Microfluidic generation of soft microgels as a tool for studying the influence of 3D microenvironments on the cellular responses upon external stimuli

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Microencapsulation of living cells in biopolymer microgels has been attracting interest due to the microgel's capability to mimic 3D microenvironments on a microscale platform [1-3]. Cells embedded in 3D gel matrices can transduce external physicochemical cues into intracellular biochemical signals, therefore exhibit *in vivo*-like physiological responses.

In this work, we demonstrate that loading gelatine microgels with human liver cells (HepG2 cell line) or probiotic bacteria (*Lactobacilllus plantarum*) using droplet microfluidics can result in: i) the ability to reflect 3D-like toxicity responses of HepG2 cells, as well as ii) the increase the survival rate of *L. plantarum* during exposure to adverse conditions in the gastrointestinal tract. The cell-loaded microgels produced in this process are covalently crosslinked with a naturally derived crosslinker, genipin. This allows the mechanical stiffness of the microgel matrix to be controlled by tuning the crosslinking degree.

Based on this *in vitro* platform, we demonstrate the optimisation of microfluidic parameters for the on-chip droplet generation system and finally determine the mechanical properties of the microgel matrix. We then compare the dose sensitivity of ethanol between 3D-encapsulated and 2D-grown HepG2 cells, and the viability of *L. plantarum* under low pH conditions under encapsulated and non-encapsulated milieux.

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