

# Package ‘plasmut’

March 26, 2024

**Type** Package

**Title** Stratifying mutations observed in cell-free DNA and white blood cells as germline, hematopoietic, or somatic

**Version** 1.0.0

**Description** A Bayesian method for quantifying the likelihood that a given plasma mutation arises from clonal hematopoiesis or the underlying tumor. It requires sequencing data of the mutation in plasma and white blood cells with the number of distinct and mutant reads in both tissues. We implement a Monte Carlo importance sampling method to assess the likelihood that a mutation arises from the tumor relative to non-tumor origin.

**License** Artistic-2.0

**Encoding** UTF-8

**biocViews** Bayesian, SomaticMutation, GermlineMutation, Sequencing

**RoxygenNote** 7.2.3

**Imports** tibble, stats, dplyr

**Depends** R (>= 4.3.0)

**Suggests** knitr, rmarkdown, tidyverse, ggrepel, magrittr, qpdf, BiocStyle, biocViews, testthat (>= 3.0.0)

**VignetteBuilder** knitr

**Config/testthat/edition** 3

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crcseq	<i>This data is an example dataset to show how to use the package</i>
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### Description

A cohort of metastatic colorectal cancer patients whose plasma and buffy coat were sequenced as part of the CAIRO5 trial. The cohort and analyses are described here: <https://pubmed.ncbi.nlm.nih.gov/36534496/>

### Value

An example DNA sequencing dataset of matched plasma and wbc colorectal cancer samples crcseq

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importance_sampler	<i>Importance sampler to estimate marginal likelihoods and Bayes factors</i>
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### Description

Importance sampler to estimate marginal likelihoods and Bayes factors

### Usage

```
importance_sampler(dat, params, save_montecarlo = TRUE)
```

### Arguments

dat	data frame with observed mutant and total counts and the analyte (plasma or buffy coat) it was taken from and the identifiers on what the mutation is (e.g., KRASG12C) and pt id
params	list with ctc, ctdna and chip a and b beta parameters reflect beliefs on what fraction of fragments belong to each class; montecarlo.samples being the number of MC samples; prior weight is the prior.weight reflects how much importance sampling to implement, closer to zero means more importance density considered
save_montecarlo	save more indepth monte carlo results

**Value**

implement importance sampling for a data set to assess probability of tumor derived mutations from sequencing results

**Examples**

```
param.list <- list(ctc=list(a=1, b=9999),
                  ctdna=list(a=1, b=9),
                  chip=list(a=1, b=9),
                  montecarlo.samples=50e3,
                  prior.weight=0.1)
dat <- data.frame(y=c(4, 1),
                  n=c(1000, 1000),
                  analyte=c("plasma", "buffy coat"),
                  mutation="mutA",
                  sample_id="id1")
importance_sampler(dat, param.list)
```

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model_w	<i>Estimate the marginal likelihood that mutations in buffy coat and cfDNA reflect CH or correspond to germline mutations. If germline, the allele frequency should be 50 percent. The prior should be diffuse enough to handle CHIP mutations which are potentially way less than 50 percent</i>
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**Description**

Estimate the marginal likelihood that mutations in buffy coat and cfDNA reflect CH or correspond to germline mutations. If germline, the allele frequency should be 50 percent. The prior should be diffuse enough to handle CHIP mutations which are potentially way less than 50 percent

**Usage**

```
model_w(dat, params)
```

**Arguments**

dat	tibble containing vectors y and n. y and n should be named
params	a list with named elements that must include the following a which is the prior expectation for number of CH or germline variants observed in the sequencing data b which is the prior expectation for number of fragments reflecting CH or germline

**Value**

list of samples, probability densities, and likelihood for non-tumor assumption

**Examples**

```
param.list <- list(ctc=list(a=1, b=9999),
                  ctdna=list(a=1, b=9),
                  chip=list(a=1, b=9),
                  montecarlo.samples=50e3,
                  prior.weight=0.1)
dat <- data.frame(y=c(4, 1),
                 n=c(1000, 1000),
                 analyte=c("plasma", "buffy coat"),
                 mutation="mutA",
                 sample_id="id1")
model_w(dat, param.list)
```

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plasma_somatic	<i>Estimate the marginal likelihood that variants identified in cell-free DNA are derived from tumor cells (ctDNA-derived)</i>
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**Description**

Estimate the marginal likelihood that variants identified in cell-free DNA are derived from tumor cells (ctDNA-derived)

**Usage**

```
plasma_somatic(dat, params)
```

**Arguments**

dat	tibble containing vectors ‘y’ and ‘n’; ‘y’ and ‘n’ should be named
params	a list with named elements that must include the following: ‘a’: prior expectation for number of plasma somatic variants observed in the plasma sequencing data ‘b’: prior expectation for number of plasma fragments not containing variants

**Value**

generate importance samples for plasma somatic model

**Examples**

```
param.list <- list(ctc=list(a=1, b=9999),
                  ctdna=list(a=1, b=9),
                  chip=list(a=1, b=9),
                  montecarlo.samples=50e3,
                  prior.weight=0.1)
dat <- data.frame(y=c(4, 1),
                 n=c(1000, 1000),
                 analyte=c("plasma", "buffy coat"),
```

```

      mutation="mutA",
      sample_id="id1")
plasma_somatic(dat, param.list)

```

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plasmut	<i>Bayesian models for estimating the origin of a sequenced DNA fragment</i>
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### Description

The plasmut package provides a Bayesian importance sampling based approach to estimate the likelihood of a mutation arising from clonal hematopoiesis or tumor

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wbc_somatic	<i>Estimate the marginal likelihood of observing somatic mutations from CTCs present in buffy coat <math>p(y_w \mid \thetaeta_w, n_w, model_S) \times p(\thetaeta_w \mid Model_S) \thetaeta_w \mid model_S \sim \text{beta}(1, 999)</math> ## sequencing error or CTC</i>
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### Description

Estimate the marginal likelihood of observing somatic mutations from CTCs present in buffy coat  $p(y_w \mid \thetaeta_w, n_w, model_S) \times p(\thetaeta_w \mid Model_S) \thetaeta_w \mid model_S \sim \text{beta}(1, 999)$  ## sequencing error or CTC

### Usage

```
wbc_somatic(dat, params)
```

### Arguments

dat	tibble containing vectors 'y' and 'n'; 'y' and 'n' should be named
params	a list with named elements that must include the following: 'a': prior expectation for number of somatic variants observed in the WBC sequencing data (either by error or from a CTC) 'b': prior expectation for number of WBCs not containing the variant

### Value

generate importance samples for wbc somatic model

**Examples**

```
param.list <- list(ctc=list(a=1, b=9999),
                  ctdna=list(a=1, b=9),
                  chip=list(a=1, b=9),
                  montecarlo.samples=50e3,
                  prior.weight=0.1)
dat <- data.frame(y=c(4, 1),
                  n=c(1000, 1000),
                  analyte=c("plasma", "buffy coat"),
                  mutation="mutA",
                  sample_id="id1")
wbc_somatic(dat, param.list)
```

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