Corporate Case Study

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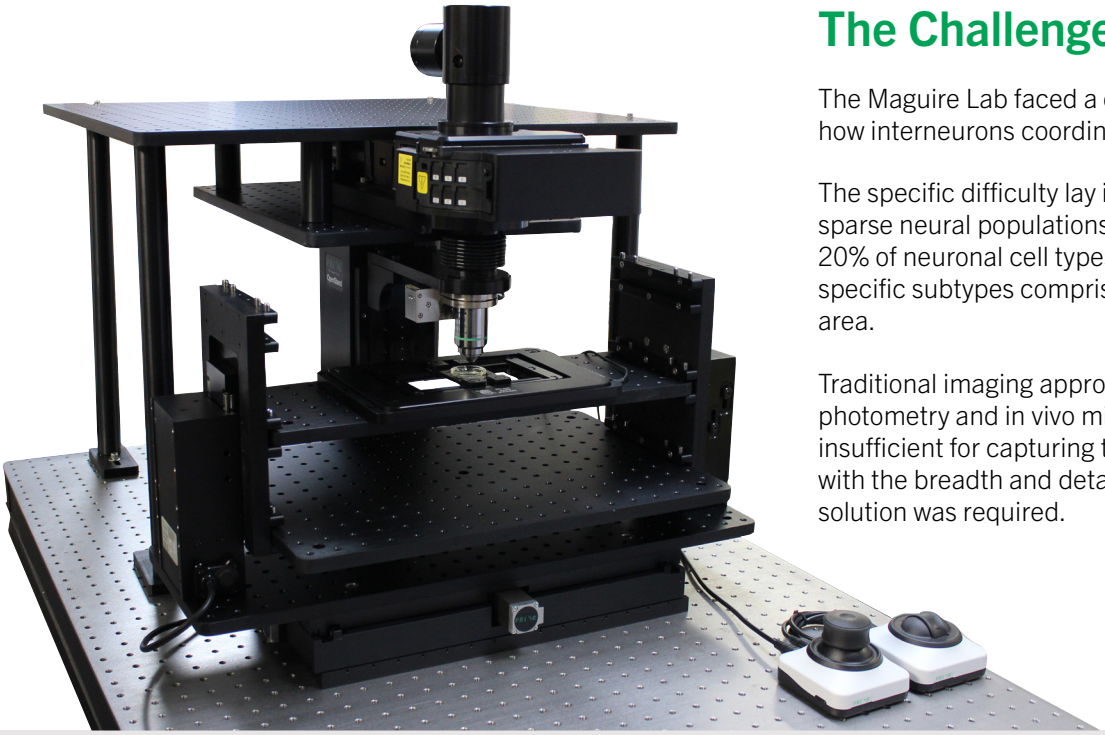
Tufts University School of Medicine
Advanced three-camera system for neurobiology

When The Maguire Lab at Tufts University School of Medicine needed a specialized system to capture simultaneous images for its research, Prior Scientific helped develop a unique three-camera widefield and confocal scanner for fluorescent imaging.



The Challenge

The Maguire Lab faced a complex challenge in studying how interneurons coordinate network activity in the brain.

The specific difficulty lay in observing and analyzing sparse neural populations. Interneurons make up only 20% of neuronal cell types in any brain region, with specific subtypes comprising just 5% of cells in a given area.

Traditional imaging approaches, including fiber photometry and in vivo microscopic imaging, proved insufficient for capturing these sparse cell populations with the breadth and detail needed, so a more customized solution was required.

About The Maguire Lab

The Maguire Lab is a research program at Tufts University School of Medicine in Massachusetts that investigates the underlying neurobiology of numerous disorders, with a focus on epilepsy and postpartum depression.

The lab's research investigates the role of GABAergic signalling and stress in the control of neural networks and the contribution to both physiology and pathophysiology.

It aims to bridge critical knowledge gaps and contribute to the development of effective treatment options.

"It felt like everyone was working as part of a team to build this together and it was a really great experience from the start to end."

All quotes from: Jamie Maguire, Ph.D; Kenneth and JoAnn G. Wellner Professor; Director, Building Diversity in Biomedical Sciences (BDBS) program

The Requirements

The Maguire Lab needed a sophisticated imaging solution that could simultaneously observe multiple cell types across a wide field of view to see the whole population structure, while also maintaining single-cell resolution.

Ultimately, their goal was to observe how the cells behave and coordinate amongst themselves in different circumstances and they needed a system that could record from multiple different cell types at the same time.

After exploring various approaches, the team identified several critical requirements for their ideal imaging system:

- Capability to record multiple cell types simultaneously.
- Wide-field view to observe entire structures.
- High-speed image acquisition.
- Multiple cameras for capturing different emission spectra.
- Low magnification while maintaining high resolution.
- Large working distance to accommodate electrophysiological chamber and equipment for simultaneous imaging and electrical recording.
- Flexibility to integrate with electrical recording equipment.

The Solution

Development of a stable, repeatable, and functional system that would operate with three separate cameras for more accurate and efficient data capture was the primary objective.

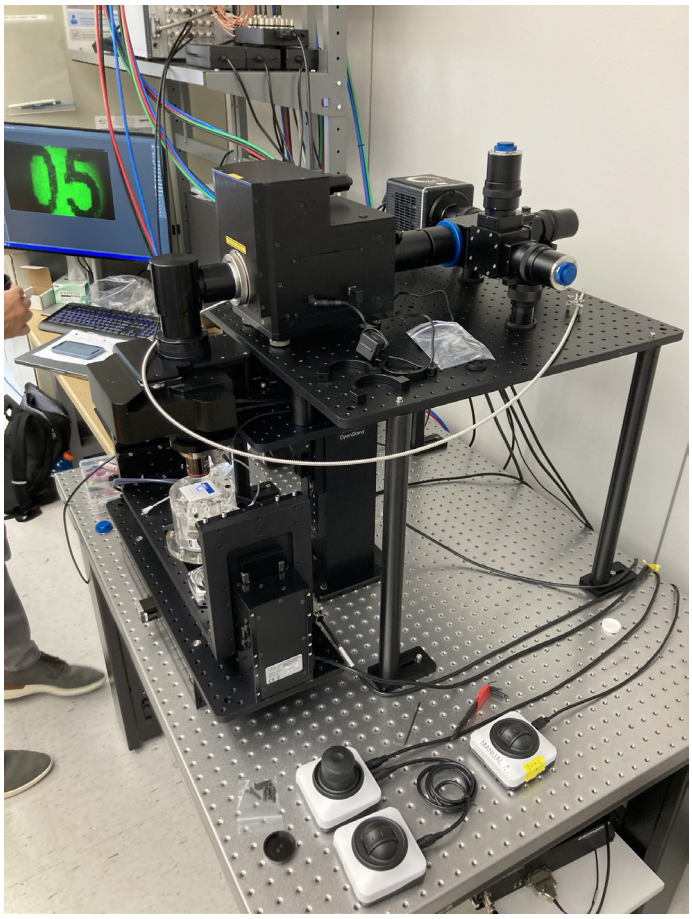
The typical solutions of using a single camera with fast filter switching via a motorized filter wheel or using a single triple-bandpass dichroic filter plus spectral unmixing were inadequate for their needs.

After evaluating multiple options, including systems from major manufacturers, the Maguire Lab determined that no off-the-shelf solution could meet its requirements.

Instead, they partnered with Prior Scientific to develop a custom imaging system built around Hamamatsu Quest cameras.

The highly collaborative implementation process saw Prior Scientific working closely with the research team to understand and meet their specific requirements.

Through collaboration with BioVision, a microscope imaging systems integrator, Prior developed a customized stand to support an upright microscope, integrating three cameras in conjunction with a Crest CICERO spinning disc confocal unit.

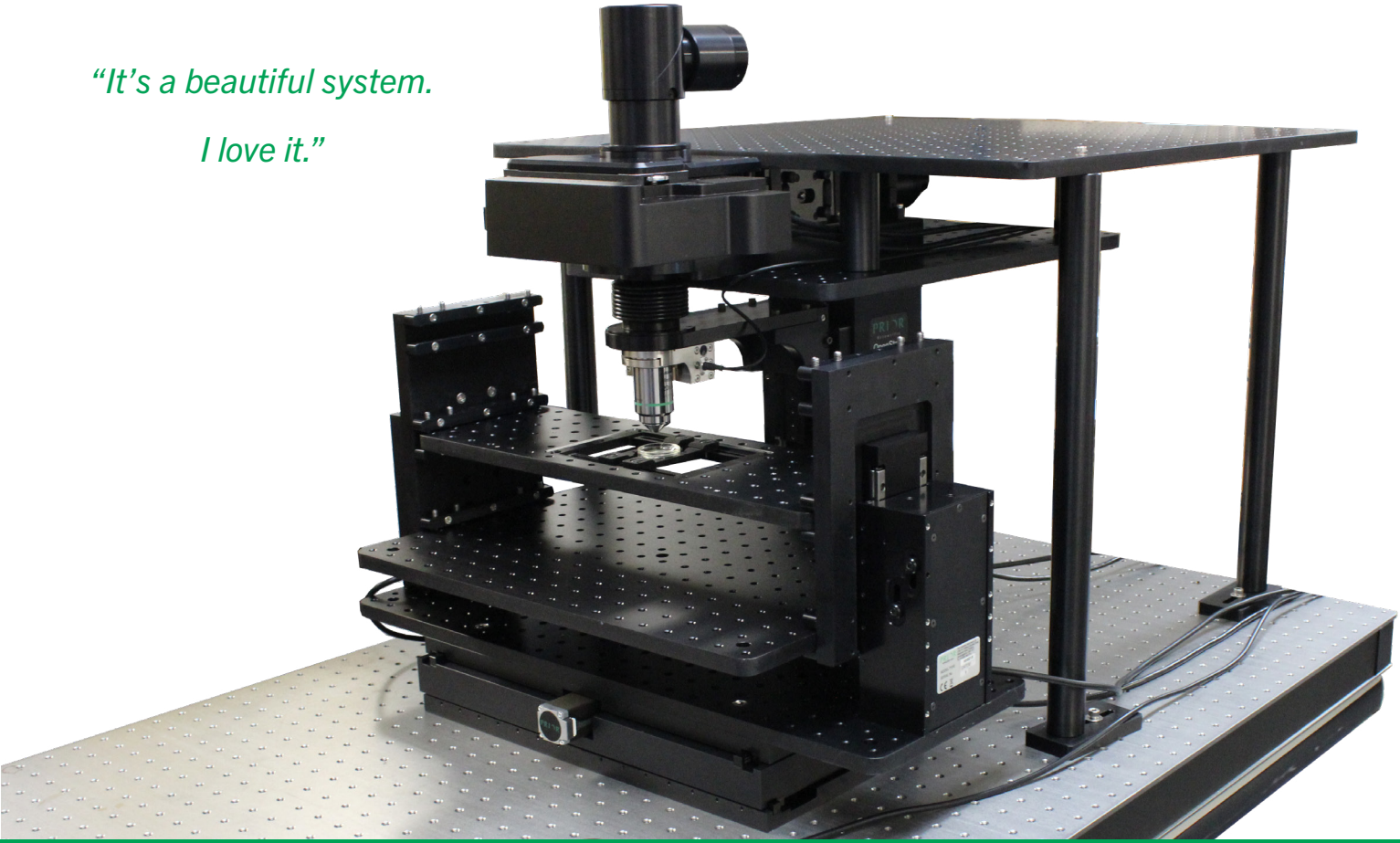


The specialized system included:

- **Platform and Mounting:** The setup uses a large 600 mm x 600 mm platform that houses the Crest Cicero unit and Prior's EPI illuminator to facilitate wide-field fluorescence, crucial for identifying precise sample locations.
- **Camera System:** Although the Crest system typically isn't designed for multi-camera setups, by using a high specification 4x magnification objective and the MultiCam from Cairn Research, it gathers sufficient light and data to provide enough signal for the three Hamamatsu Quest cameras to operate simultaneously.
- **Faraday Cage:** To minimize electrical noise during experiments, the system is enclosed in a Faraday cage, critical for supporting electrophysiology. Prior's ability to design and manufacture the system frame ensured that the entire system fitted within the volume of the cage.
- **Precision Positioning:** The inclusion of Prior's Queensgate Instruments OP800 Piezo objective positioner, known for its precision and speed, ensured accurate positioning and stacking over 800 µm, essential for the researchers' image acquisition.
- **Adjustable Shelving:** Prior's H189 physiology platform features adjustable shelf heights for imaging various sample types, from brain tissue to smaller specimens. This adaptability enables the researchers to easily reposition samples and perform a variety of experiments with the same instrument, minimizing variables between comparable datasets. Additionally, Prior's OpenStand, which forms the core of the system's frame, provides a precise motorized focusing axis with an additional 40 mm travel, further increasing flexibility.
- **Enhanced Illumination:** In addition to providing fluorescence illumination, Prior also included a flat field, white light illuminator with the system for transmitted light. This illuminator, mounted directly onto the H189, was a distinct improvement over the previous fiber bundle system.
- **Operation and Control:** The system is controlled via two ProScan III controllers and CS200 joysticks, managing up to four Z-axes. This setup enables precise manual control over sample positioning, ensuring flexibility for various experiments and sample types. Prior's multiaxis ProScan III controller and CS200 joysticks allowed Maguire Lab scientists to control all the system's axes manually and via software, ensuring flexibility for various experiments and sample types. This setup helps to keep even a complex system like this user friendly and future-proof.

"It's a beautiful system.

I love it."



The Results

The custom imaging system has transformed the research team's capabilities in several significant ways:

Expanded Data Collection

The team has made a remarkable transition from recording just one to two cells to simultaneously capturing multiple cell populations. The multiple camera system now enables researchers to observe how different neuron populations communicate in real-time and image from them simultaneously. This advancement is further enhanced by the successful integration of imaging data with electrical recordings.

"I'm just super impressed that even without the confocal how good the system is if the cells are sparse. But with the confocal enabling additional resolution, you can actually see cells that are close together and distinguish them from one another."

"I'm confident that this is going to be able to enable us to answer questions that we weren't able to answer before. And that is our ultimate goal."

Enhanced Research Capabilities

The system has opened new doors for scientific discovery and has equipped the team to pursue research questions that were previously impossible to address. Researchers can now observe cellular components and neural computations underlying behaviour patterns with exceptional clarity. The system also provides the ability to see how network states drive behavioral outcomes, offering unprecedented insight into how sparse neural populations coordinate their activity.

Competitive Advantage

The unique capabilities of the system have positioned the lab at a competitive advantage in their field. This technical has strengthened the lab's position in securing research funding and has significantly contributed to advancing scientific understanding of neural network coordination.

The system has proven transformative for the research program, enabling the team to expand their experimental approaches and create new opportunities for future research.

"Practically speaking as a lab, it gives us a tool that is really unparalleled. There's only a few people that are able to do this kind of recording and that puts us at an advantage to move the science forward. We have the ability to look at this in a way that people couldn't do before."

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