

*This is the description of Buddy the mouse that Saey wrote after first meeting Buddy.*

Buddy, a black mouse sits quietly in a dimly lit room inside a black box on a folding table. It's going to be an exciting day for Buddy, but he doesn't know that yet, says neuroscientist Jennie Young. Today, Young will place a variety of objects in Buddy's box and observe how some cells in a part of the mouse's brain involved in making memories behave while he is learning and later thinking and dreaming about the objects.

Young gets her insight into what Buddy is thinking from tiny electrodes implanted in this brain structure, called the hippocampus, deep in the mouse's brain.

In a previous study, other mice like Buddy also had electrodes implanted in their brains. But instead of memorizing objects, the mice motivated by chocolate sprinkles, ran along a track. A black and white STOP sign and abstract designs in black cardboard on the wall provided markers the mice could use to track their progress. As Buddy moves, cells in the hippocampus keep track of the positional information. Every time Buddy visits a particular corner, for instance, one cell that is designated to represent that corner will fire while cells that store information about moving along a wall stay silent. As he moves, new cells will fire in turn. Scientists can follow a mouse's progress in a maze simply by watching the order in which these place-specific cells fire.

Behind a black curtain, Young records the firing of Buddy's brain cells with a bank of computers. A speaker crackles with what sounds to the untrained listener like radio static. To Young's ear the static is the sound of memories being made. Each time an electrode detects electrical activity in one of the neurons it touches, it translates the activity to tracings on the computer screen and audible crackles.

While the mouse is awake and moving around in his box, running a maze or exploring new objects, his brain cells fire in a rhythmic pattern. Mice don't sleep in big chunks of time the way humans do. Instead, Buddy takes frequent cat naps. As he sleeps, his brain waves slow down, but small, rapid spurts of brain cell activity, called ripples, interrupt the slow rolling waves of sleep and burst above the background static. During those ripples, which last no more than a fraction of a second, the place cells fire in the same order as when the mouse was awake and exploring.

Scientists who first discovered this replay during sleep surmised that the ripples might be a way of reviewing important information from the day and making memories from those events stronger. Mice, rats and humans deprived of sleep all have trouble remembering things, but until recently, no one had a way to demonstrate directly that missing replay was responsible for the memory problem.

*This is the published opening for "The Why of Sleep," featuring Buddy the mouse.*

In a lab at MIT, a small black mouse named Buddy sleeps alone inside a box. A cone resembling a satellite dish sits atop his head. But the dish doesn't receive signals from outer space. Instead it sends transmissions from deep inside Buddy's brain to a bank of computers across the room.

Scientists like Jennie Young eavesdrop on the transmissions, essentially reading Buddy's mind, or at least that part of his mind occupied with a recent trip along a Plexiglas track littered with chocolate sprinkles. Young and her colleagues in Susumu Tonegawa's laboratory are monitoring nerve cells inside the hippocampus, one of the brain's most important learning and memory centers. Some of the cells in the sea horse-shaped hippocampus fired bursts of electrical energy as Buddy moved along the track. As he sleeps in his black box, those same cells spark to life again, replaying progress along the track in fast-forward or rapid reverse.

By recording the slumbering Buddy's brain cell activity, the scientists hope to glean clues to one of biology's greatest mysteries: the reason for sleep. Although sleep is among the most basic of behaviors, its function has proved elusive. Scientists say sleep's job is to save energy, or to build up substances needed during waking or to tear down unneeded connections between brain cells. Some emphasize sleep's special role in learning and memory. Others suggest that sleep regulates emotions. Or strengthens the immune system. And some scientists believe sleep is simply something that emerges naturally from having networks of neurons wired together.

"There are as many theories of sleep's functions as there are sleep researchers," says Mehdi Tafti, a geneticist at the University of Lausanne in Switzerland.

None of the many models for why people (and other animals) sleep can explain all of its complexity, says Robert Stickgold of Harvard Medical School in Boston. He equates proponents of the different sleep theories to blind men describing an elephant. It's a snake, or a tree or a wall, depending on which part of the elephant the men touch. Similarly, the answer to sleep's function seems to depend on what approach a given researcher takes. And each proposed idea contains inconsistencies that keep other sleep researchers from embracing it.

"There's no one theory that has enough unified evidence for it to be widely accepted," says Paul Shaw of Washington University in St. Louis.

Many sleep theories have been widely tested, though. Using brain wave recordings, genetic analyses, word tests, video games and various other methods, researchers have uncovered many of the pieces to the puzzle of sleep, even if they don't yet all fit together.