Nemonic (NExt generation MultiphOton NeuroImaging Consortium) NeuroNex hub: Advancing multiphoton imaging in neuroscience

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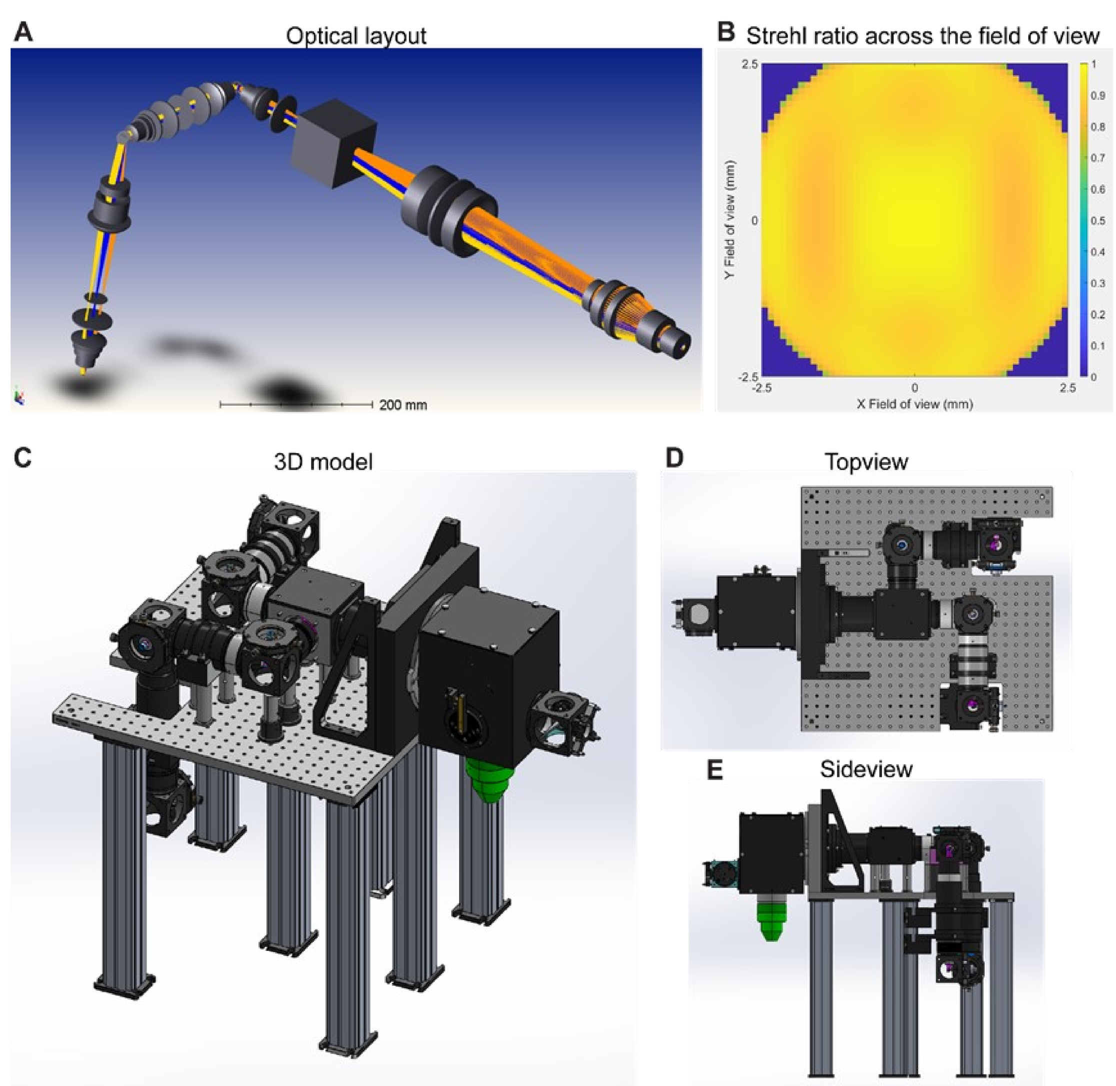
NeuroNex

Nemonic

1. Introduction

The goal of our NeuroNex hub, Nemonic, is to develop and widely disseminate state-of-the-art technology for multiphoton imaging and associated techniques to the neuroscience community, and to advance emerging technology for future innovation in multiphoton neuroimaging. We are currently running case studies using newly developed instrumentation for two- and three-photon imaging. The Nemonic project is also advancing fundamental technologies to enable untethered multiphoton imaging and stimulation in awake animals, and developing imaging modalities that are capable of enhanced resolution that use extended excitation sources yet are compatible with scattering specimens.

2. Dual Independent Enhanced Scan Engines for Large Field-of-View Three-Photon Imaging (Diesel3p)



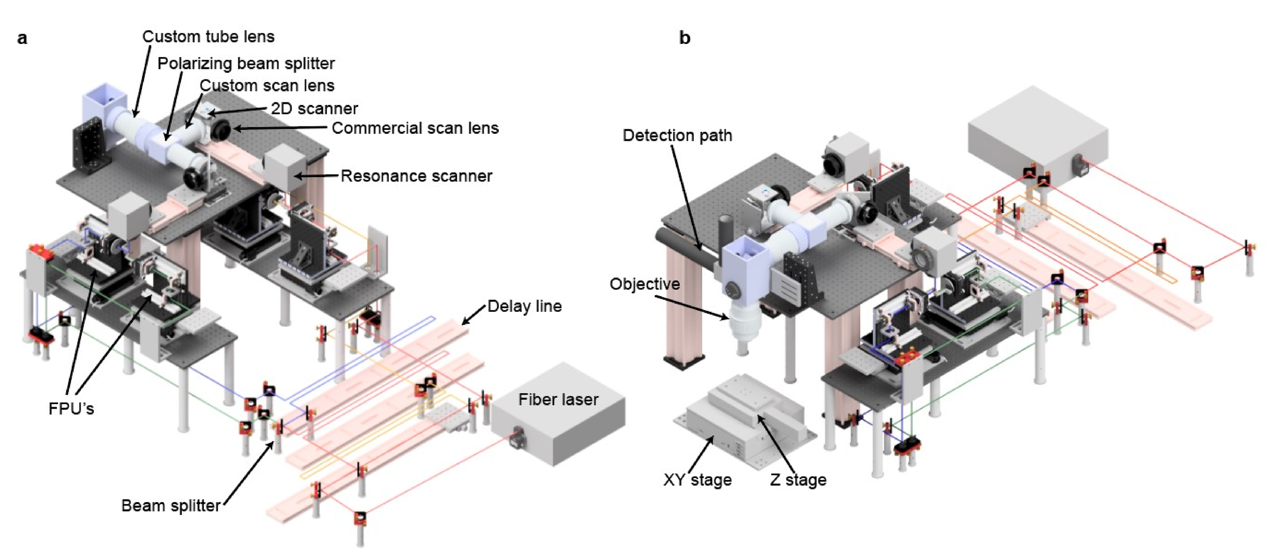
The design of the large field 3-photon imaging system. **(A)** The optical layout. **(B)** Strehl ratio across the 5x5mm field of view for 1300nm excitation wavelength at the imaging depth of 1 mm. The area of Strehl ratio > 0.8 (yellow region) is larger than a 5-mm diameter circle. **(C)** 3D mechanical model of the system **(D)** Topview. **(E)** Sideview.

Features:

- Dual independent scanning engines
- Large field of view : ~5 x 5 mm^2
- Allow simultaneous 2p + 3p imaging, achromatic at 920nm and 1300 nm
- 8-mm long working distance, 360 degree rotatable, 0.54 NA, air objective

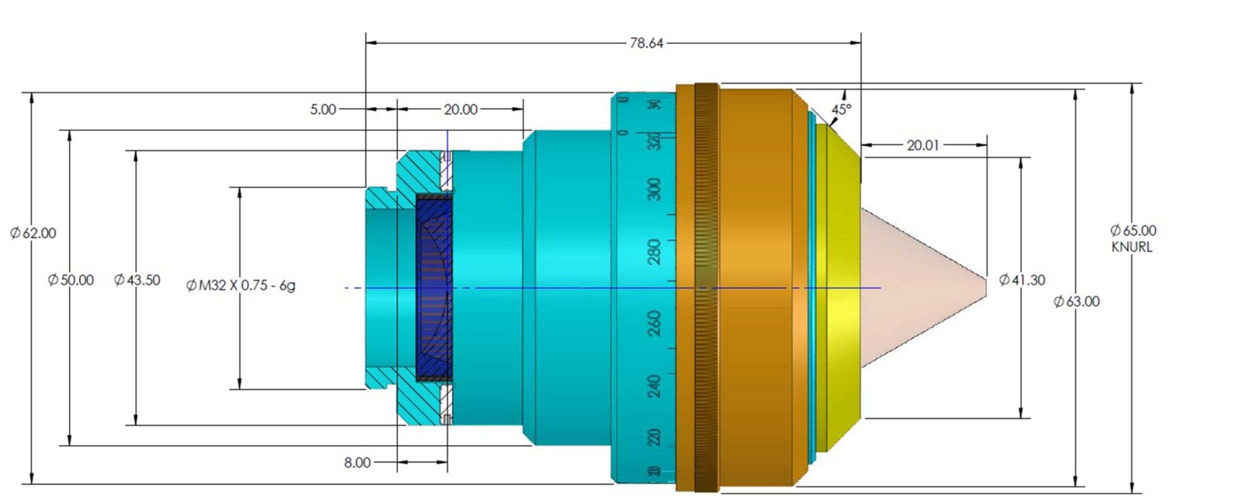
The Diesel3p design is based in part on that of Diesel2p[1], a large field-of-view two-photon microscope.

3. Quadroscope: 4-Beam Large-Field-of-View Two-Photon Microscope[2]



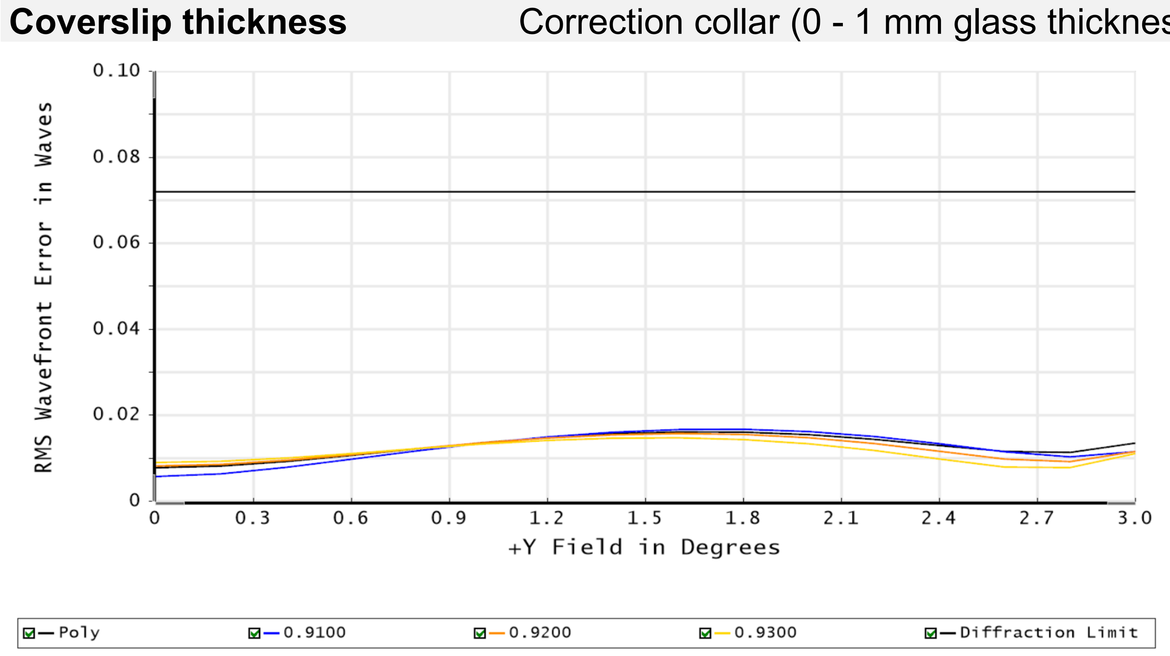
The design of the 4-beam large field two-photon microscope. (**a**) View of the microscope from the side of the beam path. (**b**) View of the microscope facing the objective and stage.

4. 20-mm Long-Working-Distance Objective for Chronic Imaging in Large Animals



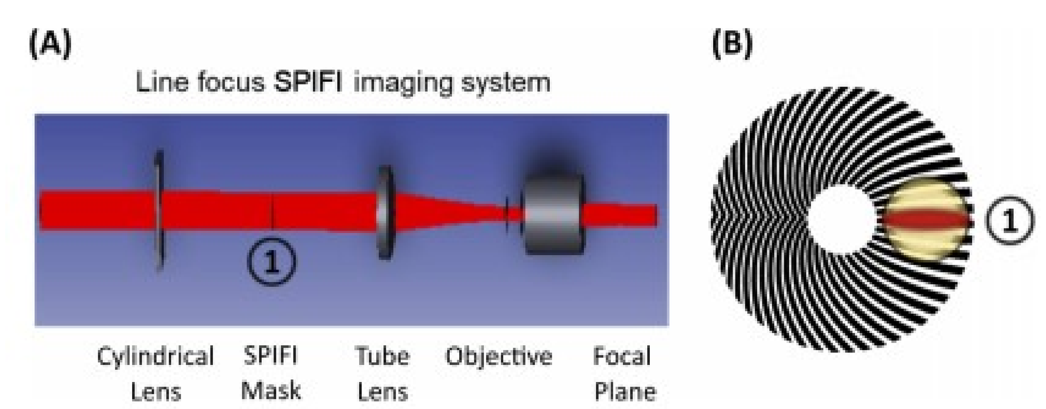
20mm working distance objective for use in animals with thick cranial window preparations, such as cats, ferrets, and non-human primates.

Design wavelength range	920nm ± 10nm
Working distance	20mm
Numerical aperture	0.5
Magnification	10 X (with 200-mm focal length tube lens)
Focal length	20 mm
Field of view	Φ2.08 mm
Scanning angles	± 3 degrees
Entrance pupil	Φ20 mm
Parfocal distance	~90 mm
Mounting thread size	M32 x 0.75
Immersion media	Air
Coverslip thickness	Correction collar (0 - 1 mm glass thickness)

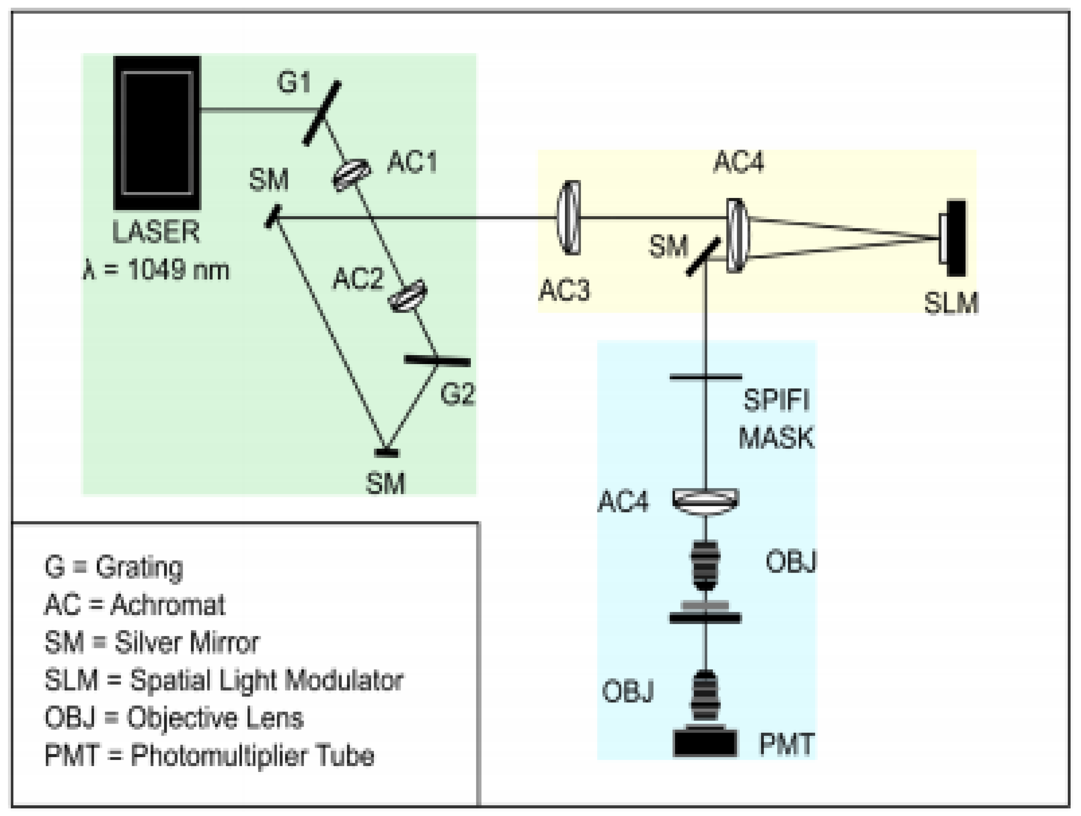


RMS Wavefront Error for the 20mm long-working-distance objective.

5. Random Access, Multifocal SPIFI (Spatial Frequency Modulated Imaging) System[3]



Spatial frequency modulated imaging (SPIFI). (**A**) The SPIFI imaging system using a cylindrical lens to produce a single 1D light sheet. (**B**) The mask at point (1) and the relative position of the cursor is shown. The area highlighted in yellow indicates the field-of-view of the microscope.



The microscope platform and relative layout of the components are displayed in the figure above. Conceptually, the system can be broken down into three sub-systems which are highlighted in green (pulse generation and dispersion compensation: SPARC system), yellow (spatial modulation with spatial light modulator (SLM)) and blue (microscopy platform with single element detection).

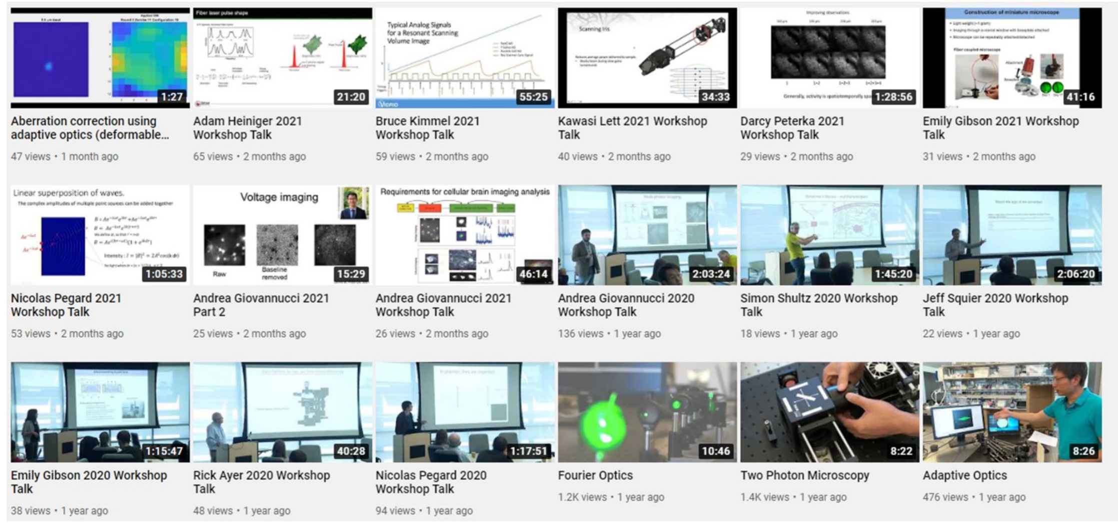
6. Mode-Locking Behavior of On-Chip Distributed Bragg Reflector Mode-Locked Laser[4]

	MLL A	MLL B	MLL C	MLL D	MLL E
Apodization	none	gaussian	gaussian	gaussian	gaussian
CR (nm/μm)	0	0.032	-0.032	-0.016	-0.032
κ at grating center (cm^{-1})	260	260	260	260	350
Threshold current (mA)	61	58	79	83	91
Wavelength at grating reflection peak (nm)	1293.1	1292.1	1297.2	1295.2	1288.4
Minimum pulse width (ps)	12.8	14.4	5.3	7.6	4.5

Summary of Mode-Locked Laser Performance.

7. Dissemination

Key pillars of our dissemination effort include sharing of designs, collaborative efforts, and easy to access online resources. Dissemination is made accessible through videos on our YouTube channel, twitter, as well as our website https://nemonic.ece.ucsb.edu/.



Lens prescriptions for imaging systems are open source, including those of the Diesel3p predecessor, Diesel2p, which is being produced by private companies (INSS and Cosys) with no patent licensing required. A modified quad version of Diesel2p, Quadroscope, is found in Jerry Chen's lab at Boston University. Diesel3p, currently being manufactured, will be assembled in Prakash Kara's lab at the University of Minnesota.

Our 20-mm long working distance objective is currently being manufactured after being preordered at cost by 9 research institutions. The Nemonic NeuroNex hub also hosts a series of high-level technical meetings on emerging technology to create headroom for even further technological development and dissemination.

In addition, we hold yearly workshops to train the next generation of neuroscientist. All materials and recorded talks are made public.

Acknowledgements

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References

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[2] Flexible Simultaneous Mesoscale Two-Photon Imaging Of Neural Activity at High Speeds. https://doi.org/10.1101/2021.04.19.440507. Clough, Mitchell ; Chen, Ichun Anderson ; Park, Seong-Wook ; Ahrens, Allison M. ; Stirman, Jeffrey N. ; Smith, Spencer L. ; Chen, Jerry L. (Preprint)

[3] Two-dimensional random access multiphoton spatial frequency modulated imaging. http://doi.org/10.1364/OE.378460. Allende Motz, Alyssa M. ; Czerski, John ; Adams, Daniel E. ; Durfee, Charles ; Bartels, Randy ; Field, Jeff ; Hoy, Christopher L. ; Squier, Jeff (January 2020, Optics Express)

[4] Integrated dispersion compensated mode-locked quantum dot laser. https://doi.org/10.1364/PRJ.397175. Zhang, Zeyu ; Norman, Justin C. ; Liu, Songtao ; Malik, Aditya ; Bowers, John E. (August 2020, Photonics Research)