ISSN: 2978-5324

Journal of Cytology & Histology Research

Research Article

Open Access

Analysis and Control of an Influenza Transmission Model

Lakshmi Sridhar N

Chemical Engineering Department University of Puerto Rico Mayaguez, USA

ABSTRACT

Influenza is a global health challenge, and effective strategies must be implemented to minimize the damage. The dynamics of influenza transmission must be understood, and control methods that are beneficial and cost-effective must be implemented. In this work, bifurcation analysis and multiobjective nonlinear model predictive control are performed on a dynamic model involving influenza. Bifurcation analysis is a powerful mathematical tool used to deal with the nonlinear dynamics of any process. Several factors must be considered, and multiple objectives must be met simultaneously. The MATLAB program MATCONT was used to perform the bifurcation analysis. The MNLMPC calculations were performed using the optimization language PYOMO in conjunction with the state-of-the-art global optimization solvers IPOPT and BARON.The bifurcation analysis revealed the existence of branchpoints in the influenza model for two different bifurcation parameters. The branch points (which cause multiple steady-state solutions from a singular point) are very beneficial because they enable the Multiobjective nonlinear model predictive control calculations to converge to the Utopia point (the best possible solution) in both models.

***Corresponding author**

Lakshmi Sridhar N, Chemical Engineering Department University of Puerto Rico Mayaguez, USA.

Received: September 05, 2025; **Accepted:** September 16, 2025; **Published:** September 19, 2025

Keywords: Bifurcation, Optimization, Control, Influenza

Background

Stilianakis et al. researched the emergence of drug resistance during an influenza epidemic using insights from a mathematical model. Alexander developed a vaccination model for transmission dynamics of influenza. studied the dynamics of two-strain influenza with isolation and partial cross-immunity. Xu et al developed a stochastic model of an influenza epidemic with drug resistance. Rambaut et al studied the genomic and epidemiological dynamics of human influenza. Lee et al researched optimal control for a pandemic influenza model involving the role of limited antiviral treatment and isolation. Qiu et al studied the transmission dynamics of an influenza model with vaccination and antiviral treatment. Tchuenche et al performed optimal control and sensitivity analysis studies of an influenza model with treatment and vaccination. Lee et al modeled the optimal age-specific vaccination strategies against pandemic influenza. Guan et al investigated the global stability of an influenza A model with vaccination. Prasad et al used a multi-modeling approach to evaluate the efficacy of layering pharmaceutical and nonpharmaceutical interventions for influenza pandemics. Chen et al performed optimal control studies of an influenza model with mixed cross-infection by age group. Le Sage et al discussed the barriers to transmission of influenza viruses. Han et al investigated the co-evolution of immunity and seasonal influenza viruses. Wang et al performed optimal control of an influenza model incorporating pharmacological and non-pharmacological interventions. This work aims to perform bifurcation analysis and multiobjective nonlinear control (MNLMPC) studies in the influenzatransmission model. The paper is organized as follows. First, the model equations are presented, followed by a discussion of the numerical techniques involving bifurcation analysis and multiobjective nonlinear model predictive control (MNLMPC). The results and discussion are then presented, followed by the conclusions [1-15].

Model Equations for the Influenzatransmission Model

The variables (s, v, is, ir, istr, irtr, r) represent thesusceptible population, vaccinated population, the population untreated with drug-sensitive strains, people untreated with drug-resistant strains, those treated with drug-sensitive strains, those treated with drug-resistant strains, and the recovered population.

The Model Equations are

$$\begin{aligned} rval &= \beta r(ir) + \beta rtr(irtr) \\ sval &= \beta s(is) + \beta str(istr) \\ tval &= rval + sval \end{aligned} \tag{1}$$

$$\begin{aligned}
\frac{ds}{dt} &= \Lambda - (tval(s)) - (\phi(s)) + ((1-u1)\omega(v)) + (\gamma(r)) - (\mu(s)); \\
\frac{dv}{dt} &= (\phi s) - ((1-u1)\omega v) - ((1-\sigma)(tval)v) - (\mu v); \\
\frac{d(is)}{dt} &= (sval(s)) + ((1-\sigma)svalv) - ((1+u2)k1is) - (is(\xi 1 + \mu + u4)); \\
\frac{d(ir)}{dt} &= (rval(s)) + ((1-\sigma)rvalv) - ((1+u3)k2ir) - (ir(\xi 2 + \mu + u4)); \\
\frac{d(istr)}{dt} &= ((1+u2)k1(is)) - (istr(ppar + \alpha 1 + \mu + u5)); \\
\frac{d(irtr)}{dt} &= ((1+u3)k2(ir)) + (ppar(istr)) - (irtr(\alpha 2 + \mu + u5)); \\
\frac{d(r)}{dt} &= (\xi 1(is)) + (\xi 2(ir)) + (istr(\alpha 1)) + (\alpha 2(irtr)) - (r(\gamma + \mu))
\end{aligned} \tag{2}$$

The Base Parameter Value are

$\Lambda = 0.0137$; μ =3.4247e-05; βs s=6.e-03;βrtr=4.02e-03; βr =1.2e-03; βrtr =1.2e-03;ϕ phi =0.03;ω=0.003; γ =0.011;σ =0.85; k1=0.7; $\xi 1$=0.25; k2=0.7; $\xi 2$=0.25; $\alpha 1$=0.3325; $\alpha 2$ =0.25;ppar=0.05;

u1, u2, u3, u4, and u5 are control parameters and are set to 0 for the bifurcation analysis.

Bifurcation Analysis
The MATLAB software MATCONT is used to perform the bifurcation calculations. Bifurcation analysis deals with 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. A commonly used MATLAB program that locates limit points, branch points, and Hopf bifurcation points is MATCONT [16,17]. This program detects Limit points (LP), branch points (BP), and Hopf bifurcation points(H) for an ODE system

$$\frac{dx}{dt} = f(x,\alpha) \tag{3}$$

$x \in R^n$ Let the bifurcation parameter be α Since the gradient is orthogonal to the tangent vector,The tangent plane at any point $w = [w_1, w_2, w_3, w_4, ...w_{n+1}]$ must satisfy

$$Aw = 0 \tag{4}$$

Where A is

$$A = [\partial f / \partial x \quad | \partial f / \partial \alpha] \tag{5}$$

where $\partial f / \partial x$ is the Jacobian matrix. For both limit and branch points, the Jacobian matrix $J = [\partial f / \partial x]$ must be singular.

For a limit point, there is only one tangent at the point of singularity. At this singular point, there is a single non-zero vector, y, where Jy=0. This vector is of dimension n. Since there is only one tangent the vector

$y = (y_1, y_2, y_3, y_4, \cdots y_n)$ must align with $\hat{w} = (w_1, w_2, w_3, w_4, \ldots w_n)$ Since

$$J\hat{w} = Aw = 0 \tag{6}$$

the n+1th component of the tangent vector $w_{n+1} = 0$ at a limit point (LP).

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

$$\begin{aligned} Az &= 0 \\ Aw &= 0 \end{aligned} \tag{7}$$

Consider a vector v that is orthogonal to one of the tangents (say w). 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 w and v are orthogonal,

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

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

Ata Hopf bifurcation point,

$$\det(2 f_x(x,\alpha) @ I_n) = 0 \tag{8}$$

@ indicates the bialternate product while I_n is the n-square identity matrix. Hopf bifurcations cause limit cycles and should be eliminated because limit cycles make optimization and control tasks very difficult. More details can be found in Kuznetsov [16-18].

Multiobjective Nonlinear Model Predictive Control (MNLMPC)
The rigorous multiobjective nonlinear model predictive control (MNLMPC) method developed by Flores Tlacuahuaz et al, was used [19].

Consider a problem where the variables $\sum_{t_i=0}^{t_i=t_f} q_j(t_i)$ (j=1, 2..n)

have to be optimized simultaneously fora dynamic problem

$$\frac{dx}{dt} = F(x,u) \tag{9}$$

t_f being the final time value, and the total number of objectivevariables and the control parameter. The single objective optimal control problem is solved individually optimizing each of the variables $\sum_{t_i=0}^{t_i=t_f} q_j(t_i)$ The optimization of $\sum_{t_i=0}^{t_i=t_f} q_j(t_i)$ will lead to the values q_j^* Then, the Mult objective optimal control (MOOC) problem that will be solved is

$$\begin{aligned} &\min\left(\sum_{j=1}^{n}\left(\sum_{t_i=0}^{t_i=t_f} q_j(t_i) - q_j^*\right)\right)^2 \\ &\textit{subject to } \frac{dx}{dt} = F(x,u); \end{aligned} \tag{10}$$

This will provide the values of multivarious times. The first obtained control value of 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 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 and confirmed as a global solution with BARON [20-22]. The steps of the algorithm are as follows

1. Optimize $\sum_{t_i=0}^{t_i=t_f} q_j(t_i)$ and obtain q_j^*.
2 . Minimize $\left(\sum_{j=1}^{n}\left(\sum_{t_i=0}^{t_i=t_f} q_j(t_i) - q_j^*\right)\right)^2$ and get the control values at various times.
3. Implement the first obtained control values
4. Repeat steps 1 to 3 until there is an insignificant difference between the implemented and the first obtained value of the control variables or if the Utopia point is achieved. The Utopia point is when $\sum_{t_i=0}^{t_i=t_f} q_j(t_i) = q_j^*$ for all j.

Sridhar demonstrated that when the bifurcation analysis revealed the presence of limit and branch points the MNLMPC calculations to converge to the Utopia solution [23]. For this, the singularity condition, caused by the presence of the limit or branch points was imposed on the co-state equation [24]. 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 MNLPMC calculations will minimize the function

$(q_1-q_1^*)^2+(q_2-q_2^*)^2$ .The Mult objective optimal control problem is

$$\min \quad (q_1-q_1^*)^2+(q_2-q_2^*)^2 \quad subject\ to\ \frac{dx}{dt}=F(x,u) \qquad (11)$$

Differentiating the objective function results in

$$\frac{d}{dx_i}((q_1-q_1^*)^2+(q_2-q_2^*)^2)=2(q_1-q_1^*)\frac{d}{dx_i}(q_1-q_1^*)+2(q_2-q_2^*)\frac{d}{dx_i}(q_2-q_2^*) \qquad (12)$$

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

$$\frac{d}{dx_i}((q_1-q_1^*)^2+(q_2-q_2^*)^2)=0 \qquad (13)$$

The optimal control co-state equation is

$$\frac{d}{dt}(\lambda_i)=-\frac{d}{dx_i}((q_1-q_1^*)^2+(q_2-q_2^*)^2)-f_x\lambda_i; \quad \lambda_i(t_f)=0 \qquad (14)$$

λ_i is the Lagrangian multiplier [24]. t_f is the final time. The first term in this equation is 0 and hence

$$\frac{d}{dt}(\lambda_i)=-f_x\lambda_i;\lambda_i(t_f)=0 \qquad (15)$$

At a limit or a branch point, for the set of ODE $\frac{dx}{dt}=f(x,u)$ f_x is singular. Hence there are two different vectors-values for $[\lambda_i]$ where $\frac{d}{dt}(\lambda_i)>0$ and $\frac{d}{dt}(\lambda_i)<0$. In between there is a vector $[\lambda_i]$ where $\frac{d}{dt}(\lambda_i)=0$. This coupled with the boundary condition $\lambda_i(t_f)=0$ will lead to $[\lambda_i]=0$ This makes the problem a unconstrained optimization problem, and the optimal solution is the Utopia solution.

Results and Discussion

The bifurcation analysis of the influenza model revealed branch points when βr and βrtr are bifurcation parameters. When was the bifurcation parameter the branch point occurred at (s, v, is, ir, istr, irtr, r,) values of (42.757781,189.151848,0,1.870419,0, 5.236455 161.018538 0.009997) (Figure. 1)

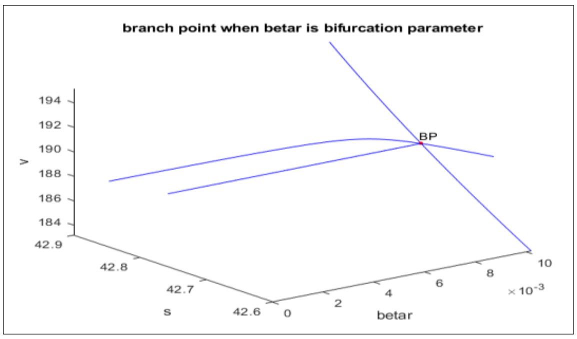

Figure 1: Branch Point (βr is the Bifurcation Parameter)

When βrtr was the bifurcation parameter the branch point occurred at (s, v, is, ir, istr, irtr, r, βrtr)

values of (42.757781, 189.151848, 0, 1.870419, 0,5.236455, 161.018538, 0.004342) (Figure. 2)

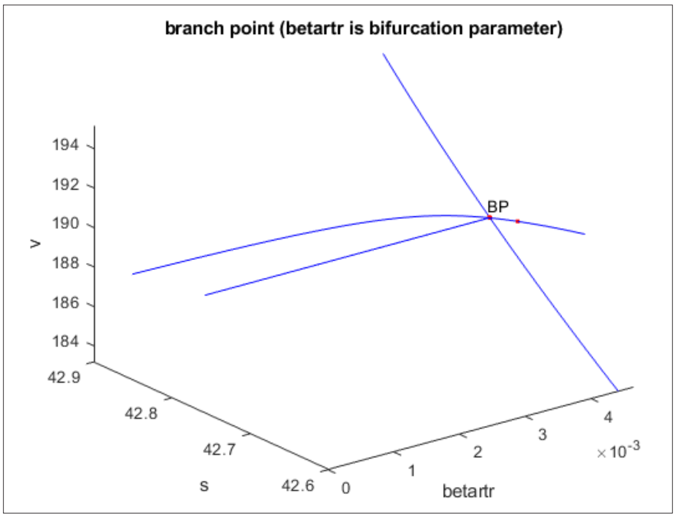

Figure 2: Branch Point (βrtr is the Bifurcation Parameter)

For the MNLMPC calculations, (0) is set to 300 and v (0) is set to 100

$\sum_{t_i=0}^{t_i=t_f} is(t_i), \sum_{t_i=0}^{t_i=t_f} ir(t_i) \sum_{t_i=0}^{t_i=t_f} istr(t_i), \sum_{t_i=0}^{t_i=t_f} irtr(t_i)$ were minimized individually and each of them led to a values0. The overall optimal control problem will involve the minimization of

$$(\sum_{t_i=0}^{t_i=t_f} is(t_i))^2+(\sum_{t_i=0}^{t_i=t_f} ir(t_i))^2+(\sum_{t_i=0}^{t_i=t_f} istr(t_i))^2+(\sum_{t_i=0}^{t_i=t_f} irtr(t_i))^2$$

was minimized subject to the equations governing the model. This led to a value of zero (the Utopia The MNLMPC values of the control variables, u1, u2 u3, u4, u5were 0.5498, 0.7725, 0.4696, 0.92579, 0.8467. The various MNMPC figures are shown in figures 3--6. The control profiles u1, u2, u3.u4,u5 (Figure. 5) exhibited noise, and this was remedied using the Savitzky-Golay filter (Figure. 6). It is seen that the presence of the limit and branch points is beneficial because it allows the MNLMPC calculations to attain the Utopia solution, validating the analysis of Sridhar [23].

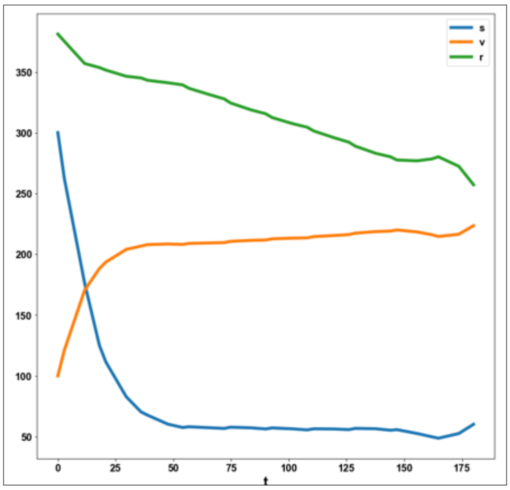

Figure 3: MNLMPC (S V R Profiles)

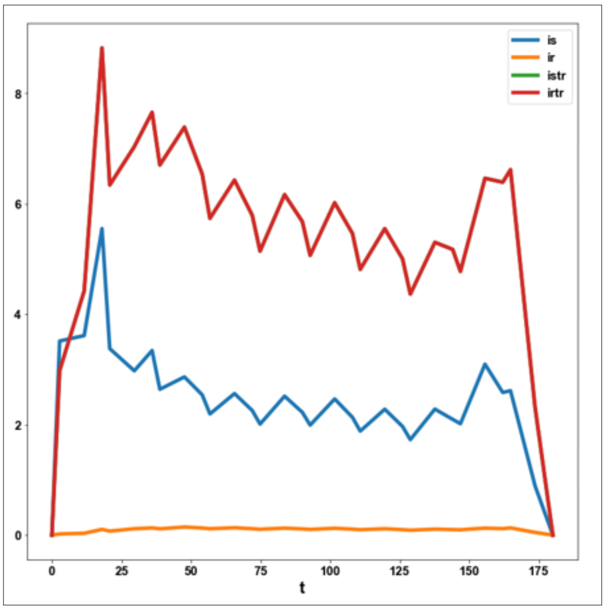

Figure 4: MNLMPC (Is Ir Istr Irtr Profiles)

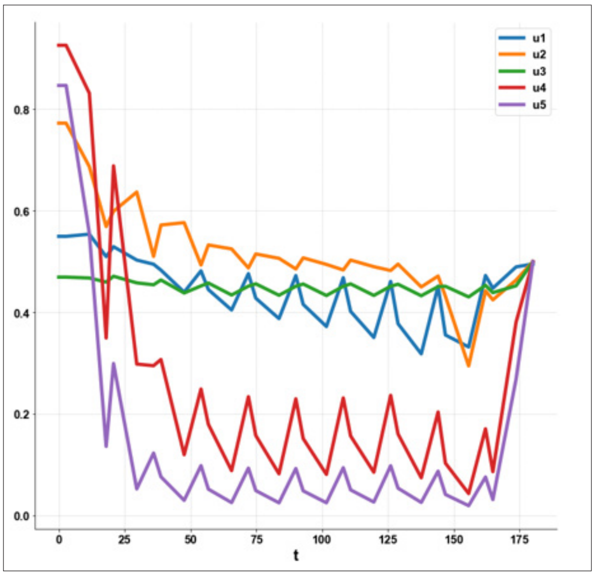

Figure 5: MNLMPC (Control Profiles with Noise)

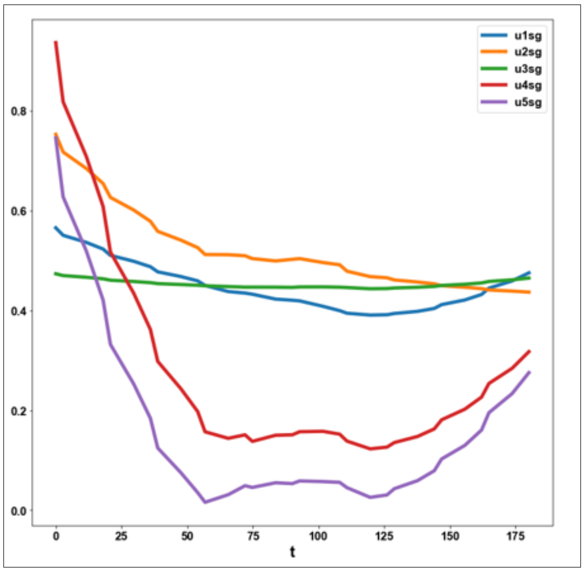

Figure 6: MNLMPC (Smooth Control Profiles; Noise Removed by Savitzky-Golay Filter)

Conclusions

Bifurcation analysis and multiobjective nonlinear control (MNLMPC) studies a dynamic influenza transmission model. The bifurcation analysis revealed the existence of branch points for two different bifurcation parameters. The branch and points (which cause multiple steady-state solutions from a singular point) are very beneficial because they enable the Multiobjective nonlinear model predictive control calculations to converge to the Utopia point (the best possible solution) in the models. A combination of bifurcation analysis and Multiobjective Nonlinear Model Predictive Control (MNLMPC)for dynamic influenza transmission models is the main contribution of this paper [25,26].

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.

Acknowledgement

Dr. Sridhar thanks Dr. Carlos Ramirez and Dr. Suleiman for encouraging him to write single-author papers

References

1. Stilianakis NI, Perelson AS, Hayden FG (1998) Emergence of drug resistance during an influenza epidemic: insights from a mathematical model. J. Infect. Dis 177: 863-873.
2. Alexander ME, Bowman C, Moghadas SM, Summers R, Gumelet AB, et al. (2004) A vaccination model for transmission dynamics of influenza. SIAM J. Appl. Dyn. Syst 3: 503-524.
3. Nuno M, Feng Z, Martcheva M, Castillo-Chavez C (2005) Dynamics of two-strain influenza with isolation and partial cross-immunity. SIAM J. Appl. Math 65: 964-982.
4. Xu Y, Allen LJS, Perelson AS (2007) Stochastic model of an influenza epidemic with drug resistance. J. Theor. Biol 248: 179-193.
5. Andrew Rambaut, Oliver G Pybus, Martha I Nelson, Cecile Viboud, Jeffery K Taubenberger, et al. (2008) The genomic and epidemiological dynamics of human influenza A virus. Nature 453: 615-619.
6. Lee S, Chowell G, Castillo-Chávez C (2010) Optimal control for pandemic influenza: the role of limited antiviral treatment and isolation. J. Theor. Biol 265: 136-150.
7. Qiu Z, Feng Z (2010) Transmission dynamics of an influenza model with vaccination and antiviral treatment. Bull. Math. Biol 72: 1-33.
8. Tchuenche JM, Khamis SA, Agusto FB, Mpeshe SC (2011) Optimal control and sensitivity analysis of an influenza model with treatment and vaccination. Acta Biotheor 59: 1-28.
9. Lee S, Golinski M, Chowell G (2012) Modeling optimal age-specific vaccination strategies against pandemic influenza. Bull. Math. Biol 74: 958-980.
10. Guan X, Yang F, Cai Y, Wang W (2022) Global stability of an influenza A model with vaccination. Appl. Math. Lett 134: 108322.
11. Pragati V Prasad, Molly K Steele, Carrie Reed, Lauren Ancel Meyers, Zhanwei Du, et al. (2023) Multimodeling approach to evaluating the efficacy of layering pharmaceutical and nonpharmaceutical interventions for influenza pandemics. Proc. Natl. Acad. Sci. USA 120: 2300590120.
12. ChenY, Zhang J, Jin Z (2023) Optimal control of an influenza model with mixed cross-infection by age group.

Math. Comput. Simul 206: 410-436.
13. Le Sage V, Lowen AC, Lakdawala SS (2023) Block the spread: barriers to transmission of influenza viruses. Annu. Rev. Virol 10: 347-370.
14. Han AX, de Jong SPJ, Russell CA (2023) Co-evolution of immunity and seasonal influenza viruses. Nat. Rev. Microbiol 21: 805-817.
15. Wang X, Cai Y (2025) Optimal control of an influenza model incorporating pharmacological and non-pharmacological interventions. Adv Cont Discr Mod 17: 1-15.
16. Dhooge A, Govearts W, Kuznetsov AY (2003) MATCONT: A Matlab package for numerical bifurcation analysis of ODEs, ACM transactions on Mathematical software 29: 141-164.
17. Dhooge A, Govaerts W, Kuznetsov YA, Mestrom W, Riet AM, et al. (2004) "CL_MATCONT"; A continuation toolbox in Matlab 161-166.
18. Kuznetsov YA (1998) Elements of applied bifurcation theory Springer,NY https://dl.acm.org/doi/10.5555/289919.
19. Kuznetsov YA (2009) Five lectures on numerical bifurcation analysis, Utrecht University, NL https://webspace.science.uu.nl/~kouzn101/NBA/nba.pdf.
20. Govaerts w JF (2000) Numerical Methods for Bifurcations of Dynamical Equilibria, SIAM https://epubs.siam.org/doi/10.1137/1.9780898719543.
21. Flores Tlacuahuac A (2012) Pilar Morales and Martin Riveral Toledo; Multiobjective Nonlinear model predictive control ofa class of chemical reactors. I & EC research 5891-5899.
22. Hart, William E, Carl D Laird, Jean-Paul Watson, David L, et al. (2020) Pyomo – Optimization Modeling in Python Second Edition. https://link.springer.com/book/10.1007/978-3-030-68928-5.
23. Wächter A, Biegler L (2006) On the implementation of an interior-point filter line-search algorithm for large-scale nonlinear programming. Math. Program 106: 25-57.
24. Tawarmalani M, Sahinidis NV (2005) A polyhedral branch-and-cut approach to global optimization, Mathematical Programming 103: 225-249.
25. Sridhar LN (2024) Coupling Bifurcation Analysis and Multiobjective Nonlinear Model Predictive Control. Austin Chem Eng 10:1107.
26. Upreti, Simant Ranjan (2013) Optimal control for chemical engineers. Taylor and Francis https://www.taylorfrancis.com/books/oa-mono/10.1201/b13045/optimal-control-chemical-engineers-simant-ranjan-upreti.