

## Live Cell Imaging with 100-nm Resolution Using Structured Illumination Microscopy

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Widefield optical microscopy is a widely used tool in live cell imaging, but its resolution is limited by the visible light's wavelength and the objective's numerical aperture. We have shown previously that using structured illumination in linear regime, the resolution limit of the widefield microscopy can be improved by a factor of 2 both laterally [1] and axially [2], but data acquisition was not fast enough for live imaging. This is mainly because that reconstructing a 2D image requires multiple (9 and 15 in 2D and 3D cases respectively) exposures under different illumination patterns and mechanical pattern switching is slow [1, 2]. Here we demonstrate a structured-illumination microscope that uses ferroelectric liquid crystal-based spatial light modulator (SLM) as the pattern generator and operates in the total internal reflection (TIR) mode. The image acquisition speed is greatly enhanced by the >1 KHz pattern switching speed of the SLM and the TIR mode that allows 2D imaging and thus only 9 exposures per time point. The microscope is capable of 100-nm resolution at frame rates up to 11 Hz for several hundred time points [3]. The speed and resolution of the microscope is demonstrated by imaging tubulin and kinesin dynamics in live *Drosophila melanogaster* S2 cells.

[1] M.G. Gustafsson, "Surpassing the lateral resolution limit by a factor of two using structured illumination microscopy," *J Microsc*, **198(Pt 2)**, 82-87 (2000).

[2] M.G. Gustafsson, L. Shao, P.M. Carlton, C.J. Wang, I.N. Golubovskaya, W.Z. Cande, D.A. Agard, and J.W. Sedat, "Three-dimensional resolution doubling in wide-field fluorescence microscopy by structured illumination," *Biophys J*, **94**, 4957-4970 (2008).

[3] P. Kner, B.B. Chhun, E.R. Griffis, L. Winoto, and M.G. Gustafsson, "Super-resolution video microscopy of live cells by structured illumination," *Nat Meth*, **6**, 339-342 (2009).