

10 YEARS OF ULTRAMICROSCOPY: OPTICS, BRAINS AND CANCER

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We published the first report on Ultramicroscopy which means here „light sheet microscopy of cleared samples with preserved endogenous fluorescence“ 10 years ago [1]. Since then the number of papers using this technique is growing exponentially and the fields of application are ever increasing. Ultramicroscopy seems to be the ideal technology for systems biology allowing for 3D imaging of whole organisms with subcellular resolution. Though it does not allow the study of living samples due to the chemical clearing applied, it is well suited for studies in developmental biology. For the investigation of many relevant problems in developmental biology it is sufficient to clear and image organisms at different time points to reconstruct their development.

I will report on our latest advances in technology and application of Ultramicroscopy. We could optically correct low power objectives with large fields of view for the study of whole organs. Recently we were able to generate light sheets with a minimal thickness in the one micrometer range and a vastly extended Rayleigh range. These light sheets are pivotal for the fast imaging of whole organisms. They allow the imaging of whole mouse brains with unprecedented detail and the study of neuronal development in whole adult drosophilae. Finally we applied Ultramicroscopy also to clinical pathology. After clearing we could image cm large pieces of human tumors in 3D with single cell resolution using enhancement of cellular autofluorescence. This approach should in future help pathological diagnostics after cancer surgery by providing thousands of optical sections through the tissue. Thus Ultramicroscopy could very soon have a significant impact in clinical medicine.

[1] H.U. Dodt, U. Leischner, A. Schierloh, N. Jährling, C.P. Mauch, K. Deininger, J.M. Deussing, M. Eder, W. Zieglgänsberger; K. Becker “Ultramicroscopy: three-dimensional visualization of neuronal networks in the whole mouse brain”, *Nat. Methods* **4**, 331-336 (2007).