

## **Sleep and wake in *C. elegans* are global brain states under tight control of arousal circuits.**

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A fundamental question in neuroscience is how global brain states like sleep and wakefulness, are reversibly generated and maintained. Specifically, how do populations of individual neurons contribute to the emergent properties of global brain states? We recently developed a technique for real-time brain-wide imaging with single cell resolution in *C. elegans* and have discovered brain-wide coordinated neuronal population activity that generates commands for behavioural action sequences in awake animals. Here we investigate global brain dynamics of sleep-wake transitions.

During developmental stages termed lethargus *C. elegans* exhibits prolonged phases of behavioural quiescence, which share fundamental properties with sleep in other animals. Using behavioural genetics, we have found a chemosensory arousal circuit involving the neuropeptide receptor NPR-1, which can trigger rapid and robust switching between behavioural quiescence and wake: in lethargic *npr-1* animals atmospheric oxygen levels induce sustained arousal, while preferred intermediate oxygen levels permit quiescence. We have exploited this paradigm to image brain-wide neuronal activity during these state transitions. Unlike the dynamical activity seen during wake which involves ~40% of neurons, we find that quiescence corresponds to sustained decreases in activity of almost all neurons including sensory, inter and motor neurons. However, a subset of GABAergic motor neurons and interneurons maintain activity during quiescence. Computational analysis of neuronal population activity reveals that quiescence is a stable attractor state embedded in the otherwise dynamical and cyclical evolution of brain-wide network activity. Furthermore, in lethargic *npr-1* animals oxygen stimulation induces a fast transition into the reversal motor command state and maintains higher levels of the cyclical awake activity, while removal of the arousal signal induces decreased wake state probability and cycles.

Based on these data we propose a model of sensory arousal operating in a top-down control manner while quiescence during lethargus is a default attractor for neural network activity in the brain.