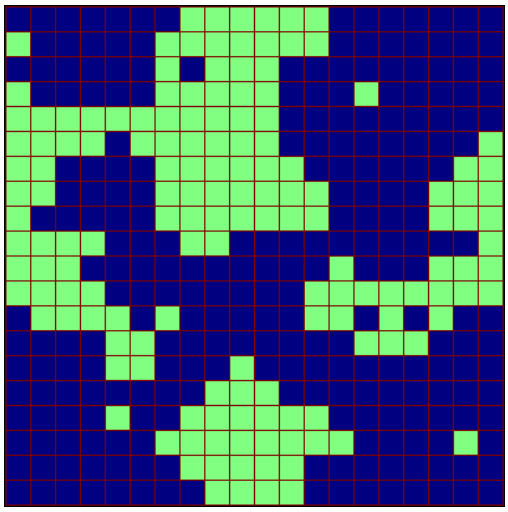
TRANSITION RATES IN THE "ELECTRICAL" ISING MODEL

The "electrical" Ising model is entirely isomorphic to the standard Ising model, so any previous literature dealing with the standard model applies here also. I use a finite model with a 20 x 20 grid, yielding 400 cells.



Energetics:

The system energy for any of the 2^{400} configurations ν is:

$$E_\nu = \sum_{ij} \left(e_i + e_j - 2e_i e_j\right)\delta\varepsilon - \sum_i \delta q e_i V \,,$$

where index *i* ranges over all 400 cells and cell values are e_i = 0 (resting) or 1 (activated). Index *j* covers all nearest-neighbor cells (north, south, east, and west) to cell *i*.

The first sum (interaction term) runs over all nearest-neighbor pairs, with care being taken not to count the same interaction twice. I use periodic boundary conditions. The interaction term is designed so that adjacent cells oriented in the same direction have zero interaction. If they are oppositely aligned, there is an energy penalty of $\delta\varepsilon$.

The second sum is the field term, driven by the voltage *V*. As cells flip from resting to activated they move a microscopic gating charge δq. Thus the system charge $q = \sum_i \delta q e_i$ ranges from 0 to $400\delta q$. I've chosen the total gating charge to be 1 eu, so δq = 0.0025 eu.

The energy ε_{en} of an individual cell can take on 10 values, depending on its own state (e = 0, 1) and the number of activated nearest neighbors (n = 0, 1, 2, 3, 4). These can be conveniently calculated ahead of time.

The possible values are: $\varepsilon_{en} = \left(2\left(2-n\right)\delta\varepsilon - \delta q V\right)e + \Delta\varepsilon n$.

We assume the whole system is in contact with a heat bath at temperature T. I prefer energy units of meV. The corresponding value of Boltzmann's constant is 0.086174 meV/K, yielding kT = 25 meV at 290 K.

Kinetics:

There are 5 activating and 5 deactivating rate constants a_i that apply to each cell i, consistent with the 10 local configurations. The rate constants are a function of the energy needed to activate the cell. This activation energy is equal to:

$$\begin{aligned}\Delta\varepsilon_n &\equiv \varepsilon_{1n} - \varepsilon_{0n} - \delta q V \\ &= 2(2-n)\delta\varepsilon - \delta q V\end{aligned}$$

Note for n = 2, there is no penalty for activation/deactivation provided V = 0. The formula describing the value of the 5 activating or "forward" rate constants α_n, which applies to a cell originally in the resting state, and surrounded by n = 0…4 activated neighbors, is given by:

$$\alpha_n = \nu \exp\left(\frac{-x\Delta\varepsilon_n}{kT}\right),$$

where ν is the pre-exponential factor, and x (the Brønsted slope) is any number between 0 and 1 (usually assigned the value 0.5). I don't ascribe any temperature-dependence to ν (implying the microscopic transition is a "bottleneck" or purely entropy-driven event) so that any temperature sensitivity of the macroscopic rate can be attributed to cell-cell interactions.

The corresponding 5 deactivating or "backward" rate constants β_n are:

$$\beta_n = \nu \exp\left(\frac{(1-x)\Delta\varepsilon_n}{kT}\right).$$

These formulas satisfy detailed balance, as evidenced by:

$$\frac{\alpha_n}{\beta_n} = \exp\left(\frac{-\Delta\varepsilon_n}{kT}\right).$$

Typical simulation parameters:

Temperature T = 290 K.

Voltage V = 0. This is for the symmetric problem. Positive or negative values of V will bias the system towards the activated (A) or resting (R) states, respectively, leading to unequal macroscopic rate constants.

Grid length = 20 x 20 $\rightarrow$ 400 cells.

Unit cell charge movement δq = 0.0025 eu $\rightarrow$ total system range: 0 to 1 eu.

Interaction energy $\delta\varepsilon$ = 24 meV (this is equal to 2J of the standard Ising model).

Pre-exponential factor ν = 20,000 kHz (= 2 x 10^7 sec^{-1}).

Brønsted slope x = 0.5.

That should be all the information you need to set up your MSM system! The remaining material relates to the Monte Carlo simulation and construction of parameters for a diffusion equation.

Kinetic Monte Carlo:

Until I gain more experience, I prefer a "brute force" simulation method to more advanced sampling schemes, so that I can be certain the model behaves appropriately. I use a similar method when simulating ion channel kinetics from a master equation, and it has worked well for me. The method is as follows:

(1) Choose starting configuration (time t = 0). I randomly assign individual cells the value of 0 or 1 according to a predetermined probability (usually 0.5, placing the configuration at the "top" of the macroscopic energy barrier).

(2) Assign to each of the 400 cells one of the 10 permissible rate constants a_i. If there are N_A active cells, then there will be $(1–N_A)$ forward rate constants, and N_A backward rate constants.

(3) Sum all the previously assigned rate constants a_i together to obtain the total rate constant a of leaving the current configuration. Then pick a uniform random number r_1, and calculate the exponentially distributed dwell time τ using the formula:

$$\tau = \frac{-\ln r_1}{a} \ .$$

(4) Pick a second random number r_2 in order to determine which cell to flip. Each cell has probability a_i/a of being chosen.

(5) Advance the simulation time t by τ, and flip the randomly chosen cell.

(6) Repeat steps 2-5 until the simulation time exceeds a certain value (usually 400 ms). I usually allow the system to equilibrate from the starting configuration before commencing data recording. Starting near the peak of q = 0.5, the system will rapidly fall into one of two macroscopic states: mostly resting cells (state R) or mostly activated cells (A).

Construction of diffusion model:

At every step k of the simulation, the following quantities were calculated: system energy E, dwell time τ, summed forward rate $\alpha = \sum_i a_i(1-e_i)$, and summed backward rate: $\beta = \sum_i a_i e_i$.

These were binned according to the value of gating charge $q = \sum_i \delta q e_i$, and running totals for each q bin were obtained.

The Helmholtz energy $A(q)$ is obtained (to within a constant) from $\exp\left(\frac{-A(q)}{kT}\right) = \frac{\sum_k \tau_k(q)}{\sum_{k,q} \tau_k(q)}$.

The additive constant can be determined from the fact that $A(0) = 0$, since system energy and configurational entropy must both be zero when all cells are in their resting positions. The potential of mean force is given by $W(q) = A(q) - qV$.

Other quantities $\langle X(q) \rangle$ were obtained through time averaging: $\langle X(q) \rangle = \frac{\sum_k \tau_k(q) X_k(q)}{\sum_k \tau_k(q)}$.

The configurational entropy can be obtained through: $TS(q) = \langle E(q) \rangle - A(q)$.

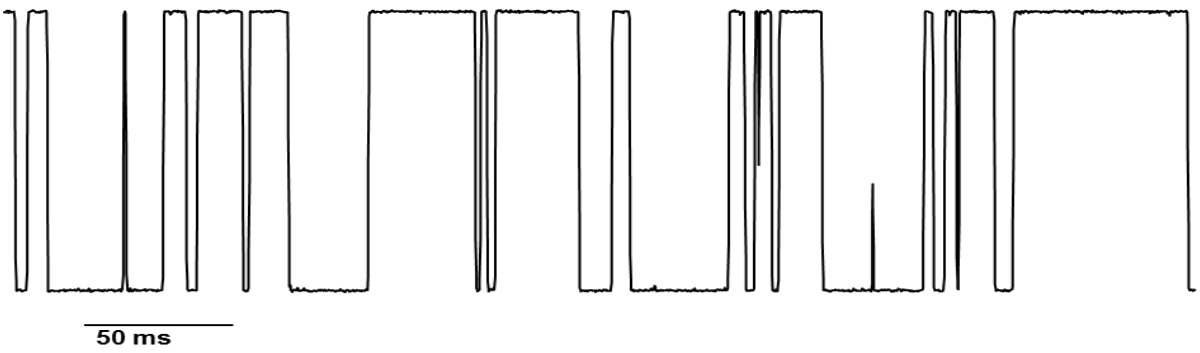
The diffusion coefficient for Brownian motion across the PMF was obtained from the standard random walk expression:

$$D(q) = 0.5\left(\langle \alpha(q) \rangle + \langle \beta(q) \rangle\right)\delta q^2 .$$

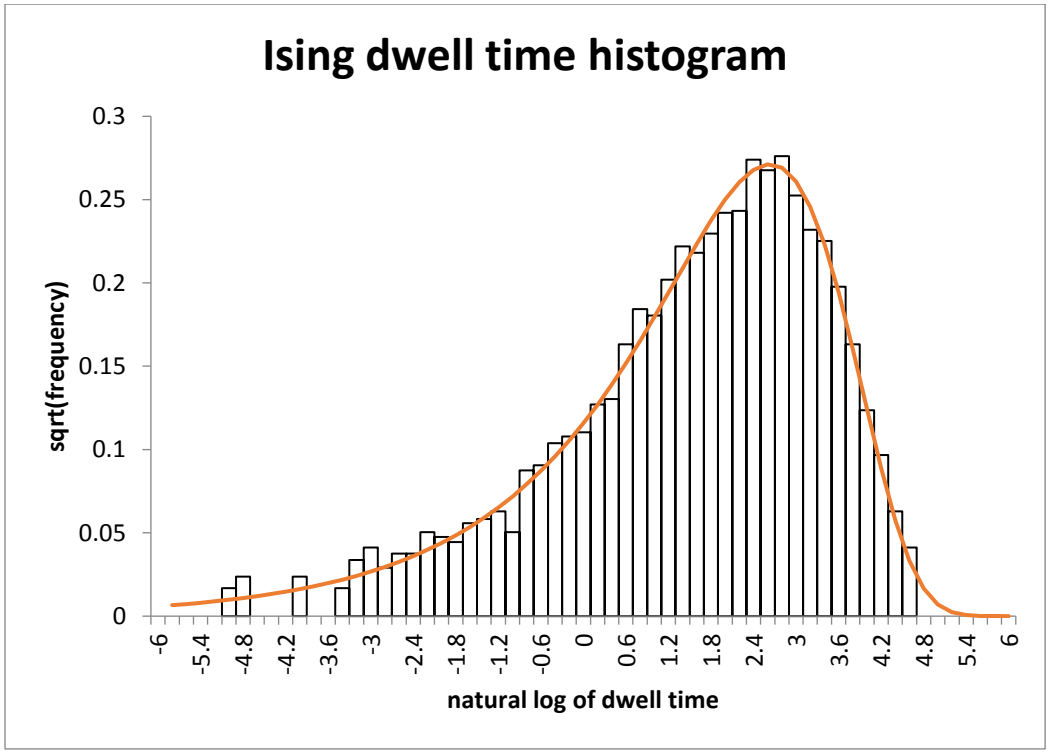
This is accurate only in the case of adequate vertical thermalization for every value of q visited during the trajectory, since the above formula uses the simulation-averaged values of the forward and backward rate constants. In fact, it overestimates the "true" value of D, as determined from analyzing mean first passage times, by about 50%.

Results from simulations:

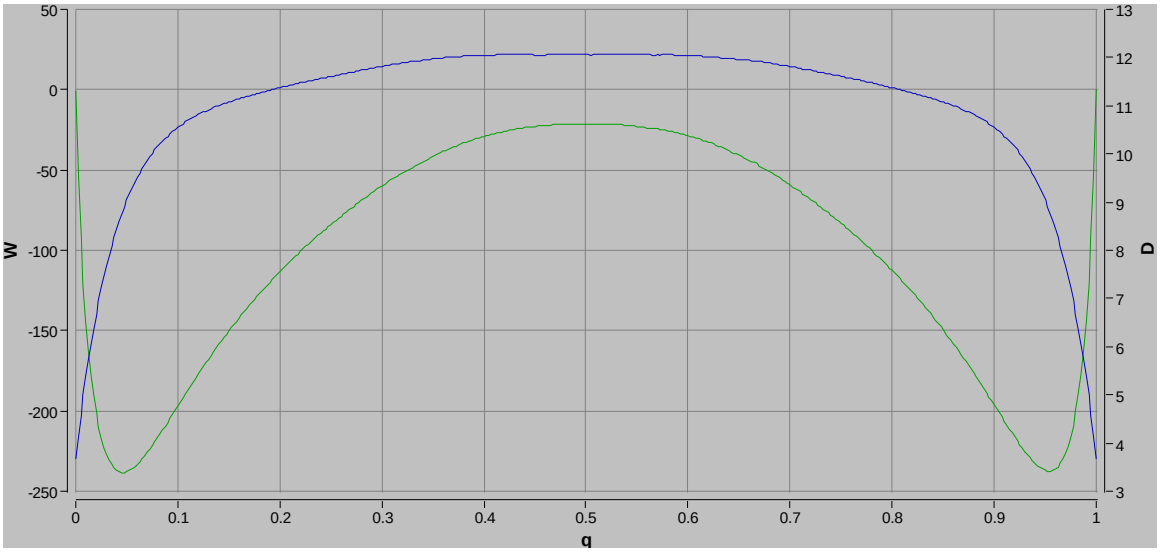
Here is a typical 400 ms trajectory of the gating charge. The reason there is so little noise apart from the large-scale fluctuations is because of low-pass filtering (which is performed independently of time averaging).



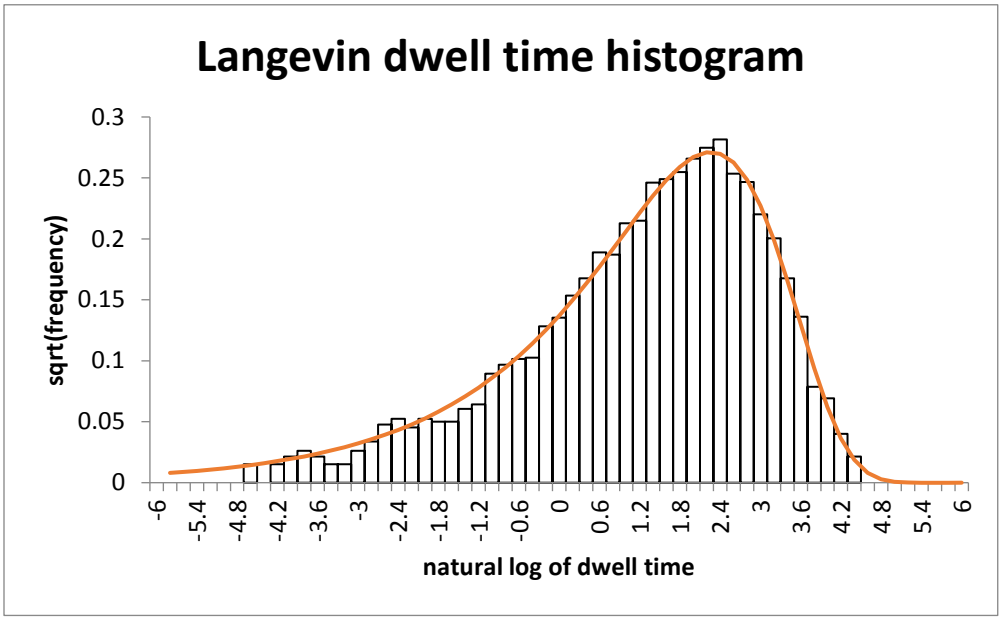
The following Sigworth-Sine transformation of the dwell time histogram for 100 trajectories like the one above shows high fidelity to an exponential distribution, with mean macroscopic dwell time = 12.53 ± 0.22 ms from binomial statistics, equivalent to a rate constant of 0.080 kHz.



From the same 100 trajectories, I constructed the Helmholtz free energy $A(q)$ (green trace, meV, labeled as W in the figure) and diffusion coefficient $D(q)$ (blue trace, eu^2/ms) using the averaging procedure detailed earlier:

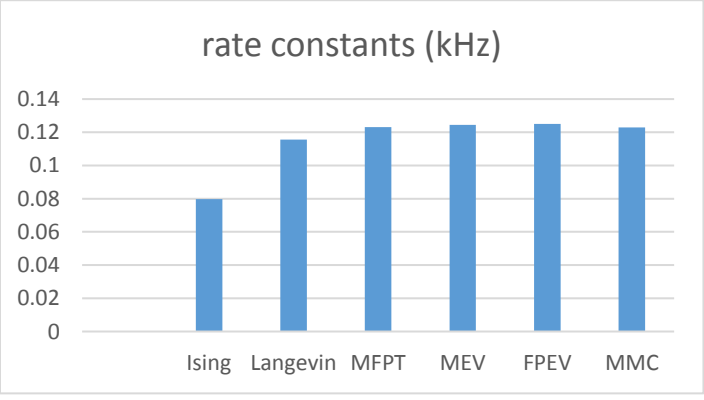


Performing Langevin dynamic simulations with the above diffusion parameters, I analyzed 100 Langevin-simulated traces with the following results: mean macroscopic dwell time = 8.68 ± 0.13 ms, equivalent to a rate constant of 0.115 kHz, nearly 50% greater than the result from the original kinetic Ising simulation.



Not being entirely trustful of my Langevin simulation algorithm, I recalculated the macroscopic rate constant using a variety of different methods: mean first passage time (MFPT); eigenvalue analysis of the Fokker-Planck (Smoluchowski) equation (FPEV) and of the linear master equation obtained from $\langle \alpha(q) \rangle$ and $\langle \beta(q) \rangle$ (MEV); and Monte Carlo simulation of the master equation (MMC).

The average of these values were 0.124 kHz, just slightly higher than the Langevin result, but obviously also substantially greater than the Ising result of 0.08 kHz.



Conclusion: The diffusion coefficient $D(q)$ computed using the rapid thermalization assumption is incorrect in predict the correct macroscopic rate constant. It follows that this assumption is incorrect, and the system is likely not Markovian with respect to the reaction coordinate q.