

# 3D Bioprinting of Model Tissues that Mimic the Tumor Microenvironment †

Florina Bojin <sup>1,2</sup>, Andreea Robu <sup>3</sup>, Maria Iulia Bejenariu <sup>4</sup>, Valentin Ordodi <sup>2</sup>, Emilian Olteanu <sup>1,5</sup>, Ada Cean <sup>2</sup>, Roxana Popescu <sup>1</sup>, Monica Neagu <sup>1,6</sup>, Oana Gavriluic <sup>1,2</sup>, Adrian Neagu <sup>1,6,7</sup>, Stelian Arjoca <sup>1,6,\*</sup>, Virgil Păunescu <sup>1,2</sup>

<sup>1</sup> Department of Functional Sciences, Victor Babes University of Medicine and Pharmacy Timisoara, Timisoara, Romania

<sup>2</sup> OncoGen Institute, Timisoara, Romania

<sup>3</sup> Department of Automation and Applied Informatics, “Politehnica” University of Timisoara, Timisoara, Romania

<sup>4</sup> Faculty of Mechanical Engineering, “Politehnica” University of Timisoara, Timisoara, Romania

<sup>5</sup> Department of Microscopic Morphology-Morphopathology, ANAPATMOL Research Center, Victor Babes University of Medicine and Pharmacy Timisoara, Timisoara, Romania

<sup>6</sup> Center for Modeling Biological Systems and Data Analysis, Victor Babes University of Medicine and Pharmacy Timisoara, 300041 Timisoara, Romania

<sup>7</sup> Department of Physics and Astronomy, University of Missouri, Columbia, MO, USA

\* Correspondence: [arjoca.stelian@umft.ro](mailto:arjoca.stelian@umft.ro) (S.A.);

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**Abstract:** The tumor microenvironment (TME) affects cancer progression. Thus, the development of TME models is needed for fundamental research and anticancer drug screening. Here, we report the biofabrication of 3D printed avascular models that mimic certain features of the TME. The tumor consists of a hydrogel droplet loaded with breast cancer cells ( $10^6$  cells/mL) encapsulated in the same type of hydrogel containing similar concentrations of primary cells (tumor-associated fibroblasts isolated from the peritumoral environment and peripheral blood mononuclear cells). Hoechst staining of cryosectioned tissue constructs showed that cells remodeled the hydrogel and remained viable for weeks. Histological sections revealed heterotypic aggregates of malignant and peritumoral cells; moreover, the constituent cells proliferated in vitro. To better understand the experimentally observed cellular rearrangements, we built lattice models of the constructs and simulated their evolution using Metropolis Monte Carlo methods. Although unable to replicate the complexity of the TME, this approach enables the self-assembly and co-culture of several cell types of the TME.

**Keywords:** breast cancer; tumor-associated fibroblasts; peripheral blood mononuclear cells; extrusion bioprinting.

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## **Conflicts of Interest**

The authors declare no conflict of interest.