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An application of simulated annealing to optimal transcranial direct current stimulation of the human brain

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Abstract: Transcranial direct current stimulation (tDCS) is known as the most effective technique for stimulating deeper brain areas. The capability of tDCS, however, strongly depends on the number of electrodes, their positions, and the amount of injected currents. This paper intends to apply the simulated annealing algorithm for determining optimal stimulation parameters in a multiple electrode scheme. The objective of the presented approach is to maximize the current density delivered to the target area under safety constraints. In order for the skin under the electrodes to be protected against temperature rises that may be caused by the stimulation, current injections are capped by a set of safety constraints. In the studies, the propagation of current density throughout the head is estimated via a 3D finite element approach in the ANSYS software package. Finally, the proposed algorithm is applied to a standard spherical four-layer human head model. The simulation results justify the capability of the established model in providing near optimal stimulation parameters. Accordingly, the presented approach provides neurologists with an effective tool to optimally stimulate the brains of patients.

Key words: Finite element method, optimal electrode placement, simulated annealing, safety constraint, transcranial direct current stimulation

1. Introduction

Transcranial direct current stimulation (tDCS) is one of noninvasive stimulation techniques in which a weak direct current (usually 1–2 mA) is delivered through a set of electrodes, i.e. cathode and anode electrodes, to the scalp [1] and the current flows through the skull. As a result of the low conductivity of the skull, in order to obtain a high current density in the brain for stimulating neurons, it is necessary to apply a large potential difference between the electrodes [2]. The approach of DC electric current to the scalp has been revealed to adjust neuronal membrane potentials [3] and to produce changes in the bioelectric activity of the brain tissue [4]. The key role of the stimulation polarity was demonstrated in [5], where it was shown that an anodal stimulation can increase the excitability while a cathodal stimulation has the reverse impact. This technique is currently used for a wide range of neurological states including depression, epilepsy, migraine, Parkinson disease, and Alzheimer disease, to name just a few [1]. This system has become more popular among neurologists due to the fact that it is inexpensive and flexible during a stimulation period [6]. As a comparison of tDCS with other stimulating techniques, transcranial magnetic stimulation (TMS), unlike tDCS, is known as a neurostimulation

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and neuromodulation technique. The TMS technique has behavioral effects and therapeutic potentials since its pulses can modulate cortical excitability. In TMS, the ratio of the maximum current density in the scalp to the maximum current density in the brain is much lower than that in electrical stimulation [2]. tDCS is used for stimulating deeper brain areas than TMS, which is usually used to stimulate cortical neurons [2,7,8].

In order to have efficient and safe brain stimulation, there are many factors that should be considered, such as the number, size, and shape of electrodes; their location; corresponding current injections; and duration of stimulations [9]. In the literature, significant efforts have been dedicated to optimizing the tDCS parameters. A brief review of the techniques developed and the assumptions made in the literature is provided in the following text in order to illustrate the contributions of this paper.

In the literature, few studies have focused on the role of optimization theories in the field of electrical stimulation. In [10], optimal electrode positions in tDCS were recommended through the evolution strategy algorithm. The placement for minimum current injection was optimized by varying the Cartesian coordinate system into a spherical system. The objective of the proposed technique was to minimize the injection current with a set of constraints to ensure that an appropriate current density is delivered to the target area.

In [11], optimal current injections associated with a set of electrodes with fixed locations were found by the simplex algorithm such that the average current density at a target area was maximized. In this paper, multiple anode and cathode electrodes were assumed to be placed at the anterior and posterior, respectively.

In order to achieve an effective and targeted tDCS stimulation, [12] used multiple small electrodes and systematically optimized their injected currents. In this approach, the maximum allowed current injection should be considered in the determination of the maximum current density in a cortical area. Based on the results, using large-pad electrodes would enhance 80% focality at the target area and 98% intensity at the cortical target area. The optimal places and corresponding current injections of a classical bipolar configuration were proposed in [13], wherein injected currents were assumed to be independent. The objective function of the developed method is to maximize the intensity and focality at a predefined target area under safety constraints. In the same paper, it was also demonstrated that the final optimal electrode configuration is dependent on the field orientation and optimization criterion.

This paper establishes a generic framework to determine the optimal stimulation parameters based on the simulated annealing (SA) technique. As the major contribution of the present paper, the new framework, unlike the existing methods, simultaneously determines the optimal number of electrodes, their locations, and the respective current injections. To the authors' best knowledge, none of the existing studies are capable of optimizing the number of connected electrodes. The maximum average current density delivered to a considered target area, which is the ultimate goal of any stimulation, is considered as the objective function of the technique. The temperature rises caused by electrical stimulation may hurt the skin under the electrodes [14]. Consideration of a set of safety constraints in order to avoid injury to the skin is the last, but not least, contribution of the current paper. For modeling the safety constraints two parameters are defined: the maximum injection current (MIC) and the maximum produced current (MPC). The former denotes the maximum allowed current injection through individual electrodes while the latter represents a maximum limit on the total current to be injected from the whole connected electrodes. A point deserving great emphasis is that the MIC and MPC are respectively determined considering the skin thermal capacity and the stimulation system power ratio. The safety constraints cap the currents injected through the electrodes by a predefined value. This distinguishes the developed framework from the existing models.

In this paper, a 3D model that was presented by Rush and Driscoll [15] is employed to model the human brain. In order to investigate the effect of tDCS on a brain, the finite element method (FEM), as the most popular approach, is used to calculate the current flows.

The remaining parts of the paper are as follows. Section 2 provides a description of the SA technique. The presented stimulation approach is thoroughly explained in Section 3. Section 4 addresses the numerical study and the simulation results. Finally, concluding remarks are comprehensively discussed in Section 5.

2. Review of simulated annealing

SA is a probabilistic metaheuristic technique that has been applied in wide areas like control engineering, machine learning, and image processing [16]. The metaheuristic approaches can be recognized as the most practical approaches for solving many complex problems, which is the case in many real-world problems that are combinatorial in nature [17]. Providing a set of near optimal solutions instead of an optimal solution that can be provided by the existing classic optimization methods is another advantage of the metaheuristic methods. By considering these methods, users are able to compromise between the accuracy of final results and computational burden.

The SA method is inspired by the process of annealing in metallurgy, wherein a heated solid is slowly cooled under the natural convection. This technique is a simple generalization of the metropolitan area algorithm [18] where the temperature parameter is known as time-varying, i.e. $T = T(t)$.

The acceptance probability of a solution is based on the following equation:

$$P(S_t \to S_{t+1}) = \begin{cases} \exp(-\frac{\Delta E(S_t)}{T(t)}), & \Delta E(S_t) \geq 0 \\ 1, & \Delta E(S_t) \leq 0 \end{cases} .$$

If t increases, $T(t)$ converges to zero based on a cooling plan whereas for $T \to \infty$ the solution is centered at the global maximum/minimum. In the hope of achieving a near global optimum solution, more new solutions are usually investigated by choosing a large value for T in the first steps, while the chance of achieving new solutions will be decreased by reducing the temperature parameter as the optimization procedure proceeds. This process leads to a focus on the proximity of the maximum/minimum solutions during the optimization process [19].

The main steps of the SA algorithm are described as follows [20]:

Step 1: In this step, different SA parameters are defined. In order to increase the chance of attaining the global optimum solution, temperature T is usually set to a large value at first. Its value will be reduced gradually as the solution procedure proceeds. Initial solution state S is the start of the iterative algorithm, and L represents the iterations for any T.

Step 2: Considering k: 1, 2, . . . , L, Steps 3 through 6 are executed.

Step 3: In this step, the SA considers a state, S', in the vicinity of the current state, S, and probabilistically decides on either moving to state S' or staying in state S.

Step 4: In this step, energy difference through $\Delta E' = P(S') - P(S)$ is computed. In this equation, $P(S)$ is known as the evaluation function.

Step 5: In this step, S' is accepted as a new current solution if $\Delta E' \prec 0$; otherwise, S' is accepted with the probability of $\exp(-\frac{\Delta E(S_t)}{T(t)})$.

Step 6: The adopted termination criterion is checked in this step. If it is satisfied, the SA procedure terminates and the current solution is reported as the final optimal solution. Otherwise, the algorithm continues to the next step. The stability of the solution in successive iterations is considered as the termination criterion. Synonymously, the considered termination criterion is approved when a predefined number of new solutions remains unchanged.

Step 7: The temperature parameter gradually decreases as the number of iterations grows and the solution procedure returns to the second step for the next iteration.

3. Materials and methods

3.1. Optimal stimulation technique

This section develops a methodology in the consideration of finding optimal locations of electrodes and their injection currents. The presented method utilizes the SA algorithm to find the global optimal solution. Figure 1 shows the step-by-step procedure of the new methodology, which is explained in the following sections.

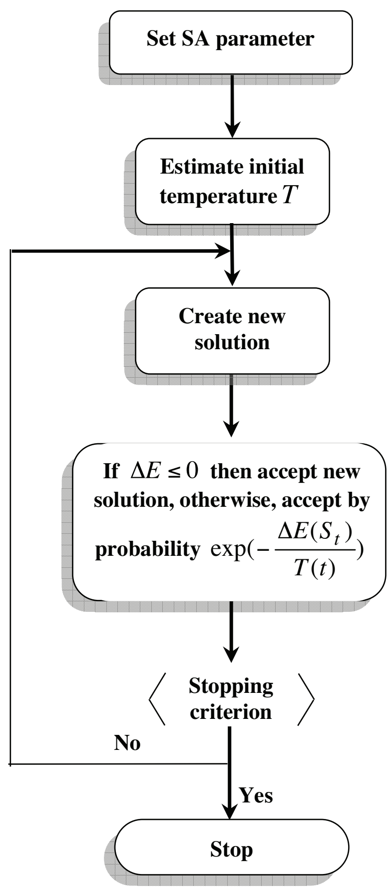

Figure 1. Step-by-step procedure of the methodology.

3.2. Structure of a candidate solution

In order to find the optimal electrode placement, a random candidate solution is created. Each candidate solution specifies the location and the number of electrodes linked to cathode and anode terminals. In the SA technique, various feasible structures can be exploited for representing a candidate solution. Choosing a proper structure for candidate solutions is one of the most influential factors on the performance of the SA technique. The location of electrodes is specified through candidate solutions. The location of electrodes is also a critical parameter. Here, placement of electrodes is based upon the 10–20 International System introduced by EasyCap [21]. This system utilizes 74 standard points for electrode locations. Electrodes can be placed at the indicated 74 points. The ground is also fixed at one of these points. Therefore, the number of all candidate points that can be connected to cathode and anode terminals is equal to 73.

As mentioned before, an individual candidate solution is represented by an array of 73 elements, each of which can be –1, 0, or +1. The value of each element indicates the type of connection of the respective standard points. The element takes +1 if the corresponding point is connected to an anode, –1 if it is connected to a cathode, and 0 otherwise.

3.3. Fitness function calculation

Fitness of the candidate solution is investigated when the candidate solution is produced. Here, the magnitude of the current density induced in a target area is picked as the fitness function. An objective function is defined as follows:

$$\text{Max } \frac{1}{\text{N}} \sum_{i=1}^{N} |J_i|,$$

where J_i is the current density evaluated at the ith node included in a target brain area, and N represents the number of nodes belonging to the target brain area.

As mentioned earlier, a set of candidate solutions is generated by the SA algorithm in each iteration. Considering the fitness function of a candidate solution, this operator creates a new solution. The procedure of calculating the fitness function is provided in this section. As discussed earlier, determining the optimal electrode locations and injected current with the aim of maximizing the current density delivered to the target area is considered as the goal of this paper.

In general, distribution of the current density throughout the brain and current density at target points can be computed by solving Laplace equations. Several commercial software packages like ANSYS and COMSOL are the most commonly used in biomedical engineering and are also proper for this case. These software packages find a solution for Laplace equations through the finite element method.

In this section, the superposition principle is adopted in order to make this process tractable. This can be done by the following steps:

1. Determine a set of target points to represent the target area in the model. The number of target points is an important parameter. Too few points might lead to inaccurate results, while too many points may make the problem computationally difficult.

2. Pick a set of possible connection points as standard locations. Obviously, final solutions will be selected among these standard locations. Without loss of generality, a well-accepted set of standard locations for electrodes is employed in this paper. This set comprises 73 standard locations and is referred to as the 10–20 International System in the literature [21].

3. Stimulate the brain by injecting 1 mA into the first standard point and estimate current density delivered to and electric potential at the considered target points. Record the obtained results and iterate this step for the next standard location. At the end of this step, the relationship between the current injection from the standard locations and current density delivered to the target points as well as electric potential of the standard locations will be obtained.

4. Establish an incidence matrix to demonstrate the relation between current density delivered to different target points and current injected into the standard electrode locations. Owing to the number of standard and target points, this matrix is 73 $\times$ 7 since 73 standard locations and 7 target points are considered.

5. Find an incidence matrix to illustrate the relation between the electric potential and current injection of the standard electrode locations. In this paper, this matrix is 73 $\times$ 73 since 73 standard locations are considered.

Employing the incidence matrices, a linear optimization problem just like that adopted in [11] is solved. The solution of this problem (i.e. the optimum current injections) is found such that the average current density delivered to the target points is maximized.

A set of constraints is considered in the problem to ensure that the obtained solution is feasible. These constraints are as follows:

- Total current injected to the electrodes attached to either of terminals, i.e. cathode or anode, must be limited to a predefined value. This value represents the maximum current that can be generated by the stimulation device.
- Current injected to individual electrodes should be restricted to a predefined value in order to prevent any skin damage.
- Electrodes connected to the same terminal should have exactly the same electric potential.
- Currents designated to the electrodes connected to the same terminal have to abide by the fundamental Kirchhoff current law.
- Total currents injected to the electrodes attached to both of the cathode and anode terminals must have the same value. In other words, the sum of the currents' flow within the electrodes connected to the cathode terminal has to be equal to the sum of the currents' flow throughout the electrodes attached to the anode terminal.

Besides the above constraints that are taken into account in the optimization problem, there is another constraint that should be checked at first. This constraint guarantees that at least one electrode is attached to each of the cathode and anode terminals. These constraints are considered in the developed framework by penalizing the fitness function. Since the electrode placement problem is a maximization problem, a small value is selected as the fitness function for a candidate solution in which one or more of the described constraints are violated. Considering the fact that the objective of the problem at hand, i.e. absolute current density in the target area, always has a positive value for feasible solutions, zero is adopted here for penalizing infeasible candidate solutions. Note that the solution procedure is not continued further for infeasible candidate solutions. The last constraint means that the fitness of a candidate solution in which either or both of the cathode and anode terminals are disconnected is equal to zero.

3.4. Stopping criterion

So far, several stopping criteria have been employed in the literature for terminating the SA procedure. Usually, generating and investigating new candidate solutions proceeds to the point where no better solution is derived in a predetermined number of consecutive iterations. Moreover, the run time is capped by a specific value that can be determined considering the inherent complexity of the problem at hand, the power of the employed processors, the available time duration, and the importance of solution optimality. Obviously, extending these bounds may increase the chance of achieving the global optimum solution. Synonymously, the extension of these limits can theoretically result in higher quality outcomes. In addition, setting a maximum number for iterations can be another stopping criterion that can be selected considering the problem characteristics and available software/hardware technologies. Clearly, the probability of achieving local optimum solutions decreases as the maximum number of iterations increases.

4. Numerical study

4.1. The 3D head model

Numerous theoretical models have been established to provide an overview of electric field and current density distribution in biological tissues [22]. It should be noted that computational models of tDCS vary in complexity from spherical head models to high resolution models based on MRI scans. All the models can correctly predict the brain current flow during the transcranial stimulation. These models also bring more accurate insight into current flow patterns [22,23].

Among the presented models, in this paper, the 3D spherical head model is employed. However, it should be noted that the established method is general and can be applied to both standard models.

The standard spherical head model [24] comprises four homogeneous and isotropic layers, namely Brain, CSF, Skull, and Scalp. The values of the radius and electric conductivity of the layers are illustrated in Table 1 [23].

Table 1. Radius and electric conductivity values.

Tissue type	Radius (cm)	Electric conductivity (s/m)
Brain	7.9	0.332
CSF	8.1	1.79
Skull	8.6	0.0083
Scalp	9.2	0.332

The electric conductivity of the layers is assumed to be only resistive. Consider that this assumption is common in brain stimulation studies.

4.2. The case under study

This section aims to provide a case study in order to demonstrate the effectiveness of the established technique. As mentioned earlier, several therapeutic tools have been exploited for a wide range of neurological disorders, namely depression, epilepsy, migraine, and Parkinson disease. Here, without loss of generality, the new technique is applied to epilepsy in the frontal lobe in the brain. In general, epilepsy is the occurrence of sporadic electrical storms that are called seizures. Frontal lobe epilepsy is the most common form of this disease and seizures are partial. Accordingly, the focus of this case study is on stimulating a prolate ellipsoid shape area in frontal lobe as a target area. The area is defined by the following parameters:

- The lengths of semiprincipal axes are 0.02, 0.02, and 0.04 m.
- The center of the area is (0.046, 0, 0.046).

The amount of current density delivered to the target area is calculated by utilizing numerical solution methods wherein continuous space is modeled by a finite number of discrete points. In this paper, in order to maintain the accuracy of the results, thousands of discrete points are used for modeling the target area. However, transferring the current density associated with these discrete points between ANSYS software and MATLAB for several iterations of SA is a complicated job. Therefore, the excessive computational burden of the optimal electrode placement problem is alleviated by replacing the whole target area by a set of target points. Note that employing too many points result in cumbersome computational complexity and selecting too few points may threaten the accuracy of results. Here, the considered ellipsoid area is modeled by its center and ends of semimajor and minor axes. This assumption significantly simplifies the solution procedure while the accuracy of the results is not jeopardized.

Here, point-like electrodes are employed to simulate the brain. By considering discrete points, the location of electrodes is modeled by the nearest point in the surface of the head. It is worth noting that the established technique is general and able to be applied to cases with different types of electrodes.

4.3. Numerical calculation

In this paper, the proposed model is created in the ANSYS software package and is shown in Figure 2. This model includes more than 4 million nodes and about 1 million hexahedral elements. A proper element in this model is Solid 231. This element is a 3D current-based element with 20 nodes and one degree of freedom, with voltage at each node. As mentioned earlier, ANSYS finds the solution of a set of Laplace equations through the finite element method. In the steady state, the divergence of current density is zero and the electric potential obeys the following equation:

$$\nabla \bullet (\sigma \nabla V) = 0.$$

In this equation, ∇ represents the gradient operator and σ is the electrical conductivity of head tissues. Here the potential difference between the two electrodes is settled so that the injected current has the required value.

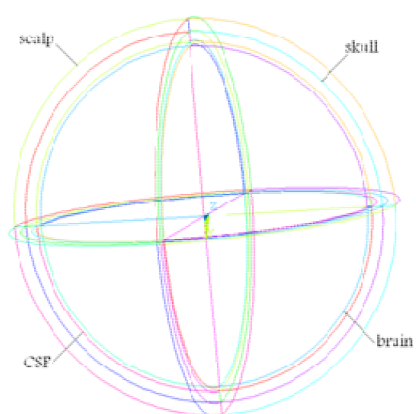

Figure 2. The spherical head model consists of four regions: scalp, skull, CSF, and brain.

The electric field E can be extracted from the scalar potential as $E = -\vec{\nabla} V$ and the current density can be calculated by using Ohm's law, $J = \sigma E$.

The ANSYS software solves the equations via an iterative linear solver in which the final solution is achieved if the solution tolerance in two consecutive iterations is less than 1e-**6**. The simulations are carried out using a personal computer with 64-bit Core i7 processors with 4 GB RAM memory.

4.4. Simulation results

In this section, the results achieved by applying the suggested methodology to the case under study are discussed. It is worth noting that the electrical stimulation can cause temperature rises that may cause burns and irritation of the skin under the electrodes [14]. Accordingly, in order to avoid damage to the skim, we have to restrict the amount of current injections. In this paper, injected currents are restricted through safety constraints in order to prevent skin damages. As mentioned heretofore, the maximum average current density at the target area is calculated as the objective function. Decision variables are picked out as the number of electrodes, their locations, and their current injections.

The tolerance of the objective function in consecutive iterations is adopted as the stopping criterion. The amount of tolerance is usually settled on the basis of a trade-off between the accuracy of the results and computational burden. Too large of a tolerance value might lead to inaccurate results, while too small of a value may make the computational burden intractable. In this paper, the tolerance is determined through engineering judgments such that the accuracy of the results is guaranteed. The minimum tolerance of the fitness function in two successive iterations is set to $1e^{-6}$.

As discussed earlier, the problem at hand has two major input parameters, namely MIC and MPC. In tDCS, restrictive factors include skin surface damages and irritation under the electrode stimulation. Therefore, MIC is determined to prevent these factors. MPC is established by attention to the stimulation device's attributes. Here, the MIC and MPC parameters are assumed to be in the range of 0.5–2 mA. In this section, comprehensive analysis is exploited to reveal the capability of the proposed method.

4.4.1. Different values of MIC

In order to design the optimal electrode locations and corresponding injected currents, different values of MIC are considered. These MIC values include 0.5, 1, 1.5, and 2 mA. In these simulations, MPC is set at 2 mA as a common limit for the safety and comfort of electrical stimulation [13]. Another point in each scenario is that the electrodes linked to each terminal are placed in the vicinity of standard points.

Table 2 gives the optimal electrode locations and injected currents for different MICs. For the sake of illustration, the location of electrodes when the MIC is set to 0.5 is illustrated in Figure 3. In this figure, cathode and anode electrodes are respectively identified by blue and red circles where the black circle demonstrates the ground.

Table 2. Optimal electrode locations and current injections for different values of MIC.

MIC	Type	Electrode locations and injected currents
0.5	Cathode	(F3,0.426), (CP1,0.448), (AF4,0.457), (CP5,0.288), (FCz,0.272)
	Anode	(C4,–0.441), (FC6,–0.5), (C6,–0.464), (TP8,–0.485)
1	Cathode	(C3,0.936), (C2,1)
	Anode	(T8,–0.967), (TP8,–0.969)
1.5	Cathode	(C6,0.970), (CP6,1.030)
	Anode	(F1,–1.123), (FCz,–0.777)
2	Cathode	(CP2,2)
	Anode	(FC6,–2)

Owing to the observations, four and five electrodes are connected to the anode and cathode respectively when the MIC is set to 0.5 mA. In this case, the maximum allowed current injection, i.e. 0.5 mA, is crossed to the anode electrode linked to point FC6.

As anticipated, when the MIC value increases, the number of electrodes connected to cathode and anode terminals is reduced. In addition, considering the minimum value of the MIC, the average current injected to the electrodes decreases, while in final case, based on the MIC and MPC, the injection current is set between electrodes. Usually it is better to use more electrodes for stimulation to ensure that the skin under the electrodes is protected against irritation and burns. Figure 4 provides the average of the total current density delivered to the target points.

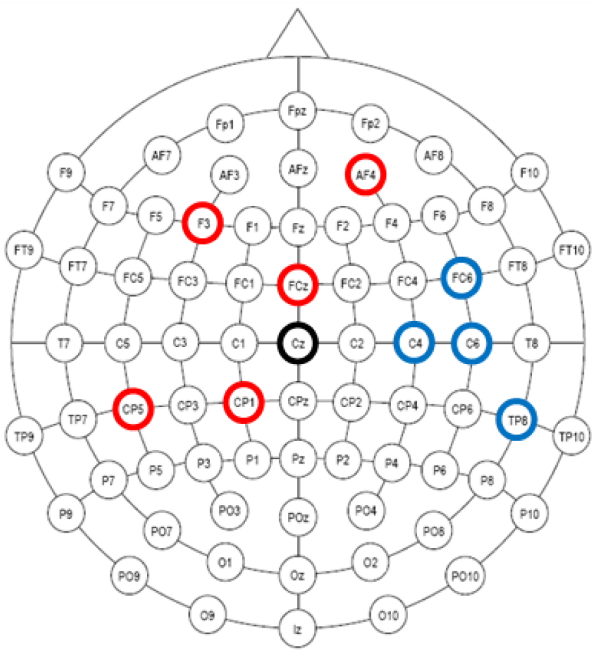

Figure 3. The location of cathode and anode electrodes when the MIC is set to 0.5 mA.

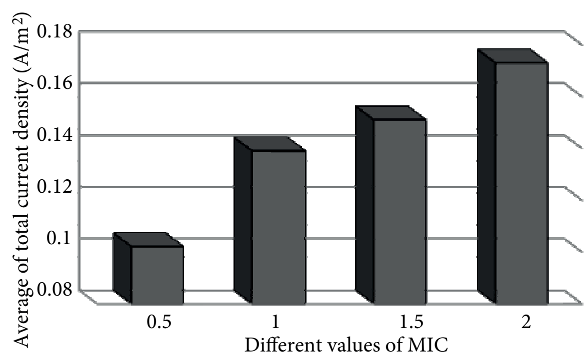

Figure 4. Average of total current density for different values of MIC.

Obviously, total current density can be estimated by $J_{total} = \sqrt{J_x^2 + J_y^2 + J_z^2}$, in which J_x, J_y, and J_z are delivered current density toward the X, Y, and Z axes, respectively. It should be noted that the average of total current density illustrates the fitness function of the proposed method.

It is observed that the average current density delivered to the target area decreases as concern about skin damages increases. On the other hand, as the number of electrodes connected to either or both cathode and anode terminals increases, the current density delivered to the target points decreases. This is due to the fact that the total produced current cannot be injected through a limited number of electrodes. Synonymously, more electrodes have to be connected to the standard points to inject a larger portion of the produced current.

4.4.2. Different values of MPC

As can be seen from the previous discussions, the MPC value has significant impacts on both the number of connected electrodes and their appropriate locations. In this section, a diverse range of the MPC values is exploited in the optimal electrode placement problem to comprehensively investigate the mentioned issue. The problem is solved for different MPC values of 0.5, 1, 1.5, and 2 mA. Note that the MIC has the constant value of 1 mA in different cases. Table 3 gives information on the optimal number of electrodes, their respective locations, and their injected currents for different values of MPC. In this case, for the sake of illustration, the location of electrodes when the MPC is set to 1.5 is illustrated in Figure 5. In this figure, cathode and anode electrodes are respectively identified by blue and red circles where the black circle demonstrates the ground.

Table 3. Optimal electrode locations and current injections for different values of MPC.

MPC	Type	Electrode locations and injected currents
0.5	Cathode	(P2,0.5)
	Anode	(F4,–0.5)
1	Cathode	(P6,1)
	Anode	(F2,–0.487), (FC2,–0.513)
1.5	Cathode	(F8,0.738), (F6,0.762)
	Anode	(CP2,–0.752), (PO4,–0.748)
2	Cathode	(C3,0.936), (C2,1)
	Anode	(T8,–0.967), (TP8,–0.969)

As expected, only one electrode is employed when the MPC is less than the MIC. A larger number of electrodes has to be connected when the MPC value increases. The average current density delivered to the target area is given in Figure 6. As can be seen, the delivered current density increases by increasing the MPC value.

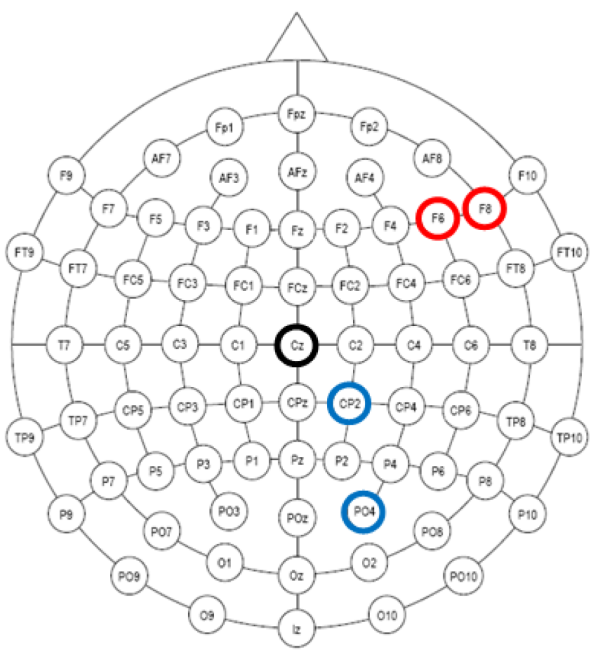

Figure 5. The location of cathode and anode electrodes when the MPC is set to 1.5 mA.

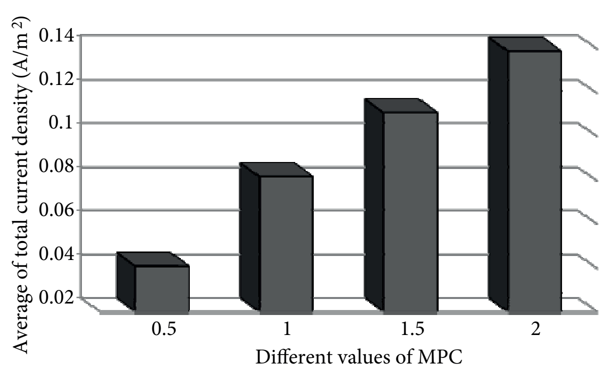

Figure 6. Average of total current density for different values of MPC.

In order to have a more effective stimulation, we have to either increase the amount of current injections or increase the number of the electrodes. The former alternative, i.e. larger current injections, is more desirable if the safety limits are not reached, while the latter, i.e. increasing the number of connected electrodes, is the only resort when the safety limits are reached. This observation can be simply expanded to the case wherein deeper brain areas need to be stimulated.

4.4.3. Dependent versus independent current injections

In this section, another aspect of optimal stimulation is discussed. As mentioned previously, a few works have been done on optimal stimulation. In [13], multiple small electrodes with independent current controls were optimized. This paper tried to find optimal electrode locations where a few terminals were available.

In the previous sections, the optimal electrode placement considering the dependent current injections was achieved. In other words, the optimal stimulation was found such that the electrodes connected to the same terminals have the same electric potential.

In this section, with attention to the availability of independent current injections, optimal electrode locations and the corresponding current injections are obtained. In this case, it is assumed that a few independent cathode and anode terminals are available. The terminals do not necessarily have the same electric potential. A set of constraints should also be considered to ensure that the number of terminals designated to either the cathode or anode and their input currents do not exceed reasonable amounts.

Table 4 compares the optimal location of electrodes, their injected currents, and the total current density delivered to the target area for both dependent and independent stimulations when the MIC is set to 1 mA. For the sake of illustration, optimized electrode location with corresponding current injection when the MIC is set to 1 mA is illustrated in Figure 7. Owing to the results, when the electrodes are supplied in a dependent manner, two electrodes are connected to both the cathode and anode terminals, whereas three electrodes are linked to the cathode and anode terminals when they can be supplied independently. In addition, as expected, larger current densities are delivered to the target area when independent supplies are employed.

Table 4. Optimal electrode locations, current injections, and total current density for dependent and independent stimulation when MIC is set to 1 mA.

Type	Dependent current	Independent current
Cathode	(C3,0.936), (C2,1)	(P8,1), (Oz,1), (Iz,1)
Anode	(T8,–0.967), (TP8,–0.969)	(FP2,–1), (F1,–1), (FC4,–1)
Total current density	0.139	0.165

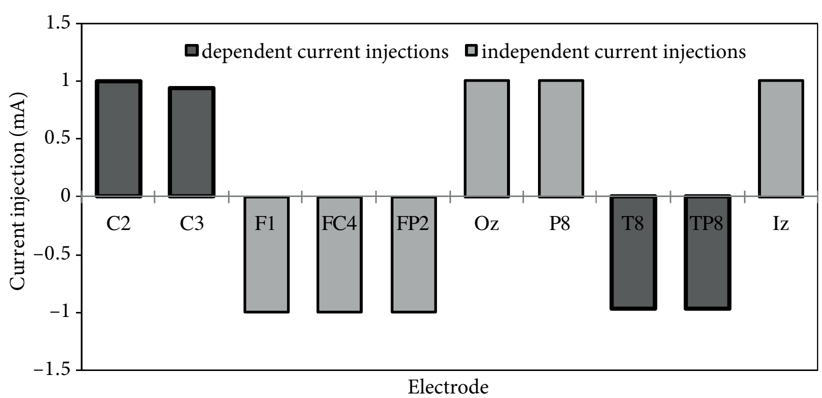

Figure 7. Optimized electrode location with corresponding current injection in different problems.

In order for a stimulation system to be able to independently supply a set of electrodes, it has to have several independent current sources. This can increase the complexity and the cost of the stimulation system. On the other hand, as shown before, a stimulation system with more independent current sources can bring greater flexibilities and hence a more effective stimulation. Therefore, there is a tradeoff between the system complexity and cost and the operation flexibility. In order to illustrate the tradeoff, the simulations are repeated for different numbers of available independent current sources and the obtained results are given in Table 5.

Table 5. Optimal electrode locations, current injections, and total current density for number of independent current sources when MIC is set to 1 mA.

Type	Number of available independent current sources				
	2	3	4	5	6
Cathode	(C4,1), (C6,1)	(TP8,1), (FT10,1)	(P8,1), (Oz,1), (Iz,1)	(Pz,1), (P6,1), (TP9,1), (O9,1)	(F4,1), (T8,1), (F6,1), (FC6,1), (F9,1),
Anode	(C1,–1), (AFz,–1)	(C3,–1), (C2,–1)	(FP2,–1), (F1,–1), (FC4,–1)	(F7,–1), (AF4,–1), (F6,–1), (FPz,–1)	(P3,–1), (O1,–1), (CP2,–1), (O10,–1), (CPz,–1)
Total current density	0.122	0.132	0.165	0.190	0.274

According to the obtained results, by raising the number of available independent current sources, the total current density delivered to the target area increases. The effectiveness of the stimulation (delivered current density) also increases as the complexity of the stimulation system (number of independent current sources) increases. This observation justifies the importance of the mentioned tradeoff between effectiveness and complexity. Another important observation is that the number of connected electrodes is not necessarily equal to the number of available independent current sources since, for example, only two electrodes are connected to anode terminals when three independent terminals are available.

5. Conclusion

An application of SA to the problem of optimal stimulation of a human head was proposed in this paper. Here, the number of electrodes, their locations, and the current flows through them were determined such that an effective stimulation was achieved. First several stimulation configurations were generated through the SA algorithm. The feasible candidate solutions among the generated configurations were analyzed by a linear optimization problem wherein optimal current injections associated with the connected electrodes were obtained. The aim of the optimization problem was to maximize the average current density delivered to the target area. In order to be sure that the skin under the connected electrodes is safe, a set of safety constraints were incorporated into the optimization problem where MIC and MPC are the main constraints. In this paper, a comprehensive case study with several sensitivity analyses was conducted to reveal the aptitude of the proposed technique. Owing to the obtained results, the average current density delivered to the target area decreases when the bounds in the safety constraints become tighter. The number of applied electrodes increases as the maximum allowed current injection decreases. In addition, it was shown that the average current density at the target area decreases as MPC decreases. Finally, it was observed that employing a set of independent current sources would increase the stimulation flexibility, thereby improving the effectiveness of the stimulation.

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