

Captured on Film

Research into a new way of collecting waterborne pathogens is part of MITRE's growing emphasis on biological defense.



“We hope that glycoprotein films will provide solutions to a variety of biodefense challenges”

— Elaine Mullen

WHEN ELAINE MULLEN FIRST arrived at MITRE as a graphic designer, she spent her days creating conceptual illustrations. In the evenings, however, Mullen would peer into a microscope. She had developed a fascination with glycoprotein films—a combination of sugars and protein.

To the aspiring researcher, the films seemed indestructible and she was curious to learn more. “I wanted to know whether glycoprotein films were permeable to certain gases and liquids,” she says.

As her research developed, Mullen, who has a biology degree, was encouraged by a MITRE colleague to patent her ideas. After her first patent was issued, Mullen's job title at MITRE's Center for Integrated Intelligence Systems changed from graphic designer to biologist. Now, as a multi-disciplinary systems engineer, Mullen is working on a MITRE-sponsored research project to develop floating films that collect and concentrate pathogens at the water surface. Monitoring water quality in U.S. rivers, lakes, and reservoirs has always been a challenge and is even more so with increased threats. “There's a need to monitor the introduction and spread of waterborne infectious disease agents to give early warnings of biological contamination,” says Mullen.

Biological defense is a new strategic focus at MITRE (see “Biological Defense”). Mullen hopes that “biocapture” films can facilitate the collection of pathogens from water samples. “The beauty of these films,” says Mullen, “is that they float in watery fluids and capture pathogens on their way to the surface where they may be gathered for further testing.”

Biological Velcro

On a molecular level, Mullen explains, the carbohydrates attached to glycoproteins are composed of sugar units that resemble tree branches. “These sugars are the key,” she says, “because they act like biological Velcro when a pathogen or biotoxin comes in contact with a specific carbohydrate sequence. In order to infect you, pathogens must first bind to your cells. They often use lectins [adhesive proteins] to grab onto host-specific sugar chains like burrs stick to animal fur.”

Mullen first discovered glycoprotein films when she was working as a freelance illustrator for scientists at the Medical College of Virginia. Her eureka moment occurred while hand-coloring a 35-mm slide of a pig that she was trying to dye the color pink. The ink, however, wouldn't adhere to the emulsion. As a last resort, Mullen added egg white, which is mostly glycoprotein, to bind the dye to the

slide. That's when she discovered a film—caused by the oil floating on the egg white solution.

“I was using a clear custard dish for the mixture and held it up to the light and looked through it,” says Mullen. “I saw the film because it was wrinkling at the interface between the oil and the mixture below. I poked it, and it moved like Saran wrap that is dented by your finger. It was strictly an accident of good fortune. Normally, when you use eggs with oil, they are in a frying pan, and you never see the films from above.”

Mullen was encouraged by her sister, a writer for the pharmaceutical industry, to consider commercial uses for glycoprotein films. But at the time there was hardly any published research, so Mullen paid a translator several hundred dollars to translate the only article she could find on the structures of egg white proteins, which had been published in a Russian journal.

A unique database

Her research at MITRE eventually reached a point where Mullen received a MITRE-sponsored research grant to learn whether glycoprotein films could capture pathogens from water. Mullen had read that carbohydrates in the whites of pigeon eggs bind to bacteria that can infect human kidneys.

To identify similar cases, she asked Baddr Shakhshsheer, a summer intern, to conduct a literature search on pathogens that produce lectins that bind to sugars

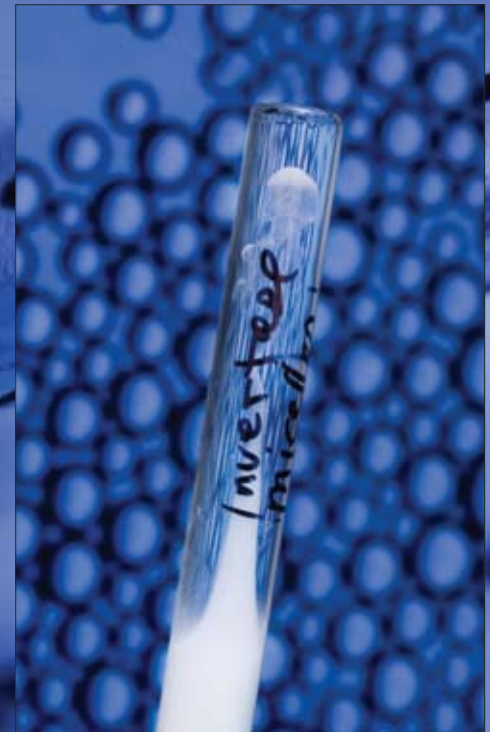
on human cell surfaces. Shakhshsheer (now attending medical school while working as a multi-disciplinary systems engineer at MITRE) put together a spreadsheet that contained about 500 citations from literature published during the past two decades on carbohydrate-binding affinities of human pathogens.

When they learned that his compilation was unique, Mullen and Shakhshsheer collaborated with a team of MITRE programmers, Web developers, and artists to produce a Web-enabled database called SugarBindDB (available free online at <http://sugarbinddb.mitre.org>). Mark Anderson, a MITRE software engineer, is currently preparing SugarBindDB for integration with other bioinformatics resources related to an emerging medical field known as the “glycobiology of disease.”

Mullen and Shakhshsheer worked with scientists at the Johns Hopkins University Applied Physics Lab to develop protocols for the quantification of biocapture. They are currently perfecting the production of uniform micelles that float to the surface within a certain time frame.

Future research opportunities include collaboration with scientists in various government and academic communities. “We hope that ultimately glycoprotein films will provide solutions to a variety of challenges related to biological defense and the remediation of infectious diseases,” says Mullen.

—David A. Van Cleave



A swirling column of micelles rising in an inverted glass vial filled with water is depicted in the cover photo. The microscopic micelles have been filled with buoyant oil and coated with a transparent film of invertase (a glycoprotein derived from baker's yeast). In the background, a digital photograph of the same micelles is projected from a microscope onto a computer screen. These micelles have been coated with the sugar, mannose, which binds several human pathogens.

BIOLOGICAL DEFENSE: NEW STRATEGIC FOCUS

Biological defense is a new area of investment for MITRE, which focuses on biotechnology to help government agencies with one of their most challenging issues: dealing with potential bio-related incidents. The company's expertise in biotechnology has expanded over the past few years, with specialists in bioinformatics, bioforensics, and bioengineering. One area of emphasis is the monitoring of the environment for the intentional introduction of bioagents.

A new Biotechnology-Nanotechnology Laboratory at MITRE supports this new strategic area. The 2,700-square-foot lab, which opened last spring on the McLean campus, also supports projects in computational biology, analysis of proteins and nucleotides, and rapid diagnosis of biological agent exposure by using non-hazardous extracts from cells previously exposed to such agents.