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Dynamic neural network architecture inspired by the immune algorithm to predict preterm deliveries in pregnant women

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ABSTRACT

There has been some improvement in the treatment of *preterm* infants, which has helped to increase their chance of survival. However, the rate of premature births is still globally increasing. As a result, this group of infants is most at risk of developing severe medical conditions that can affect the respiratory, gastrointestinal, immune, central nervous, auditory and visual systems. There is a strong body of evidence emerging that suggests the analysis of uterine electrical signals, from the abdominal surface (Electrohysterography – EHG), could provide a viable way of diagnosing true labour and even predict *preterm* deliveries. This paper explores this idea further and presents a new dynamic self-organized network immune algorithm that classifies *term* and *preterm* records, using an open dataset containing 300 records (38 *preterm* and 262 *term*). Using the dataset, oversampling and cross validation techniques are evaluated against other similar studies. The proposed approach shows an improvement on existing studies with 89% *sensitivity*, 91% *specificity*, 90% *positive predicted value*, 90% *negative predicted value*, and an overall accuracy of 90%.

1. Introduction

Preterm birth, also known as premature birth or delivery, is described by the World Health Organisation (WHO) as the delivery of babies who are born, alive, before 37 weeks of gestation [1]. In contrast, *term* births are the live delivery of babies after 37 weeks, and before 42 weeks. According to the WHO, worldwide in 2010, *preterm* deliveries accounted for 1 in 10 births [1]. In 2009, in England and Wales, 7% of live births were also *preterm.*[1] *Preterm* birth has a significant adverse effect on the newborn, including an increased risk of death and health defects. The severity of these effects increases the more premature the delivery is. Approximately, 50% of all perinatal deaths are caused by *preterm* delivery [2], with those surviving often suffering from afflictions, caused by the birth. These include impairments to hearing, vision, the lungs, the cardiovascular system and non-communicable diseases. Up to, 40% of survivors of extreme *preterm* delivery can also develop chronic lung disease [3]. In other cases, survivors suffer with neuro-developmental or behavioural defects, including cerebral palsy, motor, learning and cognitive impairments. In addition, *preterm* births also have a detrimental effect on families, the economy, and society. In 2009, the overall cost to the public sector, in England and Wales, was estimated to be nearly £2.95 billion [4]. However, developing a better understanding of preterm deliveries can help to create preventative strategies and thus positively mitigate, or even eradicate, the effects that preterm deliveries have on babies, families, and society and healthcare services.

Preterm births can occur for three different reasons. According to [2] approximately one-third are medically indicated or induced; delivery is brought forward for the best interest of the mother or baby. Another third occurs because the membranes rupture, prior to labour (*PPROM*). Lastly, spontaneous contractions (termed *preterm* labour or *PTL*) can develop. However, there is still a great deal of uncertainty about the level of risk each factor presents, and whether they are causes or effects. Nevertheless, in [2] some of the causes of *preterm* labour, which may or may not end in *preterm* birth, have been discussed. These include infection, over-distension, burst blood vessels, surgical procedures, illnesses and congenital defects of the mother's uterus and cervical weakness. Further studies have also found other risk factors for *PTL/PPROM* [7,8]. These include a previous *preterm* delivery (20%); the last two births have been *preterm* (40%), and multiple births (twin pregnancy carries a 50% risk). Other health and lifestyle factors also include cervical and uterine abnormalities, recurrent antepartum haemorrhage, illnesses and infections, any invasive procedure or surgery, underweight or obese mother,

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[1] (Gestation-specific infant mortality in England and Wales, 2009, http://ons.gov.uk).

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ethnicity, social deprivation, long working hours/late night, alcohol and drug use, and folic acid deficiency.

As well as investigating *preterm* deliveries, several studies have also explored *preterm* labour (the stage that directly precedes the delivery). However, in spite of these studies, there is no internationally agreed definition of *preterm* labour.[2] Nonetheless, in practice, women who experience regular contractions, increased vaginal discharge, pelvic pressure and lower backache tend to show Threatening Preterm Labour (*TPL*). While this is a good measure, Mangham et al., suggest that clinical methods for diagnosing *preterm* labour are insufficient [4]. Following a medical diagnosis of *TPL*, only 50% of all women with *TPL* actually deliver, within seven days [2]. In support of this, McPheeters et al., carried out a similar study that showed 144 out of 234 (61.5%) women diagnosed with *preterm* labour went on to deliver at *term* [5]. This can potentially add significant costs, and unnecessary interventions, to prenatal care. In contrast, false-negative results mean that patients requiring admittance are turned away, but then go on to deliver prematurely [6].

Predicting *preterm* birth and diagnosing *preterm* labour clearly have important consequences, for both health and the economy. However, most efforts have concentrated on mitigating the effects of *preterm* birth. Nevertheless, since this approach remains costly [1], it has been suggested that prevention could yield better results [9]. Effective prediction of *preterm* births could contribute to improving prevention, through appropriate medical and lifestyle interventions. One promising method is the use of Electrohysterography (*EHG*). *EHG* measures electrical activity in the uterus, and is a specific form of electromyography (*EMG*), the measurement of such activity in muscular tissue. Several studies have shown that the *EHG* record may vary from woman to woman, depending on whether she is in true labour or false labour and whether she will deliver *term* or *preterm. EHG* provides a strong basis for objective predication and diagnosis of *preterm* birth.

Many research studies have used *EHG* for prediction or detection of true labour. In contrast, this paper focuses on using *EHG* classification to determine whether delivery will be *preterm* or *term*. This is achieved by using a new neural network posited in this paper which is evaluated against several existing machine-learning classifiers using an open dataset, containing 300 records (38 *preterm* and 262 *term*) [10]. A signal filter and pre-selected features that are suited to classifying *term* and *preterm* records are used to produce a feature set from raw signals and is used by all classifiers. The results show that selected classifiers outperform a number of approaches, used in many other studies.

The structure of the remainder, of this paper is as follows. Section 2 describes the underlying principles of Electrohysterography. Section 3 discusses feature extraction from Electrohysterography signals. Section 4 describes machine learning and its use in *term* and *preterm* classification, while Section 5 describes the approach taken in this paper. Section 6 describes the evaluation, whilst Section 7 discusses the results before the paper is concluded in Section 8.

2. Electrohysterography

Since the late 1930s, information on the electrical activity of the uterus has been known [11]. However, it has only been in the last 20 years that formal techniques, for recording this type of activity, have appeared.

In order to retrieve *EHG* signals, bipolar electrodes are adhered to the abdominal surface. These are spaced at a horizontal, or vertical, distance of 2.5–7 cm apart. Most studies, including [10], use four electrodes although one study utilizes two [12]. In a series of other studies, sixteen electrodes were used [13–18], and a high density grid of 64 small electrodes was used in [19]. The results show that *EHG* may vary from women to women. This is dependent on whether she is in true or false labour, and whether she will deliver at *term*, or prematurely.

A raw *EHG* signal results from the propagation of electrical activity, between cells in the myometrium (the muscular wall of the uterus). This signal measures the potential difference between the electrodes, in a time domain. The electrical signals are not propagated by nerve endings; however, the exact propagation mechanism is not clear [20]. Since the late 70s, one theory suggests that gap junctions are the mechanisms responsible. Nevertheless, more recently it has been suggested that interstitial cells, or stretch receptors, may be the cause of propagation [21]. Gap junctions are groups of proteins that provide channels of low electrical resistance between cells. In most pregnancies, the connections between gap junctions are sparse, although gradually increasing, until the last few days before labour. A specific pacemaker site has not been conclusively identified, although, due to obvious physiological reasons, there may be a generalized propagation direction, from the top to the bottom of the uterus [22].

The electrical signals, in the uterus, are 'commands' to contract. During labour, the position of the bursts, in an *EHG* signal, corresponds roughly with the bursts shown in a tocodynamometer or intrauterine pressure catheter (*IUPC*). Clinical practises use these devices to measure contractions. More surprisingly, distinct contraction-related, electrical uterine activity is present early on in pregnancy, even when a woman is not in true labour. Gondry et al. identified spontaneous contractions from *EHG* records as early as 19 weeks of gestation [23]. The level of activity is said to increase, as the time to deliver nears, but shoots up especially so, in the last three to four days, before delivery [24]. As the gestational period increases, the gradual increase in electrical activity is a manifestation of the body's preparation for the final act of labour and parturition. In preparation for full contractions, which are needed to create the force and synchronicity required for a sustained period of true labour, the body gradually increases the number of electrical connections (gap junctions), between cells. In turn, this produces contractions in training.

Before analysis or classification tasks, *EHG* signals in their raw form, need pre-processing. Pre-processing can include filtering, de-noising, wavelet shrinkage or transformation and automatic detection of bursts. Recently, studies have typically focused on filtering the *EHG* signals to allow a bandpass between 0.05 Hz and 16 Hz [25–29]. However, there are some that have taken filtered *EHG* recordings to as high as 50 Hz [20]. Nevertheless, using *EHG* with such a wide range of frequencies is not the recommended method, since more interference affects the signal.

3. Feature extraction from electrohysterography signals

The collection of raw *EHG* signals is always temporal. However, for analysis and feature extraction purposes, translation, into other domains, is possible. These include a frequency representation, via Fourier Transform, [16,29–31] and wavelet transform [25,28,31–34]. The advantage of frequency-related parameters is that they are less susceptible to signal quality variations, due to electrode placement or the physical characteristics of the subjects [27]. In order to calculate these parameters, a transform from the time domain is required, i.e., using a Fourier Transform of the signal. Still, further transformation is often required before the extraction of frequency parameters. In several studies reviewed, in order to obtain frequency parameters, Power Spectral Density (*PSD*) is used. *Peak*

[2] http://bestpractice.bmj.com/best-practice/monograph/1002/basics.html.