

Analysis and Control of a Listeriosis Transmission Dynamic Model

Abstract:

Human listeriosis has a high mortality rate and poses a significant health risk. Therefore, it is crucial to develop strategies to combat this disease. Humans are primarily infected with listeriosis through the consumption of *Listeria*-contaminated foods. Implementing effective control strategies is essential to eradicate the disease. Several factors must be considered, and multiple objectives must be achieved simultaneously. Bifurcation analysis and multi-objective nonlinear model predictive control (MNL MPC) calculations are performed on a dynamic model involving listeriosis transmission. The MATLAB program MATCONT was used to perform the bifurcation analysis. The MNL MPC calculations were carried out using the optimization language PYOMO in conjunction with the advanced global optimization solvers IPOPT and BARON. The bifurcation analysis revealed the existence of a branch point in the system. This branch point (which causes multiple steady-state solutions from a single point) is beneficial because it enables the multi-objective nonlinear model predictive control calculations to converge to the Utopia point which is the best possible solution. It has been demonstrated (with computational validation) that the branch point results from the presence of two distinct separable functions in one of the equations of the dynamic model. A theorem was developed to prove this fact for any dynamic model.

Key Words: bifurcation; optimization; control; listeriosis

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Introduction:

Van den Driessche et al, (2002) [1] researched reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. Swaminathan et al (2007) [2] discussed the epidemiology of human listeriosis. Bennion et al (2008) [3] discussed strategies to decrease listeriosis mortality in the United-States. Lanzas, et al (2011) [4] developed mathematical models regarding the transmission and control of foodborne pathogens and antimicrobial resistance at preharvest. Hu et al (2016) [5] developed a modeling framework to accelerate food-borne outbreak investigations. Omondi et al (2018) [6] performed optimal control calculations for the onchocerciasis transmission model with treatment.

Osman et al (2018) [7] researched the stability analysis and modelling of Listeriosis dynamics in human and animal populations. Stout et al (2020) [8] discussed the public health impact of foodborne exposure to naturally occurring virulence-attenuated *Listeria monocytogenes*. Osman et al (2020) [9] analyzed the listeriosis transmission dynamics with optimal control. Witbooi et al (2020) [10] developed a population

model for the 2017/18 Listeriosis outbreak in South Africa. Chukwu et al (2020) [11] developed a theoretical model of listeriosis driven by cross-contamination of ready-to-eat food products. Chukwu et al (2023) [12] developed a mathematical model and performed optimal control for Listeriosis disease from ready-to-eat food products.

This work aims to perform bifurcation analysis and multiobjective nonlinear control (MNLMP) studies in two models involving the listeriosis transmission dynamics Chukwu et al, (2023) [12]. The paper is organized as follows. First, the model equations are presented, followed by a discussion of the numerical techniques involving bifurcation analysis and multi objective nonlinear model predictive control (MNLMP). The results are then presented, followed by the discussion and conclusions.

Listeriosis Model (Chukwu et al, 2023) [12]

The mathematical model comprises of sv (the scaled value of susceptible population); iv (the scaled value of infected population); lm (the scaled value of the *L. Monocytogenes*); fu (the scaled value of uncontaminated food products) and fc (the scaled value of contaminated food products) u_1 , u_2 and u_3 are the control variables. The ODE model equations are

$$\begin{aligned}\frac{d(sv)}{dt} &= \mu_h + \rho_h(1 - sv - iv) - \mu_h sv - \Lambda_h(1 - u_1) * sv \\ \frac{d(iv)}{dt} &= \Lambda_h(1 - u_1)sv - \mu_h * iv - \alpha(u_2)iv \\ \frac{d(lm)}{dt} &= rl(lm(1 - lm)) \\ \frac{d(fu)}{dt} &= \mu_f - (\Lambda_f + \mu_f)fu \\ \frac{d(fc)}{dt} &= \Lambda_f fu - (\mu_f + u_3)fc \\ \Lambda_h &= \omega_1 fc + \omega_2 lm \\ \Lambda_f &= \omega_2 lm + \omega_3 fc\end{aligned}\tag{1}$$

The base parameter values are

$$\begin{aligned}\mu_h &= 0.1; \alpha = 0.0094; \rho_h = 0.09; rl = 0.02; \omega_1 = 0.038; \omega_2 = 0.002; \omega_3 = 0.0005; \mu_f = 0.0076; \\ u_1 &= 0.5; u_2 = 0.5; u_3 = 0.5;\end{aligned}$$

Bifurcation analysis

Bifurcation analysis involves multiple steady states and limit cycles. Multiple steady states occur because of the existence of branch and limit points. Hopf bifurcation points cause limit cycles. The MATLAB software MATCONT, which is used to perform the bifurcation calculations in this work, locates limit points, branch points, and Hopf bifurcation points (Dhooge Govearts, and Kuznetsov, 2003[13]; Dhooge Govearts, Kuznetsov, Mestrom and Riet, 2004[14], Kuznetsov (1998[15]; 2009[16]) and Govaerts [2000] [17]) . This program detects Limit points(LP), branch points(BP), and Hopf bifurcation points(H) for an ODE system

$$\frac{dx}{dt} = f(x, \alpha)\tag{2}$$

$x \in R^n$ Let the bifurcation parameter be α . Since the gradient is orthogonal to the tangent vector,

The tangent plane at any point $z = [z_1, z_2, z_3, z_4, \dots, z_{n+1}]$ must satisfy

$$Az = 0\tag{3}$$

Where A is

$$A = [\partial f / \partial x \quad \partial f / \partial \alpha] \quad (4)$$

where $\partial f / \partial x$ is the Jacobian matrix. For both limit and branch points, the matrix $[\partial f / \partial x]$ must be singular. The $n+1$ th component of the tangent vector $z_{n+1} = 0$ for a limit point (LP) and at a branch point (BP), the matrix $\begin{bmatrix} A \\ z^T \end{bmatrix}$ must be singular. At a Hopf bifurcation point,

$$\det(2f_x(x, \alpha) @ I_n) = 0 \quad (5)$$

@ indicates the bialternate product while I_n is the n -square identity matrix.

Multiobjective Nonlinear Model Predictive Control (MNLMP) :

For the MNLMP calculations the procedure developed by Flores Tlacuahuaz et al (2012)[18] is used. Here $\sum_{t_i=0}^{t_i=t_f} q_j(t_i)$ ($j=1, 2..n$) represents the variables that need to be minimized/maximized simultaneously for a problem involving a set of ODE

$$\frac{dx}{dt} = F(x, u) \quad (6)$$

n is the total number of objective variables and t_f is the final time value. Let u be the control parameter vector. This MNLMP procedure

first solves the single objective optimal control problem independently optimizing each of the variables $\sum_{t_i=0}^{t_i=t_f} q_j(t_i)$ individually. The

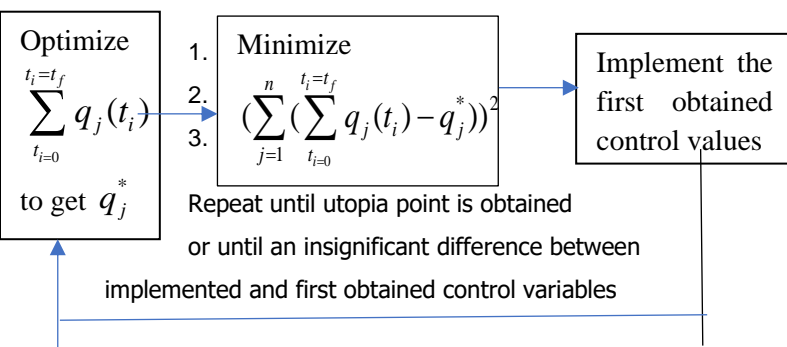
minimization/maximization of $\sum_{t_i=0}^{t_i=t_f} q_j(t_i)$ will lead to the values q_j^* . Then the optimization problem that will be solved is

$$\begin{aligned} \min & \left(\sum_{j=1}^n \left(\sum_{t_i=0}^{t_i=t_f} q_j(t_i) - q_j^* \right)^2 \right) \\ \text{subject to } & \frac{dx}{dt} = F(x, u); \end{aligned} \quad (7)$$

This will provide the values of u at various times. The first obtained control value of u is implemented and the rest are discarded. This procedure is repeated until the implemented and the first obtained control values are the same or if the Utopia point where

$\sum_{t_i=0}^{t_i=t_f} q_j(t_i) = q_j^*$ for all j is obtained. Pyomo (Hart et al, 2017)[19] is used for these calculations. Here, the differential equations are

converted to a Nonlinear Program (NLP) using the orthogonal collocation method. The NLP is solved using IPOPT (Wächter And Biegler, 2006)[20] and confirmed as a global solution with BARON (Tawarmalani, M. and N. V. Sahinidis 2005)[21]. The algorithm steps can be seen in the chart below



Sridhar (2024)[22] proved that the MNLMPC calculations to converge to the Utopia solution when the bifurcation analysis reveals the presence of limit and branch points by applying the singularity condition to the co-state equation (Upreti, 2013)[23]. If the minimization of q_1 lead to the value q_1^* and the minimization of q_2 lead to the value q_2^* . The MNLMPC calculations will minimize the function $(q_1 - q_1^*)^2 + (q_2 - q_2^*)^2$. The multiobjective optimal control (MOOC) will involve

$$\min (q_1 - q_1^*)^2 + (q_2 - q_2^*)^2 \quad \text{subject to} \quad \frac{dx}{dt} = F(x, u) \quad (8)$$

Differentiation of the objective function would yield

$$\frac{d}{dx_i} ((q_1 - q_1^*)^2 + (q_2 - q_2^*)^2) = 2(q_1 - q_1^*) \frac{d}{dx_i} (q_1 - q_1^*) + 2(q_2 - q_2^*) \frac{d}{dx_i} (q_2 - q_2^*) \quad (9)$$

The Utopia point requires both $(q_1 - q_1^*)$ and $(q_2 - q_2^*)$ are zero. Therefore,

$$\frac{d}{dx_i} ((q_1 - q_1^*)^2 + (q_2 - q_2^*)^2) = 0 \quad (10)$$

The co-state equation (Upreti, 2013)[22] is

$$\frac{d}{dt}(\lambda_i) = -\frac{d}{dx_i} ((q_1 - q_1^*)^2 + (q_2 - q_2^*)^2) - f_x \lambda_i; \quad \lambda_i(t_f) = 0 \quad (11)$$

t_f is the final time and λ_i is the Lagrangian multiplier. The first term in this equation is 0. Then

$$\frac{d}{dt}(\lambda_i) = -f_x \lambda_i; \quad \lambda_i(t_f) = 0 \quad (12)$$

At limit and branch points, for $\frac{dx}{dt} = f(x, u)$, f_x is singular. This implies that there are two different vector values for $[\lambda_i]$ where

$\frac{d}{dt}(\lambda_i) > 0$ and $\frac{d}{dt}(\lambda_i) < 0$. By continuity, there will exist a vector $[\lambda_i]$ such that $\frac{d}{dt}(\lambda_i) = 0$. With the boundary condition $\lambda_i(t_f) = 0$ the resulting solution $[\lambda_i] = 0$. This causes the optimization problem to be unconstrained optimization problem, for which the Utopia Point is a solution.

Results:

When the bifurcation analysis was performed, with r as a bifurcation parameter, two branch points (BP) were obtained at (sv, iv, lm, fu, fc, rl) values of $(1 \ 0 \ 0 \ 1 \ 0 \ 0)$ and $(0.989739 \ 0.010014 \ 1.000000 \ 0.791538 \ 0.003121 \ 0)$ (Fig. 1a).

For the MNLMPC calculations, $\sum_{t_i=0}^{t_i=t_f} iv(t_i)$, $\sum_{t_i=0}^{t_i=t_f} fc(t_i)$, $\sum_{t_i=0}^{t_i=t_f} lm(t_i)$ were minimized individually and each minimization led to a value of

0. $\sum_{t_i=0}^{t_i=t_f} fu(t_i)$ was maximized and resulted in a value of 2. The multiobjective optimal control problem will involve the minimization of

$(\sum_{t_i=0}^{t_i=t_f} fc(t_i))^2 + (\sum_{t_i=0}^{t_i=t_f} iv(t_i))^2 + (\sum_{t_i=0}^{t_i=t_f} fu(t_i) - 2)^2 + (\sum_{t_i=0}^{t_i=t_f} lm(t_i))^2$ subject to the equations of the listeriosis model. This led to a value of zero (the Utopia solution). The MNLMPC control values of u_1 , u_2 and u_3 were 0.4249; 0.487; and 0.004. Figures 1b-1h show the various MNLMPC profiles. The control profiles (u_1 u_2 u_3) exhibit noise (Fig 1g) This was remedied using the Savitzky-Golay filter (Fig. 1h).

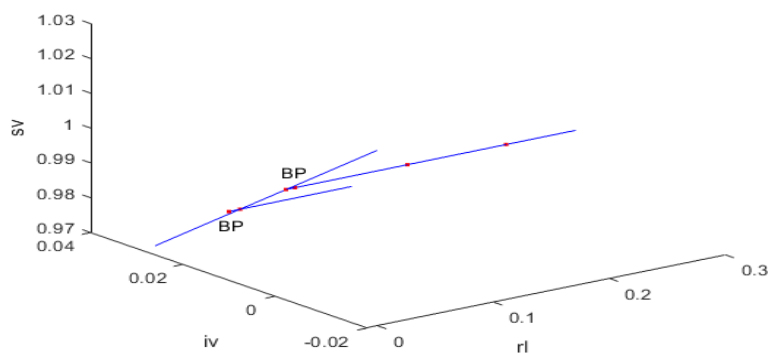


Figure 1a: Bifurcation Analysis of Listeriosis model showing branch points

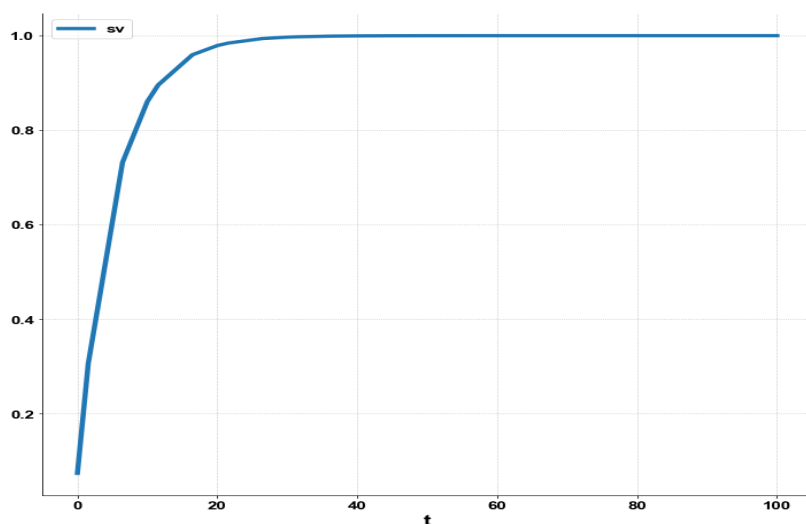


Figure 1b: MNLMPC Listeriosis model sv vs t

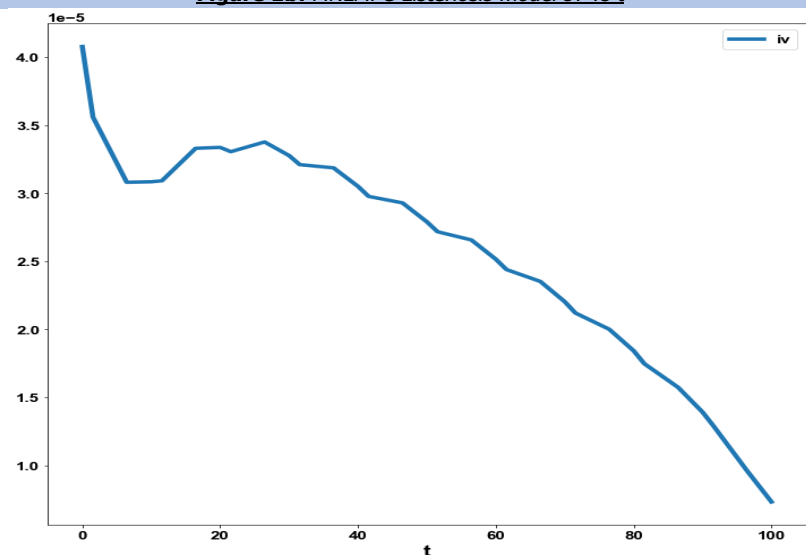


Figure 1c: MNLMPC Listeriosis model iv vs t

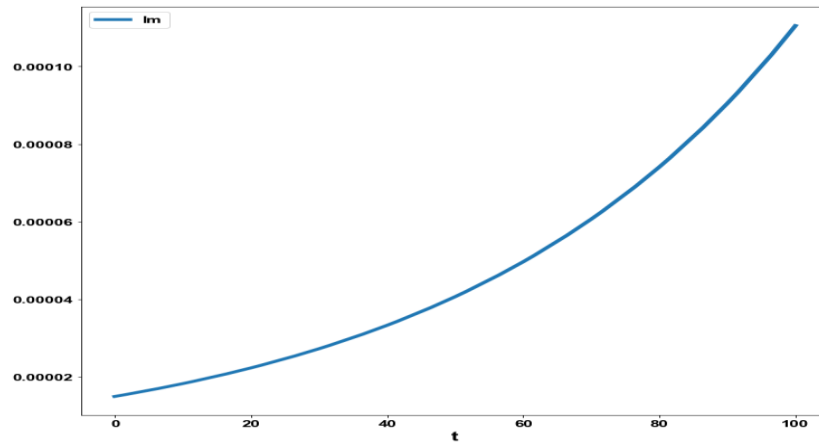


Figure 1d: *MNL MPC Listeriosis model I_m vs t*

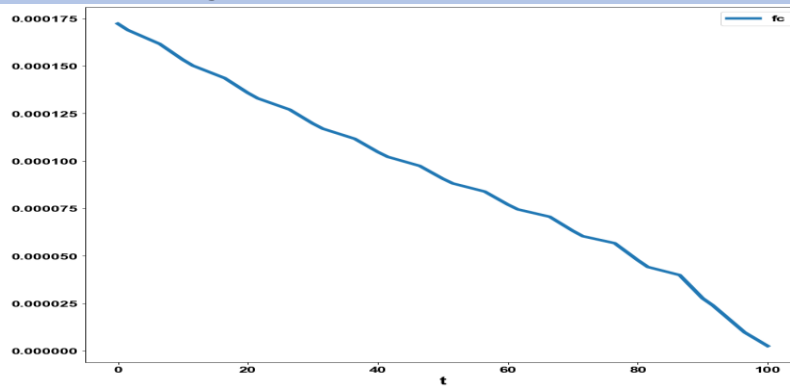


Figure 1e: *MNL MPC Listeriosis model f_c vs t*

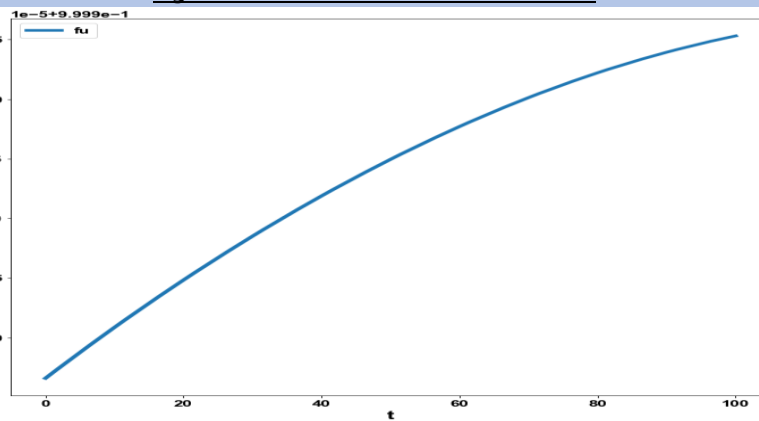


Figure 1f: *MNL MPC Listeriosis model f_u vs t*

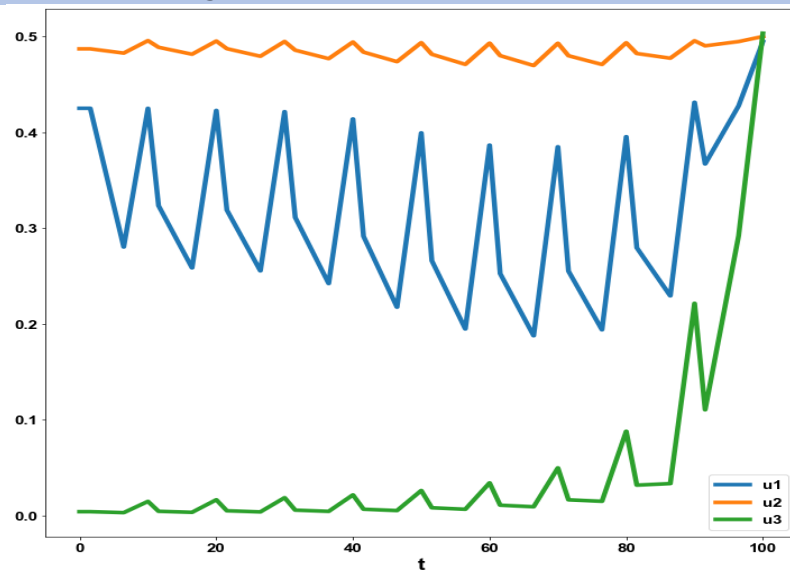


Figure 1g: *MNL MPC Listeriosis model u_1, u_2, u_3 vs t (noise exhibited)*

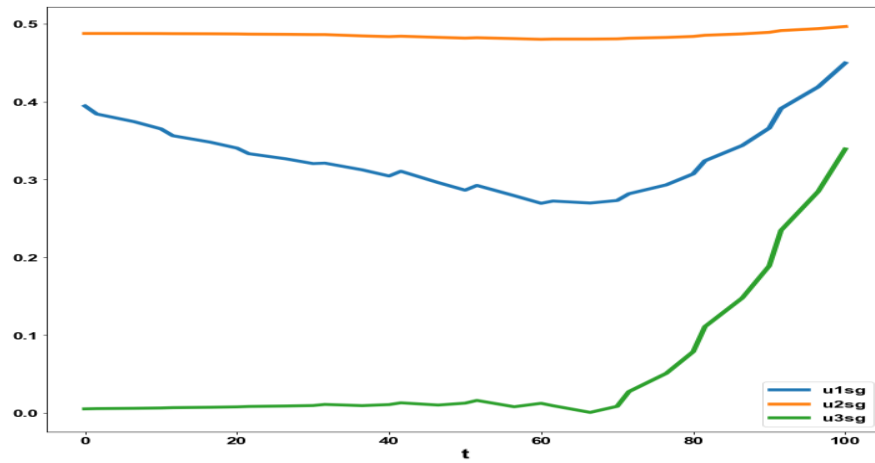


Figure 1h: MNLMPCListeriosis model u_1, u_2, u_3 vs t (noise eliminated with Savitzky Golay filter)

Discussion of results:

Theorem

If one of the functions in a dynamic system is separable into two distinct functions, a branch point singularity will occur in the system.

Proof

Consider a system of equations

$$\frac{dx}{dt} = f(x, \alpha) \quad (13)$$

$x \in R^n$. Defining the matrix A as

$$A = \begin{bmatrix} \frac{\partial f_1}{\partial x_1} & \frac{\partial f_1}{\partial x_2} & \frac{\partial f_1}{\partial x_3} & \frac{\partial f_1}{\partial x_4} & \dots & \frac{\partial f_1}{\partial x_n} & \frac{\partial f_1}{\partial \alpha} \\ \frac{\partial f_2}{\partial x_1} & \frac{\partial f_2}{\partial x_2} & \frac{\partial f_2}{\partial x_3} & \frac{\partial f_2}{\partial x_4} & \dots & \frac{\partial f_2}{\partial x_n} & \frac{\partial f_2}{\partial \alpha} \\ \dots & \dots & \dots & \dots & \dots & \dots & \dots \\ \frac{\partial f_n}{\partial x_1} & \frac{\partial f_n}{\partial x_2} & \frac{\partial f_n}{\partial x_3} & \frac{\partial f_n}{\partial x_4} & \dots & \frac{\partial f_n}{\partial x_n} & \frac{\partial f_n}{\partial \alpha} \end{bmatrix} \quad (14)$$

α is the bifurcation parameter. The matrix A can be written in a compact form as

$$A = \left[\frac{\partial f_p}{\partial x_q} \mid \frac{\partial f_p}{\partial \alpha} \right] \quad (15)$$

The tangent at any point x ; ($z = [z_1, z_2, z_3, z_4, \dots, z_{n+1}]$) must satisfy

$$Az = 0 \quad (16)$$

The matrix $\left\{ \frac{\partial f_p}{\partial x_q} \right\}$ must be singular at both limit and branch points.. The $n+1$ th component of the tangent vector $z_{n+1} = 0$ at a limit

point (LP) and for a branch point (BP) the matrix $B = \begin{bmatrix} A \\ z^T \end{bmatrix}$ must be singular.

Any tangent at a point y that is defined by $z = [z_1, z_2, z_3, z_4, \dots, z_{n+1}]$ must satisfy

$$Az = 0 \quad (17)$$

For a branch point, there must exist two tangents at the singularity. Let the two tangents be z and w . This implies that

$$\begin{aligned} Az &= 0 \\ Aw &= 0 \end{aligned} \quad (18)$$

Consider a vector v that is orthogonal to one of the tangents (say z). v can be expressed as a linear combination of z and w ($v = \alpha z + \beta w$). Since $Az = Aw = 0$; $Av = 0$ and since z and v are orthogonal,

$z^T v = 0$. Hence $Bv = \begin{bmatrix} A \\ z^T \end{bmatrix} v = 0$ which implies that B is singular.

Let any of the functions f_i are separable into 2 functions ϕ_1, ϕ_2 as

$$f_i = \phi_1 \phi_2 \quad (19)$$

At steady-state $f_i(x, \alpha) = 0$ and this will imply that either $\phi_1 = 0$ or $\phi_2 = 0$ or both ϕ_1 and ϕ_2 must be 0. This implies that two branches $\phi_1 = 0$ and $\phi_2 = 0$ will meet at a point where both ϕ_1 and ϕ_2 are 0.

At this point, the matrix B will be singular as a row in this matrix would be

$$\left[\frac{\partial f_i}{\partial x_k} \mid \frac{\partial f_i}{\partial \alpha} \right] \quad (20)$$

However,

$$\begin{aligned} \left[\frac{\partial f_i}{\partial x_k} = \phi_1 (=0) \frac{\partial \phi_2}{\partial x_k} + \phi_2 (=0) \frac{\partial \phi_1}{\partial x_k} = 0 (\forall k = 1, \dots, n) \right. \\ \left. \frac{\partial f_i}{\partial \alpha} = \phi_1 (=0) \frac{\partial \phi_2}{\partial \alpha} + \phi_2 (=0) \frac{\partial \phi_1}{\partial \alpha} \right] = 0 \end{aligned} \quad (21)$$

This implies that every element in the row $\left[\frac{\partial f_i}{\partial x_k} \mid \frac{\partial f_i}{\partial \alpha} \right]$ would be 0 and hence the matrix B would be singular. The singularity in B implies that there exists a branch point.

The two distinct equations can be obtained from the third ODE in the listeriosis model.

$$\frac{d(lm)}{dt} = rl(lm(1-lm)) \quad (22)$$

The two distinct equations are

$$\begin{aligned} rl &= 0 \\ (lm(1-lm)) &= 0 \end{aligned} \quad (23)$$

The first branch point occurs at (sv, iv, lm, fu, fc, rl) values of $(1 \ 0 \ 0 \ 1 \ 0 \ 0)$. With $rl=0$ and $lm=1$; both the distinct equations are satisfied and the theorem is validated.

The second branch point occurs at (sv, iv, lm, fu, fc, rl) values of (0.989739 0.010014 1.000000 0.791538 0.003121 0); and with $rl=0$ and $lm=0$; both the distinct equations are satisfied, validating the theorem. The MNLMPC calculations converged to the Utopia solution, justifying the analysis of Sridhar (2024) [22].

Conclusions:

Bifurcation analysis and multiobjective nonlinear control (MNLMPC) studies were performed in a listeriosis transmission model. The bifurcation analysis revealed the existence a branch point in the model. The branch point (which cause multiple steady-state solutions from a singular point) is very beneficial because it enables the Multiobjective nonlinear model predictive control calculations to converge to the Utopia point (the best possible solution) in the model. It is proved (with computational validation) that the branch point was caused by the existence of two distinct separable functions in one of the equations in the dynamic model. A theorem was developed to demonstrate this fact for any dynamic model. A combination of bifurcation analysis and Multiobjective Nonlinear Model Predictive Control(MNLMPC) for dynamic models involving listeriosis transmission is the main contribution of this paper.

Data Availability Statement

All data used is presented in the paper

Conflict of interest

The author, Dr. Lakshmi N Sridhar, has no conflict of interest.

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