

Measuring contrast processing in the visual system using SSVEP

Alex R. Wade

Daniel H. Baker

Department of Psychology and York Biomedical Research Institute, University of York, UK

Review for Vis Neurosci

Abstract:

Contrast is the currency of the early visual system. Measuring the way that the computations underlying contrast processing depend on factors such as spatial and temporal frequency, age, clinical conditions, eccentricity, chromaticity and the presence of other stimuli has been a focus of vision science for at least 100 years. One of the most productive experimental approaches in this field has been the use of the ‘steady-state visually-evoked potential’ (SSVEP): a technique where contrast modulating inputs are ‘frequency tagged’ (presented at well-defined frequencies and phases) and the electrical signals that they generate in the brain are analyzed in the temporal frequency domain. SSVEPs have several advantages over conventional measures of visually-evoked responses: they have relatively unambiguous output measures, a high SNR, and they allow us to analyze interactions between stimulus components using a convenient mathematical framework. Here we describe how SSVEPs have been used to study visual contrast over the past 70 years (Dawson, 1954). Because our thinking about SSVEPs is well-described by simple mathematical models, we embed code that illustrates key steps in the modelling and analysis. This paper can therefore be used both as a review of the use of SSVEP in measuring human contrast processing, and as an interactive learning aid.

Introduction

Neurons in the visual areas of the brain are primarily responsive to changes in cone photoreceptor activations across time and space. This property, referred to as contrast, sets the fundamental limits of our visual abilities, which remain steady over a remarkably wide range

of environmental light levels. The human response to contrast can be studied using many different techniques. Early work used psychophysical methods to measure contrast sensitivity (Campbell & Green, 1965), defined as the inverse of the lowest contrast that can be reliably detected. But neural responses can also be measured more directly using techniques such as fMRI, MEG, and EEG. Here we will describe how an EEG method known as the steady state visually evoked potential (SSVEP) technique has contributed to our understanding of human contrast processing in health, disease and throughout development.

The SSVEP is a continuous electrical response evoked in the brain by visual stimuli flickering at a constant frequency (Regan, 1966). For contrast-defined stimuli, such as sine-wave gratings, it is strongest at the occipital pole, adjacent to the early visual areas that generate the signal, although careful analysis of individual VEPs reveals multiple generators throughout visual cortex (Di Russo *et al.*, 2005, 2007). The flickering stimulus entrains neural population responses at multiples of the stimulus frequency, so continuous EEG data are typically analysed by taking the Fourier transform, and estimating the amplitude at these frequencies. Two common variants involve sinusoidal on-off flicker, where the stimulus alternates between a blank background and the peak contrast, and sinusoidal counterphase flicker, where the stimulus alternates in phase (i.e the black regions become white and the white regions become black). On-off flicker can drive independent populations of on- and off-cells in the retina once per cycle and can therefore produce a response at the fundamental flicker frequency, known as 1F, and its integer harmonics: 2F, 3F, 4F and so on. Counterphase flicker contains two transients per cycle and therefore does not produce a response at 1F, only at its even harmonics: 2F, 4F, 6F and so on. Because square-waves are spectrally broad-band, square wave flicker tends to produce more complex spectral harmonics than sine-wave flicker.

The higher harmonics of the steady-state signal are generally thought to reflect nonlinear processing in the visual system (Regan & Regan, 1988). SSVEP signals can also be elicited by periodic changes of stimulus properties other than achromatic and chromatic contrast, such as motion, stereo depth, and facial identity or expression (see Norcia *et al.*, 2015, for an overview); however our focus here is on the contrast response.

Why measure responses to contrast?

Contrast is one of the most fundamental pieces of information that the eye transmits to the brain. It can be defined as the change in cone photoreceptor activity over space (‘spatial contrast’) or time (‘temporal contrast’). Cone photoreceptors - which drive precortical opponent pathways - contribute to both chromatic and achromatic contrast, and although most of the research we describe here focuses on achromatic contrast, SSVEPs have proven to be an excellent measure of early chromatic processing as well (McKeefry *et al.*, 1996; Baseler & Sutter, 1997; Di Russo *et al.*, 2001a).

Contrast is relatively simple to define: typically, it is specified as the percentage deviation of a uniform stimulus from the background. So, for example, a disk of 100 units of cone

activation (I_{stim}) surrounded by a ‘background’ of 50 units of activation ($I_{\text{background}}$) has a contrast of $\frac{I_{\text{stim}} - I_{\text{background}}}{I_{\text{background}}} = 100\%$. Where patterns are more complex (for example, the sine-wave gratings or Gabor patches common in vision science), the Michelson (1927) definition of contrast is specified by the maximum and minimum excursions from the mean:

$$\frac{I_{\text{stimmax}} - I_{\text{stimmin}}}{I_{\text{stimmax}} + I_{\text{stimmin}}}. \quad (1)$$

These contrast definitions are appropriate both to photometric measures of stimulus contrast (for example, luminance; Lennie *et al.* (1993)) and also to definitions based on cone excitations (MacLeod & Boynton, 1979; Derrington *et al.*, 1984) which are more common in work on chromatic processing.

Although its mathematical definition is straightforward, the computations that underlie contrast processing in the brain have been the subject of intense research for many decades. The neural code for contrast, even in the earliest parts of visual cortex, is not simply a linear transform of the contrast at the retina - instead, contrast signals undergo a cascade of nonlinear processing stages that, broadly, attempt to normalise the output relative to the spatiotemporal environment. This normalization, achieved through a computation called ‘contrast gain control’ (Heeger, 1992; Foley, 1994; Carandini & Heeger, 2011) maximises the sensitivity of the visual system by making optimal use of neuronal bandwidth. As an example, a grating placed at the centre of a low-contrast background typically appears more intense than the same grating when superimposed on a high contrast background (see Figure 1; note that the code used to produce all figures in this review is available in python and R at: <https://github.com/wadelab/contrastReviewPaper>).

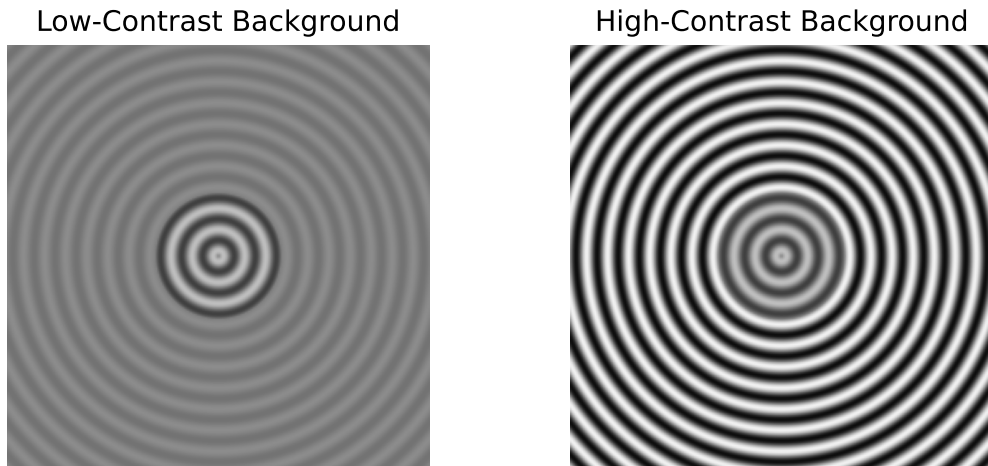


Figure 1: The perceived contrast of a stimulus depends on its context. A high contrast surround reduces the apparent contrast of the central ‘probe’ region.

A significant body of research into contrast processing is concerned with how these normalization mechanisms depend on colour (Chen *et al.*, 2000), orientation (Foley, 1994), eye of origin (Legge, 1979; Baker *et al.*, 2007), spatial and temporal frequency (Meese & Baker, 2009), location (Polat & Sagi, 1993; Tadin *et al.*, 2003; Petrov *et al.*, 2005), age (Betts *et al.*, 2005), and the presence of neurological disorders (Porciatti *et al.*, 2000; Tsai *et al.*, 2011). The SSVEP has proven to be invaluable in this research because it provides an objective readout of contrast representation at different stages of the visual system, and allows us to ‘tag’ the probe and background at separate frequencies.

Because it provides a direct read-out of neural population activity, the SSVEP signal can reveal key features of neural signal transduction. For example, by varying the peak stimulus contrast parametrically, a ‘contrast vs response’ function can be measured - where the ‘response’ is typically defined as the amplitude of the SSVEP frequency component at the stimulus frequency, or a low multiple thereof. This corresponds closely to similar functions reported by studies measuring single unit activity or local field potentials in the cortex (Shapley & Victor, 1980; Morrone *et al.*, 1982). However the SSVEP has the advantage that it is non-invasive, and so can be measured in awake, behaving human participants.

To understand the utility of the contrast SSVEP, it is helpful to identify the cascade of processing stages in the early visual system that give rise to it. In the following section we illustrate how a typical SSVEP signal measured over early visual cortex might contain information about a large number of early visual computations.

Contrast processing - linear and nonlinear

Neurons have a limited dynamic range, yet they can transmit information about visual stimuli that span many orders of magnitude. In the domain of contrast, to some extent this is accomplished at a population level - individual neurons typically implement a non-linear, sigmoidal contrast vs response (CRF) transducer (Tolhurst *et al.*, 1981; Albrecht & Hamilton, 1982) and different neurons exhibit peak sensitivity (defined as the maximum slope of the function) at different contrast levels (Carandini & Heeger, 1994; Carandini *et al.*, 1998; Busse *et al.*, 2009). A neuronal population will therefore span a sensitivity range greater than any individual member.

Individual neurons at multiple stages of the visual hierarchy also change their sensitivity depending on the average spatiotemporal contrast energy of their environment. This “normalisation” process is dynamic and nonlinear and is well-modeled by a hyperbolic ratio function in which the response of each neuron is modulated by a local ‘gain pool’ composed of the summed responses of the local neuronal population (Heeger, 1992; Busse *et al.*, 2009; Carandini & Heeger, 2011; Baker & Wade, 2017).

To better understand these processes, we will show how sinusoidal input signals might be processed by the visual system to produce SSVEPs. Figure 2 illustrates how sine waves of

different contrasts are processed in a linear system. The first panel shows the input sine wave, which would be used to modulate stimulus amplitude over time. Notice that there are five peaks in the waveform during the one second sample, so the stimulation frequency is 5Hz (F1). The second panel shows Fourier transform of the waveform, which contains a substantial peak at this frequency. If we parametrically vary the stimulus contrast (i.e. the amplitude of the waveform), the amplitude of the F1 component increases linearly with contrast (right panel).



Figure 2: Illustration of a sinusoidal input signal (left), its Fourier spectrum (middle), and how the amplitude of the first harmonic component increases with contrast (right). These calculations assume an entirely linear system.

Next we can consider the impact of a nonlinearity in processing on the responses. One of the simplest nonlinearities is the function that describes a cell’s response to different levels of contrast. In Figure 3 this is modeled by a hyperbolic ratio function resulting in a saturating non-linearity:

$$R_{\max} = \frac{C_{\text{in}}^n}{C_{50}^n + C_{\text{in}}^n}, \quad (2)$$

where R_{\max} describes the maximum response level, C_{in} is the input contrast (or the time-varying waveform), C_{50} is the ‘semi-saturation constant’ (the point at which the response is at half-maximum) and n controls the steepness of the curve (with a typical value around $n = 2$).

This nonlinearity has clear effects on signal transduction. The sinusoidal waveform is distorted by the nonlinearity, and appears frequency doubled (left panel of Figure 3; note that other nonlinearities such as rectification and squaring can have similar effects). The distortion is reflected in the Fourier spectrum (middle panel of Figure 3), which now includes responses at integer multiples (known as harmonics) of the stimulation frequency (10, 20 and 30Hz), but no response at the fundamental (5Hz). Finally, the contrast response function is now nonlinear (right panel of Figure 3). Although the hyperbolic ratio function (Equation 2) is monotonic,

the CRF resulting from measuring the amplitude of the second harmonic (2F) component contains a slight roll-off at high input contrasts. This results from the distortion of the input sine waves at high contrast due to a combination of the full-wave rectification and saturating non-linearity. Power at other harmonics increases, and the total power generated by the input is monotonic. This roll-off is often seen in experimental data and has been referred to as ‘supersaturation’ (Tyler & Apkarian, 1985; Peirce, 2007).

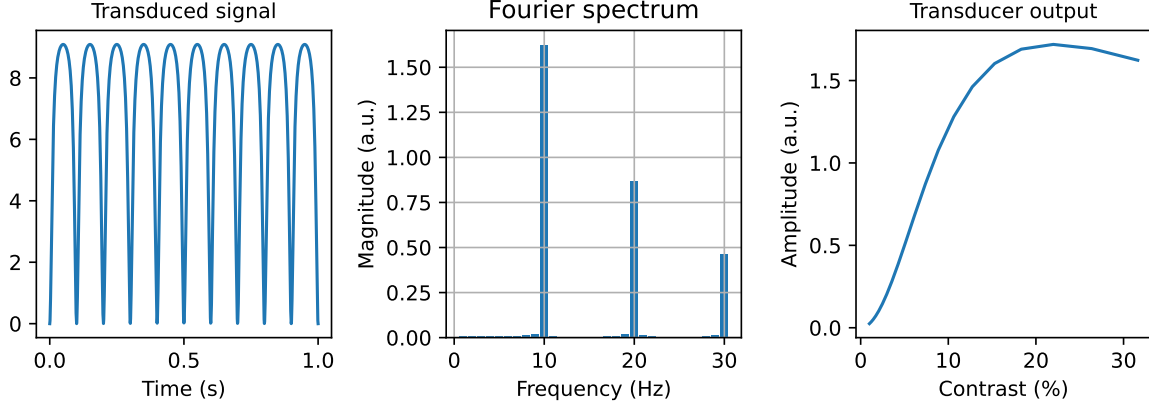


Figure 3: Illustration of how a sinusoidal input signal is affected by a nonlinear transducer. The input waveform (left panel) is frequency doubled by the squaring operator, and now features energy at the second harmonic (10Hz) and its multiple (middle panel). The contrast response function at the second harmonic is now nonlinear, and saturates at high contrasts (right panel).

To illustrate the effect of contrast gain control (Heeger, 1992), we next include a second component (a ‘mask’) that contributes to the gain pool of the first (the ‘target’). The mask stimulus will suppress the response at the target frequency, reducing its amplitude. The suppression is reciprocal - activity at the mask frequency is also reduced by the presence of the target, in a contrast-dependent manner (Busse *et al.*, 2009). At a single pair of (matched) contrast levels, we see a complex pattern of intermodulation terms in the transduced waveforms (left panel of Figure 4) and in the Fourier spectrum (middle panel of Figure 4). The two components interact generating nonlinear intermodulation terms at sums and differences of the input frequencies (F_1 , F_2). The nature of the interaction — and therefore the pattern of intermodulation terms — is determined by the computations happening as the contrast signal moves from retina to cortex (Regan & Regan, 1988).

If the two inputs were simply added together, the representation of the resulting signal in the Fourier domain would be the linear sum of the two independent signals (i.e. peaks at F_1 and F_2). However, it is important to take physiology into account. Contrast gain control reduces the amplitude of the responses via a suppressive process, which can be incorporated into our transducer function via an additional denominator term:

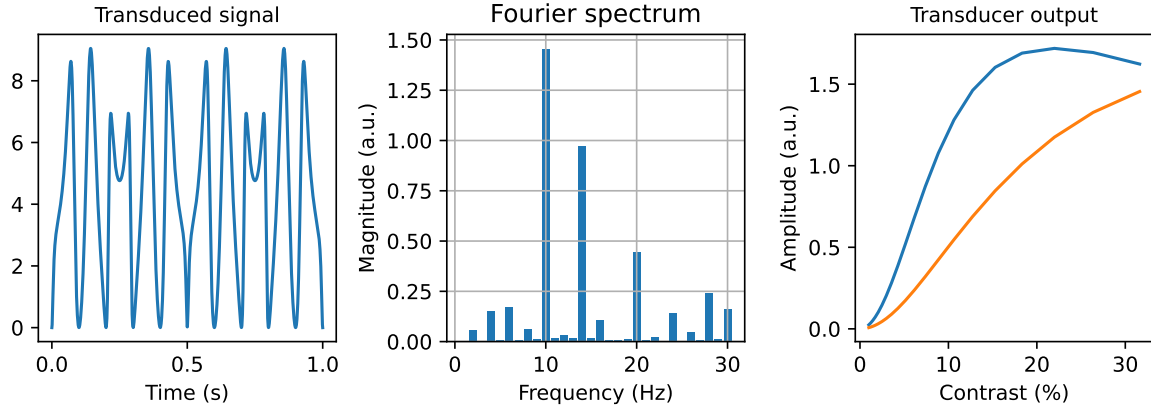


Figure 4: Demonstration of how two inputs of different frequencies are processed by a nonlinear transducer. Additional harmonics are apparent in the Fourier spectrum (middle panel), and the contrast response function is suppressed (right panel).

$$R_{\max} = \frac{C_{\text{in}}^n}{C_{50}^n + C_{\text{in}}^n + C_{\text{mask}}^n}, \quad (3)$$

where C_{mask} reflects the contrast of the mask component at a distinct frequency from that of the target. The effect of this extra term is to reduce the target response (see right panel of Figure 4). For a linear contrast axis, the contrast response function becomes shallower, whereas on a logarithmic contrast axis it maintains its steepness and shifts to the right. Suppressive effects of this kind have been obtained using SSVEP with a variety of different types of mask, including orthogonal overlaid masks, surround masks, and dichoptic masks (Burr & Morrone, 1987; Ross & Speed, 1991; Candy *et al.*, 2001; Busse *et al.*, 2009; Cunningham *et al.*, 2017; Salelkar & Ray, 2020; for a meta-analysis see Baker *et al.*, 2021).

Even without considering a spatial component, the early visual system is far more complex than the model here suggests. For example as well as cells that code positive or negative contrast in a more or less continuous manner, the retina also contains ‘transient’ cells that code temporal changes in contrast. These cells (Kuffler *et al.*, 1957; Alpern, 1971), and cells with similar properties in the LGN (Levitt *et al.*, 2001) and cortex (Hubel & Wiesel, 1959; Movshon, 1975), will introduce second harmonic components even when the stimulus itself is modulated in an on-off fashion. Analogously, in the spatial domain, so-called ‘simple cells’ are sensitive to the polarity of a spatial contrast modulation while ‘complex cells’ respond to the presence of patterned spatial contrast irrespective of its spatial position (Hubel & Wiesel, 1962). The SSVEP response to a contrast-reversing sine-wave grating therefore contains information about nonlinear computations performed across a range of retinal and cortical cell types.

The complexity of even a simple simulation of the frequency-domain signal arising from non-linear interactions is intriguing. Presumably, the signal measured from early visual cortex is

the result of a cascade of nonlinear retinal and cortical operations up to that point. It therefore contains a ‘signature’ or ‘fingerprint’ of the computational nature, order and parameters of those operations - including the shape of the transducer functions and the computations involved in signal combination. In principle, that information could be recovered from the SSVEP signal - a possibility recognised in the early days of the technique (Regan & Regan, 1988). Although characterising the complete set of computations along entire processing pathway is challenging, careful parametric variation of the input stimuli does allow us to fit models of early visual gain control using SSVEP data. For example, Tsai *et al.* (2012) demonstrated that a gain control model gave a good account of the pattern of intermodulation responses produced by two overlaid patterns flickering at different frequencies. This was achieved by passing full stimulus waveforms through the transducer nonlinearity, and calculating the Fourier spectrum of the model output. Our own work on signal combination across eyes and space similarly demonstrated close correspondence between the predictions of a computational model and empirical data in humans (Baker & Wade, 2017). More detailed modelling of intracortical recordings (Groen *et al.*, 2022) has revealed details of the timecourse of gain control effects, specifically that normalization is delayed slightly relative to the initial visual response.

Similar changes to the contrast response function might also be obtained using adaptation paradigms, in which the visual system is exposed to high contrast stimuli for long durations. Psychophysically, adaptation increases detection thresholds, but has little effect on contrast discrimination performance (Ross *et al.*, 1993), much like pattern masks (Foley, 1994). Although SSVEP adaptation effects show strong tuning for orientation (Campbell & Maffei, 1970; Vergeer *et al.*, 2018) and spatial frequency (Mecacci & Spinelli, 1976), there appear to be no studies measuring the full SSVEP contrast response function before and after an extended period of adaptation.

Measuring the development of contrast processing

An early use of the SSVEP was to provide an objective estimate of spatial contrast sensitivity in infants, without requiring behavioural responses. In well-motivated adults, psychophysical measurements of contrast sensitivity remain the gold standard. However, it is difficult and time consuming to obtain reliable psychophysical data from infants. In these cases, SSVEP measurements represent a fast and efficient method for measuring low-level visual responses (Tyler *et al.*, 1979; Braddick *et al.*, 1986; Norcia *et al.*, 1990) and the high SNR of SSVEP means that infants need only look at the screen for short periods of time.

Because SSVEP responses at detection threshold are very small, estimating a threshold is achieved by measuring the contrast response function at relatively high levels, and extrapolating back along the function (either contrast vs response measured at a constant spatial frequency or spatial frequency vs response at a constant contrast level) to estimate its intercept with the x-axis (see Figure 5). This contrast level was shown to correspond approximately with psychophysically measured detection thresholds (Norcia *et al.*, 1986).

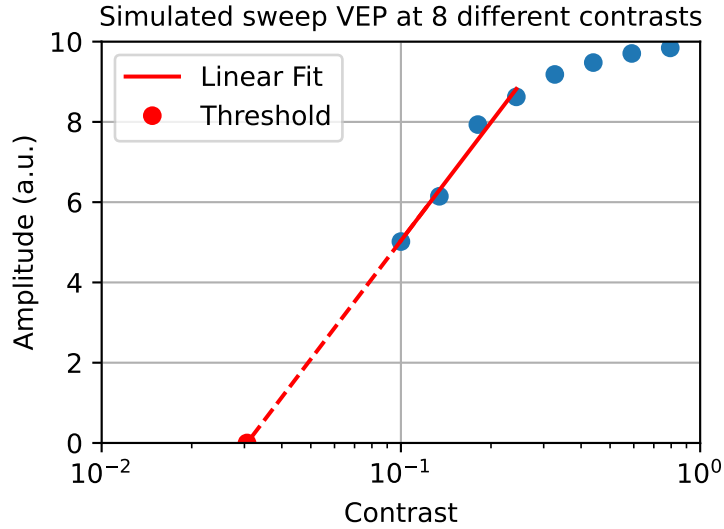


Figure 5: Sweep VEP simulation showing how a contrast detection threshold can be estimated from sweep VEP data measured at higher contrasts. The solid line is the regression fit to the lowest four data points, and the dashed line extrapolates the fit back to determine the contrast value when $y=0$, which gives a threshold estimate (red point).

A robust estimate of the threshold therefore requires the measurement of the SSVEP amplitude at many different super-threshold contrast levels. This was made faster by the development of the ‘sweep VEP’ paradigm in which the stimulus changed its contrast, spatial frequency or some other property, throughout a trial (Tyler *et al.*, 1979). To avoid hysteresis effects, the sweep is sometimes conducted both up and down in the same experiment (Tyler *et al.*, 1979; Norcia & Tyler, 1985a; Norcia *et al.*, 1990). The sweep VEP (really, a sweep ‘SSVEP’) technique is now commonly-used to obtain a rapid and objective measurement of visual acuity. In particular, because of its relative speed and simplicity, this technique has now become a standard for conducting tests of visual acuity in very young subjects or where behavioural tests are not appropriate (Ridder, 2004; Bach *et al.*, 2008; Hoffmann *et al.*, 2017; Bach & Farmer, 2020).

This approach has revealed much about the development of visual abilities in infants (Harris *et al.*, 1976; Atkinson *et al.*, 1979; Braddick *et al.*, 1986). In general, SSVEP measurements of infant vision have revealed that contrast sensitivity for both achromatic and chromatic contrast as well as stereoscopic depth perception develops earlier than had been supposed previously based on behavioural readouts (Dobson *et al.*, 1978; Norcia & Tyler, 1985b) with both chromatic and achromatic contrast detection reaching near-adult levels by around six months. Spatial acuity as measured by SSVEP reaches adult levels more slowly, but near-adult levels are recorded around one year (Norcia & Tyler, 1985b; Hamer *et al.*, 1989) compared to around six to seven years with behavioural measures (Atkinson & Braddick, 1983; Ellemberg

et al., 1999). At least some of this difference is likely due to the relative objectivity and high SNR of the SSVEP technique compared to other methods such as preferential looking, which require careful measurement of the infant’s gaze direction. However it should be noted that other groups have reported electrophysiological correlates of visual acuity that more closely match the behavioural measures (De Vries-Khoe & Spekreijse, 1982).

The SSVEP technique has also been used to study the development of the contrast gain control mechanisms described in the previous section (Candy *et al.*, 2001; Pei *et al.*, 2017). Although contrast gain control is measurable in infants as young as six weeks old (Morrone & Burr, 1986; Skoczenski & Norcia, 1998; Candy *et al.*, 2001), its development appears to be slower, with adult levels being reached at approximately 11 years (Pei *et al.*, 2017).

Contrast processing in clinical conditions

The SSVEP technique has also been used to study clinical conditions, such as diseases and developmental disorders. This can often be informative regarding the underlying mechanism that characterises the condition. Here we focus on four conditions, but there is potential to apply the method more broadly, either as a diagnostic technique, or to monitor disease severity and progression, or the efficacy of treatments.

Epilepsy is a neurological condition in which patients experience seizures - episodes of uncontrolled neural activity that can cause unconsciousness, involuntary movements and convulsions, and atypical sensory experiences. Porciatti *et al.* (2000) showed that individuals with photosensitive epilepsy generate larger steady-state signals in response to flickering visual stimuli, and their contrast response functions saturate less than those of healthy controls. This is consistent with the idea that epilepsy involves a cortical hyperexcitability that makes seizures more likely. It is also the case for individuals with idiopathic generalised epilepsy (Tsai *et al.*, 2011), a subtype of epilepsy that has a less obvious link to vision. The differences apply across the whole contrast-response function, and so resemble a response gain effect (see Figure 6a), which might be due to reduced inhibition from neighbouring neurons. Differences in SSVEP amplitudes have also been reported in individuals with migraine (Shibata *et al.*, 2008), a condition also associated with cortical hyperexcitability.

Amblyopia is a disorder of binocular vision, characterised by one eye contributing much less to perception than the other. This is often due to strabismus (squint) or anisometropia (difference in optical prescription between the eyes) during development. Contemporary accounts suggest that the amblyopic eye is suppressed by signals from the fellow eye. SSVEPs provide a convenient and objective method to characterise the difference in neural response to signals in each eye, and typically show reduced responses to stimuli in the amblyopic eye (see Figure 6b) across the contrast range (Baker *et al.*, 2015; Lygo *et al.*, 2021). There are currently many novel binocular treatments for amblyopia under development, often involving virtual reality or stereo display systems designed to encourage the two eyes to work together. The steady-state approach may be more sensitive and objective than typical acuity measurements, and also has

the potential to measure suppression between the eyes directly (e.g. Zheng *et al.*, 2019; Hu *et al.*, 2023; Du *et al.*, 2023).

Autism is a condition often associated with differences in vision (Simmons *et al.*, 2009) and other senses (MacLennan *et al.*, 2022). Pei *et al.* (2014) used a sweep-VEP method with counterphase flickering stimuli, and found weaker responses in autistic children at spatial frequencies around 8c/deg, compared with age-matched controls. This was subsequently replicated in a further pediatric sample by Vilidaite *et al.* (2018) (see Figure 6c), who additionally found weaker responses in autistic adults at the second harmonic (using on/off flicker). Interestingly this study replicated its key findings in a *Drosophila* genetic model of autism (*Nhe3* mutations), illustrating the translational potential of the steady-state approach, as well as identifying a possible biomarker for autism.

Recent work on understanding Parkinson’s disease has also used *Drosophila* genetic models. Afsari *et al.* (2014) found that mutant flies produced stronger SSVEP responses to flickering lights than control flies (see Figure 6d). The authors theorised that differences in early gain control during development might lead to visual deficits later in life. Although visual responses are a convenient assay of neural function, it is likely that the same general process applies throughout the whole brain, including in the motor system where the core Parkinson’s symptoms (tremor, rigidity, slow movement) manifest. The SSVEP differences were reduced by a kinase inhibitor that targets the dopamine system, demonstrating how model organisms can be used to test new pharmacological treatments. SSVEP responses also provide a potential method to diagnose Parkinson’s before any symptoms manifest, and to monitor the effect of treatments.

Attention and arousal

Attention exerts a profound influence on visual performance: for example, instructing people to attend covertly to a spatial location improves their performance on a target detection task significantly (Bashinski & Bacharach, 1980; Posner, 1980; Carrasco *et al.*, 2000; Cameron *et al.*, 2002; Morrone *et al.*, 2004; Pestilli *et al.*, 2009). In principle, this enhancement may be driven both by modulation of the underlying signal or noise characteristics, or by additional decision-theoretic factors such as reduction in spatial uncertainty (Petrov *et al.*, 2006; Gould *et al.*, 2007). Early experiments with non-human primates showed little evidence for attentionally-driven changes in neuronal spike rates (Luck *et al.*, 1997; McAdams & Maunsell, 1999; Mehta *et al.*, 2000a, 2000b; Marcus & Van Essen, 2002), but with the advent of spatially-resolved human brain imaging methods in the late 1990s it became apparent that spatial attention was linked to frank changes in both fMRI BOLD responses (Tootell *et al.*, 1998; Somers *et al.*, 1999; Gandhi *et al.*, 1999; Brefczynski & DeYoe, 1999; Kastner *et al.*, 1999; Buracas & Boynton, 2007; Silver *et al.*, 2007; Li *et al.*, 2008; Murray, 2008) and EEG signals (Morgan *et al.*, 1996; Müller *et al.*, 1998; Müller & Hillyard, 2000; Ding *et al.*, 2006).



Figure 6: Example contrast response functions for different clinical conditions. Panel (a) shows modelled contrast response functions for epilepsy patients (blue) and control participants (black), based on the data of Tsai et al. (2011). Panel (b) shows functions for the amblyopic (red) and fellow (black) eyes of adults with amblyopia, based on the data of Baker et al. (2015). Panel (c) shows functions for children with (green) and without (black) a diagnosis of autism, based on the data of Vilidaite et al. (2018). Panel (d) shows data from *Drosophila melanogaster* (fruit flies) from Afsari et al. (2014). One day-old flies expressing a human gene linked to Parkinson's (hLRRK-G2019S) show increased SSVEP response amplitude and sensitivity (red) compared to control animals (black).

Electrophysiological and psychophysical measurements of the effect of attention on both luminance and chromatic contrast have strongly implicated gain control as an underlying mechanism (Lu & Doshier, 1998; Di Russo & Spinelli, 1999*a*; Di Russo *et al.*, 2001*b*). These effects also appear to differ between chromatic and achromatic pathways (Di Russo & Spinelli, 1999*b*) - perhaps as a result of the different levels of nonlinear gain control in the early pre-cortical magno-, parvo- and konio-cellular pathways (Derrington & Lennie, 1984; Kaplan & Shapley, 1986; Lee *et al.*, 1990; Solomon & Lennie, 2005). In the late 2000s a comprehensive theoretical model for attentional modulation was developed that framed it as a gain control computation (Reynolds & Heeger, 2009; Boynton, 2009). This framework has proven to be influential - explaining a wide range of phenomena from the earlier literature and demonstrating subtle interactions between the size of the attentional ‘spotlight’ and the stimulus configuration which rationalise many apparent contradictions in the literature. Direct measurements of attentional modulation of achromatic SSVEP signals are broadly consistent with this model (Lauritzen *et al.*, 2010; Hou *et al.*, 2016; Martinovic & Andersen, 2018) and confirm the relatively weaker role of spatial attention on responses driven by chromatic stimuli - particularly those that isolate the opponent S-(L+M) cone pathway (Highsmith & Crognale, 2010; Wang & Wade, 2011). The gain control model of attention can also be extended to SSVEP studies of feature-based attention which show that the modulatory effects can be targeted to the most informative neuronal populations (Verghese *et al.*, 2012).

The SSVEP can also be used to study changes in visual processing *driven* by different behavioural states or overall arousal. For example, locomotion has been shown to alter neuronal excitability and spatial normalization in mice (Niell & Stryker, 2010; Ayaz *et al.*, 2013) - running mice have higher visual sensitivity and lower surround suppression compared to stationary mice. Although measuring EEG responses from locomoting humans is technically challenging, SSVEP studies (which are able to distinguish broadband noise from input signal effectively) have shown that walking also alters early visual processing, although in a manner different to that observed in mice (Benjamin *et al.*, 2018; Cao & Händel, 2019).

SSVEP measurements are typically used to measure time-invariant responses due to sustained attention. However, recent work has shown that moderately high modulation frequencies (ca 10Hz) and short analysis windows (1.5s) can also be used to track the dynamic allocation of attention across a task (Chota *et al.*, 2024) or attention to moving targets (Lissa *et al.*, 2020). The ability to track changes in attention over short time periods is also important if SSVEP is to be used for dynamic readouts - for example in a Brain Computer Interface.

Brain-computer interfaces

One widespread recent application of the SSVEP technique is in the design of brain-computer interfaces, which seek to control some aspect of a computer using neural signals. The high SNR and precise frequency resolution of SSVEPs make them an ideal candidate for this approach. Typical studies may involve presenting an array of stimuli at different flicker frequencies, and

having the participant select one either by overt attention (i.e. shifting fixation to foveate the selected stimulus) or covert attention (i.e. deploying attention to one stimulus whilst keeping fixated) (Middendorf *et al.*, 2000). Because SSVEP signals are highly sensitive to both visual field position (Di Russo *et al.*, 2007; Ales *et al.*, 2010) and attentional state (Morgan *et al.*, 1996; Müller *et al.*, 1998; Lauritzen *et al.*, 2010; Verghese *et al.*, 2012), the response to the selected stimulus will typically increase relative to the others, allowing it to be identified by an on-line algorithm. Because more than one stimulus frequency is generally present, this modulation and the associated changes in gain control will affect the entire pattern of self- and intermodulation terms, allowing the choice to be decoded by a multivariate pattern classifier.

This approach is primarily useful in situations that require the BCI to distinguish from among a small set of possibilities: for example, in early work, visual stimuli representing ‘Left’ and ‘Right’ commands in a flight simulator were distinguished robustly (Middendorf *et al.*, 2000). Although SSVEP-based BCI interfaces typically do use contrast flicker, work in this field has largely focused on optimising the stimuli or decoders to increase decoding performance and reducing visual fatigue associated with the long-term presentation of arrays of high-contrast flicker (Diez *et al.*, 2024), rather than studying visual contrast processing *per se*. We therefore note in passing that using SSVEPs to improve our understanding of early contrast processing may yield benefits to this related field.

Future directions

The SSVEP is a powerful tool for studying contrast processing. It provides a high SNR readout of neuronal activity that is unambiguously linked to the input. It is sensitive to both the amplitude and phase of the input and when combined with source imaging, it can be extracted from different cortical regions allowing researchers to track contrast processing computations across the visual pathway. Because of the high SNR, it can be measured in subjects where long recording durations are impractical (for example, infants or patients with neurological disorders) and at frequencies high enough to be effectively invisible (Herrmann, 2001; Seijdel *et al.*, 2023; Minarik *et al.*, 2023). The SSVEP is also able to ‘fingerprint’ modulators of the inputs through the harmonic and intermodulation terms they generate in the output. In principle, each nonlinearity in the visual pathway can be identified by its contribution to the frequency spectrum at different recording locations (Regan & Regan, 1988). This, in turn, allows researchers to study how contrast processing depends on spatial and temporal context, as well as changes in task, cognitive and behavioural state, and arousal.

Although visual neuroscience is a relatively old subfield, there are still outstanding questions relating to contrast processing that could be addressed by SSVEP methods. First, it is still not completely clear how contrast signals are computed in the human retina. Although we have more than a century of electrophysiological data from animals, and the broad structure of cone inputs to retinal ganglion cells is understood (Li *et al.*, 2014), we are still discovering new aspects of retinal processing that could influence the ‘coin-ing’ of the visual system’s currency

(Gollisch & Meister, 2010; Uprety *et al.*, 2022; Wang *et al.*, 2023). The ability to frequency tag both inputs (for example, cone-directed luminance contrast) and modulators (for example, stimuli that selectively drive the intrinsically-photosensitive retinal ganglion cells) is a powerful tool to explore this first stage of image generation.

Later in the visual pathway, we would like to know more about the role of corticothalamic feedback in the LGN. Although it is commonly thought of as a simple relay between the eye and the cortex, the majority of inputs to the LGN come from cortex not the eye, and there is good evidence that contrast processing in the LGN can be altered by top-down signals including attention (Sherman & Guillery, 1996; O'Connor *et al.*, 2002; Briggs & Usrey, 2007; Gouwens *et al.*, 2014). Bottom-up inputs to the LGN are segregated by eye and so responses there are often considered to be purely monocular, but it is possible that feedback signals allow some binocular computations such as interocular normalisation (Baker *et al.*, 2007; Dougherty *et al.*, 2019) to begin even at this relatively early stage. Frequency tagging inputs to different eyes or in different precortical pathways allows us to address neurons in different parts of the LGN. These techniques combined with advances in recording technology (for example, sensitive source-imaged EEG and MEG recordings that can resolve subcortical structures (Tesche, 1996; Attal *et al.*, 2012; Attal & Schwartz, 2013), noninvasive deep-brain stimulation techniques (Mohammadjavadi *et al.*, 2022) or implanted electrode arrays (Krolak-Salmon *et al.*, 2003)) may allow us to study these computations in more detail.

Finally, SSVEPs continue to provide a way of studying contrast in the cortex. Here, we are often interested in how different visual parameters interact. For example, how are signals from different eyes combined to generate both scalar contrast values and also binocular depth cues? How does contrast combination depend on the low level properties of the individual inputs such as their retinotopic location, cone contrast, spatiotemporal frequency, eye of origin and orientation? Colour vision scientists are particularly interested in how chromatic signals originating in a small number of cone-opponent retinal pathways are transformed into a perceptual colour space where the ‘unique hues’ appear to be only weakly-related to the early retinal outputs and how these computations are conditioned by the spatial and temporal properties of the scene (Wandell, 1993; Gegenfurtner, 2003; Solomon & Lennie, 2007; Stoughton & Conway, 2008; Kaneko *et al.*, 2020; Li *et al.*, 2022). All of these questions can be addressed by using SSVEP and frequency tagging to examine the computations that combine and transform the inputs at different cortical stages (Busse *et al.*, 2009; Baker & Wade, 2017; Katyal *et al.*, 2018; Chen & Gegenfurtner, 2021; Watts *et al.*, 2024). The original promise of the SSVEP approach was that the entire complex-valued frequency spectrum recorded at each location provided detailed information about the processing nonlinearities up to and including that point. In principle, this would allow researchers to uniquely fit the parameters of their computational models of visual processing (Regan & Regan, 1988). To date, the complexity of the neuronal computations at even the earliest stage of visual processing have hampered this effort - researchers typically restrict their analyses to the amplitudes of single, low-order frequency components (for example, the input frequencies or simple sums and differences of those frequencies). As our understanding of the early visual system improves, it is becoming possible to generate more realistic parameterised forward models of signal generation (Tsai

et al., 2012; Baker & Wade, 2017; Chariker *et al.*, 2020; Schrimpf *et al.*, 2020; Groen *et al.*, 2022). Feeding frequency-tagged inputs into these types of model allows us to generate synthetic SSVEP responses that can be compared with those measured in human subjects. In principle, we are therefore able to use the SSVEP to fit the parameters of early visual processing. This approach may also allow us to develop more sensitive tests for the changes in early visual processing that accompany a wide range of neurological diseases and disorders.

References

- Afsari F, Christensen KV, Smith GP, Hentzer M, Nippe OM, Elliott CJH & Wade AR (2014). [Abnormal visual gain control in a Parkinson’s disease model](#). *Human Molecular Genetics* **23**, 4465–4478.
- Albrecht DG & Hamilton DB (1982). [Striate cortex of monkey and cat: Contrast response function](#). *J Neurophysiol* **48**, 217–237.
- Ales JM, Yates JL & Norcia AM (2010). [V1 is not uniquely identified by polarity reversals of responses to upper and lower visual field stimuli](#). *Neuroimage* **52**, 1401–1409.
- Alpern M (1971). [Rhodopsin kinetics in the human eye](#). *J Physiol* **217**, 447–471.
- Atkinson J & Braddick O (1983). [Assessment of visual acuity in infancy and early childhood](#). *Acta Ophthalmol Suppl* **157**, 18–26.
- Atkinson J, Braddick O & French J (1979). [Contrast sensitivity of the human neonate measured by the visual evoked potential](#). *Invest Ophthalmol Vis Sci* **18**, 210–213.
- Attal Y, Maess B, Friederici A & David O (2012). [Head models and dynamic causal modeling of subcortical activity using magnetoencephalographic/electroencephalographic data](#). *Rev Neurosci* **23**, 85–95.
- Attal Y & Schwartz D (2013). [Assessment of subcortical source localization using deep brain activity imaging model with minimum norm operators: A MEG study](#). *PLoS One* **8**, e59856.
- Ayaz A, Saleem AB, Schölvinc ML & Carandini M (2013). [Locomotion controls spatial integration in mouse visual cortex](#). *Curr Biol* **23**, 890–894.
- Bach M & Farmer JD (2020). [Evaluation of the “freiburg acuity VEP” on commercial equipment](#). *Doc Ophthalmol* **140**, 139–145.
- Bach M, Maurer JP & Wolf ME (2008). [Visual evoked potential-based acuity assessment in normal vision, artificially degraded vision, and in patients](#). *Br J Ophthalmol* **92**, 396–403.
- Baker DH, Meese TS & Summers RJ (2007). [Psychophysical evidence for two routes to suppression before binocular summation of signals in human vision](#). *Neuroscience* **146**, 435–448.
- Baker DH, Simard M, Saint-Amour D & Hess RF (2015). [Steady-state contrast response functions provide a sensitive and objective index of amblyopic deficits](#). *Invest Ophthalmol Vis Sci* **56**, 1208–1216.
- Baker DH, Vilidaitė G & Wade AR (2021). [Steady-state measures of visual suppression](#). *PLoS computational biology* **17**, e1009507.

- Baker DH & Wade AR (2017). [Evidence for an Optimal Algorithm Underlying Signal Combination in Human Visual Cortex](#). *Cerebral Cortex (New York, NY: 1991)* **27**, 254–264.
- Baseler HA & Sutter EE (1997). [M and p components of the VEP and their visual field distribution](#). *Vision Res* **37**, 675–690.
- Bashinski HS & Bacharach VR (1980). Enhancement of perceptual sensitivity as the result of selectively attending to spatial locations. *Perception & psychophysics* **28**, 241–248.
- Benjamin AV, Wailes-Newson K, Ma-Wyatt A, Baker DH & Wade AR (2018). [The Effect of Locomotion on Early Visual Contrast Processing in Humans](#). *Journal of Neuroscience* **38**, 3050–3059.
- Betts LR, Taylor CP, Sekuler AB & Bennett PJ (2005). [Aging reduces center-surround antagonism in visual motion processing](#). *Neuron* **45**, 361–366.
- Boynton GM (2009). [A framework for describing the effects of attention on visual responses](#). *Vision Res* **49**, 1129–1143.
- Braddick OJ, Wattam-Bell J & Atkinson J (1986). [Orientation-specific cortical responses develop in early infancy](#). *Nature* **320**, 617–619.
- Brefczynski JA & DeYoe EA (1999). [A physiological correlate of the 'spotlight' of visual attention](#). *Nat Neurosci* **2**, 370–374.
- Briggs F & Usrey WM (2007). [A fast, reciprocal pathway between the lateral geniculate nucleus and visual cortex in the macaque monkey](#). *J Neurosci* **27**, 5431–5436.
- Buracas GT & Boynton GM (2007). [The effect of spatial attention on contrast response functions in human visual cortex](#). *J Neurosci* **27**, 93–97.
- Burr DC & Morrone MC (1987). [Inhibitory interactions in the human vision system revealed in pattern-evoked potentials](#). *J Physiol* **389**, 1–21.
- Busse L, Wade AR & Carandini M (2009). [Representation of concurrent stimuli by population activity in visual cortex](#). *Neuron* **64**, 931–942.
- Cameron EL, Tai JC & Carrasco M (2002). [Covert attention affects the psychometric function of contrast sensitivity](#). *Vision Res* **42**, 949–967.
- Campbell FW & Green DG (1965). [Optical and retinal factors affecting visual resolution](#). *J Physiol* **181**, 576–593.
- Campbell FW & Maffei L (1970). [Electrophysiological evidence for the existence of orientation and size detectors in the human visual system](#). *J Physiol* **207**, 635–652.
- Candy TR, Skoczenski AM & Norcia AM (2001). [Normalization models applied to orientation masking in the human infant](#). *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience* **21**, 4530–4541.
- Cao L & Händel B (2019). [Walking enhances peripheral visual processing in humans](#). *PLoS Biol* **17**, e3000511.
- Carandini M & Heeger DJ (1994). [Summation and division by neurons in primate visual cortex](#). *Science* **264**, 1333–1336.
- Carandini M & Heeger DJ (2011). [Normalization as a canonical neural computation](#). *Nat Rev Neurosci* **13**, 51–62.
- Carandini M, Movshon JA & Ferster D (1998). [Pattern adaptation and cross-orientation interactions in the primary visual cortex](#). *Neuropharmacology* **37**, 501–511.
- Carrasco M, Penpeci-Talgar C & Eckstein M (2000). [Spatial covert attention increases contrast](#)

- sensitivity across the CSF: Support for signal enhancement. *Vision Res* **40**, 1203–1215.
- Chariker L, Shapley R & Young L-S (2020). Contrast response in a comprehensive network model of macaque V1. *J Vis* **20**, 16.
- Chen C, Foley JM & Brainard DH (2000). Detection of chromoluminance patterns on chromoluminance pedestals i: Threshold measurements. *Vision Res* **40**, 773–788.
- Chen J & Gegenfurtner KR (2021). Electrophysiological evidence for higher-level chromatic mechanisms in humans. *J Vis* **21**, 12.
- Chota S, Bruat AT, Van der Stigchel S & Strauch C (2024). Steady-state visual evoked potentials reveal dynamic (re)allocation of spatial attention during maintenance and utilization of visual working memory. *J Cogn Neurosci* **36**, 800–814.
- Cunningham DGM, Baker DH & Peirce JW (2017). Measuring nonlinear signal combination using EEG. *Journal of Vision* **17**, 10–10.
- Dawson GD (1954). A summation technique for the detection of small evoked potentials. *Electroencephalography and Clinical Neurophysiology* **6**, 65–84.
- De Vries-Khoe L & Spekreijse H (1982). Maturation of luminance and pattern EPs in man. *Doc Ophthalmol Proc Ser* **31**, 461–475.
- Derrington AM, Krauskopf J & Lennie P (1984). Chromatic mechanisms in lateral geniculate nucleus of macaque. *J Physiol* **357**, 241–265.
- Derrington AM & Lennie P (1984). Spatial and temporal contrast sensitivities of neurones in lateral geniculate nucleus of macaque. *J Physiol* **357**, 219–240.
- Di Russo F, Pitzalis S, Aprile T, Spitoni G, Patria F, Stella A, Spinelli D & Hillyard SA (2007). Spatiotemporal analysis of the cortical sources of the steady-state visual evoked potential. *Hum Brain Mapp* **28**, 323–334.
- Di Russo F, Pitzalis S, Spitoni G, Aprile T, Patria F, Spinelli D & Hillyard SA (2005). Identification of the neural sources of the pattern-reversal VEP. *Neuroimage* **24**, 874–886.
- Di Russo F & Spinelli D (1999a). Electrophysiological evidence for an early attentional mechanism in visual processing in humans. *Vision Research* **39**, 2975–2985.
- Di Russo F & Spinelli D (1999b). Spatial attention has different effects on the magno-and parvocellular pathways. *Neuroreport* **10**, 2755–2762.
- Di Russo F, Spinelli D & Morrone MC (2001b). Automatic gain control contrast mechanisms are modulated by attention in humans: Evidence from visual evoked potentials. *Vision Research* **41**, 2435–2447.
- Di Russo F, Spinelli D & Morrone MC (2001a). Automatic gain control contrast mechanisms are modulated by attention in humans: Evidence from visual evoked potentials. *Vision Res* **41**, 2435–2447.
- Diez P, Orosco L, Garcés Correa A & Carmona L (2024). Assessment of visual fatigue in SSVEP-based brain-computer interface: A comprehensive study. *Med Biol Eng Comput* **62**, 1475–1490.
- Ding J, Sperling G & Srinivasan R (2006). Attentional modulation of SSVEP power depends on the network tagged by the flicker frequency. *Cerebral cortex* **16**, 1016–1029.
- Dobson V, Teller DY & Belugum J (1978). Visual acuity in human infants assessed with stationary stripes and phase-alternated checkerboards. *Vision Res* **18**, 1233–1238.
- Dougherty K, Schmid MC & Maier A (2019). Binocular response modulation in the lateral

- geniculate nucleus. *J Comp Neurol* **527**, 522–534.
- Du X, Liu L, Dong X & Bao M (2023). [Effects of altered-reality training on interocular disinhibition in amblyopia](#). *Ann N Y Acad Sci* **1522**, 126–138.
- Ellemberg D, Lewis TL, Liu CH & Maurer D (1999). [Development of spatial and temporal vision during childhood](#). *Vision Res* **39**, 2325–2333.
- Foley JM (1994). [Human luminance pattern-vision mechanisms: Masking experiments require a new model](#). *J Opt Soc Am A Opt Image Sci Vis* **11**, 1710–1719.
- Gandhi SP, Heeger DJ & Boynton GM (1999). [Spatial attention affects brain activity in human primary visual cortex](#). *Proc Natl Acad Sci U S A* **96**, 3314–3319.
- Gegenfurtner KR (2003). [Cortical mechanisms of colour vision](#). *Nat Rev Neurosci* **4**, 563–572.
- Gollisch T & Meister M (2010). [Eye smarter than scientists believed: Neural computations in circuits of the retina](#). *Neuron* **65**, 150–164.
- Gould IC, Wolfgang BJ & Smith PL (2007). [Spatial uncertainty explains exogenous and endogenous attentional cuing effects in visual signal detection](#). *J Vis* **7**, 4.1–17.
- Gouws AD, Alvarez I, Watson DM, Uesaki M, Rodgers J & Morland AB (2014). [On the role of suppression in spatial attention: Evidence from negative BOLD in human subcortical and cortical structures](#). *J Neurosci* **34**, 10347–10360.
- Groen IIA, Piantoni G, Montenegro S, Flinker A, Devore S, Devinsky O, Doyle W, Dugan P, Friedman D, Ramsey NF, Petridou N & Winawer J (2022). [Temporal dynamics of neural responses in human visual cortex](#). *J Neurosci* **42**, 7562–7580.
- Hamer RD, Norcia AM, Tyler CW & Hsu-Winges C (1989). [The development of monocular and binocular VEP acuity](#). *Vision Res* **29**, 397–408.
- Harris L, Atkinson J & Braddick O (1976). [Visual contrast sensitivity of a 6-month-old infant measured by the evoked potential](#). *Nature* **264**, 570–571.
- Heeger DJ (1992). [Normalization of cell responses in cat striate cortex](#). *Vis Neurosci* **9**, 181–197.
- Herrmann CS (2001). [Human EEG responses to 1-100 hz flicker: Resonance phenomena in visual cortex and their potential correlation to cognitive phenomena](#). *Exp Brain Res* **137**, 346–353.
- Highsmith J & Crognale MA (2010). [Attentional shifts have little effect on the waveform of the chromatic onset VEP](#). *Ophthalmic Physiol Opt* **30**, 525–533.
- Hoffmann MB, Brands J, Behrens-Baumann W & Bach M (2017). [VEP-based acuity assessment in low vision](#). *Doc Ophthalmol* **135**, 209–218.
- Hou C, Kim Y-J, Lai XJ & Verghese P (2016). [Degraded attentional modulation of cortical neural populations in strabismic amblyopia](#). *Journal of Vision* **16**, 16.
- Hu J, Chen J, Ku Y & Yu M (2023). [Reduced interocular suppression after inverse patching in anisometropic amblyopia](#). *Front Neurosci* **17**, 1280436.
- Hubel DH & Wiesel TN (1959). [Receptive fields of single neurones in the cat’s striate cortex](#). *J Physiol* **148**, 574–591.
- Hubel DH & Wiesel TN (1962). [Receptive fields, binocular interaction and functional architecture in the cat’s visual cortex](#). *J Physiol* **160**, 106–154.
- Kaneko S, Kuriki I & Andersen SK (2020). [Steady-state visual evoked potentials elicited from](#)

- early visual cortex reflect both perceptual color space and cone-opponent mechanisms. *Cereb Cortex Commun* **1**, tgaa059.
- Kaplan E & Shapley RM (1986). The primate retina contains two types of ganglion cells, with high and low contrast sensitivity. *Proc Natl Acad Sci U S A* **83**, 2755–2757.
- Kastner S, Pinsk MA, De Weerd P, Desimone R & Ungerleider LG (1999). Increased activity in human visual cortex during directed attention in the absence of visual stimulation. *Neuron* **22**, 751–761.
- Katyal S, Vergeer M, He S, He B & Engel SA (2018). Conflict-sensitive neurons gate interocular suppression in human visual cortex. *Sci Rep* **8**, 1239.
- Krolak-Salmon P, Hénaff M-A, Tallon-Baudry C, Yvert B, Guénot M, Vighetto A, Mauguière F & Bertrand O (2003). Human lateral geniculate nucleus and visual cortex respond to screen flicker. *Ann Neurol* **53**, 73–80.
- Kuffler SW, Fitzhugh R & Barlow HB (1957). Maintained activity in the cat’s retina in light and darkness. *J Gen Physiol* **40**, 683–702.
- Lauritzen TZ, Ales JM & Wade AR (2010). The effects of visuospatial attention measured across visual cortex using source-imaged, steady-state EEG. *Journal of Vision* **10**, 39.
- Lee BB, Pokorny J, Smith VC, Martin PR & Valberg A (1990). Luminance and chromatic modulation sensitivity of macaque ganglion cells and human observers. *J Opt Soc Am A* **7**, 2223–2236.
- Legge GE (1979). Spatial frequency masking in human vision: Binocular interactions. *J Opt Soc Am* **69**, 838–847.
- Lennie P, Pokorny J & Smith VC (1993). Luminance. *J Opt Soc Am A* **10**, 1283–1293.
- Levitt JB, Schumer RA, Sherman SM, Spear PD & Movshon JA (2001). Visual response properties of neurons in the LGN of normally reared and visually deprived macaque monkeys. *J Neurophysiol* **85**, 2111–2129.
- Li P, Garg AK, Zhang LA, Rashid MS & Callaway EM (2022). Cone opponent functional domains in primary visual cortex combine signals for color appearance mechanisms. *Nat Commun* **13**, 6344.
- Li PH, Field GD, Greschner M, Ahn D, Gunning DE, Mathieson K, Sher A, Litke AM & Chichilnisky EJ (2014). Retinal representation of the elementary visual signal. *Neuron* **81**, 130–139.
- Li X, Lu Z-L, Tjan BS, Doshier BA & Chu W (2008). Blood oxygenation level-dependent contrast response functions identify mechanisms of covert attention in early visual areas. *Proc Natl Acad Sci U S A* **105**, 6202–6207.
- Lissa P de, Caldara R, Nicholls V & Miellet S (2020). In pursuit of visual attention: SSVEP frequency-tagging moving targets. *PLoS One* **15**, e0236967.
- Lu Z-L & Doshier BA (1998). External noise distinguishes attention mechanisms. *Vision research* **38**, 1183–1198.
- Luck SJ, Chelazzi L, Hillyard SA & Desimone R (1997). Neural mechanisms of spatial selective attention in areas V1, V2, and V4 of macaque visual cortex. *J Neurophysiol* **77**, 24–42.
- Lygo FA, Richard B, Wade AR, Morland AB & Baker DH (2021). Neural markers of suppression in impaired binocular vision. *NeuroImage* **230**, 117780.
- MacLennan K, O’Brien S & Tavassoli T (2022). In our own words: The complex sensory

- experiences of autistic adults. *J Autism Dev Disord* **52**, 3061–3075.
- MacLeod DI & Boynton RM (1979). Chromaticity diagram showing cone excitation by stimuli of equal luminance. *J Opt Soc Am* **69**, 1183–1186.
- Marcus DS & Van Essen DC (2002). Scene segmentation and attention in primate cortical areas V1 and V2. *J Neurophysiol* **88**, 2648–2658.
- Martinovic J & Andersen SK (2018). Cortical summation and attentional modulation of combined chromatic and luminance signals. *Neuroimage* **176**, 390–403.
- McAdams CJ & Maunsell JH (1999). Effects of attention on orientation-tuning functions of single neurons in macaque cortical area V4. *J Neurosci* **19**, 431–441.
- McKeefry DJ, Russell MH, Murray IJ & Kulikowski JJ (1996). Amplitude and phase variations of harmonic components in human achromatic and chromatic visual evoked potentials. *Vis Neurosci* **13**, 639–653.
- Mecacci L & Spinelli D (1976). The effects of spatial frequency adaptation on human evoked potentials. *Vision Research* **16**, 477–479.
- Meese TS & Baker DH (2009). Cross-orientation masking is speed invariant between ocular pathways but speed dependent within them. *J Vis* **9**, 2.1–15.
- Mehta AD, Ulbert I & Schroeder CE (2000a). Intermodal selective attention in monkeys. I: Distribution and timing of effects across visual areas. *Cereb Cortex* **10**, 343–358.
- Mehta AD, Ulbert I & Schroeder CE (2000b). Intermodal selective attention in monkeys. II: Physiological mechanisms of modulation. *Cereb Cortex* **10**, 359–370.
- Michelson A (1927). *Studies in optics*. University of Chicago Press.
- Middendorf M, McMillan G, Calhoun G & Jones KS (2000). Brain-computer interfaces based on the steady-state visual-evoked response. *IEEE Trans Rehabil Eng* **8**, 211–214.
- Minarik T, Berger B & Jensen O (2023). Optimal parameters for rapid (invisible) frequency tagging using MEG. *Neuroimage* **281**, 120389.
- Mohammadjavadi M, Ash RT, Li N, Gaur P, Kubanek J, Saenz Y, Glover GH, Popelka GR, Norcia AM & Pauly KB (2022). Transcranial ultrasound neuromodulation of the thalamic visual pathway in a large animal model and the dose-response relationship with MR-ARFI. *Sci Rep* **12**, 19588.
- Morgan ST, Hansen JC & Hillyard SA (1996). Selective attention to stimulus location modulates the steady-state visual evoked potential. *Proc Natl Acad Sci U S A* **93**, 4770–4774.
- Morrone MC & Burr DC (1986). Evidence for the existence and development of visual inhibition in humans. *Nature* **321**, 235–237.
- Morrone MC, Burr DC & Maffei L (1982). Functional implications of cross-orientation inhibition of cortical visual cells. I. Neurophysiological evidence. *Proc R Soc Lond B Biol Sci* **216**, 335–354.
- Morrone MC, Denti V & Spinelli D (2004). Different attentional resources modulate the gain mechanisms for color and luminance contrast. *Vision Res* **44**, 1389–1401.
- Movshon JA (1975). The velocity tuning of single units in cat striate cortex. *J Physiol* **249**, 445–468.
- Müller MM & Hillyard S (2000). Concurrent recording of steady-state and transient event-related potentials as indices of visual-spatial selective attention. *Clin Neurophysiol* **111**, 1544–1552.

- Müller MM, Teder-Sälejärvi W & Hillyard SA (1998). [The time course of cortical facilitation during cued shifts of spatial attention](#). *Nat Neurosci* **1**, 631–634.
- Murray SO (2008). [The effects of spatial attention in early human visual cortex are stimulus independent](#). *J Vis* **8**, 2.1–11.
- Niell CM & Stryker MP (2010). [Modulation of visual responses by behavioral state in mouse visual cortex](#). *Neuron* **65**, 472–479.
- Norcia AM, Appelbaum LG, Ales JM, Cottureau BR & Rossion B (2015). [The steady-state visual evoked potential in vision research: A review](#). *Journal of vision* **15**, 4–4.
- Norcia AM & Tyler CW (1985b). [Infant VEP acuity measurements: Analysis of individual differences and measurement error](#). *Electroencephalography and Clinical Neurophysiology* **61**, 359–369.
- Norcia AM & Tyler CW (1985a). [Spatial frequency sweep VEP: Visual acuity during the first year of life](#). *Vision Research* **25**, 1399–1408.
- Norcia AM, Tyler CW & Allen D (1986). [Electrophysiological assessment of contrast sensitivity in human infants](#). *Am J Optom Physiol Opt* **63**, 12–15.
- Norcia AM, Tyler CW & Hamer RD (1990). [Development of contrast sensitivity in the human infant](#). *Vision Res* **30**, 1475–1486.
- O’Connor DH, Fukui MM, Pinsk MA & Kastner S (2002). [Attention modulates responses in the human lateral geniculate nucleus](#). *Nat Neurosci* **5**, 1203–1209.
- Pei F, Baldassi S & Norcia AM (2014). Electrophysiological measures of low-level vision reveal spatial processing deficits and hemispheric asymmetry in autism spectrum disorder. *J Vis*; DOI: [10.1167/14.11.3](#).
- Pei F, Baldassi S, Tsai JJ, Gerhard HE & Norcia AM (2017). [Development of contrast normalization mechanisms during childhood and adolescence](#). *Vision Res* **133**, 12–20.
- Peirce JW (2007). [The potential importance of saturating and supersaturating contrast response functions in visual cortex](#). *J Vis* **7**, 13.
- Pestilli F, Ling S & Carrasco M (2009). [A population-coding model of attention’s influence on contrast response: Estimating neural effects from psychophysical data](#). *Vision Res* **49**, 1144–1153.
- Petrov Y, Carandini M & McKee S (2005). [Two distinct mechanisms of suppression in human vision](#). *J Neurosci* **25**, 8704–8707.
- Petrov Y, Verghese P & McKee SP (2006). [Collinear facilitation is largely uncertainty reduction](#). *J Vis* **6**, 170–178.
- Polat U & Sagi D (1993). [Lateral interactions between spatial channels: Suppression and facilitation revealed by lateral masking experiments](#). *Vision Res* **33**, 993–999.
- Porciatti V, Bonanni P, Fiorentini A & Guerrini R (2000). [Lack of cortical contrast gain control in human photosensitive epilepsy](#). *Nature Neuroscience* **3**, 259–263.
- Posner MI (1980). [Orienting of attention](#). *Q J Exp Psychol* **32**, 3–25.
- Regan D (1966). [Some characteristics of average steady-state and transient responses evoked by modulated light](#). *Electroencephalogr Clin Neurophysiol* **20**, 238–248.
- Regan MP & Regan D (1988). [A frequency domain technique for characterizing nonlinearities in biological systems](#). *Journal of Theoretical Biology* **133**, 293–317.
- Reynolds JH & Heeger DJ (2009). [The normalization model of attention](#). *Neuron* **61**, 168–

- Ridder WH 3rd (2004). [Methods of visual acuity determination with the spatial frequency sweep visual evoked potential](#). *Doc Ophthalmol* **109**, 239–247.
- Ross J & Speed HD (1991). [Contrast adaptation and contrast masking in human vision](#). *Proc Biol Sci* **246**, 61–69.
- Ross J, Speed HD & Morgan MJ (1993). [The effects of adaptation and masking on incremental thresholds for contrast](#). *Vision Res* **33**, 2051–2056.
- Salelkar S & Ray S (2020). [Interaction between steady-state visually evoked potentials at nearby flicker frequencies](#). *Sci Rep* **10**, 5344.
- Schrimpf M, Kubilius J, Lee MJ, Ratan Murty NA, Ajemian R & DiCarlo JJ (2020). [Integrative benchmarking to advance neurally mechanistic models of human intelligence](#). *Neuron* **108**, 413–423.
- Seijdel N, Marshall TR & Drijvers L (2023). [Rapid invisible frequency tagging \(RIFT\): A promising technique to study neural and cognitive processing using naturalistic paradigms](#). *Cereb Cortex* **33**, 1626–1629.
- Shapley RM & Victor JD (1980). [The effect of contrast on the non-linear response of the y cell](#). *J Physiol* **302**, 535–547.
- Sherman SM & Guillery RW (1996). [Functional organization of thalamocortical relays](#). *J Neurophysiol* **76**, 1367–1395.
- Shibata K, Yamane K, Otuka K & Iwata M (2008). [Abnormal visual processing in migraine with aura: A study of steady-state visual evoked potentials](#). *J Neurol Sci* **271**, 119–126.
- Silver MA, Ress D & Heeger DJ (2007). [Neural correlates of sustained spatial attention in human early visual cortex](#). *J Neurophysiol* **97**, 229–237.
- Simmons DR, Robertson AE, McKay LS, Toal E, McAleer P & Pollick FE (2009). [Vision in autism spectrum disorders](#). *Vision Res* **49**, 2705–2739.
- Skoczenski AM & Norcia AM (1998). [Neural noise limitations on infant visual sensitivity](#). *Nature* **391**, 697–700.
- Solomon SG & Lennie P (2005). [Chromatic gain controls in visual cortical neurons](#). *J Neurosci* **25**, 4779–4792.
- Solomon SG & Lennie P (2007). [The machinery of colour vision](#). *Nat Rev Neurosci* **8**, 276–286.
- Somers DC, Dale AM, Seiffert AE & Tootell RB (1999). [Functional MRI reveals spatially specific attentional modulation in human primary visual cortex](#). *Proc Natl Acad Sci U S A* **96**, 1663–1668.
- Stoughton CM & Conway BR (2008). [Neural basis for unique hues](#). *Curr Biol* **18**, R698–9.
- Tadin D, Lappin JS, Gilroy LA & Blake R (2003). [Perceptual consequences of centre-surround antagonism in visual motion processing](#). *Nature* **424**, 312–315.
- Tesche CD (1996). [Non-invasive imaging of neuronal population dynamics in human thalamus](#). *Brain Res* **729**, 253–258.
- Tolhurst DJ, Movshon JA & Thompson ID (1981). [The dependence of response amplitude and variance of cat visual cortical neurones on stimulus contrast](#). *Exp Brain Res* **41**, 414–419.
- Tootell RB, Hadjikhani N, Hall EK, Marrett S, Vanduffel W, Vaughan JT & Dale AM (1998). [The retinotopy of visual spatial attention](#). *Neuron* **21**, 1409–1422.

- Tsai JJ, Norcia AM, Ales JM & Wade AR (2011). [Contrast gain control abnormalities in idiopathic generalized epilepsy](#). *Annals of Neurology* **70**, 574–582.
- Tsai JJ, Wade AR & Norcia AM (2012). [Dynamics of normalization underlying masking in human visual cortex](#). *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience* **32**, 2783–2789.
- Tyler CW & Apkarian PA (1985). [Effects of contrast, orientation and binocularity in the pattern evoked potential](#). *Vision Res* **25**, 755–766.
- Tyler CW, Apkarian P, Levi DM & Nakayama K (1979). [Rapid assessment of visual function: An electronic sweep technique for the pattern visual evoked potential](#). *Investigative Ophthalmology & Visual Science* **18**, 703–713.
- Upreti S, Adhikari P, Feigl B & Zele AJ (2022). Melanopsin photoreception differentially modulates rod-mediated and cone-mediated human temporal vision. *Isience*.
- Vergeer M, Mesik J, Baek Y, Wilmerding K & Engel SA (2018). [Orientation-selective contrast adaptation measured with SSVEP](#). *Journal of Vision* **18**, 2.
- Verghese P, Kim Y-J & Wade AR (2012). [Attention selects informative neural populations in human V1](#). *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience* **32**, 16379–16390.
- Vilidaite G, Norcia AM, West RJH, Elliott CJH, Pei F, Wade AR & Baker DH (2018). [Autism sensory dysfunction in an evolutionarily conserved system](#). *Proceedings Biological Sciences* **285**, 20182255.
- Wandell BA (1993). [Color appearance: The effects of illumination and spatial pattern](#). *Proc Natl Acad Sci U S A* **90**, 9778–9784.
- Wang AYM, Kulkarni MM, McLaughlin AJ, Gayet J, Smith BE, Hauptschein M, McHugh CF, Yao YY & Puthussery T (2023). [An ON-type direction-selective ganglion cell in primate retina](#). *Nature* **623**, 381–386.
- Wang J & Wade AR (2011). [Differential attentional modulation of cortical responses to S-cone and luminance stimuli](#). *Journal of Vision* **11**, 1.
- Watts +Dylan+J, Rozman +Ana, Somers +Lucy+P, Gunel +Bora, Racey +Chris, Barnes +Katie & Bosten +Jenny+M (2024). Tuning of cortical color mechanism revealed using steady-state visually evoked potentials. *bioRxiv*.
- Zheng X, Xu G, Zhi Y, Wang Y, Han C, Wang B, Zhang S, Zhang K & Liang R (2019). [Objective and quantitative assessment of interocular suppression in strabismic amblyopia based on steady-state motion visual evoked potentials](#). *Vision Res* **164**, 44–52.