Prediction for Periodontists by Oral Bacteria in Korean

2020 1st Semester Interdisciplinary Project

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1 Introduction

1.1 Periodontitis

Periodontitis is an inflammatory disease of the periodontium which is characterized by a progressive destruction of the tissues supporting the tooth [2]. In histopathologically, periodontitis may result periodontal pocketing, location of junctional epithelium apical to the cemento-enamal junction, loss of collagen fibers subjacent to the pocket epithelium, numerous poly-morphonuclear leukocytes in epithelium and a dense inflammatory cell infiltrate with plasma cells, lymphocytes, and macrophages [3]. Periodontits is currently assumed to progress as periodic, relatively short episodes of rapid tissue destruction followed by some prolonged intervening periods of disease remission [2].

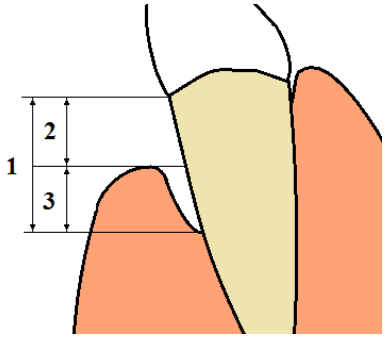


Figure 1: Diagram of Gingival Recession [1]

Periodontitis is diagnosed by measuring clinical attachment loss (CAL). Note that the CAL is the length of the figure 1-1, which is sum of gingival recession (GR) in figure 1-2, and probing depth (PD) in figure 1-3.

Periodontitis is generally believed to be a result of a host-parasite interaction in which bacteria are the determinants of periodontitis [4]. In etiology, the primary cause of periodontitis is presumed as a bacterial infection as the primary cause of periodontitis [3]. Thus, the treatment of periodontitis includes antibiotics and dental surgery.

In this manner, some medicines have been introduced for treatment. However, the success in the prevention and treatment of periodontitis has been limited. Many *in vitro* studies shows that Asian have the different bacteria from non-Asian, due to their groceries [5]. Thus, the developments of plaque and calculus in Asian differ, and may lead to distant reactions between Asian and non-Asian.

1.2 Machine Learning

Machine learning is the study of algorithms which advance spontaneously through experience. Machine learning is conjugated where is infeasible with conventional algorithms such as computer vision. Many papers show that machine learning brings out better result than human recognition.

If the feedback provides the correct answer for specific inputs, then learning problem is called supervised learning [6]. Classification is a kind of supervised learning for discrete values; regression is for continuous values.

1.3 Purpose of Research

There are many studies which have tried to find bacteria as bio-markers [7, 8]. Most of these papers, though, researched in Western people [9, 10]. As I mentioned herein-above, oral bacteria population may differ between Western and non-Western. In this approach, therefore, prediction periodontitis from machine learning which based on oral bacteria population of Korean is required.

I aimed to probe the performance of machine learning which predict the severity of periodontitis. Specifically, the purpose of this research is herein-after:

1. Classify the stage of periodontitis by oral bacteria.
2. Regress the CAL, the GR, or the PD by oral bacteria.

2 Materials

2.1 Clinical Examinations

This study included 784 samples from who visited the Department of Periodontics, Pusan National University Dental Hospital, between August 2016 and March 2019. The study protocol was approved by the Institutional Review Board of Pusan National University Dental Hospital (PNUDH-2016-019). All samples are provided written informed consent upon complete information regarding the objectives and procedures of this study.

The diagnosis of samples was completed as [11]. Also, the stage of periodontitis was categorized on the basis of the CAL as following:

- Healthy: $\leq$ 1mm
- Slight: 1-2 mm
- Moderate: 3-4 mm
- Severe: $\geq$ 5 mm

Moreover, the following patients were excluded:

- who received periodontal treatment with past six months
- who were pregnant or breastfeeding
- who refused to approve the informed consent form

The CAL was measured with a periodontal probe (PGF-W, Osung, Kwangmyung, Republic of Korea) during the clinical evaluation. All measurement were performed by two fully-experienced periodontitsts.

2.2 Analysis of Bacterial Copy

Collection of mouthwash sample and DAN extraction were performed as [12]. Also, the nine pathogens were chosen as herein-after:

1. *Porphyromonas gingivalis (Pg)*
2. *Tannerella forsysthia (Tf)*
3. *Treponema denticola (Td)*
4. *Prevotella intermedia (Pi)*
5. *Fusobacterium nucleatum (Fn)*
6. *Campylobacter rectus (Cr)*
7. *Aggregatibacter actinomycetemcomitans (Aa)*
8. *Peptostreptococcus anaerobius (Pa)*
9. *Eikenella corrodens (Ec)*

Multiplex qPCR system was optimized for the nine pathogens after the building of standard curves for each pathogen.

3 Methods

The entire program is disclosed by GitHub in `https://github.com/Fumire/Periodontist_Fall2019`.

3.1 Python Packages

Python programming language had been used to analyze data. Also, many Python modules had been adopted as hereinafter.

3.1.1 Pandas

Pandas is a Python library of rich data structures and tools for working with structured data sets common to statistics, finances, social sciences, and many other fields [13].

3.1.2 Scikit-learn: Machine Learning in Python

Scikit-learn is a Python module integrating a wide range of state-of-the-art machine learning algorithms for medium-scale supervised and unsupervised problems [14].“

3.1.3 Seaborn

Seaborn is a Python data visualization library based on *matplotlib*. It provides a high-level interface for drawing attractive and informative statistics graphics [15].

3.2 Classification

In classification, every combination of the nine pathogens, $2^9 = 512$ combinations, will be used. Also, in classification, some classes are merged into new class. For instance, healthy class and slight class could be merged, then the algorithm will be performed with four classes. As the pathogen combination, every combination of merging classes will be finished.

3.2.1 Confusion Matrix and Its Derivations

A confusion matrix is a table which displays the performance of classification algorithm. Typically, the confusion matrix is like as table 1.

Table 1: Abstract Form of Confusion Matrix

		Actual Class	
		Positive	Negative
Predicted Class	Positive	True Positive	False Positive
	Negative	False Negative	True Negative

Many derivations, such as sensitivity and specificity, come from the confusion matrix. The equation of derivations are followings:

- Sensitivity = $\frac{TP}{P}$
- Specificity = $\frac{TN}{N}$
- Precision = $\frac{TP}{TP+FP}$
- Negative predictive value = $\frac{TN}{TN+FN}$
- Miss rate = $\frac{FN}{P} = \frac{FN}{FN+TP}$
- False positive rate = $\frac{FP}{N} = \frac{FP}{FP+TN}$
- False discovery rate = $\frac{FP}{FP+TP}$
- False omission rate = $\frac{FN}{FN+TN}$
- Threat score = $\frac{TP}{TP+FN+FP}$

- Accuracy = $\frac{TP+TN}{P+N}$
- F1 score = $\frac{2TP}{2TP+FP+FN}$

Note that followed abbreviations are used:

- P: Positive
- N: Negative
- TP: True Positive
- TN: True Negative
- FP: False Positive
- FN: False Negative

3.2.2 Classification Algorithm

For classification, the followed algorithms has been used:

- K-Neighbors
- Linear Support Vector Classification (SVC)
- Poly SVC
- RBF SVC
- Sigmoid SVC
- Decision Tree
- Random Forest
- Adam Neural Network (NN)
- lbfgs NN
- Ada-Boost

These are almost every algorithm which are supported by *Scikit-learn*.

3.3 Regression

In regression, every combination of the nine pathogens, $2^9 = 512$ combinations, will be used.

3.3.1 Coefficient of Determination

Coefficient of determination, also known as R^2 or R-square, is common to use as an index of the size of the relation [16].

3.3.2 Regression Algorithm

For regression, the followed algorithm has been used:

- Linear Regression
- Ridge
- Support Vector Regression (SVR)
- Nu SVR
- Linear SVR
- Elastic Network
- K-Neighbors
- Decision Tree
- lbfgs Multi-Layer Perceptron (MLP)
- sgd MLP

These are almost every algorithm which are supported by *Scikit-learn*.

4 Results

4.1 5-class Classification

Figure 2 displays the derivations of confusion matrix in multi-class classification. Note that the values in figure 2, mean values from combinations which used same number of features will be shown.

As figure 2, the Poly-SVC algorithm has the best values with all features.

Figure 3 shows the heatmap between real and predicted classes.

4.2 4-class Classification

4.2.1 Healthy-Slight Class

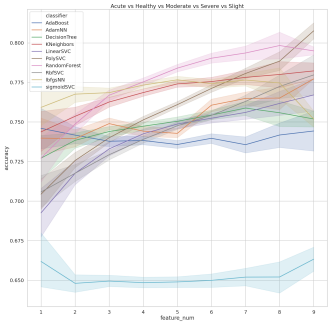
4.3 Regression

5 Discussion

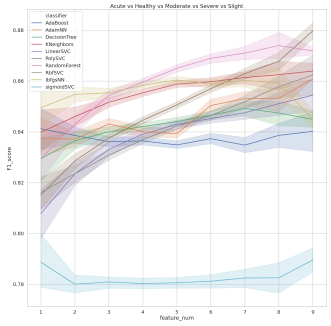
6 Acknowledgment

The relative study which based on the identical data has been submitted *American Society for Microbiology* as ”Prediction of chronic periodontitis severity using machine learning models based on salivary bacterial copy number”.

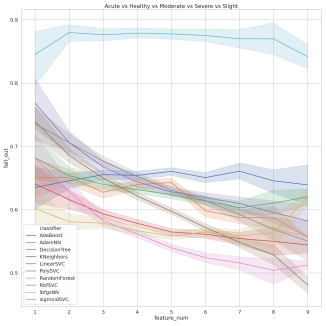
I thank all study subjects for their generous participation and the clinicians for their contributions leading to the succesful completion of this study. This work was partly supported by the Technological Innovation R&D Program (C0445482), funded by the Small and Medium business Administration (SMBA, Republic of Korea). This work also partly supported by the Next-Generation Information Computing Development Program of the National Research Foundation of Korea funded by the Ministry of Science and ICT (NRF-2016M3C4A7952635). This research work was also partly supported by the National Research Foundation (NRF) of Korea grant NRF-2017M3A9B6062026, funded by the government of Republic of Korea. I would like to thank David Whee-Young Choi for constructive criticism of the manuscript.



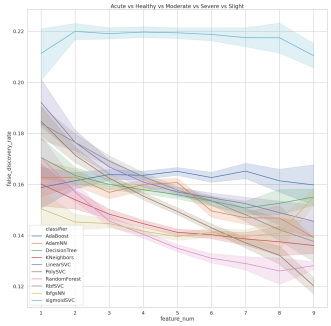
Accuracy



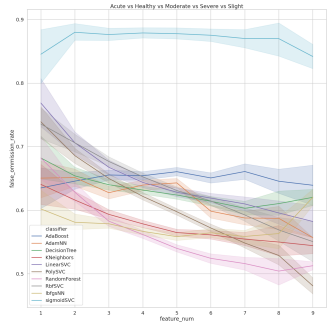
F1 score



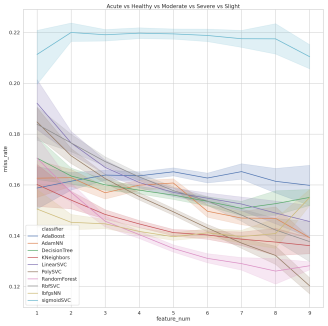
Fall-out



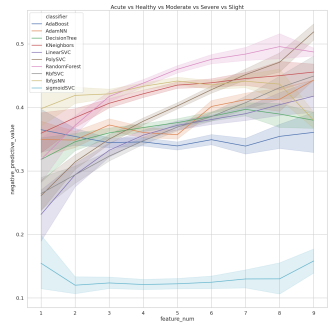
False discovery rate



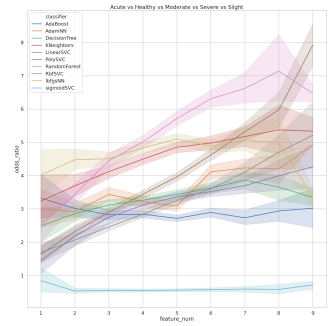
False ommision rate



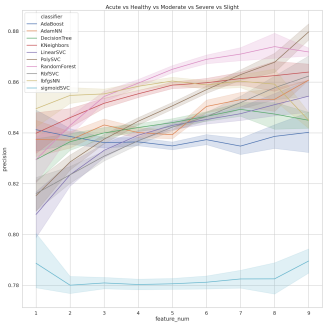
Miss rate



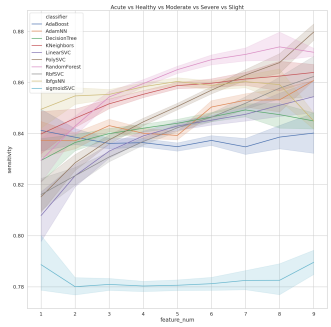
Negative predictive value



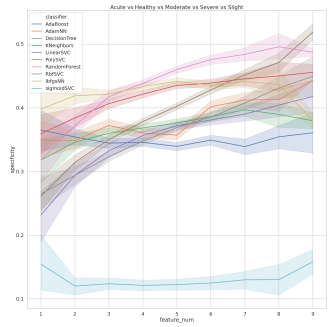
Odds ratio



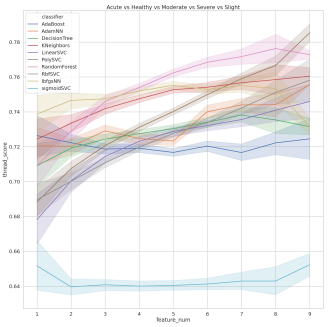
Precision



Sensitivity



Specificity



Thread score

Figure 2: Confusion Matrix Derivations from 5-class Classification

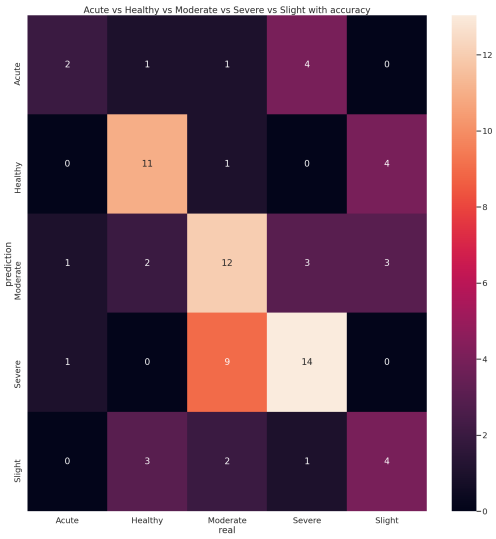


Figure 3: Heatmap Plot 5-class Classification with Poly-SVC

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