hmer: customising implausibility

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Chapter 1

Objectives

In this note we describe how to define customised implausibility measures when calibrating a model with the hmer package. Customised implausibility measures allow the hmer user to work with parameter spaces that are not necessarily rectangular, for example by imposing restrictions on parameters of the type `parameter_1 < parameter2`.

Before diving into this note, you will need to run the code contained in the box below: it will load all relevant dependencies and a few helper functions which will be introduced and used later.

Show: Code to load relevant libraries and helper functions on P18

Chapter 2

The model and calibration setup

In this section we define the model and the calibration setup for our example.

The model that we chose for demonstration purposes is the deterministic SEIRS model used in the deterministic workshop and is described by the following differential equations:

$$\frac{dS}{dt} = bN - \frac{\beta(t)IS}{N} + \omega R - \mu S \tag{2.1}$$

$$\frac{dE}{dt} = \frac{\beta(t)IS}{N} - \epsilon E - \mu E \tag{2.2}$$

$$\frac{dI}{dt} = \epsilon E - \gamma I - (\mu + \alpha)I \tag{2.3}$$

$$\frac{dR}{dt} = \gamma I - \omega R - \mu R \tag{2.4}$$

where N is the total population, varying over time, and the parameters are as follows:

- b is the birth rate,
- μ is the rate of death from other causes,
- $\beta(t)$ is the infection rate between each infectious and susceptible individual,
- ϵ is the rate of becoming infectious after infection,
- α is the rate of death from the disease,
- γ is the recovery rate and
- ω is the rate at which immunity is lost following recovery.

The rate of infection $\beta(t)$ is set to be a simple linear function interpolating between points, where the points in question are $\beta(0) = \beta_1$, $\beta(100) = \beta(180) = \beta_2$, $\beta(270) = \beta_3$ and where $\beta_2 < \beta_1 < \beta_3$. This choice was made to represent an infection rate that initially drops due to external (social) measures and then raises when a more infectious variant appears. Here t is taken to measure days. Below we show a graph of the infection rate over time when $\beta_1 = 0.3, \beta_2 = 0.1$ and $\beta_3 = 0.4$:

We now set up the emulation task, defining the input parameter ranges, the calibration targets and all the data necessary to build the first wave of emulators.

First of all, let us set the parameter ranges:

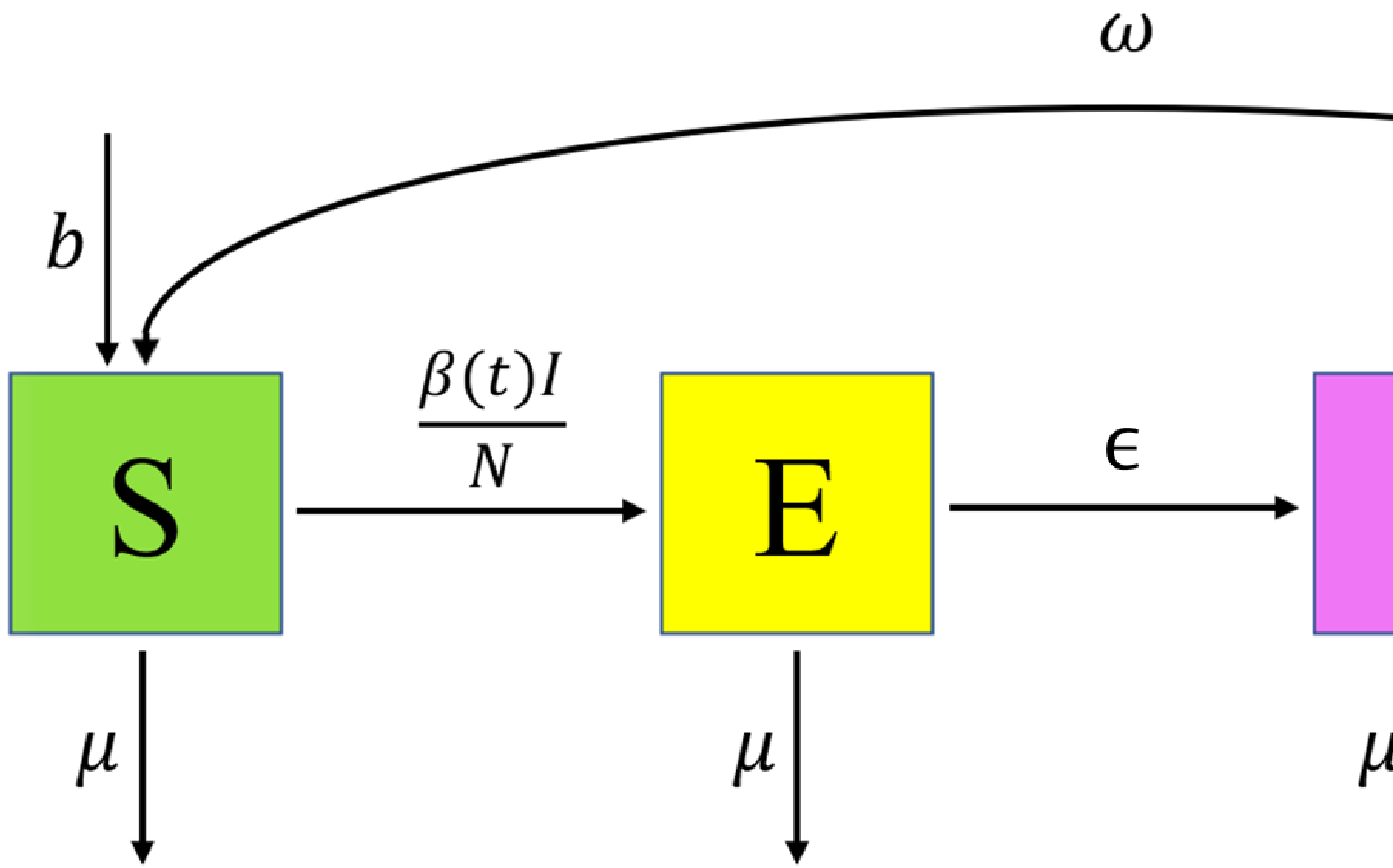


Figure 2.1: SEIRS Diagram

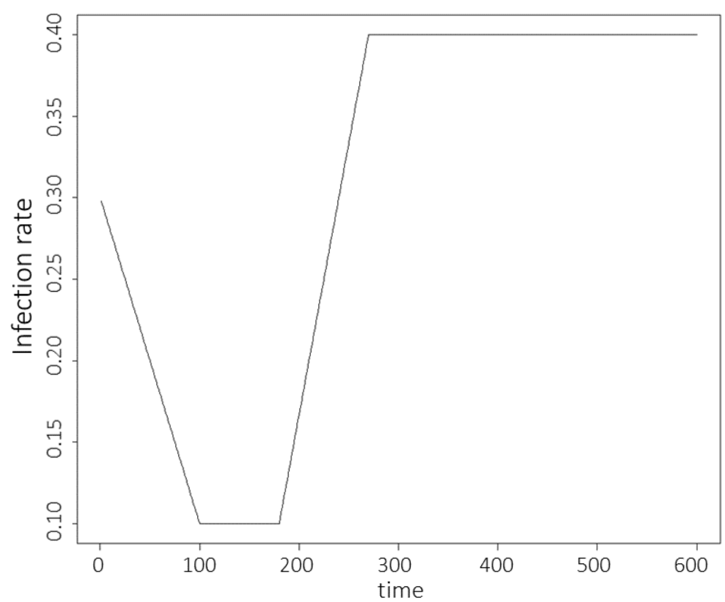


Figure 2.2: Infection rate graph

```
ranges = list(
  b = c(1e-5, 1e-4), # birth rate
  mu = c(1e-5, 1e-4), # rate of death from other causes
  beta1 = c(0.1, 0.5), # infection rate at time t=0
  beta2 = c(0.1, 0.5), # infection rates at time t=100
  beta3 = c(0.1, 0.5), # infection rates at time t=270
  epsilon = c(0.07, 0.21), # rate of becoming infectious after infection
  alpha = c(0.01, 0.025), # rate of death from the disease
  gamma = c(0.05, 0.08), # recovery rate
  omega = c(0.002, 0.004) # rate at which immunity is lost following recovery
)
```

Note that, even though β_1, β_2 and β_3 have the same initial range $[0.1, 0.5]$, when calibrating the model we want to impose $\beta_2 < \beta_1 < \beta_3$.

We then turn to the targets we will match: the number of infectious individuals I and the number of recovered individuals R at times $t = 25, 40, 100, 200, 200, 350$:

```
targets <- list(
  I25 = list(val = 115.88, sigma = 5.79),
  I40 = list(val = 137.84, sigma = 6.89),
  I100 = list(val = 26.34, sigma = 1.317),
  I200 = list(val = 0.68, sigma = 0.034),
  I300 = list(val = 29.55, sigma = 1.48),
  I350 = list(val = 68.89, sigma = 3.44),
  R25 = list(val = 125.12, sigma = 6.26),
  R40 = list(val = 256.80, sigma = 12.84),
  R100 = list(val = 538.99, sigma = 26.95),
  R200 = list(val = 444.23, sigma = 22.21),
  R300 = list(val = 371.08, sigma = 15.85),
  R350 = list(val = 549.42, sigma = 27.47)
)
```

Finally we need an initial design `wave0`, containing a well-spread set of parameter sets and the corresponding model outputs:

```
initial_LHS_training <- maximinLHS(90, 9)
initial_LHS_validation <- maximinLHS(90, 9)
initial_LHS <- rbind(initial_LHS_training, initial_LHS_validation)
initial_points <- setNames(data.frame(t(apply(initial_LHS, 1,
                  function(x) x*unlist(lapply(ranges, function(x) x[2]-x[1])) +
                  unlist(lapply(ranges, function(x) x[1]))))), names(ranges))
initial_results <- setNames(data.frame(t(apply(initial_points, 1, get_results,
                   c(25, 40, 100, 200, 300, 350), c('I', 'R')))), names(targets))
wave0 <- cbind(initial_points, initial_results)
```

Chapter 3

First wave emulators

In this section we train the first wave of emulators.

Let us start by splitting `wave0` in two parts: the training set (the first half), on which we will train the emulators, and a validation set (the second half), which will be used to do diagnostics of the emulators.

```
training <- wave0[1:90,]
validation <- wave0[91:180,]
```

We are now ready to train the emulators using the `emulator_from_data` function.

```
ems_wave1 <- emulator_from_data(training, names(targets), ranges)
```

```
## I25
## I40
## I100
## I200
## I300
## I350
## R25
## R40
## R100
## R200
## R300
## R350
## I25
## I40
## I100
## I200
## I300
## I350
## R25
## R40
## R100
## R200
## R300
## R350
```

Chapter 4

Proposing new points with custom implausibility

In this section we generate the set of points that will be used to train the second wave of emulators. **To ensure that the relationship $\beta_2 < \beta_1 < \beta_3$ is satisfied, we define a customised version of the implausibility measure.**

```
custom_imp <- function(ems, points, targets, cutoff, n, ...) {
  # Work out which points pass our restrictions beta2 < beta1 < beta3
  simple_pass <- which(points$beta2 < points$beta1 &
                       points$beta1 < points$beta3)
  # Set up an output vector
  output <- rep(FALSE, nrow(points))
  # In case all the points fail these cases return the output with all entries equal to FALSE
  if (length(simple_pass) == 0) return(output)
  # Otherwise, put the implausibility values in for the points that passed the earlier checks
  output[simple_pass] <- nth_implausible(ems, points[simple_pass,], targets,
                                         n = n, cutoff = cutoff, ...)
  return(output)
}
```

The `custom_imp` function returns the standard implausibility measure (see deterministic workshop) for parameter sets that satisfy the condition $\beta_2 < \beta_1 < \beta_3$, and it returns FALSE otherwise.

To use this customised implausibility when calling the `generate_new_design` function, we simply need to set `opts=list(accept_measure = custom_imp)`:

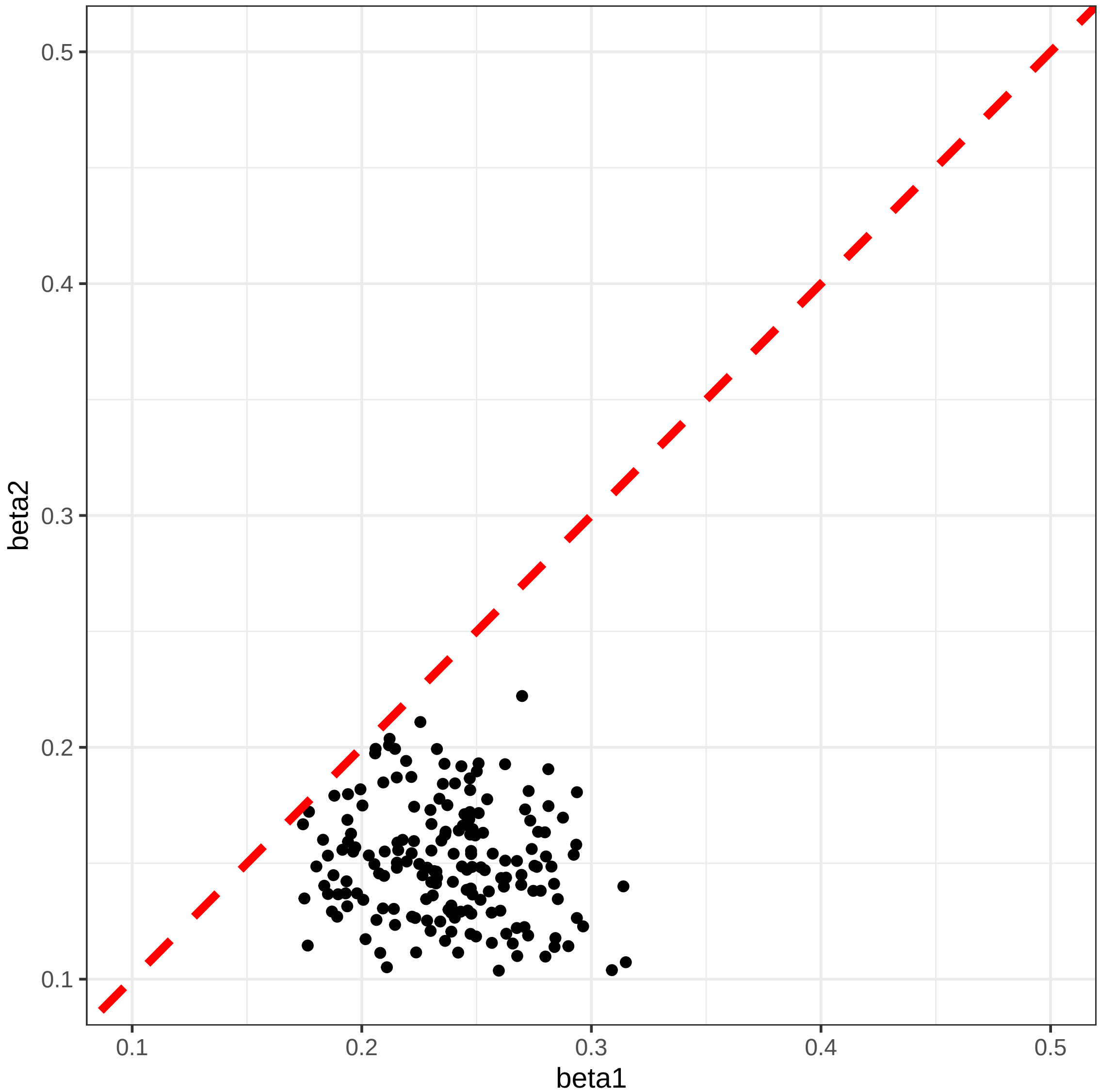
```
new_points <- generate_new_design(ems_wave1, 180, targets, verbose=TRUE,
                                  opts=list(accept_measure = custom_imp))
```

```
## Proposing from LHS...
## 84 initial valid points generated for I=4
## Performing line sampling...
## Line sampling generated 44 more points.
## Performing importance sampling...
## Importance sampling generated 62 more points.
## 46 initial valid points generated for I=3.3
## Performing line sampling...
```

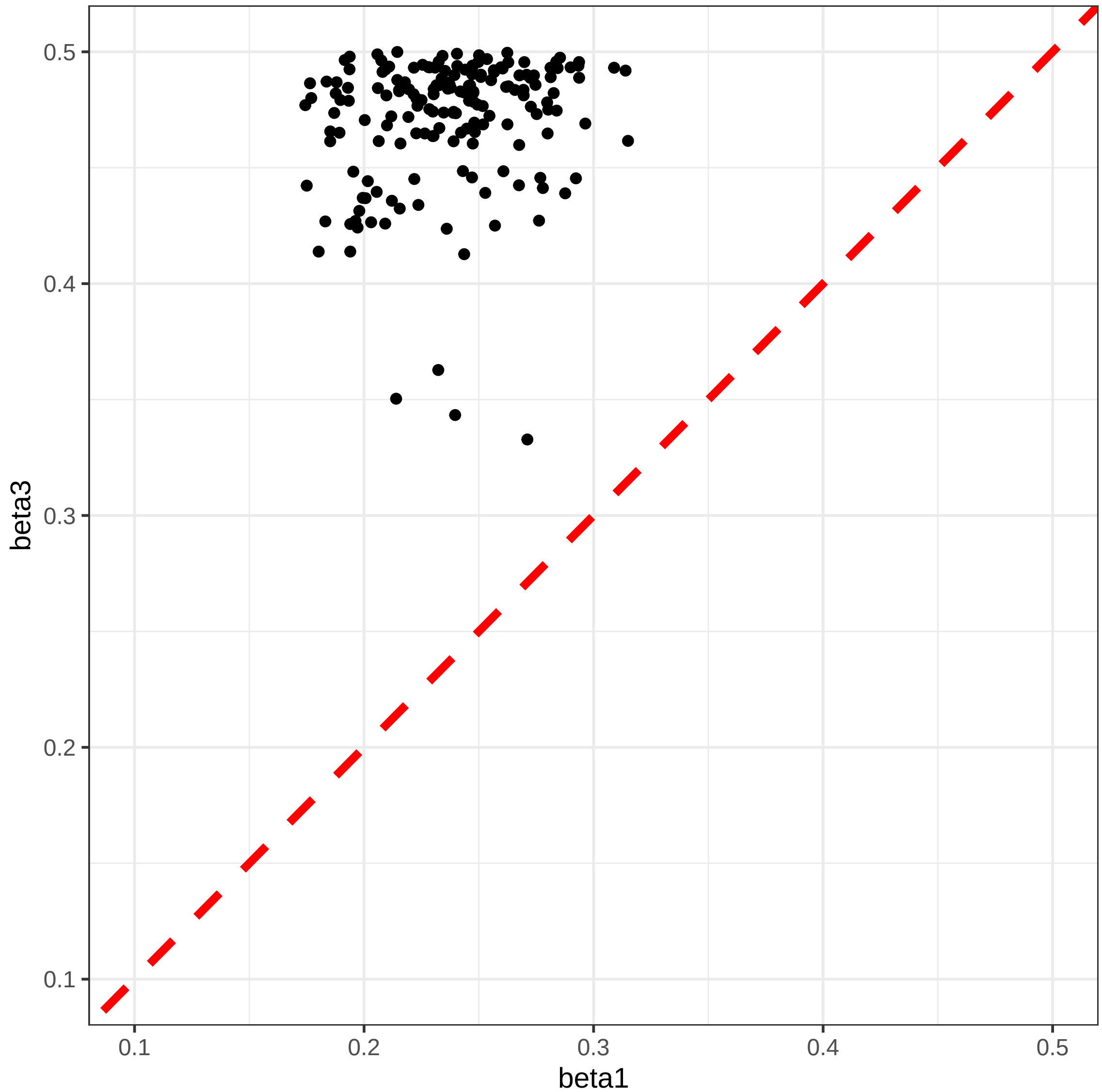
```
## Line sampling generated 38 more points.
## Performing importance sampling...
## Importance sampling generated 110 more points.
## 113 initial valid points generated for I=3
## Performing line sampling...
## Line sampling generated 33 more points.
## Performing importance sampling...
## Importance sampling generated 121 more points.
## Selecting final points using maximin criterion...
## Resample 1
## Performing line sampling...
## Line sampling generated 30 more points.
## Performing importance sampling...
## Importance sampling generated 158 more points.
## Selecting final points using maximin criterion...
```

Let us check the values of the three beta parameters for the newly generated parameter sets:

```
ggplot(new_points, aes(x = beta1, y = beta2)) + geom_point() +
       xlim(0.1,0.5) + ylim(0.1,0.5) +
       geom_abline(intercept = 0, slope = 1, color="red", linetype="dashed", linewidth=1.5) +
       theme_bw()
```




```
ggplot(new_points, aes(x = beta1, y = beta3)) + geom_point() +
       xlim(0.1,0.5) + ylim(0.1,0.5) +
       geom_abline(intercept = 0, slope = 1, color="red", linetype="dashed", linewidth=1.5) +
       theme_bw()
```



The plots clearly show that all non-implausible parameter sets at the end of the first wave satisfy the inequalities $\beta_2 < \beta_1 < \beta_3$, which is what we wanted.

From here, the history matching process continues as usual (see deterministic workshop), with the only difference being that whenever the `generate_new_design` is called, the argument `opts` needs to be set to `list(accept_measure = custom_imp)`.

Appendix A

Additional information

Code to load relevant libraries and helper functions

```
library(hmer)
library(deSolve)
library(ggplot2)
library(reshape2)
library(purrr)
library(tidyverse)
library(lhs)
set.seed(123)
############################# HELPER FUNCTIONS #############################
# `ode_results` provides us with the solution of the differential equations for a given
# set of parameters. This function assumes an initial population of
# 900 susceptible individuals, 100 exposed individuals, and no infectious
# or recovered individuals.
ode_results <- function(parms, end_time = 365*2) {
  forcer = matrix(c(0, parms['beta1'], 100, parms['beta2'], 180, parms['beta2'], 270, parms['beta3']),
                  ncol = 2, byrow = TRUE)
  force_func = approxfun(x = forcer[,1], y = forcer[,2], method = "linear", rule = 2)
  des = function(time, state, parms) {
    with(as.list(c(state, parms)), {
      dS <- b*(S+E+I+R)-force_func(time)*I*S/(S+E+I+R) + omega*R - mu*S
      dE <- force_func(time)*I*S/(S+E+I+R) - epsilon*E - mu*E
      dI <- epsilon*E - alpha*I - gamma*I - mu*I
      dR <- gamma*I - omega*R - mu*R
      return(list(c(dS, dE, dI, dR)))
    })
  }
  yini = c(S = 900, E = 100, I = 0, R = 0)
  times = seq(0, end_time, by = 1)
  out = deSolve::ode(yini, times, des, parms)
  return(out)
}
# `get_results` acts as `ode_results`, but has the additional feature
# of allowing us to decide which outputs and times should be returned.
# For example, to obtain the number of infected and susceptible individuals
# at t=25 and t=50, we would set `times=c(25,50)` and `outputs=c('I','S')`.
get_results <- function(params, times, outputs) {
  t_max <- max(times)
  all_res <- ode_results(params, t_max)
  actual_res <- all_res[all_res[,'time'] %in% times, c('time', outputs)]
  shaped <- reshape2::melt(actual_res[,outputs])
  return(setNames(shaped$value, paste0(shaped$Var2, actual_res[,'time'], sep = "")))
}
```

Return to P5