

# Two-time Beckman Awardee Keeps Laser Focus on Rewarding Research Collaborations



*Above: David Piston, PhD, 1993 Beckman Young Investigator Awardee and 2021 Beckman Center for Advanced Light-sheet Microscopy and Data Science Grantee*

"It takes a village (or more) to do productive research in today's high-tech world," explained David Piston, PhD, who serves as the Edward J. Mallinckrodt, Jr. Professor and Head of Cell Biology and Physiology at Washington University in St. Louis School of Medicine. Piston might know better than most that it really does take a village to move the needle, having also found that collaborative spirit and effort are what make research especially rewarding. Piston received a Beckman Young Investigator (BYI) award in 1993 and a grant for the Beckman Center for Advanced Light-sheet Microscopy and Data Science in 2021, both from the Arnold and Mabel Beckman Foundation. The former

supported study of three-dimensional imaging of living cell dynamics by two-photon excitation microscopy when he was in the very early stages of a tenure-track position. Nearly 30 years later, the latter funds his ongoing work optimizing multiscale light-sheet imaging.

"As long as I can remember, I planned on a career in scientific research," shared Piston, "and I have always been fascinated by lasers. I wanted to build lasers and use them to learn how matter was put together."

That fascination prompted Piston to pursue a bachelor's degree in physics from Grinnell College and a PhD in physics from the University of Illinois,

followed by a postdoc in applied physics at Cornell University. During his time in graduate school, condensed matter research was an area of study suffering from a lack of funding, and he seized on the opportunity to join Enrico Gratton's lab where he could build and use ultrafast laser spectroscopy to look at membranes and proteins.

"I knew very little about biology," he recalled, "but I really liked the collaborators and learned a lot from the biochemistry students in Gregorio Weber's and Steve Sligar's labs."

When he arrived in the lab of Watt Webb for his postdoc, the skillset he'd



*Here: Beckman Center for Advanced Light-sheet Microscopy and Data Science Grantee David Piston, PhD (second from right) with members of his lab*

honed seemed a perfect fit for a new invention: Two-photon excitation microscopy.

“The collaborators I met through that approach really opened my eyes to the range of biological questions that could be addressed by combining genetic manipulations with quantitative measurements,” reflected Piston. “I accepted a tenure-track position in biophysics at Vanderbilt University, with the goal of optimizing my quantitative imaging tools for biology. My lab at Vanderbilt was near a lot of diabetes-focused labs, and I started working on understanding the regulation of hormone secretion from pancreatic islets, which I have continued now for over 30 years. The cells that secrete insulin and glucagon are tightly coupled, with many known interactions. The concept is simple but layered with complexity given the multiple molecular pathways that all play a role.”

Then in 2015, a little over 20 years since his BYI award, Piston and the lab made the move to Washington University in St. Louis School of Medicine. When he applied to the BYI program, he was making a transition from physics toward biomedical research, and the award emphasized crossing boundaries of traditional disciplines. Piston didn't have a project ready for an R01 application for NIH funding, but the BYI program seemed to suit his career path. Reviewers agreed. Piston credited the BYI award as being crucial to his development of a rigorous new program which, three years on, led to the publication of an impactful biomedical research article. At Washington University in St. Louis, Piston's enduring fascination with lasers led him to light-sheet microscopy.

“In theory, lightsheet imaging is far superior to confocal microscopy for multidimensional imaging of live cells and tissues,” he said, “but there still isn't a consensus ‘best design’ for a lightsheet microscope. We have also encountered all the bottlenecks with data handling, processing, and visualization. We were excited to get funding to expand the breadth of our available lightsheet hardware, and to attract some help from computer scientists by funding their students. The [Beckman Foundation] RFA looked perfect to help us overcome the obstacles we were finding, and fortunately again, the reviewers agreed.”

Piston's second award from Beckman Foundation, for the Beckman Center for Advanced Light-sheet Microscopy and Data Science, is enabling him to do something he likes: Combining different approaches from genetics, molecular biology, biochemistry, physics, computer science, and mathematics to solve problems. It's doing this, he said, through interdisciplinary team funding that aids synergy between hardware and software technology and scientific applications that utilize light-sheet microscopy for discovery.

“Right now, the program is facilitating many biomedical research projects, including ones that aim to elucidate autophagy, vascular development, and primary cilia signaling,” stated Piston. “Most of our funds are going to support data curation and storage; this includes developing new tools for easy visualization of lightsheet data sets, and AI applications for segmenting and quantifying these data. Recently, we have begun to establish a foundational AI model for lightsheet data prediction and analysis.”



*Above, first and second images from top: David Piston, PhD, working in the lab*

*Above, third image from top: With Dr. Arnold O. Beckman at Beckman Center in Irvine, CA*



*Above: Images from Piston family adventures travelling around the country*

What Piston's team built was a data handling pipeline where the software is open source but the hardware environment (networking, data storage, computer infrastructure) is unique to Washington University, for researchers using light-sheet microscopy. Now, they are writing analysis modules as "stand-alone units" that will work for researchers at other institutions.

"I have been fortunate to have many talented and hardworking colleagues

over the years," he reflected. "My current lab consists of two research track faculty (both of whom also have their own projects independent from my lab), two senior scientists, a post-doc and 3 students. Having a mix of experienced researchers and trainees makes the lab a lot of fun. For the Beckman Foundation Lightsheet Microscopy Center, we have been collaborating with the groups of Bek Kamilov, a professor of computer science, and Tim Holy, a professor of neuroscience. It took us most of the first year just to figure out a shared vocabulary that we all understand efficiently – that was actually very rewarding as it forced all of us to learn a lot about each other's capabilities. Now the ideas we are working on are coming from all sides of the project, which is exciting but forces us to prioritize effort."

Something else Piston is prioritizing at this point in his career is spending more of his time trying to "pay it forward" and provide help to the next generation of scientists looking to make an impact.

"We need to do our best to level the playing field for everyone who wants

to work in research," he said. "The combination of intelligence, creativity, and grit needed to make an impact as a researcher can come from any background or gender, and we need to admit that our profession has not always been welcoming. The problems we are working on are hard, and we need to leverage all of the talent available. I am especially grateful for the opportunity to help the Beckman Foundation further these goals with my work as a reviewer for the BYI program." ■



*Above: Piston delivers remarks at a conference for the Biophysical Society*

*Image credit: All images provided courtesy of David Piston, PhD.*

*View Dr. Piston's presentation from the 2021 Beckman Symposium titled, "3D Hyperspectral Light-sheet Imaging of Pancreatic Islets on the YouTube channel of the Arnold and Mabel Beckman Foundation:*  
<https://youtu.be/GYTCVBbqZZQ>

*Visit the website of the Piston lab at Washington University in St. Louis School of Medicine:*  
<https://pistonlab.wustl.edu/>