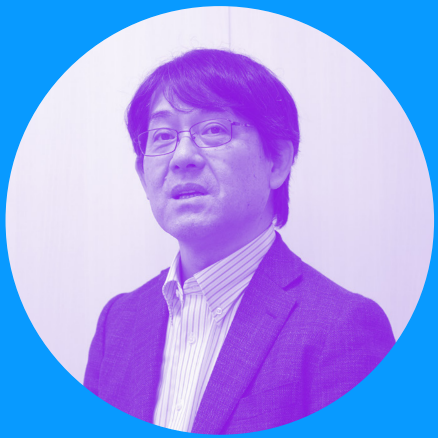

## Message to Young Readers

While the drive to conduct research that benefits others is crucial, I believe that delving into what you find mysterious or intriguing will ultimately lead to more fundamental discoveries. I encourage young people to prioritize the pursuit of interesting endeavors. Curiosity, in my opinion, is the driving force behind all meaningful discoveries.

For example, if you have a close relative suffering from a disease, it is natural to be inclined to research a cure for that specific disease. However, I believe it's more beneficial to conduct research that delves deeper into the essence of the disease. This is especially true for high school students, who should strive to have a broad perspective on things. In addition, mastering basic academic skills is crucial, so I encourage you to study diligently. In particular, proficiency in math and English will serve you well throughout your research endeavors.

I urge you to pursue intriguing endeavors. Curiosity is the driving force behind significant discoveries.

> I encourage you to prioritize exploring things that you find interesting or mysterious. This curiosity is the driving force behind fundamental discoveries.

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### What is Bio2Q?

Bio2Q is a world-class research center at Keio University. It aims to use quantum computing and AI to analyze the interaction between Human Biology and Microbiome, revealing uncharted territories of the human body and developing new treatments for intractable diseases.

It is the first private university to be selected for the World Premier International Research Center Initiative (WPI) program promoted by the Ministry of Education, Culture, Sports, Science and Technology (MEXT).


**Bio2Q**

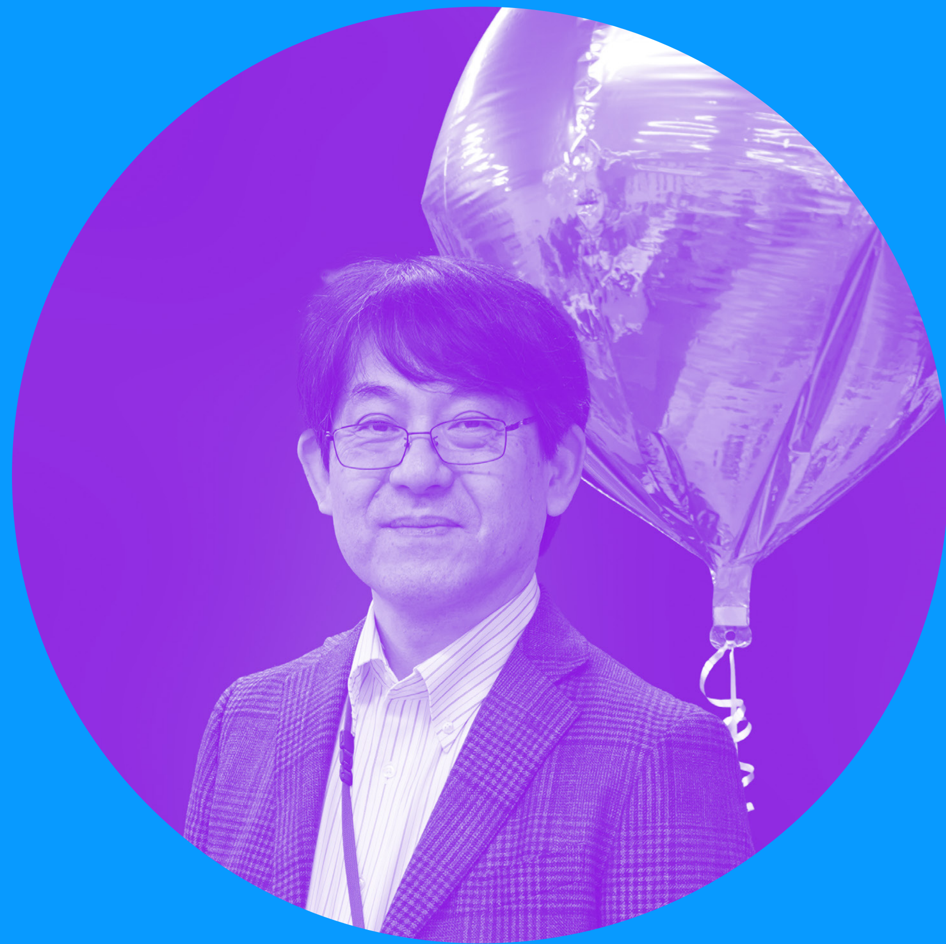
Keio University Shinanomachi Campus
35 Shinanomachi, Shinjuku-ku, Tokyo
160-8582, Japan

Email: sc-wpi-staff@adst.keio.ac.jp
Web: www.bio2q.keio.ac.jp
Tel: 03-6709-8106 (Weekdays 8:30 AM - 5:00 PM)



WPI Research Center
Keio University
Bio2Q Human Biology Microbiome Quantum Research Center


Keio University Human Biology-Microbiome-Quantum Research Center (Bio2Q)



Bio2Q Researchers

# Professor Michisuke Yuzaki

Special Advisor to Director of Bio2Q / Neuroregulation Team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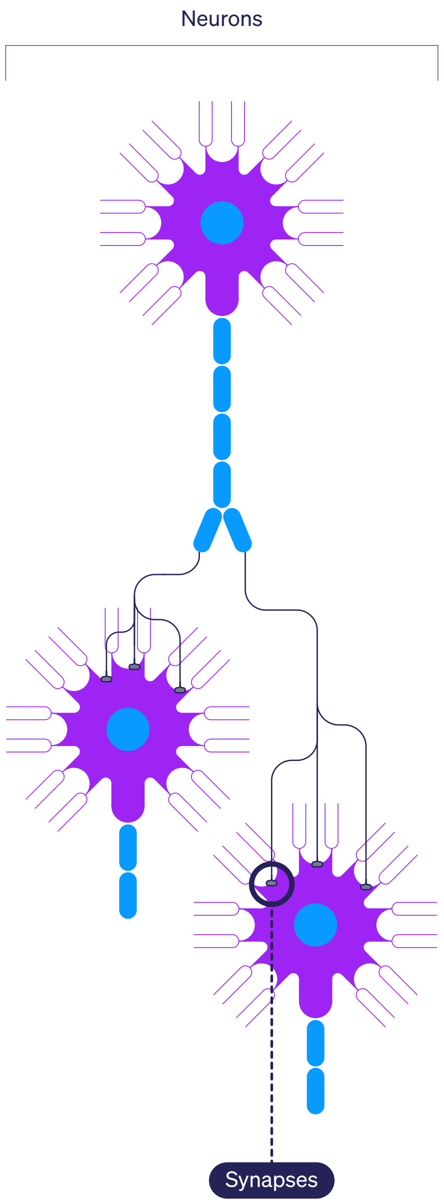



Neurons extend their processes like arms and legs to connect with other neurons. The points where they connect are called synapses.

### Please tell us about your research.

My aim is to understand brain processes related to thoughts and memories—particularly focusing on why memory deteriorates in conditions like dementia, the cause of auditory hallucinations, and attention deficits in certain mental disorders—from the perspective of brain function.

Conditions often viewed as purely physical, such as stomach ulcers and immune disorders, are linked to mental health. This insight during high school spurred my pursuit of a medical career, recognizing the importance of the mental aspects in physical illnesses. In university, I delved into psychosomatic medicine and psychiatry but soon realized my understanding of the brain was superficial. This led me to basic neuroscience, aiming to grasp brain mechanisms from the ground up.

The heart and liver function through the assembly of their respective cells, but brain cells, or neurons, require a network of connections, or synapses, to process information, think, and remember. Understanding synapse formation, modification, and elimination at the molecular level is crucial. This knowledge will help us understand neuropsychiatric and developmental disorders' pathophysiology and develop new treatment strategies for synaptic impairments.

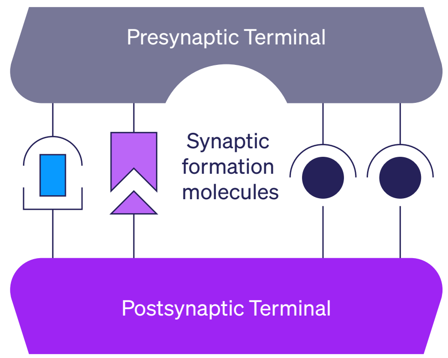
> If we want to understand how the brain functions, it is crucial to comprehend the workings of synapses.”

### What is the difference between a brain and a computer?

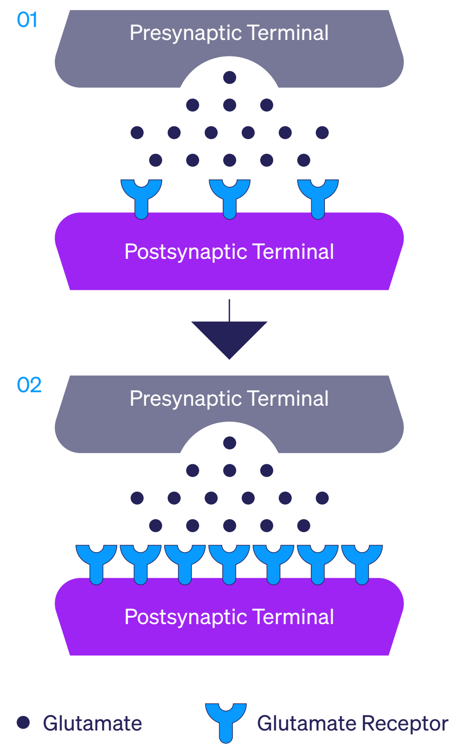
Unlike a computer whose wiring is fixed once manufactured, the brain's synaptic connections evolve with neural activity. With humans having around 20,000 genes but nearly 1,000 trillion synapses, it's clear that genes alone don't dictate the complex organization of neuronal networks. Instead, neural circuits are refined through pruning and tuning synapses in response to learning.

Our research addresses two key memory mechanisms in the brain. First, we examine how the wiring of neural circuits adapts to changes in neural activity. We've discovered that the complement family* of molecules, typically associated with immunity, is a key regulator of synapse formation and removal in the brain.

Second, we study how memory is stored at existing synapses without changing the wiring. For example, studying all night for an exam doesn't mean that new synapses will be formed by the next day. Rather, existing synapses strengthen and become more efficient at transmitting information, which is a form of memory. This process is faster and requires fewer resources than rewiring.




Between neurons, there are molecules that act like adhesives. These molecules, known as synaptic formation molecules, play a crucial role. Understanding the functions of these synaptic formation molecules may enable the recovery of lost synapses in conditions such as psychiatric disorders and developmental disabilities, potentially leading to effective treatments.




When short-to-medium-term memories are formed (Fig. 02), the number of glutamate receptors at the synaptic terminals increases. As a result, even if the same amount of glutamate is released from the presynaptic terminal, the response at the postsynaptic terminal becomes more significant.

### How are memories stored at existing synapses without rewiring?

In both computers and neural circuits, information is transmitted via electrical signals. However, in the brain, these signals are halted at synapses. A presynaptic neuron releases glutamate upon sending an electrical signa. This glutamate binds to receptors on the postsynaptic neuron, resuming the signal. Therefore, boosting the number of glutamate receptors on the postsynaptic neuron enhances information transmission, even if glutamate release is constant. On the other hand, decreasing these receptors lowers transmission efficiency. This modification in postsynaptic glutamate receptors, either increasing or decreasing, is key to forming memories and can last from several hours to several days. In the **hippocampus, for example, the number of glutamate receptors at a single synapse can double from 100 to 200 during learning.

Memory formation is not just a result of studying for an examination. Activities like exercise or musical practice can embed memories in the cerebellum, while persistent pain or drug addiction form distinct memory types. Our research aims to determine whether different memories, stored in various regions of the brain, stem from new synapse formation or from alterations in the efficiency of pre-existing synapses.

### Are there any collaborative projects with other labs at Bio2Q?

Yes, we're collaborating with Dr. Kenya Honda's lab on the study of gut bacteria and their metabolites. We know that gut bacteria produce metabolites that affect brain function, but how changes in these metabolites are detected and communicated to the brain is still unclear. Our goal is to identify the neural circuits involved in the brain-gut axis. Understanding the molecules that drive synapse formation in these circuits could enable us to alter the brain's connections from the gut, offering new avenues for disease treatment.

My interest has always been in the interplay between mind and body, a fascination that began in high school. By unraveling how the gut and its bacteria influence synapses, I aim to further explore this relationship.

*Complement family: Complement is a protein that plays a role in the innate immune system, serving as the first step in the recognition and elimination of foreign bodies. The group of proteins that share a motif with complement is called the complement family.

**Hippocampus: A region of the brain responsible for storing and organizing new episodic memories.