

# Package: spleenrbc (via r-universe)

October 29, 2024

**Title** The role of the spleen in red blood cell loss due to malaria

**Version** 0.0.1

**Description** A mathematical model of red blood cell (RBC) dynamics in a malaria infection, which includes the spleen as a separate model compartment that can retain large amounts of infected and uninfected RBCs.

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alpha_c	<i>Age-structured parasite multiplication rates (the number of released merozoites that successfully invade uRBCS of age a) in the circulation.</i>
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---

**Description**

Age-structured parasite multiplication rates (the number of released merozoites that successfully invade uRBCS of age a) in the circulation.

**Usage**

alpha\_c(u\_rbc, pmf, beta)

**Arguments**

u_rbc	The RBC count.
pmf	The parasite multiplication factor.
beta	The (age-dependent) merozoite preference for uninfected RBCs.

---

alpha_r	<i>Age-structured parasite multiplication rates (the number of released merozoites that successfully invade uRBCs of age a) in the spleen.</i>
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---

**Description**

Age-structured parasite multiplication rates (the number of released merozoites that successfully invade uRBCs of age a) in the spleen.

**Usage**

```
alpha_r(u_rbc, pmf, beta)
```

**Arguments**

u_rbc	The RBC count.
pmf	The parasite multiplication factor.
beta	The (age-dependent) merozoite preference for uninfected RBCs.

---

baseline_parameters	<i>Return the baseline parameter values, including all derived parameters.</i>
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---

**Description**

Return the baseline parameter values, including all derived parameters.

**Usage**

```
baseline_parameters(species = c("Pf", "Pv"), nospleen = FALSE, derived = TRUE)
```

**Arguments**

species	The malaria species: 'Pf' or 'Pv'.
nospleen	Whether the spleen has been removed.
derived	Whether to define parameters whose values are derived from other parameters.

---

beta	<i>Age-dependent merozoite preference for uninfected RBCs.</i>
------	----------------------------------------------------------------

---

### Description

Age-dependent merozoite preference for uninfected RBCs.

### Usage

```
beta(p, age)
```

### Arguments

p	The parameter values for the scenario.
age	The RBC age.

---

calculate_irbc_ratio	<i>Calculate the ratio of (a) the fraction of RBCs in the spleen that are infected; to (b) the fraction of RBCs in the circulation that are infected.</i>
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---

### Description

Calculate the ratio of (a) the fraction of RBCs in the spleen that are infected; to (b) the fraction of RBCs in the circulation that are infected.

### Usage

```
calculate_irbc_ratio(results)
```

### Arguments

results	A dataframe of simulation results.
---------	------------------------------------

### Value

A dataframe that includes the following columns, in addition those in results:

**iRBC\_Ratio** The ratio of infected cell fractions in the spleen and circulation.

---

credible_intervals	<i>Calculate credible intervals for each column, except "time" and "scenario".</i>
--------------------	------------------------------------------------------------------------------------

---

**Description**

Calculate credible intervals for each column, except "time" and "scenario".

**Usage**

```
credible_intervals(results, pcnt = c(50, 60, 70, 80, 90, 95))
```

**Arguments**

results	A dataframe of simulation results.
pcnt	The credible intervals to calculate, expressed as percentages.

**Value**

A dataframe with the following columns:

<b>name</b>	The statistic name (character)
<b>time</b>	The time (numeric, hours)
<b>cred_int</b>	The credible interval (ordered factor, widest to narrowst)
<b>ci_min</b>	The credible interval lower bound (numeric)
<b>ci_max</b>	The credible interval upper bound (numeric)

---

define_derived_parameters
---------------------------

*Define parameters whose values are derived from other parameters.*

---

**Description**

Define parameters whose values are derived from other parameters.

**Usage**

```
define_derived_parameters(p)
```

**Arguments**

p	The parameter values for the scenario.
---	----------------------------------------

---

delta_i	<i>Rate of infected RBC removal from the circulation into the spleen.</i>
---------	---------------------------------------------------------------------------

---

**Description**

Rate of infected RBC removal from the circulation into the spleen.

**Usage**

delta\_i(p, age)

**Arguments**

p	The parameter values for the scenario.
age	The RBC age.

---

delta_i_fold	<i>Increase in infected RBC removal into the spleen due to RBC congestion.</i>
--------------	--------------------------------------------------------------------------------

---

**Description**

Increase in infected RBC removal into the spleen due to RBC congestion.

**Usage**

delta\_i\_fold(p, net\_u\_rbc, net\_i\_rbc)

**Arguments**

p	The parameter values for the scenario.
net_u_rbc	The total number of uninfected RBCs in the circulation.
net_i_rbc	The total number of infected RBCs in the circulation.

---

delta_i_prime	<i>Rate of infected RBC reentry into the circulation from the spleen.</i>
---------------	---------------------------------------------------------------------------

---

**Description**

Rate of infected RBC reentry into the circulation from the spleen.

**Usage**

```
delta_i_prime(p, age)
```

**Arguments**

p	The parameter values for the scenario.
age	The infected RBC age(s).

---

delta_u	<i>Rate of uninfected RBC removal from the circulation into the spleen.</i>
---------	-----------------------------------------------------------------------------

---

**Description**

Rate of uninfected RBC removal from the circulation into the spleen.

**Usage**

```
delta_u(p, age)
```

**Arguments**

p	The parameter values for the scenario.
age	The RBC age.

---

delta_u_fold	<i>Increase in uninfected RBC removal into the spleen due to RBC congestion.</i>
--------------	----------------------------------------------------------------------------------

---

**Description**

Increase in uninfected RBC removal into the spleen due to RBC congestion.

**Usage**

delta\_u\_fold(p, net\_u\_rbc, net\_i\_rbc)

**Arguments**

p	The parameter values for the scenario.
net_u_rbc	The total number of uninfected RBCs in the circulation.
net_i_rbc	The total number of infected RBCs in the circulation.

---

delta_u_prime	<i>Rate of uninfected RBC reentry into the circulation from the spleen.</i>
---------------	-----------------------------------------------------------------------------

---

**Description**

Rate of uninfected RBC reentry into the circulation from the spleen.

**Usage**

delta\_u\_prime(p, age)

**Arguments**

p	The parameter values for the scenario.
age	The RBC age.



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erythropoiesis	<i>Rate of RBC production.</i>
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---

**Description**

Rate of RBC production.

**Usage**

erythropoiesis(p, u\_rbc)

**Arguments**

p	The parameter values for the scenario.
u_rbc	The RBC count.

---

hhs_asymp	<i>Red blood cell counts collected from asymptomatic Papuans who reported no fever within the preceding 24 hours (708 uninfected, 50 Pf infections, 45 Pv infections) in a cross-sectional household survey conducted in southern Papua, Indonesia.</i>
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---

**Description**

See [Pava et al., 2016](#) for details.

**Usage**

hhs\_asymp

**Format**

hhs\_asymp:

A data frame with 803 rows and the following columns:

**species** One of "Pf", "Pv", or "neg"

**total\_rbc** The red blood cell count

---

individual\_results      *Record key outputs for a single scenario.*

---

### Description

Record key outputs for a single scenario.

### Usage

```
individual_results(p, keep)
```

### Arguments

`p`                      The scenario parameters.  
`keep`                    The model state at each of the relevant time-steps.

### Value

A data frame that includes the following columns:

**scenario** The scenario number  
**time** The simulation time (hours)  
**U\_t** The number of uRBCs in the circulation  
**Ur\_t** The number of uRBCs in the spleen  
**Retic\_c\_t** The number of reticulocytes in the circulation  
**Retic\_r\_t** The number of reticulocytes in the spleen  
**I\_t** The number of iRBCs in the circulation  
**Ir\_t** The number of iRBCs in the spleen  
**Iq\_t** The number of iRBCs in the microvasculature  
**M\_t** The number of macrophages in the spleen  
**E\_t** The erythropoiesis rate  
**r\_t** The number of reticulocytes in the bone marrow  
**pmr\_c\_t\_1** The number of merozoites released in the circulation  
**pmr\_r\_t\_1** The number of merozoites released in the spleen  
**flow\_r\_to\_c** The number of reticulocytes released from the bone marrow  
**flow\_uc\_to\_r** The number of uRBCs removed from the circulation into the spleen  
**flow\_uc\_to\_r\_no\_inf** The number of uRBCs that would have been removed from the circulation into the spleen, in the absence of a malaria infection  
**flow\_ur\_to\_c** The number of uRBCs released from the spleen into the circulation  
**flow\_ur\_out** The number of uRBCs phagocytised in the spleen  
**flow\_ic\_to\_r** The number of iRBCs removed from the circulation into the spleen

**flow\_ic\_to\_q** The number of iRBCs sequestered into the microvasculature  
**flow\_ir\_to\_c** The number of iRBCs released from the spleen into the circulation  
**flow\_ir\_out** The number of iRBCs phagocytised in the spleen  
**flow\_uc\_to\_ic** The number of uRBCs in the circulation that became infected  
**flow\_ur\_to\_ir** The number of uRBCs in the spleen that became infected  
**inf\_from\_ic** The number of RBCs infected from iRBCs in the circulation  
**inf\_from\_iq** The number of RBCs infected from iRBCs in the microvasculature  
**inf\_from\_ir** The number of RBCs infected from iRBCs in the spleen  
**rho\_t** The release rate of the youngest reticulocytes  
**deltaUfold** The fold increase in uRBC removal from the circulation  
**deltaIfold** The fold increase in iRBC removal from the circulation  
**Ur\_frac\_inf** The fraction of RBCs in the spleen that become infected

---

infection\_flows\_and\_loss

*Calculate quantities related to uRBC infection and retention in the spleen due to malaria infection.*

---

### Description

Calculate quantities related to uRBC infection and retention in the spleen due to malaria infection.

### Usage

```
infection_flows_and_loss(results)
```

### Arguments

`results` A dataframe of simulation results.

### Value

A dataframe that includes the following columns, in addition those in `results`:

**U\_and\_I\_t** The value of  $U_c(t) + I_c(t)$   
**Ur\_frac\_U** the fraction of uRBCs that are retained in the spleen  
**flow\_uc\_to\_r\_inf** The retention of uRBCs due to malaria infection  
**flow\_uc\_to\_r\_ratio** The rate of uRBC retention that is due to malaria infection, relative to baseline uRBC retention  
**Uc\_loss\_ratio\_c** The ratio of uRBC retention due to malaria loss, relative to the infection of uRBCs in the circulation  
**Uc\_loss\_ratio\_cr** The ratio of uRBC retention due to malaria loss, relative to the infection of uRBCs in the circulation and the spleen

**inf\_total** The number of uRBC infections in the circulation and spleen

**inf\_from\_icq** The number of uRBC infection in the circulation due to merozoites released in the circulation and microvasculature

---

initial\_spleenrbc\_state

*Construct the initial model state.*

---

### Description

Construct the initial model state.

### Usage

initial\_spleenrbc\_state(p)

### Arguments

p                    The parameter values for the scenario.

---

lambda\_i

*Phagocytosis rate of infected RBCs in the spleen.*

---

### Description

Phagocytosis rate of infected RBCs in the spleen.

### Usage

lambda\_i(p, macrophages)

### Arguments

p                    The parameter values for the scenario.

macrophages        The macrophage count.

---

lambda_u	<i>Phagocytosis rate of uninfected RBCs in the spleen.</i>
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---

**Description**

Phagocytosis rate of uninfected RBCs in the spleen.

**Usage**

```
lambda_u(p, macrophages, age)
```

**Arguments**

p	The parameter values for the scenario.
macrophages	The macrophage count.
age	The RBC age.

---

lhs_distributions	<i>Define the distributions from which to sample values for each parameter.</i>
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---

**Description**

Define the distributions from which to sample values for each parameter.

**Usage**

```
lhs_distributions(params, lower = 0.8, upper = 1.2)
```

**Arguments**

params	A data frame that defines the parameters to be sampled.
lower	The lower bound for triangle distributions, relative to the baseline values.
upper	The upper bound for triangle distributions, relative to the baseline values.

---

parameters\_pf      *Pf parameter values for each scenario.*

---

**Description**

Pf parameter values for each scenario.

**Usage**

parameters\_pf

**Format**

parameters\_pf:

A data frame with 34 rows and 3 columns:

**name** Parameter name

**baseline** Baseline value

**dist** Sampling distribution: 'constant' or 'triangle'

---

parameters\_pv      *Pv parameter values for each scenario.*

---

**Description**

Pv parameter values for each scenario.

**Usage**

parameters\_pv

**Format**

parameters\_pv:

A data frame with 34 rows and 3 columns:

**name** Parameter name

**baseline** Baseline value

**dist** Sampling distribution: 'constant' or 'triangle'

---

`prepare_spleenrbc_snapshot`*Construct a list that will record the model state over time.*

---

**Description**

Construct a list that will record the model state over time.

**Usage**

```
prepare_spleenrbc_snapshot(p, time_steps)
```

**Arguments**

<code>p</code>	The parameter values for the scenario.
<code>time_steps</code>	The number of time-steps (hours).

---

`rbc_counts_to_haemoglobin`*Convert red blood cell counts into haemoglobin (g/dL).*

---

**Description**

For this conversion, we assume that 15 g/dL of haemoglobin corresponds to  $2.5 \times 10^{13}$  RBCs.

**Usage**

```
rbc_counts_to_haemoglobin(rbc_counts)
```

**Arguments**

<code>rbc_counts</code>	One or more RBC counts.
-------------------------	-------------------------

**Value**

Haemoglobin levels (g/dL).

**Examples**

```
rbc_counts_to_haemoglobin(1e15 * c(2.3, 2.4, 2.5, 2.6, 2.7))
```

---

rbc_steady_state	<i>The red blood cell count at homeostasis.</i>
------------------	-------------------------------------------------

---

### Description

Defined as the median red blood cell count for uninfected Papuans in the [hhs\\_asymp](#) data set.

### Usage

```
rbc_steady_state
```

### Format

```
rbc_steady_state:
A scalar value.
```

---

resolve_negative_rbc	<i>Subtract negative U values from other (positive) U values.</i>
----------------------	-------------------------------------------------------------------

---

### Description

Subtract negative U values from other (positive) U values.

### Usage

```
resolve_negative_rbc(u, t_urbc, pmf, beta_a, alpha_fun)
```

### Arguments

u	A population of red blood cells.
t_urbc	The RBC lifetime.
pmf	The parasite multiplication factor.
beta_a	The (age-dependent) merozoite preference for uninfected RBCs.
alpha_fun	The function that calculates RBC infections.



---

reticulocyte\_prod      *The reticulocyte production rate for the given normoblast population.*

---

**Description**

The reticulocyte production rate for the given normoblast population.

**Usage**

```
reticulocyte_prod(p, rho_ss, lambdaU, deltaU_a, gamma, z = 0)
```

**Arguments**

p	The parameter values for the scenario.
rho_ss	The release rate of reticulocytes from the bone marrow into the circulation at homeostasis.
lambdaU	The phagocytosis rate of uninfected RBCs in the spleen.
deltaU_a	The rate of uninfected RBC removal from the circulation into the spleen.
gamma	The normoblast population in the bone marrow.
z	The initial number of circulating reticulocytes (age of 1 hour).

---

retic\_steady\_state      *The reticulocyte production rate at homeostasis.*

---

**Description**

Returns the steady-state values for:

- normoblast population (gamma);
- reticulocyte population in the bone marrow (r\_a);
- reticulocyte population in the circulation (R\_a);
- normocyte population in the circulation (N\_a);
- RBC population in the spleen (Ur\_a); and
- circulating RBC imbalance wrt homeostasis (difference).

**Usage**

```
retic_steady_state(p)
```

**Arguments**

p	The parameter values for the scenario.
---	----------------------------------------

---

rho	<i>Age-structured release rate of reticulocytes from the bone marrow into the circulation.</i>
-----	------------------------------------------------------------------------------------------------

---

**Description**

Age-structured release rate of reticulocytes from the bone marrow into the circulation.

**Usage**

rho(p, age, u\_rbc)

**Arguments**

p	The parameter values for the scenario.
age	The reticulocyte age.
u_rbc	The RBC count (must be a scalar).

---

rho_release_age	<i>The minimum age at which reticulocytes are released from the bone marrow into the circulation.</i>
-----------------	-------------------------------------------------------------------------------------------------------

---

**Description**

The minimum age at which reticulocytes are released from the bone marrow into the circulation.

**Usage**

rho\_release\_age(p, u\_rbc)

**Arguments**

p	The parameter values for the scenario.
u_rbc	The RBC count (must be a scalar).

---

run_spleenrbc	<i>Run model scenarios.</i>
---------------	-----------------------------

---

**Description**

Run model scenarios.

**Usage**

```
run_spleenrbc(  
  scenarios = NULL,  
  days = 50,  
  time_steps = days * 24,  
  verbose = FALSE  
)
```

**Arguments**

scenarios	A dataframe of parameter combinations for each scenario.
days	The number of days to simulate.
time_steps	The number of time-steps (hours).
verbose	Whether to print a message when starting each scenario.

**Value**

A data frame whose columns capture model state variables at each time-step.

**See Also**

[individual\\_results\(\)](#) for a description of the returned data frame.

---

run_spleenrbc_model	<i>Run a single scenario and return the model state history.</i>
---------------------	------------------------------------------------------------------

---

**Description**

Run a single scenario and return the model state history.

**Usage**

```
run_spleenrbc_model(p, time_steps, debug = FALSE)
```

**Arguments**

p	The parameter values for the scenario.
time_steps	The number of time-steps (hours).
debug	Whether to check invariant properties after each time-step.

**Value**

A data frame whose columns capture model state variables at each time-step.

**See Also**

[individual\\_results\(\)](#) for a description of the returned data frame.

---

sample_parameters	<i>Create parameter samples for each scenario.</i>
-------------------	----------------------------------------------------

---

**Description**

Create parameter samples for each scenario.

**Usage**

```
sample_parameters(
  species = c("Pf", "Pv"),
  nospleen = FALSE,
  dists = NULL,
  rbc_ss = NULL,
  n_samples = 1000,
  seed = 1691987
)
```

**Arguments**

species	The malaria species: 'Pf' or 'Pv'.
nospleen	Whether the spleen has been removed.
dists	The parameter distributions from which to draw samples.
rbc_ss	The red blood cell count at homeostasis.
n_samples	The number of scenarios.
seed	The seed for the random number generator.

---

splenectomised	<i>Uninfected and infected RBC counts in the circulation and spleen of 15 asymptomatic adults in Papua, Indonesia (9 Pf infections, 6 Pv infections) who underwent splenectomy, mostly due to trauma.</i>
----------------	-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

---

**Description**

See [Kho et al., 2021](#) for details.

**Usage**

splenectomised

**Format**

splenectomised:

A data frame with 17 rows and the following columns:

**patient** Patient identifier

**infection** One of "Pf", "Pv", or "neg"

**irbc\_peri** Infected RBC count in the peripheral circulation

**irbc\_spleen** Infected RBC count in the spleen

**urbc\_peri** Uninfected RBC count in the peripheral circulation

**urbc\_spleen** Uninfected RBC count in the spleen

---

step_spleenrbc_model	<i>Update the model state by simulating forward one time-step.</i>
----------------------	--------------------------------------------------------------------

---

**Description**

Update the model state by simulating forward one time-step.

**Usage**

step\_spleenrbc\_model(p, s, t)

**Arguments**

p	The parameter values for the scenario.
s	The current model state.
t	The time for which to calculate the model state.

---

zeta	<i>Age-structured rate of RBC sequestration into the microvasculature.</i>
------	----------------------------------------------------------------------------

---

**Description**

Age-structured rate of RBC sequestration into the microvasculature.

**Usage**

zeta(p, age)

**Arguments**

p	The parameter values for the scenario.
age	The RBC age.

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