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A blocked split-plot experiment to detect the influential steps in a cell-based bioassay

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Over the last decade, 3-dimensional in vitro cell-based systems, like organs-on-chips, have gained in popularity in the pharmaceutical industry because they are physiologically relevant and easily scalable for high-throughput measurements. We wish to detect influential steps in a cell-based bio-assay using the OrganoPlate® platform developed by the company Mimetas BV. The cells are to form tubular structures grown against an extra-cellular matrix inside the wells of the culture plate. The matrix is created according to a specific protocol. Given that the quality of the matrix strongly influences the tightness of the tubular cell structures, we want to identify which of 8 factors involving features of the protocol affect that tightness. The budget is limited to 32 runs in total. As one plate can accommodate 8 runs, the runs must be spread out over 4 plates. Two factors are time-related, which makes them hard-to-change and creates a split-plot structure in the experiment. Further, batches of extra-cellular matrix material are shared among different runs. In addition, the experimenters wanted to keep track of possible edge effects on the plates based on insights from previous high-throughput platforms, so there is a need to block the runs over the positions on the plate. These features give rise to a complicated error structure and a division of the factor effects of the factors in groups with different standard errors. We developed a fractional factorial design that is compatible with the error structure so that it provides the information needed to optimize the protocol for creating the extra-cellular matrix.

Keywords

organs-on-chips, screening experiment, fractional factorial design

Primary authors: BOHYN, Alexandre (KU Leuven); GOOS, Peter (KU Leuven, Universiteit Antwerpen); Prof. SCHOEN, Eric (KU Leuven); Dr NG, Chee (Mimetas); Mrs BISHARD, Kristina (Mimetas); Mrs HAARMONS, Manon (Mimetas); Dr TRIETSCH, Sebastian (Mimetas)

Presenter: BOHYN, Alexandre (KU Leuven)

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