

IBM IEEE CAS/EDS

**AI Compute Symposium 2020**

*October 21-22*

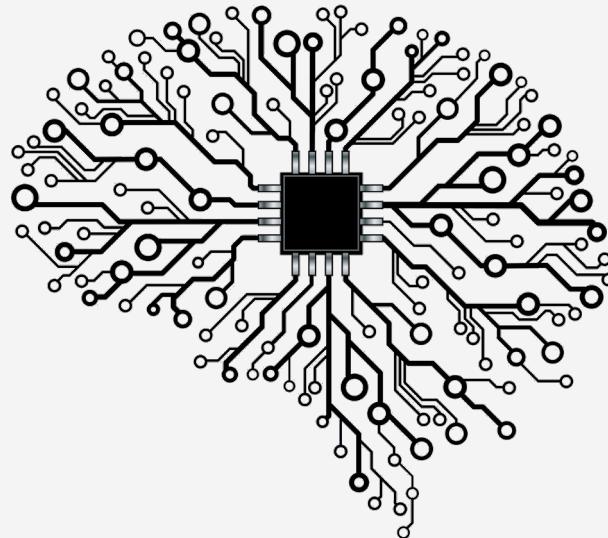
# Towards Biophysically-Based Neuromorphic Computing at Scale: Markov Abstractions of Electrochemical Reaction-Diffusion in Synaptic Transmission

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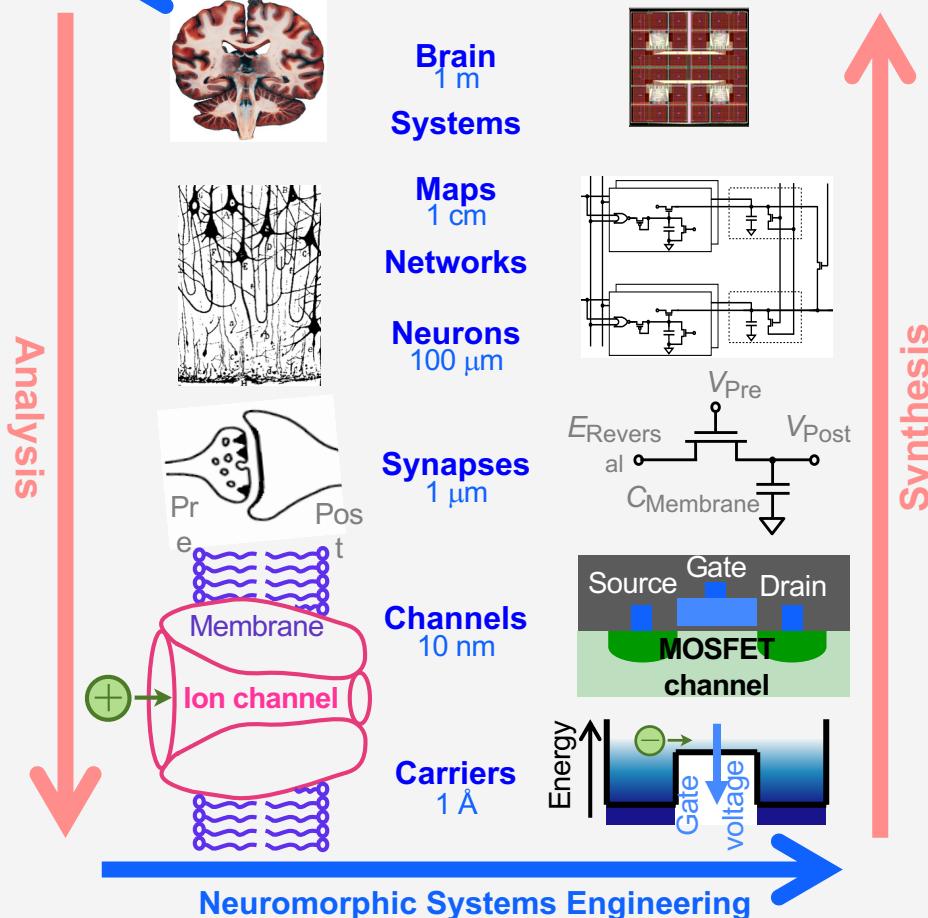
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# Background

- Neuromorphic systems are biologically inspired in design
- A tradeoff between biological realism with higher order dynamics and computational complexity
- Synaptic connections form the basis of learning and memory in both biological and artificial neural networks
- Synapses in biological systems are highly nonlinear computational units, but this complexity is often excluded from artificial models.
- Simulations including all the biological machinery for synapses have limited scaling due to computational complexity



(Gupta 2019)



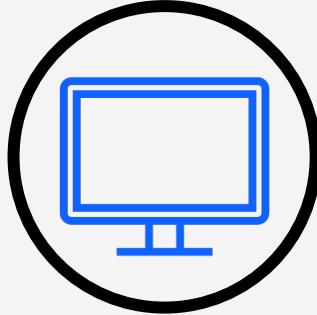
Multi-scale levels of investigation in analysis of the central nervous system (adapted from Churchland and Sejnowski 1992) and corresponding neuromorphic synthesis of highly efficient silicon cognitive microsystems. Boltzmann statistics of ionic and electronic channel transport provide isomorphic physical foundations.

G. Cauwenberghs,  
“Reverse Engineering the Cognitive Brain,”  
PNAS, 2013

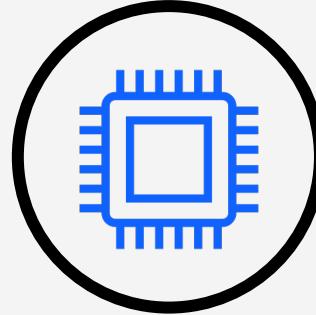
# Aims



Use experimentally obtained kinetics and parameters to build a biophysically accurate model of synaptic behavior in the brain using reaction-diffusion in a spatially realistic 3D geometry.



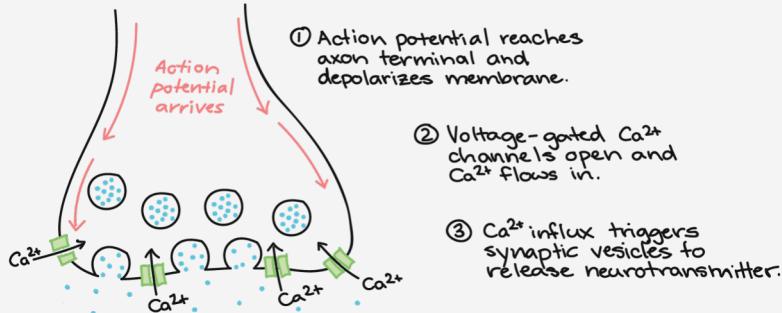
Abstract simulation details to create a computationally efficient software model for scalability while maintaining a biophysically tunable model.



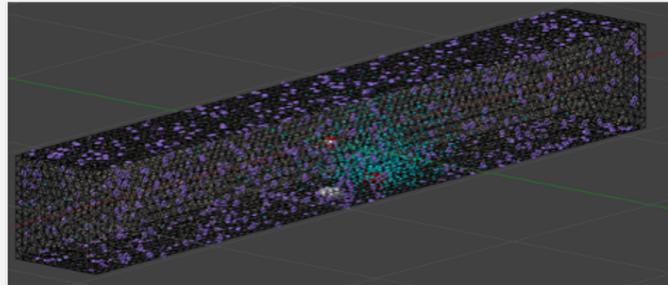
Implement biophysically tunable model into a neuromorphic hardware system.

# Methods - MCell

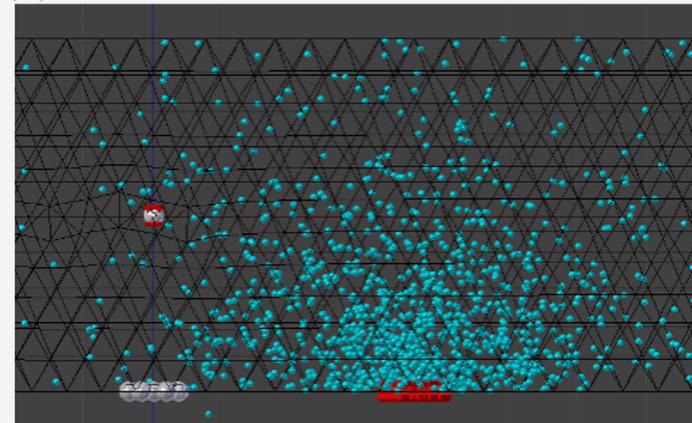
- Built physically realistic stochastic 3D reaction-diffusion system in MCell modeling software
- CA3-CA1 Schaffer collateral *en passant* synapse with experimentally obtained kinetics and parameters
- Action potential input followed by stochastic opening and closing of voltage-gated calcium channels, calcium influx to presynaptic terminal, and calcium binding buffers, pumps, and sensors mediating neurotransmitter release.



(A)

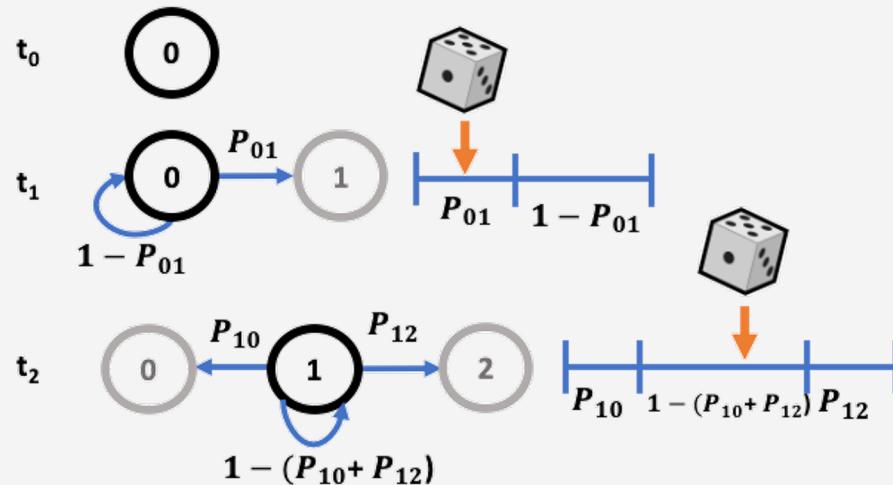
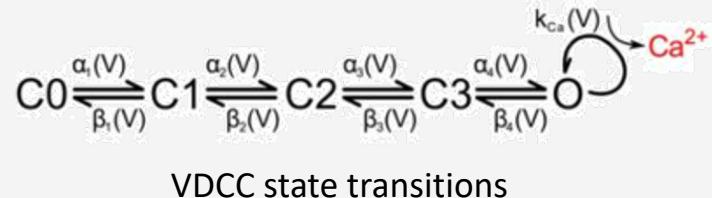


(B)

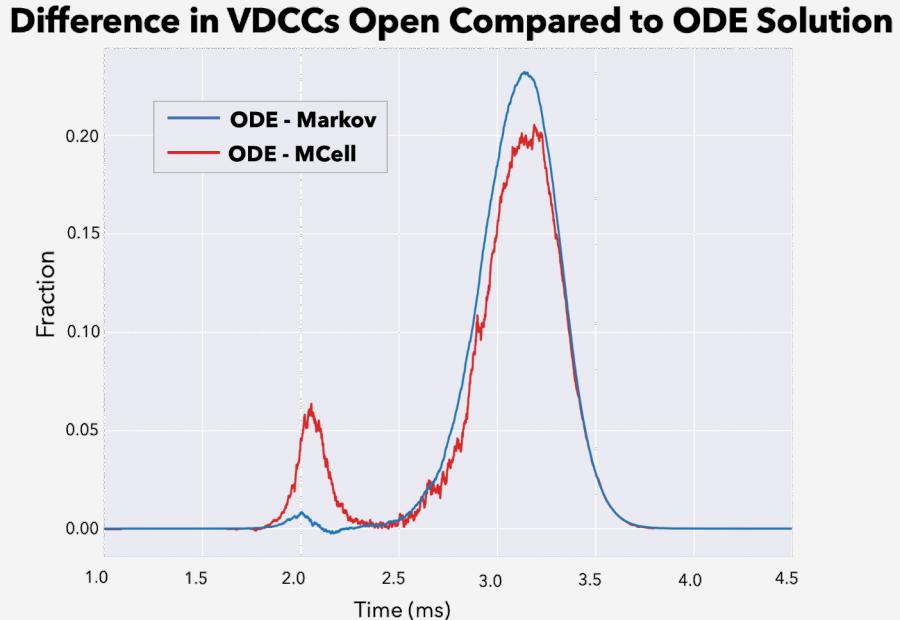
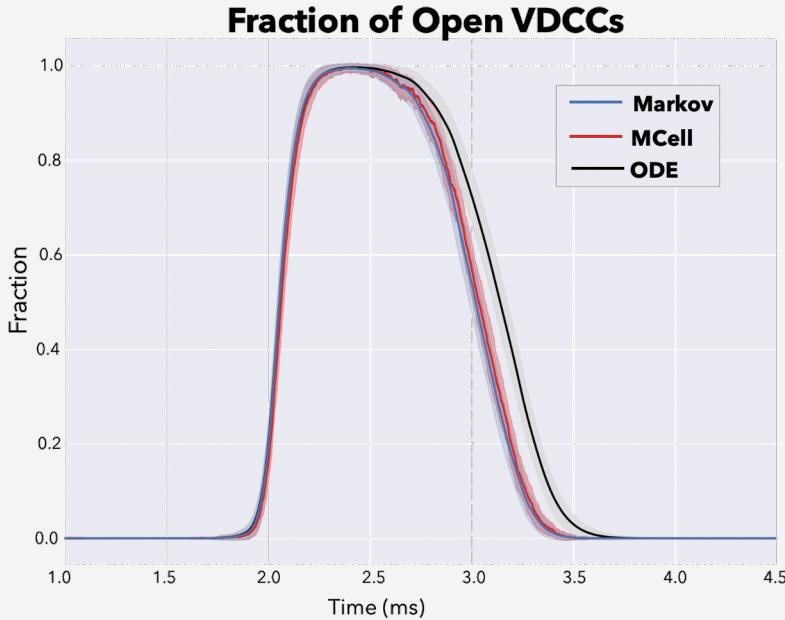


# Methods – Markov Abstractions

- Modelled action potential input and resulting voltage-dependent calcium channels (VDCCs) using Markov state transitions
- Concentration dependent calbindin buffer binding also modelled as a Markov chain
- Used multinomial sampling rather than inverse transform sampling methods to decrease number of computations per time step
- Markov abstractions were implemented using Python

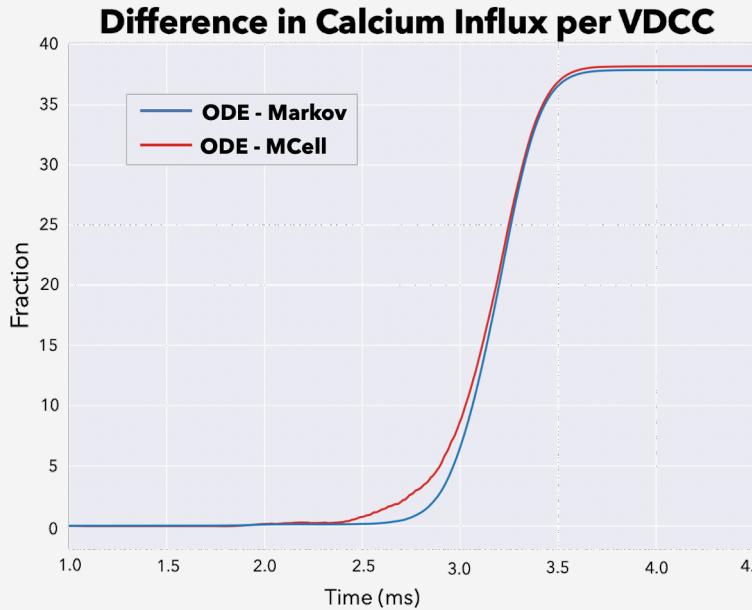
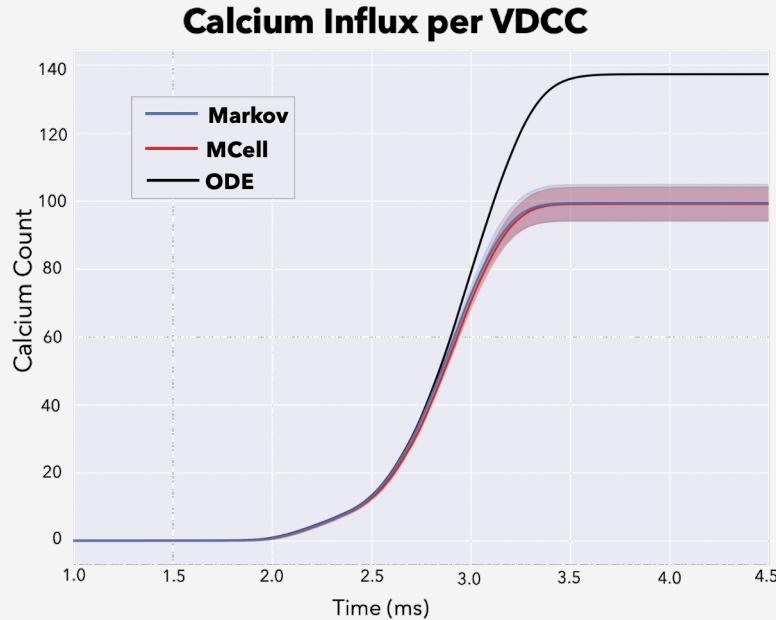


# Findings



Example comparison between Markov and MCell simulations compared to the deterministic ODE solution. There is good comparison between the Markov and Mcell simulations. The ODE overestimates the extent to which the VDCCs are open highlighting the importance of including stochasticity in the simulations.

# Findings



Calcium influx is again validated in the computationally efficient Markov model compared to the MCell model. The overestimation for open VDCCs in the deterministic solution results in higher than actual values of calcium influx through the open channels.

# Findings - Benchmarks

VDCC

	MCell	Standard Markov	Optimized Markov	<i>ODE</i> *
Runtime	$90.4 \pm 4.5$ s	$50.3 \pm 0.76$ s	$6.45 \pm 0.76$ s	$3.84 \pm 0.07$ s
Time Complexity	--	$O(NST)$	$O(T)$	$O(T)$

Calbindin

	MCell	Standard Markov	Optimized Markov	<i>ODE</i> *
Runtime	$21.08 \pm 0.26$ s	--	$2.09 \pm .06$ s	$229 \pm 7.6$ ms
Time Complexity	--	$O(NST)$	$O(T)$	$O(T)$

N: number of channels, S: number of states , T: number of timepoints

\* accuracy loss with deterministic solution

# Discussion

- Abstracted Markov model of synapse provides efficient and biophysically tunable proxy for full biological synapse model
- Runtime increases by an order of magnitude with optimized sampling scheme
- Allows for specific parameter adjustment, such as stimulus, number of VDCCs, and quantity of calbindin
- Cascade of Markov state transition modelled with efficient sampling schemes can be readily mapped onto massively parallel neuromorphic architectures