vignette

```
library(hlacoloc)
```

Introduction

HLA-coloc performs colocalization in two steps, as described in the manuscript. These are:

1. HLA gene causal signature: this uses SuSiE to assign a posterior inclusion probability (PIP) to each HLA allele.
2. HLA PIP Bayesian regression: this uses stanR to perform Bayesian regression of the PIPs in each genes separately.

Required inputs

The following dataframes are necessary to run it (for each of the two phenotypes):

1. The HLA association summary statistics. This is a dataframe with the following columns:

- `Name`: the name of the allele. These must be given in IMGT-HLA format, but can be of any field resolution though (as long as it's the same for both phenotypes).
- `z`: the z-scores of the associations.
- `beta`: the beta of the associations (if `z` is not provided).
- `se`: the standard errors (if `z` is not provided).
- `N`: the sample sizes.

2. The LD matrix (can be either in dataframe or matrix format). This is a square matrix of R coefficient for the HLA alleles above. Importantly, the order of the alleles needs to be the same in the summary statistics dataframe and in the LD matrix here.

Example

First, load the data:

The data is included in the package.

```
data("ebna","ms","r_ebna","r_ms")
```

Data snippet

Here's a snippet of the EBNA data:

```
head(ebna)
#>         Name         beta       se    N
#> 1 G*01:01:01  0.014137500 0.015906 7247
#> 2 G*01:04:04  0.076847400 0.070867 7247
#> 3 G*01:01:02 -0.017568100 0.018972 7247
#> 4 G*01:01:03  0.000931893 0.033494 7247
#> 5   G*01:05N -0.293138000 0.078049 7247
#> 6 G*01:06:01  0.002110380 0.035066 7247
r_ebna[1:5,1:5]
#>            G*01:01:01 G*01:04:04 G*01:01:02 G*01:01:03   G*01:05N
#> G*01:01:01   1.000000 -0.1573650 -0.5404320 -0.2478420 -0.0925080
#> G*01:04:04  -0.157365  1.0000000 -0.0359779 -0.0317737 -0.0171784
#> G*01:01:02  -0.540432 -0.0359779  1.0000000 -0.1419840 -0.0672568
#> G*01:01:03  -0.247842 -0.0317737 -0.1419840  1.0000000 -0.0257557
#> G*01:05N    -0.092508 -0.0171784 -0.0672568 -0.0257557  1.0000000
```

And here's a snippet of the multiple sclerosis (MS) data:

```
head(ms)
#>         Name      beta       se      N
#> 1 G*01:01:01 -0.082764 0.032331 429822
#> 2 G*01:04:04  0.059263 0.144366 429822
#> 3 G*01:01:02 -0.050757 0.043057 429822
#> 4 G*01:01:03  0.120691 0.061987 429822
#> 5   G*01:05N -0.112573 0.158904 429822
#> 6 G*01:06:01  0.155703 0.059848 429822
r_ms[1:5,1:5]
#>            G*01:01:01  G*01:04:04 G*01:01:02 G*01:01:03    G*01:05N
#> G*01:01:01  1.0000000 -0.15260200 -0.5331010 -0.2476440 -0.09820330
#> G*01:04:04 -0.1526020  1.00000000 -0.0378230 -0.0167532 -0.00766048
#> G*01:01:02 -0.5331010 -0.03782300  1.0000000 -0.1369080 -0.05690370
#> G*01:01:03 -0.2476440 -0.01675320 -0.1369080  1.0000000 -0.02644930
#> G*01:05N   -0.0982033 -0.00766048 -0.0569037 -0.0264493  1.00000000
```

Now we run HLA-coloc on EBNA and MS:

This performs the 2 steps described above in one command.

```
coloc_res<-hla_coloc(pheno1=ebna,
                     pheno1R=r_ebna,
                     pheno2=ms,
                     pheno2R=r_ms)
#> Joining with `by = join_by(Name)`
#> Joining with `by = join_by(gene)`
```

Results:

Results include the colocalization table and a plot (optional).

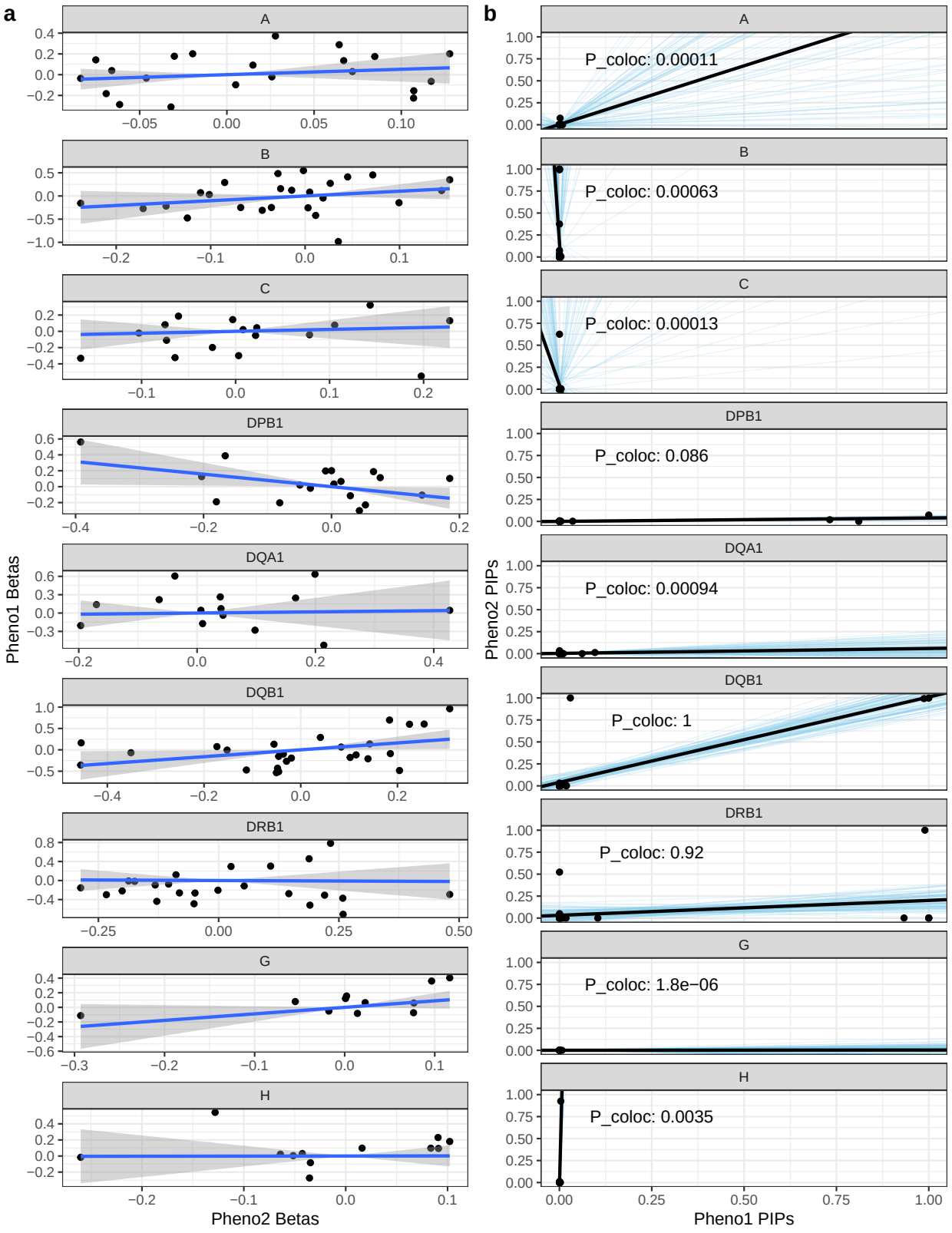
The colocalization table includes 5 columns - `gene`: the HLA gene. - `susie_coloc_prob`: the probability that SuSiE selects at least one shared HLA allele between the two traits at the given gene. - `bayes_pd`: the probability that the SuSiE posterior inclusion probabilities (PIP) correlate for each

genes. - `direction_of_correlation`: a check to make sure that the correlation between the PIPs is positive. - `hla_colocalization_probability`: the HLA colocalization probability (only valid if `direction_of_correlation` is correct). This is the product of `susie_coloc_prob` and `bayes_pd`, and is the final probability of HLA colocalization.

```
coloc_res[["hla_colocalization"]]
#> # A tibble: 9 x 5
#>   gene  susie_coloc_prob bayes_pd direction_of_correlat~1 hla_colocalization_p~2
#>   <chr>            <dbl>    <dbl> <chr>                                   <dbl>
#> 1 DQB1          1.00          1     Correct                               1.00
#> 2 DRB1          0.990         0.926 Correct                               0.916
#> 3 DPB1          0.0856        1     Correct                               0.0856
#> 4 H             0.00349       0.996 Correct                               0.00348
#> 5 DQA1          0.00129       0.732 Correct                               0.000943
#> 6 B             0.000803      0.781 Incorrect                             0.000627
#> 7 C             0.000192      0.672 Incorrect                             0.000129
#> 8 A             0.000152      0.748 Correct                               0.000114
#> 9 G             0.00000352    0.524 Correct                               0.00000184
#> # i abbreviated names: 1: direction_of_correlation,
#> #   2: hla_colocalization_probability
```

The plot has two columns. Left (a): the betas of the HLA allele summary statistics for the two traits. Right (b): the PIPs obtained from SuSiE, and the final probabilities of HLA colocalization.

```
coloc_res[["plot"]]
```


a
b
A
B
C
DPB1
DQA1
DQB1
DRB1
G
H
Pheno1 Betas
Pheno2 Betas
Pheno2 PIPs
Pheno1 PIPs
P_coloc: 0.00011
P_coloc: 0.00063
P_coloc: 0.00013
P_coloc: 0.086
P_coloc: 0.00094
P_coloc: 1
P_coloc: 0.92
P_coloc: 1.8e−06
P_coloc: 0.0035