Introduction to Modeling

The short term goal of current neurological models is to learn something about the system being modeled. While control (for instance in prosthetics), or predication (such as BlueBrain) may some day be feasible, in the short run we still have a great deal to learn about how our brain works. By learning about specific systems (the dynamics of a single person's brain), we may be able to diagnose diseases, find their causes and even someday rectify the cause. Of course by learning about various specific systems we can also learn about the general way our brains work. The reason then, for studying the BOLD model then is to be able to derive the various system parameters and understand why one brain region (say a voxel) reacts in one way, when another acts completely differently.

While the General Linear Model has been extremely effective at gleaning information about which voxels are "active" and which are not, its purpose is only to say which regions are "statistically significant". However, considering that voxels consist of millions of neurons, the reality is that a region could be active, but at some other level or time constant than expected; and be completely missed by the linear model. Studies showing activation in Cadavers of Phantoms highlight the inherant problem with the General Linear Model: a problem that mandates multiple comparison testing with very high thresholds to ensure any sort of face validity [Smith et al.(1999)Smith, Lewis, Ruttimann, Ye, Sinnwell, Yang, Duyn, and Frank]. By moving to models that actually "learn" the parameters of the model, model error will be drastically reduced allowing for much more reasonable statistical thresholds.

Of course, it is well known that many of the assumptions that the GLM makes about BOLD activation do not hold. The General Linear Model ignores the fact that the BOLD response is nonlinear, contains non-gaussian noise and most importantly that brain networks are so called "Small World Networks" [Achard et al.(2006)Achard, Salvador, Whitcher, Suckling, and Bullmore], [Smith et al.(2007)Smith, Singh, and Balsters]. Merely accounting for nonlinearities in the time-series of the BOLD response can result in significantly better estimation as shown in [Deneux and Faugeras(2006)]. But even more crucial is the recent movements away from mass- univariate models. Current mass-univariate models assume uniform connectivity from input to every voxel; yet this is obviously not the case. While violating linearity assumptions or Gaussian assumptions requires us to be more conservative, the lack of any method to switch brain circuits on and off means that any model we make for brain regions would not be Turing complete; in effect implying that humans are incapable of thought [Nordin and Banzhaf(1995)].

So called Dynamic Causal Modeling is the beginning of the next phase of neurology. DCM is the first brain study to show any significant connection between diffusion tensor imaging and actual function layout in the human brain [Stephan et al.(2009)Stephan, Titt By incorporating connections between regions and a realistic activation model, DCM corrects two of the largest problems with the GLM. While there are other techniques that may be useful in the future, they either lack physiological analogs (Artificial Neural Networks) or are extremely computationally expensive (mutual information). Given that much of the potential of the GLM has been exhausted, and that DCM is one of the first well defined methods capable of learning complicated brain circuits DCM is crucial to the future of FMRI and our understanding of the human brain.

Results

The particle filter shows great promise in being able to learn a variety of different regional activation parameters. We have performed tests with a random binary pulse train as input to a simulated region and then tested the particle filter's ability to estimate the signal parameters. Additionally random gaussian noise with an Signal-To-Noise ratio of 2.0 was added. Figure 1 shows the pulse train, the clean signal and the noisy signal, which was the input to the particle filter. A random set of system parameters was chosen to simulate the region, which the particle filter had no knowledge of other than a mean and rough variance. The tests were performed using 10,000 particles and took approximately 4 minutes to compute.

Figure 2 shows the estimated BOLD response versus the simulated data (without noise). It is clear that as the estimated BOLD response converges to the true BOLD as time progresses. This is because more and more potential states are eliminated by system's response to new input sequences. Convergence depends highly on the input signal and the weighting function thus choice of both are extremely important. We have found that an impulse train (emulated with .1 second width square waves) gives a very good response. It is also important to choose an input with some longer hold times, at least as long as than the expected time constants, which in this case was around 8 seconds. The weighting function we have chosen is based on the exponential distribution, with a variance equal to the RMS of the signal. While it is important to converge by the end of the time-series, it is often the case that converging too fast will harm the state estimation by over- emphasizing the measurements of single time points. The rate of convergence is well within control of the user of the particle filter based on the weighting function and the frequency of re-sampling. Note that resampling can cause quantization errors due to the nature of estimating a long tailed distribution with a finite number of samples.

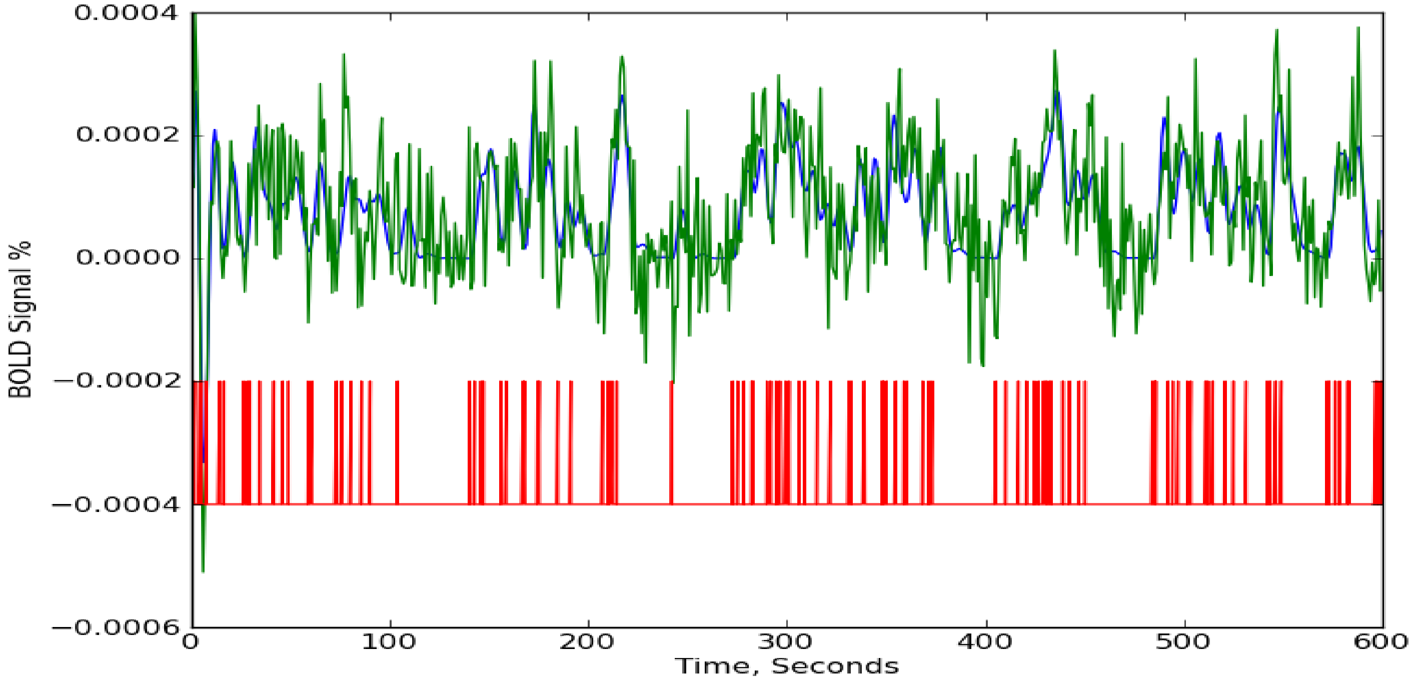

Figure 1: Simulated time-series for a single region. The red line shows the input stimulus, the blue line shows the base BOLD response, and the green line is the BOLD response with Gaussian white noise added at SNR of 2

Figure 3 shows the estimated versus simulated values for several key parameters. Notice how the variance drops as the particle filter continues. The parameters shown are V_0 which is a scaling parameter, τ_s, and τ_f which are both time constants and s_t which is a hidden state variable, estimating the flow inducing signal. Note that even though some of the parameters don't converge to the exact value, that the estimated s_t still matches the true s_t relatively well. It is often the cast that although a few parameters don't converge to their true value, one parameter may pick up the slack for another. It is of note that τ_s and τ_f do converge at least close to their true values, because they cannot be determined from steady state.

References

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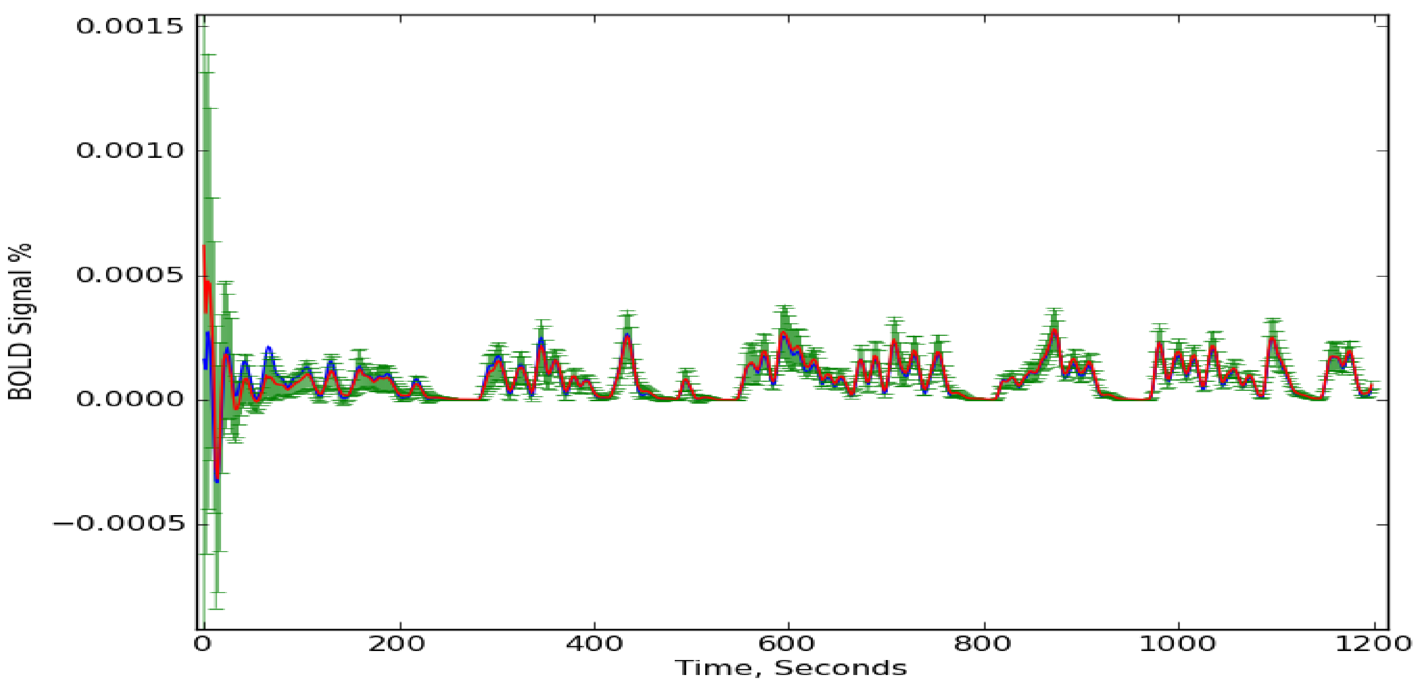

Figure 2: Particle Filter Results. The blue line is the "true" (simulated) BOLD response, the red line is the output of the particle filter with 2 standard deviations in green. Note that the error bar for time 0 is outside the scope of the image and is approximately $\pm.003$.

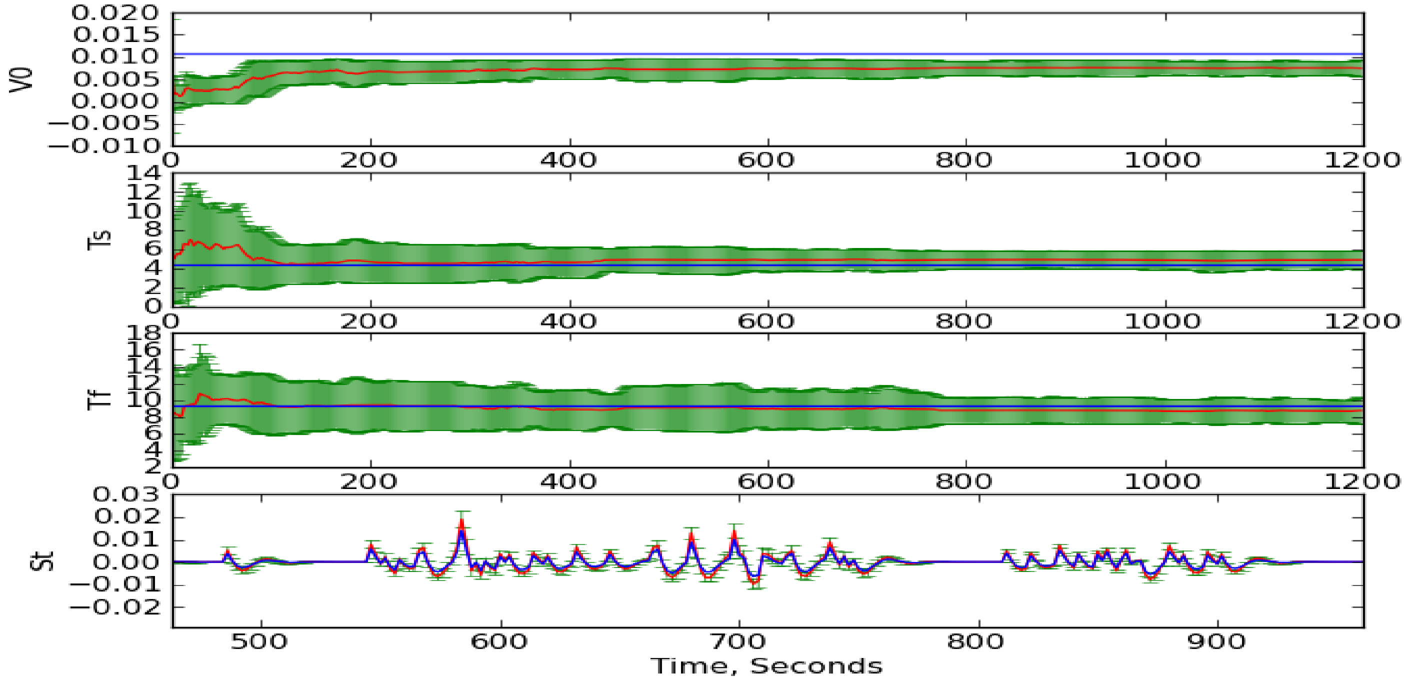

Figure 3: Particle Filter Results. The blue line is the "true" parameter and the green line is the estimated value for the parameter. Note that the timescale for S_t is different to highlight an typical stimulus response. Again 2 standard deviations are shown.

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