Research Focus

# Neurons that respond to more than one depth cue

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**The 3D orientation of a surface can be specified by perspective, motion parallax or binocular disparity. Tsutsui *et al.* have found cells in the monkey intraparietal sulcus that responded to surface orientation defined only by a texture gradient. Most of these cells also responded to orientation defined only by binocular disparity.**

Neurons in the visual cortex that respond selectively to simple visual features, such as orientation, colour and motion, are known as feature detectors. Information from distinct feature detectors is combined for at least three purposes. First, we recognize objects, such as faces, with particular combinations of features. This requires 'and' operators. Second, we scale one feature in terms of another. For example, we assess shape in terms of viewing angle and we scale binocular disparities by the square of viewing distance. This requires multiplicative operators. Finally, we recognize object properties defined by different visual features. For example, some neurons in the monkey inferior temporal cortex (part of the ventral pathway concerned with shape recognition) respond selectively to contours defined by luminance, by texture or by motion [1,2]. Furthermore, most motion-selective cells in the middle temporal area (MT; part of the dorsal pathway concerned with processing orientation and motion) respond to motion of contours defined by luminance, by contrast, by texture or by disparity [3,4]. Neurons of this type are 'or' operators and are said to be cue-invariant.

We use several distinct sources of information (depth cues) to detect the 3D structure of our visual surroundings. For example, an impression of an inclined surface is created by a texture gradient, such as that illustrated in Figure 1. The same impression of inclination is created when a display of dots presented to one eye has a horizontal shear motion imposed on it [5]. When both eyes are open, we have stereoscopic vision arising from the fact that the eyes view the world from different vantage points [6]. Thus, the impression of an inclined surface is created when the displays in Figure 2 are combined by crossing the eyes. So the same impression of depth can be produced by a texture gradient, by shear motion or by binocular disparity. We know something about the locations in the brain where each depth cue is processed.

## Detectors for distinct cues to visual depths

Neurons that respond selectively to texture gradients are found at levels beyond the primary visual cortex, particularly in the dorsal pathway leading through MT to the parietal lobe. Using functional magnetic resonance imaging (fMRI), Shikata *et al.* [7] revealed that areas within the intraparietal sulcus in humans are active when subjects discriminate between the 3D orientations of a surface defined by a texture gradient.

Some neurons in the MT respond best to motion parallax produced, for example, by moving inclined surfaces [8]. Other MT neurons respond to the second spatial derivative of motion produced by motion of 3D curved surfaces [9–11]. A patient with bilateral lesions that included V5 (i.e. MT) was unable to experience objects moving in depth even though she could perceive stationary objects [12].

Neurons sensitive to binocular disparity in local regions (disparity detectors) are found in the primary visual cortex. Neurons sensitive to gradients of disparity in the images of inclined surfaces occur at higher levels. For example, some cells in the caudal part of the lateral bank of the monkey intraparietal sulcus respond selectively to the 3D orientation of surfaces, defined only by disparity [13]. Some cells in the inferior temporal cortex respond selectively to disparity gradients depicting surfaces curved in depth [14].

## Cue-invariant detectors for depth perception

Thus, we have neurons that respond selectively to particular cues to distance. Because the cues produce the same percept, one would expect to find neurons that

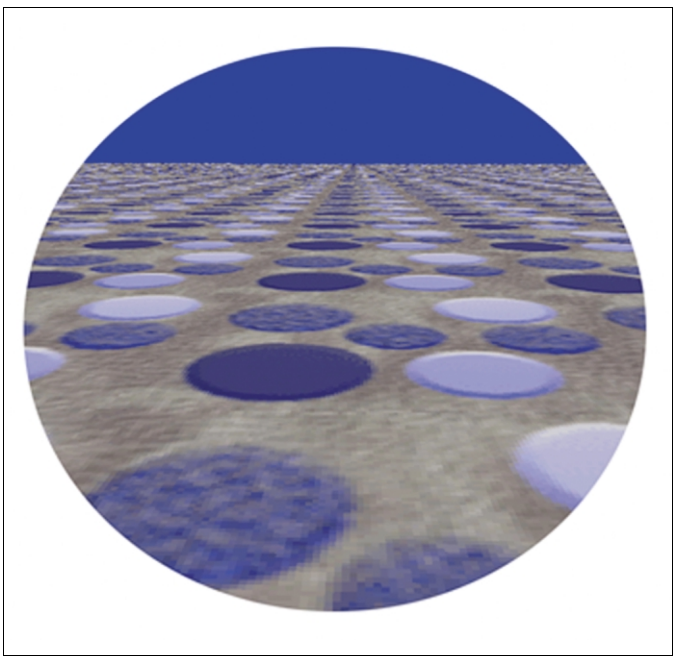

**Fig. 1.** The diminishing size and increasing density of texture elements towards the horizon creates an impression of a surface inclined in depth.

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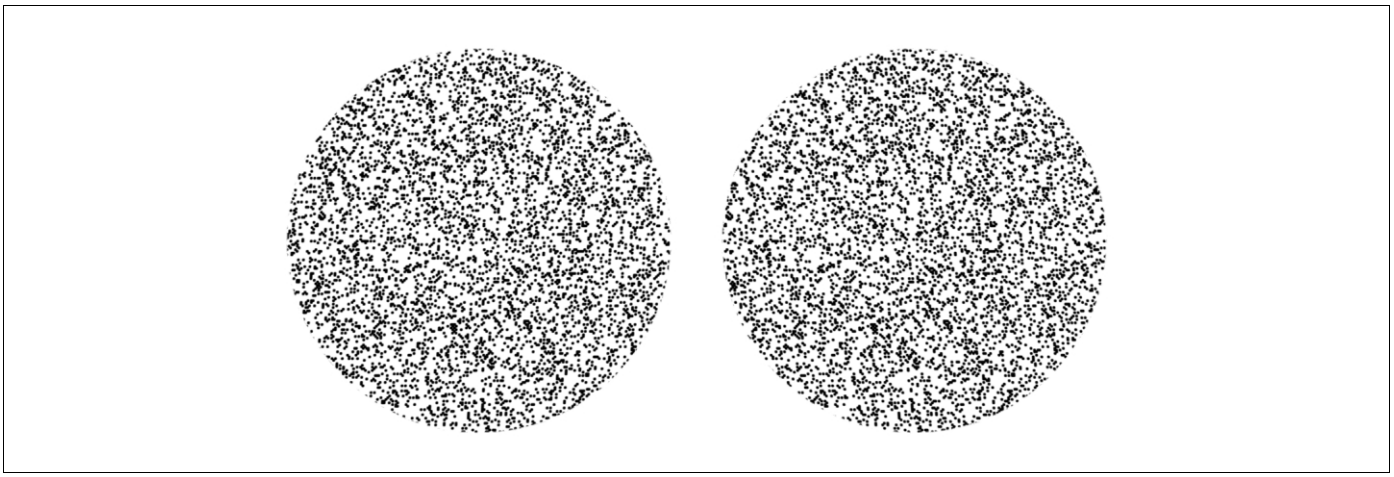

**Fig. 2**. When the eyes are converged on a point some distance sin front of or beyond the figures, the two figures will fuse to create an impression of an inclined surface.

respond to any or all of these depth cues. Cue-invariant neurons for depth cues have indeed been found. Tsutsui *et al*. [15] identified cells in the intraparietal sulcus of the monkey that responded selectively to the orientation of a surface in depth when the cue was either disparity or linear perspective. Other cells in same area responded best to motion in depth specified by looming, others to motion in depth specified by changing disparity, and still others to motion in depth defined by any of these depth cues [16].

In a recent issue of *Science* [17], Tsutsui, Sakata, Naganuma and Taira, of the Nihon University School of Medicine (Tokyo, Japan), described neurons in the intraparietal sulcus of the macaque monkey that are sensitive to surface inclination defined by either a texture gradient or a gradient of binocular disparity. They first trained two monkeys to match the inclinations of surfaces containing only the depth cue of a texture gradient, and to match the inclinations of surfaces containing only the cue of disparity. They also trained monkeys to match the inclination of a surface defined by a texture gradient to the inclination of a surface defined by disparity that was seen subsequently. They recorded from single cells in the intraparietal sulcus as alert monkeys performed the matching tasks. Seventy percent of cells responded selectively to the 3D orientation of a surface defined only by a texture gradient formed from dots or from line elements. This is the first report of single neurons that register surface orientation based on a texture gradient alone. Of these cells, 77% also responded to the orientation of the surface defined by disparity alone. This is the first report of neurons that are cue-invariant with respect to the depth cues of texture gradient and disparity.

The picture that emerges is one of many retinotopically coded visual centres that process different visual features. Some centres are organized hierarchically whereas others are in parallel. Areas also interact through lateral connections and higher centres send recurrent signals back to earlier stages. Neurons in some centres receive inputs from two or more neurons that process distinct sources of information. These neurons detect linked features, scale features and produce cue-invariant responses. The visual system is multilayered in that the output of each processing stage, not merely the output of the highest processing units in the system, is potentially available to consciousness. Thus, we are aware of the difference between an inclined surface defined by disparity, one defined by motion parallax and one defined by a texture gradient – even though the same impression of an inclined surface is produced by each type of stimulus.

In the coming years, we can expect an explosive increase in our knowledge of the ways in which information is combined in the nervous system for specific purposes. This endeavour will require the combined efforts of physiologists and psychophysicists.

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# α-Synuclein oligomerization: a role for lipids?

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**α-Synuclein is a core component of the proteinaceous aggregates observed in several neurodegenerative diseases. A central role of α-synuclein in neurodegeneration was demonstrated by the discovery of missense α-synuclein mutations in familial Parkinson's disease. However, the specific mechanism by which α-synuclein contributes to these diseases remains unclear. A recent study by Sharon *et al.* linked the presence of specific fatty acids to the appearance of α-synuclein oligomers *in vivo*. α-Synuclein oligomers might be a first step in the formation of α-synuclein aggregates present in a number of neurodegenerative diseases, although their cytotoxicity remains to be directly demonstrated.**

α-Synuclein has notoriety for being implicated in many neurodegenerative diseases. A central role for this protein in Parkinson's disease has been established with the discovery of two Parkinson's disease familial mutations. α-Synuclein is a primary component of Lewy bodies, as well as of abnormal proteinaceous aggregates present in Parkinson's disease, dementia with Lewy bodies, multiple system atrophy and other diseases [1]. However, the specific mechanism by which α-synuclein contributes to these diseases remains unclear.

## Oligomerization of α-synuclein

α-Synuclein has been found in insoluble aggregates in neurodegenerative diseases. One notion gaining support is that the primary insult leading to the deaths of relevant cell populations is formation of α-synuclein prefibrillar oligomers, rather than formation of the insoluble fibrils that are the hallmarks of many neurodegenerative diseases [2]. This phenomenon might not be confined to α-synuclein but, rather, common to soluble oligomers in general: for example, β-amyloid (Aβ) soluble oligomers in Alzheimer's disease [3], and even soluble oligomers formed by non-disease-associated proteins, have been shown to be inherently cytotoxic [4].

Evidence supporting this notion comes mostly from *in vitro* experiments. The formation of oligomeric species of α-synuclein *in vitro* was found to parallel that of Aβ, non-fibrillar oligomers of which are toxic in cell culture [2] and can disrupt cellular processes *in vivo* [5]. Further *in vitro* experiments showed that the Parkinson's-disease-related α-synuclein mutations (A30P and A53T) promote the formation of fibrillar and non-fibrillar aggregates, and 20–25 molecules of α-synuclein were found to form oligomers with pore-like morphologies [6]. Noting that the A30P and A53T mutations cause an earlier appearance of these structures than that seen with wild-type α-synuclein, Volles and Lansbury [7] posit that such a structure might be responsible for permeabilization of membranes by pre-fibrillar α-synuclein, in *in vitro* assays and possibly in *in vivo* conditions leading to the disease. Although this is intriguing, the formation of α-synuclein pre-fibrillar aggregates resembling pores has yet to be demonstrated in a cellular context. Gosavi *et al.* [8] provide correlative evidence of the disruption of Golgi complex with the appearance of α-synuclein aggregates, but the nature of the α-synuclein aggregates is unclear and the role of monomeric α-synuclein, or larger α-synuclein aggregates, cannot be ruled out.

The formation of α-synuclein oligomers can be affected by neurological injuries. Oxidative injuries, which are linked to many neurodegenerative diseases, can affect α-synuclein in several ways, including the nitration of tyrosine residues (nitrated α-synuclein has been observed in Lewy bodies) or the formation of a dopamine–α-synuclein adduct [9,10]. Consistently, both of these phenomena have effects on the formation of α-synuclein oligomers *in vitro*. Nitration induces the formation of α-synuclein oligomers and stabilizes α-synuclein polymers [9], although it can lead to the accumulation of oligomerized but pre-fibrillar species of α-synuclein [11], whereas dopamine reduces the amount of fibrillar α-synuclein in a cell-free system, possibly stabilizing a pre-fibrillar species of α-synuclein by forming a dopamine–α-synuclein adduct [10].

## α-Synuclein–lipid associations

The *in vitro* association between α-synuclein and lipid membranes, and particularly small vesicles, is well established. Although α-synuclein is generally cytosolic in its distribution, it is enriched in synaptosomal fractions of mouse and human brain, and similarities between the N terminus of α-synuclein and the lipid-binding domains of some apolipoproteins suggest a role for α-synuclein interactions with lipid membranes [12]. Further data in support of a lipid–α-synuclein interaction were observed

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