Brownian dynamics of obstructions in Lattice Microbes

Tyler M. Earnest

Luthey-Schulten group

Workshop on GPU Programming for Molecular Modeling

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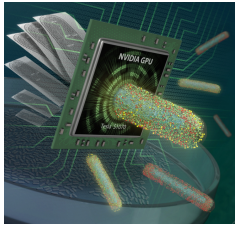
Whole-cell simulations

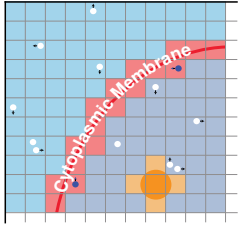
Lattice Microbes

- Simulate biochemical reactions in a cell
- Discretize cell to 3D lattice
- Add obstructions to diffusion
- Sample trajectories from RDME



$$\frac{\mathrm{d}P(\mathbf{x},t)}{\mathrm{d}t} = \mathcal{R}P(\mathbf{x},t) + \mathcal{D}P(\mathbf{x},t),$$

$$\frac{\mathrm{d}P(\mathbf{x},t)}{\mathrm{d}t} = \sum_{\nu}^{V}\sum_{r}^{R}[-a_r(\mathbf{x}_\nu)P(\mathbf{x}_\nu,t) + a_r(\mathbf{x}_\nu - \mathbf{S}_\mathbf{r})P(\mathbf{x}_\nu - \mathbf{S}_\mathbf{r},t)]$$
$$+ \sum_{\nu}^{V}\sum_{\xi}^{\pm\hat{i},\hat{j},\hat{k}}\sum_{\alpha}^{N}[-d^\alpha x_\nu^\alpha P(\mathbf{x},t) + d^\alpha(x_{\nu+\xi}^\alpha + 1)P(\mathbf{x} + 1_{\nu+\xi}^\alpha - 1_\nu^\alpha, t)].$$



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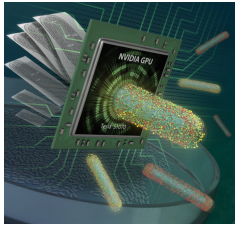
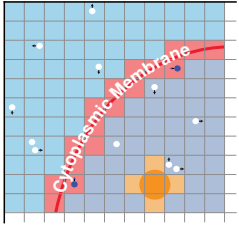


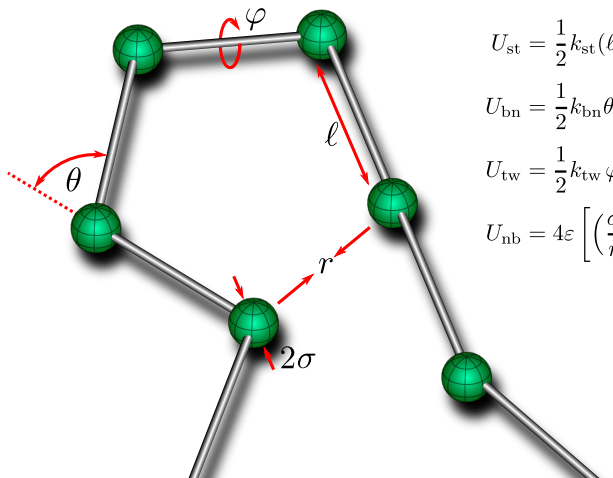
Integrate nucleoid MD with LM

- Dynamic nucleoid obstruction
- Dynamic transcription sites
- Ribosome biogenesis
- Simulate cell division



Coarse-grained MD

Force field



$$U_{\mathrm{st}} = \frac{1}{2} k_{\mathrm{st}} (\ell - \ell_0)^2$$

$$U_{\mathrm{bn}} = \frac{1}{2} k_{\mathrm{bn}} \theta^2$$

$$U_{\mathrm{tw}} = \frac{1}{2} k_{\mathrm{tw}} \varphi^2$$

$$U_{\mathrm{nb}} = 4\varepsilon \left[\left(\frac{\sigma}{r} \right)^{12} - \left(\frac{\sigma}{r} \right)^{6} \right]$$

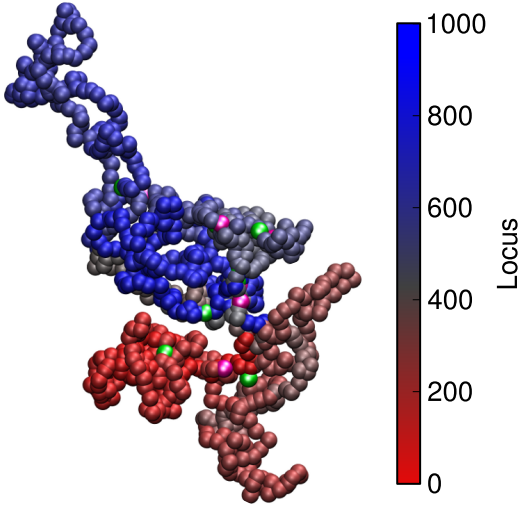
Molecular dynamics

Design of simulations

- Brownian dynamics

$$\zeta_i \, \partial_t x_i = -\partial_i U(\mathbf{x}) + \sigma_i \, \eta_i(t)$$

- Coarse-graining of DNA: 10 bp per bead, 10^5 beads
- Hard-sphere small obstructions
- Confinement potential
- Harmonic contact potentials: experimental structure



Algorithms

Molecular dynamics

1. Euler-Maruyama integration
2. Spatial-decomposition

Random number generation

1. Fast: $3N$ Gaussian random variates per timestep
2. High quality: No artificial correlations