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Nonlinearities in primate oculomotor plant revealed by effects of abducens microstimulation

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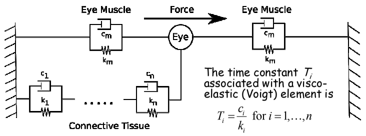
1 Introduction

It is important to characterise the dynamic behaviour of the oculomotor plant as a preliminary step towards understanding the algorithms that govern eye movement control, such as the VOR.

Previous work has determined that the oculomotor plant dynamics are linear in the case of tonic muscle activation in the anaesthetised animal (Sklavos et al., 2005). The work presented here investigates the effect of varying stimulation in the alert animal, where electrical pulses of different frequencies and duration are applied to the abducens nucleus.

The new results confirm the linearity of the passive plant (where 'passive' refers to tonically activated muscle) in the alert animal and demonstrate that the response of the plant to electrical pulses varies in a nonlinear fashion, related to the frequency of stimulation.



The time constant T_i associated with a visco-elastic (Voigt) element is

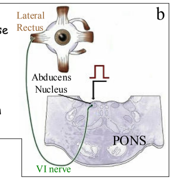
$$T_i = \frac{c_i}{k_i} \quad \text{for } i = 1,\ldots,n$$

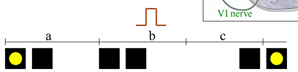
Fig. The oculomotor plant: Extraocular muscles and orbital tissue, represented by viscoelastic elements.

2 Electrical Stimulation

The abducens nucleus was identified and stimulated by pulse trains:

- 10-500ms train duration,
- 100-600 Hz amplitude,
- 0.2 ms pulse duration,
- 20uA current delivered through a microelectrode.





Each rhesus monkey (*Macaca mulatta*) was trained to perform saccadic eye movements in the gap task.

a) The fixation target was illuminated for 700-1000 ms then extinguished;
b) 100-300 ms later the abducens nucleus was stimulated;
c) 200 - 400 ms after the end of stimulation another target appeared and the animal redirected its fixation.

Eye movements were recorded with the search coil technique (at a sample rate of 500 Hz) .

3 Eye Movement Data

- Data was obtained from three animals A, B and C.
- The stimulation conditions incorporated the range of parameters shown in the table (right).
- Stimulation occurred in 1 site in animal A (head fixed) and 7 sites (both head fixed and head free) in animals B and C.
- Responses were inspected before inclusion in the modelling for obvious deviations resulting from unknown inputs.

	A	B	C
Frequency	100 Hz - 600Hz	100Hz - 500Hz	100Hz - 500Hz
Stimulation Duration	10ms-160ms	100ms - 500ms	100ms - 500ms
Number of Used Traces	102	› 400	› 400

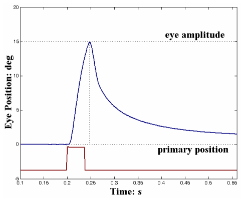


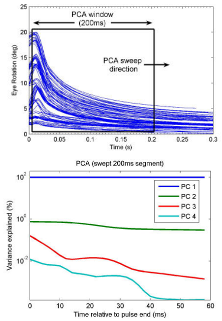
Fig. Example of change in eye-position produced by a pulse train stimulation (408 Hz, 40 ms). Unlike a saccade, the eye returns towards its initial position after stimulation ends.

4 Linear Modelling Methods

- A Principal Component Analysis (PCA) sweep in the direction of advancing time was used to indicate when time dependent processes ceased (above right).
- In the example shown this was approximately 40ms after the end of stimulation (below right).
- After this time the plant could be represented by a sum of exponential terms, such as

$$y(t) = A_1e^{-t/T_1} + A_2e^{-t/T_2} + \ldots + A_ne^{-t/T_n}$$

where $y(t)$ was the position of the eye, $T_1, T_2 \ldots T_n$ were time constants and $A_1, A_2 \ldots A_n$ were coefficients corresponding to the initial extension of the relevant Voigt element.

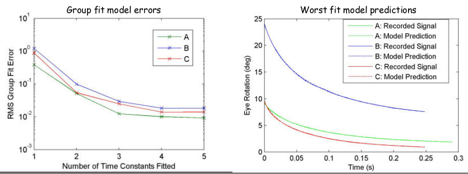


5 Linear Model of the Passive Plant

- The passive plant was found to be well described by a 3rd order model (i.e. incorporating three Voigt elements); evidence for this is shown (below left) in terms of group fit error for animals A, B and C.
- Long time-constant behaviour was observed in the data, possibly due to an integrator effect; this was modelled using a fixed long time constant, defined as 1×10^{10}s.
- The short TC of the alert animal was estimated to be approximately 0.025s; this contrasts with the results from the anaesthetised animal where the short TC was estimated as 0.01s.

Table: Time constant estimates; means and standard deviations across sites of stimulation are given for B and C

	Short TC (s)	Medium TC (s)
A	0.023	0.104
B	0.024 (0.004)	0.106 (0.031)
C	0.027 (0.014)	0.083 (0.009)



6 Effect of Starting Position

- In animal B the starting position of the eye was systematically varied from +/-25 degrees.
- Time constants could therefore be fitted separately to return movements to different orbital positions, in order to determine whether there was a variation with eye position.
- The results (shown below) demonstrate that the time constant estimates are relatively consistent across different starting positions and provides further corroboration that the assumption of approximating the passive plant by a linear time-invariant system is valid.

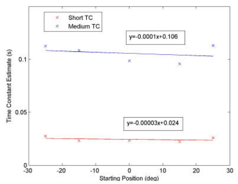


Fig. The variation in fitting time-constants separately: the data has been partitioned by starting position.

The gradient of each line of best fit is close to zero. This implies that there is no correlation between TC estimates and starting position.

7 Effect of Changing Muscle Activation

- The muscle activation can be recovered from eye movement data by inverting the linear model of the passive plant and using recordings of eye rotation as the input (see appendix A1), which was performed here using data from animal A (shown below).
- The muscle activation curves are compared to those given in Fuchs and Luschei (1971), from isometric force recordings. The data in each case is very similar, and apparently highly non-linear, with both saturation and varying rise times.

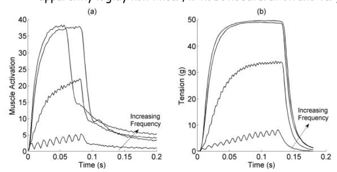
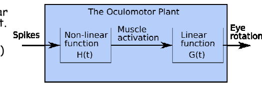


Fig. (a) Muscle activation recovered from animal A (using a set of illustrative traces). The responses correspond to stimulation frequencies of 100Hz, 200Hz, 400Hz, and 600Hz.

Fig. (b) Isometric muscle force from Fuchs and Luschei (1971). The responses correspond to stimulation frequencies of 100Hz, 200Hz, 400Hz and 500Hz.

- The implication of these results is that time-varying stimulation leads to non-linear dynamic behaviour of the oculomotor plant.
- The oculomotor plant is therefore represented here (for modelling purposes) as a linear passive component that is modified by a non-linear function during stimulation (shown right).



8 Nonlinear Modelling Methods

A linear dynamic system can be represented by an auto-regressive with exogenous input (ARX) model in input, u_t output, y_t form,

$$y_t + a_1 y_{t-1} + \ldots + a_{n_a} y_{t-n_a} = b_1 u_{t-1} + \ldots + b_{n_b} u_{t-n_b} + e_t$$

The ARX model provides a more concise representation of a system than the impulse response function. An analogous case exists for that of nonlinear systems: the non-linear ARX (NARX) model (Leontaritis and Billings 1985) can be used to represent a non-linear system as

$$y_t = f(y_{t-1},\ldots,y_{t-n_a},u_{t-1},\ldots,u_{t-n_b}) + e_t = f(\mathbf{x}_t) + e_t$$

The NARX model is useful because non-linear model descriptions that expand the current output in terms of both past inputs *and* outputs can provide a more compact representation than those that only use past inputs e.g. a Volterra series.

The input/output signals (in the NARX model) are transformed by certain basis functions $\phi_j(.)$, such as polynomials (used here), radial basis functions or wavelets, so that,

$$y_t = \sum_{j=1}^{M} \theta_j \phi_j(\mathbf{x}_t) + e_t$$

where M is the number of model terms. The NARX model is linear in the parameters θ_j, therefore they can be estimated using least squares. The significant model terms were selected in this investigation using a stepwise (orthogonal least squares) regression technique, from a superset of basis functions, up to a polynomial order of 5, with n_a=5 and n_b=5 .

9 Nonlinear Model of Muscle Activation

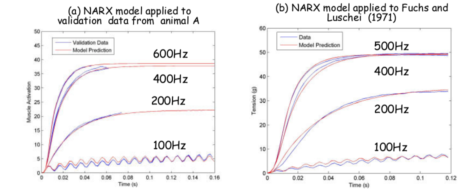
- The identified model terms are shown in the table to the right. The model notably includes input polynomial terms up to third order, consistent with that needed to represent an input saturation, which in this case is apparently frequency dependent.
- A saturation input is often represented by a static function; that is not possible in this case because the model is driven by spikes (of uniform size). This may explain why the input non-linearity is dynamic.
- The identified model was used to predict the recordings obtained in Fuchs and Luschei (1971) (with re-estimated parameters) as a further validation of the model structure.

Table: Identified NARX Model

Linear Terms	Non-linear Terms
y(t-1)	$u(t-3)^2$
y(t-2)	$u(t-3)^3$
y(t-3)	u(t-2)u(t-3)
u(t-1)	u(t-1)u(t-3)
u(t-2)	$y(t-1)u(t-3)^2$
u(t-3)	y(t-3) u(t-2) u(t-3)

(a) NARX model applied to validation data from animal A

(b) NARX model applied to Fuchs and Luschei (1971)



10 Possible Linearisation Mechanisms

- The highly non-linear appearance of the muscle activation data and corresponding dynamic (NARX) model would appear to be incompatible with previous studies from single motor unit recordings that suggest the behaviour of the oculomotor plant is approximately linear.
- To investigate this conflict the identified NARX model was simulated with inputs akin to those used in one such study, Fuchs et al. (1988). The results (shown right) are strikingly similar: the NARX model produces gain and phase changes that closely resemble those from Fuchs et al. (1988).
- There is significant variation in the gain of the system for different amplitudes of input signal modulated around 100Hz, which is not evident at 200Hz. This suggests that the identified system behaves linearly for input spike trains modulated around 200Hz and close to linear around 100Hz.
- A possible explanation for the shift in the linear operating range may be due to the fact that electrical stimulation effects are dominated by large fast units. The recordings from Fuchs et al. (1988), by contrast, were likely to be dominated by slow motor units.

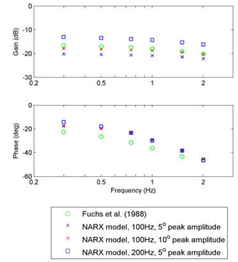


Fig. Gain and phase changes resulting from simulating the NARX model with sine wave modulated spike trains (about 100Hz and 200Hz), that produce fixed amplitude eye movements. Also shown is the equivalent information from Fuchs et al. (1988).

11 Conclusions

- Eye movements produced by electrical stimulation of the abducens nucleus were analysed to characterise the oculomotor plant in alert primate.
- The tonically activated plant in the primary position appeared approximately linear, consistent with previous studies in anaesthetised animals.
- In addition, the plant time constants appeared not to alter with orbital position over an ~50 deg range, further consistent with linearity.
- In contrast, the effects of altering muscle activation by electrical stimulation were clearly nonlinear. The nonlinearities resembled those seen in the production of isometric force in isolated lateral rectus muscle.
- The nonlinearities could be modelled using a technique derived from nonlinear system identification.
- The resultant model behaved approximately linearly for low-amplitude low-frequency movements, consistent with recordings of the firing patterns of abducens motoneurons.
- The muscle nonlinearities may present particular control problems for very fast movements such as saccades.

12 Appendix and References

A1 - Recovering the muscle activation signal

The linear model of the passive plant was defined in the state-space time-domain form as

$$\dot{\mathbf{x}}_t = A\mathbf{x}_t + Bu_t$$
$$y_t = C\mathbf{x}_t$$

where

$$A = \begin{bmatrix} -\frac{1}{T_1} & & 0 \\ & \ddots & \\ 0 & & -\frac{1}{T_4} \end{bmatrix}, \quad B = \begin{bmatrix} b_1 & \ldots & b_4 \end{bmatrix}^T, \quad C = \begin{bmatrix} 1 & \ldots & 1 \end{bmatrix}_{1\times4},$$

and the time constants were T_1=0.01s, T_2=0.1s, T_3=1s, and T_4=10s.

The input parameters (which related to relative compliances of the Voigt elements) were chosen as b_1=0.35, b_2=0.35, b_3=0.15 and b_4=0.15.

The corresponding system transfer function in the Laplace domain was

$$G(s) = C(sI - A)^{-1}B$$

The transfer function *G(s)* was inverted and simulated using the eye rotation as the input, that is,

$$\frac{u(s)}{s} = \frac{G(s)^{-1}}{s} y(s)$$

The time-domain input u_t was recovered from the signal *u(s)/s* by first order numerical differentiation.

References

Fuchs, A. F. and E. S. Luschei (1971). "Development of isometric tension in simian extraocular muscle." Journal of Physiology **219**(1): 155-166.

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