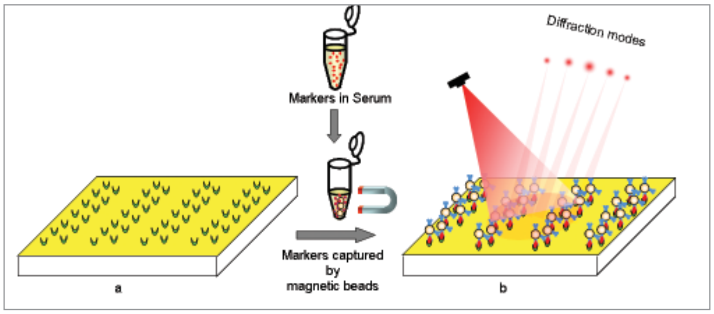
Engineering Solutions For Diagnostics

by Tanuja Koppal, PhD

As medicine moves closer to personalization and targeted therapy, the need for diagnostics that can rapidly and accurately predict and monitor the occurrence and progression of disease and drug treatments becomes critical. In an article published in the *Journal of the American Chemical Society* (Vol. 129, No. 51, Nov. 2007), Cagri Savran, Ph.D. demonstrated the use of a relatively cheap and easy-to-use biosensor for detecting serum-based protein biomarkers indicative of various types of cancers. "The main advantage of this method is its sensitivity and simplicity," says Savran. "As you can tell we are still in the development stage but we really expect this [technology] to be very useful for point-of-care diagnosis in the future."

Savran is an assistant professor at Purdue University with affiliations to the departments of Mechanical Engineering, Electrical and Computer Engineering, and Biomedical Engineering. His research interests reside at the crossroads of biology, engineering, microelectronics and nanotechnology. After completing his Ph.D. at the Massachusetts Institute of Technology in 2004, Savran returned to his alma mater to set up his research lab. Purdue had just opened the doors to the Birck Nanotechnology Center, a 187,000 sq. ft., state-of-the-art facility. "Purdue is known to be strong in engineering, but they also wanted to give pre-eminence to interdisciplinary fields, just the kinds of things I am doing right now," says Savran. "There are many professors here coming from different departments and different backgrounds. So if you are curious about something and you want to talk to somebody from a different field all you have to do is just knock on the door — everybody's under the same roof," says Savran.

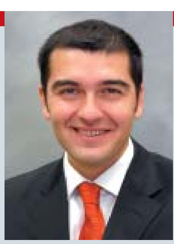


Detection of cancer markers (e.g. folate receptor, FR) by immunomagnetic diffractometry. (a) Folate-BSA patterned gold chip. (b) Diffraction grating formed by the self-assembly of FR beads. Laser illumination produces a diffraction modes.

The biosensor that Savran has built is based on one-step immunomagnetic bead-based capture, using an *in situ* assembled optical diffraction grating detection system. The magnetic beads function both as capture agents and as motifs for *in situ* assembly of the diffraction gratings. The beads are functionalized with recognition elements like antibodies that are specific to the target protein of interest. "You put these magnetic beads into a complex biological mixture and fish out the targets that are of interest to you," says Savran. The beads are then transferred onto the surface of the biosensor, which is a gold coated glass slide that is also micro-patterned with specific recognition elements. "So now you don't have to expose your sensor to the blood or other biological samples," he says.

In their recent study Savran's group used folate antibody coupled magnetic beads to detect the folate receptor, also called the folate binding protein, from serum samples. This protein is found overexpressed on the surface of various types of tumors and eventually enters the blood stream. The beads bind folate from the serum and later attach to the folate recognition elements on the micro-patterned surface of the sensor. The beads bound to the surface constitute a solid diffraction grating and illumination with a laser reveals a specific diffraction pattern. The intensities of the patterns change with the number of beads on the surface, which in turn corresponds to the amount of target protein detected.

The system that they are building for biomarker detection is very much in its infancy. "The study that is just published is actually not an optimized study," says Savran. "But we're excited because despite the fact that it was not an optimized study, those results were really good." Savran is confident that they will make significant progress in about a year or so. His group is now looking to add a flow-based system to the sensor that will allow the detection of samples in an automated and high-throughput fashion. They are also looking to miniaturize the system to enable its use as a diagnostic device. "In my lab what we are trying to do is develop things that are not only effective but also simple — simple to build and simple to put together," says Savran. "If the fabrication includes numerous steps and the instrumentation includes many components, then it becomes really easy for something to go wrong or to break. So we are trying to find the optimal point of simplicity and effectiveness."



Cagri Savran did his undergraduate studies in mechanical engineering at Purdue University and then went to MIT to pursue a Master's degree. At MIT he got interested in micro-electro-mechanical systems (MEMS) and decided to do his doctoral work in that field. He joined a group that was working on the application of MEMS to biology. At the beginning he worked on just the fabrication, modeling and characterization of MEMS-based biosensors, but as time progressed he became more drawn to biology. "Many problems are solved in traditional fields of engineering but there are still a lot of things that are not solved in biology because biological systems are a lot more complicated than engineering systems," he says. Another contributor to this trend are the improvements in automation, motion control and computer technology that have made it easier to design and simulate systems. "The bridge between fundamental sciences and engineering has not really been built until now," he says.