OMB No. 0925-0001 and 0925-0002 (Rev. 12/2020 Approved Through 02/28/2023)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.  
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Patrick La Rivière, Ph.D.

eRA COMMONS USER NAME (credential, e.g., agency login): pjlarivi

POSITION TITLE: Professor

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)

| INSTITUTION AND LOCATION | DEGREE  (if applicable) | Completion Date  MM/YYYY | FIELD OF STUDY |
| --- | --- | --- | --- |
|  |  |  |  |
| Harvard University, Cambridge, MA | A.B. | 06/1994 | Physics |
| Cambridge University, Cambridge, UK |  | 06/1995 | Hist. and Phil. of Physics |
| University of Chicago, Chicago, IL | Ph.D. | 12/2000 | Medical Physics |
|  |  |  |  |

**A. Personal Statement**

I am a research-oriented biomedical physicist with a background in inverse problems and a strong interest in emerging imaging modalities. My major research areas have been in computed tomography (both human and micro), x-ray fluorescence tomography, and computational microscopy. In computed tomography, I have developed novel approaches to sinogram restoration and spectral CT data processing that have influenced clinical practice. In X-ray fluorescence tomography, I have pioneered new imaging geometries for this emerging imaging modality that could allow for its deployment in preclinical imaging. Finally, I have begun translating my knowledge of inverse problems and image science to the field of computational microscopy, including for light sheet, polarized fluorescence, and light-field microscopy.

I am very happy to serve as a mentor and resource person to Andrew Sugraman during the course pf this project. I have substantial experience with developing synchrotron microCT techniques for biological samples. Working with Keith Cheng over the last fifteen years, we have made great progress toward optimizing sample preparation and imaging parameters for high-resolution, high-contrast phenotyping of zebrafish and other organisms and are ready to deploy these for the use of the model organism community. I have also collaborated with Bobby Kasthuri and Sean Foxley to develop pipelines allowing for imaging of the same mouse brain across MRI, synchrotron CT, and electron microscopy

**Some relevant ongoing projects include:**

1R24OD035407-01A1**06/15/2024-05/31/2028**

**NIH**

Building a Wide-field, High-resolution Histotomography Resource for Biology

**We propose to establish the groundwork for large-scale access to synchrotron microCT for biology, including a pilot imaging facility at the Lawrence Berkeley National Laboratory (LBNL) and then at Argonne National Laboratory (ANL) for histotomography, to initiate access to visualizations and histotomograms of whole, centimeter-scale model organisms and tissues, and to establish a basic set of web-based visualization and cross-referencing tools for the scientific community.**

**Role: Subcontract PI**

**Moore (La Riviere, Shroff, Colon-Ramos, Kumar; MPI) 9/1/2019 – 12/15/2024 (NCE)**

**Moore Foundation**

**Mapping neurodevelopment in developing organisms with a novel adaptive multiview microscope and automated data analysis**

**Our goal is to map the birth and migration of every cell—neuronal and non-neuronal—in a live, developing worm embryo from fertilization to maturity. We will design and build, at the Marine Biological Laboratory (MBL) in Woods Hole, MA, a novel multiview line scanning confocal microscope with integrated adaptive optics and machine-learning algorithms. This computational microscope will allow unprecedented flexibility in acquiring and interpreting high-resolution fluorescence data deep in a scattering, moving organism.**

**R35GM131843 (Oldenbourg) 06/01/2019-05/31/2025 (NCE)**

**3D imaging of cells and tissues using polarized light microscopy**

**This proposal seeks to develop instrumentation and computational approaches for multi-view polarized light microscopy, development of test targets for calibration, and applications in cell biology. The La Riviere lab will coordinate the physical and mathematical modeling for the birefringence and polarized fluorescence microscopy approaches being developed by Dr. Oldenbourg.**

**Role: Subcontract PI**

**Most relevant citations:**

1. Ding, Y., Vanselow, D.J., Yakovlev, M.A., Katz, S. R., Lin, A. Y., Clark, D. P., Vargas, P., Xin, X., Copper, J.E., Canfield, V.A., Ang, K.C., Wang, Y., Xiao, X., De Carlo, F., van Rossum, D.B., **La Riviere, P. J.,** and Cheng, K. C., “Computational 3D histological phenotyping of whole zebrafish by X-ray histotomography,” eLife (2019);8:e44898 DOI: 10.7554/eLife.44898 (2019). PMCID: PMC6559789.
2. M. A. Yakovlev, D. J. Vanselow, M. S. Ngu, C. R. Zaino, S. R. Katz, Y. Ding, D. Parkinson, S. Y. Wang, K. C. Ang, P. La Riviere & K. C. Cheng, “A wide-field micro-computed tomography detector: micron resolution at half-centimetre scale,” J. Synchrotron Rad. 29, 2022. PMCID: PMC8900834.
3. Foxley, S., Sampathkumar, V.; De Andrade, V.; Trinkle, S.; Sorokina, A; Norwood, K. **La Riviere, P.J**., Kasthuri, N., “Multi-modal imaging of a single mouse brain over five orders of magnitude of resolution,” *Neuroimage*, 238: 118250, 2021. PMCID: PMC8388011.
4. Trinkle, S., Foxley, S., Kasthuri, N., **La Rivière, P. J**., “Synchrotron x-ray microcomputed tomography as a validation dataset for diffusion MRI in whole mouse brain,” *Magnetic Resonance in Medicine*, 86, pp. 1067-1076, 2021. PMCID: PMC8076078.

**B. Positions, Scientific Appointments, and Honors**

**Positions and Scientific Appointments**

2020-pres. Professor, Department of Radiology, University of Chicago, Chicago

2018-present Associate Editor, IEEE Transactions on Computational Imaging

2017-2024 Associate Editor, IEEE Transactions on Medical Imaging

2016-2020 Charter Member, BMIT-A/ITD study section

2014-present Associate Editor, SPIE Journal of Medical Imaging

2013-present Member, Clinical Cancer and Epidemiology Peer Review Panel, ACS, Atlanta, GA

2011-2015 Chair, Imaging and Microbeam Proposal Review Panel, Advanced Photon Source

2011 to 2020 Associate Prof, Department of Radiology, University of Chicago, Chicago

2004 to 2011 Assistant Prof, Department of Radiology, University of Chicago, Chicago, Illinois

2002 to 2004 Instructor, Department of Radiology, University of Chicago, Chicago, Illinois

2000-2002 Physicist, Department of Radiology, University of Chicago, Chicago, Illinois

**Honors**

2020 Fellow, SPIE

2018 Distinguished investigator, Academy for Radiology and Biomedical Imaging Research

2016 Fellow, Marine Biological Laboratory, Woods Hole, MA

2003 IEEE Young Investigator Medical Imaging Scientist Award

**C. Contributions to Science**

**1. Development of approaches for cellular-resolution microCT**

In collaboration with Keith Cheng at Penn State Hershey Medical Center, I have worked to develop novel sample preparation and image acquisition strategies for cellular-resolution microCT using both synchrotron and benchtop microCT. Through careful staining using heavy metals and optimized determination of acquisition parameters (energy and phase-contrast settings), we have shown that whole millimeter-scale organisms and tissue samples can be reconstructed at isotropic, submicron resolution, with sufficient contrast to identify and quantify cells and cell types across the entire volume [1]. This could form the basis for a zebrafish phenome project or for studying the varieties of human tissue in health and disease. We have developed novel cameras with substantially larger fields of view [2]. Finally, in collaboration with Sean Foxley and Bobby Kasthuri, I have developed pipelines allowing for imaging of the same mouse brain across MRI, synchrotron CT, and electron microscopy [3] and shown that this pipeline has promise as a validation tool for diffusion MRI [4].

1. Ding, Y., Vanselow, D.J., Yakovlev, M.A., Katz, S. R., Lin, A. Y., Clark, D. P., Vargas, P., Xin, X., Copper, J.E., Canfield, V.A., Ang, K.C., Wang, Y., Xiao, X., De Carlo, F., van Rossum, D.B., **La Riviere, P. J.,** and Cheng, K. C., “Computational 3D histological phenotyping of whole zebrafish by X-ray histotomography,” eLife (2019);8:e44898 DOI: 10.7554/eLife.44898 (2019). PMCID: PMC6559789.
2. M. A. Yakovlev, D. J. Vanselow, M. S. Ngu, C. R. Zaino, S. R. Katz, Y. Ding, D. Parkinson, S. Y. Wang, K. C. Ang, P. La Riviere & K. C. Cheng, “A wide-field micro-computed tomography detector: micron resolution at half-centimetre scale,” J. Synchrotron Rad. 29, 2022. PMCID: PMC8900834.
3. Foxley, S., Sampathkumar, V.; De Andrade, V.; Trinkle, S.; Sorokina, A; Norwood, K. **La Riviere, P.J**., Kasthuri, N., “ Multi-modal imaging of a single mouse brain over five orders of magnitude of resolution,” *Neuroimage*, 238: 118250, 2021. PMCID: PMC8388011.
4. Trinkle, S., Foxley, S., Kasthuri, N., **La Rivière, P. J**., “Synchrotron x-ray microcomputed tomography as a validation dataset for diffusion MRI in whole mouse brain,” *Magnetic Resonance in Medicine*, 86, pp. 1067-1076, 2021. PMCID: PMC8076078.

**2. Development of novel methods for computational microscopy**

Thanks to the affiliation of the University of Chicago with the Marine Biological Laboratory in Woods Hole, I have developed many collaborations that apply my expertise in inverse problems to the development of new computational microscopy approaches. One strand, in collaboration with Hari Shroff of NIH, involves developing novel approaches to modeling and fusing multi-view data in light-sheet and confocal microscopy, including a mirror-based system to create orthogonal light sheets and capture four views of the sample [1], accelerating multi-view deconvolution [2], developing a multiview line-scanning confocal system [3], and implementing new approaches to 3D structured illumination microscopy [4].

1. Wu, Y., Kumar, A., Smith, C., Ardiel, E., Chandris, P., Christensen, R., Rey-Suarez, I., Guo, M., Vishwasrao, H.D., Chen, J., Tang, J., Upadhyaya, A., **La Riviere, P. J**., and Shroff, H., “Reflective imaging improves resolution, speed, and collection efficiency in light sheet microscopy,” *Nature Communications*, vol. 8, no. 1, p. 1452, 2017. PMCID: PMC5682293.
2. M. Guo, Y. Li, Y. Su, T. Lambert, D. D. Nogare, M. W. Moyle, L. H. Duncan, R. Ikegami, A. Santella, I. Rey-Suarez, D. Green, A. Beiriger, J. Chen, H. Vishwasrao, S. Ganesan, V. Prince, J. C. Waters, C. M. Annunziata, M. Hafner, W. A. Mohler, A. B. Chitnis, A. Upadhyaya, T. B. Usdin, Z. Bao, D. Colon-Ramos, **P. La Riviere**, H. Liu, Y. Wu, and H. Shroff, “Rapid image deconvolution and multiview fusion for optical microscopy,” *Nature Biotechnology*, 38(11):1337-1346, 2020, PMCID: PMC7642198.
3. Wu, Y., Han, Z., Su, Y, Glidewell, M., Daniels, J.S., Liu, J., Sengupta, T., Rey-Suarez, I., Fischer, R., Patel, A., Combs, C., Sun, J., Wu, X., Christensen, R., Smith, C., Bao, L., Sun, Y., Duncan, L.H., Chen, J., Pommier, Y., Shi, Y.-B., Murphy, E., Roy, S., Upadhyaya, A., Colón-Ramos, D., **La Riviere, P.J.,** Shroff, H., “Multiview super-resolution microscopy,” *Nature* 600, 279–284 (2021). PMCID: PMC8686173.
4. Li, X., Wu, Y., Su, Y., Rey-Suarez, I., Matthaeus, C., Updegrove, T.B., Wei, Z., Zhang, L., Sasaki, H., Li, Y., Guo, M., Giannini, J. P., Vishwasrao, H., Chen, J., Lee, S.-J., Shao, L., Liu, H., Ramamurthu, K. S., Taraska, J. W., Upadhyaya, A., **La Riviere, P.J.**, Shroff, H, “Three-dimensional structured illumination microscopy with enhanced axial resolution,” *Nature Biotechnology*. 2023 Jan 26:1-31. PMCID: PMC1049740.

**3. Development of novel methods for computational polarized fluorescence imaging**

We have developed a new theoretical foundation for polarized fluorescence microscopy that allows reconstruction of the 3D spatial distribution and orientation distribution of ensembles of oriented molecules. This is a significant advance over previous work, which either required assumption of isolated single molecules or was limited to 2D projection imaging of both distributions. Our approach was developed through a series of theory papers [1-3] followed by a recent preprint reporting implementation of the approach on a dual-view light sheet platform [4].

1. Chandler, T. Shroff, H., Oldenbourg, R., **La Rivière, P.J.,** “Spatio-angular fluorescence microscopy I. Basic theory,” *JOSA A*, **36**: 1334-1345, (2019). PMCID: PMC7045726.
2. Chandler, T. Shroff, H., Oldenbourg, R., **La Rivière, P.J.**, “Spatio-angular fluorescence microscopy II. Paraxial 4f imaging,” *JOSA A*, **36**: 1346-1360, (2019). PMCID: PMC7045803.
3. Chandler, T. Shroff, H., Oldenbourg, R., **La Rivière, P.J.**, “Spatio-angular fluorescence microscopy III. Constrained angular diffusion, polarized excitation, and high-NA imaging,” *JOSA A* **37**: 1465-1479 (2020). PMCID: PMC7931634.
4. Chandler, T., Guo, M., Su, Y., Chen, J., Wu, Y.,  Liu, J.,   Agashe, A., Fischer, R.S.,  Mehta, S.B., Kumar, A., Baskin, T.I.,  Jamouilĺe, V. Liu, H.,  Swaminathan, V., Nain, A., Oldenbourg, R., La Rivière, P.J., Shroff, H., “Three-dimensional spatio-angular fluorescence microscopy with a polarized dual-view inverted selective-plane illumination microscope (pol-diSPIM),” bioRxiv 2024.03.09.584243 [Preprint]. March 12, 2024. Available from: doi: https://doi.org/10.1101/2024.03.09.584243

**4. Development of algorithms and novel imaging geometries for X-ray fluorescence tomography**

I have worked for several years to develop new image reconstruction algorithms and new image acquisition strategies for X-ray fluorescence computed tomography (XFCT). X-ray fluorescence computed tomography (XFCT) is an emerging imaging modality that allows for the reconstruction of the distribution of nonradioactive elements (mostly metals) within a sample from measurements of fluorescence X-rays produced by irradiation of the sample. Many endogenous metals and metal ions, such as Fe, Cu, and Zn, play critical roles in signal transduction and reaction catalysis, while others (Hg, Cd, Pb) are quite toxic even in trace quantities.

XFCT is a stimulated emission tomography modality and thus correction for attenuation of the incident and fluorescence photons is essential if accurate images are to be obtained. We have developed three different attenuation-correction algorithms for XFCT, each more general and powerful than the last [1]. We have also proposed new data acquisition schemes to minimize attenuation [2].

In recent years, in collaboration with Ling-Jian Meng at UIUC, we have begun to explore radically different ways of measuring XFCT data. Our insight was to exploit the fact that X-ray fluorescence is a stimulated emission modality to perform selective illumination coupled with detection by pixelated cameras through collimating apertures to perform direct imaging without need for tomographic image reconstruction.

1. Meng, L. J., Li, N., and **La Rivière, P. J.,** “X-ray Fluorescence Tomography Using Emission Tomography Systems,” *IEEE Trans. Nucl. Sci*., **58**: pp, 3359-3369*,* 2011. PMCID: PMC3251222
2. Fu, G., Meng, L.-J., Eng, P., Newville, M., Vargas, P., and **La Riviere, P.J.,** “Experimentaldemonstration of novel imaging geometries for x-ray fluorescence computed tomography” Medical Physics, 40, pp. 061903 (11 pages), 2013. PMCID: PMC3663849.
3. Groll, A., George, J., Vargas, P., **La Rivière, P.J.** and Meng, L.-J., “Element Mapping in Organic Samples Utilizing a Benchtop X-Ray Fluorescence Emission Tomography (XFET) System,” IEEE Trans. Nucl. Sci., 62 (5), Oct 2015. PMCID: PMC4686274
4. DeBrosse, H.A., Chandler, T., Meng, L.-J., and La Riviere, P.J., “Joint Estimation of Metal Density and Attenuation Maps with Pencil Beam XFET,” IEEE Transactions on Radiation and Plasma Medical Sciences, vol. 7, no. 2, pp. 191-202, Feb. 2023, doi: 10.1109/TRPMS.2022.3201151.

**5. Development of sinogram restoration strategies for computed tomography**

We have a long-standing research program in sinogram restoration for computed tomography. My group has developed a novel strategy for CT data processing that entails application of a statistically principled penalized-likelihood estimation of the ideal, low-noise line integrals needed for image reconstruction from the noisy degraded transmission measurements [1]. The goal was to achieve some of the benefit of fully iterative reconstruction at a fraction of the computational cost. We collaborated with Philips Research and Development on this work [2] and some ideas were incorporated into Philips’ clinical iDose dose-reduction scheme. We showed that for quadratic penalties, we could achieve very similar performance to fully iterative reconstruction [3] and that edge-preserving penalties provided an improvement over quadratic penalties but could not match the performance of fully iterative reconstruction with edge preservation [4]. While computational power now supports the use of fully iterative in routine CT scans, there is still a role for the ideas of sinogram restoration in dynamic and spectral CT.

1. **La Rivière, P. J.**, and Bian, J., and Vargas, P. A., “Penalized-likelihood sinogram restoration for computed tomography,” *IEEE Trans. Med. Imag.,* **25,** pp. 1022–1036, 2006.
2. Forthmann, P., Kohler, T., Defrise, M., and **La Rivière, P. J.,** “Comparing implementations of penalized weighted least squares sinogram restoration,” Med. Phys. **37**, pp. 5929-5938, 2010. PMCID: PMC2988831
3. Vargas, P. A., and **La Rivière, P. J.**, “Comparison of image-domain and sinogram-domain penalized likelihood image reconstruction estimators, ” *Medical Physics*, 38, pp. 4811-4823, 2011. PMCID: PMC3172866.
4. Little K.J. and **La Rivière P. J.**, “Sinogram restoration in computed tomography with an edge-preserving penalty,” Med Phys. 2015 Mar;42(3):1307. doi: 10.1118/1.4907968. PubMed PMCID: PMC4344471.

## Complete List of Published Work in MyBibliography:

<https://www.ncbi.nlm.nih.gov/myncbi/patrick.la%20riviere.1/bibliography/public/>