# Controlled Fabrication of Functional Hydrogel Microspheres via Micromolding and Capillary Microfluidics for Biosensing and Biomacromolecular Conjugation

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Two facile microfabrication techniques for chemically functional and macroporous hydrogel microspheres are presented. First, simple micromolding exploiting surface tension-induced spontaneous formation of polymerizable fluid droplets containing a potent aminopolysaccharide chitosan or acrylic acid as the functional units followed by interfacially initiated radical polymerization leads to controlled macroporous structures and abundant primary amine or carboxylate as the conjugation handles for biomolecular conjugation. Second, capillary microfluidics enables rapid production of uniform or core-shell microspheres with equivalent chemical functionalities in a spatially discrete manner. Carbodiimide and bioorthogonal tetrazine-trans-cyclooctene cyclization reactions are enlisted to examine the interplay between inherent reaction kinetics and mass transfer limitation for carboxylate and amine moieties respectively using small and large fluorescent model proteins. Our results show that the integrated post-fabrication biomolecular conjugation approach offers promising routes for programmable production of biofunctionalized hydrogel microentities toward a large range of applications.