Chapter 6: ***Conclusion and future scope***

Contents

End is not the end, in fact E.N.D. means "Effort Never Dies".
-A. P. J. Abdul Kalam

6.1 Conclusions

In the proposed work, all the electrical parameters such as resistance, capacitance and respective ionic conductances are equally emphasized which are responsible for nerve conduction by the movement of ions through the ionic channels in order to model the proposed myelinated, demyelinated and the coupling model using electric circuit model. It is seen that an alignment parameter in the bundled nerve is also important and must be considered to design the proposed models as the NCV of the nerve in the models seem to have different values in aligned bundle and in misaligned bundle of axons.

Firstly, previous works on the physiology of a peripheral myelinated nerve demyelinated nerve is reviewed. Based on the physiology of the nerves, some primitive electric circuit models are carried out in the literature survey. It is seen that the electric models emphasizes on physiological properties of a single axon which lacks many characteristic values. In order to describe the accurate physiology of a peripheral nervous system and the mechanism underlying the physiology of a diseased nerve, different electric circuit models of peripheral nerves consisting of bundle of axons are designed using sciatic nerves of toad (equivalent to human nerve) which are further used for the recovery of the demyelinated nerve disorder.

The NCV estimated theoretically by using the electric circuit model of a peripheral myelinated nerves consisting of a bundle of axons are 40.21m/s and 52.18m/s in scattered and evenly aligned bundle of axons which are within the normal range of NCV in human nerve. Further, the NCV calculated from the repeated experiments on sciatic nerve of toad is found to be 32.90±0.21m/s which is a normal value in case of toad nerve model with a normal myelin thickness of 1.79±0.05μm as obtained from SEM image.

As witnessed from the electric circuit model of a demyelinated nerve (consisting of a bundle of demyelinated axons), there is a reduction in NCV and myelin thickness of the nerve. Further, the neuro-signals obtained from the validation experiments on toad sciatic nerve shows reduction in peaks of CAP amplitude due to the blocking of Na^+ and K^+ channels which allows the propagation of nerve impulse from one node to another node by saltatory movement. The reduction in NCV increases with increase in

demyelination as estimated theoretically by using the electric circuit model. When the same is coupled with a normal myelinated nerve, an increase in NCV values is obtained by using the electric circuit model of a coupled nerve. Moreover, the peaks of CAP amplitude are recovered to normal range in the model due to the electro-physiological properties of normal nerve in the coupled model as observed from the electric neuro signals in a toad nerve model. The neuro signals recorded from demyelinated nerves treated with 0.1µg/ml, 1µg/ml and 10µg/ml of Nk venom, the NCV were found to be 26.62±0.58m/s, 18.25±0.25m/s and 15.87±0.15m/s for their corresponding venom concentrations. An increase in the NCV by 40.36±0.12m/s, 37.50±0.11m/s and 34.85±0.14m/s are observed as the same nerve is coupled with a normal nerve in the coupled model for the same amount of crude venom concentrations. Similarly, for nerve treated with 0.1µg/ml, 1.0µg/ml and 10µg/ml of purified Nk-PLA_2, the reduction of NCV is found to be 25.62±0.81m/s, 17.10±0.13m/s and 14.46±0.58m/s. When the nerve is coupled with a normal nerve, the increase values of NCV are obtained to be 39.24±0.26m/s, 36.36±0.35m/s and 33.66±0.38m/s for 0.1µg/ml, 1.0µg/ml and 10µg/ml of Nk-PLA_2 in the coupled model. Thus, the NCV in coupled nerve (combination of nerve I treated with crude venom and normal nerve II) increases by ~34%, ~51% and ~54% for 0.1µg/ml, 1.0µg/ml and 10µg/ml respectively whereas a nerve treated with purified Nk-PLA_2 is used in the coupled nerve, the increase in NCV are found to be ~35% for 0.1µg/ml, ~53% for 1µg/ml and ~57% for 10µg/ml of purified Nk-PLA_2 respectively.

As the sciatic nerve of toads are treated with an increase dose of 3FTx, the amplitudes of both proximal and distal CAP decreases due to the presence of more number of channel blocking. The percentage of proximal CAP amplitude reduction for 0.1µg/ml, 1.0µg/ml and 10µg/ml of 3FTx are ~15%, ~16% and ~40% respectively whereas the percentage of reduced distal CAP amplitude are ~20%, ~27% and ~60%. But in the coupled nerve, the amplitudes of both proximal CAP increases by ~2%, ~9%, and ~11% whereas distal CAP amplitude are recovered by ~13%, ~27% and ~70% even if concentration of 3FTx increases from 0.1µg/ml to 10µg/ml due to suppression of electro dynamical activities of normal nerve over the demyelinated nerve.

Overall, the proposed work aims to provide a non-invasive technique for quantification of demyelination which has many scopes in the treatment of various

neurological disorders. The work also aims to present a recovery model where two nerves cross-talk and share the electro-physiological properties of one another thereby compensating the loss of axonal function due to demyelination. The functional properties for reduction of action potential in a demyelinated nerve due to channel blocking are suppressed by the physiological characteristics of normal myelinated nerve in the coupled nerve model as witnessed from the experimental results.

6.2 Scope for future works

Although the proposed work describes electric circuit model of myelinated, demyelinated and coupled nerves (between normal nerve and demyelinated nerve) for recovery and validation is performed by using toad peripheral (sciatic) nerve, there are scope of research for recovery of central demyelinated nerve by coupling with normal nerve since demyelination of central nervous system is very critical. For further speedy recovery on nerve conduction, the demyelinated nerve can be coupled in between two normal nerves in order to form a sandwich model of nerve fiber coupling. For validation of our electric circuit models (myelinated, demyelinated and coupled nerve) equivalent to human peripheral nerve, live experiments on rat or mouse model may be conducted to obtain the accuracy in physiological properties of normal and disordered nerve as well as its recovery.

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