

The Many Roles and Consequences of Stochasticity in Biological Systems

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Extrinsic vs. Intrinsic Stochasticity

Extrinsic Stochasticity

- Noise arising from random events in the environment
- Gaussian-distributed ('white') noise
- Often modeled via stochastic ODE or PDE system

Intrinsic Stochasticity

- Noise arising due to small populations of key players (for example, transcription factors)
- Modeled as a Markov process
- Often modeled via discrete stochastic (well-mixed or spatial) system

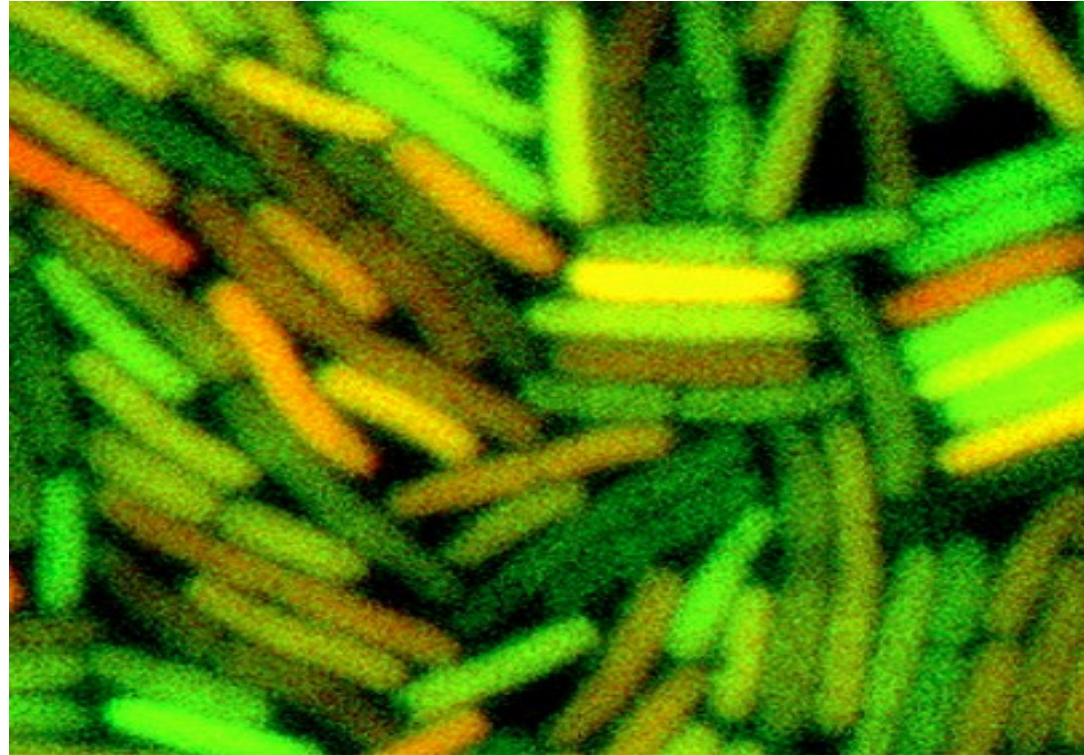
Intrinsic Stochasticity Can Have Dire Consequences!



Tasmanian Devil Disease

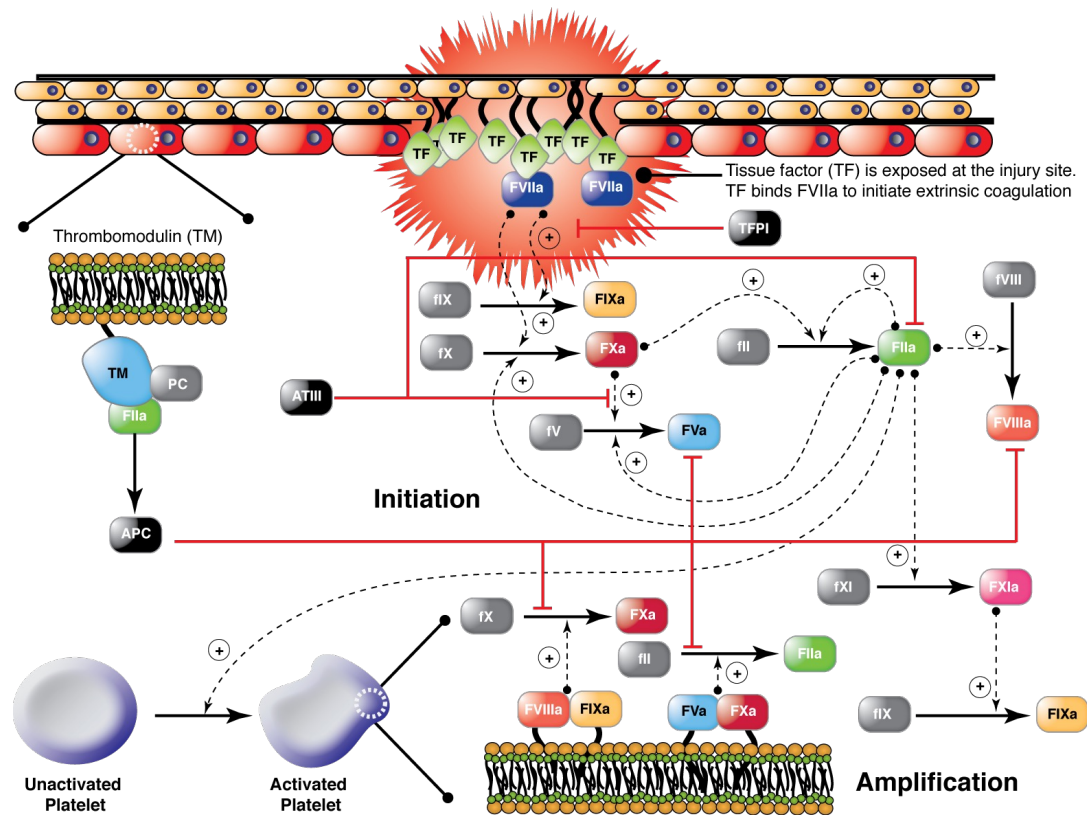


Intrinsic Stochasticity Revealed by Experiment

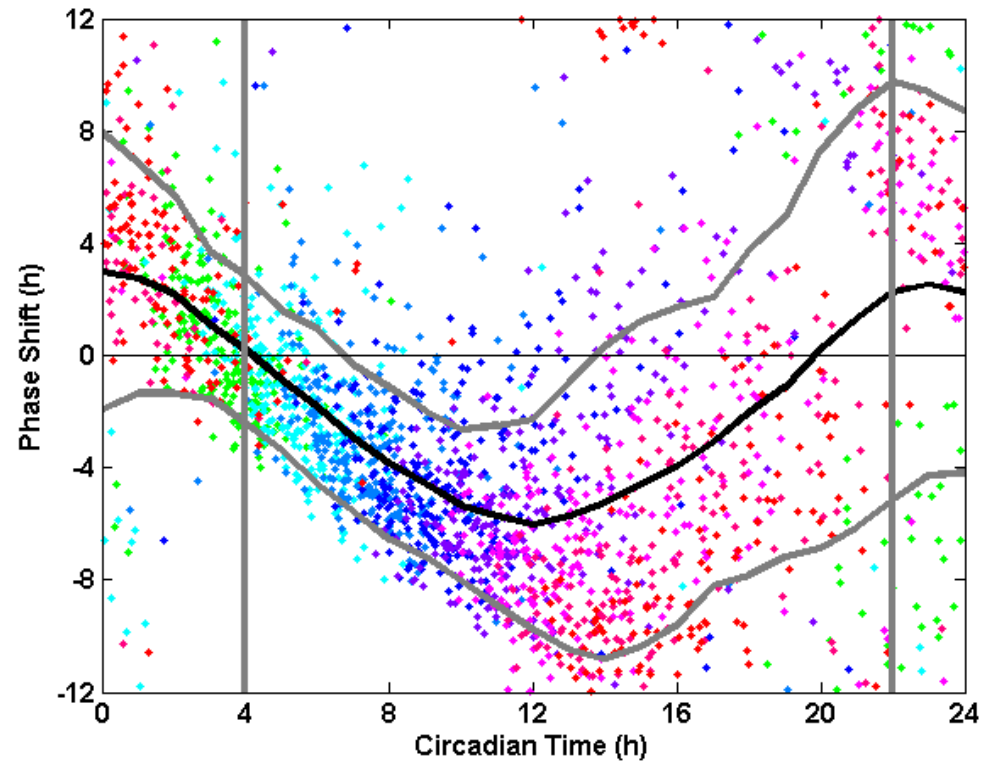


Elowitz M B et al. Science 2002;297:1183-1186
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Intrinsic Stochasticity in Medicine: The Coagulation Cascade

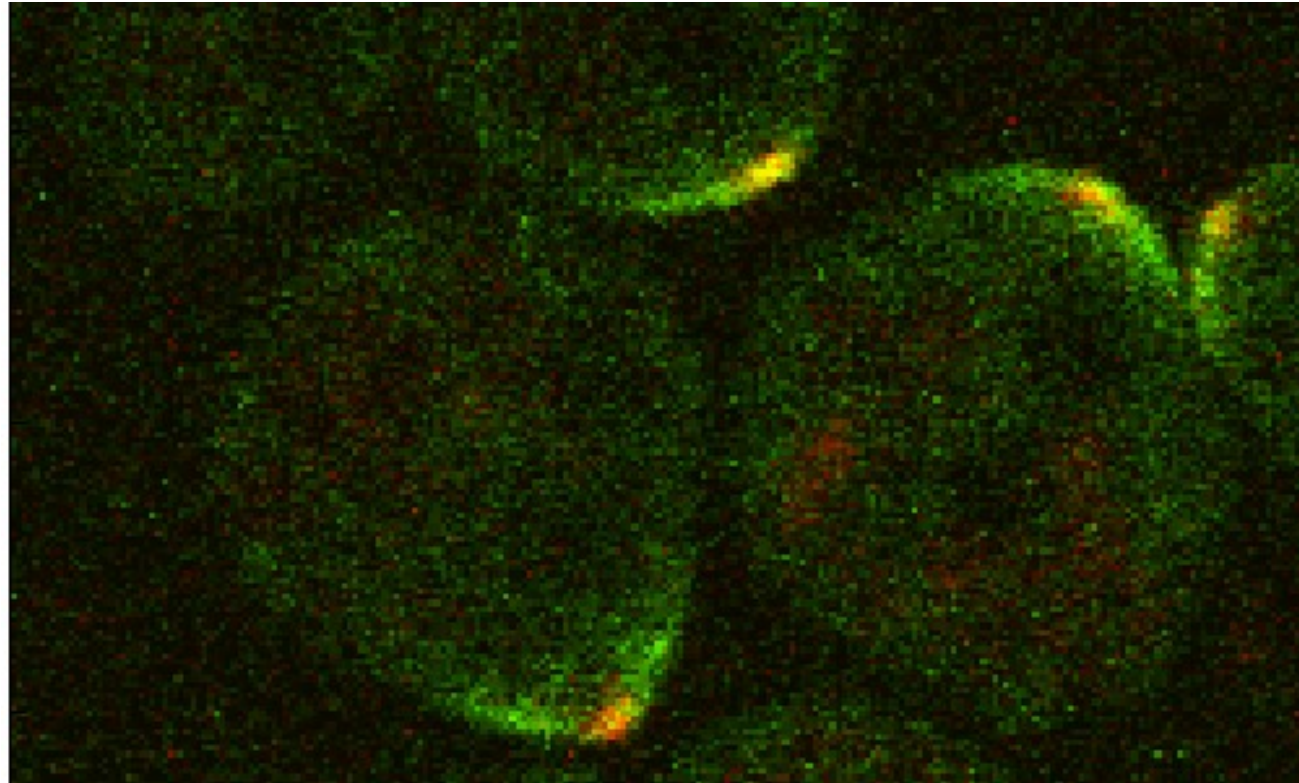


Intrinsic Stochasticity in Circadian Rhythm

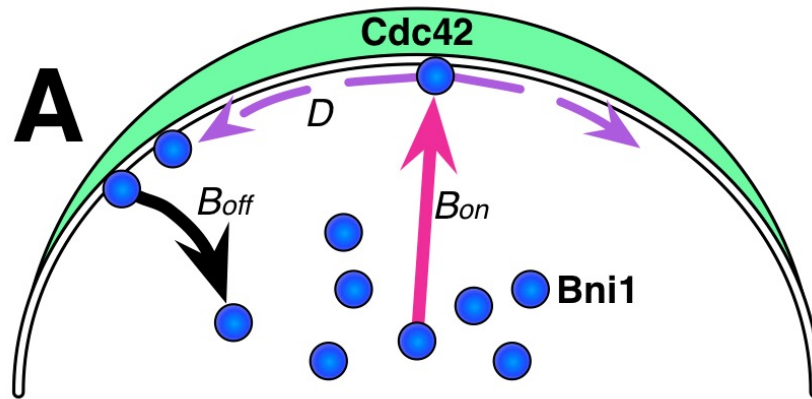


Phase response distribution

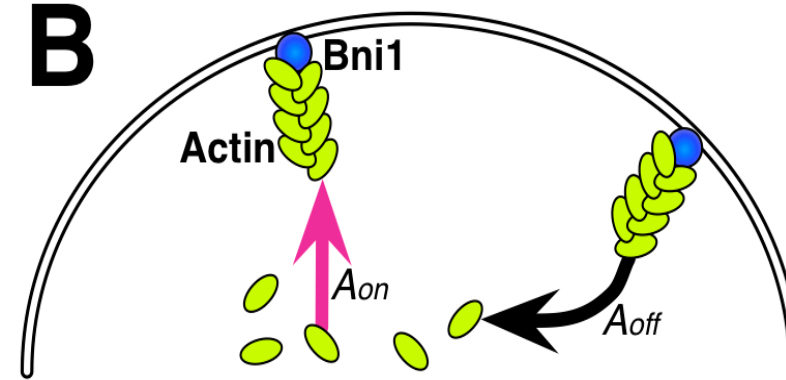
Intrinsic Stochasticity in Cell Polarization



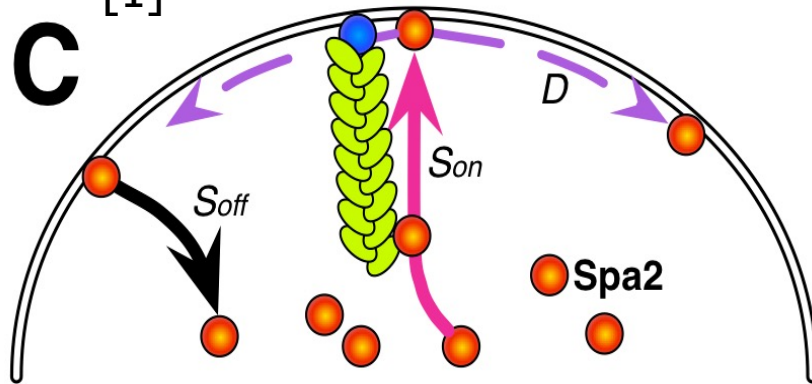
Our Polarisome Model



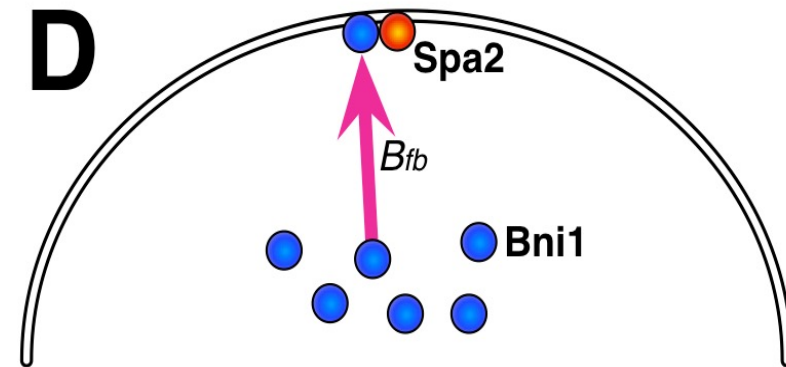
Spontaneous Recruitment
[1]



Nucleation of Actin Cables [2]

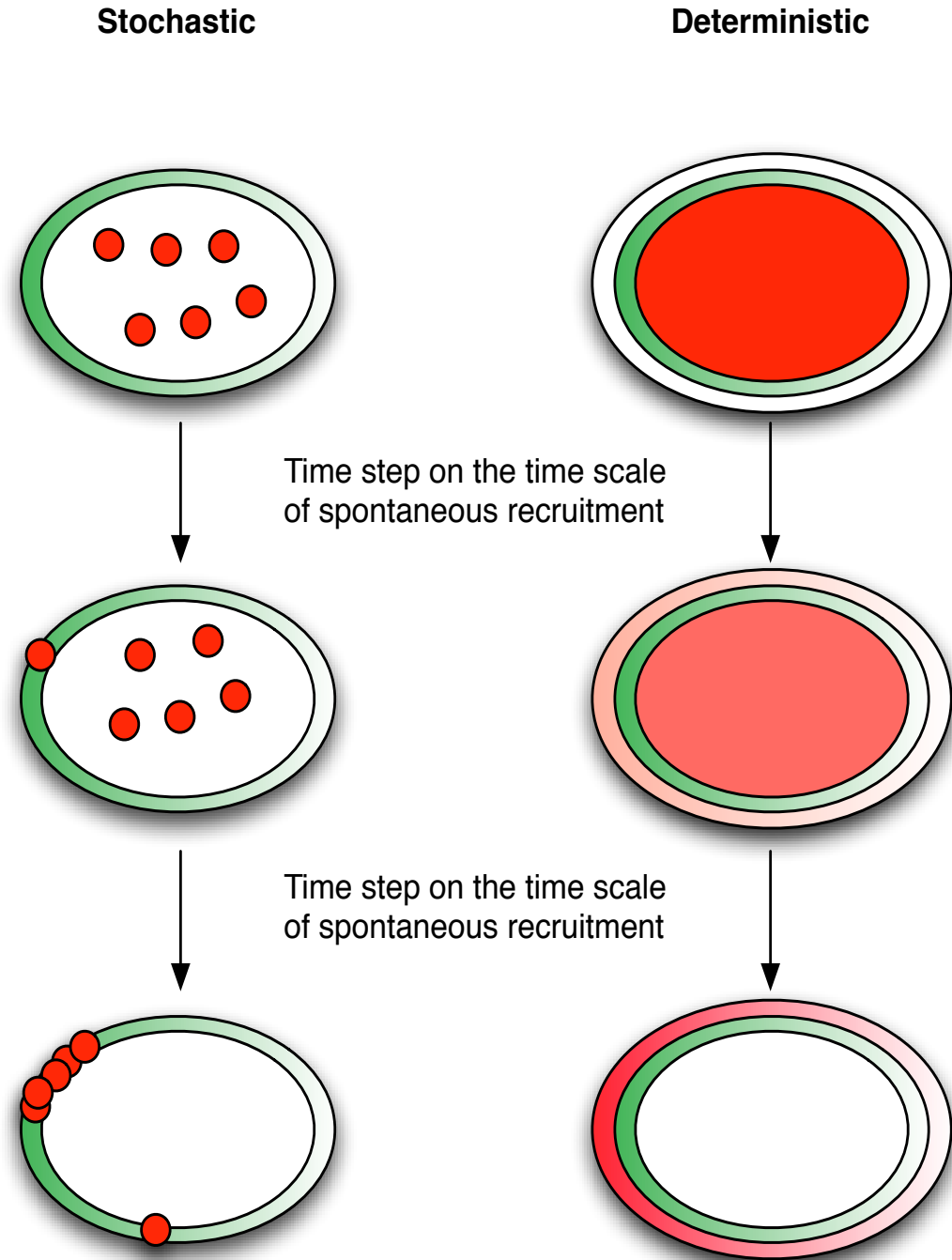


Directed transport [2]



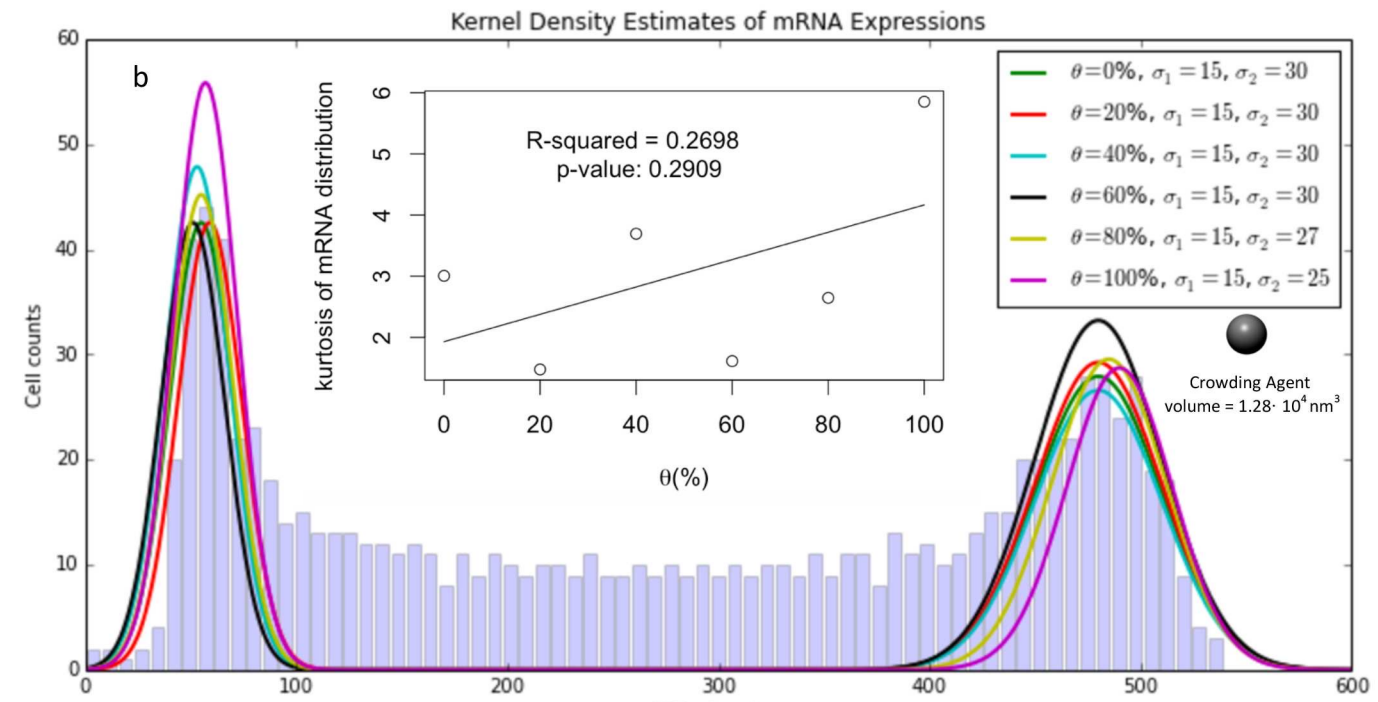
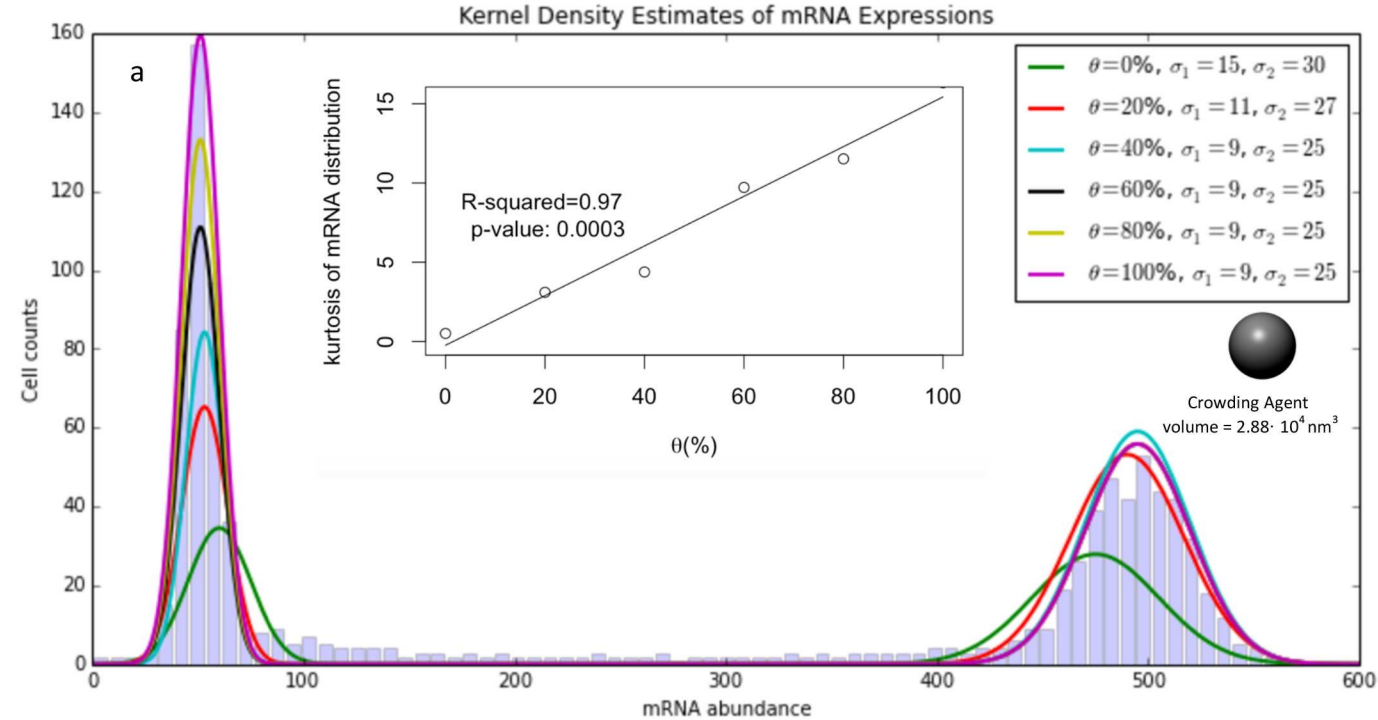
Positive feedback [2]

Stochastic Amplification

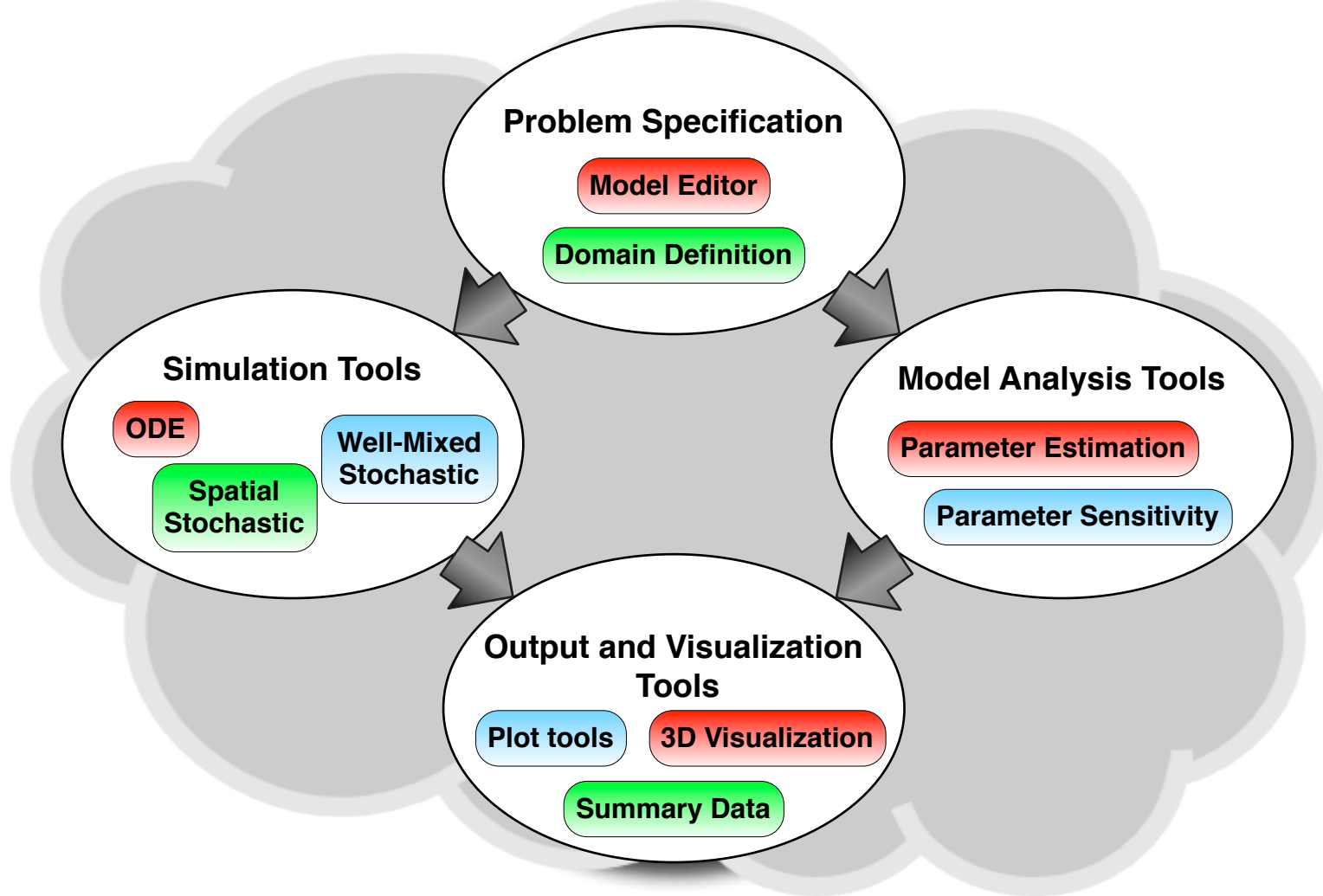


Macromolecular Crowding Regulates the Gene Expression Profile by Limiting Diffusion

Pluripotent stem cells are less crowded than more differentiated forms, resulting in greater plasticity.



www.stochss.org
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StochSS



Simulation

- Well-mixed systems: Gillespy2
 - SSA, tau-leaping, hybrid method, >80,000 downloads on Github
- Spatial stochastic systems: SpatialPy
 - Simulation of spatial deterministic/stochastic reaction-diffusion-advection problems embedded in Lagrangian reference from particle based fluid dynamics domain

Model Analysis

- Surrogate Modeling
 - Train fast metamodels of computationally expensive problems
 - Perform surrogate-assisted model reduction for large-scale models/simulators
- Inference
 - Perform likelihood-free parameter inference using parallel ABC
 - Train surrogate models (ANNs) as expressive summary statistics for likelihood-free inference
 - Infer model structure and parameters directly from data via neural ODEs (not in StochSS yet)
- Optimization
 - Optimize a specified objective function or surrogate model using a variety of approaches

Model Exploration

- Perform large distributed parameter sweep applications for any black-box model/simulator which outputs time series data
- Generate time series features and summary statistics on simulation output and visualize parameter points in feature space
- Interactive labeling of parameter points in feature space according to the users preferences over the diversity of model behaviors
- Supports semi-supervised learning and downstream classifiers

Thanks!

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Prashant Singh

Frederik Wrede

Colby Fronk

Kevin Sanft

Min Roh

Bernie Daigle

Rich Harang

... and many more!

