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New methods for assessing the control of blood flow in the brain

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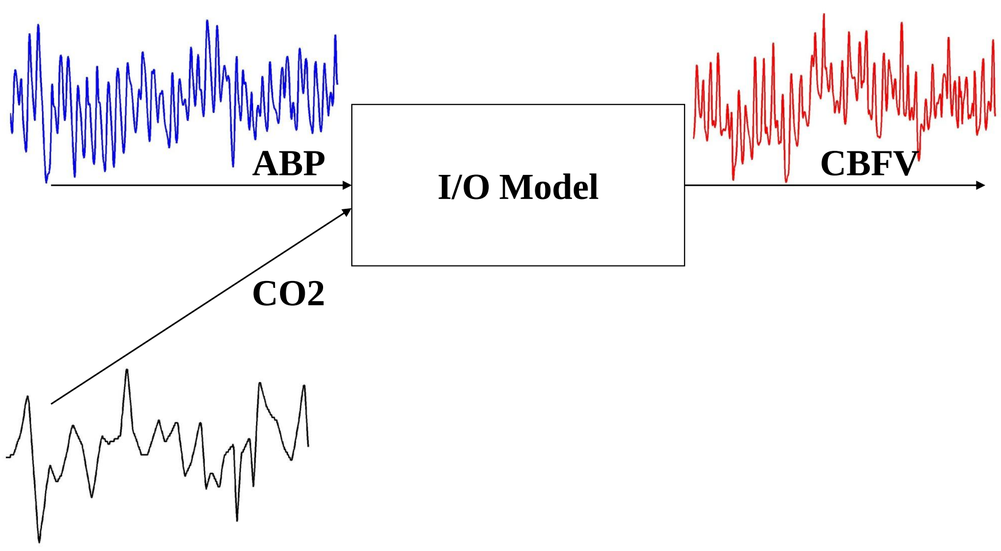
Introduction

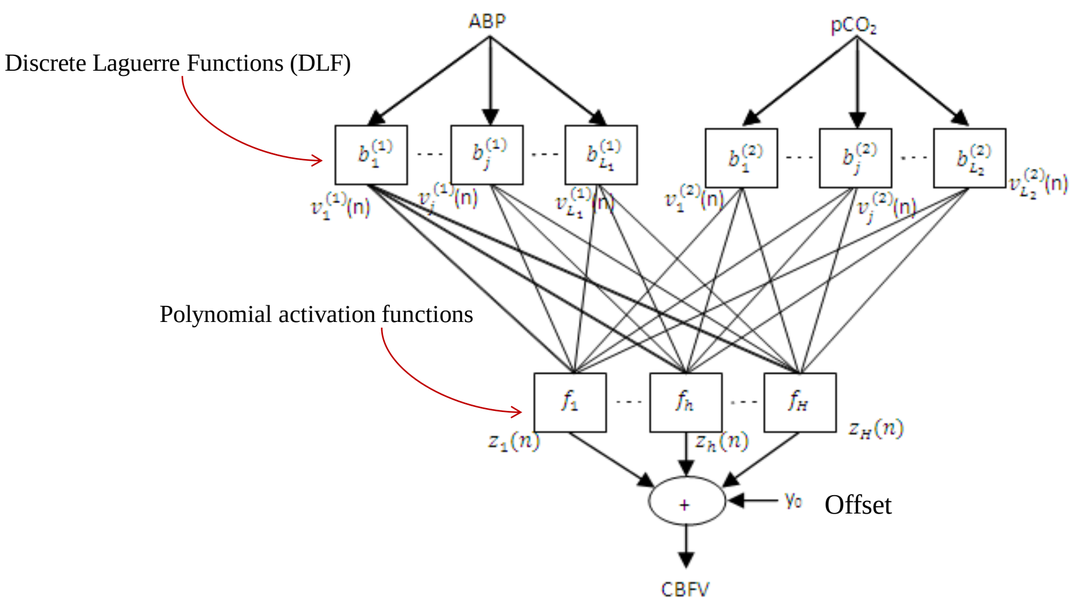
- **Cerebral autoregulation** (CA) is an active process by which blood flow to the brain is controlled at an approximately steady level despite changes in the arterial blood pressure.
- CA is considered to be an important mechanism in the development of some strokes, and also in the occurrence of the secondary damage following stroke, as well as in trauma, neonatal intracranial haemorrhage etc.
- The physiological control system is highly complex and is not fully understood.
- CA can be measured from the response of cerebral blood flow (CBF) to steady-state (static) or transient (dynamic) changes in the arterial blood pressure (ABP). The latter is generally less 'aggressive' to patients; even spontaneous variability in resting subjects can be exploited.
- There are no 'gold-standard' methods for assessing dynamic autoregulation, and clinical use is still very limited.
- Input-output models can be used to assess autoregulation, but best model structure is still unclear.
- **Objective:** find optimal model orders for nonlinear, multiple-input models based on Volterra model, and benefit of including pCO2 as a secondary input to the model.

Model-based assessment of Autoregulation

- CBF is affected by ABP, arterial CO2 pressure (pCO2), as well as other factors. This can be modelled as follows:



- Linear models can provide relatively good results, but there is evidence of nonlinearity in the autoregulatory system (3).
- Following previous work (2) we use Wiener Laguerre models, up to 2nd order.



Model comparisons

- Data from fifteen healthy adult volunteers were collected during normocapnia, hypercapnia (inhaling a 5% CO2/air mixture) and back to normocapnia, with subjects resting supine. CBFV (from transcanial Doppler Ultrasound), ABP (from a Finapres device) and pCO2 (from capnograph) were collected for approximately 5 minutes in each condition. Beat-averaged mean ABP and CBFV were obtained, and end-tidal CO2 was used as an estimate of arterial pCO2. Data were resampled at 5 Hz.
- Model parameters were estimated (least-mean-square fit) over half of each recording (training data), and evaluated over the remainder (validation data). For each model order, normalized mean-square errors (NMSE) were calculated by applying the model to the data (training and validation) and normalizing over the power of that data segment.
- Optimal orders were found for Single Input (ABP) Single Output (CBFV) and Multiple Input (ABP and pCO2), Single Output (CBFV) models, for each recording, and averaged over the 45 measurements (Table 1) .

TABLE 1 The NMSE% results for error averaged for each model.

Model	Training NMSE%	Validation NMSE%	Average Number of Parameters in model
k10 (linear, single-input)	16.21±8.51	16.28±7.08	6
k10,k01(linear two-input)	14.50±7.30	15.28±6.44	7
k10,k20,(nonlinear; self-kernels*, single-input)	15.13±7.44	16.18±7.17	6
k10,k11,(nonlinear; cross-kernels*, two-inputs)	15.18±7.49	16.14±6.97	6
k10,k01,k20,k02,k11,(nonlinear; self-kernels, cross-kernels, two-inputs)	14.16±7.70	14.60±6.13	9

* Self kernels use products of samples from the same signal, and cross-kernels use products of samples from different input signals.

- When averaging the NMSE across all recordings for each model order, the minimum was found to be 20.48%, for a linear SISO model (ABP as input) with four filterbanks (i.e. 5 parameters), giving an impulse response length of 5.4 seconds. pCO2 was not found to be included in the optimal model.

Conclusions and Outlook

- The improvement in minimal NMSE due to including pCO2 is small (table 1). The second-order self and cross-kernels showed that the nonlinearity is small, in agreement with previous work (3). This may be partly due to the small amplitude range found in spontaneous variability of ABP, pCO2 and CBFV.
- Cross-kernels (interaction between ABP and CO_2) had the strongest non-linear effect in reducing the NMSE.
- When a fixed model order is to be applied to all recordings, a 4th order SISO is recommended (minimum NMSE).
- In the continuation of this work, new experimental protocols, in which higher variations in blood pressure and pCO2 are induced, will be employed. The aim is to allow more robust detection of impaired autoregulation in patients.

References

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