

Part III – Towards in silico Cells: Simulating processes in entire cells

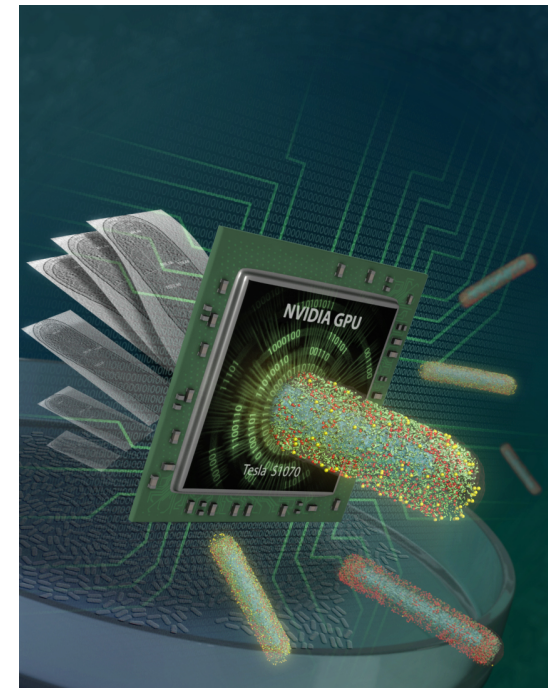
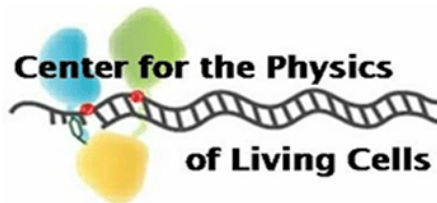
Zaida (Zan) Luthey-Schulten

Dept. Chemistry, Physics, Beckman Institute, Center for Biophysics, and

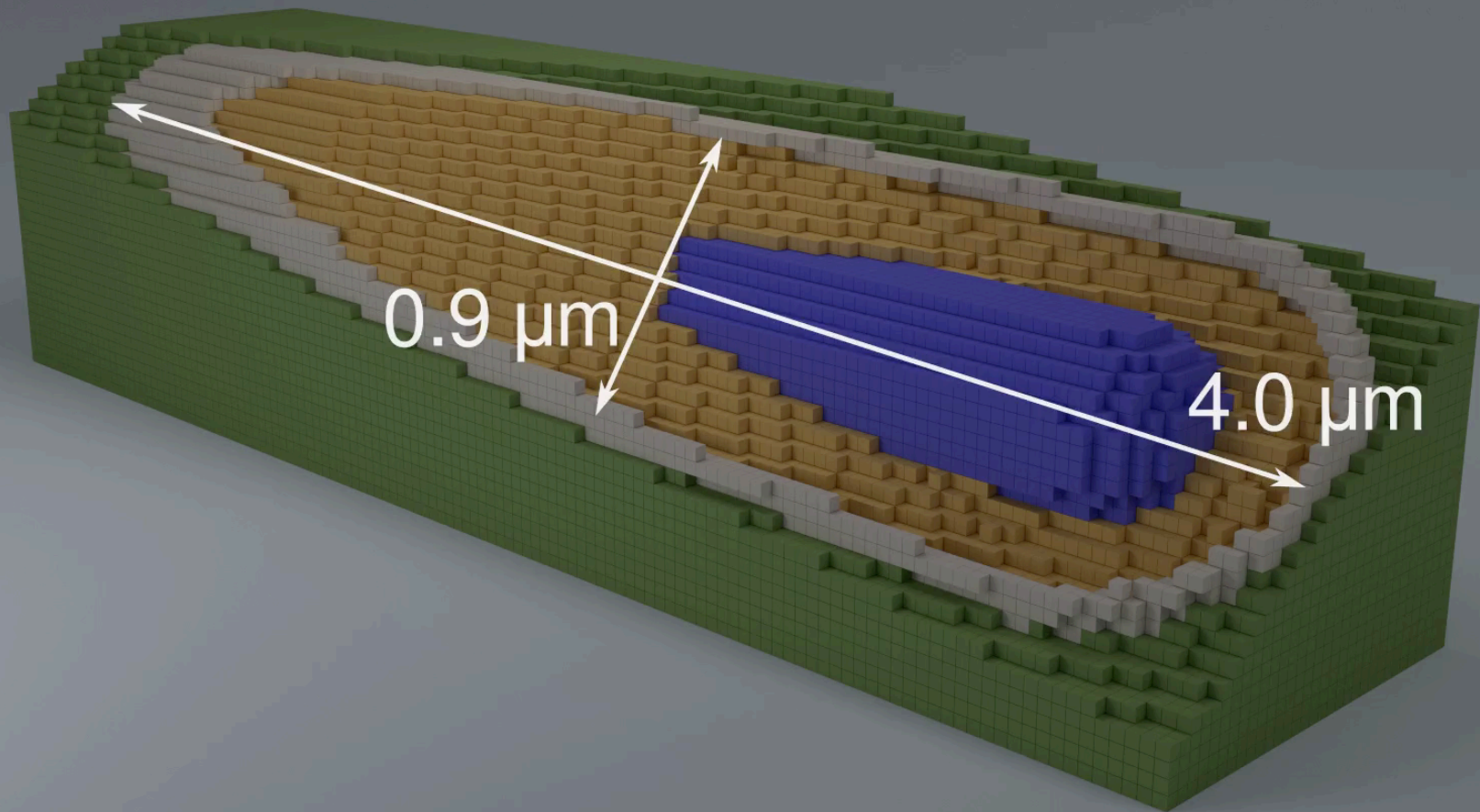
Carl Woese Institute of Genomic Biology, UIUC

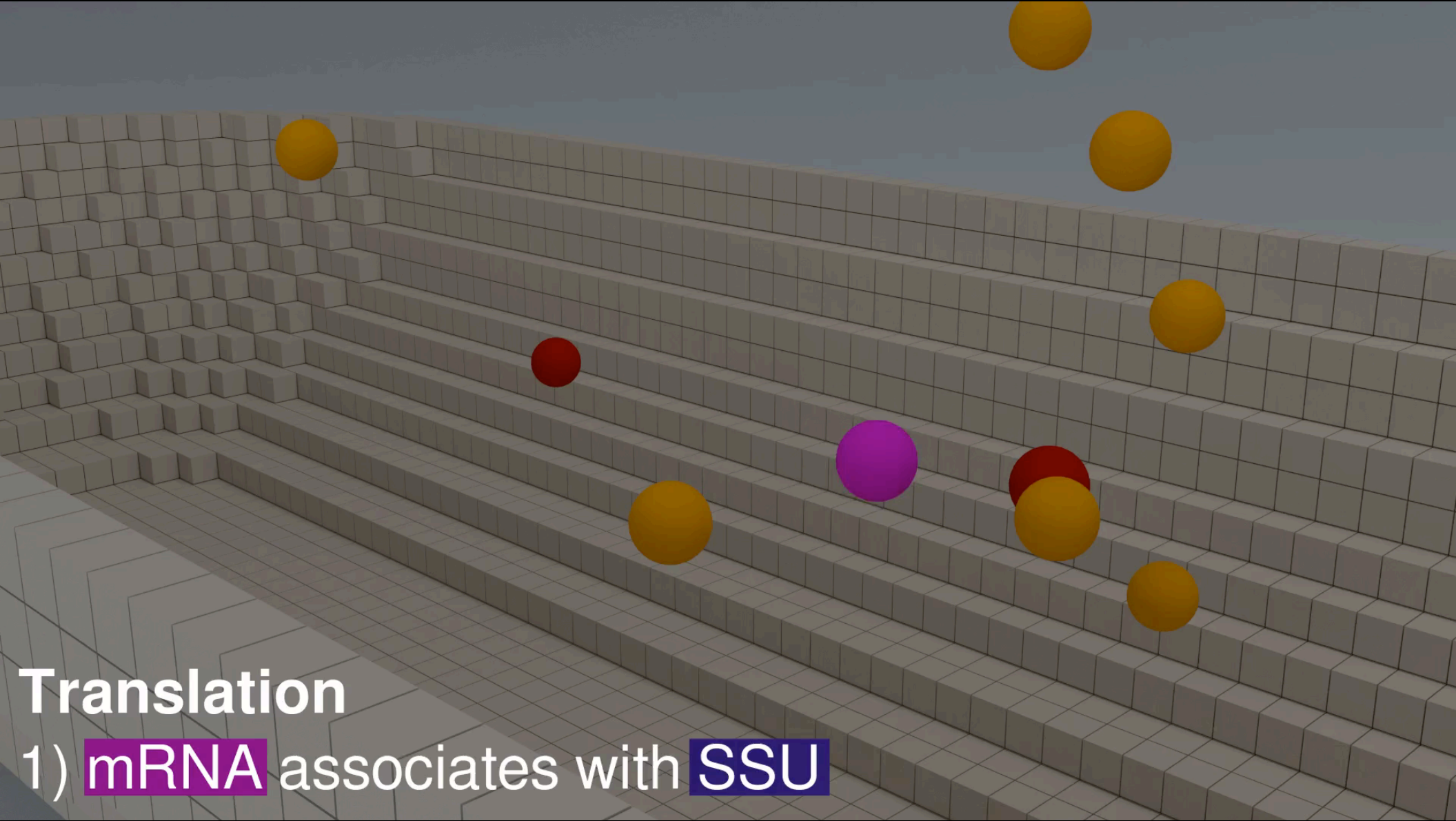
NIH Computational Biophysics Workshop, Pittsburgh, June 6-8, 2016

with **Mike Hallock and Joe Peterson**



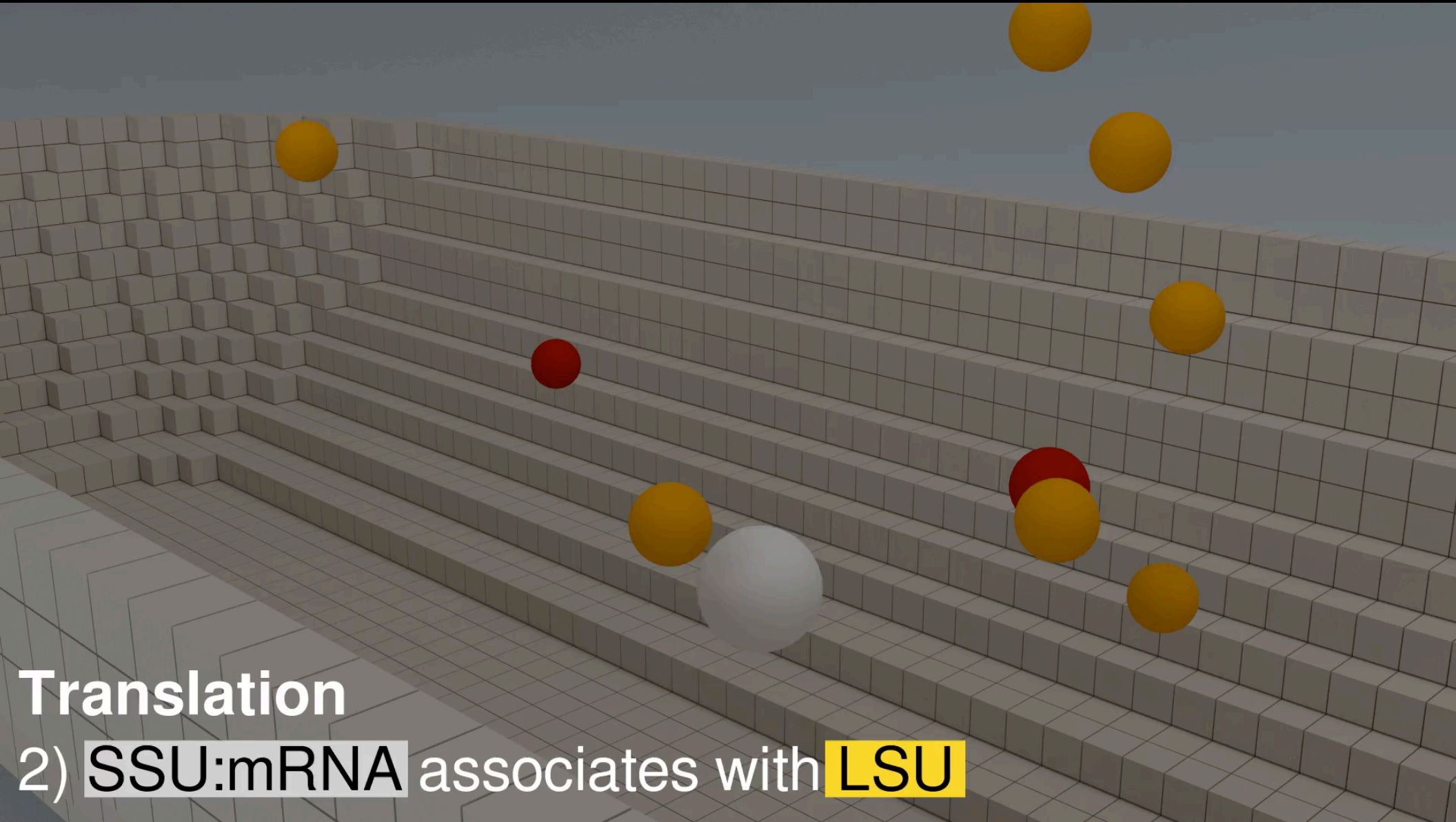
Cell dimensions





Translation

1) mRNA associates with SSU



Translation

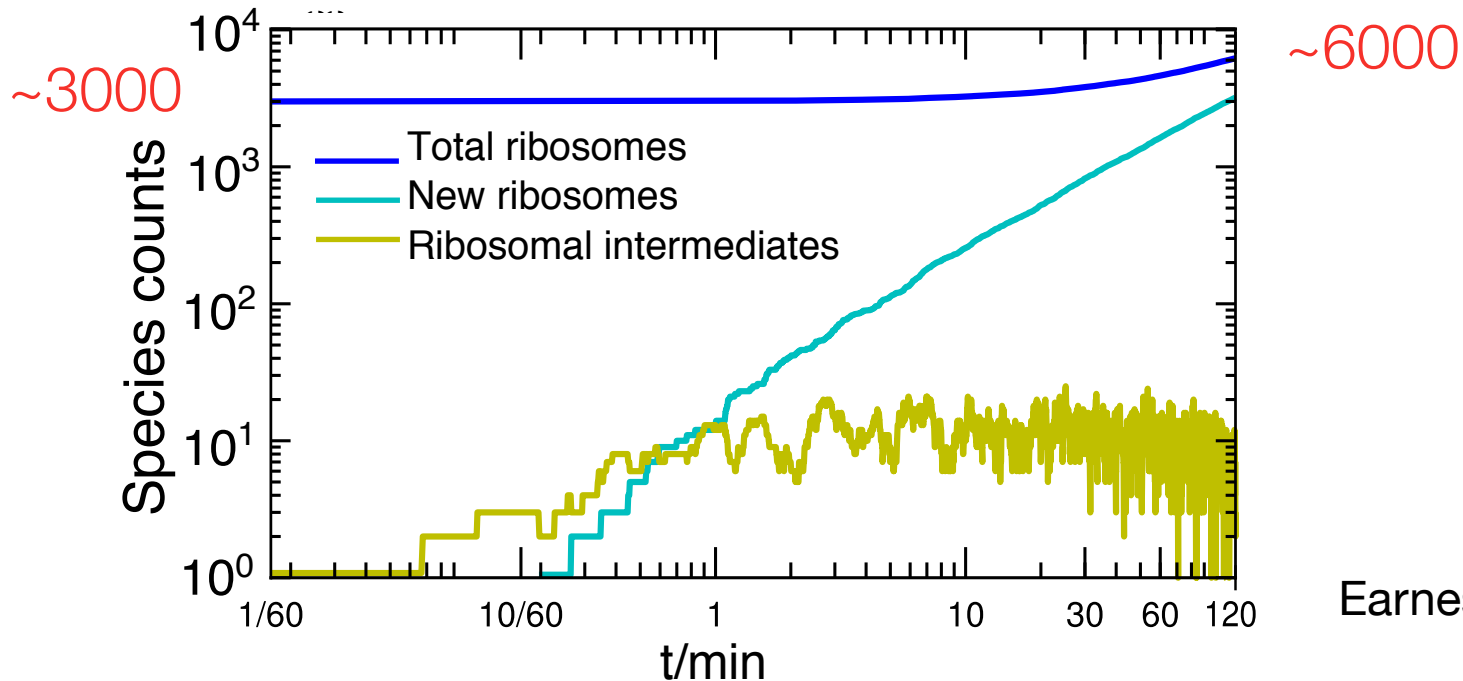
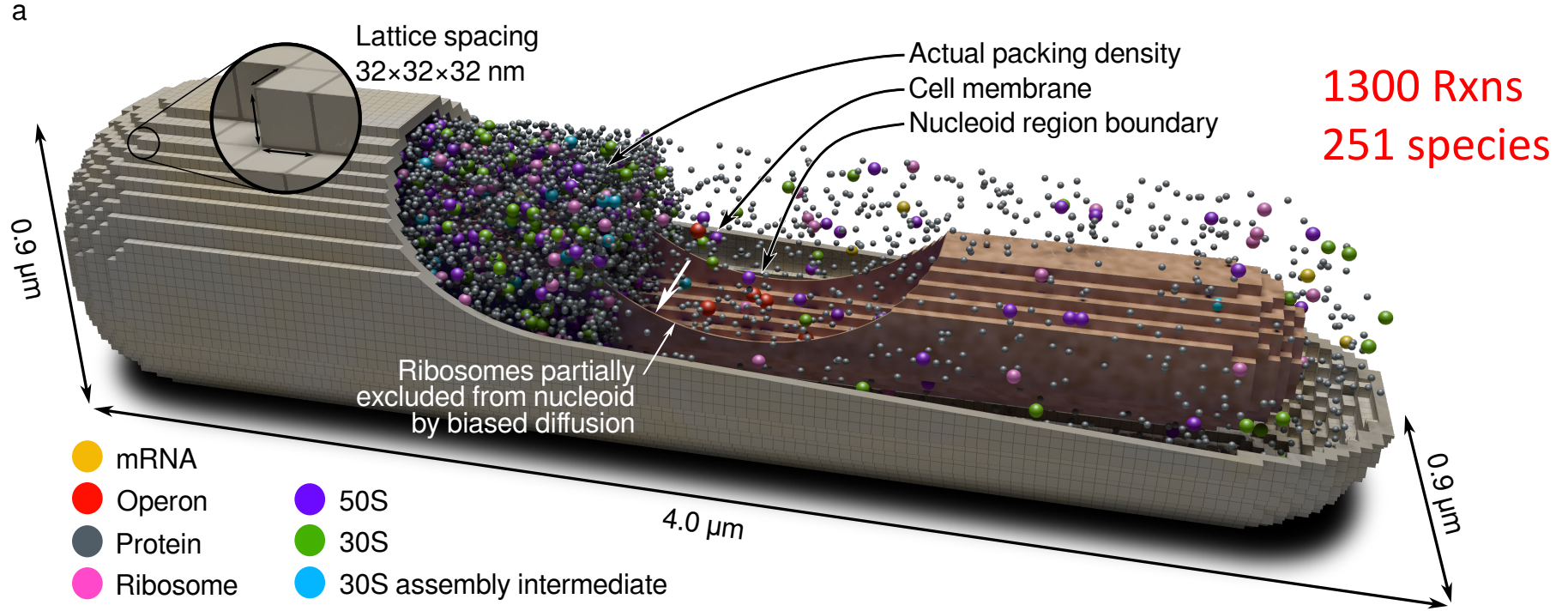
2) **SSU:mRNA** associates with **LSU**



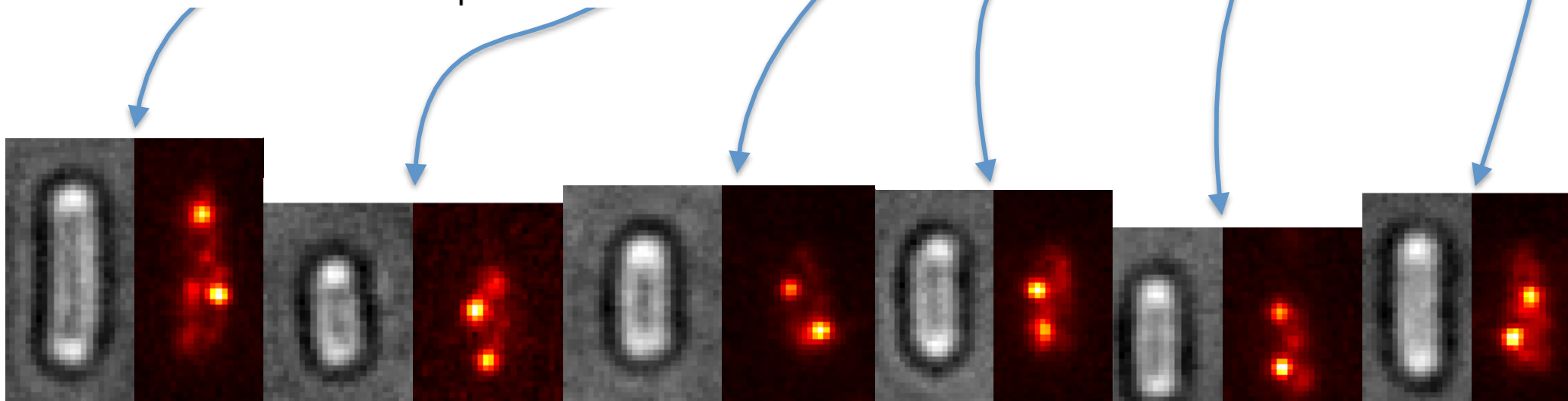
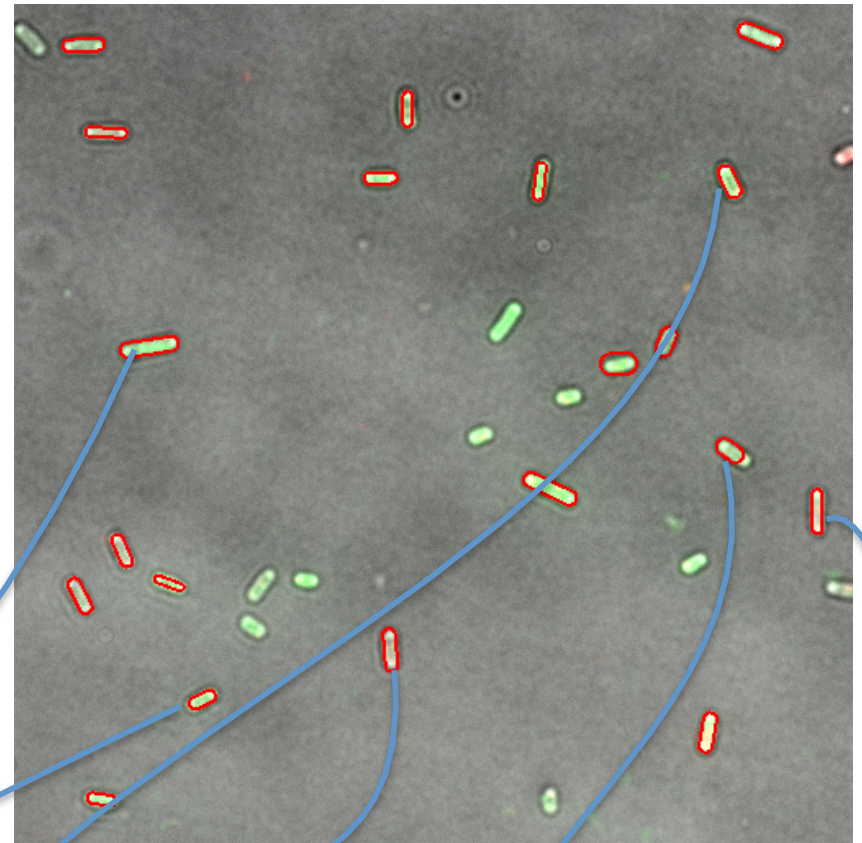
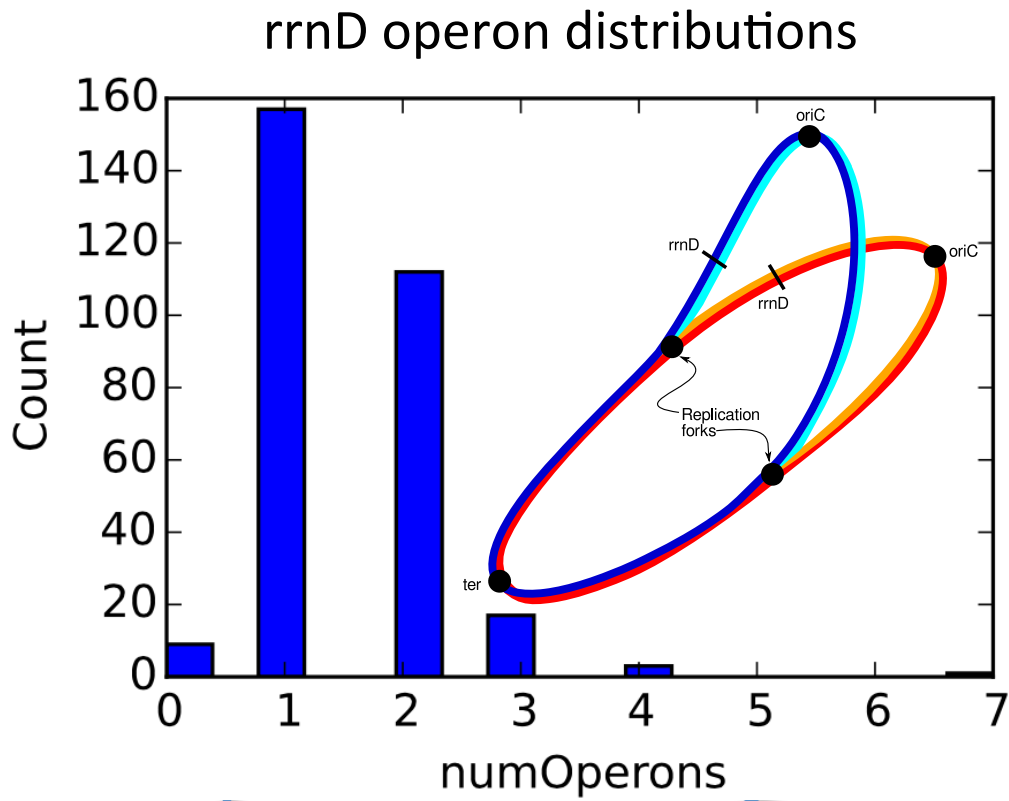
Translation

3) Ribosome produces protein with rates derived from operon structure

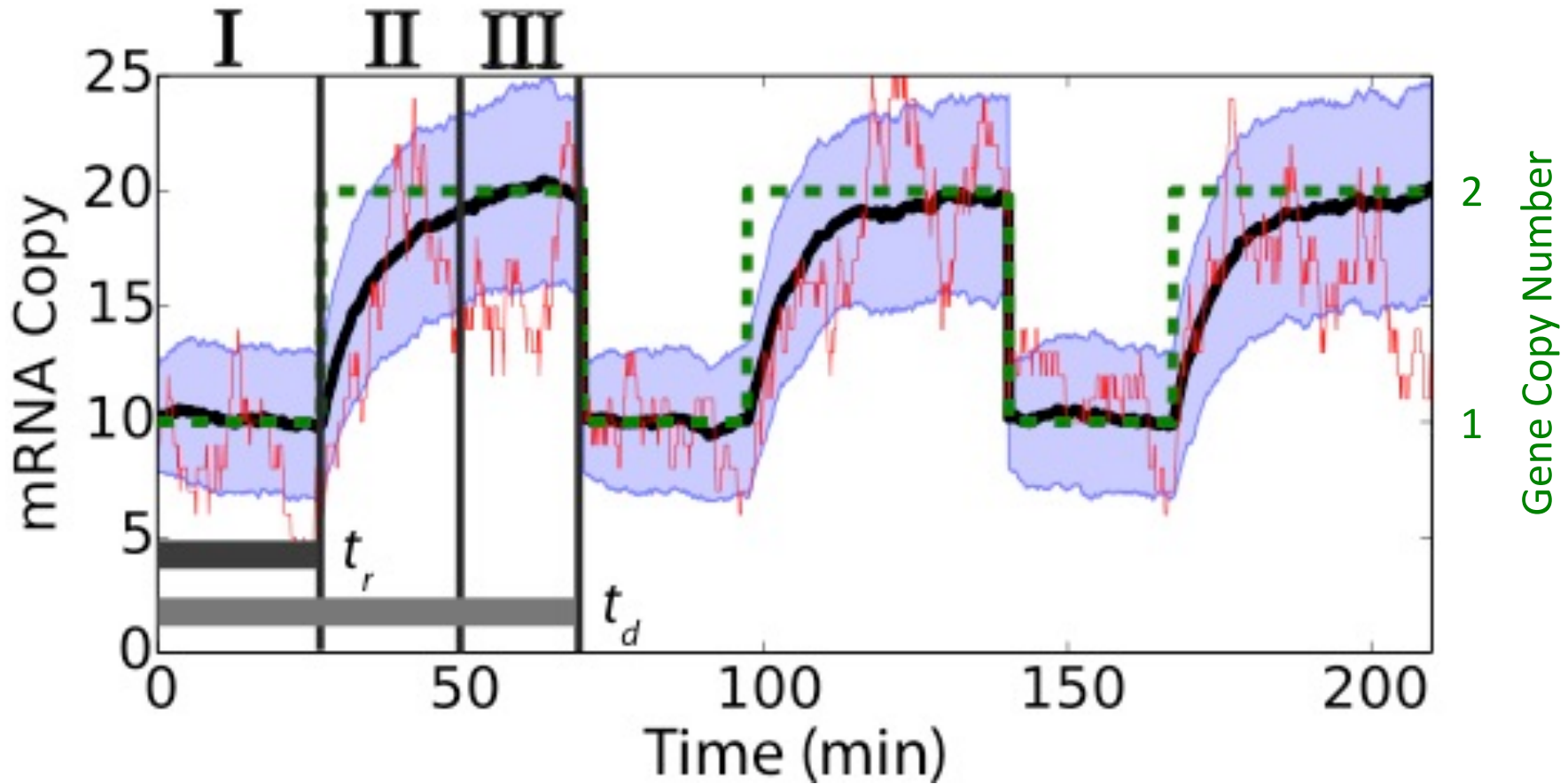
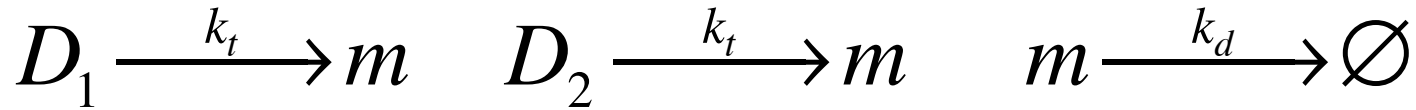
In silico Ribosome Biogenesis



Correcting for gene copies?

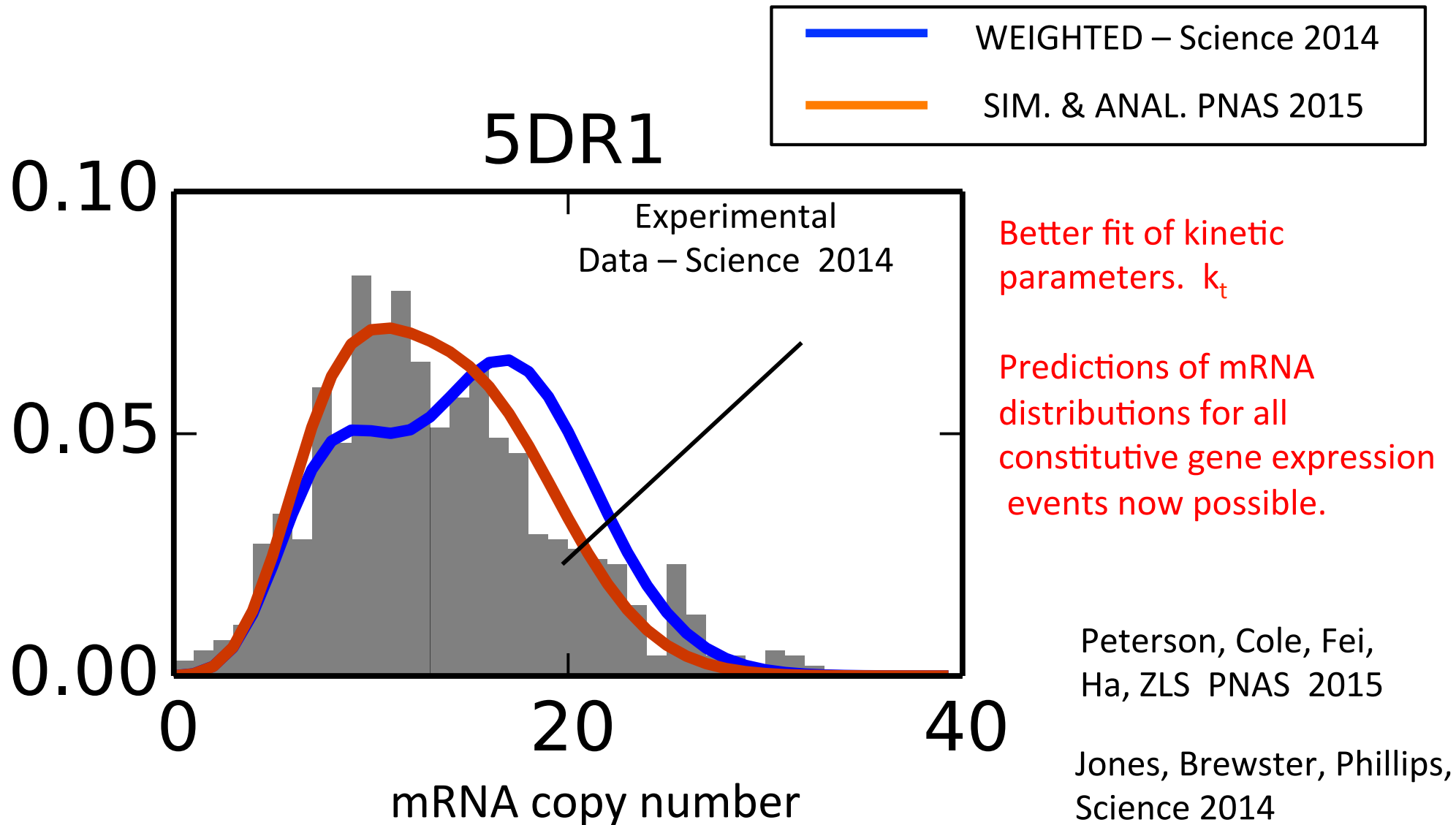


Stochastic Simulations with 2 Gene Copies



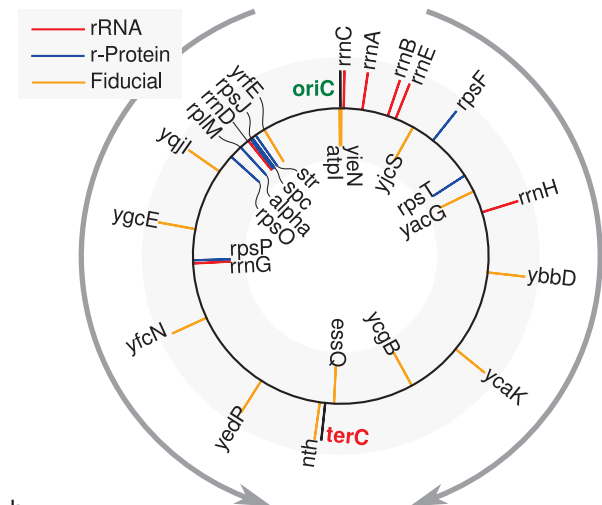
— Single trajectory — mean ■ (+/-) 1 σ - - - Gene copy number

Explicit Replication Model Matches Experimental mRNA Distributions



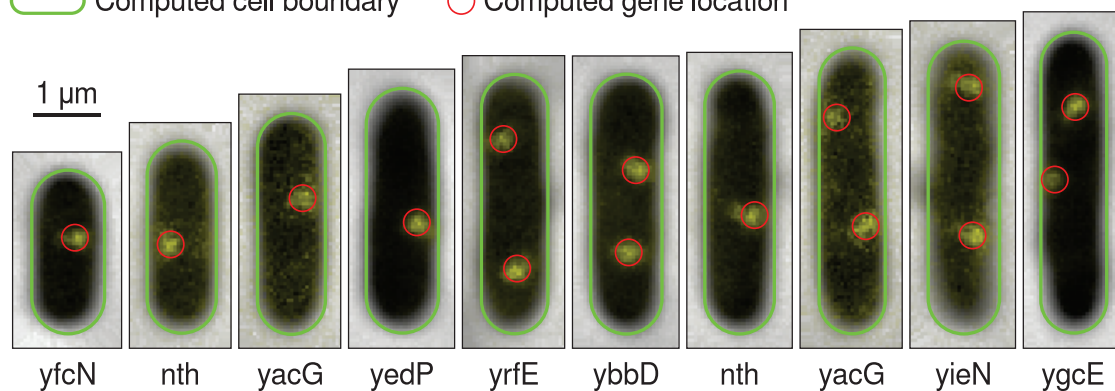
Measuring and Simulating DNA Replication

a

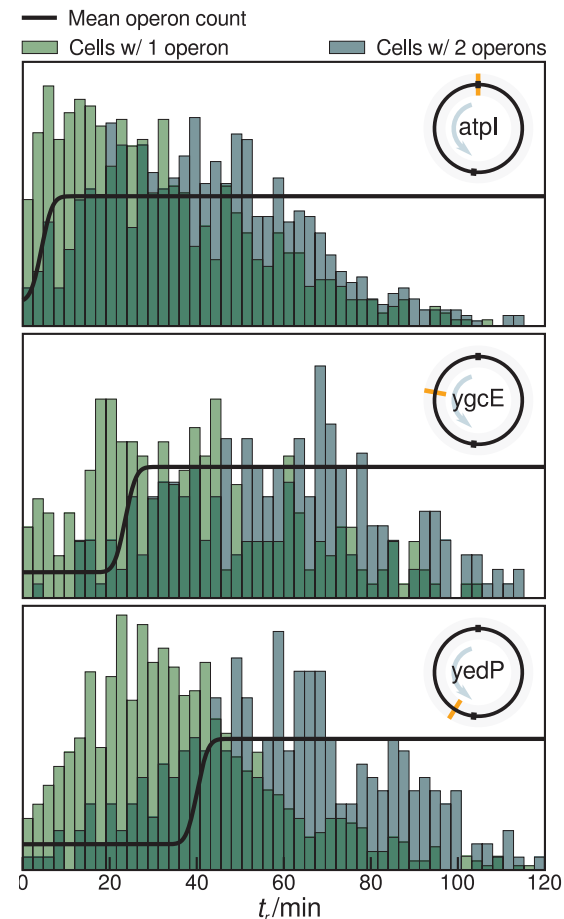


b

○ Computed cell boundary ○ Computed gene location

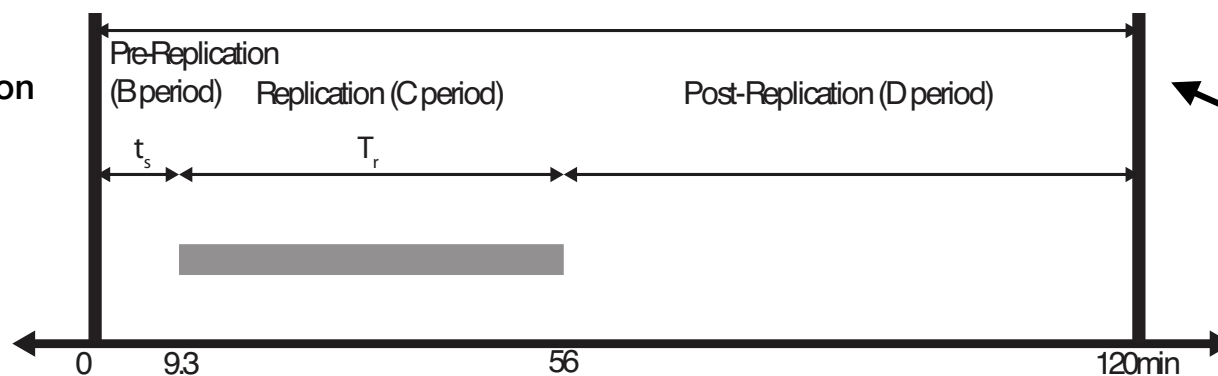


c



Initiation of Replication
9.3 min

Replication Time
45 min

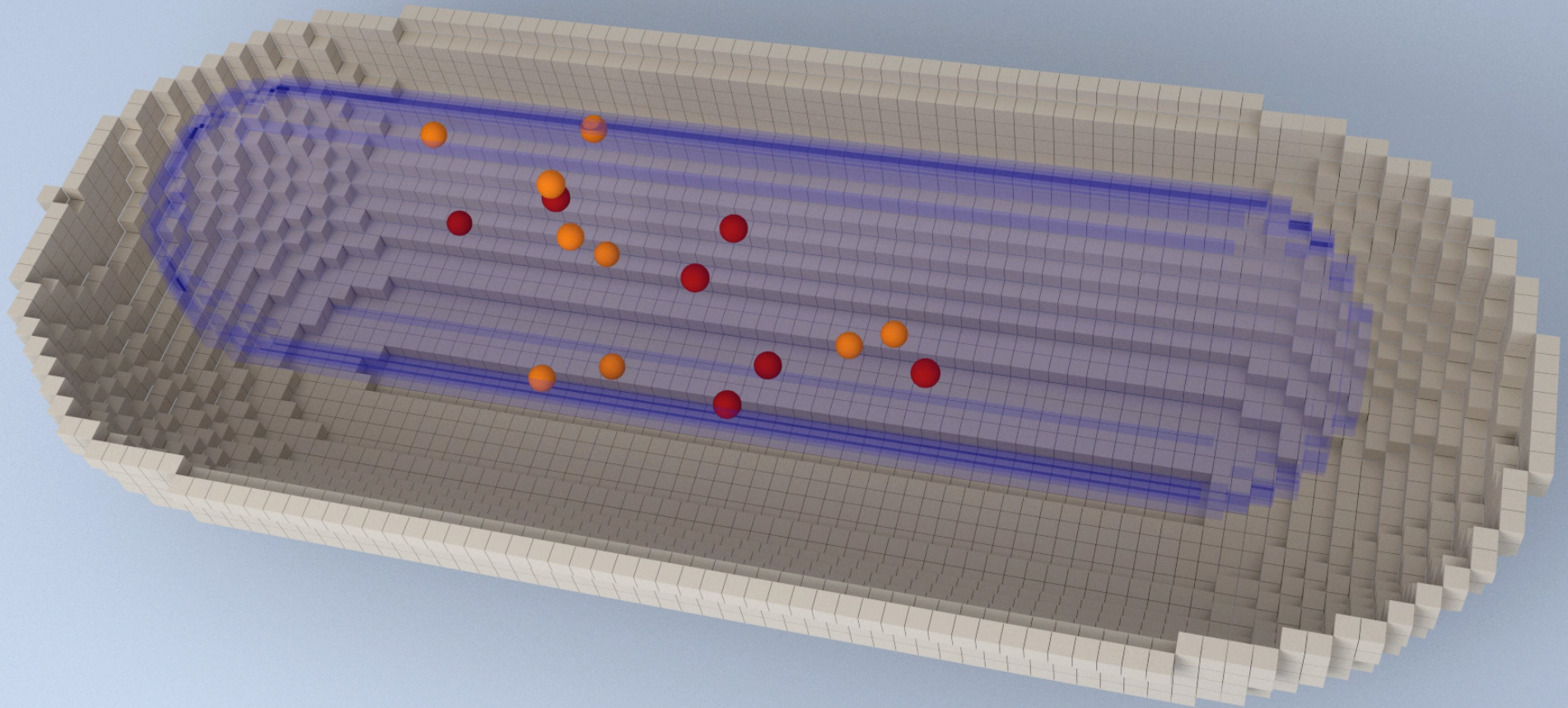


Cell Division

Dividing Cell in Lattice Microbes - Slow Growing *E. coli*

Correcting for DNA Replication

- | | | | |
|---------------------------|------------------|------------------|------------------|
| ● New SSU | ● rRNA operon | ● Intermediate 1 | ● Intermediate 4 |
| ● Translation initiation | ● r-prot. operon | ● Intermediate 2 | ● Intermediate 5 |
| ● Translation termination | ● mRNA | ● Intermediate 3 | ● Intermediate 6 |



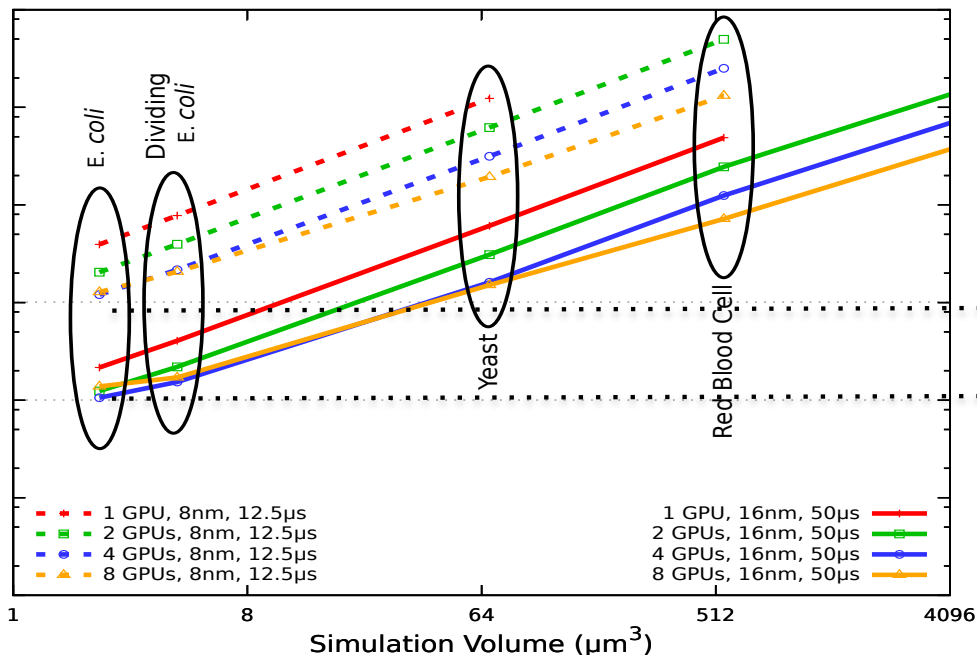
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Improving Multi-GPU Performance

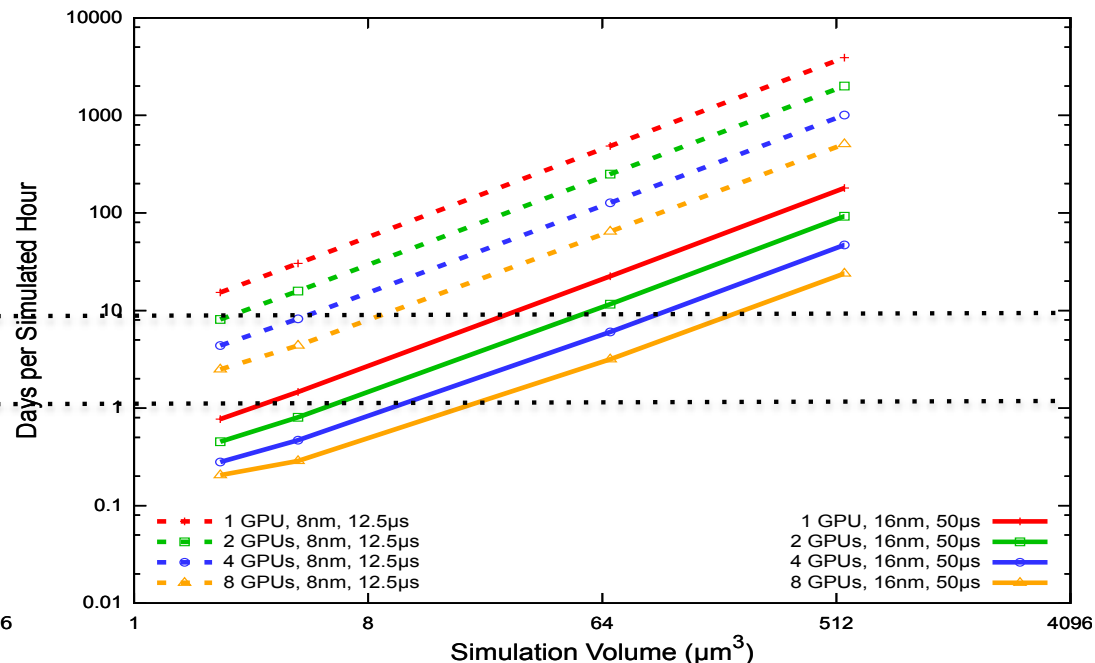
“Old” – January 2014 Hallock, et al. *Parallel Comp.*

New – Nov. 2014 *Supercomputing 2014*

Benchmark System Runtimes - NCSA Forge (Eight M2070s)



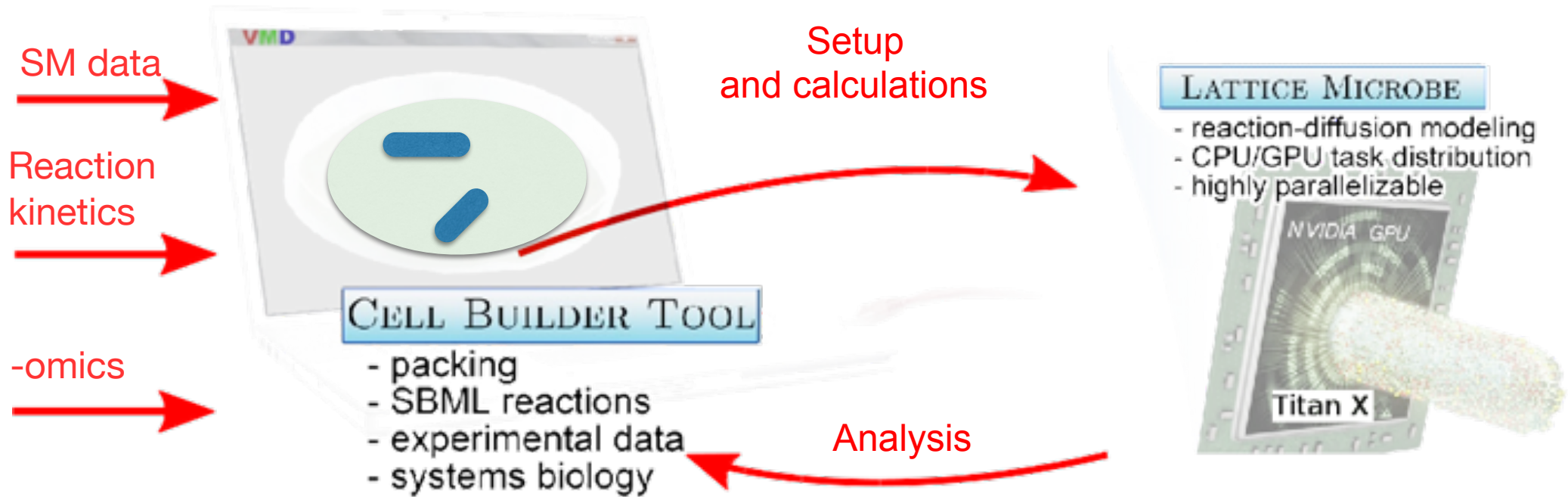
Benchmark System Runtimes - Cirrascale Eval (8x K40)



- Today -2 hr cell cycle of ~1000 rxns, 251 species in ribosome biogenesis in dividing cell requires 1 day using GTX980 / TitanX, Cuda 7.0 and LM 2.3a
- Program Lattice Microbes and PyLM with tutorials available at <http://www.scs.illinois.edu/schulten/lm/>



Facilities for GPU Parallel Computing



Tutorial - Amazon Cloud

single nodes



NSF/CPLC



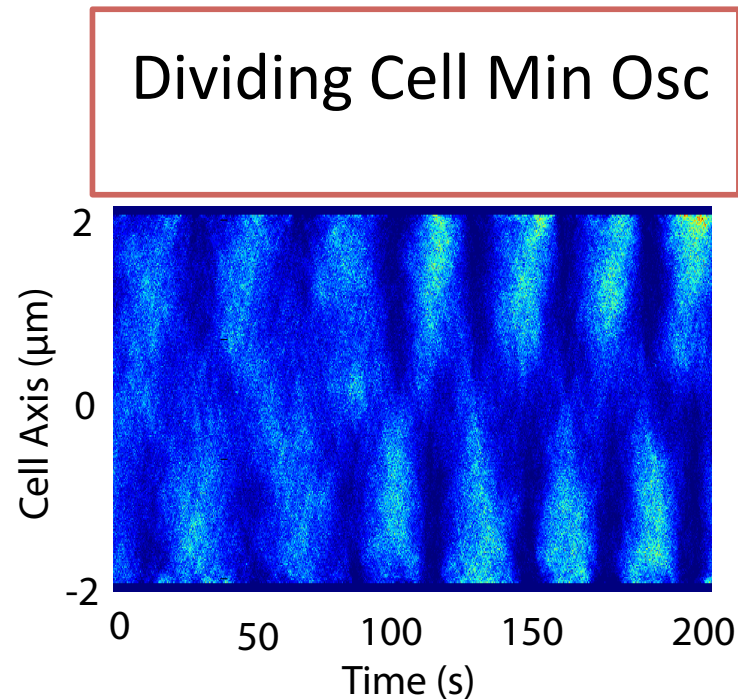
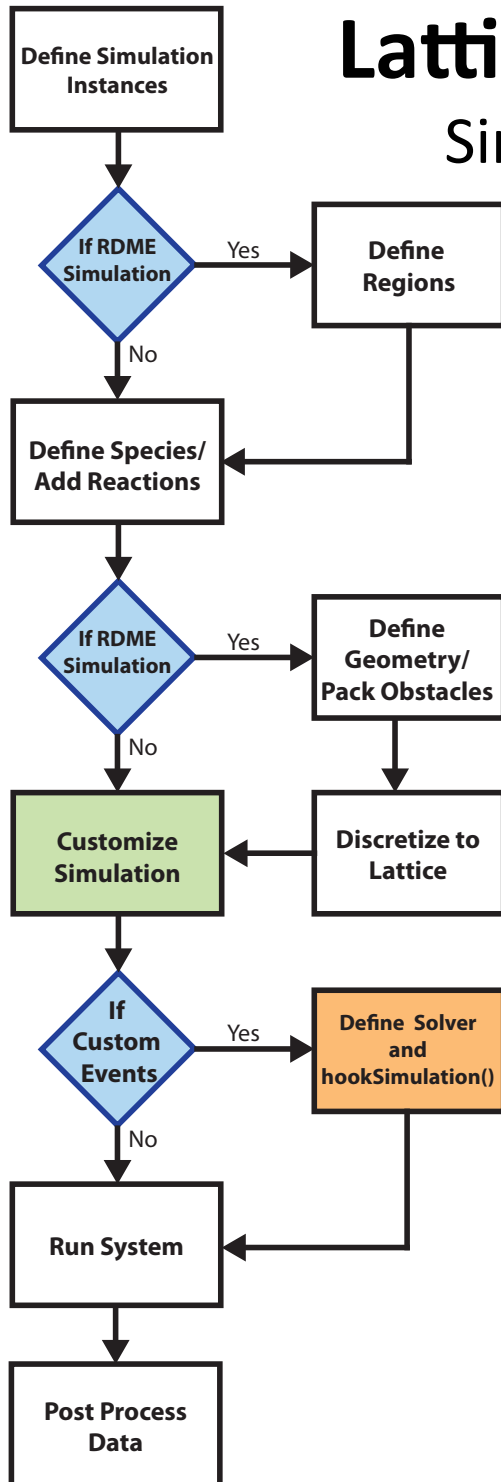
NSF/UIUC



Lattice Microbe Tutorials on the Cloud

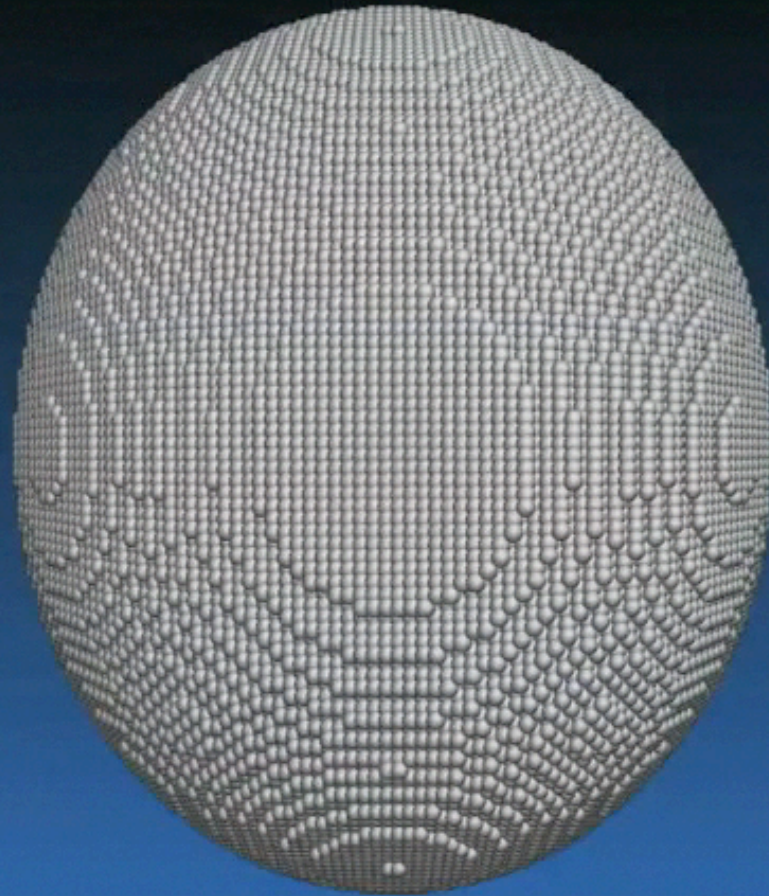
Simple Rxns, Lac Genetic Switch, Min Osc

Mike Hallock and Joe Peterson



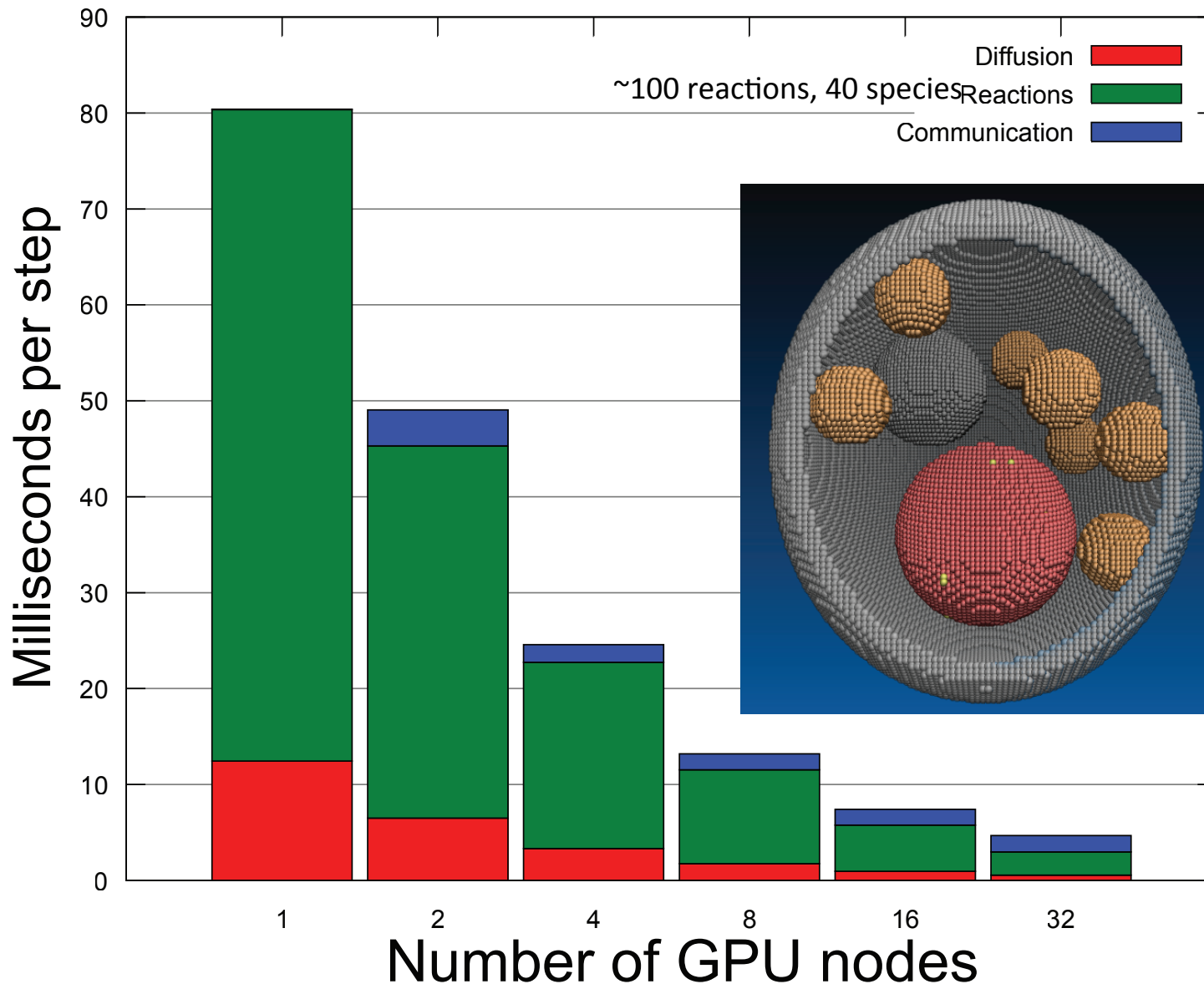
Modeling Yeast in Lattice Microbes

PyLM Shapes Demonstration by Joe Peterson



Challenges in Modeling Eukaryotic Cells

Full MPI version – Lattice Microbes



Preliminary
Results on
Galactose Switch