Instructions:
- This exam has 3 pages and 5 questions.
- Answer 50 (of 85) marks worth of questions
- You have 150 minutes to complete this exam.
- This is a closed book exam; however, you are permitted to bring one 11” × 17” sheet of notes.
- You are permitted to use a non-programmable calculator.
- Write your answers on an examination booklet. You may take this examination paper with you.

Background: The prevalence of childhood asthma is increasing in developed countries. One consequence is a need to develop accurate tests for asthma in children. Since asthma is an obstructive lung disease, it is associated with an increase in airways resistance to airflow. In adults, the gold standard test is a forced expiratory manoeuvre; the subject is asked to inhale to total lung capacity, and then to breathe out as fast as possible while airflow is monitored. Unfortunately, this test works poorly in young children, since they do not fully comply with the test instructions.

In this exam, consider an (unreasonable) approach to solve this problem – stimulating directly the breathing muscles of the child to create this maximal muscular force. An electrode is placed in the esophagus which is used to electrically stimulate the diaphragm to drive the maximum force. The advantage of such a system would be its potential improved accuracy; the disadvantage would be the electrical risks, and the level of intrusiveness felt by the child for a routine test.

1. Research Ethics and Biomedical Engineering Practice. Consider a research project to evaluate the device. Participants (children 3–5 years old) visit the lab, and are tested first by this device (D) and then by gold standard measure (G).

A. (10 marks) Write a brief ethical justification for this research project, considering the risks and benefits. Select a specific ethical framework from the ones we considered in class, and frame your arguments in terms of the categories of the ethical framework.

B. (5 marks) Why is informed consent such an important principle for research ethics? In this case, we would only have consent from the parents. Describe one ethical consideration in support of and one consideration which weighs against the use of parental consent in place of the child’s.

C. (5 marks) Such a medical device would require approval. Discuss two aspects that would be considered in assigning a medical device class to this system.

2. Sampling and statistical methods

A. (5 marks) Consider strategies to recruit volunteers for this research project. Assume asthma is fairly rare (≈ 1%) in this population. What are the advantages of stratified sampling over random sampling?
B. (5 marks) The device gives output in terms of the estimated airways resistance $R_{aw}$. The test results yield the following number of subjects in each category, rounded to the nearest integer value.

<table>
<thead>
<tr>
<th>$R_{aw}$ (kPa)</th>
<th>1.0</th>
<th>2.0</th>
<th>3.0</th>
<th>4.0</th>
<th>$\geq$ 5.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma subjects</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>Non-asthma subjects</td>
<td>30</td>
<td>12</td>
<td>6</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

If the device is used to classify subjects, there is a possibility of errors for each threshold value. Calculate the rate of type I and type II errors as a function of threshold, $R_{aw}$. Sketch the detection error trade-off curve.

C. (5 marks) In order to evaluate the discomfort of this device, a survey is added to the protocol. Typically, older subjects are more able to reply to the survey, so we don’t get responses from the youngest. Does this effect introduce a bias? Discuss briefly.

D. (5 marks) Subjects are asked to rate the discomfort of each system on a scale of 1 . . . 5. What can we conclude about how much more uncomfortable device D is than device G?

<table>
<thead>
<tr>
<th>Discomfort</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>New device (D)</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>18</td>
<td>9</td>
</tr>
<tr>
<td>Gold standard device (G)</td>
<td>9</td>
<td>18</td>
<td>9</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

3. Cells and Electrophysiology

A. (5 marks) The diaphragm is controlled by the phrenic nerve, which originates from the cervical (ie. neck) vertebra. This device is designed to send its own signals down the phrenic nerve which overpower the signals from the brain. Describe how signals propagate through a nerve axon? What will increase in the axon due to the new electrical stimulation: the firing rate? the amplitude? Are there any limits to the amplitude and firing rate?

B. (5 marks) One clear risk is that electrical stimulation in the esophagus will interfere with the heart, resulting in fibrillation. Sketch the normal electrical signal from the heart, and indicate the mechanical events which occur at each signal peak. How does the electrical signal change during ventricular fibrillation?

C. (5 marks) Asthmatic patients typically benefit from inhaled steroids, which have an anti-inflammatory effect. In the body, steroid hormones bind to receptors on proteins. What is the tertiary structure of proteins, and how does this structure help create specific binding sites on proteins?

4. Oxygen transport (heart and lungs)

A. (5 marks) During an acute asthmatic episode (attack), smooth muscles in the lung airways will constrict, increasing the airways resistance. Using a diagram of lung volumes, airflow and muscular force, discuss how breathing changes as airways resistance increases.

B. (5 marks) In such an acute condition, it may help to adopt a posture that increases functional residual capacity (FRC), such as going on hands and knees. Sketch a diagram of the forces on the abdomen, diaphragm, chest wall, and lungs in this posture. Describe how this affects FRC.

C. (5 marks) Assume a child normally breathes 15 breaths/min and 200 ml/breath (breathing 100% humidity air, at sea level, with 20% $O_2$). Cardiac output (CO) = 3 L/min, and $\dot{V}O_2 = 150$ ml $O_2$/min.
During an asthma attack, she can only manage 100 ml/breath, but all other physiological values stay constant (note that this is unrealistic). If the $S_a O_2 = 100\%$, what are the values of (a) the saturation of venous blood and (b) the concentration of expired air?

D. (5 marks) How is CO$_2$ carried in the blood? What happens to the blood when breathing is reduced, as in the previous question?

5. Biomechanics

A. (5 marks) A large fraction (40%) of bone is hydroxyapatite; this material is similar to chalk. Why is bone not brittle like chalk? Spongy bone is lighter per volume than compact bone and yet retains much of the mechanical strength. Using a diagram if necessary, explain why?

B. (5 marks) When soft tissue is stretched, the elastic modulus is low for the first fraction of the strain. At larger strains, the tissue will yield and then finally fail. Using a diagram, sketch the state of the collagen fibers in the soft tissue and explain how this affects the mechanical properties.