Spectral encoding of spatial frequency approach for imaging and characterization of 3D structures

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Probing the internal 3D structure of label-free objects, such as biological cells and tissues in their natural environments, with nano-scale accuracy and sensitivity is of great importance in many biomedical applications. Using the 3D scattering potential description of an object's structure, we present the principle of spectral encoding of 3D spatial frequency (SESF) that encodes different spatial frequencies of the scattering potential into corresponding wavelengths. The SESF principle allows us to (1) perform real-time quantitative dominant-structure imaging of a label-free object. This imaging approach produces a color map in real time in which dominant axial spatial period (or frequency) at each image point is encoded as a corresponding spectral color. We demonstrate the efficacy of real-time imaging using model systems and show the potential of this technique to detect dominant structural changes in pre-cancerous cells that are not visible using conventional microscopy. (2) We extend the SESF principle to measure the entire axial spatial period distribution for each image point. Experimental results based on characterization of cell cycle phases are presented along with comparison with structural information extracted from TEM cell images. (3) Finally, we present spectral tomographic imaging (STI), a new SESF-based integrated tomographic approach that is able to simultaneously reconstruct the 3D object with sub-micron resolution, and also provide spatially-resolved characterization of its structure that has the ability to construct local axial spatial period distribution for any 3D sub-region of interest within the object. Simulation-based examples are presented. In all three cases structural characterization is achieved with nanoscale sensitivity and accuracy.