Hot stuff. Suddenly drug companies are scrambling for synthetic chemists—and finding them in short supply.

meet the demands of their biologists. "We have vice presidents asking us why we haven't done any work on a good target," says one researcher at a midsized California-based biotech company.

That's why rent-a-chemist companies such as Albany Molecular Research and Array Biopharma in Boulder, Colorado, have seen revenues as much as double annually over the past few years, although admittedly from a small base. Each company has hired over 100 chemists, with more on the way. Although the two firms are engaged in their own drug-discovery efforts, their assembled chemical talents are largely directed at custom syntheses for partners. Albany Molecular recently placed seventh on *Business Week*'s 2001 list of hot growth companies, and Array was able to complete its initial public offering this past December when other companies refused even to try. "We have been able to capitalize on the increasing demand for high-quality chemical synthesis," says Robert Conway, Array's chief executive officer, whose company booked $5.7 million in revenues during the quarter that ended 30 June, up 152% over the same period a year earlier.

Albany Molecular and Array Biopharma are full-service companies offering a host of chemical services. Clients pay on a sliding scale based on the number of steps in the milligram-to-kilogram journey. In a recent contract, for example, Albany Molecular synthesized more than 400 compounds for use in a cardiovascular drug screen. After the contracting firm identified a lead compound from the initial 400, it came back to Albany—for an additional, larger fee—to further develop the drug candidate. Albany's partners include Eli Lilly, Aventis, and DuPont, whose spokespersons declined to comment publicly about their use of such contractors.

Other companies are smaller and specialize in a certain type of chemistry. Synthon Chiragenics in Monmouth Junction, New Jersey, makes carbohydrate-based drugs using chemistries developed by the company's founder and chief scientific officer, Rawle Hollingsworth, for example. Fluorous Technologies of Pittsburgh, Pennsylvania, is an expert in organic syntheses involving fluorine.

If chemists are in such short supply, where do these entrepreneurs find them? "We've been remarkably successful at taking people away from the major pharmaceutical companies," brags Array's Conway. Adds D'Ambra, "The market is tight, no doubt about it, but we work hard at creating a place that's attractive to good chemists." That formula includes competitive pay, plenty of stock options, and what one chemist called "the opportunity to work with other chemical heads." Says another, "It's like being in academia, only I have the chance to be rich. Why should molecular biologists have all the fun?"

And although pharmaceutical companies grumble that these chemist-entrepreneurs aren't helping to solve the problem but are merely cherry-picking from their labs, their presence hasn't set off the type of bidding war that recently swept the high-tech industry. So until the inevitable response to supply and demand increases the crop of chemists, Marzoni says that companies like his are a practical alternative. "For those companies that can't hire enough chemists, which is most of them these days, the only solution is to seek help outside the company."

–JOE ALPER

Joe Alper is a freelance writer living in Louisville, Colorado.

CREDITS: (TOP TO BOTTOM) ALBANY MOLECULAR RESEARCH; AP PHOTO/RICK RYCROFT

NATURAL DISASTERS

Researchers Target Deadly Tsunamis

Computer models, improved maps of the ocean floor, and new sensory equipment are giving scientists a handle on the causes of giant waves

ISTANBUL—When a colossal wave smashed into a spit of land along Papua New Guinea's coast on 17 July 1998, it destroyed three villages and killed more than 2100 people. That's when Costas Synolakis swung into action. The University of Southern California (USC) coastal engineer rushed to the site with an international team of tsunami scientists, including geologists, a seismologist, hydraulic engineers, and computer modelers, to find out every detail they could about the decade's most deadly tsunami. They measured marks left by the waves, surveyed damage, took statements from shaken survivors, and scrutinized seismologic and hydroacoustic data. But the evidence left them with a persistent puzzle: How could a moderate earthquake off the coast generate such a devastating tsunami, with 20-meter-high waves that impaled bodies on tree branches and smashed every structure in the 25-kilometer-long sand spit between the Pacific Ocean and the Sissano lagoon?

Three years of data collection, debate, and computer modeling may have turned up an answer. At recent tsunami conferences in Istanbul and Seattle,* and in an article being prepared for publication this fall in the *Proceedings of the Royal Society*, Synolakis, seismologist Emile Okal of Northwestern University in Evanston, Illinois, and several colleagues propose what they believe to be the culprit: an underwater landslide. Evidence of such a "slump" turned up in a detailed bathymetry survey, or map of the ocean floor, co-sponsored by the Japan Marine Science and Technology Center and the South Pacific Applied Geoscience Commission. The survey showed

Hammered. The village of Sissano, Papua New Guinea, was demolished by a tsunami in the summer of 1998.

* NATO Advanced Research Workshop, "Underwater Ground Failures on Tsunami Generation, Modeling, Risk and Mitigation," Istanbul, 23–26 May.

International Tsunami Symposium 2001, Seattle, Washington, 7–10 August.

Modeling a 3600-Year-Old Tsunami Sheds Light on the Minoan Past

The collapse of the Stronghyle volcano on the Greek island of Thera (now Santorini) in about 1600 B.C. generated a tsunami that smashed into the strongholds of the ancient Minoan civilization, Crete, and other islands in the Aegean Sea. In recent years, some archaeologists have speculated that the tsunami might have caused enough damage to doom the seafaring Minoans, whose mysterious disappearance has fueled speculation for centuries.

But recent research by tsunami modeling experts—based on data collected by geologists on coasts around the Aegean Sea—now indicates that the tsunami generated by that collapsed volcano caldera probably didn't do in the Minoans on its own. They say it could not have damaged agriculture, fishing, and society critically enough to condemn the Bronze Age Minoans, who were scattered across islands such as Crete, Rhodes, and Kos.

Sediment samples taken from the coasts of Crete, western Turkey, and other Aegean sites confirm that the volcano did indeed generate a tsunami, sedimentologist Koji Minoura of Japan's Tohoku University reported at a recent tsunami conference in Istanbul. But computer modeling of the event indicates that the waves were only between 5 and 8 meters high for most of the Minoan islands, says Greek-born tsunami modeler Costas Synolakis of the University of Southern California in Los Angeles. "At generation, the waves may have been as big as 120 meters, but they dispersed rapidly as they propagated toward Crete," Synolakis says. "The size of the wave that actually reached Crete would have been disruptive, but it would not have devastated the Minoans to the point that they abandoned their palaces."

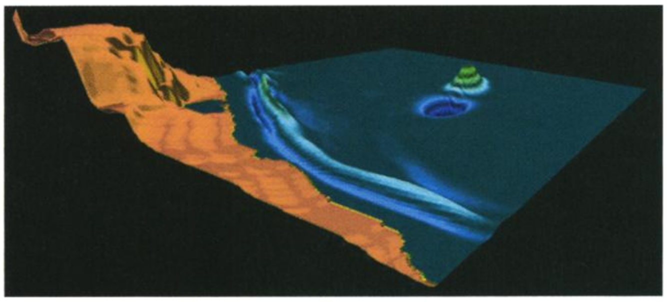
Synolakis says he doesn't know what delivered the coup de grâce to the Minoans. "There is a vexing mystery as to what eventually destroyed their world," he says. But geologist Floyd McCoy of the University of Hawaii's Windward Community College points out that the tsunami was only one of several scourges the Stronghyle eruption must have unleashed. "Add up all the regional effects of this massive eruption—ash fall, pumice drifts and fall, tsunami, earthquakes, destruction of the home base for the Cycladic culture—and no civilization could rebound, much less a Bronze Age one."

To complicate things further, experts wonder whether the tsunami was caused by the volcano's actual collapse or by the "pyroclastic flow" of scalding gases, ash, and other particles that the eruption swept into the sea. Europe's top expert on volcano-generated tsunamis, geophysicist Stefano Tinti of the University of Bologna in Italy, says that "modeling tsunamis generated by such pyroclastic flow is extremely difficult," because so many factors are involved, including the extent to which the hot gases vaporize upper layers of the sea. "We know far less about how to model the pyroclastic generation of tsunamis than we do about the more common sources, such as earthquakes and submarine landslides," says Tinti. "This is a ripe field for future research." **–R.K.**

sea-bottom scars of a major slump about 25 kilometers offshore of the Sissano lagoon. Studying seismologic and hydroacoustic data from the day of the tsunami, Okal concluded that the quake caused the slump, which in turn unleashed the deadly tsunami. And Synolakis and others on the survey team developed a computer model of the area that, they contend, confirms that such a "massive slump" offshore could have caused the Sissano tsunami. "This is the strongest evidence yet that 'local' tsunamis"—killer waves that originate just a few miles offshore of the site—"can be generated by massive underwater landslides," Synolakis says.

Some researchers dispute Synolakis's interpretation, arguing that the Sissano wave was caused mainly by the quake. But even more important than finding the cause of the Papua New Guinea tsunami, everyone agrees, are the tools developed in the search—including more sophisticated seabed imaging and computer models for tsunami generation and inundation. Marine geologist David Tappin of the British Geological Survey (BGS) calls the 3 years of ocean expeditions and scientific debates that followed the Papua New Guinea event "a watershed for tsunami research." According to Tappin, the "unprecedented depth of research" into the Sissano tsunami may allow researchers to "better understand why some areas are tsunami-prone and even to consider estimating the magnitude of the risk."

Despite those advances in bathymetry and computer modeling, other researchers argue that the most crucial challenge to tsunami research lies in gathering real-time data about killer waves before they near the shore. By spotting a tsunami early and taking its measure, proponents of such research say, scientists can help head off disaster before it strikes. Such data are now being provided by the Deep-ocean Assessment and Reporting of Tsunamis (DART) warning system, scheduled to deploy its sixth instrument this month to help predict and analyze the giant waves on the open ocean.



Making waves. In one model of the 1998 tsunami, a landslide creates a mound of water that spreads into a wall before hitting shore.

CREDIT: J. BORRERO/UNIVERSITY OF SOUTHERN CALIFORNIA

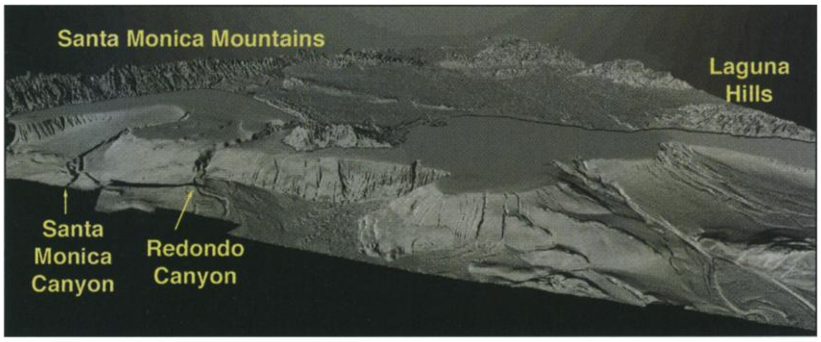
Harbor-wave history

The relation between earthquakes and tsunamis has been known for more than 2000 years—ever since the Greek historian Thucydides connected an Aegean tsunami in 426 B.C. to the quake that preceded it. Nevertheless, modern tsunami science is in its infancy. Only during the past decade have hydraulic engineers and other scientists begun using computers to model the three-dimensional evolution of tsunamis and devising inundation maps and early-warning systems for them. "Tsunamis killed more than 4000 people during the 1990s, but we have surprisingly little data to help us analyze them," says Eddie Bernard, an oceanographer who heads the U.S. National Oceanic and Atmospheric Administration's (NOAA's) Pacific Marine Environmental Laboratory (PMEL), which developed the DART system.

Tsunami generation involves intricate interactions among earthquakes, landslides, and "sympathetic" vibrations between the quake and the ocean above it. The Japanese word tsunami means "harbor wave"—a reference to the giant waves' ability to penetrate the protected harbors along Japan's coast. Although sometimes inaccurately called "tidal waves," tsunamis are produced by sudden underwater disruptions—usually undersea earthquakes but also submarine landslides and, far less often, volcanic eruptions or meteorites that hit the ocean.

The typical tsunami begins as a series of waves in the deep ocean, where they are not particularly dangerous. Although the wave pulses can race through the deep sea at speeds exceeding 700 kilometers an hour, their energy is dispersed along a wavelength as much as 750 kilometers wide. So a tsunami wave on the open sea may be just a few meters high, with a slope that's sometimes too gentle for big ships to notice. It's not until tsunamis enter shallow coastal waters that they get higher and more dangerous—often "shoaling," or squeezing together into narrow monster waves that can be as high as 10-story buildings.

Since 1990, 11 major tsunami events have struck coasts from Java to Chile, killing more than 4000 people and causing hundreds of millions of dollars in damage. In all, there were about 80 tsunamis during that decade, many of which caused little damage because they were small or struck undeveloped coastlines. The National Geophysical Data Center in Boulder, Colorado, estimated that more than 80% of the world's tsunamis appear to be generated by undersea earthquakes around the Pacific Rim, where colliding tectonic plates lead to an unusually high level of seismic activity. But Synolakis and others believe that some of those tsunamis—especially local tsunamis, which are generated just a few kilometers off the coasts they strike—may be caused mainly by offshore landslides that are shaken loose by local or more-distant quakes.



Slumpin' U.S.A. Evidence of old undersea landslides (bottom right) near Los Angeles raises fears that tsunamis could ravage the populous California coast.

CREDIT: JAMES V. GARDNER/USGS

Predicting the waves of the future

Whatever causes tsunamis, the more important challenge, Bernard believes, is to devise systems that can detect newly generated tsunamis in the deep ocean, collect information about them, and transmit it in real time to warning stations that could then evacuate threatened coastal areas. To provide a coastal warning system and to collect data about deep-sea tsunamis, NOAA has been deploying the DART system—starting in the North Pacific, along the Alaska Subduction Zone, which is the most dangerous generator of tsunamis that tend to strike Hawaii and the U.S. West Coast. Each DART assembly consists of a tsunami-detecting "bottom-pressure recorder" device on the ocean floor, which sends acoustic signals through the water to a car-sized surface buoy. The buoy transmits the data via satellite to ground stations, which relay them to NOAA'S PMEL lab and several tsunami warning stations—including stations in Alaska and Hawaii. The warning stations, as well as efforts to map the likely local impact of tsunamis at specific sites along the U.S. West Coast, are part of the U.S. National Tsunami Hazard Mitigation Program, which began in 1996.

So far, three DART instruments have been set up along the Alaska zone (near the Bering Strait), and two have been deployed closer to the Oregon coast, near the Cascadia Subduction Zone, which is thought to generate large tsunamis every few centuries. This month, a sixth DART station is being deployed in the deep ocean off South America's coast—not far from the site of the 23 June quake that generated a major tsunami along Peru's south coast. Oceanographer Frank L. Gonzalez, who directs PMEL's tsunami mapping center, says the new DART station "will intercept tsunami waves traveling from generation zones in the South American Subduction Zone to Hawaii, Japan, and other Pacific Rim countries." Gonzalez says the new equatorial DART station "will certainly help the warning centers issue faster, more reliable alerts for tsunamis generated off South America."

In the future, Bernard says, he plans to harness new science and technology to hone DART's ability to detect earthquake-generated tsunamis and spread warnings in advance. Better coverage will also be needed, he says. Bernard and his PMEL colleagues have proposed a worldwide program, tentatively called TROIKA, to deploy similar instruments in other tsunami-vulnerable regions. Such regions include the South Pacific, the Atlantic Ocean off the coast of Portugal (a 1755 tsunami destroyed much of Lisbon, killing 60,000 people), the Aegean Sea, and perhaps the Sea of Marmara and the Black Sea.

The next wave of killer waves

Despite the promise of DART and other systems for analyzing and predicting tsunamis, some experts worry that future dangers may overwhelm any defenses scientists are likely to devise. Judging from new evidence about "megatsunamis" in the distant past, such as the wave that battered the islands of the ancient Minoan civilization about 3500 years ago (see sidebar), they warn that more-destructive waves eventually will strike heavily populated coastlines, with potentially devastating impact. Ground zero is the Pacific Rim, where a seismically active "ring of fire" extending from the Bering Strait to the South Pacific unleashes earthquakes that trigger tsunamis.

Aside from the traditionally tsunami-battered Pacific islands of Japan and Hawaii, one of the most vulnerable regions is the Southern California coast. Jose Borrero, a postdoctoral researcher at USC who has worked with Synolakis in analyzing the tsunami threat along the California coast, says that "Southern California's offshore geology makes it ripe for producing tsunamis. Even a small tsunami along that coast would have a large potential for damage." Another West Coast threat comes from the Cascadia Subduction Zone, off the coasts of Washington, Oregon, and Northern California. Recent analysis of sand layers deposited in the region by ancient tsunamis suggests that one part of the Cascadia zone may be nearing a tsunami-generating earthquake, perhaps during this century.

Researchers also see potential danger in smaller seas such as the Mediterranean, the Black Sea, and even the tiny Sea of Marmara south of Istanbul. For example, a tsunami hit the French coastal city of Nice in 1979, and a small tsunami struck Izmit, Turkey, after an earthquake there in 1999. Istanbul, a metropolis of 13 million that rises along the Sea of Marmara and the Bosporus strait, could well be affected by a Marmara tsunami. "There will be another earthquake in this region, and it is likely to occur offshore, in the Sea of Marmara—making a tsunami likely," says BGS's Tappin. Ahmet C. Yalciner, an ocean engineer at Turkey's Middle East Technical University and co-director of the recent NATO tsunami workshop, fears that "underwater landslides could be a very important factor" in worsening a potential tsunami if an earthquake shakes under the Sea of Marmara.

But Bernard and others hope that advances in tsunami observation and warning systems, although powerless to influence the course of the giant waves, will help reduce the danger to vulnerable coasts. "We now have the equivalent of seismometers in the tsunami world," says Bernard. "Once we have collected data from 100 tsunamis in the deep ocean, we may have the potential to understand these complex events."

—ROBERT KOENIG