NEW METHODS FOR CTG FETAL MONITORING

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ABSTRACT
Antepartum fetal monitoring based on the classical cardiotocography (CTG) is a non-invasive and low-price tool for checking fetal status. Its introduction in the clinical routine limited the occurrence of fetal problems leading to a reduction of the precocious child mortality. Nevertheless very poor indications on fetal pathologies can be inferred from the actual CTG analysis methods, either they consist of the clinician eye inspection or of automatic algorithms. It is certain that fetal heart rate and uterine contraction carry much more information on fetal state than it is extracted by classical analysis methods. In particular Fetal Heart Rate (FHR) signal has demonstrated to provide consistent indication of his well being status and in case of fetal stress, during labor, the FHR usually shows some morphological alterations. As the methods actually used for judging a CTG trace as "abnormal" give a too low predictive value for fetal dangers, we started to develop a new computerized system for the CTG analysis. The fetal monitoring system is based on a new multiparametric analysis of FHR which includes non-linear analysis algorithms (Approximate Entropy and space state maps) of FHR. The analysis is coupled with a classification of fetal states (ABCD) by means of Neural Networks. A comparison between supervised and unsupervised networks has been done on the same set of recordings. A prototype of this new monitoring system will be implemented on the basis of HP Traceview distributed architecture.

INTRODUCTION
The introduction of cardiotocography (CTG) as a non-invasive technique for monitoring fetal conditions, allowed obstetricians to direct their attention to the antepartum period, on the basis that a major portion of the unfavorable fetal outcomes seems due to events that occur prior to the onset of labour (van Geijn, 1996). As a matter of fact, a number of risky conditions for fetal compromise has been recognized in the antepartum period, of which intrauterine growth retardation (IUGR) due to uteroplacental insufficiency and maternal type I diabetes are the predominant.

Since its introduction in the clinical routine, the use of CTG for antepartum fetal monitoring has led to a drastic reduction of intrapartum and precocious child mortality. However the actual methodology employed for judging CTG tracings has demonstrated a low predictive value for the fetal danger and high value of false positives in most cases. Indeed in the last 25 years since the introduction of CTG analysis, although the fetal and neonatal death rates have fallen considerably, the risk and severity of neurological handicap may even be rising. The conclusion of a number of recent studies is that very poor indications about fetus/newborn illness could be inferred from the actual CTG analysis (van Geijn, 1996), (Dawes et al. 1996).

The most reliable indicator of fetal condition is represented by fetal heart rate (FHR) signal, upon which CTG is based. In case of fetal stress there is a high probability (>90%) that FHR, during labour, will show some anomalies or alterations, while if FHR recording seems to be normal, chances are high that the fetus can stand the labour. Several conditions such as hypoxia, acidemia, drug induction produce noticeable variations of FHR, which are usually detected by simple eye inspection of the physician. In essence, the main characteristic of the FHR is thought to be the presence of a baseline (sinusal rhythm) on which the frequency control mechanisms act by provoking some irregularities called accelerations and decelerations. (Mantel 1990). Up to now CTG records have been analyzed by detecting and classifying mainly the changes of that hypothetical FHR base value (accelerations and decelerations) in the hope of revealing a fetal sufferance status.

Some CTG systems (Sonicaid, Hp) have tried an automatic classification of fetal states, based on the attempt to reproduce the criteria used by the clinicians, although in a quantitative way. In addition to the identification of accelerations and decelerations, also a quantitative assessment of the short term (STV) and long term (LTV) variability has been performed by the computerized CTG diagnostic systems. However the algorithmic approach, implemented on computerized automatic CTG diagnostic systems, has only led to a reduction of inter and intraobserver variability. An EEC project (Perinatal Monitoring) was pointed out to test the only commercially available system (Sonicaid
System 8000) with an initial multitrial research (van Geijn, 1993) and the results did not show a significant clinical improvement from the classic analysis by eye inspection to the automatic one. On the other hand, recent studies on HR variability signal of adult and newborn subjects emphasize that both linear and nonlinear effects contribute to the signal generation pattern (Signorini et al., 1992 and 1994). In addition it was noted that fetal distress was preceded by alterations in interbeat intervals before any appreciable change occurred in heart rate itself. If observed on long periods of time, the series obtained from the HR values are highly irregular, typical of nonlinear system behavior. Moreover, using even nonlinear analysis techniques can cluster pathological conditions. All these results lead to think that FHR regulation mechanisms show an intrinsic nonlinear behavior, i.e. FHR values can highly oscillate in time and not always tend to an equilibrium state or to a sinusoidal rhythm. Thus, FHR variation contains the information about the neural events controlling fetal heart, although the methodological tools used for clinical diagnosis up to now did not allow to extract reliable quantitative indexes linking physiopathological fetal states with FHR signal patterns.

For that reason we decided to face the problem of extracting from FHR signal both a classification of FHR patterns through ANNs, which are known to behave as non-linear classifiers, and new indexes of the non-linear behavior of FHR, presenting high sensitivity with respect to normal and pathological fetal states.

**DEVELOPMENT OF A NEW FETAL MONITORING SYSTEM**

The project we are developing has the goal to realize a new system for monitoring fetal condition, based on an appropriate and reliable analysis of FHRV. The final product of this work will be a clinical instrumentation prototype whose main characteristics are illustrated in the following. The whole system will be implemented on a PC workstation on a Windows platform. Its medium/low cost is crucial for being used in most obstetrical units.

We identify two main features that will be the kernel of a new instrument for the fetal cardiotocographic analysis. Most of these are yet implemented and have been tested on an annotated set of CTG signals as will be illustrated in the Results section.

1. **System learning ability**
   This feature is obtained by means of Neural Network (NN) techniques for the diagnostic classification of FHR patterns based on the new set of relevant parameters identified by the new mathematical tools illustrated in the following. NNs have the peculiarity of being able to learn how to perform non-linear classification of the input vectors once trained with an appropriate set of examples. Depending on the network architecture the training can be supervised – i.e. the training set consist of couples of input and desired output vectors - or unsupervised – the learning process needs only the input vectors.

2. **Linear and nonlinear multiparametric analysis of FHR**
   We evaluate the FHR characteristics by calculating linear parameters (Power spectral density estimation, variance), by extracting regularity parameters (Approximate Entropy) and by representing signal variations through Delay Maps.

   The new System Build-up has been carried out trough a modification of both the hardware and the software of an existing computerized CTG system (HP-2CTG) based on the HP-M1351A ultrasound fetal monitor. We started from the HP-2CTG system and we modified the FHRV sampling frequency, passing from the collection of 1 FHR value every 2.5 sec to 1 FHR value every 0.5 or 0.25 sec. Following the modification of the FHRV sampling frequency, the software was adapted for extracting, in a reliable way, the standard parameters (such as FHR accelerations, deceleration, etc.). Then, a first step for providing the system with learning ability was the implementation of two different NN architectures for the classification of FHR patterns based on input vectors consisting of 15 parameters automatically extracted by the 2CTG system. Once the NN has reached a stable state, the obtained clusters will be analyzed on the basis of the actual pathophysiological knowledge of FHRV indexes. The NN will then be tuned with the cases collected in the clinical tests in order to identify precise pathological classes.

   The final setup consists of a supervised NN, which will be implemented on the prototype system and trained with the clinical cases collected during the project. This NN can be re-trained by the end-user with his own cases.

   The second step consisted of the extraction of linear and nonlinear FHR global indexes including variance and Approximate Entropy. ApEn parameter quantifies the amount of regularity in data performing a detection of differences in HR that are not singled out by other classical analysis. Higher ApEn values indicate greater randomness in HR pulse. In this way, the normal fetal development should be characterized by an increasing of irregularity in HRV. As a matter of fact the complexity and the regularity properties of FHR dynamics can be useful to classify pathological situation as obtained for adult subjects and newborn infants.
On the fetal data obtained from this system we compute of the power spectral density (PSD) of the FHR by means computation based on the autoregressive modeling approach. PSD analysis provides tools for a better identification of heart rate patterns related to the Autonomic Nervous System control activity. The construction of delay maps can reveal different level of signal complexity. It could become a simple but immediate tool for physicians quantifying differences in fetal patterns. Periodic and therefore predictable patterns could be distinguished from non-periodic and unpredictable ones. FHR behavior will be evaluate by this set of quantitative parameters in time and frequency domain. They are sensitive to different pathological states as it has been demonstrated for several HRV signal conditions (Task Force ESC-NASPE, 1996).

RESULTS

Neural Networks

Neural networks have already been successfully used in CTG analysis, either for non-linear adaptive filtering in order to determine the FHR baseline (Gelmetti et al., 1994) and for various tasks related to FHR analysis (Dalton, 1994; Kol, 1995). As reported by Dalton (1994) the properties of handling complex structured data sets, the capability of learning and generalization, the representation of pattern recognition properties in a distributed fashion make NNs particularly attractive for application to maternal-fetal medicine. Two major classes can be considered among the different NN architectures: the supervised networks and the self-organizing or unsupervised ones.

The first class makes use of a supervised learning paradigm, which consists of training the network with couples of input-desired output pairs. The classification algorithm is then built-up by adjusting the weights of the network with an optimization procedure that tries to reproduce the function linking the input set to the desired output set. It has been demonstrated that a multilayered network (at least 2 layers) can approximate an arbitrary function with desired accuracy in an n-dimensional space. As a matter of fact a classification task consists of approximating an a priori unknown function which maps all the inputs coming from a set of parameters into a finite space output, representing the classes. The main problem of these networks is that the number of classes must be a-priori defined.

The self-organizing or unsupervised networks (Grossberg, 1987; Kohonen, 1987) seem to be able to overcome the problem reported before, because they show the ability to adapt themselves to variations of the inputs and to learn without the action of a supervisor. If correctly designed, these networks are able to self-adapt without loosing their stability and without forgetting or deteriorating the previously acquired knowledge. If accurately tuned, they are able to create new classes representing the clustering of parameters in the multidimensional space.

Our approach was focused on the ABCD classification of FHR patterns. The identification of FHR patterns is based upon three fetal variables: the body movements, the eye movements and the FHR variability. The occurrence and the type (random, periodic) of body movements associated with FHR patterns identify a state of fetal behavior, as shown in the Table 1.

The so-called FHR pattern classification ABCD (Njihus, 1992) have a direct relationship with the fetal behavioral states 1F to 4F. Table 2 summarizes the correspondence between FHR patterns, eye and body movements. The pattern A corresponds to the 1F state (quiet, non-REM sleep), the pattern B to the 2F state (active, REM sleep), the pattern C to the 3F state and the D to the 4F (active, jogging).

<table>
<thead>
<tr>
<th>CLASS</th>
<th>CHARACTERISTICS</th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>FHR is stable, with small oscillations (ΔFHR&lt;5bpm). Few accelerations in the occurrence of rare body movements.</td>
</tr>
<tr>
<td>B</td>
<td>FHR shows larger variations than A class (10bpm&lt;ΔFHR&lt;25bpm), with the presence of frequent accelerations during body movements.</td>
</tr>
<tr>
<td>C</td>
<td>FHR is stable, with a wide and regular oscillation (10bpm&lt;ΔFHR&lt;25bpm). Absence of fetal body movements.</td>
</tr>
<tr>
<td>D</td>
<td>FHR is unstable with frequent and large oscillations (ΔFHR&gt;25bpm). High accelerations and frequent movements.</td>
</tr>
</tbody>
</table>

Table 2. Relation between fetal heart rate and fetal movements C = coincidence of parameters matching the fetal behavioral states 1F to 4F

<table>
<thead>
<tr>
<th>Eye</th>
<th>Body</th>
<th>Heart rate</th>
</tr>
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<tbody>
<tr>
<td>C1F</td>
<td>Absent</td>
<td>Incidental A</td>
</tr>
<tr>
<td>C2F</td>
<td>Present</td>
<td>Periodic B</td>
</tr>
<tr>
<td>C3F</td>
<td>Present</td>
<td>Absent C</td>
</tr>
<tr>
<td>C4F</td>
<td>Present</td>
<td>Continuous D</td>
</tr>
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Two architectures were tested based respectively on the supervised training and on the unsupervised one: a Multilayer perceptron (MLP) trained with the adaptive backpropagation algorithm and a Kohonen self-organizing map.

**Multilayer perceptron**


The architecture of the first network was a three layer MLP, with an input layer of 15 linear neurons, a first hidden layer of 15 neurons (tansigmoid activation function), a second hidden layer of 15 neurons (tansigmoid activation function) and an output layer of 4 linear neurons. The training set consisted of 200 vectors obtained by the computerized analysis performed by the HP-2CTG system on 200 FHR windows each one lasting 5 min. The outputs were obtained by assigning to the ABCD classes the following binary vectors: class A (1,0,0,0); class B (0,1,0,0); class C (0,0,1,0); class D (0,0,0,1). The collected FHR tracings had been previously classified by the HP2CTG system (40%) and by an expert clinician (60%), in order to give a balance between automatic and human classification.

The input arrays were normalized and the MLP network was implemented by means of the Matlab Neural Networks Toolbox. The weights of the MLP were randomly initialized (initial error ~1000) and the adaptive backpropagation algorithm was used with initial learning rate =0.5. The network was trained for 77470 epochs, reaching a final error of \(-4\times10^{-5}\). The classification performance with a test set of 100 new recordings equally distributed (25 for each class) led to 96/100 of correct classifications. The 4 errors were done in tracings which had been classified with some doubts by the expert clinician.

**Self-organizing maps (Kohonen maps)**

These networks can learn to detect regularities and correlations in their input space and adapt their future responses to that input accordingly. Self-organizing maps learn to cluster groups of similar input vectors in such a way that neurons physically close together in the neuron layer respond to the similar input vectors. Their training is not supervised because the neurons adapt themselves during the iteration of input patterns presentation. This feature is highly desired in our classification task, because the output of the network cannot be biased by the judgement of the physician, even if he or she is an expert, as it happens with the MLP backpropagation training. The NN has been implemented and trained by means of SOM package (Kohonen), which is distributed free on Internet. The training set was the same as used for MLP, although the output array was not considered (not supervised training). We tried to cluster the input vectors in the parameter space on different maps (8x8, 10x10, 15x15). The best result was given by a 15x15 map (final quantization error 0.37), as shown in Fig.1.
Parameters from nonlinear analysis

Linear and nonlinear global indexes have been extracted from FHR signal. They include variance, parameters extracted from spectral analysis and Approximate Entropy which is sensitive to differences in HR that are not singled out by other classical analysis. Higher ApEn values indicate greater randomness in HR pulse. Moreover, as obtained from newborn infants, the complexity analysis seems sensitive to changes of the neural control activity on the heart. In this way, normal fetal development should be characterized by an increasing of irregularity in HRV. Complexity and regularity properties of FHR dynamics can be useful to classify pathological situation as it has been obtained for newborn infants and adult subjects.

Approximate entropy

ApEn is a statistic index which appears to have potential application to a wide variety of relatively short (>100 values) and noisy time series data (Pincus, 1995). Its computation starts from the choice of two parameter $m$ and $r$: $m$ is the length of compared runs and $r$ is really a filter. In practice we evaluate within a tolerance $r$ the regularity, or frequency, of patterns similar to a given pattern of window length $m$. From the numerical series $u(1), u(2), ..., u(N)$ and fixed $m \in \mathbb{N}$,

\[ \text{ApEn}(m, r) = \text{avg. over } i \text{ of } \ln \left( \text{conditional probability that } |u(j+m)-u(i+m)| \leq r \text{ as } |u(j+k)-u(i+k)| \leq r \text{ for } k=0,1, ..., m-1 \right). \]

ApEn measures the likelihood that runs of patterns that are close for $m$ observations remain close on next incremental comparison. It classifies both deterministic and stochastic signals requiring a reduced amount of points and it is robust against noise contamination. The presence of regularity produces smaller ApEn values and vice-versa. The value of $N$, the number of input data points is typically between 75 and 5000. Both theoretical analysis and clinical applications concluded that $m=1,2$ and $r$ between 0.1 and 0.25 SD of the input data produce good statistical validity of ApEn $(m, r, N)$. ApEn was compted on $N=300$ FHRV values (150 overlapping), $m = 1, 2$; $r = 0.1, 0.15, 0.2$. ApEn index quantifies different regularity levels in FHRV signals. Normal subject shows less regular HRV patterns. Figure 2 shows an example of FHR signal obtained from a CTG recording over 2 hours in a healthy fetus. Parameter values changes as different fetal conditions (activity (A) or quiet sleep (Q)) occur confirming their usefulness in the fetal state classification. In particular ApEn values follow the fetal behavior annotated by clinicians during CTG monitoring. PSD calculation during 2 hours recording shows different spectral patterns during activity and quiet. Spectra during Q shows LF/HF ratio <1 as it happens when the respiratory activity mediated by vagus nerve is prevalent. Moreover, spectral decomposition shows the presence of two HF contributions that can be attributed to the spontaneous “fetal respiration” activity and to the maternal respiration activity that can influence the FHRV in a reflex way. An example of delay map during Quiet is shown. It confirms the variability loss which can be observed in Q. Activity fetal states instead, are characterized by more dispersed delay maps with higher variability values and corresponding to spectra with LF/HF values > 1. Actually this multiparametric analysis has been applied to 8 fetal cases (3 Normal, 3 Pregnancy Hypertensive, 2 IUGR).

CONCLUSIONS

The obtained results confirm the importance and also the urgency of the introduction of new techniques for the fetal state classification. There is an evidence of information lack when only the traditional techniques are employed. On the other hand, the proposed methods seems to provide reliable analysis tools. This is confirmed in what follows.

Although ABCD classification of FHR patterns does not discriminate between normal and pathological labour outcomes, both the implemented NN architectures represent a noticeable step towards the automatic diagnosis based on CTG monitoring.

The MLP provides better classification results on the basis of the criteria imposed by the clinicians. Nevertheless the SOM in principle needs a larger training set to reach the same performance. Furthermore, it has the advantage of being independent of possible biases coming from human experience evaluation.

Results of multiparametric analysis are preliminary and do not allow inferring definite conclusions. The number of analyzed cases is too small for statistic analysis. ApEn value however changes as different fetal conditions (activity or quiet sleep) occur. It follows the fetal behavior annotated by the clinicians during CTG monitoring. Significant results obtained in adults and newborn infants by nonlinear techniques encourage further analysis to introduce the ApEn index in the clinical routine. The next step will be to train the networks in order to predict pathological outcomes.

The integration of all these analysis tools in the clinical CTG instrument seem a promising tool contributing to the improvement of the early diagnoses of fetal pathologies.
Figure 2: Multiparametric analysis of HRV signal (2 hours recording) for a normal, non pathological fetus (upper left panel). Results from PSD calculation (upper right) and Approximate Entropy estimators (bottom left) are shown. STD marks the estimation variance. The last panel (bottom right) reports an example of return map during quiet fetal condition.

REFERENCES