Exploring the Effects of Stochasticity on a Circuit Model of Epilepsy – A Neuroscience Gateway Project

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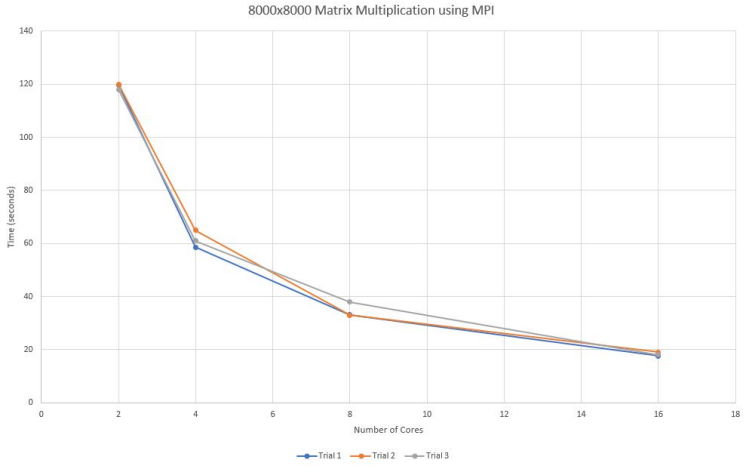
What is HPC?

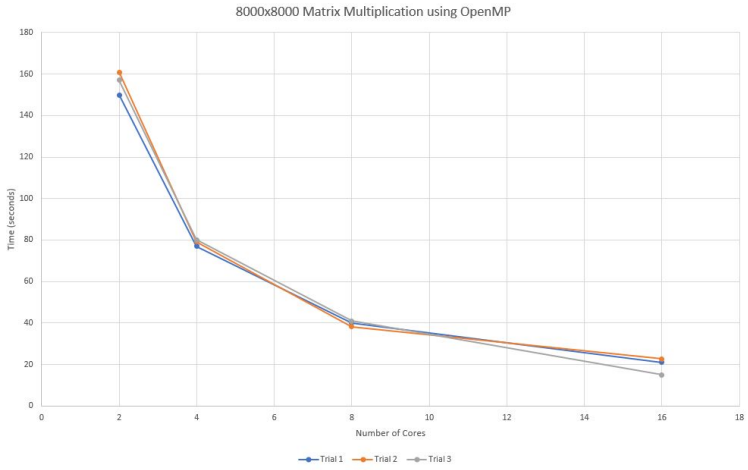
- **H**igh **P**erformance **C**omputing
- The use of multiple cores at once to perform tasks more efficiently

- Comet and Expanse supercomputers at SDSC
  - Submit a SLURM script as a job
  - A scheduler allots cores to each job
    - More cores -> longer wait time

- 2 types of parallel programming
  - Shared memory programming using 1 main memory reserve across all threads, done with OpenMP
  - Distributed memory programming using each core's small memory cache, done with MPI

OpenMP vs MPI

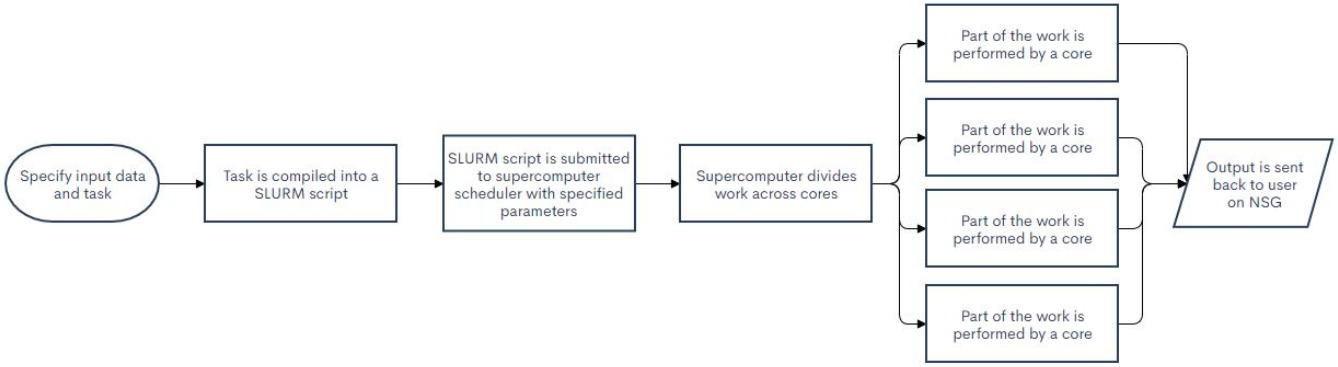




The Comet supercomputer runs tasks on multiple threads, which allows them to be completed more efficiently by splitting the load between the threads. We compared the difference between two multithreading APIs to run an example computation task. We noticed that MPI completed the example task faster than OpenMP, but the gap started to close at higher core numbers as MPI produced more diminishing returns.

NSG Portal

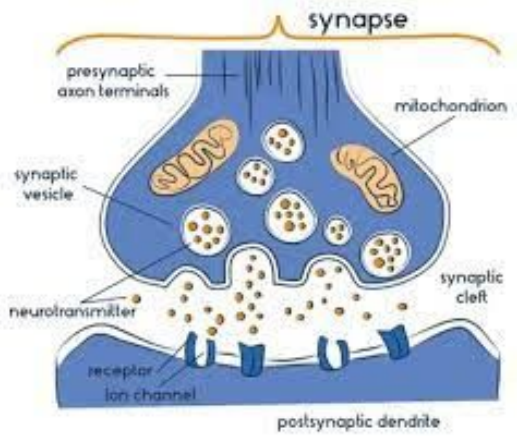
The NSG portal is a web-based interface that provides tools for neuroscientists to process large amounts of data through supercomputers

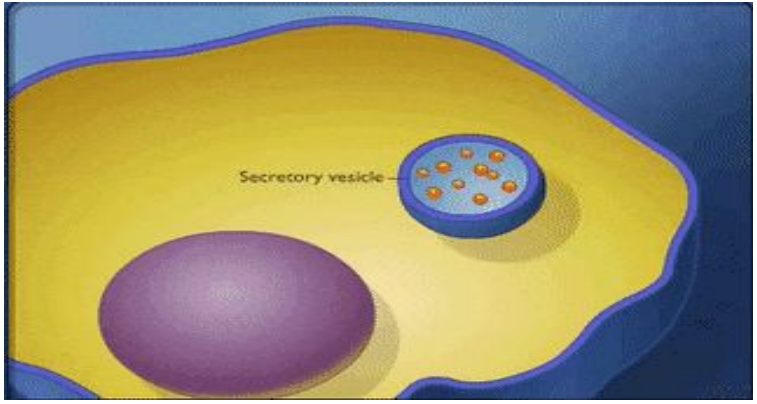


NEUROSCIENCE GATEWAY
A Portal for Computational Neuroscience

Synaptic Transmission Overview

- Neurons transmit signals through action potentials (aka “spikes”)
  - Membrane potential goes from resting state (-65 mv) to positive (~+30 mv)
- Action potentials trigger the release of neurotransmitters in **quanta**
- Quantal vesicles fuse with the presynaptic membrane > release their contents through exocytosis > neurotransmitters bind to the postsynaptic cell receptors > opens up ion channels to cause a spike in the receiving cell





What Is Stochasticity?

Something being *stochastic* means that it is described well by a random probability distribution, or that it lacks any discernible pattern.

Basis of our Experiment

- Synaptic transmissions are **stochastic** - variable success rate
  - Different # of synaptic vesicles can be released each time
  - Sometimes not enough to trigger action potentials

- Excitatory neurons release excitatory neurotransmitters that begin to trigger an action potential in the postsynaptic cell
- Inhibitory neurons release inhibitory neurotransmitters that work to “block” the action potential in the postsynaptic cell
- Excitatory neuron pathways are **more unreliable** than inhibitory neuron pathways
  - Can reach a 80% failure rate

Hypothesis of Experiment

Epilepsy occurs when a region of the brain fires spikes spontaneously

- Seizure focus- where trauma occurs (area of excited cells)

> Stimulation of the first 100 cells in the experiment

Santhakumar model of the dentate gyrus- 10% sprouting of granular cell axons > epileptic effect

- Represented by spike rasters

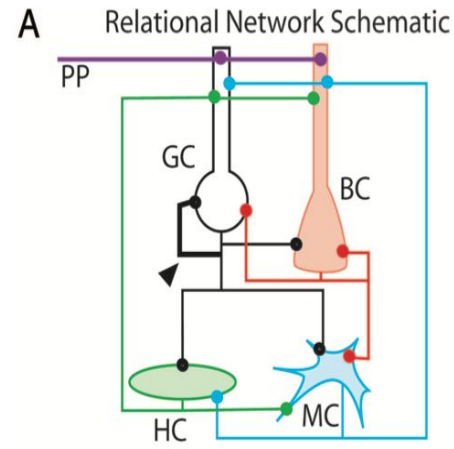
Modifications

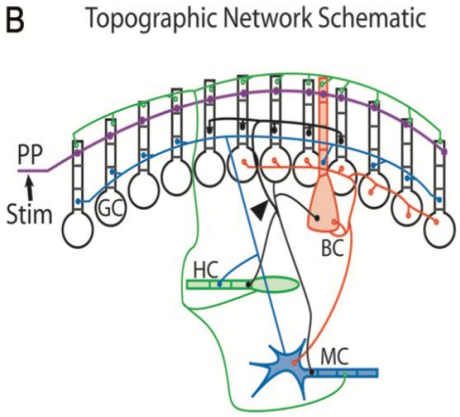
Stochastic excitatory connections - GC to GC, mossy cell to GC, GC to mossy cell

Graphs to represent number of spikes and times for first, median, and last spike

- GC = cell IDs of 0-499, MC with cell IDs of 506-520

SN- synaptic vesicle count SP1- probability of ONE vesicle's release





Data Analysis: Stochastic Effect

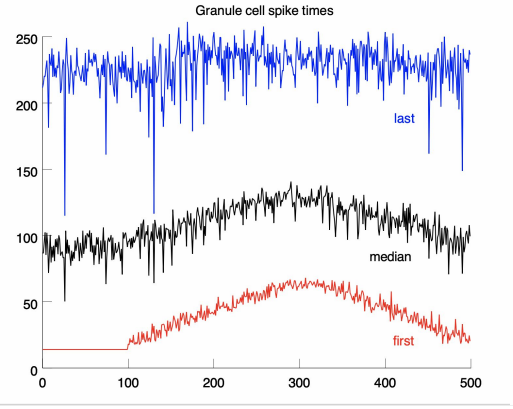
Does increasing synaptic failure rates slow down the propagation of a wave of epileptic discharges?

Peak time for the first spike to be fired:

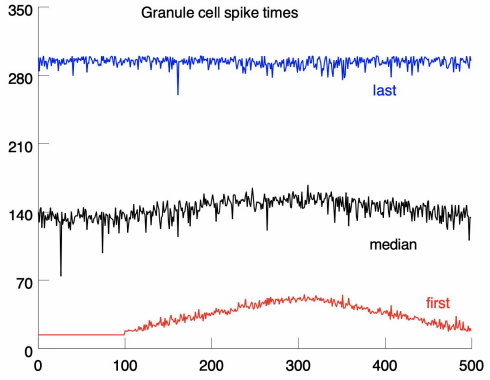
SP1 0.5, SN 6 = 46.5 ms

SP1 0.4, SN 6 = 55.5 ms

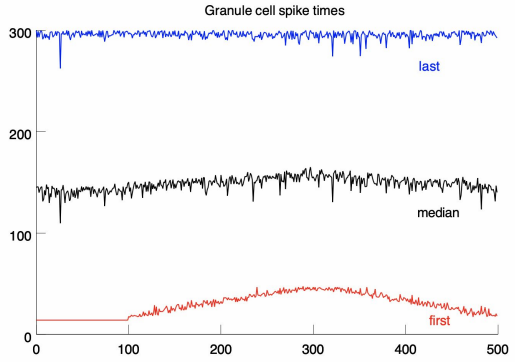
SP1 0.3, SN 6 = 68 ms



SP 0.3



SP 0.4



SP 0.5

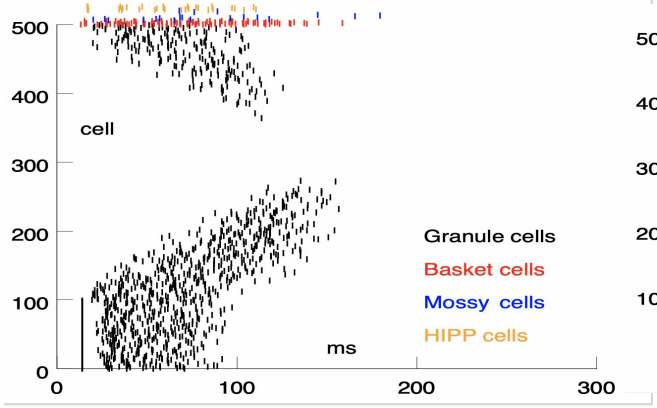
Data Analysis: Stochastic Effect

Spike rasters

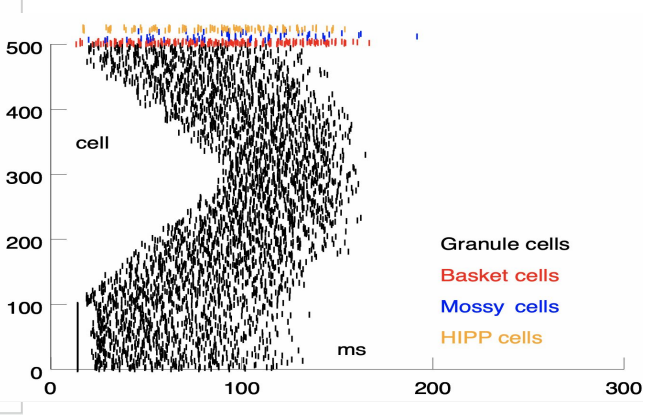
SN (synaptic vesicles) = 2

SP1 (probability of each vesicle being released)

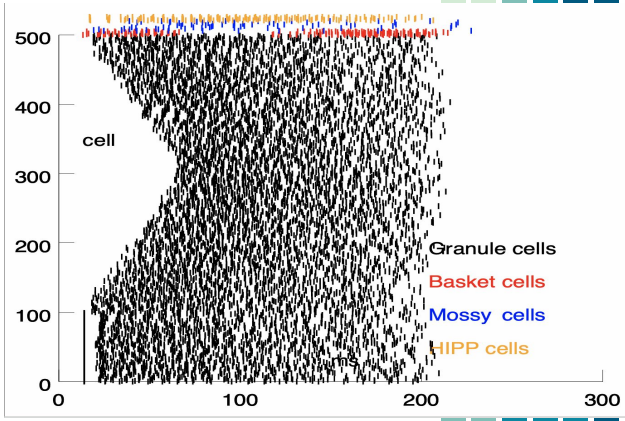
SP1 = 0.5



SP1 = 0.6

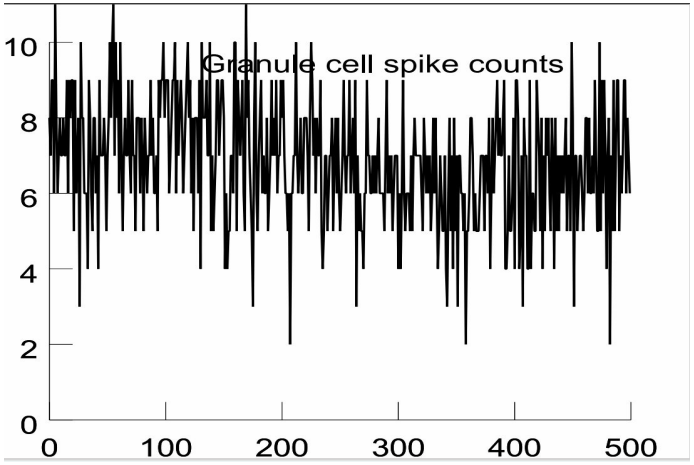


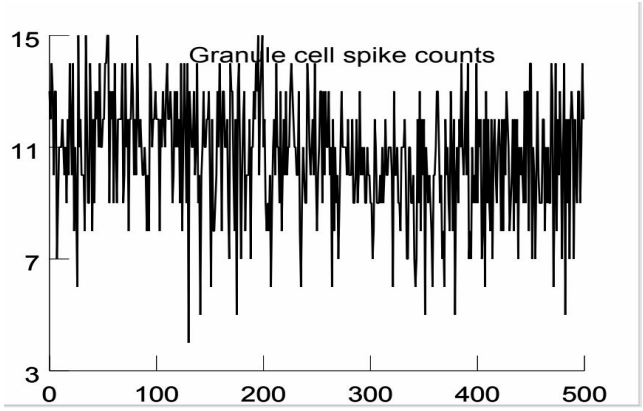
SP1 = 0.8

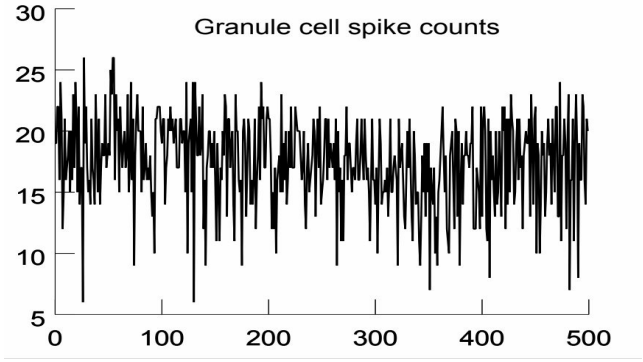


Data Analysis: Effect of SN

SP1 of 0.3 (constant)







SN of 4 (above), SN of 5 (top right), SN of 6 (bottom right)

SN	First SP1 with a complete failure
1	0.9
2	0.5
3	0.3
4	0.2
5	0.2
6	0.1

Binomial Theorem- Probabilities

k = # of synaptic vesicles released
n = total # of synaptic vesicles

Represented by the expanded binomial theorem: (p(release) + p(failure))^k

- Example: 2 vesicles released, 1 failed. p(release) = 0.6, p(fail) = 0.4
  - Probabilities can be drawn from: **$0.6^3 + 3*0.6^2*0.4 + 3*0.6*0.4^2 + 0.4^3$**

Experiment Conclusions

Increasing failure rates = more time for the signal to propagate to all cells

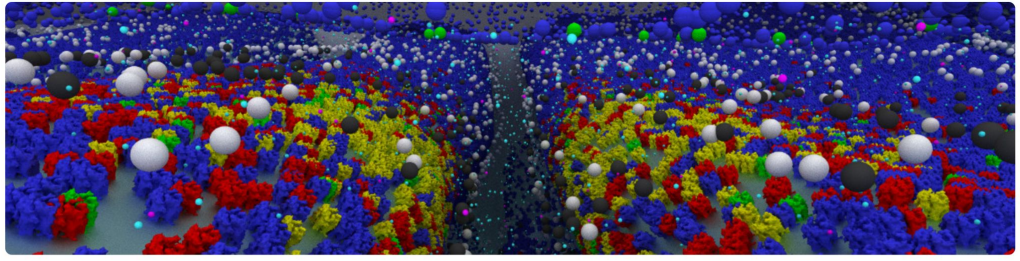
- Took longer to reach the peak time of the first spike

Increasing synaptic vesicles = faster propagation of the wave and greater signal intensity

- Shorter peak time for the first spike
- Increased numbers of spikes

Practical Applications of Stochasticity

- Artificial neural networks
  - Pattern recognition
  - Classification and categorization of objects
- Modeling of biomolecular reactions and interactions
- Run simulations to check accuracy of models



MCell
MONTE CARLO CELL