
A.2 Editorial Comment with an Excerpt from Rall (1990)

Rall, W. (1990). Perspectives on neuron modeling. In *The Segmental Motor System*, ed. M. D. Binder and L. M. Mendell. New York: Oxford University Press.

Because of space limitations, the editors have chosen not to reprint the papers of Rall that address the input-output properties of motoneuron pools involved with the segmental reflex (Rall 1955a,b; Rall and Hunt 1956). The following excerpts from Rall 1990 introduce and summarize in part the results presented in these papers.

Fractional Pool Discharge: Monosynaptic Input-Output Relation

My earliest news of Elwood Henneman came in 1954 on the day I presented my first seminar at the National Institutes of Health (NIH). Based on my Ph.D. research, this seminar included experimental results and a model for monosynaptic input-output relations in a motoneuron pool. One of the points emphasized was the need to scale the output magnitude (synchronous output volley recorded from the ventral root) relative to an elusive maximum (i.e., a complete synchronous discharge from all of the motoneurons in the pool); such scaling provides an estimate of fractional pool discharge. In the discussion following the seminar, someone mentioned that Henneman had also been concerned with estimating fractional pool discharge. It seems that both he and I had come to pursue this interest quite independently. We both explored various experimental approaches to measurement of complete pool discharge, and both recognized that posttetanic potentiation of this monosynaptic reflex (Lloyd, 1949; Eccles and Rall, 1950) provides a valuable means of demonstrating that the usual unpotentiated output represents incomplete pool discharge (Rall, 1951, 1954, 1955a, 1955b; Henneman, 1954; see also Jefferson and Benson, 1953).

My interest in this problem arose during an apprenticeship with Professors J. C. Eccles and A. K. McIntyre in Dunedin, New Zealand (1949–53). It followed from the pioneering study of the monosynaptic input-output relation that Lloyd had begun with the segmental reflex (Lloyd, 1943, 1945). On the basis of experiments by Lloyd and McIntyre in New York, and our experiments in Dunedin (Brock et al. 1951), I knew that it was important to restrict the input to a muscle nerve (triceps surae). Compared with dorsal root stimulation, this had two important advantages: (1) this restricted the input-output study to a pair of synergic motoneuron pools, in contrast to the nonfunctional combination of motoneuron pools

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provided by the segmental reflex (which includes antagonist and incomplete pools), and (2) the longer afferent conduction distance (from the hindlimb) helped to separate the effective portion from the ineffective portion of the input volley, because direct synapses to the motoneuron pool are made only by the group Ia afferent axons (which have the largest diameters, lowest electrical thresholds, and highest conduction velocities). Axons of group Ib and group II are also active in a maximal afferent volley, but they make no contribution to the effective input of the monosynaptic reflex because they make no direct synapses to the motoneuron pool; these ineffective axons have smaller diameters, higher electrical thresholds, and lower conduction velocities, such that their contamination of the experimental input record is greatest for large afferent volleys produced by large electrical stimuli. However, because groups Ia and Ib overlap in their threshold distributions, it was essential to determine the relation between the effective input and the experimental input record (Rall, 1955b). These points deserve emphasis because they were not recognized in another input-output study (Rosenblueth et al., 1949); consequently, those authors misinterpreted the plateau of their input-output relation as indicative of output saturation (i.e., complete discharge of their segmental pool); this error greatly complicated their effort to produce a theoretical model that could match their input-output curves.

Convincing evidence that the output plateau does not represent saturation (complete pool discharge) was provided by experiments that achieved four levels of reflex excitability in a single preparation (Rall, 1955b). These four levels were obtained by means of two depths of anesthesia, each used with and without brief tetanic conditioning. The four resulting input-output curves (see the left side of Fig. 1) all show an output plateau for experimental inputs greater than 70% of the maximum recorded afferent volley. It is important to understand that each output plateau corresponds to a different fraction of total pool discharge (approximately 37, 60, 72, and 84%). In other words, none of these curves showed output saturation; each plateau resulted from the ineffectiveness of the higher-threshold afferent axons (belonging to groups Ib and II), which contributed most of the upper 40% of the experimental input record. For small inputs, the effective component of the input volley (carried only by group Ia axons) grew linearly with the experimental input record (see the linear part of the dashed curve at the left in Fig. 1). Then, over the mid-range (from 20 to 70% of maximal experimental input), the normalized effective input curve bent and reached a maximum where the experimental input record was only 70% of its maximum. The shape of this dashed curve was verified by experiments with graded monosynaptic facilitation and with graded sub-threshold synaptic potentials (of the motoneuron pool) recorded in the

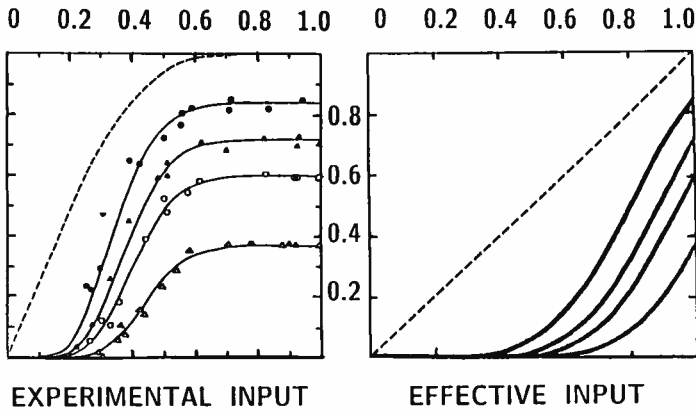


Figure 1

Output as fractional pool discharge versus two different measures of input. Each input-output curve shows an output plateau (left); transformed curves show no plateau (right). The four solid curves in the left graph were fitted to data of output versus the experimental input record (disphasic amplitude measured from intact dorsal root). The dashed line represents a normalized curve of "effective input" plotted against the experimental input record; this was based on observations of graded monosynaptic facilitation and on ventral root synaptic potentials; the linear relation for small inputs corresponds to recruitment of low-threshold group Ia fibers in the afferent muscle nerve. The ineffectiveness of increasing the experimental input volley from 60% to 100% of its maximum can be understood as resulting from the fact that the higher-threshold afferent fibers are ineffective because they belong to groups II and Ib and do not make synapses on these motoneurons. The five curves in the right panel are transformed from the five curves in the left pane; each experimental input value (abscissa, left) was replaced (in the right) by its effective input value, as defined by the ordinates on the dashed line in the left panel. This figure combines figures 2 and 6 of Rall 1955b. Straight-line fitting of the transformed data was shown in figure 4 of Rall 1955a.

ventral root. Once this dashed curve was understood, it was not surprising that the transformed input-output curves (at the right in Fig. 1) did not exhibit a plateau, because here the outputs were plotted as functions of the effective input. This transformation was the key to success in fitting the data with a relatively simple theoretical model (Rall, 1955a, 1955b).

In this model, it was assumed that the distribution of activated synaptic knobs could be treated as random over the motoneuron population. Suppose that each neuron has the same number, N , of potential synaptic sites (e.g., $N = 5000$) and that each site has the same probability, γ , of being occupied by a synapse belonging to the monosynaptic pathway (e.g., $\gamma = 0.02$); then the average number of relevant synapses per motoneuron is γN (e.g., $\gamma N = 100$). The effective input, β , ranges from 0 to 1, and for any particular value of β , we assume that $\beta\gamma$ defines the probability that a synaptic site receives an activated synapse (belonging to this pathway); thus, the average number of such activated synapses per motoneuron is $n = \beta\gamma N$ (e.g., n equals 100, 75, and 50 for β values of 1, 0.75, and 0.5, respectively). Because these probabilities were assumed to be independent,

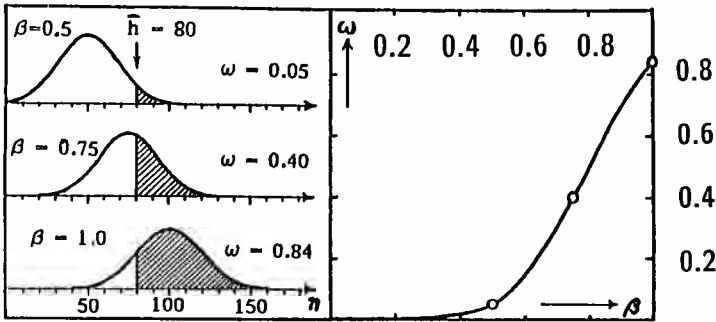


Figure 2

Schematic illustration of a mathematical model that gives output (ω) as fractional pool discharge versus effective input (β). At the left, the three input values, $\beta = 0.5, 0.75,$ and 1.0 , result in three normal distributions of the motoneuron population with respect to the number (n) of synapses activated on a motoneuron; these normal distributions are centered about mean values of 50, 75, and 100, with a standard deviation of 20; the mean threshold value is shown as 80, for the number of activated synapses needed to fire a motoneuron spike. The fractional pool discharge is shown as the shaded area under each normal distribution curve; this is the fraction of the motoneuron population for which the number of activated synapses exceeds threshold. These fractions are shown as $\omega = 0.84$ for $\beta = 1$, $\omega = 0.40$ for $\beta = 0.75$, and $\omega = 0.05$ for $\beta = 0.5$ at the left, and by the open circles on the input-output curve at the right. (Figure 1 in Rall 1955a.)

the result is a binomial (nearly Poisson) distribution of the motoneuron population with respect to the number, n , of activated synapses that each receives; the variance of this distribution is very close to n (e.g., $\text{var}(n) \approx 100$ when $\beta = 1$).

A motoneuron was assumed to fire an impulse when the number of its simultaneously activated synapses, n , exceeded some threshold number, h . The value of h was assumed to have a variability that could result both from inherent variability of motoneuron excitability and from background synaptic activity in other synapses. Because this variability in h was assumed to be independent of the variability in n , it was reasonable to approximate the combined variability of the motoneurons, with respect to their $n - h$ values, as a normal distribution with a variance, $\text{var}(n - h) = \text{var}(n) + \text{var}(h)$. In this case, good results were obtained for a normal distribution with a standard deviation very close to $\sigma = \gamma N/5$, (e.g., $\sigma = 20$).

The normal distributions in Fig. 2 are shown with $\sigma = 20$, but to simplify the diagram, these distributions are shown as though all of the combined variability were in the value of n (the number of synapses activated on an individual motoneuron). This permitted the threshold to be shown as though it were fixed at its average value, \bar{h} . The diagrams at the left illustrate how this normal distribution becomes shifted (relative to \bar{h}) for different values of effective input ($\beta = 0.5, 0.75,$ and 1.0). In each case, the shaded area of the distribution corresponds to the output, ω , as fractional

pool discharge ($\omega = 0.05, 0.40, \text{ and } 0.84$, respectively). The resulting input-output curve is shown at the right in Fig. 2.

This model has basically two theoretical parameters; both are scaled to the number γN , the average number of (direct group Ia) synapses per motoneuron (e.g., $\gamma N = 100$). One of these two parameters is the standard deviation, $\sigma/\gamma N$, of the motoneuron population with respect to the difference variable, $n - h$ (i.e., the difference between the number, n , of synapses activated on a particular motoneuron and the threshold number, h , required to fire that neuron). The other basic parameter is the average threshold value, $\bar{h}/\gamma N$. It was satisfying to find that one of these parameters had the same value for all four of the input-output curves shown in Fig. 1; i.e., $\sigma/\gamma N = 1/5$. Because of this, each input curve could be obtained by resetting the value of other parameter, $\bar{h}/\gamma N$; four values, very close to 0.80, 0.88, 0.95, and 1.07, yielded the four input-output curves of Fig. 1.

The agreement found between theory and experiment thus implied that the shift to a deeper level of anesthesia (in the experiment) was matched by an increase in the value of a single model parameter (the average threshold, \bar{h} , the motoneuron population) without a significant change in the variance or standard deviation of the population with respect to $n - h$. In addition, the effect of brief tetanic conditioning was matched by a decrease in the effective value of that same model parameter (or by an increase in the effective value of n). It may be noted that complications, such as possible departures from a normal distribution, and the possible role of higher densities of activated synapses in local zones of the soma surface were addressed in the original paper (Rall, 1955a) and found to result in similar input-output curves.

Because this model also predicted how the factor of output potentiation should depend on the level of fractional pool discharge (Fig. 5 of Rall, 1955a), it was pointed out that this could be developed into a method of estimating fractional pool discharge. Further, an extension of the model to include distinctions between homonymous and heteronymous synapses was shown to yield agreement with "cross-facilitation" of one motor pool by input from heteronymous afferents, in contrast to little or no monosynaptic "cross-discharge" in the absence of homonymous input (Figs. 6 and 7 of Rall, 1955a). A related modeling effort (Rall and Hunt, 1956) was able to account for experimental observations of the firing indices of individual motoneurons, in relation to motoneuron pool discharge, during repeated trials, for several different levels of reflex excitability.

Looking back about 33 years, it seems fair to say that these early efforts did succeed in providing explicit models that correspond reasonably well with the general concept of spatial summation in motoneuron pools, originally introduced by Denny-Brown and Sherrington (1928) and discussed

by Lloyd (1945) in terms of an “excited zone,” a “discharge zone,” and a “subliminal fringe.” The discharge zone corresponds to the shaded area in Fig. 2, while the subliminal fringe is composed of motoneurons in a band just to the left of the vertical threshold line; the excited zone probably includes the entire population for effective inputs greater than 50% of maximum.

One result of this study was to show that the shape of the input-output curve does not require spatial summation to be the very local process envisaged by Lorente de Nó (1938) and by Lloyd (1945). Moreover, another theoretical model, for passive electrotonic spread over a spherical soma, led to the conclusion that the membrane depolarization becomes essentially uniform over the closed soma surface by the time the synaptic potential reaches its maximum amplitude (Rall, 1953, 1955a, 1959); this result weighed against the validity of very local spatial summation on the motoneuron soma surface. It is interesting that the concept of local synaptic interactions has recently returned in a different context, namely, for synapses on excitable dendritic spines at distal dendritic locations (Rall and Segev, 1987, 1988).

In concluding this section on motoneuron populations, it is important to point out several limitations of these early models. No distinction was then made between motoneurons of different size or functional type; these important distinctions have been explored by Henneman and by other contributors to this volume. The assumption of random synaptic distributions was a convenience that was justified by ignorance of actual synaptic distributions. In addition, no distinction was made between different sequences of afferent fiber recruitment, and no consideration was given to distinguishing between synapses at different (proximal to distal) dendritic locations in the motoneuron population. The task of incorporating such considerations into a more comprehensive model of a motoneuron pool provides an interesting challenge for future modeling.

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