Power Analyses for SEQLinkage

Wed Apr 2 10:45:41 CDT 2014 | Let's rock and roll!

Basics

We simulate and analyze two autosomal recessive genes GJB2 and SLC26A4 and two autosomal dominant genes MYO7A and MYH9. The program takes two genes source data as input.

As we call `seqlink` from inside of the program multiple times we'd like to speed up the execution by using ramdisk of 8000MB.

```
sudo mkdir -p /ramcache
sudo mount -t tmpfs ramfs -o size=8000m /ramcache
cd /ramcache
ln -s ~/SVN/SEQLinco/simulations/LinkagePowerCalc.py pcal.py
```

Hierarchy of simulation parameters

I want to draw one figure with 4 panels. Each panel is one mode of inheritance, namely A&B are recessive and compound recessive using recessive genes; C&D are dominant and compound dominant using recessive genes. On each panel, the X-axis is sample size and Y-axis is allelic heterogeneity. Powers are contour plots of two colors, one color for new method, one for old method. The only parameter not scanned here is `--offsprings`. For now I set it in between 3 to 8. It can be varied for additional simulations in supplemental. In this figure only one of the gene pair will be reported and the complementary figure can be found in supplemental.

Linkage analysis parameters are always `-K 0.01 -W 0 -M 1`. See `seqlink -h` for details.

Example command

```
python pcal.py -g MYH9.tsv MYO7A.tsv -m dominant -r 10 --sample-size 20 \
--blueprint blueprint.txt --vanilla --tempdir /ramcache \
--run-linkage -K 0.01 --moi AD -W 0 -M 1 --output-entries 0
```

Power calculation script

Script generator:

PYTHON

```
name = 'pcal.sh'
rep = 100
batch = 50
count = 0
gdict = {'recessive': 'SLC26A4.tsv GJB2.tsv', 'compound_recessive':'SLC26A4.tsv GJB2.tsv', 'dominant':'MYO7A.tsv MYH9.tsv', 'compoun
d_dominant':'MYO7A.tsv MYH9.tsv'}
mdict = {'recessive':'AR', 'compound_recessive':'AR', 'dominant':'AD', 'compound_dominant':'AD'}
fdict = {' ': 'CHPResult.csv', '--single-markers': 'SNVResult.csv'}
with open(name, 'w') as f:
```

```
    for m in ['recessive', 'dominant', 'compound_recessive', 'compound_dominant']:
        for a in range(0, 110, 10):
            a = a * 0.01
            for s in range(5, 60, 5):
                for method in [' ', '--single-markers']:
                    count += 1
                    f.write("./pcal.py --debug -n 3 8 -g {0} -m {1} -s {2} -a {3} {4} -r {5} --ofile {9} " \
                          "--blueprint blueprint.txt --vanilla {6} --jobs 1 --run-linkage -K 0.01 " \
                          "-W 0 -M 1 --moi {7} --output-entries 0 --tempdir /ramcache/tmp >> {8}.{9}\n".\
                          format(gdict[m], m, s, a, 1-a, rep, method, mdict[m], fdict[method], "RUN%s" % count))
                    if count % batch == 0:
                       f.write("echo {}\n".format(count))
```

Use command below to run the generated script:

```
cat pcal.sh | gw-parallel -j7
```

Power calculation result

Consolidate all result data into database `PowerCalc`

```
cat CHPResult.csv.* > CHPResult.csv
cat SNVResult.csv.* > SNVResult.csv
./pcal.py --print-header | wsqlite PowerCalc -i CHPResult.csv --as CHP --header - -d","
./pcal.py --print-header | wsqlite PowerCalc -i SNVResult.csv --as SNV --header - -d","
```

To view attributes of the database

```
wsqlite PowerCalc -s
wsqlite PowerCalc -s CHP
wsqlite PowerCalc -s SNV
```

All output data and results are backed up to `0402.tar.gz` for future reference. Now let's have a rough feeling on power comparison between the methods

BASH

```
for i in recessive dominant compound_recessive compound_dominant; do
    for j in 1 2; do
        echo $i Gene$j
        echo CHP=`wsqlite PowerCalc "select avg(plod$j) from CHP where moi = '$i'"` \
        SNV=`wsqlite PowerCalc "select avg(plod$j) from SNV where moi = '$i'"`
    done
done
```

OUTPUT

```
recessive Gene1
CHP=0.727776074443 SNV=0.746848342238
recessive Gene2
CHP=0.729023265841 SNV=0.731563345514
dominant Gene1
CHP=0.528512396694 SNV=0.656528925619
dominant Gene2
CHP=0.619426496368 SNV=0.712562818265
compound_recessive Gene1
CHP=0.731162035468 SNV=0.438850488354
compound_recessive Gene2
CHP=0.727493032963 SNV=0.519363628251
compound_dominant Gene1
```

```
CHP=0.527520661156 SNV=0.521157024793
compound_dominant Gene2
CHP=0.617768595041 SNV=0.621983471074
```

Although many power values are still low at sample size 55 (meaning I need to increase sample size) and are based on small replicates (I'll increase replicates) we do observe what we expect: no power difference for recessive, slight power loss for dominant (since creating many patterns instead of using one alternative original SNV introduces noise and lowers LOD score as observed by Di), and significant power gain for compound recessive. We observed no power gain for so-called compound dominant which is counter intuitive but after more careful thinking with LOD calculations under such scenario we see this is expected: in such cases phenotype information would play a role. See variant 5 and variant 6 of the Version 0 of Supplemental figure S1.

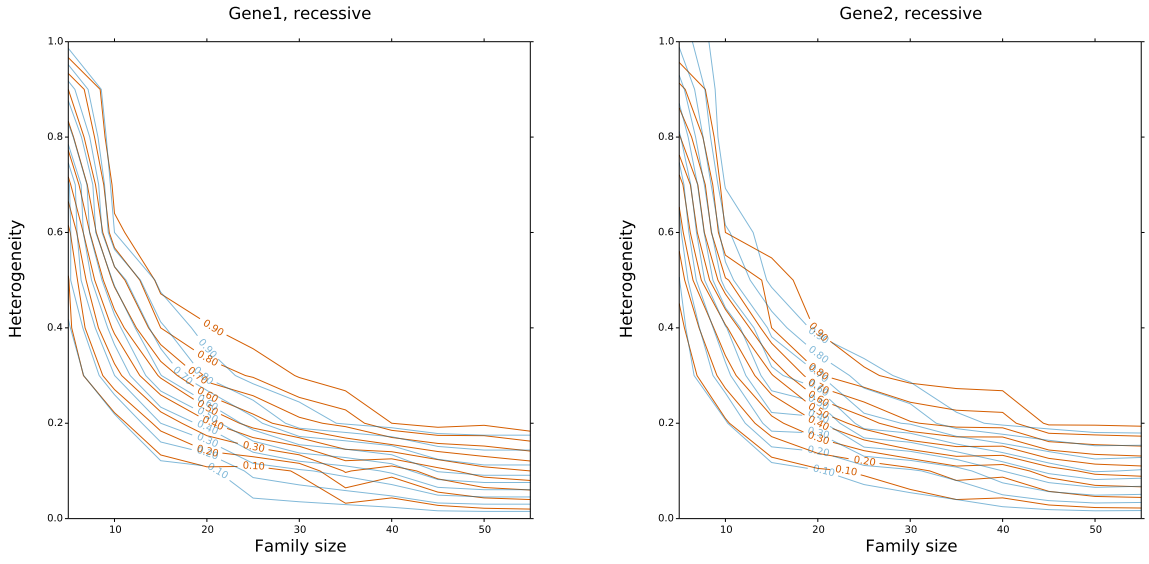
After discussion with Di we decide to add another moi, the *dominant epistatic*. But before that I need to create plots in order to decide how to adjust sample size parameters.

Thu Apr 3 14:51:32 CDT 2014 | A sleepy afternoon with voltaren all over my hands ...

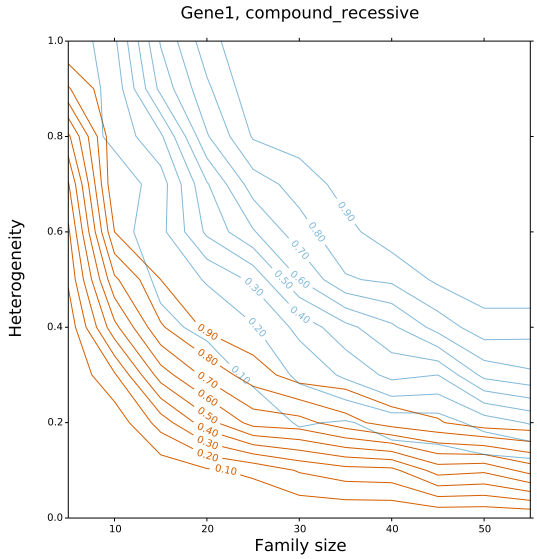
Power plot

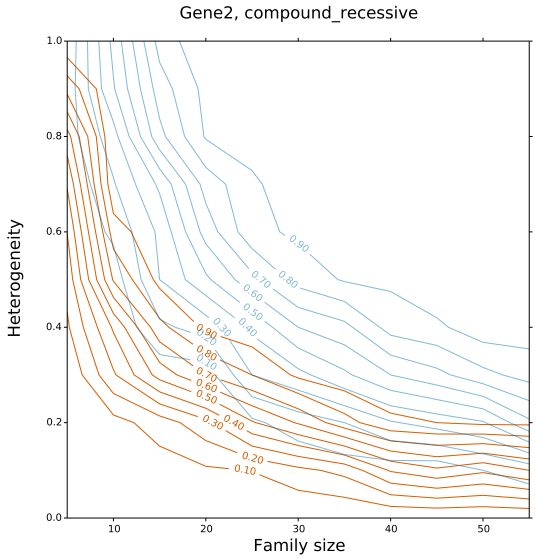
Script see `PowerContour.py` under this folder. Resulting graph below:

R

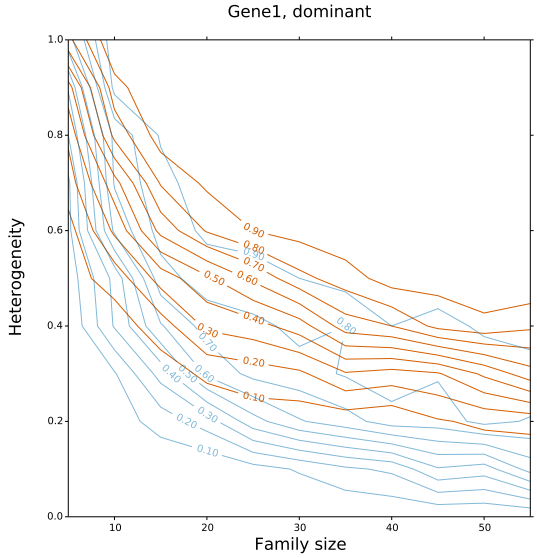


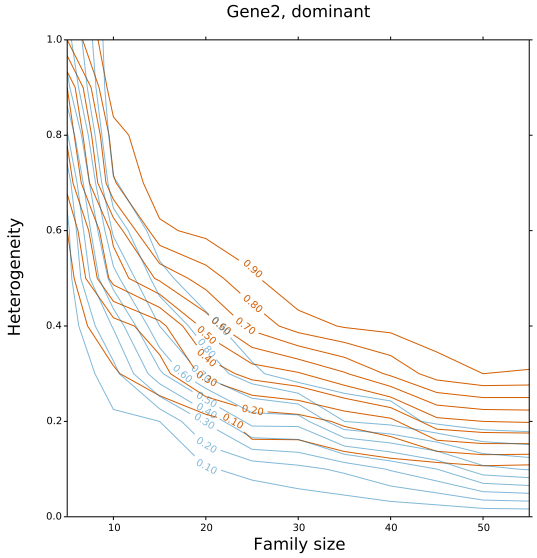
CR


Gene1, compound_recessive
Heterogeneity
Family size

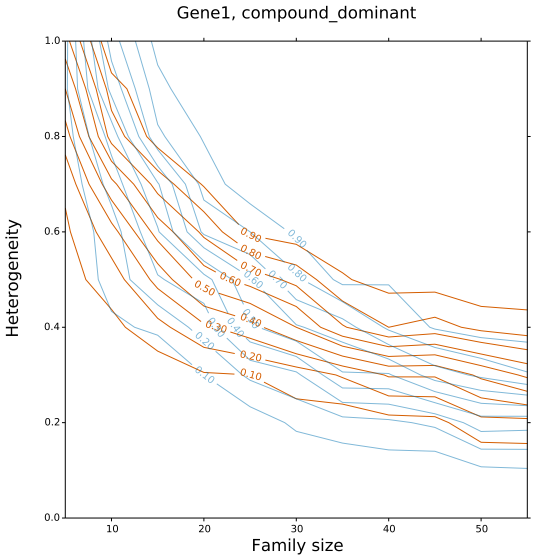

Gene2, compound_recessive
Heterogeneity
Family size

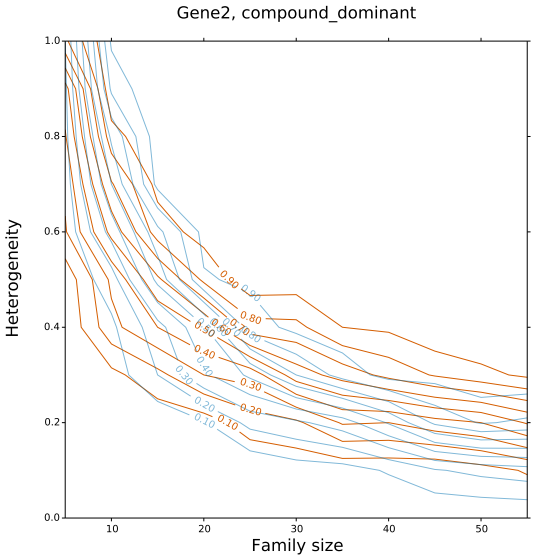
D


Gene1, dominant
Heterogeneity
Family size


Gene2, dominant
Heterogeneity
Family size

CD


Gene1, compound_dominant
Heterogeneity
Family size
1.0
0.8
0.6
0.4
0.2
0.0
10
20
30
40
50
0.90
0.80
0.70
0.60
0.50
0.40
0.30
0.20
0.10


Gene2, compound_dominant
Heterogeneity
Family size
1.0
0.8
0.6
0.4
0.2
0.0
10
20
30
40
50
0.90
0.80
0.70
0.60
0.50
0.40
0.30
0.20
0.10