Entropies for detection of Term/Preterm delivery:A Review

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Abstract

Impending preterm delivery is likely associated with a change in uterine cellexcitability, favoring conduction of electrical activity across the uterine muscles, andmyometrium. Analysis of the electrohysterogram (EHG), which is the noninvasivemeasurement of the uterine electrical activity, has therefore been investigated as a potential method for pregnancy monitoring and early diagnosis of preterm birth.Various Entropies are signal features derivedfrom information theory. They reflect the regularity of a time series and have been extensively used for analysis and characterization of physiological signals.The sample entropy and approximate entropy can detect the difference between term and preterm delivery and performance of the system can further be improved after using various entropies.

Keywords: *Electrohysterogram, Non Communicable Diseases,Approximate Entropy*

1.Introduction:

According to World Health Organization report "Born Too Soon", there are about 15 million babies born prematurely in the world among a total of about 150 million births per year. Families all around the world are affected as more than 1 in 10 babies are born preterm.Over 1 million children die each year due to complications of preterm birth. Most of the children that survives face a lifetime of disability like chronic lung disease ,learning disabilities , cerebral palsy, intellectual impairment, visual along with hearing problems and they have a strong chances of developing Non Communicable Diseases(NCD) like hypertension, diabetes and some other crucial health conditions later in life. They are physically not ready to face the world and often require special care [1]. In a systematic analysis and implications, India was given the highest rank with the highest numbers of preterm births in year 2010 with approximately 1 in 8 babies being preterm .In general most preterm births occur after 32 computed weeks of gestation. More than 90% of babies born before 28 weeks of gestation survive in high income countries but in low-income settings, only 10% of these babies or less survive [2]. Current approaches to prevention and treatment of preterm labor have been shown to be disappointingly unsuccessful [3]. Preterm Labor (PL) defined as labor before completing the 37th week of gestation is the main cause of newborn morbidity and mortality[4].On the basis of previous studies it is known that even babies born at 34–37 weeks have an increased risk of immediate complications[5]. Lots of research is going on in this field but we are still unable to diagnose, prevent and treat preterm labor. Checking efficacy of involvements that would allow this is largely influenced by the inability to accurately identify true labor with the currently used crude technology. In the case of progestin treatment for prevention of preterm birth, uterine EMG and cervical LIF are essential tools to obtain the critically needed comparative data on effectiveness of various progestin formulations and their routes of administration in different patients at high risk for preterm delivery .To find an effective prevention and treatment for preterm labor , we must find a method that will allow focusing the treatment only to patients who would, if not treated, really deliver preterm[6] ApEn was developed by Pincus as a measure of regularity to quantify levels of complexity within a time series. The ability to discern levels of complexitywithin biological data sets has become increasingly important.

2. Previous Work:

Steven M. Pincus et al. (1990) proposedtechniques to determine changing system complexity from data . Convergence of a frequently used correlation dimension algorithm to a finite valuedoes not necessarily imply an underlying deterministic model or chaos. Analysis of a recently developed family of formulas and statistics, approximate entropy (ApEn), suggests thatApEn can classify complex systems, given at least 1000 data values in diverse settings that include both deterministic chaotic and stochastic processes. The capability to discern changingcomplexity from such a relatively small amount of data holds promise for applications of ApEn in a variety of contexts.[7]

Joshua S. Richman et al. (2000) have developed a new and related complexity measure, sample entropy (SampEn) and have compared ApEn and SampEn by using them to analyze sets of random numbers with known probabilistic character. They have also evaluated cross-ApEn and cross-SampEn, which use cardiovascular data sets to measure the similarity of two distinct time series. SampEn agreed with theory much more closely than ApEn over a broad range of conditions. The improved accuracy of SampEn statistics should make them useful in the study of experimental clinical cardiovascular and other biological time series. They have developed and characterized SampEn, a new family of statistics measuring complexity and regularity of clinical and experimental time series data and compared it with ApEn, a similar family. SampEn statisticsagree much better than ApEn statistics with theory for random numbers with known probabilistic character over a broad range of operating conditions,maintain relative consistency where ApEn statistics do not, and have residual bias for very short record lengths, in a large part because of non-independence of templates. Furthermore, cross-SampEn is a more consistent measure of joint synchrony of pairs of clinical cardiovascular time series. the difficulties of ApEn analysis to the practice of counting self-matches and of cross-ApEn to the problem of unmatched templates resulting in undefined probabilities is also discussed. The differences are that SampEn does not count templates as matching themselves and does not employ a template-wise strategy for calculating probabilities. SampEn statistics provide an improved evaluation of time series regularity and should be a useful tool in studies of the dynamics of human cardiovascular physiology.[8]

Fele-Zorg et al. (2008)suggested that Sample entropy gives good results. The problem with sample entropy,lies in its extreme susceptibility to the parameter settings. If the matching pattern length, m, is too large, or if the sensitivity margin, r, is too low, within some time signals, no pattern matches can be found. The sample entropy in these cases depends only on the length of the signal and is much higher than usual. The outliers caused by this anomaly also affected the Student’s t-test, producing a low p. To avoid such erroneous results, they limited their search for suitable m and r values to those that were found to be safe while using any of the three preprocessing filters. Noticeable differences were found between the groups of records recorded early and later . The technique indicated a difference between the term and pre-term delivery groups of records. As the time of gestation progresses, the average sample entropy values for term and pre-term delivery records drop indicating higher predictability of the signals as the delivery approaches. The average sample entropy values are lower for both early and later pre-term delivery records and indicate that the signals of pre-term delivery records exhibit higher predictability than the signals of term delivery records.The signal of the pre-term delivery record shows higher predictability than that of the term delivery record.[9]

Molina-Picó et al. (2011) proposed that there is an ongoing research effort devoted to characterize the signal regularity metrics approximate entropy (ApEn) and sample entropy (SampEn) in order to better interpret there results in the context of biomedical signal analysis. Theyaddresses the influence of abnormal spikes (impulses) on ApEn and SampEn measurements. A set of test signals consisting of generic synthetic signals, simulated biomedical signals, and real RR records was created. These test signals were corrupted by randomly generated spikes. ApEn and SampEn were computed for all the signals under different spike probabilities and for 100 realizations. The effect of the presence of spikes on ApEn and SampEn is different for test signals with narrowbandline spectra and test signals that are better modeled as broadband random processes. In thefirst case, the presence of extrinsic spikes in the signal results in an ApEn and SampEn increase. In thesecond case, it results in an entropy decrease. For real RR records, the presence of spikes, often due toQRS detection errors, also results in an entropy decrease.They demonstrated that both ApEn and SampEn are very sensitive to the presence ofspikes. Abnormal spikes should be removed, if possible, from signals before computing ApEn or SampEn.otherwise, the results can lead to misunderstandings or misclassification of the signal regularity. The ApEn and SampEnperformance in the context of biomedical signal analysis andthe influence of spikes is evaluated. Neither ApEn nor SampEn should be sensitiveto spikes, especially if they are infrequent. Theoretically, Biand Ai should be big enough to cope with small variations dueto outliers, that is to say, their relative changes should be verysmall.However, our experimental study demonstrated that spikesdo influence the results of both regularity metrics. Mathematically,this is due to the fact that Bi and Ai are usually smallerthan expected. For instance, in a sinusoidal random process, forBi, although many matches are expected due to signal regularity,matches only account for the 12% of the points approximately (forr = 0.2), and in Gaussian white noise, for ten times less. The sameapplies to Ai, which is even lower than Bi. Thus, any change in thenumber of matches below the threshold r, may have a significantrelative influence on the final result, and therefore, these metricsare sensitive to outliers. Additionally, Ai and Bi can be affected in adifferent scale.It can be seen thatApEn and SampEn are influencedby the presence of spikes, spikes increase the ApEn andSampEn in regular quasiperiodic signals but the opposite happensin the case of irregular broadband random processes and thecapability to discern among types of signals based on features notapparent, seems not to be affected by the presence of spikes, providedall the classes are affected in the same manner and amount. Baseline wandering also influencesthe results of ApEn and SampEn since it reduces the number ofmatches, regardless of the signal regularity, It is very importantto screen the signals before computing ApEn or SampEn in order toassure that abnormal spikes are not present, An improvementfor ApEn or SampEn in the form of algorithm modification or newdistance measure is necessary to obtain robustness against spikes and it may be advisable for researchers to apply spike-removalalgorithms such as rank-order filters prior to the application ofApEn and SampEn in order to prevent erroneous signal regularityresults.[10]

Mahmoud Hassan et al. (2011) havecompared between three nonlinear methods,approximate entropy, correntropy and time reversibility wasdone on linear, nonlinear stationary and nonlinear nonstationarysignals in order to choose the best method to apply on real EHG signals.Indeed these signals are thought to exhibit nonlinear as well asnonstationary characteristics. Detection of nonlinearity should be the first step before any analysis of nonlinearity or nonlinear behaviorin biological signal.For the choice of best method characteristics of the signals under investigation are used to compare three methods widely used in nonlinearity detection: approximate entropy, correntropy and time reversibility.The false alarm rates with the numbers of surrogates for the three methods were computed on linear,nonlinear stationary and nonlinear nonstationary signals. The results indicate the superiority of timereversibility over the other methods for detecting linearity and nonlinearity in different signal types. The application of time reversibility on uterine electromyographic signal showed very good performance inclassifying pregnancy and labor signals. . The evolution of FAR of each methodwas computed with different surrogate numbers. The comparisondemonstrated the superiority of time reversibility in the detectionof linearity and nonlinearity of the different signals.Authors have tested EHG signals for their time reversibility property. Theresults indicate that uterine contractions during pregnancy arereversible, whereas labor contractions are temporally irreversible.They have shown that time reversibility could be a powerful tool todifferentiate between pregnancy and labor contractions.It should be pointed out that this nonlinearity measure, likeother statistical nonlinearity measures, is based on the comparisonwith surrogate data. It is not a standalone measure needing thegeneration of surrogates. Therefore, the measure would fail if thegeneration of proper surrogates fails. Since non-Gaussianity is a characteristic common to both pregnancy and laborsignals,the choice of the time reversibility parameter ismade empirically, in order to obtain the best results on the syntheticsignals and for the classification of pregnancy and laborsignals.It will be important to investigate moreclosely the influence of this parameter on the detection of linearityand nonlinearity for the different synthetic signals.The results on the real data suggest that the property of timeirreversibility is a strong characteristic for contraction measured onwomen in labor. This suggests that, for a more complete characterizationof such recordings, additional nonlinear analysis techniquesshould be applied.The results provide a very powerful method for differentiatingbetween pregnancy and labor contractions. [11]

Jennifer M. Yentes et al. (2012)proposed that Approximate entropy (ApEn) and sample entropy(SampEn) are mathematical algorithms created to measurethe repeatability or predictability within a time series and bothalgorithms are extremely sensitive to their input parameters:m (length of the data segment being compared), r (similaritycriterion), and N (length of data,especially for very short datasets, N £ 200. We suggest using N larger than 200, an m of 2and examine several r values before selecting your parameters. There is no establishedconsensus on parameter selection in short data sets, especiallyfor biological data. They examined the robustness of these two entropyalgorithms by exploring the effect of changing parametervalues on short data sets. Data with known theoreticalentropy qualities as well as experimental data from bothhealthy young and older adults was utilized.Based on their current findings, they proposed that SampEn is more reliablefor short data sets. SampEn was less sensitive to changes indata length and demonstrated fewer problems with relativeconsistency.[12]

PengRen et al. (2015) discussed that preterm delivery increases the risk of infant mortality and morbidity, and therefore developingreliable methods for predicting its likelihood are of great importance.However, to dateattempts at utilizing computational approaches to achieve sufficient predictive confidence,in terms of area under the curve (AUC) values, have not achieved the high discriminationaccuracy that a clinical application requires. They proposed a new analyticalapproach for assessing the risk of preterm delivery using EMG recordings which firstlyemploys Empirical Mode Decomposition (EMD) to obtain their Intrinsic Mode Functions(IMF). Next, the entropy values of both instantaneous amplitude and instantaneous frequencyof the first ten IMF components are computed in order to derive ratios of these twodistinct components as features. Discrimination accuracy of this approach compared tothose proposed previously was then calculated using six differently representative classifiers.Finally, three different electrode positions were analyzed for their prediction accuracy ofpreterm delivery in order to establish which uterine EMG recording location was optimal signaldata. They have shown a clear improvement in prediction accuracy of pretermdelivery risk compared with previous approaches, achieving an impressive maximum AUCvalue of 0.986 when using signals from an electrode positioned below the navel. This provides a promising new method for analyzing uterine EMG signals to permit accurateclinical assessment of preterm delivery risk. In this paper, we have demonstrated that it is possible to improve analysis of uterine EMG recordsto discriminate pregnant women at risk of preterm delivery with sufficient accuracy forpotential clinical purposes. They have classified preterm and term delivery records based on theentropy ratios of the instantaneous amplitude and the instantaneous frequency of each twoIMFs of uterine EMG signals using an EMD approach. Six different classifiers were implementedwhich revealed a mean AUC value of 0.89 and a maximum value of 0.986. A moredetailed analysis of EMG recordings from specific abdominal locations revealed that the positionwith the strongest discrimination accuracy was the one below the navel. The studysuggests that analysis of uterine EMG signals using the above approach is a very accuratemethod for discriminating women at risk of preterm delivery and may be important in clinicaluse.[13]

Massimo Mischi et al. (2017) suggested that preterm birth is a large-scale clinicalproblem involving over 10% infants. Diagnostic means for timelyrisk assessment are lacking and the underlying physiologicalmechanisms unclear. To improve the evaluation of pregnancybefore term, they have introduced dedicated entropy measures derivedfrom a single-channel electrohysterogram (EHG). Theestimation of Approximate Entropy (ApEn) and Sample Entropy(SampEn) is adjusted to monitor variations in the regularity ofsingle-channel EHG recordings, reflecting myoelectrical changesdue to pregnancy progression. In particular, modifications inthe tolerance metrics are introduced for improving robustnessto EHG amplitude fluctuations. An extensive database of 58EHG recordings with 4 monopolar channels in women presentingwith preterm contractions was manually annotated and usedfor validation. The methods were tested for their ability torecognize the onset of labor and the risk of preterm birth.Comparison with the best single-channel methods according tothe literature was performed. Results: The reference methodswere outperformed. SampEn and ApEn produced the best predictionof delivery, although only one channel showed a significantdifference ($p < 0:04$) between labor and non labor. The modifiedApEn produced the best prediction of preterm delivery, showingstatistical significance ($p<0:02$) in 3 channels. The resultswere also confirmed by the area under the receiver operatingcharacteristic curve and 5-fold cross-validation. Conclusion: Theuse of dedicated entropy estimators improves the diagnosticvalue of EHG analysis earlier in pregnancy.The changes in the EHG might manifest earlyin pregnancy, providing relevant prognostic opportunities forpregnancy monitoring by a practical single-channel solution. Entropy measures have been revisited and adjusted with theobjective of achieving noninvasive prediction of delivery anddiagnosis of preterm birth by analysis of single-channel EHGsignals. On an extended database of in-house preterm EHGmeasurements, the estimated ApEn and SampEn have shownthe best prediction of delivery, while the modified ApEn hasshown a clear advantage for early diagnosis of delivery. Theseresults prove the value of EHG entropy analysis as a tool forearly, prognostic evaluation of pregnancy.[14]

3. Conclusion:

The use of dedicated entropy estimators improves the diagnostic value of EHG analysis earlier in pregnancy. The changes in the EHG might manifest early in pregnancy, providing relevant prognostic opportunities for pregnancy monitoring. The value of EHG entropy analysis can be used as a tool for early, prognostic evaluation of pregnancy

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