Lattice light-sheet microscopy without optical lattices

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Owing to its excellent spatiotemporal resolution and low phototoxicity, Lattice light-sheet microscopy (LLSM) has revolutionized 3D imaging of subcellular structures and dynamics. To overcome the limitations of Gaussian beams, LLSM uses propagation-invariant optical lattices which are laterally scanned to create time-averaged, thin, and extended sheets of light. However, the complexity and cost of LLSM can be prohibitive for many laboratories.

Here we present the Field Synthesis theorem, which is the basis for an alternative, universal approach to create light-sheets without lateral beam scanning[1]. The Field Synthesis theorem states that any scanned light-sheet, including LLSM, can be recreated by an incoherent superposition of 1D intensity functions. This series of intensity functions is readily obtained by scanning a thin line over the pupil filter associated with the conventionally scanned light-sheet (see also figure 1). While the mathematical proof of the Field Synthesis theorem guarantees that the final, time-averaged light-sheet is identical, this new approach offers multiple advantages: 1) compared to conventional LLSM, Field Synthesis simplifies the optical train, reduces laser losses and affords for simultaneous multicolor imaging, and 2) when it is applied to light-sheets that scan a confined 2D beam (e.g. Gaussian, Bessel, Airy), the Field Synthesis approach reduces photobleaching.

In this presentation, we will discuss the theoretical foundation of the Field Synthesis theorem and its application to light-sheet microscopy. We show through numerical and experimental comparisons that Field Synthesis can indeed faithfully recreate Lattice and Bessel beam light-sheets. Multicolor imaging of cancer cell morphodynamics is presented using square lattice light-sheets generated by the Field Synthesis approach. We will discuss the potential of Field Synthesis to engineer new types of light-sheets and present preliminary results in an outlook. Due to its flexibility and simplicity, we believe that Field Synthesis will democratize advanced light-sheet microscopy, including, but not limited to, LLSM.

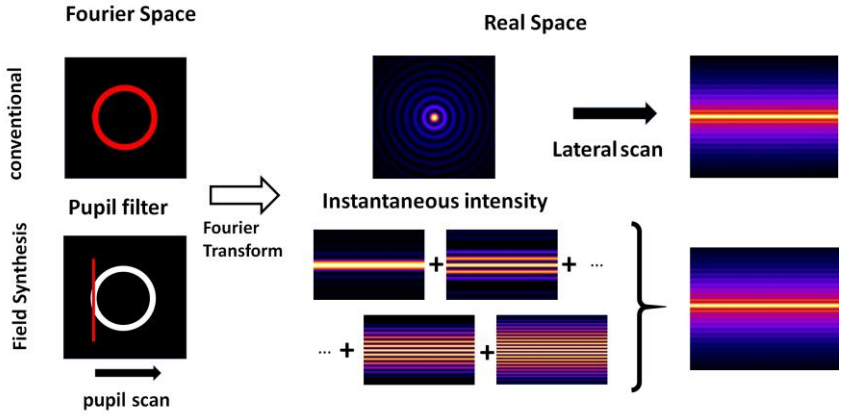

Figure 1: Comparison of conventionally scanned light-sheets (top) and the Field Synthesis approach (bottom).

[1] Chang, Bo-Jui, et al. "Universal Light-Sheet Generation with Field Synthesis." *bioRxiv* (2018): 427468.