Instructions:
- This exam has 4 pages and questions with a total of 16 subquestions.
- Answer 40 (out of a total of 80) marks worth of questions
- You have 180 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-network-connected calculator.
- Write your answers on an examination booklet. You may take this examination paper with you.

Background: During a stroke, there is the rapid loss of brain function resulting from a disturbance in the blood supply to the brain. It is a medical emergency, because it can result in neurological damage, other complications, or death\(^1\). Worldwide, stroke is the second most common cause of death\(^2\). Strokes are classified into two main types: ischemic and haemoragic\(^1\). In ischemic stroke, blood supply to a part of the brain is reduced, typically due to a blockage of blood vessels, often by a blood clot. The consequence is that the brain region becomes ischemic (with reduced O\(_2\) and increased CO\(_2\)). In haemoragic stroke, there is an accumulation of blood within the brain, often due to head injury or a ruptured aneurism (localized balloon-like widening of a blood vessel).

One possible emergency treatment for ischemic stroke is to administer thrombolytic drugs to the patient. These act as “clot busting” agents to attempt to improve blood flow and reduce ischemia. Unfortunately, administration of thrombolytic drugs to patients with haemoragic stroke is extremely dangerous, as they can worsen bleeding, and lead to death.

There is thus a clear need to rapidly distinguish between the two types of stroke, in order to determine whether a patient should be given thrombolytic drugs or not. In this exam, we consider a technology to make this determination: EIT (on which some of the prof’s colleagues are working). The details of the technology are not important for this exam, except that it is non-invasive for the patient. The only concern is that the accuracy of the technology is not perfect.

Sampling and statistical methods

Consider a study to evaluate the clinical effectiveness of EIT as a tool to choose whether patients receive thrombolytic treatment (T). Subjects arriving at the emergency department are randomized into three groups, two control groups (C1 and C2) and one experimental group (E).

1. no subjects receive treatment (C1)
2. all subjects receive treatment (C2)
3. subjects receive treatment if indicated by EIT (E)

After treatment, subjects are evaluated by a measure of mental acuity (MA). Assume that MA is measured by asking the subject to answer a set of cognitive questions; the value is the number of correct answers.

\(^1\)en.wikipedia.org/wiki/Stroke
1. (5 marks) Consider the variables in the study:
   (a) Which is the dependent and independent variable?
   (b) What kind of variable is MA (Nominal, Ordinal, Interval, Ratio scale)?
   (c) Discuss (briefly) any problems in interpreting MA, if the different tests that form part of MA were of different levels of difficulty?

2. (5 marks) We have funds for a study of size \( N = 150 \) (total subjects in all groups). We wish to detect a significant difference between the mean MA of the C1 (\( \mu_{C1} \)), and E (\( \mu_{E} \)) groups. Assume that, within each group, the standard deviation in MA scores is 2.8. **Estimate the difference** (\( \mu_{C1} - \mu_{E} \)) **we are likely to be able to detect with a statistical significance of** \( \alpha = 0.05 \).

   The following table of 1- and 2-tailed \( t \)-test values for \( \alpha = 0.05 \) may help:

<table>
<thead>
<tr>
<th>( \alpha = .05 )</th>
<th>DF= 2</th>
<th>3</th>
<th>5</th>
<th>10</th>
<th>20</th>
<th>50</th>
<th>100</th>
<th>( \infty )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-tail</td>
<td>2.92</td>
<td>2.35</td>
<td>2.02</td>
<td>1.81</td>
<td>1.72</td>
<td>1.68</td>
<td>1.66</td>
<td>1.65</td>
</tr>
<tr>
<td>2-tail</td>
<td>4.30</td>
<td>3.18</td>
<td>2.57</td>
<td>2.23</td>
<td>2.09</td>
<td>2.01</td>
<td>1.98</td>
<td>1.97</td>
</tr>
</tbody>
</table>

3. (5 marks) **What is survivorship bias?** Assume subjects that are more severely affected were less likely to survive. **Describe how survivorship bias would affect the results (would we expect a more or less significant difference between groups)?**

4. (5 marks) Assume that 10% of patients have haemoragic stroke and 90% have ischemic stroke. The technology has both a sensitivity and specificity of 0.8. **Estimate the survivorship (fraction of patients surviving) of the groups C1, C2, and E.** Use the following table of survivorship for patients who receive and do not receive treatment.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Ischemic</th>
<th>Haemoragic</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>0.80</td>
<td>0.50</td>
</tr>
<tr>
<td>Yes</td>
<td>0.90</td>
<td>0.20</td>
</tr>
</tbody>
</table>

5. (5 marks) This study has two control groups (unlike many of the studies we looked at in class): one for no treatment, and the other for uniform treatment. **Describe why two control groups is a good idea in this study**, especially considering the answer to the previous question. Specifically, how could the study be criticised, if it only contained the C1 control group?

**Research Ethics and Biomedical Engineering Practice**

6. (5 marks) **Informed consent** is a fundamental principle in research ethics. However, in this study patients are in an emergency. Delay could worsen their condition and even lead to death. If they are not conscious, then the experimenters want to get consent from their family (or whomever they are with when the ambulance arrives). Is this an ethical issue? **Use an ethical theory to argue for or against getting consent from other family members.**

7. (5 marks) The Medical Devices Bureau of Health Canada has recognized four classes of medical devices based on the level of control necessary to assure the safety and effectiveness of the device. **List and briefly describe these classes.**

   Would this EIT device be classified as a medical device? If so, **describe two considerations in classifying it, and suggest an appropriate device class.**
8. (5 marks) As medical technology becomes increasingly computerized, there is a tendency for medical staff to become less able to understand it. One example is in the comic in Fig. 1. Another example is that almost all medical equipment is used in “default” mode, with no customization. Based on the concern above, briefly discuss the two issues for a clinical engineer to consider before the purchase of new hospital technology.

Oxygen transport and biomechanics

9. (5 marks) A patient with stroke will sometimes have difficulty with balance. Consider a scenario in which the patient is pushing on a wall to maintain balance. Consider the patient’s body to be rigid with a mass of 80 kg. Draw a free-body diagram of the body when the patient is leaning at 15° into the wall. State your assumptions. What static balance equations can be written? Which are known or unknown quantities?

10. (5 marks) High blood pressure is the most important modifiable risk factor of stroke1. If a patient has a stenotic aortic valve, the heart will normally compensate by increasing blood pressure to maintain cardiac output (CO). Sketch a curve of the left ventricular pressures and volumes during the
11. (5 marks) In the previous question, we consider that the heart will compensate for the stenosis. If it is unable to do this, the condition is described as “decompensation”. Consider a heart with an end-diastolic left ventricular volume of 120 ml. Previously, when the heart was healthy, LVEF was 60% and the heart rate (HR) was 60 bpm. With the stenosis, LVEF decreased to 25% and HR increased to 100 bpm. Assume oxygen transport in the lungs is perfect and \( S_aO_2 = 100\% \). The oxygen consumption is stable at \( \dot{V}O_2 = 250 \) ml/min. Before stenosis, \( S_vO_2 = 75\% \). **Calculate the CO before and after stenosis, as well as the new value of \( S_vO_2 \).** Consider that all oxygen is transported bound to hemoglobin.

12. (5 marks) The aortic valve leaflets have a highly adaptive mechanical structure for their function. Consider that, in an experimental model, we wish to test the mechanical properties of the valve leaflets. **Describe three issues in the testing of biological materials, which must be taken into account while testing the leaflets.**

13. (5 marks) During ischemia, \( O_2 \) available to tissue decreases while blood \( CO_2 \) increases. **Describe how these chemicals are transported in the blood, and what changes happen as their concentration changes.** Use a sketch the oxy-hemoglobin dissociation curve.

**Cells and electrophysiology**

14. (5 marks) **Sketch a neuron in the brain and describe how it transmits impulses to other neurons.**

   During ischemia, the \( Na^+ \), \( K^+ \) and \( Cl^- \) pumps work more slowly. **Sketch an action potential, showing the refractory periods.** Discuss how the refractory periods may change during ischemia (considering only the effect of the slowing of the ion pump transport).

15. (5 marks) The electroencephalogram (EEG) may be used to monitor for changes in brain function during therapy for stroke. **Compare the EEG signal to the EMG and ECG. How are the signals produced? Are the signals structured or apparently random?**

   One possible way to monitor brain function would be to regularly measure a visually evoked response (VER) from the patient at each visit to the clinic. **Describe how such a VER could be measured? Why is it typical to average many VER signals?**

16. (5 marks) If the patient has a head injury, there will typically be significant swelling (due to a local accumulation of fluid). **Briefly describe some protective functions of swelling and fluid accumulation.** One way to help reabsorb such fluid would be to change the ionic concentration in the blood. **Would hyper- or hypo-tonic saline be used in this case? Explain.**