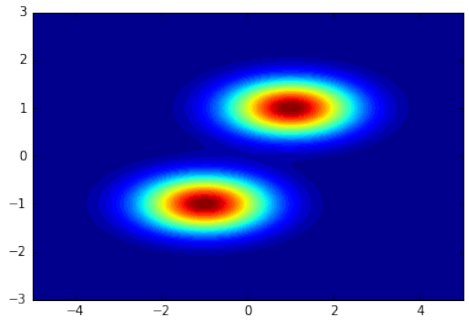
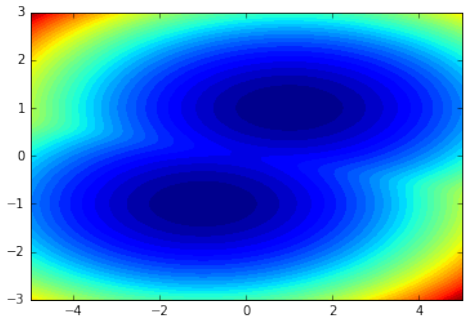
Markov state model and Hidden Markov model with orthogonal slow coordinates

In this project, you will generate a Brownian dynamics simulation of a double-well potential which is observed on a poor coordinate. You will compare the performance of Markov state models and Hidden Markov models in estimating the kinetics of the system.

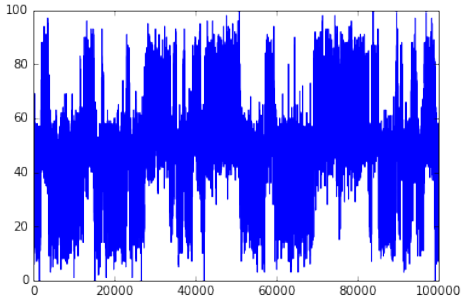
a)



b)



c)



Tasks:

1. Define a density function $f(\mathbf{x})$, where $\mathbf{x} = (x_1, x_2)$ with two modes in two dimensions which qualitatively looks like Fig. a) (the two modes should partially overlap in the x_1-coordinate)
2. Define a potential $u(\mathbf{x}) = -\log f(\mathbf{x})$
3. Implement Brownian dynamics simulation with discrete Euler discretization for this potential. The dimensionless expression for that is:

   $$\mathbf{x}_{t+\tau} = \mathbf{x}_t - \tau \nabla u(\mathbf{x}) + \sqrt{\tau}\boldsymbol{\eta}_t$$

   where $\boldsymbol{\eta}_t$ is a vector with elements sampled by a Gaussian normal distribution $\mathcal{N}(0, 1)$.
   Hint 1: Depending on your definition of f, ∇u might be complex and a bit error-prone to implement. Don't loose time this, a valid shortcut is to simply compute the derivatives with finite differences.
   Hint 2: the discretization time step τ needs to be quite small.
4. Run a sufficiently long simulation to sample many transitions. Discretize the x_1 trajectory into regular, fine bins.
5. If you have done 1-4 well, your trajectory should look similar to c) in the x_1 coordinate. You should however have about 10x the number of transitions shown in c).
6. Compute and display the implied timescales for these dynamics using Markov state models and Hidden Markov models. Compare and try to explain the differences.
7. Choose one lag time which works well with the HMM (use the same for the MSM). Plot the equilibrium distribution, the metastable memberships and the metastable distributions as a function of the bin index (i.e. corresponding to the x_1 coordinate). Compare and discuss results for MSM and HMM.
8. Compute the mean first passage times between the bins corresponding to the probability maxima / energy minima using the MSM. Compute the mean first passage times between the HMM states. Compare and discuss.