# Towards an Automated Analysis of Neuroleptics' Impact on Human Hand Motor Skills

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Abstract—The fact that neuroleptics may have a more or less noticeable influence on fine motor skills is well-known. However, up to now there is no system that allows one to measure and to quantify such an impact of neuroleptics or other drugs. This article goes a first step into this direction by demonstrating how the handwriting dynamics of a healthy person can automatically be distinguished from that of a schizophrenic and, therefore, appropriately medicated person. Moreover, it is shown that differences can be detected even for a very simple kind of hand movement. That is, the persons trace a given meander. The handwriting dynamics are measured by means of a pen equipped with force and tilt sensors (Biometric Smart Pen). Then, the parameterized script generator model proposed by Hollerbach is used in order to extract characteristic features from the measured signals, e.g., features describing deviations of measured time series from predicted model time series. These features are then used as inputs of support vector machines that classify whether the handwriting has been provided by a healthy or a diseased person.

*Index Terms*—biometric smart pen, handwriting dynamics, script generator model, support vector machine, neuroleptics, medical diagnosis

## I. INTRODUCTION

One way to measure human fine motor skills is to measure the dynamics of handwriting. This kind of biometrics allows various applications not only in the field of authentication (see, e.g., our work on signature verification in [1], [2]) but also in areas such as medical diagnosis or therapy. For example, it would be important to assess side effects of drugs in order to control the medication of patients or in the context of admission procedures for such drugs.

In principle, there are two ways of handwriting measurement and analysis: *off-line techniques* (measurement and analysis of handwriting images) and *on-line techniques* (measurement and analysis of handwriting dynamics). The latter can be realized utilizing graphic tablets that measure time series of coordinates or specific pens equipped with force and/or tilt sensors, for instance. On-line techniques certainly provide more valuable information for biomedical applications.

In this article, we compare the handwriting of mentally diseased persons and healthy persons. The disease considered here is schizophrenia, which is a mental disorder that affects cognition, behavior, and emotion. It occurs in various forms [3] with symptoms such as disorganized thinking, delusions, or hallucinations. In acute phases, persons suffering from schizophrenia receive neuroleptics. However, patients respond to this treatment in different ways. Besides the desired effects, side effects such as extrapyramidal symptoms (EPS) - certain motion disorders - can be observed. Depending on the strength of those disorders, neuroleptics are classified as either typical neuroleptics (first-generation antipsychotic drugs) or atypical neuroleptics (second-generation antipsychotic drugs). Many novel neuroleptics with minor EPS are termed to be atypical. However, this classification is disputed [4] and the question whether typical or atypical neuroleptics should be applied is lively discussed [5], [6]. To answer this question it would be very useful to quantify the impact of neuroleptics on human fine motor skills. Such a quantification would be even more important from another viewpoint: The medication of patients could be controlled individually and - hopefully more specifically than today. Also, admission procedures for neuroleptics could be enhanced by additional test methods.

This article makes an important move towards these goals by demonstrating how the handwriting dynamics of a healthy person can automatically be distinguished from that of a schizophrenic person with appropriate medication. Section II deals with the state of the art in analysis of handwriting dynamics of schizophrenic persons and in models for handwriting dynamics. Section III describes the biometric pen used in our experiments. Section IV briefly introduces the experiments themselves. Also, the most important components of our analysis framework are summarized. The handwriting model used here is set out in Section V and the characteristic features that are computed by means of this model are described in Section VI. Experimental results can be found in Section VII and Section VIII summarizes the major findings.

# II. RELATED WORK

Many mental diseases and also many drugs have an impact on fine motor skills. For example, there are significant differences in the kinematic characteristics of healthy and schizophrenic persons [7]. Also, it has been stated that kinematic effects of schizophrenia are unlike EPS induced by neuroleptics [8]. A comparison of the handwriting of patients suffering from Parkinson's disease and schizophrenic patients shows similar characteristics but with lower values of characteristic parameters for schizophrenic patients [9]. Differences in the writing speed and in the variability of writing were recognized for schizophrenic patients, patients with affective disorders, and healthy persons [10]. Influences of schizophrenia, Alzheimer's disease, and Huntington's disease on the speed and the regularity of handwriting were observed by [11], [12], [13], [14]. Deficiencies in the regularity of handwriting were stated for schizophrenic patients with druginduced parkinsonism but not for patients actually suffering from Parkinson's disease [15].

The methods for an analysis of handwriting are often very similar and simple. Usually, time series of a graphic tablet that records the pen tip position are low-pass filtered and differentiated. A segmentation technique is used to find local extrema of the y-position. For each segment, extrema and means of the time series are calculated. The means and standard deviations of those values are regarded as characteristic features.

*Handwriting models* are medical theories that either explain certain properties of handwriting or they are used to synthesize script. In the following, some of these models are briefly summarized together with some notes on how they could be used for an analysis of handwriting.

The Two-Thirds Power Law [16] states that the velocity of writing v can be expressed in terms of the curvature  $\kappa$  $(v\kappa^{\frac{1}{3}} = q)$ , where q is a constant that changes at discrete points in time. As v and  $\kappa$  can be determined from the time series of a data record, handwriting can be segmented by finding the times where  $v\kappa^{\frac{1}{3}}$  changes. The Minimum-Jerk model [17] calculates a single value, the "jerk" of a movement, and supposes that a skilled writer minimizes this value under given constraints. [18] uses the Minimum-Jerk model to quantify handwriting abilities. As those constraints determine the amount of jerk in a data record and cannot be obtained from the time series of a graphics tablet, the jerk cannot be analyzed directly. [18] uses a normalization technique without medical background to solve this problem. The model of Meulenbroeck [19] is capable of synthesizing script from a set of two-dimensional points. The arm is modeled as a kinematic chain and an optimal writing trace is found by minimizing the link rotation. Because there are several link positions for one position of the pen tip, it is impossible to determine the parameters of the model from the data of a graphics tablet. The Delta-Log-Normal model [20] composes complex movements by adding the velocities of simple movements. The parameters of those movements can be calculated from a given data record and the model was used for segmentation and movement composition. It could also be used for feature extraction, yet the parameters of the model have no medical background [21]. A similar approach is the Oscillator Model [22] with the difference that it uses oscillator functions with changing parameters for a synthesis of script. This model is described in detail in Section V.

If a script generation model is "reverted", a set of parameters could be extracted from a measured time series that allow a medical interpretation (see Section VI).

#### **III. BIOMETRIC SMART PEN FOR DATA ACQUISITION**

The Biometric Smart Pen (BiSP) is a novel ballpoint pen for the acquisition of biometric features based on handwriting dynamics [23], [24]. The device is equipped with a diversity of sensors to measure the dynamics of forces transferred in three dimensions from the refill to the force sensors and to measure the finger kinematics by means of two inclination (tilt) angles. A prototype of the BiSP device utilized here for data acquisition is shown in Figure 1.

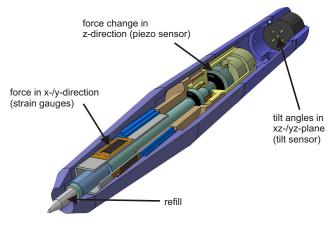


Fig. 1. Biometric Smart Pen (BiSP).

The forces resulting from handwriting on paper and transferred by the refill are monitored in horizontal directions x and y by strain gauges placed close to the front part of the refill and integrated in a half-bridge circuit. Their output signals are conditioned by a low-pass filter (with a few hundred Hz) and a single supply instrumentation amplifier. In the z-direction, defined by the longitudinal axis of the refill, the dynamics of the force are detected by a piezoelectric sensor located at the end of the refill. This sensor, which is running in a passive mode, samples the changes of the force in the z-direction. The approximately linear signals from the three force sensors are digitized with a 10 bit A/D converter at a sampling frequency of 500 Hz. The movement of the fingers holding the pen is also characterized by tilt angles  $\alpha$  and  $\beta$  with respect to the axis of the pen (refill). These angles are measured with electrolytic tilt sensors with a sampling rate of 125 Hz and a resolution of about 0.02 degrees. The recorded signals are then digitized by a 10 bit A/D converter. Altogether, the pen provides a 5dimensional time series consisting of x-force  $p_x$ , y-force  $p_y$ , and z-force changes  $p_z$ , as well as tilt angles  $\alpha$  and  $\beta$ .

The BiSP is in many respects superior to current penbased computer input devices because this pen is user friendly, uses refills that are commercially available, and handwriting can be performed on normal paper pads. A fundamental prerequisite for any analysis of dynamic handwriting patterns is a high reproducibility of signals obtained from patterns written repeatedly under optimal (i.e., identical) conditions by the same person.

## **IV. ALGORITHMIC PRE-REQUISITES**

In this article, experiments will show that it is possible to detect differences in the fine motor skills of healthy persons and schizophrenic persons medicated with neuroleptics (and, sometimes, other drugs) automatically. The time series of the BiSP will be analyzed using a script generator model. Therefor, simple drawing movements of the two groups of persons were recorded and classification rates will be determined using the recorded data.

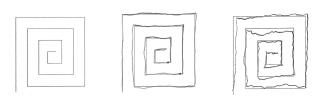
All test persons had to trace given meanders as shown in Figure 2(a) starting with the outer end point of the line. This should be done as precise as possible and with only one stroke (i.e., without interrupting the movement). The tracing of a meander requires a movement in two directions in which the wrist and the knuckles are involved. Records could be obtained for 35 schizophrenic test persons (most of them medicated with neuroleptics) and 18 healthy test persons. Figure 2 shows the traced meander and the time series of a healthy person -Figures 2(b) and 2(d) – as well as the traced meander and the time series of a diseased person - Figures 2(c) and 2(e).

First, the recorded time series are cut from the beginning to the end of the drawing movement. The force changes are discretely integrated and all time series of forces are mapped onto the same physical scale (forces in mN). Using the signals of the forces and the tilt information, the time series of the forces into the direction of writing and into a direction orthogonal to that and the writing surface are calculated using a coordinate system transformation (resulting in time series  $f_1$  and  $f_2$ ). These time series have the advantage of being widely independent of the tilt of the pen while writing [25]. Characteristic features needed for a classification are extracted using the script generator model described in the following section (Section V) and a Mahalanobis scaling method is applied to align the features. A detailed explanation of the features is set out in Section VI.

Cost-sensitive Support Vector Machines (C-SVM) are used to classify the time series using the characteristic features as inputs. SVM use a hyperplane to separate two classes [26]. For classification problems that can not be linearly separated in the input space, SVM find a solution using a nonlinear mapping from the original input space into a high-dimensional socalled feature space, where an optimally separating hyperplane is searched. Those hyperplanes are called optimal that have a maximal margin, where margin means the minimal distance from the separating hyperplane to the closest (mapped) data points (so-called support vectors). The transformation is usually realized by nonlinear kernel functions. Here, a

Gaussian kernel is used. C-SVM allow, but also minimize misclassification.

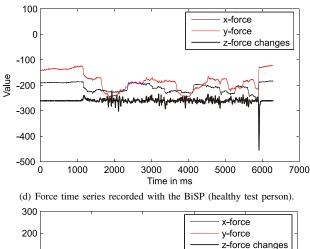
In order to determine the classification rates of the SVM, a cross-validation technique is used. This method segments the data records into k subsets of approximately equal size. In k runs, one subset is used for testing whereas the others are used for the training of the classifier. With the results from the cross-validation, the optimal set of parameters of the Gaussian kernel is found using an exhaustive search on an exponential grid.

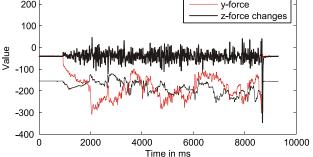


(a) Meander which had (b) Meander with line to be traced (scaled drawn by a healthy test down by a factor of person.

about two).

(c) Meander with line drawn by a schizophrenic test person.





(e) Force time series recorded with the BiSP (schizophrenic test person).

Meanders that had to be traced and recorded raw data. The two Fig. 2. persons chosen for this figure show easily distinguishable writing behavior.

#### V. AN OSCILLATOR MODEL FOR HANDWRITING

The oscillator theory of Hollerbach [22] models a twodimensional drawing or writing trace using two orthogonal oscillators and a constant movement along the direction of one of the oscillators. Let  $f:\mathbb{R}\to\mathbb{R}$  be a periodic function, then the two equations

$$\frac{\mathrm{d}x}{\mathrm{d}t} = af(\omega(t-t_0) + \Phi_x) + c_y$$

$$\frac{\mathrm{d}y}{\mathrm{d}t} = bf(\omega(t-t_0) + \Phi_y)$$

and a starting point  $(x(t_0), y(t_0))$  model a writing movement along the x- and y-direction. The parameters a and b determine the size,  $\Phi_x$  and  $\Phi_y$  the shape, and  $\omega$  the speed of the movement. The constant movement along the x-axis has speed c.

Fig. 3. The generated word "eule" (German for "owl").

TABLE I PARAMETERS OF THE WORD "EULE". f is a sinusoidal function.

time t	a	b	$\omega_x$	$\omega_y$	$\phi_x$	$\phi_y$	c
[0.00;0.26]						0.0	20
[0.26;0.61]							20
[0.61;0.82]							20
[0.82;1.05]	70.00	50.00	$5.00 \cdot 2 \cdot \pi$	$5.00 \cdot 2 \cdot \pi$	$\pi/4$	0.0	20

Hollerbach suggests sinusoidal functions as oscillators because they approximate the movements that occur in real handwriting quite well. An example of a synthesized movement can be seen in Figure 3, parameters are shown in Table I. In order to model the changes of shape during handwriting (e.g., when writing consecutive letters), the parameters  $a, b, \Phi_x$ , and  $\Phi_y$  may change at discrete points in time. The change of parameters must result in a continuously differentiable writing trace.

# VI. CHARACTERISTIC FEATURES

The oscillator theory of Hollerbach models the speed of the pen tip while writing. As the BiSP measures forces instead of positions or speeds, the model has to be modified, because the forces do not necessarily correspond directly to the speed of handwriting.

The time series of meanders traced by several persons were analyzed to find models for the forces. To model the forces, the *trigonometric trapezoid functions* we introduced in [27] can be used. The tracing of a meander requires movements into two directions. Therefore, we have to model the time series  $f_1$  and  $f_2$  (resulting from  $p_x$  and  $p_y$  by coordinate system transformation, cf. Section IV).

Definition (trigonometric trapezoid function): Let  $k \in \mathbb{N}$ ,  $a_0, \ldots, a_k \in \mathbb{R}, c_1, \ldots, c_k \in \mathbb{R}_0^+$  and  $r_1, \ldots, r_k \in \mathbb{R}^+$ . A function  $t : \mathbb{R}_0^+ \to \mathbb{R}$  is called a trigonometric trapezoid function of degree k, if

(i) 
$$t(x) = a_0$$
 for  $x \in [0, r_1]$ ,

(ii) 
$$t(x) = a_k \text{ for } x > \sum_{i=1}^k (r_i + c_i),$$
  
(iii)  $t(x) = 0.5(a_i - a_{i-1}) \left(1 - \cos(\frac{x-s}{e-s} \cdot \pi)\right) + a_{i-1} \text{ for } i \in \{1, \dots, k-1\}, \ s = \sum_{j=1}^i (r_j + c_j), \ e = s + r_{i+1}, \text{ and} x \in \left[\sum_{j=1}^i (r_j + c_j), \sum_{j=1}^i (r_j + c_j) + r_{i+1}\right], \text{ and}$ 

(

(iv) 
$$t(x) = a_i$$
 for  $i \in \{1, \dots, k-1\}$  and  $x \in \left[\sum_{j=1}^i (r_j + c_j) - c_i, \sum_{j=1}^i (r_j + c_j)\right]$ .

The intervals  $\left[\sum_{j=1}^{i} (r_j + c_j), \sum_{j=1}^{i} (r_j + c_j) + r_{i+1}\right]$  for  $i \in \{1, \dots, k-1\}$  are called *flanks* of the trapezoid function.

Trigonometric trapezoid functions resemble common trapezoid functions with the exception that the flanks are not linear but sinusoidal. This results in a better approximation of the drawing movements.

In our case, the degree k of the trigonometric trapezoid functions is given by the number of segments of a meander. As the segment boundaries (segmentation points) correspond to corners of the meander, these must be identical (i.e., at the same points in time) for the two time series records  $f_1: [0,b] \to \mathbb{R}$  and  $f_2: [0,b] \to \mathbb{R}$ . Consequently, if we fit two models (parameterized trigonometric trapezoid functions)  $t_1: [0,b] \to \mathbb{R}$  and  $t_2: [0,b] \to \mathbb{R}$  to the two time series, all the points  $c_i$  and  $r_i$  must be identical for the two models. This requirement implies additional constraints for the objective function

$$\sum_{i=1}^{2} \int_{x=0}^{b} \left( t_i(x) - f_i(x) \right)^2 dx$$

which has to be minimized considering those constraints. As we have data measured at discrete points in time, the integral can be replaced by a sum.

However, the optimization problem described above is highly nonlinear and multi-modal, and it is crucial to find a very good starting point for any iterative optimization technique (e.g., Quasi-Newton or Conjugate Gradients). Otherwise (e.g., with a randomly selected starting point), there is a high chance that any optimization technique converges in a bad local minimum of the objective function.

In order to obtain a good starting point, we initially segment the time series. In principal, the corners of a meander would be appropriate segmentation points. However, position information is not available with our biometric pen. Therefore, we use the time series  $f_1$  and  $f_2$  for segmentation. An analysis of these time series reveals that the four corner types of a meander correspond to different features of the time series: A left upper corner corresponds to a falling flank of  $f_2$ , a right upper corner to a rising flank of  $f_1$ , a bottom right corner to a rising flank of  $f_2$ , and, finally, a bottom left corner to a falling flank of  $f_1$ . However, a large number of consecutive data points corresponds to one of these patterns. Therefore, we apply additional knowledge about the approximate length of the segments to select appropriate segmentation points.

We first utilize a low-pass filter and then apply the segmentation algorithm of Brault and Plamondon [28] to the time series  $f_1$  and  $f_2$  to find appropriate candidate points for segmentation points. Basically, this algorithm has been developed to segment signatures at distinct points. Figure 4 gives an example.

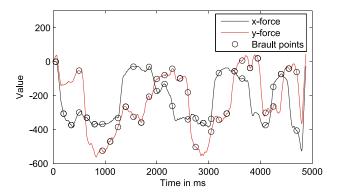


Fig. 4. Candidate points found with Brault's method.

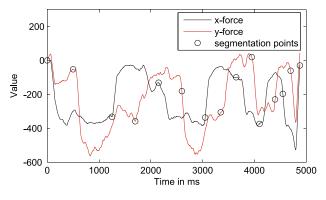


Fig. 5. Final result of the segmentation.

Then, we assess the candidate points with respect to the derivative of the time series and possibly existing level differences in a local environment around a candidate point. For the actual choice of segmentation points we pass through the time series and iteratively determine intervals which estimate the position of the respective "next" segmentation point. Within these intervals we select the candidate point with the highest rating. Figure 5 shows the candidate points selected as segmentation points. Near the end of the time series the segmentation points are closer because the vertical and horizontal lines of the meander are shorter near its center.

Next, we have to determine values for the parameters of the two models which can be used as a starting point for an optimization. For each segmentation point we determine the point for which the level difference to subsequent points is maximized. This point determines the boundary between a flank and the interval with a constant value within a segment. Now, the two models can be initialized with appropriate starting values for all parameters (cf. Figure 6).

Finally, we apply the interior-reflective Newton method [29] to improve these values, i.e., to minimize the objective function. That is, we utilize an iterative optimization method with an appropriate starting point. The result of this optimization step is shown in Figure 7. It should be mentioned again that the two time series and the respective models should not be regarded separately as additional constraints concerning the segmentation points must be met (see above).

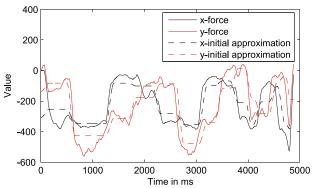


Fig. 6. Starting Function of the approximation.

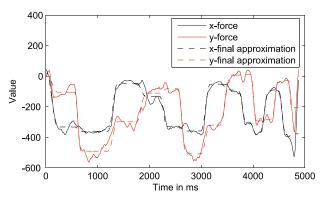


Fig. 7. Result of the iterative approximation.

In a next step, we extract characteristic features from the time series  $f_1$  and  $f_2$  as well as from the parameters of the approximating trapezoid functions. These features will be used as inputs for an SVM classifier. We compute features for the entire meander, for all segments, separately for horizontal and vertical segments, and separately for segments corresponding to the four directions of hand movement. The features reflect the drawing speed, inaccuracy, regularity, etc. Altogether, 102 features are determined. Feature selection algorithms (filter algorithms such as ReliefF and SFG; cf. [30]) were applied to assess the importance of features. Figure 8 shows the feature rating obtained in the first run of the SFG algorithm (Sequential Forward Feature Generation). The most important feature has an information gain of about 0.4. The nine most important features according to SFG, which utilizes a complete search strategy in the feature space, will be defined now.

In the following, [1; n] refers to the currently evaluated time interval, h (with  $h \le k$ ) is the currently evaluated number of segments, and  $f_1$  and  $f_2$  are the time series as mentioned before.

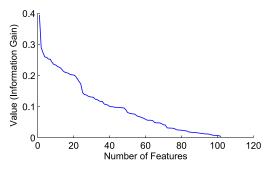


Fig. 8. Feature selection with SFG (one run).

The most important features  $m_1 - m_9$  according to the feature selection algorithm are:

• **Inaccuracy**: The inaccuracy is determined on the basis of a principal component analysis (PCA) of the two time series  $f_1$  and  $f_2$  yielding time series  $d_1$  and  $d_2$ . We assume that after the coordinate system transformation one of the force directions dominates for each segment  $(d_1)$ . If the meander would be traced perfectly, the force into the other direction  $(d_2)$  would be zero. Therefore, we compute

$$\begin{array}{rcl} Coeff_{j \in \{1, \dots, h\}} & \stackrel{\mathrm{def}}{=} & \operatorname{PCA}\left(f_{1}, f_{2}\right), \\ d_{i, j \in \{1, \dots, h\}} & \stackrel{\mathrm{def}}{=} & f_{i} \cdot Coeff_{j}, \\ error_{j \in \{1, \dots, h\}} & \stackrel{\mathrm{def}}{=} & \sqrt{\frac{1}{n} \int_{x=1}^{n} \left(d_{2}\left(x\right) - \operatorname{avg}(d_{2})\right)^{2} dx}, \\ m_{1} & \stackrel{\mathrm{def}}{=} & \operatorname{avg}_{j \in \{1, \dots, h\}}(error_{j}). \end{array}$$

• **Deviation**: The distance between the trigonometric trapezoid functions  $t_1$  and  $t_2$  and the time series  $f_1$  and  $f_2$  is the deviation of the trace from the model.

$$error_{j\in\{1,\dots,h\}} \stackrel{\text{def}}{=} \sum_{i} \sqrt{\frac{1}{n} \int_{x=1}^{n} \left(f_{i}\left(x\right) - t_{i}\left(x\right)\right)^{2} dx},$$
$$m_{2} \stackrel{\text{def}}{=} \sum_{h} \left(error_{j}\right).$$

In addition, we determine similar features for each segment:

$$\begin{array}{ll} m_3 & \stackrel{\text{def}}{=} & \operatorname{avg}_{j \in \{1, \dots, h\}} \left( error_j \right), \\ m_4 & \stackrel{\text{def}}{=} & \min_{j \in \{1, \dots, h\}} \left( error_j \right), \\ m_5 & \stackrel{\text{def}}{=} & \max_{j \in \{1, \dots, h\}} \left( error_j \right). \end{array}$$

• Flank heights: The median of the flank heights is determined by

$$\begin{aligned} & \textit{flank}_{j \in \{1, \dots, h\}} \quad \stackrel{\text{def}}{=} \quad \frac{1}{2} \sum_{i} \left( f_i \left( j \right) - f_i \left( j - 1 \right) \right), \\ & m_6 \quad \stackrel{\text{def}}{=} \quad \text{med}_{j \in \{1, \dots, h\}} \left( \textit{flank}_j \right) \end{aligned}$$

and the irregularity of the flank heights is

$$m_7 \stackrel{\text{def}}{=} \operatorname{iqr}_{j \in \{1, \dots, h\}} (\operatorname{flank}_j) / (m_6),$$

where the interquartile range is used as it is more robust to outliers than the standard deviation [31].

• **Duration**: The durations of the constant intervals and the flanks are measured by

$$\begin{array}{rcl} m_8 & \stackrel{\mathrm{def}}{=} & \mathrm{med}_{j \in \{1, \dots, h\}} \left( c_j \right), \\ m_9 & \stackrel{\mathrm{def}}{=} & \mathrm{med}_{j \in \{1, \dots, h\}} \left( r_j \right). \end{array}$$
VII. EXPERIMENTAL RESULTS

For our experiments we evaluated records of 35 schizophrenic persons (with different medications) and 18 healthy persons. Every test person provided three meander samples in each of several test sessions (between 1 and 10 sessions for schizophrenic persons and between 2 and 4 test sessions for healthy persons). The data for schizophrenic persons have been recorded at the Mental Health Institution Taufkirchen, Germany. Altogether, there are 285 meanders of schizophrenic persons and 171 meanders of healthy persons available.

For a cross-validation test, five subsets were selected in a way such that the records from one test session were either used for training or for testing, but not for both.

In a classification test with SVM (see Section IV) we want to show whether differences of the fine motor skills of healthy and schizophrenic persons can be detected automatically. Therefore, we computed the features as set out in Section VI. We determine classification rates for each of the three meanders of a test session and for all together. Results are shown in Table II. It can be stated that the classification rates are quite high. They do not differ significantly for the three meanders – we can assume that there is no familiarization effect – and are even slightly higher when all the available data are used for training and testing. In this case, we obtain a classification error of about 4.2% only.

TABLE II EXPERIMENTAL RESULTS (CLASSIFICATION RATES).

	Overall	Healthy	Healthy Schizophrenic		Max.
	(Both Classes)	(Class 0)	(Class 1)		
Meander 1	94.1%	94.9%	93.7%	79%	100%
Meander 2	94.2%	95.0%	93.7%	70%	100%
Meander 3	94.2%	94.9%	93.7%	74%	100%
Meander all	95.8%	95.9%	95.8%	88%	100%

Features which allow a good differentiation between schizophrenic and healthy persons are the inaccuracy  $m_1$  and the deviation  $m_2$ . Box plots that show the quartiles of the distributions of the two features (not scaled here) are set out in Figures 9(a) and 9(b). For schizophrenic persons the variance of feature values is noticeably higher. Furthermore, the values of the inaccuracy measure and the deviation measure are typically higher.

In future applications we want to observe and to assess the etiopathology of a specific patient during her/his clinical treatment. We are mainly interested to quantify various influences, e.g., by the type of the applied drugs (e.g., typical or atypical neuroleptics), by changes in medication, or by additional drugs Proceedings of the 2007 IEEE Symposium on Computational Intelligence in Bioinformatics and Computational Biology (CIBCB 2007)

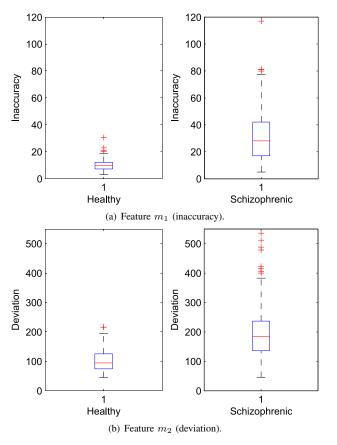
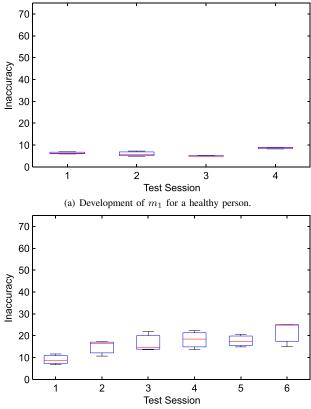


Fig. 9. Box plots of the distributions of two important features.

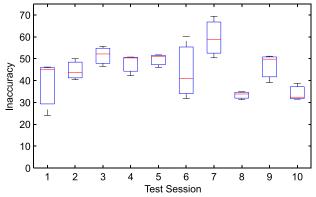
(e.g., sedatives). For the available data this is not possible as they are too heterogeneous. That is, we only have a very low number of schizophrenic patients who take one drug only. In addition, we only have a very low number of schizophrenic patients who attended five or more test sessions. However, we claim that interesting results will be obtained in future investigations: Figure 10 shows the development of the feature  $m_1$  (inaccuracy) for three persons. For the healthy person – Figure 10(a) – the values of the feature  $m_1$  do not change significantly in subsequent test sessions (low average, low variance). One of the schizophrenic patients - Figure 10(b) receives atypical neuroleptics at a relatively constant level and also sedatives. Compared to the healthy person, the variance is higher, but we also notice a deterioration of the accuracy during the clinical treatment. The other schizophrenic patient - Figure 10(c) - is alternately treated with various drugs, both atypical and typical neuroleptics. Additionally, he occasionally received an antiparkinsonian and an antidepressant. Between the seventh and the eighth test session, the patient switched from a depressive into a manic phase. At this point in time, the accuracy seems to improve suddenly.

Conclusions concerning influences of various drugs cannot be drawn at the moment. However, it can be noticed that ...

• ... the (in-)accuracy of healthy persons does not vary



(b) Development of  $m_1$  for a schizophrenic person with more or less constant medication.



(c) Development of  $m_1$  for a schizophrenic person taking various types of drugs.

Fig. 10. Box plots of the distribution of the feature inaccuracy in several consecutive test sessions.

significantly within one test session and for consecutive test sessions, cf. Figure 10(a).

• ... it seems possible to detect trends in the development of the (in-)accuracy if a schizophrenic patient is medicated at a relatively constant level, cf. Figure 10(b).

## VIII. CONCLUSION AND OUTLOOK

In this article, it is shown that it is possible to detect differences of the fine motor skills of healthy and schizophrenic persons automatically. This is even possible on a basis of relatively simple hand movements such as those effected when tracing a meander. A script generator model (Hollerbach's oscillator model) is applied to compute various characteristic features from force and tilt angle signals measured with a biometric pen. These features are subsequently classified by support vector machines.

In order to rate the fine motor skills gradually - e.g., when the etiopathology of a person must be assessed or the medication of a patient must be controlled - we must analyze a larger number of more complex hand movements. For example, patients have to write words containing the letters "ll", or to draw circles in various sizes either controlled by eye or not (cf. closed loop vs. open loop writing). For that purpose, we also have to adapt our algorithms. We also want to integrate position sensors into our pen which will make the assessment of accuracy and deviation easier and more precise. In addition to that, a grip force sensor will provide additional information. Other applications that could be realized in the future are therapy support systems for children with ADHD (attentiondeficit / hyperactivity disorder) or patients with apoplectic strokes. In [27], [32], we already investigated the influences of low temperature, physical strain, and writing with the nonpreferred (left) hand.

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