MODELLED RESPONSE OF THE ELECTRICALLY STIMULATED HUMAN AUDITORY NERVE FIBRE

by

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SUMMARY

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SUMMARY

This study determined whether the Hodgkin-Huxley model for unmyelinated nerve fibres could be more comprehensively modified to predict excitation behaviour at Ranvier nodes of a human sensory nerve fibre, as specifically applied to the prediction of temporal characteristics of the human auditory system. The model was developed in three phases. Firstly, the Hodgkin-Huxley model was modified to describe action potential dynamics at Ranvier nodes using recorded ionic membrane current data from single human myelinated peripheral nerve fibres. A nerve fibre cable model, based on a combination of two existing models, was subsequently developed using human sensory nerve fibre morphometric data. Lastly the morphological parameters of the nerve fibre model were changed to resemble a Type I peripheral auditory nerve fibre and coupled to a volume-conduction model of the cochlea.

This study is the first to show that the Hodgkin-Huxley model equations can be modified successfully to predict excitation behaviour of a generalised human peripheral sensory nerve fibre without using the Goldman-Hodgkin-Katz equations. The model includes a more comprehensive establishment of temperature dependence of the physiological and electrical parameters compared to existing models.

Two versions of the human Type I auditory nerve fibre model were developed, one simulating an undamaged (non-degenerate) fibre and another a damaged (degenerate) fibre. Comparison between predicted and measured results indicated similar transient and persistent sodium, as well as slow potassium ionic membrane currents to those found in generalised sensory nerve fibres. Results confirm that chronaxie, rheobase current, mean latency, threshold and relative refractory periods depend on the amount of degeneracy of fibres. The model could account for threshold differences observed between different asymmetric waveforms. The combination of persistent sodium and slow potassium ionic membrane currents could in part predict non-monotonic excitation behaviour observed experimentally.

A simplified method was developed to calculate electrically evoked compound action potential responses following neural excitation. It provided a computationally effective way to obtain an estimate of profile widths from the output of models that calculate neural excitation profiles, and an indirect way to estimate stimulus attenuation by calculating the value of the parameter that produces the best fit to experimental data. Results also confirmed that electrode arrays located closer to the modiolus produce more focussed neural excitation spread than more laterally located arrays.

KEY WORDS

human, auditory nerve fibre, computational model, Hodgkin-Huxley model, generalised sensory nerve fibre, ionic membrane currents, strength-duration time constant, evoked compound action potential, conduction velocity, temporal characteristics

OPSOMMING

Gemodelleerde gedrag van 'n elektries-gestimuleerde menslike ouditiewe senuweevesel

deur

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SLEUTELWOORDE

mens, ouditiewe senuweevesel, berekeningsmodel, Hodgkin-Huxley-model, veralgemeende sensoriese senuweevesel, ioniese membraanstrome, sterkte-duur tydskonstante, ontlokte saamgestelde aksiepotensiaal, geleidingspoed, temporale eienskappe

OPSOMMING

In hierdie proefskrif is 'n moontlike uitbreiding van die Hodgkin-Huxley-model vir ongemiëliniseerde senuweevesels ondersoek. Die aanpassings is daarop gemik om die opwekkingsgedrag by Ranvier-nodes van 'n menslike sensoriese senuweevesel te kan voorspel, met spesifieke toepassing op voorspelling van temporale eienskappe van die menslike ouditiewe stelsel. Die model is in drie fases ontwikkel. Gemete ioniese membraanstroomwaardes vir 'n enkele, menslike gemiëliniseerde perifere senuweevesel is gebruik om aksiepotensiaaldinamika by Ranvier-nodes te beskryf. Daarna is morfometriese inligting van menslike senuweevesels gebruik om 'n toepaslike kabelmodel, wat op twee bestaande modelle gebaseer is, te ontwikkel. Laastens is morfologiese veranderlikes van hierdie model aangepas vir 'n Tipe I ouditiewe senuweevesel en aan 'n volume-geleidingsmodel van die koglea gekoppel.

Hierdie studie is die eerste wat bewys dat vergelykings van die Hodgkin-Huxley-model suksesvol aangepas kan word om opwekkingsgedrag van 'n algemene, menslike perifere sensoriese senuweevesel te voorspel, sonder om van die Goldman-Hodgkin-Katz-vergelykings gebruik te maak. In vergelyking met bestaande modelle bevat hierdie model 'n meer uitgebreide daarstelling van die temperatuurafhanklikheid van die fisiologiese en elektriese veranderlikes.

Twee weergawes van die menslike Tipe I ouditiewe senuweevesel-model is ontwikkel, waarvan een 'n onbeskadigde (nie-gedegenereerde) vesel en die ander 'n beskadigde (gedegenereerde) vesel voorstel. 'n Vergelyking van voorspelde en eksperimenteel gemete resultate het aangedui dat kortstondige en meer blywende natrium-, sowel as stadige kaliumioon-membraanstrome bestaan, soortgelyk aan wat in algemene sensoriese senuweevesels aangetref word. Die afhanklikheid van kronaksie, reobasisstroom, gemiddelde vertraging, drempels en relatiewe refraktêre periodes tot die hoeveelheid degenerasie van vesels is aangedui. Die model kon ook drempelverskille tussen verskillende asimmetriese golfvorms voorspel. Die kombinasie van blywende natrium- en stadige kaliumioon-membraanstrome kon, gedeeltelik eksperimenteel waargeneem, nie-monotone opwekkingsgedrag voorspel.

'n Vereenvoudigde metode is ontwikkel om die elektries ontlokte saamgestelde aksiepotensiaalreaksies van neurale opwekking, te bepaal. Die metode bied 'n berekeningseffektiewe manier om profielwydtes van die uitsette van modelle wat neurale opwekkingsprofiele bereken, te voorspel. Dit verskaf ook 'n indirekte manier om stimulusverswakking te bereken deur die waarde wat gemete resultate die beste voorspel, te bereken. Resultate het ook bevestig dat elektrodeskikkings nader aan die modiolus meer gefokusde neurale opwekkingsverspreidings voorspel as meer laterale elektrodeskikkings.

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My efforts regarding this study can be summed up by the following quote:

> "Everything is vague to a degree you do not realize till you have tried to make it precise."
> – Bertrand Russell

But I enjoyed all of it.

Contents

List of abbreviations

3D	:	Three dimensional	(p. 73)
AP	:	Action potential	(p. 35)
ARP	:	Absolute refractory period	(p. 18)
ANF	:	Auditory nerve fibre	(p. 1)
ECAP	:	Electrically evoked compound action potential	(p. 2)
FE	:	Firing efficiency	(p. 20)
GHK	:	Goldman-Hodgkin-Katz	(p. 6)
GSEF model	:	Generalised Schwarz-Eikhof-Frijns model	(p. 12)
HH model	:	Hodgkin-Huxley model	(p. 4)
IPG	:	Interphase gap	(p. 101)
IPI	:	Interpulse interval	(p. 20)
MCL	:	Most comfortable level	(p. 2)
MPI	:	Masker probe interval	(p. 19)
NRT	:	Neural Response Telemetry	(p. 2)
ODE	:	Ordinary differential equation	(p. 34)
RRP	:	Relative refractory period	(p. 18)
SEM	:	Scanning electron microscopy	(p. 14)
SFAP	:	Single-fibre action potential	(p. 17)
TEM	:	Transmission electron microscopy	(p. 14)