

## Why do we sleep?

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Credit: Chau Dang, LTD Space

While we can more or less abstain from some basic biological urges—for food, drink, and sex—we can't do the same for sleep. At some point, no matter how much espresso we drink, we just crash. And every animal that's been studied, from the fruit fly to the frog, also exhibits some sort of sleep-like behavior. (Paul Sternberg, Morgan Professor of Biology, was one of the first to show that even a millimeter-long worm called a nematode falls into some sort of somnolent state.) But why do we—and the rest of the animal kingdom—sleep in the first place?

"We spend so much of our time sleeping that it must be doing something important," says David Prober, assistant professor of biology and an expert on how genes and neurons regulate <u>sleep</u>. Yes, we snooze in order



to rest and recuperate, but what that means at the molecular, genetic, or even cellular level remains a mystery. "Saying that we sleep because we're tired is like saying we eat because we're hungry," Prober says. "That doesn't explain why it's better to eat some foods rather than others and what those different kinds of foods do for us."

No one knows exactly why we slumber, Prober says, but there are four main hypotheses. The first is that sleeping allows the body to repair cells damaged by metabolic byproducts called free radicals. The production of these highly reactive substances increases during the day, when metabolism is faster. Indeed, scientists have found that the expression of genes involved in fixing cells gets kicked up a notch during sleep. This hypothesis is consistent with the fact that smaller animals, which tend to have higher metabolic rates (and therefore produce more free radicals), tend to sleep more. For example, some mice sleep for 20 hours a day, while giraffes and elephants only need two- to three-hour power naps.

Another idea is that sleep helps replenish fuel, which is burned while awake. One possible fuel is ATP, the all-purpose energy-carrying molecule, which creates an end product called adenosine when burned. So when ATP is low, adenosine is high, which tells the body that it's time to sleep. While a postdoc at Harvard, Prober helped lead some experiments in which zebrafish were given drugs that prevented adenosine from latching onto receptor molecules, causing the fish to sleep less. But when given drugs with the opposite effect, they slept more. He has since expanded on these studies at Caltech.

Sleep might also be a time for your brain to do a little housekeeping. As you learn and absorb information throughout the day, you're constantly generating new synapses, the junctions between neurons through which brain signals travel. But your skull has limited space, so bedtime might be when superfluous synapses are cleaned out.



And finally, during your daily slumber, your brain might be replaying the events of the day, reinforcing memory and learning. Thanos Siapas, associate professor of computation and neural systems, is one of several scientists who have done experiments that suggest this explanation for sleep. He and his colleagues looked at the brain activity of rats while the rodents ran through a maze and then again while they slept. The patterns were similar, suggesting the rats were reliving their day while asleep.

Of course, the real reason for sleep could be any combination of these four ideas, Prober says. Or perhaps only one of these hypotheses might have been true in the evolutionary past, but as organisms evolved, they developed additional uses for sleep.

Researchers in Prober's lab look for the genetic and neural systems that affect zebrafish sleeping patterns by tweaking their genes and watching them doze off. An overhead camera records hundreds of tiny zebrafish larvae as they swim in an array of shallow square dishes. A computer automatically determines whether the fish are awake or not based on whether they're moving or still, and whether they respond to various stimuli. Prober has identified about 500 drugs that affect their sleeping patterns, and now his lab is searching for the relevant genetic pathways. By studying the fish, the researchers hope to better understand sleep in more complex organisms like humans. "Even if we find only a few new genes, that'll really open up the field," he says. The future is promising, he adds, and for that, it'll be well worth staying awake.

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