BME331: Physiological Control Systems

Lab 2

Introduction:

In this lab, you will use a Simulink model to simulate the effects of respiration on cardiovascular function, and at the same time explore the concept of a system's **frequency response**. You will learn to collect electrocardiogram recordings on yourselves, and compare these experimental results to your analysis of the Simulink model.

Pre-lab tasks [10 marks]

Before the lab, study section 5.3.2 of the Khoo text book. The book can be accessed online through the U of T library system, at the following link: https://librarysearch.library.utoronto.ca/permalink/01UTORONTO_INST/14bjeso/alma991106900623606196. You will need to use the methods described in the text during this lab.

You will be expected to have read through the lab document beforehand, so that you know what needs to be done and can manage your time accordingly. Note that this lab includes both Simulink modeling and the analysis of electrocardiogram (ECG) recordings, and you must ensure that you have time to complete both portions.

After reading through the lab document, provide brief (1-2 sentences) answers to the following questions. Your answers must be submitted by the beginning of your first lab session.

1. Explain the concept of a frequency response.

2. Define the word "vagal", and explain its relationship to the autonomic nervous system.

3. Explain why it is preferable to compute the inter-beat interval using the QRS complex of the ECG, rather than the P or T waves.

4. Sketch an ECG signal in which the inter-beat interval is always the same. Draw a plot showing the instantaneous heart rate of this ECG as a function of time. Be sure to label all axes.

5. Sketch an ECG signal in which the inter-beat interval is NOT always the same (you can choose how it varies). Draw a plot showing the instantaneous heart rate of this ECG as a function of time. Be sure to label all axes.

Background:

Simulink Model

The model used in this lab is described in the Khoo textbook, and reproduced here in Figure 1. The input, *V*, represents lung volume changes. This respiratory activity affects both sympathetic and parasympathetic (vagal) autonomic inputs to the sinoatrial node. Inspiration decreases both types of efferent activity. The autonomic inputs are also influenced by the baroreceptor reflex. Specifically, a rise in arterial blood pressure (the variable *apb* in the model) produces a decrease in sympathetic activity and an increase in parasympathetic activity.

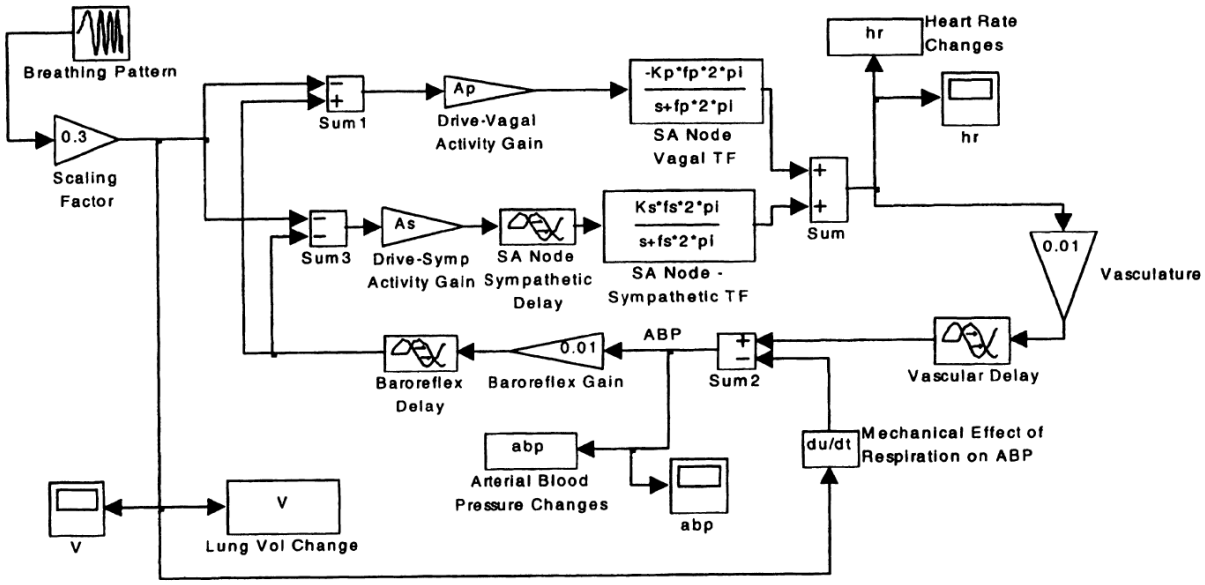

Figure 5.13 SIMULINK model of circulatory control that accounts for the effect of respiration on heart rate and arterial blood pressure.

Figure 1: Simulink model

The heart rate, *hr*, is modulated by these autonomic inputs, as follows:

- A decrease in vagal activity increases heart rate. This relationship is modeled here as low-pass filter with a cutoff frequency f_p on the order of 0.2Hz and a negative gain $-K_p$.
- An increase in sympathetic activity increases heart rate, but on a slower time scale. The transfer function is again a low-pass filter, but with a cutoff frequency f_s of 0.015Hz. In addition, there is a lag of 1-2s (set in the model to 1.7s).

Changes in heart rate are assumed to affect arterial blood pressure after a delay of 0.42s and with a simplified transfer function which is a static gain of 0.01. The baroreflex is in turn modeled as a static gain (0.01) and fixed delay (0.3s) applied to the arterial blood pressure changes.

Lastly, respiration has a direct mechanical effect on arterial blood pressure: inspiration decreases abp

while expiration increases it. This relationship is included in the model as a negative differentiator.

Note: In order to correctly relate the simulation results to the ECG data that you will collect, it is important to understand that the variable *hr* in the model is the heart **rate**. That is, when *hr* increases, the heart is beating faster. When *hr* decreases, the heart is beating slower.

Electrocardiography

Note: this section is adapted from the BioRadio "Electrocardiography 1" module.

Typical Duration and Amplitudes

The voltage of the ECG signal can vary depending on the location of the electrodes placed on the body. If the electrodes are located close to the heart, the recorded potentials can be as high as 5 mV. However, if the electrodes are placed further apart, such as at the wrists, a typical value is 1mV. Both of these measurements, however, are small compared to electrodes placed directly in contact with the heart muscle membrane. Here the potential can range as high as 110 mV. Typical amplitudes are around 1mV for the top of the Q wave to the bottom of the S wave, 0.1 – 1.3 mV for the P wave, and between 0.2 - 0.3 mV for the T wave.

The PQ interval (also known as the PR interval) is the amount of time from the beginning of the P complex to the QRS complex. This represents the amount of time between the beginning of atrial contraction and the beginning of ventricular contraction. The normal duration is approximately 0.16 seconds. Similarly, the QT interval is the time between ventricular contraction and ventricular repolarization. This is measured from the beginning of the Q wave to the end of the T wave and typically lasts 0.35 seconds. The heart rate can be determined directly from the ECG. The heart rate is the inverse of the time between similar segments in the ECG recording. For example, if the time measured between two QRS complexes is 0.8 seconds, then the number of beats per second is the inverse, 1.25 beats / second. In order to obtain the heart rate per minute, you would simply multiply by 60 seconds/minute. This would yield 75 beats per minute.

Electrode Configuration

There is a standard placement of electrodes when performing ECG recordings called a standard bipolar limb lead. A lead refers to the potential difference between two electrodes. For this lab, lead placement involves three leads, which are placed on the right arm (RA), left arm (LA), and left leg (LL). The electrodes can be attached to the wrists and inner ankle, but for clinical applications, are usually attached to the chest for a more accurate signal. Leads I, II, and III constitute the standard limb lead ECG connected as follows:

Table 1. Standard bipolar limb lead ECG configuration.

Lead	+	-
I	LA	RA
II	LL	RA
III	LL	LA

In the table, the positive and negative signs denote the polarity of the leads. So, the positive end of Lead I connects to the LA, while the negative end of Lead I connects to the RA. Using these three leads, we can form what is called Einthoven's Triangle. This is a representation of vectors demonstrating the formation of the ECG signal. In interpreting these measurements, each lead is assumed to be equivalent to measurements taken across all sides of an equilateral (Einthoven's) triangle, which is superimposed over the chest, as shown below:

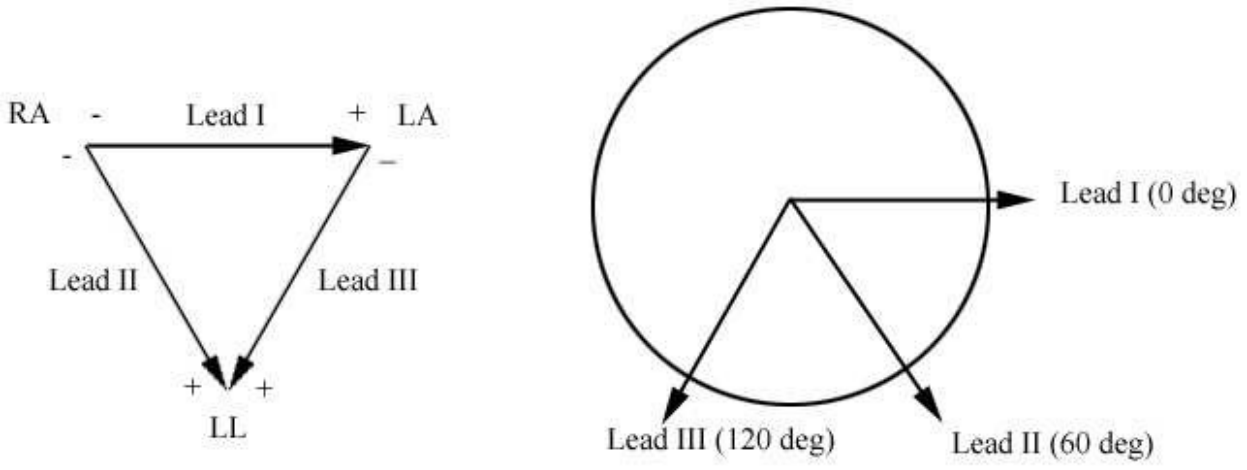

Figure 2: Einthoven's law and lead configuration.

With Einthoven's Triangle, there is an equation that relates all three vectors. Graphically, Einthoven's Law says that if the potentials of the first two leads are known, than the third lead can be found by adding the two vectors together. Mathematically, Einthoven's law states that for the potentials on each lead:

Lead I + Lead III = Lead II

Some may notice that this equation is similar to Kirchoff's Voltage law, which states that all of the voltages in a loop must equal zero. Using this equation, we only need to record two of the leads. The third lead can be determined mathematically, provided that the two leads were measured

simultaneously. Einthoven's Triangle also allows us to determine the mean electrical axis of the heart. This mean electrical axis is the vector representing the summation of all the vectors that occur in a cardiac cycle. This electrical axis can be thought of as a dipole. The dipole illustrates the strength and direction of the heart's polarization during a cardiac cycle. There are two ways of determining the mean electrical axis. Lead I measures lateral voltage and the other two measure from top to bottom. One method is to measure the magnitude of the R complex along Lead I and Lead III, and to extrapolate the vector of Lead II, which would give the magnitude and angle of the vector. A more accurate way of measuring the mean electrical axis would be to add the Q, R, and S potentials for the two leads, instead of only the R wave. The QRS potentials are measured along Lead I and III, added together, and then the mean electrical axis can be computed by finding the magnitude and direction of the vector representing Lead II. If a complete measurement of the mean electrical axis is desired, twelve leads are required, since the mean electrical axis is precisely defined in three dimensions, x, y, and z. In this lab, we will only focus on the frontal plane mean electrical axis. In normal conditions, the mean electrical axis of the heart is typically around 60 degrees.

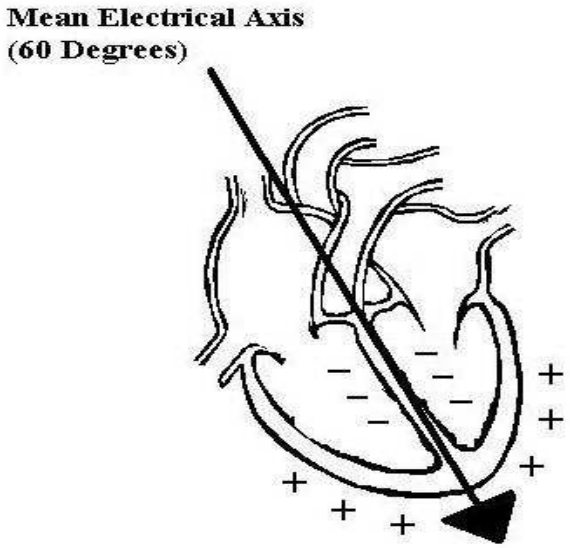

Figure 3: Mean electrical axis of the heart.

Vector Analysis of the Electrocardiogram

The ECG signal that is recorded can be derived from the Leads I-III vectors. When the ECG signal is recorded, the vector values for each of the leads changes as the atria and then ventricles contract. For example, as the QRS wave occurs, the lead I vector has a very small magnitude. This describes the slow upward growth of the lead I ECG recording. As depolarization sweeps across the atria and into the ventricles, the lead I vector begins to increase, causing the fast growth in the lead I ECG signal that is typical of the QRS complex. Then, as more of the ventricles depolarize, the lead I vector starts becoming smaller since all of the ventricular muscle has become depolarized,

causing the lead I vector to have zero or slightly negative magnitude, causing the negative slope of the ECG signal in lead I. A similar analysis can be performed on the other leads and can also explain how repolarization sweeps across the heart when the T wave occurs.

Analysis of heart rate variability

The output *hr* of the Simulink model provides the variations in the heart **rate** around a baseline (i.e., when the output increases, the heart is beating faster). In order to be able to compare the results of your modeling to your ECG data collection, you will need to convert the ECG data into heart rate data. The *instantaneous heart rate* can be defined as the inverse of the inter-beat interval (IBI). The IBI can most easily be identified by examining the time interval between two successive R complexes in the ECG. The provided MATLAB script "IBI" will detect the individual beats in your ECG data, compute the IBI values, and lastly convert this information into a plot of instantaneous heart rate. In order for these results to be accurate, you should check that the heartbeat locations indicated by the MATLAB script correspond to the heartbeats in your data. If this is not the case, you should refine the parameters "minpeakheight" and "minpeakdistance" of the function "findpeaks" until you obtain accurate detection (note that "findpeaks" occurs 3 times, be sure to change the parameters in all 3 locations).

Experimental Procedures - Simulink:

1. Model Creation in Simulink

Figure 1 is taken from the textbook by Khoo[1]. Your first task is to re-create this model in Simulink. The parameters for the model are as provided in Table 2.

Table 2: Model parameters

Parameter	Value
Ap	2.5
As	0.4
Kp	6
Ks	18
fp	0.2
fs	0.015
SA Node Sympathetic Delay	1.7
Baroreflex Delay	0.3
Vascular Delay	0.42
Breathing pattern (initial frequency)	0.005
Breathing pattern (target time)	300
Breathing pattern (frequency at target time)	0.5

[1] M.C.K. Khoo, Physiological Control Systems: Analysis, Simulation, and Estimation, IEEE Engineering in Medicine and Biology Society, Wiley & Sons, ISBN 0-7803-3408-6.

⇨ Once you are done, take a screenshot of your model. Save your model and name it “rsa”.

2. *Run the simulation using the default parameters*

Before running your simulation, go to “Simulation -> Model Configuration Parameters”. Set "Stop time" to 300 seconds, and in Solver Options set "Type" to "Fixed-step", “Solver” to “ode5”, and "Fixed-step size (fundamental sample time)" to 0.1. In the “To Workspace” sink blocks, set “Save format” to “Array”.

Execute the simulation using the default parameters and observe the output. Make sure that you understand what each input and output variable represents.

⇨ Rename the input and output variables in the Matlab workspace to V_2, abp_2 and hr_2, and save them for later analysis.

3. *Explore the frequency response of the model*

In the previous section, you used an input with varying frequency to examine how the model output varies as a function of the input frequency. In this section you will characterize the frequency response of the model in more detail, using three different methods.

First, replace the chirp input block in the previous simulation with a Band-Limited White Noise block (keep the parameters at the default values). Then, use each of the following three methods.

a) Use the Matlab code in the script provided entitled freq_response1, which is an implementation of the method described in the pre-lab. Note that you need to run the simulation first, and then apply the script to the outputs. Save the resulting plot and variables in files names “3a_plot_X.fig” and “3a_vars_X.mat”, respectively, for each output (i.e. X should be “hr” in one case and “abp” in the other).
b) Use the Simulink Spectrum Analyzer. This block can be found under “Simulink Extras/Additional Sinks”s in the Simulink block library. Connect V to the first input of this block, and the output (hr or abp, in turn) to the second input. Note that this block will analyze the frequency response while the simulation is running. Save the final Spectrum Analyzer display as “3b_plot_X.fig”.
c) Use the Matlab code in the script provided entitled freq_response2. You should replace the white noise input block with a Sine Wave block. The frequency should be set to “freq”, which will be a variable in the workspace (other parameters can be kept at the default values). The script establishes the frequency responses by explicitly sweeping the sine wave input through a range of frequencies and recording the output each time. In other words, this is a “brute force” method. It will take a few minutes to run, so you may want to start preparing the ECG portion of the lab in the meantime (see below). Save the resulting plot and output variables as “3c_plot_X.fig” and “3c_vars_X.mat”, respectively. **Note that this function will only compute**

the magnitude component of the frequency response, not the phase! This is because the time resolution at which the simulations are being run is too low for the phase calculations to be sufficiently accurate.

4. *Investigate alterations to the system*
   a) In this section, you will use the model to examine the effects of inducing a block of parasympathetic nervous modulation. This can be achieved with certain drugs, for instance Atropine. To simulate this situation, set the model parameters as follows: Ap = 0.1, Kp = 1, fp = 0.07 Hz, As = 4.0, Ks = 9 and fs = 0.015Hz. Analyze the frequency response of this modified system using the same method as in section 3a. Save the resulting plot and output variables as "4a_plot_X.fig" and "4a_vars_X.mat", respectively.
   b) In this section, you will use the model to examine the effects of inducing a block of sympathetic nervous modulation. This can be achieved with certain drugs, for instance propanolol. To simulate this situation, set the model parameters as follows: Ap = 2.5, Kp = 6, fp = 0.2 Hz, As = 0.1, Ks = 1 and fs = 0.015Hz. Analyze the frequency response of this modified system using the same method as in section 3a. Save the resulting plot and output variables as "4b_plot_X.fig" and "4b_vars_X.mat", respectively.

Experimental Procedures - Electrocardiography:

In this section, electrocardiography recordings will be collected using the BioRadio system, and used to evaluate whether the behaviour of a real physiological system corresponds to the output of the simulations.

Experimental Setup

Note: this section is adapted from the BioRadio "Electrocardiography 1" module.

During this laboratory you will record a standard three lead ECG. You should watch the setup movie included with the software prior to setting up the experiment.

1. Your BioRadio should be programmed to the "LabECGI" configuration.

2. For this laboratory you will need to use four snap electrodes from the CleveLabs Kit. Remember that the electrode needs to have good contact with the skin in order to get a high quality recording. The surface of the skin should be prepared and cleaned prior to electrode placement. For the best recordings, it is best to mildly abrade the surface with pumice or equivalent to minimize contact resistance by removing the outer dry skin layer. Attach one electrode on the palmar side of the right wrist, one on the palmar side of the left wrist, one on the left leg, and one on the right leg. **NOTE: The electrodes on the arms can be placed at the wrists and the electrodes on the legs can be placed near the ankles**.

3. After the electrodes have been placed on the subject, connect one snap lead to each of the four electrodes. Then, connect those snap leads and jumpers to input channels 1, 2, 3 and the ground using the picture below as a reference (Fig 4). Refer to your BioRadio User's guide for more information on setting up the system.

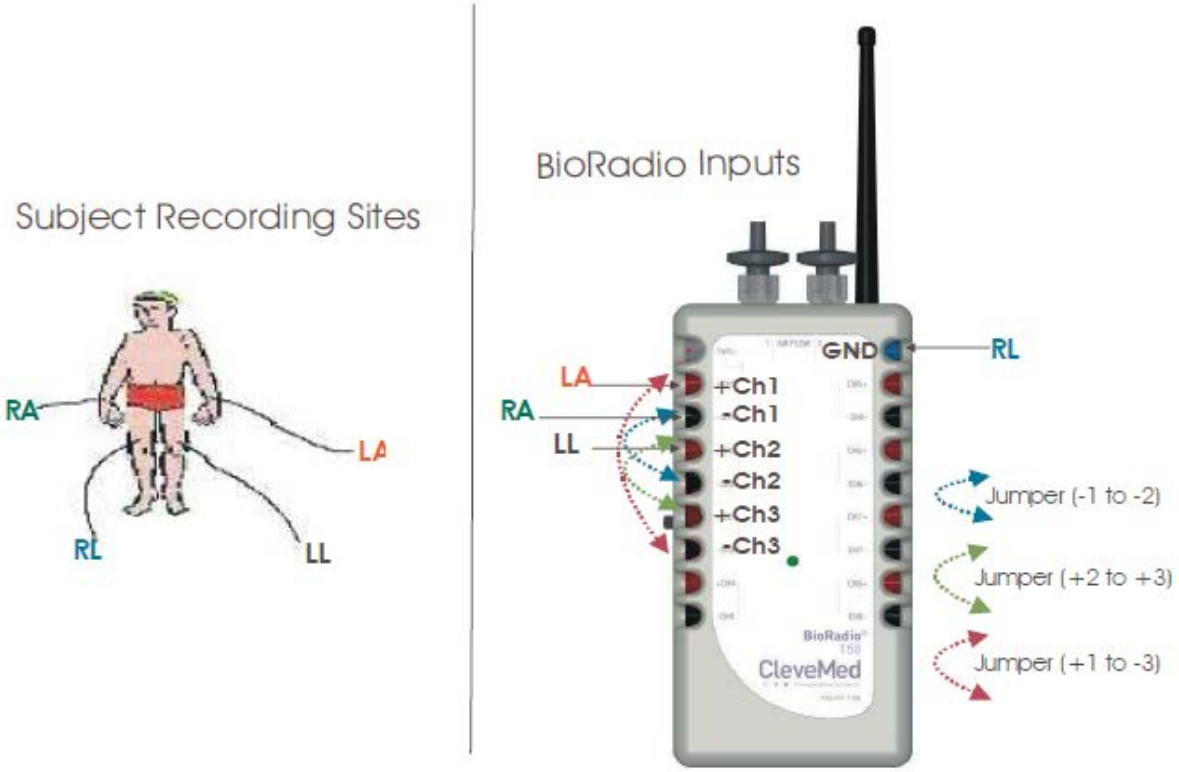

Figure 4: ECG Setup

Procedure and Data Collection

1. Run the CleveLabs Course software. Log in and select the "Electrocardiography I" laboratory session under the Basic Physiology subheading and click on the "Begin Lab" button.

2. Turn the BioRadio ON.

3. Click on the ECG data Tab and then on the green "Start" button. Three channels of ECG should begin scrolling across the screen.

4. First, you will record normal resting ECG with the subject sitting up. It is important that the subject is relaxed and still during this procedure in order to prevent artifacts from

contaminating the ECG signal.

5. For the first test, have the subject sit upright, and place his/her arm on a table or armrest. Make sure the subject is relaxed and quiet. The subject should try to breathe at a normal relaxed rate. The subject's ECG should begin scrolling across the monitor. You may need to adjust the plot scales to see the ECG clearly. Instruct the subject to relax then click on the save button and record data for approximately 1 minute. Name the data file "baseECG". Also, click on "Report" to capture a screen shot of the data scrolling. **Note**: In the saved data file, the first 3 columns correspond to your three ECG leads, and the fourth column corresponds the filtered signal that you are seeing in the Spectral Analysis tab (see step 6 below).

6. With the subject still relaxed, click on the Spectral Analysis tab to complete a spectral analysis. Depending on your surroundings, it is likely that there is some 60Hz power line noise in the signal. Note where the peak frequency of the signal occurs in the frequency domain plot. Report screen captures of the raw, unfiltered Spectral Analysis screen (show both the time domain and frequency domain plots). You may need to adjust the scaling.

7. Change the filter parameters to create a bandstop filter that will remove the 60 Hz noise from the signal and report a screen capture of the Spectral Analysis plots after filtering to verify this (again, show both the time domain and frequency domain plots).

8. Now use instead a 20 Hz low-pass filter. Report the results.

9. Repeat steps 5-8, but this time the subject should breathe very slowly. Record data for another 1 minute, and name the data file "slowECG". Record screen shots with and without filtering.

10. Repeat steps 5-8, but this time the subject should breathe very quickly. Record data for another 1 minute, and name the data file "fastECG". Record screen shots with and without filtering.

11. Next, instruct the subject to waive their left hand around in space while you are recording ECG. Save this data to file and name the file "ECGartifactleft".

12. Finally, instruct the subject to waive their right hand around in space while you are recording ECG. Save this data to file and name the file "ECGartifactright".

Report

- Your team must prepare a lab report showing the outputs that were recorded, as specified in each of the sections above (both Simulink and ECG recordings). For each section, you should include screenshots and/or graphs as appropriate to clearly illustrate your results.
- For the ECG recordings, additionally do the following:
  - Using MATLAB, import the data file "baseECG". Plot the first four beats from channel 1. Also, determine the resting heart rate of the subject based on this

recording. Repeat this for the files “slowECG” and “fastECG”. Label the P, Q, R, S and T segments of one beat on each plot.

- Using MATLAB, plot the heart rate variability in each of the three recordings “baseECG”, “slowECG” and “fastECG”, using the method described in the Background section and the provided Matlab script. Also report the standard deviations of each of the resulting hear rate signals.
- Using MATLAB, open the file “baseECG”. Einthoven’s Law stated that the sum of the potentials from all three channels should equal zero. Using this relationship, calculate what lead two should be, as if data for the first four beats was only available from leads I and III. Plot this calculated lead II, along with the measured lead II. Then, subtract the calculated lead II from the measured lead II and plot this error over time. Give a mean error between the calculated lead II and the actual lead II measurements.
- Using Einthoven’s triangle, the mean electrical axis can be approximated by adding the vectors for leads I and III, and then computing the direction and magnitude of the lead II vector, which is the mean electrical axis of the heart. To do this measurement, draw a figure similar to the one next to Einthoven’s triangle (Fig 2), except omit the line representing lead II. Use a protractor to ensure that the angle between leads I and III is 120 degrees. For both the lead I and lead III vectors, draw twenty evenly spaced tics on the vectors, ranging from 0 to 2 mV.

  One way of determining the mean electrical axis is to measure the amplitude of the R wave on leads I and III. Determine the mean amplitude of the R wave for leads I and III over three or more beats. Once known, draw a line perpendicular to the lead I and a line perpendicular to lead III vectors at the value of the R wave for the respective leads. (i.e., if the mean R wave amplitude is .8 for Lead I and .6 for Lead III, find the mark corresponding to .8 mV on Lead I, and draw a perpendicular line, and do the same for Lead III). Find the intersection of these two lines, and record the magnitude and direction of this vector. Remember that zero degrees is measured from the lead I vector. This vector we computed is the lead II vector, which indicates the mean electrical axis of the heart.

- In addition, include a Discussion section in which you will address the following questions (create a separate sub-section for each question):
  - What aspects of the experimental protocol seemed the most likely to introduce errors in the results? To what extent to you think that these issues affected the results that you are reporting, and how could the protocol be improved to address these points?
  - How do the heart rate variabilities analyzed from the ECG recordings (using the “IBI” script) relate to the results from Simulink model showing how *hr* varies based on the breathing pattern? Is the simulation reflective of the physiological data? If not, why not? In answering this question, make sure that you are considering what each result is telling you about the **changes in heart rate** as a function of the respiration rate.

- In the data files labeled “ECGartifactright” and “ECGartifactleft”, examine each of the three leads in each file. On which leads can you detect an ECG signal? On which leads is the ECG signal distorted? Explain why.
- Why was a white noise input used in the Simulink model to conduct the frequency response analysis? What is the advantage of using the chirp block, as in the original model?
- Consider the effects of the 60 Hz bandstop and 20 Hz lowpass filters that you used. What are the advantages or disadvantages of each of these two approaches?
- Based on your simulations of the sympathetic and parasympathetic blockades, which blockade has the greatest effect on the phase of *hr*? Why? Refer to the structure of the model in your answer. [Note: when comparing the phase results, focus on frequencies below approximately 0.5 Hz. Any “sawtooth” shape that you may observe in the plots at higher frequencies is simply an artefact due to phase wrapping. That is, imagine moving clockwise around a unit circle: when the phase reaches -180°, it will “jump” to +180°.]

Marking scheme

Pre-lab quiz: 5% (individual mark – pass/fail; all questions must be answered)
Simulink simulations and results: 25%
ECG experimental results: 15%
Analysis of the ECG results: 15%
Discussion questions: 30%
Clarity, organization, and language: 10%

Your lab report is due on the dates indicated in the course syllabus. Submit the report via Quercus no later than 5pm on the due date.