EE3-21 Biomedical Electronics Solutions

1. This question relates to the design of a multichannel instrument for measuring bio-potentials from neurons in the brain.

   a) Figure 1.1 shows an AC coupled bio-potential amplifier for measuring neural activity from the brain. The electrodes used have a capacitance C_E=10μF and V_{sig} and V_{os} denote the measured bio-potential and common mode offset.

      i. Give one advantage and one disadvantage of using AC rather than DC coupled bio-potential amplifiers for this application.

- Advantage: Remove common mode offset thus allowing large gain in front end. [1]
- Disadvantage: Reduction of input impedance causing potential attenuation of the signal. [1]

[Total 2 points]

      ii. Derive the input voltage to the amplifier V_{in}, and show that it is high pass function stating the equation of the cut off frequency stating any assumptions made. To aid your calculations you may use just one branch of the differential input for your analysis.

- Assuming C1<<CE we can derive: $V_{in} = (V_{sig} + V_{os}).SR_1C_1/(SR_1C_1 + 1)$ [2]
- $f_c = 1/2\pi R_1C_1$ [1]
- Note: You will loose 1 point if you don't state the assumption.

[Total 3 points]

      iii. C_1 is chosen to be 10pF. Calculate a suitable value for R_1 to give you a high pass cut off at 50 Hz.

b) $R_1 = 1/2\pi C_1 f_c = 1/2\pi(10p)(50) = 318.3M\Omega$ [2]

[Total 1 points]

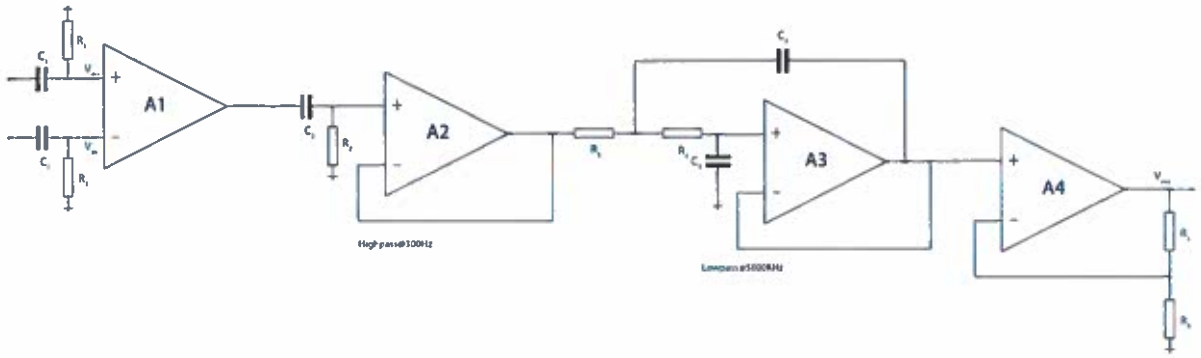
      i. It is required that this instrumentation amplifier can be connected to more than one set of electrodes using a 16X1 analogue multiplexer connected to points. A and B in Figure 1.1 and switching in multiple electrodes. Every time the multiplexer is connected a 1V transient spike appears at points A and B. State one limitation of the circuit Figure 1.1 when used in this configuration, and calculate the time taken for one complete scan of 16 electrodes assuming the multiplexer can switch to the next electrode with the spike reaches a voltage of 368mV and using this value calculate the frame rate of the system.

- Time taken to reach 368mV is one time constant=C_1R_1 = 3.183 ms [1]
- Time to scan 16 electrodes = 16x3.183ms =50.9ms [1]
- Frame rate = 1/50.9ms = 19.6 Frames per second. [2]

[Total 4 points]

c) The Bio-potential amplifier in Figure 1.1 is used as part of a monitoring system to detect the action potential signal shown in Figure 1.2. The gain of the Bio-potential amplifier is set to A=100. The output of the Bio-potential amplifier is band-pass filtered between 0.3KHz and 5KHz with a 20db/decade high-pass followed 40db/decade low-pass filter. A final gain stage is added to maximize the dynamic range between +3V to -3V.

i) Sketch the full schematic of this monitoring system, indicating suitable resistor values for you filters. You may assume all capacitors are, C=100pF for your filters.



- Schematic shown above for complete system (student needs to identify first order high pass and second order low pass (using a sallen key))[4]
- High pass value $R_2=1/2\pi C_2 f_c = 1/2\pi(100p)(300Hz)=5.3M\Omega$ [1]
- Low pass value $R_3=1/2\pi C_3 f_c = 1/2\pi(100p)(5000Hz)=318K\Omega$ [1]

[Total 6 points]

ii) Choose suitable gains and resistor values to ensure that the action potential shown in Figure 1.1 is utilizes the maximum dynamic range.

- From figure 1.2 student needs to realize that the 100uV DC is rejected and thus the maximum AC signal passing through is 150uV ptp or 100uV 0top. Realising this the maximum possible gain of the system is 3.3V/100uV=33000. [2]
- Total gain of the system 33000=A1xA2xA3xA4=100x1x1xA4. thus gain of final stage A4=330[1]
- Thus gain of last stage A4=1+R5/R4=330. therefore R5/R4=329. So we can choose R5=329K and R4=1K. [1]
- Will also accept 150uV ptp as a possible solution giving a gain of 6V/150uV
- Student gets 2/4 points for correct methodology but incorrect input signal.

[Total 4 points]

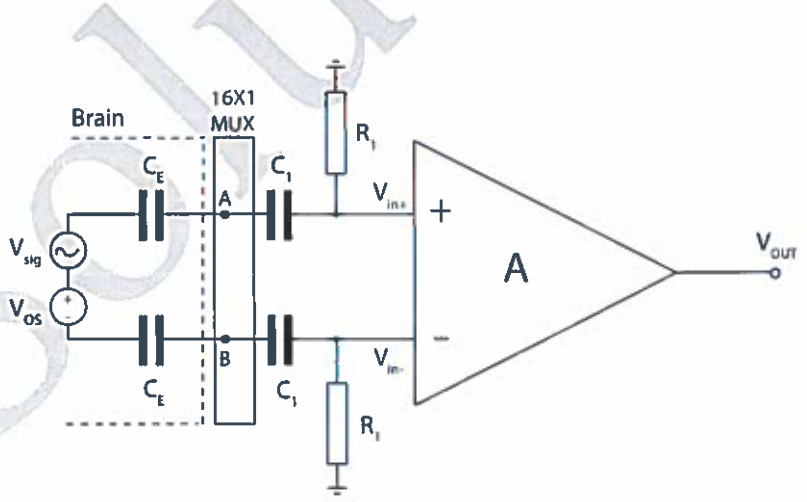


Figure 1.1

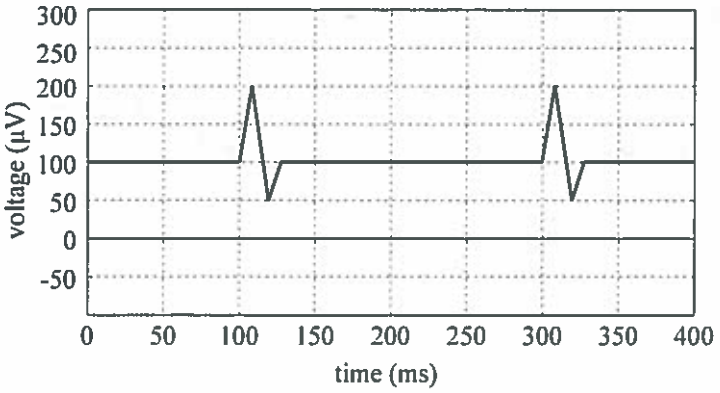


Figure 1.2

2. This question relates to electrical stimulation.

An asymmetric biphasic current waveform that is generated by an electrical stimulation circuit is shown in Figure 1.1.

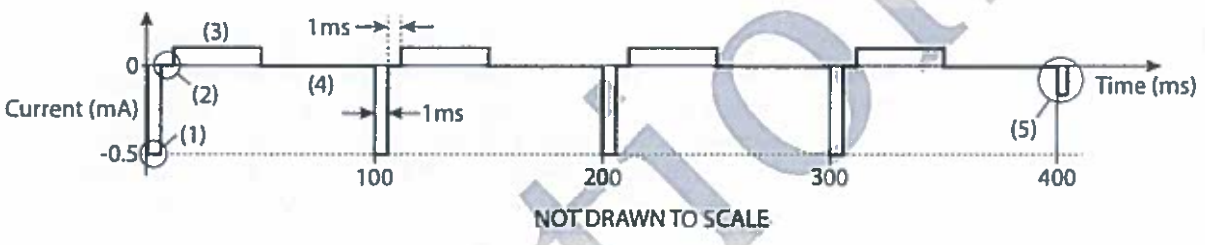


Figure 1.1

a) Give titles for phases (1), (2), (3), (4), and (5) as annotated in Figure 1.1, and briefly describe the purpose of each. [10]

(1) Cathodic phase – to provide the stimulus (charge) to activate the tissue.
(2) Interphasic delay – to allow the tissue sufficient time to activate (before applying anodic phase).
(3) Anodic phase – the recover charge that has been injected into tissue (to charge balance)
(4) Silent phase – a delay between stimulation cycles such that multiple channels can be interleaved.
(5) Shorting phase – to remove any residual charge (in case biphasic waveform is not perfectly charge balanced).

b) State one advantage and one disadvantage of using an asymmetric waveform instead of a symmetric waveform. [2]

Advantage – tissue is less prone to fatigue when stimulated successively.
Disadvantage – reduced maximum repetition rate (or scalability in case multiple channels need to be interleaved).

c) Given a 5kΩ electrode impedance, estimate the voltage headroom that is needed to generate the stimulus waveform shown in Figure 1.1. State any assumptions made. [2]

Vstimulus = Istim x Relectrode = 0.5mA x 5kΩ = 2.5V

Also assuming a further 0.5V is required for transistor circuits to operate -> total voltage headroom = 2.5V + 0.5V = 3V

d) If four stimulation channels are to be interleaved such that each channel delivers a stimulus at 10Hz, calculate the durations of phases (3) and (4), in addition to the amplitude of phase (3). [4]

If 4 channels are interleaved @ 10Hz each -> 25ms per stimulation phase.
Phase (4) is thus 75ms (during which other 3 stimulation channels are active).
Given 2ms needed for phases (1)+(2) out of 25ms -> phase (3) can thus be made to be 23ms.
Amplitude of phase (3) is thus 500uA/23 = 21.7uA.

e) Briefly describe how the magnitude of phase (5) is determined. [2]

If this is a shorting phase, the magnitude will be determined automatically when the electrodes are shorted (based on net charge build-up, and total impedance (electrode + internal impedance of circuit)). If this is part of an active balancing circuit, fixed current pulses (predefined) can be applied until the electrode voltage returns to zero.

3. Fig. 1 shows a smart contact-lens system for non-invasive measurement of tear glucose. The glucose concentration in the tear fluid is within 0.1-0.6mM for a healthy person and may go up to 1mM in patients with diabetes. The Glucose sensor comprises a working electrode (WE) with an area of 1mm^2, a reference electrode (RE) (area:0.3mm^2) and a counter electrode (CE) (area:2mm^2). The sensor readout IC receives AC power from the antenna and sends the measured data back to the transmitter. All circuits operate on a single supply with a VDD of 1.8V.

The working electrode is coated with glucose oxidase to give a peak current to glucose at VCell=0.7 V according to the following reaction:

$$\text{Glucose} + O_2 \xrightarrow{\textit{Glucose Oxidase}} \text{gluconic acid} + H_2O_2$$

$$H_2O_2 + O_2 \xrightarrow{V=0.7V} 2H^+ + 2e^-$$

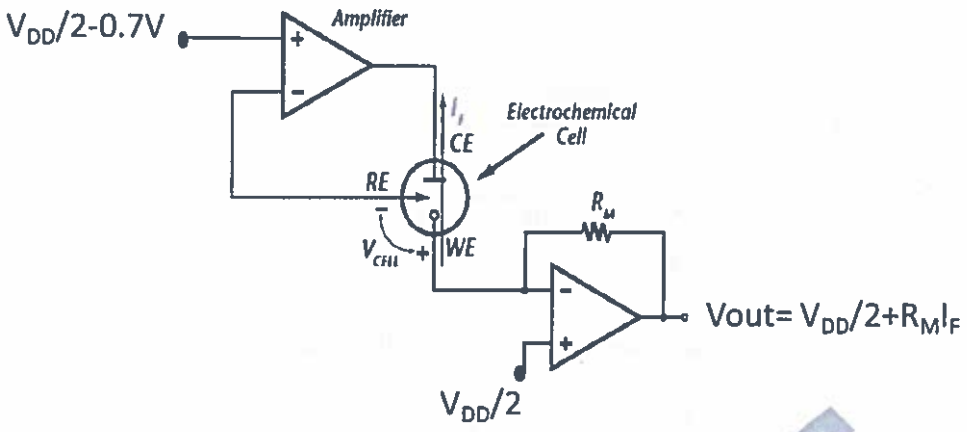
a) Calculate the peak redox current for the reaction above using the Randles Equation below. You may assume the number of electrons n is solely given by the oxidation of H_2O_2 , the scan rate is 1V/sec and the diffusion coefficient D=4.38X10^{-8} m2/s:

$$i_p = 2.69*10^5 * n^{3/2} .A .D^{1/2} .C .v^{1/2}$$

n=2
A=1mm2
D=4.38X10^{-8} m2/s
C=1mM
V=1V/sec
I= 2.69*10^5*(2)$^{1.5}$*(10^{-6})*(4.38X10^{-8})$^{0.5}$*(10^{-3})*(1)$^{0.5}$= 159 nA

[Total 2 points]

b) Design a potentiostat and trans-impedance amplifier (TIA) with opamps and resistors to apply the cell voltage and measure the sensor current, and maximize the output swing. Annotate the schematic.



[2]

V_{cell}= 0.7 V
VDD= 1.8V, $I_{F,max}$= 159nA
R_M*$I_{F,max}$=< 0.9V
Then R_M =< 5.66 MOhm

[2]
[Total 4 points]

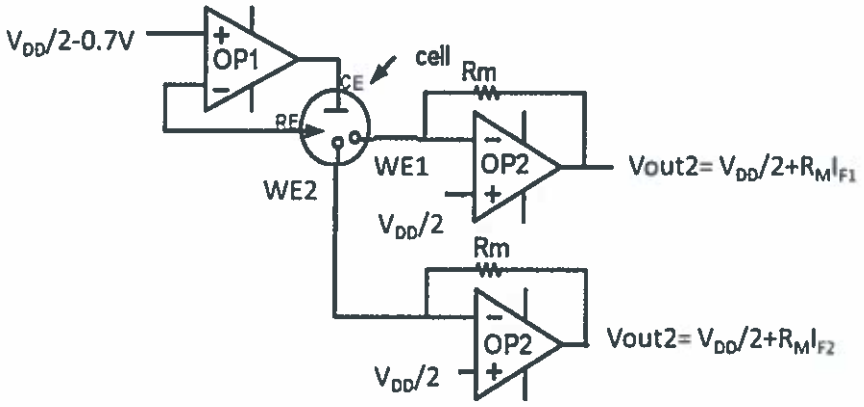
c) Describe two alternative circuits to measure the sensor current, and state one advantage for each with respect to TIA in part c. Which one is most suitable for the contact-lens and why?

Switch capacitor based TIA: adv: can be implemented on-chip as doesn't need big resistor [1]
Current-mode-potentiostat; adv: combines potentiostat and readout which means the interface system requires one less opamp and subsequently less power. [1]
Most Sutiable: The current-mode potentiostat it matches the current-to-frequency converter and doesn't require and ADC so leads to overall smaller energy consumption. [1]

[Total 3 points]

d) The interference and current drift limits the performance of the biosensing systems. Propose one method that can help to compensate these effects and redesign the circuit in part b and one of the circuits in part c to implement this method.

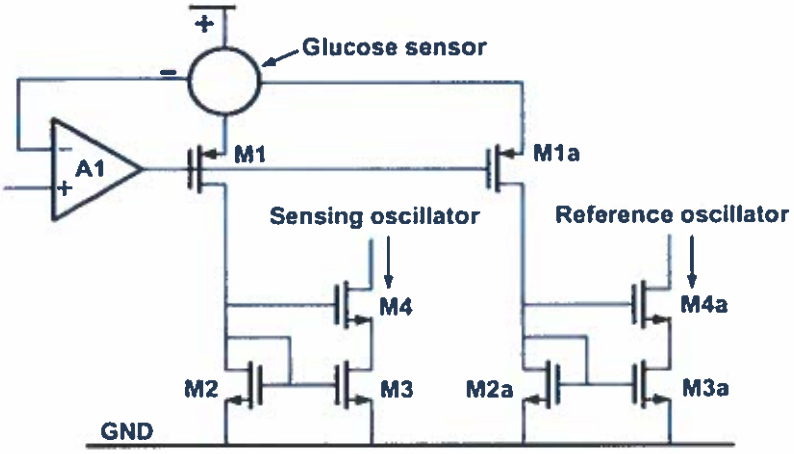
Differential measurement can be implemented to reduce the effect of drift and interferences. [1]
This can be answered with any of the resistor-mode TIAs, SC-TIA or current-mode potentiostat. The two resistors based TIA circuit :



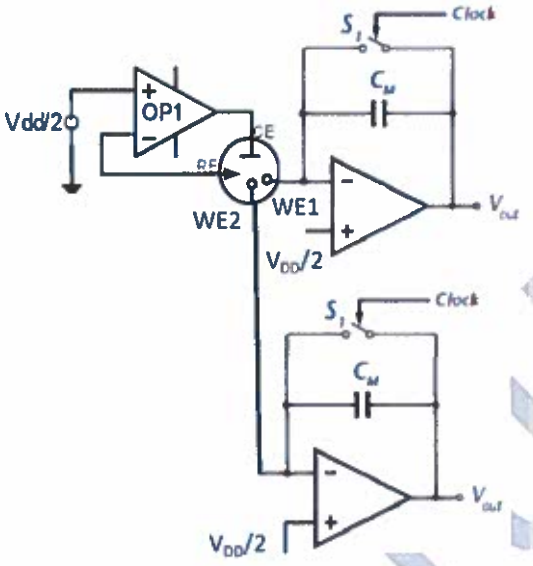
[2]

And one of the two below:

Current-mode potentiostat circuit:



Or the switch-capacitor-based TIA:



[2]

[Total 5 points]

e) **Draw the block diagram of a readout IC to interface the sensor and their connections together and to the sensor and antenna and list the function of each block.**

Main circuit blocks are:

1- Voltage rectifier: To convert ac voltage into DC

2- Energy storage capacitor: to store energy and to smooth the DC voltage

3- Voltage regulator: to make a clean, ripple-free VDD for the circuits from the rectified voltage

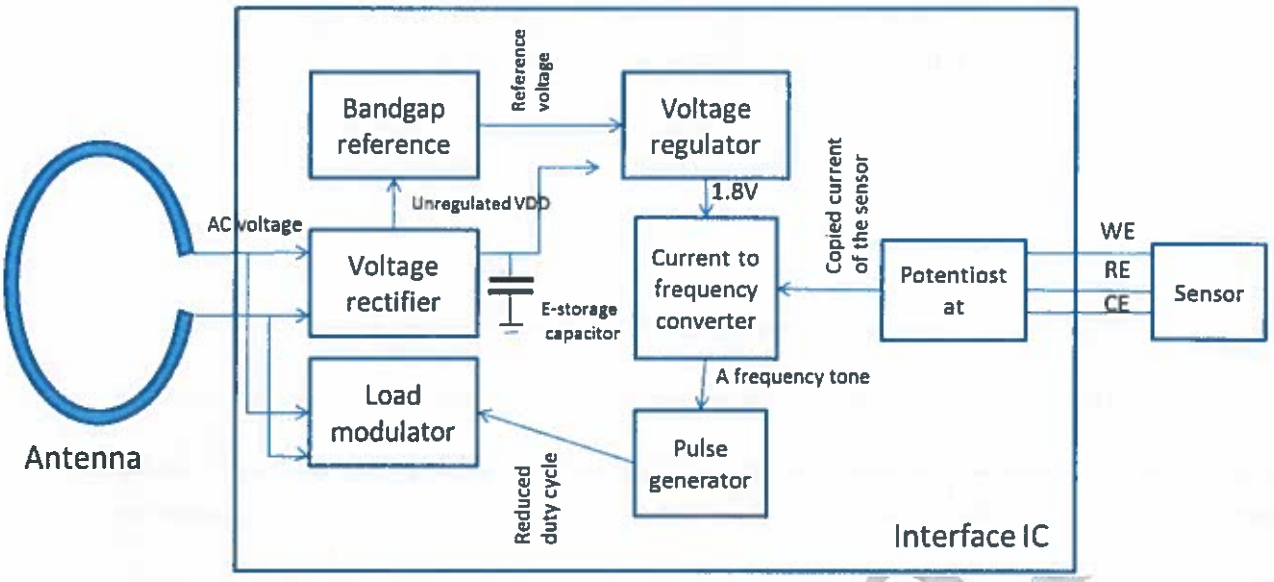
4- Bandgap reference: to make a voltage supply and temperature independent reference volage from which the regulator can produce the VDD

5- current-mode Potentiostat: to apply the cell voltage and read the sensor current

6- I-to-f converter: to produce a frequency of an oscillator proportional to the sensor current. The system then doesn't need an ADC before data communication

7- Pulse generator: to increase the pulse-width and to allow simple transfer of both main and reference oscillators

8- Antenna load modulator: to transfer the data back to the transmitter through backscattering



[Total 6 points]

4. This question relates to power management of an implantable sub-retinal prosthesis.

   a) The implanted system consumes an average power of 500µW (excluding stimulation power). Given the following parameters determine what capacity of implantable battery would be required in order to operate the device. State any assumptions that are made. [10]

Array size:	32 x 32
Electrode impedance:	100kΩ
Stimulation type:	Current-mode (symmetric biphasic pulses)
Average stimulus magnitude:	50nC
Stimulation rate (per channel):	25Hz

- To identify that the energy requirements are too high to consider a non-rechargeable battery, and thus this is considering a rechargeable battery with 1-day battery lifetime (daily recharge). [1]
- To calculate the duration of each stimulation cycle = 25Hz * 1024 channels = 25.625 stimulation cycles / sec. => 1/stim cycles per sec = 40µs (per cycle). [1]
- If cycles are biphasic and symmetrical -> 20µs cathodic phase followed by 20µs anodic phase. [1]
- Given average stimulation magnitude of 50nC -> Q=I x t => Average stimulation current is thus, I = Q/t = 50nC/0.2ms = 250µA. [1]
- Assuming the average stimulation current is 50% the maximum magnitude, then the maximum stimulation current would be 500µA. [1]
- Thus to support a 500µA current (through a 100kΩ electrode) -> Vcompliance = I x R = 1mA x 100k = 50V. This assumes that any voltage drops across other components in negligible in comparison. [1]
- Average power consumption for stimulation is therefore P = Iaverage + Vcompliance = 250µA x 50V = 12.5mW. Total average power consumption for the retinal implant during operation is thus 12.5mW + 500uW = 13mW. For a 50V supply this corresponds to an average current of 260µA. [1]

- If the device is operated for an average of 18hrs a day, then the energy capacity required for a week would be 260μA x 18hrs = 4.68mAh (assuming a 50V battery). [1]

- If this is to be boosted up from a 3V battery (assuming also losses in DC-DC conversion – e.g. 30% efficiency). a 260mAh, 3V battery should be sufficient. [2 – for identifying 50V cells done exist, and doing calculation].

b)

This question concerns the powering of implanted medical devices.

b) Thermoelectric generators (TEGs) are a possible alternative source of electrical power to batteries.

i) Draw a cross section through a TEG, labelling the important parts, and explain how the device generates electrical power.

[4]

ii) It is proposed to attach a boost power converter to a TEG that will be used to power a body worn heart rate monitor. Other than stepping up the TEG's voltage, what other important role should this converter perform and why?

[3]

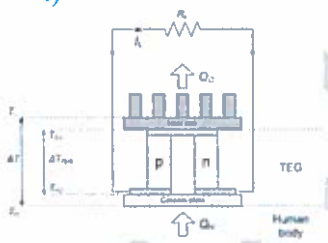
c) Inductive power transfer between coils coupled with poor coupling factor, $k<0.1$, provide a difficult challenge for the drive electronics. Explain why, and what solutions are employed.

[3]

[bookwork]

b)

i)



[2]

The TEG comprises pillars of alternating p and n type semiconductors that are connected in series electrically and in parallel thermally. Heat causes diffusion of carriers from the hot side to the cold side and the physical connectivity ensures that the charge carriers add to create a current.

[2]

[Application of knowledge from another area]

iii) The boost topology has a smooth input current which allows it to exhibit a controlled, resistive input impedance. Electrically, the TEG is a Thevenin voltage source and the boost converter is particularly amenable to maximum power point tracking.

[3]

c) Poor coupling between IPT coils (which is a natural consequence of an air gap) means the coils have significant leakage inductance and low magnetising inductance. Low k

means a need to operate with high Q factor for high efficiency – so that the large amount of reactive power associated with driving the coils does not cause excessive I^2R loss. In order to reduce the V and I rating of the power semiconductors. a combination of series and parallel resonance is utilised.

[3]

5. **Sequencing the human genome requires the identification of 3.2 billion bases of DNA that can be implemented using the process of pyrosequencing.**

   a) **Explain what DNA is and describe one of its properties that allow detection of single bases for DNA sequencing.**

[bookwork]
DNA – Deoxyribonucleic acid
To *conserve and transfer* the genetic information by replication.
DNA double helix: DNA organised in double stranded form
Complementary (matching) **base pairs**:
A-T (Adenine – Thymine) 2 hydrogen bridges
G-C (Guanine – Cytosine) 3 hydrogen bridges
Nucleotides: A nitrogenous base, a five-carbon sugar, and at least one phosphate group.

[2 points]

Properties which allows DNA sequencing:
The incorporation of one nucleotide leads to the production of pyrophosphate and most importantly to the release of a hydrogen ion from the hydroxyl group of the 3' terminal of the growing strand, leading to a change in the pH of the reaction due to the increase of the solution's acidity. We can detect this change in pH using **Ion-sensitive field effect transistors**.

[2 points]
[Total 4 points]

   b) **Explain the process of pyrosequencing, including a diagram showing the sequence of DNA bases with the signals generated for detection.**

Pyrosequencing - Insert bases ATCG sequentially and see if there is a match by monitoring the change in pH.

[2 points]

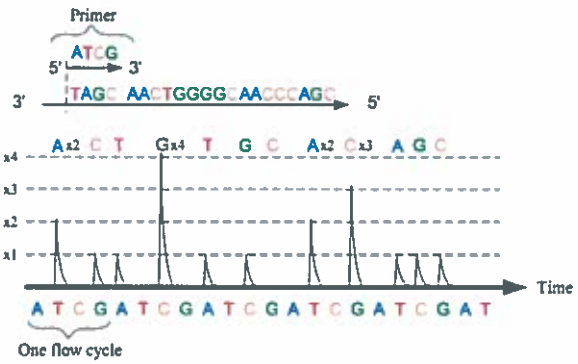


Diagram: [2 points]

[Total 4 points]

   c) **Name one sensor which is suitable for detecting DNA bases, drawing the structure of the device and listing the equations determining its operation.**

Ion-Sensitive Field Effect Transistors

- pH sensing MOS transistors.

Drain Current: $I_{DS(sat)} = \beta(V_{GS} - V_T)^2(1 + \lambda V_{DS})$

Threshold Voltage: $V_T = V_{TH(MOS)} + V_{chem}$

Chemical potential: $V_{chem} = \gamma + 2.3\alpha U_t pH$

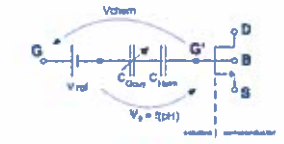
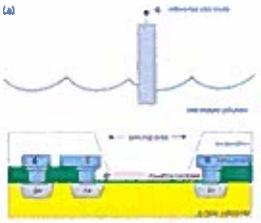
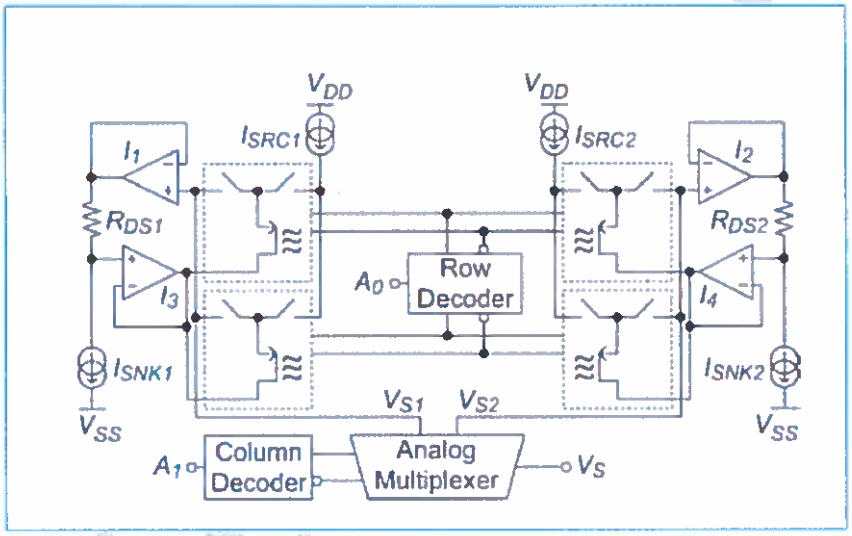


Figure 4.6: ISFET Behavioural Macromodel



[Total 4 points]

d) Draw a block level circuit schematic to show how the sensor named in part c. can be connected when scaled to millions of sensors.



[Total 5 points]

e) Explain why using this sensor has significantly reduced the cost of DNA sequencing.

ISFETs can be implemented using MOSFETs in CMOS and scaling with Moores law has allowed large scale integration to create chips with millions of sensors. We can therefore detect lot's of DNA concurrently and this has significantly reduced the cost do DNA sequencing.

[Total 3 points]