# Empirical estimation of the Grubb exponent using simultaneously acquired CBF and static magnetisation changes

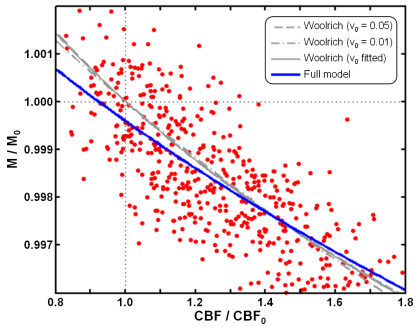
Kevin Murphy[1], Ashley D Harris[1], and Richard G Wise[1]
[1]CUBRIC, School of Psychology, Cardiff University, Cardiff, United Kingdom

***Introduction:*** For the majority of calibrated BOLD techniques, the relationship between cerebral blood volume (CBV) and cerebral blood flow (CBF) is assumed. This non-linear relationship is often described as $(CBV/CBV_0) = (CBF/CBF_0)^{\alpha}$ ,where the subscript 0 denotes baseline values. In 1974, Grubb et al. measured α to be 0.38 [1], a value that remains in common use. Recently, lower estimates of ~0.16 have been suggested based on modelling [2] and $CO_2$ challenges [3]. Increases in CBV are reflected in variation of the MR longitudinal equilibrium or static magnetisation ($M_0$). Using ASL to measure $M_0$ and CBF changes, Woolrich et al. [4] developed a simple model to calculate α. Relative CBV was determined by scaling $M_0$ changes with a baseline CBV estimate, assuming that all $M_0$ differences are related to CBV changes. However, CBV increases will cause unknown effects on extravascular spins, invalidating this assumption. This study proposes an extended model that accounts for both effects on $M_0$ to improve the measurement accuracy of α.

***Theory:*** *Woolrich model*: $(1+(1-1/v_0)*\Delta M/M_0) = (CBF/CBF_0)^{\alpha}$, where $v_0$ is an assumed baseline CBV. *Extended model*: assume two compartments, blood (B) and non-blood (NB). Baseline static magnetisation is given by $M_0 = M^{NB} + M^{B}$. During changes in CBV allow both $M^{NB}$ and $M^{B}$ to vary: $M = M_0 + \Delta M^{NB} + \Delta M^{B}$. Assume (using a principle of conservation of total volume) that changes in the non-blood compartment are proportional to changes in the blood compartment: $\Delta M^{NB} = C_1*\Delta M^{B}$. Assume that changes in M in the blood compartment are related to CBV changes: $(CBV/CBV_0) = C_2*((M^{B}+\Delta M^{B})/M^{B}) = (CBF/CBF_0)^{\alpha}$. After substituting and rearranging, we get: $M = ((1+C_1)/C_2) * (M_0 - M^{NB}) * [(CBF/CBF_0)^{\alpha} - C_2] + M_0$, where M, $M_0$ and $CBF/CBF_0$ are known and α, $M^{NB}$, $C_1$ and $C_2$ are unknowns.

***Methods:*** 15 subjects participated in 2 sessions in which scans were acquired at 3T using a PICORE QUIPSS II dual-echo ASL sequence (12 slices, 64 spiral, TE1=3.3ms, TE2=29ms, TR=2200ms, FOV=22cm, slice thickness/gap=7/1mm, TI1=600ms, TI2=1500, reps=490). Twenty to 30s blocks of visual and fingertapping tasks with separate timings were presented simultaneously whilst end-tidal $CO_2$ levels where changed at 2 minute intervals randomly between baseline, +4mmHg and +8mmHg values by adjusting inspired gases. An exponential model ($S = M e^{-TE \cdot R_2^*}$) was fit to both echoes at each time point to yield M and $R_2$* values. Tag and control M values were separated, interpolated to the TR, subtracted and averaged to yield the CBF and M time series respectively. These time series were averaged over grey matter in both the visual and motor cortices (defined by a group analysis on the $R_2$* data) for each subject, detrended and averaged across subjects for each session. Three models were fit to the four datasets (2 ROIs, 2 sessions) using a non-linear fitting routine (matlab's *nlinfit*) to yield values for α: 1) the *Woolrich model* assuming a $v_0$ value as in the original implementation, 2) an extension of the *Woolrich model* that allows the fitting routine to estimate $v_0$ and α simultaneously, and 3) the newly proposed *Extended model* (see Fig 1 for examples).

**Figure 1:** Model fits in visual cortex (sess2)




***Results:*** The results are summarised in Table 1. Assuming a baseline CBV of $v_0$=0.05, the *Woolrich model* yields reasonable α values in the visual cortex (0.168 and 0.127) but unfeasibly low values in the motor cortex (~0.04). Assuming a lower $v_0$=0.01, the motor cortex α values increase to ~0.2, thus demonstrating the need for accurate baseline CBV estimation with this model. Fitting both α and $v_0$ in the *Woolrich model* gives high but repeatable α values (~0.6) in the motor cortex with a low estimation of blood volume (~0.003). In the visual cortex, the fitting routine only reached a solution in data from one session with α=0.214 and $v_0$=0.03. Using this estimation of baseline CBV, the other session yields a similar α=0.28. Due the complexity of fitting four unknowns, the *Extended model* was only successful in one session for each of the visual and motor cortices. Fitted α were ~0.53 in both sessions with $C_1$~0.53 and $C_2$~0.94. Using these fitted constants the non-successfully fitted data yields lower α values of 0.35 and 0.24. The discrepancy between sessions demonstrates the need to fit all unknowns together for each region and session.

| | | Woolrich (fixed $v_0$) | | Woolrich (fitted $v_0$) | | Extended model | | |
|---|---|---|---|---|---|---|---|---|
| | | α ($v_0$= 0.05) | α ($v_0$= 0.01) | α | $v_0$ | α | $C_1$ | $C_2$ |
| Visual: | sess1 | 0.168 | 0.778 | 0.280 | using 0.0298 | 0.35 | using 0.57 | using 0.95 |
| | sess2 | 0.127 | 0.603 | 0.214 | 0.0298 | 0.507 | 0.57 | 0.95 |
| Motor: | sess1 | 0.041 | 0.207 | 0.615 | 0.0030 | 0.560 | 0.49 | 0.93 |
| | sess2 | 0.045 | 0.226 | 0.627 | 0.0033 | 0.240 | using 0.49 | using 0.93 |

**Table 1:** The estimated Grubb exponent, α, and other fit parameters for each of the models. When the non-linear fitting routine failed to reach a stable solution, fit parameters from the same cortex where chosen to provide an estimate of α (indicated by red).

***Discussion:*** This study proposes a model to use simultaneously acquired static magnetisation and CBF measurements to determine the Grubb exponent. We have demonstrated using the simpler *Woolrich model*, it is possible to fit for baseline CBV (rather than assuming $v_0$ as in the original implementation) alongside α to give repeatable values and to reveal regional differences. The proposed *Extended model* drops the assumption that all changes in M are related to CBV changes and allows contributions from both blood and non-blood compartments. This model can give reasonable α values along with the proportionality constants $C_1$ and $C_2$. The estimated $C_1$ value of ~0.5 indicates that for a given CBV increase, changes in M due to the blood compartment ($M^{B}$) are twice as large as non-blood compartment-related changes ($M^{NB}$). The $C_2$ value close to unity demonstrates that nearly all changes in $M^{B}$ originate from CBV increases, as expected. One drawback of this modelling approach is that the current non-linear fitting routine is prone to failure. Improvements in data quality and experimental design optimisation along with a better understanding of the fit parameters will lead to more reliable estimations of the Grubb exponent using the *Extended model*. In the future, it may be possible to estimate α on a subject-by-subject and region-by-region basis with this technique.

**References:** [1] Grubb, Stroke 5:630; [2] Griffeth, NeuroImage 58:198; [3] Chen, NeuroImage 53:383; [4] Woolrich, MRM 56:891