therapeutic products and/or non-medical biological systems with applications found as tissue substitutes, 3D cell and organ biological models, microfluidic biochips and biosensors, and tissue models for study of disease pathogenesis, drug discovery and toxicity testing. This presentation will introduce our recent research in the emerging field of cell printing and report our work on using additive technology for direct cell writing for construction of 3D cell assemble and tissue structures. Presentation topic will include: 1) introduction of direct cell writing process; 2) effect of the process parameters on cell survivability; 3) characterization of biological responses of various cells to the printing process; and 4) applications to the field of tissue science and engineering.

**(2.O14) INNOVATIVE THREE-DIMENSIONAL PLATFORM FOR COMBINATORIAL ANALYSIS OF CELL/BIOMATERIALS INTERACTIONS**

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**Introduction.** High Throughput (HT) systems are an uprising area for analysis of biomaterials properties and cell response to substrates. Combinatorial screening allows for the selection of combinations of biomaterials and/or bioactive agents in a preliminary stage of physicochemical characterization or cell behavior assessment. This leads to time and economically effective studies. To have a closer approach to in vivo settings, studies in three-dimensional (3D) conditions must be performed.

An innovative top-down photolithographic approach is here proposed to obtain biochip platforms for material/cell interaction studies using biomimetic polystyrene superhydrophobic surfaces (SHS). Cell encapsulation in alginate-based hydrogels was used for proof of concept.

**Materials and Methods.** The biochips were prepared by:

• Preparation of polystyrene SHS by a phase-inversion method;

• Generation of superhydrophilic spots by exposure of the SHS to UV/ozone radiation using hollow masks (Fig. 1A);

• Deposition of polymeric solutions mixed with cells, further crosslinked with CaCl2.

**Results and Discussion**. Superhydrophilic spots with controlled shape (squares) could be fabricated in the SHS. Alginate-based hydrogels could be deposited in the spots, keeping separate due to the wettability contrast between the spots and the rest of the substrate, even after immersion in cell culture medium.Two different cell lines - osteoblast-like (MC3T3) and fibroblast-like (L929) – previously encapsulated in the hydrogel matrices were studied after 24 hours of cell culture. The composition of the hydrogels affected cell response, leading to expected tendencies for the well-known polymer mixtures (shown in Fig. 1B).

The evaluation of cell viability and proliferation was performed by direct methods ("chip-destructive"

Materials and Methods: MTS and DNA quantification) and indirect methods (Calcein and DAPI staining image analysis). The results of both methods were consistent (Fig. 1B).

**Conclusions.** A biomimetic-inspired 3D biochip allowed for HT cell culture study and result analysis of combinatorial polymeric blends.

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**Keywords.** High-Throughput; Superhydrophobic Surfaces; Biomaterials; Cell encapsulation

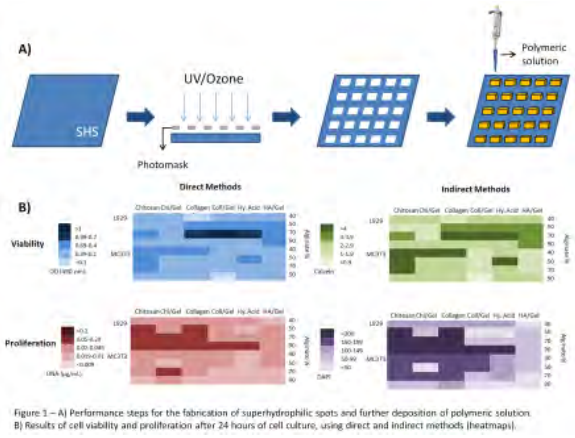


Figure 1 – A) Performance steps for the fabrication of superhydrophilic spots and further deposition of polymeric solution. B) Results of cell viability and proliferation after 24 hours of cell culture, using direct and indirect methods (heatmaps).

**(2.O15) ACOUSTICS DIRECTED MICROPARTICLE ASSEMBLY FOR BIOMEDICAL APPLICATIONS**

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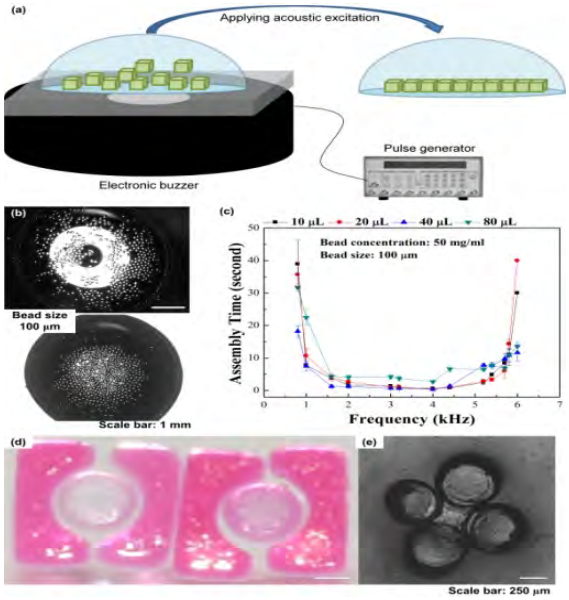
**Introduction**. Directed assembly of microgels holds great potential for applications in tissue engineering and regenerative medicine. However, there are several limitations associated with the existing techniques (hydrophilic-hydrophobic interactions, surface template) such as complexity of assembly process, involvement of organic solvents. There is still an unmet need for straightforward assembly methods. Acoustic techniques are emerging technologies offering several advantages such as decreased instrumentation complexity and gentler handling of pressure and heat sensitive biological moieties such as cells. However, acoustics have not been used for microgel assembly.

**Materials and Methods**. In this study we have developed a novel acoustic assembler to assemble microgels, Figure 1a. Microgels (PEG 1000) of different shapes were fabricated using photolithography. The microgels were deposited onto the hydrophobic surface of a petri dish where 40µL of deionized water was added to the group of microgels. The petri dish was placed above a piezo buzzer (Digi-Key, CPE-827) and exposed to acoustic vibrations produced by a pulse/function generator.

**Results.** To evaluate particle manipulation with our acoustic assembler, we assembled glass microbeads (Figure 1b-c) and microgels with different shapes (Figure 1d-e). After applying acoustic excitation, the microbeads came together at the center of the droplet within 30 sec, Figure 1b. We observed that the microbeads assembly time was dependent on excitation frequency, Figure 1c. During acoustic excitation, we observed that some microgels were immobile due to settling on their untreated surface. It was determined that a frequency sweep provoked mobility in the microgels more so than using a constant frequency, leading to the assembly of orientation specific microgels, Figure 1d-e.

**Conclusions.** In this study we report an acoustic assembler that utilizes microscale hydrogels as building blocks to create larger constructs via external acoustic fields. This approach has potential to impact multiple fields including tissue engineering, regenerative medicine, and pharmacology.

**Keywords.** Microparticle assembly, acoustics, microgels




## (2.O16) MANDIBULAR RECONSTRUCTION USING AN AXIALLY VASCULARIZED TISSUE ENGINEERED CONSTRUCT

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**Introduction.** Tissue engineering and Regenerative medicine depend mainly on the so-called extrinsic mode of neovascularization, where the neovascular bed originates from the periphery of the construct. This method is not applicable for large defects in irradiated fields.

**Materials and methods**. We are introducing a new animal model for mandibular reconstruction using intrinsic axial vascularization by the Arterio-Venous (AV) loop. Cadaveric, mechanical loading, and surgical pilot studies were performed on adult male goats. The cadaveric study aimed at defining the best vascular axis to be used in creating the AV loop in the mandibular region. Mechanical loading studies (3 points bending test) were done to put a base line for further mechanical testing after bone regeneration. A pilot surgical study was done to ensure smooth operative and post operative procedures.

**Results.** The best vascular axis to reconstruct posterior mandibular defects is the facial artery (average length 32.5±1.9mm, caliber 2.5mm), and facial vein (average length 33.3±1.8mm, caliber 2.6mm). Defects in the anterior half require an additional venous graft. The designed defect significantly affected the mechanical properties of the mandible (P value 0.0204). The animal was able to feed on soft diet from the 3rd postoperative day and returned to normal diet within a week. The mandible did not break during the period of follow up (2 months).

**Conclusions.** Our model introduces the concept of axial vascularization for mandibular reconstruction after irradiation. This is the first study to introduce the concept of axial vascularization using the AV loop for angiogenesis in the mandibular region. Moreover, this is the first study aiming at axial vascularization at the site of the defect without any need for tissue transfer (in contrast to what was done previously in prefabricated flaps). Qualitative and quantitative data on angiogenesis and osteogenesis is now being further studied by our team.

**Keywords.** Mandibular reconstruction, Axial vascularization, Bone regeneration, New animal model

## (2.P1) ALGINATE FOAMS FOR TISSUE ENGINEERING

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Scaffolds are important tools in the development of applications within tissue engineering and regenerative medicine. Scaffolds made from calcium cross-linked alginate foams are both biocompatible and biodegradable. This study presents alginate foams with controllable physical characteristics. Alginate foams are produced by mechanically agitating a dispersion of an aqueous solution of alginate, plasticizers, foaming agent, gelling agent and slowly hydrolyzing acid. An insoluble gelling ion salt, e.g. CaCO3, is used and Ca2+ ions are released as pH is lowered induced by the hydrolysis of D-glucono-delta-lactone. The wet alginate foam is then cast in specific shape using a mold, kept at ambient conditions to complete the gelling reaction, and then dried in an oven at 35-80degC. The integrity of the foams was measured using an SMS Texture Analyzer with tensile grips after the dry foam was re-hydrated in a model physiological solution. Both formulation and process were modified to produce foams with different physical characteristics as shown in the figure. Increasing the particle size of CaCO3 from 4 to 20 µm resulted in increased pore size and decreased foam strength. Increased saturation levels of gelling ions from 25 to 125% led to decreased pore size and increased foam strength and stability. There was a relationship between foam strength and alginate molecular weight. However, at similar molecular weights, stronger foams were formed using a G-rich alginate than an M-rich alginate. Generally, the foams have high pliability, they may be cut into specific shapes and sizes, they are not sticky, they can easily be folded and refolded after hydration, and they can be sutured. The foam will easily dissolve by adding agents that chelate Ca2+ such as citrate. Modifications of alginate foam formulations and the production process can be used to construct foams with physical and functional properties tailored for tissue engineering applications.

Keywords. Alginate, scaffold, tissue engineering