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# Analysis and Control of Cardiovascular Dynamic Models

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## ABSTRACT

Cardiovascular diseases (CVDs) is one of the leading causes of death in the world. It is very important to understand the dynamics of this disease and develop strategies to control it minimizing the damage as much as possible. This article involves analysis and control of two dynamic cardiovascular models. 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. Bifurcation analysis and multi-objective nonlinear model predictive control (MNLMPC) calculations are performed on two cardiovascular dynamic models. 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 branch points in both models. The branch points (which cause multiple steady-state solutions from a singular point) are very beneficial because they enable the Mult objective nonlinear model predictive control calculations to converge to the Utopia point (the best possible solution) in the models. It is proven (with computational validation) that the branch points were caused by the existence of two distinct separable functions in one of the equations in each dynamic model. A theorem was developed to demonstrate this fact for any dynamic model.

**Keywords:** Bifurcation; Optimization; Control; Heart-attack

## Background

Cardiovascular disease, often abbreviated as CVD, refers to a broad class of disorders that affect the heart and blood vessels. It remains one of the most significant global health problems, contributing to high levels of morbidity, disability and mortality across populations. Despite substantial advancements in medicine, public health awareness and treatment technologies, cardiovascular disease continues to place an enormous burden on individuals, families and societies. To understand why it holds such a prominent place among global health concerns, one must look at the biological mechanisms that underlie its development, the risk factors that predispose individuals to it, the profound social and economic consequences it entails and the ways in which prevention and treatment can mitigate its impact.

At its core, cardiovascular disease is not one singular illness but rather an umbrella term that encompasses a variety of related conditions. These include coronary artery disease, which is characterized by the narrowing or blockage of the arteries that supply blood to the heart; cerebrovascular disease, which involves the vessels supplying blood to the brain; rheumatic heart disease, which results from damage caused by rheumatic fever; congenital heart disease, which arises from structural malformations present at birth; peripheral artery disease, which affects the blood supply to limbs; and heart failure, which refers to the inability of the heart to pump sufficient blood to meet the body's needs. Of these, coronary artery disease and stroke are by far the most common and deadly, representing the majority of cardiovascular-related deaths worldwide.

The biological foundation of many forms of cardiovascular disease can be traced to a process known as atherosclerosis. Atherosclerosis involves the gradual buildup of fatty deposits or plaques, within the walls of arteries. Over time, these plaques harden and narrow the arteries, restricting blood flow and reducing oxygen delivery to vital tissues. This process is often silent, progressing without symptoms for decades, until it culminates in acute events such as heart attacks or strokes. These events occur when a plaque ruptures, forming a blood clot that obstructs circulation entirely. The damage inflicted by such blockages is often irreversible, leading to tissue death and, in severe cases, sudden death.

The development of cardiovascular disease is strongly influenced by an interplay between non-modifiable and modifiable risk factors. Non-modifiable factors include age, sex, ethnicity and genetic predisposition. As individuals grow older, the likelihood of developing cardiovascular disease rises significantly due to the cumulative wear and tear on blood vessels and the gradual decline of protective physiological mechanisms. Men are at a somewhat higher risk earlier in life, though women's risk increases substantially after menopause. Genetics can also play an important role, as family history of cardiovascular events often signals a predisposition to similar outcomes. However, it is the modifiable risk factors that explain much of the high prevalence of cardiovascular disease worldwide. These include unhealthy diets high in saturated fats, trans fats, cholesterol, salt and added sugars; physical inactivity; tobacco use; and excessive alcohol consumption. Additional contributors such as obesity, hypertension, diabetes and high cholesterol levels often arise from these lifestyle choices and amplify the likelihood of developing cardiovascular complications.

The global burden of cardiovascular disease is staggering. According to estimates from the World Health Organization, cardiovascular disease is the leading cause of death worldwide, accounting for roughly one-third of all deaths annually. This toll is not distributed evenly. While high-income countries once bore the brunt of the epidemic, improved healthcare systems, early detection and preventive interventions have helped to lower mortality rates in those regions. In contrast, low- and middle-income countries now face disproportionately high rates of cardiovascular deaths. These regions often experience rapid urbanization and lifestyle changes that increase risk exposure while lacking the resources to implement adequate prevention, screening and treatment programs. This disparity underscores the reality that cardiovascular disease is not merely a medical challenge but also a profound social and economic one, deeply linked to inequality, access to care and broader patterns of development.

The economic consequences of cardiovascular disease are equally severe. At the individual level, those who develop cardiovascular conditions often face reduced quality of life, long-term disability and financial strain due to the costs of medical treatment, hospitalization and medication. At the societal level, the economic burden extends to lost productivity, increased healthcare expenditure and the diversion of resources from other critical needs. In many countries, cardiovascular disease accounts for a substantial proportion of total healthcare spending, which places stress on both public health systems and families struggling to cope with its demands.

Despite its heavy burden, cardiovascular disease is largely preventable. The fact that so many cases can be avoided through lifestyle changes makes it a unique challenge in modern medicine. Public health strategies aimed at reducing the prevalence of risk factors have shown promising results. Anti-smoking campaigns, efforts to reduce salt intake, promotion of physical activity and initiatives to encourage healthier diets are among the most effective interventions. These population-level strategies, when combined with individual-level approaches such as regular medical checkups, blood pressure monitoring, cholesterol testing and glucose screening, can significantly reduce the incidence of cardiovascular events. Moreover, early detection plays a critical role in prevention. Identifying hypertension, diabetes and high cholesterol before they cause significant damage allows for timely interventions that can delay or even prevent the onset of cardiovascular disease.

Treatment for cardiovascular disease has also advanced dramatically over the past few decades. Pharmacological interventions, such as statins to lower cholesterol, antihypertensive drugs to control blood pressure and anticoagulants to prevent clot formation, are now widely used and have saved millions of lives. Surgical and procedural interventions, such as angioplasty, stent placement and coronary artery bypass grafting, offer lifesaving options for those with advanced disease. In cases of severe heart failure, mechanical assist devices and heart transplantation may be necessary. These treatments, though often costly and complex, demonstrate the remarkable capacity of modern medicine to prolong life and reduce suffering. Yet the challenge remains to make such treatments accessible to all populations, not just those in wealthy countries.

Beyond medical treatment, there is a growing recognition of the importance of addressing social determinants of health in tackling cardiovascular disease. Poverty, limited education, food insecurity and lack of access to safe spaces for physical activity all contribute to heightened risk and poorer outcomes. Interventions that focus solely on medical solutions without addressing these broader determinants often fall short. Consequently, holistic strategies that combine medical, behavioral and social approaches are essential. For example, urban planning that promotes walkable cities, policies that regulate unhealthy food marketing and workplace initiatives that encourage physical activity all play a role in reducing cardiovascular disease risk at the population level.

Looking to the future, cardiovascular disease presents both challenges and opportunities. Advances in personalized medicine, including genetic screening and the use of biomarkers, promise to improve risk prediction and allow for more tailored interventions. Technological innovations, such as wearable devices that monitor heart rhythms and blood pressure in real time, could empower individuals to take greater control over their health. Telemedicine offers new possibilities for expanding access to cardiovascular care in underserved regions. At the same time, emerging global health threats such as obesity and diabetes epidemics, coupled with aging populations, may further increase the prevalence of cardiovascular disease in the coming decades if preventive measures are not strengthened.

In conclusion, cardiovascular disease represents one of the most pressing health challenges of our time. Its complexity arises not only from the intricate biological mechanisms that drive it but also from the interplay of lifestyle factors, social determinants and health system limitations that shape its impact

across different populations. While the burden of cardiovascular disease is immense, it is also clear that much of it is preventable. Through a combination of public health initiatives, medical advances and societal changes, it is possible to significantly reduce its toll. Addressing cardiovascular disease requires a sustained commitment at both individual and collective levels, one that recognizes the need for healthier lifestyles, equitable access to healthcare and the integration of preventive measures into everyday life. As the world continues to grapple with this enduring health issue, the path forward lies not only in treating disease after it emerges but also in fostering conditions that allow hearts and blood vessels to remain healthy throughout the course of life.

Kraus[1], a preventive cardiologist and research scientist at Duke University, showed that both the risk of heart disease and risk factors for heart disease are strongly linked to family history. Thyfault JP[2] discussed the physiology of sedentary behavior and its relationship to health outcomes. Jibril, et al.[3] modelled and performed an optimal control analysis on sedentary behavior and physical activity in relation to cardiovascular disease. Mishra, et al.[4] provided a systematic review of the impact of cardiovascular diseases on the severity of COVID-19 patients. Harrison, et al.[5] discussed the Cardiovascular risk factors associate with the COVID disease. Clerkin, et al.[6] discussed the relationship between COVID-19 and cardiovascular disease. Evirgen, et al.[7] developed real data-based optimal control strategies for assessing the impact of the Omicron variant on heart attacks.

This work aims to perform bifurcation analysis and multiobjective nonlinear control (MNLMPC) studies in two cardiovascular disease models, which are discussed in Jibril, et al.[3] (model 1) and Evirgen, et al.[7] (model 2). The paper is organized as follows. First, the model equations are presented, followed by a discussion of the numerical techniques involving bifurcation analysis and Mult objective nonlinear model predictive control (MNLMPC). The results and discussion are then presented, followed by the conclusions.

## Model Equations

The model equations in two cardiovascular disease models; Jibril, et al.[3] (model 1) and Evirgen, et al.[7] (model 2); are described in this section.

### Model 1[3]

In this model, sv represents the sub-population involved in physical activity, iv represents the sub-population with sedentary behaviour and cv(t) represents the sub-population with cardiovascular disease.

The model equations are

$$\frac{d(sv)}{dt}=\pi+(\sigma iv)+(\gamma cv)\ -((1-u1)\beta ivsv)\ -((1-u1)\beta ivsv)-((1-u1)\alpha cvsv)+((u2+u3)(iv+cv))-\ (\mu sv)$$
$$\frac{d(iv)}{dt}=((1-u1)\beta ivsv)-((u2+u3)iv)-((\sigma+\mu+\tau)iv)$$
$$\frac{d(cv)}{dt}=((1-u1)\alpha cvsv)+(\tau iv)-((u2+u3)cv)-((\gamma+\mu+\delta)cv)$$

(1)

u1, u2 and u3 are the control parameters that represent living a healthy lifestyle, which incorporates good nutrition, weight management and getting plenty of physical activity.

The base parameter values are

$$\pi=20;\sigma=0.5;\gamma=0.2;\tau=0.15;\ \alpha=0.15;\ \beta=0.75;\ \mu=0.2;$$
$$\delta=0.08;u1=0.5;u2=0.5;u3=0.5.$$

### Model 2[7]

In this model, the variables are sv, ev, iv, ov, rv and, hv and these variables represent the susceptible, exposed, infected without Omicron, Omicron-infected, recovered and population with heart attacks. u1 and u2 are the control variables that represent self-isolation of infected individuals and other treatment alternatives such as drugs and therapy.

The model base parameters are

$$\Lambda=\ 2.9517e+03;\mu\ =3.4857e-05;\mu2\ =\ 0.8;\ \gamma1=0.0247;\gamma2=0.6;$$
$$\delta1=0.1161;\delta2=0.1085;\delta3=\ 0.5;\ \delta4=.4;\beta1=\ 0.3963;\beta2=\ 0.5;\beta3=\ 0.7;$$
$$\alpha1=0.0034;\alpha2=0.0994;\ \alpha3=0.78;\sigma\ =0.0664;\ \varepsilon1=\ 1.e-04;\ \varepsilon2\ =1.e-04;$$
$$u1=0;u2=0;$$

The model equations are

$$\frac{d(sv)}{dt}\ =\Lambda-((\mu+\gamma1)sv)-(\beta1wvev)\ -(\beta2wviv)-(\beta3wvov)$$
$$\frac{d(ev)}{dt}=(\beta1wvev(1-\varepsilon1-\varepsilon2))-((\mu+\alpha1+\sigma)ev)$$
$$\frac{d(iv)}{dt}=(\beta1\varepsilon1wvev)\ +(\beta2wviv)+(\alpha1ev)\ -((\mu+\alpha2+\delta1+\delta2+u1)iv)$$
$$\frac{d(ov)}{dt}=(\beta1\varepsilon2wvev)+(\beta3wvov)+(\sigma ev)\ -((\mu+\alpha3+\delta3+\delta4+u2)ov)$$
$$\frac{d(rv)}{dt}=(\alpha2iv)+(\alpha3ov)-(\gamma2rv)-(\mu rv)+(u1iv)+(u2ov)$$
$$\frac{d(hv)}{dt}=(\gamma1sv)+(\delta2iv)+(\delta4ov)+(\gamma2rv)-((\mu2+\mu)hv)$$
$$wv=\frac{sv}{nv}$$
$$nv=sv+ev+iv+ov+rv+hv$$

**(2)**

## Bifurcation analysis

The MATLAB software MATCONT[8,9] 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. This program detects Limit points (LP), branch points (BP) and Hopf bifurcation points(H) for an ODE system.

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

$x\in R^n$ Let the bifurcation parameter be $\alpha$ . 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

$$Aw=0\qquad(4)$$

Where A is

$$A=[\partial f/\partial x\quad|\partial f/\partial\alpha]\qquad(5)$$

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 (LP) the n+1$^{th}$ component of the tangent

vector = 0 and for a branch point (BP) the matrix $B = \begin{bmatrix} A \\ w^T \end{bmatrix}$ must be singular.

At a Hopf bifurcation point,

$$\det(2f_x(x,\alpha)@I_n) = 0 \qquad (8)$$

@ indicates the bialternate product while $I_n$ is the n-square identity matrix. More details can be found in Kuznetsov[10-12].

## Multiobjective Nonlinear Model Predictive Control (MNLMPC)

The (MNLMPC) method[13] is used.

The variables $\sum_{t_i=0}^{t_i=t_f} v_j(t_i)$ (j=1, 2..n) have to be optimized simultaneously for a dynamic problem

$t_f$ being the final time value and n the total number of objective variables and u the control parameter is used. The single objective optimal control problem is first solved optimizing each of the variables $\sum_{t_i=0}^{t_i=t_f} v_j(t_i)$ The optimization of will lead to the values $v_j^*$. This will lead to the solution of the multiobjective optimal control problem.

$$\min(\sum_{j=1}^{n}(\sum_{t_i=0}^{t_i=t_f} v_j(t_i) - v_j^*))^2$$

subject to the dynamic model equations. 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 ( $\sum_{t_i=0}^{t_i=t_f} v_j(t_i) = v_j^*$ for all j) is obtained.

Pyomo[14] is used in conjunction with IPOPT[15] and BARON[16]. Sridhar[17] demonstrated that when the bifurcation analysis revealed the presence of limit and branch points the MNLMPC calculations to converge to the Utopia solution. For this, the singularity condition, caused by the presence of the limit or branch points was imposed on the co-state equation[18]. Details of proof for this theorem can be found at Sridhar[17].

## Results

The bifurcation analysis performed with model 1 revealed two branch points at (sv, iv, cv, u1) values of (100 0 0 0.901333) and (100 0 0 0.975333). This is shown in **(Figure 1a)**.

For the MNLMPC calculations sv (0) =100; iv (0) =30; cv (0) =15.

$\sum_{t_i=0}^{t_i=t_f} sv(t_i)$ were maximized and led to a value of 200. $\sum_{t_i=0}^{t_i=t_f} iv(t_i); \sum_{t_i=0}^{t_i=t_f} cv(t_i)$ were minimized individually and produced values of 40.0634 and 17.7986. The multiobjective optimal control problem involves the minimization of $(\sum_{t_i=0}^{t_i=t_f} sv(t_i) - 200)^2 + (\sum_{t_i=0}^{t_i=t_f} iv(t_i) - 40.0634)^2 + (\sum_{t_i=0}^{t_i=t_f} cv(t_i) - 17.7986)^2$ subject to the equations governing the model. This led to a value of zero (the Utopia point). The MNLMPC values of the control variables u1 u2 and u3 were 0.2569, 0.999 and 0.999.

**(Figures 1b-1e)** show the various MNLMPC profiles. The u2 profile exhibits noise **(Figure 1d)** which was remedied using the Savitzky-Golay filter. The modified profile (u2sg) is shown in **(Figure 1e)**. The u2 and u3 profiles were identical.

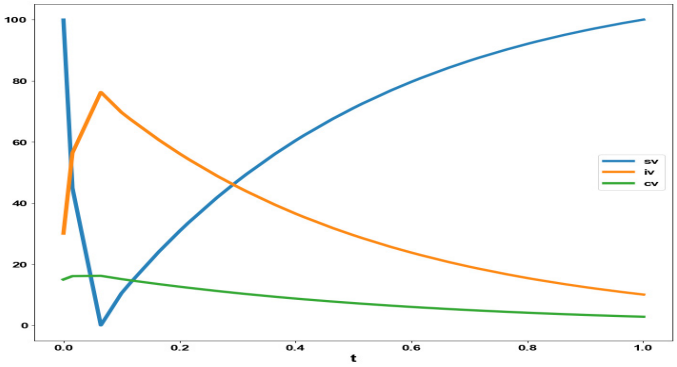


**Figure 1b:** MNLMPC for model 1 sv, iv, cv profiles.

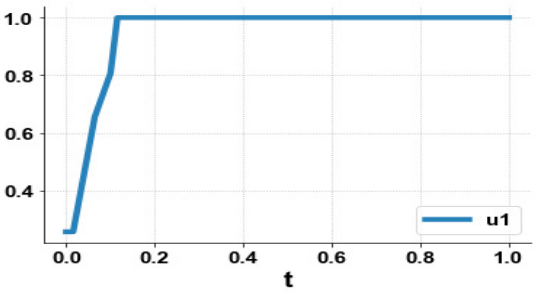


**Figure 1c:** MNLMPC for model 1 u1 profile.

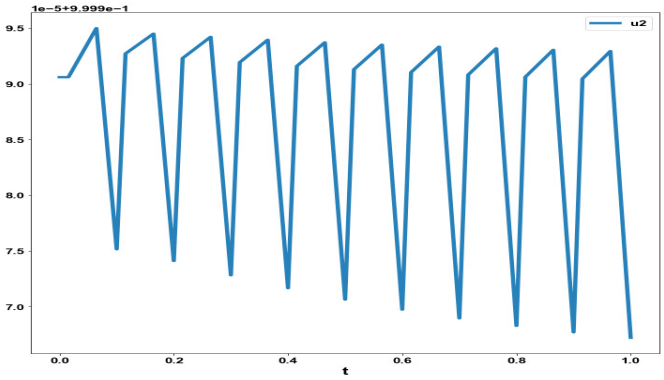


**Figure 1d:** MNLMPC for model 1 u2 profile (noise exhibited).

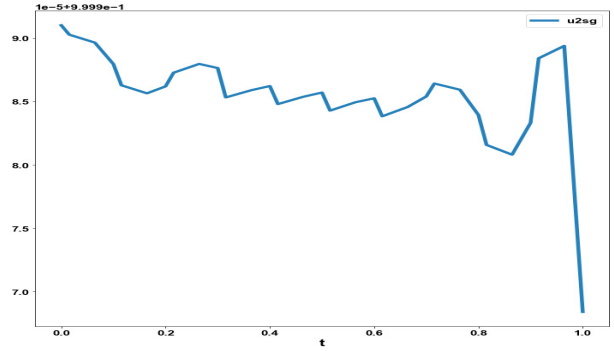


**Figure 1e:** MNLMPC for model 1 u2 profile (noise removed with Savitzky-Golay filter).

The bifurcation analysis performed (with $\beta 1$ with model 2 revealed a branch point at (sv, ev, iv ov, rv, hv, $\beta 1$ ) values of (119333.618949 0 0 0 0 3684.264957 0.072005). This is shown in **(Figure 2a)**.

For the MNLMPC calculations sv (0) =5.0e+06; iv (0) =30000; ov (0) =1300.

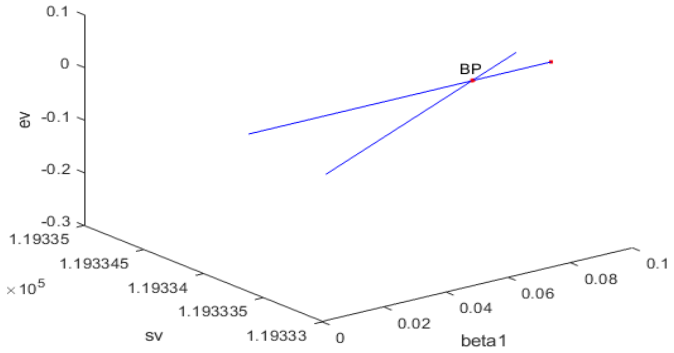


**Figure 2a:** Bifurcation Diagram for Model 2.

$\sum_{t_{i=0}}^{t_i=t_f} iv(t_i); \sum_{t_{i=0}}^{t_i=t_f} ov(t_i)$ were minimized individually and produced values of 30000 and 1300. The multiobjective optimal control problem will involve the minimization of $(\sum_{t_{i=0}}^{t_i=t_f} iv(t_i)-30000)^2+(\sum_{t_{i=0}}^{t_i=t_f} ov(t_i)-1300)^2$ subject to the equations governing the model. This led to a value of zero (the Utopia point). The MNLMPC values of the control variables u1 u2 were 0.1601 and 05602. **(Figures 2b-2d)** show the various MNLMPC profiles. The u1 u2 profile exhibits noise which was remedied using the Savitzky-Golay filter to produce the control profiles (u1sg, u2sg)) **(Figure 2d)**.

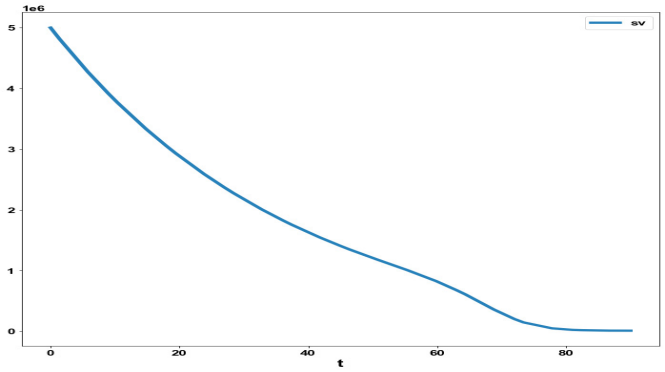


**Figure 2b:** MNLMPC for Model 2 (sv vs t).

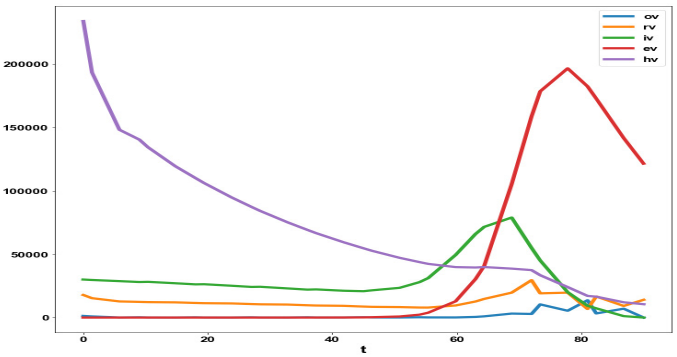


**Figure 2c:** MNLMPC for Model 2 (ov, rv, iv, ev, hv profiles).

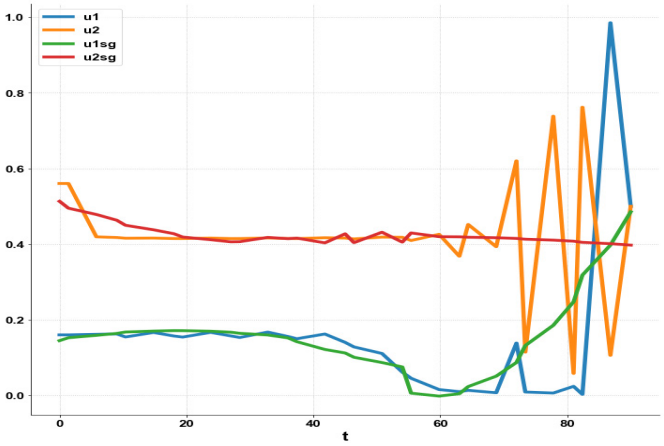


**Figure 2d:** MNLMPC for Model 2 (u1 u2 (control profiles with noise u1sg, u2sg (noise eliminated)).

## Discussion of Results

### Theorem

If at least 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

$$\frac{dx}{dt} = f(x,\alpha) \tag{16}$$

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

$$A = \begin{bmatrix} \frac{\partial f_1}{\partial x_1} & \frac{\partial f_1}{\partial x_2} & \frac{\partial f_1}{\partial x_3} & \frac{\partial f_1}{\partial x_4} & \cdots & \frac{\partial f_1}{\partial x_n} & \frac{\partial f_1}{\partial \alpha} \\ \frac{\partial f_2}{\partial x_1} & \frac{\partial f_2}{\partial x_2} & \frac{\partial f_2}{\partial x_3} & \frac{\partial f_2}{\partial x_4} & \cdots & \frac{\partial f_2}{\partial x_n} & \frac{\partial f_2}{\partial \alpha} \\ \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots \\ \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots \\ \frac{\partial f_n}{\partial x_1} & \frac{\partial f_n}{\partial x_2} & \frac{\partial f_n}{\partial x_3} & \frac{\partial f_n}{\partial x_4} & \cdots & \frac{\partial f_n}{\partial x_n} & \frac{\partial f_n}{\partial \alpha} \end{bmatrix} \tag{17}$$

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

$$A = [\frac{\partial f_p}{\partial x_q}.| \quad \frac{\partial f_p}{\partial \alpha}] \tag{18}$$

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

$$Az = 0 \tag{19}$$

The matrix $\{\frac{\partial f_p}{\partial x_q}\}$ 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 $z = [z_1, z_2, z_3, z_4, ....z_{n+1}]$) must satisfy

$$Az = 0 \quad (20)$$

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

$$\begin{aligned} Az &= 0 \\ Aw &= 0 \end{aligned} \quad (21)$$

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 where $B = \begin{bmatrix} A \\ z^T \end{bmatrix}$

Let any of the functions fi are separable into 2 functions $\phi_1, \phi_2$ as

$$f_i = \phi_1 \phi_2 \quad (22)$$

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

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

$$[\frac{\partial f_i}{\partial x_k} | \frac{\partial f_i}{\partial \alpha}] \quad (23)$$

However,

$$\begin{aligned} [\frac{\partial f_i}{\partial x_k} &= \phi_1(=0)\frac{\partial \phi_2}{\partial x_k} + \phi_2(=0)\frac{\partial \phi_1}{\partial x_k} = 0 (\forall k = 1.,,n) \\ \frac{\partial f_i}{\partial \alpha} &= \phi_1(=0)\frac{\partial \phi_2}{\partial \alpha} + \phi_2(=0)\frac{\partial \phi_1}{\partial \alpha}] = 0 \end{aligned} \quad (24)$$

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

In model 1, the first branch point occurred at (sv, iv, cv, u1) values of (100 0 0 0.901333). Here, the two distinct functions can be obtained from the third ODE in model 1 which is

$$\frac{d(cv)}{dt} = \left((1-u1)\alpha cvsv\right) + \left(\tau iv\right) - \left((u2+u3)cv\right) - \left((\gamma+\mu+\delta)cv\right) \quad (25)$$

When iv = 0 this equation reduces to

$$\frac{d(cv)}{dt} = \left((1-u1)\alpha cvsv\right) - \left((u2+u3)cv\right) - \left((\gamma+\mu+\delta)cv\right) \quad (26)$$

The two distinct equations are

$$\begin{aligned} &cv = 0 \\ &\left((1-u1)\alpha sv\right) - \left((u2+u3)\right) - \left((\gamma+\mu+\delta)\right) \end{aligned} \quad (27)$$

With cv=0; sv= 100; u1 = 0.901333, $\delta = 0.08; \gamma = 0.2;\ \alpha = 0.15;\ \mu = 0.2;\ u2 = 0.5; u3 = 0.5;$ both distinct equations are satisfied, validating the theorem.

The second branch point occurred at (sv, iv, cv, u1) values of (100 0 0 0.975333). Here, the two distinct functions can be obtained from the second ODE in model 1 which is

$$\frac{d(iv)}{dt} = \left((1-u1)\beta ivsv\right) - \left((u2+u3)iv\right) - \left((\sigma+\mu+\tau)iv\right) \quad (28)$$

The two distinct equations are

$$\begin{aligned} &iv = 0 \\ &\left((1-u1)\beta sv\right) - \left((u2+u3)\right) - \left((\sigma+\mu+\tau)\right) \end{aligned} \quad (29)$$

With iv = 0; sv= 100; u1 = 0.975333, $\sigma = 0.5; \tau = 0.15;\ \beta = 0.75;\ \mu = 0.2;\ u2 = 0.5; u3 = 0.5;$ both distinct equations are satisfied, validating the theorem.

The MNLMPC calculations converged to the Utopia solution, validating the analysis in Sridhar[17].

In model 2, the first branch point occurred at

(sv, ev, iv ov, rv, hv, $\beta 1$) values of (119333.618949 0 0 0 0 3684.264957 0.072005).

Here, the two distinct functions can be obtained from the second ODE in model 2 which is

$$\begin{aligned} &\frac{d(ev)}{dt} = (\beta 1 wvev(1-\varepsilon 1-\varepsilon 2)) - \left((\mu+\alpha 1+\sigma)ev\right) \\ &wv = \frac{sv}{nv}; nv = sv + ev + iv + ov + rv + hv \end{aligned} \quad (30)$$

The two distinct equations are

$$\begin{aligned} &ev = 0 \\ &(\beta 1 wv(1-\varepsilon 1-\varepsilon 2)) - \left((\mu+\alpha 1+\sigma)\right) = 0 \end{aligned} \quad (31)$$

With ev=0; sv = 119333.618949, hv = 3684.264957,

$\beta 1 = 0.072005;\ \varepsilon 1 = \varepsilon 2 = 1.e-04; \alpha 1 = 0.0034; \sigma = 0.0064$ both equations are satisfied, validating the theorem. Even in the case of model 2, the MNLMPC calculations converged to the Utopia solution, validating the analysis in Sridhar[17].

## Conclusions

Bifurcation analysis and multiobjective nonlinear control (MNLMPC) studies were conducted on two cardiovascular dynamic models. The bifurcation analysis revealed the existence of branch points in both models. 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 the models. It is proven (with computational validation) that the branch points were caused by the existence of two distinct separable functions in one of the equations in each 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 cardiovascular dynamic models 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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