Research in Progress

Making Waves

On March 27, 1964, the Great Alaskan Earthquake, 8.5 on the Richter scale, caused millions of dollars in damage and over a hundred deaths. Ninety-five percent of those deaths resulted not from the earthquake itself, but from a series of devastating waves — tsunamis — that propagated throughout the Pacific Ocean, causing death and destruction as far away as Hawaii, Washington, Oregon, and California.

Crescent City, California, 2,800 kilometers from the earthquake epicenter, was given four hour's notice of the tsunami's arrival. (Although these waves travel through the open ocean at 600-900 kilometers per hour, some warning is occasionally possible.) The first two waves, just two meters high, caused only minor damage. Believing that all was clear, some residents returned to begin cleaning up, only to be met by waves three and four, each about seven meters in height. These waves tossed debris around the town with remarkable force; one of them hurled a gasoline tanker truck against a building, starting a fire that spread to a nearby group of fuel storage tanks, which burned out of control for three days. The tsunami killed 11 people in Crescent City, injured 35, and destroyed 30 city blocks.

No major tsunami has struck the continental United States since that time, so in order to study them Fredric Raichlen, professor of civil engineering, has to make his own. Along with his former students, Joseph Hammack, Derek Goring, and Thierry Lepelletier, and his current students, Costas Synolakis and Jeff Zelt, Raichlen has conducted a series of experiments in two large wave tanks in which he can produce artificial tsunamis. He investigates the characteristics of these waves and the reactions of simulated harbors and shorelines to their impacts.

According to Raichlen, the word "tsunami" comes from the Japanese for "harbor wave." Scientists prefer "tsunami" to the more common, though inaccurate, term "tidal wave" since tsunamis have nothing to do with the tides. Caused by earthquakes, undersea volcanoes, landslides, or other major geological disturbances, most tsunamis are barely noticeable in the open ocean. As swells only a meter above the average sea level, even the largest tsunamis would pass harmlessly under ocean-going vessels.

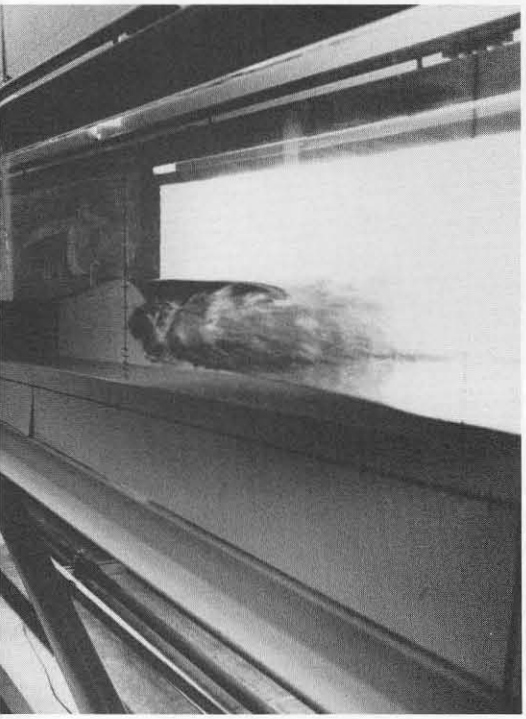
It's only when a tsunami meets the upwardly sloping ocean floor near an island or continent that its power becomes evident. Raichlen and Synolakis are studying the process of the run-up of these long waves onto beaches. Using the wave tank shown in the photo, they study three types of waves: those that travel unbroken up the beach, those that break before their arrival at the beach, and those that break on the beach itself.

As the Japanese word implies, tsunamis cause great damage within harbors. One would think that harbors with relatively narrow inlets would have a fair chance of avoiding tsunami damage. But it turns out that even certain of these harbors sustain huge amounts of damage from the waves. This happens because the inlet allows the tsunami's energy into the harbor, but then this energy has difficulty escaping. These harbors may actually be "tuned" to resonate at the frequency of the tsunami, causing waves to slosh back and forth in them like coffee in a cup. Much of Raichlen's work is involved with understanding this resonance. Raichlen and student Jeff Zelt perform experimental studies of harbor resonance in a basin 9.6 meters long by 4.7 meters wide in which they bombard simulated harbors with simulated tsunamis. These experiments are useful in developing three-dimensional numerical models of harbor resonance.

Not all of Raichlen's work deals directly with tsunamis. Another of his goals is to determine the internal kinematics of breaking water waves. For these studies, Raichlen and Jim Skjelbreia have equipped the largest of the wave tanks (a tilting one 40 meters long, 110 centimeters wide, and 61 centimeters deep) with a laser doppler velocimeter. This instrument allows them to determine the speeds of different regions of a breaking wave. To do this, laser light is reflected from naturally occurring tiny particles in the water. The faster these particles move, the more the frequency of the reflected light will shift.

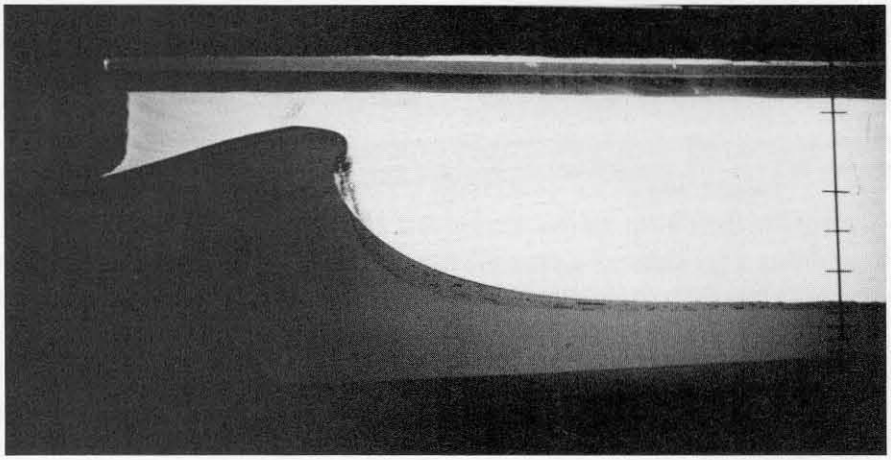
"Such measurements will be helpful in telling us how forces are distributed on a structure when waves impinge upon it," says Raichlen. And the data will also be useful in determining whether a given structure can be designed to withstand tsunamis, or whether the structure will need to be sited farther inland so that it never becomes involved.

Another group of studies, in which graduate student Francis Ting is involved, deals with the interaction of waves with underwater trenches. This



work is important for understanding the aging of navigation channels. Says Raichlen, "If you dredge a navigation channel, and waves propagate over it, you may get into some interesting problems, especially if fine sediments near the bottom turn the fluid into a density-stratified one. Waves can set up internal oscillations within a trench, affecting fluid velocities near the boundaries and modifying erosion processes."

Raichlen receives funding for his work from the National Science Foundation and the Office of Naval Research. □ — *RF*



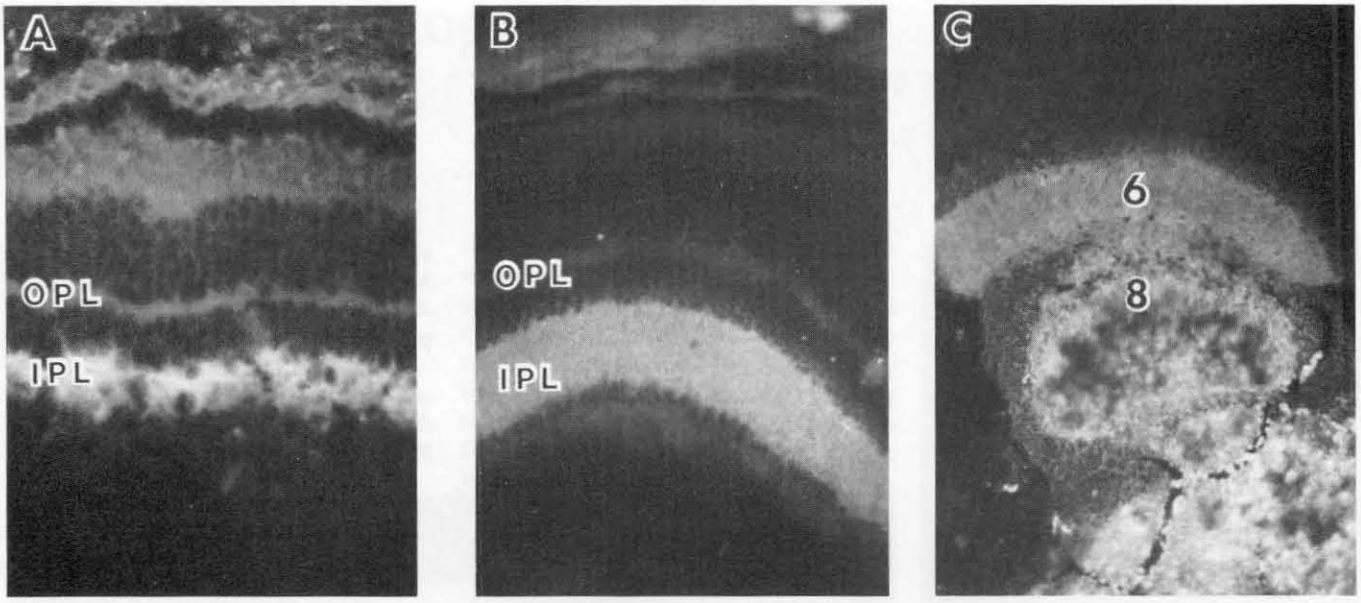
At left Fredric Raichlen and his students watch as a wave crashes in their 37.7-meter-long tank. From left, the students are Francis Ting, Costas Synolakis, and Jeff Zelt. The photo at right has caught a wave just at the point of cresting.

Fly Antibodies and Human Brains: A Marriage of Ideas

CALTECH RESEARCHERS have discovered that our brains have more in common with the brains of fruit-flies than was previously believed. Carol Miller, a visiting associate in biology, has tested a panel of 146 monoclonal antibodies (MAbs) targeted at the *Drosophila* brain on fresh-frozen sections of human brains and found, to her surprise, that over half the MAbs reacted, staining the tissue in interesting and specific ways. This unexpected finding is much more than a mere laboratory curiosity. It may help scientists understand the molecular bases of several devastating neurological disorders, among them Alzheimer's disease and amyotrophic lateral sclerosis (ALS — also called Lou Gehrig's disease).

When she's asked what possessed her to try reacting *Drosophila* antibodies with human brain tissue, Miller answers, with a laugh, "Obviously, a marriage of ideas!" For Miller, who's also Chief of Neuropathology at USC, is married to Seymour Benzer, Caltech's James G. Boswell Professor of Neuroscience. In her study of human brain disease, Miller was about to embark on a lengthy and tedious series of experiments designed eventually to lead to MAbs targeted at the sub-classes of brain cells that these diseases destroy. But Benzer already had in hand his panel of MAbs targeted at the brains of his famous fruit flies. And Miller, noting similarities between some *Drosophila* mutants and some human brain disorders, decided to give his MAbs a try.

No one, to Miller's knowledge, had ever before attempted extensive antibody cross-reactions between such distantly related species. And no one expected such a large proportion of "hits." It's not simply the number of cross-reactions that's surprising. All living things contain many similar molecules, a result of their common evolutionary origins and the constraints imposed by our earthly environment. Some of Benzer's MAbs, for example, bind to the nuclei of all cells, even those belonging to plants like onion and garlic. The really surprising thing in Miller's



One monoclonal antibody stains corresponding regions in (A) the human retina, (B) the mouse retina, and (C) the equivalent of the retina in the fruit fly's eye. IPL and OPL are the inner and outer plexiform layers. Medulla and lamina are 6 and 8.

experiments is the extent of the *specific* cross-reactivity. One *Drosophila* MAb, for example, stains only a certain subclass of cells in the hippocampus, a brain structure involved in memory that receives heavy damage in Alzheimer's disease. Another reacts preferentially with spinal cord motor neurons, which degenerate in ALS.

Like most important scientific discoveries, Miller's prompts more questions than it answers. For one thing, the nature of the molecules — the antigens — to which the antibodies bind is unknown. Are they proteins, glycoproteins, lipids, carbohydrates, or some of each? Are *Drosophila* and human antigens identical or nearly identical, or are only portions of the molecules similar? And what was the evolutionary sequence of events? Is the cross-reactivity the result of convergent evolution in which similar molecules arise from dissimilar ancestor molecules due to common environmental constraints? Or is the cross-reactivity the result of conservative evolution, in which a molecule is simply too important in one certain configuration to permit any evolutionary change, even over hundreds of millions of years?

To answer some of these questions, Miller and postdoc David Hinton are performing immuno-affinity chromatography in an attempt at purifying some of the antigens. In this technique, an antibody is first bound to a solid substrate in a column. Then homogenized brain tissue is poured through the column. The antigen molecules adhere to the immobilized antibodies and remain in the column while everything else passes through. Techniques such as amino acid sequencing can then be used to identify the antigen.

According to some preliminary data, one of these antigens is similar to the protein that makes up the "paired helical filaments," which irreversibly accumulate in, and eventually destroy, neurons in the brains of those afflicted with Alzheimer's disease. This may indicate that a related molecule resides in the normal *Drosophila* brain, encouraging Miller to believe that important aspects of Alzheimer's could be modeled in the fruit fly. This is particularly significant since to date no satisfactory animal model of Alzheimer's disease has been devised.

Miller and Hinton, along with Janet Blanks of the Doheny Eye Institute at USC Medical Center, are also working on a theoretical scheme intended to classify cross-species immunoreactivity in a hierarchical fashion by comparing the eyes of *Drosophila* and *Homo sapiens*. At the apex of the hierarchy would be antigens found only in a single cell in a single species. At its base would be those antigens found in all cells in all species. Intermediate levels of the hierarchy would, for example, group all antigens found in specific neuronal subtypes or all antigens found just in the central nervous system and nowhere else.

Obtaining fresh human brain tissue is one of the more problematic aspects of Miller's work. While animal brains can be obtained immediately after death, it is far more difficult to obtain human tissue quickly after a patient's demise. In addition, brains can't be preserved for these studies by the usual methods, since fixation in formaldehyde or related compounds destroys the reactivity of the antigens with the MAbs. Miller is in a position to ameliorate such difficulties, however, since she's in close touch with the pathology department's autopsy unit. In this way, she can occasionally obtain human brains that have been fresh-frozen less than six hours after death, a remarkably short interval for human tissue. Miller's research takes a lot of effort but it will all be worthwhile if it leads to a deeper understanding of these devastating brain disorders.

Miller's work is funded by the Amyotrophic Lateral Sclerosis Society of America, the Muscular Dystrophy Association, and the National Institutes of Health. Benzer's is funded by the National Science Foundation. □

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