Using Weighted Ensemble Sampling in Spatial Stochastic Simulations

Rory Donovan

MMBios Scientific Meeting 26/2/15

Motivation

- Biological systems are complex
- “Simple” underlying dynamics can be incredible costly to simulate directly
- Need to look for ways to increase efficiency of computations
- If rare events matter, how can we cope?

Resampling

Original Sample

Double Points, Halve Weights

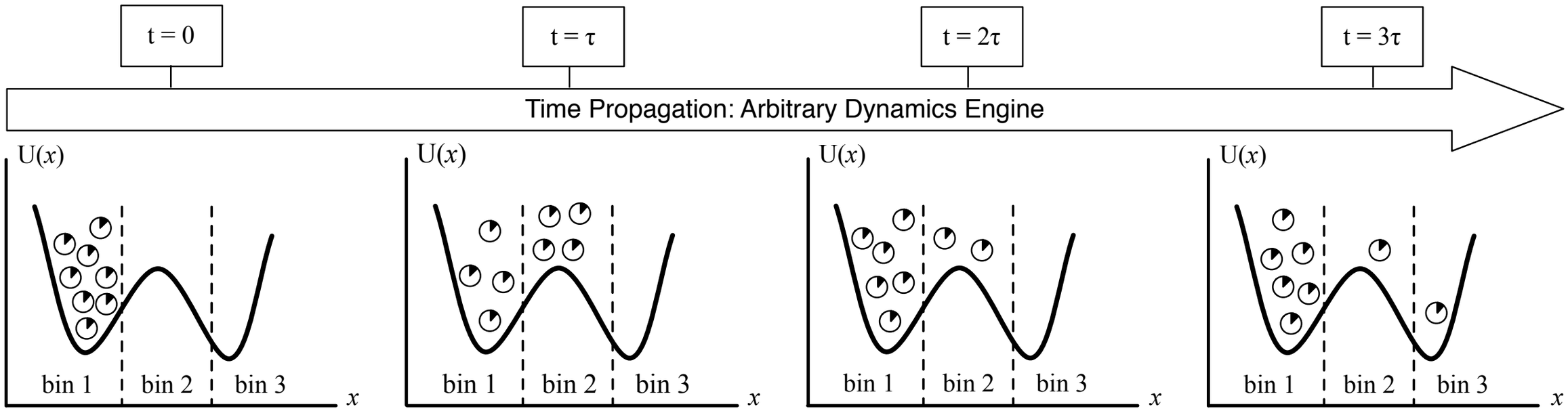
Halve Points, Double Weights

Do Both, In Different Regions

A Weighted Ensemble is Just Repeated Resampling

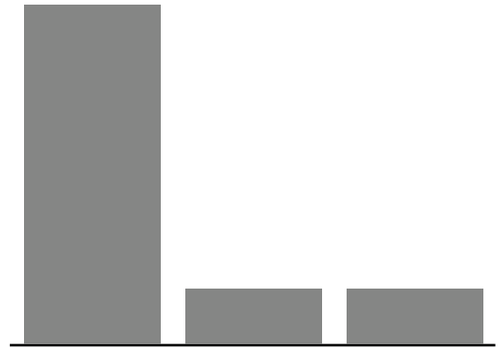
- Of any stochastic process:
  - Molecular dynamics (protein motion)
  - Chemical kinetics (cell signaling)
  - Branching processes (cancer modeling)
  - Agent based models (population dynamics)

Ensemble Sampling



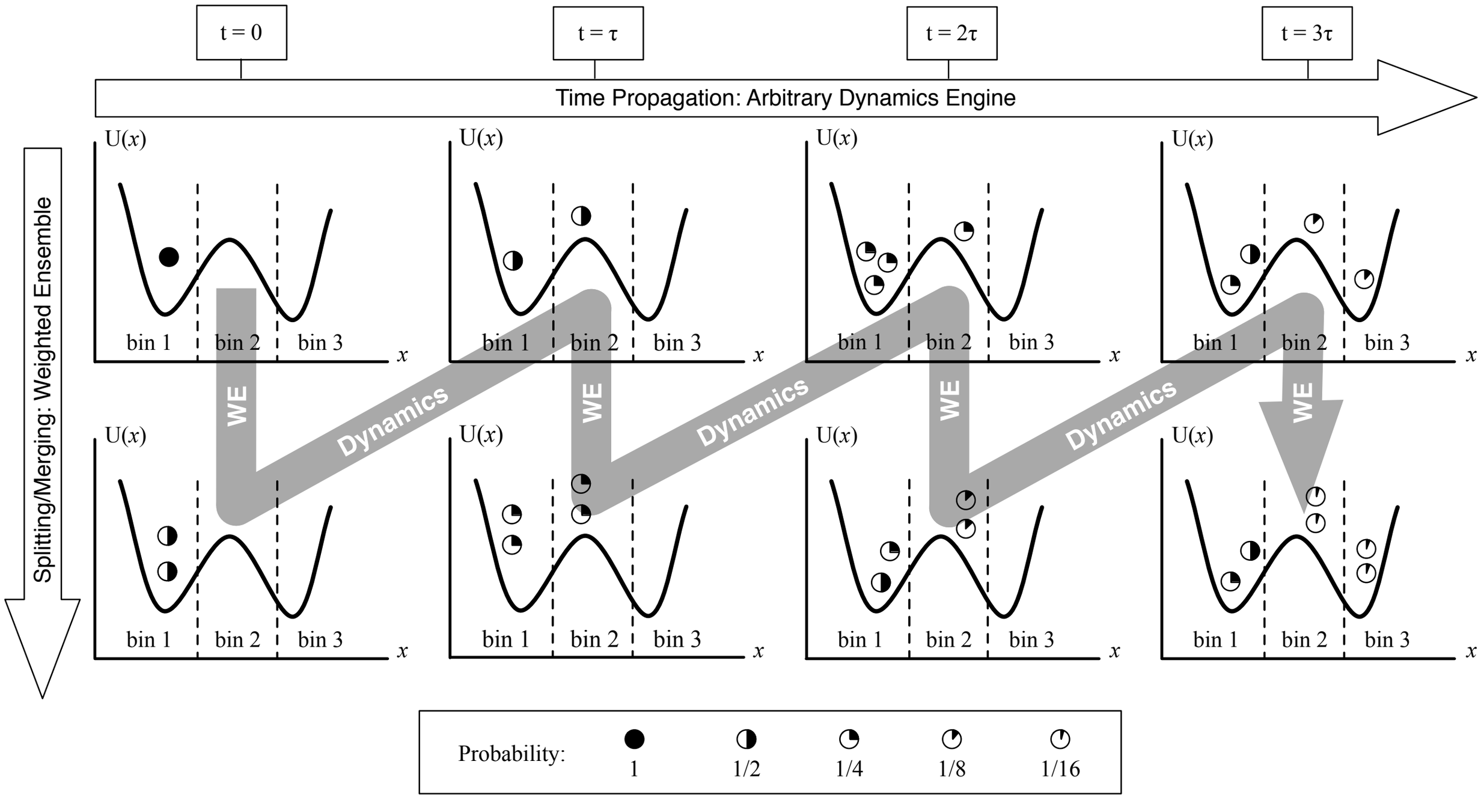
Probability: 1/8

Repeated Runs →

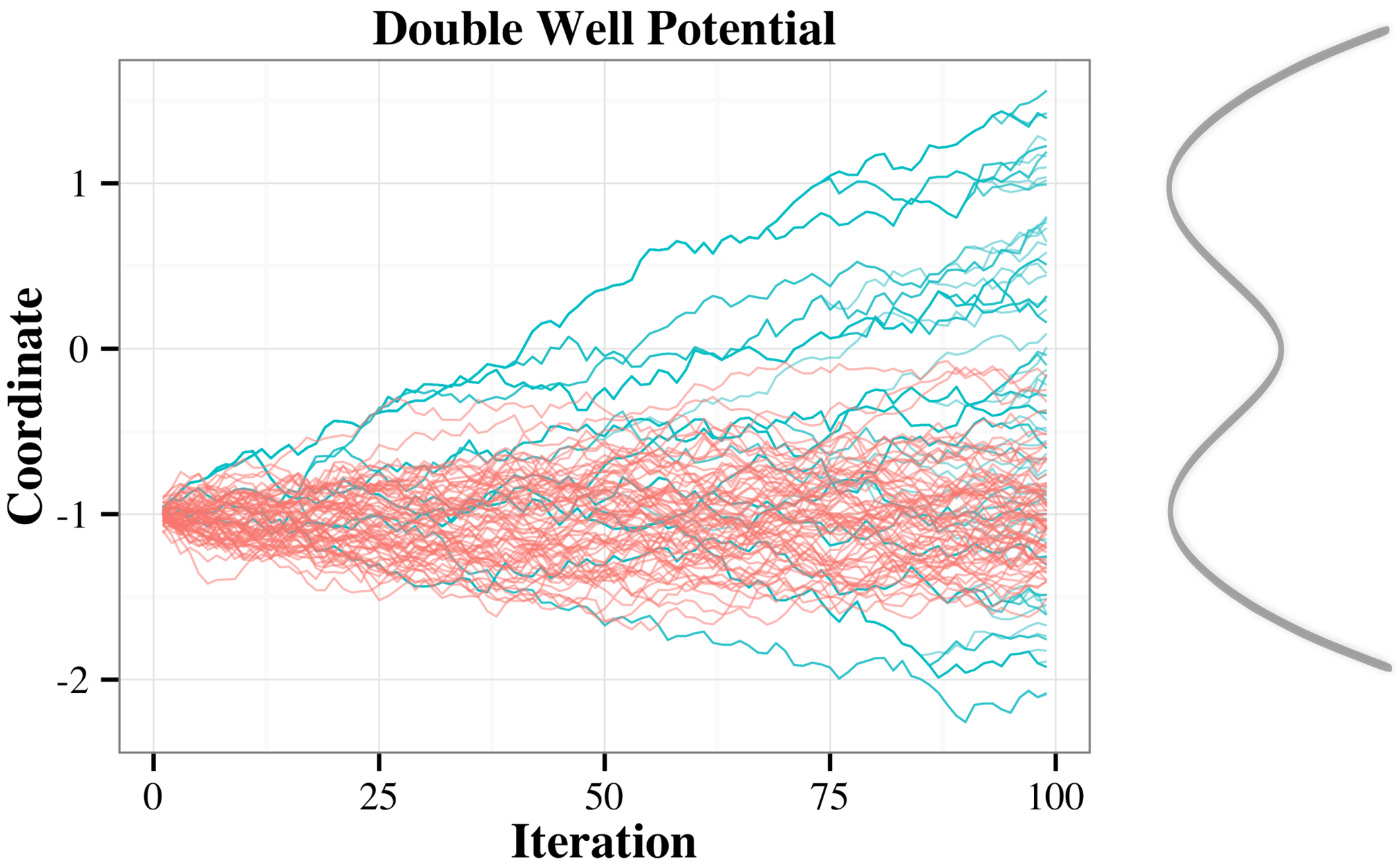


Normalized Histogram

Weighted Ensemble Sampling

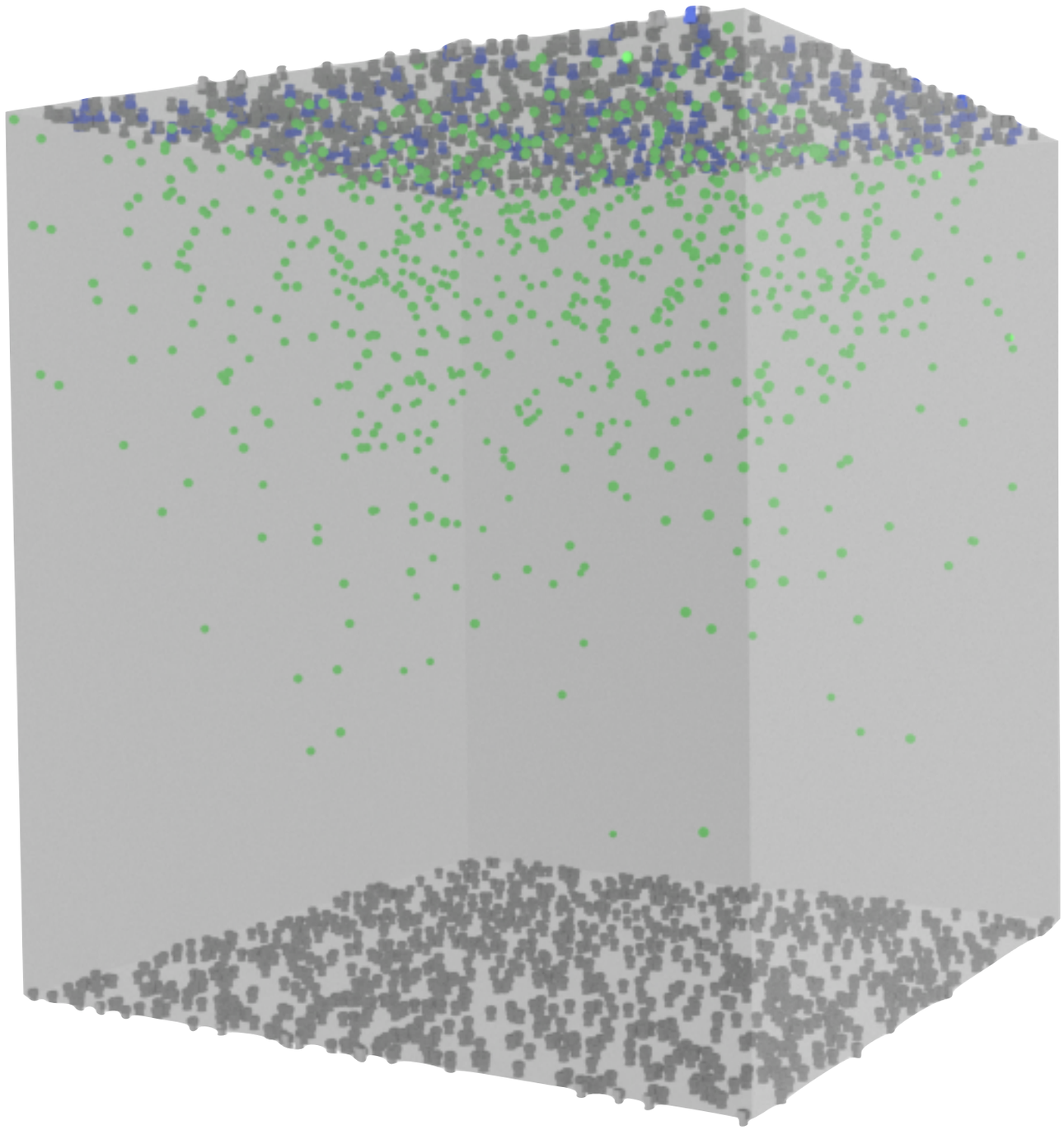


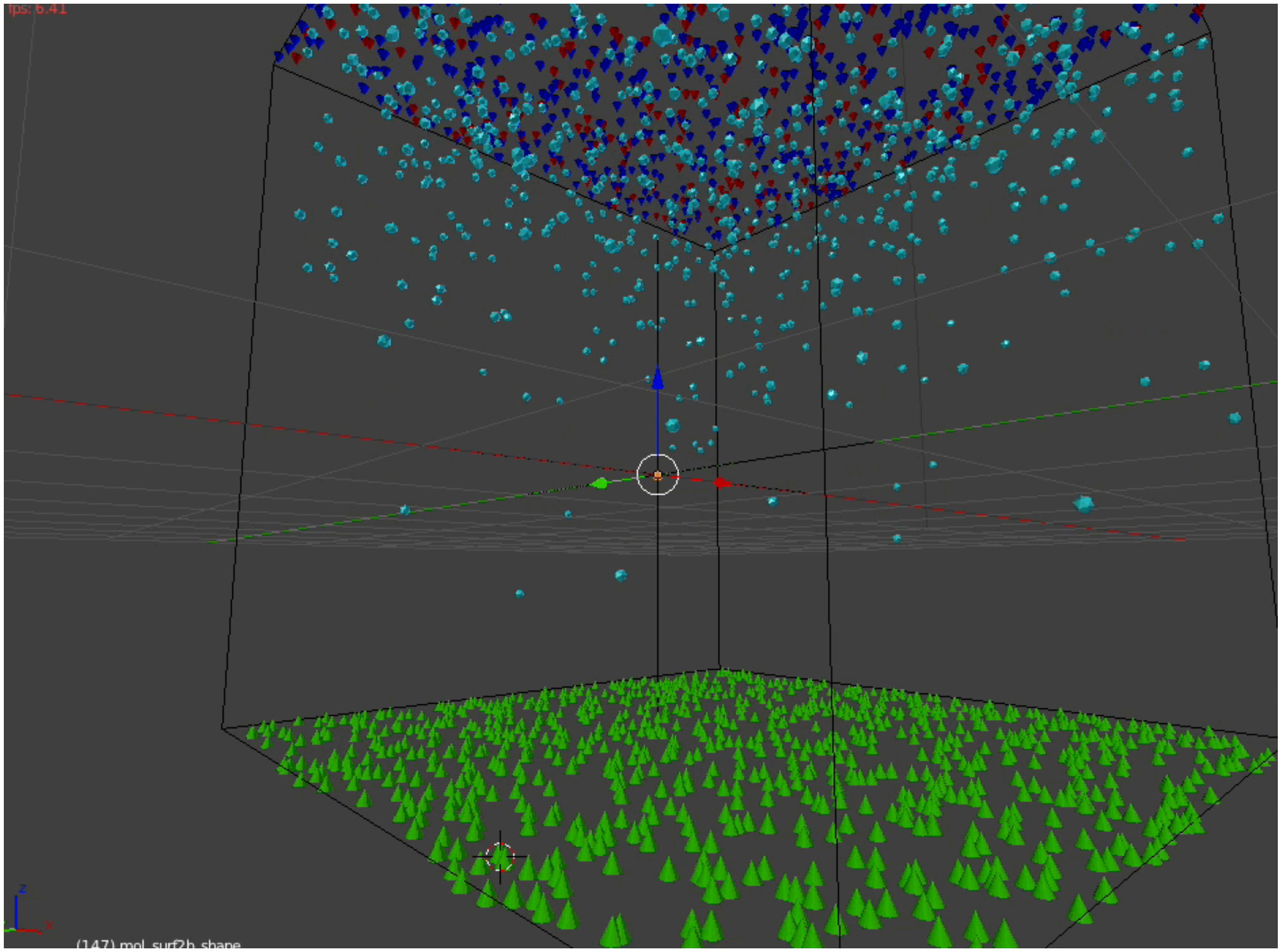
Ensembles:
Weighted vs Unweighted



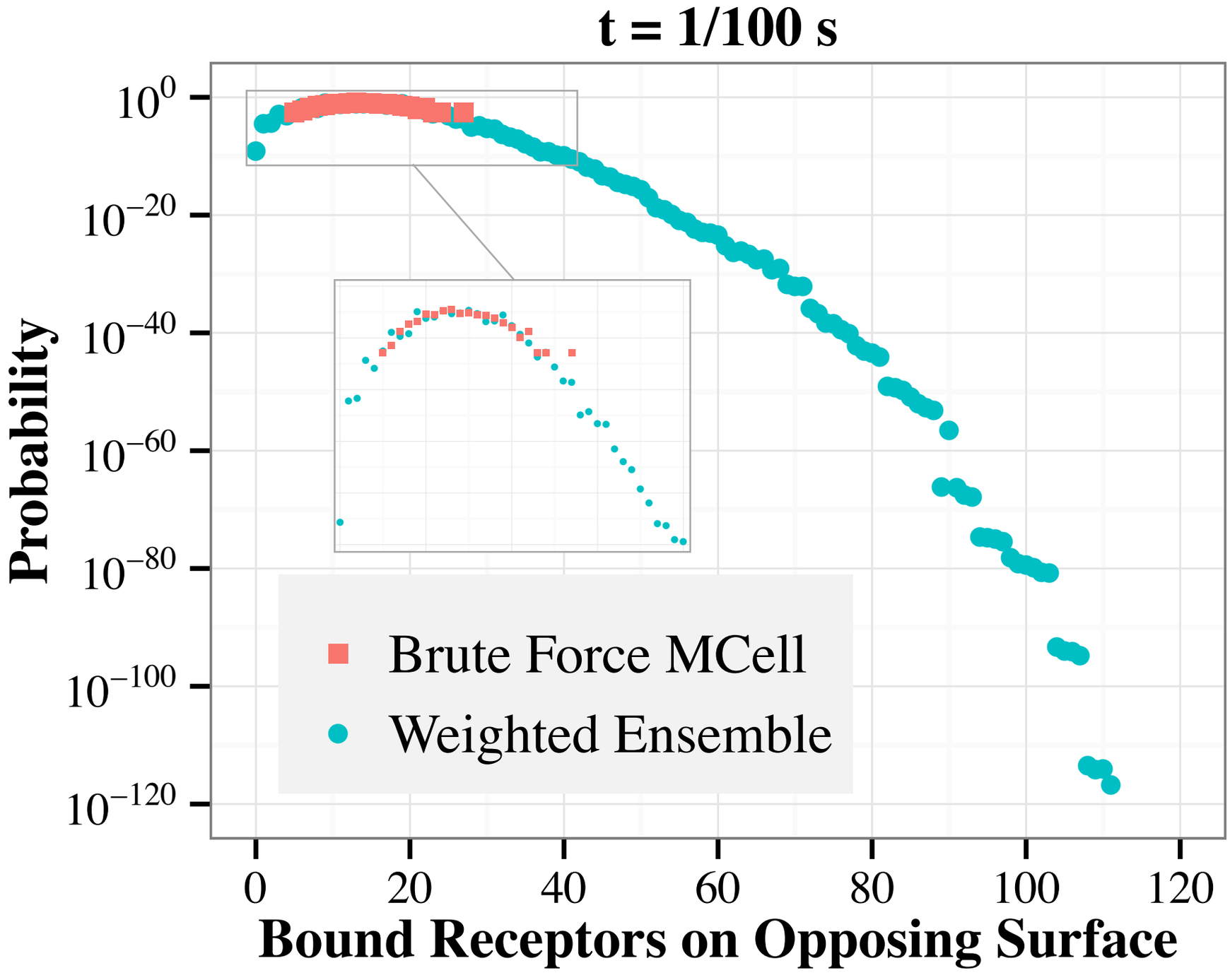
Spatial Stochastic Systems

Toy Model

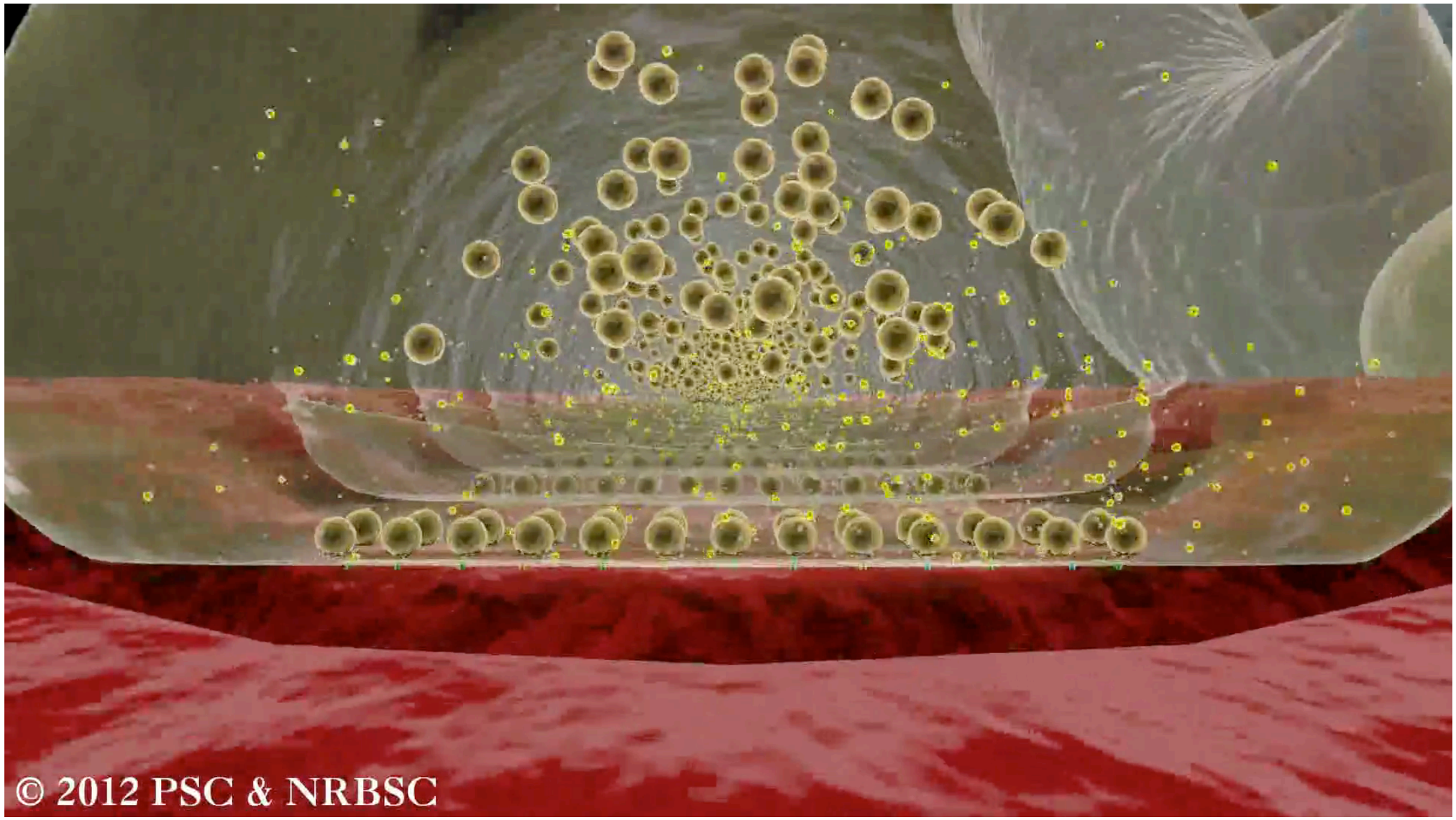



fps: 6.41
(147) mol_surf2b_shape

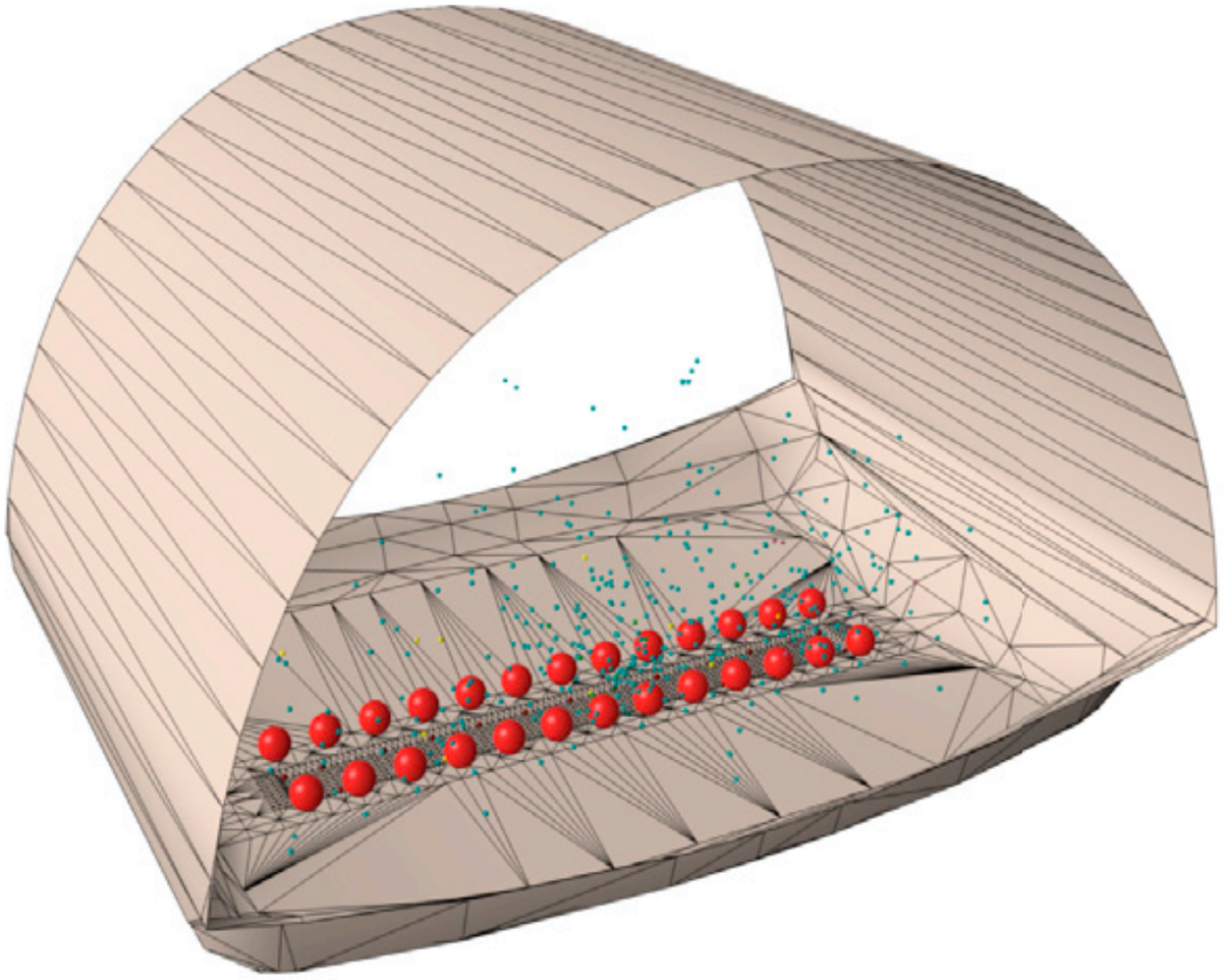
Toy Model Results

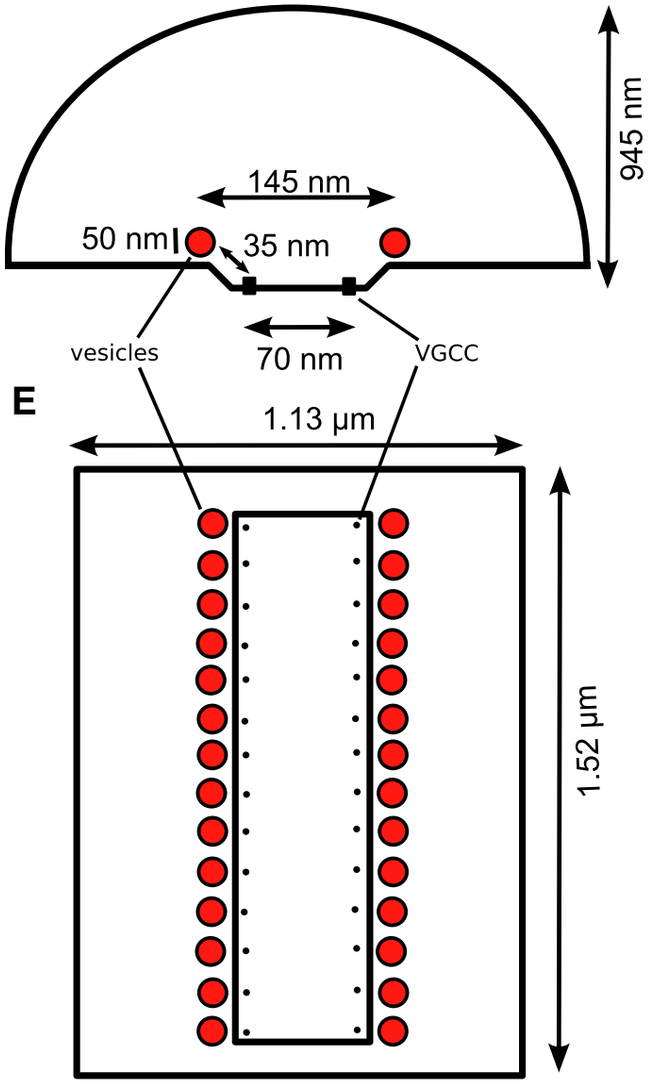


Neuromuscular Junction

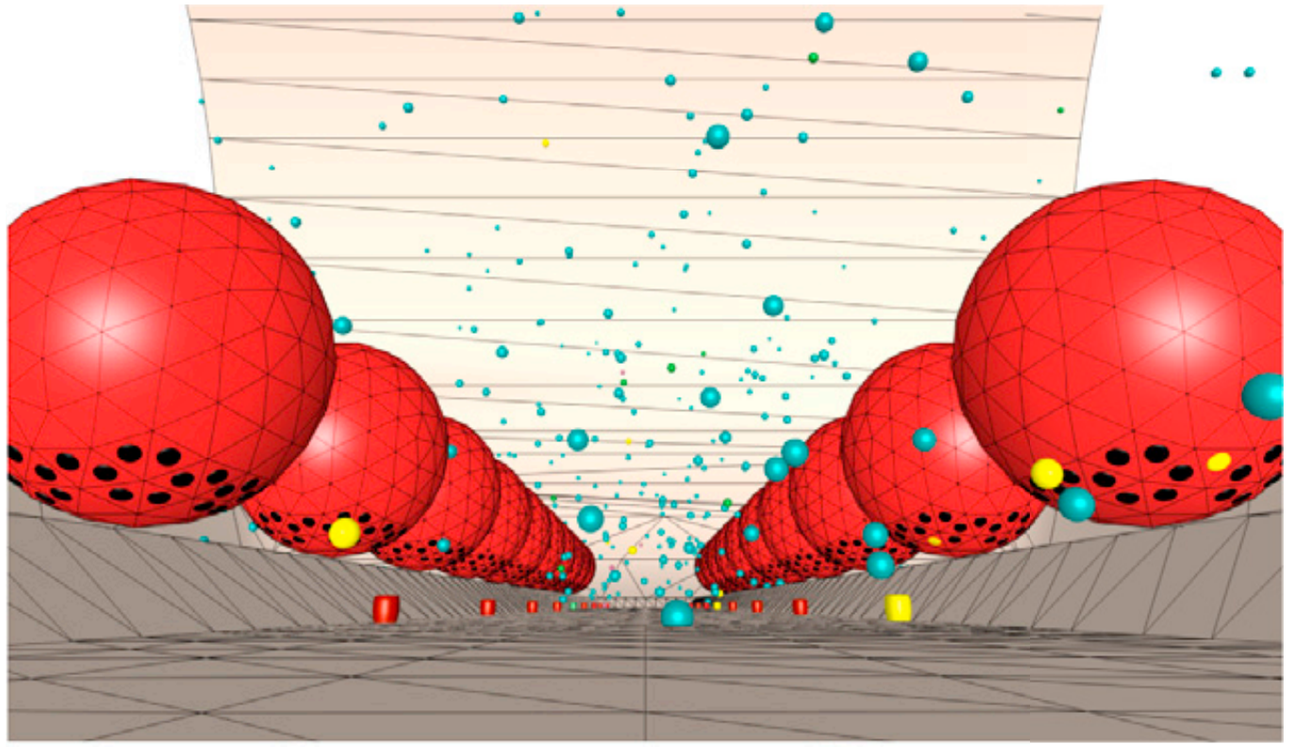


Neuromuscular Junction Model



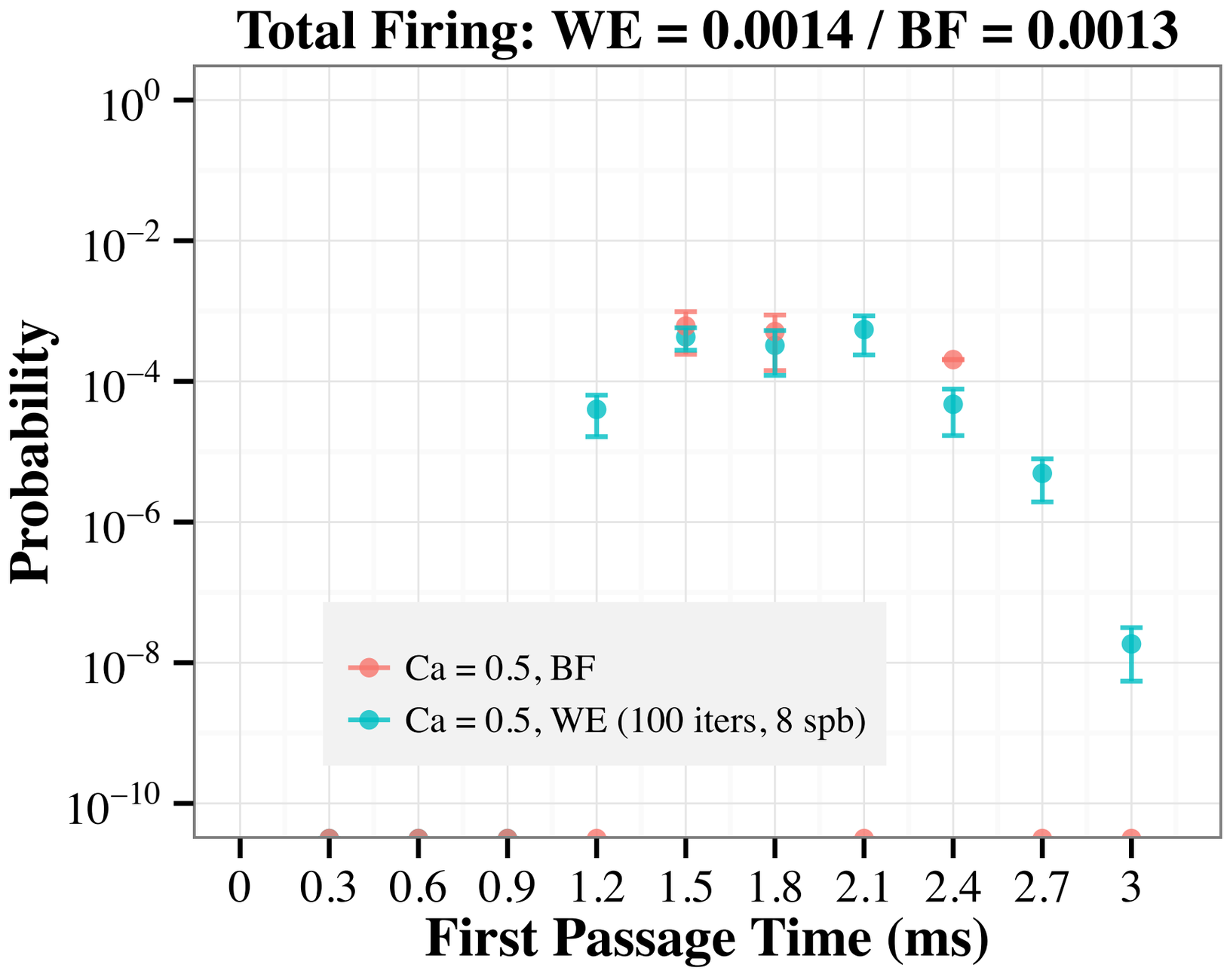


NMJ Zoomed-In

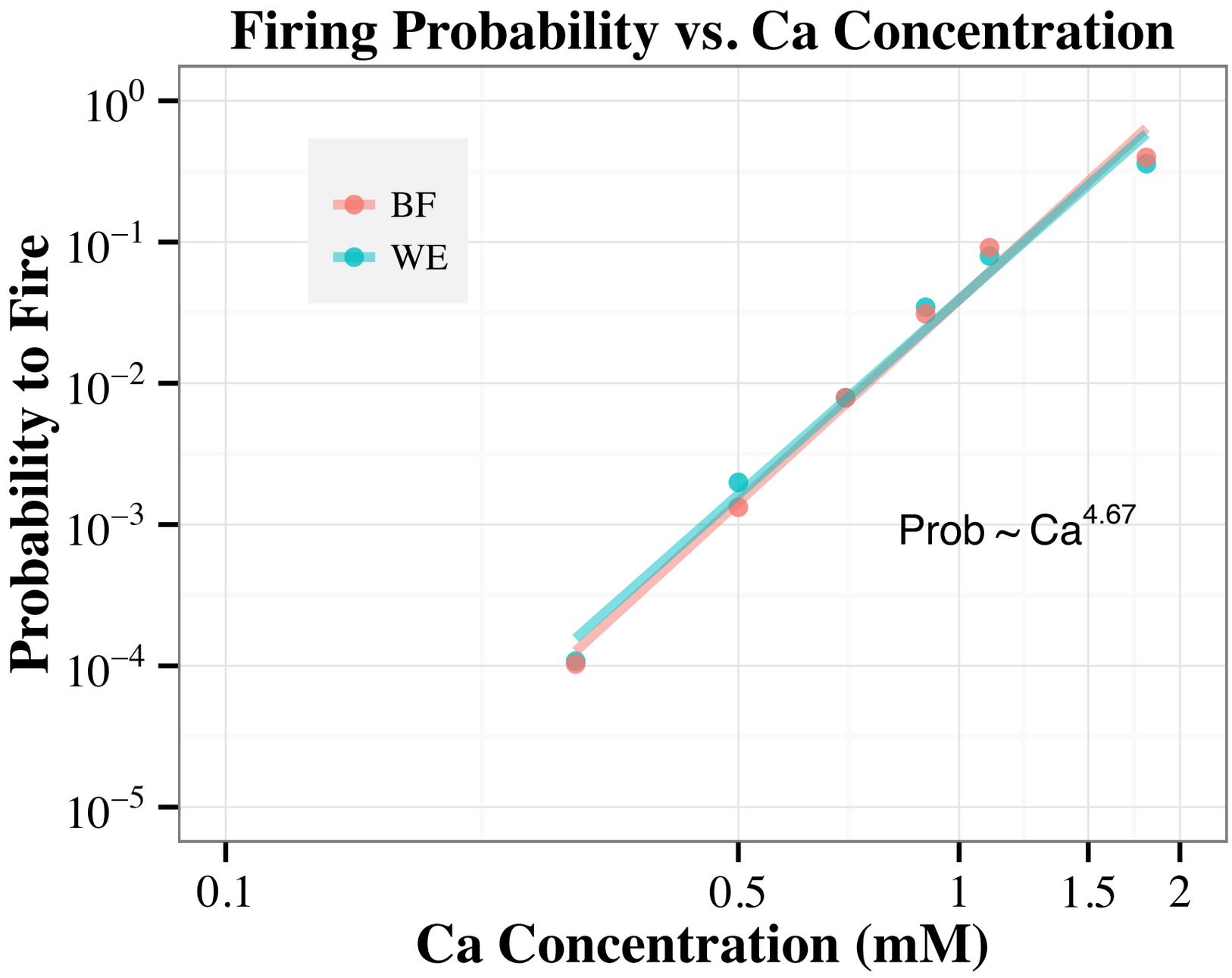


- Calcium is released from bottom, diffuses, and can bind to synaptotagmin vesicles
- Model: if enough calcium bind to one vesicle, in the right pattern, a release event occurs

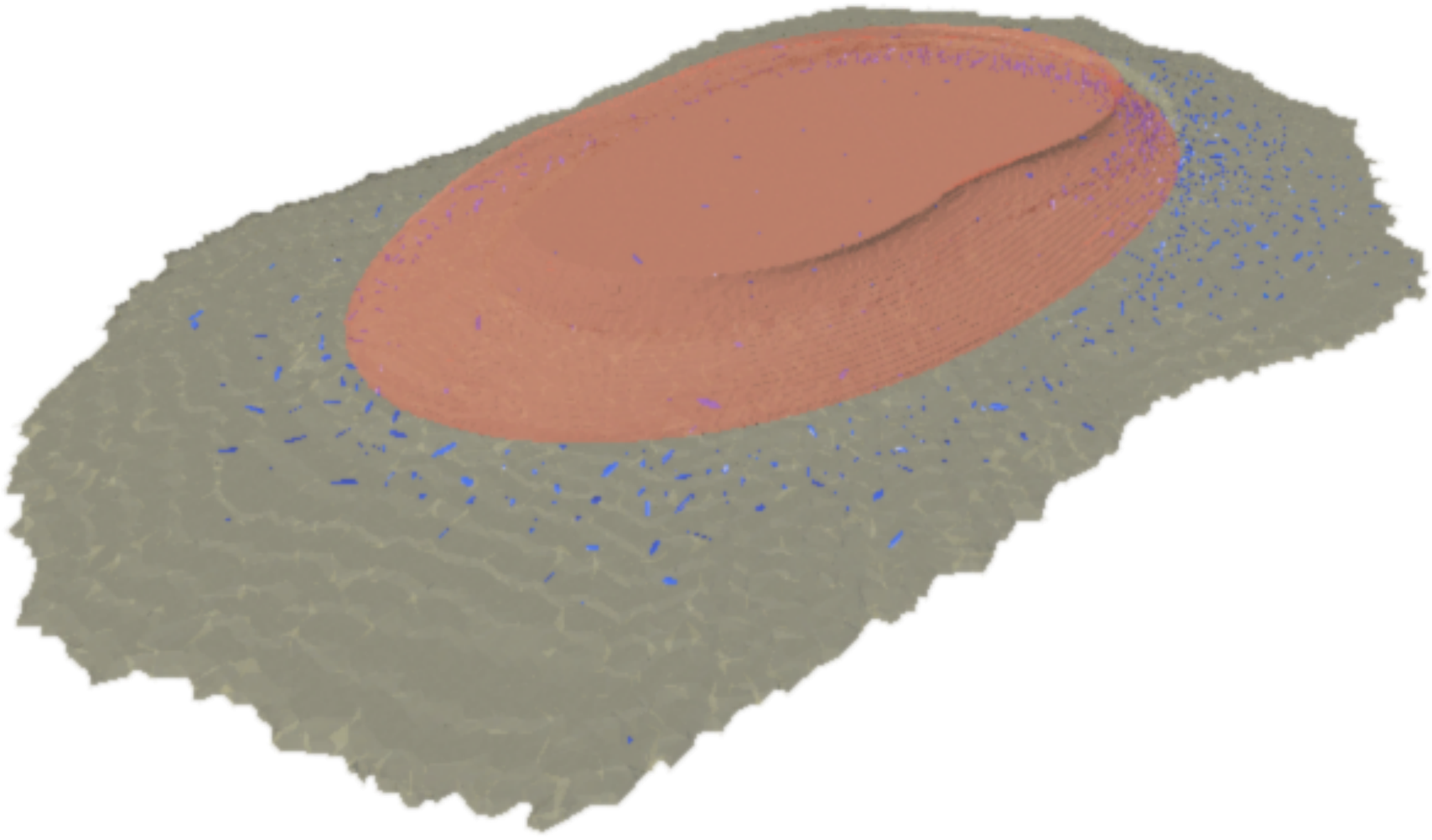
First Passage Times



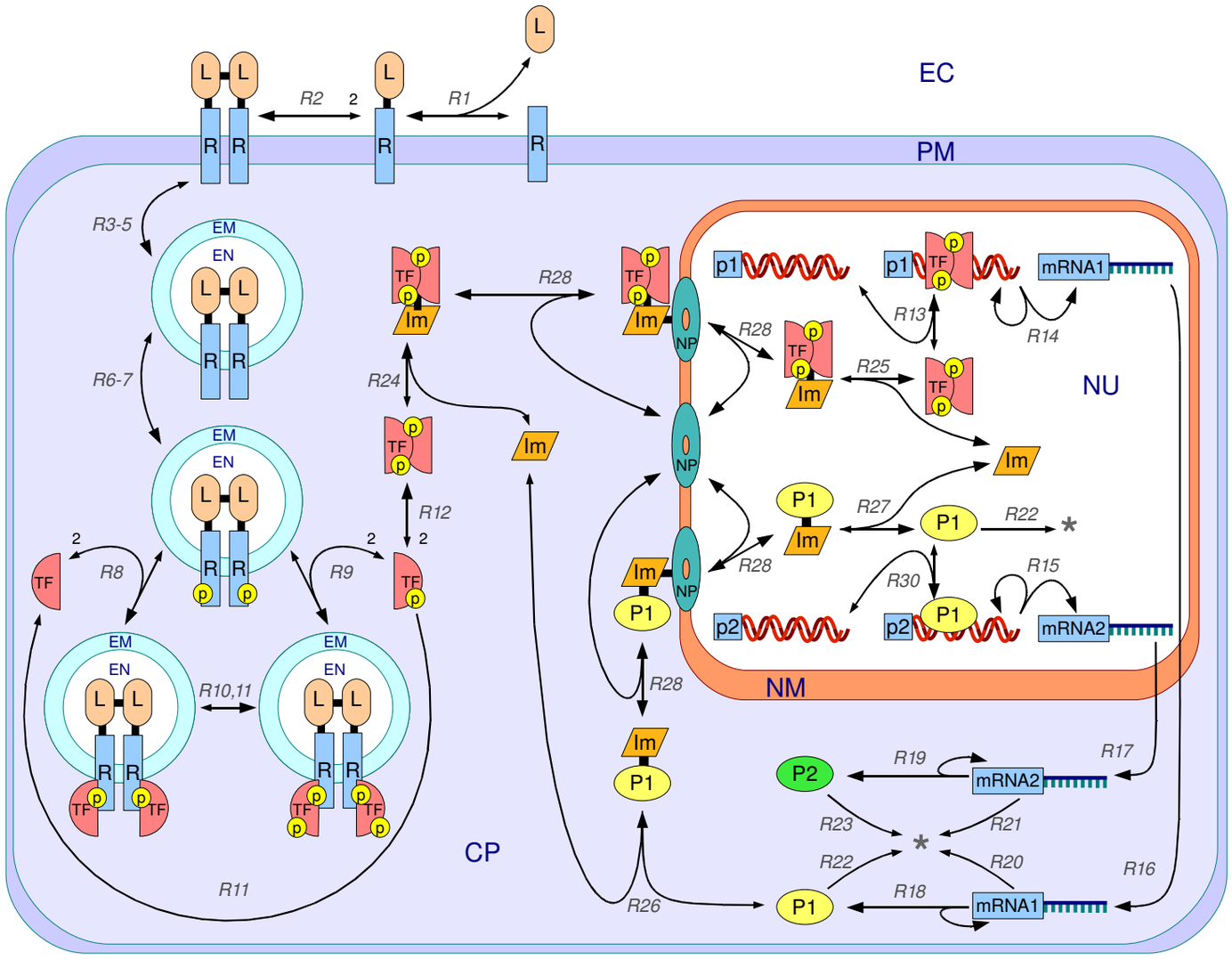
Scaling Relationship



Realistic Geometry

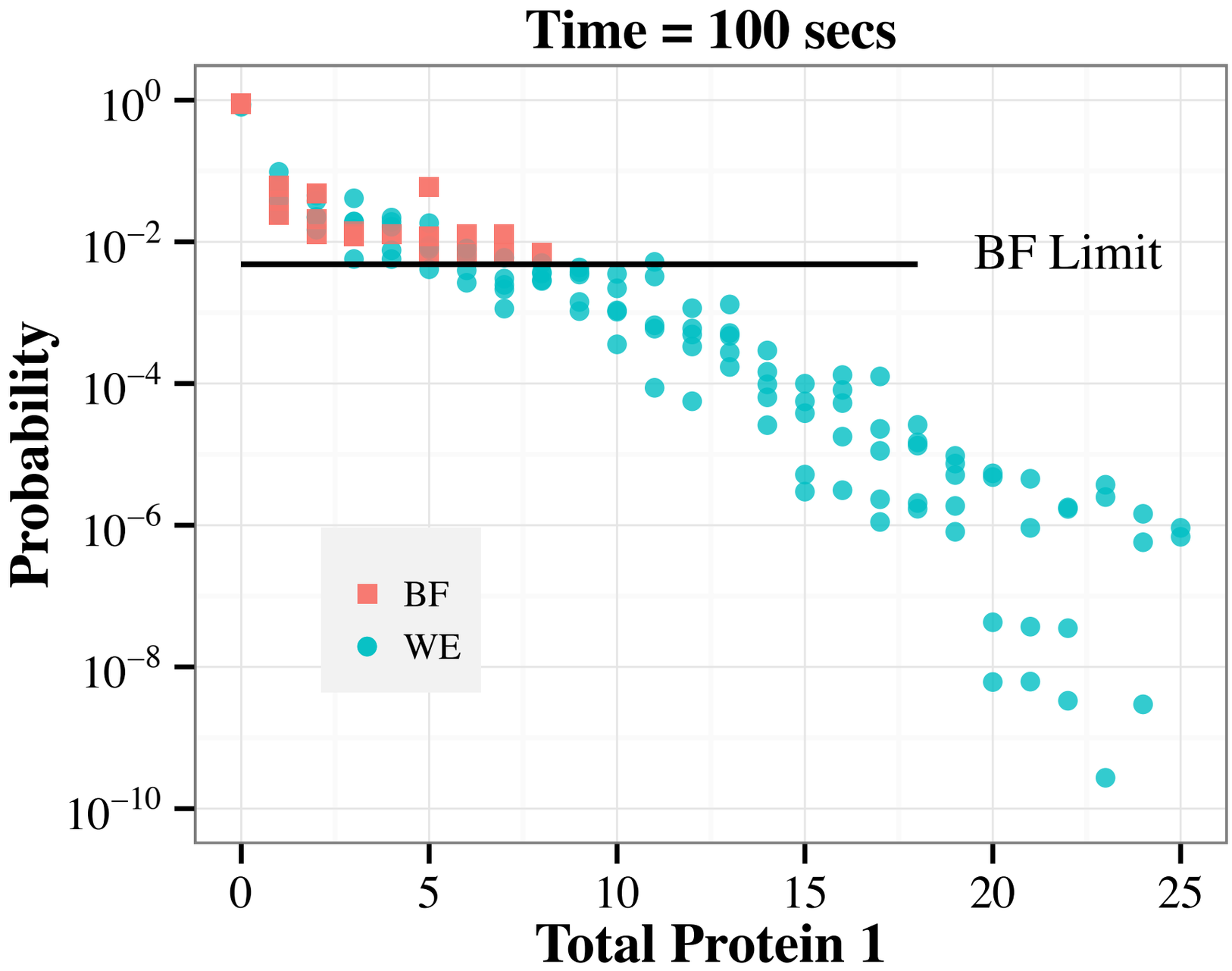


Signaling Network

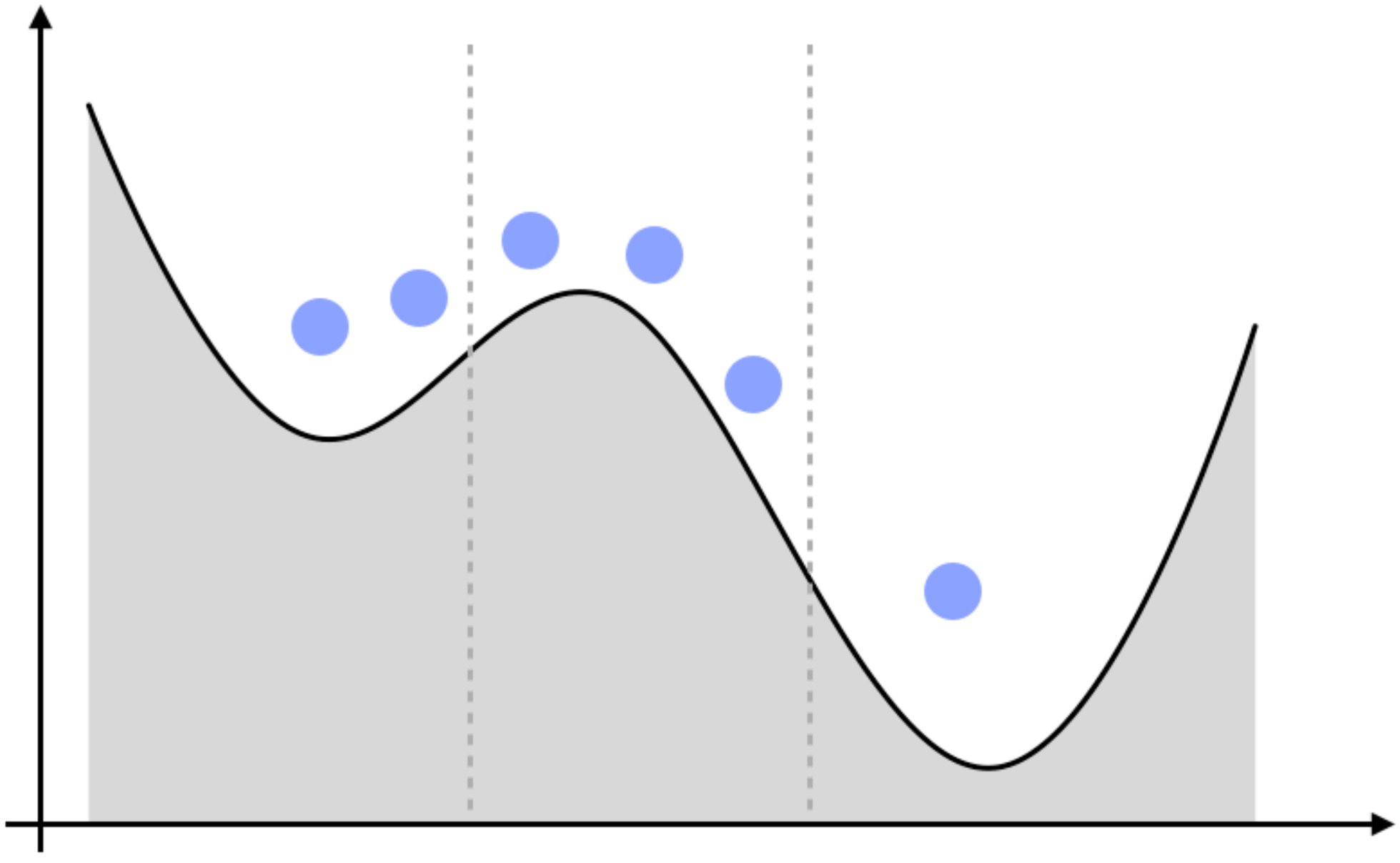


Pipeline: CellOrganizer → BioNetGen → MCell

Protein Histograms



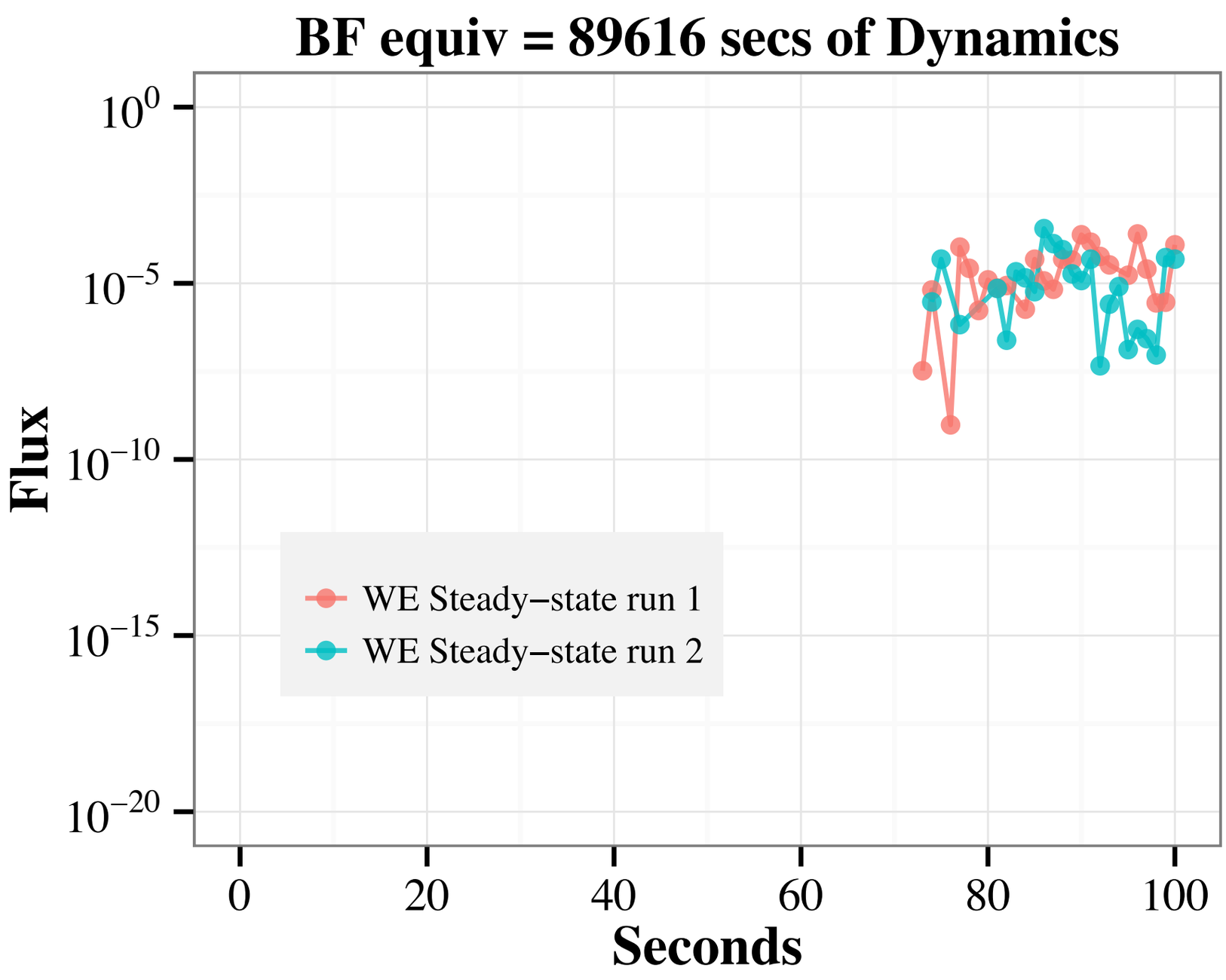
Steady-State



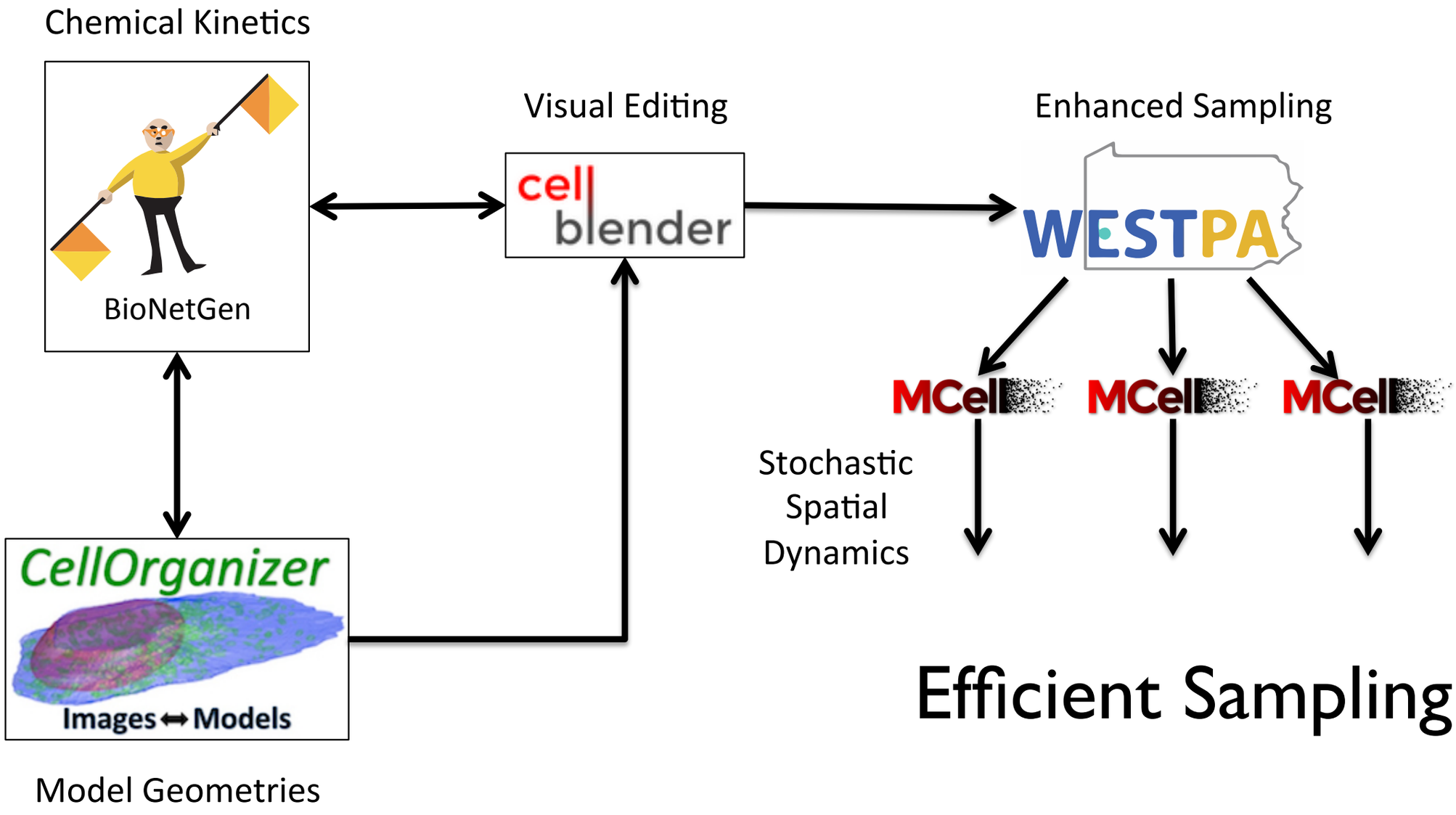
In steady state,

$$MFPT(A \rightarrow B) = 1/Flux(A \rightarrow B)$$

First Passage Times



Pipeline: MMBioS



Conclusions

- Able to sample the rare events and full distributions for stochastic systems biology models over a wide range of complexity
- Speed-up over brute-force is dramatic enough encourage the design of more complex, more realistic models
- Long time-scale behavior can be extrapolated from short simulations: can bridge dynamics over multiple timescales

Thanks

- Collaborators:
  - Jose, Devin, Markus, Jim, Bob, Dan
- Funding:
  - SF Grant No. MCB-1119091
  - NIH Grant No. P41 GM103712
  - NIH Grant No. T32 EB009403
  - NIH Grant No. GM090033
  - NSF Expeditions in Computing Grant (Award No. 0926181)