

EVPPPI_Bristol

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This is an R Markdown document which contains all the codes and results of all the EVPI and EVPPPI for the EVPPPI project in University of Bristol. Due to some update issues in the MLMC package, we currently use the functions in the package but with some modifications on codes.

The following four package are needed for MLMC functions:

```
require(parallel)
require(ggplot2)
require(grid)
require(Rcpp)
```

The following R code are for MLMC test can calculation. The first three come from the MLMC package in R (see: <https://cran.r-project.org/web/packages/mlmc/index.html>) with some new updates by Wei.

```
source("mlmc.R") #MLMC code to calculate the value to some accuracy
source("mlmc.test.R") #test function of the convergence rates and output the MLMC results
source("plot.mlmc.test.R") #function to plot the result
source("multiplot.R") #this is the function from ggplot
```

The following five R code are developed by Wei to calculate different EVPI and EVPPPI with N out samples and M^l inner samples. These can be called by **mlmc.R** to do MLMC calculations.

```
source("EVPI_1.R")
source("EVPPPI_P_1.R")
source("EVPPPI_cq_1.R")
source("EVPPPI_lor1_1.R")
source("EVPPPI_lor2_1.R")
```

EVPI

Suppose that the perfect information is available. That means by density ρ_Z we can generate samples of Z and for each sample $Z^{(n)}$ we can find the optimal decision d for that specific decision. Therefore the expected value of perfect information (EVPI) is

$$\text{EVPI} = \mathbb{E}_Z \left[\max_{d \in D} f_d(Z) \right] - \max_{d \in D} \mathbb{E}_Z [f_d(Z)].$$

and the Monte Carlo estimator on each level l with M^l inner sample is

$$\overline{\text{EVPI}}_l = \frac{1}{M^l} \sum_{m=1}^{M^l} \max_{d \in D} f_d(Z^{(m)}) - \max_{d \in D} \frac{1}{M^l} \sum_{m=1}^{M^l} f_d(Z^{(m)})$$

and MLMC estimator on each level l is

$$\overline{\text{EVPI}}_l - \frac{1}{2} \left(\overline{\text{EVPI}}_{l-1}^1 + \overline{\text{EVPI}}_{l-1}^2 \right)$$

where the $\overline{\text{EVPI}}_{l-1}^1$ uses the first M^{l-1} samples and $\overline{\text{EVPI}}_{l-1}^2$ uses the second M^{l-1} samples.

Here is the code for **EVPI_1.R** which require **Matrix**, **MASS** and **boot** packages. This function calculate N samples of the MLMC estimator on level l shown above.

```
EVPI_1 <- function(l, N) {
  require(Matrix)
  require(MASS) # mvrnorm
  require(boot) # logit, inv.logit

  # define the cost and lambda
  lamda <- 20000
  C_t1 <- 300
  C_t2 <- 30

  # calculate the number of inner samples
  M <- 2^(l+1)

  # define the mean and covariance matrix
  mu_rec <- c(0.99, 1.33)
  sigma_rec <- matrix(c(0.22, 0.15, 0.15, 0.20), 2, 2, byrow = TRUE)
  mu_rel <- c(-1.48, -0.4)
  sigma_rel <- matrix(c(0.14, 0.05, 0.05, 0.11), 2, 2, byrow = TRUE)

  # sum1 record the relavent statistics
  sum1 <- rep(0, 7)

  for(N1 in seq(1, N, by=10000)) {
    N2 <- min(10000, N-N1+1)

    # Sample all the random variables and tranform to M*N2 matrix
    P_nt_rec <- matrix(rbeta(M*N2, 6, 200), M, N2, byrow = TRUE)
    P_nt_rel <- matrix(rbeta(M*N2, 2, 100), M, N2, byrow = TRUE)

    lor_rec <- mvrnorm(M*N2, mu_rec, sigma_rec)
    lor_rel <- mvrnorm(M*N2, mu_rel, sigma_rel)

    lor_t1_rec <- matrix(lor_rec[, 1], M, N2, byrow = TRUE)
    lor_t1_rel <- matrix(lor_rel[, 1], M, N2, byrow = TRUE)
    P_t1_rec <- inv.logit(logit(P_nt_rec) + lor_t1_rec)
    P_t1_rel <- inv.logit(logit(P_nt_rel) + lor_t1_rel)

    lor_t2_rec <- matrix(lor_rec[, 2], M, N2, byrow = TRUE)
    lor_t2_rel <- matrix(lor_rel[, 2], M, N2, byrow = TRUE)
    P_t2_rec <- inv.logit(logit(P_nt_rec) + lor_t2_rec)
    P_t2_rel <- inv.logit(logit(P_nt_rel) + lor_t2_rel)

    C_rec = matrix(rnorm(M*N2, 1000, 50), M, N2, byrow = TRUE)
    C_rel = matrix(rnorm(M*N2, 2000, 100), M, N2, byrow = TRUE)
    C_no_rec = matrix(rnorm(M*N2, 2500, 125), M, N2, byrow = TRUE)

    Q_rec = matrix(rnorm(M*N2, 26, 2), M, N2, byrow = TRUE)
    Q_rel = matrix(rnorm(M*N2, 23, 3), M, N2, byrow = TRUE)
    Q_no_rec = matrix(rnorm(M*N2, 20, 4), M, N2, byrow = TRUE)

    # calculate the net benefits
```

```

NB_nt = (lamda*(P_nt_rec*(1-P_nt_rel)*Q_rec + P_nt_rec*P_nt_rel*Q_rel
              +(1-P_nt_rec)*Q_no_rec)
- (P_nt_rec*(1-P_nt_rel)*C_rec + P_nt_rec*P_nt_rel*C_rel
  +(1-P_nt_rec)*C_no_rec ))
NB_t1 = (lamda*(P_t1_rec*(1-P_t1_rel)*Q_rec + P_t1_rec*P_t1_rel*Q_rel
              +(1-P_t1_rec)*Q_no_rec)
- (C_t1 + P_t1_rec*(1-P_t1_rel)*C_rec + P_t1_rec*P_t1_rel*C_rel
  +(1-P_t1_rec)*C_no_rec ))
NB_t2 = (lamda*(P_t2_rec*(1-P_t2_rel)*Q_rec + P_t2_rec*P_t2_rel*Q_rel
              +(1-P_t2_rec)*Q_no_rec)
- (C_t2 + P_t2_rec*(1-P_t2_rel)*C_rec + P_t2_rec*P_t2_rel*C_rel
  +(1-P_t2_rec)*C_no_rec ))

# calculate the fine level and coarse level estimators
Pb = colMeans(pmax(pmax(NB_nt,NB_t1),NB_t2))
Pf = Pb-pmax(pmax(colMeans(NB_nt), colMeans(NB_t1)), colMeans(NB_t2))
if(M==2)
{
  Pc = Pb-0.5*(pmax(pmax(NB_nt[1,], NB_t1[1,]),NB_t2[1,])
              +pmax(pmax(NB_nt[2,], NB_t1[2,]), NB_t2[2,]))
} else {
Pc = Pb-0.5*(pmax(pmax(colMeans(NB_nt[1:(M/2),]),
                      colMeans(NB_t1[1:(M/2),])),colMeans(NB_t2[1:(M/2),]))
              +pmax(pmax(colMeans(NB_nt[((M/2)+1):M,]),
                      colMeans(NB_t1[((M/2)+1):M,])), colMeans(NB_t2[((M/2)+1):M,])))
}

# update the statistics
sum1[1] = sum1[1] + sum(Pf-Pc);
sum1[2] = sum1[2] + sum((Pf-Pc)^2);
sum1[3] = sum1[3] + sum((Pf-Pc)^3);
sum1[4] = sum1[4] + sum((Pf-Pc)^4);
sum1[5] = sum1[5] + sum(Pf);
sum1[6] = sum1[6] + sum(Pf^2);
sum1[7] = sum1[7] + M*N2;
}
return(sum1)
}

```

Note that $N1$ and $N2$ in this function are the trick of splitting the outer samples into a suitable size $N2=10000$ to achieve the best computational performance. If we only call the level function (e.g. $EVPI_l(1, N)$), then the number of outer samples is N . Both $N1$ and $N2$ are introduced to get the best efficiency of the matrix computation. That means, instead of computing the N out samples one by one, we compute $N2$ samples each time by using matrix computation. $N2=10000$ is the optimal size for matrix computation due to the tradeoff between the memory and speed. Then we need to do this calculation several times and $N1$ denote 1+the number of samples you have calculated. Therefore, if we want to compute $EVPI(1,33000)$, we will do the for loop four times ($N1=1, N2=10000$), ($N1=10001, N2=10000$), ($N1=20001, N2=10000$) and ($N1=30001, N2=3000$). In the last iteration, $N2=3000$ because we only need to calculate that number of the samples, which is ensured by the first line in the for loop. We also do some experiment on it by only changing the value of $N2$ range from 10 to 10^6 to do the `mlmc.test` function with the accuracy 1 and recording the running time. Here is the result:

N2	Time (s)
1e+01	142.812
1e+02	33.334
1e+03	23.683
1e+04	23.560
1e+05	24.198
1e+06	30.394

From these results, we can see that $N_2=10^4$ is the best.

The following **mlmc.test** function test the EVPI value with M^l inner samples for each level. **N** is the number of the out samples for convergence test. **L** is the max level for convergence test. **N_0** is the initial number of out samples for MLMC caculation which should be larger than the kurtosis to ensure the correct estimation of the variance. **eps.v** is the accuracy you want to achieve. You can test different accuracy using vector. **Lmin** and **Lmax** is the min and max number of levels used in MLMC. **parallel** is for parallel computing which is a integer.

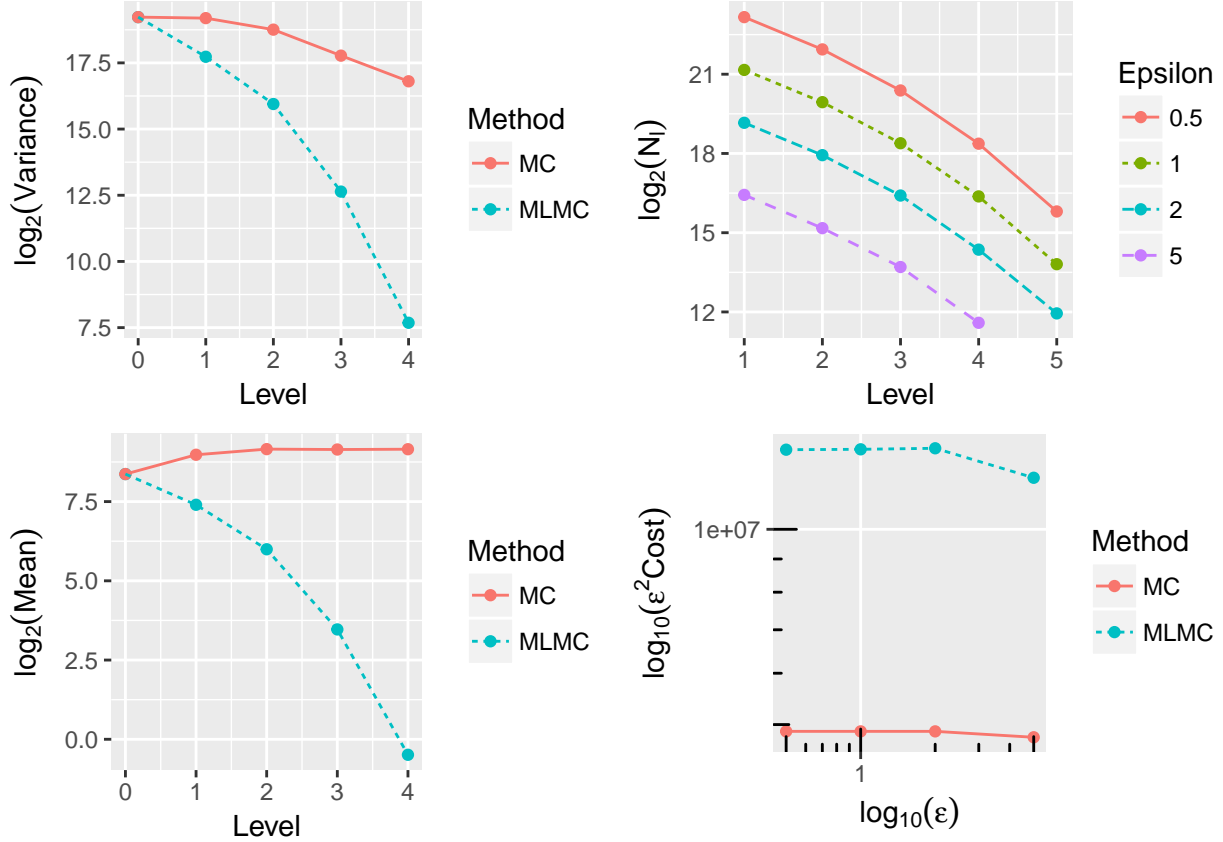
```
set.seed(666) # Set random seed to ensure the same output
# without this MLMC will give different output each time
tst <- mlmc.test(EVPI_1, M=2, N=10000,
                 L=4, N0=10000,
                 eps.v=c(0.5,1,2,5),
                 Lmin=2, Lmax=10, parallel = 32)

##
## *****
## *** Convergence tests, kurtosis, telescoping sum check ***
## *****
##
## 1   ave(Pf-Pc)   ave(Pf)   var(Pf-Pc)   var(Pf)   kurtosis   check
## -----
## 0   3.3043e+02   3.3043e+02   6.1407e+05   6.1407e+05   0.0000e+00   0.0000e+00
## 1   1.6881e+02   5.0399e+02   2.1757e+05   5.9802e+05   3.2059e+01   7.8256e-02
## 2   6.3791e+01   5.7022e+02   6.3150e+04   4.4255e+05   6.8721e+01   4.8033e-02
## 3   1.1051e+01   5.6533e+02   6.3752e+03   2.2405e+05   1.3617e+02   4.3616e-01
## 4   7.1243e-01   5.6903e+02   2.0539e+02   1.1440e+05   7.4995e+02   1.2070e-01
##
## WARNING: kurtosis on finest level = 749.945201
## indicates MLMC correction dominated by a few rare paths;
## for (information on the connection to variance of sample variances,
## see http://mathworld.wolfram.com/SampleVarianceDistribution.html
##
##
## *****
## *** Linear regression estimates of MLMC parameters ***
## *****
##
## alpha in 3.242238 (exponent for (MLMC weak convergence)
## beta in 4.132133 (exponent for (MLMC variance)
## gamma in 1.000000 (exponent for (MLMC cost)
##
## *****
## *** MLMC complexity tests ***
## *****
```

##	##	eps	value	mlmc_cost	std_cost	savings	N_1			
##	##	-----	-----	-----	-----	-----	-----	-----	-----	-----
##	0.5000	5.7501e+02	5.307e+07	1.952e+07	0.37	9384097	4022085	1369461	338880	57225
##	1.0000	5.7468e+02	1.328e+07	4.881e+06	0.37	2347260	1007127	342918	84928	14342
##	2.0000	5.7461e+02	3.333e+06	1.220e+06	0.37	586361	250699	86906	21015	3943
##	5.0000	5.6856e+02	4.803e+05	1.912e+05	0.40	88409	36904	13320	3082	

```
EVPI = tst$P[1]
```

```
plot(tst,which=c("var", "mean", "N1", "cost"),cols=2) # plot
```



The estimation of EVPI is 575.0147717 with root Mean Square Error 0.5.

EVPPI

Assume that the unknown parameters can be decomposed into two random variables as $Z = (X, Y)$ with $\Omega = \Omega_X \times \Omega_Y$ and only information of X is available. That means we can generate samples of X first and for each sample $X^{(n)}$, we can calculate the maximum of the conditional expectation of Y based on $X^{(n)}$. Therefore the expected value of partial perfect information (the value of X) is

$$\text{EVPPI} = \mathbb{E}_X \left[\max_{d \in D} \mathbb{E}_{Y|X} [f_d(X, Y)] \right] - \max_{d \in D} \mathbb{E}_Z [f_d(Z)]$$

So the conditional distribution of Y based on X is important and available. In MLMC, instead of directly estimating the EVPPI, we estimate the EVPI-EVPPI:

$$\text{DIFF} = \mathbb{E}_Z \left[\max_{d \in D} f_d(Z) \right] - \mathbb{E}_X \left[\max_{d \in D} \mathbb{E}_{Y|X} [f_d(X, Y)] \right]$$

and the Monte Carlo estimator on each level l with M^l inner sample based on $X^{(n)}$ is

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

and MLMC estimator on each level l is

$$\overline{\text{DIFF}}_l - \frac{1}{2} \left(\overline{\text{DIFF}}_{l-1}^1 + \overline{\text{DIFF}}_{l-1}^2 \right)$$

where the $\overline{\text{DIFF}}_{l-1}^1$ uses the first M^{l-1} samples and $\overline{\text{DIFF}}_{l-1}^2$ uses the second M^{l-1} samples.

EVPPI for P

Here is the code for **EVPPI_P_1.R** which require **Matrix**, **MASS** and **boot** packages:

```
EVPPI_P_1 <- function(l, N) {
  require(Matrix)
  require(MASS) # mvrnorm
  require(boot) # logit

  lamda <- 20000
  C_t1 <- 300
  C_t2 <- 30
  M <- 2^(l+1)

  mu_rec <- c(0.99, 1.33)
  sigma_rec <- matrix(c(0.22, 0.15, 0.15, 0.20), 2, 2, byrow = TRUE)
  mu_rel <- c(-1.48, -0.4)
  sigma_rel <- matrix(c(0.14, 0.05, 0.05, 0.11), 2, 2, byrow = TRUE)

  sum1 <- rep(0, 7)

  for(N1 in seq(1, N, by=10000)) {
    N2 <- min(10000, N-N1+1)

    P_nt_rec <- matrix(rep(rbeta(N2, 6, 200), M), M, N2, byrow = TRUE)
    P_nt_rel <- matrix(rep(rbeta(N2, 2, 100), M), M, N2, byrow = TRUE)

    lor_rec <- mvrnorm(N2, mu_rec, sigma_rec)
    lor_rel <- mvrnorm(N2, mu_rel, sigma_rel)

    # Generate N2 samples of P and repeat it to M*N2 matrix
    lor_t1_rec <- matrix(rep(lor_rec[, 1], M), M, N2, byrow = TRUE)
    lor_t1_rel <- matrix(rep(lor_rel[, 1], M), M, N2, byrow = TRUE)
    P_t1_rec <- inv.logit(logit(P_nt_rec) + lor_t1_rec)
    P_t1_rel <- inv.logit(logit(P_nt_rel) + lor_t1_rel)

    lor_t2_rec <- matrix(rep(lor_rec[, 2], M), M, N2, byrow = TRUE)
    lor_t2_rel <- matrix(rep(lor_rel[, 2], M), M, N2, byrow = TRUE)
    P_t2_rec <- inv.logit(logit(P_nt_rec) + lor_t2_rec)
    P_t2_rel <- inv.logit(logit(P_nt_rel) + lor_t2_rel)

    C_rec = matrix(rnorm(M*N2, 1000, 50), M, N2, byrow = TRUE)
```

```

C_rel = matrix(rnorm(M*N2,2000,100),M,N2,byrow = TRUE)
C_no_rec = matrix(rnorm(M*N2,2500,125),M,N2,byrow = TRUE)

Q_rec = matrix(rnorm(M*N2,26,2),M,N2,byrow = TRUE)
Q_rel = matrix(rnorm(M*N2,23,3),M,N2,byrow = TRUE)
Q_no_rec = matrix(rnorm(M*N2,20,4),M,N2,byrow = TRUE)

NB_nt = (lamda*(P_nt_rec*(1-P_nt_rel)*Q_rec + P_nt_rec*P_nt_rel*Q_rel
               +(1-P_nt_rec)*Q_no_rec)
- (P_nt_rec*(1-P_nt_rel)*C_rec + P_nt_rec*P_nt_rel*C_rel
   +(1-P_nt_rec)*C_no_rec ))
NB_t1 = (lamda*(P_t1_rec*(1-P_t1_rel)*Q_rec + P_t1_rec*P_t1_rel*Q_rel
               +(1-P_t1_rec)*Q_no_rec)
- (C_t1 + P_t1_rec*(1-P_t1_rel)*C_rec + P_t1_rec*P_t1_rel*C_rel
   +(1-P_t1_rec)*C_no_rec ))
NB_t2 = (lamda*(P_t2_rec*(1-P_t2_rel)*Q_rec + P_t2_rec*P_t2_rel*Q_rel
               +(1-P_t2_rec)*Q_no_rec)
- (C_t2 + P_t2_rec*(1-P_t2_rel)*C_rec + P_t2_rec*P_t2_rel*C_rel
   +(1-P_t2_rec)*C_no_rec ))

Pb = colMeans(pmax(pmax(NB_nt,NB_t1),NB_t2))
Pf = Pb-pmax(pmax(colMeans(NB_nt), colMeans(NB_t1)), colMeans(NB_t2))
if(M==2)
{
  Pc = Pb-0.5*(pmax(pmax(NB_nt[1,], NB_t1[1,]),NB_t2[1,])
               +pmax(pmax(NB_nt[2,], NB_t1[2,]), NB_t2[2,]))
} else {
  Pc = Pb-0.5*(pmax(pmax(colMeans(NB_nt[1:(M/2),]),
                        colMeans(NB_t1[1:(M/2),])),colMeans(NB_t2[1:(M/2),]))
               +pmax(pmax(colMeans(NB_nt[((M/2)+1):M,]),
                        colMeans(NB_t1[((M/2)+1):M,])), colMeans(NB_t2[((M/2)+1):M,])))
}
sum1[1] = sum1[1] + sum(Pf-Pc);
sum1[2] = sum1[2] + sum((Pf-Pc)^2);
sum1[3] = sum1[3] + sum((Pf-Pc)^3);
sum1[4] = sum1[4] + sum((Pf-Pc)^4);
sum1[5] = sum1[5] + sum(Pf);
sum1[6] = sum1[6] + sum(Pf^2);
sum1[7] = sum1[7] + M*N2;
}
return(sum1)
}

```

We can use the MLMC to calculate the value:

```

set.seed(666) # Set random seed to ensure the same output
# without this MLMC will give different output each time
tst <- mlmc.test(EVPPI_P_1, M=2, N=10000,
                 L=4, NO=10000,
                 eps.v=c(0.5,1,2,5),
                 Lmin=2, Lmax=10, parallel = 32)

```

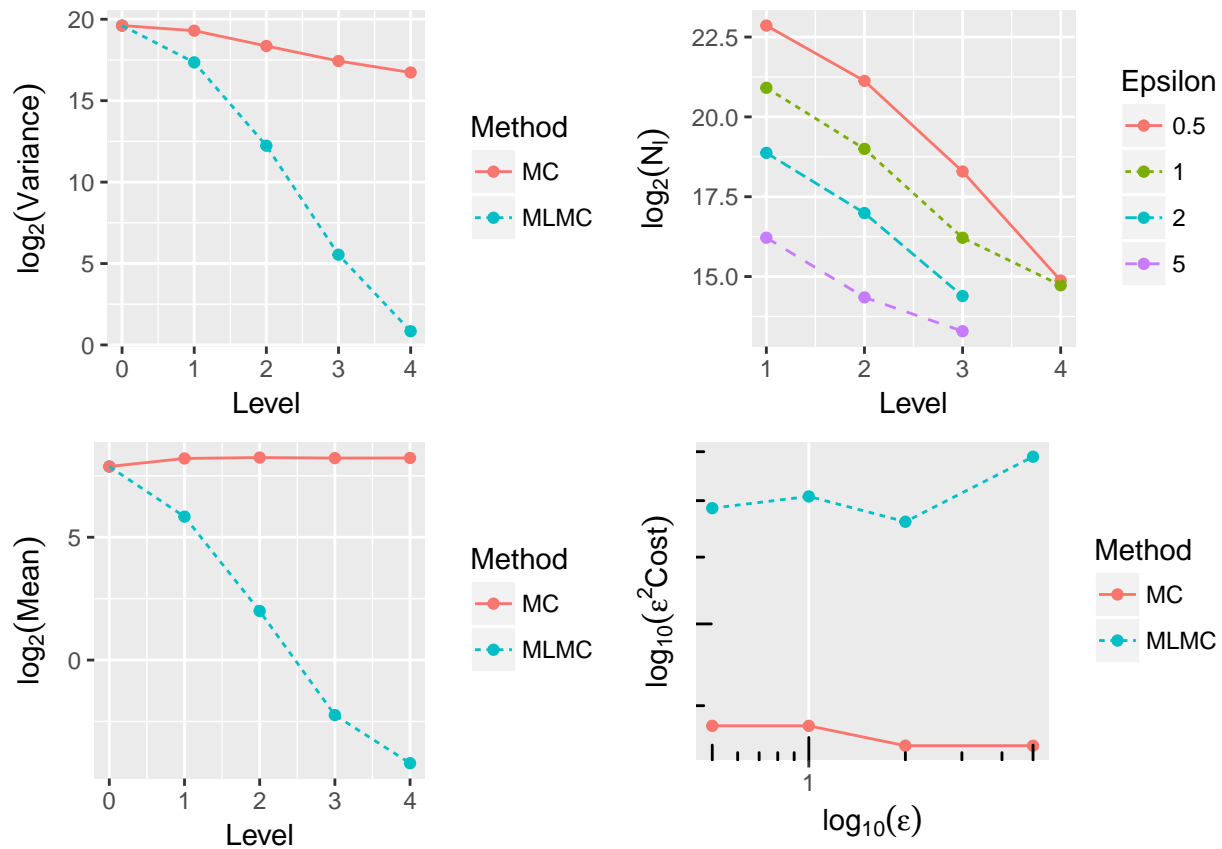
##

```

## *****
## *** Convergence tests, kurtosis, telescoping sum check ***
## *****
##
## 1    ave(Pf-Pc)    ave(Pf)    var(Pf-Pc)    var(Pf)    kurtosis    check
## -----
## 0    2.3555e+02    2.3555e+02    8.0231e+05    8.0231e+05    0.0000e+00    0.0000e+00
## 1    5.7241e+01    2.9567e+02    1.6738e+05    6.4520e+05    2.1013e+02    4.5583e-02
## 2    3.9898e+00    3.0335e+02    4.8219e+03    3.3620e+05    1.3548e+03    8.4638e-02
## 3    2.1168e-01    2.9881e+02    4.6532e+01    1.7748e+05    5.7816e+03    1.5706e-01
## 4    5.4363e-02    2.9978e+02    1.7921e+00    1.0892e+05    1.8839e+03    4.0428e-02
##
## WARNING: kurtosis on finest level = 1883.894134
## indicates MLMC correction dominated by a few rare paths;
## for (information on the connection to variance of sample variances,
## see http://mathworld.wolfram.com/SampleVarianceDistribution.html
##
##
## *****
## *** Linear regression estimates of MLMC parameters ***
## *****
##
## alpha in 3.098783 (exponent for (MLMC weak convergence)
## beta in 5.696884 (exponent for (MLMC variance)
## gamma in 1.000000 (exponent for (MLMC cost)
##
## *****
## *** MLMC complexity tests ***
## *****
##
## eps    value    mlmc_cost    std_cost    savings    N_l
## -----
## 0.5000    3.0096e+02    2.743e+07    1.514e+07    0.55    7614290    2289902    320345    30067
## 1.0000    3.0049e+02    7.081e+06    3.786e+06    0.53    1972960    523424    76009    27103
## 2.0000    3.0173e+02    1.652e+06    8.965e+05    0.54    480082    130047    21459
## 5.0000    3.0487e+02    3.157e+05    1.434e+05    0.45    76142    20845    10000

```

`plot(tst,which=c("var", "mean", "Nl", "cost"),cols=2) # plot`



The estimation of EVPPI for P is 274.0576662 with root Mean Square Error 1.

EVPPI for cq

Here is the code for **EVPPI_cq_1.R** which require Matrix, MASS and boot packages:

```
EVPPI_cq_1 <- function(l, N) {
  require(Matrix)
  require(MASS) # mvrnorm
  require(boot) # logit

  lamda <- 20000
  C_t1 <- 300
  C_t2 <- 30
  M <- 2^(l+1)

  mu_rec <- c(0.99, 1.33)
  sigma_rec <- matrix(c(0.22, 0.15, 0.15, 0.20), 2, 2, byrow = TRUE)
  mu_rel <- c(-1.48, -0.4)
  sigma_rel <- matrix(c(0.14, 0.05, 0.05, 0.11), 2, 2, byrow = TRUE)

  sum1 <- rep(0, 7)

  for(N1 in seq(1, N, by=10000)) {
    N2 <- min(10000, N-N1+1)

```

```

P_nt_rec <- matrix(rbeta(M*N2,6,200),M,N2,byrow = TRUE)
P_nt_rel <- matrix(rbeta(M*N2,2,100),M,N2,byrow = TRUE)

lor_rec <- mvrnorm(M*N2, mu_rec, sigma_rec)
lor_rel <- mvrnorm(M*N2, mu_rel, sigma_rel)

lor_t1_rec <- matrix(lor_rec[,1],M,N2,byrow = TRUE)
lor_t1_rel <- matrix(lor_rel[,1],M,N2,byrow = TRUE)
P_t1_rec <- inv.logit(logit(P_nt_rec)+lor_t1_rec)
P_t1_rel <- inv.logit(logit(P_nt_rel)+lor_t1_rel)

lor_t2_rec <- matrix(lor_rec[,2],M,N2,byrow = TRUE)
lor_t2_rel <- matrix(lor_rel[,2],M,N2,byrow = TRUE)
P_t2_rec <- inv.logit(logit(P_nt_rec)+lor_t2_rec)
P_t2_rel <- inv.logit(logit(P_nt_rel)+lor_t2_rel)

# Generate N2 samples of C Q and repeat it to M*N2 matrix
C_rec = matrix(rep(rnorm(N2,1000,50),M),M,N2,byrow = TRUE)
C_rel = matrix(rep(rnorm(N2,2000,100),M),M,N2,byrow = TRUE)
C_no_rec = matrix(rep(rnorm(N2,2500,125),M),M,N2,byrow = TRUE)

Q_rec = matrix(rep(rnorm(N2,26,2),M),M,N2,byrow = TRUE)
Q_rel = matrix(rep(rnorm(N2,23,3),M),M,N2,byrow = TRUE)
Q_no_rec = matrix(rep(rnorm(N2,20,4),M),M,N2,byrow = TRUE)

NB_nt = (lamda*(P_nt_rec*(1-P_nt_rel)*Q_rec + P_nt_rec*P_nt_rel*Q_rel
               +(1-P_nt_rec)*Q_no_rec)
- (P_nt_rec*(1-P_nt_rel)*C_rec + P_nt_rec*P_nt_rel*C_rel
   +(1-P_nt_rec)*C_no_rec ))
NB_t1 = (lamda*(P_t1_rec*(1-P_t1_rel)*Q_rec + P_t1_rec*P_t1_rel*Q_rel
               +(1-P_t1_rec)*Q_no_rec)
- (C_t1 + P_t1_rec*(1-P_t1_rel)*C_rec + P_t1_rec*P_t1_rel*C_rel
   +(1-P_t1_rec)*C_no_rec ))
NB_t2 = (lamda*(P_t2_rec*(1-P_t2_rel)*Q_rec + P_t2_rec*P_t2_rel*Q_rel
               +(1-P_t2_rec)*Q_no_rec)
- (C_t2 + P_t2_rec*(1-P_t2_rel)*C_rec + P_t2_rec*P_t2_rel*C_rel
   +(1-P_t2_rec)*C_no_rec ))

Pb = colMeans(pmax(pmax(NB_nt,NB_t1),NB_t2))
Pf = Pb-pmax(pmax(colMeans(NB_nt), colMeans(NB_t1)), colMeans(NB_t2))
if(M==2)
{
  Pc = Pb-0.5*(pmax(pmax(NB_nt[1,], NB_t1[1,]),NB_t2[1,])
               +pmax(pmax(NB_nt[2,], NB_t1[2,]), NB_t2[2,]))
} else {
  Pc = Pb-0.5*(pmax(pmax(colMeans(NB_nt[1:(M/2),]),
                       colMeans(NB_t1[1:(M/2),])),colMeans(NB_t2[1:(M/2),]))
               +pmax(pmax(colMeans(NB_nt[((M/2)+1):M,]),
                       colMeans(NB_t1[((M/2)+1):M,])), colMeans(NB_t2[((M/2)+1):M,])))
}
sum1[1] = sum1[1] + sum(Pf-Pc);
sum1[2] = sum1[2] + sum((Pf-Pc)^2);

```

```

    sum1[3] = sum1[3] + sum((Pf-Pc)^3);
    sum1[4] = sum1[4] + sum((Pf-Pc)^4);
    sum1[5] = sum1[5] + sum(Pf);
    sum1[6] = sum1[6] + sum(Pf^2);
    sum1[7] = sum1[7] + M*N2;
}
return(sum1)
}

```

We can use the MLMC to calculate the value:

```

set.seed(666) # Set random seed to ensure the same output
# without this MLMC will give different output each time
tst <- mlmc.test(EVPPI_cq_1, M=2, N=10000,
                 L=4, N0=10000,
                 eps.v=c(0.5,1,2,5),
                 Lmin=2, Lmax=10, parallel = 32)

```

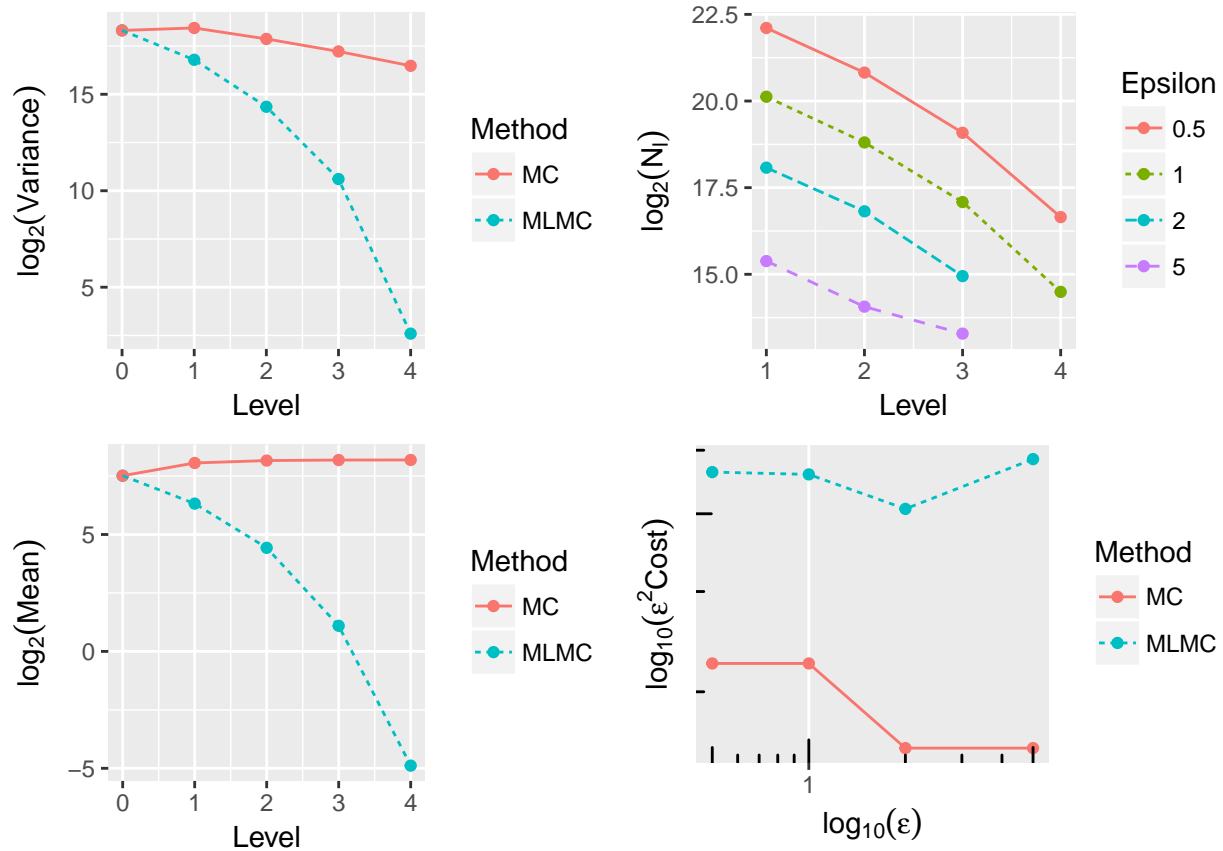
```

##
## *****
## *** Convergence tests, kurtosis, telescoping sum check ***
## *****
##
## 1    ave(Pf-Pc)    ave(Pf)    var(Pf-Pc)    var(Pf)    kurtosis    check
## -----
## 0    1.8280e+02    1.8280e+02    3.2471e+05    3.2471e+05    0.0000e+00    0.0000e+00
## 1    7.9924e+01    2.6673e+02    1.1305e+05    3.5478e+05    5.4340e+01    8.8787e-02
## 2    2.1577e+01    2.8635e+02    2.0907e+04    2.3928e+05    2.4673e+02    5.3007e-02
## 3    2.1356e+00    2.9111e+02    1.5599e+03    1.5254e+05    6.9163e+02    9.5141e-02
## 4    3.3837e-02    2.9167e+02    6.0411e+00    9.1159e+04    8.9516e+03    2.5360e-02
##
## WARNING: kurtosis on finest level = 8951.577164
## indicates MLMC correction dominated by a few rare paths;
## for (information on the connection to variance of sample variances,
## see http://mathworld.wolfram.com/SampleVarianceDistribution.html
##
##
## *****
## *** Linear regression estimates of MLMC parameters ***
## *****
##
## alpha in 4.658330 (exponent for (MLMC weak convergence)
## beta in 5.878438 (exponent for (MLMC variance)
## gamma in 1.000000 (exponent for (MLMC cost)
##
## *****
## *** MLMC complexity tests ***
## *****
##
## eps    value    mlmc_cost    std_cost    savings    N_l
## -----
## 0.5000  2.8720e+02  2.254e+07  1.302e+07    0.58  4521747  1851928  555407  102866
## 1.0000  2.8785e+02  5.598e+06  3.254e+06    0.58  1142298  458085  139031  23050
## 2.0000  2.8728e+02  1.268e+06  6.381e+05    0.50  276434  115518  31584

```

```
## 5.0000 2.8820e+02 2.340e+05 1.021e+05 0.44 42678 17149 10000
```

```
plot(tst,which=c("var", "mean", "N1", "cost"),cols=2) # plot
```



The estimation of EVPPI for C and Q is 287.8128835 with root Mean Square Error 1.

EVPPI for lor of CBT

Here is the code for **EVPPI_lor1_l.R** which require **Matrix**, **MASS** and **boot** packages:

```
EVPPI_lor1_l <- function(l, N) {
  require(Matrix) # matrix computation
  require(MASS) # multivariate normal generator
  require(boot) # logit function

  # some constants and parameters in the model
  lamda <- 20000
  C_t1 <- 300
  C_t2 <- 30
  mu_rec <- c(0.99, 1.33) # lor2
  sigma_rec <- matrix(c(0.22, 0.15, 0.15, 0.20), 2, 2, byrow = TRUE)
  mu_rel <- c(-1.48, -0.4) # lor3
  sigma_rel <- matrix(c(0.14, 0.05, 0.05, 0.11), 2, 2, byrow = TRUE)

  M <- 2^(l+1) # number of inner samples
  sum1 <- rep(0, 7)
```

```

for(N1 in seq(1, N, by=10000)) {
  # generate N2 samples together for better computational efficiency
  N2 <- min(10000, N-N1+1)

  # Generate M*N2 samples of Probability of no treatment
  P_nt_rec <- matrix(rbeta(M*N2,6,200),M,N2,byrow = TRUE)
  P_nt_rel <- matrix(rbeta(M*N2,2,100),M,N2,byrow = TRUE)

  # Generate N2 samples of lor_2 and repeat it to M*N2 matrix
  lor_rec <- mvrnorm(N2, mu_rec, sigma_rec)
  lor_rel <- mvrnorm(N2, mu_rel, sigma_rel)
  lor_t1_rec <- matrix(rep(lor_rec[,1],M),M,N2,byrow = TRUE)
  lor_t1_rel <- matrix(rep(lor_rel[,1],M),M,N2,byrow = TRUE)
  P_t1_rec <- inv.logit(logit(P_nt_rec)+lor_t1_rec)
  P_t1_rel <- inv.logit(logit(P_nt_rel)+lor_t1_rel)

  # calculate the conditional normal distribution of the lor_t2 based on N2 samples of lor_t1
  mu_t2_rec = (lor_t1_rec-mu_rec[1])*sigma_rec[1,2]/sigma_rec[1,1]+mu_rec[2];
  mu_t2_rel = (lor_t1_rel-mu_rel[1])*sigma_rel[1,2]/sigma_rel[1,1]+mu_rel[2];
  sigma_t2_rec = sqrt(sigma_rec[2,2]-sigma_rec[1,2]^2/sigma_rec[1,1]);
  sigma_t2_rel = sqrt(sigma_rel[2,2]-sigma_rel[1,2]^2/sigma_rel[1,1]);
  # Generate M*N2 samples of lor_t2 conditioned on lor_t1 and repeat it to M*N2 matrix
  lor_t2_rec = mu_t2_rec + sigma_t2_rec*matrix(rnorm(M*N2,0,1),M,N2,byrow=TRUE);
  lor_t2_rel = mu_t2_rel + sigma_t2_rel*matrix(rnorm(M*N2,0,1),M,N2,byrow=TRUE);
  P_t2_rec = inv.logit(logit(P_nt_rec)+lor_t2_rec);
  P_t2_rel = inv.logit(logit(P_nt_rel)+lor_t2_rel);

  # generate M*N2 independent inner samples
  C_rec = matrix(rnorm(M*N2,1000,50),M,N2,byrow = TRUE)
  C_rel = matrix(rnorm(M*N2,2000,100),M,N2,byrow = TRUE)
  C_no_rec = matrix(rnorm(M*N2,2500,125),M,N2,byrow = TRUE)

  Q_rec = matrix(rnorm(M*N2,26,2),M,N2,byrow = TRUE)
  Q_rel = matrix(rnorm(M*N2,23,3),M,N2,byrow = TRUE)
  Q_no_rec = matrix(rnorm(M*N2,20,4),M,N2,byrow = TRUE)

  # calculate the NB value for all 3 treatments of all samples using formula (5.1)
  NB_nt = (lamda*(P_nt_rec*(1-P_nt_rel)*Q_rec + P_nt_rec*P_nt_rel*Q_rel
    +(1-P_nt_rec)*Q_no_rec)
    - (P_nt_rec*(1-P_nt_rel)*C_rec + P_nt_rec*P_nt_rel*C_rel
    +(1-P_nt_rec)*C_no_rec ))
  NB_t1 = (lamda*(P_t1_rec*(1-P_t1_rel)*Q_rec + P_t1_rec*P_t1_rel*Q_rel
    +(1-P_t1_rec)*Q_no_rec)
    - (C_t1 + P_t1_rec*(1-P_t1_rel)*C_rec + P_t1_rec*P_t1_rel*C_rel
    +(1-P_t1_rec)*C_no_rec ))
  NB_t2 = (lamda*(P_t2_rec*(1-P_t2_rel)*Q_rec + P_t2_rec*P_t2_rel*Q_rel
    +(1-P_t2_rec)*Q_no_rec)
    - (C_t2 + P_t2_rec*(1-P_t2_rel)*C_rec + P_t2_rec*P_t2_rel*C_rel
    +(1-P_t2_rec)*C_no_rec ))

  # the first term in estimator (9.1)
  Pb = colMeans(pmax(pmax(NB_nt,NB_t1),NB_t2))

```

```

# DIFF estimator (9.1) with M inner samples for level l
Pf = Pb-pmax(pmax(colMeans(NB_nt), colMeans(NB_t1)), colMeans(NB_t2))

# Average of two DIFF estimator with M/2 inner samples for level l-1
if(M==2)
{
  Pc = Pb-0.5*(pmax(pmax(NB_nt[1,], NB_t1[1,]),NB_t2[1,])
               +pmax(pmax(NB_nt[2,], NB_t1[2,]), NB_t2[2,]))

} else {
  Pc = Pb-0.5*(pmax(pmax(colMeans(NB_nt[1:(M/2),]),
                       colMeans(NB_t1[1:(M/2),])),colMeans(NB_t2[1:(M/2),]))
               +pmax(pmax(colMeans(NB_nt[((M/2)+1):M,]),
                       colMeans(NB_t1[((M/2)+1):M,])), colMeans(NB_t2[((M/2)+1):M,])))
}

# update all the statistics needed by MLMC
sum1[1] = sum1[1] + sum(Pf-Pc);
sum1[2] = sum1[2] + sum((Pf-Pc)^2);
sum1[3] = sum1[3] + sum((Pf-Pc)^3);
sum1[4] = sum1[4] + sum((Pf-Pc)^4);
sum1[5] = sum1[5] + sum(Pf);
sum1[6] = sum1[6] + sum(Pf^2);
sum1[7] = sum1[7] + M*N2;
}
return(sum1) # return statistics
}

```

We can use the MLMC to calculate the value:

```

set.seed(666) # Set random seed to ensure the same output
# without this MLMC will give different output each time
tst <- mlmc.test(EVPPI_lor1_l, M=2, N=10000,
                 L=4, NO=10000,
                 eps.v=c(0.5,1,2,5),
                 Lmin=2, Lmax=10, parallel = 32)

```

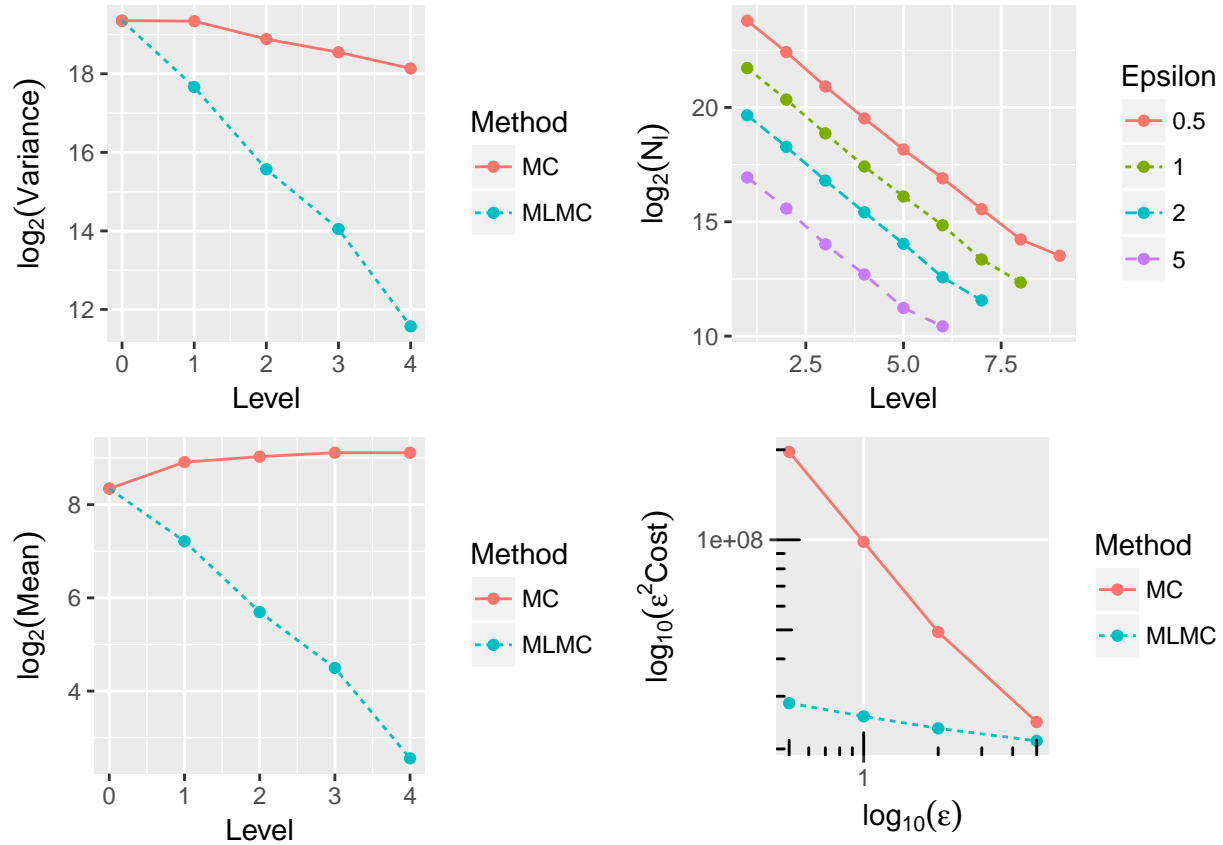
```

##
## *****
## *** Convergence tests, kurtosis, telescoping sum check ***
## *****
##
## 1   ave(Pf-Pc)   ave(Pf)   var(Pf-Pc)   var(Pf)   kurtosis   check
## -----
## 0   3.2492e+02   3.2492e+02   6.6945e+05   6.6945e+05   0.0000e+00   0.0000e+00
## 1   1.4834e+02   4.8171e+02   2.0766e+05   6.6378e+05   4.8424e+01   1.3479e-01
## 2   5.1858e+01   5.2265e+02   4.8650e+04   4.8418e+05   6.6135e+01   2.1006e-01
## 3   2.2573e+01   5.5440e+02   1.6945e+04   3.8341e+05   9.3511e+01   2.1159e-01
## 4   5.8828e+00   5.5381e+02   3.0403e+03   2.8826e+05   2.0209e+02   1.7826e-01
##
## WARNING: kurtosis on finest level = 202.085385
## indicates MLMC correction dominated by a few rare paths;
## for (information on the connection to variance of sample variances,
## see http://mathworld.wolfram.com/SampleVarianceDistribution.html

```

```
##
##
## *****
## *** Linear regression estimates of MLMC parameters ***
## *****
##
## alpha in 1.570001 (exponent for (MLMC weak convergence)
## beta in 2.000076 (exponent for (MLMC variance)
## gamma in 1.000000 (exponent for (MLMC cost)
##
## *****
## *** MLMC complexity tests ***
## *****
##
## eps      value      mlmc_cost      std_cost      savings      N_l
## -----
## 0.5000  5.6865e+02  1.138e+08  7.872e+08      6.92  14556679  5620269  1983560  752775  293384
## 1.0000  5.6864e+02  2.570e+07  9.839e+07      3.83  3457486  1332890  478818  175349  70573
## 2.0000  5.6762e+02  5.858e+06  1.230e+07      2.10  827542  318042  114507  43726  16814
## 5.0000  5.6584e+02  8.516e+05  9.839e+05      1.16  125874  49029  16553  6638  2404
```

`plot(tst,which=c("var", "mean", "Nl", "cost"),cols=2) # plot`



The estimation of EVPPI for lor of CBT is 6.3664424 with root Mean Square Error 1.

EVPPI for lor of antidepression

Here is the code for **EVPPI_lor2_1.R** which require **Matrix**, **MASS** and **boot** packages:

```
EVPPI_lor1_1 <- function(l, N) {
  require(Matrix)
  require(MASS) # mvrnorm
  require(boot) # logit

  lamda <- 20000
  C_t1 <- 300
  C_t2 <- 30
  M <- 2^(l+1)

  mu_rec <- c(0.99,1.33)
  sigma_rec <- matrix(c(0.22,0.15,0.15,0.20),2,2,byrow = TRUE)
  mu_rel <- c(-1.48,-0.4)
  sigma_rel <- matrix(c(0.14,0.05,0.05,0.11),2,2,byrow = TRUE)

  sum1 <- rep(0, 7)

  for(N1 in seq(1, N, by=10000)) {
    N2 <- min(10000, N-N1+1)

    P_nt_rec <- matrix(rbeta(M*N2,6,200),M,N2,byrow = TRUE)
    P_nt_rel <- matrix(rbeta(M*N2,2,100),M,N2,byrow = TRUE)

    lor_rec <- mvrnorm(N2, mu_rec, sigma_rec)
    lor_rel <- mvrnorm(N2, mu_rel, sigma_rel)

    # Generate N2 samples of lor_t2 and repeat it to M*N2 matrix
    lor_t2_rec <- matrix(rep(lor_rec[,2],M),M,N2,byrow = TRUE)
    lor_t2_rel <- matrix(rep(lor_rel[,2],M),M,N2,byrow = TRUE)
    P_t2_rec <- inv.logit(logit(P_nt_rec)+lor_t2_rec)
    P_t2_rel <- inv.logit(logit(P_nt_rel)+lor_t2_rel)

    # calculate the conditional normal distribution of the lor_t1 based on N2 samples of lor_t2
    mu_t1_rec = (lor_t2_rec-mu_rec[2])*sigma_rec[1,2]/sigma_rec[2,2]+mu_rec[1];
    mu_t1_rel = (lor_t2_rel-mu_rel[2])*sigma_rel[1,2]/sigma_rel[2,2]+mu_rel[1];
    sigma_t1_rec = sqrt(sigma_rec[1,1]-sigma_rec[1,2]^2/sigma_rec[2,2]);
    sigma_t1_rel = sqrt(sigma_rel[1,1]-sigma_rel[1,2]^2/sigma_rel[2,2]);

    # Generate M*N2 samples of lor_t2 conditioned on lor_t1 and repeat it to M*N2 matrix
    lor_t1_rec = mu_t1_rec + sigma_t1_rec*matrix(rnorm(M*N2,0,1),M,N2,byrow=TRUE);
    lor_t1_rel = mu_t1_rel + sigma_t1_rel*matrix(rnorm(M*N2,0,1),M,N2,byrow=TRUE);
    P_t1_rec = inv.logit(logit(P_nt_rec)+lor_t1_rec);
    P_t1_rel = inv.logit(logit(P_nt_rel)+lor_t1_rel);

    C_rec = matrix(rnorm(M*N2,1000,50),M,N2,byrow = TRUE)
    C_rel = matrix(rnorm(M*N2,2000,100),M,N2,byrow = TRUE)
    C_no_rec = matrix(rnorm(M*N2,2500,125),M,N2,byrow = TRUE)

    Q_rec = matrix(rnorm(M*N2,26,2),M,N2,byrow = TRUE)
    Q_rel = matrix(rnorm(M*N2,23,3),M,N2,byrow = TRUE)
```



```

Q_no_rec = matrix(rnorm(M*N2,20,4),M,N2,byrow = TRUE)

NB_nt = (lamda*(P_nt_rec*(1-P_nt_rel)*Q_rec + P_nt_rec*P_nt_rel*Q_rel
               +(1-P_nt_rec)*Q_no_rec)
- (P_nt_rec*(1-P_nt_rel)*C_rec + P_nt_rec*P_nt_rel*C_rel
   +(1-P_nt_rec)*C_no_rec ))
NB_t1 = (lamda*(P_t1_rec*(1-P_t1_rel)*Q_rec + P_t1_rec*P_t1_rel*Q_rel
               +(1-P_t1_rec)*Q_no_rec)
- (C_t1 + P_t1_rec*(1-P_t1_rel)*C_rec + P_t1_rec*P_t1_rel*C_rel
   +(1-P_t1_rec)*C_no_rec ))
NB_t2 = (lamda*(P_t2_rec*(1-P_t2_rel)*Q_rec + P_t2_rec*P_t2_rel*Q_rel
               +(1-P_t2_rec)*Q_no_rec)
- (C_t2 + P_t2_rec*(1-P_t2_rel)*C_rec + P_t2_rec*P_t2_rel*C_rel
   +(1-P_t2_rec)*C_no_rec ))

Pb = colMeans(pmax(pmax(NB_nt,NB_t1),NB_t2))
Pf = Pb-pmax(pmax(colMeans(NB_nt), colMeans(NB_t1)), colMeans(NB_t2))
if(M==2)
{
  Pc = Pb-0.5*(pmax(pmax(NB_nt[1,], NB_t1[1,]),NB_t2[1,])
               +pmax(pmax(NB_nt[2,], NB_t1[2,]), NB_t2[2,]))
} else {
  Pc = Pb-0.5*(pmax(pmax(colMeans(NB_nt[1:(M/2),]),
                        colMeans(NB_t1[1:(M/2),])),colMeans(NB_t2[1:(M/2),]))
               +pmax(pmax(colMeans(NB_nt[((M/2)+1):M,]),
                        colMeans(NB_t1[((M/2)+1):M,])),colMeans(NB_t2[((M/2)+1):M,])))
}
sum1[1] = sum1[1] + sum(Pf-Pc);
sum1[2] = sum1[2] + sum((Pf-Pc)^2);
sum1[3] = sum1[3] + sum((Pf-Pc)^3);
sum1[4] = sum1[4] + sum((Pf-Pc)^4);
sum1[5] = sum1[5] + sum(Pf);
sum1[6] = sum1[6] + sum(Pf^2);
sum1[7] = sum1[7] + M*N2;
}
return(sum1)
}

```

We can use the MLMC to calculate the value:

```

set.seed(666) # Set random seed to ensure the same output
# without this MLMC will give different output each time
tst <- mlmc.test(EVPPI_lor2_l, M=2, N=10000,
                 L=4, NO=10000,
                 eps.v=c(0.5,1,2,5),
                 Lmin=2, Lmax=10, parallel = 32)

```

```

##
## *****
## *** Convergence tests, kurtosis, telescoping sum check ***
## *****
##
## 1   ave(Pf-Pc)   ave(Pf)   var(Pf-Pc)   var(Pf)   kurtosis   check

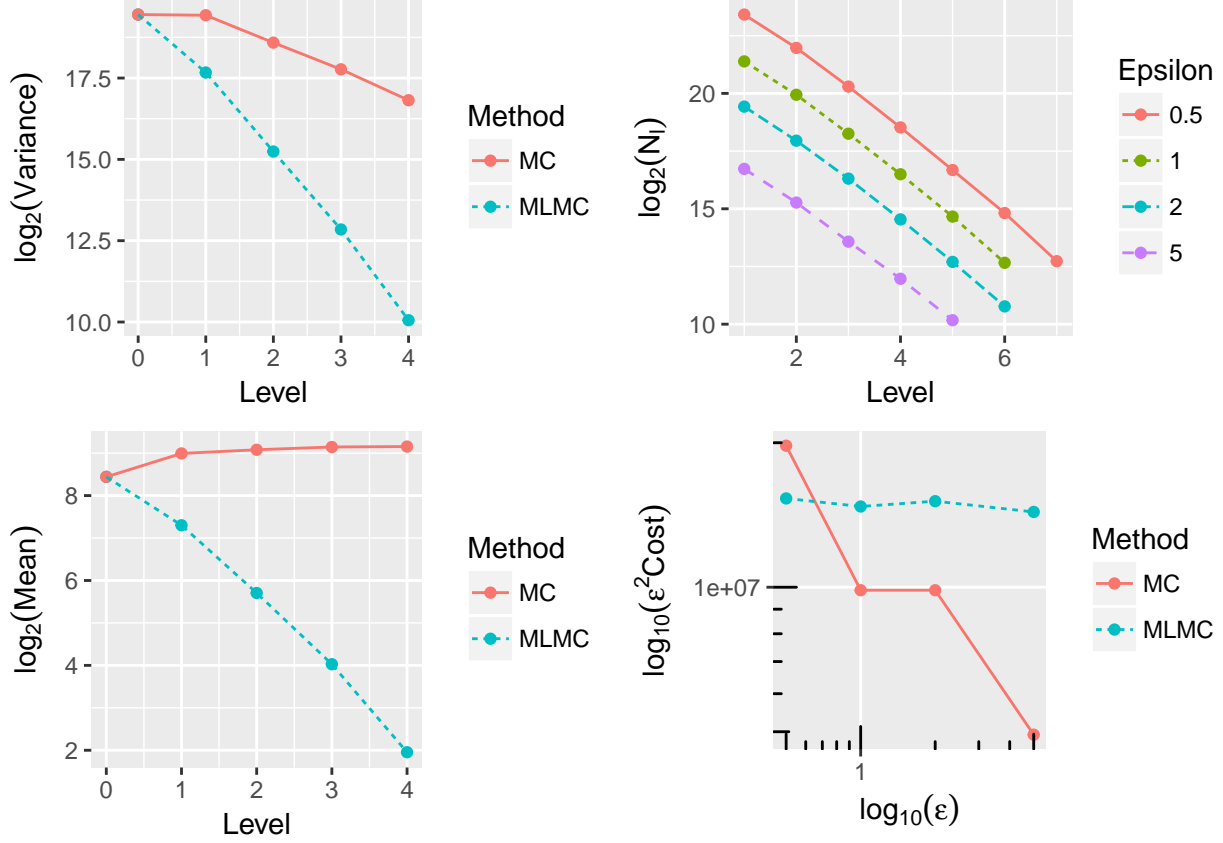
```

```

## -----
## 0  3.4775e+02  3.4775e+02  7.1715e+05  7.1715e+05  0.0000e+00  0.0000e+00
## 1  1.5773e+02  5.0980e+02  2.0861e+05  7.0674e+05  4.2171e+01  6.7084e-02
## 2  5.2193e+01  5.4122e+02  3.8737e+04  3.9428e+05  7.2387e+01  4.1580e-01
## 3  1.6311e+01  5.6624e+02  7.3573e+03  2.2332e+05  8.1351e+01  2.4485e-01
## 4  3.8734e+00  5.7030e+02  1.0637e+03  1.1552e+05  2.5227e+02  7.4581e-03
##
## WARNING: kurtosis on finest level = 252.273782
## indicates MLMC correction dominated by a few rare paths;
## for (information on the connection to variance of sample variances,
## see http://mathworld.wolfram.com/SampleVarianceDistribution.html
##
##
## *****
## *** Linear regression estimates of MLMC parameters ***
## *****
##
## alpha in 1.876090 (exponent for (MLMC weak convergence)
## beta in 2.593240 (exponent for (MLMC variance)
## gamma in 1.000000 (exponent for (MLMC cost)
##
## *****
## *** MLMC complexity tests ***
## *****
##
##      eps      value  mlmc_cost  std_cost  savings      N_l
## -----
## 0.5000  5.7475e+02  6.124e+07  7.886e+07      1.29  11191739  4111534  1287314  377388  104929
## 1.0000  5.7251e+02  1.473e+07  9.858e+06      0.67  2740902  1006357  312613  92423  25917
## 2.0000  5.7708e+02  3.777e+06  2.464e+06      0.65   704854  253380  81059  23819  6646
## 5.0000  5.6872e+02  5.740e+05  1.972e+05      0.34   108657   39503  12210  4006  1153

```

`plot(tst,which=c("var", "mean", "Nl", "cost"),cols=2) # plot`



The estimation of EVPPI for lor of antidepressant is 0.2655106 with root Mean Square Error 1.

Summary

MLMC works well for all the calculations and starts to show the computational savings when calculating the EVPPI for lor, i.e. involving the conditional sampling.

Comparison with QMC

For comparison, we set the **mean square error (MSE)** to be 0.25 ($\epsilon = 0.5$) and divide it into two parts: **weak error:** 0.25, **variance:** 0.1875.

We first run the **MLMC** function to achieve the required MSE, which gives the computational costs of the MLMC and standard MC. Then, by using the same number of inner samples, we do QMC on the outer samples and achieve the required variance. This kind of comparison is relatively unfair for MLMC, since other algorithms do not need to find the required number of inner samples.

Table 2: Comparison of Computational Cost (10^6)

	Standard MC	MLMC	QMC
EVPPI_P	15.14	26.93	5.63
EVPPI_cq	13.02	22.85	5.12
EVPPI_lor1	787.20	108.50	8.19