

9/25/03 This is the multidivtime.readme file

This file contains information about the multidivtime program and related files.

The main headings in this file are:

## **I. multicntrl.dat**

## **II. To run the multidivtime program ...**

## **III. Interpreting the results of the multidivtime program**

**(throughout this document, technical details judged to be less risky to ignore are in an *italic* font)**

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## **I. multicntrl.dat**

Most desired changes will probably involve modifying the multicntrl.dat file that is copied below.

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```
/* the following lines are all needed in multicntrl.dat ...
   do not add or delete lines but change entry on left of each
   line as you see fit ... */
example.tree
3 ... number of genes ... FOLLOWING LINES CONTAIN ONLY NAMES OF DATA
FILES
oest.Gene1
oest.Gene2
oest.Gene3
10000 ... numsamps: How many times should the Markov chain be sampled?
100 ... sampfreq: How many cycles between samples of the Markov chain?
100000 ... burnin: How many cycles before the first sample of Markov chain?
1.5 ... rttm: a priori expected number of time units between tip and root
1.5 ... rttmsd: standard deviation of prior for time between tip and root
0.07 ... rtrate: mean of prior distribution for rate at root node
0.07 ... rratesd: standard deviation of prior for rate at root node
0.4 ... brownmean: mean of prior for brownian motion constant "nu"
0.4 ... brownsd: std. deviation of prior for brownian motion constant "nu"
/* the following lines are all needed (i.e., do not delete them) but you may
   not want to alter entries unless you are familiar with the computer code */
1.0 ... minab: parameter for beta prior on proportional node depth
0.1 ... newk: parameter in Markov chain proposal step
```

```

0.5 ... othk: parameter in Markov chain proposal step
0.5 ... thek: parameter in Markov chain proposal step
100.0 ... bigtime: number higher than time units between tip and root could
           be in your wildest imagination
/* the program will expect the entry below to be the number of constraints
   and then the specified number of constraints should follow on
   subsequent lines */
3 ... number of constraints on node times
L 5 1.0
L 7 1.1
U 7 1.4
0 ... number of tips which are not collected at time 0
0 ... nodata: 1 means approximate prior, 0 means approximate posterior
0 ...commonbrown: 1 if all genes have same tendency to change rate, 0 otherwise
-----

```

The line ...

example.tree

is the line that specifies the rooted ingroup topology along with the outgroup taxa. The format of this file is explained in the estbranches.readme file.

The lines below indicate that there are 3 genes in the multigene data set and the output files from the estbranches program for the three genes are names oest.Gene1, oest.Gene2, and oest.Gene3.

```

3 ... number of genes ... FOLLOWING LINES CONTAIN ONLY NAMES OF DATA
FILES
oest.Gene1
oest.Gene2
oest.Gene3

```

Markov chain Monte Carlo (MCMC) approaches (such as the one implemented in multidivtime ) approximate distributions of interest. The quality of the approximation improves as the length of the Markov chain increases. In multidivtime, the Markov chain completes burnin + sampfreq\*(numsamps-1)+1 cycles. The first burnin cycles of the Markov chain are not used for approximating the posterior distributions of interest. No samples from the first burnin cycles are taken. Instead, the first sample is taken at cycle burnin+1. Reasonable choices for values of burnin and sampfreq depend on the data set. High values are more likely to lead to good approximations of posterior distributions than low values. On the other hand, the amount of computation time required is proportional to the number of cycles of the Markov chain.

The Achilles' heel of MCMC approaches is that they may need too much computational time to get a good posterior distribution approximation. To get a hint of whether the MCMC approach is working well, one technique is to see if separate runs of the Markov chain yield similar approximations.

rttm is the mean of the prior distribution for the time separating the ingroup root from the present. rttmsd is the standard deviation of this prior distribution. Choice of the values for rttm and rttmsd depends on what is known by the user regarding the sequences and organisms being studied.

rtrate and rratesd are respectively the mean and standard deviation of the prior distribution for the rate of molecular evolution at the ingroup root node. Choosing a reasonable value of rtrate is difficult. My usual strategy is not statistically rigorous but it seems to work reasonably well. First, I use the `estbranches` program to estimate amounts of evolution from the ingroup root to the ingroup tips. These estimated amounts of evolution from the ingroup root to the ingroup tips will differ depending on the tips. I usually pick an amount that is close to the median of the amount of evolution for the different tips. I'll refer to this amount as X. Remembering that the amount of evolution is a rate multiplied by a time, I set rtrate to X divided by rttm. For the value of rratesd, a big standard deviation (e.g., setting rratesd to equal rtrate) may be reasonable when there is little knowledge about evolutionary rates.

SLIGHTLY RELEVANT: You are free to set the time units to be what you want. Of course, you want to then adjust the units for the rates to correspond to the units for the times. For example, let's say that rtime should be about 20 million years and rtrate should be about 0.1 changes per 10 million years. You could make rtime equal to 2.0 where 1.0 time unit is 10 million years. You could then make rtrate equal to 0.1. My preference is to make the time units such that rtime is between 0.1 and 10 time units. This is the range where the MCMC proposal parameters seem to be best for achieving convergence of the Markov chain.

brownmean and brownsd set the mean and standard deviation of the prior distribution for  $\tau$  (the variance in logarithm of rate of molecular evolution for an amount of time  $\tau$  is  $\tau$  multiplied by  $t$ ). We are still working on what is a good choice for the value of brownmean. My current favorite strategy is to have  $\text{rttm} \times \text{brownmean}$  be about 1 or 2. I wish I had a more reasoned approach. My current approach for setting brownsd is to have it equal to brownmean. This generates a pretty flexible prior, I think. If brownmean is set equal to 0.0, then the program analyzes the data with a molecular clock (i.e., evolutionary rates are forced to be constant over time).

*minab sets the prior for the times of the interior nodes given the time of the root. In the section describing changes subsequent to the Thorne et al. 1998 paper, "a" is used instead of "minab". High values of minab (values greater than 1) specify a prior where*

*internal node times "repel" each other. Low values of minab (values lower than 1) cause internal node times to "attract" one another. I recommend trying a value for minab that is 1.0 or slightly greater than 1. To be honest, I have not done much exploration with values that differ from 1.0.*

*newk, thek, othk have to do with proposed states for the Metropolis-Hastings algorithm. It's probably a good idea not to change them unless you look at the multidivtime.c code.*

bigtime is a number that is absolutely positively way bigger than the age of any node in the data set

The number of node of constraints on node ages needs to be specified. In the example, there are three constraints. They are specified with the following three lines ...

```
L 5 1.0  
L 7 1.1  
U 7 1.4
```

The "L" of the first of the three lines indicates that the Lower bound for the age of node 5 is 1.0 time units.

The "L" of the second of the three lines indicates that the Lower bound for the age of node 7 is 1.1 time units.

The "U" of the third line indicates that the Upper bound for the age of node 7 is 1.4 units.

The 3 lines below are not in the multicntrl.dat file ...

```
2 ... number of tips which are not collected at time 0  
T 0 0.2  
T 3 0.3
```

... If these 3 lines replaced the line ...

0 ... number of tips which are not collected at time 0

... then they would indicate that 2 tips (Tip 0 and Tip 3) are isolated at time 0.2 and 0.3 respectively. By default, all other tips are assumed to be isolated at time 0.0, where time 0.0 is represents the time of the most recently isolated sequences.

0 ... nodata: 1 means approximate prior, 0 means approximate posterior

The above line should be 1 to approximate the prior and it should be 0 to approximate the posterior.

0 ...commonbrown: 1 if all genes have same tendency to change rate, 0 otherwise

The commonbrown value determines whether a multigene analysis will force all genes to have identical expected rate variation over time (commonbrown = 1) or whether genes are allowed to vary in how far from a clock they are (commonbrown = 0). I usually analyze data sets by trying both options. commonbrown = 0 is the more biologically attractive but commonbrown = 1 seems to be more robust to poorly specified prior distributions for the autocorrelation parameter (i.e. poor specification of brownmean and brownsd).

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## **II. To run the multidivtime program**

You should type something like:

```
multidivtime example > & out.example &
```

The ">& out.example &" part of the above command specifies that multidivtime will run in the background and will send its output to a file named out.example. Alternatively, the ">& out.example &" part can be eliminated and the results will be sent to the screen instead.

The "example" part of the above command specifies that output file names produced by the multidivtime program will have the suffix "example"

tree.example will be a file that has estimates of branch times

node.example is a file that contains detailed information about the Markov chain run.

samp.example contains samples from the Markov chain in a formatted file. The "samp" files can become quite large. They are useful for exploring convergence and for importing into visualization packages such as R or Splup, but otherwise you may want to delete the "samp" files.

ratio.example contains relative probability ratios for the parameter values sampled by the MCMC program. You may want to delete this ratio.example file after a run.

When the multidivtime program is invoked with the specific suffix "numbers", the program is written to abort soon after printing out the node numbers assigned by the multidivtime program. This node number information can then be used to specify which

node numbers are being constrained in the multicntrl.dat file. Once the constraints are set, multidivtime can then be run with some suffix other than "numbers" to do the desired analysis.

### III. Interpreting the results of the multidivtime program

The file out.example was produced by typing:

```
multidivtime example > out.example &
```

The out.example file and comments are included below.

```
-----  
out.example - lines with comments begin with #  
-----  
  
Suffix for output files from this run is example  
#data pertaining to the MCMC run will be put in various files  
#with a suffix that is "example"  
Random number seed from file inseed is 483439889  
#the program reads the initial seed for the random number generator  
#from a file named "inseed"  
Taxon named Outgroup is part of the outgroup  
# above line or lines list outgroup taxa - this is one check of whether  
# program is reading tree in the fashion that you intend  
Root node number of master tree is 8  
Here are node numbers of other internal nodes on master tree:  
#the assignment of numbers to nodes can be found below  
(Taxon_A:0,((Taxon_B:1,Taxon_C:2):6,(Taxon_D:3,Taxon_E:4):5):7);  
Number of genes= 3  
Name of gene 0 is oest.Gene1  
Name of gene 1 is oest.Gene2  
Name of gene 2 is oest.Gene3  
Master Sequence 1 (Taxon_B) is absent in gene data set 0  
#above line indicates that Taxon_B was not found in the data  
# set for oest.Gene1. As mentioned above, taxa can be missing  
# for some genes.  
Approximate the posterior version  
# above indicates that it is posterior and not prior being approximated  
Genes differ in tendencies to change rates over time  
# above means that "commonbrown" option in multicntrl.dat  
# was set to 0  
sampfreq 100 numamps 10000 burnin 100000
```

```

newk 0.100 othk 0.500 thek 0.500
brownmean 0.400 brownsd 0.400
browngamr 1.000 browngamlam 2.500
rttm 1.500 rttmsd 1.500 minab 1.000
timegamr 1.000 timegamlam 0.667
rtrate 0.0700 rratesd 0.0700
rategamr 1.000 rategamlam 14.286
nbranches= 8 nnodes= 9
ntips = 5 nintnodes = 3
bigtime = 100.000
# for multigene data sets, we may be interested in whether a pair
# of genes is changing rate in a correlated fashion. To investigate
# this question, we must approximate the distribution of our
# test statistic under the null hypothesis that genes change rate in an
# uncorrelated fashion. The Thorne and Kishino (2002, Sys Biol, 51:689-702)
# paper describes the details of this hypothesis test. The line below
# indicates that 1000 values will be generated to approximate the distribution
# of our test statistic under the null hypothesis
starting at semi-random guess
# message above means that initial state of Markov chain is randomly selected
# Below is a list of information about each node in the tree, where
# the first number in a line is the number of the node to which the
# rest of the line refers.
# "t=" tells the time of a node for the initial state
# of the Markov chain. "hight=" tells the highest (oldest)
# allowed time for the node. "lowt=" tells the lowest (youngest)
# possible time for a node. "rt=" tells the rate at the node for
# the initial state in the Markov chain
# "pnode=" is the node number of the parent node.
0:t= 0.0000 hight= 0.0000 lowt= 0.0000 rt= 1.5463 pnode= 8
1:t= 0.0000 hight= 0.0000 lowt= 0.0000 rt= 1.0094 pnode= 6
2:t= 0.0000 hight= 0.0000 lowt= 0.0000 rt= 1.7320 pnode= 6
3:t= 0.0000 hight= 0.0000 lowt= 0.0000 rt= 1.4069 pnode= 5
4:t= 0.0000 hight= 0.0000 lowt= 0.0000 rt= 1.9141 pnode= 5
5:t= 1.2319 hight= 1.4000 lowt= 1.0000 rt= 1.7273 pnode= 7
6:t= 1.2373 hight= 1.4000 lowt= 0.0000 rt= 1.6789 pnode= 7
7:t= 1.2373 hight= 1.4000 lowt= 1.1000 rt= 1.2945 pnode= 8
8:t= 1.2375 hight= 100.0000 lowt= 1.1000 rt= 1.5463 pnode= -1
Each gene initialized to have same rate at node 0!
# Below would be different if specifications of different sampling times
# for different tips had been made in the multicntrl.dat file
All sequences (tips) isolated at same time
POSTERIOR INTERVAL from probability 0.02500 to 0.97500
(i.e. 250 -th lowest value to 9750 -th lowest value)

```

```

# Above means that 95% "credibility" intervals will be estimated by
# sorting samples (in this case 10000 samples) from the Markov chain and
# and then reporting the 250th and 9750 lowest sampled values
# for each parameter (parameters include rates at nodes, times of nodes, etc.
#
#the Markov chain Monte Carlo routine goes through many cycles
#Each cycle consists of steps where a change to a rate on a branch or a
#time of a node is proposed. On the next many lines, the number of times
# that the proposed changes succeeded ("nsuc") or failed ("nfail")
# along with the proportion of successes ("psuc") are listed. If any
# of the "psuc" values is extremely low (e.g. less than 0.01), this may
# indicate that the Markov chain is getting "stuck" and the procedure
# is not working. Some proposal types may not be used for certain
# kinds of analyses (e.g., when a molecular clock is assumed)
Consflate: nsuc= 958917 nfail= 140984 psuc= 0.87182
Bothflate: nsuc= 959171 nfail= 140730 psuc= 0.87205
Rateflate[0]: nsuc= 499647 nfail= 600254 psuc= 0.45427
Partrateflate[0]: nsuc= 641077 nfail= 458824 psuc= 0.58285
Rateflate[1]: nsuc= 244440 nfail= 855461 psuc= 0.22224
Partrateflate[1]: nsuc= 360753 nfail= 739148 psuc= 0.32799
Rateflate[2]: nsuc= 212785 nfail= 887116 psuc= 0.19346
Partrateflate[2]: nsuc= 319409 nfail= 780492 psuc= 0.29040
Timeflate: nsuc= 332123 nfail= 767778 psuc= 0.30196
Partconsflate: nsuc= 400854 nfail= 699047 psuc= 0.36445
Partbothflate: nsuc= 400653 nfail= 699248 psuc= 0.36426
Parttimeflate: nsuc= 331580 nfail= 768321 psuc= 0.30146
RATE[gene 0][node 0] nsuc= 833230 nfail= 266671 psuc= 0.75755
RATE[gene 1][node 0] nsuc= 592464 nfail= 507437 psuc= 0.53865
RATE[gene 2][node 0] nsuc= 503714 nfail= 596187 psuc= 0.45796
RATE[gene 0][node 1] nsuc= 1043126 nfail= 56775 psuc= 0.94838
RATE[gene 1][node 1] nsuc= 856718 nfail= 243183 psuc= 0.77890
RATE[gene 2][node 1] nsuc= 748804 nfail= 351097 psuc= 0.68079
RATE[gene 0][node 2] nsuc= 962157 nfail= 137744 psuc= 0.87477
RATE[gene 1][node 2] nsuc= 501519 nfail= 598382 psuc= 0.45597
RATE[gene 2][node 2] nsuc= 818778 nfail= 281123 psuc= 0.74441
RATE[gene 0][node 3] nsuc= 673761 nfail= 426140 psuc= 0.61257
RATE[gene 1][node 3] nsuc= 960552 nfail= 139349 psuc= 0.87331
RATE[gene 2][node 3] nsuc= 844182 nfail= 255719 psuc= 0.76751
RATE[gene 0][node 4] nsuc= 1007753 nfail= 92148 psuc= 0.91622
RATE[gene 1][node 4] nsuc= 777647 nfail= 322254 psuc= 0.70702
RATE[gene 2][node 4] nsuc= 845317 nfail= 254584 psuc= 0.76854
RATE[gene 0][node 5] nsuc= 847673 nfail= 252228 psuc= 0.77068
RATE[gene 1][node 5] nsuc= 661745 nfail= 438156 psuc= 0.60164
RATE[gene 2][node 5] nsuc= 523177 nfail= 576724 psuc= 0.47566

```



```

RATE[gene 0][node 6] nsuc= 898194 nfail= 201707 psuc= 0.81661
RATE[gene 1][node 6] nsuc= 670682 nfail= 429219 psuc= 0.60977
RATE[gene 2][node 6] nsuc= 534318 nfail= 565583 psuc= 0.48579
RATE[gene 0][node 7] nsuc= 855459 nfail= 244442 psuc= 0.77776
RATE[gene 1][node 7] nsuc= 770996 nfail= 328905 psuc= 0.70097
RATE[gene 2][node 7] nsuc= 671276 nfail= 428625 psuc= 0.61031
ROOT rate constrained to equal rate of node 0
RATE CHANGE[gene 0][node 9] nsuc= 940062 nfail= 159839 psuc= 0.85468
RATE CHANGE[gene 1][node 9] nsuc= 948955 nfail= 150946 psuc= 0.86276
RATE CHANGE[gene 2][node 9] nsuc= 977332 nfail= 122569 psuc= 0.88856
TIME 5: nsuc= 467680 nfail= 632221 psuc= 0.42520
TIME 6: nsuc= 243451 nfail= 856450 psuc= 0.22134
TIME 7: nsuc= 463143 nfail= 636758 psuc= 0.42108
TIME 8: nsuc= 545683 nfail= 554218 psuc= 0.49612
#In the samples of the Markov chain, the proportion of time
# for the sample from an internal node to a tip relative
# to the time from the ingroup root to a tip
# can be calculated. The following lines list these proportions
# and their sample standard deviations. The estimated 95% credibility
# interval are the final two numbers
# on each line (for nodes 0-4, the 95% interval goes from 0.0000 to 0.0000
# because times of the tip nodes are forced to be 0.0000 here
Prop. Node 0 to Root= 0.00000 (S.D. = 0.00000) ( 0.00000, 0.00000)
Prop. Node 1 to Root= 0.00000 (S.D. = 0.00000) ( 0.00000, 0.00000)
Prop. Node 2 to Root= 0.00000 (S.D. = 0.00000) ( 0.00000, 0.00000)
Prop. Node 3 to Root= 0.00000 (S.D. = 0.00000) ( 0.00000, 0.00000)
Prop. Node 4 to Root= 0.00000 (S.D. = 0.00000) ( 0.00000, 0.00000)
Prop. Node 5 to Root= 0.58085 (S.D. = 0.04025) ( 0.50231, 0.66080)
Prop. Node 6 to Root= 0.52830 (S.D. = 0.04773) ( 0.43536, 0.62378)
Prop. Node 7 to Root= 0.66188 (S.D. = 0.03705) ( 0.58843, 0.73360)
#the following line lists the approximate posterior mean and standard
# deviation of the time from ingroup root to tip and the 95% interval
Root Depth = 1.94240 (S.D. = 0.15916) ( 1.64508, 2.26649)
# Below begins a list of estimated rates for each node with each gene
# When viewing the rate estimates, remember that the rates at the beginning
# node and ending node of one branch are forced to be identical. In this
# case, Nodes 0 and 8 are forced to have identical rates.
Rate[Gene 0,Node 0]= 0.01023 (S.D. = 0.00236) ( 0.00590, 0.01509)
Rate[Gene 0,Node 1]= 0.02937 (S.D. = 0.05172) ( 0.00160, 0.12983)
Rate[Gene 0,Node 2]= 0.03114 (S.D. = 0.01607) ( 0.00467, 0.06532)
Rate[Gene 0,Node 3]= 0.19406 (S.D. = 0.02638) ( 0.14560, 0.24783)
Rate[Gene 0,Node 4]= 0.00891 (S.D. = 0.00561) ( 0.00107, 0.02217)
Rate[Gene 0,Node 5]= 0.02502 (S.D. = 0.00644) ( 0.01339, 0.03874)
Rate[Gene 0,Node 6]= 0.02913 (S.D. = 0.01100) ( 0.01112, 0.05375)

```

Rate[Gene 0,Node 7]= 0.02179 (S.D. = 0.00609) ( 0.01142, 0.03527)  
 Rate[Gene 0,Node 8]= 0.01023 (S.D. = 0.00236) ( 0.00590, 0.01509)  
 # Below lists the estimated autocorrelation parameter for Gene 0  
 Rate Change[Gene 0] = 1.02292 (S.D. = 0.43777) ( 0.41561, 2.11239)  
 Rate[Gene 1,Node 0]= 0.06879 (S.D. = 0.00910) ( 0.05229, 0.08797)  
 Rate[Gene 1,Node 1]= 0.15809 (S.D. = 0.06869) ( 0.03440, 0.29668)  
 Rate[Gene 1,Node 2]= 1.13127 (S.D. = 0.14473) ( 0.87039, 1.43902)  
 Rate[Gene 1,Node 3]= 0.04057 (S.D. = 0.02169) ( 0.00701, 0.08984)  
 Rate[Gene 1,Node 4]= 0.15981 (S.D. = 0.03668) ( 0.08913, 0.23336)  
 Rate[Gene 1,Node 5]= 0.11750 (S.D. = 0.02281) ( 0.07419, 0.16373)  
 Rate[Gene 1,Node 6]= 0.21882 (S.D. = 0.05349) ( 0.11754, 0.32867)  
 Rate[Gene 1,Node 7]= 0.13545 (S.D. = 0.03052) ( 0.08326, 0.20260)  
 Rate[Gene 1,Node 8]= 0.06879 (S.D. = 0.00910) ( 0.05229, 0.08797)  
 Rate Change[Gene 1] = 0.86538 (S.D. = 0.37191) ( 0.35746, 1.76167)  
 Rate[Gene 2,Node 0]= 0.16235 (S.D. = 0.01899) ( 0.12768, 0.20208)  
 Rate[Gene 2,Node 1]= 0.39883 (S.D. = 0.10956) ( 0.17123, 0.60456)  
 Rate[Gene 2,Node 2]= 0.26669 (S.D. = 0.09686) ( 0.06774, 0.45288)  
 Rate[Gene 2,Node 3]= 0.17129 (S.D. = 0.05939) ( 0.05333, 0.28645)  
 Rate[Gene 2,Node 4]= 0.17053 (S.D. = 0.05875) ( 0.05150, 0.28343)  
 Rate[Gene 2,Node 5]= 0.28201 (S.D. = 0.04893) ( 0.19642, 0.38968)  
 Rate[Gene 2,Node 6]= 0.40017 (S.D. = 0.07846) ( 0.26999, 0.57788)  
 Rate[Gene 2,Node 7]= 0.33019 (S.D. = 0.06972) ( 0.22248, 0.49191)  
 Rate[Gene 2,Node 8]= 0.16235 (S.D. = 0.01899) ( 0.12768, 0.20208)  
 Rate Change[Gene 2] = 0.46463 (S.D. = 0.34254) ( 0.09266, 1.38325)  
  
 br 0 samp mean= 0.01971 ( 0.00406) est. = 0.01875 ( 0.01189, 0.02769)  
 br 1 samp mean= 0.02980 ( 0.02889) est. = 0.04053 ( 0.00844, 0.08567)  
 br 2 samp mean= 0.03067 ( 0.00651) est. = 0.12787 ( 0.01834, 0.04362)  
 br 3 samp mean= 0.12264 ( 0.01272) est. = 0.01640 ( 0.09795, 0.14803)  
 br 4 samp mean= 0.01900 ( 0.00386) est. = 0.00837 ( 0.01163, 0.02674)  
 br 5 samp mean= 0.00367 ( 0.00126) est. = 0.00814 ( 0.00153, 0.00646)  
 #the next lines list the mean and standard deviation of  
 #the estimated posterior distribution of times for particular nodes  
 # and the 95% interval is also listed  
 Actual time node 0 = 0.00000 (S.D. = 0.00000) ( 0.00000, 0.00000)  
 Actual time node 1 = 0.00000 (S.D. = 0.00000) ( 0.00000, 0.00000)  
 Actual time node 2 = 0.00000 (S.D. = 0.00000) ( 0.00000, 0.00000)  
 Actual time node 3 = 0.00000 (S.D. = 0.00000) ( 0.00000, 0.00000)  
 Actual time node 4 = 0.00000 (S.D. = 0.00000) ( 0.00000, 0.00000)  
 Actual time node 5 = 1.12399 (S.D. = 0.07099) ( 1.00693, 1.26010)  
 Actual time node 6 = 1.02197 (S.D. = 0.08360) ( 0.86141, 1.18014)  
 Actual time node 7 = 1.28155 (S.D. = 0.07545) ( 1.13225, 1.39491)  
 Actual time node 8 = 1.94240 (S.D. = 0.15916) ( 1.64508, 2.26649)

#the last part of the output lists the rank correlation coefficient  
# for each pair of genes and then the approximate P-value for  
#evaluating the null hypothesis that the pair of genes change rate  
#independently

For rank corr. between genes 0 and 1, the observed  
value is 0.0238095 and this is equalled or exceeded 0.559 of  
the time when these 2 genes evolve independently

For rank corr. between genes 0 and 2, the observed  
value is 0.3333333 and this is equalled or exceeded 0.370 of  
the time when these 2 genes evolve independently

For rank corr. between genes 1 and 2, the observed  
value is 0.4047619 and this is equalled or exceeded 0.261 of  
the time when these 2 genes evolve independently

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(this is the end of multidivtime.readme file)