



## UKE Paper of the Month February 2024

### Synaptic wiring motifs in posterior parietal cortex support decision-making

Aaron T. Kuan, Giulio Bondanelli, Laura N. Driscoll, Julie Han, Minsu Kim, David G. C. Hildebrand, Brett J. Graham, Daniel E. Wilson, Logan A. Thomas, Stefano Panzeri, Christopher D. Harvey & Wei-Chung Allen Lee

*(Giulio Bondanelli is co-first author and Stefano Panzeri is co-senior co-corresponding author)*

[Nature. 2024 Feb 21](#)

#### ABSTRACT:

The posterior parietal cortex exhibits choice-selective activity during perceptual decision-making tasks. However, it is not known how this selective activity arises from the underlying synaptic connectivity. Here we combined virtual-reality behaviour, two-photon calcium imaging, high-throughput electron microscopy and circuit modelling to analyse how synaptic connectivity between neurons in the posterior parietal cortex relates to their selective activity. We found that excitatory pyramidal neurons preferentially target inhibitory interneurons with the same selectivity. In turn, inhibitory interneurons preferentially target pyramidal neurons with opposite selectivity, forming an opponent inhibition motif. This motif was present even between neurons with activity peaks in different task epochs. We developed neural-circuit models of the computations performed by these motifs, and found that opponent inhibition between neural populations with opposite selectivity amplifies selective inputs, thereby improving the encoding of trial-type information. The models also predict that opponent inhibition between neurons with activity peaks in different task epochs contributes to creating choice-specific sequential activity. These results provide evidence for how synaptic connectivity in cortical circuits supports a learned decision-making task.

#### STATEMENT:

*Decision-making is possibly the most studied topic in cognitive neuroscience, with wide implications in fields from social sciences to economics to artificial intelligence. Over decades of research, thousands of models of how it may be implemented in the brain have been proposed. Yet, we did not know which decision-making computation was implemented in the brain, because we did not know the connections between the neurons and the computations that these connections made. In highly interdisciplinary work, we combined electron microscopy anatomy, functional imaging of many neurons with single-cell resolution in mice performing decision-making, and advanced neural network mathematical modelling to unravel for the first time the circuit diagram and the computations in the cerebral cortex that lead to decision making. As a result of this tour-de-force, we have derived for the first time the “physics” equations that tell us how a brain decides. The basic computation is the winner-takes-it-all: neurons that have the stronger evidence to support correct decision-making shut down the others with weaker evidence. This work was supported by a highly competitive grant from the USA NIH BRAIN initiative (R01 R01NS108410 jointly awarded to the 3 co-corresponding authors), the first of this kind at UKE. The joint NIH award and the continued strong collaboration with the highly prestigious institutions in Boston contributes strongly to the internationalization and excellence of UKE and UHH.*

#### BACKGROUND:

The entire computational modelling work in this study was performed by the Institute of Neural Information Processing led by Stefano Panzeri who holds a Nucleus Professorship at UKE since 2021, funded by the university of excellence funds of the Universität Hamburg. It was part of the postdoctoral training work of Dr Giulio Bondanelli within the NIH BRAIN Initiative grant (R01NS108410). Both UKE authors have original training in theoretical physics and now perform interdisciplinary research devoted to understand how brain circuits process information.