Bias forces in well-tempered metadynamics

Siva Dasetty

Notes | 07.07.20

---

1. Single CV

According to well-tempered metadynamics [1], bias potential (V_{bias}) deposited at any time (t) along a single collective variable (CV) with respect to CV at every iteration ($niter$),

$$V_{\text{bias}}\left(\text{CV},\ t_{\text{niter}}\right)_{\text{CV}_t} = V_{\text{bias}}\left(\text{CV},\ t_{niter-1}\right)_{\text{CV}_t} + w \times \exp\left\{-\frac{1}{2}\left(\frac{(\text{CV}-\text{CV}_{\text{niter}})}{\sigma}\right)^2\right\}_{\text{CV}_t}$$

- In standard metadynamics [2], $w = w_0$
- In well-tempered metadynamics [1], $w = w_0 \times \exp\left(-\frac{V_{\text{bias}}(\text{CV},\ t_{\text{niter}}\ )}{k_B \Delta T}\right)$

Force at every timestep (t) due to deposited bias potential:

$$F_{\text{bias}}(\text{r}, t) = \ -\left\{\frac{dV_{\text{bias}}\left(\text{CV}, t_{\text{niter}}\right)}{\text{dCV}}\right\}_{\text{CV}_t} \times \frac{\text{dCV}}{\text{dr}_t}$$

Substituting $V_{\text{bias}}\left(\text{CV},\ t_{\text{niter}}\right)$ in the first term of the RHS in the above equation

$$\left\{\frac{dV_{\text{bias}}\left(\text{CV}, t_{\text{niter}}\right)}{\text{dCV}}\right\}_{\text{CV}_t} = \left\{\frac{d\left[V_{\text{bias}}\left(\text{CV},\ t_{niter-1}\right) + w \times \exp\left\{-\frac{1}{2}\left(\frac{(\text{CV}-\text{CV}_{\text{niter}})}{\sigma}\right)^2\right\}\right]}{\text{dCV}}\right\}_{\text{CV}_t}$$

- Helper function: Derivative of Gaussian at any iteration

$$\left\{\frac{d\left[w \times exp\left\{-\frac{1}{2}\left(\frac{(\text{CV}-\text{CV}_{\text{niter}})}{\sigma}\right)^2\right\}\right]}{\text{dCV}}\right\}_{CV_t}$$
$$= \left\{-w \times \frac{(\text{CV}-\text{CV}_{\text{niter}})}{\sigma^2} \exp\left\{-\frac{1}{2}\left(\frac{(\text{CV}-\text{CV}_{\text{niter}})}{\sigma}\right)^2\right\}\right\}_{\text{CV}_t}$$

Substituting helper function in $\left\{\frac{dV_{\text{bias}}(\text{CV}, t_{\text{niter}})}{\text{dCV}}\right\}_{\text{CV}_t}$

$$\left\{\frac{dV_{\text{bias}}\left(\text{CV},t_{\text{niter}}\right)}{\text{dCV}}\right\}_{\text{CV}_t}=$$

$$\left\{\sum_{iter\leq niter-1}\left[-w\times\frac{\left(\text{CV}-\text{CV}_{\text{niter}}\right)}{\sigma^2}\exp\left\{-\frac{1}{2}\left(\frac{\left(\text{CV}-\text{CV}_{\text{niter}}\right)}{\sigma}\right)^2\right\}\right]\right.$$
$$\left.-w\times\frac{\left(\text{CV}-\text{CV}_{\text{niter}}\right)}{\sigma^2}\exp\left\{-\frac{1}{2}\left(\frac{\left(\text{CV}-\text{CV}_{\text{niter}}\right)}{\sigma}\right)^2\right\}\ \right\}_{\text{CV}_t}$$

2. N CVs

Bias potential every n number of iterations (niter):

$$\begin{aligned}&V_{\text{bias}}\left(\text{CV}_1,\text{CV}_2,\dots\text{CV}_n,\ t_{\text{niter}}\right)_{\text{CV}_{1,t},\text{CV}_{2,t},\dots,\text{CV}_{n,t}}\\ &=V_{\text{bias}}\left(\text{CV}_1,\text{CV}_2,\dots\text{CV}_n,t_{niter-1}\right)_{\text{CV}_{1,t},\text{CV}_{2,t},\dots,\text{CV}_{n,t}}\\ &\quad+w\times\prod_{i=1..N}\exp\left\{-\frac{1}{2}\left(\frac{\left(\text{CV}_i-\text{CV}_{i,\ niter}\right)}{\sigma_i}\right)^2\right\}_{\text{CV}_{i,\ t}}\end{aligned}$$

- In standard metadynamics, $w=w_0$
- In well-tempered metadynamics, $w=w_0\times\exp\left(-\frac{V_{\text{bias}}\left(\text{CV}_1,\text{CV}_2,\dots\text{CV}_n,t_{\text{niter}}\ \right)}{k_B\Delta T}\right)_{\text{CV}_{1,\ niter},\text{CV}_{2,\ niter},\dots,\text{CV}_{n,niter}}$

Force at every timestep due to bias potential:

$$F_{\text{bias}}\left(t\right)=\ -\sum_{i=1,..N}\left\{\frac{dV_{\text{bias}}\left(\text{CV}_1,\text{CV}_2,\dots\text{CV}_n,t_{\text{niter}}\right)}{\text{dCV}_i}\right\}_{\text{CV}_{i,t}}\times\frac{\text{dCV}_i}{\text{dr}_t}$$

Substituting $V_{\text{bias}}\left(\text{CV}_1,\text{CV}_2,\ C_{\text{niter}}\right)$ in the first term of the RHS of $F_{\text{bias}}\left(t\right)$

$$\left\{\frac{dV_{\text{bias}}\left(\text{CV}_1,\text{CV}_2,\dots\text{CV}_n,t_{\text{niter}}\right)}{\text{dCV}_i}\right\}_{\text{CV}_{i,t}}=$$

$$\left\{\frac{d\left[V_{\text{bias}}\left(\text{CV}_1,\text{CV}_2,\ \dots\text{CV}_n,t_{niter-1}\right)+w\times\prod_{i=1..N}\exp\left\{-\frac{1}{2}\left(\frac{\left(\text{CV}_i-\text{CV}_{i,\ niter}\right)}{\sigma_i}\right)^2\right\}\right]}{\text{dCV}_i}\right\}_{\text{CV}_{i,t}}$$

- Helper function: Derivative of Gaussian (gDerv) with respect to CV_1 at any iteration

$$\left\{ \frac{d\left[w \times \prod_{i=1..N} \exp\left\{-\frac{1}{2}\left(\frac{(\mathrm{CV}_i - \mathrm{CV}_{i,\ niter})}{\sigma_i}\right)^2\right\}\right]}{\mathrm{dCV}_1} \right\}_{\mathrm{CV}_{1,\ t}}$$

$$= \left\{ -w \times \frac{(\mathrm{CV}_1 - \mathrm{CV}_{1,niter})}{\sigma_1^2} \exp\left\{-\frac{1}{2}\left(\frac{(\mathrm{CV}_1 - \mathrm{CV}_{1,\ niter})}{\sigma_1}\right)^2\right\} \times \prod_{i=2..N} \exp\left\{-\frac{1}{2}\left(\frac{(\mathrm{CV}_i - \mathrm{CV}_{i,\ niter})}{\sigma_i}\right)^2\right\} \right\}_{\mathrm{CV}_{1.t}}$$

Substituting helper function in general case i.e., $\left\{\frac{dV_{\mathrm{bias}}(\mathrm{CV}_1,\mathrm{CV}_2,\ldots\mathrm{CV}_n,t_{\mathrm{niter}})}{\mathrm{dCV}_i}\right\}_{\mathrm{CV}_{i,t}}$

$$\left\{\frac{dV_{\mathrm{bias}}\left(\mathrm{CV}_1,\mathrm{CV}_2,\ldots\mathrm{CV}_n,t_{\mathrm{niter}}\right)}{\mathrm{dCV}_i}\right\}_{\mathrm{CV}_{i,t}} =$$

$$\left\{ \sum_{iter \le niter-1} \left[-w \times \frac{(\mathrm{CV}_i - \mathrm{CV}_{i,niter})}{\sigma_i^2} \exp\left\{-\frac{1}{2}\left(\frac{(\mathrm{CV}_i - \mathrm{CV}_{i,\ niter})}{\sigma_i}\right)^2\right\} \times \prod_{j\neq i, j=1..N} \exp\left\{-\frac{1}{2}\left(\frac{(\mathrm{CV}_i - \mathrm{CV}_{i,\ niter})}{\sigma_i}\right)^2\right\} \right] \right.$$

$$\left. -w \times \frac{(\mathrm{CV}_i - \mathrm{CV}_{i,niter})}{\sigma_i^2} \exp\left\{-\frac{1}{2}\left(\frac{(\mathrm{CV}_i - \mathrm{CV}_{i,\ niter})}{\sigma_i}\right)^2\right\} \times \prod_{j\neq i, j=1..N} \exp\left\{-\frac{1}{2}\left(\frac{(\mathrm{CV}_i - _{\mathrm{CV}}\ i, niter)}{\sigma_i}\right)^2\right\} \right\}_{\mathrm{CV}_{i,t}}$$

Combining the two terms in RHS,

$$\left\{\frac{dV_{\mathrm{bias}}\left(\mathrm{CV}_1,\mathrm{CV}_2,\ldots\mathrm{CV}_n,t_{\mathrm{niter}}\right)}{\mathrm{dCV}_i}\right\}_{\mathrm{CV}_{i,t}} =$$

$$\left\{ \sum_{iter \le niter} \left[-w \times \frac{(\mathrm{CV}_i - \mathrm{CV}_{i,niter})}{\sigma_i^2} \exp\left\{-\frac{1}{2}\left(\frac{(\mathrm{CV}_i - \mathrm{CV}_{i,\ niter})}{\sigma_i}\right)^2\right\} \times \prod_{j\neq i, j=1..N} \exp\left\{-\frac{1}{2}\left(\frac{(\mathrm{CV}_i - \mathrm{CV}_{i,\ niter})}{\sigma_i}\right)^2\right\} \right] \right\}_{\mathrm{CV}_{i,t}}$$

In terms of gaussianDerv (gDerv) and gaussian (g),

$$\left\{ \frac{dV_{\text{bias}} \left(\text{CV}_1, \text{CV}_2, \dots \text{CV}_n, t_{\text{niter}} \right)}{\text{dC}V_i} \right\}_{\text{CV}_{i,t}}$$

$$= \left\{ \sum_{iter \leq niter} \left[w \times gDerv(\text{CV}_i - \text{CV}_{i,niter}, \sigma_i) \times \prod_{j \neq i, j=1..N} g \left(\text{CV}_i - \text{CV}_{i,niter}, \sigma_i \right) \right] \right\}_{\text{CV}_{i,t}}$$

[1] A. Barducci, G. Bussi, and M. Parrinello, *Well-Tempered Metadynamics: A Smoothly Converging and Tunable Free-Energy Method*, Physical Review Letters **100**, 020603 (2008).

[2] A. Laio and M. Parrinello, *Escaping Free-Energy Minima*, Proceedings of the National Academy of Sciences **99**, 12562 (2002).