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# A Complexity Analysis for Normal Cerebral Blood and CSF Flow

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# A Complexity Analysis for Normal Cerebral Blood and CSF Flow

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## Abstract

Cerebro-spinal fluid (CSF) exhibits pulsatile flow due to systolic and diastolic blood flow in cerebral arteries and veins. We describe an investigation of the relationship between CSF flow and arterial & venous blood flow using principle component analysis (PCA). The study used Phase-Contrast Magnetic Resonance Images (PC-MRI) of 16 volunteers with no known CSF abnormalities. The immediate outcome is a linear model relating normal flows, which can be used as a comparative tool to identify abnormal flows due to disease. However, the PCA analysis also places an upper limit on the number of independent parameters required in any non-linear, physical model of the system. This could ultimately inform the development of such a model, allowing identification of the underlying biological mechanisms leading to abnormal flow in disease.

## 1 Introduction

It is widely believed that abnormal behaviour in CSF flow is due to changes in ventricular size, aqueductal diameter, brain tissue compliance, and cerebral blood flow [1]. In diseases such as vascular dementia and hydrocephalus, the normal equilibrium between blood and CSF flow is disturbed, and it is important to know the mechanisms of these flows and their relationship.

PC-cine MRI can be used to observe the flow through Basilar (BA) & Carotid (CA) Arteries, Superior Sagittal Sinus (SSS) and Aqueduct (AQ), Foramen Magnum (FM) with different velocity encoding [2]. We acquired 16 images within one heart beat by averaging over 3-4 minute scanning duration depending on each subject's heart rate.

In previous work [3], we explored the possibility of developing a physical model of cerebral blood and CSF flows, based on the identification of an equivalent electrical circuit. Instability in the model parameters during optimisation indicated over-specification of this model, leading to a requirement for an estimation of the number of independent modes of variation in the data. In this paper, we describe the use of PCA to explore correlations amongst measurements of cerebral blood and CSF flows in 16 normal volunteers. The resulting linear model of normal flows can immediately be used to identify abnormality due to disease. The flows must be subject to linear correlations due to conservation of fluid: an instructive analogy is provided by Kirchhoff's Laws, the set of linear relationships based on conservation of current that are used to analyse arbitrary electrical circuits. Therefore, the analysis provides a valid empirical model of the flow processes. However, PCA analysis also provides an upper limit on the number of independent modes of variation in the flow data. This estimate can inform the development of non-linear, physical models of normal flow. Ultimately, such models could provide a comparative tool for identifying the biological origins of abnormal flows due to disease.

## 2 Materials and Methods

### 2.1 Subjects and MR Image Acquisition

In this study, we have included 16 healthy male volunteers (mean age 35.5) with no known neuro-biological abnormality. For each subject, we acquired flow images of CSF at AQ and FM, arterial blood flow images at BA, CA, and venous blood flow at SSS. Sagittal T1-weighted images and phase-contrast angiography scout images

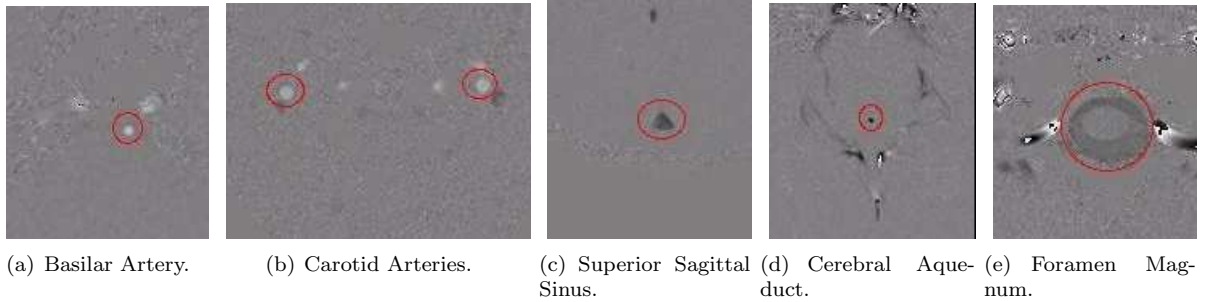


Figure 1: Typical MR images of the vessels in which flows were measured.

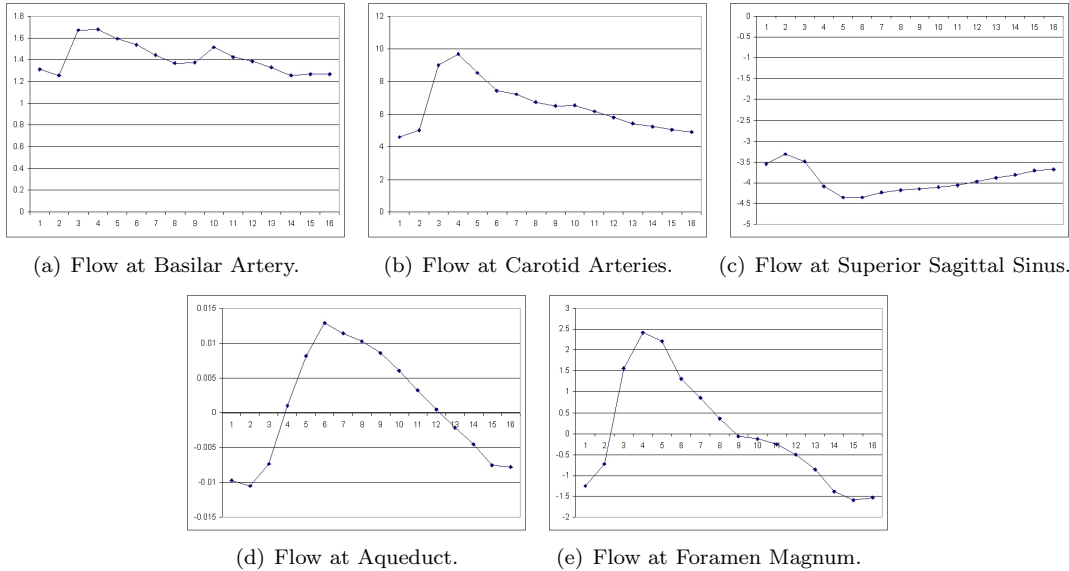


Figure 2: Mean flow results.

were acquired to identify acquisition plane for each subject. Images acquired are for one heart beat and there are 16 retrospectively cardiac-gated cine-PC images. All subjects are scanned at 3T Phillips medical system using electrocardiogram (ECG) cardiac gating. Image parameters were flip angle 10-15, 5-7mm slice thickness, TR 8.82 - 22.13, and TE 8.14 - 14.39.  $V_{enc}$  (velocity encoding) for AQ & FM is set at 10cm/sec, 90cm/sec for BA and CAR, and 60cm/sec for SSS. Scan time depended on the subject's heart rate and was usually 3-4 min for each region: total scanning time was 20-30min including scout imaging.

## 2.2 Image processing

Typical images at a single time point for each regions are shown in Figure 1. High intensity values represent systolic flows, and low values represent diastolic flows. AQ and FM sequences contain both systolic & diastolic flows, BA & CA sequences contain only systolic positive flow images, and SSS sequence contain diastolic negative flow images only.

Flows	AQ	BA	CA	FM	SSS
AQ	1.0	-	-	-	-
BA	0.42	1.0	-	-	-
CA	0.47	<b>0.95</b>	1.0	-	-
FM	0.56	<b>0.92</b>	<b>0.97</b>	1.0	-
SSS	<b>0.95</b>	0.43	0.47	0.54	1.0

Table 1: Correlation values between flow means

The AQ flow was computed by fitting velocity images in the region over the cerebral aqueduct with a quadratic function, and integrating the area under this curve for positive values of the fitted function. The BA & CA flow

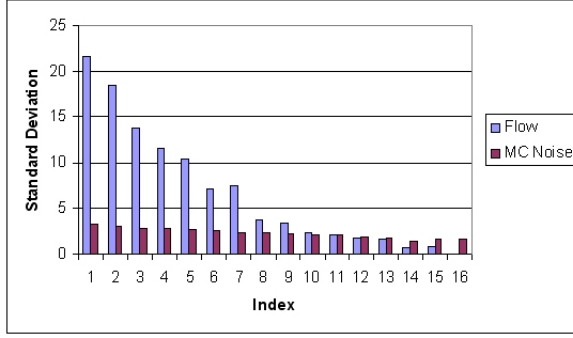


Figure 3: Histogram of standard deviations

was estimated from the sum of flow values in the foot-to-head direction within the region of the arteries, defined by thresholding the magnitude flow images. The flow into the FM and SSS is obtained in the same way as BA flow, but in the future FM regions could be automatically located using active shape models.

Typical flow curves obtained from the MR images are shown in Figure 2. Note that FM flow follows closely to CA & BA flow and peak delay between CA & BA flow and AQ flow. Correlations between the various flow measurements were calculated, and are given as absolute values in Table 1. Significant correlations ( $\geq 0.75$ ) are shown in bold. There are strong correlations between arterial in flows and CSF flow at FM, and venous out flow and aqueductal flow. However, there is no apparent correlation between arterial and venous blood flow.

### 2.3 Principle Component Analysis

The data consisted of five flow measurements  $k$  (AQ, BA, CA, FM, SSS) for each of the 16 subjects  $i = 1 \dots N$ , with 16 time points for each flow. They were concatenated into one 80-dimensional vector for each subject, giving a  $16 \times 80$  data matrix. The aim was to apply PCA in a quantitative statistical manner, explicitly making use of singular-value decomposition (SVD) as a hyperplane fit to the data. This procedure required that all of the input data had homogeneous errors. Therefore, each individual flow measurement  $x_{k,i}$  was first weighted by the standard deviation  $\sigma_k$  ( $k = 1 \dots 5$ ) derived from reproducibility experiments. The covariance matrix of  $K_{x'}$  of the input data was then calculated for all  $N$  subjects using

$$K_{x'} = \frac{1}{N-1} \sum_i^{i=N} (\mathbf{x}'_i - \mathbf{m}_{x'}) (\mathbf{x}'_i - \mathbf{m}_{x'})^T \quad (1)$$

where  $\mathbf{x}'_i = \mathbf{x}_i / \sigma_{\mathbf{k}}$  and  $\mathbf{m}_{x'}$  is mean value for each time point of flow. This produced an 80x80 dimensional matrix. SVD was then applied to perform PCA on the covariance matrix, using

$$A = UWV^T \quad (2)$$

where  $A =$  covariance matrix  $K_x$  (80x80), and  $W$  is a diagonal matrix whose values are the eigenvalues of the  $K$  matrix.  $U$  and  $V$  are 80x80 orthogonal matrices whose columns are the eigenvectors ( $\mathbf{e}_j$ ) of the  $K$  matrix.

## 3 Results

An 80-dimensional Monte-Carlo simulation was performed using a unit Gaussian noise model, in order to estimate the noise in the analysis. The results of square-root eigenvalues from the flow data and synthetic Monte-Carlo noise are shown in Figure 3. Figure 4 shows the first seven eigenvectors. The eigenvalues converge to the noise from the 8<sup>th</sup> onwards, indicating that a purely linear model of this flow data can be generated using only seven parameters.

## 4 Conclusions

Diseases such as vascular dementia and hydrocephalus may destroy the equilibrium normally present between cerebral blood and CSF flows. The ability to model the flow processes present in normal subjects would allow the

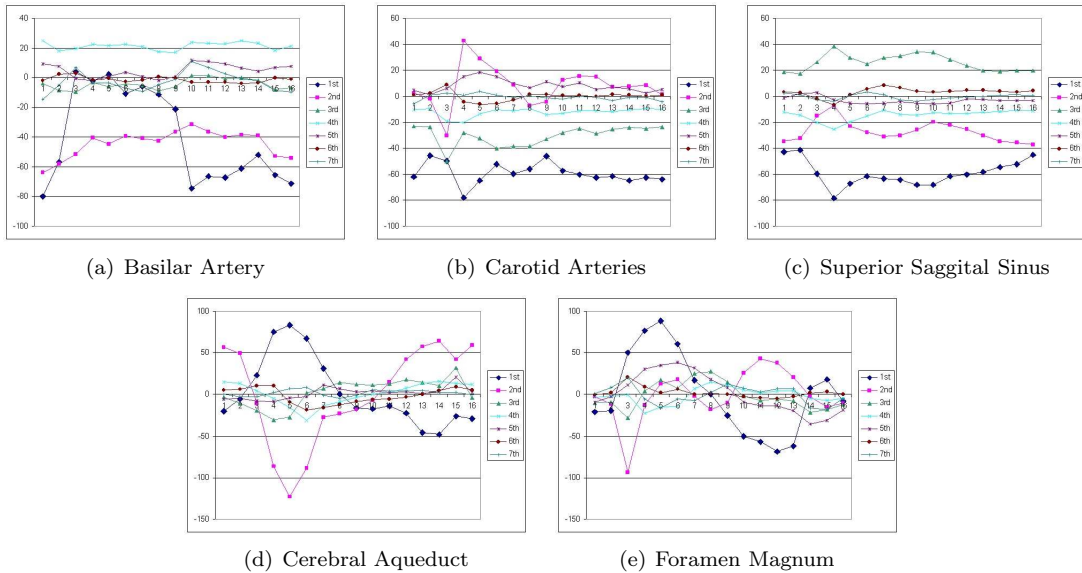


Figure 4: First 7 Eigenvectors for each 16 elements, weighted by their eigenvalues.

identification of these disease-related abnormalities. In previous work [3], we explored the possibility of developing a physical model of cerebral blood and CSF flows, based on the identification of an equivalent electrical circuit. Instability in the model parameters during optimisation indicated over-specification of this model, leading to a requirement for an estimation of the number of independent modes of variation in the data.

In the wider context, this work acts as an exemplar for the quantitative application of PCA. By ensuring that the input data have homogeneous errors, the singular-value decomposition applied in PCA is explicitly used as a hyperplane fit. This allows the extracted eigenvalues to be interpreted as measures of the signal present above the background noise level i.e. as an absolute measure of the information content of the data. In this paper we have described such an estimation process, and have demonstrated that a purely linear model of cerebral flow requires only seven parameters. As stated in the introduction, conservation of flow volume implies that such a low parameter system would be expected. This is to be contrasted with previous work [4] in which the non-linear transformation applied to quantitative measurements of flow in order to obtain a space of uniform errors resulted in a non-linear system that could not be compactly described using PCA. The resulting linear model described here is immediately applicable as an empirical model of the normal flow processes, and so can be compared to flows observed in disease states in order to identify any abnormalities. However, a physical (non-linear) model of the flows would have greater utility since it would, in addition, allow identification of the underlying biological origins of the abnormal flow states. The work presented here can be used to inform the development of such a model, placing an upper limit on the number of parameters required and thus avoiding problems due to over-specification. Alternatively, independent component analysis (ICA) could be used to approach such a physical model.

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