Incubator-independent cell-culture perfusion platform for continuous long-term microelectrode array electrophysiology and time-lapse imaging

Abstract:
Most in vitro electrophysiology studies extract information and draw conclusions from representative, temporally limited snapshot experiments. This approach bears the risk of missing decisive moments that may make a difference in our understanding of physiological events. This feasibility study presents a simple benchtop cell-culture perfusion system adapted to commercial microelectrode arrays (MEAs), multichannel electrophysiology equipment and common inverted microscopy stages for simultaneous and uninterrupted extracellular electrophysiology and time-lapse imaging at ambient CO2 levels. The concept relies on a transparent, replica-casted polydimethylsiloxane perfusion cap, gravity- or syringe-pump-driven perfusion and preconditioning of pH-buffered serum-free cell-culture medium to ambient CO2 levels at physiological temperatures. The low-cost microfluidic in vitro enabling platform, which allows us to image cultures immediately after cell plating, is easy to reproduce and is adaptable to the geometries of different cell-culture containers. It permits the continuous and simultaneous multimodal long-term acquisition or manipulation of optical and electrophysiological parameter sets, thereby considerably widening the range of experimental possibilities. Two exemplary proof-of-concept
long-term MEA studies on hippocampal networks illustrate system performance. Continuous extracellular recordings over a period of up to 70 days revealed details on both sudden and gradual neural activity changes in maturing cell ensembles with large intra-day fluctuations. Correlated time-lapse imaging unveiled rather static macroscopic network architectures with previously unreported local morphological oscillations on the timescale of minutes.