UNDERSTANDING BIOINKS FOR EXTRUSION BIOPRINTING WITH LIGHT SHEET FLUORESCENCE MICROSCOPY

Alessia Candeo, Aly Abdelrahman, Soher Jayash, George Morgan, James E Moore Jr, and Gowsihan Poologasundarampillai
Dipartimento di Fisica, Politecnico di Milano, Piazza Leonardo da Vinci 32, I-20133 Milano, Italy
School of Dentistry, University of Birmingham, Birmingham, B5 7EG, UK
Department of Bioengineering, Imperial College London, South Kensington, SW7 2AZ, UK
E-mail : alessia.candeo@polimi.it

KEY WORDS: Bioprinting, light-sheet fluorescence microscopy, additive manufacturing, flow

Additive manufacturing currently sees extrusion-based 3D bioprinting as the leading technology for producing tissue constructs mainly thanks to its simple concept, to the ability to produce constructs at centimetre-scale and to the rapid developments in bioinks. Extrusion bioprinting delivers cells embedded in a hydrogel via a nozzle of <500 μm on a platform. During the extrusion process, the printing parameters and the hydrogel flow behaviour are responsible for mechanically damaged as they pass through the capillary. Indeed, the full understanding of the flow behaviour at the nozzle and the possibility to regulate the printing parameters according to the observed flow are becoming fundamental. Up to now, the study of bioinks, of their behaviour in the nozzle and their impact on printing and cell viability relies on rheological measurements before printing, and on biological assays post printing. When the flow itself at the nozzle level is considered, the community counts on in silico modelling with no experimental data to confirm the theoretical behaviour. Here, we present an investigation based on light sheet florescence microscopy (LSFM) to image and quantify flow of cell-laden hydrogels through a capillary. Quasi-real time images of the flow of different inks in a capillary of 400 μm internal diameter were acquired at various depths at a frame rate of 35 Hz with a light time of 6.3 ms. Moreover, 4D dataset of the whole capillaries were recorded showing possible inhomogeneity of the materials. Cells were annotated and tracked to extract velocity profiles and shear rate to quantify flow and fluid behaviour. Events like eddies formation, fluid compressions and cracking not predicted by modelling were observed. Our work shows the importance of monitoring the flow and change the printing paramenters on-the-go, with LSFM being the most indicate method for the study of bioinks. The experimental observation of hydrogels together with the cells embedded in them flowing through capillaries offered the possibility to enrich what is already known about some state of the art material and feed this into modelling.