Problem Set 1

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Reading

Reading. A. Borst & L. N. Groschner, *How Flies See Motion*, Annu. Rev. Neurosci. **46**:17–37 (2023) — in particular Figures 1, 4 and 5. A. D. Gonzalez-Suarez *et al.*, *Excitatory and inhibitory neural dynamics jointly tune motion detection*, Curr. Biol. **32**:3659–3675 (2022). Optional: L. N. Groschner, J. G. Malis, B. Zuidinga & A. Borst, *A biophysical account of multiplication by a single neuron*, Nature **603**:119–123 (2022).

The question

The introduction lecture and the following lecture on the motion detection in fly ended with a one-line algorithm: a direct input B, two delayed flanking inputs A and C, output $S_A \times S_B \div S_C$. T4 is the neuron in which every ingredient of such a scheme has actually been measured. Decide how much of the real circuit that one line captures, and where it stops being true.

The two models

Model A (algorithmic). Three inputs sample the visual field at azimuths $-\Delta\varphi$, 0, $+\Delta\varphi$, delivering contrast signals $u_A(t)$, $u_B(t)$, $u_C(t)$. Each arm applies a causal linear temporal filter and adds a positive baseline,

$$S_A = a_0 + K_{\tau_A} * u_A, \qquad S_B = b_0 + K_{\tau_B} * u_B, \qquad S_C = c_0 + K_{\tau_C} * u_C, \qquad R = \frac{S_A S_B}{S_C}.$$

The kernel. Everything in Problem 1 depends on the *shape* of K, not only on a delay, so we state it explicitly. Take the normalised alpha function

$$K_\tau(t) = \frac{t}{\tau^2}\, e^{-t/\tau}\, \Theta(t), \qquad \int_0^\infty K_\tau(t)\, dt = 1, \qquad K_\tau(0) = 0, \qquad \text{peak at } t = \tau. \tag{1}$$

Two features will matter and should be kept in view: K_τ is **causal** ($K_\tau(t) = 0$ for $t < 0$), and it has a **rising phase** ($K_\tau(0) = 0$, so the arm responds not to the input's present value but to its recent history). For comparison you will also need the pure low-pass kernel

$$h_\tau(t) = \frac{1}{\tau} e^{-t/\tau}\,\Theta(t), \tag{2}$$

which is causal but has no rising phase, $h_\tau(0^+) = 1/\tau$.

Neither form is a measurement. The temporal kernels of Mi1, Tm3, Mi4, CT1 and Mi9 have been obtained by reverse correlation with stochastic visual stimuli (Gonzalez-Suarez *et al.*, Curr. Biol. 2022), and they are neither (1) nor (2): they are biphasic, with an undershoot, so each arm is band-pass rather than low-pass. Part 1(c) and part 2(c) are about whether that difference matters.

Model B (biophysical). One isopotential compartment,

$$C_m \frac{dV}{dt} = -g_L(V-E_L) - g_{\mathrm{inh}}(t)(V-E_{\mathrm{inh}}) - g_{\mathrm{exc}}(t)(V-E_{\mathrm{exc}}), \qquad g_{\mathrm{inh}} = g_9 + g_G,$$

where g_9 is the Mi9 (GluClα) conductance and g_G the GABAergic one.

Parameters: $\Delta\varphi = 5°$, $\tau_A = \tau_C = 150$ ms, $\tau_B = 20$ ms, $g_L = 0.10$ nS, $E_L = -68$ mV, $E_{\mathrm{exc}} = 0$ mV, $E_{\mathrm{inh}} = -70$ mV.

1. The algorithm on its own *(30 pts)*

(a) Let $R(t) = \sum_i (k_i * u_i)(t)$ for arbitrary causal linear filters k_i. Show that the time-averaged response to a drifting sinusoidal grating is the same for both directions of motion. Conclude what kind of nonlinearity a direction-selective detector needs. Note that this conclusion is independent of the kernel shape — it is the last statement in this problem that will be.

(b) Take impulse inputs $u_i(t) = C\,\delta(t - t_i)$ and let $\tau_B \to 0$, so that arm B reports the instantaneous contrast. For preferred-direction (PD) motion at velocity v, $(t_A, t_B, t_C) = (-\Delta t_s, 0, +\Delta t_s)$ with $\Delta t_s = \Delta\varphi/v$; for null-direction (ND) motion the order reverses. Expanding R to second order in the input-driven parts of S_A, S_B, S_C, evaluate the time integral of the $S_A S_B$ term and of the $S_B S_C$ term for PD and for ND. Show that the first is non-zero only for PD and the second only for ND, and identify which of the two properties of K_τ listed above is responsible.

(c) Still with impulse inputs, now keep τ_B finite, so that arm B applies K_{τ_B}.

  (i) Evaluate the correlation $\int K_{\tau_A}(t+\Delta t)\,K_{\tau_B}(t)\,dt$ as a function of $\Delta t > 0$, find the interval Δt^* that maximises it, and hence the preferred velocity $v^* = \Delta\varphi/\Delta t^*$. Evaluate numerically.

(ii) Repeat the calculation with the low-pass kernel (2) in place of (1) in both arms. Show that the result is monotonic in v, so that no preferred velocity exists.

(iii) State the conclusion in one sentence: which property of the kernel sets the preferred speed, and which merely sets the direction selectivity? What does (ii) tell you about how much of this circuit is captured by the word "delay"?

2. Mapping the circuit onto the algorithm *(30 pts)*

(a) Using Figure 4a,b, assign Mi9, Mi1+Tm3 and Mi4+C3+CT1 to the arms A, B, C of a T4a cell. The assignment must follow from your answer to 1b, not from the figure's colours. Explain in two sentences why the dendritic tip has to point *against* the preferred direction.

(b) Mi9 is an OFF cell, is glutamatergic, and acts on GluClα, a glutamate-gated chloride channel. Read the sign and the spatial offset of its receptive field off Figure 5b, then write out the full chain of signs from "brightness rises in the tip column" to "T4 depolarises."

(c) From Figure 5c,d, rank the three measured input traces by their time of peak, separately for PD and ND motion, and estimate a peak time for each. Is the ordering the one your answer to 1b requires? Are τ_A and τ_C in fact equal, as the parameter list assumes? Finally, identify the feature of the measured traces that neither (1) nor (2) reproduces, and say — using 1(c) — what it would do to the velocity tuning.

3. From conductances to arithmetic *(40 pts)*

(a) With $E_{\mathrm{inh}} = E_L$, derive the steady state of Model B and put it in the form $V_{\mathrm{ss}} - E_L = (E_{\mathrm{exc}} - E_L)\, g_{\mathrm{exc}}/(g_L + g_{\mathrm{inh}} + g_{\mathrm{exc}})$. State the limit in which this becomes a clean division by g_{inh}, and what fails outside that limit.

(b) *Disinhibition is multiplication.* Let $g_9(t) = \bar{g}_9[1 - m\tilde{S}_A(t)]$ with $0 \le m\tilde{S}_A \le 1$. Expand $V_{\mathrm{ss}} - E_L$ to first order in $m\tilde{S}_A$ and exhibit the term proportional to $g_{\mathrm{exc}}\tilde{S}_A$. Why is a *decrease* of an inhibitory conductance a multiplication rather than an addition?

(c) Show that the steady state of Model B can be written *exactly* in the form $S_A S_B / S_C$, and give explicit expressions for S_A, S_B, S_C in terms of g_9, g_G, g_{exc}, g_L. Then identify the catch: the S_C you obtain is not a function of the C arm alone. Consequently, predict the outcome of an experiment that manipulates Mi9 and Mi4 *together*, and state how that prediction

differs from the one made by a factorised three-arm model. This is the single sharpest difference between the algorithm and the biophysics — make the statement precise.

(d) *Reading conductances off the data.* In Figure 5c,d the membrane potential $V(t)$ and the input resistance $R_{\mathrm{in}}(t)$ were measured together. Show that

$$g_{\mathrm{exc}}(t) = \frac{V(t) - E_L}{R_{\mathrm{in}}(t)\,(E_{\mathrm{exc}} - E_L)}, \qquad g_{\mathrm{inh}}(t) = \frac{1}{R_{\mathrm{in}}(t)} - g_L - g_{\mathrm{exc}}(t),$$

stating the assumptions required. Read V and R_{in} off the figure at several points along the PD and ND traces — at minimum at rest, at the peak of R_{in}, and at the peak of V — and sketch $g_{\mathrm{exc}}(t)$ and $g_{\mathrm{inh}}(t)$ for both directions. What has happened to the inhibitory conductance at the R_{in} peak in PD? What does the resting value of g_{inh} say about Mi9 in an unstimulated cell, and why does the algorithm need exactly such a tonic level? Mi1 and Tm3 are not direction selective: what does that predict about $g_{\mathrm{exc}}(t)$ in the two directions, and does your decomposition agree?

(e) *GluClα knockdown* (Figure 5f). Write down what Model A predicts when S_A is clamped at a_0, and what Model B predicts when $\bar{g}_9 = 0$, for the response amplitude and for the width of the directional tuning. The data show responses that are *larger* in nearly all directions and tuning that is close to isotropic. Which model accounts for the increase in amplitude, by what mechanism, and what does that tell you about the status of the baseline a_0 in Model A?

Note. Derivations in full. Where you read values off a published figure, state the numbers you read and treat them as measurements with an error bar: an answer accurate to within a factor of two, with its uncertainty stated, is worth more here than three digits. Where you are asked to predict an experiment, one paragraph suffices, but specify what is manipulated, what is measured, and which model the outcome would falsify.