News Release

Title

Dialysis membrane-enforced microelectrode array measurement of diverse gut electrical activity

Key Points

○ The gut is an extremely long tube in the body, and features of motility differ greatly among sections, reflecting their functions. Therefore, investigations into mechanisms underlying gut motility require a technique that can handle high diversity and complexity of spatio-temporal electrical activities.

○ We thus developed a dialysis membrane-enforced microelectrode array technique that enables detection of a variety of electrical activities in micro-regions of the gut in a wide range of frequencies.

○ We show several representative observations and analyses, such as the propagation of neuro-transmission-evoked tonic potentials, and a cooperating multitude of colonic electric oscillators referred to as a myoelectric complex.

Summary

Assoc. Prof. Shinsuke Nakayama and research associates (Ms Naoko Iwata, and Chiho Takai) at the Department of Cell Physiology, Nagoya University Graduate School of Medicine (Dean: Kenji kadomatsu) developed a dialysis-membrane-enforced microelectrode array (MEA) technique for highly spatio-temporal analysis of biological electric activity through the collaborative research work including student research projects.

The gut is an extremely long tube in the body that is divided into several sections, including the stomach, duodenum, ileum, and colon. Motility features differ greatly, even between subsections of each section and also change depending on their functional state. Furthermore, multiple control systems of excitable cellular organizations overlap throughout the gastrointestinal (GI) tract, cooperating properly to yield smooth and elaborate movements. Therefore, investigations into the underlying mechanisms require a technique that can handle the high diversity and complexity of electrical activities in the gut for appropriate measurements and analyses.

In this study, we thus developed a dialysis-membrane-enforced MEA technique. Sheets of muscle piled below a dialysis membrane were fixed between the strings of the anchor, and mounted on MEA. Small molecules such as gas, ions and metabolites were able to be exchanged through the membrane, maintaining a physiological environment and allowing for continuous spontaneous electrical activity. Additionally, the use of dialysis membranes improved electric separation between sensing electrodes to support measurements of regional electrical activity independently. In various sections of the gut, we recorded characteristic spontaneous electric activity, and performed spatio-temporal

analysis and potential mapping for visual demonstration. Especially, in the colon, the dialysis membrane-enforced MEA enabled the assessment of the spatial distribution of the myoelectric complex (slow oscillations preceded by rapid oscillations; transient spike activity). Furthermore, propagation of excitatory neuro-transmission-evoked tonic potentials was observed in the ileum.

As presented in the example measurements and analyses, we introduce a useful technique to investigate a variety of electrical cooperation and coordination underlying functional movements of the gut. We hope that this technique can also be applied to studies of genetic modifications and pharmaceutical examinations.

This study was published in a scientific journal "Biosensors and Bioelectronics" (online).

Research Background

The gut is an extremely long tube in the body that is divided into several sections, including the stomach, duodenum, ileum, and colon. Motility features differ greatly even between the subsections of each section, and these can also change depending on their functional state. Furthermore, multiple control systems of excitable cellular organizations overlap throughout the gastrointestinal (GI) tract, cooperating properly to yield smooth and elaborate movements. Therefore, investigations into the mechanisms underlying gut motility thus require a technique that can appropriately measure and analyze electrical activities spatio-temporally, despite high diversity and complexity.

Research Results

In this study, we thus developed a dialysis-membrane-enforced MEA technique, that enabled us to measure characteristic features of spatio-temporal electrical activity in various sections of the gut.

Sheets of muscle piled below a dialysis membrane were fixed between the strings of the anchor, and mounted on MEA. Small molecules such as gas, ions and metabolites were able to be exchanged through the membrane, maintaining a physiological environment for continuous spontaneous electrical activity (Figure 1). Thus, the use of dialysis membranes enabled us to perform MEA recordings over a long period. In addition, the use of dialysis membranes improved the electric separation between sensing electrodes to support measurements of regional electrical activity independently.

In the stomach, ileum and colon, we recorded characteristic spontaneous electric activity, and performed spatio-temporal analysis and potential mapping for visual demonstration. 1) Especially, in the colon, the dialysis-membrane-enforced MEA enabled to assess the spatial distribution of the myoelectric complex (slow oscillations preceded by rapid oscillations; transient spike activity) (Figure 3). 2) Furthermore, the propagation of neuro-transmission-evoked tonic potentials was observed in the ileum (Figure 2).

This study was published in a scientific journal "Biosensors and Bioelectronics" (online).

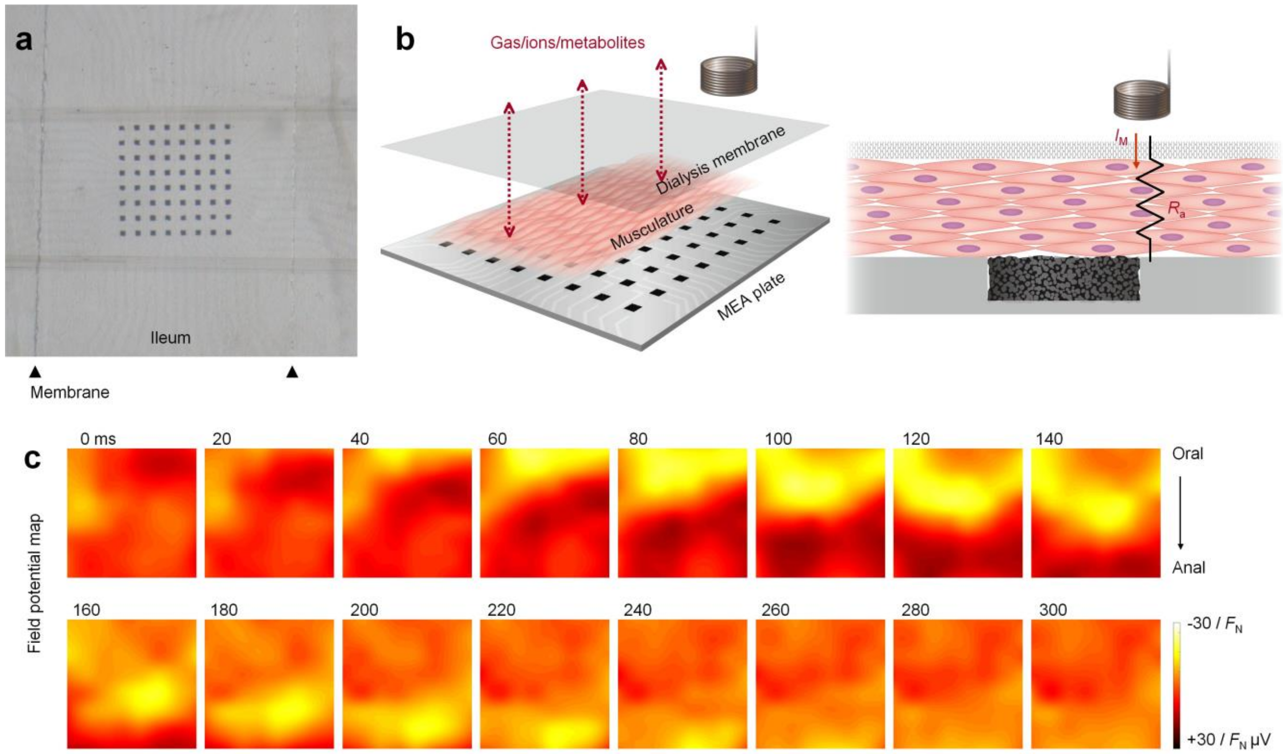

Figure 1. Dialysis membrane-enforced microelectrode array recording of muscle sheets isolated from the ileum of mice. (a,b) Muscle sheets were mounted between a piece of dialysis membrane and MEA plate. (c) Filed potential mapping show propagating pacemaker activity from the oral to anal direction. I_M: cell membrane current. R_a: Access resistance.

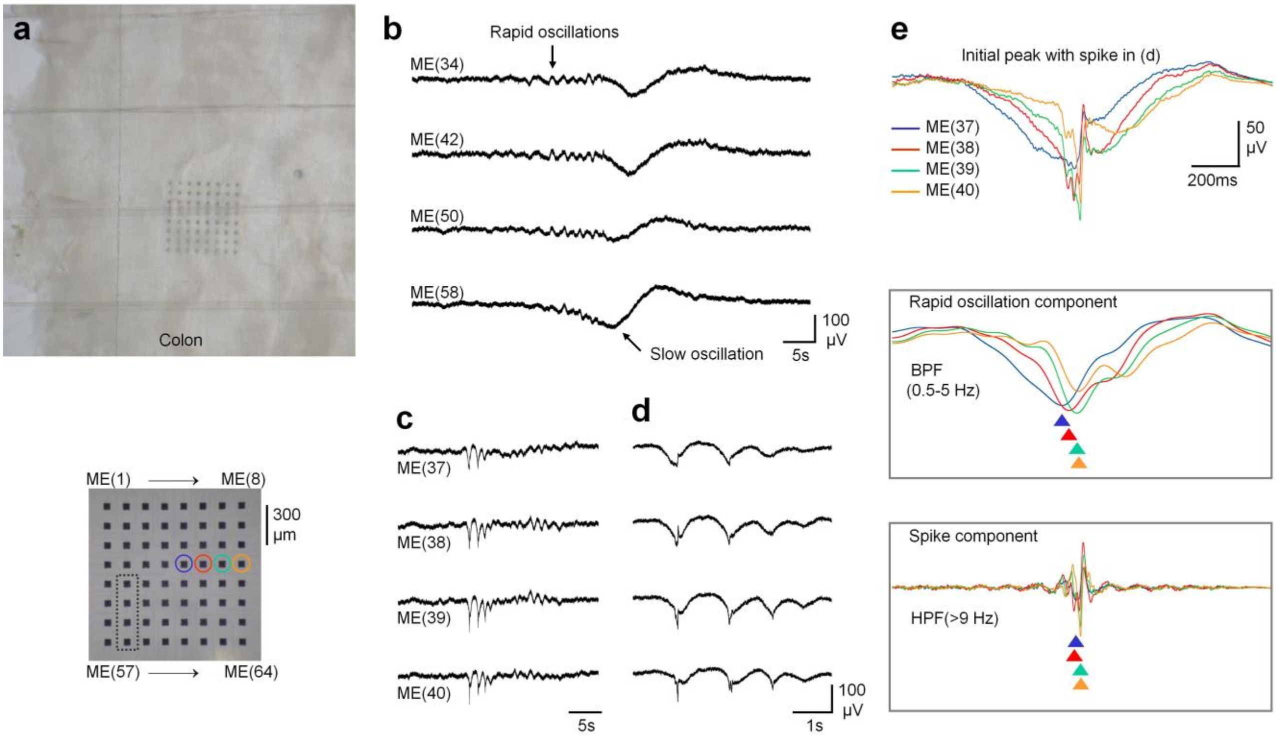

Figure 2. An example of measurement of myoelectric complex in the colon. (a) Photograph of colonic muscle sample on MEA. (b) Slow oscillating potentials preceded by rapid oscillating potentials with small amplitude. (c,d) Trains of rapid oscillating potentials observed in different regions. (e) The initial rapid oscillating potentials in (d) overlapping with a spike-like fast potential in the four horizontal MEs are superimposed (upper panel). Separation of rapid oscillation (middle) and spike component (lower). BPF: band pass filter. HPF: high-pass filter.

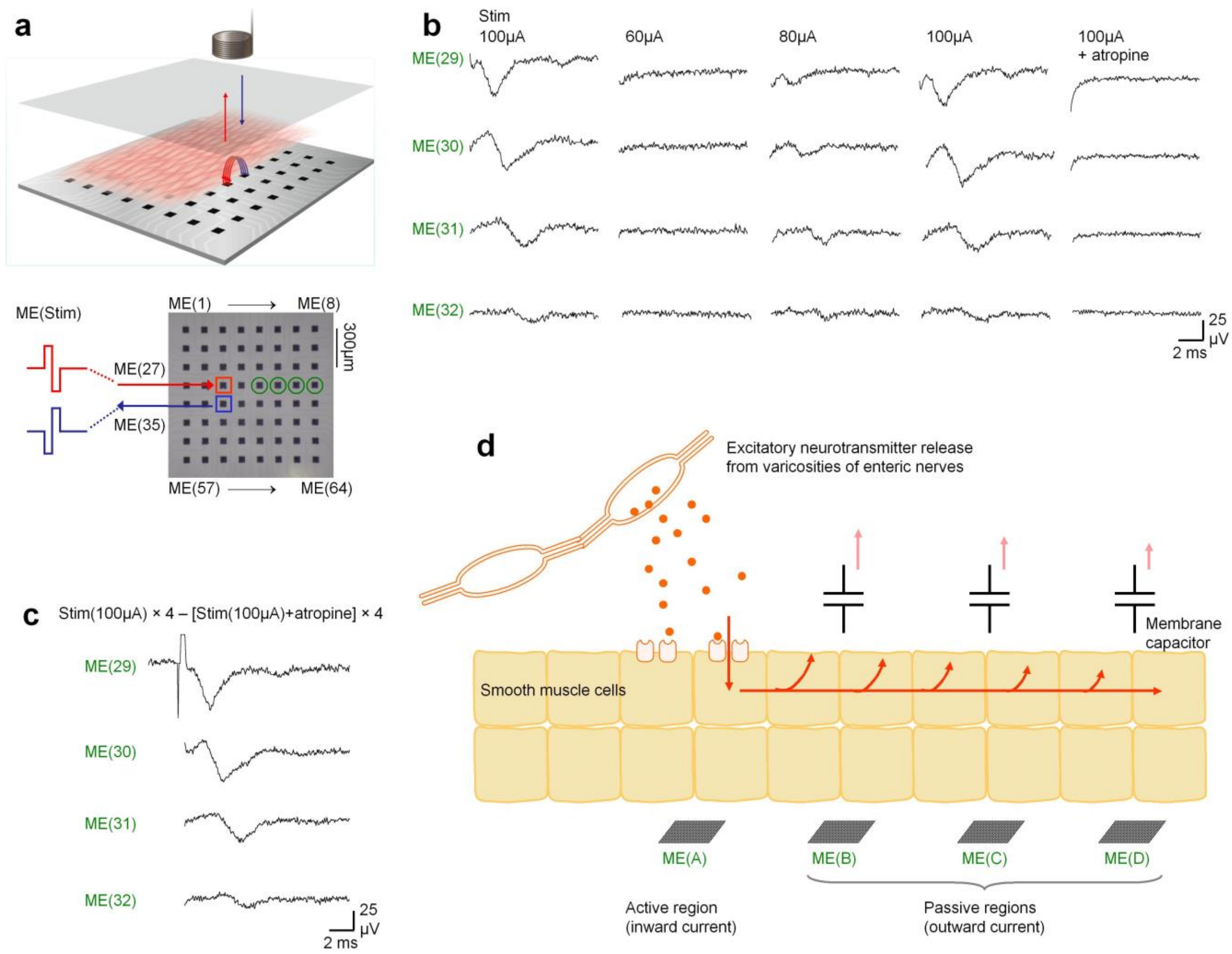

Figure 3. Propagation of electric stimulus-evoked potentials. (a) Sample preparation and stimulus procedure. Electric current was applied in ME(27, 35), and field potentials were measured in other MEs. (b) Evoked potentials measured at ME(29-32). (c) Average of four field potentials evoked by ±100 μA. Simulating current surge was compensated by subtracting the evoked potentials in the presence of atropine. (d) Schematic representation of electro-tonic potential propagation upon neuro-muscular junction transmission. Excitatory neurotransmitter-induced inward current in smooth muscle cells near ME(A) intercellularly propagates, charging the membrane capacitor in adjacent cells. MEs(B-D) thus detect outward current.

Research Summary and Future Perspective

Dialysis membrane-enforced MEA enabled stable measurements of spatio-temporal electrical activities over a wide frequency range: from the propagation of excitatory junction potentials and spike potentials to slowly oscillating pacemaker potentials in the gut.

Coordinated movements are required in functional motility of the gut, such as propelling and mixing food. Recently, it has become clearer that gut motility makes a significant contribution to human health through the brain-gut interaction, symbiosis of microbiota, immunity, etc. On the other hand, the inclusions of numerous types of food, drugs and genetic modifications are likely to affect coordinated movements of the gut. For example, in irritable bowel syndrome (IBS), a prevailing functional disease, these factors overlap impairing gut motility. In future studies, the present technique could be useful for functional characterization of various excitable tissues in health and disease.

Publication

Naoko Iwata, Takumi Fujimura, Chiho Takai, Kei Odani, Shin Kawano, Shinsuke Nakayama (2017). Dialysis membrane-enforced microelectrode array measurement of diverse gut electrical activity. *Biosensors and Bioelectronics* 94, 312-320.

DOI：http://doi.org/10.1016/j.bios.2017.03.002

Japanese ver.

https://www.med.nagoya-u.ac.jp/medical_J/research/pdf/Biosensors and Bioelectronics_20170530.pdf