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DOI: 10.1016/j.cub.2010.01.008

## Sensorimotor Transformation: From Visual Responses to Motor Commands

A recent study reveals how vision-based estimates of self-motion are passed on to premotor descending neurons which connect to various motor centres in the fly nervous system.

Holger G. Krapp

The ability to control movements requires our nervous system to perform at least two fundamental tasks. One is to constantly monitor how we are moving and whether our movements deviate from a desired path. And the other is to generate compensatory motor commands should any deviations occur. The first part involves sensory modalities, including vision and the inner ear organ, which provide us with information about our movements and the orientation of our body relative to the world. The second part relies on appropriate action of our muscular or motor systems. One of the most challenging questions in neurobiology is: how is sensory information transformed into appropriate motor action? Wertz *et al.*

[1] have studied the electrical responses of individual nerve cells that connect visual interneurons in the fly brain to motor areas in the animal's thorax: they found that the signals of these premotor descending neurons provide a more robust indication of the fly's motions in space than the signals of the visual interneurons from which they receive input.

Non-neurobiologists tend not to consider sensorimotor transformation as a particular challenge. We are normally quite good at controlling our movements without even thinking about it, but the way our nervous system does it involves a massive amount of neural computing power. What is more, in humans, parts of almost all brain areas contribute when it comes to movement control.

Neurobiologists working on the neural principles underlying sensorimotor transformations, therefore, are dealing with quite a degree of complexity. Luckily, applying a reductionist approach, the complexity may at least partly be reduced.

Instead of trying to work out the visuomotor transformation required to create, for instance, a landscape painting, we could confine ourselves to something more humble. This could be the visual control of gaze and locomotion, a reflex-like behaviour seen in all animals endowed with eyes. And also, instead of looking at one of the most complex nervous systems of all, which arguably is the human one, we could look at something considerably smaller: the nervous system of a fly. Despite the fact that its entire nervous system consists of less than  $4 \times 10^5$  neurons — ridiculously few compared to the  $10^{12}$  neurons in our own brain — a fly achieves a degree of sophistication in terms of visuomotor control unmatched by any man-made device. Just convince yourself by watching their spectacular flight manoeuvres.

Similarly unmatched is our level of understanding of the functional organization of the fly nervous system.

Research over many decades has established the wiring of most of the fly's neural circuits [2]. Furthermore, electrophysiological and imaging studies monitoring neuronal activities, combined with quantitative behavioural input–output analyses and computational modelling, have revealed a number of general principles in neural processing — many of them contributing to visual gaze and flight control [3–5].

A key advance in working out what we know today about fly visuomotor control came from behavioural studies into motion vision. It was quite obvious that the ability to use visual information for motor control was critically dependent on the existence of a mechanism that allows animals and humans to distinguish between visual motion in different directions. How the visual system solves this task was first discovered in a beetle [6]. Later on, experimental and theoretical studies — many of them in flies — confirmed the functional structure of the so-called elementary movement detector (EMD). An EMD is activated when visual motion takes place in its preferred direction and is inhibited upon motion in the opposite null-direction [7].

Why was this discovery so important for visuomotor control? Whenever we are moving around, the entire visual world is continuously shifted across our eyes. The resulting retinal image shifts, or optic flow fields, have long been identified as a rich source of self-motion information [8]. The reason is that the overall pattern of retinal motion depends on how we are moving. If we move forward, for instance, an optic flow pattern is generated that looks fundamentally different than that we face when rolling our head (Figure 1B, grey arrows). As a rule of thumb, during translation local optic flow is in the same direction at opposite positions in the visual field while during rotation the flow at those positions is in opposite directions. Thus, by analysing the direction of motion within optic flow patterns, the visual system can infer what self-motion has caused them. And a necessary condition for such an analysis is the ability to distinguish between visual motion in different directions.

This is generally true for all visually oriented animals and well supported

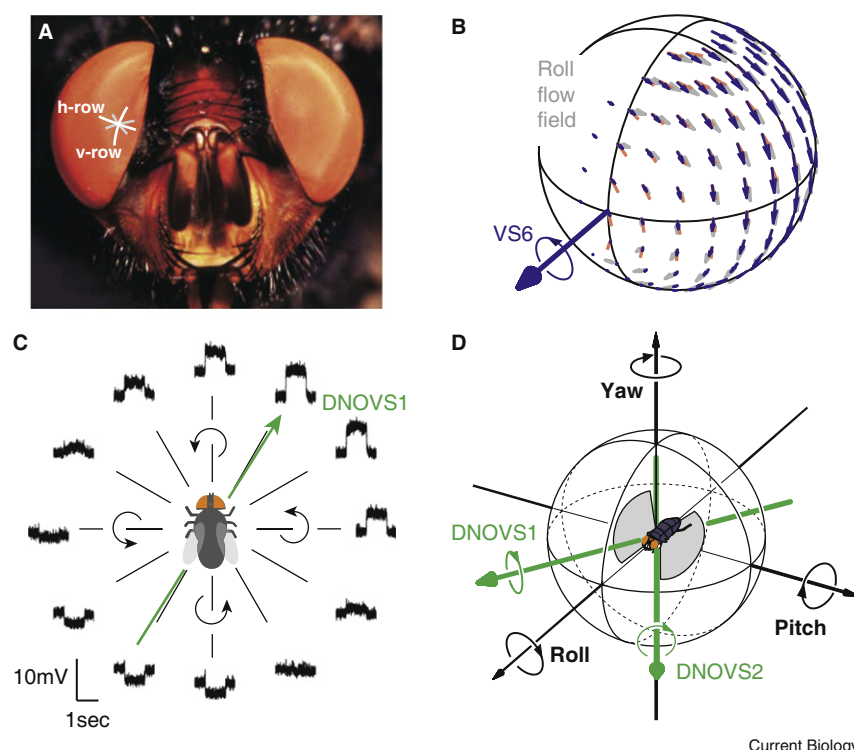


Figure 1. Transforming local retinal image shifts into estimates of self-motion.

(A) The blowfly *Calliphora vicina* has massive compound eyes each consisting of several thousand individual facets. Each facet, or ommatidium, measures the light level at a tiny patch of the visual field. Elementary movement detectors (EMDs) analyse the direction of visual motion by correlating the light levels at neighbouring ommatidia along the hexagonal eye lattice. The analysis takes place in sensory coordinates given by the local lattice orientation. V-rows are defined by the arrangement of next-neighbouring ommatidia, h-rows are the result from the combination of the two oblique rows, which are also defined by next neighbouring ommatidia. The motor systems, however, require signals which are provided in coordinates that fit the pulling plane of the muscles controlling head and body movements. (B) The transformation between retinal coordinates and motor coordinates takes place by selectively integrating local motion signals. Optic flow generated by roll-rotation consists of a specific distribution of vectors indicating the relative velocity and direction of retinal image motion (grey background arrows). The VS6 cell integrates the signals of those EMDs whose preferred direction matches the direction of local optic flow vectors in a roll flow field. The blue arrows show the resulting local preferred directions in the receptive field of the VS6 cell. Note that the local preferred directions of VS6 roughly coincide with the local orientation of the hexagonal eye lattice (orange bars). The output signals of VS6 are passed on to motor and descending neurons and can be used to control head and body movements around the animal's roll axis. Other tangential cells signal different self-motion components. (C) The electrical responses of DNOVS1 when the fly encounters wide-field motion patterns mimicking various horizontal rotations. The neuron prefers rotations around an axis 32° off the fly's roll axis. (D) Preferred rotation axes of DNOVS1 and DNOVS2. Photograph (A): courtesy Roland Hengstenberg, data in (C,D) taken from [1], data in (B) re-plotted from [5,9].

from first principle [5]. But how does the nervous system analyse optic flow to monitor self-motion? That is where the fly has proven to be an excellent model system to study. Its prominent compound eyes — which grant the animal panoramic vision — indicate already that the fly is well adapted to visually estimate its self-motion. Flies employ thousands of EMDs analysing directional motion along the facet rows of its hexagonal eye lattice (Figure 1A). The output signals of the

EMDs are then connected to the extended input arborizations of interneurons called tangential cells living in the lobula plate, the third visual neuropil in the fly brain [2]. These tangential cells were shown to have certain properties essential for self-motion estimation: they respond to visual motion in a directionally selective way and they have extended receptive fields, sometimes even exceeding an entire visual hemisphere [3,5].

Detailed studies of the local motion preferences within their receptive fields revealed that tangential cells integrate the output of EMDs in a selective way. Each tangential cell receives input only from those EMDs for which the preferred direction matches the direction of local retinal image shifts in a specific optic flow field, and thus during particular self-motions [9]. For instance, the distribution of local preferred directions in the receptive field of the 10 VS-cells — a distinct subpopulation of tangential cells — suggested that these cells encode the fly's rotations around horizontal body axes. Figure 1B (blue arrows) shows the receptive field organization of the VS6 cell. Another subpopulation of tangential cells, the HS-cells, is in charge of encoding rotations around slightly diverging vertical axes [5]. HS-cells have also been suggested to assess the distance to objects in the surroundings when the fly is drifting after a sharp turn [10].

Work over the last couple of years has further detailed our knowledge about a variety of clever computational principles which help the fly tangential cells to robustly estimate self-motion components. This is by no means trivial because local EMD signals are ambiguous as they not only depend on the direction and speed of motion but also on the distributions of visual contrast in the surrounding [7]. Besides spatially integrating thousands of EMD signals evolution has designed a few other tricks to solve the problem. HS-cells, for instance, form networks of connections involving the left and the right part of the fly visual system which helps to tell apart forward translation and yaw rotation [11]. And VS-cells were shown to be connected with their next neighbours via electrical synapses [12]. For one, this explains the enormous extent of these cells' receptive fields.

More importantly for the fly's ability to estimate self-motion is that the chain-like connectivity between VS-cells further mitigates the confounding effect local contrast variations may have on their output signals — the unfortunate property they would otherwise inherit from the inputting EMDs. The robustness of encoding self-motions is also increased by banning non-linear processing steps, including any gain control mechanisms, to the tangential cell dendrites while their outputs may

be linearly combined with those from other tangential cells or with signals from other sensory modalities [13]. These principles are quite important for a successful sensorimotor transformation because the signals controlling the fly's gaze and flight should ideally depend only on the self-motion component but not on the visual layout of the surroundings.

What self-motions do the premotor descending neurons encode? We knew already that the VS-cells measure rotations around horizontal body axes [9]. And studies on the receptive fields of neck motor neurons receiving direct and indirect input from HS- or VS-cells roughly reflect the preferred self-motion axes of the tangential cells [14]. Although the preferred self-motions of the descending neurons DNOVS1 and DNOVS2 were predicted based on the neurons' local motion preferences [15], their responses to global optic flow-like motion patterns had not been measured before. Wertz *et al.* [1] designed a straight forward experiment. They put a fly in the centre of a cylindrical visual stimulation set-up, similar to a flight simulator. While recording the electrical signals from DNOVS1 and DNOVS2 the scientists generated wide-field motion patterns mimicking rotations of the fly around various horizontal body axes. The strongest increase or decrease of the neurons' electrical potential occurred when the pattern was rotated around a specific horizontal body axis in the counter clockwise or clockwise direction, respectively. All other simulated rotation axes tested made the neurons respond at intermediate levels. For DNOVS1 the results are shown in Figure 1C.

From these experiments Wertz *et al.* [1] worked out that both DNOVS1 and DNOVS2 measure rotations of the fly which are about plus and minus 30° off the animal's roll axis (Figure 1D). They also found out that the robustness of the signals — that is, the reliability with which descending neurons indicate specific self-motions — is greater than it is in the tangential cells they receive input from. When repeatedly confronted with rotations of a naturalistic wide-field pattern the response variance relative to the mean descending neuron responses is significantly smaller than in tangential cells. How this increased robustness

is established is not yet known. But one potential explanation might be that information from both eyes is combined, a mechanism found in fly neck motor neurons [14] and suspected to be in place at least for some descending neurons [1].

Wertz *et al.* [1] have set the stage to even further extend our knowledge on how sensory information is conveyed to the motor system in flies for gaze and flight control. They have confirmed that the selective integration of ambiguous local motion information results in signals indicating the animals self-motion. The robustness with which certain rotations are encoded is further increased along distinct processing stages of the sensorimotor pathway: from the integration of local signals on the tangential cell dendritic input arborizations, their axons and again at the level of their target neurons.

Some pressing questions still remain unanswered: For instance, what is the logic behind the specific choice of the rotation axes the tangential cells, motor neurons and descending neurons cover? Recently it was proposed that the specific arrangement of the tangential cell preferred rotation axes establishes a non-orthogonal motor coordinate system that simplifies the detection and control of the fly's natural modes of motion when airborne [16]. And secondly, how are signals from other sensory modalities linked in to even further fine-tune motor commands the fly uses to keep its gaze level and to maintain aerodynamic stability [16]? First studies on the latter question suggest that such multisensory integration takes place at all levels, from the tangential cells to the motor and descending neurons [17–19].

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DOI: 10.1016/j.cub.2010.01.024

## Evolution: Postponing Extinction by Polyandry

**Sex-ratio meiotic drive occurs when males produce a predominance of X-chromosome bearing sperm and an inordinate number of daughters. A driving X causes highly female-biased sex ratios and the risk of extinction. Polyandry can rescue a population from extinction.**

Michael J. Wade

Meiotic drive is the failure of ‘fair’ Mendelian meiosis in heterozygous individuals, such that they produce gametes carrying a preponderance of one allele instead of the expected equal proportions of two alleles. Meiotic drive can be detected only in the progeny of heterozygotes and only if one allele produces a recognizable phenotype. Meiotic drive involving a sex chromosome,  $X^{SR}$  (where the superscript ‘SR’ stands for sex ratio), is easy to detect, because every mating involves a heterozygote (males are the heterogametic or XY sex in many species, including fruit flies), the sex of an offspring is a readily recognizable phenotype, and the expected ratio of sons to daughters is 1:1. Mendelian meiosis results in males producing equal numbers of X-chromosome bearing and Y-chromosome bearing sperm, while XX females produce only X-bearing eggs. Meiotic drive is a violation of Mendelian meiosis such that  $X^{SR}Y$  males produce almost exclusively  $X^{SR}$  sperm and few if any Y-bearing sperm. As a result, their offspring are overwhelmingly daughters and few, if any, sons. In a population, the selective advantage of a driving  $X^{SR}$  relative to a wild-type

X-chromosome is nearly two-fold, making sex-ratio meiotic drive one of the strongest known evolutionary forces. In theory, the population sex ratio is a simple function of the frequency of  $X^{SR}$ . As the  $X^{SR}$  chromosome spreads relentlessly, it would ultimately result in a population composed entirely of females, which will go extinct [1–3]. However, the observed frequency of  $X^{SR}$  in natural populations is low: less than 25% in natural populations of *Drosophila pseudoobscura* [4]. Furthermore, in laboratory experiments, the frequency of  $X^{SR}$  often tends to decline [5] and extinction takes place rarely or never. This gives rise to the question that has absorbed research geneticists for decades: what are the evolutionary forces that limit meiotic drive? The study of meiotic drive offers the rare opportunity to investigate conflict between opposing selective forces and between different levels of selection (gametic, individual and group) while the evolutionary conflict is in progress.

An experimental study by Trevor Price, Gregory Hurst and Nina Wedell [6], published in this issue of *Current Biology*, marks an important step forward in our understanding of the evolutionary forces that limit the effects of meiotic drive. Their work rests on the

earlier observations [7] that discovered that in *Drosophila pseudoobscura* males with an  $X^{SR}$ -chromosome ( $X^{SR}Y$  males) produce only half the amount of functional sperm of normal,  $X^+Y$  males (where  $X^+$  indicates a normal, wild-type X-chromosome). Mechanistically, it turns out that, in the development of the gametes of  $X^{SR}Y$  males,  $X^{SR}$  bearing sperm survive at the expense of Y-bearing sperm, reducing by half the total amount of functional sperm. Thus, the mechanism responsible for the apparent meiotic drive appears to contain the seeds for its own limitation in that  $X^{SR}Y$  males will suffer a severe handicap in reproductive competition with normal males because they have fewer sperm. However, early research into the sperm competitive ability or ‘virility’ of  $X^{SR}Y$  relative to  $X^+Y$  males was conflicting or ambiguous [8–12] and models showed that the expected fitness effects, especially in the presence of frequency-dependent mating and re-mating, should be complex [12–15] with the possibility of multiple, stable intermediate equilibria.

In their study, Price and colleagues [6] established 48 populations using *D. pseudoobscura* recently isolated from a wild population, each with a frequency of 30% of the  $X^{SR}$  chromosome, mirroring the natural frequency in their source population. Each population was founded with 60 males and 60 females and subsets of 12 populations were subjected to different and artificially controlled mating treatments. In the monandrous treatment, sexually mature females were mixed with males for four hours before being isolated away from males — it is known that females will