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NAMRL- 1280 **IAM**-R600

A PROCEDURE FOR THE ANALYSIS OF NYSTAGMUS AND OTHER EYE MOVEMENTS

Graham R. Barnes

June 1981

NAVAL AEROSPACE MEDICAL RESEARCH LABORATORY
PENSACOLA, FLORIDA

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Naval Medical Research and Development Command
M0933.PN.004-0005
MR.041.01.03-0156

Joint Report

Reviewed by	Approved and Released by
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23 June 1981

SUMMARY PAGE

THE PROBLEM

The variety of stimulus waveforms used in vestibular research and in clinical testing requires a versatile procedure for quantitatively analysing oculomotor responses.

FINDINGS

A new procedure was developed to analyse oculomotor responses to many forms of vestibular and/or visual stimuli used in experimental work and in clinical practice. The main advantage of the procedure lies in the simplicity of the basic algorithm which enables fairly rapid data analysis of a variety of response forms on a medium-speed computer working in a high-level language. For slow phase analysis, detection of saccades is carried out by a simple threshold procedure based upon the expected response form, and regression procedures are used to obtain stimulus-response correlation and slope (gain) measures. The procedure provides measures of gain, phase and directional preponderance for responses to sinusoidal stimuli.

This report was written while the author was a visiting scientist at the Naval Aerospace Medical Research Laboratory. The algorithm was adapted by Dr. Barnes to NAMRL equipment which is similar, though not identical, to data processing equipment at the Royal Air Force Institute of Aviation Medicine, Farnborough, England. The major work on program development was accomplished by Dr. Barnes before his visit.

INTRODUCTION

There are already many examples of procedures for the analysis of nystagmus (1,2,13), some of which are able to perform on-line analysis with a suitably fast computer. Most of these procedures involve the use of some fairly complex algorithm for distinguishing between fast and slow phases of the eye movement. The motivation for developing a different procedure in our laboratory was threefold. The first, and foremost, reason was an essentially practical one. As a research group with continually varying computational needs, we opted for the installation of a fairly powerful desktop computer (Hewlett-Packard 9845S) which could be easily programmed by experimenters in a high-level language (BASIC) without the assistance of a dedicated computer programmer. The drawback inherent in the use of such a computer is that it is relatively slow compared with those which use machine-code instructions. There was thus an incentive to develop an analysis procedure which would combine the superior pattern-recognition characteristics of the human operator with a relatively simple method of detecting the occurrence of fast phases.

The second reason for developing a new procedure came about as a result of the need to analyse the oculomotor responses to voluntary head movements. In these responses the peak slow-phase eye velocity was frequently very high (> 100 deg/sec) and the normal procedures for detecting fast phases, which might frequently be reduced to 100-150 deg/sec, were inadequate. The third point was that a reliable method was required for detecting fast phases in the oculomotor response to many different types of stimuli. In particular, there was a need to be able to analyse the responses to a high frequency visual pursuit task in which the fast phases are likely to be in the same direction as the slow-phase eye movements.

There are two means by which the improvement in processing time has been achieved. The first is that the detection of saccades is carried out by a simple threshold procedure based upon the expected form of the response. The threshold limits can be set up by the operator, although an automatic procedure is available for those responses which are unlikely to differ greatly from the population norm. The second feature is that there is no attempt in the analysis to interpolate between slow phases in order to reconstitute the cumulative slow-phase eye position. Instead, the points corresponding to the fast-phase components are simply discarded, leaving only slow-phase eye velocity points for subsequent statistical analysis.

THE FAST-PHASE DETECTION PROCEDURE

DATA PREPARATION

Prior to any data analysis a number of analogue and digital techniques are used to prepare the data. First the eye movement recording signal (normally an electro-oculographic recording) is filtered by an analogue low-pass filter (Kemo VBF/19) with a 48 dB/octave roll-off at 50 Hz. If the stimulus is also to be recorded, as it is during an oscillatory stimulus, then it is also filtered in a similar manner so that any phase distortion of the waveform will apply equally to both stimulus and response. The filtered signals are passed through an analogue-digital converter (Microconsultants Modular 15) which is capable of sampling up to eight channels simultaneously, using a parallel sample and hold module. The sampling rate and number of channels to be sampled can be set up prior to data acquisition under computer control.

The digitised data are fed directly into the computer (Hewlett-Packard 9845S) using Direct Memory Access, a rapid procedure with a transfer rate of 20,000 words/sec.* Analogue signals obtained from experiments are normally recorded on a multichannel tape recorder rather than being digitised on-line and stored in the computer. It is felt that this method gives greater flexibility should it ever be necessary to analyse the records in a different manner. The advantage of using Direct Memory Access is that it enables the analogue tape to be replayed at many times the recording rate (up to 32 x on our own recorder - a Racal-Thermionic Store 4-D) and so drastically reduce the data acquisition time.

If the recorded eye movement signal is still noisy despite the analogue filtering, the computer program incorporates a subroutine to apply a digital filter as an operator-specified option. The filter is of the auto-regressive type developed by Lynn (10,11). The filter introduces no phase distortion, but great care must be used in selecting the original sampling rate if this procedure is to be used. It is particularly useful when attempting to analyse EOG signals induced by a periodic stimulus of frequency greater than 1 to 2 Hz, where the signal to noise ratio may be severely diminished.

All the operations performed on the eye movement signals are actually carried out on the eye velocity signal. Thus, before any further processing can take place the eye displacement signal is digitally differentiated, using a two-point difference method, as shown below:

$$\dot{\theta}_i = (\theta_{i+1} - \theta_{i-1}) / 2.Dt$$

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*Equipment components at NAMRL which differ from some of those described in this section were adapted by the author to accomplish versatile quantitative eye movement analysis. At NAMRL the analog signals are recorded on a cassette recorder (Phillips Mini-Log 4 or a TEAC R 80). These signals, without analog filtering, are played back into a Hewlett-Packard multiprogrammer, Model 6942A, which incorporates three plug-in cards: an analog-to-digital converter, timer-pacer, and memory card. The multiprogrammer under the control of the Hewlett-Packard 9845T computer samples, digitizes, and stores the data on the memory card where they are transferred to the computer memory upon request. This process is limited by memory card capacity to 4096 readings per channel, and is slower than the direct memory access method used at IAM.

where $\dot{\theta}_i$ = eye velocity at time t = i.Dt

θ_i = eye displacement at time t = i.Dt

Dt = sampling increment(s)

If the stimulus is a periodic waveform, then it is also differentiated and stored along with the original waveform to be used in the subsequent statistical analysis.

The eye velocity signal is presented on the computer graphics display as shown in Figure 1. In this example, in which the stimulus is a sinusoidal waveform at 0.1 Hz, the stimulus velocity is also displayed. This exhibits the typical response of the vestibulo-ocular reflex, in which the slow-phase eye velocity is modulated in accord with the stimulus waveform but is in the compensatory direction. (N.B. The polarity of the stimulus waveform is reversed in Figure 1.) The slow phase is interspersed with brief high velocity spikes of reversed polarity, representing the differentiated fast phases. Figure 1 also shows, for completeness, the eye displacement signal, though it is not normally displayed to the operator during the analysis on the computer visual display unit (VDU).

SETTING-UP THRESHOLD LIMITS FOR SINUSOIDAL STIMULI

The procedure which is used for fast-phase detection is one in which the expected response is used to set up velocity thresholds for the assessment of slow and fast phases. The procedure is illustrated in Figure 1 for a sinusoidal stimulus, although the procedure is similar for other types of stimuli as will be shown later.

The first step is to estimate the characteristics of the stimulus waveform. The frequency is calculated by finding the zero cross-over points, and the peak velocity is estimated by integration of the first half-cycle of the stimulus waveform. Only a complete number of cycles is used for the analysis, which enables any offset in the stimulus waveform signal to be identified and removed. The graphics display has a cursor facility in which the position of one horizontal and one vertical line can be made to move in a direction perpendicular to the line. In the manual mode of threshold determination these cursor lines are brought up on the display screen so as to overlay the eye velocity waveform. The first set is aligned with the vertical cursor indicating the position of the first peak of the stimulus waveform and with the horizontal cursor indicating the estimated level of peak slow-phase eye velocity. This estimate is taken to be the peak stimulus velocity level multiplied by the normal gain factor (approximately 0.7) for the vestibulo-ocular reflex when recorded in the dark (5). If the position of the vertical cursor does not coincide with the peak slow-phase eye velocity, or in other words, if there is a phase difference between stimulus and response, the cursor is adjusted appropriately. Likewise if the horizontal cursor does not give a good estimate of peak eye velocity, it can be maneuvered in order to do so. A second set of cursors then allows the

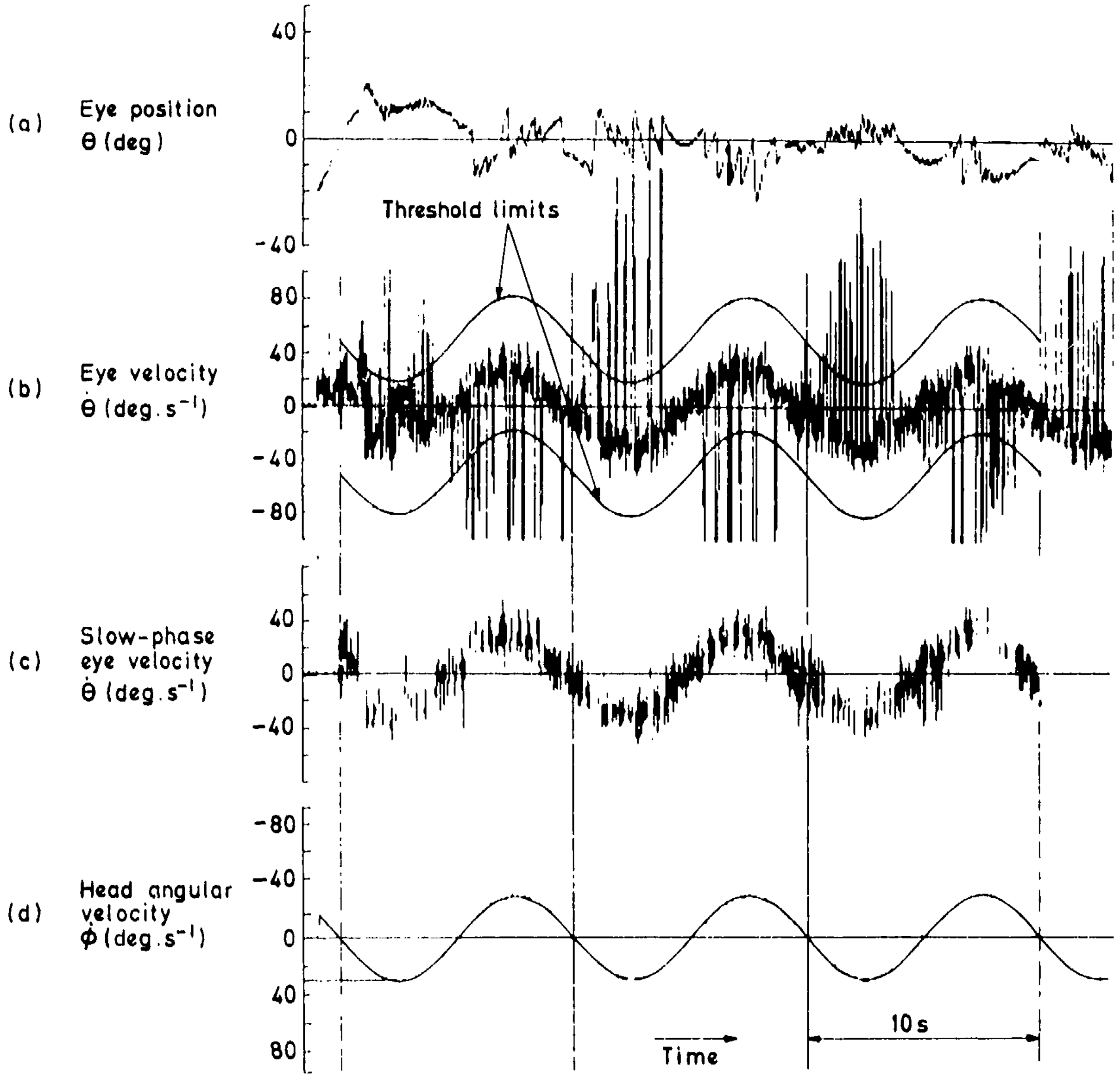

Figure 1

An illustration of the manner in which stimulus-related threshold limits are set up to dissociate the fast- and slow-phase components of nystagmus elicited in response to a 0.1 Hz sinusoidal oscillation of the head about the yaw axis.
(a) Eye position signal (EOG) sampled at 20-ms intervals. (N.B. The steplike nature of the signal is a common aberration produced by such computer graphics systems.)
(b) The differentiated EOG signal with fast and slow phases present.
(c) The eye velocity signal after fast phases have been removed.
(d) The stimulus, reversed in polarity for simplification of analysis. The analysis is normally carried out on ten cycles of the response, although only three are displayed here for clarity.

position and magnitude of the troughs of the response to be estimated. If there is any directional preponderance in the response, this method allows the difference between the peak and trough velocities to be used as an estimate of that offset.

In this manner an estimate of peak slow-phase eye velocity together with any offset and phase change with respect to the stimulus waveform have been obtained. The next step is to use this estimate to set up threshold limits on either side of the estimated response waveform. This threshold is normally taken to be ± 50 deg/sec, and a set of small cursor lines is brought up to indicate where the threshold line will pass in relation to the first peak. If this threshold level is felt to be insufficient for the noise level of the eye movement signal, then it can be increased by moving the cursor the appropriate distance in the direction of the ordinate. The threshold is not normally decreased below 50 deg/sec when analysing eye movements recorded by EOG because of the inherent noise in the signal. When a suitable threshold has been assigned, the threshold limits are plotted by the computer graphics in relation to the eye velocity waveform, as shown in Figure 1.

THRESHOLD LIMITS FOR TRANSIENT RESPONSES

In many types of vestibular stimuli the oculomotor response is transient, decaying, or changing with respect to time in a manner which is not always easy to correlate with the stimulus. In such examples, two methods of setting threshold limits have been adopted. First, for those responses which are reasonably predictable, an estimate of the slow-phase velocity is obtained, based upon established population norms. For example, the response of the lateral semicircular canals to a rapid deceleration from a constant angular velocity exhibits an exponential decay of slow-phase eye velocity which is governed predominantly by a time constant of approximately 15 seconds, as shown in Figure 2. Accordingly, the threshold limits may be set up on the assumption that the response exhibits such a form (Figure 2), and this will be adequate even for quite large variations in the actual time constant. Second, if the response is not easily predicted in terms of some simple mathematical representation, the operator is allowed to manipulate cursors in order to simulate the slow-phase velocity with as many straight-line segments as are necessary. This technique is particularly useful in analysing the responses to a caloric irrigation as shown in Figure 3.

THE ELIMINATION OF FAST PHASES

Every point which lies outside the threshold limits is taken to represent a fast-phase eye movement. The advantage of this procedure is that it allows fast phases of fairly low velocity (> 50 deg/sec) to be detected. One of the problems inherent in any procedure which operates on digitised data is that the process of sampling the data effectively filters it. Thus the peak level of the digitised data during a fast phase may not represent true peak. This is illustrated in Figure 4, where sampling point 8 is seen not to occur at actual peak velocity. This effect is made worse when the sampling rate is reduced. Most fast

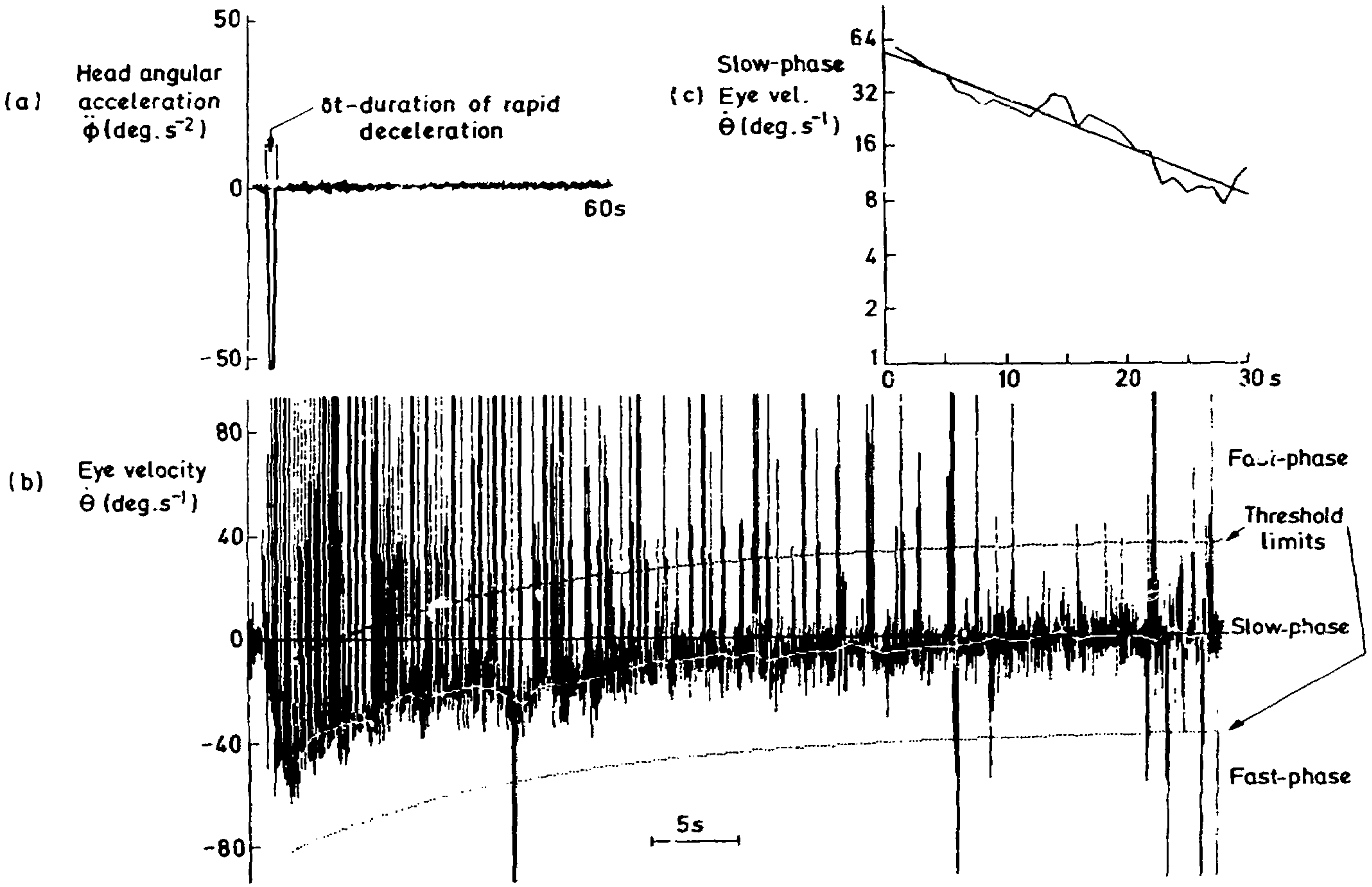

Figure 2

The exponentially decaying response of the vestibulo-ocular reflex to a rapid deceleration from constant angular velocity at 100 deg/sec.

(a) The deceleration stimulus from which the initiation of the response is calculated.

(b) The differentiated EOG signal (eye velocity) with exponentially decaying threshold limits as indicated. The line drawn through the centre of the slow-phase points indicates the slow-phase velocity, averaged at 1-sec intervals, after removal of fast phases.

(c) A log-linear plot of slow-phase eye velocity against time, from which the time constant and peak level of the response may be estimated.

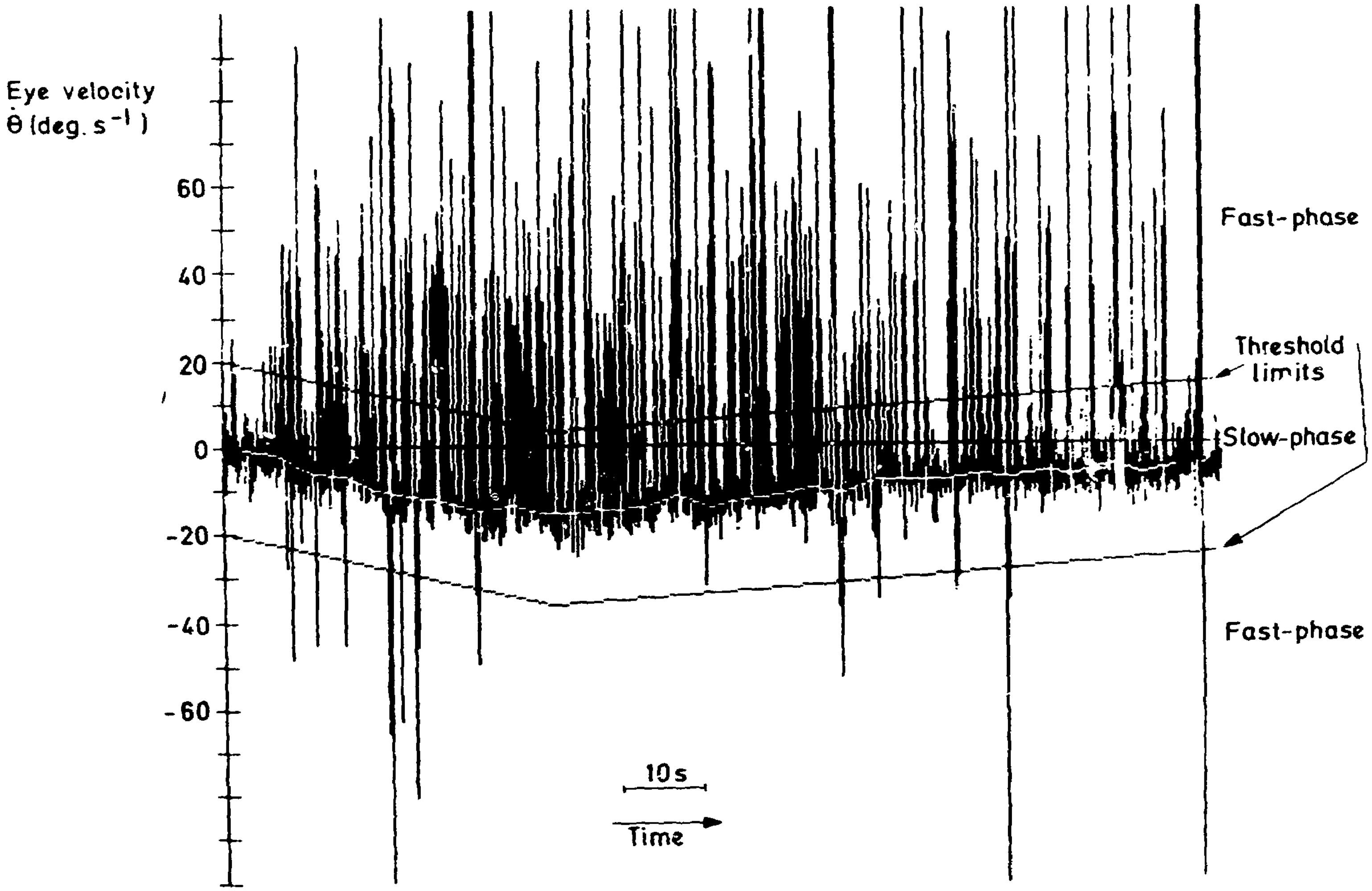

Figure 3

The manner in which straight-line segments are used as threshold limits to dissociate the fast- and slow-phase components in the response to caloric irrigation of the external auditory canal. The line drawn through the centre of the slow-phase components represents the slow-phase velocity, averaged at 4-sec intervals, after removal of the fast phases.

phases in vestibular nystagmus last for 20-60 ms (14). It is therefore necessary, in normal circumstances, that the sampling interval not be increased beyond 20 ms and it should preferably be 10 ms or less. If any analysis of fast-phase characteristics is to be carried out, the sampling interval should be approximately 5 ms or less. However, even if there are only one or two samples per fast-phase movement, the technique for threshold detection still works adequately.

The sampled points (e.g., 7, 8, 9, and 10 in Figure 4) that lie outside the threshold limits are automatically discarded from the analysis. In addition, in order to ensure that no component of the fast phase remains, one point preceding the first point above threshold (point 6 in Figure 4) and one point following the last point above threshold (point 11 in Figure 4) are also discarded. The rate at which the signal is sampled is critical in this process. It has been determined empirically that the number of occasions on which there is any remnant of the fast phase is negligible if the sampling interval is greater than or equal to 20 ms if the threshold is set at 50 deg/sec. This is partially supported by the recorded velocity profiles of saccadic eye movements (8) in which the velocity tends to exceed 50 deg/sec well within the first 10 ms of the response. Consequently, if the sampling interval is less than 10 ms, the number of points below the threshold which are discarded should be increased appropriately. Conversely, if the sampling interval is too great (> 40 ms), the process of casting out data points may result in some slow-phase points being unnecessarily lost.

This procedure for eliminating the fast phases is common to all the methods of analysis. However, the reduced data are statistically analysed in different ways for different types of stimuli. In the following section, an outline of these procedures is given.

ANALYSIS OF REDUCED DATA

ANALYSIS OF SINUSOIDAL RESPONSES USING REGRESSION PROCEDURES

One of the problems associated with discarding data in the manner just described is that the data cannot be subjected to the more conventional forms of frequency domain analysis, such as the Fourier Transform, because the data points are no longer equi-spaced. However, it is still possible to obtain a direct correlation between the stimulus and the response using a regression procedure. This may be best illustrated, as in Figure 5, by plotting eye velocity ($\dot{\theta}$) against head velocity ($\dot{\phi}$) for data of the type exhibited in Figure 1. If the eye velocity is almost exactly compensatory for head velocity (i.e., there is negligible phase error), then the slow-phase eye movements will be disposed in a straight line which passes through the origin. The slope of this line, which should be negative, represents the gain of the response. In Figure 5, the threshold limits, defined in Figure 1, appear as straight lines enclosing the slow-phase data points. The fast-phase components lie outside the threshold within the circled areas.

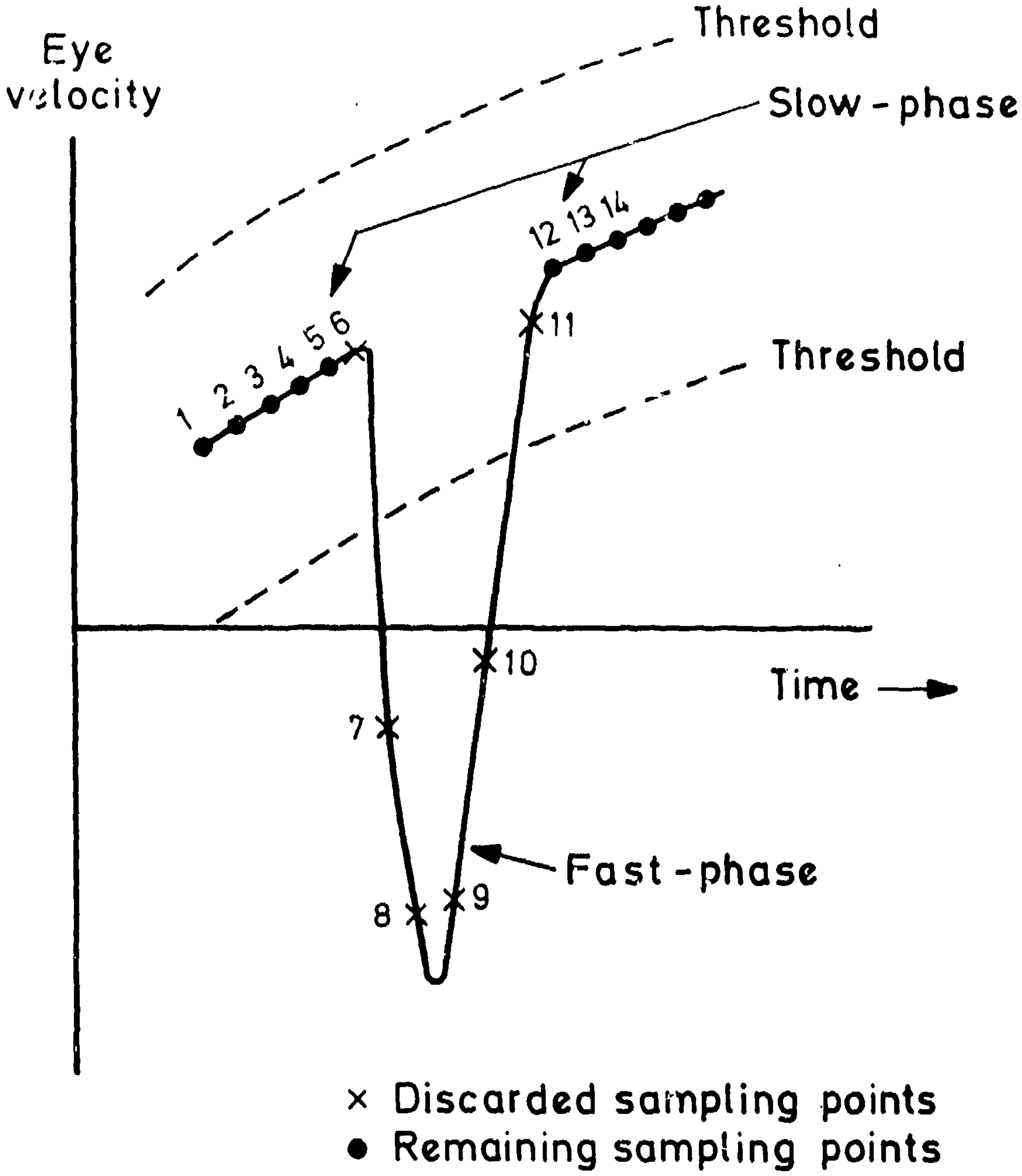

Figure 4

An illustration of the method by which fast-phase eye movements are detected and discarded, using simple threshold limits on the eye velocity waveform. When a data point (e.g., point 7) lies outside the threshold, both that point and points within the preceding 20 ms are discarded from the analysis.

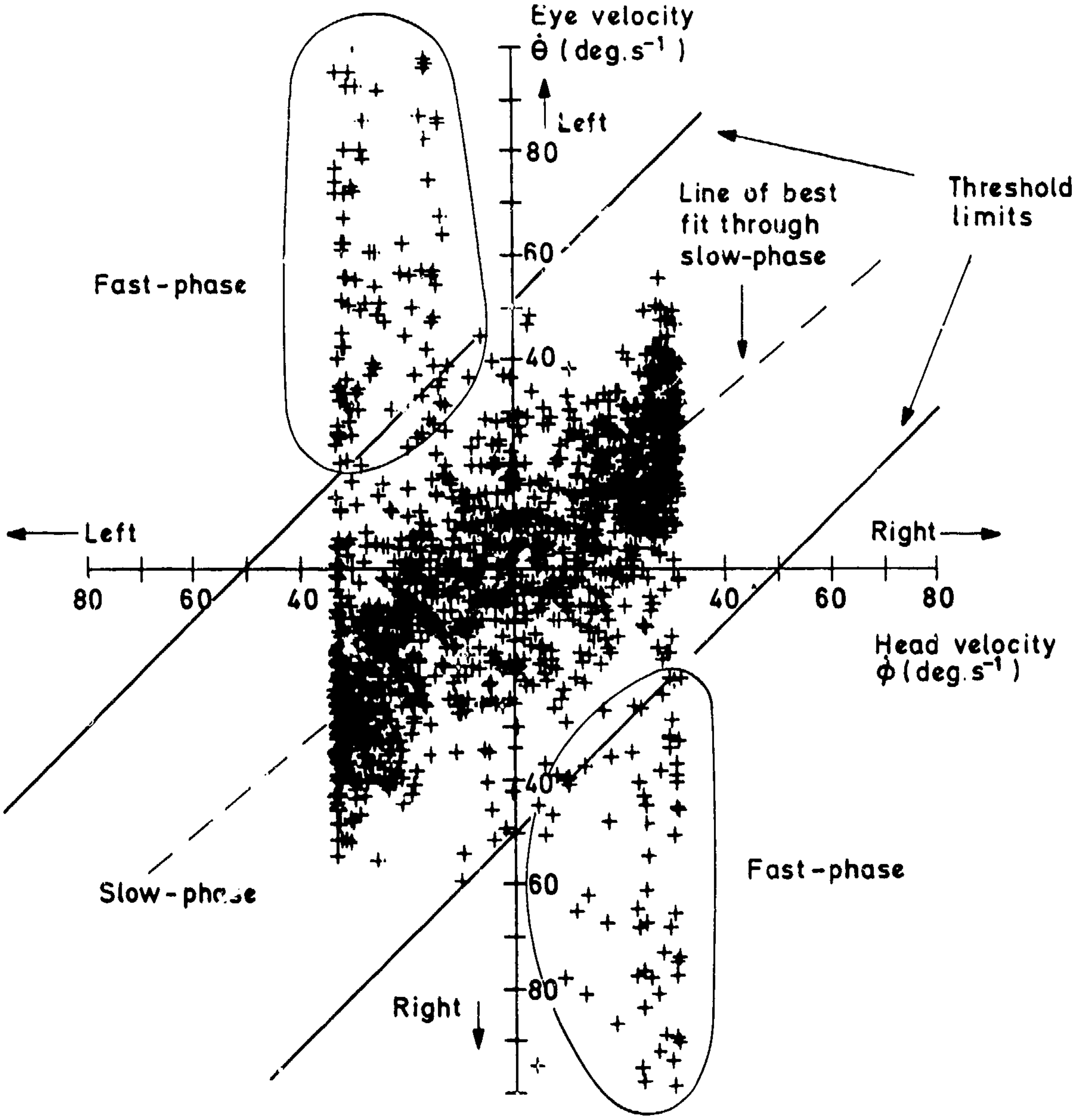

Figure 5

An illustration of the manner in which slow-phase and fast-phase components of the eye velocity signal may be dissociated when eye velocity is plotted against head velocity for the response to a sinusoidal oscillation as shown previously in Figure 1.

Since eye velocity ($\dot{\theta}$) should be proportional to head velocity ($\dot{\phi}$), it is possible to carry out a linear regression on the slow-phase points to obtain an accurate determination of the slope and intercept. For this purpose the sampled data points of the stimulus waveform which are paired with the fast phase of the eye velocity waveform are also discarded. However, if there is any phase difference between $\dot{\theta}$ and $\dot{\phi}$, the slow-phase points in Figure 5 appear as an ellipse, not a straight line. It is possible to obtain an indication of this phase error if the correlation is made between eye velocity, head velocity, and head acceleration $\ddot{\phi}$. That is, it is assumed that the data points will fit an equation of the form:

$$\dot{\theta} = A\dot{\phi} + B\ddot{\phi} + C \qquad (1)$$

where A, B, and C are constants of proportionality.

If head velocity is a sinusoidal function then

$$\dot{\phi} = \Omega \sin \omega t \quad \text{and} \quad \ddot{\phi} = \Omega\omega \cos \omega t \qquad (2)$$

where Ω = peak stimulus velocity (deg/sec).

Substituting these values in equation (1) gives

$$\dot{\theta} = A\Omega \sin \omega t + B\Omega\omega \cos \omega t + C \qquad (3)$$

$$= \sqrt{A^2 + B^2 \omega^2}\, \Omega \sin (\omega t - \psi) + C \qquad (4)$$

where $\psi = \tan^{-1} \frac{B\omega}{A}$.

In this manner it is possible to extract the gain ($\sqrt{A^2 + B^2 \omega^2}$), phase ($\psi$), and directional preponderance (C) from the response. In addition, it is possible to apply more complex regression equations to extract any nonlinearities from the response.

ANALYSIS OF TRANSIENT RESPONSES USING MODEL PREDICTIONS

As discussed earlier, some stimuli applied to the vestibular apparatus give rise to transient eye movement responses which cannot be directly correlated with the stimulus. However, it is possible to establish models of oculomotor performance (5) which have a sound physiological basis, and the response can be fitted, using regression procedures, to such a model. The models used may be much more complex than those simple representations which were first used to establish threshold limits.

An example of the type of response which can be fitted in this manner is that shown in Figure 6. The stimulus is a ramp-step angular velocity function (an acceleration pulse) applied to the horizontal semicircular canals. The slow-phase eye velocity rises to a peak value at the end of the acceleration and then decays in an exponential manner. The response cannot be modeled by a single exponential since the reversal

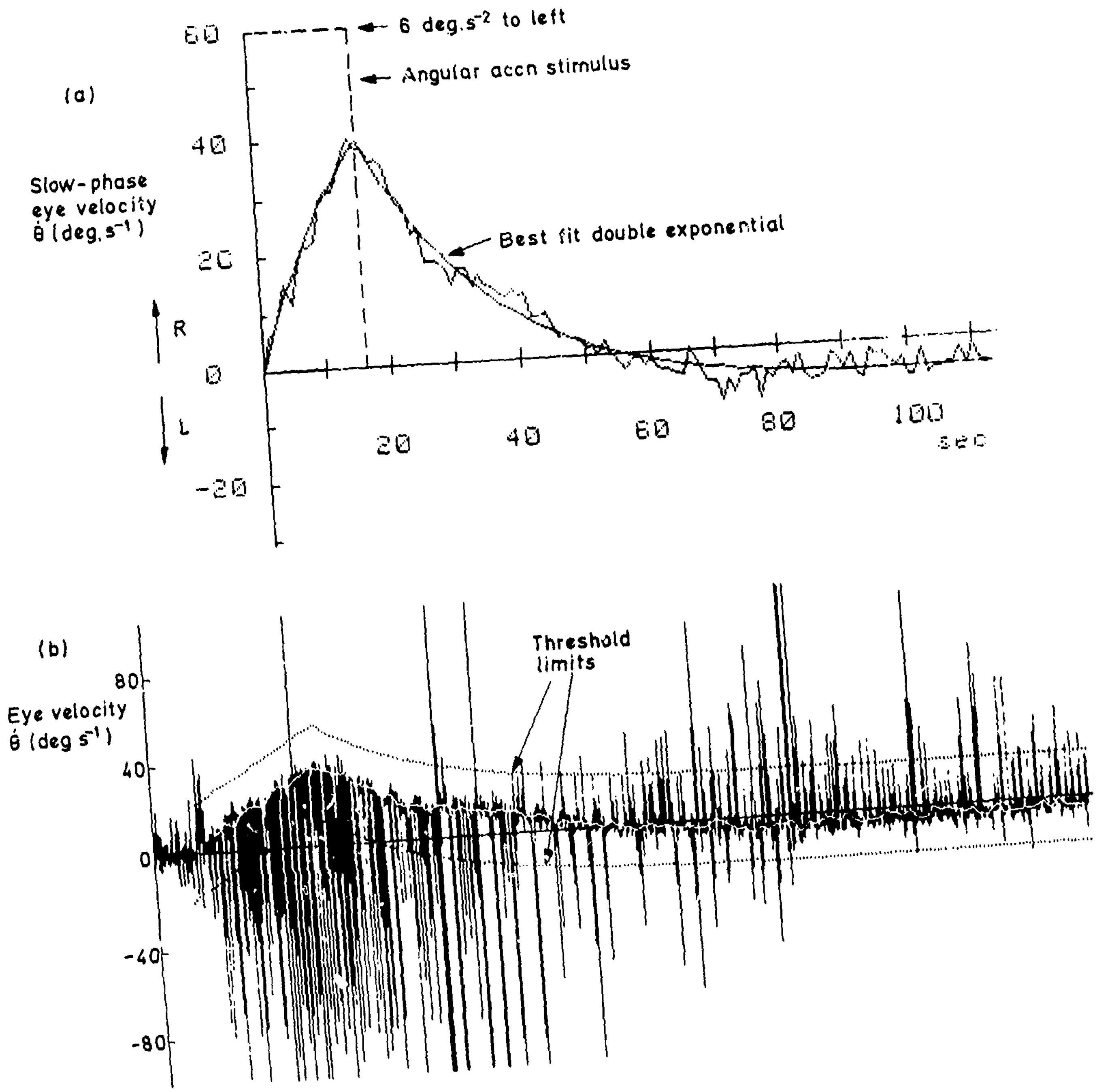

Figure 6

The response of the vestibulo-ocular reflex to a ramp-step head angular velocity stimulus (i.e., an angular acceleration pulse of 6 deg/sec^2 for 16 sec). In (b), the threshold limits are set up as if the response were that of a simple first-order system (time constant 15 sec) whereas in (a) the extracted average slow-phase velocity is best fitted by a more complex second-order model exhibiting properties of adaptation.

after 20-30 seconds indicates the presence of a second time-dependent component which is normally referred to as adaptation (6,15). The response can be adequately modeled (5) using a transfer function of the form

$$\frac{\dot{\theta}}{\ddot{\phi}} = - \frac{K_C \, T_B \, T_{AD} s}{(1+T_B s)(1+T_{AD} s)} \tag{5}$$

where K_C is a constant of proportionality (approx. 0.7)

T_{AD} is the time constant of adaptation (approx. 80-100 sec)

T_B is the long time constant of the canal-ocular response (approx. 15 sec).

The response of equation (5) to an acceleration pulse (level α) is

$$\dot{\theta} = \alpha \, K_C \, F(t)$$

where

$$F(t) = (e^{-t/T_{AD}} - e^{-t/T_B}) \qquad \text{for } 0 < t < \tau$$

$$= (1 - e^{\tau/T_{AD}}) \, e^{-t/T_{AD}} - (1 - e^{\tau/T_B}) \, e^{-t/T_B} \qquad \tau < t$$

This equation can be fitted to the data by assuming initial estimates for T_{AD} and T_B and then using an iterative multiple regression procedure (3) to obtain new estimates of T_{AD}, T_B, and K_C which are within acceptable limits of accuracy.

This procedure can be carried out without modification on the data points which remain after the fast-phase components have been discarded. However, this frequently involves a large number of data points which can result in a long processing time because of the iterative procedure. Consequently, a technique for reducing the data points is normally used. This is carried out by averaging the number of data values which are remaining within consecutive time bins of specific duration (say, 1 sec for the type of response shown in Figure 6), a method which is only suitable for responses varying slowly with time.

ANALYSIS OF TRANSIENT RESPONSES USING ARBITRARY DESCRIBING FUNCTIONS

On occasions it is only necessary to extract one or two important features from a response rather than to characterise it in terms of a meaningful model. An example is the caloric response in which the peak slow-phase velocity and the time-to-reach peak are two of the most important variables which can be used to identify abnormalities of vestibular function. Models of the caloric response have been developed (6,12) but are complex and would not be easily fitted using a regression procedure. However, in order to extract the important variables it is sufficient to fit the data with a simple power law regression. A 5th order solution is normally used for caloric analysis, giving a fit through the data points as shown in Figure 7. Peak slow-phase velocity

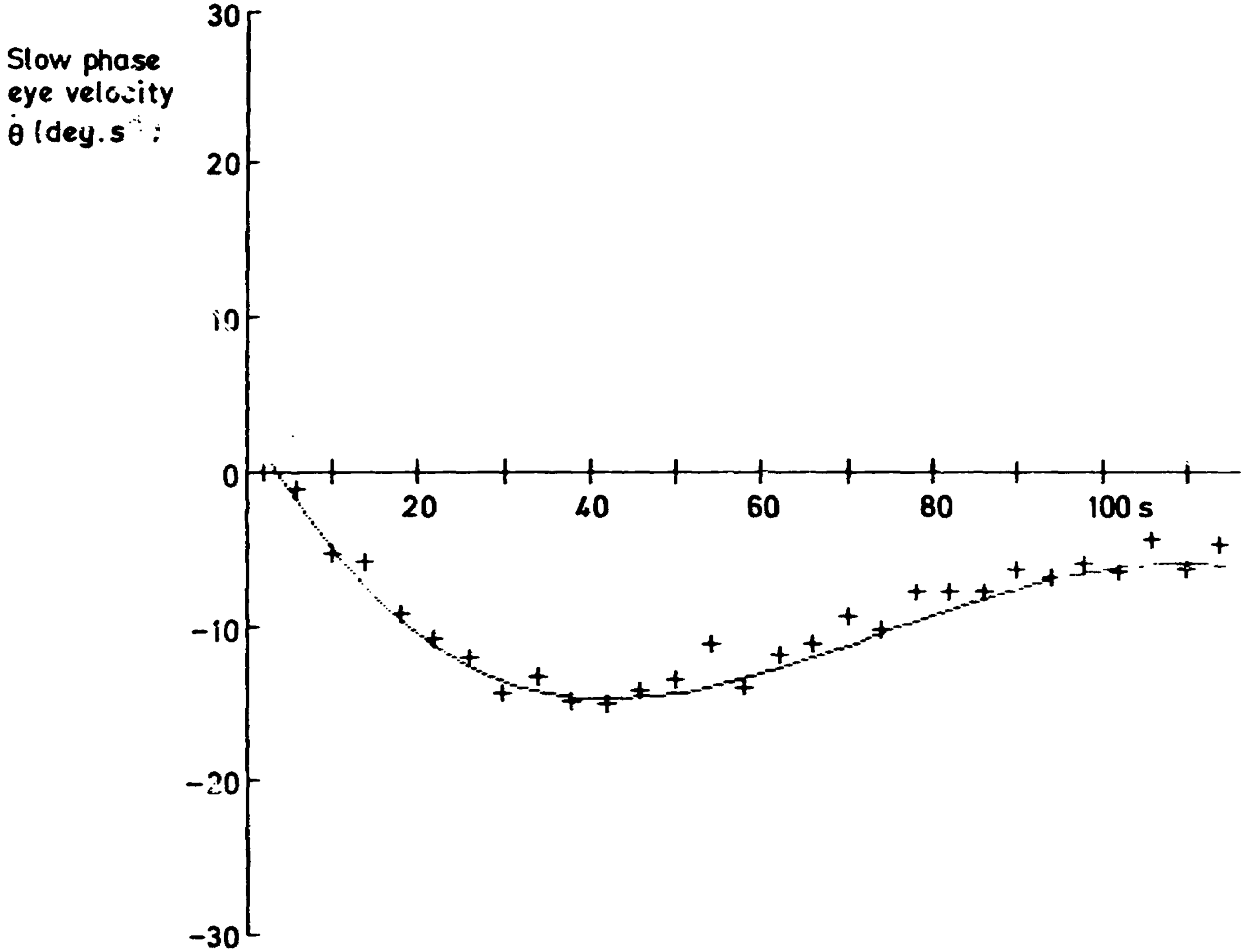

Figure 7

The slow-phase eye velocity obtained by a caloric irrigation (see Figure 3), fitted by a 5th-order power function of time, from which peak velocity and the time to reach peak may be extracted.

and time to peak are then easily derived from the parameters of the fitted equation.

CONCLUSIONS

A new procedure for analysing nystagmus and other oculomotor responses has been described. The main advantage of this procedure lies in the simplicity of the basic algorithm which enables the data to be analysed fairly rapidly on a medium-speed computer working in a high-level language. The method has been found particularly useful for analysing responses of the vestibulo-ocular reflex in which the slow-phase eye velocity may be very high, as, for example, during voluntary head movements, but is also applicable to many other forms of vestibular responses, to pursuit tracking responses, and to optokinetic responses. In addition, because the analysis is carried out on eye velocity data and because regression procedures are used for statistical analysis, it is not necessary to manufacture new data points to interpolate across the gaps left by the discarded fast phases.

The principal disadvantage of the technique described here is that unless a reasonable prior estimate of the slow-phase eye velocity can be made, it is unsuitable for on-line analysis. This problem can be overcome for certain types of stimuli such as caloric irrigation in which the slow-phase response is normally only in one direction and is of relatively low velocity compared with the fast phases. It has also been found that in experiments on normal human subjects, the response differs sufficiently little from that of the population norm that analyses can be carried out automatically. One further aspect of this procedure which carries a slight penalty is that in order to cut down the amount of data points stored and thus decrease processing time, the sampling rate must be kept as low as possible (optimally 10-20 ms). This precludes the possibility of analysing the characteristics of the fast-phase eye movements in any detail and also makes it difficult to analyse nystagmus in which the saccadic frequency is very high (e.g., in older patients and those using nicotine). However, these two problems may still be adequately addressed if a longer processing time is tolerable.

The procedure described here has been used to analyse the responses in many different forms of experiments (4,7,9) and in routine clinical analyses and has been found to be reliable in its detection and elimination of fast phases. Comparisons of analyses carried out in this manner with those carried out by hand using a beat-by-beat slope-fitting procedure have established that the method is accurate. In addition, it is less susceptible to the inclusion (or exclusion) of data values which the human operator subjectively might feel should (or should not) be included in the analysis.

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1. REPORT NUMBER NAMRL- 1280 and IAM-R600	2. GOVT ACCESSION NO. AD-A112 603	3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) A Procedure for the Analysis of Nystagmus and Other Eye Movements		5. TYPE OF REPORT & PERIOD COVERED Joint Report
		6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s) Graham R. Barnes		8. CONTRACT OR GRANT NUMBER(s)
9. PERFORMING ORGANIZATION NAME AND ADDRESS Naval Aerospace Medical Research Laboratory Naval Air Station Pensacola, Florida 32508		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS M0933.PN.004-0005 MR.041.01.03-0156
11. CONTROLLING OFFICE NAME AND ADDRESS Naval Medical Research and Development Command National Naval Medical Center Bethesda, Maryland 20014		12. REPORT DATE 23 June 1981
		13. NUMBER OF PAGES 18
14. MONITORING AGENCY NAME & ADDRESS(if different from Controlling Office)		15. SECURITY CLASS. (of this report) Unclassified
		15a. DECLASSIFICATION/DOWNGRADING SCHEDULE

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18. SUPPLEMENTARY NOTES

This procedure was adapted for use with NAMRL equipment, and the report was written while the author was a visiting scientist at NAMRL; but it is based upon program development accomplished by Dr. Barnes at the Royal Air Force Institute of Aviation Medicine.

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

Eye movement analysis; Algorithm; Automated electro-oculography; Nystagmus

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

A new procedure was developed to analyse oculomotor responses to many forms of vestibular and/or visual stimuli used in experimental work and in clinical practice. The main advantage of the procedure lies in the simplicity of the basic algorithm which enables fairly rapid data analysis of a variety of response forms on a medium-speed computer working in a high-level language. For slow phase analysis, detection of saccades is carried out by a simple threshold procedure based upon the expected response form, and regression (over)

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S/N 0102-LF-014-6601

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procedures are used to obtain stimulus-response correlation and slope (gain) measures. The procedure provides measures of gain, phase, and directional preponderance for responses to sinusoidal stimuli.