Mathematics and Neuroscience Merge To Shed Light on Learning

~ A Q&A with Nathaniel Sawtell, Larry Abbott and Salomon Muller ~

What can a fish tell us about the brain and our senses? At Columbia's Zuckerman Institute, two labs with different expertise — one in experimental neuroscience, the other in mathematical modeling — have teamed up to find out.

When we walk along a busy street, we can easily distinguish moving people and cars from stationary objects, even though the entire world before our eyes is sweeping past us. Our brains employ unparalleled computing power to make this possible. To understand this computational ability, Nathaniel Sawtell, PhD, and Larry Abbott, PhD, study fish that sense their environment with electrical pulses. They use their findings to build mathematical models that explain how the brain learns to perform these kinds of complex computations. By investigating this form of learning, these scientists' interdisciplinary work also has implications for machine learning technologies based on the brain.

We spoke with Drs. Sawtell and Abbott, as well as doctoral candidate Salomon Muller, about their latest discoveries, published recently in the journal Cell.

What is the big question you hope to answer with your research?

Nathaniel Sawtell: The ability to perceive and experience our world is effortless, but behind the scenes our brain is constantly performing sophisticated computations. A key feature of this process that we want to understand is how the brain can recognize and process external sensory stimuli, such as sounds and sights generated by the outside world, like the car whizzing by, while tuning out those sensory stimuli that we generate from our own movements; how it distinguishes between the 'self' and the 'other.' It turns out that this ability requires a form of learning.

Larry Abbott: We want to learn how the brain processes information about the environment while simultaneously updating its knowledge about how to react to that environment. This type of concurrent learning and updating is difficult for computers to accomplish — but the brain does it automatically.

Salomon Muller: Our work investigates how clusters of neurons, called circuits, make perceiving and learning possible. We believe that understanding this process will reveal critical clues to how the brain works and solves problems.

How did you go about investigating this question? And what can these investigations teach about the human brain?

NS: We focus our investigations on the elephant-nose fish, an animal that emits and detects electrical pulses to perceive and navigate its surroundings. In particular, we study a structure in the fish's brain called the electrosensory lobe. This structure is very similar to the cerebellum, an ancient brain structure that is present in all vertebrates, including in people.

The electrosensory lobe helps the elephant-nose fish use its electrical pulses to detect nearby objects. For example, these pulses enable the fish to sense the minute electrical fields produced by the prey it wishes to eat. Remarkably, the fish can sense these small electrical fields even while the fish itself is producing much larger electric signals. We studied how this is done.

LA: These capabilities make this fish a powerful model for studying how circuits in the brain can cancel out self-generated sounds, or the effects of its own movement, thereby distinguishing between external and internal stimuli. In addition, this is a great system for exploring how brain circuits both process information and learn at the same time, and enable us to think about what happens when those circuits are disrupted.

What did you uncover about the cerebellum in your study?

NS: Previous work had shown that the fish's electrosensory lobe, which is similar to the cerebellum, contains several layers of neurons stacked on top of each other. In this study, we discovered that neurons in the middle layer do something incredible.

LA: Most neurons generate bursts of electricity to communicate. But, importantly, these middle-layer neurons produce two different types of electrical bursts — one for learning and the other for communication.

SM: Earlier research had observed these dual signals but had not deciphered their role. We developed a mathematical model demonstrating that these signals actually emanate from different regions of the same neuron, and that this compartmentalized organization is what enables the circuit to learn on the go.

What impact could these findings have on medicine and technology?

NS: As we mentioned, the fish's electrosensory lobe is remarkably similar to our own cerebellum. Recent evidence strongly suggests that our brains follow similar rules as those that allow fish to learn with flexibility and adaptability. Understanding those rules will help us to figure out how the brain grows and develops, as well as what goes wrong in disease when this circuitry gets disrupted. One example is tinnitus, or ringing in the ears. Tinnitus is a common and, in some cases, debilitating condition that is hypothesized to arise because of a malfunction of circuits in the human brain that normally function to cancel out self-generated sounds. Our work in the elephant-nose fish has the potential to inform efforts investigating the underlying mechanisms of this disorder.

LA: These findings could lead to machine-learning algorithms that more closely resemble what the brain does. At present, such algorithms divide learning and processing or communicating into two separate phases. The biological discovery we uncovered in our research suggests a new path forward: a learning mechanism that can do both things at once.

Your research brings together experimental neuroscience with theoretical neuroscience. Why are collaborations like these important?

NS: The brain is the most complex thing we know of. Building sophisticated mathematical models is absolutely essential for understanding how it works, because they give a roadmap for experimentalists like me to use as I continue to delve deeper into the mechanisms of learning.

LA: As a neuroscientist who was originally trained in physics, I obviously have a background different from Nate Sawtell's, but rather than that getting in the way of our collaborations, we use our different approaches to great advantage. Building bridges between mathematics and biology makes for successful collaborations that drive science, medicine and technology forward.

SM: As a doctoral candidate here at Columbia's Zuckerman Institute, I have been mentored by both Drs. Abbott and Sawtell, which has been incredibly rewarding. In neuroscience, you often take things apart to understand them. Our collaboration allows us to also put the pieces back together; our focus is not on solving a one piece of a problem, but on understanding a system with all of its pieces.

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