5.4 FREQUENCY RESPONSE OF A MODEL OF CIRCULATORY CONTROL

The regulation of heart rate and systemic blood pressure is achieved in the short-term primarily through the feedback control via the arterial baroreflexes. However, both cardiovascular variables are continually perturbed by respiration. Breathing can affect heart rate and arterial blood pressure through a number of mechanisms. First, respiratory-induced intrathoracic pressure changes exert a direct effect on arterial pressure which, in turn, affects heart rate through the baroreflexes. Secondly, the present evidence suggests a direct coupling between the respiratory pattern generator in the medulla and the autonomic centers that influence heart rate. Thirdly, vagal feedback from the pulmonary stretch receptors during breathing has been shown to reflexively affect heart rate. And, finally, changes in heart rate can lead to changes in cardiac output which, in turn, produce arterial blood pressure fluctuations that alter heart rate through the baroreflexes. The overall effect of respiration on heart rate, commonly referred to as the *respiratory sinus arrhythmia*, can be quantified in terms of a frequency response function. Changes in phase and/or magnitude of this frequency response function would suggest changes in one of the factors that influence autonomic control of heart rate.

5.4.1 The Model

The model of circulatory control that we will examine was developed by Saul and coworkers (1991) from the Harvard Medical School and Massachusetts Institute of Technology. The SIMULINK implementation of this model (filename: "`rsa.mdl`") is shown in Figure 5.13. Respiration, measured in the form of lung volume change, V, is assumed to directly affect the autonomic inputs to the sinoatrial node: inspiration leads to decreases in both vagal and sympathetic efferent activity (note signs in summing blocks). The model does not distinguish between respiratory input from the pulmonary stretch receptors from the central drive that originates in the medullary centers. Feedback from the baroreceptors also directly influences the autonomic inputs to the heart: a rise in arterial blood pressure, `abp`, produces a decrease in sympathetic activity and an increase in parasympathetic activity. During inspiration, the decrease in vagal efferent activity acts on the sinoatrial node to increase heart rate, `hr`. The transfer function that models the dynamics of this relationship is a simple low-pass filter with a cutoff frequency (fp) that is on the order of 0.2 Hz and a negative gain, $-K_p$. In contrast, the response of the sinoatrial node to sympathetic stimulation is considerably slower. In addition to a latency of 1–2 s, the transfer function that characterizes the dynamics of sympathetic activity to heart rate conversion has a cutoff frequency, fs, of 0.015 Hz. In this case, the gain is positive.

Changes in heart rate are assumed to affect arterial blood pressure after a delay of 0.42 s. For simplicity, the transfer function representing the properties of the arterial vasculature is assumed static with a gain of 0.01 (mm Hg) min bt^{-1}. As well, since the

transduction of abp into baroreceptor output occurs with very rapid dynamics, we assume that the baroreflex can be adequately represented by a static gain (equal to 0.01) in series with a fixed delay of 0.3 s. Finally, the direct mechanical effects of respiration on abp are modeled as a negative differentiator, i.e., inspiration tends to decrease abp while expiration tends to increase it. Thus, the model simulates respiratory sinus arrhythmia by allowing the direct autonomic stimulation of heart rate. As well, the resulting changes in heart rate and the direct mechanical effects of respiration produce fluctuations in abp, which subsequently affect hr via the baroreflexes.

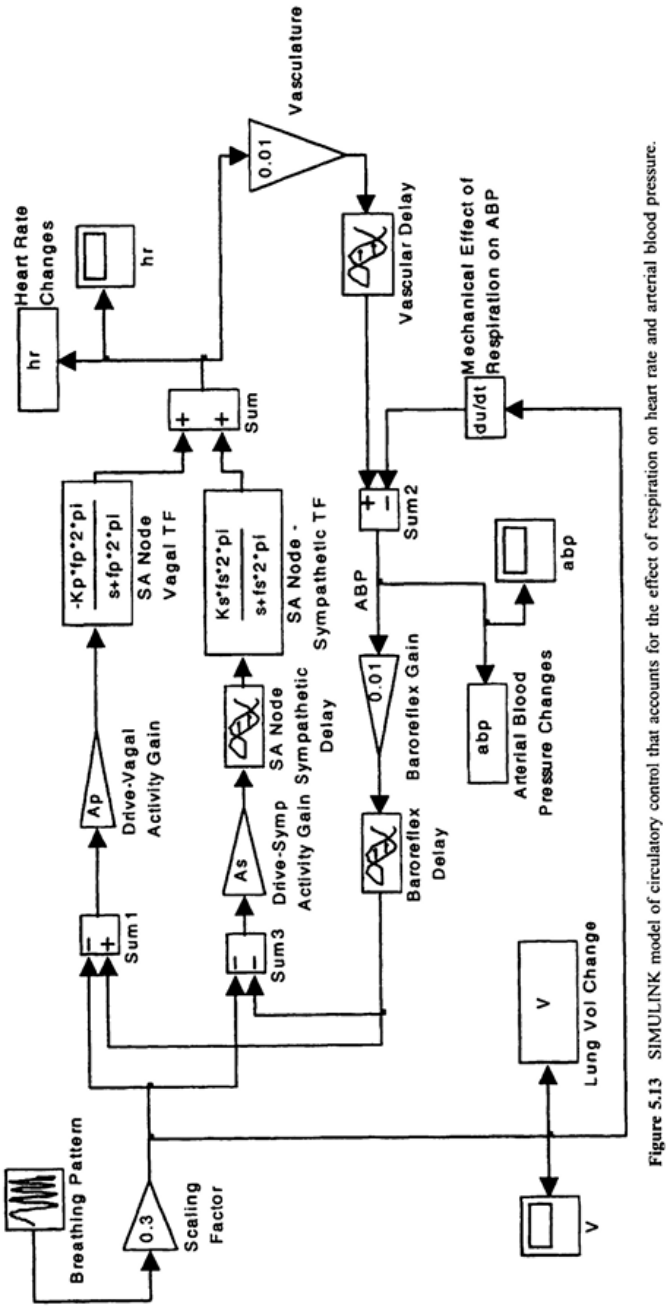

Figure 5.13 SIMULINK model of circulatory control that accounts for the effect of respiration on heart rate and arterial blood pressure.

5.4.2 Simulations with the Model

To determine the frequency response of the circulatory control model, we employ a source block that produces a `chirp` signal. This is a sine wave, the frequency of which increases linearly with time. In our case, we set the parameters of the chirp block such that we start off with a frequency of 0.005 Hz and end with a frequency of 0.5 Hz after a duration of 300 s (simulation time). Since the amplitude of the chirp signal is not adjustable, a gain block of 0.3 is included between the source block and the rest of the model. This limits the peak-to-peak amplitude of the "respiration signal" to 0.6 liter. Before starting the simulation, the m-file "`rsa_var.m`" has to be executed in order to assign values to the adjustable parameters of the model. The following nominal parameter values represent the normal subject in supine posture: SA node vagal transfer function gain, $K_p = 6$; SA node sympathetic transfer function gain, $K_s = 18$; SA node vagal transfer function cutoff frequency, $f_p = 0.2$ Hz; SA node sympathetic transfer function cutoff frequency, $f_s = 0.015$ Hz. The relative weight factors for the conversion of respiratory drive or baroreflex drive to efferent neural activity are: A_p (for the vagal branch) = 2.5 and A_s (for the sympathetic branch) = 0.4.

Figure 5.14 displays the results obtained from one simulation run; for the sake of clarity, only 100 s of the simulated "data" are shown. The top panel shows the chirp signal (respiratory input) used to stimulate the model. The corresponding changes in heart rate predicted by the model are displayed in the middle panel. Note that at low frequencies, heart rate fluctuates almost in synchrony with lung volume change; however, at the higher frequencies, it tends to lag respiration. Also, the amplitude of the heart rate signal decreases with increasing frequency, underscoring the low-pass nature of the overall frequency response. The predicted behavior of arterial blood pressure is somewhat different: as frequency increases, the respiratory-induced changes in `abp` become larger. This results from the growing influence of the direct mechanical effects of breathing on blood pressure as frequency increases.

5.4.3 Frequency Response of the Model

Using the method described in Section 5.3.2, the frequency response of the model can be deduced from the input and simulated output. Instead of inserting the `Spectrum Analyzer` block, the reader can also save the input (`V`) and output (`hr` or `abp`) variables to the `Workspace`, and use the following MATLAB code (saved as "`rsa_tf.m`") to deduce the frequency response:

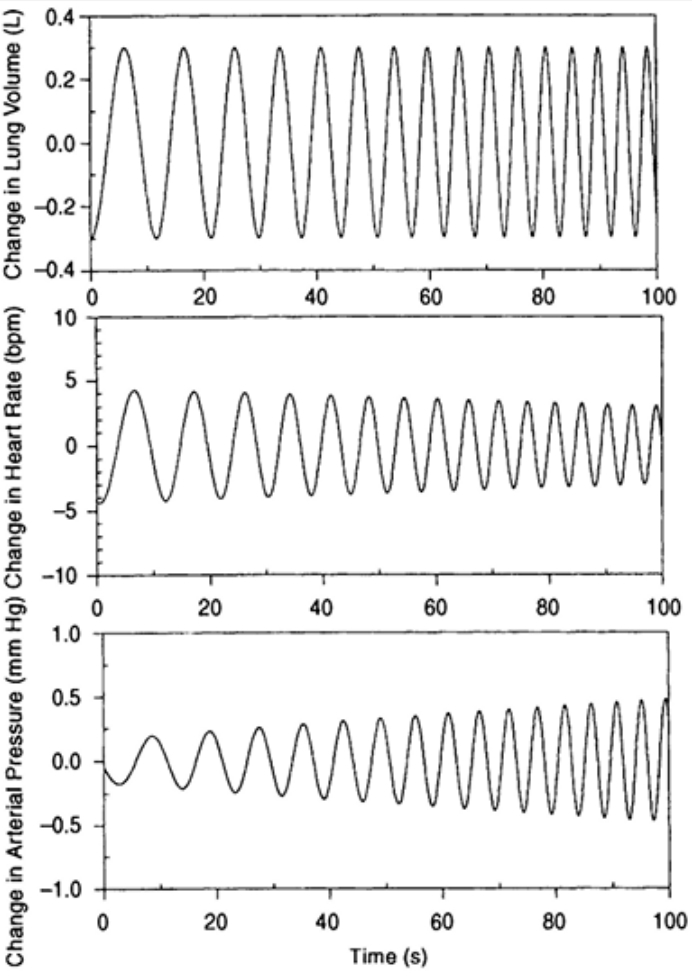

Figure 5.14 Responses in heart rate and arterial blood pressure to a controlled breathing pattern (slow-to-high frequency), as predicted by the SIMULINK model of circulatory control ("normal" conditions).

```
% We assume the sampling interval is 0.1 s so that N = 3000
% for a total simulation time of 300 s
>>freq = [0:1/300:5]';
% compute Power spectrum of V and Cross-spectrum between
% V and hr
>> Pv = psd(V, N, 10);
>> Pvhr = csd(V, hr, N,10);
% compute Frequency Response magnitude and phase
>> Hvhr = Pvhr./Pv;
>> Hvhrmag =abs(Hvhr);
>> Hvhrpha = angle(Hvhr)*180/pi;
```

The chirp signal is useful as an input waveform since it produces a reasonably broad spectrum over the frequency range of interest: 0 to 0.4 Hz. Figure 5.15 displays the magnitude (top panel) and phase (lower panel) components of the frequency response between respiration and heart rate estimated for the simulated supine normal subject (solid curves). The low-pass nature of the magnitude response is clearly evident; however, the frequency response values toward the low (0 Hz) and high (0.4 Hz) ends of the range displayed cannot be regarded as accurate since most of the spectral power of the chirp input is contained in the frequencies in the middle of this range.

The results of two other simulation cases are also presented in Figure 5.15. The first simulates how the frequency response of the respiratory sinus arrhythmia would change if the "subject" were given a dose of atropine ("+Atropine", dashed curves) that produces complete *parasympathetic blockade*. In addition, the model parameters are also modified to simulate the subject in a standing posture, when the sympathetic influence on heart rate is enhanced. Under such conditions, heart rate control would be modulated predominantly by the sympathetic nervous system. Not surprisingly, the resulting frequency response magnitude curve shows a substantial increase at frequencies below 0.03 Hz and a large decrease at frequencies higher than 0.1 Hz. The phase curve shows a much steeper slope, indicating an

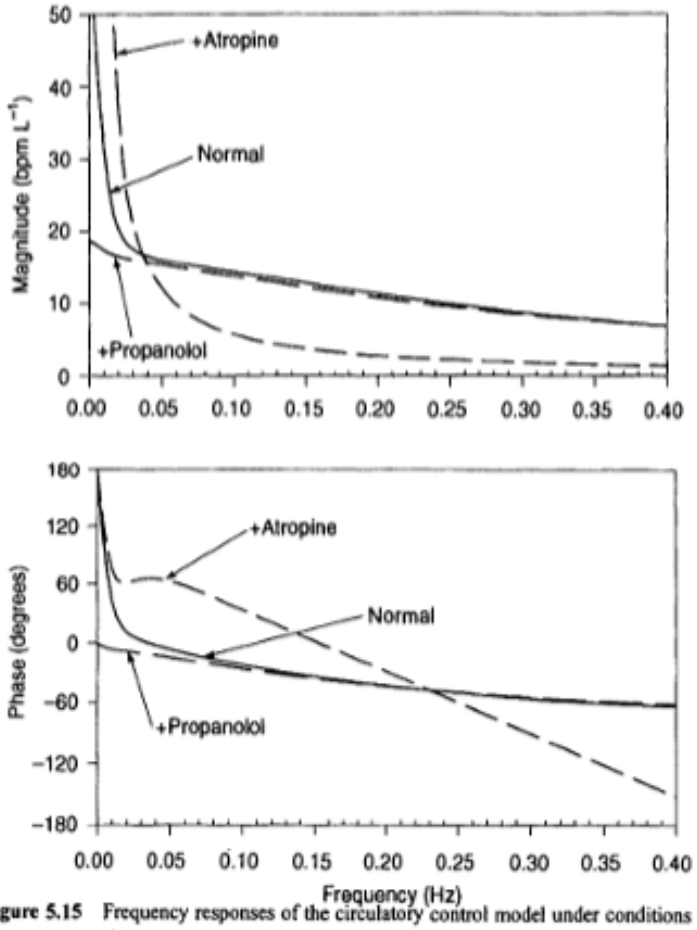

Figure 5.15 Frequency responses of the circulatory control model under conditions that simulate normal heart rate control, complete β-adrenergic blockade ("+Atropine"), and complete parasympathetic blockade ("+Propanolol").

increase in the lags inherent in the system. The values of the model parameters employed here are: $A_p = 0.1$, $K_p = 1$, $f_p = 0.07$ Hz, $A_s = 4.0$, $K_s = 9$ and $f_s = 0.015$ Hz.

In the other simulation case, the "subject" is given a dose of propanolol, which produces *β-adrenergic blockade*. Furthermore, we assume a supine posture, thus making vagal modulation the predominant mode of control. The frequency response curves corresponding to this condition are labeled "+Propanolol". Compared to the control case, there is little change in the frequency response above 0.05 Hz. However, loss of sympathetic modulation leads to a significant decrease in frequency response magnitude and phase at the very low frequencies. Under this "purely vagal" state, the phase difference between respiration and heart rate is relatively small over the 0 to 0.4 Hz range, indicating that the respiratory-induced changes in heart rate occur rapidly. The parameter values used to represent this state are: $A_p = 2.5$, $K_p = 6$, $f_p = 0.2$ Hz, $A_s = 0.1$, $K_s = 1$, $f_s = 0.015$ Hz.