

Understanding cell interactions is a snap

NANOBIOTECHNOLOGY

Understanding the complex signaling between cells is difficult because current methods are inadequate to manipulate tissue *in vitro*. Researchers at the University of California, San Diego and Massachusetts Institute of Technology have now fabricated a Si device with interlocking fingers coated with polystyrene to culture cells for the study of intercellular interactions [Hui and Bhatia, *Proc. Natl. Acad. Sci. USA* (2007) **104**, 5722]. The fingers of the comb can be separated easily, held in contact, or positioned at a constant distance using integrated snap-locks, and the device is compatible with common 12-well plates.

The researchers investigated the interaction of rat hepatocytes with 3T3 fibroblasts cells using the device. Hepatocytes cultured alone rapidly lose their liver-specific function *in vitro*, but when cultured together with a variety of other cells, can maintain their function for weeks. "Hepatocytes were a good choice since the effects of their interaction with certain support cells is so pronounced," says Elliot E. Hui. When the hepatocytes are placed in direct contact with fibroblasts for 18 hours, then separated at a fixed distance of 80 μm , the liver cells remain viable for at least two weeks because of interaction with soluble factors secreted by the fibroblasts. Without the initial contact, the hepatocytes fail to secrete albumin, which is used to gauge liver function. "We have also had good results with cardiac muscle cells, various developmental progenitors, and bone marrow stroma," says Hui. "The surface of our device is basically the same as a standard cell culture plate, so we expect it to be broadly compatible with many cell types."

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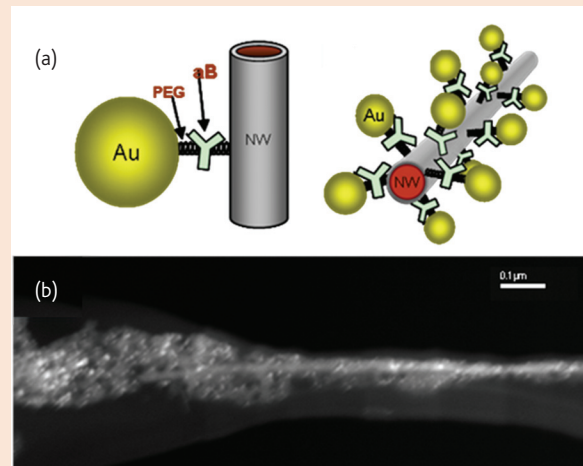
Detecting proteins with excitons and plasmons

NANOBIOTECHNOLOGY

Researchers at the University of Michigan, Ohio University, and Pusan National University in Korea have constructed molecular spring assemblies to optically detect proteins in solution [Lee *et al.*, *Nat. Mater.* (2007) **6**, 291]. The assemblies are composed of Au nanoparticles attached to CdTe nanowires via poly(ethylene glycol), or PEG, linkers conjugated with antibodies.

The device relies on the interaction between excitons, bound electron and hole pairs in the semiconducting nanowires, and plasmons, quantized oscillations of the conduction electrons in the metallic nanoparticles. The researchers conjugated antistreptavidin to the PEG linkers and then exposed the nanostructures to solutions with varying concentrations of streptavidin. When the nanowires are excited optically, shifts of up to 10 nm in the emission spectra are observed.

The researchers attribute this shift to changes in the distances between the nanoparticles and nanowires and have developed a theoretical framework to explain the sensor effect in terms of the exciton mobility. "For a strong effect, the exciton drift time inside a nanowire should be comparable with the exciton lifetime," explains Alexander O. Govorov of Ohio University. Decreasing the distance between the nanoparticle and nanowire decreases the exciton lifetime, leading to a blue shift in the emission spectrum of the exciton. The choice of nanowire and nanoparticle material are critical parameters to device performance.



(a) Cartoon of the molecular spring assembly and (b) transmission electron micrograph of a CdTe nanowire decorated with Au nanoparticles. (Courtesy of Nicholas A. Kotov.)

Replacement of Au with Ag nanoparticles, for example, would change the resonance frequency of the plasmons, explains Nicholas A. Kotov of the University of Michigan. "The exciton frequency then has to be changed to match it, in order to observe the same effects." Govorov adds that to observe the blue shift, the exciton and plasmon energies should be close. "For Au nanoparticles and CdTe nanowires, this resonance is achieved," he says. "Ag nanoparticles have a higher energy plasmon, so nanowires with a higher energy exciton such as InGaN are required."

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Polymer coat protects cells

NANOMEDICINE

Type I diabetes results when beta islet cells in the pancreas fail to produce insulin. Transplanting healthy cells has been used as a treatment, but with varying success. Now a team at The University of Chicago has devised a method to encapsulate individual islet cells in thin shells of cross-linked poly(ethylene glycol), or PEG, that permits normal glucose regulation and protects cells from a detrimental immune response [Wyman *et al.*, *Small* (2007) **3**, 683].

The researchers trapped the cells at the interface between an aqueous layer floating on top of a denser chlorinated hydrocarbon oil. They then drew the cells into a spout, using a technique called selective withdrawal, where they were coated with a PEG precursor solution. The cells were then exposed to a green laser to induce photoinitiators to form a PEG hydrogel. "PEG has many advantages as an encapsulation material," explains Sidney R. Nagel. "In particular it is

nonreactive with the immune system and has an established history as a material that can be implanted into the human body for a wide range of approved clinical applications." When the encapsulated cells are exposed to various levels of glucose, insulin secretion similar to unmodified cells is observed. "Islets remain alive and viable throughout the encapsulation process," says Marc R. Garfinkel. "The coats do not pose a diffusion barrier to glucose or insulin as there is no time lag in the insulin response." The coating also prevents fluorescently labeled protein molecules (lectin) from reaching cells. Lectin is smaller than immunoglobulin, which is involved in the immune response that destroys islet cells. The results indicate that encapsulation is a sufficient barrier to harmful large molecules but permeable enough to allow small molecules like water and glucose to enable cells to operate.

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