San Francisco data - New Model

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1 Supporting tools

First, we load the libraries and custom functions that support the analysis.

```
library(bayesplot)
library(cmdstanr)
library(dplyr)
library(extraDistr)
library(GGally)
library(ggplot2)
library(reshape2)
library(ggpubr)
library(ggridges)
library(gridExtra)
library(kableExtra)
library(lubridate)
library(Metrics)
library(patchwork)
library(posterior)
library(purrr)
library(readr)
library(readsdr)
library(readxl)
library(writexl)
library(scales)
library(stringr)
library(tidyr)
library(viridisLite)
# Custom functions
source("./R/helpers.R")
source("./R/plots.R")
# source("./R/incidence_comparison.R")
# Custom model functions
source("./R/mdls/generate_deSolve_components.R")
source("./R/mdls/utils.R")
source("./R/mdls/arrange_variables.R")
source("./R/mdls/extract_variables.R")
source("./R/mdls/stan_ode_function_2.R")
source("./R/mdls/plots_2.R")
# Backup folder
fldr <- "./backup_objs/san_francisco_ext_202210"</pre>
dir.create(fldr, showWarnings = FALSE, recursive = TRUE)
```

2 Data

We read the xls file that contains the incidence data and transform it into a format suitable for the analysis.

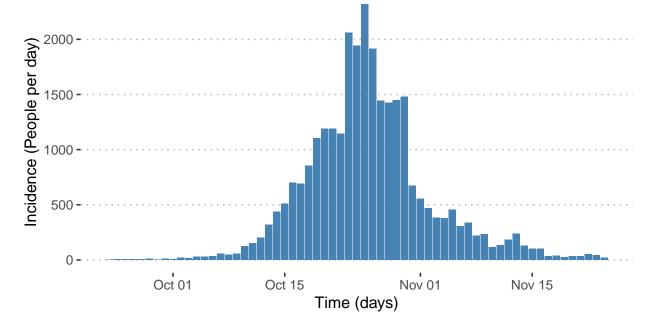
```
# Change according to input data
flu_data <- read_xls("./data/rsif20060161s03.xls", range = "A6:C69") %>%
  rename(time = Time, y = Cases) %>%
  mutate(time = time + 1,
```

```
Date = ymd(Date),
         Week = epiweek(Date))
flu_data
## # A tibble: 63 x 4
##
      Date
                   time
                             y Week
##
      <date>
                  <dbl> <dbl> <dbl>
                                   39
##
    1 1918-09-23
                             4
                      1
    2 1918-09-24
                      2
                                   39
##
                             5
                                  39
##
    3 1918-09-25
                      3
                             5
    4 1918-09-26
                      4
                             7
                                   39
##
##
    5 1918-09-27
                             9
                                   39
##
    6 1918-09-28
                      6
                            10
                                   39
    7 1918-09-29
                      7
                             4
##
                                   40
##
    8 1918-09-30
                      8
                            13
                                   40
    9 1918-10-01
                             9
##
                                   40
                     10
## 10 1918-10-02
                            20
                                   40
```

2.1 Daily data

... with 53 more rows

For this graph and the remaining figures, ggplot2 provides the framework for creating visualisations. Here, we show the daily case notifications during the autumn wave of the influenza pandemic (Spanish flu) in the city of San Francisco, California, from 1918 to 1919.



3 Calibration workflow

3.1 Prior information - $\pi(\theta)$

The following list corresponds to the time-independent variables and initial conditions of the SEIR model that will be fitted to the San Francisco data. For each parameter, we indicate their prior knowledge. We construct prior distributions for parameters for which we cannot obtain direct estimates and present them in a density plot.

First of all, as one of the parameters (the recovery rate for hospitalized class) of the model is calculated as follows:

$$\gamma_2 = 1/(1/\gamma_1 - 1/\alpha)$$

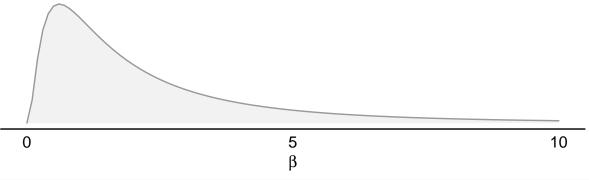
If γ_1 is greater than α , the parameter would take a negative value, which is impossible.

To solve this, the following can be done:

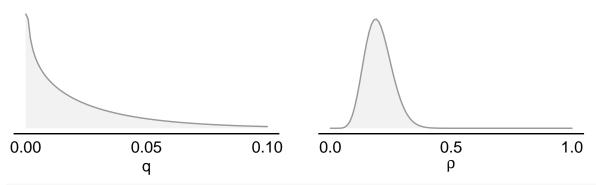
$$\gamma_1 = \omega * \alpha$$

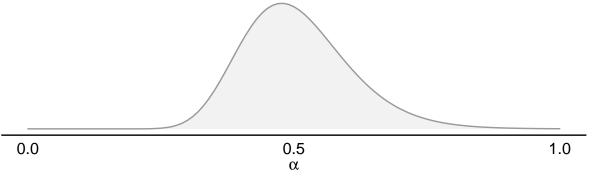
Where ω is a new parameter bounded between 0 and 1. In this way, we always make sure that γ_1 is never greater that α . We would estimate ω instead of γ_1 so that we could work with less stringent priors.

- Initial population: N(0) = 550000 [People]
- Initial death: D(0) = 0 [People]
- Initial recovered: R(0) = 0 [People]
- Initial diagnosed and reported: J(0) = 0 [People]
- Initial asymptomatic and partially infectious: A(0) = 0 [People]
- Initial susceptible: S(0) = N(0) E(0) I(0) [People]
- •
- Birth and natural death rates: $\mu = 1$ / (60 * 365) [1 / day]
- Rate of progression to infectious: k = 1 / 1.9 [1 / day]
- •
- Recovery rate: $\gamma_1 = \omega * \alpha [1 / \text{day}]$
- Recovery rate for hospitalized class: $\gamma_2 = \frac{1}{\frac{1}{\gamma_1} \frac{1}{\alpha}} [1 / \text{day}]$
- Mortality rate: $\delta = \frac{CFP}{1-CFP}(\mu + \gamma_2)$ [1 / day] (being Case fatality proportion CFP = deaths / cases = $\frac{1908}{28310} = 0.067$)
- •
- Initial infected: $I(0) \sim lognormal(1,1)$ [People]
- Initial exposed: $E(0) \sim lognormal(1,1)$ [People]
- Rate of effective contacts per infected individual: $\beta \sim lognormal(0.5, 1)$ [1 / day]
- Relative infectiousness of the asymptomatic class: $q \sim beta(0.75, 30)$
- Proportion of clinical infections: $\rho \sim beta(10, 40)$
- Diagnostic rate $\alpha \sim lognormal(-0.75, 0.1)$ [1 / day]
- Auxiliary parameter: $\omega \sim beta(2,2)$

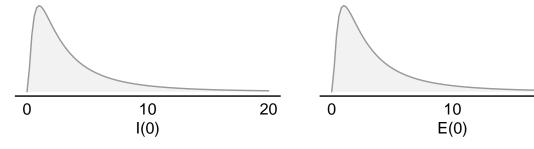


```
g2 \leftarrow ggplot(NULL, aes(c(0, 0.1))) +
  geom_area(stat = "function", fun = dbeta, fill = "grey95",
            colour = "grey60", args = list(shape1 = 0.75, shape2 = 30)) +
  scale_x_continuous(breaks = c(0, 0.05, 0.1)) +
  theme_pubr() +
 labs(y = "",
      x = "q") +
 theme(axis.line.y = element_blank(),
       axis.ticks = element_blank(),
        axis.text.y = element_blank())
g3 \leftarrow ggplot(NULL, aes(c(0, 1))) +
  geom_area(stat = "function", fun = dbeta, fill = "grey95",
            colour = "grey60", args = list(shape1 = 10, shape2 = 40)) +
  scale_x_continuous(breaks = c(0, 0.5, 1)) +
  theme_pubr() +
 labs(y = "",
       x = bquote(rho)) +
  theme(axis.line.y = element_blank(),
        axis.ticks = element_blank(),
       axis.text.y = element_blank())
print(g2 + g3)
```





```
0.0 0.5 1.0 w
```



3.2 Prior predictive checks

First, we describe the SEIR model.

```
# parameters
stp_time <- nrow(flu_data)
parameters <- list(start = 1, stop = stp_time-1, dt = 1/32)

#levels
levels <- list(
    # The entire population is assumed susceptible at the beginning of the pandemic wave
    list(name = "S", equation = "BR-IR-HR1", initValue = 550000),
    list(name = "E", equation = "IR-ER-HR2", initValue = 0),
    list(name = "A", equation = "AR-RR11-HR3", initValue = 0),
    list(name = "I", equation = "PR-DR-RR12-HR4", initValue = 0),
    list(name = "J", equation = "DR-RR2-MR-HR5", initValue = 0),
    list(name = "R", equation = "RR11+RR12+RR2-HR6", initValue = 0),</pre>
```

20

```
list(name = "D", equation = "MR", initValue = 0),
 list(name = "C", equation = "DR", initValue = 0)
# variables
vars <- list(</pre>
 list(name = "gamma_1", equation = "omega*alpha"),
 list(name = "DR", equation = "I*alpha"),
 list(name = "delta", equation = "(cfp/(1-cfp))*(mu+gamma_2)"),
  list(name = "MR", equation = "J*delta"),
  list(name = "gamma_2", equation = "1/((1/gamma_1)-(1/alpha))"),
  list(name = "RR2", equation = "J*gamma_2"),
  list(name = "RR12", equation = "I*gamma 1"),
  list(name = "RR11", equation = "A*gamma_1"),
  list(name = "PR", equation = "rho*ER"),
  list(name = "AR", equation = "(1-rho)*ER"),
  list(name = "ER", equation = "E*k"),
  list(name = "lambda", equation = "((I+J+q*A)*beta)/N"),
  list(name = "IR", equation = "lambda*S"),
  list(name = "HR6", equation = "mu*R"),
  list(name = "HR5", equation = "mu*J"),
  list(name = "HR4", equation = "mu*I"),
  list(name = "HR3", equation = "mu*A"),
  list(name = "HR2", equation = "mu*E"),
 list(name = "HR1", equation = "mu*S"),
 list(name = "BR", equation = "mu*N"),
 list(name = "N", equation = "S+E+I+A+J+R")
variables <- arrange_variables(vars)</pre>
# constants
# According to the tests performed, these initial values do not affect the first part of the analysis.
# Check for the second part
constants <- list(</pre>
  list(name = "mu", value = 1/(60*365)), # As specified in the paper
  list(name = "beta", value = 1.25),
 list(name = "q", value = 0.02),
  list(name = "k", value = 1/1.9), # As specified in the paper
  list(name = "rho", value = 0.36),
  # list(name = "gamma_1", value = 0.4),
 list(name = "omega", value = 0.5),
  list(name = "alpha", value = 1),
 list(name = "cfp", value = 0.067), # As specified in the paper
 list(name = "IO", value = 0),
  list(name = "E0", value = 0)
model_structure <- list(parameters = parameters,</pre>
                        levels = levels,
                        variables = variables,
                        constants = constants)
deSolve_components <- get_deSolve_elems(model_structure)</pre>
```

```
model <- list(
  description = list(constants = constants),
  deSolve_components = deSolve_components
)</pre>
```

Then, we draw 500 samples from the prior distribution and simulate the model with these inputs. Given the computational burden of this process, we save the results in an RDS file.

```
file_path <- file.path(fldr, "prior_sims.rds")</pre>
           <- 500
n_sims
pop_size
           <- 550000
if(!file.exists(file_path)) {
  set.seed(300194)
  E_0_sims
                 <- rlnorm(n_sims, 1, 1)
  I_0_{sims}
               <- rlnorm(n_sims, 1, 1)</pre>
  beta_sims
               <- rlnorm(n_sims, 0.5, 1)
                <- rbeta(n_sims, 0.75, 30)</pre>
  q_sims
                <- rbeta(n_sims, 10, 40)</pre>
  rho_sims
               <- rlnorm(n_sims, -0.7, 0.2)</pre>
  alpha_sims
  omega_sims
                 <- runif(n_sims, 0.01, 0.99)</pre>
  consts_df <- data.frame(beta</pre>
                                      = beta sims,
                                      = q_sims,
                             q
                             rho
                                      = rho_sims,
                             omega
                                      = omega_sims,
                             alpha
                                      = alpha_sims)
  stocks_df <- data.frame(S = pop_size - E_0_sims - I_0_sims,
                             E = E_0_{sims}
                             I = I_0_{sims}
                             C = I_0_{sims}
  sens_o <- sd_sensitivity_run(model$deSolve_components, start_time = 0,</pre>
                                 stop_time = stp_time, timestep = 1 / 32,
                                 multicore = TRUE, n_cores = 4,
                                 integ_method = "rk4", stocks_df = stocks_df,
                                 consts_df = consts_df)
  saveRDS(sens_o, file_path)
} else {
  sens_o <- readRDS(file_path)</pre>
```

We check if the data obtained (sens_o) contain any NA values

```
anyNA(sens_o)
```

[1] FALSE

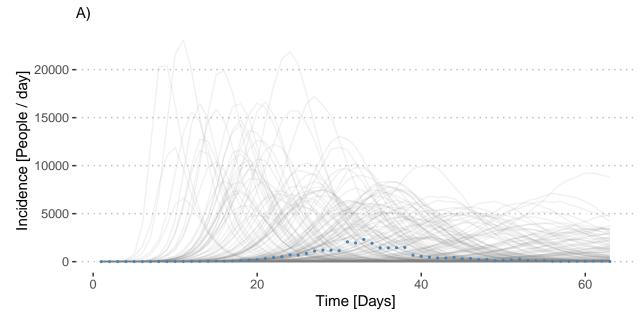
And we show the values of the variables to see at a glance the range of values in which they move (minimum, maximum, average value...).

```
summary(sens_o)
```

```
##
        time
                                                               Α
                   Min. :
   Min. : 0.00
                                                  0.00
##
                                5.9
                                      Min. :
                                                                      0.0
                                                         \mathtt{Min}.
   1st Qu.:15.75
                   1st Qu.:546028.7
                                      1st Qu.:
                                                  0.07
                                                         1st Qu.:
   Median :31.50
                   Median :549931.2
                                      Median :
                                                  4.67
                                                                      7.5
##
                                                         Median:
##
   Mean :31.50
                   Mean :469079.4
                                      Mean : 4605.90
                                                         Mean : 17669.4
##
   3rd Qu.:47.25
                   3rd Qu.:549983.5
                                      3rd Qu.:
                                                181.24
                                                         3rd Qu.:
                                                                    653.5
   Max. :63.00
                         :549999.4
                                             :292989.00
                   Max.
                                      Max.
                                                         Max. :423648.6
##
         Ι
                            J
                                               R
                                                                  D
##
   Min. :
               0.00
                      Min. :
                                   0.00
                                          Min. :
                                                      0.0
                                                            Min. :
                                                                        0.000
##
   1st Qu.:
               0.01
                      1st Qu.:
                                   0.01
                                          1st Qu.:
                                                     11.1
                                                            1st Qu.:
                                                                        0.160
   Median :
               0.79
                      Median :
                                   0.77
                                          Median :
                                                     40.4
                                                            Median :
                                                                        0.529
   Mean : 813.74
                      Mean : 3292.57
                                          Mean : 53966.7
                                                            Mean : 572.359
##
##
   3rd Qu.:
              28.83
                      3rd Qu.:
                                51.29
                                          3rd Qu.: 1222.8
                                                            3rd Qu.: 11.664
                      Max. :159863.95
                                          Max. :546642.8
                                                            Max. :10047.971
##
   Max. :43965.77
##
         С
                                               DR
                          gamma_1
                                                                gamma_2
##
   Min. :
                0.10
                       Min. :0.005775
                                          Min. :
                                                     0.000
                                                             Min. : 0.00585
                5.40
                                          1st Qu.:
                                                     0.005
##
   1st Qu.:
                       1st Qu.:0.122716
                                                             1st Qu.: 0.16214
   Median :
               15.37
                       Median: 0.243265
                                          Median :
                                                     0.380
                                                             Median: 0.50080
##
   Mean : 11839.53
                       Mean :0.251356
                                          Mean : 391.707
                                                             Mean : 1.74781
##
   3rd Qu.:
              362.27
                       3rd Qu.:0.374964
                                          3rd Qu.:
                                                    14.094
                                                             3rd Qu.: 1.46937
##
   Max. :194074.97
                       Max. :0.667106
                                          Max. :23725.558
                                                             Max. :46.74746
##
        RR2
                            RR12
                                               RR11
                                                                   ER
                       Min. :
                                           Min. :
                                                                  :
##
   Min. :
               0.000
                                   0.000
                                                      0.00
                                                                          0.00
                                                             \mathtt{Min}.
               0.006
                       1st Qu.:
                                                             1st Qu.:
##
   1st Qu.:
                                   0.003
                                           1st Qu.:
                                                      0.06
                                                                          0.04
##
   Median :
               0.275
                       Median :
                                   0.137
                                           Median:
                                                      1.38
                                                             Median :
                                                                          2.46
   Mean : 300.166
                       Mean : 115.106
                                           Mean : 1569.97
                                                             Mean : 2424.16
             12.166
                                           3rd Qu.: 90.61
                                                                       95.39
##
   3rd Qu.:
                       3rd Qu.:
                                   3.864
                                                             3rd Qu.:
   Max. :15621.565
                                                             Max. :154204.74
##
                       Max. :16214.361
                                           Max. :67041.21
                            HR5
##
       HR6
                                             HR4
                                                                 HR3
                       Min. :0.000000
                                          Min. :0.000000
                                                             Min. : 0.000000
   Min. : 0.000000
   1st Qu.: 0.000506
                                                             1st Qu.: 0.000009
##
                       1st Qu.:0.000000
                                          1st Qu.:0.0000005
##
   Median: 0.001843
                       Median :0.000035
                                          Median :0.0000362
                                                             Median: 0.000343
   Mean : 2.464233
                       Mean :0.150345
                                          Mean :0.0371570
                                                             Mean : 0.806821
                       3rd Qu.:0.002342
##
   3rd Qu.: 0.055837
                                          3rd Qu.:0.0013166
                                                             3rd Qu.: 0.029842
##
   Max. :24.960859
                       Max. :7.299724
                                          Max. :2.0075696
                                                             Max. :19.344683
##
       HR2
                           HR1
                                                N
                                                               delta
##
   Min. : 0.000000
                       Min. : 0.000269
                                           Min. :539952
                                                           Min. :0.000423
##
   1st Qu.: 0.000003
                       1st Qu.:24.932817
                                           1st Qu.:549988
                                                           1st Qu.:0.011647
   Median: 0.000213
                       Median :25.111015
                                           Median :550000
                                                           Median :0.035966
##
   Mean : 0.210315
                                           Mean :549428
##
                       Mean :21.419149
                                                           Mean :0.125516
   3rd Qu.: 0.008276
                       3rd Qu.:25.113401
                                           3rd Qu.:550000
                                                           3rd Qu.:0.105521
   Max. :13.378493
                       Max. :25.114126
                                           Max. :550000
                                                           Max. :3.357002
##
##
         MR
                            PR
                                               AR
                                                                 lambda
##
              0.0000
                                   0.00
                                                             Min. :0.000000
   Min. :
                       Min. :
                                                      0.00
                                          Min. :
              0.0004
   1st Qu.:
                       1st Qu.:
                                   0.01
                                          1st Qu.:
                                                      0.03
                                                             1st Qu.:0.000000
   Median :
             0.0198
                                   0.46
                                                             Median :0.000005
##
                       Median :
                                          Median:
                                                      1.97
##
   Mean : 21.5661
                       Mean : 514.47
                                          Mean : 1909.69
                                                             Mean :0.038166
   3rd Qu.: 0.8741
                       3rd Qu.: 19.48
                                          3rd Qu.:
                                                     75.33
                                                             3rd Qu.:0.000617
##
   Max. :1121.8093
                       Max. :39060.49
                                          Max. :115144.25
                                                             Max. :4.470358
##
         IR
                             BR
                                                               beta
                                             mu
##
         :
                0.00
                             :24.66
                                            :4.566e-05
                                                          Min. : 0.04298
                       Min.
   Min.
                                       Min.
##
   1st Qu.:
                0.02
                       1st Qu.:25.11
                                       1st Qu.:4.566e-05
                                                          1st Qu.: 0.73783
                                       Median :4.566e-05
##
   Median :
                2.31
                       Median :25.11
                                                          Median: 1.56744
                                       Mean :4.566e-05
##
   Mean : 2463.75
                       Mean :25.09
                                                          Mean : 2.52610
```

```
3rd Qu.:
              90.39
                       3rd Qu.:25.11
                                       3rd Qu.:4.566e-05
                                                           3rd Qu.: 2.79864
##
   Max.
         :291191.17
                            :25.11
                                       Max.
                                             :4.566e-05
                                                                 :41.38231
                       Max.
                                                           Max.
##
         q
                             k
                                             rho
                                                              omega
##
          :7.811e-05
                       Min.
                              :0.5263
                                       Min.
                                               :0.07457
                                                          Min.
                                                                 :0.01303
  Min.
##
   1st Qu.:6.352e-03
                       1st Qu.:0.5263
                                       1st Qu.:0.16445
                                                          1st Qu.:0.25914
##
  Median :1.630e-02
                       Median :0.5263
                                       Median :0.19684
                                                          Median :0.49874
  Mean :2.522e-02
                       Mean :0.5263
                                        Mean :0.19996
                                                          Mean :0.50033
   3rd Qu.:3.565e-02
                       3rd Qu.:0.5263
                                        3rd Qu.:0.23209
                                                          3rd Qu.:0.74175
##
##
   Max.
          :1.495e-01
                       Max.
                            :0.5263
                                        Max.
                                               :0.42402
                                                          Max.
                                                                 :0.98887
##
                                          ΙO
                                                      ΕO
                                                                 iter
       alpha
                         cfp
  Min.
          :0.2632
                    Min.
                           :0.067
                                    Min.
                                           :0
                                                Min. :0
                                                            Min. : 1.0
                                                            1st Qu.:125.8
##
  1st Qu.:0.4385
                    1st Qu.:0.067
                                    1st Qu.:0
                                                1st Qu.:0
## Median :0.4918
                    Median :0.067
                                                Median :0
                                    Median :0
                                                            Median :250.5
## Mean
         :0.5067
                          :0.067
                                    Mean
                                                Mean
                                                                  :250.5
                    Mean
                                          :0
                                                      :0
                                                            Mean
## 3rd Qu.:0.5632
                    3rd Qu.:0.067
                                    3rd Qu.:0
                                                3rd Qu.:0
                                                            3rd Qu.:375.2
                                                                   :500.0
## Max.
          :0.8424
                    Max.
                          :0.067
                                    Max.
                                          :0
                                                Max.
                                                      :0
                                                            Max.
file_path <- file.path(fldr, "sens_inc.rds")</pre>
if(!file.exists(file_path)) {
 set.seed(346282)
 sens_inc <- predictive_checks(n_sims, sens_o) # dist = "pois"</pre>
 saveRDS(sens_inc, file_path)
} else {
 sens inc <- readRDS(file path)</pre>
}
```

Here, we plot the results of the prior predictive checks. Dots indicate the actual data.



We can see that there are simulations that do not present changes in any of the compartments as shown in the following image:

```
sens_o5 <- filter(sens_o, iter == 5)

plt <- sens_o5[ , c("time", "S", "E", "A", "I", "J", "R", "D")]
plt <- melt(plt , id.vars = 'time', variable.name = 'compartment')

ggplot(plt, aes(x = time, y = value)) +
  geom_line(aes(colour = compartment)) +
  theme_pubclean() +
  labs(subtitle = "iter = 5")</pre>
```





4e+05 **-**

value

2e+05 -----



But there are also simulations that do show changes in the compartments. For example, iteration 250:

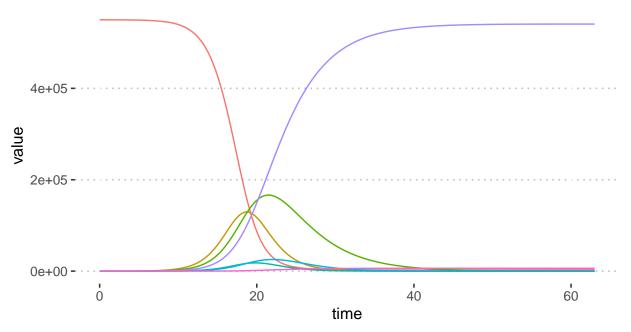
```
sens_o250 <- filter(sens_o, iter == 250)

plt <- sens_o250[ , c("time", "S", "E", "A", "I", "J", "R", "D")]
plt <- melt(plt , id.vars = 'time', variable.name = 'compartment')

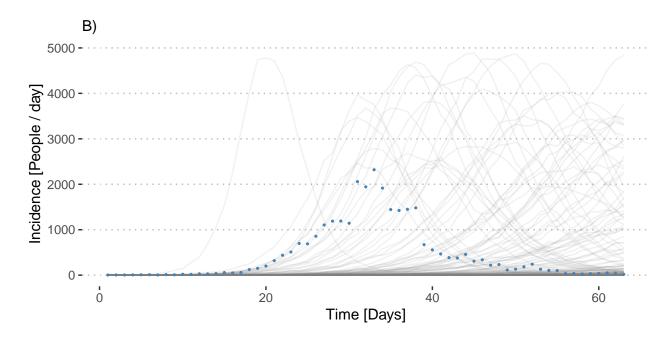
ggplot(plt, aes(x = time, y = value)) +
  geom_line(aes(colour = compartment)) +
  theme_pubclean() +
  labs(subtitle = "iter = 250")</pre>
```







In the above simulations, it can be seen that the prior distribution produces simulations far off the actual data. To have a closer inspection, we filter out trajectories whose peak is greater than 5000 new cases in a day.



3.2.1 Measurement model

In this section, we discuss the choice of the measurement model and how we use prior predictive checks to guide such a decision. Initially, we opt for the default choice, i.e., the normal distribution. This choice implies that, at every time step, the difference between the measurement and the true value (error) follows a normal distribution. Additionally, this distribution entails that the error across all time steps is similar (homoscedasticity). In other words, the magnitude of the error is indifferent to the magnitude of the true value, an assumption that may seem unrealistic. As could be expected, the normal distribution adds a new unknown, the standard deviation (δ). To test this model, we assume $\delta \sim Cauchy(0,1)$, and simulate 500 trajectories.

Next, we consider the Poisson distribution given that it has been used in the empirical treatment of count data, particularly concerning counts of events per unit of time. This distribution lifts the constraint of equal variance across measurements as the error magnitude is proportional to the true number of reported individuals at each time step. As with the normal distribution, we generate 500 simulations.

Finally, to count data, the Negative Binomial distribution is an alternative to the Poisson should the latter fail to capture overdispersion in the data. We model such overdispersion in the Negative Binomial's scale parameter ($\phi \sim \text{Half-normal}(0,1)$). We can see that the trajectories generated by the Negative Binomial are more dispersed than the ones produced by the Poisson distribution. Nevertheless, in this case, they do not provide a more accurate representation of the data. Consequently, we adopt the Poisson distribution as the measurement model.

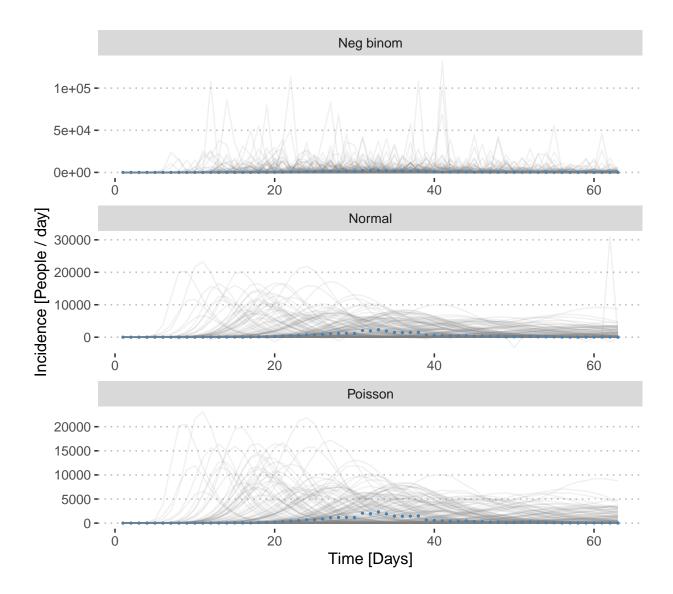
In addition, in the "The reproduction number for influenza" article, the following is stated:

"The stochastic version of the model is formulated as usual by taking the rates on the right-hand side of the population equations to determine the mean change λ over the time τ of the several population classes, which is in practice extracted from a probability distribution $P[\lambda]$ with average λ . In the estimation procedure described below, P is taken to be a Poisson distribution, which is the maximal entropy distribution for a discrete process for which only the average is known. If information is also available about the statistics of fluctuations, a more general distribution, such as a Negative Binomial, can be employed instead."

```
set.seed(102667)

pois_meas <- sens_inc %>% mutate(dist = "Poisson")
```

```
# Normal distributed measurements
norm_meas <- predictive_checks(n_sims, sens_o, "norm") %>%
       mutate(dist = "Normal")
# Negative binomial measurements
{\tt nbinom\_meas} \begin{tabular}{ll} \begin{t
        mutate(dist = "Neg binom")
meas_df <- bind_rows(pois_meas, norm_meas, nbinom_meas)</pre>
n1 \leftarrow ggplot(meas_df, aes(x = time, y = y)) +
        geom_line(aes(group = iter), alpha = 0.1, colour = "grey50") +
        geom_point(data = flu_data, aes(x = time, y = y), size = 0.5,
                                                    colour = "steelblue") +
        facet_wrap(~dist, ncol = 1, scales = "free") +
        theme_pubclean() +
        labs(y
                                             = "Incidence [People / day]",
                                                = "Time [Days]",
                           subtitle = "")
print(n1)
```



3.3 Fitting

For calibrating SD models in Stan, it is necessary to create a file written in Stan's own language. This kind of file structures the code in blocks. For this example, five blocks are necessary: Functions, data, parameters, transformed parameters, and model. Here model refers to prior distributions and the likelihood (measurement model). The SD model is considered a function, which can be constructed from the model specification. This translation is possible thanks to the function stan_ode_function_2 (a modification of the stan_ode_function from the readsdr package). Similarly, readsdr supports the creation of the data block. The other blocks must be built manually.

```
stan_data <- stan_data("y", type = "int", inits = FALSE)</pre>
stan_params <- paste(</pre>
 "parameters {",
 " real<lower = 0>
                              beta;",
 " real<lower = 0, upper = 1> q;",
 " real<lower = 0, upper = 1> rho;",
 " real<lower = 0, upper = 1> omega;",
 " real<lower = 0, upper = 1> alpha;",
 " real<lower = 0, upper = 55000> I0;",
 " real<lower = 0, upper = 55000> E0;",
"}", sep = "\n")
stan_tp <- paste(</pre>
 "transformed parameters{",
 " vector[n_difeq] o[n_obs]; // Output from the ODE solver",
 " real x[n_obs];",
 " vector[n_difeq] x0;",
 " real params[n_params];",
 " x0[1] = 550000 - E0 - I0;",
 " x0[2] = E0;",
 " x0[3] = 0;",
 " x0[4] = I0;",
 " x0[5] = 0;",
 " x0[6] = 0;",
 " x0[7] = 0;",
 " x0[8] = I0;",
 " params[1] = beta;",
 " params[2] = q;",
 " params[3] = rho;",
 " params[4] = omega;",
 " params[5] = alpha;",
 fun_exe_line,
 " x[1] = o[1, 8] - x0[8];",
 " for (i in 1:n_obs-1) {",
 " x[i + 1] = o[i + 1, 8] - o[i, 8] + 1e-5;",
 " }",
 "}", sep = "\n")
stan_model <- paste(</pre>
 "model {",
 " omega ~ uniform(0.01, 0.99);",
 " beta
          ~ lognormal(0.5, 1);",
 " q
            ~ beta(0.75, 30);",
 " rho
            ~ beta(10, 40);",
 " alpha ~ lognormal(-0.7, 0.2);",
 " IO
            ~ lognormal(1, 1);",
 " E0
            ~ lognormal(1, 1);",
 " y
            ~ poisson(x);",
 "}",
 sep = "\n")
stan_gc <- paste(</pre>
```

We show below the code contained in the Stan file.

```
cat(stan_text)
```

```
## functions {
##
     vector SEIR(real time, vector y, real[] params) {
##
       vector[8] dydt;
##
       real gamma_1;
       real DR;
##
       real gamma_2;
##
##
       real RR2;
##
       real RR12;
       real RR11;
##
##
       real ER;
##
       real HR6;
##
       real HR5;
       real HR4;
##
##
       real HR3;
##
       real HR2;
##
       real HR1;
##
       real N;
##
       real delta;
       real MR;
##
##
       real PR;
##
       real AR;
##
       real lambda;
##
       real IR;
##
       real BR;
       gamma_1 = params[4]*params[5];
##
       DR = y[4]*params[5];
##
##
       gamma_2 = 1/((1/gamma_1)-(1/params[5]));
       RR2 = y[5]*gamma_2;
##
##
       RR12 = y[4]*gamma_1;
##
       RR11 = y[3]*gamma_1;
##
       ER = y[2]*0.5263157895;
##
       HR6 = 4.56621e-05*y[6];
##
       HR5 = 4.56621e-05*y[5];
##
       HR4 = 4.56621e-05*y[4];
##
       HR3 = 4.56621e-05*y[3];
```

```
##
       HR2 = 4.56621e-05*v[2];
##
       HR1 = 4.56621e-05*y[1];
       N = y[1]+y[2]+y[4]+y[3]+y[5]+y[6];
##
##
       delta = (0.067/(1-0.067))*(4.56621e-05+gamma_2);
##
       MR = y[5]*delta;
       PR = params[3]*ER;
##
##
       AR = (1-params[3])*ER;
       lambda = ((y[4]+y[5]+params[2]*y[3])*params[1])/N;
##
##
       IR = lambda*y[1];
##
       BR = 4.56621e-05*N;
##
       dydt[1] = BR-IR-HR1;
##
       dydt[2] = IR-ER-HR2;
       dydt[3] = AR-RR11-HR3;
##
##
       dydt[4] = PR-DR-RR12-HR4;
##
       dydt[5] = DR-RR2-MR-HR5;
##
       dydt[6] = RR11+RR12+RR2-HR6;
##
       dydt[7] = MR;
       dvdt[8] = DR;
##
##
       return dydt;
##
## }
## data {
##
     int<lower = 1> n_obs;
     int<lower = 1> n_params;
##
##
     int<lower = 1> n_difeq;
##
     int y[n_obs];
##
     real t0;
##
     real ts[n_obs];
## }
## parameters {
##
     real<lower = 0>
                                 beta;
##
     real<lower = 0, upper = 1> q;
     real<lower = 0, upper = 1> rho;
##
##
     real<lower = 0, upper = 1> omega;
##
     real<lower = 0, upper = 1> alpha;
##
     real<lower = 0, upper = 55000> I0;
     real<lower = 0, upper = 55000> E0;
##
## }
## transformed parameters{
     vector[n_difeq] o[n_obs]; // Output from the ODE solver
##
##
     real x[n obs];
     vector[n_difeq] x0;
##
     real params[n_params];
##
##
     x0[1] = 550000 - E0 - I0;
##
     x0[2] = E0;
     x0[3] = 0;
##
##
     x0[4] = I0;
##
     x0[5] = 0;
     x0[6] = 0;
##
##
     x0[7] = 0;
##
     x0[8] = I0;
##
    params[1] = beta;
##
    params[2] = q;
##
     params[3] = rho;
```

```
##
     params[4] = omega;
##
     params[5] = alpha;
##
     o = ode_rk45(SEIR, x0, t0, ts, params);
     x[1] = o[1, 8] - x0[8];
##
##
     for (i in 1:n_obs-1) {
##
       x[i + 1] = o[i + 1, 8] - o[i, 8] + 1e-5;
##
     }
## }
## model {
             ~ uniform(0.01, 0.99);
##
     omega
##
     beta
             ~ lognormal(0.5, 1);
##
             ~ beta(0.75, 30);
     q
             ~ beta(10, 40);
##
     rho
##
             ~ lognormal(-0.7, 0.2);
##
     ΙO
             ~ lognormal(1, 1);
##
     ΕO
             ~ lognormal(1, 1);
##
             ~ poisson(x);
     У
## }
## generated quantities {
     real log_lik;
##
     log_lik = poisson_lpmf(y | x);
## }
```

To perform the calibration via HMC, we must provide Stan with the calibration parameters. We specify 2,000 iterations (1,000 for warming-up and 1,000 for sampling) and four chains. We also supply the number of parameters to be fitted for the SD model, the number of stocks (n_difeq), the simulation time, and San Francisco's data.

```
# Path to cmdstan
set_cmdstan_path("/Users/redondo/cmdstan")
          <- "./backup_objs/san_francisco_ext_202210"</pre>
file_path <- file.path(fldr, "fit.rds")</pre>
if(!file.exists(file_path)) {
  stan_d <- list(n_obs = nrow(flu_data),
                         = flu_data$y,
               n_{params} = 5,
               n_{difeq} = 8,
                t0
                         = 0,
                         = 1:length(flu_data$y))
                ts
mod <- cmdstan_model(stan_filepath)</pre>
fit <- mod$sample(data</pre>
                                    = stan_d,
                                    = 553616.
                   chains
                                    = 4
                   parallel_chains = 4,
                   iter_warmup
                                    = 1500,
                   iter_sampling
                                    = 500.
                                    = 5,
                   refresh
                   save_warmup
                                    = TRUE,
                   output dir
                                    = fldr)
                   # adapt_delta
                                      = 0.99
                                      = 0.1
                   # step_size
```

```
fit$save_object(file_path)
} else {
  fit <- readRDS(file_path)
}</pre>
```

We note that the execution ends with the following information:

\texttt{ All 4 chains finished successfully.

Mean chain execution time: 5432.4 seconds.

Total execution time: 5758.2 seconds. }

Although the model is complex, execution has taken too long.

We generated this file from \$fit\$cmdstan_diagnose()

3.3.1 Diagnostics

Processing complete.

Before inspecting the samples, Stan returns global diagnostics to the user about the sampling process. It is expected that the result is free from divergent iterations or indications of pathological behaviour from the Bayesian Fraction of Missing Information metric. Also, iterations that saturate the maximum tree depth indicate a complex posterior surface. The Stan manual provides intuitive interpretations of these metrics.

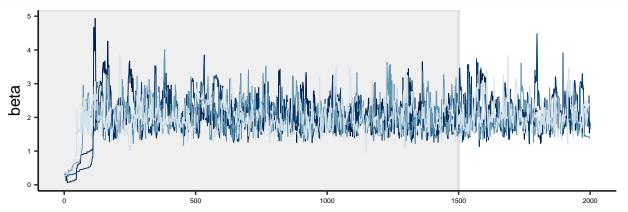
```
fileName <- file.path(fldr, "diags.txt")</pre>
if(!file.exists(fileName)) {
  diagnosis <- fit$cmdstan_diagnose()</pre>
  writeLines(diagnosis$stdout, fileName)
} else {
  readChar(fileName, file.info(fileName)$size) %>% cat()
}
## Processing csv files: /Users/redondo/R/SDR_Bayes-master/backup_objs/san_francisco_ext_202209/flu_poi
## , /Users/redondo/R/SDR_Bayes-master/backup_objs/san_francisco_ext_202209/flu_poisson_new-20221014085
## , /Users/redondo/R/SDR_Bayes-master/backup_objs/san_francisco_ext_202209/flu_poisson_new-20221014085
## , /Users/redondo/R/SDR_Bayes-master/backup_objs/san_francisco_ext_202209/flu_poisson_new-20221014085
##
##
## Checking sampler transitions treedepth.
## 4 of 8000 (0.05%) transitions hit the maximum treedepth limit of 10, or 2^10 leapfrog steps.
## Trajectories that are prematurely terminated due to this limit will result in slow exploration.
## For optimal performance, increase this limit.
##
## Checking sampler transitions for divergences.
## 1107 \text{ of } 8000 \text{ (13.84\%)}  transitions ended with a divergence.
## These divergent transitions indicate that HMC is not fully able to explore the posterior distribution
## Try increasing adapt delta closer to 1.
## If this doesn't remove all divergences, try to reparameterize the model.
## Checking E-BFMI - sampler transitions HMC potential energy.
## E-BFMI satisfactory.
## Effective sample size satisfactory.
## Split R-hat values satisfactory all parameters.
```

As we can see, the diagnostics indicate that we must change either the priors, the model or some of its parameters if we want to achieve satisfactory results.

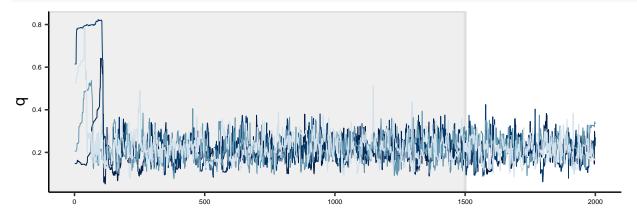
3.3.1.1 Trace plots

A common approach to inspect calibration results is to check for convergence in trace plots.

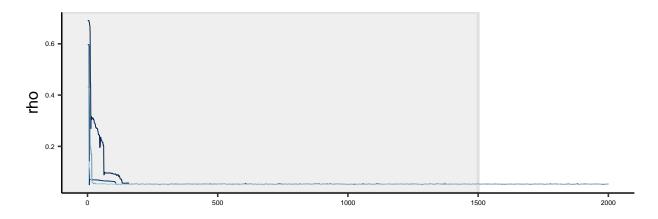
```
b1 <- trace_plot_2(fit, pars = c("beta"), n_samples = 2000, n_warmup = 1500) +
    theme(axis.text = element_text(size = 5))
print(b1)</pre>
```



```
b2 <- trace_plot_2(fit, pars = c("q"), n_samples = 2000, n_warmup = 1500) +
    theme(axis.text = element_text(size = 5))
print(b2)</pre>
```

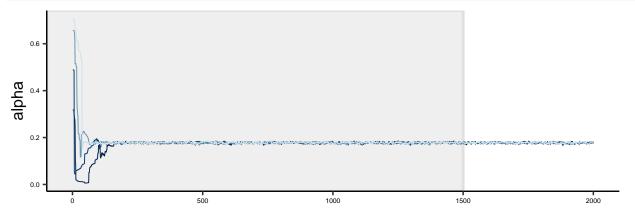


```
b3 <- trace_plot_2(fit, pars = c("rho"), n_samples = 2000, n_warmup = 1500) +
    theme(axis.text = element_text(size = 5))
print(b3)</pre>
```

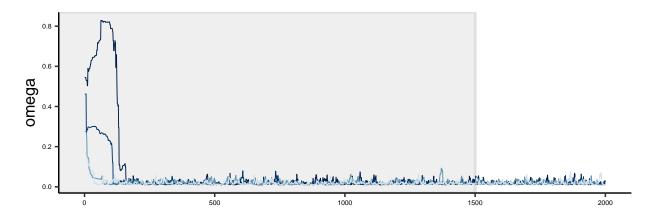


```
Chain -1 - 2 - 3 - 4
```

```
b5 <- trace_plot_2(fit, pars = c("alpha"), n_samples = 2000, n_warmup = 1500) +
    theme(axis.text = element_text(size = 5))
print(b5)</pre>
```

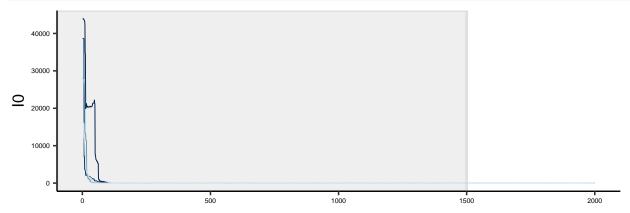


```
b4 <- trace_plot_2(fit, pars = c("omega"), n_samples = 2000, n_warmup = 1500) +
    theme(axis.text = element_text(size = 5))
print(b4)</pre>
```

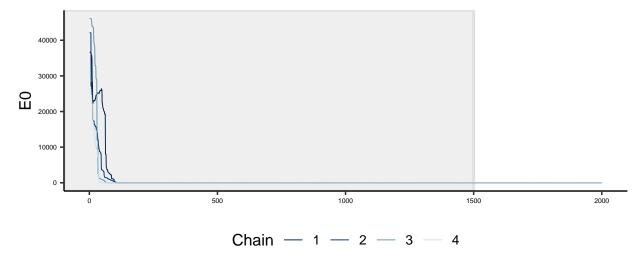


Chain — 1 — 2 — 3 — $\frac{1}{4}$

```
b6 <- trace_plot_2(fit, pars = c("IO"), n_samples = 2000, n_warmup = 1500) +
    theme(axis.text = element_text(size = 5))
print(b6)</pre>
```



Chain -1 - 2 - 3 - 4



We can see...

3.3.1.2 Potential scale reduction factor (\hat{R}) & Effective Sample Size (\hat{n}_{eff})

 \widehat{R} is a convergence diagnostic, which compares the between- and within-chain estimates for model parameters and other univariate quantities of interest. If chains have not mixed well, R-hat is larger than 1. It is recommended to run at least four chains by default and only using the sample if R-hat is less than 1.01 [@Vehtari_2021]. Stan reports R-hat, which is the maximum of rank normalized split-R-hat and rank normalized folded-split-R-hat, which works for thick-tailed distributions and is sensitive also to differences in scale.

For each parameter θ , we split each chain from the sampling phase in two halves. That is, from **four** chains of 1000 draws each one, we obtain **eight** split chains of 500 draws each one. Then, we label the simulations as $\theta_{ij} (i=1,...,N;j=1,...,M)$, where N is the number of samples per split chain, M is the number of split chains, and S=NM is the total number of draws from all chains. We subsequently transform these simulations to their corresponding rank normalized values z_{ij} . According to @Vehtari_2021, we replace each value θ_{ij} by its rank r_{ij} within the pooled draws from all chains. Second, we transform ranks to normal scores using the inverse normal transformation and a fractional offset via Equation 1:

$$z_{ij} = \Phi^{-1} \left(\frac{r_{ij} - 3/8}{S - 1/4} \right) \tag{1}$$

Using these normal scores, we calculate \hat{R} following the formulation proposed by @gelman2013bayesian. Initially, we compute B and W, the between- and within-sequence variances, respectively:

$$B = \frac{N}{M-1} \sum_{j=1}^{M} (\bar{z}_{.j} - \bar{z}_{..})^2, \text{ where } \bar{z}_{.j} = \frac{1}{n} \sum_{i=1}^{n} z_{ij}, \ \bar{z}_{..} = \frac{1}{M} \sum_{j=1}^{M} \bar{z}_{.j}$$
 (2)

$$W = \frac{1}{M} \sum_{j=1}^{M} s_j^2, \text{ where } s_j^2 = \frac{1}{N-1} \sum_{i=1}^{n} (z_{ij} - \bar{z}_{.j})^2$$
 (3)

Then, we can estimate $\widehat{var}^+(\theta|y)$, the marginal posterior variance of the parameter, by a weighted average of W and B:

$$\widehat{var}^{+}(\theta|y) = \frac{N-1}{N}W + \frac{1}{N}B\tag{4}$$

From (3) and (4), we obtain the rank normalized split \hat{R} :

$$\widehat{R} = \sqrt{\frac{\widehat{var}^+(\theta|y)}{W}} \tag{5}$$

To obtain the rank normalized folded-split \widehat{R} , we simply transform the simulations (Equation 6) and then apply the procedure described above (Equations 1-5).

$$\zeta_{ij} = |\theta_{ij} - median(\theta)| \tag{6}$$

For MCMC draws, we define the estimated effective sample size as

$$\hat{n}_{eff} = \frac{MN}{1 + 2\sum_{t=1}^{T} \hat{\rho}_t} \tag{7}$$

This quantity requires an estimate of the sum of the correlations ρ up to lag T (the first odd positive integer for which $\hat{\rho}_{T+1} + \hat{\rho}_{T+2}$ is negative). The correlation at any specific lag t (Equation 8) depends upon the estimate \widehat{var}^+ and the Variogram at each t (Equation 9).

$$\hat{\rho_t} = 1 - \frac{V_t}{2\widehat{var}^+} \tag{8}$$

$$V_t = \frac{1}{M(N-t)} \sum_{j=1}^{M} \sum_{i=t+1}^{N} (z_{i,j} - z_{i-t,j})^2$$
(9)

We use the term *bulk effective sample size* to refer to the effective sample size based on the rank normalized draws. To ensure reliable estimates of variances and autocorrelations needed for \hat{R} and \hat{n}_{eff} , @Vehtari_2021 recommend that the rank-normalized effective sample size must be greater than 400 (100 per chain).

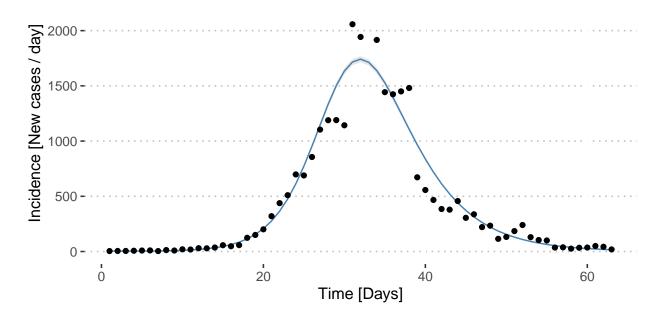
par	ess_bulk	rhat
beta	189.5047	1.033044
q	191.6735	1.033221
rho	299.5844	1.006239
$gamma_1$	398.9158	1.004438
alpha	263.1130	1.004162
I(0)	211.4549	1.026631
E(0)	516.4998	1.007880

As we can see, neither the values of the effective sample size nor the values of R meet the desired minimums to be able to use the estimations.

3.3.1.3 Check deterministic fit

Once the computation has been deemed satisfactory, we subsequently check that the model's expected value captures the underlying trajectory of the data. The reader should take into account that in each sampling iteration, Stan generates a trajectory from the SD model. We compare these simulated time series against the measured incidence (dots) to visually examine whether the trend is consistent with the data. The solid blue line denotes the mean trajectory, and the grey shaded area indicates the 95 % credible interval.

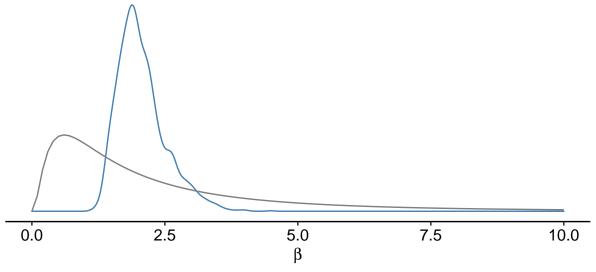
```
posterior_df <- fit$draws() %>% as_draws_df()
# We add the fixed constants
samples_normal <- posterior_df[ , pars_hat] %>%
  mutate(mu = 1/(60*365), k = 1/1.9, cfp = 0.067) \%
  mutate(
   gamma_1 = omega*alpha,
   gamma 2 = 1/((1/gamma 1) - (1/alpha)),
   delta = (cfp/(1-cfp))*(mu+gamma_2),
   R0 = (beta*k)/(k+mu) * (rho*((1/(gamma 1+alpha+mu))+(alpha/((gamma 1+alpha+mu)*(gamma 2+delta+mu)))
   0 = alpha / (alpha+gamma_1+mu),
   11 = "Normal"
         )
y_hat_df_norm <- extract_timeseries_var("x", posterior_df)</pre>
summary_df <- y_hat_df_norm %>% group_by(time) %>%
  summarise(lb = quantile(value, c(0.025, 0.975)[[1]]),
            ub = quantile(value, c(0.025, 0.975)[[2]]),
            y = mean(value))
ggplot(summary_df, aes(x = time, y)) +
  geom_ribbon(aes(ymin = lb, ymax = ub), fill = "grey90") +
  geom_line(colour = "steelblue") +
  geom_point(data = flu_data) +
  theme pubclean() +
  labs(y = "Incidence [New cases / day]", x = "Time [Days]")
```

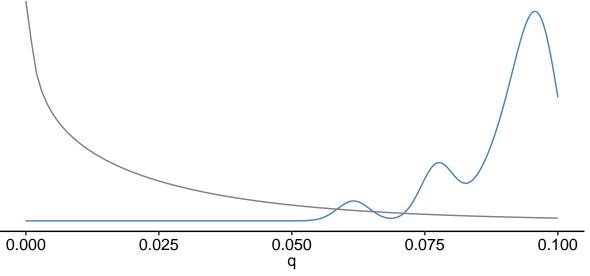


3.3.2 Posterior information

3.3.2.1 Prior & posterior comparison

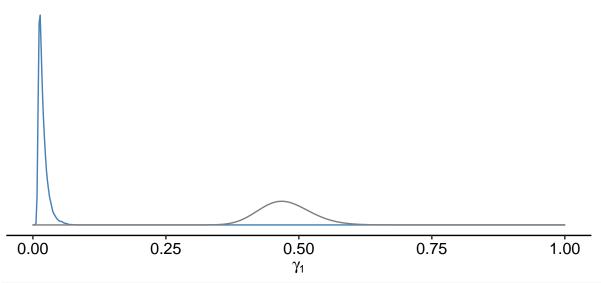
A critical goal of model calibration is to gain information from the data about the parameters of interest. One way to accomplish such a purpose is through the comparison of marginal prior and marginal posterior distributions. Namely, we evaluate the knowledge acquired from the process.

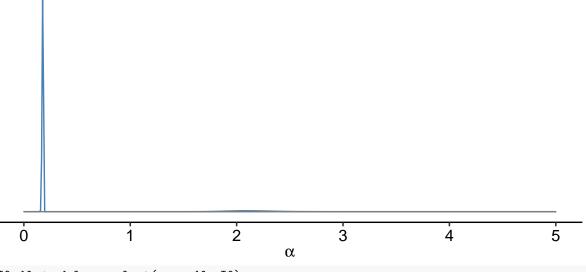




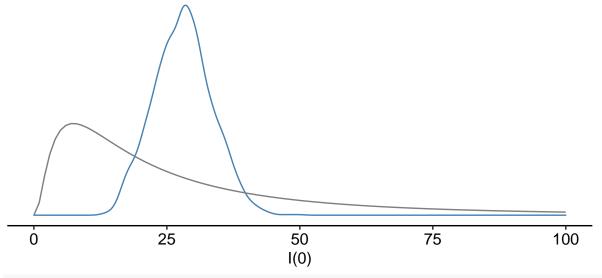
```
rho_df <- dplyr::select(pars_df, rho)
base <- ggplot(rho_df, aes(x = rho)) +</pre>
```

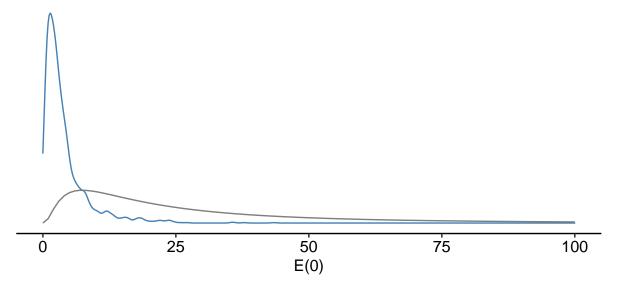
```
0.00 0.25 0.50 0.75 1.00 ρ
```





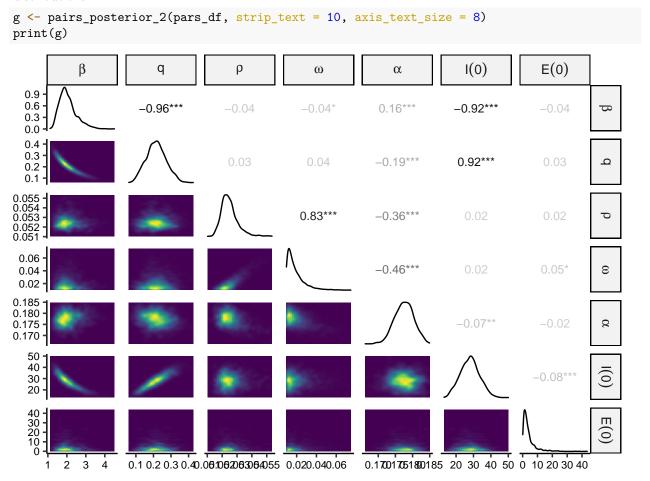
```
IO_df <- dplyr::select(pars_df, I0)
base <- ggplot(IO_df, aes(x = I0)) +
  geom_density(colour = "steelblue") +</pre>
```





3.3.2.2 Pair plots

This plot helps us evaluate parameter interactions or joint distributions. The lower triangular shows, through heat maps, the concentration of values in the x-y plane among all possible parameter pairs. The upper triangular quantifies such interactions by the correlation coefficients. The diagonal displays marginal posterior distributions.



4 Original Computing Environment

```
sessionInfo()
## R version 4.1.2 (2021-11-01)
## Platform: x86_64-apple-darwin17.0 (64-bit)
## Running under: macOS Big Sur 10.16
##
## Matrix products: default
           /Library/Frameworks/R.framework/Versions/4.1/Resources/lib/libRblas.0.dylib
## BLAS:
## LAPACK: /Library/Frameworks/R.framework/Versions/4.1/Resources/lib/libRlapack.dylib
##
## locale:
## [1] en_US.UTF-8/en_US.UTF-8/en_US.UTF-8/C/en_US.UTF-8/en_US.UTF-8
## attached base packages:
## [1] stats
                 graphics grDevices utils
                                                datasets methods
                                                                    base
##
## other attached packages:
## [1] viridisLite_0.4.1 tidyr_1.2.1
                                                               scales_1.2.1
                                             stringr_1.4.1
##
  [5] writexl_1.4.0
                          readxl_1.4.1
                                             readsdr_0.2.0
                                                               readr_2.1.3
## [9] purrr_0.3.5
                          posterior_1.3.1
                                             patchwork_1.1.2
                                                               Metrics_0.1.4
## [13] lubridate_1.8.0
                                                               ggridges_0.5.4
                          kableExtra_1.3.4
                                            gridExtra_2.3
## [17] ggpubr_0.4.0
                          reshape2_1.4.4
                                             GGally_2.1.2
                                                               ggplot2_3.3.6
## [21] extraDistr_1.9.1 dplyr_1.0.10
                                             cmdstanr_0.5.0
                                                               bayesplot_1.9.0
## loaded via a namespace (and not attached):
## [1] httr_1.4.4
                             jsonlite_1.8.2
                                                   carData_3.0-5
## [4] distributional_0.3.1 highr_0.9
                                                   tensorA_0.36.2
## [7] cellranger 1.1.0
                             yaml 2.3.5
                                                   pillar 1.8.1
## [10] backports_1.4.1
                             glue_1.6.2
                                                   digest_0.6.29
## [13] RColorBrewer_1.1-3
                             ggsignif_0.6.4
                                                   checkmate_2.1.0
## [16] rvest_1.0.3
                             colorspace_2.0-3
                                                   htmltools_0.5.3
## [19] plyr_1.8.7
                             pkgconfig_2.0.3
                                                   broom_1.0.1
## [22] webshot 0.5.4
                             processx 3.7.0
                                                   svglite 2.1.0
## [25] tzdb_0.3.0
                             tibble_3.1.8
                                                   generics_0.1.3
## [28] farver_2.1.1
                             car_3.1-0
                                                   ellipsis_0.3.2
## [31] withr_2.5.0
                             cli_3.4.1
                                                   magrittr_2.0.3
## [34] ps_1.7.1
                             evaluate_0.17
                                                   fansi_1.0.3
## [37] MASS_7.3-58.1
                             rstatix_0.7.0
                                                   xm12_1.3.3
## [40] tools_4.1.2
                             hms_1.1.2
                                                   matrixStats_0.62.0
## [43] lifecycle_1.0.3
                             munsell_0.5.0
                                                   compiler_4.1.2
## [46] systemfonts_1.0.4
                             rlang_1.0.6
                                                   grid_4.1.2
## [49] rstudioapi_0.14
                             labeling_0.4.2
                                                   rmarkdown_2.17
## [52] gtable_0.3.1
                             abind_1.4-5
                                                   reshape_0.8.9
## [55] rematch_1.0.1
                             R6_2.5.1
                                                   knitr_1.40
                             utf8 1.2.2
## [58] fastmap 1.1.0
                                                   stringi 1.7.8
## [61] Rcpp_1.0.9
                             vctrs_0.4.2
                                                   tidyselect_1.2.0
## [64] xfun_0.33
```