ENGINEERING TRIPOS PART IIA

Wednesday, 9th May 2012 2.30 to 4pm

Module 3G3 **Answer**: CRIB

INTRODUCTION TO NEUROSCIENCE

*Answer not more than **three** questions.*

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
There are no attachments

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

Version: Final

1 (a) The following questions are about hearing.

(i) Describe the mechanisms by which different frequencies of sound can be localised.

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).

(ii) Describe the mechanical and neural mechanisms by which each neuron in the cochlear nerve becomes selective for a particular frequency of sound. [50%]

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 electomotile 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.

(b) The following questions are about multisensory integration.

(i) In the presence of a visual and an auditory stimulus, what features of these stimuli determine the degree of enhancement (facilitation) seen in superior colliculus?

Answer: Enhancement is related to three features own the stimuli. First, the two stimuli must be co-localised in space. Second, they must occur synchronously for maximum enhancement - which decreases as the temporal offset between the stimuli increase. Finally, the enhancement show inverse

effectivenesss with greater enhancement seems for weaker stimuli.

(ii) You can see the width of an object and also feel its width using touch. When generating a single estimate of the object's width, describe the computations the brain performs and the rationale behind them. [50%]

Answer: The estimate is a weighted average of the visual and haptic estimates $\hat{x} = wx_v + (1-w)x_h$ with the weighting depending on the noise variances in the two sources, that is $w = \sigma_h^2/(\sigma_v^2 + \sigma_h^2)$. Therefore, the brain needs estimates of the sensory variance in the two modalities, needs to calculate the weighting w and apply this to the final estimate. The advantage of this procedure is that it results in the most accurate estimate that is the minimum variance estimate (assuming the sensors are unbiased).

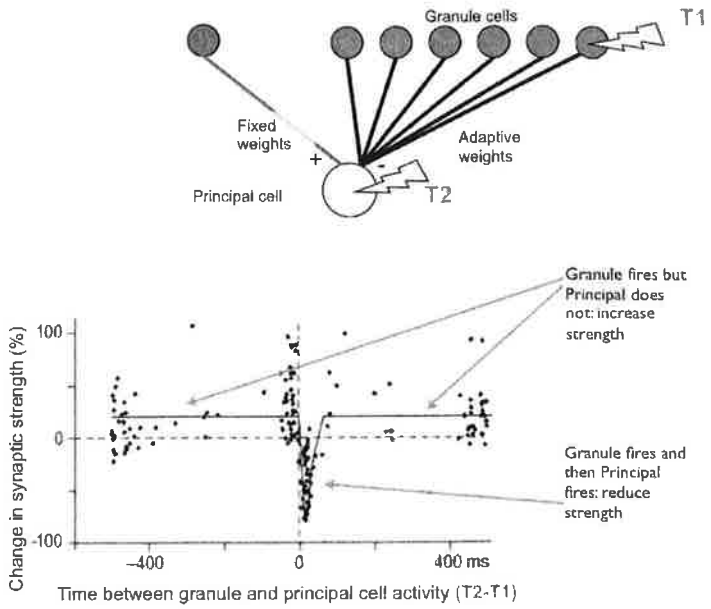
2 (a) With regard to synaptic learning:

(i) Describe what is meant by anti-hebbian learning.

Answer: Anti-Hebbian learning describes a particular class of learning rule by which synaptic plasticity can be controlled. These rules are based on a reversal of Hebb's postulate, and therefore can be understood as dictating reduction of the strength of synaptic connectivity between neurons following a scenario in which a neuron directly contributes to production of an action potential in another neuron. Often the synapse strengthens slightly if the action potential at a synapse does not cause an action potential post-synaptically.

(ii) Describe (including a diagram) the circuit and mechanism of learning in the cerebellar-like structure of the weakly electric fish.

Answer:



Research on the weakly electric fish has demonstrated that the electrosensory lateral-line lobe (ELL) receives sensory input from electroreceptive sensory organs which utilize a self-generated electrical discharge (called an EOD; electric organ discharge) to extract information

from the environment about objects in close proximity to the fish. The cerebellar-like structure is responsible for filtering the input to remove predictable components of the input. The principal cells receive input from both the sensory surface (fixed input) and from the granule cells (from all sensory modalities and efference copy). The synaptic weight between the granule and principal cells undergoes anti-hebbian modification. Therefore if the Granule fires but Principal does not the synapse will slowly increase strength whereas if Granule fires and then Principal fires the synapse will reduce strength (see figure).

(iii) What are the benefits of anti-hebbian learning for sensory processing in the weakly electric fish and what behavioural evidence is there that humans process sensory information in a similar manner? [40%]

Answer: By predictively cancelling the expected sensory feedback the fish can be attuned to unexpected sensory inputs in the environment such as predators or prey. Sensory cancellation is also seen in humans such as in our inability to tickle ourselves and our underestimation of self-produced forces.

(b) A person plans a movement so as to use a knife to cut an apple in half.

(i) What roles might forward (predictive) models play during the movement?

Answer: Forward models can be used to anticipate the consequences of the motor command so that the control system uses the predictive signal rather than wait for the delayed feedback (or combine the two for accurate state estimations). In addition the predictions can be used for sensory cancellation so as to be more attuned to unexpected sensory events.

(ii) Why is redundancy of the human arm beneficial for improving the accuracy of such movements?

Answer: Redundancy allows for different movement to be chosen so as to minimise the negative effects of signal dependent noise. In additions by altering the configuration of the arm stiffness can be controlled for the task.

(iii) How, and why, might stiffness of the arm be different in this task and in cutting a loaf of bread? [40%]

Answer: The stiffness is likely to increase perpendicular to the knife

for the apple but not the bread. This is because the apple-knife interface is unstable in this direction and increasing stiffness can increase stability. In the bread condition the interface is stable and stiffness can be reduced.

(c) What features of the auditory and motor systems make cochlear implants currently more successful than brain driven neuromotor prostheses? [20%]

Answer: The auditory system has a very clear representation that is a line ton topic map that allows the electrodes to directly stimulate the appropriate inner hair cells. In motor cortex the coding is not well understood and the requirement to map the output ono a multidimensional output divide such as a robotic interface adds further complexity.

3 (a) This question is about GABAergic transmission.

(i) Some GABA receptors (so-called GABA-A receptors) act by directly opening a chloride channel. Explain how the release of GABA by a presynaptic cell influences the membrane potential of the postsynaptic cell through these receptors. [10%]

Answer: Cl^- is a negatively charged ion and its concentration is much higher outside the cell than inside it. Therefore when the Cl^- channel of the GABA-A receptor opens Cl^- enters the cell hyperpolarising it. As a consequence, GABA release of a presynaptic cell hyperpolarises (decreases the membrane potential of) the postsynaptic cell.

(ii) The gradient of chloride in certain neurons during development (when the nervous system is not yet mature) is opposite to that in normal, mature neurons. Explain the postsynaptic effect of GABAergic transmission in these neurons during development. [5%]

Answer: In these neurons, the Cl^- concentration is higher inside the cell than outside. Therefore when the Cl^- channel of the GABA-A receptor opens Cl^- leaves the cell depolarising it. As a consequence, GABA release of a presynaptic cell depolarises (increases the membrane potential of) the postsynaptic cell.

(iii) There are also metabotropic GABA receptors (so-called GABA-B receptors) that result in the opening of potassium channels via a G-protein-mediated cascade. Describe how the postsynaptic effect of GABA-B receptors are similar to or differ from those of GABA-A receptors. [10%]

Answer: K^+ is a positively charged ion and its concentration is much higher inside the cell than outside. Therefore when the K^+ channel of the GABA-B receptor opens K^+ leaves the cell hyperpolarising it. As a consequence, GABA release of a presynaptic cell also hyperpolarises (decreases the membrane potential of) the postsynaptic cell through GABA-B receptors, as through GABA-A receptors, but here this effect is mediated by K^+ rather than Cl^- ions. Since GABA-A receptors are ionotropic (because they directly open an ion channel) while GABA-B receptors are metabotropic, another difference is that the effects of GABA-B receptors will appear (and vanish) much more slowly.

(iv) In some cells, the reversal potential of chloride is above the resting

membrane potential, but only by a few millivolts. However, the activation of GABA-A receptors is said to inhibit the cell in the following sense: when these receptors are activated at the same time as the glutamate receptors (by a different set of presynaptic cells), the firing rate of the postsynaptic neuron is lower than if only the glutamate receptors were activated. Explain how this is possible. [40%]

Answer: Glutamate receptors depolarise the cell. If this depolarisation is large enough the membrane potential of the postsynaptic cell exceeds the threshold for action potential generation and it will start generating action potentials. However, when GABA-A receptors open, the membrane potential will be drawn towards their reversal potential. Even though this reversal potential is above the resting membrane potential, it is still below the threshold potential at or above which the cell is when it is stimulated through glutamate receptors. Thus, under these circumstances the activation of GABA-A receptor decreases pushes the membrane towards more negative values thereby decreasing its firing rate.

(b) The following questions are about the gill-withdrawal reflex in the Aplysia.

(i) Describe the experimental procedure for sensitising the gill-withdrawal reflex in the Aplysia.

(ii) A sensitisation experiment is performed. State how each of the following quantities change in response to stimulating the siphon before and after sensitisation (i.e. do they increase, decrease or stay the same after sensitisation):

A. number of action potentials emitted by sensory neurons that respond to siphon touch

B. magnitude of potassium current in the synaptic terminal of these sensory neurons

C. amount of calcium influx into synaptic terminal of the sensory neurons

D. amount of transmitter released by the sensory neurons

E. amount of transmitter released by the motor neurons responsible for gill withdrawal [35%]

Answer: Sensitisation can be achieved by repeatedly presenting the animal with a noxious stimulus (eg. by delivering a weak electric shock to the tail) – without pairing it with an otherwise harmless stimulus (eg. touching the siphon). As a result, the response to the otherwise harmless stimuli will also be amplified. In response to stimulating the siphon over the course of sensitisation:

(i) number of action potentials emitted by sensory neurons: does not change

(ii) magnitude of potassium current in the synaptic terminals of sensory neuron: decreases

(iii) amount of calcium influx into synaptic terminals of sensory neuron: increases

(iv) amount of transmitter released by sensory neuron: increases

(v) amount of transmitter released by motor neuron: increases

4 (a) An in vivo experiment found that the size of (field) EPSPs in CA1, in response to Schäffer collateral stimulation, was larger after a session of active exploration of the environment than before it. The conclusion drawn from this study was that exploration induces LTP. Give an alternative explanation of the findings, and describe control experiments in which one could show that exploration itself is neither necessary nor sufficient for increasing the size of EPSPs. [40%]

Answer: These findings could also be explained by active exploration raising the temperature of the animals (including its brain) thus leading to larger EPSPs without actual synaptic plasticity. In a control experiment animals could be gently heated up while they are still (not exploring) and show that EPSPs are increased after this – thus demonstrating that exploration is not necessary for larger EPSPs. Another control experiment could keep animals' head at a fixed temperature while they are exploring the environment and show that in this case there is no change in the size of EPSPs – thus demonstrating that exploration is not sufficient for larger EPSPs

(b) Describe the main differences between the Rescorla-Wagner and temporal-difference theories of classical conditioning. In your answer address the following points:

(i) In these theories, how do the different key quantities (CS, US, predictions, prediction weights and errors) depend on time?

Answer: The Rescorla-Wagner theory (RW) only considers time in terms of subsequent trials while the temporal-difference theory (TD) also considers within-trial time. As a consequence, in RW there is a single value for the level of each CS and the amount of the US in a trial, while in TD all these quantities vary as functions of (discrete) time within a trial. As a further consequence, the predictions (ie. responses) of the animal and thus prediction weights and prediction errors are also quantified by a single scalar per trial (and per stimulus for weights) in RW, but as time-varying functions within a trial in TD.

(ii) What are the quantities that animals are trying to predict according to these theories?

Answer: In RW, the quantity predicted by the animal is the amount of US appearing at the end of the trial, in TD it is the total (cumulative) amount of US appearing from a given time point until the end of the trial.

(iii) Which theory involves an element of bootstrapping, what kind of bootstrapping is it, and why is it necessary in the theory?

Answer: In TD, predictions of this total amount of US need to be made at every time point within the trial, while the true total amount of US can only be known at the end of the trial. Thus, the exact prediction error (truth minus prediction) would also only be known at the end of the trial and could not be made at the same time when the prediction is made (time points within the trial). To circumvent this, the true total amount of US is approximated at any given time within the trial by the amount of US in the next time step plus the prediction of the total US in that time step. This approximate total US is then used to compute the prediction error at that time which is then used to change the corresponding prediction weights such that in the next trial the predictions are improved. Thus, an estimate (the prediction of total US at time t in the trial) is improved by using another estimate (the prediction of total US at time $t+1$ in the trial) – this is bootstrapping. In RW, there is no need for such bootstrapping, because predictions only need to be done once per trial and after each prediction the corresponding true value is discovered.

(iv) What are the predictions these theories make about what happens in

secondary conditioning? [60%]

Answer: RW incorrectly predicts that the secondary CS becomes a conditioned inhibitor and thus there would be no response when it is presented alone. TD predicts the secondary CS becomes to predict the primary CS and thereby the arrival of the US and thus that there will be a response when it is presented alone.

END OF PAPER