Physical Sciences
RESEARCH IN PROGRESS

Physics of Fluids Shows Promise for Coating of Transplanted Cells

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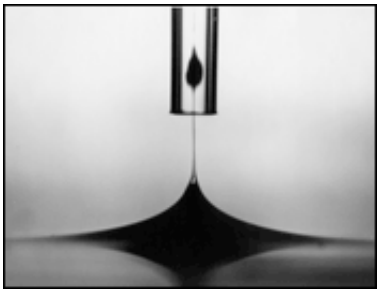
By Steve Koppes

University scientists have developed one of the world's smallest shrink-wrapping systems, one motivated by the need to protect insulin-producing transplanted cells from the body's immune system.



Sidney Nagel, the Stein-Freiler Distinguished Professor in Physics, and Milan Mrksich, Associate Professor in Chemistry, have completed the first major step in developing a coating to protect islets from the immune system. They have developed on of the world's smallest shrink-wrap systems, one that may eventually be used for cell transplantation in patients suffering from diabetes mellitus.

Diabetes mellitus damages or destroys the body's ability to produce insulin, a protein that regulates the body's use of sugar. Surgeons can transplant the cells that produce insulin, called the Islets of Langerhans, from pigs to humans. The body, however, attacks the cells as foreign invaders.

Sidney Nagel, the Stein-Freiler Distinguished Service Professor in Physics, said researchers are a long way from coating islets for actual transplantation, but they have completed the first major step.

He and Milan Mrksich, Associate Professor in Chemistry, led a team of scientists that developed a coat thick enough to protect islets from the immune system, yet thin enough to allow insulin and other nutrients to flow out of the cells and into the body.

"We don't know the limits of how small we could make the coats," Nagel said. The team successfully coated particles ranging in size from 100 microns--approximately the width of two human hairs--to 300 microns, the size variation of the Islets of Langerhans.

"We demonstrated that we can go down to roughly the 10-micron range for the coat size, which is what we were aiming for, and that we have control of the thickness of the coat," Nagel said. The Chicago team described its system in the Friday, April 13 issue of the journal Science. Graduate students Itai Cohen, Hui Li and James Hougland were co-authors.

Nagel began working on the project after learning of the need for such a process from Horacio Rilo, formerly Assistant Professor in Surgery, now at the University of Cincinnati. Nagel and Mrksich then came together through the University's multidisciplinary Materials Research and Science Engineering Center. "Sid's group has been looking at a lot of interesting physics that involve different fluids flowing past one another," Mrksich said. "The neat thing is that Sid had a way of coating particles with a liquid layer, so he could take a particle, a microbead, and wrap it with a layer of water and have this whole thing stabilized in a bath of oil."

The method used to coat the particles is called selective withdrawal. The process can occur when one liquid sits atop a layer of another liquid and yet they do not mix, much like oil and water. By inserting a tube into the top layer and applying just a little suction, only the top layer will be withdrawn. With the application of additional suction, the lower layer becomes entrained in the flow, too.

"If you put the particles to be coated in the lower fluid, then they will be entrained in the flow as well and go up the spout," Nagel said. "By changing various flow rates and the height of the spout, you can change the thickness of the coat."

The concept is actually quite simple.

"You can do this with your mouth and a straw," he said. "Every time you suck up a little piece of ice in the bottom of your iced tea, you're getting something of the phenomenon."

Mrksich's group used polymer chemistry to further process the particles after Nagel and Cohen had coated them via selective withdrawal. Polymers are compounds that chemists engineer for specific purposes.

"We picked a few routine polymer systems and showed that they could be applied to this particle coating," Mrksich said. "This work established the flexibility of this approach, that it's possible to coat a whole variety of different particles with a range of different polymers."

The technology potentially could be developed for use in drug-delivery implants as well as for Islets of Langerhans transplantation.

"There's a big industry concerned with implantable systems that can release drugs," Mrksich said. Many of these systems require that the implant have a drug reservoir along with a barrier that can selectively release the drug at the appropriate dosage, while also protecting the implant from rejection.
"This system of Nagel's really permits unprecedented flexibility in controlling the size of these microparticles and especially in controlling the delivery of molecules and proteins across that coating."

The next step for the team is to develop a system that can reliably coat large numbers of microparticles at once and to learn how to uniformly coat even smaller particles. "If this method could be extended to particles measuring only a few microns, it could be very important for creating artificial organelles that could be put into cells to influence cell behavior," Mrksich said. Organelles, he explained, are micron-sized cellular components that carry out specific functions.

"If we could create beads that were loaded with drugs or had other activities and coat them so that the cell could take them up and pull them into its interior, the method would give us a way of adding new functions, new properties, to cells," he said.