ENGINEERING TRIPOS PART IB

Example 60 minutes

Sample Questions for Paper 8, Section G

ENGINEERING FOR THE LIFE SCIENCES

*Answer not more than **two** questions.*

(Note that the actual exam paper will only have three questions to choose from.)

All questions carry the same number of marks.

*The **approximate** percentage of marks allocated to each part of a question is indicated in the right margin.*

STATIONERY REQUIREMENTS
Single-sided script paper

SPECIAL REQUIREMENTS

You may not start to read the questions printed on the subsequent pages of this question paper until instructed that you may do so by the Invigilator

1 (a) Both Optical Coherence Tomography (OCT) and Ophthalmic Ultrasound (US) are based on broadband pulses with relatively short duration. A pulse P has frequency ω_0 and a duration $2a$, defined by:

$$P = \begin{cases} (1 - \left|\frac{t}{a}\right|)\, e^{j\omega_0 t} & -a < t < a \\ 0 & \text{otherwise} \end{cases}$$

What is the bandwidth of this pulse, defined in terms of the frequency difference between the spectral nulls closest to ω_0? How does the bandwidth relate to the depth resolution of the technique? [40%]

Answer: We can calculate the bandwidth of the pulse by taking the Fourier Transform:

$$\begin{aligned}
\mathscr{F}(P) &= \int_0^a (1-\frac{t}{a}) e^{j\omega_0 t} e^{-j\omega t}\, \mathrm{d}t + \int_{-a}^0 (1+\frac{t}{a}) e^{j\omega_0 t} e^{-j\omega t}\, \mathrm{d}t \\
&= \left[\frac{1-\frac{t}{a}}{j(\omega_0-\omega)} e^{j(\omega_0-\omega)t} + \int \frac{1}{aj(\omega_0-\omega)} e^{j(\omega_0-\omega)t}\, \mathrm{d}t \right]_o^a + \Big[\ldots \Big]_{-a}^0 \\
&= \left[\frac{1-\frac{t}{a}}{j(\omega_0-\omega)} e^{j(\omega_0-\omega)t} - \frac{e^{j(\omega_0-\omega)t}}{a(\omega_0-\omega)^2} \right]_0^a + \left[\frac{1+\frac{t}{a}}{j(\omega_0-\omega)} e^{j(\omega_0-\omega)t} + \frac{e^{j(\omega_0-\omega)t}}{a(\omega_0-\omega)^2} \right]_{-a}^0 \\
&= -\frac{e^{j(\omega_0-\omega)a}}{a(\omega_o-\omega)^2} + \frac{2}{a(\omega_0-\omega)^2} - \frac{e^{-j(\omega_0-\omega)a}}{a(\omega_o-\omega)^2} \\
&= \frac{1}{a(\omega_o-\omega)^2} \left[2 - \left(e^{j(\omega_0-\omega)a} + e^{-j(\omega_0-\omega)a} \right) \right] \\
&= \frac{2}{a(\omega_o-\omega)^2} \Big(1 - \cos(\omega_0-\omega)a \Big)
\end{aligned}$$

Hence the first nulls around the centre frequency ω_0 occur at $\cos(\omega_0 - \omega)a = 1$, i.e. $(\omega_0 - \omega)a = \frac{\pi}{2}$. The bandwidth is therefore $\frac{\pi}{a}$, or in terms of frequency $\frac{1}{2a}$.

The depth resolution of the technique is given by the auto-correlation distance of the imaging pulse, which is proportional to the pulse length a. Hence the resolution is inversely proportional to the bandwidth of the pulse.

(b) To acquire three-dimensional data in either OCT or US it is necessary to gather an array of samples in three directions.

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(i) Compare and contrast the methods used to scan in each direction for OCT and US. [20%]

Answer: In OCT the lateral scanning (both x and y) is achieved by physically moving the optics, usually by use of a galvanometric mirror. The lateral sample spacing can therefore be adjusted to any level, though increasing the sample density will also increase the acquisition time. Axial (depth, or z) scanning in Time-domain OCT is achieved by moving the reference mirror, and in Spectral-domain OCT is controlled by the number and frequency spacing of the CCDs in the linear CCD array.

In Ultrasound, the lateral scanning in one dimension is usually achieved electronically, by using a different set of piezo-electric elements in the ultrasound transducer. Scanning in the other (elevational) dimension (or sometimes rotational) is achieved by physical movement of the transducer, usually with a stepper motor. Axial scanning is achieved by sampling of the ultrasound echo as it is received — the sample rate and the speed of sound in the medium determine the sample spacing.

(ii) How does *image resolution* differ from *sample spacing*? What are the typical image resolutions in each dimension for OCT and US? [20%]

Answer: Image resolution describes the extent to which a single point is blurred when it is imaged. On the other hand, sample spacing refers to the distance between individual measurements which make up an image. Although the sample spacing is often set to be a little less than the image resolution, the two are completely independent of each other.

In OCT, the lateral resolution in both dimensions is typically $15\,\mu$m (except for non-commercial systems using adaptive optics which can achieve up to $2\,\mu$m), and the axial (depth) resolution is slightly better than $5\,\mu$m. In ultrasound, the lateral resolution is very variable, but is typically 0.5 mm at best, and the elevational resolution is typically 1 mm at best. The axial (depth) resolution can be up to $200\,\mu$m, depending on frequency.

(iii) What are the issues which need to be considered when displaying a 2D slice through such 3D data? [20%]

Answer: If displaying a 2D slice through 3D data, the regular 2D array of pixels on a typical display will not coincide with the location of the samples in the 3D volume. Hence *interpolation* or *approximation* is required to find

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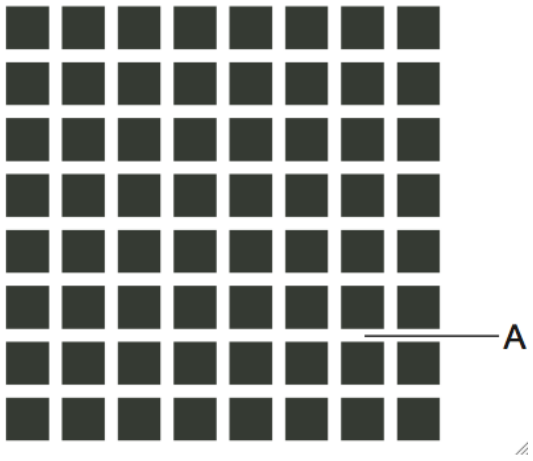
values for the sampled data at the display points. The interpolation algorithm should be chosen dependent on how we believe the real data behaves, and affects what the displated slice will look like. Some algorithms generate very smooth data and others generate discontinous data. Either approach could be correct, depending on the circumstances.

Another factor in displaying a slice through a 3D data set is the orientation of the display. Some features of OCT and ultrasound are aligned with the direction of travel of the light or the sound waves. For instance, a strong reflector of sound or light will not allow the signal to pass through to deeper tissue, and hence deeper tissue will appear very dark. Randomly orientated slices through 3D data are not aligned with the direction of travel and hence can make the appearance of such features confusing.

2 (a) Describe the receptive field properties of ganglion cells in the retina. [15%]

Answer: Ganglion cells have roughly circular receptive fields from a few minutes of arc at fovea, to few degrees at periphery. On-centre ganglion cells have a excitatory receptive field centre and inhibitory surround thereby respond optimally to differential illumination (see figure). Off-centre ganglion cells have an inhibitory receptive field centre and excitatory surround. There are also colour opponent cells which are either red-green or blue-yellow

(b) When viewing the grid below, illusory darks spots appear at the 4-way intersections of the white stripes. Based on your knowledge of a ganglion cell's receptive field explain why these spots may occur at these intersections but not on the lines at the midpoints of the squares such as location A. [15%]



Answer: Illusory grey spots are perceived at the intersections because a retinal ganglion cell receptive field lying at the intersection of the cross has more light falling on its inhibitory surround than a receptive field that lies between two black squares. Consequently, its excitatory centre is suppressed to weaker activity (see figure).

(c) Why do the illusory spots in (b) not appear on intersections that you are

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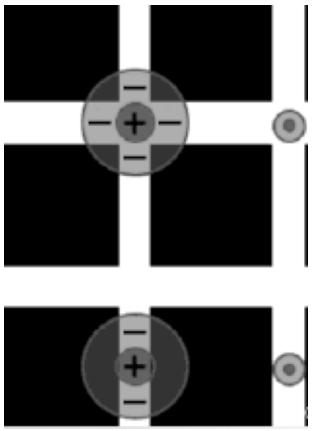

directly looking at? [10%]

Answer: The ganglion cell receptive field at the fovea is much smaller than in the periphery so when directly viewing an intersection the entire receptive field lies within the white lines thereby abolishing the illusion.

(d) The brain uses many cues to determine the distance to objects in the world. A good painter can reproduce many of them. What cues are available to determine that a painted scene does not truly have depth? [20%]

Answer: The cues that an artist can not include in a painting are

- •Accommodation cues due to the adjustment of the focal length of the lens
- •Motion parallax which is the result of changing positions of an object in space due to either the motion of the object or of the viewer's head
- •Convergence cues due to the angle made by the two viewing axes of a pair of eyes
- •Binocular disparity: the disparity between images of the same object projected onto the retinas

(e) In colour vision the visual system uses colour opponent channels of L+M+S, L-M, and S-(L+M) from the L, M and S retinal photoreceptors. Why is it thought that the visual system generates these colour opponent channels? [20%]

Answer: The spectral composition of natural objects has been studied and it has been shown that the first three Principal Components of these spectral curves are the colour opponent channels which suggest that recoding into these three opponent channels

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preserves the greatest amount of information about the spectral composition needed to distinguish between objects (or decorrelates the input).

(f) Describe behavioural and neurophysiological evidence that the visual system processes different spatially frequencies within an image independently. [20%]

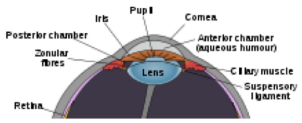
Answer: Behavioural evidence comes from a) fatigue of one spatial frequency leads to shift in perception for the population of spatial frequencies (spatial frequency aftereffect) b) detecting the difference between images depends on the difference in their components (e.g. square wave vs. sine way example) and c) the phase with which two different frequency spatial gratings are combined does not alter the threshold for their detection. Neurophysiological evidence from the cell in visual cortex that show receptive field properties which are wavelet like (sinusoid windowed by a Gaussian) of varying spatial frequencies.

3 (a) (i) Describe the anatomy and function of the lens and the cornea in the eye.

Answer: The cornea is the transparent external surface of the eye, covering the pupil (opening) and iris (coloured part). The cornea contributes the majority $(2/3)$ of the eye's focussing power but is fixed focus. The (crystalline) lens sits behind the iris and contributes the remainder $(1/3)$ of the eye's focussing power. The focal distance of the eye is altered by changing the shape of the lens via the action of the ciliary muscles.

(ii) How do cells in the lens and cornea receive nutrients?

Answer: Because both the lens and cornea need to remain optically transparent, they must not contain blood vessels. The cells in each tissue must therefore receive nutrients via diffusion. The eye secretes a clear fluid called the aqueous humour that carries nutrients throughout the eye. The cornea also receives oxygen via diffusion at the external air interface via the tear fluid.



(iii) Describe at least two ways that the eye changes with aging. Explain how these affect eye function and how these conditions are treated by eye doctors. [35%]

Answer: Cataracts are opacities of the lens which can block light and obstruct vision. Cataracts are treated by removing the lens and replacing it with a polymer artificial lens implant. This is one of the oldest medical implant sugeries still in use today. Early lenses were PMMA and rather stiff but modern lenses tend to be more flexible (and thus foldable for minimally-invasive insertion) using materials such as silicone rubber. Lenses currently in development (but not yet in general use) are "accommodating" in that they are attached to the ciliary muscles to try and restore original lens-like function.

Presbyopia is a change in the geometry and mechanical properties of the lens with aging, causing it to become less deformable and thus less responsive to actions of the ciliary muscles in adjusting eye focus. Current treatment is the use of reading glasses (including biofocals) although a variety of glasses-free alternatives are currently under development

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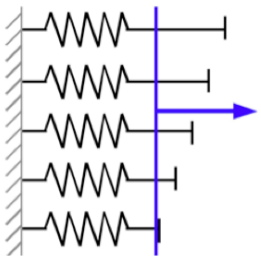
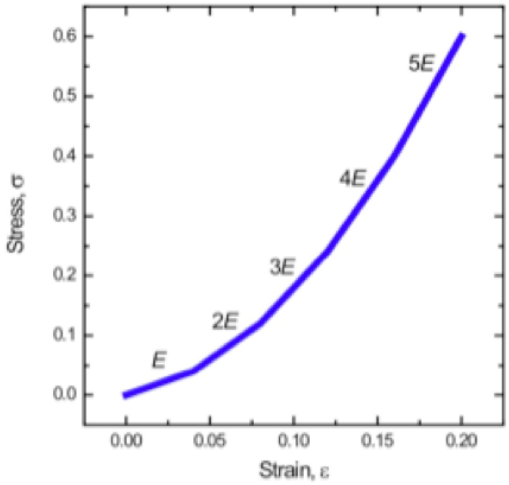
(b) (i) Given the following phenomonenological model for sequential spring recruitment, and assuming that the stiffness of each spring is E and the springs are evenly distributed in space, draw the stress-strain response for the model. Describe how this model relates to the mechanical responses observed in biological materials.



Answer: If all springs have equal stiffness and are equally spaced, they are sequentially recruited such that each time a strain increment increases by a fixed amount, the stiffness of the material increases by E. This gives rise to a stress-strain response that is approximately quadratic, i.e. $\sigma = c\varepsilon^2$ where c is a constant. This is considered a good model of collagenous soft tissues, in which it is thought that as the strain increases, more collagen fibrils are "recruited" either by re-orientation or by uncrimping of intrinsic waviness in their structure, such that with each increasing strain increment there are more parallel collagen fibrils bearing load.



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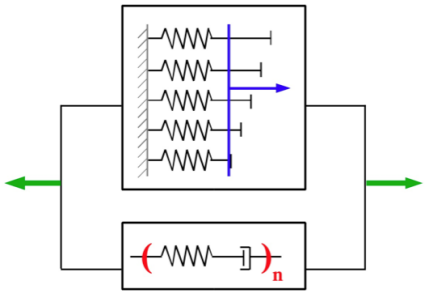
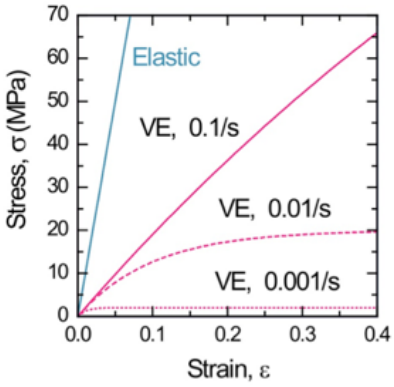
(ii) The model in (i) is now modified to add a second component, a Maxwell viscoelastic model in parallel with the original sequential recruitment model. How does this alter the stress-strain response drawn in part (i)? [45%]



Answer: When a viscoelastic element is added in parallel with the quadratic recruitment model, the stress-strain response does become strain rate dependent. However, this effect is far smaller than would be observed in the linear Maxwell model in isolation, because as the strains increase the stiffness of the quadratic elastic model starts to dominate the overall response and so the strain-rate effect is smaller than would be expected in a linearly viscoelastic material, as is shown in the following plots. Again, this is consistent with the observed responses of soft biological materials.



(c) A cornea has a thickness of 350 μm, an elastic modulus of 0.3 MPa, and an intrinsic permeability of 8.2×10^{-17} m^2. What is the time constant for pressure-induced transport through the cornea assuming the viscosity of water is 1 mPa s? [20%]

Answer: The time constant $\tau = \frac{h^2}{E\kappa}$ where $\kappa = \frac{k}{\eta}$

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h = tissue thickness
E = elastic modulus
κ = hydraulic permeability
k = instrinsic permeability
η = the viscosity of water.

Substituting and calculating gives 4.98 s, a quite physiologically reasonable result!

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4 (a) Explain with mathematical definitions what efficient encoding means for a single neuron. [20%]

Answer: Let the response properties of a neuron be characterised by $\mathrm{P}_{\mathrm{resp}}(r|s)$, giving the probability of the cell generating response r if the stimulus has value s. Let the probability distribution of the stimulus as found in the natural environment be described by the distribution $\mathrm{P}_{\mathrm{stim}}(s)$. Efficient coding is achieved by the neuron if its response distribution is such that the mutual information between its responses and the stimulus, $\mathrm{MI}(r,s) = \int_{-\infty}^{\infty}\int_{-\infty}^{\infty} \mathrm{P}(r,s) \log \frac{\mathrm{P}(r,s)}{\mathrm{P}(r)\,\mathrm{P}_{\mathrm{stim}}(s)}\, dr\, ds$ is maximised, where $\mathrm{P}(r,s) = \mathrm{P}_{\mathrm{resp}}(r|s)\,\mathrm{P}_{\mathrm{stim}}(s)$ and $\mathrm{P}(r) = \int_{-\infty}^{\infty} \mathrm{P}(r,s)\, ds$. Information maximisation can only be studied under some constraints about the response characteristics of the neuron, otherwise some degenerate response distribution (that allows arbitrarily high or low responses, or zero response variability) would be obtained as "optimal".

(b) Explain with mathematical definitions what entropy maximisation means for a single neuron and its relation to information maximisation. [20%]

Answer: Let us use the distributions $\mathrm{P}_{\mathrm{resp}}(r|s)$ and $\mathrm{P}_{\mathrm{stim}}(s)$ as defined above. Then the overall (marginal) distribution of the responses of a neuron is $\mathrm{P}(r) = \int_{-\infty}^{\infty} \mathrm{P}_{\mathrm{resp}}(r|s)\,\mathrm{P}_{\mathrm{stim}}(s)\, ds$. Entropy maximisation is achieved by the neuron if its response distribution is such that the (differential) entropy of its response distribution $\mathrm{H}(r) = -\int_{-\infty}^{\infty} \mathrm{P}(r) \log \mathrm{P}(r)\, dr$ is maximised under some constraints as for information maximisation. For example, the minimal and maximal response of the neuron or its mean response may be constrained to have some specific values. Entropy maximisation also achieves information maximisation if the conditional entropy of the responses, $\mathrm{H}(r|s) = -\int_{-\infty}^{\infty}\int_{-\infty}^{\infty} \mathrm{P}_{\mathrm{resp}}(r|s) \log \mathrm{P}_{\mathrm{resp}}(r|s)\, dr\, \mathrm{P}_{\mathrm{stim}}(s)\, ds$ is sufficiently small relative to the (unconditional) response entropy: $\mathrm{H}(r|s) \ll \mathrm{H}(r)$, because $\mathrm{MI}(r,s) = \mathrm{H}(r) - \mathrm{H}(r|s)$.

(c) In a (fictional) new species a neuronal type encodes in its firing rate the overall brightness of the visual field, characterised by a single scalar s that can take values between 0 and $s_{\max}$ (measured in some appropriate physical units). We want to test our hypothesis that this neuron achieves information maximisation (in the response entropy maximisation sense) with respect to this stimulus.

(i) We know that the relevant constraint under which the neuron has to operate is that its mean firing rate must be 10 Hz. What should the firing rate

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distribution of the neuron be according to our hypothesis? [25%]

Answer: The maximum entropy distribution for a given mean (for non-negative quantities, such as firing rates) is the exponential distribution. Thus, the firing rate distribution of the neuron should be $\mathrm{P_r}(r) = \frac{1}{10\ \mathrm{Hz}} e^{-\frac{r}{10\ \mathrm{Hz}}}$.

(ii) The overall brightness of the visual field under natural conditions is found to be distributed uniformly within its range. How should the firing rate of the neuron, r, depend on the stimulus, s, according to our hypothesis? Please choose one of the following options and explain your choice.

A. $r = 10\ \mathrm{Hz} \cdot e^{-\frac{s}{s_{\max}}}$

B. $r = \frac{1}{10}\ \mathrm{Hz} \cdot e^{-\frac{s}{s_{\max}}}$

C. $r = 10\ \mathrm{Hz} \cdot e^{\frac{s}{s_{\max}}}$

D. $r = \frac{1}{10}\ \mathrm{Hz} \cdot e^{\frac{s}{s_{\max}}}$

E. $r = 10\ \mathrm{Hz} \cdot \ln \frac{1}{1-\frac{s}{s_{\max}}}$

F. $r = \frac{1}{10}\ \mathrm{Hz} \cdot \ln \frac{1}{1-\frac{s}{s_{\max}}}$

[35%]

Answer: The correct answer is E: $r = 10\ \mathrm{Hz} \cdot \ln \frac{1}{1-\frac{s}{s_{\max}}}$. This is because the optimal tuning curve, $r(s)$, must satisfy the following condition in general: $r'(s) = \frac{\mathrm{P_{stim}}(s)}{\mathrm{P_r}(r(s))}$. In our case, $\mathrm{P_{stim}}(s) = \frac{1}{s_{\max}}$, and $\mathrm{P_r}(r) = \frac{1}{10\ \mathrm{Hz}} e^{-\frac{r}{10\ \mathrm{Hz}}}$, and so it must be true that $r'(s) = \frac{10\ \mathrm{Hz}}{s_{\max}} e^{\frac{r(s)}{10\ \mathrm{Hz}}}$. For the tuning curve in E, it is easy to see that both sides of this last constraint evaluate to $\frac{10\ \mathrm{Hz}}{s_{\max}} \cdot \frac{1}{1-\frac{s}{s_{\max}}}$, therefore this tuning curve is optimal.

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