Stratified Markov Chain Monte Carlo

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Sampling Problems

What is the probability of finding a protein in a given conformation?

Bayesian inference for ODE model of circadian rhythms.

Figure from Phong, et al, PNAS, 2012

Compute sample from
Boltzmann distribution.

Figure from Folding@home

Compute sample from
posterior distribution.
Markov Chain Monte Carlo (MCMC)

**Goal:** Compute $\pi(g) := \int g(x)\pi(dx)$.

**MCMC Method:** Choose Markov chain $X_n$ so that

$$\lim_{N \to \infty} \frac{1}{N} \sum_{n=0}^{N-1} g(X_n) = \pi(g).$$

"$X_n$ samples $\pi$."

---

**MCMC trajectory $X_n$**

**Target Density $\pi$**
Difficulties with MCMC

Multimodality: Multimodality $\implies$ slow convergence

Tails: Need large sample to compute small probabilities, e.g. $\pi ([M, \infty))$.
Sketch of Stratified MCMC

1. Choose family of strata, i.e. distributions $\pi_i$ whose supports cover support of target $\pi$.

2. Sample strata by MCMC.

3. Estimate $\pi(g)$ from samples of strata.

**Typical Strata:** $\pi_i(dx) \propto \psi_i(x)\pi(dx)$ for “localized” $\psi_i$.

**Why Stratify?**

- Strata may be *unimodal*, even if $\pi$ is *multimodal*
- Can concentrate sampling in *tail*
History of Stratification

**Surveys:** [Russian census, late 1800s], [Neyman, 1937]

**Bayes factors:** [Geyer, 1994]

**Selection bias models:** [Vardi, 1985]

**Free energy:** [Umbrella Sampling, 1977], [WHAM, 1992], [MBAR, 2008]

**Ion channels:** [Berneche, et al, 2001]

**Protein folding:** [Boczkó, et al, 1995]

**Problems:**

1. WHAM/MBAR are complicated iterative methods . . .
2. No clear *story* explaining benefits of stratification.
3. Stratification underappreciated as a *general* strategy.
4. Need good *error bars* for adaptivity.
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**BvK, et al:** Propose Eigenvector Method for Umbrella Sampling, develop *story, error bars, stratification* for *dynamical quantities* . . .
Eigenvector Method for Umbrella Sampling (EMUS)

[BvK, et al]

- **Bias Functions:** \( \{\psi_i\}_{i=1}^{L} \) with
  \[
  \sum_{i=1}^{L} \psi_i(x) = 1 \text{ and } \psi_i(x) \geq 0.
  \]
  
  **Note:** User chooses bias functions.

- **Weights:** \( z_i = \pi(\psi_i) \)

- **Strata:** \( \pi_i(dx) = z_i^{-1} \psi_i(x) \pi(dx) \)
Goal: Write $\pi(g)$ in terms of averages over strata $\pi_i(dx) = \frac{\psi_i(x)\pi(dx)}{z_i}$.

First, decompose $\pi(g)$ as weighted sum:

$$\pi(g) = \int g(x) \sum_{i=1}^{L} \psi_i(x) \pi(dx)$$

$$= \sum_{i=1}^{L} z_i \int g(x) \frac{\psi_i(x)\pi(dx)}{z_i} = \sum_{i=1}^{L} z_i \pi_i(g).$$
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$$
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$$

$\psi_i$’s sum to one

$$
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How to express weights $z_i = \pi(\psi_i)$ as averages over strata?

$$z_j = \pi(\psi_j) = \sum_{i=1}^L z_i \pi_i(\psi_j) \quad \iff \quad z^T = z^T F,$$

where $F_{ij} = \pi_i(\psi_j)$. 

\[ \text{eigenproblem} \quad \text{overlap matrix} \]
Eigenvector Method for Umbrella Sampling (EMUS)

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**eigenproblem**

**overlap matrix**
**Eigenvector Method for Umbrella Sampling (EMUS)**

[BvK, et al]

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$$
\begin{align*}
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    \text{eigenproblem} & \quad \text{overlap matrix}
\end{align*}
$$

**Why does eigenproblem determine $z$?**

1. $F$ is stochastic; $z$ is a probability vector.
2. If $F$ irreducible, $z$ is *unique* solution of eigenproblem.
Recall: \( \pi(g) = \sum_{i=1}^{L} z_{i} \pi_{i}(g) \), and \( z^T = z^T F \) for \( F_{ij} = \pi_{i}(\psi_{j}) \).

**EMUS Algorithm:**

1. Choose bias functions \( \psi_{i} \) and processes \( X_{n}^{i} \) sampling the strata.
2. Compute \( \bar{g}_{i} := \frac{1}{N_{i}} \sum_{n=1}^{N_{i}} g(X_{n}^{i}) \) to estimate \( \pi_{i}(g) \).
3. Compute \( \bar{F}_{ij} := \frac{1}{N_{i}} \sum_{n=1}^{N_{i}} \psi_{j}(X_{n}^{i}) \) to estimate \( F \).
4. Solve eigenproblem \( \bar{z}^T = \bar{z}^T \bar{F} \) to estimate weights \( z \).
5. Output \( g^{EM} = \sum_{i=1}^{L} \bar{z}_{i} \bar{g}_{i} \).
Eigenvector Method for Umbrella Sampling (EMUS)
[BvK, et al]

Recall: \( \pi(g) = \sum_{i=1}^{L} z_i \pi_i(g) \), and \( z^T = z^T F \) for \( F_{ij} = \pi_i(\psi_j) \).

EMUS Algorithm:

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Key Point: Simplicity of EMUS enables analysis of stratification.
EMUS Analysis: Outline

1. Sensitivity of $g^{EM}$ to sampling error.

2. Dependence of sampling error on choice of strata.

3. Stories involving multimodality and tails.
For $F$ irreducible and stochastic, let $z(F)$ be the unique solution of

$$z(F)^T = z(F)^T F.$$ 

$P_i^F[\tau_j < \tau_i]$: probability of hitting $j$ before $i$, conditioned on starting from $i$, for a Markov chain on $1, \ldots, L$ with transition matrix $F$.

Theorem [BvK, et al]:

$$\frac{1}{2} P_i^F[\tau_j < \tau_i] \leq \max_{m=1,\ldots,L} \left| \frac{\partial \log z_m(F)}{\partial F_{ij}} \right| \leq \frac{1}{P_i^F[\tau_j < \tau_i]} \leq \frac{1}{F_{ij}}.$$ 

Led to new perturbation bounds for Markov chains [BvK, et al].
Quantifying Sensitivity to Sampling Error II

Assumption: CLT holds for MCMC averages:

\[ \sqrt{N_i} (\bar{g}_i - \pi_i(g)) \xrightarrow{d} N(0, C(\bar{g}_i)) \quad \text{asymptotic variance} \]

Theorem [BvK, et al]: \( \sqrt{N} (g^\text{EM} - \pi(g)) \xrightarrow{d} N(0, C(g^\text{EM})) \), where

\[
\frac{C(g^\text{EM})}{\text{var}_\pi(g)} \lesssim \sum_{i=1}^{L} \left( \sum_{j \neq i} \frac{1}{P_i^F[\tau_j < \tau_i]^2} \right) \times \frac{\sum_{j=1}^{L} C(\bar{F}_{ij})}{\kappa_i} + z_i^2 \left( \frac{C(\bar{g}_i)}{\kappa_i} \right). 
\]

Notation: \( N \) is total sample size, with \( N_i = \kappa_i N \) from \( \pi_i \).
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Dependence of Sampling Error on Strata I

Write $\pi(dx) = Z^{-1} \exp(-V(x)/\varepsilon)$ for some potential $V$:

Assume bias functions $\psi_i$ piecewise constant:

Assume $X^i_t$ is overdamped Langevin with reflecting boundaries:

$$dX^i_t = -\nabla V(X^i_t)dt + \sqrt{2\varepsilon}dB^i_t \quad + \quad \text{reflecting BCs}$$
Dependence of Sampling Error on Strata II

Let \( \pi(dx) = Z^{-1} \exp(-V(x)/\varepsilon) \) for some potential \( V \):

\[
\frac{C(\bar{g}_i)}{\text{var}_{\pi_i}(g)} \lesssim \frac{D^2}{\varepsilon} \times \exp \left( \frac{\max_{\text{supp} \pi_i} V - \min_{\text{supp} \pi_i} V}{\varepsilon} \right).
\]

**Theorem** [BvK, et al]: For overdamped Langevin with reflecting BCs,

Notation: \( D \) is diameter of support of \( \pi_i \).
EMUS Analysis: Outline

1. Dependence of sampling error on choice of strata.

2. Sensitivity of $g^{EM}$ to sampling error.

3. Stories involving multimodality and tails.
EMUS and Multimodality

Let \( \pi(dx) = Z^{-1} \exp(-V(x)/\varepsilon) \) for double well \( V \):

Asymptotic variance of naïve MCMC grows \textit{exponentially} as \( \varepsilon \downarrow 0 \).

\textbf{Theorem [BvK, et al]:}
For right choice of strata (\( L \propto \varepsilon^{-1} \)), asymptotic variance of EMUS estimate \( g_{EM} \) grows \textit{polynomially} as \( \varepsilon \downarrow 0 \).
EMUS and Tails

**Goal:** Compute $\pi([M, \infty)) = \int_M^{\infty} \pi(dx)$.

For a broad class of distributions $\pi$, relative asymptotic variance of MCMC grows *exponentially* as $M \uparrow \infty$.

**Theorem** [BvK, et al]:
For right choice of strata, relative asymptotic variance of EMUS grows *polynomially* as $M \uparrow \infty$. 
Example: EMUS for Bayesian Inference

- **Goal:** Fit set of thicknesses of 485 stamps by mix of 3 Gaussians:

- **Parameters:** means $\mu_1 \leq \mu_2 \leq \mu_3$, precisions $\lambda_1, \lambda_2, \lambda_3$, weights, etc

- **Bayesian method:** Define *posterior distribution* on parameter space.
Example: EMUS for Bayesian Inference

- **Parameters:** means $\mu_1 \leq \mu_2 \leq \mu_3$, precisions $\lambda_1, \lambda_2, \lambda_3$, weights, etc
- **Objective:** Compute marginal in $\log_{10} \lambda_1$ and $\log_{10} \lambda_2$.
- **Strata:** Cylinders over grid of regions in $\log_{10} \lambda_1$, $\log_{10} \lambda_2$ plane:

![Diagram showing support of typical stratum]
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Asymptotic variances of EMUS vs. unbiased MCMC for marginal in $\log \lambda_1$: 

![Graph showing comparison between EMUS and unbiased MCMC for marginal in $\log \lambda_1$. The graph plots $\log_{10}$ of the asymptotic variance against $\log_{10}(10^{0.01 m^2})$. The EMUS line is blue, and the No Bias line is orange. The graph highlights the variance differences between the two methods.](image-url)
Conclusions

- We present and analyze EMUS, a stratified MCMC method, and we derive practical error bars for EMUS estimator [BvK et al, JCP, 2016].

- Our analysis required development of new perturbation estimates for stochastic matrices [BvK et al, SIMAX, 2015].

- We clearly identify classes of problems for which stratification is beneficial, and we propose novel applications in statistics [BvK et al, 2019+].

- We analyze and improve a stratification method for computing dynamical quantities [BvK et al, SIREV, 2017].

- **Ongoing Work:** Convergence of NEUS, automatic methods for determining strata, comparison with other rare event sampling methods, . . .