FEATURE RELEVANCE ASSESSMENT IN AUTOMATIC INTER-PATIENT HEART BEAT CLASSIFICATION

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- Keywords: Heart beat classification, AAMI standards, Support vector machines, Unbalanced data, Feature selection, Inter-patient classification.
- Abstract: Long-term ECG recordings are often required for the monitoring of the cardiac function in clinical applications. Due to the high number of beats to evaluate, inter-patient computer-aided heart beat classification is of great importance for physicians. The main difficulty is the extraction of discriminative features from the heart beat time series. The objective of this work is the assessment of the relevance of feature sets previously proposed in the literature. For this purpose, inter-patient classification of heart beats following AAMI guidelines is investigated. The class unbalance is taken into account by using a support vector machine (SVM) classifier that integrates distinct weights for the classes. The performances of the SVM model with an appropriate selection of features are better than those of previously reported inter-patient classification models. These results show that the choice of the features is of major importance, and that some usual feature sets do not serve the classification performances. In addition, the results drop significantly when the class unbalance is not taken into account, which shows that this issue must be addressed to grasp the importance of the pathological cases.

1 INTRODUCTION

The analysis of the electrocardiogram (ECG) signal provides critical information on the cardiac function of patients. Long-term recordings of the ECG signal are, for example, required for the clinical diagnosis of some disease conditions, and for the evaluation of new drugs during phase-one studies by pharmaceutical groups. Such long-term recordings are usually obtained using the popular Holter recorders.

These systems are ambulatory heart activity recording units delivering signal storing capabilities ranging from 24 to 48 hours and thus providing with data of hundreds to thousands of heart beats. The analysis is usually performed off-line by cardiologists, whose diagnosis may rely on just a few transient patterns. Due to the high number of beats to evaluate, this task is very expensive and reliable visual inspection is difficult. Computer-aided classification of pathological beats is therefore of great importance.

However, this is a difficult task in real situations. First, several sources of noise pollute the ECG signal. Among these, power line interferences, muscular artifacts, poor electrode contacts and baseline wandering due to respiration can sometimes be identified. Second, the classes are very unbalanced since a vast majority of the heart beats are normal healthy beats and just a small number of beats are pathological, though those are of major importance. Third, artificial intelligence methods require the extraction of discriminative features from the heart beat time series. The extraction of the information available in the ECG signal into a set of relevant features requires proper expertise because it is difficult and crucial.

Computer-aided heart beat classification has been addressed previously in the literature. Several features characterizing the heart beats and several classification models have been investigated (Clifford et al., 2006). However, very few reported works follow the standards defined by the American Association for Medical Instrumentation (AAMI), which makes it very difficult to assess the relative merits of the methods and of the proposed extracted features (Association for the Advancement of Medical Instrumentation, 1998). Also, the unbalanced classes issue is usually not taken into account. Furthermore, most of proposed methods require labeled beats from the tested patient in the training of the model and actually perform what could be referred to as "intra-patient" classification. By contrast, "inter-patient" classification consists in classifying the beats of a new tested patient according to a reference database built from data coming from other patients. This is a much harder task of generalization but it is also much more useful since labeled beats from a new patient are usually not timely available in real situations.

In this work, *inter-patient* classification of heart beats following the AAMI guidelines is investigated. First, the class unbalance is taken into account by using a support vector machine classifier that integrates distinct weights for the classes depending on their priors. Second, a large number of distinct features proposed in the literature are combined and evaluated, and a discussion is made about the relevance of each type of features.

The following of this paper is organized as follows. Section 2 briefly reviews the state of the art in heart beat classification. Section 3 provides a short overview of the theoretical background for the mathematical methods used in this work. Section 4 describes the methodology followed by the experiments and Section 5 presents the results.

2 STATE OF THE ART

This section provides a short review of the state of the art in supervised heart beat classification. Two kinds of heart beat classification paradigms can be distinguished, corresponding to either *intra-patient* classification or *inter-patient* classification.

Inter-patient classification consists in classifying the beats of a new tested patient according to a reference database and a model built from data from other patients. This process thus implies generalization from one patient to another. As far as intra-patient classification is concerned, the reference database must contain previously labeled beats from the tested patient. The results that can be achieved are naturally better than when inter-patient classification is performed, but the patient labeled beats are usually not available in real situations. Furthermore, because pathological beats can be very rare, there is no guarantee that the few training beats that would be labeled for this patient would contain representatives for each class; and the classifier could possibly fail in predicting something it has not learned.

Despite these major drawbacks, the majority of previously reported work is about *intra-patient* classi-

fication. Different models have been proposed for this task, including neural networks (Osowski and Hoai, 2001), *k*-nearest neighbors (Christov et al., 2006), hidden Markov models (Cheng and Chan, 1998) and support vector machines (Melgani and Bazi, 2008). A comprehensive review of *intra-patient* classification methods and their results can be found in (Clifford et al., 2006).

As far as *inter-patient* classification is concerned, the first study to establish a reliable *inter-patient* classification methodology following AAMI standards is (Chazal et al., 2004). A linear discriminant analysis (LDA) classifier model is trained and the results are evaluated on an independent test set. The unbalanced classes issue is addressed by introducing weights in the linear discriminant functions. In (Park et al., 2008), these classification results are improved on the same dataset using SVM and other features. Hierarchical SVMs are used to reduce the effect of unbalanced classes.

The classification performances heavily rely on the extraction of relevant features from the heart beat time series. A variety of features have been proposed to characterize the heart beats. The representation of the heart beat signal by the coefficients of Hermite basis functions expansions is introduced for a clustering application in (Lagerholm et al., 2000), and later used for classification by (Osowski et al., 2004) and (Park et al., 2008). Another type of features that has been proposed is the representation of the heart beats by higher order statistics, and in particular the cumulants of order 2, 3 and 4 (Osowski and Hoai, 2001).

Another widely used group of features is morphological features (latter referred to as segmentation features) (Christov et al., 2006; Chazal et al., These features require the annotation of 2004). PQRST waves and then summarize the morphology of the heart beat series by their duration, area, Q-T intervals, S-T intervals, the height of the QRS complex, etc. In most of previously reported works, the successive time differences between the R spikes of heart beats (later referred to as R-R intervals) are always combined to the other features. However, the intrinsic relevance of each type of features remains unknown. In this paper, this relevance is investigated using feature selection techniques (François, 2008; Guyon et al., 2006).

3 THEORETICAL BACKGROUND

This section provides a brief theoretical background on mathematical methods that are used in this work.

3.1 Support Vector Machines

A support vector machine (SVM) is a supervised learning method that was first introduced by Vapnik (Vapnik, 1999). The two-classes case is described here, because its extension to multiple classes is straightforward by applying the one-against-all or one-against-one methods. Let us first define the *p* dimensional feature vector $\mathbf{x}_k = \{x_k^1, x_k^2, ..., x_k^p\}$ and the associated class value $y_k \in \{-1, 1\}$ for a given heart beat *k* with *k* ranging from 1 to *K*, *K* being the total number of heart beats.

SVMs are linear machines that rely on a preprocessing to represent the features in a higher dimension, typically much higher than the original feature space. With an appropriate non-linear mapping $\phi(\mathbf{x})$ to a sufficiently high dimensional space, finite data from two categories can always be separated by a hyperplane. In SVMs, this hyperplane is chosen as the one with the largest margin.

Assume each observation \mathbf{x}_k has been transformed to $\mathbf{z}_k = \boldsymbol{\varphi}(\mathbf{x}_k)$. The equation of the hyperplane in the augmented space is defined as $g(\mathbf{z}) = \mathbf{a}^t \mathbf{z}$ where both the weight and the transformed pattern vectors are augmented by $a_0 = w_0$ and $z_0 = 1$ respectively. A separating hyperplane thus ensures that

$$y_k g(\mathbf{z}_k) \ge 1 \quad k = 1, \dots, K. \tag{1}$$

The distance from any hyperplane to a transformed pattern \mathbf{z} is $|g(\mathbf{z})|/||\mathbf{a}||$, and Eq. 1 implies that

$$\frac{y_k g(\mathbf{z}_k)}{||\mathbf{a}||} \ge b \quad k = 1, \dots, K \tag{2}$$

where it is assumed that *b* is an existing positive margin. The objective is then to find the weight vector **a** that maximizes *b*. As the solution vector can be scaled arbitrarily, the constraint $b||\mathbf{a}|| = 1$ is usually imposed, which is equivalent to minimizing $||\mathbf{a}||^2$. By constructing the Lagrangian, this *primal* optimization can be reformulated in a so-called *dual* form that maximizes

$$L(\boldsymbol{\alpha}) = \sum_{k=1}^{K} \alpha_k - \frac{1}{2} \sum_{k=1}^{K} \sum_{j=1}^{K} \alpha_k \alpha_j y_k y_j \mathbf{z}_k^t \mathbf{z}_j, \quad (3)$$

with respect to the Lagrange multipliers α_k associated to inequalities 1, subject to the constraints

$$\sum_{k=1}^{K} y_k \alpha_k = 0 \qquad 0 \le \alpha_k \le C \tag{4}$$

where C represents the regularizing parameter and determines the balance between the complexity of the model and the classification error. These equations can be efficiently solved using quadratic programming. For this type of optimization, there exist many highly effective learning algorithms. A common method for solving the problem is Platt's Sequential Minimal Optimization (SMO) algorithm, which breaks the problem down into 2-dimensional subproblems that may be solved analytically, eliminating the need for a numerical optimization algorithm such as conjugate gradient methods (Platt, 1999).

In the dual form, the explicit form of the mapping function φ must not be known as long as the kernel function $K(\mathbf{x}_i, \mathbf{x}_j) = \varphi(\mathbf{x}_i)\varphi(\mathbf{x}_j)$ is defined. The kernel can for example be the linear kernel $K(\mathbf{x}_i, \mathbf{x}_j) = \mathbf{x}_i^t \mathbf{x}_j$ or the radial basis function kernel $K(\mathbf{x}_i, \mathbf{x}_j) = exp(-\gamma ||\mathbf{x}_i - \mathbf{x}_j||^2)$ where γ is a kernel parameter to be tuned.

3.2 Hermite Basis Functions

The representation of the heart beat signal via Hermite basis functions (HBF) was first introduced by (Lagerholm et al., 2000) for a clustering application and later by (Osowski et al., 2004) for classification. This approach exploits similarities between the shapes of HBF and typical ECG waveforms. Let us denote the heart beat signal by x(t). Its expansion into a Hermite series of order N is written as

$$x(t) = \sum_{n=0}^{N-1} c_n \phi_n(t, \sigma)$$
(5)

where c_n are the expansion coefficients and σ is the width parameter. $\phi_n(t, \sigma)$ are the Hermite basis functions of the *n*th order defined as follows:

$$\phi_n(t,\sigma) = \frac{1}{\sqrt{\sigma 2^n n! \sqrt{\pi}}} e^{-t^2/2\sigma^2} H_n(t/\sigma) \qquad (6)$$

where $H_n(t/\sigma)$ is the Hermite polynomial of the *n*th order. The Hermite polynomials satisfy the following recurrence relation:

$$H_n(x) = 2xH_{n-1}(x) - 2(n-1)H_{n-2}(x)$$
(7)

with $H_0(x) = 1$ and $H_1(x) = 2x$.

The higher the order of the Hermite polynomial, the higher its frequency of changes in the time domain, and the better the capability of the expansion in Eq. 5 to reconstruct the signal (Clifford et al., 2006). The width parameter σ can be tuned to provide a good representation of beats with large differences in durations. The coefficients c_n of the HBF expansion can be estimated by minimizing the sum of squared errors using singular value decomposition and the pseudoinverse technique. These coefficients summarize the shape of the heart beat signal and can be treated as the features used in the classification process.

3.3 Higher Order Statistics

The statistical properties of the heart beat signal can be represented by its higher order statistics (HOS). The cumulants of order two, three and four are usually used (Osowski and Hoai, 2001). Assuming the heart beat signal x(t) has a zero mean, its cumulant C_x^i of order *i* can be computed as follows:

$$C_x^2(\tau_1) = E\{x(t)x(t+\tau_1)\}$$

$$C_x^3(\tau_1,\tau_2) = E\{x(t)x(t+\tau_1)x(t+\tau_2)\}$$

$$C_x^4(\tau_1,\tau_2,\tau_3) = E\{x(t)x(t+\tau_1)x(t+\tau_2)x(t+\tau_3)\}$$

$$-C_x^2(\tau_1)C_x^2(\tau_3-\tau_2)$$

$$-C_x^2(\tau_2)C_x^2(\tau_3-\tau_1)$$

$$-C_x^2(\tau_3)C_x^2(\tau_2-\tau_1)$$

where *E* is the expectation operator and τ_1, τ_2, τ_3 are the time lags.

4 METHODOLOGY

Let us assume that a reference database has been obtained and labeled by a cardiologist, with all pathologies of interest being represented. Given a new ECG signal, for example recorded using an Holter system, one wants to use the information contained in the reference database in order to predict the pathologies present in the new signal.

4.1 ECG Filtering

The filtering procedure defined in (Chazal et al., 2004) is used in this work. The ECG signal is first filtered by two median filters. The first median filter is of 200 msec width and removes the QRS complexes and the P waves. The resulting signal is then processed with a second median filter of 600 msec width to remove the T waves. The signal resulting from the second filter operation contains the baseline wanderings and can be subtracted from the original signal. Powerline and other high frequency artifacts are then removed from the baseline corrected signal with a FIR filter.

4.2 Heart Beat Extraction

Several computer-aided annotation algorithms have been reported in the literature in order to automatically detect the characteristic points of the ECG (Clifford et al., 2006). The standard *ecgpuwave*¹ segmentation software provided with the MIT-BIH database is used to provide estimates of such characteristic points. Nevertheless, even the best annotation algorithms sometimes fail in detecting the exact beginning of the beats (the start of the P wave). However, the R spike has a very high detection rate and can be used as a more reliable marker. Defining a static window around the R spike is thus a safer way to separate the beats without missing a large amount of data. A window of 250 msec before and after the R position is used in this work.

4.3 Feature Extraction

Five groups of features are extracted from each heart beat: R-R intervals, Hermite basis function expansion coefficients, higher order statistics, segmentation features and patient-normalized segmentation features.

- 1. R-R intervals: This group consists of six features built from the R-R interval series. The first three features are the R-R interval to the previous beat, the R-R interval to the next beat and the average of R-R intervals in a window of 10 surroundings beats. The other next three interval features correspond to the ratio between the previous three values and their mean value for this patient. These last features are thus independent from the mean normal behavior of the heart of patients, which can naturally be very different between individuals, possibly misleading the classifier.
- 2. Segmentation features: A large variety of 24 features are computed from the estimated characteristic points. Some of these features are a boolean flag indicating the presence/absence of QRS, P and T waves. If the waves are present, their duration, maximum and minimum values, area, standard deviation, skewness and kurtosis are computed as features. The complete list of segmentation features can be found in (Christov et al., 2006).
- 3. HBF coefficients: The parameters for computing the HBF expansion coefficients as defined in (Park et al., 2008) are used. The order of the Hermite polynomial is set to 20, and the width parameter σ is estimated so as to minimize the reconstruction error. Figure 1 shows a normal beat and its reconstruction from the estimated HBF coefficients.
- 4. Higher order statistics: The 2nd, 3rd and 4th order cumulant functions are computed. The parameters as defined in (Osowski et al., 2004) are used: the lag parameters range from -250 msec to 250 msec centered on the R spike and 10 equally spaced sample points of each cumulant are used as

¹see http://www.physionet.org/physiotools/software-index.shtml

features, for a total of 30 features. Figure 2 shows an example of cumulants for a normal beat.

5. Patient-normalized segmentation features: This group of features contains the same features as the segmentation group, but the values are normalized by their mean value for each patient. The normalization is obviously not applied to boolean segmentation features. Here again, the objective is to make each feature independent from the mean behavior of the heart of a patient, because it can naturally be very different between individuals.



Figure 1: (1) A normal ECG beat and (2) its reconstruction from HBF coefficients.



Figure 2: (1) A normal ECG beat (2) its cumulant of the 2nd order (3) its cumulant of the third order and (4) its cumulant of the fourth order.

4.4 Classification Model

Classification models based on SVMs with the *one-against-one* multi-class strategy are considered in this study. The training of the model is performed on a reference database, and this model is then applied to get a prediction of the class label of new heart beats from another patient. Several types of kernels are evaluated in this study, and the linear kernel always outperforms the other kernels. As this is in accordance with previous works on heart beat classification using SVMs (Park et al., 2008), only the results with the linear kernel are reported here.

The relative proportions of the classes of the available training examples influence dramatically the performances of the SVM classifier. If a few number of classes dominates the training data, the performances of SVM drop significantly (Yinggang and Qinming, 2006). One solution to this problem is to randomly downsample the larger classes, but this results in a waste of potentially useful data. A better solution followed in this work is to include all training examples but reduce the contribution of dominating classes in the training process.

This is achieved by weighting the parameter C of class i in Eq. 4 to w_iC . The problem is to find the optimal w_i values. In a two-class problem, it can easily be estimated by cross-validation. In a multi-class problem, this is much more difficult; in our experiments these values are set according to the prior probabilities of each class in the training data. Let us define n_i , the number of beats in class *i*. The weight associated to each class *i* is then set as $w_i = n_i/N$ where N is the total number of beats. Intuitively, the addition of weights in the classifier for small classes means that more attention is given to pathological classes and less to normal beats. This is in accordance with doctors who clearly prefer that a healthy patient is wrongly diagnosed ill rather than an ill patient is diagnosed healthy and left untreated.

4.5 **Performance Evaluation**

In a heart beat classification task, around 90% of beats are normal beats and a dummy classifier which would always predicting the normal class would get 90% accuracy. For this reason, it is important to look at class accuracies separately and to use the average of these class accuracies as performance measure rather than considering the overall classification accuracy.

Normal beats (N)	Supraventricular ectopic	Ventricular ectopic beats	Fusion beats (F)
	beats (S)	(V)	
Normal beats	Atrial premature beat	Premature ventricular contraction	Fusion of ventricular and normal beats
Left bundle branch block beats	Aberrated atrial prema- ture beat	Ventricular escape beats	
Right bundle branch block beats	Nodal (junctional) pre- mature beats		
Atrial escape beats	Supraventricular prema- ture beats		
Nodal (junctional) espace beats			

Table 1: Grouping of the MIT-BIH labeled heart beat types according to the AAMI standards.

5 EXPERIMENTS AND RESULTS

Data from the MIT-BIH arrhythmia database (Goldberger et al., 2000) are used in our experiments. The database contains 48 half-hour long ambulatory recordings obtained from 48 patients, for a total of approximatively 110'000 heart beats labeled into 15 distinct types. Following the AAMI recommendations, the four recordings with paced beats are rejected and the MIT-BIH labeled types are then grouped into four more clinically relevant heart beat classes (Association for the Advancement of Medical Instrumentation, 1998) (see Table 1 for grouping details):

- **N-class** includes beats originating in the sinus node (normal and bundle branch block beat types);
- S-class includes supraventricular ectopic beats;
- V-class includes ventricular ectopic beats (VEBs);
- **F-class** includes beats that result from fusing normal and VEBs.

The dataset configuration is the same as in (Chazal et al., 2004; Park et al., 2008). The 44 available recordings are divided in two independent datasets of 22 recordings each with approximatively the same ratio of heart beats classes. The first dataset is the training set, and is used to build the model. The second dataset is the test set, and is used to obtain an independent measure of the performances of the classifier. Table 2 shows the number of beats in each class and their frequencies in the two datasets.

All features introduced in Section 4.3 are computed and all the possible combinations of the five feature groups are evaluated with the weighted SVM model, for a total of 31 configurations. Table 3 holds the most interesting results out of the 31 configurations, together with the results of previously reported models that also followed AAMI guidelines and *interpatient* classification. The best and worst results of the SVM model when no weights are defined ("raw" models) are also shown in the table.

The most remarkable observation is that when R-R features are not included in the model, is has been impossible to obtain more than 55.4% of mean accuracy. The other feature groups, when included alone in the model, always lead to an accuracy below 50%.

Best overall performances are obtained with the combination of R-R intervals and segmentation features with 83.0% accuracy. The addition of any other features to this selection always leads to a lower accuracy. In particular, the normalization of the segmentation features with respect to each patient provides a lower accuracy when these features are coupled with R-R intervals than when their non normalised version is used. It is also interesting to note that R-R interval features yield 80.8% of accuracy by themselves and are clearly the most important features to include in the model.

The weights included in the SVM to take the unbalanced class ratio into account are also of major importance. If no weights are defined, the best average accuracy that can be obtained by the SVM model decreases to 54.3%, with an accuracy of only 7.4% for class S and of 33.0% for class F which is clearly unacceptable.

The weighted SVM model with the best selection (or any of the top three selections in Table 3) achieves performances significantly higher than previously reported models, with a reduced number of features. Furthermore, the weighted SVM model yields better results for each of the pathological classes with a class accuracy always over 80%.

	N	S	V	F	Total
Training	45801	938	3708	414	50861
	90.05%	1.84%	7.29%	0.81%	100%
Test	44202	1835	3204	388	49629
	89.06%	3.7%	6.46%	0.78%	100%

Table 2: Distribution of heart beat classes in the two independent datasets.

Table 3: Selection of the most interesting results out of the 31 configurations with the weighted SVM model (sorted in decreasing average accuracy). Best and worst results of the SVM model with no weights ("raw" SVM) are also displayed. Results of previously reported comparable models are also included.

Model	Feature sets			Results						
	R-R	Seg	HBF	HOS	NSeg	N	S	V	F	Avg.
Weighted SVM	•	•				75.1	89.3	86.9	80.7	83.0
(Top 5)	•					77.8	63.8	86.9	94.6	80.8
	•	•	•	•		75.4	89.4	75.4	66.8	76.8
	•		•			83.8	78.7	73.0	35.1	67.6
	•				•	88.5	78.6	74.2	4.6	61.5
(Selected)		•				63.2	61.5	80.2	16.8	55.4
	•	•	•	•	•	79.5	28.8	73.8	3.6	46.4
					•	78.0	25.9	78.7	0.3	45.7
				•		78.1	2.1	60.8	6.2	36.8
(Bottom 3)			٠			47.8	13.5	57.4	15.2	33.5
		•	٠		•	75.2	3.7	52.6	0.8	33.1
		•			•	68.5	4.5	53.7	1.0	31.9
"Raw" SVM	•	•	•	•		96.2	7.4	80.5	33.0	54.3
(Best and worst)			•			100.0	0	0	0	25.0
Hierar. SVM (Park et al., 2008)	•		•	•		86.2	82.6	80.8	54.9	76.1
Weighted LDA (Chazal et al., 2004)		•				86.7	53.3	67.3	71.6	69.7

6 CONCLUSIONS

The classification of heart beats is of great importance for clinical applications involving the long-term monitoring of the cardiac function. The main difficulty is the extraction of discriminative features from the heart beat time series. The goal of this work is the assessment of the relevance of feature sets often used in the literature. Five feature groups are considered: R-R intervals, segmentation features, HBF coefficients, higher-order statistics and patient-normalized segmentation features.

For this purpose, this work has followed and motivated the use of:

- *AAMI guidelines* for the establishment of reliable classifiers and for the evaluation of their relative merits;
- *inter-patient* rather than *intra-patient* classification;
- weighted multi-class SVM models to address the

class unbalance problem;

- preprocessing and dataset preparation according to the literature;
- and the *average class accuracy* as performance measure.

Best results are obtained with the combination of R-R intervals and segmentation features, with an average class accuracy of 83.0%. Any addition of features to these two groups leads to a lower performance. In particular, the normalization of the segmentation features with respect to each patient provides a lower accuracy when these features are coupled with R-R intervals. When R-R intervals are not added in the model, it has been impossible to obtain more than 55.4% (obtained by the segmentation features alone) which is unacceptable. To the opposite, it is interesting to observe that R-R intervals alone already lead to 80.8% of average accuracy.

These results show that R-R intervals are clearly the most significant features to include in a heart beat classification problem. The second most important features are morphological features. The other feature groups such as Hermite basis function expansion coefficients, higher-order autocorrelation statistics and patient-normalized features do not seem to serve the classification performances.

These results obtained with the weighted SVM model and R-R intervals combined to segmentation features are significantly better than previously reported *inter-patient* classification models. In particular, the classification performances for the pathological classes are always improved with more than 80%; those classes are of crucial importance for the diagnosis. Furthermore, these performances are achieved with a reduced number of features. The choice of the features is thus a task of major importance, as a bad selection or too many features can lead to unaceptable results.

Another important issue for classification of heart beats resides in the class unbalance, which is met with weights being included in the SVM model. Indeed, the average accuracy obtained by the model with our best feature selection decreases from 83.0% to 54.3%, with an accuracy of only 7.4% for class S and of 33.0% for class F when these weights are removed, leading to rather useless models that are unable to grasp the importance of the pathological cases.

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