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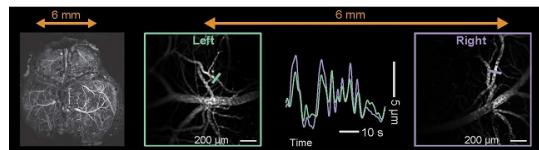
## UC San Diego Researchers Solve Mystery of Oxygenation Connections in the Brain

Scientists have known that areas of the brain with similar functions—even those in different brain hemispheres—connect to share signals when the body rests, but they haven't known how this "resting-state connectivity" occurs. Now, scientists in the Neurophysics Laboratory at the University of California San Diego may have the answer. Using an advanced form of optical microscopy designed by David Kleinfeld and Philbert Tsai in the UC San Diego

Department of Physics, postdoctoral fellow Celine Mateo and colleagues studied tiny changes in the diameter of brain blood vessels across the entire cortex of a mouse. Their findings, published in the Oct. 26 issue of the journal *Neuron*, revealed a cascade of interactions that explains how oxygen levels correlate over large distances in the brain, as detected by fMRI—the major tool used by neuroscientists and psychologists to study the involvement of different brain areas in human behavior. The scientists say their results have immediate impact on human health and medicine applications, including higher resolution imaging methods to study connections within the brain.

"One impact of our results is to use MRI and directly study fluctuations in the diameter of blood vessels across the brain," said Kleinfeld, a distinguished professor in the Divisions of Biological Sciences and Physical Sciences, noting a project already underway with colleagues at Massachusetts General Hospital.

During their study of brain interactions, UC San Diego researchers observed the slow variation in amplitude of high frequency electrical signals in the resting brain normally associated with attention span. This slow variation—periods of 10 seconds—in electrical signal amplitude corresponds with slow vibrations in the muscles surrounding arterioles in the brain. The muscles then contract and relax rhythmically, changing the diameter of the arterioles and modulating the oxygen levels in neighboring brain tissue. This effect is particularly notable



Researchers used advanced brain imaging techniques to match corresponding blood vessels in left and right hemispheres of the brain and discovered that variations in their respective diameter track each other over time. Image courtesy of Celine Mateo

when it occurs between brain regions across the two cortical hemispheres. When the research team repeated these measurements in mice that lacked anatomical connections between brain hemispheres, however, the synchronization decreased.

Mateo explained that the research furthers the understanding of how blood vessels dynamically help the brain maintain its homeostasis—the tendency of the body to seek and maintain a condition of balance within its internal environment.

“Our next question is to ask how blood vessels participate on the regenerative effect of sleep,” said Mateo. “We hope that applying our arsenal of optical and genetically engineered tools will advance our understanding of this fascinating subject.”

Only in the past 25 years have scientists discovered that changes in the magnetic properties of hemoglobin—a protein of red blood cells that contains iron and carries oxygen—can be used as a surrogate to measure brain activity. The resulting technique, called BOLD fMRI, became the standard means by which researchers have measured what parts of the brain are activated during different mental activities.

In addition to UC San Diego’s Kleinfeld and Mateo, coauthors of this important study include Per Knutsen and Andy Shih. The work was funded by the National Institute of Mental Health (grants MH108503 and MH111438) as part of the NIH BRAIN program, the National Institute of Neurological Disease and Stroke (grants NS082097 and NS097265), the National Institute of General Medical Sciences (grant GM12345), and the National Science Foundation (grants PHY-153264 and OIA-1539034).

The first students to enroll at UC San Diego in 1960 were graduate students in the Department of Physics. Part of the Division of Physical Sciences, the department is ranked #16 by U.S. News and World Report. The Division of Biological Sciences, ranked #14, was also established early at the university. Today, UC San Diego biology is one of the most frequently declared undergraduate majors on campus.

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