
Preface

Stem cells, 3D tissue models, bioprinting, artificial organs and regenerative medicine are becoming widely accepted as new venues in pursuit of human knowledge. The growing need and substantial progress experienced by these biomedical science and engineering areas over the recent years lead mankind to the coming ‘age of biomaterials’.

The multidisciplinary territory of 3D tissue models formed by the successful fusion of developmental and cell biology, physics, chemistry, mathematics and engineering holds great promise for translational applications such as cancer biology, regenerative medicine, ‘clinical trial on chip’ and personalized medicine-aided ‘healthy ageing’. However, newcomers and even experts working with 3D tissue models should not be mistaken by apparent ease of growing artificial tissues—with some exceptions, a great number of technical challenges exist, which must be faced and solved. Thus, the microheterogeneity and the single-cell level analysis of metabolism, hypoxia, cell proliferation status and other biomarkers have to be measured, quantitatively and with *live tissue* material. Indeed, majority of research groups try to avoid these issues and still rely on the use of fixed or artificially treated, optically cleared tissue samples or end-point assays inherited from the twentieth century, without realizing that the ‘future’ is already here.

Live cell imaging uses novel microscopy techniques and extensively developing probe chemistries to help in facing and solving this problem.

For example, imaging depth can be significantly improved using multiphoton and light-sheet microscopy approaches; on the other hand, the coevolution of fluorescence and phosphorescence lifetime imaging microscopies and data analysis algorithms combined with nanoparticles and new probe chemistries allows to significantly extend the number of measured parameters, creating truly multi-parametric quantitative imaging approach. The area is still very young and immature and needs strong commitment from the users to become widespread and start bringing up its results. To this end, the aim of our book is to bring together some of the leaders and pioneers in the area, to share their experience and provide easy to adapt and modify protocols, methods and techniques.

The book first introduces the reader into the *state of the art* of 3D tissue models, their general compatibility with live cell imaging and advanced imaging options (FLIM and PLIM microscopies) and highlights the available probes and sensors, which are ready to use for multi-parametric imaging in 3D (Chaps. 1, 2, 3, and 4). To extend the scope of the book, Chap. 5 provides a

brief methodological overview in the manufacturing process of 3D scaffold materials, highly useful in creating, maintaining and optimizing the 3D tissue models. The following chapters comprehensively cover most of the available applications of multi-parametric imaging and provide experimental protocols, full of technical details, necessary to guide the beginner in this area: sequential FLIM-PLIM imaging of O₂ and cell cycle in intestinal organoids is described in Chap. 6, intracellular pH imaging in tumour models is described in Chap. 7, technical tips on setting up FLIM microscope and analysis of autofluorescence are described in Chap. 8, high-resolution imaging of Ca²⁺ in live brain is described in Chap. 8 and example of viscosity imaging is described in Chap. 9. Some advanced applications, which can be potentially compatible with FLIM and PLIM, conclude the book: light-sheet microscopy for in situ monitoring of cancer cell invasion (Chap. 10) and Raman microscopy (Chap. 11). Overall, the applications are selected in order to (i) cover the majority of available and successfully used measurement options (including endogenous cofactors, exogenous dyes, nanoparticles and genetically encoded biosensors) and (ii) provide an overview of the practical use of available imaging platforms—from inexpensive laser-scanning systems to two-photon FLIM and light-sheet microscopes. Most of the ‘missing’ applications are discussed in introductory Chaps. 1, 2, 3, and 4.

I wish to thank all the contributors for joining me in this venture, and I believe that altogether the final book represents a comprehensive starting reference guide for the multi-parametric analysis of 3D tissue models, will serve its main function to invite and engage the new people in the area and will remain highly useful for generations of scientists.

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