Chapter 5

Parameter estimation of conductance model of neuron

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5.1 An overview

Conductance based neuron models (e.g. H-H type models) are highly nonlinear and involve many electrophysiological variables and parameters. Among these parameters, some of them can be measured experimentally while other parameters cannot be measured experimentally. Under such circumstances, for finding the good set of model parameters, parameter estimation techniques are to be used. A commonly used approach is the estimation method introduced by Hodgkin-Huxley which is associated with the voltage- clamp technique. Though this method may be taken as a reference method, but for every model, use of voltage clamp technique and finding the associated mathematical expression is very difficult to carry out for neurophysiologists.

Different methods have already been developed in order to estimate the parameters of conductance based model of neurons. L.Buhry et al had estimated parameters using differential evolution algorithm for a neuro-mimetric analog IC designed by them [7-10]. They have taken fast spiking neuron model as a reference signal. Similarly other authors like David Csercsik et al had also estimated parameters in GnRH neuron (responsible for hormones in neuroendocrine reproductive system) which revealed many important characteristics such as firing potential, depolarization amplitude, average frequency etc [20-21]. However, in the last fourteen years, nature-inspired metaheuristic algorithms have attracted much attention in the area of optimization. In the last two decades, many new algorithms such as genetic algorithm, particle swarm optimization, differential evolution, bat algorithm, firefly algorithm and cuckoo search have been the focus of research in the field of optimization.

In this chapter, three nature inspired algorithms was considered for estimation of Hodgkin-Huxley formalism to find the efficient algorithm for estimating the model parameters of conductance based model of neuron. This efficient algorithm is then used to estimate the parameters of the NEUROAchFET.

5.2 Determination of suitable parameter estimation method in conductance based H-H model

To determine the superior method for estimation of parameters in H-H conductance based model, three methods was considered. The three methods are: Genetic Algorithm (GA), Particle Swarm Optimization (PSO) and Firefly algorithm (FA). These algorithms were simulated in MATLAB using fitness function to estimate parameters and compared with reference signal which was obtained from Hodgkin and Huxley.

Here, Hodgkin-Huxley mathematical equations was taken as fitness function. A fitness function is required to estimate the parameters for determination of the closeness of the values to reference model. The fitness function of the neuron model was taken from equation (2.13) in Chapter 2. The optimization algorithms were applied to the fitness function [41] and compared with the reference signal. A reference signal was obtained from Hodgkin –Huxley (Fig.2.9) shown in Chapter 2. The parameters were estimated using the algorithms and the values were recorded. For estimating the parameters in action potential, equation (2.13) was taken as fitness function. Equation 2.13 was rewritten as shown in equation (5.1). All the other related variables was described in section 2.3.5. p, q and r is represented as number of gating variables for potassium and sodium ions respectively as explained in section 2.3.5.

$$I = C_M \frac{dv}{dt} + \overline{g_K} n^p (V - V_K) + \overline{g_{Na}} m^q h^r (V - V_{Na}) + \overline{gl}(V - V_l) \tag{5.1}$$

All the parameters such as gating variables, conductances of sodium, potassium, leakage and resting potentials were estimated using GA, PSO and FA. Estimation of parameters for sodium and potassium current were also done and fitness function was derived from equation (2.13) in Chapter 2.The detailed program of each estimation method is given in the Appendix.

5.2.1 Estimation of the parameters in H-H model using GA

Genetic algorithm (GA) is an evolutionary algorithm which imitates the process of evolution. GA follows the Darwin's principle of selection of the best. To optimize a solution, a fitness function is always required. A fitness function is defined so that the optimum solution can be evaluated. Fitness value is assigned to evaluate the optimality of the solution. The flow chart of the algorithm is shown in Fig.5.1.

In the first step, population is initialized with the help of fitness function. Population size shows how many chromosomes are available in the population. Too many populations will slow down the algorithm. But, very less population is also not favorable since there will be less chance in exploring the search space. In selection process, the best and favorable solutions are kept and others are discarded. It follows the selection of the best criteria and the best solutions are multiplied eliminating the bad solutions. A solution can be identified as favourable or unfavourable by its fitness value. A fitness value is defined so that the solutions obtained can be determined how close it is to the optimal solution. The solutions are ranked from highest to lowest values. It is a factor to rank the solution and find the optimal solution. In the GA, Roulette wheel and proportionate selection method was used [37]. From the solutions, parents are selected by their fitness value. The better fitness value (chromosome) has more chances of selection. Next step is the crossover, where the new population is created by using previous population available with the help of selection operator. This operator exchanges the gene information between the populations. From the population, two parents are chosen and two offsprings are produced interchanging genes from each parent. Point of selection is random and probability of crossover determines whether the crossover will take place or not. Crossover rate shows how often crossover occurs. If it is 100%, then whole of the population will undergo crossover i.e. the new population will be formed from the parts of the chromosome of the parents. If it is 0%, the new population will be the exact copy of the older population and there will be no crossover. Mutation is introduced to have a sudden change in the chromosome to maintain diversity in the population. In binary mutation, a sudden change occurs where 1 is converted to 0 and vice versa. In continuous genetic algorithm, a random number is introduced for mutation. Probability of mutation is kept low for steady convergence otherwise it will not converge easily and will search randomly for the solution.100% mutation rate means that the whole chromosome is altered and 0% ensures there is no change. Mutation rate is performed to prevent the solution from falling to local extreme. But mutation should not occur very often because it may go for random search. Elitism is the preservation of best solutions since the best solution may get destroyed due to mutation and crossover. The process described is iterated until best solution is found. The number of iteration is fixed prior to the process taking place. For GA, population size was taken as 300, mutation rate was taken as 0.2 and selection rate was 0.5.

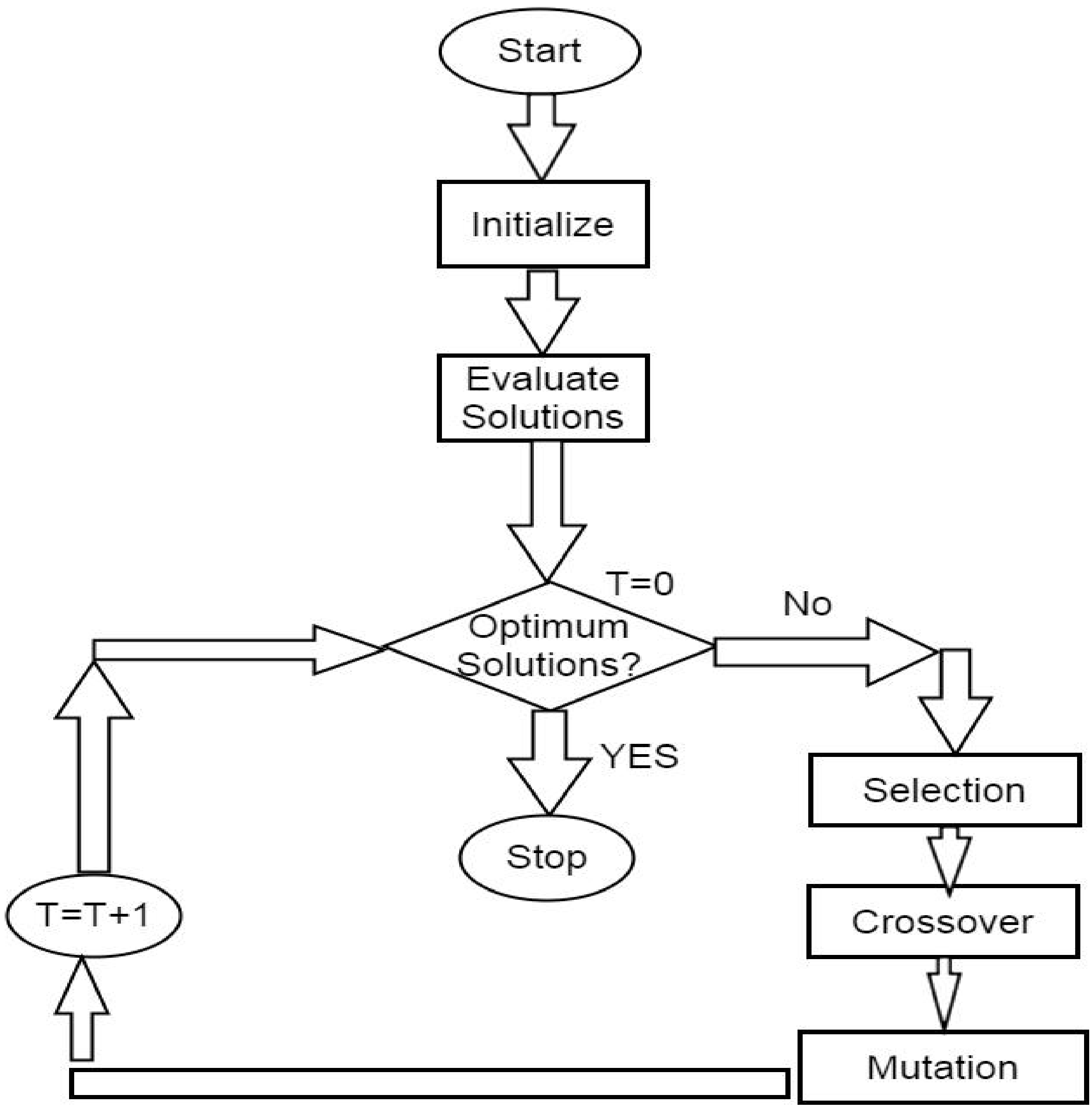

Fig.5.1: Flow chart for Genetic Algorithm

Fig.5.2 shows the estimation of parameters related to action potential by GA. Reference signal taken was of H-H model. Fig.5.3 and Fig. 5.4 shows estimation of parameters for sodium and potassium current by GA. Table 5.1 shows the theoretical and estimated parameters of H-H model for action potential and their respective sodium current and potassium current.

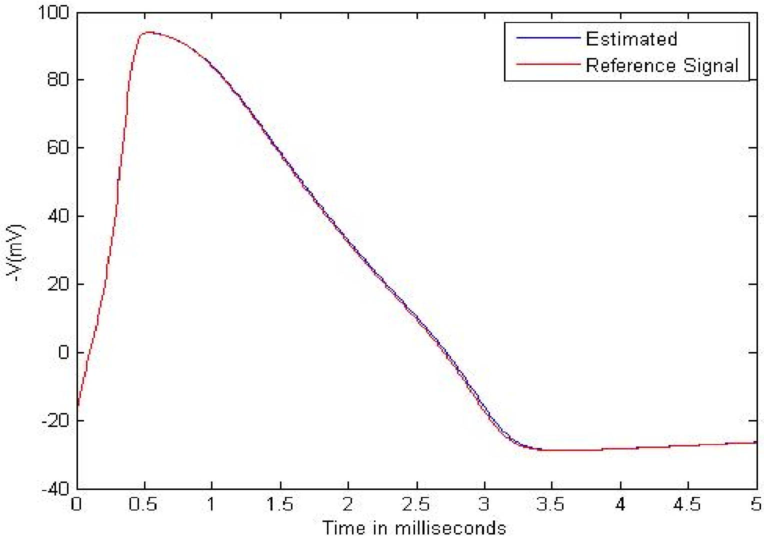

Fig.5.2: Parameter estimation of action potential for H-H model by GA.

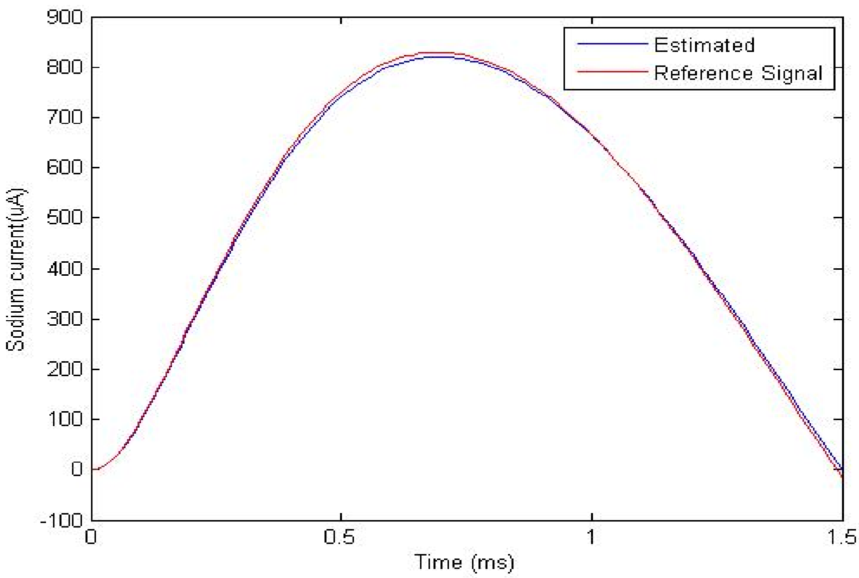

Fig.5.3: Estimation of parameters of sodium current by GA.

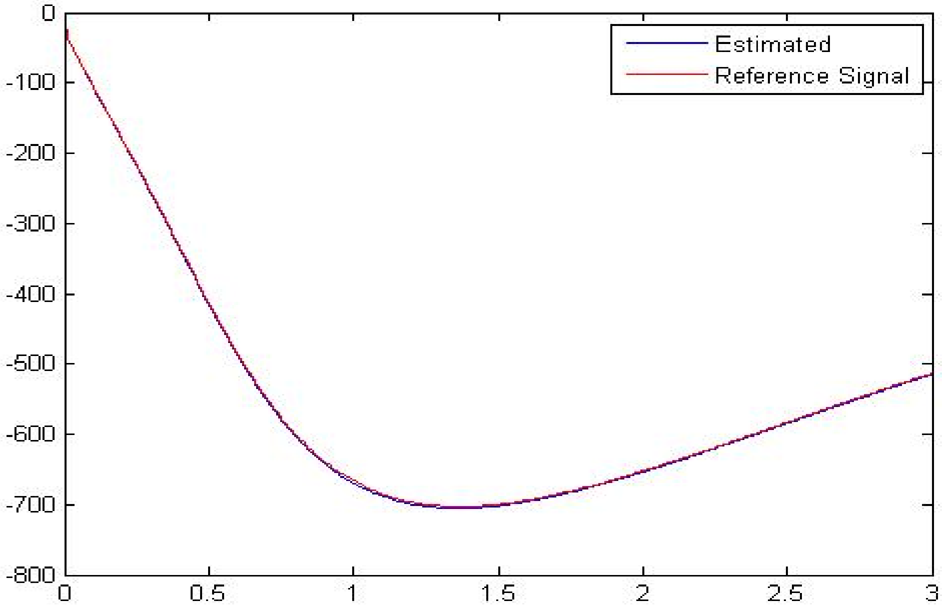

Fig.5.4: Parameter estimation of potassium current by GA.

Table 5.1: Theoretical and estimated values using GA

Parameters	Reference [H-H] values	Estimated Values
$\overline{g_{Na}}$ (m.mho)	120	117
$\overline{g_k}$ (m.mho)	36	33
$\overline{g_l}$ (m.mho)	0.3	0.29
C_M (µF)	1	0.5
V_{Na} (mV)	-115	-110
V_K (mV)	12	11.4
V_l	-10.613	-10.9
p	4	4
q	3	3
r	1	1

5.2.2 Estimation of the parameters in H-H model using PSO

PSO is an optimization method developed by Dr. Eberhart and Dr. Kennedy in 1995 inspired from bird flocking. PSO is similar with GA in many ways but it does not

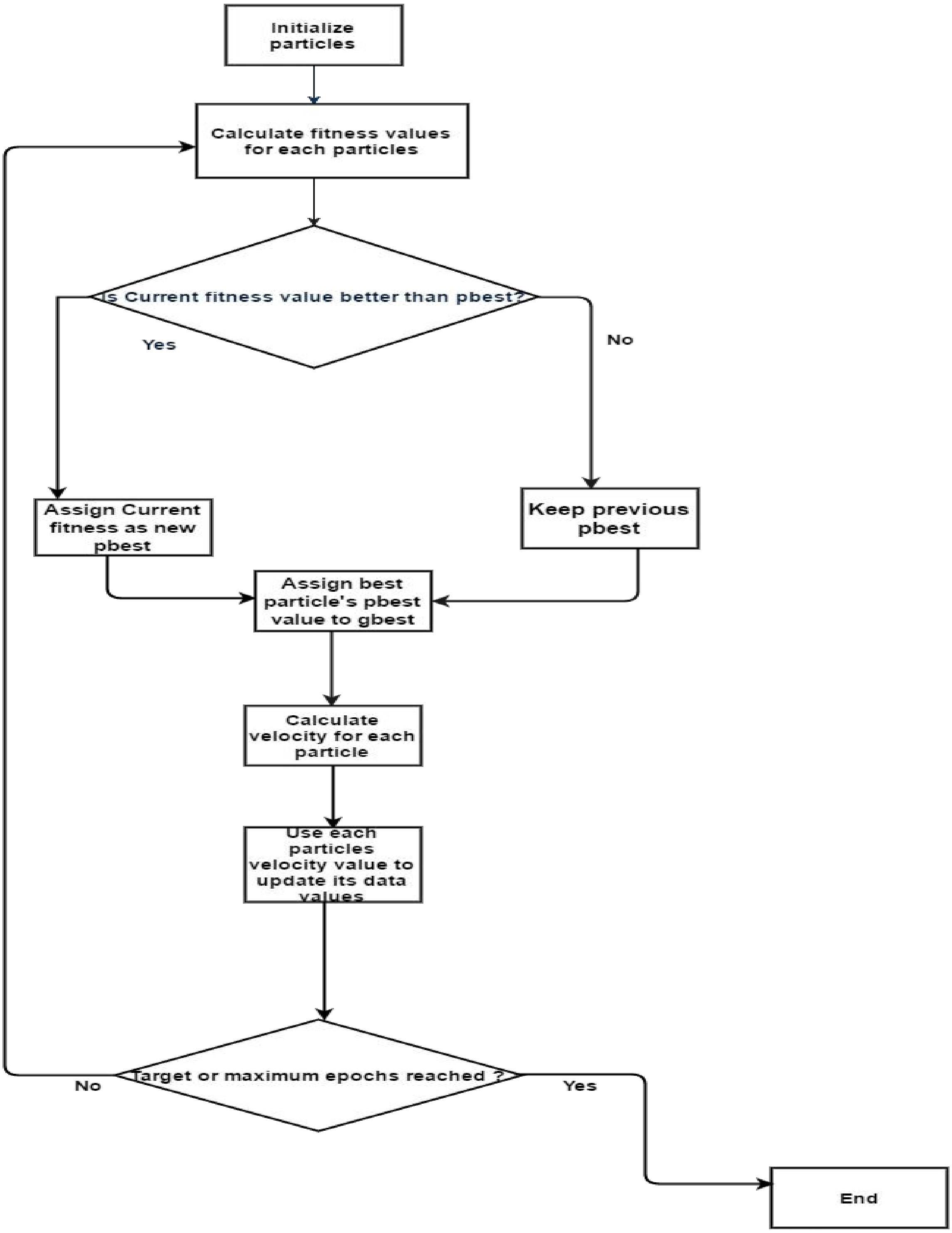

Fig.5.5: Flow chart for Particle Swarm Optimization

consider mutation, crossover factor [57]. A population of random solution is generated and finds optimum solution by updating the generation. The obtained solutions flock towards the best possible solution obtained so far (fitness value). In PSO, each particle searches for the best solution obtained so far. This value is called pbest. Another neighboring particle which takes into account the best value obtained is called lbest. The particle who takes into account the whole population and all the best values obtained to find the best solution is called global best(gbest).PSO changes the velocity and acceleration towards p_{best} and l_{best} value. A random term is generated for acceleration of the values towards p_{best} and l_{best}. PSO is used in many applications for optimization purpose and other specific problem.PSO has got many advantages such as it is easy to use, lesser value to adjust and a cheaper way. The process is best described in the Fig.5.5. In PSO, population size can vary between 100 to 300.

The parameters are estimated using PSO by using the same fitness function in GA. Fig.5.6 shows the parameters related to action potential estimated by PSO. Fig.5.7 and Fig.5.8 show estimation of parameters for sodium and potassium current by PSO. Table 5.2 shows the estimation of parameters for action potential, sodium channel and potassium channel.

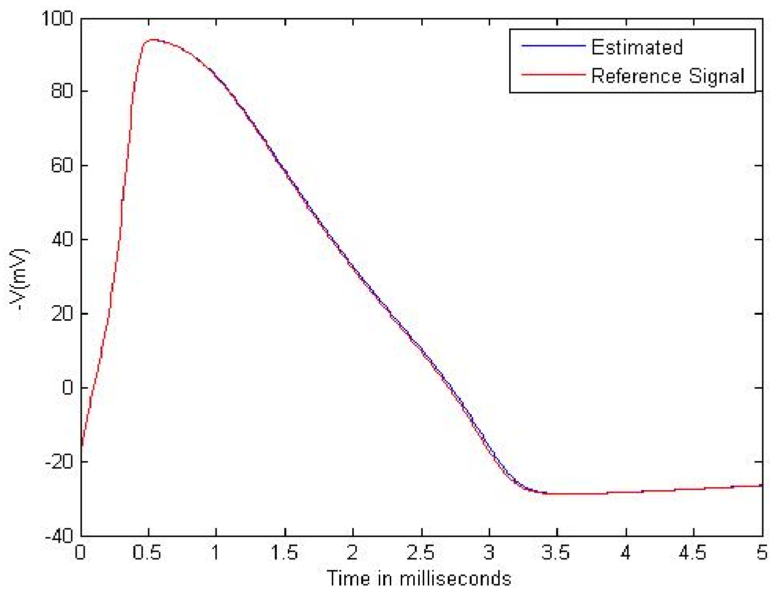

Fig.5.6: Parameter extraction of action potential by PSO using H-H signal as the reference.

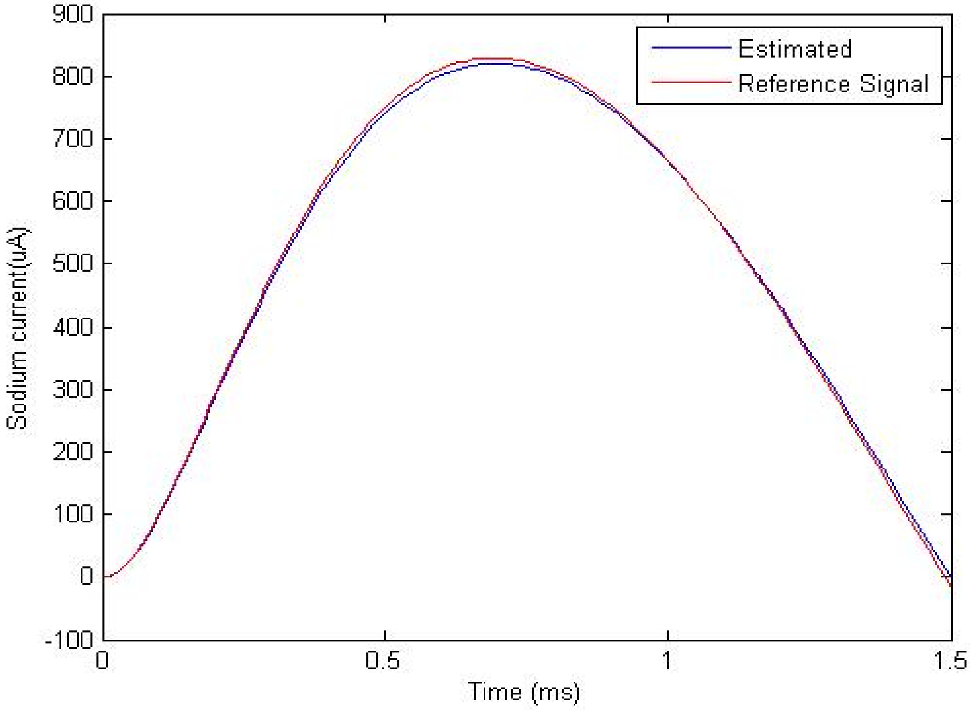

Fig.5.7: Estimation of parameters of sodium current by PSO.

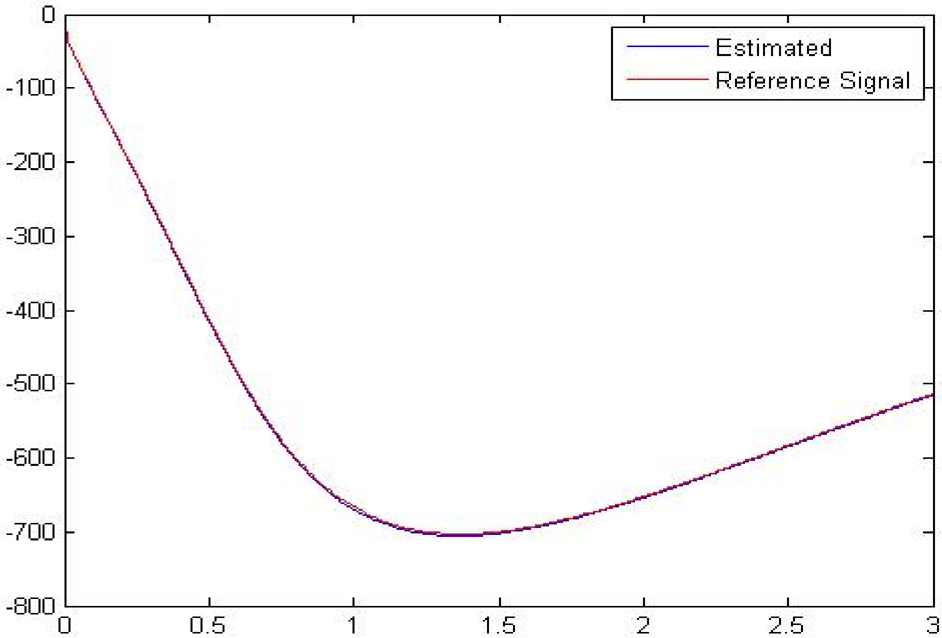

Fig.5.8: Estimation of parameters using PSO for potassium current.

Table 5.2: Estimation of parameters using PSO.

Parameters	Reference [H-H] values	Estimated Values
$\overline{g_{Na}}$ (m.mho)	120	118
$\overline{g_k}$ (m.mho)	36	35
$\overline{g_l}$ (m.mho)	0.3	0.3
C_M (μF)	1	0.7
V_{Na} (mV)	-115	-111
V_K (mV)	12	11.7
V_l	-10.613	-10.9
p	4	4
q	3	3
r	1	1

5.2.3 Estimation of the parameters in H-H model using FA

Firefly algorithm is also a biologically inspired algorithm proposed by Xin-She Yang and it is a powerful tool for numerical optimization. FA uses the characteristics of fireflies with the following conditions [104-107]:

i. Fireflies are unisex and they get attracted towards each other regardless of their sex.

ii. Attractiveness depends on the brightness of the fireflies. A less brighter firefly will attract towards the brighter firefly. Brightness of a firefly decreases with distance and their attractiveness. The firefly moves randomly when there is no brighter firefly.

iii. Objective function determines the brightness of a firefly. Maximization of problem is done by making it directly proportional to the objective function.

The logic of the firefly algorithm is described below:

Brightness *I* is directly proportional to the fitness function at point *x* (equation (5.2),

$$I(x) \infty f(x) \tag{5.2}$$

Brightness is affected by distance between two fireflies (*i* and *j*) and other disturbances like noise etc. Distance between two fireflies is denoted as r_{ij} (carteseian distance) [104-107]. Therefore, light intensity $I(r)$ is given as :

$$I(r) = I_s/r^2 \tag{5.3}$$

I_s is the light intensity at source. With a fixed light absorption coefficient *Y*, the light intensity *I* varies with distance *r*, i.e.

$$I(r) = I_0 e^{-Yr} \tag{5.4}$$

Where I_0 is the initial light intensity. When $r \neq 0$ and combined effect of inverse square law and absorption is taken in Gaussian form:

$$I(r) = I_0 e^{-Yr^2} \tag{5.5}$$

For function decreasing monotonically, equation (5.5) reduces to:

$$I(r) = \frac{I_0}{1+Yr^2} \tag{5.6}$$

The above two equations (5.5) and (5.6) are same and their series expansion at $r = 0$ is:

$$e^{-Yr^2} = 1 - Yr^2 + \frac{1}{2}Y^2r^4 + \ldots.., \tag{5.7}$$

$$\frac{1}{1+Yr^2} = 1 - Yr^2 + \frac{1}{2}Y^2r^4 + \ldots.., \tag{5.8}$$

As it is said that firefly attractiveness depends on the light intensity of the adjacent firefly, therefore attractiveness β of a firefly is:

$$\beta(r) = \beta_0 e^{-Yr^2} \tag{5.9}$$

β_0 is the attractiveness at $r = 0$. It is faster to calculate $1/(1+r^2)$ than e^{-Yr^2} (exponential function). So, above equation is replaced by $\beta = \frac{\beta_0}{1+Yr^2}$ for faster calculation.

Equation (5.9) is a characteristic distance $1/\sqrt{Y}$ over the change of attractiveness from β_0 to $\beta_0 e^{-1}$.

Attractiveness function can be defined now as a monotonically decreasing function as

$$\beta(r) = \beta_0 e^{-\Upsilon r^2} \tag{5.10}$$

The attractiveness of a firefly by another firefly is determined by equation (5.11):

$$x_i = x_i + \beta_0 e^{-\Upsilon r^2_{ij}} \left(x_j - x_i\right) + \alpha(rand - \frac{1}{2}) \tag{5.11}$$

The second term is due to attraction and third term is the randomization parameter. rand is a random number generator from 0 to 1.

Basic algorithm is as under:

Objective function f(x), $x=(x_1,\ldots,x_d)^T$

Generate initial population of fireflies x_i *(i=1,2,…n)*

Light intensity I_i *at* x_i *is determined by* $f(x_i)$

Define light absorption coefficient γ

while (t< MaxGeneration)

for i = 1: n all n fireflies

for j = 1:i all n fireflies

if ($I_j > I_i$), Move firefly i towards j in d-dimension; **end if**

Attractiveness varies with distance r via exp [-γr]

Evaluate new solutions and update light intensity

end for j

end for i

Rank the fireflies and find the current best

End while

Postprocess results and visualization

Firefly is more efficient and have more success rate than PSO and GA [104-107].It can be made better if the randomness is reduced since it is observed that the

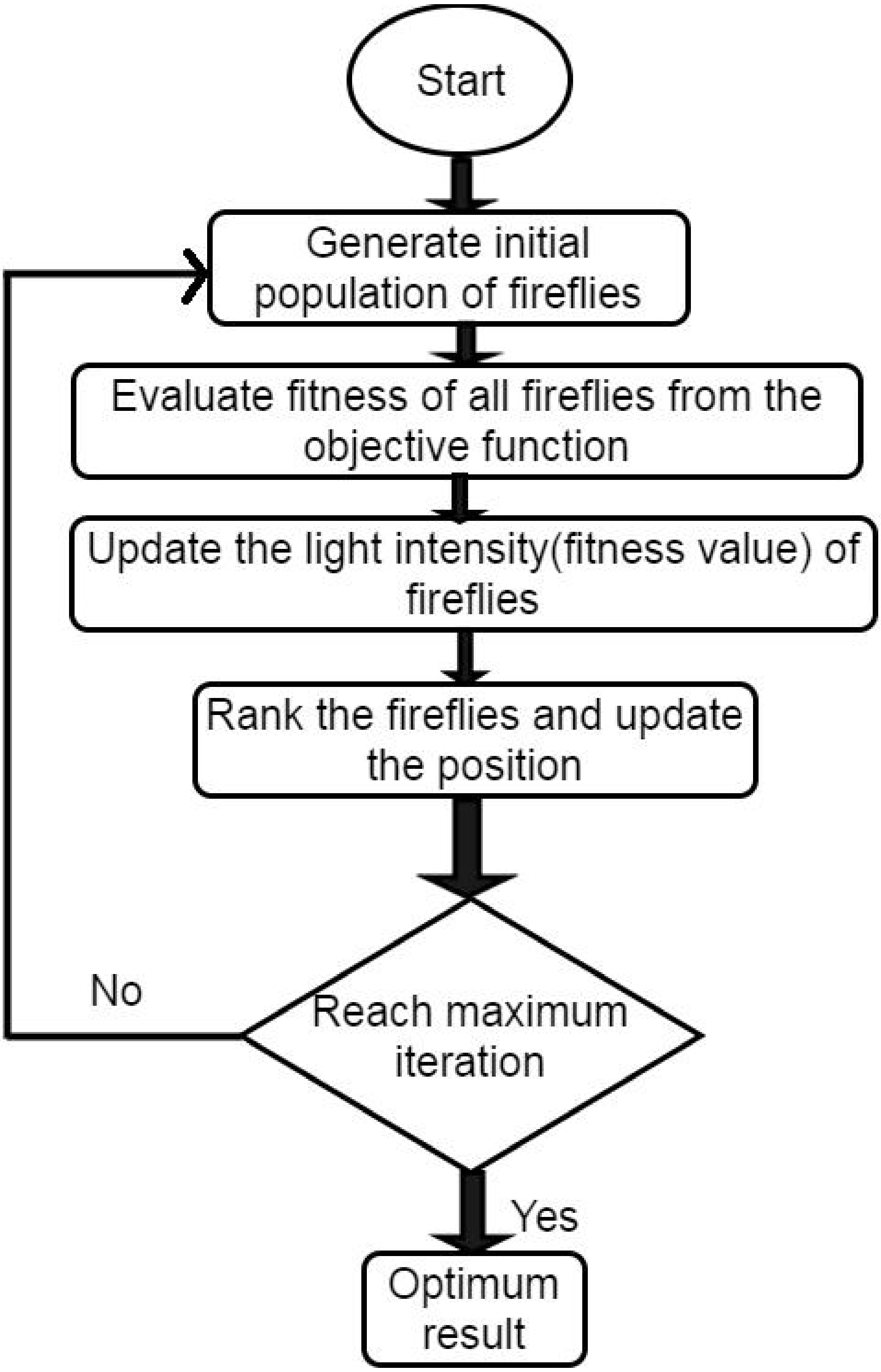

Fig.5.9: Flow chart of firefly algorithm

values are changing when optimum solution is reached. Flow chart of firefly algorithm is shown in Fig. 5.9.

In FA, population size was taken as 100, light absorption coefficient (Y) was taken as 1, attraction coefficient (β) was taken as 0.2, alpha equal to 0.2 was taken. For estimation purpose in H-H conductance based neuron model, equation 5.1 is taken into account for fitness function. Fig. 5.10 shows the estimation of parameters using FA in action potential. Similarly, parameter estimation done for sodium and potassium current are shown in Fig. 5.11 and Fig. 5.12 respectively. Table 5.3 shows the paramters estimated using FA for action potential and their respective sodium current and potassium current.

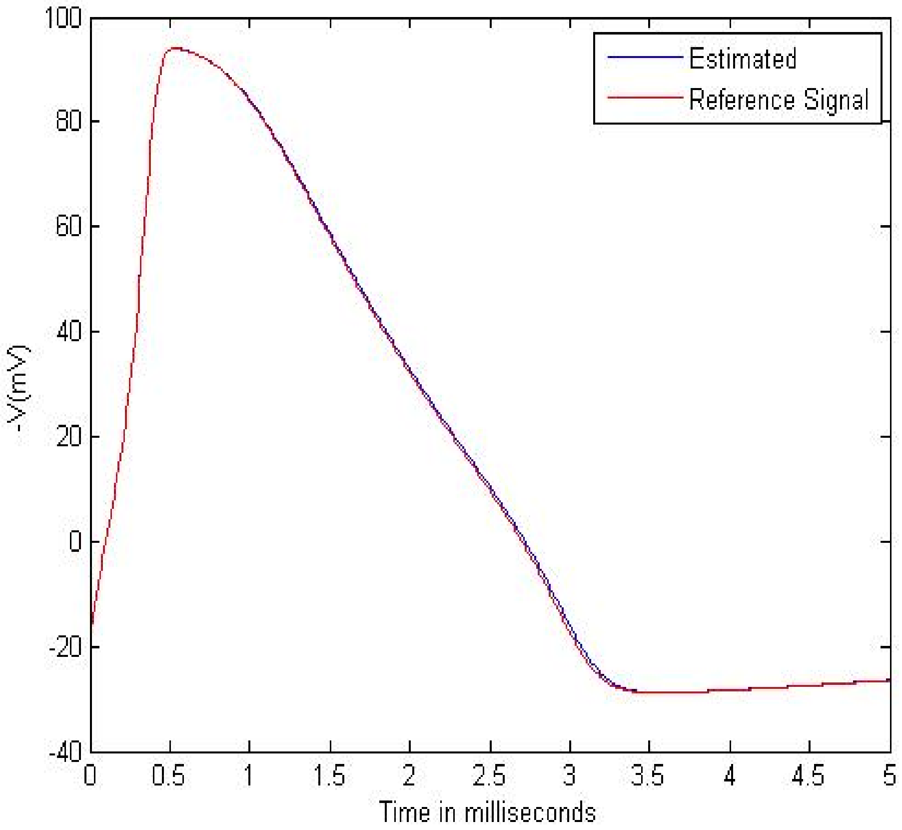

Fig.5.10: Parameter estimation of action potential by FA.

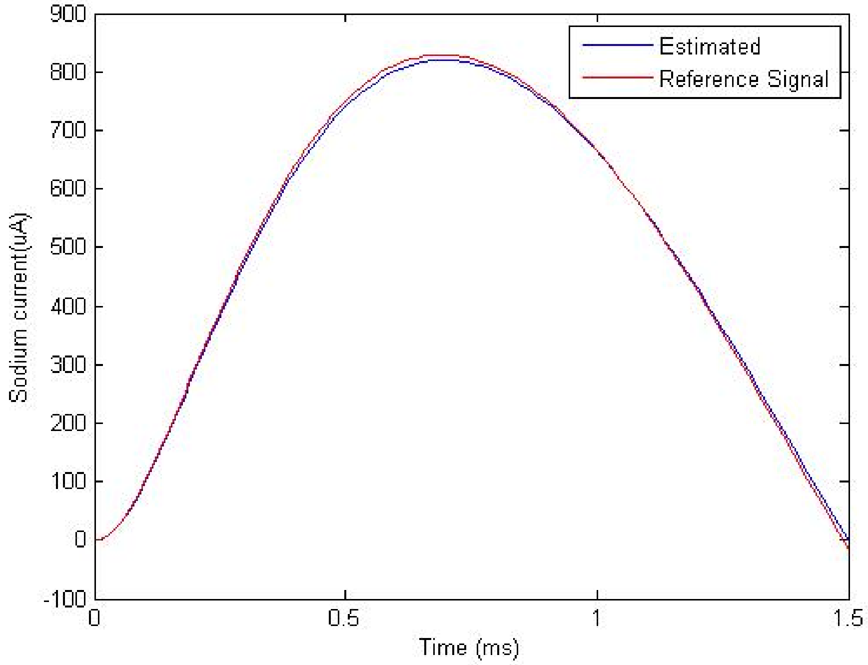

Fig.5.11: Estimation of sodium current parameters using FA.

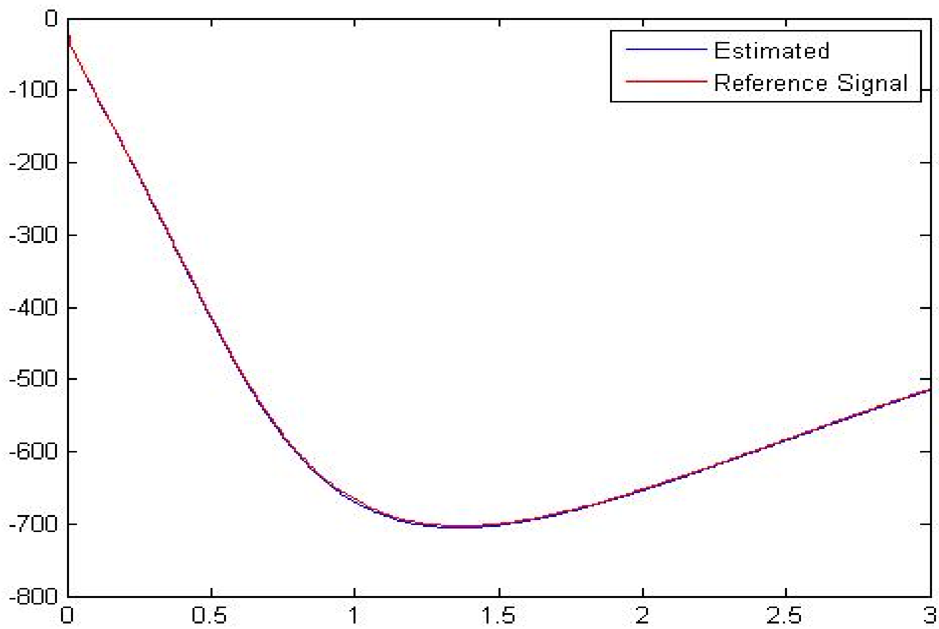

Fig.5.12: Parameter estimation of potassium current using FA

Table 5.3 : Estimation of parameters using FA

Parameters	Reference [H-H] values	Estimation Values
$\overline{g_{Na}}$ (m.mho)	120	120
$\overline{g_k}$ (m.mho)	36	36
$\overline{g_l}$m.mho)	0.3	0.31
C_M (μF)	1	1
V_{Na} (mV)	-115	-115
V_K (mV)	12	12
V_l	-10.613	-10.6
p	4	4
q	3	3
r	1	1

5.3 Comparison of GA, PSO and FA

Estimation of parameters was done by varying the iteration process from 100 to 600 in steps of 100. Fig.5.13 shows the relative error versus generations in GA for estimating the parameters in action potential. Fig.5.14 and Fig.5.15 shows the relative error found using PSO and FA for estimating parameters in action potential. It was observed that exact value estimation was achieved by FA in 300 iterations with no relative error while GA and PSO had some relative error till 600 iterations. Relative error is calculated in percentage. It was observed that the values obtained by FA were more closer to H-H model .Estimated parameters of GA and PSO was different from the values of H-H based model. FA was found to be more efficient, faster and number of iteration required was lesser than other methods[104-107].It uses randomness factor and global communication to find the best value.

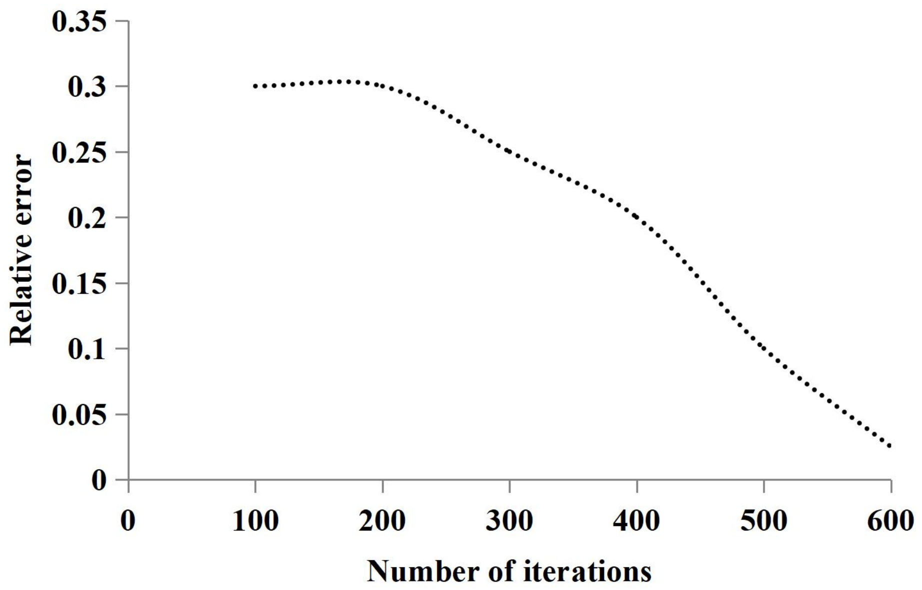

Fig.5.13: Relative error in GA versus number of iterations

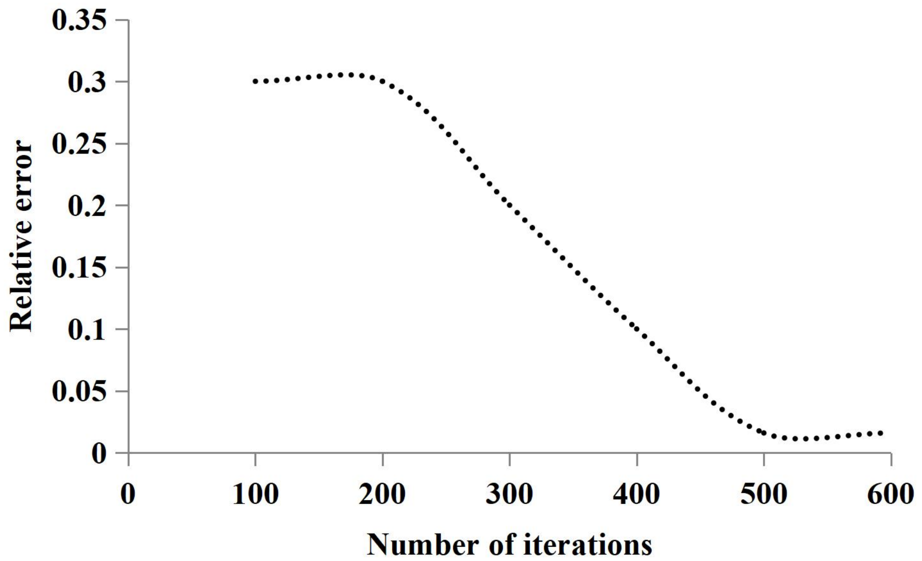

Fig.5.14: Relative error in PSO versus number of iterations

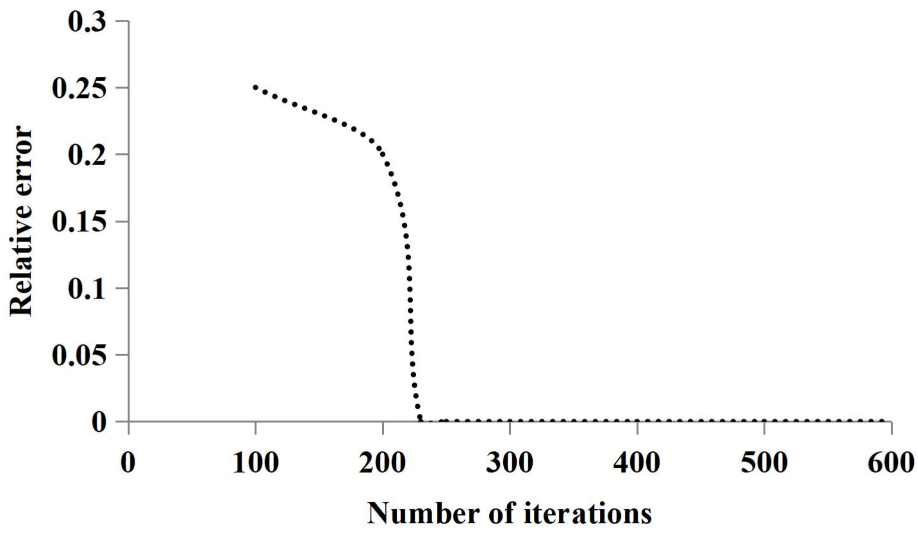

Fig.5.15: Relative error in FA versus number of iterations

5.4 Estimation of the parameters of NEUROAchFET using the best estimation method

The best algorithm was used to estimate the parameters for NEUROAchFET. Here, the reference signal taken was the signals obtained from NEUROAchFET. The estimated signals used the fitness function shown in equation (5.1). The algorithm was simulated in MATLAB.

5.4.1 Estimation of the parameters of the NEUROAchFET using FA

Since it was observed that FA is the most suitable method for estimation of parameters in conductance based H-H model, FA was used to estimate the parameters for NEUROAchFET circuit. Fig.5.16 shows the estimated and measured signals for estimating the parameters related to action potential. Measured signals are the ones obtained from NEUROAchFET. The fitness function (equation 5.1) was used to estimate the parameters using FA for the signals obtained in Chapter 4. With the help of FA, parameters related to potassium and sodium current was also estimated and shown in Fig.5.17 and Fig 5.18. The estimated values of the signals obtained from the circuit were similar to the H-H model. Table 5.4 shows the parameters estimated for

NEUROAchFET. The parameters were also estimated for Roy neuron model using FET and compared in Table 5.4 [41,83]. It shows that the values of the parameter of NEUROAchFET (estimated) matches with H-H model.

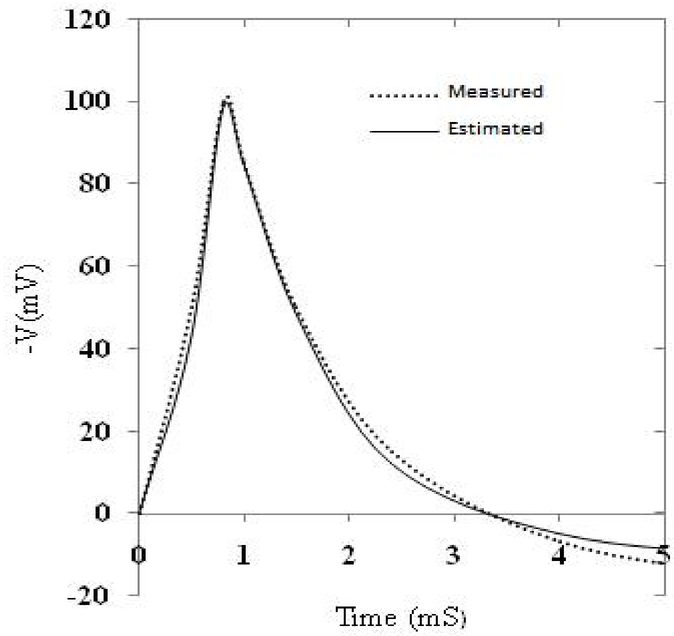

Fig.5.16: Parameter estimation of action potential in NEUROAchFET using FA.

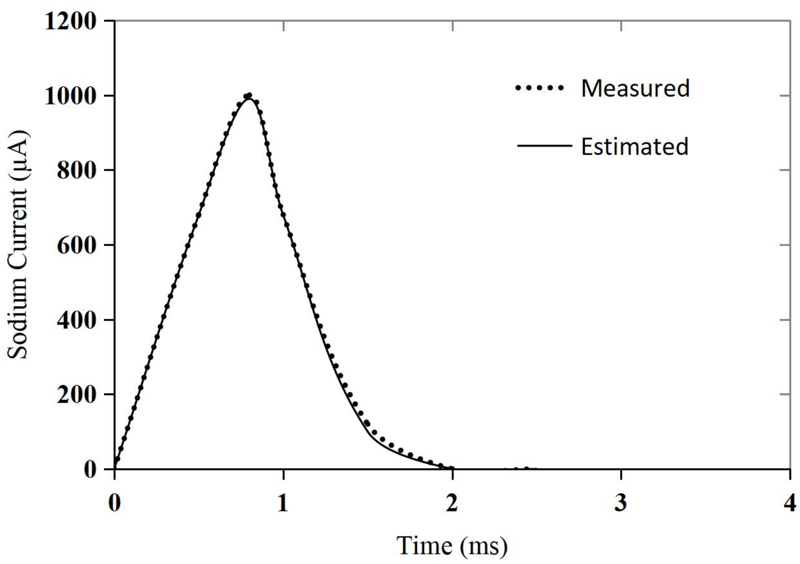

Fig.5.17: Estimation of sodium current in NEUROAchFET using FA.

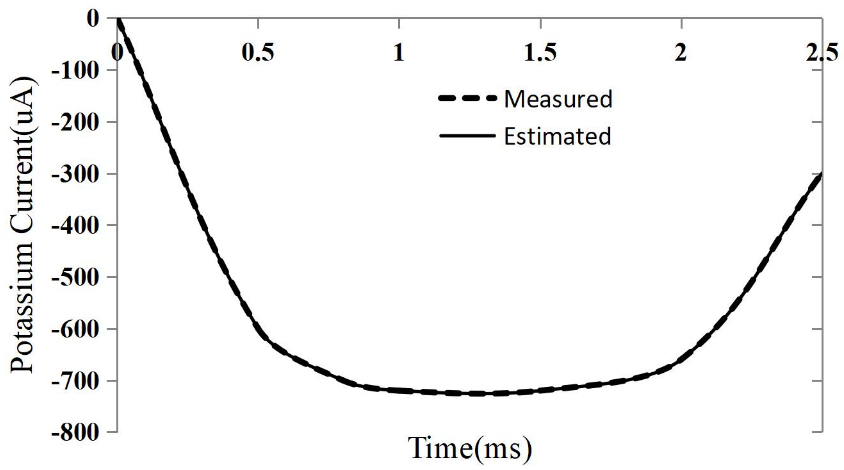

Fig.5.18: Estimation of parameters using FA for potassium current in NEUROAchFET.

Table 5.4: Estimation of parameters using FA in NEUROAchFET

Parameters	H-H model (Range)	Roy Model	Estimated by FA for NEUROAchFET
$\overline{g_{Na}}$ (m.mho)	120 — 260	124	130
$\overline{g_k}$ (m.mho)	26 — 49	37	40
$\overline{g_l}$ (m.mho)	0.13 — 0.50	0.3	0.31
C_M (μF)	0.8 — 1.5	1	1
V_{Na} (mV)	-95 — -119	-114	-112
V_K (mV)	9 — 14	12	14
V_l	-4 — -22	-10.613	-10.6
p	4	4	4
q	3	3	3
r	1	1	1

The estimated values obtained from NEUROAchFET signals was compared with other models and found to be in good agreement (Fig. 5.19).

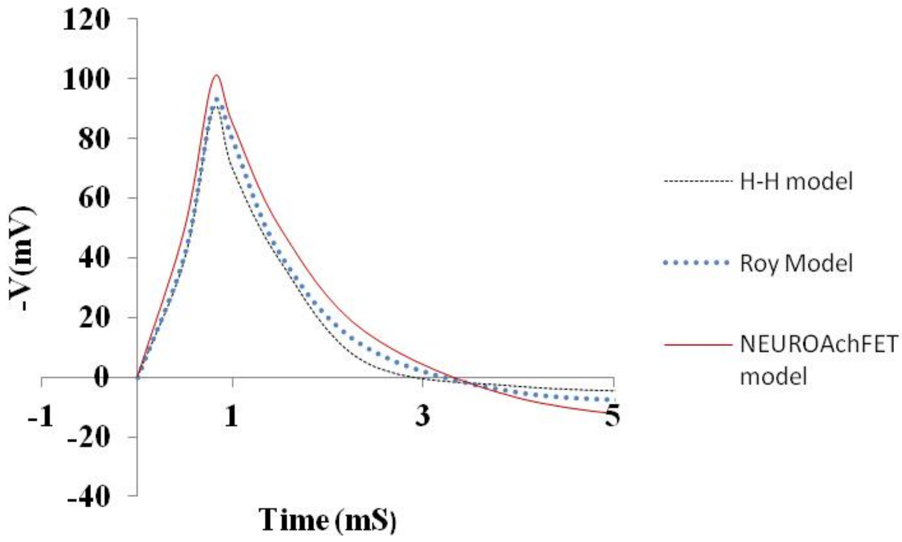

Fig.5.19: Action potential obtained from H-H model, Roy model and NEUROAchFET model

5.5 Summary

In this work, Firefly method of parameter estimation was applied to extract the parameters of NEUROAchFET model, which showed better results than other optimization methods. Various parameters such as sodium conductance, potassium conductance, equilibrium potential of sodium and potassium and leakage conductance were estimated together. FA automatically considers the inter-dependency of the parameters. The estimated parameters showed close proximity with H-H data making the circuit valid from biological point of view. FA was found to be quite fast and accurate for estimation of all the parameters of a neuron model simultaneously and also, easy to fit data than other traditional methods. Thus, this estimation method can be used to estimate the parameters of different types of spikes in neuron models for study and research purpose.