Available online at www.sciencedirect.com

ScienceDirect

Current Opinion in Neurobiology

A comparative approach to closed-loop computation

E Roth[1,4], S Sponberg[1,2,4] and NJ Cowan[3]

Neural computation is inescapably closed-loop: the nervous system processes sensory signals to shape motor output, and motor output consequently shapes sensory input. Technological advances have enabled neuroscientists to close, open, and alter feedback loops in a wide range of experimental preparations. The experimental capability of manipulating the topology—that is, how information can flow between subsystems—provides new opportunities to understand the mechanisms and computations underlying behavior. These experiments encompass a spectrum of approaches from fully open-loop, restrained preparations to the fully closed-loop character of free behavior. Control theory and system identification provide a clear computational framework for relating these experimental approaches. We describe recent progress and new directions for translating experiments at one level in this spectrum to predictions at another level. Operating across this spectrum can reveal new understanding of how low-level neural mechanisms relate to high-level function during closed-loop behavior.

Addresses
[1] Department of Biology, University of Washington, Seattle, WA 98195, United States
[2] Department of Physiology and Biophysics, University of Washington, Seattle, WA 98195, United States
[3] Department of Mechanical Engineering, Johns Hopkins University, Baltimore, MD 21218, United States

Corresponding author: Cowan, NJ (ncowan@jhu.edu)

[4] ER and SS contributed equally.

Current Opinion in Neurobiology 2014, **25**:54–62

This review comes from a themed issue on **Theoretical and computational neuroscience**

Edited by **Adrienne Fairhall** and **Haim Sompolinsky**

0959-4388/$ – see front matter,

http://dx.doi.org/10.1016/j.conb.2013.11.005

Introduction

In his seminal 1948 book entitled ''Cybernetics,'' Norbert Wiener proffered that neural computation is a fundamentally closed-loop process [1]:

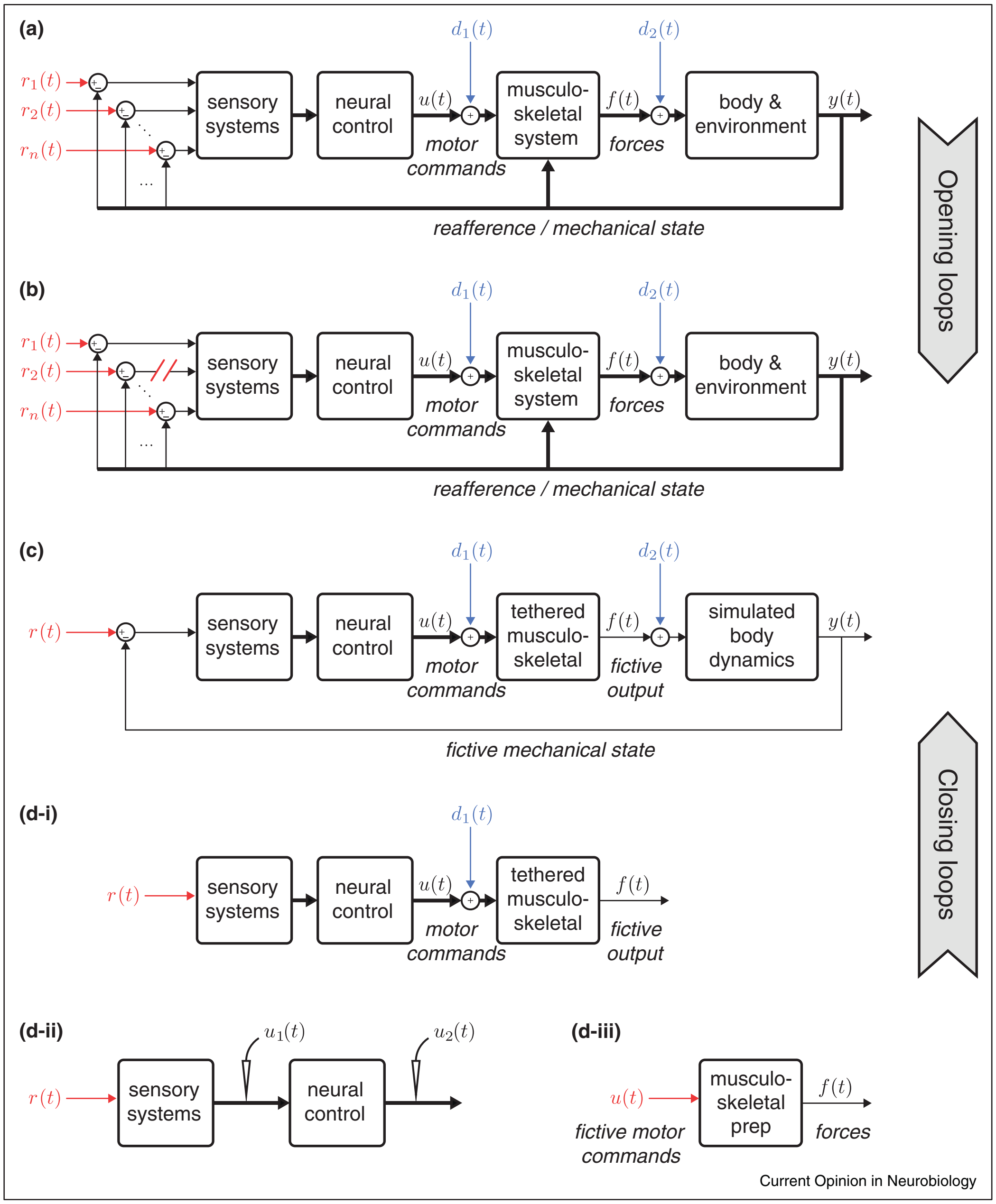
> The central nervous system no longer appears as a self-contained organ, receiving inputs from the senses and discharging into the muscles. On the contrary, some of its most characteristic activities are explicable only as circular processes, emerging from the nervous system into the muscles, and re-entering the nervous system through the sense organs...

This circular process is *closed-loop feedback*; sensing governs action, action changes the state of the animal in its environment, and these changes are perceived via sensing. This contrasts with *open-loop* processes, where information flows unidirectionally and the output of the system does not influence the sensory inputs. Understanding how behavior arises from the physiological complex of sensory, neural, and motor subsystems requires an understanding of how information flows through this network that is inescapably closed loop.

Technological limitations have historically required a focus on open-loop responses of individual mechanisms or subsystems within the nervous system. Recent progress has enabled unprecedented access to physiological signals across a spectrum of experimental conditions, spanning open-loop neurophysiology to artificially closed-loop preparations to perturbed free behavior (Figure 1). But, there remains a gap: the primary mathematical tools in computational neuroscience are statistics, information theory, and dynamical systems theory. Largely absent from that list is feedback control theory. Control theory can be thought of as a subfield of dynamical systems theory—after all, the addition of feedback loops merely alters the dynamics of a system. However, feedback control is a general and flexible means to achieve goal-directed ends, reject task-irrelevant disturbances, and govern system-level behavior. The dynamics of a feedback-controlled system can bear little resemblance to the open-loop response. Feedback can render fragile systems robust and unstable systems stable. For example, in human postural control, the body acts as an inverted pendulum (which is unstable), but under the control of the nervous system, the dynamic response shares the stable character of a hanging pendulum [2••].

Control theory furnishes a common language for quantifying and interpreting behavior of the whole animal or its subsystems in the closed-loop context. In what follows, we describe approaches to experimentally opening and closing feedback loops (Figure 1), present a control theoretic framework for interpreting and interrelating results across this spectrum of experimental paradigms, and then provide concrete examples showing how to use empirical results from one configuration to make quantitative predictions about system behavior in another.

Figure 1



A spectrum of experimental topologies. At all levels of the spectrum, we can record a variety of signals, including motor output, $u(t)$, force output, $f(t)$, and mechanical state, $y(t)$. We can perturb the system to modify behavior via modulations to reference signals $r_i(t)$ (red) or disturbances $d_i(t)$ (blue), which can be injected to motor commands or added to musculoskeletal forces. Thin lines represent signals with one (or very few) dimensions, while heavier lines represent potentially high-dimensional signals. **(a)** Free, intact behavior has multiple closed loops. The animal's movement (change in its mechanical state) is fed back via multiple sensory modalities. Only relative motion is measured by the nervous system, so self motion is intrinsically subtracted from exogenous reference signals $r_1(t)$ through $r_n(t)$ that represent these different sensory modalities (e.g. vision, olfaction, mechanoreception). **(b)** Working down the spectrum, if an individual sensory modality is inhibited, then the topology changes and the corresponding feedback loop is opened. **(d)** The bottom of the spectrum includes many fully open-loop conditions from rigidly tethered behavioral experiments (d-i) to reduced electrophysiological (d-ii) and *ex vivo* musculoskeletal (d-iii) preparations. **(c)** Working up the spectrum, we close the loop around these preparations in an individual modality by simulating the changes in the mechanical state of the body (fictive mechanical state), feeding that signal back, and subtracting it from the reference signal.

Experimentally closing and opening loops

Experimental paradigms run the gamut from free behavior (which can involve dozens of closed loops) to open-loop, feedforward physiological experiments. In Figure 1, we organize a coarse spectrum of experimental paradigms by the degree to which they preserve closed loops at the behavioral level. *Block diagrams* provide an intuitive means for depicting mechanistic models at many scales of resolution. Blocks represent subsystems while arrows depict signals. Together these define the topology of the experiment, where ''topology'' refers to how the component subsystems are interconnected.

Perturbed Free Behavior. Figure 1a depicts the block diagram for a freely behaving animal; multiple, parallel sensory streams are filtered through the nervous system to govern locomotion. In this paradigm, perturbations have been largely limited to exogenous sensory stimuli [3–6] or mechanical disturbances [7–10] and means for measuring behavior have been similarly noninvasive (e.g. kinematic data extracted from video or motion capture). By considering the behavioral output in response to perturbation signals we can quantify performance of the closed-loop system in terms of a behavior-level model. Then, by substituting models for ''known'' blocks, we can use the empirical model at the behavior level to infer dynamics of other subsystems [11•].

Suppressed Sensorimotor Loops in Free Behavior. Working down the spectrum, Figure 1b depicts experiments in which sensorimotor loops are selectively 'opened', but behavior remains largely intact. This class of experiments has been the most sparsely investigated.

Traditionally a sensorimotor loop is opened in one of two ways, by inhibiting or ablating part of the sensory circuit or by eliminating the stimulus. However, ablation and inhibition can degrade multiple pathways, seriously limiting or wholly eliminating behavior. In removing or degrading particular sensory cues [12], animals can reweight the contributions of other modalities [13•], and if sensory reweighting is not the phenomenon being investigated, the change can be confounding. In a less deleterious approach, the sensory reference can be actively clamped in real-time by feeding back the animal's kinematic states to cancel reafference [3]. In this way, the selected sensory modality is still intact and excited, but the animal loses control authority over it.

Open-loop neuroethology. Unlike free behavior, which is inherently closed-loop, the dominant experimental paradigm in systems neuroscience is at the other end of the spectrum. It involves the presentation of stimuli to elicit downstream responses in partially intact or restrained preparations. ''Downstream'' emphasizes the fact that the system is investigated in a feedforward manner, devoid of its (closed-loop) behavioral context (Figure 1d). These preparations afford sophisticated instrumentation, enabling researchers to relate complex spatiotemporal stimuli to neural responses. Tethered preparations where the animal's response does not impact sensory stimuli are open-loop (Figure 1d-i), but this category also includes *in vitro* electrophysiology of sensory encoding and neural circuit characterization (Figure 1d-ii). To explore the open-loop dynamics of the motor subsystem, we can also isolate the musculoskeletal system with a ''work loop'' preparation and characterize the response (Figure 1d-iii), namely the conversion of motor commands into force and power [14,15•].

Closing feedback loops around reduced/restrained preparations.

Acute electrophysiology in an artificially closed loop (i.e. virtual reality) is now possible in an increasing variety of animal systems [16•,17,18••] (Figure 1c). These systems are adaptions of behavioral preparations in which a (mostly) intact animal is tethered in such a way to preserve motor output, for example, a flying insect is glued to a wire [19,20] or a walking animal is suspended over a treadmill or trackball [16•,21]. Such preparations enjoy topological simplicity: low-dimensional fictive motor output is fed back to a sensory input after being subtracted from a reference. The ''simulated body dynamics'' are often taken to be a simple linear gain. Even though the dynamics of tethered responses often differ from free behavior, there are benefits of the closed-loop topology—whether natural or virtual—such as stability and robustness. In addition, one can directly relate open-loop mechanism to closed-loop behavior, while simultaneously performing electrophysiological and imaging techniques.

A control theoretic framework for traversing the experimental spectrum

Linear dynamics are often dismissed because the constituent subsystems of animal behaviors are nonlinear (e.g. sensory tuning curves [22], muscle mechanics [14,15•,23]). But, many behaviors, such as standing upright in humans [24], visual scene stabilization in fruit flies [25•,26,27], and thigmotaxis in cockroaches [28–30], involve operating near a putative equilibrium—the domain where linearized models are most faithful to the underlying dynamics.

A dynamical model can take a variety of forms, including systems of differential equations, an impulse response function, or a transfer function in the frequency domain. System identification techniques fit these models empirically, using observations of the system output in response to sufficiently rich perturbations of the stimuli, such as sums of sinusoids [31•,32••], band-limited noise [2••], or binary m-sequences [33]. Alternatively, models can be derived from first principles [34,35].

Feedback is transformative (as compared to feedforward series or parallel connections) in that it fundamentally changes the dynamical character of a system. As a result, often the effects of feedback are not immediately intuitive. *Stability*—e.g. a hawkmoth recovers from sensed mechanical perturbations by moving its abdomen [20,32••]—and *robustness*—e.g. the moth maintains hovering flight despite asymmetric damage to its wings [36]—are typical of evolved, biological behaviors and these properties are afforded by well-tuned feedback control systems. As such, a principled approach to interpreting low-level mechanisms in the context of feedback is necessary. Control theory provides tools for interpreting these models in the context of an experimental topology—either synthesizing subsystem models into a behavioral prediction or decomposing a behavioral model to infer or constrain functional subsystems.

The central tool for probing the system dynamics and identifying a model, no matter the topology, is the application of *perturbations* and recording of the corresponding responses. Exogenous *reference signals*—those that modulate the goal or equilibrium of the behavior—are perturbations that the organism attempts to track. Hence, the system tends to propagate reference modulations through to a change in the output. Examples include moving the visual reference during optomotor tracking and fixation in flies [3,16•,19,37], or modulating the position of a refuge during a shelter-seeking behavior in electric fish [12,31•], and can include the coupling and decoupling of multiple modalities (e.g. separating the visual and mechanical contributions to a moth's turning response [20]).

Disturbances contrast with reference modulations in that the system should minimize their impact on system state. Disturbances frequently take the form of perturbing forces or torques and can have a variety of temporal signatures: impulsive like a poke, wind gust, and cannon blast [7,9,8,38,10]; repeated and broad spectrum such as with rough terrain [39]; or persistent such as for a lasting step-change in headwind. On the motor side, experimental alteration of motor commands during free behavior act as disturbances that can reveal the role of individual muscles during closed-loop locomotion [40,41] and can be directly connected to their open-loop physiological responses [15•].

Reference modulations and mechanical disturbances provide an effective means to determine system dynamics and they are particularly powerful when used in concert [2••]. But there are other types of perturbations that can provide critical insight into closed-loop computation that are not investigated in this paper. For example, *modifications* to system parameters (i.e. changing the dynamics of a block) can include changing the physical properties of the animal's biomechanics (e.g. mass, stiffness, or shape [36]) and state-dependent changes (neuromodulatory or behavioral) to sensorimotor processing [42–44].

Examples

In the examples that follow, we review several studies that have begun to open and close loops to traverse the experimental spectrum in Figure 1. We focus particular attention on those studies that explicitly use control theoretic modeling to translate between two (or more) experimental topologies.

Translating free behavior into open-loop physiology

Control theory can generate testable hypotheses to guide the open-loop physiological investigation of neural mechanisms based on system identification of the closed-loop behavior [45]. This is especially powerful in the context of a biomechanical model. For example, fast-running cockroaches use their antennae as tactile probes to track along surfaces. Mechanoreceptors along the antenna detect curves, dips, and protrusions of the adjacent surface, which can be thought of as modulatory perturbations to the reference signal [28]. A control-theoretic model of the whole-animal behavior (Figure 1a) predicted that the nervous system should encode both distance and rate-of-approach to the wall in order to ensure stability. Subsequent open-loop electrophysiological recordings (Figure 1d) not only revealed encoding of both distance and rate-of-approach in the primary sensory afferents but also filtering of the sensory signal that matched the time course of the motor response [29]. This work further motivated the open-loop characterization of the antennal mechanics which are themselves tuned to behavior [30].

Predicting behavioral consequences of open-loop mechanisms

Using a neuromechanical model, one can predict closed-loop behavioral responses (Figure 1a) from open-loop measurements (Figure 1d). Such analysis provides a mechanistic interpretation of the open-loop response. For example, the visuomotor transform of the abdomen of a tethered, behaving moth was integrated with a model of free flight [32••]. This model demonstrated the feasibility of the abdominal reflex response to stabilize flight. That work makes a precise behavioral prediction—in the form of a predicted behavioral transfer function—that can be tested in future studies. Similarly, wide-field motion sensitive neurons in flies can be interpreted as instantiating an optimal feedback control system as is common in engineering design [46]. One could couple this control-theoretic model with a model of flight to predict responses to perturbations of the free-flight behavior.

Closing the loop around restrained or reduced preparations

For systems amenable to artificially closed loops, the experiment is readily transitioned from closed to open loop (or vice versa) by setting the feedback gain to zero, facilitating interpretation between Figure 1c to and from Figure 1d-i. However, in open-loop preparations (Figure 1d-i–iii) there is no guarantee that the neuromechanical subsystems operate near a behaviorally relevant equilibrium, and thus this hypothesis must be directly tested. Ejaz et al. validated that cell behavior in closed loop is consistent with prior electrophysiological descriptions of visual motion sensitive cells in flies by using a closed-loop fly–robot interface in which the rotation of a visual scene was modulated by electrophysiological measurements [47].

Conversely, the local linearization afforded by closed-loop experimentation (Figure 1c) may mask interesting mechanistic nonlinearities (e.g. saturation). One approach to this is the replay paradigm [37], which tests how well a closed-loop model captures the behavior of the underlying feedforward mechanism [26]. The animal is first presented a stimulus in artificially closed-loop and the error signal, $r(t) - y(t)$ in Figure 1c, is recorded. This error signal (optic flow in the case of the fly optomotor behavior) is subsequently replayed in an open-loop preparation, yielding two experiments with identical sensory percepts.

A completely different category of behaviors are those such as escape and avoidance which naturally involve *unstable* equilibria; prolonged observations of these responses are difficult in free behavior [18••]. For example, in the fruit fly, rapidly looming visual scenes induce a turning response *away* from the focus of expansion. Reiser and Dickinson characterized the turning response to patterns of expansion at different speeds and emanating from different azimuthal positions, presented in open loop [48]. The open-loop responses (Figure 1d-i) generated a prediction for the initiation of the expansion avoidance response which was in turn validated in tethered, closed-loop behavior (Figure 1c) and during free flight (Figure 1a).

Opening closed loops during behavior

Traversing the spectrum of topologies by selectively opening individual feedback pathways during intact behavior (a to b in Figure 1) has received much less attention than the prior three examples. In perhaps the clearest example, Lockhart and Ting [13•] used an optimal control model to predict patterns of muscle activation during responses to postural perturbations. They then eliminated one type of proprioceptive feedback and were able to show that, after an adaptation period, the resulting changes in muscle activation were consistent with sensory reweighting prescribed by the same optimal control framework.

While these previous results rely on an elegant coupling of experiment and model, experimental assays on different topologies can generate testable predictions even without an *a priori* model of the system dynamics. The example in Figure 2 depicts a hypothetical set of three complementary experiments for parsing the contributions of visual and olfactory processing in a flower-tracking behavior in the flying moth. It uses the frequency domain tools of control theory to extract a testable, quantitative prediction. Input–output relationships of block or systems of blocks are represented here in the frequency domain by a *transfer function*, such as, $G(s)$. The argument, s, is the Laplace complex frequency variable and is dropped for convenience. In this representation, a composite system reduces to an algebraic expression of its constituent subsystems. The transfer function of two blocks, G_1 and G_2, in series becomes a multiplication of their frequency domain representations, G_1G_2. The representation of parallel pathways is a summation, $G_1 + G_2$. If G is in a unity feedback loop, then the closed-loop transfer function is $G/(1 + G)$. These simple tools are sufficient to make rejectable hypotheses linking low-level mechanisms to intact behavior, as described in Figure 2.

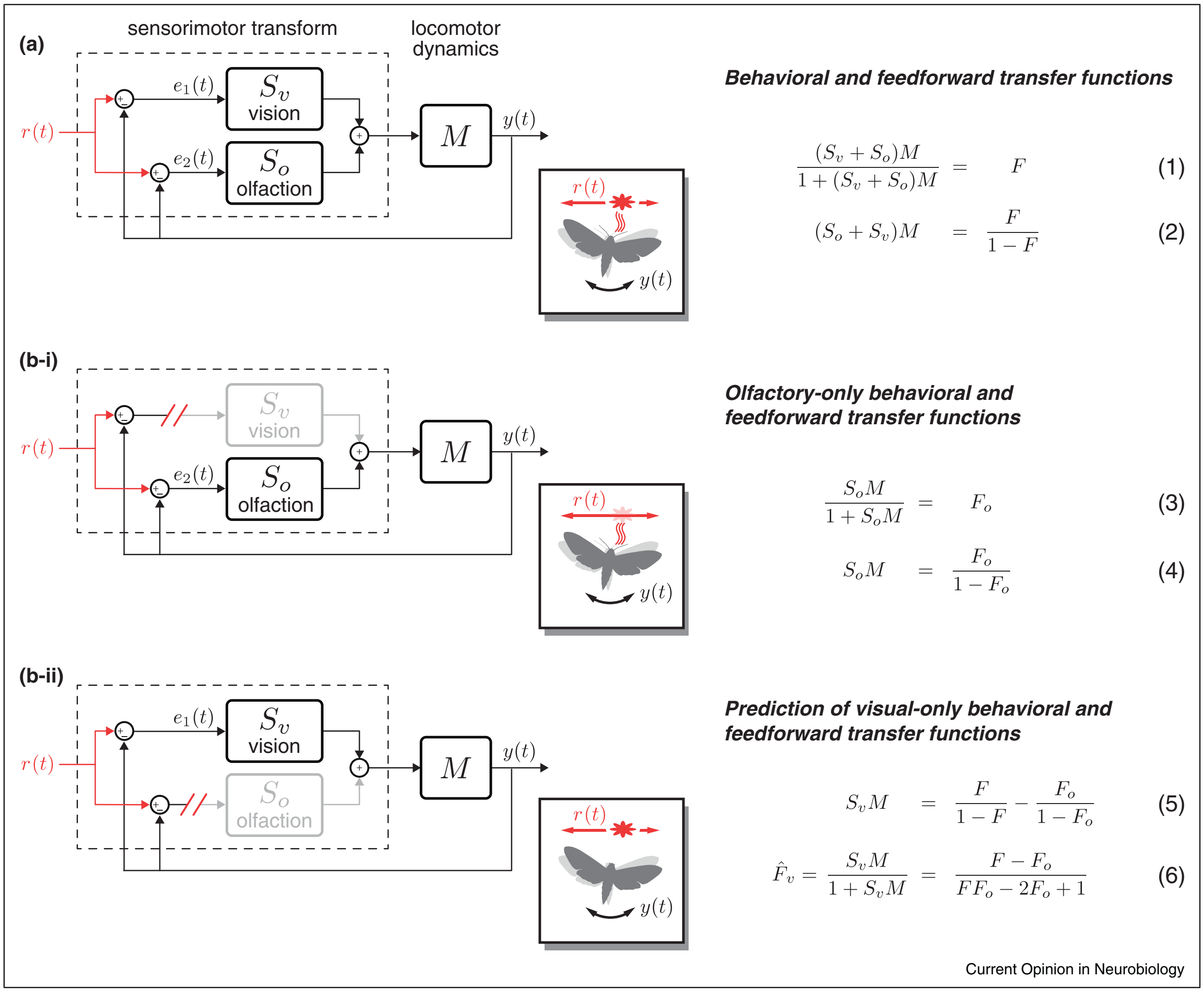
Challenges and horizons

Our effort now should be to rigorously traverse this range of experimental systems using control theory to make specific, testable predictions between the levels. With this in mind, there are several outstanding challenges to address at the intersection of control theory and neuroethology.

Applying linear methods to complex, nonlinear biological systems

Linear control theory provides a useful framework for the quantitive analysis and modeling of behavioral responses and their underlying mechanisms at many scales. While nonlinear dynamics are required to capture many neuromechanical phenomena, linear analyses provides an essential first step. Linearized models provide an excellent initial hypothesis of behavior, precisely because they are rejectable [31•,32••]. The linearity assumption can be supported using a coherence analysis [18••] or, more directly, by testing that the superposition and scaling properties are preserved in the input–output pairs [31•,32••]. Even when a system has nonlinear properties, the failure of linearity can in itself reveal interesting principles of neural computation [18••,31•]. Moreover, many tools exist to characterize nonlinear systems. Poincaré maps and Floquet analysis allow us to apply linear systems identification and control theoretic tools to capture periodic systems' behavior [49]. Other nonlinearities common in biology are context-dependency [44] and adaptation or learning [31•]. While these phenomena alter the linear system properties, they frequently occur over sufficiently long timescales such that for a given context, a linear model retains its efficacy. For example, even if the gains or specificity in fly visual processing

Figure 2



Examples of opening loops in free behavior. In free behavior, the animal tracks a moving stimulus that presents both visual and olfactory cues [5]. The closed-loop behavioral transfer function, F, is experimentally determined from the movement of the flower, $r(t)$, and the moth's position $y(t)$. We hypothesize a topology with parallel sensing pathways **(a)** which puts F in the context of the subsystems S and M (Eqn 1). The S transfer functions encompass the sensory systems and neural control blocks from Figure 1. The M transfer function includes musculo-skeletal and body dynamics. From the measurement of the closed-loop transfer function we can calculated the feedforward (open-loop) transform as $(S_o+S_v)M$ (Eqn 2). This experiment can be repeated in the dark (if the behavior persists) or with an invisible object, thereby opening the visual feedback loop (**b**-i). We now identify a closed-loop transfer function based on closed-loop olfactory-only tracking, F_o, and calculate the feedforward olfactory-only pathway S_oM (Eqns 3, 4). The above two experiments provide a direct, quantitative, and rigorous means to predict responses in a novel topology. Specifically, note that from these two results, we can predict the feedforward response of visual-only tracking, S_vM (Eqn 5) Thus, by simple algebra, we can calculate the predicted closed-loop behavioral response to a visual-only stimulus, $\hat{F_v}$ (Eqn 6). In a final experiment (b-ii), we leave vision intact and inhibit olfaction (e.g. by ablating the antennae or eliminating the odor source), thereby directly measuring F_v and comparing it to the prediction, $\hat{F_v}$. Disagreement between the prediction and the experiment can indicate sensory reweighting or reveal unmodeled subsystems and interconnections.

changes between quiescence and flight [42,43], optomotor frequency response functions may be applied in each context to quantify the performance differences.

Reconciling neural signals with control theory

Our goal in this paper is to identify the parameterization, topology, and performance of the combined neuromechanical system. However, control theoretic approaches can fall short when we do not know *a priori* what signals or variations in signals are necessarily relevant to a controlled behavior. Towards this end, we must be able to integrate the information theoretic and statistical descriptions typically applied to neural encoding with control-theoretic models for the locomotor mechanics and feedback processes.

Dimensionality reduction approaches for identifying a feature basis of high-dimensional signals can extract relevant representations of complex biological signals [50]. Advances on principal component analysis feature discrimination have led to efficient representations of motor cortex activity that is predictive of individual trial-to-trial variability in motor tasks [51]. Other methods explicitly maximize the mutual information between two sets of signals [52,53]. Sets of motor commands can be reduced to muscle synergies and compared across behaviors or individuals [54,55]. As methods move towards simultaneous reduction of high-dimensional input and output data, we may pare down the myriad signals across the nervous system to a number tractable for a controls analysis, providing a reasonable parameterization of the signals relevant to system identification.

Discriminating neural and mechanical contributions to control

Mechanics and neural processing are tuned to interface with one another for the control of behavior. Recording *only* the references and output mechanical states permits the identification of sensorimotor pathways. Characterizing the individual contributions of neural and mechanical transformations further requires measuring and manipulating signals and systems within the block diagram. In practice, simulating closed-loop dynamics (Figure 1c) and opening individual sensorimotor loops (Figure 1b) require access to the intervening neural signals, motor commands, and internal forces during restrained or free behavior (e.g. $d_1(t)$ and $d_2(t)$ in Figure 1). Fortunately, the emergence of new technologies allow unprecedented tractability in recording and observing intact, behaving animals. Miniature backpacks allow electrophysiological and dynamics measurements from moderate to large sized insects [56,57], computer vision advances allow for the rapid analysis of high-speed or long-lasting video recordings [58,59], and the modern genetic toolkit enables not just the elimination of individual genes or sensors, but their enhancement, reversible silencing, optical control, and selective expression [60].

Acknowledgements

We would like to thank Tom Daniel, Michael Dickinson, Jon Dyhr, Eric Fortune, Andrew Lamperski, Manu Madhav, Eric Rombokas, Ari Rosenberg, Sarah Stamper, Erin Sutton, Marie Suver, Eric Tytell and Tim Warren for insightful discussions and critical review of this manuscript. This material is based upon work supported by the National Science Foundation under grant nos. CISE-0845749 (N. Cowan) and IOS-1243801 (D. Padilla) and the Komen Endowed Chair and AFOSR grant nos. FA9550-11-1-0155 (T. Daniel) and FA9550-10-1-0368 (M. Dickinson) and the Paul G. Allen Family Foundation (T. Daniel).

References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

1. Wiener N: *Cybernetics: or Control and Communication in the Animal and the Machine*. New York: John Wiley and Sons, Inc.; 1948, .

2. •• Kiemel T, Zhang Y, Jeka JJ: **Identification of neural feedback for upright stance in humans: stabilization rather than sway minimization**. *J Neurosci* 2011, **31**:15144-15153.

By injecting perturbations simultaneously at multiple points in the feedback loop one can obtain a model of the system as a whole, and, simultaneously, the dynamics of individual transfer functions. The functional significance of the neural feedback system can then be interpreted based, for example, on optimal control predicitons

3. Fry SN, Rohrseitz N, Straw AD, Dickinson MH: **Visual control of flight speed in *Drosophila melanogaster***. *J Exp Biol* 2009, **212**:1120-1130.

4. Barron A, Srinivasan MV: **Visual regulation of ground speed and headwind compensation in freely flying honey bees (*Apis mellifera* L.)**. *J Exp Biol* 2006, **209**:978-984.

5. Balkenius A, Dacke M: **Learning of multi-modal stimuli in hawkmoths**. *PLoS One* 2013, **8**:e71137.

6. Willis MA, Avondet JL, Zheng E: **The role of vision in odor-plume tracking by walking and flying insects**. *J Exp Biol* 2011, **214**:4121-4132.

7. Jindrich DL, Full RJ: **Dynamic stabilization of rapid hexapedal locomotion**. *J Exp Biol* 2002, **205**:2803-2823.

8. Ristroph L, Bergou AJ, Ristroph G, Coumes K, Berman GJ, Guckenheimer J *et al.*: **Discovering the flight autostabilizer of fruit flies by inducing aerial stumbles**. *Proc Natl Acad Sci U S A* 2010, **107**:4820-4824.

9. Daley MA, Biewener AA: **Leg muscles that mediate stability: mechanics and control of two distal extensor muscles during obstacle negotiation in the guinea fowl**. *Philos Trans R Soc B* 2011, **366**:1580-1591.

10. Vance JT, Faruque I, Humbert JS: **Kinematic strategies for mitigating gust perturbations in insects**. *Bioinspir Biomim* 2013, **8**:016004.

11. • Tytell ED, Holmes P, Cohen AH: **Spikes alone do not behavior make: why neuroscience needs biomechanics**. *Curr Opin Neurobiol* 2011, **21**:816-822.

The authors describe the essential role that mechanics play in shaping behavior. In particularly, this review paper highlights the necessity of interpreting neural mechanism in the context of a closed sensorimotor loop that includes muscles, musculoskeletal system, body, and environment

12. Stamper SA, Roth E, Cowan NJ, Fortune ES: **Active sensing via movement shapes spatiotemporal patterns of sensory feedback**. *J Exp Biol* 2012, **215**:1567-1574.

13. • Lockhart DB, Ting LH: **Optimal sensorimotor transformations for balance**. *Nat Neurosci* 2007, **10**:1329-1336.

This paper integrates a mechanical model of postural balance, together with a PID controller to capture details of EMG recordings during perturbed stance. The modeling framework requires remarkably few fitting parameters, and in fact the PID gains are predicted by a simple optimal controller. An exciting feature of the approach is the selective blocking of certain afferents (much like in Figure 2), and the application of control theory to predict both behavioral responses and EMGs after optimal reweighting

14. Josephson RK: **Dissecting muscle power output**. *J Exp Biol* 1999, **202**:3369-3375.

15. • Sponberg S, Libby T, Mullens CH, Full RJ: **Shifts in a single muscle's control potential of body dynamics are determined by mechanical feedback**. *Philos Trans R Soc B* 2011, **366**:1606-1620.

In this paper the authors altered motor commands with single action potential resolution in freely running and standing cockroaches. They showed that the closed-loop transformation of these disturbances into movement changed with behavioral context. Not only was the magnitude impacted, but the direction and sign of the effect changed as well. The companion paper showed how these responses arise from shifts in the open-loop neuromuscular transformation

16. • Bahl A, Ammer G, Schilling T, Borst A: **Object tracking in motion-blind flies**. *Nat Neurosci* 2013, **16**:730-738.

The optomotor response (the stabilization of wide-field motion) in flies has largely been explained by motion-sensitive circuits in the lobula plate. By genetically inhibiting the motion-sensitive pathways to lobula plate (temperature-sensitiveshibire), the authors isolate a parallel motion insensitive

pathway (likely encoding positional cues). Tethered flies walking on a floating ball treadmill were recorded fixating moving wide-field patterns (motion stimulus with little positional cues) as well as stripes (both motion and positional cues) in closed-loop; in experiments where shibire is activated, flies no longer respond to wide-field motion, but the stripe-fixation behavior persists

17. Engert F: **Fish in the matrix: motor learning in a virtual world**. *Front Neural Circuits* 2012, **6**:125.

18. •• Madhav MS, Stamper SA, Fortune ES, Cowan NJ:: **Closed-loop stabilization of the jamming avoidance response reveals its locally unstable and globally nonlinear dynamics**. *J Exp Biol* 2013, **216**:4272-4284 http://dx.doi.org/10.1242/jeb.088922.

The authors examine a sensorimotor behavior — the Jamming Avoidance Response in weakly electric knife fish — by using three separate experimental topologies. The experimental results were interrelated using control systems theory, as described in this perspective. The first experimental topology stabilized the behavior around the unstable equilibrium. The second experimental topology was a behavioral clamp, which served to virtually open a feedback loop. The model that was fit to the data from the first two topologies was used to predict responses in a third: free behavior. The model predicted the responses accurately and predicted a nonlinear bifurcation in the system response which was verified experimentally.

19. Reiser MB, Dickinson MH: **A modular display system for insect behavioral neuroscience**. *J Neurosci Meth* 2008, **167**:127-139.

20. Hinterwirth AJ, Daniel TL: **Antennae in the hawkmoth *Manduca sexta* (Lepidoptera, Sphingidae) mediate abdominal flexion in response to mechanical stimuli**. *J Comp Physiol* 2010, **196**:947-956.

21. Spence AJ, Nicholson-Thomas G, Lampe R: **Closing the loop in legged neuromechanics: an open-source computer vision controlled treadmill**. *J Neurosci Meth* 2013, **215**:164-169.

22. Lavzin M, Rapoport S, Polsky A, Garion L, Schiller J: **Nonlinear dendritic processing determines angular tuning of barrel cortex neurons in vivo**. *Nature* 2012, **490**:397-401.

23. Brezina V, Orekhova IV, Weiss KR: **The neuromuscular transform: the dynamic, nonlinear link between motor neuron firing patterns and muscle contraction in rhythmic behaviors**. *J Neurophysiol* 2000, **83**:207-231.

24. van der Kooij H, Peterka RJ: **Non-linear stimulus–response behavior of the human stance control system is predicted by optimization of a system with sensory and motor noise**. *J Comp Neurol* 2011, **30**:759-778.

25. • Aptekar JW, Shoemaker PA, Frye MA: **Figure tracking by flies is supported by parallel visual streams**. *Curr Biol* 2012, **22**:482-487.

The authors explore visually mediated fixation responses in tethered behaving flies, parsing the contributions of a moving textures (elementary motion, EM) and moving figures (figure motion, FM, presented as regions of coherently moving textures) to the locomotor response. The visual scene is perturbed using uncorrelated m-sequences (pseudorandom binary sequences) for EM and FM. Predictive input-ouput models are generated for the two responses using a correlation analysis between the output (wingbeat asymmetry) and each motion input. Rather than opening a loop by presenting only FM or EM in successive experiments, a clever choice of input signals allows for the parallel processing streams to be identified concurrently

26. Roth E, Reiser MB, Dickinson MH, Cowan NJ: **A task-level model for optomotor yaw regulation in Drosophila melanogaster: a frequency-domain system identification approach**. *IEEE Conference on Decision and Control, IEEE*. 2012:3721-3726.

27. Censi A, Straw AD, Sayaman RW, Murray RM, Dickinson MH: **Discriminating external and internal causes for heading changes in freely flying drosophila**. *PLoS Comp Biol* 2013, **9**:e1002891.

28. Cowan NJ, Lee J, Full RJ: **Task-level control of rapid wall following in the American cockroach**. *J Exp Biol* 2006, **209**:1617-1629.

29. Lee J, Sponberg SN, Loh OY, Lamperski AG, Full RJ, Cowan NJ: **Templates and anchors for antenna-based wall following in cockroaches and robots**. *IEEE Trans Robot* 2008, **24**:130-143.

30. Mongeau JM, Demir A, Lee J, Cowan NJ, Full RJ: **Locomotion and mechanics mediated tactile sensing: antenna reconfiguration simplifies control during high-speed navigation in cockroaches**. *J Exp Biol* (in press), http://dx.doi.org/10.1242/jeb.083477.

31. • Roth E, Zhuang K, Stamper SA, Fortune ES, Cowan NJ: **Stimulus predictability mediates a switch in locomotor smooth pursuit performance for *Eigenmannia virescens***. *J Exp Biol* 2011, **214**:1170-1180.

In this study, the authors characterize the frequency response of a refuge-tracking behavior. Disparities between the responses to sinusoids and pseudo-random sums-of-sinusoids reveals a non-linearity which suggests an adaptive estimation mechanism contributes to the behavior. The experimental assays, modeling approach and analyses applied in this paper are extensible to many goal-directed behaviors

32. •• Dyhr JP, Daniel TL, Morgansen KA, Cowan NJ: **Flexible strategies for flight control: an active role for the abdomen**. *J Exp Biol* 2013, **216**:1523-1536.

This paper characterized the open-loop transfer function from vision to abdominal actuation in the hawkmoth, *Manduca sexta*. They discovered a feedback pathway from wide-field motion detection to flexing of the large abdomen, which can both pitch the body and shift the location of the center of mass. Pitch is an inherently unstable mode for a hovering insect, therefore requiring feedback control. The authors modeled the physical dynamics of abdominal actuation, which serves as a model of the plant. Coupling the open-loop transfer function to these plant dynamics in a closed loop topology, the authors were able to demonstrate that visual control of abdominal flexion was sufficient to stabilize the pitching mode of flight

33. Theobald JC, Ringach DL, Frye MA: **Visual stabilization dynamics are enhanced by standing flight velocity**. *Biol Lett* 2010, **6**:410-413.

34. Tytell ED, Hsu CY, Williams TL, Cohen AH, Fauci LJ: **Interactions between internal forces, body stiffness, and fluid environment in a neuromechanical model of lamprey swimming**. *Proc Natl Acad Sci U S A* 2010, **107**:19832-19837.

35. Sefati S, Neveln ID, Roth E, Mitchell T, Snyder JB, MacIver MA *et al.*: **Mutually opposing forces during locomotion can eliminate the tradeoff between maneuverability and stability**. *Proc Natl Acad Sci U S A* 2013, **110**:18798-18803 http://dx.doi.org/10.1073/pnas.1309300110.

36. Fernández MJ, Springthorpe D, Hedrick TL: **Neuromuscular and biomechanical compensation for wing asymmetry in insect hovering flight**. *J Exp Biol* 2012, **215**:3631-3638.

37. Heisenberg M, Wolf R: **Reafferent control of optomotor yaw torque in *Drosophila melanogaster***. *J Comp Physiol A* 1988, **163**:373-388.

38. Revzen S, Burden SA, Moore TY, Mongeau JM, Full RJ: **Instantaneous kinematic phase reflects neuromechanical response to lateral perturbations of running cockroaches**. *Biol Cybern* 2013, **107**:179-200.

39. Sponberg S, Full RJ: **Neuromechanical response of musculo-skeletal structures in cockroaches during rapid running on rough terrain**. *J Exp Biol* 2008, **211**:433-446.

40. Sponberg S, Spence AJ, Mullens CH, Full RJ: **A single muscle's multifunctional control potential of body dynamics for postural control and running**. *Philos Trans R Soc B* 2011, **366**:1592-1605.

41. Sponberg S, Daniel TL: **Abdicating power for control: a precision timing strategy to modulate function of flight power muscles**. *Proc Roy Soc B* 2012, **279**:3958-3966.

42. Maimon G, Straw AD, Dickinson MH: **Active flight increases the gain of visual motion processing in drosophila**. *Nat Neurosci* 2010, **13** 393–U29.

43. Suver MP, Mamiya A, Dickinson MH: **Octopamine neurons mediate flight-induced modulation of visual processing in *Drosophila***. *Curr Biol* 2012, **22**:2294-2302.

44. Maimon G: **Modulation of visual physiology by behavioral state in monkeys, mice, and flies**. *Curr Opin Neurobiol* 2011, **21**:559-564.

45. Cowan NJ, Fortune ES: **The critical role of locomotion mechanics in decoding sensory systems**. *J Neurosci* 2007, **27**:1123-1128.

46. Hyslop A, Krapp HG, Humbert JS: **Control theoretic interpretation of directional motion preferences in optic flow processing interneurons**. *Biol Cybern* 2010, **103**:353-364.

47. Ejaz N, Krapp HG, Tanaka RJ: **Closed-loop response properties of a visual interneuron involved in fly optomotor control**. *Front Neural Circuits* 2013, **7**: http://www.frontiersin.org/Neural_Circuits/10.3389/fncir.2013.00050/abstract.

48. Reiser MB, Dickinson MH: **Visual motion speed determines a behavioral switch from forward flight to expansion avoidance in drosophila**. *J Exp Biol* 2013, **216**:719-732.

49. Revzen S, Guckenheimer JM: **Finding the dimension of slow dynamics in a rhythmic system**. *J R Soc Interface* 2012, **9**:957-971.

50. Bialek W, De Ruyter Van Steveninck R, Tishby N: **Efficient representation as a design principle for neural coding and computation**. *IEEE International Symposium on Information Theory, IEEE*. 2006:659-663.

51. Churchland MM, Cunningham JP, Kaufman MT, Foster JD, Nuyujukian P, Ryu SI *et al.*: **Neural population dynamics during reaching**. *Nature* 2012, **487**:51-56.

52. Fitzgerald JD, Sincich LC, Sharpee TO: **Minimal models of multidimensional computations**. *PLoS Comp Biol* 2011, **7**:e1001111.

53. Tishby N, Pereira FC, Bialek W: **The information bottleneck method**. *Allerton Conf Comm Comp* 1999:368-377.

54. Tresch M, Jarc A: **The case for and against muscle synergies**. *Curr Opin Neurobiol* 2009, **19**:601-607.

55. Safavynia SA, Ting LH: **Task-level feedback can explain temporal recruitment of spatially fixed muscle synergies throughout postural perturbations**. *J Neurophysiol* 2012, **107**:159-177.

56. Spence AJ, Revzen S, Seipel J, Mullens C, Full RJ: **Insects running on elastic surfaces**. *J Exp Biol* 2010, **213**:1907-1920.

57. Harrison RR, Fotowat H, Chan R, Kier RJ, Olberg R, Leonardo A *et al.*: **Wireless neural/EMG telemetry systems for small freely moving animals**. *IEEE Trans Biomed Circ Syst* 2011, **5**:103-111.

58. Kabra M, Robie AA, Rivera-Alba M, Branson S, Branson K: **JAABA: interactive machine learning for automatic annotation of animal behavior**. *Nature Methods* 2013, **10**:64-67.

59. van Breugel F, Dickinson MH: **The visual control of landing and obstacle avoidance in the fruit fly *Drosophila melanogaster***. *J Exp Biol* 2012, **215**:1783-1798.

60. Clark DA, Freifeld L, Clandinin TR: **Mapping and cracking sensorimotor circuits in genetic model organisms**. *Neuron* 2013, **78**:583-595.