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Development and application of a neuroinformatics environment for neuroscience and neuroethology

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ABSTRACT

Insect brains are excellent models for analyzing neuronal function in moderately complex central nervous systems due to the vast potential they offer for revealing the intricate details of the workings of a biological neural network. For a systematic approach to understanding neuronal mechanisms, it is important to integrate research results from various fields, such as morphology, physiology and immunohistochemistry. We are developing a database system, the *Bombyx Neuron Database (BoND)* for assembling and sharing experimental and analytical data. The system is designed and developed based on experimental data, mostly obtained from intracellular recordings. A new WWW technology, CMS (Content Management System), was implemented in our system. That is, PHP-based CMS, XOOPS, provides several functions for web-based database management, for instance, user accounting, web page designing and data backup. The *BoND* was developed by our original database module of XOOPS, in order to deal with electrophysiological and anatomical data. Research resources from various fields are combined in the database for realizing a conjunction of experiments and analysis, which will assist progress in understanding neural network mechanisms as a virtual laboratory.

1. Introduction

The ultimate goal of neuroethology is the systematic understanding of animal behavior based on the activities in the neural circuits of the individual. Insects are suitable creatures for this purpose because their brain consists of a simpler structure with fewer cells in comparison to the brains of vertebrates. The number of neurons in insect brains is estimated at 10^{5-6} while it is estimated to range at about 10^{10-11} in the human brain. Therefore, it is much easier to investigate the relationship between information processing and neuronal activities within insect brains, making insects well-suited as model animals for the analysis of mechanisms related to functions under various environmental conditions (Hildebrand, 1996; Kuwana, Nagasawa, Shimoyama, & Kanzaki, 1999; Webb, 2001).

Furthermore, the mechanisms underlying sensory perception and control of behavior in individuals or groups of individual (super-organisms) of social insects have recently received much attention, since they employ simple and robust algorithms useful for solving a wide range of engineering problems (Quijano & Passino, 2007a, 2007b). As a result, the investigation of insect nervous systems has become an interdisciplinary field of research integrating areas from molecular biology to behavioral science.

The silkworm moth, *Bombyx mori,* is a domesticated insect whose behavioral repertoire is extremely simple. The imagines do not feed at all and male silkworm moths hardly move in the absence of sex pheromone stimuli. However, when a male moth is exposed to the pheromone, it shows a stereotypical zigzag walking pattern toward the pheromone source (Kanzaki & Shibuya, 1992; Kramer, 1975; Obara, 1979). As male silkmoths specifically display this simple behavior, it is a realistic goal to describe the entire neural circuitry involved in generating the zigzag walking pattern and hence understand its mechanism. We have been investigating this behavior at the molecular, cellular and network levels with regard to olfactory information processing and behavioral control mechanisms (Iwano et al., in press; Kanzaki, Ikeda, & Shibuya, 1994; Kanzaki, Nagasawa, & Shimoyama, 2005; Kanzaki & Shibuya, 1992; Namiki & Kanzaki, 2008; Seki & Kanzaki, 2008; Wada & Kanzaki, 2005).

We have accumulated much information on neural processing involved in this behavior, such as the morphology and physiology of single neurons, immunohistochemistry, voltage sensitive dye and calcium imaging, and behavioral responses. In this work, computer and network environments have become indispensable to manage and share the increasing amount of experimental data.

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Neuroinformatics is a new concept to advance the application of information science and technology for the utilization of research resources accumulating in such neuroscientific fields, thus yielding an understanding of the essential mechanisms of the information processing occurring in the brain and neural system (Dashti, Ghandeharizadeh, Stone, Swanson, & Thompson, 1997; Pittendrigh & Jacobs, 2003; Rueden, Eliceiri, & White, 2004; The OECD Working Group on NI, 2003; van Pelt, van Ooyan, & Uylings, 2001). It is also considered to provide a valuable research resource for various fields such as engineering, agriculture and medicine.

In this study, we developed a database system for the administration of various experimental data regarding *Bombyx* neurons, and implemented an environment enabling the consolidation and utilization of data in terms of brain specimens including confocal laser scan microscope images, physiological and histochemical experimental data. This system introduces functions for searching, extraction and classification of accumulated experiment records based on location in the brain, morphology, response characteristics, and other parameters. It makes possible to advance efficiently and accurately by performing operations traditionally based on experimenters' memories and intuition. In addition, all the brain specimens used in experiments are stored in a refrigerator for later use in the laboratory, and the system may be effectively applied to the selection of samples for further experiments and the organization of specimens.

One of the latest web technologies, Content Management System (CMS), was applied in this development. CMS is widely used for building and managing the Internet portal site. As the system is designed for use with a web browser-based user interface, publication and sharing of data on the Internet are accomplished easily. It may be applied as a basic tool for uniformly managing experimental data, the publication of data presented in papers (Ikeno et al., 2007). Furthermore, it can be used for constructing the Internet portal site as well as for data sharing through the setting of access restrictions. Further development will permit this system to evolve into a standard database system in the field of neuroinformatics.

2. System configuration

It is necessary to deal with a considerable and ever-increasing volume of experimental data. It must be easy to use and the data management system should be accessible through web browsers, because the web system is the most common user interface for databases. The eXtensible Object Oriented Portal System, XOOPS (http://www.xoops.org/, http://xoopscube.org/), which is a free software CMS, uses MySQL (http://www.mysql.com/) as database format, Apache (http://www.apache.org/) as web server, and is developed by Hypertext Preprocessor scripting language (PHP, http://www.php.net/). XOOPS has been demonstrated to be capable to support fairly large-scale web sites in practical application, and has important advantages in terms of extensibility due to its modular architecture. Our development takes advantage of such characteristics of XOOPS, utilizing among others, its functions for user management, network access. A low-cost practical database system was achieved as a result. New functions were developed and implemented by focusing on areas important for the management of neuron-based experimental data.

2.1. System configuration and environment

A system validation of the developed database system, *Bombyx Neuron Database* (BoND), was implemented under the environment shown in Fig. 1. The hardware was a personal computer running the widely used Windows XP (Microsoft Co. Redmond, WA) with RAID1 mirroring disk system. By sharing the data files under the Windows network file system, access from Windows application software was provided to clients connected over a network. Moreover, the system may be ported to other operating systems supported by XOOPS, such as UNIX-like systems including Linux and Mac OS X. On the client side, any system having web browsing capabilities can be used for database access. Confocal laser scan microscope images are obtained as a LSM file format from the database and handled by the LSM Image Browser (http://www.zeiss.de/Imagebrowser, Carl Zeiss Co., Jena, Germany) in conjunction with the database. A hierarchical folder (directory) structure is used to manage experimental data files as shown in Fig. 2. Each experimental datum is stored as one content corresponding to a brain sample. A unique ID number is applied to each content and data files stored in the folder named by this ID. Experimental data files were classified and saved in different subfolders named with experimental theme (morphology, physiology, etc.). Regarding morphology data, the confocal laser scan microscope of Carl Zeiss Co. creates a database file (mdb file) containing the image recording conditions along with a sequence of image files (lsm files), which were stored in the 'LSM' folder. A thumbnail image file of neuron morphology, which is referred to from the thumbnail index page and the detail page, constructed from LSM images was placed in the subfolder (such as, img1) of 'thumbnail' folder.

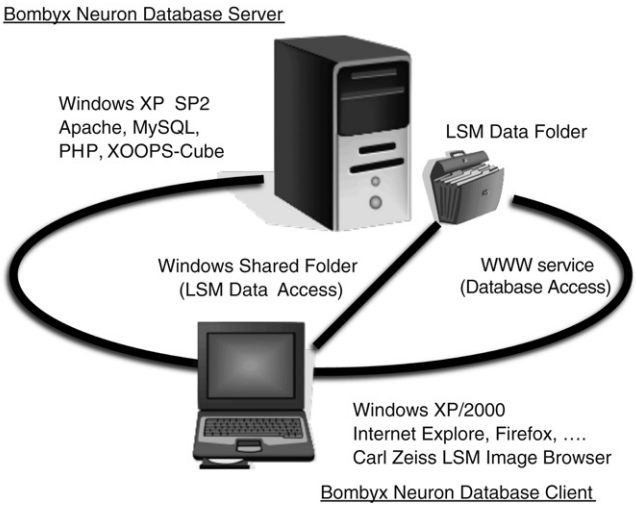

Fig. 1. Configuration of Bombyx Neuron Database system (BoND). BoND is implemented as a module in a CMS system, XOOPS. Users can access BoND by Web browser and observe the 3D-image through Windows network file system by LSM browser.

Electrophysiological experimental data were placed in the 'physiology' folder, creating a subfolder corresponding to the experimental conditions (control, light, etc.), and saving the data files. Image files of graphs for experimental data are also saved in the subfolder (e.g. img2) of the thumbnail folder, which can be assigned by an administrator. When other new experiments are conducted on the sample, a new folder can be created for deposit of newly obtained data.

2.2. Functions of the database system

The database system implements the following functions in order to manage experimental data related to neuron morphology and responses.

I. **Operation from a web browser:** All operations, such as data registration and browsing, can be performed via a web browser.