

Package ‘R0’

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Type Package

Title Estimation of R0 and Real-Time Reproduction Number from Epidemics

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Depends R (>= 2.13.0), MASS

Description Estimation of reproduction numbers for disease outbreak, based on incidence data. The R0 package implements several documented methods. It is therefore possible to compare estimations according to the methods used. Depending on the methods requested by user, basic reproduction number (commonly denoted as R0) or real-time reproduction number (referred to as R(t)) is computed, along with a 95% Confidence Interval. Plotting outputs will give different graphs depending on the methods requested : basic reproductive number estimations will only show the epidemic curve (collected data) and an adjusted model, whereas real-time methods will also show the R(t) variations throughout the outbreak time period. Sensitivity analysis tools are also provided, and allow for investigating effects of varying Generation Time distribution or time window on estimates.

License GPL (>= 2)

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R0-package	<i>Estimation of R0 and Real-Time Reproduction Number from Epidemics</i>
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Description

Estimation of reproduction numbers for disease outbreak, based on incidence data. The R0 package implements several documented methods. It is therefore possible to compare estimations according to the methods used. Depending on the methods requested by user, basic reproduction number (commonly denoted as R_0) or real-time reproduction number (referred to as $R(t)$) is computed, along with a 95% Confidence Interval. Plotting outputs will give different graphs depending on the methods requested : basic reproductive number estimations will only show the epidemic curve (collected data) and an adjusted model, whereas real-time methods will also show the $R(t)$ variations throughout the outbreak time period. Sensitivity analysis tools are also provided, and allow for investigating effects of varying Generation Time distribution or time window on estimates.

Details

Package:	R0
Type:	Package
Title:	Estimation of R0 and Real-Time Reproduction Number from Epidemics
Version:	1.2-6
Date:	2015-05-21
Author:	Pierre-Yves Boelle, Thomas Obadia
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License: GPL (≥ 2)
 LazyLoad: yes

Author(s)

Pierre-Yves Boelle, Thomas Obadia

check.incid	<i>Check incid in the input</i>
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Description

Checks incid in the input. For internal use only.

Usage

```
check.incid(incid, t = NULL,
            date.first.obs = NULL,
            time.step = 1)
```

Arguments

incid	An object (vector, data.frame, list) storing incidence
t	An optional vector of dates.
date.first.obs	Optional date of first observation, if t not specified
time.step	Optional. If date of first observation is specified, number of day between each incidence observation

Details

For internal use. Called by estimation methods to format incidence input.

check.incid handles everything related to incidence content integrity. It is designed to generate an output which comply with estimation functions requirements. Epidemic data can be provided as an epitools object (see below) or as vectors (incidence, dates, or both). When dates are provided, they can be in a separate t vector, or computed with the first value and a time step. In the end, the function returns a list with "epid" and "t" values. If you plan on using estimation functions on their own (and not through est.R0), be aware that any incorrect input format will result in erratic behavior and/or crash.

Object incid is either a list or data.frame. Expect item/column "\$dates" and/or "\$stratum3". This is expected to work with objects created by epitools package (tested with v0.5-6).

Epicurve.dates returns (among other things) a list with \$dates object. This list gives incidence per day. Other epicurve methods return \$dates along with a \$time_period object and a \$stratum3,

which contains respectively daily incidence data aggregated by the given time period, and the same data with colnames that comply with R standard time notation.

E.g.: `epicurve.weeks` returns `$dates`, `$weeks` and `$stratum3`. `$stratum3` object is a list of dates (correct syntax), where each date is repeated to reflect the incidence value at this time.

Incidence data should not contain negative or missing values.

Incidence data and time vector should have the same length.

Value

A list with components `incid` and `t`.

Author(s)

Pierre-Yves Boelle, Thomas Obadia

Examples

```
#Loading package
library(R0)

## Data is taken from the paper by Nishiura for key transmission parameters of an institutional
## outbreak during 1918 influenza pandemic in Germany
data(Germany.1918)
Germany.1918

## check.incid will extract names from the vector and coerce them as dates
check.incid(Germany.1918)

## Had Germany.1918 not have names() set, output would have been with index dates
## To force such an output, we here impose t=1:126.
## Erasing names(Germany.1918) would have produced the same
## If so, then the epid$t vector returned will be replacement values.
check.incid(Germany.1918, t=1:126)

## You can also choose not to provide a complete date vector, but to only
## indicated the first day of the observation, and the number of days between each
## observation. In this example we will assume a time step of 7 days.
check.incid(Germany.1918, date.first.obs="1918-01-01", time.step=7)

## Finally, if no names() are available for the dataset and date.first.obs is not provided,
## setting time.step to any integer value will generate a t vector starting
## from 1 and incrementing by the time.step parameter.
```

est.GT

Find the best-fitting GT distribution for a series of serial interval

Description

Find the best-fitting GT distribution for a series of serial interval

Usage

```
est.GT(infector.onset.dates = NULL,
       infectee.onset.dates = NULL,
       serial.interval = NULL,
       request.plot = FALSE,
       ...)
```

Arguments

```
infector.onset.dates      Vector of dates for infector symptoms onset.
infectee.onset.dates      Vector of dates for infectee symptoms onset.
serial.interval           Vector of reported serial interval.
request.plot              Should data adjustment be displayed at the end?
...                       Parameters passed to other functions (useful for hidden parameters of generation.time)
```

Details

Generation Time distribution can be estimated by two inputs methods. User can either provide two vectors of dates or a unique vector of reported serial intervals. If two vectors are provided, both onset.dates vectors should be of same length. Element i is the onset date for individual i . This means that infector k (symptoms on day `infector.onset.dates[k]`) infected infectee k (symptoms on day `infectee.onset.dates[k]`) If only `serial.interval` is provided, each record is assumed to be the time elapsed between each pair of infector and infectee.

When `request.plot` is set to TRUE, a graphical output provides standardized histogram of observed data along with the best-fitting adjusted model.

Value

A `R0.GT` object that complies with [generation.time](#) distribution requirements of the R0 package

Author(s)

Pierre-Yves Boelle, Thomas Obadia

Examples

```
#Loading package
library(R0)

# Data taken from traced cases of H1N1 viruses.
data(H1N1.serial.interval)
est.GT(serial.interval=H1N1.serial.interval)

## Best fitting GT distribution is a gamma distribution with mean = 3.039437 and sd = 1.676551 .
## Discretized Generation Time distribution
## mean: 3.070303 , sd: 1.676531
```

```
## [1] 0.0000000000 0.1621208802 0.2704857362 0.2358751176 0.1561845680 0.0888997193 0.0459909903
## 0.0222778094 0.0102848887 0.0045773285 0.0019791984 0.0008360608 0.0003464431 0.0001412594

# The same result can be achieved with two vectors of dates of onset.
# Here we use the same data, but trick the function into thinking onset dates are all "0".
data(H1N1.serial.interval)
est.GT(infectior.onset.dates=rep(0,length(H1N1.serial.interval)),
      infectee.onset.dates=H1N1.serial.interval)
```

 est.R0.AR

Estimate R0 from attack rate of an epidemic

Description

Estimate R0 from attack rate of an epidemic.

Usage

```
est.R0.AR(AR = NULL,
          incid = NULL, pop.size = NULL,
          S0 = 1, checked = FALSE,
          ...)
```

Arguments

AR	Attack rate as a percentage from total population
incid	Sum of incident cases, possibly in the form of a vector of counts.
pop.size	Population size in which the incident cases were observed.
S0	Initial proportion of the population considered susceptible.
checked	Internal flag used to check whether integrity checks were ran or not.
...	parameters passed to inner functions

Details

For internal use. Called by est.R0.

In the simple SIR model, the relation between R0 and the Attack Rate is in the form $R0 = -\ln((1 - AR)/S0)/(AR - (1 - S0))$.

If the population size is provided, the variance of R0 is estimated using the delta method. The hypothesis are that of homogeneous mixing, no more transmission (epidemic ended), no change in transmission or interventions during the epidemic. This estimate may be correct in closed populations, and may be less valid in other cases.

The correction for incomplete susceptibility is based on the SIR model equations.

CI is computed for the attack rate considering the population size ($CI(AR) = AR + / - 1.96 * \text{sqrt}(AR * (1 - AR)/n)$), and so the CI for the reproduction number is computed with this extreme values.

Value

A list with components:

epid	The vector of incidence, after being correctly formatted by <code>check.incid</code> . Used only by <code>plot.fit</code> .
R	The estimate of the reproduction ratio.
conf.int	The 95% confidence interval for the R estimate.
AR	Original attack rate.
begin.nb	First date of incidence record. Used only by <code>plot.fit</code> .
end.nb	Last date of incidence record. Used only by <code>plot.fit</code> .
method	Method used for the estimation.
method.code	Internal code used to designate method.

Note

This is the implementation of the formula by Dietz (1993).

Author(s)

Pierre-Yves Boelle, Thomas Obadia

References

Dietz, K. "The Estimation of the Basic Reproduction Number for Infectious Diseases." *Statistical Methods in Medical Research* 2, no. 1 (March 1, 1993): 23-41.

Examples

```
#Loading package
library(R0)

## Woodall reported an attack rate of 0.31 in a population of 1732 during
## the 1957 H2N2 influenza pandemic ('Age and Asian Influenza, 1957', BMJ, 1958)

est.R0.AR(pop.size=1732, AR=0.31)
# Reproduction number estimate using Attack Rate method
# R : 1.19698[ 1.179606 , 1.215077 ]

est.R0.AR(AR=0.31)
# Reproduction number estimate using Attack Rate method.
# R : 1.19698

est.R0.AR(pop.size=1732, incid=31)
# Reproduction number estimate using Attack Rate method
# R : 1.009057[ 1.005873 , 1.012269 ]

est.R0.AR(pop.size=1732, incid=c(2,3,4,7,4,2,4,5))
# Reproduction number estimate using Attack Rate method
# R : 1.009057[ 1.005873 , 1.012269 ]
```

```
est.R0.AR(pop.size=1732, incid=c(2,3,0,7,4,2,0,5))
# Reproduction number estimate using Attack Rate method
# R : 1.006699[ 1.003965 , 1.009453 ]
```

 est.R0.EG

Estimate R from exponential growth rate

Description

Estimate R from exponential growth rate.

Usage

```
est.R0.EG(epid, GT, t = NULL,
  begin = NULL, end = NULL,
  date.first.obs = NULL,
  time.step = 1, reg.met = "poisson",
  checked = FALSE,
  ...)
```

Arguments

epid	object containing epidemic curve data. see Details.
GT	generation time distribution
t	Vector of dates at which incidence was calculated
begin	At what time estimation begins
end	Time at which to end computation
date.first.obs	Optional date of first observation, if t not specified
time.step	Optional. If date of first observation is specified, number of day between each incidence observation
reg.met	Regression method used. Default is "poisson" (for GLM), but can be forced to "linear".
checked	Internal flag used to check whether integrity checks were ran or not.
...	parameters passed to inner functions

Details

For internal use. Called by est.R0.

method "poisson" uses Poisson regression of incidence. method "linear" uses linear regression of log(incidence)

CI is computed from the $1/M(-r)$ formula using bounds on r from the Poisson regression.

Value

A list with components:

R	The estimate of the reproduction ratio.
conf.int	The 95% confidence interval for the R estimate.
r	Exponential growth rate of the epidemic.
conf.int.r	Confidence interval of the exponential growth rate of the epidemic.
Rsquared	The deviance R-squared measure for the considered dates and model.
epid	Original epidemic data.
GT	Generation time distribution used in the computation.
data.name	Name of the data used in the fit.
begin	Starting date for the fit.
begin.nb	The number of the first day used in the fit.
end	The end date for the fit.
end.nb	The number of the last day used for the fit.
fit	Method used for fitting.
pred	Prediction on the period used for the fit.
method	Method for estimation.
method.code	Internal code used to designate method.

Note

This is the implementation of the method provided by Wallinga & Lipsitch (2007).

Author(s)

Pierre-Yves Boelle, Thomas Obadia

References

Wallinga, J., and M. Lipsitch. "How Generation Intervals Shape the Relationship Between Growth Rates and Reproductive Numbers." *Proceedings of the Royal Society B: Biological Sciences* 274, no. 1609 (2007): 599.

Examples

```
#Loading package
library(R0)

## Data is taken from the paper by Nishiura for key transmission parameters of an institutional
## outbreak during 1918 influenza pandemic in Germany)

data(Germany.1918)
mGT<-generation.time("gamma", c(3, 1.5))
```

```
est.R0.EG(Germany.1918, mGT, begin=1, end=27)
## Reproduction number estimate using Exponential Growth
## R : 1.525895[ 1.494984 , 1.557779 ]
```

 est.R0.ML

Estimate the reproduction number by maximum likelihood

Description

Estimate the reproduction number by maximum likelihood

Usage

```
est.R0.ML(epid, GT, import = NULL,
  t = NULL, begin = NULL,
  end = NULL, date.first.obs = NULL,
  time.step = 1, range = c(0.01,
    50), unknown.GT = FALSE,
  impute.incid = FALSE,
  checked = FALSE,
  ...)
```

Arguments

epid	the epidemic curve
GT	generation time distribution
import	Vector of imported cases.
t	Vector of dates at which incidence was calculated
begin	At what time estimation begins
end	Time at which to end computation
date.first.obs	Optional date of first observation, if t not specified
time.step	Optional. If date of first observation is specified, number of day between each incidence observation
range	Range in which the maximum must be looked for
unknown.GT	When GT distribution is unknown, it is estimated jointly. See details.
impute.incid	Boolean value. If TRUE, will impute unobserved cases at the beginning of the epidemic to correct for censored data
checked	Internal flag used to check whether integrity checks were ran or not.
...	parameters passed to inner functions

Details

For internal use. Called by est.R0.

White & Pagano (2009) detail two maximum likelihood methods for estimating the reproduction ratio. The first (and used by default in this package) assumes that the serial interval distribution is known, and subsequently the likelihood is only maximised depending on the value of R. The second method can be used if the serial interval distribution is unknown: in that case, the generation time is set to follow a Gamma distribution with two parameters (size, shape), and the optimization routine finds the values of R, size and shape that maximize the likelihood. However, the epidemic curve must be long enough to account for a whole generation. The authors showed that this is achieved when the cumulated amount of incident cases reaches 150. When using this method, the flag `unknown.GT` must be set to TRUE. `GT` must still be provided with a `R0.GT`-class object, however its mean and sd will be recycled as starting value for the optimization routine.

The principle of the methods described by White & all is to compute the expected number of cases in the future, and optimise to get R using a Poisson distribution.

CI is achieved by profiling the likelihood.

Value

A list with components:

<code>R</code>	The estimate of the reproduction ratio.
<code>conf.int</code>	The 95% confidence interval for the R estimate.
<code>epid</code>	Original or augmented epidemic data, depending whether <code>impute.incid</code> is set to FALSE or TRUE.
<code>epid.orig</code>	Original epidemic data.
<code>GT</code>	Generation time distribution used in the computation.
<code>begin</code>	Starting date for the fit.
<code>begin.nb</code>	The number of the first day used in the fit.
<code>end</code>	The end date for the fit.
<code>end.nb</code>	The number of the last day used for the fit.
<code>pred</code>	Prediction on the period used for the fit.
<code>Rsquared</code>	Correlation coefficient between predicted curve (by <code>fit.epid</code>) and observed epidemic curve.
<code>call</code>	Call used for the function.
<code>method</code>	Method used for fitting.
<code>method.code</code>	Internal code used to designate method.

Note

This is the implementation of the method provided by White & Pagano (2009).

Author(s)

Pierre-Yves Boelle, Thomas Obadia

References

White, L.F., J. Wallinga, L. Finelli, C. Reed, S. Riley, M. Lipsitch, and M. Pagano. "Estimation of the Reproductive Number and the Serial Interval in Early Phase of the 2009 Influenza A/H1N1 Pandemic in the USA." *Influenza and Other Respiratory Viruses* 3, no. 6 (2009): 267-276.

Examples

```
#Loading package
library(R0)

## Data is taken from paper by Nishiura for key transmission parameters of an institutional
## outbreak during the 1918 influenza pandemic in Germany)

data(Germany.1918)
mGT<-generation.time("gamma", c(2.45, 1.38))
est.R0.ML(Germany.1918, mGT, begin=1, end=27, range=c(0.01,50))
# Reproduction number estimate using Maximum Likelihood method.
# R : 1.307222[ 1.236913 , 1.380156 ]

res=est.R0.ML(Germany.1918, mGT, begin=1, end=27, range=c(0.01,50))
plot(res)

## no change in R with varying range
## (dates here are the same index as before. Just to illustrate different use)
est.R0.ML(Germany.1918, mGT, begin="1918-09-29", end="1918-10-25", range=c(0.01,100))
# Reproduction number estimate using Maximum Likelihood method.
# R : 1.307249[ 1.236913 , 1.380185 ]
```

est.R0.SB

Estimate the time dependent reproduction number using a Bayesian approach

Description

Estimate the time dependent reproduction number using a Bayesian approach. All known data are used as a prior for next iteration (see Details).

Usage

```
est.R0.SB(epid, GT, t = NULL,
          begin = NULL, end = NULL,
          date.first.obs = NULL,
          time.step = 1, force.prior = FALSE,
          checked = FALSE,
          ...)
```

Arguments

epid	the epidemic curve
GT	generation time distribution
t	Time at which epidemic was observed
begin	At what time estimation begins. Just there for "plot" purposes, not actually used
end	At what time estimation ends. Just there for "plot" purposes, not actually used
date.first.obs	Optional date of first observation, if t not specified
time.step	Optional. If date of first observation is specified, number of day between each incidence observation
force.prior	Set to any custom value to force the initial prior as a uniform distribution on [0;value]
checked	Internal flag used to check whether integrity checks were ran or not.
...	parameters passed to inner functions

Details

For internal use. Called by est.R0.

Initial prior is an unbiased uniform distribution for R, between 0 and the maximum of $\text{incid}(t+1) - \text{incid}(t)$. For each subsequent iteration, a new distribution is computed for R, using the previous output as new prior.

CI is achieved by a cumulated sum of the R posterior distribution, and corresponds to the 2.5% and 97.5% thresholds

Value

A list with components:

R	vector of R values.
conf.int	95% confidence interval for estimates.
proba.Rt	A list with successive distribution for R throughout the outbreak.
GT	Generation time distribution used in the computation.
epid	Original epidemic data.
begin	Begin date for the fit.
begin.nb	Index of begin date for the fit.
end	End date for the fit.
end.nb	Index of end date for the fit.
pred	Predictive curve based on most-likely R value.
data.name	Name of the data used in the fit.
call	Complete call used to generate results.
method	Method for estimation.
method.code	Internal code used to designate method.

Note

This is the implementation of the method provided by Bettencourt & Ribeiro (2008).

Author(s)

Pierre-Yves Boelle, Thomas Obadia

References

Bettencourt, L.M.A., and R.M. Ribeiro. "Real Time Bayesian Estimation of the Epidemic Potential of Emerging Infectious Diseases." PLoS One 3, no. 5 (2008): e2185.

Examples

```
#Loading package
library(R0)

## Data is taken from the paper by Nishiura for key transmission parameters of an institutional
## outbreak during 1918 influenza pandemic in Germany)

data(Germany.1918)
mGT <- generation.time("gamma", c(3,1.5))
SB <- est.R0.SB(Germany.1918, mGT)

## Results will include "most likely R(t)" (ie. the R(t) value for which the computed probability
## is the highest), along with 95% CI, in a data.frame object
SB
# Reproduction number estimate using Real Time Bayesian method.
# 0 0 2.02 0.71 1.17 1.7 1.36 1.53 1.28 1.43 ...

SB$Rt.quant
# Date R.t. CI.lower. CI.upper.
# 1 1918-09-29 0.00 0.01 1.44
# 2 1918-09-30 0.00 0.01 1.42
# 3 1918-10-01 2.02 0.97 2.88
# 4 1918-10-02 0.71 0.07 1.51
# 5 1918-10-03 1.17 0.40 1.84
# 6 1918-10-04 1.70 1.09 2.24
# 7 1918-10-05 1.36 0.84 1.83
# 8 1918-10-06 1.53 1.08 1.94
# 9 1918-10-07 1.28 0.88 1.66
# 10 1918-10-08 1.43 1.08 1.77
# ...

## "Plot" will provide the most-likely R value at each time unit, along with 95CI
plot(SB)
## "Plotfit" will show the complete distribution of R for 9 time unit throughout the outbreak
plotfit(SB)
```

 est.R0.TD

Estimate the time dependent reproduction number

Description

Estimate the time dependent reproduction number according to Wallinga & Teunis.

Usage

```
est.R0.TD(epid, GT, import = NULL,
          n.t0 = NULL, t = NULL,
          begin = NULL, end = NULL,
          date.first.obs = NULL,
          time.step = 1, q = c(0.025,
                               0.975), correct = TRUE,
          nsim = 10000, checked = FALSE,
          ...)
```

Arguments

epid	epidemic curve.
GT	generation time distribution.
import	Vector of imported cases.
n.t0	Number of cases at time 0.
t	Vector of dates at which incidence was measured.
begin	At what time estimation begins. Just here for "plot" purposes, not actually used
end	At what time estimation ends. Just here for "plot" purposes, not actually used
date.first.obs	Optional date of first observation, if t not specified
time.step	Optional. If date of first observation is specified, number of day between each incidence observation.
q	Quantiles for R(t). By default, 5% and 95%
correct	Correction for cases not yet observed (real time).
nsim	Number of simulations to be run to compute quantiles for R(t)
checked	Internal flag used to check whether integrity checks were ran or not.
...	parameters passed to inner functions

Details

For internal use. Called by est.R0.

CI is computed by multinomial simulations at each time step with the expected value of R.

Value

A list with components:

R	vector of R values.
conf.int	95% confidence interval for estimates.
P	Matrix of who infected whom.
p	Probability of who infected whom (values achieved by normalizing P matrix).
GT	Generation time distribution used in the computation.
epid	Original epidemic data.
import	Vector of imported cases.
pred	Theoretical epidemic data, computed with estimated values of R.
begin	Starting date for the fit.
begin.nb	The number of the first day used in the fit.
end	The end date for the fit.
end.nb	The number of the last day used for the fit.
data.name	Name of the data used in the fit.
call	Call used for the function.
method	Method for estimation.
method.code	Internal code used to designate method.

Note

This is the implementation of the method provided by Wallinga & Teunis (2004). Correction for estimation in real time is implemented as in Cauchemez et al, AJE (2006).

If imported cases are provided, they are counted in addition to autonomous cases. The final plot will show overall incidence.

Author(s)

Pierre-Yves Boelle, Thomas Obadia

References

Wallinga, J., and P. Teunis. "Different Epidemic Curves for Severe Acute Respiratory Syndrome Reveal Similar Impacts of Control Measures." *American Journal of Epidemiology* 160, no. 6 (2004): 509.

Examples

```
#Loading package
library(R0)

## Data is taken from the paper by Nishiura for key transmission parameters of an institutional
## outbreak during 1918 influenza pandemic in Germany)
```



```

data(Germany.1918)
mGT<-generation.time("gamma", c(3, 1.5))
TD <- est.R0.TD(Germany.1918, mGT, begin=1, end=126, nsim=100)
# Warning messages:
# 1: In est.R0.TD(Germany.1918, mGT) : Simulations may take several minutes.
# 2: In est.R0.TD(Germany.1918, mGT) : Using initial incidence as initial number of cases.
TD
# Reproduction number estimate using Time-Dependent method.
# 2.322239 2.272013 1.998474 1.843703 2.019297 1.867488 1.644993 1.553265 1.553317 1.601317 ...

## An interesting way to look at these results is to agregate initial data by longest time unit,
## such as weekly incidence. This gives a global overview of the epidemic.
TD.weekly <- smooth.Rt(TD, 7)
TD.weekly
# Reproduction number estimate using Time-Dependant method.
# 1.878424 1.580976 1.356918 1.131633 0.9615463 0.8118902 0.8045254 0.8395747 0.8542518 0.8258094..
plot(TD.weekly)

```

estimate.R

Estimate R0 for one incidence dataset using several methods

Description

Estimate R0 for one incidence dataset using several methods.

Usage

```

estimate.R(epid = NULL,
           GT = NULL, t = NULL,
           begin = NULL, end = NULL,
           date.first.obs = NULL,
           time.step = 1, AR = NULL,
           pop.size = NULL,
           S0 = 1, methods = NULL,
           checked = TRUE, ...)

```

Arguments

epid	Name of epidemic dataset
GT	Generation Time repartition function
t	Date vector
begin	Begin date for estimation. Can be an integer or a date (YYYY-mm-dd or YYYY/mm/dd)
end	End date for estimation. Can be an integer or a date (YYYY-mm-dd or YYYY/mm/dd)
date.first.obs	Optional date of first observation, if t not specified
time.step	Optional. If date of first observation is specified, number of day between each incidence observation

AR	Attack rate as a percentage from total population
pop.size	Population size in which the incident cases were observed. See more details in est.R0.AR documentation
S0	Initial proportion of the population considered susceptible
methods	List of methods to be used for R0 estimation/comparison. Must be provided as <code>c("method 1", "method 2", ...)</code>
checked	Internal flag used to check whether integrity checks were ran or not.
...	Parameters passed to inner functions

Details

Currently, supported methods are Exponential Growth (EG), Maximum Likelihood (ML), Attack Rate (AR), Time-Dependant (TD), and Sequential Bayesian (SB). See references below.

Value

A list with components:

estimates	List containing all results from called methods.
epid	Epidemic curve.
GT	Generation Time distribution function.
t	Date vector.
begin	Begin date for estimation.
end	End date for estimation.

Author(s)

Pierre-Yves Boelle, Thomas Obadia

References

- [est.R0.EG](#): Wallinga, J., and M. Lipsitch. "How Generation Intervals Shape the Relationship Between Growth Rates and Reproductive Numbers." *Proceedings of the Royal Society B: Biological Sciences* 274, no. 1609 (2007): 599.
- [est.R0.ML](#): White, L.F., J. Wallinga, L. Finelli, C. Reed, S. Riley, M. Lipsitch, and M. Pagano. "Estimation of the Reproductive Number and the Serial Interval in Early Phase of the 2009 Influenza A/H1N1 Pandemic in the USA." *Influenza and Other Respiratory Viruses* 3, no. 6 (2009): 267-276.
- [est.R0.AR](#): Dietz, K. "The Estimation of the Basic Reproduction Number for Infectious Diseases." *Statistical Methods in Medical Research* 2, no. 1 (March 1, 1993): 23-41.
- [est.R0.TD](#): Wallinga, J., and P. Teunis. "Different Epidemic Curves for Severe Acute Respiratory Syndrome Reveal Similar Impacts of Control Measures." *American Journal of Epidemiology* 160, no. 6 (2004): 509.
- [est.R0.SB](#): Bettencourt, L.M.A., and R.M. Ribeiro. "Real Time Bayesian Estimation of the Epidemic Potential of Emerging Infectious Diseases." *PLoS One* 3, no. 5 (2008): e2185.

Examples

```

#Loading package
library(R0)

## Outbreak during 1918 influenza pandemic in Germany)
data(Germany.1918)
mGT<-generation.time("gamma", c(3, 1.5))
estR0<-estimate.R(Germany.1918, mGT, begin=1, end=27, methods=c("EG", "ML", "TD", "AR", "SB"),
                  pop.size=100000, nsim=100)

attributes(estR0)
## $names
## [1] "epid"      "GT"      "begin"   "end"     "estimates"
##
## $class
## [1] "R0.sR"

## Estimates results are stored in the $estimates object
estR0
## Reproduction number estimate using Exponential Growth method.
## R : 1.525895[ 1.494984 , 1.557779 ]
##
## Reproduction number estimate using Maximum Likelihood method.
## R : 1.383996[ 1.309545 , 1.461203 ]
##
## Reproduction number estimate using Attack Rate method.
## R : 1.047392[ 1.046394 , 1.048393 ]
##
## Reproduction number estimate using Time-Dependent method.
## 2.322239 2.272013 1.998474 1.843703 2.019297 1.867488 1.644993 1.553265 1.553317 1.601317 ...
##
## Reproduction number estimate using Sequential Bayesian method.
## 0 0 2.22 0.66 1.2 1.84 1.43 1.63 1.34 1.52 ...

## If no date vector nor date of first observation are provided, results are the same
## except time values in $t are replaced by index

```

generation.time

Generation Time distribution

Description

Create an object of class GT representing a discretized Generation Time distribution.

Usage

```

generation.time(type = c("empirical",
                        "gamma", "weibull",

```

```
"lognormal"), val = NULL,
truncate = NULL,
step = 1, first.half = TRUE,
p0 = TRUE)
```

Arguments

type	Type of distribution.
val	Vector of values used for the empirical distribution, or c(mean, sd) if parametric.
truncate	Maximum extent of the GT distribution.
step	Time step used in discretization.
first.half	First probability computed on half period.
p0	Is probability on day 0 0

Details

How the GT is discretized may have some impact on the shape of the distribution. For example, the distribution may be discretized in intervals of 1 time step starting at time 0, i.e. [0,1), [1,2), and so on. Or it may be discretized as [0,0.5), [0.5, 1.5), ... (the default).

If the GT is discretized from a given continuous distribution, the expected duration of the Generation Time will be less than the nominal, it will be in better agreement in the second discretization.

If p0 is TRUE (default) then the generation time distribution is set to 0 for day 0.

If no truncation is provided, the distribution will be truncated at 99.99 percent probability.

Value

A list with components:

GT	The probabilities for each time unit, starting at time 0.
time	The time at which probabilities are calculated.
mean	The mean of the discretized GT.
sd	The standard deviation of the discretized GT.

Author(s)

Pierre-Yves Boelle, Thomas Obadia

Examples

```
#Loading package
library(R0)

# GT for children at house(from Cauchemez PNAS 2011)

GT.chld.hsld1<-generation.time("empirical", c(0,0.25,0.2,0.15,0.1,0.09,0.05,0.01))
plot(GT.chld.hsld1, col="green")
GT.chld.hsld1
```

```

# Discretized Generation Time distribution
# mean: 2.729412 , sd: 1.611636
# [1] 0.00000000 0.29411765 0.23529412 0.17647059 0.11764706 0.10588235 0.05882353
# [8] 0.01176471

GT.chld.hsld2<-generation.time("gamma", c(2.45, 1.38))
GT.chld.hsld2
# Discretized Generation Time distribution
# mean: 2.504038 , sd: 1.372760
# [1] 0.0000000000 0.2553188589 0.3247178420 0.2199060781 0.1144367560
# [6] 0.0515687896 0.0212246257 0.0082077973 0.0030329325 0.0010825594
#[11] 0.0003760069 0.0001277537

# GT for school & community
GTs1<-generation.time("empirical", c(0,0.95,0.05))
plot(GTs1, col='blue')

plot(GT.chld.hsld1, ylim=c(0,0.5), col="red")
par(new=TRUE)
plot(GT.chld.hsld2, xlim=c(0,7), ylim=c(0,0.5), col="black")

```

Germany.1918

Germany.1918 exemple dataset

Description

Temporal distribution of Spanish flu in Prussia, Germany, from 1918-19

Usage

```
data(Germany.1918)
```

Format

The format is: num [1:126] 10 4 4 19 6 13 28 23 35 27 ...

Source

Peiper O: Die Grippe-Epidemie in Preussen im Jahre 1918/19. Veroeffentlichungen aus dem Gebiete der Medizinalverwaltung 1920, 10: 417-479 (in German).

References

Nishiura H. Time variations in the transmissibility of pandemic influenza in Prussia, Germany, from 1918-19. In: Theoretical Biology and Medical Modelling

Examples

```
data(Germany.1918)
## maybe str(Germany.1918) ; plot(Germany.1918) ...
```

GT.chld.hsld *2009 A/H1N1 observed Generation Time distribution*

Description

Observed generation time distribution for children in household for the 2009 A/H1N1 influenza pandemic.

Usage

```
data(GT.chld.hsld)
```

Format

The format is: num [1:8] 0 0.25 0.2 0.15 0.1 0.09 0.05 0.01

Source

S. Cauchemez, A. Bhattarai, T.L. Marchbanks, R.P. Fagan, S. Ostroff, N.M. Ferguson, et al., Role of Social Networks in Shaping Disease Transmission During a Community Outbreak of 2009 H1N1 Pandemic Influenza, *Pnas*. 108 (2011) 2825-2830.

Examples

```
data(GT.chld.hsld)
## maybe str(GT.chld.hsld) ; plot(GT.chld.hsld) ...
```

H1N1.serial.interval *H1N1 serial interval sample*

Description

Data taken from traced cases of H1N1 viruses.

Usage

```
data(H1N1.serial.interval)
```

Format

The format is: num [1:355] 1 1 3 2 1 2 1 3 2 4 ...

Details

Vector of values that represents the time lag between symptoms onset for pairs of infector/infectee, for a dataset of complete traced cases. Each value accounts for a pair of infector/infectee. This serial interval is often substituted for the generation time distribution, as it is easier to observe.

Examples

```
data(H1N1.serial.interval)
## maybe str(H1N1.serial.interval) ; plot(H1N1.serial.interval) ...
```

impute.incid

Optimization routine for incidence imputation

Description

When first records of incidence are unavailable, tries to impute censored cases to rebuild longer epidemic vector

Usage

```
impute.incid(CD.optim.vect,
             CD.epid, CD.R0, CD.GT)
```

Arguments

CD.optim.vect	Vector of two elements (multiplicative factor, log(highest imputed data) to be optimized
CD.epid	Original epidemic vector, output of check.incid()
CD.R0	Assumed R0 value for the original epidemic vector
CD.GT	Generation time distribution to be used for computations

Details

This function is not intended for stand-alone use. It optimizes the values of vect, based upon minimization of deviation between actual epidemics data and observed generation time. The optimized function is [censored.deviation](#), which returns the deviation used for minimization. Stand-alone use can be conducted, however this assumes data are all of the correct format.

Value

A vector with both imputed incidence and source available data.

Author(s)

Pierre-Yves Boelle, Thomas Obadia

`inspect.data`*Inspect input data for common issues*

Description

Inspect input data and look for common mistakes. The function does not return any object but yields warnings with suggestions as to how to clean inputs before running estimation routines.

Usage

```
inspect.data(incid, t = NULL,  
             GT = NULL)
```

Arguments

<code>incid</code>	An object (vector, data.frame, list) storing incidence
<code>t</code>	An optional vector of dates
<code>GT</code>	Generation Time repartition function

Details

`inspect.data` looks for common issues that could affect estimation routines. Such issues include too low incidence counts, leading/trailing zeros, non-integer values... Before any checks are conducted, the data are passed to `check.incid` that will try and guess the format of the data.

A not-so-uncommon issue is to provide non-integer counts for incidence, for example when working with aggregated data that represent averaged number of cases across different communities. This however does not agree well with parametric likelihood that assume exponential growth over the early stage of an epidemic or Poisson distribution of cases, where non-integer values will cause calculations to fail.

Missing values may cause issues if not handled properly. By default, `check.incid()` will recast missing values to zero. Leading and trailing NA's should be omitted entirely from the input. Gaps found between available data may also cause issues if they span over a period that's longer than the total generation time. A warning is raised to inform on these possible issues.

Likewise, leading and tailing zeros would cause similar issues. `Begin` will default to the first value and end to the peak one. Just in case, these will be inspected here too. Sequence of 0s exceeding the length of the generation time will also yield a warning.

Scarce data may also cause errors when optimizing likelihood functions. A time-series of incidence spanning for a duration shorter than that of the generation time distribution is likely to correspond to an index case that hasn't yet infected all its offsprings. This would bias estimates downwards and should be taken into account when interpreting results.

Author(s)

Pierre-Yves Boelle, Thomas Obadia

`plot.R0.S`*Plot objects from `sensitivity.analysis`*

Description

Plots objects from `sensitivity.analysis`

Usage

```
## S3 method for class 'R0.S'  
plot(x, what = "heatmap",  
      time.step = 1, skip = 5,  
      ...)
```

Arguments

<code>x</code>	Result of <code>sensitivity.analysis</code> (class R0.S)
<code>what</code>	Specify the desired output. Can be "heatmap" (default), "criterion", or both.
<code>time.step</code>	Optional. If date of first observation is specified, number of day between each incidence observation
<code>skip</code>	Number of results to ignore (time period of X days) when looking for highest Rsquared value.
<code>...</code>	Parameters passed to inner functions

Details

For internal use. Called by `plot`.

Value

A data frame with best R0 measure for each possible time period, along with corresponding begin/end dates

`$max.Rsquared` Best R0 measure for each time period, as measured by their Rsquared value.

Author(s)

Pierre-Yves Boelle, Thomas Obadia

 plotfit

Generic S3 method to plot either "R0.R" and "R0.sR" objects

Description

Generic S3 method to plot either "R0.R" and "R0.sR" objects

Usage

```
plotfit(x, all = TRUE,
        xscale = "w", SB.dist = TRUE,
        ...)
```

Arguments

x	Object for which the fit should be plotted.
all	Should the whole epidemic curve be shown
xscale	Scale to be adjusted on X axis. Can be "d" (day), "w" (week (default)), "f" (fornight), "m" (month).
SB.dist	Should R distribution throughout the epidemic be plotted for SB method? (default: TRUE)
...	parameters passed to plot.R

Details

plot.fit is designed to either call plot.fit.R0.R or plot.fit.R0.sR. This S3 Method allows for plotting the goodness of fit of a model to the original epidemic curve provided by user. Depending on the method of estimation, the graphical output will vary: - EG, ML and TD methods will show the original epidemic curve, along with the best-fitting prediction model - AR will only show the epidemic curve, since no actual model is computed - RTB will display 9 density curves for the R distribution throughout the epidemic

Author(s)

Pierre-Yves Boelle, Thomas Obadia

\$GT.sd	Range of standard deviations used for tested GTs.
\$R	Computed value for Reproduction Number given GT.type, GT.mean and GT.sd.
\$conf.int[1]	The lower limit of 95% CI for R.
\$conf.int[2]	The upper limit of 95% CI for R.

Author(s)

Pierre-Yves Boelle, Thomas Obadia

sa.time

Sensitivity analysis of basic reproduction ratio to begin/end dates

Description

Sensitivity analysis of reproduction ratio using supported estimation methods.

Usage

```
sa.time(incid, GT, begin = NULL,
        end = NULL, est.method,
        t = NULL, date.first.obs = NULL,
        time.step = 1, res = NULL,
        ...)
```

Arguments

incid	incident cases
GT	generation time distribution
begin	Vector of begins date of the estimation of epidemic
end	Vector of end dates of estimation of the epidemic
est.method	Estimation method used for sensitivity analysis
t	Dates vector to be passed to estimation function
date.first.obs	Optional date of first observation, if t not specified
time.step	Optional. If date of first observation is specified, number of day between each incidence observation
res	If specified, will extract most of data from a R0.R-class result already generated by est.R0 and run sensitivity analysis on it.
...	parameters passed to inner functions

Details

By varying different pairs of begin and end dates, different estimates of reproduction ratio can be analyzed.

'begin' and 'end' vector must have the same length for the sensitivity analysis to run. They can be provided either as "dates" or "numeric" values, depending on the other parameters (see [check.incid](#)). If some begin/end dates overlap, they are ignored, and corresponding uncomputed data are set to NA. Also, note that unreliable Rsquared values are achieved for very small time period (begin ~ end). These values are not representative of the epidemic outbreak behaviour.

Value

A list with components as a data frame:

df	data.frame object with all results from sensitivity analysis.
df.clean	the same object, with NA rows removed. Used only for easy export of results.
mat.sen	Matrix with values of R0 given begin (rows) and end (columns) dates.
begin	A range of begin dates in epidemic.
end	A range of end dates in epidemic.

Author(s)

Pierre-Yves Boelle, Thomas Obadia

sensitivity.analysis *Sensitivity analysis of basic reproduction ratio to begin/end dates*

Description

Sensitivity analysis of reproduction ratio using supported estimation methods.

Usage

```
sensitivity.analysis(incid,  
  GT = NULL, begin = NULL,  
  end = NULL, est.method = NULL,  
  sa.type, res = NULL,  
  GT.type = NULL, GT.mean.range = NULL,  
  GT.sd.range = NULL,  
  t = NULL, date.first.obs = NULL,  
  time.step = 1, ...)
```

Arguments

<code>incid</code>	incident cases
<code>GT</code>	generation time distribution
<code>begin</code>	Vector of begins date of the estimation of epidemic
<code>end</code>	Vector of end dates of estimation of the epidemic
<code>est.method</code>	Estimation method used for sensitivity analysis
<code>sa.type</code>	string argument to choose between "time" and "GT" sensitivity analysis.
<code>res</code>	If specified, will extract most of data from a R0.R-class result already generated by <code>est.R0</code> and run sensitivity analysis on it.
<code>GT.type</code>	Type of distribution for GT (see <code>GT.R</code> for details)
<code>GT.mean.range</code>	mean used for all GT distributions throughout the simulation
<code>GT.sd.range</code>	Range of standard deviation used for GT distributions. Must be provided as a vector.
<code>t</code>	Dates vector to be passed to estimation function
<code>date.first.obs</code>	Optional date of first observation, if <code>t</code> not specified
<code>time.step</code>	Optional. If date of first observation is specified, number of day between each incidence observation
<code>...</code>	parameters passed to inner functions

Details

This is a generic call function to use either `sa.time` or `sa.GT`. Argument must be chosen accordingly to `sa.type`. Please refer to `sa.time` and `sa.GT` for further details about arguments.

'begin' and 'end' vector must have the same length for the sensitivity analysis to run. They can be provided either as "dates" or "numeric" values, depending on the other parameters (see `check.incid`). If some begin/end dates overlap, they are ignored, and corresponding uncomputed data are set to NA. Also, note that unreliable Rsquared values are achieved for very small time period (`begin ~ end`). These values are not representative of the epidemic outbreak behaviour.

Value

An sensitivity analysis object of class "R0.S" with components depending on sensitivity analysis type.

Author(s)

Pierre-Yves Boelle, Thomas Obadia

Examples

```
#Loading package
library(R0)

## Data is taken from the paper by Nishiura for key transmission parameters of an institutional
## outbreak during 1918 influenza pandemic in Germany)
```

```

data(Germany.1918)

## For this exemple, we use the exact same call as for the internal sensitivity analysis function

## sa.type = "GT"

## Here we will test GT with means of 1 to 5, each time with SD constant (1)
## GT and SD can be either fixed value or vectors of values
## Actual value in simulations may differ, as they are adapted according to the distribution type
tmp<-sensitivity.analysis(sa.type="GT", incid=Germany.1918, GT.type="gamma", GT.mean=seq(1,5,1),
                        GT.sd.range=1, begin=1, end=27, est.method="EG")

## Results are stored in a matrix, each line dedicated to a (mean,sd) couple
plot(x=tmp[,"GT.Mean"], xlab="mean GT (days)", y=tmp[,"R"], ylim=c(1.2, 2.1), ylab="R0 (95% CI)",
     type="p", pch=19, col="black", main="Sensitivity of R0 to mean GT")
arrows(x0=as.numeric(tmp[,"GT.Mean"]), y0=as.numeric(tmp[,"CI.lower"]),
       y1=as.numeric(tmp[,"CI.upper"]), angle=90, code=3, col="black", length=0.05)
## One could tweak this example to change sorting of values (per mean, or per standard deviation)
## eg: 'x=tmp[,c('GT.Mean')]' could become 'x=tmp[,c('GT.SD')]'

## sa.type="time"

mGT<-generation.time("gamma", c(2.6,1))
sen=sensitivity.analysis(sa.type="time", incid=Germany.1918, GT=mGT, begin=1:10, end=16:25,
                       est.method="EG")
# ...
# Warning message:
# If 'begin' and 'end' overlap, cases where begin >= end are skipped.
# These cases often return Rsquared = 1 and are thus ignored.
## A list with different estimates of reproduction ratio, exponential growth rate and 95%CI
## with different pairs of begin and end dates in form of data frame is returned.
## If method is "EG", results will include growth rate and deviance R-squared measure
## Else, if "ML" method is used, growth rate and R-squared will be set as NA

## Interesting results include the variation of R0 given specific begin/end dates.
## Such results can be plot as a colored matrix and display Rsquared=f(time period)
plot(sen, what=c("criterion","heatmap"))
## Returns complete data.frame of best R0 value for each time period
## (allows for quick visualization)
## The "best.fit" is the time period over which the estimate is the more robust

# $best.fit
#   Time.period Begin.dates End.dates      R Growth.rate  Rsquared CI.lower. CI.upper.
# 92           15 1970-01-08 1970-01-23 1.64098  0.1478316 0.9752564 1.574953 1.710209

```

sim.epid

*Epidemic outbreak simulation***Description**

Generates several epidemic curves with specified distribution and reproduction number.

Usage

```
sim.epid(epid.nb, GT,
         R0, epid.length,
         family, negbin.size = NULL,
         peak.value = 50)
```

Arguments

epid.nb	Number of outbreaks to be generated.
GT	Generation time distribution for the pathogen. Must be a R0.GT-class object.
R0	Basic reproduction number.
epid.length	Length of the epidemic.
family	Distribution type for the new cases, either "poisson" or "negbin".
negbin.size	Over-dispersion parameter, if family is set to "negbin".
peak.value	Threshold value for incidence before epidemics begins decreasing

Details

This function is only used for simulation purposes. The output is a matrix of n columns (number of outbreaks) by m rows (maximum length of an outbreak).

When using rnbinom with "mean" and "size" moments, the variance is given by $\text{mean} + \text{mean}^2/\text{size}$ (see ?rnbinom). One should determine the size accordingly to the R0 value to increase the dispersion. From the previous variance formula, if $\text{Var}(X) = k \cdot R0$, $\text{size} = R0/(k-1)$

Author(s)

Pierre-Yves Boelle, Thomas Obadia

Examples

```
#Loading package
library(R0)

## In this example we simulate n=100 epidemic curves, with peak value at 150 incident cases,
## and maximum epidemic length of 30 time units.
## Only the outbreak phase is computed. When the peak value is reached, the process is stopped
## and another epidemic is generated.
sim.epid(epid.nb=100, GT=generation.time("gamma",c(3,1.5)), R0=1.5,
         epid.length=30, family="poisson", peak.value=150)

# Here, a 30*100 matrix is returned. Each column is a single epidemic.
```

sim.epid.indiv	<i>Influenza-like illness simulation (individual-based model)</i>
----------------	---

Description

Generates several epidemic curves on a individual-based model

Usage

```
sim.epid.indiv(beta,  
               Tmax, n = 1, family = "poisson",  
               negbin.size = NULL)
```

Arguments

beta	Contact rate in the SEIR model.
Tmax	Maximum length of the epidemic (cases infected after this length will be truncated).
n	Number of epidemics to be simulated (default is 1)
family	Distribution of offspring (default is "poisson").
negbin.size	If family is set to "negbin", sets the size parameter of the negative binomial distribution.

Value

A matrix with epidemics stored as columns (incidence count)

Note

This is not the final version. This is the exact function as used in the manuscript (Obadia et al., 2012). It will be properly implemented to conform with other objects of the package in future releases.

The epidemic is simulated using a branching process, with infinite number of susceptibles to allow for exponential growth. The model used follows the Crump-Mode-Jagers description, with S/E/I/R description of the natural history. Latent and infectious period follow parametrized Gamma distributions typical of influenza. An index case is first introduced, and offspring is sampled from a negative binomial distribution, with mean $\beta * I$ and variance $negbin.size * \beta * I$, to allow for overdispersion.

Author(s)

Pierre-Yves Boelle, Thomas Obadia

smooth.Rt

Smooth real-time reproduction number over larger time period

Description

Smooth real-time reproduction number over larger time period

Usage

```
smooth.Rt(res, time.period)
```

Arguments

res	An object of class "R0.R", created by any real-time method (currently implemented: TD and SB)
time.period	Time period to be used for computations.

Details

Regrouping Time-Dependant R(t) values, or even Real Time Bayesian most-likely R values (according to R distributions) should take into account the Generation Time. Results can be plotted exactly the same as input estimations, except they won't show any goodness of fit curve.

Value

A list with components:

R	The estimate of the reproduction ratio.
conf.int	The 95% confidence interval for the R estimate.
GT	Generation time distribution used in the computation.
epid	Original or augmented epidemic data, depending whether impute.values is set to FALSE or TRUE.
begin	Starting date for the fit.
begin.nb	The number of the first day used in the fit.
end	The end date for the fit.
end.nb	The number of the last day used for the fit.
data.name	The name of the dataset used.
call	Call used for the function.
method	Method used for fitting.
method.code	Internal code used to designate method.

Author(s)

Pierre-Yves Boelle, Thomas Obadia

Examples

```

#Loading package
library(R0)

## This script allows for generating a new estimation for RTB and TD methods.
## Estimations used as input are agregated by a time period provided by user.
## Results can be plotted exactly the same was as input estimations,
## except they won't show any goodness of fit curve.
data(Germany.1918)
mGT <- generation.time("gamma", c(3,1.5))
TD <- estimate.R(Germany.1918, mGT, begin=1, end=126, methods="TD", nsim=100)
TD
# Reproduction number estimate using Time-Dependant method.
# 2.322239 2.272013 1.998474 1.843703 2.019297 1.867488 1.644993 1.553265 1.553317 1.601317 ...
TD$estimates$TD$Rt.quant
#   Date      R.t. CI.lower. CI.upper.
# 1      1 2.3222391 1.2000000 2.4000000
# 2      2 2.2720131 2.7500000 6.2500000
# 3      3 1.9984738 2.7500000 6.5000000
# 4      4 1.8437031 0.7368421 1.5789474
# 5      5 2.0192967 3.1666667 6.1666667
# 6      6 1.8674878 1.6923077 3.2307692
# 7      7 1.6449928 0.8928571 1.6428571
# 8      8 1.5532654 1.3043478 2.2608696
# 9      9 1.5533172 1.0571429 1.7428571
# 10    10 1.6013169 1.6666667 2.6666667
# ...

TD.weekly <- smooth.Rt(TD$estimates$TD, 7)
TD.weekly
# Reproduction number estimate using Time-Dependant method.
# 1.878424 1.580976 1.356918 1.131633 0.9615463 0.8118902 0.8045254 0.8395747 0.8542518 0.8258094..

TD.weekly$Rt.quant
#   Date      R.t. CI.lower. CI.upper.
# 1      1 1.8784240 1.3571429 2.7380952
# 2      8 1.5809756 1.3311037 2.0100334
# 3     15 1.3569175 1.1700628 1.5308219
# 4     22 1.1316335 0.9961229 1.2445302
# 5     29 0.9615463 0.8365561 1.0453074
# 6     36 0.8118902 0.7132668 0.9365193
# 7     43 0.8045254 0.6596685 0.9325967
# 8     50 0.8395747 0.6776557 1.0402930
# 9     57 0.8542518 0.6490251 1.1086351
# 10    64 0.8258094 0.5836735 1.1142857
# 11    71 0.8543877 0.5224719 1.1460674
# 12    78 0.9776385 0.6228070 1.4912281
# 13    85 0.9517133 0.5304348 1.3652174
# 14    92 0.9272833 0.5045045 1.3423423
# 15    99 0.9635479 0.4875000 1.5125000
# 16   106 0.9508951 0.5000000 1.6670455
# 17   113 0.9827432 0.5281989 1.8122157

```

```
# 18 120 0.5843895 0.1103040 0.9490928
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