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 -n 20 \
--blueprint blueprint.txt --tempdir /ramcache \
--run-linkage -K 0.01 --moi AD -W 0 -M 1 --output-entries 0
```

Power calculation script

Script generator:

PYTHON

```python
name = 'pcal.sh'
rep = 500
batch = 50
count = 0
gdict = {'recessive': 'SLC26A4.tsv GJB2.tsv', 'compound_recessive':'SLC26A4.tsv GJB2.tsv',
         'dominant':'MYO7A.tsv MYH9.tsv'}
mdict = {'recessive':'AR', 'compound_recessive':'AR', 'dominant':'AD'}
fdict = {' ': 'CHPResult.csv', '--single-markers': 'SNVResult.csv'}
folder = ''
```

```
with open(name, 'w') as f:
    for m in ['recessive', 'dominant', 'compound_recessive']:
        for a in [' ', '-a']:
            for p in [i * 0.01 for i in range(0, 110, 10)]:
                for n in range(5, 81, 1):
                    for method in [' ', '--single-markers']:
                        if count % batch == 0:
                            folder = 'B' + str(count / batch + 1)
                            mkdir = 'mkdir -p {};'.format(folder)
                        else:
                            mkdir = ''
                        count += 1
                        f.write("{12}./pcal.py --debug -s 3 8 -g {0} -m {1} -n {2} -p {3} {4} -r {5} "\
                                "--ofile {9} {10} --blueprint blueprint.txt {6} --jobs 1 "\
                                "--run-linkage -K 0.01 -W 0 -M 1 --moi {7} --output-entries 0 "\
                                "> {11}/{8}.{9}\n".\
                                format(gdict[m], m, n, p, 1-p, rep, method, mdict[m],
                                       fdict[method], "RUN%s" % count, a, folder, mkdir))
```

Use command below to run the generated script on desktop:

```
cat pcal.sh | gw-parallel -j 7
```

Or on cluster:

pbs

```
#PBS -o info/log
#PBS -e info/err
#PBS -N SLSimulation
#PBS -t 5-81%50
cd $PBS_O_WORKDIR
mkdir -p info
rm -rf info/*
rep=500
MOI=( 'recessive' 'dominant' 'compound_recessive' ) #MOI in simulation
Mmap=( 'AR' 'AD' 'AR' ) #MOI in mlink
Gmap=( 'SLC26A4.tsv GJB2.tsv' 'MYO7A.tsv MYH9.tsv' 'SLC26A4.tsv GJB2.tsv' ) #gene pairs
Mtype=( ' ' '--single-marker' )
Fmap=( 'CHPResult.csv' 'SNVResult.csv' ) #result
N=$PBS_ARRAYID #family number
count=0
for m in $(seq 0 2)
do
        for a in ' ' '-a'
        do
                for pN in $(seq 0 10 100)
                do
                        p=$(bc <<< "${pN}/100")
                        q=$(bc <<< "1 - ${p}")
                        for t in 0 1
                        do
                                mkdir -p FAM$N
                                ./LinkagePowerCalc.py --debug -s 3 8 -g ${Gmap[$m]} \
                                -m ${MOI[$m]} -n $N -p $p $q -r $rep \
                                      --ofile FAM${N}RUN$count $a --blueprint blueprint.txt \
                                ${Mtype[$t]} --jobs 1 --run-linkage -K 0.01 -W 0 -M 1 \
                                --tempdir /mnt/ram --moi ${Mmap[$m]} --output-entries 0 \
                                > FAM${N}/${Fmap[$t]}.RUN${N}.$count
                                count=$(bc <<< "$count + 1")
                        done
                done
        done
done
```

makefile

```
run:
        qsub SubmitJobs.pbs
clean:
        rm -rf RUN* FAM* info/* B* cache/
test:
        PBS_O_WORKDIR=. PBS_ARRAYID=6 bash SubmitJobs.pbs
.PHONY: run clean test
```

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 `040*.tar.gz` for future reference. Now let's have a rough feeling on power comparison between the methods

BASH

```
for k in 0 1; do
    for i in recessive dominant compound_recessive; do
        for j in 1 2; do
            echo $i Gene$j, allelic heterogeneity $k
            echo CHP=`wsqlite PowerCalc "select avg(plod$j) from CHP where moi = '$i' and ahet = $k"` \
            SNV=`wsqlite PowerCalc "select avg(plod$j) from SNV where moi = '$i' and ahet = $k"`
        done
    done
done
```

Results below are based on data from `0403.tar.gz`:

OUTPUT

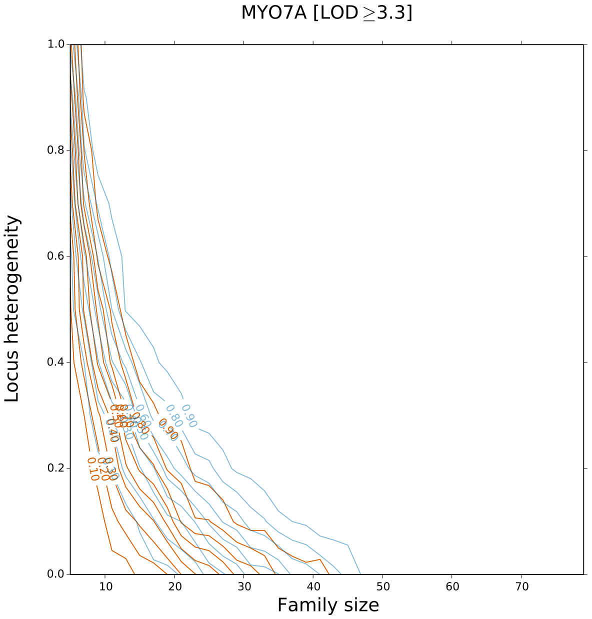
Thu Apr 3 14:51:32 CDT 2014 | A sleepy afternoon with voltaren all over my hands ...

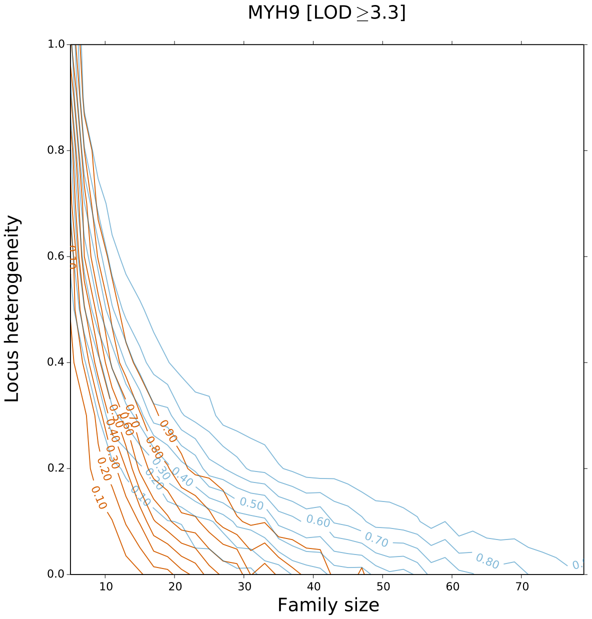
Power plot

Script see `PowerContour.py` under this folder. Graphs below are based on data from `0403.tar.gz`:

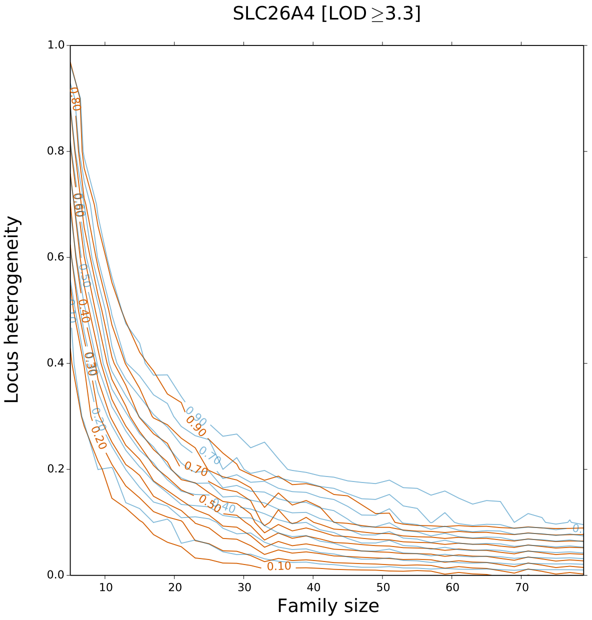
Without allelic heterogeneity

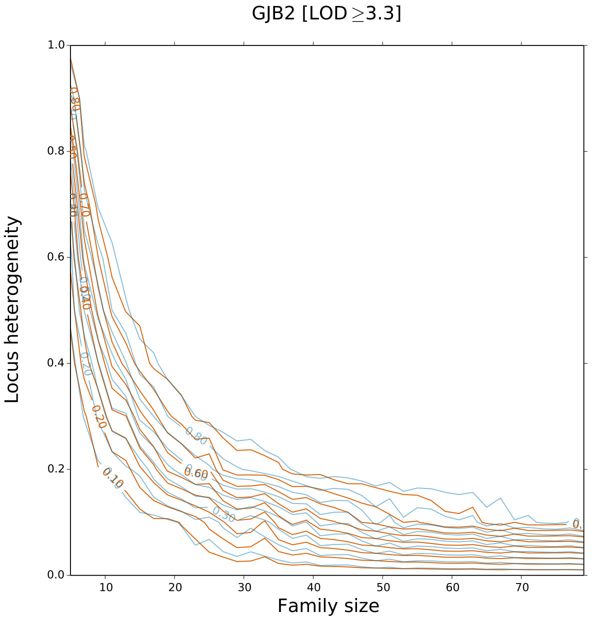
Dominant



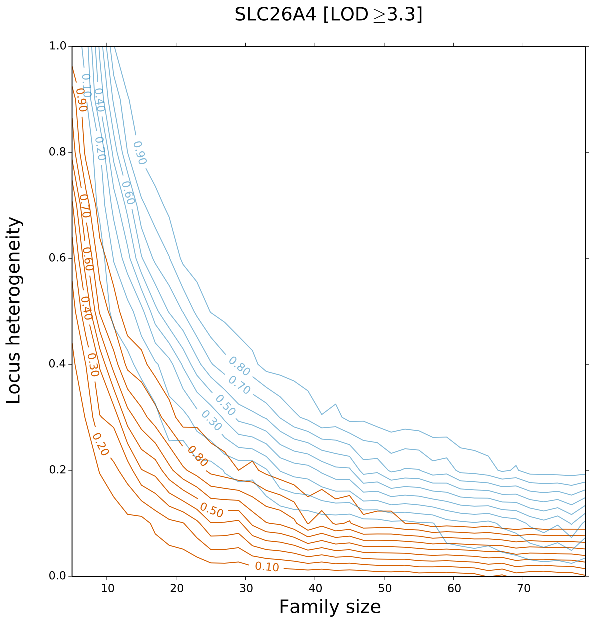


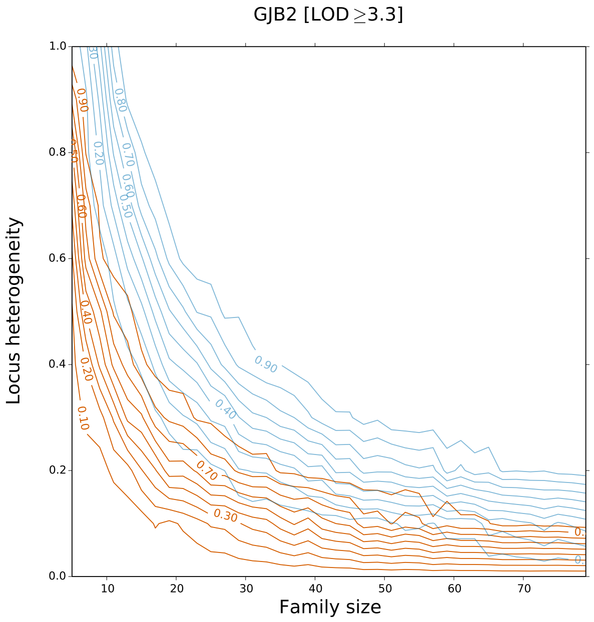
Recessive





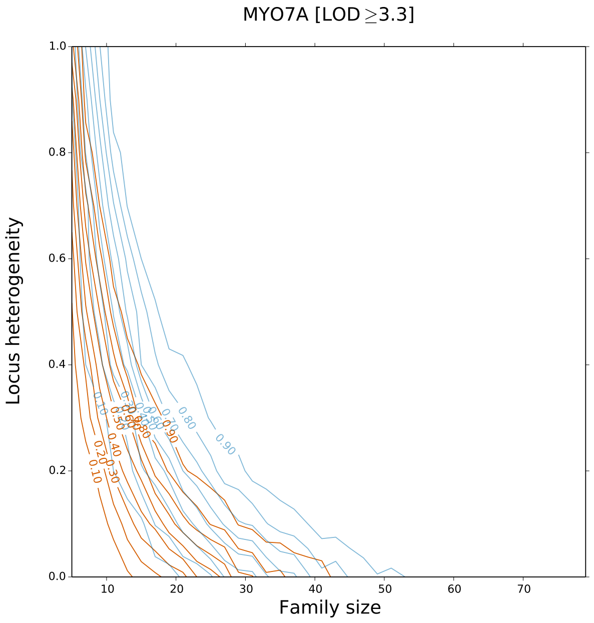
Compound recessive

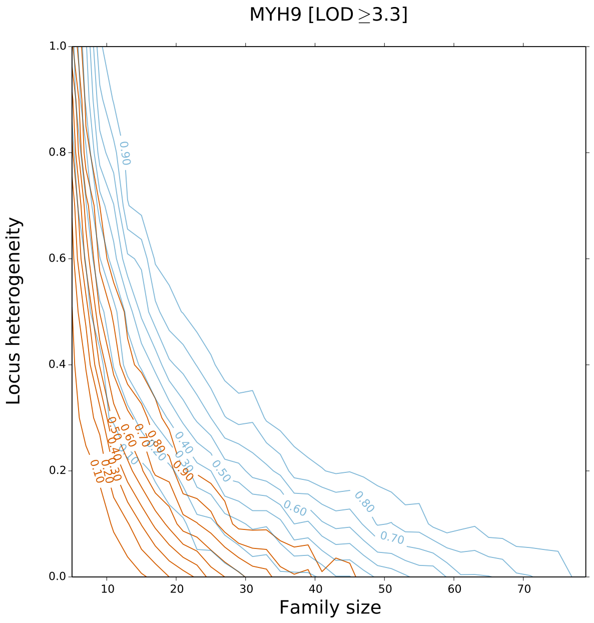




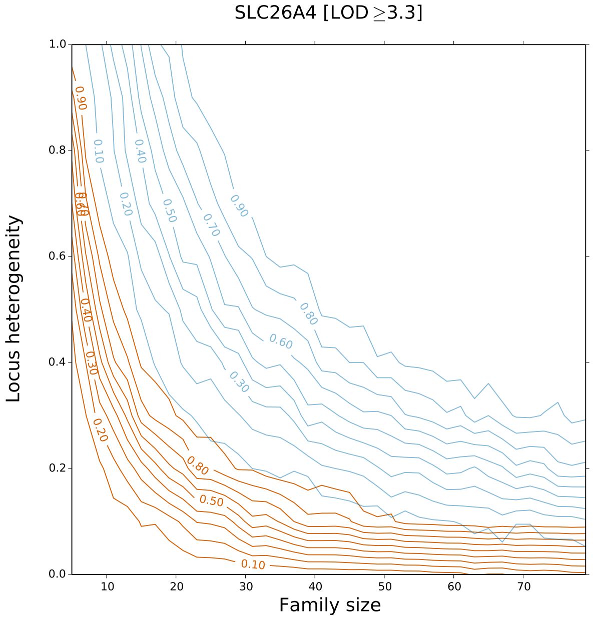
With allelic heterogeneity

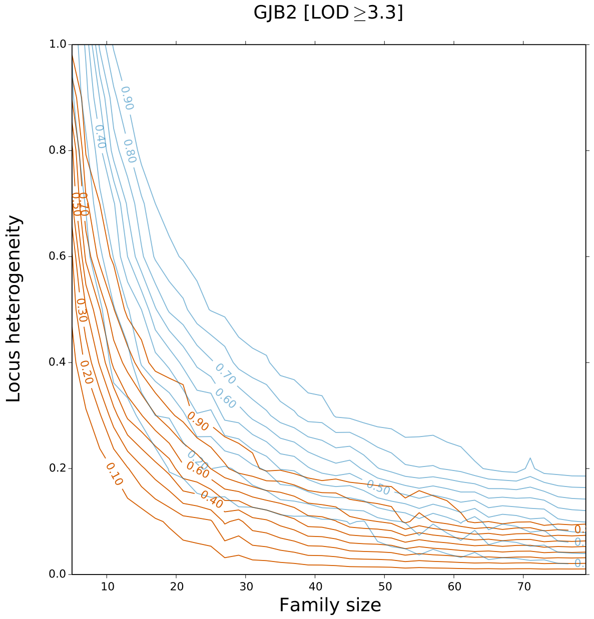
Dominant



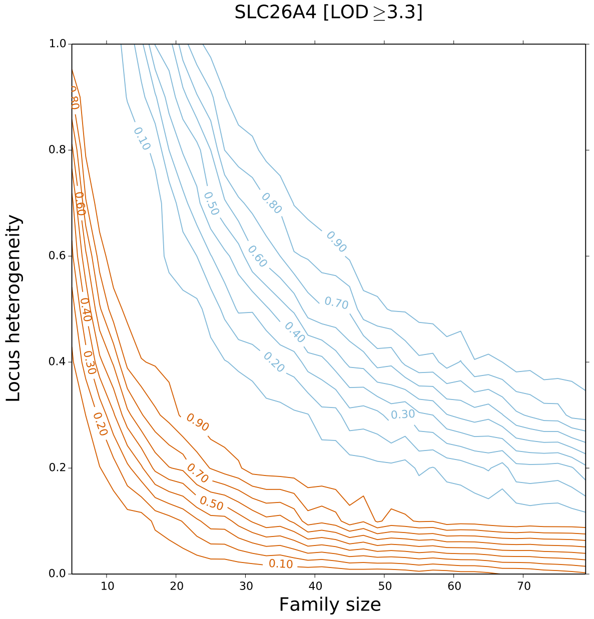


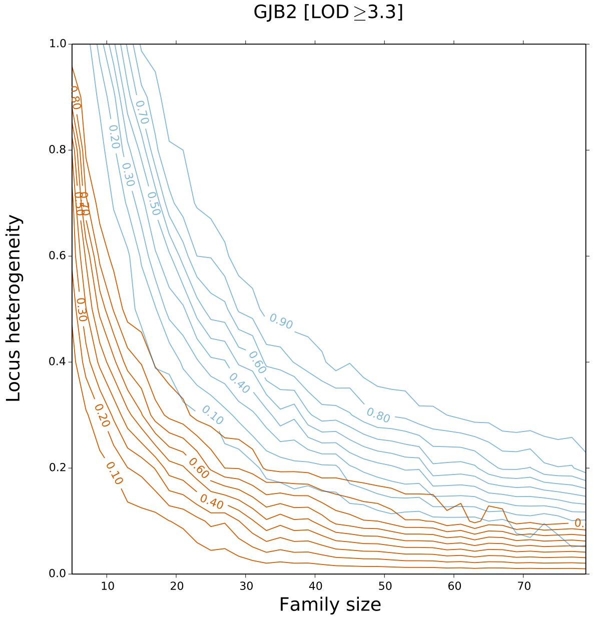
Recessive





Compound recessive


SLC26A4 [LOD ≥3.3]
Locus heterogeneity
Family size


GJB2 [LOD ≥3.3]
Locus heterogeneity
Family size