Robust Control Design of Heart Rate Response during Treadmill Exercise under Parametric Uncertainty*

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Abstract—**Rehabilitation (Rehab) exercise can benefit cardiac patients as it can promote the recovery and improve the heart wellness. However, heart failure (HF) patients can only take mild exercise, since excessive exercise may lead to fatal events. It is important to control the exercise intensity at a desired level to maximize exercise benefit. Heart Rate (HR) is an essential factor for measuring exercise intensity. Mathematical models of HR can be used to study exercise physiology. However, HR models involve model uncertainty, resulting from model calibration or variability in patients. It is important to quantify the effect of uncertainty on HR prediction for optimizing exercise intensity, such as treadmill speed. A probabilistic model-based control design is presented in this work to obtain an optimal treadmill speed for Rehab exercise in the presence of uncertainty. To obtain a computationally tractable formulation, the generalized polynomial chaos (gPC) theory is used to propagate uncertainty via a model to HR predictions, and predict slow-acting responses such as peripheral local metabolism that can be used to evaluate exercise outcome for individual patients. The speed control of treadmill is formulated as an optimization problem that can maximize the exercise outcome, while minimizing the slow-acting effects. The effectiveness of the proposed control design was experimentally verified with simulations, showing potentials in the exercise control of individual patients.**

I. INTRODUCTION

Automatic exercise system is important for rehabilitation and analysis of cardio respiratory kinetics [1], for which heart rate (HR) is a common physiological parameter that can be used for exercise protocol design [2, 3]. During exercise, the cardiovascular system will increase the delivery of blood and oxygen to muscles as the metabolic demand increases, which can result in an increase in HR response and stroke volume. Mathematical models, describing the cardiovascular system during exercise, have been developed to understand exercise physiology and investigate etiology of HR response [1, 3].

A major challenge of cardiac rehabilitation is the design of optimal exercise protocol for patients in different conditions, in order to maintain the HR at desired levels. Several control strategies have been proposed, including PID control [4] and model reference control [5]. However, most of these control methods are based on linear models of the HR response during exercise, which cannot provide an optimal exercise protocol, due to the nonlinear characteristic of HR response [6]. It is useful to optimize the exercise protocol and study the control of HR response with nonlinear models.

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Model uncertainty is another challenge for the design and control of HR. Such an uncertainty may originate from model calibration using noisy data or may result from variability of individual patients such as cardiovascular fitness. To improve the reliability and accuracy of model-based control design, it is necessary to account for uncertainty and evaluate its effect on HR during exercise. Monte Carlo (MC) simulations-based uncertainty analysis is one of the most popular techniques, but MC is computationally demanding, since it generally requires many simulation-runs to obtain an accurate result. Recently, the generalized polynomial chaos (gPC) expansion has been studied by a few authors in different disciplines [7, 8, 9], which can provide a probabilistic description of uncertainty and its effect on model predictions such as HR [10].

This paper aims to design an optimal exercise protocol via robust control of HR with nonlinear model in the presence of parametric uncertainty. A probabilistic approach is developed to optimize treadmill speed, which can find a tradeoff between maximizing the exercise outcome and minimizing the slow-acting effects on individual patients. The paper is organized as follows. In Section II, the non-linear dynamic models of HR response and the theoretical background of gPC are given. A nonlinear optimization problem for treadmill speed design is presented in Section III, followed by results in Section IV and a brief conclusion in Section V.

II. THEORETICAL BACKGROUND

A. Nonlinear models of human heart rate response

The deterministic nonlinear state space model of the HR response during treadmill exercise is described as [1]:

$$\dot{x}_1 = -a_1 x_1 + a_2 x_2 + a_6 u^2 \tag{1.a}$$

$$\dot{x}_2 = -a_3 x_2 + \phi(x_1) \tag{1.b}$$

$$HR(t) = 4.0 x_1 + HR_{rest} \tag{1.c}$$

where the initial condition is defined as $x_1(0) = x_2(0) = 0$, and the function $\phi(\cdot)$ is given as follows:

$$\phi(x_1) = \frac{a_4 x_1}{1 + \exp(-(x_1 - a_5))} \tag{1.d}$$

The HR_{rest} is the resting HR response and equals to 74 *bpm* (beats per minute) in this current work. The input u is the speed of the treadmill in *km*/*h* that needs to be adjusted so that the output $HR(t)$ matches a desired HR response. The variable x_1 describes the change in HR due to Rehab exercise. The second variable x_2 is used to describe the complex slow-acting effects, including hormonal systems, peripheral local metabolism, and dehydration. For example, the accumulation of metabolic byproducts in the case of peripheral local metabolism, e.g., K^+, H^+, PO_4^{3-}, lactic acid, and other metabolites, can cause the vasodilatation and hyperemia in muscles [11]. This will cause a reduction in total peripheral resistance that further induces a decrease in arterial blood pressure. To adjust blood pressure, cardiac outputs need to be increased, which means that the stroke volume and HR will be increased via the baroreceptor reflex [12]. Consequently, variable x_2, e.g., the metabolites from peripheral local metabolisms, can affect the HR during exercise. Parameters in (1) can be calibrated with parameter estimation technique such as Levenberg-Marquardt [1]. Table I shows the calibration results, where the mean value of $\hat{a}_i$, and the standard deviation $\delta\hat{a}_i$ (δ=0.05) are given. The confidence interval of a parameter $\hat{a}_i$ is defined as $[\hat{a}_i - \delta\hat{a}_i, \hat{a}_i + \delta\hat{a}_i]$).

TABLE I. ESTIMATION OF PARAMETERS AND THEIR UNCERTAINTY (CONFIDENCE INTERVAL=$[\hat{a}_i - \delta\hat{a}_i, \hat{a}_i + \delta\hat{a}_i]$)

Para	$\boldsymbol{a_1}$	$\boldsymbol{a_2}$	$\boldsymbol{a_3}$	$\boldsymbol{a_4}$	$\boldsymbol{a_5}$	$\boldsymbol{a_6}$
$\hat{a}_i$	1.84	24.32	6.36×10^{-2}	3.21×10^{-3}	8.32	0.38
$\delta\hat{a}_i$	0.36	4.36	1.95×10^{-2}	6.84×10^{-4}	0.44	0.019

B. Sensitivity analysis with Sobol index

Some parameters in the HR model may have significant effect on model predictions. The Sobol sensitivity index is first used to identify these parameters [13], which is a fractional contribution of the variance in HR. This calculates the *total sensitivity index* that measures the main effects of a given parameter and all the interactions involving this parameter. For instance, if three parameters are studied, i.e., a_1, a_2, and a_3. The *total effect* of a_1 on HR, i.e., y=x_1, is calculated as:

$$S_{T_{a_1}} = S_{a_1} + S_{a_1,a_2} + S_{a_1,a_3} + S_{a_1,a_2,a_3} \quad (2)$$

where $S_{T_{a_1}}$ is the total sensitivity index (*total effect*) of a_1, S_{a_1} is the 1st order sensitivity index (*main effect*), S_{a_1,a_2} and S_{a_1,a_3} are the 2nd order sensitivity index. The 3rd order sensitivity index S_{a_1,a_2,a_3} defines the interaction among all parameters.

To quantify the effect of parametric uncertainty on HR, i.e., y=x_1 in (1), the sensitivity index can be calculated as:

$$v = V_{p_i}[E(y|a_i)]/V(y) \quad (3)$$

where $a_i$is the i^{th} parameter, $E(y|a_i)$ is the mean value of y conditioned on a_i, and $V(y)$ is the total variance in HR.

Sobol sensitivity analysis uses decomposition of variance to compute sensitivity indices. The key is to rewrite the output $y = f(\boldsymbol{a})$ into summands of variance with combinations of $\{a_i\}$ in an increasing dimensionality, where $\boldsymbol{a}$ is a vector of parameters, $\boldsymbol{a}$=$\{a_i\}(i = 1,\cdots,k)$. The output is defined as:

$$f(\boldsymbol{a}) = f_0 + \sum_{i=1}^{k} f_i(a_i) + \sum_{i<j}^{k} f_{ij}(a_i,a_j) + \cdots + f_{1,\cdots,k}(a_1,\cdots,a_k) \quad (4)$$

where f_0 is a constant, and can be calculated as:

$$f_0 = \int_{\Omega^k} f(\boldsymbol{a})\, d\boldsymbol{a} \quad (5)$$

where Ω^k is a k-dimensional parameters space defined by $\boldsymbol{a}$. The total variance can be calculated as:

$$V = \int_{\Omega^k} f^2(\boldsymbol{a})\, d\boldsymbol{a} - f_0^2 \quad (6)$$

Based on (6), the total variance can be decomposed in a similar way as done for the model output in (4), which gives:

$$V(y) = V = \sum_{i}^{k} V_i(a_i) + \sum_{i<j}^{k} V_{ij}(a_i,a_j) + \cdots + V_{1,\cdots,k}(a_1,\cdots,a_k) \quad (7)$$

where

$$V_i = V_{a_i}(E_{a\sim i}(y|a_i)); \quad (8)$$

$$V_{ij} = V_{a_i a}(E_{a\sim ij}(y|(a_i,a_j))) - V_{a_i}(E_{a\sim i}(y|a_i) - V_{a_j}(E_{a\sim j}(y|a_j)); \ldots\ldots \quad (9)$$

In (8) and (9), $V_{(*)}$ is the variance, E is the mean value, and $a{\sim}i$ denotes all parameters except a_i. Analogously, as done in (3), the *main effect* S_{a_i} for the *i^th^* parameter is calculated as:

$$S_{a_i} = V_{a_i}/V \quad (10)$$

where S_{a_i} is the *main effect* of the i^{th} parameter. The *total effect* can be estimated with (2), representing the *main effect* plus higher order effect due to interactions. Sobol sensitivity indices, e.g., the *main effect* and *total effect*, are approximated using techniques such as Monte Carlo (MC) simulations [14].

C. Generalized polynomial chaos expansion

The generalized polynomial chaos (gPC) approximates an uncertain parameter as another random variable with a prior distribution. Let define the nonlinear HR model as:

$$\dot{\boldsymbol{x}} = f(t,\boldsymbol{x},\boldsymbol{\theta},\boldsymbol{p}) \quad (11)$$

where $\boldsymbol{x}$ contains HR change and slow-acting effects with an initial value of $\boldsymbol{x}_0$, $\boldsymbol{\theta}$ is a vector of fixed parameters, and $\boldsymbol{p}$ is uncertain parameters. To propagate the effect of $\boldsymbol{p}$ onto $\boldsymbol{x}$, each parameter p_i (i=1,2,…,n_p) in $\boldsymbol{p}$ is approximated with a random variable from $\boldsymbol{\xi} = \{\xi_i\}$ as:

$$p_i = p_i(\xi_i) \quad (12)$$

where ξ_i is the i^{th} random variable. Based on the gPC theory, both $\boldsymbol{p}$ and $\boldsymbol{x} = \{x_j\}$ can be estimated with a set of orthogonal polynomial basis functions $\Phi_j(\boldsymbol{\xi})$ as:

$$p_i(\xi_i) = \sum_{k=0}^{\infty} \hat{p}_{i,k}\Phi_k(\xi_i) \approx \sum_{k=0}^{q} \hat{p}_{i,k}\Phi_k(\xi_i) \quad (13)$$

$$x_j(t,\boldsymbol{\xi}) = \sum_{k=0}^{\infty} \hat{x}_{j,k}(t)\Phi_k(\boldsymbol{\xi}) \approx \sum_{k=0}^{Q} \hat{x}_{j,k}(t)\Phi_k(\boldsymbol{\xi}) \quad (14)$$

where $\hat{p}_{i,k}$ and $\hat{x}_{j,k}$ are the gPC coefficients, and $\{\hat{p}_{i,k}\}$ are calculated such that $p_i(\xi_i)$ follows a prior distribution of p_i. Coefficients $\{\hat{x}_{j,k}\}$ are calculated with nonlinear models (1) and a Galerkin projection [10], by projecting (1.a) and (1.b) onto each one polynomial chaos basis function $\{\Phi_k(\boldsymbol{\xi})\}$ as:

$$\langle \dot{\boldsymbol{x}}, \Phi_k(\boldsymbol{\xi})\rangle = \langle f(t,\boldsymbol{x})(t,\boldsymbol{\xi}), \boldsymbol{p}(\boldsymbol{\xi}), \Phi_k(\boldsymbol{\xi})\rangle \quad (15)$$

For practical application, (13) is often truncated to a finite number of terms, i.e., q. Hence, the total number of terms in (14) can be approximated as a function of an arbitrary order q in (13) that is necessary to estimate a priori known distribution of $\boldsymbol{p}$ and the number (n_p) of uncertain parameters in $\boldsymbol{p}$ as:

$$Q = ((n_p + q)!/(n_p!\,q!)) - 1 \quad (16)$$

As seen in (16), the number of terms Q in (14) increases as the q and/or n_p increases. Also, the inner product between two vectors in (15) is defined as:

$$\langle \psi(\boldsymbol{\xi}), \psi'(\boldsymbol{\xi})\rangle = \int \psi(\boldsymbol{\xi}), \psi'(\boldsymbol{\xi})W(\boldsymbol{\xi})d\boldsymbol{\xi} \quad (17)$$

where the integration is calculated over the entire domain of $\boldsymbol{\xi}$, and $W(\boldsymbol{\xi})$is the weighting function, i.e., probability density function (PDF) of $\boldsymbol{\xi}$. Once the coefficients of gPC expansion in (14) are available, it is possible to rapidly compute statistical moments of $\boldsymbol{x}$ at time t as a function of $\{\hat{x}_{j,k}\}$ as:

$$E\left(x_j(t)\right) = E\left(\sum_{i=0}^{Q} \hat{x}_{j,i}(t)\phi_i\right) = \hat{\boldsymbol{x}}_{j,i}(t)E(\phi_i) + \sum_{i=1}^{Q} E(\phi_i) = \hat{\boldsymbol{x}}_{j,0}(t) \tag{18}$$

$$\begin{aligned} Var\left(x_j(t)\right) &= E\left(x(t) - E\left(x_j(t)\right)^2\right) \\ &= E\left(\left(\sum_{i=0}^{Q} \hat{x}_{j,i}(t)\phi_i - \hat{x}_{j,(i=0)}(t)\right)^2\right) \\ &= E\left(\left(\sum_{i=0}^{Q} \hat{x}_{j,i}(t)\phi_i\right)^2\right) = \sum_{i=0}^{Q} \hat{x}_{j,i}(t)^2\, E(\phi_i^2) \end{aligned} \tag{19}$$

From (18) and (19), the mean of $\boldsymbol{x}$ in (1.a) can be calculated with gPC coefficient $\hat{x}_{j,k=0}$, while the higher order statistical moment, e.g., variance, is computed with other coefficients. Also, the PDFs of $\boldsymbol{x}(t)$ can be approximated by sampling from the prior distribution of $\boldsymbol{\xi}$, and substituting samples into (14). The gPC coefficients ensure the rapid calculation of PDF of $\boldsymbol{x}$, thus reducing the computational burden for the optimization-based control design of treadmill speed as discussed below.

III. Treadmill Speed Control Design

A. Treadmill speed control via optimization

Using statistical moments of $\boldsymbol{x}$ calculated with (18) and (19), the treadmill speed design can be formulated as follows. Consider a time index set $\daleth = \{1, 2, \cdots t_k\}$, an optimal speed sequence $u^* := [u_1, u_2, \cdots u_k]^\daleth$ that finds a tradeoff between maximizing exercise objective and minimizing the slow-acting effects at time instant t_k can be defined as:

$$\begin{aligned} u^* := \underset{u^*}{\arg\min} \quad \{ & \omega_1 \sum_{i=1}^{t_f} \left(x_{1,m}(i) - x_{1,ref}\right)^2 \\ & + \omega_2 \sum_{i=1}^{t_f} x_{1,v}(i) + \omega_3 \sum_{i=1}^{t_f} \left(x_{2,m}(i)\right. \\ & \left. - x_{2,max}\right)^2 + \omega_4 \sum_{i=1}^{t_f} x_{2,v}(i) \} \end{aligned} \tag{20}$$

where $x_{1,m}$ is the mean value of HR in (1.a) over time index set $\daleth$, $x_{1,ref}$ is the desired HR which is a given prior, $x_{1,v}$ is the variance of predicted HR, $x_{2,max}$ is the allowed maximum slow-acting effects such as dehydration, $x_{2,v}$ is the variability of slow-acting effects, $\{\omega_{i=1,\cdots,4}\}$ are weights that penalize the contribution of each term to the total cost, and $t_f \in \daleth$. Note that all quantities are calculated with gPC coefficients of $\boldsymbol{x}$.

B. Constraints for optimization defined in (20)

The optimization problem (20) is evaluated over the time index set $\daleth$. In addition, absolute value function constraints are applied to decision variable (i.e., speed of treadmill) and model responses (i.e., HR change and slow-acting effects).

Using the gPC coefficients, it is possible to compare the PDF of model outputs, e.g., x_1, at different time instant in $\daleth$. The overlap can be used as an indicator to determine if model predictions have significantly changes. For example, if the overlap is very large, see Fig.1 (b), it can be assumed that the treadmill speed and uncertainty have not significantly affect HR. Thus, the speed can be further changed, vice-versa if the overlap is very small, see Fig. 1 (b). For simplicity, heuristic approach is used to introduce constraints in (20).

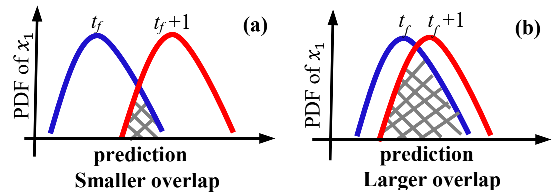

Figure 1. Demonstration of optimzation constraints

To avoid dramatic changes in treadmill speed, absolute values constraints are used for HR x_1. For two consecutive time instants, t_k and t_{k+1}, the PDFs of x_1 at t_k and t_{k+1} can be estimated with the gPC theory. Let assume the allowable changes in speed as $\Delta \mathrm{u}_{t_k,t_{k+1}}$, then constraints is expressed as: $\left|\Delta \mathrm{u}_{t_k,t_{k+1}}\right| \le \mu A$, where μ is a tuning factor to manipulate the allowable change, and A denotes the overlap. Also, hard speed constraints of treadmill can be used to ensure exercise safety.

IV. Results and Discussion

A. Parametric Uncertainty Screening with Sobol Index

To elaborate the effects of parametric uncertainty on model predictions, perturbations were used in parameters in Table I. For each parameter, 100 samples were randomly generated from a confidence region of $[\hat{a}_i - \delta\hat{a}_i, \hat{a}_i + \delta\hat{a}_i])$ to calculate the *main* and *total effect*. Based on the Sobol indices, the half-normal probability diagram [15] was used to show the effect of uncertainty on HR, which can be computed as:

$$\left[\Phi^{-1}\left(0.5 + \frac{0.5[i - 0.5]}{k}\right), \varepsilon_{a_i}\right] \tag{21}$$

where i=1,⋯,6 is the index of a_i in Table I, Φ^{-1} is the inverse of the cumulative distribution function of normal distribution, $\{\varepsilon_{a_i}\}$ is the *main* or *total effect* of each parameter from Sobol analysis. Fig. 2 shows the *total effect* of uncertainty on HR x_1 in (1.a). As seen, it was found that the *total effect* of a_1 has considerable influence on x_1 compared to other parameters. Thus, a_1 was chosen as the most sensitive uncertainty in this work. It is worth mentioning that same results were observed for slow-acting variable x_2, but the result is not shown.

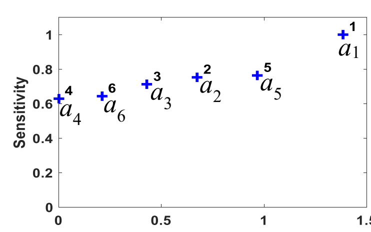

Figure 2. Half-normal plot of the total effects of model parameters on HR response (x_1)

B. Generation of gPC model for Optimization

The inner product in (17) is possible for monomial or polynomial terms, but approximation is needed, when the model is non-monomial, e.g., the nonlinear function $\phi(x_1)$ in (1.d). Note that $\phi(x_1)$ is approximately zero when x_1 is small, whereas $\phi(x_1)$ can be defined with a linear function, i.e., $a_4 x_1$. Thus, a piecewise function is used to approximate $\phi(x_1)$ to facilitate rapid calculations of gPC coefficients.

$$\phi(x_1) = \begin{cases} 0.01 a_4 x_1 & x_1 < 5 \\ a_4 x_1 (0.16 x_1 - 0.45) & 5 \leq x_1 \leq 10 \\ a_4 x_1 & x_1 > 10 \end{cases}$$

C. Treadmill Speed Control Design

Consider parameter a_1 as the uncertainty, for any specific time index set $\daleth = \{1, 2, \cdots\ t_k\}$, the cost in (20) is minimized with respect to the treadmill speed. In this case study, hard speed constraints are applied to the treadmill speed, i.e., the speed can be varied within 2 km/h and 7 km/h. For the absolute value constraints, μ is 0.1, and equal weights are used in (20).

TABLE II. EVALUATION OF CONTROL PERFORMANCE

Control strategy	***Speed*** (km/h)	***Cost***	***Variability***
Without optimization	5	1029	8.32
Optimization (k =100)	4.8432	4.04	2.13
Optimization (k =20)	3.2289	1.22	0.44

Table II shows the results for three speed control strategies. In the first case study, a constant speed (i.e., 5 km/h) was used, while the optimization (20) was used in the second and third case studies. For the second case study, 100 time instants were used, i.e., k =100, whereas k is 20 in the third case study. For comparison, the cost in (20) and the variability in slow-acting effect x_2 were calculated. As seen in Table II, in the presence of uncertainty in a_1, the improvement with optimization (20) is significant. Also, it was found that when a smaller number of time instants was used in $\daleth$, the speed obtained from (20) is smaller, since the variability in slow-acting effect is smaller when the speed is lower. The reduced speed will increase the exercise time, thus increases the contribution of the first term in (20) to the total cost. This shows the tradeoff between the exercise objective and the slow-acting effects.

C. Computational Efficiency

As aforementioned, model uncertainty is inevitable due to intrinsic variability resulting from individual patients. Since the objective here is to extend the proposed method to online tuning of treadmill speed for each patient, it is important to assess the computational cost. The optimization problem (20) can be solved with Monte Carlo (MC) simulations. It was found that the optimization of (20) can be finished in ~1-2 seconds with the gPC model on an Intel Core i7 desktop and the search of optimum was completed approximately with 50-60 evaluations. On the other hand, using MC simulations, about 1 min was required to evaluate (20) with 100 samples of uncertain parameter a_1. Thus, 50-60 function evaluations of (20) may take about an hour, which is significantly higher, as compared to the proposed gPC-based optimization.

V. CONCLUSION

A gPC expansion-based method is proposed to propagate uncertainty in model parameter onto an objective function of a robust optimization problem, which can be used to control the speed of treadmill during exercise of rehabilitation. The proposed method is proved to be more efficient than Monte Carlo simulations-based method, thus making it is attractive for online control of treadmill speed. In addition, the method can be applied to more complicated model of the heart rate (HR) response, where more than more or even all parameters are uncertain. However, this is left for further work.

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