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 the stochastic engine MESORD 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.

Two new directions have been explored:

(1) Importing real 3D morphology (reconstructed from electron microscopy serial sections) into the model instead of an idealized one built by combination of geometric primitives. This required a major modification of the software and is still under way.

(2) Attempt to build very large scale geometry with over 10^6 voxels and 10^7 individual molecular species. This has revealed some limitations in the simulation engine, triggering a major revision by the authors.

3. Conclusion

Using the RSCC has allowed us to efficiently conduct complex simulations to complement our other experimental approaches. 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. The next major release will make use of GPU-acceleration (in collaboration with Upsalla Univ. , Sweden)

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 2009, 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 years, with no publications involving simulations done on the RSCC.

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

Most of the efforts this year has been devoted to solving software issues. The model development, however has been steadily pursued and should allow to run simulation with unprecedented level of accuracy once the engine issues are solved.