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WEIZMANN INSTITUTE OF SCIENCE

Science Tips

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Cell on a Chip Reveals Protein Behavior

For years, scientists around the world have dreamed of building a complete, functional, artificial cell. Though this vision is still a distant blur on the horizon, many are making progress on various fronts. Prof. Roy Bar-Ziv and his research team in the Weizmann Institute's Materials and Interfaces Department recently took a significant step in this direction when they created a two-dimensional, cell-like system on a glass chip. This system, composed of some of the basic biological molecules found in cells – DNA, RNA, proteins – carried out one of the central functions of a living cell: gene expression, the process by which the information stored in the genes is translated into proteins. More than that, it enabled the scientists, led by research student Yael Heyman, to obtain "snapshots" of this process in nanoscale resolution.

The system, consisting of glass chips that are only 8 nanometers thick, is based on an earlier one designed in Bar-Ziv's lab by Dr. Shirley Daube and former student Dr. Amnon Buxboim. After being coated in a light-sensitive substance, the chips are irradiated with focused beams of ultraviolet light, which enables the biological molecules to bind to the substance in the irradiated areas. In this way, the scientists could precisely place DNA molecules encoding a protein marked with a green fluorescent marker in one area of the chip and antibodies that "trap" the colored proteins in an abutting area. When they observed the chips under a fluorescence microscope, the area in which they had placed the antibodies turned a glowing bright green. This meant that the DNA instructions had been copied into RNA molecules, which were in turn translated into fluorescent green proteins. The green proteins were then ensnared by the antibodies.

Next, the scientists asked whether their cell-like system could reproduce complex structural assemblies of naturally-occurring proteins. This time, they attached a viral gene to the chips' surface encoding a protein that can self-assemble into a nanotube. With the help of Dr. Sharon Wolf of the Electron Microscopy Unit, they observed a forest of minuscule tubes sprouting from the antibody area under an electron microscope.

The researchers then sought a way to produce and trap multiple proteins simultaneously by confining each protein in the area of its gene on the chip. On top of the chip to which the DNA encoding green proteins was bound, the scientists added a solution with a second gene encoding a red protein. The resulting red and green proteins competed for binding on the antibody traps, yielding a graded spatial separation in which the antibodies closest to the green genes had the highest concentration of green protein, with red concentrations rising farther afield. The results of this research recently appeared in *Nature Nanotechnology*.

Bar-Ziv: "We have shown that it is possible to build a protein 'production line' outside of the cell and use it to observe a spectrum of protein activities." In the future, such a system may move from enabling the observation of proteins to providing the basis for techniques to create complex, active protein structures on demand. ❙

Prof. Roy Bar Ziv's research is supported by the Yeda-Sela Center for Basic Research; and the Carolito Stiftung.

Causing Collapse

Weizmann Institute researchers suggest one can affect an atom's spin by adjusting the way it is measured

One of the most basic laws of quantum mechanics is that a system can be in more than one state – it can exist in multiple realities – at once. This phenomenon, known as the superposition principle, exists only so long as the system is not observed or measured in any way. As soon

as such a system is measured, its super-position collapses into a single state. Thus, we, who are constantly observing and measuring, experience the world around us as existing in a single reality.

The principle of superposition was first demonstrated in 1922 by Otto Stern and Walther Gerlach, who observed the phenomenon in the spin of silver atoms. Spin is the intrinsic magnet in quantum particles, and when a particle's spin is in superposition, it points in more than one direction at the same time. (Instead of the north and south of magnets, these are referred to as up and down.) Dr. Roee Ozeri and research students Yinnon Glickman, Shlomi Kotler and Nitzan Akerman, of the Physics of Complex Systems Department studied how the spin of a single atom collapsed from superposition to one state when it was observed with light. They "measured" the atom by shining laser light on it. Just as our eyes observe the world by absorbing the photons – light particles – scattered in our direction by objects, the researchers observed the process of spin collapse in the atoms by measuring the scattered photons. In results that appeared recently in *Science*, they showed that the direction that a photon takes as it leaves the atom is the direction that the spin adopts when superposition collapses.

Next, the team measured the polarization of the emitted photon and found that the observed polarization determines the effect of measurement on the spin. This suggests that an observer can influence the collapse of superposition just by adjusting the orientation of his photon-polarization measurement apparatus.

The reason for this "action-at-a-distance" is that the spins of the measured atoms and the emitted photons were entangled. That is, even after they were separated, a measurement of one of them instantaneously affected the other.

The experiment is an important step in understanding the measurement process in quantum systems. ❙

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Programmed Destruction

Stroke, heart attacks and numerous other common disorders result in a massive destruction of cells and tissues called necrosis. It's a violent event: As each cell dies, its membrane ruptures, releasing substances that trigger inflammation, which in turn can cause more cellular necrosis. A new Weizmann Institute study may help develop targeted therapies for controlling the tissue destruction resulting from inflammation and necrosis.

The study, conducted in the laboratory of Prof. David Wallach of the Biological Chemistry Department, focused on a group of signaling enzymes, including caspase 8, which was discovered by Wallach nearly two decades ago. Earlier studies by scientists in the United States, China and Europe had shown that this group of proteins induces "programmed," or deliberate, necrosis intended to kill off damaged or infected cells. This revelation had generated the hope that by blocking the induction of necrotic cell death by these proteins, it might be possible to prevent excessive tissue damage in various diseases.

But in the new study, reported in *Immunity*, Wallach's team sounds a warning. The researchers have revealed that under conditions favoring inflammation – that is, in the presence of certain bacterial components or other irritants – the same group of signaling enzymes can trigger an entirely different process in certain cells. It can activate a previously unknown cascade of biochemical reactions that causes inflammation more directly, without inducing necrosis, by stimulating the production of hormone-like regulatory proteins called cytokines. The research, mainly based on experiments in transgenic mice lacking caspase 8 in certain immune cells, was spearheaded by postdoctoral fellow Dr. Tae-Bong Kang. Team members Seung-Hoon Yang, Dr. Beata Toth and Dr. Andrew Kovalenko made important contributions to the study.

These findings suggest that prior to developing targeted necrosis-controlling therapies, researchers need to learn more about the signals transmitted by caspase 8 and its molecular partners: Since this signaling can lead to several entirely different outcomes, the scientists need to determine when exactly it results directly in necrosis and when it does not. Clarifying this matter is of enormous importance: Tissue necrosis occurs in a variety of disorders affecting billions of people, from the above-mentioned stroke and heart attack to viral infections and alcoholism-related degeneration of the liver.

Prof. David Wallach's research is supported by the Leona M. and Harry B. Helmsley Charitable Trust; and Merck Serono. Prof. Wallach is the incumbent of the Joseph and Bessie Feinberg Professorial Chair.