[PHAICELL] Coherent quantitative phase microscopy: revisiting the basics and proposing novel numerical reconstruction methods with applications for advanced label-free bio-imaging
Principal Investigator: PhD Maciej Trusiak, Warsaw University of Technology (Faculty of Mechatronics)

Quantitative Phase Microscopy (QPM) stands out among modern label-free imaging techniques as extremely capable high-contrast approach. "Label-free" means that the sample is not treated with staining nor fluorescence labeling, and can be imaged based on its endogenous contrast agent, i.e., refractive index (introducing measurable optical phase delay). This non-phototoxic non-destructive imaging technique brings biology and metrology closer as it generates quantitative map of live bio-structure (cell mass, volume, surface area and their evolution in time) upgrading visualization of the sample to its stain-free non-invasive optical measurement and enabling precise diagnostics. **The problem to be solved within the PHAICELL** project is connected with the fact that QPM went very dynamically into an application-oriented development, whereas there are still fundamental limits of quantitative phase imaging to be studied. Moreover, basing on exploration of these limits, novel numerical reconstruction techniques will be developed to overcome selected obstacles of currently available QPM systems like, for instance, limited information capacity and phase sensitivity. On top of these fundamental and numerical studies new experimental applications will be considered in the PHAICELL project. These studies are expected to produce new important advances in biomedicine, in particular in stem cell analysis and neurobiology, which we plan to study with our partners from Mossakowski Medical Research Center (MMRC); spermatozoon analysis, which we will study in collaboration with our partners from University of Valencia (ULVC); and fish cells, microplastic pollution and antimicrobial bacteria resistance screening that we will study with our partners from The Arctic University of Norway (UiT). It is important to note that investigations in cooperation with MMRC will be conducted utilizing modified grating-based multi-beam phase microscope – the WUTscope 2.0. The original version of this novel microscope was built in the Institute of Micromechanics and Photonics WUT during the very successful OPUS 13 (PI: Maciej Trusiak) project and constitutes a world-wide unique phase microscope based on diffraction grating with unseen compactness. Throughout PHAICELL we plan to modernize the WUTscope from both numerical and experimental points of view and perform installations in UiT and UVLC of preferably 3D printed systems to facilitate on-site investigations of interesting bio-samples.

In the PHAICELL project we unprecedentedly aim at exploring and defining the limits of QPM in terms of high-speed imaging in low photon flux regime, very noisy interferograms processing and strong bio-object absorption of light, and push these limits. There is a strong world-wide noticeable need to fill the indicated gaps within QPM technology. It is highlighted by increasing number of scientific publications in high impact journals and widely used popular commercial products (e.g., Nanolive). PHAICELL will exploit advanced techniques both in experimental developments, i.e., pseudothermal light sources, custom made waveguide structured, unique WUT-designed phase microscope, and numerical advancements, i.e., adaptive local iterative filtering, variational mode decomposition etc.. Through novelty-driven methodology PHAICELL will attempt to surpass the current state-of-the-art in QPM and enable high-speed, low light intensity noninvasive bio-imaging with limited signal and increase phase contrast accuracy. Biomedical collaborators will ensure the challenging nature of the applications and their timeliness.

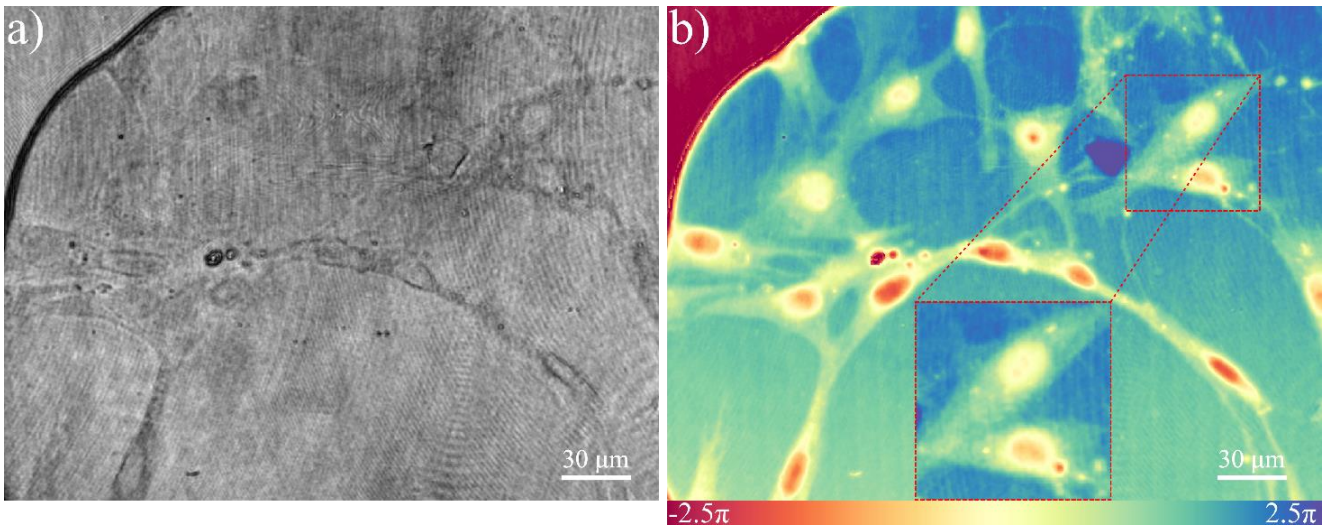

Fig. 1 (a) mesenchymal stem cells seen in the bright field microscope, (b) the same cells seen under the WUTscope. High contrast and highly-specific imaging is to be highlighted and further expanded on dynamic imaging under harsher experimental conditions.