UAF researchers adapt Stanford method to make transparent brains

By Weston Morrow, wmorrow@newsminer.com | Posted: Tuesday, May 19, 2015 12:08 am

FAIRBANKS — For years, neurologists and other researchers studying the functions of animal brains have been forced to cut brains into hundreds or even thousands of tiny slices to study them through microscopes.

That changed in 2014 when researchers at Stanford University developed a method to take a normally opaque brain and turn it entirely transparent. Turning a brain transparent might not seem to have many practical scientific benefits, but the beauty of the process is that it allowed researchers to study small rodent brains under microscopes as a whole.

Instead of cutting mouse brains into hundreds of 50-micron slices and studying each one individually, researchers were able to place an entire mouse brain under the microscope and study the intimate details of their specific interest while also seeing it in the still-complete whole. The process was dubbed “CLARITY” by lead researcher Karl Deisseroth.

Most innovations, however exciting, come with a catch, though. For a lab like Deisseroth’s at Stanford, the cost of CLARITY is minimal, but the drawback of CLARITY is that it’s prohibitively expensive for small labs — like ones at the University of Alaska Fairbanks.

That’s where UAF undergraduate Matt Vanagel came into the picture. While in a biochemistry class at UAF, Vanagel came across an article on CLARITY and thought it might provide a great boon to research being conducted by several researchers at UAF, including professor Kelly Drew and Ph.D. student Carla Frare.

Frare and Drew had been studying hibernation using rats, taking the rat brains and studying their neural processes by examining the brain slices.

“We were really thinking this technique would help this project out a lot and probably a lot of others at UAF,” Vanagel said. “I kind of thought that trying to implement CLARITY into her research might save a lot of time and give a more complete picture.”

The only problem was the cost, but Vanagel wasn’t going to let that stop him. He began, with the help of UAF chemistry professor Brian Rasley, looking into ways CLARITY’s results might be replicated with the use of cheaper substitute reagents. The Stanfored method required a specific reagent that cost as much as $450 per milliliter. On top of that, it required several expensive lab

instruments UAF — and many other schools and labs — simply didn't have.

Vanagel searched around and was eventually able to find a solution that, instead of costing $450 per mililiter, cost only 20 cents per mililiter.

In addition to that, the CLARITY method required an electric stimulation to speed up the process. Vanagel decided to see how long the process might take if he let the effect simply take place passively, without stimulation.

The result was slower, taking weeks instead of days to work on a single-centimeter brain section, but it was much more affordable, and it worked.

Vanagel's method still has limitations compared to the CLARITY method. For instance, the microscopes UAF has access to cannot examine an entire rat brain in one piece — the brains need to be split into several sections — but the handful of sections is vastly preferable to the hundreds of slices that had to be dealt with before.

In the end, Vanagel was able to essentially replicate the results of the CLARITY method with just a fraction of the cost, helping to open the groundbreaking method to researchers in small labs at UAF and perhaps ultimately even around the world.

Vanagel, from Eagle River, graduated from UAF last week with a bachelor's degree, but his work will continue to support research at UAF and will be carried on by others at the school like Rasley, Drew and Frare.

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