

Peak production of rhythmic proteins occurs at two times of day

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Sleep disorders are reported to affect 50 to 70 million Americans, and have been linked to obesity and diabetes, as well as depression and other psychiatric disorders. Circadian cycles are driven by biological clocks that regulate behaviors such as sleep. Environmental or genetic alterations of the circadian clock contribute to jet lag, sleep disorders, and psychiatric disorders.

In a new study published 5 November in the open access journal *PLOS Biology*, Rob Jackson, who is professor at Tufts University School of Medicine (TUSM) and member of the neuroscience and genetics faculties at the Sackler School of Graduate Biomedical Sciences at Tufts, and colleagues have examined a large group of rhythmically produced proteins in cells that make up the circadian clock (also called clock cells) of the fruit fly *Drosophila*. Surprisingly, they find that a majority of the proteins are produced during two intervals of the [circadian cycle](#), the middle of the day or middle of the night.

"The circadian clocks of fruit flies and humans share molecular components, making the fruit fly an outstanding model for genetic studies focused on circadian behavior," said first author Yanmei Huang, research assistant professor of neuroscience at TUSM and a member of Jackson's team.

This study uses an innovative ribosome profiling technique to reveal the complete circadian program of [protein](#) synthesis (the 'circadian translome') within these clock cells. Fruit flies were collected at

different times of the circadian cycle, and mRNAs bound to ribosomes were isolated from clock cells; they were identified and quantified using RNA sequencing methods to document patterns in [protein production](#).

Messenger RNAs (mRNAs) carry instructions for protein production in a process called translation. Jackson's team used translational profiling, a method that indirectly reveals the production of proteins, and RNA sequencing to determine exactly when proteins in clock cells are produced from mRNAs. They identified 1,069 mRNAs, including hundreds of novel mRNAs that show peaks in translation at certain times of the day.

Proteins formed from these 1,069 mRNAs were classified by their biological function. Among the proteins whose functions are known, the researchers found that proteins required for similar functions were produced at the same times. Proteins required for metabolism show peak production during the day, while proteins required for cell growth show peak production during the night.

The researchers hope that by identifying the specific times proteins are produced in clock cells and their functions, they can better understand how the [circadian clock](#) regulates protein production and the body's biological systems. This, in turn, will provide insight into diseases and [psychiatric disorders](#) caused by disruptions in the circadian system.

"This highly synchronized protein production is a novel discovery. For the first time in any organism, we identified proteins within clock cells that show 24-hour rhythms of production," said senior author Rob Jackson.

Jackson's research in *Drosophila* has focused on genes and neural circuits that regulate circadian behavior. Some of his other recent work, in collaboration with postdoctoral associate Dr. Fanny S. Ng showed that

astrocytes, a type of glial cell in the brain, are critical in regulating [circadian rhythms](#).

More information: Huang Y, Ainsley JA, Reijmers LG, Jackson FR (2013) Translational Profiling of Clock Cells Reveals Circadianly Synchronized Protein Synthesis. *PLoS Biol* 11(11): e1001703. [DOI: 10.1371/journal.pbio.1001703](#)

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