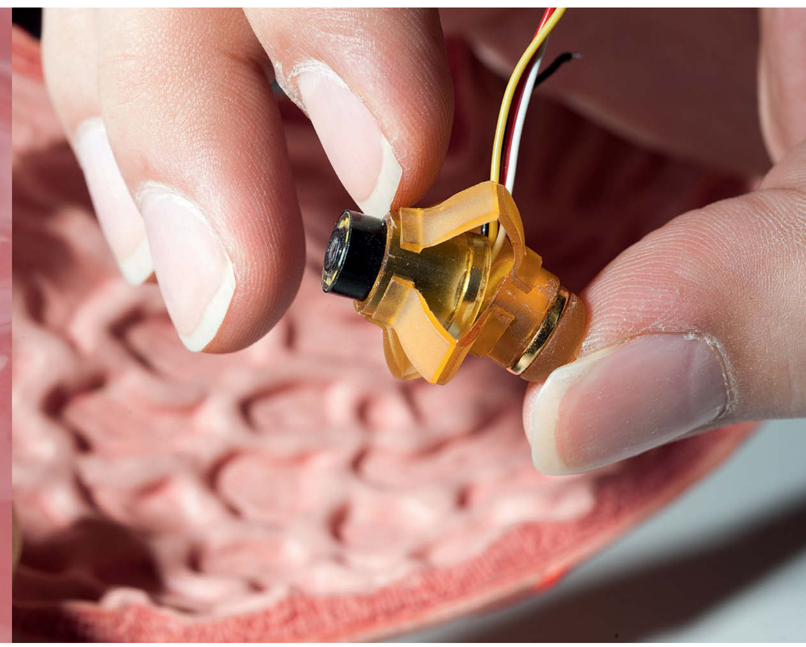
Diagnostics with a Stomach Pill



Gastroscopy usually requires patients to swallow an endoscope tube. Although camera-carrying capsules are also suitable for the task, it is still not possible to control them. Scientists at the **Max Planck Institute for Intelligent Systems** in Stuttgart plan to change all that. And their tiny capsule-shaped robots can do a lot more than merely take snapshots of the stomach's interior.

TEXT **TIM SCHRÖDER**

Photos: MPI for Intelligent Systems (left), Tom Pingel (right)

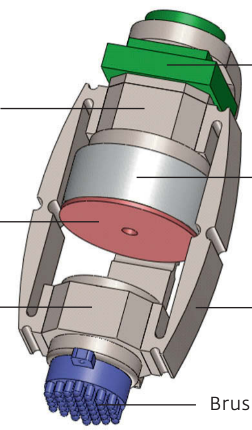
Left to right The MASCE capsule endoscope that Max Planck researchers in Stuttgart are developing is 24 millimeters long. It can be flattened so that it's unable to leave the stomach. MASCE is guided through the stomach with the help of a magnet, as demonstrated here by Donghoon Son.

Photos: Tom Pingel (2)

Gastroscopy is an unpleasant procedure. Anyone who has had to undergo diagnostic gastroscopy because of persistent abdominal pain will know how strange it feels to swallow a long tube. The tube, called a gastroscope, contains a fiber-optic cable that transmits images from a camera at the tip of the tube to a monitor outside the body. Gastroscopy today is a routine procedure. Doctors use it to search for inflammation or tumors in the stomach and duodenum. For patients, it is always a cause of distress.

For the past ten years or so, doctors have therefore resorted to a small high-tech alternative in individual cases – capsule endoscopes: miniature cameras the size of a lozenge. Patients only need to swallow the capsule to launch it on a journey through the gastrointestinal tract, during which the camera snaps hundreds of photos, which it transmits wirelessly to a storage device that the patient attaches to his or her belt for a few hours.

Doctors use capsule endoscopy when blood occurs in a patient's stool and the wound can't be located by gastroscopy or colonoscopy. In such cases, the bleeding source is often in the small intestine, which can't be reached from outside the body. Capsule endoscopy is ideal for examinations in the narrow confines of the small intestine. However, in the relatively large stomach or colon, it is a matter of luck wheth-



Above MASCE is fitted with a camera (green). Two magnets, one at either end, help to guide the capsule endoscope and also to open the lid (red) of the chamber in which drugs or micro-grippers are transported. The latter can be used to take tissue samples. A brush-like silicone structure (blue), to which the micro-grippers stick, collects the samples.

Right-hand page Metin Sitti heads the Department of Physical Intelligence at the Max Planck Institute for Intelligent Systems in Stuttgart. He is developing robots whose abilities reside in their construction or material.

er the diseased tissue actually falls in the camera's field of view. Moreover, the images tend to be blurred in those organs, as the distance from the capsule to the wall of the organ changes constantly, and are only coincidentally in focus. The problems arise because, unlike a camera at the tip of a conventional endoscope, capsule endoscopes can't be controlled from outside.

For some time now, scientists have therefore been working on capsules that patients can swallow like pills. Such capsules should be guidable, making them suitable for investigations of the stomach and colon. Within the framework of an EU project that ended four years ago, experts at a number of companies and scientific institutions developed a robot capsule that moves through the stomach and intestine like an insect on tiny legs. However, the crawling movement consumed so much power that the robot's on-board energy supply was soon depleted.

Other research teams therefore prefer robot capsules containing magnetic particles or components that allow them to be controlled by magnetic fields outside the body. As the magnetic field moves, the round capsule follows the magnetic field, rolling slowly along in the stomach. As tests in the lab have shown, this mode of locomotion works very well.

Metin Sitti is also developing capsule robots that can be controlled by means of external magnetic fields. He calls them millibots. Measuring only a few millimeters in length, they are initially being optimized for exploring the stomach. Doctoral student Donghoon Son and other members of Sitti's team have guided the millibots, which are in the shape of drug capsules, through artificial silicone stomachs and real pig's stomachs for many hours.

ABILITIES INHERENT IN THE CONSTRUCTION OR MATERIAL

Getting such machines to move about is one of Metin Sitti's fields of expertise. He has developed long-legged robots that glide across the surface of puddles like pond skaters, and flying machines that flutter about like butterflies. For many years he taught mechanical engineering at Carnegie Mellon University in Pittsburgh, and for the past year he has headed the new Department of Physical Intelligence at the Max Planck Institute for Intelligent Systems in Stuttgart.

Physical intelligence – the term initially sounds like an oxymoron, because a robot's mind is usually thought to reside in its software. "Physical intelligence means that a machine's intelligence or abilities reside primarily in its construction or material – not just in its control system," explains Metin Sitti; for example the pond skater, which distributes its weight through its long legs in such a way that it floats on water, using surface tension to support it.

Sitti and his coworkers are extremely creative in finding new materials to make their robots better adapted for specific applications than would be possible with conventional robots composed of steel, plastic and electronic components. Their millibot capsules are a prime example. Unlike conventional capsule endoscopes, they don't have a hard shell. Instead, the 24-millimeter-long devices are held together by strips of soft polyurethane plastic, a material that is used in a similar form for the soles of running shoes. The capsules, which are egg-shaped like rugby balls, are fitted with small magnets at the top and bottom.

Graphic: MPI for Intelligent Systems

Photo: Tom Pingel

Thanks to their flexible shell, the small rubber capsules have the unusual ability to contract. Each polyurethane strip has a fold running across its width, so that an external magnetic field can cause the strips to fold together, flattening the capsule. To this end, an external magnetic field first pulls the capsule against the stomach wall in an upright position. When the researchers increase the strength of the magnetic field, this causes the capsule's internal magnets to move toward each other.

Because the material is elastic, as soon as the magnetic field decreases, the polyurethane strips return to their original shape, and the millibots regain their capsular form. Sitti calls the tiny machines MASCE, short for magnetically actuated soft capsule endoscopes.

A robot that can be squashed like a rubber ball doesn't sound very high tech. But the deformable millibots are special. Capsule endoscopes can usually only roll sideways or tumble while taking photos. Due to their deformability, however, they are in command of a very different kind of movement, which gives them completely new abilities.

Metin Sitti and his colleagues have developed a tiny chamber that opens when MASCE is compressed in a magnetic field – and closes again when the magnetic field diminishes. In the laboratory, the researchers have thereby been able to release tiny amounts of ink, spurt for spurt.

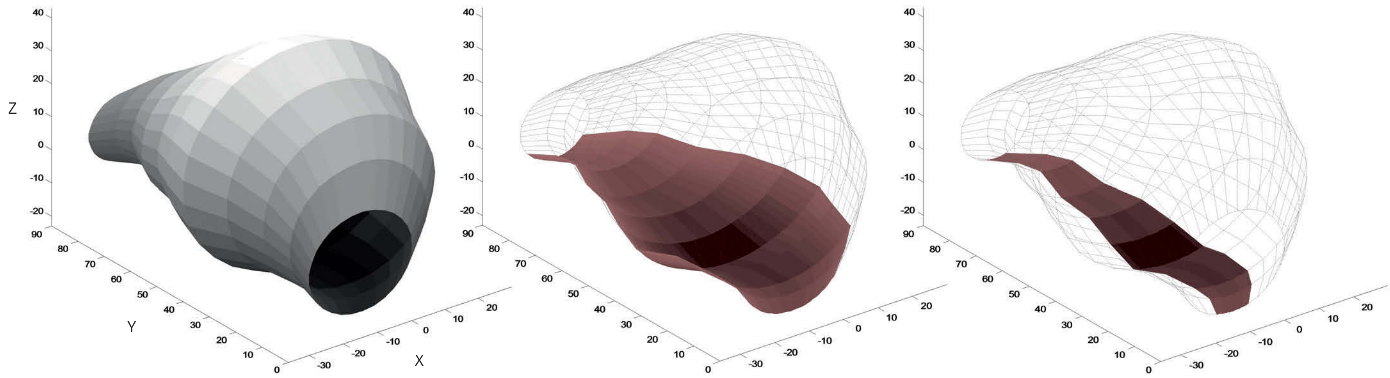
MASCE RELEASES SMALL AMOUNTS OF ACTIVE SUBSTANCES

"We imagine that in the future doctors will be able to release small quantities of drugs, for example to target inflammation or individual tumors," says Sitti. Many people, especially elderly patients, don't tolerate medicines when they swallow them.

"MASCE can release small quantities of drugs directly at the desired site in a much more targeted manner," Sitti says. This would reduce stress to the patient. It is even conceivable for MASCE to dwell in the stomach for several days in order to treat an inflammation or a tumor over an extended period.

Normally, objects pass through the outlet of the stomach, the pylorus, into the duodenum after a short time. The MASCE capsule would be no different. In order for it to release drugs to target an inflammation or tumor for an extended period, the researchers have therefore developed a second type of egg-shaped capsule that can be compressed into a thick disc-like shape by an external magnetic field. It then keeps that shape until the magnetic field is switched off. The capsule can thus remain in the stomach for several days. This MASCE variant contains namely two magnets – one at either end of its longitudinal axis – whose strength is not normally sufficient to compress the capsule. However, an external magnet can move the magnets toward each other so that their attractive force is sufficiently strong without help from outside.

Conversely, as soon as the treatment is completed, an external magnetic field can weaken the attractive force between



Above Regardless of the patient's position, a capsule endoscope only reaches part of the stomach. The size of the working space (middle and right) depends on the ratio between the capsule weight and the strength of the guiding magnetic field. For the entire organ to be examined, the patient has to change position several times.

Below MASCE is controlled by means of a copper wire coil that generates a magnetic field. The magnetic particles of a sensor, visible as metallic dots on the green plate, determine its position and orientation.

Right-hand page To reconstruct the spatial structure of the stomach wall, Mehmet Turan (right) guides a stereo camera with a tube through the stomach model. Meanwhile, Donghoon Son (left) checks the quality of the resulting 3D image.

Graphic: IEEE Transactions on Robotics, vol. 28, no. 1, February 2012; photo: Tom Pingel

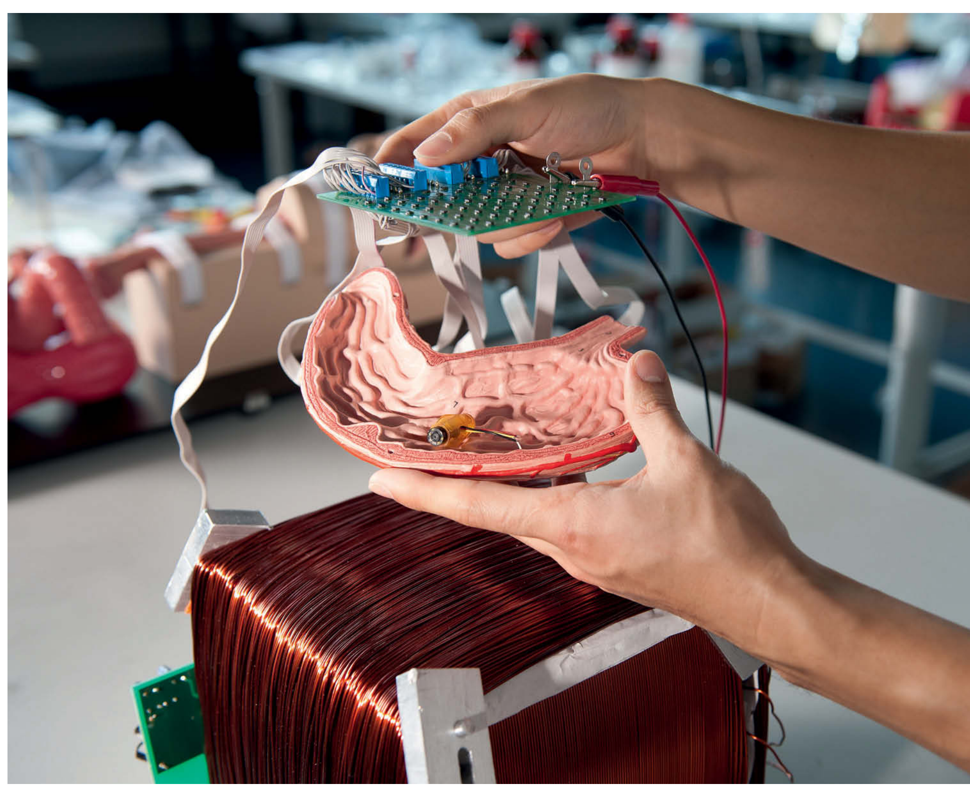
the capsule magnets. The capsule then snaps back to its original shape and is able to pass through the pylorus.

Together with the research group headed by materials scientist David Gracias of Johns Hopkins University in Baltimore, Sitti has integrated another important function in the MASCE millibot – the ability to perform biopsies. Doctors usually take samples of the mucosa during gastroscopy in order to examine suspected tissue for inflammation or cancer in the lab. To do so, the doctor pushes a kind of wire with small forceps into the gastroscope.

MICRO BIOPSY GRIPPERS BITE INTO TISSUE

Until now, capsule endoscopes have not been able to remove tissue samples. By contrast, the MASCE millibot can. Together with David Gracias, Metin Sitti had the idea of equipping MASCE with tiny grippers only a few micrometers in width. These micro-grippers resemble small stars whose points draw together like claws and bite into surrounding tissue when they warm up to body temperature. The prongs consist of a metallic layer and a polymer layer that expand at different rates as the temperature rises, causing the prongs to bend.

The skill lies in triggering the minuscule grippers at the right place, for example not until the capsule reaches the stomach. A biopsy experiment



proved successful. Metin Sitti filled the small chamber of the MASCE with micro-grippers and positioned it with the help of a magnetic field on a piece of pig's stomach. When the capsule was compressed in the magnetic field, the micro-grippers fluttered down onto the tissue. When the researchers increased the temperature, the micro-grippers snapped shut.

"For a while, we wondered how we could collect the micro-grippers again. Finally, we happened on the idea of coating one end of the MASCE capsule with a brush-like silicone structure to capture the micro-grippers," Sitti explains. That, too, proved successful in experiments. The researchers manipulated MASCE into an upright position in a magnetic field and pressed the capsule endoscope, together with its silicone brush, firmly against the tissue. Some of the micro-grippers were indeed caught in the silicone and were then transported away with MASCE. Of course, Sitti admits, a micro-gripper can only collect a small amount of tissue. However, he believes the quantity is sufficient for laboratory analyses.

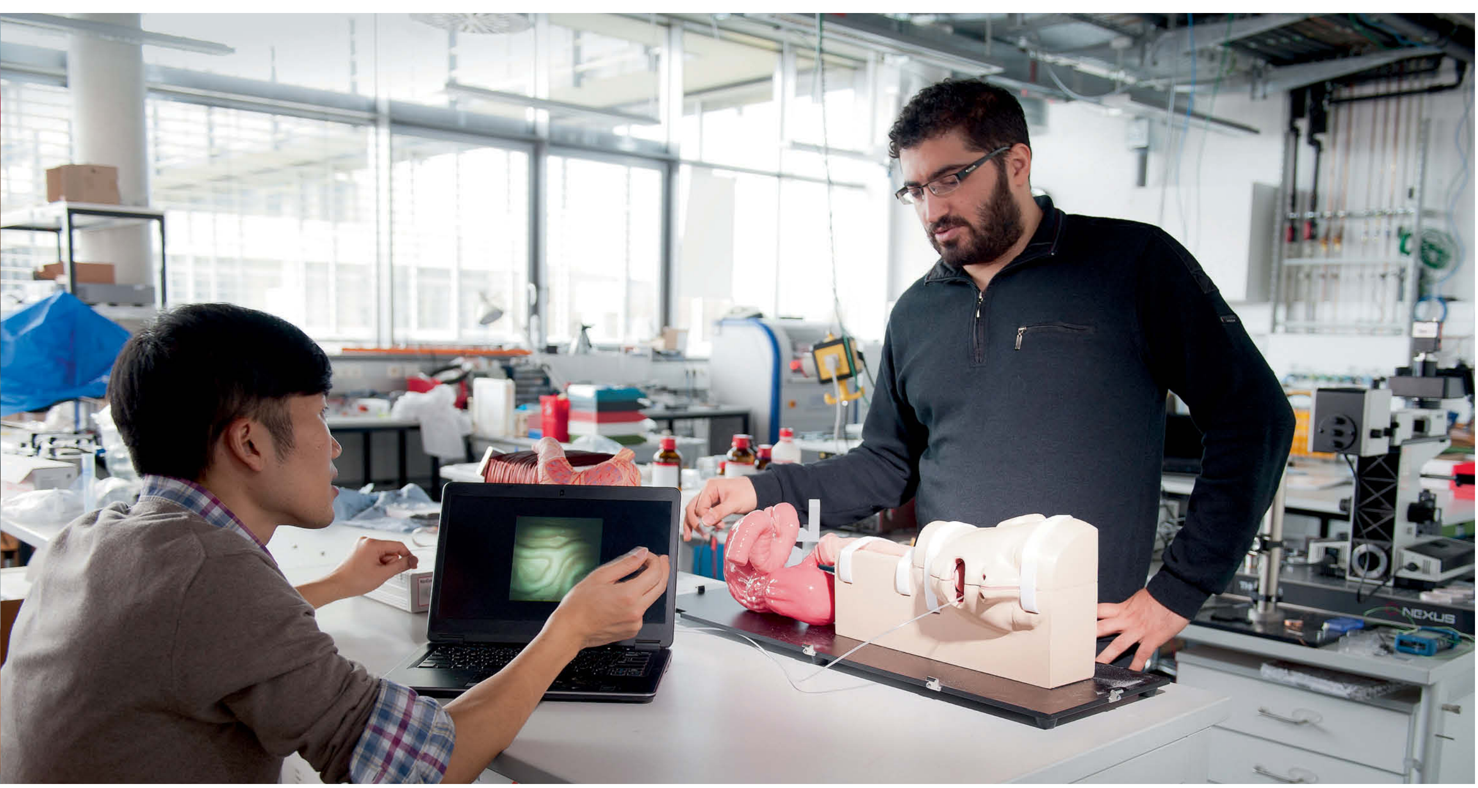
Metin Sitti can also imagine using the micro-grippers in the colon in the future. The problem is that they would have already snapped closed before reaching the colon, having travelled through the body for several hours. However, they could be heated by means of an external magnetic field, Sitti says – similar to the way in which a pot is heated on an induction cooker.

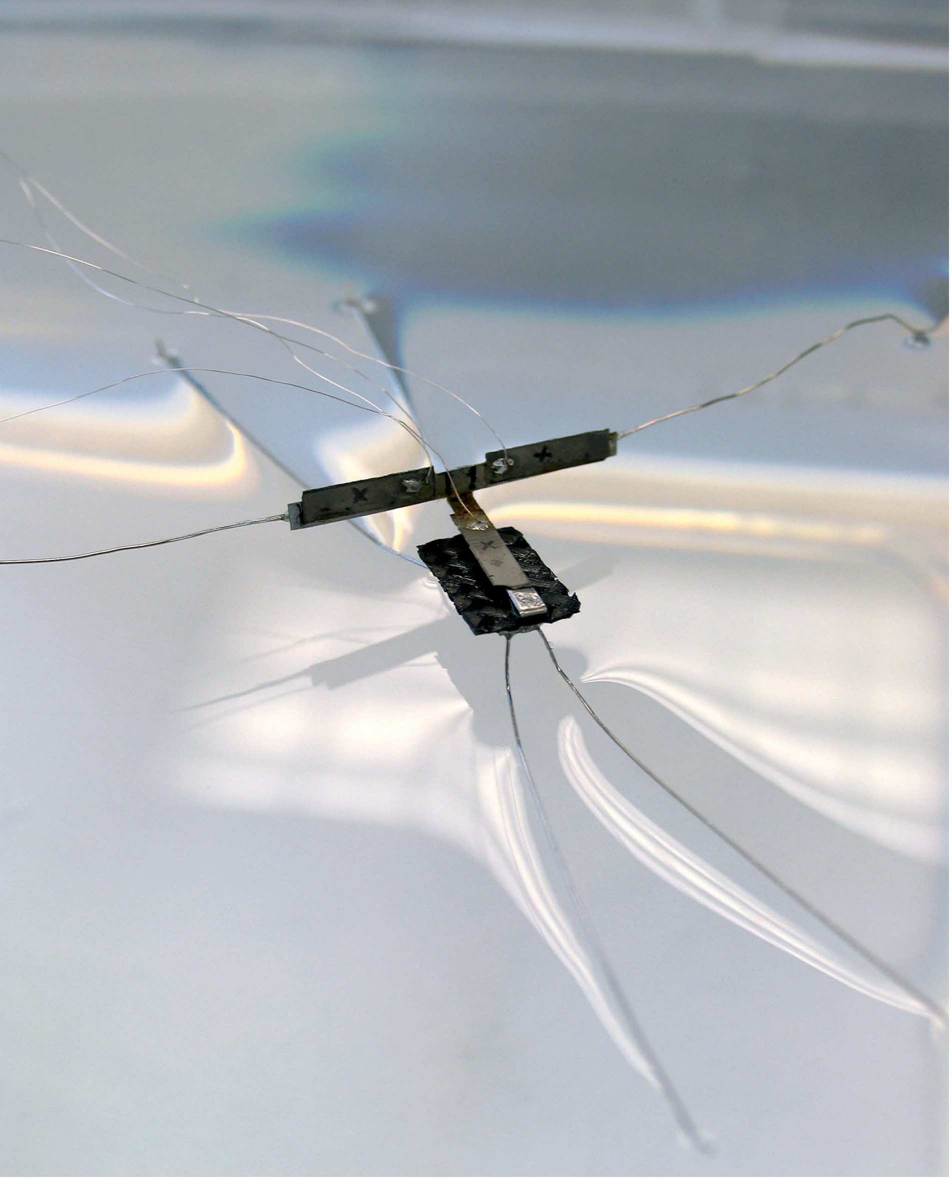
MASCE is still not refined enough for use in patients, but Metin Sitti has already shown that the intelligent polyurethane capsule endoscopes can do a lot more than their conventional precursors, which can only take photographs. Nevertheless, several challenges remain.

Later use in patients presupposes the ability to position MASCE with pinpoint accuracy. To do so, it must be possible to move the magnetic field and the capsule it controls very precisely. The future user must also be able to tell from the camera image which part of the stomach is actually being viewed. Today, a doctor using a conventional gastroscope navigates by rotating the camera at the end of the long tube back and forth.

But how can you know what a capsule is viewing as it tumbles through the stomach? "Ultimately, we want to develop a system that a doctor can use

Photo: Tom Pingel





The capsule endoscope is just one example of how the Stuttgart-based Max Planck researchers use design and material properties to impart abilities to a robot. Guided by these principles, they have also developed an artificial pond skater.

in real time to view the stomach or other parts of the gastrointestinal tract, as with a conventional gastroscope," says Mehmet Turan, a doctoral student in Sitti's department who is in charge of analyzing the images from MASCE.

The image quality, however, is still too poor to achieve that: the small MASCE camera has a resolution of only 250 x 250 pixels, and many of the images it produces are blurred. The problem is compounded by reflections from the moist, shiny mucosa, which disrupts the image, and the peristaltic movements of the stomach.

Mehmet Turan's task is to overcome MASCE's weaknesses. Turan studied electrical engineering and computer science and is an expert in computer vision. He is currently concerned with the question of how robots are able to perceive and analyze their environment – and especially how even poor images can be utilized with the help of computers. "I'm trying to solve the problem by having the computer analyze and merge many individual images, or frames. In this way, we can overcome weaknesses in an image by means of information contained in other images."

A PRECISE 3D MAP OF THE INTERIOR OF THE STOMACH

Mehmet Turan's ultimate future goal is to produce a precise 3D map of the interior of the stomach for every patient, allowing doctors to use MASCE to navigate accurately. The map should resolve structures smaller than one millimeter. Tumors and inflamed areas should also be clearly distinguishable. "To target tumors with drugs using a capsule endoscope, doctors must know precisely where the diseased tissue is located. This is only possible if we coordinate the magnetic field control with the image produced by MASCE," says Turan.

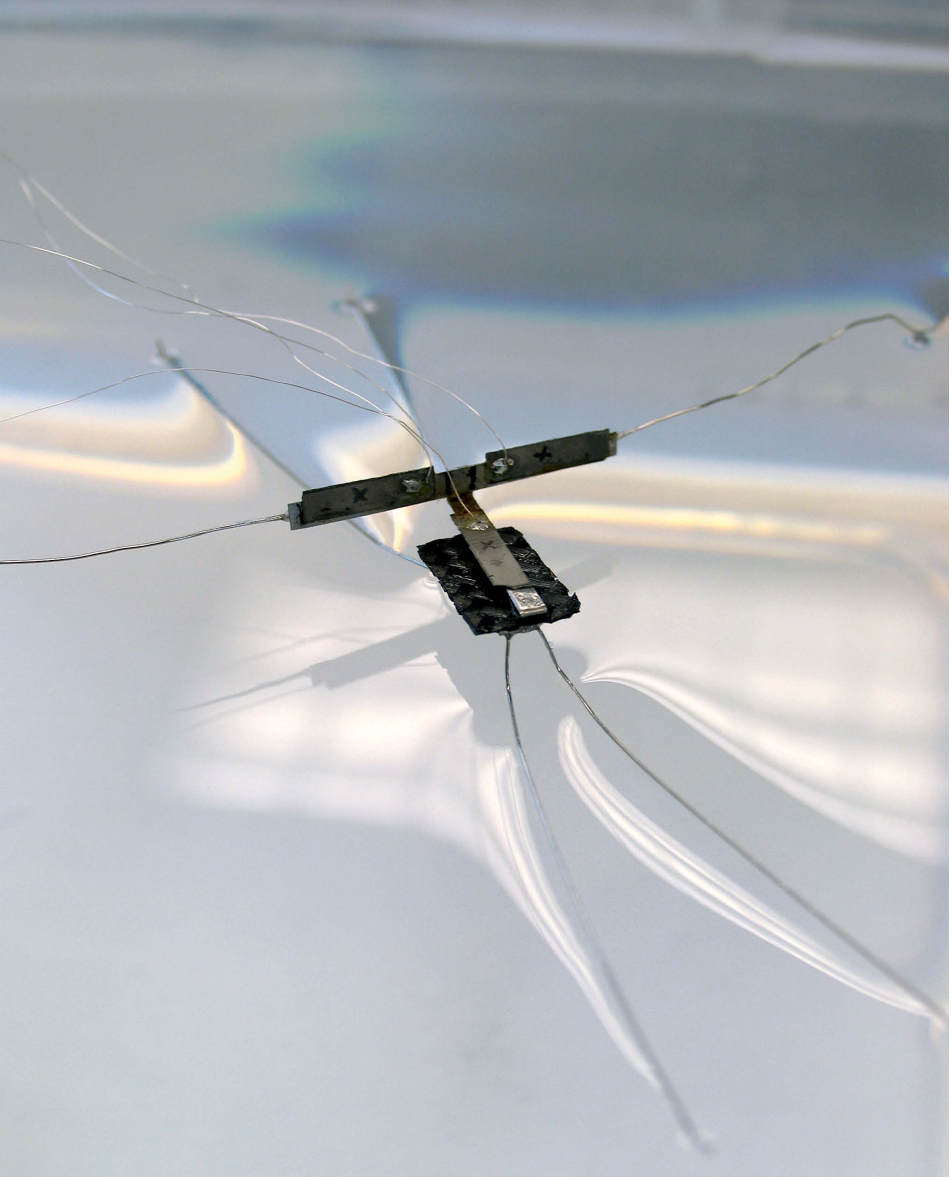
The researcher's task is difficult, not least because the gastric mucosa looks the same everywhere. "When a machine views a landscape, there are clear objects or structures it can use for orientation. There are no such landmarks in the stomach." Turan is therefore trying to extract landmarks from multiple frames to help the computer orient itself. Experts speak of distinguishable features, or corners. In the stomach, these can be particularly prominent folds in the mucosa or blood vessels.

Another advantage of such landmarks is that the computer is able to fix a position more quickly. That's important if the images are to be analyzed and relayed later in real time. A major challenge is estimating depth. As is generally known, animals have two eyes because stereovision enables them to better recognize how far away objects are. Each eye views a distant scene from a slightly different perspective.

However, the camera currently installed in MASCE has only one lens. It is therefore difficult to judge from its images how deep structures, for example folds, lie within the gastric mucosa. Turan also plans to solve this problem in the coming months with the help of machine learning. During analysis of the frames, the computer will take its bearings from landmarks in the organ, for example folds or other elevations. Multiple frames taken from various angles will then be compared to calculate the three-dimensional topology of the surface.

That will be important in the future in order to release micro-grippers or drugs with millimeter precision. As the

Photo: MPI for Intelligent Systems



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