Dictionary-based Support Vector Machines for Unsupervised Ischemia Detection at Rest with CP-BOLD Cardiac MRI

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Introduction: A noninvasive imaging approach that can identify ischemic myocardial territories without requiring provocative stress or administration of contrast agents could be immensely valuable in the detection of acute coronary syndromes. Recent studies have demonstrated that Cardiac Phase-resolved Blood-Oxygen-Level Dependent (CP-BOLD) MRI[1] may be one such method. The identification of ischemic territories from CP-BOLD relies on the fact that in healthy conditions myocardial signal intensity varies in a way that it is maximal in systole and minimal in diastole (with some possible slight shifts,[2-3] see example in Fig. 1), whereas in disease scenarios this behavior does not hold. To determine these patterns post-processing is required. Initial methods relied on segmental indicators, defined as ratios of signal intensities typically between end systole and diastole.[1] More recently, approaches adopting techniques from fMRI namely Independent Component Analysis (ICA),[4] or from structural dictionary learning,[5] have been developed to take advantage of information across the cardiac cycle and were tested on synthetic data. However, both methods utilize fixed thresholds to identify ischemic patterns in time series and do not offer statistical interpretation.

Purpose: We hypothesize that we can combine recent advances in machine learning theory and statistical permutation testing to provide a method for unsupervised pixel-level ischemia detection with CP-BOLD. Since obtaining pixel-level time series from real CP-BOLD data does require precise registration and segmentation, this study uses synthetic data, for which the location of ischemic territories is known a priori. This permits the absolute quantification of performance without introducing bias due to errors in other processing steps (such as registration and segmentation).

Methods: Generation of synthetic time series: For simulation purposes, synthetic time series were obtained from real CP-BOLD data[1] of 10 canines, using a dictionary learning approach.[2] Several datasets **Y** were then generated, each one referring to a single subject and containing a chosen number (N_I) of synthetic ischemic time series out of a total number of N time series. Each time series represents the evolution of CP-BOLD signal intensity at a certain 'pixel' of the myocardium. The extent of ischemia[6] of a particular Y is then expressed as the ratio $\mathbf{IE = N_I / N}$. Unsupervised ischemia detection with DB-SVM: The basic premise of the proposed method is that, given an input dataset Y, a normal pattern (remote to ischemia) is found, and automatically each time series is labeled accordingly, i.e. the algorithm decides if the related myocardial location follows the normal pattern or not (and thus must belong to an ischemic territory). For each Y, the Nx1 vector of originating statuses (1=remote, 0=ischemic), denoted as **GT**, is known. The goal of the algorithm is to retrieve an equally sized vector of labels **L**; perfect detection accuracy is when L equals GT for all entries. The approach relies on the observation that remote to ischemia a cyclic pattern exists,[2-3] and that this pattern can be found via structural dictionary learning.[5] The algorithm was then designed as an iterative procedure consisting of two steps. In the *first step* dictionary sparse decomposition $Y_{L=1}=D^C X^C+D^G X^G$ is performed, where D^C is a "circulant" dictionary containing shifted versions of the cyclic pattern, and D^G is a compact dictionary accounting for general signal variability (both dictionaries are learned). The dictionary-based model is intended to linearly represent the supposedly remote time series, where at the beginning all the time series are considered remote. The *second step* takes advantage of the trained dictionary-driven model and actually labels each time series, relying on One-class Support Vector Machines (One-Class SVM)[7] classifier. This algorithm essentially tries to learn the statistical support of the most populous class (the normal one) and penalizes input time series (the anomalous ones) if they do not satisfy the statistics of the normal class. The penalty mechanism was modified to incorporate the related dictionary reconstruction error: thus, anomaly is defined as time series that do not fit the dictionary model. The two steps are iteratively repeated until convergence is reached as shown in Fig. 2, forming the proposed DB-SVM. Inference via permutations: To obtain a statistical confidence on the output labels obtained, permutation testing, extensively employed in functional MRI (fMRI), was adopted. Data were permuted (by shuffling row-wise each time series) and the process outlined above was repeated. Under permutation testing an output label vector L with all zeros (all anomalies) is expected, and by counting the number of wrong assignments normalized by the number of permutations (10000) a p-value was obtained. Statistical analysis: Experiments were conducted varying N and IE. The accuracy values of the algorithm(s) were recorded and differences were evaluated with a paired Wilcoxon signed rank test.

Results: Table 1, shows the comparison of the proposed method (DB-SVM) with an ICA-based ischemia detector[4] (ICA) and a simple One-class SVM classifier,[7] i.e. without dictionary learning (SVM). DB-SVM achieves a higher accuracy (statistically significant) than ICA, across the range of N and IE considered. Fig. 3 shows an example of the obtained probabilistic map overlaid on a real image, solely for visualization purposes.

Discussion: The novelty of the proposed algorithm resides in the combination of a dictionary-learning step and an unsupervised classifier. The alternation of the two procedures is beneficial for both learning a better pattern for the remote time series and improving classification, with dictionary learning effectively "guiding" the SVM classifier. By accounting for shifts, the algorithm takes advantage of them as means of defining the remote pattern.

Conclusions: This work demonstrates that the identification of ischemic territories with CP-BOLD MRI at rest is possible at a higher accuracy than other state-of-the-art methods. Moreover, the probabilistic interpretation of the results here proposed provides confidence to the expert, allowing him/her to threshold according to desired significance, as commonly done in fMRI. While further investigations are necessary to validate this method with data from real experiments, when combined with accurate myocardial registration and segmentation, this could provide a powerful visualization and analysis technique for CP-BOLD at rest, thus accelerating the translation of this truly non-invasive approach to the diagnosis of ischemic heart diseases.

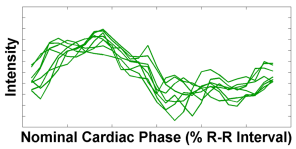

Fig. 1. Example CP-BOLD time series obtained from several regions in the myocardium of an animal in baseline conditions showing the presence of a common cyclic pattern.

Table 1. Accuracy (mean ± std) in % of ICA, SVM, and DB-SVM, with variable N and IE. (*denotes statistical significance DB-SVM vs ICA)

	N=150			N=50		
IE	**ICA**	**SVM**	**DB-SVM**	**ICA**	**SVM**	**DB-SVM**
40%	92±6	89±1	98±1*	79±6	87±1	89±5*
33%	87±6	82±1	97±2*	84±6	79±2	88±8
25%	87±5	74±1	97±2*	85±7	72±1	93±5*

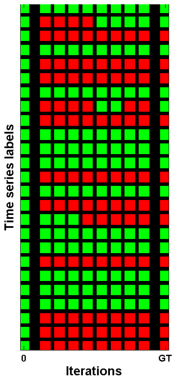

Fig. 2. Evolution of the label vector **L** (green=remote, red=ischemia), across several iterations of the DB-SVM algorithm. The last column on the right is the vector of originating statuses **GT**. While initially assuming that all time series are normal, observe that after a few iterations it converges to closely match the ground truth.

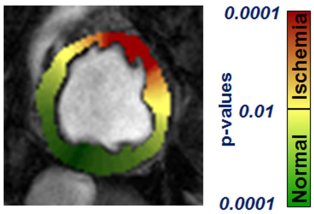

Fig. 3. Synthetic example of ischemia likelihood obtained with DB-SVM, visualizing p-values (the darker the color-shade, the more likely the pixel belongs to the assigned class).

References: (1) Tsaftaris et al., *Circ Cardiovasc Img, 6(2)*:311-9 2013; (2) Rusu et al., *IEEE TMI, 33(7)*:1422-1433 2014; (3) Boschetto et al., *Proc. ISMRM, 22*: 1588 2014; (4) Morisi et al., *Proc. ISMRM, 22*: 2055 2014; (5) Rusu & Tsaftaris, *MICCAI, 8674*: 562-569 2014; (6) Tsaftaris et al., *JMRI, 35(6)*:1338-48 2012; (7) Schölkopf et al., *J. Neural Comput. 13(7)*:1443-1471 2001.