

# Press Release

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## How brains surrender to sleep IMP researchers use roundworms to study basic principles of sleep

*Scientists at the Research Institute of Molecular Pathology (IMP) in Vienna study fundamental aspects of sleep in roundworms. Using advanced technologies, they monitor the activity of all nerve cells in the brain while they are falling asleep and waking up. The journal Science publishes their ground-breaking results this week.*



The illustration shows two worms: the top one is sleeping and most of its nerve cells are quiet, the second is awake with many of its nerve cells vigorously active. © IMP

Sleep is a universal trait in animals: every nervous system seems to regularly undergo and require states of relaxation, during which brain activity is drastically altered. Sleep is vital, as we experience in our daily lives, but scientists are still debating why this is the case.

A team of neurobiologists led by Manuel Zimmer of the IMP Vienna used the roundworm *C. elegans* to study in detail how the brain switches between wakefulness and sleep. Their results suggest that in tired animals sleep is a ground state of the brain that spontaneously establishes itself as long as strong external stimuli from the environment are absent.

Manuel Zimmer compares such a state to a marble resting in a valley; to push it uphill requires some effort, but it will roll back by itself when left on its own. The equivalent is to arouse a sleeping worm, thereby pushing its brain into wakefulness, but if still tired and left unperturbed it will fall back to sleep. Scientists who deal with complex dynamical systems use the term 'attractor' for such processes. 'We propose this attractor mechanism as an efficient means how overarching states like sleep and wakefulness can propagate throughout an entire brain', says Zimmer.

### Worms as models for sleep research

*C. elegans* was chosen as a model for sleep research because its nervous system consists of only 302 neurons. It is small enough for advanced microscopy approaches enabling access to the activity of all nerve cells in the brain at single-cell precision. This was key for obtaining new insights when monitoring the widespread reconfigurations that the brain undergoes between wakefulness and sleep.

Another challenge that the scientists faced was to control when worms would fall asleep and wake up. PhD-students Annika Nichols and Tomáš Eichler established an intriguing experimental system using variable oxygen concentrations as a switch. In their natural

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habitat, *C. elegans* live in soil where abundant microorganisms keep oxygen levels low. The researchers showed that under these preferred conditions the worms felt comfortable and could fall asleep, provided they were tired. Nichols and Eichler found that fresh air with atmospheric oxygen content alarms sleeping animals, causing them to rapidly wake up. 'This opened a door to effectively switch between the sleep and wake states during our experiments', says Nichols.

### **A neural meter for tiredness**

Nichols went on and recorded the activity of all neurons in the brain while triggering switches between sleep and wakefulness. She found that during sleep, most nerve cells that are vigorously active during wakefulness, become silent. However, a few specific types of nerve cells stay alert. One of these types, termed RIS, was previously shown to promote sleep by excreting a sleep substance. Nichols showed that RIS activity is already elevated in awake animals that are prone to sleep, hinting that it is a measure of how tired the brain is.

### **Sleep as a default attractor state of the brain**

When monitoring the activity of the brain as it fell asleep, Nichols made an interesting discovery: her computer analyses indicated that neuronal network activity spontaneously converged to a quiet and stable state. Originally, the researchers had assumed that RIS cells would force the nervous system into quiescence much like a conductor who silences the orchestra after the final chord. However, the new data suggest that RIS seems to act more like a mediator who negotiates an agreement between all players, followed by a collective action. The advantage of this scenario is that the dramatic changes between wakefulness and sleep can be triggered by rather subtly turning some of the regulatory knobs in the brain.

Despite the many differences between a worm brain and the human brain, these results provide a promising model for studying fundamental principles of brain organisation.

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### **Original Publication**

A global brain state underlies *C. elegans* sleep behavior. Annika L. A. Nichols, Tomáš Eichler, Richard Latham, Manuel Zimmer. *Science* 356, 23 June 2017.

### **Illustration**

An illustration can be downloaded and used free of charge in connection with this press release: <https://www.imp.ac.at/news>.

Caption: The illustration shows two worms: the top one is sleeping and most of its nerve cells are quiet, the second is awake with many of its nerve cells vigorously active.

### **About the IMP**

The Research Institute of Molecular Pathology (IMP) in Vienna is a basic biomedical research institute largely sponsored by Boehringer Ingelheim. With over 200 scientists from nearly 40 nations, the IMP is committed to scientific discovery of fundamental molecular and cellular mechanisms underlying complex biological phenomena. In particular, research at the IMP addresses topics in molecular and cellular biology; structural biology and biochemistry; gene expression and chromosome biology; stem cell biology and development; immunology and cancer; and neuroscience. The IMP is located at the Vienna BioCenter.

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### **About the Vienna BioCenter**

Vienna BioCenter (VBC) is a leading life sciences location in Europe, offering an extraordinary combination of research, business and education on a single campus. About 1.700 employees, 86 research groups, 17 biotech companies, 1.300 students, and scientists from more than 40 nations create a highly dynamic environment of international standards.

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### **VBC PhD Programme**

Much of the work underlying this publication was done by doctoral students at the IMP, enrolled in the Vienna BioCenter PhD Programme. Find out more about training opportunities for young scientists: [www.imp.ac.at/career/phd-master/](http://www.imp.ac.at/career/phd-master/)