High-Speed Plasmonic Structured Illumination Microscopy

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BACKGROUND

Modern optical microscopy has been the key to advancing our understanding of structures and functions of living cells. A major disadvantage, however, has been its diffraction-limited spatial resolution, that is, resolving only features no smaller than half the wavelength used. Several approaches have been developed to overcome this drawback, e.g.: near-field scanning optical microscopy which scans a sharp tip over the object; stimulated emission depletion microscopy, which focuses the irradiation spot to below the diffraction limit; stochastic optical reconstruction microscopy, which locates single fluorophore molecules; and structured illumination microscopy (SIM), which superposes a light pattern on an object with sub-wavelength features to produce fringe patterns that can be optically measured and de-convolved to form a high-resolution image. Significant spatial resolution improvement can be gained using these techniques but with low imaging speed as a trade-off. Standard or linear SIM offers, at most, only a factor-of-two resolution improvement because the illumination pattern used is diffraction-limited. Non-linear SIM applied to fluorescence microscopy achieves >2 resolution enhancement by introducing higher harmonics to the illumination pattern through the nonlinear, saturated fluorescence response; this technique entails additional limitations (e.g., sample heating/damage, need to acquire more images) and is not applicable to scattering.

TECHNOLOGY DESCRIPTION

UC San Diego researchers have developed a method and apparatus to perform fast, nanoscale optical microscopy using structured illumination provided by tunable plasmon interference patterns. The invention is referred to as plasmonic structured illumination microscopy (PSIM). Surface plasmons—electromagnetic waves formed by collective oscillations of electrons at a metal/dielectric interface—propagate such that their wavelength is *shorter* than that of light of the same frequency. Hence, plasmons enable illumination patterns with spatial resolution superior to that attainable by direct use of light and standard optics. In the invention, multiple measurements are obtained with different phase-shifts between the object and plasmonic illumination pattern, which are needed for high-resolution image reconstruction. Phase tuning is implemented using a fast, programmable space light modulator, thus making high-speed data acquisition and dynamic imaging studies possible. PSIM can achieve at least 3- to 5-fold spatial resolution improvement compared with conventional optical microscopy and imaging speeds of ≥ 50 frames/second. It can be implemented for both scattering and fluorescence microscopy, including non-linear SIM, and promises to be a breakthrough tool for studies requiring sub-diffraction-limited resolution and ultra-fast dynamic imaging (e.g., Brownian motion, neurotransmitter imaging).

STATE OF DEVELOPMENT

This invention has a patent pending and is available for sponsored research and/or licensing.

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	8,836,948	09/16/2014	2009-202

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OTHER INFORMATION

KEYWORDS

structured illumination microscopy, SIM, surface plasmon, fluorescence microscopy, sub-diffraction-limit imaging, super resolution

CATEGORIZED AS

- **Engineering**
  - Other

RELATED CASES

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