# Modeling of Hippocampal Memory Functions and Taste Cell Sensory Reception to Pave the Way for Novel Neuro-Devices

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***Abstract*-- The goal of our COE program is to develop electronic neuro-devices that lead to realize dedicated VLSI chips. One of the fields in the COE program is the "Neurophysiology and Electrochemistry." The aims of the field are to develop a physiology-base hippocampal model that performs sequence learning and prediction of memory sequences and to develop a taste cell network model that detects chemical signals with high sensitivity. We will also talk about how we collaborate with other fields toward the goal of our COE program.**

## I. Introduction

Recent advancements of brain science and modeling of natural neural systems have brought us the possibility of designing novel electronic neuro-devices that perform brain functions. The Department of Brain Science and Engineering in the Graduate School of Life Science and Systems Engineering of Kyushu Institute of Technology was founded in 2000 to open up a new field "Brain-Inspired Information Technology" and took off to pave the way for a new paradigm of information technology.

Our program "The World of Brain Computing Interwoven out of Animals and Robots" headed by Takeshi Yamakawa was selected in 2003 as a 21st Century Center of Excellence Program of the Ministry of Education, Culture, Sports, Science and Technology, Japan. Since the aim of this COE program coincides exactly with the aim of our department, the establishment of the foundations of Brain-Inspired Information Technology is now being boosted by the COE program.

The aim of our COE program is to develop electronic neuro-devices that lead to realize dedicated VLSI chips including memory devices, sensory devices, information integration devices, motor control devices and so on. The Brain-Inspired Information Technology covers a wide range of the information technology based on the information processing systems containing neuro-devices. Therefore, neuro-devices that perform brain functions are technical foundations of the Brain-Inspired Information Technology.

Our COE program consists of five fields: Neurophysiology and Electrochemistry, Psychology and Human Operation, Mathematics and Linguistics, Brain-Like Integrated Circuits, and Robotics. The role of the field "Neurophysiology and Electrochemistry" is to develop models based on the physiological knowledge of memory and sensory reception mechanisms of the central nervous system and to explore the way for the electronic devices with the physiology-base models.

Specifically, major goals are to develop a hippocampal model that performs sequence learning and prediction of memory sequences and to develop a taste cell network model that detects chemical signals with high sensitivity. In this paper, we will focus on these two topics and talk about what our research is heading and how we collaborate with other fields toward the goal of our COE program.

## II. Brain-Inspired Memory Model

The most important function that is inherent in the whole brain and forms the basis of higher brain functions is learning and memory. The brain learns environment by changing connection weight between neurons depending on the sensory information and memorizes the results by maintaining patterns of connection weight for a long time.

Memory systems in the brain not only store single events but also connect stored memories by further learning. Memory systems are furthermore connected directly with excellent brain functions such as motor control, spatial recognition, information integration, decision making, and so on. These features are quite different from those of current memory devices used in computers. In other words, learning, memory, and functional execution progress simultaneously on the same networks in the brain. This indicates that the information processing in the brain is a novel paradigm of the information technology.

The hippocampus is one of the most important sites in the brain that governs memory functions. A distinctive function of the hippocampus is to learn a sequence of places so that animals can recognize the places where they are.

Hayashi and his collaborators found neuro-chaos using molluscan single neurons in 1982 [1] and provided evidence for chaotic field responses of the rat hippocampus and primary somatosensory cortex in 1995 and 1996 [2,3]. After that, they developed a hippocampal CA3 network model based on physiological knowledge and unveiled the mechanisms that the CA3 network caused chaotic responses to a periodic stimulation in spite of an assembly of a large number of neurons [4].

Hayashi et al also found that the stochastic resonance took place in the hippocampal CA1 network with the aid of projection of irregular activity of the CA3 network through Schaffer collaterals and subthreshold signal through the perforant path fibers [5]. They therefore proposed a memory recall model due to stochastic resonance; a memory pattern embedded in connection weight of Schaffer collateral synapses in CA1 can be recalled by the stochastic resonance.

The hippocampal CA3 contains recurrent synapses that are subject to spike-timing dependent plasticity (STDP) [6, 7]. When firing of the presynaptic neuron precedes firing of the postsynaptic neuron, the synaptic connection is potentiated little by little by STDP function. When the neurons fire in reverse order, the synaptic connection is depressed little by little. Yoshida and Hayashi have demonstrated that radial propagation of neuronal activity is organized in CA3 with recurrent synapses that are subject to STDP algorithm when theta burst stimulation is fed to a local site in CA3, as shown in Fig. 1 [8]. Since this radial propagation is maintained in CA3 for a while after quit of the stimulation, this dynamical pattern is a short-term memory while maintaining spontaneous spatiotemporal activity.

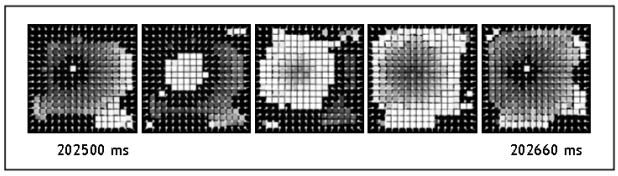


Fig. 1 Radial propagation of neuronal activity in CA3 after quit of 8 Hz stimulation. Radial propagation continues repeatedly like a ripple spreading on the surface of water. White squares indicate excited pyramidal cells. Intervals between panels are 40 ms.

Furthermore, Yoshida and Hayashi have demonstrated that a cluster of neurons learning a temporal sequence can be produced in CA1 using the radial propagation of neuronal activity in CA3 as illustrated in Fig. 2 [9]. Theta burst signals are successively fed to different sites in CA3 and CA1 respectively. The CA3 network repeats radial propagation of neuronal activity from the stimulus sites, like ripples spreading on the surface of water. Since the radius of the ripples depends on the time when signals are fed, the distribution of ripples reflects the sequence of signals. Firing of neurons on the ripples with different radii therefore links signals that are successively fed to different sites in CA3. In other words, delay by the radial propagation makes the neuronal activity possible to coincide temporally with responses to following signals. Since CA3 pyramidal cells on the ripples fire at almost the same time, Schaffer collateral synapses that connect the firing CA3 pyramidal cells to their common CA1 pyramidal cells are finally potentiated. This cluster of CA1 neurons is maintained for a long time. This would be an important mechanism for sequence learning.

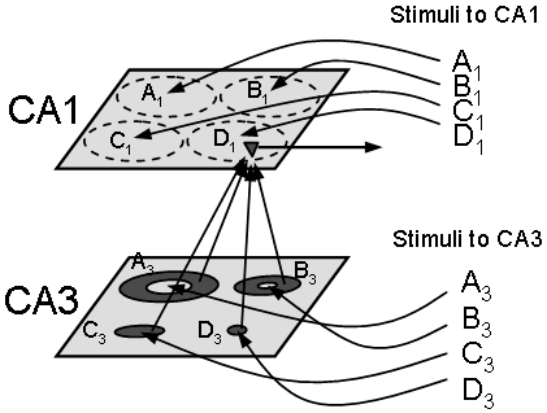


Fig. 2 Coding of a temporal sequence. Four burst signals (A3-D3 and A1-D1) were fed successively to four regions of CA3 and CA1. A cluster of neurons that learned temporal order of signals was produced in CA1.

It is true that it is possible to take a step toward neuro-devices because of great advancement of brain science. In fact, the research results mentioned above have formed basis of neuro-devices that perform sequence learning and process sensory information based on the consequent memory. However, there are still several unsolved issues on learning mechanisms of the hippocampus: for example, physiological mechanisms of phase/rate coding of place information in a theta cycle, phase advancement of place cell firing when animals traverse the place field, and so on. New ideas based on new physiological knowledge are necessary to develop good physiology-base models that can learn sequential information.

Ishizuka, a member of our COE program, has studied physiological features of the hippocampus for many years and has published papers on input-output relations of hippocampal neurons, plastic changes in synapses, mechanisms of rhythm generation, and so on [10,11]. Natsume who is also a member of COE program study hippocampal theta rhythm and is particularly interested in relations between synaptic long-term potentiation (LTP) and the theta rhythm [12]. Their parts in the COE program are to get new physiological knowledge useful for developing a physiology-base hippocampal memory model.

On the other hand, it is far less easy to fabricate the brain-inspired integrated circuits using only digital circuit

techniques. If we try to do so, analog features of information processing in the brain would be spoiled, and complex digital circuits with many transistors would be required sometimes. Techniques of merged analog-digital circuits are then required and collaboration with a research group in other fields is necessary.

Morie, a member of COE program, in the field "Brain-Like Integrated Circuits" have studied analog-digital architecture and has designed a resistor fuse network for global image segmentation, an oscillator network for image extraction, Gabor-type wavelet transformation for image processing, dynamic-link architecture for flexible image matching [13-15]. These have been implemented as VLSIs. Physiology-base hippocampal memory models would be transformed into electronic neuro-devices by extended researches on merged analog-digital integrated circuits.

Miki in the filed "Brain-Like Integrated Circuits" has studied soft integrated circuits that have functional and structural adaptabilities to environment change. It has been demonstrated that these circuits can be used for feature extraction and knowledge acquisition from sequential data [16]. These circuit techniques would be useful to fabricate hippocampal memory devices that perform sequence learning. The hippocampal memory devices must also be adaptable to environment change.

The aim of the present research program is to develop a hippocampal memory model that performs sequence learning, prediction of memory sequences, and functional execution simultaneously and to make a step toward electronic neuro-devices. These neuro-devices that mimic hippocampal functions are indispensable to a new field "Brain-Inspired Information Technology."

## III. Brain-Inspired Sensor Model

Taste buds are the taste sensors of vertebrates. In mammals, taste buds exist on tongues, soft palates, pharynx, and epiglottis. They contain four types of taste bud cells (TBCs): type I to type IV cells. Type I to type III cells are elongated cells and their apical portions receive taste stimuli fed through taste pores. Type I and type II cells are referred to as the dark cell and the light cell, respectively, because of the difference between their electron densities. Electron density of the type III cell is similar to that of the type II cell. The type IV cell is the basal cell that is the precursor of other types of TBCs.

In the frontal two-thirds of mouse tongues, taste buds consist of ~50 TBCs. Among these TBCs, only type III cells have synaptic contacts with taste nerves and can transmit taste information to the brain. However, it remains to be investigated if the type III cells express receptor sites for taste substances. Interestingly, type II cells that have no synaptic contacts with taste nerves express receptor sites. These recent understandings suggest that type II cells sense taste substances and transfer taste information to type III cells, and then the type III cells transmit the taste information to the brain. Thus, type III cells may integrate taste information obtained from several type II cells before the type III cells transmit the information to the brain. In other words, taste buds might work as a micro-brain.

Yoshii and his colleagues tested the interactions between type II and type III cells using in-situ whole-cell patch clamp and optical recording techniques (Fig. 3) [17]. Patch clamp studies have showed that some of the TBCs generate depolarizing or hyperpolarizing receptor potentials in response to taste substances. Optical recordings using a voltage-sensitive dye have showed that such chemosensitive TBCs tend to form colonies. The formation of such colonies suggests the existence of cross talk between TBCs, which is usually eliminated from artificial sensors.

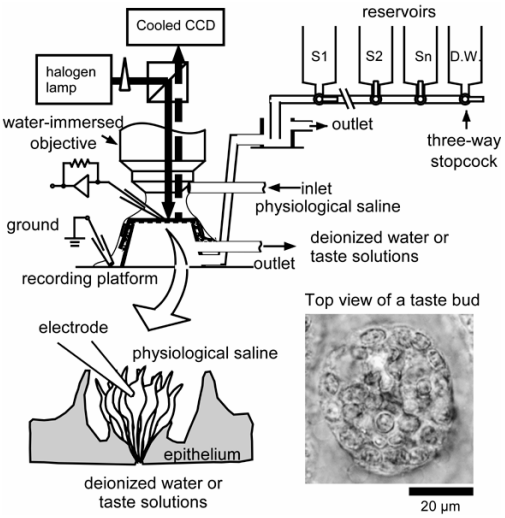


Fig. 3 Experimental set up for in-situ patch clamp and optical recordings. Peeled lingual epithelium mounted on a recording platform is placed under a microscope equipped with a water-immersed objective. TBCs are injected with probe dyes under voltage-clamp conditions. The solid and broken arrows indicate the excitation and fluorescence paths respectively. Receptor membranes of TBCs facing inside the platform and basolateral membranes of TBCs facing the objective are irrigated separately. The reservoirs, S1-Sn and D.W., are for stimulating solutions and deionized water. The photograph shows a single taste bud.

Yoshii and his colleagues are now investigating molecular mechanisms of the cross talk between TBCs (Fig. 4). They have revealed gap junctions between TBCs and neurotransmitter receptors on TBCs (unpublished data). In general, gap junctions are intercellular channels that connect cells both electrically and chemically, since they permeate small ions such as $Na^+$, $K^+$, $Cl^-$, and $Ca^{2+}$, besides second messengers such as cAMP and IP3 that modulate cellular functions electrically and biochemically. Neurotransmitter receptors also chemically connect cells to each other. When a subgroup of TBCs releases

neurotransmitter, other TBCs expressing their receptors would receive taste information.

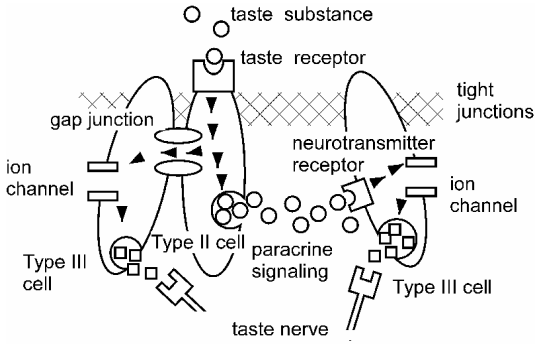


Fig. 4 A hypothetical TBC network formed by gap junctions and paracrine systems. Type II cells generate second messengers in response to taste substances. These second messengers diffuse into type III cells through gap junctions and elicit receptor potentials by opening ion channels on the cells. The type III cells then release neurotransmitters and activate taste nerves. These second messengers also generate receptor potential (not shown) to release neurotransmitters that diffuse into interstitial spaces to activate neurotransmitter release sites on the type III cells.

Tateno and Miki are designing sensors with cross talk because animal taste receptors appear to take advantage of the cross talk to increase the sensitivity. Tateno is doing simulation of the interaction between TBCs using a Hodgkin-Huxley neuron network. Gap junctions and other ion channels including neurotransmitter receptors are assigned conductances, and their opening and closing are expressed by high and low conductances respectively. Cell membranes are assigned conductances in parallel to capacitance, and solutions inside and outside cells are also assigned conductances. Tateno will make a computer model of a single TBC first and connect the cells to develop a taste cell network model to investigate features of the interaction between cells in a taste bud.

Miki is designing a single hardware TBC and will realize an electronic TBC network as a taste bud model. Moreover, he will assemble taste buds into an electronic taste bud network. His final goal is to produce a bio-inspired silicon sensor.

## IV. Summary

We explained our major aims, development of a hippocampal memory model and a taste cell network model, oriented to electronic neuro-devices. It was also mentioned how we collaborated with researchers in other fields toward the goal of our COE program.

Researchers in a wide range of research field from fundamental research on brain functions to applied research on electronic devices must advance interdisciplinary collaboration in order to establish a new field "Brain-Inspired Information Technology." If these researchers do research independently, the new field would not be established. Even if these researches are simply merged into a single group, nothing happens. We have to establish the fundamental techniques for Brain-Inspired Information Technology. The point is that researchers must seep out of their own field into other different fields for collaboration.

We must develop physiology-base models that perform some brain functions and then extract essential mechanisms of brain functions by simplification and abstraction of the physiology-base models in order to design electronic neuro-devices. At this point, our part is very important in our COE program and we must know matters required to design electronic devices.

On the other hand, researchers engaging in research on electronic devices must also seep out of their own field into the neuroscience. Then, they must study how they change the design techniques of devices and what they should think out as new design techniques in order to bring out distinctive features of the information processing mechanisms in the brain.

Close relation and interplay between different research fields would bring fruitful research results, and neuro-devices would be produced consequently as fundamental techniques of Brain-Inspired Information Technology.

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