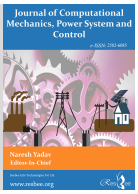
Vol.5 No.2 April 2022

Journal of Computational Mechanics, Power System and Control

Received 10 December, Revised 28 February, Accepted 25 March



Shark Optimization Algorithm: Drug Dosage Estimation in Cancer Chemotherapy

Anbhazhagan P
Associate Professor
Department of Computer Science and Information Technology
Kebri Dehar University, Ethiopia

Abstract: Chemotherapy is a medicine that is frequently exploited to treat cancer; the cancer cells widen as well as propagate more rapidly than the other cells in body. Although chemotherapy is a capable technique to analyze several types of cancers, treatment involves threat as it reasons side effects because of inappropriate drug practice. Thus, this research proposes a robust controller to control the dosage of the drug which is performed in parameter estimation. Additionally, a Modified Regularized Error Function (MREF)-Extended Kalman Filter (EKF) is adopted to approximate tumor cells as well as it can be used for different circumstances. In addition, the overfitting problem happens at the time of the drug dosage estimation which is resolved by exploiting this method. Furthermore, to improve the proposed model performance, the primary condition of EKF is fine-tuned using Shark Optimization Algorithm (SOA). Finally, the preeminence of the developed technique is revealed regarding the error analysis.

Keywords: Cancer, Chemotherapy, Controller, Drug, Treatment, Overfitting

Nomenclature

Abbreviations	Descriptions
GWO	Grey Wolf Optimization
MREF	Modified Regularized Error Function
RMSE	Root Mean Square Error
pCR	pathological Complete Remission
GA	Genetic Algorithm
TN	Triple-Negative
MIMO	Multiple Input Multiple Output
PSO	Particle Swarm Optimization
MA	Memetic Algorithm
MAE	Mean Absolute Error
EKF	Extended Kalman Filter
GSA	Gravitational Search Algorithm
FM	Forward Movement
NEF-EKF-ISF	Nonlinear Error Function based EKF with Improved Scaling Factor

1. Introduction

Generally, chemotherapy is the most important treatment modality for cancer patients as well as it includes the employ of parenteral or oral chemotherapeutic agents to monitor the growth of the tumor as well as to extend the endurance time of patients. Into the bloodstream, the chemotherapeutic agents will go through and arrive at the cancerous cells and normal host cells all through the body. Therefore, the most important difficult disadvantage seen in oncology is the toxicity of chemotherapeutics. Besides these conditions, numerous kinds of research encountered mathematical approaches to recognize the growth of tumors in the chemotherapy as well as formulate the best chemotherapy schedules which ascertain the drug's dosage administrated to the cancer patients by means of the objectives of increasing the therapeutic efficiency on tumor cells as well as reducing the normal cells toxicity [6]. Meanwhile, chemotherapy has both benefits as well as drawbacks. Still, if a patient is unsure regarding the starting

https://doi.org/10.46253/jcmps.v5i2.a2

diagnosis else reappearance, it is highly useful to go for chemotherapy [7]. One more notable feature of chemotherapy is the materialization of drug confrontation, generally seen in cancer patient's treatment. If "tumor cells produce resistance to chemotherapeutic agents, enduring treatment might no longer be effectual as well as the oncologists have to, consequently, conclude a novel chemotherapy schedule". Nevertheless, there are a restricted amount of chemotherapy regimens to treat each category of cancer efficiently.The main objective of some studies is to devise an optimal control problem as well as resolve it. The chemotherapeutic schedule is attained as diminishes the load of the tumor; the negative features of drugs on healthy cells are taken into consideration. For MIMO Cancer Immunotherapy, a new Feedback Linearization Control is developed. A technique of predictive control with a moving horizon is exploited to decide the optimal dosing of cancer chemotherapy. An optimal immunotherapy manage of destructive tumor growth was developed. An adaptive control approach was exploited to control the usage of the drug, as well as the performance of the three unsure approaches, was evaluated. The optimal control theory was employed and shows the stability and efficacy of the optimization model to minimize cancer load excluding the tumor is not eradicated.

The major contribution of this research is to develop a robust controller to control drug dosage by means of a new noise factor as well as an error function. Here, a new approach is proposed a novel algorithm known as the Shark optimization algorithm to fine-tune the primary state of EKF.

2. Related Works

In 2021, Ying Cheng et al [1], developed pembrolizumab–chemotherapy extended endurance vs. placebo–chemotherapy with convenient toxicity as well as the conserved or enhanced health-associated of life quality in Chinese patients with metastatic squamous NSCLC. The performance analysis exhibits that aid pembrolizumab–chemotherapy as initial-line treatment in this population. In 2019, XIN FENG *et al.,* [2], worked on the viewpoint to predict pCR by employing only nodal sizes of the primary three treatments. An optimal feature combination for each breast cancer sub-kind was observed from real nodal sizes of the primary three treatments as well as nodal sizes of subsequently 3 treatments predicted from those of the initial 3 ones. The prediction was estimated using measures Avc D. A True Negative breast cancer patient might be an opinion of pCR Avc D subsequent to using soon three treatments. In any case, Avc D was attained for all 4 breast cancer subtypes examined in this paper. In 2021, Muhammad Zubair *et al*., [3], worked on the variable structure on the basis of the nonlinear control approaches presented to minimize the tumor cells, protect a secure amount of healthy cells, remain the immune cells over a definite value, and make sure an appropriate number of chemotherapy drug. In 2020, Peilian Wang *et al*., [4], formulated competent amalgamation chemotherapy schedules, which establish drugs dosages administered to cancer patients. The conventional cell cycle-specific model was employed; the method of obtaining drug resistance was integrated to typify cell growth. Then, the purpose of optimal chemotherapy schedule for patients was devised as a nonlinear optimization issue, with the objective of reducing not merely the quantity of tumor cells. To overwhelm the complexity in examining an acceptable solution to the issue because of its nonlinear nature MA with a developed local search scheme was developed. In 2020, Utkarsha L. Mohite and Hirenkumar G. Patel [5], worked on a robust controller which examines drug dosage besides from estimation of parameters here, and a NEF-EKF-ISF was developed. In reality, the error was calculated by employing the traditional difference function and it was utilized to update the procedure of EKF in the conventional models.

3. Adopted Non-Linear Control Theory

A new non-linear controller model is developed which verifies the association of tumor cells with normal cells as well as immune cells. Eq. (1) to (3) indicates a non-linear system which $B(n)$, $T(n)$ as well as $ID(n)$ represents a number of the tumor, normal as well as immune cells at a time n. As a result, drug injections are represented as the control inputs. The chemotherapeutic drug effect is represented as $v_1(n), v_2(n)$ and $v_3(n)$ correspondingly. Moreover, immune cell type is taken into consideration which reduces the size of the tumor using a kinetic process. In addition, the technique is taken into consideration of immunity cells, and their growth is enthused by T-cells. The cell total population is presumed to be destroyed by exploiting the drug with different levels. Eq. (1) indicates that Lymph node, as well as bone marrow models, are a steady resource for ID cells.

$$\overrightarrow{ID} = st + \frac{\rho ID \cdot T}{\alpha + T} - p_1 ID \cdot T - t_1 IB - y_1 v_1 IB \quad (1)$$

$\frac{\rho ID \cdot T}{T}$ represents saturation with terms like ρ and α that directly shows that immune cells are encouraged using tumour cells. $q_1 ID \cdot T$ represents contest amongst tumour as well as immune cells which

reason immune cell loss. $y_1 v_1 ID$ represents immune cell loss as well as $t_1 ID$ represents that immune cells are insolvent at t_1 nature death rates. In Eq. (2), $r_1 T(1 - c_1 T)$ represents tumour cell's development with r_1 growth rate as well as t_1^{-1} carrying ability. The inconsistency amid the rates of growth as well as death is shown using logistic growth terms [6]. $p_2 ID \cdot T$ represents disagreements amid tumor as well as immune cells which results in losses of tumour cells. Similarly, $p_3 TB$ represents differences between normal and tumour cells which reasons tumour cell loss as well as $y_2 v_2 Q$ signifies tumour cells loss.

$$\vec{T} = r_1 T(1 - c_1 T) - p_2 ID \cdot T - p_3 TV - y_2 v_2 T \tag{2}$$

$r_2 B(1 - c_2 B)$ signifies normal cells population growth with r_2 growth rate as well as t_2^{-1} in eq. (3). Moreover, $p_4 QB$ represents divergences amid tumor and normal cells which causes normal cell loss and $y_3 v_3 B$ represents normal cell losses. Moreover, y_1, y_2 and y_3 represents chemotherapy's effect on destroying cell growth.

$$\vec{B} = r_2 B(1 - c_2 B) - p_4 TB - y_3 v_3 B \tag{3}$$

4. Adaptive Controlling System

In this research, an adaptive robust control system is adopted for 3rd -order nonlinear approach. The aforesaid controller tries to mark out the system conditions with suitable optimum values. In order to accomplish the objective, the number of cells is calculated with the optimum values as well as error waveforms are produced on the basis of that drug dosage proposed. In addition, constraints are calculated as well as used in the controller loop to model a robust system. Eq. (4) and (5) describe the reformulation of eq. (1) to (3) which describes the 3rd order model of a tumour.

$$\begin{bmatrix} \overrightarrow{ID} \\ \vec{T} \\ \vec{B} \end{bmatrix} = \begin{bmatrix} 1 & 0 & 0 \\ \frac{ID \cdot T}{\alpha + T} & 0 & 0 \\ -T.ID & 0 & 0 \\ -ID & 0 & 0 \\ 0 & T & 0 \\ 0 & T^2 & 0 \\ 0 & -T^2 & 0 \\ 0 & -ID & 0 \\ 0 & -TD & 0 \\ 0 & 0 & T \\ 0 & 0 & -T^2 \\ 0 & 0 & -TB \end{bmatrix}^T \begin{bmatrix} st \\ \rho \\ p_1 \\ t_1 \\ r_1 \\ r_1 c_1 \\ p_2 \\ p_3 \\ r_2 \\ r_2 t_2 \\ p_4 \end{bmatrix} - \begin{bmatrix} y_1 ID v_1 \\ y_2 T v_2 \\ y_3 B v_3 \end{bmatrix} \tag{4}$$

$$\begin{bmatrix} v_1 \\ v_2 \\ v_3 \end{bmatrix} = \begin{bmatrix} \frac{1}{T} & 0 & 0 \\ \frac{T}{\alpha + T} & 0 & 0 \\ -D & 0 & 0 \\ -1 & 0 & 0 \\ \frac{-ID}{ID} & 0 & 0 \\ 0 & 1 & 0 \\ 0 & -T & 0 \\ 0 & ID & 0 \\ 0 & -T & 0 \\ 0 & \frac{-T}{T} & 0 \\ 0 & 0 & 1 \\ 0 & 0 & -B \\ 0 & 0 & -T \\ 0 & 0 & \frac{-B}{B} \end{bmatrix}^T \begin{bmatrix} \frac{st}{y_1} \\ \frac{\rho}{y_1} \\ \frac{p_1}{y_1} \\ \frac{t_1}{y_1} \\ \frac{1}{y_1} \\ \frac{r_1}{y_2} \\ \frac{r_1 c_1}{y_2} \\ \frac{p_2}{y_2} \\ \frac{p_3}{y_2} \\ \frac{1}{y_2} \\ \frac{r_2}{y_3} \\ \frac{r_2 c_2}{y_3} \\ \frac{q_4}{y_3} \\ \frac{1}{y_3} \end{bmatrix} \tag{5}$$

Eq. (6) indicates the regression vectors. Eq. (7) denotes parameters are resaved with the estimated values as well as appropriate equations in the scenario of uncertainties. Subsequently, to formulate a steady model, the states like immune, normal as well as tumour cells mark out their associated optimum values that are exhibited in eq. (8), where positive values are shown γ_1, γ_2 and γ_3. (ID_t and $\overrightarrow{ID_t}$), (T_t and $\vec{T}_t$) as well as (B_t and $\vec{B}_t$) implies the immune cell's optimum values and derivation of immune cell, tumour cell as well as a normal cell. In eq. (6), the eq. (8) is replaced in order to achieve the eq. (9)

$$H_1 = \left[\frac{1}{ID} \quad \frac{T}{\alpha + T} \quad -T \quad -1 \quad \frac{-ID}{ID}\right]$$
$$H_2 = \left[1 \quad -T \quad -ID \quad -B \quad \frac{-T}{T}\right] \tag{6}$$
$$H_3 = \left[1 \quad -B \quad -T \quad \frac{-B}{B}\right]$$

$$\bar{\theta}_1 = \left[\frac{\overline{st}}{\bar{y}_1} \quad \frac{\bar{\rho}}{\bar{y}_1} \quad \frac{\bar{p}_1}{\bar{y}_1} \quad \frac{\bar{t}_1}{\bar{y}_1} \quad \frac{1}{\bar{y}_1}\right]^T$$
$$\bar{\theta}_2 = \left[\frac{\bar{r}_1}{y_2} \quad \frac{\bar{r}_2 \bar{c}_2}{y_2} \quad \frac{\bar{c}_2}{\bar{y}_2} \quad \frac{\bar{c}_3}{\bar{y}_2} \quad \frac{1}{\bar{y}_2}\right]^T \tag{7}$$
$$\bar{\theta}_3 = \left[\frac{\overline{ra}_2}{\bar{y}_3} \quad \frac{\overline{ra}_2 \bar{c}_2}{y_3} \quad \frac{\bar{c}_4}{\bar{y}_3} \quad \frac{1}{\bar{y}_3}\right]^T$$

$$\overrightarrow{ID} = \overrightarrow{ID}_t - \gamma_1(ID - ID_t)$$
$$\vec{T} = \vec{T}_t - \gamma_2(T - T_t) \tag{8}$$
$$\vec{B} = \vec{B}_t - \gamma_3(B - B_t)$$

$$H_1\left(\overrightarrow{ID}_t - \gamma_1(ID - ID_t), ID, B, T\right) = \left[\frac{1}{ID} \quad \frac{T}{\alpha + T} \quad -T \quad -1 \quad \frac{-\overrightarrow{ID}_t - \gamma_1(ID - ID_t)}{ID}\right]$$
$$H_2\left(\vec{T}_t - \gamma_2(T - T_t), ID, B, T\right) = \left[1 \quad -T \quad -1 \quad -B \quad \frac{-\vec{T}_t - \gamma_2(T - T_t)}{Q}\right] \tag{9}$$
$$H_3\left(\vec{B}_t - \gamma_3(B - B_t), ID, B, T\right) = \left[1 \quad -B \quad -T \quad \frac{-B_t - \gamma_3(B - B_t)}{B}\right]$$

Eq. (10) states control law where, $\bar{\theta}_1$, $\bar{\theta}_2$ as well as $\bar{\theta}_3$ represents vector variables. Additionally, eq. (11) represents the adaptation law to compute the vector constraint, where Γ_1, Γ_2 as well as Γ_3 signifies symmetric positive constant metrics. Eq. (12) states error vector of tumour, immune, as well as normal cell and it is indicated using $\ddot{\vec{T}}$, $\overleftrightarrow{ID}$ as andwell as $\vec{B}$.

$$\begin{cases} v_1 = H_1 \bar{\theta}_1 \\ v_2 = H_2 \bar{\theta}_2 \\ v_3 = H_3 \bar{\theta}_3 \end{cases} \tag{10}$$

$$\dot{\bar{\theta}}_1 = \overleftrightarrow{ID} \cdot ID \cdot \Gamma_1 H_1^T \text{sign}(y_1)$$
$$\dot{\bar{\theta}}_2 = \ddot{\vec{T}} \cdot T \cdot \Gamma_2 H_2^T \text{sign}(y_2) \tag{11}$$
$$\dot{\bar{\theta}}_3 = \dot{\vec{B}} \cdot B \cdot \Gamma_3 H_3^T \text{sign}(y_3)$$

$$\overleftrightarrow{ID} = ID - ID_t \tag{12}$$

4.1. Kernel Function

In reality, to compute the immune cells, it is essential to use a nonlinear observer. At first, on the basis of eq. (13), a discrete-time nonlinear system is designed, wherein w_k represents processing noise as well as x_k represents the measurement noises. The foremost purpose of this research is to adopt a new noise factor named as m. The combination of m might tends to system state disturbances that are reduced using the adopted model. Moreover, as stated in Eq. (14), x_k and w_k are fixed as ZWGN with two covariance metrics and it is stated as Q and R, wherein b_k represents measurement vector such as normal and tumor cells as well as a_k signifies system states and these vectors are stated in eq. (15). In addition, proposed model is used to tune primary state w_k in Eq. (13). On basis of eq. (1), (2) as well as (3), the

cancer chemotherapy scheme attains f^* and eq. (11) consists of the estimating constraints employed in the EKF observer. Therefore, on the basis of eq. (16), f^* is modeled.

$$\begin{aligned} b_k &= f(b_{k-1}, u_{k-1}) + w_k \\ a_k &= Ub_k + x_k + m \end{aligned} \tag{13}$$

$$\begin{aligned} &\left\{w_k w_j^T\right\} = R\delta_{kj} \quad R > 0, \\ &\left\{x_k x_j^T\right\} = Q\delta_{kj} \quad Q > 0 \end{aligned} \tag{14}$$

$$\left\{w_k x_j^T\right\} = 0$$

$$\begin{aligned} b_k &= \left[ID_k \quad T_k \quad B_k\right]^T \\ a_k &= \left[T_k \quad B_k\right]^Q \end{aligned} \tag{15}$$

$$f^* = \begin{bmatrix} \overline{st} + \dfrac{\overline{\rho} ID_k T_k}{\overline{\alpha} + T_k} - \overline{p}_1 ID_k T_k - \overline{t}_1 ID_k - \overline{y}_1 v_{1k} ID_k \\ \overline{r}_1 T_k (1 - \overline{c}_1 T_k) - \overline{p}_2 ID_k T_k - \overline{p}_3 T_k B_k - \overline{y}_2 v_{2k} T_k \\ \overline{r}_2 B_k (1 - \overline{c}_2 B_k) - \overline{p}_4 T_k B_k - \overline{y}_3 v_{3k} B_k \end{bmatrix} \tag{16}$$

Using EKF the varied states are estimated such as prediction as well as update.

Prediction: As stated in eq. (17), the prediction of $\vec{b}_{k|k-1}$ as well as associated error covariance matrix $PR_{k|k-1}$ is designed.

Update: As stated in eq. (18), PQ_k and $\vec{b}_k$ are estimated, wherein k_k stated as Kalman gain.

$$\begin{aligned} \vec{b}_{k|k-1} &= \left(\vec{b}_{k-1}\right)f \\ PQ_{k|k-1} &= Er_k PQ_{k-1} Er_k^T + R_k \end{aligned} \tag{17}$$

$$\begin{aligned} Er_k &= \frac{\partial f(b)}{\partial b}|_{b=\vec{b}_{k-1}} \\ \vec{b}_k &= \vec{b}_{k|k-1} + k_k\left(a_k - U_k \vec{b}_{k|k-1}\right) \\ k_k &= PQ_{k|k-1} U^T{}_k \left(U_k PQ_{k|k-1} U^T{}_k + Q_k\right)^{-1} \\ PQ_k &= \left(PQ^{-1}{}_{k|k-1} + U^T{}_k Q^{-1}{}_k U_k\right)^{-1} \end{aligned} \tag{18}$$

4.2. Covariance Matrix Estimation

The estimation of KF is based upon how user selects precise Q_k and R_k for various applications. Usually, Q_k as well as R_k are constant matrixes, which are attained using the trial and error model. Nevertheless, definite problems have occurred in election process, and therefore for enhancement, a novel estimation of covariance matrix is proposed in [7] on the basis of the kernel-based error function. As a conservatory, a novel scaling factor is included with error function as used in [8]. Moreover, developed model aspires to ascertain a new error function as calculated in Eq. (19). T harmonic mean of RMSE and MAE amid h_k and $\vec{b}_k^+$ is calculated that is taken into consideration as the error function. o_k states measurement function, h_k as well as $\vec{b}_k^+$ signifies actual and estimated value in eq. (19). The augmentation is performed with error measure calculation to achieve better performance, wherein differential estimate of error measure ∂e_k is calculated on the basis of Eq. (20).

$$e_k = HM\left[MAE\left(h_k, \vec{b}_k^+\right), RMSE\left(h_k, \vec{b}_k^+\right)\right] \tag{19}$$

$$\partial e_k = \exp\left(\frac{e_k}{e_k^-}\right) \cdot e_k \tag{20}$$

Q **Estimation:** In eq. (21), the Q_k evaluation is stated, which, H_k indicates the covariance matrix of novelty. As a result, as stated in eq. (20), Q_k is estimated in ∂e_k. Furthermore, Eq. (23) exhibits the Q_k evaluation, which b represents the system state number as well as the enhancement factor V.

$$Q_k = G_k - U_k^{[1]} PQ_k^- U_k^{[1]T} \tag{21}$$

$$V = Q_{k-1} + \left(\partial e_k \partial e_k^T + U_k^{[1]} PQ_k^- U_k^{[1]T}\right) \tag{22}$$

$$Q_k = \frac{\log(V)}{b} \tag{23}$$

Additionally, the scaling factor is involved which facilitates updating procedure as coarse-grained as well as fine-tuned. As stated in eq. (24), the V SF represents the scaling factor as calculated in Eq. (25). Here, σe signifies standard deviation and n exhibits a number of instants, as well as we signifies weight which is calculated in Eq. (26), which In signifies prior and present instants, CIn indicates present instants. σe denotes calculated in Eq. (27), which nu represents a number of data points, x_i represents each data value as well as $\vec{y}$ represents x_i mean.

$$V = Q_{k-1} + \left(\partial e_k \partial e_k^T + U_k^{[1]} P Q_k^- U_k^{[1]T}\right) \times [SF] \tag{24}$$

$$SF = \frac{\sigma e}{n} \sum_{i=1}^{n} we_i \tag{25}$$

$$we = \frac{In}{CIn} \tag{26}$$

$$\sigma e = \sqrt{\sum_{i=1}^{nu} \frac{(x_i - \vec{x})^2}{nu - 1}} \tag{27}$$

Estimation of R **:** On the basis of eq. (28), the process noise is calculated in order to estimate R_{k-1}. The average estimation of R concerning time is stated in Eq. (29), which α represents the forgetting factor (0.3 as per [8]) and k_k represents Kalman gain.

$$w_{k-1} = b_k - \Phi(b_{k-1}, v_{k-1}) \tag{28}$$

$$R_k = \alpha R_{k-1} + (1-\alpha)\left(k_k t_k t_k^T k_k^T\right) \tag{29}$$

The proposed approach tries to optimize the primary state (w_k) using the optimization approach. The objective function *(OF)* of the proposed paper which is exhibited in Eq. (30), which $\mathrm{Sum}((So)^2)$ signifies regularized term, e denotes the error, and *So* represents an arbitrary solution.

$$OF = \mathrm{Min}\left[\mathrm{Mean}(e) + \mathrm{Sum}\left((So)^2\right)\right] \tag{30}$$

4.3Proposed SOAModel

The SOA is considered a powerful optimization approach. It is extensively exploited in diverse cases, like solving mathematical functions [13]. In the SOA, rotational movement of sharks is an important operator for engrossing local optimums. In SOA, some suppositions are performed, as well as they are stated below [12]:

a) The wounded fish is represented as the prey to sharks.

b) The sharks attempt to discover injured fish by attaining blood particles from wounded fish's body.

c) The velocity of wounded fish is avoided over the velocity of the shark.

In proposed model, sharks' locations are taken into consideration as candidate solutions for optimization issues [12]:

$$S_j^l = \left[s_{j,1}^l, s_{j,2}^l, \ldots\ldots\ldots, s_{j,ND}^l\right] \tag{31}$$

wherein S_j^l represents the j^{th} initial location, $s_{j,l}^l$ represents k^{th} dimension of j^{th} shark represents and ND represents the count of decision variables. The velocity of the shark's change is stated as below:

$$|v_{j,k}^i| = \min\left[|\eta_i . r_1 \frac{\partial(of)}{\partial(s_k)}| s_{k,k}^i + \alpha \cdot r_2 \cdot v_{j,k}^{i-1}|, |\beta, v_{j,k}^{i-1}|\right] \tag{32}$$

wherein β represents velocity limiter, $v_{j,k}^i$ represents k^{th} dimension of the j^{th} shark velocity, α represents inertia coefficient, r_1, r_2 represents arbitrary numbers of the objective model as well as η_i represents an arbitrary number. The sharks carry out FM by exploiting the preceding location as well as the velocity of sharks:

$$p_j^{i+1} = S_j^i + V_j^i \cdot \Delta t_i \tag{33}$$

wherein p_j^{i+1} represents the new position of j^{th} shark based on the FM, S_j^i represents the current location of j^{th} shark, as well as Δt_i represents a time interval.

From local optimums the sharks employ rotational movement to get away:

$$Q_j^{i+1,m} = P_j^{i+1} + r_3 P_j^{i+1}, m = 1, \ldots\ldots, M \tag{34}$$

wherein $Q_j^{i+1,m}$ represents the position of sharks subsequent to rotational movement, M represents the count of points in local search as well as r_3 represents an arbitrary number.

If a maximization issue is taken into consideration, the ending position of sharks is computed as below:

$$S_j^{i+1} = \arg\max[of(P_j^{i+1}), of(Q_j^{i+1,1}), \ldots\ldots\ldots, of(Q_j^{i+1,M}) \quad (35)$$

For each agent, the objective model is computed. The optimal shark with the optimal objective model is ascertained. Subsequently, the position, as well as the velocity of the sharks, is updated.

5. Experimentation Procedure

In this section, performance analysis of the adopted chemotherapy controller model, called SFO has experimented. Here, the experimentation was performed concerning the error analysis. Moreover, the analysis was performed for 3 varied noise levels 0.41, 0.43, and 0.55. These noise levels were indicated as noise levels 1, 2, and 3 for immune cells, tumour cells, and normal cells. Here, adopted technique has experimented with the traditional techniques namely GWO [14], GA [15], GSA [16], and PSO [15].

Tables 1, 2 and 3 exhibit analysis of the adopted method with the traditional approaches on tracking requisite values of the tumour, normal and immune cells. Here, the analysis is performed for 3 varied noise levels like 0.41, 0.43, and 0.55. When seeing the attained results, the proposed controller model has attained the adjacent best values when compared with the conventional models. Therefore, minimum estimated values are obtained using tumour cells which disclose the nonappearance of tumour cells. Therefore, the adopted model reveals to be improved in minimizing the growth of tumour with the best drug dosage.

6. Conclusion

The major objective of this research was to adopt a novel controller to regulate drug dosages that were carried out in the parameter estimation. Subsequently, an MREF-EKF was developed to estimate tumor cells that were developed under different circumstances. Additionally, the primary phase of the EKF was tuned via the Shark Optimization Algorithm model. Finally, performance analysis was performed to authenticate the enhancement of the adopted technique with the existing models. By analyzing the results, the adopted technique attained better results while differentiated from the conventional techniques.

Table 1: Performance analysis of adopted and existing techniques regarding noise level 1

Methods	GWO	GA	PSO	GSA	Proposed model
Immune Cells (mol)	0.850104	0.850104	0.850104	0.850104	0.850104
Tumour Cells (mol)	0.024156	0.023878	0.024005	0.024156	0.023878
Normal Cells (mol)	0.846477	0.845477	0.846487	0.846466	0.846454

Table 2: Performance analysis of adopted and existing techniques regarding noise level 2

Methods	GWO	GA	PSO	GSA	Proposed model
Immune Cells (mol)	0.650104	0.650104	0.650104	0.650104	0.650104
Tumour Cells (mol)	0.024036	0.023861	0.023886	0.024036	0.02386
Normal Cells (mol)	0.846432	0.846355	0.846222	0.846677	0.846890

Table 3: Performance analysis of adopted and existing techniques regarding noise level 3

Methods	GWO	GA	PSO	GSA	Proposed model
Immune Cells (mol)	0.960104	0.960104	0.960104	0.960104	0.960104
Tumour Cells (mol)	0.043331	0.043164	0.043188	0.043331	0.043164
Normal Cells (mol)	0.841254	0.848976	0.843421	0.846876	0.846899

Compliance with Ethical Standards

Conflicts of interest: Authors declared that they have no conflict of interest.

Human participants: The conducted research follows the ethical standards and the authors ensured that they have not conducted any studies with human participants or animals.

Reference

[1] Ying ChengLi ZhangLuis Paz-Ares,"Pembrolizumab Plus Chemotherapy for Chinese Patients With Metastatic Squamous NSCLC in KEYNOTE-407", JTO Clinical and Research Reports, 25 September 2021.

[2] X. Feng et al., "Accurate Prediction of Neoadjuvant Chemotherapy Pathological Complete Remission (pCR) for the Four Sub-Types of Breast Cancer," IEEE Access, vol. 7, pp. 134697-134706, 2019.

[3] M. Zubair, I. A. Rana, Y. Islam and S. A. Khan, "Variable Structure Based Control for the Chemotherapy of Brain Tumor," IEEE Access, vol. 9, pp. 107333-107346, 2021.

[4] P. Wang, R. Liu, Z. Jiang, Y. Yao and Z. Shen, "The Optimization of Combination Chemotherapy Schedules in the Presence of Drug Resistance," in IEEE Transactions on Automation Science and Engineering, vol. 16, no. 1, pp. 165-179, Jan. 2019.

[5] Mohite, Utkarsha L. and Patel, Hirenkumar G, "Robust controller for cancer chemotherapy dosage using nonlinear kernel-based error function" Bio-Algorithms and Med-Systems, vol. 16, no. 4, pp. 20190056, 2021.

[6] H. Schattler, U. Ledzewicz, “Optimal Control for mathematical models of cancer therapies”, Springer, 2010.

[7] Utkarsha L. MohiteHirenkumar G. Patel,"Optimization assisted Kalman filter for cancer chemotherapy dosage estimation", Artificial Intelligence in Medicine, vol.119, 20 August 2021.

[8] Shahrokh Akhlaghi, Ning Zhou and Zhenyu Huang, "Adaptive Adjustment of Noise Covariance in Kalman Filter for Dynamic State Estimation", Systems and Control, pp. 1-5, 2017.

[9] B. R. Rajakumar, "Impact of Static and Adaptive Mutation Techniques on Genetic Algorithm", International Journal of Hybrid Intelligent Systems, vol. 10, no. 1, pages: 11-22, 2013.

[10] B. R. Rajakumar, "Static and Adaptive Mutation Techniques for Genetic algorithm: A Systematic Comparative Analysis", International Journal of Computational Science and Engineering, vol. 8, no. 2, pages: 180-193, 2013.

[11] S. M. Swamy, B. R. Rajakumar and I. R. Valarmathi, “Design of Hybrid Wind and Photovoltaic Power System using Opposition-based Genetic Algorithm with Cauchy Mutation”, IET Chennai Fourth International Conference on Sustainable Energy and Intelligent Systems (SEISCON 2013), Chennai, India, Dec. 2013.

[12] Ye-fei TianRui-jin LiaoSaeid Gholami Farkoush,"Placement and sizing of EESS bundled with uncertainty modeling by two-stage stochastic search based on improved shark smell optimization algorithm in micro-grids", Energy Reports6 August 2021.

[13] Lina XuYujuan SiHomayoun Ebrahimia,"Medical image fusion using a modified shark smell optimization algorithm and hybrid wavelet-homomorphic filter", Biomedical Signal Processing and Control27 February 2020.

[14] Rupam Gupta Roy,"Rescheduling Based Congestion Management Method Using Hybrid Grey Wolf Optimization - Grasshopper Optimization Algorithm in Power System", Journal of Computational Mechanics, Power System and Control,vol. 2, no. 1, January 2019.

[15] Gayathri Devi K.S,"Hybrid Genetic Algorithm and Particle Swarm Optimization Algorithm for Optimal Power Flow in Power System",Journal of Computational Mechanics, Power System and Control, vol. 2, no. 2, April 2019

[16] Amal Abdulrahman Juma Al Raisi," Hybrid Particle Swarm Optimization and Gravitational Search Algorithm for Economic Dispatch in Power System",Journal of Computational Mechanics, Power System and Control, vol. 3, no. 3, July 2020