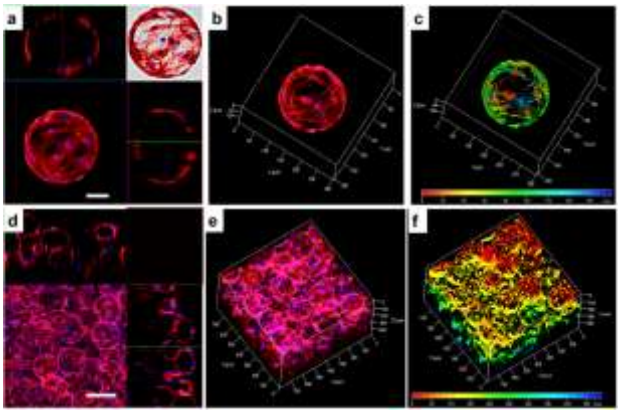

Figure 7. Confocal images of Individual cell-seeded hydrogel particles and scaffold-free by assembling.

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