A BOLD Sampling Scheme to Improve the Estimation of Voxel-wise Encoding Model Parameters

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Abstract

Encoding models are a widely used data driven technique to derive functional models like the sensitivity profiles of voxels to sets of stimulus features. They are typically estimated using linear regression techniques to find a model that uses sets stimulus features as input to predict fMRI BOLD activity of a voxel as output. The regression weights represent the functional model (e.g. a voxel's receptive field). Sampling rate differences between stimulus and BOLD which can render the estimated model uninterpretable. This is typically counteracted by temporally down sampling the stimulus, which is undesirable as it causes information loss. Here we use simulations to first demonstrate that higher stimulus than fMRI sampling rates combined with regular BOLD sampling make the estimation of encoding models noisy and hard to interpret. We then demonstrate that a novel re-sampling based technique that samples the BOLD response at irregular temporal intervals alleviates these problems and allows to use the stimulus feature space with full temporal resolution for encoding model estimation.

Keywords: encoding model; re-sampling; quality assessment; fMRI; BOLD; simulation

Introduction

Encoding models are widely used for data-driven derivation of neural processing models. They are particularly useful when continuous realistic stimuli are used. They are used to associate measures of observed brain activation with features of interest derived from sensory stimuli, actions, etc. The model coefficients are interpreted as the sensitivity profile of the neural population to the stimulus features (Holdgraf et al. 2017).

A common approach to estimating encoding models is to set up a multivariable linear regression in which the predictor variables consist of stimulus features preceding the current brain activation measures. In standard experiments, both the stimulus and the brain activity are sampled at regular intervals. Furthermore, in fMRI experiments, the stimulus is typically sampled at higher rates than the BOLD response. One problem with this sampling scheme is that a linear regression predictor matrix constructed at full temporal stimulus resolution will have elevated correlations among predictors, leading to biased model coefficient estimates and thereby rendering the encoding model uninterpretable. The standard approach to mitigate this problem is to down sample the stimulus features to the BOLD sampling rate (e.g., de Heer et al. 2017). However, this is undesirable because it removes temporal stimulus variations from the model estimation that may have been relevant in driving the BOLD response.

Our study has two aims: First, we demonstrate and quantify the detrimental effects of different BOLD and stimulus sampling rates on the estimation of encoding model parameters and their predictive performance. Second, we develop and test a new BOLD re-sampling scheme with irregular temporal sampling and show that it improves the estimation of encoding model coefficients at stimulus sampling rates higher than the BOLD sampling rate. We use an fMRI BOLD simulation framework in which the ground truth of brain activity, noise, and encoding model are known. This allows for assessment of the accuracy of the model's BOLD predictions and the quality of the model.

Methods

The encoding model approach is rooted in linear systems theory. A basic assumption is that the stimulus is convolved with an impulse response function to obtain the observed brain activity. The encoding model estimation step recovers the impulse response function as the coefficients of a multivariable linear regression.

In order to generate realistic data we simulated an fMRI experiment in which an acoustic stimulus is presented and BOLD data from a brain voxel sensitive to the sound pressure envelopes are recorded. We convolve the sound pressure wave with a standard hemodynamic impulse response function (HRF, 15s duration) to obtain the voxel's simulated BOLD response. The sound pressure wave and the BOLD response were regularly sampled with 25 ms and 850 ms inter-sample interval, respectively. We added different levels of realistic fMRI noise generated with the BrainIAK toolbox (Ellis et al. 2020) to obtain five SNR (0.1, 0.25, 0.5, 1, 2) levels in the noisy BOLD signal.

The encoding model estimation step aims to recover the HRF. We estimated a multivariable regression model using scikit-learn. We used the 15-second sound envelope intervals (34 samples) before each BOLD sample as predictors. The BOLD time course (850 ms inter-sample interval) was the predicted variable. The regression coefficients are the estimated encoding model. They should ideally have the same values as the HRF used for convolution. We used a cross-validated L2 regularized optimization to estimate the coefficients. We assessed the BOLD prediction accuracy using leave-one-run out cross-validation.

We investigated two sampling schemes. In the first, the BOLD response predicted in the encoding model was sampled at the regular sampling rate and predicted from the stimulus time series at the high sampling rate. This was expected to distort the encoding model. In the second, the BOLD response predicted in the encoding model was sampled with varying intervals. We first up sampled the BOLD response to the sampling rate and then randomly picked up sampled data from the interval between two actual BOLD samples. This simulates BOLD sampling with a known temporal jitter and produced the same number of samples as the regular sampling scheme. Importantly, we constructed the regression model with the past stimulus samples for sampled BOLD time point. We repeated the encoding model estimation 100 times with different random samples and averaged the results. We expected that the irregular sampling scheme improves the estimation of the encoding model coefficients.

We assessed model quality by calculating the coefficient of determination (COD) between the predicted and the noisy BOLD response as well as the ground truth BOLD response without noise. Moreover, we compared the estimated model coefficients to the ground truth HRF.

Results

Because of space restrictions we report here only the results for SNR=0.5. However, the conclusions generalize to the other SNRs tested, in particular the realistic lower SNRs.

With the regular sampling scheme the COD calculated between the noisy and the predicted BOLD response was on average 0.19 (STD 0.07) which is realistic for a typical fMRI experiment. Interestingly, when comparing the predicted to the ground truth BOLD response it we found that the model predicted the BOLD response nearly perfectly (COD 0.96; STD 0.01). This indicates that the COD was dominated by the noise when estimated from the noisy data. Next we compared the encoding model coefficients to the ground truth HRF. We found that the COD for the encoding model is around zero (COD -0.34; STD 0.76). Together these results indicate that although the encoding model estimated from the regularly sampled models is wrong and should not be interpreted, it still makes good BOLD predictions.

With the irregular sampling scheme the COD calculated between the noisy and the predicted BOLD response is 0.6 (STD 0.12) and the COD between the ground truth and the estimated BOLD is 0.99 (STD 0.0). This indicates that BOLD prediction improved with the irregular sampling scheme. Importantly, the COD between the ground truth HRF and the model coefficients was 0.91 (STD 0.01), indicating a nearly perfect HRF reconstruction. Together these results indicate that the encoding model obtained with the irregular sampling scheme recovers the HRF well and predicts the BOLD response well.

Discussion

In this work we investigated the effects of stimulus and BOLD sampling schemes on the quality of BOLD predictions and model interpretability in an encoding model analysis. Our results indicate that even at a moderate SNR of 0.5 regular sampling of the BOLD response combined with a higher sampling rate of of the stimulus renders the encoding model coefficients uninterpretable. Importantly, The newely introduced irregular sampling scheme can greatly improve the quality of the estimated encoding model coefficients making the model better interpretable.

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