[TRUE_QPI] High spatio-temporal throughput truly 2D/3D quantitative phase imaging at single-cell level

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Cells are the basic units defining structure and function of living organisms through their growth and differentiation, interaction and communication, aging and apoptosis etc. Research applications such as cell biology, rapid clinical diagnosis and drug screening, require fast and non-destructive functional testing of live cells in big clusters. However, studies based on the single-cell level require thousands of time and manpower consuming analyses to examine all population (cluster) and are especially cumbersome in fluorescent microscopic imaging due to the need of sample labelling and related phototoxicity. Single-cell analysis approach is gaining more and more attention in the life sciences as a capable tool for providing a feasible technical solution enabling fundamental and systematical investigation of the biological composition and cellular heterogeneity in multicellular live cell colonies and tissues. However, in order to overcome the consequential contradiction between "small individuals" and "large colonies", it is urgent to develop new optical imaging techniques for label-free single-cell analysis unveiling subcellular structure in an ensemble of the population. They will allow to precisely locate and accurately measure single cells of interest automatically in dynamically changing highly heterogeneous population, as often only very few cells carry important information (e.g., state of mutation, markers of disease status like Circulating Tumor Cells etc.)

Envisioned research project focuses on establishing new fundamental theories, optoelectronic (optical engineering) systems, and reconstruction algorithms for realizing label-free (non-fluorescent), high-throughput, high-resolution, interferometric and non-interferometric quantitative phase imaging (QPI – 2D imaging) and refractive index tomography (RIT – 3D imaging). Through altering the coherence of the multiplexed illumination and devising novel computational imaging algorithms we will gain experimentally and numerically driven crucial improvement of phase signal to noise ratio and break the space-time bandwidth product limit of the microscopic systems. There are three main scientific work packages within INTENCITY:
(1) developing high-precision 2D QPI methods for imaging unlabeled live cells based on low-coherence common-path digital holographic microscopy and Fourier ptychographic microscopy;
(2) studying 3D RIT realized in interferometric (phase tomography) and non-interferometric (3D ptychography) coding, understanding fundamental links between non-interferometric ptychographic and interferometric tomographic 3D reconstructions, advancing them through novel algorithms and proposing completely new optical microscope for hybrid phase tomography and ptychography – the ShengScope (Fig.1);
(3) comprehensive biomedical imaging and measurements conducted with biological partners to help, in a feed-back loop, optimize the ShengScope layout and reconstruction software and through new opto-numerical methods within this novel system address some of the most challenging questions in single-cell analysis, e.g., for stem cell research and cervical cancer screening.

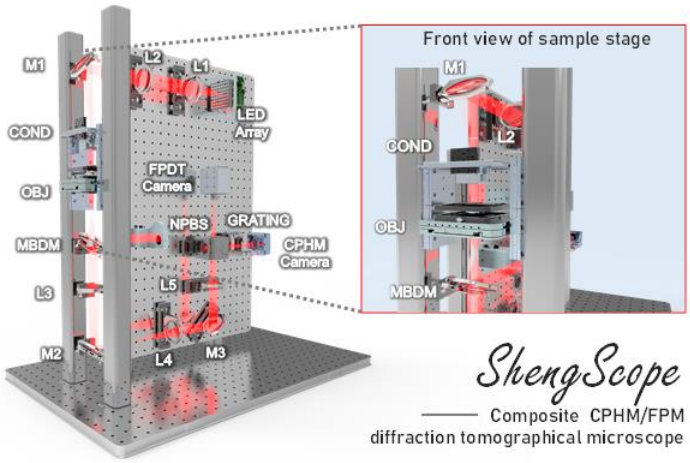

Fig. 1. Prototype layout of the ShengScope– employing 2D/3D phase imaging solutions and merging them into a standalone device poised to address important biomedical challenges in cooperation with biomedical partners. The inset shows the front view of the illumination beam and the sample stage.

The main impact of the research is expected to ensure the theoretical foundation and technical support for the next generation of label-free imaging tools for 2D/3D single-cell analysis enabling life scientists to efficiently study large populations with single-cell precision and subcellular details with easy sample preparation and no contamination. Jointly designed, implemented and tested by WUT/NJUST complementary teams, novel ShengScope will produce a major impact on single-cell label-free investigation empowered by phase microscopy and tomography enabling fast, accurate and non-invasive quantitative diagnosis and cell-culture/tissue analysis.

The main objectives of this project are based on merging complementary expertise of two research teams possessing strong background in experimental interferometric optical metrology (WUT) and non-interferometric quantitative phase imaging (NJUST). Importantly, project envisions close day-to-day remote cooperation of both teams in pursue of the ultimate goal – design, implementation and testing of novel hybrid phase microscope and tomograph with unique layout and dedicated computational architecture to allow for a innovative merger of non-interferometric ptychography and interferometric phase imaging. The expertise and dedication of both teams is crucial as this project could not have been conducted by a single side, which makes in perfectly suitable for SHENG 3 Initiative.