A Unified Mathematical Modelling Framework in Food Science: Three Pool Model

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Abstract

Different empirical and inactivation models applied in the estimation of parameters and modelling of phenomena in food microbiology, generalized Lotka Voltera approach used to describe the interaction of microorganisms, mechanistic models utilized to provide more insight into the underlying dynamic can all be unified as variations of a new model known as three pool model. Compared against the aforementioned methods which are applicable in specific applications with some limitations, the present model turns out to be less complex with general applicability, low number of parameters and preferably to explain the mechanism of the phenomenon of interest. To illustrate the generality of the model, three different examples are reported.

Contents

1. INTRODUCTION

Description of kinetics in micro-organisms can be classified into two major classes: The primary model and the secondary model. Primary models describe the changes of the attribute of interest in time. According to the behavior of micro-organisms during food processing and storage, primary models can be divided into inactivation models and growth models. The survival can be considered as the slow growth or slow inactivation and the only difference from growth or inactivation is the larger time scales. In order to predict microbial survival or growth curves, some empirical and mechanistic mathematical models have been used. In fact, most of empirical models have no or little microbiological or physiological basis, which make the interpretation of some model parameters difficult and their performances do not match observed microbiological outcomes. To produce a more accurate mathematical model, more mechanisms are necessary to interpret model parameters with a biological basis (Zwietering 2002).

1.1. Empirical Models

Empirical Models are extensively used in the estimation of parameters and modelling of phenomena. An excellent overview of primary models used in food science can be found in (Van Boekel 2008). Here some commonly used empirical models are given.

1.1.1. Baranyi and Roberts Model. The ordinary differential equation for the Baranyi and Roberts model is (Baranyi et al. 1993):

$$\frac{dq(t)}{dt} = \mu q(t) \quad 1.$$
$$q(0) = q_0 \quad 2.$$

$$\frac{dN(t)}{dt} = \mu\alpha(t)N(t)(1 - \frac{N(t)}{N_{max}}); \alpha(t) = \frac{q(t)}{1+q(t)}; N(0) = N_0 \quad 3.$$

where q_0 and $q(t)$ are the quantities which are related to the critical substance necessary for growth and characterize the physiological state of the culture in the moment of inoculation and later time, respectively. μ is the specific growth rate, expressed in $[1/h]$. N_0 , N_{max} and $N(t)$ are initial, maximal and actual cell concentration, respectively, expressed in $[CFU/g]$. The adjustment function, which takes into account the lag phase during which the population adapts to the new environment is denoted by $\alpha(t)$. Also, instead of using parameter q_0, the quantity $q_0 = \frac{1}{e^h - 1}$ is usually used.

1.1.2. Modified Gompertz Model. The ordinary differential equation for the modified Gompertz model is:

$$\frac{dy}{dt} = yBln(\frac{C}{y}) \quad 4.$$

and

$$y(0) = A + Cexp[-e^{BM}] \quad 5.$$

where A, C, B and M are model parameters and y is the natural logarithm of the cell concentration. In the practical implementation, we have encountered some issues related to the division by zeros in the modified Gompertz model. The $y = ln(y)$ is used to remove the division by y, which is causing sometimes problems. The transformed modified Gompertz model is defined as follows:

$$\frac{dy}{dt} = B(ln(C) - y) \quad 6.$$

and,

$$y(0) = ln(C) - e^{BM} \quad 7.$$

1.1.3. Inactivation models. The classically well known model to describe the inactivation of micro-organisms is a thermal death time model. The model is as follows (Whiting 1997):

$$\begin{cases} \frac{dN}{dt} = -kN(0 \leq t < +\infty) \\ N(0) = N_0 \, (N_0 > 0; t = 0) \end{cases} \quad 8.$$

In which N is the number of micro organisms. However, some shoulder phase are often observed in practice. To address this problem, a modified model to capture the effect of the shoulder phase is proposed (Buchanan et al. 1993):

$$\log(N) = \begin{cases} \log(N_0) & (t \leq \lambda) \\ \log(N_0) - k(t-\lambda) & (t \geq \lambda) \end{cases} \quad 9.$$

In which λ is the shoulder phase.

1.2. Mechanistic Models

The mechanistic models are usually much more complex and include more parameters to be estimated. However, such models can yield more insight into the underlying dynamic. Zwietering etal. proposed two different mechanistically based models To describe the lag phase in bacteria. These models resulted in two different equations, but can express the same effect (Zwietering 2002). In one model, with the assumption that at first, rhe component B should be made and then it is converted to C before the cells can divide and also the number of molecules C per cell (p) is constant, we have:

$$A \overset{k_a}{\rightarrow} B \overset{k_b}{\rightarrow} C \quad 10.$$

$$\begin{cases} \frac{dB}{dt} = (k_a - k_b B)X \\ \frac{dC}{dt} = p\frac{dX}{dt} \end{cases} \quad 11.$$

Then in another model with assumptions considering the exponentially growth of bacteria and normally distributed lag phase, the mechanistic model is as follows:

$$\begin{cases} \frac{dN}{dt} = \mu N; t > \lambda \\ Ln(\frac{N}{N_0}) = \mu(t-\lambda) \end{cases} \quad 12.$$

Where N is the number of micro-organisms, N_0 the number at $t = 0$ (until $t < \lambda$), μ the specific growth rate and λ the lag time. These two models describe the lag phase and explain some steps inside of the lag pool in TPM.

In another mechanistic point of view, mass and energy balances were used to provide an overview of the complete product line including the different stages (freezing, dispense, chilled, transfer) and the interactions between the different stages. The goal was to quantitatively describe all aspects of microbial kinetics in a process line in view of the wide range of important factors involved. Applying both predictive microbiology and HACCP (Hazard Analysis Critical Control Points) offered to find the critical points in the product line quantitively. The growth and exchange between the dead spaces and the bulk product flow in continuous system is made. The balances for the main stream and the dead spaces can be written as (Zwietering 1997):

$$\begin{cases} V_1\frac{dN_{out}}{dt} = F_p(N_{in} - N_{out}) + F_e(N_d - N_{out}) + \mu N_{out}V_1 + \frac{r_c}{1000p} \\ V_d\frac{dN_d}{dt} = F_e(N_{out} - N_d) + \mu_d N_d V_d \end{cases} \quad 13.$$

In which F_e is flow from the bulk stream , volume V_1 , to the dead volume, volume V_d, F_p is the main bulk flow, μ is the grwth rate, N_{out} the number of micro-organisms in

the main flow, N_d the number of micro-organisms in the dead pool and r_c is the external contamination rate.

Another interesting area in which mechanistic models can play an important role is the interaction of microorganisms. Empirical studies using ine species results in a mathematical model to predict the variations of microorganisms in foods. However, foods can include a complex microflora with interactions between the different species. A mechanistic model has been proposed to describe the interaction of two microorganisms, L . curvatus and E . cloacae growing in a broth culture (Zwietering 1997). The main factors of interaction are the glucose concentration S, the lactic acid concentration P and the pH of the medium. The effects of S, P and pH on the specific growth of pure cultures of L . curvatus and E . cloacae is presented using the following differential equations (Martens 1998):

$$\begin{cases} \frac{dX_{Lc}}{dt} = \mu_{Lc} X_{Lc} \\ \frac{dX_{Ec}}{dt} = \mu_{EC} X_{EC} \end{cases} \quad 14.$$

In which X_{Lc}, X_{Ec} are the accumulation of L . curvatus and E . cloacae,and μ_{Lc}, μ_{Ec} are the specific growth rates.

$$\mu = \mu_{opt}(\frac{S}{S + KS_{Lc}})(\frac{4(pH - pH_{minLc})(pH_{maxLC} - pH)}{(pH_{maxLC} - pH_{minLC})^2}) - b_1 P \quad 15.$$

In which μ_{opt} is the growth rate at optimal conditions. KS_{Lc} is the Monod constant and b_1 is a regression parameter for the description of the effect of P on the specific growth rate of L . curvatus.

2. General idea

When a population of bacteria experiences a new environmental situation they often need time to adapt to the new situation. Some bacteria even may not be able to adjust and die other will enter the exponential growth phase after a a lag phase. Motivated by this we divide a bacterial population into three pools (**Figure 1**):

- $L(t)$: the fraction of the population doing nothing - being in the lag phase
- $D(t)$: the fraction of the population undergoing cell death
- $G(t)$: the fraction of the population growing and dividing

2.1. No back-flow from G and D to L

The pools G and D are unidirectionally connected with the pool L. We assume for simplicity that there is no link between G and L. The suggested model can be cast in the following two reactions:

$$L \xrightarrow{\lambda} G \quad 16.$$
$$L \xrightarrow{\mu} D \quad 17.$$
$$G \xrightarrow{\alpha} 2G \quad 18.$$
$$G \xrightarrow{\mu'} D \quad 19.$$
$$D \xrightarrow{\beta} \emptyset \quad 20.$$

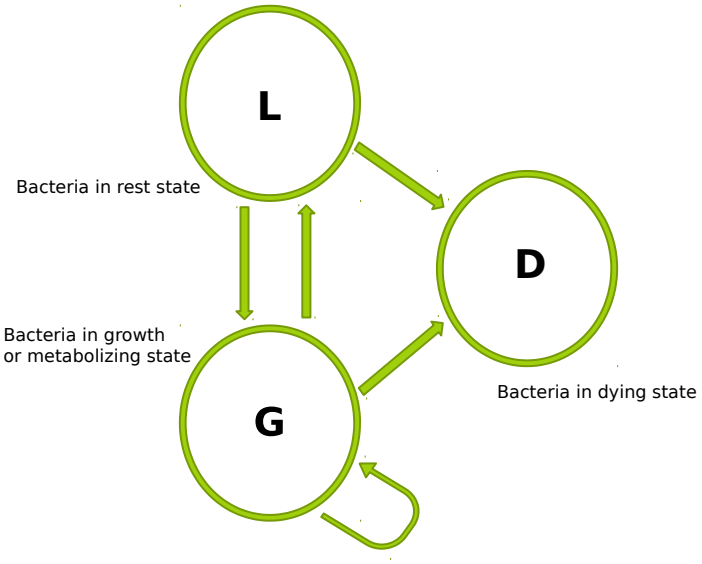

Figure 1

Schematic representation of exchange between three states or pools.

The fraction G of the exponentially growing cells will go to steady state due to limitations in resources. λ is the rate by which cells go from the lag phase to the growth phase; μ is the rate by which cells go from the lag phase to the state in which they die; α is the growth rate of the healthy population; β is the rate by which the cells are removed from the D pool. Note that one could further simplify this model to a two pool or state model by omitting the pool D and removing cells with rate β directly from pool L. The relevant question here is whether cells in the pool D still contribute to the limitation of the resources by, e.g., occupying space or consuming important nutrients. If yes, the three pool model would be advantageous, if not the two pool model is sufficient with the advantages of having one parameter less.

The dynamics of the three pool model can be captures by the coupled system of ordinary differential equations (the two pool model can be achieved by setting $D \equiv 0$ and replacing μ with β):

$$\dot{L} = -(\mu + \lambda)L \tag{21.}$$

$$\dot{G} = \lambda L + \alpha G \left(1 - \frac{L + G + D}{N_t}\right) - \mu' G \tag{22.}$$

$$\dot{D} = \mu L + \mu' G - \beta D \tag{23.}$$

to be solved with the initial conditions $L(0) = n_0$, $G(0) = 0$, and $D(0) = 0$, where n_0 is the initial bacterial population. N_t denotes the maximal size of the total bacterial population due to environmental limitations (**Figure 2**). For $\mu' = 0$ the equations for L and D can be

readily integrated resulting in:

$$L(t) = n_0 e^{-(\mu+\lambda)t} \tag{24.}$$

$$D(t) = n_0 \mu e^{-\beta t} \frac{1 - e^{-(\mu+\lambda-\beta)t}}{\mu + \lambda - \beta}. \tag{25.}$$

For constant parameters μ, λ, and β the integrals for L and D can be put into the differential equation for G. However, for time dependent parameters, e.g. for a dependence on a non-static, dynamic temperature, it appears to be not advantageous to use the analytical results for L and D and work instead with all three equations for L, G, and D. It is interesting to see what type of equations result for the total bacterial population $n = L + G + D$:

$$\dot{G} = \lambda L + \alpha G \left(1 - \frac{n}{N_t}\right) \tag{26.}$$

$$\dot{n} = -\beta D + \alpha G \left(1 - \frac{n}{N_t}\right). \tag{27.}$$

with the initial conditions $G(0) = 0$ and $n(0) = n_0$. These equations have a clear interpretation, are derived from simple principles, and are different from the popular Barayni-Roberts and modified-Gompertz models. A notable difference is that the growth rate α is time independent. For the functions L and D it holds: $\lim_{t\to\infty} L(t) = \lim_{t\to\infty} D(t) = 0$. It follows immediately that $\lim_{t\to\infty} G(t) = N_t$. The equation exhibit a lag phase and an initial drop due to cell death. To find a substantial initial drop one needs $\beta\mu \gg \alpha\lambda$. The lag time t_L can be approximated by the time at which half of the initial population is in the growth phase, i.e., $n_0 = 2G(t_L)$. Assuming $L \ll N_t$ we can ignore the non-linear term in the equation for G, which gives rise to:

$$1 = 2\int_0^{t_L} \lambda L(t) e^{\alpha(t_L - t)} dt \tag{28.}$$

$$1 = 2\lambda e^{\alpha t_L} \frac{1 - e^{-(\mu+\lambda+\alpha)t_L}}{\mu + \lambda + \alpha}. \tag{29.}$$

For $\alpha > \mu + \lambda$ t_L can be approximated by:

$$t_L \approx -\frac{1}{\alpha} \ln\left(\frac{2\lambda}{\mu + \lambda + \alpha}\right). \tag{30.}$$

The lag time t_L diverges very slowly, logarithmically with $\lambda \to 0$.

2.2. Back-flow from G to L

We explore now the idea that under certain conditions, as sudden change in the environment, part of the population G will enter a lag-phase, i.e., there is a back-flow from G to L.

$$L \xrightarrow{\lambda} G \tag{31.}$$

$$L \xrightarrow{\mu} D \tag{32.}$$

$$G \xrightarrow{\alpha} 2G \tag{33.}$$

$$G \xrightarrow{\gamma(t)} L \tag{34.}$$

$$D \xrightarrow{\beta} \emptyset \tag{35.}$$

The rate $\gamma(t)$ depends on the rate of change of the environment. Stronger and quicker changes will lead to a higher rate γ. Let the change in the environment be in temperature T (**Figure 3**).

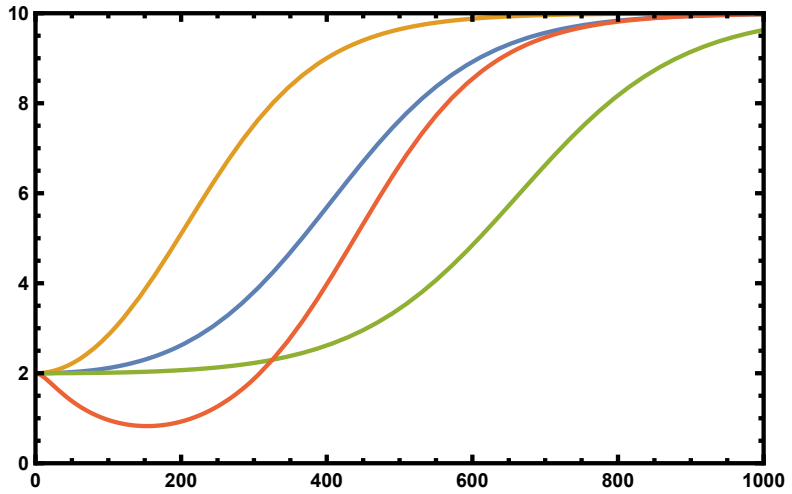

Figure 2

The dynamics of the sum of $n = L + G + D$, the size of the bacteria population. Short lag times, $\lambda = 10^{-2}$, orange curve. Intermediate lag time, $\lambda = 10^{-3}$, blue curve. Long lag time, $\lambda = 10^{-4}$, green curve. For all three curves $\mu = 0$ (no dying bacteria). Significant dip for intermediate lag time and dying bacteria, $\lambda = 10^{-3}$, $\mu = 10^{-2}$. The other parameters are the same for all curves and read: $\alpha = 1.1 \times 10^{-2}$, $\beta = 10^{-1}$, $n_0 = 2$, $N_t = 10$.

2.3. Maxwell type of stress - strain relation

We propose a kind of visco-elastic Maxwell type of stress-strain relation and write down the ordinary differential equation for γ to be:

$$\dot{\gamma} = \Gamma \left| \dot{T} \right| - \delta\gamma. \tag{36.}$$

We assumed that the direction of the temperature change does not matter, i.e., a change from $T = 2$ to $T = 12$ has the same effect as a change from $T = 14$ to $T = 4$. Γ is a scaling factor and δ is the relaxation time for the temperature disturbance. Integration of this equation yields (with $\gamma(0) = 0$):

$$\gamma(t) = \Gamma \int_0^t \left| \dot{T}(t') \right| e^{-\delta(t-t')} dt'. \tag{37.}$$

After some manipulation of this equation we find:

$$\gamma(t) = \Gamma\delta \left| \left[T[t] - T[0]e^{-\delta t} - \delta \int_0^t T(t') e^{-\delta(t-t')} dt' \right] \right|. \tag{38.}$$

This representation of the rate $\gamma(t)$ has the advantage that it only involves $T(t)$ and does not require the calculation of the derivative of T. If T exhibits n temperature jumps, one finds:

$$\gamma(t) = \Gamma \sum_{i=1}^{n} |\Delta T_i| \, \theta(t - t_i) e^{-\delta(t-t_i)}. \tag{39.}$$

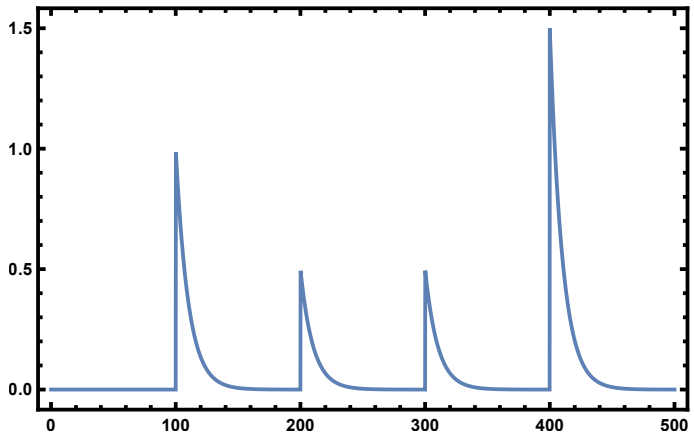

Figure 3

The back-flow rate γ, by which the growing bacterial population G goes back to the lag-phase population L. Shown is the rate γ for four temperature jumps at $t = 100, 200, 300, 400$ with the temperature difference $\Delta T = 10, 5, 5, 15$. The parameters are $\Gamma = 1$, $\delta = 0.1$.

The ordinary differential equations for the pool model with environmental-shock based back-flow read:

$$\dot{L} = \gamma(t)G - (\mu + \lambda)L \tag{40.}$$

$$\dot{G} = \lambda L - \gamma(t)G + \alpha G\left(1 - \frac{L + G + D}{N_t}\right) \tag{41.}$$

$$\dot{D} = \mu L - \beta D \tag{42.}$$

This model has already seven parameters. The solution for one temperature jump of $\Delta T = 10$ at $t = 400$ is given in **Figure 4**.

3. Extending the Three Pool Model

In the previous sections the saturation of the growth pool G was achieved by using the logistic growth function. To base the TPM on elementary elements, we include several additional element.

3.1. Resource dependence

We aim to include a resource pool which is used by the growing bacteria. Once the pool is depleted the growth of the bacteria stops. The simplest way to include this is:

$$\dot{G} = \alpha_0 RG \tag{43.}$$

$$\dot{R} = -\alpha_0 RG \tag{44.}$$

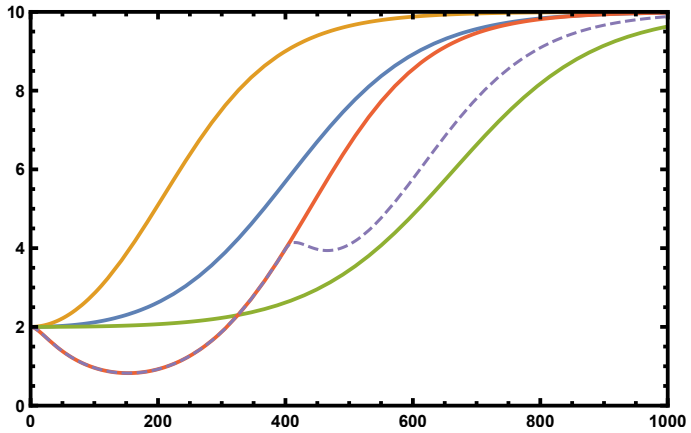

Figure 4

The dynamics of the sum of $n = L + G + D$, the size of the bacteria population. The curves are the same as in Figure 2, besides the dashed line. Short lag times, $\lambda = 10^{-2}$, orange curve. Intermediate lag time, $\lambda = 10^{-3}$, blue curve. Long lag time, $\lambda = 10^{-4}$, green curve. For all three curves $\mu = 0$ (no dying bacteria). Significant dip for intermediate lag time and dying bacteria, $\lambda = 10^{-3}$, $\mu = 10^{-2}$. Temperature shock, $\Delta T = 10$, for intermediate lag time and dying bacteria, $\lambda = 10^{-3}$, $\mu = 10^{-2}$, $\delta = 0.1$, dashed curve. The other parameters are the same for all curves and read: $\alpha = 1.1 \times 10^{-2}$, $\beta = 10^{-1}$, $n_0 = 2$, $N_t = 10$.

Exploiting $R + G =$const$= C$ we find:

$$\dot{G} = \alpha_0 (C - G) G \tag{45.}$$

$$\Leftrightarrow \dot{G} = \alpha_0 C \left(1 - \frac{G}{C}\right) G \tag{46.}$$

Writing $\alpha := \alpha_0 C$ and $C = N_t$ this is of course the logistic growth equation. We insert this now into the simplest version of the TPM. To this end we assume that the bacteria only leave the lag-phase if there are nutrients, i.e., resources. Otherwise they stay in the lag-phase:

$$\dot{L} = -\lambda R L \tag{47.}$$

$$\dot{G} = \lambda R L + \alpha R G \tag{48.}$$

$$\dot{R} = -\frac{\alpha}{N_t} R G \tag{49.}$$

We rescaled R by N_t, such that it is dimensionless. One note about R: the pools L and G represent number of bacteria (or number of bacteria per unit area/volume) while R represents an abstract resource pool. Let say $G = N_B/V$ and $[G] = 1/V$, where N_B is number of bacteria and V is the volume. Then $R = N_R/V$ and $[R] = 1/V$, where N_R is the number of resource molecules (or any appropriate unit, e.g., mol). Then $[\alpha_0] = V/s$, $[N_t] = 1/V$, and $[\alpha] = 1/s$. For homogeneous densities it is equivalent to consider the total amount, i.e., multiplying L and G by the volume. In this case $[L] = [G] = [N_t] = 1$.

Turning back to the equations above we can state: $L + G + N_t R = N_t$. For $t = 0$ we have $n_0 + N_t R_0 = N_t$ (given $L_0 = n_0$ and $G_0 = 0$) and from this: $N_t R_0 = N_t - n_0$. Using

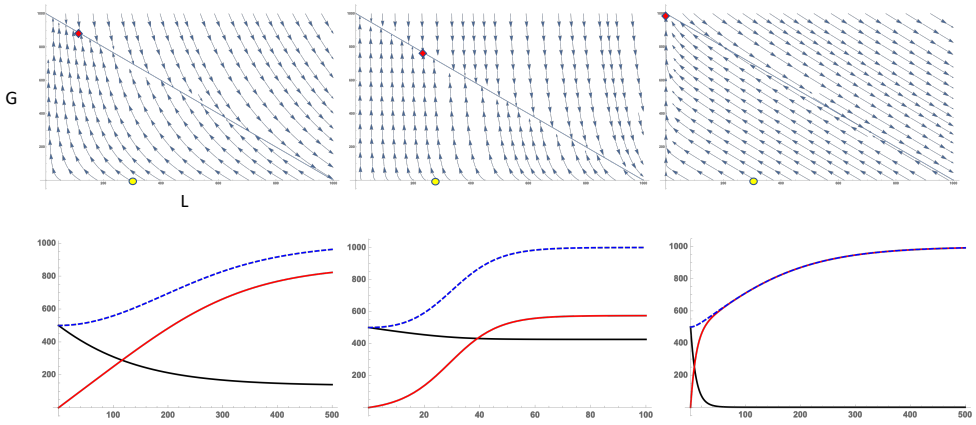

Figure 5

Upper panel: Phase portraits of the dynamics of the TPM with resource limitation. Abscissa: L and ordinate: G. Yellow circles indicate the initial condition, red Left: case $\lambda \approx \alpha$, $\lambda = 0.01$, $\alpha = 0.01$. Middle: case $\lambda \ll \alpha$, $\lambda = 0.01$, $\alpha = 0.2$. Right: case $\lambda \gg \alpha$, $\lambda = 0.2$, $\alpha = 0.01$. For all cases $G(t = 0) = 0$, $L(t = 0) = 500$, $N_t = 1000$. Lower panel: Dynamic of the pools L (black solid line), G (red solid line), and $T = G + L$ (blue dashed line).

this we eliminate R and arrive at:

$$\dot{L} = -\lambda \left(1 - \frac{L+G}{N_t}\right) L \tag{50.}$$

$$\dot{G} = \lambda \left(1 - \frac{L+G}{N_t}\right) L + \alpha \left(1 - \frac{L+G}{N_t}\right) G \tag{51.}$$

The steady state is $L_s + G_s = N_t$. However, it depends on the initial conditions and the parameters what L_s and G_s are. There is no way to determine L_s and G_s besides solving the dynamical equations, i.e., the steady state cannot be determined directly by solving a set of algebraic equations. To see this we determine the nullclines: the first nullcline is $G = N_t - L$ and the second is $G = N_t - L$, i.e., the nullclines coincides. Every point on the line $G = N_t - L$ is a fixed point. This can be seen in Fig. 5.

For $\lambda \ll \alpha$ the lag-pool is not emptied before all resources are consumed. As a consequence the lag-pool is non-zero in steady-state. In contrast, for $\lambda \gg \alpha$ the lag-pool is depleted before the resources are consumed, i.e., the lag-pool is zero in steady state.

3.2. Back-flow from the growth- to the lag-pool

The pool G represents the bacteria being in the metabolizing state. Once the resources are depleted the bacteria go back to the rest or lag-phase (needs to be checked). This can be modelled by:

$$\dot{L} = -\lambda_f RL + \mathcal{B}(R)G \tag{52.}$$

$$\dot{G} = \lambda_f RL + \alpha RG - \mathcal{B}(R)G \tag{53.}$$

$$\dot{R} = -\frac{\alpha}{N_t} RG \tag{54.}$$

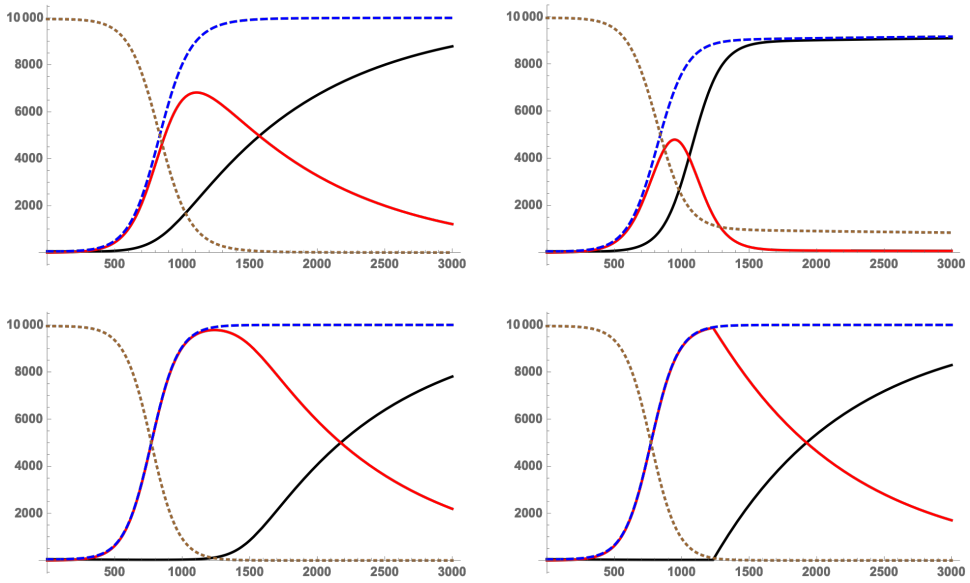

Figure 6

The dynamics of L (black solid line), G (red solid line), and $T = L + G$ (blue dashed line) for different back-flow models. The brown dashed line denotes the resource pool. Upper left: $\mathcal{B}_1$, Upper right: $\mathcal{B}_2$ with $n = 1$. Lower Left: $\mathcal{B}_3$ with $K = 10^{-3}$, $n = 1$. Lower right: $\mathcal{B}_4$ with $K = 10^{-3}$. In all cases: $\lambda_b = 10^{-3}$, $\lambda_f = 10^{-3}$, $\alpha = 10^{-2}$, $L(0) = 50$, $G(0) = 0$, $N_t = 10^4$.

The function $\mathcal{B}$ captures how the bacteria go back to the lag-phase when resources are limited. Some simple choices:

$$\mathcal{B}_1 = \lambda_b \tag{55.}$$

$$\mathcal{B}_2 = \frac{\lambda_b}{R^n} \tag{56.}$$

$$\mathcal{B}_3 = \frac{\lambda_b K^n}{K^n + R^n} \tag{57.}$$

$$\mathcal{B}_4 = \lambda_b \theta (K - R) \tag{58.}$$

Note that $\mathcal{B}_1$, $\mathcal{B}_2$,and $\mathcal{B}_4$ are limiting case of $\mathcal{B}_3$:

$$\mathcal{B}_1 = \lim_{K \to \infty} \mathcal{B}_3 \tag{59.}$$

$$\mathcal{B}_2 = \lim_{\substack{K \to 0 \\ \lambda_b K^n = \text{const}}} \mathcal{B}_3 \tag{60.}$$

$$\mathcal{B}_4 = \lim_{n \to \infty} \mathcal{B}_3 \tag{61.}$$

The parameter λ_b controls how quickly the bacteria go from the G to the L pool.

3.3. Waste production

The bacteria consume R and produce W. It is the accumulation of the bacteria waste which is responsible for the spoilage of food products. In order to take this into account we add an equation for the waste production:

$$\dot{L} = -\lambda_f RL + \mathcal{B}(R)G \quad 62.$$
$$\dot{G} = \lambda_f RL + \alpha RG - \mathcal{B}(R)G \quad 63.$$
$$\dot{R} = -\frac{\alpha}{N_t} RG \quad 64.$$
$$\dot{W} = \mathcal{F}(R, G). \quad 65.$$

The function $\mathcal{F}$ denotes the model for the waste production rate. We shall discuss two possible models:

$$\mathcal{F}_1(R, G) = \kappa\alpha RG = -\kappa N_t \dot{R} \quad 66.$$
$$\mathcal{F}_2(R, G) = \kappa G \quad 67.$$

Model $\mathcal{F}_1$ results in waste accumulation in steady state $W_1^s = \lim_{t\to\infty} W_1(t) = \kappa(N_t - n_0)$. To see this we note $\dot{W}_1 = \kappa(\dot{L} + \dot{G})$, which yields: $W_1(t) = \kappa(L(t) + G(t) - n_0)$ where we used $W_1(0) = G(0) = 0$, $L(0) = n_0$. This model assumes that waste is only produced when the bacteria grow and divide.

Model $\mathcal{F}_2$ results in $W_2(t) = \kappa \int_{t_0}^{t} G(t')dt'$. As long as $G > 0$ waste is produced, no matter whether the amount of bacteria is still growing. The amount of waste depends therefore on the back-flow model employed, which can be seen in Fig. 7.

4. The TPM as a generalised Lotka-Volterra model (gLV)

The TPM can be readily extended to more than one bacteria. Hereby is the interesting case that the bacteria interact via:

- Competition for common nutrients
- Influence by production of specific substances:
  - Mutual activation
  - Mutual inhibition

In general, a combination of these options will be the case. We will, however, focus on the discussion of the separate instances.

4.1. Competition for common nutrients

We consider for simplicity only one common resource pool. This stands either for one specific nutrient pool or subsumes all relevant nutrients. The simplest pool model for bacterial species A and B encompassing lag-phases, growth-phases and a common resource pool is given by (no back-flow to the lag-pool):

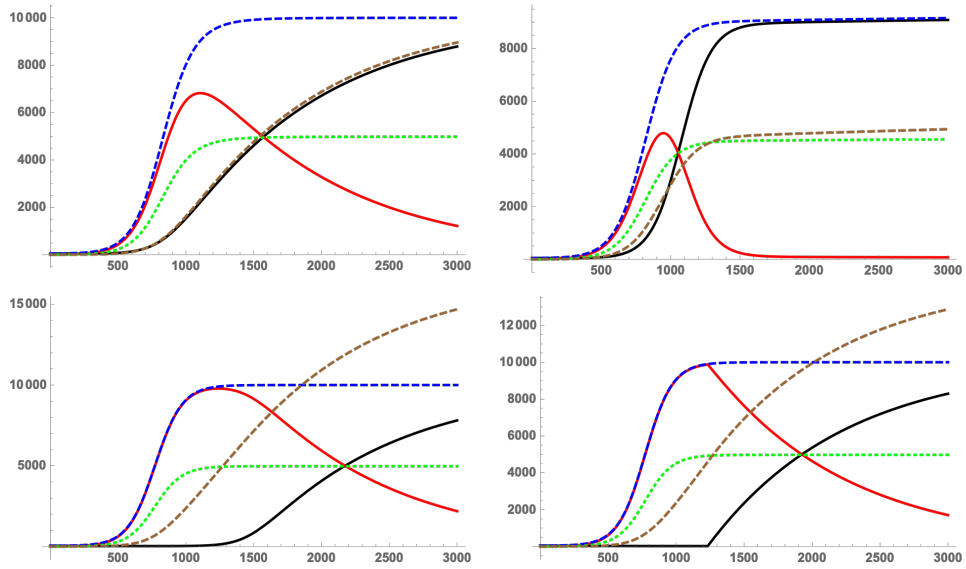

Figure 7

The dynamics of W_1 (green dotted line) and W_2 (brown dashed line). The other curves show L, G, and $T = L + G$ for different back-flow models as described in Fig. 6. $\kappa = 0.5$ for W_1 and $\kappa = 10^{-3}$ for W_2.

$$\dot{L}_A = -\lambda_A R L_A \tag{68.}$$

$$\dot{L}_B = -\lambda_B R L_B \tag{69.}$$

$$\dot{G}_A = \lambda_A R L_A + \alpha_A R G_A \tag{70.}$$

$$\dot{G}_B = \lambda_B R L_B + \alpha_B R G_B \tag{71.}$$

$$\dot{R} = -\frac{\alpha_A}{N_t} R G_A - \frac{\alpha_B}{N_t} R G_B \tag{72.}$$

We again rescaled the resource pool with N_t and find

$$R = 1 - \frac{L_A + G_A + L_B + G_B}{N_t} \tag{73.}$$

$$R_0 = 1 - \frac{n_A + n_B}{N_t}. \tag{74.}$$

Inserting Eq. 73 into Eqs. 68 - 71 yields:

$$\dot{L}_A = -\lambda_A L_A + \frac{\lambda_A}{N_t} \left(L_A + G_A + L_B + G_B\right) L_A$$

$$\dot{L}_B = -\lambda_B L_B + \frac{\lambda_B}{N_t} \left(L_A + G_A + L_B + G_B\right) L_B$$

$$\dot{G}_A = \lambda_A L_A - \frac{\lambda_A}{N_t} \left(L_A + G_A + L_B + G_B\right) L_A + \alpha_A G_A - \frac{\alpha_A}{N_t} \left(L_A + G_A + L_B + G_B\right) G_A$$

$$\dot{G}_B = \lambda_B L_B - \frac{\lambda_B}{N_t} \left(L_A + G_A + L_B + G_B\right) L_B + \alpha_B G_B - \frac{\alpha_B}{N_t} \left(L_A + G_A + L_B + G_B\right) G_B$$

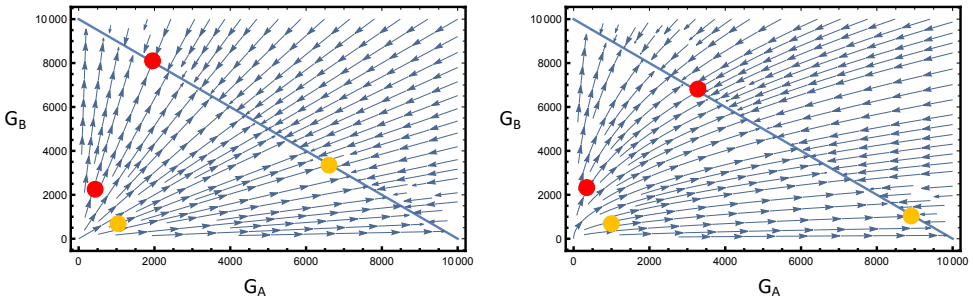

Figure 8

Phase portraits of the competition model given by Eqs. 75. Left: Equivalent species. The initial abundance decides about the steady state abundance. $\alpha_A = \alpha_B = 0.01$. Right: The growth rate of species A exceeds growth rate of species B, $\alpha_A = 0.01$, $\alpha_B = 0.005$. $N_t = 10^4$ in both cases.

which has the structure of a generalised Lotka-Volterra system. In order to better see this, we set $L_A = L_B = 0$:

$$\dot{G}_A = \alpha_A G_A \left(1 - \frac{G_A}{N_t}\right) - \frac{\alpha_A}{N_t} G_A G_B \tag{75.}$$

$$\dot{G}_B = \alpha_B G_B \left(1 - \frac{G_B}{N_t}\right) - \frac{\alpha_B}{N_t} G_A G_B. \tag{76.}$$

For $N_t \gg \alpha_{A/B}$ the equations decouple. The null-clines of the system given by Eqs. 68 - 71 coincide and are given by $N_t = L_A + G_A + L_B + G_B$. If $\lambda_{A/B} > \alpha_{A/B}$ the lag-pools are completely depleted before the depletion of the resource pool stops the dynamics. To simplify the investigation of the systems dynamics we therefore ignore the L_A and L_B dimension and only consider the dynamics on the centre-manifold given by the $G_A \times G_B$ plane. The corresponding phase-plot is shown in Fig. 9. The advantage in using the pool model in contrast to using Lotka-Volterra directly is that all parameters have a clear meaning and consistent parameter relations arrive naturally. And a species can have more than one internal state. However, it is instructive to rewrite the system by setting $x_1 \equiv G_A$, $x_2 \equiv G_B$, and $\mathbf{x} = (x_1, x_2)^T$:

$$\dot{\mathbf{x}} = A\mathbf{x} + \frac{1}{2}\mathbf{x}B\mathbf{x} \tag{77.}$$

$$A = \begin{bmatrix} \alpha_A & 0 \\ 0 & \alpha_B \end{bmatrix} \tag{78.}$$

$$B = \frac{-2}{N_t} \begin{bmatrix} \alpha_A & \alpha_A \\ \alpha_B & \alpha_B \end{bmatrix} \tag{79.}$$

The pool model, in contrast to the classical Lotka-Volterra approach, allows for far more flexibility. Non-linear functional responses can be introduced without any problem (see how section 4 for an extended discussion).

4.2. Mutual inhibition

The simplest way to introduce inhibition of species A by species B is via a growth rate of species A depending on the abundance of species B. For sake of simplicity we ignore the lag pool and write for a mutual inhibition:

$$\dot{G}_A = \mathcal{B}_A(G_B) G_A \left(1 - \frac{G_A + G_B}{N_t}\right) \tag{80.}$$

$$\dot{G}_B = \mathcal{B}_B(G_A) G_B \left(1 - \frac{G_A + G_B}{N_t}\right). \tag{81.}$$

The function $\mathcal{B}_{A/B}$ captures the inhibiting effects in an effective way. It is straight forward to make the mechanism of inhibition more explicit by, e.g., introducing a waste pool. One possible choice for $\mathcal{B}$ is:

$$\mathcal{B}(G) = \frac{\alpha}{1 + KG}. \tag{82.}$$

This corresponds to the case $W \sim G$, where W is the waste (or whatever one chooses to call it) of species A affecting species B. If the waste accumulates one needs to replace G by $\int G dt$. Keeping it simple yields:

$$\dot{G}_A = \frac{\alpha_A G_A}{1 + K_B G_B} \left(1 - \frac{G_A + G_B}{N_t}\right) \tag{83.}$$

$$\dot{G}_B = \frac{\alpha_B G_B}{1 + K_A G_A} \left(1 - \frac{G_A + G_B}{N_t}\right). \tag{84.}$$

One can distinguish two limiting cases: *i*) $K_{A/B} \ll N_t$ and *ii*) $K_{A/B} \gg N_t$. In the first case the inhibition is of minor importance and could be ignored. In the latter case one can simplify the equations, given n_A and n_B are non-zero:

$$\dot{G}_A = \tilde{\alpha}_A \frac{G_A}{G_B} (1 - G_A - G_B) \tag{85.}$$

$$\dot{G}_B = \tilde{\alpha}_B \frac{G_B}{G_A} (1 - G_A - G_B). \tag{86.}$$

We introduced the rescaled growth rates $\tilde{\alpha}_A = \alpha_A/(N_t K_B)$ and $\tilde{\alpha}_B = \alpha_B/(N_t K_A)$. Note that $[\tilde{\alpha}] = \mathrm{s}^{-1}$. Rescaling time with $\tilde{\alpha}_A$ and defining the dimensionless parameter

$$\psi = \tilde{\alpha}_B/\tilde{\alpha}_A \tag{87.}$$

$$\psi = \frac{K_B \alpha_B}{K_A \alpha_A} \tag{88.}$$

results in:

$$\dot{G}_A = \frac{G_A}{G_B} (1 - G_A - G_B) \tag{89.}$$

$$\dot{G}_B = \psi \frac{G_B}{G_A} (1 - G_A - G_B). \tag{90.}$$

We can separate three cases:

$$\psi > 1: \quad \text{Species B growth faster and/or inhibits A stronger} \tag{91.}$$

$$\psi = 1: \quad \text{A and B are equivalent} \tag{92.}$$

$$\psi < 1: \quad \text{Species A growth faster and/or inhibits B stronger} \tag{93.}$$

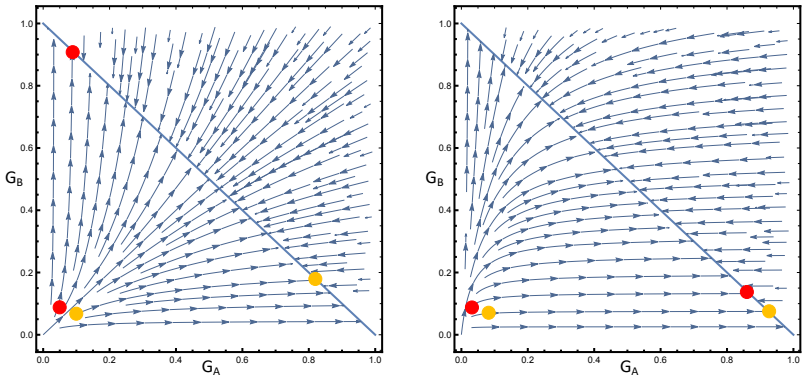

Figure 9

Simplified mutual inhibition model given by Eqs. 85. Left: Both species are equivalent, $\psi = 1$. Right: Species A exceeds (growth faster and/or suppresses stronger) species B, $\psi = 10$.

4.3. Mutual activation/Mutuality

In case of mutual activation each of the two species benefit from the presence of the other. For sake of clarity we omit again the lag pool and write:

$$\dot{G}_A = \mathcal{B}_A(W_B, R)G_A \tag{94.}$$
$$\dot{G}_B = \mathcal{B}_B(W_A, R)G_B \tag{95.}$$
$$\dot{R} = -\mathcal{B}_A(W_B, R)G_A - \mathcal{B}_B(W_A, R)G_B \tag{96.}$$
$$\dot{W}_A = \mathcal{F}_A(R, G_A) \tag{97.}$$
$$\dot{W}_B = \mathcal{F}_B(R, G_B). \tag{98.}$$

W_A and W_B denote the substance produced by species A and B, respectively. The functions $\mathcal{B}_A(W_B, R)$ and $\mathcal{B}_B(W_A, R)$ capture the resource dependent growth. Setting $\mathcal{B}_A(W_B, R) = \alpha_A W_B R$, $\mathcal{B}_B(W_A, R) = \alpha_B W_A R$, $\mathcal{F}_A(R, G_A) = \kappa_A R G_A$, $\mathcal{F}_B(R, G_B) = \kappa_B R G_B$, rescaling G_A, G_B, and W_B with N_t, W_A with κ_A/α_A, time with $\alpha_A N_t^2$, defining $\phi = \kappa_A \alpha_B/(\alpha_A^2 N_t)$, and $\psi = \kappa_B/(\alpha_A N_t)$ results in:

$$\dot{G}_A = W_B G_A \left(1 - G_A - G_B\right) \tag{99.}$$
$$\dot{G}_B = \phi W_A G_B \left(1 - G_A - G_B\right) \tag{100.}$$
$$\dot{W}_A = G_A \left(1 - G_A - G_B\right) \tag{101.}$$
$$\dot{W}_B = \psi G_B \left(1 - G_A - G_B\right). \tag{102.}$$

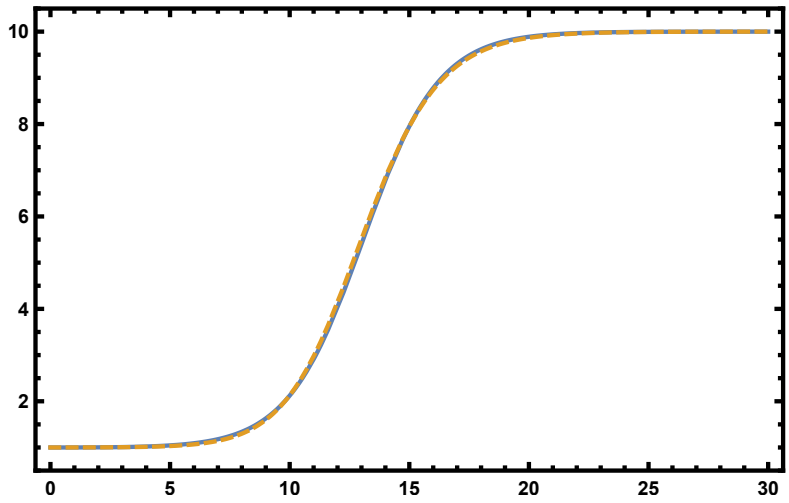

Figure 10

Comparison of the Barayni-Roberts model (dashed line) and the Three-Pool model (solid line). The parameters are $\alpha = 0.7$, $\lambda = 1.5^{-3}$, $\mu = 0$, $\beta = 0$, $N_t = 10$ for the Three-Pool Model and $\alpha = 0.588$, $\rho = 10^{-3}$, $\nu = 0.77$, $N_t = 10$ for the Barayni-Roberts model.

5. Examples of application of TPM

5.1. Comparison to the Barayni-Roberts Model

The equation for the Barayni-Roberts model is given by:

$$\dot{n} = \alpha(t) n \left(1 - \frac{n}{N_t}\right) \tag{103.}$$

$$\alpha(t) = \alpha_m \frac{\rho e^{\nu t}}{1 + \rho e^{\nu t}}. \tag{104.}$$

The initial and maximal are $\alpha(0) = \alpha_m \rho$ and $\lim_{t\to\infty} \alpha(t) = \alpha_m$. The parameters ρ and ν modulate the lag-phase. ρ should be sufficiently smaller than α_m to result in very small initial growth. However, the parameters ρ and ν lack a clear meaning. To compare this with the three-pool model one has to set $\mu = 0$, i.e., no dying bacteria ($D \equiv 0$). Because the total bacteria population n is $n = G + L$ we can write $G = n - L$ and with this we find:

$$\dot{n} = \alpha G \left(1 - \frac{n}{N_t}\right) \tag{105.}$$

$$\dot{n} = \alpha (n - L) \left(1 - \frac{n}{N_t}\right) \tag{106.}$$

$$\dot{n} = \alpha \left(n - e^{-\lambda t}\right) \left(1 - \frac{n}{N_t}\right). \tag{107.}$$

Notably, the pool model has a different structure and has one parameter less. All parameters can be given a clear meaning. Although the structure is different both models can produce the same results and in this sense they are equivalent as can be seen in Figure 10.

To compare the TPM with the Barayni-Roberts and modified Gompertz model, in practice, we have used a real, time-domain data from VION producer including minute steak of loin product. The data consists of temperature in degree of centigrade, time in hours, mean and standard deviation of the cell density of microorganisms in log10 [CFU/g] for total viable count (TVC). In **Figure 11**, it is observed that the fitted primary model for three models are the same. In fact, they can provide the same results and they are equivalent.

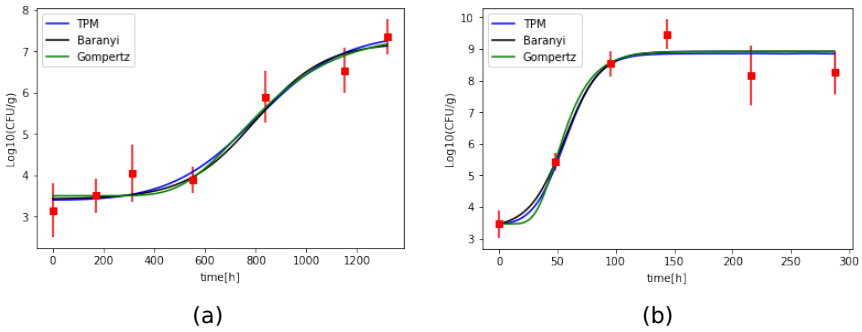

Figure 11

Comparison of the TPM with the Barayni-Roberts and modified Gompertz model for TVC in Pork loin (a) Temperature = 2 °C,(b) Temperature = 15 °C .

5.2. Comparison to the gLV

While the gLV model has a range of applications in studying microbial communities, it also has a number of limitations.

1. The gLV can only describe pair-wise interactions, for example, when a cross-feeding relationship between two species is weakened by the production of the exchanged metabolite by a third species, the gLV is no longer able to be extended in more than two species scenario.
2. The environmental effects such as variable temperature or spatial structure are not considered.
3. There are some assumptions such as homogeneous populations, constant interaction

strength.

4. The interactions are assumed to be bilinear which means the growth rate of a species will change proportionally to the abundance of its interaction species. But the scenario in the real world is different. For example, when the concentration of a substrate produced by a species is high, the enzyme activity rather than the substrate concentration limits the rates of biochemical reactions.

5.3. Capturing the intermediate lag phases of microbial behavior in non-isothermal conditions

The rapid environmental changes can cause intermediate lag phases. Large temperature variations, as an example, applied during the microbial growth phase can lead to an intermediate lag phase known as a transient adaptation of the growth rate (Huang 2003). However, the obtained mechanistic knowledge can only build a basis for population-based models. At present, there is no dynamic model to describe an intermediate lag phase. Incorporating the complex microbial adaptation mechanisms into the predictive models is a challenge to be overcome.

SUMMARY POINTS

1. The TPM proposed a unified mathematical modelling framework in food microbiology.
2. The advantagrs of TPM include description of the kinetics with general applicability, low number of parameters to be less complex, and preferably to explain the mechanism of the phenomenon of interest.

DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

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