Liquid crystal droplets discovered to be exquisitely sensitive to an important bacterial lipid

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A recent discovery involving liquid crystals could lead to a replacement test for the presence of endotoxins. Current tests involve the use of horseshoe crab blood, which is blue due to a protein called hemocyanin, the oxygen-carrying pigment the blood contains. This image shows a horseshoe crab in sand at Monomoy National Wildlife Refuge, Mass. Credit: Bill Perry, U.S. Fish and Wildlife Service

(PhysOrg.com) -- In the computer displays of medical equipment in hospitals and clinics, liquid crystal technologies have already found a major role. But a discovery reported from the University of Wisconsin-Madison suggests that micrometer-sized droplets of liquid crystal, which have been found to change their ordering and optical appearance in

response to the presence of very low concentrations of a particular bacterial lipid, might find new uses in a range of biological contexts.

Detecting endotoxin, a lipid-polysaccharide combination that is found in the outer membranes of many types of bacteria, is a standard way to establish the presence of bacterial contamination in a wide range of drugs, medical supplies and equipment. The current technology is based on a complex mixture of proteins isolated from the blood of a horseshoe crab, says Nicholas Abbott, a professor and the chair of chemical and biological engineering at UW-Madison.

Abbott, an expert in surfaces of soft materials, knows that liquid crystals have highly useful properties. "An unusual characteristic of a liquid crystal is that information travels through it over long distances. Many past studies have shown that events at a surface of a liquid crystal, which might affect just one layer of molecules, can trigger a change in the ordering of the liquid crystal that propagates as deep as 100,000 molecules away from the interface."

In a paper published Friday, May 20, in *Science*, Abbott and colleagues showed that concentrations of endotoxin in the picogram/milliliter range were enough to trigger a change in the appearance of liquid crystalline droplets visible in a light microscope. "When we investigated the behavior of endotoxin with the liquid crystalline droplets, we were surprised to find that we could decrease the concentration of endotoxin to extremely low levels and still see that change in the ordering of the liquid crystals."

Abbott initially thought that the changes in the liquid crystalline droplets would be due to the adsorption of the endotoxin to the surfaces of the droplets, but the concentration was too low to justify this explanation. So Abbott and his graduate students I-Hsin Lin and Dan Miller along with

colleagues in the NSF-sponsored UW-Madison Materials Research Science and Engineering Center determined that "the transition was not driven by adsorption of endotoxin over the surface of the liquid crystalline droplet, but instead by localization of the endotoxin at defects in the liquid crystal droplets."

The localization of impurities to defects is "ubiquitous" in material science, Abbott says, "and it appears that a similar phenomenon is occurring here, which then triggers the transition in the liquid crystal droplet. This is a fundamentally different mechanism that gives rise to a level of sensitivity which is 10,000 to 100,000 higher than surface-driven transitions seen in past studies of liquid crystalline systems, and it suggests the basis for a very high level of sensitivity in detection." Abbott also comments that "defect-driven ordering transitions in liquid crystalline systems have not been reported previously, and it is also highly surprising that it is so specific to the particular structure of endotoxin."

The defect-driven phenomenon that Abbott found could be more broadly applicable than endotoxin, but he says "endotoxin in itself is pretty important. Endotoxin comes from the outer membrane of Gram-negative bacteria, and is considered a key indication of bacterial infection." Animal immune systems themselves are tuned to respond to endotoxin, Abbott says, and the Food and Drug Administration requires testing for endotoxin on equipment used to make vaccines, drugs, intravenous fluids and many other devices and materials.

The current FDA-approved test for endotoxin is based on the blood of horseshoe crabs, which have evolved to combat infection by clotting their blood in the presence of endotoxin. Horseshoe crabs are captured, bled and then returned to the water. The horseshoe crab test is the "gold standard assay" for endotoxin, Abbott says, "but our system so far seems a bit more sensitive and does not involve any biological components. The

change in optical appearance of the droplets is quite striking, and it occurs within a minute."

The discovery could be the start of a long road to commercialization, but Abbott cautions, "We have found a fundamental phenomenon, but it's a long path to have a validated technology that can replace the horseshoe crab assay."

Horseshoe crabs are some of the most primitive multicellular organisms surviving on Earth, but Abbott believes they would still appreciate not having to donate blood quite so often.

Provided by University of Wisconsin-Madison