Studies with "manufactured" biomaterials promise advances in medicine, such as more effective drugs and methods for diagnosing disease.

Synthetic Membranes: Copying Mother Nature

Imitating the biological complexities found in Mother Nature is no easy task. Nevertheless, scientists working at SNS and the nearby CNMS are trying to emulate the molecular activity that occurs at biological interfaces—the boundary areas within living cells. The researchers are building bio-inspired, biocompatible synthetic membranes to help them understand the interactions between synthetic materials and biomolecules.

"We're taking our inspiration from Mother Nature," says researcher, Brad Lokitz. "In the body and in nature, lots of biological processes happen at interfaces and membranes, so we're trying to mimic nature in a very basic way to gain some insight into these processes."

In addition to Lokitz, the research effort includes John Ankner, Jamie Messman, and Dean Myles of ORNL; Mike Kilbey and Jimmy Mays of ORNL and the University of Tennessee; and Juan Pablo Hinestrosa of Clemson University.

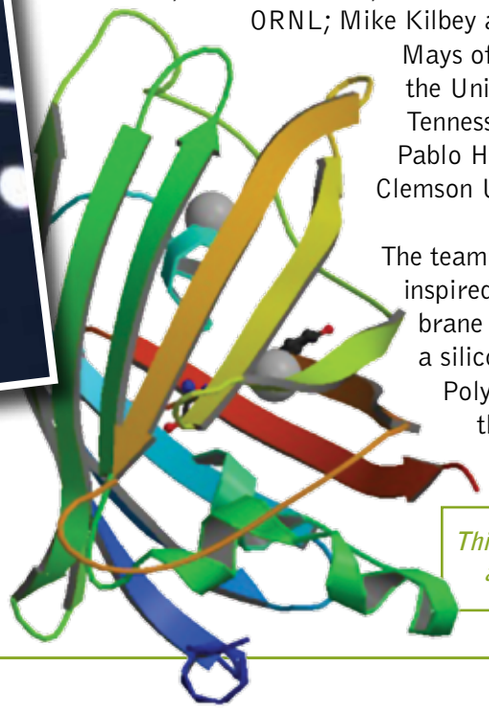
The team's bio-inspired membrane starts with a silicon base. Polymers are then attached more or less evenly across the surface of the silicon. These polymer strands provide a framework, or scaffold, for the biomolecules that are added later.

"The design is somewhat similar to a hairbrush," says Lokitz. "If you take a hairbrush and turn it over, the base of the brush would be the silicon substrate and the bristles that extend out would be the polymer."

It has taken several attempts to come up with a process that results in a polymer framework that has a uniform thickness and is evenly distributed across the surface, but the results have been worth the trouble. "In order to use neutrons to study the sample, it needs to be very uniform on the molecular level," says Lokitz. "The rougher the surface is, the less information you can extract from it, so we want the surfaces to be as molecularly smooth as possible. Just now we're getting to the point that we can reproducibly prepare samples that are sufficient to take over to SNS and obtain good results."

The team is using the SNS's Liquids Reflectometer to study both the polymer scaffold itself and the attached biomolecules. One of the reflectometer's specialties is using neutrons to investigate the boundaries between hard and soft matter—like the bio-inspired surface Lokitz and his colleagues are working with.

Lokitz notes that having SNS right next door to CNMS provides a synergistic opportunity to perform nanoscience research at two state-of-the-art facili-



This green fluorescent protein (GFP) variant is shown as a representative protein for future binding studies.

ties. "We can create our samples at CNMS, walk next door, and test them at a world-class facility. As we're running our test, we pretty much get immediate feedback. If we see that we need to do something different, we can go back to CNMS, tweak our procedure, and then go back next door to continue the testing."

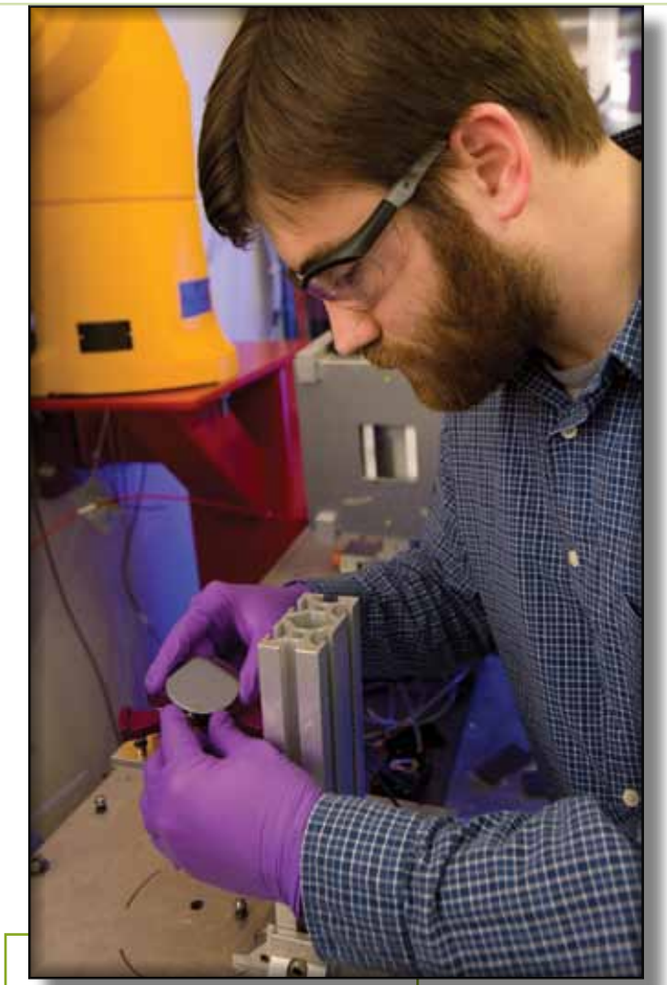
Once a satisfactory scaffold is in place, researchers "functionalize" it by starting a chemical reaction that allows the biomolecules to bind themselves to the polymers. Researchers then examine the scaffold looking for several things: how the attached biomolecules affect the structure and organization of the polymer scaffold, how being attached to the scaffold affects the stability and structure of the biomolecules, and whether the biomolecules can still perform their biological functions when attached to the scaffold.

The Liquids Reflectometer is able to characterize the thickness, density, and orientation of the polymers. It is also very sensitive to small changes in density or thickness, so it provides researchers with an opportunity to study minute variations in the scaffold or the attached biomolecules.

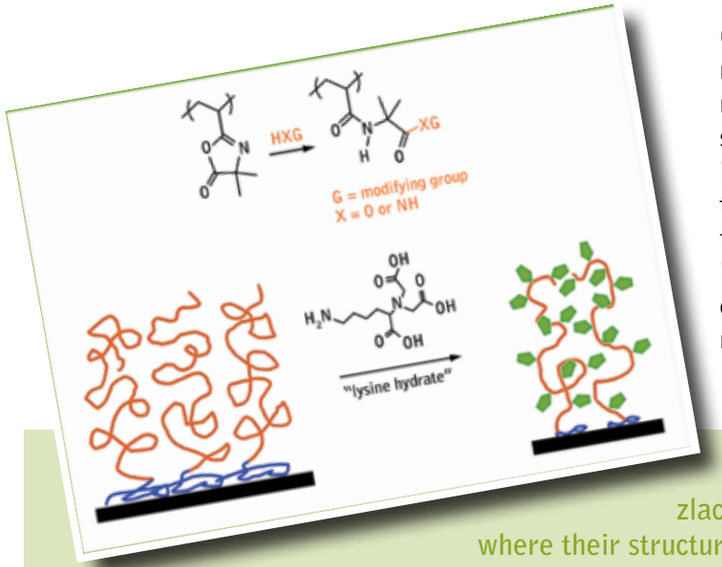
"We can look at the surface with just the polymer attached and get an idea of the layer thickness and composition." Lokitz says. "Then when we functionalize the layer—attach the biomolecules—and look at it again, the instrument is sensitive enough to notice those small changes."

"For example," Lokitz says, "Right now we're using lysine hydrate as a model compound and are evaluating its ability to bind proteins after it's attached to the scaffold. "

Overall, the project aims to develop expertise in using neutron scattering to prepare and investigate soft material scaffolds that can be used to create bio-inspired membranes. Because interfaces play a key role in biological processes, developing robust platforms that can be used to examine structure-property-function relationships of biomolecules attached at interfaces is crucial to bridging biology and biological processes to the development of next-generation materials, devices, and processes.



Brad Lokitz examines a sample at the SNS Liquids Reflectometer.



The research team has made scaffolds based on a novel class of block copolymer called vinyldimethylazlactone (VDMA). The VDMA block copolymers allow proteins and enzymes to be confined to interfaces, where their structure and stability can be examined at the molecular level. This knowledge can provide a foundation for developing more complex bio-inspired systems.

Above: reaction of VDMA with lysine hydrate. Once the polymer scaffold (orange) is attached to the substrate (blue), biomolecules (green) are attached to the individual polymer strands. Researchers then examine the scaffold to see how the biomolecules affect the structure of the scaffold, how being attached to the scaffold affects biomolecules, and whether the biomolecules can still perform their biological functions.