



# ***British Society for Clinical Electrophysiology of Vision***

## ***6<sup>th</sup> Annual Meeting***

***Hosted by the School of Optometry & Vision  
Sciences, Cardiff University***

***15<sup>th</sup> & 16<sup>th</sup> September 2008***





## Welcome

We are delighted to be able to welcome you to Cardiff, a city with heritage, ambition, and a distinctive character. It is home to the Millennium Stadium, Cardiff Castle and the filming of the BBC's *Dr Who*.

Cardiff is well established as 'Europe's Youngest Capital' but its history dates back more than 2000 years to the Romans. It was once one of the busiest ports in the world, exporting the coal which fuelled the industrial revolution.

The famous Tiger Bay docklands have been substantially transformed into Cardiff Bay, a modern development of homes, shops, offices, visitor attractions and the National Assembly for Wales, all surrounding a huge freshwater lake.

We are especially delighted to be able to welcome you into the School's new home, a modern, state-of-the-art facility. Our new home includes a much improved professional clinic and world-class research facilities. The atrium is also used to display art work, so please feel free to view this at your leisure.

It now remains for us to thank all of those involved in making this conference possible, and we hope that you enjoy your time in Cardiff.

Rachel North  
Alison Binns  
Tom Margrain  
Margaret Woodhouse  
Conference Organisers



We would like to thank all our sponsors for their generous support of BriSCEV 2008. With special thanks to Diagnosis UK Ltd who also sponsored the 'Drinks Reception' and Roland Consult for their sponsorship of the 'tea and biscuits'.

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Colin	Barber	Nottingham University
Alison	Binns	School of Optometry & Vision Sciences, Cardiff University
Mike	Bradnam	Royal Hospital for Sick Children Glasgow
Karen	Bradshaw	
George	Brimlow	Nottingham University
Mary	Broadbery	Northern Ireland Region Royal Victoria Hospital
Lawrence	Brown	Sheffield Teaching Hospitals NHSFT
Malcolm	Brown	Royal Liverpool University Hospital
Ruth	Campbell	Moorfields Eye Hospital
Andrew	Carter	Moorfields Eye Hospital
Kong Yien	Chin	
Charles	Cottrill	Oxford Eye Hospital
Jenny	Cumiskey	School of Optometry & Vision Sciences, Cardiff University
Claire	Delaney	Manchester Royal Eye Hospital
Wolfgang	Drexler	School of Optometry & Vision Science, Cardiff University
Jon	Erichsen	School of Optometry & Vision Science, Cardiff University
Lesley	Farrell	Glasgow Caledonian University
A C	Fisher	Department of Medical Physics & Clinical Engineering
Alison	Foulis	Gartnavel General Hospital
Maryke	Fox	Nottingham University
Lisa	Fox	Nottingham University
Paul	Gerry	RD & Exeter NHS Foundation Trust
Richard	Hagan	Royal Liverpool University Clinical Engineering Department
Ruth	Hamilton	Royal Hospital for Sick Children Glasgow
Sam	Hayton	Birmingham Children's Hospital
J	Hermens	Netherlands
Liesbeth	Hoeks	Radboud Hospital
Chris	Hogg	Moorfields Eye Hospital
Graham	Holder	Moorfields Eye Hospital
Cameron	Hudson	Cardiff University & Optical Express
Beverley	Holland	Nottingham University
Deepthy	Jayakrishnan	Nottingham University
Tony	Johnston	Eye Out-Patient Department Aberdeen Royal Infirmary
Adrian	Jones	School of Optometry & Vision Science, Cardiff University
Anni	Jowett	Nottingham University
David	Keating	Gartnavel General Hospital Ophthalmology
Susanne	Kelly	Stoke Mandeville Hospital Department of Ophthalmology
Charlotte	Latham	School of Optometry & Vision Sciences, Cardiff University
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Katie	Mortlock	School of Optometry & Vision Sciences, Cardiff University
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## **BriSCEV Cardiff 2008**



Daphne	McCulloch	Glasgow Caledonian University
Michelle	McIntosh	Glasgow Caledonian University
Tessa	Mellow	Great Ormand Street Hospital for Children
Laura	Milner	Clinical Engineering Royal Liverpool University
Magella	Neveu	Moorfields Eye Hospital
Rachel	North	School of Optometry & Vision Science, Cardiff University
Stuart	Parks	Gartnavel General Hospital
Neil	Parry	Manchester Royal Eye Hospital
Madeline	Perry	Bristol Eye Hospital
Anthony	Robson Rohan	Moorfields Eye Hospital
Don Gerard	Jayamanne	Doncaster Royal Infirmary
David	Sculfor	Stoke Mandeville Hospital Department of Ophthalmology
Uma	Shahani	Glasgow Caledonian Department of Vision Science
Richard	Smith	Stoke Mandeville Hospital
Paul GD	Spry	Bristol Eye Hospital
Tim	Stark	Visual Electro-Diagnostic Clinic
Jo	Steen	Oxford Eye Hospital
Dorothy	Thompson	Great Ormand Street Hospital for Children
Vivien	Thorpe	Yorkhill Hospital Clinical Physics
Sinead	Walker	Gartnavel General Hospital
Yaqin	Wen	Nottingham University
John	Wild	School of Optometry & Vision Sciences, Cardiff University
Clive	Wolsley	Northern Ireland Medical Physics
Maggie	Woodhouse	School of Optometry & Vision Sciences, Cardiff University
Ashley	Wood	School of Optometry & Vision Sciences, Cardiff University



Monday 15th September

- |                     |   |
|---------------------|---|
| <b>11.30 -12.30</b> | <b>Clinical Case Presentations</b>          |
| <b>12.45</b>        | <b>Welcome – Professor Tim Wess</b>         |
| <b>1.00 – 2.00</b>  | <b>Session 1 – ERG analysis</b>             |
| <b>2.00-3.15</b>    | <b>Coffee, Posters &amp; Exhibition</b>     |
| <b>3.15 – 4.15</b>  | <b>Antarctic Experience.....Dr C Hudson</b> |
| <b>4.15 -5.00</b>   | <b>AGM</b>                                  |
| <b>5.15 – 6.00</b>  | <b>Drinks reception</b>                     |
| <b>6.00</b>         | <b>Coach departs for Cardiff Castle</b>     |
| <b>6.30</b>         | <b>Tours around Castle</b>                  |
| <b>7.30</b>         | <b>Welsh Banquet</b>                        |



## **ANALYSING THE FLICKER ERG: COMPARISON OF TIME AND FREQUENCY DOMAINS.**

Hamilton R <sup>1,2</sup>, Boulton R <sup>2,3</sup>, Thorpe V <sup>1</sup>, Bradnam MS <sup>1,2</sup>, Bach M <sup>4</sup>

1. Clinical Physics, Royal Hospital for Sick Children, Glasgow, UK
2. Clinical Physics University of Glasgow, Glasgow, UK
3. Clinical Physics, Princess Royal Maternity, Glasgow, UK
4. Ophthalmology, University of Freiburg, Germany

**Purpose:** To assess which peak(s) of the flicker ERG is (are) best to measure and to compare findings in the time and frequency domains.

**Methods:** Flicker ERGs were recorded from eight normal control subjects. White, 2.51 phot cd s m<sup>-2</sup> flashes generated by a xenon strobe were delivered at 30.303 Hz into a Ganzfeld bowl (background luminance of 70 cd m<sup>-2</sup>). ERGs were recorded using skin electrodes on the lower eyelid. Averaging was employed to render adequate quality recordings. Time domain: amplitude and implicit time (IT) of the fifteen peaks were noted. For assessment of the best peak to measure, data was averaged over all 10 subjects. For comparison with frequency domain results, each subject's ERG was summarised by average peak amplitude and an average peak IT. Frequency domain: an FFT algorithm was implemented in Microsoft Excel after shortening the data sample to 495 ms (a multiple of the stimulation interval, 33 ms) and resampling at 1024 Hz to preserve 512 (29) data points (Excel's FFT algorithm requires 2n data points). The phase of the signal at 30.303 Hz was noted. Amplitude was added for the first four harmonics if a significant signal was present, and doubled to make it analogous to peak-to-trough amplitude in time domain. Phase was converted to an analogue of implicit time ('delay'; ms).

**Results:** In the time domain, ERG peaks did not differ from each other in either implicit time (from the preceding stimulus) or amplitude, although the first peak was the largest. Average peak IT measured in the time domain was 1.4 ms shorter than the delay of the 30.3 Hz component measured in the frequency domain (19.2 ms vs 20.6 ms;  $T=-4.38$ ,  $P=0.001$ ). There was no difference between amplitude measured in the time domain and amplitude of the 30.3 Hz component measured in the frequency domain (25.4  $\mu$ V vs 28.1  $\mu$ V;  $T=-1.64$ ,  $P=0.135$ ).

**Discussion:** The ISCEV Standard implies that every peak should be studied in a flicker ERG recording. The current study suggests that, if only one peak is examined, all peaks are equally good candidates to represent the whole trace. This is the case despite the use here of bursts of flicker (rather than a continuous stimulus) which can distort signals with an underlying single-flash waveform.

The results here show that a signal analysed in the frequency domain will manifest itself as a millisecond slower and the same amplitude as in the time domain. Analysing steady-state signals in the frequency domain has some advantages over time domain analysis, especially in low signal-to-noise conditions, but the relation between results obtained in each domain should be clearly understood.



## **A MULTILAYERED APPROACH TO THE AUTOMATIC ANALYSIS OF MFERG WAVEFORMS: THE ARTIFICIAL NEURAL NETWORK**

Alison Foulis, Stuart Parks, David Keating

ElectroDiagnostic Imaging Unit, Tennent Institute of Ophthalmology, Gartnavel General Hospital, Glasgow, UK

**Purpose:** The multifocal ERG (mfERG) provides spatial and temporal information on the retina's function in an objective manner making it a valuable tool for diagnosing retinal abnormalities, however interpretation of the signals is often difficult. A system capable of automatically classifying the waveforms and comparing serial visits would therefore be advantageous.

**Method:** A multilayered approach is being studied to achieve this goal. A range of information will be included such as, analysis of the Fourier domain profiles, wavelet transforms, filters, signal to noise ratio mapping, amplitude and latency information and the use of artificial neural networks (ANN). Waveforms will be studied both individually and in a spatial context. This study describes the application of ANNs to classify the mfERG.

Waves were to be categorized as either normal, reduced in amplitude, delayed, reduced and delayed or as having no significant response. A number of approaches were taken in an attempt to yield the highest performance. These included looking at the type of data used to train the network (synthetically created waveforms versus true clinical data) and the use of one network versus a multiple network solution (i.e. the combined output of three networks with one dedicated to timing, one to amplitude and one to the presence of a response). Factors such as the network architecture, the neuron transfer function and the number of training iterations were all varied until an optimal performance was achieved for each method. All networks were trained using 800 waveforms and were then tested on 450 previously unseen clinical responses. The performance of the network was assessed by comparing its classification for a wave with that stated by an experienced operator.

**Results:** A feed-forward back-propagation network with one hidden layer was found to yield the optimal performance for each experiment. When presented with the unseen clinical waves, the network trained using synthesised responses classified 70% of them correctly. When the clinically trained network was presented with the same waves, an accuracy of 79% was achieved. Finally the multiple network approach successfully classified 85% of the mfERG responses. Waves close to the timing and amplitude boundaries were the most problematic for the network.

**Conclusion:** The use of three networks, trained on clinical data yielded the most successful results. ANNs are a viable component in a multilayered approach to simplify the interpretation and analysis of the mfERG waveforms.





## EYE\_EDT\_ToolBox: OPEN SOURCE METHODS FOR PROCESSING AND MODELLING VISUAL ELECTROPHYSIOLOGICAL SIGNALS

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Dept. of Medical Physics & Clinical Engineering, and Clinical Eye Research Centre,  
Royal Liverpool University Hospital, Liverpool UK

Introduction: Whilst bandwidths are specified in ISCEV methodological 'recommendations', the scientific rationale for these specifications is somewhat difficult to justify. Very loose definitions of frequency response are used, most often with little attention to order and phase response: there is no appreciation signal mathematical morphology and no regard to the statistics of response characterisation (through cardinal points or 'cursor-positioning'). Consequently, across a range laboratories using differing equipment, the identification of 'information' from the 'data' of recordings is variable, and establishing realistic inter-institutional norms and standards is unrealistic. This is clearly a legacy of analogue signal processing. However, modern and available digital computing can provide explicitly-specified analyses which are easily implemented and completely circumvent these limitations. The requirement is to introduce the general theory of the readily available mathematical techniques to the critical clinical community and to equipment manufactures, and to provide practically-realizable tools so that clinical best practice can advance.

Methods: The PERG is taken as an illustrative example, but the methods can be applied directly to other responses such as the transient VEP, and the focal and full-field ERGs. The mathematical tools are realised in the MatLab programming language and are freely available as open source downloads for the experienced MatLab user, or implemented over the Internet from any simple 'web page' browser. The heart of the analyses is the *synchronous Dynamical Embedding Matrix* (sDEM) which forms the basic structure for optimal Fourier-based filtering and a robust structure for identification and elimination of spontaneous artefacts within a systematic statistical framework. Signal recoveries are achievable in highly challenging signal-to-noise ratio recordings and amenable to accurate 'automatic cursoring' inferred from local polynomial estimates with explicitly determined  $p$  values. Whilst the underlying techniques are complicated, their detailed understanding is absolutely not necessary for the Clinical User: the ToolBox and its web page interface make them very straight forward to apply to real and synthetic test data.

Results: The effects of differing bandwidth-limiting regimes of *ad hoc* user-chosen specifications applied to exemplar clinical PERGs with a range of signal-to-noise will be demonstrated graphically without recourse to unfamiliar mathematics. The relative sensitivity and robustness of cardinal point identification ('cursoring positions') in noise will be illustrated. A web page modelling tool for investigating the statistics of signal estimation in user-specified noise conditions will be illustrated by a 'click-and-go' (*sic!*) Internet session with the remote Liverpool MatSOAP server. A working RPC example of FIR filtering and adaptive artefact rejection (in the EYE\_EDT\_ToolBox) called from the Espion Instrument (Diagnosys LLC) will be demonstrated for a series of clinical PERGs.

Conclusions: The application of modern mathematical techniques in visual electrophysiology to signal recovery, statistical description and modelling is very long overdue. The EYE\_EDT\_ToolBox allows the Clinical User, the Researcher and the Equipment Manufacturer to address this shortcoming.



**WHERE'S THE B-WAVE? THE OBJECTIVE ANALYSIS OF ERGS WITH A POOR SIGNAL TO NOISE RATIO.**

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Cardiff University

**Purpose:** To demonstrate three techniques which allow improved objectivity in the evaluation of low amplitude ERGs, such as the focal rod ERG.

**Methods:** Focal rod ERGs were recorded from two individuals. Extensively averaged ERGs were recorded to provide a 'gold standard' response with an optimal signal-to-noise ratio. Ten individual traces were also recorded and averaged offline. This 'noisy' trace was then processed in three ways: i) Using a statistical method, the outliers (outside 2SD of the mean) were subtracted and a new average obtained. ii) Using Fourier analysis, the high frequency noise (9<sup>th</sup> harmonic and above) was removed from the signal. iii) The Fourier analysed trace was then fitted with a model based on the sum of three gamma functions, which correspond approximately to the photoreceptor, bipolar and inner retinal components of the ERG. The amplitudes and implicit times of a- and b-waves of the response were assessed at each stage of analysis. These processing techniques were also applied to real data recorded in previous studies to demonstrate the clinical utility of the approach.

**Results:** The two traces of 250 averages were very repeatable. When only 10 traces were averaged the amplitudes of both a- and b- waves tended to be overestimated. Both the Fourier and the modelling approach allowed objective evaluation of the peaks of the a- and b-waves. The amplitudes of the Fourier smoothed/modelled traces were very similar to the 'gold standard' focal rod ERGs consisting of 250 averages. The Fourier and modelling approaches allowed an objective assessment of previously collected 'noisy' focal rod ERG and multifocal ERG data obtained from participants in other studies.

**Conclusions:** Fourier analysis and modelling of focal rod ERG data allowed the extraction of objective information about the amplitude and implicit time of the a- and b-waves even when their location was unclear. This reduced recording time by allowing fewer averages to be taken. Furthermore, the three component model also provided information about the characteristics of the underlying sub-components, which may ultimately have more clinical relevance than a- and b-wave assessment. These analytical techniques could be beneficial in the objective interpretation of other types of low amplitude ERG responses.



**24 HR DAYLIGHT AND CIRCADIAN RHYTHM CHANGES – AN  
ANTARCTIC STUDY**

Dr Cameron Hudson  
School of Optometry and Vision Sciences,  
Cardiff University &  
Optical Express

During the austral summer of 2007/08, optometrist, Cameron Hudson, embarked upon a 700 mile trans-Antarctic expedition to the South Pole. His aim was not only to successfully complete the journey but also raise public awareness of the importance of eye health examinations, support the work of three vision charities and to carry out a novel research project into human vision. Cameron and his two other team mates investigated the impact of the 24hr daylight environment in Antarctica on their circadian rhythms. The team wore Actigraph wrist activity monitors throughout the 57 day expedition to monitor their sleep-wake cycle. Samples of saliva and buccal swabs were obtained at predetermined intervals throughout the expedition to measure the level of melatonin and presence of 'clock-genes' in the body, respectively. The project was inspired by work presented during the 2006 BRISCEV meeting at Stoke-Mandeville hospital and Cameron will provide an update and overview of the expedition findings so far.



# **POSTER - ABSTRACTS**

**(alphabetical order)**



**LUMINANCE-RESPONSE FUNCTIONS FOR VEPs TO FULL FIELD FLICKER STIMULATION.**

Sayed Al Abdlsaed<sup>1</sup>, Michelle A McIntosh<sup>1</sup>, Richard G Boulton<sup>2</sup>, Ruth Hamilton<sup>2</sup>,  
Daphne L McCulloch<sup>1</sup>

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<sup>2</sup>Glasgow University, Glasgow. Scotland, UK

**Purpose:** Associations between flash luminance and VEP amplitude are notably difficult to characterize for transient flash stimuli because of high variability amplitude and waveform. Steady-state VEPs (SS-VEPs) to luminance flicker are more easily characterized in the frequency domain and earlier work in our lab has shown that VEP amplitudes saturate at far lower luminance levels than do ERGs to similar flickering stimuli. We will characterise the luminance-response profile of VEPs and photopic ERGs for stroboscopic flicker and for sinusoidally modulated flicker.

**Methods:** Participants will be healthy adult volunteers with no visual or ocular motor dysfunction and corrected visual acuity of 6/6 (0.0 Log MAR) or better in each eye. SS-VEPs are recorded binocularly and monocularly (using a light excluding patch) to full field flicker stimuli generated using LEDs in a ganzfeld (Espion Colordome«). Two modes of flicker will be presented: stroboscopic flash (5 ms pulses on a photopic background of 30 cd/m<sup>2</sup>) and sinusoidally modulated flicker (mean luminance 50 cd/m<sup>2</sup>) presented at 7.32 Hz. Both stimuli are presented in 15 steps ranging from sub-threshold to the maximal available (33 cd/s/m<sup>2</sup> and 100% modulation respectively). VEPs are recorded at Oz referenced to Fz and the ERG is recorded using an HK loop electrode. The magnitude of Fourier components of the SS-VEPs and flicker ERGs at the fundamental stimulus frequency and the double harmonic (14.6 Hz) (F2) will be fit by least squares functions to calculate the saturated magnitudes and sensitivity (luminance at semi saturation).

**Results:** Preliminary data indicate that VEPs show higher sensitivity and saturate at lower levels than ERGs for both stroboscopic and sinusoidal stimuli.

**Conclusions:** The parameters will be used for comparison with luminance response functions of infant groups during development.



## **DECIMATION OF BINARY SEQUENCES FOR MULTIFOCAL RECORDING**

Malcolm Brown, Anthony Fisher, Richard Hagan, Anne Small

Clinical Engineering Dept. and Clinical Eye Research Centre  
Royal Liverpool University Hospital, UK

### **Purpose**

To optimise the decimation of binary sequences for use in multifocal recording with particular reference to use of short sequences, and to provide an educational tool.

### **Methods**

We have created a mathematical tool to examine a binary sequence and check its properties. With a given set of restrictions entered by the user, such as the number of separate channels required, the number of base periods in the recording epoch, which (how many) higher-order Kernels to test for etc., the tool will find a set or sets of sequences from the master sequence which have the least number of possible overlaps or contaminations between channels.

### **Results**

The task can be reduced to a set of formulae. Published examples of decimation include simple methods of selection of the stimulating sequences such as maximum or equal separation. Our tool shows these methods to be unsuitable.

### **Conclusions**

Using this tool, binary sequences can be tested for suitability in multifocal recording. Not surprisingly, short sequences provide only a limited number of options when a large number of channels are required, and are therefore most in need of examination and optimisation.



## **ELECTRICAL IMPEDANCE MEASUREMENT ON THE SCLERA/CORNEA**

Malcolm Brown, Laura Milner, Anthony Fisher, Richard Hagan

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University Hospital, Liverpool UK

**Purpose:** To investigate the methods and currents used to measure electrode impedance especially in relation to scleral/corneal electrodes. This work was undertaken to assist in the debate regarding the risks of measuring electrode impedances at the eye.

**Methods:** A number electrode impedance meters and electrophysiology recording systems in common use in the UK were investigated to establish the methods by which electrode impedance is measured and in particular what currents and waveforms are used.

**Results:** In general, the frequency ranges were 10-100Hz and currents passed through the electrodes varied from  $<1\mu\text{A}$  to  $50\mu\text{A}$ . There were some aspects of the results which were difficult to understand in relation to connection/disconnection of other electrodes.

**Conclusions:** All of the devices tested use currents below the limits ( $100\mu\text{A}$  in normal condition and  $500\mu\text{A}$  in single fault conditions) set for the safety of medical devices (IEC60601-1) with Type BF patient connections, which is the appropriate classification for biological amplifiers recording from the eye. Most of the items tested delivered currents which were an order of magnitude lower than the above, but the  $1\mu\text{A}$  limit recommended in the ISCEV Calibration Guidelines (2003), was not always achieved. Our measurements were continuous measurements, and could not take account of all possible transient currents arising from switching events.



**INVESTIGATION OF THE EFFECTS OF OXYGEN INHALATION ON THE SCOTOPIC OSCILLATORY POTENTIALS IN SUBJECTS WITH DIABETES MELLITUS**

J. Cumiskey<sup>1</sup>, N. Drasdo<sup>1</sup>, DR Owens<sup>2</sup>, RV North<sup>1</sup>

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<sup>2</sup>School of Medicine, Cardiff University, Cardiff, UK

**PURPOSE:** It has been proposed that the retina is subject to sub-clinical levels of tissue hypoxia prior to the development of diabetic retinopathy (DR), in patients with Diabetes Mellitus (DM), and reduced oscillatory potential (OP) amplitudes in these subjects may indicate this. The aim of this study was to record OPs in order to investigate possible signs of hypoxia in the inner retinal layers, and, if found, to what extent its effects on retinal function may be reversed by oxygen (O<sub>2</sub>) inhalation.

**METHODS:** Twenty-three Type 2 DM subjects with no visible retinopathy (NDR), mean disease duration 7.3 years, mean age 62.3 years (SD±5.6), 14 Type 2 DM subjects with background retinopathy (BDR), mean disease duration 11.7 years, mean age 63.1 years (SD±8.3) and 21 age-matched controls, mean age 60.0 years (SD±10.8), were recruited. OPs were recorded monocularly following 20 minutes dark adaptation to ISCEV standards. Subjects inhaled 100% O<sub>2</sub> for 5 minutes through a 60% Ventimask. This procedure was repeated: a) after 2 minutes of O<sub>2</sub> inhalation and b) 2 minutes, c) 7 minutes and d) 12 minutes after mask removal.

**RESULTS:** O<sub>2</sub> inhalation increased summed OP amplitudes in the BDR group across time (p=0.006, RM ANOVA) with a significant increase of 36.7% (p=0.040, Bonferroni pairwise comparisons) 12 minutes after mask removal. Non-significant increases in summed OP amplitude were found in both the control (p=0.087) and NDR (p=0.359) groups. OP1 amplitude was also found to increase significantly across time in the BDR group (p=0.041, RM ANOVA) though this did not reach significance with Bonferroni pairwise comparisons. OP3 amplitude increased in the NDR group (p=0.005, RM ANOVA) with a significant increase in amplitude 7 minutes after mask removal, (p=0.020, Bonferroni pairwise comparisons).

**CONCLUSIONS:** OP amplitudes were found to be smallest in DM patients with BDR and both summed OP and OP1 amplitudes were found to significantly increase following O<sub>2</sub> inhalation in this group. OP3 was also found to significantly increase following O<sub>2</sub> inhalation in the NDR group. These increases may reflect a reduction of inner retinal hypoxia in these subjects with O<sub>2</sub> inhalation.





## **A COMPACT REPRESENTATION OF THE TRANSIENT PERG USING THE DISCRETE WAVELET TRANSFORM**

A.C.Fisher, R.P.Hagan, M.C.Brown

Dept. of Medical Physics & Clinical Engineering, and Clinical Eye Research Centre,  
Royal Liverpool University Hospital, Liverpool, United Kingdom

**Purpose:** To describe a robust minimum parameter graphical model of the clinical PERG waveform for optimal recovery from recordings of poor signal-to-noise ratio (SNR)

**Introduction:** The PERG waveform as described in the ISCEV Standard is characterised by 3 coordinate-pairs ('cardinal points') in time  $\sim$ [35, 50, 95]ms and amplitude, requiring just 6 numbers. However, even with a conservative bandwidth of [1 ... 45]Hz, Fourier Series decomposition requires a minimum of 15 numbers (to describe the DC-term and the first 7 harmonics). Further, recent artificial neural network models (e.g. SPoC [www.liverpooleye.org](http://www.liverpooleye.org)) have required  $\geq$  16 numbers. Clearly, without a system of constraints, the standard practice of reporting the PERG with only 3 cardinal points is under-determined and consequently ambiguous. In the model presented here, such constraints are provided by a single simple template applied to a two-level wavelet decomposition of the data.

**Method:** A reference structure is constructed from the ISCEV PERG model comprising: i. a detrended bandlimited zero-extended template; ii. a weighting vector emphasising 'regions of interest' close to cardinal point times. The data are decomposed into low-frequency (high scale) and high-frequency (low scale) components by discrete wavelet transformation. Each of these decompositions are Pearson crosscorrelated under scale, time-displacement and amplitude perturbation with the template weighted by the weighting vector. This results in  $2 \times 3$  numbers which define the 6 parameter model.

This model was tested against noise-free clinical PERG waveforms (with unequivocal 'cardinal points') to which realistic  $1/f$  Gaussian noise [white ... Brownian] over a range of SNRs was added.

**Results:** In all trials the 6 parameter model recovered the cardinal points as least as effectively as the SPoC Expert System but additionally reproduced the underlying waveform 'exactly' as judged by the human eye.

**Conclusion:** The model can be effectively applied during data acquisition to recover the underlying PERG. Its 6 parameters can be tested in real-time using bootstrap statistical sampling to optimise the recovery process and minimise recording times. A web-based interactive demonstration will be accessible over the Internet via a MatSOAP connection ([www.matsoap.org.uk](http://www.matsoap.org.uk)) at [www.liverpooleye.org](http://www.liverpooleye.org). The software written will be made available 'open source' as the Liverpool Eye-EDT-ToolBox for MatLab®.



**ERG RESPONSE SMEARING INTO 'UNUSED' M-SEQUENCES AT FAST STIMULATION RATES.**

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**Purpose:** To determine the number of sequences (within an m-sequence family) that have a tangible signal (considering linear and non-linear components) relating to visual stimulus run by a single m-sequence.

**Methods:** The ability of the m-sequence to encode and decode the electrical activity of several areas down just one recording channel has made the mfERG a reality. What makes this possible is that by shifting an m-sequence (which is a pseudo binary random sequence) by one step a daughter m-sequence is created that has no correlation to the first mother sequence. At fast stimulus rates the time between sequence steps is not sufficient to contain all the response and part of the response may be captured in the neighbouring sequences (Note not neighbouring hexagons). A single hexagon was used to stimulate the retina (to avoid mutual kernels) driven by a single 511 long ( $n=9$ ) sequence at 6 different rates. 20 normal volunteers participated and recording was made with thread electrode, with pupils dilated with 1 % tropicamide. Stimulus had peak luminance at 120cd/m<sup>2</sup> and was near 100% contrast with surround held at 60cd/m<sup>2</sup>. Ethical approval was obtained from the Local Regional Ethical Committee and all subjects gave informed, written consent.

**Results:** At the fastest rate ( $bp=16.67ms$ ) there were 32 sequences easily identifiable as having power above the ambient noise. At this rate five clusters of signal were identified centred around the first order, second order, third order kernels as well as the second and third slice of the second order. Whilst other higher order kernels may be present they are not readily seen in this cohort of 20 subjects above background noise. At a slower rate ( $bp=83ms$ ) only one sequence was determined to have a significant response above the noise level.

**Conclusion:** This practical data would suggest that it is impossible to run a 19 hexagon stimulus with a base period as short as 16.7ms without clashes from higher orders and higher numbers of hexagons would have further clashes. It would also suggest that at a slower rate  $bp=83ms$  only one sequence need be excluded from the decimation for each stimulating hexagon. Overall this study suggests that short sequences are best used when there are a limited number of stimulating hexagons or when the stimulus is slowed down.



**A SIMPLE, LOW COST, SCALABLE GANZFELD STIMULATOR**

Chris Hogg  
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Purpose; To develop a simple flexible ganzfeld stimulator for animal work.

Methods; A design has been developed that allows the stimulator, constructed from low cost readily available components, to be scaled from small rodents to much larger animals or human subjects.

Results; Circuit designs and examples of ERGs recorded from two species will be shown, whilst detailed construction information will be made available on the internet.

Conclusions; A versatile stimulator can be manufactured from readily available parts by most laboratories with a small amount of technical expertise.

Acknowledgements;

Scientific workshops at the Institute of Ophthalmology carried out the machining of parts for the prototype device discussed, (Paul Johnson and Ian Macartney).



## **HOW MUCH CHANGE MATTERS?**

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**Purpose:** To determine the inter-trial variability of pattern reversal VEP, (pVEP), measures of amplitude and time to peak of the main positivity 'p100'.

**Methods:** PVEPs were recorded 24 times over an eight-week period from 2 healthy participants. The subjects viewed a plasma screen with both eyes open from a distance of 1 metre. High contrast, black and white checks of side subtense 50', 25' and 12.5' pattern reversed 3/s in a 28 degree test field. The different sized checks were presented in a pseudo-random order. 3 runs, each of 100 trials, were acquired to each stimulus from an active electrode placed at Oz referred to a mid-frontal electrode at aFz. The amplitude of N80-P100 and the peak times of P100 were measured.

**Results:** P100 amplitude and time to peak were stable across sessions and did not depend upon the order of check size presentation. Standard deviations on average were 10.5% of the mean for amplitude and 1.3% of the mean for time to p100 peak. Variation in amplitude was greater than time to peak. Reasons for this variation are multi-factorial, but from our experience relate primarily to subject alertness and attention to the stimuli.

**Conclusion:** This study provides rules of thumb to help determine whether changes of pVEP amplitude and time to peak are clinically significant between serial recordings, once confounding variables have been taken into account.



## **ARTEFACT CONTROL IN MULTIFOCAL RECORDING**

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**Purpose:** To investigate the problems of artefact control in multifocal ERG recording.

**Background:** For synchronous signal averaging as used for VEP and ERG recording, a very basic artefact rejection system can be used which simply decides to leave large amplitude or other unsuitable recordings out of the grand average. For multifocal recording this is unsatisfactory because the entire recording must be submitted for decoding. The inclusion of erroneous or saturated sections of the recording seriously degrades the decoding process.

**Methods:** We recorded the original ERG signal data from entire multifocal ERG sessions with the subject purposefully introducing artefacts by blinking and eye movements. The signal during the artefacts were examined in detail. We then compared these artefactual signals with the amended recordings from a commercial mfERG system (Roland Retiscan) that employed artefact rejection tools.

**Results:** Blink artefacts in particular are enormous (>2 orders of magnitude larger) in contrast to the mfERG response, and usually take the form of a large spike in one direction followed by a complementary spike of alternative polarity and then return on an exponential path to the baseline. On comparison of the raw artefactual data with the Roland Retiscan ('biofile') data, we could characterise methods for removing sections of signal where artefacts occur and replacing with sections of uncontaminated signal. The effect the artefact rejection method had on the amended signal was also examined.

**Conclusions:** Blink artefacts with open-eye electrodes cause problems and the recording may be seriously damaged before, during and after detection of artefacts. We understand some systems make no attempt to control these contaminations, but we note the Retiscan uses a technique by which the 'biofile' recording is suspended whilst the machine repeats the previous half second of stimulus sequence and continues the recording when the artefact has passed. In this way the integrity of the sequence and the 'biofile' are maintained and contain no artefactual sections. There may be room for improvement in these methods by exclusion of the immediate prior and post artefact epochs since they are also subject to substantial baseline movements.



## THE PHOTOPIC NEGATIVE RESPONSE: DTL VS. SKIN ELECTRODES, INTEROCULAR DIFFERENCES AND INTENSITY RESPONSE FUNCTIONS.

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**Introduction.** The photopic negative response (PhNR) of the electroretinogram (ERG), a negative deflection following the b-wave elicited under certain stimulating conditions, was first described about a decade ago. It is presumed to originate in the inner retina and is therefore of considerable interest to those interested in ocular conditions where the inner retinal dysfunction is found, such as glaucoma. We report the preliminary findings of a pilot study comparing the PhNR recorded using DTL and skin active electrodes.

**Methods.** 18 healthy control subjects were recruited from within the School of Optometry and Vision Sciences at Cardiff University. Photopic ERGs were recorded with dilated pupils (min. 7mm) to a series of flashes of red light (Lee filter 026, "Bright Red") ranging from 0.02 to 1.5 cd.s/m<sup>2</sup>, presented over a continuous short wavelength background (Schott glass filter BG28, luminance ~3.8 log scot tds). ERGs were recorded simultaneously with DTL and skin electrodes, both referred an electrode placed 3cm behind the outer canthus. Between 40-200 averages were acquired, depending on the stimulus luminance. For the purposes of this study, the PhNR was measured from baseline to the lowest trough following the b-wave, in accordance with typical practice in this group.

**Results.** A photopic ERG with PhNR was obvious at higher intensities with both electrode types, but often difficult to distinguish at the lowest intensities with the skin electrodes. Skin electrode amplitudes were 40-50% lower than DTL electrode responses.

**Conclusions.** Preliminary analysis of data shows that the PhNR can be reliably recorded using skin electrodes at intensities typically reported in the literature and that the reduction in PhNR amplitude with skin electrodes is consistent with the reduction in a-wave and b-wave amplitudes found in this and previous studies. Further work currently underway includes investigating alternative methods of measuring the PhNR amplitude and assessing inter-session repeatability



**STEADY STATE PATTERN VEPS: ONSET-OFFSET CHECKS ARE MORE EFFECTIVE THAN PATTERN REVERSAL FOR FREQUENCY DOMAIN DETECTION**

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**Purpose:** Steady-state VEPs (SS-VEPs) are used in applications that require rapid, quantitative signal detection. SS-VEP signals vary with presentation mode and with temporal presentation rate. We compare two modes of pattern presentation: pattern reversal (PR) and pattern onset-offset (ON-OFF) across a range of presentation rates.

**Methods:** Participants were 10 healthy adult volunteers (aged 18-25), with no visual or ocular motor dysfunction. Pattern stimuli were high-contrast, ISCEV-standard, small checks (0.25 degree check width) presented in PR and ON-OFF modes. Five temporal rates between 3.42 and 18.6 were used. PR checks were presented at the reversal rate and ON-OFF stimuli were presented at the cycle frequencies (50% duty cycle alternated with luminance-matched grey). In addition, full-field, square-wave modulated flicker (50% duty cycle, 200 cd/m<sup>2</sup>) stimuli were presented at the same rates. Signals were averaged for an integer number of cycles using total periods of 40s or less. The magnitude and signal-to-noise ratio (SNR) of Fourier components of the SS-VEPs were compared at the fundamental stimulation rates (F1) and at double these rates (F2) using ANOVA with Bonferroni corrections.

**Results:** Overall, ON-OFF presentation of checks produced larger VEPs and SNRs than did PR at both F1 and F2 ( $p < 0.01$ ). For both presentation modes SS-VEP signals were strongest for temporal rates between 7.14 and 12.7 (reversals/s or Hz for PR and ON-OFF respectively) probability of detection of F1, F2 or both. However, the frequency response functions differed between the presentation modes; at both F1 and F2 SS-VEPs for ON-OFF checks followed a high pass function with similar magnitude and SNR values for frequencies up to 12.5 Hz. For PR checks the SS-VEPs were band pass with significantly low magnitude and SNRs values at the high and low reversal rates. Differences between ON-OFF and PR were significant for stimulation rates of 3.4 for F1 and F2 and at 4.6 Hz for F2. Interestingly, the full field ON-OFF luminance flicker produces SS-VEPs with a band-pass frequency response function similar to that of the PR checks with undetectable signals at low and high stimulation rates

**Conclusions:** SS-VEPs to luminance flicker and to PR checks are poorly detected for presentation rates below 5 and above 15 Hz. In contrast, checks presented in the ON-OFF mode elicit strong SS-VEPs for stimulation frequencies as low as 3.4 Hz. Using relatively short presentation times, SS-VEPs in young adults are strongest when presented at 7-13 Hz with signal detection at F1 and F2.

**Acknowledgements:** This work was supported by Individual Mobility Grant RF3006-2006 from European Commission awarded to Elena Prokofyeva.



## **STROBOSCOPIC AND SQUARE WAVE FLICKER VEPS FOR VISUAL PATHWAY ASSESSMENT.**

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**Purpose:** Steady-state VEPs (SS-VEPs) to luminance flicker are useful for evaluation of visual pathways, particularly for those who have poor fixation or limited co-operation. SS-VEP waveforms are influenced by the luminance profile of the flicker. We compare stroboscopic and square wave flicker across a range of stimulus frequencies to compare the normal frequency response characteristics for SS-VEPs to these common modes of flicker presentation.

**Methods:** Participants were 10 healthy adult volunteers (aged 18-25), with no visual or ocular motor dysfunction and corrected visual acuity of 6/6 (0.0 Log MAR) or better in each eye. SS-VEPs were recorded binocularly to full field flicker stimuli generated using LEDs in a ganzfeld (Espion Colordome®). Two modes of flicker were presented: square wave modulated (ON-OFF with 50% duty cycle, 200 cd/m<sup>2</sup>) and stroboscopic flash (5 ms pulses, 10 cd.s/m<sup>2</sup>) presented at six temporal frequencies, 3.42, 4.64, 7.32; 12.7, 18.6 and 38.1 Hz. The magnitude of Fourier components of SS-VEPs at the fundamental stimulus frequencies (F1) and double harmonics (F2) and the signal-to-noise ratios (SNR) were compared using ANOVA with Bonferroni corrections.

**Results:** For both modes of stimulation, flicker at 7.3 and at 12.7 Hz elicited a significant SS-VEP in all participants ( $p < 0.05$ ), usually for both at F1 and F2. Using these recording parameters, the SS-VEP was also detectable in 9/10 subjects at 4.6 and 18.6 Hz but poorly detected for the slowest (3.4 Hz) and fastest (38 Hz) flicker rates. SS-VEP magnitudes are larger for F1 than for F2 ( $p < 0.001$ ). Square wave modulated flicker gave higher SNR values at F1 than those for stroboscopic flicker ( $p = 0.001$ ); this difference was significant individually for 12.6 and 18.6 Hz flicker (post hoc tests,  $p < 0.01$ ). F2 harmonics were best detected from 4.6 to 12.7 Hz but did not differ between the modes of stimulation.

**Conclusions:** Flickering stimuli elicit reliable SS-VEPs in young adults using flicker rates between 7 and 19 Hz. Square wave modulated flicker has an advantage over stroboscopic flicker as it elicits higher SNRs. These parameters can be used to assess the visual pathways of patients with poor fixation.

**Acknowledgements:** This work was supported by Individual Mobility Grant RF3006-2006 from European Commission awarded to Elena Prokofyeva.





**A NYSTAGMUS OR POSSIBLE ALBINISM CHECKLIST FOR EYES WITHOUT OBVIOUS PATHOLOGY: PRELIMINARY RESULTS**

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**Purpose:** To evaluate the preliminary findings obtained since the introduction of a check list to assist in the diagnosis of the cause of congenital, uniplanar nystagmus in patients without obvious ocular pathology and cases of possible albinism.

**Methods:** In January 2008 a new checklist was introduced within the Ophthalmology Department of the Royal Hospital for Sick Children (Yorkhill). The checklist contains the causes of nystagmus for which clinical signs are not present or are subtle: albinism, optic nerve hypoplasia, chiasmal pathology, congenital stationary night blindness, achromatopsia, periventricular leucomalacia and a history of methadone exposure in utero. The checklist is employed to establish the diagnosis efficiently. Routine electrophysiological assessment is carried out as part of the work-up. This involves VEP recording to assess chiasmal routing and latency and amplitude of responses, full-field ERG recording and, where required, estimation of acuity using steady-state VEPs.

**Results:** To date the following diagnoses have been established: idiopathic nystagmus (3); retinal abnormality (1) and delayed visual maturation (1). Further cases are anticipated.

**Conclusions:** Congenital nystagmus is seen infrequently in ophthalmology clinics and clinicians may not have the range of diagnostic possibilities immediately to hand; diagnosis can thus be elusive. The aim of the checklist is to facilitate efficient and accurate diagnosis in these cases. These preliminary results demonstrate the use of electrophysiological assessment in diagnosing the cause of nystagmus. The future plan is to use the checklist as an audit tool to compare clinical findings and electrophysiological results with the aim of assessing the performance of electrophysiological tests in diagnosing albinism.



**CHANGES IN OCT LAMINAR STRUCTURE BUT NOT MFERG TIMING IN THE CENTRAL RETINA IN RETINITIS PIGMENTOSA.**

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**Aim:** To investigate relationships between retinal morphology and retinal function in patients with retinitis pigmentosa (RP) using optical coherence tomography (OCT) and multifocal electroretinography (mfERG).

**Methods:** 14 patients with RP who had visual acuities of 0.2logMAR or better and Humphrey central fields of 10° or larger participated in the study along with 16 normal control subjects. The amplitudes and timings of the mfERG responses were compared to spatially corresponding measures of retinal layer thickness from OCT within the macula region (central 12°).

**Results:** Eyes with RP demonstrated thinning of the photoreceptor retinal (PR) layer and thickening of mid-inner retinal (MIR) layers beyond the fovea. mfERG amplitude was reduced in all regions, whereas mfERG timing was only significantly delayed at a retinal eccentricity of 6-12° and was otherwise preserved within the foveal and parafoveal retina (0-6°). PR layer thickness was correlated with mfERG amplitude across the macula region. mfERG timing was correlated with the total change in retinal thickness (combined PR thinning and MIR thickening) at an eccentricity of 6-12°.

**Conclusions:** The relationship between mfERG timing and retinal thickness in RP is dependent on retinal eccentricity. Preserved timing in the central retina (0-6°) despite significant disruption to retinal laminar structure could be suggestive of inner retinal remodelling or functional redundancy. Cone system activity derived from mfERG amplitude appears to be related to the thickness of the photoreceptor layer in the macula region.

**Funding:** Northern Ireland Research and Development Office.



## **THE COMPARATIVE PERFORMANCE OF TWO DTL VARIANTS IN RECORDING THE ERG**

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**Purpose:** To compare the performance of two commercially available DTL ERG electrodes in a double blind trial using a method previously established by Vaegan et al (ARVO 2008, Abstr # 2225) which creates linear scaling transfer functions for both means and standard deviations of amplitudes and peak times.

**Methods:** Two DTL electrode variants, the DTL plus Model D141 (Diagnosys LLC, Cambridge UK) and another fabricated by the Department of Clinical Engineering, Liverpool UK were used. Both are multi-filament ca 5cm long, low impedance (ca 300 ohm) fibres with non allergenic adhesive pads each end. The Liverpool model is in a closed sterile pack. The eye with each electrode was randomized. After >7mm dilation ISCEV standard bilateral ERGs and 19 area mfERGs were recorded in 6 normal persons and 5 patients with symmetrical bilateral disease. The data were sorted by electrode type named only as A and B and sent to ACF for interpretation and cursoring. To increase the correlation of the fitted functions, measures included components with the widest possible range. Amplitudes varied from the bright flash ERG to the 3 ring averages of the first order kernel mfERG. The two regression equations, constrained to pass through zero, of the relationship ( $A=bB$  and  $B=cA$ ) of the means and s.d.s of each measure were calculated. The 'true' exponents were estimated by averaging the first and the inverse of the second exponent ( $(b+1/c)/2$ ) while the error of estimate was given from  $b-1/c$ . Coefficient of variation (amplitude exponent / s.d. exponent) or SNR of A and B were compared and the significance of the difference from a ratio of 1.0 calculated. Spreadsheets containing the amplitudes and times to peak of each component and their means and standard deviations (s.d.s) with each electrode (identified only as type A and type B) were sent to a third location for comparison. Responsibility for clinical procedures and masking of A and B was assumed by V; ACF independently performed the data analysis; TW unmasked identities A & B and summarized the results. The identity of types A and B was then unmasked.

**Results:** Here we report the 3 amplitude measures: the mean mfERG P1, the scotopic bright flash a wave and the photopic bright flash b wave. Measures from the two electrode types were both stable and reliable. Non-parametric analysis of each covariate by Kolmogorov-Smirnov technique ('measures of distribution') and Mann-Witney for paired data did not reject the null hypothesis (for  $\alpha=0.5$ ) that the samples of electrodes performed identically. Thus there is no indication that a transfer function other than 1.0 should be applied, however, the signal-to-noise ratio for the Liverpool variant was significantly greater ( $p<0.5$ ) the Model Plus D141

**Conclusion:** This study suggests that the DTL plus D141 and Liverpool variant electrodes perform similarly and that, with caution, could be used interchangeably. The complete experiment will use far higher numbers of test subjects and will establish whether a multivariate parametric statistical analysis will still support the conclusions.



## **A COMPARISON OF REFERENCE ELECTRODE POSITION AND TYPE FOR MONOCULAR ERG RECORDING**

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**Purpose:** The electroretinogram (ERG) amplitude is affected by the type and position of reference electrode used. It is desirable to elicit the largest amplitude (signal) possible when recording an ERG trace, this helps achieve a good signal to noise ratio (SNR). A poor SNR can limit the usefulness of an ERG recording; this can be a significant problem if the signal is small, such as when recording a focal ERG.

**Method:** 18 healthy subjects were recruited and focal 41Hz flicker ERG (20°Ø, 595nm stimulus) traces were obtained using an active DTL electrode and 4 different reference electrodes. Reference skin electrodes were positioned at 1, 3 and 5 cm, from the outer canthus of the test eye, and a DTL reference electrode placed in the contralateral eye.

**Results:** Increased skin electrode position from the outer canthus resulted in larger ERG amplitudes elicited. Results demonstrate a significant difference in amplitude with skin electrode position whilst the DTL reference produced comparable amplitudes to the skin electrode in the 3cm position.

**Conclusion:** This study highlights the importance of consistent and accurate reference electrode positioning. The contralateral DTL was shown to be an effective alternative to traditional reference skin electrodes, whilst also demonstrating practical benefits.



Tuesday 16<sup>th</sup> September

**9.15 Keynote Lecture 1 – Professor Wolfgang Drexler**

**OPTOPHYSIOLOGY: NON-INVASIVE OPTICAL PROBING  
OF DEPTH RESOLVED RETINAL PHYSIOLOGY**

**10.15 -11.30 Coffee, Posters & Exhibition**

**11.30-12.30 Session 2 – Novel Techniques**



**OPTOPHYSIOLOGY: NON-INVASIVE OPTICAL PROBING OF DEPTH  
RESOLVED RETINAL PHYSIOLOGY**

Professor Wolfgang Drexler

School of Optometry and Vision Sciences,  
Cardiff University,  
Cardiff

Optical coherence tomography (OCT) is an emerging non-invasive, optical medical diagnostic imaging modality, which enables *in vivo* cross-sectional tomographic visualization of intraretinal microstructure. Recent developments in ultrabroad bandwidth laser as well as OCT technology enable three-dimensional ultrahigh resolution OCT with unprecedented axial resolution, approaching resolution levels of conventional histopathology, enabling optical biopsy of the living human retina. In addition, extensions of OCT are recently under development that should provide non-invasive *depth resolved* functional imaging of the investigated tissue, including extraction of spectroscopic, blood flow or physiologic tissue information.

Optophysiology – an optical analogue to electrophysiology - has been developed to measure depth resolved light-induced intrinsic optical signals of the retina at different wavelengths *in vitro* and *in vivo*. Preliminary results indicate a more pronounced contribution to the total backscattering change originating from the proximal layers of the retina, especially the photoreceptor layer. Optophysiology might be a useful extension to OCT for extracting intrinsic optical signals of the living human retina, to provide significant information about the origin of these stimulus-induced signals and to enable the differentiation and early detection of pathologies via localized functional state.



**MULTIMODAL IMAGING: A NEW TOOL TO INVESTIGATE THE RELATIONSHIP BETWEEN MACULAR STRUCTURE AND FUNCTION IN RETINAL DISEASE**

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**Purpose:** To investigate the effects of retinal disorders with macular involvement on macular structure and corresponding function using multimodal imaging (MMI), a new imaging modality which combines a scanning laser ophthalmoscope, optical coherence tomography and micro-multifocal ERG (micro-mfERG).

**Methods:** A prototype OCT/SLO system (OTI; Toronto, Canada) was modified to integrate an organic light emitting diode (OLED) display into the optics of the system. A high resolution micro-mfERG stimulus covering up to the central 24 degrees was projected onto the OLED display. During the 8 minute micro-mfERG recording time, OCT scanning was performed in both coronal (C-scan) and transverse (B-scan) planes in multiple locations to allow structural and functional information to be collected for all the stimulated areas. Accurate patient fixation during the recordings was ensured by monitoring the SLO channel.

55 patients with conditions affecting the macula (14 with a macular hole, 25 with age-related macular degeneration and 16 with other conditions) have been assessed using MMI and the structural and functional information obtained has been correlated. 12 patients with a macular hole and 15 patients with age-related macular degeneration (ARMD) have been re-assessed with MMI post-treatment and the structural and functional changes observed.

**Results:** MMI was well tolerated by all patients tested with good patient compliance observed in all recordings. Good correlation was observed between structural and functional alterations in most patients although in some cases functional abnormalities extended wider than structural alterations. In patients with ARMD there was generally good correspondence between the area of structural alterations and macular dysfunction however most patients did not show significant functional improvements post-treatment even though OCT confirmed improvements in macular structure. In patients with a macular hole, pre-treatment MMI showed varying degrees of functional loss. Post-treatment MMI showed anatomical closure in all patients accompanied by improvements in micro-mfERG amplitudes but persistence of timing delays. The patients tested with other conditions generally showed good correlation between the area of structural alterations and macular dysfunction.

**Conclusions:** MMI provides a means of simultaneously imaging the surface, substructure and function of the macula at multiple discrete sites. The results presented illustrate that disease processes do not necessarily result in corresponding deficits in macular structure and function. MMI is well tolerated by patients and may help in improving our understanding of disease processes and in assessing the success of surgical or pharmacological interventions for various disorders affecting the macula.



## **SERIAL IMAGING AND FUNCTIONAL CORRELATES OF HIGH DENSITY RINGS OF FUNDUS AUTOFLUORESCENCE IN DIFFERENT RETINAL DYSTROPHIES.**

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<sup>2</sup>Institute of Ophthalmology, University College London, UK.

**Purpose:** To examine the evolution and functional significance of parafoveal rings of high density fundus autofluorescence (AF) in patients with different retinal dystrophies.

**Methods:** One hundred patients with retinal dystrophy were ascertained who had a parafoveal ring of high density AF. Seventy five had a clinical diagnosis of retinitis pigmentosa (RP) or Usher syndrome with a visual acuity of 6/9 or better; 20 of 75 had repeat AF imaging after periods of up to 7 years. Twenty five others included cases of cone or cone-rod dystrophy (GUCA1A, RPGR, RIMS1) or cone dystrophy with supernormal rod ERG (KCNV2). International-standard full-field and pattern ERG (PERG) testing were performed. Some underwent fine matrix mapping (FMM).

**Results:** a) The AF ring radius correlated positively with PERG P50 amplitude in RP ( $r=0.80$ ,  $p<0.05$ ,  $N=75$ ). The ring encircled areas of preserved photopic function. Serial AF revealed progressive ring radius reduction in 10 of 20 cases at rates of 1.5-12% per year.

b) In the 25 patients with different forms of cone or cone-rod dystrophy, AF rings resembled those seen in RP or encircled areas of central RPE atrophy. Cross-sectional analysis over 5 decades revealed that AF ring size was related to age in KCNV2 cases ( $r=0.77$ ,  $p<0.05$ ,  $N=7$ ). Two cases (RPGR, RIMS1) showed progressive ring expansion. There was an inverse relationship between P50 and ring size in those with detectable PERGs.

**Conclusions:** High density AF rings progressively constrict in a high proportion of patients with RP and good visual acuity. The rate of ring constriction varies between patients. The rings correlate with measures of macular function and may be of prognostic value in predicting preservation of central vision in RP. Progressive ring expansion may occur in different forms of cone and cone-rod dystrophy as central macular RPE atrophy develops.





## **CORRECTING FOR RETINAL MACULAR PIGMENT DISTRIBUTION IMPROVES CHROMATIC SELECTIVITY OF LARGE-FIELD BLUE-YELLOW VEPS.**

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2 Faculty of Medicine, University of Manchester

3 Moorfields Eye Hospital, London

4 Institute of Ophthalmology, London

**Purpose:** The optical density of macular pigment (MPOD) varies widely across the population and, within a single individual, across the macula. This can alter sensitivity to stimuli in the blue region of colour space. For example, blue-green (B/G) and blue-yellow (B/Y) isoluminance can be markedly affected and this is commonly exploited in psychophysical methods of measuring MPOD. We have developed a VEP test which allows objective measurement of isoluminance for a series of concentric annular B/G gratings which allow an estimate of MPOD and distribution. The results correlate well with different psychophysical assessments. The same stimulation protocol can be used to create grating stimuli which are isoluminant across the whole stimulated field and we have successfully generated blue-green and blue-yellow onset VEPs to large stimuli.

**Methods.** Large (18deg diameter) and small (3deg diameter) B/Y gratings were displayed on a high resolution colour monitor. Spatial frequency was 2c/deg and mean luminance was 10cd/sq m. The chromatic axis was rotated until the B/Y border in a bipartite field was minimally distinct, thus specifying a tritanopic confusion axis for each individual. Isoluminance was set for the centre of both stimulus fields (0.6 deg diameter) using heterochromatic minimum flicker photometry (HFP; 10Hz). The 18deg stimulus was additionally adjusted to compensate for laterally distributed MP by specifying minimum flicker for 9 concentric annular regions around the fovea. On-off VEPs were recorded to the following gratings: 18deg tritan (isoluminant for the centre and each annulus), 18deg tritan and 3 deg tritan (both isoluminant for centre), and 18deg achromatic. Temporal contrast sensitivity was measured by setting pattern and movement thresholds for each of these stimuli at a range of temporal frequencies.

**Results.** The signature of a chromatic VEP is a marked onset negativity which is not seen in the offset response. Using the large multiple annular isoluminant grating, we recorded chromatic-selective negative polarity VEPs. With a single isoluminant setting the 18 deg field elicited positive achromatic components. The magnitude of this effect was related to the MPOD. Psychophysically-determined temporal contrast sensitivity functions were low-pass for the multiple annular isoluminant field with resolution limit at about 10Hz; using the standard 18deg field achromatic intrusion increased and temporal resolution was about 20Hz.

**Conclusions.** Multiple annuli can be used to generate large isoluminant tritan stimuli that compensate for individual differences in MPOD and distribution. The method provides a selective method of activating koniocellular (B/Y) mechanisms using large chromatic fields and allows improved analysis of the blue-cone-driven visual pathway.



**NEAR INFRARED OPTICAL IMAGING: A COMPLEMENTARY IMAGING  
APPROACH TO USE IN CONJUNCTION WITH VEPS?**

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**Purpose:** To use functional near infrared optical brain imaging to measure blood flow in active muscle and brain tissue during sensory and motor tasks.

**Methods:** Functional near infrared (fNIR) optical brain imaging is an emerging non-invasive technology for measuring the dynamic changes in blood haemoglobin levels in activated brain areas during perceptual and cognitive tasks. This technology provides a balance between the time resolution of electro- and magnetoencephalography (E/MEG) and event-related potentials (ERPs) and spatial resolution of functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) for probing superficially areas of the brain cortex. Here we report preliminary data recorded from normal adult subjects using a 2-channel NIRS system (Oxiplex TS, ISS).

**Results:** The data were recorded on the forehead in response to eye opening and closing, over motor cortex whilst flexing of the forearm and over occipital cortex (over V1) in response to contrast reversing checkerboard patterns.

**Conclusion:** We consider the efficacy of this technique in imaging brain function within the clinical setting.



**1.30-2.30 Keynote Lecture 2 – Dr JT Erichsen**

**A WING GUIDED BY AN EYE: A SIDEWAYS LOOK AT BIRD VISION**

**2.30 -4.00 Session 3 – Clinical Electrophysiology**

**4pm**

**Meeting Ends**



## **A WING GUIDED BY AN EYE: A SIDEWAYS LOOK AT BIRD VISION**

Dr. Jonathan T. Erichsen  
School of Optometry & Vision Sciences  
Cardiff University  
Cardiff

### Abstract:

The purpose of this talk is to introduce the bird as a model system for studies of vision. Although the avian eye and visual pathways have a surprising amount in common with humans, there are also many fundamental differences. Both the similarities and the differences present us with a range of possibilities for understanding, amongst other things, the function of the fovea, the importance of optical adaptations, the purpose of colour vision, eye development and the operation of visuomotor responses. In addition, the structural properties of the visual system can place significant constraints on various behaviours. A good example of this is the distinctive head bobbing of some birds when they walk. Our neuroscience studies of the visual response to a close object (the near response) have revealed that the circuitry is conserved across many vertebrate species, including birds. Recently we have discovered that manipulations of this circuitry can have a direct influence on the development of the eye and its refractive state. We believe that further investigations of these pathways from a comparative perspective will help identify general organisational principles that will in turn inform studies of experimental myopia. At the very least, however, you will hopefully come away with a better appreciation of the bird's eye view of the world and how studies using the bird may enhance our understanding of vision.



**ON THE DIFFERENTIATION BETWEEN FUNDUS ALBIPUNCTATUS AND  
RETINITIS PUNCTATA ALBESCENS.**

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**Purpose:**

To compare and contrast the phenotypic variation in patients with fundus albipunctatus (FA) and retinitis punctata albescens (RPA).

**Methods:** A cohort of patients with fundus albipunctatus was assessed by clinical examination, electrophysiology and autofluorescence imaging. Electrophysiology was performed to incorporate the relevant ISCEV Standards; significant additions included the use of red stimulation under dark adaptation and the use of extended dark adaptation (DA; usually one eye overnight). Most patients gave permission for DNA screening which confirmed RDH5 mutation. A cohort of patients with RPA consequent upon CRALBP mutation was similarly ascertained.

**Results:** Patients with FA showed a variable degree of cone dysfunction, with only some patients showing full-field cone ERG abnormalities. Patients with RPA had marked cone system abnormalities. Rod specific ERGs were undetectable in FA patients after standard DA, but there was pronounced recovery of rod system function following extended DA, when rod system ERGs could return to normal. Red stimulation under DA suggested that recordings under DA were arising from the cone system, in keeping with loss of rod function consequent upon defective rhodopsin regeneration. Patients with RPA could show limited recovery following extended DA, but normalization was not observed.

**Conclusion:** The value of accurate electrophysiological characterization in the differentiation between FA and RPA is confirmed. The importance of an extended period of dark adaptation prior to ERG is stressed.



**MONITORING THE PROGRESSION OF MONOCULAR OPTIC NEURITIS WITH  
MULTIFOCAL VISUAL EVOKED POTENTIALS AND OTHER FUNCTIONAL  
MEASURES: A CASE STUDY.**

Maryke Fox 1, Colin Barber 1

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University Hospitals NHS Trust

**Purpose:** To monitor changes following an acute episode of monocular optic neuritis using the multifocal VEP and to compare the results to other functional measures.

**Methods:** We monitored a patient who was diagnosed with left optic neuritis following presentation to eye casualty with acute visual field loss and headache. Visual acuity, colour contrast sensitivity and mfVEP testing were recorded from the patient over a period of a year following an acute episode of left optic neuritis. The right eye was unaffected but an MRI brain scan showed lesions indicating a high probability of this patient subsequently developing multiple sclerosis. mfVEP responses were grouped in quadrant rings and quadrants and peak amplitude and latency compared between eyes and between visits. To minimize test-retest variation, peak latencies and amplitudes from the left eye were plotted as percentages of those from the right eye.

**Results:** The VA in the left eye was NPL in the acute stage. 8 months after onset vision had returned to 0.0(LogMAR). VA in the right eye was better than 0.0(LogMAR) throughout. Colour contrast sensitivity in the left eye on the protan axis improved significantly over the follow-up period but remained poor on the tritan axis. Colour vision in the right eye was normal throughout the follow-up period. mfVEP: Peak latency was difficult to measure on some of the quadrant rings because the signal was small and the peaks broad. It was easier to measure the peak amplitude with confidence. Both peak latencies and amplitudes improved markedly between the first and second visit (1 month and 4.5 months after onset respectively) and then showed little improvement for the rest of the follow-up period. After the initial improvement there was no significant interocular difference in peak latency and the peak amplitudes in the affected eye were, on average, 40% of the amplitudes from the unaffected eye.

**Conclusions:** VA can improve markedly following an episode of acute optic neuritis but colour vision and mfVEP peak amplitudes can remain abnormal for at least a year after the event.



**OPTIC NERVE HYPOPLASIA (ONH) AND AND OPTIC ATROPHY CO-EXISTING  
SIGNS OF CONENITAL RETINAL GANGLION CELL DYSPLASIA.**

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2. Childrens Hospital Los Angeles, and Keck School of Medicine, University of Southern California. Los Angeles, CA, USA.

**Purpose:** Optic nerve hypoplasia (ONH), congenital dysplasia of the retinal ganglion cells, is characterized by small optic nerves and is often associated with other congenital brain malformations. In addition, a substantial proportion of affected children demonstrate pallor of the optic nerves indicating that hypoplasia may coexist with optic atrophy. We examine the associations between pallor and severity of hypoplasia on electrophysiologic measures and visual prognosis in a large cohort of children with ONH.

**Methods:** Participants were 85 children with ONH (16% unilateral cases) enrolled in the Childrens Hospital Los Angeles prospective study of prenatal and clinical risk factors in ONH. They were recruited before 36 months of age and have completed assessment of visual acuity at 5 years of age. Initial assessments included ERGs and VEPs to photopic flash and to pattern-reversal checks as well as fundus photography with chloral hydrate sedation. ONH severity was assessed using the disk diameter to disk-macula ratio (DD/DM). Pallor, graded from photographs by a expert masked observer (MSB) was present in 40% of fixating eyes. Only the fixating or better-seeing eye of each participant was analysed to exclude amblyopia as the aetiology of visual impairment (94% have strabismus).

**Results:** Three of the measures recorded at the initial assessment were useful for establishing the visual prognosis at 5 years of age: the amplitude of the flash VEP to (Spearman's rank correlations,  $p < 0.001$ ), the threshold check size for pattern VEPs ( $p > 0.01$ ) and the amplitude of the N95 component of the pattern ERG to 4-degree checks ( $p < 0.02$ ). Both severity of ONH and pallor were independently associated with visual outcome and with the threshold VEP check size, demonstrating that pallor is an additional risk factor in eyes with a similar DD/DM. The DD/DM was also significantly associated with the amplitudes the flash VEP and of the N95 of the PERG. The P50 of the PERG and the photopic flash ERGs had no prognostic value.

**Conclusions:** Optic nerve pallor is frequently associated with ONH and indicates an additional risk of visual impairment in affected eyes. In the present study, the threshold check size for VEPs was significantly more elevated in eyes with both optic nerve pallor and ONH compared with those who had ONH only.

**Acknowledgements:** This research was supported in part by The One Small Voice Foundation, the Carnegie Trust for the Universities of Scotland, and by NIH General Research Center (GCRG) grant (M01 RR00043).



**ASYMMETRICAL OCULAR HYPOPIGMENTATION WITH INTER-OCULAR DIFFERENCES IN THE INTER-HEMISPHERIC SYMMETRY OF THE VEP.**

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**Purpose:** Melanin production in the RPE occurs early in ocular genesis and is critical to visual pathway development. Disruption of melanin synthesis can result in ocular hypopigmentation and visual pathway misrouting. The aim of this study is to use VEP techniques to investigate chiasmal decussation of the visual pathways in patients with inter-ocular differences in RPE pigmentation. Patients with Waardenburg Syndrome are also examined.

**Methods:** Four patients with asymmetrical inter-ocular pigmentation (Patients 1-4, mean age  $34 \pm 19$  yrs) and two patients with Waardenburg Syndrome (Patients 5 and 6, 6 and 11 yrs) were examined. VEPs to pattern appearance (PappVEP) and flash (FVEP) stimulation were recorded using 5 active electrodes. ERGs and fundus photography were also performed.

**Results:** All patients presented with fundal hypopigmentation of one or both eyes. Patients 1, 3 and 4 had bilateral foveal hypoplasia; patients 2 and 3 had iris transillumination; and patients 2, 3 and 4 had nystagmus. Patient 5 had heterochromia (right eye = blue iris; left eye = brown iris) and patient 6 had blue irises.

**Fundus photography:** Patients 1-5 showed asymmetrical pigmentation between the eyes and pigment distribution differed between eyes. Retinal blood vessel patterns did not differ between eyes regardless of pigmentation.

**VEPs:** In patients 1-4, FVEP and PappVEPs from the more pigmented eye showed no significant inter-hemispheric difference in amplitude/latency. FVEP and PappVEPs from the less/minimally pigmented eye showed a significant inter-hemispheric difference in amplitude/latency. In patients 5 and 6, FVEP and PappVEPs showed no significant inter-hemispheric difference in amplitude/latency from either eye. ERGs from both eyes of all patients were normal.

**Conclusion:** During development melanin deposition in one eye appears to be independent of deposition in the other eye. Subsequently, its influence on chiasmal decussation of the hemispheric projections may also be independent between eyes. Four patients with inter-ocular differences in RPE pigmentation demonstrate asymmetrical VEPs in the eye with the least amount of pigment, whereas the fellow eye is normal. In addition, RPE hypopigmentation in Waardenburg Syndrome appears to have no effect on the visual pathways. This suggests that the underlying mechanisms associated with hypopigmentation in albinism are different to those in Waardenburg Syndrome.





## **THE VISIBLE SPECTRUM - THE MAGIC OCTAVE**

Malcolm Brown

Clinical Engineering Dept. & Clinical Eye Research Centre, Royal Liverpool  
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Infra-red vision and Xray eyes would be very useful! Further, why not listen to the radio, see television or use the cell-phone and SatNav networks directly, without apparatus. Why is vision limited to just one octave of the vast electromagnetic spectrum?

It appears that the photometric (visible) spectrum arises from a co-incidence of three unrelated properties to give vision between about 400 and 700nm in humans and from 320 to 740nm across the entire animal spectrum:

1. The spectrum of light leaving the sun (black body at 5800K) has a broad peak at 500nm, halving at 370 and 730nm
2. Earth's atmosphere is only transparent to light between 300 and 700nm
3.
  - a. The lens must prevent short wavelength (UV) light entering the eye to prevent ionising radiation damage to the retina
  - b. Long wavelength (Infrared) photons have limited energy. Some fish and amphibians can sense up to 740nm, but these are all cold blooded.

Evolutionary pressures will have acted to consolidate this position since plants enjoy, absorb and reflect light from the same octave of illumination, and we have to see them to eat.