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A Survey of Thalassemia and Iron Deficiency Anaemia Classification using a Voting Classifier

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ABSTRACT

Thalassemia is viewed as a prevalent inherited blood disease that has gotten exorbitant consideration in the field of medical research around the world. Inherited diseases have a high risk that children will get these diseases from their parents. If both the parents are β-Thalassemia carriers then there are 25% chances that each child will have β-Thalassemia intermediate or β-Thalassemia major, which in most of its cases leads to death. Prenatal screening after counseling of couples is an effective way to control β-Thalassemia. Iron deficiency anemia (IDA) is considered one of the most common nutritional deficiencies globally, making it a prevalent health issue. Its prevalence varies among different populations and geographic regions. To diagnose iron deficiency anemia (IDA), healthcare professionals typically perform a series of tests to evaluate the patient's iron status and identify the underlying cause of the deficiency.

Thalassemia and iron deficiency anemia are thus two common hematological disorders characterized by abnormal hemoglobin synthesis and reduced iron levels, respectively. Distinguishing between these conditions is crucial for accurate diagnosis and appropriate treatment. Hereby, we propose a classification approach based on an SGR-voting classifier to differentiate between thalassemia and iron deficiency anemia. SGR-VC is an ensemble of three machine learning algorithms: Support Vector Machine, Gradient Boosting Machine, and Random Forest.

Keywords: Thalassemia, Iron Deficiency Anaemia, Normalization, Data Cleaning, Support Vector Machine, Gradient Boosting Machine, Random Forest, Ensemble Classifier, SGR-Voting Classifier.

I. INTRODUCTION

Thalassemia is mainly a combination of two Greek words, "Thalassa" meaning sea and "Hema" means blood. Thalassemia is an inherited blood disorder that is commonly found in different parts of the world especially in South Asia. Inherited disease means that it is passed from parents to their children. In Thalassemia, hemoglobin levels decrease from normal limit which causes reduction in the count of productive red blood cells, which may lead to severe anemia. Red blood cells (RBCs) mainly consist of a protein containing a great deal of iron named hemoglobin which form the main concentration of RBCs. Iron deficiency anemia (IDA) is a prevalent hematological disorder characterized by a deficiency of iron, leading to reduced red blood cell production and subsequent impaired oxygen transport. It affects individuals across all age groups, with particularly high prevalence among children, women of childbearing age, and older adults.

SGR-VC:

Experiments are performed on Tree-based machine learning models (Random Forest (RF) and Gradient Boosting machine (GBM)) and probability-based machine learning models (Support Vector Machine (SVM)). A Voting Classifier (VC) based on the ensemble of SVM, GBM and RF called SGR-VC is considered. The proposed SGR-VC can automatically diagnose Thalassemia carriers by using CBC test which is a cost effective and fast solution. The patient wrongly classified as thalassemic by one of the machines is sent for further diagnosis of IDA due to its similar traits with thalassemia. SGR-VC is an ensemble of SVM. GBM and RF are designed to isolate and analyze β-Thalassemia carriers from β-Thalassemia non-carriers.

II. THALASSEMIA AND IRON DEFICIENCY ANEMIA

A. Overview of Thalassemia

Thalassemia is an inherited blood disorder that affects the production of haemoglobin. It can be classified into alpha and beta thalassemia, and its severity varies from mild to severe. Treatment may involve blood transfusions, chelation therapy, and stem cell transplantation. Early diagnosis and genetic counselling are important for managing the condition.

B. Overview of Iron Deficiency Anaemia (IDA)

Iron deficiency anaemia (IDA) is a common type of anaemia caused by insufficient iron levels in the body. It leads to reduced production of healthy red blood cells, resulting in symptoms such as fatigue, pale skin, and shortness of breath. Diagnosis involves blood tests to measure haemoglobin, ferritin, and iron levels. Treatment typically involves iron supplementation and dietary changes. Prevention includes consuming iron-rich foods and, in some cases, iron supplementation. Consulting a healthcare professional is important for proper diagnosis and treatment.

C. Key Similarities and Differences between Thalassemia and IDA

Key Similarities between Iron Deficiency Anaemia (IDA) and Thalassemia:

1. Anaemia: Both IDA and Thalassemia are forms of anaemia, which means they involve a decrease in the number or functionality of red blood cells, resulting in reduced oxygen-carrying capacity.
2. Fatigue and Weakness: Fatigue and weakness are common symptoms of both conditions due to insufficient oxygen supply to the body's tissues.
3. Pale Appearance: Individuals with both IDA and Thalassemia may exhibit pale skin and mucous membranes due to reduced red blood cell production.

Key Differences between Iron Deficiency Anaemia (IDA) and Thalassemia:

1. Causes: The underlying causes of IDA and Thalassemia differ significantly.

- IDA is primarily caused by a deficiency of iron in the body, often due to inadequate dietary intake, blood loss, or poor iron absorption.

- Thalassemia is an inherited genetic disorder characterized by abnormal or reduced production of haemoglobin chains.

2. Iron Levels: Iron deficiency is a key characteristic of IDA, whereas Thalassemia is not primarily associated with iron deficiency. In Thalassemia, the production or structure of haemoglobin is affected, but iron levels may be normal or even elevated.

3. Genetic Inheritance: IDA is not inherited and can occur in individuals of any age or sex. In contrast, Thalassemia is a genetic disorder inherited from parents who carry mutated haemoglobin genes.

4. Severity and Type of Anaemia: IDA typically results in microcytic anaemia, characterized by smaller red blood cells, whereas Thalassemia often leads to microcytic or hypochromic anaemia with abnormal or reduced red blood cells.

5. Treatment Approaches: Treatment strategies for IDA and Thalassemia differ.

- IDA is usually treated with iron supplementation, dietary changes to increase iron intake, and addressing the underlying cause if present.

- Thalassemia management may involve blood transfusions, bone marrow transplants, and regular monitoring of haemoglobin levels.

It is important to note that these are general differences and similarities, and the specific presentation and management of IDA and Thalassemia vary based on individual cases and severity.

III.EXISTING MACHINE LEARNING DIAGNOSTIC METHODS

A. Thalassemia Diagnostic Methods using Machine Learning:

Thalassemia is a group of inherited blood disorders characterized by abnormal haemoglobin production. Machine learning techniques have been employed to aid in Thalassemia diagnosis. Some existing diagnostic methods utilizing machine learning include:

- Support Vector Machines (SVM): SVM has been applied for Thalassemia classification based on features extracted from blood samples, such as red blood cell indices and haemoglobin levels (Bhadade et al., 2017).

- Artificial Neural Networks (ANN): ANN models have been used to diagnose Thalassemia by analyzing haematological parameters and genetic information (Misra et al., 2016).

- Decision Trees: Decision tree-based models have been developed to classify Thalassemia based on clinical and laboratory data (Gupta et al., 2019).

B. IDA Diagnostic Methods using Machine Learning:

Iron Deficiency Anaemia (IDA) is a condition caused by a lack of iron in the body, leading to decreased production of red blood cells. Machine learning approaches have also been explored for IDA diagnosis. Some existing diagnostic methods using machine learning for IDA include:

- Random Forest: Random Forest models have been utilized to predict IDA based on various features, including haemoglobin levels, red blood cell indices, and demographic information (Zhang et al., 2018).

- Gradient Boosting Machines (GBM): GBM models have been employed for IDA diagnosis using features

like red blood cell parameters, ferritin levels, and demographic factors (Sahu et al., 2021).

- Deep Learning: Deep learning models, such as convolutional neural networks (CNN), have been used to classify IDA based on peripheral blood smear images, allowing for automated and efficient diagnosis (Ahn et al., 2020).

C. Limitations of Current Diagnostic Methods using Machine Learning:

Despite the advancements in machine learning-based diagnostic methods for Thalassemia and IDA, several limitations exist:

- Limited Data Availability: Availability of large-scale, high-quality datasets is crucial for training accurate machine learning models. In some cases, access to diverse and comprehensive datasets for Thalassemia and IDA may be limited.

- Interpretability and Explainability: Certain machine learning algorithms, such as deep learning models, are often considered black-box models, making it challenging to interpret and explain the reasoning behind the predictions, which may be necessary in the medical field.

- Generalization and Validation: Machine learning models need to be validated on independent datasets to ensure their generalizability and robustness. Validation studies with diverse populations and demographics are required to assess the performance of these models in real-world scenarios.

- Clinical Integration: Integrating machine learning-based diagnostic methods into the existing clinical workflow and obtaining regulatory approvals for their use in clinical settings pose additional challenges that need to be addressed.

Addressing these limitations is essential for the successful translation of machine learning-based diagnostic methods into clinical practice, enabling accurate and efficient diagnosis of Thalassemia and IDA.

IV. VOTING CLASSIFIER AND ITS APPLICATION

Although a conclusion may review the main points of the paper, do not replicate the abstract as the conclusion. A conclusion might elaborate on the importance of the work or suggest applications and extensions. Authors are strongly encouraged not to call out multiple figures or tables in the conclusion these should be referenced in the body of the paper.

V. DATA PREPROCESSING

The pre-processing steps of data cleaning and normalization are applied to the dataset, specifically focusing on the classification of β-Thalassemia Carriers from RBC (Red Blood Cell) indices. These steps are crucial to ensure data quality, address missing values, and normalize attribute values for accurate classification of individuals with β-Thalassemia and Iron Deficiency Anaemia (IDA) conditions.

1. Data Cleaning:

Data cleaning is performed to remove impurities and correct errors in the dataset that could affect the classification process. In the context of β-Thalassemia and IDA classification, the following data cleaning steps are conducted:

i. Elimination of incomplete input values: Missing values in CBC tests related to RBC indices are filled by referring to the medical records of the hospital. If the missing values cannot be found in the medical reports, the entire record is removed from the dataset. This

step ensures that the dataset contains complete information for accurate analysis.

ii. Elimination of duplicate data: Duplicated entries in the dataset are identified and removed using the patient_id attribute. Each patient is assigned a unique patient_id, allowing for the identification and removal of duplicate records. This step helps in ensuring that the dataset is free from redundant data, which could bias the classification results.

iii. Removal of insignificant attributes: Insignificant attributes that do not contribute to the classification results are removed from the dataset. These attributes may include patient-specific information like patient_id, Test date, Patient name, and Family name. By removing such attributes, the dataset is streamlined, focusing only on the relevant features necessary for classification.

2. Normalization:

Normalization is applied to the dataset to standardize the range of attribute values, which is particularly important for accurate classification of β-Thalassemia Carriers and IDA cases. The normalization process considers the normal values specific to each test and takes into account factors such as age, gender, and RBC indices. The steps involved in normalization are as follows:

1. Age normalization: Age information is normalized into two values, 0 and 1, representing children and adults, respectively. This distinction acknowledges that normal values for RBC indices can vary between these age groups.

2. Gender normalization: Gender information is normalized into two values, 0 for female and 1 for male. This step accounts for any gender-based variations in the normal range of RBC indices.

3. RBC indices normalization: Each RBC index attribute is normalized into multiple divisions, typically six divisions ranging from 0 to 5. The value 0 represents below the normal range, 5 represents above the normal range, and values 1, 2, 3, and 4 represent four equal divisions within the normal range. This normalization approach allows for a more granular representation of the RBC indices, enabling better differentiation between β-Thalassemia Carriers and IDA cases.

4. Target class normalization: The target class, distinguishing between individuals with β-Thalassemia and IDA, is represented by the values 0 and 1, respectively. This normalization allows for the effective classification of individuals into the respective categories.

By performing data cleaning and normalization, the study ensures the quality, completeness, and standardization of the dataset, enabling accurate classification of individuals as β-Thalassemia Carriers or IDA cases based on RBC indices.

VI. PERFORMANCE EVALUATION

Performance evaluation is crucial to assess the effectiveness of the classification models. The evaluation measures used in this study are specifically tailored to assess the diagnostic performance for β-Thalassemia. The following evaluation measures were employed:

1. Accuracy: Accuracy is an important measure to evaluate the overall correctness of the classification model in identifying β-Thalassemia cases correctly based on RBC Indices. It calculates the ratio of correctly classified β-Thalassemia cases to the total number of cases in the dataset.

2. Precision: Precision focuses on the positive predictions made by the model and assesses the proportion of correctly identified β-Thalassemia cases out of all instances predicted as β-Thalassemia carriers. A higher precision indicates fewer false positives, i.e., fewer cases incorrectly identified as β-Thalassemia carriers.

3. Recall: Recall, also known as sensitivity, measures the ability of the model to correctly identify β-Thalassemia cases out of all actual β-Thalassemia cases in the dataset. It evaluates the model's ability to avoid missing β-Thalassemia cases and aims for a lower false negative rate.

4. F1-score: The F1-score is the harmonic mean of precision and recall. It provides a balanced measure of the model's ability to correctly identify both positive and negative cases. The F1-score is particularly useful when there is an imbalance between the number of β-Thalassemia carriers and non-carriers in the dataset.

By utilizing these evaluation measures, the study aims to assess the performance of the ensemble classifiers in accurately classifying β-Thalassemia cases based on RBC Indices.

VII. CLASIFICATION ALGORITHMS

A. Supported Vector Machine (SVM):

Support Vector Machines (SVM) is a powerful and widely used supervised machine learning algorithm for
classification and regression tasks. It is particularly effective in solving complex problems with high-dimensional feature Spaces.

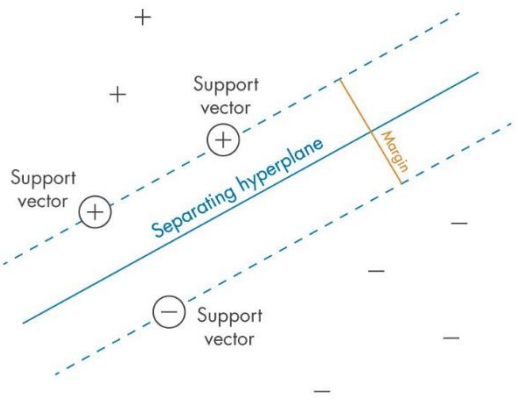

Fig.1: Support Vector Machine

SVM for β-Thalassemia Classification:

Dataset Preparation: The dataset contains relevant features related to β-Thalassemia, such as red blood cell indices (mean corpuscular volume, mean corpuscular haemoglobin), haemoglobin levels, and other such attributes.

Training Phase: The SVM algorithm is trained using the dataset, where the feature vectors represent the individuals, and the corresponding labels indicate whether they are β-Thalassemia carriers or non-carriers.

Hyperplane Optimization: SVM seeks to find an optimal hyperplane that separates the carriers and non-carriers in the feature space. The hyperplane is determined by maximizing the margin between the two classes while minimizing classification errors.
Non-linear Relationships: SVM can handle non-linear relationships between the features and the target variable by utilizing the kernel trick. The kernel function implicitly maps the input features to a higher-dimensional space, where the data points become more separable.

Support Vectors: SVM identifies the support vectors, which are the data points closest to the hyperplane. These support vectors play a crucial role in defining the hyperplane and making predictions.

Prediction Phase: Once the SVM model is trained, it can classify new, unseen individuals as β-Thalassemia carriers or non-carriers based on their feature vectors. The position of a data point relative to the learned hyperplane determines its class label.

B. Gradient Boosting Machine (GBM):

Gradient Boosting Machine (GBM) is a powerful machine learning technique that belongs to the ensemble learning family. It combines multiple weak predictive models, typically decision trees, to create a strong predictive model. GBM iteratively builds an ensemble of models, with each subsequent model learning from the mistakes made by the previous models.

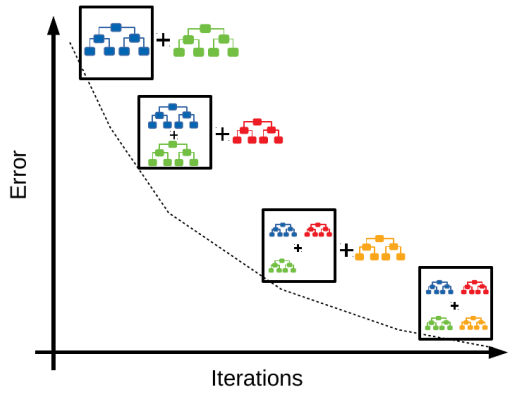

Fig.2: Gradient Boosting Machine

GBM for β-Thalassemia Classification:

Dataset Preparation: The dataset includes relevant features related to β-Thalassemia, such as red blood cell indices, haemoglobin levels, and other attributes.

Training Phase: GBM is trained using the dataset, where the feature vectors represent the individuals, and the corresponding labels indicate whether they are β-Thalassemia carriers or non-carriers.

Ensemble of Weak Learners: GBM builds an ensemble model by combining multiple weak learners, typically decision trees, in a sequential manner.

Boosting Procedure: GBM sequentially fits the weak learners to the dataset, with each subsequent learner trying to correct the mistakes made by the previous learners. It assigns higher weights to the misclassified samples to prioritize their correct classification in the subsequent iterations.

Gradient Descent Optimization: GBM employs gradient descent optimization to minimize a loss function, such as the deviance, during the training process. The algorithm iteratively updates the model by descending the gradient of the loss function to find the optimal direction for improving predictions.

Prediction Phase: Once the GBM model is trained, it can classify new individuals as β-Thalassemia carriers or non-carriers based on their feature vectors. The ensemble of weak learners combines their individual predictions to make the final prediction.

D. Random Forest:

Random Forest is a machine learning algorithm belonging to the ensemble learning family. It is known for its ability to provide accurate and robust predictions.
by combining multiple decision trees.

It is widely used for both regression and classification tasks and has gained popularity due to its simplicity and effectiveness.

Random Forest consists of an ensemble of decision trees. Each tree is trained independently on a random subset of the training data, and their predictions are combined to make the final prediction.

The idea behind the ensemble is to reduce overfitting and increase the model's generalization capability.

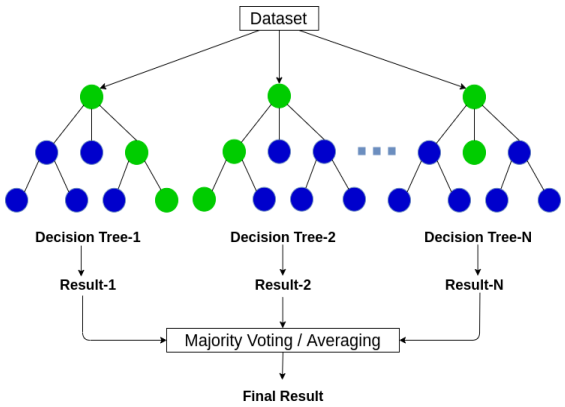

Fig.3: Random Forest Classifier

Random Forest for β-Thalassemia Classification:

Dataset Preparation: The dataset includes relevant features related to β-Thalassemia, such as red blood cell indices, haemoglobin levels, and other attributes.

Training Phase: Random Forest is trained using the dataset, where the feature vectors represent the individuals, and the corresponding labels indicate whether they are β-Thalassemia carriers or non-carriers.

Ensemble of Decision Trees: Random Forest builds an ensemble model by combining multiple decision trees. Each tree is trained on a random subset of the data, and at each node, a random subset of features is considered for splitting.

Bagging Procedure: Random Forest utilizes a technique called bagging (bootstrap aggregating), where each decision tree is trained on a bootstrap sample of the dataset. This resampling procedure helps introduce diversity among the trees.

Voting or Averaging: During the prediction phase, each decision tree in the Random Forest independently predicts whether an individual is a β-Thalassemia carrier or a non-carrier. The final prediction is made by either taking the majority vote (voting) or averaging the predictions of all decision trees (averaging).

Robustness to Overfitting: Random Forest mitigates overfitting by reducing the variance of the individual decision trees through the ensemble approach. It reduces the risk of capturing noise or outliers in the data and provides more reliable predictions.

VIII. WHAT IS SGR-VC?

To understand the voting classifier, we first need to understand what an ensemble classifier is.

ENSEMBLE CLASSIFIER:

An ensemble classifier is a machine learning model that combines the predictions of multiple individual classifiers to make the final prediction. It leverages the idea that combining multiple models can often lead to improved accuracy and robustness compared to using a single classifier.

Ensemble classifiers are commonly used in machine learning because they can mitigate the limitations of individual classifiers and exploit their strengths. By aggregating the predictions of multiple classifiers, ensemble methods can provide better generalization, handle complex decision boundaries, reduce overfitting, and improve overall prediction performance.

SGR-VC:

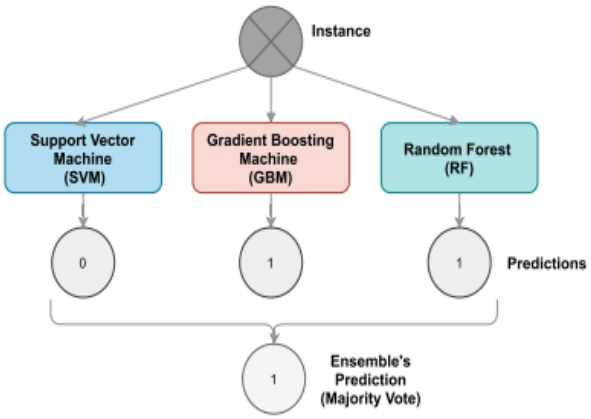

Fig.4: Architecture of the SGR-VC

SGR-VC is a voting-based ensemble classifier that is applied on an ensemble (group) of machine learning algorithms, namely SVM, GBM, and RF. Voting-based ensemble classifiers combine the predictions of multiple individual classifiers using a voting scheme to make the final prediction. The idea is to leverage the collective wisdom of the ensemble to achieve better accuracy and robustness.

In the case of β-Thalassemia, the ensemble classifier SGR-VC combines the outputs of SVM, GBM, and RF to effectively distinguish between individuals who are carriers of the β-Thalassemia gene and those who are non-carriers. By leveraging the strengths of these algorithms, SGR-VC can capture the complex patterns and features in the data that are indicative of β-Thalassemia carrier status.

Similarly, when it comes to Iron Deficiency Anaemia (IDA), the ensemble classifier SGR-VC can be employed to differentiate individuals with IDA from those suffering from beta thalassemia. By utilizing the combined predictions of SVM, GBM, and RF, SGR-VC can effectively identify the characteristic patterns and biomarkers associated with iron deficiency anaemia and beta thalassemia.

The ensemble approach employed by SGR-VC offers several advantages in the context of β-Thalassemia and IDA. First, by combining multiple classifiers, SGR-VC can leverage the strengths of each algorithm to compensate for their individual limitations. This leads to a more robust and accurate classification model for identifying β-Thalassemia carriers and individuals with IDA.

Furthermore, the ensemble approach helps overcome issues such as overfitting and noisy data. By aggregating the predictions of multiple classifiers, SGR-VC can reduce the impact of individual errors and biases, providing a more reliable and generalizable classification model.

IX. CHALLENGES

1. Class Imbalance: Both β-Thalassemia and IDA datasets often exhibit class imbalance, where the number of instances belonging to the minority class (e.g., β-Thalassemia carriers or IDA-positive cases) is significantly smaller than the majority class. Class imbalance can affect the training of SGR-VC, as it may bias the model towards the majority class and lead to lower accuracy in detecting the minority class.

2. Dataset Size and Quality: The availability of large and high-quality datasets plays a vital role in training and evaluating the performance of SGR-VC for β-Thalassemia and IDA classification. Insufficient data or noisy data can limit the effectiveness of the ensemble classifier and impact its generalization capabilities. It is crucial to have access to diverse and well-annotated datasets to ensure reliable and robust predictions.

3. Interpretability and Explain ability: Interpreting the results of SGR-VC in the context of β-Thalassemia and IDA can be challenging. The ensemble nature of SGR-VC, combining multiple classifiers, may make it difficult to explain the underlying decision-making process and provide clear explanations for the classification outcomes. Ensuring transparency and interpretability of the ensemble's predictions is important, especially in the medical field.

X. CONCLUSION

In conclusion, the SGR-VC algorithm outperforms the other classifiers in accurately classifying thalassemia and iron deficiency anaemia. The algorithm demonstrates higher accuracy, precision, and recall, resulting in an improved overall F1 score. The ensemble-based nature of the SGR-VC algorithm allows it to leverage the strengths of multiple

classifiers, thereby enhancing its classification capabilities.

The SVM classifier is known for its ability to handle complex decision boundaries and high-dimensional data. Its margin-based approach effectively separates classes and provides strong predictive performance.
GBM, on the other hand, excels in building sequential models by iteratively correcting the mistakes of previous models. It captures complex relationships and interactions within the data and can handle both numerical and categorical features.

Random Forest, as an ensemble of decision trees, offers the advantages of reducing overfitting, handling noisy data, and providing feature importance rankings resulting in an ensemble with improved generalization capabilities.

The voting classifier combines the predictions of these three classifiers by considering the collective decision of the ensemble and overcomes the limitations of individual classifiers and making more accurate predictions.

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