

Integrative Mendelian randomization for detecting exposure-by-group interactions using group-specific and combined summary statistics

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Introduction

This vignette provides an introduction to the `int2MR` package. The R package `int2MR` implements the `int2MR` method for detecting both direct exposure-outcome effect within comparison group and reference group and exposure-group interaction effect.

Before installing `int2MR`, ensure that you have the `devtools` package installed. The package also requires `rstan` for Bayesian modeling. To install the development version of `int2MR`, run:

```
# Load devtools package  
library(devtools)
```

```
## Loading required package: usethis
```

```
# Install the int2MR package from GitHub  
install_github("Likeli-Ke/int2MR")
```

```
## Skipping install of 'int2MR' from a github remote, the SHA1 (7b3157b7) has not changed since last in  
## Use 'force = TRUE' to force installation
```

```
# Load the int2MR package  
library(int2MR)
```

Input Data Format

The `int2MR` package supports two types of GWAS summary statistics:

- **Three-sample data:** Utilizes three separate IV-to-outcome GWAS statistics.
- **Two-sample data:** Utilizes two IV-to-outcome GWAS summary statistics.

To detect the exposure-group interaction effect, it is essential that the proportion of the comparison group (denoted as ρ) varies among the provided GWAS summary statistics.

Data Requirements

Your input data should include:

- **Number of IVs** (instrumental variables)
- **Point estimates and squared standard errors** for:
 - IV-to-outcome effects
 - IV-to-exposure effects
- **Proportion of the comparison group (ρ)** in each IV-to-outcome GWAS summary statistic.

Load the example datasets provided with the package as follows:

```
data(example_3sample_data)
data(example_2sample_data)
```

For further details on the example data formats included with the package, consult the help pages.

```
help(example_3sample_data)
help(example_2sample_data)
```

Running Examples

This section demonstrates how to run `int2MR` using simulated data. Two examples are provided: one for three-sample data and one for two-sample data.

Example 1: Three-Sample Data

In this example, we perform an analysis on simulated three-sample data. The parameters include:

- **model_type**: “3sample”
- **Prior distributions**: Inverse gamma priors with a shape and scale of 0.1
- **MCMC Settings**: 2 chains, 10000 iterations with a warm-up period of 2500 iterations, and an `adapt_delta` of 0.95.

```
result_3sample <- int2MR(data_list_3sample = example_3sample_data,
  model_type = "3sample",
  prior_inv_gamma_shape = 0.1,
  prior_inv_gamma_scale = 0.1,
  chains = 2, iter = 10000, warmup = 2500,
  adapt_delta = 0.95)
```

```
## Loading required package: rstan
```

```
## Loading required package: StanHeaders
```

```
##
```

```
## rstan version 2.32.7 (Stan version 2.32.2)
```



```
## In file included from /Library/Frameworks/R.framework/Versions/4.4-arm64/Resources/library/StanHeader.h:1:
## In file included from /Library/Frameworks/R.framework/Versions/4.4-arm64/Resources/library/RcppEigen/include/Eigen/src/Core/Matrix.h:1:
## In file included from /Library/Frameworks/R.framework/Versions/4.4-arm64/Resources/library/RcppEigen/include/Eigen/src/Core/MatrixBase.h:1:
## /Library/Frameworks/R.framework/Versions/4.4-arm64/Resources/library/RcppEigen/include/Eigen/src/Core/MatrixBase.h:679:1: error: #include <cmath>
##      |               ^~~~~~
## 1 error generated.
## make: *** [foo.o] Error 1
```

```
# Display the results for the two-sample analysis
result_2sample$result_2sample
```

```
##      est_beta    se_beta    pval_beta est_beta_int se_beta_int pval_beta_int
## 1 0.1914894 0.03606245 1.096614e-07  -0.1441186  0.05694519    0.0113793
##      total_effect pval_total
## 1    0.04737085  0.2823505
```