

CELLULAR AND SYSTEMS MODELING - HW6

Student: Shu-Ting Cho (shc167@pitt.edu)

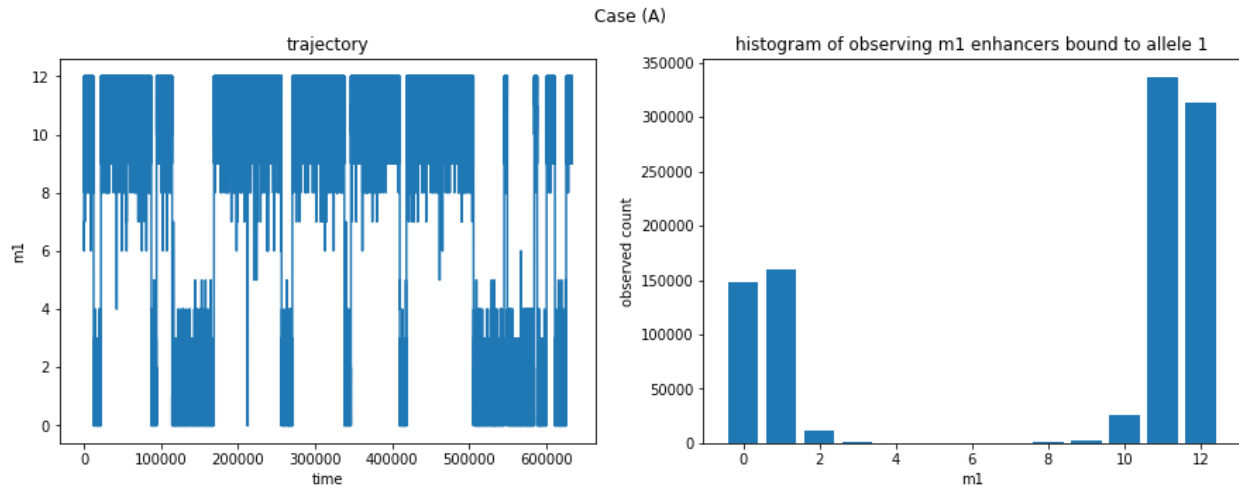
In this exercise, you are asked to write a computer code to simulate the enhancer binding model described in the main text and reproduce the results shown in Fig. 3B of the OR book chapter. Consider two alleles that are epigenetically active, and the number of enhancers $M = 12$. You will simulate four cases,

- A) symmetric case: $\varepsilon_1 = \varepsilon_2 = \varepsilon$, $\delta = -0.5 k_B T$;
- B) asymmetric case: $\varepsilon_1 = \varepsilon$, $\varepsilon_2 = \varepsilon + 0.5 k_B T$, $\delta = -0.5 k_B T$;
- C) symmetric without cooperativity: $\varepsilon_1 = \varepsilon_2 = \varepsilon$, $\delta = 0$;
- D) asymmetric case without cooperativity: $\varepsilon_1 = \varepsilon$, $\varepsilon_2 = \varepsilon + 0.5 k_B T$, $\delta = 0$.

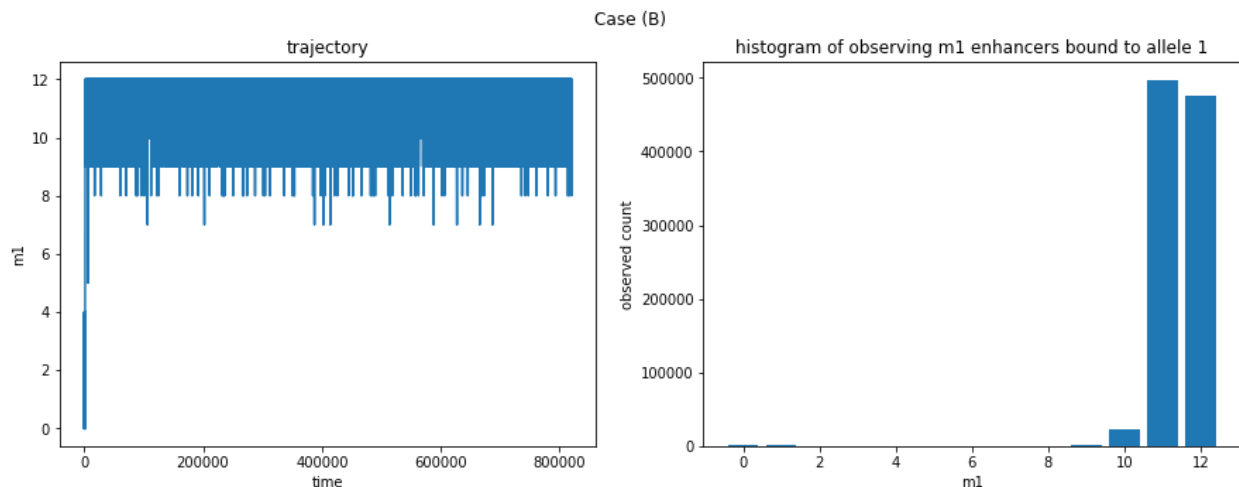
- 1) (30 points) For each case, simulate a long or multiple trajectories, plot histograms of observing m_1 enhancers bound to allele 1 (so $m_2 = M - m_1$ enhancers bound to allele 2).

observed count, without resampling

A) symmetric case: $\varepsilon_1 = \varepsilon_2 = \varepsilon$, $\delta = -0.5 k_B T$



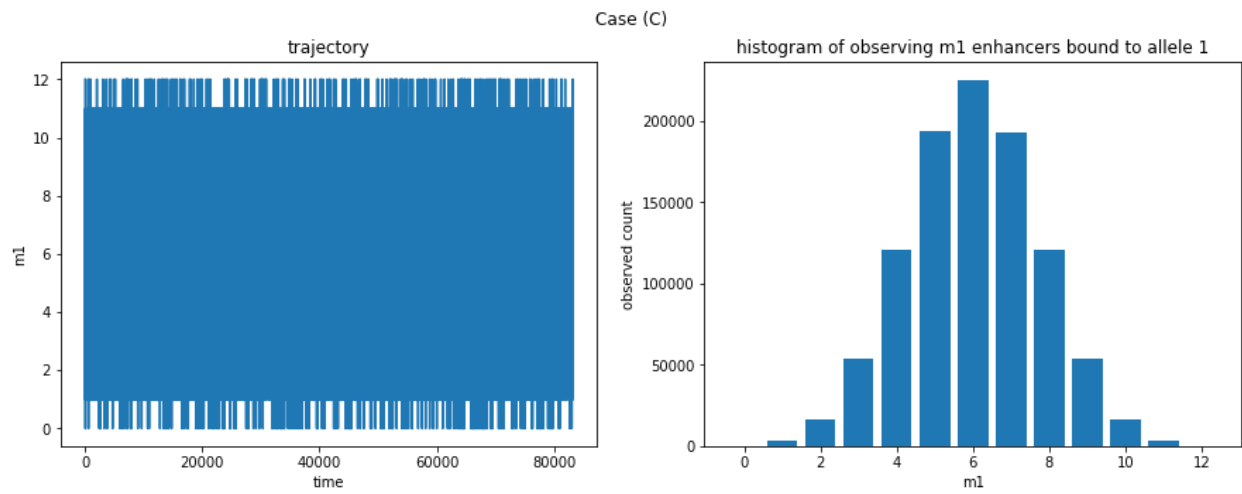
B) asymmetric case: $\varepsilon_1 = \varepsilon$, $\varepsilon_2 = \varepsilon + 0.5 k_B T$, $\delta = -0.5 k_B T$



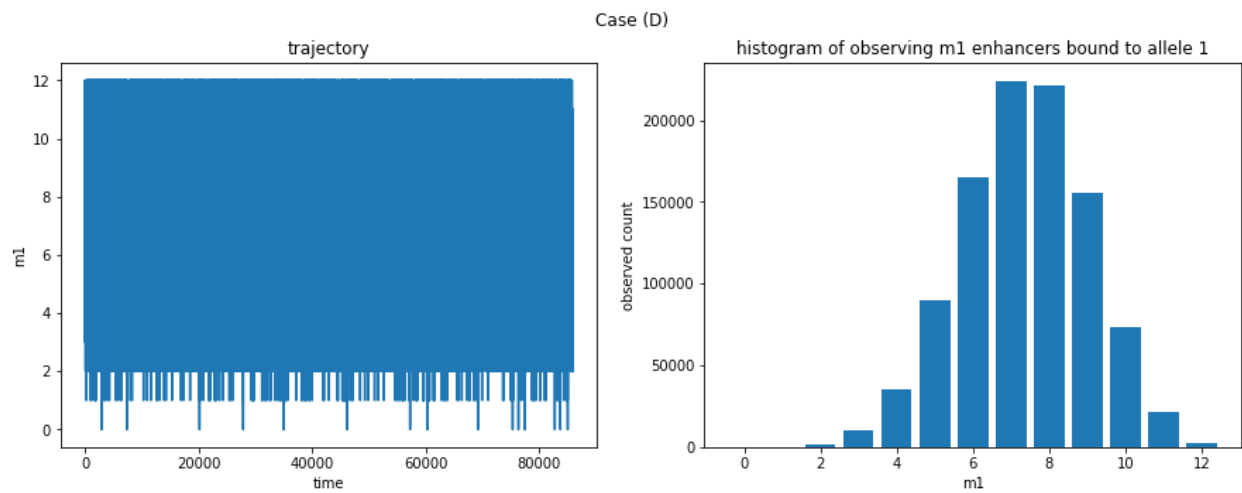
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C) symmetric without cooperativity: $\varepsilon_1 = \varepsilon_2 = \varepsilon$, $\delta = 0$



D) asymmetric case without cooperativity: $\varepsilon_1 = \varepsilon$, $\varepsilon_2 = \varepsilon + 0.5 k_B T$, $\delta = 0$



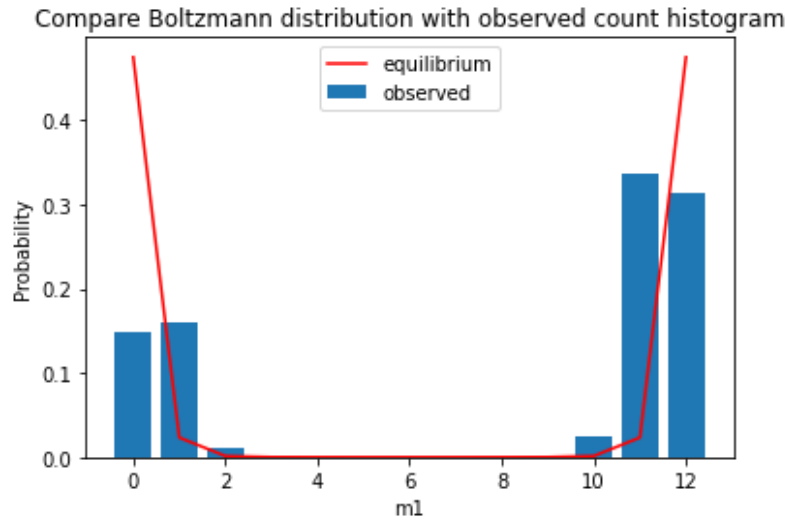
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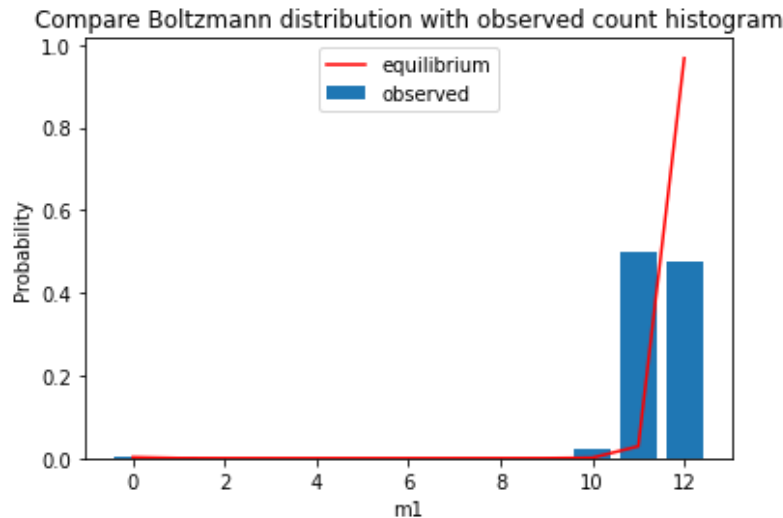
- 2) (10 points) Convince yourself that the total free energy of a configuration with m_1 enhancers bound to allele 1 is $E_{m_1} = m_1 \varepsilon_1 + m_2 \varepsilon_2 + \frac{m_1(m_1-1)}{2} \delta + \frac{m_2(m_2-1)}{2} \delta$. Then the equilibrium probability of observing such configuration is given by the Boltzmann distribution, $P_{m_1} = \frac{\frac{M!}{m_1!m_2!} \exp(-E_{m_1}/k_B T)}{\sum_{m_1=0}^M \frac{M!}{m_1!m_2!} \exp(-E_{m_1}/k_B T)}$. Compare the Boltzmann distribution with what you obtained in question 1.

With a lower free energy, the probabilities of m_1 falls into those value are higher. Therefore, the Boltzmann distribution P_{m_1} would give us similar trend as we observed from the long (to equilibrium) simulations.

(A) symmetric case: $\varepsilon_1 = \varepsilon_2 = \varepsilon$, $\delta = -0.5 k_B T$



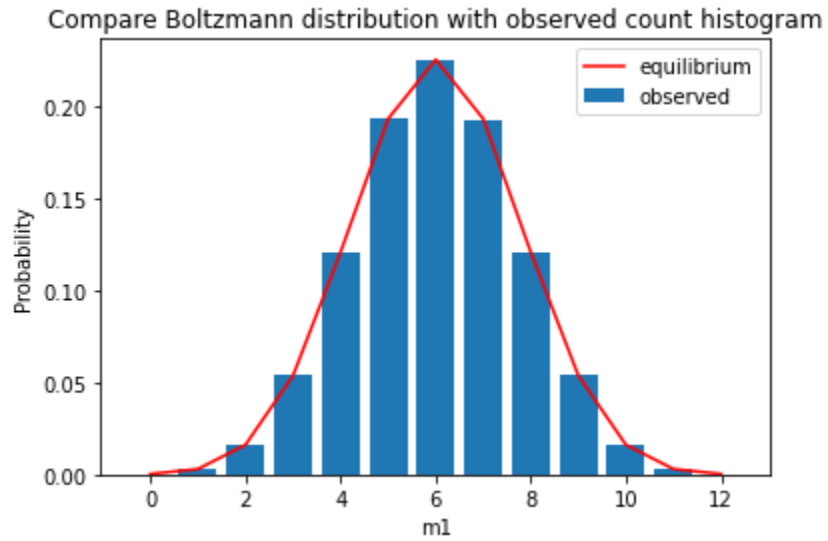
(B) asymmetric case: $\varepsilon_1 = \varepsilon$, $\varepsilon_2 = \varepsilon + 0.5 k_B T$, $\delta = -0.5 k_B T$



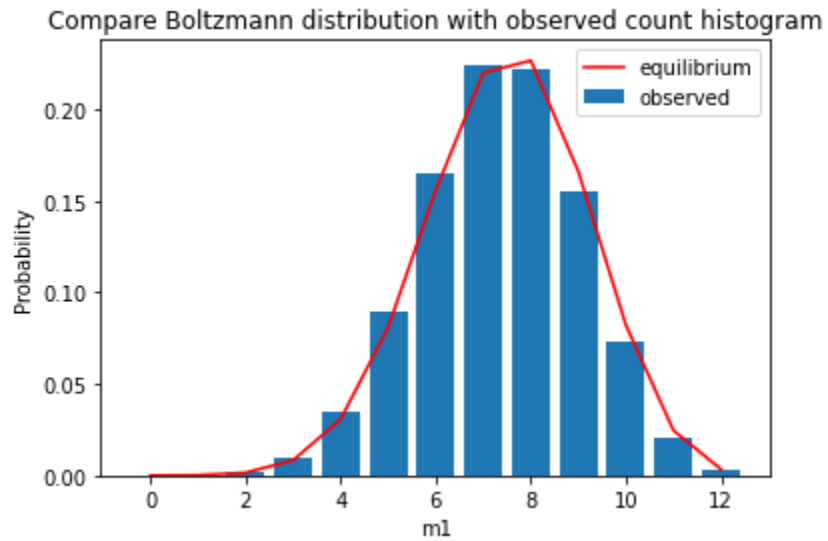
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(C) symmetric without cooperativity: $\varepsilon_1 = \varepsilon_2 = \varepsilon$, $\delta = 0$



(D) asymmetric case without cooperativity: $\varepsilon_1 = \varepsilon$, $\varepsilon_2 = \varepsilon + 0.5 k_B T$, $\delta = 0$



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- 3) (10 points) Compare the symmetric (asymmetric) case with and without cooperativity, and discuss how the qualitative shape of the distribution changes.

Based on the distribution we can see that when there is cooperativity, almost all the enhancers would bound to the same allele. For the symmetric case, the enhancers would all bind to allele 1 and after some time they would all bind to allele 2. For the asymmetric case, since allele 1 is more preferable than allele 2, almost all enhancers are bound to allele 1 throughout the equilibrium stage.

When there is no cooperativity, each enhancer would choose which allele it wants to bind freely without looking at the neighbors, thus we observed the histogram of m_1 is a normal distribution with its mean = $M/2$. For the asymmetric case where allele 1 is preferable, we can see that the peak of the bell curve is shifting to the right because the probability of an enhancer binding to allele 1 is higher than it binding to allele 2.