Discussion

Gregory Kovacs

C: I would like to point out the value of research when an application or engineered use has not yet been identified – basic science work.

A: I enthusiastically support the value of basic scientific research However, in this talk I am focusing on the value of research that is "pulled" from needs rather than pushed from a technology perspective. Both types of engineering development can coexist well.

Q: Can we solve limitations in scaling down drug delivery devices by introducing the drug externally?

A: This is how it is done now, for the most part. Implants include reservoirs for the drug, which can be refilled by injecting through the skin and through a fill port.

Q: Is progress being made in harvesting energy from within the body to address the challenges in scaling down power sources?

A: Work is going on within companies. A description was given of schemes that utilize mechanical motion to power a device, similar to winding a watch. The issue with such an approach is that rechargeable power sources cannot be depended upon entirely, so you still need to include a primary (non-rechargeable) battery.

Q: How can these microtechnologies be used for biohazard detection?

A: At some level they enable it, but from a systems perspective, quite often one needs to sample large volumes of air or water, and that requires larger, higher-powered equipment. Once the sample is obtained (and sometimes concentrated to improve sensitivity), the microtechnologies can really help.

Yasuharu Koike

Q: Does this technique use pattern matching?

A: No.

Q: People with spinal cord injuries cannot control muscles directly. Can you make a model for those people?

A: If we use FES (Functional Electrical Stimulation) techniques, we can capture the data related to muscle activities and movement.

Q: I was wondering how long one can use muscle interface.

A: We can use this interface for a long time without fatigue.

Q: Can you apply this technique for involuntary muscles, for example those regulating gut movement?

A: If we find the neurons related to those muscles, we can use this technique.

Karl F. Böhringer

Q: How long can you record with your MEMS electrodes?

A: We recorded up to a couple of minutes. The main reasons why we did not record longer were (a) we saw some damage to cells from the implant procedure coupled with signal degradation over time, and (b) for the initial demonstration of the technology we were satisfied with a short recording period.

Q: How did you confirm that the signals you were reading were actually intracellular?
A: This point could be debated, but signal size and the shape of the signal were consistent with intracellular behavior.

Q: There is "art" behind the use of capillaries to make intracellular measurements. Is there less "art" in the use of MEMS electrodes?
A: We are still at an earlier stage with these MEMS probes, and they are still more difficult to handle and control. The sharper the tip, the less damage to the cell. Micromachining does provide a sharper probe and more controlled dimensions than a glass capillary tube approach.

Q: With PEG-tetraglyme coating, do they actually resist foreign body response in an animal model?
A: I am not an expert in this area. In the short recordings we did see the proper response in our studies (i.e., PEG-coated electrodes performed better than uncoated electrodes). In work with V. Pan at the University of Washington over several days, foreign body response on substrates with PEG patterns was studied., and PEG coating greatly reduced protein adsorption.

Mihoko Otake

Q: How do you validate the schizophrenia model through experiments?
A: We will do fMRI imaging with schizophrenic subjects whose dopamine and/or serotonin receptors are blocked by blockers in order to weaken the inhibitory network. We will test if the comparative regions are activated in voluntary movement.

Q: Do we really need the inhibitory network? We might be able to describe over-attribution and under-attribution of schizophrenic subjects without the inhibitory network.
A: It might be possible to describe over-attribution and under-attribution of schizophrenic subjects if only the "interpretation" of the activity of comparative regions is altered. However, the existence of inhibitory networks is suggested if the activity of comparative regions is inactive when over-attribution occurs.

Q: Is Gourmet developed by Prof. Doi's group?
A: Yes. Gourmet is the module for model integration that is included in the multiscale simulation package for the soft material "OCTA." Prof. Doi told me that the module is not only for soft material models but any kind of model. I decided to make use of the module because it is effective to integrate multiscale neural models.

Q: Is this study led by Prof. Doi?
A: No. Prof. Doi is the PI of JST's CREST program, which is a grant program for research groups. "The bidirectional multiscale neural simulation project" is supported by JST's PRESTO program, which is a grant program for young researchers, not for groups. I am the PI of the project.

Q: There are many symptoms in schizophrenia. Are visual, auditory, olfactory, and tactile hallucinations also described using the same model?
A: Yes. The model can describe symptoms such as images, voices, smells, and senses of touch are synthesized by subjects but cannot be recognized as such because of deficits in prediction of sensory feedback.

Q: Schizophrenia is a complex disorder. What is the future direction of this study?
A: Here we showed a model that describes the abnormal sense of schizophrenic subjects who sometimes attribute their own actions to the intentions of others and may perceive themselves as

causing events that they in fact do not control. There are microscopic and macroscopic hypotheses including deficits in dopamine, serotonin, glutamatergic neurotransmission, or neurogenesis caused by genetic and environmental conditions. For example, Prof. Osumi supports the hypothesis of neurogenesis disorder. Different hypotheses are associated with each other. We would like to integrate different models on the same simulation in order to understand multiple aspects of brain activity for both health and disease. Future work includes multiscale simulation of schizophrenia that describes different experimental results without conflicts.