THE SISO MONOSYNAPTIC REFLEX THRESHOLD AND GAIN: RELATIONSHIP TO MOTONEURON POOL PARAMETERS

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Abstract – **Single-input single-output (SISO) synapse models describe the input firing-rate – output firing-rate relationship of a motoneuron (MN) pool. While the MN pool is very complex, containing many MNs with a range of properties, the SISO model contains very few parameters: a presynaptic threshold, a linear postsynaptic gain, and some form of output firing-rate saturation. In this study, the parameters of the SISO synapse model are related to the patterns of MN recruitment and rate coding in the MN pool. Using this general analysis, SISO models are then generated for two specific MN pools, one healthy, one unhealthy. It is concluded that the SISO model represents healthy synaptic behaviour well, even across large ranges of input firing-rates. Estimation of SISO models for unhealthy behaviour, however, should be treated with caution.**
***Keywords* - synapse, model, motoneuron pool, reflex, muscle**

I. INTRODUCTION

Mathematical models of the human neuromuscular system are used to explore the neural mechanisms that underlie movement [1]. These models seek to describe the interaction of muscles, muscle sensors, synapses, control from the central nervous system, and biomechanics. As a result the mathematical model dimensionality (i.e. number of 'tuneable' variables) of these models increases with the complexity and size of the system. To maintain tractable analysis and understanding of the system's equations, simplified models of the neuromuscular system's physiology are frequently used.

The monosynaptic reflex arc is an example of a complex physiological system that has been represented by a mathematical model of low dimensionality. Fig. 1 represents a piecewise-linear single-input single-output (SISO) model that has been utilised in previous research [2,3]. One input firing-rate (*IFR*) is subjected to a pre-synaptic threshold (T_{PRE}) and linear post-synaptic gain (G_{LIN}) to produce one output firing-rate (*OFR*). After *IFR* reaches a value (T_{SAT}), no more increase in *OFR* is observed. In a mathematical neuromuscular model, this *OFR* will typically activate a muscle model that uses one contractile element to represent the motor unit (MU) pool.

The true physiology of the reflex arc involves many pre-synaptic nerves with individual input firing-rates, both excitatory and inhibitory, making many synaptic connections to the motoneurons of the motoneuron (MN) pool of a muscle [4]. The physiological multiple-input multiple-output (MIMO) structure is modelled by the SISO system with three parameters T_{PRE}, G_{LIN}, and T_{SAT}.

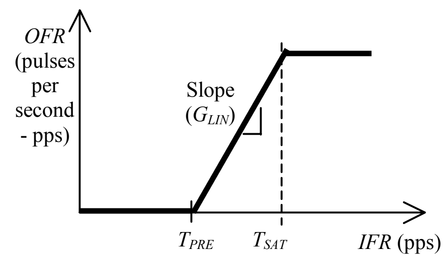

Figure 1. A simple piecewise-linear SISO synapse model.

This work attempts to ascertain the nature of the relationship between the MIMO synaptic physiology and the piecewise-linear SISO synapse model in Fig. 1. It will also highlight possible pitfalls in the estimation of the piecewise-linear SISO synapse model.

II. METHODOLOGY

A single MN's synaptic behaviour will be mathematically described in a general sense. The multiple input and multiple output firing-rates of the MN pool will be reduced to a single input and a single output firing-rate. The relationship between these single input and output firing-rates of the MN pool will be related to MN recruitment and rate coding. Piecewise-linear SISO synapse models, such as in Fig. 1, will be then fitted to the input-output relationship of one healthy and one unhealthy MN pool.

A) The single MN pool input firing-rate and the MN pool synapses

The multiple excitatory inputs to the MN pool are first averaged together to give one input firing-rate, *IFR*. Taking into account the eventual saturation of the synapse and assuming that the pre-synaptic *IFR* is linearly related to excitatory post-synaptic current by a factor k_i, the output firing-rate of the i^{th} MN, OFR_i, is:

$$OFR_i = \left[u\left(k_i IFR - Pthres_i\right) - u\left(k_i IFR - Pmax_i\right)\right]\times$$
$$\left[\left(k_i IFR - Pthres_i\right)G_{MNi}(k_i IFR) + Ethres_i\right] \quad (1)$$
$$+\,u\left(k_i IFR - Pmax_i\right)Emax_i$$

where $Pthres_i$ is the post-synaptic current threshold, $Pmax_i$ is the maximum effective current (beyond which no further increases in OFR_i occur), $G_{MNi}(k_i IFR)$ is the MN's input current – output firing-rate gain,

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$Ethres_i$ is the initial firing-rate of the MN on recruitment, and $Emax_i$ is the maximum OFR_i for the i^{th} MN. $u(\bullet)$ is the unit-step function.

B) The single MN pool output firing-rate

The single output firing-rate of the MN pool, OFR, must simultaneously represent the firing-rate of many MNs. As piecewise-linear SISO synapse models typically activate muscle models designed from single fibre experiments [1], the OFR will be determined by the average firing-rate per muscle fibre. Estimating the number of muscle fibres per MU as the ratio of the i^{th} MU tetanic force, $fmax_i$, to the total tetanic muscle force, $FMAX$, one obtains:

$$OFR = \sum_i OFR_i \frac{fmax_i}{FMAX} = \frac{1}{FMAX} \sum_i OFR_i \, fmax_i \tag{2}$$

Filling in for OFR_i (1) and using experimental values for $Pthres_i$, $Pmax_i$, $G_{MNi}(k_i IFR)$, $Ethres_i$, $Emax_i$, and $fmax_i$ one can produce a plot of IFR against OFR from which a piecewise-linear SISO synapse model can be generated.

C) Relating MU behaviours to SISO models

1) The threshold parameters, T_{LIN} and T_{SAT} of the piecewise-linear model can be readily related to the IFR that activates the first MN, i.e. $\min(Pthres_i/k_i)$ and the IFR at which the last MN reaches its maximum output firing-rate, i.e. $\max(Pmax_i/k_i)$.

2) One can differentiate (2) with respect to IFR to determine an expression for the 'gain' between the single input firing-rate and the single output firing-rate of the MN pool, G_{POOL}:

$$G_{POOL}(IFR) = \frac{\mathrm{d}(OFR)}{\mathrm{d}(IFR)} = \frac{1}{FMAX} \frac{\mathrm{d}\left(\sum_i OFR_i \, fmax_i\right)}{\mathrm{d}(IFR)}$$

Noting that Eq. 1 is continuous for all i, and assuming all $Pthres_i$ are different, G_{POOL} expands to following expression:

$$G_{POOL} = \frac{fmax_i Ethres_i \delta(k_i IFR - Pthres_i)}{FMAX} + \sum_{\substack{MNs\ in \\ active \\ region}} \frac{fmax_i}{FMAX} \left[\begin{array}{c} k_i G_{MNi}(k_i IFR) \\ + (k_i IFR - Pthres_i) \dfrac{\mathrm{d}(G_{MU\,i}(k_i IFR))}{\mathrm{d}(IFR)} \end{array} \right] \tag{3}$$

where 'MNs in active region' is defined as all the MNs activated but not yet firing at their maximum firing-rate, and □(•) is a dirac-delta function.

This expression for G_{POOL} (3) contains two terms, the first describing the effect of MN recruitment, the second the effect of MN rate coding. By integrating these two terms individually with respect to IFR it is possible to see the relative contribution of these two physiological principles to the lumped parameterisation of 'post-synaptic gain' in piecewise-linear models.

D) Fitting the piecewise-linear models

If the OFR at $IFR = T_{SAT}$ is known, the piecewise-linear SISO model's gain, G_{LIN}, can be derived using T_{PRE} and ignoring (3). The accuracy of this method relies on little variation in G_{POOL} when IFR lies between T_{PRE} and T_{SAT}. Indeed, better fits of the piecewise-linear model can be achieved if accuracy of the upper threshold T_{SAT} is sacrificed and (3) is used instead. T_{SAT} can be argued to be the least important parameter. It is of little functional importance as it only plays a part in neuromuscular dynamics at high levels of activation when muscle force output is also becoming saturated. In this work, therefore, the piecewise-linear SISO model parameters will be visually estimated from the plot of IFR against OFR (Eq. 2), with emphasis on the accuracy of T_{PRE} and G_{LIN} to the detriment of T_{SAT} accuracy.

III. Results

Healthy and unhealthy MN pool synaptic behaviours were modelled. The MN pool was based on data from the cat medial gastrocnemius, assumed to contain 280 MUs [5]. The relationship between IFR and a MN's post-synaptic current, represented by the k_i, was set to 10^{-9} A/(pulses per second (pps)) for all MNs.

A) Healthy MN pool

In Heckman and Binder [5], every MN in the MN pool was assigned an individual $Pthres_i$, $Pmax_i$, $Ethres_i$, $Emax_i$, and $fmax_i$ based on experimental data from the literature. A piecewise-linear expression with two linear regions defined by two thresholds ($Pthres1_i$ and $Pthres2_i$) was used to represent the i^{th} MN's input-output gain, G_{MNi}. Fig. 2 shows a plot of IFR against the resulting OFR (3), along with the individual contributions to the IFR-OFR relationship due to the MN recruitment and rate coding), and the visual estimation of the piecewise-linear SISO model.

B) Unhealthy MN pool

After central nervous system trauma, all MNs in the affected muscles have often been reported to have smaller presynaptic recruitment thresholds and a reduced range of values across the MN pool. This behaviour is frequently paralleled with reduced initial firing-rates, a reduction in rate coding, and lower maximum firing-rates of the MNs [6]. The resulting modifications to the healthy MN pool synaptic behaviour are detailed in Table I. The healthy MN pool parameters are given for comparison. Fig. 3 presents results for the unhealthy MN pool in a similar fashion to Fig. 2. Figure 4 shows two alternative estimations of the piecewise-linear SISO model from the *IFR-OFR* relationship resulting from the unhealthy synaptic behaviours.

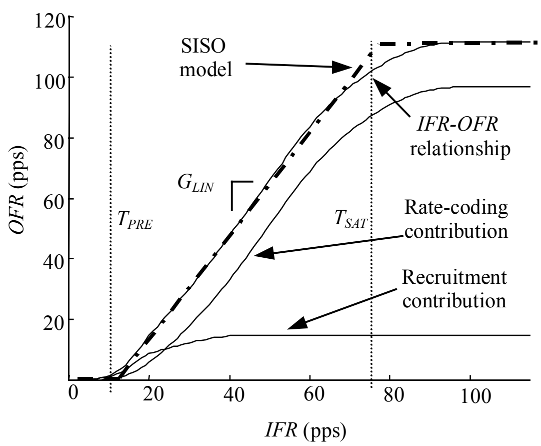

Figure 2. The *IFR-OFR* relationship for the healthy MN pool, along with the contribution of MN recruitment and rate coding. The piecewise-linear SISO model (heavier dash-dot line) was visually estimated from the *IFR-OFR* relationship.

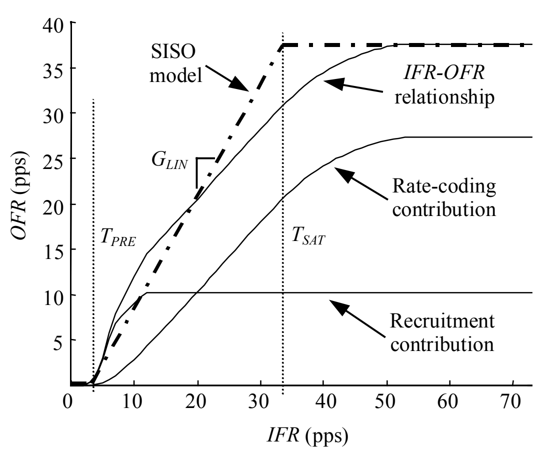

Figure 3. The *IFR-OFR* relationship for the unhealthy MN pool, along with the contribution of recruitment and rate coding. The piecewise-linear SISO model (heavier dash-dot line) was visually estimated from the *IFR-OFR* relationship.

TABLE I
HEALTHY AND UNHEALTHY MN POOL PARAMETERS

Parameter	Values (in ranges where appropriate) and Units	
	Healthy MN Pool	Unhealthy MN Pool
$Ethres_i$ (initial firing-rate)	8 – 17.5 pps	6 – 12 pps
$Emax_i$ (maximum firing-rate)	22 – 70 pps	12 – 36 pps
G_{MNi} input-output gain for 'active region' 1	1.5 pps/nA	3.0 pps/nA
G_{MNi} input-output gain for 'active region' 2	0.75 pps/nA	1.5 pps/nA
$Pthres1_i$ (presynaptic threshold for 'active region' 1)	3.5 – 40 nA	2 – 12 nA
$Pthres2_i$ (presynaptic threshold for 'active region' 2)	14.8 – 75.4 nA	8 – 40 nA

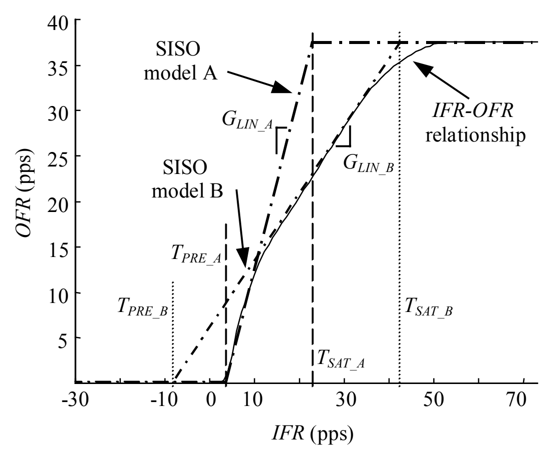

Figure 4. Two other piecewise-linear SISO models representing the unhealthy MN pool (long dash-dot and dash dot). The dashed vertical lines define the two thresholds, T_{PRE} and T_{LIN}, for model A, the dotted vertical lines represent the thresholds for model B.

IV. DISCUSSION

A) The IFR-OFR relationship interpreted with respect to MN recruitment and rate-coding

The *IFR-OFR* relationship, defined by $G_{POOL}(IFR)$, has been shown to be dependant on both MN recruitment and rate-coding. The dirac-delta functions in the expression for G_{POOL} (3) indicate that increases in *OFR* due to MN recruitment are controlled by small increments in *IFR*. In contract, the increases in G_{POOL} due to MU rate coding occur over much larger IFR ranges (Fig. 2).

It should be noted that when the last MU is recruited the muscle produces around 70% of maximum muscle force [4]. Therefore the further increases in G_{POOL} after this point are not as functionally significant as one might infer from examination of Fig. 2. Indeed MU firing-rates rarely reach the value required for maximum muscle force *in vivo* [7].

B) Piecewise-linear SISO model estimation from IFR-OFR relationship derived from MN pool data

Fig. 2 shows the piecewise-linear SISO synapse model fitted to the *IFR-OFR* relationship for the healthy MN pool. The linear approximation is seen to be quite reasonable, even over large ranges of *IFR*. It only loses accuracy at high *OFR,* which has been argued to be of limited functional relevance. The healthy distributions of MN properties in the MN pool have yielded this result. The MN recruitment and rate coding appear to be balanced in such a manner that the rise in G_{POOL} due to MN recruitment at low *IFR* offsets the lower contribution of MN firing-rate increases at low *IFR*.

The unhealthy MN pool 'active region' in Fig. 3, is less linear (due to the disruption in the balance between MU recruitment and rate coding) and consequently the piecewise-linear fit does a poorer job in mimicking the MU pool's *IFR – OFR* relationship. The piecewise-linear SISO model does still predict, however, a lowering of the presynaptic threshold and a higher post-synaptic gain, both of which would be expected after central nervous system trauma [2].

C) Piecewise-linear SISO model estimation from IFR-OFR relationship derived from clinical experiment

The above estimations of the piecewise-linear SISO model rely on detailed knowledge of the MN pool's properties. In a clinical situation, such information is unavailable and research is performed to evaluate it [2]. As shall be seen, however, very different descriptions of a subject's injury can be concluded depending on data gathered.

In Fig. 4 the integrated G_{POOL} from the unhealthy MN pool is presented with two possible piecewise-linear SISO model fits. We shall assume that the MN pool under examination is always tonically active due to an upper motoneuron disorder, e.g. cerebral palsy, and changes in *IFR* are directly related to afferent firing changes, e.g. muscle spindle activation during stretch.

With low tonic muscle activation, the synaptic reflexes would be best characterised by the piecewise-linear SISO model A. Under higher levels of tonic activation, the piecewise-linear SISO model B would be more accurate. Both models appear to be clinically reasonable. Piecewise-linear model A has predicted a slightly lower presynaptic threshold, T_{PRE_A}, and a higher postsynaptic gain, G_{LIN_A}. The tonic activation of the muscle would be assumed to be spindle-driven as a reduction in the spindle mediated *IFR* would reduce the *OFR* to zero. With the piecewise-linear model B, however, G_{LIN_B} has remained largely unchanged from the healthy MN pool synaptic behaviour, but now a larger decrease in T_{PRE_B} is predicted. The negative value implies that even if the afferent firing dropped to zero, the muscle would remain active, i.e. that the tonic muscle activation is centrally mediated. Therefore, depending on the part of the *IFR-OFR* curve to which the piecewise-linear SISO model is fit, different neural behaviours are predicted.

V. CONCLUSION

A piecewise-linear SISO synapse model was derived from a generalised analysis of MN pool behaviour. Using data from the literature the piece-wise linear model was seen to be a good, simple approximation to the overall MIMO healthy MN pool behaviour. This holds even for large ranges in input firing-rate. Care must be taken, however, in experimental estimation of these models, particularly when the relative contributions of MU recruitment and MU rate-coding to muscle activations have been disrupted.

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