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Jellies and their twinkling protein

Glowing with a cool inner light, jellyfish exude tranquillity. On a molecular level, though, the substance that gives them their ghostly glow is a bit flashier: The individual molecules of variants of green fluorescent protein (GFP) blink repeatedly when excited with a laser, a new study shows.

Some smaller organic molecules can also blink, says Roger Y. Tsien of the University of California, San Diego in La Jolla, but GFP is one of the first molecules known to do so at room temperature under "normal biological conditions." Tsien, William E. Moerner, and their colleagues describe their findings in the July 24 NATURE.

The protein coils itself into the shape of a barrel, with three amino acids in the center serving as the light-emitting chromophore (SN: 10/5/96, p. 212). The scientists examined two mutant forms that give off a brighter, yellow light rather than the normal bluish green glow.

By immobilizing the protein molecules in a gel and illuminating them with light 488 nanometers (nm) in wavelength, the researchers could see the molecules emit light for a few seconds, darken, then turn on again. The cycle repeated itself for several minutes before the molecules stayed dark for a long time, apparently turned off for good.

Shining 405-nm light on the molecules for a few minutes reactivated them, however. Following this treatment, illumination with the original light caused the molecule to glow and blink again.

This unusual switching behavior may make GFP a useful material for optical data storage, the researchers suggest. One bit of data could be stored by a single molecule of GFP rather than by macroscopic dots of bacteriorhodopsin, another light-responsive protein with data storage potential (SN: 3/8/97, p. 140).

"To me, [the study] says that even single molecules have dynamic processes



The Pacific Northwest jellyfish, Aequorea victoria, glows bright with GFP, an intriguing fluorescent protein.

of their own," says George N. Phillips Jr. of Rice University in Houston. "You can't just go by the snapshots of what they look like."

The mechanism behind the blinking has yet to be explained. "There must be some kind of conformational change," says S. James Remington of the University of Oregon in Eugene. Moerner suggests that changes in the charge around the chromophore are responsible. Experiments to determine GFP's structure immediately after excitation with light may provide some answers, Phillips says.

"The whole field of structural biology is moving from one where static images are generated to one where dynamic processes are appreciated more," he adds. "This is a striking example of how if you ignore the dynamics, you'll miss all sorts of interesting things." —*C. Wu*

Secrets underlie lethal heart condition

Genetic mutations that can cause the heart to stop suddenly in otherwise healthy people are proving to be more varied and insidious than researchers had suspected. The condition, called long QT syndrome, may also be more prevalent than the currently estimated rate of 1 in 9.000.

Long QT syndrome is an inherited disease that causes a rapid heartbeat, fainting, and sometimes death—most often, apparently, during stress. It could account for half of the approximately 8,000 sudden, unexplained deaths among children and adults each year, says G. Michael Vincent, a cardiologist at the University of Utah School of Medicine in Salt Lake City.

Researchers have identified mutations in several genes, any one of which can produce the heart problems. Three of these genes had been detected by 1996 (SN: 1/13/96, p. 31), two were discovered in the last year, and another is suspected. Carriers of one of these mutated genes have a 50 percent chance of passing it on to their children. In rare cases, the mutation can cause deafness, too.

The condition gets its name from the unusually long interval between two points, labeled Q and T, on an electrocardiogram (EKG), which records a person's heart rhythm. The excessive interval signals that cells in the heart aren't recharging fully between beats. Sudden jolts of fear, excitement, or physical exertion may increase this already long gap. The person suffers arrhythmia, a fluttery heartbeat that pumps insufficient blood to the brain, and faints. The worst episodes conclude with the heart's stopping, causing death, Vincent says.

Recent findings on the syndrome continue to turn up surprises.

For example, the QT interval can vary greatly in people who have the syndrome, even among those who are related. Moreover, genetic screening made possible by the new findings turns up many potential cases that would have gone undetected in the past, says Katherine Timothy, research coordinator of the Utah team. For 10 to 15 percent of those who have one of the characteristic mutations, an EKG shows no sign of the ailment.

Another 30 percent of carriers have borderline long QT intervals, Vincent reported last week at an American Heart Association seminar in Portland, Ore. "That further complicates the diagnosis." He believes that these slightly longer than normal intervals could be present in as many as 1 in 5,000 people.

Long QT syndrome is treatable. Early diagnosis is especially important because the disorder causes many deaths during puberty. Beta blockers, which inhibit the nervous system's influence on the heart, are effective against long QT syndrome in about 90 percent of cases. "Beta blockers slow the heart rate and make the heart resistant to irregular rhythms," says Charles R. Bridges Jr., a heart surgeon at the University of Pennsylvania in Philadelphia. The recent QT findings are "fascinating stuff," he adds.

Scientists have recently come to suspect that a low-protein diet or drug use can also trigger the heart problem in people with long QT syndrome. Several people with the condition have died while smoking marijuana, and one died while using cocaine, Vincent says. Anecdotal evidence suggests that some prescription medications may also exacerbate the condition.

One rare form of long QT syndrome is accompanied by congenital deafness, but only when both parents pass along a copy of a defective gene. Studies in mice, published earlier this year, indicate that this gene variant may be recessive, unlike the other long QT mutations.

Women are diagnosed with long QT syndrome more often than men, Vincent says. Women normally have slightly longer QT intervals and thus may be more susceptible to the syndrome's effects, he suggests. In addition, many boys who die of unidentified causes may in fact have succumbed to long QT syndrome, leaving fewer men than women with the syndrome. "That skews the subsequent evaluation," he says.

Because long QT syndrome so often goes undiagnosed, the Utah researchers have amassed data by surveying relatives of people suspected of having had it. After READER'S DIGEST published a story on Vincent's work in 1996, 2,500 people called his office to relate an unexplained sudden death, usually of a young person, in the family. Vincent is now seeking funding to investigate those cases. —N. Seppa