



# Recent Research Using Meadowlark Optics Spatial Light Modulators

Meadowlark Optics, Inc.  
5964 Iris Parkway  
Frederick, CO 80504

[www.meadowlark.com](http://www.meadowlark.com)  
[slmsupport@meadowlark.com](mailto:slmsupport@meadowlark.com)  
+1 303-833-4333

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## Imaging in Scattering or Turbid Media

**Overview:** Adaptive optics was first utilized to correct for aberrations that are introduced when imaging through atmospheric turbulence. In monochromatic imaging systems or laser communication systems wavefront correction is most easily accomplished by adding a liquid crystal spatial light modulator to the imaging system. By applying an equal and opposite phase to the SLM it is possible to restore diffraction limited images. In recent years, much of the research on atmospheric turbulence correction is translating to biology, where biological systems introduce scattering and turbidity. For example, SLMs can be used in STED microscopes for deep tissue imaging. In order to maintain the structure of the excitation and depletion sources, the aberrations that the sources will encounter when passing through the sample must be pre-corrected for. Similarly SLMs used in multi-photon imaging systems are used to pre-correct for scattering and aberrations the illumination will encounter when exciting deep tissue targets.

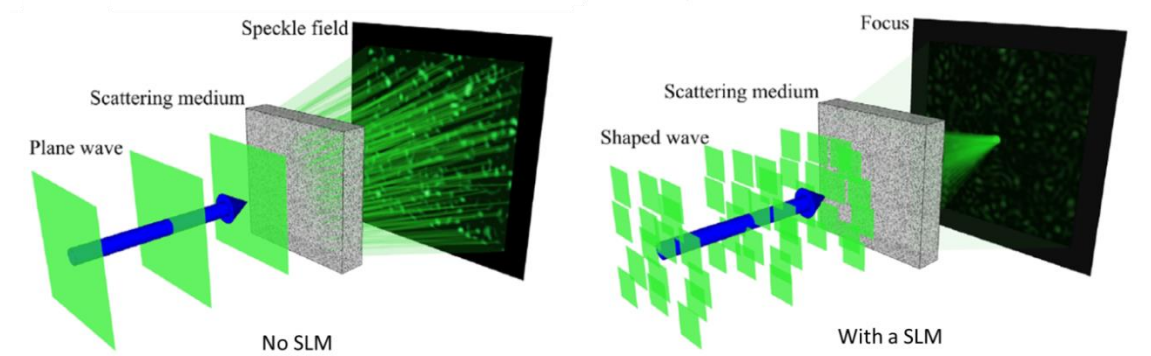


Figure 1 Hemphill, A. S., Tay, J. W., & Wang, L. V. (2016). Hybridized wavefront shaping for high-speed, high-efficiency focusing through dynamic diffusive media. *Journal of biomedical optics*, 21(12), 121502.

**Critical requirements:** For this market the SLM must offer high resolution, phase stability, and high speed switching. The SLM resolution determines the ability to correct for complex aberrations. High phase stability ensures temporally stable excitation which is important when imaging in scattering media with significant losses. High speed SLMs allow for real time adaptive optics.

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## Volumetric Imaging

**Overview:** In order to understand biological functions at a system level it is necessary to image interconnectivity of processes in real time. This is particularly relevant in neuroscience, where the BRAIN initiative is funding research to understand how the brain functions, and how that function is altered by disease. This requires imaging with single cell resolution within a volume as large as possible. There are multiple approaches to volumetric imaging. Light sheet microscopy enables low intensity illumination across a plane of the sample such that large field of view imaging with minimized optical heating is achieved. Similarly scanning a Bessel beam throughout a volume enables compression of a volume of activity into a single plane for deep tissue large field-of-view high-speed imaging.

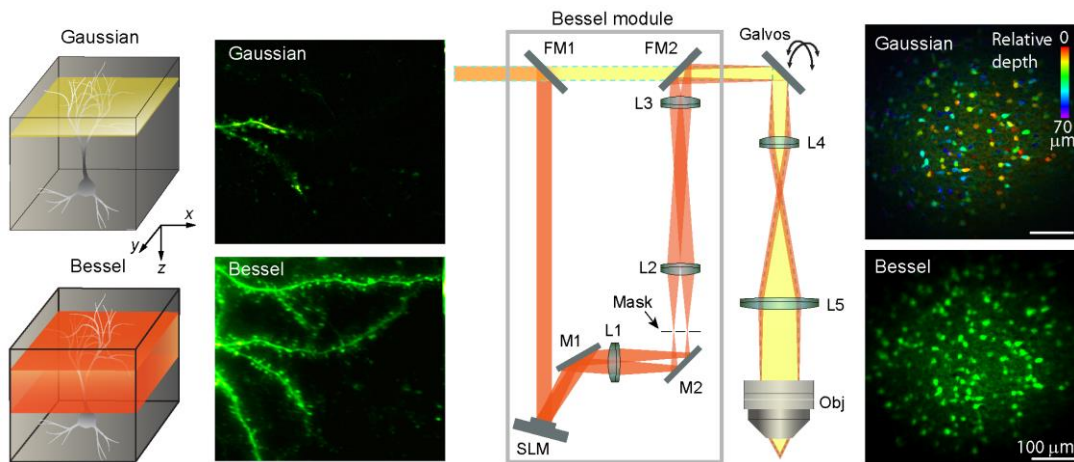


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**Critical requirements:** For this market the SLM must offer high resolution, and high speed switching. The SLM resolution allows the axial intensity of the illumination to be tuned to compensate for losses when imaging through highly scattering tissue. The switching speed of the SLM determines the rate at which the illumination can be scanned axially to extend the volume of imaging.

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## Optogenetics

**Overview:** Despite extensive research, brain function and neurological diseases are poorly understood. Complexities arise from the quantity of neurons in the brain and from the densely interconnected networks of intermixed cell types. There is a need for methods that noninvasively probe the underlying micro-circuitry in the brain with single-cell resolution.

Over the last decade, calcium imaging and photoactivation have emerged as solutions to this problem, providing all-optical means to monitor and manipulate circuit activity. Calcium imaging uses calcium indicators that bind with calcium to alter the fluorescence characteristics of neurons. When a neuron fires, there is an uptake of calcium into the cell body. If the firing neuron is illuminated with an excitation source during the firing event, then the fluorescence emission increases, generating an optical response that corresponds to electrical activity. Complementary to calcium imaging is photoactivation, which can use photosensitive proteins (optogenetics) or optochemical (caged) compounds to manipulate firing patterns either by causing neurons to fire or by silencing neurons. This combination of calcium imaging and photoactivation offers a means for neuroscientists to record the spatiotemporal dynamics of activity and map physical structure of circuits with single-cell resolution.

Liquid crystal spatial light modulators act as a programmable lens that can be used to manipulate the wavefront of the excitation source. In its simplest form, the SLM can be used as a programmable prism, redirecting light to a single focal point with a lateral shift. By adding prism functions together, the SLM can be used to create multiple focal points within a 2D plane. Furthermore, by adding weighting functions and lens functions, the SLM can redirect light to hundreds of focal points with a programmable intensity in a 3D volume. In two-photon microscopes, LC-SLMs enable multisite 3D scanless excitation for photoactivation, as well as high-speed volumetric imaging to record a volume of circuit activity. This combination provides neuroscientists with a toolbox for in vivo studies deep within the cortex to better understand the physical structure of neural circuits, the relationship of firing patterns, external stimuli and the resulting behavior, and how these processes are altered by neurological disease.

**Critical requirements:** For this market the SLM must provide high resolution, high phase stability, low losses, and high speed switching. The SLM resolution determines the field of view of the neural circuits that can be studied. High phase stability ensures temporally stable excitation. Low losses are important for studies of large scale neural circuits where light is divided among the number of neurons under study. High speed switching allows the programmability of the excitation to match rates of naturally occurring circuit dynamics.

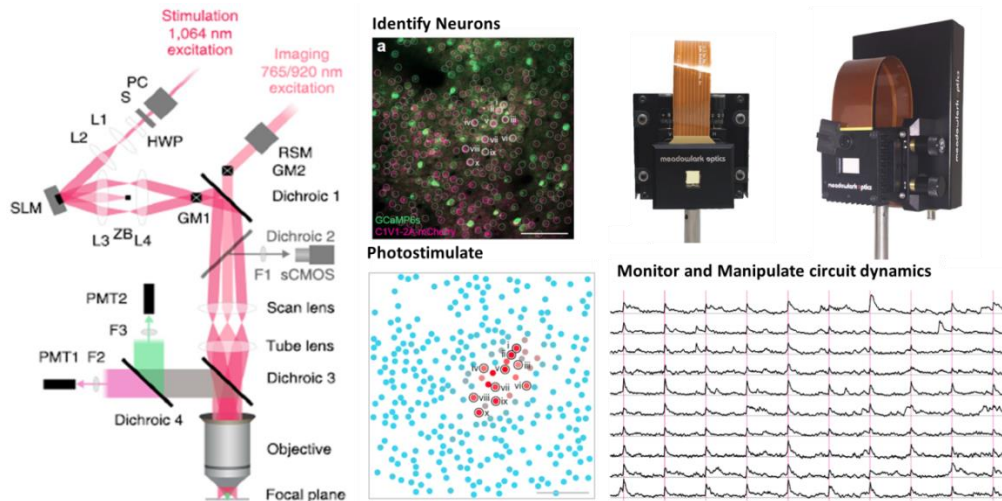


Figure 3 Zhang, Z., Russell, L. E., Packer, A. M., Gauld, O. M., & Häusser, M. (2018). Closed-loop all-optical interrogation of neural circuits in vivo. *Nature methods*, 15(12), 1037.

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## Fiber-based Optical Manipulation

**Overview:** Fiber optic communications have long been of interest, but more recently the technology is being coupled with SLMs for imaging deep in tissue where scattering would otherwise prevent optical techniques from being practical. Much research is focused on imaging through multi-mode fibers due to the small form factor that minimizes damage to surrounding tissue. The challenge of imaging with multi-mode fibers is that manipulation of the fiber alters the phase error that the fiber introduces. High speed SLMs are used not only to remove the phases errors, but also to target excitation at the end of the fiber.

**Critical requirements:** For this market the SLM must provide high resolution, high phase stability, and high speed switching. The SLM resolution determines the ability to correct for aberrations introduced by the fiber and the ability to selectively redirect excitation after propagating through the fiber. High phase stability ensures temporally stable excitation and imaging. High speed allows for real time phase correction in as any handling of the fiber disrupts the phase of propagation.

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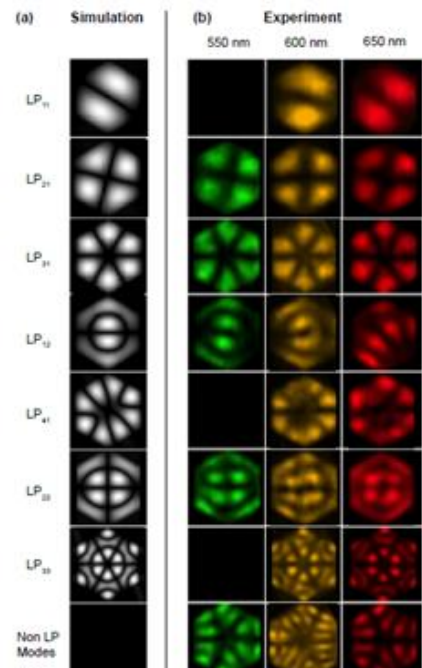


Figure 4 Ruskuc, A., Koehler, P., Weber, M. A., Andres-Arroyo, A., Frosz, M. H., Russell, P. S. J., & Euser, T. G. (2018). Excitation of higher-order modes in optofluidic photonic crystal fiber. *arXiv preprint arXiv:1807.08806*.

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## PSF Engineering

**Overview:** With the recent award of the Nobel Prize to Betzig and Moerner there has been a significant increase in awareness of point spread function (PSF) engineering. In this case the SLM is placed in the emission arm of a microscope. Moerner demonstrated use of PSF engineering with a Meadowlark Optics SLM for super-resolution imaging and 3D localization of fluorescence emitters. PSF engineering has been demonstrated to enable a microscope to image a sample using multiple imaging modalities simultaneously change between modalities non-mechanically. This allows for imaging of structures with a weak refractive index, and for quantitative measurement of phase structures. Imaging modalities that have been demonstrated include: spiral phase imaging, dark field imaging, phase contrast imaging, differential interference contrast imaging, and extended depth of field imaging.

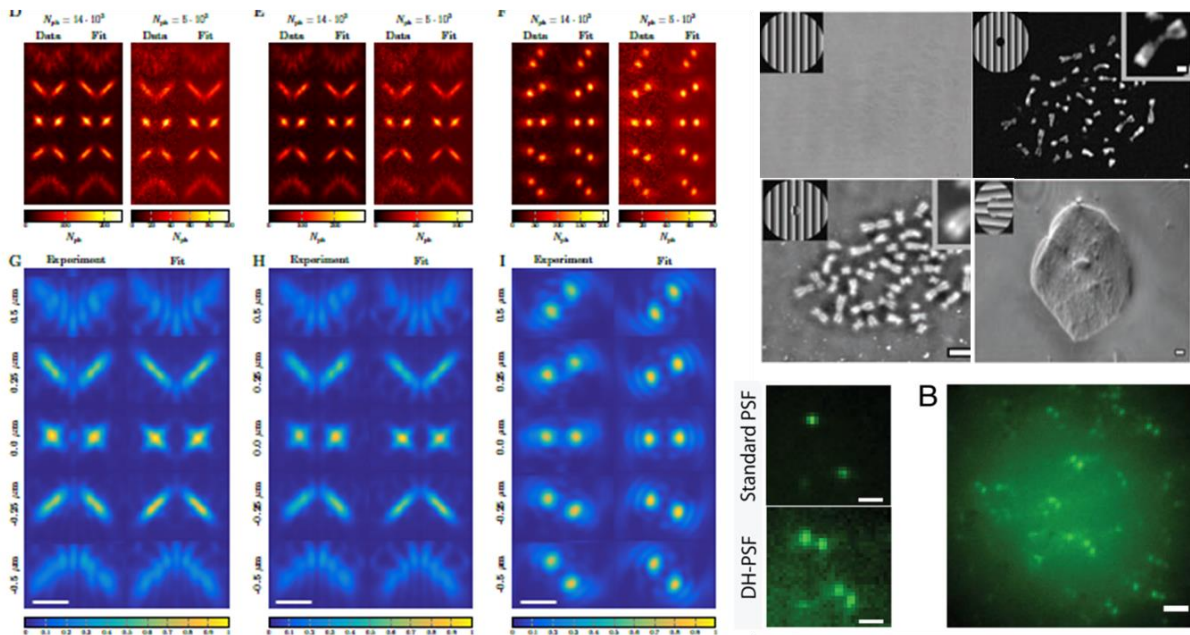


Figure 5 (left) Siemons, M., Hulleman, C. N., Thorsen, R. Ø., Smith, C. S., & Stallinga, S. (2018). High precision wavefront control in point spread function engineering for single emitter localization. *Optics express*, 26(7), 8397-8416. (right top) Maurer, Christian, et al. "What spatial light modulators can do for optical microscopy (right bottom) Pavani, Sri Rama Prasanna, et al. "Three-dimensional, single-molecule fluorescence imaging beyond the diffraction limit by using a double-helix point spread function."

**Critical requirements:** For this market it is important that the SLM minimize optical losses. PSF engineering uses a SLM to manipulate the wavefront in the emission path of the microscope. There is a lack of signal in fluorescence imaging without adding losses. Use of a SLM with a high fill factor minimizes losses to diffraction. High resolution SLMs are ideal for creating the complex phase functions required for 3D localization, and high speed allows for real time deep tissue super-resolution imaging.

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## General Microscopy

**Overview:** Much research is aimed at improving imaging in a variety of conditions such as: correcting for spherical aberrations in 3D imaging far from the ideal focal plane, correcting for motion related artifacts, and developing new imaging modalities. In each case the SLM is used as a powerful tool to supplement and enhance capabilities of traditional microscopes.

**Critical requirements:** Due to the breadth of this category the requirements of the SLM are specific to the scope of the research. Meadowlark's wide range of product options and customizations enable the SLM to be tuned to match the requirements of each new approach to microscopy.

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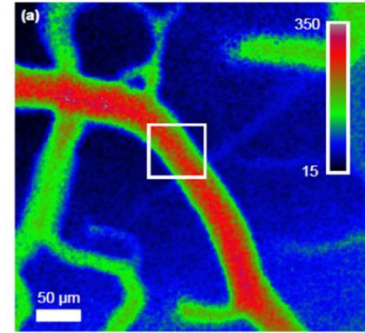


Figure 6 Ringuette, D., Sigal, I., Gad, R., & Levi, O. (2015). Reducing misfocus-related motion artefacts in laser speckle contrast imaging. *Biomedical optics express*, 6(1), 266-276.

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## Holographic Optical Tweezing (HOT)

**Overview:** Holographic optical tweezing uses tightly focused laser beams to manipulate the 3D position of objects within a field of view. This can be used for research in fundamental physics, biological studies, and cold atom trapping. The SLM is used to modulate the phase of an incident laser beam to create a 3D volume of focal points. Objects with a higher refractive index than the surrounding media are pulled toward the waist of the focal points, allowing the ability to manipulate the position of objects with diameters ranging from 10 nm to 100  $\mu\text{m}$  with micron scale control.

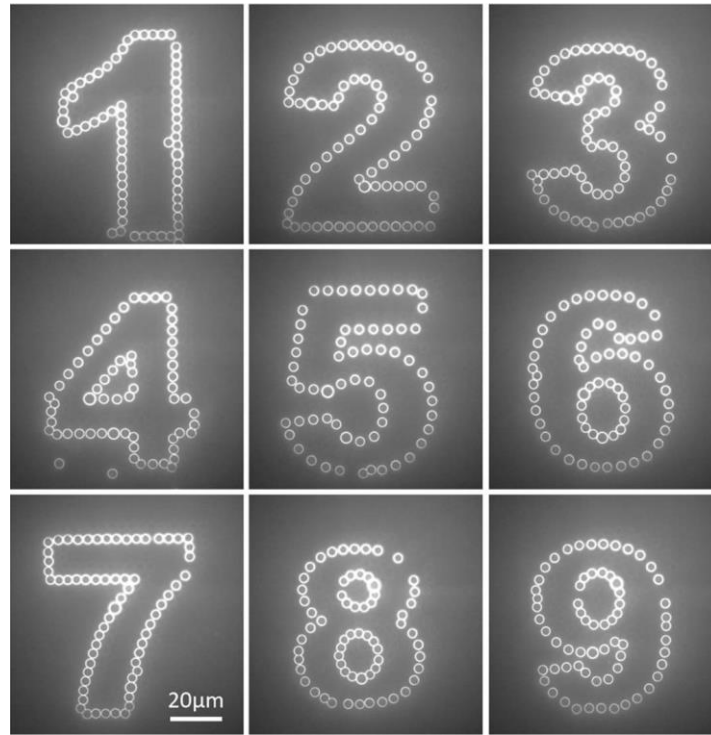


Figure 7 Shaw, L. A., Chizari, S., & Hopkins, J. B. (2018). Improving the throughput of automated holographic optical tweezers. *Applied optics*, 57(22), 6396-6402.

**Critical requirements:** For this market the SLM must provide high resolution, high phase stability, and high speed. The resolution of the SLM determines the field of view that objects can be manipulated in and the number of traps that can be created which determines the throughput of experimental studies. The phase stability of the SLM allows the incident power to be minimized while maintaining a stable trap. Use of a high speed SLM has been demonstrated as a means to dynamically dampen Brownian motion to maximize trap strength and minimize required incident power to maintain a stable optical trap. For work with biological samples, limiting the incident power and duration of exposure are critical to maintaining viability.

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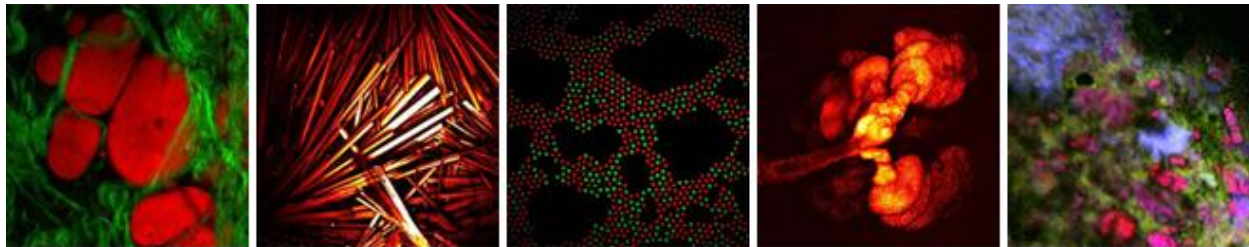
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## Pulse Shaping

**Overview:** By modulating the phase and/or amplitude of spectral component of broadband femtosecond lasers it is possible to generate arbitrarily shaped ultrafast optical waveforms. Applications for this technology include optical communications, biomedical optical imaging, high power laser amplifiers, quantum control, and laser-electron beam interactions. The typical implementation utilizes a grating to spatially separate spectral components of a femtosecond laser onto an SLM. The SLM can simultaneously introduce a phase bias and diffraction grating to control the phase and amplitude of each spectral component. The reflected light from the SLM is recombined to form an ultra-short pulse. Shaped pulses can be used to tune excitation in CARS microscopes, for spectroscopy, for machining and laser marking, nonlinear microscopy, and communications.



**Critical requirements:** This market requires phase stability, and resolution such that a single SLM can modulate the phase and amplitude of spectral components. 2D SLMs are ideal if the lateral resolution is sufficiently high for the range of wavelengths being modulated. The columns of the SLM are then utilized as diffraction gratings to superimpose amplitude modulation on the phase bias.

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