Tumoral Angiogenesis Optimizer: A new bio-inspired based metaheuristic

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Abstract

In this article, we propose a new metaheuristic inspired by the morphogenetic cellular movements of endothelial cells (ECs) that occur during the tumor angiogenesis process. This algorithm starts with a random initial population. In each iteration, the best candidate selected as the tumor, while the other individuals in the population are treated as ECs migrating toward the tumor's direction following a coordinated dynamics through a spatial relationship between tip and follower ECs. EC movements mathematical model in angiogenic morphogenesis are detailed in the article. This algorithm has an advantage compared to other similar optimization metaheuristics: the model parameters are already configured according to the tumor angiogenesis phenomenon modeling, preventing researchers from initializing them with arbitrary values. Subsequently, the algorithm is compared against well-known benchmark functions, and the results are validated through a comparative study with Particle Swarm Optimization (PSO). The results demonstrate that the algorithm is capable of providing highly competitive outcomes. Also the proposed algorithm is applied to a real-world problem. The results showed that the proposed algorithm performed effective in solving constrained optimization problems, surpassing other known algorithms.

Keywords: Tumoral angiogenesis optimizer, metaheuristic, global optimization, artificial intelligence.

1 Introduction

Optimization is a broad concept that permeates various domains, from engineering design to business planning, from internet routing to environmental sustainability. Businesses seek to maximize profits while minimizing costs, engineers strive to optimize the performance of their designs while minimizing expenses, and sustainability studies aim to minimize environmental harm in resource exploitation. Nearly everything we do is, in some way, related to optimizing something. Consider, for instance, vacation planning, where we seek to maximize enjoyment while minimizing costs [?, ?, ?, ?, ?, ?, ?, ?, ?].

Mathematical optimization addresses these problems using mathematical tools. However, it has the drawback that many algorithms, especially gradient-based search methods, are local search techniques. Typically, these searches begin with an assumption and attempt to improve the quality of solutions. For unimodal functions, convexity ensures that the final optimal solution is also a global optimum. For multimodal objectives, the search may become trapped in a local optimum. Another limitation lies in solving optimization problems with high-dimensional search spaces; classical optimization algorithms fail to provide suitable solutions because the search space grows exponentially with problem size, rendering exact techniques impractical. Moreover, the complexities of real-world problems often prevent verifying the uniqueness, existence, and convergence conditions that mathematical methods require [?, ?].

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Metaheuristics, on the other hand, are becoming powerful methods to solve many challenging optimization problems. They are known for their ability to find global optima. Classic examples include genetic algorithms, ant colony optimization, and particle swarm optimization, among others. Metaheuristics find applications across science, technology, and engineering fields [?, ?, ?, ?].

In recent years, there has been a growing interest in nature-inspired, human behavior-inspired, and physics-inspired metaheuristics, such as the Moth Search Algorithm, Grey Wolf Optimizer, Gold Rush Optimizer, Bat-Inspired Algorithm, Ebola optimization search algorithm, and the Gravitational Search Algorithm [?, ?, ?, ?, ?]. These algorithms address different optimization problems, but there is no one-size-fits-all algorithm that provides the best solution for all optimization problems. Some algorithms perform better than others for specific problems. Hence, the search for new heuristic optimization algorithms remains an open problem.

In this paper, we introduce a novel optimization algorithm inspired by the morphogenetic cell movements of ECs that occur during tumor angiogenesis, namely, the Tumoral Angiogenesis Optimizer (TAO). This article is structured as follows: In Section 2, we describe an agent-based model that explains the behavior of endothelial cells during angiogenesis. This model, along with the PSO algorithm, inspired our optimization algorithm, which is detailed in Section 3. In Section 4, a comparative study with the PSO algorithm is presented, considering test functions. In the same section, two constrained optimization problems are addressed, specifically, the problem of minimizing the Rosenbrock function with a cubic and a linear constraint, and the Cantilever Beam Design Problem. Finally, conclusions and possible new researches are presented in Section 5.

2 Angiogenic cell movements mathematical model

Morphogenetic cell movements generate diverse tissue and organ shapes, and questions arise regarding whether these movements share common principles and how cells coordinate behaviors. Angiogenesis, a morphogenetic cell movement, involves the emergence of new vascular networks. Vascular ECs work collectively to form dendrite structures, with several molecular players identified. However, the cellular mechanisms underlying angiogenesis remain largely unknown. Understanding these processes would bridge the gap between molecules and angiogenic morphogenesis.

To gain deeper insights into morphogenesis, a group of researchers developed a system that combines time-lapse imaging with computer-assisted quantitative analysis. This approach allowed for a thorough investigation of the behaviors of ECs driving angiogenic morphogenesis in an in vitro model [?]. The discoveries revealed that EC behaviors are considerably more dynamic and intricate than previously believed, with individual ECs frequently changing their positions, including instances of tip cell overtaking [?]. The phenomenon of dynamic tip cell overtaking had also been reported by another research group [?]. These revelations led the researchers to ponder the following question: How are the movements of individual ECs integrated into the highly dynamic and complex multicellular process that culminates in the formation of ordered architectures? Mathematical and computational modeling strategies have proven invaluable for shedding light on the biological intricacies underlying angiogenic morphogenesis, especially when employed alongside quantitative experimental approaches [?, ?, ?, ?]. Over time, a variety of models, encompassing continuum, discrete, and hybrid approaches, have been developed to explore different facets of angiogenesis across various biological scales [?, ?, ?]. Recent advancements have introduced cell-based models, such as cellular potts and agent-based models, designed to uncover the biological implications of angiogenesis predictively. These models enable the dissection of the molecular and cellular mechanisms involved in processes like sprouting [?, ?, ?, ?] and cell rearrangement [?].

In [?], one-dimensional an agent-based model was developed in order to simulate the behaviors of ECs during the elongation of blood vessels. In this models, individual ECs are represented as agents aligned along the axis of vessel elongation, which forms an emerging sprout in the vascular network. Each cell (agent) behaves autonomously in accordance with a set of specific rules: For each step, t, each agent, i, has a position, $x_i(t)$, a cell migration speed, $v_i(t)$ ($v_i = v_1$ or v_2, where $v_2 < v_1$), and a cell migration direction, $D_i(t)$ ($D = +1$ (anterograde) or $D_i = -1$

(retrograde)). For each step, v_i and D_i satisfy the following rules:

1. Speed transition rule: If $v_i(t) = v_1$, it can change to $v_i(t+1) = v_2$ with a probability p. If $v_i(t) = v_2$, it can change to $v_i(t+1) = v_1$ with a probability s. In the absence of these conditions, motility remains unchanged, i.e., $v_i(t+1) = v_i(t)$.

2. Direction transition rule: If $D_i(t) = -1$, then with a probability r, motility changes to $D_i(t+1) = +1$. If at the last step $D_i(t) = +1$, then with a probability s, motility changes to $D_i(t+1) = -1$. In the absence of these conditions, the direction remains unchanged, i.e., $D_i(t+1) = D_i(t)$.

Furthermore, from the set $X_t = \{x_j(t)\}_j$, we consider $\max X_t$ and $\max\{\min\{x_j, x_k\}\}_{j\neq k}$, which are respectively the largest and second largest elements among the set X_t. We define (i,t) satisfying a tip EC restriction condition if $\max X_t - \max\{\min\{x_j, x_k\}\}_{j\neq k} > d$, where d is the tip-follower threshold for restriction of tip EC movement. If the tip EC restriction condition is satisfied, $v_i(t) = v_2$ is adopted as the tip EC speed. This models the fact that more mature ECs play a crucial role in controlling or regulating the mobility of tip ECs.

The agents update their position based on the following equation:

$$x_i(t+1) = x_i(t) + v_i(t+1)D_i(t+1), \tag{1}$$

together with the tip EC restriction condition.

3 Tumoral Angiogenesis Optimizer

In this section, we will explain our optimization algorithm. As we have just seen, during the angiogenesis process, there are local rules that ECs follow, but there is also global communication through which more mature ECs can regulate the migration speed of tip ECs during the formation of new blood vessels. These cells migrate towards the direction where there is a gradient of growth factors, such as vascular endothelial growth factor (VEGF), which attracts cells to the tissue where vascularization is needed. In the context of tumor angiogenesis, tumors can secrete a signaling protein to stimulate the formation of new blood vessels that grow towards the tumor to supply it with oxygen and nutrients, which is essential for its growth and survival.

This global communication among ECs reminds us of the PSO algorithm, which was initially introduced by James Kennedy and Russell Eberhart in 1995 [**?**], where global communication plays a central role and inspires us to formulate our algorithm as follows:

TAO is initialized with a population of random solutions within the problem's search space. The initial migration speeds are all set to v_1, and the initial migration directions are all set to 1, i.e., $v_i(0) = v_1$ and $D_i(0) = 1$ for each individual i in the initial population.

In each iteration, the algorithm seeks optima by updating the individuals in the population, and the solution with the best fitness is referred to as "the tumor", and the other solutions, referred to as "cells," migrate through the problem's search space towards the tumor following the following dynamics:

$$x_i(t+1) = x_i(t) + v_i(t+1)D_i(t+1)(tumor(t) - x_i(t)) + \gamma^t r, \tag{2}$$

where $x_i(t)$ and $tumor(t)$ are, respectively, the position of cell i and the best solution in iteration t. The migration speed, $v_i(t)$, and migration direction, $D_i(t)$, follow the rules 1 and 2, explained earlier, with respect to the direction from cell $x_i(t)$ to $tumor(t)$. Additionally, for each cell, the distance it has traveled throughout the algorithm is recorded, and this information is used to check if the restriction of tip EC movement is satisfied. To simulate the branching of blood vessels, we use the random vector r, which allows us to modify the direction of $tumor(t) - x_i(t)$ above its normal plane. This provides diversity among the cells and ensures good exploration. The parameter γ is a learning parameter, which, based on our empirical study, should be in the range $[0.2, 0.7]$.

Parameters v_1, v_2, p, s, q, and d already set according [**?**], which, since the search spaces can be rescaled, provides an advantage compared to other metaheuristics where calibrating the involved parameters can be a very challenging task. From the pseudocode **??**, it is relatively

Algorithm 1: Tumoral Angiogenesis Optimizer Algorithm

Data: Objective function, $f(x)$, model parameters, population size, max number of iterations and search region

Result: Approximate optimum, x^+, and $f(x^+)$

```
Initialize the cells population;
Initialize the cellular migration speed;
Initialize cellular migration directions;
Tumor(0) = the best search cell;
while t < Max number of iterations do
    Check if tip EC restriction condition is satisfied;
    foreach Cell do
        Check rules 1. and 2.;
        Update the positions of the cells from equation (??);
        Tumor(t) = the best search cell;
    return Tumor and f(Tumor).
```

straightforward to implement TAO algorithm in any programming language. Table **??** shows values used in this paper.

v_1	v_2	p	q	r	s	d
5.332	0.938	0.0416891	0.234	0.194	0.240	55

Table 1: Parameter values used in this paper.

4 Validation and comparation

4.1 Unconstrained optimization problems

In order to evaluate the performance of our algorithm, we applied it to 6 standard benchmark functions. The function descriptions are detailed in Table **??**.

Given the stochastic nature of the meta-heuristic algorithms, their performance cannot be accurately assessed based on a single run. In order to evaluate the approach comprehensively, multiple trials with independently initialized populations are conducted. Consequently, this study reports results obtained from 30 trials, with a population size of 100 and maximum number of 500 iterations employed for both low- and high-dimensional problems.

Function	Name	Dimension	Range	Minimum
$F_1 = \sum_{i=1}^{n} x_i^2$	Sphere	20	$[-100, 100]^n$	0
$F_2 = \sum_{i=1}^{n} 100\left(x_i - x_{i-1}^2\right) + (x_{i-1} - 1)^2$	Rosenbrock	10	$[-30, 30]^n$	0
$F_3 = x^2 + y^2 + 25\left(\sin^2(x) + \sin^2(y)\right)$	Eggcrate	2	$[-2\pi, 2\pi]^2$	0
$F_4 = \sum_{i=1}^{n} (x_i + 0.5)^2$	Step	30	$[-5.12, 5.12]^n$	0
$F_5 = 10n + \sum_{i=1}^{n} \left[x_i^2 - 10\cos(2\pi x_i)\right]$	Rastrigin	10	$[-5.12, 5.12]^n$	0
$F_6 = -\sum_{i=1}^{n} \sin(x_i)\left[\sin\left(\frac{ix_i^2}{\pi}\right)\right]^{20}$	Michalewicz	5	$[0, \pi]^n$	-4.6877...
$F_7 = \sum_{i=1}^{n} ix_i^2$	Sum Squares	30	$[-10, 10]^n$	0

Table 2: Classical benchmark problems.

In order to compare the performance of TAO algorithm we will use standard PSO. Let's remember that the PSO algorithm has the following equations to update the velocities and positions of the particles for each particle i:

$$\begin{cases} v_i(t+1) = wv_i(t) + c_1 r_1(p_{i_{best}} - x_i(t)) + c_2 r_2(g_{best} - x_i(t)) \\ x_i(t+1) = x_i(t) + v_i(t+1), \end{cases} \tag{3}$$

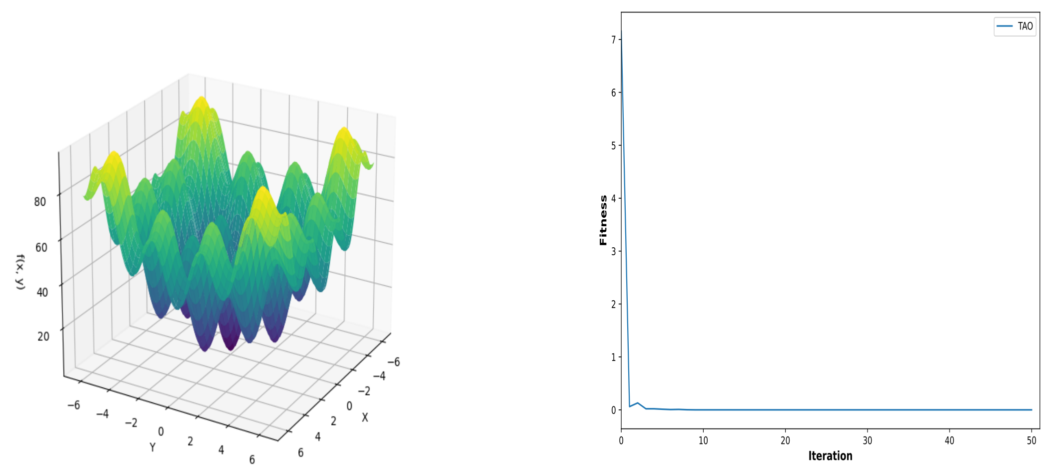
where $v_i(t)$, $x_i(t)$ and $p_{i_{best}}$ are, respectively, the velocity, position and personal best value of particle i at time t. Furthermore, w is the inertial weight, c_1 shows the individual coefficient, c_2 signifies the social coefficient, r_1, r_2 are random numbers uniformly distributed in $[0,1]$, g_{best} is the global best, and shows the best solution found by all particles (entire swarm) until tth iteration. Usually $c_1 = c_2 \in [1.8, 2.0]$. We used $c_1 = c_2 = 2$ [**?**].

The inertia weight w is inspired by the particle swarm optimization algorithm and is calculated using the equation:

$$w = w_{max} - \frac{w_{max} - w_{min}}{t_{max}} t, \tag{4}$$

where t is the current iteration step, t_{max} is the maximum iteration step, w_{max} is the maximum inertia weight, and w_{min} is the minimum inertia weight. Usually, $w_{max} = 0.9$ and $w_{min} = 0.4$ [**?**, **?**].

The initial velocities in the PSO algorithm are set to zero, as empirical evidence has shown this to be the most effective approach [**?**].



(a) The eggcrate function.

(b) Convergence curve of TAO algorithm.

Figure 1: Using TAO algorithm with population size = 50 and maximum number of iterations = 50, we obtain the approximation x^+=(1.3119482e-9, 3.9670538e-9), and $f(x^+)$ =4.5444231e-16.

The statistical results of TAO and PSO on the benchmark problems presented in Table indicate that the proposed algorithm outperforms both in all cases.

4.2 Constrained optimization problems

In this subsection, we will consider optimization problems with constraints.

4.2.1 Rosenbrock function constrained with a cubic and a line

Let us first consider the problem of minimizing the Rosenbrock function subject to two inequality constraints: one is a cubic constraint, and the other is linear. This is a nonlinear constrained optimization problem with a global optimum at $x^* = (1, 1)$, with $f(x^*) = 0$.

Function	Parameters	PSO	TAO
	Beast	0.0416891	1e-07
F_1	Mean	1.7180551	1.0434957
	Standard deviation	1.4389095	0.8459855
	Beast	2.7253815	0.0058221
F_2	Mean	8.5999977	6.9607255
	Standard deviation	4.6557892	5.0302997
	Beast	0.0000000	0.0000000
F_3	Mean	0.0000000	0.0000000
	Standard deviation	0.0000000	0.0000000
	Beast	0.306966	5.5e-06
F_4	Mean	0.7906888	0.0010151
	Standard deviation	0.2765826	0.0015117
	Beast	1.6399746	0.9899181
F_5	Mean	7.3307733	8.4788214
	Standard deviation	3.5371322	5.4759516
	Beast	-4.8693888	-4.6458954
F_6	Mean	4.6169278	-3.9887314
	Standard deviation	0.141926	0.5212977
	Beast	0.6684421	0.181605
F_7	Mean	8.0236676	1.9926416
	Standard deviation	6.2222502	1.7023876

Table 3: Statistical results of benchmark functions.

$$\min_{(x,y)\in[-100,100]^2} \quad f(x,y) = (1-x)^2 + 100(y-x^2)^2 \tag{5}$$

Subject to:

$$g_1(x) : (x-1)^3 - y + 1 \leq 0$$

$$g_2(x) : x + y - 2 \leq 0.$$

In order to address the problem, we will introduce a penalty function to transform the constrained problem into an unconstrained problem. One way to do this is to define the function:

$$F(x,y) = f(x,y) + r_1 \max\{g_1(x), 0\} + r_2 \max\{g_2(x), 0\},$$

where functions $\max\{g_i(x), 0\}$ measure the extent to which the constraints are violated, and r_i are known as penalty parameters, which must be estimated [**?**, **?**]. Thus, problem (**??**) can be rewritten as:

$$\min_{(x,y)\in[-100,100]^2} \quad F(x). \tag{6}$$

Using the metaheuristic proposed in this article we obtain $r_1 = 0.01$, $r_2 = 0.05$ and the approximate solution: $x^+ = (0.93744360.8786004)$, with $f(x^+) = -0.0040689$. This results in a relative error of approximately $\epsilon \approx 0.0965690$.

4.2.2 Cantilever Beam Design Problem

The Cantilever Beam Design Problem is a significant challenge in the fields of mechanics and civil engineering, primarily focused on minimizing the weight of a cantilever beam. In this problem, the beam consists of five hollow elements, each with a square cross-section. The goal is to determine the optimal dimensions of these elements while adhering to certain constraints (see figure **??**).

The mathematical expression governing this problem and its associated constraints are represented by equation (**??**).

$$\min_{0.01 \le x_1, x_2, x_3, x_4, x_5 \le 100} \quad f(x_1, x_2, x_3, x_4, x_5) = 0.06224(x_1 + x_2 + x_3 + x_4 + x_5) \tag{7}$$

Subject to:

$$g(x) : \frac{61}{x_1^3} + \frac{37}{x_2^3} + \frac{19}{x_3^3} + \frac{7}{x_4^3} + \frac{1}{x_5^3} \le 1.$$

In order to address problem (**??**), we reformulate it as an unconstrained problem as follows:

$$\min_{0.01 \le x_1, x_2, x_3, x_4, x_5 \le 100} \quad F(x_1, x_2, x_3, x_4, x_5), \tag{8}$$

where $F(x_1, x_2, x_3, x_4, x_5) = f(x_1, x_2, x_3, x_4, x_5) + r \max\{g(x) - 1, 0\}$ and $r = 4.455068564365$. Subsequently, we apply TAO algorithm using a population of 100 individuals and a maximum of 300 iterations. Then, we obtain $r = 4.455068564365$ and the approximate solution: $x^+ = (6.01601588, 5.30917383, 4.49432957, 3.50147495, 2.15266534)$, with $f(x^+) = 1.33652057$.

Table 4 lists the best solutions obtained by TAO and various methods: artificial ecosystem-based optimization (AEO), ant lion optimizer (ALO), coot optimization algorithm (COOT), cuckoo search algorithm (CS), gray prediction evolution algorithm based on accelerated even (GPEAae), interactive autodidactic school (IAS), multi-verse optimizer (MVO), symbiotic organisms search (SOS) and hunter-prey optimizer (HPO) [**?**].

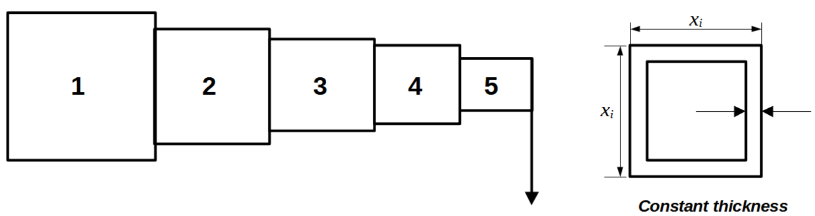


Figure 2: Cantilever Beam Design Problem.

The comparative outcomes are presented within Table **??**. These results clearly demonstrate that the TAO algorithm we propose presents a superior solution for addressing this problem.

Algorithm	Optimal values					Optimal weight
	x_1	x_2	x_3	x_4	x_5	
TAO	6.01601588	5.30917383	4.49432957	3.50147495	2.15266534	1.33652057
HPO	6.00552336	5.30591367	4.49474956	3.51336235	2.15423400	1.33652825
AEO	6.02885000	5.31652100	4.46264900	3.50845500	2.15776100	1.33996500
ALO	6.01812000	5.31142000	4.48836000	3.49751000	2.15832900	1.33995000
COOT	6.02743657	5.33857480	4.49048670	3.48343700	2.13459100	1.33657450
CS	6.0089000	5.30490000	4.50230000	3.50770000	2.15040000	1.33999000
GPEAae	6.0148080	5.30672400	4.49323200	3.50516800	2.15378100	1.33998200
IAS	5.9914000	5.30850000	4.51190000	3.50210000	2.16010000	1.34000000
MVO	6.0239402	5.30601120	4.49501130	3.49602200	2.15272610	1.33995950
SOS	6.0187800	5.30344000	4.49587000	3.49896000	2.15564000	1.33996000

Table 4: Comparison results for the cantilever design problem.

5 Conclusiones

In this paper, we introduce a novel metaheuristic algorithm named the Tumoral Angiogenesis Optimizer (TAO), drawing inspiration from the morphogenetic cellular movements of ECs that occur during the tumor angiogenesis process. Based on the results obtained from mathematical benchmark functions, TAO outperforms the standard PSO. Furthermore, our algorithm has demonstrated successful solutions to two constrained optimization problems. Notably, in the context of the Cantilever Beam Design Problem, it outperformed several well-established metaheuristics.

This article can be expanded and improved with several research directions for future studies. First of all, it can be improved by studying the process of tumor angiogenesis in more detail. Secondly, it would be interesting to consider more test functions and practical real-world problems. Finally, the phenomena of cell appearance and death can be considered.

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