Received: March 23, 2024. Revised: April 10, 2024.

INASS

International Journal of
Intelligent Engineering & Systems

http://www.inass.org/

Development of Intelligent Control Strategy for an Anesthesia System Based on Radial Basis Function Neural Network Like PID Controller

Ahmed Sabah Al-Araji[1]* **Khulood Eskander Dagher[2]** **Mohammed Najm Abdullah[1]**

[1]*Computer Engineering Department, University of Technology-Iraq, Baghdad, Iraq*
[2]*Al-Khwarizmi College of Engineering, University of Baghdad, Baghdad, Iraq*
* Corresponding author's Email: Ahmed.s.alaraji@uotechnology.edu.iq

Abstract: This paper presents an adaptive neural network acting like a proportional-integral-derivative (PID) controller that uses an intelligent meta-heuristic technique to improve the drug infusion rate (propofol) as a manipulated variable in closed-loop control of anesthesia systems using the Bispectral Index (BIS) as the primary controlled variable. The effect of propofol on the human body is modelled using the pharmacokinetic (PK) and pharmacodynamics (PD) models. A physiological dataset of patients, including gender, weight, height, age, and the like, determines the parameters of the PK/PD mathematical model. The proposed controller seeks to provide the optimal propofol control action, which is in charge of swiftly, precisely, and accurately maintaining a triad of hypnosis, analgesia, and neuromuscular blockade by infusing several drugs that are specific to each state. To train this neural network like a PID controller with the radial basis function (RBF) in a neuron, the meta-heuristic method is employed. The first technique is particle swarm optimization (PSO), which has been widely used in both data estimation and training because of its quick computing speed, while the second technique is the chaotic PSO algorithm, and the third technique is the modified CPSO algorithm (MCPSO). The fundamental proposed procedures of the MCPSO algorithm use the chaos method, including the coefficients of acceleration, and remove the two random parameters from the velocity update equation to generate more randomness in the search space to quickly solve the local minima problem. The PSO, CPSO, and MCPSO meta-heuristic algorithms use the mean square error (MSE) performance index to find and optimize the optimal or the nearly ideal gain parameters of the nonlinear neural network to function like a PID controller. The simulation results show that the proposed controller for different physiological dataset patients is characterized by its efficacy and resilience in terms of controlling the depth of the hypnosis state and the infusion rate of the anesthetic drug during surgery in order to avoid under- or over-dosing of the drug for the patient through the desired value of BIS (50) with minimizing the steady-state error, which is equal to zero without any oscillation. Moreover, the comparison results showed that the proposed RBF-NN-PID controller enhanced the time in one minute to reach the depth of anesthesia at the moderate hypnotic state when compared to the fractional-order adaptive high-gain controller, in which the time to reach the depth of anesthesia is two minutes. In contrast, the adaptive neuro-fuzzy controller reached the depth of anesthesia in three minutes. Therefore, the time was improved by 50% and 67%, respectively. In particular, the surgery BIS index was kept at the BIS desired 50 at the moderate hypnotic state without any error and with no oscillation at steady-state.

Keywords: Anesthesia system, Chaotic particle swarm optimization, Propofol rate, Radial basis function, Neural network like PID controller.

1. Introduction

In simple terms, anesthesia is the medical profession's means of guaranteeing that a patient's body remains painless throughout surgical procedures. On the other hand, the anesthetic was first used almost a century ago. In particular, propofol has been the best agent for intravenous technique-maintained anesthesia since the mid-1980s [1]. Deep anesthesia could not be achieved before the automatic control was activated. In contrast to all other clinical drug treatments for anesthesia, the prompt onset of anesthetic medications and the required, regular

monitoring of their potentially harmful symptoms are distinct. In theory, a closed-loop controller might be used to generate a personalized general anesthetic without the need for expensive and time-consuming hereditary pre-screening [2]. Regarding the amount of duties they complete each day, the number of anesthesiologists has increased in recent years. They use physiological indicators and their intuition to balance the dosage of hypnotics and muscle relaxants. In particular, the anesthesiologist functions as a manual feedback controller in certain ways [3]. Moreover, many types of anesthetic drug controllers were developed in the anesthetic system to keep the patient's depth of hypnotic at a BIS index value of 50 at the surgical procedure band. For instance, the authors in [4] proposed an intelligent controller based on a neural network and a fuzzy logic algorithm to enhance the depth of hypnotics for no cardiac surgery. They used nine rules for the fuzzy logic controller and a neural network for the identifier to improve and fasten the output signal BIS, which reached the desired value of 50 with steady-state error. However, the drawbacks of this controller are that the Jacobean of the PK/PD model based on the multi-layer neural perceptron has insufficient learning that leads to errors in the output and that the propofol control action has a big spike in the response. In addition, the authors in [5] explained an advanced regulatory system based on the PID controller and the model predictive controller (MPC)for first-order plus time-delay approximation of the PK/PD model to modify the level of patients' hypnotic during surgical operation, and they used the trial-and-error method to tune the parameters of the PID controller and the prediction horizon for the weights of the MPC. However, the issue with this controller is that the model is built as a first-order model, while in fact, the PK/PD model is of third-order, which leads the actual BIS to reach the steady state in 10 minutes for a moderately hypnotic state with a value of 50. In [6], the authors described the control of anesthesia concentration using a PID controller using a trial-and-error method for tuning the controller parameters to obtain the propofol control action for the PK-PD model. Nevertheless, the problem with this PID controller is that the trial-and-error method for tuning the controller parameters leads to small errors with undershoots in the BIS response. Furthermore, in [7], the authors designed an adaptive neuro-fuzzy controller for anesthesia using the linear PK/PD patient model. The authors used three membership values and two variable gains with the trial-and-error method to obtain the two control gains in the control law. As a result, the controller generates a quick and suboptimal value of the propofol control action, which causes a slight oscillation in the BIS index value at 3 minutes without error in the steady-state response. However, the issue with this controller is that the two control gains in the control law obtained from the trial-and-error method led to errors in the output response of BIS because the propofol control action generated from the control law was not the optimal control action. Moreover, in [8], the authors proposed a fractional order controller that was built for the linear PK/PD model, using an adaptive high-control gain that starts from 1000 for all patients using the trial-and-error method to obtain the control law gain. Therefore, the controller generates a fast but non-optimal value of the propofol control action, which leads to an actual BIS value of zero at the steady-state error at 2 minutes to reach the moderate hypnotic state at a 50 BIS value. However, the limitation of this controller is that the only high-control gain value in the control law obtained from the trial-and-error method led to the long-time reaching of the moderate hypnotic state. However, in [9], the authors illustrated an adaptive Smith predictor controller based on the inverse Hill equation for generating the propofol drug that provided the expected performance, including fast transient, small under-overshoot, and limited BIS oscillation. However, this controller's drawback is that the estimation of the hill coefficient is built as a linear slope, which leads the actual BIS to reach the steady state with less settling time and a small offset error. In [10], the authors provided a comprehensive overview of the different types of controllers that were used in the anesthesia system from 2017 to 2022. As a result of this survey, the PID controller represents 35% of the controllers used in the anesthesia system, 28% for model predictive controllers, 13% for fuzzy logic controllers, 13% for neural network controllers, and 11% for other controllers.

In this work, the problem definition is that the time challenge to reach the depth of anesthesia for the patient in a surgical operation is the BIS index value within the minimum amount of time possible. This problem essentially involves the regulation of the propofol infusion drug rate to avoid under- or over-dosing of the drug for the patient that leads to hypotension and postoperative adverse reactions during surgical operations or after them. Specifically, the main objective of this research is to determine the fast and optimal propofol-infusion rate control action in order to enhance the performance of the anesthesia depth based on the BIS index value during the patients' surgical operations by implementing the proposed off-line nonlinear RBF-NN-PID controller

and using a three-heuristic algorithm based on the chaos method.

In particular, the main scientific contribution of this work is to find and tune the optimal or near-optimal control gain parameters of the nonlinear RBF-NN-PID controller using the proposed MCPSO algorithm based on the chaos method that uses the coefficients of acceleration and removes the two random parameters from the velocity update equation to generate more randomness in the search space to quickly solve the local minima problem. This method leads to obtaining the fast and optimal value of the rate of anesthetic drug control action that will be injected into the patient-based PK/PD model to quickly track and stabilize the patient's depth of anesthesia and keep it at a surgery BIS index value within a suitable time to avoid under- or over-dosing of the drug for the patient that leads to hypotension and postoperative adverse reactions during surgical operations or after them.

This paper is organized as follows: In Section 2, the pharmacokinetic and pharmacodynamic mathematical models are shown. In Section 3, the control strategy design is elucidated. In Section 4, the simulation's outcomes are displayed. The key findings from this work and upcoming research are given in Section 5.

2. Mathematical model

The mathematical modeling of dynamic systems is the first and most crucial stage in the controller design process. Particularly, a more thorough comprehension of the system's behaviour results in a more effective controller design, which is made more challenging to grasp by the complex, nonlinear, and changing dynamics of physiological systems. Based on pharmacokinetics (PK) and pharmacodynamics (PD) [11], the classic compartmental model of anesthesia is presented in this section, as illustrated in Fig. 1 and in Table 1. In the PK portion of this model, there are three major compartments and one effect site compartment located in the PD sector. The propofol infusion rate and the BIS index value, respectively, are the PK/PD model's single input and single output [10].

When patients receive injections of drugs, those substances move to different parts of the human body. In this regard, determining the amount of injectable medication that really reaches the target is crucial. The PK model offers a mathematical depiction of drug distribution in the human body.

The three important compartments in this model are shown in Fig. 1. It is recognized that essential organs, including the liver, brain, and blood, are

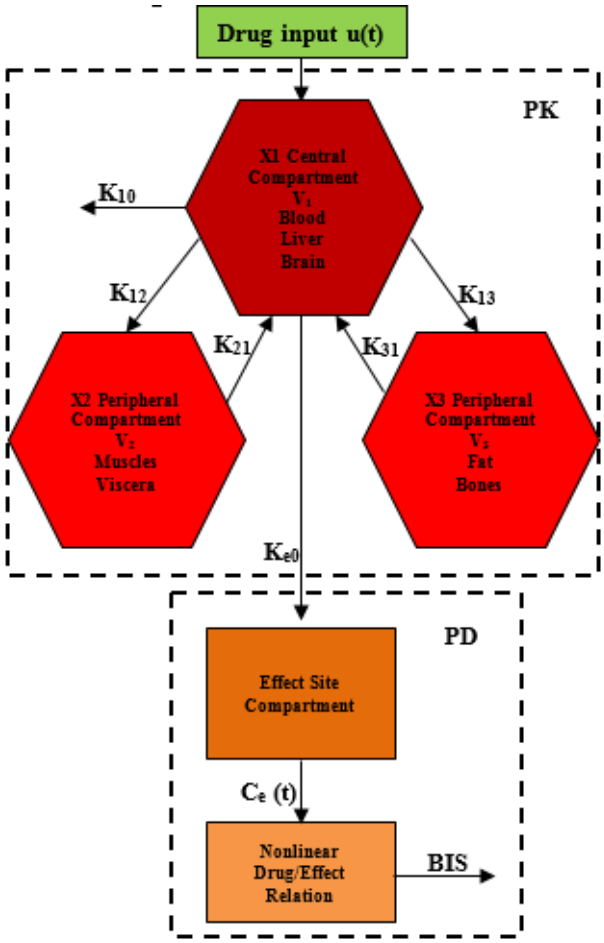

Figure. 1 The anesthesia model based on PK/PD compartment

located in the core compartment sometimes referred to as compartment V_1. The peripheral compartments V_2 and V_3 indicate other bodily sections that receive the infused drugs. The muscles and viscera in compartment V_2 are physiological tissues with good blood flow and rapid movement. Conversely, because compartment V_3 is composed of bone and fat, which are two anatomical elements with restricted blood flow, it has a sluggish dynamic [7,8,10]. The balancing equation for the drug concentration Xi (mg) in the ith 1, 2, and 3 compartments can be established as given below to create this model [7,8]:

$$\dot{X}_1(t) = u(t) - K_{12}X_1(t) - K_{13}X_1(t) - K_{10}X_1(t) + K_{21}X_2(t) + K_{31}X_3(t) \quad (1)$$

$$\dot{X}_2(t) = K_{12}X_1(t) - K_{21}X_2(t) \quad (2)$$

$$\dot{X}_3(t) = K_{13}X_1(t) - K_{31}X_3(t) \quad (3)$$

where, $X_1(t)$, $X_2(t)$, and $X_3(t)$ are for three different compartments. $X_1(t)$ stands for the main blood

Table 1. Definition of the PK/PD model parameters

Symbols	Definition
V1	The volume of liver, brain, and blood located in compartment 1
V2	The volume of muscles and viscera in compartment 2
V3	The volume of bone and fat in compartment 3
$X_1(t)$	The stands for the main blood compartment
$X_2(t)$	The peripheral fast compartment, such as muscles and the Viscera
$X_3(t)$	The slow dynamics compartment, such as fat or bones
u(t)	The propofol infusion rate into the blood in (mg/min)
K_{12}	The transfer of anesthesia (1/min) from the first compartment to the second compartment
K_{21}	The transfer of anesthesia (1/min) from the second compartment to the first compartment
K_{13}	The transfer of anesthesia (1/min) from the first compartment to the third compartment
K_{31}	The transfer of anesthesia (1/min) from the third compartment to the first compartment
K_{10}	The elimination rate constant (1/min)
W	The weight (kg) of the patient
H	The height (cm) of the patient
lbm	The lean body mass
A	The age (in years) of the patient
C_{l1}	The clearance of compartment 1 (L/min)
C_{l2}	The clearance of compartment 2 (L/min)
C_{l3}	The clearance of compartment 3 (L/min)
$C_p(t)$	The plasma concentration to the infusion rate
$C_e(t)$	The drug concentration in the effect site compartment

compartment, $X_2(t)$ represents the peripheral fast compartment, such as muscles and the Viscera, $X_3(t)$ represents the slow dynamics compartment, such as fat or bones, and *u(t)* is the propofol infusion rate into the blood in (mg/min).

The transfer rate of anesthesia concentration from different compartments is defined by the term "K," and the unit is 1/min. The transfer of anesthesia from the first compartment to the second is denoted by K_{12}. While from the second to the first, it is denoted by K_{21}. Similarly, K_{31} and K_{13} follow the transfer of anesthesia concentration from the third to the first compartments and vice versa [10]. The relation between these parameters and the patient specifications, such as weight (kg), height (cm), lean body mass (lbm), gender (male or female), and age (in years), could be described as follows [12,13].

$$\left.\begin{aligned} K_{10} &= \frac{C_{l1}}{V_1} \\ K_{12} &= \frac{C_{l2}}{V_1} \\ K_{13} &= \frac{C_{l3}}{V_1} \\ K_{21} &= \frac{C_{l2}}{V_2} \\ K_{31} &= \frac{C_{l3}}{V_3} \end{aligned}\right\} \tag{4}$$

where,

$$\left.\begin{aligned} V_1 &= 4.27 \\ V_2 &= 18.9 - 0.39(A-53) \\ V_3 &= 238 \end{aligned}\right\} \tag{5}$$

$$C_{l1} = 1.89 + 0.0456(W-77) - 0.0681(lbm-59) + 0.0264(H-177) \tag{6}$$

$$C_{l2} = 1.29 - 0.024(A-53) \tag{7}$$

$$C_{l3} = 0.836 \tag{8}$$

$$lbm(male) = 1.1W - 128\frac{W^2}{H^2} \tag{9}$$

$$lbm(female) = 1.07W - 148\frac{W^2}{H^2} \tag{10}$$

The corresponding PK model can be expressed as $C_p(t)$ relating the plasma concentration to the infusion rate [6].

$$C_p(t) = \frac{X_1(t)}{V_1} \tag{11}$$

As given in Eq. (12) [7], $C_e(t)$ representing the drug concentration in the effect site compartment of the PD model might be computed using the plasma concentration derived from the PK model.

$$\dot{C}_e(t) = K_{e0}(C_p(t) - C_e(t)) \tag{12}$$

where K_{e0} is the drug elimination rate from the effect site compartment and is the inclusion rate of drug metabolism. The BIS index value is obtained from the sigmoidal nonlinearity Hill equation via the effect site compartment $C_e(t)$, EC_{50} is the drug concentration at the half maximal effect, and "g" is

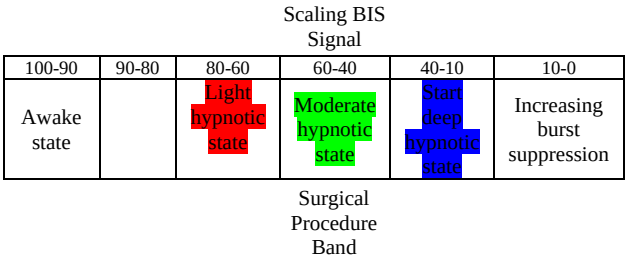

Figure. 2 General surgery BIS index value [7,10]

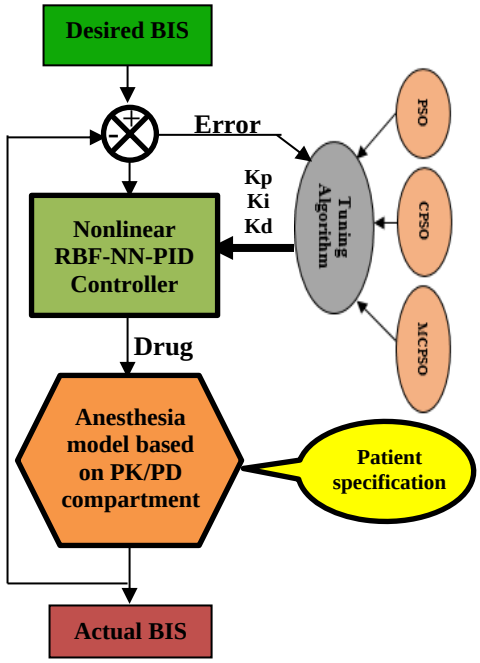

Figure. 3 The proposed nonlinear RBF-NN-PID controller for the anesthesia system

the nonlinearity degree of the function as follows [6-8]:

$$BIS(t) = BIS_0\left(1 - \frac{C_e(t)^g}{EC_{50}^g + C_e(t)^g}\right) \quad (13)$$

or

$$BIS(t) = E_0 - E_{max}\left(\frac{C_e(t)^g}{EC_{50}^g + C_e(t)^g}\right) \quad (14)$$

where, BIS_0 is the index value in an awake state, and it is equal to 100.
E_0 denotes the initial BIS value when $C_e(t)$=0, while E_{max} is the maximum effective site concentration.

The desired BIS index value in the surgical procedure band ranges from 40 to 60 as a scaling BIS signal. However, its nominal value is 50 based on the Bi-spectral index for different hypnotic states, as shown in Fig. 2 [7,10].

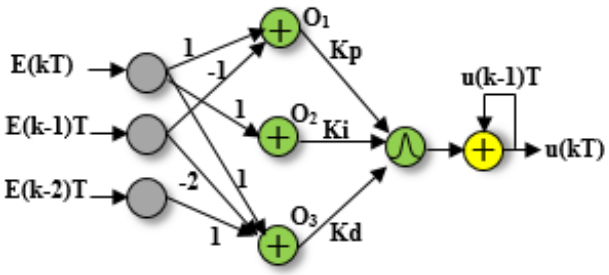

Figure. 4 The proposed nonlinear RBF-NN-PID controller structure

3. Adaptive neural network like PID controller

In this section, an adaptive radial basis function neural network like the PID controller is considered to control the depth of anesthesia via suitable drug infusion rate control action. Fig. 3 illustrates the control strategy of the anesthesia system and presents the suggested meta-heuristic technique, which is suitable for exploring and exploiting the global extreme solution to find and tune the gain control parameters of the neural network to function like a PID controller.

3.1 Control strategy design

The proposed structure of the nonlinear RBF-NN-PID controller is shown in Fig. 4, based on Gaussian neural networks, which have been found to be powerful schemes for learning complex input-output nonlinear mapping and have been used in the learning and control of nonlinear dynamic systems.

The RBF neural network feedforward algorithm is calculated according to Eq. (15) [14], which describes the discrete PID controller as follows:

$$PID(kT) = PID(k-1)T + Kp(E(kT) - E(k-1)T) + Ki(E(kT)) + Kd(E(kT) - 2E(k-1)T + E(k-2)T) \quad (15)$$

where Kp, Ki, and Kd are the control gain parameters of the PID controller. Therefore,

$$O_1(kT) = E(kT) - E(kT - T)) \quad (16)$$

$$O_2(kT) = E(kT) \quad (17)$$

$$O_3(kT) = E(kT) - 2E(kT - T) + E(kT - 2T) \quad (18)$$

The error signal between the desired BIS index value and the actual BIS level is the input for the RBF neural network. The sum of these signals is calculated as follows:

$$net(kT) = (K_p O_1(kT) - c)^2 + (K_i O_2(kT) - c)^2 + (K_d O_3(kT) - c)^2 \quad (19)$$

where c is the center of the geometric shape of the Gaussian functions of neurons.

The activation function output of the RBF-NN is as follows [15,16]:

$$H(net(kT) = ae^{-(\frac{net(kT)}{\sigma^2})} \quad (20)$$

where a and σ are the maximum amplitude and the width of the geometric shape of the Gaussian functions of neurons, respectively.

The final value of the propofol drug control action of the hypnosis depth is given in Eq. (21):

$$u(kT) = u(k-1)T + H(net(kT)) \quad (21)$$

The control gain parameters of the nonlinear RBF-NN-PID controller can be found and tuned by the off-line (PSO, CPSO, and MCPSO) algorithms in order to obtain the optimal or near-optimal propofol infusion drug control action for the PK/PD model to keep the desired BIS index value in the surgical procedure band ranging from 40 to 60 as a scaling BIS signal to prevent hypotension and postoperative adverse reactions. However, its nominal value is 50 based on the Bi-spectral index for a moderately hypnotic state.

Three meta-heuristic techniques, including PSO, CPSO, and MCPSO algorithms, will be used in this work. Eq. (6) [17, 18] is used as the cost function to determine the mean square error of every solution in all optimization algorithms:

$$MSE = \sum_{It}^{ITmax}[\frac{1}{K}\sum_{i}^{K}((BIS_{desired}(i) - BIS_{actual}(i))^{2})] \quad (22)$$

where, *ITmax* is the maximum number of iterations and *K* denotes the maximum number of samples.

The PSO, CPSO, and MCPSO algorithms are used for swarming the control gain parameters (Kp, Ki, and Kd) toward the best correct solution found in the previous iterations. The aim is to effectively search the result space, eventually converge on the minimum BIS error solution, and discover better solutions along the way based on the nonlinear RBF-NN-PID controller.

3.2 Control parameters tuning algorithms

The PSO algorithm belongs to the population-based evolutionary algorithms, which draw inspiration from studies on swarms, including fish schools and bird flocks [19]. More specifically, the PSO process is started with a set of (Npop) randomly chosen particles {Kp, Ki, Kd}. As every particle in the group symbolizes a point that moves across a (Dim)-dimensional search space, the positions of the particles indicate multiple potential sets of unknown parameters that need to be idealized. The rate at which the particle's location changes is determined by its velocity, while its fitness or quality measure is determined by its position inside the search space [14,20].

The vector ($Kpid_{particle\,i}$) = [$Kpid_{\text{particle},1}$, $Kpid_{\text{particle},2}$, …, $Kpid_{\text{particle},i}$], where (i) is the particle's index, while the vector ($Vpid_{\text{particle},i,}$) = {V$pid_{\text{particle},1}$, $Vpid_{\text{particle},2}$, …, V$pid_{\text{particle},i}$}, which is limited within the range of $Vpidmax_{\text{particle}}$ = {V$pidmax_{\text{particle},1}$, V$pidmax_{\text{particle},2}$, …, V$pidmax_{\text{particle},i}$}, representing the velocity.

The velocity is forced to its proper value if it is beyond certain limits. The i[th] particle can seek its local optimal place by altering its velocity in this manner. Based on its own flight expertise, each particle modifies its trajectory toward a particular place and disseminates collective knowledge among the particles. In addition, each particle has an iteration that varies its speed from one location to another, and it retains the best position it has found thus far in the vector $Lpid\_best_{\text{particle},i}$ = {$Lpid\_best_{\text{particle},1}$, $Lpid\_best_{\text{particle},2}$, …, $Lpid\_best_{\text{particle},i}$}.

The best global particle or solution up to this point is represented by the global best position, which is then kept in the vector $Gpid\_best_{\text{particle}}$ = {$Gpid\_best_{\text{particle},1}$, $Gpid\_best_{\text{particle},2}$, …, $Gpid\_best_{\text{particle},i}$} among all the best individual locations of particles.

Each iteration modifies each particle's location and velocity in accordance with Eqs. (23) and (24) [14], and the parameters' definitions are shown in Table 2.

$$Vpid_{particle,i}^{k+1} = w \times Vpid_{particle,i}^{k} + c_1 r\left(Lpid\_best_{particle,i}^{k} - (Kpid)_{particle,i}^{k}\right) + c_2 r(Gpid\_best_{particle}^{k} - (Kpid)_{particle,i}^{k}) \quad (23)$$

$$(Kpid)_{particle,i}^{k+1} = (Kpid)_{particle,i}^{k} + Vpid_{particle,i}^{k+1} \quad (24)$$

According to the description in [21], the basic steps of the CPSO algorithm involve finding and fine-tuning the parameters of the nonlinear RBF-NN-PID controller and incorporating the chaos method into

Table 2. Definition of the PSO parameters

Symbols	Definition
W	Inertia weight 0.731
$Vpid_{particle,i,k}$	Particle speed at iteration k
c_1 ,c_2	Acceleration constants (1.39,1.39)
r_1,r_2	Random values between (0,1)
$(Kpid)^k_{particle,i}$	At k[th] iteration, the i[th] (Kp, Ki, Kd) particle
$Lpid\_best_{particle,i}$	The best i[th] (Kp, Ki, Kd) particle in local fitness.
$Gpid\_best_{particle}$	The best (Kp, Ki, Kd) particle in global fitness

Table 3. Definitions of the CPSO parameters

Parameter	Definition with value
β^1	0.3 deterministic value
μ	4 constant value
W	0.831 inertia weight
W_{min}	0.25 minimum weight
W_{max}	0.95 maximum weight
IT	Current iteration number
IT_{max}	The maximum iterations number
c_1, c_2	Coefficients of parameter acceleration [1.39, 1.39]
$Vpid_{particle,i,k}$	At k[th] iteration, the i[th] (Kp, Ki, Kd) particle velocity
$(Kpid)^k_{particle,i}$	At k[th] iteration, the i[th] (Kp, Ki, Kd) particle
$Lpid\_best_{particle,i}$	The best i[th] (Kp, Ki, Kd) particle in local fitness.
$Gpid\_best_{particle}$	The best (Kp, Ki, Kd) particle in global fitness

the PSO algorithm to increase the randomness in the PSO algorithm's search to solve the local minima problem.

$$\beta^{k+1} = \mu \times \beta^k(1-\beta^k) \qquad 0 < \beta^1 < 1 \tag{25}$$

$$W = W_{max} - [(W_{max} - W_{min}) \times (\frac{IT}{IT_{max}})] \tag{26}$$

$$W_{new} = W \times \beta^{k+1} \tag{27}$$

As a result, the particle updates its equations for position and velocity, which are as follows [21]:

$$\begin{aligned} Vpid^{k+1}_{particle,i} &= W_{new,k} \times Vpid^k_{particle,i} + \\ c_1 r\left(Lpid\_best^k_{particle,i} - (Kpid)^k_{particle,i}\right) &+ c_2 r(Gpid\_best^k_{particle} - (Kpid)^k_{particle,i}) \end{aligned} \tag{28}$$

Table 4. Definitions of the MCPSO parameters

Parameter	Definition with value
β^1	0.3 deterministic value
μ	4 constant value
W	0.831 inertia weight
W_{min}	0.25 minimum weight
W_{max}	0.95 maximum weight
IT	Current iteration number
IT_{max}	The maximum iterations number
c_{1-min}	0.1 minimum weight for c_1
c_{1-max}	1.9 maximum weight for c_1
c_{2-min}	0.1 minimum weight for c_2
c_{2-max}	1.9 maximum weight for c_2
$Vpid_{particle,i,k}$	At k[th] iteration, the i[th] (Kp, Ki, Kd) particle velocity
$(Kpid)^k_{particle,i}$	At k[th] iteration, the i[th] (Kp, Ki, Kd) particle
$Lpid\_best_{particle,i}$	The best i[th] (Kp, Ki, Kd) particle in local fitness.
$Gpid\_best_{particle}$	The best (Kp, Ki, Kd) particle in global fitness

$$(Kpid)^{k+1}_{particle,i} = (Kpid)^k_{particle,i} + Vpid^{k+1}_{particle,i} \tag{29}$$

Table 3 illustrates the CPSO parameters' definitions that are used in the numerical simulation. The fundamental proposed procedures of the MCPSO algorithm use the chaos method in each of c_1 and c_2 acceleration coefficients and remove the two random parameters (r_1 and r_2) from the velocity update equation in order to generate more chaotic randomness in the search that depends on $c_{1-new}$and $c_{2-new}$for the proposed MCPSO algorithm and to quickly solve the local minima problem, as follows:

$$c_1 = c_{1-max} - [(c_{1-max} - c_{1-min}) \times (\frac{IT}{IT_{max}})] \tag{30}$$

$$c_{1-new} = c_1 \times \beta^{k+1} \tag{31}$$

$$c_2 = c_{2-max} - [(c_{2-max} - c_{2-min}) \times (\frac{IT}{IT_{max}})] \tag{32}$$

$$c_{2-new} = c_2 \times \beta^{k+1} \tag{33}$$

As a result, the suggested particle modifies its location and velocity equations, which are as follows:

$$\begin{aligned} Vpid^{k+1}_{particle,i} &= W^k_{new} \times Vpid^k_{particle,i} + \\ c^k_{1-new}\left(Lpid\_best^k_{particle,i} - (Kpid)^k_{particle,i}\right) &+ c^k_{2-new}(Gpid\_best^k_{particle} - (Kpid)^k_{particle,i}) \end{aligned} \tag{34}$$

$$(Kpid)^{k+1}_{particle,i} = (Kpid)^{k}_{particle,i} + Vpid^{k+1}_{particle,i} \quad (35)$$

The definitions of the MCPSO parameters utilized in the numerical simulation are shown in Table 4.

4. Simulation results

We implemented the proposed off-line nonlinear RBF-NN-PID controller with three meta-heuristics (PSO, CPSO, and MCPSO) for the PK/PD model using the numerical fourth-order Runge-Kutta (4RK) method based on the MATLAB package with a 0.1 minutes sampling time. This controller improved and controlled the depth of the hypnosis state and the drug infusion rate (propofol) during surgery operations and improved the time to reach the moderate hypnotic state at BIS of 50, preventing patients from being under- or overdosed, which could cause hypotension and postoperative adverse reactions. The first dataset includes four different patients with the physical specifications of (gender, age, height, weight, EC50, and g), as given in Table 5 [8]. Then, the parameters of the PK/PD model, as shown in Table 6, are based on the Eqs. (4)-(10), where Ke0 is a constant value (0.456 (1/min)). In this regard, the proposed offline nonlinear RBF-NN-PID controller settings for the search space areas are displayed for each patient in Table 7, which is suitable for exploring and exploiting the global extreme solution to find and tune the gain control parameters of the proposed controller. Therefore, we examined the efficacy and performance of the proposed controller using the off-line method for tuning the parameters based on PSO, CPSO, and MCPSO algorithms with a population size that equals 50 particles and a maximum number of iterations that equals 50. Moreover, the definitions of the parameters for the tuning algorithms in Tables 2, 3, and 4 are adopted. The response of the suggested closed-loop infusion drug propofol nonlinear RBF-NN-PID controller for patient #1 at the desired BIS that equals 50 is shown in Fig. 5. From Fig. 5, the fast response of BIS reaches the desired BIS of 50 after ten samples, which means 1 minute, and the patient will enter the moderate hypnotic state at time 0.1 minute when using the proposed MCPSO tuning algorithm for the RBF-NN-PID controller to generate the optimal propofol drug control action. When using the CPSO tuning algorithm for the RBF-NN-PID controller, the response of BIS is fast and reaches 50 after fifteen samples, which means 1.5 minutes, and the patient will enter the moderate hypnotic state at time 0.3 minutes. When using only the PSO tuning algorithm, the response reached the desired BIS at 3 minutes after thirty samples, and the patient will enter the moderate hypnotic state at time 0.4 minutes. The best values of the RBF-NN-PID control parameters

Table 5. The definitions of physical specifications [8]

Patient	Gander	A	H	W	EC_{50}	g
#1	F	40	163	54	6.33	2.24
#2	F	50	163	83	6.44	2.18
#3	M	28	164	60	4.93	2.46
#4	M	42	179	78	4.82	1.85

Table 6. The parameters of the PK/PD model

Patient	K_{10}	K_{12}	K_{13}	K_{21}	K_{31}
#1	0.389	0.375	0.195	0.0668	0.0035
#2	0.556	0.319	0.195	0.0679	0.0035
#3	0.342	0.442	0.195	0.0659	0.0035
#4	0.425	0.363	0.195	0.0670	0.0035

Table 7. The suggested search space regions of the control parameters for each patient

Kp	*Ki*	*Kd*
-1.5 to +1.5	-2 to +2	-1 to +1

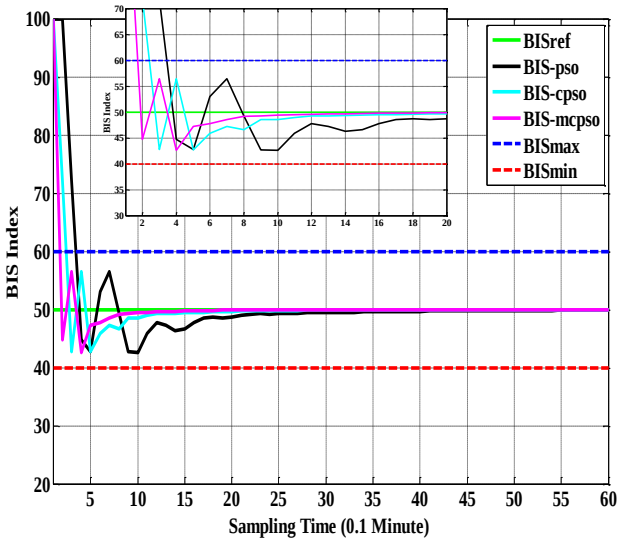

Figure. 5 The BIS response for patient #1 of the closed-loop RBF-NN-PID controller

Table 8. The optimal parameters' values for the three algorithms

Algorithms	K_p	K_i	K_d
PSO	-0.437	-0.241	-0.881
CPSO	-0.543	-0.235	-0.766
MCPSO	-0.521	-0.225	-0.757

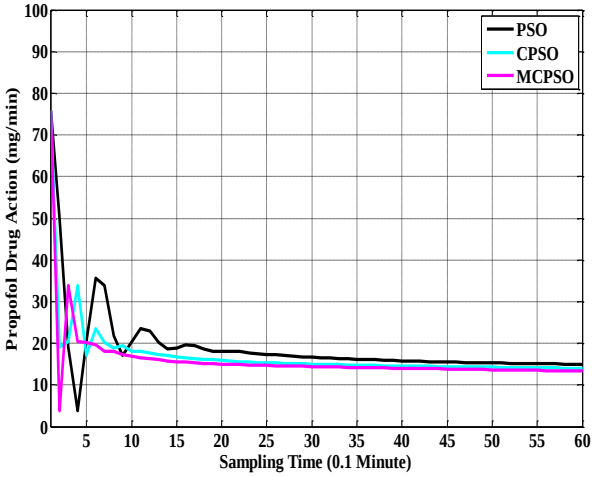

Figure. 6 The propofol drug rate response

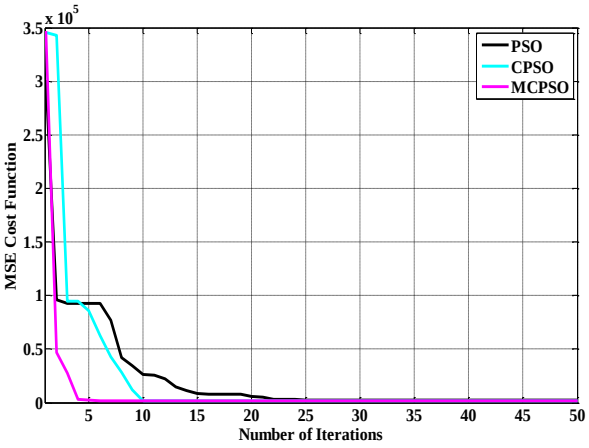

Figure. 7 The response of the cost function (MSE) for all methods

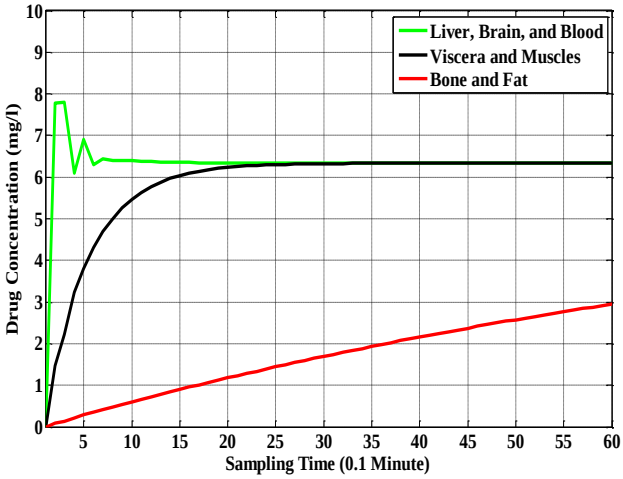

Figure. 8 The response of the plasma concentration in the PK model

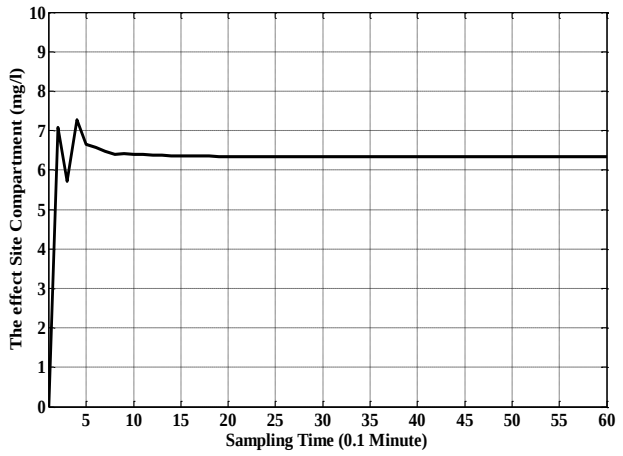

Figure. 9 The response of the concentration of the drug in the effect site compartment

for patient #1 by employing PSO, CPSO, and the proposed MCPSO algorithms are displayed in Table 8. Fig. 6 shows the output response of the propofol drug action of the RBF-NN-PID controller when the desired BIS value suddenly decreases from 100 to 50 in a moderately hypnotic state. The proposed controller quickly and optimally calculates the propofol drug action value to control the depth of the hypnosis state. Based on Eq. (22), the response of the cost function (MSE), which is used in the three tuning algorithms, during 50 iterations is shown in Fig. 7.

In particular, the proposed MCPSO algorithm reaches the minimum value of MSE at 5 iterations, the CPSO algorithm reaches it at 10 iterations, and the PSO algorithm reaches it at 25 iterations. Specifically, the chaos method is applied in the proposed MCPSO algorithm in the three parts of Eq. (34) in parameters (W_{new}, c_{1-new}, and c_{2-new}) in order to increase the stochastic randomness in the search for the MCPSO algorithm and to solve the local minima problem as fast as possible. On the other hand, the CPSO algorithm uses only one chaos parameter (W_{new}). In the PSO algorithm, the chaos method was not applied. Fig. 8 shows the response of the plasma concentration in the PK model for the core compartments of the liver, brain, and blood. Moreover, the viscera and muscles are fast-moving, well-perfused bodily tissues, while the bone and fat have a slow dynamic because they are bodily components with limited blood flow. Fig. 9 shows the concentration of the drug in the effect site compartment $C_e(t)$ in the PD model that was obtained from the plasma concentration in the PK model. The outcomes of evaluating the proposed RBF-NN-PID controller using the proposed MCPSO algorithm for patient #1 in different surgery BIS index values, including the light hypnotic state of 70, the moderate hypnotic state of 50, and the start deep hypnotic state of 25 in terms of fast response,

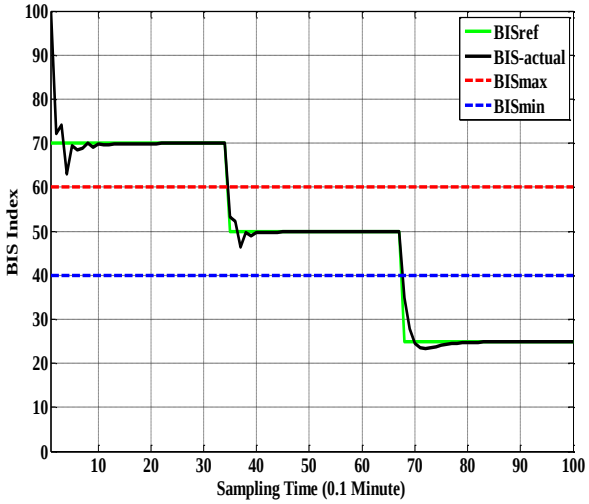

Figure. 10 The surgery BIS response for different states

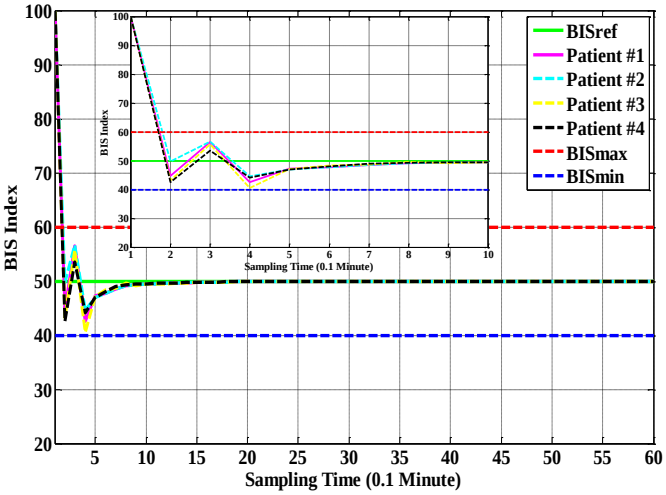

Figure. 12 The BIS response for four patients [8] of the closed-loop RBF-NN-PID controller

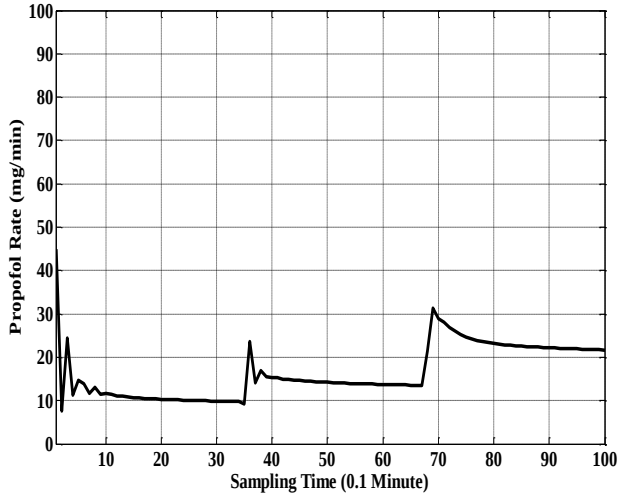

Figure. 11 The propofol drug rate response for different states of BIS surgery

Table 9. The definitions of physical specifications [7]

Patient	Gander	A	H	W	EC_{50}	g
#1	F	36	163	50	6.76	4.29
#2	F	28	164	52	8.44	4.1
#3	M	37	187	75	8.02	2.1
#4	M	42	179	78	4.82	1.85

Table 10. The parameters of the PK/PD model

Patient	K_{10}	K_{12}	K_{13}	K_{21}	K_{31}
#1	0.377	0.397	0.195	0.0665	0.0035
#2	0.386	0.442	0.195	0.0659	0.0035
#3	0.342	0.442	0.195	0.0659	0.0035
#4	0.425	0.363	0.195	0.0670	0.0035

accurately maintaining a triad of hypnosis, and optimally generating the propofol drug action are shown in Figs. 10 and 11, respectively. Fig. 12 shows the performance of the proposed controller using the off-line method for tuning the parameters based on MCPSO algorithms and using the parameters' definition in Tables 4, 5, and 6 for four patients [8] at a desired BIS that equals 50. From Fig. 12, the fast response of BIS reaches the desired BIS of 50 in 1 minute, and all patients will enter the moderate hypnotic state at 0.1 minutes. The second dataset includes four different patients with physical specifications of (gender, age, height, weight, EC50, and g), as given in Table 9, [7]. Then, the parameters of the PK/PD model are shown in Table 10, and they are based on the Eqs. (4)-(10), where Ke0 is a constant value (0.456 (1/min)). Fig. 13 shows the performance of the proposed controller for another dataset [7] of four patients at a desired BIS that equals 50. From Fig. 13, the fast response of BIS reaches the desired BIS of 50 in 1 minute, and patients #1, #2, and #4 will enter the moderate hypnotic state at time 0.1 minutes, while patient #3 will enter the moderate hypnotic state at time 0.25 minutes. To validate the effectiveness of the proposed optimization algorithms (MCPSO) for tuning the parameters of the RBF-NN-PID controller in terms of reaching the moderate hypnotic state at a minimum time and for displaying the time enhancement percentage, Eq. (36) is used.

$$Enhancement\ Time\ (\%) = 100\left(1 - \frac{Time\ for\ Ess\ to\ reach\ \ zero\ by\ the\ proposed\ method}{Time\ for\ Ess\ to\ reach\ \ zero\ by\ other\ method}\right) \quad (36)$$

Table 11 shows the comparison of the simulation

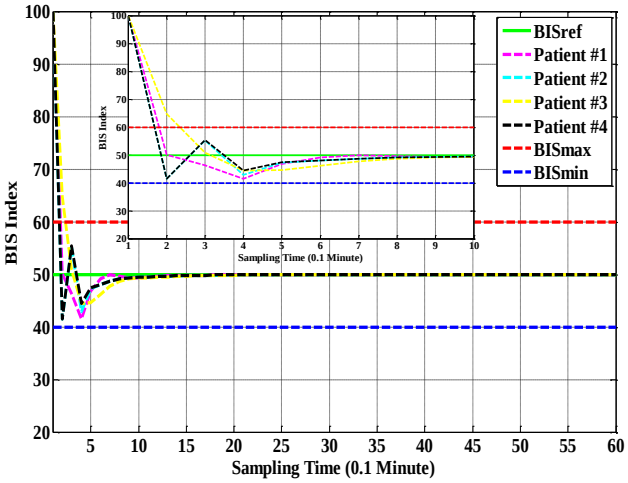

Figure. 13 The BIS response for four patients [7] of the closed-loop RBF-NN-PID controller

Table 11. Comparing the simulation results with other controller's designs.

Type of control algorithm	**Tuning algorithm**	**Steady-State Error and time to reach the moderate hypnotic state**	**Enhancement in the time to reach the moderate hypnotic state (%)**
Fractional order controller [8]	Adaptive high gain	E_{ss}=0 T=2 min	50% when using MCPSO
Adaptive Neuro-Fuzzy controller [7]	Trial and error	E_{ss}=0 T=3 min	67% when using MCPSO
The proposed RBF-NN-PID	PSO	E_{ss}=0, T=3 min	
	CPSO	E_{ss}=0T=1.5 min	
	The Proposed MCPSO	E_{ss}=0, T=1 min	

results for the suggested nonlinear RBF-NN-PID controller utilizing the tuning algorithms (PSO, CPSO, and the proposed MCPSO) and the results of other types of controllers that are taken from the dataset from [7, 8], as given in Tables 5 and 9.

The fractional order controller in [8] was built for the linear PK/PD model, and it uses the adaptive high control gain for all patients starting from 1000 using the trial-and-error method to obtain the control law gain. Therefore, the controller generates a fast but non-optimal value of the propofol control action, which leads to an actual BIS value at a steady-state error of zero at 2 minutes to reach the moderate hypnotic state at a 50 BIS value. In contrast, the proposed nonlinear RBF-NN-PID controller uses the proposed heuristic method (MCPSO) with the PK/PD model, and the controller has generated optimal or near-optimal propofol control action based on the best parameters obtained by the proposed MCPSO optimization algorithms, which leads to reaching the moderate hypnotic state level of 50 BIS in 1 minute without error in the steady state and with no oscillation. By using Eq. (36), the comparison results showed that the nonlinear RBF-NN-PID enhanced the time to 1 minute to reach the moderate hypnotic state by 50% when compared to the fractional order controller [8] that reached the moderate hypnotic state in 2 minutes, taking into account the same dataset and the same operation conditions. The adaptive neuro-fuzzy controller in [7] was designed for the linear PK/PD patient model. It uses three membership values and two variable gains with the trial-and-error method to obtain the two control gains in the control law. As a result, the controller generates a quick and suboptimal value of the propofol control action, which causes a slight oscillation in the BIS index value at 3 minutes without error in the steady-state response. On the other hand, the proposed nonlinear RBF-NN-PID controller using the proposed heuristic method (MCPSO) with the PK/PD model has generated optimal or near-optimal propofol control action based on the best parameters obtained by the proposed MCPSO optimization algorithms, which leads to reaching the moderate hypnotic state level of 50 BIS in 1 minute without error in the steady-state and with no oscillation. By using Eq. (36), the comparison results showed that the nonlinear RBF-NN-PID enhanced the time to 1 minute to reach the moderate hypnotic state by 67% when compared to the adaptive neuro-fuzzy controller [7], which reached the moderate hypnotic state in 3 minutes, considering the same dataset and the same operation conditions.

In summary, the simulation results demonstrate that the suggested nonlinear RBF-NN-PID controller with the proposed MCPSO algorithm can generate the best propofol infusion rate control action, which allows the linear PK/PD patient model to track the required depth of anesthesia with the least amount of tracking error and minimum time to reach the moderate hypnotic state, achieving the optimal performance in various patients' datasets.

5. Conclusions

The main scientific contribution of this work is to find and tune the optimal or near-optimal control gain

parameters of the nonlinear RBF-NN-PID controller using the proposed MCPSO algorithm based on the chaos method. Specifically, this method uses the coefficients of acceleration and removes the two random parameters from the velocity update equation in order to generate more chaotic randomness in the search space in order to quickly solve the local minima problem, leading to obtaining the fast and optimal value of the rate of anesthetic drug control action that will be injected into the patient-based PK/PD model. This process is done to quickly track and stabilize the patient's depth of anesthesia and keep it at a surgery BIS index value within a suitable time to avoid under- or over-dosing of the drug for the patient that leads to hypotension and postoperative adverse reactions during surgical operations or after them.

Consequently, the MCPSO method was suggested using the auto-tuned control strategy of the proposed RBF-NN-PID controller, and it works incredibly well to solve the following issues:

- At the target BIS value of 50, the depth of anesthesia is superbly monitored and sustained at a typical moderate hypnotic state of (60-40) without oscillation in the steady state.
- In order to increase the stochastic randomness in the search for the proposed algorithm and to solve the local minima problem, the chaos method was applied in the three parts of Eq. (34) in parameters (W_{new}, c_{1-new}, and c_{2-new}), resulting in the suggested MCPSO algorithm, which has the offline tuning control parameters of kp, ki, and kd.
- The propofol-infusion rate control action was optimized to improve the surgery BIS index response with high tracking precision of the measured output without a spike or saturation condition.
- The minimum tracking error for the surgical BIS index is equal to zero.
- The comparison results showed that the proposed RBF-NN-PID controller enhanced the time in one minute to reach the depth of anesthesia at the moderate hypnotic state when compared to the fractional-order adaptive high-gain controller, in which the time to reach the depth of anesthesia is two minutes. In contrast, the adaptive neuro-fuzzy controller reached the depth of anesthesia in three minutes. Therefore, the time was improved by 50% and 67%, respectively.

In order to manufacture anesthesia systems, the experimental work of the proposed RBF-NN-PID controller with the proposed MCPSO optimization algorithm will be implemented in the future in an embedded system based on an FPGA development board or an Arduino card with a propofol infusion drug pump device.

Conflicts of Interest

The authors declare no conflict of interest.

Author Contributions

For the linear PK/PD model, Ahmed S. Al-Araji, Khulood E. Dagher, and Mohammed Najm Abdullah developed the nonlinear RBF-NN-PID controller. Ahmed S. Al-Araji proposed the meta-heuristic MCPSO technique. For the datasets of patients, Khulood E. Dagher outlined the suggested control strategy based on PSO and CPSO. The suggested simulation findings from this work were addressed by all authors.

References

[1] Y. Kotani, A. Pruna, and G. Landoni, "Mechanisms of Action of the Detrimental Effect of Propofol on Survival", *Journal of Cardiothoracic and Vascular Anesthesia*, Vol. 37, No. 11, pp. 2176-2180, 2023.

[2] A. Mehr, S. I. Shah, M. Shaban, M. Shahid, and M. M. Awais, "Automatic Anesthesia Depth Control System For Isoflurane Concentration', In: *Proc. of International Conf. on Applied Sciences and Technology (IBCAST)*, Islamabad, Pakistan, pp. 476-489, 2022.

[3] S. Krishnakumar, B. Janney, W. A. Snowfy, S. J. Sharon, and S. V. Kumar, "Automatic anaesthesia regularization system (AARS) with patient monitoring modules", *International Journal of Engineering and Technology*, Vol. 7, No. 2, pp. 48-52, 2018.

[4] N. Eshghi, M. Aliyari, and M. Teshnehlab, " Anesthesia Control Based on Intelligent Controllers", In: *Proc. of International Conf. on Bioinformatics and Biomedical Engineering*, Beijing, China, pp. 1-4, 2009.

[5] S. Yelneedi, S. Lakshminarayanan, and G. P. Rangaiah, "Advanced Regulatory Controller for Automatic Control of Anesthesia", In: *Proc. of International Conf. of Automatic Control*, Seoul, Korea, pp. 11636-11641, 2008.

[6] U. Shola, and V. Neelanarayanan, "Control of Anesthesia Concentration using PID Controller", *International Journal of Innovative Technology and Exploring Engineering*, Vol. 8, No. 6, pp. 356-360, 2019.

[7] M. J. Khodaei, M. H. Balaghi, A. Mehrvarz, and N. Jalili,"An Adaptive Multi-critic Neuro-fuzzy Control Framework for Intravenous Anesthesia Administration", *IFAC-Papers OnLine*, Vol. 51, No. 34, pp. 202-207, 2019.

[8] M. B. Alavi, and M. Tabatabaei, "Control of Depth of Anesthesia using Fractional-Order Adaptive High-Gain Controller", *IET Systems Biology*, Vol. 13, No. 1, pp. 36-42, 2019.

[9] B. Patel, H. Patel, P. Vachhrajani, D. Shah, and A. Sarvaia, "Adaptive Smith Predictor Controller for Total Intravenous Anesthesia Automation", *Biomedical Engineering Letters*, Vol. 9, pp. 127-144, 2019.

[10] A. T. Namel, and M. A. Sahib, "A Comprehensive Review on Automated Control of Anesthesia: Recent Methods, Challenges and Future Trends", *Wasit Journal for Pure Science*, Vol. 2, No. 2, pp. 291-315, 2023.

[11] O. Vandemoortele, L. N. Hannivoort, F. Vanhoorebeeck, M. M. R. F. Struys, and H. E. M. Vereecke, "General Purpose Pharmacokinetic-Pharmacodynamic Models for Target-Controlled Infusion of Anaesthetic Drugs: A Narrative Review", *Journal of Clinical Medicine*, Vol. 11, No. 9, pp. 1-14, 2022.

[12] T. W. Schnider, C. F. Minto, P. L. Gambus, C Andresen, D. B. Goodale, S. L. Shafer, and E. J. Youngs 'The Influence of Method of Administration and Covariates on the Pharmacokinetics of Propofol in Adult Volunteers', *Anesthesiology*, Vol. 88, No. 5, pp. 1170-1182, 1998.

[13] T. Hallynck, H. Soep, J. Thomis, J. Boelaert, R. Daneels, and L. Dettli, "Should Clearance be Normalised to Body Surface or to Lean Body Mass?" *British journal of Clinical Pharmacology*, Vol. 11, No. 5, pp. 523-526, 1981.

[14] M. N. Abdullah, and K. E. Dagher, "Airborne Computer System Path-Tracking Based Multi-PID-PSO Controller Design", *International Journal of Intelligent Engineering and Systems*, Vol. 14, No. 3, pp. 403-411, 2021, doi: 10.22266/ijies2021.0630.33.

[15] S. B. Shinde, K. Lahari, K. C. Garimella, V. S. Sree, N. K. Pikle, G. S. Bhavekar, P. Borkar, S. Badhiye, and M. Raghuwanshi, "Experimental Analysis of Heart Disease Prediction Using Machine Learning with Emphasis on Hyper Parameter Tuning and Recursive Feature Elimination", *International Journal of Intelligent Engineering and Systems*, Vol. 16, No. 6, pp. 85-100, 2023, doi: 10.22266/ijies2023.1231.08.

[16] N. T. Pham, and T. D. Le, "A Novel FOC Vector Control Structure Using RBF Tuning PI and SM for SPIM Drives", *International Journal of Intelligent Engineering and Systems*, Vol. 13, No. 5, pp. 429-440, 2020, doi: 10.22266/ijies2020.1031.38.

[17] K. E. Dagher, "Design of an Adaptive Neural Voltage-Tracking Controller for Nonlinear Proton Exchange Membrane Fuel Cell System Based on Optimization Algorithms", *Journal of Engineering and Applied Sciences*, Vol. 13, No. 15, pp. 6188-6198, 2018.

[18] F. A. S. AL-Taie, and A. S. Al-Araji, "Development of Predictive Voltage Controller Design for PEM Fuel Cell System based on Identifier Model", *International Journal of Intelligent Engineering and Systems*, Vol. 16, No. 2, pp. 343-360, 2023, doi: 10.22266/ijies2023.0430.28.

[19] S. M. Hussein, and A. S. Al-Araji, "Enhancement of a Path-Finding Algorithm for the Hovercraft System Based on Intelligent Hybrid Stochastic Methods", *International Journal of Intelligent Engineering and Systems*, Vol. 17, No. 2, pp. 346-364, 2024, doi: 10.22266/ijies2024.0430.29.

[20] A. A. Kareem, B. K. Oleiwi, and M. J. Mohamed, "Planning the Optimal 3D Quadcopter Trajectory Using a Delivery System-Based Hybrid Algorithm", *International Journal of Intelligent Engineering and Systems*, Vol. 16, No. 2, pp. 427-439, 2023, doi: 10.22266/ijies2023.0430.34.

[21] K. E. Dagher, and M. N. Abdullah, "Airborne Computer System Based Collision-Free Flight Path Finding Strategy Design for Drone Model", *International Journal of Intelligent Engineering and Systems*, Vol. 14, No. 6, pp. 234-248, 2021, doi: 10.22266/ijies2021.1231.22.