Dry dissection of disparity divergence eye movements using independent component analysis

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Received 11 August 2005; received in revised form 27 March 2006; accepted 30 March 2006

Abstract

Dry dissection, a concept developed by Lawrence Stark, includes a variety of techniques designed to isolate internal neural control components by using cleverly designed stimulus or measurement protocols. As envisioned by Stark, the concept applies only to motor systems that have multiple stimulus inputs and/or response behaviors. A new application of independent component analysis (ICA) can be used to extend the dry dissection concept to identify motor components from a single, isolated response. It is only necessary that multiple responses can be obtained to the same stimulus. This “ensemble ICA” technique is well suited to analyze various eye movement behaviors as even isolated motor systems often include multiple control processes. Here we apply ensemble ICA to vergence eye movements: the inward (convergence) or outward (divergence) turning of the eyes that allows us to view images at various distances. Previous studies concerning the dynamics of convergence and divergence eye movements have produced varied, sometimes contradictory, results: most studies report that convergence is considerably faster than divergence, but opposite results have also been reported. Experimental results have shown that the dynamics of divergence movements depend on the initial vergence position while those of convergence do not: divergence eye movements in response to targets initially near to the subject can attain peak velocities twice that of those driven by more distant targets. To determine the underlying cause of this behavior, ensemble ICA was applied to divergence responses. Results show that both convergence and divergence contain a sustained (step-like) and a transient (pulse-like) control component, but the amplitude of the transient component in divergence is dependent on initial stimulus position.

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Keywords: Vergence eye movements; Dry dissection; Disparity vergence; Independent component analysis; Eye movements; Motor control

1. Introduction

In the early 1960s, Lawrence Stark proposed a general strategy for utilizing multiple input and output channels to gain information about internal neural configurations, a strategy he termed “dry dissection” [1]. The dry dissection concept encompassed a variety of experimental protocols in which stimuli are carefully controlled to evoke only one neural control component. Additionally, selective measurement techniques can be used to isolate the responses evoked by a single component.

Dry dissection approaches have been particularly successful in isolating the various overlaying neural control components that control human eye movements. Eye movement control systems frequently involve multiple inputs and outputs. For example, the “oculomotor near triad” has three different motor outputs, vergence, lens focusing (accommodation), and pupil size changes, and these three responses are driven by two major stimuli, blur and retinal disparity, along with several minor stimuli. Dry dissection approaches work quite well with the oculomotor near triad and some other oculomotor systems, but traditional dry dissection methods cannot be applied to isolated stimulus–response combinations. However, some single stimulus–response combinations may be mediated by multiple neural components.
Disparity vergence is only one of five distinct control processes responsible for guiding or positioning the eyes. Other eye movement systems include the saccadic, smooth pursuit, vestibular, and accommodative systems vergence. The disparity vergence system, in conjunction with the accommodative vergence system, mediates inward and outward turning eye movements that are used to align stereoscopically paired images on the foveae. Since multiple control systems are involved (disparity and blur-driven\(^1\) systems), traditional dry dissection techniques are required to isolate the disparity vergence system by using a special stimulus device that optically decouples blur and disparity. Using such an unphysiological stimulus (normally disparity stimulation is coupled to blur stimulation through simple trigonometry) to isolate the disparity vergence control system is an archetypical example of the dry dissection approach.

Early behavior indicated that the disparity vergence system may be composed of two control subcomponents. The control structure of this system is embodied in the “dual mode theory” which states that the vergence response is guided by two components: an open-loop transient component which generates a pulse-like neural signal, and a feedback, sustained component that generates a step-like neural signal [2–4]. The transient component improves the dynamics of the response by making the initial portion of the movement faster while the feedback component is responsible for the accuracy of the final position. An ensemble application of principle component analysis (PCA) has confirmed that two components could account for most of the variability found in vergence eye movements, implying that two systems are primarily responsible for the combined response [5].

Unfortunately, classical dry dissection techniques are not able to isolate subcomponents of the disparity vergence response. While neurophysiological studies in animals also provide evidence of a two component structure [6], in humans, it is not possible to record signals directly from the motoneurons. To isolate the components of the disparity vergence system, the methods of dry dissection need to be extended so that they can be applied to a system with a single input and a single response. If multiple observations can be produced from the same stimulus, a novel application of independent component analysis (ICA) can be used to isolate any subcomponent [5,7]. Essentially, each component contributes to the response-to-response variability and ICA can resolve these components based on their contributions to the overall variability.

Controversy exists regarding the relative dynamics of convergence and divergence. Several studies report that convergence is faster than divergence [3,8–10] by as much as double [10], while other studies report pure divergence and convergence to have approximately the same velocity characteristics [11]. We have shown that the dynamics of divergence movements depend on the initial position, but the dynamics of convergence movements do not [12]. Divergence movements to the same amplitude step stimulus are faster, attaining higher peak velocities, if they begin close to the subject compared to those that begin some distance from the subject. Conversely, convergence movements show about the same peak velocities to equal amplitude step stimuli irrespective of their initial distance. Thus, depending on the initial location of the stimulus, the relationship between convergence and divergence dynamic properties (i.e., which is faster) can vary dramatically.

The mechanism underlying this substantial difference in behavior is the focus of this work. Some insight can be gained from recent experiments that show that the vergence response to a fixed step-like stimulus can be modified by stimulus history [5,13,14]. Given an appropriate training stimulus, the dynamics of a convergent response to a fixed, constant test stimulus can be augmented to produce responses with large peak velocities and overshoot characteristics [13]. Alternatively, a different training stimulus can be used to diminish convergence dynamics so that responses to the same test stimulus are substantially slower [5,12,14]. Component decomposition using ICA has been applied to convergence responses under these different adaptive conditions and has shown that it is the transient component that is being modified. Specifically, modification of the amplitude of the convergence transient component can produce a strong adaptive change in the overall convergence response [5,14]. Recently, Alvarez et al. [14] have shown that an adaptive protocol can also modify divergence movements, and the transient component is also likely to be involved.

Here enhanced dry dissection using ICA will be applied to divergence responses to confirm that these movements are also mediated by two underlying control processes and to determine how such subcomponents vary with initial position. Applying ICA to divergence responses, we will show that the divergence is indeed guided by two components analogous to those found in convergence and that it is the amplitude of the transient component that is influenced by initial position.

2. Methodology

Four subjects (18–60 years old) participated in this study. Two subjects were male, and two were female. All subjects signed informed consent forms before the experiments that were approved by the New Jersey Institute of Technology (NJIT) Institutional Review Board (IRB). Head position was stabilized using a custom chin rest to avoid any influence from the vestibular system. All subjects were able to perform the task easily. One subject was highly trained and aware of the goals of this study while the other three subjects were inexperienced and naïve to the goals of the study.

2.1. Experimental design

Disparity vergence stimuli were presented using a dynamic haploscope constructed from two computer monitors that generated a symmetrical stimulus of paired vertical lines. Essentially two vertical lines are presented to each eye separately through partially reflecting mirrors. These lines were the only objects seen by subject during the experiment, and as they were at a constant distance (40 cm), accommodative and proximal cues

\(^{1}\) The blur-driven accommodative system will be less active in older individuals who are presbyopic.
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Fig. 1. An ensemble of 53 individual disparity vergence responses to a 4° divergent step. The initial position was 6°.

associated with depth information related to the target distance were minimized [15].

During an experimental session, pure divergent stimuli were presented: the stereographically paired lines moved symmetrically. All stimuli were step changes of 4° amplitude, but beginning at different initial distances from the subject. The “near” stimulus began at an initial vergence position of 20° and the “far” stimulus at 8°. During an experimental run, both divergent and convergent stimuli were randomly presented at a random time to discourage subject prediction that might influence vergence dynamics [16,17].

The application of ICA used here requires a number of repetitive responses to the same stimulus for the behavior being analyzed. Simulations indicated that 10–20 individual responses were sufficient to determine accurate estimates of the two components. Our analysis used from 15 to 53 individual responses to the various vergence step stimuli. One of the larger divergence data sets from one subject is shown in Fig. 1.

Eye movements were recorded using an infrared limbus tracking system (λ = 950 nm) manufactured by Skalar Iris (model 6500). The manufacturer reports a resolution of 2 min of arc. All eye movements were well within the system’s ±25° linear range. Since the nonlinearities of our system were small, a maximum of 5% [4], we used a two-point calibration: one taken before and the other after each individual response. Data acquisition was done at a sampling rate of 200 Hz, which is well above the Nyquist frequency for vergence eye movements.

2.2. Data analysis

This study is concerned with movement dynamics, so movements that contained small saccades during the final, steady-state portion were analyzed as long as the saccades in the two eyes cancelled in the net vergence response. The calibrated left and right eye movements were subtracted to yield the net disparity vergence movement. When displayed graphically, convergence was plotted as positive, and divergence was plotted as negative. The velocity response was computed using a two-point central difference algorithm [18]. Data were analyzed by measuring the magnitude of the peak velocity and decomposed using ICA.

ICA is a form of “blind source separation” (BSS) that can isolate individual components from a mixture provided the components are non-Gaussian and sufficiently independent...
ICA has also been described as a non-Gaussian version of factor analysis and somewhat similar to PCA [22,23]. In fact, an extensive study of the application of factor analysis to ensemble vergence response data was undertaken, but none of the standard approaches such as “varimax” were able to identify the underlying components in simulated data.

The basic principles behind ICA are well described in number of references [19–23] and will be only briefly mentioned here. The ICA model is a generative model: it attempts to explain how the components are mixed to generate the observed signals based on a linear mixing model [23]:

\[
x = As + \text{noise},
\]

where \( x \) and \( s \) are random vectors of size \( m \) (the number of mixtures, or individual responses in our application), and \( n \) (the number of underlying sources, or components in our application).

![Diagram](A) Schematic diagram of the pulse–step model that was used to evaluate the ICA approach. There is a variable delay element in the step generator path. (B) Signal patterns produced by the pulse and step components. A number of model parameters were varied randomly to simulate movement-to-movement variability.

![Graphs](A) An ensemble of simulated convergence responses produced by the pulse–step model outlined in Fig. 2. Model parameters were randomly varied on a response-to-response basis to produce variability between responses. (B) Ensemble standard deviation of the model response ensemble shown in A (dashed line) along with the ensemble standard deviation calculated from two different human convergence response ensembles (solid lines).
The noise vector represents the disturbances in the form of additive noise independent of the source vector \( s \). The goal of ICA is to identify the linear mixing matrix \( A \). Inverting the mixing matrix produces an “unmixing” matrix, \( U = A^{-1} \), that can be used to estimate the unobservable source vector \( s \) (\( s = Ux \)). This is accomplished by linear transformations of the data set (i.e., rotations and scalings) with the goal of optimizing some objective function related to statistical independence, such as a measure of non-Gaussianity, or more generally, some measure of mutual information. There are quite a number of different approaches for estimating \( A \), differing primarily in the objective function that is optimized and the optimization method [23]. Since both the mixing process \( A \) and the sources \( s \) are unknown, these techniques are part of a larger family known as Blind Source Separation (BSS) [20,23].

In this application, the signals produced by the neural control components of vergence eye movements constitute the latent variables \( s \), and the mixing matrix \( A \) accounts for their movement-to-movement variability. The ensemble of motor responses (Fig. 1) is taken as the components of the signal vector, \( x \). The critical assumptions in ICA are that the variables are statistically independent and have non-Gaussian distributions. This latter is essential since it is the non-Gaussianity of the data set that is often optimized. While vergence responses are certainly non-Gaussian, the initial portions of these responses may not be independent due to a stimulus-induced synchronization of the driving neural sources. In other words, even if the underlying neural sources are independent, their activation by a common stimulus induces a temporary correlation between their responses. As these responses continue, this “stimulus effect” diminishes so that the components become independent during the latter portion of the response. To avoid this stimulus-induced synchronization, the evaluation of the mixing matrix, \( A \), was performed only on the latter portion of the responses.

The time period following maximum ensemble variance (close to the time of peak velocity) was found to provide sufficient component independence to permit accurate determination of the mixing matrix. The mixing matrix, \( A \), obtained from the truncated responses was inverted in the algorithm we used to give the unmixing matrix, \( U \), which was then applied to the entire response (including the initial portion) to estimate the underlying motor components, \( s \).

Another important assumption in the ICA model is that the independent sources not only exist, but undergo instantaneous linear mixing to produce the sensor signal. While no biological process is likely to be truly linear, extensive eye movement data indicate that separate neural signals, such as those from version and vergence neural centers do combine more or less linearly. Moreover, most models of the oculomotor plant are linear [9].

Several popular ICA algorithms can be downloaded from the Web as MATLAB script files. In this study, we used the “Jade” algorithm for real-valued signals developed by J.-F. Cardoso (available at: http://sig.enst.fr/~cardoso/stuff.html); however, the “FastICA” algorithm developed by the ICA Group at the Helsinki University worked equally well (available at: http://www.cis.hut.fi/projects/ica/fastica/fp.html). Both these algorithms provide preprocessing that uses PCA to reduce the dimensionality of the data set. In our analysis, data dimensionality was reduced to two based on results from a PCA-based study of the number of components [5].

Simulations showed that the algorithms produced more accurate results if the data sets were symmetrical, so each response was modified by adding the inverted response to the end of the actual response to make the ensemble data symmetric along the time axis (that is, the responses have the format of periodic functions). While this operation does not add any new information to the data set, it does change its statistical properties. Specifically, a modified, symmetrical data set showed more than one order of magnitude greater difference in the ratios between the first three eigenvalues as compared to the original data set. This improvement influenced the selection of principal components during the preprocessing of PCA-based data reduction operation and gave much more accurate component decompositions on simulated data. After the ICA analysis, the inverted responses were discarded.

Due to inherent ambiguities, ICA cannot determine the scale of the components. The initial pre-response period was used to establish a zero reference for the components; that is, both components are assumed to be zero or at some fixed base level. To determine the amplitude, we note that the sum of the two components should equal the average response. Hence, the amplitude of the individual components was adjusted until their sum equalled the average response. Since there were only two components with quite different time characteristics, the amplitude scaling was uniquely determined by matching the average response. Amplitude scaling was implemented using the MATLAB basic optimization routine “fminsearch” which uses the Nelder–Mead simplex, or direct search, method. After scaling,
the sum of the two components matched the ensemble average response almost exactly.

2.3. ICA validation

The ability of ensemble ICA to isolate components was evaluated using simulated responses from a quantitative model of the disparity vergence system [24]. Unlike experimental data it is possible to obtain the normally hidden components from model simulations. To simulate responses with realistic movement-to-movement variability, several model variables were perturbed by adding or subtracting a small random variable before each simulation. The model used is essentially a pulse–step model (i.e., the controller was simulated using pulse and step components) with a second-order plant, Fig. 2. The model parameters that were varied included: pulse latency, step latency, pulse height, pulse width, step height, step risetime, and the major time constant representing the oculomotor plant (in fact, all the model parameters except the plant minor time constant which has negligible influence on dynamics).

A simulated convergence response ensemble is shown in Fig. 3A. The response-to-response variability of the model parameters was adjusted so that the standard deviation of the simulated response ensemble was approximately the same as that seen in a human response ensemble, Fig. 3B.

Averages of the model’s internal components were then compared with the components estimated by ICA for the model’s responses, Fig. 4. A very close match is observed between the internal components and those found by ICA using the model’s external responses. Hence, ICA decomposition of a response ensemble provides a good estimate of the average behavior of the underlying, internal components.

3. Results

Typical individual divergence eye movements are shown for four subjects in Fig. 5. The upper traces are velocity and the lower traces are vergence position. The dashed line shows responses that began near to the subject while the solid line shows responses that had more distant initial positions. Although

Fig. 5. Divergence responses to 4° step stimuli that began either near (dashed line) or far (solid line) from subject. The difference in dynamics is evident.
ICA analysis of response ensembles was done to determine if divergence movements consist of multiple components and how these components influence the dynamic difference seen in Fig. 5. Horng et al. [26–28] postulate that divergence is composed primarily of the sustained component. They further speculate that if a transient component is present, it would have to be smaller than the transient found in convergence. However, they did not report the initial position of the stimuli and we have shown this to have a strong influence on the dynamics of divergence.

Applying ICA decomposition to ensembles of divergence responses shows the underlying components of movements that began close to (left plots) or further from (right plot) the subject, Fig. 7. For both subjects, it is evident that the transient component is larger in responses that begin close to the subject. These results indicate that the transient component is dependent on the initial stimulus condition and is responsible for the difference observed in divergence dynamics.

4. Discussion

Since divergence dynamics are dependent on initial position and convergence dynamics are not, any comparison between the two will depend on initial condition and should take this into account. This may account for the differences in convergence versus divergence velocities reported by different groups [8,11].

The ICA decomposition shows the underlying neural components, but after they have been modified by the plant. Thus, it is not possible to determine if the dynamic differences in these components (Fig. 5) are due to differences in the neural control signals or to nonlinearities in the neuromuscular plant. The fact that position dependent dynamics is only
found in divergence movements suggests that a neural control process is involved; however, it is also possible that the near (20°–16°) divergence movements were more strongly influenced by plant nonlinearities than the near (16°–20°) convergence movements.

A control-based explanation is supported by some primate neurophysiologic studies. These studies have shown that different cells exist for convergence and divergence movements [6,25] and that convergence cells are more prevalent than divergence cells in the midbrain specifically within the mesencephalic reticular formation [25]. Thus, divergence is not simply a negative convergence movement but a separate neurophysiological system. The neural control strategy of the two systems may be different. Evidence of burst and burst-tonic cells shows that combinations of a transient and a sustained neural signal are used for both convergence and divergence movements. The divergence cells may fire with more synchronization for near stimuli creating a pulse with a greater magnitude and stronger kinematics compared to divergence responses to stimuli further from the subject. It is also possible that the divergence cell pool may be dependent on the initial position and thus different cells are responsible for stimuli at different distances from the subject.

5. Conclusion

Classical dry dissection methods have been used to isolate the disparity vergence eye movements. These studies have shown that dynamics of divergence eye movements are dependent on the initial stimulus position. The closer the stimulus is to the subject, the faster the responses. Conversely, convergence is not dependent on the initial stimulus position. An extension of dry dissection based on ICA was used to isolate the underlying components of divergence eye movements. This decomposition showed that two neural control components are active in divergence eye movements and that changes in the transient component may be responsible for the differences in divergence dynamics seen at different initial positions. However, the influence of nonlinearities in the extraocular muscles cannot be ruled out.
Acknowledgment

This work was funded in part by Essilor International.

References


John Semmlow was born in Chicago, in 1942, and received the BSEE degree from the University of Illinois in Champaign in 1964. Following several years as a design engineer for Motorola, Inc., he entered the Bioengineering Program at the University of Illinois Medical Center in Chicago, receiving the Ph.D. in 1970. He has held faculty positions at the University of California, Berkeley, and the University of Illinois, Chicago, and currently holds a joint position as Professor of Surgery, UMDNJ- Robert Wood Johnson Medical School and Professor of Biomedical Engineering at Rutgers University, New Jersey. In 1985 he was a NSF/CNRS Fellow in the Sensormotor Control Laboratory of the University of Provence, Marseille, France. He was appointed a Fellow of the IEEE in 1994 in recognition of his work in acoustic detection of coronary artery disease, a Fellow of AIMBE in 2003, and a Fellow of BMES in 2005. He was founding chair of the International Conference on Vision and Movement in Man and Machines, first held in Berkeley in 1995. His primary research interests include discovering strategies for how the brain controls human motor behavior such as eye movements, the characteristics of the aging eye and lens, the development of improved imaging technologies, particularly in the eye, and medical instrumentation. He has a wide range of outside interests: he is President of the Board of the New Brunswick Chamber Orchestra; leader of the Rutgers Folk dancers, an avid, if somewhat dangerous, skier, an enthusiastic, mediocre tennis player, and he enjoys the slow, but nonetheless very expensive hobby of sailing.