Version HS/2

EGT3
ENGINEERING TRIPOS PART IIA - CRIB

Tuesday, 29th April 2014 14.00-15.30

Module 3G3

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.*

*Write your candidate number **not** your name on the cover sheet.*

STATIONERY REQUIREMENTS
Single-sided script paper

SPECIAL REQUIREMENTS TO BE SUPPLIED FOR THIS EXAM
CUED approved calculator allowed

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

1 (a) Write short notes:

(i) on the advantages and disadvantages of local and intensity coding schemes for location; [15%]

Answer: Local coding schemes make the discrimination of stimuli easy, but require a large number of neurons, particularly when the dimension of the coded location is large (combinatorial explosion). Intensity coding schemes require few neurons to encode location, but are more sensitive to noise and make it hard to represent multiple stimuli.

(ii) on behavioural evidence for multisensory integration; [15%]

Answer: When animals are trained to localize low-intensity auditory and visual stimuli, the combination of the two stimuli evokes more correct responses than the sum of the correct responses for the individual stimuli. This cannot be explained by a model in which the two modalities are processed independently.

(iii) comparing the attentional pop-out effect and serial visual search. [15%]

Answer: The attentional pop-out effect arises when a target object differs from surrounding distractors in a single elementary visual feature such as color, orientation or illumination. The time it takes to detect the target is then independent of the number of distractors it is surrounded by. When the target is different from the distractors in more than one of those features (or does not pop out for some other reason), subjects fall back on a serial search strategy. The time to find the target then increases with the number of distractors the target object is surrounded by.

(b) Explain the structure and function of the middle ear, illustrating your answer with a diagram. What properties of the middle ear might explain why people find that their own recorded voice sounds strange? [25%]

Answer: The middle ear lies between the eardrum (also called the tympanic membane) and the oval window. It contains three small bones (the malleus, incus and stapes) known as the ossicles.
The purpose of the middle ear is to transmit sounds arriving at the eardrum to the cochlea through the oval window. This involves impedence matching since air has a low acoustic impedence whereas the fluid filled cochlea has a high acoustic impedence. The middle ear achieves this by collecting sounds over the relatively large area of the eardrum and focussing them onto the much smaller area of the stapes footplate which is about twenty times smaller. The ossicles provide some additional amplification (roughly 1.3 times) much like a system of levers, but their main purpose is to allow regulation of the mechanical coupling. For example, when a tiny muscle called the stapedius contracts, this reduces the motion of the stapes thereby protecting the delicate structures of the inner ear from loud noises. This muscle is controlled by an unconscious reflex triggered by continuous loud sounds.

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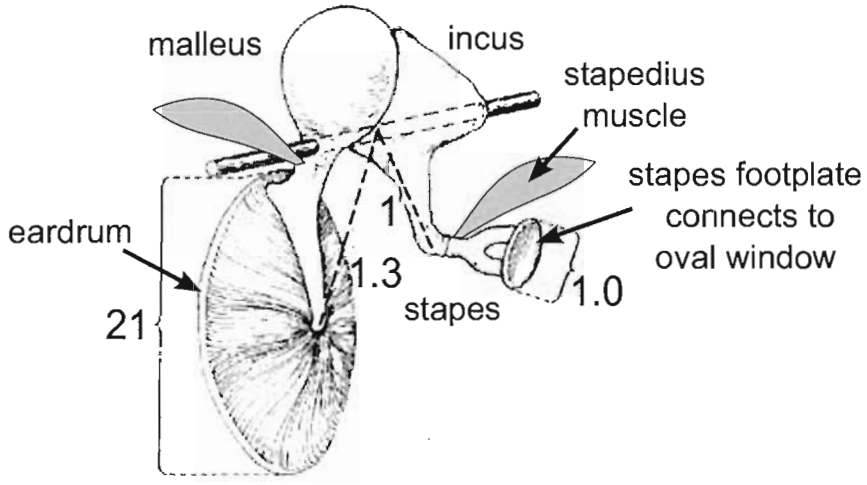
The stapedius reflex affects frequencies differentially and is engaged automatically when a person speaks. It may therefore help explain why people find that their own recorded voice sounds strange and unfamiliar.



(c) In comparison to normal hearing, electrical hearing using cochlear implants is limited in terms of the range of frequencies that can be heard, the frequency resolution, and pitch discrimination. Using your knowledge of cochlear implants, explain the nature and origin of these limitations. [30%]

Answer:

- Frequency range: Due to anatomical constraints, electrode implantation is normally only possible over the first turn of the cochlea (roughly limited to 1.5kHz-20kHz). This means that cochlear implant listeners have little or no low frequency hearing (10Hz-1.5kHz).
- Frequency resolution: Electrode arrays usually contain about 20 electrodes and the electrical stimulation spreads sideways further reducing frequency resolution to about 10 independent channels. This is a poor replacement for 3000 inner hair cells in a healthy human cochlea.
- Pitch discrimination: The limited frequency resolution of cochlear implants reduces spectral cues for pitch. In normal hearing, temporal fine structure cues arising from phase locking also contribute. However, the electrical stimulation employed in cochlear implants uses a constant pulse rate in each channel which does not preserve these cues. Consequently pitch discrimination by implantees is very poor, often failing to distinguish pitches which differ by half an octave or more.

2 (a) This question is about perceptual decision making.

(i) Describe the drift-diffusion model for perceptual decision making. [20%]

Answer: The drift-diffusion model assumes that decisions in a two-alternative forced choice task are

made when a decision variable reaches one of two decision bounds. During the trial, the decision variable performs a biased random walk. The bias, also called the "drift", scales with the strength of the stimulus (for random dot kinematograms, this is the coherence of the pattern) and controls how often and how quickly the decision variable reaches either of the decision bounds. The noise in the random walk accounts for variability in the reaction times. The model aims at reproducing the probabilities of the subject's choices as well as the distribution of reaction times.

(ii) Describe two properties of neuronal responses in the lateral intraparietal area of macaque monkeys that support their interpretation as neural correlates of the decision variable in the drift-diffusion model. [20%]

Answer: While the monkey is viewing random dot kinematograms, some neurons in the lateral intraparietal area increase their firing rate with a rate that increases with the coherence of the random dot kinematogram, similar to the decision variable in the drift-diffusion model (property 1). When the time courses of the firing rate for different coherences are temporally aligned to the time of the behavioural response, all firing rate curves increase up to a similar firing rate, suggesting that a decision is made when the firing rate reaches a "decision bound" (property 2).

(b) This question is about the neuronal resting potential and action potential generation.

(i) Explain how the permeability of the cell membrane for sodium and potassium ions affects A) the reversal potentials for these ions and B) the resting potential of the cell. [20%]

Answer: The reversal potential for a specific ion is determined by the equilibrium of the osmotic and the electric flux of the given ion across the membrane. Because both fluxes are proportional to the membrane permeability, the reversal potentials for sodium and potassium are independent of the respective membrane permeabilities. The resting potential is determined by an equilibrium of different currents (e.g., sodium and potassium currents), which scale with the respective permeabilities. Therefore, the resting potential is determined by the relative degree of permeability for sodium and potassium.

(ii) Hyperkalemia is a serious and potentially lethal medical condition in which the extracellular concentration of potassium ions is pathologically increased. Explain what happens to the neuronal resting potential in response to rising extracellular potassium concentration. [15%]

Answer: An increase in the extracellular concentration of potassium decreases the concentration difference between the intra- and extracellular space. Therefore, the reversal potential of potassium increases (becomes less hyperpolarized) and with it the resting potential of the cell.

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(iii) During the development of hyperkalemia, the extracellular potassium concentration rises relatively slowly (compared to neuronal time scales) over a course of minutes or hours. Explain the effects such a slow rise in extracellular potassium concentration has on voltage-gated sodium and potassium channels and how it affects the generation of action potentials. [25%]

Answer: Let us think of the resulting gradual increase in resting potential as a sequence of small membrane potential increases. Each of these steps slightly increases the number of open sodium channels, which quickly inactivate. The number of sodium channels that can be opened therefore gradually decreases with increasing extracellular potassium concentrations. Because potassium channels do not inactivate, the number of open potassium channels gradually increases. The cell is therefore slowly driven into a state that resembles that during the refractory period, with many inactivated sodium channels and many open potassium channels. It therefore becomes increasingly difficult to trigger action potentials.

3 This question is about the properties of synaptic transmission in four different synapse types:

type 1 – the presynaptic cell is excitatory and the postsynaptic cell is excitatory;
type 2 – the presynaptic cell is excitatory and the postsynaptic cell is inhibitory;
type 3 – the presynaptic cell is inhibitory and the postsynaptic cell is excitatory;
type 4 – the presynaptic cell is inhibitory and the postsynaptic cell is inhibitory.

(a) Describe the sequence of cellular-molecular events during synaptic transmission for each of the above synapse types. For each type, include in your answer the name of a relevant neurotransmitter. [40%]

Answer:

In all types: the presynaptic action potential travels down the axon of the presynaptic cell and arrives at the presynaptic terminal, the presynaptic membrane becomes depolarised, voltage gated Ca^{2+}-channels open, Ca^{2+} influx to the presynaptic cell, presynaptic vesicles fuse with the presynaptic membrane and release their neurotransmitter content, neurotransmitter molecules diffuse across the synaptic cleft and bind to receptors in the postsynaptic membrane. As a result of transmitter-receptor binding, ion channels will open in the postsynaptic membrane. (When the receptor is ionotropic, the ion channel is the same molecule as the receptor itself; when the receptor is metabotropic, the ion channel is a different molecule that is opened through a cascade of reactions initiated by the receptor.) The different cases differ in the kind of ions that enter or leave the postsynaptic cell through the channel opened by transmitter-receptor binding:

In types 1 and 2, the ions have a reversal (or Nernst-)potential above the resting membrane potential, such as Na^+ or Ca^{2+}. As a result, either positive ions enter the postsynaptic cell or negative ions leave it, so that it becomes more positively charged, i.e. depolarised, resulting in an excitatory postsynaptic potential (EPSP). The neurotransmitter could be glutamate.
In types 3 and 4, the ions have a reversal (or Nernst-)potential below the resting membrane potential, such as K^+ or Cl^-. As a result, either negative ions enter the postsynaptic cell or positive ions leave it, so that it becomes more negatively charged, i.e. hyperpolarised, resulting in an inhibitory postsynaptic potential (IPSP). The neurotransmitter could be GABA.
Note that the valence of the ion to which the ion channel is permissive does not determine alone whether an EPSP or IPSP occurs, because its reversal potential also plays a role, and also that only the type of the presynaptic cell matters in determining the course of events during synaptic transmission, i.e. types 1 and 2 are equivalent for the purposes of this question, as are types 3 and 4.

(b) In which of the above synapse types can AP5 have an affect on synaptic transmission? For those in which it can, explain under what conditions and how it alters A) the sequence of cellular-molecular events described in (a) and B) the shape of the postsynaptic response. [40%]

Answer:

AP5 is an antagonist of the NMDA receptor, of which the natural ligand is glutamate. It can only have an effect on excitatory synaptic transmission, i.e. in types 1 and 2 (and it will have no effect in types 3 and 4). In these cases, it will have an effect if transmission is glutamatergic, i.e. the transmitter is glutamate, the postsynaptic cell has NMDA receptors, and these receptors significantly contribute to the postsynaptic response under normal conditions. For this latter condition it is necessary that the postsynaptic cell is sufficiently depolarised at the time of presynaptic activation, either because it also has a large number of AMPA receptors that also bind glutamate and have a depolarising effect, or because other sources of depolarisation (other presynaptic cells firing, or the experimenter injecting current) act at the same time. The effect of AP5 under this conditions will be blocking the NMDA receptors so that they don't open, thus reducing the amount of positive current entering the postsynaptic cell, i.e. abolishing the NMDA component of the EPSP, thereby decreasing its magnitude and also its duration, as the NMDA component is slower than the AMPA component. The most important effect is that less (or no) Ca^{2+} enters the postsynaptic cell, which prevents the initiation of synaptic plasticity which otherwise might occur.

(c) For each of the above synapse types, give an example in the gill withdrawal reflex pathway of the Aplysia, or state if there are no examples for it in this pathway. For each example synapse you provide, describe how its strength changes in habituation. [20%]

Answer:

type 1: sensory neuron→motor neuron synapse, becomes weaker in habituation

type 2: sensory neuron→inhibitory interneuron synapse, becomes weaker in habituation

type 3: inhibitory interneuron→motor neuron synapse, becomes weaker in habituation

type 4: no example

4 (a) Describe how the Morris water maze is used to study spatial memory. In your answer include a description of the basic experimental setup, the behavioural measures that are used to quantify learning, and also the procedures by which one can ensure that behaviour is not based on navigational strategies that are independent of spatial memory. [30%]

Answer:

The Morris water maze is a tank (~1 m diameter) filled with water and with walls that don't have any obvious visual cues around them. In each trial, the animal is placed at the periphery of the tank, and needs to swim until it finds a small (~ 10 cm diameter) platform on which it can stand. Rats will prefer standing on the platform to swimming so they will be naturally motivated to find the platform as fast as they can. The location of the platform remains fixed over several trials so that the animal has a chance of learning this location over repeated exposure to the task. Learning can be quantified using a variety of measures, such as escape latency (the time it takes the animal to find the platform), path length (total distance travelled until finding the platform), or in an 'extinction' setting (i.e. using catch trials when the platform is not actually available) time spent (searching the platform) in goal area or goal quadrant of the maze (relative to time spent in other areas / quadrants of the maze). The following procedures are important for a well controlled experiment. The rat needs to be started from a random position around the periphery of the maze in each trial to make sure that it does not employ a simple route-following strategy – i.e. it doesn't just remember when to turn left or right. The platform must be invisible slightly submerging it under water level, and making the water opaque (e.g. with milk) to ensure that the rat cannot simply look and see where it needs to go but must use its spatial memory to remember the location of the platform.

(b) This question is about reward learning in stochastic, non-stationary environments, i.e., environments in which rewards are stochastic and their probabilities may change over time. Each experiment described below uses a novel conditioned stimulus (CS). All experiments start with 10 baseline trials, in which no CS or reward (US) is given, followed by 100 conditioning trials in all of which the CS is given. The experiments differ in the way the US is delivered in the 100 conditioning trials.

Experiment 1: US is delivered in all of the 100 conditioning trials.
Experiment 2: US is delivered in a random 50% of the 100 conditioning trials.
Experiment 3: US is delivered in all of trials 11-35 and 61-85, but not in trials 36-60 and 86-110.
Experiment 4: US is delivered in a random 75% of trials 11-60, and a random 25% of trials 61-110.

(i) In each experiment, plot the response and the *squared* prediction error as computed by the Rescorla-Wagner rule for two cases: when the learning speed is high (~0.9), and when the learning speed is low (~0.05). (Note that it is the

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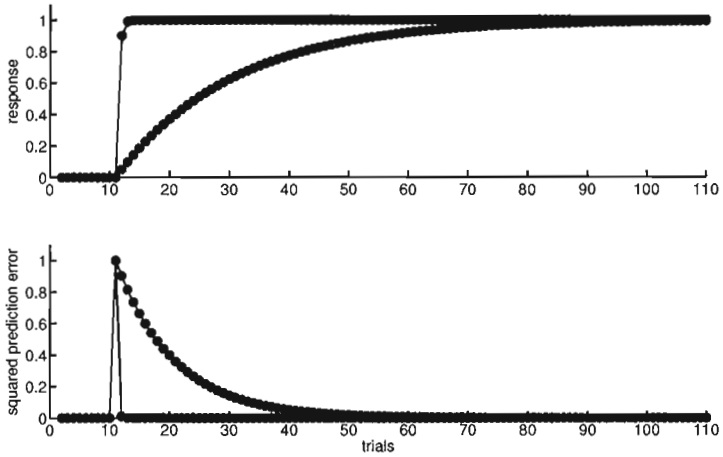
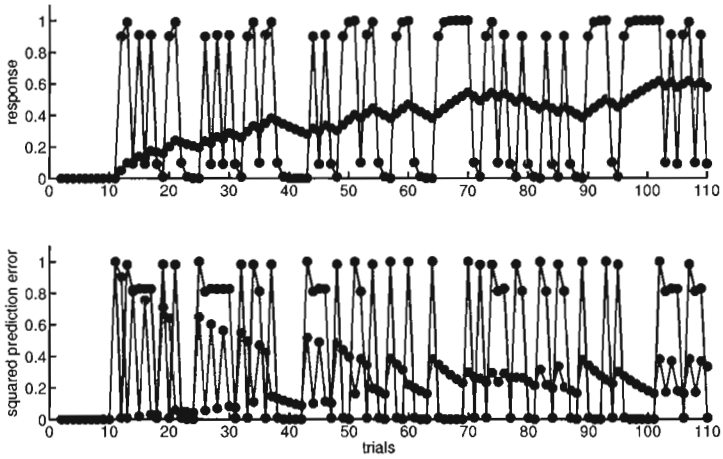
squared, not the signed prediction error that needs to be plotted.) [40%]

Answer:

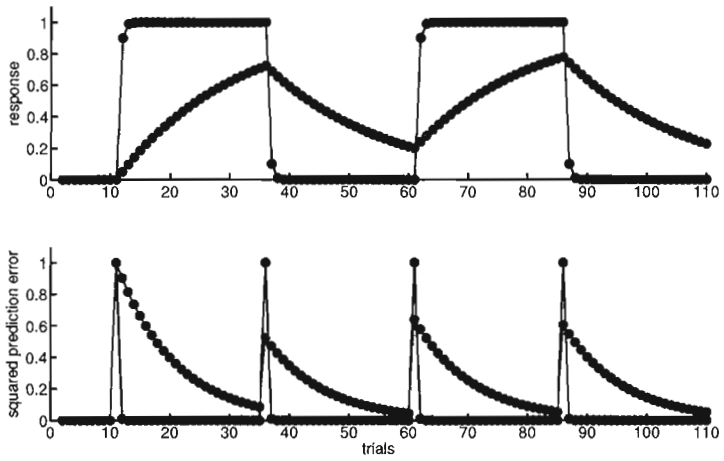
Experiment 1:



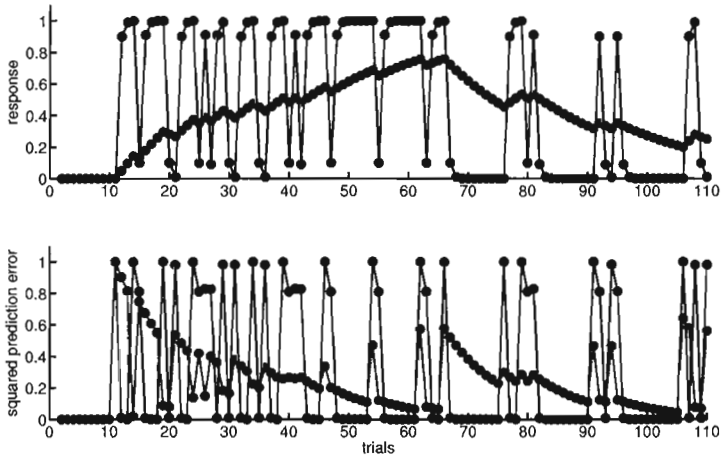
Experiment 2:



Experiment 3:



Experiment 4:



On all plots, black is for high, grey is for low learning speed.

(ii) Describe the role of the *squared* prediction error in the Rescorla-Wagner learning theory. [10%]

Answer:

The squared prediction error is central to the Rescorla-Wagner learning theory because that is the quantity that the theory assumes animals are trying to minimise over trials, and indeed the Rescorla-Wagner rule is derived as performing stochastic gradient descent on this quantity, i.e. it is guaranteed to minimise it (at least on average).

(iii) Different environments can vary in their stochasticity (i.e., how stochastically rewards are given), and their non-stationarity (i.e., how often reward probabilities change). Explain with reasons how these two factors influence whether a high or a low learning speed is more advantageous.

[20%]

Answer:

Fast learning (high learning speed) makes the response on a trial be very close to the reward on the previous trial. This means it makes the response either 0 or 1, and also that it tracks changes in the reward very rapidly. Slow learning (low learning speed) makes the response hover around the average reward experienced over a number of previous trials. This means that it makes the response graded, and tracking changes in reward more slowly. Therefore, fast learning will be more advantageous for rapidly changing deterministic environments, whereas slow learning will be advantageous for more stationary, and more stochastic environments.

END OF PAPER

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