Directed Assembly of Microscale Hydrogels via Magnetics

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Statement of Purpose: Directed assembly of microscale hydrogels (microgels) is a promising method for constructing complex three-dimensional (3D) geometries that mimic repeating functional units within the human body (*e.g.*, lobule in liver, islet in pancreas). Several methods have been proposed to assemble the microgels, but many are limited by process complexity, low throughput potential, and the use of organic solvents [1, 2]. A simple directed assembly process with high throughput potential is still an unsatisfied step towards recreating *in vivo* tissue structures and functions.
Here we propose a novel magnetic directed assembly method for fabricating 3D construct using microgels. Magnetic nanoparticles (MNPs) were encapsulated in the microgels and manipulated using externally applied magnets. Incorporation of MNPs into microgels creates a new biomaterial that maintains the biocompatibility of hydrogels while contributing additional capabilities for culture, magnetic manipulation and complex 3D assembly of microgels [3,4].

Methods: Microgels (PEG, MW 1000) of different sizes and shapes were fabricated using photolithography. These microgels were fabricated by encapsulating iron (II, III) oxide MNPs within the hydrogels. These M-gels (magnetic nano-particle encapsulated microgels) were attracted with the use of neodymium magnets of 1 tesla power (**Figure 1a**). They were secondary cross-linked along with 5 µl of prepolymer solution for the stability of the structure.

Results: Complex 3D constructs of the microgels were achieved through magnetic directed assembly with precise spatial control. We observed the formation of a 10 mm diameter single layer spheroid within 5 seconds of introducing the magnetic rod. With such time control and varying the concentration of MNPs (0.3%-2%) multi-layer spheroids were fabricated (**Figure 1b**). We achieved a various complex structures using the flexible templates such as arc, dome, sphere and tubular constructs **(Figure 1c-f)**. The observed M-gel assembly confirm that the gravitational force can be balanced by the magnetic force applied via permanent magnets.

Conclusions: Here we reported a directed assembly method of microgels as building blocks via magnetics into larger constructs that mimic *in vivo* structures. These results envisage that this method holds the potential to impact multiple fields including tissue engineering, stem cell technology, regenerative medicine, and pharmacology.

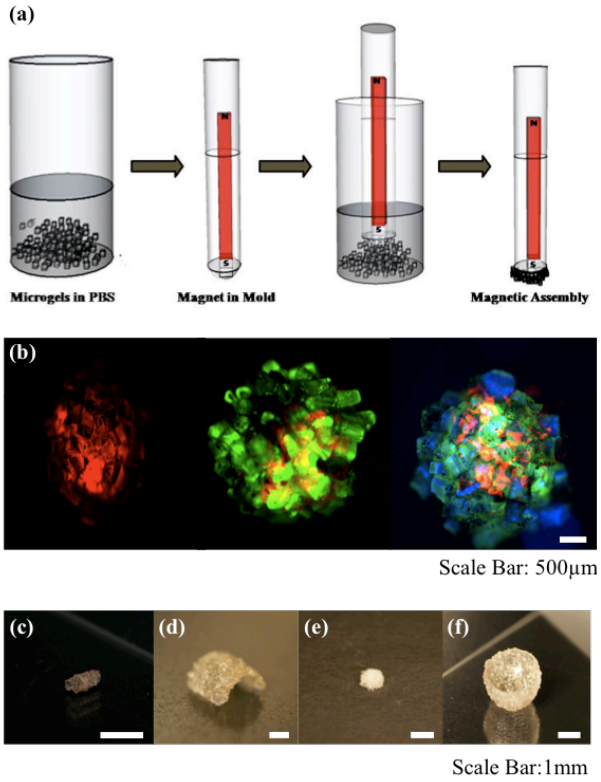

Figure 1. Directed assembly of microgels. (a) Schematic of magnetic assembly; **(b)** Magnetically assembled three-layer sphere; **(c-f)** Magnetically assembled 3D structures.

References:

1. Pampaloni, F., et al.,*The third dimension bridges the gap between cell culture and live tissue*. Nature reviews, 2007.8(10): p. 839-845.
2. Griffith, L.G., Swartz, M.A. *Capturing complex 3D tissue physiology in vitro*. Nature reviews, 2006.**7**(3): p. 211-224.
3. Souza GR, *et al.* (2006) Networks of gold nanoparticles and bacteriophage as biological sensors and cell-targeting agents. *Proceedings of the National Academy of Sciences of the United States of America* 103(5):1215-1220.
4. Souza GR, *et al.* (2008) Bottom-Up Assembly of Hydrogels from Bacteriophage and Au Nanoparticles: The Effect of Cis- and Trans-Acting Factors. *PLoS One* 3(5):e2242..