

## My notes on the BOLD model in the current literature (Sept 2003)

Ying Zheng, Dept of Psychology, Univ of Sheffield, UK

The BOLD signal is related to the transverse relaxation rate of deoxyhaemoglobin  $R_2^*$  as

$$\frac{\Delta BOLD}{BOLD} \cong -T_E * \Delta R_2^* \quad (1)$$

where  $T_E$  is the echo time,  $\Delta R_2^*$  is the difference between  $R_2^*$  and its baseline value. Ogawa et al (1993) used Monte Carlo simulation to show that for large blood vessels (radius  $> 8\mu m$ )  $R_2^*$  is linearly related to the blood volume fraction  $V_f$  and the susceptibility induced frequency shift  $\nu$ . For small blood vessels (radius  $< 8\mu m$ ),  $R_2^*$  is quadratically related to  $\nu$ .

A more explicit model relating  $R_2^*$  to blood susceptibility as well as the magnetic field strength was derived by Yablonskiy and Haacke (1994) assuming blood vessel network as randomly distributed cylinders with random directions of their axes. The model can be written as

$$R_2^* = \frac{4\pi}{3} \gamma B_0 V_f \Delta \chi_{b-w} \quad (2)$$

where

$\Delta \chi_{b-w}$  = susceptibility difference between blood and water (see Appendix at the end)

$B_0$  = external magnetic field strength

$\gamma$  = angular gyromagnetic ratio (i.e. the ratio of the magnetic moment of a rotating charged particle to its angular momentum).

=  $2.675 \times 10^4$  rad/sec/Gauss for the hydrogen nucleus

= 42.58 MHz in 10 kG

=  $2\pi \times 42.58 \times 10^6$  rad/s.

The assumptions made in deriving the above model are:

- (a) the average number of objects in the volume of interest is much greater than 1;
- (b) the volume fraction of blood is much smaller than 1;
- (c) the radius of a blood vessel is much smaller than both its length and curvature, and the blood vessel length is much larger than the average distance between the vessels;
- (d) the model was derived assuming the medium extend to infinity.

The last assumption may seriously affect the accuracy of the model if the area of interest lies near the surface of the brain.

From my Appendix at the end, equation (2) can be re-written as

$$R_2^* = \frac{4\pi}{3} \gamma \mathcal{B}_0 V_f H_{ct} [(1-S)\Delta\chi_{r-o} + \Delta\chi_{o-w}] \quad (3)$$

where

$H_{ct}$  = haematocrit concentration;

$S$  = blood oxygen saturation;

$\Delta\chi_{r-o} = 1.83 * 10^{-7}$  (cgs) = susceptibility of deoxygenated haemoglobin with respect to oxygenated haemoglobin;

$\Delta\chi_{o-w} = -0.26 * 10^{-7}$  (cgs) = susceptibility of oxygenated haemoglobin with respect to water.

Because  $\Delta\chi_{o-w}$  is seven times smaller than  $\Delta\chi_{r-o}$ , most models seem to ignore  $\Delta\chi_{o-w}$ . However even at low saturation  $S = 0.5$ , contribution from the  $\Delta\chi_{o-w}$  term will account for 22% of the signal  $R_2^*$ . At higher saturation  $S = 0.7$ , contribution from the  $\Delta\chi_{o-w}$  term will account for 32% of the signal  $R_2^*$ . Hence it may not be wise to discard the term  $\Delta\chi_{o-w}$  in eqn.(3) above. As  $\Delta\chi_{o-w}$  is negative, ignoring it has the effect of over-estimating the relaxation rate  $R_2^*$ .

Nevertheless, Yablonskiy and Haacke (1994) has ignored the  $\Delta\chi_{o-w}$  term, consequently producing the model:

$$R_2^* = \frac{4\pi}{3} \gamma \mathcal{B}_0 V_f H_{ct} (1-S)\Delta\chi_{r-o} \quad (4)$$

The term  $\Delta\chi$  in their model is equivalent to  $H_{ct}\Delta\chi_{r-o}$  in the above equation. And the choice of  $\Delta\chi = 0.8 * 10^{-7}$  implies the assumption that the haematocrit concentration is 0.44.

The model for the BOLD signal can thus be written as

$$\begin{aligned} \frac{\Delta BOLD}{BOLD} &\cong -T_E * \Delta R_2^* \\ &= -T_E * (R_2^* - R_{20}^*) \\ &= -T_E * \frac{4\pi}{3} \gamma \mathcal{B}_0 H_{ct} \Delta\chi_{r-o} \{V_f (1-S) - V_{f0} (1-S_0)\} \\ &= T_E * \frac{4\pi}{3} \gamma \mathcal{B}_0 H_{ct} \Delta\chi_{r-o} V_{f0} (1-S_0) \left\{ 1 - \frac{V_f (1-S)}{V_{f0} (1-S_0)} \right\} \end{aligned} \quad (5)$$

By noting that  $V_f (1-S)$  and  $V_{f0} (1-S_0)$  are the volumes of deoxyhemoglobin and its baseline respectively, and that the quantity

$$M = T_E * \frac{4\pi}{3} \gamma B_0 H_{ct} \Delta\chi_{r-o} V_{f0} (1 - S_0) \quad (6)$$

is a function of physical parameters of the magnet and the baseline values only, eqn.(5) can be re-written as

$$\frac{\Delta BOLD}{BOLD} \cong M(1 - q) \quad (7)$$

where  $q = \frac{Hbr}{Hbr_0} = \frac{V_f(1 - S)}{V_{f0}(1 - S_0)}$ . In most circumstances,  $q$  is less than unity. Under these conditions,  $M$  is the upper bound for the BOLD signal. Conditions under which  $q$  is greater than unity will be discussed later. In such cases, negative BOLD signals will be obtained.

**Now doing it properly.....**

If the model is to include the  $\Delta\chi_{o-w}$  term, then the BOLD signal can be calculated from

$$\frac{\Delta BOLD}{BOLD} \cong M(1 - q) + M'(1 - v) \quad (8)$$

where

$$M' = T_E * \frac{4\pi}{3} \gamma B_0 H_{ct} \Delta\chi_{o-w} V_{f0} \quad (9)$$

and

$$v = \frac{V_f}{V_{f0}} \quad (10)$$

As  $v$  is greater than unity during neural stimulation, the BOLD estimation using eqn.(8) will be less than that using eqn.(7).

## Appendix: Susceptibility

The magnetic susceptibility  $\chi$  of a solution containing a paramagnetic agent is defined as the ratio of the magnetisation in the solution to the corresponding magnetising force. Deoxyhaemoglobin is paramagnetic and hence becomes magnetised when subjected to external magnetic force. The BOLD signal is a measure of changes in deoxyhaemoglobin due to changes in neural activity.

To find the deoxygenated blood susceptibility, the following model is used (Weisskoff and Kiihne, 1992):

$$\chi_{blood} = H_{ct} S \chi_{ox} + H_{ct} (1 - S) \chi_{deox} + (1 - H_{ct}) \chi_{plasma} \quad (A1)$$

where  $H_{ct}$  is the concentration of the haematocrit, i.e., the fraction by volume taken up by the red blood cells,  $S$  is the oxygen saturation, and  $\chi_{blood}$ ,  $\chi_{ox}$ ,  $\chi_{deox}$  and  $\chi_{plasma}$  are the volume susceptibilities of the blood, oxy- and deoxy-generated haemoglobin and plasma respectively. Clearly the susceptibility of blood is dependent on the level of oxygen saturation as well as the concentration of the haematocrit. Normally we assume that the concentration of the haematocrit remains constant.

The imaging experiment used by Weisskoff and Kiihne did not measure  $\chi_{blood}$  directly, but rather the difference in susceptibility between blood and water:

$$\Delta\chi_{b-w} = \chi_{blood} - \chi_{water} \quad (A2)$$

Because the susceptibility of plasma and that of water are almost identical, eqn.(A1) becomes

$$\Delta\chi_{b-w} = H_{ct} S \Delta\chi_{o-w} + H_{ct} (1 - S) \Delta\chi_{r-w} \quad (A3)$$

where

$$\Delta\chi_{o-w} = \chi_{ox} - \chi_{water}, \quad \Delta\chi_{r-w} = \chi_{deox} - \chi_{water} \quad (A4)$$

By plotting the variable  $\frac{\Delta\chi_{b-w}}{H_{ct}}$  against  $(1 - S)$ , Weisskoff and Kiihne fitted a straight line through the data obtained by varying  $H_{ct}$  between 13 to 80% and saturation between 20 to 98%. If eqn.(A3) is re-written as

$$\frac{\Delta\chi_{b-w}}{H_{ct}} = (1 - S) \Delta\chi_{r-o} + \Delta\chi_{o-w} \quad (A5)$$

where  $\Delta\chi_{r-o} = \Delta\chi_{r-w} - \Delta\chi_{o-w}$  is the susceptibility between fully deoxygenated and fully oxygenated red blood cells, we can see that the slope of the straight line is  $\Delta\chi_{r-o}$ , and the intercept of the straight line is  $\Delta\chi_{o-w}$ . According to Weisskoff and Kihne (1992),

$$\Delta\chi_{r-w} = 1.57 \times 10^{-7} \text{ cgs}, \quad \Delta\chi_{o-w} = -0.26 \times 10^{-7} \text{ cgs}, \quad \text{and} \quad \Delta\chi_{r-o} = 1.83 \times 10^{-7} \text{ cgs} \quad (\text{A6})$$

Note. cgs (centimetres-grams-seconds) system vs. the S.I. units (mks: metres-kilograms-seconds):  $\chi(\text{mks}) = 4\pi\chi(\text{cgs})$ .