# Brett Jesse Graham, PhD

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## *In Brief*

A neurophysiologist by training, an engineer by necessity. I am:

- proficient in electrical, mechanical and software design, construction and testing
- skilled in computer vision, embedded systems design, imaging technologies, and rapid prototyping
- adept programmer in several languages: Python, C/C++, Javascript, Matlab
- motivated and tenacious learner

## *Current Position*

2017-present Neuroengineer, Center for Brain Science, Harvard University

*Project*: Design and fabricate scientific instrumentation for 40+ labs
*Supervisor*: Ed Soucy PhD, http://ntcore.org

## *Education and Employment*

2013-2017 Electron Microscopy Engineer, Harvard Medical School

*Project*: GridTape methodology and instrumentation
*Lab PI*: Wei-Chung Allen Lee PhD, http://lee.hms.harvard.edu/

2009-2013 Postdoctoral Researcher in Visual Neurophysiology, Harvard University

*Project:* High-throughput electrophysiology in rat visual cortices
*Lab PI:* David Cox PhD, http://coxlab.org

2004-2009 PhD in Behavioral Neuroscience, University of Delaware

*Dissertation:* A functional study of the teleost nucleus isthmi:
Sensing and attending to objects in the immediate environment
*Advisor:* David PM Northmore PhD

2000-2003 BA in Psychology, Millersville University of Pennsylvania

## *Awards and Honors*

2008-2009 Psychology Department Dissertation Award
2008-2009 University Dissertation Fellowship
2007-2008 Psychology Department Teaching Fellow

## ***Technical Skills***

### *Engineering*

Proficient in CAD/CAM programs for mechanical design and production (Solidworks, Autodesk Inventor, Mastercam) and printed circuit board layout (Eagle, KiCad). Trained machinist (Manual and 5-axis CNC Mill, Manual and CNC Lathe, Waterjet), Skilled in the use of rapid prototyping tools (Laser Cutter, 3D printers). Licensed amateur radio operator (general class, KB1WTX).

### *Methods Development*

Designed, constructed and validated novel methods for eyetracking in awake rodents, structured light 3-D scanning for high resolution stereology, vacuum component design, nanoscale motion control and automation.

### *Computer Programming*

Demonstrated proficiency in many programming languages: Python, C/C++, R, Java, Matlab, and Javascript. Projects include analysis of big data (>100 TB datasets), control of embedded linux and microcontroller systems, visual stimulus presentation, automated image processing, data visualization, computer numeric motion control and system monitoring. Examples and open source code available at: https://github.com/braingram/

### *Extracellular Electrophysiology*

Setup and performed in vivo recordings from the visual system in paralyzed fish and awake head-fixed rats. Designed and constructed custom recording hardware from off-the-shelf professional audio equipment and discrete components. Programmed custom software for the presentation of visual stimuli, acquisition of 32 channel silicon microelectrode data, and analysis of large (tens of terabytes) datasets.

### *Computational Modeling*

Designed and programmed biologically constrained models of fish midbrain visual processing. Applied these models to the real-world problem of visual object avoidance in an unmanned aerial vehicle (Air Force SBIR, AF081-069).

## ***Publications***

Hildebrand D, Cicconet M, Torres R, Choi W, Quan T, Moon J, Wetzel A, Champion A, **Graham B**, Randlett O, Plummer G, Portuges R, Bianco I, Saalfeld S, Baden A, Lillaney K, Burns R, Vogelstein J, Schier A, Lee WC, Jeong WK, Lichtman J, Engert F (2017) Whole-brain serial-section electron microscopy in larval zebrafish. *Nature,* 545, 345-349.

Lee WC, Bonin V, Reed M, **Graham B**, Hood G, Glattfelder K & Reid RC (2016) Anatomy and function of an excitatory network in the visual cortex. *Nature*, 532(7599), 370-374.

Own C, Murfitt M, Own L, Brittain D, da Costa N, Reid RC, Hildebrand D, **Graham B** & Lee WC (2015) Reel-to-Reel Electron Microscopy: Latency-Free Continuous Imaging of Large Sample Volumes. *Microscopy and Microanalysis*, 21(S3), 157-158.

Zoccolan D, **Graham B**, & Cox D (2010) A self-calibrating, camera-based eye tracker for recording of rodent eye movements. *Frontiers in Neuroscience*. 4(193).

Ortiz F E, **Graham B,** Spagnoli K & Kelmelis E J (2009) Biologically inspired collision avoidance system for unmanned vehicles. *SPIE Proceedings*. 7332(1), 73320B.

**Graham B J** & Northmore D P M (2007) A spiking neural model of midbrain visuomotor mechanisms that avoids objects by estimating size and distance monocularly. *Neurocomputing*, 70(10-12), 1983-1987.

**Graham B J** & Northmore D P M (2006) A model of proximity measurement by the teleost nucleus isthmi. *Neurocomputing*, 69(10-12), 1281-1285.

Northmore D P M & **Graham B J** (2005) Avoidance behavior controlled by a model of vertebrate midbrain mechanism. *Lecture Notes in Computer Science*, 3561, 338-345.

## ***Patents***

**Graham B**, Lee WC & Hildebrand D (2016) GridTape Imaging Stage. U.S. Provisional Patent Application Application 62/420,550, Nov 10, 2016

Hildebrand D, **Graham B** & Lee WC (2016) GridTape for Fast Nanoscale Imaging. U.S. Provisional Patent Application Application 62/325,747, Apr 21, 2016

## ***Notable Projects***

### *GridTape, novel sample collection, processing and imaging for connectomics*

**Motivation:** Mapping neural circuits (connectomics) requires collection of peta-scale image datasets with resolution of a few nanometers per pixel and regions of interest that span more than a cubic millimeter. Technological advancements are necessary to reduce the time and effort required to collect these datasets

**Plan:** Design, build, test and deploy new material, methodology, instrumentation and software to speed-up and automate connectomics dataset collection.

**Execution:** Helped design a novel sample substrate on which serial ultra-thin sections of tissue could be collected and imaged. Scaled and automated production of this substrate to make millimeter cube datasets possible. Modified hardware and wrote control software for sample processing instrumentation to allow accurate automated ultra-thin section collection. Designed, machined, constructed, tested, and deployed an in-vacuum imaging stage capable of nanometer resolution movements and automated sample exchange. Modified a transmission electron microscope with a camera array capable of acquiring at rates up to 1.68 gigapixels per second.

**Result:** The methods and instrumentation are being used to generate several connectomics datasets. Hundreds of meters of sample substrate have been produced, thousands of sections have been collected and processed and over a petabyte of raw data have been collected using the developed imaging system that has been adopted by the Allen Institute, Princeton University and other institutions.

### *High-throughput electrophysiology in awake behaving rats*

**Motivation:** Laboratory rats are not common subjects in studies of the visual system. Although they are capable of complex visual form recognition, little is known about their higher-level visual processing.

**Plan:** Develop and build an electrophysiological rig to acutely record brain activity in an awake rat performing a visual identification task. The rig must be capable of recording: eye movements, behavioral measures (animal state, response to stimuli, etc), electrode position, and brain activity in 32 locations simultaneously.

**Execution:** Constructed a 32 channel recording system to monitor brain activity using off-the-shelf professional audio equipment (10x savings and improved performance compared to neuroscience-specific hardware). Combined a commercial 3D scanning tool with custom software to capture high-resolution (better than 50 micron) scans of skull landmarks during surgery that are then used with a custom 3D navigation program to position the electrode during recording sessions. Finalized automated calibration software for and tested the accuracy of a custom built rat eye tracker. Coded an automated analysis and visualization pipeline that processes large datasets (several terabytes) collected from this rig and displays analyzed results using a web server.

**Result:** To date, almost 3 TB of raw data have been collected and analyzed using this rig. The results have produced a detailed map of stimulus selectivity and tolerance covering the majority of visual cortical areas.

### *Measuring the response to visual and hydrodynamic stimuli in the fish midbrain*

**Motivation:** In fish, the majority of sensory processing occurs in the midbrain. Previous work discovered a subdivision that responds preferentially to approaching visual stimuli which could be used to identify impending collisions, a problem of great interest to robotics and engineering.

**Plan:** Develop and build an apparatus to present visual and hydrodynamic stimuli to a paralyzed fish while recording midbrain activity. The total budget could not exceed $2000.

**Execution:** Built and tested amplifier boards from discrete components (integrated circuits, resistors, capacitors). Wrote software to: measure voltages from a National Instruments data acquisition device, present visual stimuli using OpenGL, and measure the location of hydrodynamic stimuli using an ultrasonic range finder attached to a microcontroller board running custom firmware.

**Result:** Using this rig, data were collected for two experiments. The first parametrically described the response of the approach selective midbrain subdivision to visual objects and debunked two theories that attempted to describe how the subdivision signals impending collisions. Data from the second study revealed that this subdivision does not respond to the approach of hydrodynamic stimuli in a similar, approach-selective manner.

## ***Abstracts and Conference Presentations***

**Graham B** (April 2017) GridTape. Invited talk, Max Planck/HHMI Connectomics Conference, Berlin, Germany.

Marra K, **Graham B**, Carouso S & Cox D (Mar, 2012) Implementation of a Peltier-based cooling device for localized deep cortical deactivation during in vivo object recognition testing. APS Meeting Abstracts, Boston, MA.

**Graham B**, Carouso S & Cox D (Nov, 2011) High resolution stereotaxy using structured light imaging. Poster session at Society for Neuroscience, Washington, DC.

Ortiz F E, Spagnoli K & **Graham B** (Apr, 2009) Biologically inspired collision avoidance system for unmanned vehicles. Presented at SPIE: Defense, Security and Sensing, Orlando, FL.

**Graham B J** & Northmore D P M (Nov, 2008) Sensing the distance of looming objects from a monocular visual image: a parametric examination of the teleost nucleus isthmi. Poster session presented at Society for Neuroscience, Washington, DC.

**Graham B J** & Northmore D P M (Feb, 2008) Monocular proximity derivation in the teleost midbrain. Poster session presented at Computational and Systems Neuroscience, Salt Lake City, UT.

**Graham B J** & Northmore D P M (Oct, 2006) Bi-directional communication of posterior commissure axons between the nuclei isthmi in a teleost. Poster session presented at Society for Neuroscience, Atlanta, GA.

**Graham B J** & Northmore D P M (July, 2006) Spiking neuron models based on midbrain mechanisms that guide visual behavior. Poster session presented at Computational Neuroscience Meeting, Edinburgh, Scotland.

**Graham B J** & Northmore D P M (July, 2005) A model of proximity measurement by the teleost nucleus isthmi. Poster session presented at Computational Neuroscience Meeting, Madison, WI.

## *Grants*

2008 Improvements to Sense and Avoid (SAA) Systems for Unmanned Aircraft Systems (UAS), Air Force SBIR, AF081-069.
Fernando E. Ortiz PhD, Principal Investigator (EM Photonics)
**Brett Graham PhD** (Consultant, University of Delaware)
David PM Northmore PhD, (Consultant, University of Delaware)

## *Teaching Activities*

### *Instructor*

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| Spring 17 | Freshman Physics Seminar |
| Fall 17, Spring 17 | Arduino for Neurobiologists |
| Fall 07, Spring 08 | Sensation and Perception (Psyc 310) |

### *Teaching Assistant*

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| Spring 07 | Measurement and Statistics (Psyc 209) |
| Fall 04 - Spring 07 | Sensation and Perception (Pysc 310), Lab Instructor |
| Fall 06 | Sensation and Perception (Psyc 310, online course) |
| Fall 06 | Developmental Psychology (Psyc 350) |
| Fall 05 | Brain and Behavior (Psyc 314) |