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Optimal experimental design for improving the estimation of growth parameters of *Lactobacillus viridescens* from data under non-isothermal conditions

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ABSTRACT

In predictive microbiology, the model parameters have been estimated using the sequential two-step modeling (TSM) approach, in which primary models are fitted to the microbial growth data, and then secondary models are fitted to the primary model parameters to represent their dependence with the environmental variables (e.g., temperature). The Optimal Experimental Design (OED) approach allows reducing the experimental workload and costs, and the improvement of model identifiability because primary and secondary models are fitted simultaneously from non-isothermal data. *Lactobacillus viridescens* was selected to this study because it is a lactic acid bacterium of great interest to meat products preservation. The objectives of this study were to estimate the growth parameters of *L. viridescens* in culture medium from TSM and OED approaches and to evaluate both the number of experimental data and the time needed in each approach and the confidence intervals of the model parameters. Experimental data for estimating the model parameters with TSM approach were obtained at six temperatures (total experimental time of 3540 h and 196 experimental data of microbial growth). Data for OED approach were obtained from four optimal non-isothermal profiles (total experimental time of 588 h and 60 experimental data of microbial growth), two profiles with increasing temperatures (IT) and two with decreasing temperatures (DT). The Baranyi and Roberts primary model and the square root secondary model were used to describe the microbial growth, in which the parameters b and T_{min} (±95% confidence interval) were estimated from the experimental data. The parameters obtained from TSM approach were $b = 0.0290$ (±0.0020) [1/(h$^{0.5}$ °C)] and $T_{min} = -1.33$ (±1.26) [°C], with $R^2 = 0.986$ and RMSE = 0.581, and the parameters obtained with the OED approach were $b = 0.0316$ (±0.0013) [1/(h$^{0.5}$ °C)] and $T_{min} = -0.24$ (±0.55) [°C], with $R^2 = 0.990$ and RMSE = 0.436. The parameters obtained from OED approach presented smaller confidence intervals and best statistical indexes than those from TSM approach. Besides, less experimental data and time were needed to estimate the model parameters with OED than TSM. Furthermore, the OED model parameters were validated with non-isothermal experimental data with great accuracy. In this way, OED approach is feasible and is a very useful tool to improve the prediction of microbial growth under non-isothermal condition.

1. Introduction

The development of mathematical models considering microbial behavior and the application of statistics and computational simulations have resulted in successful predictions of microbial growth in foods subject to a wide range of environmental conditions. The well-known classification of primary and secondary models was established more than 20 years ago (Whiting and Buchanan, 1993) and have been widely used. However, the values of the model parameters depend on the approach used for their estimation, and thus, the parameter estimation is still a very important issue to be investigated.

The two-step modeling (TSM) approach is the traditional approach used to estimate the primary and secondary model parameters, which consists of the sequential fitting of the models. First, the primary model is fitted to the experimental growth data under static environmental conditions to estimate the growth parameters (μ_{max}, λ, y_{max}, and y_0 are the most common parameters). Then the secondary model is fitted to the primary model parameters to assess their dependence with the environmental conditions (e.g., temperature, pH, a_w) (Whiting and Buchanan, 1993). After these two modeling steps, the

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parameters should be validated with new experimental data which were not used in the estimation steps. A lot of experimental data are needed to obtain the model parameters with TSM approach. Despite its high workload, costs, and experimental efforts, the TSM approach has been the most reported in the literature (Elias et al., 2016; Juneja et al., 2009; Longhi et al., 2013; Tremarin et al., 2015, among others).

The optimal experimental design (OED) approach was introduced in predictive microbiology at the end of the 1990s (Cunha et al., 1997; Grijspeerdt and Vanrolleghem, 1999; Versyck et al., 1999) as an alternative approach to estimate primary and secondary model parameters from experiments optimally designed. In the OED approach, the experiments are designed optimizing a certain criterion based on the Fisher Information Matrix, which takes into account the model sensitivity to the parameters variations, to the experimental noise and to the constraints of the system under study (Balsa-Canto et al., 2008; Bernaerts et al., 2000; Franceschini and Macchietto, 2008; Munack, 1989). The experimental data are obtained at the optimal designed conditions, and then, the parameters are estimated with the simultaneous fitting of the primary and secondary models to the data. In general, experimental time, costs, and workload are reduced with the OED approach, and the model parameters had smaller confidence intervals than those estimated from TSM approach (Brandão et al., 2001). Even with these advantages, the OED approach has not been widely used in predictive microbiology, maybe because of the complexity of the calculations in the optimization step.

The temperature of chilled foods usually varies during transport, in retail stores and at home, influencing the kinetics of microbial growth (Kilcast and Subramaniam, 2000; Van Impe et al., 1992). The temperature increase in the sub-optimal temperature range decreases the adaptation time and increases the maximum specific growth rate of the spoilage bacteria, which tends to reduce the food shelf life and quality (Elias et al., 2016; Longhi et al., 2013; McDonald and Sun, 1999). Experiments performed at non-isothermal condition can help to extract the influence of temperature variations on the microbial growth parameters (Versyck et al., 1999). It is important for predictive microbiology because the transposition of results from static conditions to dynamic conditions is, sometimes, not acceptable (Valdramidis et al., 2008). In the other words, parameters estimated under dynamic conditions (OED approach) can be more accurate than parameters obtained under static conditions (TSM approach) since they were obtained from optimal dynamic conditions.

Microbial growth is the most common cause of food spoilage, which can be noticeable by visible aspects (slime), texture modifications (polymer degradation), and/or undesirable flavor (Gram et al., 2002). The shelf life of meat and meat products has been linked to the growth of lactic acid bacteria, from which the *Lactobacillus* has been indicated as one of the main genus (Borch et al., 1996; Nychas et al., 2008), and the *Lactobacillus viridescens* has been reported as one of the main specific spoilage organisms (Dušková et al., 2013). In the literature, the growth parameters of spoilage microorganisms have been estimated with TSM approach, and for our knowledge, there are no studies for spoilage microorganisms with OED approach.

The objectives of this study were to apply the OED approach to estimate the growth parameters of *L. viridescens* and to compare OED and TSM approaches by assessing the fitting goodness and experimental work required.

2. Materials and methods

2.1. Microorganism

Lyophilized *L. viridescens* (CCT 5843 ATCC 12706, Lot 22.07) was purchased from André Tosello Foundation of Tropical Cultures (Campinas, Brazil). The strains were rehydrated, grown into Man, Rogosa and Sharpe (MRS) broth (Acumedia Manufactures, Michigan, USA), and stored at −24 °C in Eppendorf tubes containing MRS:glycerol medium (4:1 in volume, respectively).

2.2. Experimental procedures

Before inoculation, the strains of *L. viridescens* were reactivated in MRS medium at 30 °C for 18 h. Microbial growths were performed in 250 mL Erlenmeyer flasks with 160 mL of MRS medium and initial concentration of approximately 10^3 CFU/mL. The flasks were placed in incubators (Dist, Florianópolis, Brazil) with temperature control, which was recorded by data loggers (Testo 174, Lenzkirch, Germany) every 5 min. The experiments were performed in duplicate under isothermal (4 °C, 8 °C, 12 °C, 16 °C, 20 °C, and 30 °C) and non-isothermal conditions (as described below). All experiments were conducted until reaching the stationary growth phase.

The microbial growth under non-isothermal conditions was assessed by shifting between predetermined temperature plateaus. Two increasing temperature profiles (IT) (4 °C, 8 °C, 12 °C, and 16 °C ($IT_{4–8–12-16}$), and 12 °C, 16 °C, 20 °C, and 25 °C ($IT_{12–16–20-25}$)) and two decreasing temperature profiles (DT) (16 °C, 12 °C, 8 °C, and 4 °C ($DT_{16–12–8-4}$), and 25 °C, 20 °C, 16 °C, 12 °C, 8 °C, and 4 °C ($DT_{25–20–16-12-8-4}$)) were selected. The time to shift (t_{shift}) between each plateau were optimally designed by the OED approach.

Temperature profiles were chosen based on preliminary tests (experiments under different temperature plateaus) and previous studies (Bernaerts et al., 2002; Longhi et al., 2013). Each temperature profile was composed by, at least, four temperature plateaus that would improve the model parameter decorrelation and enlarge the sub-optimal temperature range (from 4 to 25 °C considering increasing and decreasing temperature profiles). The maximum temperature difference between plateaus was 5 °C, aiming to avoid intermediate lag phases. One experimental data at each t_{shift} and, at least, three experimental data at each temperature plateau were collected, improving the confidence of parameters estimation (Grijspeerdt and De Reu, 2005).

Experimental growth data under dynamic refrigeration temperature were used to validate the TSM and OED model parameters obtained. Four different temperature profiles were chosen, in which the temperature switched between two plateaus after a regular time interval, as follows: 5 °C and 11 °C after each 24 h ($TP_{5–11(24h)}$); 5 °C and 11 °C after each 12 h ($TP_{5–11(12h)}$); 5 °C and 8 °C after each 12 h ($TP_{5–8(12h)}$); and 3 °C and 10 °C after each 12 h ($TP_{3–10(12h)}$).

2.3. Growth modeling

The Baranyi and Roberts primary model (Baranyi and Roberts, 1994), shown in Eqs. (1) and (2), was used to describe the microbial growth. The square root secondary model (Ratkowsky et al., 1982), shown in Eq. (3), was used to describe the dependence of μ_{max} parameter with the temperature. In Eqs. (1), (2), and (3), y [ln CFU/mL] is the natural logarithm of the cell concentration N [CFU/mL] at time t [h], Q [dimensionless] is related to the physiological state of the cells at time t, μ_{max} [1/h] is the maximum specific growth rate, y_{max} [ln CFU/mL] is the natural logarithm of the maximum cell concentration, T [°C] is the temperature, T_{min} [°C] is the theoretical minimal temperature for microbial growth, and b [1/($h^{0.5}$ °C)] is an empirical parameter. The initial conditions to solve Eqs. (1) and (2) are $y(0) = y_0$ and $Q(0) = Q_0$, respectively, in which y_0 [ln CFU/mL] is the value of the natural logarithm of initial cell concentration, and Q_0 [dimensionless] is the value related to the initial physiological state of cells.

$$\frac{dy}{dt} = \mu_{max}\left[\frac{1}{1+\exp(-Q)}\right][1-\exp(y-y_{max})] \quad (1)$$

$$\frac{dQ}{dt} = \mu_{max} \quad (2)$$

$$\sqrt{\mu_{max}} = b(T-T_{min}) \quad (3)$$

2.4. Optimal experimental design

The basic concepts of OED approach were described in detail by Franceschini and Macchietto (2008) and Versyck et al. (1999). The OED approach applied in this study followed the method proposed by Bernaerts et al. (2000); Bernaerts et al. (2002) and Grijspeerdt and De Reu (2005). In summary, each t_{shift} between plateaus in each experimental setup was obtained by minimizing the *E*-modified criteria (the ratio of the largest to the smallest eigenvalue of FIM) of the Fisher Information Matrix (FIM), shown in Eq. (4).

$$\mathrm{FIM} = \int_0^{t_f} \left(\frac{\partial y}{\partial p}\right)^T W \left(\frac{\partial y}{\partial p}\right) dt \tag{4}$$

in which $(\frac{\partial y}{\partial p})$ is the sensitivity matrix (i,j) of the model response (y_i) to the model parameters (p_j) variation; $(\frac{\partial y}{\partial p})^T$ is the transpose of $(\frac{\partial y}{\partial p})$; W is a weighting matrix; and t_f is the final experimental time. The sensitivity functions are calculated by numerical integration of their associated differential equations. The y_0 and y_{max} parameters were assumed as the real values of the experimental curves, and the values of b and T_{min} parameters of the square root secondary model obtained in TSM approach were used as nominal parameters for computing the FIM.

The fully relative sensitivity functions were chosen for this study, as proposed by Bernaerts et al. (2002), because model parameters exhibit a considerable difference in order of magnitude.

2.5. Parameter estimation

The experimental data under isothermal conditions were used to estimate the parameters by the TSM approach. The primary model (Eqs. (1) and (2)) was fitted to growth data (y vs. t) generating the primary model parameters, and subsequently, the secondary model (Eq. (3)) was fitted to the primary model parameters as a function of the temperature.

Non-isothermal growth data were used to estimate the parameters of the Baranyi and Roberts primary model and the square root secondary model simultaneously, fitting the equations to the growth data of each profile and applying the OED approach to calculate the t_{shift} values for the next profile. The parameters were estimated by three different approaches: IT-OED (the two increasing temperature experiments together), DT-OED (the two decreasing temperature experiments together), and OED (the four increasing and decreasing temperature experiments together).

Fitting procedure was performed with the *solver add-in* available in the software Office Excel 2010 (Microsoft, Redmond, WA, USA) that uses the *GRG non-linear* solving method. Five different values of initial try obtained randomly were evaluated in the parameter estimation (to avoid local minimum). The differential equations were solved using the Runge–Kutta 4th-order method, applying the adequate initial conditions to each model.

The 95% confidence intervals (CI) of the model parameters (Eq. (5)) and the 95% prediction bounds of the mathematical models (Eq. (6)) were computed in the fitting procedure.

$$\mathrm{CI} = \mathrm{par} \pm t_n \sqrt{S} \tag{5}$$

$$\mathrm{IP} = y_{pdt} \pm t_n \sqrt{vSv^T} \tag{6}$$

in which par is the parameter estimated by the fitting, t_n is computed using the inverse of Student's t cumulative distribution function, S is a vector of the diagonal elements from the estimated covariance matrix of the coefficient estimates, $(X^TX)^{-1}s^2$, X is the Jacobian of the fitted values with respect to the parameters, X^T is the transpose of X, s^2 is the mean squared error, and v is defined as the Jacobian evaluated at a specified predictor value.

The coefficient of determination (R^2, Eq. (7)) and the root mean squared error (RMSE, Eq. (6)) were used to assess the ability of the mathematical models in representing the growth data.

$$R^2 = 1 - \frac{\sum_{i=1}^{n}\left[y_{obs(i)} - y_{pdt(i)}\right]^2}{\sum_{i=1}^{n}\left[y_{obs(i)} - \overline{y_{obs}}\right]^2} \tag{7}$$

$$\mathrm{RMSE} = \sqrt{\frac{\sum_{i=1}^{n}\left[y_{obs(i)} - y_{pdt(i)}\right]^2}{n - n_p}} \tag{8}$$

in which n is the number of experimental data, n_p is the number of parameters of the model, y_{pdt} is the value predicted by the mathematical model, y_{obs} is the observed experimental data, and $\overline{y_{obs}}$ is the mean value of the observed experimental data.

The bias factor (Eq. (9)) and the accuracy factor (Eq. (10)) (Ross, 1996) were used to assess the ability of the mathematical models in predicting the growth data under non-isothermal conditions.

$$\mathrm{bias} = 10^{\sum_{i=1}^{n}\frac{\log\left(\frac{y_{pdt(i)}}{y_{obs(i)}}\right)}{n}} \tag{9}$$

$$\mathrm{accuracy} = 10^{\sum_{i=1}^{n}\frac{\log\left|\frac{y_{pdt(i)}}{y_{obs(i)}}\right|}{n}} \tag{10}$$

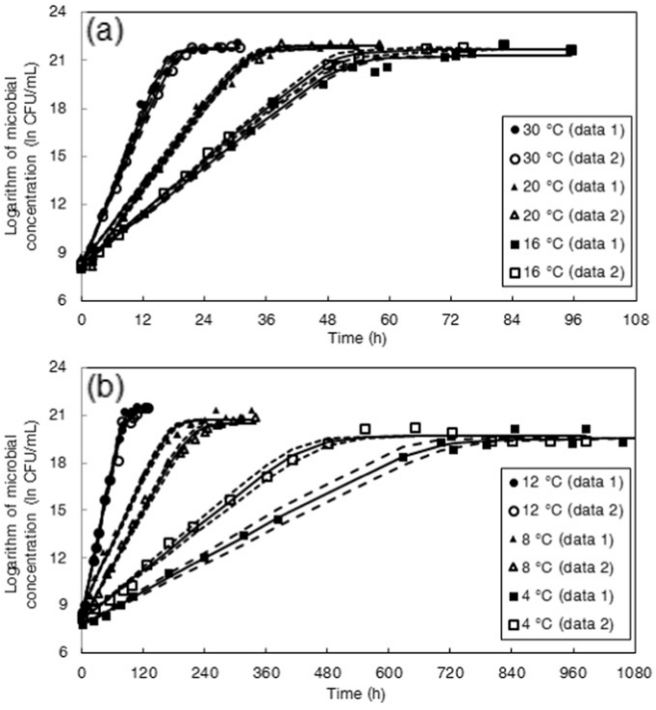

Fig. 1. First step of TSM approach: fitting of the Baranyi and Roberts primary model (solid lines) to the experimental data (symbols) of the growth of *L. viridescens* under isothermal conditions at (a) 30 °C, 20 °C, and 16 °C; (b) 12 °C, 8 °C, and 4 °C; and 95% prediction bounds of the mathematical model (dashed lines).

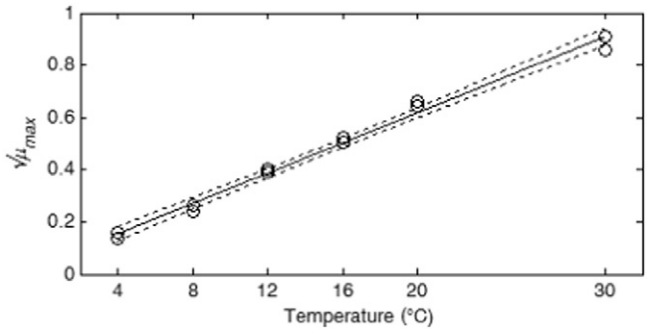

Fig. 2. Second step of TSM approach: fitting of the square root secondary model (solid line) to the μ_{max} parameter data (symbols), and 95% prediction bounds of the mathematical model (dashed lines).

Table 1
Values of the square root model parameters b and T_{min} (±95% confidence intervals), and the statistical indexes (R^2 e RMSE) of the model fitting obtained in each approach.

Approach	b [1/(h$^{0.5}$ °C)]	T_{min} [°C]	R^2	RMSE
TSM	0.0290 (±0.0020)	−1.33 (±1.26)	0.986	0.581
IT-OED	0.0314 (±0.0019)	0.12 (±0.71)	0.995	0.317
DT-OED	0.0295 (±0.0019)	−1.57 (±1.05)	0.999	0.259
OED	0.0316 (±0.0013)	−0.24 (±0.55)	0.990	0.436

3. Results and discussion

The experimental data collected at six isothermal conditions (4 °C, 8 °C, 12 °C, 16 °C, 20 °C, and 30 °C) and the fitted Baranyi and Roberts primary model are shown in Fig. 1. In all model fitting under isothermal conditions, a very short lag time was observed, and thus, the microorganism was considered fully adapted. The values of the y_{max} parameter were similar in all model fitting (average value of y_{max} equal to 21.09, with standard deviation of 0.82). In a second step, the square root secondary model was fitted to the μ_{max} parameter data, as shown in Fig. 2. The values of the b and T_{min} parameters of the square root secondary model for the TSM approach are shown in Table 1, as well as the statistical indexes R^2 and RMSE of the fitting.

The four non-isothermal experiments ($IT_{4–8–12–16}$, $IT_{12–16–20–25}$, $DT_{16–12–8–4}$, and $DT_{25–20–16–12–8–4}$) used to estimate the model parameters with the OED approach were optimized computing the FIM. The optimal times to shift the temperature ($t_{shift(n)}$) and the final experimental time (t_f) found in the optimization are shown in Table 2. The experimental data collected at the four experiments were used to estimate simultaneously the parameters of the Baranyi and Roberts primary model and the square root secondary model. The experimental data as well as the fitting of the models are shown in Fig. 3. The values of b and T_{min} parameters of the square root secondary model, from the OED approach, are shown in Table 1, as well as the statistical indexes R^2 and RMSE of the fitting.

Besides, the experimental data of the non-isothermal experiments were used to estimate the model parameters in each case: the two increasing temperature profiles (IT-OED), the two decreasing temperature profiles (DT-OED), and the four increasing and decreasing temperature profiles (OED). The values of b and T_{min} parameters of the square root secondary model for the IT-OED and DT-OED are shown in Table 1, as well as the statistical indexes R^2 and RMSE of the model fitting.

The results presented in the Table 1 show that the values of b and T_{min} parameters, estimated with IT-OED, DT-OED, and OED, were close to the parameters estimated with the traditional TSM approach. However, smaller confidence intervals of the model parameters were found with IT-OED, DT-OED, and OED. Furthermore, best statistical indexes R^2 and RMSE were found with the OED approach, in comparison with the results of the traditional TSM approach.

Table 2
Optimal times to shift (t_{shift}) and total experimental time (t_f) found in the computation of the FIM for each temperature profile.

Experiment	t_{shift1} (h)	t_{shift2} (h)	t_{shift3} (h)	t_{shift4} (h)	t_{shift5} (h)	t_f (h)
$IT_{4–8–12–16}$	63.0	91.5	105.0			168.0
$IT_{12–16–20–25}$	20.1	32.0	40.0			60.0
$DT_{16–12–8–4}$	11.9	32.0	72.9			192.0
$DT_{25–20–16–12–8–4}$	4.3	10.8	20.7	37.5	71.6	168.0

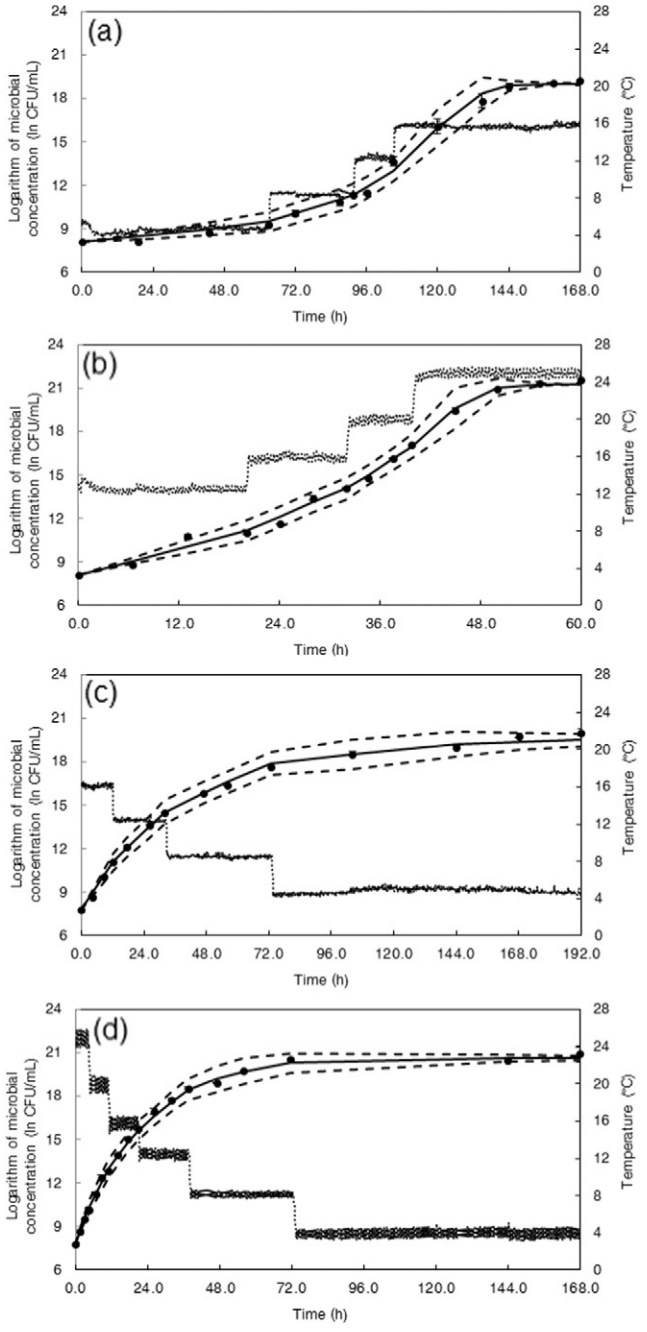

Fig. 3. Unique step of OED approach: simultaneous fitting of the Baranyi and Roberts primary model and square root secondary model (solid lines) to the experimental data (symbols) of the growth of *L. viridescens* under optimal non-isothermal conditions for profiles (a) $IT_{4–8–12–16}$, (b) $IT_{12–16–20–25}$, (c) $DT_{16–12–8–4}$, and (d) $DT_{25–20–16–12–8–4}$; the experimental temperature profile (dotted lines), and 95% prediction bounds of the mathematical model (dashed lines).

Table 3
Number of experimental data and time needed to estimate the model parameters in each condition (isothermal and optimal non-isothermal).

Temperature	Experimental time (h)	Experimental data
4	2257	38
8	668	41
12	251	29
16	191	33
20	112	28
30	61	27
Total of TSM	**3540**	**196**
4-8-12-16	168	14
12-16-20-30	60	14
Subtotal of IT-OED	228	28
16-12-8-4	192	14
25-2016-12-8-4	168	18
Subtotal of DT-OED	360	32
Total of OED	**588**	**60**

The number of experimental data and the resulting experimental time needed to estimate the model parameters in each approach are shown in Table 3. One observes that the lower incubation temperatures result in higher experimental time to obtain the microbial growth curve. This relation was clearly observed comparing the results under isothermal conditions, in which 63.8% of the experimental time (2257 h) was spent in the kinetic at 4 °C. On the other hand, reliable model parameters at low temperatures are essential in the study of shelf life of refrigerated foods, and thus, experiments in low temperatures are essential to validate the mathematical model and avoid extrapolation. A great advantage of the OED approach is the optimal duration time of the experiment in each temperature plateau. In the experiment at 4 °C, only 63.0 h was spent for the $IT_{4–8–12-16}$ profile, 119.1 h for the $DT_{16–12–8-4}$ profile, and 96.4 h for the $DT_{25–20–16-12-8-4}$ profile. Furthermore, in the OED approach, a relative temperature range is analyzed in each experiment instead of only a constant temperature. These experimental characteristics result in smaller number of experimental data and shorter time to estimate the model parameters, as can be seen in Table 3.

The results presented in the Table 3 show that a total experimental time of 3540 h and 196 experimental data were needed to estimate the model parameters with TSM approach. On the other hand, only a total experimental time of 588 h and 60 experimental data were needed to estimate the model parameters with OED approach.

TSM and OED model parameters were validated by comparing model predicted values to experimental data of non-isothermal growth curves at four different temperature profiles ($TP_{5–11(24h)}$, $TP_{5–11(12h)}$, $TP_{5–8(12h)}$ and $TP_{3–10(12h)}$), as shown in Fig. 4. The statistical indexes (RMSE, bias factor and accuracy factor) obtained in this validation step are shown in Table 4. In all cases, RMSE value was close to zero, and bias factor and accuracy factor values were close to one, indicating the validity of the estimated TSM and OED model parameters. RMSE values and accuracy factor values obtained by predictions with the OED model parameters were lower than the same indexes in predictions using TSM model parameters (exception to RMSE value of the $TP_{5–8(12h)}$ profile). Furthermore, the bias factor values obtained by predictions with OED model parameters were closer to the unit than the bias factor values estimated when using TSM model parameters. Therefore, comparing the statistical indexes, OED model parameters led to a slightly better prediction of the experimental data under non-isothermal condition than the TSM model parameters, although model predictions and 95% prediction bounds were very similar to both TSM and OED (as shown in Fig. 4).

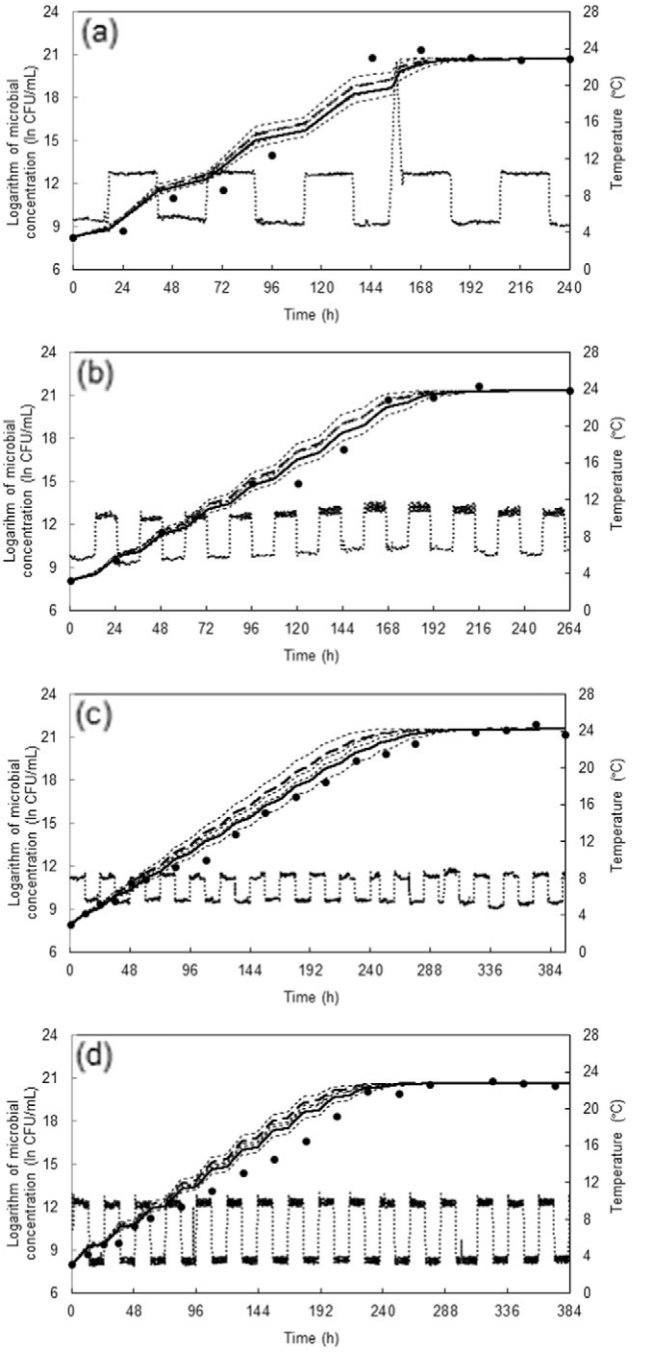

Fig. 4. Predictions of the growth of *L. viridescens* under non-isothermal conditions by TSM (dashed bold lines) and OED (continuous bold lines) model parameters, 95% prediction bounds of the mathematical model (dashed lines), experimental data of the microbial growth (symbols), experimental temperature profiles (dotted lines).

4. Conclusion

The results presented in the current study show that the OED approach allows estimating the microbial growth parameters with smaller confidence intervals and best statistical indexes than those estimated from the TSM approach. Furthermore, in the OED approach, only 31% of experimental data and 17% of time were needed than those needed by the TSM approach. The OED model parameters were validated with non-isothermal experimental data with great accuracy. In this way, the OED approach should be widely applied to estimate the model parameters in predictive microbiology.

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Table 4
Statistical indexes (RMSE, bias factor, and accuracy factor) obtained in the validation of model parameters of the TSM and OED approaches under four different non-isothermal conditions.

Temperature profile	Approach	RMSE	Bias factor	Accuracy factor
$TP_{5-11(24h)}$	TSM	1.116	1.033	1.062
	OED	1.100	1.020	1.057
$TP_{5-11(12h)}$	TSM	0.915	1.028	1.033
	OED	0.677	1.012	1.028
$TP_{5-8(12h)}$	TSM	1.518	1.019	1.073
	OED	1.627	0.982	1.065
$TP_{3-10(12h)}$	TSM	1.321	1.065	1.066
	OED	0.991	1.048	1.050

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ijfoodmicro.2016.06.042.

References

Balsa-Canto, E., Alonso, A.A., Banga, J.R., 2008. Computing optimal dynamic experiments for model calibration in predictive microbiology. J. Food Process Eng. 31, 186–206.

Baranyi, J., Roberts, T., 1994. A dynamic approach to predicting bacterial-growth in food. Int. J. Food Microbiol. 23, 277–294.

Bernaerts, K., Versyck, K.J., Van Impe, J.F., 2000. On the design of optimal dynamic experiments for parameter estimation of a Ratkowsky-type growth kinetics at suboptimal temperatures. Int. J. Food Microbiol. 54, 27–38.

Bernaerts, K., Servaes, R.D., Kooyman, S., Versyck, K.J., Van Impe, J.F., 2002. Optimal temperature input design for estimation of the square root model parameters: parameter accuracy and model validity restrictions. Int. J. Food Microbiol. 73, 145–157.

Borch, E., Kant-Madmansb, M.L., Blixt, Y., 1996. Bacterial spoilage of meat products. Int. J. Food Microbiol. 33, 103–120.

Brandão, T.R.S., Oliveira, F.A.R., Cunha, L.M., 2001. Design of experiments for improving the precision in the estimation of diffusion parameters under isothermal and non-isothermal conditions. Int. J. Food Sci. Technol. 36, 291–301.

Cunha, L.M., Oliveira, F.A.R., Brandão, T.R.S., Oliveira, J.C., 1997. Optimal experimental design for estimating parameters of the Bigelow model. J. Food Eng. 33, 111–128.

Dušková, M., Kameník, J., Karpíšková, R., 2013. *Weissella viridescens* in meat products-a review. Acta Vet. 82, 237–241.

Elias, S.O., Alvarenga, V.O., Longhi, D.A., Sant'Ana, A.S., Tondo, E.C., 2016. Modeling growth kinetic parameters of salmonella Enteritidis SE86 on homemade mayonnaise under isothermal and nonisothermal conditions. Foodborne Pathog. Dis. http://dx.doi.org/10.1089/fpd.2015.2045 (ahead of print).

Franceschini, G., Macchietto, S., 2008. Model-based design of experiments for parameter precision: State of the art. Chem. Eng. Sci. 63, 4846–4872.

Gram, L., Ravn, L., Rasch, M., Bruhn, J.B., Christensen, A.B., Givskov, M., 2002. """"Food spoilage—interactions between food spoilage bacteria. Int. J. Food Microbiol. 78, 79–97.

Grijspeerdt, K., De Reu, K., 2005. Practical application of dynamic temperature profiles to estimate the parameters of the square root model. Int. J. Food Microbiol. 101, 83–92.

Grijspeerdt, K., Vanrolleghem, P., 1999. Estimating the parameters of the Baranyi model for bacterial growth. Food Microbiol. 16, 593–605.

Juneja, V.K., Melendres, M.V., Huang, L., Subbiah, J., Thippareddi, H., 2009. Mathematical modeling of growth of *Salmonella* in raw ground beef under isothermal conditions from 10 to 45 °C. Int. J. Food Microbiol. 131, 106–111.

Kilcast, D., Subramaniam, P., 2000. Chapter 1—Introduction. In: Kilcast, D., Subramaniam, P. (Eds.), The Stability and Shelf Life of Foods. CRC Press, Boca Raton, pp. 1–22.

Longhi, D.A., Dalcanton, F., Aragão, G.M.F., Carciofi, B.A., Laurindo, J., 2013. Assessing the prediction ability of different mathematical models for the growth of *Lactobacillus plantarum* under non-isothermal conditions. J. Theor. Biol. 21, 88–96.

McDonald, K., Sun, D.W., 1999. Predictive food microbiology for the meat industry: a review. Int. J. Food Microbiol. 52, 1–27.

Munack, A., 1989. Optimal feeding strategy for identification of Monod-type models by fed-batch experiments. In: Fish, N., Fox, R., Thornhill, N. (Eds.), Computer Applications in Fermentation Technology: Modelling and Control of Biotechnological Processes. Elsevier, Amsterdam, pp. 195–204.

Nychas, G.J.E., Skandamis, P.N., Tassou, C.C., Koutsoumanis, K.P., 2008. Meat spoilage during distribution. Meat Sci. 78, 77–89.

Ratkowsky, D., Olley, J., McMeekin, T., Ball, A., 1982. Relationship between temperature and growth-rate of bacterial cultures. J. Bacteriol. 149, 1–5.

Ross, T., 1996. Indices for performance evaluation of predictive models in food microbiology. J. Appl. Bacteriol. 81, 501–508.

Tremarin, A., Longhi, D.A., Salomão, B.C.M., Aragão, G.M.F., 2015. Modeling the growth of *Byssochlamys fulva* and *Neosartorya fischeri* on solidified apple juice by measuring colony diameter and ergosterol content. Int. J. Food Microbiol. 193, 23–28.

Valdramidis, V.P., Geeraerd, A.H., Bernaerts, K., Van Impe, J.F.M., 2008. Identification of non-linear microbial inactivation kinetics under dynamic conditions. Int. J. Food Microbiol. 128, 146–152.

Van Impe, J.F., Nicolaï, B.M., Martens, T., Baerdemaeker, J.D., Vandewalle, J., 1992. Dynamic mathematical model to predict microbial growth and inactivation during food processing. Appl. Environ. Microbiol. 58, 2901–2909.

Versyck, K.J., Bernaerts, K., Geeraerd, A.H., Van Impe, J.F., 1999. Introducing optimal experimental design in predictive modeling: a motivating example. Int. J. Food Microbiol. 51, 39–51.

Whiting, R., Buchanan, R., 1993. A classification of models in predictive microbiology—reply. Food Microbiol. 10, 175–177.