# Molecular 'fishing' technique paves way for advanced hand-held sensing devices

February 12 2007

A new molecular "fishing" technique developed by researchers at Duke University and Duke's Pratt School of Engineering lays the groundwork for future advances in hand-held sensing devices.

Hand-held devices used for medical testing or environmental and food-safety monitoring could quickly and precisely measure concentrations of virtually any chemical substance, including blood proteins, toxic pollutants and dangerous biological agents, in a test solution, according to the researchers.

The researchers describe the chemical methodology that would enable such devices in this week's online early edition of the journal *Proceedings of the National Academy of Sciences*.

The new technique uses an atomic force microscope (AFM), a device for observing the surface of individual molecules and measuring the force of interactions among them. The AFM includes a tiny cantilever arm with a sharp tip that scans the surface of atomic specimens, and monitoring the deflection of the cantilever provides information about the force of molecular interactions.

The researchers use the AFM's cantilever as a fishing rod, which they bait with a sample of the chemical to be measured in order to catch "fish," actually proteins known to specifically bind the target chemical. They dangle the chemical "worm" in a solution that contains the target chemical and also is stocked with the protein fish. Because the fish are easier to catch with the baited cantilever when there are fewer free worms to compete with, the researchers can quantify the amount of chemical in solution by tallying the number of successful catches.

"As you sample the surface with the AFM cantilever fishing rod, the number of times you get a 'bite' provides a measure of the chemical concentration," said chemistry professor Eric Toone of Duke University.

The team also included mechanical engineering and materials science professors Rob Clark and Piotr Marszalek, both of Duke's Pratt School. All three investigators are members of Duke's Center for Biologically Inspired Materials.

Their method could be adapted for virtually any chemical of interest by varying the identity of the molecular worms and fish, according to the researchers.

While the current process requires about 200 pulls on the cantilever rod and takes hours to provide an accurate reading, it could be made much faster in a very straightforward way, the researchers said. "To get enough pulls, you can either pull one rod 200 times or pull 200 rods once," Clark said. "The test could be made massively parallel and very fast."

In demonstrating the new method using lactose molecules as the worms and a protein called galectin 3 as the fish, the researchers relied on computerized AFM controls to lower the baited cantilever toward the solution a billionth of a meter at a time.

"Instead of plunging into the surface, we approached it step by step in order to minimize the number of interactions to one, maybe two, molecules," Marszalek said.

Based on the force measured on the AFM rod as it was withdrawn from the solution, the researchers judged each attempt either as nonbinding, meaning they didn't catch anything or made only passing contact, or as binding. When galectin 3 fish bound the lactose bait, withdrawal of the cantilever registered a greater force. They repeated the process until the bait had made some form of contact at least 350 times.

They found, as expected, that the probability of binding varied with the concentration of lactose in the solution. At low concentrations, binding occurred with the greatest frequency. As the concentration rose, the likelihood of binding declined. The researchers used that probability of binding to calculate the chemical concentration.

The researchers suggest that the method eventually could be incorporated into devices similar to hand-held personal digital assistants. Such devices likely could be made adaptable, they said, testing for different chemicals by simply switching out a chip.

AFM fishing has advantages over other testing methods that rely on heat or changes in optical properties, the researchers said.

"Although broadly applicable, such techniques require long sampling times and equipment that isn't suitable for use in the field," Toone said. Additionally, methods that depend on optical characteristics generally require the testing solution to be clear, precluding their use on blood, milk or any other opaque solution.

The researchers said they will continue to examine the fundamental biophysics that underlie the new method and to develop practical applications.

Source: Duke University