The circadian clock is like an orchestra with many conductors

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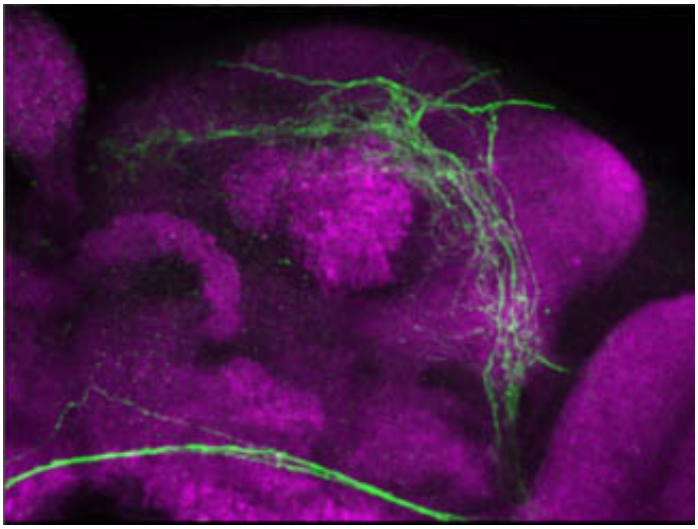


A fly brain (the shape of which is shown in magenta) with green fluorescent protein expressed in clock neuron projections. Credit: University of Michigan

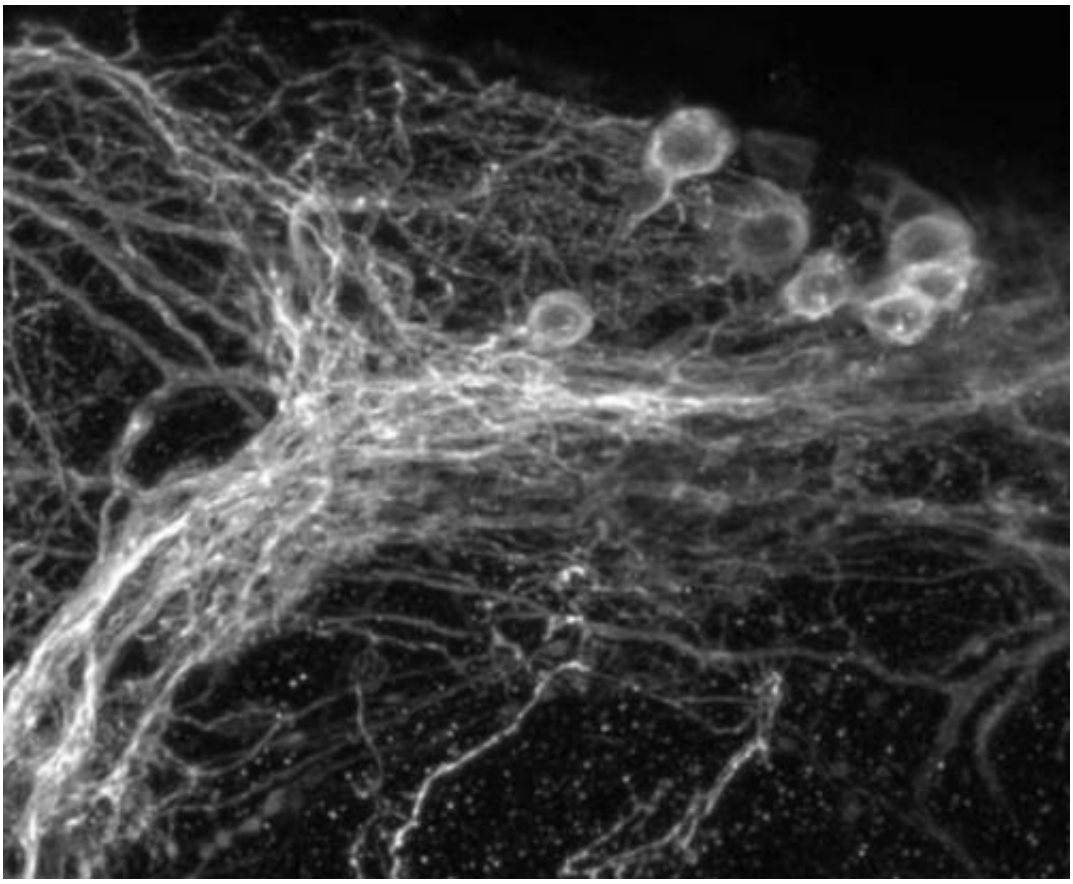
You've switched to the night shift and your weight skyrockets, or you wake at 7 a.m. on weekdays but sleep until noon on weekends—a social jet lag that can fog your Saturday and Sunday.

Life runs on rhythms driven by circadian clocks, and disruption of these cycles is associated with serious physical and emotional problems, says Orie Shafer, a University of Michigan assistant professor of molecular, cellular and developmental biology.

Now, new findings from Shafer and U-M doctoral student Zepeng Yao challenge the prevailing wisdom about how our body clocks are organized, and suggest that interactions among neurons that govern circadian rhythms are more complex than originally thought.

Yao and Shafer looked at the circadian clock neuron network in fruit flies, which is functionally similar to that of mammals, but at only 150 clock neurons is much simpler. Previously, scientists thought that a master group of eight clock neurons acted as pacemaker for the remaining 142 clock neurons—think of a conductor leading an orchestra—thus imposing the rhythm for the fruit fly circadian clock. It is thought that the same principle applies to mammals.

Interactions among clock neurons determine the strength and speed of circadian rhythms, Yao says. So, when researchers genetically changed the clock speeds of only the group of eight master pacemakers they could examine how well the conductor alone governed the orchestra. They found that without the environmental cues, the orchestra didn't follow the conductor as closely as previously thought.



These are clock neurons in a small region of the fly brain. Credit: University of Michigan

Some of the fruit flies completely lost sense of time, and others simultaneously demonstrated two different sleep cycles, one following the group of eight neurons and the other following some other set of neurons.

"The finding shows that instead of the entire orchestra following a single conductor, part of the orchestra is following a different conductor or not listening at all," Shafer said.

The findings suggest that instead of a group of master pacemaker neurons, the clock network consists of many independent clocks, each of

which drives rhythms in activity. Shafer and Yao suspect that a similar organization will be found in mammals, as well.

"A better understanding of the circadian clock mechanisms will be critical for attempts to alleviate the adverse effects associated with circadian disorders," Yao said.

Disrupting the circadian clock through shift work is associated with diabetes, obesity, stress, heart disease, mood disorders and cancer, among other disorders, Yao says. The International Agency for Research on Cancer classified shift work that disrupts circadian rhythms as a human carcinogen equal to cancer-causing ultraviolet radiation.

More information: "The Drosophila Circadian Clock is a Variably Coupled Network of Multiple Peptidergic Units," by Z. Yao et al. *Science*, 2014.

Provided by University of Michigan

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