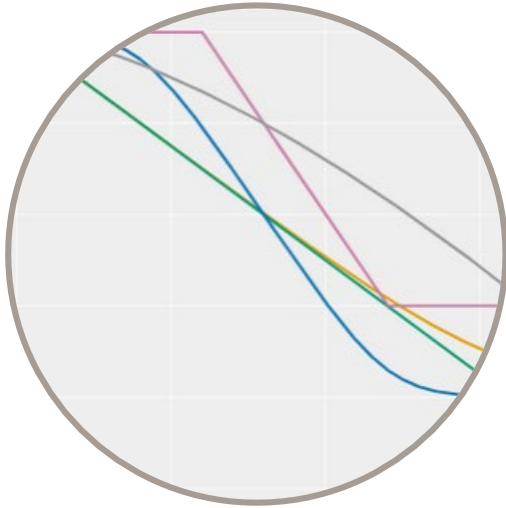


biogrowth & bioinactivation - making predictive microbiology a bit easier

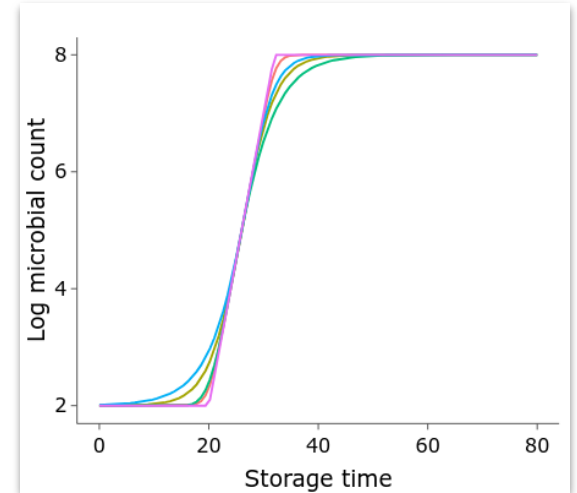
IAFP Software Fair Series

Alberto Garre, postdoc at Wageningen University



We know our RTE product is safe... but
One day, it was on the sun for one hour

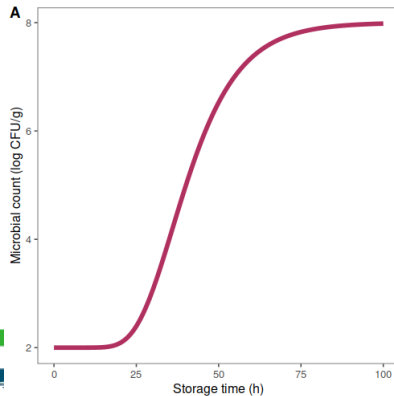
What should we do?



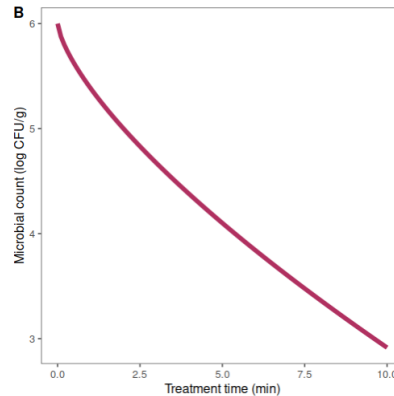
Predictive microbiology

Part of food science that develops and validates mathematical models to predict the microbial response within the food chain

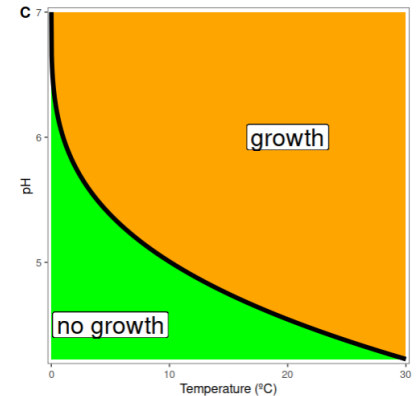
Growth



Inactivation



Growth boundary



Predictive microbiology is mature now

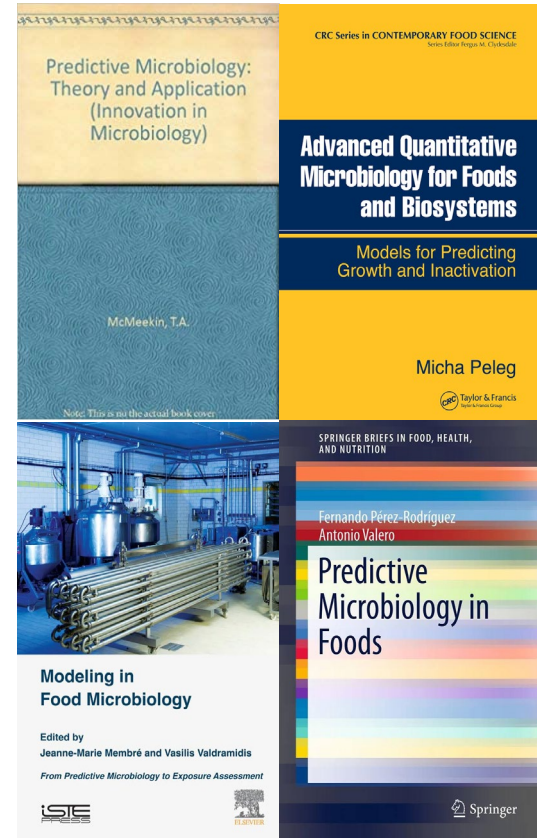
~100 or 50 years old

Main principles defined

Established experimental methodologies

Sheared modeling approaches

Included in some regulations



(Some) applications of predictive micro

Process design

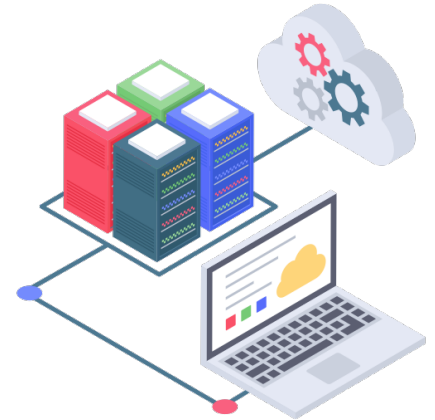
Shelf life estimation

HACCP plans

Food Safety Objectives

Quantitative Microbial Risk Assessment

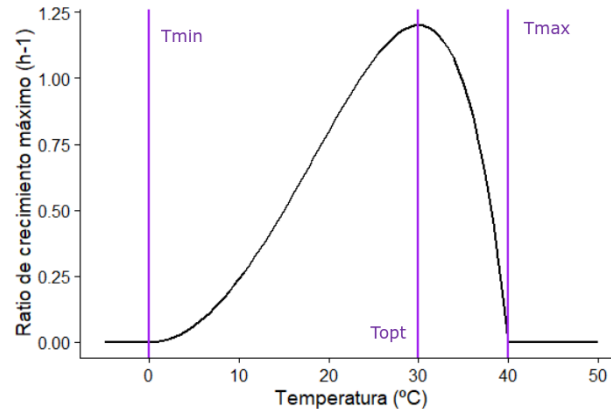
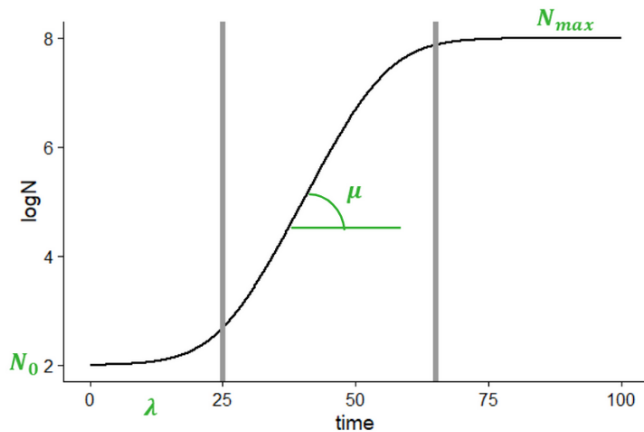
Education



The usual modelling approach

Primary model: relationship between the microbial count and the elapsed time

Secondary model: relationship between the kinetic parameters and the environment (temperature, pH...)

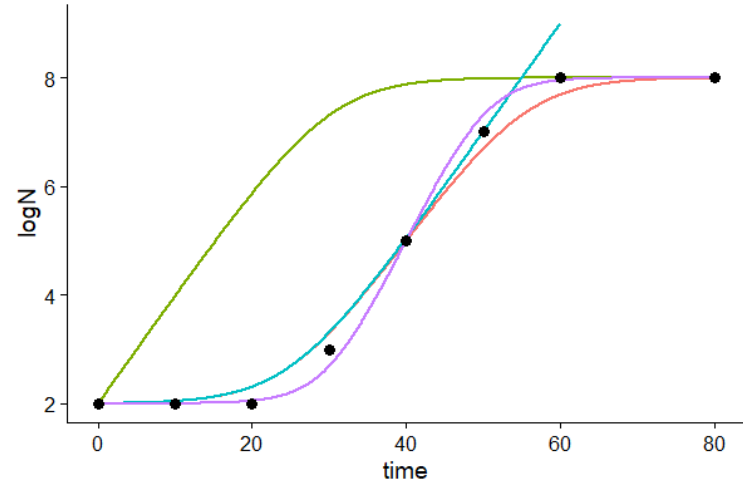


Model fitting is central in predictive microbiology

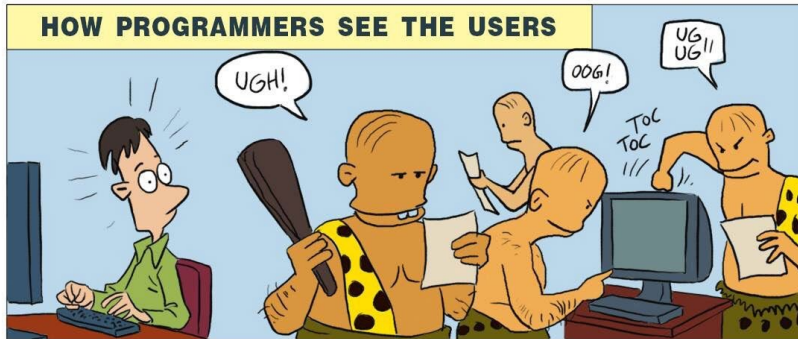
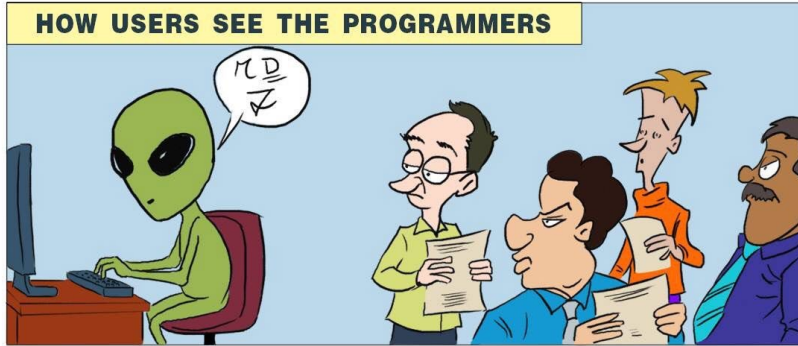
Parameters cannot be known

They are estimated from data

Always question validity



Issue: predictive micro cannot be done by hand



Methodology well established...
but complex

Fitting of non-linear models can be
complicated (identifiability).


Dynamic growth requires models in
differential equations.

Software can bridge this gap


During the last years several applications to make life easier

Simplify and facilitate the model process

Cover practically every step of QMRA/shelf life estimation



Food Microbiology
Volume 45, Part B, February 2015, Pages 290-299



Software for predictive microbiology and risk assessment: A description and comparison of tools presented at the ICPMF8 Software Fair

Fanny Tenenhaus-Aziza ^a ✉, Mariem Ellouze ^b ✉



Current Opinion in Food Science
Volume 44, April 2022, 100814



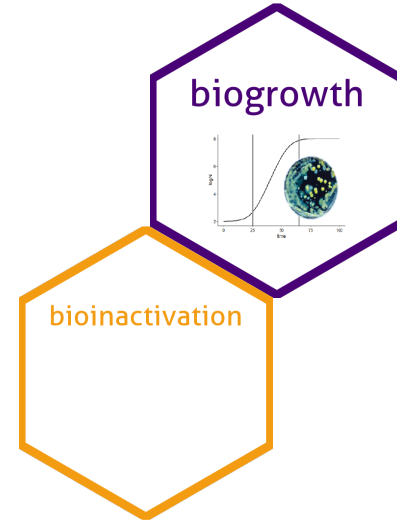
New software solutions for microbiological food safety assessment and management

Arícia Possas ✉, Antonio Valero ✉, Fernando Pérez-Rodríguez

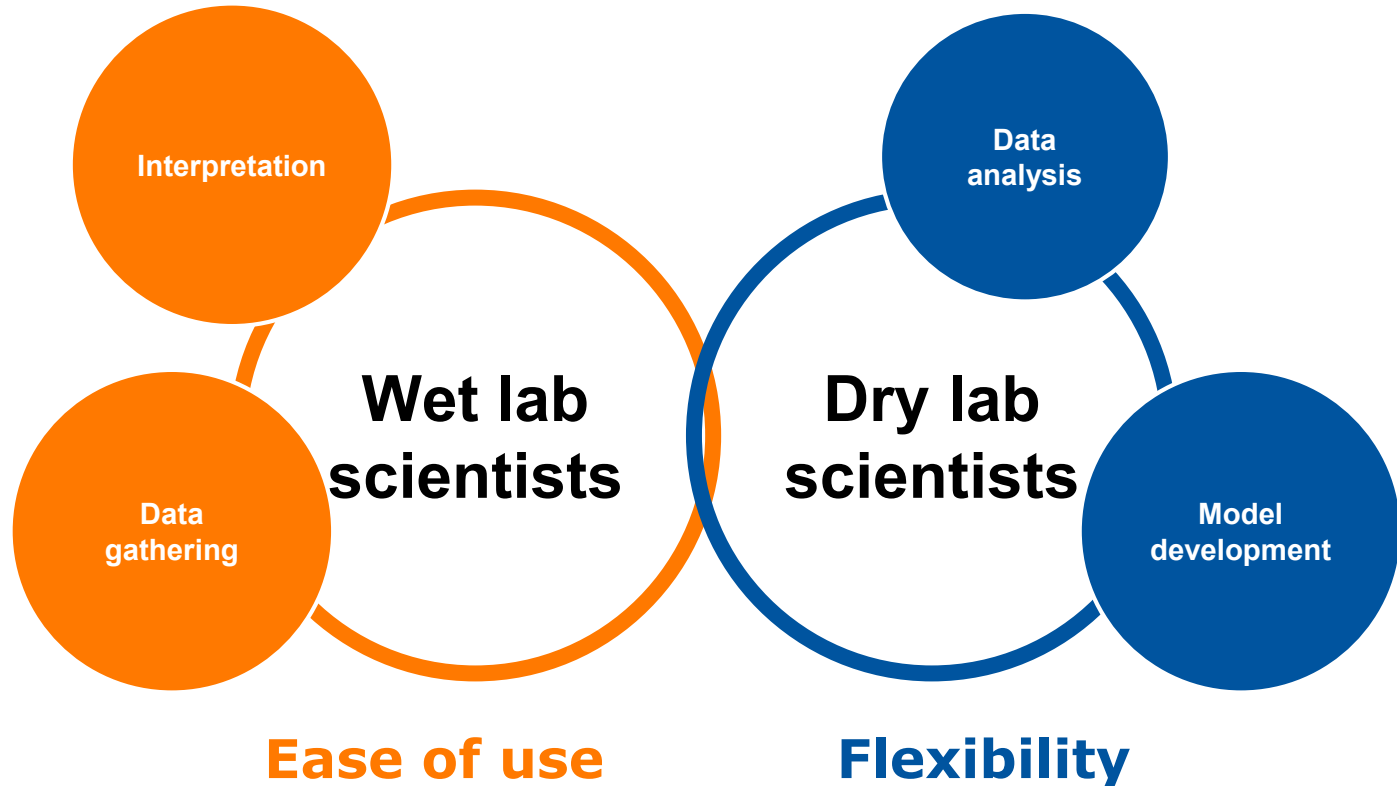
biogrowth & bioinactivation

Main goal: facilitate predictive microbiology

- Model fitting & calculation of predictions
- Isothermal & dynamic conditions
- Deterministic & stochastic
- Model comparison



Who may use these tools?



An architecture to make everyone happy

An R package

- Core functions for predictive microbiology
- Integration in other workflows, automation...
- **Flexibility**



An online application

- User-friendly interface to the R package
- Additional functions for model interpretation
- **Ease of use**



Transparency as a principle

Open Code

```
30 print.DynamicGrowth <- function(x, ...) {
31
32   cat("Growth prediction under dynamic conditions\n\n")
33
34   env <- names(x$env_conditions)
35   cat(paste("Environmental factors included:", paste(env, collapse = " ", "\n\n")))
36
37   cat("Parameters of the primary model:\n")
38   print(unlist(x$primary_pars))
39   cat("\n")
40
41   for (i in 1:length(x$sec_models)) {
42     cat(paste("Secondary model for ", names(x$sec_models)[i], ":\n", sep = ""))
43     print(unlist(x$sec_models[[i]]))
44     cat("\n")
45   }
46
47 }
```

Detailed manuals

This module includes a variety of primary inactivation models commonly used in predictive microbiology. The user can select among them using ①. Then, the values of the model parameters must be defined using the numeric inputs ②. Note that the contents of this box are updated according to the inactivation model selected. For details about the models implemented, please look at Appendix A.

Implementation details

(Adapted) Full Ratkowsky model

The full Ratkowsky model (Ratkowsky et al, 1983) is an extension of the square-root model by Ratkowsky (Ratkowsky et al, 1982) that accounts for the decline of the growth rate for temperatures higher than the optimal one. It is described by the following equation

$$\sqrt{\mu} = b(X - X_{min})(1 - e^{c(X - X_{max})})$$

where X is the value of the environmental factor, X_{min} is the theoretical minimum value for growth, X_{max} is the theoretical maximum value for growth, b is a parameter that defines the slope of the curve for suboptimal temperatures and c defines the slope for superoptimal temperatures.

Due to structural identifiability and compatibility with the other models, to use it as a gamma factor, this model must be modified so it is defined within [0, 1]. This can be done by defining a function such as

$$Y_{Ratkowsky} = \left(\frac{\sqrt{\mu(X)}}{\sqrt{\mu_{opt}}} \right)^2$$

Code examples

Because the temperature during the simulation equals the cardinal parameter X_{opt} , the predicted population size is identical to the one calculated using `predict_isothermal_growth` for the Baranyi model when $\mu = \mu_{opt}$ and $\lambda = \frac{\ln(1+1/Q_0)}{\mu_{opt}}$.

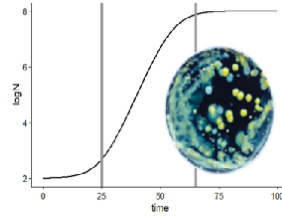
```
lambda <- Q0_to_lambda(q0, mu_opt)

my_model <- "Baranyi"
my_pars <- list(logN0 = 2, logNmax = 8, mu = mu_opt, lambda = lambda)

static_prediction <- predict_isothermal_growth(my_model, my_times, my_pars)

plot(static_prediction) +
  geom_line(aes(x = time, y = logN), linetype = 2, data = dynamic_prediction$simulation,
           colour = "green")
```

biogrowth



Features of biogrowth

Predictions

- Isothermal conditions
- Parameter uncertainty
- Dynamic conditions
- Any number of factors
- Several models

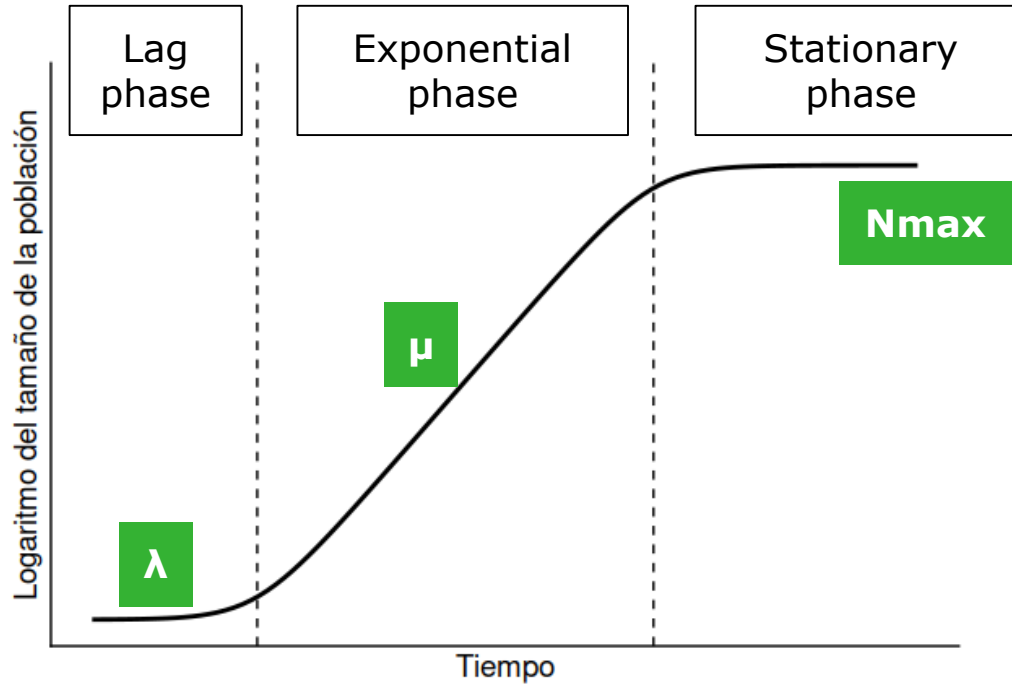
Other

- Visualization
- Statistical summaries
- Goodness of fit
- Results export

Model fitting

- Primary models
- Dynamic experiments
- Global fitting
- Cardinal parameters
- Fixing any parameter
- Any number of factors
- Several models

Isothermal growth



Primary models in *biogrowth*

Baranyi

$$\log N(t) = \log N_{max} + \log \frac{1 + \exp(\ln(10)\mu(t - \lambda)) - \exp(-\ln(10)\mu\lambda)}{\exp(\ln(10)\mu(t - \lambda)) - \exp(-\ln(10)\mu\lambda) + 10^{\log N_{max} - \log N_0}}$$

modified Gompertz

$$\log N(t) = \log N_0 + C \left(\exp \left(- \exp \left(\frac{e \cdot \mu}{C} (\lambda - t) + 1 \right) \right) \right)$$

Logistic

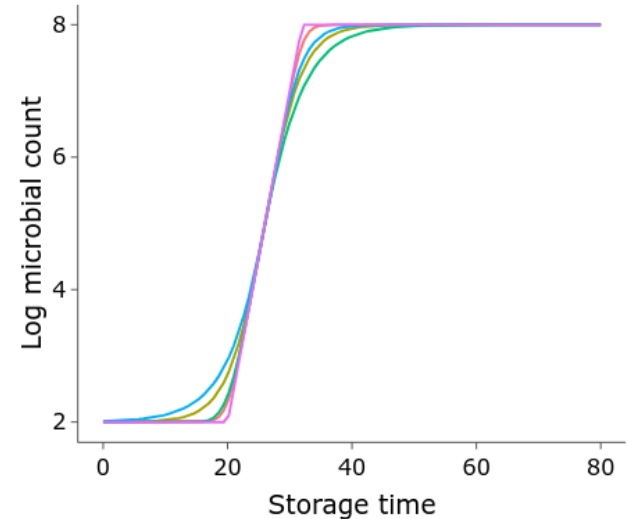
$$\log N(t) = \log N_0 + \frac{C}{1 + \exp \left(\frac{4\mu}{C} (\lambda - t) + 2 \right)}$$

Richards

$$\log N(t) = \log N_0 + C \left[1 + \nu \cdot \exp \left(1 + \nu + \frac{\mu}{C} (1 + \nu)^{1+1/\nu} (\lambda - t) \right) \right]^{-1/\nu}$$

Trilinear

$$\log N(t) = \begin{cases} \log N_0 & \text{if } t < \lambda \\ \log N_{max} & \text{if } t > t_{stat} \\ \log N_0 + \mu(t - \lambda) & \text{otherwise} \end{cases}$$

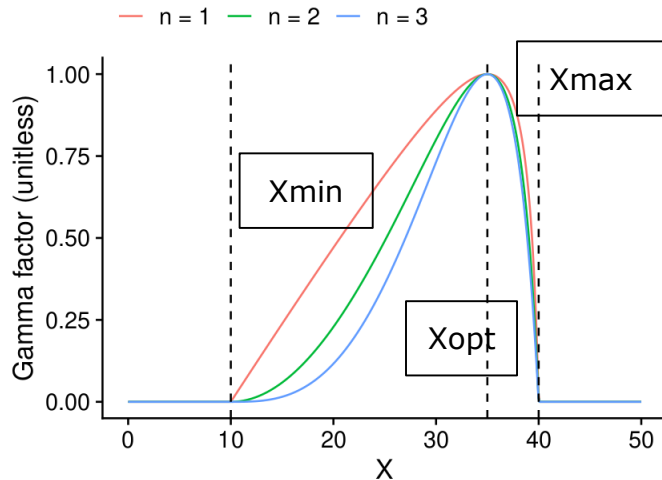


Secondary modelling - gamma concept

Hypotheses:

- each suboptimal factor (pH, aw, T...) reduces the growth rate
- each effect is independent

$$\mu(t) = \mu_{opt} \cdot \gamma_1(X_1(t)) \cdot \dots \cdot \gamma_n(X_n(t)); i \in 1, \dots, k$$



Models included

- Cardinal parameter model
- Full Ratkowsky model
- Zwietering-type models

The *biogrowth* R package

Available from CRAN


`install.packages("biogrowth")`

Extensively documented



biogrowth: Modelling of Population Growth

Modelling of population growth under static and dynamic environmental conditions. Includes functions for model fitting and making prediction under isothermal and dynamic conditions. The methods (algorithms & models) are based on predictive microbiology (See Perez-Rodriguez and Valero (2012, ISBN:978-1-4614-5519-6)).

Version: 0.2.0
Depends: R (≥ 2.10)
Imports: [deSolve](#) (≥ 1.28), [tibble](#) (≥ 3.0.3), [dplyr](#) (≥ 0.8.5), [FME](#) (≥ 1.3.6), [MASS](#) (≥ 7.3), [rlang](#) (≥ 0.4.7), [purrr](#) (≥ 0.3.4), [ggplot2](#) (≥ 3.3.2), [cowplot](#) (≥ 1.0.0), [lamW](#) (≥ 1.3.0), [tidyr](#) (≥ 1.0.2), [formula.tools](#) (≥ 1.7.1)
Suggests: [knitr](#), [rmarkdown](#), [tidyverse](#) (≥ 1.3.0)
Published: 2021-01-27
Author: Alberto Garre  [aut, cre], Jeroen Koomen [aut], Heidy den Besten [aut], Marcel Zwietering [aut]
Maintainer: Alberto Garre <garre.alberto at gmail.com>
License: [GPL-3](#)
NeedsCompilation: no
Materials: [README NEWS](#)
CRAN checks: [biogrowth results](#)

Downloads:

Reference manual: [biogrowth.pdf](#)
Vignettes: [Publication ready figures with biogrowth](#)
[Modelling population growth with biogrowth](#)
[Using dynamic models for static environmental conditions](#)

Package source: [biogrowth_0.2.0.tar.gz](#)
Windows binaries: r-devel: [biogrowth_0.2.0.zip](#), r-release: [biogrowth_0.2.0.zip](#), r-oldrel: [biogrowth_0.2.0.zip](#)
macOS binaries: r-release (arm64): [biogrowth_0.2.0.tgz](#), r-release (x86_64): [biogrowth_0.2.0.tgz](#), r-oldrel: [biogrowth_0.2.0.tgz](#)
Old sources: [biogrowth archive](#)

Linking:

Please use the canonical form <https://CRAN.R-project.org/package=biogrowth> to link to this page.

Just a few lines

```
3 ## We will use the multiple_experiments data set
4
5 data("multiple_experiments")
6
7 ## For each environmental factor, we need to defined a model
8
9 sec_names <- c(temperature = "CPM", pH = "CPM")
10
11 ## Any model parameter can be fixed
12
13 known <- list(Nmax = 1e8, N0 = 1e0, Q0 = 1e-3,
14             temperature_n = 2, temperature_xmin = 20, temperature_xmax = 35,
15             pH_n = 2, pH_xmin = 5.5, pH_xmax = 7.5, pH_xopt = 6.5)
16
17 ## The rest require starting values for model fitting
18
19 start <- list(mu_opt = .8, temperature_xopt = 30)
20
21 ## We can now call the fitting function
22
23 global_fit <- fit_multiple_growth(start, multiple_experiments, known, sec_names)
24
25 ## Parameter estimates can be retrieved with summary
26
27 summary(global_fit)
28
29 ## Any single environmental factor can be added to the plot using add_factor
30
31 plot(global_fit, add_factor = "temperature")
32
```

Parameters:

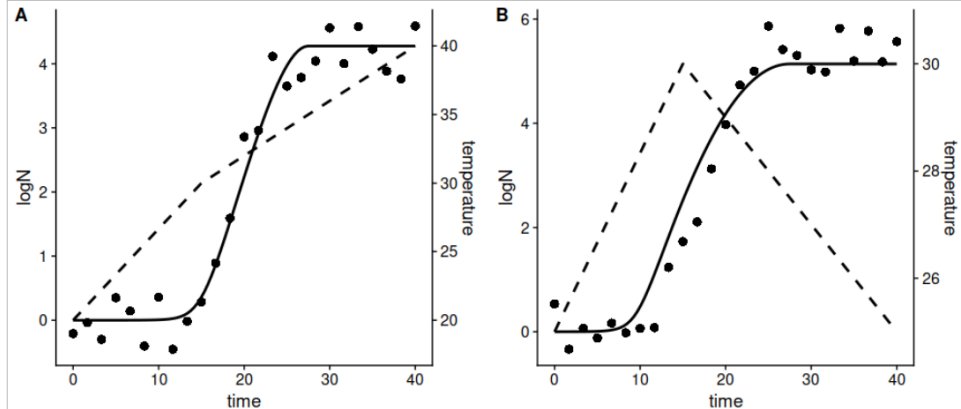
	Estimate	Std. Error	t value	Pr(> t)
mu_opt	0.54196	0.01222	44.35	<2e-16 ***
temperature_xopt	30.62396	0.18728	163.52	<2e-16 ***

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 0.4282 on 48 degrees of freedom

Parameter correlation:

	mu_opt	temperature_xopt
mu_opt	1.0000	0.8837
temperature_xopt	0.8837	1.0000

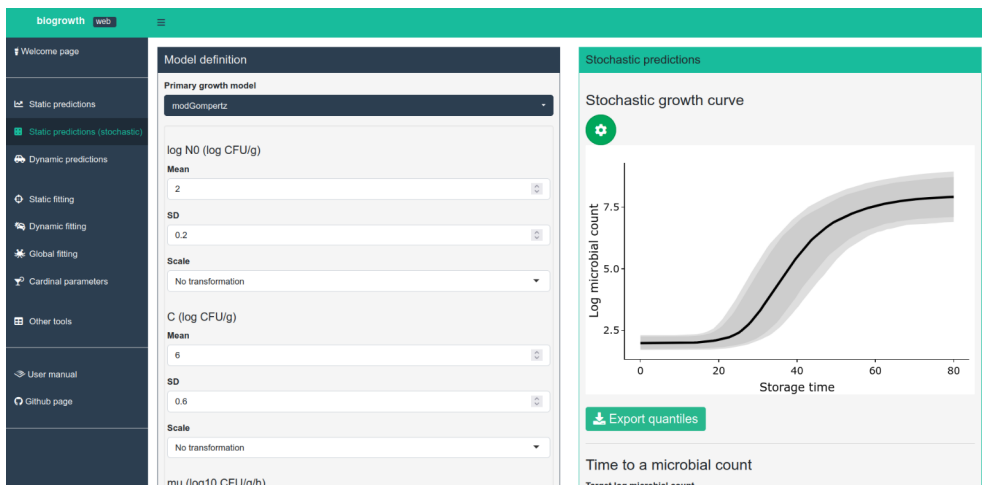




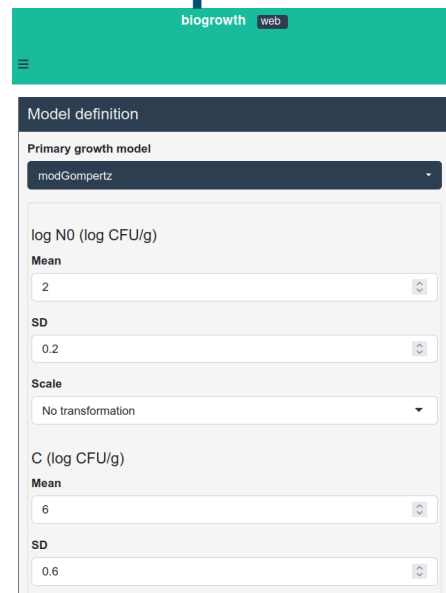
The online version of *biogrowth*

<https://foodmicrowur.shinyapps.io/biogrowth/>

PC



smartphone



Open code



<https://github.com/albgarre/biogrowth>

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albgarre / biogrowth

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albgarre Updated the NEWS 10 days ago 174

R	Updated the labels of plot.FitSecond...	10 days ago
data	Included two new datasets	21 days ago
man	Included two new datasets	21 days ago
vignettes	Updated the parameters of the vign...	10 days ago
.Rbuildignore	Improved the README file	7 months ago
.gitignore	Small changes for CRAN	8 months ago
DESCRIPTION	Added times to predict.FitDynamicG...	4 months ago
NAMESPACE	Implemented formula interface for pr...	5 months ago
NEWS.md	Updated the NEWS	10 days ago
README.Rmd	Updated the README file	4 months ago
README.md	Edited README.md	4 months ago
cran-comments...	Prepared for CRAN	7 months ago

Releases

No releases published
Create a new release

Packages

No packages published
Publish your first package

Contributors 2

- albgarre Alberto ...
- Jeroen-K Jeroen ...

https://github.com/albgarre/biogrowth_web

albgarre / biogrowth_web

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albgarre Added a help page to the static predi... 11 days ago 35

man	Added a help page to the static predi...	11 days ago
README.Rmd	Improved the README file	7 months ago
README.md	Improved the README file	7 months ago
example_cardi...	Fitting cardinal parameters	9 months ago
example_dyna...	Dynamic prediction	9 months ago
example_dyna...	Added a few changes to make every...	8 months ago
example_dyna...	Added a few changes to make every...	8 months ago
example_dyna...	Added a few changes to make every...	8 months ago
example_globa...	I had forgotten to commit the expa...	7 months ago
example_globa...	I had forgotten to commit the expa...	7 months ago
example_static...	Added a few changes to make every...	8 months ago
my_body.R	Added a help page to the static predi...	11 days ago
server.R	Added a help page to the static predi...	11 days ago

Releases

No releases published
Create a new release

Packages

No packages published
Publish your first package

Languages

- R 100.0%

Live demonstration

<https://foodmicrowur.shinyapps.io/biogrowth/>

Steps

- Fitting primary growth models
- Fitting cardinal growth models (temperature & pH)
- Validation under dynamic conditions
- Fitting dynamic growth models



bioinactivation

Features of *bioinactivation*

Predictions

- Isothermal conditions
- Dynamic conditions
- Parameter uncertainty
- Several models

Other

- Visualization
- Statistical summaries
- Goodness of fit
- Results export

Model fitting

- Primary models
- Two-step fitting
- One-step fitting
- Dynamic models
- Fixing any model parameter
- Several models

Isothermal models included in *bioinactivation*

Bigelow

$$\log N = \log N_0 - t/D$$

Geeraerd

$$\log N = \log N_{res} + \log_{10} \left(\frac{(10^{\log N_0 - \log N_{res}} - 1) \cdot e^{k \cdot SL}}{(e^{k \cdot t} + e^{k \cdot SL} - 1) + 1} \right)$$

Peleg

$$\log N = \log N_0 - b \cdot t^n$$

2 pop. Weibull

$$N = N_0 / (1 + 10^\alpha) [10^{-(t/\delta_1)^{p_1} + \alpha} + 10^{-(t/\delta_2)^{p_2}}]$$

Mafart

$$\log N = \log N_0 - (t/\delta)^p$$

Metselaar

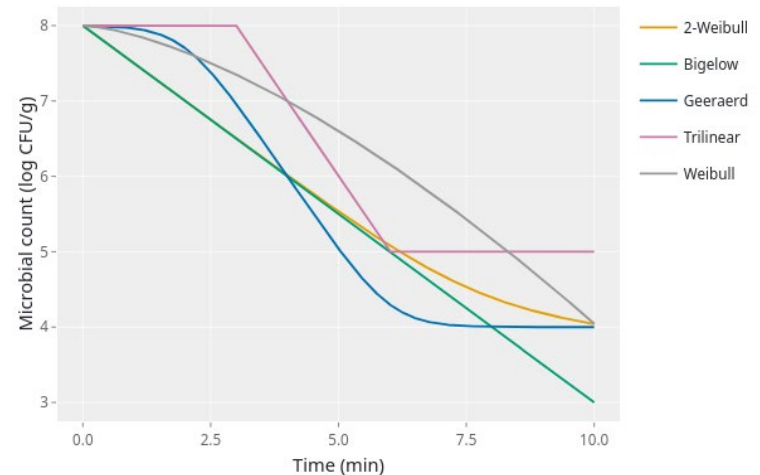
$$\log N = \log N_0 - \Delta (t/(\Delta D_\Delta))^p$$

Trilinear model

$$\log N = \log N_0; t < SL$$

$$\log N = \log N_{res}; t > t_{res}$$

$$\log N = \log N_0 - (t - SL)/D; \text{ otherwise}$$



Dynamic models included in *bioinactivation*

Bigelow

$$\frac{d\log_{10}N}{dt} = -\frac{1}{D(T)}$$

$$\log_{10}D(T) = \log_{10}D(T_{ref}) - \frac{T - T_{ref}}{z}$$

Geeraerd

$$\frac{dN}{dt} = -\frac{1}{1 + C_c} k_{max}(T) N \left(1 - \frac{N_{res}}{N}\right)$$

$$k_{max}(T) = k_{max}(T_{ref}) 10^{-(T - T_{ref})/z}$$

Mafart

$$\frac{d\log_{10}S}{dt} = -p \left(\frac{1}{\delta(T)}\right)^p t^{p-1}$$

$$\log_{10}D(T) = \log_{10}D(T_{ref}) - \frac{T - T_{ref}}{z}$$

Peleg

$$\frac{d\log_{10}S}{dt} = -b(T) n \left(\frac{-\log_{10}S}{b(T)}\right)^{\frac{n-1}{n}}$$

$$b(T) = \ln \left(1 + e^{k_b(T - T_c)}\right)$$

The *bioinactivation* R package

Available from CRAN

`install.packages("bioinactivation")`

Extensively documented

<https://github.com/albgarre/bioinactivation>



bioinactivation: Mathematical Modelling of (Dynamic) Microbial Inactivation

Functions for modelling microbial inactivation under isothermal or dynamic conditions. The calculations are based on several mathematical models broadly used by the scientific community and industry. Functions enable to make predictions for cases where the kinetic parameters are known. It also implements functions for parameter estimation for isothermal and dynamic conditions. The model fitting capabilities include an Adaptive Monte Carlo method for a Bayesian approach to parameter estimation.

Version: 1.2.3
Imports: [dplyr](#) (≥ 0.4.1), [deSolve](#) (≥ 1.11), [FME](#) (≥ 1.3.2), [lazyeval](#) (≥ 0.1.10), [ggplot2](#) (≥ 2.0.0), [MASS](#) (≥ 7.3-39), graphics (≥ 3.1.3), stats (≥ 3.1.3), [rlang](#) (≥ 0.1.2), [purrr](#) (≥ 0.3.2)
Suggests: [knitr](#) (≥ 1.9), [testthat](#) (≥ 0.9.1), [rmarkdown](#) (≥ 1.12)
Published: 2019-08-01
Author: Alberto Garre [aut, cre], Pablo S. Fernandez [aut], Jose A. Egea [aut]
Maintainer: Alberto Garre <garre.alberto at gmail.com>
License: [GPL-3](#)
NeedsCompilation: no
Citation: [bioinactivation citation info](#)
Materials: [NEWS](#)
CRAN checks: [bioinactivation results](#)

Just a few lines

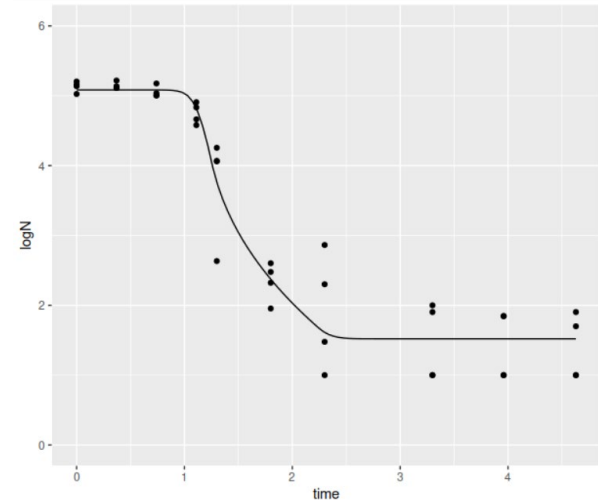
```
1
2 data(dynamic_inactivation) # The example data set is used.
3
4 simulation_model <- "Peleg" # Peleg's model will be used
5
6 dummy_temp <- data.frame(time = c(0, 1.25, 2.25, 4.6),
7                             temperature = c(70, 105, 105, 70)) # Dummy temp. profile
8
9 ## Set known parameters and initial points/bounds for unknown ones
10
11 known_params = c(temp_crit = 100)
12
13 starting_points <- c(n = 1, k_b = 0.25, N0 = 1e+05)
14 upper_bounds <- c(n = 2, k_b = 1, N0 = Inf)
15 lower_bounds <- c(n = 0, k_b = 0, N0 = 1e4)
16
17 dynamic_fit <- fit_dynamic_inactivation(dynamic_inactivation, simulation_model,
18                                       dummy_temp, starting_points,
19                                       upper_bounds, lower_bounds,
20                                       known_params)
21
22 plot(dynamic_fit)
23 summary(dynamic_fit)
```

Parameters:

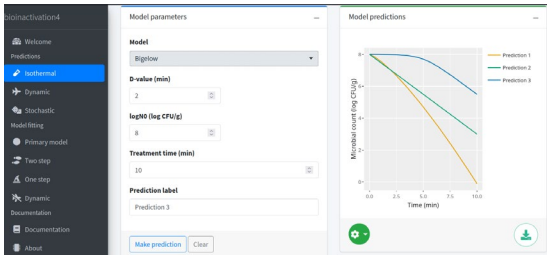
	Estimate	Std. Error	t value	Pr(> t)
n	4.186e-01	7.757e-02	5.397	4.12e-06 ***
k_b	6.596e-01	3.212e-02	20.531	< 2e-16 ***
N0	1.213e+05	3.137e+04	3.865	0.000433 ***

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 0.4328 on 37 degrees of freedom



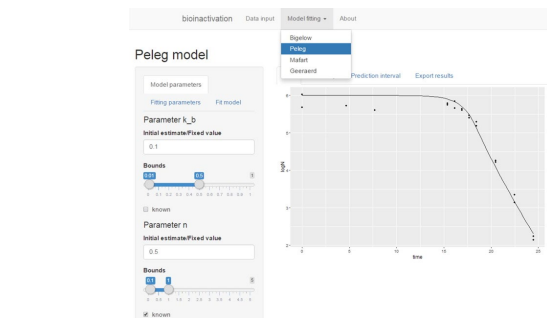
The web version



2022

bioinactivation4

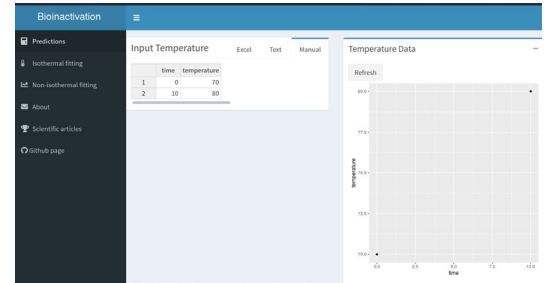
Complete interface to the package
Improved & modernized interface
Additional editing tools



2017

bioinactivation FE

Extended functions
One-step fitting
Dynamic predictions



bioinactivation SE

Illustration of the package
Fitting dynamic experiments

Open code



<https://github.com/albgarre/bioinactivation>

albgarre / **bioinactivation** Public

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albgarre Got rid of all the mutate_ b6746c6 on Jul 5, 2021 124 commits

R	Got rid of all the mutate_	8 months ago
data	Updated training set documentation.	6 years ago
inst	CRAN submission	3 years ago
man	Got rid of select_	8 months ago
tests	Increased the tolerance of the tests.	6 years ago
vignettes	Fixed the vignette	3 years ago
.gitignore	Included graphics in ggplot2.	6 years ago
DESCRIPTION	Got rid of all the mutate_	8 months ago
NAMESPACE	Got rid of all the mutate_	8 months ago
NEWS.md	Prepared for CRAN re-submission	3 years ago
README.Rmd	Extended README file.	6 years ago
README.md	Update README	3 years ago
cran-comments.md	Prepared for CRAN re-submission	3 years ago

README.md

bioinactivation: a package for modelling microbial inactivation in R.

The **bioinactivation** package implements several function for the modelization of microbial inactivation in R. It includes:

<https://github.com/albgarre/bioinactivation4>

albgarre / **bioinactivation4** Public

<> Code Issues Pull requests Actions Projects Wiki Security Insights Settings

main 1 branch 0 tags Go to file Add file Code

albgarre Updated the README file c75cbf2 14 days ago 28 commits

R	Improved the residual table	14 days ago
www	Added the pics in the carousel	14 days ago
.gitignore	Initial commit	8 months ago
LICENSE	Initial commit	8 months ago
README.md	Updated the README file	14 days ago
Rplot01.png	Updated application	5 months ago
example_1step.csv	Updated application	5 months ago
example_1step.xlsx	Updated application	5 months ago
server.R	Implemented the 2 step module	7 months ago
ui.R	Added a link to the manual	14 days ago

README.md

bioinactivation4

The bioinactivation package for R includes several function for building and applying microbial inactivation models (Garre et al., 2017). This package is available on CRAN, making it easy to install in any computer with R. The package is Open Source, with the source code available on GitHub:

Live demonstration

<https://foodlab-upct.shinyapps.io/bioinactivation4/>

Steps

- Fitting primary inactivation models
- Fitting secondary models: one & two-step approach
- Validation under dynamic conditions
- Fitting dynamic inactivation models

Additional reading



Food Research International
Volume 93, March 2017, Pages 66-74



Bioinactivation: Software for modelling dynamic microbial inactivation

Alberto Garre ^a, Pablo S. Fernández ^a  , Roland Lindqvist ^b, Jose A. Egea ^c



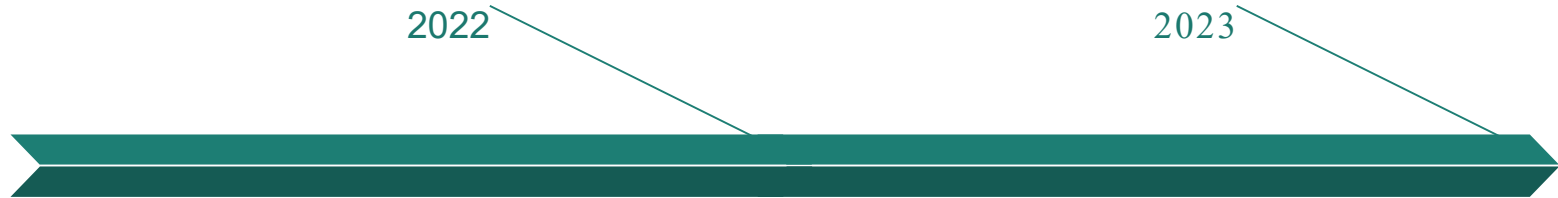
Food Research International
Volume 112, October 2018, Pages 353-360



Bioinactivation FE: A free web application for modelling isothermal and dynamic microbial inactivation

Alberto Garre ^a, Marta Clemente-Carazo ^a, Pablo S. Fernández ^a  , Roland Lindqvist ^b, Jose A. Egea ^c  

Roadmap



biogrowth package
update

bionactivation4
release

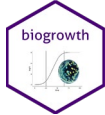
biogrowth web
optimize
new features
release

bionactivation
modernize

Conclusions

- *bioinactivation* and *biogrowth* try to make life easier
- They can ease focusing on the most relevant parts of a study
- They are free, open and transparent
- Users decide software quality
- Your feedback is essential for improving the tools

Acknowledgements



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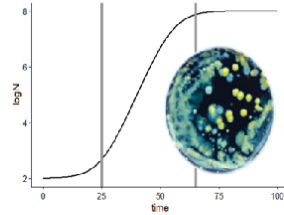
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backup slides

biogrowth



Fitting primary models



bioinactivation

Isothermal fitting