WastewaterRe Code Summary

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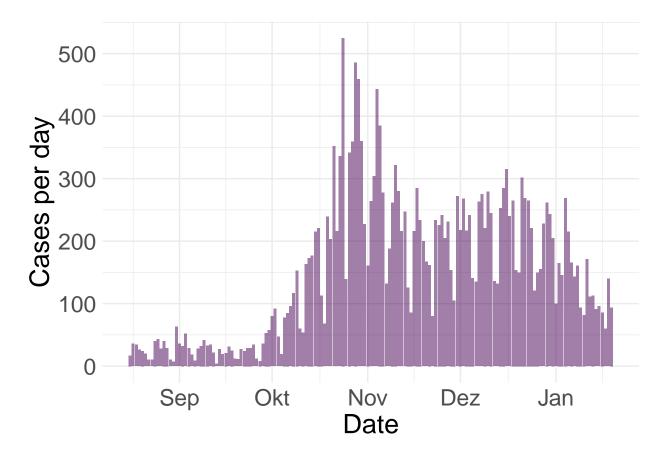
4/25/2022

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'))

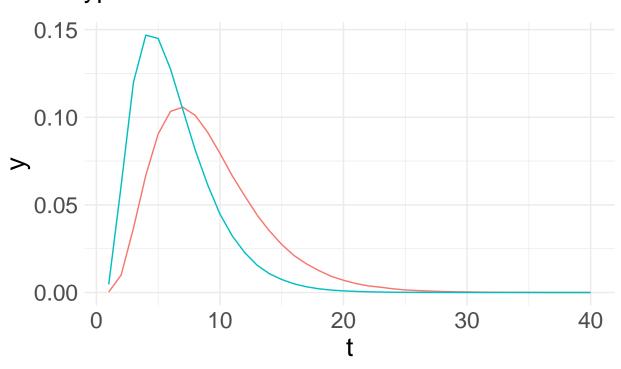
constant_delay_distributions <- list("Simulated" = get_vector_constant_waiting_time_distr(
    IncubationParams$shape, IncubationParams$scale,
    OnsetToCountParams$shape, OnsetToCountParams$scale),
    "Symptoms" = get_vector_constant_waiting_time_distr(
        IncubationParams$shape, IncubationParams$scale,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

constant_delay_distributions</pre>
```

```
 [73] \ \ 0.000000 \ \ 0.000000 \ \ 0.000000 \ \ 0.000000 \ \ 0.000000 \ \ 0.000000 \ \ 0.000000 
##
##
$Symptoms
##
[1] 0.004607 0.060842 0.119950 0.146859 0.144965 0.127522 0.104273 0.081281
[9] 0.061620 0.044772 0.032270 0.022803 0.015629 0.010728 0.007410 0.004959
[17] 0.003283 0.002125 0.001411 0.000936 0.000634 0.000401 0.000265 0.000161
##
[25] 0.000107 0.000067 0.000041 0.000033 0.000022 0.000010 0.000003 0.000004
[33] 0.000002 0.000002 0.000001 0.000001 0.000000 0.000000 0.000001 0.000000
##
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)
          [,1]
                           [,3]
                                   [,4]
##
                   [,2]
                                           [,5]
                                                   [,6]
## [3,] 0.036610 0.010062 0.000276 0.000000 0.000000 0.000000 0.000000
## [4,] 0.067133 0.036610 0.010062 0.000276 0.000000 0.000000 0.000000
## [5,] 0.090271 0.067133 0.036610 0.010062 0.000276 0.000000 0.000000
## [6,] 0.103354 0.090271 0.067133 0.036610 0.010062 0.000276 0.000000
## [7,] 0.106364 0.103354 0.090271 0.067133 0.036610 0.010062 0.000276
# 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 %>%
```

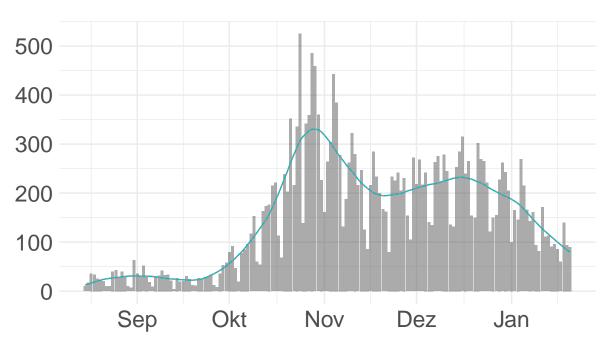
```
arrange(date) %>%
    filter(cumsum(value) > 0)
head(data_subset)
## # A tibble: 6 x 9
             region value data_type source variable country
##
     date
                                                                  date_type
              <chr> <dbl> <chr>
                                     <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 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 the

```
do_deconvolution <- function(
  incidence_data,
  days_further_in_the_past = 30,
  verbose = FALSE,
  delay_distribution_matrix,
  initial_delta,
   max_iterations = 100
) {
  # use mode of 'constant_delay_distribution'. -1 because indices are offset by one as the delay can be</pre>
```

```
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$value,
    original_incidence,
    delay_distribution_matrix = delay_distribution_matrix,
    max_delay = days_further_in_the_past,
    max_iterations = max_iterations,
    verbose = verbose)
  deconvolved_dates <- first_guess %>% pull(date)
  result <- tibble(date = deconvolved_dates, value = final_estimate)</pre>
  result <- result %>%
    filter(date <= maximal_date - first_guess_delay)</pre>
 return(result)
bootstrap_replicate_i <- 0 # looping index</pre>
max_iterations <- 100</pre>
verbose <- FALSE
data_type_subset <- unique(data_subset$data_type)[1]</pre>
is_local_cases <- TRUE</pre>
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
new_deconv_data = deconvolveIncidence(orig_cases,
                                         incidence_var = inc_var,
                                         getCountParams('incubation'),
                                         getCountParams(pasteO(inc_var, '_zh')),
                                         smooth_param = TRUE, n_boot = 50)
```