1 (a) The following questions are about hearing.

(i) Describe the processes that allow sound to be decomposed into different frequencies in the inner ear.

Answer: Vibrations of the oval window set up travelling waves in the basilar membrane. The membranes mechanical properties change over its length from its base being narrow, thick and stiff to the apex being wide, thin and pliant. This leads to each portion of the membrane being tuned to maximally vibrate for a particular frequency of sound from high frequencies at the base (20KHz) to low frequencies at the apex (20Hz). This leads to a logarithmically spaced tonotopic map. Outer hair cells amplify the signal through their electromotile properties and the inner hair cell transduce the motion into action potentials. Each inner hair cell is tuned to respond to a particular frequency thereby reducing cross-talk and each successive hair cell differs by around 0.2% in frequency.

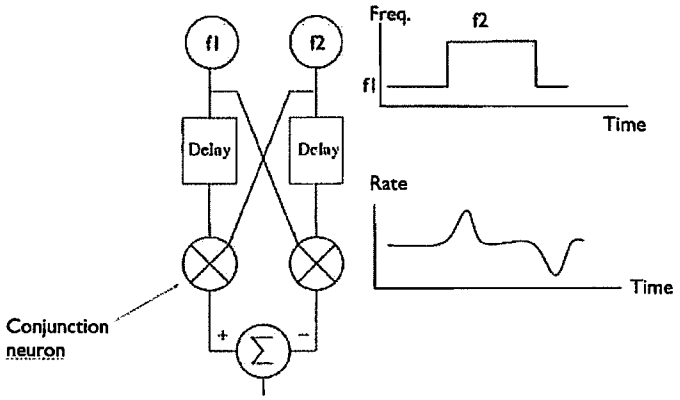
(ii) Describe the mechanisms that allow sound to be localised. Include in your description details of how these mechanisms apply to sounds of different frequencies.

Answer: There are both monaural and binaural cues. Monaural cues rely on the head related transfer function which determines the frequency dependent attenuation of sound that depend on location relative to the head. The pinna acts as a 10KHz notch filer due to reflections leading to cancellation with the prominence of the notch depending on elevation. In addition, higher frequencies are attenuated with distance so that for known spectra such as speech the frequency content is a cue to distance. Binaural cues are sound intensity differences which are best for high frequencies (>3KHz) and timing differences which are best for low frequencies (<1.5 KHz).

(iii) Describe how neurons in the auditory pathway may become tuned to particular changes in sound frequency over time such as an increase or decrease in frequency.

Answer: One possible mechanism is that neurons tuned for different frequencies are connected to conjunction neurons both directly as well as through a delay. A final comparator then leads to a system that can respond positively to an increasing stimulus and negatively to a decreasing stimulus (see figure).

(cont.



[50%]

(b) The following questions are about vision.

(i) Write brief notes on

A. Complex cells

Answer: Complex cells are found in primary visual cortex and respond to oriented lines moving in a particular direction. Their properties are thought to be created from a set of simple cells of similar orientation but spatially separated connecting to the complex cell through a set of delay lines. Complex cells do not respond to spots of lights and little to stationary stimuli. They tend to have larger receptive fields than simple cell and account for around 75% of cell in the primary visual cortex.

B. Retinotopic maps

Answer: A retinotopic map is one in which the spatial retinal topography is maintained. That is the receptive fields of adjacent cells are spatially related. Most cortical areas continue to have retinotopic maps although there is a substantial magnification of the foveal part of the map in primary visual cortex.

C. Optical imaging of the brain

Answer: In optical imaging, a voltage-sensitive dye is (usually) used on the surface of an exposed region of the brain which changes its reflectance properties with electrical activity. Using special illumination and high-speed cameras it is possible to record the activity of a population of neurons.

D. The contrast-sensitivity function

Answer: The contrast-sensitivity function relates the minimal spatial contrast of a sinusoidal pattern that can be perceived (vs. uniform grey) to the spatial frequency of the sinusoid. The function tends to peak at 4-5 cycles/degree.

(TURN OVER for continuation of Question 1

E. Physiological depth cues

Answer: There are 4 cues to depth that are physiological rather than psychological: Accommodation that adjusts the focal length of the lens, motion parallax, convergence angle of the eye and binocular disparity (useful for less than 30m)

(ii) The brain is said to code efficiently for colour. Explain what this means and the evidence that supports the statement.

Answer: The brain represents colour with regard to the natural variation of reflectance. Examination of principal components analysis of the spectral reflectance of objects suggest that the first three PCA reflect different opponency processes in terms of the [L]ong, [M]edium and [S]hort wavelength: that is L+M+S, L-M and S-(L+M). Evidence for this comes form fatigues experiments in colour space and from neuronal recording of such opponency. [50%]

2 (a) Write brief notes on:

(i) Label-line codes

Answer: The receptors and initial neural channels for the different senses are independent. Each sensory neuron responds to only one modality. We can "label" each sensory neuron ("line") by the modality it codes.

(ii) Coarse coding

Answer: Neurons have large overlapping receptive fields. Position is encoded by the ensemble activity. Can represent multiple stimuli. No need to estimate rate over a long time period. For example, humans can perform two-point discrimination of 1.4mm but the sensors' receptive fields are around 7 x 7 mm.

(iii) Tapped delay lines

Answer: Tapped delay lines can be used to detect motion (simple cells to complex cells) or to determine time delays between signals in auditory localisation.

(iv) The role of gamma efferents in spindles

Answer: The gamma efferents innervate the polar region of the spindle which are contractile. Without the gamma innervation when the muscle contracts the spindle would become unloaded and insensitive to further shortening. The active control through the gamma activation maintains the dynamic range of the receptor. This uses a combined alpha-gamma activation pattern.

(v) Reflex reversal

Answer: Different behavioural contexts can show reflex reversal and these can be learned. When standing on a platform that is translated backwards the achilles tendon is stretched leading to a reflex response that rights the subject. However, a similar stretch can be induced by tilting the platform backwards but now the response would cause greater instability and over the series of a few trials the reflex changes sign causing inhibition of muscle showing that the reflex reverses. [50%]

(b) The following questions are about the action potential.

(i) What is a reversal potential and what determines its value?

Answer: Ions are subject to two forces driving them across the cell membrane: chemical gradient and electrical gradient. There is an equilibrium potential where the two gradients balance= -75mV for K^+ (given by Nernst equation). This is the reversal potential for K^+ as perturbation of the membrane potential from this reverses the net direction of ion flux. The value depends on the permeability of the membranes to the ions and their

(TURN OVER for continuation of Question 2

concentrations intra- and extra-cellularly.

(ii) What are the roles of voltage-sensitive ion channels in the action potential?

Answer: The actual process of the action potential generation occurs in four steps, consecutive, but overlapping. These steps are all opening and/or closing of ion gates, and subsequent changes in membrane potentials.

1) The first step is the resting state, where all active ion channels are closed. Almost all voltage gated sodium and potassium gates are closed. However some potassium is leaking out via leakage channels, and even smaller amounts of sodium are diffusing in.

2a) This phase actually consists of two substeps. As the membrane is depolarised to threshold, voltage gated sodium channels begin to open. By the time threshold potential is reached, enough voltage gated sodium channels (vgsc) are opened that the potential is now self generating, being driven on by the influx of Na+. With the vast majority of the vgsc opened Na+ floods into the cell, further depolarising the cell, and increasing the membranes permeabliliy to sodium by over 1000 times. Eventually the cell lets in so many positively charged sodium ions that the membrane potential goes from -70mV to +30mV.

2b) As the membrane potential reaches 0mV, and the cell interior becomes more and more positive, sodium entry becomes less rapid, as the electrical gradient starts to repel the ions. Furthermore in less than a millisecond of reaching threshold the sodium gates begin to close, albeit slowly. This additionally causes the membrane to start to loose permeablility with regard to the sodium ions. As the net influx of sodium declines, and then finally stops, the membrane has reached its maximum depolarisation at about +30mV.

3) As the membrane potential approaches +30 mV, voltage gated potassium channels open and positively charged potassium ions begin to flow out of the cell. This begins to repolarise the cell by reducing the excess internal positive charge and moving the membrane potential closer to the resting potential. At this point the cell is basically impermeable to sodium and very permeable to potassium which rapidly flows out of the cell down both its electrical (initially) and chemical gradients.

4) Potassium efflux (exiting) continues past the resting potential of -70 mV due to the slow closing voltage gated potassium channels. This causes a hyperpolarisation known as undershoot which takes the membrane potential to around -75mV. Soon afterward the cell returns to resting potential.

(iii) Describe the factors that can increase action potential propagation velocity.

Answer: The speed of propagation depends on how quickly the voltage settles to a new level and depends on both axial resistance Ra and membrane capacitance Cm. Lowering Ra allows quick spread and lowering Cm require less charge to be deposited. Therefore, conduction can be increased by increasing axon diameter (area), or myelination. Myelination increases the membrane thickness by about hundredfold and therefore decreases the membrane capacitance. This requires less charge to be deposited for the same change

(cont.

and voltage. Therefore by covering the axon, the action potential can jump between the gaps between the myelin (the nodes). Such white-matter therefore allows for fast propagation and the channels are only present at the nodes. [50%]

3 (a) State for each of the following substances whether they are neurotransmitters produced by the brain, neurotransmitter agonists, neurotransmitter antagonists, secondary messengers, or retrograde messengers:

(i) NMDA

(ii) glutamate

(iii) serotonin

(iv) NO

(v) AP5

(vi) Ca^{2+}

(vii) dopamine

(viii) AMPA

(ix) cAMP

(x) GABA

Answer:

(i) NMDA: agonist

(ii) glutamate: neurotransmitter

(iii) serotonine: neurotransmitter

(iv) NO: retrograde messenger

(v) AP5: antagonist

(vi) Ca^{2+}: secondary messenger

(vii) dopamine: neurotransmitter

(viii) AMPA: agonist

(ix) cAMP: secondary messenger

(x) GABA: neurotransmitter

[20%]

(b) Describe the main neural pathway involved in the gill withdrawal reflex of Aplysia and the sequence of events in this pathway during a reflex response.

Answer: There are about 24 sensory neurons in the abdominal ganglion of Aplysia that innervate the siphon. When the siphon receives a tactile stimulus these neurons become activated and excite their

(cont.

postsynaptic partners, including both inhibitory and excitatory interneurons as well as motor neurons – all located in the same ganglion. There are about 6 motor neurons innervating the gill. These motoneurons receive direct monosynaptic connection from the sensory neurons as well as indirect connections (through the interneurons). The direct pathway uses glutamate as its neurotransmitter. The activated motor neurons then cause the withdrawal of the gill. [30%]

(c) Explain what changes at the cellular level underlie the following three aspects of LTP as measured in extracellular recordings:

(i) increased amplitude of the population EPSP,

Answer: The amplitudes of EPSPs in individual cells (as could be measured intracellularly) have increased, and as they add up they create a larger extracellularly measured population EPSP. [10%]

(ii) increased amplitude of the population spike,

Answer: The amplitudes of EPSPs in individual cells (as could be measured intracellularly) have increased, and so more cells reach the firing threshold and fire action potentials in response to the stimulus. Also, because latencies have decreased (see next point), the action potentials occur more synchronously which further increases the amplitude of the population spike since. [20%]

(iii) decreased latency of the population spike.

Answer: The amplitudes of EPSPs in individual cells (as could be measured intracellularly) have increased, but this means that their initial slopes have also increased proportionally. Thus cells that for which the amplitude of EPSP exceeds the firing threshold will also reach the threshold earlier. [20%]

4 (a) Explain how the NMDA receptor acts as a coincidence detector. Include in your explanation which cellular-molecular events need to coincide for detection, and how detection of coincidence is signalled by the NMDA receptor?

Answer: The opening of the NMDA receptor requires the coincidence of two events: glutamate (or an agonist thereof) needs to bind to it on the extracellular side, and the membrane in which it is embedded needs to become depolarised sufficiently such that the Mg^{2+} ion blocking it is removed. The receptor signals the detection of these two events by opening and thus becoming permeable for several ions, most importantly for Ca^{2+} ions which then flow into the cell and act as second messengers there. [30%]

(b) Describe the differences between associative and non-associative forms of learning in Aplysia at the level of behaviour.

Answer: Associative learning requires two different stimuli to be presented simultaneously, or in close temporal contiguity, during training, and the result (eg. enhanced responding) will be specific to the (conditioned) stimulus used during training. Non-associative forms of learning do not require two different stimuli (as in habituation) or don't require the two kinds of stimuli to be presented simultaneously (as in sensitisation) during training, and the effects will not be specific to the stimuli used during training. [20%]

(c) Describe three different experimental conditions in which it can be shown that the activity of dopaminergic cells is consistent with a temporal difference error signal.

Answer: In a classical conditioning experiment:

(i) before training, dopaminergic activity increases for some time after the presentation of the US, but not at the time of the CS;

(ii) after training, dopaminergic activity increases for some time after the presentation of the CS, but not at the time of the US when it is delivered;

(iii) after training, dopaminergic activity decreases for some time after the time when the US ought to be presented when in fact it was omitted despite the CS having been presented earlier in the trial.

[30%]

(d) Describe what is the standard consolidation theory, and how experiments with hippocampal lesions support it?

Answer: Standard consolidation theory (SCT) states that declarative memories are first stored in the hippocampus and over the course of hours, days, or even weeks (depending on the species) they become gradually independent of the hippocampus and presumably supported by the neocortex. Experiments supporting SCT test the retrieval of memories at different delays with and without hippocampal lesions preceding the test and lead to the following results. In control animals, (without hippocampal lesions)

(cont.

performance is high when tested soon after acquisition, and gradually declines with longer delays before retrieval is tested. In animals with hippocampal lesions, performance is negligible when lesioned and then tested soon after acquisition, but it gradually increases as the delay between acquisition and lesioning (and hence testing) is increased, reaching the performance levels of control animals (as appropriate for long delays). [20%]

END OF PAPER