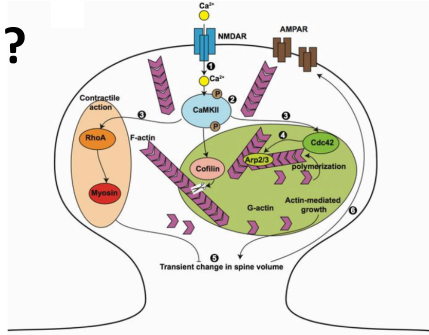


Multiscale theory of synapse function with model reduction by machine learning

What will be delivered?



Model

Fundamental **model** of synaptic morphogenesis that:

- ✓ Mechanistically links calcium signaling to actin cytoskeleton growth
- ✓ Incorporates knowledge from disparate spatiotemporal scales using ML
- ✓ Integrates existing signaling pathways and growth mechanisms which were previously studied in isolation

Theory

- ✓ **Theory** for ML model reduction of spatial reaction networks, e.g. calcium signaling
- ✓ **Theory** for ML model reduction of dynamical graph grammars, e.g. actin reorganization
- ✓ **Theory** for fast parallel multiscale simulation algorithms of spatially embedded graphs

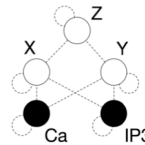
Software

- ✓ **Software** library in C++ and Python for training ML models
- ✓ **Software** that integrates the popular reaction-diffusion software MCell with the library for training ML models
- ✓ **Software** library built on the Cabana C++ library, ready for exascale-computing projects
- ✓ **Data and model sharing platform** for sharing MCell and ML models

What is new inside?

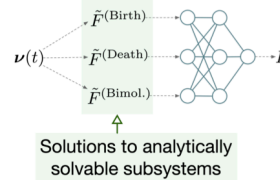
Physics-informed ML with Dynamic Boltzmann distributions (DBDs)

(1) Reduced model probability distribution
 $p \sim \tilde{p} = \frac{1}{Z} \exp[-E(\nu(t))]$

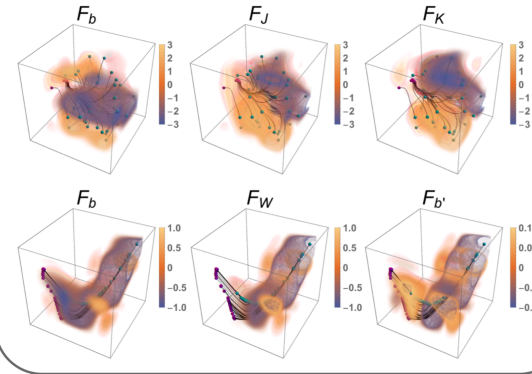


(2) Differential equation **to be learned** describing time evolution

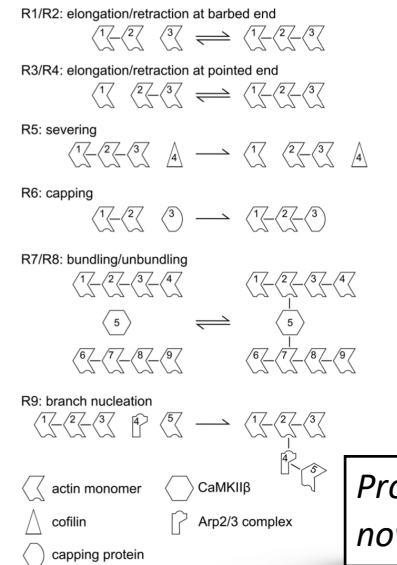
$$\frac{d\nu}{dt} = F(\nu(t); \mathbf{u})$$



Data-driven reduced model of calcium regulation of actin



Dynamical graph grammar (DGG) for actin growth



Prototype now exists

How will this change current practice?

Exploit ML revolution and DGGs for ...

- scaling up multiscale realistic modeling of synapses;
- enabling human understanding & analysis of complex models

End Users

MCell modelers; Bio-mathematicians; other modeling platform builders; Specialists in drug-evoked synaptic plasticity, Alzheimers disease, ...; Specialists in the biological substrates of learning.
 Data: All synaptic pathway relevant data notably including imagery.

E. Mjolsness/UC Irvine,
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