

Step 1. Creating annotations and computed LD-score

- a. Create annotation matrix for each chromosome. All = All SNPs, Conserved = SNP within conserved genes +/- 50kb.

SNP	CHR	BP	A1	A2	All	Conserved
rs1	22	1	T	C	1	1
rs2	22	1000	A	G	1	1
rs3	22	20001	A	G	1	0
...
...
rs1001	22	10002	C	T	1	0

- b. Computing LD-scores with pre-computed UK Biobank LD matrices.

```
python compute_ldscores_from_ld.py \  
  --annot annotation/annotations.22.annot.parquet \ #file in step a  
  --ukb \  
  --out lsdsc/ldsc.22.parquet #ldsc score file
```

Step 2. Computing prior causal probabilities with PolyFun

- a. Reformat GWAS summary data

```
python munge_polyfun_sumstats.py \  
  --sumstats gwas/gwas_sumstats.gz \ #input gwas summary  
  --n 327209 \  
  --out gwas/sumstats_munged.parquet \ #gwas reformatted summary  
  --min-info 0.6 \  
  --min-maf 0.001
```

- b. Run PolyFun with L2-regularized S-LDSC

```
python polyfun.py \  
  --compute-h2-L2 \  
  --no-partitions \  
  --output-prefix l2_r_sldsc/prior \ #output l2-r-s-ldsc results  
  --sumstats gwas/sumstats_munged.parquet \ #reformatted gwas  
  --ref-ld-chr ldsc/ldsc. \ #ldsc score file from step 1  
  --w-ld-chr ukb/weights. #From baseline-LF 2.2.UKB
```

Step 3. Fine mapping with SuiSE using pre-computed summary LD information from the UK Biobank

- a. Perform fine mapping for each LD block with prior causal probabilities and without

```
#run fine-mapper  
python finemapper.py \  
  --ld LD_temp/chr1_46000001_49000001 \ #LD block LD file  
  --sumstats l2_r_sldsc/prior.22.snpvar_ridge_constrained.gz \  
  --n 327209 \  
  --chr 22 \  
  --start 46000001 \ #start of LD block  
  --end 49000001 \ #end of LD block  
  --method susie \  
  --max-num-causal 5 \  
  --out finemap_LDblock/finemap.UKB.1.46000001.49000001.gz  
  
--non-funct #add this command if don't want to use priors causal probabilities
```

- b. Aggregating the results

```
python aggregate_finemapper_results.py \  
  --out-prefix finemap_LDblock/finemap.UKB \  
  --chr 22 \  
  --sumstats l2_r_sldsc/prior.22.snpvar_ridge_constrained.gz \  
  --out finemap_agg/polyfun_agg.txt
```