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Physiological oxygen measurements *in vitro*-Schrödinger's cat in 3D cell biology

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After the development of 3D cell culture methods in the middle of the last century and the plethora of data generated with this culture configuration up to date, it could be shown that a three-dimensional arrangement of cells in most of the cases leads to a more physiological behavior of the generated tissue. However, a major determinant for an organotypic function, namely, the dissolved oxygen concentration in the used *in vitro*-system, has been neglected in most of the studies. This is due to the fact that the oxygen measurement in the beginning was simply not feasible and, if so, disturbed the measurement and/or the *in vitro*-system itself. This is especially true for the meanwhile more widespread use of 3D culture systems. Therefore, the tissues analyzed by these techniques can be considered as the Schrödinger's cat in 3D cell biology. In this perspective paper we will outline how the measurement and, moreover, the regulation of the dissolved oxygen concentration in *in vitro*-3D culture systems could be established at all and how it may be possible to determine the oxygen concentration in organoid cultures and the respiratory capacity via mito stress tests, especially in spheroids in the size range of a few hundred micrometers, under physiological culture conditions, without disturbances or stress induction in the system and in a high-throughput fashion. By this, such systems will help to more efficiently translate tissue engineering approaches into new *in vitro*-platforms for fundamental and applied research as well as preclinical safety testing and clinical applications.

KEYWORDS

physiological oxygen concentration, *in vitro*, 3D cell culture, organoid, microcavity sensor arrays, optical O₂ measurement

1 Introduction

Since the introduction of 3D cell culture techniques by (Holtfreter et al., 1944; Moscona et al., 1957) in the middle of the last century, it has been shown that three-dimensional *in vitro*-approaches are superior to their two-dimensional counterparts in many respects. This superiority is characterized by changes in key cellular parameters that influence the organotypic behavior such as morphology (Paschmann et al., 2013; Li et al., 2017), ability to establish cell-cell and cell-matrix contacts (Druel et al., 2017; Kapalczyńska et al., 2018; Yamada et al., 2022), proliferation behavior (Kapalczyńska et al., 2018; Souza et al., 2018), metabolism (Tidwell et al., 2022; Rybkowska et al., 2023),

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National Library of Medicine (U.S.), 1979 First multi year cumulation covers six years 1965 70 **Neonatal Physiological Measurements** Peter Rolfe, 2013-10-22 Neonatal Physiological Measurements documents the proceedings of the Second International Conference on Fetal and Neonatal Physiological Measurements The book is organized into eight parts The papers in Part I deal with general topics on the monitoring of newborn infants Part II presents studies on cerebral hemodynamics Part III focuses on blood gas analysis Part IV examines respiratory measurements while Part V presents investigations into sudden infant death syndrome Part VII covers applications of nuclear magnetic resonance spectroscopy Part VIII takes up neonatal monitoring technologies for developing countries Part VIII the Appendix contains two keynote speeches The first discusses the measurement of human umbilical venous blood flow in utero The second paper discusses the measurement of fetal heart rate variation **Analyzing Network Data in Biology and Medicine** Nataša Pržulj, 2019-03-28 Introduces biological concepts and biotechnologies producing the data graph and network theory cluster analysis and machine learning using real world biological and medical examples *Fetal Physiological Measurements* Peter Rolfe, 2013-10-22 Fetal Physiological Measurements provides information pertinent to the fundamental aspects of fetal and neonatal physiological measurements This book discusses the accuracy of ultrasound autocorrelation method Organized into seven parts encompassing 45 chapters this book begins with an overview of the various factors that cause fetal heart sounds to differ from those after birth This text then examines the importance of phonocardiography in monitoring the fetal cardiovascular system Other chapters consider the significant relationship between the fetal heart rate patterns and uterine activity wherein each uterine contraction represents a stress for the fetus This book discusses as well the assessment of fetal motor activity in utero which became feasible after the introduction of real time ultrasound into obstetrics The final chapter deals with the primary causes of neurological morbidity and mortality related to determinable events in the neonatal period This book is a valuable resource for obstetricians pediatricians physiologists and biomedical engineers National Library of Medicine Current Catalog National Library of Medicine (U.S.), 1965 *Principles and Practice of Blood-gas Analysis* A. P. Adams, C. E. W. Hahn, 1979 **Colloid Chemistry, Theoretical and Applied: Biology and medicine** Jerome Alexander, 1928 Biology for Medical Entrance (All in One), 2nd Edition Srivastava, Santosh Kumar, 2014 A Book on Biology for Medical Entrance **Issues in Analysis, Measurement, Monitoring, Imaging, and Remote Sensing Technology: 2011 Edition**, 2012-01-09 Issues in Analysis Measurement Monitoring Imaging and Remote Sensing Technology 2011 Edition is a ScholarlyEditions eBook that delivers timely authoritative and comprehensive information about Analysis Measurement Monitoring Imaging and Remote Sensing Technology The editors have built Issues in Analysis Measurement Monitoring Imaging and Remote Sensing Technology 2011 Edition on the vast information databases of

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