GWA Meta-Analysis METAL practical

In this practical we will run a GWA meta-analysis using METAL
http://www.sph.umich.edu/csg/abecasis/metal/
Documentation can be found at the metal wiki:
http://genome.sph.umich.edu/wiki/Metal_Documentation

Start by making a working folder and copying the practical files to it. In a new terminal window:

```
mkdir metal-practical

cp /faculty/meike/2013/metal-practical/* metal-practical/

cd metal-practical
```

METAL is flexible. It can run:

- fixed effects meta-analysis
- heterogeneity tests
- effect size, sample size, or weighted meta-analysis

It requires a *driver file*, which

- describes the input files
- defines meta-analysis strategy
- names output file

In the current practical we will run a meta-analysis on two files.

1. Check format of results files

- Ensure all necessary columns are available
- Modify files to include all information

METAL uses certain columns and you will use them depending on the kind on analyses method you choose. The following columns are used

- SNP
- OR
- SE [for standard error meta-analysis]
- P-value [for Z-score meta-analysis]
- N/weight column [If we had two samples of different sizes]

We will run meta-analysis based on effect size and on test statistic. For the weights of test statistic, I've assumed that the sample sizes are the same (METAL defaults to weight of 1 when no weight column is supplied).

Earlier this week you have ran your own GWA on SNPs on Chr 20 genotyped on a small number of cases and controls and we created an extra dataset. So, the current meta-analysis will be based on two datasets. In the 'real' world the number of datasets is often larger (and in that respect the preparation and QC-ing very time consuming and important).

Step 2. Prepare driver file

- Ensure headers match description
- Crosscheck each results file matches Process name

```
# PERFORM META-ANALYSIS based on effect size and on test statistic

# Loading in the input files with results from the  participating samples
# Note: Order of samples is …[sample size, alphabetic order,..]
# Phenotype is ..
# MB March 2013

MARKER  SNP
 ALLELE  A1 A2
 PVALUE  P                          specifies column names
 EFFECT  log(OR)
 STDERR  SE

PROCESS results1.txt                processes two results files
 PROCESS results2.txt

OUTFILE meta_res_Z .txt             Output file naming

ANALYZE                             Conducts Z-based meta-analysis from test statistic

CLEAR                               Clears workspace

SCHEME STDERR                       Changes meta-analysis scheme to beta + SE

PROCESS results1.txt                processes two results files
 PROCESS results2.txt

OUTFILE meta_res_SE .txt            Output file naming

ANALYZE                             Conducts effect size meta-analysis
```

Step 3. Run METAL

```
metal < metal_run_file
```

metal is the command and *metal_run_file* is the driver file

This will output information on the running of METAL things to standard out [the terminal]
It will spawn 4 files:

- 2 results files: meta_res_Z1.txt and meta_res_SE1.txt
- 2 info files: meta_res_Z1.txt.info and meta_res_SE1.txt.info

Step 4. Looking at your results

Load your results into HAPLOVIEW. The METAL output file have a different header (*marker* instead of *SNP*), so we have to change the header

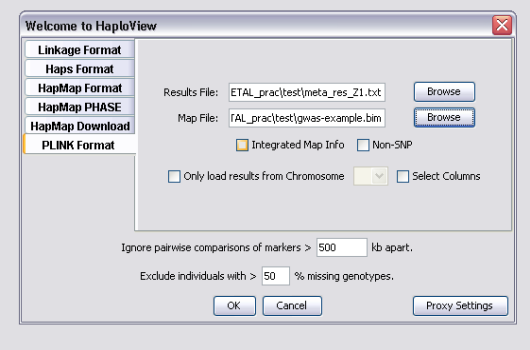
In the same directory run:

```
./reformat.sh
```

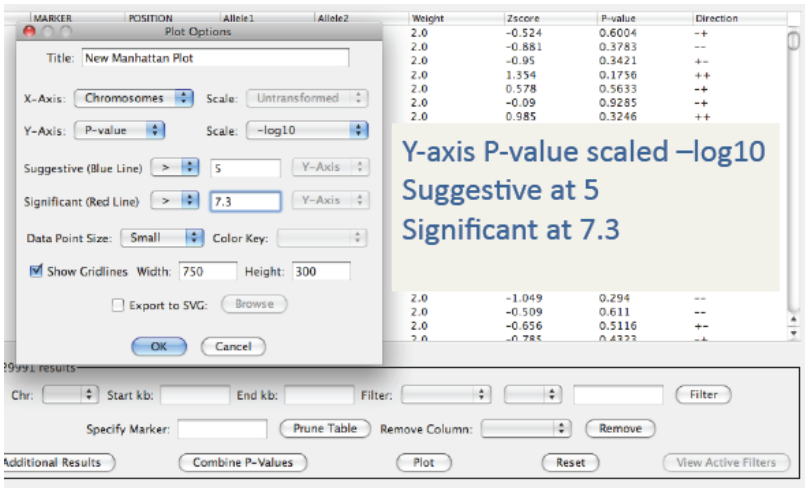
This changes 1st column name to SNP

We can then load the meta-analysis results files into haploview

- Load in the meta_res_Z1.txt
- Make sure to include the bim file that Jeff used earlier (gwas-example.bim)



We would like to plot the results in a Manhattan plot



*** Which SNP has the lowest p-value?**