

Spatiotemporal ^1H NMR Spectroscopy of 3D Cell Models

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ABSTRACT

The emergence of three-dimensional cell cultures representing tissue features closely, that are weakly reproduced by standard two-dimensional systems, requires adapting established analytical techniques to investigate these challenging new models. It is especially desired to obtain spatially resolved data for living organoids giving insight into transport processes and biochemical characteristics of domains differently provided with nutrition supply and waste product removal. Within this work we present an NMR-based approach to dynamically obtained radial metabolite profiles for cell spheroids, one of the most frequently used 3D models. Our approach combines an easy to reproduce custom-made measurement design maintaining incubator conditions without inhibition of the NMR experiment, with a spatial selective NMR pulse sequence. To overcome the inherently low sensitivity of NMR spectroscopy we modified the selective sequence to achieve faster acquisition and employed a commercially available cryo NMR probe. Finally, radial metabolite profiles could be obtained via double Abel inversion of the measured one-dimensional intensity profiles. Applying this method to Ty82 cancer cell spheroids clearly demonstrates the spatial resolution, for instance confirming exceedingly high lactate and strongly decreased glucose concentrations in the oxygen-depleted core of the spheroid. Furthermore, we dynamically investigate the process of cell death and metabolite degradation after maintaining a spheroid under incubator conditions for several days.