PHYSIOLOGICAL CONTROL SYSTEMS (VS ARTIFICIAL ONES)

1) Physiological **VERSATILITY** (vs fixed tasks):
integration of various open loop and closed loop regulation strategies.

2) Unknown components → **SYSTEM IDENTIFICATION** → laws derived from data (black-box) vs. internal models based on known artificial components (white-box). Even when we know some physiological law based on physical considerations we don't know the value of the parameters for that specific subject in that specific condition. This is called a "gray-box", the parameters of which must be identified by fitting specific data.

3) Extensive **CROSS-COUPLING** (it. *interazioni*):

Example: contributions of interrelated systems to the muscle stretch reflex

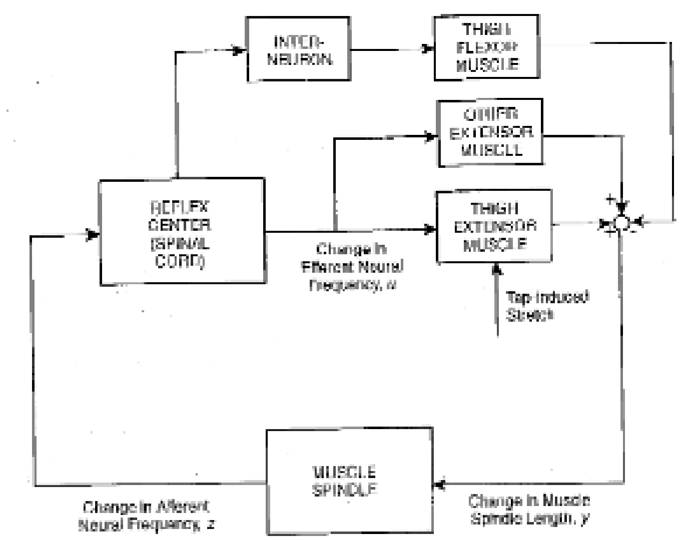

Figure 1.4 Contributions of interrelated systems to the muscle stretch reflex.

More examples:
arterial pressure control - low pressure and high pressure areas - blood volume control - control of flow in organs and limbs - thermo-regulation - renal activity - intracranial pressure …

4) **ADAPTIVE** control mechanisms and **HIERARCHICAL** structure:

Example: adaptive characteristics of the muscle stretch reflex

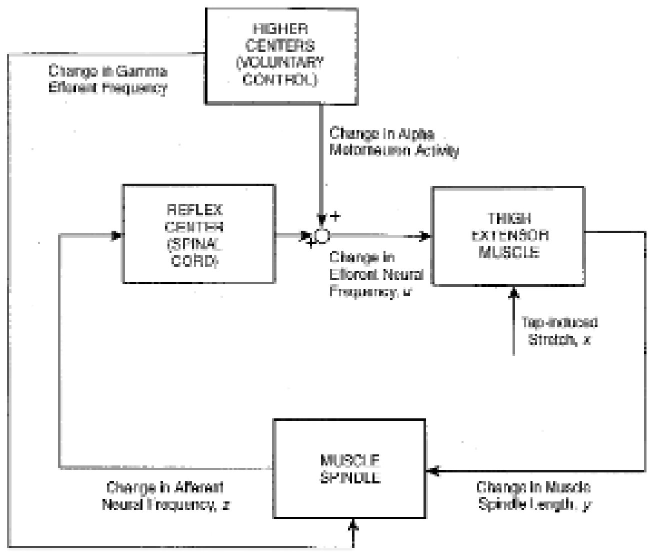

Figure 1.5 Adaptive characteristics of the muscle stretch reflex.

5) **EMBEDDED** (it. "intrinseco") negative feedback and set point:

Note: we will go into this counter-intuitive though central concept in the "Equilibrium chapter" and provide examples.

Definition: creation of feedback working point not through a comparison of measure and an external set-point but by satisfying feedforward and feedback non-linear static characteristics.
By linearizing around the working point, this can be represented as a virtual "set-point", however an embedded not an external one!

Adaptation of the working point is obtained by adapting the control loop non-linear features (see examples in the Equilibrium chapter), not by moving an external set-point (who should move it?!).

6) Generally, **NON-LINEAR** features of both control and plant.

1.3 SYSTEMS ANALYSIS: FUNDAMENTAL CONCEPTS

Prior to analyzing or designing a control system, it is useful to define explicitly the major variables and structures involved in the problem. One common way of doing this is to construct a *block diagram*. The block diagram captures in schematic form the relationships among the variables and processes that comprise the control system in question. Figure 1.1 shows block diagrams that represent open-loop and closed-loop control systems in canonical form. Consider first the open-loop system (Figure 1.1a). Here, the *controller* component of the system translates the input (r) into a controller action (u), which affects the *controlled system* or "*plant*" thereby influencing the system output (y). At the same time, however, external disturbances (x) also affect plant behavior; thus, any changes in y reflect contributions from both the controller and the external disturbances. If we consider this open-loop system in the context of our previous example of the heating system, the heater would be the controller and the room would represent the plant. Since the function of this control system is to regulate the temperature of the room, it is useful to define a *set-point*, which would

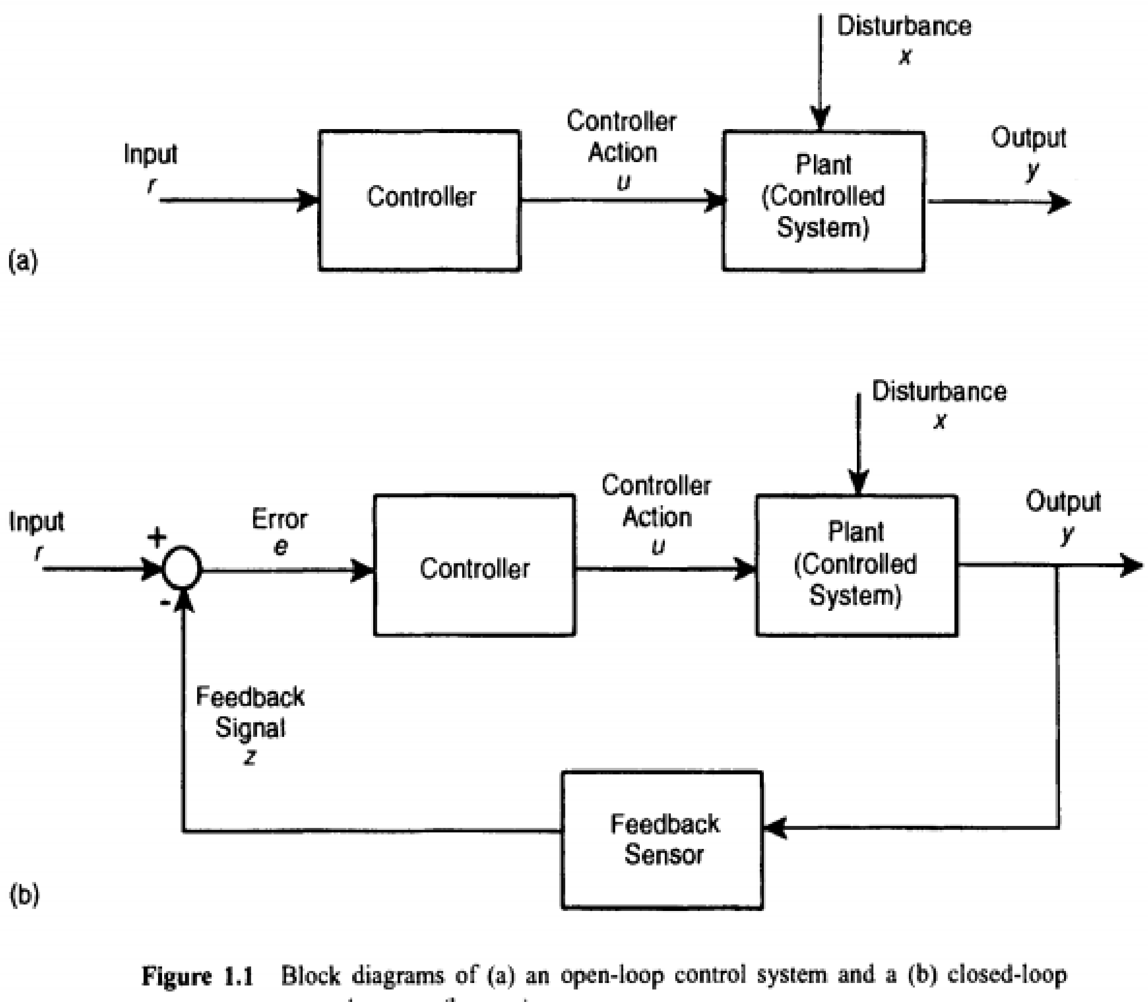

Figure 1.1 Block diagrams of (a) an open-loop control system and a (b) closed-loop control system (bottom).

correspond to the desired room temperature. In the ideal situation of no fluctuations in external temperature (i.e., $x = 0$), a particular input voltage setting would place the room temperature exactly at the set-point. This input level may be referred to as the *reference input value*. In linear control systems analysis, it is useful (and often preferable from a computational viewpoint) to consider the system variables in terms of *changes* from these reference levels instead of their absolute values. Thus, in our example, the input (r) and controller action (u) would represent the deviation from the reference input value and the corresponding change in heat generated by the heater, respectively, while the output (y) would reflect the resulting change in room temperature. Due to the influence of changes in external temperature (x), r must be adjusted continually to offset the effect of these disturbances on y.

As mentioned earlier, we can circumvent this limitation by "closing the loop." Figure 1.1b shows the closed-loop configuration. The change in room temperature (y) is now measured and transduced into the feedback signal (z) by means of a feedback sensor, i.e., the thermostat. The feedback signal is subsequently subtracted from the reference input and the error signal (e) is used to change the controller output. If room temperature falls below the set-point (i.e., y becomes negative), the feedback signal (z) would also be negative. This feedback signal is subtracted from the reference input setting ($r = 0$) at the *mixing point* or *comparator* (shown as the circular object in Figure 1.1b), producing the error signal (e), which is used to adjust the heater setting. Since z is negative, e will be positive. Thus, the heater setting will be raised, increasing the flow of heat to the room and consequently raising the room temperature. Conversely, if room temperature becomes higher than its set-point, the feedback signal now becomes positive, leading to a negative error signal, which in turn lowers the heater output. This kind of closed-loop system is said to have *negative feedback*, since any changes in system output are compensated for by changes in controller action in the *opposite* direction.

Negative feedback is the key attribute that allows closed-loop control systems to act as regulators. What would happen if, rather than being subtracted, the feedback signal were to be *added* to the input? Going back to our example, if the room temperature were to rise and the feedback signal were to be added at the comparator, the error signal would become positive. The heater setting would be raised and the heat flow into the room would be increased, thereby increasing the room temperature further. This, in turn, would increase the feedback signal and the error signal, and thus produce even further increases in room temperature. This kind of situation represents the *runaway* effect that can result from *positive feedback*. In lay language, one would refer to this as a *vicious cycle* of events. Dangerous as it may seem, positive feedback is actually employed in many physiological processes. However, in these processes, there are constraints built in that limit the extent to which the system variables can change. Nevertheless, there are also many positive feedback processes (e.g., circulatory shock) that in extreme circumstances can lead to the shut-down of various system components, leading eventually to the demise of the organism.

1.4 PHYSIOLOGICAL CONTROL SYSTEMS ANALYSIS: A SIMPLE EXAMPLE

One of the simplest and most fundamental of all physiological control systems is the *muscle stretch reflex*. The most notable example of this kind of reflex is the *knee jerk*, which is used in routine medical examinations as an assessment of the state of the nervous system. A sharp tap to the patellar tendon in the knee leads to an abrupt stretching of the extensor muscle in the thigh to which the tendon is attached. This activates the muscle spindles, which are stretch receptors. Neural impulses, which encode information about the magnitude of the stretch, are sent along afferent nerve fibers to the spinal cord. Since each afferent nerve is synaptically connected with one motorneuron in the spinal cord, the motorneurons get activated and, in turn, send efferent neural impulses back to the same thigh muscle. These produce a contraction of the muscle, which acts to straighten the lower leg. Figure 1.2 shows the basic components of this reflex. A number of important features of this system should be highlighted. First, this and other stretch reflexes involve reflex arcs that are monosynaptic, i.e. only two neurons and one synapse are employed in the reflex. Other reflexes have at least one interneuron connecting the afferent and efferent pathways. Secondly, this closed-loop regulation of muscle length is accomplished in a completely involuntary fashion, as the name "reflex" suggests.

A third important feature of the muscle stretch reflex is that it provides a good example of negative feedback in physiological control systems. Consider the block diagram representation of this reflex, as shown in Figure 1.3. Comparing this configuration with the general closed-loop control system of Figure 1.1, one can see that the thigh muscle now corresponds to the plant or controlled system. The disturbance, x, is the amount of initial stretch produced by the tap to the knee. This produces a proportionate amount of stretch, y, in the muscle spindles, which act as the feedback sensor. The spindles translate this mechanical quantity into an increase in afferent neural traffic (z) sent back to the reflex center in the spinal cord, which corresponds to our controller. In turn, the controller action is an increase in efferent neural traffic (u) directed back to the thigh muscle, which subsequently contracts in order to

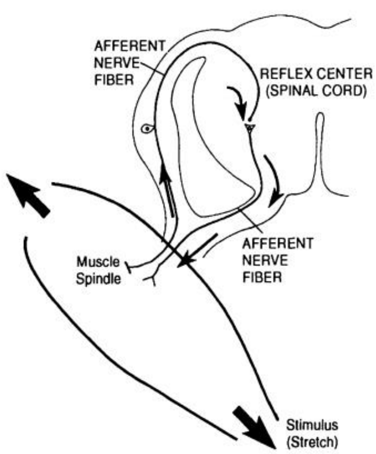

Figure 1.2 Schematic illustration of the muscle stretch reflex. (Adapted from Vander *et al.*, 1997).

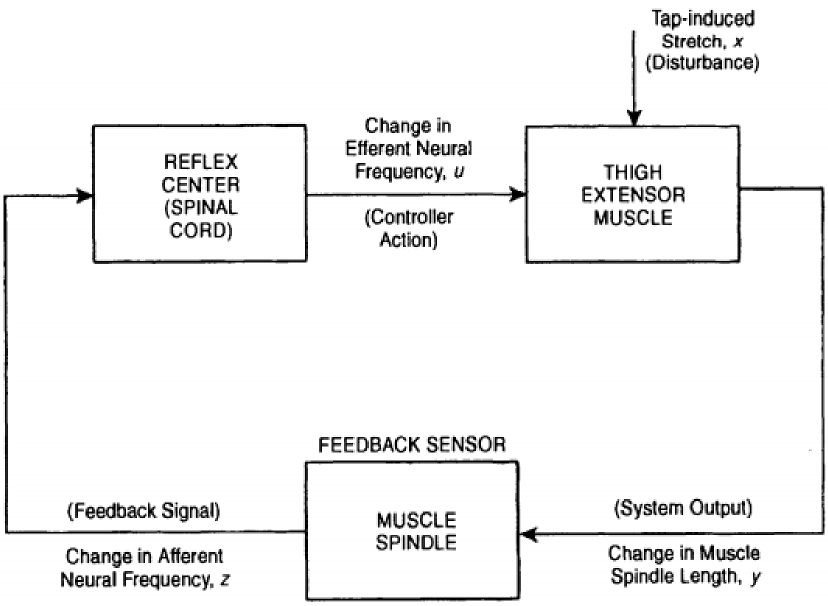

Figure 1.3 Block diagram representation of the muscle stretch reflex.

1.5 DIFFERENCES BETWEEN ENGINEERING AND PHYSIOLOGICAL CONTROL SYSTEMS

While the methodology of systems analysis can be applied to both engineering and physiological control systems, it is important to recognize some key differences:

- An engineering control system is designed to accomplish a defined task, and frequently, the governing parameters have been fine-tuned extensively so that the system will perform its task in an "optimal" manner (at least, under the circumstances in which it is tested). In contrast, physiological control systems are built for versatility and may be capable of serving several different functions. For instance, although the primary purpose of the respiratory system is to provide gas exchange, a secondary but also important function is to facilitate the elimination of heat from the body. Indeed, some of the greatest advances in physiological research have been directed at discovering the functional significance of various biological processes.
- Since the engineering control system is synthesized by the designer, the characteristics of its various components are generally known. On the other hand, the physiological control system usually consists of components that are unknown and difficult to analyze. Thus, we are confronted with the need to apply system identification techniques to determine how these various subsystems behave before we are able to proceed to analyzing the overall control system.

- There is an extensive degree of *cross-coupling* or interaction among different physiological control systems. The proper functioning of the cardiovascular system, for instance, is to a large extent dependent on interactions with the respiratory, renal, endocrine, and other organ systems. In the example of the muscle stretch reflex considered earlier, the block diagram shown in Figure 1.3 oversimplifies the actual underlying physiology. There are other factors involved that we omitted and these are shown in the modified block diagram shown in Figure 1.4. First, some branches of the afferent nerves also synapse with the motorneurons that lead to other extensor muscles in the thigh that act synergistically with the primary muscle to straighten the lower leg. Secondly, other branches of the afferent nerves synapse with interneurons which, in turn, synapse with motorneurons that lead to the flexor or antagonist muscles. However, here, the interneurons introduce a polarity change in the signal, so that an increase in afferent neural frequency produces a decrease in the efferent neural traffic that is sent to the flexor muscles. This has the effect of relaxing the flexor muscles so that they do not counteract the activity of the extensor muscles.
- Physiological control systems, in general, are *adaptive*. This means that the system may be able to offset any change in output not only through feedback but also by allowing the controller or plant characteristics to change. As an example of this type of feature, consider again the operation of the muscle stretch reflex. While this reflex plays a protective role in regulating muscle stretch, it also can hinder the effects of

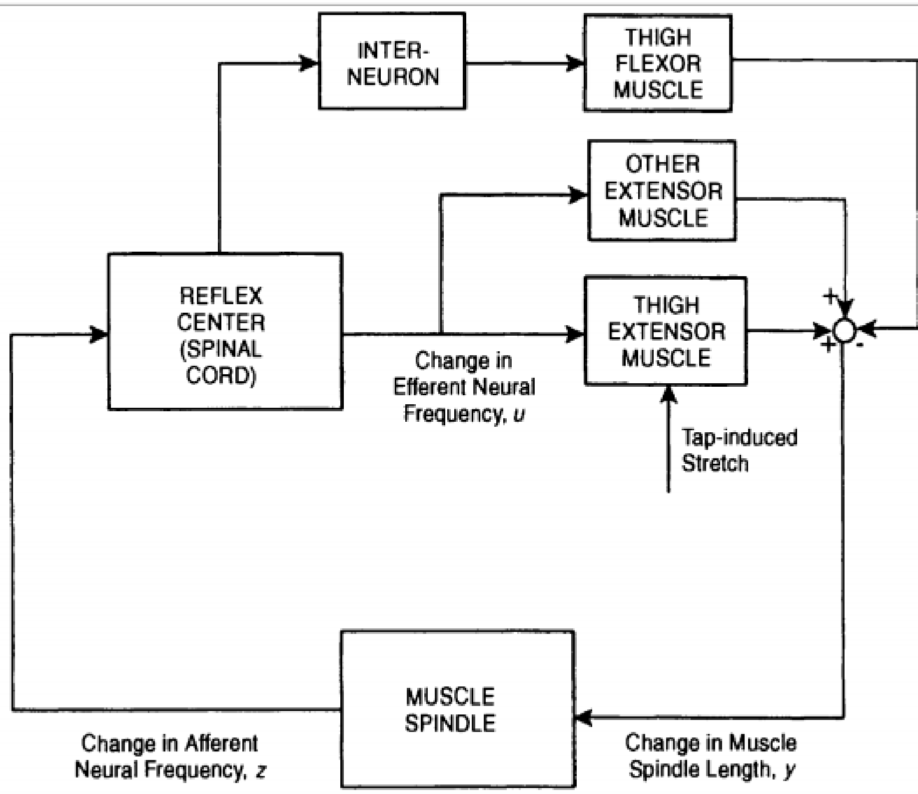

Figure 1.4 Contributions of interrelated systems to the muscle stretch reflex.

voluntary control of the muscles involved. For instance, if one voluntarily flexed the knee, the stretch reflex, if kept unchanged, would come into play and this would produce effects that oppose the intended movement. Figure 1.5 illustrates the solution chosen by Nature to circumvent this problem. When the higher centers send signals down the alpha motorneurons to elicit the contraction of the flexor muscles and the relaxation of the extensor muscle, signals are sent simultaneously down the efferent gamma nerves that innervate the muscle spindles. These gamma signals produce in effect a resetting of the operating lengths of the muscle spindles, so that the voluntarily induced stretch in the extensor muscles is no longer detected by the spindles. Thus, by this clever, adaptive arrangement, the muscle stretch reflex is basically neutralized.

- At the end of Section 1.4, we alluded to another difference that may be found between physiological control systems and simpler forms of engineering control systems. In Figure 1.1, the feedback signal is explicitly subtracted from the reference input, demonstrating clearly the use of negative feedback. However, in the stretch reflex block diagram of Figure 1.3, the comparator is nowhere to be found. Furthermore, muscle stretch leads to an *increase* in both afferent and efferent neural traffic. So, how is negative feedback achieved? The answer is that negative feedback in this system is "built into" the plant characteristics: increased efferent neural input produces a *contraction* of the extensor muscle, thereby acting to counteract the initial stretch. This kind of *embedded* feedback is highly common in physiological systems.

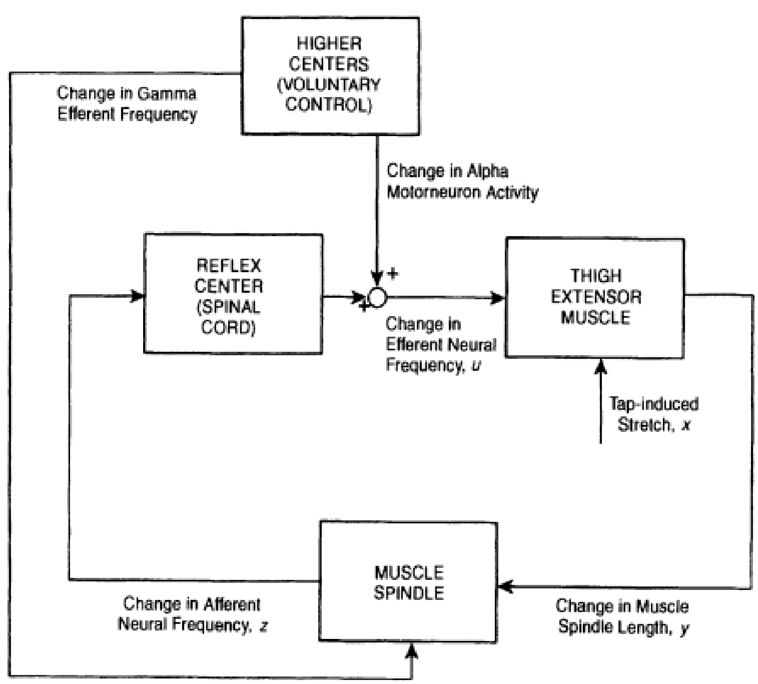

Figure 1.5 Adaptive characteristics of the muscle stretch reflex.

- One final difference is that physiological systems are generally nonlinear, while engineering control systems can be linear or nonlinear. Frequently, the engineering designer prefers the use of linear system components since they have properties that are well-behaved and easy to predict. This issue will be revisited many times over in the chapters to follow.

2.3 LINEAR MODELS OF PHYSIOLOGICAL SYSTEMS: TWO EXAMPLES

In this section, we will derive the mathematical formulations that characterize the input–output properties of two simple physiological models. The first model provides a linearized description of lung mechanics (Figure 2.6). The airways are divided into two categories: the larger or central airways and the smaller or peripheral airways, with fluid mechanical resistances equal to R_C and R_P, respectively. Air that enters the alveoli also produces an expansion of the chest-wall cavity by the same volume. This is represented by the connection of the lung (C_L) and chest-wall (C_W) compliances in series. However, a small fraction of the volume of air that enters the respiratory system is shunted away from the alveoli as a result of the compliance of the central airways and gas compressibility. This shunted volume is very small under normal circumstances at regular breathing frequencies, but becomes progressively more substantial if disease leads to peripheral airway obstruction (i.e., increased R_P) or a stiffening of the lungs or chest-wall (i.e., decreased C_L or C_W). We account for this effect by

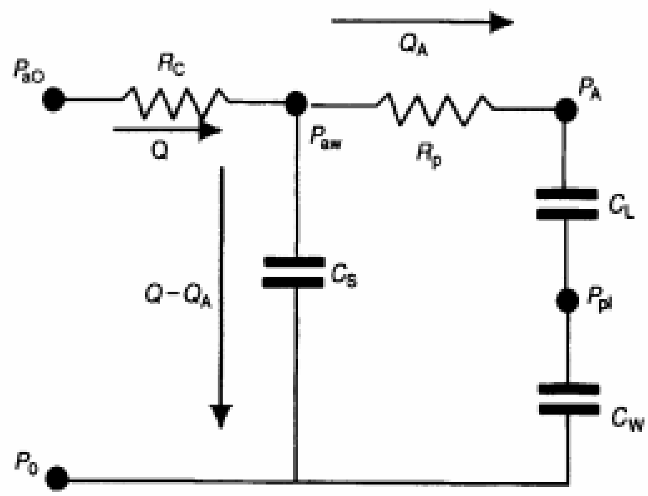

Figure 2.6 Linear model of respiratory mechanics.

placing a shunt compliance, C_S, in parallel with C_L and C_W. The pressures developed at the different points of this lung model are: P_{ao} at the airway opening, P_{aw} in the central airways, P_A in the alveoli and P_{pl} in the pleural space (between the lung parenchyma and chest wall). These pressures are referenced to P_0, the ambient pressure, which we can set to zero. Suppose the volume flow-rate of air entering the respiratory system is Q. Then, the objective here is to derive a mathematical relationship between P_{ao} and Q.

From Kirchhoff's Second Law (applied to the node P_{aw}), if the flow delivered to the alveoli is Q_A, then the flow shunted away from the alveoli must be $Q - Q_A$. Applying, Kirchhoff's First Law to the closed circuit containing C_S, R_P, C_L, and C_W, we have

$$R_P Q_A + \left(\frac{1}{C_L} + \frac{1}{C_W}\right) \int Q_A \, dt = \frac{1}{C_S} \int (Q - Q_A) \, dt \tag{2.14}$$

Applying Kirchhoff's First Law to the circuit containing R_C and C_S, we have

$$P_{ao} = R_C Q + \frac{1}{C_S} \int (Q - Q_A) \, dt \tag{2.15}$$

Differentiating Equation (2.14) and Equation (2.15) with respect to time, and subsequently reducing the two equations to one by eliminating Q_A, we obtain the equation relating P_{ao} to Q:

$$\frac{d^2 P_{ao}}{dt^2} + \frac{1}{R_P C_T} \frac{dP_{ao}}{dt} = R_C \frac{d^2 Q}{dt^2} + \left(\frac{1}{C_S} + \frac{R_C}{R_P C_T}\right) \frac{dQ}{dt} + \frac{1}{R_P C_S} \left(\frac{1}{C_L} + \frac{1}{C_W}\right) Q \tag{2.16}$$

where C_T is defined by

$$C_T = \left(\frac{1}{C_L} + \frac{1}{C_W} + \frac{1}{C_S}\right)^{-1} \tag{2.17}$$

The second example that we will consider is the linearized physiological model of skeletal muscle, as illustrated in Figure 2.7. F_0 represents the force developed by the active contractile element of the muscle, while F is the actual force that results after taking into account the mechanical properties of muscle. R represents the viscous damping inherent in the tissue, while C_P (parallel elastic element) and C_S (series elastic element) reflect the elastic

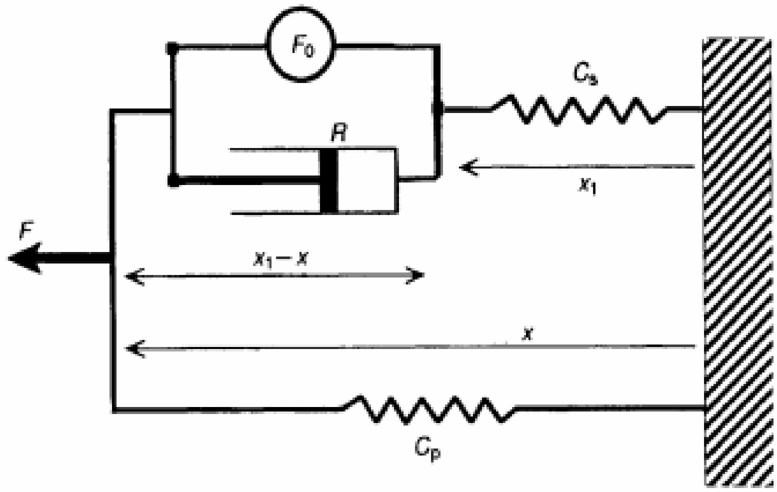

Figure 2.7 Linear model of muscle mechanics.

storage properties of the sarcolemma and the muscle tendons, respectively. First, consider the mechanical constraints placed on the model components as a result of the parallel configuration. If spring C_P is stretched by an incremental length x, the entire series combination of R and C_S will also extend by the same length. Furthermore, the sum of the force transmitted through the two branches of the parallel configuration must equal F. However, although the sum of the extensions of C_S and R will have to equal x, the individual length contributions from C_S and R need not be equal. Thus, if we assume C_S is stretched a length x_1, then the extension in the parallel combination of R and F_0 will be $x - x_1$. The velocity with which the dashpot represented by R is extending is obtained by differentiating $x - x_1$ with respect to time, i.e., $d(x - x_1)/dt$.

Using the principle that the force transmitted through C_S must be equal to the force transmitted through the parallel combination of F_0 and R, we obtain the following equation:

$$\frac{x_1}{C_S} = R\left(\frac{dx}{dt} - \frac{dx_1}{dt}\right) + F_0 \qquad (2.18)$$

Then, using the second principle, i.e., that the total force from both limbs of the parallel combination must sum to F, we have

$$F = \frac{x_1}{C_S} + \frac{x}{C_P} \qquad (2.19)$$

Eliminating x_1 from Equation (2.18) and Equation (2.19) yields the following differential equation relating F to x and F_0:

$$\frac{dF}{dt} + \frac{1}{RC_S}F = \left(\frac{1}{C_S} + \frac{1}{C_P}\right)\frac{dx}{dt} + \frac{1}{RC_S C_P}x + \frac{F_0}{RC_S} \qquad (2.20)$$

Note that in Equation (2.20), under steady-state, isometric conditions (i.e., the muscle length is constrained to be constant), $x = 0$, $dx/dt = 0$ and $dF/dt = 0$, which leads to the result $F = F_0$. Therefore, under steady-state isometric conditions, the force developed by the muscle model will reflect the force developed by the active contractile element of the muscle.

2.4 DISTRIBUTED-PARAMETER VERSUS LUMPED-PARAMETER MODELS

The models that we have considered up to this point are known as *lumped-parameter models*. A given property of the model is assumed to be "concentrated" into a single element. For example, in the lung mechanics model (Figure 2.6), the total resistance of the central airways is "lumped" into a single quantity, R_C, even though in reality the central airways are comprised of the trachea and a few branching generations of airways, each of which has very different fluid mechanical resistance. Similarly, a single constant, C_L, is assumed to represent the compliance of the lungs, even though the elasticity of lung tissue varies from region to region. In order to provide a more realistic characterization of the *spatial* distribution of system properties, it is often useful to develop a *distributed-parameter model*. This kind of model generally takes the form of one or more partial differential equations with time and some measure of space (e.g., length or volume) as independent variables.

A distributed-parameter model can be viewed as a network of many infinitesimally small lumped-parameter submodels. To illustrate this relationship, we will derive the governing differential equation of a distributed-parameter model of the passive cable characteristics of an unmyelinated nerve fiber. As shown in Figure 2.8, the nerve fiber is