Computers and Chemical Engineering 82 (2015) 13–24

Contents lists available at ScienceDirect

Computers and Chemical Engineering

journal homepage: www.elsevier.com/locate/compchemeng

Optimal drug infusion profiles using a Particle Swarm Optimization algorithm

M. Elisa Montain, Aníbal M. Blanco, J. Alberto Bandoni *

Planta Piloto de Ingeniería Química (UNS-CONICET), Camino La Carrindanga km. 7, 8000 Bahía Blanca, Argentina

ARTICLE INFO

Article history:
Received 29 September 2014
Received in revised form 29 April 2015
Accepted 30 May 2015
Available online 12 June 2015

Keywords:
Dynamic optimization
Cardiorespiratory model
Drug infusion
Particle Swarm Optimization

ABSTRACT

The dynamic optimization of the administration of therapeutic drugs in simulated patients is proposed. The approach is based on a non-linear discontinuous cardiorespiratory model, which has been conceived to simulate the effect of inotropic and vasoactive drugs as well as anesthetic agents. A stochastic technique (Particle Swarm Optimization), within the context of the control vector parameterization approach, is adopted to identify the infusion profiles of various drugs in order to track, as close as possible, the set-points on several variables of medical interest. Two different medical procedures are investigated in order to test the efficiency and robustness of the algorithm: a congestive heart failure and the unclamping of an aortic vessel. Due to the conflicting nature of the different objectives, compromise solutions are obtained in all cases.

1. Introduction

The most critical variables to be controlled in intensive care units are mean arterial pressure, mean pulmonary arterial pressure, cardiac output and depth of anesthesia. The control of such variables is achieved through the administration of various drugs and anesthetic agents. Drugs commonly used are sodium nitroprusside and phenylephrine to regulate mean arterial pressure, dopamine to control cardiac output, nitroglycerin to regulate mean pulmonary arterial pressure, propofol to induce anesthesia and isoflurane to maintain the anesthetic state.

In practice, physicians are responsible for adjusting the doses of drugs in order to keep the hemodynamic and anesthetic variables within acceptable levels, performing the task of a closed loop controller. The design of automatic controllers to assist physicians in this process has been addressed by the Process Systems Engineering community. For example, Yelneedi et al. (2009a,b) evaluated the robustness of advanced control strategies for the regulation of hypnosis with propofol in a broad range of patients. In general, the most popular control strategies considered are (Dua and Pistikopoulos, 2010; Gentilini et al., 2001; Gopinath et al., 1995; Isaka and Sebald, 1993; Kwok et al., 1997; Rao et al., 2000; Uemura et al., 2006; Yu et al., 1992): multirate model predictive control, model predictive control, cascade internal model control and multi-parametric model based control, among others. Model based controllers use non-linear physiological models to simulate human processes such as blood circulation, respiration and distribution of substances among the organs (Yelneedi et al., 2009a,b; Yu et al., 1992). The performance criteria commonly adopted is the minimization of the settling times of the variables of interest. Some of the controllers have been tested with relative success on animals and on patients undergoing a specific disease (Dua and Pistikopoulos, 2010; Gentilini et al., 2001; Gopinath et al., 1995).

Knowing in advance the optimal infusion profiles of the drugs to be administered to a patient, provided by a dynamic optimization problem, can potentially improve the quality of the treatment in surgical and intensive care environments. Infusions can be designed in order to prevent exceeding concentration limits of the drugs which might impact, for example, on the time spent by the patient in the post-operative care unit recovering from anesthesia. A patient-specific physiological model within a dynamic optimizer can also be used by the anesthesiologists to carry out "what if" and failsafe analysis for various scenarios that may arise during surgery. In a closed loop framework, the optimal infusion profiles can be fed as set-points to the control system since the open-loop optimal controls are rarely applied directly in practice, due to the presence of uncertainty such as model mismatch, process disturbance and variation in initial conditions. Moreover, the knowledge in advance of an open-loop optimal control law for a given process can offer an estimate on how far the system is from the optimal operation and help to identify possible improvement actions (Chachuat, 2007).

* Corresponding author. Tel.: +54 291 4861700; fax: +54 291 4861600.
E-mail addresses: mmontain@plapiqui.edu.ar (M.E. Montain), ablanco@plapiqui.edu.ar (A.M. Blanco), abandoni@plapiqui.edu.ar (J.A. Bandoni).

http://dx.doi.org/10.1016/j.compchemeng.2015.05.026
0098-1354/

Nomenclature

Parameters

C_{a1}	1° systemic arterial capacitance
$C_d(inyectable)$	drug concentration in vein chamber
$C_d(inhalable)$	drug concentration in lung chamber
$C_d(organs)$	drug concentration in organ chamber
C_j	vessel elasticity in cardiovascular chamber j
C_{p1}	1° pulmonary arterial capacitance
C_{v1}	1° systemic venous capacitance
C_{v1BARO}	1° systemic venous capacitance influenced by the baroreceptor
C_{v2}	2° systemic venous capacitance
Eff_{Ca1}	effect of drugs on 1° systemic arterial capacitance
Eff_{Cp1}	effect of drugs on 1° pulmonary arterial capacitance
Eff_{Cv1}	effect of drugs on 1° systemic venous capacitance
Eff_{Emaxlv}	effect of drugs on the maximal left systolic elastance
Eff_{Ra2}	effect of drugs on 2° systemic arterial resistance
Eff_{Ra3}	effect of drugs on 3° systemic arterial resistance
Eff_{Rl1}	effect of drugs on 1° pulmonary venous resistance
Eff_{Vunv1}	effect of drugs on 1° systemic venous unstressed volume
E_{maxlv}	maximal left systolic elastance
$E_{maxlvBARO}$	maximal left systolic elastance influenced by the baroreceptor
E_{maxrv}	maximal systolic right ventricular elastance
H	heart rate
L_j	flow inertia in cardiovascular chamber j
P_{AA}	partial pressure of drug in alveoli
P_{CO_2}	partial pressure of CO_2 in alveoli
P_j	blood pressure in cardiovascular chamber j
P_{O_2}	partial pressure of O_2 in alveoli
Q_{a3}	flow rate at the systemic capillary section
Q_j	blood flow in cardiovascular chamber j
Q_{p3}	Flow rate at the pulmonary capillary section
R_{a1}	1° systemic arterial resistance
R_{a2}	2° systemic arterial resistance
R_{a2BARO}	2° systemic arterial resistance influenced by the baroreceptor
R_{a3}	3° systemic arterial resistance
R_{a3BARO}	3° systemic arterial resistance influenced by the baroreceptor
R_j	viscous loss term in cardiovascular chamber j
R_{l1}	1° pulmonary venous resistance
V_j	blood volume in cardiovascular chamber j
V_{unj}	unstressed volume in cardiovascular chamber j
V_{unv1}	1° systemic venous unstressed volume
$V_{unv1BARO}$	1° systemic venous unstressed volume influenced by the baroreceptor
V_{unv2}	2° systemic venous unstressed volume

Acronyms

BIS	Bispectral index
CO	Cardiac output
CVP	Control Vector Parameterization
DAEs	Differential-algebraic equations
DOA	Depth of anesthesia
DP	Dopamine
EEG	Electroencephalogram
ISO	Isoflurane
IVP	Initial value problem
MAP	Mean arterial pressure
MPAP	Mean pulmonary arterial pressure
NLP	Non-linear programming problem
NTG	Nitroglycerin
OF	Objective function
PFL	Propofol
PNP	Phenylephrine
PSO	Particle Swarm Optimization
SNP	Sodium nitroprusside
SQP	Succesive quadratic programming

The dynamic optimization approach is extensively used to aid in the design and operations of industrial systems (Adams and Seider, 2008; Balsa-Canto et al., 2005; Barton et al., 1998, 2000; Biegler, 2010; Carrasco and Banga, 1997; Galán and Barton, 1998; Vassiliadis et al., 1994). The most popular application is the determination of optimal operating policies in batch processes. Other applications include the design of operating procedures for process start-up, shut-down and changeover, the design of emergency shutdown systems, and the optimal design of inherently dynamic processes such as those operated in a batch, semi-continuous and/or periodic manner (Carrasco and Banga, 1997; Barton et al., 2000; Schlegel et al., 2005).

Besides its development, according to our knowledge there are practically no reports in the open literature on applications of the dynamic optimization strategy to physiological systems. In this article, the drug infusion optimization problem is formulated as a dynamic optimization problem (or open loop control problem) to find the input profiles of the manipulated variables (drug infusion rates) that minimize the off-sets of the hemodynamic and anesthetic variables with respect to appropriate set-points over a finite time interval. For this purpose, a detailed physiological simulation model is used and the Particle Swarm Optimization (PSO) strategy within a Control Vector Parameterization (CVP) approach is adopted to conduct the dynamic optimization. It is worth mentioning that the problem is inherently multi-objective, since it is desired to control several variables simultaneously.

In the next section the used physiological model is described. In Section 3 the basic concepts of dynamic optimization problems are presented followed by the description of the PSO algorithm (Section 4). In Section 5 implementation details of the proposed approach are presented. In Section 6, the results of the addressed case studies are detailed followed by a conclusions and future work section.

2. Physiological model

The adopted physiological simulation model is built up on models available in the literature for the following processes: cardiovascular dynamics, baroreflex, respiration, transport and distribution of substances and pharmacologic effects of drugs. The integrated model, reported in Montain et al. (2014), provides the time profiles of the main hemodynamic and pharmacodynamic variables under many different scenarios of drug infusion for therapeutic purposes. A brief description of each sub model and the corresponding references are provided below. In Fig. 1, the interconnection among the sub models is depicted.

2.1. Cardiovascular and baroreflex model

The cardiovascular system model is a lumped pulsatile model that captures the main features of the blood circulation. The different organs are represented by a series of interconnected elastic chambers, representing the pumping heart and vascular systems (systemic and pulmonary circulation). For a complete description of this model see Ottesen et al. (2004).