Development of a modular phase microscope based on TIE

Bachelor or Master thesis project
Computational Systems Biology group, D-BSSE, ETHZ
Anticipated start date: 2023

Background and Objective

Quantitative phase microscopy is an emerging technology to study biophysical properties inside a cell such as density, cell mass and dynamics. Depending on the light source they are more or less invasive on the cellular well being. The development of fast, electronic tunable lenses as well as advances in optical theory enable direct quantification of the phase using the transport of intensity equation (TIE) and wide-field illumination. A modular, easy to use add one module would facilitate the usage of quantitative phase microscopy in research and could be used as independent method to cross validate other approaches. In this project we consider the in-house developed prototype based on an Arduino driven electronic tunable lens (ETL) as a starting point for a microscopy add-on module implementation[1–3]. The final assembled module will be driven using a custom, Python based GUI and implement the TIE for the phase reconstruction. To validate the system polystyrene beeds of known size or other suitable nano materials could be used. Finally, the budding yeast *Saccharomyces cerevisiae* grown under different nutrient conditions (SDmin with high, low d-Glucose) will be observed over multiple generations using strains with suitable cell cycle marker (i.e a prototrophic haploid FRY2095, Myo1-mKate2 (3x), Whi5-mKOkappa (1x)) with an emphasis of mass transport from mother to bud.

Project tasks

1. Familiarization with the quantitative phase theory and relevant literature.
2. Implementation of the add on module by designing suitable 3D printed parts to hold the lens (similar to the Thorlabs rail system).
3. Implementation of the TIE algorithm and control software using the existing Arduino prototype.
4. Run calibration experiments with beads or similar materials.
5. Run biological experiments using the strain FRY2095[4], the microfluidic device CellClamper[5], CellX[6,7] YouScope[8].
6. (Optional) Run a beads experiment with the spatial light interference microscopy module (SLIM)[9] in paralel for direct comparision of the retrived densitiyes and cell masses.
7. (Optional) In depth analysis of differences using Fourier analysis to determine differences of the two technologies.

General:

The thesis will include a written report (in English language, with critical assessment of the work) and an oral presentation of the work in our group(s). Additionally, we expect comprehensible written, test driven code development using version control. The delivered hardware and code will be tested for the expected functionality and the aforementioned criteria prior to the thesis evaluation.

Required skills:

Good rapid prototyping skills (3D design & printing); Good programming skills (OOP), preferentially experience with C++ and Python; Knowledge in optics, camera sensors, image generation and processing and electronics; basic knowledge in Molecular biology and the model organism yeast; basic knowledge in statistics and experimental design.

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References:

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