# WastewaterRe Code Summary

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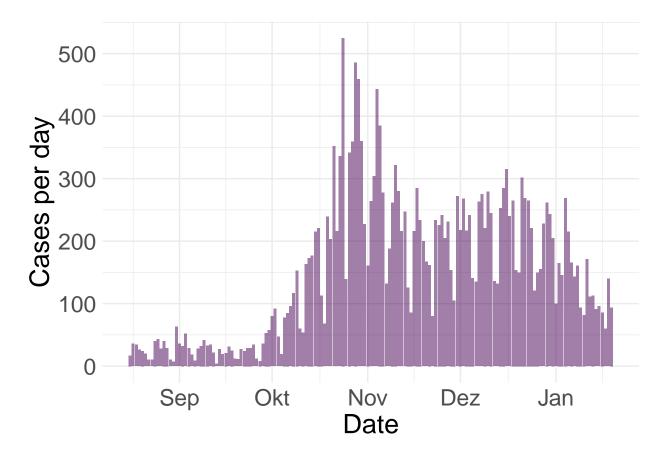
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### Summary of code used in WastewaterRe Paper by Huisman et. al

- wastewater Zurich.R
- Initial data manipulation (outside of complicated, nested functions)
- Wastewater ("Flow") data
  - flow data is loaded with col\_names = c('date', 'cases', 'cases\_smooth', 'flow', 'n1\_smooth', 'n2\_smooth')
  - gene data is loaded with col\_names = c('date', 'n1', 'n2'),
  - missing values in flow data are imputed by linear interpolation:

#### - Case data

- Catchment level clinical case data: missing values are set to 0
- Intuition: a positive case is most likely reported for the next day if the actual day was missing



#### - Deconvolution of Case data

Region: CHE

Data type: infection\_confirmed

## ##

- Let C denote the observed cases and D denote the delay distribution ("transfer function") from true underlying incidence  $I_{cc}$  to C.
- Then,  $C = I_{cc} * D$  is the convolution of true incidence  $I_{cc}$  and delay function D.
- Thus, in order to obtain an estimate for the underlying true incidence, which we want to use to obtain our Shedding Load Distribution (SLD), we need to do a deconvolution of observed cases and delay distribution.

### - deconvolveIncidence()

• Let's have a closer look at the called function wrapper:

```
deconvolveIncidence <- function(df, incidence_var = 'n1',</pre>
                                 IncubationParams, OnsetToCountParams,
                                 smooth_param = FALSE, n_boot = 50){
  infection_df <- addUselessColumns(df, inc_var = incidence_var)</pre>
  constant_delay_distributions <- list("Simulated" = get_vector_constant_waiting_time_distr(</pre>
    IncubationParams$shape, IncubationParams$scale,
    OnsetToCountParams$shape, OnsetToCountParams$scale),
    "Symptoms" = get vector constant waiting time distr(
      IncubationParams$shape, IncubationParams$scale,
      (0, 0)
  estimatedInfections <- get_infection_incidence_by_deconvolution(</pre>
    infection_df,
    is local cases = T,
    constant_delay_distribution = constant_delay_distributions[['Simulated']],
    constant_delay_distribution_incubation = constant_delay_distributions[["Symptoms"]],
    max_iterations = 100,
    smooth_incidence = smooth_param,
    empirical_delays = tibble(),
    n_bootstrap = n_boot,
    verbose = FALSE)
  return(estimatedInfections)
}
```

• Apparently, the actual deconvolution function takes as input the infection time series, and the delay distributions 1) incubation and 2) symptom onset to reporting as vectors that sum up to 1.

```
inc_var <- "confirmed"

IncubationParams <- getCountParams('incubation')
OnsetToCountParams <- getCountParams(pasteO(inc_var, '_zh'))

constant_delay_distributions <- list("Simulated" = get_vector_constant_waiting_time_distr(
    IncubationParams$shape, IncubationParams$scale,
    OnsetToCountParams$shape, OnsetToCountParams$scale),
    "Symptoms" = get_vector_constant_waiting_time_distr(
        IncubationParams$shape, IncubationParams$scale,
        0, 0))

constant_delay_distributions</pre>
```

```
## $Simulated

## [1] 0.000249 0.009954 0.036585 0.066823 0.090698 0.103189 0.106403 0.100766

## [9] 0.091679 0.079801 0.066626 0.054616 0.044358 0.035327 0.027431 0.021192

## [17] 0.016095 0.012188 0.009252 0.006966 0.005238 0.003821 0.002739 0.002111

## [25] 0.001569 0.001222 0.000834 0.000623 0.000456 0.000338 0.000244 0.000163

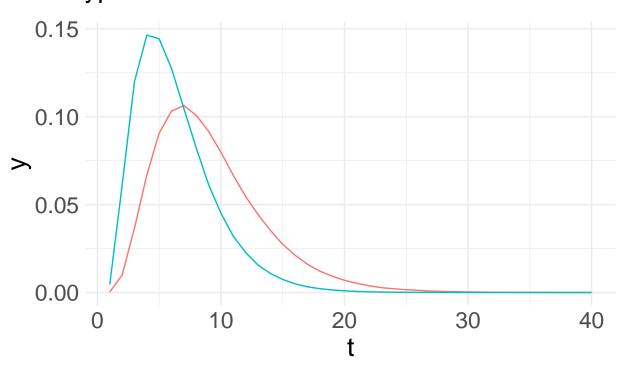
## [33] 0.000107 0.000102 0.000062 0.000050 0.000038 0.000020 0.000002 0.000012

## [41] 0.000008 0.000008 0.000008 0.000000 0.000000 0.000000 0.000000 0.000001
```

```
[57] 0.000000 0.000000 0.000000 0.000000 0.000001 0.000000 0.000000 0.000000
     [73] \ \ 0.000000 \ \ 0.000000 \ \ 0.000000 \ \ 0.000000 \ \ 0.000000 \ \ 0.000000 \ \ 0.000000 
   ##
##
  $Symptoms
##
    [1] 0.004537 0.060809 0.119930 0.146395 0.144358 0.127380 0.104666 0.082200
    [9] 0.061414 0.045133 0.032019 0.022757 0.015633 0.010843 0.007424 0.004925
    [17] \quad 0.003259 \quad 0.002169 \quad 0.001461 \quad 0.000961 \quad 0.000626 \quad 0.000390 \quad 0.000266 \quad 0.000147 \quad 0.000626 \quad 0.000666 \quad 0.
##
    [25] 0.000120 0.000065 0.000043 0.000019 0.000024 0.000014 0.000005 0.000005
    ##
    sum(constant_delay_distributions[[1]])
## [1] 1
sum(constant_delay_distributions[[2]])
## [1] 1
T_max \leftarrow 40
```

### Shape of used delay distributions

# type — Incubation — Symptom Onset to Reporting



• detail question: What goes on inside the following function?! I know what the result is so this is not too important to sort out :)

```
scale = c(scale_incubation, scale_onset_to_report))
  f <- Vectorize(function(x){</pre>
    if(x < 0) {
      return(0)
    } else if(x < 0.5) {
     return(F_h(0.5))
    } else {
      return(F_h(round(x + 1E-8) + 0.5) - F_h(round(x + 1E-8) - 0.5))
    }
 })
# Where the following function is called
make_ecdf_from_gammas <- function(shape, scale, numberOfSamples = 1E6) {</pre>
  draws <-
    rgamma(numberOfSamples, shape = shape[1], scale = scale[1]) +
    rgamma(numberOfSamples, shape = shape[2], scale = scale[2])
 return(Vectorize(ecdf(draws)))
}
```

# - get\_infection\_incidence\_by\_deconvolution()

```
## Actual deconvolution function..
get_infection_incidence_by_deconvolution <- function(</pre>
 data_subset,
  constant delay distribution,
  constant_delay_distribution_incubation = c(),
  is onset data = F,
  is_local_cases = T,
  smooth_incidence = T,
  days_incl = 21,
  empirical delays = tibble(),
  n_{bootstrap} = 5,
  days_further_in_the_past = 30,
  days_further_in_the_past_incubation = 5,
  max_iterations = 100,
  verbose = FALSE) {
  #TODO make the days_further_in_the_past type specific
  if(nrow(data_subset) == 0) {
    return(tibble())
  data_type_subset <- unique(data_subset$data_type)[1]</pre>
  # exclude leading zeroes
  data_subset <- data_subset %>%
    arrange(date) %>%
    filter(cumsum(value) > 0)
```

```
if(nrow(data_subset) == 0) {
   return(tibble())
 }
 minimal_date <- min(data_subset$date) - days_further_in_the_past
 maximal_date <- max(data_subset$date)</pre>
 all_dates <- seq(minimal_date, maximal_date, by = "days")
 is_empirical = (nrow(empirical_delays) > 0)
 if(verbose && is_empirical) {
    cat("\tEmpirical delay distribution available\n")
 }
# We can ignore this as default setting is_onset_data = FALSE
#
    if( is_onset_data ) {
#
      delay_distribution_matrix_incubation <- get_matrix_constant_waiting_time_distr(
#
        constant_delay_distribution_incubation,
#
        all dates)
#
#
      initial\_delta\_incubation \leftarrow min(which(cumsum(constant\_delay\_distribution\_incubation) > 0.5)) - 1
#
#
#
      if (unique (data_subset region) [1] != "ESP") { # hack to workaround weirdness of Spanish data
#
#
        # account for additional right-truncation of onset data (needs to be reported first)
#
        if(is_empirical) {
#
          delay_distribution_matrix_onset_to_report <- get_matrix_empirical_waiting_time_distr(
#
            empirical_delays,
#
            seq.Date(min(data\_subset\$date), max(data\_subset\$date), by = "days"))
#
#
          delay_distribution_matrix_onset_to_report <- get_matrix_constant_waiting_time_distr(
#
            constant_delay_distribution,
#
            seq.Date(min(data_subset$date), max(data_subset$date), by = "days"))
#
        7
#
#
        data subset <- data subset %>%
#
          complete(date = seq.Date(min(date), max(date), by = "days"), fill = list(value = 0))
#
#
        Q_{vector\_onset\_to\_report} \leftarrow apply(delay\_distribution\_matrix\_onset\_to\_report, MARGIN = 2, sum)
#
#
        #TODO remove
#
        # if(unique(data_subset$reqion)[1] == "ESP") { # hack to work around spanish data between sympt
#
           right_truncation <- 3
#
            # need to offset the Q vector by how many days were truncated off originally
#
            Q_vector_onset_to_report \leftarrow c(rep(1, right_truncation), Q_vector_onset_to_report[1:(length(0, right_truncation))]
        # }
#
#
#
        data_subset <- data_subset %>%
#
          mutate(value = value / Q_vector_onset_to_report) %>%
#
          mutate(value = if_else(value == Inf, 0, value))
#
```

```
#
   } else {
# Also, is_empirical = FALSE per default and we don't supply empirical delays.
    # if(is empirical) {
       delay_distribution_matrix_onset_to_report <- get_matrix_empirical_waiting_time_distr(</pre>
    #
          empirical delays,
    #
          all_dates[(days_further_in_the_past_incubation + 1):length(all_dates)])
    #
    #
        delay_distribution_matrix_incubation <- get_matrix_constant_waiting_time_distr(</pre>
    #
          constant_delay_distribution_incubation,
    #
          all_dates)
    #
      initial_delta_incubation <- min(which(cumsum(constant_delay_distribution_incubation) > 0.5)) -
      initial_delta_report <- median(empirical_delays$delay, na.rm = T)</pre>
    # } else {
      delay_distribution_matrix <- get_matrix_constant_waiting_time_distr(</pre>
        constant_delay_distribution,
       all_dates)
      initial_delta <- min(which(cumsum(constant_delay_distribution) > 0.5)) - 1
      # take median value (-1 because index 1 corresponds to zero days)
 # }
  # }
 results <- list(tibble())
 ## bootstrapping is performed on the log_diff = log_value - log_loess
 ## and is converted back to original scale afterwards
 for (bootstrap_replicate_i in 0:n_bootstrap) {
   if (verbose == T) {
              Bootstrap replicate: ", bootstrap_replicate_i, "\n")
      cat("
   if (bootstrap_replicate_i == 0) {
      time_series <- data_subset</pre>
   } else {
      time_series <- get_bootstrap_replicate(data_subset)</pre>
## Now, the original or bootstrapped time series is smoothed by LOESS
   if (smooth_incidence == T) {
      smoothed_incidence_data <- time_series %>%
        complete(date = seq.Date(min(date), max(date), by = "days"),
                 fill = list(value = 0)) %>%
       mutate(value = getLOESSCases(dates = date, count_data = value, days_incl))
```

```
raw_total_incidence <- sum(time_series$value, na.rm = TRUE)</pre>
      smoothed_total_incidence <- sum(smoothed_incidence_data$value, na.rm = T)</pre>
## Reweighting to make sure that sums match??
      if (smoothed total incidence > 0) {
        smoothed_incidence_data <- smoothed_incidence_data %>%
          mutate(value = value * raw_total_incidence / smoothed_total_incidence)
     }
   } else {
      smoothed_incidence_data <- time_series %>%
        complete(date = seq.Date(min(date), max(date), by = "days"),
                 fill = list(value = 0))
    # is_onset_data = FALSE per default
    # if (is_onset_data) {
       deconvolved_infections <- do_deconvolution(smoothed_incidence_data,</pre>
    #
                                                      delay_distribution_matrix = delay_distribution_matr
    #
                                                      days_further_in_the_past = days_further_in_the_past
    #
                                                      initial_delta = initial_delta_incubation,
    #
                                                     max iterations = max iterations,
                                                     verbose = verbose)
    # } else {
    # is_empirical = FALSE as well in our setting
      # if(is_empirical) {
          # perform the deconvolution in two steps
          deconvolved_symptom_onsets <- do_deconvolution(smoothed_incidence_data,</pre>
                                                           delay_distribution_matrix = delay_distribution
      #
                                                           days_further_in_the_past = days_further_in_the
      #
                                                           initial_delta = initial_delta_report,
      #
                                                           max_iterations = max_iterations,
      #
                                                           verbose = verbose)
      #
      #
          deconvolved_infections <- do_deconvolution(deconvolved_symptom_onsets,</pre>
      #
                                                       delay distribution matrix = delay distribution mat
      #
                                                       days_further_in_the_past = days_further_in_the_pas
      #
                                                       initial_delta = initial_delta_incubation,
      #
                                                       max_iterations = max_iterations,
                                                       verbose = verbose)
      # } else {
        deconvolved_infections <- do_deconvolution(smoothed_incidence_data,</pre>
                                       delay_distribution_matrix = delay_distribution_matrix,
                                       days_further_in_the_past = days_further_in_the_past,
                                       initial_delta = initial_delta,
                                       max_iterations = max_iterations,
                                       verbose = verbose)
       }
    # }
```

```
deconvolved_infections <- deconvolved_infections %>%
      slice((days_further_in_the_past -5 + 1):n())
    data_type_name <- paste0("infection_", data_type_subset)</pre>
    ## dataframe containing results
    deconvolved infections <- tibble(</pre>
      date = deconvolved infections$date,
      region = unique(time_series$region)[1],
      country = unique(time_series$country)[1],
      source = unique(time_series$source)[1],
      local_infection = is_local_cases,
      data_type = data_type_name,
      replicate = bootstrap_replicate_i,
      value = deconvolved_infections$value
    results <- c(results, list(deconvolved_infections))</pre>
  }
  return(bind_rows(results))
}
```

- Essentially, what happens is: the wrapper function creates the vectors of delay distributions for 1) incubation and 2) symptom onset to reporting and supplies it to the actual deconvolution function. Then, the function get\_matrix\_constant\_waiting\_time\_distr creates a T by T lower-diagonal matrix with the vectorized delay distributions as columns starting at the diagonal element (see below for illustration).
- bootstrapping is performed on log\_diff = log\_value log\_loess where log\_value = log(value + 1). Afterwards, the bootstrapped time series is transformed back to original scale: ts\_boot = exp(log\_diff + log\_loess) 1. In each of the n\_bootstrap = 50 iterations, the deconvolution is performed.

• Let's check what shape the returned matrix delay\_distribution\_matrix has:

```
constant_delay_distributions <- list("Simulated" = get_vector_constant_waiting_time_distr(
    IncubationParams$shape, IncubationParams$scale,
    OnsetToCountParams$shape, OnsetToCountParams$scale),
    "Symptoms" = get_vector_constant_waiting_time_distr(</pre>
```

```
IncubationParams$shape, IncubationParams$scale,
     (0, 0)
constant_delay_distribution <- constant_delay_distributions[['Simulated']]</pre>
constant_delay_distribution_incubation <- constant_delay_distributions[["Symptoms"]]</pre>
dates seq <- seq(date("2021-01-01"), date("2021-01-01")+6, by = "days")
# Check Matrix for small N
get_matrix_constant_waiting_time_distr(
       constant_delay_distribution,
       dates seq)
                           [,3]
                                   [,4]
##
          [,1]
                   [,2]
                                           [,5]
                                                   [,6]
## [3,] 0.036571 0.010002 0.000297 0.000000 0.000000 0.000000 0.000000
## [4,] 0.066968 0.036571 0.010002 0.000297 0.000000 0.000000 0.000000
## [5,] 0.090729 0.066968 0.036571 0.010002 0.000297 0.000000 0.000000
## [6,] 0.103512 0.090729 0.066968 0.036571 0.010002 0.000297 0.000000
## [7,] 0.106210 0.103512 0.090729 0.066968 0.036571 0.010002 0.000297
# Verify that Matrix indeed only includes vectorized delay distribution
all.equal(constant_delay_distribution[1:7],
       get matrix constant waiting time distr(
       constant_delay_distribution, dates_seq)[,1])
## [1] TRUE
```

# "stepwise" function call

```
days_further_in_the_past <- 30</pre>
incidence_var <- inc_var <- 'confirmed'</pre>
head(orig_cases)
## # A tibble: 6 x 2
##
     date
             confirmed
                     <dbl>
     <date>
## 1 2020-08-15
                        10
## 2 2020-08-16
                        17
## 3 2020-08-17
                        36
## 4 2020-08-18
                        34
## 5 2020-08-19
                        26
## 6 2020-08-20
data_subset <- infection_df <- addUselessColumns(orig_cases, inc_var = incidence_var)</pre>
  # exclude leading zeroes
 data_subset <- data_subset %>%
```

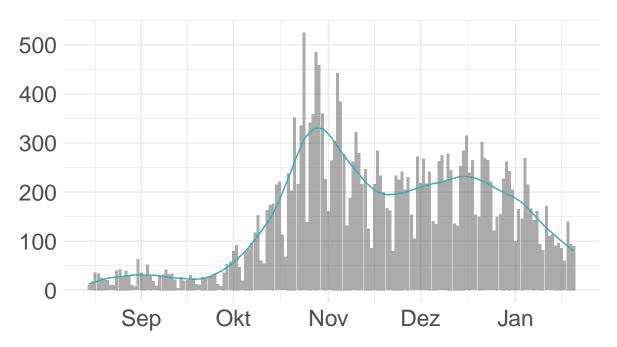
```
arrange(date) %>%
    filter(cumsum(value) > 0)
head(data_subset)
## # A tibble: 6 x 9
             region value data_type source variable country
##
     date
                                                                  date_type
              <chr> <dbl> <chr>
                                     <chr> <chr>
##
                                                      <chr>
                                                                  <chr>
     <date>
## 1 2020-08-15 CHE
                        10 confirmed ETH incidence Switzerland report
                        17 confirmed ETH incidence Switzerland report
## 2 2020-08-16 CHE
## 3 2020-08-17 CHE
                       36 confirmed ETH incidence Switzerland report
                       34 confirmed ETH incidence Switzerland report
## 4 2020-08-18 CHE
## 5 2020-08-19 CHE
                       26 confirmed ETH incidence Switzerland report
## 6 2020-08-20 CHE 24 confirmed ETH incidence Switzerland report
## # ... with 1 more variable: local_infection <lgl>
 minimal_date <- min(data_subset$date) - days_further_in_the_past</pre>
 maximal date <- max(data subset$date)</pre>
 all_dates <- seq(minimal_date, maximal_date, by = "days")
# Create actual delay_distribution_matrix
delay_distribution_matrix <- get_matrix_constant_waiting_time_distr(constant_delay_distribution,all_dat
initial_delta <- min(which(cumsum(constant_delay_distribution) > 0.5)) - 1
```

#### - Smoothing by LOESS

```
days_incl = 21
time_series <- data_subset</pre>
smoothed_incidence_data <- time_series %>%
        complete(date = seq.Date(min(date), max(date), by = "days"),
                 fill = list(value = 0)) %>%
        mutate(value = getLOESSCases(dates = date, count_data = value, days_incl))
      raw_total_incidence <- sum(time_series$value, na.rm = TRUE)</pre>
      smoothed_total_incidence <- sum(smoothed_incidence_data$value, na.rm = T)</pre>
## Reweighting to make sure that sums match
      if (smoothed_total_incidence > 0) {
        smoothed_incidence_data <- smoothed_incidence_data %>%
          mutate(value = value * raw_total_incidence / smoothed_total_incidence)
      }
sum(smoothed_incidence_data$value) == raw_total_incidence
## [1] TRUE
smoothed_incidence_data_raw <- time_series %>%
        complete(date = seq.Date(min(date), max(date), by = "days"),
                 fill = list(value = 0)) %>%
        mutate(value = getLOESSCases(dates = date, count_data = value, days_incl))
ggplot() +
```

### LOESS smoothing results for reported case incidence





# do\_deconvolution()

- After putting together the necessary inputs the actual deconvolution function do\_deconvolution() is called.
  - smoothed\_incidence\_data
  - delay\_distribution\_matrix
  - initial\_delta: index at which cumsum of delay distribution vector exceeds median
- do\_deconvolution() function:

```
do_deconvolution <- function(
  incidence_data,
  days_further_in_the_past = 30,
  verbose = FALSE,
  delay_distribution_matrix,
  initial_delta,
  max_iterations = 100
) {</pre>
```

```
# use mode of 'constant_delay_distribution'. -1 because indices are offset by one as the delay can be
  first_guess_delay <- ceiling(initial_delta)</pre>
  if (verbose) {
    cat("\tDelay on first guess: ", first_guess_delay, "\n")
 first_recorded_incidence <- with(filter(incidence_data, cumsum(value) > 0), value[which.min(date)])
  last_recorded_incidence <- with(incidence_data, value[which.max(date)])</pre>
  minimal_date <- min(incidence_data$date) - days_further_in_the_past</pre>
  maximal_date <- max(incidence_data$date)</pre>
  first_guess <- incidence_data %>%
    mutate(date = date - first_guess_delay) %>%
    complete(date = seq.Date(minimal_date, min(date), by = "days"),
             fill = list(value = first_recorded_incidence)) %>% # left-pad with first recorded value
    complete(date = seq.Date(max(date), maximal_date, by = "days"),
             fill = list(value = last_recorded_incidence)) %>% # right-pad with last recorded value
    arrange(date) %>%
    filter(date >= minimal_date)
  original_incidence <- incidence_data %>%
    complete(date = seq.Date(minimal_date, maximal_date, by = "days"),
             fill = list(value = 0)) %>%
    pull(value)
  final_estimate <- iterate_RL(</pre>
    first_guess$value,
    original_incidence,
    delay_distribution_matrix = delay_distribution_matrix,
    max_delay = days_further_in_the_past,
    max_iterations = max_iterations,
    verbose = verbose)
  deconvolved_dates <- first_guess %>% pull(date)
 result <- tibble(date = deconvolved dates, value = final estimate)
  result <- result %>%
    filter(date <= maximal_date - first_guess_delay)</pre>
 return(result)
# setting function arguments
bootstrap_replicate_i <- 0 # looping index</pre>
max iterations <- 100
verbose <- FALSE
data_type_subset <- unique(data_subset$data_type)[1]</pre>
is_local_cases <- TRUE</pre>
incidence_data <- smoothed_incidence_data</pre>
```

```
# use mode of 'constant_delay_distribution'. -1 because indices are offset by one as the delay can be
  (first guess delay <- ceiling(initial delta))
## [1] 7
 if (verbose) {
    cat("\tDelay on first guess: ", first_guess_delay, "\n")
  (first_recorded_incidence <- with(filter(incidence_data, cumsum(value) > 0), value[which.min(date)])
## [1] 12.38484
  (last_recorded_incidence <- with(incidence_data, value[which.max(date)]))</pre>
 minimal_date <- min(incidence_data$date) - days_further_in_the_past
 maximal_date <- max(incidence_data$date)</pre>
 incidence_data %>%
   head(10)
## # A tibble: 10 x 9
                region value data_type source variable country
                                                                   date_type
##
                <chr> <dbl> <chr>
                                      <chr> <chr>
                                                        <chr>>
      <date>
                                                                   <chr>>
## 1 2020-08-15 CHE
                       12.4 confirmed ETH incidence Switzerland report
## 2 2020-08-16 CHE
                       14.5 confirmed ETH incidence Switzerland report
                       16.4 confirmed ETH incidence Switzerland report
## 3 2020-08-17 CHE
## 4 2020-08-18 CHE
                       18.3 confirmed ETH incidence Switzerland report
## 5 2020-08-19 CHE
                      20.5 confirmed ETH incidence Switzerland report
## 6 2020-08-20 CHE
                      22.5 confirmed ETH incidence Switzerland report
## 7 2020-08-21 CHE
                      24.1 confirmed ETH incidence Switzerland report
## 8 2020-08-22 CHE
                     25.2 confirmed ETH
                                           incidence Switzerland report
## 9 2020-08-23 CHE
                        26.2 confirmed ETH
                                             incidence Switzerland report
## 10 2020-08-24 CHE
                        26.9 confirmed ETH
                                              incidence Switzerland report
## # ... with 1 more variable: local_infection <lgl>
 incidence_data %>%
   tail(10)
## # A tibble: 10 x 9
##
                region value data_type source variable country
                                                                   date_type
                <chr> <dbl> <chr>
                                       <chr> <chr>
      <date>
                                                        <chr>>
##
  1 2021-01-11 CHE
                       127. confirmed ETH
                                              incidence Switzerland report
## 2 2021-01-12 CHE
                       122. confirmed ETH
                                             incidence Switzerland report
## 3 2021-01-13 CHE
                       116. confirmed ETH
                                             incidence Switzerland report
## 4 2021-01-14 CHE
                       111. confirmed ETH
                                            incidence Switzerland report
## 5 2021-01-15 CHE
                       105. confirmed ETH incidence Switzerland report
## 6 2021-01-16 CHE
                       99.7 confirmed ETH
                                            incidence Switzerland report
## 7 2021-01-17 CHE
                       94.6 confirmed ETH
                                             incidence Switzerland report
                      89.3 confirmed ETH
## 8 2021-01-18 CHE
                                             incidence Switzerland report
## 9 2021-01-19 CHE
                      84.3 confirmed ETH
                                             incidence Switzerland report
## 10 2021-01-20 CHE
                      79.7 confirmed ETH
                                             incidence Switzerland report
```

```
## # ... with 1 more variable: local_infection <lgl>
  first_guess <- incidence_data %>%
    mutate(date = date - first_guess_delay) %>%
    complete(date = seq.Date(minimal_date, min(date), by = "days"),
             fill = list(value = first_recorded_incidence)) %% # left-pad with first recorded value
    complete(date = seq.Date(max(date), maximal_date, by = "days"),
             fill = list(value = last_recorded_incidence)) %>% # right-pad with last recorded value
    arrange(date) %>%
    filter(date >= minimal_date)
  first_guess %>%
    head(10)
## # A tibble: 10 x 9
##
                 region value data_type source variable country date_type
##
      <date>
                 <chr> <dbl> <chr>
                                         <chr>
                                                 <chr>>
                                                          <chr>
                                                                  <chr>
##
   1 2020-07-16 <NA>
                          12.4 <NA>
                                         <NA>
                                                 <NA>
                                                          <NA>
                                                                  <NA>
##
   2 2020-07-17 <NA>
                          12.4 <NA>
                                         <NA>
                                                 <NA>
                                                          <NA>
                                                                  <NA>
    3 2020-07-18 <NA>
                          12.4 <NA>
                                         <NA>
                                                 <NA>
                                                          <NA>
                                                                  <NA>
## 4 2020-07-19 <NA>
                         12.4 < NA >
                                         <NA>
                                                 <NA>
                                                          <NA>
                                                                  <NA>
## 5 2020-07-20 <NA>
                         12.4 <NA>
                                         <NA>
                                                 <NA>
                                                          <NA>
                                                                  <NA>
## 6 2020-07-21 <NA>
                          12.4 <NA>
                                         <NA>
                                                 <NA>
                                                          <NA>
                                                                  <NA>
   7 2020-07-22 <NA>
                          12.4 <NA>
                                         <NA>
                                                 <NA>
                                                          <NA>
                                                                  <NA>
## 8 2020-07-23 <NA>
                          12.4 <NA>
                                         <NA>
                                                 <NA>
                                                          <NA>
                                                                  <NA>
## 9 2020-07-24 <NA>
                          12.4 <NA>
                                         <NA>
                                                 <NA>
                                                          <NA>
                                                                  <NA>
## 10 2020-07-25 <NA>
                          12.4 <NA>
                                         <NA>
                                                 <NA>
                                                          <NA>
                                                                  <NA>
## # ... with 1 more variable: local_infection <lgl>
  first_guess %>%
    tail(10)
## # A tibble: 10 x 9
##
      date
                 region value data_type source variable country
                                                                        date_type
                 <chr> <dbl> <chr>
                                         <chr> <chr>
##
      <date>
                                                           <chr>>
                                                                        <chr>
##
  1 2021-01-11 CHE
                          89.3 confirmed ETH
                                                 incidence Switzerland report
   2 2021-01-12 CHE
                          84.3 confirmed ETH
                                                incidence Switzerland report
## 3 2021-01-13 CHE
                         79.7 confirmed ETH
                                                 incidence Switzerland report
## 4 2021-01-14 <NA>
                         79.7 <NA>
                                         <NA>
                                                 <NA>
                                                           <NA>
                                                                        <NA>
## 5 2021-01-15 <NA>
                         79.7 <NA>
                                         <NA>
                                                 <NA>
                                                           <NA>
                                                                        <NA>
## 6 2021-01-16 <NA>
                          79.7 <NA>
                                         <NA>
                                                 <NA>
                                                           <NA>
                                                                        <NA>
## 7 2021-01-17 <NA>
                          79.7 <NA>
                                         <NA>
                                                 <NA>
                                                           <NA>
                                                                        <NA>
## 8 2021-01-18 <NA>
                          79.7 <NA>
                                         <NA>
                                                 <NA>
                                                           <NA>
                                                                        <NA>
## 9 2021-01-19 <NA>
                          79.7 <NA>
                                         <NA>
                                                 <NA>
                                                           <NA>
                                                                        <NA>
## 10 2021-01-20 <NA>
                          79.7 <NA>
                                         <NA>
                                                 <NA>
                                                           <NA>
                                                                        <NA>
## # ... with 1 more variable: local_infection <lgl>
  original_incidence <- incidence_data %>%
    complete(date = seq.Date(minimal_date, maximal_date, by = "days"),
             fill = list(value = 0)) %>%
    pull(value)
  final_estimate <- iterate_RL(</pre>
    first_guess$value,
```

```
original_incidence,
  delay_distribution_matrix = delay_distribution_matrix,
  max_delay = days_further_in_the_past,
  max_iterations = max_iterations,
  verbose = verbose)

deconvolved_dates <- first_guess %>% pull(date)

result <- tibble(date = deconvolved_dates, value = final_estimate)

result <- result %>%
  filter(date <= maximal_date - first_guess_delay)

restult_RL <- result</pre>
```

### iterate\_RL()

- do\_deconvolution() is another wrapper function for iterate\_RL(), which implements the Richardson-Lucy Algorithm.
- This algorithm starts with a shifted and extended version of the original dataset as initial\_estimate = first\_guess. Specifically, the time series of reported cases is shifted by 7 days in the past, 30 days are added to the left and the resulting 30 missing values left and 7 right are imputed using the first and last observation of reported cases, respectively.
- Additional inputs to the function are:
  - original\_incidence: smoothed original time series of cases
  - delay\_distribution\_matrix: The matrix presented above
  - threshold\_chi\_squared = 1
  - max\_iterations = 100
  - $\max_{delay} = 30$

### **Function**

```
iterate_RL <- function(
   initial_estimate,
   original_incidence,
   delay_distribution_matrix,
   threshold_chi_squared = 1,
   max_iterations = 100,
   max_delay,
   verbose = FALSE) {

   current_estimate <- initial_estimate
   N <- length(current_estimate)
   N0 <- N - max_delay
   chi_squared <- Inf
   count <- 1

   delay_distribution_matrix <- delay_distribution_matrix[1:length(current_estimate), 1:length(current_estimate)
   truncated_delay_distribution_matrix <- delay_distribution_matrix[(1 + max_delay):NROW(delay_distribution_matrix])</pre>
```

```
Q_vector <- apply(truncated_delay_distribution_matrix, MARGIN = 2, sum)
while(chi_squared > threshold_chi_squared & count <= max_iterations) {
    if (verbose) {
        cat("\t\tStep: ", count, " - Chi squared: ", chi_squared, "\n")
    }

    E <- as.vector(delay_distribution_matrix %*% current_estimate)
    B <- replace_na(original_incidence/E, 0)

    current_estimate <- current_estimate / Q_vector * as.vector(crossprod(B, delay_distribution_matrix current_estimate <- replace_na(current_estimate, 0)

    chi_squared <- 1/NO * sum((E[(max_delay + 1): length(E)] - original_incidence[(max_delay + 1) : length(E)] }

    return(current_estimate)
}</pre>
```

#### Stepwise examination

```
# setting missing arguments
initial_estimate <- first_guess$value</pre>
max_delay <- days_further_in_the_past</pre>
threshold_chi_squared <- 1</pre>
# initialize RL algorithm: starting value is
  current_estimate <- initial_estimate</pre>
  # length of output series
 N <- length(current_estimate)</pre>
  # length of original series
  NO <- N - max_delay
  chi_squared <- Inf</pre>
  count <- 1
  # subset delay_distribution_matrix
  delay_distribution_matrix <- delay_distribution_matrix[1:length(current_estimate), 1:length(current_e
  {\it \# subset delay\_distribution\_matrix \ to \ obtain \ a \ 159 \ x \ 189 \ matrix}
  # in order to compute weighting vector
  truncated_delay_distribution_matrix <- delay_distribution_matrix[(1 + max_delay):NROW(delay_distribut
  # column sums (sum of weights from original series to incidence estimate)
  Q_vector <- apply(truncated_delay_distribution_matrix, MARGIN = 2, sum)
  while(chi_squared > threshold_chi_squared & count <= max_iterations) {</pre>
    if (verbose) {
      cat("\t\tStep: ", count, " - Chi squared: ", chi_squared, "\n")
```

```
# P x u (wiki)
   E <- as.vector(delay_distribution_matrix %*% current_estimate)
    \# d / (P x u)
   B <- replace_na(original_incidence/E, 0)</pre>
   current_estimate <- current_estimate / Q_vector * as.vector(crossprod(B, delay_distribution_matrix</pre>
   current estimate <- replace na(current estimate, 0)</pre>
    chi_squared <- 1/N0 * sum((E[(max_delay + 1): length(E)] - original_incidence[(max_delay + 1) : len
    count <- count + 1
 }
(final_estimate <- current_estimate)</pre>
##
     [1] 12.03129 12.01429 11.97833 11.95466 11.92945 11.94037
                                                                    11.98400
##
     [8] 11.98460 11.98466 11.99222
                                      11.99631 12.00785 12.01729
                                                                    12.02201
##
   [15] 12.04036 12.05631 12.07801 12.09261 12.11959 12.15131 12.18766
##
   [22] 12.22819 12.27919 12.34037 14.54178 16.53884 18.66581 21.11161
   [29] 23.55298 25.51549
##
                             26.93477
                                       28.05062
                                                 28.80114 29.38114
                                                                    30.11299
##
   [36] 30.86677 31.46687
                             31.96849 32.21024
                                                 32.09833 31.77875
                                                                    31.50753
##
   [43] 31.32591 31.06703 30.72711 30.14189 29.15640 28.00582
                                                                    26.87387
   [50] 25.78023 24.81179
                             24.16521 23.65563 22.99370 22.45045
                                                                    22.08068
##
   [57] 21.59997 21.26583 21.28476 21.79234
                                                 22.69131 23.84333
                                                                    25.74037
##
   [64] 28.64571 32.06017 35.34603 39.00140 43.16522 47.47466
                                                                    52.40903
## [71] 57.98623 63.93842 70.34174 77.00854 83.61032 91.24982 99.78046
## [78] 107.88923 116.16043 125.22731 134.52248 143.44985 152.62299 164.00945
## [85] 177.99264 192.84128 208.72858 225.99939 243.19068 260.76497 280.11675
   [92] 296.85747 312.76462 327.81731 336.66821 342.07027 347.32129 348.77687
## [99] 346.25926 342.79042 335.69048 325.84509 315.55403 304.33770 292.18620
## [106] 280.35170 270.24136 260.90075 251.20727 242.85431 235.60297 227.65024
## [113] 218.96912 211.71971 206.02085 200.85696 196.04262 192.29178 190.04285
## [120] 188.71099 188.27828 188.99994 190.54861 192.32490 194.17451 195.90618
## [127] 197.88651 200.82107 203.96784 206.34525 208.71727 211.30716 213.66360
## [134] 215.38870 217.25633 219.18098 220.36835 221.07242 222.60904 224.79407
## [141] 226.65334 228.60672 230.73977 232.65494 234.00518 234.94542 234.70448
## [148] 233.19836 231.63610 229.87113 226.54198 223.13174 220.40247 216.67768
## [155] 211.88142 207.51302 203.70518 200.11499 196.72238 193.11841 190.19042
## [162] 187.54769 183.93546 179.97338 175.48214 169.82303 162.95004 155.59946
## [169] 148.25667 140.53153 133.69992 126.75294 119.81223 114.39011 108.82158
## [176] 103.14554 97.71854 92.29851 87.17600 81.96468 76.97901 72.34955
## [183] 71.88838 71.40393 70.91009 70.43287 70.00383 69.68736 69.64088
```

#### Further stepwise processing

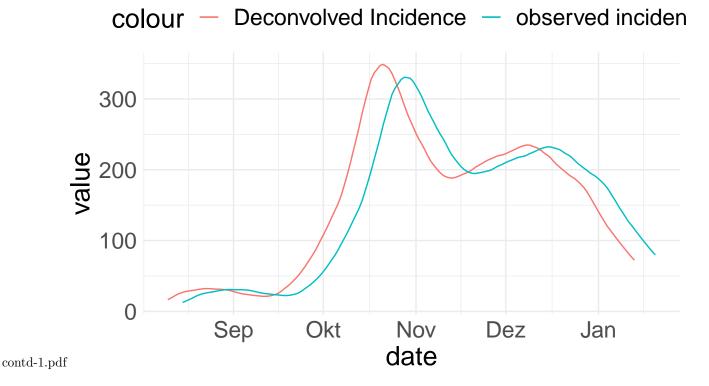
```
## do_deconvolution()
deconvolved_dates <- first_guess %>%
  pull(date)

result <- tibble(date = deconvolved_dates, value = final_estimate)</pre>
```

```
result <- result %>%
    filter(date <= maximal_date - first_guess_delay)</pre>
result %>%
 head(10)
## # A tibble: 10 x 2
##
     date
                value
##
                 <dbl>
      <date>
## 1 2020-07-16 12.0
## 2 2020-07-17 12.0
## 3 2020-07-18 12.0
## 4 2020-07-19 12.0
## 5 2020-07-20 11.9
## 6 2020-07-21 11.9
## 7 2020-07-22 12.0
## 8 2020-07-23 12.0
## 9 2020-07-24 12.0
## 10 2020-07-25 12.0
deconvolved_infections <- result</pre>
## get_infection_incidence_by_deconvolution()
deconvolved_infections <- deconvolved_infections %% slice((days_further_in_the_past -5 + 1):n())
   data_type_name <- paste0("infection_", data_type_subset)</pre>
    ## dataframe containing results
   deconvolved_infections <- tibble(</pre>
     date = deconvolved_infections$date,
     region = unique(time_series$region)[1],
     country = unique(time_series$country)[1],
     source = unique(time_series$source)[1],
     local_infection = is_local_cases,
     data_type = data_type_name,
     replicate = bootstrap_replicate_i,
     value = deconvolved_infections$value
    )
ggplot() +
  geom_line(aes(x = date, y = value, color = "Deconvolved Incidence"), data = deconvolved_infections) +
 geom_line(aes(x = date, y = value, color = "observed incidence"), data = incidence_data) +
  ggtitle("Incidence estimate based on Richardson-Lucy deconvolution",
         subtitle = "- RL deconvolution is performed by Huisman et. al to estimate ground truth infect
```

### Incidence estimate based on Richardson-Lucy deconvolution

- RL deconvolution is performed by Huisman et. al to estimate ground truth infection



## Richardson-Lucy deconvolution applied to cases

- Iterative deconvolution procedure to recover underlying image (or time series in our case) that has been blurred by a *known* point spread function (PSF)
- Converges to the Maximum-Likelihood (MLE) solution under the assumption that the data follows a poisson distribution, which is great for us as we have count data.
- Recall our original deconvolution problem:  $C = I_{cc} * D$  where we are interested in estimating the ground truth infection incidence time series  $I_{cc}$ .
- Then,  $C_t = \sum_j \mathbf{P}_{t,j} \cdot I_{cc}^j$  are the observed cases at day t, where  $\mathbf{P}$  is delay\_distribution\_matrix. As mentioned above, this matrix is a T by T lower-diagonal matrix with the vectorized delay distributions as columns starting at the diagonal element created by the function get\_matrix\_constant\_waiting\_time\_distr(). (see above for illustration).
- Following the RL algorithm:

$$I_{cc}^{i+1} = I_{cc}^{i} \left( \frac{C}{\mathbf{P} \cdot I_{cc}^{i}} \times \mathbf{P} \right)$$

, where the division is elementwise.

• For our purpose, however, we need a small adjustment to correct for the fact that we might observe infections that are not fully transmitted into the wastewater:

$$I_{cc}^{i+1} = \frac{I_{cc}^{i}}{\mathbf{P}_{[31:189,1:189]}^{\mathbf{T}} \cdot \mathbf{1}} \left( \frac{C}{\mathbf{P} \cdot I_{cc}^{i}} \times \mathbf{P} \right)$$

#### - RL deconvolution in R

```
## RL deconvolution in R
Q_vector <- apply(truncated_delay_distribution_matrix, MARGIN = 2, sum)

while(chi_squared > threshold_chi_squared & count <= max_iterations) {
    if (verbose) {
        cat("\t\tStep: ", count, " - Chi squared: ", chi_squared, "\n")
    }
    # P x u (wiki)
    E <- as.vector(delay_distribution_matrix %*% current_estimate)
    # d / (P x u)
    B <- replace_na(original_incidence/E, 0)

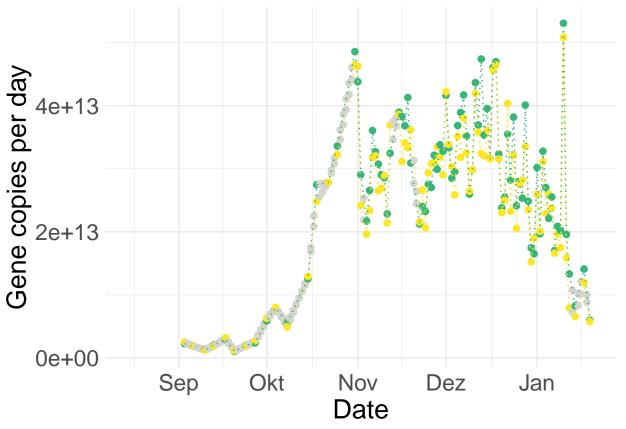
current_estimate <- current_estimate / Q_vector * as.vector(crossprod(B, delay_distribution_matrix))
    current_estimate <- replace_na(current_estimate, 0)

chi_squared <- 1/NO * sum((E[(max_delay + 1): length(E)] - original_incidence[(max_delay + 1) : length(E)] - count <- count <-
```

#### - Normalisation of Wastewater Data

```
## Normalisation of WW data ####
# Min observed
norm_min <- min(raw_data_ZH$n1, raw_data_ZH$n2)</pre>
### ALL Normalised WW DATA ####
ww data = bind rows(raw data ZH) %>%
 mutate(norm_n1 = n1/norm_min,
       norm_n2 = n2/norm_min)
ww_data
## # A tibble: 139 x 12
##
              cases cases_smooth
                                  flow n1_smooth n2_smooth
     date
                                                             n1
                                                                     n2
            <dbl>
##
                         <dbl>
     <date>
                                <dbl>
                                          <dbl>
                                                   <dbl>
                                                           <dbl>
                                                                  <dbl>
                                         1.81e12 2.04e12 2.27e12 2.54e12
## 1 2020-09-03 53
                           33 158459
## 2 2020-09-04 38.7
                          33.4 156052. 1.94e12 2.18e12 2.14e12 2.32e12
## 3 2020-09-05 24.3
                          33.8 153644.
                                        2.06e12 2.31e12 2.00e12 2.10e12
## 4 2020-09-06 10
                                         34.1 151237
## 5 2020-09-07 15.5
                           32.5 147888. 2.02e12 2.18e12 1.73e12 1.71e12
                           30.9 144540. 1.85e12 1.92e12 1.58e12 1.55e12
## 6 2020-09-08 21
## 7 2020-09-09 26.5
                           29.3 141191. 1.68e12 1.66e12 1.44e12 1.38e12
                                         ## 8 2020-09-10 32
                           27.7 137842
## 9 2020-09-11 22.7
                           27.9 132288. 1.57e12 1.45e12 1.55e12 1.44e12
                                         1.62e12 1.50e12 1.81e12 1.67e12
## 10 2020-09-12 13.3
                           28.1 126733.
## # ... with 129 more rows, and 4 more variables: orig_data <lgl>, region <chr>,
## # norm_n1 <dbl>, norm_n2 <dbl>
```

```
# Plot raw data #####
plot_raw_ww_data <- ww_data %>%
  dplyr::select(date, orig_data, region, N1 = n1, N2 = n2) %>%
  pivot_longer(cols = c(N1, N2)) %>%
  mutate(name_orig = ifelse(!is.na(orig_data), name, 'Imputed'))
ww_data_plot <- ggplot() +</pre>
  geom_point(data = plot_raw_ww_data, aes(x=date, y= value, colour = name_orig),
             size = 2, show.legend = F) +
  geom_line(data = plot_raw_ww_data %>% filter(orig_data),
            aes(x=date, y= value,colour = name), linetype = 'dotted', show.legend = F) +
  labs(x = 'Date', y='Gene copies per day') +
  scale_x_date(limits = c(as_date('2020-08-15'), as_date('2021-01-20'))) +
  scale_colour_manual(values = c(viridis(4)[3:4], 'lightgrey'),
                      labels = c('N1', 'N2', 'Imputed'),
                      breaks = c('N1', 'N2', 'Imputed'),
                      name = 'Variable') +
  labs(colour = 'Variable')
ww_data_plot
```



### - Deconvolution of case data with given SLD

```
##### Deconvolve and Estimate WW Re #####
config_df = expand.grid("region" = c('ZH'),
                         'incidence_var' = c('norm_n1', 'norm_n2'),
                         'FirstGamma' = 'incubation',
                         'SecondGamma' = 'benefield' )
config_df
     region incidence_var FirstGamma SecondGamma
## 1
         ZH
                  norm_n1 incubation
                                        benefield
## 2
         ZH
                  norm_n2 incubation
                                        benefield
getCountParams(as.character(config_df[1, 'FirstGamma']))
## $shape
## [1] 2.743164
##
## $scale
## [1] 1.932075
getCountParams(as.character(config_df[1, 'SecondGamma']))
## $shape
## [1] 0.929639
##
## $scale
## [1] 7.241397
getCountParams(as.character(config_df[2, 'FirstGamma']))
## $shape
## [1] 2.743164
##
## $scale
## [1] 1.932075
getCountParams(as.character(config_df[2, 'SecondGamma']))
## $shape
## [1] 0.929639
## $scale
## [1] 7.241397
deconv_ww_data <- data.frame()</pre>
Re_ww <- data.frame()</pre>
for(row_i in 1:nrow(config_df)){
  new_deconv_data = deconvolveIncidence(ww_data %>% filter(region == config_df[row_i, 'region']),
                                         incidence_var = config_df[row_i, 'incidence_var'],
                                         getCountParams(as.character(config_df[row_i, 'FirstGamma'])),
                                         getCountParams(as.character(config_df[row_i, 'SecondGamma'])),
                                         smooth_param = TRUE, n_boot = 50)
```

```
new_deconv_data <- new_deconv_data %>%
    mutate(incidence_var = config_df[row_i, 'incidence_var'])
  ##### Get Re #####
  new_Re_ww = getReBootstrap(new_deconv_data)
  new_Re_ww <- new_Re_ww %>%
   mutate(variable = config_df[row_i, 'incidence_var'],
           region = config df[row i, 'region'])
  deconv_ww_data <- bind_rows(deconv_ww_data, new_deconv_data)</pre>
 Re_ww = bind_rows(Re_ww, new_Re_ww)
## estimating Re for data source: ETH ...
    Region: ZH
       Data type: infection_norm_n1
##
## estimating Re for data source: ETH ...
##
    Region: ZH
       Data type: infection_norm_n2
```

### - Scanning of different SLDs

• They are scanning across 600 different combinations of mean x sd.

```
#Scan across deconvolution parameters ####
# Uncommented because this takes about 2 hrs per scan
for (incubationParam in c('zero', 'incubation')){
  for (incidence var in c('norm n1')){
    for (canton in c('ZH')){
      proc_data <- ww_data %>% filter(region == canton)
      plotData_subset <- plotData %>% filter(region == canton)
      # the scan values
      meanOpts = seq(0.5, 15, 0.5)
      sdOpts = seq(0.5, 10, 0.5)
      deconv_results = cbind(expand_grid(meanOpts, sdOpts),
                              'rmse_cc' = NA, 'coverage_cc' = NA, 'mape_cc' = NA,
                              'rmse_h' = NA, 'coverage_h' = NA, 'mape_h' = NA)
      for (row_id in 1:nrow(deconv_results)){
         deconv_config = try(deconvolveIncidence(proc_data, incidence_var,
                                                 getCountParams(incubationParam),
                                                 getGammaParams(deconv_results[row_id, 'meanOpts'],
                                                                deconv_results[row_id, 'sdOpts']),
                                                 smooth_param = TRUE, n_boot = 50))
         if('try-error' %in% class(deconv_config)){
          deconv results[row id, c('rmse cc', 'coverage cc', 'mape cc')] = c(Inf, 0, Inf)
          deconv_results[row_id, c('rmse_h', 'coverage_h', 'mape_h')] = c(Inf, 0, Inf)
```

```
Re_config = getReBootstrap(deconv_config)
         deconv_results[row_id, c('rmse_cc', 'coverage_cc', 'mape_cc')] = compareTraces(Re_config, plot
                                                                                            filter(data_t;
       }
       write_csv(deconv_results, paste0('.../scan/deconv_', incubationParam, '_',
                                         canton, '_', incidence_var, '.csv'))
     }
  }
}
###############
# Results of the scan
# Where:
Restimates <- Re_cases %>%
 mutate(region = 'ZH') %>%
  mutate(data_type = recode_factor(data_type,
                            infection_confirmed = "Confirmed cases",
                            infection_hospitalised = "Hospitalized patients",
                            infection_death = "Deaths") ) %>%
 mutate(countryIso3 = 'CHE')
date_ranges <- Re_ww %>%
  group_by(region) %>%
  summarise(min_date = min(date),
            max_date = max(date))
plotData <- Restimates %>%
  filter(region %in% c('ZH'),
         estimate_type == 'Cori_slidingWindow',
         date >= date_ranges[date_ranges$region == 'ZH', ]$min_date,
         date <= date_ranges[date_ranges$region == 'ZH',]$max_date )</pre>
compareTraces <- function(Re_i, Re_j){</pre>
  compare_df = Re_i %>%
   left_join(Re_j, by = 'date', suffix = c(".i", ".j")) %>%
   mutate(se = (median_R_mean.i - median_R_mean.j)^2,
           rele = abs((median_R_mean.j - median_R_mean.i)/median_R_mean.j),
           coverage = (median_R_mean.i > median_R_lowHPD.j) & (median_R_mean.i < median_R_highHPD.j) )</pre>
  se = compare_df %>% pull(se)
  rele = compare_df %>% pull(rele)
  coverage = compare_df %>% pull(coverage) %>% sum(na.rm = T) /length(Re_i$date)
 rmse = sqrt(sum(se, na.rm = T)/length(Re i$date))
  mape = sum(rele, na.rm = T)/length(Re_i$date)
 return(c(rmse, coverage, mape))
```