Neurobiology and Human/Animal Behaviour
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problem set #1 solutions

QUESTIONS FROM LECTURE #1

1. (a) pros-, (the first), mes- (the middle), rhomb- (diamond-shaped)
(b) tel- di- mes- met- myel

2. The notochord, derived from mesoderm, signals the overlying ectoderm to begin the process of neurulation, whereby the ectoderm becomes neuroectoderm.

3. The cephalic flexure brings the prosencephalon downwards so that it abuts the developing hindbrain. This geometry allows the oculomotor nerves to find the developing eyes.

4. The embryonic rhombencepholon is subdivided into several rhombomeres. The particular rhombomeric fates of cells are determined by levels of FGF-8 ('FGF' standing for 'fibroblast growth factor') and other transcription factors.

QUESTIONS FROM LECTURE #2

1. Though it may seem counterintuitive that the compartment with *more* of a positive ion has the more negative potential, one has to consider what's keeping these positive ions where they are. Two opposing gradients are at work. The concentration gradient impels these ions to move across the membrane in order to equalise their concentrations on either side (and therefore to maximise entropy). If the system is at equilibrium and the ions are *not* moving along their concentration gradient, then it must be the case that the electrochemical gradient is exactly opposing the concentration gradient and thereby making the net ion current zero. In order for this to happen, the side of the membrane that has more of these positive ions must be electrically negative relative to the other side. In terms of physical chemistry, the concentration gradient is a manifestation of the entropy term $-T\Delta S$ and the electrochemical gradient is a manifestation of the enthalpy term ΔH in the equation for Gibbs free energy, $\Delta G = \Delta H - T\Delta S$.

2. Using the Goldman Equation, you should get -92mV, 7.5mV, and 0.73mV, respectively.

3. Metabotropic receptors can amplify signals, since each step in the signalling cascade can be repeated many times by the same activated protein or second messenger. This amplification property is particularly desirable in retinal photoreceptors – a completely dark-adapted photoreceptor can respond to a single photon. In addition, metabotropic signalling can produce long-term changes in the postsynaptic neuron, since second messengers can activate transcription factors and other enzymes that affect gene expression and cellular metabolism and structure. Ionotropic receptors, though they cannot amplify or effect long-term change, can act much more quickly than metabotropic receptors since their effects depend only on ion current flow.

4. Chemical synapses are unidirectional, and signals mediated by different neurotransmitters can interact in varied and complex ways. The drawback is that chemical transmission is slow in comparison to electrical transmission. Gap junctions are found in electrically active tissues such as heart muscle in which precise synchrony must be maintained.

5. The NMDA receptor's voltage-current relationship when its gate is open is nonlinear; it does not follow Ohm's Law. To draw a loose analogy, the NMDA receptor behaves like a transistor rather than a resistor. This property is important because it means that the NMDA receptor can function like a logic gate in an electronic computer, combining inputs in a nonlinear manner. At the resting membrane potential, magnesium ions just outside the neuron are attracted to the neuron's electrically negative interior, and block the channel like a stopper sucked into a drain. So if glutamate binds to an NMDA receptor when the postsynaptic neuron is at resting potential, not much happens: the inward sodium and calcium currents remain very nearly zero, since sodium and calcium ions can't get past the magnesium. However, if glutamate binds to the NMDA receptor when the neuron has already been somewhat depolarised by other (non-NMDA) receptor activity, then the magnesium will not be blocking the channel, and NMDA receptor activation will produce a high inward current of sodium and calcium ions.

QUESTIONS FOR LECTURE #3

1. The portions of the channel's membrane-spanning segments that are exposed to the interior of the membrane are lipophilic, consisting in general of uncharged, non-polar amino acid residues. The portions exposed to the cytoplasm and to the extracellular fluid, in contrast, are hydrophilic. The

embedded position is thus the state of least potential energy.

2. Does it consist of seven transmembrane segments? If so, it's a G-protein-coupled receptor.

3. Depleting extracellular calcium, using a calcium chelator, abolishes exocytosis. Intracellular injection of a calcium-dependent dye demonstrates that exocytosis is correlated with calcium influx.

4. (a) The sodium current that forms the spike of the action potential will be abolished. If the membrane can be brought near threshold by means other than the sodium current (*e.g.* by artificial current injection), the delayed-rectifier potassium current will be intact.
(b) The action potential and the relative refractory period will be prolonged.
(c) The action potential will be lower in amplitude, since it won't have time to peak before the voltage-gated sodium channels begin to inactivate.
(d) The effect of this mutation would be rather like removing the delay from the delayed-rectifier potassium current: a low-amplitude repolarisation would begin simultaneously with the high-amplitude depolarisation, decreasing the summed amplitude of the action potential. This almost exactly what happens in the case of the chemically-gated kainate/quisqualate glutamate receptor, whose reversal potential is near 0mV, between the Na^+ and K^+ reversal potentials.

5. During the absolute refractory period, the membrane cannot produce an action potential, because the inactivation gates on its sodium channels have closed. During the longer, relative refractory period, more than the normal amount of depolarisation is needed in order to reach the threshold for an action potential, since the delayed-rectifier potassium current is still active and must be overcome.

6. Shunting inhibition occurs when a depolarising, inward current source at a relatively distal synapse completes a circuit with a hyperpolarising current sink at a relatively proximal synapse. (The terms 'source' and 'sink' are borrowed from the terminology of electrical engineering; they refer to the idea that every current must be part of a complete circuit; every source must eventually be matched with a sink in order to avoid a buildup of electrical charge within the system.) The proximal, inhibitory synapse 'vetos' the effect of the distal, excitatory synapse.

7. Synaptic facilitation is a short-term increase in the efficacy of a synapse, mediated by accumulation of intracellular calcium. Synaptic depression occurs when repeated activation of a synapse has exhausted the presynaptic neuron's store of vesicles. Post-tetanic potentiation is an increase in transmitter release, caused by calcium-mediated priming of vesicles.

8. A node of Ranvier is an interruption in the myelin sheath surrounding an axon. Voltage-gated channels are concentrated at nodes of Ranvier. In an unmyelinated axon, the speed of propagation of the action potential depends very strongly on the time that it takes for voltage-gated sodium channels in adjacent patches of membrane to open, and ion currents flow radially in and out of the axon. Myelination, in contrast, forces current to flow longitudinally, along the axon from one node of Ranvier to the next. Since the speed of propagation of this electrical signal far exceeds the speed at which signals can be conducted by the micromechanical opening and closing of ion channel gates, conduction in myelinated axons is much faster than in unmyelinated axons. The electrical signal does dissipate with distance, though, and this is why nodes of Ranvier are necessary in order to regenerate the action potential periodically along the axon – without the nodes of Ranvier, signals would decay below the action potential threshold, and conduction would fail.

QUESTIONS FOR LECTURE #4

1. The choroid plexus is located on the roofs of the ventricles. It produces cerebrospinal fluid.

2. An anastomosis is a communication between arteries. The circle of Willis is an anastomosis comprising the posterior cerebral, posterior communicating, middle cerebral, anterior cerebral, and anterior communicating arteries.

3. Consider the effects of a localised drop in pressure, for example the sort caused by a clot in a local distribution of the arterial system, with a regional or systemic drop in pressure. In the former case, redundancy in the blood supply is a benefit since the circumscribed area affected by the blockage can be fed from alternative supplies without any significant adverse effect on blood pressure in those supplies. In the latter case, a large-scale drop in pressure most affects the 'watershed' areas at the edges of neighbouring perfusion territories, making these areas vulnerable to ischaemic damage.

4. Intuitively, it may seem that the magnetic resonance signal in activated areas would decrease: since more oxygen is being extracted, the amount of deoxyhaemoglobin should increase, and thus the spoiling effect of magnetic susceptibility gradients surrounding deoxyhaemoglobin-filled capillaries should be heightened. In fact, work by Kamil Ugurbil's magnetic resonance imaging group at the University of Minnesota has shown that this is exactly what happens during the short time immediately following the initial activation of a brain region. Conventional fMRI can't see this initial dip in MR signal, though, since it's almost immediately swamped by a large increase in blood flow due to autoregulation – the region becomes flooded with more oxygenated blood than it can use, and so there is a net increase in the MR signal.