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Optimizing Nerve Cuff Stimulation of Targeted Regions Through Use of Genetic Algorithms

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Abstract— **A nerve cuff electrode is a viable technology for use in a neuroprostheses system to restore loss of function due to neurological injury. The Flat Interface Nerve Electrode (FINE) is a nerve cuff that gently reshapes the nerve to bring the axons closer to the stimulating contacts. The overall goal of this work is to optimize nerve cuff stimulation in upper extremity nerves. Recently, highly efficient and accurate linear models of neuronal activation have been developed in our lab. Using the fast calculations from the newly developed linear activation method, nerve stimulation parameters such as current pulse width and pulse amplitude at many electrode contacts can be explored by employing optimization algorithms. Finite element nerve models with high density electrodes were constructed based on upper extremity cadaveric nerve cross sections. An objective function was developed to target specific groups of nerve fascicles and minimize overlap amongst these groups. By changing the objective function and using a genetic search algorithm, stimulation parameters can be optimized for many contacts.**

I. INTRODUCTION

Human intraoperative experiments demonstrate that selective nerve activation is feasible when using the Flat Interface Nerve Electrode (FINE) without optimization [6, 8]. These experiments are informative but large parameter space exploration is limited due to time and costs. Field steering has been shown to improve selectivity [2, 9, 10, and 12] but applying field steering to multicontact electrodes is challenging because of the many combined permutations of parameters. Optimizing nerve cuff stimulation parameters may provide enhanced selectivity. Simulations are an efficient method to investigate important aspects in nerve cuff electrode stimulation. Anatomically based computer simulations of the femoral nerve cuff electrode for use in a standing device [7] have shown the FINE to be functionally selective and applicable for a standing neuroprosthesis. The simulation methods were validated by human intraoperative experiments. These simulations determined neuronal excitation by using a nonlinear neuronal activation method [5]. When this method is applied to millions of axons, it requires several months to solve [7].

A newly developed linear algorithm [4] has allowed fast calculations of neuronal excitation for thousands of neurons in seconds. The linear methods have enabled the rapid exploration of a large parameter space. Coupling the linear method with a large parameter search space can provide optimal parameters for nerve cuff stimulation. An objective function was developed to optimize important outcomes of nerve cuff stimulation for the FINE in a human median nerve. The objective function developed is a tool that can incorporate any electrode configuration for any nerve cross section and calculate optimal parameters needed to achieve user defined target groups. Our hypothesis is that a large parameter search space can be used to selectively activate target groups using a high density nerve cuff electrode. Calculating the optimal parameters of the nerve cuff will indicate the capabilities of the nerve cuff and guide electrode design. The goal of this study is to design an optimized stimulus paradigm for selective activation of contiguous groupings of fascicles in a multi-fasciculated nerve and evaluate the paradigm's efficacy.

II. METHODS

A. Constructing Finite Element Models

Anatomically based simulations were constructed from human cadaveric cross sections of the median nerve. The nerve cross sections consist of an epineurium containing the fascicles. Fascicles are bundles of axons consisting of the endoneurium and are surrounded by the perineurium. Images of histological cross sections of the median nerve were imported into MATLAB (The MathWorks, Inc., Natick, MA) and the vertices of the fascicles and epineurium were recorded using a custom MATLAB software package. The thickness of the perineurium was set to 3% of the fascicular diameter [3].

Two dimensional templates were imported into Maxwell 3D v12 (Ansys Corporation, Canonsburg, PA). The 2D template was extruded 60 mm to create 3D finite element models. Conductances were assigned to the various tissues [1] (Table 1). A high density FINE was modeled around the nerve with 36 contacts. Each contact had a dimension of .5 x .5 mm and was insulated on all sides by silicone except for the face flush with the nerve. The contacts in the simulations were located .2 mm from the nerve. The nerve cuff model

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TABLE 1

Material	Conductivity (S/m)
Perineurium	.0021
Endoneurium	.57 (longitudinal)
	.083 (transverse)
Epineurium	.083
Saline	2.0

Modeling Conductivities assigned to the finite element model structures [1].

was surrounded by saline with a dimension of 300 x 300 x 300 mm. The simulations were solved with a -1 mA stimulus applied to each contact separately for a total of 36 simulations.

B. Calculating Axonal Activation and Selective Activation

One hundred axons were randomly placed in each fascicle. A bimodal distribution axon diameter range of 4-16 μm [3] was employed in this study to determine a realistic spatial extent of activation within the fascicle. The offset from the center of the node of ranvier was randomly distributed and each axon had 21 nodes of ranvier. The potential fields calculated at each contact with a unit stimulus of -1 mA were scaled with the amplitude of the active contacts and added to calculate the resulting potential. The calculated voltage fields were interpolated at each node.

The interpolated voltages were then applied to the linear approximation method to determine axonal activation [4]. The linear approximation method is a double decay exponential function that determines activation of neuronal excitation. It requires the second spatial difference of the voltage along the axon, the voltage magnitude at the nodes, and the pulse width of the stimulus in order to determine axonal activation.

Selective activation of a target group (S_{TG}) was calculated by subtracting the fraction of axons activated outside the target group (Recruitment Cost, RC_c) from the fraction of axons activated within the target group (Recruitment Benefit, RB_c) shown in equation (1.1) [7].

$$S_{TG} = RB_c - RC_c \quad (1.1)$$

C. Developing an Objective Function

The O matrix was used to calculate components of the objective function (1.1) using the MATLAB Genetic Algorithm toolbox. The O matrix shown below was calculated for each set of contact amplitudes with a constant pulse width of 100 μs. The columns in the matrix correspond to specific axons throughout the entire cross section. The row number corresponds to the cathodic contact number from contact 1 through 36. Each row is the result of anode surround stimulation (Fig. 1). A value of 1 in the matrix indicates the axon was activated and a 0 indicates the axon was not activated.

$$O = \begin{vmatrix} 1/0 & \dots & 1/0 \\ \vdots & & \\ 1/0 & \dots & 1/0 \end{vmatrix}$$

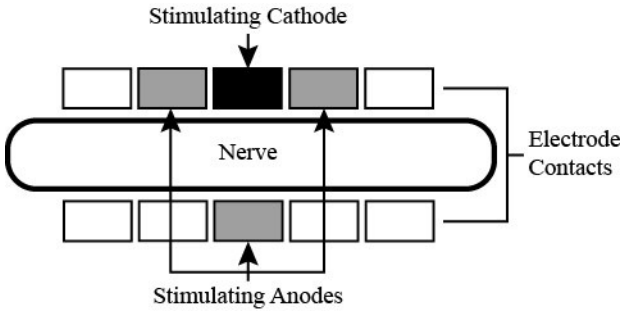

Fig. 1. The surrounding anode stimulation paradigm was optimized for each target group by the objective function (1.2). Each stimulating contact set consists of one cathode and three surrounding anode contacts. The pulse width was set to 100 μs and the current amplitudes were varied to minimize objective function (1.2).

The contact configurations were constrained to one cathode and three surrounding anodes for each activated target group (Fig. 1). The final solution to the search algorithm consists of cathodic and anodic amplitudes that activate all target groups selectively.

Minimizing the objective function (1.2) drives the result towards an optimal solution for selective stimulation of the target regions. The O matrix is manipulated to quantify each component in equation 1.2.

$$F_{obj} = W_1 * T_{axons} + W_2 * L_{axons} + W_3 * R_{axons} + W_4 * M_{axons} + W_5 * G_{axons} \quad (1.2)$$

T_{axons} =Number of axons within a **Traced** group

L_{axons} =Number of total axons activated at **Least** once

R_{axons} =Number of **Redundantly** stimulated axons across different sets of activating contacts

M_{axons} =Number of contacts that activate **More** than 20 axons

G_{axons} =Number of axons that are in a **Group** larger than 300 axons

The T_{axons} component compares the O matrix to all the specified target regions and determines which contact set yields a result closest to one of the target regions. The chosen activation result is penalized for any differences in activation from the chosen target region. To ascertain a solution where all target regions are activated, the L_{axons} component penalizes the function if not all axons within the cross section are activated at least once. The R_{axons} component penalizes the objective function if there are axons activated more than once between each activating set of contacts. The M_{axons} component increases the number of contacts activated which increases the number of optimal solutions available. The G_{axons} component penalizes the function when the group activated contained more than three fascicles since all target groups selected included two or three fascicles.

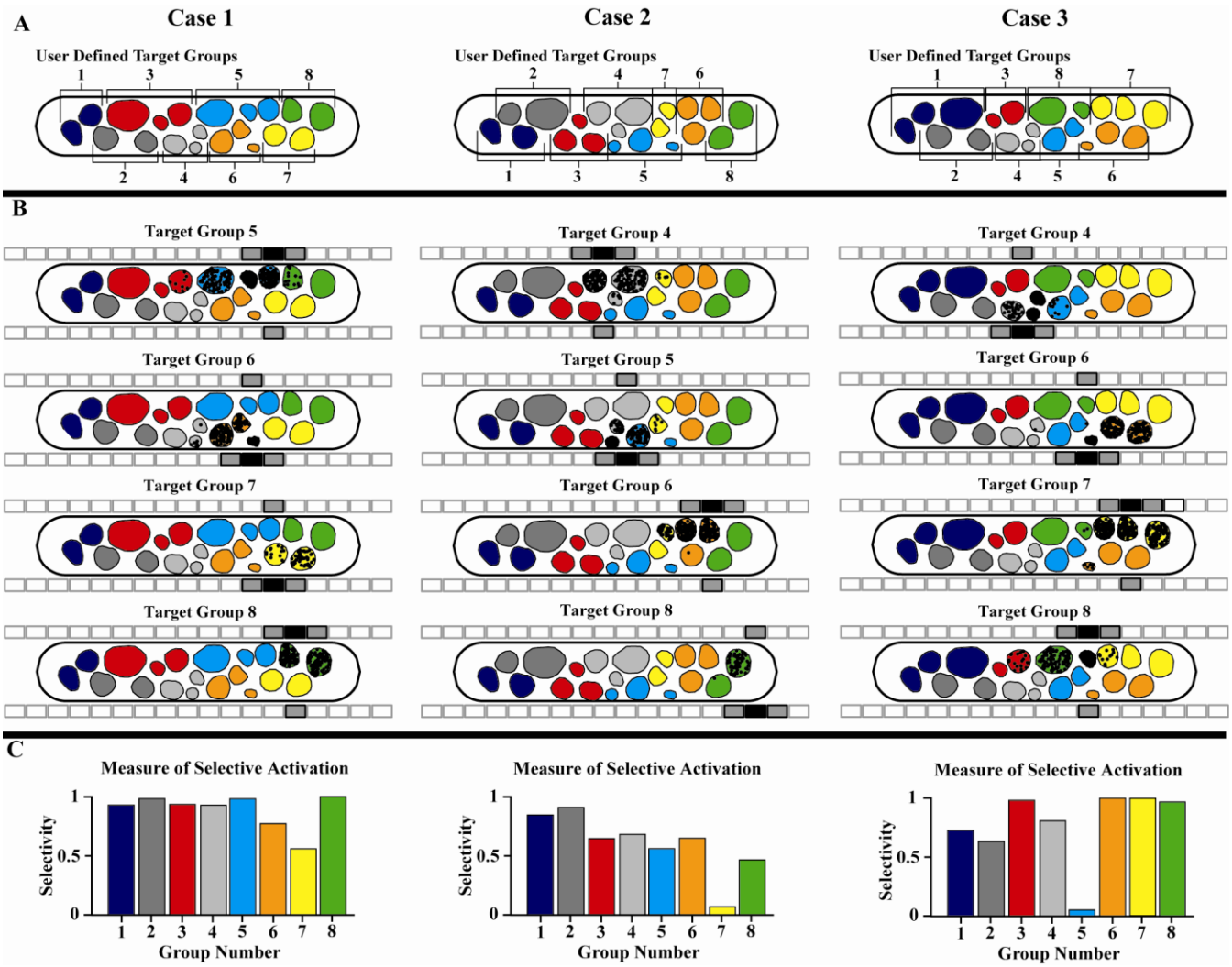

Fig. 2. Each case represents a set of user defined contiguous groupings of fascicles. Panel A shows the target regions defined for each case. The nerve cross sections shown are 2 D representations of the finite element models that were constructed. Panel B shows select examples of target groups activated from stimulation parameters determined through the genetic search method. The black dots represent the locations of axons that were activated. The black contacts are cathodic and the surrounding gray contacts are anodic. These cases demonstrate that an optimal solution can be obtained for most contiguous target groups. Selective activation of target group 7 from Case 2 and group 5 from Case 3 was not achieved and their results are not shown. Panel C shows the selectivity values for each of the target group configurations. All groups were activated selectively except for group 7 in Case 2 and group 5 in Case 3. Both of the groups that were not activated selectively contained one fascicle located deep within the nerve.

W_n are the corresponding weights which were chosen to scale the magnitude of the five different components. If a component was being maximized, W_n had a negative value. Multiple combinations of weights were tested and the weights that produced the most favorable outcome were selected. The values used in the simulations for W_1, W_2, W_3, W_4, and W_5 were 10, -1, 1, -100 and 1, respectively. The stimulation parameters that yielded the smallest objective function value calculated with equation 1.2 were selected as the solution. To test the algorithm, we optimized several arbitrarily selected contiguous groups of fascicles.

III. RESULTS

In order to demonstrate optimization for any contiguous target groupings, three different cases are shown in Figure 2. Only target regions within the right half of the nerve cross section are shown. The groups in case 1 contained fascicles which were located superficially. These groups were all activated separately. The fascicles in groups from case 2 included both superficial and deep fascicles. All of the groups in case 2 were activated selectively except for group 7. The target groups in case 3 also contained groups with fascicles located both superficial and deep. In Case 3, group 5 contained a deep fascicle and was not able to be activated separately from the nearby group. The groups most fully recruited across all cases contained fascicles that were located superficially.

The selectivity values [7] were calculated for all three cases and are shown in Figure 2 C. All groups across all three cases were recruited selectively above 46% except for two groups. The two groups that were not activated selectively were group 7 from case 2 and group 5 from case 3. These two groups consisted of two fascicles where one fascicle was located deep within the cross section and the

other fascicle was located superficially in the cross section.

IV. DISCUSSION

The stimulation paradigm implemented consisted of a constrained set of four contacts. All activation sets for all the target groups in the three cases shown in Figure 2 were solved in 48 minutes. The anode surround stimulation paradigm was selected because with the surrounding anodes, the field intensity can be focused to smaller regions. The pulse width was held constant in order to decrease the number of parameter permutations. Allowing more contacts and the pulse width to be unconstrained would result in more control of the field shaping but would increase the computation time. Additional field steering could yield more selective results but it is beyond the scope of this initial trial.

These results are representative of those for all contiguous groups and could be generated for any arbitrary contiguous groupings of fascicles. It was difficult to trace fascicular groups to specific muscles in the median nerve cross section that was used as a template in the simulations. We chose to group the fascicles into eight separate arbitrary groupings. The nerve cross section consisted of 20 fascicles and each group was set to contain 2-3 fascicles that were contiguous. Superficial groups that consisted of similar sized fascicles along a horizontal axis of symmetry were activated the most selectively. Both of the groups with selectivity values below 46% consisted of two fascicles with one fascicle located in the middle of the cross section. Fascicles surrounded by other fascicles were difficult to activate using cuff electrodes with a single cathode, surround anode stimulation configuration.

The objective function developed indicates that a search algorithm can be implemented to determine optimal stimulation parameters for any contiguous target groups. An additional aspect that could provide improvement would be a constraint on the recruited axons outside the target group. The number of axons activated outside the target penalizes the function but the fraction of each fascicle activated does not affect the objective function. For example, the objective function has the same value for 100% of one fascicle activated outside the target as it does for 5 fascicles with 20% activation. The fraction of the activation of each fascicle recruited outside the region is important and could be incorporated into the objective function. It is preferable to have a small fraction of multiple fascicles than full activation of a single fascicle that innervates an antagonist muscle.

Although the cross section must be known *a priori*, the genetic search algorithm is not constrained to a specific cross section. A cross section must be predefined to apply to the genetic search method but target regions are defined by the user. The same objective function can be applied to many variations of the same cross sections. Varying the fascicular locations within the same cross section and applying these variations to the genetic search method allows for investigating the effect of redistributing the fascicles within the cross section. Reshaping of the nerve due to the FINE may cause fascicular redistribution and its effect on selectivity can be studied through use of the genetic search method.

Additionally, the objective function can be further modified for use in experimental stimulation. The current objective function (1.2) is calculated from axonal activation of computer simulations to achieve selective activation of user defined target groups. The target of the objective function can be defined as an EMG signal of interest. The stimulation parameters would then be optimized to selectively activate the EMG signals of interest which would not require information of the internal nerve anatomy.

V. CONCLUSIONS

A genetic search algorithm can find optimal stimulation parameters for arbitrary target regions in the nerve model. The genetic search method can be applied to any nerve cross section with user defined contiguous groups of fascicles. Additionally, a modified genetic search method can be employed for use in real stimulation. These techniques offer an attractive method to improve selectivity of nerve cuff electrodes for neuroprostheses.

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