Robot Pills

A voyage through the human body is no longer mere fantasy. Tiny devices may soon perform surgery, administer drugs and help diagnose disease

BY PAOLO DARIO AND ARIANNA MENCIASSI

THE MOVIE *FANTASTIC VOYAGE,* the story of a miniaturized team of doctors traveling through blood vessels to make lifesaving repairs in a patient's brain, was pure science fiction when it came out in 1966. By the time Hollywood remade the film in 1987 as *Innerspace,* a comedy, real-world engineers had already begun building prototypes of pill-size robots that could voyage through a patient's gastrointestinal tract on a doctor's behalf. Patients began swallowing the first commercially built pill cameras in 2000, and since then doctors have used the capsules to get unprecedented views of places, such as the inner folds of the small intestine, that are otherwise difficult to reach without surgery.

One important aspect of *Fantastic Voyage* that has remained fantasy is the notion that such tiny pill cameras could maneuver under their own power, swimming toward a tumor to get a biopsy, checking out inflammation in the small intestine, or even administering drug treatments to an ulcer. In recent years, however, researchers have made great strides in converting the basic elements of a passive camera pill into an active miniature robot. Advanced prototypes, now being tested in animals, have legs, propellers, sophisticated imaging lenses and wireless guidance systems. Soon these tiny robots may be ready for clinical trials. Right now they are testing the limits of miniaturized robotics.

TRANSFORMING PASSIVE PILLS

THE DIGESTIVE TRACT is the first frontier. The first wireless camera pill, M2A, introduced in 1999 by the Israeli company Given Imaging, and subsequent models established the usefulness of examining the gastrointestinal tract with a wireless device. The practice, known as capsule endoscopy, is now routinely used in medicine. Unfortunately, the lack of human control in a passive camera pill leads to a high rate of false negative results—the cameras miss problem areas, which is unacceptable for a diagnostic tool. If the purpose of peering inside the body is to screen for disease or to get a closer look at a suspected problem, a doctor wants most of all to be able to stop the camera and maneuver it to inspect a region of interest.

Transforming a passive capsule into a more reliable device for gastrointestinal screening requires adding moving appendages, or actuators, to propel the pill through the body or act as tools for manipulating tissues. Operating those moving parts demands two-way high-speed wireless data transmission of images and instructions. The pills must, in effect, become tiny robots able to respond quickly to a technician's orders. All these components need sufficient power to complete their tasks during a journey that could last up to 12 hours. And all this must fit into a two-cubic-centimeter container—about the size of a Gummi Bear—that a patient can comfortably swallow.

The same year M2A debuted, the Intelligent Microsystem Center (IMC) in Seoul, Korea, initiated a 10-year project to develop a new generation of capsular endoscopes with advanced features. Such a robotic pill would have onboard sensors and a light source for imaging. It would have mechanisms for delivering drug therapies and taking biopsies. And it would have the ability to locomote, under an endoscopist's wireless remote control. Since 2000, additional companies and research groups have entered the field. For instance, 18 European teams formed a consortium with the IMC to develop capsular robots for cancer detection and treatment. Our group at the Scuola Superiore Sant'Anna in Pisa, Italy, with the medical supervision and guidance of Marc O. Schurr of novineon in Tubingen, Germany, handles the scientific and technical coordination of that project, called VECTOR, for versatile endoscopic capsule for gastrointestinal tumor recognition and therapy.

These academic and industry groups have come up with many innovative ideas. In particular, they have posed a variety of solutions to the central challenge: how to control the movement of capsular devices inside the body. Most of them take one of two fundamental approaches.

The first entails directing the movement of the capsule with onboard actuators—moving parts such as paddles, legs, propellers or similar appendages integrated into the shell of the device and capable of deploying once the pill is inside the digestive tract. The actuators, powered by miniature motors, are most often used to direct the capsule's movements, but in some designs legs can also push aside tissue around the capsule, to get a better look at something or to help the capsule pass through a collapsed section of intestine. Motors and actuator mechanisms such as gears are pretty large compared with the total volume of a swallowable capsule, which makes the integration of other essential parts—the imaging sensor or a therapeutic module such as a biopsy tool— challenging. In addition, to distend tissue, a capsule must exert a significant force—equivalent to 10 or 20 times its weight. The ef-

KEY CONCEPTS

- Pill cameras made possible unprecedented internal views of the entire digestive tract, but the uses and accuracy of those passive capsules are limited.
- Active pill-size robotic capsules are being developed for use in screening, diagnosis and therapeutic procedures.
- Miniaturizing robotic components to perform tasks inside the body poses novel engineering challenges. Those challenges are giving rise to creative solutions that will influence robotics and other medical technologies in general.

—The Editors

FRANK HÜLSBÖMER

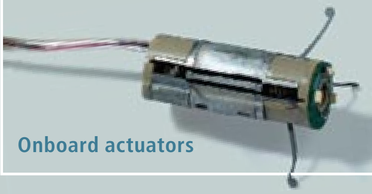
[IN THE WORKS]

MINI BOTS FOR A WIDE RANGE OF JOBS

To make miniature robots that can operate in the digestive tract, engineers must find ways of wirelessly controlling their locomotion and fine movements. And they must fit the required tools, imaging sensors and power supply into a capsule small enough for a patient to swallow. Here are some examples of the diverse tasks engineers want tiny robots to do and the ways they are trying to overcome the technical challenges.

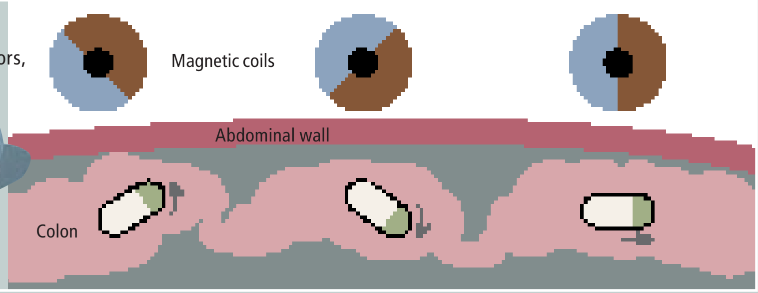
LOCOMOTION

The movements of endoscopic robots can be controlled either by onboard actuators, such as legs, paddles, propellers or cilialike appendages, or by magnetic fields generated outside the patient's body.



Onboard actuators

Magnetic propulsion

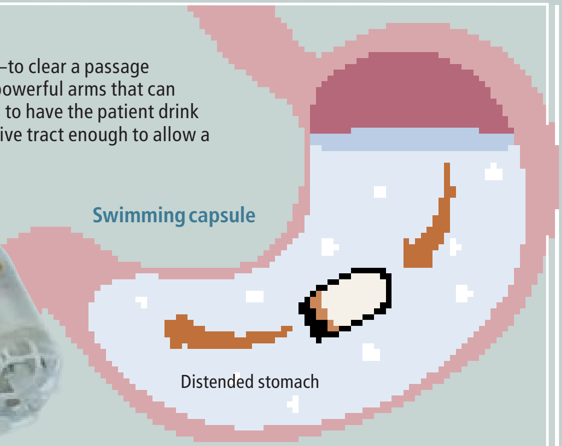


TISSUE DISTENSION

One way to push tissue out of the way—to clear a passage or to gain a view—is to give the robot powerful arms that can push. A less energy-intensive method is to have the patient drink water (*right*), which distends the digestive tract enough to allow a propeller-driven capsule to maneuver.

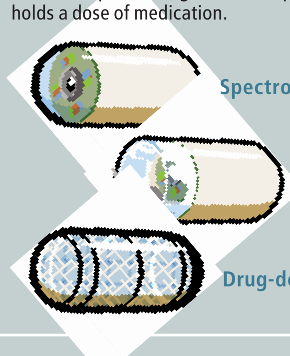
Capsule with arms

Swimming capsule



DIAGNOSIS/TREATMENT

A capsule can carry a wide range of tools: a spectroscopic camera that sees cells underneath the surface layer of tissue; a clip for taking a tissue biopsy; or a well that holds a dose of medication.



fort requires high torques from the motors, which consumes considerable power (approximately half a watt). This power drain puts a strain on battery technology, which limits how long these devices can operate.

To conserve battery power, the best trade-off might be to use actuators only for propulsion and find other ways to distend tissue. Having a patient drink half a liter of clear liquid just before swallowing a propeller-driven capsule, for instance, would distend the stomach for up to 20 minutes before the fluid drains away into the small intestine. In that time, the pill could swim around under wireless control and examine the stomach lining.

The bulk and power requirements of onboard actuators have led some researchers to focus on another approach: applying magnetic fields generated outside the body to remotely control the movement of the capsules. In 2005 Olympus and Siemens introduced a magnetic guidance system for its passive camera pill that causes the pill to rotate. The corkscrew motion generates a light friction that helps the capsule burrow through narrow stretches of the digestive tract, such as the small intestine, according to literature from Siemens.

Although using magnets to guide an endoscopic capsule through the intestines is straightforward, achieving reliable control with magnets alone is extremely difficult. Magnetic fields lose power with distance, and with the irregular geometry of the intestine, sudden changes in field strength can cause the capsule to jump or can entirely sever magnetic control over the pill. In practice, this instability may cause an operator to lose contact with the pill and to be unable to find it again. It is possible to compensate by adding more magnets, which would give greater control and stability, but that might require cumbersome configurations of the electromagnetic coils.

TAILORED HYBRIDS

IN LIGHT OF the limitations of both internal and external approaches to controlling capsule movements, we believe that we need to combine these

[THE AUTHORS]

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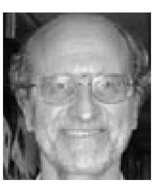
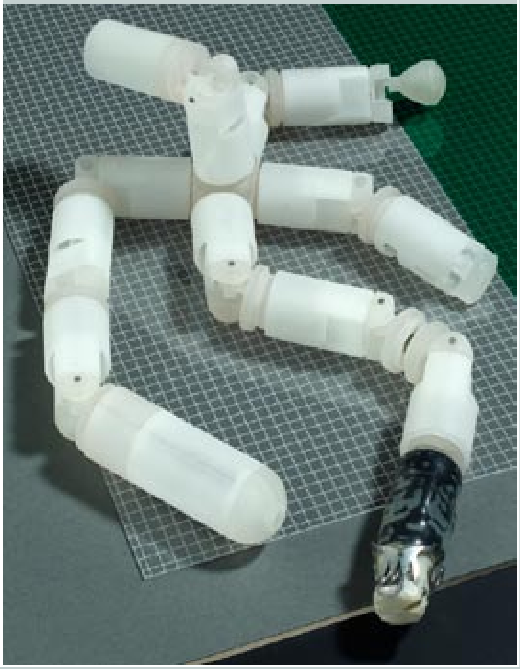


REMOTE SURGERY

One way to expand the range of tasks that robot pills can perform is to design them for self-assembly. The patient would swallow a dozen or more pills; once inside the stomach, the pills would combine with one another to form one big, powerful robot. Surgeons would operate the device wirelessly. When the surgery was complete, the robot would break apart into capsules, which would pass harmlessly through the digestive tract.

Possible surgical configuration



two methods to find a solution that will be comfortable for the patient and offer reliable diagnostics. External magnetic locomotion is adequate for a rough positioning of a capsule inside the intestine; leglike actuators are useful to shift position or maneuver for a better view.

Our research group has designed such a hybrid capsule with four motor-driven legs and tested it in a pig, whose intestines are the same dimensions as those of humans. The capsule's legs remain closed while the device is being swallowed and during most of its trip through the digestive tract. An external magnetic field generator held close to the abdomen guides the capsule forward. When the capsule reaches a segment of intestine whose walls have collapsed, it lifts the surrounding tissue by extending its legs, which move the capsule slightly forward through the opening.

In most areas of the small and large intestines, a hybrid locomotion system would provide the control doctors need for thorough visual inspection. Different situations will call for different solutions. The VECTOR project, for instance, has developed three capsule concepts for the small intestine alone: one is a passive camera pill for normal screening; a second is a diagnostic capsule with active locomotion and spectroscopic imaging that can detect abnormalities underneath the tissue surface. The same spectroscopic sensor is incorporated in the third planned VECTOR capsule, which would also carry a biopsy tool that could take a tissue sample and store it inside the capsule, to be retrieved when the capsule exits the patient.

The ability to perform biopsies and other more complex therapeutic actions, such as surgical procedures, would make capsular endoscopic robots an even more powerful medical tool. But critical problems such as power supply, space constraints and limited torque make many more ambitious therapeutic tasks requiring complicated motions and multiple actuators impossible to achieve with a single two-cubic-centimeter pill.

For these reasons, we are now working on an advanced concept: surgical robots that configure themselves inside the body. Here is how it might work. The patient would drink a stomach-distending fluid, then swallow as many as 10 or 15 capsules. Each capsule would be a miniaturized component with magnets at either end. Once inside the stomach, the capsules, under remote guidance, would quickly assemble themselves into the desired configuration. A surgeon would then use the assembled robot as a wireless tool that can operate without the need to make a single incision from outside the body. When the surgery is done, the magnetic bonds between the capsules could be reconfigured or broken, allowing the parts to make their exit harmlessly through the digestive tract.

We have an early prototype based on two-centimeter capsules with customizable internal parts and actuators. One or more capsules could have a camera, others could have onboard tools, and all would be controlled wirelessly.

Miniaturized robotic components may eventually find wider use throughout the body for a variety of purposes. Guidance systems and camera sensors developed for capsule endoscopy are already influencing related biomedical technologies, such as the newest versions of traditional endoscopes and laparoscopic surgery tools. Beyond health care, these technologies are part of a broad trend toward miniaturization and wirelessly controlled multifunctional robotics. Capsule robots will undoubtedly have an influence on robotic machines in the larger world. ■

HYBRID CAPSULE guided by external magnets navigates the colon of a pig, using extendable legs to adjust its position and push aside tissue.

FRANK HÜLSBÖMER (*left*); COURTESY OF ARIANNA MENCIASSI (*right*)

MORE TO EXPLORE

Wireless Capsule Endoscopy: From Diagnostic Devices to Multipurpose Robotic Systems. Andrea Moglia, Arianna Menciassi, Marc Oliver Schurr and Paolo Dario in *Biomedical Microdevices,* Vol. 9, No. 2, pages 235–243; December 12, 2006.

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