



Electric impedance spectroscopy feature extraction for tissue classification with electrode embedded surgical needles through a modified forward stepwise method

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ABSTRACT

There has been a growing interest in developing electric impedance sensing surgical tools for tissue identification during surgery. A key facet of this development is identifying distinct features that can be used to identify tissues from one another. This paper explores several feature extraction techniques and classification methods applied to electric impedance data. Furthermore, a modified forward stepwise method is proposed. The method introduces a scoring metric to help select features to add to the model, that is based off of the coefficient of variation and overlapping index from the feature's probability density functions for each of the classes. The proposed and existing methods were applied to spectral data measured at 23 frequencies, from 132 samples across 6 different tissues including ex-vivo bovine kidney, liver and muscle, poultry liver, as well as freshly excised canine testicle and ovary samples. These methods were able to successfully find impedance spectra features for the investigated biological tissues. The best predictive accuracy was with Boruta feature extraction and a Random Forest classifier but without significantly reducing the number of features in the classifier model. The proposed method was able to reduce the number of features in the model to an average of 5.8 features for all tested classifiers. These methods may have use in finding features to discriminate other tissue types, possibly to aid in targeting lesions in minimally invasive cancer treatment surgeries.

1. Introduction

Stereotactic surgeries describe a minimally invasive procedure that is used to locate a target inside the body. These procedures have evolved since their original development in 1951 [1]. Broadly speaking, stereotactic surgery involves a rigid frame connected to the patient to position surgical tools and an imaging method to localise the target. The methodology has been used for radio-neurosurgery [1], brain stimulation for treating psychiatric illness [5] and needle based breast cancer biopsy [22], among others.

Stereotactic breast biopsy is one of the leading surgical techniques used to diagnose breast cancer. X-ray or CT imaging is typically used to mark the location of suspicious lesions, such that the biopsy needle can be placed accordingly. For real-time guidance, ultrasound imaging is used in some procedures to localise the tools and locate suspect lesions. However, it is well-recognised that ultrasound imaging is not always reliable, and can result in inaccurate needle placement. This can lead to multiple biopsy cores required for pathology assessment as the tissue captured from one needle is appreciably small and may not contain sig-

nificant amount of the target lesion. There has been a growing interest in developing new technologies and methods that can supplement the current biopsy procedures including better needle path planning, imaging, and embedding sensors on the needles. Other needle based procedures, such as prostate brachytherapy [20] and percutaneous nephrolithotomy [21] are also heavily dependent on tool placement and could also benefit from similar improvements.

To supplement the current imaging methods and procedures, innovative improvements to the surgical tools have been attempted that can sense the properties of nearby tissue. Notably, force sensors installed on surgical needles have been used to sense the change in stiffness between healthy tissue and cancerous tumours [24]. There has also been a growing interest in using electric impedance sensing needles, to monitor changes in the tissue impedance at the needle tip [13]. Studies have shown that carcinoma of the breast, healthy connective tissue, and adipose tissue, have distinct dielectric features [2,10]. The method known as electric impedance spectroscopy (EIS) is the analysis of the electric impedance at different stimulus frequencies. There have been several

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attempts at incorporating electrodes into biopsy needles [11,26] to perform EIS.

To be able to perform EIS, two or more electrodes are required. Two commonly used arrangements are bipolar and tetrapolar: two and four electrodes respectively. In a bipolar arrangement, for example, voltage can be applied across the electrodes and the current measured in line. A tetrapolar arrangement may have the current injected across one electrode pair and the voltage measured across the other pair. Both configurations have been used in the development electric impedance sensing surgical needles.

As seen in [10], landmark impedance features for differentiating carcinoma from healthy tissue can be seen at near direct-current and at 125 kHz. Similar landmark features can be seen in other organs, such as the prostate, where it has been reported that cancer could be discriminated against benign tissues by observing the permittivity component of the impedance at 100 kHz [7]. Other developments include a feature extraction method for impedance spectroscopy data using the information theoretic criterion [25] and single-layer feed-forward neural networks [3,9].

With the ability to sense the electric impedance at the tip of a biopsy needle, it is possible to classify the tissue while performing stereotactic surgery using the EIS data. This improvement to the procedure may reduce the number of required biopsy samples, as the surgeon can be notified prior to extraction if the needle is inside the lesion. The techniques proposed may also be valid for other tissues that are valid for stereotactic surgery, including the liver, brain, and lung, provided that the target lesion has different electric impedance than the surrounding tissue.

The mechanisms behind the electric impedance of tissues has been long studied, and is not trivial. As the frequency of the electric stimulus changes, the impedance is known to change. These changes in tissue impedance are often described as being tied to the so-called α , β and γ dispersions, and are seen in the approximate ranges of 1 Hz to several kHz, 1 kHz to several MHz, and upwards of 1 GHz respectively. While it may seem desirable to measure the impedance at multiple frequencies to have a better understanding of the tissue's behaviour, this luxury may not be feasible in real-time applications such as stereotactic surgery. One then may argue to focus purely on the high frequency measurements, but there may be impedance features at lower frequencies that can be more helpful in discriminating between two tissue classes. The question then becomes how to identify the critical landmark features that should be used for tissue classification.

There are multiple methods to extract critical features from a data set [18]. The forward stepwise and backward stepwise methods are popular for regression model development as they are relatively simple to implement. In forward stepwise analysis, one would typically start with a null model; a model with no predictors. Each of the measured features are added individually to the null model, and the classification accuracy is tested. The most successful feature is then used in the next iteration of the model and the process continues. Metrics such as coefficient of determination, coefficient of variation, and Bayesian information criterion are often used to consider when predictors should stop being added.

One of the issues with these types of greedy approaches is the limited number of model solutions considered. There may exist another model that with the correct combination of features, would present a better solution, but is not considered due to an earlier decision in the model building process. For example, there may be certain features that, on their own, are not effective classification features but when combined with other features, result in a more powerful model. In other words, the method may progress down a path that does not achieve the global best classifier. Furthermore, should two or more features improve the model equally, there needs to be some criteria to select between them. To this end, a more stochastic approach to model building could be used to consider a more diverse set of models.

One could consider that the wrapper approach to the feature extraction problem called Boruta [17] would fall in this category. In Boruta, the goal is to find which features in a data set are relevant. The algorithm uses the Random Forest classifier to develop an importance metric alongside the so-called "shadow" features; an existing feature in the data set that has been randomly reorganised. With this combination, the method is able to determine which features are deemed as important to the classification problem. In some research papers, Boruta has performed the best when compared to other Random Forest based feature selection methods [16]. While Boruta has been criticised for its computational complexity, recent updates to the algorithm have lessened this concern for some data sets [8]. Nevertheless, as a heuristic algorithm, this method comes with the associated drawbacks of such methods.

The unique contribution presented in this paper is the investigation on how to define features for ex-vivo tissue classification by comparing different classifiers and feature extraction methods. This analysis includes a novel algorithm where a model is constructed from a null base model and additional features are added as they improve classification accuracy. To overcome indecisiveness in which feature to add, a scoring criteria based on the training data statistics is incorporated.

The paper is structured by first introducing the new feature selection method and algorithm. These methods are tested on EIS electric impedance data for a variety of tissues: 132 samples across 6 different tissues, measured at 23 frequencies. Tissues measured include bovine kidney, liver and muscle, poultry liver, and canine testicle, and ovary samples. The results of the paper first present the predictive accuracy of the model with all features, then that of the models with the feature extraction techniques. The paper then concludes with a discussion of the results, suggested improvements, and future work.

2. Materials and methods

2.1. Proposed modified forward stepwise method

2.1.1. Data primer

The method proposed in this paper is developed to address a continuous value multivariate classification problem. As many classifiers are built upon the notion of basing future probability on previous measurements, the training data for a measured feature should be similar to other measurements. To this end, the data should be normally distributed. The Shapiro-Wilk test [23] can be used to determine if the data for all samples are normally distributed. The test involves calculating the statistic W ,

$$W = \frac{(\sum_{u=1}^n \mathbf{a}_u \mathbf{q}_{(u)})}{(\sum_{u=1}^n \mathbf{x}_u - \mu_u)^2} \quad (1)$$

where $\mathbf{q}_{(u)}$ is the u th order statistic. The coefficients \mathbf{a}_u are determined through,

$$(a_1, \dots, a_n) = \frac{\mathbf{m}^T \boldsymbol{\sigma}^{-1}}{\sqrt{\mathbf{m}^T \boldsymbol{\sigma}^{-1} \boldsymbol{\sigma}^{-1} \mathbf{m}}} \quad (2)$$

where $\boldsymbol{\sigma}$ is the covariance matrix, \mathbf{m} are the expected values of the order statistics sampled from the standard normal distribution.

Provided that the measurements in the training data set follow a Gaussian distribution, many classification algorithms become available to use.

2.1.2. Proposed feature scoring method

Considering a two class classification problem, it is desirable that the numerical features have distinctly separate values. In many applications a feature x may share similar values between two classes. To quantify the severity of shared values, the overlapping index [19] η be-

tween these two arbitrary classes c_1 and c_2 can be determined, see Fig. 5. The overlapping index is evaluated by computing the area underneath the intersection of the probability density functions for these classes [19],

$$\eta(x|c_1, x|c_2) = \int_{-\infty}^{\infty} \min(f(x|c_1), f(x|c_2)) dx \quad (3)$$

As these are probability density functions, the area under either curve will sum to unity. Thus $0 \leq \eta \leq 1$, where a value of 0 would indicate that these features have no overlap in values, and 1 indicates identical values between the two classes.

However, the overlapping index on its own is not sufficient. As seen in Fig. 5, two classes may have a small overlap value, due to a large standard deviation σ of the data for the feature of that class. To quantify the spread of data about the mean value μ , the coefficient of variation v for i th feature for the j th class can be calculated,

$$v(x_i|c_j) = \frac{\sigma}{\mu} \quad (4)$$

Smaller values of v indicate that the data is more closely gathered about the mean, which would suggest that future measurements would also be near the mean value.

To then quantify how likely one is able to discern between the i th feature of two arbitrary classes, a novel scoring metric SC can be used,

$$SC(x|c_1, x|c_2) = \eta(x|c_1, x|c_2)v(x_i|c_1)v(x_i|c_2) \quad (5)$$

Ultimately, SC can be used to gauge how similar a feature is between two classes. A smaller value of SC indicates low similarity between the classes at the feature.

2.1.3. Algorithm to Extract Features

The objective in developing the classification model is to maximise prediction accuracy with only as many predictors are needed. Additional predictors in the model may be redundant, which would increase measurement time, or possibly harm predictive accuracy [6]. In the development of models with a high number of features, it is not realistic to perform an exhaustive search of all possible predictor combinations, as it is computationally expensive. Researchers often turn toward forward stepwise analysis for constructing their classifier [6].

To address some of these limitations, this paper develops a method inspired by the popular forward stepwise analysis method, where individual features are initially used and additional features are added if they improve classification accuracy.

A modification to the forward stepwise analysis is proposed here, where a statistical analysis of the data is used to guide the method towards a better performing classifier. These candidate features are selected through investigating normality tests, calculating the tissue variance, evaluating the standard deviation of the tissue samples, and distribution overlap evaluations.

With the null base model created, the predictive accuracy of this model should be determined with each feature added to the model. This should be accomplished by training the classifier with the training data set, then predicting the classes of a validation data set, and recording the number of true positives and incorrect classifications.

Algorithm 1: Modified Forward Stepwise Analysis to Extract Features

The iterative portion of the algorithm is then implemented, where an additional feature is added to the previous iteration's model and testing the model's accuracy, until a stopping criteria is met. These stopping criteria are at the discretion of the programmer and could be as simple as the number of desired features in the model, a decrease in prediction accuracy through an iteration, or involve an over-fitting penalty function threshold.

In the event that two or more features would equally improve the predictive accuracy of the model, the scoring criteria in (5) is used. The feature with the smallest score should suggest a feature that, relatively speaking, would most reliably improve the model.

Pseudocode for this algorithm is provided in Algorithm 1. As an example, one iteration of the algorithm is illustrated in Fig. 6, where a feature is added to the model based on its score value.

In this study, the proposed forward stepwise algorithm (Modified) described in Algorithm 1 was implemented in *Python 3.8.5*. The stopping criteria were set to add features until the next iteration model would have the classification accuracy that would decrease the model performance, or a maximum of 7 features had been added to the model.

2.2. Classifier & feature extraction methods

The sequential feature selection method was implemented using *scikit-learn 0.24*, with the stopping criteria set to extract 7 features. The Boruta feature selection method was provided by Daniel Homola in the *boruta.py* Github repository [8]. [17]. The Boruta algorithm was configured to automatically determine the number of estimators, a verbosity of 2, and the Random Forest classifier within the algorithm was set to use balanced class weights and a maximum tree depth of 5.

2.3. Classification methods

Several classification methods could be utilised for this application, including quadratic discriminant analysis (QDA), support vector machine classifier (SVM), k-nearest neighbours (kNN), Naive Bayes (NB), and Random Forest (RF) [4,15,27]. Each of these classifiers will be used in this study to have a deeper understanding of the potential of tissue classification from electric impedance data, as well as a comparison of the feature extraction methods.

For this study, the QDA classifier, NB classifier, and the SVM classifier were configured to the default values from *scikit-learn 0.24.2*. The k-Nearest Neighbours (kNN) classifier was set up to consider 3 neighbours, with uniform weights, and to use standard Euclidean distance as the metric. The Random Forest (RF) classifier used 10 estimators, with bootstrapping enabled. The remaining parameters for the kNN and RF classifiers were left as the default values from *scikit-learn 0.24.2*.

Data was collected for 9 runs for each feature selection method and classifier pairing.

3. Results

The results of this paper are split into two stages. The first stage of results presents the gathered EIS data from the tissues. The second set of results compares the predictive accuracy from the different feature selection and classification methods (see Fig. 1).

3.1. Tissue measurement

A modified brachytherapy needle developed in [12] uses a bipolar electrode arrangement in combination with the an impedance spectroscopy analyzer (Quadra from Eliko, Tallin, Estonia) to measure the tissue electric impedance at the tip, refer to Fig. 2. The investigated organs include.

- 22 samples of ex-vivo poultry liver;
- 22 samples of ex-vivo bovine liver;
- 22 samples of ex-vivo bovine kidney;
- 22 samples of ex-vivo bovine muscle;
- 22 samples of freshly excised canine testicle;
- 22 samples of freshly excised canine ovary;

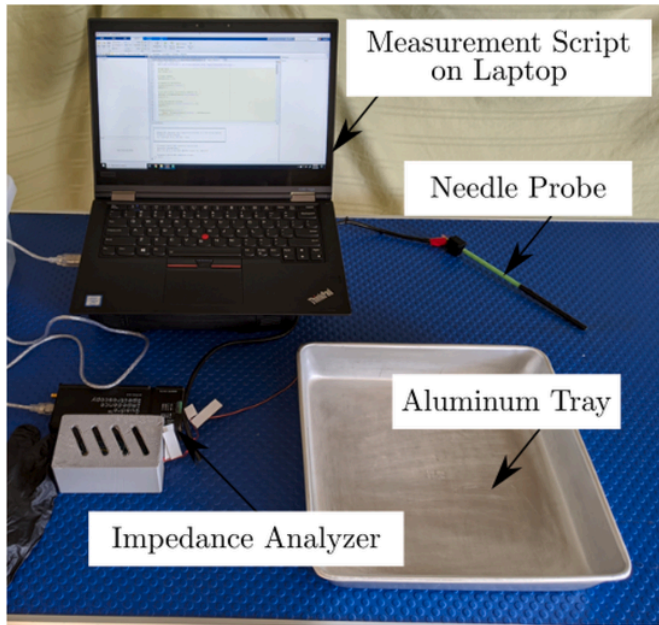


Fig. 1. Experimental setup for measuring the tissue samples. The impedance spectroscopy analyzer was connected to a coaxial bipolar electrode embedded needle.

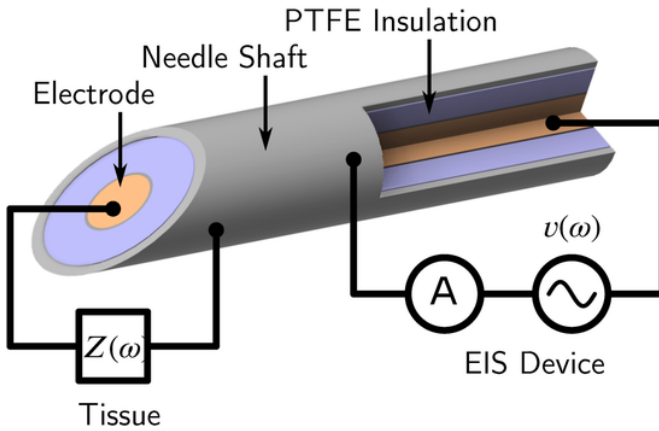


Fig. 2. CAD model of a bipolar electrode arrangement electrode embedded needle. The two electrodes are the coaxial core electrode and the needle shaft and are separated by polytetrafluoroethylene (PTFE). A sinusoidal voltage of frequency ω is applied across the electrodes and the current is measured inline. With the frequency, current, and voltage known the impedance $Z(\omega)$ can be determined. Image from [12], reused with permission.

The organs were trimmed of connective tissue and fat where applicable. The canine organs were measured at a local veterinarian hospital that were conducting scheduled spay and neuter surgeries. These ovary and testicle samples were measured immediately following excision during surgery. The poultry liver, bovine liver, bovine kidney and bovine muscle were purchased from a local butcher, where they were refrigerated below -4°C . The samples were kept refrigerated until they were segmented into pieces and trimmed of unwanted connected tissue. The kidney samples were cut to expose the cross section of each lobe. The needle probe was inserted into the renal cortex for all kidney samples, see Fig. 3. For the bovine muscle, the meat was cubed into approximately 2 cm samples. The needle probe was inserted parallel with the direction of the muscle fibres. Remaining strands of fat in the samples were avoided during insertion. All tissue samples were recorded at 20°C room temperature and the same needle probe was used for all

measurements. The needle probe was cleaned and sanitised between each use.

The impedance spectroscopy device was ground-ded with the aluminium tray that the tissue samples would be placed on during measurements. At a single frequency, the impedance magnitude and phase were measured 10 times and averaged. The impedance was measured following a 4.2 V excitation signal at the following frequencies in Hz,

$$f = \begin{bmatrix} 10.42 & 20.83 & 31.25 & 100 & 114.58 & 300 & \dots \\ 322.92 & 700 & 1100 & 1700 & 2300 & 3100 & \dots \\ 11000 & 17000 & 23000 & 31000 & 43000 & 61000 & \dots \\ 89000 & 127000 & 179000 & 251000 & 349000 & & \end{bmatrix}$$

With the current data available there are $2N$ variables available for classification: magnitude and phase at N frequencies.

In total, across the tissue types, 132 samples were measured. The measured impedance for each tissue was inspected for outlier or noisy data. Ultimately, one sample from each type was discarded, resulting in 126 samples used in the experiments.

3.1.1. Data preparation & analysis

The measurement samples were separated into three categories: test, train and validation. The data was initially partitioned with a 70/30% split for test and training data. The training data was further split into a validation data set, also using a 70/30% split. The split-training and validation data sets are used with the feature extraction method. After the feature extraction, the training and validation data sets are then combined to train the classifier to be used on the test data.

The average impedance for some of these samples are shown in Fig. 4. It is observed that the average impedance for these tissues indeed differ, and could potentially be used for classification. It is evident that the measurements for any of the presented tissues contain variation in the impedance across the samples along the frequency spectrum. The question is then raised if there is a way to determine key features as others have seen in [7,10], such that measurements need only be taken at these frequencies without compromising, or potentially improving, classification accuracy. This is the objective of the feature selection study.

3.2. Feature observations in EIS data

The results of the Shapiro-Wilk test confirmed that all sample measurements were normally distributed.

The variance across all samples for all tissues revealed that the greatest variance occurs at 10.42 Hz for the magnitude and at 114 Hz for the phase. For both magnitude and phase, the variance was smallest at 349 kHz, the highest measured frequency.

The standard deviation for all tissues revealed that the smallest deviation in the magnitude occurs at 349 kHz. The phase showed similar results for muscle, ovaries and testes, but the bovine liver, poultry liver and bovine kidney had the smallest standard deviation in the range of 1700–3100 Hz.

The probability density function for each tissue is constructed at all features. It was desired to find where there was minimal overlap in values for all tissues. Using any two functions the area can be estimated through integration, see Fig. 5. Analysis of the overlap metric for all tissue combinations reveals there was no single feature that is distinctly unique for all tissues. There are, however, some features with low overlap for multiple tissues, such as the magnitude at 349 kHz in Fig. 5.

The above metrics do not reveal a clear feature (or combination thereof) that should be automatically included in any of the classifier models. The analysis does reveal that there are features that are more likely to be seen in new samples. Namely, the highest measured frequency features have the lowest standard deviation, suggesting future test samples would yield similar values, thus making them reliable pre-

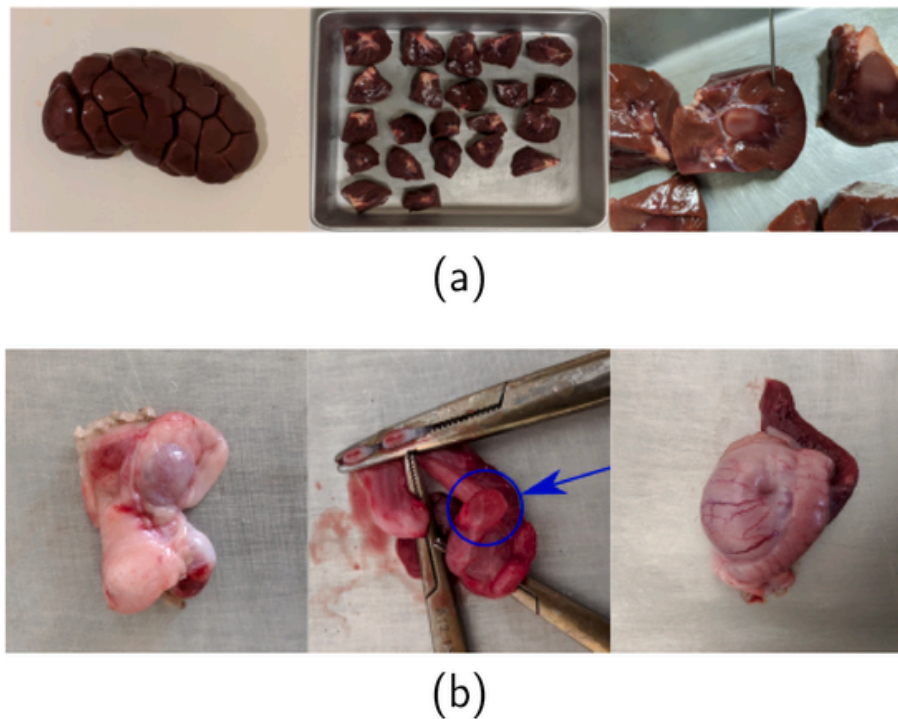


Fig. 3. (a) Preparation of the bovine kidney samples. The kidney was sectioned into 22 pieces and placed on an aluminium tray. The needle was inserted into the same location across the other samples. The other ex-vivo tissue samples received similar preparation. (b) Examples of the freshly excised tissue collected during data collection. From left to right, ovary, ovarian cyst, testicle.

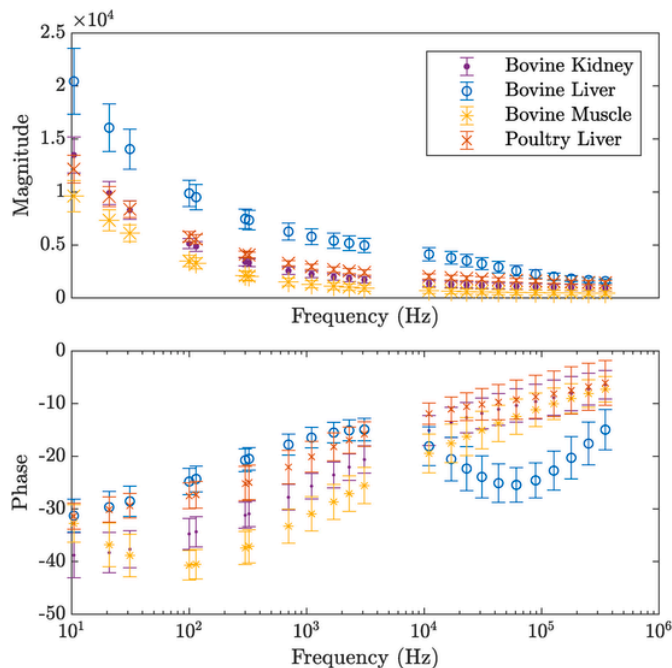


Fig. 4. The average electric impedance for 15 samples of 4 tissues in the database training set with standard deviation.

dictors. Regardless, in this study all models started without any features.

3.3. Classification & performance

The collected EIS data was then used with the methods to determine the most effective combination. The Boruta, SFS, and proposed Modified feature extraction methods were used to construct models for the

classifiers. The average accuracy from 9 runs for each classifier and feature selection method is presented in Table 1. The average number of extracted features from each of the selection methods are listed in Table 2. The average most precise combination found with this study was Boruta feature extraction with a Random Forest classifier at 90%. However, the single best run performance was found to be 97% using a support vector machine classifier and the proposed Modified method. Interestingly, this model was built with 6 features representing only the phase information of the impedance. However, as shown by the standard deviation across all of the selection methods, the SVM classifiers had volatile swings in predictive accuracy across the different runs. Despite this, the Modified method had on average better performance with the SVM classifier than the other selection methods.

The Modified method and SFS had relatively comparable performance in predictive accuracy. Both of these methods outperformed Boruta with all classifiers except with the Random Forest classifier.

Illustrated in Fig. 7 are the samples in the training data set where some clustering can be seen for several classes at the features shown. The Boruta feature selection typically selected all, or all but one, feature as significant. As a result, there is little difference in using all features and using the Boruta models. With the SFS method, its stopping criteria was set to provide 7 features, so all models were built with this criteria. The proposed Modified method provided the least amount of features.

As a comparison, a model with all features and a model generated with the proposed Modified method were used with a SVM classifier and are shown in Fig. 8. It is evident that using the model with fewer features improved the predictive accuracy of the classifier.

4. Discussion & conclusion

This paper presented different feature extraction methods and classifiers to use with electric impedance spectra for ex-vivo tissue classification. The experiments in this paper investigate three feature selection techniques and five different classification methods. The results of the experiments suggest that for most of the classifiers used, the predictive

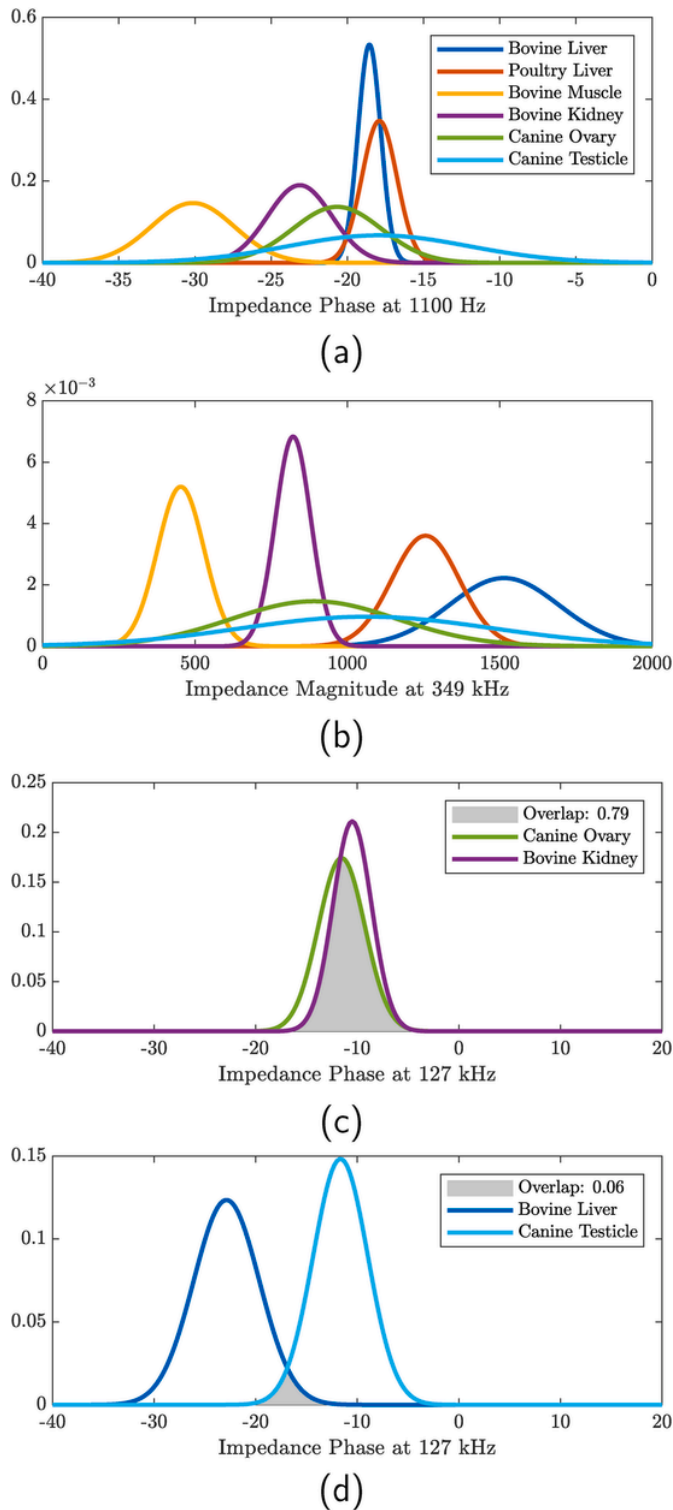


Fig. 5. (a) Distribution of the impedance phase at 1100 Hz feature, where there is significant overlap in the tissues, which would discourage its use in the classifier model. (b) The magnitude at 349 kHz feature illustrates a scenario where there is still a significant amount of overlap in some of the tissues, but there are distinct regions for some tissues, suggesting that it could be a possible inclusion in the classifier model. (c) Quantifying the overlap between the distributions of two tissues with similar values. (d) A smaller overlap indicates that the tissues are less likely to share a similar value.

accuracy increased on average when using a reduced number of features in the model.

While the performance of SFS and the proposed Modified method were comparable, the results of this study highlight its effectiveness in reducing the number of features needed to obtain similar predictive accuracy. Reducing the number of frequencies to measure the electric impedance is useful in developing these sensor embedded surgical tools for real-time tissue classification. Focusing solely on the predictive accuracy, it was seen in this study that the RF classifier performed the best, even with a large number of features in the model. Another advantage of the RF classifier is that it was the most consistent across the runs and classifiers, as shown by the small standard deviation. By comparison, the SVM classifier was the least consistent across all the classifiers and runs.

In this study the classification models were built using the measured impedance directly from the EIS device. Another approach to consider is to fit the measurements to an equivalent circuit model and using the estimated impedance from the circuit model at specific frequencies, or using the circuit element values (resistance, capacitance, etc.) similar to the work in [14].

Improvements could be made to the method proposed in this paper to further increase its performance. The similarity scoring metric could incorporate the skew of the training data, or replace the overlapping index with the probability Jaccard. Accounting for collinearity in features could be a useful addition to the method and remove redundant features being added to the model.

It should be stated that there are limitations to this study. Notably, with the tissue sample measurements split into the test and training data sets, there was a limited amount of data to build the model from. It is expected that having a larger number of samples for each tissue would improve the robustness when building the model, and having a larger test data set would reinforce, or possibly refute in the case of over fitting, the effectiveness of the classifier. Furthermore, it would be worthwhile to investigate a larger variety of tissues than those mentioned in this paper. The EIS measurements of cancerous and healthy tissues are of particular interest in determining if there are any specific frequencies of where it is easiest to differentiate the tissues by electric impedance.

Lastly, one might expect that there could be different performance of the classifiers by altering the parameters from those selected in the study. For example, changing the number of neighbours to consider in the kNN classifier, or a different kernel function in the SVM classifier.

Beyond the scope of this study, the proposed feature extraction method may be applicable to other continuous multivariate classification problems. It may be worthwhile to investigate the applicability of this relatively simple feature extraction.

Declaration of competing interest

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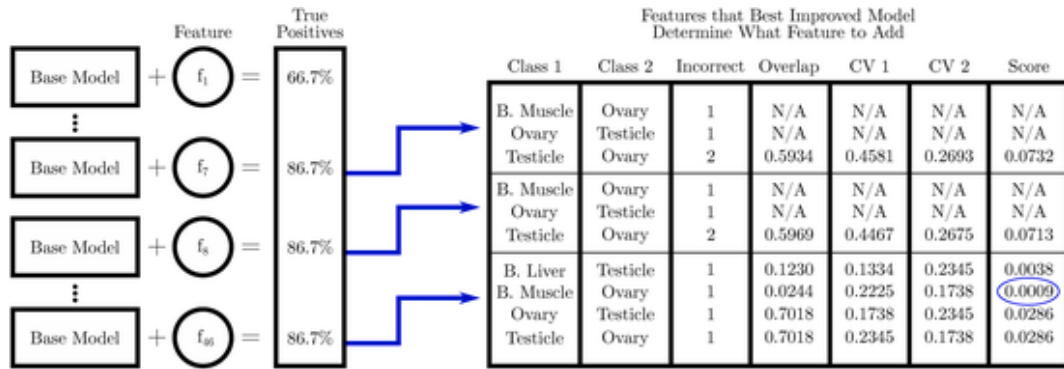


Fig. 6. The first iteration of the modified forward stepwise method illustrated with the EIS data. Each of the remaining features are added to base model separately, and the true positives classifications are evaluated. This iteration revealed that there were three features that would improve the model by the same amount. A closer inspection of the classification results is needed to determine which of the three features should be added. For a given feature, the worst classification pair is selected, to see if it can be improved. The overlap η between these features and the corresponding v are calculated. The score is calculated using (5). The feature with the lowest score will be added to the model. In this example f_{46} , the impedance phase at 349 kHz, is added to the next iteration of the model. This feature is removed from the remaining features, and the process repeats until the stopping criteria is met.

Table 1

Feature extraction method & classifier accuracy.

| | All | Boruta | SFS | Modified |
|-----|---------|---------|---------|----------|
| QDA | 43 ± 12 | 44 ± 10 | 85 ± 6 | 86 ± 6 |
| NB | 80 ± 6 | 85 ± 4 | 88 ± 5 | 86 ± 7 |
| kNN | 80 ± 6 | 75 ± 4 | 77 ± 7 | 76 ± 6 |
| SVM | 56 ± 12 | 58 ± 11 | 59 ± 14 | 68 ± 15 |
| RF | 84 ± 5 | 90 ± 4 | 78 ± 6 | 81 ± 3 |

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Table 2

Average number of extracted features.

| All | Boruta | SFS | Modified |
|-----|--------|-----|----------|
| 46 | 45 | 7 | 5.8 |

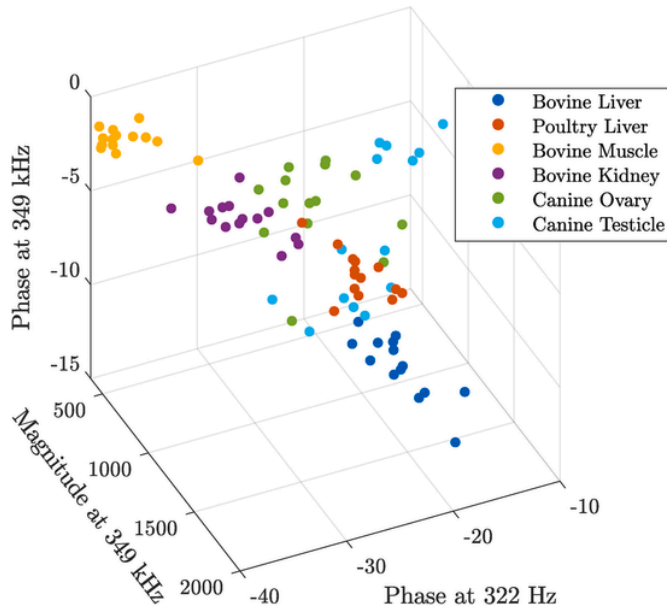


Fig. 7. A scatter plot showcasing three of the six extracted features of the training data in a model built with the Modified method and a QDA classifier. Clusters for some of the tissues are distinctly evident, suggesting that these features could be used to discriminate the tissues.



Fig. 8. (a) A confusion matrix of a test data set using the SVM classifier with the all features in the model. (b) A confusion matrix of another test data set using the SVM classifier with a 6-feature model built with the proposed Modified method. The classifier was able to correctly identify most samples, showing drastic improvement when using select features over all features.

Algorithm 1: Modified Forward Stepwise Analysis to Extract Features

Result: Which features help predict the classes
 Use (3) to get η for every class pair and feature;
 Use (4) to calculate v for each feature;
while a stop condition is not met **do**
 for the number of remaining unused features **do**
 Add feature to current version of model;
 Determine model accuracy;
 Record best performance;
 end
 if More than one new feature had same best improvement to model accuracy **then**
 Determine worst misclassifications;
 Get score using (5) with v and η ;
 Select feature with smallest score;
 end
 Add best performing feature to model;
end

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