ANALYTICAL CHEMISTRY

Light Touch Identifies Wisps of Rogue DNA

When anthrax-laden letters contaminated a U.S. Senate building and a Washington, D.C., postal facility last fall, it often took days to get the results back from the lab. Federal officials longed for a quick and accurate detector, but "current techniques don't fit the bill," says Chad Mirkin, a chemist at Northwestern University in Evanston, Illinois. Now Mirkin and his colleagues have developed a sensitive biological assay that they hope will make other methods obsolete.

On page 1536, Mirkin's team of chemists describes an assay that, unlike more conventional methods of detecting genetic material, doesn't rely on the polymerase chain reaction (PCR) to boost its sensitivity. PCR limits a test's speed and often increases its false-positive rate. The new technique currently can detect DNA or RNA at a concentration of about 20 femtomolar: about one part in 3 trillion for an aqueous solution. That's hundreds of times better than most other methods, says Mirkin, who has plans to improve its sensitivity by another order of magnitude or two.

"It's a very exciting technique," says chemist Mark Wightman of the University of North Carolina, Chapel Hill. "It's a really neat and simple way to ID specific DNA and RNA fragments—and it doesn't seem to be pie in the sky."

The technique starts by making an open-face chemical sandwich out of two components, each primed to recognize a target strand of DNA or RNA. On one side is a chip covered with DNA strands, each designed to snag a fragment of the genetic material of the biological agent it needs to recognize, such as anthrax or HIV. On the other side is a set of gold nanoparticles, each also covered with DNA that will attach to a target's genetic material.

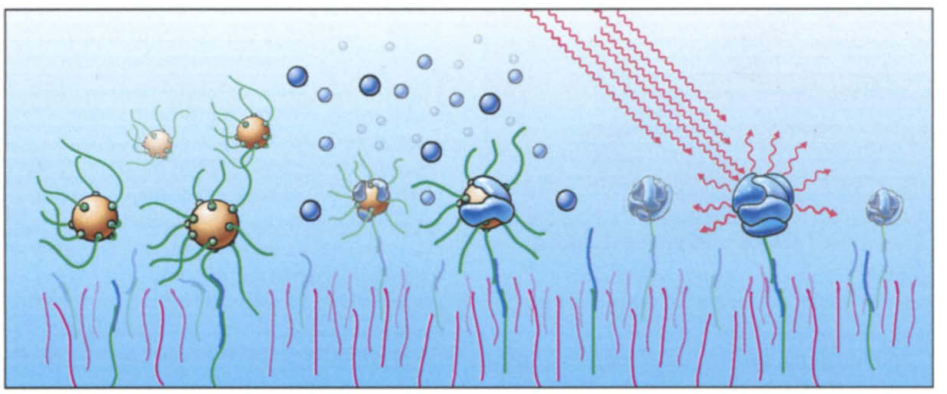
The researchers pour a solution contaminated with target substances over the chip. When the target strands bind to the complementary DNA strands on the chip, a bit of each target strand remains jutting above the forest of DNA for the treated gold nanoparticles to latch onto. Then the team soaks it in a solution of gold nanoparticles, whose attached DNA snags onto the loose ends of the target strands. By anchoring gold particles to the chip, the target strands flag their presence (see figure, below).

Ordinarily, it would be tough to detect these gold nanoparticles, especially in small concentrations. To make them easier to spot, the team tags each of them with a Raman dye, a chemical that scatters light in a distinctive way as photons make the molecule vibrate. Then the researchers expose the chip-gold sandwich to a solution of silver ions that coat the gold nanoparticles with silver, strengthening the dye's scattering properties.

When the team zaps the chip with a laser, each spot that has been exposed to the target material—the regions that are covered with silver-covered nanoparticles—scatters light. Different dyes scatter different colors. As a result, the researchers can test for several targets at a time, by color-coding the targets to make anthrax, say, blue and HIV yellow.

Other assays, such as those that use fluorescent dyes, can also assign different colors to different targets. But the Raman technique is more versatile, Mirkin says, offering a wider choice of dyes and scattering light over a relatively narrow part of the spectrum. That makes it easier to cram several different dye labels into the same frequency range. "We can put in 10 different dyes, giving you 10 distinct signatures" over a certain region of the spectrum, says Mirkin. "You can't do it with fluorescence. You can't even come close."

The Raman technique will have to win over biologists wedded to other methods, with cost an important consideration. But according to Wightman, the technique is ripe for the marketplace. Potential applications include use as a bioweapons sensor or diagnostic test that can be performed at a clinic rather than being sent to a lab. Mirkin has helped found Nanosphere, a company based in Northbrook, Illinois, to exploit the commercial feasibility of these nanoparticle-based techniques. –CHARLES SEIFE



Metal detector. In new DNA test, gold nanoparticles bind to target strands and get silver-plated. Then radiation scattered from a laser beam picks out the targets.

NEUROSCIENCE

Sight, Sound Converge In Owl's Mental Map

The barn owl is a deadly hunter. Using hearing to pinpoint the scurrying of a mouse or other small animal, it swoops out of the night sky and dispatches its prey. To guide its lethal accuracy, the owl uses a mental map tuned to the location of sounds.

But this map cannot maintain itself on sound alone; it requires visual information to continually update its accuracy. But despite years of searching, only now have researchers been able to find out how those visual cues reach the map. On page 1556, Eric Knudsen and his colleagues at Stanford University School of Medicine report that they have discovered a "gate" in the brain that, when opened, allows the auditory map to receive the visual information it needs.

"The novel thing about this study is not that there is visual input into an auditory area; there are many demonstrations of that," says neuroscientist Andrew King of the University of Oxford, U.K. There have also been previous examples of gating, in which some kinds of neural input are allowed into a brain area only under certain conditions. But what makes this work "really important," says Alexander Grunewald of the University of Wisconsin, Madison, who has studied gating of sensory information in monkeys, is that this picture is more complete than others because the researchers know just how the gated information is used.

Knudsen's group showed in the early 1980s that the owl brain contains a map of auditory space in an area called the external nucleus of the inferior colliculus (ICX). Each ICX neuron responds to sounds from a certain location. The brain computes the location using differences in the timing or intensity with which the sound reaches the two ears. Knudsen's team showed in 1993 that this auditory map is modified by visual information. This is key to the map's function, says Yoram Gutfreund, a postdoc with Knudsen and lead author on the current paper, because any changes in the hearing in one or both ears—caused by changes in

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