density of human ocular media. Optom Vis Sci 2001;78:386–395.
21. Hunold W, Malessa P. Spectrophotometric determination of melanin pigmentation of the human fundus oculi. Ophthalmic Res 1974;6:355–362.
22. Highman VN, Weale RA. Rhodopsin density and visual threshold in retinitis pigmentosa. Am J Ophthalmol 1973; 75:822–832.
23. Carr RE, Ripps H, Siegel IM, Weale RA. Rhodopsin and the electrical activity of the retina in congenital night blindness. Invest Ophthalmol Vis Sci 1966;5:497–507.
24. Liem AT, Keunen JE, van Norren D. Clinical applications of fundus reflection densitometry. Surv Ophthalmol 1996;41: 37–50.
25. Augsten R, Konigsdorffer E, Schweitzer D, Strobel J. Nonproliferative diabetic retinopathy-reflection spectra of the macula before and after laser photocoagulation. Ophthalmologica 1998;212:105–111.
26. Landrum JT, Bone RA, Kilburn MD. The macular pigment: a possible role in protection from age-related macular degeneration. Adv Pharmacol 1997;38:537–556.
27. Delori FC, Goger DG, Dorey CK. Age-related accumulation and spatial distribution of lipofuscin in rpe of normal subjects. Invest Ophthalmol Vis Sci 2001;42:1855–1866.
28. Berendschot TTJM, et al. Influence of lutein supplementation on macular pigment, assessed with two objective techniques. Invest Ophthalmol Vis Sci 2000;41:3322–3326.

OCULAR MOTILITY RECORDING AND NYSTAGMUS

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INTRODUCTION

This chapter will discuss the different types of eye movements generated by the ocular motor system, the advantages and disadvantages of commonly used recording systems, the requirements for accurate calibration of those systems, and the use of eye-movement recordings in research.

What Can We Record and Why? A Brief Introduction to Types of Eye Movements and Why We Record Them

Humans are highly visually driven animals. Our hearing may be inferior to that of the owl and our sense of smell far poorer than a dog's, but our visual acuity is excelled by few other species. High resolution vision, however, creates a bandwidth problem—if we processed our entire visual field simultaneously at maximal resolution, we would need so many optic nerve fibers to carry visual information back to the brain that our eyes might not fit into our heads. The solution that has evolved is to make the resolution of the retina—the light-sensitive neural layer of the eye—inhomogeneous. Visual acuity in the central 1° of the visual field is maximal, but it falls off rapidly as one moves toward the periphery. What keeps us from ever being aware of this fact is the nearly incessant motion of our eyes, which use a number of interconnected control systems to direct our gaze to an object of interest and to keep it fixated in the face of target and body movement. Considerable processing in the visual areas of the brain is needed to integrate the discontinuous flow of visual images into the clear, stable perception of the world that we usually experience.

EYE MOVEMENTS

The types of eye movements to be discussed here all play a part in the maintenance of vision. There are only 6 muscles per eye, arranged in opposing pairs and moving in a relatively constrained way by virtue of the anatomy of the orbit. Although each type of eye movement serves a specific purpose and is generated by partially distinct brain mechanisms, they nonetheless interact in the course of normal life. Examination and recording of eye movements has a surprisingly long history, going back to the pioneering work of Dodge and Cline (1). Eye-movement recording has enjoyed a number of advantages over the analysis of other motor control mechanisms. The following sections will briefly describe each type of eye movement, what purpose it serves, and why one might wish to record it.

Version and Vergence

The ocular motor system may be divided into two major subsystems: one that controls version (conjugate or conjunctive) eye movements, and one that controls vergence (disconjugate or disjunctive) eye movements. Saccades, pursuit, vestibuloocular, and optokinetic eye movements are types of version movements, and convergent and divergent refixations and pursuits are types of vergence eye movements. Patients may exhibit eye-movement abnormalities stemming from disorders in the version or vergence subsystem and both nystagmus and saccadic intrusions may be disconjugate, even uniocular. Recording systems used for all eye movements should be capable of independently recording data from both eyes, regardless of whether they are presumed to be conjugate, which is especially important when recording patients but is also applicable to normal individuals because conjugacy is not absolute. It is a common misconception that one can record "conjugate" movements from one eye only and presume the other eye is moving in exactly the same manner. In this chapter, only methods that fulfill this requirement are considered, regardless of either the experimental paradigm (version or vergence) or the subject population (normal or patient).

Saccades

Saccades are the fastest eye movements made, with velocities at times approaching 1000°/s. We make them nearly incessantly during our waking hours and during rapid eye movement sleep. Although at the end of each saccade only the most central area around the fixation location is seen with maximal acuity, our brains are able to integrate the rapidly acquired series of such images into a single, unified perception of the world. Saccades may be horizontal, vertical, or oblique, which has implications for their recording, as will be discussed below. Evaluation of saccades may be grouped broadly into assessment of the saccades themselves and analysis of where they go as an individual views a scene or an image. Some eye trackers are more suitable for one sort of study than another. In particular, some methods are poorly suited to vertical and completely unsuited to torsional eye movements, where as others may have insufficient temporal resolution for assessment of latency or accuracy but excel at mapping sequences of fixations in two dimensions. In this discussion, a somewhat arbitrary distinction will be drawn between the detailed evaluation of individual saccades (as is often done clinically) and the assessment of scanpaths (as is sometimes used in a clinical setting but more often used in studies of man-machine interaction).

Inherent Saccadic Characteristics.

Accuracy. Saccadic accuracy is usually expressed in terms of gain (eye position/target position). Most commonly, if a refixation were comprised of multiple steps toward the target, the gain would be based only on the first step. Gain may be either abnormally high or abnormally low in different neurological conditions.

Latency. Latency is the time between stimulus onset and onset of eye movement. In humans, latency may range from 80 to several hundred ms, depending on the task and the age and health of the patient. Normally, saccades made in anticipation of target motion are excluded, unless stimuli with predictable location and timing are used. To be measured accurately, data must be acquired at a rate permitting the precise resolution of saccade timing (e.g., 500 Hz). Thus, a 25 or 30 Hz video-based system would be useless for this application.

Peak Velocity. Peak velocity can be measured either using analog electronics or, more commonly now, by off-line differentiation using software. Peak velocity is affected by fatigue, sedating drugs, and diseases that affect the cells in the brainstem that generate the fast, phasic component of saccadic innervation. Again, very low frame rates will make accurate calculation of peak velocity impossible, as it would not be possible to measure the rate of change in eye position. Indeed, if the sampling rate is too low, small saccades may be lost altogether, as they could be completed between samples (or video frames).

Scanpaths. Scanpaths can be divided into the descriptions of how individuals view a scene and nystagmus scanpaths that describe the eye trajectories about a fixation point in an individual with nystagmus. The former contain refixation saccades and periods of fixation whereas the latter contain the oscillatory nystagmus movements, braking, and foveating saccades, plus intervals of relatively stable fixation, if present.

Clinical Applications. Demonstration of how individuals (including patients) view a scene is probably the most familiar application of eye movement recording. In these applications, the "fine structure" of each saccade is of less interest than knowledge of where the saccades take the eyes and in what sequence. The classic work of Yarbus demonstrated the stereotyped way in which individuals view faces (2). As these investigations are focused on how cognitive processes control gaze, such work can be used to examine how patients with Alzheimer's disease (3) examine a novel scene or how individuals with schizophrenia attempt to judge the emotions expressed in a face. For scanpath analyses, high temporal resolution is unnecessary and spatial resolution on the order of a degree, not minute of arc, is acceptable. A wide linear range for vertical and horizontal eye movements is essential, however. Unobtrusiveness and minimal obstruction of the visual field are highly desirable when behavior is to be interfered with as little as possible.

Commercial Applications (Usability Studies, Man-Machine Interactions). Commercial applications are probably one of the most rapidly growing areas of eye movement research; it involves evaluating how humans interact with human displays. Here, the goal may be to see how a web page is examined or where a pilot is looking in a cockpit. The technical requirements for the eye tracker are essentially the same as for clinical applications. An exception is the area of gaze-contingent displays, where the endpoint of a saccade is predicted from recording its beginning, and the display is updated in high resolution only at that point. Such applications impose stricter temporal and spatial resolution criteria.

Nystagmus Scanpaths. Plots of the horizontal vs. vertical motion of nystagmus patients' eye movements during fixation of a stationary target provide insight into their ability to foveate the target in a stable (i.e., low retinal-slip velocity) and repeatable (i.e., low variance in the mean positions of target foveation intervals) manner. Nystagmus phase-plane (eye position vs. eye velocity) and scanpath plots were developed to study the foveation periods present in many of the waveforms seen in infantile nystagmus (4–8). They are important methods that provide insight into how individuals with such oscillations can achieve high visual acuity. The recording equipment for nystagmus scanpaths and phase-planes needs to be both accurate and of sufficient bandwidth to record the small saccades imbedded in nystagmus waveforms.

Smooth Pursuit. A correlate of having only a small part of the retina—the fovea—with high spatial resolution is that if a moving object is to be seen clearly, it must be tracked precisely, so that its image remains on the fovea, which is the function of the smooth pursuit system. The brain substrates underlying smooth pursuit are, to a degree, separable from those of the saccadic system, but, as a recent review has noted (9), a high degree of parallelism exists. Given that the two systems must work together for successful tracking, this fact is not surprising. For example, if you hear a bird call in the sky and decide to follow it, you must first locate it with a saccade (and possibly a head movement). Your pursuit system then keeps your gaze on the bird, but if it moves too swiftly for this system, it can be reacquired by a saccade and tracking can the recommence. If it is lost again, the pattern repeats. Indeed, if pursuit gain (eye velocity/target velocity) is low or even zero, objects can still be tracked by repeated saccades, giving rise to the clinical observation of "cogwheel pursuit."

In contrast to the many roles that saccades serve, pursuit eye movements are rather specialized for tracking. We all can generate saccades at will, even in the absence of targets, but voluntary generation of smooth pursuit is extremely rare and of poor quality. When recorded, it may be examined qualitatively for the presence of saccades or the smooth tracking segments can be separated out and their gain analyzed. As a result of the bilateral organization of motor control in the brain, it is possible to have a unidirectional pursuit abnormality, which may be of diagnostic value. However, bilaterally reduced smooth pursuit is nonspecific, as it may result from boredom, inattention, alcohol, fatigue, as well as pathology. As the pursuit system cannot track targets moving at greater than approximately 2 Hz, the requirements for its recording are not very demanding. If pursuit velocity is to be derived, however, then a low-noise system with appropriate low-pass filtering is essential to prevent the velocity signal from being swamped by noise. A low-noise system is also crucial in computer analysis of smooth pursuit because the algorithm used to identify saccades must ensure that none of the saccade is included in the data segment being analyzed as pursuit. If the pursuit component of the eye movement is only 5°/s and portions of saccades with velocities $\leq 30°$/s are included, pursuit gain calculations may be highly inaccurate, which is a concern when commercial systems incorporating proprietary algorithms are being used in clinical settings where this possibility has not been anticipated. See Calibration (below) for more information.

Vestibulo-Ocular Response (VOR)

The VOR is a fast reflex whose purpose is to negate the effects of head or body movement on gaze direction. Acceleration sensors in the semicircular canals provide a head-velocity input to the ocular motor system that is used to generate an eye-velocity signal in the opposite direction. The sum of head and eye velocity cancel to maintain steady gaze in space. The VOR is tuned to negate fast head movements and works in concert with the optokinetic reflex (see below), which responds to lower frequency background motion.

Rotational Testing. For vision to be maximally effective, it must continue to work properly as humans move around in the environment. Consider what would happen if the eyes were fixed in the head as one walked about—the image falling on the retina would oscillate with every step. Every turn of the head would cause the point of regard to sweep away from the fovea. Relying on visual input to compensate would be far too slow to generate an accurate compensatory input. Therefore, humans possess the semicircular canals, three approximately (but not precisely) orthogonal transducers of rotational motion, as part of each inner ear. Only three neurons separate the canals from the extraocular muscles that move the eyes. The canals are filled with fluid and, as the head moves, the inertia of the fluid causes it to lag behind, stimulating displacement-sensitive hair cells at the base of each canal. With only two synapses between sensory transducer and motor effector, the core of the VOR pathway can act very rapidly. Note, however, that constant velocity rotation elicits a signal that eventually decays to baseline, as the fluid eventually ceases to lag behind the canals (i.e., it moves with the same rotational velocity as the canals). Of course, prolonged constant velocity rotations are not part of our evolutionary history and are rarely encountered in daily life.

As the function of the VOR is to facilitate the maintenance of stable gaze as we move around in the environment, it makes intuitive sense to assess it in a moving subject. The most common way to make this assessment is to measure the horizontal component of the VOR as the patient is rotated while in the seated position. Spring-loaded Barany chairs were eventually superseded by electrically driven chairs, which could be driven with velocity steps, sinusoidally, or with more complex inputs. Step inputs may be used to quantify the time constant of decay of the VOR, whereas the other inputs can be used to generate gain and phase plots. Directional asymmetries or abnormal gains can be readily detected with such testing. Such tests are also carried out not only under baseline conditions, with the patient in complete darkness, but also with the VOR suppressed (patients fixate a target rotating with them) or enhanced (patients fixate an earth-fixed target).

Rotary chair testing has several shortcomings, particularly for low frequencies (e.g., 0.05 Hz). It takes a long time to obtain several cycles of data, during which time the patient may be lulled to sleep by the slow rotation in the dark. Alerting tasks (e.g., mental arithmetic) can be used to overcome this shortcoming, but the overall testing time may be quite long. Stimuli such as pseudo-random binary sequences have been used, with data analyzed by cross-correlation (10) in order to obtain results across a wide range of frequencies more rapidly. Another limitation, however, is that in order to obtain VOR data with a chair, the entire patient must be rotated, which limits the frequency range of the technique, because rotations of, for example, a 100 kg individual at 2 Hz would require very high forces. In addition, high frequency rotations increase the likelihood that because of inertia, the patient would not rotate precisely in phase or with the same amplitude as the chair. Systems are available that record eye movement and sense head movement during patient-initiated head shaking, which allows for testing at more physiological frequencies, but it requires a cooperative patient.

A fundamental problem with rotary chair testing is that although directional differences can be detected, localizing pathology to one ear is difficult. Obviously, rotating only one side of the head is impossible, and the "push-pull" nature of the vestibular system (due to the juxtaposed semicircular canals in the ears) makes lateralization difficult. For this reason, the next test remains valuable, in spite of its shortcomings.

Caloric Testing. Introduced by Barany in 1903, caloric testing is probably the most widely used of all vestibular tests. When carried out using EOG, it is still often referred to as "electronystagmography" (ENG), a term that is sometimes mistakenly applied to all forms of eye-movement recording. It involves the irrigation of the ear canal with either warm water or cold water, which alters the behavior of the horizontal semicircular canal on the side being irrigated. Cold water simulates reduced ipsilateral activity and warm water simulates an irritative lesion; the temperature of the water thus determines the direction of the resulting induced nystagmus fast phase in the way described by the acronym COWS: cold, opposite; warm, same. Vestibular nystagmus frequency and amplitude can readily be assessed for each ear at various temperature levels, which remains the only practical way to assess each side of the vestibular system independently. However, caloric stimulation has the appreciable shortcoming that it is a dc input to the vestibular system. It thus assesses the function of the system far from its physiological frequency range of several Hertz.

Optokinetic Response (OKR)

The OKR is a slow reflex whose purpose is to negate the effects of retinal image movement on gaze direction. Velocity sensors in the retina provide an input to the ocular motor system that is used to generate an eye-velocity signal in the same direction, maintaining gaze on the moving background. The OKR is tuned to respond to slow retinal image movement and works in concert with the VOR (see above), which responds to high frequency head motion.

Full-Field. The optokinetic nystagmus (OKN) response, like the VOR, may be induced in healthy individuals with appropriate visual stimuli. The fundamental form of the optokinetic response is induced by motion of all (or most) of the visual field, which elicits a slow eye movement in the direction of the stimulus, with a fast phase bringing the eyes back toward their initial position. This response continues as long as the stimulus continues. If one considers how the VOR decays with continuous motion and has low gain at very low frequencies, then it can be seen that the OKR and the VOR are functionally additive. Indeed, the relationship between OKR and VOR can be readily observed by anyone who has sat gazing out of a train window and felt himself moving, only to discover that it was the adjacent train which was pulling out of the station. The optokinetic stimulus evokes activity in the vestibular nuclei of the brain, and this activity elicits a sense of motion—the most common way to activate the vestibular system. This visually-induced motion percept is known as linearvection if the motion is linear and as circularvection if the stimulus is rotational. The nature of OKN differs depending on whether the stimulus is actively followed or passively viewed.

Small-Field (Hand-Held Drum, Tape). Although "train nystagmus" may be relatively easy to induce in the real world, presentation of a full-field OKN stimulus in a clinical setting requires a stimulus that essentially surrounds the patient. For this reason, OKN is more often tested using either a small patterned drum or a striped tape, both of which can be easily held in the examiner's hands. Although the OKN induced in this way looks no different than that deriving from a full-field stimulus, it is primarily a smooth pursuit response, whereas the full-field OKN includes both pursuit components as well as responses deriving from subcortical pathways, including the lateral geniculate body, accessory optic system, nucleus of the optic tract, and the brain stem and cerebellar circuitry governing eye movements.

Spontaneous Nystagmus & Saccadic Intrusions or Oscillations

Diagnostic Classification. In addition to induced nystagmus, some subjects exhibit either spontaneous or gaze-evoked nystagmus or saccadic intrusions or oscillations. The waveforms and other characteristics of these movements often have diagnostic value; accurate calibration of the data is necessary to extract diagnostic information or to deduce the mechanisms underlying the genesis of an intrusion or oscillation (nystagmus or saccadic).

Nystagmus Versus Saccadic Oscillations. The first distinction to be made when spontaneous oscillations are present is to distinguish between the many types of nystagmus and saccadic intrusions and oscillations. Both the slow-phase waveforms and their relationships to target foveation (placement of the target image on the small, high resolution portion of the retina) help in making this determination. Although the details of these determinations are beyond the scope of this chapter, the basic difference is that nystagmus is generated and sustained by the slow phases, whereas saccadic intrusions and oscillations are initiated by saccades that take the eyes off-target.

Congenital Versus Acquired Nystagmus. If nystagmus is present, determination of its origin is necessary (i.e., is it congenital or acquired?). Again, this field is complex and cannot be fully discussed here. Suffice is to say, certain nystagmus waveforms exist that are pathognomonic of congenital nystagmus; they, along with characteristic variations with gaze angle, convergence angle, or fixating eye, help to determine whether a nystagmus is congenital or acquired.

OCULAR MOTOR RECORDING SYSTEMS

Overview of Major Eye-Movement Recording Technologies

The following are descriptions of the more common technologies used to record the eye movements of both normals and patients. Technical descriptions, engineering, and physics of these and other methods may be found elsewhere in this volume (see "Eye Movement Measurement Techniques"). Emphasis in this chapter will be on the abilities of different types of systems and the calibration requirements to provide accurate eye-movement data in the basic and clinical research settings.

Electrooculography. *Theory of Operation.* Electrooculography (EOG) is the only eye-movement recording method that relies on a biopotential, in this case, the field potential generated between the inner retina and the pigment epithelium. This signal may approach 0.5 mV or more in amplitude. If two electrodes are placed on either side of, and two more above and below, the orbit (along with a reference electrode on the forehead or ear), then as the eye rotates in the orbit, a voltage proportional to the eye movement may be recorded, because one electrode becomes more positive and the other more negative with respect to the reference electrode. The technique is one of the oldest and most widespread and has been the standard for assessment of eye movements related to vestibular function. When the term ENG is seen, it is generally EOG that is used.

Characteristics. EOG has the considerable advantage that it requires only a high impedance, low noise instrumentation amplifier for its recording and that the voltage is linearly proportional to eye movement over most of its range. Such amplifiers are relatively inexpensive in comparison with many other eye-tracking technologies. As the electrodes are placed on the skin adjacent to the eye, no contact occurs with the eye itself and no obstruction of any part of the visual field exists. It also is unaffected by head motion, because the electrodes move with the head.

Applications. In theory, the EOG can be used anywhere eye movements are to be recorded. However, as the following section will show, it has a number of inherent limitations that practically eliminate it from many applications. Its widest use remains in the assessment of vestibular function and for the recording of caloric nystagmus and the vestibulo-ocular reflex. It is unsuited for use in environments with changing levels of illumination, as normal physiological processes will change the resting potential of the EOG and thus alter its relationship with amplitude of eye movement. EOG can be used in the assessment of saccades and smooth pursuit, but the low-pass filtering generally required will lead to artificially lowered saccade peak velocities. EOG has occasionally been used in scanpath studies, but its instability and fluctuating gain make it undesirable for this application, because if scenes differing in mean luminance are presented, the EOG will gradually change amplitude.

Limitations. Although conceptually simple and easy to implement, EOG has many shortcomings. One is that because the electrodes are placed on the surface of the facial skin, the EOG is not the only signal they detect. If the patient is nervous or clenches his or her teeth, the resulting electromyographic (EMG) activity in the facial muscles will be recorded as well, with the result that the signal actually recorded is the sum of the desired EOG and the unwanted EMG. As the spectra of the two signals overlap, no amount of filtering can completely separate them.

Another significant problem with EOG is the fact that, like many biopotential recordings, it is prone to drift. Some of this droft may reflect electrochemical changes at the electrode, causing a shift in baseline, which was particularly a problem when polarizable electrodes were used in the early days of the technique. Even nonpolarizable electrodes such as the commonly used Ag-AgCl button electrodes may still yield a varying baseline when first applied. Furthermore, the potential also shifts with changes in illumination. Indeed, assessment of this response to light is itself a clinical tool. This baseline variability can lead to the temptation to use an ac-coupled amplifier in the recording of the EOG, which has frequently been done, particularly in the ENG literature. Although not a problem if the only data required is nystagmus frequency, significant distortion occurs when ac-coupling is used to record saccades. The apparent drift back toward the center closely resembles a saccade whose tonic innervational component is inadequate. Noise and drift limit the resolution of EOG to eye movements of no less than 1°; this threshold may be even higher in a nervous patient or an elderly patient with slack, dry skin. An additional limitation undercuts the EOG's otherwise significant advantage in being able to record vertical eye movements, which is the overshooting seen on vertical saccades. It has long been suggested that the lids, moving somewhat independently of the globe, act as electrodes on the surface of the globe, conducting current in parallel to the other current path between globe and electrodes (11).

Another more practical drawback to the use of EOG when used for recording the movements of both eyes horizontally and vertically is that a total of nine electrodes are required (see Fig. 1). Each must be individually adhered to the patient and must be carefully aligned if spurious crosstalk between horizontal and vertical motion is to be avoided. Even if only horizontal motion is to be recorded, five accurately placed electrodes are still needed. A common but unfortunate clinical shortcut has been to use only three—two at either outer canthus of the eye and one

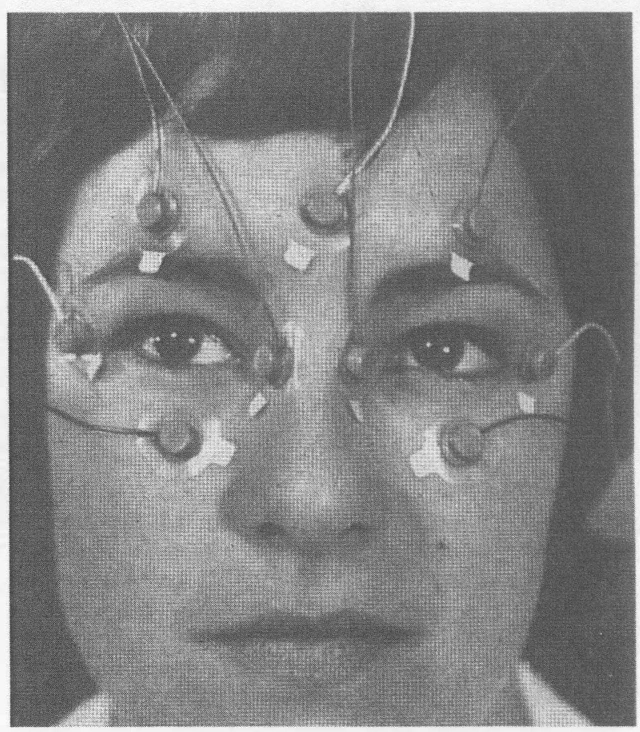

Figure 1. EOG electrodes arranged to record the horizontal and vertical eye movements of both eyes. Reference electrode is in the center of the forehead.

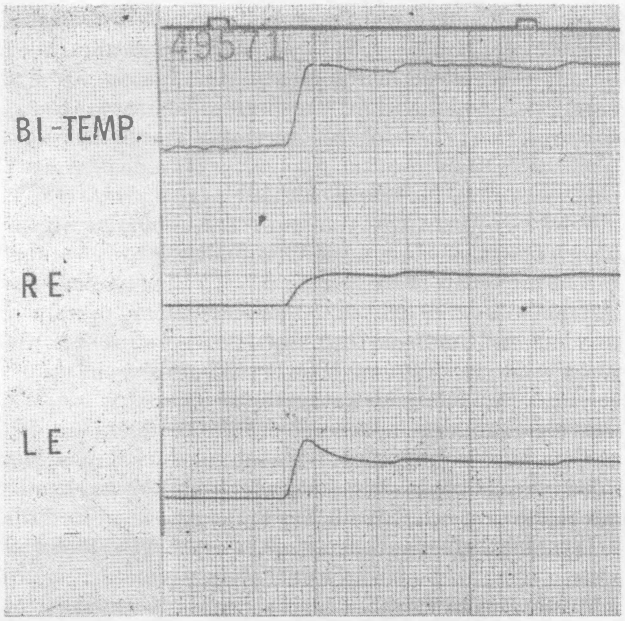

Figure 2. False saccadic trajectory from bitemporal EOG electrodes resulting from the summation of the individual saccadic trajectories shown below.

for reference. This shortcut effectively records a "cyclopean" eye by summing the potentials obtained from each eye. Although eye movements other than vergence are conjugate in normal individuals, it is not generally normal individuals who are seen for clinical evaluation. Figure 2 illustrates how an overshooting and an undershooting eye movement may be combined to give the appearance of a perfect saccade. For this reason, both ac-coupling and bitemporal electrode placement should be avoided when anything other than the crudest information about eye movement is desired.

Infrared Reflectance.

Theory of Operation. Although photographic recording of eye movements dates back to 1901 (1), such methods remained cumbersome to use, especially when they required frame-by-frame analysis of the location of some marker on the eye. Optical levers, where a beam of light was reflected from a mirror attached by a stalk to a scleral contact lens, offered the opportunity for precise registration of eye position, but occluded the view of the eye being recorded. As might be imagined, they were also unpleasant to wear. An alternative recording method that also makes use of reflected light relies on the differential reflectivity of the iris and sclera of the eye to track the limbus—the boundary between these structures. The earliest versions of this system were developed by Torok et al. (12) and refined by several investigators over the years (13–15). Although the number of emitters and detectors vary between designs, they share the same fundamental principle; that is, the eye is illuminated by chopped, low intensity infrared light (to eliminate the effects of variable ambient lighting). Photodetectors are aimed at the limbus on either side of the iris. As the eye moves, the amount of light reflected back onto some detectors increases and onto others decreases. The difference between the two signals provides the output signal. As would be expected, these signals are analog systems, so that the output of the photodetectors is electronically converted into a voltage that corresponds to eye position. Figure 3 shows an IR system mounted on an earth-fixed frame (a), spectacle

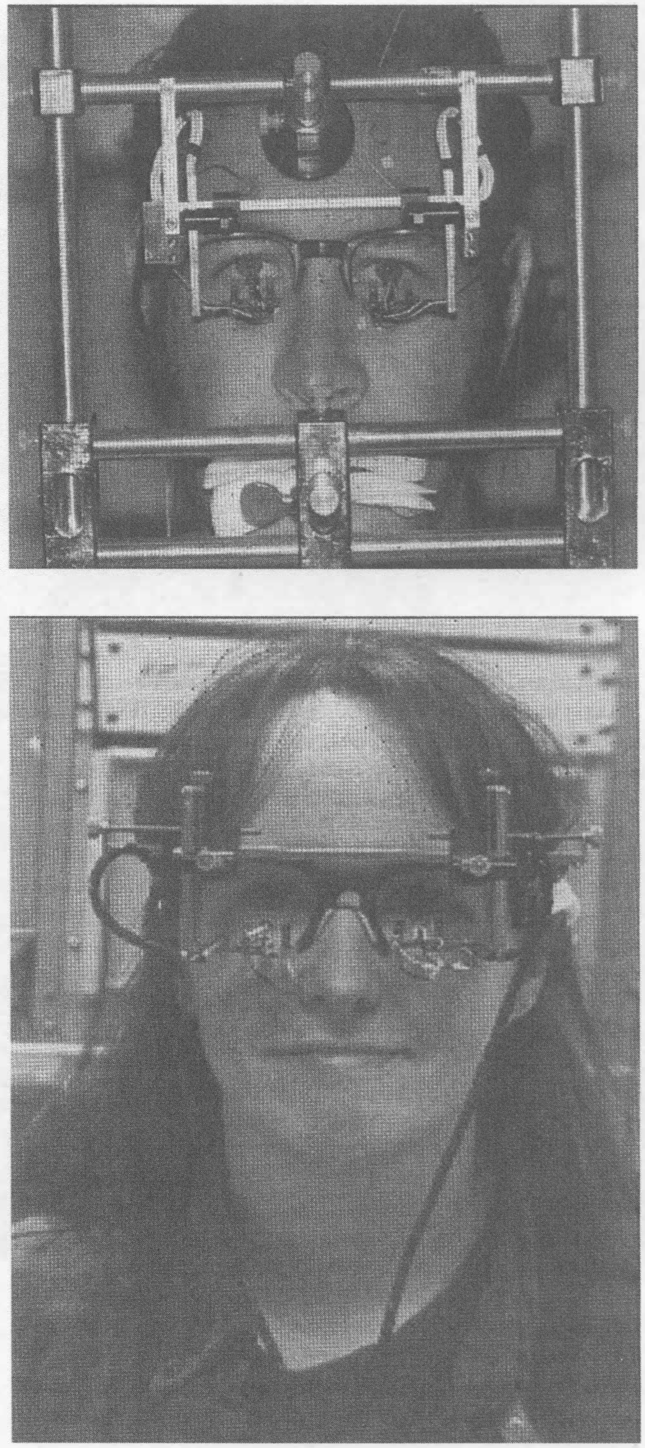

Figure 3. IR system to measure the horizontal eye movements of both eyes shown mounted on an earth-fixed frame (a) and spectacle frame (b) for human subjects and on a spectacle frame for a canine subject (c).

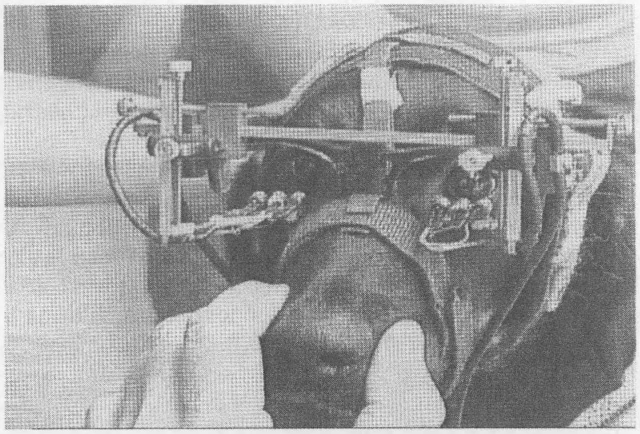

Figure 3. (*Continued*)

frame (b), and spectacle frame on a dog (c). Figure 4 shows an IR system mounted in goggles on a child (a) and a dog (b).

Characteristics. These systems offer a number of advantages over EOG, at least for the examination of horizontal eye movements. As the signal is not a biopotential, it is free of the instability found in the EOG; it is also immune to interference from muscle artifact and changes in electrode potentials. Unlike some earlier photographic methods, the device does not occlude the eyes, as the sensors and emitters are positioned above or below the eye. The field of view is somewhat obstructed by the emitter/detector, in contrast to EOG. Resolution is of the order of minutes of arc. Assuming that nothing disturbs the sensors, a shaken head or a rubbed eye, for example, stability is excellent. Thus, the question of using ac-coupling, as in many electronystagmographic applications of the EOG, never occurs. System bandwidth is generally on the order of 100 Hz, which is sufficient to capture fine details of saccades.

The linear range of these systems generally is between $\pm15^\circ$ and 20° in the horizontal plane and half this amount or less in the vertical plane (which requires vertical orientation of the detectors or summation of the signals from horizontally-oriented detectors).

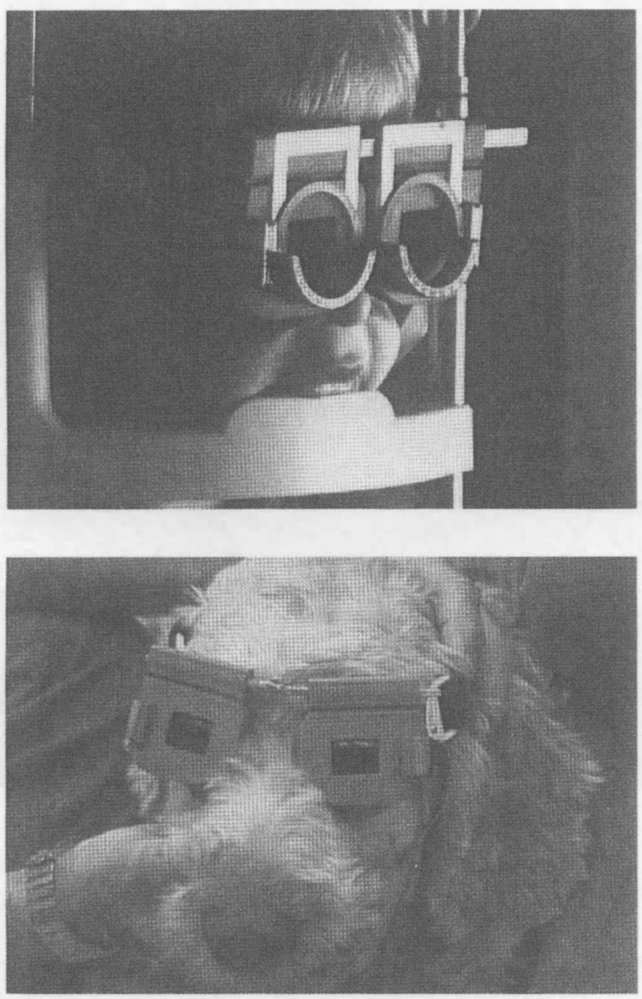

Figure 4. IR system to measure the horizontal and vertical eye movements of both eyes shown mounted in goggles for a human subject (a) and a canine subject (b).

Applications. IR limbus trackers are probably second only to EOG in their range of applications. Their ability to resolve fine detail with low noise makes them excellent for conditions where subtle features of the eye movement are important; examples include analyses of saccadic trajectories or analysis of small corrective saccades within a nystagmus waveform. An important advantage over EOG is that if eye velocity is to be calculated, the resulting signal is far less noisy than the derivative of an EOG recording, especially where broadband EMG noise has contaminated the signal developing from the eye. These systems are well suited to studies of any sort of eye movement that falls within their linear operating range in the horizontal plane. As they are generally head-mounted, they will tolerate modest head movement, but if the stimuli are fixed in the environment, such movement will certainly cause a loss of baseline and may move the tracker outside its linear range, which makes head stabilization highly desirable, especially when stimuli are presented at gaze angles where subjects would normally make both a head movement and an eye movement to acquire the target. Finally, IR systems are noninvasive, a major advantage for many patients and for children.

Limitations. One of the biggest shortcomings of these systems is their poor performance for vertical eye movement, their near-uselessness for oblique eye movements, and their complete lack of value for torsional eye movements. Although the limbus is clearly visible over a wide range of eye positions in the horizontal plane, the eyelids obscure its top and bottom margins. Although a degree of vertical tracking can be obtained by virtue of the differential reflectivity of the iris and pupil, the range over which this is possible is limited, again in part because of occlusion of the lids. Oblique movement suffers from inherent crosstalk because, as eye position changes in one plane, the sensitivity to motion in the other plane will vary, which is a hindrance to using these systems for studies of reading, scanpath analysis, or other applications where 2D eye movements are important. The use of the systems in rotational testing is also limited by the range of allowable gaze angles and by the possible slippage of the head mounting on the head if accelerations are sufficiently high. Their suitability for small children also varies; some of the systems do not fit small heads well, although if precise calibration is not important, one can generally record patients as young as 3 years. These systems are not generally appropriate for use with infants. The one exception is for diagnosing nystagmus from its waveform by simply holding the sensors in front of the eyes, which can be done for even the smallest infants (e.g., a premature infant still in an incubator).

Scleral Search Coil.

Theory of Operation. Robinson developed the Scleral Search Coil technique in 1963 (16). It relies on the principle that a coil of wire in an alternating magnetic field induces a voltage proportional to the area of the coil, the number of turns, and the number of field lines. This latter measure will vary with the sine of the angle the coil makes with the magnetic field. In the basic configuration, two orthogonal pairs of field coils are used, each modulated by phase-locked square wave sources either operating in quadrature (i.e., one signal 90° phase-shifted relative to the other) (16) or at a different frequency (e.g., 50 and 75 kHz) (17). An annular contact lens with a very fine coil of wire is placed on the eye, so that it surrounds the cornea (or in animals, is surgically implanted under the conjunctiva). Figure 5 shows an annular search-coil contact lens on the eye of a subject. Components of the induced voltage generated by the horizontal and vertical signals can be separated via phase-sensitive detectors. Note that this method of recording horizontal and vertical components of eye movement eliminates the crosstalk present in 2D recordings made by limbus trackers. With an appropriately wound coil added to the lens, torsional eye movements may also be recorded. This technique is the only one able to record torsion with high bandwidth.

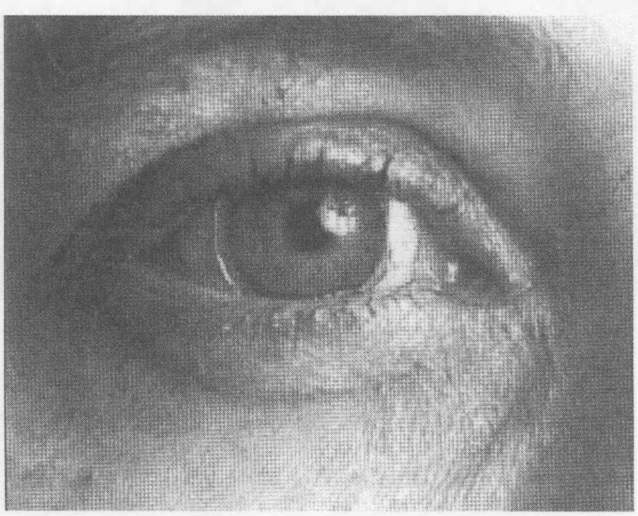

Figure 5. An annular search-coil contact lens used to measure the horizontal and vertical eye movements of a human subject. The fine wire from the imbedded coil exits at the nasal canthus.

Characteristics. This technology serves as the "gold standard" for eye-movement recording. Resolution is in seconds of arc and the linear range ± 20°, with linearization possible outside this range, because the nonlinearity follows the sine function. The signals are extremely stable, because their source is determined by the geometry of coil and magnetic field alone. In the usual configuration, the maximum angle that can be measured is 90°. Although the eyes cannot rotate this far in the head, if the head is also allowed to turn (and its position recorded by a head coil), a net change of eye position > 90° is possible. A solution to this problem was developed whereby all the field coils were oriented vertically, generating a magnetic field whose vector rotates around 360°. Now, the phase of the field coil varies linearly over 360° of rotation (18,19), which is most often used for horizontal eye movements, with vertical and torsional eye movements recorded using the original Robinson design.

Applications. As the search-coil system provides such high quality data, it can be used in nearly any application where stability, bandwidth, and resolution are paramount and free motion by the subject is not essential. However, recent evidence suggests that the coils themselves may alter the eye movements being measured (20). Nonetheless, the low noise level and ability to independently record horizontal, vertical, and torsional movements at high bandwidth and high resolution still make this the gold standard of eye-movement recording techniques.

Limitations. As a result of their size, search-coil systems are clearly not suited for ambulatory studies or those carried out in other real-world settings such as a vehicle. The system also cannot be adapted to use in fMRI scanners, unlike IR limbus trackers or video-based systems. Search coils are invasive, making them unsuitable for some adult patients and for most children. A small risk of corneal abrasion exists when the coil is removed, but this risk is generally minor. Use of the coil in infants or small children would be undesirable, because they could not be instructed not to rub their eyes while the coil was in place. Another practical issue associated with the technology is the cost of the coils, which have a single supplier, have a limited lifetime, and are relatively expensive (> US$100 each). As recommended duration of testing with the coils is 30 minutes or less, long duration studies are also precluded.

Digital Video.

Theory of Operation. Although electronic systems that locate and store the location of the center of the pupil in a video image of the eye were developed in the 1960s, often in combination with pupil diameter measurement (21,22), video-based eye trackers became a major force in eye-tracking technology when digital rather than analog image analysis was implemented. If the camera is rigidly fixed to the head, then simply tracking this centroid is sufficient to identify the location of the eye in its orbit. However, if there is even slight translational movement of the camera with respect to the eye, a large error is introduced: 1 mm of translation equals 10° of angular rotation in the image. For this reason, video systems also track the specular reflection of a light source in the image in addition to the pupil centroid. As this first Purkinje image does not change with rotation but does change with translation, whereas the pupil center changes with eye rotation as well as translation, their relative positions can be used to compensate for errors induced by relative motion occurring between the head and camera. Figure 6 shows a digital video system in use on a human subject (a) and on dogs (b and c).

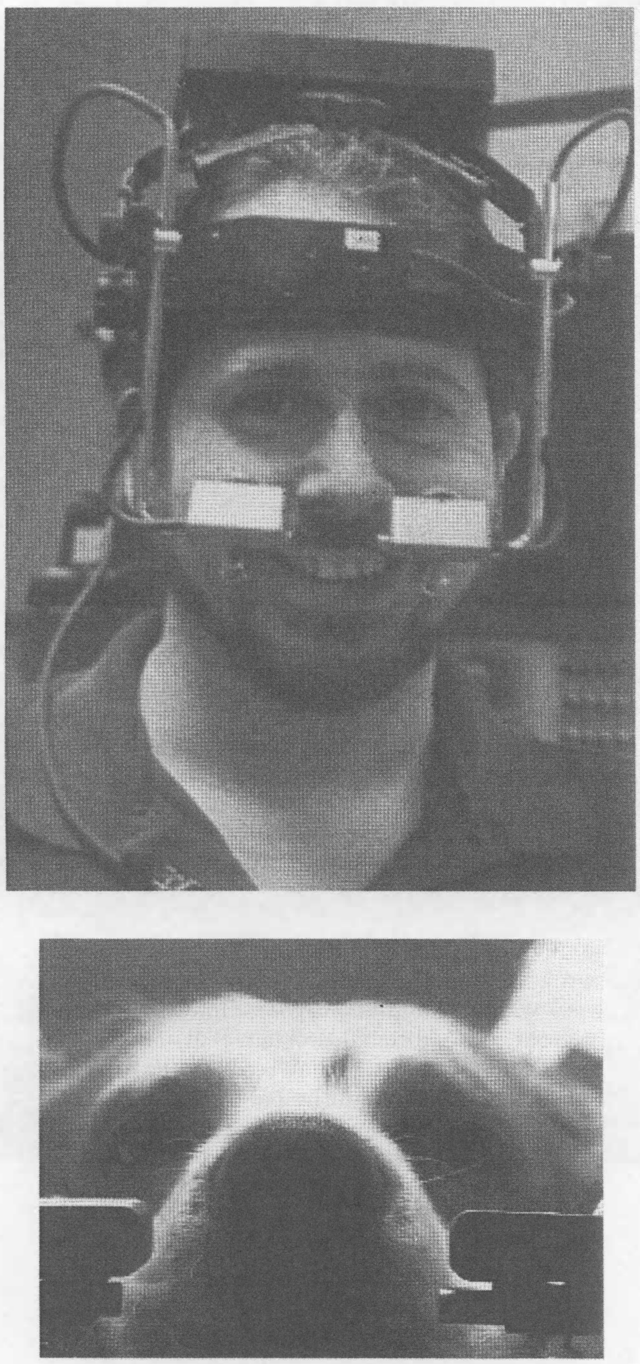

Figure 6. A high-speed digital video system to measure the horizontal and vertical eye movements of both eyes for a human subject (a) and canine subjects (b and c).

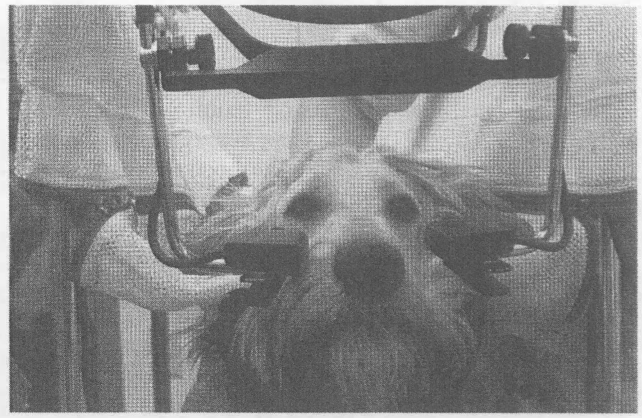

Figure 6. (*Continued*)

Characteristics. Assuming that the axes of the head and camera are aligned, then video-based systems are capable of recording both horizontal and vertical eye movements over a relatively wide range (often $\pm 30^\circ$ horizontally, somewhat less vertically). Resolution is better than EOG but generally somewhat less than for IR or search-coil systems, often in the range of 0.5°. As analog video systems use a raster scan to represent an image, spatial resolution is limited by the nature of the video system used (e.g., PAL or NTSC). Bandwidth is limited by the frame rate of the video system. If conventional analog video is used, then frame rates are 50 Hz for PAL and 60 Hz for NTSC. These rates impose a maximum bandwidth of 25 and 30 Hz, respectively. Although adequate for examination of slow eye movements, these frame rates are inadequate for assessment of saccades; indeed, very small saccades could be completed within the inter-frame interval. Systems using digital video are free from the constraints imposed by broadcast TV standards and can make use of higher frame rate cameras—several now operate at 250 or 500 Hz. Generally, a frame rate versus resolution trade-off exists—higher frame rates imply lower image resolution. However, continued improvement in digital video technology and ever faster and cheaper computers continue to improve performance.

Although older video tracking systems often required a good deal of "tweaking" of brightness and contrast settings in an effort to obtain a reliable image of the pupil, many recent systems have more streamlined set-up protocols. In the past, some systems internally monitored fixation on calibration targets and rejected data that were unstable, thereby making the systems unsuitable for use with patients with nystagmus. However, default calibration settings generally permit data to be taken and the nystagmus records can then be retrospectively calibrated.

Applications. In principle, digital video is the most flexible of all eye-movement recording technologies. Some systems use cameras mounted on the head, using either helmets or some other relatively stable mounting system. Other systems use remote cameras, often mounted adjacent to or within a computer stimulus display. Systems used in vehicles may use either remote cameras or helmet-mount cameras. In addition to conventional clinical eye-movement testing, video systems, especially remote camera models, are increasingly being used in commercial applications such as advertising studies and usability analyses of websites. For such applications, the unobtrusiveness of the technology and the need to only monitor fixations rather than to study saccade dynamics makes even relatively low-frame-rate video ideal. Such systems are also excellent for use with infants and small children, who may be induced to look at some attractive display on a screen but who generally respond poorly to head-mounted apparatus. Remote systems that track more than one first Purkinje image can cope with a wider range of head movements, making the systems even less restrictive for the subjects. Some video systems can also analyze torsional eye movements by identifying some feature on the iris and then tracking changes in its orientation from frame to frame. High-speed (500 Hz) digital video systems are seeing increased use in basic and clinical laboratories, challenging magnetic search coils as the method of choice.

Limitations. The problems associated with calibrating patients whose eyes are never still have already been discussed. As noted before, the other serious limitations of some of these systems are their somewhat limited spatial resolution and bandwidth. Both parameters can be optimized, but doing so leads to marked increases in price. However, unlike other eye-tracking technologies, the limiting factors for high-speed, digital video eye-movement recording systems are the cameras and computing power. As the enormous general consumer market rather than the quite small eye-movement recording market drives improvements in both technologies, improvements can be anticipated to occur much faster than they would otherwise. Even within the eye-tracking field, the development of commercial uses for the technology will facilitate its advance faster than the smaller and less prosperous academic research community.

OCULAR MOTOR RECORDING TECHNIQUES

How Do We Record and Later Calibrate and Analyze Subjects' Eye Movements?

The initial recording and *post-hoc* calibration and analysis of eye movements require following a protocol conducive to both accurate calibration and obtaining the data specific to a particular study. Decades of experience have resulted in the following recording procedures and caveats and in the development of software that allows accurate calibration and linearization of the data.

Real-Time Monitoring. When recording subjects (especially patients), it is necessary to monitor the eye channels in real-time to ensure that the subject is following instructions, which is also imperative when calibrating subjects (see below). Unlike highly dedicated and motivated graduate students, most subjects quickly become bored by the task at hand or distracted and fail to fixate or pursue the stimuli; others may have difficulty doing so. Real-time monitoring via a strip chart or computer display allows the experimenter to detect and correct such failures with a simple verbal instruction encouraging the subject (e.g., "follow the target" or "look at the target").

Monocular Calibration. The key to obtaining accurate eye-movement data that will allow meaningful analysis is monocular calibration; that is, calibration of each eye independently while the other is behind cover. Too often, potentially accurate, commercially available recording systems are seriously compromised by built-in calibration techniques that erroneously presume conjugacy, even for so-called normal subjects. Just as bitemporal EOG makes it impossible to determine the position of either eye individually (see Fig. 2), so do calibration techniques carried out during binocular viewing of the stimuli. Most commercially available software calibration paradigms suffer from this fatal flaw, rendering them totally inappropriate for most clinical research and seriously compromising studies of presumed normal subjects. For methods that depend on subject responses to known target positions (e.g., IR or digital video), both the zero-position adjustment and gains at different gaze amplitudes in each direction must be calibrated for each eye during short intervals of imposed monocular fixation (i.e., the other eye occluded); for methods where precalibration is possible (e.g., magnetic search coils), the zero adjustment for each eye in each plane must also be made during imposed monocular fixation.

Linearization and Crosstalk Minimization. In addition to monocular calibration, linearization is required of most systems, even within the stated "linear" regions of those systems. As a result of different facial geometries and the inability to position the sensors in the precisely optimal positions for linearity, these systems are usually not linear over the range of gaze angles needed for many studies. System responses may be linearized by taking data during short intervals (5 s) of monocular fixation at all gaze angles of interest (e.g., 0°, ± 15°, ± 20°, ± 25°, and ± 30°) and applying post-recording linearization software. Even Robinson-type search coils need an arcsine correction for a linear response. For IR and video-based systems measuring eye motion in both the horizontal and vertical planes, crosstalk is a major problem due to sensor placement. Crosstalk can also be minimized post recording, using software written for that purpose. However, IR systems suffer from the additional problem that, as vertical eye position changes, a change may occur in the sensors' aim regions at the left and right limbal borders, which means that for a diagonal eye movement, the horizontal gain is an unknown function of vertical eye position, making IR systems essentially unsuitable for the recording of oblique eye movements.

All of the problems discussed above are accentuated when recording subjects with ocular motor oscillations, such as nystagmus. In these cases, the experimenter must be familiar with the type of nystagmus the subject has and be able to identify the portions of their waveforms that are used for target foveation. It is the "foveation periods" that are used to set the zero-position and gains at each target position; without them, accurate calibration is impossible.

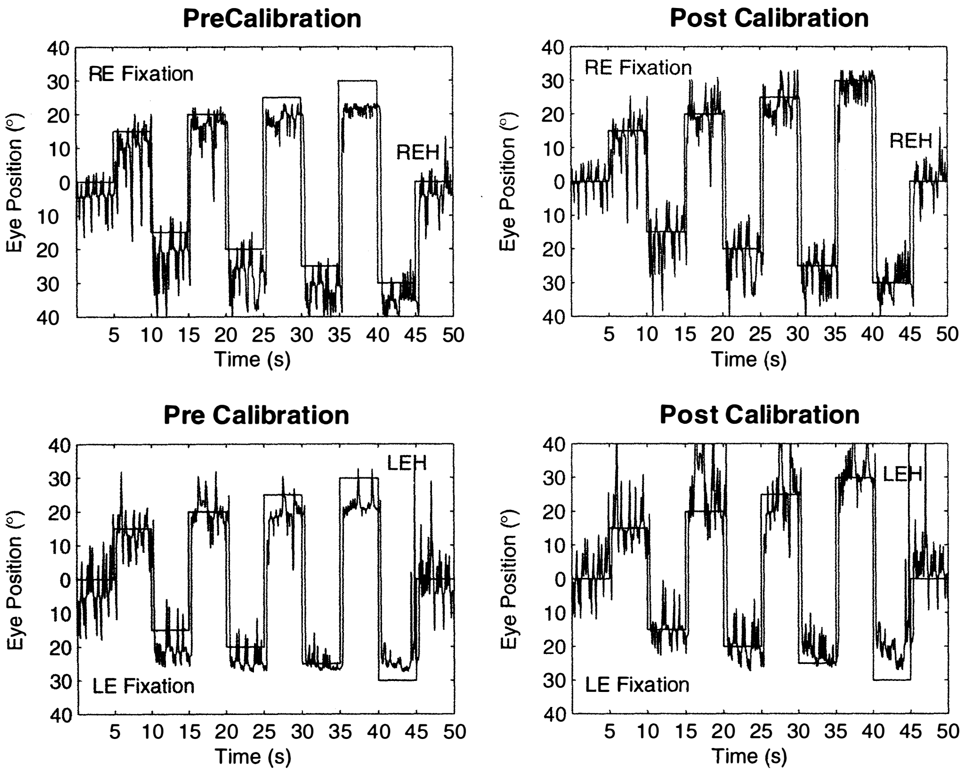

Figure 7. Monocular fixation precalibration and postcalibration (horizontal) records for the right (REH) and left (LEH) eye. Compare the offsets and nonlinear precalibration responses to the bias-adjusted, calibrated, and linearized postcalibration responses. Note the failure of the subject to look at the −30° target during LE fixation. In this figure and Fig. 8, target position is shown by the alternating direction, increasing offset, solid line.

The rest of the nystagmus waveform is irrelevant to target foveation and should be ignored during calibration. With a little practice, investigators can easily determine exactly where the subject with nystagmus is looking, which eye is fixating, and where the other eye is located with respect to the target; they can also determine periods of inattention by the associated waveform changes. Figure 7 demonstrates precalibration and postcalibration (horizontal) records of each eye made under imposed monocular fixation, and Fig. 8 shows the results of applying those calibration factors to a record made during binocular "viewing" of the targets. Note that the fixating eye is easily determined as well as the angle/position of the strabismic eye. Unfortunately, investigators with little or no experience in recording subjects with nystagmus are often reduced to using the average eye position during long periods of presumed binocular fixation to approximate calibration of subjects with nystagmus (and probably strabismus). Averaging anathema to accurate calibration and renders most potentially accurate recording systems (e.g., search coils) no better than bitemporal EOG. Needless to say, the results and conclusions of such studies must be highly suspect and are often incorrect; they exemplify how even the most sophisticated hardware and software can be misused, and prove the old adage, "garbage in, garbage out."

CONCLUSIONS

During the past 40 years, advances in eye-movement recording systems, coupled with the control-systems approach brought to the field by biomedical engineers, have resulted in an explosion of basic and clinical ocular motor research, at the systems as well as single-cell levels. Using the measurement systems and recording and calibration techniques described above, great strides have been made in our understanding of the ocular motor system. Animal studies have provided understanding at the single-cell and cell-network (bottom-up) levels, giving rise to computer models of small portions of the ocular motor system with neuroanatomical correlations. Normal human studies have allowed characterization of ocular motor behavior under a variety of stimulus conditions, giving rise to functional, top-down computer models of ocular motor behavior. Finally, studies of patients with many congenital and acquired ocular motor disorders have provided insights into the functional structure of the ocular motor system, which was not forthcoming from studies of normals (23,24). These latter studies have resulted in robust, behavioral models of the ocular motor system that are able to simulate normal responses and patient responses to a variety of ocular motor stimuli (25–27).

At present, accurate eye-movement recordings are an integral part of the diagnosis of both congenital and acquired forms of nystagmus, and of saccadic intrusions and oscillations. In addition, they provide objective measures of therapeutic efficacy that are related to visual function in patients afflicted with disorders producing ocular motor dysfunction. Indeed, ocular motor studies of the effects of a specific surgical procedure for congenital nystagmus produced an entirely new type of "nystagmus" surgery for both congenital and acquired nystagmus (28–31). This surgery (named "tenotomy") simply requires

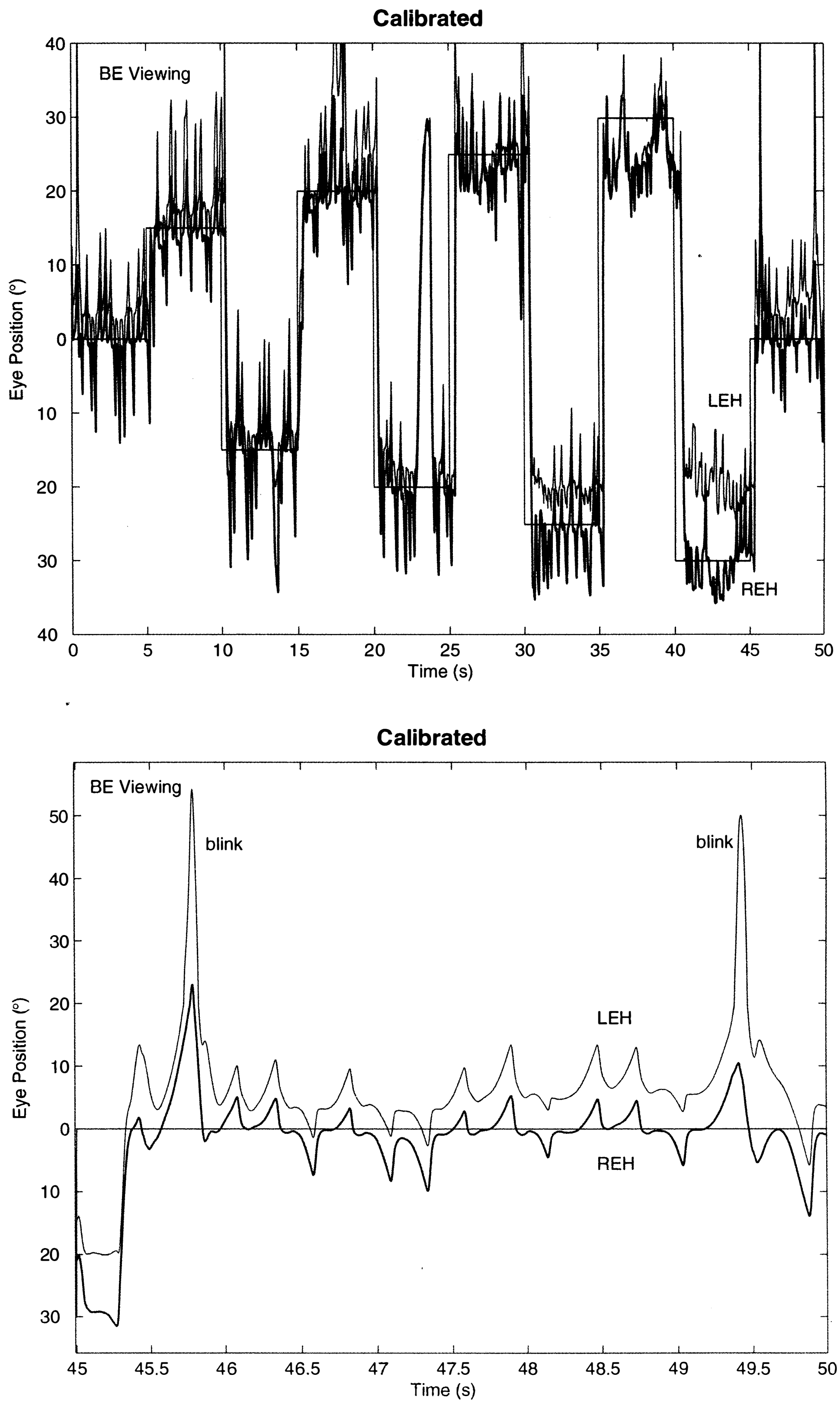

Figure 8. Calibrated binocular viewing records of both eyes (a) and final primary-position segment (b). Note the preference for RE fixation in left gaze and in the final primary-position segment, with the LE 3–5° esotropic. Note also how well the flat foveation periods of the RE line up on the 0° target despite the alternating direction of the nystagmus.

removal and reattaching, at their original insertion points, each of the four extraocular muscles in the plane of the nystagmus. Tenotomy represents a radical paradigm change from the "strabismus" surgeries that preceded it and has resulted in new insights into the anatomic structures responsible for proprioceptive signals from the extraocular muscles and their neurophysiologic role in the control of eye movements (32–34).

BIBLIOGRAPHY

1. Dodge R, Cline TS. The angle velocity of eye movements. Psychol Rev 1901;8:145–157.
2. Yarbus AL. Eye Movements and Vision. New York: Plenum Press; 1967.
3. Daffner KR, Scinto LF, Weintraub S, Guinessey JE, Mesulam MM. Diminished curiosity in patients with probable Alzheimer's disease as measured by exploratory eye movements. Neurology 1992;42:320–328.
4. Dell'Osso LF, Van der Steen J, Steinman RM, Collewijn H. Foveation dynamics in congenital nystagmus I: Fixation. Doc Ophthalmol 1992;79:1–23.
5. Dell'Osso LF, Van der Steen J, Steinman RM, Collewijn H. Foveation dynamics in congenital nystagmus II: Smooth pursuit. Doc Ophthalmol 1992;79:25–49.
6. Dell'Osso LF, Van der Steen J, Steinman RM, Collewijn H. Foveation dynamics in congenital nystagmus III: Vestibulo-ocular reflex. Doc Ophthalmol 1992;79:51–70.
7. Dell'Osso LF, Leigh RJ. Foveation period stability and oscillopsia suppression in congenital nystagmus. An hypothesis. Neuro Ophthalmol 1992;12:169–183.
8. Dell'Osso LF, Leigh RJ. Ocular motor stability of foveation periods. Required conditions for suppression of oscillopsia. Neuro Ophthalmol 1992;12:303–326.
9. Krauzlis RJ. Recasting the smooth pursuit eye movement system. J Neuriphysiol 2004;91:591–603.
10. Furman JM, O'Leary DP, Wolfe JW. Application of linear system analysis to the horizontal vestibulo-ocular reflex of the alert rhesus monkey using pseudorandom binary sequence frequency sinusoidal stimulation. Biol Cyber 1979;33:159–165.
11. Barry W, Jones GM. Influence of eyelid movement upon electro-oculographic recording of vertical eye movements. Aerospace Med 1965;36:855–858.
12. Torok N, Guillemin VJ, Barnothy JM. Photoelectric nystagmography. Ann Otol Rhinol Laryngol 1951;60:917–926.
13. Young LR. Measuring eye movements. Am J Med Electr 1963;2:300–307.
14. Kumar A, Krol G. Binocular infrared oculography. Laryngoscope 1992;102:367–378.
15. Reulen JP, Marcus JT, Koops D, de Vries FR, Tiesinga G, Boshuizen K, et al. Precise recording of eye movement: The IRIS technique. Part 1. Med Biol Eng Comput 1988;26: 20–26.
16. Robinson DA. A method of measuring eye movement using a scleral search coil in a magnetic field. IEEE Trans Bio Med Electron 1963;BME(10):137–145.
17. Remmel RS. An inexpensive eye movement monitor using the scleral search coil technique. IEEE Trans Biomed Eng 1984;31:388–390.
18. Hartmann R, Klinke R. A method for measuring the angle of rotation (movements of body, head, eye in human subjects and experimental animals). Pflügers Archiv (Suppl); 362:R52.
19. Collewijn H. Eye movement recording. In: Carpenter RHS, Robson JG, eds. Vision Research: A Practical Guide to Laboratory Methods. Oxford: Oxford University Press; 1999.
20. Frens MA, van der Geest JN. Scleral search coils influence saccade dynamics. J Neurophysiol 2002;88:676–691.
21. Young LR. Recording eye position. In: Clynes M, Milsum JH, eds. Biomedical Engineering Systems. New York: McGraw-Hill; 1970. pp 1–2.
22. Marchant J. The oculometer: NASA, 1967. Report No. CR-805.
23. Abel LA, Dell'Osso LF, Daroff RB. Analog model for gaze-evoked nystagmus. IEEE Trans Biomed Eng 1978;BME(25): 71–75.
24. Abel LA, Dell'Osso LF, Schmidt D, Daroff RB. Myasthenia gravis: Analogue computer model. Exp Neurol 1980;68:378–389.
25. Dell'Osso LF, Jacobs JB. A normal ocular motor system model that simulates the dual-mode fast phases of latent/manifest latent nystagmus. Biolog Cybernet 2001;85:459–471.
26. Dell'Osso LF. Nystagmus basics. Normal models that simulate dysfunction. In: Hung GK, Ciuffreda KJ, eds. Models of the Visual System. New York: Kluwer Academic/Plenum Publishers; 2002. pp 711–739.
27. Jacobs JB, Dell'Osso LF. Congenital nystagmus: Hypothesis for its genesis and complex waveforms within a behavioral ocular motor system model. JOV 2004;4(7):604–625.
28. Dell'Osso LF. Extraocular muscle tenotomy, dissection, and suture: A hypothetical therapy for congenital nystagmus. J Pediatr Ophthalmol Strab 1998;35:232–233.
29. Dell'Osso LF, Hertle RW, Williams RW, Jacobs JB. A new surgery for congenital nystagmus: Effects of tenotomy on an achiasmatic canine and the role of extraocular proprioception. JAAPOS 1999;3:166–182.
30. Hertle RW, Dell'Osso LF, FitzGibbon EJ, Yang D, Mellow SD. Horizontal rectus muscle tenotomy in patients with infantile nystagmus syndrome: A pilot study. JAAPOS 2004;8:539–548.
31. Hertle RW, Dell'Osso LF, FitzGibbon EJ, Thompson D, Yang D, Mellow SD. Horizontal rectus tenotomy in patients with congenital nystagmus. Results in 10 adults. Ophthalmology 2003;110:2097–2105.
32. Büttner-Ennever JA, Horn AKE, Scherberger H, D'Ascanio P. Motoneurons of twitch and non-twitch extraocular fibres in the abducens, trochlear and oculomotor nuclei of monkeys. J Comp Neurol 2001;438:318–335.
33. Büttner-Ennever JA, Horn AKE, Graf W, Ugolini G. Modern concepts of brainstem anatomy. From extraocular motoneurons to proprioceptive pathways. In: Kaminski HJ, Leigh RJ, eds. Neurobiology of Eye Movements. From Molecules to Behavior—Ann NY Acad Sci 956. New York: NYAS; 2002. pp 75–84.
34. Hertle RW, Chan C, Galita DA, Maybodi M, Crawford MA. Neuroanatomy of the extraocular muscle tendon enthesis in macaque, normal human and patients with congenital nystagmus. JAAPOS 2002;6:319–327.

See also ELECTRORETINOGRAPHY; EYE MOVEMENT, MEASUREMENT TECHNIQUES FOR.

OCULOGRAPHY. See OCULAR MOTILITY RECORDING AND NYSTAGMUS.

OFFICE AUTOMATION SYSTEMS

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INTRODUCTION

The purpose of this article is to help people in fields, such as healthcare, engineering, sales, manufacturing, consulting, and accounting to understand office automation systems

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