icant blood-flow increases while subjects awaited the electric shock. Blood flow reflects the activity of discrete groups of brain cells.

Although a brain structure called the amygdala did not light up in the PET study, there is much evidence it plays an important role in anxiety production, Reiman notes.

He and his co-workers previously studied people with panic disorder, which is characterized by recurrent anxiety attacks. An infusion of sodium lactate launches an anxiety attack in many panic disorder patients. PET images show that before lactate infusion these individuals have uneven blood flow and disturbed oxygen metabolism in the parahippocampal gyrus, another part of the temporal lobes. During a lactate-induced anxiety attack, blood flow increases in the temporal poles, the same regions implicated in nonpanic anxiety.

The parahippocampal gyrus feeds information to the temporal poles, Reiman says.

While PET is a promising tool in the study of normal emotions, "we're going to have to develop creative new ways to induce emotions in the laboratory," Reiman says. — *B. Bower*

Cell-like biosensor opens ionic floodgates

Tiny things become quite apparent when their presence triggers huge effects. Take the pufferfish poison tetrodotoxin. A relatively few molecules deactivate neurons by plugging membrane pores, or channels, which control the cross-membrane travel of many thousands of sodium ions during a neural impulse. In most animals, vanishingly small amounts of tetrodotoxin have the extremely obvious effect of death.

Scientists are learning how to build ion channels into silicon-based biosensors that they hope will announce the presence of minuscule amounts of neurotransmitters, drugs and workplace or battlefield poisons. "We are trying to build a generic sensor for a range of compounds that have specific physiological effects," says biochemist Frances S. Ligler of the Naval Research Laboratory in Washington, D.C. For instance, the poisons tetrodotoxin, saxitoxin and μ-conotoxin differ chemically, but they all block sodium ion channels by binding to the proteins that make up the channels. She estimates that several more years of development lie ahead for a reliable biosensor of this type.

Sodium, calcium and other ion channels pepper cell membranes, which are made of two fragile layers of long lipid molecules that mix well with water on one end but are oily on the other. The oily, or hydrophobic, ends form the interior of the lipid bilayer by bunching together to avoid contact with the watery environments inside and outside the cells. The hydrophilic heads of the lipids make up the membrane's interior and exterior surfaces. Spanning the two-molecule-thick bilayer are the ion channels, whose openings are regulated by a variety of biologically important molecules. With the new type of biosensor, Ligler and her colleague Thomas L. Fare hope to use the bilayer-bound channels as tiny detectors of channel-binding compounds. Such binding causes large changes in ionic currents — monitored by an underlying silicon electrode — and should give away the presence of the binding molecules.

To make the biosensors, the researchers use a strong acid to etch tiny pores into the surface of a silicon electrode on which they assemble an "asymmetric bilayer" made of a standard, cell-like layer of individual lipid molecules and a layer of polymerized lipids. "This makes the bilayer tougher" than a regular cell membrane, Ligler says. During the assembly, the researchers also include any of a variety of ion channels — calcium channels from bovine brain tissue, for instance. The porous surface of the electrode provides spaces below the membrane into, and from which, ions can flow through channels.

Using silicon as the current-detecting electrode, the researchers see no obstacles to building their biosensors with complex electronic circuitry that will amplify tiny signals from changing ionic currents, subtract background noise or even recognize exactly which of many possible molecules is binding to the channel proteins at any one time to cause changes in ionic flow.

"We are building a biosensor that will detect a broad class of compounds as opposed to one that is highly specific," Ligler says. Many biosensor developers attach antibodies or enzymes — which bind or recognize only one or a few compounds — to electrodes to make biosensors that exclusively detect, say, glucose or dopamine. "Ion-channel proteins bind a variety of compounds," Ligler stresses. And because biosensors made with the channels do not work by binding only specific chemical structures, they should detect even unknown compounds that may have the same physiological consequences. Ligler is describing the new electrode in Hawaii this week at the Molecular Electronics — Science and Technology Conference. — *I. Amato*

Weakness for alcohol borne by muscles

A new study of a homogeneous population of alcoholics with no signs of sickness reveals that long-term, heavy alcohol consumption damages the heart in one-third of alcoholics and skeletal muscles in almost half. "It is very clear that [alcohol's toxic effects on muscle] are significant and far more widespread than anybody previously thought," says pathologist Emanuel Rubin of Jefferson Medical College in Philadelphia, a coauthor of the study.

The research also demonstrates for the first time, he says, that beyond a certain high level of lifetime alcohol consumption, muscle weakness is proportional to the amount of alcohol consumed.

"So the more alcohol consumed in a lifetime, the less the strength of the heart and the less the strength of the [skeletal] muscles," Rubin says. "But this is not to say that one or two drinks a day will damage you in any way. You have to drink a lot for a long period of time to get these effects."

His team found skeletal muscle disease in people who consumed a lifetime dose of more than 13 kilograms per kilogram of body weight. For a 154-pound man, this corresponds to drinking more than 12 ounces of 86-proof whiskey a day for 20 years.

Rubin and his co-workers studied 50 white men aged 25 to 59 who voluntarily entered an alcohol treatment unit in Barcelona, Spain. All held stable jobs and had supportive families. In addition, all were "reasonably well nourished," so the effects found in the study "have nothing to do with nutrition," Rubin says. These individuals were compared with an age-matched control group of 50 white male physicians who were not heavy drinkers.

Using a force-measuring machine to assess the strength of each man's deltoid muscle, the researchers found the alcoholics significantly weaker than the controls; 42 percent were very weak. And by microscopically examining muscle tissue samples from the subjects, the researchers detected irreversible changes, such as cell death and scarring, in 46 percent. In contrast, the 10 samples taken from controls were entirely normal. The findings appear in the Feb. 16 NEW ENGLAND JOURNAL OF MEDICINE.

Noninvasive heart scans revealed abnormal heart function in 33 percent of the alcoholics but normal function in all the controls. Six alcoholics with severely weakened hearts underwent diagnostic biopsies, all of which revealed multiple signs of cardiac muscle breakdown due to alcohol, Rubin says. None of these alcoholics suffered from coronary artery disease.

"There was a very good correlation between damage to [skeletal] muscle and damage to the heart," Rubin says. Heart and skeletal muscles share certain features, such as striations. He concludes, therefore, that "alcohol is a toxin for striated muscle regardless of where it is." — *I. Wickelgren*