

Computational Modeling of a Biological Network

Implementing the Rescorla-Wagner Learning Rule: A Simulation Study

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1 Introduction

The ability of animals to predict the causal structure of their environment, enabling them to exert anticipatory control over behavior, is a fundamental aspect of learning (Dickinson, 2001). This predictive capacity spans across diverse animal species and has intrigued scientists since the pioneering research of Ebbinghaus, Pavlov, and Thorndike, sparking extensive debates about the mechanisms underlying learning processes (Kandel et al., 2014).

Associative olfactory learning, a cornerstone of learning, involves forming associations between odors (conditioned stimuli, CS) and unconditioned stimuli (US), resulting in the establishment of appetitive or aversive memories (Quinn et al., 1974; Tempel et al., 1983). One influential theory in the realm of associative learning is the Rescorla-Wagner rule, introduced by Rescorla and Wagner in 1972. This rule posits that the change in the strength of an association between a conditioned stimulus (CS) and an unconditioned stimulus (US) is proportional to the magnitude of the prediction error, quantifying the difference between the expected and actual US intensity:

$$\Delta V = \alpha \cdot \beta \cdot (\lambda - V_{\text{total}})$$

Here, ΔV signifies the change in CS's associative strength, α controls the learning rate, β denotes US salience, λ represents CS associability, and V_{total} reflects total CS associative strength.

The Rescorla-Wagner rule provides insights into how animals update their expectations based on environmental outcomes and has been applied extensively to explain various forms of associative learning, including classical and operant conditioning paradigms. The intricate neural networks within the brain, particularly the mushroom body, play a central role in enabling fruit flies to develop both approach-based (positive) and avoidance-based (negative) learning responses to odors (McGuire et al., 2001).

Olfactory perception begins with odorants binding to olfactory sensory neurons in the antennae, which then connect to Projecting Neurons (PNs) (Masse et al., 2009). Most antennal lobe projection neurons extend dendrites to a single

glomerulus and bifurcate axons to innervate the lateral horn and the MB (Jeffreys et al., 2007). The mushroom body transforms olfactory sensory information into learned behavioral responses, with PNs' axons synapsing with Kenyon cells' (KCs) dendrites in the MB calyx. The parallel axons of KCs form the mushroom body lobes, selectively engaging specific subpopulations of KCs without spatial preference (Campbell et al., 2013).

Three KC classes extend parallel fibers forming the mushroom body lobes, synapsing with MB output neurons (MBONs) (Busch et al., 2009). MBONs' dendrites extend into the lobes, projecting axons outside of the mushroom body. Modulatory input neurons, including dopaminergic neurons (DANs) and octopaminergic neurons (Mao and Davis, 2009), also innervate the lobes, defining specific 'subdomains' within each lobe (Pech et al., 2013).

Dopaminergic neurons (DANs), the predominant modulatory neurons within the mushroom body, locally modify KC-MBON synapses through dopamine action (Waddell, 2013). DAN activity during learning is required, and externally induced DAN activation can serve as the unconditioned stimulus (US) in associative learning (Liu et al., 2012). D1-like dopamine receptors within KCs are essential for olfactory memory formation (Kim et al., 2007).

With inspiration from these findings, we undertake a modeling effort to replicate the mushroom body's central connectome, with a primary focus on simulating associative learning. Employing an evolutionary perspective, our endeavor initiates with a primitive structure, deviating from the actual mushroom body. Throughout this evolutionary simulation, we strive to comprehend challenges and address them within this context. This simulation's outset involves a reversed relationship between approach behavior and rewarding the US, contrary to the mushroom body's inherent structure.

2 Primitive Structure

2.1 Connectome

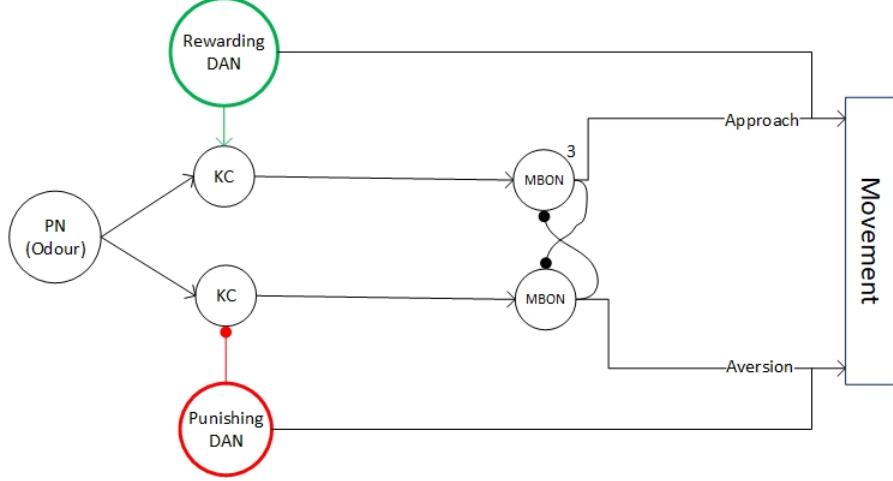


Figure 1: Primitive structure for associative learning based on MB anatomical findings

$$dk_1/dt = -\mu k_1 + \alpha CU_1 \quad (1)$$

$$dk_2/dt = -\mu k_2 + \alpha CU_2$$

$$dM_1/dt = -\nu M_1 + \gamma k_1 - \beta M_2$$

$$dM_2/dt = -\nu M_2 + \gamma k_2 - \beta M_1$$

(2)

If we consider the CU constant, then the dynamical system could be presented as:

$$d/dt \begin{bmatrix} k_1 \\ k_2 \\ M_1 \\ M_2 \end{bmatrix} = \begin{bmatrix} -\mu & 0 & 0 & 0 \\ 0 & -\mu & 0 & 0 \\ \gamma & 0 & -\nu & -\beta \\ 0 & \gamma & -\beta & -\nu \end{bmatrix} \begin{bmatrix} k_1 \\ k_2 \\ M_1 \\ M_2 \end{bmatrix} \quad (3)$$

To define the coefficient of the system in a way that ensures an asymptotically stable system, we employed the 'Routh and Hurwitz' methods, resulting in the following coefficients:

$$d/dt \begin{bmatrix} k_1 \\ k_2 \\ M_1 \\ M_2 \end{bmatrix} = \begin{bmatrix} -1 & 0 & 0 & 0 \\ 0 & -1 & 0 & 0 \\ 1 & 0 & -3 & -2 \\ 0 & 1 & -2 & -3 \end{bmatrix} \begin{bmatrix} k_1 \\ k_2 \\ M_1 \\ M_2 \end{bmatrix} \quad (4)$$

2.2 K Cells

We computed the steady state of each cell as follows:

$$0 = -\mu k + \alpha CU \quad (5)$$

$$k_0 = \frac{\alpha CU}{\mu}$$

$$0 = -\nu M_1 + \gamma k_1 - \beta M_2$$

$$M_0 = \frac{\gamma k_1 - \beta M_2}{\nu}$$

To explore the impact of \mathbf{k} on the alteration of \mathbf{M} steady state, we plotted the difference between the steady states of the two \mathbf{M} cells, ($M_1 - M_2$), as a function of different values of \mathbf{K} cells:

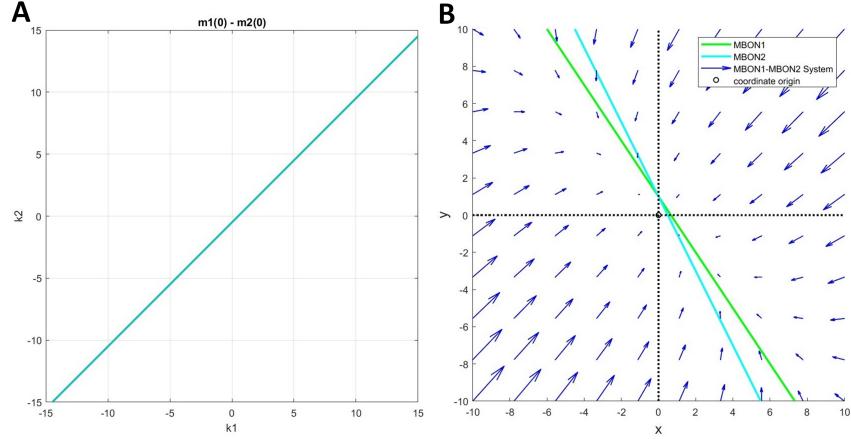


Figure 2: **A:** Difference between the steady states of two M cells based on different values of K's. **B:** Steady-state and nullclines of the system

2.3 Simulating System

2.3.1 Introducing Constant CS*US

Each K cell has two inputs: CS and US. CS is the same for each set of K cells, but one of them acquires a rewarding US, and the other receives a punishing US.

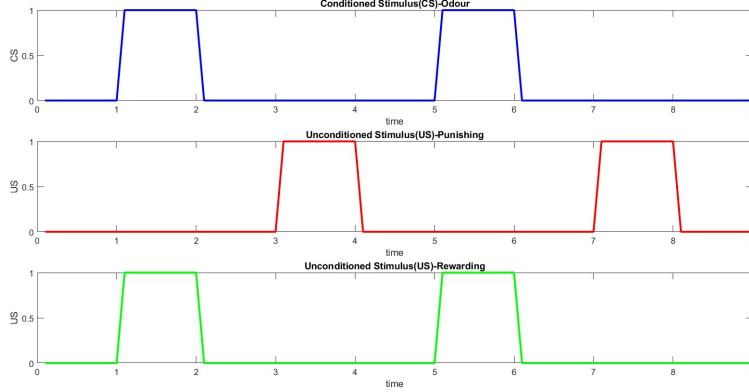


Figure 3: Order of presenting CS and US during the time course

2.3.2 K Cell Activity

Experimental studies have revealed that Kenyon cells in the mushroom body exhibit a phenomenon known as "Coincidence Detection." This phenomenon is observed specifically in the axons of the mushroom body's Kenyon cells and is elicited by forward pairing with time intervals akin to those needed for behavioral conditioning. Notably, the forward pairing of neuronal depolarization and octopamine results in a sub-additive effect on cAMP. Elevating intracellular cAMP facilitates calcium transients in mushroom body neurons, suggesting that cAMP elevation can induce presynaptic plasticity (Tomchik and Davis, 2009). We formulated the activity of K cells using the following equations:

$$dk/dt = -\mu k + \alpha CU$$

$$k_t = \frac{CU^2}{CU_{\frac{1}{2}}^2 + CU^2}$$

$$k_{t+1} = k_t + (k_0 - k_t)(1 - \exp^{-dt/\tau_k}) = k_0 + (-k_0 + k_t) \exp^{-dt/\tau}$$

In these equations, the term $\frac{CU^2}{CU_{\frac{1}{2}}^2 + CU^2}$ functions as a sigmoidal hard function (positive rectifying), and the term $CU_{\frac{1}{2}}$ represents the predefined inflection point. We introduced a gain factor to represent the amplitude of K cell responses, which is activated only when both CS and US occur together.

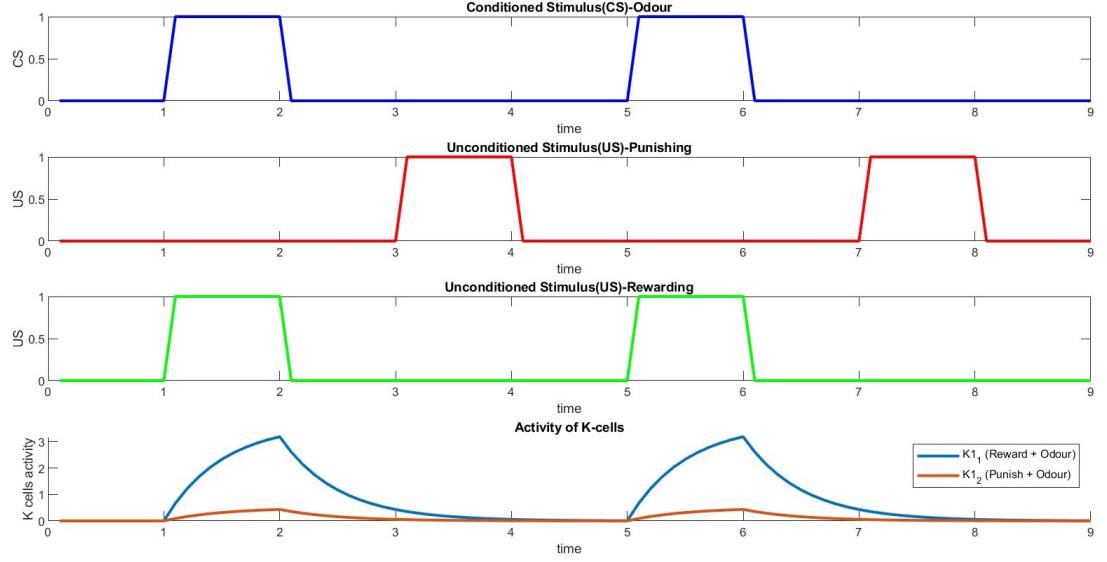


Figure 4: Response of K cell to the order of CS and US. As the coincidence detector, we defined a gain factor for the response of K cells. As seen in the last part of the figure, K cells that receive both CS and US together exhibit a significantly higher amplitude of response compared to those receiving CS alone.

2.4 M Cells

We defined the activity equations for M cells as follows:

$$\begin{aligned}
 M_0 &= \gamma k_1 - \beta M_2 \\
 M_t &= \frac{k_t}{k_{\frac{1}{2}}^2 + k_t^2} \\
 M_{t+1} &= M_0 + (M_t - M_0)(e^{-dt/\tau_M})
 \end{aligned} \tag{6}$$

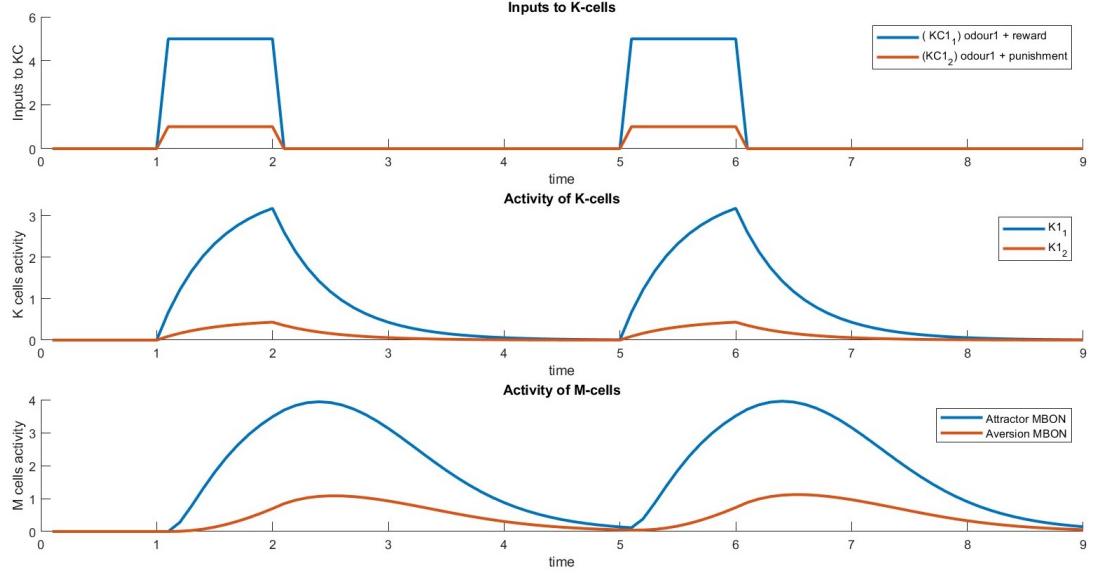


Figure 5: Activity of M cells in response to K cells' input. M cell responses to K cell activity with delay and accurately represent the amplitude of inputs.

3 Implementing Plasticity

Experimental studies have shown that synapses between K and M cells are the primary sites of plasticity in the mushroom body (Hancock et al., 2022). An appropriate plasticity rule for our system should encompass three key attributes:

1. It must incorporate the Hebbian rule.
2. It must account for extinction phenomena.
3. It must ensure system stability.

3.1 Simple Function

To assess whether our system can appropriately respond to synaptic alterations, we initially implemented a simple function that increases the coefficient from k_1 to M_1 with a constant term after each input, and decreases the coefficient from k_2 to M_2 .

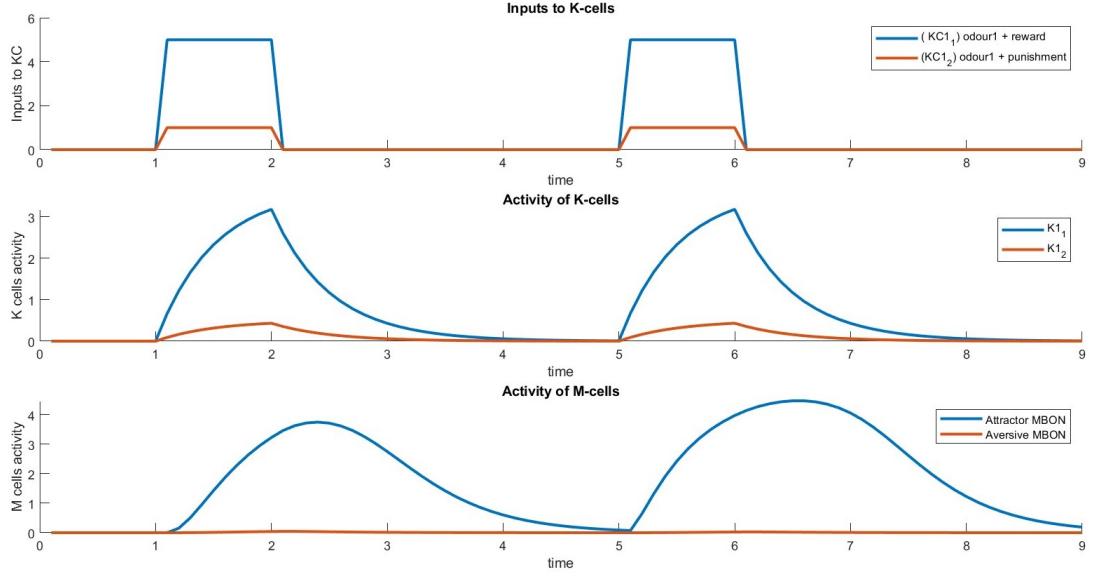


Figure 6: Implementation of the simple function

As shown in Fig18, implementing the simple function does indeed alter the response of M_1 to frequent inputs from k_1 to M_1 . Compared to Fig17, the activity of M_1 demonstrates a higher magnitude and a longer period of depolarization in response to the second input. By increasing the difference between the weights of M cell connections, the effect of mutual inhibition is enhanced, resulting in a reduced response of the M cell that doesn't receive CS and US simultaneously.

3.2 BCM

First, we applied the BCM (Bienenstock, Cooper, and Munro) rule (Bienenstock et al., 1982) to our system:

$$\begin{aligned}\tau_w \frac{dw}{dt} &= vu(v - \theta) \\ \tau_\theta \frac{d\theta}{dt} &= v^2 - \theta\end{aligned}$$

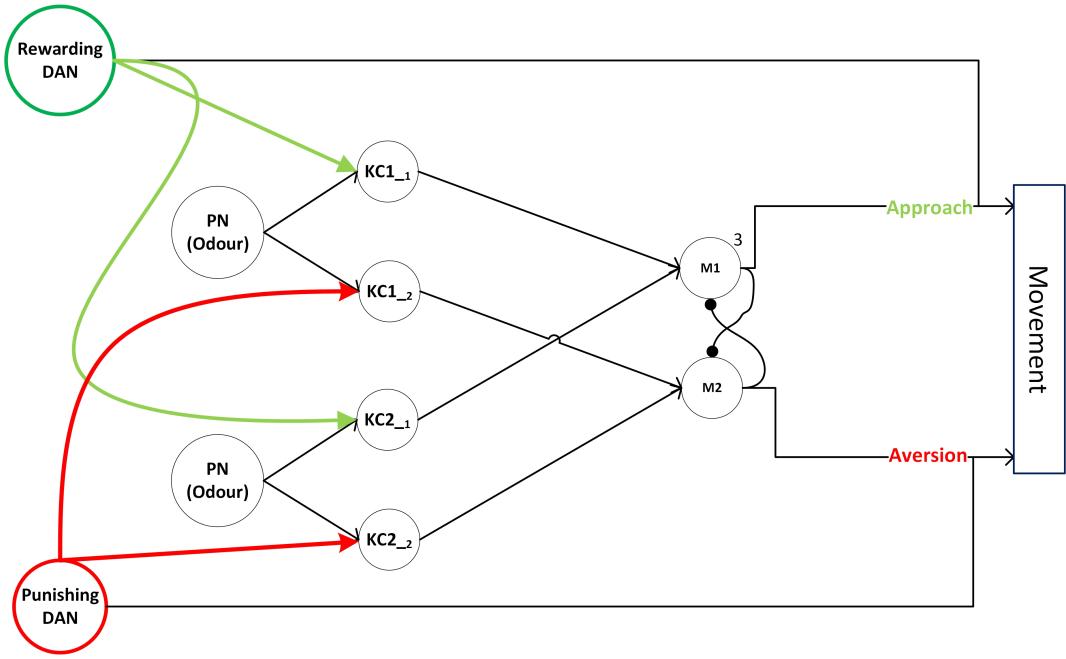


Figure 7: Schematic representation of the two-CS system. As depicted, each series of K cells connected to both types of M cells(attraction and aversion) to provide the ability for each CS to coupled with rewarding or Punishing US.

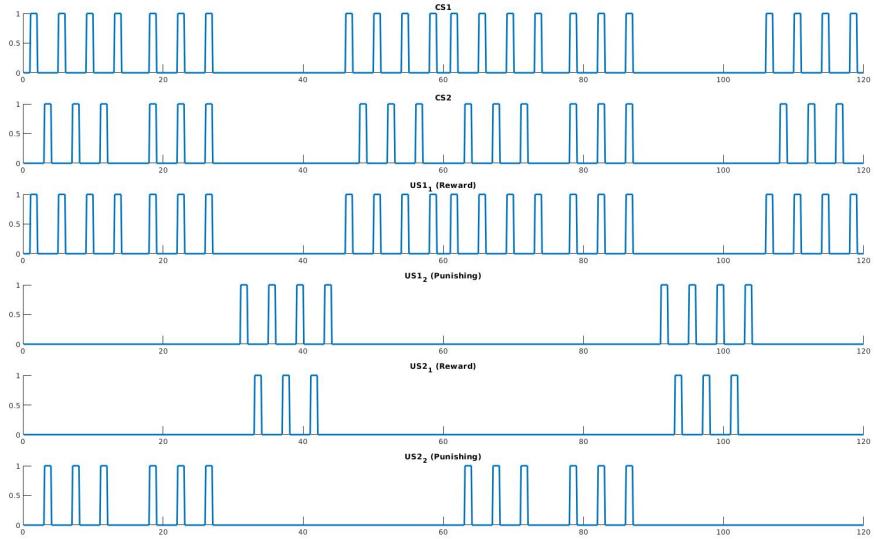


Figure 8: Sequences of CS and US. All of the K cells were introduced by the US (Rewarding or Punishing) but not at the same time for each series of K cells. Sequences designed somehow to first CS coupled more with rewarding the US and the second one with punishing.

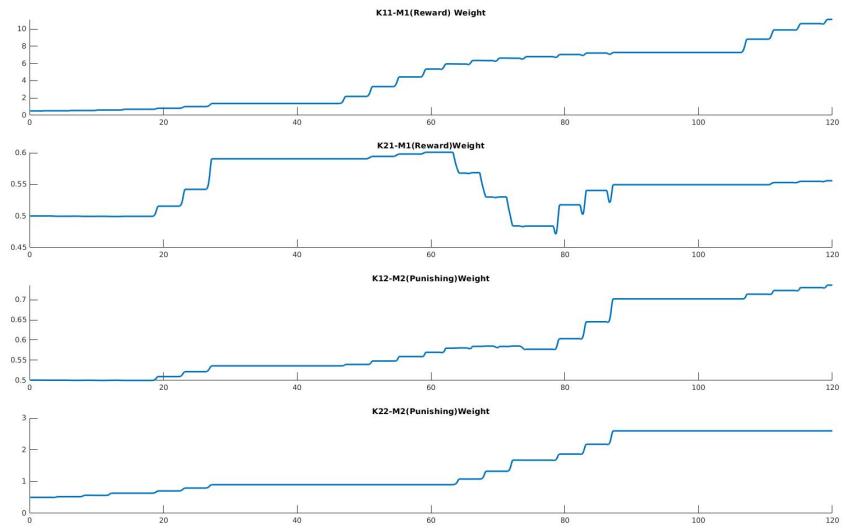


Figure 9: K cell-M cells synapses weight changes during time, implying BCM rule. As you could see, the weight of coupled synapses (first and last one) increased dramatically but for the others, increasing was slight.

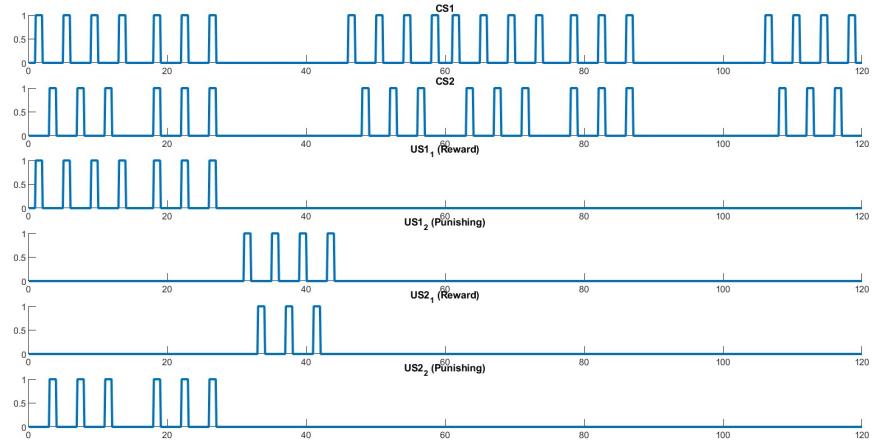


Figure 10: Stimulus sequence for evaluating extinction phenomena for BCM rule. Initially, CS coupled with the US exactly like the Fig20, but after that CS was introduced to the system solely.

the result of weight changes is as follows:

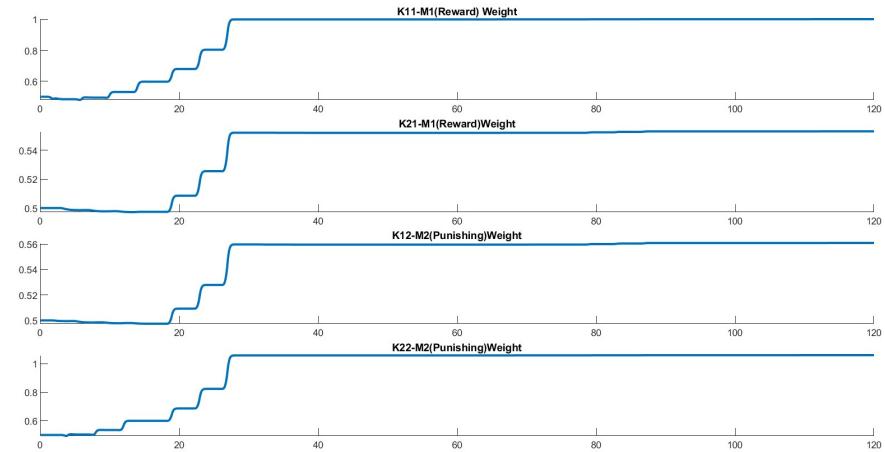


Figure 11: BCM rule's weight changes for extinction phenomena. after the initial training phase, by introducing CS solely, the weight of K-M synapses does not decrease (as expected) but remains at a steady level.

This rule is characterized by a Hebb-like product of the presynaptic activity and a nonlinear function, $\theta(v, \theta)$, of the postsynaptic activity, v . For low values of postsynaptic activity ($\theta < v$), θ is negative; for $\theta > v$, θ is positive. The rule stabilizes by allowing the modification threshold, θ , to vary as a super-linear function of the previous activity of the cell.

Initially, we introduced this rule to our two-KC system as shown in Fig 19. BCM defines plasticity based on the competition among different inputs to a specific synapse. As a result, our model did not provide a good estimation for the functionality of the BCM rule. To address this, we expanded our model to a two-odor system with four K cells (Fig 7). The sequence of CS and US was adjusted to introduce competition among different inputs (Fig 20). After implementation, we evaluated the effect of input on the weights between KCs and M cells (Fig 21). The weights of coupled synapses (e.g., $KC1_1 - M1$ and $KC2_2 - M2$) increased significantly, while the other connections showed only slight increases due to the low amplitude input from CS or US alone.

During our implementation, we discovered that if a neuron only excited with one specific input for an extended period, the effect would be anti-Hebbian.

Next, we evaluated the performance of the BCM rule on extinction phenomena. We changed the input such that during the initial period, the agent was trained with coupled CS and US, followed by CS presentation alone (Fig 10). The results of weight changes are shown in Fig 11. Contrary to our expectation, the weights of K-M synapses did not decrease during the non-coupled CS presentation, indicating that the BCM rule couldn't support extinction phenomena.

3.3 Short-Term Facilitation (STF)

STF refers to a phenomenon in which synaptic efficacy changes over time based on the history of presynaptic activity. STF is caused by calcium influx into the axon terminal after spike generation, which increases the release probability of neurotransmitters. We implemented STF using the following equations:

During synaptic events:

$$P_{eff} \rightarrow P_{eff} + f_F(1 - P_{eff}) \quad 0 \leq f_F \geq 1$$

Between synaptic events:

$$\tau_P \frac{dP_{eff}}{dt} = P_0 - P_{eff} \quad ,$$

$$P_{eff}(t) = P_0 + (P_{ini} - P_0)(e^{-dt/\tau_P})$$

By implementing this rule, we introduced the stimulus defined in Fig 20 to the system. Weight changes resulting from the STF rule are shown in Fig 12. This rule successfully supported both the Hebbian learning and extinction phenomena. However, implementing this rule with a continuous time scale poses a challenge. This becomes evident when evaluating the responses of M cells (Fig 13). Although the M cells exhibit qualitatively appropriate responses, their shapes do not appear satisfactory due to the discrete-time definition challenge.

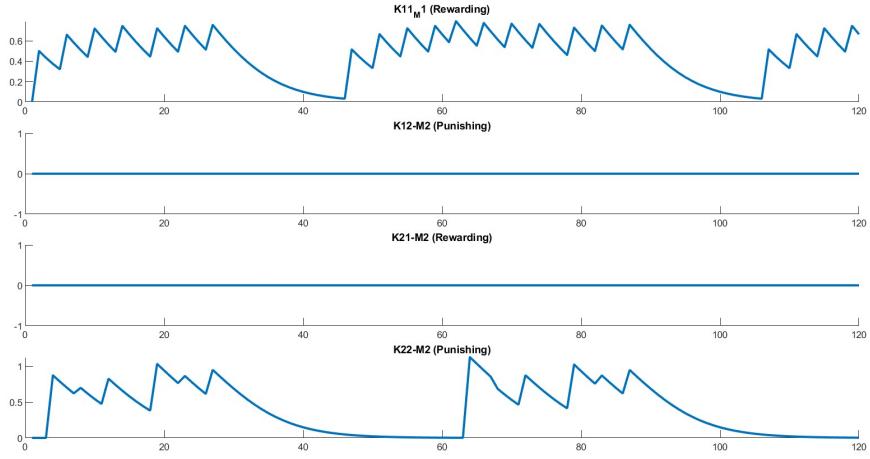


Figure 12: Weight changes for STF rule. We observed both Hebbian learning and extinction phenomena in this plot.

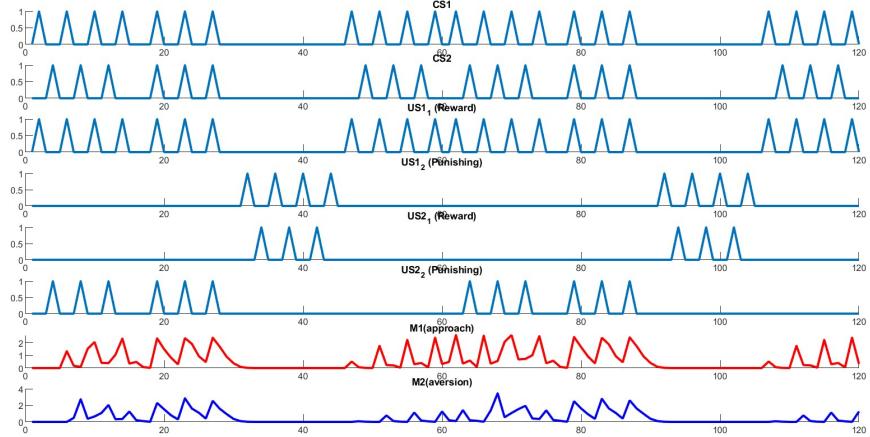


Figure 13: Stimulus and M cell responses. M cells respond appropriately to the coupled stimulus. Due to the discrete-time definition challenge, the shape of M cell responses does not seem optimal.

4 Extinction

Our simulation design involved a training phase (CS + US), followed by presenting the CS alone to assess whether the M cell continued firing even after the removal of the US. We expected our model to first exhibit Hebbian learning, maintaining firing post-US elimination, and to represent extinction phenomena - the synaptic weight between K-M cells decreasing with frequent CS presentation.

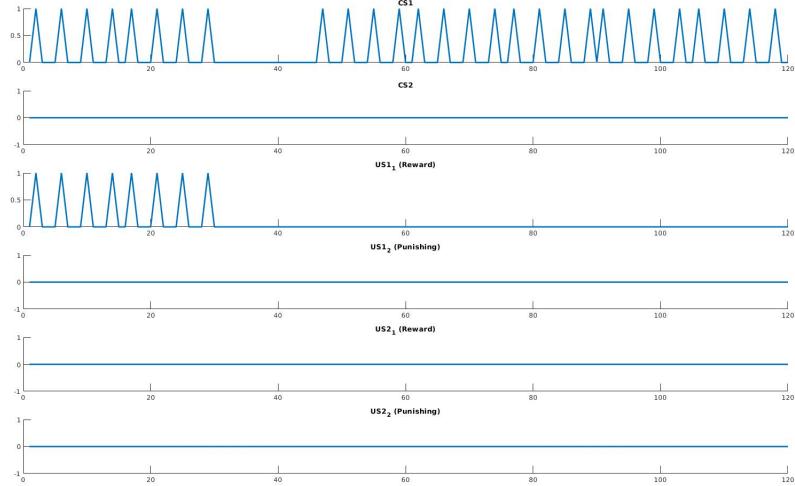


Figure 14: Stimulus used to simulate extinction phenomena.

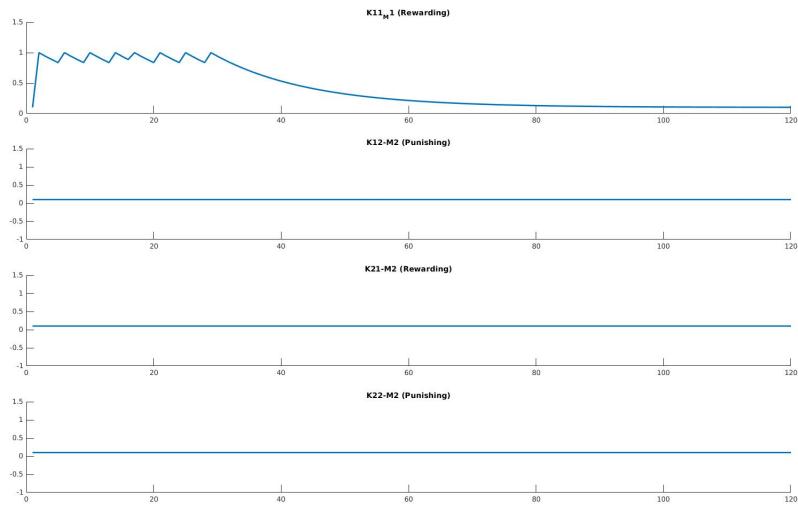


Figure 15: Plot of K→ M synaptic weight changes during extinction trials.

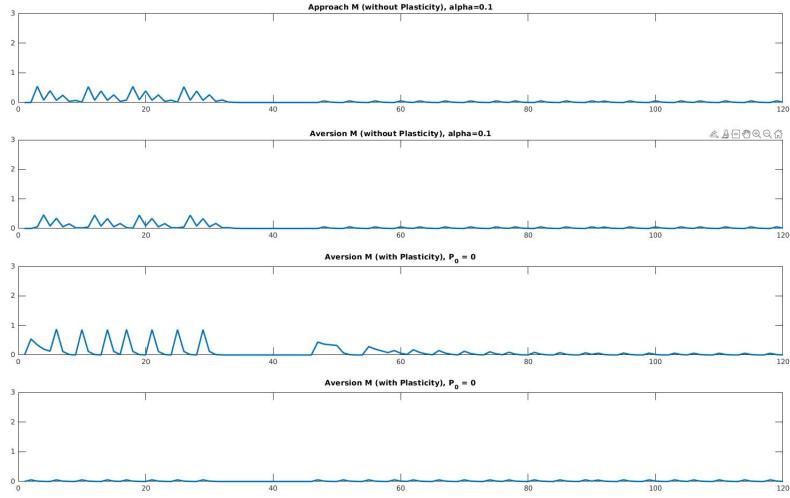


Figure 16: Plot of M cell activity. The upper rows depict non-plastic connections, while the lower rows depict plastic ones. The peculiar M cell shape during the test phase can potentially be adjusted by altering the M cell's activation function and time span.

As seen in Fig 16, the facilitated model shows extended firing during the CS unassociated test phase compared to the non-plastic model. Over time, the firing amplitude decreases after frequent unassociated stimulation.

Our next inquiry was whether, after extinction, our system could associate the previously presented CS with the opposite kind of US. We aimed to verify if our model retained its ability to represent dynamic environmental features.

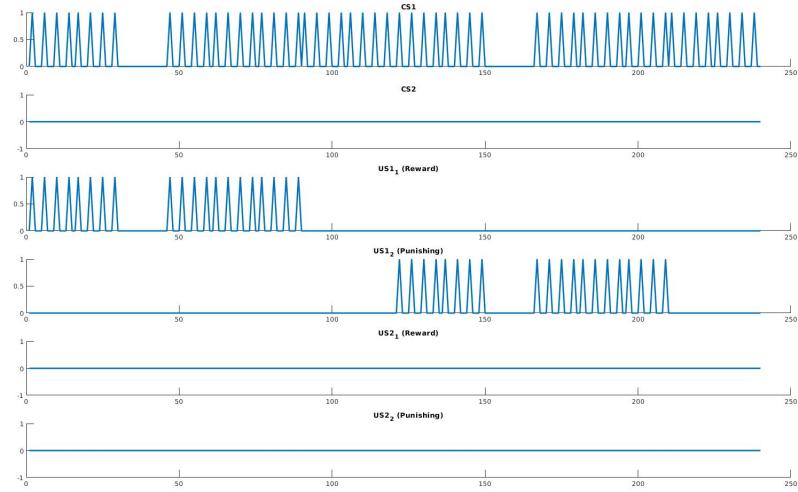


Figure 17: Stimulus sequence in the two-phase stimulation trial.

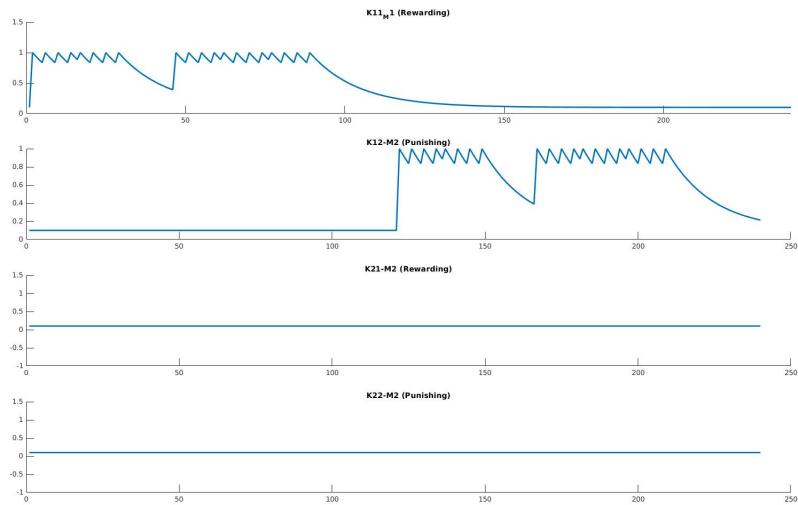


Figure 18: Synaptic weight changes in the two-phase stimulation trial.

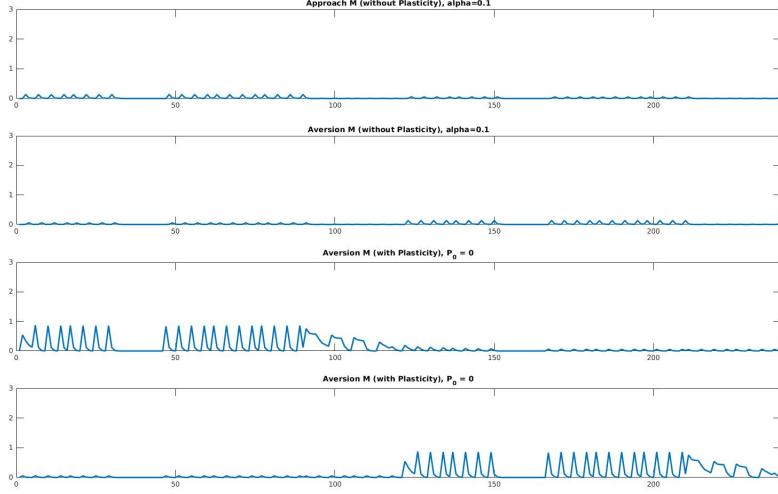


Figure 19: M cell activity in the two-phase stimulation trial.

While the environment lacks both opposite US (rewarding and punishing), our system displays the capacity to relearn novel situations. After the first training phase, the system undergoes forgetting (weight relaxation to initial values), priming itself for new associations.

5 Reciprocal Connection between K Cells and u

Mushroom body input neurons (MBINs) are Dopaminergic and Octopaminergic neurons that carry US signals to the MB. Recent studies revealed comparable K cell-MBIN connections (Eichler et al., 2017). KC-to-MBIN connections could potentially be depolarizing. Untrained odors can activate DANs in adult Drosophila (Riemensperger et al., 2005; Mao and Davis, 2009), akin to brief activations seen in monkeys, interpreted as salience signals (Schultz, 2015). Modulating KC-to-MBIN strength could explain DAN activation changes in Drosophila (Riemensperger et al., 2005; Mao and Davis, 2009), bees, and monkeys (Menzel, 2012; Schultz, 2015). Additionally, dopamine receptors within Drosophila KCs are crucial for memory formation (Waddell, 2013).

We introduce new connections by modifying the dynamical equations for K and u (MBIN) cells:

$$\begin{aligned}\frac{dk}{dt} &= -\alpha k(t) + \beta u(t) \\ \frac{du}{dt} &= -\alpha u(t) + \beta k(t)\end{aligned}\quad (7)$$

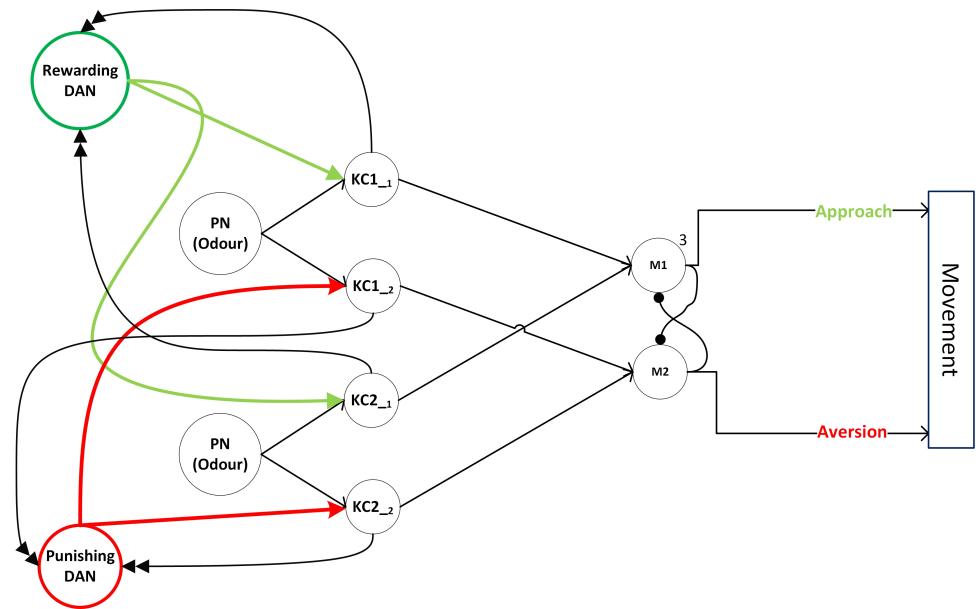


Figure 20: Schematic representation of the two-CS system with K-u-reciprocal-connection. K cell backpropagation affects the same u cell that introduces the US.

By employing the previous extinction stimulus (Fig 14), we examined the new connection's impact on the test phase.

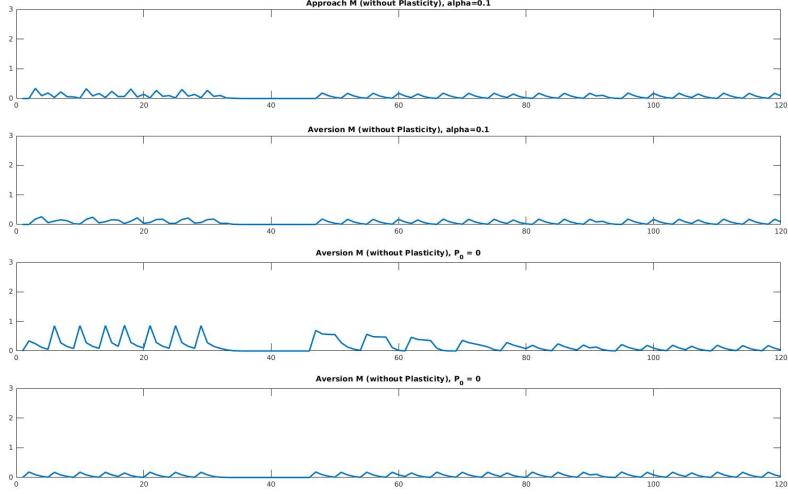


Figure 21: M cell activity in the $K \rightarrow u$ model. M cells in associated connection exhibit an extended firing period during the test phase compared to non- $K-u$ connections.

Fig 21 demonstrates the new model's prolonged response to the unassociated CS, unlike the non- $K-u$ connection model. Although the plasticity rule has not been introduced to $K-u$ connections yet, experimental evidence suggests its necessity.

Currently, our system replicates Hebbian and extinction phenomena but not conditioning and reverse conditioning. Moreover, the system can represent relief learning, where the CS following US termination associates with the opposite US effect (Mancini et al., 2019).

6 Backpropagation from M to u

Previous research reveals M cells innervate U cells within and outside the Mushroom body (Eichler et al., 2017). Feedback connections between MBONs and DANs exist in adult Drosophila (Ichinose et al., 2015). These M to U feed-across motifs potentially play roles in conflicting memory formation, reversal learning, and enhancing modulatory input flexibility (Das et al., 2014; Aso et al., 2014). Delayed M cell excitation to U could mimic reverse learning.

7 Dopaminergic Plasticity Rule

Various plasticity rules have been used to describe dopamine's effect on $k \rightarrow M$ synapses. Recent models implement reward prediction error (RPE), driven by the difference between output (MBON) and reinforcement (DAN) predictions (Zhao et al., 2021; Springer and Nawrot, 2021). Neuronal dynamics in fruit flies suggest neither Hebbian nor RPE rules perfectly capture MB plasticity (Schleyer et al., 2020). Investigating new plasticity rules approximating dopaminergic function is crucial.

The dopaminergic rule should fulfill certain conditions:

1. Ensure forgetting, saturation, and stability.
2. Coincidence of u and $k \rightarrow$ depression in $k \rightarrow M$.
3. u excitation $\rightarrow M$ excitation.
4. k excitation \rightarrow potentiation in $k \rightarrow M$.

8 Conclusion

In conclusion, our computational modeling effort aimed to replicate the complex biological network within the fruit fly's mushroom body, focusing on associative learning processes. Through an evolutionary approach, we constructed a primitive structure based on known anatomical and physiological findings. The Rescorla-Wagner learning rule served as the foundational framework, guiding our exploration of associative olfactory learning mechanisms.

We systematically introduced and tested various plasticity rules, aiming to capture essential features of biological synaptic plasticity. We began with simpler functions, progressing to more intricate models like the BCM rule and Short-Term Facilitation (STF). While some models exhibited Hebbian learning and extinction phenomena, challenges persisted, including the discrete-time definition and the lack of robustness in representing various aspects of associative learning, such as conditioning and reverse conditioning.

Our exploration extended to introducing reciprocal connections between K cells and modulatory input neurons (MBINs) and implementing backpropagation from output neurons (MBONs) to MBINs. These additional connections were inspired by biological findings and aimed to enhance the model's flexibility in representing diverse learning scenarios.

Furthermore, we delved into the challenging domain of dopaminergic plasticity rules, essential for capturing the intricate dynamics of reward prediction errors and reinforcement learning. Although no single plasticity rule perfectly replicated dopaminergic function, our efforts shed light on the complexities involved in bridging computational models with biological reality.

Despite the challenges faced and the limitations of our current model, our work serves as a stepping stone in understanding the intricate processes underlying associative olfactory learning. Moving forward, it is crucial to continue

refining our models, incorporating more nuanced plasticity rules, and integrating the wealth of experimental data becoming available. As our understanding deepens and computational power advances, we inch closer to unraveling the mysteries of how biological systems learn, adapt, and make predictions about their environments.

References

- Aso, Y., Sitaraman, D., Ichinose, T., Kaun, K. R., Vogt, K., Belliart-Guérin, G., Plaçais, P.-Y., Robie, A. A., Yamagata, N., Schnaitmann, C., et al. (2014). Mushroom body output neurons encode valence and guide memory-based action selection in drosophila. *Elife*, 3:e04580.
- Bienenstock, E. L., Cooper, L. N., and Munro, P. W. (1982). Theory for the development of neuron selectivity: orientation specificity and binocular interaction in visual cortex. *Journal of Neuroscience*, 2(1):32–48.
- Busch, S., Selcho, M., Ito, K., and Tanimoto, H. (2009). A map of octopaminergic neurons in the drosophila brain. *Journal of Comparative Neurology*, 513(6):643–667.
- Campbell, R. A., Honegger, K. S., Qin, H., Li, W., Demir, E., and Turner, G. C. (2013). Imaging a population code for odor identity in the drosophila mushroom body. *Journal of Neuroscience*, 33(25):10568–10581.
- Das, G., Klappenbach, M., Vrontou, E., Perisse, E., Clark, C. M., Burke, C. J., and Waddell, S. (2014). Drosophila learn opposing components of a compound food stimulus. *Current biology*, 24(15):1723–1730.
- Dickinson, A. (2001). Causal learning: Association versus computation. *Current Directions in Psychological Science*, 10(4):127–132.
- Eichler, K., Li, F., Litwin-Kumar, A., Park, Y., Andrade, I., Schneider-Mizell, C. M., Saumweber, T., Huser, A., Eschbach, C., Gerber, B., et al. (2017). The complete connectome of a learning and memory centre in an insect brain. *Nature*, 548(7666):175–182.
- Hancock, C. E., Rostami, V., Rachad, E. Y., Deimel, S. H., Nawrot, M. P., and Fiala, A. (2022). Visualization of learning-induced synaptic plasticity in output neurons of the drosophila mushroom body γ -lobe. *Scientific reports*, 12(1):1–14.
- Ichinose, T., Aso, Y., Yamagata, N., Abe, A., Rubin, G. M., and Tanimoto, H. (2015). Reward signal in a recurrent circuit drives appetitive long-term memory formation. *Elife*, 4.
- Jefferis, G. S., Potter, C. J., Chan, A. M., Marin, E. C., Rohlfing, T., Maurer Jr, C. R., and Luo, L. (2007). Comprehensive maps of drosophila higher olfactory centers: spatially segregated fruit and pheromone representation. *Cell*, 128(6):1187–1203.
- Kandel, E. R., Dudai, Y., and Mayford, M. R. (2014). The molecular and systems biology of memory. *Cell*, 157(1):163–186.
- Kim, Y.-C., Lee, H.-G., and Han, K.-A. (2007). D1 dopamine receptor dda1 is required in the mushroom body neurons for aversive and appetitive learning in drosophila. *Journal of Neuroscience*, 27(29):7640–7647.

- Liu, C., Plaçais, P.-Y., Yamagata, N., Pfeiffer, B. D., Aso, Y., Friedrich, A. B., Siwanowicz, I., Rubin, G. M., Preat, T., and Tanimoto, H. (2012). A subset of dopamine neurons signals reward for odour memory in drosophila. *Nature*, 488(7412):512–516.
- Mancini, N., Hranova, S., Weber, J., Weiglein, A., Schleyer, M., Weber, D., Thum, A. S., and Gerber, B. (2019). Reversal learning in drosophila larvae. *Learning & Memory*, 26(11):424–435.
- Mao, Z. and Davis, R. L. (2009). Eight different types of dopaminergic neurons innervate the drosophila mushroom body neuropil: anatomical and physiological heterogeneity. *Frontiers in neural circuits*, 3:5.
- Masse, N. Y., Turner, G. C., and Jefferis, G. S. (2009). Olfactory information processing in drosophila. *Current Biology*, 19(16):R700–R713.
- McGuire, S. E., Le, P. T., and Davis, R. L. (2001). The role of drosophila mushroom body signaling in olfactory memory. *Science*, 293(5533):1330–1333.
- Menzel, R. (2012). The honeybee as a model for understanding the basis of cognition. *Nature Reviews Neuroscience*, 13(11):758–768.
- Pech, U., Pooryasin, A., Birman, S., and Fiala, A. (2013). Localization of the contacts between kenyon cells and aminergic neurons in the drosophila melanogaster brain using splitgfp reconstitution. *Journal of Comparative Neurology*, 521(17):3992–4026.
- Quinn, W. G., Harris, W. A., and Benzer, S. (1974). Conditioned behavior in drosophila melanogaster. *Proceedings of the National Academy of Sciences*, 71(3):708–712.
- Riemensperger, T., Völler, T., Stock, P., Buchner, E., and Fiala, A. (2005). Punishment prediction by dopaminergic neurons in drosophila. *Current biology*, 15(21):1953–1960.
- Schleyer, M., Weiglein, A., Thoener, J., Strauch, M., Hartenstein, V., Weigelt, M. K., Schuller, S., Saumweber, T., Eichler, K., Rohwedder, A., et al. (2020). Identification of dopaminergic neurons that can both establish associative memory and acutely terminate its behavioral expression. *Journal of Neuroscience*, 40(31):5990–6006.
- Schultz, W. (2015). Neuronal reward and decision signals: from theories to data. *Physiological reviews*, 95(3):853–951.
- Springer, M. and Nawrot, M. P. (2021). A mechanistic model for reward prediction and extinction learning in the fruit fly. *ENeuro*, 8(3).
- Tempel, B. L., Bonini, N., Dawson, D. R., and Quinn, W. G. (1983). Reward learning in normal and mutant drosophila. *Proceedings of the National Academy of Sciences*, 80(5):1482–1486.

- Tomchik, S. M. and Davis, R. L. (2009). Dynamics of learning-related camp signaling and stimulus integration in the drosophila olfactory pathway. *Neuron*, 64(4):510–521.
- Waddell, S. (2013). Reinforcement signalling in drosophila; dopamine does it all after all. *Current opinion in neurobiology*, 23(3):324–329.
- Zhao, C., Widmer, Y. F., Diegelmann, S., Petrovici, M. A., Sprecher, S. G., and Senn, W. (2021). Predictive olfactory learning in drosophila. *Scientific reports*, 11(1):1–17.