

Markov Abstractions of Biochemical Stochastic Reaction-Diffusion Models of Synaptic Transmission for Efficient Neuroscientific Simulations



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Abstract

Progress in computational neuroscience towards understanding brain function is challenged both by the complexity of molecular-scale electrochemical interactions at the level of individual neurons and synapses, and the dimensionality of network dynamics across the brain covering a vast range of spatial and temporal scales. Our work abstracts the highly detailed, biophysically realistic 3D reaction-diffusion model of a chemical synapse to a compact internal state space representation for efficient large-scale simulations while preserving biologically interpretable tunable parameters.

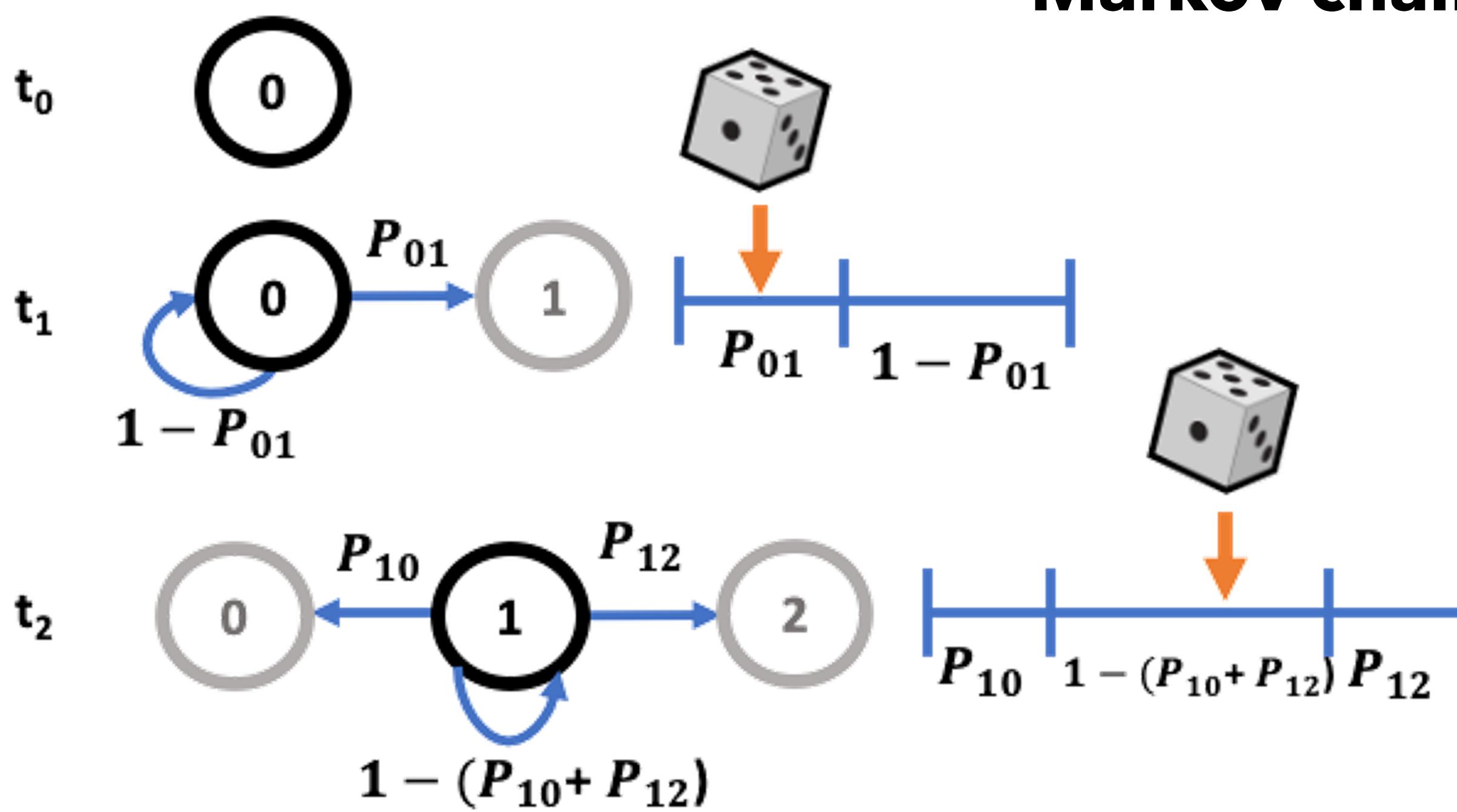
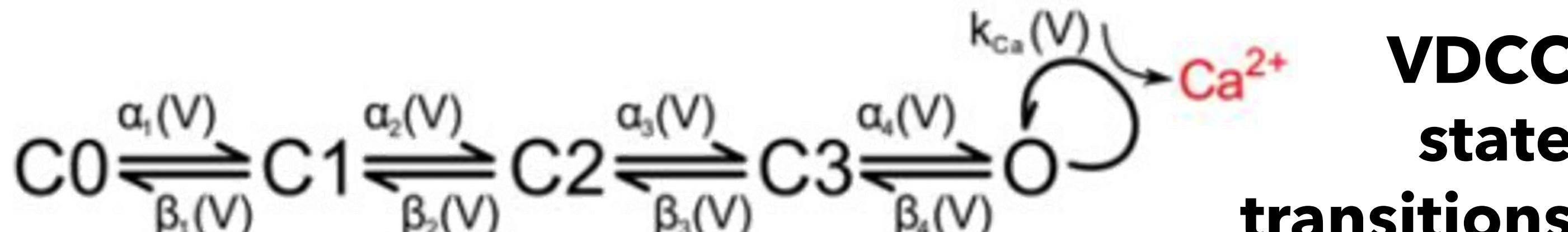
Introduction

Large-scale simulations of brain function vary in their biological realism from more realistic Hodgkin-Huxley type models being difficult to implement and not as scalable, while less realistic integrate-and-fire (I&F) architectures being easier to implement but do not capture complex dynamics of neural networks [1, 2].

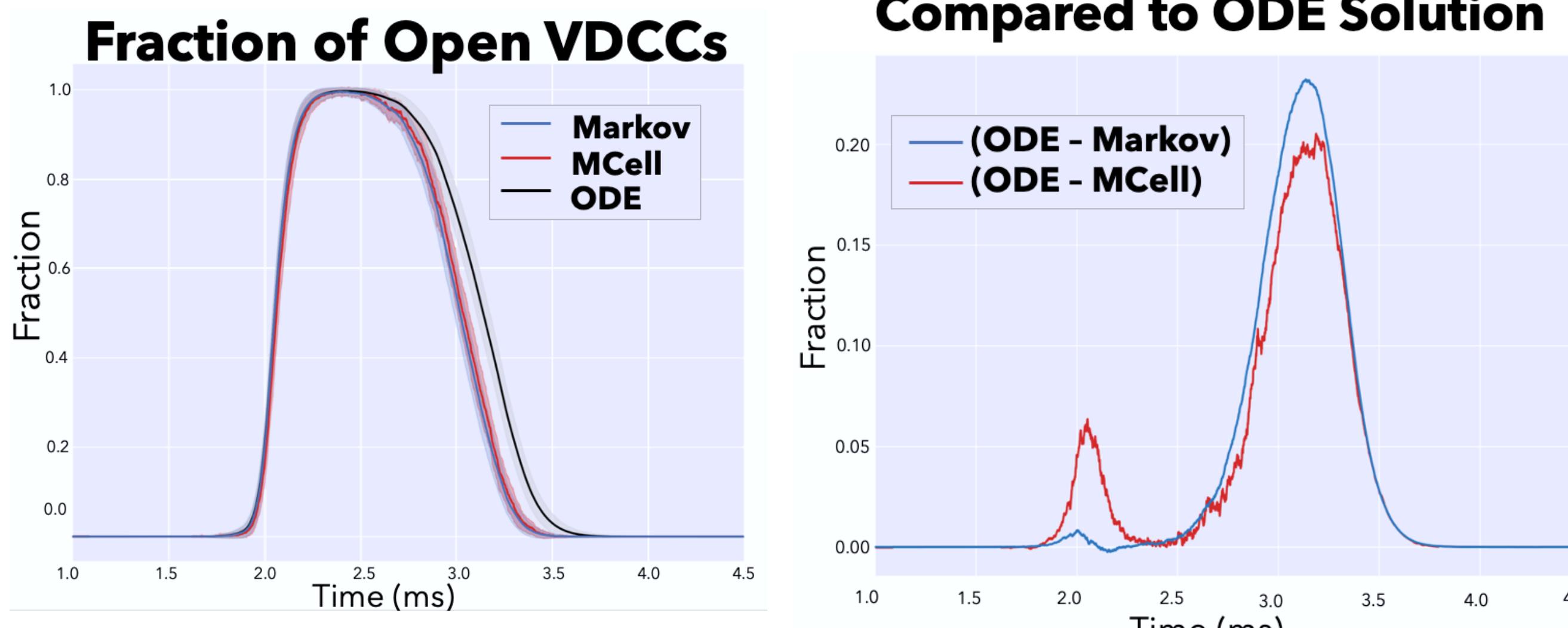
Synapses form the connections between neurons and the strength of these connections changes over time, forming the basis of learning and memory in both biological and artificial neural networks. The computations in synapses are highly nonlinear in nature, but in artificial neural networks, synaptic strength is typically reduced to a single value, which is updated to a specific task. Our work addresses the need for a more biophysically realistic model of the synapse with biologically tunable parameters to represent synaptic plasticity, while offering efficient real-time implementation for neuroscientific simulations.

Methods

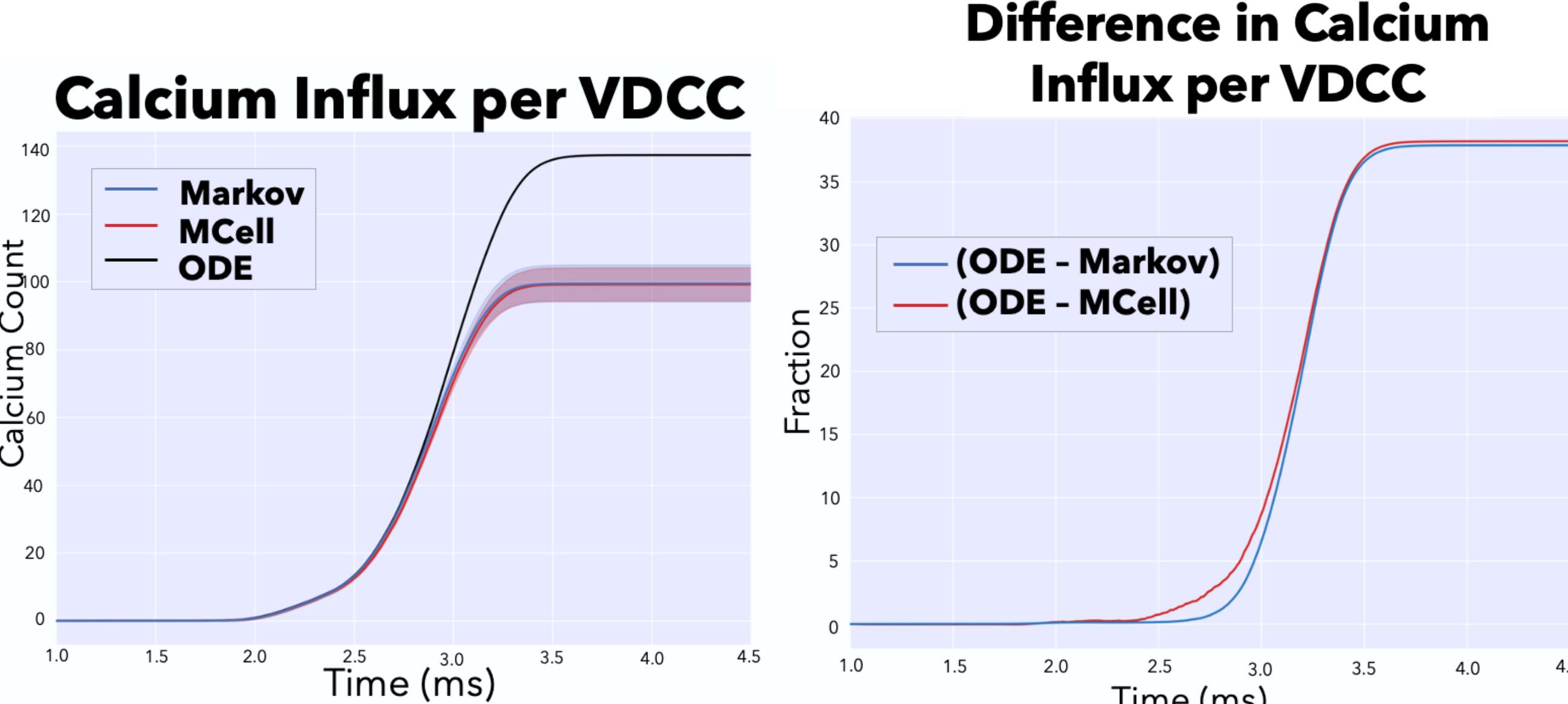
- (A)
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- Built physically realistic stochastic 3D reaction-diffusion system in MCell modeling software
 - CA3-CA1 Schaffer collateral en passant synapse with experimentally obtained kinetics and parameters [3,4]
 - Action potential input followed by stochastic opening and closing of voltage-gated calcium channels, calcium influx to presynaptic terminal, and calcium binding buffers, pumps, and sensors mediating neurotransmitter release.
- (B)
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Simulation Results



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.



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.

Benchmark Results

VDCC	Runtime	Floating Point Operations
MCell	90.4 ± 4.5 s	--
Standard Markov	109.2 ± 0.9 s	$7.01 (\pm .02) \times 10^7$
Multinomial Markov	9.40 ± 0.1 s	$1.26 (\pm .01) \times 10^7$
ODE (Euler)*	10.05 ± 0.1 s	7.73×10^7

Calbindin	Runtime	Floating Point Operations
MCell	21.08 ± 0.26 s	--
Standard Markov	--	$4.612 (\pm .002) \times 10^7$
Multinomial Markov	$2.37 \pm .02$ s	$2.72 \times 10^7 \pm (8 \times 10^3)$
ODE (Euler)*	$0.72 \pm .01$ s	1.60×10^7

N: number of channels, S: number of states , T: number of timepoints
* accuracy loss with deterministic solution

Discussion

Our abstracted Markov model of synapse provides efficient and biophysically tunable proxy for full biological synapse model. The runtime decreases by an order of magnitude with optimized sampling scheme. Floating point operations decrease by over a factor of two between standard Markov sampling and our multinomial Markov sampling in the VDCC simulations and decreases by three orders of magnitude in the calbindin simulations due to the quantity of calbindin binding reactions that take place in a typical simulation.

These biologically tunable models allow for specific parameter adjustment, such as stimulus, number of VDCCs, and quantity of calbindin. Cascades of Markov state transition modelled with efficient sampling schemes can be readily mapped onto large-scale neuroscientific simulations of brain function and learning.

References

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Acknowledgement

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