

# Nonlinear stochastic deconvolution of bolus-tracking MRI: assessment and comparison on simulated data vs other methods in presence/absence of dispersion

F. Zanderigo<sup>1</sup>, A. Bertoldo<sup>2</sup>, G. Pillonetto<sup>1</sup>, C. Cobelli<sup>1</sup>

<sup>1</sup>Information Engineering, University of Padova, Padova, Italy, <sup>2</sup>Information Engineering, University of Padova, Padova, ITALY, Italy

**Introduction.** Bolus tracking MRI allows to quantify cerebral blood flow (CBF), volume (CBV) and mean transit time (MTT) by deconvolution from arterial input function, AIF(t), and tissue concentration, C(t), measures:  $C(t)=CBF \cdot [AIF(t) \otimes R(t)]$  (eq.1), where R(t) is the tissue residue function. In particular, one obtains  $R^*(t)=CBF \cdot R(t)$  and estimates CBF from its maximum value. The most commonly used deconvolution method is singular value decomposition (SVD) [1], a nonparametric technique which is extremely fast, but shows some limitations: presence of nonphysiological oscillations in R(t) and dependence of estimated CBF values on selected threshold value as well as delay and dispersion in AIF [2,3]. More recently, other improved deconvolution approaches have been proposed including SVD using a Block-Circulant matrix (BC) [4] and Tikhonov Regularization (TIKH) [5]. In [6] we proposed a new nonlinear stochastic regularization method (NSR) able to account for smoothness and non-negativity of R(t) and to handle dispersion of AIF. Here NSR is tested and validated on simulated data and results compared to those obtained by using SVD, BC, and TIKH.

## Materials and Method

**Simulated Data.** Data were simulated by following the same method of [1,5] with a gamma-variate AIF, a fixed CBF value typically found in normal grey matter, and two models for R(t), an exponential and a gamma-variate function to simulate the case of absence or presence of bolus dispersion, respectively. The tissue noise-free curve was obtained from eq.1, and then S(t) signals were generated from  $S(t)=S_0 \exp(-k \cdot C(t) \cdot TE)$  (eq.2) with  $S_0=100$ ,  $TE=80$  ms, k selected to achieve a peak signal drop of 40% (value typically found in human grey matter) and Gaussian noise with two signal-to-noise ratios  $SNR=10$  and  $SNR=50$  was added to the data. Noisy tissue concentration time curves were generated using eq.2 and the noisy S(t) signals. The simulations were repeated 100 times for each R(t).

**Deconvolution methods.**  $R^*(t)=CBF \cdot R(t)$  was calculated by SVD as described in [1], with the commonly used threshold of 20% of the maximum singular value; BC with the optimal threshold values indicated in [4]; TIKH as described in [5] with two methods for selecting the optimal regularization parameter, i.e. L-curve and generalized cross validation (GCV) criteria; NSR as described in [6, 7]. NSR is a Bayesian method which exploits a model of the unknown input only allowing nonnegative values.

**Results.** Figure 1 shows, in time logarithmic scale (the time scale was shifted by 1sec to improve the quality of the plot visualization), the mean  $R^*(t)$  curve (100 simulations,  $SNR=50$ ) obtained with absence and presence of dispersion (upper panel: exponential R(t); lower panel: gamma variate R(t)) with SVD, BC, TIKH, and NSR. The black solid lines represent the true  $R^*(t)$ , grey solid lines the mean solutions, the dashed lines mean  $\pm$  SD of the solutions. For both R(t) models, as expected [2,4] SVD underestimates the peak of  $R^*(t)$  and introduces oscillations which are more pronounced in case of bolus dispersion. BC performs less satisfactory than SVD without bolus dispersion and slightly better in the dispersed case, but nonphysiological oscillations and negative values are still present. TIKH\_gcv mean solutions are smoother and estimate fairly well the peak of the function, but show oscillations and large SD values. Finally, NSR presents an excellent performance both in the exponential as well as the dispersed case: the estimated  $R^*(t)$  function shows narrow confidence intervals, a smooth nonnegative shape with no oscillations and a good estimation of peak values. However, NSR performs slightly better when dispersed case is considered. NSR is also superior in comparison with SVD, BC, and TIKH both in presence and absence of dispersion when  $SNR=10$  is considered (not shown).

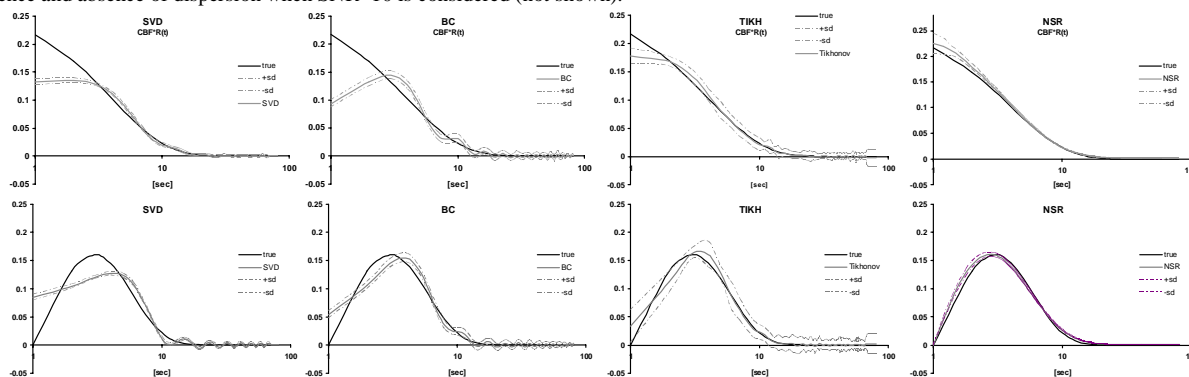


Figure 1

Table 1 shows the Root Mean Square Error (RMSE) between simulated-true and estimated peak of  $R^*(t)$ :  $RMSE_{peak} = ((\sum_i [\max(R^*(t_i)) - \max(R^*_{true}(t_i))]^2) / 100)^{1/2}$ , and the RMSE between the total estimated and the true  $R^*(t)$ :  $RMSE_{total} = (\sum_i [(1/N) \cdot \sum_j (R^*(t_j) - R^*_{true}(t_j))]^2)^{1/2} / 100$ , with  $N$ =number of samples, for both  $SNR=10$  and  $SNR=50$ . The smallest RMSE values are shadowed in Table 1. RMSE values confirm that NSR produces the most accurate estimate of the true  $R^*(t)$ , especially when bolus dispersion is considered. Note that since TIKH with GCV criteria demonstrated to have a superior performance over TIKH with LCC, TIKH with GCV results are shown in Figure 1 and Table 1.

	RMSE <sub>peak</sub>				RMSE <sub>total curve</sub>			
	SVD	BC	TIKH	NSR	SVD	BC	TIKH	NSR
<b>SNR=50</b>								
no dispersion	0.082	0.073	0.040	0.008	0.010	0.016	0.008	0.002
dispersion	0.033	0.007	0.008	0.003	0.011	0.009	0.010	0.004
<b>SNR=10</b>								
no dispersion	0.072	0.071	0.063	0.040	0.015	0.025	0.016	0.007
dispersion	0.028	0.020	0.140	0.017	0.017	0.021	0.022	0.008

Table 1

ischaemic grey matter CBF values. NSR succeeds in detecting positive and smoothed residue functions without the need to fix any threshold value, and allowing to detect only positive (i.e. physiological) and smoothed  $R^*(t)$ .

**Discussion** NSR deconvolution method is able to estimate with good accuracy the physiological shape of  $R^*(t)$  both in the case of presence and absence of dispersion. Additional our simulation studies (not shown) confirm these results also for tissue concentration time curves with typical white matter and

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