Richard Mann, PhD

Tracing the Steps that Guide Movement

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Richard Mann, PhD, is the Higgins Professor of Biochemistry and Molecular Biophysics at Columbia University and a principal investigator at the Mortimer B. Zuckerman Mind Brain Behavior Institute. Dr. Mann completed postdoctoral training at Stanford University Medical Center. He received his PhD from the Massachusetts Institute of Technology and his BSc. from Cornell University..

For Richard Mann, PhD, answers to some of biology's biggest puzzles, such as how our brains direct our muscles to move, can be found in the tiniest of places.

A man walks into a bar. But how did he do it?

To many people, this may sound like the setup to a joke. But to Richard Mann, PhD, a principal investigator at Columbia's Mortimer B. Zuckerman Mind Brain Behavior Institute, this is one of the incredibly complex questions that he is attempting to answer.

"On the surface, the mechanisms that guide movement — even something as simple as how we put one foot in front of the other — are actually extraordinarily complex," says Dr. Mann. "For example, your leg contains more than two dozen muscles. How does the brain know to direct that one specific muscle in your leg to move, but not the one next to it? I want to be able to answer that question in precise detail."

In his lab, Dr. Mann studies the motor neuron, a type of brain cell that stimulates muscle movement. Motor neurons send instructions to muscles using axons, long branches that extend from the bodies of these cells and attach to muscles. He wants to understand how the features of motor neurons — what they look like, what they do and where they are located — give each neuron its individual identity. His ultimate goal is determine how that identity guides a neuron's behavior.

As a graduate student at the Massachusetts Institute of Technology, Dr. Mann's interest in the biology of cells steered him toward the field of genetics. After all, says Dr. Mann, the way in

which genes inside each cell get switched on and off in a precisely timed sequence is what ultimately makes one cell different from the next.

Throughout his career, Dr. Mann has studied the fruit fly. Compared to humans or even mice, the fruit fly bears several advantages. For one, its genome has been largely decoded; scientists know the function of many of its approximately 17,000 genes. They can also manipulate how, where and when a gene is turned on. From that information figure out how genes affect a fly's growth and development.

"But we wanted to go further to see how those manipulations affect a fly's behavior, such as its ability to move," says Dr. Mann. "The only problem was that no tools were available to do this. So that's when we came up with the idea for Flywalker."

Flywalker is a combination apparatus and software program that pays close attention to an insect's steps. The insect strolls over a piece of glass in the device. At the same time, light beamed

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into the glass bends — much in the same way that light shimmers in a swimming pool — resulting in bursts of light where the fly touches the glass. A video camera captures those bursts and then feeds them into software that reconstructs the fly's movements, step by step.

To develop the system, Dr. Mann teamed up with Columbia physicist Szabolcs Marka, PhD. They shared Flywalker with the scientific community in 2013. Soon after, Drs. Mann and Marka created a modified version of their program to monitor the movement of mice, aptly named Mousewalker. Both programs were distributed as open-source projects, so that anyone could replicate, and improve upon, the original design. Today, both Flywalker and Mousewalker are vital tools used by many labs around the world.

Ultimately, Dr. Mann's work on imaging fly movement will lead to insights into our own locomotion. This is because many of the genes, and even the circuitry connecting neurons to each other, involved in movement in the fly are also serve the same purpose in humans.

"It's fascinating to me that such a small genome and nervous system, which we observe in the fruit fly can produce such complex structures and behaviors," says Dr. Mann. "How this happens is a big part of what I'm trying to find out."