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‘MICRO-SWIMMERS’ MAY SOON HELP WITH DRUG DELIVERY

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Varied tactics: By changing the pH of the solution or by triggering it with light, the researchers showed that drug release could be activated. | Photo Credit: Special Arrangement

In the 1966 Hollywood film, *Fantastic Voyage*, a group of scientists enter the bloodstream of a colleague to remove a blood clot from his brain, by shrinking themselves and their submarine, Proteus, to the size of a cell. This element of science fiction is on its way to becoming a reality, as recent research aims at moving microbots into the bloodstream to deliver drugs. Speaking of this work, Varun Sridhar from Max Planck Institute for Intelligent Systems (MPI-IS), Stuttgart, Germany, says, “Our work has shown that it is possible to use light as a fuel to move microbots in real-body conditions with intelligent drug-delivery that is selectively sensitive to cancer cells.” The research is led by MPI-IS and Max Planck Institute for Solid State Research (MPI-FKF), Stuttgart, Germany.

Imagine trying to swim in a pool of honey. Any effort to push backwards and thus generate forward motion would be hindered by the high viscosity of the honey. At the microscopic level, the viscosity of even water is overwhelming. “A Hollywood film can take liberties; miniaturising a submarine is all that is [needed]. However, in real life, locomotion of microscopic swimmers is not that simple,” says Metin Sitti, a director at MPI-IS, who is part of the collaboration.

Made from the two-dimensional compound poly (heptazine imide) carbon nitride (aka PHI carbon nitride), these microbots are nothing like the miniaturised humans. They range from 1-10 micrometre (a micrometre is one-millionth of a metre) in size, and can self-propel when energised by shining light.

The PHI carbon nitride microparticles are photocatalytic. “Like in a solar cell, the incident light is converted into electrons and holes. These charges drive reactions in the surrounding liquid,” explains Dr. Sridhar. The charges react with the fluid surrounding them. This reaction, combined with the particle's electric field, makes the microbots (micro-swimmers) swim.

“As long as there is light, electrons and holes are produced on the surface of the swimmers, which in turn react to form ions and an electric field around the swimmer. These ions move around the particle and cause fluid to flow around the particle. So this fluid flow causes the micro-swimmers to move,” said Dr. Sridhar, “With light, we not only move the microbots but can direct their motion towards a specific goal.”

Just like the fragrance of incense wafts from a region of high concentration to low, the ions move from the bright surface of the micro-swimmer to the rear end. The diffusion of the swimming medium in one direction propels the micro-swimmer in the opposite direction. This is like a boat moving in the direction opposite to the oar strokes.

The particles are nearly spherical, and the incident light illuminates one-half of the sphere, leaving the other dark. As photocatalysis is light-driven, it occurs only on the brightened hemisphere. As the ions move from the bright side to the dark side, micro-swimmers march towards the direction of the light source.

The design of micro-swimmers or making them move in a particular direction is not new. “The body fluids and blood contain dissolved salts. When salts are present, the salt ions stop the reaction ions from moving freely as they will just bind or recombine with them and stop them. So all the chemically propelled swimmers can't swim in solutions containing salts." says Filip Podjaski, an author of the paper published in *Science Robotics.*

For example, when dissolved in water, common salt (NaCl) breaks up into sodium (Na^{+}) and chloride (Cl^{-}) ions. These ions will neutralise the ions created by the photocatalytic reaction, thereby impeding the self-propulsion.

To overcome this challenge, the researchers examined various materials such as titanium dioxide and cobalt monoxide and finally zeroed on polyheptazine imide (PHI) carbon nitride. While carbon nitride is an excellent photo-catalyst, the two-dimensional PHI has a sponge-like structure full of pores and voids and charge storage properties.

The researchers found that the ions in the salty solution passed through the pores of PHI carbon nitride. Thus, there was little or no resistance from the salt ions. Experiments were carried out in sample solutions as highly concentrated as water from the dead sea. "Salt ions present in the swimming medium do not affect the propulsion. Our organic material allows the ions to pass through them freely," says Bettina Lotsch, a director at MPI-FKF, and co-author of the paper.

In addition to transporting salt ions from the fluid, the voids and pores on the microparticles worked as cargo bays and could soak up large amounts of drug. The researchers found that Doxorubicin, a drug used to treat cancer, was readily absorbed. By changing the pH of the solution or by triggering it with light, the researchers showed the drug release could be activated.

"The material also has an intelligent charge-storage property to store electrons when light is present. The environment of cancer cells is characterised by low oxygen. The stored electrons are sensitive to it. We use that to deliver drugs, targeting the cancer cells," explains Dr. Sridhar.

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