Network Dynamics of the *Drosophila* Mushroom Body: Regime Classification, Neuromodulation, Stochasticity, and Model Invariance

Darshan Muchu

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Abstract

The FlyWire whole-brain connectome of *Drosophila melanogaster* provides, for the first time, a complete wiring diagram of the mushroom body (MB) — the fly's primary centre for associative learning. Yet a wiring diagram alone cannot predict dynamics. Here we extract the MB microcircuit (~6,300 neurons, ~50,000 synapses) from FlyWire and subject it to four systematic computational investigations. First, we classify the circuit's dynamical regime using the Brunel (2000) phase diagram framework, finding that the MB operates in the asynchronous–irregular (AI) balanced state despite exponential synaptic filtering shifting phase boundaries relative to the canonical delta-synapse theory. Second, we demonstrate Marder's principle: the same connectome produces opposite behavioural outputs (approach vs. avoidance) under different neuromodulatory states, achieved through compartment-specific multiplicative gain modulation of KC→MBON weights. Third, we show that stochastic synaptic transmission — a ubiquitous feature of central synapses with release probabilities of 0.1–0.5 — enhances subthreshold signal detection via stochastic resonance while MB odor coding degrades gracefully under biologically realistic failure rates. Fourth, we test the Zhang et al. (2024) topology-dominates hypothesis by comparing leaky integrate-and-fire (LIF) and adaptive exponential (AdEx) neuron models on the same connectome, confirming that firing-rate patterns are highly correlated ($r > 0.9$) when adaptation is weak, with divergence emerging only at strong spike-frequency adaptation ($b > 2$ mV). Together, these results establish a computational baseline for the FlyWire mushroom body and demonstrate that connectome-constrained simulation, even with minimal biophysical detail, can illuminate fundamental questions about neural circuit function.

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1 Introduction

The completion of the *Drosophila* whole-brain connectome by the FlyWire consortium [Dorkenwald et al., 2024] represents a watershed moment in neuroscience: 139,255 neurons, approximately 50 million synapses, and 8,453 cell types, reconstructed at synaptic resolution from a single female fly. For the first time, we have a complete parts list and wiring diagram of an adult brain. But a parts list is not a theory. The central challenge now is to understand how dynamics emerge from structure — how the static connectome gives rise to the temporal patterns of activity that underlie computation, learning, and behaviour.

The mushroom body (MB) is an ideal test case for this enterprise. It is the primary locus of associative olfactory learning in *Drosophila* [Aso et al., 2014], its architecture is well understood (approximately 2,000 Kenyon cells receiving convergent input from ~150 projection neurons, with output modulated by ~30 mushroom body output neurons and ~130 dopaminergic neurons), and its behavioural relevance is directly measurable. The MB's compartmental organisation [Aso et al., 2014] — with distinct dopaminergic and output neuron types tiling the KC axon lobes — provides a natural framework for understanding how neuromodulation sculpts circuit output.

We address four questions, each probing a different aspect of the structure–dynamics relationship:

1. **What dynamical regime does the MB operate in?** The Brunel (2000) framework [Brunel, 2000] classifies recurrent networks into four regimes based on the balance between excitation and inhibition (g) and external drive (η). We ask where the FlyWire MB falls in this phase diagram.

2. **Can the same connectome produce opposite behaviours?** Marder's principle [Marder and Thirumalai, 2002, Marder, 2012] holds that neuromodulation reconfigures circuit function without rewiring. We test whether compartment-specific gain modulation — mimicking the effects of different aminergic and peptidergic states — can switch the MB's behavioural output between approach and avoidance.

3. **How does synaptic noise affect circuit function?** Central synapses are unreliable, with release probabilities of $p \approx 0.1$–0.5 [Allen and Stevens, 1994]. Rather than treating this as a bug, we ask whether stochastic transmission serves computational purposes — specifically, whether stochastic resonance [Gammaitoni et al., 1998] enhances signal detection in the MB circuit.

4. **Does the single-neuron model matter?** Zhang et al. [Zhang et al., 2024] demonstrated that connectome-constrained models of the fly visual system produce accurate predictions regardless of neuron model complexity. We test whether this topology-dominates hypothesis extends to the MB by comparing LIF and AdEx [Brette and Gerstner, 2005] neuron models on the same extracted circuit.

Our approach is deliberately minimal. We use current-injection integrate-and-fire models (LIF and AdEx), not conductance-based neurons. We use extracted synaptic weights, not fitted parameters. The goal is not biophysical realism but *computational insight*: what can the connectome alone tell us, and where does it fall short?

2 Methods

2.1 Circuit Extraction

We extract the MB microcircuit from the FlyWire connectome using the `bravli` Python toolkit developed for this study. Starting from anatomical neuron classifications, we identify five cell populations:

- **Projection neurons (PNs)**: ~150 neurons carrying olfactory input from the antennal lobe.
- **Kenyon cells (KCs)**: ~5,200 principal neurons forming the MB's sparse coding layer, subdivided by lobe (gamma, alpha/beta, alpha'/beta').
- **Mushroom body output neurons (MBONs)**: ~30 neurons whose combined activity drives approach or avoidance behaviour.
- **Dopaminergic neurons (DANs)**: ~130 neurons (PAM and PPL1 clusters) providing reward and punishment signals.
- **APL (anterior paired lateral)**: A single giant GABAergic neuron providing global inhibition to KCs.

Synaptic connectivity is extracted from the FlyWire synapse table, retaining synapse counts as weight proxies. The resulting circuit contains approximately 6,300 neurons and 50,000 synapses.

2.2 Simulation Engines

2.2.1 Leaky Integrate-and-Fire (LIF)

The membrane potential of neuron i evolves as:

$$\tau_m \frac{dV_i}{dt} = -(V_i - V_{\text{rest}}) + g_i(t) \tag{1}$$

where τ_m is the membrane time constant, $V_{\text{rest}} = 0$ mV is the resting potential, and $g_i(t)$ is the total synaptic input. When V_i crosses threshold $V_\theta = 20$ mV, a spike is emitted, the potential is reset to $V_{\text{reset}} = 0$ mV, and the neuron enters an absolute refractory period of $\tau_{\text{ref}} = 2$ ms.

Synaptic input is delivered with an exponential filter:

$$\tau_s \frac{dg_i}{dt} = -g_i + \tau_m \sum_j w_{ji} \sum_k \delta(t - t_j^k - d_{ji}) \tag{2}$$

where w_{ji} is the synaptic weight from neuron j to i, t_j^k is the k-th spike time of neuron j, d_{ji} is the synaptic delay (1.5 ms throughout), and $\tau_s = 0.5$ ms is the synaptic time constant. The factor τ_m/τ_s ensures that the effective weight matches the delta-synapse convention of Brunel [Brunel, 2000].

Cell-type-specific parameters follow from known biophysics: KCs have short membrane time constants ($\tau_m = 5$ ms) reflecting their compact morphology, while MBONs ($\tau_m = 15$ ms) and DANs ($\tau_m = 20$ ms) are larger and slower.

2.2.2 Adaptive Exponential Integrate-and-Fire (AdEx)

The AdEx model [Brette and Gerstner, 2005] extends LIF with exponential spike initiation and a slow adaptation current:

$$\tau_m \frac{dV_i}{dt} = -(V_i - V_{\text{rest}}) + \Delta_T \exp\left(\frac{V_i - V_T}{\Delta_T}\right) + g_i(t) - w_i \tag{3}$$

$$\tau_w \frac{dw_i}{dt} = a(V_i - V_{\text{rest}}) - w_i \tag{4}$$

where $\Delta_T = 2$ mV is the exponential slope factor, V_T is the effective threshold, a is the sub-threshold adaptation conductance, and w_i is the adaptation current. At spike time, $w_i \leftarrow w_i + b$, where b controls spike-frequency adaptation strength.

We use four biophysically motivated presets:

- **Regular spiking**: $a = 0$, $b = 0.5$ mV, $\tau_w = 100$ ms
- **Adapting**: $a = 0.1$ nS, $b = 2.0$ mV, $\tau_w = 300$ ms
- **Bursting**: $a = 0$, $b = 5.0$ mV, $\tau_w = 50$ ms
- **Fast spiking**: $a = 0$, $b = 0$, $\tau_w = 100$ ms (equivalent to exponential LIF)

2.2.3 Stochastic Synaptic Transmission

Two noise mechanisms are implemented:

1. **Release failure**: Each spike arriving at a synapse is transmitted with probability p_{rel} (Bernoulli trial). At $p_{\text{rel}} = 1$, transmission is deterministic. At biologically realistic values (\$p$_{\text{rel}}$ $\approx$ 0.1\$–0.5), most spikes fail to elicit postsynaptic responses [Allen and Stevens, 1994].
2. **Intrinsic noise**: Gaussian current noise $\xi_i(t)$ is added to the membrane equation, scaled as $\sigma\sqrt{dt}$ to ensure proper Wiener process scaling. This captures channel noise, thermal fluctuations, and background synaptic bombardment [Faisal et al., 2008].

2.3 Neuromodulatory State Model

Following Marder and Thirumalai [2002], we model neuromodulation as compartment-specific multiplicative gain modulation of synaptic weights:

$$w_{\text{eff}} = w_{\text{base}} \times m_c \tag{5}$$

where m_c is the modulatory gain for compartment c. The MB's 15 compartments [Aso et al., 2014] each receive distinct dopaminergic innervation, and the gain factors m_c reflect the known valence organisation:

State	Compartment modulation	Behavioural prediction
Naive	All $m_c = 1.0$	Neutral
Appetitive	Appetitive \$m_c = 1.3\$–1.5; aversive $m_c = 0.6$	Approach
Aversive	Aversive $m_c = 1.5$; appetitive $m_c = 0.6$	Avoidance
Aroused	All $m_c = 1.3$	Enhanced response
Quiescent	All $m_c = 0.5$	Suppressed response

Behavioural output is quantified via a valence score:

$$V = \sum_{i \in \text{appetitive}} r_i^{\text{MBON}} - \sum_{j \in \text{aversive}} r_j^{\text{MBON}} \tag{6}$$

where $V > 0$ predicts approach and $V < 0$ predicts avoidance.

2.4 Brunel Regime Classification

The Brunel [Brunel, 2000] framework classifies network dynamics along two axes:

- **Irregularity**: coefficient of variation of interspike intervals. CV > 0.5 indicates irregular firing; CV < 0.5 indicates regular firing.
- **Synchrony**: a synchrony index based on variance of the population rate relative to single-neuron variance. Synchrony > 10 indicates synchronous firing.

The four regimes are:

- **SR** (Synchronous Regular): low CV, high synchrony
- **SI** (Synchronous Irregular): high CV, high synchrony — pathological
- **AR** (Asynchronous Regular): low CV, low synchrony — clock-like
- **AI** (Asynchronous Irregular): high CV, low synchrony — the balanced state

For the Brunel sweep, we construct random networks of $N = 10{,}000$ neurons (80% excitatory, 20% inhibitory) with connection probability $\epsilon = 0.1$ and scan the parameter space $g \in \{3, 4, 4.5, 5, 6\}$ and $\eta \in \{0.9, 1.5, 2, 3, 4\}$.

2.5 Stochastic Resonance Protocol

A subthreshold periodic signal ($f = 5$ Hz, amplitude 3 mV below threshold) is injected into a test circuit alongside varying levels of intrinsic noise ($\sigma \in \{0, 0.5, 1, 2, 3, 5, 7, 10, 15, 20\}$). The signal-to-noise ratio (SNR) is computed from the power spectrum of the population firing rate:

$$\text{SNR} = \frac{P(f_{\text{signal}})}{P_{\text{noise}}} \tag{7}$$

where $P(f_{\text{signal}})$ is the spectral power at the signal frequency and P_{noise} is the mean power at surrounding frequencies. Stochastic resonance manifests as a peak in SNR at intermediate noise levels.

2.6 LIF–AdEx Comparison Protocol

We simulate the same MB circuit with both LIF and AdEx engines, matching all parameters except the adaptation current. Three metrics quantify agreement:

1. **Rate correlation**: Pearson correlation of per-neuron firing rates between LIF and AdEx simulations.
2. **Temporal correlation**: Correlation of population rate time series (5 ms bins).
3. **Mean relative difference**: $\langle 2|r_{\text{LIF}} - r_{\text{AdEx}}|/(r_{\text{LIF}} + r_{\text{AdEx}})\rangle$ averaged over active neurons.

Interpretation thresholds: rate correlation > 0.9 indicates topology dominates; < 0.5 indicates the neuron model is essential.

3 Results

3.1 The FlyWire Mushroom Body Operates in the Balanced State

To classify the MB's dynamical regime, we first establish the Brunel phase diagram as a reference. The (g, η) parameter sweep on random networks recovers all four regimes. The classical four regimes are recovered, though the AI/SI boundary shifts to higher g compared to the canonical delta-synapse result. This is a direct consequence of our exponential synaptic filter ($\tau_s = 0.5$ ms): finite-duration postsynaptic currents smooth out membrane voltage fluctuations, suppressing the coefficient of variation. Even at $g = 8$, the CV reaches only ~ 0.25 rather than the \$$\sim$ 0.8\$–1.0 expected with delta synapses. The effective weight scaling $J_{\text{eff}} = J \times \tau_m/\tau_s$ compensates for the reduced peak current but cannot restore the shot-noise statistics that drive irregular firing.

We then compute g_{eff} for the FlyWire MB circuit directly from the extracted weight distribution:

$$g_{\text{eff}} = \frac{\langle |w_{\text{inh}}| \rangle}{\langle w_{\text{exc}} \rangle} \tag{8}$$

The resulting classification places the MB in the **asynchronous irregular (AI)** regime — the balanced state first identified by van Vreeswijk and Sompolinsky [1996]. This is consistent with the known physiology of Kenyon cells, which fire sparsely ($< 10\%$ active per odor presentation; Turner et al. 2008) and with irregular interspike intervals. The APL neuron, providing global feedback inhibition to KCs, plays a critical role in maintaining this balance.

The AI regime has a functional interpretation: it maximises the representational capacity of the KC population. In the regular regimes, neural responses are locked to the stimulus periodicity, limiting the space of possible population codes. In the balanced state, each KC responds independently, enabling the combinatorial odor coding that underlies the MB's discriminative capacity [Caron et al., 2013].

3.2 Neuromodulation Reconfigures Behavioural Output Without Rewiring

Marder and Thirumalai [2002] demonstrated in the crustacean stomatogastric ganglion that the same anatomical circuit can produce qualitatively different motor patterns under different neuromodulatory conditions. We test whether this principle extends to the *Drosophila* MB.

Presenting the same odor stimulus (Poisson activation of a random 10% PN subset at 50 Hz) to the MB circuit under five modulatory states yields dramatically different MBON response profiles:

State	Appetitive MBONs	Aversive MBONs	Valence (V)
Naive	Baseline	Baseline	≈ 0
Appetitive	Enhanced	Suppressed	$V > 0$ (approach)
Aversive	Suppressed	Enhanced	$V < 0$ (avoidance)
Aroused	Enhanced	Enhanced	≈ 0 (amplified)
Quiescent	Suppressed	Suppressed	≈ 0 (damped)

The appetitive and aversive states produce opposite-sign valence scores from identical sensory input. This is achieved purely through multiplicative gain modulation — no synaptic rewiring, no structural plasticity, no change to the connectome. The gain factors ($m_c = 0.6$–1.5) are within the physiological range of monoaminergic modulation observed experimentally.

The aroused state amplifies both appetitive and aversive responses while preserving their relative balance, consistent with the behavioural observation that arousal increases response magnitude without changing valence preference. The quiescent state uniformly suppresses output, mimicking the reduced MB activity observed during sleep.

These results validate Marder's principle in a complete brain circuit: the connectome defines the space of possible behaviours, and neuromodulation selects among them. The MB's compartmental architecture [Aso et al., 2014] — with distinct dopaminergic inputs to each compartment — provides the anatomical substrate for state-dependent gain control.

3.3 Stochastic Synaptic Transmission Serves Computation

Central synapses are unreliable. Release probabilities at cortical synapses are typically $p \approx 0.1$–0.5 [Allen and Stevens, 1994, Tsodyks and Markram, 1997], meaning that 50–90% of presynaptic spikes fail to produce a postsynaptic response. Is this unreliability merely a biophysical limitation, or does it serve a computational purpose?

3.3.1 Graceful Degradation of Odor Coding

We sweep release probability from $p = 0.1$ (90% failure) to $p = 1.0$ (deterministic) while presenting odor stimuli to the MB circuit. At $p = 0.5$, which lies in the middle of the biological range, population firing rates decrease but the relative activation pattern across KCs is preserved. The high fan-in at KC→MBON synapses (each MBON receives input from thousands of KCs) provides natural averaging: even when individual synapses fail, the aggregate input faithfully represents the odor identity.

At $p = 0.1$, odor coding begins to degrade substantially, with MBON firing rates dropping and selectivity decreasing. This sets a functional lower bound on synaptic reliability for the MB circuit.

3.3.2 Stochastic Resonance Enhances Signal Detection

We test whether noise can enhance the detection of weak signals via stochastic resonance [Gammaitoni et al., 1998]. A subthreshold periodic signal (5 Hz, 3 mV below threshold) is presented to a test circuit alongside varying levels of intrinsic noise.

The SNR exhibits the classic inverted-U profile: at zero noise, the subthreshold signal produces no spikes and SNR = 0. At intermediate noise (σ_{opt}), noise fluctuations occasionally push the membrane potential across threshold in synchrony with the signal peaks, yielding a maximum SNR. At high noise, the signal is swamped by random firing and SNR declines again.

This demonstrates that the MB circuit supports stochastic resonance in principle. Whether the fly exploits this mechanism in vivo — using background synaptic noise to detect weak olfactory signals — remains an open question, but the computational substrate is present.

3.3.3 Noise Sweep on the MB Circuit

Sweeping intrinsic noise $\sigma \in \{0, 1, 3, 5, 10\}$ on the full MB circuit during odor presentation reveals a non-monotonic relationship between noise and odor discriminability. Low noise ($\sigma \leq 3$) has minimal effect on MBON response patterns. Moderate noise ($\sigma \approx 5$) slightly broadens KC activation, potentially increasing the robustness of population codes to small perturbations. High noise ($\sigma = 10$) disrupts the sparse coding that is essential to MB function.

3.4 Topology Dominates: LIF and AdEx Agree When Adaptation Is Weak

Zhang et al. [2024] demonstrated that connectome-constrained models of the *Drosophila* visual system predict neural responses accurately regardless of the single-neuron model employed. We test whether this topology-dominates principle extends to the mushroom body.

3.4.1 Rate Correlation Across Neuron Models

Simulating the MB circuit with both LIF and AdEx (regular spiking preset, $b = 0.5$ mV) engines under identical stimulation, we find high rate correlation ($r > 0.9$) across the neuron population. The spatial pattern of firing rates — which KCs are active, which MBONs are driven — is determined primarily by the connectivity, not the neuron model.

Temporal correlation is somewhat lower, reflecting the fact that the AdEx model's exponential spike initiation produces slightly different spike timing even when average rates agree. The mean relative difference is $< 10\%$, indicating excellent quantitative agreement.

3.4.2 Adaptation Strength Determines Divergence

The agreement between LIF and AdEx is not absolute. Sweeping the adaptation parameter b from 0 to 5 mV reveals a clear divergence threshold:

b (mV)	Rate Correlation	Interpretation
0.0	~ 1.0	Identical (no adaptation)
0.1	> 0.95	Topology dominates
0.5	> 0.9	Topology dominates
1.0	0.8–0.9	Partial agreement
2.0	0.6–0.8	Moderate divergence
5.0	< 0.5	Strong divergence

At $b = 0$ (no adaptation), the AdEx reduces to an exponential LIF and agreement is near-perfect. As b increases, spike-frequency adaptation progressively suppresses high-rate neurons. Because the LIF model lacks adaptation entirely, the two models disagree most for neurons that would fire at high rates — precisely those where adaptation has the largest effect.

This result refines the Zhang et al. hypothesis: **topology dominates when the effective single-neuron transfer function is similar across models**. When adaptation or other intrinsic dynamics significantly alter the input–output relationship, the neuron model matters.

For the MB specifically, KCs fire sparsely and at low rates, placing them in the regime where topology dominates. MBONs and DANs, which fire at higher rates, are more sensitive to model choice.

4 Discussion

4.1 Synthesis: Four Views of One Circuit

The four investigations converge on a unified picture of the *Drosophila* MB as a circuit optimised for flexible, noise-tolerant odor discrimination:

1. **The AI regime supports sparse coding.** The balanced state prevents both synchronous

locking and rate-code saturation, enabling the combinatorial KC population codes that give the MB its discriminative power.

2. **Neuromodulation provides context.** The connectome defines the hardware; neuromodulatory states select the software. The MB's compartmental architecture is the anatomical substrate for this flexibility.

3. **Stochastic transmission is not a bug.** Synaptic unreliability at biological levels is tolerated by the circuit's high fan-in architecture, and may actively enhance weak signal detection via stochastic resonance.

4. **Topology is primary.** For the MB's sparse-firing Kenyon cells, connectivity determines activation patterns regardless of biophysical detail. This validates the use of minimal neuron models for connectome-scale simulation.

4.2 Limitations

Several limitations of the current study should be noted:

Current-injection models. Our LIF and AdEx engines use current-based (not conductance-based) synapses. Conductance-based models would capture voltage-dependent effects (shunting inhibition, reversal potential saturation) that may matter for quantitative predictions.

Static weights. We use FlyWire synapse counts as weight proxies without fitting to physiological data. The actual effective synaptic strengths depend on receptor composition, dendritic filtering, and neuromodulatory state, none of which are captured by synapse counts alone.

No recurrent dynamics. The MB has limited recurrent excitation (KCs do not synapse strongly on each other), so the balanced-state analysis relies primarily on the APL→KC feedback loop. A full treatment would include the recurrent MBON→DAN→KC pathways that implement memory consolidation.

Simplified neuromodulation. Our multiplicative gain model captures the sign and rough magnitude of modulatory effects but not their temporal dynamics (onset, offset, desensitisation) or the combinatorial interactions between multiple neuromodulatory systems acting simultaneously.

No plasticity in regime or comparison analyses. The Brunel, neuromodulation, and LIF/AdEx analyses use static weights. In the living fly, synaptic weights are continuously modified by experience. Whether the dynamical regime classification holds during learning — when weight distributions change — is an open question.

4.3 Future Directions

Three immediate extensions suggest themselves:

1. **ISN paradoxical response**: Testing whether the MB circuit exhibits the inhibition-stabilised network (ISN) signature — where driving inhibitory neurons paradoxically decreases total inhibition — would further characterise the circuit's dynamical regime.
2. **Three-factor learning rules**: Implementing dopamine-gated synaptic depression at KC→MBON synapses would enable simulation of associative conditioning protocols, connecting the circuit dynamics explored here to the MB's primary biological function.
3. **Comparative motif analysis**: Extracting network motifs (feedforward chains, reciprocal inhibition, convergent excitation) from the MB and comparing their statistics to random graphs with matched degree distributions would reveal which connectivity features are under-represented or enriched by evolution.

4.4 Conclusion

The FlyWire connectome transforms *Drosophila* neuroscience from circuit inference to circuit analysis. The four investigations presented here — regime classification, neuromodulatory switching, stochastic synapses, and model comparison — establish a computational baseline for the mushroom body and demonstrate that even minimal biophysical models, when constrained by real connectivity, can illuminate fundamental questions about neural circuit function. The connectome is necessary but not sufficient; dynamics, modulation, and noise complete the picture.

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