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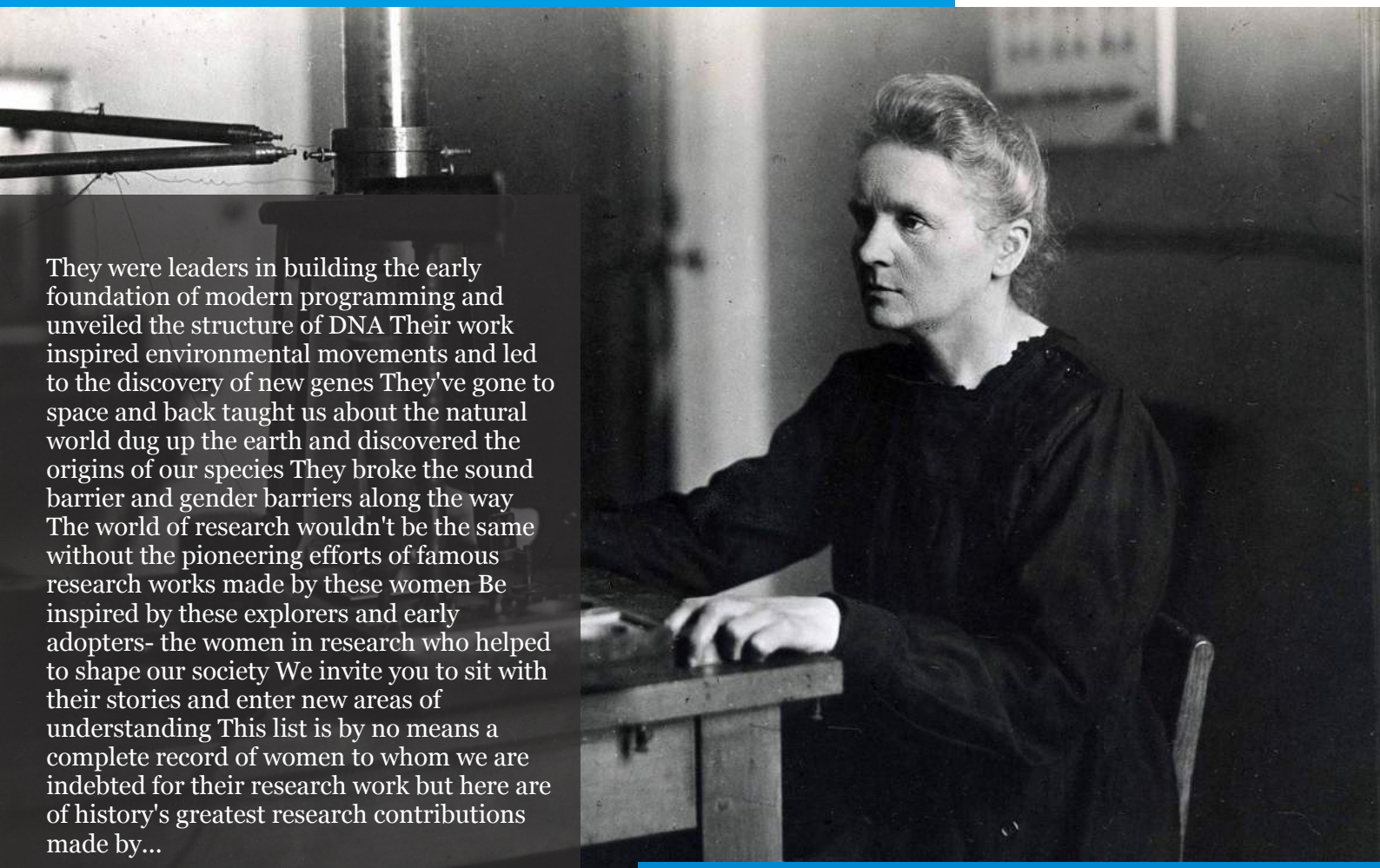

They were leaders in building the early foundation of modern programming and unveiled the structure of DNA Their work inspired environmental movements and led to the discovery of new genes They've gone to space and back taught us about the natural world dug up the earth and discovered the origins of our species They broke the sound barrier and gender barriers along the way The world of research wouldn't be the same without the pioneering efforts of famous research works made by these women Be inspired by these explorers and early adopters- the women in research who helped to shape our society We invite you to sit with their stories and enter new areas of understanding This list is by no means a complete record of women to whom we are indebted for their research work but here are of history's greatest research contributions made by...

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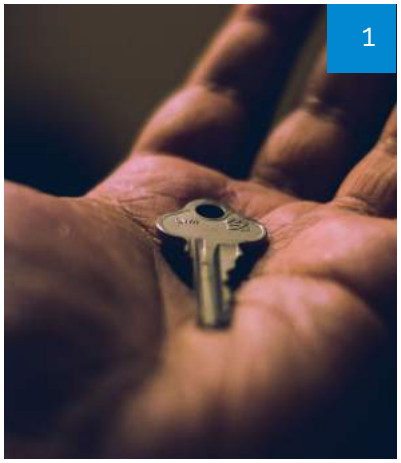

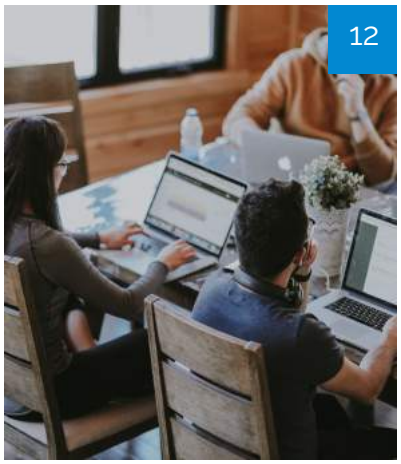

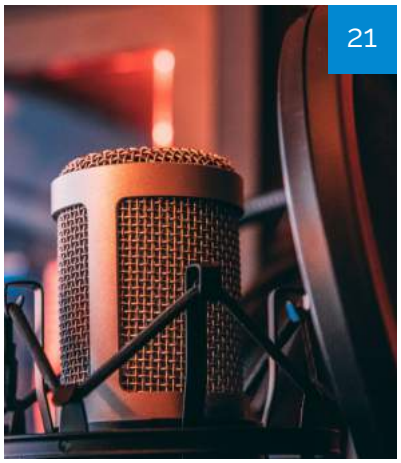

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Jocaxian Protection for Database Passwords

Joao Carlos Holland de Barcellos

São Paulo University

ABSTRACT

We will show a new database password protection method that can be used in programming languages, specially in those that are interpreted, where the executable code is humanly readable as well, being able to leave the database password exposed, with the risks of information theft and data changes.

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ABSTRACT

We will show a new database password protection method that can be used in programming languages, specially in those that are interpreted, where the executable code is humanly readable as well, being able to leave the database password exposed, with the risks of information theft and data changes.

I. INTRODUCTION

In several interpreted programming languages, such as, for instance: PHP, Lisp, Python, Java etc.. whenever we need to access a database we must provide - among other parameters - a password for the programming-language bank opening command, and thus, inside the program we'll have to pass this password to the opening command.

Therefore, the password becomes dangerously exposed in the program that stays on the application server

We must note that, in several cases, mainly on especially in multilayer architectures, the database server, where the corporate data stay, can be much more important than the application servers, so it would not make much sense to spend 'fortunes' on protecting of this server if the entire bank vulnerability is on the application servers where passwords are exposed.

Here also goes the saying: "The safety of the chain is not higher than its weakest link"[03].

II. CRYPTOGRAPHY

A slightly more secure way would be to store the encrypted database password in a constant in the source program, or in an external file.

However, since the decrypt function is in interpreted code, which is humanly readable, it could be easily copied and executed by the intruder, and so - again

- the database password could be decrypted and revealed.

III. PRECOMPILERS AND OBFUSCATORS

A precompiler transforms the source code into an intermediate language (not humanly readable) that can then be executed by an interpreter program.

However, many precompilers have tools that "decompile" the compiled code. Let's look at the PHP language:

"...No protection guarantees 100% safety. Even the best paid solutions presented above are not 100% secure. The site zendecode.com, for example, claims to instantly decompile Zend Guard code and Icon Cube ...."

An obfuscator is a program that makes source code extremely difficult to understand. It does this, for example, by taking the comments of the programs, changing the name of the variables, the name of the functions, taking out the indentations, etc ...

Of course this makes the process of finding the password in the source program daunting a little more, but with a little patience it is still possible to find it.

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IV. COMPILED LANGUAGES

It is important to note that, depending on the danger and importance of the database, not even compiled languages can safely hide database passwords because there are decompiler programs [06] and disassemblers [07] that can convert the executable code back in a source program, that is, it does the reverse work of compilation, and again, the database's password could be dangerously exposed.

V. THE JOCAXIAN METHOD

One solution to this problem is to tie / merge / encrypt the Database (BD) password with the User ID (ID) and the System User password.

In this way, the intruder, even in possession of the source programs, will not be able to find the database password without knowing the password and the user ID.

As the user ID / password is not stored on the application server - and strictly speaking, nowhere - because it is entered by the user when it is identified ('logged in') in the system

- it is extremely difficult to discover the database password without this data.

In order to implementing this method we will basically need two functions:

The first is used to merge (or shuffle or encrypt) the database password with the user ID and password:

Blend_DB_password=merge(User_ID, User_Password, DB_password);

The second is used to 'undo' (or unscramble or decrypt) the password (previously merged) using the user ID and password:

BD_password = unmerge (User_ID, User_Password, Blended_DB_Password)

This way, the DB password would be visible only in the program variables at runtime, and not statically saved in the source program.

The Pre Password Table Of course we will need a Table (let's call it the Pre-Password Table) to store the merged passwords, which would be formed by one line for each user of the system.

A possible implementation of the Pre_Password table would be having 3 fields per line:

(ID_USER_HASH, PASSWORD_USER_HASH, BLENDED_DB_PASSWORD)

This table could be written as a text table on the application server itself or, in the case of relatively many users, in *another* database, intended to store only this table and of course, with another own password and unprotected.

VI. A SIMPLE IMPLEMENTATION

Of course the user ID / password comes from a data field of the application at run time, that is, it comes from fields that the user fills out of his terminal and, therefore, don't need to be recorded on any part of the system.

Our Pre_Password Table could so be formed by 3 fields:

The first field of the table, USER_ID_HASH, would be a field with HASH of the user ID, such as the HASH function that could be , as example, the sum of the bytes of its ID multiplied by the order in which this byte appears in the string.

The second field of the table, the PASSWORD_USER_HASH, would be just a field with the HASH of the user's password. This field is not really necessary but would, along with USER_ID_HASH, be used to form a key that would identify which line of the PreSenha table is located the user, and then find the field that really matters: the MERGED_DB_PASSWORD.

The third field the MERGED_DB_PASSWORD would be formed by a reversible function that associates the USER_ID , USER_PASSWORD and the DB_PASSWORD.

As an example, we could have, in case of numerical fields:

MERGED_DB_PASSWORD = merge (USER_ID, USER_PASSWORD, DB_PASSWORD) = HASH (USER_ID + USER_PASSWORD) + DB_ PASSWORD
And its reverse function:

DB_PASSWORD = unmerge (USER_ID, USER PASSWORD, MERGED_DB_PASSWORD) = MERGED_DB_PASSWORD - HASH (USER_ID + USER_PASSWORD)

Simple Example

To exemplify and make it easy, let's assume that all passwords are numeric up to 5 digits.
Thus, using prime numbers [05], we could write:

USER_HASH_PASSWORD=REST_DI ISION((USER_PASSWORD * 104711) , 9991)

USER_ID_HASH= "X" + USER_ID; // (to simplify)

For the merge function let's use the sum function as an example (in practice a more complicated function must be used):

Merge function (USER_ID, USER_PASSWORD, DB_PASSWORD)=DB_PASSWORD*2017 + USER_PASSWORD;
So that:

DB_MERGED_PASSWORD = DB_PASSWORD * 17 + USER_PASSWORD;

And the unmerge function would be:

Unmerge function (USER_ID, USER_ PASSWORD,DB_MERGED_PASSWORD) = (DB_MERGED_PASSWORD
USER_PASSWORD) / 17;

Trivial Example for Elucidation

Let's consider 2 users and their passwords as an example: MARIA, 1234
JOAO , 999

If the password of our BD is, for example: **54321**, and using the functions of the 'simple example' above, we will have in our PRE_PASSWORD table:

ID_HASH,PASSWORD_HASH,
DB_MERGED_PASSWORD (XMARIA, 9762, 924.691) (XJOAO ,519, 933.456)

When the system receives the user data (when logged in): ID = JOAO ; USER_PASSWORD = 999
It calculates the HASH of the user ID and password, in this example: HASH_ID= XJOAO

HASH_PASSWORD = REST_DIVISION((999 * 104711) / 9991) = 519

With this composite key (XJOAO, 519) the program finds the line, in the Pre_Password table, which contains the merged password, in our example = 933.456

And it uses the unmerge function = (933.456 - 999) / 17 = 54321 and retrieves the database password ☺

VII. CONCLUSION

We have seen that database security (DB) is sometimes much more important than applications. And, as the link of a chain, the security and privacy of the DB is no greater than the security and privacy of application servers.

To make DB security even greater and break the weak link of application servers is unnecessary, and often even pointless, to overshadow source programs, which embeds database passwords, rather than this, is better merge (encrypt) the password of the DB with the ID and Password of the user so that it becomes almost impossible to get it by an intruder out of the system.

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5 How to compile a PHP file?_https://softwareengineering.stackexchange.com/questions/369122/can-i-compile-php-to-hide-the-code
5 Number Theory/10000 cousins https://primes.utm.edu/lists/small/10000.txt
6 Decompiler https://en.wikipedia.org/wiki/Decompiler
7 Disassembler https://en.wikipedia.org/wiki/Disassembler

An Efficient Method of Vehicle Registration Number Plate Extraction and Recognition using Image

S M Sohel Rana, M. Humayun Kabir, Md. Shohel Rana & Sanjoy Kumer Sarker

Islamic University

ABSTRACT

Due to increasing population, the number of vehicles is growing day by day. These increases numbers of vehicles create various problems for traffic police such as signal light violations, parking problems, wrong lane violations and toll booth violations. This research will be helpful to control these traffic violations for traffic police. Moreover, it will also be helpful for the other number plate extraction and character recognition applications. We proposed in this research car registration number extraction and character or number recognition. This research will be able to extract and recognize alphanumeric characters in a given image. The final output will be stored in a text file. This file will have extracted alphanumeric characters. This technology will be, cost effective, fast and highly accurate. In this research we will try various algorithms and logics in MATLAB and find best process to extract number plate and recognition of alphanumeric each character. The main goal of this research is to reduce the manpower, cost, time and to make the process quick and highly available.

Keywords: character recognition, extraction, alphanumeric character, traffic.

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Keywords: character recognition, extraction, alphanumeric character, traffic.

Author α σ ρ: Dept. of Electrical and Electronic Engineering, Islamic University, Kushtia.
ω: Dept. of Information and Communication Engineering, Islamic University, Kushtia.

I. INTRODUCTION

In recent world, the number of vehicle is increasing day by day. According to a recent survey, the number of vehicle on the roads reached more millions last year which creates new challenges for traffic police such as red light violations, wrong lane violations, parking problems, & toll booth violations. There need various automate processes to control that violation in addition to increasing traffic police. To resolve this issue traffic police installed plenty of surveillance devices such as traffic light cameras, parking booth cameras or toll booth cameras. It requires man-power to check these images, note down the vehicle's registration number and forward it to the appropriate department to take an action on rule violators [1, 2]. Extraction of vehicle registration numbers and alphanumeric characters is the main topic of our research. Vehicle registration number is a unique identity for all vehicles in a given state. It represents a legal license to ply on the road. Therefore, the registration number is the primary, most widely accepted, human readable and mandatory identifier for motor vehicles.

II. LITERATURE REVIEW

Chittode J S has developed an algorithm based on morphological operations for number plate recognition to monitor and manage parking services [3]. The ROI is another method area which includes the number plate from which alphanumeric characters are recognized. Paunwala proposed a method for directional segmentation which finds ROI using morphological processing [4]. In the case of image

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acquisition and number plate recognition system Lekhna proposed an effective algorithm which is NPR algorithm [5]. Chunyu C et al. [6] has developed a technique named global matching of CBP for recognition of vehicle license number plate from vehicle image. This technique has implemented using MATLAB and characters are recognized using edge detection segmentation. Singh M et al. [7] developed an efficient approach works on opening and closing of morphological operations. It has been done for segmentation process of alphanumeric characters. Recognition is done using the template matching. Kranti S et al. [8] presented a methodology for number plate extraction name. This methodology mainly deals with edge detection and window filtering method which are used in this methodology and give efficient results. Ganapathy V et al. [9] developed a methodology for Malaysian vehicles. This methodology is mainly based on morphological analysis and results extraction of number plate with 95% accuracy.

III. PROPOSED METHOD

These sections include a proposed algorithm for vehicle number plate extraction and alphanumeric number recognition. The algorithm of proposed method is shown below.

Proposed algorithm consists of following steps:

1. Image acquisition
2. RGB to gray scale image
3. Gray scale to binary image
4. Vertical Edge Detection
5. Dilation of an Image
6. Extraction of number plate
7. Enhance number plate
8. Segmentation of characters
9. Load and read templates
10. Comparison and recognition
11. Storing in file

3.1 Image acquisition

The first section is "Image acquisition. Images and videos is taken by a high resolution cameras. With the help of the image acquisition toolbox in MATLAB we can detect a camera easily. Using a camera, the project accepts an image path in MATLAB code. This research is suitable for all kinds of image. Figure 1 shows an input image.

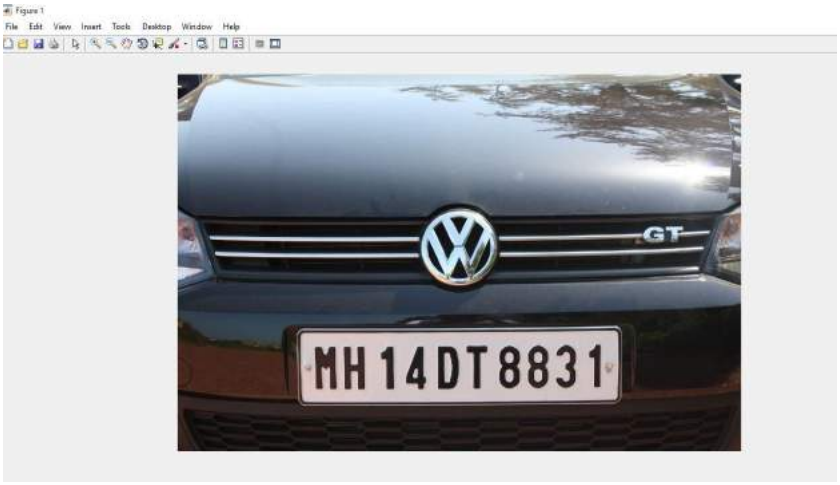
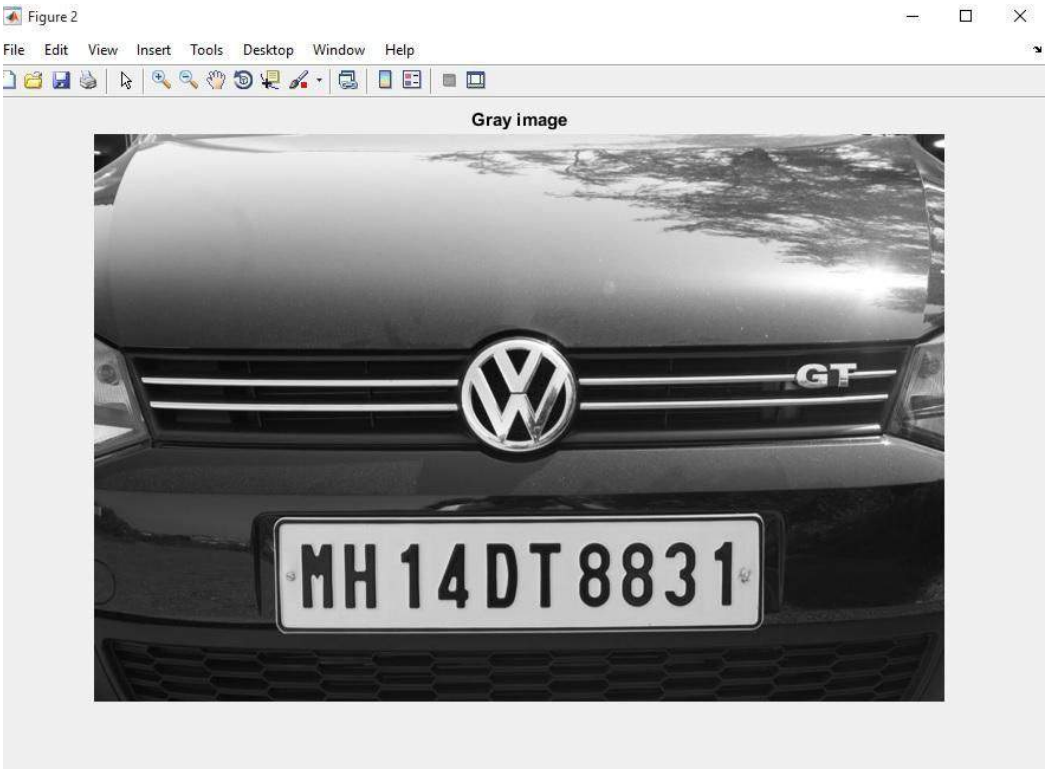


Figure 1: Image acquisition

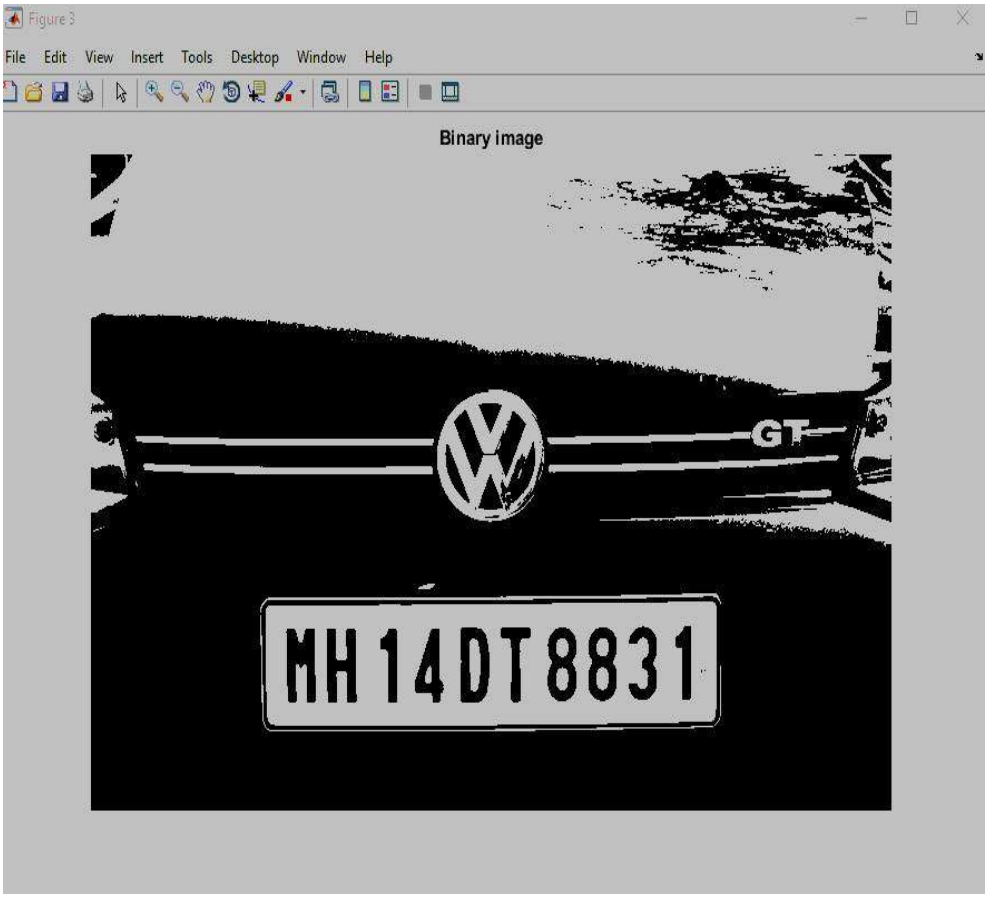
3.2 RGB to gray scale image

In this section RGB to grayscale conversion takes place by using rgb to gray function. A gray scale image is also known as a black and white image in which. Black is the weakest intensity and white is the strongest intensity. RGB to gray image is shown in figure 2.



3.3 Gray scale to binary image

In this case im2bw' function is used for binarization of an image. The Otsu method has been used to converter into two color images black and white.The pixel values above this threshold value turn into white and values below this threshold turns into black. Binary image is shown in figure 3.



3.4 Vertical Edge Detection

This section used to detect vertical edge by using Sobel operator and the result is shown in figure 4 after applying Sobel operator to binary image.

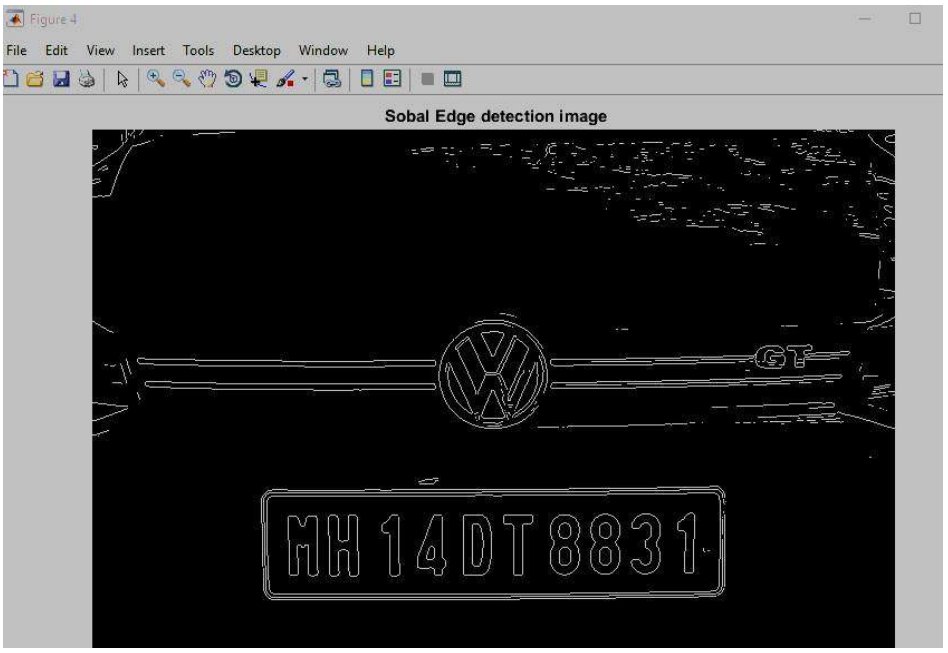
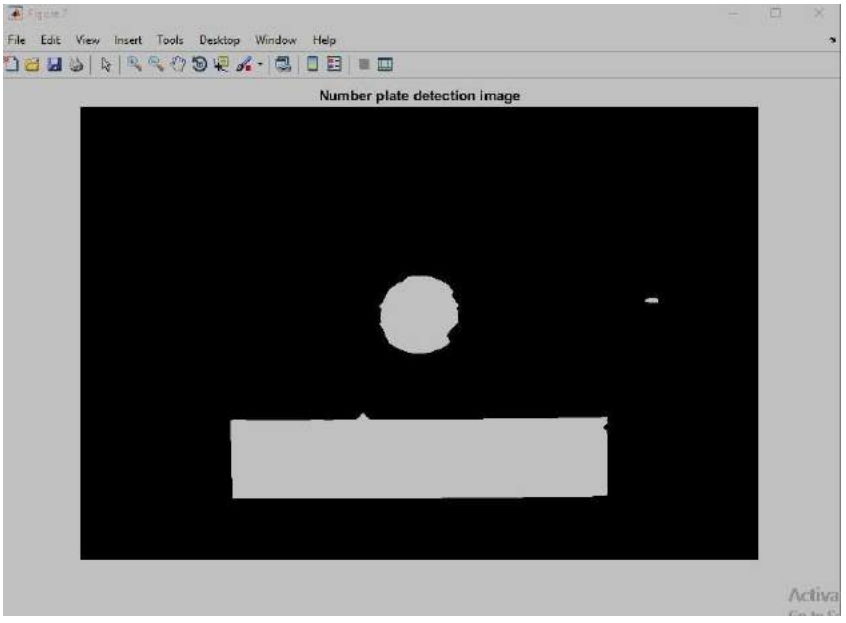


Figure 4: Vertical Edge detection.

3.5 Dilation of an Image

These operations are mainly used to remove unwanted noise from the image. In this step, image has been dilated. Dilation is a process for filling holes by using MATLAB toolbox imfill function in an image, sharpen edges of an object maximize brightness and connect the broken lines. Dilation of an image is shown in figure 5 and after filling holes is shown in figure 6. Then morphological opening and erode operations are used to detect the of candidate number plate area by using imerode function and its result in shown in figure 7.



3.6 Extraction of number plate

After the number plate detection, the original number plate area is extracted and the row and column indices of plate area by connected component analysis. Original extracted number plate area is shown in figure 8.

Figure 8: Extraction of number plate.

3.7 Enhance number plate

Theoriginal extracted number plate consists of various noise or unwanted holes. So the enhancement of the original number plate is done and the result of enhancement number plate is shown in figure 9.

Figure 9: Enhance number plate

3.8 Segmentation of characters

After enhancing plate, the 'bwlabel' function helps for the segmentation and labeling of the characters. It is used to separates each character and labels them according to the sequence. 'imresize' is another function which is used to resize the segmented images and make them same size, Moreover, the 'imcrop' function is use to crop the segmented characters. Horizontal and vertical histogram has been used for segmentation based on threshold value. Depend on Starting and ending points by horizontal direction each character is extracted is shown in figure 10.

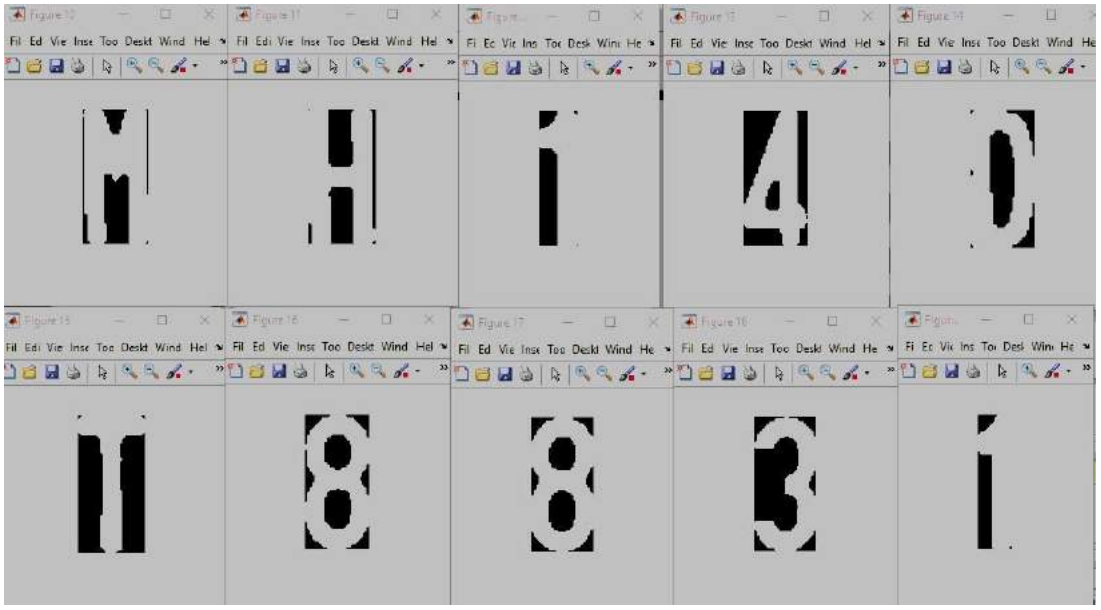


Figure 10: Segmentation of Characters.

3.9 Load and read templates

In this step, we loads template image including 0 to 9 and a to z character for the comparison of characters for recognition.

3.10 Comparison and recognition

In this step, comparison of extracted characters with templates takes place and output of this step is the extracted letters or characters. It is easier to check and read each and every segment. The 'corr2' function compares and finds the minimum difference between the pixels. Recognition of each character is shown in figure 11.

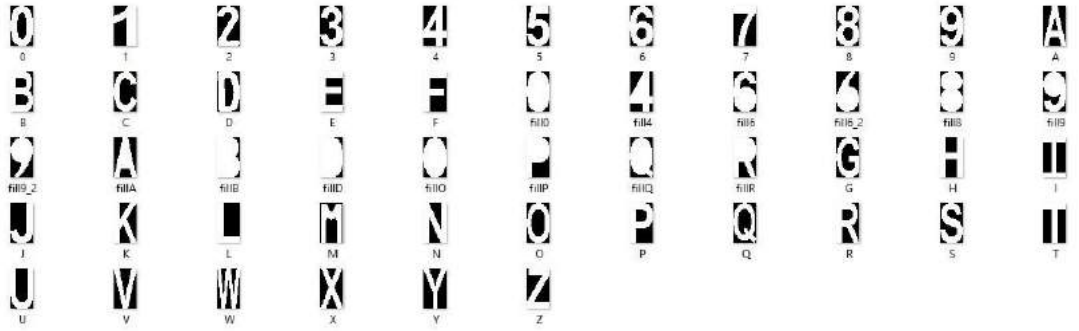
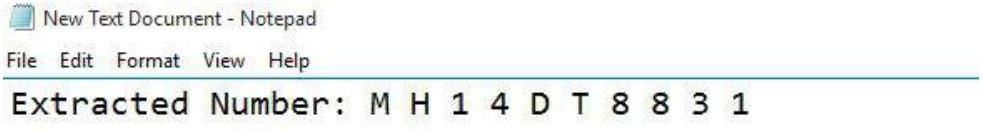


Figure 11: Comparison and recognition

3.11 Storing in file

In this step, after extracting character from number plate with complete information is stored in file as shown in figure 12.



IV. EXPERIMENTAL RESULTS

This proposed system work all types of input image for number plate extraction and recognition. In this case we have tested more than 133 input images which are different sizes and colors. This system work all time a day more accurately and user friendly. The input images are taken in different illumination. The result of proposed system is shown in table 1.

Table 1: Result of proposed system.

Total Image	Successfully number plate Extracted and Recognition	Success Rate (%)
133	132	99.25

V. CONCLUSION

This research is able to process an input image of any format and successfully computed all the modules. Moreover, all the functions have been implemented perfectly. Users can directly find the extracted alphanumeric characters in the result text file. The results provided by car registration number plate extraction and recognition system are successfully tested on various images with accuracy 99.25%.

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Feedback on the Performance of Students in their Information Technology Module

Leovigildo Lito d. Mallillin

ABSTRACT

This study aims to identify the performance of the students in their information technology module along the area of operating system, microsoft word, microsoft excel, microsoft powerpoint, internet, and I.T. basic knowledge. The study comprised of two hundred eighty (280) respondents. They are officially registered at Gulf College under the Center of Foundation Studies in the A.Y. 2017-2018. They belong to GFP Block 2 and have registered information technology as part of their module.

Descriptive method is utilized in the study because it involves collections of quantitative information that can be tabulated along a continuum in numerical form, such as their feedback on the skills in their information technology practical examination. It describes categories of information such as their skills in operating system, microsoft office, internet and I.T. basic knowledge.

Keywords: performance of students in I.T., operating system, microsoft word, excel, powerpoint, internet, basic I.T knowledg.

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The two non-probability sampling techniques namely, Convenience Sampling and Purposive Sampling are employed in the study.

Results show that operating system, microsoft word and internet are excellent and impressive, however, microsoft excel, powerpoint and basic information knowledge are very poor as based on the result of their feedback during their practical examination.

Keywords: performance of students in I.T., operating system, microsoft word, excel, powerpoint, internet, basic I.T knowledge.

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I. INTRODUCTION

Information technology is one of the modules and requirements of the Center of Foundation Studies. Information technology contributes to the learning process of students and will be useful in their future, whether in their own work or in their own business. This enhances students in their computer literacy as part of their learning in the module as this has been explored by (Xu & Chen, 2016) as the approach of information digitalization or computer process that improves the learning and teaching environment of the students. The authors further stressed that application of information technology has become the concerned of the modern technology as compared to their computer literacy programme in their module particularly on the success information of basic computer application among the students. This guaranteed the techniques in teaching in the information technology among the students that promotes teaching effectiveness by applying basic information technology knowledge and with different information literacy.

Nevertheless, information technology module provides foundation and knowledge of the students to utilise the MS office application such as powerpoint, word and excel. The information technology functions prepare students in the basic processing of computer. It suits them the application of data manipulation for their learning enhancement and literacy in the module. However, information technology deals with basic keyboard skills, since information technology is designed to help students transform their knowledge on their hands off keyboarding, techniques and styles of the application of MS office. Systems and application is the process that

establishes the needed information and knowledge extended to the learners. MS windows and office tools including Word, Excel, Powerpoint, and Internet application are the process of creating of giving information or system in the students learning process (Gokhale, 2015).

The learning outcome of the students demonstrates the ability to analyse the main functions of computer system and how they work in sequence to process information. Information system has been the major concerned since the beginning of the electronic digital computer age and operating cycles. The module is designed for the student process and information, this helps them to understand the advantage and limitations of the state-of-the-art in the basic knowledge to information technology because of the functions of that application (Siewiorek and Swarz, 2017). Moreover; the description of the different functions hardware components such as CPU, storage systems, types of memories like RAM, ROM and common input and output devices has been a part of their knowledge in the module. The system for the support of the hardware provides both services in association with the learning knowledge of the students. They are given background to identify the said hardware in such a way that information are given to the students particularly on the different functions of the different hardware in the computer (Adamczyk, et.al., 2016).

On the other hand, the module explains the different types of software, operating system, application software and programme software among them which is a part of their feedback in the summative practical examination to include the different types of computers, network computers, laptops and PDAs. A device consists of hardware and software taught among the students to explore a wide range of system configuration and requires a wide range of hardware and software capabilities on the application of their module and as a part of their summative feedback. This also provides systematic application and development that required efforts among students (Brunner, et. al, 2011).

This module has 60 hours of whole class contact over the semester. In the class hour, students will be working with their tutor and other fellow students. Students have regularly tutor time with their module tutor. Students will take part in the formative exercises. This develops their skills in information technology. Student will be working for their own various task and activity required for them. The performance of the students is based on the marks during the practical examination given to them. This is where they will be given feedback for any room of improvement on their information technology module, lectures are available, class hours are used as complementary learning activities (Asarta and Schmidt, 2017).

Formative feedback helps to prepare students for their formal assessment. It gives practice in building their skills in information technology. Learning the skills in the information technology module requires students to practice and help them build competencies in information technology module. This describes the assessment formative feedback questions given to students during their final practical examination to determine their skills in the operating system, microsoft office application, internet and information technology basic knowledge (Dunaway and Orblych, 2011).

Statement of the Problem

1. What is the performance of students in their information technology module along the area of

a. operating system,
b. microsoft word,
c. microsoft excel,
d. microsoft powerpoint,
e. internet, and
f. I.T. basic knowledge?

II. RESEARCH DESIGN

The study employed the quantitative research particularly the descriptive method because it

involves collections of quantitative information that can be tabulated along a continuum in numerical form, such as their feedback on the skills in their information technology practical examination. It describes categories of information such as their skills in operating system, microsoft office, internet and I.T. basic knowledge. Descriptive research involves gathering data that describes events and then organizes, tabulates, depicts, and describes the data collection. It often uses visual aids such as graphs and charts to aid the reader in understanding the data distribution. Because the human mind cannot extract the full import of a large mass of raw data, descriptive statistics are very important in reducing the data to manageable form. When in-depth, narrative descriptions of small numbers of cases are involved, the research uses description as a tool to organize data into patterns that emerge during analysis (Pierce, 2017).

2.1 Research Subject

The subjects of the study are the students of Gulf College under the Center of Foundation Studies who are officially registered in the A.Y. 2017-2018. They belong to GFP Block 2 and have registered Information Technology as part of their module. Two Hundred Eighty (280) students are utilised in the study.

2.2 Research Technique

The study employed the two nonprobability sampling techniques namely, Convenience Sampling and Purposive Sampling. Convenience Sampling and Purposive Sampling are Nonprobability Sampling Techniques that a researcher uses to choose a sample of subjects/units from a population. It generates results that will be used to create generalizations pertaining to the entire population on the performance and skills of the respondents' particularly on feedback area of operating system, microsoft office application, internet and I.T. basic knowledge skills (Etikan, Musa and Alkassim, 2016).

2.4 Research Instrument

For data gathering purposes, the research used a feedback form on the result of the assessment of the students in their skills on operating system, microsoft word, microsoft excel, Microsoft powerpoint, internet and I.T. basic knowledge using the following scale:

1. Performance of the students in the area of operating system

Scale	Descriptive Level
6	Excellent
5	Very Good
4	Good
3	Satisfactory
2	Poor
1	Very Poor

2 Performance of the students in the area of microsoft word

Scale	Descriptive Level
6	Excellent
5	Very Good
4	Good
3	Satisfactory
2	Poor
1	Very Poor

3 Performance of the students in the area of microsoft excel

Scale	Descriptive Level
6	Excellent
5	Very Good
4	Good
3	Satisfactory
2	Poor
1	Very Poor

4 Performance of the students in the area of microsoft powerpoint

Scale	Descriptive Level
6	Excellent
5	Very Good
4	Good
3	Satisfactory
2	Poor
1	Very Poor

5 Performance of the students in the area of internet

Scale	Descriptive Level
6	Excellent
5	Very Good
4	Good
3	Satisfactory
2	Poor
1	Very Poor

6 Performance of the students in the area of I.T. basic knowledge

Scale	Descriptive Level
6	Excellent
5	Very Good
4	Good
3	Satisfactory
2	Poor
1	Very Poor

III. RESULT OF THE STUDY

Table 1: Performance of the students in their information technology module

Operating System	Frequency	Percentage
✓ Excellent	135	48
✓ Very Good	23	8
✓ Good	61	22
✓ Satisfactory	12	4
✓ Poor	24	9
✓ Very Poor	25	9
Microsoft Word		
✓ Excellent	100	36
✓ Very Good	31	11
✓ Good	41	15
✓ Satisfactory	24	9
✓ Poor	42	15
✓ Very Poor	42	15
Microsoft Excel		
✓ Excellent	44	16
✓ Very Good	27	10
✓ Good	44	16
✓ Satisfactory	17	6
✓ Poor	73	26
✓ Very Poor	75	27
Microsoft PowerPoint		
✓ Excellent	30	11
✓ Very Good	50	18
✓ Good	24	9
✓ Satisfactory	30	11
✓ Poor	40	14
✓ Very Poor	106	38
Internet		

✓ Excellent ✓ Very Good ✓ Good ✓ Satisfactory ✓ Poor ✓ Very Poor	222 1 0 2 2 53	79 0 0 1 1 19
I.T. Basic Knowledge		
✓ Excellent ✓ Very Good ✓ Good ✓ Satisfactory ✓ Poor ✓ Very Poor	54 42 23 37 39 85	19 15 8 13 14 30

Table 1 shows the performance of the respondents in their information technology module during their assessment and during their practical examination. As observed in the table, performance of students along the area of operating system is excellent, with a frequency of 135 or 48% among the respondents, performance of students along the area of Microsoft word shows excellent, with a frequency of 100 or 36% among the respondents, performance of students along the area of microsoft excel is very poor, with a frequency of 75 or 27% among the respondents, performance of students along the area of microsoft powerpoint is very poor, with a frequency of 106 or 28% among the respondents, performance of students along the area of internet is excellent, with a frequency of 222 or 79% among the respondents and performance of students along the area of I.T. basic knowledge is very poor, with a frequency of 85 or 30% among the respondents.

IV. DISCUSSION

As based on the result of the assessment and as based on the result of their practical examination, performance in every skills vary depends on the knowledge and interest of the respondents. The approach of the assessment is designed on the needs and skills of the students, focusing on their knowledge and need in the information technology module. This module plays an important role on the learning skills of the students (Mislevy, et. al., 2017).

On the performance of the respondents along the area of operating system shows impressive because the respondents got a high mark which is excellent for the reasons that the module tutor taught them the proper way of making that skill of operating system as part of the module outcome. The operating system is a file name and data where the students save their work output for purposes of monitoring the result of their practical examination. It is a requirement for them to develop during their assessment. Students are required to follow this requirements as part of their assessment in the operating system and labelled with their name and I.D. number (Preece, Rogers and Sharp, 2015).

On the other hand, performance of the students along the area of microsoft word shows excellent because most of the respondents fall on that category. Microsoft word is known everywhere. Everybody has knowledge on using microsoft word. They have the mastery on how to type a text, however; need to improve more on the command in that activity. Microsoft word is not just typing a word, it also involves, changing of font styles, sizes, inserting, headers and footers, line spacing, margin, data capturing, editing and designs to name few of the features of microsoft word. The microsoft words contains document type by the students with corresponding guide

questions for them to follow. It is an application of the module output taught among them. Several guide questions are given to them to perform as their task in the microsoft office word skills (Bedi and Partridge, 2011).

Nevertheless, performance of the students along the area of microsoft excel is very poor. This shows that they have limited knowledge in performing the task. They have limited knowledge on the fundamental operations in columns, rows, computations, graph, alignment to name few on the basic functions of microsoft excel application. Though different functions on excel has been taught to them. They cannot grasp to follow unlike on the other application of microsoft office operations. Microsoft excel involves summarizing, reporting and analyzing data. It is needed in the computation to make the task easy and comfortable. Students are being taught the basic on how to use the microsoft office excel in an effective and efficient way because it provides approaches and improves for the analysis of data. The concept therefore is easier and designed for students to learn in preparation for their future work. Learning the formula in utilising the microsoft excel makes the task easier and comfortable to the user (Winston, 2016).

Additionally, performance of the students along the area of microsoft popwerpoint shows very poor. Though the basic concept in creating powerpoint design is complicated because they have to consider the animation, transition, designs, number of slides and the font size. They know what to do but during the actual assessment the learners have forgotten all the principles. It might be that they are not used to it. They will just use the powerpoint in their presentation once in a life time. This needs to be practiced from time to time for a better mastery on the concept of creating a powerpoint slides. They know how to design but they have lack knowledge on the concept on what they will put in the slides. They are confused and have no enough knowledge on the slides they are going to put in the slides. They have problems on creating designs, animation, transition and have problems on the contents of the slides. Powerpoint is more effective instructional medium of knowledge because it demonstrated instruction benefits among the learners. The effect of varied digital presentation tools or powerpoint plays an important role on the part of the students because they will use it in their project and presentation to all their modules and it is focused on how presentation technologies used for the acquisition knowledge of the students (Chou, Chang and Lu, 2015).

Furthermore, performance of students along the area of internet shows excellent. Learners are exposed to internet and they have the knowledge on the proper usage of internet. With the latest trend of technology now, it is strongly evident that this kind of application is just easy to utilise. Just log in with their password and then they can send the message. What is important is they have their username with their password. Others are not because they have forgotten their user name and their password. The dynamics of internet to students measures their capacity in the proper usage because they are provided the moodle with their username and password. This is only exclusively used in the college by the students needed in the uploading of their assignment and sending their project as part of the development of their module. This has been expounded by (Dimpfl and Jank, 2016) that latter is measured by internet search queries related to their assignment, work and performance.

Similarly, performance of students along the area of basic information technology knowledge is very poor. Students are not familiar with the application of the basic information technology knowledge. They are provided the materials for them to master but still they cannot. It shows that students are weak in terms of self-mastery. They need to push them to master but they have limited knowledge perhaps they did not develop yet their proper study habits on the mastery of the basic knowledge in the information technology. They are particular on the hands off application rather than mastery of the theory and concept in basic information technology. Mastering, memorizing, reading and understanding digital text that is

organized in a non-linear hypertext format can be challenging for students as it requires a more self-directed selection of text pieces compared to reading linear texts and hands off application and theory. The differences in students' skills in comprehending digital text can be explained by their behavior and various underlying skills. Students' behavior was operationalized by their selection of task-relevant hypertext pages; students' abilities in terms of mastering, memorizing, reading linear texts, dealing with computer interfaces more generally and evaluating the usefulness of online information were considered as underlying skills. The basic information technology or computer skills and evaluating online information would explain performance in digital reading above and beyond reading skills measured with linear texts (Hahnel, Goldhammer, Naumann and Kröhne, 2016).

V. CONCLUSIONS

As based on the result of the study, knowledge of students in their information technology module varies depends on their interest. Respondents answer on operating system, microsoft powerpoint and internet show impressive, however, others did not make it. They are not familiar with the application of the operating system, micrsoft word and internet, Similarly, to those students who are weak in internet are those students who have no user name and password.

Subsequently, learners ability in microsoft excel, microsoft powerpoint and basic information technology are not that impressive because they did not get the correct format and correct application of the excel, powerpoint and basic knowledge of information technology.

VI. RECOMMENDATIONS

Module tutors in information technology should focus on the application of microsoft office like excel and powerpoint because this is needed by the respondents. This also includes the basic information technology knowledge. Functions on the application of the different microsoft office must be given emphasis as this is important among the learners.

Likewise on the functions of operating system, microsoft word and internet, respondents must be given activities based on their interest, this serves as a motivating factors among them to improve their skills in the information technology skills.

Future researchers need to explore more on the other activities not tackled in this study to better improve the information technology module.

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Speaker Identification of Whispering Sound: Effectiveness of Timbre Audio Descriptors

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ABSTRACT

Identification of a person from the whispered voice is challenging task as many variations are observed in the speech attributes of the same the speaker in whispered and neutral mode. The success of the speaker identification system relies on the selection of good audio features and this paper mainly focus on the feature selection for the task. There are hundreds of audio features available for sound description, but their performance depends upon the type of the database. The motivation of this paper is to investigate the suitability of timbre features for whispered database. The choice of timbre features is due to their perceptual and multidimensional approach. However, all the features may not be contributing to the maximum speaker identification accuracy. Hence, a careful selection of limited audio descriptors from the available large set is essential to increase the speaker identification with low process time. The Hybrid Selection method is used to select the well-performing audio descriptors from all available descriptors in MPEG-7. Five timbre features namely roll-off, roughness, brightness, irregularity and MFCC are found outperforming for the database used. Here, a comparison of results is being done among traditional MFCC feature and timbre features where later reported an absolute accuracy of 10.4%. The database consist of about 480 utterances including neutral and whispered speech mode. K-NN classifier with three nearest neighbour and Euclidean distance is used.

Keywords: speaker identification, feature extraction, mpeg-7, musical information retrieval, timbre features, whispered speech.

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Speaker Identification of Whispering Sound: Effectiveness of Timbre Audio Descriptors

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ABSTRACT

Identification of a person from the whispered voice is challenging task as many variations are observed in the speech attributes of the same speaker in whispered and neutral mode. The success of the speaker identification system relies on the selection of good audio features and this paper mainly focus on the feature selection for the task. There are hundreds of audio features available for sound description, but their performance depends upon the type of the database. The motivation of this paper is to investigate the suitability of timbre features for whispered database. The choice of timbre features is due to their perceptual and multidimensional approach. However, all the features may not be contributing to the maximum speaker identification accuracy. Hence, a careful selection of limited audio descriptors from the available large set is essential to increase the speaker identification with low process time. The Hybrid Selection method is used to select the well-performing audio descriptors from all available descriptors in MPEG-7. Five timbre features namely roll-off, roughness, brightness, irregularity and MFCC are found outperforming for the database used. Here, a comparison of results is being done among traditional MFCC feature and timbre features where later reported an absolute accuracy of 10.4%. The database consist of about 480 utterances including neutral and whispered speech mode. K-NN classifier with three nearest neighbour and Euclidean distance is used.

Keywords: speaker identification, feature extraction, mpeg-7, musical information retrieval, timbre features, whispered speech.

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I. INTRODUCTION

Due to basic differences in the vocal efforts while whispered and neutral mode, there exist differences in their characteristics in terms of structure, positions of formants, spectral slope and energy. The formants in whispered speech are shifted to the higher frequency which may not be captured by widely used Mel Frequency Cepstral Coefficient [1]. Speech modes are classified as neutral, loud, shouted, soft, and whispered, where whisper exhibits very low energy and minimum spectral slope. A low spectral slope indicates that energy contents in case of the whisper are concentrated in high frequency. Such variations degrade the performance of the speaker identification system developed for neutral speech when tested with whispered voice [1]. Hence, use of the perceptual feature which can accommodate the whisper-neutral variability is emphasized. Whispered speech has a low signal-to-noise ratio (SNR), hence using only high SNR whispers for identification are suggested. It is also mentioned that identification accuracy can be increased if a comparison is made by only unvoiced part in neutral and whispered samples of the same speaker as unvoiced part in both the modes remains almost the same [1-2]. Linear Frequency Cepstral Coefficient feature (LFCC) is also useful for a whispered sound, as formants are shifted to the higher frequency [3]. Using a feature mapping technique in [4], an additional enhancement of 10% in identification is found. But the delay is introduced as the feature mapping is being done in the testing phase. Another approach to feature transformation from neutral to whispered speech is adapted in [5], overcome the problem of system speed as the processing is done in training phase only.

London Journal of Research in Computer Science and Technology

In reference [6], the combined feature vector of Mel Frequency Cepstral Coefficient (MFCC) and Gammatone Frequency Cepstral Coefficients (GFCC) are used for speaker identification. Results are compared with three classifiers namely LBG-VQ, Gaussian mixture model (GMM) and back propagation neural network (BPNN) which are found to be 59.2%, 70.9% and 84.7% respectively. Also, it had demonstrated the use of the neural network with 14 inputs of the combined feature vectors of MFCC and GFCC and 90 neurons in its output layer to classify the speakers. The hidden layer uses 17 neurons. However, this number requires investigation through trial and error method. Here a Genetic algorithm is used for reduction in feature dimension of MFCC and GFCC. When first Principal Component investigation is applied, 39 feature vectors each of MFCC and GFCC is reduced to 24 feature vectors. Further GA (Genetic algorithm) is applied and feature vectors reduce to 24 features. Two similarity measures are used in speaker identification namely distance and the highest frequency [7]. In the distance measure, speaker samples assigned to codebook having a minimum distance. In the second method, along with the minimum distance, the codebook having the highest frequency pair of input voice sample is selected. Sound files are also processed with Least Mean Square (LMS) and reported the highest speaker identification accuracy as 82.35% with the distance measure and 90.72% with the frequency measure. In reference [8], the vectors in the low dimensional space named as i-vectors are addressed for speaker identification to accommodate both speaker and channel variability. I-vector method proposed a single space which is named the total variability space. The identification accuracy is investigated in three environments namely clean background, White noise and Babble noise environment. Improved Locality Preserving Projections (LPP) with i- vector reported improvements in Equal Error Rate (EER) and Min Detection Cost Function (MinDCF). EER and MinDCF with improved LPP are found 4.45 and 0.17 respectively compared to 7.32 and 0.53 with use of GMM. Linear Discriminant Analysis (LDA) dimension reduction method is also used which reduces the feature dimension to 200 compared to 512 in UBM.

MPEG-7 is rich with many perceptual based audio descriptors and the best performing audio descriptors can be found by Hybrid Selection Method [9]. This method is used for singer identification from North Indian classical music which is more complex due to a separation of vocal from this music. Hence, only limited and sufficient perceptual features combination (namely RMS energy, brightness and fundamental frequency) are selected by Hybrid Selection method and successfully used. The singer identification accuracy using K-means classifier offered the accuracy of about 70%. MPEG-7 descriptors are mainly found to be used for the singer and musical instrument identification with few efforts of a speaker, gender or age identification but in neutral mode of speech. To reduce the size of MPEG-7 descriptors, speech features are extracted with a spectrum basis projection like Principal Component Analysis (PCA). While an experiment of the speaker and gender recognition, use of Independent Component Analysis (ICA) had proven the best compared to Normalized Audio Spectrum Envelope (NASE) and PCA [10]. Timbre features such as vibrato and the attack-decay are used for singer identification and analyses harmonic content and the dynamic characteristics of sound. It is stated that spectral envelope is a base to distinguish between two different musical instruments even playing the same note and amplitude which is a perceptual work indeed. feature is found effective and accuracy reported as 87.8% in segment level singer identification [11].

II. ANALYSIS OF WHISPERED SPEECH

This section analyses the whispered speech to its neutral counterpart from the spectrogram. Further, it explains the limitations of a whispered speaker identification method on the basis of unvoiced part only.

2.1 Attributes of Whispered Speech

Speech characteristics in whispered mode drastically change compared to neutral speech. The whisper is generated due to air passing through vocal constriction without vibrations and hence, the periodic structure is not found. The formants in whispered speech shifts to higher frequencies and their bandwidth also expand compared to neutral speech [12].

Spectrogram shown below is generated using PRAAT for the sentence "If it doesn't matter who wins, why do we keep score?" both in neutral and whispered mode. From formant analysis, it is observed that the formants F1 and F2 are shifted to higher frequency compared to neutral speech and formant bandwidth also increases.

Spectrogram for: (a) Neutral speech (b) Whispered speech

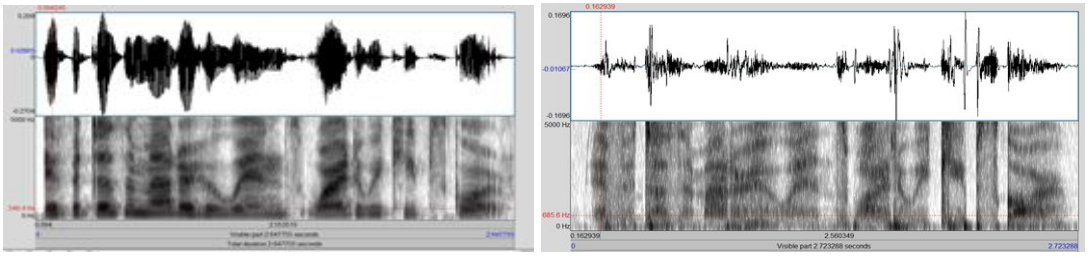

Fig. 1: Spectrogram for the same sentence and the same speaker in neutral and whispered Speech

The average formants values for all speakers in the database (described in section 4.a) are observed as below:

Table 1: Comparative average formant values and Bandwidth of F1 and F2 for neutral and whisper speech

Sr.	Type of sound	Formant Frequency (Hz)		Median of Bandwidth (Hz)	
		F1	F2	F1	F2
1.	Neutral	345-524	1814-2016	265.75	189.34
2.	Whisper	413-681	1895-2135	545.50	356.33

In addition to the formant and bandwidth shift, such other variations [13] in the whispered speech compared to neutral, makes the speaker identification task difficult.

2.2 Comparison between neutral an whispered speech by unvoiced utterances only

It is stated that the unvoiced part of speech in both whispered and neutral speech remains almost constant. Hence, it may be good choice to execute neutral-whisper speaker identification using unvoiced utterances only. A voiced or unvoiced decision is based on a range of zero-crossing rate (ZCR) and energy values together i.e. Low energy and high ZCR confirm an unvoiced decision [14].

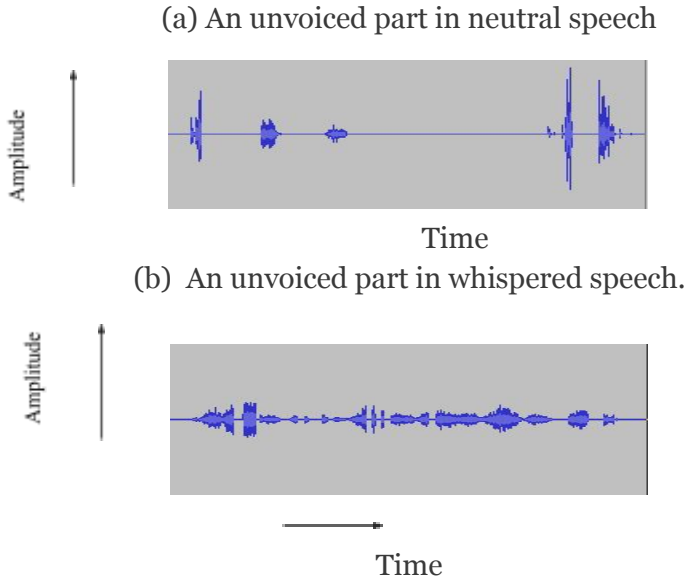

Fig.2: An unvoiced part in neutral and whispered speech

However, the unvoiced part in neutral voice is very small as shown in Fig. 2. It means a major part of the sound signal is not involved in the comparison process; hence there may be a loss of the intelligence. As fixed frame size is used while speech processing, the same frame may include voiced and unvoiced portion which confuses the decision.

III. AUDIO DESCRIPTORS AND TIMBRE

Audio Descriptors represent unique speaker dependent attributes. Specific attributes are identified and used as per suitability to the particular application. One can extract attributes in a time domain or frequency domain. Fourier transform is a widely used tool for visualizing the useful and sufficient characteristics of sound for classification in a most convenient way. MPEG-7 consists of rich and different classes of audio descriptors suitable for a variety of applications. The elements of the audio framework of a MPEG-7 standard are:

Descriptors (D): It includes timbrel temporal descriptor, timbrel spectral descriptors, basic spectral descriptors, spectral basis descriptors, signal parameter descriptors and silence descriptors.

Description schemes (DSs): It is way of integrating the relationships between the components of descriptors which supports other applications. It includes musical instrument, melody description audio signature, general sound recognition and indexing, and spoken content.

A description definition language (DDL): The DDL is syntax in schema language which is useful to express and combine audio descriptors and description schemes. It is a very powerful element in MPEG-7 which makes possible for user to create extension and modify descriptors, DSs and or even to define new ones [15].

Timbre is not understood clearly to the researchers and everyone has defined it in own way [16].

Definition 1: cannot be quantified like any other physical quantity but defined as a perceptual and subjective attribute of sound.

Definition 2: Timbre owe to many unknown dimensions, where the qualities and importance of feature are not very clear. Though cannot be mapped to a one-dimensional scale, it is even not uncoupled from the other one-dimensional components.

It is stated in [16] that trained musicians can "easily" identify instruments from a musical tone, but the error rates by machine are found higher. This fact pointed out the need of incorporating perceptual based method for extracting unknown useful information which cannot be done by traditional way.

IV. SYSTEM DESCRIPTION

The detailed process of the speaker identification of the whispered sound and components used in this paper are explained in Fig. 4.

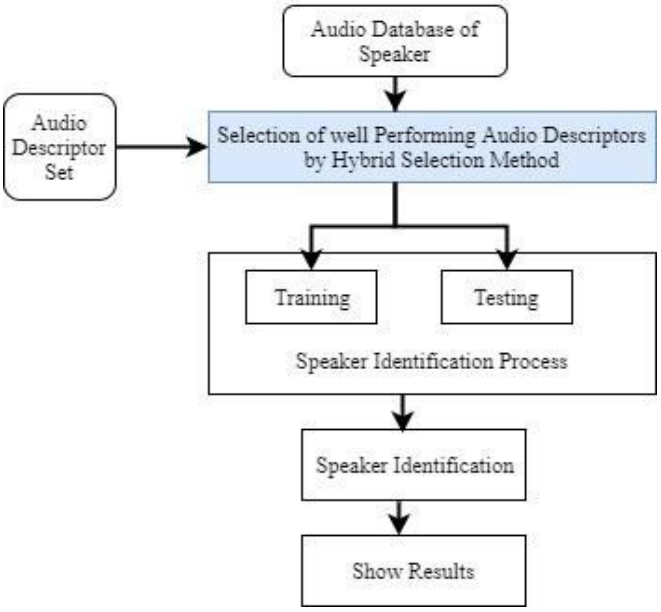

Fig. 3: System block diagram for Speaker Identification of whispered sound

The speaker identification mainly includes three steps: feature extraction, training and testing. Our system uses database of 24 speakers consisting audio samples both in neutral and whispered mode. Hybrid Selection method examines the performance of all probable audio descriptors and eliminates low performing descriptors. Selected timbre audio features are used for training the system. A whispered query given for testing is classified by K-NN classifier and identified speaker identity is declared.

4.1 Audio Database of Speakers

Speaker database consist of 24 speakers, about 10 samples each in both neutral and whispered mode. It includes 17 male and 7 female candidates. The database includes utterances in English language having duration of 2-3 seconds. Acer TravelMate 8000 series notebook was used for recordings, with a sampling frequency of 16 kHz and stored as 16-bit PCM-encoded WAV files. As the recorded speech (neutral and whispered both) is having bandwidth below 8 kHz, sampling frequency is selected according to the nyquist criteria. While recording the database, phonetically balanced sentences from TIMIT database are selected. The recording is done in a room with no acoustic conditioning to check the robustness of the proposed system in a bit noisy environment.

4.2 Hybrid selection method for finding the best Feature for speaker identification in whispers

MPEG-7 standards defined more than 52 audio descriptors including all low level descriptors. Using all of the descriptors will make the system complex; moreover all of them are not useful in the whispered database. The various dimension reducing algorithms like PCA, Sequential forward generation (SFG) or Sequential backward generation (SBG) are suggested. The SFG

algorithm starts with an empty set of features and adds new well performing feature at each level. The process continues adding new feature for identification task until no further improvement is found. The SBG process is similar to SFG but starts with a full set of features and eliminates those features giving the lowest results until no further fall in result is found [16]. Methods more of less similar to SFG or SBG can be adopted for its ease of implementation.

The Hybrid Selection Algorithm used in this paper is demonstrated below. The results confirmed our assumption that perceptually motivated timbre features are most suitable for the speaker identification within the whispered database. When the algorithm is executed for our database; the features namely roll-off, roughness, brightness, irregularity and MFCC are found to be giving the best identification accuracy. The performances of audio descriptors are also the database dependent [17]. Musical Information Retrieval (MIR) toolbox is easily incorporated in the Matlab environment. It makes use of functions available in public-domain tool boxes such as the auditory toolbox (Slaney, 1998), NetLab (Nabney, 2002), or SOM toolbox (Vesanto, 1999). MIR toolbox is adopted for easy use and computation simplicity. Among the selected timbre features, irregularity & roll-off are based on an envelope analysis while roughness & brightness are the spectrum based analysis and MFCC uses the Mel spectrum.

The algorithm described below is similar to SBG which starts with set of all probable features and goes about eliminating the low performing features at successive level.
The steps followed for the algorithm are as below:

1. Take all the probable Audio Descriptors (ADs).
2. *Level 1*: Test all of them separately and calculate classification accuracy for each.
3. Rearrange all ADs in the descending order of accuracy and choose only first three ADs giving highest accuracy.
4. *Level 2*: Now the selected ADs are appended with all ADs, one by one, and the best three feature vector as a combination of two ADs are passed to the next level.
5. *Level 3*: Feature vector of two ADs are appended by the third AD sequentially and the best vectors of three ADs are passed to the next level.
6. *Level n*: This is the last iteration before (n+1) level, where the further addition of AD does not increase the accuracy.

After the last iteration, the identification accuracy is maximum with the audio descriptors namely Roll-off, roughness, irregularity, brightness and, Mel Frequency Cepstral Coefficient (MFCC) which is proven in result section.

4.3 Timbre audio descriptor significance and Vector space

This section covers the definitions, significance [17-19], and vector space of timbre audio descriptors. It also compares the feature values for inter-speaker and intra-speaker voice samples.
Roll-off frequency: The roll-off is useful for distinguishing voiced from an unvoiced speech from envelope nature. Hence, roll-off is very important descriptor in whispered speech. It is estimated from the major energy (85% or 95%) concentrated below the frequency bins selected. Mathematically,

$$\sum_{i=1}^{R} S_t[n] = 0.85 \times \sum_{i=1}^{N} S_t[n] \qquad (1)$$

Roughness: Average roughness is found by *mir-roughness* function which estimates the average variance between all peaks of the spectrum of the signal. Another way, roughness can find the presence of harmonics generally higher than the 6th harmonic.

Brightness: It is the midpoint of the energy distribution of the frequency.

Irregularity: It analyses all peaks of the spectrum, and variations are calculated among successive peaks which is elaborated by,

$$\sum_{k=1}^{n} (a_k - a_{k+1})^2 / \sum_{k=1}^{n} a_k^2 \qquad (2)$$

For better speaker identification, it is desired that the feature vectors used for the different speakers should exhibit discriminative property. Three features namely brightness, irregularity and roughness (for the sake of example) are plotted as a three-dimensional vector in the 3-D space as shown in fig. 4. For each speaker sample, three features mentioned above are considered as three dimensions of a vector and every sample of similar speaker uses a unique colour. Fig. 4 shows that all the samples of the same speaker are located nearby which indicates intra-speaker similarity. While every speaker sample is sufficiently isolated from every other speaker.

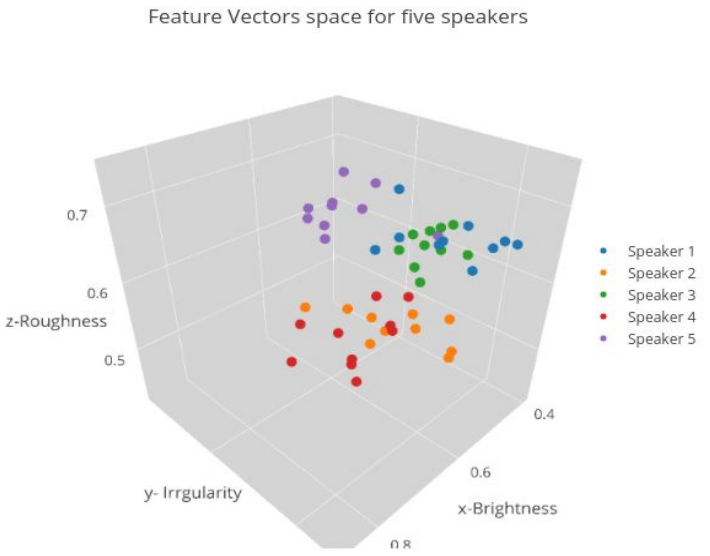

Fig. 4: Feature vectors in 3-D space for five speakers each with 10 samples

Fig.5 shows the acoustic distance for selected timbre features as Roll-off, Roughness, Brightness andregularity. Four samples of speakers are investigated w.r.t. above features. Here, two speech samples of two different speakers are used for illustration. SP1_1 and SP1_2 are samples of speaker 1 while SP2_1 and SP2_2 are samples of speaker 1. From below plot, it is depicted that there is an appreciable similarity in the acoustic distances of speaker samples of the same speaker i.e. acoustic distances for two samples of speaker 1 (SP1_1 and SP1_2) and speaker 2(SP2_1 and SP2_2) are nearby. On the other hand, acoustic distances of two different speakers (SP1_1 and SP2_1, SP1_1 and SP2_2, SP1_2 or SP2_1, SP1_2 or SP2_2) are discriminatory.

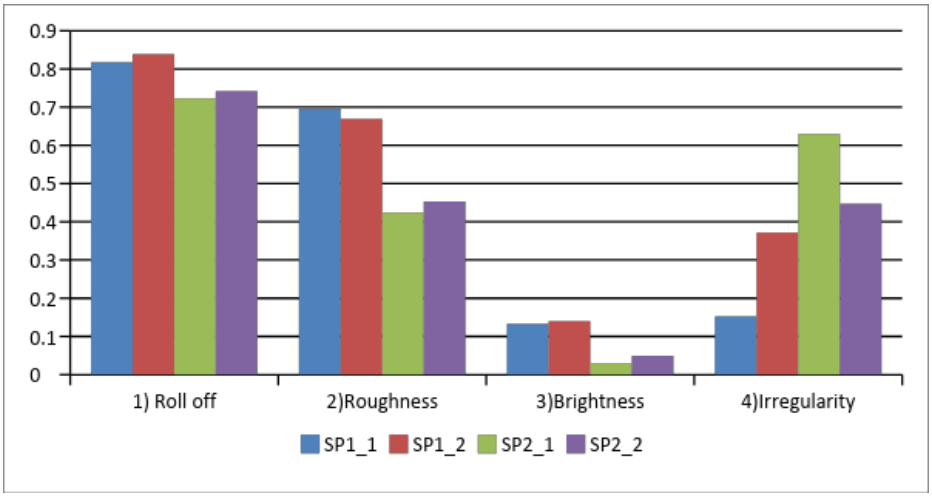

Fig. 5: Inter-speaker and intra-speaker feature comparison

The distance models are presented as a compact and easy way to understand raw data which can be useful the informational redundancy detaining of the audio descriptors [20]. Here, MFCC is not included in the feature vector due to large dimension (20 coefficient) which would make the representation somewhat redundant and unclear. While actual execution, Roll-off, Roughness, Brightness, irregularity and 20- MFCC coefficients form a vector which is used as a representation of unique characteristics of the individual speaker. The discrimination ability among selected features and different speakers is investigated by the standard deviation. The following table shows the standard deviation (σ) analysis. Standard deviation (σ) estimates the tendency of an individual elements of a group to deviate from the mean value (μ) for the group. A low standard deviation means that the group elements are distributed to be close to the mean, while a high value indicates that the data points are widely spread from the expected value (mean).

$$\sigma = \sqrt{\frac{1}{N}\sum_{i=1}^{N}(x_i - \mu)^2} \qquad (3)$$

Individual feature values of five speakers with 10 samples are tabulated in independent arrays first. Then the intra-speaker standard deviation for each audio descriptor is calculated and listed as below.

Table 2: Standard deviation for five Speakers pertaining to the selected timbre features

Selected Feature	Standard Deviation				
	SP_1	SP_2	SP_3	SP_4	SP_5
1) Roll-off	0.059773	0.067684	0.036448	0.041838	0.162628
2) Brightness	0.030004	0.039599	0.022873	0.026962	0.036932
3) Roughness	0.045886	0.126484	0.178834	0.024304	0.056731
4) Irregularity	0.082886	0.101791	0.141807	0.10608	0.117716
5) MFCC	0.083468	0.072469	0.046284	0.080897	0.035945

From the above table, the intra-speaker deviation for every feature is found to be very small which implies the small variations in the samples of the same speaker. Secondly, the standard deviation for every independent feature of the same speaker is different. Also, the standard deviation is different for every other speaker pertaining to all individual features. Hence, intra-speaker similarity and discrimination for inter-feature and inter-speaker acoustic properties can be predicted. As mentioned earlier, the identification process uses all selected features in the

form of vector. Hence, it is recommended to analyse inter-speaker discrimination on the basis of a feature vector. Hence, the standard deviation between all the samples of the same speaker for each feature are arranged in the form of an array (feature vector) and a box chart is represented for all 24 speakers in the database. Every speaker is represented by a range of values with min, max and,median. A major observation is noted here that each speaker shows a discriminative range of values w.r.t. feature vector.

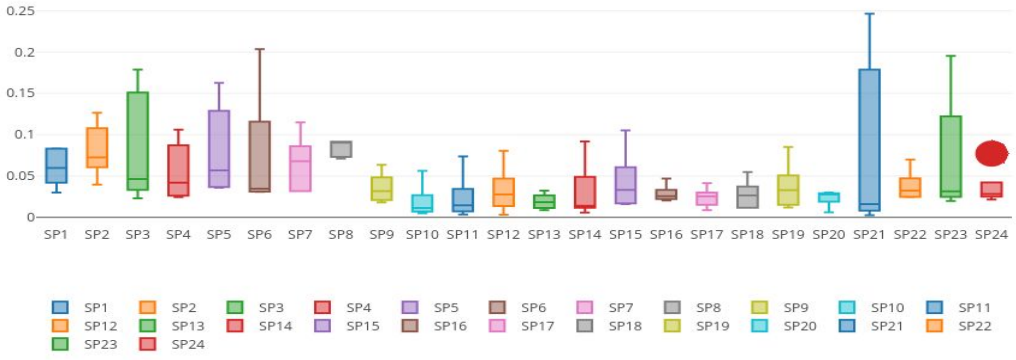

Fig. 5: A box chart for 24 speakers with all selected features as a vector

4.4 K-NN classifier K-Nearest Neighbor (KNN) Classifier

The KNN classifier lazy learning algorithm which does not require the prior knowledge of data. K-NN offers variations based on a number of nearest neighbors (k), a distance function (d), and a decision rule. For an audio file X_n with n samples, a new query vector is labeled a class based on the minimum distance from the predefined classes. Mathematically, it is a matter of calculating a posteriori class probabilities P (wi|x) as

$$P\,(w_i|x) = \frac{k_i}{k} \,.\, P(w_i) \qquad (4)$$

where ki is the number of vectors which belongs to class w_i within the subset of k vectors[21]. A large value of k is recommended, in general, to reduce the effect of noise on the accuracy. Also, the odd value of k is chosen for binary classification [22]. The results are also affected by the way of calculating distances between the training and testing vectors by various distance metrics available.

V. RESULTS

The system is initially trained and tested with the whispered voice samples for the selection of well-performing features suitable for whispered voice. Here, 80% samples are used while training and 20% samples were used while testing. Results are compared with only MFCC features and timbre features (zero-crossing, brightness, roughness, roll-off and irregularity) including MFCC. The K-NN classifier is used for classification.

Table 3 elaborates selection of audio descriptors on the basis of the best classification results for the whispered database. The best audio descriptors found are namely MFCC, roll-off, brightness, irregularity and roughness.

Table 3: Classification accuracy using MFCC only and timbre with MFCC for five speakers

Sr. No.	Audio Descriptors	Combination*		
		MFCC+Roll-off+Brightness+Roughness	MFCC+Roll-off+Brightness+Irregularity	MFCC+Roll-off+Roughness +Irregularity
1.	MFCC	....	....	....
2.	Attack-time	48	32	42
3.	Attack-slope	46	18	20
4.	ZCR	34	36	30
5.	Roll-off	....	....	....
6.	Brightness	....	....	74
7.	Irregularity	74	....	....
8.	Roughness	....	74	....

It is seen that classification accuracy is increasing as we go about appending the audio descriptors and it is maximum as 74% when all five descriptors mentioned above are appended. However, when attack-time and attack-slope and zero-crossing are added in the feature vector, the accuracy suddenly drops, hence they are eliminated.

A baseline system using traditional MFCC features and k-NN classifier as described in [23] is used. We could have used some state of the art classifier, however our focus of study is on the performance of timbre features for whispered database and use of other good classifier is left for future scope. Again, K-NN is proven to be the simplest and efficient classifier invariety of applications. As a thumb rule, 80% neutral samples are used for training and 20% whispered samples are used for testing.

Comparative testing accuracy using MFCC-KNN and timbre with MFCC-KNN is shown in Table 4 below.

Table 4: % Testing accuracy of Speaker identification with MFCC only and Timbre with MFCC

No. of speakers	Training (neutral) samples	Testing (whispered) samples	MFCC only	Timbre with MFCC
4	32	8	62.5	75.0
8	64	16	68.7	81.2
12	96	24	66.6	75.0
16	128	32	65.6	71.8
20	160	40	47.5	65.0
24	192	48	41.6	52.0

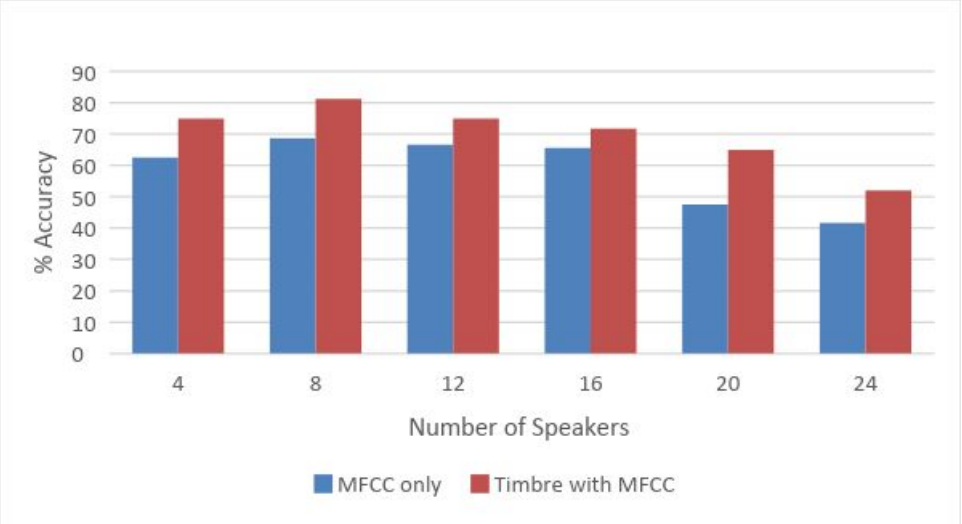

Fig. 7: Comparative identification results by Timbre features and MFCC features

Above results are observed with best performing timbre features and KNN classifier.

VI. CONCLUSIONS

The paper contributes (1) Creation of whispered-neutral speaker adaption database, (2) Analysis of whispered speech to know the limitations of a method like speaker identification on the basis unvoiced part only (3) Selection of the best audio descriptors useful for whispered speech database. (4) Analysis of timbre features on the basis of standard deviation for intra-speaker similarity and inter-speaker and inter-feature discrimination ability. (5) Further, experimental results proved that the perceptual based timbre features which are selected by Hybrid Selection Algorithm (brightness, roughness, roll-off, irregularity and MFCC) are found outperforming giving an enhancement in accuracy by 10.4% compared to traditional MFCC features only.

It is obvious that the set of well-performing feature depends upon the database used. By using a possible number of different databases of same kind e.g. whispered speech, list of most common and best-performing features can be known. Also, the robustness of timbre features can be investigated in depth by adding known and controlled noise in the noise-free (standard) speaker database.

K-NN classifier used here. However, use of any other advance classifier is recommended to enhance the results further, retaining the same feature extraction module used in the above work.

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In Silico Analysis of Single Nucleotide Polymorphisms (SNPs) of Three Isoforms of Human Nitric Oxide Synthase (nNOS, iNOS, eNOS) Genes

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ABSTRACT

The three isoforms of Nitric Oxide Synthase (NOS) synthesize free radical nitric oxide (NO), which has numerous protein targets in human body.Several vital processes are regulated and/or mediated by NO in nervous, immune and cardiovascular systems. Hence, alteration on NO level leads to pathological conditions in particular cells or tissues. Prior to conduction population genetic research, listing and identifying the most deleterious SNPs that may have strong relation with a particular disease is crucial. Hence, the aim of this study was to determine the functional non-synonymous Single Nucleotide Polymorphisms (nsSNPs) with emphasis on the exon regions for the neuronal, Inducible and Endothelial Nitric Oxide (nNOS, iNOS, eNOS) genes. Data from dbSNP database were functionally and structurally analyzed using different bioinformatics softwares. In the exon region, 222 SNP (from total 5293), 203 SNPs (from 1441) and 195 SNP (from 782) in nNOS, iNOS and eNOS, respectively were analyzed. Results of SIFT and PolyPhen predicted six SNPs in nNOS, iNOS, and seven SNPs in eNOS genes as damaging.

Keywords: nitric oxide synthase (NOS), nitric oxide (NO), single nucleotide polymorphisms (SNPs), bioinformatics softwares.

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ABSTRACT

The three isoforms of Nitric Oxide Synthase (NOS) synthesize free radical nitric oxide (NO), which has numerous protein targets in human body.Several vital processes are regulated and/or mediated by NO in nervous, immune and cardiovascular systems. Hence, alteration on NO level leads to pathological conditions in particular cells or tissues. Prior to conduction population genetic research, listing and identifying the most deleterious SNPs that may have strong relation with a particular disease is crucial. Hence, the aim of this study was to determine the functional non-synonymous Single Nucleotide Polymorphisms (nsSNPs) with emphasis on the exon regions for the neuronal, Inducible and Endothelial Nitric Oxide (nNOS, iNOS, eNOS) genes. Data from dbSNP database were functionally and structurally analyzed using different bioinformatics softwares. In the exon region, 222 SNP (from total 5293), 203 SNPs (from 1441) and 195 SNP (from 782) in nNOS, iNOS and eNOS, respectively were analyzed. Results of SIFT and PolyPhen predicted six SNPs in nNOS, iNOS, and seven SNPs in eNOS genes as damaging. Whereas, I-mutant server showed decrease stability of proteins encoded by them. Then CPH modeler 3.2 and Chimera software version 1.2 showed structure of these proteins. Further, Proscan version 1.7 server, Promotor 2.0 prediction server and TSSG prediction program identified cis regulatory elements in the above genes. Interestingly, most deleterious SNPs found in this study have not reported yet, especially in eNOS.

Keywords: nitric oxide synthase (NOS), nitric oxide (NO), single nucleotide polymorphisms (SNPs), bioinformatics softwares.

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I. INTRODUCTION

Single Nucleotide Polymorphisms (SNPs) represent the most frequent form of polymorphism in the human genome.[1,2]. Nitric oxide synthases (NOSs) synthesize the metastable free radical nitric oxide (NO), it is an unorthodox messenger molecule, has numerous targets enzymes and proteins [3,4]. There are three isoforms of NOS: endothelial (eNOS), neuronal (nNOS), and inducible (iNOS)[5]. Neuronal NOS (nNOS) gene located within chr12, reference Sequence: NG_011991.2. It is calcium-dependent and produces low level of NO as a cell signaling molecule. It constitutively expressed in specific neurons of the brain. It has been identified by immunohistochemistry in: spinal cord, sympathetic ganglia, peripheral nitrergic nerves, epithelial cells of various organs, kidney (macula densa cells), adrenal glands, islet cells of pancreatic, and vascular smooth muscle. The major source of nNOS in mammalians, is the

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skeletal muscle.nNOS has been implicated in modulating learning, memory, and neurogenesis. Disturbance in NO signaling , contribute to a variety of neurodegenerative pathologies such as excitotoxicity following stroke, multiple sclerosis, Alzheimer's, and Parkinson's diseases.Also Freudenberg mentioned in his review , some variants of nNOS associated with development of Psychiatric diseases such as Major depression, bipolar disorders, Autistic Spectrum disorder (ASD), Obsessive Compulsive disorder(OCD), Anxiety disorders, and Schizophrenia (Freudenberg et, al 2015[6-10]. In addition there are two researches done in 2012, and 2013 showed that here is significant association between some SNPs in nNOS and ischemic stroke [11,12]. Inducible (iNOS) gene located in: chr17, reference Sequence NG_011470.1. It encode calcium-independent enzyme that produces large amounts of NO.It identified basically in macrophages and express virtually in any cell or tissue that can be cytotoxic on parasitic microorganisms as well as on some tumor cells [13].Also can be expressed in cells when induced by bacterial lipopolysaccharide, cytokines, and other inducing agents . So, non-immune cells can be induced and affect the adjacent cells, for example ,Cytokine-activated endothelial cells, have been shown to lyse tumor cells, and induced hepatocytes kill malaria sporozoites. Also, it involved in non-specific allograft rejection[7,14-17]. Moreover excessive release of NO by iNOS plays a major role in septic shock, it lower the blood pressure predominantly due to it is effect in the vascular wall[18]. Interestingly, genetic variations in iNOS are involved in resistance to malaria as mentioned in research done by Maria de Jesus Trovoada, and her colleges in 2014 [19].

Endothelial NOS (eNOS) gene located in chr7, reference sequence NG_011992.1(NCBI). It encodes calcium-dependent NOS that produce low levels of NO, mostly it expressed in endothelial cells, and has been detected in cardiac myocytes, platelets, certain neurons of the brain, in syncytio-trophoblasts of the human placenta and in LLC-PK1 kidney tubular epithelial cells [7,17]. Physiological functions of eNOS include: vasodilation, inhibition of platelet aggregation and adhesion, inhibition of leucocyte adhesion,vascular inflammation, and Control of vascular smooth muscle proliferation. Furthermore, NO has been shown to inhibit DNA synthesis, mitogenesis, and proliferation of vascular smooth muscle cells [20,21], and has a role in Stimulation of angiogenesis postnatal, also had been found to be critical for collateral formation and angiogenesis post-ischemia [22]. One of the meta-analysis revealed that eNOS 4b/polymorphisms could be a risk factor for coronary artery disease, particularly in African populations [23]. Other research conclude that, (A-->G) change in eNOS is one of the most important variant associated with susceptibility to essential hypertension [24].Moreover, NOS is known to decrease the bioavailability of NO in sickle patients and play a role in different phenotypic presentation in patients, so every deleterious SNPs may affect the severity and outcome of the disease in sickle patients.

As Goldstein DB said in his paper, much attention of researches focused to date has focused on three polymorphisms in the eNOS gene which are: (-786T>C (rs2070744), intron 4 27-base-pair repeat, and Glu298Asp (rs1799983)), and this limits the study of eNOS to an isolated"candidate polymorphism" rather than a "candidate gene [25]. Therefore , identifying other pathological variants is required to carry out other genetic researches -the Same approach has been used to investigate the effect of nsSNP of HLA–*DRB1* and HLA-*DQB1* genes[26], so this study was done to identify the most deleterious SNPs in each isoform, and to determine the effect of them in structure and function and stability of proteins, that may contribute with other molecules to cause diseases.

II. MATERIAL AND METHODS

Softberry (http://www.softberry.com/),and is the most The data of SNPs of the 3 isoform of human NOS genes was collected from National Center for

Biological Information (NCBI) web site. The information of the SNP (i.e protein accession number and SNP ID) of these isoform was retrieved from NCBI dbSNP. (http://www.ncbi.nlm.nih.gov/snp/) and Swiss Prot databases (http://expasy.org/),

2.1 In silico analysis of the functional impact of coding nsSNPs using

(SIFT) software (Sorting Tolerant From Intolerant),(http://blocks.fhcrc.org/sift/SIFT.html) is an online bioinformatics tool used to predict whether an amino acid substitution will affect the protein function or not.[27]. The main underlying principle of this program is that it generates alignments with a large number of homologous sequences, and assigns scores to each residue ranging from zero to one. Scores close to zero indicate evolutionary conservation of the genes and intolerance to substitution, while scores close to one indicate tolerance to substitution only [28]. *(PolyPhen) software:* Is an online bioinformatics program (http://genetics.Bwh.harvard.edu/pph2/), automatically predict the consequence of an amino acid change on the structural and functional protein level. The program search for protein 3D structures, do multiple alignments of homologous sequences and amino acid contact information in several protein structure databases, then calculate position-specific independent count scores (PSIC) for each of two variants, and then computes the PSIC scores difference between two variants. The higher PSIC score difference, indicate that the functional impact of particular amino acid substitution is likely to occur [29, 30].

2.2 Identification of cis regulatory elements using

1. PROSCAN version 1.7 Web Promoter Scan Service

It predicts promoter regions based on homologies with putative eukaryotic Pol II promoter sequences. The site is serviced and maintained by Dr. Dan Prestridge at the Advanced Biosciences Computing Center, University of Minnesota. (http://bimas.dcrt.nih.gov/molbio/proscan/)

2 Promoter 2.0 Prediction Server

It predicts transcription start sites of vertebrate Pol II promoters in DNA sequences. It has been developed as a frequently updated database of simulated transcription factors that interact with sequences in promoter regions. It builds on principles that are common to neural networks and genetic algorithms. The site is serviced and maintained by Steen Knudsen at The Center for Biological Sequence Analysis at the Technical University of Denmark. (http:/www.cbs.Dtu.dk/services/Promoter/)

3 TSSG

This is the tool that used in Recognition of human Pol II promoter regions and transcription start sites, located in accurate mammalian cis element prediction program. Also has the fewest false positive predictions[31].

2.3 Prediction of the protein stability using

1) I-Mutant server

To support the results and to predict the stability of deleterious SNPs, I-Mutant2.0 online software has been used (http://folding.biofold. org/i-mutant/i-mutant2.0.html). It is a web server using for automatic prediction of protein stability changes upon single-site mutations, the result is a sign of DDG (the free energy change), positive sign (+) indicates increase of stability, negative sing (-) indicates decrease of stability.

2.4 Modeling of the deleterious SNPs using

1) CPH model 3.2 server

It has been used to predict the 3D structure for those proteins with an unknown 3D structure model. It is a protein homology modeling server, where the template recognition is based on profile to profile alignment, guided by secondary structure and exposure predictions. http://www.cbs.dtu.dk/services/CPHmodels/.

2) Chimera software version 1.8.1

This is a homology modeling software that has been used to generate the mutated models of each of the selected PDB (protein database) entries. This software is used to browse respectively locate the 3D structure of the specific protein and then alter the native amino acid with a mutated one to then look for structural effect that may produce. The outcome is then a graphic model depicting the mutation [32].

2.5 Analysis of the deleterious SNPs using project hope

It is online software (http://www.Cmbi.ru.nl/hope) has been used to build an automatic mutant analysis server that analyzes the structural and functional effects of point mutations, it is easy to understand and deal with and provide attractive results for the researchers [33]. It evaluate the effect of the mutation on the following features: Contacts made by the mutated residue, structural domains in which the residue is located, modifications on this residue and known variants for this residue.

III. RESULTS

Table 1: Shows numbers of SNPs in regions of nNOS, iNOS ,and eNOS genes (based on the dbSNP database)

		Number of SNPs	
sNPS	nNOS	iNOS	eNOS
Exons	222	203	195
5UTR	19	29	2
3UTR	145	43	8
Introns and other	4907	1166	477

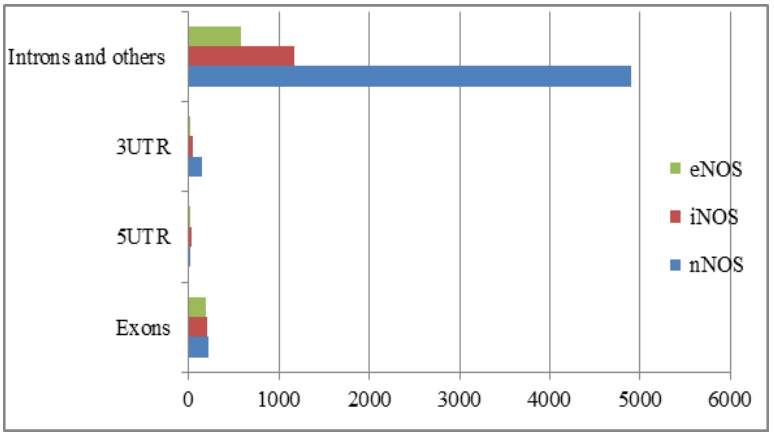

Figure 1: Bar chart represents the distribution of 3′ UTR, 5′ UTR, Exons and intronic and other SNPs for nNOS, iNOS and eNOS genes (based on the dbSNP database)

Table 2: Shows List of deleterious nsSNPs of iNOS that were analyzed using SIFT and Polyphen software's, And also result of I-Mutant server

Rs id nNOS	Position	Sift Score	Prediction	Poly2 Score	Predioction in PolyPhen	Stability
rs 56308341	R23H	0.01	DAMAGINE	1	Probably damaging	Decrease
rs 76839820	TI05M	0.01	DAMAGINE	1	Probably damaging	Decrease
rs 78402290	R19c	0.01	DAMAGINE	1	Probably damaging	Decrease
rs80348085	R48S	0.01	DAMAGINE	1	Probably damaging	Decrease
rs 78422671	R1129H	0.02	DAMAGINE	0.903	Probably damaging	Decrease
rs 55922940	L216P	0.01	DAMAGINE	0.814	Possible damaging	Decrease
Rs id iNOS	Position	Sift Score	Prediction in Sift Score	Poly2 Score	Predioction in PolyPhen	Stability
rs 28944201	R1009C	0.02	DAMAGINE	0.984	Probably damaging	Decrease
rs 406104261	R506W	0.02	DAMAGINE	0.996	Probably damaging	Decrease
rs 112588673	R452Q	0.01	DAMAGINE	0.99	Probably damaging	Decrease
rs 143835443	L720F	0.05	DAMAGINE	0.97	Probably damaging	Decrease
rs 150704221	R750H	0.01	DAMAGINE	0.821	Possible damaging	Decrease
145383683	V1037l	0.02	DAMAGINE	0.456	Possible damaging	Decrease
Rs id eNOS	Position	Sift Score	Prediction in Sift Score	Poly2 Score	Predioction in PolyPhen	Stability
rs 146141837	R1172C	0.01	DAMAGINE	1	Probably damaging	Decrease
rs 14178 7079	R530Q	0.01	DAMAGINE	0.984	Probably damaging	Decrease
rs 143324164	R128W	0.01	DAMAGINE	0.993	Probably damaging	Decrease
rs 145711802	F172L	0.03	DAMAGINE	0.937	Possible damaging	Decrease
rs 141456642	E156K	0.03	DAMAGINE	0.935	Possible damaging	Decrease
rs 145000830	Q411H	0.02	DAMAGINE	0.591	Possible damaging	Decrease
rs 3918232	V827M	0.04	DAMAGINE	0.476	Possible damaging	Decrease

Table 3: Shows results of proscan version 1.7 and tssg of n*NOS*gene

No	Strand	Promoter Location	No.	Stand	Promoter Location
1	Forward	5317 to 5567	16	Forward	140126 to140376
2	Forward	5591 to 5841	17	Forward	145087 to 145337
3	Forward	15511 to 15761	18	Forward	149576 to 149826
4	Forward	22122 to 22372	19	Forward	154991 to 155241
5	Forward	34103 to 34335	20	Reverse	157321 to 157071
6	Forward	35351 to 35601	21	Reverse	142595 to142345
7	Forward	37430 to 37680	22	Reverse	118101 to 117851
8	Forward	40608to 40858	23	Reverse	98357 to 98107
9	Forward	42576 to 42826	24	Reverse	89682 to 89432
10	Forward	43442to 43692	25	Reverse	56773 to 56523
11	Forward	72314 to 72564	26	Reverse	35798 to 35548
12	Forward	106229 to 106479	27	Reverse	18620 to 18370
13	Forward	114649 to 114899	28	Reverse	5845 to 5595
14	Forward	128185 to 128435	29	Reverse	5411 to 5161
15	Forward	131052 to 131302			

Table 4: Shows result of proscan version 1.7 and tssg of *eNOS and iNOS* genes

eNOS Promoter		iNOS Promoter		
No	Strand	Location	Stand	Location
1	Forward	2376 to 2626	Forward	2869 to 3119
2	Forward	18192 to 18442	Forward	6509 to 6759
3	Forward	22274 to 22524	Forward	16614 to 16864
4	Reverse	22746 to 22496	Forward	37132 to 37382
5	Reverse	18539 to 18289	Reverse	37784 to 37534

6	Reverse	11775 to 11525	Reverse	25471 to 25271
7	Reverse	9846 to 9596	Reverse	3137 to 6887
8	Reverse	2873 to 2623		

Table 5: Shows results of promotor 2.0 Prediction Server of nNOS, INOS , and eNOS genes

Rs id nNOS	Position	Sift Score	Prediction	Poly2 Score	Predioction in PolyPhen	Stability
rs 56308341	R23H	0.01	DAMAGINE	1	Probably damaging	Decrease
rs 76839820	TI05M	0.01	DAMAGINE	1	Probably damaging	Decrease
rs 78402290	R19c	0.01	DAMAGINE	1	Probably damaging	Decrease
rs80348085	R48S	0.01	DAMAGINE	1	Probably damaging	Decrease
rs 78422671	R1129H	0.02	DAMAGINE	0.903	Probably damaging	Decrease
rs 55922940	L216P	0.01	DAMAGINE	0.814	Possible damaging	Decrease
rs id inos	Position	Sift Score	Prediction in Sift Score	Poly2 Score	Predioction in PolyPhen	Stability
rs 28944201	R1009C	0.02	DAMAGINE	0.984	Probably damaging	Decrease
rs 406104261	R506W	0.02	DAMAGINE	0.996	Probably damaging	Decrease
rs 112588673	R452Q	0.01	DAMAGINE	0.99	Probably damaging	Decrease
rs 143835443	L720F	0.05	DAMAGINE	0.97	Probably damaging	Decrease
rs 150704221	R750H	0.01	DAMAGINE	0.821	Possible damaging	Decrease
145383683	V1037l	0.02	DAMAGINE	0.456	Possible damaging	Decrease
rs id enos	Position	Sift Score	Prediction in Sift Score	Poly2 Score	Predioction in PolyPhen	Stability
rs 146141837	R1172C	0.01	DAMAGINE	1	Probably damaging	Decrease

rs 14178 7079	R530Q	0.01	DAMAGINE	0.984	Probably damaging	Decrease
rs 143324164	R128W	0.01	DAMAGINE	0.993	Probably damaging	Decrease
rs 145711802	F172L	0.03	DAMAGINE	0.937	Possible damaging	Decrease
rs 141456642	E156K	0.03	DAMAGINE	0.935	Possible damaging	Decrease
rs 145000830	Q411H	0.02	DAMAGINE	0.591	Possible damaging	Decrease
rs 3918232	V827M	0.04	DAMAGINE	0.476	Possible damaging	Decrease

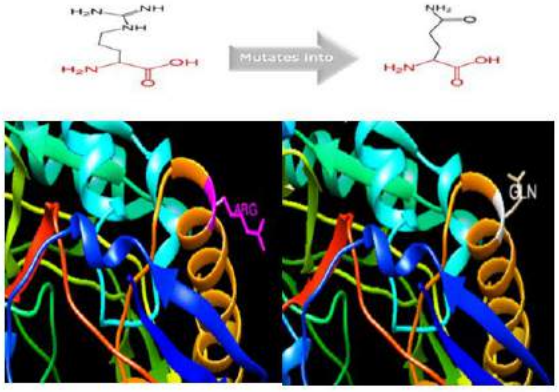

Figure 2: Shows Structure model (cartoon shape) of wild type amino acid Arginine (R)of *i*NOS in "stick" (magenta color) (left), and mutant type Glutamine (Q) in "stick" (grey color) at position 452 using chimera software

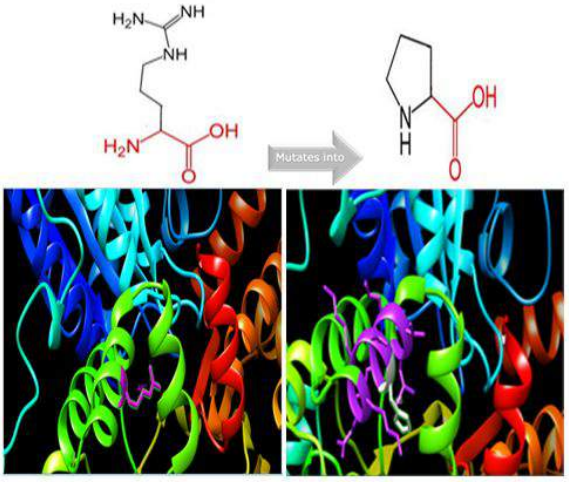

Figure 3: Shows Structure model (cartoon shape) of wild type amino acid (R) in "stick" (Magenta color) (left), and mutant type (H) in "stick" (Grey color) of nNOS gene (right) at position 1129 using chimera software

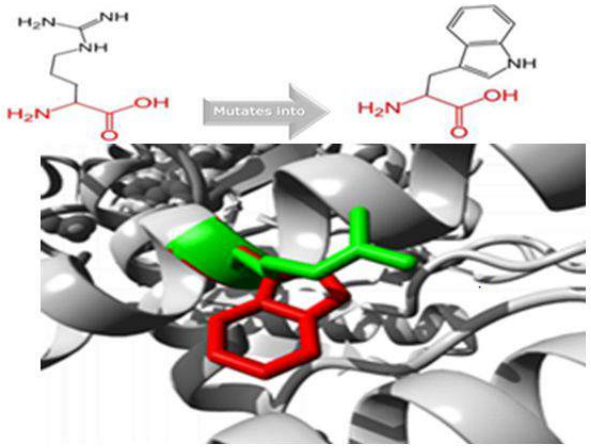

Figure 4: Shows wild amino acid (R) and mutant one (w) in position128 in eNOS gene and Close-up of the mutation using project hope. The protein is colored grey, the side chains of both the wild-type and the mutant residue are shown and colored green and red respectively

IV. DISCUSSION

Nitric oxide synthase is an enzyme, with three isoform (i.e. nNOS, iNOS, eNOS) synthesis Nitric oxide (NO), as messenger molecule and neurotransmitter; it plays an important role in regulation and modulation of a lot of processes in the nervous, immune, and cardiovascular systems. From the database of single nucleotide polymorphisms in a national center of biotechnology (NCBI), 5293, 1441, and 782 SNPs in nNOS, iNOS, ande NOS respectively, were obtained and categorized as shown in figure 1, table1. So an effort was done to identify most deleterious SNPs that can affect the structure, function and stability of the proteins that encode these genes . SNPs was submitted to the SIFT as well as to the PolyPhen server, their prediction are six damaging SNPs in both nNOS and INOS ,and 7 damaging SNPs in eNOS as shown in tables 2. It has been reported in two studies done in 2002 and 2010 in Japanese population, SNP (C276T) and SNP (rs41279104) in nNOS are significantly associated with schizophrenia, with p value of allelic frequency = 0.000007. and p value of genotype = 0.0013 , allelic p =), respectively [34,35]. Also mentioned in two studies, one done by Manso, H. and his colleages , and other in Chinese population, SNPs in nNOS (rs2293050, rs2139733, rs7308402 and rs1483757) were significantly associated with susceptibility to stroke and ischemic stroke (rs7308402) respectively,[11,12]. rs1800780 in the eNOS associated with susceptibility to essential hypertension as reported in B. Yang et. al, 2013[24].

I- mutant server's result showed that, some deleterious SNPs decrease the stability of these proteins while the other increase it as shown in tables 2. To visualize the effect of these damaging SNPs, cph modeler sever, Chimera software and project hope has been used for probably damaging SNPs as shown in figure 2,3,4. Important point is that, only one 3D structure of nNOS (1129) , iNOS (452), and eNOS (128) were done from all other damaging SNPs, the problem is that, there is no pdb id for protein encoding these genes, in addition, there is no full structure done for these isoforms , then protein sequence were checked again for their 3D structural using pBLAST analysis and also protein data bank (pdb), they showed similarity is very weak association with proteins found in data bank http://www.rcsb.org/pdb/home/home.do, so, visualization of 3D structure of deleterious SNPs that found just in chain C -which extent from 755 to 1418- and chain A- from 83 to 505- and from 76 to 480 in nNOS, iNOS, and eNOS respectively has been appeared. Hap map project (http://hapmap.ncbi.nlm.nih.gov/) and 1000 genome project has been used to check the allelic frequency of these damaging SNPs that has been appeared in chains of the protein encoded genes, SNP (rs78422671) in nNOS which is missense transition mutation from G To A that change the amino acid sequence from Arginine (R**)** – hydrophilic- to Histidine (H)- hydrophilic- not found in Hap Map project, in 1000 genome project (MAF = 0.0002/1). SNP (rs112588673) in iNOS ,which is missense transition mutation from G to A, that convert the amino acid from Arginine (R)- hydrophilic - to

Glutamine (Q)- hydrophilic-, not found neither in HapMap project, nor in 1000 genome project. The last SNP (rs143324164) in eNOS ,which is missense transition mutation from C to T, that convert he amino acid from Arginine (R)- hydrophilic - to t tryptophan (W)

- Aromatic , hydrophobic -, it was not found in HapMap project, but was found in 1000 genome project with MAF = 0.0004/2 . Furthermore, cis regulatory elements in three genes (nNOS, iNOS, and eNOS) were determined, as shown in tables 4,5,6. Numbers of promotor start sites by Proscan version 1.7 server is equal to that came out by TSSG prediction program , but differ from the results when Promotor 2.0 prediction server was used , so this server less reliable than others two. Combination of clinical evidences, and in silico analyses strongly recommended to increase our knowledge and to understand the effect deleterious SNPs and their role in the pathogenesis of the NO related diseases. Hence, these most deleterious SNPs may constitute distinct genetic markers that may be used as powerful mutation-screening in disease epidemiological studies.

V. CONCLUSION

Bioinformatics field is a powerful field nowadays worldwide and used in all fields of life sciences. Six SNPs in both (nNOS, iNOS) ,and seven SNPs in eNOS genes as damaging., these deleterious SNPs will affect the bioavailability of nitric oxide, and thus will contribute in the pathogenesis of human immune, neuro and cardiovascular diseases.

IV. RECOMMENDATION

More researches are warranted to detect the deleterious SNPs that come out from this study. x-ray crystallography and NMR must be done for other chain of the Three isoforms of human NOS , in order to be able to do 3d structure of them and to visualize the mutation that may occur on them

Disclosure statement.

The authors declare that, there is no conflict of interest regarding the publication of this paper.

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