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CHAPTER 2.7

Dynamics of saccadic oscillations

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Abstract: The brainstem circuitry underlying saccades is symmetrical with respect to the midline. The oculomotor behaviour generated by the circuitry depends on a combination of signals passed along fibre tracts and less easily identifiable connections, such as those across the midline. The midline crossing connections are often affected by developmental disorders which give rise to unstable eye movements (see J. Jen, this volume). The connections at the levels of the colliculus, pause cells, and neural integrator generate different dynamical mechanisms for the development of instabilities, which can be identified in eye movement recordings using phase space analysis techniques.

Keywords: fixed point; phase plane; hopf bifurcation; saccade; nystagmus

Introduction

Disorders of horizontal fixation

The normal saccadic system behaves in a remarkably machine-like fashion, producing 3–4 saccades during every second of our waking lives, all with similar main sequence characteristics. This consistency makes it hard to explain the disorders of normal saccadic behaviour which are found clinically (Ramat et al., 2007). For example, the visual systems of albinos typically show a number of distinctive features which include an underdeveloped retina, abnormal routing of the nerve fibres in the brain, nystagmus, and strabismus. Despite these distinctive features, the eye movement disorders which can be recorded from the patients are relatively varied (Collewijn et al., 1985; Timms et al., 2006), as illustrated in Fig. 1A.

Midline circuitry for horizontal saccades

The saccadic system provides a good starting point for determining how oculomotor disorders arise, because of the extensive knowledge of the neurophysiology of the system (Scudder et al., 2002; Sparks, 2002). The mechanics of the oculomotor plant are heavily damped so that a burst of innervation is required to make a fast eye movement and a tonic change of innervation is required to counter the spring stiffness of the plant. The burst of innervation is delivered by burst cells and a neural integrator converts the burst to a step change in innervation. In addition, the pause cells fire steadily when the eye is fixating the target, and inhibit the burst cells. The behaviour of the normal saccadic system can be characterised by the

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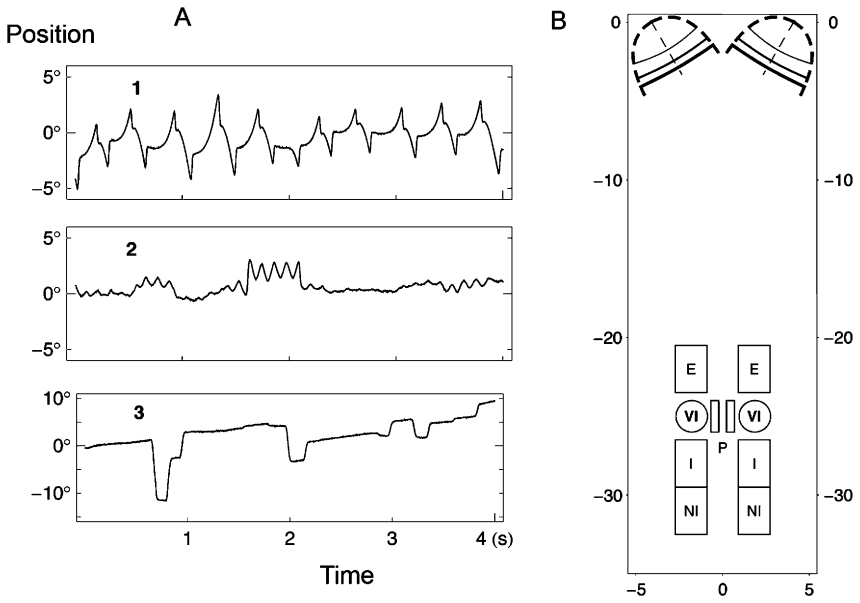

Fig. 1. (A) Three examples of horizontal disorders of fixation recorded from subjects with albinism. (1) Nystagmus, (2) intermittent fine pendular nystagmus, and (3) macrosaccadic oscillations (see Timms et al., 2006 for details of the stimulus and recording technique). (B) Schematic diagram of the relative anatomical proximity of some of the classes of neurons responsible for horizontal saccadic eye movements.

relationships between saccade amplitude and duration and peak velocity, which are referred to as the main sequence.

One noticeable feature of abnormal fixation is that horizontal disorders of fixation are much more common than vertical disorders. The most obvious difference between the horizontal and vertical eye movement systems is that the horizontal system is symmetric with respect to the midline (see Fig. 1B). This requires coordination of signals across the midline via fibre tracts and commisures, and also by fibres crossing the midline. The latter may be more vulnerable to because of the guidance required to ensure successful completion of their connections. Following from this hypothesis, one can go on to ask if different types of oculomotor oscillation are related to failure of different midline crossing connections. This question is addressed with respect to the disorders illustrated in Fig. 1A. Before examining the different disorders the concepts needed to characterise instability are introduced.

Instabilities of fixation

Fixed points

A useful tool for characterising the behaviour of a system is provided by the geometrical technique according to which the state of the system is described by a point in a state space and successive states trace out a curve in state space, known as a trajectory. A trajectory which arrives at a point corresponding to an equilibrium state of the system will stay at the point, which is referred to as a fixed point. In practice, while a trajectory in the neighbourhood of a stable fixed point will be guided towards the point, a trajectory near an unstable fixed point will be guided towards the point in some directions, and repelled from it in other directions in state space. In the context of the oculomotor system, steady fixation corresponds to a stable fixed point, and drifts and oscillations occur when the fixed point becomes unstable. Although it is known that in the case of the oculomotor disorder of nystagmus the state space of fixation is at least three dimensional

(Abadi et al., 1997), the different types of oculomotor instabilities can be revealed by a projection of the state space trajectories into a two dimensional phase plane plot of velocity against position (Dell'Osso et al., 1992). An example of the phase plane trajectory of a single saccade is shown in Fig. 2A. This tool will be use to illustrate how the different oculomotor disorders shown in Fig. 1A can emerge from the normal behaviour of the system.

Neural integrator drift

Stable fixation requires that the eye comes to rest at a particular position and does not move away from that position. On a plot of eye velocity against eye position all stable fixation points will lie on a horizontal line through the origin (Goldman et al., 2002). This relationship has been used to recover the parameters of the neural integrator. The behaviour of the neural integrator can be modelled by a first order, linear differential equation:

$$\frac{dp}{dt} = \frac{p}{\lambda} + v_{\text{bias}}$$

where p is the eye position signal, λ the time constant of the integrator, and v_{bias} the constant velocity bias on the input to the integrator. It follows from this equation that the values of both the time constant and the velocity bias can be recovered from a least squares fit to a plot of inter-saccadic velocities against inter-saccadic eye positions (Goldman et al., 2002).

Phase plane analysis can be adapted to identify that the drift shown in Fig. 1A3 is due to an abnormal bias in the neural integrator. If only the position and velocity signals from the intervals between saccades are plotted, then the data is expected to lie on a straight line. The slope of the line is equal to the time constant of the integrator and the offset of the line is equal to the bias on the integrator. The integrator is unstable if the slope is negative and the offset is non-zero.

Burst cell oscillations

The fine pendular nystagmus shown in Fig. 1A2 is an example of a microsaccadic oscillation. Such oscillations have been identified as saccadic

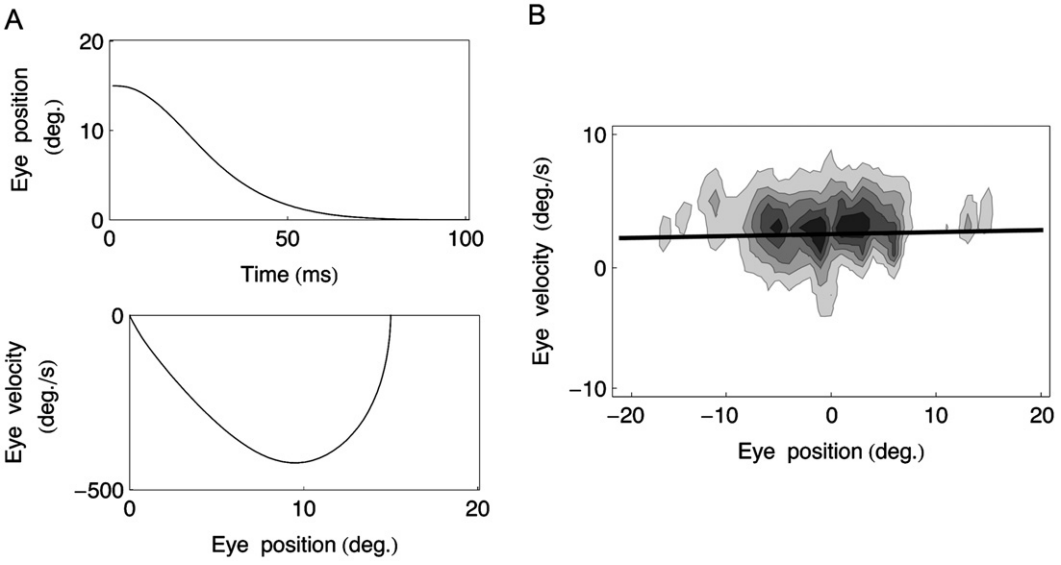

Fig. 2. (A) An example of the phase plane representation of a single saccade. The time course of the saccade is plotted above and the trajectory of the saccade in the phase plane is plotted below. (B) Histogram of the frequency of position and velocity combinations from the phase plane which occur during inter-saccadic intervals. These points were identified by having a velocity of less than 10 degrees/s. The best linear fit to the data is shown by the thick line.

because the particular duration and peak velocity of each movement lie on an extension of the main sequence for small saccades. Both modelling (Ashe et al., 1991; Ramat et al., 2005; Laptev et al., 2006) and experimental results (Ramat et al., 2005) have shown that incomplete inhibition of the burst cells by the pause cells results in high-frequency oscillations.

As illustrated in Fig. 3, the oscillations correspond to closed loops in the phase plane and the dynamical mechanism by which the instabilities develop can be shown to involve a Hopf bifurcation (Laptev et al., 2006). One of the definitive features of the Hopf bifurcation, that distinguishes it from other oscillation generating mechanisms, is that the amplitude of the oscillation grows with the square of the distance from the fixed point. This behaviour can be clearly seen in the simulations plotted in Fig. 3.

Splitting of the pause cells

The final example of an oculomotor instability involves the changes with gaze angle in a nystagmus waveform similar to that shown in Fig. 1A1. The trajectories for nystagmus cycles at different gaze angles can all be plotted on the same phase plane diagram as shown in Fig. 4, which also illustrates the changes in the waveforms. Also plotted in Fig. 4 are the locations of the fixed

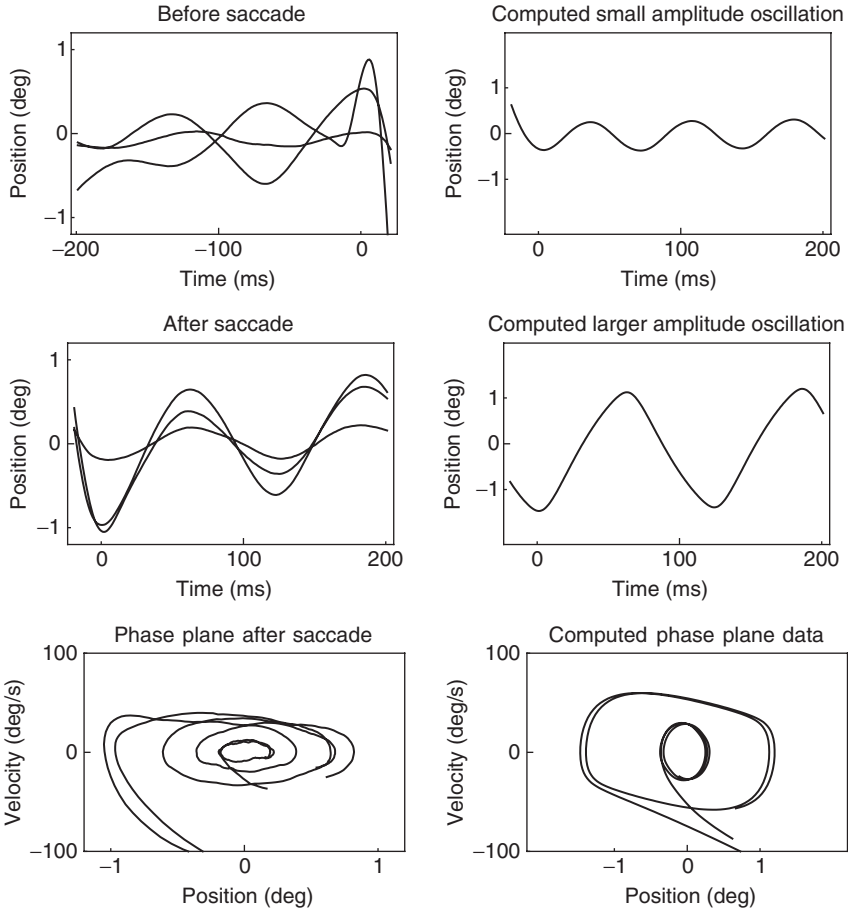

Fig. 3. Measured and modelled microsaccadic oscillations. Both sets of oscillations have their phase reset by voluntary saccades. The simulated waveforms become oscillatory through a Hopf bifurcation mechanism, and in accordance with this mechanism become increasingly sinusoidal as their amplitude decreases.

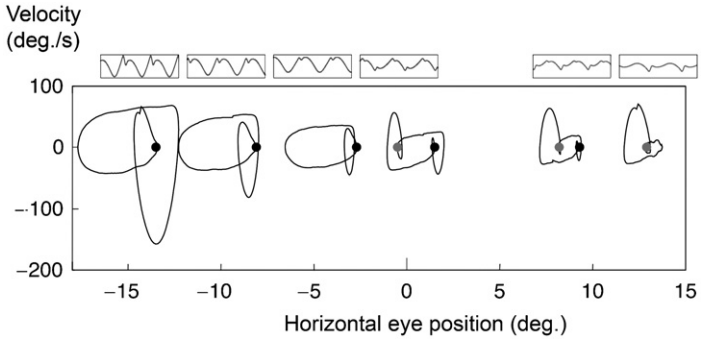

Fig. 4. Examples of nystagmus waveforms recorded from a subject with his head supported by a chin rest. Thirty seconds of fixation was recorded at each target position, which lay in the range from 15 degrees left to 15 degrees right and were located 5 degrees apart. Consistent oscillations were obtained from all target directions except 5 degrees right. Examples of the oscillations are plotted in boxes along the top of the figure. Each box encloses 1 s of eye movement recording and the vertical extent of the box corresponds to 6 degrees of gaze angle. In the phase plane representations the system follows a clockwise path round the loops, drifting away from the fixed point and being brought back by a small saccade. The fixed points of the leftward directed saccades are plotted in black and those of the rightward directed saccades are shown in grey. It is apparent that in the straight ahead direction the two fixed points do not coincide.

points for each waveform. When the target is between the straight ahead direction and 10 degrees to the right of the subject there are two fixed points. If it is assumed that the pause cells fire at the end of a saccade the presence of two fixed points implies that with a single target direction the pause cells can resume firing at two different fixation directions.

Conclusion

A number of horizontal oculomotor disorders appear to be related to failure of the normal development of midline crossing connections in the brainstem. Targets close to the naso-temporal boundary of the retina are represented on both the left and right halves of the colliculus and mutual inhibition between the halves is required to ensure that accurate saccades are generated (van Opstal and van Gisbergen, 1989; Tabareau et al., 2007). Damage to these lateral connections has been shown to result in incessant saccades in the monkey (Carasig et al., 2006). Microsaccadic oscillations occur when activity cycles between the left and right excitatory burst cells. This cycling will only occur with nonlinear mutual inhibition between the burst cells. Although more speculative, it may be that early-onset nystagmus oscillations involve interactions between two groups of pause cells, one of which fires when the target is imaged at a point on the left of the fovea and one of which fires when a target is imaged on the right of the fovea.

The effects of failure of the normal development of midline crossing connections can be investigated experimentally using two recently developed techniques of nonlinear systems analysis. Initially, the experimenter will not know the dimension of the state space of the abnormal fixation system and will have to assume that state space has at least three dimensions since it is known that early-onset nystagmus has at least this dimensionality (Abadi et al., 1997; Akman et al., 2006). A straightforward extension of the phase plane to three dimensions can be effected by plotting not just the position and velocity but also the acceleration of the eye. The fixed points of the system can be found directly from the eye movement recordings by using a technique of nonlinear dynamics which has been adapted for eye movement data by Theodorou and Clement (2007). Once the fixed points have been found, the dimensionality and stability of the system at the fixed points can be estimated by a local principal component method applied to eye movement data by Abadi et al. (1997) and Akman et al. (2006). These techniques enable direct comparison of experimentally measured and simulated eye

movement disorders. They can be used to test if the two sets of data have the same number of fixed points and the same dimensionality at each fixed point (Akman et al., 2006).

Once an oscillation is established it is not always possible to establish how it developed. The nonlinear systems approach is based on investigating how the behaviour of the eye movement system changes as a parameter is continuously varied. In many cases, once a patient develops an oscillation they cannot eliminate it by changing a parameter of the system such as gaze angle. So for investigating clinical conditions, the nonlinear dynamics approach will have to be adapted to consist of investigating the dynamics of a range of subjects with a given condition. For example, the hypothesis of a Hopf bifurcation underlying microsaccadic oscillations could be tested by pooling data from many subjects with different sized oscillations to see if the oscillations are more sinusoidal at smaller amplitudes.

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References

Abadi, R.V., Broomhead, D.S., Clement, R.A., Whittle, J.P. and Worfolk, R. (1997) Dynamical systems analysis: a new method of analysing congenital nystagmus waveforms. Exp. Brain Res., 117: 355–361.

Akman, O.E., Broomhead, D.S., Clement, R.A. and Abadi, R.V. (2006) Nonlinear time series analysis of jerk congenital nystagmus. J. Comput. Neurosci., 21: 153–170.

Ashe, J., Hain, T.C., Zee, D.S. and Schatz, N.J. (1991) Microsaccadic flutter. Brain, 114: 461–472.

Carasig, D., Kush, P., Fucito, M., Ramcharan, E. and Gnadt, J.W. (2006) Irrepressible saccades frm a tectal lesion in a Rhesus monkey. Vision Res., 46: 1161–1169.

Collewijn, H., Apkarian, P. and Spekreijse, H. (1985) The oculomotor behaviour of human albinos. Brain, 108: 1–28.

Dell'Osso, L.F., Van der Steen, J., Collewijn., H. and Steinman, R.M. (1992) Foveation dynamics in congenital nystagmus. I. Fixation. Doc. Ophthalmol., 79: 1–23.

Goldman, M.S., Kaneko, C.R.S., Major, G., Aksay, E., Tank, D.W. and Seung, H.S. (2002) Linear regression of eye velocity on eye position and head velocity suggests a common oculomotor neural integrator. J. Neurophysiol., 88: 659–665.

Laptev, D., Akman, O.E. and Clement, R.A. (2006) Stability of the saccadic system. Biol. Cybern., 95: 281–287.

Ramat, S., Leigh, R.J., Zee, D.S. and Optican, L.M. (2005) Ocular oscillations generated by coupling of brainstem excitatory and inhibitory saccadic burst neurons. Exp. Brain Res., 160: 89–106.

Ramat, S., Leigh, R.J., Zee, D.S. and Optican, L.M. (2007) What clinical disorders tell us about the neural control of saccadic eye movements. Brain, 130: 10–35.

Scudder, C.A., Kaneko, C.R.S. and Fuchs, A.F. (2002) The brainstem burst generator for saccadic eye movements. A modern synthesis. Exp. Brain Res., 142: 439–462.

Sparks, D.L. (2002) The brainstem control of saccadic eye movements. Nat. Neurosci. Rev., 3: 952–964.

Tabareau, N., Bennequin, D., Berthoz, A., Slotine, J.-J. and Giraud, B. (2007) Geometry of the superior colliculus mapping and efficient oculomotor computation. Biol. Cybern., 97: 279–292.

Theodorou, M. and Clement, R.A. (2007) Fixed point analysis of nystagmus. J. Neurosci. Methods, 161: 134–141.

Timms, C., Thompson, D., Russell-Eggitt, I. and Clement, R.A. (2006) Saccadic instabilities in albinism without nystagmus. Exp. Brain Res., 175: 45–49.

van Opstal, A.J. and van Gisbergen, J.A.M. (1989) A nonlinear model for collicular spatial interactions underlying the metrical properties of electrically elicited saccades. Biol. Cybern., 60: 171–183.