Individualised Optimisation of Modelled Cerebral Oxygenation Near-Infrared Spectroscopy Signals

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Abstract: Responses of NIRS signals in a healthy volunteer are predicted using a model of brain circulation. Optimisation using partial data is shown to increase the model's predictive power which can aid the interpretation of NIRS signals in individuals.

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1. Introduction

Noninvasive measurements of cerebral circulation and metabolism have the potential to significantly increase our understanding of the healthy and injured brain. Improvements in techniques such as near-infrared spectroscopy (NIRS) [1] can provide valuable information and offer the potential for developing multimodal monitoring strategies, in particular in neurointensive care. However, the interpretation of NIRS and other measured signals requires understanding not only of the physics of the measurement process, but also the underlying physiology. At the same time such techniques provide scope for acquiring large quantities of data, therefore, developments in measurement techniques alone are insufficient, and naturally require corresponding developments in analysis. This leads to the use of methodologies where modelling, of physiology and the measurement process, play a key role. In this paper, the predictions of a previously developed model of brain circulation and metabolism [2], termed BrainSignals, are compared with a representative data set measured from a healthy volunteer undergoing a series of drops in inspired oxygen [3].

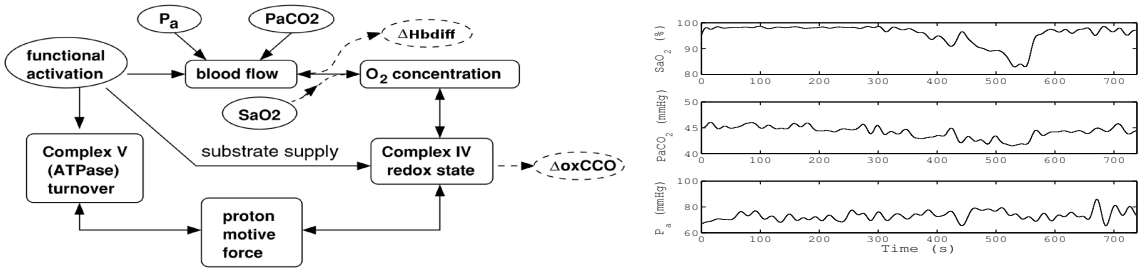
Optical measurements made *in vivo*, as presented here, can have considerable physiological and measurement noise, despite this, preliminary studies [4] suggest that qualitative trends in certain measurements can be predicted with some consistency. To be of use in a clinical context a model must be able to give insight not only into averaged behaviour of the signals, but also the behaviour of individuals, who may display a wide range of natural physiological and pathophysiological variation, giving rise to optical measurements which may not be straightforward to interpret. Given prior information/data for an individual the success of subject-specific reparametrisation of the model is characterised via its ability to reproduce NIRS data for that individual. In this case the prior information takes the form of a training set of partial data from the full experiment.

2. Methodology

Details of the experimental protocols and measurement methodologies are provided in [3]. In short, heart rate, mean arterial blood pressure (P_a), inspired oxygen concentration (FiO_2) and arterial oxygen saturation (SaO_2) were measured continuously. A continuous wave NIRS broadband spectrometer (BBS) developed in-house [3] was used to monitor brain tissue haemodynamics. The first five minutes of the study monitored the subject at normoxia. after which nitrogen was added to the inspired gases until SaO_2 fell to 80%, at which point FiO_2 was returned to normal for a further five minutes. This procedure was repeated three times, during which end tidal carbon dioxide tension ($EtCO_2$) and breathing rate were measured continuously and fed back to the subject in order to allow normocapnea to be maintained. Data from the experiment was manually divided into the three challenges by choosing time-points in the middle of the periods of normoxia between hypoxemic challenges.

2.1. The BrainSignals model

The BrainSignals model is described in [2], and available for download at [5]. This model is a simplification of the large scale BRAINCIRC model in [6] and was constructed to aid interpretation of measured signals (such as those described above), thus allowing, model performance to be better evaluated against *in vivo* data and maximising the clinical relevance of the model, the basic structure of the model is illustrated in Fig. 1a. Several parameters which were either expected to have large physiological variation between individuals or can be hard to measure have been given



(a) Model inputs are enclosed in solid ovals, while outputs of NIRS measured signals are enclosed in dashed ovals

(b) Input signals for a single challenge

Fig. 1: Summary of the main inputs, variables and processes in the model used in this study.

"typical" values in the model. Optimising these parameters via data from individuals, as carried out here, is a natural progression in developing the use of the model.

Inputs to the BrainSignals model were three measured systemic signals (Fig. 1b): mean P_a, SaO_2 and $EtCO_2$ (which was assumed to be equal to arterial partial pressure of CO_2, a model input parameter). It should be noted that the experimental protocol allowed for hypoxemic episodes which were neither necessarily of the same magnitude nor of the same duration. A single challenge cannot simply be treated as a drop in oxygen, as a number of other systemic effects may be simultaneously occurring, thus extrapolating from one hypoxemic challenge to the next becomes nontrivial. The signals used to provide comparison between the modelled and measured data were the NIRS signals derived from the difference in the changes in tissue oxy- and deoxy-haemoglobin concentrations ΔHbdiff. The unweighted mean distance between measured and modelled values of ΔHbdiff during the challenge gives a quantifiable measure of the success of the model at reproducing the signals.

2.2. *Model optimisation*

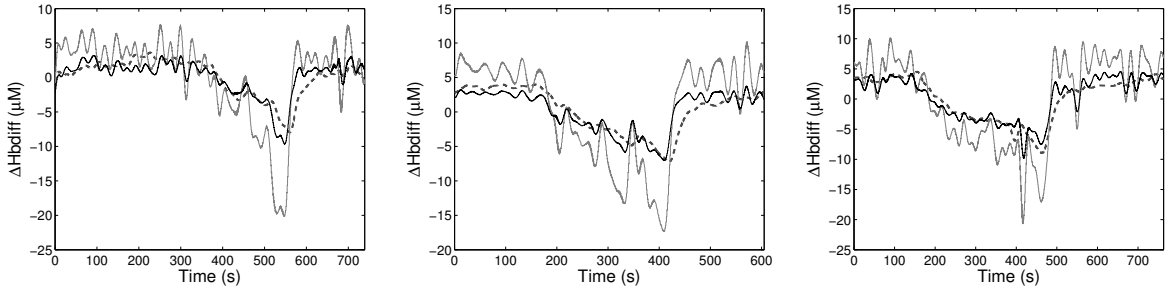
Discussion with clinical collaborators used to establish which model parameters might be expected to show widest physiological variation and were potentially of most clinical use, combined with preliminary sensitivity analysis led to a choice of seven model parameters to be altered in the optimisation: the normal venous-arterial volume ratio, VARn, blood concentration of haemoglobin [Hb], a typical arteriolar radius r_n, a dimensionless parameter u, representing normal energy demand, R_O and R_P, the strength of cerebral blood flow (CBF) regulation in response to arterial O_2 levels and changes in blood pressure respectively, τ_P, the typical time-constant for the pressure autoregulation response. All other model parameters were fixed at default values.

For each of the three challenges, an optimisation was carried out to find values of the seven optimisation parameters which minimised the distance between the model and the data. To assess the ability of the optimisation process to improve the model's prediction of unseen data, the optimisation of one challenge was used to predict the behaviour of the other challenges. The overall prediction factor is the average percentage improvement in the distances pre and post optimisation obtained from using each optimisation to predict the remaining unseen challenges. This value quantifies the average increase in predictability of the signal during a challenge given knowledge of one other challenge.

3. Results

The modelled and measured signals for each challenge are shown in Fig. 2, the corresponding values of distances along with the average of all 3 challenges are shown in the first two rows of Table 1. These numbers quantify the maximal ability of the model-class to reproduce the signals individually. From Table 1 we see that the average weighted distance between modelled and measured ΔHbdiff was reduced from 0.908 to 0.261, an improvement of 71.26%. The prediction factors for each challenge, and their average, are presented in the third row of Table 1. This row is read as follows: consider the entry for challenge 1 this value means that the prediction of the value of ΔHbdiff for challenge 1 was on average 66.94% improved by optimisating the model to data from a different challenge. Table 1 shows that on average there is a considerable improvement in the prediction of ΔHbdiff, following model individualisation.

In addition to the haemoglobin chromophores, changes in oxidation state of the Cu_A centre in cytochrome *c* oxidase (ΔoxCCO) known to be a significant NIR absorber were measured. Table 1 shows that the distances between the unoptimised model and the measured data for all three challenges are small and the improvement post optimisation averaged 13.64%. However, whilst on average the prediction factors show a small improvement, for challenge 3 when optimising the model on data from the other challenges results in a small decrease in predictive accuracy.



(a) Challenge 1 (b) Challenge 2 (c) Challenge 3

Fig. 2: Modelled and measured ΔHbdiff signals during hypoxic challenges. Bold lines are the optimised model output, grey lines the unoptimised model while the dashed lines are measured data.

Table 1: Signal-to-data distances and prediction factors for each challenge and the average for all three challenges.

ΔHbdiff	Challenge 1	Challenge 2	Challenge 3	Average
Unoptimised distances	0.853	0.983	0.889	0.908
Optimised distances	0.273	0.260	0.250	0.261
Prediction factors	66.94%	71.01%	62.08%	66.67%
ΔoxCCO				
Unoptimised distances	0.254	0.224	0.233	0.237
Optimised distances	0.215	0.194	0.205	0.205
Prediction factors	7.87%	3.57%	-2.58%	2.96%

4. Discussion

We have shown that the BrainSignals model has some success at simultaneously reproducing qualitative and quantitative behaviour of NIRS measured physiological signals during a hypoxemic challenge. Even prior to optimisation *with default parameter values* the measured and modelled values appeared on visual inspection to be a reasonable match. As all three challenges show significant differences post optimisation, a mismatch between modelled and measured values of ΔHbdiff may be at least partly attributable to the choice of model parameters. As ΔHbdiff is a difference between two measured signals ΔHbO_2 and ΔHHb it is possible that some correlated measurement errors cancel, leading to an improved signal-to-noise ratio. For the ΔoxCCO signals the signal-to-noise ratios were low and the unoptimised model could reasonably reproduce the measured signals. However, the optimisation process did not greatly reduce the model-to-data distance. It is worth noting the interpretation of the physiological meaning of ΔoxCCO is nontrivial, having been extensively investigated as a marker of cellular oxygen metabolism and a measure of cerebral well being.

Interpretation of optical measurements is key to their use in clinical applications, from the preliminary results presented in this work it can be seen that there is scope for modelling in the interpretation of NIRS signals and for individualisation to improve the predictive performance of the model. Thus, loosely speaking, knowledge of the NIRS data during one challenge for an individual improves the ability of the model to predict the behaviour of NIRS signals in subsequent challenges. However, further analysis is required across a larger study of both individuals and signals.

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