A flash of insight: Chemist uses lasers to see proteins at work

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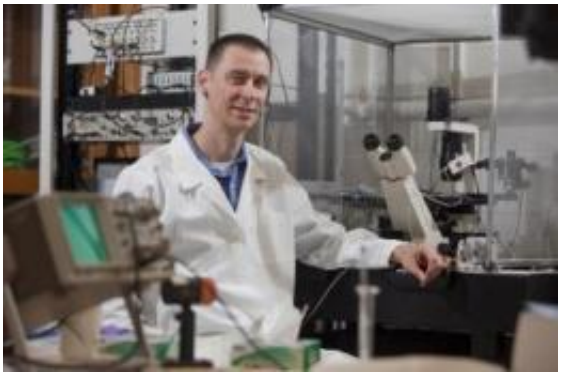

Binghamton University researcher Christof Grewer thinks he has an important brain transport protein -- glutamate transporter -- figured out and he's taking aim with lasers. Credit: Jonathan Cohen

Binghamton University researcher Christof Grewer thinks he has an important brain transport protein – glutamate transporter – figured out. And he's using a novel approach to spy on them by taking aim with lasers.

Grewer, a biophysical chemist, studies glutamate transport proteins, miniscule components of our brains that move glutamate among cells. Glutamate, an important molecule in cellular metabolism, is also a neurotransmitter. He explains his research on these tiny proteins in the brain using an analogy: imagine never having seen a car before and trying to determine what makes the vehicle run.

"We would be interested in seeing what happens when the car is moving, and we'd take pictures of that," he says. "We'd see the pistons moving, and that would be the beginning of understanding."

Scientists know the transport proteins are important, and they know they move glutamate in and out of cells through a sort of door in the cell wall, known as a glutamate transporter. But exactly how the proteins trigger those doors in the cell wall, and what makes them move glutamate to the inside or outside of a cell, is unknown.

Learning how those triggers function could have major implications for human health. For example, during a stroke, when blood and oxygen to the brain are restricted, brain cells release glutamate into the space surrounding them. That starts a toxic chain that can kill brain cells and harm certain brain functions. Knowing how the glutamate molecules are transported through cell walls could one day lead to drugs that help or halt the transport.

Grewer — one of perhaps two dozen researchers in the world who work on this problem — switches analogies as he continues describing the way these proteins move.

"Think about people being transported in an elevator in a tall building," he says. "So in order for that to work, the door of the elevator has to open, and then the person has to step into the elevator. And then the elevator brings you to a higher floor, and then the door has to open, and the person has to walk out."

In this case, glutamate molecules are the people. The elevator cars are the glutamate transporters. And the electricity and wires that move elevator doors are — well, that's what he's trying to figure out. Grewer's brainstorm was to create a method that uses lasers to trigger the transports' action. By controlling when the movement happens, he can

document it. It all goes back to his analogy of photographing a car's pistons. Taking snapshots may illuminate how the transporters and glutamate molecules work together.

Grewer stumbled onto the glutamate transporters. When he was a graduate student in physical chemistry at Johann Wolfgang Goethe-University in Frankfurt, Germany, his research focused on chemistry and light. His introduction to biochemistry — and to glutamate receptors — came during a post-doctoral fellowship at
Cornell University.

"We were trying to activate these receptors on a very fast time scale," he says. "It's not that easy to do."

His background in chemistry and physics brought fresh insight to the lab. What if, he thought, a flash of light could help trigger the transport process? By timing the reactions, the researchers could better capture what happens during the glutamate transfer.

"They were so interesting to me that I just had to stay with them," Grewer says of glutamate transporters. "I thought, that is just the most amazing thing to study."

Most biochemical research on the brain focuses on possible cures and many researchers are experimenting with known drugs to judge their effect on brain function.

In most proteins, and in biology, researchers know what the genetic code and the DNA look like. The number of proteins in the body is also a known factor. But what's not unclear is how these proteins function. And that's where Grewer's work comes in. He has become a pioneer in the usage of lasers, which although used on other types of proteins, has not been used before in this area of study.

Provided by Binghamton University