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OPTIMISING THE CONNECTIVITY COEFFICIENTS IN THE SOMATOSENSORY PATHWAY USING GENETIC ALGORITHMS

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ABSTRACT

The interacting questions of consciousness, awareness and depth of anaesthesia are challenging and timely. A neuronal network of the somatosensory pathway relating to administration of narcotic/hypnotic drugs for surgical anaesthesia has been developed. It employs spatially distributed and lumped-parameter modelling, and is a derivative of other established neuronal models. It comprises 22 ODE (Ordinary Differential Equations) and has many connectivity parameters which require careful selection. The initial model used connectivity coefficients proportional to the average number of synaptic contacts between the relevant cortical cellular components based on histological examination. While giving reasonable correspondence to experimental data from rats, the manual adjustment of these crudely estimated coefficients was both tedious and not entirely satisfactory. In this paper, the connectivity terms have been optimised using global GA (Genetic Algorithm) tuning. The GA is seeded with the previously established synaptic weighted estimates. It is shown that very good agreement with physiological data has been achieved in an automated fashion. The resultant connectivity coefficients can now be investigated for probing likely areas of uncertainty for further detailed anatomical studies.

INTRODUCTION

The literature discusses extensively, based on physiological experiments, the structure and functioning of the somatosensory cortex and its role in anaesthesia processing (Angel 1993; Treede et al. 1999; Kaas and Collins 2001). To alleviate the dependence upon animal experiments, a neuronal network of the somatosensory pathways, as shown in Figure 1, was proposed previously (Ting et al. 2003) by the researchers to provide a framework for a wide range of hypothesis testing in exploring the anaesthetic mechanisms/dynamics. Though the structure is realistic and parsimonious, it is valuable as a paradigm on which a series of anaesthetic phenomena have been explored in a focused scientific manner. Analytical studies were not undertaken due to the lack of physiological information and the complexity of the model, and hence existing neuronal models and physiological parameters were utilised in the proposed pathway model. By comparison with responses from anaesthetised rats, the model's responses are able to describe the dynamics of somatosensory evoked responses (SER) under general anaesthesia. However, one of the major problems in application of the proposed model is the insufficient knowledge on the numbers of inter-neuron synaptic contacts which are normally roughly counted in histological studies (White 1989).

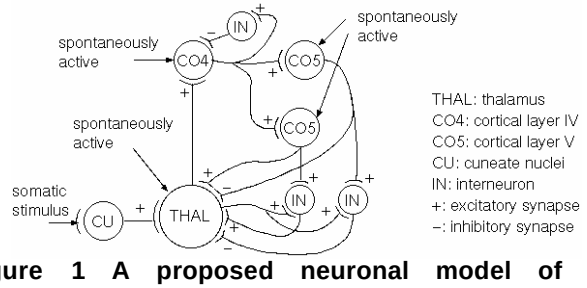

Figure 1 A proposed neuronal model of the somatosensory pathways (Ting et al. 2003).

In Figure 1, the number of either excitatory or inhibitory synapses per neuron is represented using a connectivity

coefficient accounting for the average number of synaptic contacts between the correlating cells (Wilson and Cowan 1972). The connectivity coefficients can be partially derived from costly and time-consuming histological studies (White 1989; Jansen and Rit 1995), but mainly as a compromised result from simulations (Ting et al. 2003). This inherent drawback gives simulation responses with a big discrepancy from physiological responses although a similarity in between exists. There is a certain, subject-dependent combination of the connectivity coefficients in light of physiology (Tsodyks et al. 1998), but it was not successful in previous work and hence coefficient selection was mainly induced by trial-and-error. Thus, it would be beneficial to derive a set of optimal coefficients based on which simulation responses may be more coincident to physiological responses. In lieu of physiology, the derived optimal combination of coefficients may be used as a guideline in exploring the synaptic distribution in the brain.

RESEARCH METHODS

Network Modelling of the Somatosensory Pathway

Modelling the Neuron Cells

A neuron can be seen as the construction of synapses, cell body, and axon hillock using the concept of lumped modelling (Lopes da Silva et al. 1982). The synapses convert incoming signals into membrane potentials. Membrane potentials, either temporally or spatially distributed, are integrated by the cell body. The integration is then converted to nerve impulses at the axon hillock if the voltage reaches a threshold potential. Finally, the nerve impulses are transmitted through the axons.

Physiological experiments show that the EPSPs and IPSPs have impulse responses and can be lumped as follows (Lopes da Silva et al. 1982):

$$h_e(t) = \begin{cases} Aate^{-at}, & t \geq 0 \\ 0, & t < 0 \end{cases} \quad (1)$$

$$h_i(t) = \begin{cases} Bbte^{-bt}, & t \geq 0 \\ 0, & t < 0 \end{cases} \quad (2)$$

with $A = 3.25\text{mV}$, $B = 22\text{mV}$, $a = 100\text{s}^{-1}$, $b = 50\text{s}^{-1}$. A and B represent the amplitude gains of the PSP functions and a and b the transmission lag constants.

The interneuron has its own transfer function (Jansen and Rit 1995):

$$h_d(t) = \begin{cases} Aa_d te^{-a_d t}, & t \geq 0 \\ 0, & t < 0 \end{cases} \quad (3)$$

where $a_d \approx a/3$ means that the interneuron has a latency 3 times longer than the cortical cells. The axon hillock model is lumped as (Freeman 1987):

$$s(u) = \frac{2e_0}{1 + e^{g(n_0 - n)}} \quad (4)$$

where $g = 0.56mV^{-1}$, $e_0 = 2.5Hz$, $n_0 = 6mV$.

Because of the lack of sufficient physiological information, both cortical cells and interneurons are assumed to have the same hillock model. This approach has been used by several researchers in modeling various nervous pathways such as the visual pathway by Jansen and Rit (1995), alpha EEG rhythm by Rotterdam et al. (1982), the olfactory pathway by Freeman (1987), and the somatosensory pathway by Ting et al. (2003).

Network for Numerical Simulation

A block diagram of the physiological pathway of Figure 1 is obtained by applying the above linear synaptic transfer functions and the nonlinear hillock activation function to each cell in the pathway and is shown in Figure 2. Constants $C_{\#}$ represent the connectivity coefficients which account for the average number of synaptic contacts between the correlating cells (Wilson and Cowan 1972). Based on the pathway network and the neuronal models we can construct a set of 22 ODEs suitable for numerical solution to describe dynamics of the pathway in various aspects of neurophysiological studies (Ting et al. 2003).

The block representation of Figure 2 was solved using numerical techniques with a fourth-order Runge-Kutta-Fehlberg (RKF4) method under a fixed step length. Responses recorded on the scalp corresponding to the integrated current generated by the membrane potential fluctuations of the cortical cells. Hence the model validation signals are obtained by collecting results of y_5-y_7 for the output of the primary somatosensory cortex cells in layer IV.

A noticeable difficulty encountered in dealing with model simulation is the selection of the connectivity coefficients – sixteen coefficients exist in the model, ie. $C_k, k = 1 \cdots 16$, which are not well known yet. The literature gives only partial and inaccurate information on the connectivity coefficients. Hence, to arrive at an oscillatory evoked response more realistic to physiological responses, it has been a laborious task in manually selecting the coefficient values in accordance to the histological literature and existing similar works.

Our previous work adopted a combination of the connectivity coefficients as below: C_1=C, C_2=0.25C, C_3=0.1C, C_4=C, C_5=C, C_6=C, C_7=C, C_8=0.25C, C_9=C, C_{10}=0.1C, C_{11}=0.8C, C_{12}=0.1C, C_{13}=0.1C, C_{14}=C, C_{15}=C and C_{16}=C with C=135 being decided by trial and error. Since large changes of the connectivity coefficients can make the system unstable, the above selection was maintained constant throughout all simulations. This is physiologically reasonable since the number of synaptic contacts should be a constant under normal conditions (Thomson and Deuchers 1994).

Pilot Simulation Results

The 22 ODEs of the network model in Figure 2 were implemented in GNU C++ on Linux workstations. The ODEs were solved using the fourth-order Runge-Kutta-Fehlberg (RKF4) method with a fixed step length. A sweep is envisaged to consist of 500 samples at sampling rate of 500 Hz. The sampling period in the RKF4 integration is divided into 50 steps for a better resolution. Fifty (50) raw responses are averaged to give an evoked response, this being the so-called ensemble averaging.

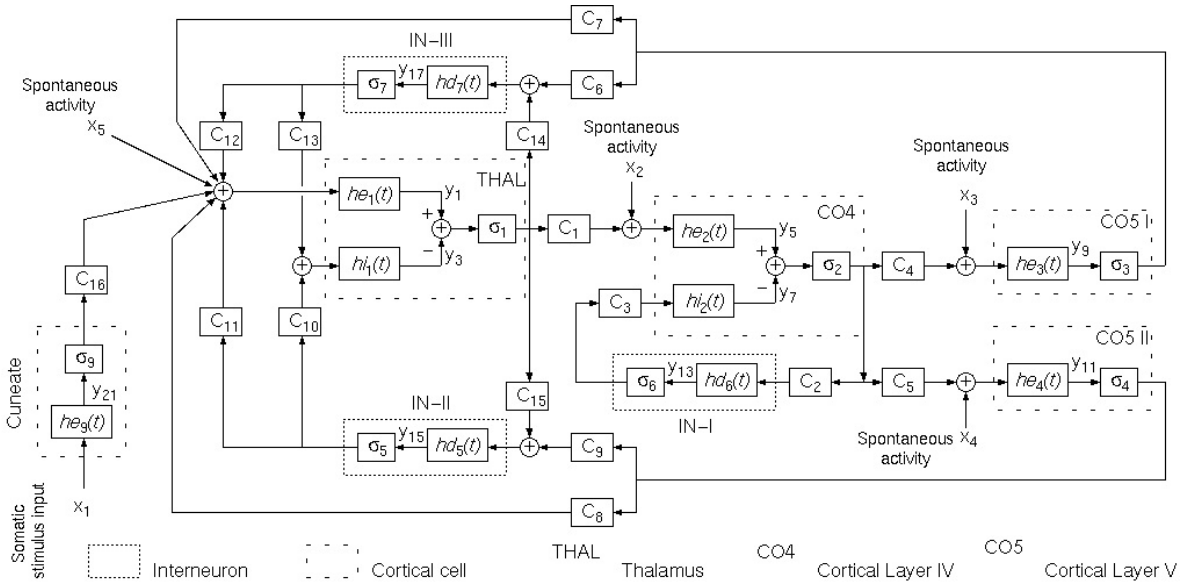

Figure 2. Detailed block diagram of the proposed model for the somatosensory pathways of Figure 1.

The responses representing the post-synaptic membrane potentials occur at the respective neuron.

A monotonic function was used to mimic the somatic stimulus (Jasen and Rit 1995):

$$x_1(t) = q \cdot \left(\frac{t}{w}\right)^n \cdot e^{-t/w} \tag{5}$$

with $n = 7$, $w = 0.005$, and $q = 0.5$. Stimuli generated using the above function were applied to the cortical model at the 50th sample time of each sweep. Spontaneous activities, $x_2 \cdots x_5$, applied to the cortical cells from the surroundings were assumed to be a random disturbance with a magnitude range of (120,320) impulse per second representing the instantaneous frequencies.

In analogy to SEPs recorded from living subjects, we are able to define the usual terms relating to SEP analysis as shown in Figure 3. Figure 3a is a response recorded from a urethane-anaesthetised rat. In Figure 3b, obtained from the model, the onset, initial positive peak and initial negative trough are also well defined. These indices are used as neurophysiological indicators in clinical applications (Angel and LeBeau 1992).

The Need for Optimised Connectivity Coefficients

The connectivity coefficients employed in the above study were kept constant through the whole process of simulation. This is the major drawback of this cortical model in that it does not have sufficient knowledge on real connectivity coefficients. Variations of the coefficient values make the system outcomes to differ from the animal data and be unstable. Though constant, the connectivity coefficients during simulation simply follow the nature law if the synaptic contacts are not damaged by either chemicals (drugs) or physical disturbances (Thomson and Deuchers 1994). However, the above simulation result implies that there exists an optimal combination of the connectivity coefficients which produce more realistic responses in comparison with physiological data. This concept is well recognised by those who use artificial neural networks (ANN) in solving engineering problems. In ANN applications, the weightings connecting neural elements are optimised using a learning engine. Being motivated by the success of ANN learning, we employed Genetic Algorithms to determine an optimal combination of the connectivity coefficients with the aim to give more realistic simulation results.

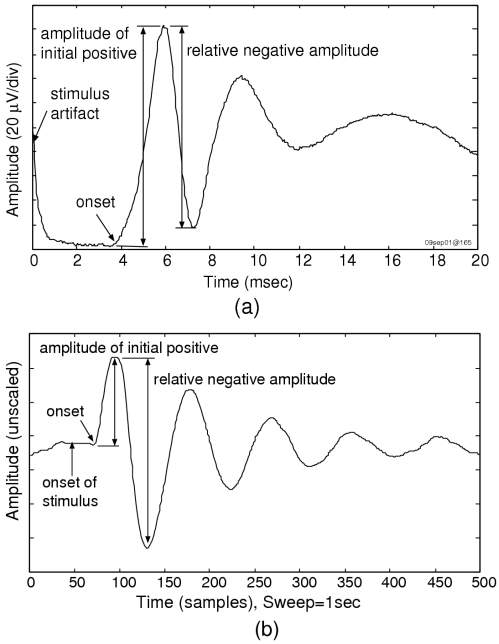

Figure 3. A simulation response in analogy to a realistic SEP sweep: (a) from an anaesthetized rat, (b) simulation result.

OPTIMISATION OF CONNECTIVITY COEFFICIENTS

The Need of Optimisation

The optimisation of the connectivity coefficients is a problem to simultaneously search for multiple, competing solutions. Traditionally, this problem is solved using either a calculus-based or numerical technique(mainly dynamic programming) (Tang et al. 1996). The former may result in local optima while the latter is only suitable for problems of moderate size and is time consuming in computation. The Genetic Algorithm(GA) is a search process based on the law of natural selection and genetics. Usually, a simple GA consists of three operations: selection, genetic operation, and replacement. Because of its simplistic implementation procedure, the GA is used as an optimisation tool in this study for searching the optimal combination of the connectivity coefficients. The GA has also been used in construction of ANNs for engineering applications (Maniezzo 1994; Angeline et al. 1994). For details of the GA the readers are referred to the large volume of literature.

Optimisation with Genetic Algorithms

In this study, the GA is employed to arrive at global optimisation of the connectivity coefficients. The connectivity coefficients are described as a population which comprises a group of chromosomes, from which the connectivity coefficients are randomly selected in accordance with our previous work. The fitness values of the all chromosomes are evaluated by calculating the objective function in a decoded form. A parent group of chromosomes is selected from the population to generate the offspring by the defined genetic operations. The fitness of the offspring is evaluated in a similar fashion to their parents. The chromosomes in the current population are then replaced by their offspring, based on a certain replacement strategy.

The GA cycle is repeated till a desired termination criterion is reached. If all go well throughout this process of simulated evolution, the best chromosome in the final population can become a highly evolved solution to the problem. A top-level description of the GA employed in this study is itemised below and is shown in Figure 5:

1. Randomly generate an initial population.
2. Calculate the fitness $F(x_i)$ of each chromosome x_i in the current population $X(t)$.
3. Create new chromosomes $X_r(t)$ by mating current chromosomes, applying mutation and recombination as the parent chromosomes mate.
4. Delete numbers of the population to make room for new chromosomes.
5. Compute the fitness of $X_r(t)$ and insert those with a higher fitness into the population.
6. Go to step 2 till end test or the best chromosomes reached.

In step 1, parameters of the initial population are normally selected to 1 to 4 times the number of parameters being sought (Lee and Fan 2000). Hence the number of generations is set to 25. An 8-bit binary encoding scheme is employed. The length of bit number is a compromise between accuracy and computation time.

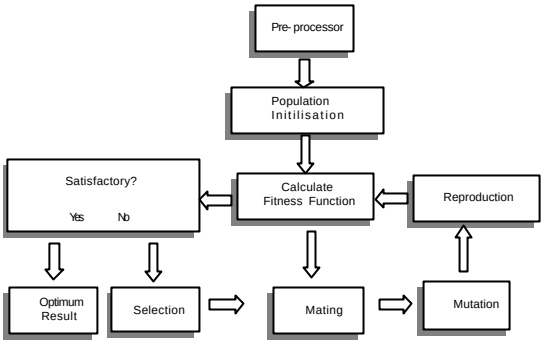

Figure 5. A GA cycle.

The status of each chromosome is evaluated using an objective function. The objective function calculates the fitness of a new population of chromosomes. The objective (fitness) function is defined as:

$$F(x_i) = \frac{1}{0.1 + J_0} \tag{6}$$

with $J_0 = \sum_{j=1}^{N}\sum_{i=1}^{N}\left\| x_{\max,i} - x_{\min,j} \right\|^2$,

where $x_{\max,i}$ and $x_{\min,j}$ are the maximum/minimum of chromosome x_i after encoding and N is the number of chromosomes. The adoption of 0.1 in the denominator prevents the calculation from an overflow error in division. A population with a higher fitness is used for reproducing a new generation based on the roulette wheel selection method (Tang et al. 1996). Mating is a process based on which chromosomes of populations exchange in the mating pool. The mating rate is 0.6 in this study. While mating allows chromosomes to exchange chromosomes, the process of mutation opens a door for new chromosomes to be part of the population. Mutation enhances the parameter search zone so that possible local optimisation can be avoided. In this study the mutation probability is set to 0.01. The elitism strategy (Wall 1996) is used in step 5 for retaining the best fit chromosomes in the old generation while the remaining are substituted with new chromosomes.

This simple GA engine is combined with the network model of the somatosensory pathways of Figure 2. The connectivity coefficients are encoded, mated, mutated and then reproduced to a globally optimised combination $\tilde{C}$. $\tilde{C}$ is furthermore refined with the following iterative learning algorithm:

$$\hat{C} = \tilde{C} + \frac{1}{1+e} \tag{7}$$

with parameters as defined in Figure 6. The learned coefficients $\hat{C}$ stipulate the somatosensory model and hence a new sweep of simulated evoked-response is obtained. The optimisation and learning operations are terminated when the simulated response

y_b matches the animal data y_{ref} within a tolerable range, with the criterion defined below:

$$ISI = \sum (y_{ref} - y_b)^2 \quad (8)$$

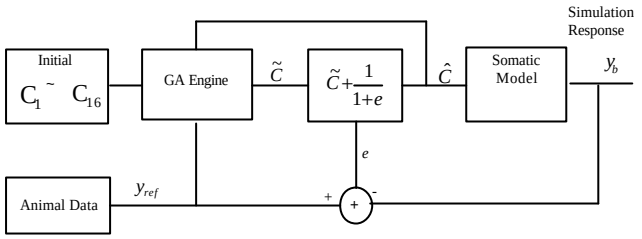

Figure 6. The GA optimizer.

TENTATIVE SIMULATION RESULTS AND DISCUSSION

The GA-based simulator was implemented using the C++ language based on an object-oriented approach. The GA operation was realised using the open-source GAlib, a C++ library of Gas components available freely at http://lancet.mit.edu/da/.

The animal response of Figure 3a is used as the reference data y_{ref} in GA optimisation of Figure 6. The numerical simulator for the somatosensory pathways is identical to that for Figure 3b with the same neuronal parameters. Connectivity coefficients used for Figure 3b are used as initial value in coefficient optimisation. The following GA parameters are adopted during simulation: population size (25), generations (500), mutation rate (0.01), mating rate (0.6), and convergence rate (0.99). A pilot study shows that the optimisation converges after 120 generation of iteration as shown in Figure 7. Hence the simulation terminates at 120th generation to save computational time.

An optimal combination of the connectivity coefficients are obtained and then fixed in the whole course of SEP simulation. Figure 8 shows a sweep of simulation response with parameter search ranges as summarized in Table 1.Comparing Figure 3.b and Figure 7 it is seen that the latter matchesthe animal data well. The promising simulation result implies that there exists an optimal combination of the connectivity coefficients in a living subject. This is physiologically reasonable as the number of synaptic contacts in the brain is unlikely to change with time except when brain lesions occur.

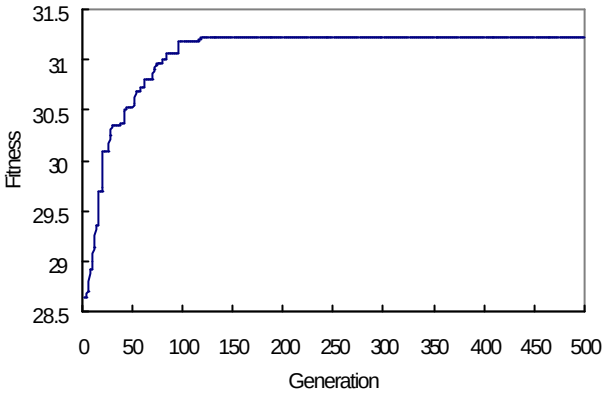

Figure 7. The fitness profile in learning.

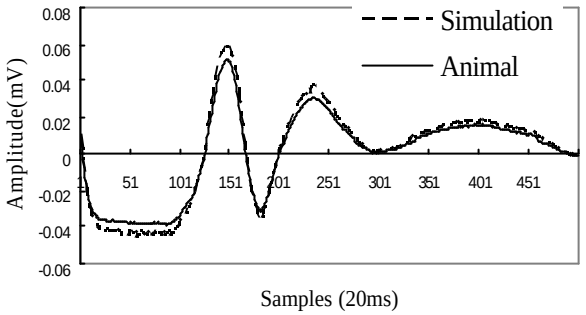

Figure 7. GA-optimised simulation results.

Table 1. Search ranges of connectivity for optimization and optimized coefficients.

	C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}	C_{11}	C_{12}	C_{13}	C_{14}	C_{15}	C_{16}
Upper Bound	135	37.5	14.8	139	139	139	139	139	139	14	139	14	14	139	139	139

Lower Bound	135	30	12.1	122	122	122	122	30	122	12	122	12	12	122	122	122
Optimised	135.8	34.15	13.6	135.7	135.67	135.7	134	35.5	133.3	14.4	108.88	14.6	14.77	135.54	133.76	133.76

CONCLUSIONS

The proposed somatosensory neuronal model shown in Figure 1 was initially simulated based on "best guess" connectivity coefficients. The scenario gave promising simulation responses from a physiologically-based structure and components. Though the result was promising, there still exists a big discrepancy between realistic responses from a living subject and the simulation responses. This is understandable since the connectivity coefficients were derived by trial, which do not account for actual combination in living subject. This is inevitable as it is really difficult to count the actual synaptic distributions or obtain even a rough estimate by histology.

The GA-based simulator was implemented using the C++ language based on an object-oriented approach. The pathway of Figure 1 consists of spatially distributed cortical neurons. Each cortical neuron represents a population of neurons in the respective area. Hence it would be natural and challenging to utilise clustering computing to construct a parallel computing platform and hence facilitate its computational speed (Dorigo and Maniezzo 1992). We may expect that each neuron population of the pathway can be decomposed into unique computing units. Based on this approach a real-time nervous simulation system may be possible in the near future.

This simulation result of this pilot study reveals that it would be valuable to use the optimised connectivity coefficients as a guideline for histology in counting the number of synaptic contacts in the brain. Further works should be conducted to explore several physiological aspects of the application of this GA-based simulator.

ACKNOWLEDGMENTS

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