

Dopamine for performance evaluation—Insights from songbirds

Vikram Gadagkar*

Department of Neuroscience, Zuckerman Mind Brain Behavior Institute, Columbia University,
New York, NY, United States

*Corresponding author: e-mail address: vg2481@columbia.edu

Introduction

Internally-guided reinforcement learning

Rumor has it that the great pianist Arthur Rubinstein was walking along the streets of New York when a pedestrian approached him and asked, “How do I get to Carnegie Hall?” Rubinstein pondered this for a second and said, “Practice!” Indeed, many of our motor skills are not innately programmed but are acquired through a process of trial and error, or practice. We all know that becoming an expert at singing, playing the piano, or excelling at tennis can take years, and sometimes a lifetime, of practice. Much of our understanding of the neural mechanisms underlying trial-and-error or reinforcement learning (RL) comes from the study of animals engaged in various tasks motivated by primary rewards like food or juice (Sutton & Barto, 2018). A rat in a box with a lever will learn, through trial and error, to press the lever for a food reward. Classic experiments in the 1950s by Olds and Milner showed that we can remove food from the equation if we hook up the lever to an electrode with which the rat can self-stimulate its dopamine neurons (Olds & Milner, 1954). In this case, the rat will learn to press the lever not for food, but for a pulse of dopamine.

We are all familiar with the addictive properties of dopamine but dopamine signals also seem ideally suited for trial and error or RL. Wolfram Schultz and colleagues recorded the response of midbrain dopamine neurons that project to the basal ganglia of a monkey that was trained to associate a light cue with a juice reward 1 s later (Schultz et al., 1997)—see also Chapter 18. Since the light was presented at random, the appearance of the light was a better-than-expected outcome or a positive prediction error and was signaled by a phasic activation in

dopamine neuron firing. One second later when the monkey expected juice, if the reward was withheld, that constituted a worse-than-expected outcome or negative prediction error and was signaled by a phasic suppression in dopamine neuron firing. In other words, these dopamine neurons encoded reward prediction error (RPE), the difference between actual and predicted reward. The phasic activations and suppressions of dopamine neuron firing are thought to positively and negatively reinforce preceding motor acts, thus leading to learning. The idea is that when dopamine increases, the motor actions that presumably led to the unexpected reward are positively reinforced, making them more likely to be repeated in the future; when dopamine decreases, the actions that led to an unexpected lack of reward are negatively reinforced, making them less likely to be repeated. The discovery of RPE has been highly influential and provides hope that other such general principles might be revealed by systems neuroscience. However, most of our motor skills such as speaking or playing a musical instrument, are not learned in the pursuit of immediate food or juice rewards; they are instead learned by comparing ongoing performance to internal goals. How are such internally-guided motor sequences evaluated by the brain?

The songbird is an ideal model for internally-guided reinforcement learning

Zebra finches do not learn to sing for primary rewards like food or juice. The adult zebra finch song is a naturally-learned, highly stereotyped, complex motor sequence. The song typically consists of 2–7 song elements called syllables, that are repeated again and again. Juvenile

male zebra finches, not unlike human infants (Doupe & Kuhl, 1999), begin their vocal journey with babbling, which lacks the spectral and temporal structure of adult song. Juvenile males memorize the song of an adult male tutor, often the father, to form an auditory template, and spend the next couple of months of their development learning to make a copy of the tutor's song (Fig. 22.1A) through a process that looks very similar to trial-and-error learning or practice (Doya & Sejnowski, 1995; Fee & Goldberg, 2011; Mackevicius & Fee, 2018; Tchernichovski et al.,

2001). How does the zebra finch brain accomplish this impressive feat?

Much of our understanding of the neural circuits underlying reward-based trial-and-error learning in mammals comes from the study of basal ganglia-thalamocortical loops including dopamine projections to the basal ganglia (Costa, 2007; Wickens et al., 2003). Many of these neural circuits are evolutionarily conserved (Colquitt et al., 2021; Pfenning et al., 2014) and zebra finches also possess basal ganglia-thalamocortical loops (Fig. 22.1B) with similar dopamine projections (Bottjer, 1993; Doupe et al., 2005). Zebra finches offer several advantages as a model system in neuroscience (Burke & Schmidt, 2020). First, song is a highly stereotyped and quantifiable behavior. Second, the zebra finch brain contains a discrete set of interconnected brain regions called the "song system" that is dedicated to learning and producing song. Third, these brain regions are organized into tight clusters of cells called nuclei that permit targeted recording and manipulation (Fig. 22.1C). Similar to the dopamine projections to the basal ganglia in mammals, we focus here on the projection from the ventral tegmental area (VTA) to the singing-related basal ganglia nucleus Area X (VTA_X), more than 95% of which is dopaminergic (Person et al., 2008). Motivated by the mammalian literature on external RPE, it had been hypothesized that these dopamine neurons in VTA could transmit a conceptually similar error signal for song learning, even though song is internally evaluated (Fee & Goldberg, 2011; Kubikova & Košál, 2010).

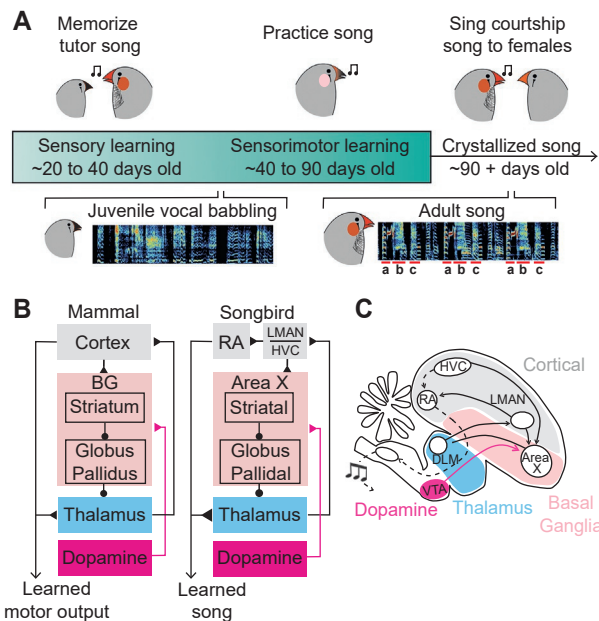


FIG. 22.1 The songbird as a model for internally-guided reinforcement learning. (A) The zebra finch song-learning process. Juvenile male zebra finches first memorize the song of their tutor during the sensory phase, then learn to make a copy of the tutor's song with practice during the sensorimotor phase, and ultimately perform the song to females during courtship in adulthood. Juvenile vocal babbling lacks the spectral and temporal structure and stereotypy of adult song, which consists of repeated motifs of ~2–7 song syllables. (B) The song system consists of basal ganglia-thalamocortical loops including a dopamine projection to the basal ganglia nucleus Area X. These circuits are evolutionarily conserved and correspond to mammalian circuits extensively studied in the context of reward-based RL. (C) Schematic representation of the avian song system. The motor pathway (*dashed lines*) consists of the projection from HVC to RA. A second input to RA comes from LMAN, the output nucleus of the anterior forebrain pathway (AFP) required for song learning (*solid black lines*). The AFP consists of a basal ganglia-thalamocortical loop spanning Area X, DLM, and LMAN. Note the dopamine projection from the nucleus VTA to Area X (*magenta line*). The stereotypy of song, a naturally learned complex motor sequence, the presence of a dedicated neural circuit for the learning and production of song, and the nucleated brain structures permitting targeted recording and manipulation, make the songbird an ideal model system for internally guided RL. HVC, proper name; RA, robust nucleus of the arcopallium; LMAN, lateral magnocellular nucleus of the anterior nidopallium; DLM, dorsolateral thalamus, medial part; VTA, ventral tegmental area. *No permission required.*

Dopamine neurons encode performance prediction error in singing birds

To test if dopamine neurons convey an error signal for song learning (Fig. 22.2A), Gadagkar et al. recorded from antidromically identified Area X-projecting VTA neurons (Fig. 22.2B) in singing birds while changing the perceived quality of particular song syllables (Gadagkar et al., 2016). To change song quality, the authors used a distorted auditory feedback (DAF) paradigm, where 50% of the renditions of a particular target syllable were distorted with auditory feedback (Fig. 22.2C and D). To ensure that the feedback sounded similar to a normal zebra finch song, they took a 50 ms snippet of a different syllable and played it over the target syllable. The specific hypothesis was that a distorted syllable sounds wrong or worse than expected to the bird and should cause negative prediction error signals. VTA_X neurons were suppressed after distorted syllables, consistent with a negative prediction error. Remarkably, these same neurons were activated after undistorted target syllables even though these syllable renditions were left completely unmodified (Fig. 22.2E and F). Their interpretation was that since 50% of the renditions of

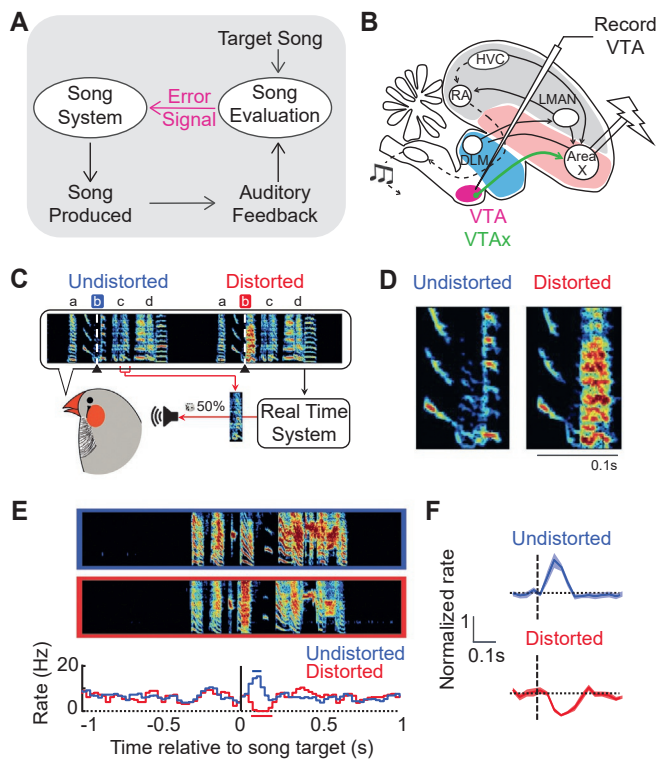


FIG. 22.2 Dopamine neurons encode performance prediction error. (A) Juvenile zebra finches memorize a tutor (target) song and need to listen to themselves (auditory feedback) to learn their songs. It had been hypothesized that a comparison of the auditory feedback of ongoing song to the stored memory of the target song (template) results in an “error signal” that is used for song learning via reinforcement. (B) Neurons that project from VTA to Area X (VTA_X) were antidromically identified. A stimulation electrode was used to activate Area X and a backpropagating antidromic signal was recorded on the recording electrode to confirm the projection. (C) Example of displaced distorted auditory feedback (DAF). A 50 ms snippet of syllable “c” was played back with a speaker during the production of target syllable “b” (target time, *black triangles*, and *white dashed lines*). Randomly interleaved renditions of the target syllable were left undistorted (*distorted target syllable*, *red box*; *undistorted target syllable*, *blue box*). (D) Expanded view of the target syllable showing an undistorted rendition (*left*) and a distorted rendition (*right*). (E) Example VTA_X neuron showing performance prediction error (PPE). Undistorted song motif (*blue box*), distorted song motif (*red box*), and firing rate histograms for undistorted (*blue*) and distorted (*red*) motifs aligned to the song target time. Horizontal bars, significant deviations from baseline. This neuron was suppressed after distortions and activated at the precise timepoint in the song when a distortion might have occurred but did not. (F) Normalized responses to undistorted (*top*) and distorted (*bottom*) syllables for 17 error-encoding neurons (*line and shading*, mean \pm SEM). Adapted from Gadagkar, V., Puzerey, P. A., Chen, R., Baird-Daniel, E., Farhang, A. R., & Goldberg, J. H. (2016). Dopamine neurons encode performance error in singing birds. *Science*, 354(6317), 1278–1282.

the target syllable were distorted with feedback, the expected quality of the target syllable was lowered for the bird; an undistorted target syllable thus sounded better-than-expected to the bird and was signaled by a phasic dopamine activation.

If this interpretation of the dopamine activation after undistorted target syllables as a better-than-expected signal is correct, the magnitude of the dopamine activation should depend on the probability of error. If the probability of error is high, an undistorted syllable is more surprising and should cause a higher dopamine activation; if the probability of error is low, an undistorted target syllable is less surprising and should lead to a lower dopamine activation. To test this specific hypothesis, Gadagkar et al. next performed a “two-target” experiment, where they recorded the activity of VTA_X neurons while distorting two different target syllables, Target-1 50% of the time, as before, and an additional Target-2 only 20% of the time. Consistent with this hypothesis, they observed a significantly smaller activation in VTA_X neuron firing for the less surprising undistorted Target-2 compared to the more surprising undistorted Target-1. These results suggest that birds not only compare their ongoing song to the template or goal but also to their recent practice; i.e., whether their current song is closer or farther away to the ultimate goal (the template) compared to recent practice. Such a comparison to recent practice could allow small improvements toward the goal to be reinforced even if the current performance is distant from the ultimate goal, as in a juvenile early in learning. Thus, similar to RPE in mammals, VTA_X neurons in zebra finches encode a better-than-expected and worse-than-expected dopamine signal, not for external rewards like food for juice but instead for performance outcomes—whether the bird’s own performance is better or worse than expected. These dopamine signals are therefore called performance prediction errors (PPE). The discovery of PPE identified the long-sought-after error signal for song learning and more broadly showed that the principle of dopaminergic prediction error (and the brain’s reward circuitry) can generalize to the internally-guided learning of complex motor sequences. Just as RPE serves to reinforce behaviors that maximize rewards, PPE can be used to reinforce high-quality motor performance. In this conceptualization, a better-than-expected motor performance (relative to an internal goal or standard) can be thought of as intrinsically “rewarding,” similar to how unexpectedly received food or juice is rewarding.

Optogenetic dopamine activation is sufficient to drive changes in song

In the distorted auditory feedback paradigm as implemented by Gadagkar et al. above, target syllables were randomly distorted with a certain probability, independent of any features of the syllables produced. This was to ensure that the observed dopamine response could be attributed exclusively to the auditory feedback and not

to any aspect of motor production. However, previous studies have demonstrated that if auditory feedback is provided contingent on the pitch of a target syllable, birds learn to modify the syllable pitch (Figure 22.3A) to avoid feedback (Andalman & Fee, 2009; Tumer & Brainard, 2007). For example, if low-pitch syllable variants are distorted with feedback, birds move the pitch up within hours, and vice versa. This paradigm, called contingent auditory feedback (CAF), suggests that birds can use auditory feedback as an “error signal” to modify their songs. The discovery of dopaminergic PPE (Gadagkar et al., 2016) now

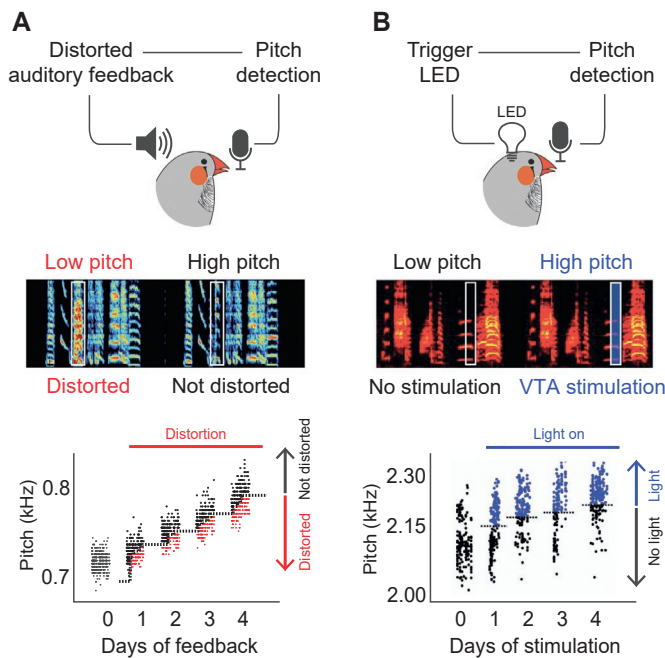


FIG. 22.3 Optogenetic stimulation of dopamine neurons drives song changes. (A) Contingent auditory feedback (CAF) drives learning. Schematic representation of the CAF protocol (top). The pitch of a target syllable is monitored continuously and whenever the measured pitch falls below a set threshold, the syllable is distorted with auditory feedback. Spectrogram of example song renditions (middle). Undistorted target syllable (left) and distorted target syllable (right) are shown enclosed in a white box. CAF-induced pitch changes in the target syllable (bottom). Each dot represents the mean pitch of a target syllable rendition. Target syllable renditions with the pitch below the threshold (dotted line) were distorted. (B) Schematic representation of optogenetic stimulation protocol (top). The pitch of a target syllable is monitored continuously and whenever the measured pitch falls above a set threshold, VTA axon terminals in Area X were activated. Spectrogram of example song renditions (middle). Low-pitch rendition (left) did not trigger optogenetic stimulation while a high-pitch rendition (right) triggered stimulation (target syllable enclosed in white box). Optogenetic stimulation-induced pitch changes in the target syllable (bottom). Each dot represents the mean pitch of a target syllable rendition. Target syllable renditions with a pitch above the threshold (dotted line) triggered stimulation. (A) Adapted from Gadagkar, V., Puzerey, P. A., Chen, R., Baird-Daniel, E., Farhang, A. R., & Goldberg, J. H. (2016). Dopamine neurons encode performance error in singing birds. *Science*, 354(6317), 1278–1282. (B) Adapted from Mooney, R. (2022). *Birdsong*. *Current Biology*, 32 (Original work published 2022).

provides a neural mechanism for the behavioral song modifications seen in CAF experiments, that distortion-induced dopamine suppressions (and activations on undistorted syllable renditions) lead to the observed pitch changes. Consistent with this hypothesis, lesions to the dopamine input to Area X in a related songbird, the Bengalese finch, reduced the magnitude of CAF-induced pitch changes (Hoffmann et al., 2016).

If the distortion-induced pitch changes are indeed caused by dopamine suppressions, it should be possible to modify syllable pitch by pitch-contingent dopamine activation. To investigate whether dopamine can drive changes in song, two independent groups optogenetically activated or inhibited VTA_X neurons in a pitch-contingent manner (Hisey et al., 2018; Xiao et al., 2018). Stimulating VTA_X terminals in Area X was sufficient to drive changes in syllable pitch toward the targeted frequencies (Fig. 22.3B); decreasing the activity of VTA_X terminals moved the pitch away from the targeted frequencies, consistent with the expectation from the VTA_X neuron firing observed in the feedback experiments described above. Furthermore, D1 receptor antagonists blocked these dopamine-dependent song changes. These optogenetic experiments elegantly demonstrated that dopamine signals to the song system basal ganglia Area X are sufficient to drive changes in song, complementing the correlational electrophysiological recordings of a dopamine PPE in VTA_X neurons (Gadagkar et al., 2016).

Dopamine neurons evaluate natural fluctuations in performance quality

If dopamine encodes performance prediction error, spontaneous dopamine activity should evaluate natural fluctuations in behavior, independent of any experimentally induced perturbations. In other words, dopamine should act as a real-time performance monitor during ongoing behavior. The Gadagkar et al. study showing that dopamine encodes PPE (Gadagkar et al., 2016) used an external sound to control song quality, thus raising the question of whether the dopamine system is simply using song timing to develop an expectation about the external DAF sound; the dopamine system would need to evaluate the quality of natural fluctuations of song for song learning. To directly address this question, Duffy et al. looked for significant relationships (Fig. 22.4A) between spontaneous VTA_X firing and natural (unperturbed) fluctuations in ongoing song (Duffy et al., 2022). They parametrized natural song into a low-dimensional set of eight song features (Fig. 22.4B) and used a Gaussian process (GP) regression model to fit the relationships between rendition-to-rendition fluctuations in song

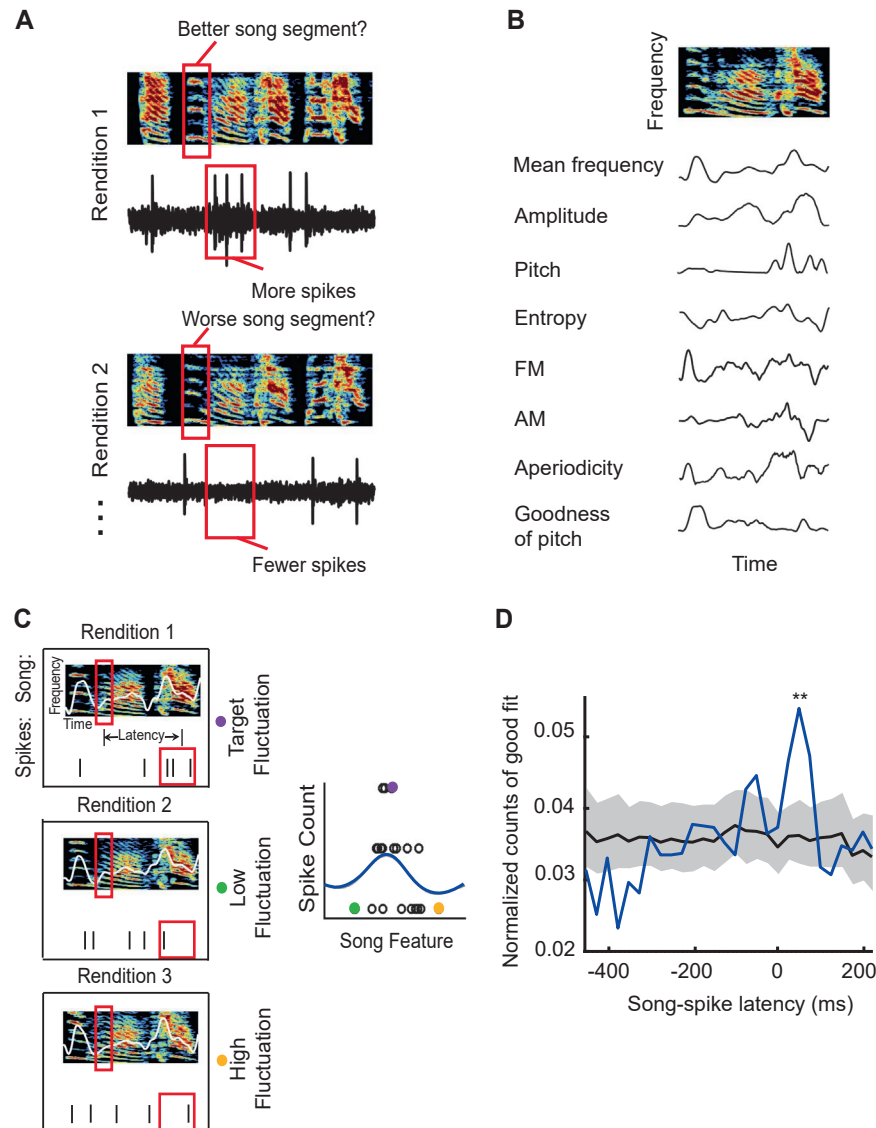


FIG. 22.4 Dopamine neurons evaluate natural variations in performance quality. (A) Schematic representation of the hypothesis that natural variations in song quality should also result in dopamine error responses. If dopamine has a reinforcing effect on performance, a “better” song segment should lead to more spikes and a “worse” song segment should lead to fewer spikes. Song windows and spike windows are shown in red boxes. (B) Natural song syllables (song syllables that were never distorted) were parametrized into eight time-varying song features. (C) Schematic representation of fitting natural song fluctuations to spike counts within the specific song and spike time windows (red boxes). Local song feature values (white line represents a single song feature for illustration) were used to predict local spike counts after a brief latency using a Gaussian process (GP) model. If a bird is trying to maintain its song, the “target” feature value should result in more spikes, and deviations from this target should lead to fewer spikes. A spike count-song feature plot is expected to have a peak at the target song feature value (right), which can be fit with the GP model (blue line). Such fits were generated for all song features and all natural syllables recorded in the dataset. (D) The latency distribution of predictive fits over 22 error-encoding VTA neurons shows a significant peak in the number of responses at a positive latency of about 50 ms (** $P < 0.01$). The blue line shows real data and the black line with gray shading shows the mean \pm SD for shuffled data, where the syllable renditions and spike trains were shuffled. A positive latency is consistent with an evaluative process and 50 ms is consistent with the latencies observed in the DAF experiments. Adapted from Duffy, A., Latimer, K. W., Goldberg, J. H., Fairhall, A. L., & Gadagkar, V. (2022). Dopamine neurons evaluate natural fluctuations in performance quality. *Cell Reports*, 38(13).

feature values and VTA_X spike counts. By binning both song feature values and spike count in sliding windows, they asked if significant relationships between song features and spike counts exist and if so, at what song-spike latencies they occur (Fig. 22.4C). Across all

recorded VTA_X neurons and all natural (unperturbed) syllables, they found that song variations were most predictive of spiking at a positive latency of 0–100 ms (Fig. 22.4D). A positive latency is consistent with an evaluative (as opposed to a premotor) process since

the predicted spikes occur after the song fluctuation. Furthermore, the latency of 0–100 ms was remarkably similar to the observed latencies to DAF perturbations (0–150 ms) in the feedback experiments (Gadagkar et al., 2016). Taken together, these results showed that dopamine neuron firing evaluates natural fluctuations in song quality (with a PPE-like response) independent of any external feedback or perturbations.

If VTA_X neurons evaluate natural fluctuations in song quality, this leads to predictions about the form of the song-spike relationships. If a bird is trying to maintain its song, typical variations should be followed by more spikes and deviations should be followed by fewer spikes (a “stabilizing” form). On the other hand, if the bird is trying to make modifications to its song, the form should be “directional,” with more spiking in the direction of the desired modification and less spiking in the opposite direction. Assuming there is a single “best” version of the song, we do not expect multiple spiking maxima in a “disruptive” form. Duffy et al. next investigated the tuning curve shapes of the song-spike relationships using generalized linear models (GLM) with both linear and quadratic features. The predominant form of song-spike relationships was found to be either directional or stabilizing, consistent with the hypothesis that a PPE-like signal should respond most strongly to a single “best” version of song. In other words, the form of the song-spike relationships was consistent with the birds either maintaining or making small corrections to their songs. These results provide strong evidence from both the timing and the tuning properties, that dopamine neuron firing can evaluate the performance of a natural behavior, independent of any external perturbation.

Dopaminergic error signals retune to social feedback during courtship

The studies discussed in the previous sections demonstrate that just as dopamine RPE signals could allow hungry or thirsty animals to approach and learn from food- or water-predicting cues, dopamine PPE signals could enable internally-guided learning of complex motor sequences (see also Chapter 21). Dopamine prediction error signals have also been observed in response to social outcomes, suggesting that dopamine could mediate reinforcement across a wide range of behaviors (Dai et al., 2022; Hu et al., 2021; Solié et al., 2022; Xie et al., 2023). The generality of dopamine reinforcement mechanisms raises the question of how dopamine can evaluate outcomes in complex environments with multiple objectives. Roeser and Gadagkar et al. addressed this question by using dopamine fiber photometry (Sun et al., 2018) to record dopamine responses in male zebra finches that were simultaneously thirsty,

sexually motivated, and actively practicing their songs (Roeser, Gadagkar, et al., 2023). They tested two mutually inclusive hypotheses. First, dopamine signals could be dynamically modulated to suit the current priority (Allen et al., 2019; Sakata & Brainard, 2009); for example, dopamine signals to water cues could retune to social outcomes if courtship is a higher priority than thirst. Second, different dopamine pathways could be anatomically segregated based on objective (Menegas et al., 2018); for example, singing-related error signals could be routed specifically to striatal areas dedicated to vocal communication.

By recording dopamine signals associated with quenching thirst, singing a good song, and courting a mate while male zebra finches could retrieve water, evaluate song, or court a female (Fig. 22.5A and B), Roeser and Gadagkar et al. found evidence to support both hypotheses. When male zebra finches were alone, water reward-related dopamine signals were observed in both Area X and a striatal region MST that is not connected with the nucleated song system and receives dopamine input from a separate group of neurons in VTA (Person et al., 2008; Ramarao et al., 2023). And remarkably, when courting a female, water-related dopamine responses as well as dopamine song performance error signals diminished (Figure 22.5C). The observation that dopamine reward and performance error signals are reduced while singing to a female suggests the possibility that the dopamine system becomes retuned to new outcomes, such as positive feedback from the female during courtship. Female zebra finches do not sing but produce short vocalizations called “calls” that are thought to provide affiliative feedback and reinforcement for bonding, suggesting they may influence the dopamine system (Hernandez et al., 2016; Zann, 1996). They found that while female calls that were produced when the male was not singing resulted in small and unreliable responses in Area X and MST, female calls that overlapped with male song evoked large and reliable dopamine release but primarily in Area X (Figure 22.5D and E). These results suggest that the dopamine system handles coexisting drives with two different mechanisms. First, anatomically distinct dopamine pathways can carry different signals; water reward signals were broadcast to both striatal regions while vocal performance signals were routed to Area X, the specific striatal area specialized for communication. Second, dopamine signals can be flexibly retuned to the highest or current objective; both water reward and song-related performance error signals were diminished and dopamine was instead activated by male song-aligned female calls during courtship. More broadly, these results suggest that the dopamine self-evaluation system, active during solo “practice,” may be turned down during audience-directed “performance” and dopamine could instead become tuned to social feedback from the audience.

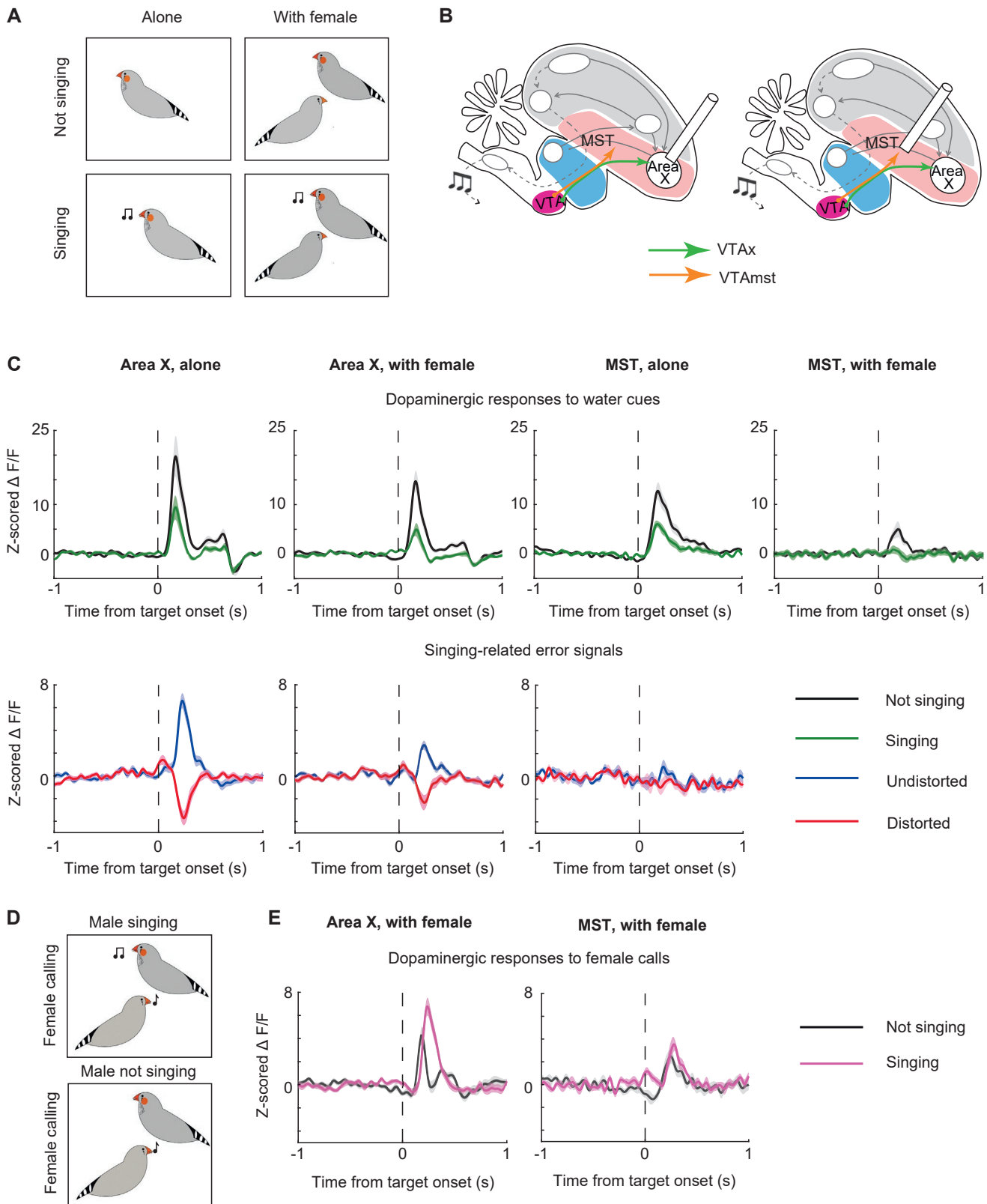


FIG. 22.5 Dopaminergic error signals retune to social feedback during courtship. (A) Dopamine responses to water cues and singing-related error signals were recorded in two striatal regions, Area X and MST, in four conditions: when adult male zebra finches were alone and not singing, alone and singing, with a female and not singing, and with a female and singing female-directed song. (B) Zebra finch brain schematics showing the two recording sites for dopamine fiber photometry. Area X is the singing-related basal ganglia that receives a dopamine projection from VTA; the medial striatal area (MST) is a region that lacks connectivity with the nucleated song system and receives a projection from a separate group of dopamine neurons in the VTA. (C) Dopamine responses to water cues (*top row*) and singing-related error signals (*bottom row*) are diminished during courtship. While dopamine responses to water cues were found in both Area X and MST, singing-related error signals were observed only in Area X. *Line and shading*, mean \pm SEM. (D) Dopamine responses to female calls were recorded during female-directed singing and nonsinging periods. (E) Dopamine responses to female calls were substantially higher when the calls overlapped ongoing song than during nonsinging. Dopamine responses to female calls, similar to singing-related error signals, were primarily observed in Area X. *Line and shading*, mean \pm SEM. Adapted from Roeser, A., Gadagkar, V., Das, A., Puzerey, P. A., Kardon, B., & Goldberg, J. H. (2023). Dopaminergic error signals retune to social feedback during courtship. *Nature*, 623(7986), 375–380.

Future directions: The causes and consequences of dopamine performance error

Does dopamine guide vocal learning during development?

RL algorithms have contributed to some of the biggest recent advances in artificial intelligence and machine learning (Botvinick et al., 2019), from mastering Chess and Go (Schrittwieser et al., 2020) to the automated discovery of novel algorithms (Fawzi et al., 2022)—see also Chapters 24 and 26. Although dopamine has long been thought to also underlie the acquisition of motor skills through reinforcement in biological systems (Markowitz et al., 2023), directly testing this has been challenging. The discovery of a dopaminergic PPE in adult birds (Gadagkar et al., 2016) strongly suggests that dopamine guides vocal learning during development, in line with decades of speculation on the role of dopamine in the song-learning process. To investigate the role of VTA_X neurons in juvenile song copying, Hisey et al. (2018) used an intersectional genetic method to ablate these neurons during development. They found that birds with VTA_X neurons ablated during the sensorimotor phase made significantly worse copies of their tutor song compared to controls. Next, they found that infusing a D1-receptor antagonist into Area X during the sensorimotor phase prevented the song from improving during the infusion period, further supporting the role for dopamine in song learning. We are now in a position to directly test the role of dopamine in the vocal learning process. Complete vocal trajectories of song learning can be recorded in the lab, and recent advances in supervised and unsupervised computational methods permit low-dimensional parametrizations of these vocalizations (Duffy et al., 2022; Goffinet et al., 2021). Concurrent advances in dopamine recording techniques such as dopamine fiber photometry (Sun et al., 2018) now allow the simultaneous monitoring of vocalization-aligned dopamine transients in Area X (Roeser, Gadagkar, et al., 2023). Datasets of song learning trajectories and associated dopamine levels will allow us to directly test if dopamine guides vocal learning during development. Recording dopamine levels associated with the developmental trajectory of a complex natural behavior will also help identify the kind of RL algorithms used by the brain for motor skill learning (Kollmorgen et al., 2020; Toutounji et al., 2024; Wood, 2021).

How is the dopamine performance error signal constructed?

The discovery that VTA_X neurons encode PPE (Gadagkar et al., 2016) presents an opportunity to

delineate how neural circuits construct the error signal. To signal PPE, these circuits must perform a moment-by-moment comparison of the ongoing song not just to the template but also to a timestep-dependent prediction of song quality. Ever since imitative learning was described in songbirds almost six decades ago, the hunt has been on for the auditory template (Konishi, 1965; Marler, 1970), but now for the first time, we have access to the end result of the comparison involving the template, which is the error signal (Gadagkar et al., 2016). Can we trace our way back from the dopamine PPE signal to uncover how neural circuits make predictions and comparisons (Chen & Goldberg, 2020) for motor skill learning? The first step would be to investigate the contributions of the inputs to VTA. One major input is from a high-order auditory cortical area called ventral intermediate arcopallium (AIV) which is necessary for song learning and sends error signals to VTA (Bottjer et al., 2000; Mandelblat-Cerf et al., 2014). A second prominent input to songbird VTA comes from the ventral pallidum (VP), which is also required for song learning and exhibits performance error signals (Chen et al., 2019). Kearney et al. found that pitch-contingent optogenetic stimulation of AIV_{VTA} terminals negatively reinforces syllable pitch while stimulation of VP_{VTA} terminals positively reinforces syllable pitch (Kearney et al., 2019), suggesting that these inputs drive opposing effects on VTA neurons, consistent with previous electrophysiological results. Other inputs to VTA such as the subthalamic nucleus (STN) and lateral habenula (LHb) have also been shown to be involved in song learning and error computation (Das & Goldberg, 2022; Roeser, Teoh, et al., 2023). Elucidating the circuitry that connects auditory areas to VTA enabling the storage and comparison of the template and generation of expectations of song will have important implications well beyond song learning for the neural basis of procedural memories and skill learning (Ikeda et al., 2020).

How is the dopamine performance error signal used for song learning?

Although dopamine prediction error signals are thought to positively and negatively reinforce preceding motor actions for learning, the mechanisms by which downstream basal ganglia-thalamocortical loops use these error signals are an active area of research (Costa, 2007; Wickens et al., 2003)—see also, e.g., Chapters 15, 21, and 26. Even the precise relationships between the activity of medium spiny neurons (MSNs) in the striatum and behavior is a topic of intense debate (Singh Alvarado et al., 2021). The discovery of a dopamine PPE (Gadagkar et al., 2016), along with the advantages of the birdsong system, provides a unique opportunity to address these

questions. First, the zebra finch song is highly stereotyped, permitting precise correlations between neural activity and behavior. Second, the anterior forebrain pathway (AFP), or the learning pathway of the song system consists of a basal ganglia-thalamocortical loop dedicated to singing. Third, the AFP forms a closed, topographically organized loop all the way down to the song-producing muscles, thus enabling parallel circuits to control distinct channels of motor output. A detailed mechanistic model involving dopamine-modulated cortico-striatal plasticity has been proposed for song learning but many of the key components of this model remain to be tested (Fee & Goldberg, 2011). Area X, the song-related basal ganglia, is a striato-pallidal structure with cell types similar to mammals including D1 and D2 MSNs (Farries et al., 2005). Future work delineating how the various cell types in Area X (Goldberg et al., 2010; Goldberg & Fee, 2010) use the dopamine PPE signal to orchestrate the learning of a complex motor sequence like birdsong promises to reveal fundamental principles of motor control.

Dopamine beyond performance evaluation

The discovery that the dopamine system can retune to female vocalizations during courtship (Roeser, Gadagkar, et al., 2023) opens up the intriguing possibility that social feedback might be able to influence motor output via the dopamine system. While the role of social feedback in vocal learning has been well demonstrated in human infants (Elmlinger et al., 2023), the importance of active social feedback in nonhuman animals is not well studied. Recent studies indicate that social feedback from females (West & King, 1988) might permit juvenile zebra finches to make better copies of their tutor songs (Carouso-Peck & Goldstein, 2019; Bistere et al., 2024). Future work will investigate the neural mechanisms by which social feedback is integrated to enhance the song-learning process. The songbird is also emerging as a powerful model to investigate the role of dopamine beyond performance evaluation and motor learning. Dopamine input from the periaqueductal gray to the premotor nucleus HVC is involved in representing tutor songs in juveniles (Tanaka et al., 2018) and coordinating female-directed song and courtship displays in adults (Ben-Tov et al., 2023). Dopamine in songbirds has also been shown to be involved in the motivation to sing (Riters, 2012), as a reinforcement signal to promote monogamy (Tokarev et al., 2017), and in shaping female song preference to male song (Barr et al., 2021). The tractable neural circuitry and rich courtship behaviors in songbirds present a unique opportunity for future work to elucidate the role of dopamine in mediating various aspects of social behavior.

Conclusions: Dopamine prediction error signals for internally-guided motor learning

The principle of a dopaminergic RPE has been highly influential and stands as a prime example of a “general principle” of brain function revealed by systems neuroscience (Schultz et al., 1997). RPEs provide an RL mechanism through which animals can approach and learn from primary external rewards like food or juice. However, many of our motor skills like speaking or playing an instrument are not learned for food or juice rewards but instead learned by comparing ongoing motor performance to an internal goal. Song learning in zebra finches has emerged as a powerful model to investigate the role of dopamine in such internally-guided RL for motor performance (Mooney, 2022; Wood, 2021; Woolley, 2019). Using a variety of state-of-the-art techniques such as awake-behaving electrophysiology, computational methods, and optogenetics, the dopamine projection to Area X, the singing-related basal ganglia, has been shown to encode performance prediction error that could be used for song learning (Duffy et al., 2022; Gadagkar et al., 2016; Hisey et al., 2018; Xiao et al., 2018). These results suggest that the same reward circuitry that has been so extensively studied in neuroscience is a much more general-purpose system that can also permit the learning of complex motor sequences through internally-guided RL. Using dopamine fiber photometry and leveraging the context-dependent switch in song, from solo “practice” to female-directed courtship “performance,” it was discovered that the dopamine PPE signal, present while practicing alone, is substantially diminished during courtship and dopamine is instead activated by female vocalizations (Roeser, Gadagkar, et al., 2023). These findings demonstrate the social modulation of dopamine error signals and suggest that the dopamine system may flexibly switch from self-evaluation during motor practice to potentially receiving social feedback during audience-directed performance. The songbird presents a unique opportunity for future work investigating whether the dopamine PPE signal is used for song learning during development, how it is constructed by upstream circuits, how it can then be used by downstream basal ganglia-thalamocortical loops to learn song, and how social feedback might influence motor learning and performance through the dopamine system.

Acknowledgments

I thank Malavika Eswaran for assistance with figures, Arnav Raha for the zebra finch drawings, and funding support from: NIH/NINDS K99/R00 Pathway to Independence Award, NIH DP2 New Innovator Award, the Searle, McKnight, and Klingenstein-Simons Scholar Awards, and the Konishi Neuroethology Research Award.

References

- Allen, W. E., Chen, M. Z., Pichamoorthy, N., Tien, R. H., Pachitariu, M., Luo, L., & Deisseroth, K. (2019). Thirst regulates motivated behavior through modulation of brainwide neural population dynamics. *Science*, 364(6437).
- Andalman, A. S., & Fee, M. S. (2009). A basal ganglia-forebrain circuit in the songbird biases motor output to avoid vocal errors. *Proceedings of the National Academy of Sciences*, 106(30), 12518–12523.
- Barr, H. J., Wall, E. M., & Woolley, S. C. (2021). Dopamine in the songbird auditory cortex shapes auditory preference. *Current Biology*, 31(20), 4547.
- Ben-Tov, M., Duarte, F., & Mooney, R. (2023). A neural hub for holistic courtship displays. *Current Biology*, 33(9), 1640.
- Bistere, L., Gomez-Guzman, C. M., Xiong, Y., & Vallentin, D. (2024). Female calls promote song learning in male juvenile zebra finches. *Nature Communications*, 15, 8938.
- Bottjer, S. W. (1993). The distribution of tyrosine hydroxylase immunoreactivity in the brains of male and female zebra finches. *Journal of Neurobiology*, 24(1), 51–69.
- Bottjer, S. W., Brady, J. D., & Cribbs, B. (2000). Connections of a motor cortical region in zebra finches: Relation to pathways for vocal learning. *Journal of Comparative Neurology*, 420(2), 244–260.
- Botvinick, M., Ritter, S., Wang, J. X., Kurth-Nelson, Z., Blundell, C., & Hassabis, D. (2019). Reinforcement learning, fast and slow. *Trends in Cognitive Sciences*, 23(5), 408–422.
- Burke, J. E., & Schmidt, M. F. (2020). *Neural control of birdsong encyclopedia of life sciences* (pp. 345–355). Wiley.
- Carouso-Peck, S., & Goldstein, M. H. (2019). Female social feedback reveals non-imitative mechanisms of vocal learning in zebra finches. *Current Biology*, 29(4), 631.
- Chen, R., & Goldberg, J. H. (2020). Actor-critic reinforcement learning in the songbird. *Current Opinion in Neurobiology*, 65, 1–9.
- Chen, R., Puzerey, P. A., Roeser, A. C., Riccelli, T. E., Podury, A., Maher, K., Farhang, A. R., & Goldberg, J. H. (2019). Songbird ventral pallidum sends diverse performance error signals to dopaminergic midbrain. *Neuron*, 103(2), 266.
- Colquitt, B. M., Merullo, D. P., Konopka, G., Roberts, T. F., & Brainard, M. S. (2021). Cellular transcriptomics reveals evolutionary identities of songbird vocal circuits. *Science*, 371(6530).
- Costa, R. M. (2007). Plastic corticostriatal circuits for action learning: What's dopamine got to do with it? *Annals of the New York Academy of Sciences*, 1104, 172–191.
- Dai, B., Sun, F., Tong, X., Ding, Y., Kuang, A., Osakada, T., ... Lin, D. (2022). Responses and functions of dopamine in nucleus accumbens core during social behaviors. *Cell Reports*, 40(8), 111246.
- Das, A., & Goldberg, J. H. (2022). Songbird subthalamic neurons project to dopaminergic midbrain and exhibit singing-related activity. *Journal of Neurophysiology*, 127(2), 373–383.
- Doupe, A. J., & Kuhl, P. K. (1999). Birdsong and human speech: Common themes and mechanisms. *Annual Review of Neuroscience*, 22, 567–631.
- Doupe, A. J., Perkel, D. J., Reiner, A., & Stern, E. A. (2005). Birdbrains could teach basal ganglia research a new song. *Trends in Neurosciences*, 28(7), 353–363.
- Doya, K., & Sejnowski, T. (1995). A novel-reinforcement-model-of-birdsong-vocalization-learning. *NIPS*, 7(1995), 101–108.
- Duffy, A., Latimer, K. W., Goldberg, J. H., Fairhall, A. L., & Gadagkar, V. (2022). Dopamine neurons evaluate natural fluctuations in performance quality. *Cell Reports*, 38(13).
- Elmlinger, S. L., Schwade, J. A., Vollmer, L., & Goldstein, M. H. (2023). Learning how to learn from social feedback: The origins of early vocal development. *Developmental Science*, 26(2).
- Farries, M. A., Ding, L., & Perkel, D. J. (2005). Evidence for “direct” and “indirect” pathways through the song system basal ganglia. *Journal of Comparative Neurology*, 484(1), 93–104.
- Fawzi, A., Balog, M., Huang, A., Hubert, T., Romera-Paredes, B., Berekatain, M., ... Kohli, P. (2022). Discovering faster matrix multiplication algorithms with reinforcement learning. *Nature*, 610(7930), 47–53.
- Fee, M. S., & Goldberg, J. H. (2011). A hypothesis for basal ganglia-dependent reinforcement learning in the songbird. *Neuroscience*, 198, 152–170.
- Gadagkar, V., Puzerey, P. A., Chen, R., Baird-Daniel, E., Farhang, A. R., & Goldberg, J. H. (2016). Dopamine neurons encode performance error in singing birds. *Science*, 354(6317), 1278–1282.
- Goffinet, J., Brudner, S., Mooney, R., & Pearson, J. (2021). Low-dimensional learned feature spaces quantify individual and group differences in vocal repertoires. *eLife*, 10.
- Goldberg, J. H., Adler, A., Bergman, H., & Fee, M. S. (2010). Singing-related neural activity distinguishes two putative pallidal cell types in the songbird basal ganglia: Comparison to the primate internal and external pallidal segments. *Journal of Neuroscience*, 30(20), 7088–7098.
- Goldberg, J. H., & Fee, M. S. (2010). Singing-related neural activity distinguishes four classes of putative striatal neurons in the songbird basal ganglia. *Journal of Neurophysiology*, 103(4), 2002–2014.
- Hernandez, A. M., Perez, E. C., Mulard, H., Mathevon, N., & Vignal, C. (2016). Mate call as reward: Acoustic communication signals can acquire positive reinforcing values during adulthood in female zebra finches (*Taeniopygia guttata*). *Journal of Comparative Psychology*, 130(1), 36–43.
- Hisey, E., Kearney, M. G., & Mooney, R. (2018). A common neural circuit mechanism for internally guided and externally reinforced forms of motor learning. *Nature Neuroscience*, 21(4), 589–597.
- Hoffmann, L. A., Saravanan, V., Wood, A. N., He, L., & Sober, S. J. (2016). Dopaminergic contributions to vocal learning. *Journal of Neuroscience*, 36(7), 2176–2189.
- Hu, R. K., Zuo, Y., Ly, T., Wang, J., Meera, P., Wu, Y. E., & Hong, W. (2021). An amygdala-to-hypothalamus circuit for social reward. *Nature Neuroscience*, 24(6), 831–842.
- Ikeda, M. Z., Trusel, M., & Roberts, T. F. (2020). Memory circuits for vocal imitation. *Current Opinion in Neurobiology*, 60(1), 37–46.
- Kearney, M. G., Warren, T. L., Hisey, E., Qi, J., & Mooney, R. (2019). Discrete evaluative and premotor circuits enable vocal learning in songbirds. *Neuron*, 104(3), 559.
- Kollmorgen, S., Hahnloser, R. H. R., & Mante, V. (2020). Nearest neighbours reveal fast and slow components of motor learning. *Nature*, 577(7791), 526–530.
- Konishi, M. (1965). The role of auditory feedback in the control of vocalization in the white-crowned sparrow 1. *Zeitschrift für Tierpsychologie*, 22(7), 770–783.
- Kubikova, L., & Košťál, L. (2010). Dopaminergic system in birdsong learning and maintenance. *Journal of Chemical Neuroanatomy*, 39(2), 112–123.
- Mackevicius, E. L., & Fee, M. S. (2018). Building a state space for song learning. *Current Opinion in Neurobiology*, 49, 59–68.
- Mandelblat-Cerf, Y., Las, L., Denissenko, N., & Fee, M. (2014). A role for descending auditory cortical projections in songbird vocal learning. *eLife*, 2014(3).
- Markowitz, J. E., Gillis, W. F., Jay, M., Wood, J., Harris, R. W., Cieszkowski, R., Scott, R., Brann, D., Koveal, D., Kula, T., Weinreb, C., Osman, M. A. M., Pinto, S. R., Uchida, N., Linderman, S. W., Sabatini, B. L., & Datta, S. R. (2023). Spontaneous behaviour is structured by reinforcement without explicit reward. *Nature*, 614(7946), 108–117.
- Marler, P. (1970). A comparative approach to vocal learning: Song development in white-crowned sparrows. *Journal of Comparative and Physiological Psychology*, 71(Pt. 2), 1–25.
- Menegas, W., Akiti, K., Amo, R., Uchida, N., & Watabe-Uchida, M. (2018). Dopamine neurons projecting to the posterior striatum reinforce avoidance of threatening stimuli. *Nature Neuroscience*, 21(10), 1421–1430.

- Mooney, R. (2022). Birdsong. *Current Biology*, 32, 2022.
- Olds, J., & Milner, P. (1954). Positive reinforcement produced by electrical stimulation of septal area and other regions of rat brain. *Journal of Comparative and Physiological Psychology*, 47(6), 419–427.
- Person, A. L., Gale, S. D., Farries, M. A., & Perkel, D. J. (2008). Organization of the songbird basal ganglia, including area X. *Journal of Comparative Neurology*, 508(5), 840–866.
- Pfenning, A. R., Hara, E., Whitney, O., Rivas, M. V., Wang, R., Roulhac, P. L., Howard, J. T., Wirthlin, M., Lovell, P. V., Ganapathy, G., Mouncastle, J., Moseley, M. A., Thompson, J. W., Soderblom, E. J., Iriki, A., Kato, M., Gilbert, M. T. P., Zhang, G., Bakken, T., ... Jarvis, E. D. (2014). Convergent transcriptional specializations in the brains of humans and song-learning birds. *Science*, 346(6215).
- Ramarao, M., Jones, C., Goldberg, J. H., Roeser, A., & Cooper, B. G. (2023). Songbird mesostriatal dopamine pathways are spatially segregated before the onset of vocal learning. *PLoS ONE*, 18(11), e0285652.
- Riters, L. V. (2012). The role of motivation and reward neural systems in vocal communication in songbirds. *Frontiers in Neuroendocrinology*, 33(2), 194–209.
- Roeser, A., Gadagkar, V., Das, A., Puzerey, P. A., Kardon, B., & Goldberg, J. H. (2023). Dopaminergic error signals retune to social feedback during courtship. *Nature*, 623(7986), 375–380.
- Roeser, A., Teoh, H. K., Chen, R., Cohen, I., & Goldberg, J. (2023). The songbird lateral habenula projects to dopaminergic midbrain and is important for normal vocal development. *bioRxiv*.
- Sakata, J. T., & Brainard, M. S. (2009). Social context rapidly modulates the influence of auditory feedback on avian vocal motor control. *Journal of Neurophysiology*, 102(4), 2485–2497.
- Schrittwieser, J., Antonoglou, I., Hubert, T., Simonyan, K., Sifre, L., Schmitt, S., ... Atari, M. (2020). Go, chess and shogi by planning with a learned model. *Nature*, 588(7839), 604–609.
- Schultz, W., Dayan, P., & Montague, P. R. (1997). A neural substrate of prediction and reward. *Science*, 275(5306), 1593–1599.
- Singh Alvarado, J., Goffinet, J., Michael, V., Liberti, W., Hatfield, J., Gardner, T., Pearson, J., & Mooney, R. (2021). Neural dynamics underlying birdsong practice and performance. *Nature*, 599(7886), 635–639.
- Solié, C., Girard, B., Righetti, B., Tapparel, M., & Bellone, C. (2022). VTA dopamine neuron activity encodes social interaction and promotes reinforcement learning through social prediction error. *Nature Neuroscience*, 25(1), 86–97.
- Sun, F., Zeng, J., Jing, M., Zhou, J., Feng, J., Owen, S. F., Luo, Y., Li, F., Wang, H., Yamaguchi, T., Yong, Z., Gao, Y., Peng, W., Wang, L., Zhang, S., Du, J., Lin, D., Xu, M., Kreitzer, A. C., ... Li, Y. (2018). A genetically encoded fluorescent sensor enables rapid and specific detection of dopamine in flies, fish, and mice. *Cell*, 174(2), 481.
- Sutton, R. S., & Barto, A. G. (2018). *Reinforcement learning: An introduction* (2nd ed.). Cambridge: The MIT Press.
- Tanaka, M., Sun, F., Li, Y., & Mooney, R. (2018). A mesocortical dopamine circuit enables the cultural transmission of vocal behaviour. *Nature*, 563(7729), 117–120.
- Tchernichovski, O., Mitra, P. P., Lints, T., & Nottebohm, F. (2001). Dynamics of the vocal imitation process: How a zebra finch learns its song. *Science*, 291(5513), 2564–2569.
- Tokarev, K., Bruno, J. H., Ljubčić, I., Kothari, P. J., Helekar, S. A., Tchernichovski, O., & Voss, H. U. (2017). Sexual dimorphism in striatal dopaminergic responses promotes monogamy in social songbirds. *eLife*, 6.
- Toutounji, H., Zai, A. T., Tchernichovski, O., Hahnloser, R. H. R., & Lipkind, D. (2024). Learning the sound inventory of a complex vocal skill via an intrinsic reward. *Science Advances*, 10(13).
- Tumer, E. C., & Brainard, M. S. (2007). Performance variability enables adaptive plasticity of ‘crystallized’ adult birdsong. *Nature*, 450(7173), 1240–1244.
- West, M. J., & King, A. P. (1988). Female visual displays affect the development of male song in the cowbird. *Nature*, 334(6179), 244–246.
- Wickens, J. R., Reynolds, J. N. J., & Hyland, B. I. (2003). Neural mechanisms of reward-related motor learning. *Current Opinion in Neurobiology*, 13(6), 685–690.
- Wood, A. N. (2021). New roles for dopamine in motor skill acquisition: Lessons from primates, rodents, and songbirds. *Journal of Neurophysiology*, 125(6), 2361–2374.
- Woolley, S. C. (2019). Dopaminergic regulation of vocal-motor plasticity and performance. *Current Opinion in Neurobiology*, 54, 127–133.
- Xiao, L., Chattree, G., Oscos, F. G., Cao, M., Wanat, M. J., & Roberts, T. F. (2018). A basal ganglia circuit sufficient to guide birdsong learning. *Neuron*, 98(1), 208.
- Xie, Y., Huang, L., Corona, A., Pagliaro, A. H., & Shea, S. D. (2023). A dopaminergic reward prediction error signal shapes maternal behavior in mice. *Neuron*, 111(4), 557–570.e7.
- Zann, R. A. (1996). *The zebra finch: A synthesis of field and laboratory studies*. Oxford University Press: Oxford University Press.