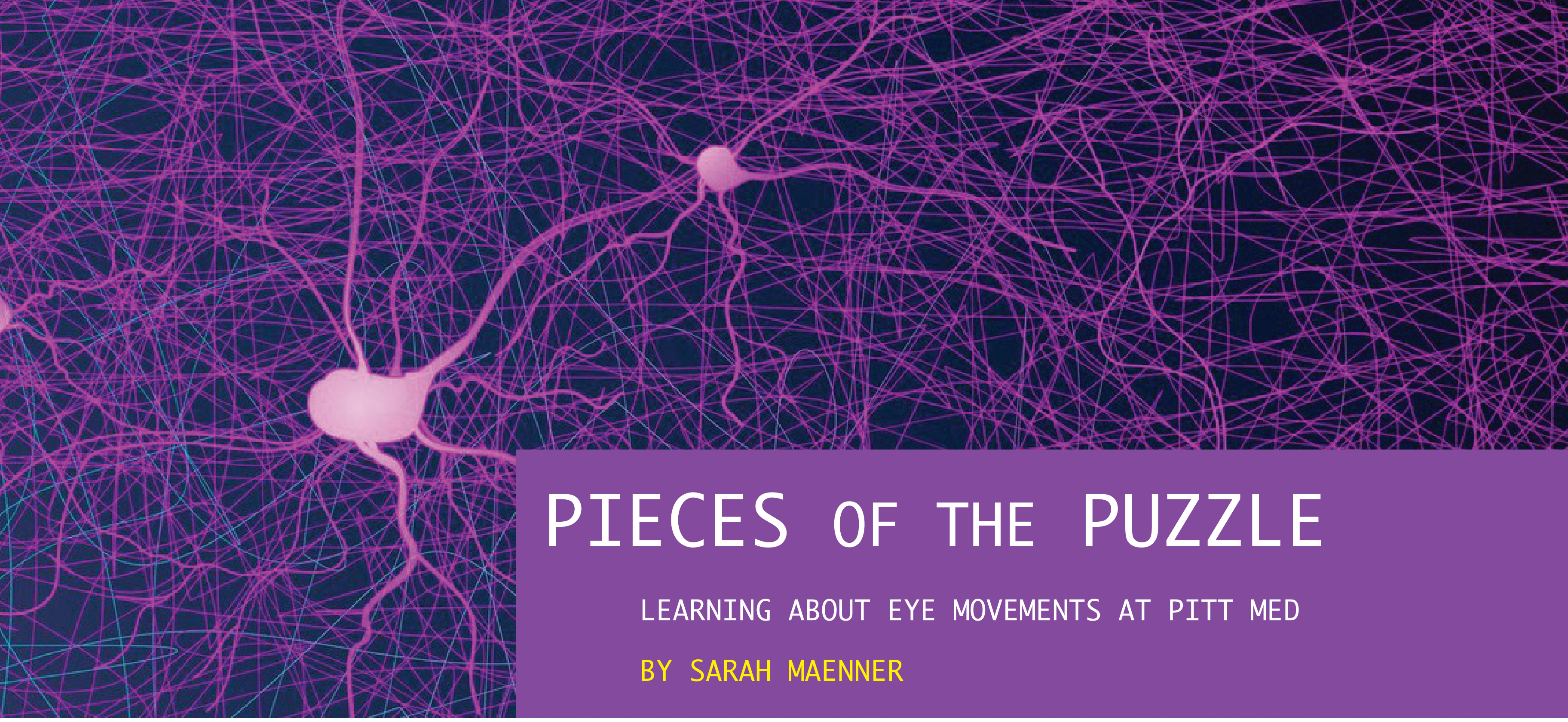

# PIECES OF THE PUZZLE

## LEARNING ABOUT EYE MOVEMENTS AT PITT MED

BY SARAH MAENNER

The monkey concentrates intently in a dark room, its face illuminated by the bright computer screen before it. On the screen, dots travel to the left, then return to the center to begin moving to the right. The monkey watches the dots. As its eyes follow them, first left and then right, a computer outside the room records data from electrodes within the monkey's brain on the activity of brain cells, or neurons. When the monkey's eyes move left: *beep*! When the monkey's eyes move right: *silence*. In this experiment, we have learned that some neurons are only active when the eyes move in a certain direction. In this way, the scientists who are studying these neurons get to see how the monkey's behavior and the neurons' activity interact in real time. The scientists are excited: this is the kind of excitement which drives whole careers.

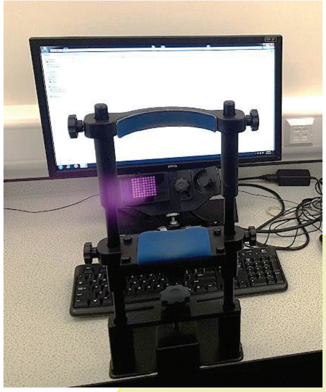

Photo from: Chassy et. al., 2017

**An example experimental setup of a head-rest, eye-tracker, and computer monitor for use in human experiments.**

"It gives me goosebumps, and it's the cool, exciting, awesome thing that I've always said, when that stops being exciting to me is probably when I should stop doing what I'm doing," says Dr. J. Patrick Mayo, principal investigator of this particular laboratory. Dr. Mayo is an Assistant Professor of Ophthalmology at the University of Pittsburgh School of Medicine, and he and his lab study the interaction of vision and eye movements as well as the neural mechanisms of that interaction. Put another way, they study how our eye movements affect what we see, and what happens in our brains as we move our eyes. He studies a subfield of neuroscience which recognizes that our eyes are not merely cameras which "wiggle around" and faithfully record everything in the environment. Instead, they require us to keep objects of interest within a certain part of our visual field, called the fovea. To do this, we move our eyes in certain ways: quick movements, called "saccades," jump from one region of the visual field to another, and much slower and more deliberate movements, called "smooth pursuit" (or simply "pursuit"), follow an object of interest.

To study these movements and their neural representations, visual scientists use a combination of experiment designs. The most common of these are behavioral studies and electrophysiological studies. Behavioral studies focus on the eye movements and determining which are used in certain scenarios. These studies have been used for about a hundred years, and they are accessible since they don't require much specialized equipment and are also non-invasive. In contrast, electrophysiological studies are more invasive; they measure the electrical activity of neurons by inserting electrodes into the brain. They use certain equipment, which can be limited by technological capabilities and costs. Because of these limitations, visual scientists know much about visual perception but not as much about the neural mechanisms behind that perception. *How* we see is therefore the question that Dr. Mayo asks, so the lab joins the field's increasing use of electrophysiological studies, as in the opening scene.

Over the last few decades, while electrophysiological studies have become more common, researchers don't often study neuron activity in both sides of the brain simultaneously. The brain is divided into two halves, or hemispheres, and each hemisphere controls related but distinct functions. This is called lateralization. In terms of vision, the right hemisphere of the brain processes information coming from the left side of the visual field, and the left hemisphere processes the right. It is similar for motion; the right hemisphere moves the left half of the body, and the left hemisphere moves the right half of the body. Most electrophysiological experiments only study neuron activity in one hemisphere at a time, but Dr. Mayo believes this to be an oversight: "If we can record in both hemispheres at the same time, we could try to make some…observations about communication between the two hemispheres… And what the information that's being carried in each hemisphere over time [is]. Is it, you have information on the left side and then it gets passed to the right side? Those sorts of questions." Due to technological restrictions, these questions are currently mostly unanswered. Dr. Mayo estimates there are only around five published papers which investigate electrophysiology in both hemispheres simultaneously: one of which is his own post-doctoral work.

To this, I suggested he is "the guy" who studies this. He responded that it may be true, although he didn't intend to fall into this niche in particular. It just so happens that these methods are helpful to answer the questions he finds compelling. To Dr. Mayo, "the simpler the question, the better," and while his research may not be, in his words, the "big, sexy, fancy" work that is immediately noticed by journalists and papers, it is still important in breaking down those larger, high-level questions. In a field like neuroscience, a field full simple and complicated unknowns, it is the bite-size and study-able questions which, slowly but surely, advance our knowledge of the universe and of ourselves.

The lab doesn't focus on curing one disease in particular, such as Alzheimer's disease or Huntington's disease, but instead tries to establish the general mechanisms behind movement so that researchers of these diseases have knowledge from which to draw. That is, the lab aims for wide applicability. Why the visual system? “The way things work for the visual system may be the way in which things work [for other movement systems].” Studying how arm movements are initiated may, in the end, teach us much of the same information, but simplicity is the name of the game. Eye movements are easier to study because there are only a few muscles involved and about as many directions they can move the eyes in. Simplicity keeps the questions more practical and the answers clearer.

Photo courtesy of: Mac Mayo, 2023

The lab at Kennywood, June 2023 (from left to right): Dr. Mayo, Sarah Maenner, Zixuan Xiao, Emily Lopez, Kendra Noneman, Maria Chroneos.

In order to answer their questions, the lab needs subjects. Like the rest of the subfield, they often study monkeys (or, in science jargon, non-human primates), in particular, rhesus monkeys. These primates are not-so-distant cousins of humans, so their visual systems are similar to ours, and they can easily learn behaviors for an experiment. In coordination with hospitals and patients, human subjects are also becoming more popular. Dr. Mayo's lab has teamed up with another lab in the department, led by Dr. Marlene Behrmann, to study eye movements in children with epilepsy.

The epilepsy was so severe in those cases that when the children were young, they needed to have half of their brain removed in a procedure called hemispherectomy. When the procedure is done at a young enough age, it works surprisingly well, with a very good chance of curing the epilepsy and with a high chance of recovery. From these patients, we learn just how adaptable the brain is: the remaining hemisphere is able to take over some of the functions that would have been controlled by the half that was removed.

However, one half of the brain will not be able to recover all of these lost functions, so these patients also teach us how clever the brain can be. Even when it can't adapt anatomically, it can take what it can do and utilize those functions in creative ways. In the study, the patients were meant to pursue a target going both left and right, and they appeared to be able to do that, despite the loss of one hemisphere. Because eye movements can be recorded so precisely, the researchers found something surprising: “You can see that they're doing smooth pursuit in one direction using their intact hemisphere, and then in the other direction, they're doing something that kind of looks like pursuit but is not actually pursuit, and they're actually making saccades.” Pursuit would have been ideal in that situation, but it wasn't possible anymore, and saccades worked well enough—and “well enough” is all you need.

This study was a re-do of a paper from the 1970s which had only one subject, though this time there were around twenty subjects, leading to more robust results. It was led by doctoral student Maria Chroneos, a trainee in both Dr. Behrmann's and Dr. Mayo's labs. There have been several graduate students from both Pitt and Carnegie Mellon University working in the lab over the years, along with a handful of undergraduates, mostly from Pitt's Department of Neuroscience and School of Engineering. As principal investigator, one of Dr. Mayo's roles is to mentor these students as they grow into scientists by passing along his knowledge of techniques, along with his enthusiasm. “I appreciate much more helping pass that enthusiasm along to other people, [which is] almost more rewarding [than doing the experiments myself] because my influence or my contribution to the field of science is vastly larger if there's more people going out there doing things.”

Life as a principal investigator, or PI, is very different from life as a researcher in someone else's lab. As a student or postdoctoral researcher (“postdoc”), scientists can spend hours a day running experiments, but as leader of the group, PIs have a much more administrative role. “Most days are some sequence of meetings, either administrative meetings, collaboration meetings, or trainee meetings. So it's just meetings, meetings, meetings. And some science talks thrown in there.” When he can, Dr. Mayo also manages to squeeze in science writing, which is mostly in the form of applying for grants. Science writing is a useful skill because in order to write a successful application, he must understand the concepts and methods well enough to be able to convince an observer that his projects are worth their resources. These grant reviewers are a challenging audience to write to since they often know the basics of neuroscience but are not themselves visual scientists. Therefore, Dr. Mayo has to balance a “slippery slope”: assume that they have less knowledge and risk looking “dumb,” or assume that they have a background that they don't and risk losing their comprehension and thus their resources.

There are other challenges, too. In particular, working within the “behemoth machine” of the university and hospital system can be tough because so many people have so many different opinions of how things should be run. But that's nothing compared to the main challenge: the sheer vastness of the unknown. The field is so young, and the brain is so complicated, that every time we learn something, it generates dozens more questions. Can we dare to hope to ever understand it in its entirety? In the present, neuroscientists are still trying to get their bearings, which in practice oftentimes results in failure.

The frustration of failure is luckily combatted by the constancy of curiosity, and scientists are a constant and curious bunch. It's a discipline all about the discovery and joy of the *new*. At the end of an experiment, when the data are collected and the results are analyzed, you have something new to show the world: a piece of knowledge which no one else has ever known. “That's the wild thing about neuroscience, what we're doing right now,” Dr. Mayo says. “And those things could be totally small and trivial, something that you're not gonna blow someone's mind with, but at the same time, it is your little puzzle piece that you're putting onto the board to make the whole picture.” Day by day, the lab works to add their pieces to the wider puzzle, one eye movement at a time. ■