Post-doctoral position in microscopy

Desired skills/expertise:

- Can design and construct microscopy systems
- Familiar with structured illumination microscopy
- Labview
- Matlab
- Solidworks (or similar 3D CAD)
- Zemax (or similar lens design software)
- Has experience with translating technology to the clinic
- Familiar with basic image processing

Project description/Job description:

Histopathology is the clinical standard for tissue diagnosis. However, histopathology has several limitations including that it requires tissue processing, (sectioning and staining the tissue) which can take 30 minutes or more, and requires a highly trained pathologist to diagnose the tissue. With these features taken together, it is difficult to diagnose tissue at the point of care using histopathology.

Optical microscopy is a powerful technique to obtain high-resolution images of tissue morphology in real-time at the point-of-care, without the need for fixing, sectioning, and staining. In particular, fluorescence microscopy has been combined with vital fluorescent stains to visualize micro-anatomical features.

In conventional fluorescence microscopy, the entire field of view is uniformly illuminated with the excitation light. This creates a problem as fluorophores outside the plane of focus are also excited and emit photons, generating a significant amount of unwanted background fluorescence. This in turn significantly degrades contrast of features of interest in the focal plane. This is a common issue in wide-field fluorescence microscopy and several specialized techniques exist to reject background fluorescence, such as fluorescence confocal microscopy. While extremely effective in rejecting background fluorescence, confocal microscopy requires specialized optics in the form of rapid scanning mirrors and adjustable pinhole collection, which increases the cost and hinders the intra-operative clinical feasibility. In addition, the amount of photons collected at each beam scan position is limited, so the system requires a sensitive detector (such as a photomultiplier tube). Further, because of the small field of view, the beam position has to be raster scanned to be able to survey an area that is in on the order of square millimeter to square centimeter. An alternative approach to reject background fluorescence is using structured illumination microscopy (SIM), where the entire field of view is illuminated with a defined spatial pattern and scanning of a focal spot is not required. Other than the use of patterned illumination, the illumination and collection geometry is identical to that of conventional fluorescence microscopy, so a standard CCD may be used for detection. SIM has been shown to perform equivalently (and at times better) than confocal microscopy with respect to optical sectioning and SNR, particularly in superficial tissues. However, SIM has the added advantage of full-field illumination and non-descanned detection, thus lowering the complexity compared to confocal scanning systems, and increasing the speed with which microscopy of large tissue areas can be performed.

Our group has constructed a bench-top wide-field structured illumination fluorescence microscope and has validated the use of SIM for imaging excised tumor margins from a mouse sarcoma model. However, we would like to extend this analysis to the clinic. In order to measure freshly excised tissue we will need to design and construct a portable SIM system that can fit on a cart. This portable SIM system could be left in the Radiology

suite at the Cancer Center and used to image freshly excised breast biopsy specimens, which we have previously imaged with a high resolution fluorescence microendoscope.

Specific tasks:

- Design and construct a portable SIM system
- Optimize system with computer aided modeling
- Measure a cohort of breast biopsies in the clinic
- Analyze images with a previously validated image processing technique developed in our lab
- Compare results to study completed with the high resolution fluorescence microendoscope
- Mentor and provide guidance to graduate and undergraduate students
- Assist with writing and submitting grants
- Manuscript preparation

Interested postdoctoral applicants should send the following information to msk22@duke.edu:

- Cover Letter
- CV
- Publication List
- Summary of research accomplishments and research interests