KYUSHU UNIVERSITY

Public Relations Initiative, Kyushu University
744 Motooka Nishi-ku Fukuoka, 819-0395
TEL: +81-92-802-2443 FAX: +81-92-802-2139
E-MAIL: sysintlkh@jimu.kyushu-u.ac.jp
URL: https://www.kyushu-u.ac.jp

PRESS RELEASE (2025/9/16)

Scientists create a mathematical model that explains esophageal motility disorders

Scientists bridge mathematics and clinical medicine to reveal how esophageal muscle movements during swallowing typically occur and the root causes behind swallowing difficulties.

Fukuoka, Japan—For most people, swallowing is second nature, but how does it occur, and why do some people have difficulty with it? Researchers at Kyushu University in Japan have started to tackle these questions by developing a mathematical model that recreates the muscle movements of the esophagus that occur during swallowing. The model, reported in *Royal Society Open Science*, also replicates muscle dynamics seen in various esophageal motility disorders, revealing insights into their underlying causes and opening up new avenues for treatment.

A major symptom of esophageal motility disorders is difficulty in swallowing, known clinically as dysphagia, which affects millions worldwide. Dysphagia greatly impacts quality of life, sometimes resulting in malnutrition, dehydration, or even life-threatening complications such as aspiration pneumonia.

When we swallow, it triggers esophageal peristalsis, a process in which the muscles of the esophagus involuntarily contract and relax in a wave-like motion, pushing the swallowed contents toward the stomach. Although seemingly simple, recent advances in observational techniques, such as high-resolution manometry which measures esophageal pressure, have revealed a hidden complexity to these movements.

"For example, the lower esophageal sphincter, which is the valve between the esophagus and the stomach, acts like an on-off switch, opening only at the right moment to let food through. Also, when we swallow multiple times in row, the swallows suppress each other and only the last contraction is passed along, a phenomenon known as deglutitive inhibition," says first author Professor Takashi Miura from Kyushu University's Faculty of Medical Sciences. "However, we didn't have a model that could recreate all these complex esophageal movements or esophageal motility disorders."

In a collaboration with Josai University and Hokkaido University, the research team used simple mathematical equations in combination with high-resolution manometry to create a model that mimics the entire esophageal motility process. The model includes signaling that occurs in the brain and in the local nerve networks in the esophagus, as well as the contraction and relaxation of the esophageal muscles and lower esophageal sphincter.

By adjusting a few key parameters in their equations—such as the strength of nerve signals, the firing threshold of the nerves, or the strength of the muscle contractions—the researchers were also able to simulate a wide range of known disorders described in the Chicago Classification, the international classification scheme for esophageal motility disorders.

"Our model therefore can provide enormous theoretical insight into what could be the underlying causes behind these disorders," says Miura.

The implications are far-reaching. In the future, clinicians may be able to use a more advanced version of the model to identify multiple potential root causes for each patient. "By systemically changing the model parameters, we could identify numerous potential causes that could give rise to the patient's symptoms, whereas a doctor may only be able to suggest one or two," suggests Miura. "This expands the number of avenues to try in order to treat the disorder."

The model could also help guide drug discovery, by simulating the effects of drugs for different esophageal motility disorders before they reach clinical trials.

However, the current model still has some limitations for clinical use. For example, the model only examines how swallowing occurs when taking in liquid, rather than food. "Once you add in food, there are so many factors to consider, such as the food size, shape, texture and how it deforms the shape of the esophagus. This greatly increases the complexity of the model."

The model also only accounts for muscle contraction in one dimension, from the mouth to the gut. The team now plans to expand the model into two dimensions to capture even more complex patterns of esophageal motion, such as "jackhammer esophagus", where the esophagus twists and distorts in shape from the violent muscle contractions.

"This is just the first step toward building a theoretical framework for swallowing," said Miura. "With further development, it may help guide new treatments and ultimately improve quality of life for patients with dysphagia."

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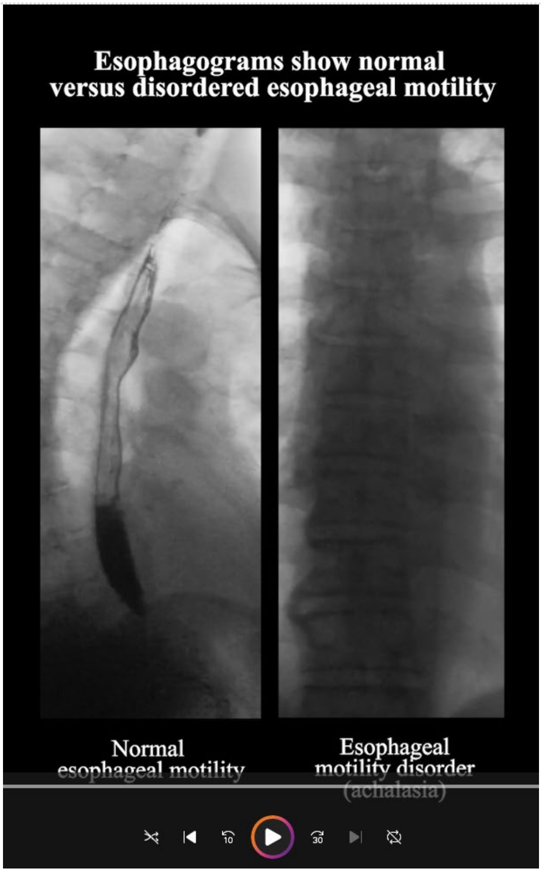
For more information about this research, see "A mathematical model of human oesophageal motility function" Takashi Miura, Hiroshi Ishii, Yoshitaka Hata, Hisako Takigawa-Imamura, Kei Sugihara, Shin-Ichiro Ei, Xiaopeng Bai, Eikichi Ihara and Yoshihiro Ogawa, *Royal Society Open Science,* https://doi.org/10.1098/rsos.250491

About Kyushu University
Founded in 1911, Kyushu University is one of Japan's leading research-oriented institutes of higher education, consistently ranking as one of the top ten Japanese universities in the Times Higher Education World University Rankings and the QS World Rankings. The university is one of the seven national universities in Japan, located in Fukuoka, on the island of Kyushu—the most southwestern of Japan's four main islands with a population and land size slightly larger than Belgium. Kyushu U's multiple campuses—home to around 19,000 students and 8000 faculty and staff—are located around Fukuoka City, a coastal metropolis that is frequently ranked among the world's most livable cities and historically known as Japan's gateway to Asia. Through its VISION 2030, Kyushu U will "drive social change with integrative knowledge." By fusing the spectrum of knowledge, from the humanities and arts to engineering and medical sciences, Kyushu U will strengthen its research in the key areas of decarbonization, medicine and health, and environment and food, to tackle society's most pressing issues.



Video. 1. Esophagograms showing normal esophageal motility and an esophageal motility disorder (achalasia). In healthy swallowing, liquid quickly passes from the mouth to the stomach. In individuals with esophageal motility disorders, this process is disrupted. Credit: Eikichi Ihara, Kyushu University

[Contact]
Takashi Miura, Professor
Faculty of Medical Sciences, Department of Anatomy and Cell Biology
Tel: +81-92-642-6048
E-mail: miura.takashi.869@m.kyushu-u.ac.jp