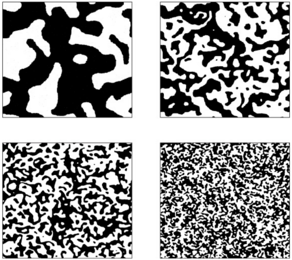
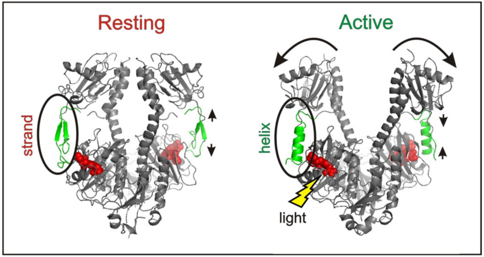
Boltzmann Generators

F. Noé[1]

December 8, 2018

Limitations of Monte Carlo Sampling





- **Input**: Reduced Potential Energy $u(\mathbf{x})$ in coordinates $\mathbf{x} \in \mathbb{R}^n$, e.g. $u(\mathbf{x}) = U(\mathbf{x})/k_B T$ (canonical ensemble).
- **Aim**: Generate *independent* Samples from Equilibrium Distribution.

$$\mu(\mathbf{x}) \propto e^{-u(\mathbf{x})}$$

- **Problem**: For large n, subvolume of low-energy configurations is vanishingly small compared to $\mathbb{R}^n$ and has a complex shape.
  - No protocol to place all n degrees of freedom is known such that direct MC sampling (proposal + rejection or reweighting) works.
  - Standard approach: MD/MCMC with local moves $\rightarrow$ sampling problem.

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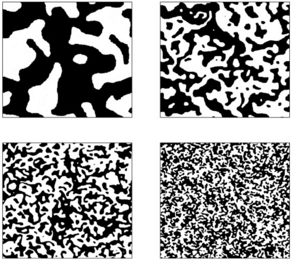

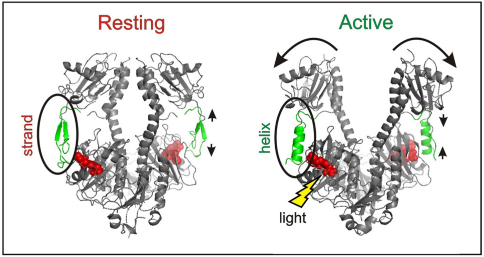

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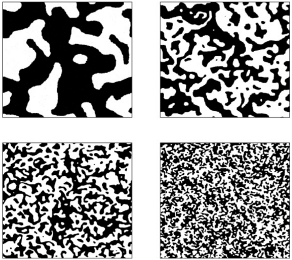

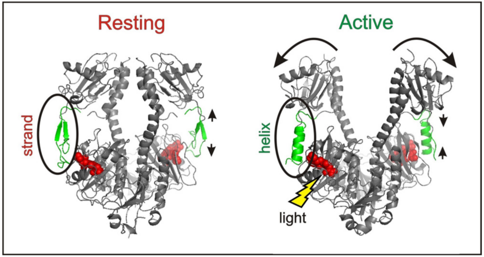

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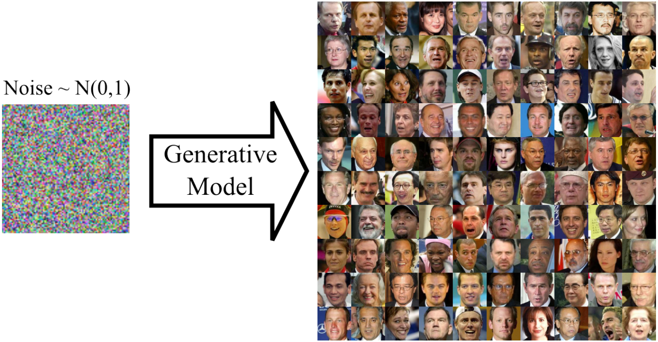
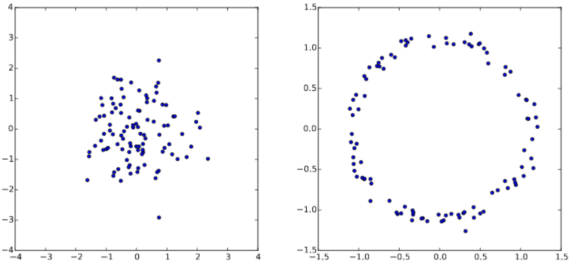
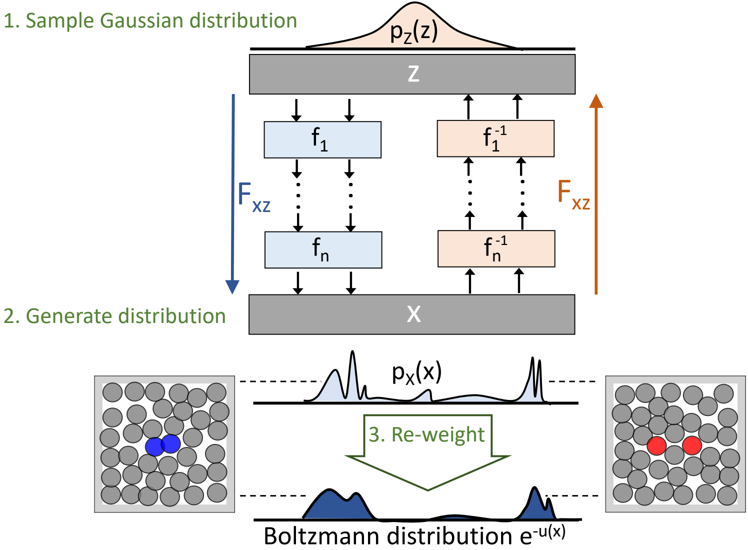
Idea: Use Generative Neural Networks





Boltzmann Generators[1]



[1] https://arxiv.org/abs/1812.01729

- Invertible transformation:

$$\mathbf{z} = F_{xz}(\mathbf{x};\theta)$$
$$\mathbf{x} = F_{zx}(\mathbf{z};\theta).$$

- Jacobians:

$$\mathbf{J}_{zx}(\mathbf{z};\theta) = \left[\frac{\partial F_{zx}(\mathbf{z};\theta)}{\partial z_1}, \ldots, \frac{\partial F_{zx}(\mathbf{z};\theta)}{\partial z_n}\right]$$
$$\mathbf{J}_{xz}(\mathbf{x};\theta) = \left[\frac{dF_{xz}(\mathbf{x};\theta)}{dx_1}, \ldots, \frac{dF_{xz}(\mathbf{x};\theta)}{dx_n}\right]$$

- Transformation of random variables:

$$\begin{aligned} p_X(\mathbf{x}) &= p_Z(\mathbf{z}) \left|\det \mathbf{J}_{zx}(\mathbf{z})\right|^{-1} \\ &= p_Z(T_{xz}(\mathbf{x})) \left|\det \mathbf{J}_{xz}(\mathbf{x})\right| \end{aligned} \tag{1}$$

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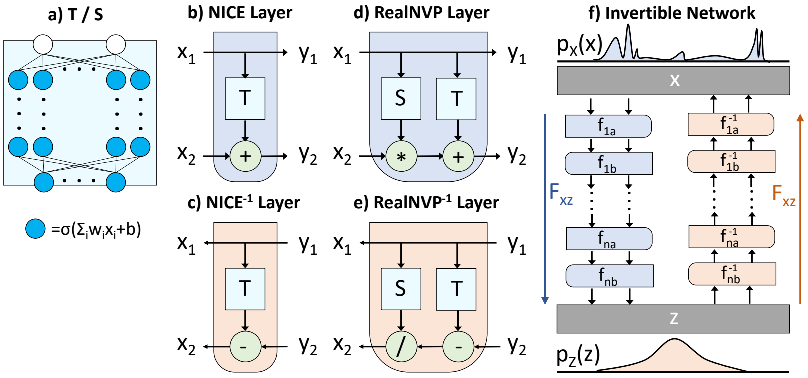

- **NICE**: Dinh, Krueger, Y. Bengio, ICLR 2015
- **RealNVP**: Dinh, Sohl-Dickstein, S. Bengio, ICLR 2017
- More advanced flow operations (e.g., normalizing flows)

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Invertible network components

Layer	f_{xz}	$\lvert\det \mathbf{J}_{xz}\rvert$	f_{zx}	$\lvert\det \mathbf{J}_{zx}\rvert$
NICE	$\begin{aligned}\mathbf{z}_1 &= \mathbf{x}_1\\ \mathbf{z}_2 &= \mathbf{x}_2 + T(\mathbf{x}_1;\theta)\end{aligned}$	1	$\begin{aligned}\mathbf{x}_1 &= \mathbf{z}_1\\ \mathbf{x}_2 &= \mathbf{z}_2 - T(\mathbf{y}_1;\theta)\end{aligned}$	1
Scaling, Exp	$\mathbf{z} = \mathrm{e}^{\mathbf{k}} \circ \mathbf{x}$	$\mathrm{e}^{\sum_i k_i}$	$\mathbf{x} = \mathrm{e}^{-\mathbf{k}} \circ \mathbf{z}$	$\mathrm{e}^{-\sum_i k_i}$
RealNVP	$\begin{aligned}\mathbf{z}_1 &= \mathbf{x}_1\\ \mathbf{z}_2 &= \mathbf{x}_2 \odot \exp(S(\mathbf{x}_1;\theta))\\ &\quad + T(\mathbf{x}_1;\theta)\end{aligned}$	$\mathrm{e}^{\sum_i S_i(\mathbf{x}_1;\theta)}$	$\begin{aligned}\mathbf{x}_1 &= \mathbf{z}_1\\ \mathbf{x}_2 &= (\mathbf{z}_2 - T(\mathbf{x}_1;\theta))\\ &\quad \odot \exp(-S(\mathbf{z}_1;\theta))\end{aligned}$	$\mathrm{e}^{-\sum_i S_i(\mathbf{z}_1;\theta)}$

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Learning Problem

- **Distributions**:

$$\begin{array}{rcccl} \text{Prior} & \mu_Z(\mathbf{z}) & \xrightarrow{F_{zx}} & p_X(\mathbf{x}) & \text{generated} \\ \text{Boltzmann} & \mu_X(\mathbf{x}) & \xrightarrow{F_{xz}} & p_Z(\mathbf{z}) & \text{generated} \end{array}$$

- **Aim**: sample configurations $\mathbf{x}$ from **Boltzmann distribution**

$$\mu_X(\mathbf{x}) = Z_X^{-1} e^{-u(\mathbf{x})} \tag{3}$$

- **Prior distribution**: Sample input in $\mathbf{z}$ from isotropic Gaussian:

$$q_Z(\mathbf{z}) = \mathcal{N}(\mathbf{0}, \sigma^2 \mathbf{I}) = Z_Z^{-1} e^{-\frac{1}{2}\|\mathbf{z}\|^2/\sigma^2}, \tag{4}$$

Prior energy:

$$u_Z(\mathbf{z}) = -\log q_Z(\mathbf{z}) = \frac{1}{2\sigma^2}\|\mathbf{z}\|^2 + \text{const}$$

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Latent KL divergence

- Loss function:

$$J = \underbrace{w_{ML} J_{ML}}_{\text{max likelihood}} + \underbrace{w_{KL} J_{KL}}_{\text{Kullback–Leibler}} + \underbrace{w_{RC} J_{RC}}_{\text{reaction coordinate}}.$$

- KL divergence between generated $p_X(\mathbf{x})$ and Boltzmann distribution:

$$\begin{aligned} \mathrm{KL}_\theta [\mu_Z \parallel p_Z] &= \int \mu_Z(\mathbf{z}) [\log \mu_Z(\mathbf{z}) - \log p_Z(\mathbf{z};\theta)] \, \mathrm{d}\mathbf{z}, \\ &= -H_Z - \int \mu_Z(\mathbf{z}) \log p_Z(\mathbf{z};\theta) \mathrm{d}\mathbf{z}, \\ &= -H_Z - \int \mu_Z(\mathbf{z}) [\log \mu_X(F_{zx}(\mathbf{z};\theta)) + \log |\mathbf{J}_{zx}(\mathbf{z};\theta)|] \, \mathrm{d}\mathbf{z}, \\ &= \underbrace{-H_Z + \log Z_X}_{\text{const}} + \underbrace{\mathbb{E}_{\mathbf{z}\sim\mu_Z(\mathbf{z})} [u(F_{zx}(\mathbf{z};\theta)) - \log |\mathbf{J}_{zx}(\mathbf{z};\theta)|]}_{\text{free energy}} \end{aligned}$$

- KL loss:

$$J_{KL} = \mathbb{E}_{\mathbf{z}\sim\mu_Z(\mathbf{z})} [u(F_{zx}(\mathbf{z};\theta)) - \log |\mathbf{J}_{zx}(\mathbf{z};\theta)|] . \qquad (5)$$

- See also:
  - $\mathrm{KL}_\theta [q_Z \parallel p_Z]$ equals *probability distillation loss* (van den Oord et al, *PMLR 2018*).
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Problem: sampling $\mathbf{x} \sim \mu(\mathbf{x})$ is difficult and our goal!

- **Maximum Likelihood** loss for initial data distribution $\rho(\mathbf{x})$:

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Reaction coordinate loss

- Loss function:

$$J = \underbrace{w_{ML} J_{ML}}_{\text{max likelihood}} + \underbrace{w_{KL} J_{KL}}_{\text{Kullback}-\text{Leibler}} + \underbrace{w_{RC} J_{RC}.}_{\text{reaction coordinate}}$$

- Reaction coordinate loss:

$$J_{RC} = \int p(R(\mathbf{x})) \log p(R(\mathbf{x}))\, \mathrm{d}R(\mathbf{x})$$
$$= \mathbb{E}_{\mathbf{x} \sim p_X(\mathbf{x})} \log p(R(\mathbf{x})).$$

- Implementation:
  - Reaction coordinate function R is user input
  - Min and max bounds are given
  - $p(R(\mathbf{x}))$ is computed as a batchwise kernel density estimate.

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$$\begin{aligned} J_{RC} &= \int p\left(R(\mathbf{x})\right) \log p\left(R(\mathbf{x})\right) \,\mathrm{d}R(\mathbf{x}) \\ &= \mathbb{E}_{\mathbf{x} \sim p_X(\mathbf{x})} \log p\left(R(\mathbf{x})\right). \end{aligned}$$

- Implementation:
  - Reaction coordinate function R is user input
  - Min and max bounds are given
  - $p\left(R(\mathbf{x})\right)$ is computed as a batchwise kernel density estimate.

[1] https://arxiv.org/abs/1812.01729

Reaction coordinate loss

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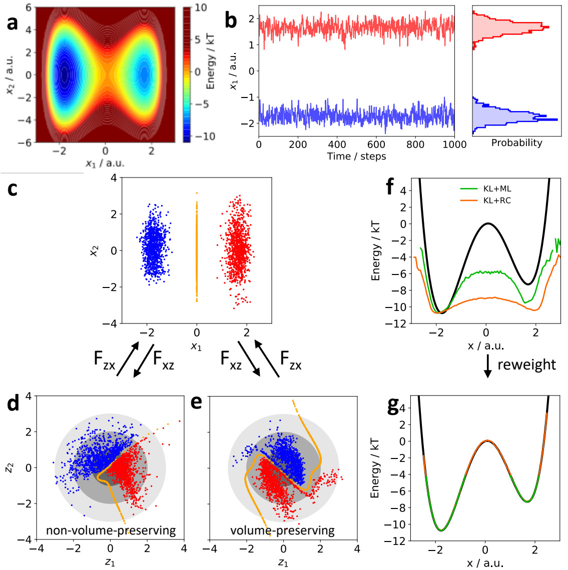
Boltzmann Generator - 1D Example



Reweighting

- Probability reweighting: assign to each generated configuration $\mathbf{x}$ the statistical weight:

$$w_X(\mathbf{x} \mid \mathbf{z}) = \frac{\mu_X(\mathbf{x})}{p_X(\mathbf{x})} = \frac{p_Z(\mathbf{z})}{\mu_Z(\mathbf{z})}. \tag{6}$$
$$\propto \mathrm{e}^{-u_X(T_{zx}(\mathbf{z}))+u_Z(\mathbf{z})+\log|\det(\mathbf{J}_{zx}(\mathbf{z}))|}$$

- Weighted expectation values

$$\mathbb{E}[O] \approx \frac{\sum_{i=1}^{N} w_X(\mathbf{x}) O(\mathbf{x})}{\sum_{i=1}^{N} w_X(\mathbf{x})}.$$

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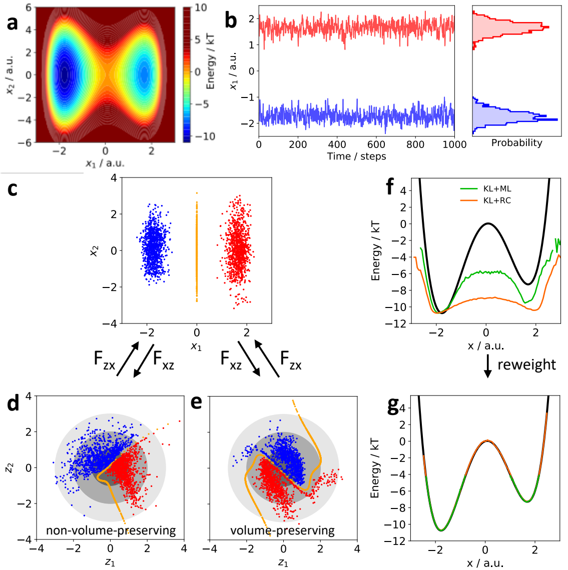
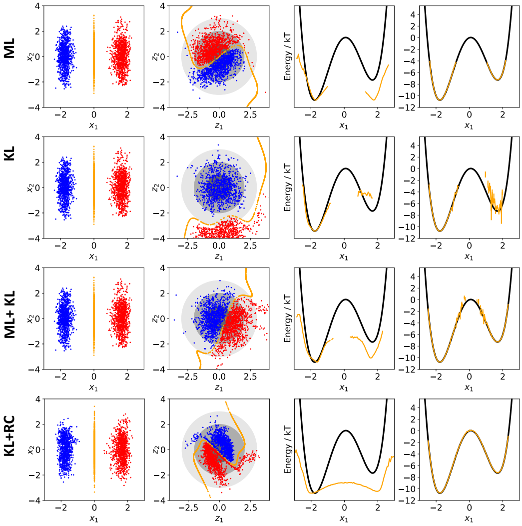


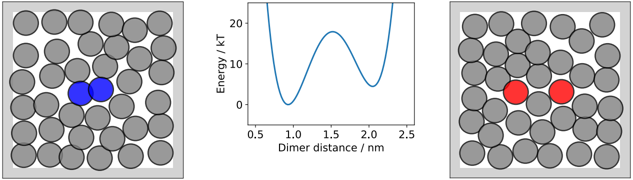
Different training methods



Architecture $\mathrm{N_{10}S}$, $nl_{layers} = 2$, $nl_{hidden} = 100$, $\sigma = \tanh$

[1]https://arxiv.org/abs/1812.01729

Boltzmann Generator - Particle dimer

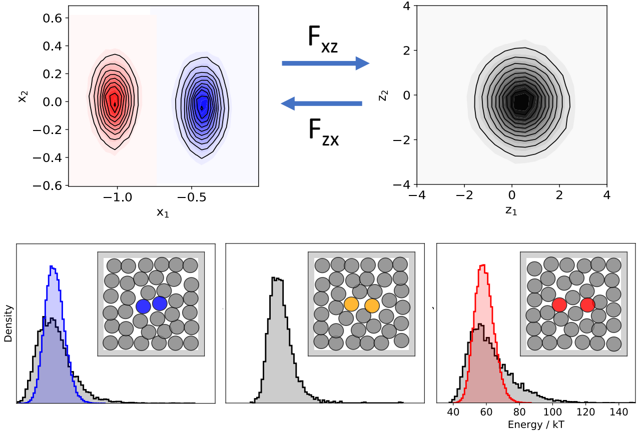


- Configuration: $\mathbf{x} = \left[\mathbf{x}_{1x}, \mathbf{x}_{1y}, \mathbf{x}_{2x}, \mathbf{x}_{2y}, \ldots, \mathbf{x}_{(n_s+2)x}, \mathbf{x}_{(n_s+2)y}\right]$
- Dimer distance $d = \|\mathbf{x}_1 - \mathbf{x}_2\|$, **potential energy**:

$$
\begin{aligned}
U(\mathbf{x}) = \frac{1}{4}a(d-d_0)^4 - \frac{1}{2}b(d-d_0)^2 + c(d-d_0)^4 \\
+\varepsilon \sum_{i=1}^{n+1} \sum_{j=i+1, j\neq 2}^{n+2} \left(\frac{\sigma}{\|\mathbf{x}_i - \mathbf{x}_j\|}\right)^{12} \\
+\,\text{box potential}
\end{aligned}
$$

[1] https://arxiv.org/abs/1812.01729

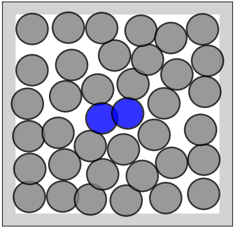
Boltzmann Generator - Particle dimer

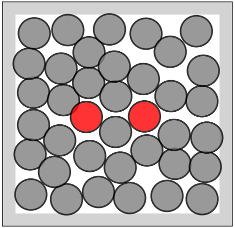


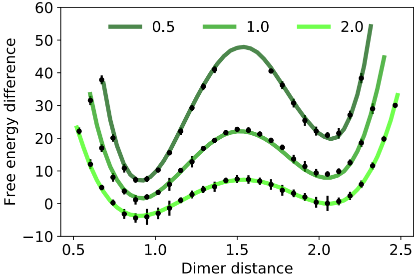
Architecture R_8, $nl_{layers} = 3$, $nl_{hidden} = 200$, $\sigma = \tanh$, $w_{KL} = 1$, $w_{ML} = 0.01$, $w_{RC} = 10$

[1] https://arxiv.org/abs/1812.01729

Boltzmann Generator - Particle dimer



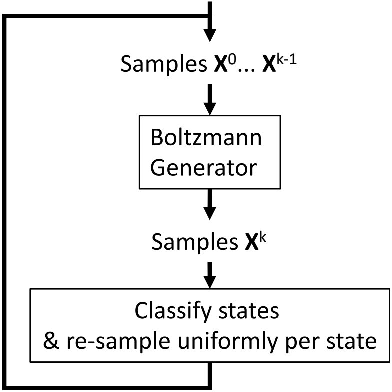




7 orders of magnitude speedup compared to MD

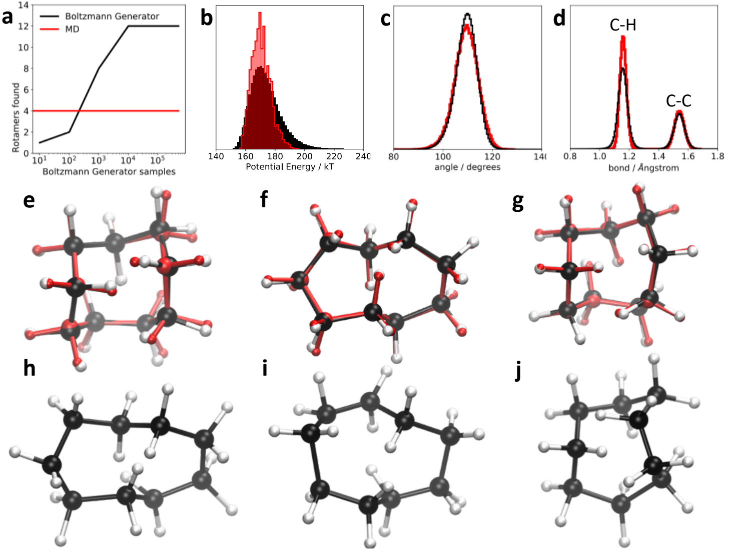
[1]https://arxiv.org/abs/1812.01729

Iterative exploration



[1] https://arxiv.org/abs/1812.01729

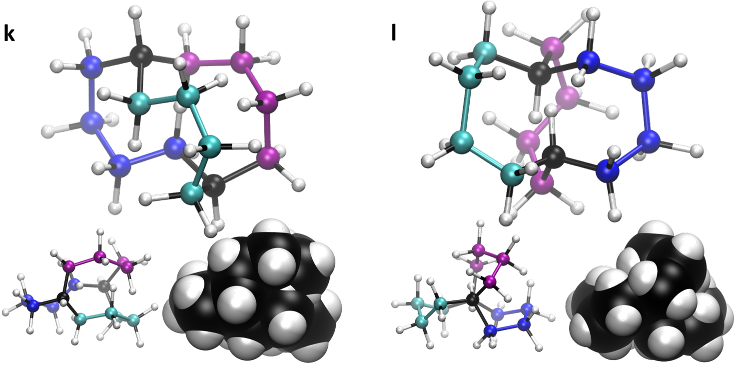
Boltzmann Generator - Hydrocarbons



$R_4,\ nl_{layers} = 2,\ nl_{hidden} = 100,\ \sigma = \tanh,\ w_{KL} = 0.01,\ w_{ML} = 1$

[1]https://arxiv.org/abs/1812.01729

Boltzmann Generator - Hydrocarbons



R_4, $nl_{layers} = 2$, $nl_{hidden} = 100$, $\sigma = \tanh$, $w_{KL} = 0.01$, $w_{ML} = 1$

[1] https://arxiv.org/abs/1812.01729

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Positions available!