Science In The Cloud

Joseph L. Hellerstein
Computational Discovery Department
Google
Seattle, Washington USA
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Agenda

- Supercomputing in the cloud
  - Application to computational chemistry
- Computational discovery for brain science
  - Brain science 101
  - Simulating sleep-wake cycles
- Lessons learned, random musings
$4,829-per-hour supercomputer built on Amazon cloud to fuel cancer research

By Jon Brodkin | Published 2 days ago

~50K cores
~6.7K EC2 instances
$4,828.85 per hour
We’re pleased to announce a new academic research grant program: Google Exacyle for Visiting Faculty. Through this program, we’ll award up to 10 qualified researchers with at least 100 million core-hours each, for a total of 1 billion core-hours. The program is focused on large-scale, CPU-bound batch computations in research areas such as biomedicine, energy, finance, entertainment, and agriculture, amongst others. For example, projects developing large-scale genomic search and alignment, massively scaled Monte Carlo simulations, and sky survey image analysis could be an ideal fit.
G-Protein Coupled Receptors (GPCR)

- GPCRs enable the exchange of molecules between cells and their environment.
- 40% of pharmaceuticals target GPCRs.
Dynamics of GPCRs
Brain Simulation Case Study

- Brain science 101
- Simulating sleep wake cycles in the cat brain.
<table>
<thead>
<tr>
<th>Animal</th>
<th>Neurons (M)</th>
<th>Neuron-M per brain-g</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sea slug</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Mouse</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>Cat</td>
<td>300</td>
<td>10</td>
</tr>
<tr>
<td>Human</td>
<td>100,000</td>
<td>71.4</td>
</tr>
</tbody>
</table>
Figure 12-38  Essential Cell Biology, 2/e. (© 2004 Garland Science)
Synapses Connect Neurons

#synapses ~ 1,000 X #Neurons
Examples of High Level Brain Wirings
Mapping Function to Brain Anatomy

Phineas Gage: A Gruesome but True Story About Brain Science
by John Fleischman

Phineas Gage was truly a man with a hole in his head. A railroad construction foreman, Phineas was blasting rock near Cavendish, Vermont, in 1848 when a thirteen-pound iron rod was shot through his brain. Miraculously, he survived another eleven years and became a textbook case in brain science. But he was forever changed by the accident, and what happened inside his brain...more
Brodmann's Areas in the Human Brain

- Primary visual cortex (V1)
- Primary somatosensory cortex
- Primary motor cortex
- Secondary visual cortex (V2)
- Associative visual cortex (V3, V4)
- Anterior prefrontal cortex
- Primary visual cortex (V1)
Details of Sensory Motor Areas
Can a brain simulation reproduce sleep-wake cycles?

Model

- Point model of 65K neurons
- Statistical model of neural circuits
- Calibrate from empirical data
Model Parameterizations

- Neurons (65K)
  - Ion channels, propagation delays, types
- Synapses (~65M)
  - Neurotransmitter, weights on neurons, connections

Hundreds of parameters!!!
Models of Neuron Firings

A dynamic threshold ($\tilde{\theta}$) is defined for each cell that determines at which membrane potential the cell should fire

$$\frac{d\theta}{dt} = - (\theta - \theta_{eq})/\tau_\theta$$

The change in membrane potential $V$ for each neuron is as follows

$$\frac{dV}{dt} = [ - g_{NaL}(V - E_{Na}) - g_{KL}(V - E_K) - I_{syn} - I_{int}]/\tau_m - g_{spike}(V - E_K)/\tau_{spike}$$

where the conductances for the sodium leak ($g_{NaL} = 0.2$) and potassium leak ($g_{KL} = 1.0–1.85$) are the primary determinants of the resting membrane potential. Conductance units are dimensionless.
Study Summary

- Discovered simulation parameters that: (a) are consistent with empirical sleep-wake cycles and (b) satisfy a set of biological constraints.

- But...
  - Is the model over-fitted?
  - Very time-consuming to explore the parameter space to determine if there is a consistent parameter set.
  - Ad hoc methodology
    - How systematically build model?
    - How diagnose model errors (e.g., concept of diagnostics in statistics)?
  - Little engineering rigor
    - No concept of tests that relate simulation results to biology
Why Science in the Cloud?

- Burst capacity
  - Access to many thousands of cores
- Reproducibility
  - Investigators use the same computational tools and data
- Sharing
  - Build on the results of others
- Efficient use of scarce research dollars
  - Avoid investments in infrastructure with a short lifetime
System Challenges

- Fine grain parallelism on a commodity infrastructure
- Low friction scaling
  - Scientists should focus on science not programming distributed systems.
- Interactive exploratory analysis at scale.
- Introspective batch processing.
- Multi-cloud support
  - Data are big & distributed
  - Commercial science requires both public and private clouds
Science Methodology Challenges

- Systematic model development that is calibrated with empirical data
- Testing methodology
- Integrate models at multiple levels of granularity
- Standardized schemas so can share data
  - But accommodate rapid evolution of knowledge
- Create a culture of software engineering among scientists
  - Software is the lab notebook for computational discovery