Control Mechanism Modeling of Human Cardiovascular-Respiratory System

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Outline

- Mathematical modeling of cardiovascular and respiratory systems
- Problem formulation of cardiorespiratory control mechanism
- Proposed optimal control algorithm
- Experimental results
- Conclusions

Introduction

- Noncommunicable diseases like cardiovascular and respiratory diseases are one of the major leading causes of death in the world.
- Mathematical models of the underlying physiological systems will greatly help in providing more diagnostic information.
- They quantify the complex interactions between several systems, and can be used to predict certain diseases in advance which alter the normal system function.

Related Work

- Grodins models the cardiovascular system using a feedback regulator.[1]
  - The cardiovascular system is divided into two subsystems: a controlling system (containing medullary cardiac and vasomotor centers, and endocrine glands which operate on the heart and blood vessels) and a controlled system (containing mechanical and gas exchange elements).
- Guyton *et al.* develop a system model of the circulatory regulation by dividing the circulatory system into 18 major subsystems such as circulatory dynamics, capillary membrane dynamics, pulmonary dynamics, vascular stress relaxation, etc.[2]

[1] F. S. Grodins, "Integrative cardiovascular physiology: a mathematical synthesis of cardiac and blood vessel hemodynamics," *The Quarterly Review of Biology*, vol. 34, no. 2, pp. 93-116, 1959.

[2] A. C. Guyton, T. G. Coleman, and H. J. Granger, "Circulation: overall regulation," *Annual Review of Physiology*, vol. 34, pp. 13-46, 1972.

Related Work

- Kappel and Peer develop a model of the response of the cardiovascular system to constant workload on a person after a period of complete rest.[3]
  - In this process, the baroreceptor control loop plays a central role. This local control mechanism is modeled using the four compartment model of the cardiovascular system.
- Aittokallio *et al.* develop a model of the respiratory control system, which describes the gas exchange between pulmonary blood, tissue capillary blood, venous blood and tissue compartments.[4]

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[3] F. Kappel and R. O. Peer, "A mathematical model for fundamental regulation processes in the cardiovascular system," *Journal of Mathematical Biology*, vol. 31, pp. 611-631, 1993.

[4] T. Aittokallio, M. Gyllenberg, O. Polo, and A. Virkki, "Parameter estimation of a respiratory control model from noninvasive carbon dioxide measurements during sleep", *Mathematical Medicine and Biology*, vol. 24, no. 2, pp. 225-249, 2007.

Related Work

- Batzel *et al.* model the cardiovascular-respiratory control system with transport delays.[5]
  - The cardiovascular and respiratory control systems are modeled by a linear negative feedback control which minimizes a quadratic cost function denoting an optimal system performance.

[5] J. J. Batzel, S. Timischl-Teschl, and F. Kappel, "A cardiovascular-respiratory control system model including state delay with application to congestive heart failure in humans", *Journal of Mathematical Biology*, vol. 50, no. 3, pp. 293-335, 2005.

Proposed Model

- Local control mechanisms (baroreceptor control loop and respiratory control loop) play a key role in stabilizing the cardiovascular-respiratory system under different conditions.
- Here, we focus on modeling these control mechanisms as the human body goes from awake state to stage 4 non-REM sleep state.
- We formulate this mechanism as an optimal control problem.

Proposed Model

- Limitations of existing models:
  - The cardiovascular-respiratory system model is nonlinear. Batzel *et al.* solve this optimal control problem by linearizing the system at the final sleep steady state.
  - However, linearizing the system at just one point is not optimal. Moreover, it is difficult to know the final sleep steady state values of all the states in practice.
- Challenges:
  - The system model is nonlinear and involves time delay.

Our Approach

- We propose an iterative algorithm to solve the optimal control problem.
- We initially start with a nominal state and input sequences, and iteratively update these sequences to get the final optimal sequences.
- In each iteration, the system is linearized with the sequences obtained from the previous iteration. Using the linearized system, we formulate the optimal control problem as a convex optimization problem and solve it using interior-point methods.

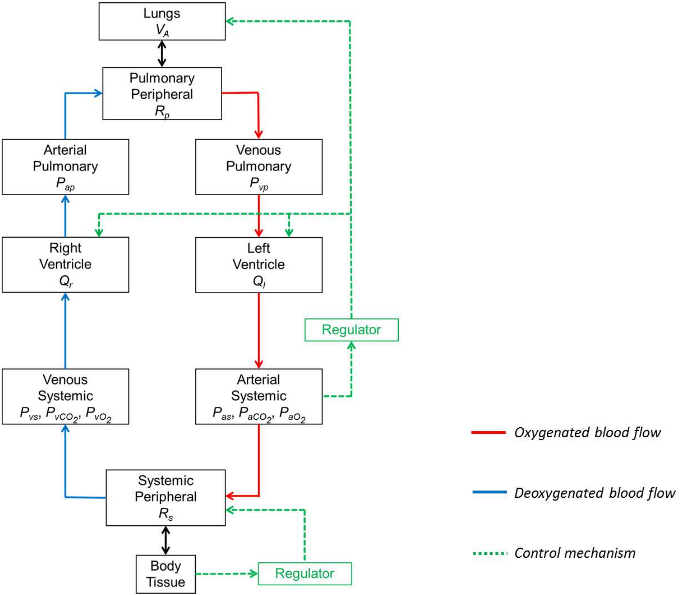
Cardiorespiratory System Model

- We adopt the cardiovascular-respiratory system model used by Batzel *et al.* [5].
- The model is described by a set of 13 delay differential equations. The delay represents the transport delay between the cardiovascular and respiratory systems.
- The model has 13 state variables and 2 control input variables:

$$\begin{aligned}\mathbf{x}(t) = [&P_{aCO_2}(t), P_{aO_2}(t), C_{vCO_2}(t), C_{vO_2}(t), P_{as}(t), P_{vs}(t),\\ &P_{vp}(t), S_l(t), S_r(t), \sigma_l(t), \sigma_r(t), H(t), \dot{V}_A(t)]^T,\\ \mathbf{u}(t) = [&\dot{H}(t), \ddot{V}_A(t)]^T.\end{aligned}$$

- The transition from an awake state to stage 4 non-REM sleep state can be modeled by stabilizing P_{aCO_2}, P_{aO_2}, and P_{as} states.

Model Block Diagram



Optimal Control

- We formulate the optimal control problem that transfers the cardiorespiratory system from awake to sleep steady states as,

$$\mathbf{u}^{\star}(t) = \arg\min_{\mathbf{u}} \int_{t_0}^{t_f} \Big(q_1(x_1(t)-\bar{x}_1)^2 + q_2(x_2(t)-\bar{x}_2)^2 + q_5(x_5(t)-\bar{x}_5)^2 + r_1 u_1^2(t) + r_2 u_2^2(t) \Big)\, dt,$$

subject to the system model:

$$\dot{x}_i(t) = F_i(\mathbf{x}(t), \mathbf{x}(t-\tau)) + \mathbf{b}_i^T\, \mathbf{u}(t), \quad t \in [t_0, t_f],$$
$$\mathbf{x}(t) = \mathbf{x}_0(t), \quad t \in [t_0-\tau, t_0],$$
$$\mathbf{u}(t) \leq \mathbf{0},$$

where $i = 1, 2, ..., 13$, $\bar{x}_i$ is the final steady state value of state i, $\mathbf{x}_0(t)$ is the given initial history, q_i and r_j's are positive coefficients that assign weight to the state and input terms in the above cost function.

Discrete-time Optimal Control

- For ease of optimization, we first discretize the system using the first-order Euler approximation as,

$$\begin{aligned} x_i[k+1] &= g_i\left(\mathbf{x}[k], \mathbf{x}[k-a], \mathbf{u}[k]\right) \\ &= x_i[k] + h\, F_i\left(\mathbf{x}[k], \mathbf{x}[k-a]\right) + h\, \mathbf{b}_i^T\, \mathbf{u}[k]. \end{aligned}$$

- Using this discrete-time system, we reformulate the optimal control problem as,

$$\begin{aligned} \min_{\mathbf{U}} \quad & \sum_{k=0}^{N-1} \left(\mathbf{x}[k] - \bar{\mathbf{x}}\right)^T \mathbf{Q}_0 \left(\mathbf{x}[k] - \bar{\mathbf{x}}\right) + \mathbf{u}[k]^T \mathbf{R}_0 \mathbf{u}[k] \\ & + \left(\mathbf{x}[N] - \bar{\mathbf{x}}\right)^T \mathbf{Q}_0 \left(\mathbf{x}[N] - \bar{\mathbf{x}}\right) \\ \text{s.t.} \quad & \mathbf{x}[k+1] = \mathbf{g}\left(\mathbf{x}[k], \mathbf{x}[k-a], \mathbf{u}[k]\right), \quad \mathbf{u}[k] \leq \mathbf{0}, \end{aligned}$$

where $N = \frac{t_f - t_0}{h}$, $\mathbf{U} = \{\mathbf{u}[0], \mathbf{u}[1], ..., \mathbf{u}[N-1]\}$ is the optimal control input sequence, $\bar{\mathbf{x}} = [\bar{x}_1, \bar{x}_2, 0, 0, \bar{x}_5, 0, ..., 0]^T$, $\mathbf{Q}_0$ is a 13×13 diagonal matrix with $[q_1, q_2, 0, 0, q_5, 0, ..., 0]^T$ as its main diagonal, and $\mathbf{R}_0$ is a 2×2 diagonal matrix with $[r_1, r_2]^T$ as its main diagonal.

State Augmentation

- We further convert the higher order difference equations into first-order difference equations by augmenting the states $\{\mathbf{x}[k], \mathbf{x}[k-1], ..., \mathbf{x}[k-a]\}$ to construct a new state vector as,

$$\mathbf{z}[k] = \left[\mathbf{x}[k]^T, \mathbf{x}[k-1]^T, ..., \mathbf{x}[k-a]^T\right]^T.$$

- With this new state vector, the system can be written as,

$$z_i[k+1] = f_i\left(\mathbf{z}[k], \mathbf{u}[k]\right) = g_i\left(\mathbf{z}[k], \mathbf{u}[k]\right), \ \ i = 1, 2, ..., 13,$$
$$z_i[k+1] = f_i\left(\mathbf{z}[k], \mathbf{u}[k]\right) = z_{i-13}[k], \ \ i = 14, ..., 13(a+1).$$

Iterative Linear Quadratic Regulator

- The constraint, $\mathbf{z}[k+1] = \mathbf{f}\left(\mathbf{z}[k], \mathbf{u}[k]\right)$, is nonlinear. This makes the optimal control problem nonconvex.
- For Iteration 0, set initial nominal sequences $\mathbf{u}_0[k]$ and $\mathbf{z}_0[k]$. The system is first linearized around these nominal sequences as,

$$\delta\mathbf{z}[k+1] = \mathbf{A}_k\, \delta\mathbf{z}[k] + \mathbf{B}_k\, \delta\mathbf{u}[k],$$

  where $\delta\mathbf{z}[k] = \mathbf{z}[k] - \mathbf{z}_0[k]$, $\delta\mathbf{u}[k] = \mathbf{u}[k] - \mathbf{u}_0[k]$, $\mathbf{A}_k = \nabla_{\mathbf{z}}\, \mathbf{f}\left(\mathbf{z}_0[k], \mathbf{u}_0[k]\right)$ and $\mathbf{B}_k = \nabla_{\mathbf{u}}\, \mathbf{f}\left(\mathbf{z}_0[k], \mathbf{u}_0[k]\right)$.

Optimal Control Problem

- We reformulate the optimal control problem as,

$$\begin{aligned}\min_{\delta\mathbf{U}} \quad \tilde{J} = \sum_{k=0}^{N-1} \frac{1}{2}\left(\delta\mathbf{z}[k]-\delta\bar{\mathbf{z}}[k]\right)^T\mathbf{Q}\left(\delta\mathbf{z}[k]-\delta\bar{\mathbf{z}}[k]\right) \\ +\frac{1}{2}\left(\delta\mathbf{u}[k]-\delta\bar{\mathbf{u}}[k]\right)^T\mathbf{R}\left(\delta\mathbf{u}[k]-\delta\bar{\mathbf{u}}[k]\right) \\ +\frac{1}{2}\left(\delta\mathbf{z}[N]-\delta\bar{\mathbf{z}}[N]\right)^T\mathbf{Q}\left(\delta\mathbf{z}[N]-\delta\bar{\mathbf{z}}[N]\right) \\ \text{s.t.} \quad \delta\mathbf{z}[k+1] = \mathbf{A}_k\,\delta\mathbf{z}[k]+\mathbf{B}_k\,\delta\mathbf{u}[k], \\ \mathbf{u}_0[k]+\delta\mathbf{u}[k]\leq \mathbf{0},\end{aligned}$$

where $\delta\bar{\mathbf{z}}[k] = \bar{\mathbf{z}} - \mathbf{z}_0[k]$, $\delta\bar{\mathbf{u}}[k] = -\mathbf{u}_0[k]$, and $\delta\mathbf{U} = \{\delta\mathbf{u}[0], \delta\mathbf{u}[1], ..., \delta\mathbf{u}[N-1]\}$.

- We use interior-point methods to solve the above convex problem.

Nominal Sequences Update

- After computing the optimal $\delta\mathbf{u}[k]$, we update the nominal input sequence as,

$$\mathbf{u}[k] = \mathbf{u}_0[k] + \delta\mathbf{u}[k], k = 0, 1, ..., N-1.$$

- To update the nominal state sequence, we simulate the nonlinear system, $\mathbf{z}[k+1] = \mathbf{f}\left(\mathbf{z}[k], \mathbf{u}[k]\right)$, with the above updated nominal input sequence.

Optimal Control Algorithm

- Initialize: $\mathbf{u}_{(0)}[k] = \mathbf{0}$, $\mathbf{z}_{(0)}[k+1] = \mathbf{f}\left(\mathbf{z}_{(0)}[k], \mathbf{u}_{(0)}[k]\right)$, $k = 0, 1, ..., N-1$.

repeat

Find the optimal $\delta\mathbf{u}[k]$.

Input update: $\mathbf{u}_{(i)}[k] = \mathbf{u}_{(i-1)}[k] + \delta\mathbf{u}[k]$.

State update: $\mathbf{z}_{(i)}[k+1] = \mathbf{f}\left(\mathbf{z}_{(i)}[k], \mathbf{u}_{(i)}[k]\right)$.

until

$||J_{(i)} - J_{(i-1)}||_2 < \epsilon$

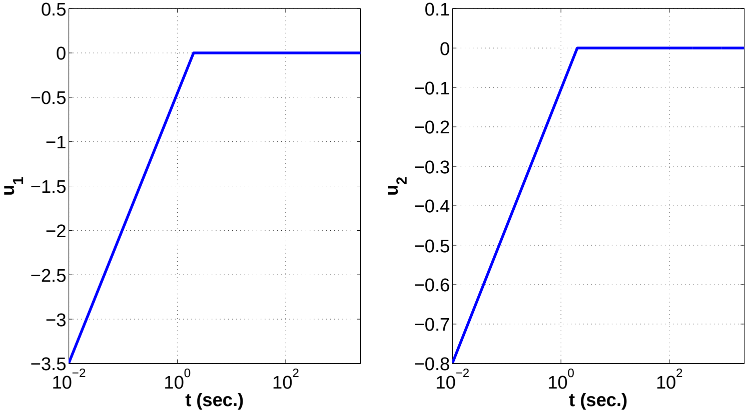
Experimental Results

- We first calculate the steady state values of all system states in both awake and sleep stages by running the discrete-time system for a long period of time with zero control inputs.

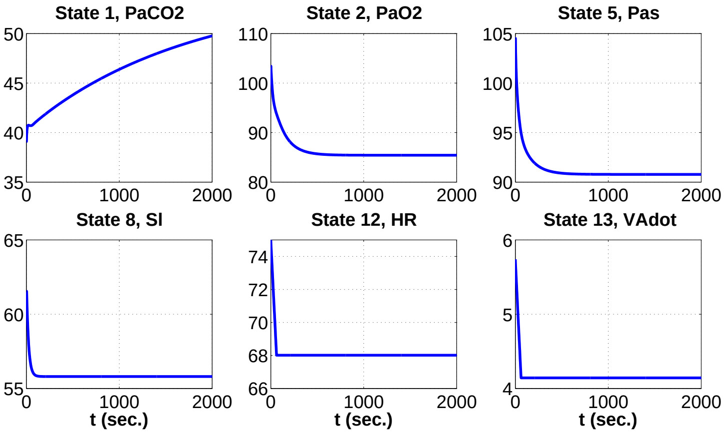
$$\bar{\mathbf{x}}_a = [39.0974, 103.4, 0.5563, 0.1273, 104.5, 3.515, 7.857, 61.54, 4.691, 0, 0, 75, 5.736]^T,$$
$$\bar{\mathbf{x}}_s = [51.0767, 89.1, 0.6386, 0.1187, 91.23, 3.788, 7.742, 55.79, 4.253, 0, 0, 68, 4.392]^T.$$

- The transition of the cardiovascular-respiratory system from awake to sleep states is modeled by stabilizing the states $P_{aCO_2}(t)$, $P_{aO_2}(t)$, and $P_{as}(t)$ to their corresponding sleep steady state values: $\bar{x}_1 = 51.0767$, $\bar{x}_2 = 89.1$, $\bar{x}_5 = 91.23$.

Optimal Control Input Sequences

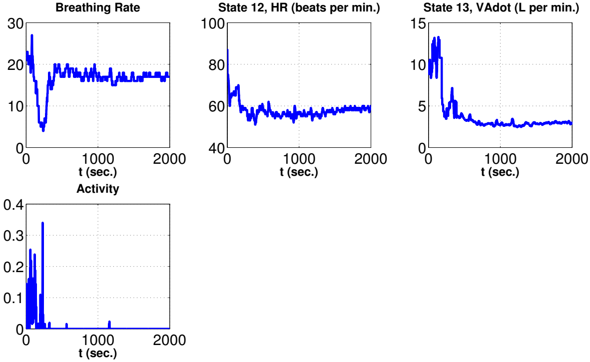


Optimal State Trajectories



Real State Trajectories

- To validate our simulation results, we collected real data from a healthy 25-year-old male subject using Hexoskin biometric smart shirt.
- The measured physiological signals of the subject during awake to sleep transition are shown below.



Conclusions

- In this paper, we studied how to model the control mechanism of the cardiovascular-respiratory system during the transition from an awake state to stage 4 non-REM sleep state.
- A cardiovascular-respiratory system model with transport delays is adopted.
- An iterative algorithm is proposed to find the optimal control inputs that drive the cardiovascular-respiratory system from awake state to sleep state.
- Simulation results show the effectiveness of the proposed method. The system states converge close to their sleep steady state values.
- Comparison with real physiological signals shows that the control mechanism model can catch the system dynamics of the subject from awake to sleep state.