hoangtn / extTADA

Unwatch 4 Star 1 Fork 0

Code Issues 1 Pull requests 0 Projects 0 Wiki Settings Insights

Branch: master extTADA / examples / extTADA_MultipleSteps.ipynb Find file Copy path

Hoang Nguyen Update files 55a3cdb 5 minutes ago

0 contributors

39.6 MB Download History

extTADA for separate steps

This example describes steps to obtain results for de novo data. There are many steps used in this example. Users can use this example to customize plots/parameters for publications.

Some main steps:

1. Estimate genetic parameters using MCCMC.
2. Use these parameters to calculate FDRs for each gene.

Load source files of extTADA

In [7]:
```
fileR <- dir("../script", ".R$")
for (ii in fileR)
    source(paste0("../script/", ii))
```

```
Loading required package: ggplot2
Loading required package: StanHeaders
rstan (Version 2.16.2, packaged: 2017-07-03 09:24:58 UTC, GitRev: 2e1f913d3ca3)
For execution on a local, multicore CPU with excess RAM we recommend calling
rstan_options(auto_write = TRUE)
options(mc.cores = parallel::detectCores())
locfit 1.5-9.1   2013-03-22
```

In [8]:
```
N = list(dn = 1077, ca = 3157, cn = 4672)
inputData <- read.table("../data/SimulationDataDNandCC.txt", header = TRUE, as.is = TRUE)

head(inputData)
```

Out[8]:

	Gene	mut_lof	mut_mis3	dn_lof	dn_mis3	cc_case1	cc_case2	cc_control1	cc_control2
1	G1	9.996657e-07	4.54062e-07	0	0	0	0	0	0
2	G2	1.420491e-07	1.04146e-10	0	0	0	0	0	0
3	G3	2.144318e-06	3.35199e-06	0	0	0	0	0	0
4	G4	3.981797e-06	7.82154e-06	0	0	0	0	0	0
5	G5	9.14698e-08	1.04146e-10	0	0	0	0	0	0
6	G6	3.779929e-06	2.85364e-06	0	0	0	0	0	0

In [ ]:
```
```

In [9]:
```
allDNData <- inputData[, paste0("dn_", c("mis3", "lof"))]
allMutData <- inputData[,paste0("mut_", c("mis3", "lof"))]
head(data.frame(allMutData, allDNData))
```

Out[9]:

	mut_mis3	mut_lof	dn_mis3	dn_lof
1	4.54062e-07	9.996657e-07	0	0
2	1.04146e-10	1.420491e-07	0	0
3	3.35199e-06	2.144318e-06	0	0
4	7.82154e-06	3.981797e-06	0	0
5	1.04146e-10	9.14698e-08	0	0
6	2.85364e-06	3.779929e-06	0	0

Use the function *extTADA* to sample values of parameters

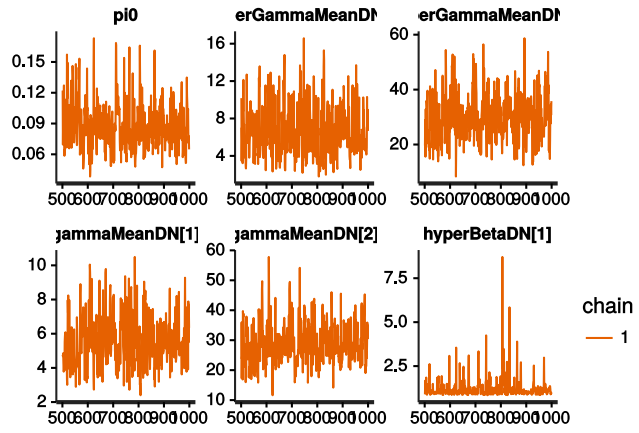
In [10]:
```
mcmcDD <- extTADAmcmc(modelName = DNextTADA, #extTADA for only de novo data
                      dataDN = allDNData, mutRate = allMutData,
                      Ndn = rep(N$dn, 2), ## There are two de novo categories
                      nIteration = 1000)
```

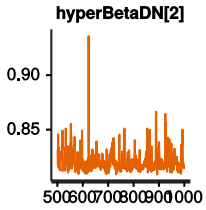
```
There are 19358 genes in this analysis

=============FIRST TIME ===============
```

```
Sampling with nter = 1000 and nThin = 1


The model DNextTADA is used

In file included from /home/hoangnguyen/R/x86_64-pc-linux-gnu-library/3.2/BH/include/boost/config.
hpp:39:0,
                 from /home/hoangnguyen/R/x86_64-pc-linux-gnu-library/3.2/BH/include/boost/math/to
ols/config.hpp:13,
                 from /home/hoangnguyen/R/x86_64-pc-linux-gnu-library/3.2/StanHeaders/include/sta
n/math/rev/core/var.hpp:7,
                 from /home/hoangnguyen/R/x86_64-pc-linux-gnu-library/3.2/StanHeaders/include/sta
n/math/rev/core/gevv_vvv_vari.hpp:5,
                 from /home/hoangnguyen/R/x86_64-pc-linux-gnu-library/3.2/StanHeaders/include/sta
n/math/rev/core.hpp:12,
                 from /home/hoangnguyen/R/x86_64-pc-linux-gnu-library/3.2/StanHeaders/include/sta
n/math/rev/mat.hpp:4,
                 from /home/hoangnguyen/R/x86_64-pc-linux-gnu-library/3.2/StanHeaders/include/sta
n/math.hpp:4,
                 from /home/hoangnguyen/R/x86_64-pc-linux-gnu-library/3.2/StanHeaders/include/src/
stan/model/model_header.hpp:4,
                 from file12e0d5afd7c.cpp:8:
/home/hoangnguyen/R/x86_64-pc-linux-gnu-library/3.2/BH/include/boost/config/compiler/gcc.hpp:186:
0: warning: "BOOST_NO_CXX11_RVALUE_REFERENCES" redefined [enabled by default]
 #  define BOOST_NO_CXX11_RVALUE_REFERENCES
 ^
<command-line>:0:0: note: this is the location of the previous definition

SAMPLING FOR MODEL '493590f0b50b55273a713acc3c2b8395' NOW (CHAIN 1).

Gradient evaluation took 0.020208 seconds
1000 transitions using 10 leapfrog steps per transition would take 202.08 seconds.
Adjust your expectations accordingly!


Iteration:   1 / 1000 [  0%]  (Warmup)
Iteration: 100 / 1000 [ 10%]  (Warmup)
Iteration: 200 / 1000 [ 20%]  (Warmup)
Iteration: 300 / 1000 [ 30%]  (Warmup)
Iteration: 400 / 1000 [ 40%]  (Warmup)
Iteration: 500 / 1000 [ 50%]  (Warmup)
Iteration: 501 / 1000 [ 50%]  (Sampling)
Iteration: 600 / 1000 [ 60%]  (Sampling)
Iteration: 700 / 1000 [ 70%]  (Sampling)
Iteration: 800 / 1000 [ 80%]  (Sampling)
Iteration: 900 / 1000 [ 90%]  (Sampling)
Iteration: 1000 / 1000 [100%]  (Sampling)

 Elapsed Time: 134.752 seconds (Warm-up)
               132.583 seconds (Sampling)
               267.335 seconds (Total)
```

Take a quick look at the traces of parameters

In [11]:
```
options(repr.plot.width=5, repr.plot.height=5)
stan_trace(mcmcDD)
```





In [12]:
```
mcmcDD
```

Out[12]:
```
Inference for Stan model: 493590f0b50b55273a713acc3c2b8395.
1 chains, each with iter=1000; warmup=500; thin=1;
post-warmup draws per chain=500, total post-warmup draws=500.

                         mean se_mean   sd     2.5%      25%      50%      75%
pi0                      0.09    0.00 0.02     0.05     0.07     0.09     0.10
hyperGammaMeanDN[1]      6.60    0.17 2.67     2.60     4.61     6.13     8.15
hyperGammaMeanDN[2]     29.60    0.61 8.35    15.19    23.50    29.30    34.62
gammaMeanDN[1]           5.53    0.11 1.49     3.18     4.48     5.26     6.46
gammaMeanDN[2]          28.87    0.50 6.78    17.56    24.23    28.07    32.96
hyperBetaDN[1]           1.22    0.04 0.60     0.86     0.94     1.05     1.25
hyperBetaDN[2]           0.82    0.00 0.01     0.81     0.81     0.82     0.82
lp__                 -1771.70    0.10 1.49 -1775.23 -1772.46 -1771.41 -1770.64
                        97.5% n_eff Rhat
pi0                      0.14   184    1
hyperGammaMeanDN[1]     12.61   248    1
hyperGammaMeanDN[2]     47.23   189    1
gammaMeanDN[1]           8.87   174    1
gammaMeanDN[2]          43.57   185    1
hyperBetaDN[1]           2.73   233    1
hyperBetaDN[2]           0.85   243    1
lp__                 -1769.71   220    1

Samples were drawn using NUTS(diag_e) at Mon Jul 17 21:47:42 2017.
For each parameter, n_eff is a crude measure of effective sample size,
and Rhat is the potential scale reduction factor on split chains (at
convergence, Rhat=1).
```

Use the function *estimatePars* of extTADA to obtain modes, and credible intervals (ID) of parameters

In [13]:
```
pars0 <- estimatePars(pars = c('pi0',
                               'hyperGammaMeanDN[1]', 'hyperGammaMeanDN[2]',
                               'hyperBetaDN[1]', 'hyperBetaDN[2]'),
                      mcmcResult = mcmcDD)
```

```
====
Only pi and hyper parameters are estimated in this step
extTADA does not calculate HPDs for hyper betas, just their medians
===
```

In [14]:
```
pars0
```

Out[14]:

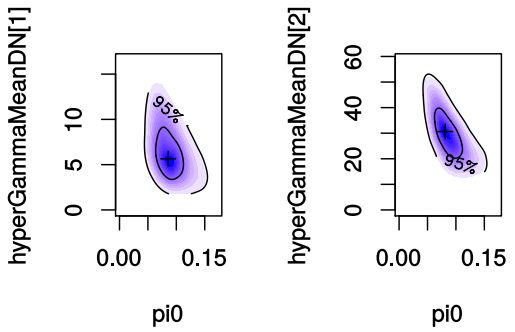
	Mode	lCI	uCI
pi0	0.07889561	0.04738143	0.13488191
hyperGammaMeanDN[1]	5.570321	2.253059	12.083404
hyperGammaMeanDN[2]	29.32103	13.84757	46.75609
hyperBetaDN[1]	1.045378	1.045378	1.045378
hyperBetaDN[2]	0.8178659	0.8178659	0.8178659

Use the function *plotParHeatmap* of extTADA to draw heatmaps of pairs of pars

In [15]:
```
options(repr.plot.width=4, repr.plot.height=3)
par(mfrow = c(1, 2))
plotParHeatmap(pars = c("pi0", "hyperGammaMeanDN[1]"), mcmcResult = mcmcDD)
plotParHeatmap(pars = c("pi0", "hyperGammaMeanDN[2]"), mcmcResult = mcmcDD)
```

```
Warning message:
```

```
In plot.xy(xy, type, ...): font width unknown for character 0x1Warning message:
In plot.xy(xy, type, ...): font metrics unknown for character 0x1Warning message:
In plot.xy(xy, type, ...): font width unknown for character 0x1Warning message:
In plot.xy(xy, type, ...): font metrics unknown for character 0x1
```



Use function *calculateFDR* of extTADA to obtain FDRs of genes

In [20]:
```
##Get gene list
geneName <- inputData[, 1]
##Set parameters: use pars0 above
parsFDR <- list(gammaMeanDN = pars0[, 1][2:3],
                betaDN = pars0[, 1][4:5],
            pi0 = pars0[, 1][1],
            nfamily = rep(ntrioDD, 2))

dataFDR <- calculateFDR(pars = parsFDR,
                        dnData = allDNData, mutData = allMutData,
                        geneName = geneName)
```

```
No parameters for case-control data;  therefore, these categories are not calculated in this step.
```

In [21]:
```
head(dataFDR)
```

Out[21]:

	Gene	dn_mis3	dn_lof	mut_mis3	mut_lof	BF	PP	qvalue
651	G651	2	2	3.01758e-06	1.078392e-06	20785.65	0.9994386	0.000561369
13294	G13294	0	3	9.19223e-06	8.024558e-06	2434.837	0.9952279	0.00266673
13582	G13582	0	2	7.85352e-07	7.324984e-07	716.2537	0.9839614	0.00712403
2815	G2815	0	2	4.94616e-06	2.519077e-06	384.3445	0.9705192	0.01271323
8387	G8387	0	2	3.92051e-06	3.447629e-06	314.9663	0.9642575	0.01731908
9500	G9500	0	2	4.89887e-06	3.585234e-06	293.1533	0.9616998	0.02081593

In [22]:
```
dim(dataFDR[dataFDR$qvalue < 0.1, ])
dim(dataFDR[dataFDR$qvalue < 0.05, ])
```

Out[22]:
1. 18
2. 8

Out[22]:
1. 11
2. 8