# Research Outline of Research Areas

**Mechanical self-transformation of living systems**
http://multicellular-mechanics.org

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| Number of Research Area | : | 22A302 | Term of Project : | FY2022-2026 / FY2020-2024 |
| Head Investigator | : | MOTEGI Fumio | | |
| Research Institution | : | Institute for Genetic Medicine, Hokkaido University | | |

## 1. Details of Research Area

Elucidating the design principles of multicellular organisms is a fundamental challenge for researchers in the field of life science. Global order of an organism generally develops from local interactions among molecules and cells. Collectively, these interactions—referred to as *self-organization*—give rise to the emergent properties of fate, form, and function of cells, ultimately leading to morphogenesis of tissues and organs. Mechanical forces that cause changes in size, shape, and position of cells are integral to morphogenesis, and recent studies have highlighted the potential for mechanical forces to modulate cellular fate and function, suggesting the existence of a complex feedback between forces and cellular physiology.

This Research Area aims to develop new paradigms of morphogenesis through quantitative and holistic evaluation of how mechanical forces control emergent properties of self-organizing feedback in developing organisms. We will develop cutting-edge technologies to investigate mechanical processes and determine the magnitude and distribution of forces within cells and extracellular spaces. With this insight, we will understand how these forces elicit self-organizing feedback leading to progressive self-tuning transformation of multicellular systems over longer timescales.

Our Planned Research is composed of three Research Groups: A01 and A02 will elucidate mechanical self-organization in a diverse array of multicellular systems, while B01 will develop novel techniques in the measurement and analysis of mechanics, as well as theoretical methods to model and numerically simulate self-organization. Through close and organic collaborations within this multi-disciplinary group, we expect to reveal novel insights into mechanical self-organization and achieve a paradigm shift in the understanding of biological design principles.

## 2. Call for Proposals and Expectations for Publicly Offered Research, etc.

We are calling for Publicly Offered Research that will conduct quantitative measurement and analysis of mechanical forces by incorporating and inventing new methods from physics and chemistry. In addition, we expect Publicly Offered Research to investigate the physiological functions of mechanics by manipulating forces within cells and tissues while employing theoretical analyses. We also seek Publicly Offered Research that will investigate a wide range of mechanical self-organization events. The projects will be expected to not only complement and strengthen the Planned Research, but also to take up the challenge of establishing unique systems and innovative techniques to further accelerate the overall research aims.

We expect the A03 Research Group to be aimed at investigating self-organization of unique biological systems including, but not limited to, "*ex vivo* analysis of tissue morphogenesis," "formation of organoids derived from differentiated stem cells," and "reconstituted systems by restructuring cellular interactions." These projects will improve our understanding of extracellular mechanics and reveal how multicellular systems sense and respond to external forces. In addition, we encourage challenging proposals involving, for example, the use of "unconventional model animals and plants" and investigating "nonbiological forces" (e.g., gravity, atmospheric or water pressure, and geomagnetism). A proposal targeting disease and aging would also be considered if it fits the overall objectives.

The B02 Research Group should aim at developing innovative techniques for the quantitative measurement, manipulation, and evaluation of various types of forces in multicellular systems. Particularly, proposals on the development of force biosensors and force-measuring technologies that can be applied to cell surfaces, nuclear membranes, and the lumenal surfaces of embryos or tubular organs are highly welcomed. We encourage the development of new technologies for the manipulation of in vivo forces such as optogenetics, material engineering, and MEMS technology. B02 also welcomes "dry" research proposals focused on theoretical investigation and mathematical modeling of mechanical self-organization.

## 3. Research Group, Upper Limit of Annual Budget and Number of research projects scheduled to be selected

| Research Group Number | Research Group | Upper Limit of Annual Budget (Million yen) | Number of research projects scheduled to be selected |
|---|---|---|---|
| A03 | Research on mechanically self-organizing multi-cellular systems | 5.00 (wet)<br>3.00 (dry) | 12<br>5 |
| B02 | Development of techniques for measurement, manipulation, and theoretical analysis of mechanical self-organization | | |

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