Applied Statistical Modelling and Inference in Ophthalmology:

Analysis of visual field and video data for glaucoma patients.

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Abstract

Eyesight is arguably the most important of our senses with the eye absorbing 80% of external information from our surroundings. The field of ophthalmology studying the anatomy, physiology and diseases of the eye, is of extreme importance. Many methods exist to measure vision and the eye, creating a large range of interesting datasets. We developed methods to analyse three datasets from subjects with glaucoma, the second leading cause of blindness worldwide.

Visual field testing using standard automated perimetry, is the most common method for monitoring glaucoma progression. A numerical matrix representing the dimmest intensity seen by a particular locus on the eye is outputted. This can be thought of as a map, and disease mapping techniques applied. We employed conditional autoregressive priors to account for the spatial correlation structure in the visual field results, in a way that respects the physiological and optical properties of the eye. Model diagnostics showed our model superior to the currently used point-wise linear regression methods.

Visual field mean deviation, the mean light intensity across all loci adjusted for age matched controls, provides a global estimate of glaucoma progression. We investigated the shape of the relationship between mean deviation and time over long series of visual fields using splines. We considered imposing a monotonic non-increasing constraint. When a curve deviated from being linear or monotonic non-increasing, this was an indication of physiological or treatment change in the eye.

We developed methods to extract and analyse data from video sequences of retinal venous pulsation, observed as change in blood flow, varying with the cardiac cycle. Video sequences were divided into individual frames, and the mean pixel intensity was calculated separately for three vessel segments representing the artery, lower vein and upper vein. Simple harmonic

terms modelled the periodic component of the trend. The non-periodic trend, caused by patient movement, was modelled by linear splines. An autoregressive process modelled error correlation. Retinal blood flow has been linked to many diseases, so the characteristics of these curves have clinical importance.

Publications arising from this thesis

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List of Abbreviations

AGIS	Advanced Glaucoma Intervention Study
AIC	Akaike information criterion
asb	Apostilbs
AUC	Area under the curve
BLUP	Best linear unbiased predictor
BYM	Besag, York and Mollie model (disease mapping)
CAR	Conditional autoregressive
CIGTS	Collaborative Initial Glaucoma Treatment Study
dB	Decibels
DIC	Deviance information criterion
DLS	Differential light sensitivity
EMGT	Early Manifest Glaucoma Trial
GPA	Glaucoma progression analysis
IOP	Intraocular pressure
ICP	Intracranial pressure
LTF	Long term fluctuation
MCMC	Markov chain Monte Carlo
MD	Mean Deviation
OAG	Open-angle glaucoma
ODF	Ophthalmodynamic force
PLR	Point-wise linear regression
POAG	Primary open-angle glaucoma
POBF	Pulsatile ocular blood flow
REML	Residual maximum likelihood estimation
RGB	Red-green-blue colour model
ROC	Receiver operating characteristic
SAP	Standard automated perimetry
SITA	Swedish interactive threshold algorithm (SAP method)
SMR	Standard mortality ratio
SPROG	Our model in Chapter 4 (Spatial Progression)
STF	Short term fluctuation
SVP	Spontaneous vein pulsation
VPSG	Vein Pulsation Study Trial in Glaucoma
VF	Visual Field

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