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Eunok Jung
Konkuk University

Charles F. Babbs
Purdue University, babbs@purdue.edu

Suzanne Lenhart
University of Tennessee - Knoxville

Vladimir A. Protopoescu

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Eunok Jung, PhD[a], Charles F. Babbs, MD, PhD[b], Suzanne Lenhart, PhD[c], Vladimir A. Protopopescu, PhD[d]

[a] Department of Mathematics
Konkuk University
1 Hwayang-dong, Gwangjin-gu
Seoul 143-701, Republic of Korea

[b] Department of Basic Medical Sciences
Purdue University and Indiana University School of Medicine
1246 Lynn Hall
West Lafayette IN 47907-1246, USA

[c] Department of Mathematics
University of Tennessee
Knoxville TN 37996-1300, USA

[d] Oak Ridge National Laboratory
Computer Science and Mathematics Division
Oak Ridge TN 37831-6016, USA

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Address for correspondence and reprints:

Charles F. Babbs, MD, PhD
1426 Lynn Hall
Purdue University
West Lafayette IN 47907-1246, USA
E-mail: babbs@purdue.edu
Voice: 765-496-2661, Fax: 765-494-0781

ABSTRACT

Objective: To apply the mathematical techniques of optimal control theory (OCT) to a validated model of the human circulation during cardiopulmonary resuscitation (CPR), so as to discover improved waveforms for chest compression and decompression that maximize the systemic perfusion pressure (SPP). **Methods:** The human circulatory system is represented by seven difference equations, which describe the pressure changes in systemic vascular compartments caused by chest compression. The forcing term is the intrathoracic pressure generated by the external chest compression, which is taken as the "control" variable for the system. The optimum waveform of this forcing pressure as a function of time, determined from OCT, maximizes the calculated SPP between the thoracic aorta and the superior vena cava over a period of 13.3 sec of continuous chest compression under clinically realistic conditions. **Results:** The optimal waveform included both compression and decompression of the chest to the maximum allowable extent. Compression-decompression waveforms were rectangular in shape. The frequency of optimal compression-decompression was 90/min. The duty cycle (compression duration / cycle time) was 40 percent. The SPP for the optimum control waveform was 36 mmHg vs. 25 mmHg for standard CPR. **Conclusions:** OCT suggests that both compression and decompression of the chest are needed for best hemodynamics during CPR.

Key Words: ACD-CPR, Cardiopump®, decompression, duty cycle, impedance, heart arrest, hemodynamics

INTRODUCTION

External cardiopulmonary resuscitation (CPR) has not changed fundamentally since it was first introduced in the 1960's by Kouvenhoven, Jude, and Knickerbocker. Not surprisingly perhaps, survival rates from sudden cardiac death, treated with lay rescuer or professional rescuer CPR, have remained similarly stable, ranging from 2 to 5 percent for long term survival from out-of-hospital cardiac arrest in adults, and from 10 to 20 percent for long term survival from in-hospital cardiac arrest[1-3].

Over the past half century, the challenge of improving resuscitation success has attracted many investigators, who have proposed several modifications of conventional external CPR with three letter acronyms. These include SVC-CPR for simultaneous ventilation and compression[4], IAC-CPR for interposed abdominal compression[5,6], HIC-CPR for high impulse compression[7,8], ACD-CPR for active compression-decompression[9,10], and, more recently, CCC-CPR for continuous chest compression CPR without ventilation[11-13]. Although large numbers of patients are needed to achieve statistical significance when baseline survival rates are low[14], significant improvement in resuscitation success in humans across multiple studies has been demonstrated for three-rescuer IAC-CPR[15,16], and recently for standard CPR with an impedance threshold valve, designed to augment negative pressures in the chest between compressions, and thereby improve pump filling[17-19]. Such advances keep hope alive that improvement in resuscitation methods can indeed

translate to improved outcome. Thus the question of which technique of CPR is "optimal" remains an open and legitimate research problem.

A recent and rather radical proposal in basic cardiopulmonary resuscitation is the concept of chest compression only CPR, advocated by Hallstrom[13] in Seattle and by investigators at the University of Arizona[20,21] . According to this proposal, pauses in chest compression for rescue breathing in adult cardiac arrest victims may be unnecessary—or even harmful—if chest compressions are interrupted and all circulation stops. Advocates of this approach suggest that the paradigm of continuous chest compression and no formal ventilation produces sufficient motion of air in and out of the lungs for adequate oxygenation of the reduced volume of blood flowing through the lungs each minute during CPR. Continuous chest compression CPR is not only simple and easy to remember for lone rescuers; it also provides a more straightforward problem for theorists, since abrupt interruptions of chest compression for ventilation are not needed.

The objective of this paper is to offer a fresh, interdisciplinary approach to the problem of CPR optimization with continuous chest compressions, namely, the application of optimal control theory (OCT) to a model of the human cardiovascular system during cardiac arrest. OCT is a standard mathematical technique that can be applied to complex dynamical systems with known physical constraints, in order to specify a control variable that maximizes (or minimizes) a particular performance criterion for the system. OCT has been applied quite successfully to problems in economics, robotics, and space flight[22-26], but to the best of our knowledge has not been applied to CPR. In the present application the goal of OCT is to specify the "best waveform" for chest compression (or decompression) during CCC-CPR. By best waveform we mean the pattern of imposed intrathoracic pressure as a function of time that maximizes systemic blood flow during external chest compression and cardiac arrest. The optimal waveform could have any shape, any frequency, and could be symmetrical or asymmetrical. In this sense OCT is a very general and powerful method that is unbiased by conventional thinking. If OCT were applied to the problem of maximizing blood flow during CPR, it could provide results that would be hard to obtain by trial and error or by the synthesis of data from varying clinical and animal models in the relatively underfunded and challenging area of resuscitation research.

To apply OCT one must have a so-called "state space" model of the complex system to be controlled. Suitable models of the human cardiovascular system have been developed for studies of CPR[27], in which the instantaneous pressures in each vascular compartment describe the state of the system at any point in time. Difference equations can be written that define the rate of change of pressure in each compartment[27], thus setting the formal stage for use of OCT. The forcing function for the system is the force applied to the chest, which induces intrathoracic pressure variations. The physical constraints of the system include practical limits on the amount of positive and negative pressure that can be reasonably developed within the chest.

Now, what key variable in CPR needs to be optimized? There is good evidence that such a key physiologic predictor of resuscitation success is mean systemic perfusion pressure (SPP)[28-31] or specifically the thoracic aortic pressure minus the right atrial pressure,

averaged over the time steps in the resuscitation period. Assuming that SPP is a reasonable performance criterion for CPR, the problem is well set for application of OCT to determine the best possible waveform for chest compression.

Here we report the results of this interdisciplinary analysis. The results confirm the importance of generating some degree of negative intrathoracic pressure during the chest recoil phase of CPR. These theoretical results may help drive much-needed consensus toward genuinely optimal chest compression technique in external CPR.

METHODS

Mathematical model for optimal control

We apply the optimal control strategy for increasing blood flow to a validated model of the human circulation, developed by one of us[27] and illustrated in Figure 1. In this model, heart and blood vessels are represented as a network of resistances and compliances, the values of which are based upon normal human anatomy and physiology. The model describes the adult human circulation and can be represented by seven difference equations, with time as the discrete underlying variable. Assumptions of the model are minimal and include the definition of compliance (volume change / pressure change), and Ohm's Law (flow = pressure / resistance). As a control input, we chose the pressure waveform developed within the chest as a function of time caused by external compression or decompression by the rescuer. The pressure state variables are as follows:

P_1 pressure in abdominal aorta

P_2 pressure in inferior vena cava

P_3 pressure in carotid arteries

P_4 pressure in jugular veins

P_5 pressure in thoracic aorta

P_6 pressure in right heart and superior vena cava

P_7 pressure in thoracic pump (i.e. pulmonary vasculature and left heart).

The resistances between vascular compartments, R, and the compliances of vascular compartments, C, are defined in the legend of Figure 1. Time is discretized into small steps Δt. At step n, when elapsed time is $n\Delta t$, the pressure vector denoted by $P(n) = (P_1(n), P_2(n), \ldots$ describes all seven pressures in the system and therefore its state at time step, n. The "state space" for the model is the 7-dimensional space including all seven pressures at each point in time.

Using the definition of compliance and Ohm's law, as described in reference[27], one can describe the evolution of pressures within the system over time by a set of difference equations that give the time rate of change of pressure within each compartment as a function of all the other pressures. The difference equations for pressures read:

$$P_1(n+1) = P_1(n) + \Delta t \frac{1}{C_{aa}}\left[\frac{1}{R_a}(P_5(n) - P_1(n)) - \frac{1}{R_s}(P_1(n) - P_2(n))\right]$$

$$P_2(n+1) = P_2(n) + \Delta t \frac{1}{C_{ivc}}\left[\frac{1}{R_s}(P_1(n) - P_2(n)) - \frac{1}{R_v}(P_2(n) - P_6(n))\right]$$

$$P_3(n+1) = P_3(n) + \Delta t \frac{1}{C_{car}}\left[\frac{1}{R_c}(P_5(n) - P_3(n)) - \frac{1}{R_h}(P_3(n) - P_4(n))\right]$$

$$P_4(n+1) = P_4(n) + \Delta t \frac{1}{C_{jug}}\left[\frac{1}{R_h}(P_3(n) - P_4(n)) - \frac{1}{R_j}V(P_4(n) - P_6(n))\right]$$

$$P_5(n+1) = P_5(n) + f_p(u(n) - u(n-1)) +$$
$$\frac{\Delta t}{C_{ao}}\left[\frac{1}{R_o}V(P_7(n) - P_5(n)) - \frac{1}{R_c}(P_5(n) - P_3(n)) - \frac{1}{R_a}(P_5(n) - P_1(n)) - \frac{1}{R_{ht}}(P_5(n) - P_6(n))\right]$$

$$P_6(n+1) = P_6(n) + f_p(u(n) - u(n-1)) +$$
$$\frac{\Delta t}{C_{rh}}\left[\frac{1}{R_j}V(P_4(n) - P_6(n)) + \frac{1}{R_v}(P_2(n) - P_6(n)) + \frac{1}{R_{ht}}(P_5(n) - P_6(n)) - \frac{1}{R_i}V(P_6(n) - P_7(n))\right]$$

$$P_7(n+1) = P_7(n) + u(n) - u(n-1) + \frac{\Delta t}{C_p}\left[\frac{1}{R_i}V(P_6(n) - P_7(n)) - \frac{1}{R_o}V(P_7(n) - P_5(n))\right].$$

These equations are also referred to as the state equations. The numerical values of the various vascular resistances and compliances, *R* and *C*, are given in reference[27]. Note that the forgoing are linear equations except for the valve function *V,* which describes the action of the input (tricuspid) and output (aortic) values of the thoracic pump and of Niemann's venous valves in the internal jugular veins. Here V is defined as $V(s) = s$ if $s \geq 0$ and $V(s) = 0$ if $s \leq 0$. To be rigorous mathematically, one should approximate the valve function by a smooth function that is differentiable at zero. Such a smooth function would actually be more realistic from a mechanical/engineering standpoint than the idealized valve function.

The variable *u* is the control variable, or the "unknown" intrathoracic pressure that we wish to optimize. The increment in this forcing function *u(n) - u(n - 1)* is the amount that intrathoracic pressure is changed at teach time step as a result of chest compression. In principle, the intrathoracic pressure *u* may be the result of any conceivable manipulation, including compression or decompression of the chest, positive or negative pressure

ventilation, inflation and deflation of a balloon within the chest, or the action of an impedance threshold device[32].

The thoracic pump factor, f_p, allows one to model both the thoracic pump and cardiac pump mechanisms of blood flow during CPR. The thoracic pump mechanism moves blood through fluctuations in global intrathoracic pressure[33,34]. This mechanism is most prominent in adults. To model thoracic pump CPR the pressures in all intrathoracic compartments (the pump compliance, representing the heart and lungs, the thoracic aorta, and the right heart and thoracic venae cavae) are augmented by the full forcing pressure, $u(n) - u(n-1)$. That is, to model a pure "global" intrathoracic pressure pump $f_p = 1$.

Alternatively, the cardiac pump mechanism moves blood through compression of the cardiac ventricles only. This mechanism is most prominent in children. To model cardiac pump CPR pressure in the pressure in the central "pump" chamber only is augmented by the forcing pressure, and $f_p = 0$. In many persons a combination of cardiac pump and thoracic pump mechanisms is believed to operate[35-37]. To model this situation, the pressure in the chest pump is augmented by the full forcing pressure and the pressure in the thoracic aorta and vena cavae are augmented by a fraction $0 \le f_p \le 1$ of the forcing pressure. Here we shall use the thoracic pump factor $f_p = 0.75$, which represents the state of affairs in a typical adult resuscitation.

We use N time steps, ranging from 0 to $N-1$, and the initial data for pressures are entered at $n = 0$. Typically $P(0) = (P_1(0), P_2(0), \ldots$ is taken as 5 mmHg in all vascular compartments. Then we use the discrete evolution system above to construct a marching solution for successive small increments of time, Δt, typically 0.005 sec. Use of a time increment that is too coarse results in unstable oscillations of computed pressures; however, decreasing the value of Δt can restore stability.

The control set is:

$U = \{(u(0), u(1), \ldots$ $\ldots$

The notation above means that at each time step n the control is bounded between two pre-assigned values, K_1 and K_2, which represent practical limits that are physiologically and medically reasonable for the chest compression and suction (negative pressure). In this paper the values of these bounds are +60 mmHg and – 20 mmHg, respectively. We note that to obtain a practical compression waveform that can be repeated indefinitely, if necessary, the value of the control at the end of the process is equal to its initial value, $u(N-1) = u(0)$.

Optimal Control Approach

In OCT a waveform, *u,* representing the time history of the forcing intrathoracic pressure, is chosen to maximize (or minimize) a particular time-domain *performance index, J* . The maximum *J* is sought over all possible waveforms, *u*, and corresponding trajectories, P(n), during a particular time interval, here 0 to 13.3 seconds of continuous chest compression, which is the time required for 20 uninterrupted compressions at a rate of 90 compressions/minute. In the present problem J is the mean SPP minus a cost function, namely

$$J(u) = \sum_{n=1}^{N} \left[P_5(n) - P_6(n) \right] - \sum_{n=0}^{N-2} \frac{B}{2} u^2(n),$$

where the constant *B* models the specific cost (financial, medical, or otherwise quantified) of implementing the control. The first term represents the summed pressure differences between the thoracic aorta and the vena cava, ($P_5 - P_6$), which is proportional to the mean SPP. The second term represents the cost of implementing the control and has the double effect of stabilizing the control problem and allowing for an explicit characterization for the optimal control. In the life-saving situation of CPR, as opposed to typical economic and engineering problems, we are willing to pay any reasonable cost to generate adequate intrathoracic pressure. For technical reasons, *B* is not allowed to be zero. Hence, in the present application we chose very small values of $B \sim 0.0001$. Doubling or tripling the value of *B* did not significantly change the results, so for this CPR problem we are dealing with a regime in which cost is not an issue. Our goal is to maximize $J(u)$, i.e., to find a u^* such that $J(u^*) = \max_u J(u)$.

This discussion can be made mathematically rigorous whereby we are able to explicitly characterize the optimal control. For technical details we refer to our previous paper[38]. However, to give the flavor of the argument, we mention the following. Since our goal is to maximize the objective performance function, *J*, this would imply a differentiation with respect to the controls; however since *J* depends on the controls both directly and indirectly (i.e., through *P)*, we have to make sure that the maps

$$u, \text{ control } \rightarrow P(u), \text{ state pressures}$$

and

$$u, \text{ control } \rightarrow J(u), \text{ objective function}$$

are differentiable in a suitable sense. For sufficiently small time steps Δt, the existence and uniqueness of the optimal control can be shown[38]. Moreover, we have shown that the optimal control is completely and explicitly characterized in terms of the solution of the optimality system, which consists of the state equations, adjoint equations, and the optimality condition. The adjoint system is a system of seven difference equations that complements the seven state equations for pressures and the optimality condition expresses

simply the requirement that the objective function *J* attain its maximum at the optimal control[38].

The numerical implementation of this optimal control solution involves an iterative method. The iterative method starts with an initial guess for the control values. Using this control, the pressure (state) equations are evolved forward for *N* time steps. Using the values of the state variables calculated during this initial sweep and the final conditions, the adjoint system is solved backwards for *N* time steps. At this point, the controls are updated using the latest values of the state and adjoint variables. The forward and backward sweeps are repeated until a stable solution for the optimal control is found. This technique to solve the optimality system is widely used[39,40].

RESULTS

Figure 2 shows tracings of intrathoracic pressure as a function of time for a 13.3 second window, representing 20 compressions at 90/min with no pauses for ventilation. Figure 2(a) shows the waveform for standard-CPR as a reference. Figure 2(b), shows the optimal control waveform, $u^*(t)$, given the practical upper and lower limits of chest pressure in our problem (-20 mmHg to +60 mmHg). The physiological parameters are the same as in Babbs' work[27]. The time step is 0.005 *s*. The parameter *B* is 0.0001. With the optimal control waveform the mean systemic perfusion pressure, SPP, is 36.1 mmHg, which is much greater than SPP of 24.7 mmHg in the standard CPR model.

In the waveform of Figure 2(b) the positive and the negative control values represent compression and decompression of the chest, respectively. In particular, they represent the intrathoracic pressure pulses caused by external chest compression or decompression. Importantly, the optimal control waveform includes both compressions and decompressions to the maximal allowable extent (from + 60 mmHg to –20 mmHg). Chest decompression during CPR could be created in practice by using a plunger-like device as the Ambu Cardiopump® or by using an intrathoracic pressure regulator device, which applies gentle suction to the endotracheal tube between positive pressure ventilations[32]. The decompressions are longer lasting than the compressions, resembling those in active compression-decompression (ACD) CPR. The optimal duty cycle for chest compression is approximately 40 percent, leaving 60 percent of cycle time for pump filling. The “noise” in the last three beats of the optimal control is an end effect artifact.

DISCUSSION

We applied OCT to the problem of CPR without any preconceived notions about what the results should be. Only two requirements were specified in advance: the rudimentary resistive-capacitative plumbing of the cardiovascular system and physically realistic limits on maximal and minimal pressures in the chest. There was no preconceived requirement for negative pressure, or for any particular range of compression rates or duty cycles or for a simple, repeatable pattern of the optimal control within the 13.3-second window. The

fact that OCT found a solution incorporating both compression and decompression of the chest, confirms much recent work by Lurie and coworkers concerning the value of modest negative intrathoracic pressure during chest recoil to enhance pump filling during CPR. For example, studies in anesthetized pigs have demonstrated greater venous return and greater perfusion pressures during standard CPR when an impedance threshold device is attached to the airway[41,42] to prevent inrush of air through the trachea during chest recoil until a critical "cracking pressure" is reached. This device also improves the effectiveness of active compression-decompression or ACD-CPR, by preventing "decompression of the decompression"—that is by preventing an inrush of air through the trachea as the chest is actively expanded by withdrawal of a plunger device. The strategy of encouraging modest negative intrathoracic pressure during chest recoil has already proved successful in improving clinical outcome in human victims of sudden cardiac death[17-19]. The agreement of the OCT waveform with these concepts already developed in animal experiments and in clinical trials provides independent confirmation of their validity, since no bias toward any particular solution was included in the problem definition or in the analysis.

One alternative and complementary way to overcome sluggish filling of the chest pump during CPR is the application of interposed abdominal compressions with IAC-CPR[43-45]. This strategy forces blood into the chest from the abdomen and can be quite effective. It requires less force and less specialized equipment to generate a given positive pressure in the abdomen by pushing on it, than to generate an equivalent negative pressure in the chest by pulling on it. From a hemodynamic standpoint the results on the venous side are similar, and there is the added benefit of abdominal aortic counterpulsation with IAC, which tends to boost total output and perfusion of the heart and brain[46,47].

In the future, we plan to implement OCT on an IAC-CPR model and find the optimal profiles for both chest and abdominal compression-decompression. A recent paper by one of us[48] contains a numerical model with 14 equations involving chest and abdomen compressions and decompressions. Various waveforms were explored to improve SSP by simulated evolution. The most effective waveforms included the maximal allowable compression and decompression of both chest and abdomen in patterns similar to those found in the present paper for chest compression only CPR.

The present study has limitations similar to those of any theoretical study. Issues of safety and complications of the proposed compression waveform are not addressed. More complex models could have been studied, incorporating for example more compartments, the mass and inertia of blood, or the effects of specific patterns of positive pressure ventilations. Here for simplicity we specifically excluded manipulation of abdominal pressure. Nevertheless, the results of this first-ever application of optimal control theory to CPR are interesting—perhaps less so in the exact numerical values of the solution than in the strategy they imply—the active decompression of intrathoracic pressure to increase venous return to the pump. This strategy can be realistically implemented in a variety of ways by human rescuers or by non-fatiguing mechanical devices. Although progress toward exploiting the benefits of negative intrathoracic pressure in CPR had temporarily stalled because of mixed results with ACD or plunger CPR[15,49], in retrospect it is becoming apparent that the failure of studies of ACD-CPR to show benefit was more due to

difficulties in its implementation than to validity of its concept. Perhaps it is now time to move beyond calls for more research and to implement available techniques to increase venous return between chest compressions.

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FIGURES AND LEGENDS

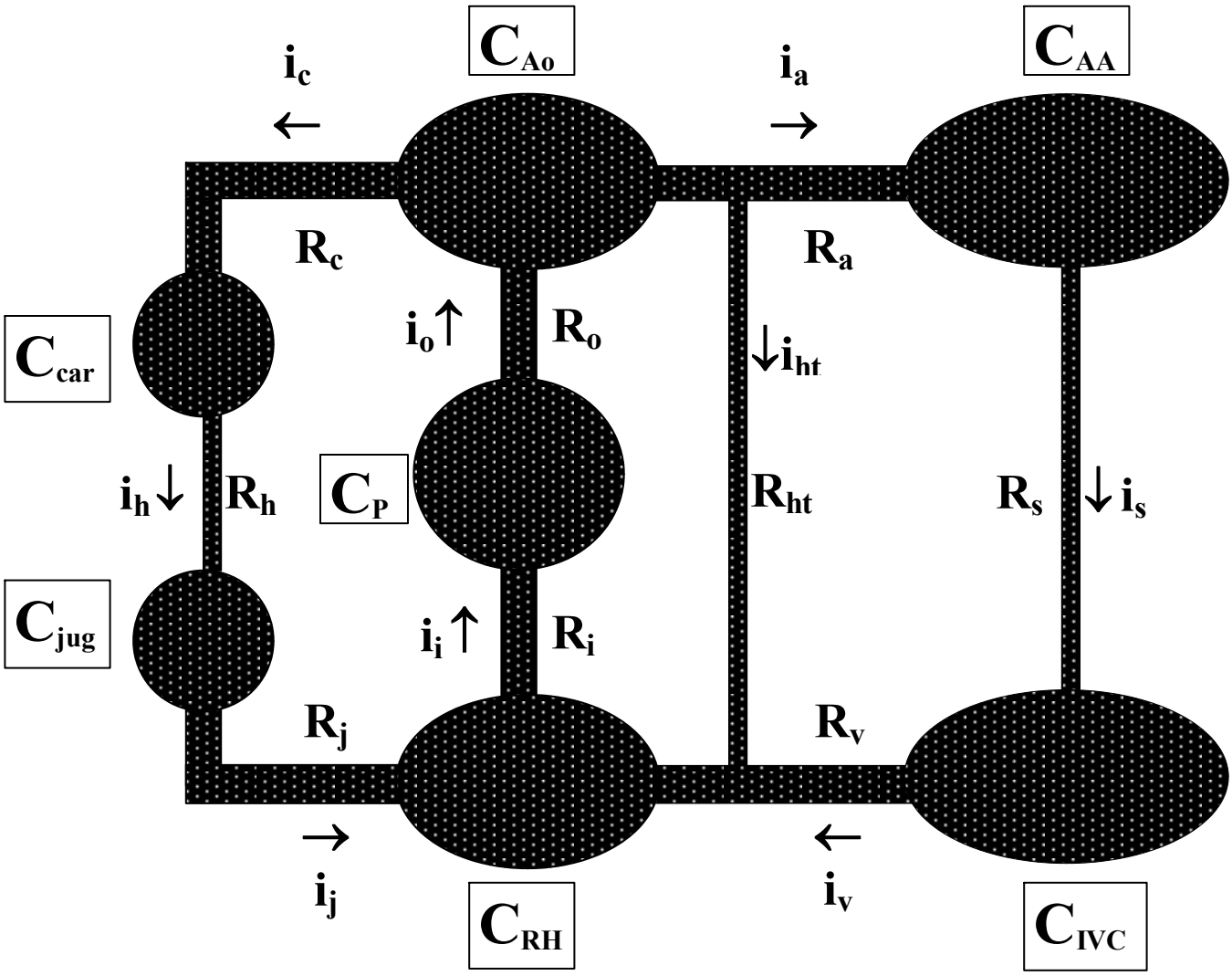

FIGURE 1. Model of the human circulatory system. Subscripts of the compliances represent: Ao thoracic aorta, RH right heart, P pump, AA abdominal aorta, IVC inferior vena cava, car carotid artery, jug jugular veins. Subscripts of the resistances represent: o pump output, i pump input, v subphrenic vena cava, j jugular veins, h head and arms, c carotid arteries, a aorta, s subphrenic organs, ht coronary vessels of the heart.

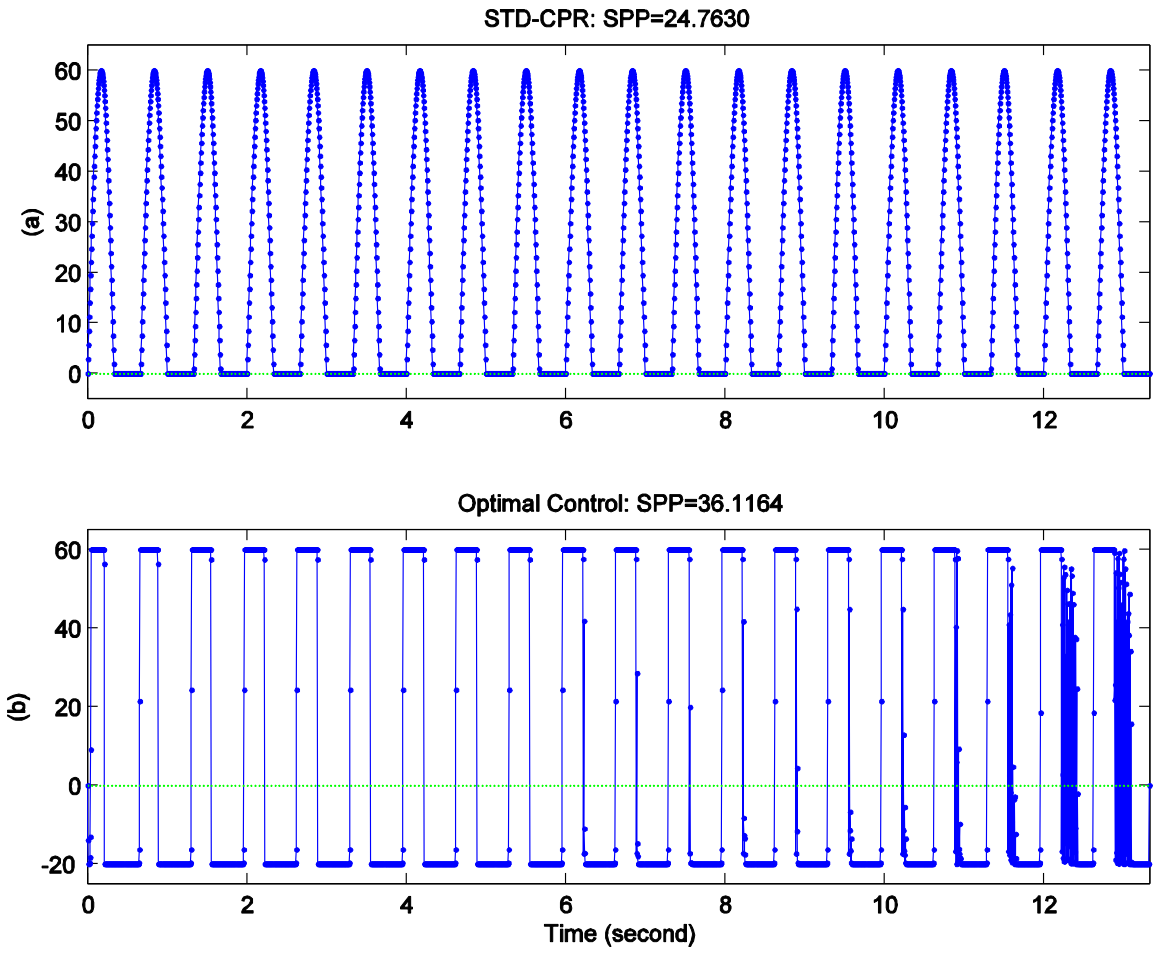

FIGURE 2. Chest compression waveforms resulting from optimal control theory. (a) Intrathoracic pressure for standard CPR with chest compression only, ranging from 0 to 60 mmHg. (b) Intrathoracic pressure for optimal control CPR with chest compression only, ranging from –20 to 60 mmHg.