Gatsby Computational Neuroscience Unit
Neuroscience Candidacy 2012

Written Examination
26-27 Jan 2012

Part I

This part has 20 short questions. Answer all of them, to the best of your ability. Each is worth 4 marks. No reference materials are allowed.

It should take no more than 3 hours.

1. Consider a synapse that can both facilitate and depress. The release probability, p, behaves as follows:

   - Every time there is a spike, the probability, p, increases by a factor of $f_F(1-p)$ and, with probability p, it decreases by a factor of $(1-f_D)p$. Both factors are relative to the probability immediately before the spike.
   - Between spikes, p decays back to its equilibrium value of p_0 with time constant τ.

   Write down a differential equation describing the time-evolution of p.

2. Explain, via biophysical mechanisms, how the weight change of a synapse during learning can depend on *both* pre-synaptic and post-synaptic activity.

3. If you doubled the axial resistance, r_L, in a passive dendrite (assumed to be infinitely long and uniform), what would happen to the electrotonic length?

4. Assuming the standard Hodgkin Huxley model, show, by sketching steady-state I-V (current-voltage) curves, that if the steady state m current, $m_\infty(V)$, activates at too high a voltage, or the steady state h current, $h_\infty(V)$, inactivates at too low a voltage, slowly increasing the voltage will not result in a spike.

5. Name one major excitatory and one major inhibitory neurotransmitter in the brain.

6. You perform simulations of a large, randomly connected network of excitatory and inhibitory neurons in which the synapses are current-based. The network operates at low firing rates in the asynchronous regime. You notice that a small perturbation to the firing rate decays as

$$\delta\nu \propto e^{-\lambda t}\cos(\omega t)\,.$$

   A friend of yours claims, based on years of experience with the standard Wilson and Cowan equations, that if you were to increase the connection strengths of all the neurons by 10%, both λ and ω would increase by almost exactly 10%, with the increase getting closer and closer to 10% as the network gets larger (assuming you scaled the weights appropriately with network size). Explain why your friend is wrong.

7. To build a Hopfield network with spiking neurons, you use connectivity that yields the following excitatory and inhibitory synaptic drives (denoted h_i^E and h_i^I, respectively),

$$\begin{aligned} h_i^E(t) &= \frac{1}{N^{1/2}}\sum_j W_{ij}^{EE} g_j^E(t) - \frac{1}{N^{1/2}}\sum_j W_{ij}^{EI} g_j^I(t) + \frac{1}{N}\sum_j J_{ij} g_j^E(t) \\ h_i^I(t) &= \frac{1}{N^{1/2}}\sum_j W_{ij}^{IE} g_j^E(t) - \frac{1}{N^{1/2}}\sum_j W_{ij}^{II} g_j^I(t) \end{aligned}$$

   where J_{ij} is the standard Hopfield connectivity,

$$\begin{aligned} J_{ij} &= \sum_\mu \xi_i^\mu \xi_j^\mu \\ \xi_i^\mu &= \begin{cases} 1 & \text{with probability } 1/2 \\ -1 & \text{with probability } 1/2\,, \end{cases} \end{aligned}$$

   and $g_j^E(t)$ and $g_j^I(t)$ are the excitatory and inhibitory current pulses associated with each spike; that is, whenever there is a spike on excitatory neuron j, $g_j^E(t)$ increases by a small amount, and then decays back toward zero, and similarly for $g_j^I(t)$. Coupling is all-all, and the Ws and Js are $\mathcal{O}(1)$.

   Explain why there is a factor of $1/N$, and not $1/N^{1/2}$, in front of the sum containing J_{ij}.

8. Sketch the form of spike-response current that would lead a GLM model to exhibit bursting, with slow adaptation in the burst rate given constant input. Take care to ensure that the spike trains generated will look biologically plausible.

9. Explain the difference between the model fit by the STC method and a second-order Volterra model. Under what conditions would the the two classes of model (STC and second-order Volterra) be identical?

10. As visual contrast falls, the visual system—from the retina upwards—often switches from emphasising local boundaries in the scene to smoothing over larger regions. Discuss why this might be.

11. What is colour constancy? Where in the brain might you expect to find neuronal correlates of constancy?

12. Consider a neuron whose spiking is described renewal process with the ISI distribution

$$p(\tau) = \begin{cases} 0 & \tau < \tau_{\text{ref}} \\ \lambda e^{-\lambda(\tau - \tau_{\text{ref}})} & \tau \geq \tau_{\text{ref}} \end{cases}$$

    Show a typical spike train $\{t_i\}$ from this cell as points along a line, and sketch the corresponding function $u(t)$ which would rescale time so that the rescaled spike events $\{u(t_i)\}$ would be Poisson distributed.

13. Give an example of a neural population that uses a "Cartesian" code. Why do you think that this coding strategy might have evolved in the case you chose—why not a joint distributed code?

14. What is spike-time dependent plasticity? What determines the degree of competition it leads to for multiple synapses onto the same postsynaptic neuron is compared with conventional rate-based Hebbian learning? Justify your answer.

15. What are the direct and indirect pathways through the striatum? What significance does the difference have for the control of action?

16. What are likely to be the major differences between the contribution of the cerebellum and the striatum to decision-making and control?

17. What are the dorsal and ventral visual processing streams? What sort of major functional connections would you expect between them?

18. What is the signature of a silent synapse? Do you think it would be silent in practice in vivo?

19. Define phase precession in the context of place cells. Outline a mechanism which might be able to instantiate it.

20. What is a concurrent variable interval schedule of reinforcement. Why might it lead to probability matching?

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Neuroscience Candidacy 2011

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28 Jan 2011

Part II

This part contains 12 questions, of which you need to answer 10. Each is worth 12 marks.

It should take no more than 5 hours.

1. Consider a neuron that obeys the set of equations

$$\begin{aligned} \tau \frac{dV}{dt} &= -(V - V_L) - g_0 x (V - V_0) \\ \tau_x \frac{dx}{dt} &= \frac{1}{1 + \exp[(V - V_x)/\Delta V]} - x \end{aligned}$$

where

$$\begin{aligned} \tau &= 10 \text{ ms} \\ \tau_x &= 100 \text{ ms} \\ g_0 &= 5 \\ V_L &= -60 \text{ mV} \\ V_0 &= 0 \text{ mV} \\ V_x &= -50 \text{ mV} \\ \Delta V &= 5 \text{ mV}. \end{aligned}$$

You voltage clamp the cell at -65 mV for a time much larger than τ_x, and then suddenly step the voltage to -40 mV. Sketch, qualitatively, the current that flows through your electrode as a function of time. Does the current flow into the cell or out of it? Indicate on the plot the initial and the final value of the current, assuming that the membrane resistance is 100 MΩ.

2. A linear integrate and fire neuron evolves according to

$$\tau \frac{dV}{dt} = -(V - \mathcal{E}_L) + \sum_j W_{ij} g_j(t)(V - \mathcal{E}_j).$$

Assuming you know $g_j(t)$ for all j, write down an exact expression for $V(t)$. For simplicity, let $V(t = 0) = \mathcal{E}_L$. (This expression will involve integrals you can't do.) Now assume that $g_j(t)$ can be characterized by a mean, $\overline{g}$, plus fluctuating terms, where the fluctuating terms are stationary and exhibit temporal correlations that decay with time (i.e., for all j and k, $\langle \delta g_j(t) \delta g_k(t') \rangle$ goes to zero when $|t - t'|$ is large). If you approximate $g_j(t)$ by $\overline{g}$ and solve for $V(t)$, how does the error in $V(t)$ scale with time? I'm looking for an expression of the form $f\left(\mathcal{O}(t^\alpha)\right)$; all you need to do is tell me the function, f, and the exponent, α.

3. Consider the standard Hopfield model,

$$x_i(t + 1) = \text{sign}\left(\frac{1}{N} \sum_{j,\mu} \xi_i^\mu \xi_j^\mu x_j(t) \right)$$

where

$$\xi_i^\mu = \begin{cases} 1 & \text{with probability } 1/2 \\ -1 & \text{with probability } 1/2, \end{cases}$$

the sum on i runs from 1 to N (there are N neurons) and the sum on μ runs from 1 to p (there are p memories). At time t,

$$x_i = \begin{cases} \xi_i^\mu & \text{with probability } q \\ -\xi_i^\mu & \text{with probability } 1 - q. \end{cases}$$

Write down an expression for the probability that $x_i(t + 1) = \eta_i^\mu$.

4. You do an experiment in which you add channel rhodopsin to about 10% of the excitatory cells in a network. You shine enough light to increase the firing rate of those neurons by 1 Hz, on average. You find that the firing rates of the other excitatory neurons drop. Explain why. Assume you can treat the network as randomly connected and operating in the balanced regime.

5. Consider an experiment in which subjects need to estimate the position of their hand on a table-top at about chest level. They can use both proprioceptive and visual information. Because of the joint angles involved, proprioceptive information is rather precise in depth, but may generate relatively large errors along the horizontal axis. Conversely, vision is precise horizontally, but poor at judging depth. Assume that all errors are Gaussian distributed and that neither modality is biased.

   Suppose the observer's hand is actually 20 cm away, directly in front of the centre of her chest. Sketch the following quantities for a single (typical) trial on the same figure:

   - A distribution representing the observer's belief about her hand position based on proprioceptive information alone.
   - A distribution representing the observer's belief about her hand position based on visual information alone.
   - A distribution representing the observer's belief about her hand position based on both proprioceptive and visual information.

   Now, assuming that the observer always reports the most likely location for the hand based on the available sensory information, sketch the distributions of the following quantities *across* trials on a second figure:

   - The distribution of reports obtained with the observer's eyes closed.
   - The distribution of reports obtained for the location of an artificial hand placed by the experimenter and seen but not touched by the observer.
   - The distribution of point-estimates obtained for the location of the observer's own hand when her eyes are open.

   Finally, repeat the drawings above for the case that an artificial discrepancy is introduced between vision and proprioception by placing horizontally-displacing prisms in front of the observer's eyes.

6. Consider a population of neurons that show monotonic linear tuning for a stimulus s. That is, the firing rate of neuron i is $f_i(s) = g_i s$. Assume the standard deviation of the spike count for each neuron is the same value σ. Describe in terms of g_i the structure of stimulus-independent correlation between all the neurons which would maximise the Fisher Information about s. You may assume that the spike counts are Gaussian distributed.

7. Compare Fisher information and (Shannon) average mutual information. How are they related? Discuss the relevance of each to neuroscience.

8. Two neurons respond to a punctate stimulus at time $t = 0$ by producing spikes distributed as an inhomogeneous Poisson process with rates:

$$\lambda_i(t) = g_i e^{-(t-\tau_i)/2\beta} \Theta(t - \tau_i)$$

   for $i = 1, 2$. $\Theta(\cdot)$ is the Heaviside function.

   - Suppose first that g_i and τ_i are constant. What is the expected cross-covariogram (i.e. shuffle-corrected cross-correlogram) between these cells' spike trains?
   - Now, suppose the g_i vary from trial to trial, with correlation coefficient ρ. Now what is the expected cross-covariogram. Sketch the function.
   - Finally, consider the possibility that the τ_i also covary. It is difficult to find a closed-form expression in this case, but sketch the shape of function you would expect, comparing it the one above.

9. In what sense does hyperbolic discounting of the future lead to the possibility of intertemporal choice conflict between present and future selves? Show how this can lead to commitment behaviour, making a choice at one time to wait for a moderate-sized reward to avoid being faced with a choice at a later time between a smaller sooner, and a larger later reward.

10. What is a synaptic eligibility trace? Define the TD(λ) learning rule. What happens at $\lambda = 1$? What basis could there be for choosing λ appropriately?

11. Consider a pure Hebbian learning rule driven by anticorrelations, with $\dot{\mathbf{v}} = \begin{pmatrix} 1 & -a \\ -a & 1 \end{pmatrix} \mathbf{v}$, where $a > 0$.

    If hard constraints are imposed such that $0 \leq v_1, v_2 \leq 1$ (by suppressing changes in just the variable(s) that would lead outside these bounds), derive the range(s) of initial values of $\mathbf{v}$ that will end up at $\mathbf{v} = (1, 1)$.

12. Discuss different ways of normalizing the synaptic efficacy of a neuron. Illustrate your answer by drawing a picture of possible constraint lines in a 2d case, and show the flow of the weights associated with this normalization. What effect does normalization have on the ultimate outcome of plasticity in cases such as the formation of ocular dominance columns