The Neuromuscular Transform: The Dynamic, Nonlinear Link Between Motor Neuron Firing Patterns and Muscle Contraction in Rhythmic Behaviors

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Brezina, Vladimir, Irina V. Orekhova, and Klaudiusz R. Weiss. The neuromuscular transform: the dynamic, nonlinear link between motor neuron firing patterns and muscle contraction in rhythmic behaviors. J. Neurophysiol. 83: 207–231, 2000. The nervous system issues motor commands to muscles to generate behavior. All such commands must, however, pass through a filter that we call here the neuromuscular transform (NMT). The NMT transforms patterns of motor neuron firing to muscle contractions. This work is motivated by the fact that the NMT is far from being a straightforward, transparent link between motor neuron and muscle. The NMT is a dynamic, nonlinear, and modifiable filter. Consequently motor neuron firing translates to muscle contraction in a complex way. This complexity must be taken into account by the nervous system when issuing its motor commands, as well as by us when assessing their significance. This is the first of three papers in which we consider the properties and functional role of the NMT. Physiologically, the motor neuron–muscle link comprises multiple steps of presynaptic and postsynaptic Ca$^{2+}$ elevation, transmitter release, and activation of the contractile machinery. The NMT formalizes all these into an overall input-output relation between patterns of motor neuron firing and shapes of muscle contractions. We develop here an analytic framework, essentially an elementary dynamical systems approach, with which we can study the global properties of the transformation. We analyze the principles that determine how different firing patterns are transformed to contractions, and different parameters of the former to parameters of the latter. The key properties of the NMT are its nonlinearity and its time dependence, relative to the time scale of the firing pattern. We then discuss issues of neuromuscular prediction, control, and coding. Does the firing pattern contain a code by means of which particular parameters of motor neuron firing control particular parameters of muscle contraction? What information must the motor neuron, and the nervous system generally, have about the periphery to be able to control it effectively? We focus here particularly on cyclical, rhythmic contractions which reveal the principles particularly clearly. Where possible, we illustrate the principles in an experimentally advantageous model system, the accessory radula closer (ARC)–opener neuromuscular system of Aplysia. In the following papers, we use the framework developed here to examine how the properties of the NMT govern functional performance in different rhythmic behaviors that the nervous system may command.

INTRODUCTION

Cyclical, rhythmic behaviors such as biting, chewing and swallowing, breathing, and many different kinds of locomotion feature prominently in the behavioral repertoires of both vertebrates and invertebrates (Gray 1968; Pearson 1993; Stein et al. 1997). Such behaviors appear to unfold in an integrated and efficient manner, but this can only be if their muscular plant is successful in operating within specific constraints. Usually a number of muscles are involved, and the contractions of each muscle must be appropriate in amplitude and timing, not just in themselves but in relation to those of the other muscles. Furthermore, although the basic pattern of the behavior may be stereotyped, its parameters can often vary over a wide range to meet behavioral demands: for instance, the behavior can speed up or slow down manyfold. The muscles must remain effectively coordinated throughout. Finally, at different times the same muscles may be used in different behaviors, with different contraction and coordination requirements.

In the nervous system, such rhythmic behaviors are generated by central pattern generators (CPGs) (Harris-Warrick et al. 1992; Marder and Calabrese 1996; Pearson 1993; Stein et al. 1997). Neurons of the CPG fire cyclically in various patterns and phase relationships; the patterned activity is distributed to motor neurons (in some cases these may themselves be elements of the CPG) and to the muscles. Like the behaviors they generate, CPGs exhibit plasticity that modulates the basic pattern or even reconfigures the CPG entirely to switch between different behaviors (Dickinson 1995; Harris-Warrick et al. 1992; Katz 1995; Stein et al. 1997).

Thus a set of neurons with a certain complex pattern of activity drives a set of muscles to contract, likewise, in a certain complex, functionally meaningful pattern. It is easy to assume (especially because experimental work often focuses on just one or the other) that the linkage between these two halves of the whole system is straightforward, so that, for instance, changes seen in the pattern of activity of the CPG will automatically be read out as similar changes in the pattern of muscle contractions, and furthermore will constitute functional changes in the behavior. However, this is often not so.

Figure 1 illustrates this in the case of a pair of antagonistic muscles whose alternating contractions combine in an oscillatory movement that must meet a certain criterion for functional behavior. This illustration is in fact based on the functioning of a real system, the accessory radula closer (ARC)–opener neuromuscular system of Aplysia (Cohen et al. 1978; Evans et al. 1996; Weiss et al. 1992, 1993). The opposing contractions of the two muscles (top), driven by alternating bursts of motor neuron firing (middle), produce a combined movement (bot-
FIG. 1. Example of the problem: decreasing cycle period distorts and eventually completely eliminates functional rhythmic behavior. This figure uses some real experimental data to update the conceptual model of Weiss et al. (1992, 1993) of the functioning of the antagonistic radula closer-opener neuromuscular system of *Aplysia*. The radula is a handlike structure that the animal protrudes from its mouth to grasp food; the radula must alternately close to grip the food while it is being pulled in and open to release the food into the esophagus. The accessory radula closer (ARC, or I5) muscle (Cohen et al. 1978) is a larger and stronger muscle than the antagonistic radula opener muscle complex I7-I10 (Evans et al. 1996).

Left column, top: actual recording of length of the ARC muscle (in a reduced preparation, however, isolated from the opener), showing contractions produced by firing of its motor neuron B15 in a slowly cycling pattern (schematized below), with burst duration $d_{\text{intra}} = 5.1$ s, interburst interval $d_{\text{inter}} = 9.1$ s, intraburst frequency $f_{\text{intra}} = 14$ Hz, and so cycle period $P = 14.2$ s, duty cycle $F = 0.36$, and mean frequency $\bar{f} = 5$ Hz (for definitions see Fig. 2 and Input firing patterns in RESULTS). Shown are 2 cycles after the contractions had stabilized at their steady-state shape and amplitude. The record used for the antagonist (i.e., radula opener) muscle (downward from the fully relaxed line) is, for the sake of simplicity in this conceptual illustration, just the ARC record inverted, scaled to $\frac{1}{3}$ amplitude, and half-cycle out of phase. Left, bottom: the net movement has been derived by summation of the contraction waveforms of the 2 antagonist muscles. It is assumed that functional behavior (repetitive, alternating closing and opening of the radula) requires that the movement make transitions across the zero line, marked axis of functional movement (cf. Weiss et al. 1992, 1993). Middle: as in left, but with the cycle period decreased $9$-fold ($d_{\text{intra}} = 0.58$ s, $d_{\text{inter}} = 1.02$ s, and so $P = 1.6$ s, but $F$, $f_{\text{intra}}$, and $\bar{f}$ as before). Thin traces predict the contractions and movement that would be recorded in an ideal period-invariant system: i.e., the records, left, simply compressed in time without distortion. Thick traces show the contractions of the ARC muscle that were actually produced by the faster firing pattern, and further records derived from them as before. Right: 2 cycles from the middle column at an expanded time resolution (expanded again by the same factor of $9$ by which the period was compressed). It can be seen that the decrease in cycle period has entirely eliminated functional behavior: the net movement (thick trace, bottom right) no longer makes the transitions across the zero line that close and open the radula. Although this is primarily a conceptual illustration, it is worth noting that it is not grossly inconsistent with what is known about the functioning of the intact closer-opener neuromuscular system in vivo (see Paper II). In particular, the slow cycle period used here is entirely physiological, and the fast one only slightly faster than physiological (e.g., Susswein et al. 1976, 1978; Weiss et al. 1986).
which, to be functional, must alternately cross the axis of functional movement. At slow cycle speed (left), this is possible. However, as the neural circuitry decreases the cycle period in an attempt to speed up the behavior (middle, expanded at right), the muscle contractions change shape so that the behavior does not simply become compressed in time, as one might naively expect, but becomes increasingly distorted and eventually completely dysfunctional (bottom right).

Analysis of such phenomena can be regarded as a problem in pattern dependence. How do different patterns of neuronal firing translate, through what we may call the neuromuscular transform (NMT), to muscle contractions and to functional behavior? We have recently presented some general ideas about pattern dependence in biological processes (Brezina et al. 1995–1997). Here and in the following paper (Brezina and Weiss 2000, henceforth referred to as Paper II), we expand and apply these ideas to the neuromuscular problem in particular. We consider the problem theoretically from first principles and, whenever possible, use the Aplysia ARC-opener neuromuscular system as a real illustration. The aim is to develop a framework with which to answer such questions as: What parameters of the firing pattern are important for different parameters of contraction and functional behavior? Can it be said, even, that certain parameters of the firing pattern “code” for certain parameters of contraction and behavior? Given a firing pattern, what contractions and behavior will it produce? Conversely, given a behavioral requirement, what firing patterns are optimal? It will be seen that, with a fixed NMT, behaviors with certain parameters are not possible with any firing pattern. However, as we show in the last paper in this series (Brezina et al. 2000, referred to as Paper III), the range of possible behaviors can be greatly expanded by appropriately tuning the NMT through peripheral neuromuscular plasticity and modulation.

**METHODS**

Motor neuron–evoked contractions of the ARC muscle of Aplysia were measured as in previous studies (Brezina et al. 1995–1997). Briefly, motor neuron B15 was intracellularly stimulated to fire spikes in the desired pattern; to assure control over the pattern, each spike was elicited by a separate brief current injection. (The patterns used are described in Input firing patterns in RESULTS.) The muscle contracted isotonically against a light load; length was measured with an isotonic transducer.

**RESULTS**

**General strategy**

We begin by considering an elementary motor unit: a single muscle controlled by a single motor neuron. Firing of the motor neuron evokes contraction of the muscle via a sequence of intermediate steps, including propagation of the action potentials into the motor neuron terminals, release of transmitter, reception and propagation of the signal in the muscle, elevation of Ca^{2+}, and activation of the contractile machinery. The quantitative details of these intermediate steps are, in general, unknown. However, the first and last elements in the sequence, namely the firing of the motor neuron and the contraction of the muscle, are easily measurable, and every pattern of firing produces some observable state of contraction of the muscle. This allows us to represent the overall activity of the motor unit by a lumped input-output relation, the neuromuscular transform (NMT)

\[
\text{INPUT} \quad \begin{array}{c}
\text{Motor neuron firing frequency} \\
\text{f(t)}
\end{array} \quad \begin{array}{c}
\text{NMT} \\
\text{NMT} \\
\text{OUTPUT} \\
\text{Muscle contraction amplitude} \\
\text{c(t)}
\end{array}
\]

where \( f \) and \( c \) (defined more precisely below) are instantaneous measures of the input and output at any particular time \( t \). In general, \( f \), and therefore \( c \), varies with \( t \).

We now structure the input \( f \) in different temporal patterns: that is, we consider different input waveforms \( f(t) \). For rhythmic contractions, periodically repeating patterns are most relevant. Because in these papers we wish to emphasize general principles, for simplicity we will restrict our quantitative consideration to a set of canonical patterns, those describing firing of the motor neuron in regular repetitive bursts (like those in Fig. 1, for example; a precise definition follows in the next section). This is a natural set of elementary patterns, already of obvious physiological significance yet simple enough to keep the more technical aspects of computation and presentation of the results relatively straightforward. The approach and the principles that we will illustrate using these canonical patterns can be readily extended to more complex patterns.

Having selected a pattern, we feed it through the NMT. As will be seen, the important properties of the NMT are its nonlinearity and its time dependence, fundamental properties of NMTs generally. However, again for the sake of illustrative simplicity, we will focus quantitatively on just two NMTs. One is a simple mathematical model whose properties are completely defined so that their effects on the output can be fully understood. We can then compare the behavior of a real, experimental NMT, the Aplysia ARC-muscle NMT.

We now ask, when the input pattern is fed through the NMT, what output emerges? We can examine the whole contraction waveform \( c(t) \) or concentrate only on key parameters such as the peak or the mean contraction. In these papers we will be concerned primarily with the steady-state output achieved after sufficiently long repetition of the input pattern.

How does the output differ when the input is structured in different patterns? We will analyze what parameters of the input are important in determining various parameters of the output. Does the firing pattern contain a “code” by means of which particular parameters of motor neuron firing selectively control particular parameters of muscle contraction? Conversely, what information must the motor neuron, and the nervous system generally, have about the periphery to be able to control it effectively?

In Paper II, we then add the fact that the contractions must meet certain criteria for functional behavior. Every firing pattern produces some state of contraction of the muscle, but is it a functionally appropriate state? We can examine this by defining for the muscle, or for several interacting muscles, a behavioral task and a corresponding measure of how well, if at all, the task is being performed. We will define several tasks of increasing complexity for our elementary motor unit, for an antagonistic pair of two such units, and finally a realistic task for the real Aplysia ARC-opener neuromuscular system. It will be seen that relatively few firing patterns produce functional behavior, and even fewer produce efficient functional behavior.
Conversely, functional behaviors with certain parameters are not possible with any firing pattern.

Finally, in Paper III, we use this foundation to examine how functional behavior may be expanded and optimized by appropriately tuning the NMT through peripheral neuromuscular plasticity and modulation.

We proceed as much as possible visually, through suitable graphical illustrations of the important concepts; the underlying mathematics and other more technical points can be found in the APPENDICES. The most frequently used symbols are summarized in Table 1. The DISCUSSION may be read independently for a nontechnical overview of the issues, results, and their biological implications. Papers II and III are organized similarly.

**Input firing patterns**

First, we must select a suitable time-dependent variable (for simplicity, just one) to formally describe the firing of the elementary motor neuron. We could take the continuous waveform of membrane voltage or, better, extract from it the timing of discrete spikes. For our purposes, however, it is most convenient to process the latter still further (by taking the reciprocal of the interspike interval) into a higher-order continuous variable, the “instantaneous” motor neuron firing frequency, $f$. The limits inherent in this discrete-to-continuous conversion will not be significantly felt in our work here. (Indeed, our work will enable us to say when those limits become significant: APPENDIX 1.)

**TABLE 1. Principal symbols used in this and the following papers**

<table>
<thead>
<tr>
<th>$t$</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>$f$</td>
<td>Firing frequency</td>
</tr>
<tr>
<td>$f(t)$</td>
<td>Firing pattern or waveform</td>
</tr>
<tr>
<td>$\langle f \rangle$</td>
<td>Mean firing frequency</td>
</tr>
<tr>
<td>$d_{\text{intra}}$</td>
<td>Burst duration</td>
</tr>
<tr>
<td>$d_{\text{inter}}$</td>
<td>Interburst interval</td>
</tr>
<tr>
<td>$P$</td>
<td>Cycle period</td>
</tr>
<tr>
<td>$F$</td>
<td>Duty cycle</td>
</tr>
<tr>
<td>$\phi$</td>
<td>Parameters of the model NMT</td>
</tr>
<tr>
<td>$\alpha, \beta, p, q$</td>
<td>Overall time constant of the NMT</td>
</tr>
<tr>
<td>$\tau_{\text{contr}}$</td>
<td>Time constant of contraction</td>
</tr>
<tr>
<td>$\tau_{\text{relax}}$</td>
<td>Time constant of relaxation</td>
</tr>
<tr>
<td>$c$</td>
<td>Contraction</td>
</tr>
<tr>
<td>$c(t)$</td>
<td>Contraction waveform</td>
</tr>
<tr>
<td>$\xi$</td>
<td>Period-wise maximum contraction</td>
</tr>
<tr>
<td>$\xi$</td>
<td>Period-wise minimum contraction</td>
</tr>
<tr>
<td>$\langle \xi \rangle$</td>
<td>Period-wise mean contraction</td>
</tr>
<tr>
<td>$[c(t)]_\infty$</td>
<td>Contraction waveform in the dynamical steady state</td>
</tr>
<tr>
<td>$c_\infty$</td>
<td>Maximum contraction in the dynamical steady state</td>
</tr>
<tr>
<td>$\xi_\infty$</td>
<td>Minimum contraction in the dynamical steady state</td>
</tr>
<tr>
<td>$\langle \xi \rangle_\infty$</td>
<td>Mean contraction in the dynamical steady state</td>
</tr>
<tr>
<td>$m$</td>
<td>Measure of functional movement</td>
</tr>
<tr>
<td>$m_\infty$</td>
<td>Measure of functional movement in the dynamical steady state</td>
</tr>
</tbody>
</table>

We can now consider different patterns of $f$. Temporal pattern is defined only over an interval of time, not at any single time point. Different patterns of $f$ are thus expressed in different waveforms $f(t)$; for our purposes the two will be synonymous. Our entire approach in this work is geared toward studying, as the basic unit, whole intervals of $f(t)$, and the corresponding intervals of $c(t)$, rather than their individual points.

Our canonical set of input waveforms, describing firing in regular repetitive bursts, is essentially the set of all waveforms that have the form sketched in the middle of Fig. 2 (more precisely, see APPENDIX A). Each such waveform is characterized by the structure of a single period, which then repeats endlessly. A single period, and therefore the whole waveform, can be completely defined by just three independent parameters. The most elementary triplet of parameters is that of the burst duration $d_{\text{intra}}$, interburst interval $d_{\text{inter}}$, and intraburst firing frequency $f_{\text{intra}}$, as indicated on the sketch in Fig. 2. (Note that the interburst frequency is always zero; patterns in which it is not are not members of the canonical set.) Another parameter triplet that is often used to describe such waveforms is that of the cycle period $P$, duty cycle (fraction of the period occupied by the burst) $F$, and mean (period-averaged) firing frequency $\langle f \rangle$. These are composite parameters, derived from the elementary ones using the relations

$$d_{\text{intra}} + d_{\text{inter}} = P \quad (2a)$$
$$d_{\text{intra}}P = F \quad (2b)$$
$$f_{\text{intra}}F = \langle f \rangle \quad (2c)$$

Finally, an intermediate parameter triplet of $P, F,$ and $f_{\text{intra}}$ is obtained by applying Eqs. 2a and 2b but not 2c.

The three parameter triplets constitute three alternative descriptions of the canonical set of waveforms. We will call them the $(d_{\text{intra}}, d_{\text{inter}}, f_{\text{intra}})$, $(P, F, \langle f \rangle)$, and $(P, F, f_{\text{intra}})$ representations. We now introduce a geometric point of view, which we will employ extensively throughout this work, designed to conceptually organize the set of waveforms and allow the whole set to be transformed through the NMT as a unit. Geometrically, the three representations can be pictured as alternative three-dimensional input spaces whose coordinates are the members of the triplet (Fig. 2, top). Every point in each space represents a canonical waveform, and every canonical waveform is represented in each space (see further APPENDIX A). How the spaces correspond to one another is given by Eqs. 2. Because Eqs. 2b and 2c are not linear, lines and planes in one space may correspond to curves and curved surfaces in another. The thick and thin meshes plotted in the spaces in Fig. 2 illustrate this for two particular subsets of the canonical set.

Why are we interested in three different descriptions of the same set of waveforms? It is because, by using different coordinates, they make explicit different parameters of the input pattern that may be important in different situations. For instance, the cycle period $P$, the parameter of interest in a problem like that in Fig. 1, is explicit in the $(P, F, \langle f \rangle)$ and $(P, F, f_{\text{intra}})$ representations but not in the $(d_{\text{intra}}, d_{\text{inter}}, f_{\text{intra}})$ representation. The $(P, F, \langle f \rangle)$ representation, but not the other two representations, makes explicit the mean firing frequency $\langle f \rangle$; a horizontal plane in that space represents all canonical patterns...
with the same mean density of spikes, just arranged in different ways. Thus each space emphasizes different parameters of the input pattern, and, when the spaces are then transformed through the NMT, the effect of those parameters on the output is immediately apparent. Numerous examples of this will be seen below.

Clearly, more complex patterns would require spaces of more dimensions to represent them. A general representation of arbitrary input patterns would require an infinite number of dimensions. Our three-dimensional spaces are, in fact, reductions of this general space, possible because we have restricted our patterns to just a small subset with a special structure.

**NMTs**

The real *Aplysia* ARC-muscle NMT that we will use should more precisely be called the B15-ARC NMT, because it involves only one of the muscle’s two motor neurons, neuron B15. We will not use the other, B16-ARC, NMT, although we will discuss generally how to analyze systems composed of multiple motor neurons as well as multiple muscles.

The B15-ARC NMT, like any other real NMT, is a priori unknown. We have no defining formula for it. Fundamentally, however, a transform is just a specification of the output that is produced for any particular input. If need be, this can be an explicit listing (APPENDIX B). We can begin to define the NMT, therefore, by correlating particular input waveforms \( f(t) \) with...
their corresponding output waveforms $c(t)$. In Fig. 3A we have done this for a set of input waveforms that are also members of our canonical set (APPENDIX A), namely steady, continuous firing at various frequencies. We will show later that the information obtained with this special subset of input waveforms can be sufficient to define the NMT completely.

We see in Fig. 3A1 that, when motor neuron B15 begins to fire steadily, the ARC muscle contracts with a broadly sigmoidal time course, at first slowly (the contraction begins, in fact, only after some delay), then faster, and finally slower again, eventually reaching a steady-state contraction, $c_\infty$. All phases of the time course become faster, and $c_\infty$ becomes greater, as the firing frequency $f$ increases. These dependencies on $f$, too, are sigmoidal, with no contraction at all until some threshold value of $f$, and saturation at large $f$; the steady-state $c_\infty(f)$ relation is shown in Fig. 3A2. When the motor neuron stops firing, the muscle relaxes with an exponential time course (Fig. 3B1). Overall, then, the B15-ARC NMT is highly nonlinear with respect to both time and the firing frequency $f$, and has a characteristic time scale (quite slow, of the order of seconds) that can be described by a characteristic time constant (APPENDIX C). Qualitatively, these properties are very typical of real NMTs generally. Quantitatively, in their characteristic speed in particular, NMTs of course differ considerably.

Implicit in any such description of a real NMT is a prior decision concerning the output variable, $c$. What, exactly, is being measured? In Fig. 3A, and elsewhere in this work where we have used the B15-ARC NMT, we measured the length of the muscle contracting isotonically against a constant light load. We could alternatively measure length under (probably...
more behaviorally realistic) auxotonic, variable-load conditions, or force under isometric conditions. The important qualitative properties of the NMT would most likely be the same: force measurements would probably yield a figure much like Fig. 3A. However, because the same input $f$ would be transformed to a different output $c$ in each case, formally we would be describing a different, although physiologically and functionally related, NMT. [In any case, throughout this work we represent active contraction produced by motor neuron firing as positive, upward movement of $c(t)$, even though this corresponds to decrease in length.]

The other NMT that we will work with is a simple mathematical model. In this case we do know the NMT a priori. It is implicitly defined by the kinetic schema

\[
\frac{af''(t)}{[1 - a(t)]} \stackrel{\beta}{\longrightarrow} a(t); \quad a'(t) = c(t)
\]

where $0 \leq a(t) \leq 1$ and $\alpha, \beta, p, q$ are constants, or by the corresponding equations

\[
\frac{da(t)}{dt} = a\dot{f}(t)[1 - a(t)] - \beta a(t); \quad a'(t) = c(t)
\]

Here, the input $f$ controls the rate of a time-dependent reaction of an intermediate, $a$, on which the output $c$ then depends. We found this model useful in our previous work (Brezina et al. 1997) because it can exhibit very different properties depending on the values of the parameters $\alpha, \beta$, and especially $p$ and $q$. In our work here, unless noted otherwise, we will use the “standard” parameter values $\alpha = 1, \beta = 1, p = 1, q = 3$. As can be seen in Fig. 3B, with these values the model NMT reproduces all of the qualitative properties of the real B15-ARC NMT. It too, produces output that increases sigmoidally with both time and $f$, with a characteristic time scale. The primary point, however, is not to model the real NMT in the conventional sense. Rather, the model NMT, by exhibiting important properties in a simple and well-defined way, allows us to clearly analyze their effects on the output.

Output contractions

When an input waveform $f(t)$ is fed through the NMT, an output waveform $c(t)$ emerges. Examples with steady input were seen in Fig. 3, and a preliminary idea of the output waveforms that are produced by bursting input patterns may be gained from Figs. 4 and 5, for the real B15-ARC NMT and the model NMT, respectively. Clearly, even with simple input, the output of the NMT can be quite complex. Its analysis is facilitated, however, by our geometric point of view.

Some questions may require that we consider the whole output waveform. In the same way that we constructed geometric input spaces to collectively represent and relate to each other our input waveforms, we can construct output spaces for output waveforms. Insofar as the shapes of the output waveforms are more complex and variable, to represent them completely such spaces would need to have a correspondingly greater number of dimensions. (See, however, the next section.) A general representation of arbitrary output waveforms (as of arbitrary input waveforms) would require an infinite number of dimensions.

Fortunately, many questions concern, rather than the whole output waveform, just a small number of functionally important parameters of it. We will consider three such parameters: the peak (maximum) contraction, $\bar{c}$; the minimum contraction, $\underline{c}$; and the mean contraction, $\langle c \rangle$. [As discussed in the next section, our output waveforms $c(t)$ will always be periodic with the same period $P$ as the corresponding input waveform $f(t)$. The period $P$ is thus the natural basic interval for our study. Each period of $c(t)$ yields a single value of $\bar{c}, \underline{c}$, and $\langle c \rangle = \frac{1}{P} \int_{P} c(t) \, dt$.] Each of these single parameters can be represented in a reduced one-dimensional output space, that is, a line. Later, in Paper II, we will devise more complex parameters to measure how well the contractions are performing a behavioral task. These will still be single parameters, however, and so capable of being represented in one-dimensional output spaces.

In all cases, we wish to see which inputs yield which outputs, not just individually but collectively: that is, how an input space is globally transformed into an output space. But this collective specification is the NMT (more precisely, the part of it that we have chosen to focus on with our reduced input and output spaces), no longer in an implicit definition such as Schema 3 or Eq. 4 but as its explicit solution. It can be represented in a combined space that is the product of the input and output spaces. With a three-dimensional input space and a one-dimensional output space—our canonical situation—we have a four-dimensional space to represent the NMT. As will be evident in the next section, all of this is no more than a generalization to higher dimensions of the familiar procedure of plotting an independent variable on a horizontal axis (a one-dimensional input space), a dependent variable on a vertical axis (a one-dimensional output space), and the relation of the two variables in the plane defined by the two axes (a two-dimensional product or input-output space).

Existence of mappings

Before proceeding to specific analysis, we must clarify one important issue. In what way is the NMT a transform? A transform, or, in the mathematical definition, a function or mapping, is a single-valued relation: each input maps to one, and only one, output. Of what aspects of the NMT is this true, and under what circumstances? This issue is important because a mapping provides us with a simple definition of control. If an input always maps to the same, predictable output, we may reasonably say that the input controls the output. We can apply this idea to whole waveforms—overall control of the muscle by the motor neuron—or to specific parameters. As will be seen, controllability then conveniently classifies different physiological situations.

We will discuss the existence of mappings with the aid of Fig. 4. Figure 4C shows time courses of contractions produced by the real B15-ARC NMT, as in Fig. 3A but now not only with steady firing, but also four representative bursting patterns.

At this point, it is instructive to retreat for a moment from viewing waveforms in units of periods to the elementary pointwise view. The period-wise case will then be entirely analogous. Point-wise, the complete, unredacted input-output space is just two-dimensional: the $(f, c)$ plane. It is so simple because all information about how successive points are related in waveforms has been discarded. Figure 4A plots the trajectory through the $(f, c)$ plane of two of the contractions in Fig. 4C,
with steady firing and for one period of one of the bursting patterns. (The horizontal arrows above the records in C indicate the sections plotted in A and B.)

At any time \( t \), there is, of course, a single value of the input \( f \), and a single value of the output \( c \). (In other words, \( f \) and \( c \) are functions of \( t \).) In that the NMT takes in that value of \( f \), and puts out that value of \( c \), it appears to be a transform (cf. APPENDIX D). However, the point of our geometric representation is to eliminate time as an explicit variable and consider all events simultaneously. Then, clearly, there is no single-valued mapping of \( f \) to \( c \); in the \((f, c)\) plane in Fig. 4A we see, for each plotted \( f \), multiple values of \( c \), corresponding to sections of the trajectory where \( c \) is changing even though \( f \) remains constant. Intuitively, Fig. 4C suggests that the value of \( c \) at any moment must reflect, as well as \( f \), also the immediately preceding value of \( c \). To predict \( c \) exactly requires knowledge of the complete state of the system, the pair \((f, c)\) (precisely, see APPENDIX E, I).

Knowing just \( f, c \) can only, at best, be predicted to be in some likely range.

However, as time progresses, with constant \( f \), we see in Fig. 4A (and Fig. 3A1) that each trajectory monotonically approaches a special state: the steady state. Thus the range in which, knowing just \( f, c \) might be expected to be, narrows with time and converges to the steady-state mapping \( c_\omega(f) \), a one-dimensional curve across the \((f, c)\) plane in Fig. 4A (taken from Fig. 3A2). The model NMT, we know from solving Eq. 4 (see next section), approaches the steady state asymptotically as \( t \to \infty \); the real B15-ARC NMT, we see in Fig. 3A1, reaches it quite fast, if we consider that what is significant, functionally as well as experimentally, is only some close enough approximation (cf. APPENDIX B, and later).

We proceed similarly for the period-wise case. Fig. 4B shows a reduced three-dimensional input-output space, the \((P, F, \bar{c})\) space with \( P \) and \( F \) as the input parameters and the peak contraction \( \bar{c} \) as the output, with the trajectories of the four bursting patterns in Fig. 4C. (All four patterns had the same \( f \), allowing us to omit this fourth dimension.) Again, there is no single-valued mapping of the input \((P, F)\) to the output \( \bar{c} \); to predict \( \bar{c} \) exactly requires knowledge of the complete state of the system, the triplet \((P, F, \bar{c})\) (APPENDIX E, 2). But, with time, all trajectories converge monotonically to the steady-state mapping \( \bar{c}_\omega(P, F) \), the two-dimensional surface in Fig. 4B. (We will describe later how to compute this surface.)

The same behavior is found in every input-output space that we
multidimensional space to represent every possible state, how far it progresses toward them will be an important
steady state of the system, even though point-wise it has not system stabilizes at \[ f(t) \] (APPENDIX E, 2).^1

With our NMTs, each output space behaves in this way because each, when joined to a sufficient input space, is in fact sufficient to distinctly represent every whole output waveform \( c(t) \) that can be produced by any canonical \( f(t) \) (APPENDIX E, 2). We do not need, after all, an infinite-dimensional or even a multidimensional space to represent every possible \( c(t) \): a one-dimensional space for a single parameter such as \( \bar{c} \), \( \bar{\xi} \) or \( \bar{\epsilon} \) is enough. In other words, for a particular \( f(t) \), a parameter such as \( \bar{c} \), \( \bar{\xi} \) or \( \bar{\epsilon} \) uniquely specifies the whole period of \( c(t) \) that yielded it (and vice versa, of course; consequently, any one of \( \bar{c} \), \( \bar{\xi} \) and \( \bar{\epsilon} \) uniquely specifies the other two). Fundamentally, all of this reflects the fact that an NMT can produce only a restricted set of output waveforms (cf. APPENDIX I). Only certain shapes are possible. In our case, only one type of shape is possible, for which a one-dimensional space provides an optimal—complete, distinct, and compact—representation. Any output space of more than one dimension will not provide a compact representation, in the sense that, for any \( f(t) \), it will contain points that cannot be reached with that \( f(t) \). Just as our reduced three-dimensional input spaces provide equivalent optimal representations of our restricted set of input waveforms, output spaces reduced to just one dimension such as \( \bar{c} \), \( \bar{\xi} \) or \( \bar{\epsilon} \) provide equivalent optimal representations of the restricted set of output waveforms.

In each such output space, the steady-state point represents a unique steady-state output waveform, \( c(t) \) (Fig. 4C). Because there is a period-wise mapping to it from \( f(t) \), \( c(t) \) is periodic with the same period \( P \) as \( f(t) \), and each period of \( c(t) \) is identical. \( c(t) \) yields a unique value of \( \bar{c} \), \( \bar{\xi} \) and \( \bar{\epsilon} \), and of any other parameter that can be defined by a period-wise mapping from \( c(t) \), including our functional performance parameters in Paper II.

Note in Fig. 4 that, with bursting input, period-wise the system stabilizes at \( c(t) \), in what we may call the dynamical steady state of the system, even though point-wise it has not reached a true steady-state \( c(t) \). Indeed, periodic \( f(t) \) and \( c(t) \) correspond to a cycle in the elementary \((f, c)\) plane (Fig. A4). During each burst when \( f = f_{\text{intra}} \), \( c \) rises toward \( c_{\text{a}}(f_{\text{intra}}) \), and during each interburst interval when \( f = 0 \), \( c_{\text{b}}(0) = 0 \). Although, in general, it reaches neither true steady state, how far it progresses toward them will be an important consideration in the following sections. With steady input, the two kinds of steady state necessarily coincide.

For any input, our model NMT, and apparently also the real B15-ARC NMT, has just a single steady state point-wise, and a single steady state period-wise; otherwise the mappings we have discussed would not exist. Such simple behavior is typical of many real NMTs. With some NMTs we may find, however, that for some inputs the dynamical steady state of the system consists of multiple points in the output space (alternative steady states that the system may reach from different regions of the space) or that it is itself periodic, or even that it does not have any recognizable simple structure. We have presented this section (and the associated APPENDIX E) in some detail partly to suggest how such possibilities, too, might be studied by our approach, essentially by expanding it into a more complete dynamical systems analysis. We will return to the physiological significance of such possibilities later, when we consider the implications of the ideas introduced in this section for controllability. First, however, we will examine the actual steady-state output produced by the model NMT, and by the real B15-ARC NMT.

Steady-state output of the model NMT

For any waveform \( f(t) \) as input to Eq. 4, and knowing the current state of the system—any state, not just the steady state—we can compute the corresponding output waveform \( c(t) \) (APPENDIX E). If necessary, we can do this numerically. With our canonical input waveforms, however, we can readily obtain analytic solutions (APPENDIX F). The output waveform has the general shape discussed in the last section. During each burst when \( f = f_{\text{intra}} \), \( c \) moves toward \( c_{\text{a}}(f_{\text{intra}}) \), and during each interburst interval when \( f = 0 \), \( c_{\text{b}}(0) = 0 \). In general these movements are unequal so that the waveform gradually rises, or falls, over successive periods (exactly like the output of the B15-ARC NMT in Fig. 4C). In the dynamical steady state of the system, however, the two movements—rise during the burst and fall during the interburst interval—must be equal and opposite. This requirement immediately gives us the unique steady-state waveform \( c(t) \) (three examples, to be discussed below, are shown in Fig. 5). Period-wise, we thus compute the dynamical steady state reached with bursting input just as, point-wise, we do the true steady state reached with steady input, by equating the appropriate opposing fluxes and converting our knowledge of the kinetics of \( c \) into knowledge of its absolute steady-state amplitude.

From \( c(t) \), we then obtain analytic expressions for \( c_{\text{a}} \), \( c_{\text{b}} \), and \( c_{\text{c}} \) (APPENDIX F). We can write these expressions in terms of one or another of our alternative triplets of input parameters. To see how our set of inputs maps globally to the set of outputs, we need simply examine these expressions, or their graphic representations in the appropriate input-output spaces.

As we have discussed, these are four-dimensional spaces, in which the steady state occupies a three-dimensional volume. Four dimensions are already unmanageable graphically. We will therefore usually show representative three- or even two-dimensional sections through the complete four-dimensional space, obtained by setting one or two of the input parameters to constant values (as, in effect, we did in Fig. 4B). In a three-dimensional section the steady state appears as a two-dimensional surface, and in a two-dimensional section as a one-dimensional curve. Various such plots can be seen in Figs. 6–9.

To understand the input-output mapping, it is most convenient to begin with the input in the \((P, F, \langle f \rangle)\) representation.

\(^1\) In stating these principles for the B15-ARC NMT, we are assuming that it behaves in certain ways, specified in APPENDIX E, as simply as the model NMT. This is a reasonable assumption, consistent to a first approximation with the available evidence, although clearly not absolutely correct. We will maintain this assumption through to the end of RESULTS, then consider how such an assumption might be relaxed in the DISCUSSION.
As we have already noted, this representation explicitly allows us to decompose the input into two components: \( \langle f \rangle \), the mean firing frequency or density of motor neuron spikes, and \((P, F)\), the temporal arrangement of those spikes. In our previous work (Brezina et al. 1997) we reserved the term “pattern” technically just for the latter.

The output then depends on both components, filtered in different ways through their interaction with the properties of the NMT. Broadly, we can think of the output as being dependent on \( \langle f \rangle \) according to the steady-state mapping \( c_\infty(\langle f \rangle) \), but then modified, in a complex but predictable manner, by a factor that depends on the pattern \((P, F)\) (as well as \( \langle f \rangle \)). This factor, which we technically termed “pattern dependence,” was the focus of our previous work. We found that, with a time-dependent NMT such as the model NMT, key determinants of pattern dependence are the time scale of the input pattern relative to that of the NMT, and the shape—the degree and kind of nonlinearity—of the NMT (Brezina et al. 1997). The interaction of these elements can be envisioned intuitively as follows. The nonlinearity of the NMT only appears on time scales longer than \( \tau \), the time constant of the NMT. The input pattern exists on time scales shorter than \( P \), the cycle period. Only when \( P > \tau \), so that the nonlinearity and the pattern overlap and interact, does pattern dependence become expressed, and modifies the output from its basic value of \( c_\infty(\langle f \rangle) \).

This can be seen in Fig. 6, which shows sections through the mappings \( \bar{c}_\infty(\langle f \rangle, F, P) \), \( c_\infty(\langle f \rangle, P, F) \), and \( \langle c_\infty(\langle f \rangle, F, P) \rangle \) for one particular value of \( \langle f \rangle \). The shapes of these surfaces reflect, therefore, just changing pattern dependence, modifying the output up (lighter tone) or down (darker tone) from the basic value of \( c_\infty(\langle f \rangle) \). Lower and higher values of \( \langle f \rangle \) give similar surfaces layered, respectively, below and above the ones shown, although gradually changing in shape with \( \langle f \rangle \), as will be apparent in subsequent figures.

In the \( F \) direction, each surface begins at \( c_\infty(\langle f \rangle) \) when \( F = 1 \) (steady input; front edge). Pattern dependence becomes ex-

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**FIG. 5.** Steady-state output waveforms \([c(\langle t \rangle)]_\infty\) produced by the model NMT, illustrating their appearance as the time scale of the input pattern, \( P \), varies relative to the time constant of the NMT, \( \tau \). These are plots of Eq. F1 with the standard parameter values \( \alpha, \beta, p = 1, q = 3 \). The gray bars mark the phases when \( f = f_{\text{intra}} \). In all cases \( F = \frac{1}{3}, f_{\text{intra}} = 1.5, \langle f \rangle = 0.5 \). The input pattern \((\langle f \rangle)\) is thus identical in all cases, except on different time scales. In all cases \( \tau = 1 \) (APPENDICES C and F). Locations A–C in Fig. 6A are shown, although gradually changing in shape with \( \langle f \rangle \), as will be apparent in subsequent figures.

**FIG. 6.** Parameters \( \bar{c}_\infty, c_\infty \), and \( \langle c_\infty \rangle \) of the steady-state output of the model NMT: overall view of their dependence on input parameters, \( (P, F, \langle f \rangle) \). These are plots over a broad range of \( P \) and \( F \) of the steady-state mappings \( \bar{c}_\infty(\langle f \rangle, P, F) \), \( c_\infty(\langle f \rangle, P, F) \), and \( \langle c_\infty(\langle f \rangle, P, F) \rangle \) given by Eqs. F4–F6 with the standard parameter values \( \alpha, \beta, p = 1, q = 3 \). In all cases \( \langle f \rangle = 0.5 \); these are therefore only representative sections, at \( \langle f \rangle = 0.5 \), through the general mappings \( \bar{c}_\infty(\langle f \rangle, P, F) \), \( c_\infty(\langle f \rangle, P, F) \), and \( \langle c_\infty(\langle f \rangle, P, F) \rangle \). Extended log scales have been used to show a broad range of \( P \) and \( F \) and to emphasize the asymptotic behavior of \( \bar{c}_\infty, c_\infty \), and \( \langle c_\infty \rangle \) at its extremes. Higher values of \( \bar{c}_\infty, c_\infty \), and \( \langle c_\infty \rangle \) are shown in lighter tone, lower values in darker tone. In B, when \( P \gg \tau \) and \( F < 1 \), \( \bar{c}_\infty \rightarrow 0 \), off scale (Eq. G2). \( \tau = 1 \) (APPENDICES C and F). Locations A–C in A correspond approximately to the 3 waveforms \([c(t)]_\infty\) in Fig. 5, A–C.
pressed as $F$ decreases, as the input pattern itself develops—as the spikes are grouped into progressively more extreme bursts—and engages the nonlinearity of the NMT. In the $F$ direction, therefore, output increased above $c_{\infty}(f)$ reflects what we may call “positive” pattern dependence—greater output as spikes are grouped into bursts—and output decreased below $c_{\infty}(f)$ “negative” pattern dependence—greater output as spikes are dispersed into steady firing. Output remaining precisely at $c_{\infty}(f)$ is pattern independent: the arrangement of spikes is immaterial to the output.

We wish now to emphasize, however, the $P$ direction. Demonstrating the critical importance of the relative time scales of the input pattern and the NMT, we see that each surface is divisible into two regions of distinct pattern dependence and therefore distinct output, above and below $P \approx \tau$. (To emphasize this we have used extended log scales, in Fig. 6 only.) The characteristic output seen in each region can be understood by examining the limiting values that the output tends to when $P \ll \tau$ or $P \gg \tau$, when the NMT, in effect, becomes time independent and the output ceases to vary with $P$. How $\overline{c}_{\infty} = c_{\infty}$, and $\langle c \rangle_{\infty}$ depend on input parameters in these two cases is shown in Figs. 7 and 8, respectively; typical shapes of $[c(t)]_{\infty}$ in the two cases can be seen in Fig. 5, A and C.

The case when $P \ll \tau$, when the input pattern is much faster than the NMT, is simple. In the extreme, when the pattern can be considered infinitely fast or the NMT infinitely slow, $c$ does not, within any particular period, sense changes in $f$ at all (Fig. 5A). It makes no progress either toward $c_{\infty}(f_{\text{intra}})$ during each burst, or toward $c_{0}(0) = 0$ during each interburst interval, but simply stabilizes somewhere between the two. Then $\overline{c}_{\infty} = c_{\infty} = \langle c \rangle_{\infty} = [c(t)]_{\infty} = \text{constant}$. The only question is whether the output stabilizes at the same constant for every input pattern. If so, the output is pattern independent. Indeed, as Fig. 7, left, shows, the output of the model NMT with the standard parameter values is pattern independent. When $P \ll \tau$, the output always has the basic, unmodified value of $c_{\infty}(f)$ (Fig. 7, middle), depending just on $f$, the mean density of motor neuron spikes, regardless of $(P, F)$, their pattern. Intuitively, no pattern dependence is expressed because the input pattern cannot engage the nonlinearity of the NMT, because on time scales much shorter than $\tau$ the nonlinearity of the NMT remains completely undeveloped: the NMT is effectively linear (see APPENDIX G, 1; Brezina et al. 1997).

We see in Fig. 7 the utility of our different input representations. The relevant part of the $(P, F, (f))$ input space, transformed through the NMT, generates a simple, immediately comprehensible output structure (left). In contrast, the same input in the $(d_{\text{intra}}, d_{\text{inter}}, f_{\text{intra}})$ representation, for instance (right), does not yield immediate insight. More specifically, we reiterate that pattern dependence in our precise technical definition is explicit only when the input is in the $(P, F, (f))$ representation, where each surface shows the output produced by all possible patterns of the same number of spikes. This is not true, for example, in the $(P, F, f_{\text{intra}})$ representation, where the number of spikes is not conserved as the pattern changes.

The case when $P \gg \tau$, when the input pattern is much slower than the NMT, is just the opposite. In this case $c$ progresses very far toward $c_{\infty}(f)$. In the extreme, when the pattern can be considered infinitely slow or the NMT infinitely fast, $c$ relaxes instantaneously all the way to the new value of $c_{\infty}(f)$, either $c_{\infty}(f_{\text{intra}})$ or $c_{\infty}(0) = 0$, whenever $f$ changes (Fig. 5C). Then the output can be found simply by examining the $c_{\infty}(f)$ relation. Intuitively, on time scales much longer than $\tau$, the nonlinearity of the NMT is fully developed, pattern dependence is fully expressed, and fully modifies the output.

Clearly, $\overline{c}_{\infty} = c_{\infty}(f_{\text{intra}})$ (Fig. 8A; APPENDIX G, 2). Now it is input in the $(d_{\text{intra}}, d_{\text{inter}}, f_{\text{intra}})$ representation that generates an immediately comprehensible output structure (Fig. 8A, middle and right), whereas input in the $(P, F, (f))$ representation (left) does not, although it does show that $\overline{c}_{\infty}$ is now pattern dependent. There is only “positive” pattern dependence. Each surface (except that with zero input) rises monotonically as $F$ decreases, the exact shape depending on $F$ and also $(f)$ in a way that directly reflects the monotonically increasing but nonlinear $c_{\infty}(f_{\text{intra}})$ relation (Brezina et al. 1997).

Similarly, $\overline{c}_{\infty} = c_{\infty}(0) = 0$, except when $d_{\text{intra}} = 0$ or $F = 1$ (steady input), when $\overline{c}_{\infty} = c_{\infty}(f_{\text{intra}}) = c_{\infty}(f)$ (Fig. 8B). Here there is extreme “negative” pattern dependence.

The case of $\langle c \rangle_{\infty}$ is more complex and interesting (Fig. 8C). Input in the $(d_{\text{intra}}, d_{\text{inter}}, f_{\text{intra}})$ representation is not immediately helpful (right). The most comprehensible output structure is generated with input in the $(P, F, f_{\text{intra}})$ representation (middle). Indeed, $\langle c \rangle_{\infty} = F_{\text{intra}}c_{\infty}(f_{\text{intra}})$ (APPENDIX G, 2). With input in the $(P, F, (f))$ representation (left), the properties of the $c_{\infty}(f_{\text{intra}})$ relation again translate into pattern dependence. In this case, the sigmoidal shape of the relation generates both “positive” and “negative” pattern dependence (Brezina et al. 1997). “Negative” pattern dependence, associated with downward curvature of the relation—that is, its saturation—predominates, but is overlain by “positive” pattern dependence, associated with upward curvature of the relation, over a limited range of small $F$ and $(f)$. Removing the upward curvature, by
setting $q = 1$ rather than $q = 3$ (see Fig. 3B2), would eliminate the “positive” pattern dependence. To eliminate the “negative” pattern dependence too, and make $\langle c \rangle_\infty$ completely pattern independent not just for fast, but also for slow patterns (as indicated by the outlined surface in Fig. 8C, left), indeed for all patterns, would require removing the saturation of the $c_\infty(f_{\text{intra}})$...
We have examined, then, the extremes when $P \ll \tau$ and $P \gg \tau$. The most physiologically relevant patterns, however, are those on intermediate time scales, around $P \approx \tau$. Here $c$ makes significant progress toward, but does not reach, $c_a(f_{\text{intra}})$ and $c_a(0) = 0$ in each cycle period (Fig. 5B). Over this relatively narrow range of time scales, pattern dependence and output make a rapid transition between the picture that we observed with very fast patterns ($P \ll \tau$) and that observed with very slow patterns ($P \gg \tau$). As a consequence, output parameters are very sensitive to input parameters in this range, now not just to $F$ but also $P$, or $d_{\text{intra}}$ and $d_{\text{inter}}$. Figure 9 again shows $c_{\text{intra}}$, $c_{\text{inter}}$, and $\langle c \rangle_{\text{intra}}$ for input in the $(d_{\text{intra}}, d_{\text{inter}}, f_{\text{intra}})$ representation. These are two-dimensional sections, for various combinations of values of the input parameters, through the complete four-dimensional spaces, with $c_{\text{intra}}$, $c_{\text{inter}}$, and $\langle c \rangle_{\text{intra}}$ all plotted together in each panel for comparison. It is clear, once more, how the output—$c$, or any parameter such as $c_{\text{intra}}$, $c_{\text{inter}}$, or $\langle c \rangle_{\text{intra}}$—of the model NMT, because of the simple dynamical behavior that we have described, can never move outside the boundaries set by $c_a(f_{\text{intra}})$ (dotted line) and $c_a(0) = 0$ (horizontal axis in each panel). Where it is within those boundaries and how closely it approaches them, however, varies greatly, and changes very rapidly with small changes in input parameters in this intermediate, physiologically relevant range. We will examine the consequences of this further in Paper II, when we ask the output to perform a behavioral task.

Steady-state output of the B15-ARC NMT

We can use exactly the same strategies and concepts that we described in the last section to analyze the output of the real B15-ARC NMT. Indeed, because the dynamical behavior of the B15-ARC NMT is qualitatively similar to that of the model NMT, so is its output.

The only difference in our approach stems from the different ways in which the NMTs are defined. For the model NMT we have a general formula (Eq. 4) whose solutions, for every input pattern, constitute the complete NMT. For the B15-ARC NMT, however, we have no general formula, only some of the specific solutions, namely those for steady firing shown in Fig. 3A.

The conventional modeling strategy would be to work backward from the available specific solutions to reconstruct a general formula that might have produced them, which could then be used to generate all other solutions too. A plausible simple model of the B15-ARC NMT might indeed look much like our model NMT. However, the backward step is not uniquely determined. Any finite set of solutions—especially the approximate, variable outputs of a real NMT—is compatible with many models. Selecting a particular one introduces, explicitly or implicitly, a host of additional assumptions. We will therefore avoid this strategy and see what can be done just with the data itself. In essence, we wish to see whether, from just a part of the NMT, we can recreate the whole.

We have already seen how, when $P \gg \tau$, steady-state pattern dependence and output depend simply on the shape of the $c_a(f)$ relation. In the last section we described this for the model NMT, but exactly the same is true for a real, empirical NMT (Brezina et al. 1997). From just the information in Fig. 3A2, therefore, we can determine the steady-state output—the whole contraction waveform $[c(t)]_{\text{intra}}$, or a parameter such as $c_{\text{intra}}$, $c_{\text{inter}}$, or $\langle c \rangle_{\text{intra}}$—of the B15-ARC NMT when $P \gg \tau$.

There is a more powerful and complete strategy, however. In
Existence of mappings, we noted that, point-wise, to predict \( c \) requires knowledge of the pair \((f, c)\); this knowledge is in fact also sufficient, certainly for the model NMT (APPENDIX E, I). If this is true also for the B15-ARC NMT, then contraction trajectories beginning at the same contraction amplitude \( c \), with the same motor neuron firing \( f \), will be identical whatever higher-order, period-wise pattern that firing is part of. We can therefore simply take appropriate sections of such records as those in Fig. 3A1 obtained with steady firing to reconstruct contraction waveforms produced by bursting patterns, now not just those where \( P \gg \tau \) but by all canonical patterns. We can do this for any state, not just the steady state. Starting with any value of \( c \), we can reconstruct the whole waveform \( c(t) \) as \( c \) moves toward \( c_{\text{intra}} \) during each burst and toward \( c_{\infty}(0) = 0 \) during each interburst interval. In general the two movements are unequal so that \( c(t) \) progressively rises, or falls, over successive periods (as we saw in Fig. 4C). In the dynamical steady state of the system, the movements must be equal and opposite, and this gives us the unique waveform \([c(t)]_{\infty}\), and so \( \bar{c}_{\infty}, \hat{c}_{\infty}, \) and \( \langle c \rangle_{\infty} \). Exactly as with the model NMT, we convert our knowledge of the kinetics of \( c \) into knowledge of its absolute steady-state amplitude.

In Fig. 10 we have used this kind of approach (for details see APPENDIX I) to reconstruct, from just the records obtained with steady firing in Fig. 3A1, the steady-state contractions predicted for a variety of bursting patterns. Figure 10A shows several examples of whole waveforms \([c(t)]_{\infty}\) (black traces); Fig. 10B shows the predicted \( \bar{c}_{\infty}, \hat{c}_{\infty} \) and \( \langle c \rangle_{\infty} \) (meshes), in the \((P, F, f)\) input representation, for one value of \( f \) (again, therefore, these are just sections through the complete four-
dimensional spaces). As we discussed in connection with the model NMT, plots in the format of Fig. 10B reflect changing pattern dependence.

To test these predictions, we have then carried out a series of experiments, actually firing motor neuron B15 in these bursting patterns and recording the actual contractions of the ARC muscle. The results are superimposed in Fig. 10A (gray traces) and B (scatter points).

The agreement between the predicted and the actual contractions is remarkably good. This suggests that our simple view of the dynamical behavior of the B15-ARC NMT is, to a first approximation, valid. The point-wise output of the B15-ARC NMT, like that of the model NMT, depends to a first approximation just on \( f \) and \( c \), and so contains all the information needed to predict the period-wise output (see further the discussion). Under these circumstances, it is indeed possible to use just a part of the NMT, such as that for steady firing, to recreate the whole. Furthermore, we can immediately understand what we see in Fig. 10 on exactly the same principles that we described for the model NMT.

Thus, reflecting the time dependence of the B15-ARC NMT, in the plots of Fig. 10B we see pattern dependence and output change around \( P = \tau \), of the order of several seconds (cf. Fig. 3A1). With patterns faster than this, contractions become, to a first approximation, pattern independent (see Appendix I). With slower patterns, substantial pattern dependence develops. In Fig. 10B1, because the \( c_\infty(f) \) relation increases monotonically (Fig. 3A2), we see just “positive” pattern dependence of \( c_\infty \). In Fig. 10B2, we see \( c_\infty \) tend to \( c_\infty(0) = 0 \). In Fig. 10B3, because the \( c_\infty(f) \) relation is sigmoidal, we see positive pattern dependence of \( c_\infty \), which predominates at the small \( f \) chosen here, but already hints of developing “negative” pattern dependence at large \( P \) and small \( F \). The proportion of negative to positive pattern dependence would increase with \( f \). Qualitatively, all of this is as with the model NMT. Quantitatively, however, the B15-ARC NMT is more complex (compare Fig. 3, A and B), and as a result additional features (most notably, the region of “positive” pattern dependence of \( c_\infty \)) become significant especially in the intermediate, physiologically relevant range of time scales.

**Input-output control and coding**

Under what circumstances can we say that the input controls the output? When can we say that the firing of the motor neuron controls the contraction of the muscle, or more specifically, that a certain parameter of the firing pattern controls a certain parameter of the contraction?

As we have already mentioned, a convenient precise definition of control is provided by an input-output mapping. If an input produces a unique, predictable output, then we can say that the input controls the output: if the nervous system applies the input through the NMT, it can be certain of the output that will emerge, and by varying the input, it can vary the output in a predictable way. If, on the other hand, the input produces different outputs at different times depending on the circumstances, such as the values of additional parameters, then that input, by itself, does not control the output.

From our discussion in *Existence of mappings* above, we see that, with our NMTs, the firing pattern never controls the contraction except in the dynamical steady state of the system. Except then, the input waveform \( f(t) \) never controls the output waveform \( c(t) \). Furthermore, never, except in the steady state, does \( f(t) \), or any of its parameters, control any of the individual output parameters \( \bar{c}, \bar{\zeta} \), and \( \zeta \). This follows immediately from the one-to-one correspondence between \( c(t) \) and each of its parameters (see *Existence of mappings* and Appendix E, 2): in other words, from the extremely restricted shape of \( c(t) \).

In the dynamical steady state, the firing pattern does control the contraction. The input waveform \( f(t) \), and so any set of parameters that completely describes it—for our canonical patterns, the triplets \( (d_{\text{intra}}, d_{\text{inter}}, f_{\text{intra}}) \) or \( (P, F, \langle f \rangle) \), for instance—controls the output waveform \( [c(t)]_\infty \) and consequently its parameters \( \bar{c}_\infty, \bar{\zeta}_\infty \), and \( \zeta_\infty \).

We can now ask, does any smaller subset of the input parameters, or any single parameter, control any of the output parameters? Looking at the output of our NMTs that we plotted in Figs. 6–10, and particularly at the output in the physiologically relevant, intermediate range of time scales in Figs. 9 and 10, the intuitive answer appears to be, in general, no.

However, we can sharpen our discussion of this question by considering the very closely related question of input-output coding. This question has recently been asked, in the neuromuscular context, for example by Morris and Hooper (1998). Does the motor neuron firing pattern contain within it “codes” for specific features of the muscle contractions, such as \( \bar{c}_\infty, \bar{\zeta}_\infty \), and \( \zeta_\infty \)?

Clearly, the concepts of coding and control are essentially equivalent: both seek an input-output mapping. Coding has often been interpreted, however, in a somewhat restricted way. Morris and Hooper (1998), for instance, searched for codes in a real neuromuscular system by examining plots of several “natural” parameters of the firing pattern—simple parameters such as \( f_{\text{intra}} \) and \( P \)—against several contraction parameters for straight-line relationships. Experimentally, it may be impractical to do more than this. Here, however, we are in a position to relax the restrictions implicit in this procedure in two ways. First, it will be instructive to consider that the coding parameter (or, in our equivalent concept, the controlling parameter) need not be any one of the simple, “natural” input parameters, but may be some arbitrary function \( \mathcal{F} \) of any or all of them, for example \( \mathcal{F}(d_{\text{intra}}, d_{\text{inter}}, f_{\text{intra}}) \). (Indeed, \( P, F, \langle f \rangle \) are themselves already composite, albeit still simple, functions of \( d_{\text{intra}}, d_{\text{inter}}, \) and \( f_{\text{intra}} \).) Second, the code need not be linear. A nonlinear code—as long as it remains a code, a single-valued function—may be more efficient. As we suggest in the discussion, the two restrictions have more to do with analytic convenience than biological function.

Nevertheless, analytically, we will retain the linear restriction for the moment. The most restricted form of the coding problem is as follows: for a coded or controlled output parameter \( \mathcal{C} \), can we find a coding or controlling input parameter \( \mathcal{F} \) such that \( \mathcal{F} = \mathcal{C} \)? If we can answer this form of the question, we can answer the question in general, because we can relax the equality between \( \mathcal{F} \) and \( \mathcal{C} \) into an arbitrary linear or nonlinear mapping (see Appendix K).

Our discussion so far in fact already contains a surprisingly simple and complete answer to the coding problem. If and only if there is a mapping from the input to \( \mathcal{C} \), then the input contains a unique code \( \mathcal{F}_{\mathcal{C}} \) such that \( \mathcal{F}_{\mathcal{C}} = \mathcal{C} \). This follows immediately from our view of coding as mapping, and the
definition of mapping as a single-valued relation. With our NMTs, therefore, the firing pattern does not contain a code for any such parameter as \( \bar{c}_1 \), \( \bar{c}_2 \), or \( \langle c \rangle \) except in the dynamical steady state of the system. In the dynamical steady state, however, a code exists for each of \( \bar{c}_1 \), \( \bar{c}_2 \), and \( \langle c \rangle \), and is unique. This is because \( \bar{c}_1 \), \( \bar{c}_2 \), and \( \langle c \rangle \) are given by, and can be computed from, the input in one and only one way. When \( \bar{c}_1 = \bar{c}_2 \), indeed, the mapping \( \bar{c}_1 = \bar{c}_2 \) is equivalent to \( \bar{c}_1(P, F, \langle f \rangle) \), say, is precisely the code \( \bar{c}_1 \) (Fig. 2). From this we see, too, that because the values of \( \bar{c}_1 \), \( \bar{c}_2 \), and \( \langle c \rangle \) are different, their codes must be different also.) But we have already computed all of these mappings: those we have plotted in Figs. 6–10. Thus, Figs. 6–10 can all equally be regarded as plots of the codes \( \bar{c}_1 \), \( \bar{c}_2 \), and \( \langle c \rangle \).

An important fact follows from this. In studying Figs. 6–10, we saw how the mappings depended, in general, in a complex fashion on \( \bar{c}_1 \) of all the input parameters. The same is therefore true for the codes. For the model NMT, for instance, the codes \( \bar{c}_1 \), \( \bar{c}_2 \), and \( \langle c \rangle \) in the \( (P, F, \langle f \rangle) \) input representation and substituting \( \bar{y} = \alpha(f)e^P \frac{1}{P} \) for compactness, are

\[
\begin{align*}
\bar{c}_1 &= \left\{ \begin{array}{l}
\alpha(f)^p \left[ 1 - \exp[-P(\bar{y} + \beta F)] \right] \\
\alpha(f)^p \left[ 1 - \exp[-P(\bar{y} + \beta F)] \right]
\end{array} \right. \\
\bar{c}_2 &= \left\{ \begin{array}{l}
\alpha(f)^p \left[ 1 - \exp[-P(\bar{y} + \beta F)] \right] \\
\alpha(f)^p \left[ 1 - \exp[-P(\bar{y} + \beta F)] \right]
\end{array} \right. \\
\langle c \rangle &= \left\{ \begin{array}{l}
\alpha(f)^p \left[ 1 - \exp[-P(\bar{y} + \beta F)] \right] \\
\alpha(f)^p \left[ 1 - \exp[-P(\bar{y} + \beta F)] \right]
\end{array} \right.
\end{align*}
\]

and, with \( q = 3 \)

\[
\begin{align*}
\bar{c}_1 &= \left\{ \begin{array}{l}
2P\beta \exp[\bar{y} - (1 + 3)] \\
+ \exp[3(\bar{y} + 2F + \beta)] \\
+ 4\exp[\bar{y} + 2F + \beta] \\
+ 4\exp[3(\bar{y} + 2F + \beta)] \\
+ 2\exp[1 - F + \beta] \\
+ 2\exp[1 - F + \beta] \\
+ 4\exp[\bar{y} + 2F + \beta] \\
- \exp[2(\bar{y} + 2F + \beta)] \\
+ 2\exp[1 - F + \beta] \\
+ 2\exp[1 - F + \beta] \\
- \exp[2(\bar{y} + 2F + \beta)] \\
- \exp[2(\bar{y} + 2F + \beta)] \\
- \exp[2(\bar{y} + 2F + \beta)] \\
- \exp[2(\bar{y} + 2F + \beta)] \\
- \exp[2(\bar{y} + 2F + \beta)] \\
- \exp[2(\bar{y} + 2F + \beta)] \\
- \exp[2(\bar{y} + 2F + \beta)] \\
- \exp[2(\bar{y} + 2F + \beta)] \\
- \exp[2(\bar{y} + 2F + \beta)]
\end{array} \right. \\
\bar{c}_2 &= \left\{ \begin{array}{l}
3\beta \\
\alpha(f)^p \left[ \frac{\bar{y}}{F} \right] \\
\exp[-3\beta \exp[3P \beta F]] \\
- \exp[3P \beta F] \\
- \exp[3P \beta F] \\
- \exp[3P \beta F] \\
- \exp[3P \beta F]
\end{array} \right. \\
\langle c \rangle &= \left\{ \begin{array}{l}
6\beta \exp[\bar{y} - (1 + 3)] \\
- \exp[\bar{y} - (1 + 3)] \\
- \exp[\bar{y} - (1 + 3)] \\
- \exp[\bar{y} - (1 + 3)] \\
- \exp[\bar{y} - (1 + 3)] \\
- \exp[\bar{y} - (1 + 3)] \\
- \exp[\bar{y} - (1 + 3)]
\end{array} \right.
\end{align*}
\]

(These are Eqs. F4–F6 from APPENDIX F, of which sections were plotted in Figs. 6–8.) Each of these codes is a different, complex function of all three simple parameters \( P, F, \) and \( \langle f \rangle \). Thus, although a code is guaranteed to exist and can actually be computed, it will not be, in general, any one of the simple, “natural” input parameters, several of these, or even a simple combination of them, but some complex function of all of them. And, because the code is unique, no simpler one exists.

This does not mean, of course, that the code cannot be approximated by simpler functions. Such approximations improve in accuracy, and acceptable approximations can be obtained with progressively simpler functions, as the set of inputs is restricted, especially to certain regions of the input space. We saw this happen when \( P \ll \tau \) and \( P \gg \tau \); in the former case, for instance, the codes in Eq. 5 simplified (Fig. 7) to just \( \bar{c}_1 = \bar{c}_2 = \bar{c}_1 \approx \bar{c}_2 \approx \bar{c}_1 \approx \bar{c}_2 \) (when \( p = 1 \)). In this part of the input space, in other words, the three exact, general codes combining all three parameters \( P, F, \) and \( \langle f \rangle \) in different complex ways are all well approximated by the same relatively simple function of just \( \langle f \rangle \). (Because here \( \bar{c}_1 = \bar{c}_2 = \bar{c}_1 \approx \bar{c}_2 \approx \bar{c}_1 \approx \bar{c}_2 \), all three codes can be the same.)

It is worth pointing out the geometric view of this. We discussed earlier how we constructed our alternative input spaces with different sets of input parameters as dimensions (Fig. 2) so that, when the spaces were transformed through the NMT, the different effects of those parameters would immediately be apparent in the output structure. Clearly, if we find an input space that structures the output so as to vary along just one of the input dimensions, then that identifies the code (perhaps a nonlinear form of it; see APPENDIX K). When \( P \ll \tau \), this happens, approximately, when one of the input dimensions is \( \langle f \rangle \) (Fig. 7, left). More generally, therefore, our discussion here shows that it is possible to transform the input spaces in Fig. 2 into yet another input space (a different one for \( \bar{c}_1, \bar{c}_2, \) and \( \langle c \rangle \)), with \( \bar{c}_3 \) as one of the dimensions, along which the output will vary, linearly and exactly, not just when \( P \ll \tau \) but for all canonical patterns.

Clearly, then, the code exists relative to the sets of inputs being considered. The general codes in Eqs. 5 are exact over our whole set of canonical input patterns. From the general codes, we can derive different local codes that will be good approximations over different regions of the input space. Because only parts of the input space, and only approximate output, will be physiologically significant, such approximations are all that the nervous system need deal with. But knowledge of the unique general codes gives us a complete overview. It allows us to compare the quality of different local approximations and shows how various local codes must relate to each other; for instance, the local code must be very different on either side of \( \tau \) (see, e.g., Fig. 6). Conversely, we see that an experimentally determined code will be an approximate local one, depending heavily on the number and range of input parameters that are varied in the experiment.

**DISCUSSION**

The nervous system issues motor commands to muscles to generate behavior. All such commands must, however, pass through a filter that we have here called the NMT. The NMT transforms patterns of motor neuron firing into shapes of muscle contractions. This work is motivated by the fact that the NMT is far from being a straightforward, transparent link between motor neuron and muscle. The NMT is a dynamic, nonlinear, and modifiable filter. Consequently, motor neuron firing translates to muscle contraction in a complex way. This complexity must be taken into account by the nervous system when issuing its motor commands. It means, too, that observing the motor activity of the nervous system in isolation may not provide much insight into the significance of that activity in the behaving animal. When motor neurons or the CPG that drives them are observed to change their patterns of activity in various ways, for instance when modulators and drugs are applied, what changes, if any, would actually result in muscle contractions and behavior? Often, this question is ignored; when acknowledged, it is often left as too complex for sys-
tematic study. At the same time, it is clear in a variety of both invertebrate and vertebrate muscles that the NMT can transform the motor output of the nervous system in quite unexpected ways. What we have tried to do here is to develop a conceptual framework within which the connection between motor neuron activity and muscle contractions can be analyzed, understood, and predicted. Using this framework, we have then examined how the connection is governed by different basic properties of the NMT. We have geared our work not so much toward understanding in great detail the exact mechanical response of the muscle, but more toward providing a basis on which to consider (in the following papers) the functional performance of the neuromuscular unit in different behavioral tasks that the nervous system may command.

All of this is just as relevant to nonrhythmic as to rhythmic contractions and behaviors. We have focused here on the latter because, apart from their intrinsic importance, they dramatize the consequences of different properties of the NMT (as contraction accumulates over successive cycles to very different degrees) while at the same time imposing tighter and clearer functional constraints. Similarly, although the same issues arise in all motor neuron–driven muscles, in both vertebrates and invertebrates, our relatively simple illustrative examples—where we suppose, for instance, that the motor neuron fires in regular bursts, that the muscle contracts slowly, and that the same muscle, with a single set of properties, is required to respond appropriately to a broad range of firing patterns in different behaviors—are most immediately reminiscent of invertebrate neuromuscular systems, such as the Aplysia ARC-opener system.

Overview of approach and results

Physiologically, the motor neuron–muscle link comprises a sequence of steps, each with its own complex and only partially known dynamics: steps such as elevation of the presynaptic Ca$^{2+}$ concentration and release of transmitter (e.g., Fisher et al. 1997; Tank et al. 1995), elevation of Ca$^{2+}$ in the muscle (Rüegg 1992), and activation of the contractile machinery (Rüegg 1992; Woledge et al. 1985). The NMT lumps together these individual steps into an overall input-output relation, between the motor neuron firing pattern and contraction of the muscle, and so, too, between various parameters of the former and various parameters of the latter. Because the individual steps can have very different dynamics in different muscles in the same animal and across species, so can the overall NMT (Hoyle 1983). The characteristic speed of NMTs, for instance, differs over several orders of magnitude.

We wish to know how the NMT converts inputs to outputs, not just individually but collectively, for whole sets of related inputs, so that we can see how the output changes as the input varies in different ways. The approach that we have described here is essentially an elementary dynamical systems approach. We treat the NMT as a dynamical system whose operation can be represented geometrically in a multidimensional input-output space. This space has as its input dimensions parameters describing the set of firing patterns of interest, and as its output dimensions the contraction features of interest. Any definable contraction parameter may be studied in this way. Here we worked with elementary parameters such as the maximum, minimum, and mean contraction of a single muscle, but, as will be seen in Paper II, we can equally well take some complex functional readout of the interaction of several muscles: in essence, a whole behavior. Because the input pattern has its existence over intervals rather than points of time, we study the dynamics of the system interval-wise, here for instance period-wise. The input-output operation of the NMT is now visible in the structure of the input-output space.

The output depends on how the input pattern engages and interacts with the properties of the NMT. The two key properties of the NMT are the shape of its nonlinearity, and its characteristic time scale, relative to the time scale of the input pattern. We have analyzed the interaction of these elements in some detail, in particular for the steady-state output. A valuable tool in this analysis was the concept of pattern dependence, in a precise, technical sense, which we developed in our previous work (Brezina et al. 1997) as a measure of how the output varies with different temporal arrangements of the same, fixed amount of input, here a fixed mean firing frequency or spike density. Using this concept, the interaction between the elements may informally be summarized as follows. Pattern dependence of different kinds (we distinguished, in particular, positive pattern dependence, where the output increases as the spikes are grouped into bursts, and negative pattern dependence, where the converse occurs) arises when the input pattern engages different kinds of nonlinearities in the shape of the NMT. In a typical time-dependent NMT such as the two we examined here, however, these nonlinearities only appear on time scales longer than the characteristic time constant of the NMT. On shorter time scales, the NMT is effectively linear. But the input pattern exists only on time scales shorter than the cycle period. On longer time scales, what is perceived is simply the mean frequency of firing: the input is unpatterned. Only when the cycle period is longer than the time constant of the NMT, therefore, so that the time scales of the input pattern and of the NMT overlap, does the pattern engage the nonlinearities in the NMT and the pattern dependence appear. Thus there is a certain symmetry between the two elements. Both pattern and nonlinearity must be present for the mean contraction, for instance, to be pattern dependent; it becomes pattern independent—a function simply of the mean frequency of spikes, regardless of their temporal arrangement—if the input becomes unpatterned, or if the NMT becomes linear.

We have illustrated these ideas using a mathematical model NMT with completely known properties, and found very similar behavior in the real B15-ARC NMT of Aplysia. Phenomena of the same sort, analyzable on the same principles, have been noted in numerous muscles of both invertebrates and vertebrates (see, e.g., Burke et al. 1976; Hooper et al. 1999; Hoyle 1983; Josephson and Stokes 1987; Morris and Hooper 1997, 1998; Partridge 1966; Partridge and Benton 1981; Stokes and Josephson 1994). Pattern dependence (although not always in our precise definition) is recognized to be a prominent and physiologically important feature of the output of many muscles (Bevan et al. 1992; Gillyard and Kennedy 1969; Stein and Parmiggiani 1979; Zajac and Young 1980). Phenomena of the same origin emerge in work-loop analysis and other quasi-functional assays of muscular performance (Caiozzo and Baldwin 1997; Josephson 1993; Stevens 1996).

The dynamical structure of the NMT then has immediate implications for motor neuron–muscle control and coding (see Motor neuron–muscle control and coding).
Extensions of analysis

In results, we discussed simple examples, but in such a way as to suggest also how more complex cases could be dealt with. These would generally require expansion of our representational and computational apparatus, but not necessarily any more complex principles. Obvious extensions include the following.

MORE COMPLEX FIRING PATTERNS. Here we worked with a canonical set of elementary bursting patterns requiring for complete description just three parameters, and so three dimensions of the input space. More complex patterns would require more input dimensions. However, the key factor would still be the relative time scales of the pattern and the NMT. On time scales shorter than the time constant of the NMT, for instance, if the NMT becomes linear, pattern of any kind—no matter how complex, regular or irregular, constant, systematically varying, or random—is irrelevant to the output. Thus, in a pattern containing fast components or irregularities superimposed on a basic slow component, only the latter would be significant.

MORE MOTOR NEURONS, MORE MUSCLES. Here we worked with an elementary motor unit of one motor neuron driving one muscle. More complex physical plant—multiple motor neurons driving one muscle, one motor neuron driving multiple muscles, multiple motor units jointly producing some behavior—would again require a higher-dimensional space. Complex cross-connections of motor neurons, inhibitory as well as excitatory, to muscles occur in invertebrates (Atwood 1976; Hoyle 1983), to some extent even at the Aplysia ARC muscle (see Paper II). In the following papers we will deal with one configuration of multiple motor units jointly producing a behavior, namely the antagonistic pair of two motor units.

MORE COMPLEX NMT DYNAMICS. Here we have studied two rather simple NMTs, with dynamics governed, to a first approximation, by just two variables, the instantaneous firing frequency and contraction amplitude, with sigmoidal dependence on time and frequency, evolving monotonically to a single steady state. Many NMTs have such properties, and even these simple properties are capable, as we saw, of quite complex transformations of the motor neuron firing pattern.

Muscle physiology and biomechanics is known to be full of complicating processes and interactions, however. Presynaptically, transmitter release undergoes facilitation and depression (Fisher et al. 1997; Zucker 1989). Postsynaptically, muscle length, force, and speed depend on each other and on the load and stretch by other muscles (Partridge and Benton 1981; Ruegg 1992; Woledge et al. 1985). There are modulatory effects (see Paper III). All of these factors can a priori be expected to depend on the motor neuron firing pattern, furthermore not just on the instantaneous pattern, but on its history, and their own history too. The awareness of such complications is often what discourages systematic study of the NMT. How can these complications be accommodated within our framework?

The general answer is that, by developing a framework and principles, such as those above, that are relatively abstract—that deal, ultimately, with the dynamical structure, not its physical interpretation—we can indeed incorporate all of these factors in our analysis. They will appear simply as distortions of the structure of the dynamical space, for example as changes in the shapes of such surfaces as those in Figs. 6–10, and in some cases as additional variables or dimensions of the space. Roughly, we can say that the complicating factors will affect most the quantitative output of the NMT, less so its qualitative aspects, such as the number of dimensions or steady states, and least of all the overall framework and principles.

The key to dealing with each specific factor of this kind lies, in fact, in its history dependence. Indeed, the dynamical system approach in general can be thought of as one that seeks to represent the dynamical system in terms of a set of variables whose present values—the present state of the system—are sufficient to completely summarize its history, and predict its future.

Most generally, factors that affect the existing dynamical structure of the NMT, but vary independently of it (external modulation of the NMT by a hormone, for instance) will appear as one or more additional dimension orthogonal to the existing ones.

Of more immediate interest to us here, however, are factors that depend to a greater or lesser degree on the existing structure, in particular, like the output contraction itself, on the input firing pattern. Again, such factors can be classified according to their time scale relative to that of the input patterns of interest.

Factors that relax very slowly appear, on the time scale of interest, as essentially independent, as well as fixed. They can be treated as fixed background parameters rather than dynamical variables. We must not forget, however, that the structure of the NMT may change considerably depending on their values; for example, on the degree of tonic modulation (Paper III) or load (e.g., Partridge 1966). For any quantitatively accurate prediction of the output of the NMT, in a particular behavior for instance, we must therefore be sure to know the NMT with the appropriate settings of such parameters. The nervous system, too, must have this knowledge (see Motor neuron–muscle control and coding).

Factors that relax very fast are likewise already implicitly included in the existing structure of the NMT. They, in effect, have no independent history: their history is completely correlated with the history of another dynamical variable. For example, the fastest components of facilitation of transmitter release (Fisher et al. 1997) will always have relaxed to steady state on the time scale of the relatively slow input patterns that we applied here to the B15-ARC NMT. All of its output that we see, in Figs. 3A, 4, and 10, for instance, will therefore already contain the contribution of any such facilitation. Such fast processes may account for the quantitatively more complex structure of the B15-ARC NMT as compared to the model NMT.

It is factors that relax on an intermediate time scale, comparable to that of the input patterns of interest, that require particular attention. Here, we found that, for the set of patterns that we tested, the dynamics of the B15-ARC NMT—like those of the model NMT for all patterns—could be accounted for by just two variables, the instantaneous firing frequency and contraction amplitude. The whole history of the response of the system to the firing pattern, in other words, was summarized in the output, the contraction amplitude itself. There
were no “hidden” factors that had any different relation to the firing pattern in this parameter range.  

Only if the dynamics are as simple as just described is it possible to predict, as we did, the structure of the complete NMT from just a part of it, such as the contractions produced with steady firing, without having a specific model of the NMT. Had we found our prediction to be significantly inaccurate, we would have had either to determine the response of the NMT to different firing patterns purely empirically, or to develop a model of the NMT that specified additional “hidden” variables, and so dimensions of the dynamical space, to account for the extra pattern dependence that we found.

Additional dimensions do not necessarily change the qualitative structure of the NMT’s steady state—a higher-dimensional system can still converge on a single steady-state point—but they multiply the possibilities in this regard. Indeed, some real NMTs may have multiple steady states that they may reach from different parts of the dynamical space. Quasi-multistability appears, for instance, as a result of catch or latch phenomena in some invertebrate as well as vertebrate muscles (Burke et al. 1970, 1976; Ruegg 1971, 1992; Twarog and Muneoka 1972; Wilson and Larimer 1968). Steady states that are periodic, or even more complex, are possible (see Motor neuron–muscle control and coding). Expanded into a more complete form, the dynamical systems framework is ideal for the detection and study of such more complex dynamical behaviors (see, e.g., Jackson 1989; Thompson and Stewart 1986).

Applications of these principles will be seen in Paper III, when we expand the structure of the NMT to incorporate plasticity and modulation.

**Motor neuron–muscle control and coding**

The dynamical structure of the NMT is the medium through which all motor neuron–muscle control and coding must occur. Here we have interpreted issues of control and coding in the most elementary physiologically meaningful way, in terms of input-output predictability. If the motor neuron, or more generally the nervous system, sends a firing pattern through the NMT, under what circumstances and to what extent can it be sure of the contraction that will result? Are there parameters of the pattern that it can vary to predictably manipulate desired parameters of the contraction? Or, to put the question another way, what knowledge must the nervous system have, about the pattern or about the system as a whole, to be able to perform such prediction and manipulation?

Using as our analytic tool the existence of single-valued input-output mappings, we saw that, knowing just the firing pattern, the motor neuron cannot predict the resulting contraction, except when the contraction has reached a steady-state point. (Usually, this will entail any other dynamical variables of the NMT reaching steady-state points as well.) This is because the output depends not just on the input, but also, as we discussed in the last section, on the history of the system, summarized by its complete present state. But this history diminishes in significance as the system converges to the steady state. In the steady state, the history is, in effect, forgotten.

For our two NMTs, the history is completely summarized by one variable, the contraction amplitude itself. Thus the nervous system can predict future contractions exactly, under all circumstances, if, as well as the firing pattern, it knows the present contraction amplitude. More generally, for any NMT, it must know the values of all of the dynamical variables. But to a limited extent it can substitute for this complete knowledge just a memory of the firing pattern. In particular, if it only knows that the pattern has lasted long enough, it can conclude that the contraction and its parameters have approached as close as desired to their unique, predictable, steady-state values.

In any case, for the nervous system to explicitly compute the output, it must also know the quantitative structure of the NMT. To what extent such computation actually goes on, and the required knowledge is actually represented in the nervous system, will be an issue below.

The functional implication of all this is that stereotyped, repetitive contractions, especially if fine tolerances are not essential, can be satisfactorily controlled in a purely feed-forward way. The nervous system simply sends through the NMT the repetitive pattern that predicts the desired steady-state output, knowing that after no more than a few cycles the output will be close enough to that value. [This is somewhat reminiscent of the equilibrium point hypothesis that has been proposed to explain even nonrepetitive movements of vertebrates (see, e.g., Bizzi et al. 1991).] Sensory feedback to report the actual present output will tend to be required, on the other hand, if transitions from one behavior to another are to be controlled precisely, and in precise, nonstereotyped, nonrepetitive behaviors: wherever, it is the transient, rather than the steady-state, output that is of essence. Feedback does indeed appear to be particularly important in such situations (Houk and Rymer 1981; Pearson 1993; Stein et al. 1997).

For our two NMTs, the history of the system is completely summarized by the contraction amplitude, a variable that is easily reported by sensory feedback. This allows complete prediction of future contractions. But the future output of more complex NMTs, with “hidden” dynamical variables, may not be completely predictable, even with feedback of the present output, in non–steady-state situations.

It is also possible that the system may not settle to a completely predictable and controllable steady-state point. For example, some muscles exhibit myogenic as well as neurogenic contractions. This is the case in many vertebrate smooth muscles (Hoyle 1983; Wood 1989), the leech heart (Calabrese and Maranto 1984; Maranto and Calabrese 1984), and a number of other invertebrate muscles, especially when exposed to contraction-potentiating modulators and hormones (Evans and Myers 1986; Kuhlman et al. 1985; Meyrand and Marder 1991).
Often there is a continuum of contractile behavior with increasing concentration of the modulator, from ordinary neurogenic contractions, through a phase where the motor neuron firing only triggers or entrains myogenic contractions, to spontaneous myogenic contractions (cf. Hoyle et al. 1999). This corresponds to a continuum of predictability and controllability of the muscle by the motor neuron. Formally similar situations occur in other muscle types, for instance asynchronous insect flight muscle (Hoyle 1983).

It is worth briefly distinguishing two reasons for such behavior. In a more complex NMT, the steady state may not be a point, but, for example, a cycle. Alternatively, it may be a point, but one whose value varies along one of the dimensions of the NMT, which then amounts to, in essence, an extra input independent of the motor neuron firing pattern.

In such cases, where there appear to be extra factors or inputs perturbing the NMT as it is currently conceived, incomplete predictability may once again be remedied analytically by enlarging the scope—the number of variables or dimensions—of the system to incorporate the perturbations, and physiologically by providing the relevant information to the controlling neurons. Incomplete controllability, similarly, invites us to consider additional, perhaps higher-order, parameters of the output that may still be controlled. For example, when motor neuron firing merely triggers contractions, it no longer controls their overall waveform or maximum, minimum, or mean amplitude, but it still controls their frequency. Indeed, our two NMTs, too, control this parameter at all times, not just in the steady state.

From our initial elementary definition of control, our discussion has now led us to something closer to the more general idea of controllability employed in control theory (e.g., Jacobs 1993; Stengel 1994). Rather than asking merely whether an input predicts the immediately corresponding output, the question becomes whether an input can drive the system, and its output, to some desired state at some time in the future. Here predictability and controllability part company. The output may be completely predictable, yet not fully controllable, because no available input may be able to produce the desired output. With our two NMTs, simple outputs are fully controllable: any steady-state maximum, minimum, or mean contraction can be produced by some canonical firing pattern, indeed, as Figs. 6–10 show, redundantly by many of them. But controllability decreases as the desired output grows more complex. At least one pattern can still be found to produce any combination of maximum and minimum contraction. But no canonical pattern (indeed, no firing pattern at all) can further combine a given maximum and minimum contraction with arbitrarily fast rates of transition between them. This is because, as we saw in Results, all of these parameters are mutually dependent, by virtue of the fact that our NMTs (and, to a greater or lesser extent, all NMTs) can produce only a restricted set of contraction shapes (see further Appendix I). This will have important functional consequences in the following papers.

When the input pattern does predict and control the output, can we then identify within the input pattern a “code” for the output? This question is usually asked, and studied by examining various empirical input-output relationships (e.g., Morris and Hooper 1998), in the hope of finding simple codes between the “natural” parameters of the input and output, such that, say, the intraburst firing frequency will code—and, it is usually expected, code linearly—for the maximum contraction, the burst duration will code for the mean contraction, and so on. To predict and control that output parameter, the nervous system would then need to know and be able to vary just that input parameter; the rest of the structure of the input pattern would be irrelevant.

Indeed, we saw that, if an input-output mapping exists, as it does in the steady state, then a code exists, because in essence it is that mapping. There is a unique code in the firing pattern for each such parameter as the steady-state maximum, minimum, and mean contraction. If we know the NMT, we can compute these codes (e.g., Eqs. 5 in Results).

But, although a code exists, it is not simple. In general we can expect each code to be a different complex, nonlinear function of all of the input parameters (as Eqs. 5 illustrate). Because the code is unique, no simpler code—in particular, no code by just one or another of the simple, “natural” input parameters—exists. The complexity of the code directly mirrors the complexity of the NMT through which the firing pattern must pass to produce the contractions.

Certainly, these complex codes can, to different degrees, be approximated by simpler codes. Because always some range of output is functionally acceptable, such approximations will be all that the nervous system need deal with. However, very different approximations will be accurate in different regions of the input space. Thus, as we saw in Figs. 7 and 8, quite different aspects of the firing pattern will be most critical for a particular contraction parameter, and the same aspect perhaps for different parameters, with patterns faster and slower than the time constant of the NMT. In their study of neuromuscular output in the lobster, Morris and Hooper (1997, 1998) found such phenomena.

All of this raises a fundamental issue. While the concept of a “code” is valuable to us analytically, to what extent is it actually used by the nervous system? A code implies the existence of two complementary operations, of encoding and decoding. The second would be done by the NMT; the first, presumably, by the nervous system. Consider what the nervous system would have to do to perform an encoding in the way that, with the information in this paper, we would do it. Given a desired value of a contraction parameter, the task is to compute a set of values for the parameters of the firing pattern that will produce it. To do this, the nervous system would have to compute complex functions like those in Eqs. 5, or rather their inverses. This would have to be done not just for one, but simultaneously for multiple contraction parameters, mutually dependent, and all dependent on the same parameters of the firing pattern. Depending on the relative numbers of the firing-pattern and contraction parameters involved and on the structure of the NMT, there may be multiple solutions (e.g., Figs. 6–10), one solution, or no solutions at all (Appendix I; Paper II). Finally, all of these computations would alter with external influences (or, if these are incorporated into the NMT, in different regions of a more complex NMT) such as modulation of the NMT (Paper III). In sum, because the encoding mirrors the decoding, and the decoding is done by the NMT, the nervous system would have to have an internal representation of the current structure of the NMT. The nervous system would, in essence, have to be capable of an overview of the
structure of the NMT of the kind that we have in Eqs. 5 or in Figs. 6–10.

Certainly in relatively simple systems such as the Aplysia ARC system, a much more plausible picture is of just a single operation, straightforwardly performed by the NMT. The nervous system generates various firing patterns that, when sent through the NMT, produce various contractions. But the nervous system does not choose these patterns based on any calculation of their expected effect. Indeed, it does not choose them at all, in any immediate sense. Rather, those patterns and contractions produce what ultimately matters, efficient behaviors (Paper II), and the nervous system, together with the NMT, has evolved as an integrated, automatic mechanism to generate just that subset of patterns and contractions. The system moves automatically only along certain paths through the dynamical space of the NMT. We have an overview of the whole space and so can see what consequences other patterns, too, would bring, but the nervous system does not.

From this perspective, the problems above are no longer problematic. External influences such as modulation are simply parts of the automatic mechanism (Paper III). The nonlinearity and complexity of the structure of the NMT, while difficult from our analytic perspective, simply reflect its implementation by real biological processes. Biological processes are intrinsically dynamic, nonlinear, and connected in networks of divergent-convergent interactions whereby, just as we see in the NMTs, each input parameter influences multiple output parameters, and multiple input parameters influence each output parameter (see Brezina and Weiss 1997). The structure is naturally complex and nonlinear; to make it simple and linear would require, paradoxically, additional complexity. To look for simple, linear codes is thus probably a misconceived enterprise. Similar conclusions have been reached concerning the distributed representation of more abstract aspects of movement at higher levels in the vertebrate nervous system (e.g., Alexander et al. 1994; Fetz 1994).

In fact, the complex, nonlinear structure of the NMT has positive advantages. As with other biological networks (Brezina and Weiss 1997), we can think of the structure of the NMT as embodying “hard-wired” information on the basis of which multiple inputs and outputs are automatically coordinated and integrated. Thus, for instance, a change in any one parameter of the firing pattern leads to coordinated changes in all of the contraction parameters. The nonlinearities in the structure vary the sensitivity in different regions of the input space, usually maximizing it in the intermediate, physiological parameter range. Different NMTs have quantitatively different nonlinearities, on different time scales. As a result, they respond preferentially to, and can be differentially controlled by, different firing patterns. It is interesting in this context that muscles that generate, for each motor neuron spike, a spike and a relatively standard twitch in the muscle—most notably, of course, vertebrate skeletal muscles—have NMTs that may, consequently, be somewhat more linear. In these, more of the integrative work may be performed by the CNS.

In the following two papers, we go on to use the conceptual framework that we have developed here to examine the functional role of the NMT.

APPENDIX A

Input firing patterns

Precisely, the canonical set includes only waveforms with the following parameter values: $d_{\text{intra}} > 0$, $d_{\text{inter}} \geq 0$, $f_{\text{intra}} \geq 0$; or $P > 0$, $0 < F \leq 1$, $\langle f \rangle \geq 0$. In particular, we exclude $P = 0$ and consequently $d_{\text{intra}} = 0$ and $F = 0$ (cf. Eq. 2 in RESULTS) because they have no useful meaning, would yield singularities in the output (e.g., in Eqs. F4 and F5 below), and because, when they are excluded, there is then one-to-one correspondence among the three representations in Fig. 2. Any point in one space maps to a point in the other two spaces. Furthermore, every point in each space maps to a canonical waveform, and every canonical waveform maps to a point in each space, except when $d_{\text{inter}} = 0$, $F = 1$, or when $f_{\text{intra}} = \langle f \rangle = 0$. We include these values and the corresponding waveforms in the canonical set because they represent two important special kinds of input, namely steady, continuous firing and zero input, respectively. In the former case $f_{\text{intra}} = \langle f \rangle$ is given but $d_{\text{intra}} = P$ is unspecified; the single waveform of steady, continuous firing at any particular frequency is therefore represented by a horizontal line in the rear plane of each space in Fig. 2. In the latter case both $d_{\text{intra}}$ and $d_{\text{inter}}$, or $P$ and $F$, are unspecified; the single waveform of zero input is therefore represented by the whole bottom plane of each space. However, when transformed through an NMT, all points in each line or plane yield the same output, as required.

In defining the canonical waveforms with just three parameters, we have ignored the phase of the waveforms. All input waveforms $f(t)$ [and similarly output waveforms $\psi(t)$] that can be superimposed by translation along the $t$ axis are considered to be identical; $t$ is relative rather than absolute. This is appropriate because our main focus here is not on the temporal relationships between different waveforms, but rather on the internal structure of individual waveforms. See also APPENDIX D.

APPENDIX B

Real and ideal NMTs

Our model NMT is an ideal NMT, defined continuously for every $t$ and $f$ in the relevant real-valued interval. The real B15-ARC NMT, however, is defined, strictly, only at those finitely many, isolated values of $t$ and $f$ where measurements were actually made. This permits an explicit input-output listing of the NMT. However, taking just this as our formal definition of the NMT creates significant problems. If the measurements are made at different values of $t$ and $f$, we will have a different listing and so, formally, a different NMT. Furthermore, owing to experimental variability and error, even a duplicate set of measurements at the same $t$ and $f$ will always be slightly different, again giving, formally, a different NMT. We would prefer to consider all such NMTs as being, in fact, the same NMT. Finally, many of our arguments rely, explicitly or implicitly, on continuity. In this work we therefore adopt, for simplicity, the usual “naïve” view that there exists a single, continuously defined, ideal NMT, to which the experimental measurements are just different approximations. The usual course would be to use the experimental data to create the most likely specific model of the ideal NMT. We avoid any such specification (see Steady-state output of the B15-ARC NMT in RESULTS), but simply add to our limited experimental listing of the NMT the assumption that an underlying ideal NMT exists. The NMT is defined “completely” if the experimental listing is a sufficiently accurate and sufficiently complete approximation.

APPENDIX C

Time constant of the NMT

Clearly, no single time constant describes the whole complex time course of $c$, even when $f$ is constant, in Fig. 3A1, or in Fig. 3B1.
Further, the time constant varies with $f$, and for each bursting input waveform there are consequently two time constants, for $f = f_{\text{inter}}$ and $f = 0$ (see APPENDIX F). The time scale of the NMT, therefore, is better described by a range of characteristic times. For simplicity, however, we usually lump them all together under the generic designation $\tau^*$. 

APPENDIX D

Delay in the NMT

Due to cumulative delay in the sequence of steps underlying a real NMT, the output corresponding to any input does not occur at the same time, but some time later. Strictly, all relations that we establish between input and output must correct for this to be meaningful. We could allow for it with a formal delay in our definition of the NMT (e.g., in Eq. 4 for the model NMT). In the B15-ARC NMT, however, the delay appears insignificantly short relative to the slow time scale of the NMT. We therefore simply ignore this complication.

APPENDIX E

NMT dynamics

1) Point-wise, the $(f, c)$ plane is a state space completely filled with flow of trajectories $[f(t), c(t)]$, determined, in the case of the model NMT, by solutions of Eq. 4 with the input $f(t)$; we assume that, to a first approximation, the B15-ARC NMT behaves similarly (cf. APPENDIX 1, Steady-state output of the B15-ARC NMT in results, and the discussion). Here as well as in 2), we omit for simplicity any bounds that may restrict the space, e.g., $f \geq 0$, $c \geq 0$. The two variables $f$ and $c$ are necessary and sufficient to determine the evolution of the system. Any starting point $[f(0), c(0)]$ and $f(t)$ defined over the next time interval $\Delta t$ uniquely determine $c(t_0 + \Delta t)$. For the same $f(t)$, the trajectories are nonintersecting. A steady state is just a point where $c$ remains constant if $f$ does. The model NMT, and apparently also the B15-ARC NMT, monotonically approaches a unique steady state $c_n(f)$ (APPENDIX F). Indeed, in a bounded state space $(f, c)$, the approach to a unique $c_n(f)$ must be monotonic.

2) Period-wise, as a consequences of 1), a space with sufficient input and output dimensions to distinctly represent each $f(t)$ and $c(t)$ is a state space with properties analogous to those in 1) (except that the system is now discrete in time).

For any canonical $f(t)$ [we may omit steady input for which all of the following holds in degenerate form, but which is better treated simply as in 1)], we can write the corresponding $c(t)$ in period $n$ as

$$
c_{n}(t') = \begin{cases} 
c_{n,\text{inter}}(t') & \text{if } 0 \leq t' \leq d_{\text{inter}} \\
c_{n,\text{intra}}(t' - d_{\text{inter}}) & \text{if } d_{\text{inter}} \leq t' \leq P 
\end{cases}
$$

where $t'$ is the time since the beginning of the period, $c_{\text{intra}}$ the interburst output corresponding to $f = f_{\text{inter}}$, and $c_{\text{inter}}$ the interburst output corresponding to $f = 0$. By 1), $c_{\text{intra}}$ and $c_{\text{inter}}$ are simply sections of trajectories from the point-wise state space $(f, c)$. $c_{\text{intra}}$ evolves monotonically toward $c_{n}(f_{\text{inter}})$, and $c_{\text{inter}}$ toward $c_{n,\text{inter}}(0)$. Successive $c_{\text{intra}}$ and $c_{\text{inter}}$ and so successive periods $c_0$ and $c_{n-1}$ are continuous: $c_{\text{intra}}(d_{\text{inter}}) = c_{\text{inter}}(0)$ designate the same time point, as do $c_{n}(P) = c_{n,\text{inter}}(P - d_{\text{inter}}) = c_{\text{inter}}(d_{\text{inter}}) = c_{n,\text{inter}}(0) = c_{n+1}(0)$. Furthermore, all periods $c_n$ producible with any particular $f(t)$ can be ordered by a single point, for instance their initial point $c_0(0)$, such that, for any two periods $c_0$ and $c_1$, if $c_1(0) > c_1(0)$ then $c_{n}(0) > c_{n+1}(0)$, and if $c_1(0) = c_1(0)$ then $c_{n}(0) = c_{n+1}(0)$, at every time point $t'$. With continuity in $c$ assured from 1), there is then continuous one-to-one correspondence between the whole period $c_0$, each point $c_{n}(t')$, and parameters such as $c_{\text{intra}}$ and $c_{\text{inter}}$. Each evolves monotonically: for successive periods, $c_0(0) > c_{n+1}(0)$ implies that $c_{n+1}(0) > c_{n+2}(0)$, and $c_0(0) < c_{n+1}(0)$ implies that $c_{n+1}(0) < c_{n+2}(0)$, until the system reaches a dynamical steady state when $c_0(0) = c_{\text{inter}}(0)$. This last equality is the necessary and sufficient condition for the steady state. We can rewrite it as

$$
c_{\text{inter}}(0) = c_{\text{inter}}(d_{\text{inter}})
$$

or as

$$
\Delta c_{\text{inter}} = -\Delta c_{\text{inter}}
$$

where $\Delta c_{\text{inter}} = c_{\text{inter}}(d_{\text{inter}}) - c_{\text{inter}}(0)$, the interburst change in $c$, and $\Delta c_{\text{inter}} = c_{\text{inter}}(d_{\text{inter}}) - c_{\text{inter}}(0)$, the interburst change in $c$. There is just one such steady state: for the model NMT, this is best seen if we recast Eq. 2b in terms of the intermediate $a$, for which everything in this appendix holds just as for $c$, because it is simply $c^2$ (Eq. 4). As $a$ increases, $\Delta c_{\text{inter}}$ monotonically decreases through zero at $a = a_\infty(f_{\text{inter}}) > 0$, while $\Delta c_{\text{inter}}$ monotonically increases from zero at $a = a_\infty(0) = 0$ (Eqs. FIb and FIc). There is one and only one point where $\Delta c_{\text{inter}} = -\Delta c_{\text{inter}}$. The same applies to be true, in this case for $c$ itself, for the B15-ARC NMT (Eqs. IIb and IIc).

APPENDIX F

Output of the model NMT

Solving Eq. 4 for a canonical $f(t)$, we can rewrite Eq. 1 as

$$
c_{n}(t') = a^2(t') = \begin{cases} 
a_{\text{inter}}^2(t') & \text{if } 0 \leq t' \leq d_{\text{inter}} \\
a_{n,\text{inter}}^2(t' - d_{\text{inter}}) & \text{if } d_{\text{inter}} \leq t' \leq P 
\end{cases}
$$

where, with $\tau = (a^2 + \beta)^{-1}$ and $a(f) = a^2(f)$

$$
a_{\text{inter}}(t') = a_{\text{inter}}(f_{\text{inter}}) - [a_{\text{inter}}(f_{\text{inter}}) - a_{\text{inter}}(0)] \exp[-\tau(f_{\text{inter}})]
$$

$$
a_{n,\text{inter}}(t') = a_{n,\text{inter}}(0) - [a_{n,\text{inter}}(0) - a_{\text{inter}}(0)] \exp[-\tau(f_{\text{inter}})]
$$

The instantaneous conversion relation $d'' = c$ operates on the whole output waveform, each of its points, and parameters such as the maximum or minimum output (but not, in general, the mean output: $(c) \neq \langle d'' \rangle$). Also, we have

$$
c_{n}(f) = a^2(f) = \left[ \frac{a_{\text{inter}}^2}{a_{\text{inter}}^2 + \beta} \right]^g
$$

Using the interconversion $f_{\text{inter}}F = \langle f \rangle$, we note that

$$
c_{n}(f_{\text{inter}}) = \left[ \frac{a_{\text{inter}}^2}{a_{\text{inter}}^2 + \beta} \right]^g = \left[ \frac{a(f)^p}{a(f)^p + \beta F} \right]^g
$$

and

$$
c_{n}(F) = \left[ \frac{a_{n,\text{inter}}^2}{a_{n,\text{inter}}^2 + \beta F} \right]^g
$$

When $F = 1$, $f_{\text{inter}} = (f)$, and $c_{n}(f_{\text{inter}}) = c_{n}(f)$. In the dynamical steady state of the system, $a_{\text{inter}}(0) = a_{\text{inter}}(d_{\text{inter}})$ (Eq. 2a). We recall also that $a_{\text{inter}}(d_{\text{inter}}) = a_{\text{inter}}(0)$. Because $a_\infty(f_{\text{inter}}) > a_\infty(0)$, the first point is the steady-state minimum $a_\infty$, the second point the steady-state maximum $a_\infty$. Replacing $a_{\text{inter}}(0)$ with $a_{\text{inter}}(d_{\text{inter}}) = a_\infty$, in Eq. FIb, $a_{\text{inter}}(0)$ with $a_{\text{inter}}(0)$ in Eq. FIc, and solving the system of Eqs. FI for $a_\infty$ and $a_\infty$, we obtain the unique steady-state output waveform

$$
\begin{bmatrix} a_{\text{inter}}^2(t') \end{bmatrix} = \left[ \frac{a_{\text{inter}}^2}{a_{\text{inter}}^2 + \beta} \right]^g
$$

$$
\begin{bmatrix} c(t') \end{bmatrix} = \left[ \frac{a_{\text{inter}}^2}{a_{\text{inter}}^2 + \beta} - a_\infty \right] \exp[-(a_{\text{inter}}^2 + \beta t')]^g
$$

if $0 \leq t' \leq d_{\text{inter}}$

$$
\begin{bmatrix} a_{\text{inter}}^2(t' - d_{\text{inter}}) \end{bmatrix} = [a_{\infty} \exp[-\beta(t' - d_{\text{inter}})]^g
$$

if $d_{\text{inter}} \leq t' \leq P$
with maximum and minimum output, in the \((d_{intra}, d_{inter}, f_{intra})\) and \((P, F, f, (f))\) representations,

\[
\dot{c}_e = a^e = \left( \frac{\alpha_{f_{intra}}}{\alpha_{f_{intra}} + \beta} \right) \left( 1 - \exp\left[ -\left( \frac{\alpha_{f_{intra}}}{\alpha_{f_{intra}} + \beta} \right) d_{intra} \right] \right) + \left( \frac{\alpha(f)}{\alpha(f) + \beta F} \right) \left( 1 - \exp\left[ -\left( \frac{\alpha(f)}{\alpha(f) + \beta F} \right) d_{inter} \right] \right)
\]

\[
\zeta_e = a^\zeta_e = \left( \frac{\alpha_{f_{intra}}}{\alpha_{f_{intra}} + \beta} \right) \left( 1 - \exp\left[ -\left( \frac{\alpha_{f_{intra}}}{\alpha_{f_{intra}} + \beta} \right) d_{intra} \right] \right) \exp\left[ \left( \frac{\alpha_{f_{intra}}}{\alpha_{f_{intra}} + \beta} \right) d_{intra} \right]
\]

The mean steady-state output is

\[
(c)_e = \frac{1}{P} \int_0^P \left[ c(t') \right] \, dt'
\]

\[
= \frac{1}{P} \left( \int_0^{d_{intra}} \left[ a_{f_{intra}}(t') \right] \, dt' + \int_{d_{intra}}^P \left[ a_{f_{intra}}(t' - d_{intra}) \right] \, dt' \right)
\]

which, for any \(q = 1, 2, 3, \ldots\), has a straightforward but lengthy explicit solution (for \(q = 3\), see Eq. 5e).

When \(d_{inter} = 0\) or \(F = 1\) (steady input), Eqs. F4–F6 yield \(\dot{c}_e = \zeta_e = (c)_e = c_e(f_{intra}) = c_e(f)\).

**APPENDIX G**

**Steady-state output of the model NMT when \(P \ll \tau\) and \(P \gg \tau\)**

1) \(P \ll \tau\). Taking the limits of Eqs. F4–F6, we obtain

\[
\lim_{P \to 0} \dot{c}_e = \lim_{P \to 0} \zeta_e = \lim_{P \to 0} (c)_e = \left( \frac{\alpha(f)}{\alpha(f) + \beta F} \right)^q
\]

which yields \(\lim \dot{c}_e = \lim \zeta_e = \lim (c)_e = c_e(f)\) when \(P = 1\).

Alternatively, when \(P \to 0\) and \([c(t)]_0 = \text{constant}\), say \(c^*\) (cf. Fig. 5A), we can solve Eq. 4 simply by equating the mean rates of increase and decrease of \(c\). For a canonical \(f(t)\), we have \(\alpha_{f_{intra}}(1 - \sqrt{c^*})FP = \beta \sqrt{c^*} F\), which yields \(c^* = \left( \frac{\alpha_{f_{intra}}(\sqrt{c^*})}{\alpha_{f_{intra}} + \beta F} \right)^q\), equivalent to Eq. GI. The output is pattern independent if and only if \(c^*\) is the same if \(f\) is). With \(f = f_{intra}, F = constant\), \(c^*\) is constant if and only if \(P = 1\). Then \(c^* = c_e(f)\), as required. In other words, for pattern-independent output \(c^*\) at some \(f\), when \(P = 0\) and \([c(t)]_0 = \text{constant}\), a necessary and sufficient condition is that the rate of change of \(c\) be linear with \(f\) around \(c^*\).

The above implies further that Eqs. F1 can simplify to pattern-independent output as \(P \to 0\) only as long as the terms \(\tau\) and \(a_e\) remain related to each other in a particular way, namely by the relations \(\tau = \alpha f + \beta f^{-1}\), \(a_e = \alpha f\), that derives from the original differential Eq. 4 that becomes linear as \(P \to 0\). Eqs. F1 with arbitrary \(\tau\) and \(a_e\) are, in general, no longer solutions of any such differential equation and do not simplify to pattern-independent output as \(P \to 0\) (cf. Paper III).

For a more general treatment of the relationship between linearity and pattern dependence see Brezina et al. (1997).

2) \(P \gg \tau\). Taking the limits of Eqs. F4–F6, we obtain

\[
\lim_{P \to \infty} \dot{c}_e = \lim_{P \to \infty} \zeta_e = \left( c_e(f_{intra}) \right) \text{ if } F = 1
\]

\[
\lim_{P \to \infty} \dot{c}_e = \lim_{P \to \infty} \zeta_e = \left( c_e(f) \right) \text{ if } F < 1
\]

**APPENDIX H**

**Ideal linear NMT**

The defining equation, corresponding to Eq. 4 for the model NMT, is \(dc(t)/dt = af(t) - \beta c(t)\), with solutions and behavior as in APPENDICES E and F with appropriate modifications, in particular

\[
\tau(f) = 1/\beta, \quad c_e(f) = af/\beta
\]

and, corresponding to Eq. F6

\[
(c)_e = \alpha(f)/\beta = c_e(f)
\]

**APPENDIX I**

**Output of the B15-ARC NMT**

According to APPENDIX E, contractions produced by the B15-ARC NMT are described by Eq. F1b, where, if the point-wise evolution of the system truly depends on \(f\) and \(c\) only (APPENDIX E, f), \(c_{intra}\) and \(c_{inter}\) are the unique trajectory sections defined by the initial values \(c = c_{inter}(0)\) and \(c_{inter}(0), \) with input \(f = f_{inter}\) and \(0,\) maintained for \(\Delta t = d_{inter}\) and \(d_{inter}\) respectively. [And, by definition, \(c_{inter}(0) = c_{inter}(d_{inter})\).] These trajectories are identical whenever these values occur, whatever the period-wise pattern. We can therefore take sections of records such as those in Fig. 3A I obtained with steady firing to reconstruct contraction waveforms produced by bursting patterns.

In the dynamical steady state, Eq. E2 must also be satisfied. We must find trajectory sections \(c_{intra}\) and \(c_{inter}\) such that not only \(c_{inter}(0) = c_{inter}(d_{inter})\) but also \(c_{intra}(0) = c_{intra}(d_{inter})\). [Because the system is monotonic and \(c_{intra}(f_{inter}) > c_{intra}(0)\), the former is \(c_{intra}\) the latter \(c_{inter}\).] Without an analytic expression for \(c(f)\) in the case of the B15-ARC NMT, we can only find such \(c_{intra}\) and \(c_{inter}\) by iterative numerical search.

However, we can obtain immediate expressions for the steady-state \(c_{intra}\) and \(c_{inter}\) if we make the simplifying assumption that the contraction kinetics depend, to a first approximation, only on \(f\) and not on \(c\), that they behave like the exponential kinetics of the intermediate \(a\) in the model NMT (Eqs. 5b and 5c). If so, we can take an arbitrary section of the record obtained with steady firing at the correct \(f\) and simply scale it appropriately. We designate records obtained with steady firing at \(f = f_{inter}\) and \(f = 0,\) respectively, as \(c_{f=inter}(t^*)\) and \(c_{f=0}(t^*)\) where \(t^*\) is the time since the start of firing or cessation of firing, respectively. We take sections beginning with \(t^* = 0\). This gives us

\[
[c(t')]_e = \left\{ \begin{array}{ll} [c_{inter}(t')]_e & \text{if } 0 \leq t' \leq d_{inter} \\ [c_{inter}(t') - c_{inter}(0)]_e & \text{if } d_{inter} \leq t' \leq P \end{array} \right. (Ia)
\]

where \(c_{inter}(0) = 0\) and \(c_{inter}(0) = 0\) (Fig. 3A), Eqs. 1b and 1c reduce to

\[
[c_{inter}(t')]_e = c_{f=inter}(t') \left( 1 - \frac{c_{f=inter}(0)}{c_{inter}(0)} \right) + \zeta_e
\]

\[
[c_{inter}(t')]_e = c_{f=inter}(t') \left( \frac{\zeta_e}{c_{inter}(0)} \right) + \zeta_e
\]
If we now recall that, also, \( \epsilon_{\text{intra}} = [c_{\text{intra}}(d_{\text{intra}})]_c \) and \( \epsilon_{\text{extra}} = [c_{\text{extra}}(d_{\text{extra}})]_c \), we find

\[
\epsilon_{\text{extra}} = c_{\text{extra}}(0)\varphi, \quad \epsilon_{\text{intra}} = c_{\text{intra}}(d_{\text{intra}})\varphi
\]  

(12)

where

\[
\varphi = \frac{c_{\text{intra}}(d_{\text{intra}})}{c_{\text{extra}}(d_{\text{extra}})[c_{\text{extra}}(d_{\text{extra}}) + c_{\text{intra}}(f_{\text{intra}})] - 1} + c_{\text{extra}}(0)
\]

Finally

\[
(c)_c = \frac{1}{P} \int_0^P \left[ \epsilon(t') \right] \, dt' = \frac{1}{P} \int_0^{t_{\text{extra}}} \left[ c_{\text{intra}}(t') \right] \, dt' + \frac{1}{P} \int_{t_{\text{extra}}}^{P} \left[ c_{\text{intra}}(t' - d_{\text{intra}}) \right] \, dt'
\]  

(13)

which, without an analytic expression for \( c(t) \), must be evaluated numerically.

Although the kinetics of \( a \) in the model NMT are truly independent of \( a \) in the way assumed by Eqs. 11–13, those of \( c \) produced by the B15-ARC NMT (or indeed by the model NMT) clearly do vary with \( c \) to some extent, departing from the exponential (becoming sigmoidal) particularly at small \( r^* \) and small (nonzero) \( f \) (Fig. 3). To the extent that they do, the reconstruction using the simplifying assumption of Eqs. 11–13, and that without it, will differ, most significantly at short \( P \) (see Fig. 10B) where, with \( r^* = 0 \), the former will predict smaller \( c \) than the latter. Given the actual kinetics of \( c \), reconstruction using the assumption amounts to adding to the simple pointwise \((f, c)\) state space in APPENDIX E, I an extra state variable sensitive to the history of firing. This may not be entirely inappropriate (see DISCUSSION). In any case, the two reconstructions are similar enough that both are probably consistent with the experimental data in Fig. 10B.

APPENDIX J
Discrete spikes in fast patterns

Our conversion of the timing of discrete spikes to the “instantaneous” firing frequency \( f \) is most satisfactory for very slow patterns that hold \( f \) steady over many interspike intervals, loses accuracy as the pattern speeds up, and becomes meaningless when each burst comes to contain just one spike, roughly when \( P \) shortens below the limit \( P^* = 2/(f) \). Different patterns can then still of course be specified in terms of the continuous variable \( f \), but in terms of discrete spikes they are all indistinguishable from each other and identical simply to steady firing at \( f \). Because no pattern can be produced, output necessarily becomes pattern independent. For a real NMT that must operate with real spikes, \( P^* \) is a real, physiologically significant limit and reason why contractions must become pattern independent with fast patterns. In Fig. 10B, with \( f \approx 5.7 \) Hz, \( P^* = 0.35 \) s. However, the contractions already come close to being pattern independent at values of \( P \) significantly longer than this: the B15-ARC NMT does not distinguish patterns as fast as \( P^* \) in any case. In general, if an NMT becomes linear on time scales shorter than \( \tau \), and \( \tau > P^* \), then any shortcomings of \( f \) in describing the real spike pattern will not be significant (Brezina et al. 1997).

APPENDIX K
Linear and nonlinear coding

In RESULTS we consider only the most restricted form of the coding problem, where, for a coding input parameter \( F \) and coded output parameter \( \epsilon \), \( \epsilon = \epsilon(F) \). But we can easily relax the equality between \( \epsilon \) and \( \epsilon \) is related to an arbitrary code \( \bar{F} \), which codes for \( \epsilon \) through an arbitrary linear or nonlinear mapping \( g \), in a straightforward way. Because \( g(\bar{F}) = \epsilon \), therefore also \( g(\bar{F}) = \bar{F} \). Because \( g \) is a function of \( \bar{F} \) only, all of the simple input parameters that are combined in \( \bar{F} \) must already be similarly combined in \( \bar{F} \).

APPENDIX L
Controlrability and factors restricting the set of outputs of the NMT

Expanding our elementary definition of control to the more general idea of system controllability in essence turns around the question of output-space representation. We now ask, not so much what outputs will emerge from the NMT and what output space is needed to represent them, but rather, given an output space, what parts of it can be reached with a particular input (cf. Existence of mappings in RESULTS) and, more importantly, with any input? The answer has to do with how restricted, relative to the given output space, is the set of outputs—shapes of output waveforms \( c(t) \) and their parameters—that the NMT can actually produce. Informally, we can distinguish three factors that determine this.

1) The available input set. From a restricted set of \( f(t) \), an NMT cannot generate arbitrary \( c(t) \), but only a correspondingly restricted subset. Most important is the dimensionality of the input set. Through an input-output mapping, in the steady state for instance, an NMT can continuously reach and control an output space of no greater number of dimensions than the number of independent input dimensions. Thus the three dimensions of our canonical set of input patterns can control—vary separately from one another, as opposed to in an obligatorily linked fashion—no more than three contraction parameters.

2) The extra dimensionality of a more complex NMT correspondingly expands the dimensionality of the reachable output space, although quite possibly only transiently; in the steady state, the system may well collapse back to the limit given by 1). See Extensions of analysis and Motor neuron–muscle control and coding in the DISCUSSION.

3) Finally, the particular dynamical structure of the NMT plays a very important role in determining what, within the possibilities of 1) and 2), is actually achieved. For instance, by 1), our set of canonical patterns certainly has sufficient dimensionality to control two contraction parameters, say \( \epsilon_{\text{extra}} \) and \( \epsilon_{\text{intra}} \). However, as we saw in RESULTS, practically significant differential control of these can be achieved only with patterns that are slow relative to the time constant of the NMT. With fast patterns, \( \epsilon_{\text{extra}} \) and \( \epsilon_{\text{intra}} \) are always essentially identical. In this part of the space, the dynamical structure of the NMT is such that the same, single dimension of the pattern \( (f, c) \), if the NMT becomes linear, comes to control both output parameters, and the other dimensions become irrelevant.

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