



Advanced Monte-Carlo Sampling Schemes for Value of Information Estimation

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Objective

- To explore the potential of advanced Monte-Carlo sampling schemes to reduce computational cost of estimating Expected Value of Partial Perfect Information (EVPI).
- Quasi Monte-Carlo (QMC) and Multilevel Monte-Carlo (MLMC) estimation are compared with Nested Monte-Carlo (NMC) for a cost-effectiveness model in depression.

Methods

Expected Value of Partial Perfect Information (EVPI)

- Economic models calculate net benefit $f_d(X, Y)$ for decision d and sets of possibly correlated input parameters X and Y .
 - The EVPI for X (e.g. quality of life following treatment) is
- $$E_X \left[\max_{d \in D} E_{Y|X} [f_d(X, Y)] \right] - \max_{d \in D} E_{X,Y} [f_d(X, Y)]$$
- It is the expected improvement in decision making given perfect information about X .

Nested Monte Carlo (NMC)

- The Nested Monte-Carlo estimator for EVPI is NMC
- $$\frac{1}{N} \sum_{n=1}^N \max_{d \in D} \frac{1}{M} \sum_{m=1}^M f_d(X^{(n)}, Y^{(m,n)}) - \max_{d \in D} \frac{1}{MN} \sum_{n=1}^N \sum_{m=1}^M f_d(X^{(n)}, Y^{(m,n)})$$
- This requires N samples of $X^{(n)}$ and M samples $Y^{(m,n)}$ conditional on each $X^{(n)}$
 - This nested simulation is biased due to Jensen's inequality and computationally intensive.

Multilevel Monte-Carlo (MLMC)

- To apply MLMC to EVPI we instead estimate the quantity
- $$DIFF = EVPI - EVPPI = E_{X,Y} \left[\max_{d \in D} f(X, Y) \right] - E_X \left[\max_{d \in D} E_{Y|X} [f_d(X, Y)] \right]$$
- The NMC estimator with 2^l inner samples based on $X^{(n)}$ is

$$\widehat{DIFF}_l = \frac{1}{2^l} \sum_{m=1}^{2^l} \max_{d \in D} f_d(X^{(n)}, Y^{(n,m)}) - \max_{d \in D} \frac{1}{2^l} \sum_{m=1}^{2^l} f_d(X^{(n)}, Y^{(n,m)})$$

- MLMC generates a sequence of differences $\widehat{DIFF}_l - \widehat{DIFF}_{l-1}$ and estimates the telescoping sum

$$E[\widehat{DIFF}_L] = E[\widehat{DIFF}_0] + \sum_{l=1}^L E[\widehat{DIFF}_l - \widehat{DIFF}_{l-1}]$$

- For low l , $\widehat{DIFF}_l - \widehat{DIFF}_{l-1}$ is cheap to evaluate, for high l it has a low variance so few samples are needed to estimate its expectation
- The MLMC estimator using N_l outer samples for each level l is

$$\widehat{DIFF} = \sum_{l=1}^L \frac{1}{N_l} \sum_{n=1}^{N_l} (\widehat{DIFF}_l^{(l,n)} - \widehat{DIFF}_{l-1}^{(l,n)})$$

- Unlike NMC, MLMC provides an estimate of the estimation bias

$$E[\widehat{DIFF}_{L+1} - \widehat{DIFF}_L] \sim \sum_{l=L+1}^{\infty} E[\widehat{DIFF}_l - \widehat{DIFF}_{l-1}] = DIFF - E[\widehat{DIFF}_L]$$

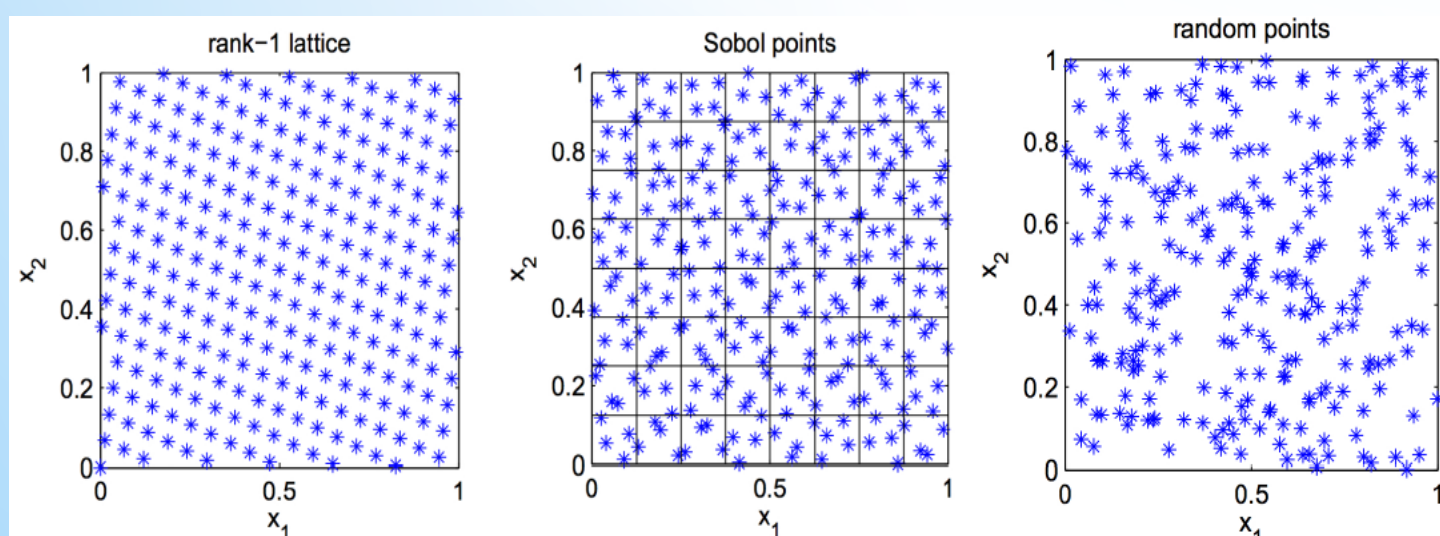
- The MLMC scheme can estimate EVPI to a given Mean Square Error (MSE) ε^2 , the sum of variance and square of bias, and at a cost which is $O(\varepsilon^{-2})$.
- The number of levels L is chosen to achieve a bias $\leq 0.5\varepsilon$ and N_l is chosen to achieve variance $\leq 0.75\varepsilon^2$.

Quasi Monte-Carlo (QMC)

- Assuming g is a real-valued function and X is a random variable with cumulative distribution F , we estimate $E[g(X)]$ by

$$\frac{1}{N} \sum_{n=1}^N g(X_i)$$

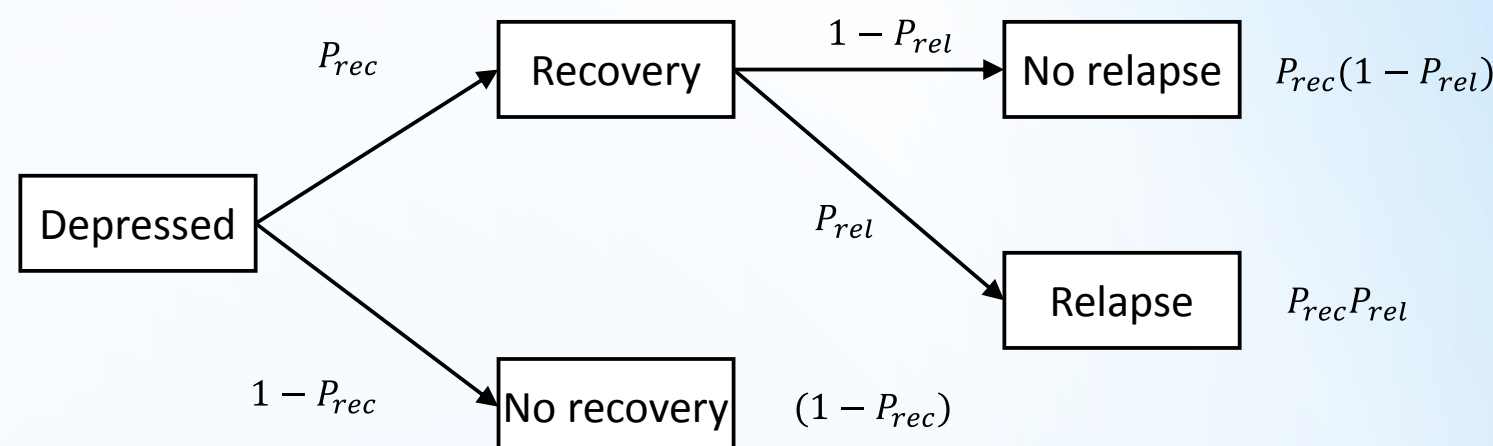
- where $X_i = F^{-1}(U_i)$ and $\{U_i\}$ are uniformly distributed in $[0,1]$.
- Standard MC chooses U_i for X_i randomly.
- QMC chooses U_i for X_i systematically.
- QMC is deterministic and achieves a better convergence rate of the error than MC
- For EVPI, only apply QMC to outer samples N as not many inner samples M are needed for accuracy.
- A confidence interval for estimated EVPI can be provided using randomized QMC.
- Randomized QMC is unbiased and has much lower variance than NMC.



Example of QMC uniform random number generation in 2-dimensions for 256 points using rank-1 lattice points or a Sobol sequence.

Example Model

- We applied our method to a constructed example of a decision tree for depression informed by a Network Meta-Analysis (NMA) conducted in WinBUGS.



- The same structure, but with different probabilities of recovery and relapse, were used for treatment by antidepressant and by cognitive behavioural therapy (CBT).
- Mean costs and Quality Adjusted Life Years (QALYs) of final states were assumed to run over a 30 year time horizon.

Parameter	Recovery, no relapse	Recovery, relapse	No recovery
Mean Costs	$N(1000,50)$	$N(2000,100)$	$N(2500,125)$
Mean QALY	$N(26,2)$	$N(23,3)$	$N(20,4)$

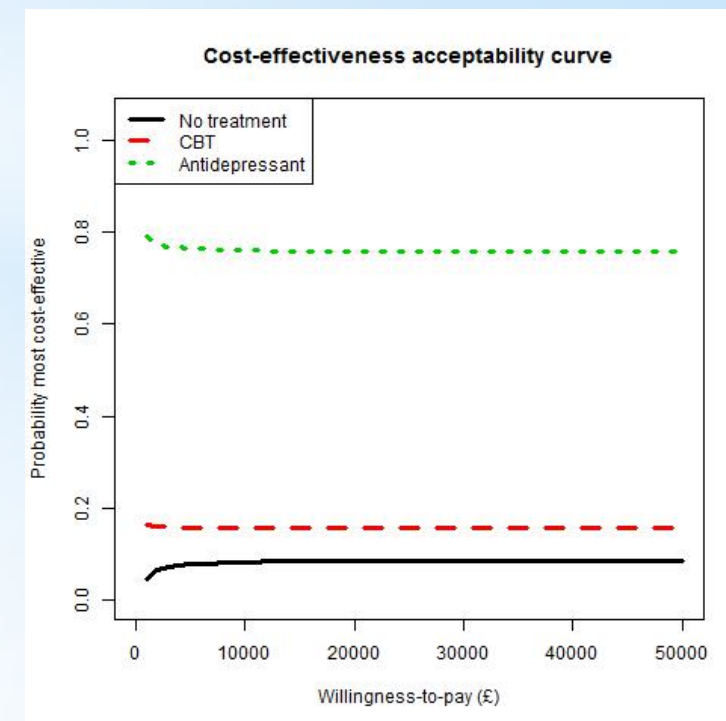
- The NMA provided log odds ratios (lor) of recovery and relapse on treatments vs no treatment based on a network of 5 trials.
- We approximated Markov Chain Monte Carlo samples from posterior distributions using

$$\begin{pmatrix} \text{lor}_{2,rec} \\ \text{lor}_{3,rec} \end{pmatrix} \sim MVN \left(\begin{pmatrix} 0.99 \\ 1.33 \end{pmatrix}, \begin{pmatrix} 0.22 & 0.15 \\ 0.15 & 0.20 \end{pmatrix} \right), \quad \begin{pmatrix} \text{lor}_{2,rel} \\ \text{lor}_{3,rel} \end{pmatrix} \sim MVN \left(\begin{pmatrix} -1.48 \\ -0.40 \end{pmatrix}, \begin{pmatrix} 0.14 & 0.05 \\ 0.05 & 0.11 \end{pmatrix} \right)$$

- Absolute probabilities of recovery and relapse on no treatment were set as $Beta(6,200)$ and $Beta(2,100)$ distributions.
- Fixed treatment costs of 0,300, and 30 were assumed for no treatment, antidepressants, and CBT, respectively.

Results

- We pre-specified the Mean Squared Error (MSE) to 0.25 and use MLMC to choose level L at which bias is less than 0.5ε .
- We then use 2^L inner samples for NMC and QMC to ensure all three have same bias.
- Total EVPI at this MSE was estimated at 574.9 (573.4, 576.4).
- We run NMC and QMC to achieve same MSE as MLMC and compare computational cost (standardised regardless of computer).
- Both MLMC and QMC outperformed NMC in an example with 20 treatments, but MLMC outperformed QMC.



Sets of parameters (no. parameters)	EVPI**	NMC	MLMC	QMC
Probabilities (6)	301.1 (299.6, 302.6)	15.14	26.93	5.63
Costs and QALYS (6)	288.1 (286.6, 289.6)	13.02	22.85	5.12
CBT treatment effects* (2)	568.6 (567.1, 570.1)	787.20	108.50	8.19
Antidepressant treatment effects* (2)	574.0 (572.5, 575.5)	78.90	61.86	6.23

*Log odds ratios of recovery and relapse relative to no treatment.

**EVPI value estimated by MLMC, values in brackets are 99% credible intervals defined by $\pm 3\varepsilon$.

Conclusions and further work

- MLMC and QMC can provide substantial computational savings over NMC.
- MLMC can provide estimation of the bias in EVPI and EVPPI estimates.
- MLMC performed best for smaller number of correlated parameters.
- For the simple case with few treatment options, QMC was best, but more complex examples found MLMC to be best.
- We are exploring real world examples, including atrial fibrillation.

References

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