Most probable transition pathway of biological SDEs

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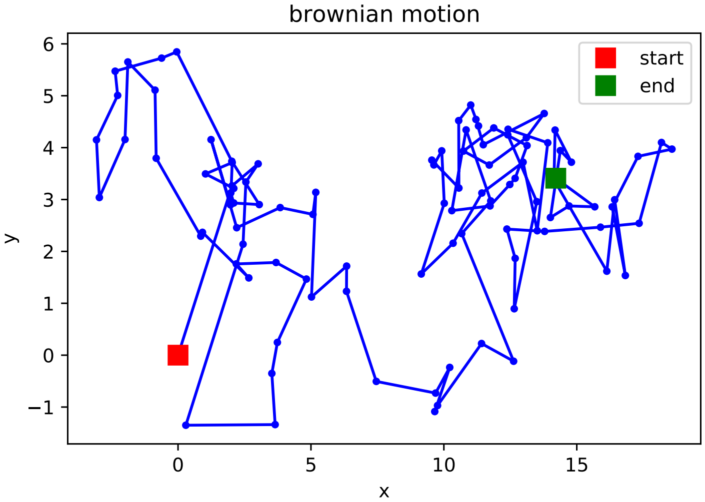
- All physical systems are "noisy"
- Noise: think of Brownian motion
- Accounts for sudden changes in system
- Many biological processes are stochastic: mutation, gene regulation, etc.

Brownian Motion



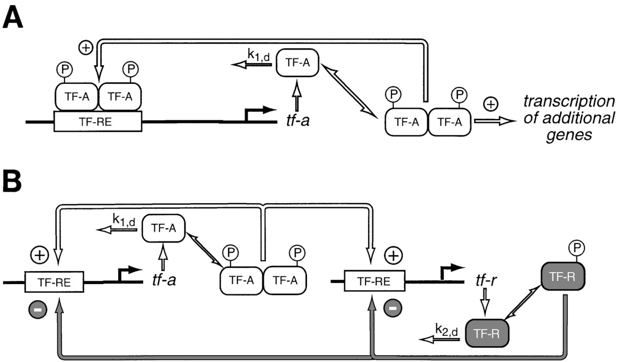
What's an SDE?

The definition of a *stochastic differential equation* given a stochastic process X_t, drift function $f(X_t, t)$, and diffusion function $\sigma(X_t, t)$:

$$dX_t = f(X_t, t)dt + \sigma(X_t, t)dB_t \tag{1}$$

Think: f determines direction, σ denotes noise intensity

The Biology (Smolen et al.)



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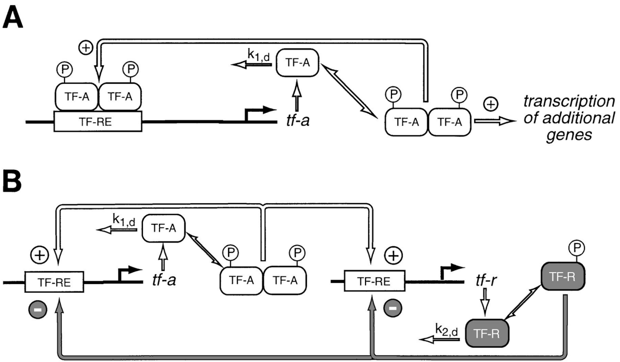

$$\frac{d[\text{TF A}]}{dt} = \frac{k_{1,f}[\text{TF A}]^2}{[\text{TF A}]^2 + K_{1,d}} - k_{1,d}[\text{TF A}] + r_{1,\text{bas}} \qquad (2)$$

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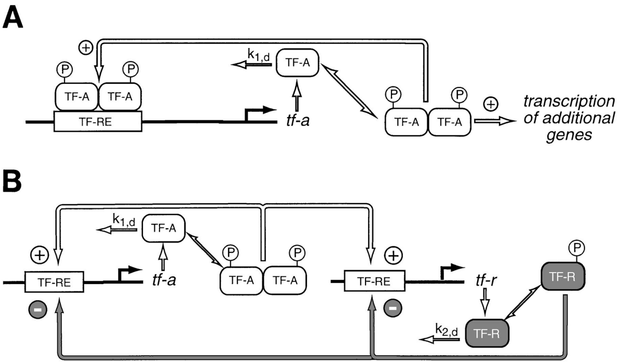

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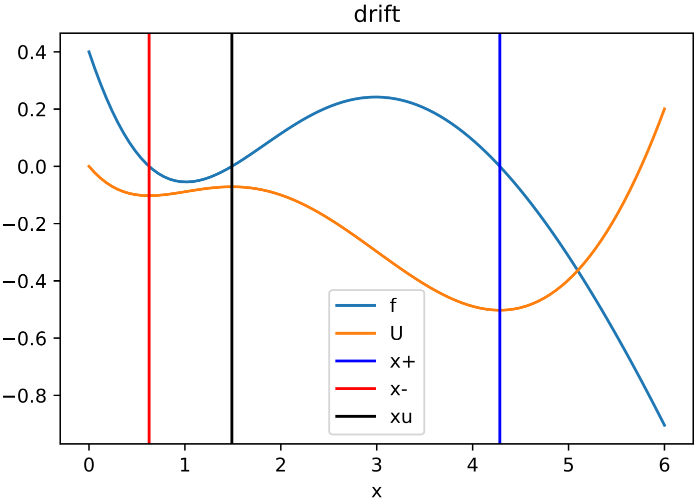
Let this be our f and we use constant noise $\sigma = 0.10$.

Our Model



Simulation

Given f and σ, we simulate the SDE with the Euler-Maruyama method.

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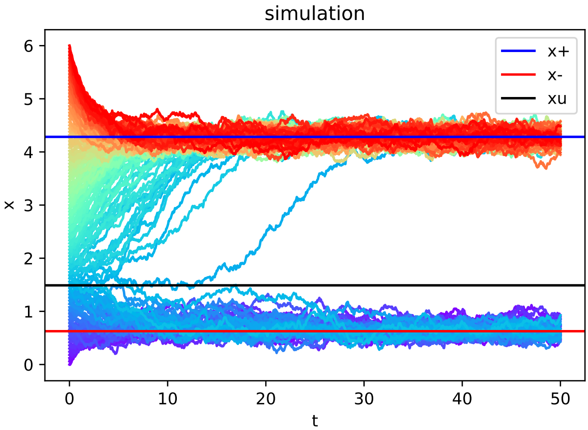
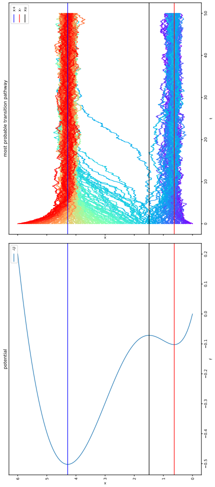


Model against Potential



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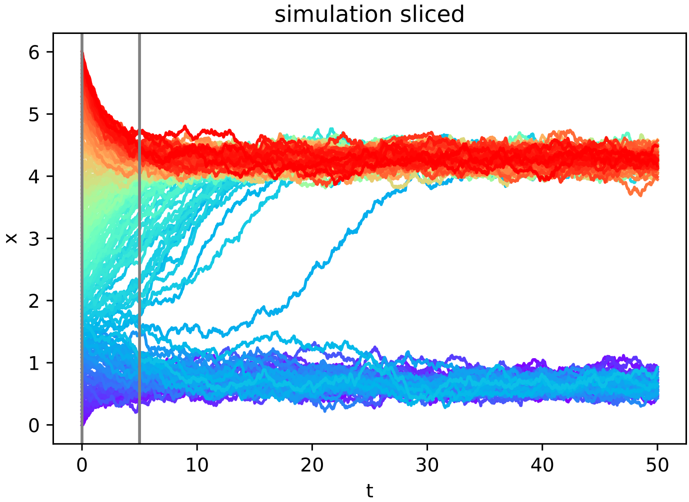
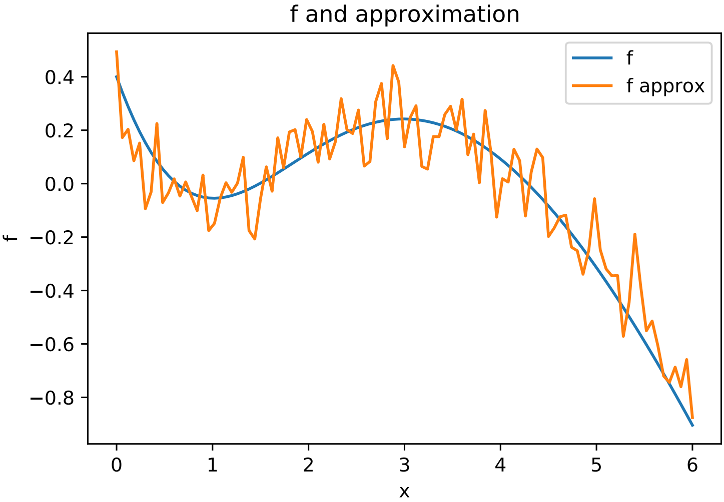
found by Dai et al. (2020). Proof involves stochastic version of Taylor expansion.

Simulation Zoom-In



Learned f



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- Solving analytically is very difficult
- The shooting method lets us find the "velocity" that minimizes the "loss"

The Shooting Method

We rewrite our second order ordinary differential equation into a first order:

$$\begin{cases} v = \dot{z} \\ \dot{v} = \frac{\epsilon^2}{2} f''(v) + f'(v) f(v) \end{cases} \tag{7}$$

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Mean Path vs Learned Path

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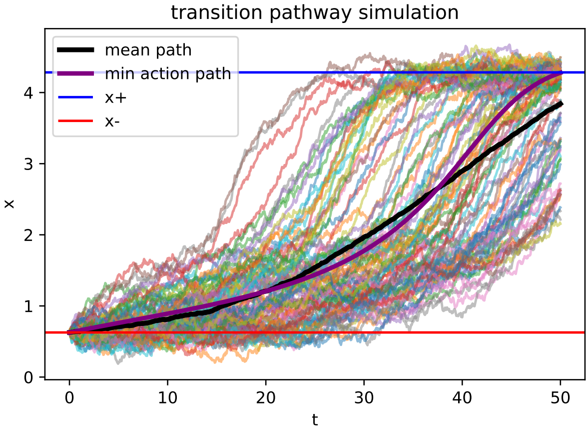
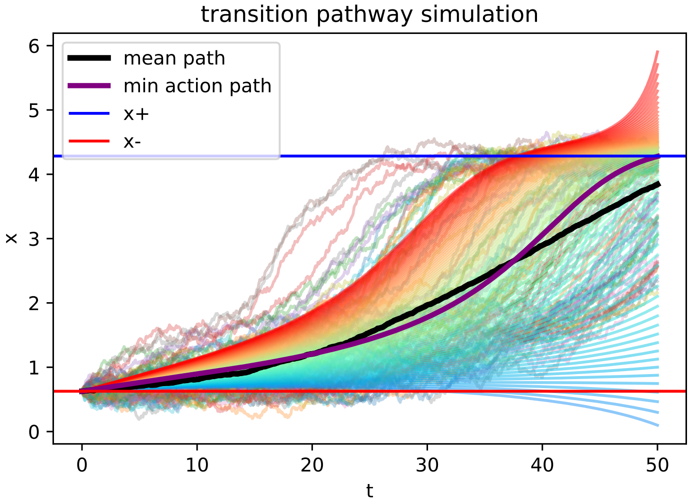


Learned Probable Pathway



Future Work

- Fine tune/optimize specific data extraction and fitting
- Other stochastic information: mean exit time
- Consider higher dimensional data: consider the second transcription factor TF-R
- Applying machine learning techniques to estimating pathway distribution (needed for higher dimensions)
- Applications outside of biology

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- M. Dai, J. Duan, J. Liao, X. Wang. Maximum Likelihood Estimation of Stochastic Differential Equations with Random Effects Driven by Fractional Brownian Motion. arXiv, 2001.01412, 2020.
- P. Smolen, D. A. Baxter, and J. H. Byrne. Frequency selectivity, multistability, and oscillations emerge from models of genetic regulatory systems. American Journal of Physiology-Cell Physiology, 274:531-542, 1998.
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