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Let Music Sound while She Doth Make Her Choice

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To attract females during courtship, *Drosophila melanogaster* males sing songs with motifs of varying temporal structure. In this issue of *Neuron*, Clemens et al. (2015) identify a song feature indicating male fitness and propose a neural mechanism for how it may be extracted from the auditory signal by female flies.

Probably the most important way that animals use acoustic signals is to advertise their sexual fitness. Mapping out how such vocalizations drive conspecifics' actions is difficult because both the acoustic signal and the response may be complex. However, the response of females to the songs sung by male *Drosophila melanogaster* fruit flies during natural courtship (von Schilcher, 1976) may be an example of natural decision-making behavior with just the right combination of patterned stereotypy, well-defined behavior, and readily quantifiable variability to allow this particular case to be resolved.

Drosophila courtship songs are composed of bouts of singing interleaved with long pauses, with each song bout itself consisting of two song modes: sine song (a low-frequency "humming") and pulse song (a series of short pulses of high amplitude) (von Schilcher, 1976) (Figure 1A). The songs of different species typically differ in the intervals between pulses during pulse song (Ritchie et al., 1999). Coen et al. (2014) recently demonstrated through a robust statistical analysis that much song variability within a species, previously thought to be random, could be explained by the male fly's recent sensory experience during courtship with a female. The authors of a new study in this issue of *Neuron* (Clemens et al., 2015) have now performed a detailed analysis of the song patterns produced by the male and corresponding female responses to determine what song features appear to contain the fitness information that the female uses to decide whether to mate. Further, by characterizing neural responses during passive listening, they were able to propose a neural algorithm for the extraction of these relevant patterns.

To identify which song features influenced female behavior (i.e., indicated male fitness) most, Clemens et al. (2015) recorded both the male songs and female walking speed while male and female flies engaged in natural courtship. They then correlated each of several hand-picked song features (such as song bout duration, sine song duration, pulse song duration, interpulse interval, etc.) with female speed and showed that the duration of male song bouts was the most important factor governing the female's slowing down (taken as an approximate measure of attraction).

To understand the neural mechanisms by which the female's nervous system extracts such features from the full auditory signal and transforms them into output motor decisions, the authors patch-clamped nonspiking neurons in the ventrolateral protocerebrum (VLP) and antennal mechanosensory and motor complex (AMMC) in the antennal lobe of immobile females exposed to both artificial and natural song segments. The experimenters used the results to build adaptive linear-nonlinear neural models that predicted membrane potential as a function of recent song history. Most neural responses were surprisingly simple: they could be predicted by simply linearly filtering the song stimulus, although including an adaptation term did improve the model slightly. The bank of neural filters spanned a wide range of timescales and had a slightly biphasic character. These responses were very consistent across different stimulus types. This high predictability allowed the

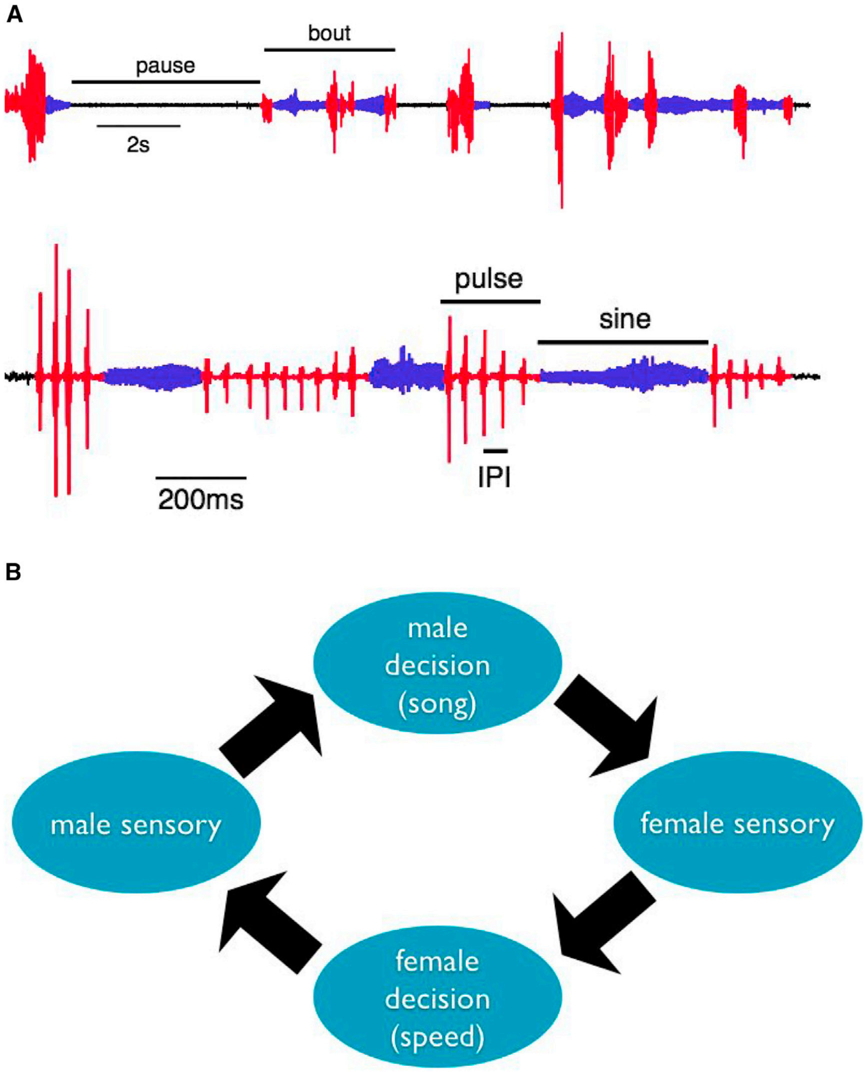

Figure 1. *Drosophila* Courtship Songs and Decision-Making Process
(A) Examples of *Drosophila melanogaster* courtship song with pauses, bouts, sine mode (blue), pulse mode (red), and interpulse interval (IPI) indicated (reproduced from Clemens et al., 2015).
(B) The cyclical decisionmaking process during *Drosophila* courtship.

experimenters to infer the female VLP and AMMC activity during *naturalistic* courtship behaviors, during which patch-clamp recording is extremely difficult. This in turn allowed the construction of a potential decoder by which the AMMC/VLP representation of song might be transformed into motor signals controlling the female's walking speed. For this, the bimodal nature of the filter turned out to be key. By separately rectifying the positive and negative filter outputs, a decoder could extract two distinct song features, the total amount of song and the number of bout onsets, from a single input signal. The ratio of these two signals yields the important variable—the bout duration. Multiplicative and divisive combination of neural signals is a frequently occurring motif, e.g., in normalization (Carandini and Heeger, 2012) and in computations like looming (Gabbiani et al., 2002). An explicit representation of this computed variable and the decision process itself is yet to be found. However, together with the lab's work characterizing male song modulation (Coen et al., 2014), this work provides the skeleton of an elegant cyclical description of the male-female decision-making process during courtship (Figure 1B).

Currently, compromises are inevitable in simultaneously recording neural activity and natural behavior: often the animal's free movement must be restricted to allow precise recording. This work demonstrates how computational modeling can be used to transcend these limitations: instead of recording both activity and behavior during a single experiment, in this case the experimenters observed that the simplicity of the neural responses strongly implied that responses recorded during passive listening could be used as a surrogate for those during active behavior. This is certainly the hope driving studies of insect behavior, such as flying odor tracking, in tethered preparations (e.g., Bhandawat et al., 2010), as recording from neurons while flies are actively flying in a wind tunnel is at present impossible. Of course, this technique relies strongly on the assumption that the response models generalize across behavioral conditions, in particular that the female's locomotion does not modulate neural responses to song. Flight, for example, is known to affect the gain, if not the tuning, of visual responses (Maimon et al., 2010); here a future challenge will be to demonstrate that locomotion or engagement in courtship does not affect the filter structure and timescales of these auditory responses.

The relatively simple structure of *Drosophila* song and the easily quantifiable courtship responses provide an opportunity to gain a rich understanding of this important example of decision-making. What might be necessary to achieve this level of understanding of other sensory decision paradigms in which the input signals are more complex and the behavioral choices harder to identify? There are two major challenges to framing such a decision-making process in natural behavior. One is to segment behavior into discrete states, such that "decisions" are transitions between these states, driven by sensory input. The other is to identify the sensory signals that are maximally informative about the decisions.

Here, the authors took advantage of the fact that *Drosophila* songs are clearly composed of sequences of stereotyped motifs (pulse song, sine song, pause) and that behavioral responses could be well-described by walking speed alone. In the general case, one would like to use the data to discover low-dimensional or discrete representations of the relevant variables. However, while machine-learning algorithms do exist to segment arbitrary signals, such as the movements of honeybees or fruit flies, into statistically differentiated dynamical regimes (Fox et al., 2009; Berman et al., 2014), these techniques are often only useful when segments are already identifiable by eye and one simply seeks to automate the segmentation process. Ideally, one would like to learn reduced representations of two or more predictively linked variables (e.g., stimulus and behavior) simultaneously. One such "dual dimensionality reduction," based on the method of partial least-squares, a variant of cross-correlation analysis, was recently used to identify coding principles involved in control of flight muscles in the hawkmoth (Sponberg et al., 2015). Other "dual" methods of simultaneously identifying simple representations of both input and output, such as coclustering (Dhillon et al., 2003), may also prove useful in the analysis of future data sets. Indeed, such an analysis may reveal that the walking trajectories of female flies during courtship are best described not as sequences of speeds but rather as song-feature-dependent transitions among a discrete set of movement states, as is observed in male "dances" during courtship (Spieth, 1974). The recent work of Clemens et al. (2015) provides great encouragement that the neural substrates that govern such sensory-driven decisions will be decodable.

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The Decision Path Not Taken

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Real-life decisions often involve multiple intermediate choices among competing, interdependent options. Lorteije et al. (2015) introduce a new paradigm for dissecting the neural strategies underlying such decisions.

Decisions in the laboratory typically require a single choice, between two or more options. But in real life, decisions are often hierarchical, requiring multiple choices that define a path through a decision tree. Hierarchical decisions can be made with an explicitly serial strategy—choosing one of the highest-level branches first, then moving on to lower-level decisions within that branch. This happens, for example, when we use a phone app to choose a restaurant by picking a neighborhood first, then choosing a cuisine available in that neighborhood, then a price point within the range for that cuisine, etc. (Figure 1A, "Serial"). The serial strategy saves time and effort—at each choice point, we eliminate the need to consider anything further down the non-chosen branches.

But what happens if we make a more rapid and intuitive decision about where to eat? The decision is certainly influenced by the same interacting factors—where we feel like traveling, what we feel like eating, how much we want to spend. Our internal decision-making process could follow the same steps, deciding on a neighborhood first, then a cuisine, etc. But that sounds a bit clunky and suspiciously digital. Shouldn't our extremely parallel wetware use a more parallel strategy? Maybe our brains should compare all restaurants at once, rating each based on a combination of neighborhood, cuisine, and price. This amounts to evaluating all possible paths through the decision tree in parallel (Figure 1B, "Parallel Path"). It might work, if we only know a few restaurants. But most of us know dozens at least, and comparing them all simultaneously would be a tall