Neural network modelling of human electroencephalogram patterns

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A general regression neural network model with different processing elements (PE) fits the observed electroencephalogram signals (EEG) of the human brain during awake, sleep and rapid eye movement (REM) stages. The number of PEs required for simulation could be an indication of the complexity of the EEG pattern. About 6.5 times more PEs are required to simulate the signal during alert eyes open (β waves) than alert eyes closed (α waves) stage. Also, half the number of PEs are required to simulate sleep stage 4 when compared to simulating sleep stage 2. REM sleep requires more number of PEs to simulate than sleep stage 4. PEs required to simulate short duration 'petit mal' epileptic seizure less than those required to simulate β waves, but more than those required to simulate REM state. In most cases a correlation exists between the number of PEs and the fractal dimension.

THE neuron is the fundamental cellular unit of the nervous system and, especially the human brain. The central nervous system is a neural network of about 10^{11} neurons, all of them interconnected in the form of a dense matrix. The neocortex is under the influence of external stimuli as well as input from subcortical areas. The axon or the output path of a neuron splits up and connects to dendrites or input paths of other neurons through a junction known as a synapse. The electrical activity of the brain is routinely measured from the scalp and analysed for abnormalities. It is used in the search for sleep disorders.

Electroencephalogram (EEG) is related to the firing pattern of the neurons in the neighbourhood of the cerebral cortex. Cells continuously receive pulses, especially at dendrites, from other neighbouring neurons. The pulses are transmitted at synapses. Certain incoming pulses generate excitatory waves, while others generate inhibitory waves of electric current in the recipients. These dendritic currents are fed through the cell body to a region at the start of the axon. These currents enter the extracellular space after crossing the cell membrane. The cell calculates the overall strength of the currents, which is indicated by changes in voltage across the membrane, by adding all the excitatory and subtracting all the inhibitory currents. If the sum is above a threshold value then the neuron fires (i.e. an output from the neuron is generated). Although the activity of real neurons is very complex what is described above is an oversimplification of the process of synaptic integration.

The mechanism producing each EEG tracing sums up the currents initiated at the dendrites. The tracing shows the excitatory state of group of neurons rather than of individual neurons, because the extracellular space is criss-crossed by currents from thousands of cells[1]. EEG tracings of living beings generally oscillate and are very irregular, but nevertheless follow a pattern. They may have a high-frequency component superimposed on low-frequency signals. Recent progress in the theory of nonlinear dynamical systems has provided new methods for the study of EEG time series data. Global properties of the brain EEG patterns at various stages of activity and inactivity, are being analysed using the theory of chaos, Lyapunov exponent, auto-correlation function, power spectra and fractal dimension[2–4]. Activity of a small subset of neurons in the presence and absence of a synchronized oscillatory signal is modelled using differential equations and the results analysed using spatial auto-correlation function and correlation dimension[5].

Neural network computer programs try to simulate neuronal activity. In an artificial neural network, the unit analogous to the biological neuron is referred to as a processing element (PE)[6,7]. In spite of the fact that simple interconnected networks do not completely simulate the dynamic properties of real neurons, they are useful in gaining insight into universal principles of distributed systems. Also, a trained network has striking similarities to actual neurons and can suggest functional roles of neurons with input and output that are hard to grasp intuitively. Back propagation network has been used to process chaotic EEG signals[8].

A neural network consists of many processing elements joined together through connection weights which correspond to the synaptic strength of neural connections. Data to the network is presented at input layer and the response of the network to the given data is stored in the output layer. It is speculated that the training or learning of neural network model is similar to the way humans or animals are trained by reinforcement technique, where certain synapses that connect the neurons selectively get strengthened leading to increase in the gain.

We attempt here to simulate the different types of EEG patterns emanating from human brain during activity (eyes closed and open, epileptic seizure stages) and inactivity (sleep stages 2, 4 and REM stages) using a general regression neural network model.

Back propagation partially recurrent and cascade correlation neural network models have been used to simulate non-average single trial multi-channel EEG data produced during the side finger movement[9]. The cascade correlation neural network model was found to predict the obs signals well.

Neural network models have been used to train on ECG signals of patients with anterior and myocardial

infarction and the network was later used for prediction of abnormalities[10]. Back propagation model has also been used for detecting spikes and seizures during epileptic fits[11], for simulating the oscillatory activity observed in the visual cortex[12], and olfactory system[13]. Very little work is reported on simulating the EEG brain signals during various sleep stages, eyes open and closed stages. A trained neural network model can help in identifying sleep disorders, changes in sleep pattern and variation in sleep patterns between individuals.

Two networks that are well suited for modelling, prediction and classification are back-propagation (BP) and general regression neural network (GRNN)[14]. BP network is a general purpose nonlinear regression technique which attempts to minimize global error. The main advantages of the GRNN over the BP network are (i) it can handle non-stationary or noisy data; (ii) it can be effectively used with sparse data. This network was proposed by Donald Specht of the Lockheed Palo Alto Research Laboratory.

Each PE in the network has several inputs and outputs. The output path of a PE is connected to the input path of another PE through connection weight. The input signal is multiplied by the weight before it is sent to the PE. All the weighted signals are summed up and fed as the input to the PE. This signal is transformed and sent to the output path of the PE. A neural network normally has one input, one output and at least one hidden layer and, there may be several PEs in each layer. During learning stage the weights are manipulated so that for a given set of input signals, the outputs estimated by the network match the actual values.

GRNN uses a statistical equation for calculating the conditional mean Y of a scalar random variable y given a measurement X of a vector random variable x. The conditional mean is statistically the most probable value for the random variable Y for given X. The vector random variables x and y correspond to the ensemble of inputs and outputs of the network. The equation for conditional mean requires knowledge of the joint probability density function (PDF) of the random variable x and y.

In GRNN, the PDFs are obtained from the training vectors using Parzen estimation. Parzen estimation is a non-parametric estimation procedure which approximates a density function by constructing it out from many PDFs and, it takes the form of a Gaussian distribution (bell-shaped curve). The parameter used in the exponential term of the Gaussian equation is estimated from the input vectors and their centre and, is given by the square root of the sum of square of the difference between the input vectors and the centre. It is also known as the Euclidean distance (D_t). This type of summation is called Euclidean summation and is suitable for most of the problems. The estimate for the conditional mean for the output vector is given by

$$Y(X)=\frac{\sum_{t=1}^{T}[Y^{(t)}\exp(-D_t^2/2\sigma^2)]}{\sum_{t=1}^{T}[\exp(-D_t^2/2\sigma^2)]},$$

where $\{[X^{(t)}, Y^{(t)}]: t = 1, \ldots T\}$ is a set of training sample input/output pairs, D_t is the Euclidean distance between x and $X^{(t)}$ and N is the number of input modes of the network.

$$D_t=\sqrt{\sum_{i=1}^{N}(x_i-X_i^{(t)})^2}.$$

σ, the width parameter $= S/T^{E/N}$, $0 < E < 1$.

At the start of the learning cycle, the number of pattern (or hidden) PE can be set to the number of data vectors in the training file and later changed depending upon the network performance. Three parameters which control the learning process are the radius of influence, reset factor and time constant.

If the input vectors or training samples are large, the estimate for conditional mean becomes both time and memory-intensive. So the input vectors are grouped together (or clustered) and the average value of the groups are used in the calculations in order to decrease the simulation time. Any input vector is assigned to a nearest group if its distance to the centre of a previously established kernel is less than the radius of influence, otherwise a new kernel is established. A very small value for radius of influence will lead to a large number of clusters and hence increased computational time. Whereas, a large value will give fewer clusters and hence loss of sensitivity and possibly poor data fit.

PEs whose contributions in the summation are very small are termed as non-winning PEs. All the output weights from each of these non-winning PEs are multiplied

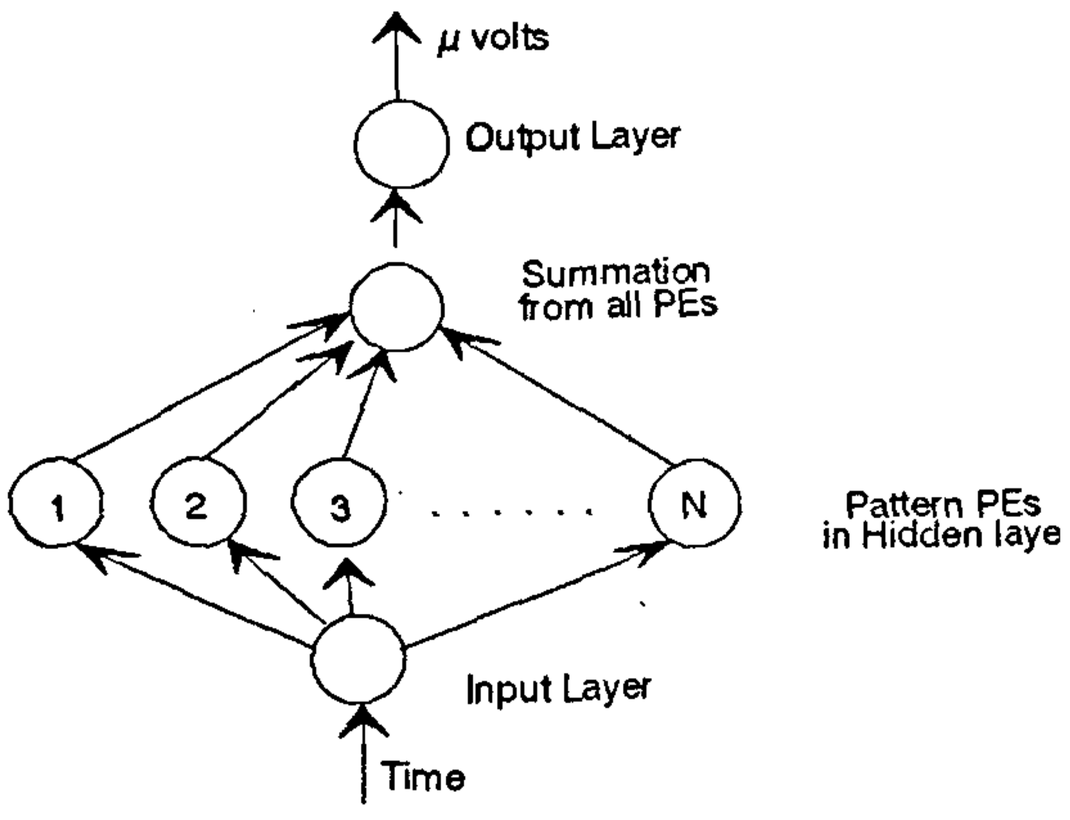

Figure 1. A general regression neural network for the EEG problem

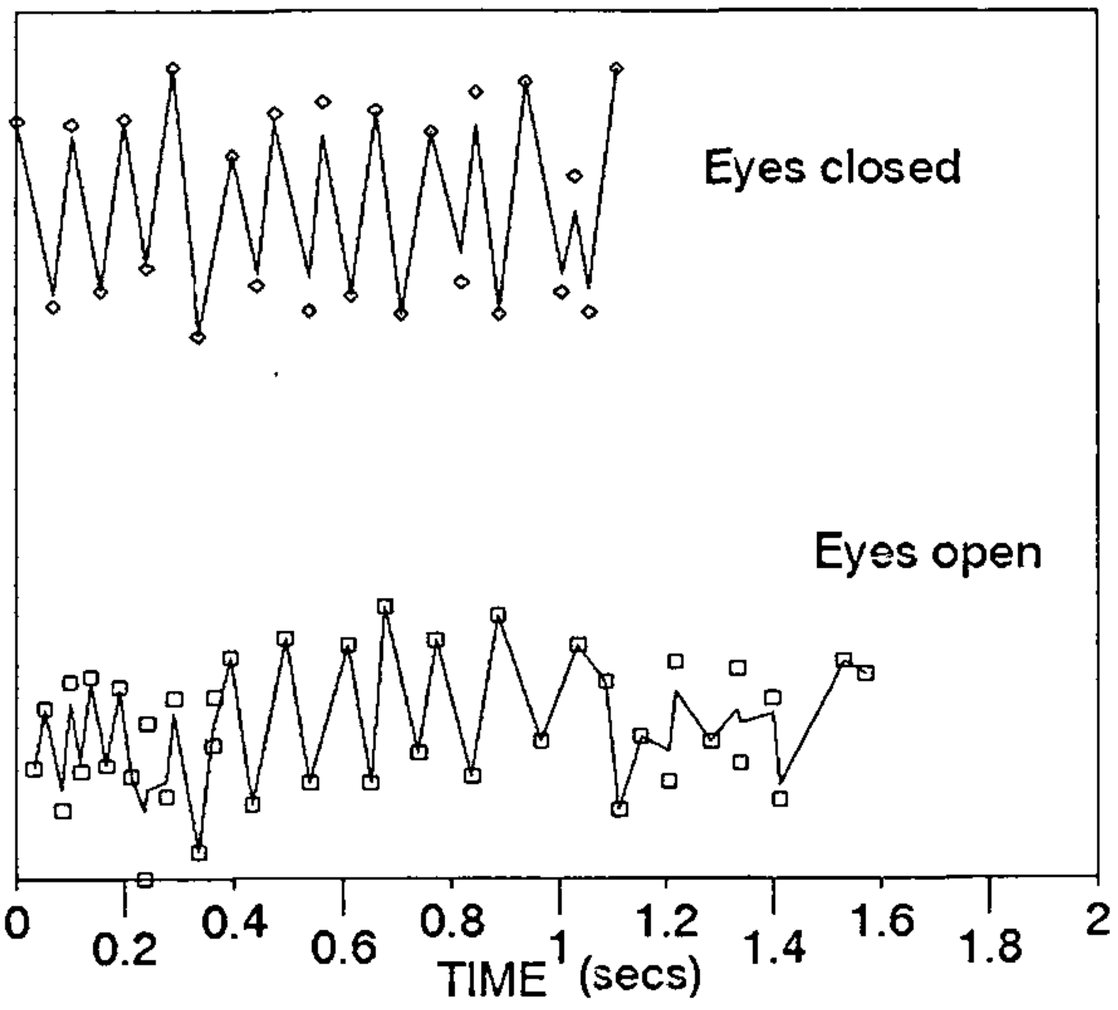

Figure 2. Comparison of human EEG data (points) and GRNN model simulation (continuous lines) during the stages of eyes open (9950 PEs) and eyes closed (1500 PEs). (Number of PEs required for simulation are given in brackets. *Y* axis is not to scale but presented arbitrarily to show the fit between the model and the simulation. *Y* axis ranges for eyes open and closed are 10 and 60 μV respectively.)

by a numeric term (called forgetting function), whose value decreases in an exponential fashion. The value of the time constant in the exponential term decides how fast the weights decay. When the weights become smaller than the ratio, reset factor/number of PEs, then the particular weight is set to zero. A large time constant could lead to slow decay of the weight from non-winning PE. The suggested value for radius of influence, reset factor and time constant are 0.05, 0.01 and 1000 respectively. In all the simulations about 10000 learning cycles were employed. Figure 1 shows a typical GRNN with a single input and single output, in this case time and μV respectively, and several pattern PEs in the hidden layer.

The EEG patterns were simulated by GRNN network. NeuralWorks Explorer (NeuralWare Inc., Pittsburgh, USA), a software running on a PC 386 equipped with a math coprocessor, was used for these studies[15]. The human EEG brainwave data were read from the figures given in references 3 and 4. The blown-up figures were scanned using a flat bed optical scanner, digitized and the data points were read into a computer program using a mouse and a cursor. The data points were uniformly spaced out in time. Time versus μV were read out from the digitized data. About 5000 data points were collected from each pattern signal, 80% of the data was used by the neural network model for fitting and the remaining 20% of the data was used for comparing model predictions with actual values.

The goodness-of-fit (root mean square error = RMSE) is obtained by calculating the square root of the mean of the sum-of-squares of the difference between model predictions and the actual data. Generally RMSE decreases as the PEs are increased. The simulations were performed by systematically increasing the number of PEs until the corresponding RMSE reaches a minimum value or remains unchanged. The PEs reported in the paper correspond to the lowest RMSE. In all the figures, points represent observed values and continuous lines are the neural network model predictions. In the figures only a few data points are shown for the sake of clarity. Also, data points near peaks and valleys are shown because maximum differences are generally expected between model predictions and data at these points.

An alert and active brain produces beta waves, which are high frequency low amplitude events (~ 10 μV) (ref. 4). As the eyes are closed, the relaxing individual produces alpha waves, with an average frequency of 10 cycles/s and amplitudes of the order of 60 μV. Alpha waves are well ordered and much more coherent than beta waves. Figure 2 shows the comparison of EEG data with simulation of both these waves with a GRNN network model. The alpha waves were simulated with 1500 PEs, whereas the beta waves were simulated with 9900 PEs. Both the simulations were carried out with 10,000 learning cycles and, radius of influence of 0.0001. A very low radius of influence indicates that no clustering of PEs was done. From the figure it could be noticed that the model is able to predict the observed behaviour reasonably well. Beta waves have fine structure, hence require more PEs (by an order of 6.5) to simulate than the well-ordered alpha waves. As the brain reaches a relaxed stage (alpha) from an alert one (beta), the number of neurons in an active state in the brain possibly decreases, which is very clearly seen from the number of PEs required for simulation.

In sleep the individual drifts in and out of four stages of sleep. Sleep stage 2 is a light stage, with slightly coherent waves of amplitude of 70 μV. Sleep stage 4, is a deep sleep stage, with amplitude of 120 μV and about 3–5 cycle/s. The four stages of sleep are followed by the rapid eye movement sleep (REM) in which he dreams. In the REM stage the cerebral activity reverts to a non-coherent state, with an amplitude of about 30 μV. All these three sleep stages are simulated with a GRNN network having 4000, 2000 and 2500 PEs respectively. Figure 3 compares the data with the simulation. As the sleep enters the deep stage 4 from stage 2, the number of PEs decreases by half, indicating that the number of neurons active in the brain also decreases, possibly by half. The number of PEs required to simulate REM sleep is more than that required to simulate sleep stage 4, but less than that required to simulate stage 2. The EEG brain wave data shown in Figures 2 and 3 were taken from reference 4.

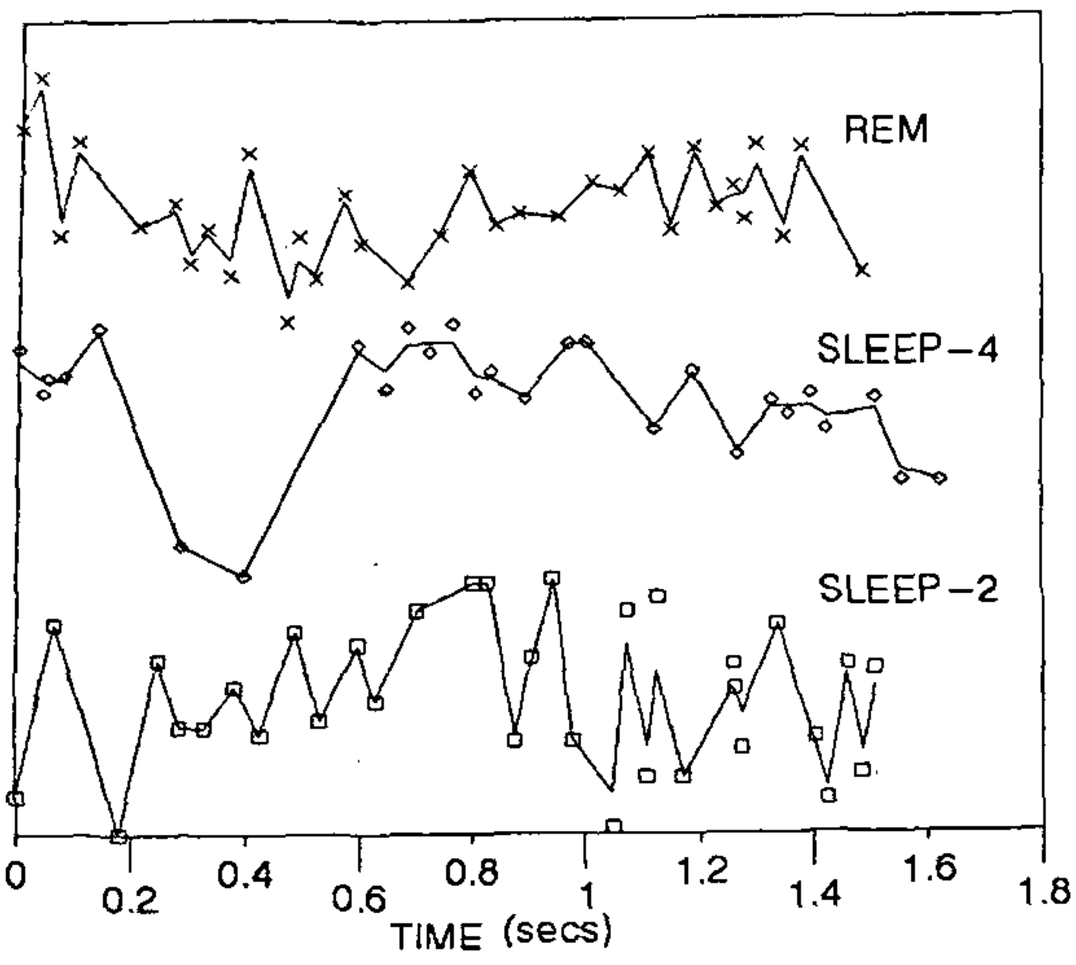

Figure 3. Comparison of human EEG data (points) and GRNN model simulation (continuous lines) during sleep stage 2 (4000 PEs), sleep stage 4 (2000 PEs) and REM sleep (2500 PEs). (Number of PEs required for simulation are given in brackets. *Y* axis is not to scale but presented arbitrarily to show the fit between the model and the simulation. *Y* axis ranges for sleep stages 2, 4 and REM are 70,120 and 30 μV respectively.)

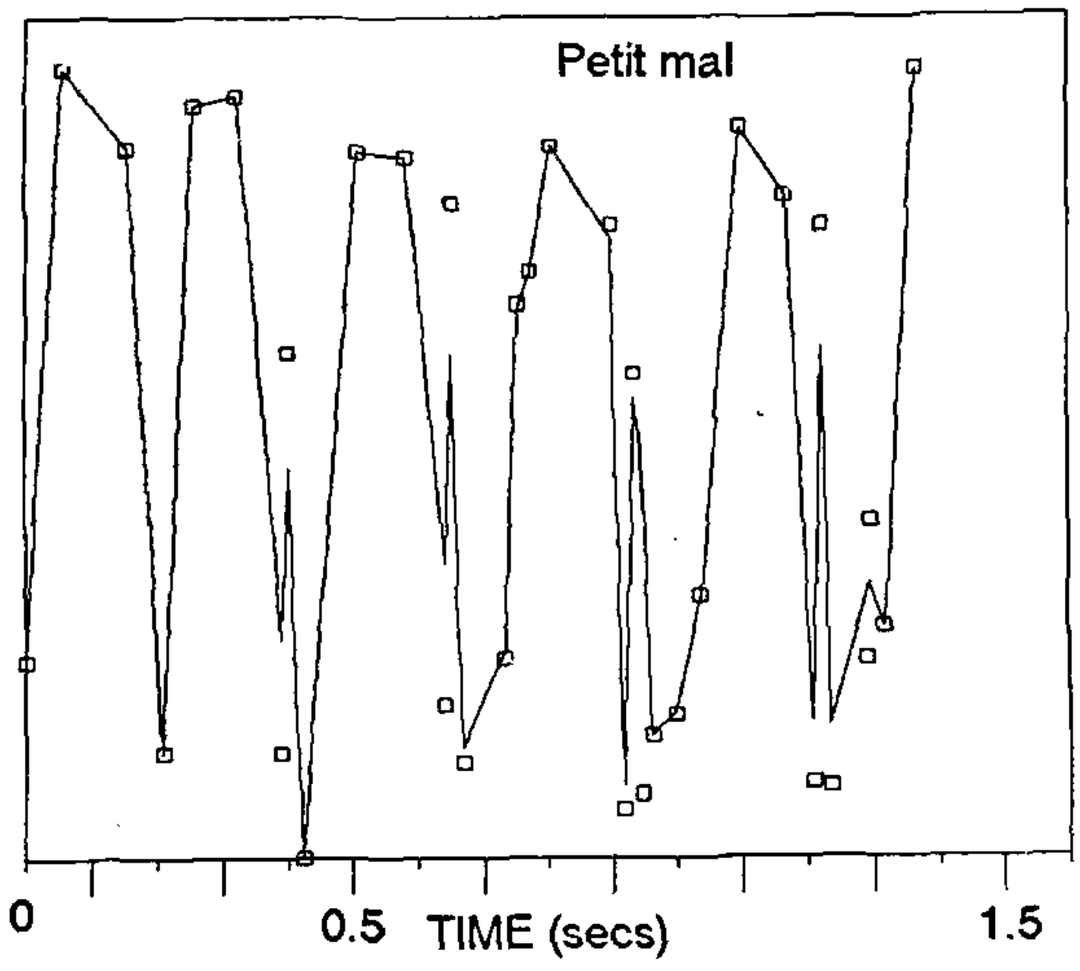

Figure 4. Comparison of human EEG data (points) and GRNN model simulation (continuous line) during petit mal seizure (5000 PEs). (Number of PEs required for simulation are given in brackets. *Y* axis range for petit mal seizure is 120 μV.)

There are several forms of epilepsy and, seizure of short duration (~5 s) is known as 'petit mal'[3]. This type generally invades the entire cerebral cortex and shows a bilateral symmetry between the two hemispheres. During the seizure the EEG activity switches to an apparent oscillating mode. Figure 4 compares the data and the

Table 1. Comparison of human cerebral activity, number of PEs required in the GRNN neural network model for simulation and the fractal dimension of the EEG signals

Activity	Number of PEs required for simulation	Fractal dimension (from refs 2–4)
Eyes open	9950	9.7
Eyes closed	1500	6.6
Sleep stage 2	4000	5.0
Sleep stage 4	2000	4.05
REM	2500	8.2
Petit mal	5000	2.05

simulation carried out with a GRNN network, of the EEG pattern of the epileptic stage with 5000 PEs. The model appears to simulate the epileptic waves fairly well. It appears that the number of neurons taking part during the seizure is more than the normal REM stage but less than the eyes open active stage. The EEG data of 'petit mal' was taken from reference 3.

Table 1 lists the number of PEs required for simulating the EEG waves at various stages of brain activity. It also gives the fractal dimension, which is a measure of the minimum number of variables required to describe the signal[2–4]. Fractal dimension also measures the temporal coherence of the phenomena and follows qualitatively the degree of arousal. The fractal dimension decreases from the eyes open to the eyes closed stages, and so does the number of PEs required for simulating these two states. A similar trend in fractal dimension and number of PEs is observed in the case of sleep stages 2 and 4. Although the fractal dimension in the case of REM sleep is high, the number of PEs required for simulation is low. The fractal dimension of the EEG signals during the REM stage and epileptic seizure are 8.2 and 2.05 respectively, indicating a large reduction in the complexity of the signals. The neural network model studies indicate that the number of PEs required for both these stages are 2500 and 5000 respectively. The PEs required for simulating 'petit mal' seizure should have been much lower than this value. The RMSE in all cases is of the order of 0.05 to 0.07 (error margin of about 5 to 7%), indicating a good data fit.

This paper describes the modelling and simulation of the EEG patterns observed during the various stages of human activities. The simulations were carried out with general regression neural network model. The number of neurons required to simulate the EEG patterns and rhythms could be reasonably explained based on the brain activity. Most number of PEs are required to simulate beta waves observed during an active brain with eyes open. This is followed by 'petit mal' seizure. A correlation exists between number of PEs and fractal dimension in some cases. It should be borne in mind that

the number of PEs required for simulating a particular activity estimated from modelling, cannot be equal to the number of neurons in the brain taking part in the activity. But, the ratio of PEs estimated by modelling for two activities may be an indication of the ratio of active neurons in the brain during two activities. Although another neural network model, namely back propagation model, was not able to fit these EEG patterns, other neural network models could also be attempted.

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Response of IgG sub-classes to diethylcarbamazine therapy in bancroftian filarial patients

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The response of IgG subclasses to diethylcarbamazine (DEC) treatment was studied in bancroftian filariasis patients. On the basis of clinical signs and parasitological examination, a total of 22 patients were categorized into asymptomatic microfilaraemics (AS-Mfmic; $n = 12$) and symptomatic amicrofilaraemics (S-AMfmic; $n = 10$). The subjects were treated with DEC (300 mg/day) for 21 days. Before treatment, AS-Mfmic cases showed higher levels of IgG_1 and IgG_4 than the S-AMfmics whereas IgG_2 was higher in S-AMfmics than in AS-Mfmics. DEC caused more than 90% reduction in microfilaraemia by day 30 since the start of treatment in AS-Mfmics, while S-AMfmics remained amicrofilaraemic throughout the study period. In AS-Mfmics, DEC treatment enhanced IgG_4 and decreased IgG_1 levels while IgG_2 and IgG_3 remained unaffected. In S-AMfmics, DEC treatment caused decrease in IgG_1, IgG_3 and IgG_4, while IgG_2 level remained unchanged. We report that DEC therapy brings about changes in specific IgG_1 and IgG_4 in AS-Mfmics and IgG_1, IgG_3 and IgG_4 in S-AMfmics.

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FILARIAL parasite initiates immune response in its host at both cellular and humoral levels. Clinical expression of filariasis, therefore, reflects not only the duration and intensity of infection but also the degree and character of different types of immunologic responses. Asymptomatic microfilaria (mf) carriers have depressed antibody- and cell-mediated immune responses while acute manifestations and chronicity are associated respectively with an intermediate and hyper-immune response[1–4].

The major immunoglobulins involved in the antifilarial antibody responses in human host are IgG, IgM, and IgE[3,5,6]. IgG is the major immunoglobulin detectable in all categories of filarial subjects and the clinical severity of the infection is directly related to this isotype[7]. Recent studies have also shown that different categories of filarial subjects have different IgG subclass profiles. Specific IgG_1 and IgG_3 are predominant in chronic lymphatic filariasis whereas IgG_4 is elevated in mf carriers and tropical pulmonary eosinophilia cases[8,9]. As IgG_4 was suggested to indicate the presence of parasites[8,10], Wamae *et al.*[11] used it as an indicator of adulticidal efficacy of diethylcarbamazine (DEC) or ivermectin in microfilaraemic (bancroftian) human subjects. However, whether DEC can also bring about alteration in other subclass responses in bancroftian filarial patients is not known. We report here the response of IgG subclasses to DEC treatment (shortly after cessation of the treatment) in symptomatic amicrofilaraemic and asymptomatic microfilaraemic bancroftian patients.

Patients reporting to the outdoor clinic of King George's Medical College, Lucknow for treatment of various ailments, were examined for filariasis. The patients were from Lucknow and its adjoining areas which are known to be endemic to bancroftian filariasis. A