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Fitting and Comparing Microbial Population Growth Models

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Abstract

Microbial growth modeling has roots in the mathematical principles of population dynamics formulated during the early 19th century. Today, the foundations that these models laid are crucial in predicting how microbial populations grow. Despite centuries of progress in this field, no singular model has been found that best suits all growth data [16]. This study aims to explore some of the potential reasons behind this by fitting four models to a dataset of microbial growth assembled from 10 different sources [2, 3, 6, 8, 19, 22, 20, 26, 27, 30]. The models (Quadratic, Cubic, Gompertz and Logistic) are a mix of linear and nonlinear models that account for different types of growth. After fitting the models to all data, R-squared and AICc values were calculated, which revealed that, some models will greatly outperform others depending on the data. Overall, the Gompertz model was the best-fitting model in terms of R-squared but not AICc which accounts for model complexity. When this is factored in, the logistic model outperforms it, likely because the data better suits it, and because it is less complex. However, the overall results also suggest that there is no singular model that can be applied to all experiment scenarios and that model use has to be carefully considered for each experiment with contextual knowledge. Future research efforts should ideally focus on clarifying model use scenarios for different variables and units.

1 Introduction

The use of quantitative modeling in microbiology has been an extremely important field of research for decades. Early work - such as Malthus's exponential growth model (1798) and Verhulst's logistic equation (1838) - laid the foundation for understanding how populations grow. These foundations (especially the logistic equation) led to a variety of different breakthroughs across mathematical fields and continue to have relevance today. Over decades, these models were improved upon and used in more and more fields, eventually including microbial growth modeling in the early 20th century [16]. Even in this sub-field of population modeling, the knowledge gained has been applied to various fields ranging from medicine to agriculture to environmental ecology. Microbial growth modeling helps predict when food spoils, it informs on the efficacy of antibiotics, it can help maximize yield of foods that use fermentation and much more [12, 5]. The scientific process in which such models are most often used is model selection, where multiple candidate models are fit to the data and compared to each other. Comparisons usually aim to balance goodness of fit (how well the model explains the data) with parsimony (avoiding unwanted complexity) [29]. Both of these concepts have metrics tied to them such as R-squared, which captures how well the model fits the data, and AIC factors in and penalizes model complexity. A major benefit of model selection is that models can not only describe the phenomenon seen in the data (phenomenological models) but also the biomechanics behind the phenomenon (mechanistic models). As an example, linear models like the cubic and quadratic models are phenomenological because the parameters used to not explicitly map to an underlying biological mechanism, they are simply fit to the data. Despite not explaining any of the biology behind the data, both models can accurately describe growth trends, especially the cubic model which can capture all 4 phases of growth (lag, exponential, stationary/stable and death) due to its "saddle" shape (Fig. 1) [7].

Similarly, the logistic and Gompertz models also capture most phases excluding the death phase due to their sigmoidal shapes, but unlike the cubic model, these aim to explain the data by using actual biological concepts such as carrying capacity and growth rate [25]. Each model is a tradeoff between simple or complex, linear or nonlinear, and phenomenological or mechanistic, all of which have their own benefits and drawbacks [18].

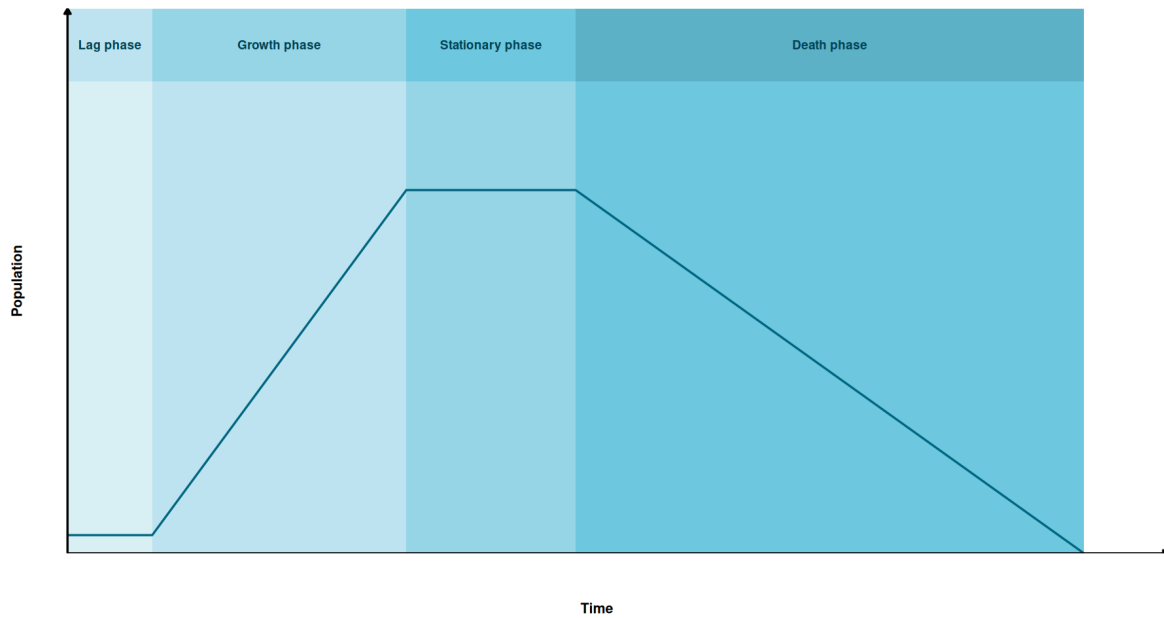


Figure 1: Simplified microbial growth phases visualized, modified from [18].

Model	Parameters	Linear vs. Non-linear	Phenomenological vs. Mechanistic
Quadratic	3	Linear	Phenomenological
Cubic	4	Linear	Phenomenological
Logistic	3	Non-linear	Mechanistic)
Gompertz	4	Non-linear	Mechanistic

Table 1: Visualizing tradeoffs by comparing growth models along key dimensions.

The following aims to compare the predictive ability and generalisability of each model across a varied dataset including 45 bacterial species, 18 different growth mediums, 4 different units of growth and temperatures ranging from 0-37 Celsius. Overall, the Gompertz and cubic models are expected to perform best when measured by R-squared values, simply because they have the most parameters. When measured by AIC (or AICc in this case) the logistic model is expected to perform best, due to its lesser complexity and ability to capture a lag phase.

2 Methods

2.1 Data Wrangling

All bacterial growth data was collected from 10 separate research articles and subsetting by citation. Afterwards, any obvious errors such as negative weight were removed and a threshold of 6 datapoints per experiment was implemented, leaving a total of 302 subsets.

2.2 Model Definitions

All models, excluding the Gompertz, were fit using their standard formula:

Quadratic model:

$$N_t = ax^2 + bx + c \quad (1)$$

Cubic model:

$$N_t = ax^3 + bx^2 + cx + d \quad (2)$$

Logistic model:

$$N_t = \frac{N_0 K e^{rt}}{K + N_0 (e^{rt} - 1)} \quad (3)$$

Four-parameter Gompertz model:

$$\log(N_t) = N_0 + (N_{max} - N_0) e^{-e^{\frac{r_{max} \exp(1)}{(N_{max} - N_0) \log(10)} + 1} (t_{lag} - t)} \quad (4)$$

Where the parameters represent:

- N_t : Population at time t
- N_0 : Initial population size
- N_{max} : Maximum population size
- K : Carrying capacity
- r : Intrinsic growth rate
- r_{max} : Maximum intrinsic growth rate
- t_{lag} : Lag time before exponential growth phase

2.3 Model fitting

All statistical analysis was performed using R. Linear models were fit as polynomial regressions and non-linear models were fit using a least squares algorithm called the Levenberg-Marquardt algorithm also known as the damped least-squares method. To identify optimal parameters for each non-linear model, parameters were randomly drawn 100 times from a normal distribution with a mean equal to the natural log of the minimum population size $\log(N_0)$ and a standard deviation of 0.1. This same logic was applied the maximum population size K . In order to find the best

r_{max} value, the maximum value of the second derivative of r was taken as that would reveal its steepest slope. Final parameter values were chosen based on which ones produced the best fit (or highest R^2). The Levenberg-Marquardt algorithm requires an input of starting values for K , N_0 , t_{lag} and r_{max} . K will logically be near peak population size, N_0 near minimum population size and t_{lag} will end once the exponential growth phase begins. The starting value of r_{max} was chose as 0.1 simply because it is a reasonable guess based on the literature. The algorithm also requires lower bounds, which were mostly set to extreme values to allow the model some flexibility or set to the minimum of what is biologically possible (such as a t_{lag} of 0).

Since the Gompertz model uses $\log(N_t)$, all other models had to be log-transformed too (using the natural logarithm). In addition, the log of the growth data itself was used in each model. This was done to ensure that resulting measures of model success (R^2 and $AICc$) were comparable, since comparing from linear space to log-space (or vice versa) would mean comparing these metrics which come from fundamentally different response variables (N_t vs $\log(N_t)$). The idea of bringing the cubic, quadratic and logistic models into log-space after model fitting in order to calculate an R^2 and $AICc$ value was rejected. Since these model parameters were optimized to minimize residuals in linear space, log-transforming residuals post-hoc would introduce a mismatch in optimization objective with the evaluation metric and would also distort errors since the logarithm compresses larger values more than smaller values.

Once all model fitting had concluded, each individual R^2 value was manually calculated and each $AICc$ was calculated using an R package. $AICc$ was favoured over AIC or BIC due to the low sample size within each subset of data, and from this a resulting Akaike Weight was also calculated. A resulting dataframe was then created which included each experiments R^2 , $AICc$ and Akaike Weight (A.W.) per model, in addition to temperature and growth units used in the experiments. Temperature values were placed into "10-width" bins (bins that encompass 10 degrees celsius each), to simplify analysis. These bins were based on mesophilic (an organism that thrives in moderate temperatures) and psychophilic (an organism that thrives in cold temperatures) ranges [10]. All results are derived from this final dataframe.

2.4 Computing Tools

As mentioned, all computing and analysis was conducted in R (version 4.3.3), using packages "minipack.lm" for non-linear models, "tidyverse" for data manipulation and poltting, "AICcmodavg" for calculating $AICc$ values and Akaike Weights and lastly "parallel" for parallel processing. A simple bash script was used to run the R script and generate plots of each data subset with models overlaid.

3 Results

Overall, the mechanistic models performed the best on all metrics of model success. To compare models, all groups that where missing a model because it failed to converge where pruned leaving 267 groups. Each time a model "beat" the others a tally was added to that model. This helped determine the best singular model for each group of data, but it does not inform on how well the models did in relation to each other. Some models might have R^2 values extremely close to the winner but this method will not capture that relationship. A simple method to account for this is to observe the mean of each model success metric for each model.

When analyzing data by growth units, two significant findings were observed. When growth was measured by CFU (colony forming units), the Gompertz model outperformed all other models

Models	Quadratic	Cubic	Logistic	Gompertz
R^2 "wins"	0	72	79	116
AICc "wins"	45	25	138	59
Total "wins"	45	97	217	175

Table 2: Comparison of models based on R^2 and AICc "wins". Akaike Weight "wins" are identical to AICc "wins".

Models	Quadratic	Cubic	Logistic	Gompertz
Mean R^2	0.85	0.91	0.93	0.80
Mean A.W.	0.19	0.10	0.50	0.21

Table 3: Comparison of models based on mean R^2 and mean Akaike Weight. Mean AICc are not shown due to some AICc being infinite.

in all metrics. When this was measured by OD 595 (optical density at 595nm), the logistic model outperformed all other models in all metrics. Similarly, when analyzing by temperature a pattern emerged where the Gompertz model performance declined with increasing temperature and the logistic model performance increased.

	Cubic	Gompertz	Logistic	Quadratic
CFU	10%	90%	-24%	-42%
OD 595	30%	-86%	60%	-79%
0 to 10	80%	52%	-30%	-21%
10 to 20	-10%	5%	-4%	11%
20 to 30	-30%	-52%	30%	-5%
30 to 37	-70%	-33%	26%	5%

Table 4: Percentage increase in mean Akaike Weight (compared to baseline) when analyzing data by growth unit and temperature. Model performance increases are tinted green while decreases are tinted red. Note: the remaining two units of growth measurement are not included in this table.

4 Discussion

At an initial glance, the fundamental question of which model performs best can be challenging to answer. The Gompertz model seems to both have the most "wins" but also the lowest mean R^2 , while the logistic model has a competitive R^2 and the highest mean R^2 , but vastly outperforms the other models in terms of all AICc metrics. This finding is also seemingly dependent on the units used and the temperature at which the experiments were conducted at. Understanding the models step by step can help clarify the underlying causes of this phenomenon.

The Gompertz model is characterised by its ability to capture a lag phase, an exponential phase and a stable phase [14]. This immediately provides a possible answer as to why the Gompertz performed worse at higher temperatures. All species in the dataset are generally mesophilic and therefore tend to have a longer or more pronounced lag phase at colder temperatures [15, 28]. At higher temperatures, cells do not need to adjust to their environment as much and therefore the

lag phase is often shorter or nonexistent. As for the models drastic change in performance with different units, it helps to understand how these are measured. OD 595 measurements reflect overall turbidity which can include nonviable cells and debris. If a cell dies for instance, the debris left behind will be captured by the OD 595 measurement, meaning that these measurements can have less pronounced lag and stable phases, directly leading to worse performance of the Gompertz model which relies on these phases to be present [13]. Which also explains why CFU seems to improve how well the Gompertz model works, since CFU is a direct measure of viable cells and also tends to be less noisy than OD 595 measurements, meaning that any trends found are less likely to be obscured by noise [17].

Conversely, the logistic model (in this specific case) has the same factors influencing it. The specific method applied to the model means that instead of the classic sigmoid curve of the logistic model, which may be able to capture a lag phase, the model used is unlikely to do so. This is due to the fact that all models were log-transformed (excluding the Gompertz), meaning that the classic sigmoid curve was transformed into something resembling a quadratic polynomial (Fig. 2).

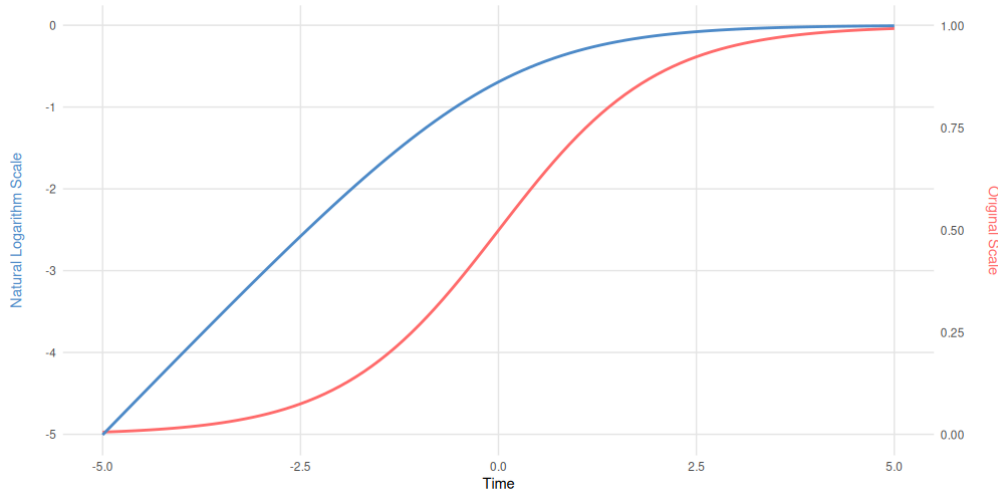


Figure 2: Dual-axis comparison of the logistic growth model (red) vs its log-transformed (blue) counterpart, using $K = 1$ and $r = 1$.

Because this model now cannot capture a lag phase effectively, it naturally performs better in cases where a lag phase is small or not present at all. Meaning that both higher temperatures and OD 595 as a measurement of growth would suit this model over the Gompertz (Fig. 3).

Of note is that the cubic model, despite theoretically being able to capture all phases of growth, it generally performed worse than the previously mentioned models. Within models where a death phase was present, it generally outperformed other models. This aligns with previous research findings that state that cubic models perform well when death phases are present [24]. However, models with a protracted stable phase and no death phase notably caused issues because the "saddle" could not be "stretched" long enough (Fig. 4).

Despite frequently performing well in terms of R^2 , its higher parameter count (4) and its overfitting tendency led to it having the lowest mean A.W. out of all models, even when compared to the quadratic model. This highlights the importance of complexity in model selection, since the only other model with the same parameter count (the Gompertz model) similarly performed worse in all Akaike metrics when compared to R^2 [9]. Conversely, the quadratic model, despite its very poor performance when measured by R^2 , performed much better once complexity was factored in,

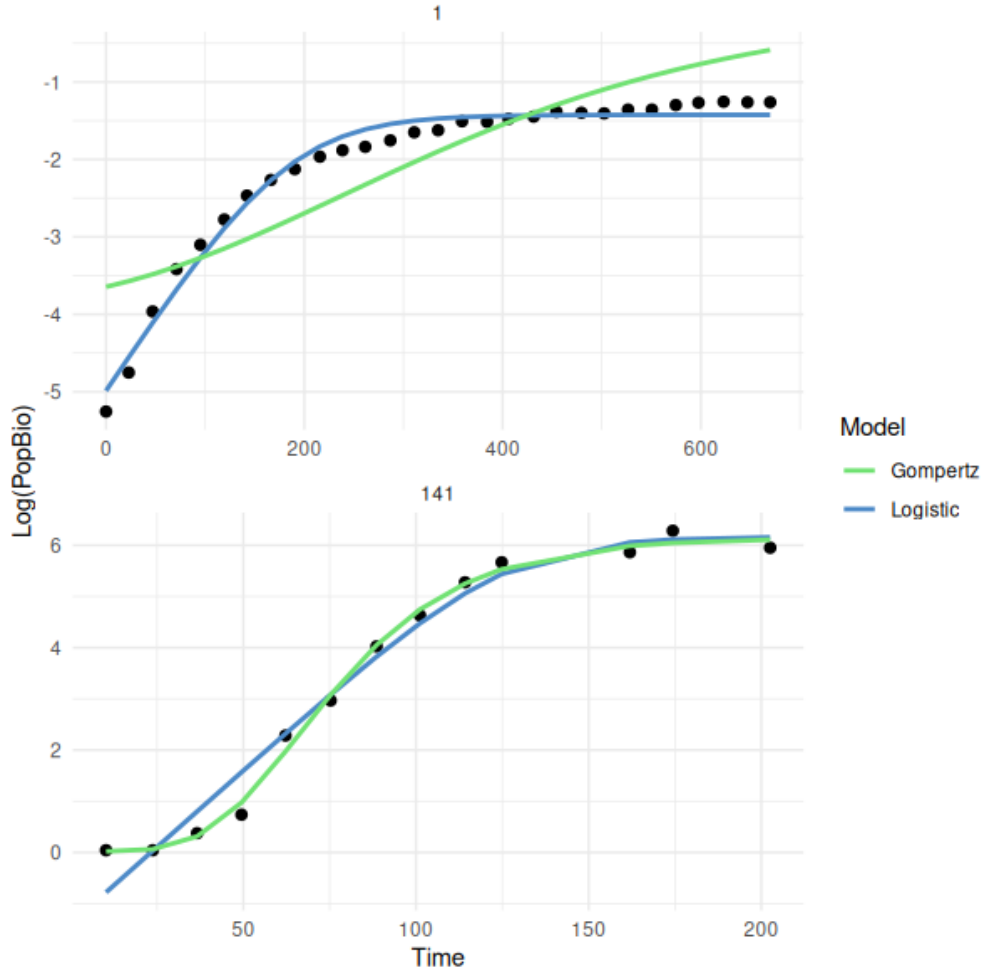


Figure 3: Example groups 1 and 141, which show how the Gompertz performs better when a clear lag phase is present compared to the logistic model.

almost being on par with the Gompertz model.

Another point of note is that R^2 by itself can be a misleading metric [23]. The Gompertz model had the worst mean R^2 , yet also had the most "wins" due to the fact that it had both extremely good fits and a very poor fits. Since the literature generally agrees that A.W. are superior when comparing models, this metric will be used to judge ultimate model success [4]. When evaluated on this metric the results did not align with expectations.

Specifically, the fact that the logistic model performed very well in terms of R^2 and A.W. was the main unexpected finding. Prior judgment of the logistic models success relied on the fact that it was assumed to be used in its non-transformed version, essentially meaning that it would replicate what the Gompertz model did but with a less clearly defined lag phase and stable phase. Since it was log-transformed and the data generally did not have many pronounced lag phases, it essentially performed like a "better" quadratic model. So not only did it fit exceptionally well, it also had few parameters (3) making it the best-performing model.

Similarly unexpected and along the same lines, are the results of the quadratic model, which nearly had the same mean A.W. as the Gompertz despite a poor R^2 performance. Both metrics of model success were expected to loosely align with each other (and they generally do), but the

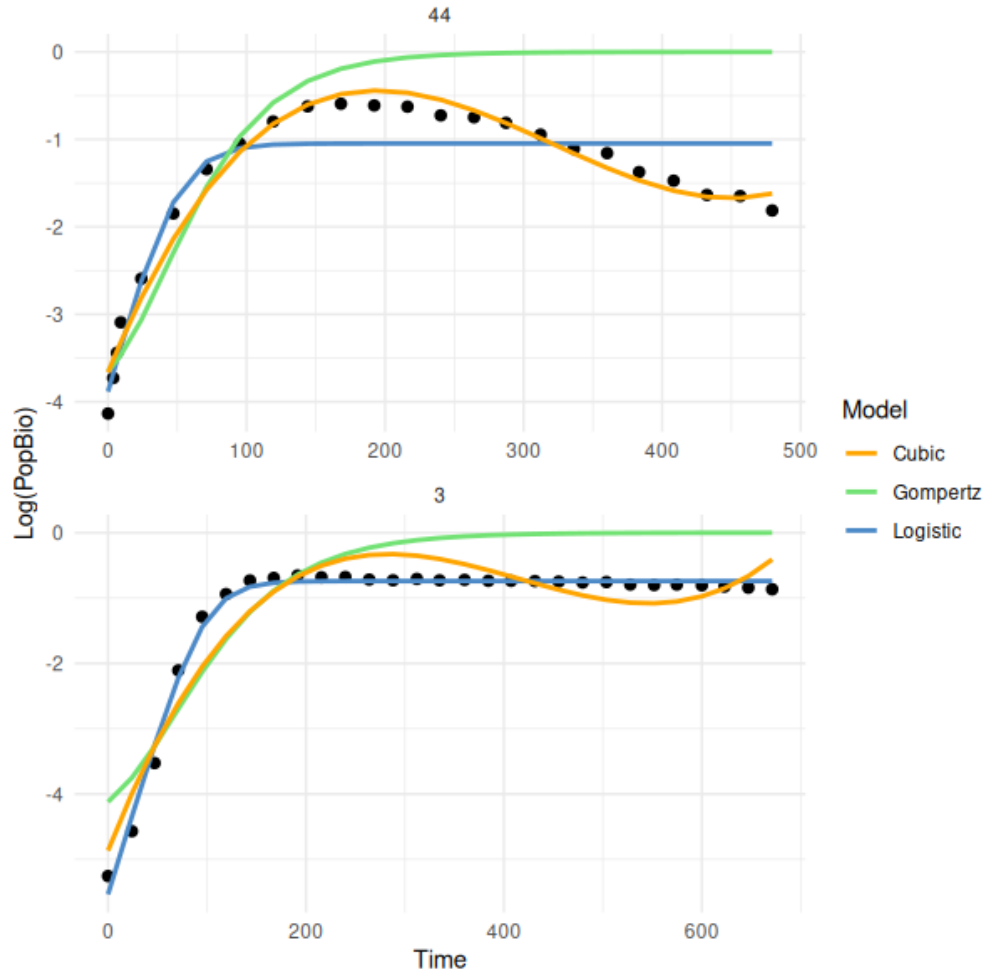


Figure 4: Example group 44, showing how the cubic model captures a death phase and example group 3 showing how the saddle could not be stretched long enough due to a long stable phase.

quadratic model showcased the importance of low parameter count (3).

On the other hand, a result that was expected was the general success of mechanistic models vs phenomenological models, aligning with previous research in this field [21, 18, 5]. The Gompertz model was expected to perform better, but this could easily be due to the data or minor errors in parameter selection. Overall, results proved that there cannot be a one-size-fits-all approach to model selection and that the models used are not generalizable to all data of microbial growth [11, 18]. As an example: units of measurement, medium, PH, temperature and experiment length are all important factors that can influence whether or not a model works [1].

Ideally, future research would focus on clarifying which models are appropriate for which experiment scenarios. A literature review publishing a guide on model selection for different scenarios could be published as just one singular paper, but could massively simplify the process of model selection for research that is yet to come.

References

- [1] Simen Akkermans and Jan F. Van Impe. Mechanistic modelling of the inhibitory effect of pH on microbial growth. *Food Microbiology*, 72:214–219, June 2018.
- [2] Young-Min Bae, Ling Zheng, Jeong-Eun Hyun, Kyu-Seok Jung, Sunggi Heu, and Sun-Young Lee. Growth characteristics and biofilm formation of various spoilage bacteria isolated from fresh produce. *Journal of Food Science*, 79(10):M2072–2080, October 2014.
- [3] Joey R. Bernhardt, Jennifer M. Sunday, and Mary I. O'Connor. Metabolic Theory and the Temperature-Size Rule Explain the Temperature Dependence of Population Carrying Capacity. *The American Naturalist*, 192(6):687–697, December 2018.
- [4] Nicholas P. Danks, Pratyush N. Sharma, and Marko Sarstedt. Model selection uncertainty and multimodel inference in partial least squares structural equation modeling (PLS-SEM). *Journal of Business Research*, 113:13–24, May 2020.
- [5] Daniel S. Esser, Johan H. J. Leveau, and Katrin M. Meyer. Modeling microbial growth and dynamics. *Applied Microbiology and Biotechnology*, 99(21):8831–8846, November 2015.
- [6] Liane Aldrichi Galarz, Gustavo Graciano Fonseca, and Carlos Prentice. Predicting bacterial growth in raw, salted, and cooked chicken breast fillets during storage. *Food Science and Technology International*, 22(6):461–474, September 2016.
- [7] Blanca E. Garcia, Emmanuel Rodriguez, Yolocuauhtli Salazar, Paul A. Valle, Adriana C. Flores-Gallegos, O. Miriam Rutiaga-Quñones, and Raul Rodriguez-Herrera. Primary Model for Biomass Growth Prediction in Batch Fermentation. *Symmetry*, 13(8):1468, August 2021.
- [8] C. O. Gill and K. M. DeLacy. Growth of *Escherichia coli* and *Salmonella typhimurium* on high-pH beef packed under vacuum or carbon dioxide. *International Journal of Food Microbiology*, 13(1):21–30, May 1991.
- [9] Yuanlin Gu, Hua-Liang Wei, and Michael M. Balikhin. Nonlinear predictive model selection and model averaging using information criteria. *Systems Science & Control Engineering*, 6(1):319–328, January 2018.
- [10] Eoin Gunnigle, Jeppe L. Nielsen, Matthew Fuszard, Catherine H. Botting, Jerome Sheahan, Vincent O'Flaherty, and Florence Abram. Functional responses and adaptation of mesophilic microbial communities to psychrophilic anaerobic digestion. *FEMS Microbiology Ecology*, 91(12):fiv132, December 2015.
- [11] Dimitrios-Georgios Kontopoulos, Arnaud Sentis, Martin Daufresne, Natalia Glazman, Anthony I. Dell, and Samraat Pawar. No universal mathematical model for thermal performance curves across traits and taxonomic groups. *Nature Communications*, 15(1):8855, October 2024.
- [12] Ehsan Mahdinia, Shaowei Liu, Ali Demirci, and Virendra M. Puri. Microbial Growth Models. In Ali Demirci, Hao Feng, and Kathiravan Krishnamurthy, editors, *Food Safety Engineering*, pages 357–398. Springer International Publishing, Cham, 2020.
- [13] Portia Mira, Pamela Yeh, and Barry G. Hall. Estimating microbial population data from optical density. *PLOS ONE*, 17(10):e0276040, October 2022.

- [14] S. Murunga and Festus A. Were. Predicting Microbial Growth In Anaerobic Digester Using Gompertz And Logistic Models - IRE Journals. 3:198–205, 2019.
- [15] Akihiro Ohnishi, Akihiro Nagano, Naoshi Fujimoto, and Masaharu Suzuki. Phylogenetic and physiological characterization of mesophilic and thermophilic bacteria from a sewage sludge composting process in Sapporo, Japan. *World Journal of Microbiology and Biotechnology*, 27(2):333–340, February 2011.
- [16] N. S. Panikov. 1.20 - Microbial Growth Dynamics. In Murray Moo-Young, editor, *Comprehensive Biotechnology (Second Edition)*, pages 257–283. Academic Press, Burlington, January 2011.
- [17] Katia Peñuelas-Urquides, Licet Villarreal-Treviño, Beatriz Silva-Ramírez, Liliana Rivadeneyra-Espinoza, Salvador Said-Fernández, and Mario Bermúdez de León. Measuring of *Mycobacterium tuberculosis* growth: A correlation of the optical measurements with colony forming units. *Brazilian Journal of Microbiology*, 44:287–290, 2013.
- [18] Micha Peleg and Maria G. Corradini. Microbial Growth Curves: What the Models Tell Us and What They Cannot. *Critical Reviews in Food Science and Nutrition*, 51(10):917–945, December 2011.
- [19] J. D. Phillips and M. W. Griffiths. The relation between temperature and growth of bacteria in dairy products. *Food Microbiology*, 4(2):173–185, April 1987.
- [20] S. Rohini Karnat, M. V. R. K. Sarma, and D. Somashekar. Study of changes in functional properties of fermented Idli batter during storage under different temperature conditions. *Food and Humanity*, 3:100377, December 2024.
- [21] Monica Roman and Dan Selișteanu. Modeling of microbial growth bioprocesses — Equilibria and stability analysis. *International Journal of Biomathematics*, 09(05):1650067, September 2016.
- [22] Norman G. Roth and Robert B. Wheaton. Continuity of psychrophilic and mesophilic growth characteristics in the genus *arthrobacter*. *Journal of Bacteriology*, 83(3):551–555, March 1962.
- [23] Shokrya Saleh. MODEL SELECTION VIA ROBUST VERSION OF R-SQUARED. *Journal of Mathematics and Statistics*, 10(3):414–420, October 2014.
- [24] Mohd Yunus Shukor. Test for the presence of autocorrelation in the modified Gompertz model used in fitting of *Burkholderia* sp. strain Neni-11 growth on acrylamide. *Bioremediation Science and Technology Research (e-ISSN 2289-5892)*, 4(2):25–27, December 2016.
- [25] Matthew J. Simpson, Alexander P. Browning, David J. Warne, Oliver J. Maclaren, and Ruth E. Baker. Parameter identifiability and model selection for sigmoid population growth models, October 2021.
- [26] K Sivonen. Effects of light, temperature, nitrate, orthophosphate, and bacteria on growth of and hepatotoxin production by *Oscillatoria agardhii* strains. *Applied and Environmental Microbiology*, 56(9):2658–2666, September 1990.
- [27] C. J. Stannard, A. P. Williams, and P. A. Gibbs. Temperature/growth relationships for psychrotrophic food-spoilage bacteria. *Food Microbiology*, 2(2):115–122, April 1985.

- [28] J. T. Trevors, A. K. Bej, N. Mojib, J. D. van Elsas, and L. Van Overbeek. Bacterial gene expression at low temperatures. *Extremophiles*, 16(2):167–176, March 2012.
- [29] Si Zhu and Guibing Chen. Numerical solution of a microbial growth model applied to dynamic environments. *Journal of Microbiological Methods*, 112:76–82, May 2015.
- [30] M. H. Zwietering, J. C. de Wit, H. G. A. M. Cuppers, and K. van 't Riet. Modeling of Bacterial Growth with Shifts in Temperature. *Applied and Environmental Microbiology*, 60(1):204–213, January 1994.