

New non-invasive, label-free monitoring approach for 2D and 3D cell culture

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Two major issues of cell-based toxicological and drug response assays are the lack of the temporal component of endpoint assays, and the strong dependency of reproducibility and significance on the quality and condition of the cells used. Thus there is a tremendous need to provide insight into the usually inaccessible processes inside the incubator. We developed a novel lensfree imaging method exploiting the optical properties of the cell itself for imaging inside the incubator, which allows non-invasive, super compact, label-free, live-cell monitoring. By applying AI to determine key cell culture parameters such as confluence, proliferation, and cell motility [1], high-quality, automated, objective, and real-time data can be collected. Applying our lensfree microscopy (LM) method, we find that memory effects from heterogeneous cell culture conditions lead to an increase of variance during subsequent assays like e.g. omics-readouts [2] or other cell based assays, like wound healing assays, motility and proliferation assays significantly. Furthermore, our LM is also suitable for 3D applications and will enable quantification of organoid growth dynamics and interactions. Our approach dramatically increases control and processing speed. In the context of the reproducibility crisis, we hope to make a contribution in the direction of standardization of cell-based research in the future.

References

- [1] M. Rempfler et al., "Tracing cell lineages in videos of lens-free microscopy," *Med. Image Anal.*, vol. 48, pp.147-161, 2018.
- [2] P. Bortel, G. Hagn, L. Skos, A. Bileck, V. Paulitschke, P. Paulitschke, L. Gleiter, T. Mohr, C. Gerner and S. Meier-Menches, "Memory effects of prior subculture may impact on the quality of multi-omic perturbation profiles in colon carcinoma cells", *PNAS*, 2024.

