Multiscale Quantitative Phase Imaging for Biomedical Applications

Gabriel Popescu
Quantitative Light Imaging Laboratory, Department of Electrical and Computer Engineering, Beckman Institute of Advanced Science and Technology, University of Illinois at Urbana-Champaign, Urbana, IL 61801, USA
gpopescu@illinois.edu

Light scattering limits the quality of optical imaging of *unlabeled* specimens: too little scattering and the sample is transparent, exhibiting low contrast, and too much scattering washes the structure information altogether. As a result, current instruments, target specifically either the thin (low-scattering) specimens or the optically thick (multiply scattering) samples. We developed spatial light interference microscopy (SLIM) as a high-sensitivity, high-resolution label-free imaging method, which open new applications for studying structure and dynamics. Color SLIM (cSLIM) is a recent development that allows the phase imaging of *stained* tissue slices. Using specimens prepared under the standard protocols in pathology, cSLIM yields simultaneously the typical image that the pathologist is accustomed to (e.g., H&E, immunochemical stains, etc.) and a quantitative phase image, which provides new information, currently not available in bright field images (e.g., collagen fiber orientation).

However, SLIM works best for thin specimens, such as single cell layers and tissue slices. To expand this type of imaging to thick, multiply scattering media, we developed gradient light interference microcopy (GLIM). GLIM exploits the principle of low-coherence interferometry to extract phase information, which in turn yields strong, intrinsic contrast of transparent samples, such as single cells. Because it combines multiple intensity images that correspond to controlled phase shifts between two interfering waves, GLIM can suppress the incoherent background due to multiple scattering. We demonstrate the use of GLIM to image various samples, including standard micron size beads, single cells, cell populations, bovine embryos, and live brain slices. GLIM operates as an add-on to a conventional microscope and overlays seamlessly with the existing channels (e.g., fluorescence). Its recent reflection geometry implementation (epi-GLIM) allows for imaging bulk tissues.

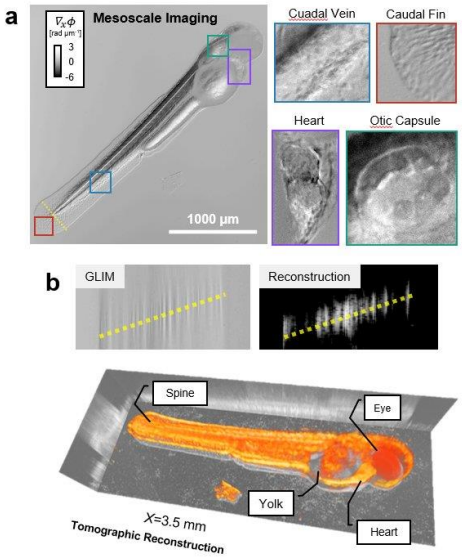

Figure. Live zebra fish tomography using epi-GLIM (Nature Comm., 2019).

References:

1. Kim, T., R. J. Zhou, M. Mir, S. D. Babacan, P. S. Carney, L. L. Goddard and G. Popescu (2014). "White-light diffraction tomography of unlabeled live cells." Nature Photonics **8**(3): 256-263.
2. Horstmeyer, R., R. Heintzmann, G. Popescu, L. Waller and C. Yang (2016). "Standardizing the resolution claims for coherent microscopy." Nature Photonics **10**: 68-71.
3. Kandel, M. E., C. Hu, G. Naseri Kouzehgarani, E. Min, K. M. Sullivan, H. Kong, J. M. Li, D. N. Robson, M. U. Gillette, C. Best-Popescu and G. Popescu (2019). "Epi-illumination gradient light interference microscopy for imaging opaque structures." Nature Communications **10**(1): 4691.
4. Nguyen, T. H., M. E. Kandel, M. Rubessa, M. B. Wheeler and G. Popescu (2017). "Gradient light interference microscopy for 3D imaging of unlabeled specimens." Nat Commun **8**(1): 210.
5. Park, Y., C. Depeursinge and G. Popescu (2018). "Quantitative phase imaging in biomedicine." Nature Photonics **12**(10): 578.
6. Popescu, G. (2011). Quantitative phase imaging of cells and tissues. New York, McGraw-Hill.

Bio

Gabriel Popescu is a Professor in Electrical and Computer Engineering, University of Illinois at Urbana-Champaign. Following his BS and MS in Physics from University of Bucharest, he received his Ph.D. in Optics in 2002 from the School of Optics/ CREOL (now the College of Optics and Photonics), University of Central Florida. He continued his training with the late Michael Feld at M.I.T., working as a postdoctoral associate. He joined Illinois in August 2007 where he directs the Quantitative Light Imaging Laboratory (QLI Lab) at the Beckman Institute for Advanced Science and Technology. Dr. Popescu served as Associate Editor of Optics Express and Biomedical Optics Express, Editorial Board Member for Journal of Biomedical Optics and Scientific Reports. He authored two books, edited another book, authored 175 journal publications, 220 conference presentations, 32 patents, gave 220 lecture/plenary/invited talks. He founded Phi Optics, Inc., a start-up company that commercializes quantitative phase imaging technology. He is a Fellow of OSA and SPIE, and senior member of IEEE.