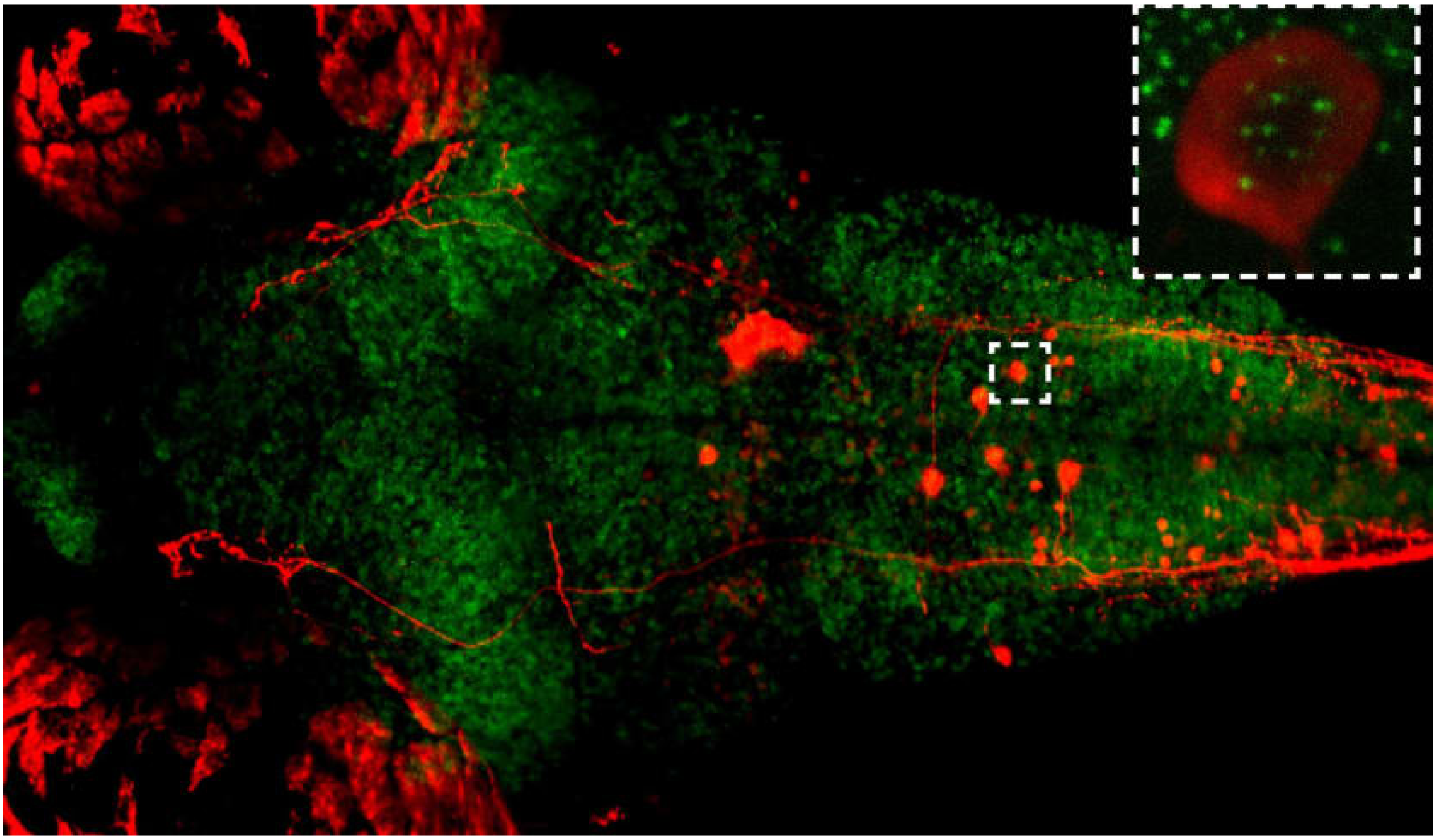

Imaging chromosome dynamics (green) in single neuron (red, dashed box) in live baby zebrafish Credit: David Zada / Lior.Appelbaum@biu.ac.il

World News

Why Do We Need Sleep? Israeli Scientists Solve the Mystery

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We all sleep. From jellyfish to frilled-neck lizards to flying squirrels to humans, the need for sleep is universal. But the biological reason why sleeplessness ultimately leads to death has always been a mystery.

Now a paper from Bar-Ilan University published Tuesday in the journal Nature Communications presents a groundbreaking theory: that when we sleep, our nerve cells take a break from their usual function, freeing their resources to reduce DNA damage that was accumulated during wakefulness.

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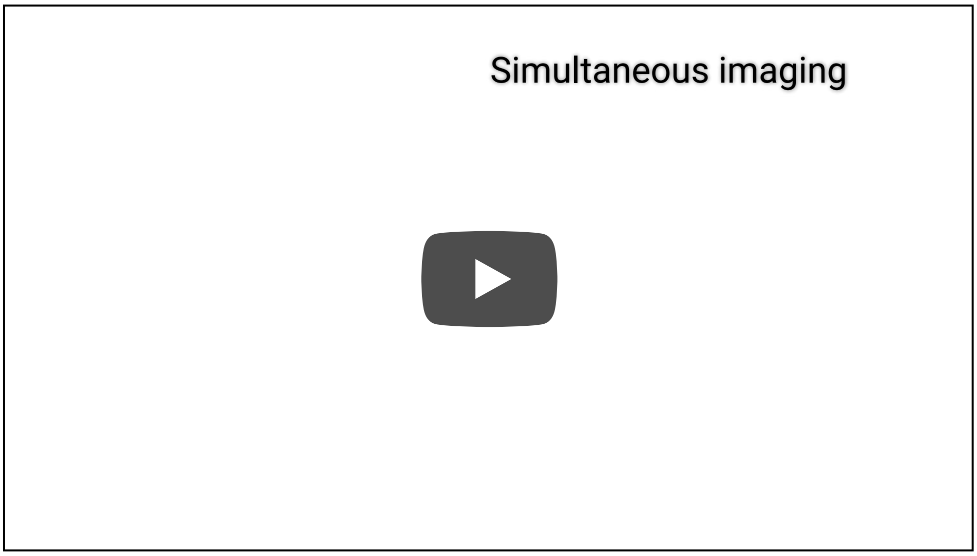
Haaretz Weekly Episode 17 Credit: Haaretz

Sleep makes no evolutionary sense in that it's an insanely vulnerable time for the slumberer. You're more likely to get eaten by a predator than when you're awake. So why would we evolve to need sleep?

It’s well established that loss of sleep affects brain performance such as memory and learning, from fruit flies to humans. This strongly argues that sleep is biochemically essential, and that sleep deprivation causes some kind of gradual systems collapse in the brain.



Simultaneous imaging of chromosome dynamics (red) and neuronal activity (green) in live zebrafish. Credit: David Zada

Now Prof. Lior Appelbaum – of Bar-Ilan University’s Mina and Everard Goodman Faculty of Life Sciences and Gonda (Goldschmied) Multidisciplinary Brain Research Center – believes he and his colleagues have discovered the biological why. Appelbaum supervised the study led by grad student David Zada.

Based on observing single neurons in live transparent fish during sleep and wakefulness, they concluded that if the organism doesn’t sleep, its cells don’t “power down”

Accruing neuronal DNA disrepair may explain how sleep and sleep disturbances affect brain performance, even aging and various brain disorders, the team postulates.

“When the organism whole sleeps, we can now define single sleeping cells,” Appelbaum told Haaretz. “Here for the first time we show how the sleep of the organism affects movement of chromosomes and DNA maintenance in specific single neurons.”

Sleep and the single cell

The fish in question were zebrafish, stripy freshwater minnows that originally hailed from the Himalayas and, being appropriately hardy, have become a popular aquarium pet – and research subject.

Animated illustration of the main findings

Why we need sleep[Credit: David Zada

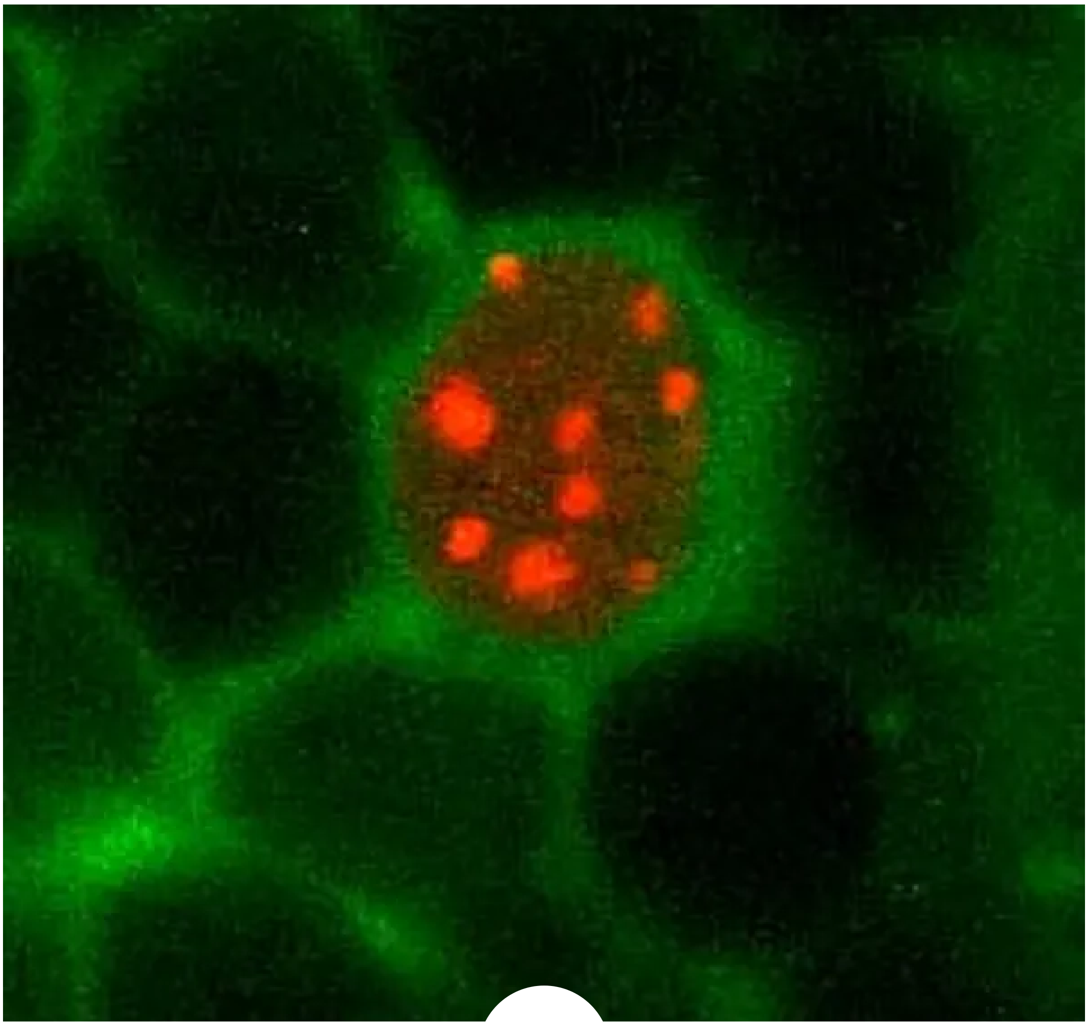
Fortunately for brain researchers, when zebrafish are young, they're transparent. Even their skulls are transparent, rendering them ideal for observational research of what's happening in their little brains. Importantly, like humans, zebrafish sleep during the night.

All our cells have DNA, with the exception of red blood cells in humans and some other animals. From the moment each cell comes into being, its DNA starts to suffer damage. All sorts of things can damage DNA, such as oxidants, sunbathing (in the case of skin cells) and even neuronal activity itself.

But the damage should be repaired by DNA repair enzymes, in theory.

Asked how exactly they could see when a zebrafish neuron was online or offline, Appelbaum says the researchers developed a method to mark chromosomes in the fish's DNA and track their movement inside the neuron. Their imaging achieved the resolution of seeing these chromosomes in the individual fish brain neurons.

Using 3D time-lapse photography and live baby zebrafish with marked chromosomes, the researchers discovered that when the fish is awake, chromosome movement in the cell nuclei is diminished and DNA damage accumulates. If wakefulness persists, this damage can reach unsafe levels.



Simultaneous imaging of chromosome dynamics (red) and neuronal activity (green) in live zebrafish. Credit: David Zada / Lior.Appelbaum@biu.ac.il

After prolonged sleep deprivation, neuronal cells can die. But during sleep, chromosome movement is faster. This fast movement is the expression of efficient nucleus maintenance.

In other words, sleep normalizes the levels of DNA damage in each individual neuron, the researchers say.

DNA maintenance isn't efficient enough when the organism and its nerves are awake; the organism requires an offline sleep period with reduced input to the brain for the repair to be proper.

"It's like potholes in the road," Appelbaum says. "Roads accumulate wear and tear, especially during daytime rush hours, and it's most convenient and efficient to fix them at night, when there's light traffic."

What about non-neuronal cells? Do they also fix their DNA when the animal is sleeping? Possibly not.

The researchers tested two other cell types, Appelbaum says: endothelial cells (vascular system) and glial cells. They didn't find differences in chromosome dynamics and DNA damage between day and night. "We suggest that this mechanism is specific to neurons. However, future work should test these processes in other cell types, such as muscles," he says.

When neurons go offline

The bottom line is that when the fish sleeps, movement surrounding the chromosomes escalates, and that increase in activity was shown to be essential to efficient DNA repair.

there is evidently some DNA repair in the neurons. But the balance tilts toward repair only when the zebrafish sleeps.

Experiments bolstered the finding; for instance, by making the fish sleep in the middle of its daytime wakefulness period by putting melatonin in the water, and filming the sleep-dependent increase of chromosome movements and efficient repair. Or by chemically inducing DNA damage in the fish – which was followed by increased sleep and normalization of this damage.

Appelbaum notes that we've known for a hundred years that sleep aids memory and learning, and brain performance in general, but the question remained what it did at the level of the single neuron. Now we know.

"We believe that under normal conditions, when we're tired, the accrued damage to the neuronal DNA somehow signals the brain to go to sleep," he says.

Asked if all neurons sleep when the organism does, and if they all probably sleep similarly, Appelbaum points out that our brains don't shut down during sleep; they enter another state.

"Maybe different neurons need different amounts of sleep," he says. "Also, it's likely that not every neuron can go to sleep when it feels like. This would cause chaos, and the brain has to function properly during the day. Evolution developed the brain with a consolidated, synchronized period of sleep dedicated to cellular maintenance."

The next phase of the research will be to look for neurons that are especially active during sleep, region by region of the brain. Another question is what happens to our DNA ones dreaming. Research published last year concluded that animals as far down as lizards can dream too.

An association with neurodegenerative diseases is also possible. Chronic sleep loss may increase the risk for neuronal cell death due to DNA damage. Appelbaum notes that one symptom of many brain diseases is insomnia.

Doctoral student David Zada was the first author of the study, with co-authors Dr. Tali Lerer-Goldshtein, Dr. Irina Bronshtein and Prof. Yuval Garini, all from Bar-Ilan University.

3D imaging of chromosome dynamics in two “dancing” cells in the brain of live zebrafish. Credit: 3D imaging of chromosome dynamics in two “dancing” cells in the brain of live zebrafish.