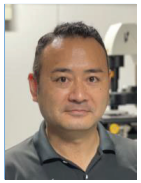
【Grant-in-Aid for Transformative Research Areas（B）】

Creation of multi-scale 4D biology（Ma-ru-tto Biology）



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Research Area Information	Number of Research Area : 23B303　Project Period (FY) : 2023-2025 Keywords : Multi-scale, 4D imaging, aging, biophotonics

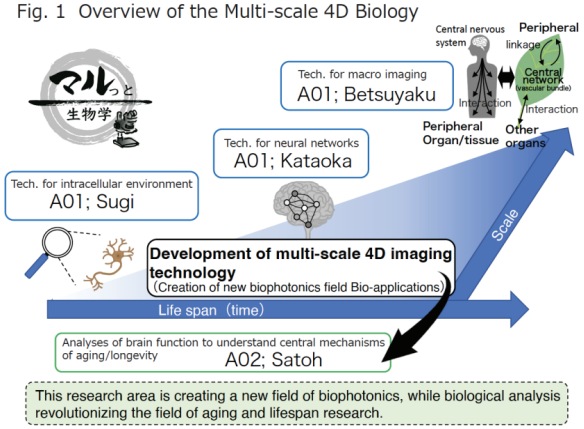
Purpose and Background of the Research

●Outline of the Research

Clarification of brain-centered mechanisms of aging/longevity and the initial timing of declines in biological function with age is expected to revolutionize the field of aging research. However, analyses within only "local time" and "local tissues" over the life course provide minimal information from the whole body. In this study, we will develop a novel multi-scale 4D imaging technique, allowing us to analyze the process of functional declines at multiple levels (molecular, cellular, neural network, and individual whole body) over the life course, entirely (Fig. 1). This novel technique will provide a great insight into comprehensive mechanisms by which the brain controls aging and longevity in mammals.

Our research, which totally differs from conventional bioimaging, will open new avenues for biophotonics. Multi-scale 4D biology is a highly unique research area that will revolutionize the field of aging and lifespan through biological analysis using mice, nematodes, and plants.

Fig. 1 Overview of the Multi-scale 4D Biology

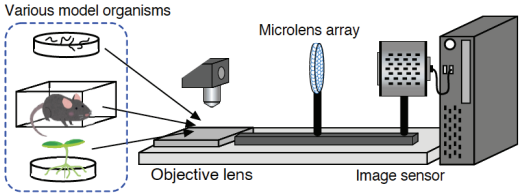


●Background of the Research

With the development of molecular biology and genetic techniques since the 1990s, mechanisms of functional declines in each organ or tissue with age has been further understood not only in lower eukaryotes, but also in mammals.

In this research area, several age-related phenomena will be analyzed in living organisms from various angles using the novel multi-scale 4D imaging technique. Furthermore, to utilize this technique is best suited approach for long-term events such as aging. Therefore, further progression of this research area will have a significant impact in the field of aging research.

Fig. 2 Development of a novel multi-scale 4D imaging technique



Development of 'multi-scale 4D imaging technology' for real-time measurement of 3D dynamics of living organisms in a single shot at multiple scales

●Purpose of the Research

We will develop and utilize the novel multi-scale 4D imaging technique using light-field (LF) microscopy, which enables to obtain nano-resolution image of 3D space with single camera shot.

High-resolution LF microscope captures images of samples through multiple micro-lens arrays (a series of small round lenses). The single camera shot can obtain 3D depth information. No spatial scanning is needed.

In this research area, the LF microscope will be combined with originally developed techniques of visualization and qualified/quantified measurements at multiple levels (e.g. molecular, cellular, neural network, and individual whole body). This combination will lead to newly develop the multi-scale 4D imaging technique (Fig. 2).

Useful utilization of this technique will be demonstrated by elucidating aging mechanisms.

Expected Research Achievements

In this research area, research group **A01** will develop the multi-scale 4D imaging technique at multiple levels, and research group **A02** will assess brain function by the newly developed multi-scale 4D imaging technique and physiological analyses.

📌Research group **A01**: Development of the multi-scale 4D imaging technique in a variety of model organisms as follows:

Sugi Group: Single shot of intracellular environment in worms
Kataoka Group: Visualization of neural networks in the brain of mice
Betsuyaku Group: Macro imaging of immunoreaction in the whole-body of plants

📌Research group **A02**: Analyses of brain function to understand central mechanisms of aging/longevity

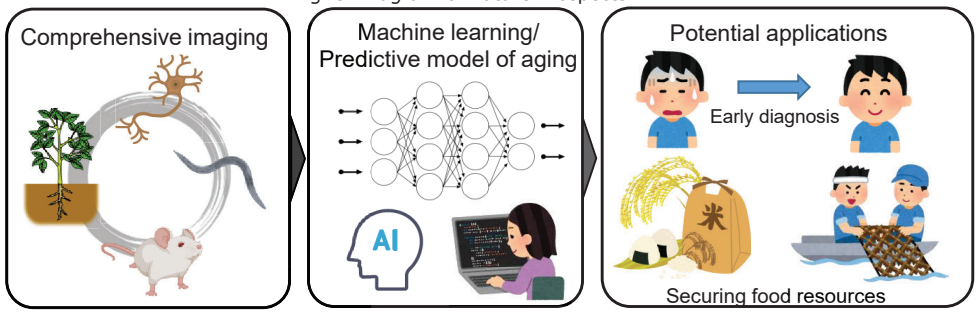
Satoh Group: Elucidation of the role of hypothalamic neurons in the central mechanisms of aging/longevity by assessing its function at the molecular, cellular, and organismal levels using the multi-scale 4D imaging technique.

● Expected results･development and impact connected to social life

Machine learning will be performed based on images obtained from various model organisms. As a result, predictive models of aging itself and/or the initial timing of functional declines can be constructed. This model will be utilized for several applications such as (i) extension of healthy lifespan, (ii) early diagnosis of diseases, and (iii) securing food resources from Earth (Figure 3).

In addition, long-term observation of the same individual subjects will contribute to the principles related to animal welfare and the 3Rs perspective.

Fig. 3 Diagram of Future Prospects



Homepage Address, etc.	Currently under preparation