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## Studying the brain across scales using imaging and physics

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Functional Magnetic Resonance Imaging (fMRI) is a powerful tool to map brain activity non-invasively. Over the past 25 years, fMRI has become widely used in neuroscience research and is the foundation of tens of thousands of published studies. However, fMRI does not measure neurons directly. Instead, in the most common form of fMRI called Blood Oxygen Level Dependent (BOLD), changes in the concentration of paramagnetic deoxyhemoglobin in the blood are detected. Although changes in blood oxygenation are correlated with neural activity, a quantitative relation has not been established, limiting the interpretation of data and the power of fMRI to study the brain in health or disease.

Animal models provide invaluable insight into brain physiology for studying questions such as the cellular origin of fMRI. In mice, state-of-the-art optical technologies have been developed to probe neuronal activity as well as blood flow and oxygenation across spatial scales while manipulating cell-type-specific neuronal activity. However, translating such detailed results from laboratory animals into predictions relevant for human imaging requires both technical and theoretical efforts.

In the first part of this talk, I will demonstrate a framework for imaging the brain of awake behaving mice across scales, from two-photon microscopy in individual  $\sim 10$  micron wide cerebral arterioles and cells, to macroscopic fMRI. I will then show how high-resolution 3D images of cerebral vasculature measured in mice can be graphed into a connected network to model blood circulation using simple laws of physics. In this model, deep learning as well as equations of fluid dynamics, gas diffusion and the physics of magnetic resonance are leveraged to predict human brain imaging signals and improve their interpretation. Potential applications in neuroscience and fundamental cancer research will be discussed.

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