

Spinal Sensorimotor System Part IV: The PPSL Network

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The PPSL Network

The motoneuron level (MNL) network is the “network of networks” that directly converges on the spinal cord system’s motoneurons (MNs). The propriospinal level (PPSL) network has the MNL for its immediate target, and given the level of complexity we have already seen at the MNL, it should be no surprise that the PPSL network is considerably more difficult for neurobiologists to probe. When a network’s target is a motoneuron, there is comparatively little doubt about what the direct function of the MNL network involves. In one way or another, its role is to activate or inhibit the proper groups of muscles at the proper time in the execution of a reflex or a voluntary movement. For the PPSL network, which targets interneurons (INs) at both the MNL and within the PPSL, the significance of signal processing with which any particular IN is involved is at least one level removed from direct MN activity and consequently interpretation becomes a major issue for neurobiologists. In this sense, exploration of the PPSL networks is handicapped by the same sort of “what does this do?” issues that confront neuroscience research of the brain.

It is therefore not surprising that few PPSL circuits have been identified and mapped out, nor that very, very few PPSL INs have been identified. Most, but not all, PPSL INs lie in the dorsal horn where they are in a position to process afferent signals as they enter from the peripheral nerves. We saw an example of this in Part I (figure 2 below). Even for this simple circuit, we did not discuss the function of the subnetwork made up of the islet, marginal, projection, and stalked cells; the reason we did not is that the specific function of this network is not entirely clear. What we do know about the PPSL network can be briefly summarized as follows.

1. The PPSL can be characterized as a “network of interacting networks” topology.
2. The outputs of PPSL subnetworks project to either the MNL, to ascending tracts back to the brain, or make propriospinal projection to other segments of the spine.
3. The PPSL contains one or more central pattern generators (CPGs), probably within each spinal segment, that coordinate the timing of various muscles during complex movements.
4. The PPSL is probably responsible for activating or inhibiting subassemblies in MNL networks, thereby providing the variable switching structure control system scheme we discussed previously.
5. Some descending tract control signals from the brain contact INs at the PPSL, and at least some of these connections involve metabotropic signaling (which makes sense considering the length of time required to execute long muscle movement sequences in voluntary locomotion).

Among the many things not known about PPSL networks is whether or not long-term potentiation or long-term depression (i.e. “motor learning”) takes place within the PPSL. By way of contrast, it is well-established that motor learning takes place within the cerebellum. But whether or not this motor learning is augmented by motor learning phenomena within the spinal cord is entirely unclear.

Most PPSL INs have not yet been identified. Certainly some PPSL INs are involved in integrating sensory and descending tract information, and respond to this information by exerting control over MNL networks. It is likely that the group II dorsal horn INs (IIDH-INs) mentioned

in Part III play this role. Probably one of the key roles for these PPSL INs is in the co-opting of the flexor reflex in the execution of voluntary movements. Other generic classes of PPSL INs include the following.¹

1. Flexor reflex afferent (FRA) INs, which mediate spinal responses to cutaneous, joint and at least some of the group II afferent pathways;
2. Primary afferent depolarization (PAD) Ins, which are responsible for effecting **presynaptic inhibition** of afferent pathway signals;
3. Proprioceptive relay interneurons (PR-INs), including some propriospinal interneurons (P-INs), which supply control signals to the INs at the MNL in the same and different spinal segments; and
4. Ascending tract interneurons (T-INs), which relay information from the spinal circuits back to the brain.

From the analysis of afferent signal pathways reaching MNL INs, we can safely conclude that most subnetworks at the PPS level are only one or two neurons “deep”. Individually, then, it seems likely that specific subnetworks in the PPSL are going to be fairly simple networks. On the other hand, observable behavior of coordinated muscle movements makes it very likely that PPSL subnetworks have extensive lateral, reciprocal connections with other subnetworks at their own level. Mutual lateral inhibition and excitation of subnetworks at the same level does, of course, greatly complicate the analysis of individual subnetwork behaviors. Thus, what we can learn from the findings of neurobiology largely consist of “functional” rather than “circuit” relationships. To put this another way, we know, e.g., that the spinal segment contains at least one CPG coordinating agonist-antagonist muscle movements (and perhaps also coordinating muscle synergists on both sides of the spinal cord), but we do not know the details of how these CPGs are constructed, or even if there is one CPG or many CPGs in a spinal segment. **I anticipate that the biggest challenge for our EC algorithms is going to be in coming up with putative subnetworks that implement PPSL functionalities.**

Presynaptic Inhibition by PAD Interneurons

Up until now when we have talked about inhibitory interneurons the inhibition evoked has been postsynaptic. This is the type of “classic” inhibition that gets modeled by negative synaptic weights in conventional artificial neuron models, and by dedicated inhibitory synapses in the BAN neuron model. The types of synapses involved in postsynaptic inhibition are axodendritic and axosomatic synapses (i.e. the synapse is between an axon and either a dendrite or the soma). Presynaptic inhibition involves one or the other of two different sorts of synapse, the axoaxonal synapse (i.e. the synapse is made between two axons) and the axodendritic triad (see figure 2 below). We discussed axoaxonal synapse in the previous tech brief on synaptic modulation when we talked about heterosynaptic plasticity.²

In the spinal cord presynaptic inhibition is tied to the observation of depolarization in primary afferent nerve fibers evoked by axoaxonal signaling. The phenomenon is called “primary

¹ E. Jankowska, “Interneuronal relay in spinal pathways from proprioceptors,” *Progress in Neurobiol.* (1992), **38**: 335-378.

² R. Wells, “Synaptic weight modulation and adaptation part I: introduction and presynaptic mechanisms,” May 15, 2003.

afferent depolarization” or PAD. Hence, the inhibitory interneuron is called a PAD-IN.¹ Because in many cases depolarization is regarded as a sign of excitation in a postsynaptic cell, it may at first seem strange that PAD should be an inhibitory mechanism. However, the terminals of the afferent nerve fibers in the spinal cord tend to have resting potentials more negative than the Nernst potential³ for chloride (Cl^-), which is about -70 mV. The inhibitory action at the axoaxonal synapse in PAD inhibition causes an increase in the membrane conductance for Cl^- , which in turn raises the membrane potential of the afferent fiber closer to the Nernst potential for Cl^- . This is depolarization, but the amount of depolarization is not enough to excite an action potential (AP). Rather, the increase Cl^- conductance acts to shunt excitatory currents in the axon, which reduces the amplitude of any action potentials that fiber is conducting. The net effect is to reduce the amount of neurotransmitter (NTX) emitted at the axon terminal², and this is an inhibitory action.

PAD inhibition is rarely a complete inhibition. By this I mean that it reduces the amount of NTX released by the axon terminal being inhibited, but it does not completely suppress NTX release by that fiber terminal. Rather, the action of PAD inhibition is that of a short-term decrease in the synaptic weight between the afferent fiber and its target postsynaptic neuron. In terms of hardware modeling, this corresponds to decreasing the Hamming weight of the weight-setting register in figure 5 of our tech brief on dendritic computation.⁴ Physiologically, the NTX used by PAD-INS is GABA (γ -aminobutyric acid), which is one of the principal inhibitory NTXs in the central nervous system. This NTX not only depolarizes afferent nerve fibers, but it can also, in the case of an axodendritic triad (where the PAD-IN synapses simultaneously with both the afferent fiber and the dendrite of the fiber’s postsynaptic target), hyperpolarize the target cell.

PAD inhibition is slow-acting, both in onset and in abatement. Figure 1 illustrates the time course of the effect of presynaptic inhibition of a Ia afferent fiber on a monosynaptic reflex in a gastrocnemius muscle MN.⁵ Generally, induction of PAD inhibition requires several volleys of

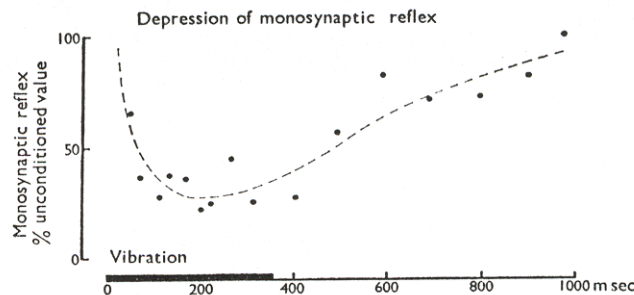


Figure 1: Effect of PAD inhibition on monosynaptic muscle reflex. The data is expressed as percentage of uninhibited reflex action. The figure is taken from Matthews⁵. Inhibition was induced by vibrating the semitendinosus muscle at 200 vibrations per second, thereby exciting Ia fibers.

³ The Nernst potential is the name given the “battery” that models the contribution of a particular ion to the cell’s membrane potential in the Hodgkin-Huxley model of the neuron. The H-H model is the basic biophysical model of the behavior of excitable membranes, and for this model Hodgkin and Huxley won the 1963 Nobel Prize in medicine. All artificial neuron models are approximations of one or more aspects of the Hodgkin-Huxley model. The H-H model is a nonlinear circuit model. A diagram of the basic H-H circuit can be found in our IECON’02 paper by Wells and Barnes, “Delay resistor implementation of integrators in biomimic artificial neurons, Proc. IECON’02, pp. 3186-3190.

⁴ R. Wells, “Dendritic computation in multi-compartment neurons,” undated.

⁵ P.B.C. Matthews, *Mammalian Muscle Receptors and Their Central Actions*, London: Edward Arnold Ltd., 1972, pp. 385-394.

relatively high-frequency AP bursts to come in on the afferent nerve that stimulates the inhibition. As figure 1 illustrates, the action of PAD inhibition is a couple of orders of magnitude slower than direct synaptic action. This leads me to hypothesize that the NTX receptor on the presynaptic terminal of the afferent being inhibited must be a metabotropic receptor, e.g. a GABA_B receptor, since such slow action requiring such a strenuous excitation to invoke is typical of metabotropic signaling and is not typical of ionotropic channels (i.e. the ionotropic GABA_A receptor).⁶

PAD-INs are named for the afferent they depolarize.¹ An IN inhibiting group Ia afferents is called a PAD_{Ia}-IN; one that inhibits group Ib afferents is called a PAD_{Ib}; one inhibiting group II afferents is a PAD_{II}; etc. PAD inhibitory pathways generally include more than one IN but not necessarily more than two. Only a couple dozen PAD-INs have been identified to date, and it is typically the case that PAD-INs must be inferred on the basis of indirect experimental clues (some of which we are about to look at). It is thought that PAD_{Ia}- and PAD_{Ib}-INs are located in laminae VI and VII of the spinal cord gray matter (the intermediate zone near the motoneuron pools). PAD-INs of other afferents (muscle group III and IV, cutaneous, etc.) are thought to reside in laminae I – III of the dorsal horn. This is where the islet cell is found (see Figure 2), and the islet cell is thought to be a PAD-IN inhibiting A δ cutaneous afferents via the axodendritic triad synapse shown in the inset of figure 2.

As you might guess from the metabotropic descending tract axon shown in the inset of figure 2, the actions of PAD-INs can be modulated from higher motor control centers in the brain. NE is norepinephrine; 5-HT is serotonin. The descending tract axon will use one or the other, but not both, as a NTX to modulate the excitability of the islet cell. The notation in the figure is meant to indicate the possible presence of more than one descending tract connection to the islet cell.

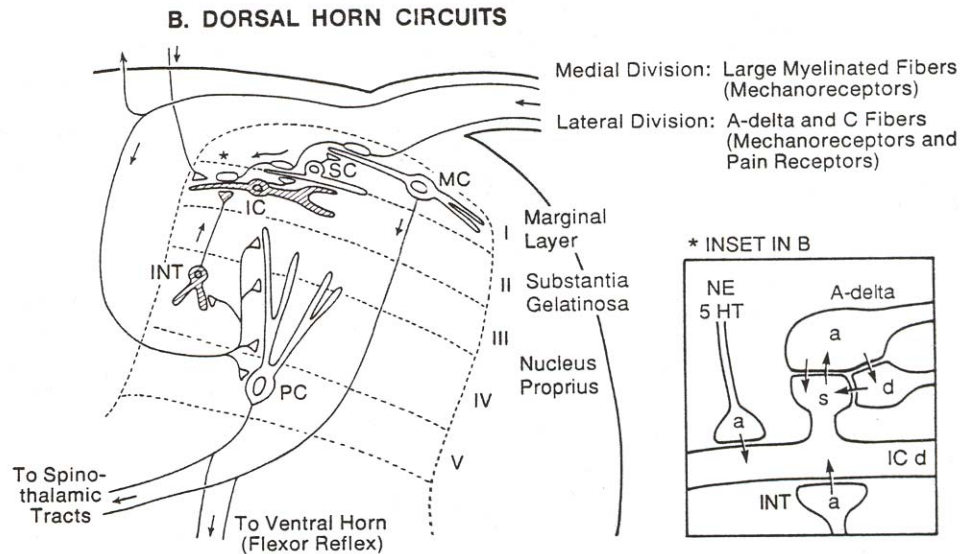


Figure 2: The islet cell PAD circuit in the dorsal horn. This figure was previously presented as figure 15 in Part I. IC = islet cell; SC = stalked cell; MC = marginal cell; INT = unidentified interneuron; PC = projection cell. The inset also illustrates an axodendritic triad (a-s-d). The islet cell is GABA-ergic (uses GABA as its NTX), which is what identifies it as a PAD-IN. Note the complicated four-way interaction in the triad synapse shown in the inset. The stalked cell (dendrite d in the inset) is not GABA-ergic.

⁶ R. Wells, “Modulation channels in biomimic artificial neurons,” *Proc. 28th Ann. Conf. Indust. Electron. (IECON’02)*, Seville, Spain, Nov. 5-8, 2002, pp. 3209-3214.

Another common aspect of PAD networks is indicated in figure 2. Observe that there is a lateral division pathway for the mechanoreceptor and pain receptor fibers that runs through the marginal cell (MC) to the flexor reflex pathway to the ventral horn. The MC is co-excited by the stalked cell (SC), which itself receives inhibitory input from the islet cell (IC). Thus, in addition to direct PAD action on the afferent fibers, the IC exerts a disynaptic influence on the MC through inhibition of the SC. What this tells us is that PAD networks can also have lateral connection to FRA networks in the PPSL.

Group Ia and Group Ib PAD inhibition. In most cases PAD inhibition of group Ia afferents is most effectively activated by Golgi tendon organ afferents (group Ib afferents). Hultborn et al. have examined presynaptic inhibition of group Ia afferents that make monosynaptic contact with motoneurons.^{7,8} They found that Ia afferents from heteronymous muscles could evoke presynaptic inhibition of homonymous Ia afferents from the agonist muscle. Figure 3 is a sketch of the PAD network mediating this effect.

We recall that the Ia muscle spindle most effectively senses velocity of the muscle contraction. Thus, we could expect that vibration of the muscle enhances the presynaptic inhibition. This is in fact the case, as illustrated in Figure 4⁷. In the experiment leading Hultborn et al. to figure 4, it was interesting to note that presynaptic inhibition of the reflex was initially preceded by a brief facilitation of the reflex action. This is illustrated for the soleus muscle and for the quadriceps in figure 5. It is thought that this early facilitation is due to the spread of the vibration to the homonymous muscle spindles.

We have seen in earlier parts of this tech brief that Ia afferents converge on motoneurons from various synergist muscles. The presynaptic inhibition of these Ia afferents from stimulation

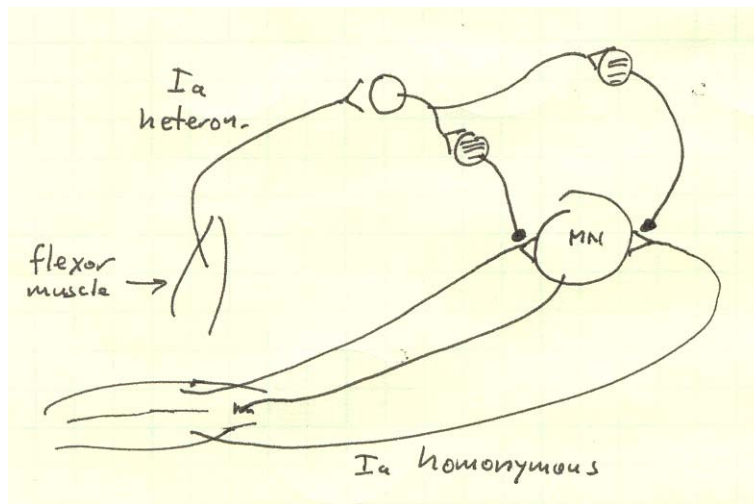


Figure 3: Sketch of presynaptic inhibition of homonymous Ia afferents by heteronymous Ia afferents. The motoneuron drives the agonist muscle (which in Hultborn et al. was a triceps surae muscle). The PAD inhibitory pathway from heteronymous Ia afferents to the presynaptic terminal of the homonymous Ia afferents are disynaptic. The action of this pathway is to reduce the positive feedback from Ia afferents to the motoneuron. Dark-hatched INs are inhibitory PAD-INS. Open circles are excitatory.

⁷ H. Hultborn, S. Meunier, C. Morin, and E. Pierrot-Deseilligny, "Assessing changes in presynaptic inhibition of Ia fibres: a study in man and the cat," *J. Physiology* (1987), **389**: 729-756.

⁸ —, "Changes in presynaptic inhibition of Ia fibres at the onset of voluntary contraction in man," *J. Physiology* (1987), **389**: 757-772.

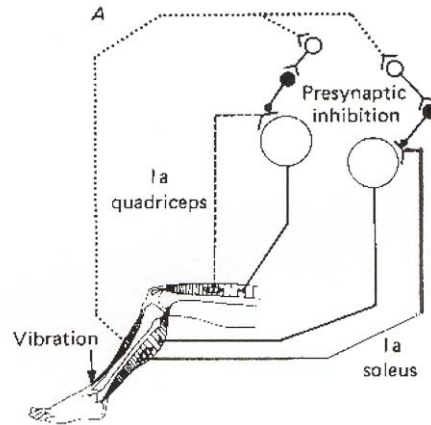


Figure 4: Presynaptic inhibition of Ia afferents from the quadriceps and soleus through vibration of the tibialis anterior tendon. The vibration was applied as three short shocks of 200 Hz each. Open circles are excitatory INs; filled circles are inhibitory PAD-INs.

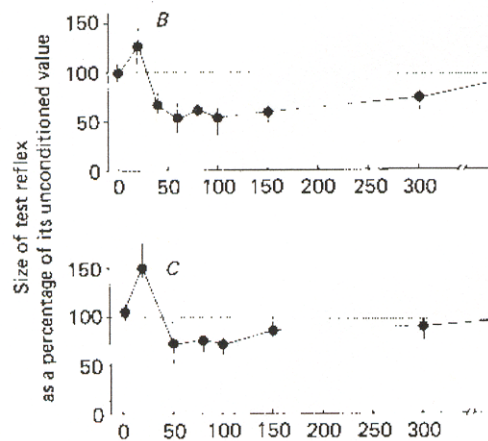


Figure 5: Time course of presynaptic facilitation for the pathways in figure 4. The time scale is in msec. and the size of the test reflex is expressed in percentage of unstimulated reflex response. Note the brief interval of facilitation at the beginning. This is believed to be due to the spread of the vibration stimulus to the muscle spindles of the soleus (B) and quadriceps (C) muscle spindles.

of heteronymous muscles affects these synergist Ia afferents equally with those from the agonist muscle. This is illustrated in Figure 6 below. Hultborn et al. were not particularly clear as to their reason for representing the inhibitory pathways as involving two inhibitory PAD_{Ia}-INs, as shown in the figure, rather than in speculating that the inhibition was due to a single PAD_{Ia}-IN projecting to the presynaptic terminals of both Ia presynaptic terminals for the quadriceps and soleus muscles. However, if there are separate PAD_{Ia}-INs mediating inhibition in these two pathways, then one consequence would be that other modulatory (control) signals converging on the PAD-INs would permit independent control of the amount of inhibition applied to these separate positive-feedback pathways from the synergist muscles. There is evidence that indicates that convergence of spindle afferent stimulants for presynaptic inhibition takes place on the first order INs in the PAD pathway (the excitatory IN in figure 6), but it is not clear whether or not the

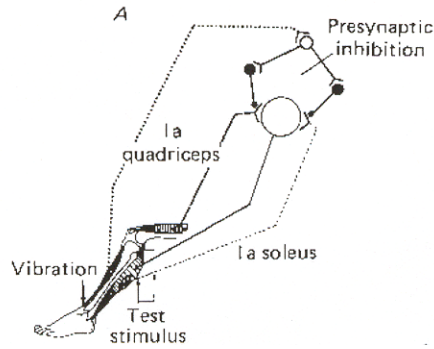


Figure 6: Presynaptic inhibition of both agonist and synergist Ia afferents by heteronymous Ia afferents. The inhibition is again preceded by a brief facilitation, similar to that of figure 5, prior to the onset of reflex inhibition.

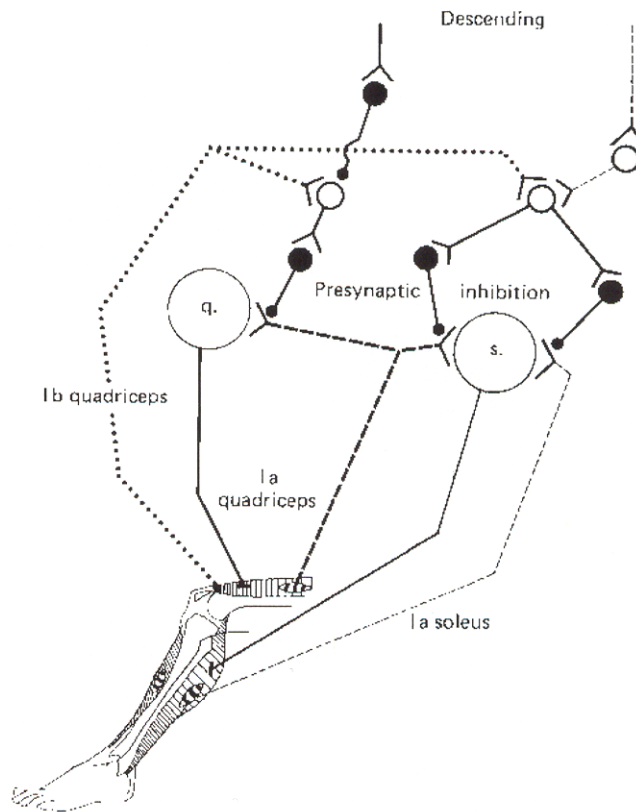


Figure 7: Ib-evoked presynaptic inhibition of Ia afferents. Open circles are excitatory, closed circles are inhibitory INs. The two motoneurons are quadriceps (q) and soleus (s). The figure also illustrates descending tract pathways from higher brain centers by which voluntary movement commands affect the inhibitory pathways. In the network shown here, convergence of the command signals takes place at the first order (excitatory) INs.

convergence of control signals takes place preferentially on the inhibitory PAD-INs (as it does with the islet cell in figure 2).

The cases just illustrated are for Ia afferents inhibiting Ia afferents. I mentioned earlier that Ib afferents exert a stronger inhibitory effect on Ia afferents than is the case where the inhibiting pathway is sourced from Ia spindles. The inhibitory pathway is illustrated in Figure 7, which also

includes putative descending control pathways modulating the PAD inhibition.⁸ In terms of the pathway from group Ib afferent to group Ia presynaptic inhibition, this network is of the same basic connectionist character as the previous figures. What is interesting here, however, is the convergence of descending tract control pathways at the first-order PAD pathway INs. The descending tract for the quadriceps muscle inhibits the PAD pathway (which is to say that it allows the positive feedback from quadriceps group Ia spindle afferents to the quadriceps MN to take place). The descending tract control signal converging on the PAD pathways to the soleus muscle is excitatory (which is to say that it promotes presynaptic inhibition of the homonymous Ia feedback to the soleus MN by the quadriceps Ib afferent). In Hultborn et al.'s experiment, PAD inhibition was measured during voluntary contraction of the quadriceps muscle. The descending control pathway shown in figure 7 is such as to promote contraction of the quadriceps while inhibiting reflex contraction of the soleus. This is what we would expect for the act of extending the leg. Note, however, that if the subject were trying to stand on tiptoes, the calf muscles (soleus) would have to contract, and so to maintain this position presynaptic inhibition of group Ia feedback to the soleus MN would be undesirable. Thus, either removal of the descending tract excitation would be required (and this would have to be sufficient to break the Ib feedback path), or else yet another inhibitory descending tract signal converging on the first-order excitatory IN for the soleus pathway would be needed.

Presynaptic inhibition of the reciprocal Ia inhibitory pathway. Presynaptic inhibition also plays a role in mediating the myotatic reflex. We recall that this reflex is the one which is handled by the inhibitory Ia-IN (see part III of this tech brief). This example of PAD presynaptic inhibition is interesting because it illustrates a fairly complex instance of motor control circuitry. The dynamics of the myotatic reflex involve not only the Ia-IN but also the actions of Renshaw cell (RC) recurrent inhibition of the MN. Fu et al. showed⁹ that reciprocal Ia inhibition often exhibits two “phases”, one due to the combined actions of the Ia-IN and the RC, the other involving presynaptic inhibition.

A simplified diagram of Fu et al.'s experiment is shown in Figure 8. They applied a controlled stretch to the agonist muscle (either a quadriceps muscle, Q, or a triceps surae muscle, G-S), and measured the monosynaptic reflex response to a twitch applied to the antagonist muscle (either the posterior biceps and semitendinosus muscle, PBSt, deep peroneous, DP, or the tibialis anterior muscle, TA). The goal of their experiment was to determine the relative “gains” of Ia afferents vs. Renshaw cell inhibition.

Fu et al. observed that at lower values of stretch in the agonist muscle, the inhibition of the antagonist was determined primarily by the Ia-IN pathway. They found that the firing rate of the Ia sensory neuron increased more or less linearly with stretch length. In most cases the antagonist reflex decreased linearly with increasing agonist stretch up to a point, after which the amount of reflex response reached a plateau in decline. This is illustrated in Figure 9 below. The plateau set in at an agonist stretch length of about 5 or 6 mm. The antagonist reflex response then would hold constant with increasing agonist stretch until a second breakpoint occurred, typically at around 15 mm of agonist stretch. The antagonist reflex then began to decline, again more or less linearly, from that point.

Fu et al. concluded from this that the reciprocal inhibition of the antagonist showed two “phases”, corresponding to the initial Ia-IN mediated inhibition and the later second inhibition. Their hypothesis is that the second phase is caused by the onset of presynaptic inhibition. During

⁹ T.-C. Fu, H. Hultborn, R. Larsson, and A. Lundberg, “Reciprocal inhibition during the tonic stretch reflex in the decerebrate cat,” *J. Physiol.* (1978), **284**: 345-369.

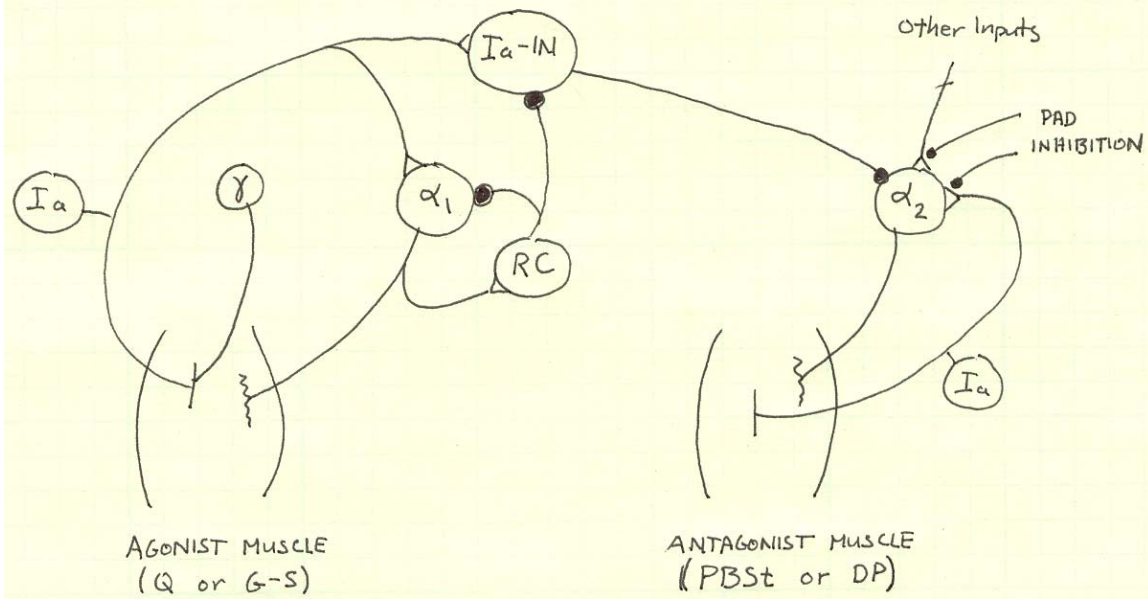


Figure 8: Simplified diagram of reciprocal Ia inhibition tested by Fu et al. A stretch was applied to the agonist muscle and the monosynaptic twitch reflex of the antagonist muscle was measured to determine the amount of inhibition undergone by its motoneuron, α_2 . Ia = Ia sensory neuron; RC = Renshaw cell; Ia-IN = Ia inhibitory interneuron. Q = quadriceps muscle; G-S = triceps surae muscle; PBSt = posterior biceps and semitendinosus muscle; DP = deep peroneus muscle. They also tested the antagonist tibialis anterior (TA) muscle.

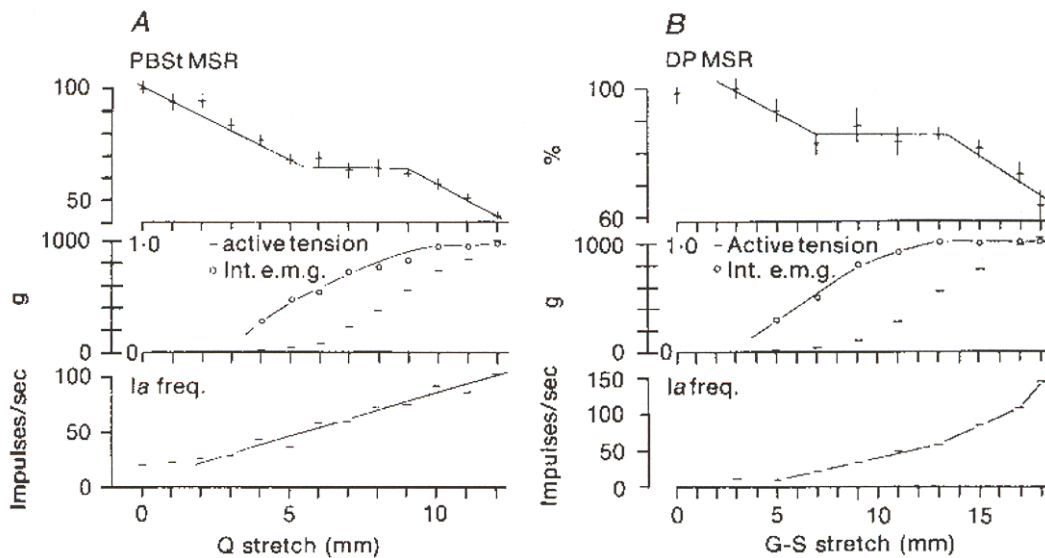


Figure 9: Typical result from Fu et al.'s experiment. (A) is the result for agonist Q and antagonist PBSt. (B) is the result for agonist G-S and antagonist DP. MSR = monosynaptic reflex. The top curves show the percentage decline in antagonist reflex response. The bottom curves give the average firing rate of the agonist Ia sensory neuron vs. stretch length. The center curves plot the active tension measured in the agonist muscle and its motoneuron activity as determined by electromyogram (e.m.g.).

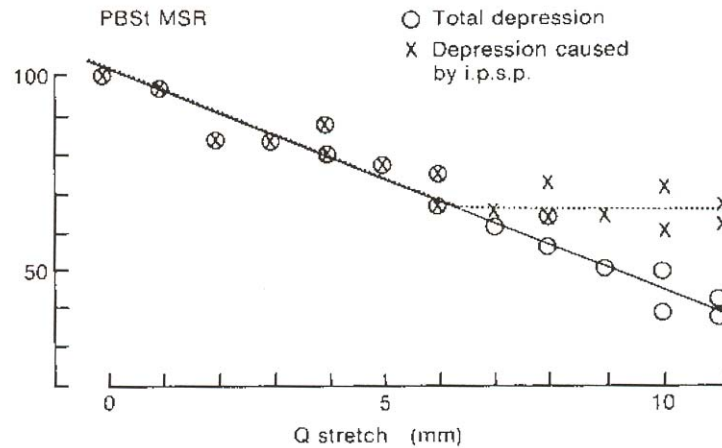


Figure 11: Separation of Ia-IN mediated inhibition (x) from total antagonist inhibition. The case illustrated in this figure corresponds to row 3 column 2 in figure 10.

their test results, 39 were instances with no second phase and no peak in e.m.g. activity. There were 10 cases where a second phase was observed, equally split between cases with and without a peak in e.m.g. activity. There were 15 cases where no plateau in antagonist inhibition was observed at all. There are 18 cases that are not consistent with pure Ia-IN mediated inhibition (row 1 columns 2 and 3; row 2 column 1, and row 3 column 1). Fu et al. concluded that row 1 column 2 cases are due to presynaptic inhibition for the second phase of antagonist reflex depression. They also were able to determine that row 3 column 2 involves both pre- and postsynaptic (i.e., Ia-IN mediated) inhibition. Figure 11 illustrates how they were able to break out the postsynaptic inhibition mediated by the Ia-IN from the total antagonist reflex inhibition. Row 1 column 3 is also indicative of presynaptic PAD inhibition. It is not clear what the mechanism is for the row 3 column 1 cases, but the lack of e.m.g. activity implies that there is no Ia-IN mediated inhibition from the agonist muscle involved in it. Row 2 column 1 they attribute to a purely presynaptic mechanism (since no change in e.m.g. is observed in this case).

The nature of their experiment was such that it was not possible to identify the PAD-INS involved in the presynaptic inhibition. (This is why figure 8 does not show the PAD pathway to the Ia afferents converging on the antagonist MN). In summary, Fu et al. found: 1) that presynaptic inhibition is a factor in the reciprocal Ia inhibition of antagonists; and 2) that Ia excitation of the Ia-IN and recurrent inhibition of the Ia-IN by the Renshaw cell comes to a “balance” such that Ia-IN inhibition of the antagonist MN reaches a saturation value, beyond which the Ia-IN exerts no additional influence on the α_2 MN.

FRA - GRA Pathways

Without doubt, one of the principal tasks of the PPSL network is the processing of flexor reflex afferent information and the incorporation of descending tract central command signals into this pathway for voluntary movement. In addition, we saw in Part III that some muscle spindle afferents make polysynaptic connection to interneurons in the MNL network, and all such pathways are mediated by INs in the PPSL network. As defined by Eccles and Lundberg in 1959, group III muscle afferents, high threshold joint afferents, and cutaneous afferents are called flexor reflex afferents (FRAs) when they converge on common interneurons or when they act together in producing a reflex (i.e. the flexor reflex). When muscle spindle afferents, e.g. group II

afferents, also join in with FRAs in controlling motor response, they are collectively called “general reflex afferents” or GRAs.¹⁰

It is unfortunately the case that it is very difficult to obtain the kinds of measurements on INs at the PPSL that would permit the kind of “map making” for these networks that has been accomplished for the INs in the MNL circuits. Thus, most of our knowledge of PPSL networks is rather more “functional” than specific. The literature tends to discuss these pathways in terms of “black box” networks projecting to motoneurons. Obviously such a depiction in a diagram subsumes our MNL INs into this “black box”. Nonetheless, we can get some idea about what is going on within the PPSL through latency analysis on pathways converging on MNs and MNL INs (which we have discussed in Part III). Insofar as group II spindle afferents and FRAs are concerned, the picture that emerges from the literature is one of “pathway fractionation”, a term that basically means there are a lot of parallel pathways through subnetworks converging down on MNL interneurons and motoneurons. The picture this suggests is illustrated in Figure 12, where obviously we have subsumed the MNL INs within the “IN subnetworks” displayed in the figure.

One key piece of evidence that supports the hypothesis that INs in PPSL subnetworks integrate a large number of afferent pathways before passing down the information they convey

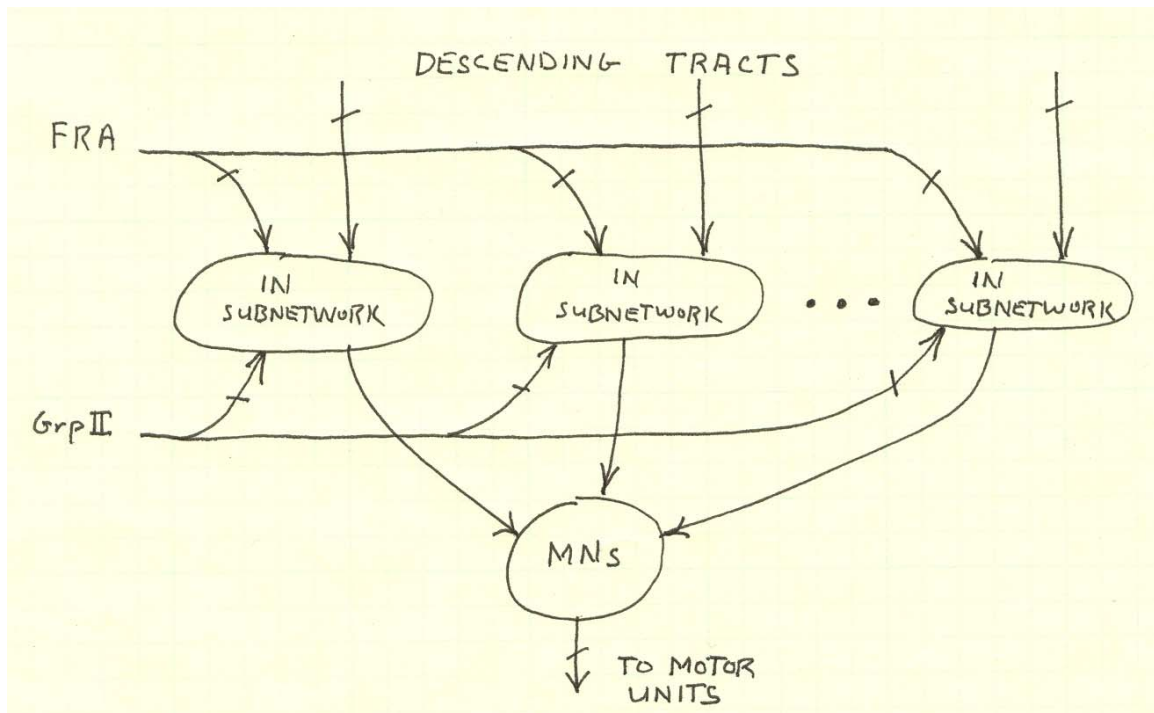


Figure 12: Fractionated network model of convergence on motoneurons. The MNL interneurons have been taken into the IN subnetworks depicted in this figure. Not shown are lateral connections among the subnetworks and group I afferent inputs into these networks and into the motoneurons (MNs).

¹⁰ A. Lundberg, K. Malmgren, and E.D. Schomburg, “Reflex pathways from group II muscle afferents. 3. Secondary spindle afferents and the FRA: a new hypothesis,” *Exp. Brain Res.* (1987), **65**: 294-306.

to MNL INs is the phenomenon of nonlinear summation at the level of the MNs.¹¹ When several group II pathways converge at a MN, it is usually the case that the resulting postsynaptic potentials observed show a deficit from what would be expected if all the group II afferent effects summed linearly. The deficit from a linear summation for group II afferents is in the range of 35-40% down from what a linear sum should yield. Lundberg et al. make the hypothesis that this deficit is largely due to occlusion from shared interneuronal discharges that “shut the gate” on some of these group II signals. Thus, summation deficit is regarded as a kind of minimal measure of how many group II afferents from different muscles converge at a common interneuron. The reasoning behind this is that if these afferents had their own pathways to the motoneuron, the effect produced by simultaneously arriving APs on the MN would be stronger than what is actually observed. On the other hand, if these afferents converge instead on a common IN, they could evoke a stronger firing activity from that IN, but converging multiple pathways down to the activity from a single axon (running from the IN to the MN) would evoke less of a response at the MN.

Another bit of evidence supporting the fractionated subnetworks model is obtained by the observation that FRAs tend to exhibit spatial facilitation. “Spatial facilitation” merely means that co-activation of afferents from different parts of the body facilitates MN or IN responses. This is the sort of behavior one would expect if an IN in the pathway required the summation of a larger number of afferents before it would produce an AP. Different MNs are stimulated by different combinations of afferent sources; e.g. a given cutaneous afferent might evoke response from motoneuron “A” if it is co-active with afferents from muscles W and X, but might evoke response from motoneuron “B” if it is co-active with afferents from muscles Y and Z.

This general theme is illustrated in Figure 13.^{12,13} In this figure ipsilateral FRAs (i-FRAs) and contralateral FRAs (co-FRAs) both converge on the MN, along with a vestibulospinal tract (or a long propriospinal tract) input pathway. Lateral inhibition among the MNL INs provides the capability for one side or the other to dominate the MN response. FRA volleys can facilitate the response of the descending tract (or a long propriospinal tract) IN. Lundberg summarizes the following hypotheses for these FRA pathways.

1. The afferents comprising the FRA converge on common interneurons. Evidence we will consider shortly will indicate that this common IN is at the PPSL rather than the MNL.
2. The FRA have access to a number of alternative spinal reflex pathways. This is the main point illustrated in figure 12.
3. There are mutual inhibitory interactive connections at an interneuronal level between the alternative reflex pathways from the FRA. Figure 13 illustrates mutual lateral inhibition at the MNL, but the mutual inhibition Lundberg is discussing in this hypothesis also includes an inhibition that takes place at the PPSL. We will examine this in more detail in just a bit.
4. The interneurons of different alternative reflex pathways from the FRA can be activated by descending pathways from the higher motor centers. Again, this hypothesis covers not only the descending tract pathway in figure 13, but also descending control at the PPSL.

¹¹ —, “Reflex pathways from group II muscle afferents. 2. Functional characteristics of reflex pathways to α -motoneurons,” *Exp. Brain Res.* (1987), **65**: 282-293.

¹² E. Jankowska, A. Lundberg, and D. Stuart, “Propriospinal control of last order interneurons of spinal reflex pathways in the cat,” *Brain Res.* (1973), **53**: 227-231.

¹³ A. Lundberg, “Multisensory control of spinal reflex pathways,” *Prog. in Brain Res.* (1979), **50**: 11-28.

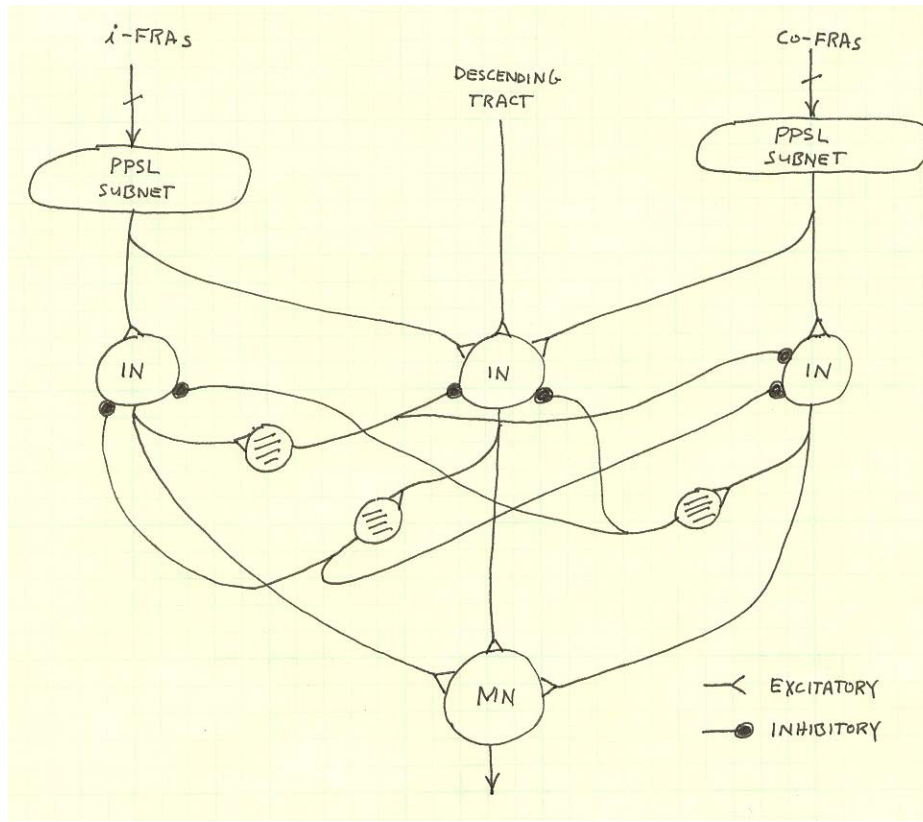


Figure 13: Convergence of ipsilateral and contralateral FRAs and descending tract signals on a motoneuron. (Modified from Jankowska¹² and Lundberg¹³). The interneurons in the figure belong to the MNL network, along with the inhibitory INs mediating lateral inhibition among them. The ipsilateral FRAs (i-FRAs) and contralateral FRAs (co-FRAs) are afferent to interneurons in the PPSL networks. The descending tract signal is a vestibulospinal fiber. The center “descending tract” IN can also be excited by long propriospinal fibers. Volleys from the FRAs can produce facilitation of the descending tract/ propriospinal tract IN in the center of the figure. Lateral inhibition among MNL INs can allow FRAs from one side to dominate the MN control by gating off FRAs from the other side.

5. Some of the afferents belonging to the FRA are excited during an active limb movement. Although nociceptors are not excited by ordinary limb movements (e.g., it usually doesn't hurt to walk), many cutaneous sensors, joint sensors, and group III muscle afferents (and, of course, group Ia, group Ib and group II spindle afferents) are excited from active limb movement. These afferents provide “spatial data” on body position, and this is what makes co-opting the FRA pathway by command signals during locomotion useful.

The alternative pathways of hypothesis 4 above can be divided into two classes. The first class consists of “short latency” reflex pathways, and this is the class represented by figure 13. For purposes of the following discussion we will refer to a member of this class as an “A” network. The other class, which we will call a “B” network, consists of networks exhibiting a late and long-lasting reflex response to FRA signals. “A” and “B” networks seem to come in pairs, in the sense that the same FRAs are input signals to both networks. Furthermore, there is evidence of lateral inhibition between these networks. Finally, there is compelling evidence pointing to an organization of network “B” based on a half-center network, which is the precursor for the formation of a central pattern generator (CPG). Figure 14 is a sketch of the general schema of this arrangement.

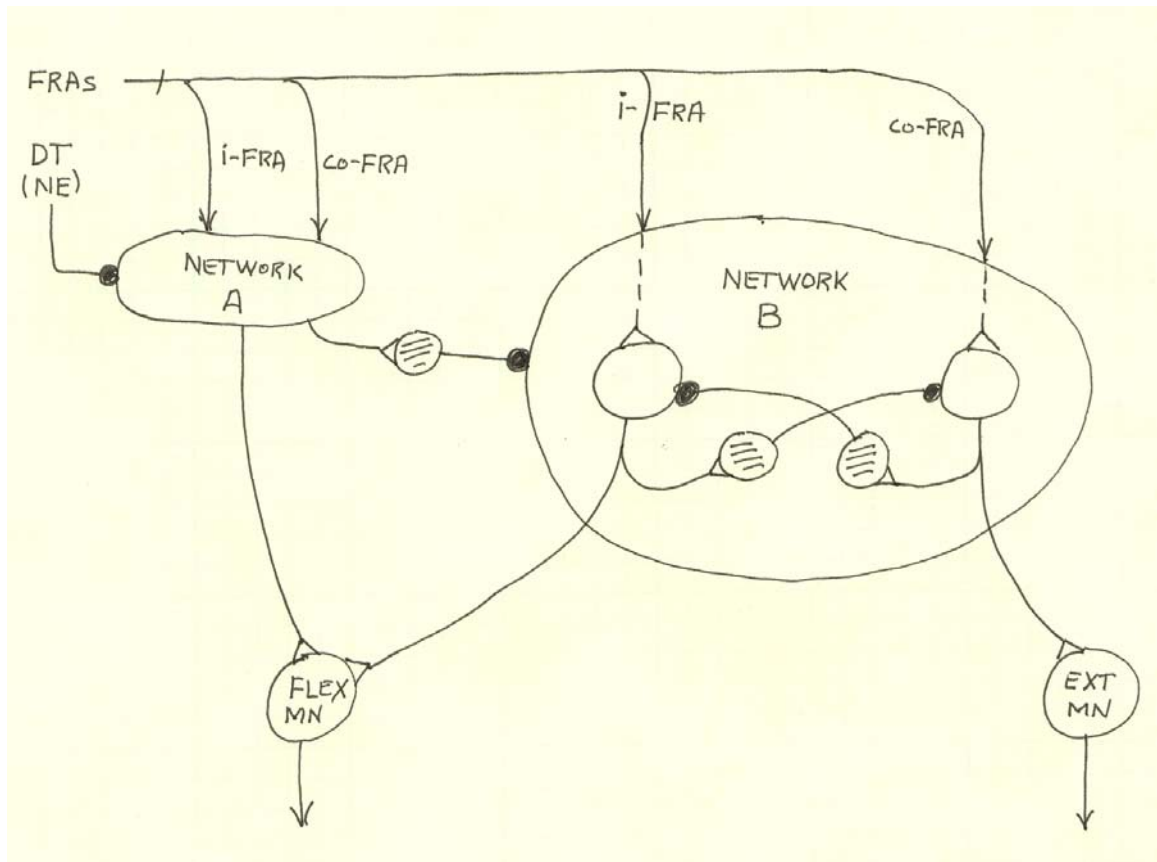


Figure 14: General schema of “A” – “B” FRA network pathways. (Modified from Lundberg¹³). DT = descending tract. NE = norepinephrine (the NTX for the DT). FLEX MN = flexor motoneuron. EXT MN = extensor motoneuron. The dashed lines in network B (----) denote possible polysynaptic pathways from the afferent input. Network A is the network of figure 13. The network A output to the inhibitory IN probably is sourced by a PPSL interneuron. The INs shown within network B are connected in a half-center topology and are probably last order PPSL interneurons. NE is a metabotropic NTX, and its application to network A causes the release of inhibition of network B. The DT input is probably applied to the PPSL subnetworks of figure 13, but the details of this network are not known. However, since the latency through network A is short, the PPSL subnetwork is possibly only a single IN deep. The details of the subnetwork within network B to which the inhibitory input from A is connected are not known, but it is possible that this inhibitory input makes monosynaptic contact with the last-order flexor IN in network B. When network B is enabled and a strong i-FRA volley is applied to it, alternating bursts of activity are produced in the flexor and extensor motoneuron nerves (see figure 15).

Unfortunately, most of the details of network B are still unknown. However, experimental evidence tends to indicate that the INs comprising the half-center network are last-order INs within the network. Furthermore, the EPSPs induced in the flexor MN by network B, and the relatively slow onset and long duration of these EPSPs, is consistent with the hypothesis that these INs use metabotropic second messenger signaling.⁶ Motoneuron nerve activity evoked by a signal from network B in response to a strong i-FRA volley is shown in Figure 15(a). Figure 15(b) shows the EPSPs induced in the flexor MN by network A and by network B. Figure 15(a) is the classic behavior that is to be expected from the actions of a CPG. Note that in order for network B to be capable of signaling to the MNs, the inhibition of network B from network A must first be released. Release of this inhibition is evoked by a noradrenergic (NE) signal from the descending tract input to network A. It is possible that the lateral inhibition of network B by network A is applied directly to the last-order INs shown in network B in figure 14.

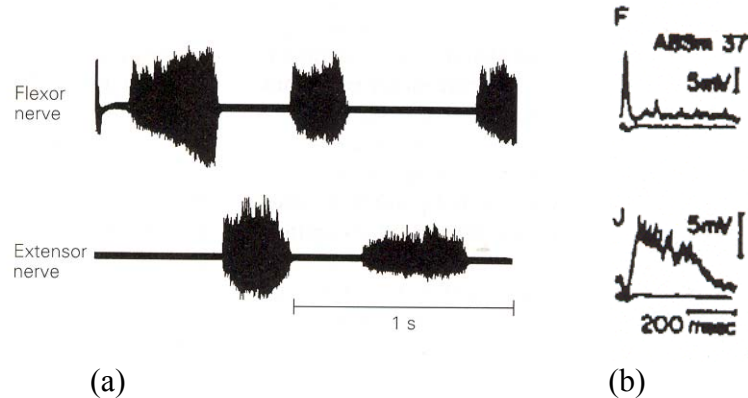


Figure 15: Motor nerve activity and EPSPs registered in the flexor MN from networks A and B. Figure 15(a) illustrates alternating AP bursts in the flexor and extensor nerves following a strong i-FRA volley to network B when network A is disabled by NE input. Figures 15(b) are measured EPSPs registered in the flexor motoneuron from network A (“F” figure) and from network B (“J” figure). The EPSP induced by network A is consistent with an ionotropic synaptic channel. However, the EPSP registered from network B is of such a duration and slow time course as to be consistent with metabotropic synaptic signaling. This implies that the IN projecting to the flexor MN from network B communicates with the MN, and with the inhibitory IN within network B, through a metabotropic second messenger cascade. This hypothesis is also consistent with the long burst lengths registered in the motor nerve activity in (a).

If it is true that the last-order INs in network B use metabotropic second messenger signaling to the MNs, then it follows that these INs belong to the PPSL network. This is because the INs we placed in the MNL in Part III use ionotropic signaling to the MNs. It might also be true that the FRA inputs to the network contact these INs directly, but it seems more likely that they first converge, in different patterns, on other INs (first order INs) which integrate the patterns of inputs and signal to the last order INs of the CPG. The advantage of this two-layer network topology is that it would provide a simpler means of processing joint and limb position information during locomotion. It is already known that rhythmic motoneuron firing patterns during locomotion (e.g. as in walking) depend on joint positions and vary during the four stepping phases in walking (as we noted previously in Part III).¹⁴

Contralateral FRA inputs to network B excite extensors and inhibit flexors (just the opposite behavior from i-FRA inputs). In addition to the FRA inputs to network B depicted in figure 14, this network also receives feedback from group I muscle spindle afferents. Strong stimulation of group Ib afferents (Golgi tendon organ afferents) is capable of interrupting the rhythmic excitation of flexors. This is illustrated in Figure 16. In addition to the group I pathways we have previously discussed (in Part III), this figure illustrates a feedback pathway from group I afferents to network B of figure 14. This pathway is mediated by an excitatory group I interneuron located within the PPSL network. The last order extensor IN in the CPG projects to what we would have to call one of Jankowska’s “Ib-EINs” in the MNL network (cf. Part III). Note that if the signaling by the CPG neurons to the MNs is metabotropic, as the evidence suggests, then it is also likely to be metabotropic in the connection to the “Ib-EIN”, although it is not necessarily true that this must be the case. (Whether a synapse is ionotropic or metabotropic depends on the types of postsynaptic receptors the target cell expresses at the synapse. Most NTX chemicals can bind to either ionotropic or metabotropic receptors).

¹⁴ S. Grillner and S. Rossignol, “Contralateral reflex reversal controlled by limb position in the acute spinal cat injected with clonidine i.v.,” *Brain Res.* (1978), **144**: 411-414.

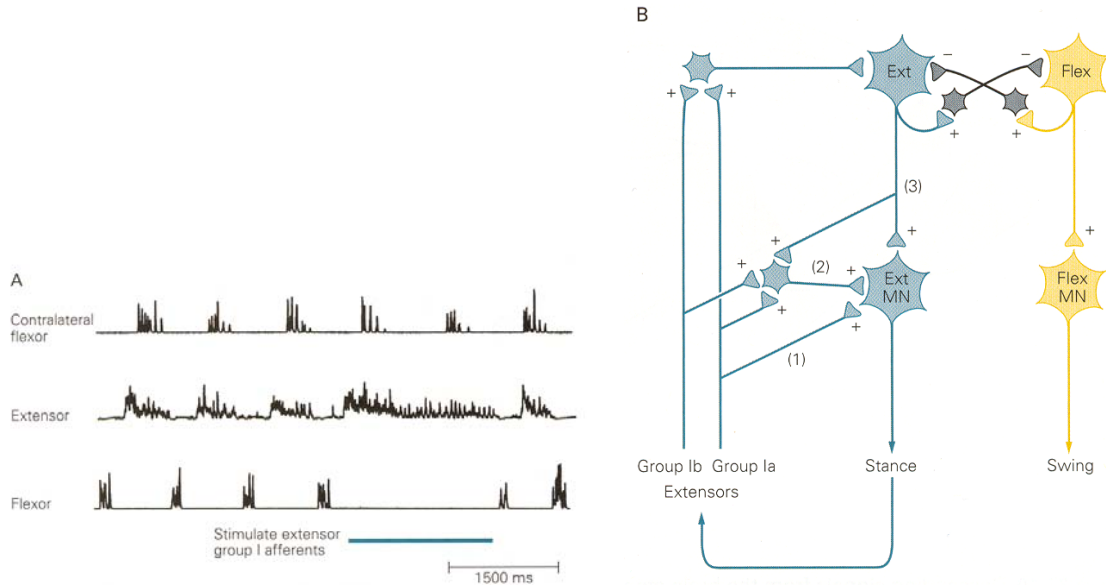


Figure 16: Interaction of group I afferents with CPG action of network B.¹⁵ Stimulation of group Ib afferents from ankle extensor muscles inhibits burst firing in ipsilateral flexors and prolongs the burst in the ipsilateral extensors during walking, as shown in (A). The timing of flexor activity in the contralateral leg is not affected. Stimulation of group Ib afferents from extensors prevents initiation of the swing phase. (B) illustrates the feedback pathways for the group I extensor afferents. + = excitatory synapse, - = inhibitory synapse. The half-center CPG from network B is shown at the top right of the figure. The IN at the top left of the figure is an excitatory IN (which we would probably have to call a “group I IN”) in the PPSL network. The IN mediating the path marked (2) in the figure is one of Jankowska’s “Ib-EINs” and belongs to the MNL network. Note that this IN receives excitatory stimulation from the last order extensor IN in the CPG, which most likely is a metabotropic signal. We should also take note that the network configuration illustrated in figures 13-16 must be repeated on both sides of the spinal segment, since identical control is required for each side of the body. Although no feedback connections leading to the flexor MN (except for the indirect pathway through the CPG) are shown in this figure, it is likely that the group I afferents from the extensor could also help mediate inhibition of the flexor MN via the inhibitory Ib-IN we discussed in Part III.

The network organization we have been discussing must of course be bilateral. In other words, the network topology we have depicted must be repeated on both sides of the spinal segment. This is because appropriate motor control and timing must be applied to both sides of the body during locomotion. Coordination of the two sides can be signaled through the contralateral projections of the FRAs.

Group II and group III muscle afferents modulate the activity of PPSL networks. Motor nerve patterns evoked by the CPG during locomotion are not fixed, stereotyped patterns, but rather depend on limb position as well as other muscle and joint positions (e.g. the hip position). Group II and group III afferents are signals that provide a “gating” mechanism for timing the required switching of the half-center networks. There is some evidence to indicate that at least part of this gating action is mediated through the PPSL subnetworks in network A.¹³ Figure 17 illustrates convergence of FRA pathways with modulation by group II and group III afferents.¹⁰ The IN receiving monosynaptic group II input is the IIVH-EIN we discussed in Part III. The IN at

¹⁵ K. Pearson and J. Gordon, “Locomotion,” in *Neural Science*, 4th ed., E. Kandel, J. Schwartz, and T. Jessell (eds.), NY: McGraw-Hill, 2000, pp. 737-755.

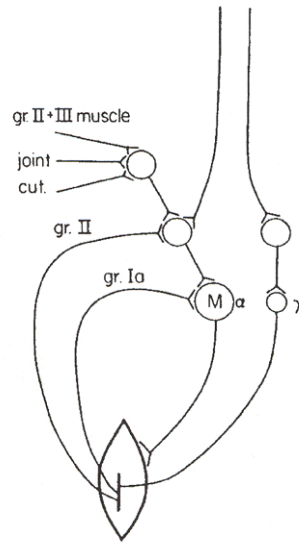


Figure 17: Modulation pathways for group II and group III muscle afferents. The IN receiving monosynaptic group II inputs and projecting directly to the α -MN is a IIVH-EIN located in the MNL network. The IN at the top left of the figure belongs to the PPSL subnetwork of figure 13. The unlabeled inputs coming down from the top of the figure are supraspinal and propriospinal tract signals. This schematic has been simplified by leaving out the connections to the α -MN we have depicted in the previous figures, and the MNL networks we discussed in Part III. The unlabeled IN projecting to the γ -MN represents the MNL INs in the γ -MN network discussed in Part III of this tech brief.

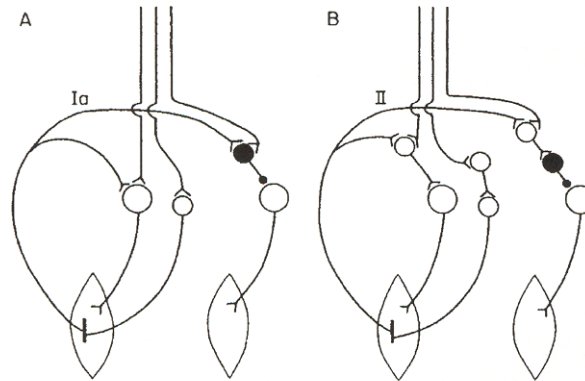


Figure 18: Group II inhibitory pathway to the antagonist MN. (A) illustrates the inhibitory pathway for group Ia muscle spindle afferents via the Ia-IN. (B) depicts the group II inhibitory pathway, and we can note the similarity between the two figures. The PPSL IN of figure 17 is omitted from the figure. The IN at the upper right in (B) is a group II EIN, but this one belongs to the PPSL rather than the MNL network. It projects to an inhibitory IIVH-IIN in the MNL network, forming a trisynaptic pathway to the antagonist MN.

the upper left of the figure is an integrating IN in the PPSL subnetwork of figure 13. As the figure indicates, the FRA pathway from this IN to the α -MN is trisynaptic. As for the details of what comprises these FRA-GRA inputs, refer to the discussion of the IIVH-IN in part III.

Figure 17 illustrates the excitatory pathway for group II afferents and the FRA-GRA pathways. It is important for us to keep in mind that along with this excitation of the agonist MN, these afferents also effect an inhibitory pathway to antagonist MNs.¹⁰ This is illustrated in Figure

18. Figure 18(A) merely repeats what we said in Part III regarding the reciprocal Ia inhibitory pathway mediated by the Ia-IN in the MNL network. Figure 18(B) is the inhibitory pathway for group II afferents. The agonist muscle is shown on the left, the antagonist on the right. The agonist INs are the same as depicted in figure 17, except for the fact that the figure omits the PPSL IN mediating the FRA-GRA pathway. The excitatory IN at the upper right of (B) is a group II EIN, but it is located in the PPSL network and is not the IIVH-EIN of the MNL network that we discussed in Part III. It is probably one of the IIDH-EINs mentioned in Part III. The inhibitory IN shown in (B) is the IIVH-IIN in the MNL that we discussed in Part III of this tech brief.

In examining figure 18, it is worth bearing in mind that there must be a similar network (i.e. figures 17 + 18) making connections to what in figure 18 is the antagonist muscle network. We can expect that the FRA-GRA connections will show differences in terms of what is projected to the antagonist. This is because one of these two muscles will be an extensor, the other a flexor. It is known that flexor α -MNs are the main target of excitatory interneurons in group II pathways, while extensors are the main target of inhibitory interneurons in group II pathways.¹ However, “main target” does not mean “only target” and excitatory group II INs have access to extensor MNs, and inhibitory group II INs have access to flexor MNs. In terms of FRA afferents, flexor MNs are predominantly excited from ipsilateral FRAs, while extensor MNs are predominantly excited from contralateral FRAs.

In addition, we saw in Part II that there are FRA-GRA pathways to γ -MNs, with group II pathways preferentially targeting dynamic γ -MNs, and group III pathways preferentially targeting static γ -MNs. The circuits in the PPSL networks forming pathways to γ -MNs are not known, but it is reasonable to use the topologies illustrated in the previous figures as a starting point for the γ -MNs.¹ It is not unlikely that the principal differences in pathways to flexor and extensor α -MNs and to γ -MNs is likely to be in the sources of the afferents and their number participating in those pathways. Data on the distribution of sources was presented in Part III.

FRA and Presynaptic Inhibition

Flexor reflex afferents also are implicated in pathways that evoke presynaptic inhibition of group Ia muscle spindle afferents. This appears to be an important constituent in control and stabilization of the flexor reflex. In addition, FRA-evoked presynaptic inhibition provides us with some additional clues about the internal structure of PPSL networks A and B.¹⁶

FRA-evoked presynaptic inhibition of Ia afferents shows itself to be capable of very specific targeting of particular pathways. It is this specificity that provided the first clue that presynaptic inhibition could be effected via interneurons and that PAD inhibition was localized to specific presynaptic terminals of Ia afferents. That FRA pathways are the source of this inhibition was indicated by the observation that FRA volleys produced dorsal root potentiation (DRP), i.e. depolarization of nerves in the dorsal root.

We saw earlier that Ia afferents could evoke PAD inhibition of Ia afferents. Volleys in the FRAs are known to effectively depress PAD evoked by volleys of Ia afferents from flexors in Ia afferents from other muscles. The time course over which DRP remains depressed following FRA volley is relatively lengthy, which to me suggests that the mechanism in the FRA pathway

¹⁶ A. Lundberg, “Integration in the reflex pathway”, in *Proc. 1st Nobel Symposium: Muscular Afferents and Motor Control*, June 1965, Södergarn, Sweden, R. Granit (ed.), NY: John Wiley & Sons, 1966, pp. 275-305.

involves metabotropic signaling⁶, which has a much longer time course than ionotropic signaling. Figure 19 illustrates a typical DRP depression vs. time response.

Concurrently, the FRA volleys remove presynaptic inhibition acting upon Ia EPSPs in extensor MNs that had been evoked by Ia afferents. In other words, if Ia volleys had previously evoked presynaptic inhibition of the Ia pathway to extensor MNs, FRA volleys could remove this inhibition. Lundberg's presentation of these findings in 1965¹⁶ was hampered a great deal by lack of data available at that time, but in light of later results, most of which we have already presented in this tech brief, it is possible to add some detail to the pathway circuits he presented. The effect of which we currently speak appears to involve PPSL interneurons in network A of figure 14. Figure 20 illustrates a hypothetical network A topology suggested by the available data.

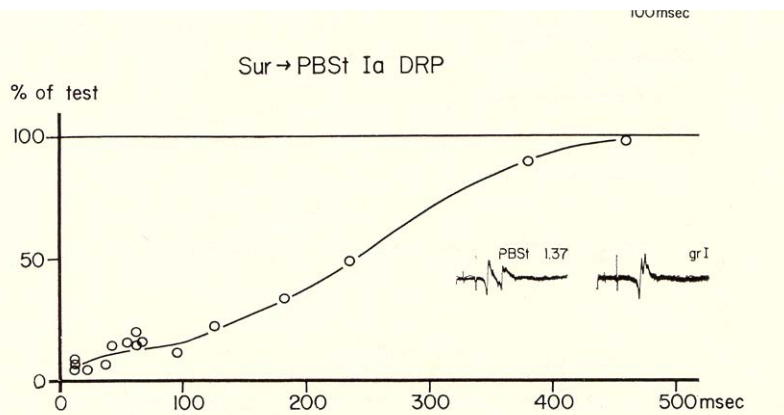


Figure 19: Depression in dorsal root potential due to FRA volleys. The time scale over which Ia afferent evoked PAD inhibition of other Ia afferents is depressed is consistent with metabotropic signaling mechanisms.

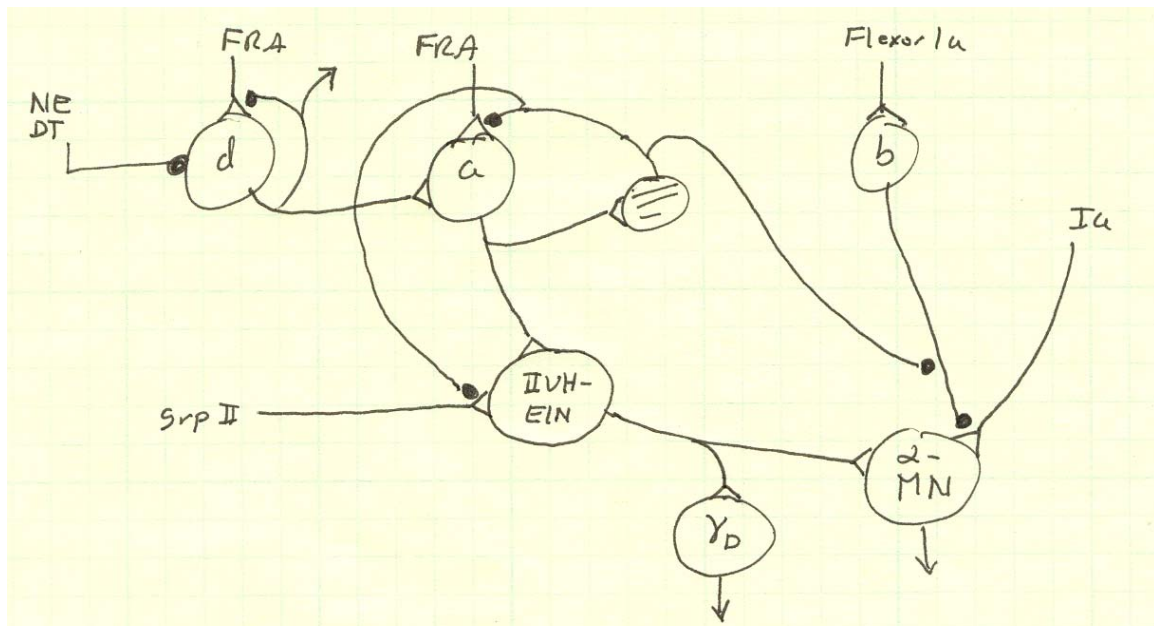


Figure 20: Putative "A" network illustrating FRA-evoked presynaptic inhibition. The two MNs and the IIVH-EIN belong to the MNL network level. The other interneurons, d-IN, a-IN, b-IN and the inhibitory IN belong to PPLS network A of figure 14.

There are several things to note in figure 20. First, the “d” interneuron (“d-IN”) receives an inhibitory noradrenergic (NE) input from a supraspinal descending tract. This synapse is metabotropic, and so inhibition of d-IN by NE is relatively long-lasting. I propose the hypothesis that the d-IN is the interneuron mediating inhibition of network A, and that inhibition of d-IN has the collateral effect of enabling the activity of network B in figure 14. (This is what the arrow shown going off from d-IN is meant to indicate in this figure; we will discuss that arrow’s pathway shortly). The second thing to note is that the axon of the d-IN makes both an excitatory contact with the a-IN and an inhibitory presynaptic connection to FRA presynaptic terminals at d-IN’s own input. The only kinds of NTXs capable of both these actions from the same axon are NTXs that can bind to metabotropic receptors which initiate long-lasting second messenger signaling processes.⁶ Although d-IN has not been specifically identified (so far as I know), ACh is an NTX that is known to have both excitatory and inhibitory metabotropic receptors.¹⁷ I make the hypothesis that the recurrent presynaptic inhibition of d-IN is evoked through metabotropic activation of the G-protein-dependent inward-rectifier potassium (GIRK) channel, and that the excitatory synapse it makes with the a-IN is likewise a G-protein-activated second messenger process. Thus, excitation of the d-IN by FRA produces a long-lasting excitatory bias of a-IN which, although not sufficient by itself to cause the a-IN to produce action potentials, “enables” a-IN to respond to the FRA converging on it. When d-IN is inhibited by NE, the a-IN loses this necessary “bias” and is effectively “gated off”.

The a-IN in combination with the inhibitory IN has three actions. First, FRA-evoked excitation of the a-IN produces excitatory bias of a MNL IIVH-EIN, which lowers the IIVH-EIN’s threshold insofar as the ability of group II muscle afferents to excite it is concerned. Note that the IIVH-EIN targets both an α -MN and a dynamic γ -MN for the same muscle. This is consistent with Appelberg et al.’s earlier finding that group II spindle afferents preferentially target dynamic γ -MNs (see Part II). I propose that the a-IN synapse with the IIVH-EIN (and also with the inhibitory IN) is ionotropic (that is, it is a normal, fast-acting NTX-gated ion channel).

Second, activation of the a-IN excites an inhibitory IN that targets two effects. The first of these is a presynaptic inhibition of FRAs converging on the a-IN. This type of recurrent inhibition has the function of regulating and stabilizing the maximum firing rate of the a-IN in response to FRAs. This action also inhibits the transmission of group II afferents via the IIVH-EIN. The other effect of the inhibitory IN (and this is the third of the three FRA-evoked actions of a-IN) is an axoaxonal inhibition of the signaling path from the b-IN shown in figure 20. The b-IN is a PPSL interneuron that responds to Ia afferents from flexors by inhibiting Ia excitation of the extensor MN shown in the figure. This is the mechanism by which DRP depression, such as shown in figure 19, is effected by FRA volleys. To be consistent with figure 19, this axoaxonal inhibition would have to be effected by a metabotropic receptor such as the GABA_B receptor. Interneuron b-IN has also not been identified, but it is likely to be located in the dorsal horn.

The original evidence leading to our division of the PPSL structure into an A and a B network was based upon experiments where the subject animal was administered the drug DOPA. DOPA is a precursor molecule for dopamine, norepinephrine (NE), and serotonin (5-HT). DOPA experiments also showed that there is a slow, long-lasting suppression of PAD by FRAs. This action we associate with the B network. Figure 21 illustrates the hypothetical network pathways mediating this effect.

¹⁷ B. Hille, *Ion Channels of Excitable Membranes*, 3rd ed., Sunderland, MA: Sinauer Associates, 2001, pp. 219, 231.

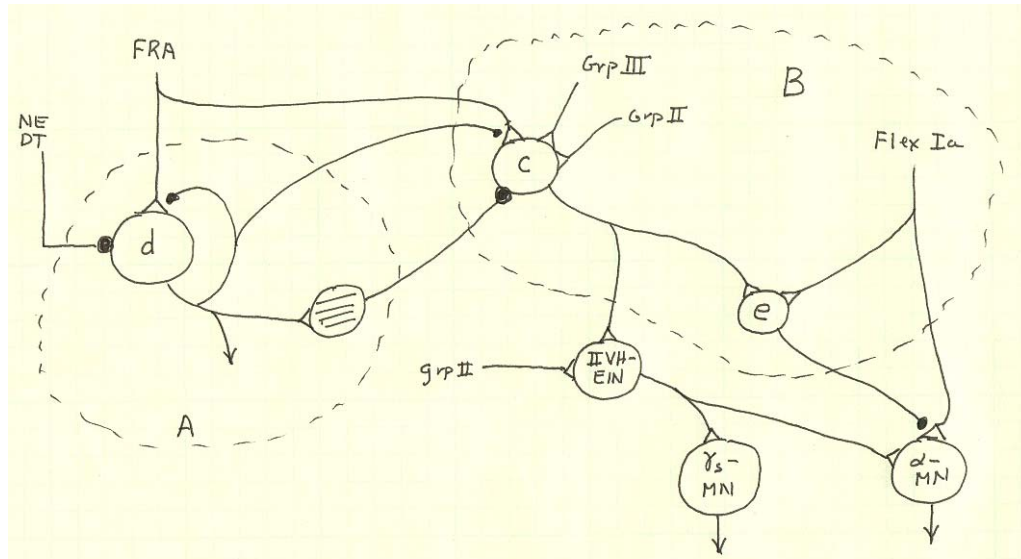


Figure 21: B network presynaptic inhibition of Ia afferents and group II facilitation by FRA volleys.

Interneurons “c” and “e” belong to PPSL network B. The d-IN belongs to PPSL network A. Within network A, the d-IN projects to yet another inhibitory IN, which corresponds to the inhibitory IN in figure 14. Inhibition of the d-IN by the NE signal from the descending tract (DT) disables the A network and enables the B network after a recovery latency. (Recall that the d-IN is presumed to employ metabotropic signaling). Release of the c-IN by the d-IN enables the FRA pathway to the MNs and the II VH-EIN at the MNL. Unlike the A network in figure 20, where activation of the a-IN inhibits group II transmission, activation of the c-IN enables group II transmission to the extensor MN and to a static γ -MN. Because group III afferents favor static γ -MNs, I propose that this is the principal pathway for group III excitation of the so-called “ α - γ loop”. The e-IN is excited by c-IN APs, but still requires Ia afferent input from flexors in order to mediate presynaptic inhibition of these afferents (with accompanying DRP). The arrow leaving the d-IN goes to the other neurons depicted in figure 20.

When the d-IN in network A is active, it effectively gates off the c-IN in network B. (Recall that we presume the actions of the d-IN are metabotropic). When d-IN is inhibited by descending tract signals (using the metabotropic NTX norepinephrine, NE), this releases the inhibition of FRA pathways into network B. FRA and group III afferents are now free to facilitate group II afferents to the α -MN and to a static γ -MN. (Recall from Part II that group III muscle afferents favor excitation of γ -MNs). We may likewise suppose that c-INS are first-order interneurons in the FRA pathway to the half-center CPG network of figure 14. Whether this requires two c-INS in network B (one for ipsilateral, one for contralateral FRAs) remains to be seen.

Propriospinal and Ascending Tract Efferents

An efferent is an output signal. In addition to motor nerve efferents, spinal cord networks also produce efferents that feed to other spinal cord segments (propriospinal tracts) and that send what are, in effect, “status signals” back up the spinal cord to higher centers in the brain (ascending tracts).

In the strict sense, any IN that projects to targets in other spinal segments is a propriospinal (P-IN) interneuron. Many of the INs we have already named project to nearby segments and so are in the strict sense P-INS. Of special note are those P-INS making very long projections (the so-called “long P-INS”). These are located in the cervical segments, which control neck, shoulders, arms, and hands. Part of controlling lumbar circuits in voluntary movement involves what have

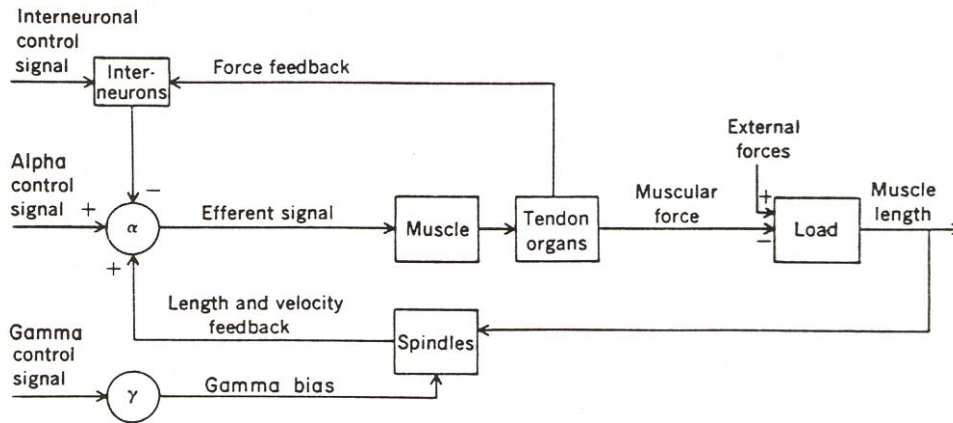


Figure 22: Simplified block diagram of motor control servo system. The lines in the diagram should be regarded as bussed signals. The circles labeled α and γ represent the MNL networks of INs as well as the MNs. The alpha control signals come from descending supraspinal tracts and long propriospinal P-INs, and play the role of activating or inactivating selected muscles for an intended movement or outcome. The interneuronal control bus, also of supraspinal and propriospinal origin, provides a reference for the intended force to be employed in the movement such that if the actual force applied exceeds the reference inhibitory signals are applied to the appropriate α -MNs. A part of the control signal input to this block, as well as a part of the alpha control signal bus, is made up of coordinating signals from long propriospinal INs that provide “error signals” conveying information about the position and motion of the rest of the body. This diagram is incomplete in the sense that it does not show ascending tract signals going back to the higher coordinating centers in the brain stem and cerebellum. These coordinating centers are part of the body’s overall “feedback control system”, but their primary focus is on the overall body state rather than the state of individual muscles. Direct control of individual muscles belongs to the “servo system” shown here.

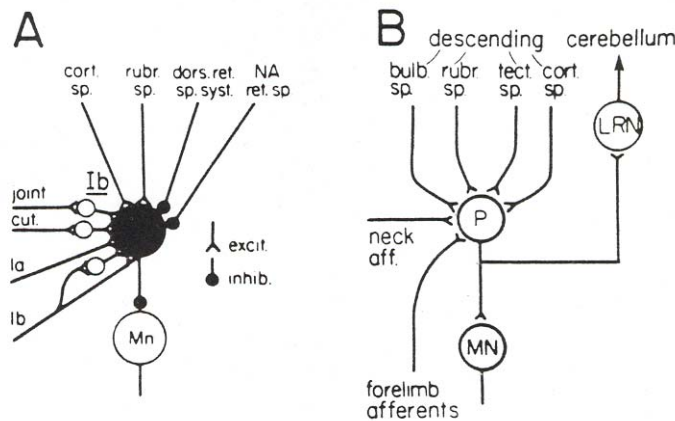


Figure 23: Comparison of the Ib-IN (A) and the cervical long P-IN (B). Both INs receive descending tract command signals of supraspinal origin, and both project to MNs. The function of the P-IN is to integrate afferent information from the neck and forelimbs (arms, in human beings) and apply this information to setting the excitation level in lumbar MNs. These neck and limb afferents include FRA pathways, mediated by PPSL networks that are probably similar to those we have already discussed. The P-IN also projects to the inhibitory Ia-IN (not shown), and it has a collateral that ascends to the lateral reticular nucleus (LRN) in the brain stem. This project to the LRN updates the higher integrating centers with body state and posture information, and is used by the brain to alter descending tract signals.

been termed “motor programs” executed in supraspinal command circuitry in the cerebellum and brain stem. Part of the execution of these “motor programs” involves what is known as the “mind

set” mechanism, whereby intended movement is signaled to spinal neurons as a kind of “reference signal.” This information can be thought of as analogous to the “reference signal” or “set point” signal employed in classical servo control systems, e.g. Figure 22. The interneuronal control signals, alpha control signals, and gamma control signals shown in this figure convey this “set point” information to the servo circuitry that directly controls muscle activation and inactivation. One primary function of long propriospinal interneurons is to convey control signals to the lumbar circuitry to stimulate corrective movements when overall body posture, position, or movement departs from the intended body state.

Figure 23 illustrates the long cervical P-IN in comparison to the inhibitory Ib-IN. The P-IN is an integration center for afferent information from peripheral nerves in the cervical segments. It receives descending tract information from the bulbospinal, rubrospinal, tectospinal, and corticospinal tracts. It returns FRA information to the lateral reticular nucleus (LNR) in the brain stem, which coordinates rhythmic activities in several limbs during voluntary locomotion. This coordination leads to changes in descending tract command signals that correct movement and posture when the body state does not match the intended movement.¹⁸ The P-IN also transmits this information to MNs and Ia-INs in the lumbar region, where it targets specific muscle groups as required in order to coordinate whole-body posture and movement.

In effect, the brain maintains a “map” of actual body state and a “map” of desired body state. The job of the motor control system is to see to it that these maps match up. When they do not match, the motor control system must execute the appropriate coordinated movements to bring the actual into agreement with the desired. It is not out of place here to make a comment or two regarding the analogy between the motor control system and engineering servo systems. A “servo” is a type of control system that incorporates two distinct control functions. The first, and probably most familiar to you, is called the “regulator.” A regulator’s job is to see to it that the output of the “plant” being controlled matches a desired, static reference signal. The biological equivalent of this is posture. A regulator’s primary function is the rejection of and correction for disturbances that tend to move the output of the “plant” away from the desired reference state.

The second job of a servo system is called tracking (sometimes called “following”). A tracking system’s function is to make the output of the “plant” follow (“track”) a time-varying reference signal. For example, when a disk drive executes a “seek” it moves the recording and playback heads to a different track on the disk. Disk drives are designed to do this as quickly as possible in order to minimize the amount of time required to access the data. Whereas a regulator makes the system be “stiff” (resistant to change), a tracker has just the opposite effect, namely to make the system change quickly and expeditiously, correcting for disturbances as it goes. It may perhaps be obvious to you that these two functions, regulation and tracking, are to some extent contrary to each other. In a disk drive during the execution of a seek, the normal regulator control pathways are disabled and a new set of control pathways, designed to expedite the desired change, are put in place. At the end of the seek (called the “settle phase”), the regulator pathways are re-enabled so that the system may resume the task of regulating head position over the data track. During a seek, the disk controller produces a desired position and velocity trajectory (the “desired response” that is the reference for the control of moving the disk head). The “seek control” circuitry (including the firmware executed by a microcontroller that “runs” the servo system) is tasked with making the actual position and velocity match this desired profile.

The analogy between this and biological motor control should be obvious. Execution of voluntary movement is the analog of tracking, instant-by-instant, the desired body positions that

¹⁸ V.B. Brooks, *The Neural Basis of Motor Control*, NY: Oxford University Press, 1986, pp. 88-90.

reflect the intent of the movement. Maintenance of posture, on the other hand, is the analog of the servo regulator function. In order to perform either function, but especially in order to be able to execute the tracking servo task, ascending signals conveying information about the actual body state must be returned to the higher coordinating centers in the brain. At the spinal cord level, this is carried out by ascending tract interneurons (T-INs). The cervical P-IN in figure 23 plays such a role by means of the collateral it projects to the LNR. The benefit of this “short loop” back to the brain is speed; the higher centers do not have to wait for information to come back from the long loops that pass through the peripheral nervous system in order to tell if the gross body state matches the desired map. However, for detailed control and corrective actions, the brain does require more detailed (if still highly integrated) information from specific “counties” in the body map. This is where T-INs in the lower parts of the spinal cord come into the picture.

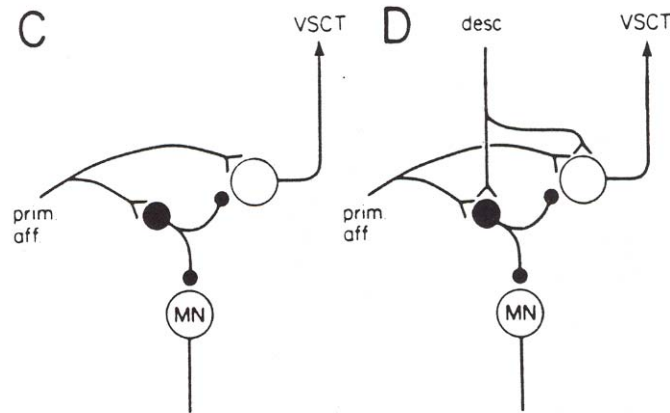


Figure 24: Two examples of T-IN PPSL circuits returning primary afferent information to the ventral spinocerebellar tract. Open circles are excitatory neurons, filled circles are inhibitory Ia-INs. (C) illustrates a T-IN that monitors the input and output of a Ia-IN. Since the primary afferent pathway to the MN is in this case inhibitory, the T-IN in effect “compares” the afferent input to the actual signal going to the MN and signals the cerebellum (via the VSCT) if MN is not actually inhibited. (D) illustrates much the same thing except this time the comparison is expanded to include descending tract command information.

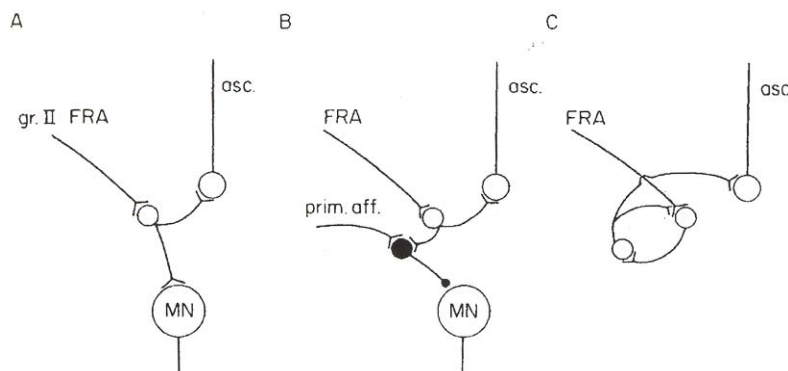


Figure 25: T-INs relaying group II and FRA information to the brain. These circuits are not “comparators” like those of figure 24. Instead, they transmit integrated information about FRA-GRA pathways. In (A) actual MN excitation responding to a GRA reflex pathway is signaled. (B) illustrates transmission of FRA information intended to cause MN inhibition. This is data regarding body state rather than actual MN state. (C) illustrates a special channel to the cerebellum that signals FRA-evoked presynaptic inhibition of an FRA-GRA pathway IN.

Figure 24 illustrates two PPSL network circuits that compare primary afferent signals, whose actions should be to inhibit the MN, to whether or not the MN is actually being inhibited. It transmits the outcome of this comparison to the cerebellum via the ventral spinocerebellar tract (VSCT). The figure illustrates in (C) a simple comparison of primary efferents only. (D) shows how descending tract command information can be incorporated into the comparison. This figure illustrates what is probably the most common function of T-INs, namely comparison of commands with the actual state of MN excitation.

Group II and FRA pathway information is also relayed to coordinating brain centers by T-INs. Figure 25 illustrates three PPSL circuits conveying interneuron activity to the brain. Note that in figure 25C the network imputes a presynaptic, recurrent facilitation of FRA converging on the interneuron, an action that is capable of producing a lengthy burst signal in the ascending pathway. In all three cases, the conveyed information reflects how FRA is exerting control over MN activity.

Summary

This brings us to the close of this tech brief. The PPSL networks have the function of integrating information over a wide spatial region of the body, controlling the reflex arc, and co-opting the basic reflex circuitry of the MNL networks in the execution of voluntary movement. The PPSL is comprised of a fractionated collection of interacting subnetworks, each typically only one or two neurons deep. Its two principal tasks involve the proper incorporation of FRA signals to target specific MNs for activation or inactivation, and to provide feedback information to higher coordinating centers in the brain. This feedback not only provides the brain with data required to form its “actual” body map, but also to provide information that allows comparison of actual with desired body maps.

Compared to the MNL, the PPSL is the least well understood part of the spinal cord system. Probably the majority of its neurons are dorsal horn INs, but at least some of them are located in the intermediate zone or the ventral horn. We can probably best regard the PPSL networks presented here as “basic themes” from which more specific “variations on a theme” can be evolved or designed. This is a less satisfactory state of knowledge than we would have if the PPSL networks were better mapped out and understood. But I’m afraid that for at least now this is probably the best we can do for our background research into bipedal locomotion.

Left almost untouched by this tech brief is the issue of the supraspinal control system. This topic merits attention, but for at least the next year or two it is probably well beyond what we can do with regard to the bipedal locomotion problem. It has perhaps become apparent in the closing section of Part IV that descending tract command signals are of a more dynamical than static nature. It would naturally follow from this that by not presenting more data on supraspinal control this tech brief is leaving us somewhat under-equipped for the task at hand. However, I can offer two final observations. First, any electromechanical platform we might build as part of implementing a bipedal system is going to be far less complicated than a cat or a human, so how much good more current knowledge of descending tract command signals would do us is somewhat problematic. Second, the brain is far more complicated than the spinal cord. In the case of the spinal cord we at least have a rather unambiguous output, namely muscle movement. In the case of the brain, what functions are actually being carried out by its various cell assemblies is far less easy to figure out. One way we might perhaps be able to make lemonade out of the current shortcomings in our data could be to figure out through EC algorithms what kinds of descending tract control signals are necessary to carry out SSMS functions properly. If we can do that, it will

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provide a foundation for future projects aimed at addressing the higher brain functions involved in biomimic robotics.

R. Wells
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