

**SINGLE-MOLECULE OBSERVATION
AT HIGH SPEED IN LIVING TISSUE
BY LIGHT-SHEET BASED FLUORESCENCE MICROSCOPY**

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The capability to observe single molecules in cells and tissue in real-time will fundamentally deepen our understanding of molecular physiological processes. Here we introduce a methodology that combines the optical sectioning effect of light sheet-based microscopy and ultrasensitive high-speed imaging [1, 2]. Using this approach we succeeded to observe small, single biomolecules in solution, living cells and tissue with an unprecedented speed and signal-to-noise ratio. Single molecule observation could be performed in biological samples such as cell nuclei of intact living tissue, e.g fluorescent molecules in salivary gland cell nuclei of *Chironimus tentans* larvae [2, 3]. We measured intranuclear diffusion coefficients of tracer molecules and determined the effective nuclear viscosity. In particular, for the first time ever we directly visualized the intranuclear trafficking and nuclear export of native mRNA molecules packed into messenger ribonucleoprotein particles (mRNPs) in salivary gland cell nuclei, which were marked by the fluorescence labelled RNA binding protein hrp36, the *C. tentans* homologue of mammalian hnRNP A1.

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