

# PY541 PS6

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## Problem 1: Wolff (Sethna 8.8)

(a)

In Metropolis algorithm, the correlation time is very long. For Wolff, on the other hand, the correlation time is very short. The dynamics of the spin flip is changing at almost every step. The speedup is significant.

(b)

We define a spin up site has energy of  $+J$ , and a spin down site has energy of  $-J$ . Thus, we can say that the interaction energy, that is, the difference in energy between adjacent sites, is 0 if the spins of two adjacent sites have same direction, and  $2J$  if the spins are opposite. In the case where a cluster of spin ups flips to spin downs, each boundary segments adjacent to a spin up gains energy of  $2J$ , whereas each boundary segments adjacent to a spin down loses energy of  $-2J$ . If we denote  $n_{\uparrow}$  = number of cluster edges adjacent to a spin up site and  $n_{\downarrow}$  = number of cluster edges adjacent to a spin down site, we can say that the energy gain due to the flip is  $\Delta E_{\uparrow} = 2J \times n_{\uparrow}$  and energy loss due to the flip is  $\Delta E_{\downarrow} = -2J \times n_{\downarrow}$ . Thus, without the loss of generality, we can say that the change in energy due to a cluster flip is given by:

$$E_B - E_A = \Delta E_{\uparrow} + \Delta E_{\downarrow} = 2(n_{\uparrow} - n_{\downarrow})J \quad (1)$$

(c)

Detailed balance requires the probability flux from a state to another balances the probability flux backwards. That is,  $P_{\alpha\beta}\rho_{\beta}^* = P_{\beta\alpha}\rho_{\alpha}^*$ . In our case, we have  $P_{\alpha\beta} = \Gamma_{A \rightarrow B}$ ,  $P_{\beta\alpha} = \Gamma_{B \rightarrow A}$ ,  $\rho_{\beta} = e^{-\beta E_B}$ , and  $\rho_{\alpha} = e^{-\beta E_A}$ . Therefore, the detailed balance imposes the following relationship:

$$\Gamma_{A \rightarrow B} e^{-\beta E_A} = \Gamma_{B \rightarrow A} e^{-\beta E_B} \quad (2)$$

On the other hand, we have

$$\Gamma_{A \rightarrow B} = \sum_{\alpha} P_{\alpha}^C (1-p)^{n_{\uparrow}} \quad (3)$$

$$\Gamma_{B \rightarrow A} = \sum_{\alpha} P_{\alpha}^C (1-p)^{n_{\downarrow}} \quad (4)$$

Plugging in the expressions, we have the relation

$$\sum_{\alpha} P_{\alpha}^C (1-p)^{n_{\uparrow}} e^{-\beta E_A} = \sum_{\alpha} P_{\alpha}^C (1-p)^{n_{\downarrow}} e^{-\beta E_B} \quad (5)$$

$$(1-p)^{n_{\uparrow}-n_{\downarrow}} = e^{-2\beta(n_{\uparrow}-n_{\downarrow})J} \quad (6)$$

Therefore, we have the expression for the probability  $p$ :

$$p(T) = 1 - e^{2J/k_B T} \quad (7)$$

## Problem 2: Entropy Increases! Markov Chains (Sethna 8.12)

(a)

Let's use the induction argument on  $M$ . Assume that the statement is true for  $M$ . If the statement is true for  $M = 1$ , as well as  $M + 1$ , then we know that the statement is true in general.

It is straightforward to see that for  $M = 1$ , the relation holds for a concave function  $g$ :

$$g(\mu x) \geq \mu g(x) \quad (8)$$

Let's now look at  $M + 1$  case.

$$g\left(\sum_{\alpha=1}^{M+1} \mu_{\alpha} x_{\alpha}\right) = g\left(\mu_{M+1} x_{M+1} + \sum_{\alpha=1}^M \mu_{\alpha} x_{\alpha}\right) \geq \mu_{M+1} g(x_{M+1}) + \sum_{\alpha=1}^M \mu_{\alpha} g(x_{\alpha}) = \sum_{\alpha=1}^{M+1} \mu_{\alpha} g(x_{\alpha}) \quad (9)$$

Thus, we can see that the statement is true for  $M + 1$ . Therefore, we have proven that, for a concave function  $g(x)$  over the domain  $x \geq 0$ ,

$$\boxed{g\left(\sum_{\alpha=1}^M \mu_{\alpha} x_{\alpha}\right) \geq \sum_{\alpha=1}^M \mu_{\alpha} g(x_{\alpha})} \quad (10)$$

**(b)**

The free energy of  $n$ th state is given by:

$$F^{(n)} = \sum_{\alpha} \rho_{\alpha}^{(n)} E_{\alpha} + k_B T \rho_{\alpha}^{(n)} \log(\rho_{\alpha}^{(n)}) \quad (11)$$

Similarly, the free energy of  $n + 1$ th state is given by:

$$F^{(n+1)} = \sum_{\alpha} \rho_{\alpha}^{(n+1)} E_{\alpha} + k_B T \rho_{\alpha}^{(n+1)} \log(\rho_{\alpha}^{(n+1)}) \quad (12)$$

but we have the relation

$$\rho_{\alpha}^{(n+1)} = \sum_{\beta} P_{\alpha\beta} \rho_{\beta}^{(n)} \quad (13)$$

Thus, we can express the free energy at  $n + 1$ th state in terms of  $\rho_{\beta}^{(n)}$ :

$$\begin{aligned} F^{(n+1)} &= \sum_{\alpha\beta} P_{\alpha\beta} \rho_{\beta}^{(n)} E_{\alpha} + k_B T P_{\alpha\beta} \rho_{\beta}^{(n)} \log(P_{\alpha\beta} \rho_{\beta}^{(n)}) \\ &= \sum_{\alpha\beta} P_{\beta\alpha} \frac{\rho_{\alpha}^{*}}{\rho_{\beta}^{*}} \rho_{\beta}^{(n)} E_{\alpha} + k_B T P_{\beta\alpha} \frac{\rho_{\alpha}^{*}}{\rho_{\beta}^{*}} \rho_{\beta}^{(n)} \log\left(P_{\beta\alpha} \frac{\rho_{\alpha}^{*}}{\rho_{\beta}^{*}} \rho_{\beta}^{(n)}\right) \end{aligned} \quad (14)$$

where we have used detailed balance in the last equality. Defining a concave function  $g(x) = -x \log(x)$  and using the relation found in part (a), we can further develop the relation as:

$$\begin{aligned} F^{(n+1)} &= \sum_{\alpha\beta} P_{\beta\alpha} \frac{\rho_{\alpha}^{*}}{\rho_{\beta}^{*}} \rho_{\beta}^{(n)} E_{\alpha} - k_B T g\left(\sum_{\alpha\beta} P_{\beta\alpha} \frac{\rho_{\alpha}^{*}}{\rho_{\beta}^{*}} \rho_{\beta}^{(n)}\right) \\ &\leq \sum_{\alpha\beta} \rho_{\beta}^{(n)} \left[ E_{\alpha} + k_B T \left( \log\left(\frac{\rho_{\alpha}^{*}}{\rho_{\beta}^{*}}\right) + \log(\rho_{\beta}^{(n)}) \right) \right] = F^{(n)} \end{aligned} \quad (15)$$

where we have flipped the direction of inequality along with flipping the signs. In short, we have  $\boxed{F^{(n+1)} \leq F^{(n)}}$ .

This means that the free energy decreases for a Markov chain, which means that the entropy increases for Markov chains.

### Problem 3: Stochastic Cells (Sethna 8.10)

**(a)**

The monomer concentration decreases by two whenever two monomers dimerize. This happens with a rate of  $k_b$ , so concentration decreases by  $-2k_b[M]^2$  for a unit time. On the other hand, the concentration increases by two

whenever a dimer dissociates, so the concentration increases by  $2k_u[D]$ . The net change in dimer concentration  $[M]$  with respect to time is given by:

$$\boxed{\frac{dM}{dt} = -2k_b[M]^2 + 2k_u[D]} \quad (16)$$

The dimer concentration is the opposite, but we should take note that only one dimer is produced or dissociated. Thus,

$$\boxed{\frac{dM}{dt} = k_b[M]^2 - k_u[D]} \quad (17)$$

To find the equilibrium concentrations, set Eq. 16 to 0 and solve the following system of equations:

$$\begin{cases} \frac{dM}{dt} = -2k_b[M]^2 + 2k_u[D] = 0 \\ [M] + 2[D] = N \end{cases} \Rightarrow [M(t = \infty, N)] = -\frac{k_u}{4k_b} + \frac{\sqrt{k_u^2 + 8Nk_bk_u}}{4k_b} \quad (18)$$

Setting  $N = 2, 90, 10100$ , along with  $k_b = 1$  and  $k_u = 2$ , we can see that

$$\begin{cases} [M(\infty, 2)] = \frac{4\sqrt{k_u}}{\sqrt{k_u} + \sqrt{16k_b + k_u}} \Rightarrow [M(0, 2)] = 1 \text{ nM} \\ [M(\infty, 90)] = -\frac{k_u}{4k_b} + \frac{\sqrt{720k_bk_u + k_u^2}}{4k_b} \Rightarrow [M(0, 90)] = 9 \text{ nM} \\ [M(\infty, 10100)] = -\frac{k_u}{4k_b} + \frac{\sqrt{80000k_bk_u + k_u^2}}{4k_b} \Rightarrow [M(0, 10100)] = 100 \text{ nM} \end{cases} \quad (19)$$

The numerical solutions with the plots are attached below as a Mathematica notebook.

(b)

Below are the plots simulating dimerization reaction using Monte Carlo method. The blue curves represent the continuum solution, and the orange curves are the discrete simulations.

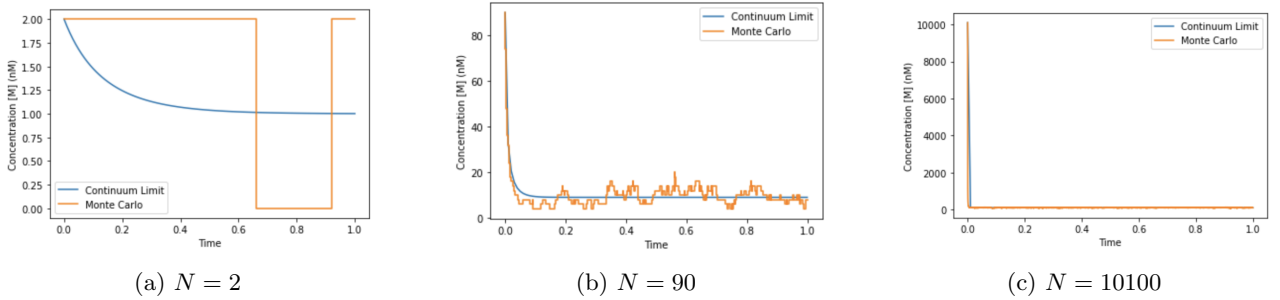


Figure 1: Monte Carlo vs continuum limit

We can observe that at  $N = 90$ , the plots somewhat agree, with some fluctuations. At  $N = 10100$ , the plots almost completely agree.

(c)

Below are the averages for stochastic dimerizations.

We are already getting some reasonable plots for  $N = 2$ . At  $N = 90$ , we are getting a remarkable agreement with the continuum limit.

## Problem 4: Kinetic Proof Reading (Sethna 8.23)

(a)

We have

$$\frac{\rho_E^*}{\rho_{E'A}^*} = e^{\beta(\varepsilon_{E'A} - \varepsilon_E)} \quad (20)$$

$$\frac{\rho_E^*}{\rho_{E'G}^*} = e^{\beta(\varepsilon_{E'G} - \varepsilon_E)} \quad (21)$$

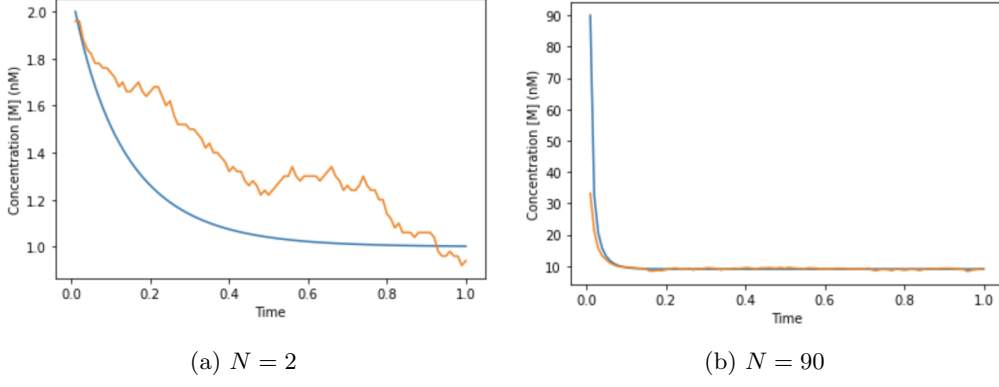


Figure 2: Average of stochastic dimerization

We assume  $\rho_E^* \approx 1$ , so

$$\rho_{E'A}^* = e^{-\beta(\varepsilon_{E'A} - \varepsilon_E)} = \frac{\alpha}{\mu_A} \quad (22)$$

$$\rho_{E'G}^* = e^{-\beta(\varepsilon_{E'G} - \varepsilon_E)} = \frac{\alpha}{\mu_G} \quad (23)$$

For most of  $E$  to remain unbound,  $\varepsilon_E \ll \varepsilon_{E'A}, \varepsilon_{E'G}$ . That is, the free energy of the unbound state should be a lot less than those of bound states.

Detailed balance requires

$$\rho_E^* \alpha = \rho_{E'A}^* \mu_A \quad (24)$$

$$\rho_E^* \alpha = \rho_{E'G}^* \mu_G \quad (25)$$

The failure rate is given by:

$$f_\rho^* = \frac{\rho_{E,G}^*}{\rho_{E,A}^*} = \frac{\mu_A}{\mu_G} \quad (26)$$

We can notice that not assuming  $\rho_E^* \approx 1$  introduces the  $\rho_E^*$  term at the first equality of Eq. 26, but the term cancel out, resulting in the same form even without the assumption.

(b)

$$\begin{aligned} f_{\text{naive}} &= \frac{\rho_{E,G}^*}{\rho_{E,A}^*} = \exp[\beta(\varepsilon_{E,A}^* - \varepsilon_E) - \beta(\varepsilon_{E,G}^* - \varepsilon_E)] \\ &= \exp[-\beta(\varepsilon_{E,G}^* - \varepsilon_{E,A}^*)] = \exp\left[-\frac{5}{(0.616)}\right] \approx 2.985 \times 10^{-4} \end{aligned} \quad (27)$$

To agree with the failure rate match with the experimental value,

$$-\frac{\Delta\varepsilon}{0.616} = \log(10^{-9}) \Rightarrow \Delta\varepsilon = -12.75 \frac{\text{kcal}}{\text{mol}} \quad (28)$$

(c)

Detailed balance gives

$$\begin{aligned} \rho_E^* \alpha &= \rho_{E'A}^* \mu_A & \rho_E^* \alpha &= \rho_{E'G}^* \mu_G & \Rightarrow \rho_{E'A}^* &= \frac{\rho_{E'A}^* \beta}{\eta} = \frac{\alpha \beta}{\mu_A \eta} \\ \rho_{E'A}^* \beta &= \rho_{E'A}^* \eta & \rho_{E'G}^* \beta &= \rho_{E'G}^* \eta & \Rightarrow \rho_{E'G}^* &= \frac{\rho_{E'G}^* \beta}{\eta} = \frac{\alpha \beta}{\mu_G \eta} \\ \rho_E^* \lambda &= \rho_{E'A}^* \sigma_A & \rho_E^* \lambda &= \rho_{E'G}^* \sigma_G \end{aligned} \quad (29)$$

Thus, the failure rate becomes:

$$f_\rho^* = \frac{\rho_{E'G}^*}{\rho_{E'A}^*} = \frac{\alpha \beta}{\mu_G \eta} \frac{\mu_A \eta}{\alpha \beta} = \frac{\mu_A}{\mu_G} \quad (30)$$

Therefore, the failure remains same as in part (a).

Assuming  $\rho_E \approx 1$ , from the detailed balance, we get the following:

$$\rho_{E'A}^* = \frac{\lambda}{\sigma_A}, \text{ and } \rho_{E'G}^* = \frac{\lambda}{\sigma_G} \quad (31)$$

Using these expressions, we have for the failure rate

$$f_{\text{rate}} = \frac{\rho_{E'G}^*}{\rho_{E'A}^*} = \frac{\lambda}{\sigma_G} \frac{\sigma_A}{\lambda} = \frac{\sigma_A}{\sigma_G} \quad (32)$$

Cyclic detailed balance says

$$(\rho_E^* \lambda)(\rho_{E'A}^* \eta)(\rho_{EA}^* \mu_A) = (\rho_E^* \alpha)(\rho_{EA}^* \beta)(\rho_{E'A}^* \sigma_A) \quad (33)$$

$$(\rho_E^* \lambda)(\rho_{E'G}^* \eta)(\rho_{EG}^* \mu_A) = (\rho_E^* \alpha)(\rho_{EG}^* \beta)(\rho_{E'G}^* \sigma_A) \quad (34)$$

From this, we get

$$\lambda \eta \mu_A = \alpha \beta \sigma_A \quad (35)$$

$$\lambda \eta \mu_G = \alpha \beta \sigma_G \quad (36)$$

Finally, combining the two equations, we get

$$\boxed{\frac{\sigma_A}{\sigma_G} = \frac{\mu_A}{\mu_G}} \quad (37)$$

(d)

The cyclic detailed balance does not hold for the kinetic proofreading diagram, because in kinetic proofreading, there is an ATP that is used to fuel the transition between  $EA$  to  $E'A$ , which is not reversible. For the cyclic detailed balance to hold, the reaction should look the same whether it goes  $EA \rightarrow E'A$  or  $E'A \rightarrow EA$ , which is not true in kinetic proofreading. The environment loses an ATP and gains AMP per clockwise reaction.

(e)

$$\text{error ratio} = f = \frac{\rho_{E'G}^*}{\rho_{E'A}^*} = \exp[-\beta(\varepsilon_{E'G} - \varepsilon_{E'A} + \delta\Xi)] \quad (38)$$

(f)

The matrix can be built with the rates of the following transitions:

$$M_{\text{Mark}} = \begin{pmatrix} E \rightarrow E & EA \rightarrow E & E'A \rightarrow E \\ E \rightarrow EA & EA \rightarrow EA & E'A \rightarrow EA \\ E \rightarrow E'A & EA \rightarrow E'A & E'A \rightarrow E'A \end{pmatrix} \quad (39)$$

Thus, the matrix for 8.28 is given by:

$$M_{\text{Mark}}^{8.28} = \begin{pmatrix} 1 - \alpha - \lambda & \mu_A & \sigma_A \\ \alpha & 1 - \mu_A - \beta & \eta \\ \lambda & \beta & 1 - \sigma_A - \eta - \omega \end{pmatrix} \quad (40)$$

For 8.29, we have basically the same matrix, but with greater  $\beta$  and smaller  $\eta$ , since the  $\text{ATP} \rightarrow \text{AMP}$  reaction makes  $EA \rightarrow E'A$  much more likely than the reverse. I will denote the reaction rates  $\tilde{\beta}$  and  $\tilde{\eta}$ , where  $\tilde{\beta} > \beta$  and  $\tilde{\eta} < \eta$ .

$$M_{\text{Mark}}^{8.29} = \begin{pmatrix} 1 - \alpha - \lambda & \mu_A & \sigma_A \\ \alpha & 1 - \mu_A - \tilde{\beta} & \tilde{\eta} \\ \lambda & \tilde{\beta} & 1 - \sigma_A - \tilde{\eta} - \omega \end{pmatrix} \quad (41)$$

(g)

Imposing cyclic detailed balance, we have:

$$\frac{\lambda \eta \mu_A}{\lambda \eta \mu_G} = \frac{\alpha \beta \sigma_A}{\alpha \beta \sigma_G} \Rightarrow \sigma_A = \frac{\lambda \eta \mu_A}{\alpha \beta}, \text{ and } \sigma_G = \frac{\lambda \eta \mu_G}{\alpha \beta} \quad (42)$$

Using Mathematica, we recover the simple expression we obtained for  $f_{\text{naive}}$

$$\text{FullSimplify}\left[\frac{(\alpha \beta + \beta \lambda + \lambda \mu g) (\eta \mu a + \beta \sigma a + \mu a \sigma a)}{(\alpha \beta + \beta \lambda + \lambda \mu a) (\eta \mu g + \beta \sigma g + \mu g \sigma g)} /. \left\{\sigma a \rightarrow \frac{\lambda \eta \mu a}{\alpha \beta}, \sigma g \rightarrow \frac{\lambda \eta \mu g}{\alpha \beta}\right\}\right]$$

$$\frac{\mu a}{\mu g}$$

(h)

When we set  $\lambda = \eta = 0$ , we have

$$f = \frac{\beta \sigma_A + \mu_A \sigma_A}{\beta \sigma_G + \mu_G \sigma_G} \quad (43)$$

For small  $\beta$ , the expression reduces to

$$f = \frac{\mu_A \sigma_A}{\mu_G \sigma_G} \quad (44)$$