Handwritten Processing for Pre Diagnosis of Alzheimer Disease

Donato Impedovo Ieee member[1], Giuseppe Pirlo[2], Donato Barbuzzi[2],
Alessandro Balestrucci[2] and Sebastiano Impedovo[2]
[1]Department of Electrical and Electronic of the Bari Polytechnic, Bari, Italy
[2]Department of Computer Science of "Aldo Moro", Bari University, Via Orabona 4, 70125 Bari, Italy

Keywords: Neuromuscular Transfer Function, Handwritten Data Analysis, Alzheimer Disease.

Abstract: Based on neuromuscular transfer function of the handwriting system, in this paper a non invasive pre diagnosis system for Alzheimer disease alert is proposed. It is well known in fact, that writing originates from spike trains produced within the Central Nervous System (CNS) and more specifically, inside the 4-th and the 6-th regions of the Bradman's map and then transmitted through the first and second order axons to the spinal cord to control the muscles involved in the handwriting as the arm, the forearm, the hand and the pen or pencil utilized for the writing. More specifically, in this work is proposed a new method, not invasive, for early diagnosis of degenerative disability, it can be also useful for monitoring activities related to the progression of neuromuscular disease in order to evaluate the changing related also to the efficiency of the therapies used. Benefit can be obtained not only for the medical field but also for the pharmaceutical developments. Specifically in the paper, the results of some experiments have been focused by considering a certain number of persons some of which affect by Alzheimer disease.

1 INTRODUCTION

Biometrics, from the Greek: Bios that means "life" and Metros that means "measure", is the discipline devoted to the study of variables related to the physicality of individuals in order to measure their value (Boldrini, M., 1934) and to use them to the creation of applications that are used in several fields i.e. finger prints generally used for social end military goals to certificate the identity of a person. See fig.1 (Medugno, V., Valentino, S., Acampora, G., 1999).

Bioengineering is recognized worldwide as an emerging discipline aimed at generating a better understanding of biological phenomena and produce technologies for health with benefit of the society.

The Bioengineering operates in several areas:

- Technological,
- Industrial,
- Scientific,
- Clinical,
- Hospital.

The goal which it arises is twofold:

- Improvement of knowledge about the functioning of biological systems;
- Development of new methodologies and diagnostic tools for treatment and rehabilitation (Biondi, E., Cobelli, E., 2001).

Figure 1: Fingerprint, signature, personal handwritten strokes.

In this paper specifically the handwriting is considered as a biometric entity and it is investigated in depth.

After this short introduction on the biometry, the paper presents: in sec. 2 the human neuromuscular

Impedovo D., Pirlo G., Barbuzzi D., Balestrucci A. and Impedovo S..
Handwritten Processing for Pre Diagnosis of Alzheimer Disease.
DOI: 10.5220/0004900701930199
In *Proceedings of the International Conference on Biomedical Electronics and Devices* (BIODEVICES-2014), pages 193-199
ISBN: 978-989-758-013-0

system involved in the hand writing process; in sec. 3 the problem of the stability in handwriting emphasizing the most stable part of a writing and showing the influence of a disease on these parts. Finally in sec. 4 some results are reported by processing handwritten sample produced by some Alzheimer illness affected patients by stressing the relationship between stability regions and disease insurgence.

2 ANATOMICAL AND NEURO-PHYSIOLOGICAL ASPECTS OF HANDWRITING

The handwriting as neuromuscular activity is described by starting from the neurophysiologic point of view and arriving to the mechanics of the neuromuscular system that allows the handwriting.

During the years of his live, a writer acquires at subconscious level some graph logic features that are synthesized in graphic strokes made increasingly clear, safe, fast and unique, here called personal strokes, that remain unchanged over time.

By looking at handwriting, it must be said that humans have different types of movements: "automatic" and "volunteers"; writing movements are a combination of this two type. The ability to move is made possible by the neurons in the cerebral cortex of the motor area (Brodmann's area 4, also called the primary motor area) at the origin of the *pyramidal system,* that provide at the voluntary movements of the muscles and the planning of the motor gesture. The motor area controls all voluntary movements, between these areas relative to the fine movements of the hand between which the movements necessary for writing; the voluntary movement interacts with the involuntary movement which belongs to the pre-motor area (area 6) which starts the extra-pyramidal system. For writing-motor processes are crucial sensory information, properly those of the sphere proprioceptive (kinaesthetic and sensitivity) that allow a continuous and accurate movements (Guyton, A.C., Hall, J.E., 2006), (Cattaneo, L., 1989).

This information, as well as through the mediation of the cerebellum and of the specific sensory areas, also converge directly on neurons of the areas of motor skills (motor neurons and neuromuscular junctions) and then operate without the intervention of conscious perceptions. The cerebellum has an important influence on all movements of the arm, as a consequence, the

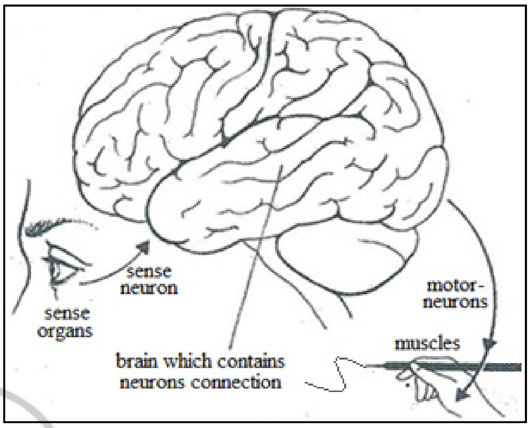


Figure 2: Example of the use of neurons to sense, motion and connection.
(source: http://www.analisidellascrittura.com/Image/neurofisiologia1(1).jpg)

behaviour of handwriting, allowing to perform all movements with precision and harmony.

Alzheimer's disease is the most common form of irreversible disabling degenerative dementia with onset senile, and his one of first and is considered one of the most serious diseases to social impact (Borri, M., 2012), (Meek, P.D., McKeithan, E.K., Schumock, G.T., 1998), (Zhu, C.W., Sano, M., 2006). In the brain of the patient is evident brain atrophy, a sign of the death of neurons, which does reduce the overall volume of the brain, which is filled with cerebrospinal fluid and it does enlarge the ventricles (Vallar, G., Papagno, C., 2007). The diagnosis is usually confirmed by specific behavioural assessments and cognitive tests, often followed from imaging magnetic resonance, but the computer-images based diagnostics allows only and solely to ascertain the presence and effects of cortical atrophy.

The first symptoms that appear are: impaired memory and not aware of the disease. The course of the disease and the symptom modes may be different for each individual patient.

Clinical features: Alzheimer's gets worse, new symptom joins to the existing, can be added aphasia, agnosia and apraxia.

Having been in his youth a large volume of activity mental/cognitive represents a protective factor against Alzheimer's. The disease can be recognized only with the neuropsychological examination and not with the instrumental diagnosis, and the main diagnosis of Alzheimer's occurs only through clinical evaluation actually (Waldemar, G., Dubois, B., Emre, M., et al, 2007).

A complete description of the neuromuscular system is reported in the former paper presented to the CIBB 2013 Nice (F) (Impedovo, S., et al, 2013) by looking the anatomic, physiologic and mathematical aspects, also the data acquisition devices used for investigation is over there described. In this paper is instead treated the relation between handwriting of suspected disease person, affected by the Alzheimer pathology, and illness persons.

3 STABILITY MEASURE OF HANDWRITING

The database (Impedovo, S., 2013) developed and used at Intelligent System Laboratory of the "Aldo MORO" Bari University: (ISUNIBA), utilizes a certain number of handwritten words representing the "mamma" word, produced exactly by 15 subjects affected by Alzheimer disease, 16 without any pathology, 7 namely with senile deficits of various kind and 5 affected by other neuromuscular disease, for a total of 43 persons. Each person has written the "mamma" word 5 times. In the database there are 215 specimen.

All the images are described in “bmp” format and represented in black and white. They are named according the code: “xxx\m-xxx-yy.bmp” for injured subjects and “xxx\s-xxx-yy.bmp” for illness subject, where xxx is the number of the writer and yy is the test number.

The goal of the research is to investigate the stability of handwritten "mamma" word and it has been done by comparing the results obtained by hilliness and injured subjects.

Therefore the proposed approach is a way for a non invasive analysis to investigate on the wealth status in persons suspected of disease affections. It must be said that the choice of the mamma word has been due to the fact that it is one of the first learned in speaking and writing and one of the last that is forget in the human live.

For each specimen processing algorithms have been used in order to compare each one whit the others in the data base. In fact after a pre processing for noise removal each specimen (Larkins, 2009) has been normalized at a standard dimension.

The median noise removal algorithm has been used just by coloring the 8 neighboring pixels with different colors for each pixel and averaging the value. The results of the techniques is reported in the next images.

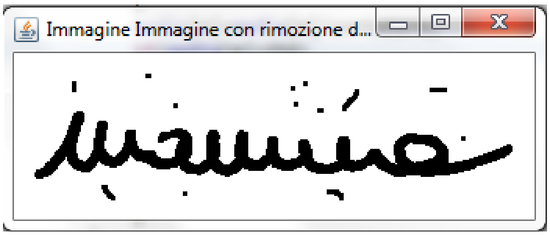


Figure 3: Image affected by noise.

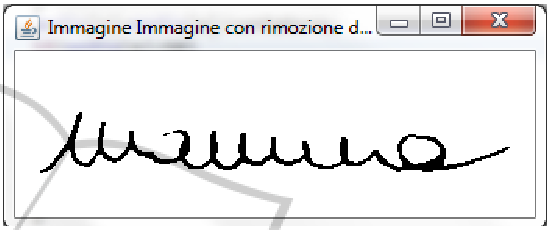


Figure 4: Image with noise removed.

The word dimension normalization has been obtained by using a specific software based namely on the reduction of number of pixels along x and y direction to a fixed number and the results are reported in the two specimen in the following, the first being the original and the second the normalized one.

Figure 5: Original image.

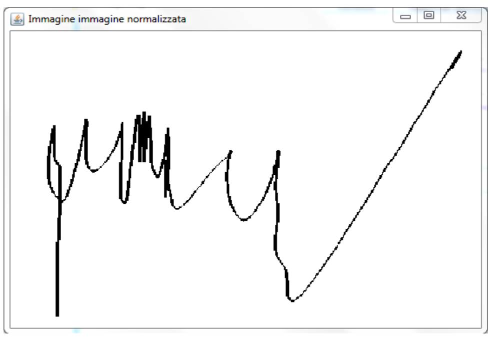


Figure 6: Normalized image.

The Equimass Grid techniques has been used to split each image in elementary parties. This technique, as it is well known, consists in dividing the image in non uniform sub regions obtained by dividing the image with horizontal and vertical lines on the base of the black pixels included in each region according to the formula :

$$Ma = \frac{M}{n}$$

Where Ma is the number of black pixels included in each horizontal or vertical direction of the specimen area (Larkins, R.L., 2009). In the following is reported the results of the algorithm application for a given specimen consisting of 10 by 10 subregions.

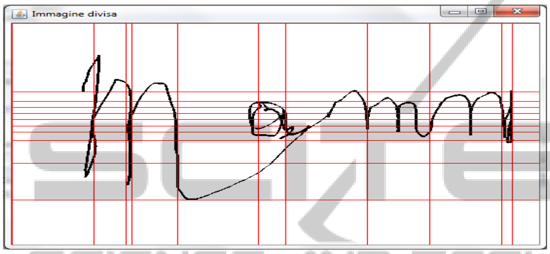


Figure 7: Equimass Grid Algorithm Application Result for a the given Specimen.

For each stroke into a sub region, the waiting vector is computed. It consists of twenty values computed on the base of the black pixels detected in the containing sub region. In the next figure are reported the results of the horizontal and vertical division but also the results of the oblique divisions along the main and secondary diagonals .

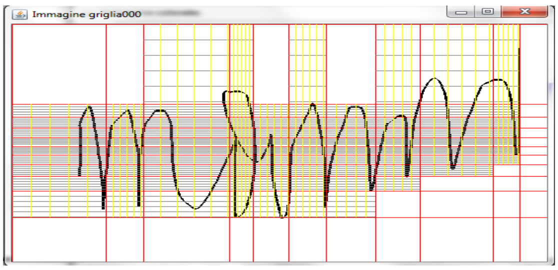


Figure 8: Horizontal and vertical division

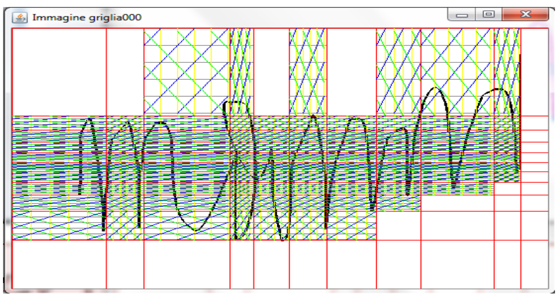


Figure 9: Horizontal, vertical and principal and secondary diagonal divisions.

In order to compare two vector the cosine similarity has been used, more specifically it is divided for the vector length in order to normalize the results just according to the following formula.

$$CosSim(Vp, Vj) = \frac{\vec{Vp} * \vec{Vj}}{|\vec{Vp}| * |\vec{Vj}|} = \frac{\sum_{i=1}^{t}(Wip * Wij)}{\sqrt{\sum_{i=1}^{t} Wip^2} * \sqrt{\sum_{i=1}^{t} Wij^2}}$$

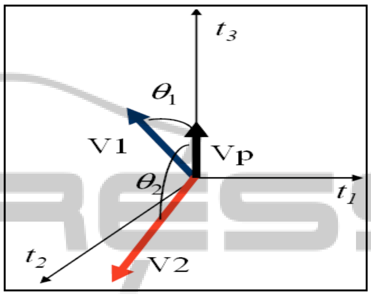
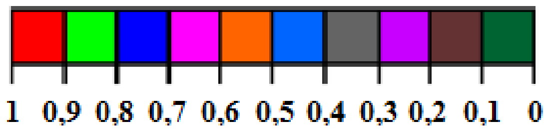


Figure 10: Graphic illustration of the cosine similarity

By taking into account the former similarity, computed region by region, the stability of the writing is computed for each region. At this purpose the similarity average value among all the regions is used according the formula:

$$stability = \frac{\sum_{i=1}^{r} Sij}{r}$$

where r represents the total region number, *S* is the similarity, "*i*" the tract under consideration and "*j*" the region name. As matter of fact the stability is a decimal number represented by a color according the code scale here reported:



In the next image by using this code are represented the different stability region by region for the spacemen under consideration.

The Yoshimura approach (Yoshimura, I.Isao, Yoshimura, M.Mitsu, 1991) for classification is used to train the learning phase and to measure the disease by comparing the characteristic of the stroke in the patient with that in the data base recorded in the learning phase. The result is a Boolean value that measure the disease of the patient.

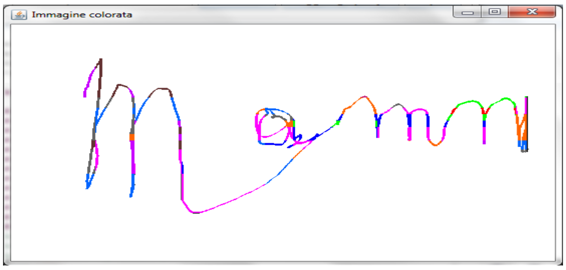


Figure 11: Different stable regions in a fragment of the mamma words.

About the Yoshimura approaches it must be said that:
for an unknown input specimen to the system, let it be F', the system compute the distance $d1', d2', d3'$ between F' and the corresponding values in the injured subjects $F1, F2, F3$ in the database. For this operation are considered only the three must stable regions. The distances $d1', d2', d3'$ between these strokes and the reference strokes $F1, F2, F3$ infact are:

$d1' =$ distance between F' and $F1$,
$d2' =$ distance between F' and $F2$
$d3' =$ distance between F' and $F3$

The maxima distance $dmax'$ among $d1', d2', d3'$ and the minima distance dmin among $d1', d2', d3'$ are then considered to evaluate the subject under test and it is considered as an injured one only if $dmax' < dmin$, and on the contrary he is estimated as an hilliness subject if it results: $dmax' > dmin$.

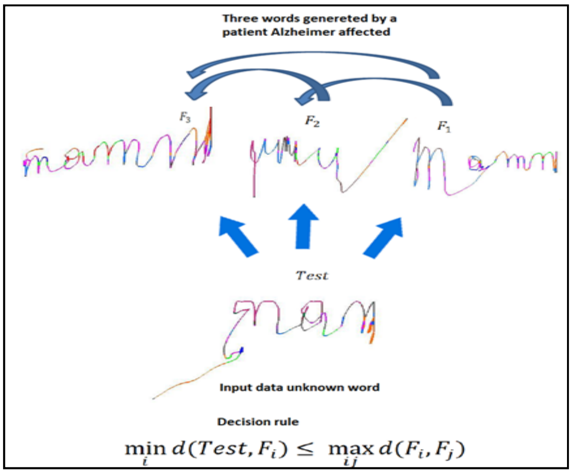


Figure 12: Yoshimura similarity approach example.

Obviously it will be the medical doctor that will suggest new clinical test in the first case.

The Software Diagram in use is divided in packages as in the figure here in the following:

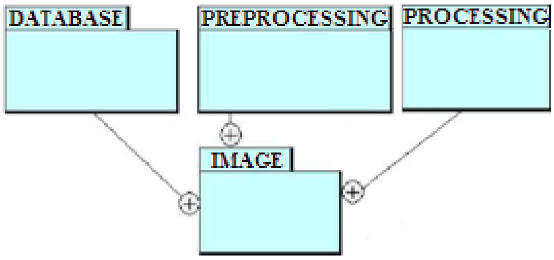


Figure 13: Class diagram applied on each word.

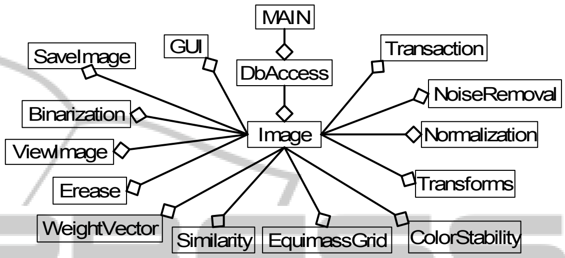


Figure 14: Class Diagram.

In the following some experimental results about the Stability are reported: firstly the 10 table for Alzheimer injured patients, divided in sub region of the grid and colored:

Patient 1

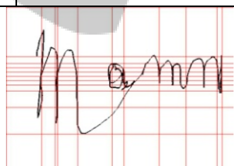
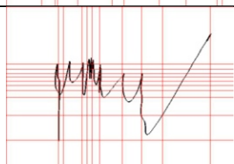
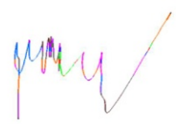
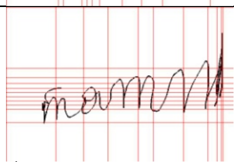
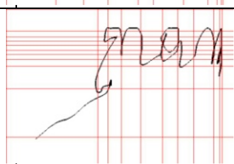
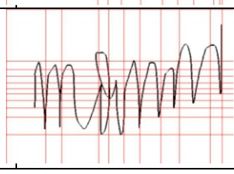
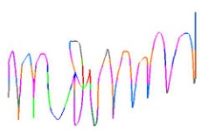
N	Grid	Color
1		
2		
3		
4		
5		

Figure 15: Table for the first patient.

similarly also the tables for the 2nd,3-rd,4-th,5-th,6-th,7-th ,8-th,9-th and
the 10-th patient have been considered and computed the related maps.

Also the 10 maps for illness subjects have been computed and in the following there is one of them :

Hillness subject 1-st

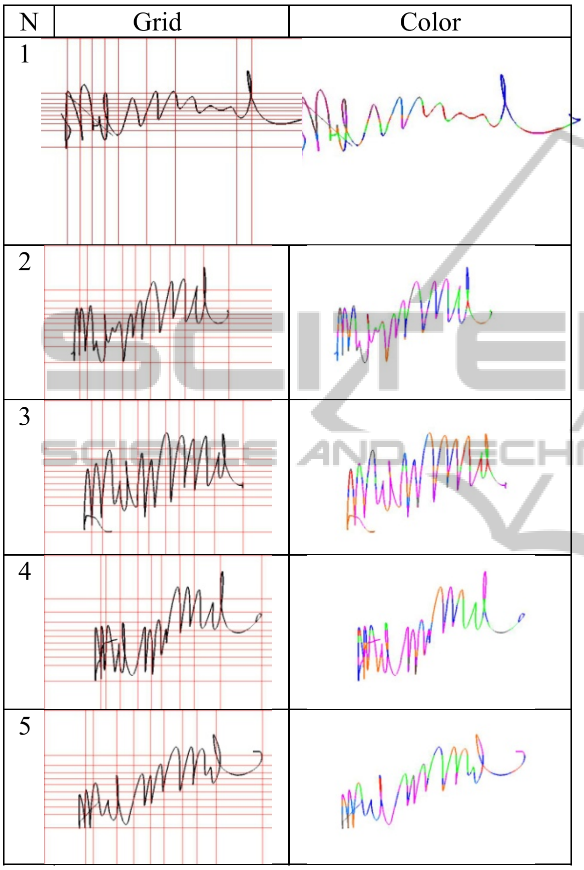


Figure16: Table for the first hilliness patient.

4 STATISTICS

By using the colored pie diagram, the statistics have been obtained and some of the results are in the following:

Upper part of the first illness subject.

Example of computation for the upper part light violet:

13:2 = 100: x

X = 2*100÷13= 7,69

In the same way have been processed all the other parts of all the data in the data base and the experiments concluded that the middle part of the word is much more stable than lower and upped

Color	Upper part	Middle part	Lower part
Violet	15,38%	0%	0%
Dark green	7,69%	1,72%	0%
Brown	15,38%	12,07%	0%
Light violet	7,69%	1,72%	8,33%
Gray	7,69%	15,52%	8,33%
Cyan	23,08%	10,34%	41,67%
Orange	0%	10,34%	25%
Pink	7,69%	24,14%	8,33%
Blue	7,69%	8,62%	8,33%
Green	7,69%	13,80%	0%
Red	0%	1,72%	0%

parts in injured persons but in any case they are less stable than in respect to illness subject.

Also two error type have been considered:

- I type error False Rejection Rate (FRR)
- II type error False Acceptance Error (FAR)

The first error type occurs if a stroke produced by a illness subject is rejected and of the second type if a stroke produced by an injured subject is accepted.

In the following the results obtained analyzing only the stable parts of the word are reported.

FRR: 12,5%
FAR: 32%

instead by considering all the zones the results obtained have been:

FRR: 0%
FAR: 14,7%

5 CONCLUSIONS

The experimental results shown that are the lower and upper parts of the handwritten word mamma that are more affected in stability by the Alzheimer disease instead the middle part of the word remain almost stable, obviously it is necessary investigate more in dept in order to define specific parameters for this personal disease but these evaluation are encouraging to continue on this direction of the research and also defining others similarity measure as we are starting to do.

REFERENCES

Boldrini, M., 1934. *Biometria e antropometria*, Giuffrè.
Medugno, V., Valentino, S., Acampora, G., 1999. *Sistemi di elaborazione dell'informazione: Sicurezza su Reti,* University of Salerno. Italy.

Biondi, E., Cobelli, E., 2001. *Storia della Bioingegneria,* Pàtron.

Guyton, A.C., Hall, J.E., 2006. *Fisiologia Medica,* Elsevier.

Cattaneo, L., 1989. *Anatomia del sistema nervoso centrale e periferico dell'uomo*, Monduzzi.

Borri, M., 2012. *Storia della malattia di Alzheimer*, Il Mulino. Bologna.

Meek, P.D., McKeithan, E.K., Schumock, G.T., 1998. *Economic considerations in Alzheimer's disease. Pharmacotherapy*, Pharmacotherapy Publications Inc.

Zhu, C.W., Sano, M., 2006. *Economic considerations in the management of Alzheimer's disease*, Dovepress Journal.

Vallar, G., Papagno, C., 2007. *Manuale di Neuropsicologia,* Il Mulino.

Waldemar, G., Dubois, B., Emre, M., et al, 2007. *Recommendations for the diagnosis and management of Alzheimer's disease and other disorders associated with dementia*, NCBI. USA.

Impedovo, S., Balestrucci, A., Rollo, A., Impedovo, D., Pirlo, G., Mangini, F. M., Barbuzzi, D., Sarcinella, L., O'Reilly, C., Plamondon, R., 2014. *Writing generation model for health care neuromuscular system investigation*, Springer-Verlag, in press. Nice(F).

Impedovo, S., 2013. ISUNIBA Database http://www.di.uniba.it/~impedovo/ISUNIBA.htm.

Larkins, R.L., 2009. *Off-line Signature Verification*, University of Waikato.

Yoshimura, I.Isao, Yoshimura, M.Mitsu, 1991. *Off-line writer verification using ordinary characters as the object.*, PR(24), No. 9.