One Dimensional Weighted-Ensemble Brownian (WEB) Dynamics Simulation

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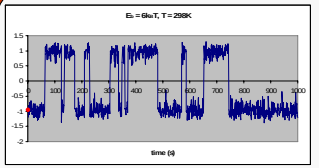
Introduction

Pharmaceuticals that cure illness, treat disease, and improve quality of life are the byproducts of our greater understanding of how the human body functions. In the last century, our knowledge of human anatomy and physiology has penetrated beyond the level of organ systems, organs, differentiated tissue cells, organelles, and nucleic acids to the very molecules of functionality themselves, proteins.

Abstract

It is difficult to determine high-energy conformations of proteins, because they exist in their high energy states for too short of a time to acquire laboratory data. The alternative for determining high-energy protein conformations outside the laboratory is through a dynamics simulation. Most algorithms for dynamics simulations are incapable of simulating a protein long enough to identify a protein's high energy conformation. However, Huber and Kim's weighted-ensemble Brownian (WEB) dynamics simulation surpasses its contemporary algorithms.

The WEB method makes such an improvement on standard Brownian algorithms that it is capable of producing the same length of real-time simulation as standard Brownian methods at a fraction of the computing time.

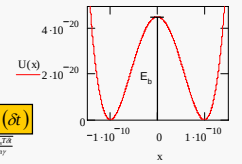


Brownian Dynamics Simulation of one Particle in Double-Welled Energy Coordinate

Method

$$U(x) = E_b\left[\left(\frac{x}{d}\right)^2 - 1\right]^2$$

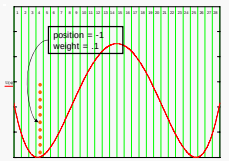
$d = 1\text{Å}$ $\quad E_b = 11k_BT$



Brownian Algorithm:

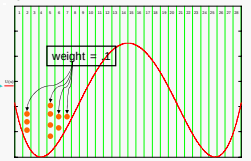
$$x_{i+1} = x_i + F_i \times (m\gamma)^{-1} \times \delta t + X_i(\delta t)$$

$F_i = -\frac{dU}{dx}\Big|_{x_i}$ $\quad m = \frac{1k_BTs^2}{\text{Å}^2}$ $\quad \delta t = .001\text{s}$ $\quad \gamma = 1s^{-1}$ $\quad X_i(\delta t) = \pm\sqrt{\frac{2k_BT\delta t}{m\gamma}}$

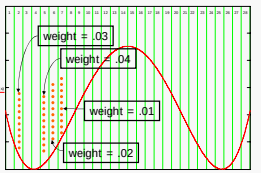


Initial System
- 10 Evenly-weighted particles
- 28 bins
- Run each particle forward 100 time steps (.1s)

$$\sum_{i=1}^{N} w_i = 1$$



Modification Event
- Calculate weight of particles in each bin
- Split/Combine particles so that each active bin (any bin with one or more particles in it) has 10 particles
- Assign 1/10 of total bin weight to all 10 particles in each active bin



Continue until 1,000 modification events are completed

$$\frac{100 \text{ iterations}}{1 \text{ modification event}} \times 1{,}000 \text{ modification events} = 100{,}000 \text{ iterations}$$

$$100{,}000 \text{ iterations} \times \frac{.001 \text{ second}}{1 \text{ iterations}} = 100 \text{ second simulation}$$

Conclusion

- The WEB method yields the same results as a standard Brownian method if permitted to run indefinitely → approaching the Boltzmann distribution
- The WEB method allows more particles to cross the energy barrier earlier on in the simulation → less computing time necessary for determining a change in equilibrium
  - WEB: 9 Energy Barrier Crossing Events
  - Standard Brownian: None
- The WEB method's ability to reduce the iterations necessary to produce a large-scale energy change can be applied to larger 3-D systems, such as proteins, to determine high energy conformations

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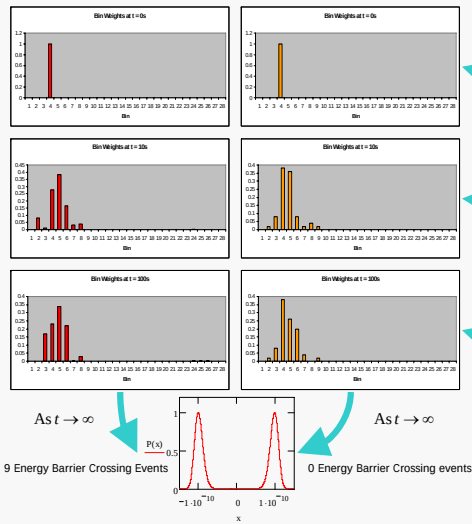
Results



To prove the advantage of using a WEB algorithm over a standard Brownian algorithm, we compared a simulation generated by the WEB method to a simulation generated by a standard Brownian algorithm.

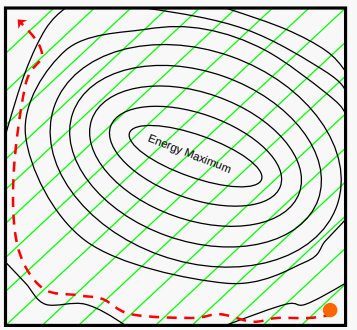
In both simulations, all evenly-weighted particles begin at the same initial position (-1 Å)

At 10 seconds real time into the simulation, a small number of particles in the WEB simulation have already crossed the energy barrier, while none in the standard Brownian simulation have overcome the boundary

At the end of the both simulations, the WEB simulation is beginning to approximate the theoretical bimodal distribution, while no particles have even crossed the energy barrier in the standard Brownian simulation

If both simulations are allowed to run indefinitely, they will approximate the theoretical Boltzmann Distribution

Continued Research



The WEB method can be extended to two-dimensional energy coordinate systems and beyond. Just as the energy coordinate of a one-dimensional system is divided up into bins, the contour map of a two-dimensional system's energy coordinate is partitioned as well. However, one must take precaution in deciding how to assign bins. Bin division lines should be approximately perpendicular to the direction of particle movement.

References

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