Project Title:

Simulation of molecular signaling during synaptic plasticity, in Purkinje neuron.

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1. Background and purpose of the project, relationship of the project with other projects

The project is to use realistic simulation to study the molecular and cellular mechanisms of synaptic plasticity in the cerebellum. The simulation is built from our own experimental results on protein distribution and dynamic modifications and the predictions are tested experimentally on living brain tissue. The model is also used as a tool to guide the analysis of single molecule tracking experiments performed in the lab.

Specific usage status of the system and calculation method

The project uses two stochastic engines MESORD and Smoldyn to simulate interaction / diffusion of molecules in discretized spatial model of neuronal dendrites.

2. Result

Several models have been implemented and exploration of the parameter space has been conducted using concomitant runs, in different cell geometries. The simulations suggest that the morphology of the cellular compartment plays a significant role in the processing of intracellular signals.

Last year, we identified some major limitations of the MesoRD simulation engine and the problems are currently under assessment by the original authors. As an alternative, we have been evaluating the Smoldyn engine which does not require spatial discretization and has an explicit concept of membrane (lacking in MesoRD). This has been the main task of an intern (Y-T Clochard).

3. Conclusion

Using the RSCC has allowed us to efficiently conduct parallel comparison of different simulation engines on complex simulations of spatially resolved reactions. We have received expert technical support from the RSCC support staff.

4. Schedule and prospect for the future

The model development has been hampered by some short-comings of the simulation engine, but those difficulties are being addressed.

5. If you wish to extend your account, provide usage situation (how far you have achieved, what calculation you have completed and what is yet to be done) and what you will do specifically in the next usage term.

In 2010, efforts have been devoted mainly to solving theoretical and software issues as well as designing new experimental approaches to measure protein behavior in neurons, to extract accurate simulation parameters and generate datasets to which simulation output can be compared. For these reasons, our CPU use this year has been reduced compared to previous year. In FY2011, we will re-run all simulations using the updated simulation engine to ensure that previously obtained results can be reproduced and were not caused by the identified software problems. This is expected to require significant amount of computation, over several weeks.

6. If you have a “General User” account and could not complete your allocated computation time, specify the reason.

7. If no research achievement was made, specify the reason.

Fiscal Year 2010 List of Publications Resulting from the Use of RICC

[Publication]

Spike timing-dependent plasticity as the origin of the formation of clustered synaptic efficacy engrams. Iannella NL, Launey T, Tanaka S. Front Comput Neurosci. 2010 Jul 14;4. pii: 21.

[Proceedings, etc.]

[Oral presentation at an international symposium]

[Others]