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# Noninvasive *In-Situ* Measurement of Blood Lactate Using Microwave Sensors

A. Mason\*, O. Korostynska, J. Louis, L. E. Cordova-Lopez, B. Abdullah, J. Greene, R. Connell, and J. Hopkins

**Abstract—Goal:** This paper reports a novel electromagnetic sensor technique for real-time noninvasive monitoring of blood lactate in human subjects. **Methods:** The technique was demonstrated on 34 participants who undertook a cycling regime, with rest period before and after, to produce a rising and falling lactate response curve. Sensors attached to the arm and legs of participants gathered spectral data, blood samples were measured using a Lactate Pro V2; temperature and heart rate data was also collected. **Results:** Pointwise mutual information and neural networks are used to produce a predictive model. The model shows a good correlation ( $R = 0.78$ ) between the standard invasive and novel noninvasive electromagnetic wave based blood lactate measurements, with an error of 13.4% in the range of 0–12 mmol/L. **Conclusion:** The work demonstrates that electromagnetic wave sensors are capable of determining blood lactate level without the need for invasive blood sampling. **Significance:** Measurement of blood metabolites, such as blood lactate, in real-time and noninvasively in hospital environments will reduce the risk of infection, increase the frequency of measurement and ensure timely intervention only when necessary. In sports, such tools will enhance training of athletes, and enable more effecting training regimes to be prescribed.

**Index Terms—**Electromagnetic wave, microwave, non-invasive, point of care, sensor, wearable.

## I. INTRODUCTION

LACTATE is key in two fundamental metabolic processes, glycolysis and oxidative phosphorylation, which serve as the basis for energy production in the human body [1]. Glycolysis is the process of converting glucose into the intermediate molecule pyruvate. Oxidative phosphorylation completes the process, in conjunction with oxygen, to form carbon dioxide;

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both processes also result in the production of adenosine triphosphate (ATP) which provides energy for cells to function.

When the body is in a resting and/or healthy non-active state, lactate levels in the blood stream are maintained at a relatively low steady state. According to Andropoulos [2], whole blood lactate should be in the range 0.2–1.7 mmol/L in a healthy patient, with some variation noted based on age. However, when stress is introduced to the body (e.g., via exercise or acute illness) the energy requirements of the body can alter significantly. Typically, glycolysis can accelerate rapidly to meet the new energy demand; however, oxidative phosphorylation does not. This means that the body produces significant amounts of pyruvate, which it must then convert to lactate (via the enzyme lactate dehydrogenase, or LDH) so that glycolysis can continue accelerating and producing both pyruvate and ATP. Once the lactate level in the cells becomes saturated, it will be transported into the blood stream; during acute exercise lactate may exceed 20 mmol/L, as shown by Goodwin *et al* [3] for example. In a healthy person post-exercise, the lactate level will steadily drop back to normal levels, with oxidative phosphorylation being able to clear the excess lactate.

When the stress placed on the body is due to illness, the tendency for the body to accumulate lactate is prolonged, perhaps resulting in lactic acidosis. It is therefore commonplace in contemporary medicine for lactate to be used as a means to evaluate the severity of acute illness, diagnose disease states, predict mortality, and assess response to resuscitation [4]. Furthermore, in sport, lactate is one of the most often measured parameters when performance testing athletes and prescribing exercise intensities [3].

Current off-the-shelf *Point of Care* (PoC) technologies (further detailed in Section II) necessitate a blood sample. While steps have been taken to speed up the process of measurement and analysis, the requirement of extracting blood is still considered a major inconvenience. In a hospital environment, this carries significant infection control risks, and the frequency of sampling is rarely sufficient for clinicians to understand whether intervention is necessary. Leading clinicians at Alder Hey Childrens Hospital (Liverpool, UK) suggest that even if patient blood is sampled and measured 4–6 times per day, as may be the case in intensive care environments, this does not readily enable one to understand if the lactate level is rising (i.e., worsening condition) or falling (i.e., recovery). Furthermore, in cases where the patient is an infant, the amount of blood available is small and so extraction of even 1–3 ml of blood represents a significant

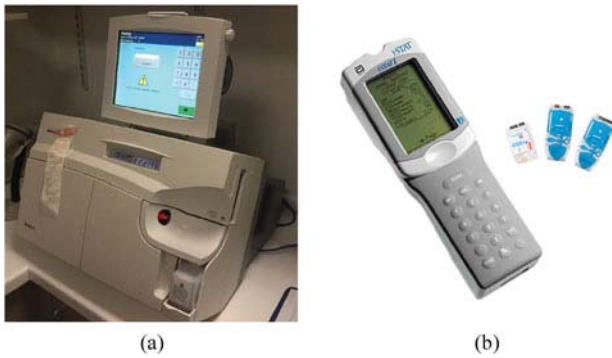


Fig. 1. (a) An example of a Siemens BGA used by the authors, with capacity to measure and predict 24 different parameters based on an input of approx. 0.1 ml of blood, and (b) a handheld Abbott BGA offering a greater level of portability and requiring 65  $\mu$ L blood volume.

percentage of overall blood volume if sampling frequently and leads to considerable stress to the patient.

For athletes, the issue of blood volume is less challenging since they are typically adult and in a good state of health. However, blood sampling is still cumbersome in sport since athletes typically have to reduce exercise intensity (or stop altogether) to provide a measurement which prohibits continuous high resolution monitoring during exercise.

This paper describes the use of a microwave-based sensor for the measurement of lactate non-invasively by simple application to the skin of a subject. The authors have worked in this area for some years [5]–[9] mainly considering in-vitro measurement of lactate and the varying types of microwave-based sensor design depending on specific applications. This work takes a considerable step forward, and shows the potential of in-vivo application of the sensor technology with human participants in a controlled environment.

## II. STATE OF THE ART IN LACTATE MONITORING

In a clinical environment blood gas analysis has become an integral part of patient monitoring, particularly in the case of acute illness (i.e., in emergency wards or intensive care units), with clinical staff relying upon inclusion of blood gas analysers (BGAs) to assist in diagnostic workups and development of treatment plans [10]. A BGA, such as that shown in

Fig. 1(a), can directly measure pH, partial pressure of oxygen ( $PO_2$ ) and carbon dioxide ( $PCO_2$ ), a variety of electrolytes, and various metabolites including glucose, lactate, blood urea nitrogen, and creatinine [11]. Compared with laboratory analysis, a BGA offers rapid measurement time (approx. 1 minute, excluding sampling and transit times) and a wealth of information upon which assessment of patient condition can be made. It is no surprise therefore that the BGA has become the gold standard against which clinicians compare emerging point of care technologies.

Measurement with a BGA is not without its drawbacks however, since the process of extracting blood from a patient is an invasive procedure, with potential complications which include artery occlusion, digital embolisation leading to digital



Fig. 2. Lactate Pro V2 LT-1730 in use by the authors.

ischemia, sepsis, local infection, pseudoaneurysm, hematoma, bleeding, and skin necrosis [12]. As a result of infection risk, resource availability, and patient capacity to provide blood, BGA does not give a high resolution assessment of patient condition over time, which many clinicians argue would provide information relevant to understanding the necessity and form of intervention. Furthermore, the drive toward more point of care monitoring equipment located at the patient bedside has clinicians looking toward smaller and more portable devices. Some attempts to produce portable BGAs, such as the Abbott i-STAT device illustrated in Fig. 1(b), have been commercialised and studies show they give levels of accuracy for lactate comparable with larger desktop systems [13]. However, the required blood volume (65  $\mu$ L), long sampling times (approx. 65 seconds) and skilled handling procedure preclude use at the bedside.

BGAs offer a broad range of measurements, but a number of devices have been released to the market that offer single metabolite measurement. These are typically based on an electrochemical principle, using an electrochemically sensitised strip which, when exposed to blood, changes its electrical properties. When inserted into a device designed to interface with these strips, users are able to obtain a lactate reading within 15–60 seconds. While these devices still require blood to be extracted from a subject, the volume requirement is significantly lower than a BGA—for example the Lactate Pro V2 LT-1730 system (see Fig. 2) used regularly by the authors requires only 5  $\mu$ L of blood.

An in-depth study [14] considered the reliability of such handheld electrochemical devices, concluding that although all devices tested exhibited varying characteristic (error, accuracy), all could be used for longitudinal studies and have particular relevance in prescribing exercise regimes. A smaller study [15] also demonstrated that such electrochemical sensors give acceptable results in clinical settings, and some are approved for medical use, however there is little evidence to show significant uptake in this context. This is perhaps due to uncertainty regarding the unknown sources of error with point of care devices (e.g., temperature, operator training, equipment condition, etc.) when compared with clinical laboratory facilities [16], and the remaining infection control risk due to extraction of blood, albeit in smaller volumes. In addition, some caution against the use of a fingertip test for lactate due to inferior accuracy. Gaiieski *et al.* [17] note that this may not be an issue in all patients,

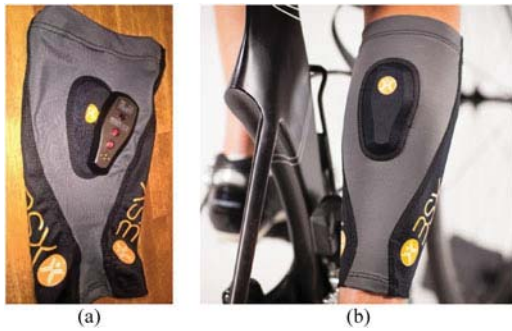


Fig. 3. BSX Insight athlete lactate prediction system, (a) with sensor removed from its wearable sleeve and (b) as worn by a cyclist.

164 but compares the case of those undergoing intensive care with  
 165 those presenting at emergency departments. In the former case,  
 166 patients will be given significant volumes of intravenous fluid  
 167 which, coupled with continued capillary leak and decreased in-  
 168 travascular osmotic pressure, can lead to diffuse tissue oedema  
 169 [18]. In the latter case however, patients are often hypovolemic,  
 170 potentially decreasing the amount of extravascular fluid that  
 171 enters a fingertip blood sample.

172 Devices such as the Lactate Pro and i-STAT represent the  
 173 current state-of-the-art in terms portable point of care systems  
 174 for determining absolute blood lactate, and work continues in  
 175 this field to improve cost, reliability and accuracy. A compre-  
 176 hensive review of electrochemical sensor techniques to realise  
 177 lactate measurement has been produced by Singh *et al* [19],  
 178 and work by other researchers continues to improve this field  
 179 through new fabrication techniques and methods to move toward  
 180 wearables, with researchers utilising sweat rather than blood for  
 181 lactate measurements [20], [21]. The desire for devices to be  
 182 wearable is well known across a range of blood metabolites, to  
 183 remove completely the need for blood extraction and revolu-  
 184 tionise healthcare practices.

185 The options for non-invasive lactate monitoring remain lim-  
 186 ited for practitioners in either healthcare or sports, and perhaps  
 187 the best example to reach the market is the BSX Insight lactate  
 188 prediction system (see Fig. 3). This is a validated [22] wear-  
 189 able system to predict *lactate threshold*, the point at which the  
 190 concentration of blood lactate begins to exponentially increase  
 191 during exercise. This system uses near infrared (NIR) sensors  
 192 to monitor oxygenation in the gastrocnemius muscle and, via  
 193 a patented algorithm, detects inflection points in the muscle  
 194 oxygenation curve at increased workloads.

195 Other optical based techniques for monitoring lactate are ev-  
 196 ident in the literature [23]–[27], however little of that work  
 197 appears to have made a significant presence on the PoC market.  
 198 Largely speaking, these types of devices combine a chemical  
 199 approach (e.g., a colour change) which then infers a lactate con-  
 200 centration. However, these suffer from the same drawback as  
 201 current electrochemical methods, namely the limited reusabil-  
 202 ity of the sensitive elements of the device themselves. Boldt  
 203 [16] demonstrates that costs from such point of care devices  
 204 depend on many factors which can be categorised in terms of  
 205 *pre-analytical*, *analytical* and *post-analytical* costs which may

vary from one organisation to the next thus making the cost  
 benefit difficult to establish.

### III. ELECTROMAGNETIC WAVE SENSORS

A review of the current state of the art reveals that techniques  
 available to practitioners in both clinical and sports contexts  
 present challenges for measuring lactate in real-time. Most  
 systems rely upon the extraction of blood, which presents in-  
 fection risks and is a barrier to providing high-resolution lactate  
 information. Furthermore, the single use model of portable  
 electrochemical PoC devices, such as the Lactate Pro and others  
 described in [14] pose challenges for clinical environments in  
 terms of budgeting and training. While there have been steps  
 to move toward wearable devices, those reported recently in  
 the research domain, particularly for monitoring sweat, have a  
 limited lifespan and therefore present similar issues.

Therefore, the authors have proposed the use of an electro-  
 magnetic (EM) wave sensor system, operating at microwave  
 frequencies, to provide a chemical-free sensor for real-time  
 monitoring of athletes. Although the main aim of the authors  
 has been to develop the system for medical use, it is clear  
 also that the technology has relevance to sport science, namely  
 the monitoring of athletes to ensure applicability of training  
 regimes, as well as to assist in their prescription.

EM wave sensors operating at microwave frequencies are  
 seeing an increasing interest across a variety of applications,  
 including for measurements in the food industry [28]–[31], for  
 water analysis [33], as well as for in-vitro, minimally-invasive  
 [36], [37] and non-invasive [38]–[40] medical purposes. The  
 sensors can typically be characterised as requiring low power  
 (< 1 mW) while retaining a good level of penetration into a  
 target material so that they may assess properties beneath a  
 surface—in this case, determination of blood lactate through the  
 skin of a subject. The sensors are also highly adaptable, with  
 cavities, fluidic channels, flexible and even fabric based devices  
 being demonstrated by researchers. It is these characteristics,  
 combined with their low-cost, that make them an interesting  
 proposition across so many potential application areas.

In this work, measurements from the EM wave sensor (de-  
 scribed in Section IV) are captured in the form of S-parameters  
 for reflected ( $S_{11}$ ) and transmitted ( $S_{21}$ ) energy. As energy is  
 coupled into the sensor, both the  $S_{11}$  and  $S_{21}$  signals vary de-  
 pending upon properties of the analyte presented to the sensor,  
 such as conductivity and permittivity [40]. Conductivity is a  
 measure of a material's ability to conduct an electric current,  
 whereas permittivity is a measure of how an electric field is af-  
 fected by a dielectric medium. This is determined by the ability  
 of a material to polarise in response to the field, and reduce the  
 total electric field inside the material. Therefore, permittivity  
 ( $\epsilon_r$ ) as defined in (1) relates to a material's ability to transmit  
 an electric field and is a complex value which varies with fre-  
 quency, and accounts for both the energy stored by a material  
 ( $\epsilon'$ ) as well as any losses of energy ( $\epsilon''$ ) which might occur.

$$\epsilon_r = \epsilon' + j\epsilon'' \quad (1)$$

258 The permittivity of a material is derived from a number of  
 259 characteristics (e.g., temperature, chemical structure, molecu-  
 260 lar composition, etc.) and is a measure of various polarisation  
 261 phenomena that occur over different frequency ranges when  
 262 exposed to an alternating EM field [41]. This causes dipolar  
 263 polarisation in polar molecules (such as lactate), which causes  
 264 them to rotate over a time period proportional to their dipole  
 265 moment and local conditions (e.g., viscosity). Since there is a  
 266 delay between the dipolar polarisation and the applied alternat-  
 267 ing EM field, dispersions exist whereby the molecule does not  
 268 have sufficient time to fully align to the field, giving rise to di-  
 269 electric relaxation in the microwave region of the EM spectrum.  
 270 A number of mathematical models have been developed by Cole  
 271 and Cole [42], Cole and Davidson [43], [44] and Havriliak and  
 272 Negami [49] to explain relaxation phenomena. It is based upon  
 273 these principles that EM wave sensors, operating at microwave  
 274 frequencies, can selectively detect molecules such as lactate.

#### 275 IV. METHODOLOGY

276 This section of the paper describes the sensor used during  
 277 the work, the testing regime employed using cyclists to test the  
 278 sensor response to lactate levels, and detail regarding placement  
 279 of the sensor itself on participants.

##### 280 A. Test Regime

281 A testing regime was designed to enable the development of a  
 282 lactate profile in participants. The regime was based on the use  
 283 of a Lode Excalibur Sport ergometer, which enables increase  
 284 in pedal resistance up to 1500 W. The protocol adhered to was  
 285 phased as follows:

- 286 1) Begin with a rest period after fitment of sensors and other  
 287 preparation for 5 minutes to enable stabilisation of a base-  
 288 line lactate level;
- 289 2) Warmup for a period of 5 minutes at 80 W, encourag-  
 290 ing participants to maintain a constant cadence (approx.  
 291 70-80 rpm) throughout;
- 292 3) Increment resistance every 2 minutes by 20 W, maintain-  
 293 ing similar cadence, and maintain resistance increment  
 294 regime until cyclist cadence falls below 60 rpm, indicat-  
 295 ing exhaustion.
- 296 4) Conclude with a 10-minute rest period to observe falling  
 297 lactate post-exercise.

298 Throughout this test regime, measurements were taken with  
 299 various devices as follows:

- 300 1) EM wave sensor measurements, comprising an  $S_{11}$  and  
 301  $S_{21}$  spectra, every 30 seconds (see Sections IV-B and  
 302 IV-C for detail of the sensor and placement).
- 303 2) Blood lactate measurements using a Lactate Pro V2 elec-  
 304 trochemical analyser, drawing blood samples from the tip  
 305 of a finger on the left hand. In respect of the test regime,  
 306 measurements were taken at the beginning and end of  
 307 phase 1, the end of phase 2, every minute during phase 3,  
 308 and then every 2 minutes during phase 4. This device was  
 309 chosen not only due to its use in research work noted by  
 310 other authors, but also due to it being one of the only such  
 311 devices with medical approval.

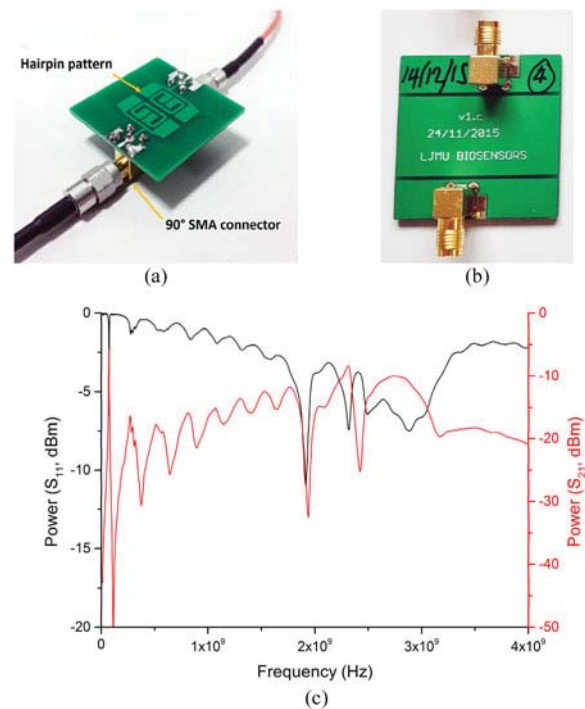


Fig. 4. The (a) top view and (b) bottom view of the physical sensor used in this work, and (c) S-parameter measurements (10 MHz–4 GHz).

- 3) Temperature measurements using a thermocouple taped  
 to the arm and leg of participants.
- 4) Heart rate via a Polar V800 chest strap and watch com-  
 bination.

All data was date and time stamped so that it could be re-  
 spectively synchronised for comparison and analysis. Testing  
 took place between December 2015 and May 2016, with 34  
 participants being recruited for the trial. The majority of the  
 participants were male and aged between 25 and 40; 20% of  
 the test subjects were female. There is no significant difference  
 noted in expected blood lactate levels in these groups [2]. In to-  
 tal, from all participants, 367 lactate measurements were taken  
 using the Lactate Pro V2 device, which acted as the reference  
 method in this study.

##### 326 B. Electromagnetic Wave Sensor

For this work, a so-called *hairpin resonator* configuration  
 of sensor has been designed and constructed as illustrated  
 in Fig. 4(a). The sensor dimensions are 40 mm × 40 mm ×  
 1.6 mm ( $l \times w \times h$ ), with coaxial (SMA) feeds to the decou-  
 pled hairpin conductors.

The sensor is manufactured via a standard etching process,  
 and the substrate is FR4 epoxy glass coated with a biocompat-  
 ible mask that helps to prevent leeching of the copper conductor  
 when worn by test subjects. The SMA connector contacts,  
 shown as exposed in Fig. 4(a) were also masked with insulat-  
 ing tape when in use to prevent direct conductor contact with  
 the skin. The rear of the sensor has a discontinuous ground plane  
 that isolates ports 1 from port 2, as pictured in Fig. 4(b). This  
 is to enable resonance of the device, while also ensuring that

341 the generated EM energy is directed toward the test material  
 342 and providing the hairpin pattern with shielding from outside  
 343 sources of interference.

344 S-parameter measurements for the sensor in air are illustrated  
 345 in Fig. 4(c), showing that the sensor tends to resonate at approx.  
 346 2 GHz. The sensor is designed such that the EM field closely  
 347 coupled to the surface of the sensor, so that the field may pen-  
 348 etrate through the skin of a target and interact with the fluids  
 349 beneath. Maintaining a field close to the sensor surface has some  
 350 advantages, namely that of reducing interference from objects  
 351 other than the surface to which it is directly attached. The hair-  
 352 pin configuration of the device supports this notion well, and  
 353 has the primary reason for its use.

354 Each sensor was connected to a separate Rohde and Schwarz  
 355 ZVL13 Vector Network Analyser (VNA), and  $S_{11}$  and  $S_{21}$   
 356 measurements were recorded every 30 seconds via a bespoke  
 357 LabView interface. The equipment was configured to capture  
 358 data between 10 MHz and 4 GHz, with 4000 discrete data points  
 359 recorded. The equipment was set to output 0 dBm (1 mW)  
 360 power. The system configuration was selected based upon discus-  
 361 sion with the project partners, as well as knowledge obtained  
 362 in prior published (e.g., [5], [6], [8], [39]) and unpublished  
 363 work. Previous work suggested that lactate and similar metabo-  
 364 lites were quantifiable within this selected frequency range,  
 365 although some uncertainty of the precise response frequency  
 366 was present due previous work being ex-situ. From a commer-  
 367 cial perspective, it was desirable to have an upper limit of 4  
 368 GHz to limit unit cost and size of a future “all-in-one” wearable  
 369 solution.

### 370 C. Sensor Placement

371 The sensor was placed on the left arm and leg of each partici-  
 372 pant; the leg due to this being the source of lactic acid production  
 373 during exercise, and the arm due to blood being drawn from the  
 374 finger tip for lactate measurement. Specific placement on the  
 375 leg was over the *Rectus femoris* muscle and on the wrist approx.  
 376 one-third distance between the wrist and elbow joints, where  
 377 there would be significant blood flow owing to the *Arteriove-*  
 378 *nous fistula*. The left side of each participant was chosen simply  
 379 due to accessibility within the testing space itself; the setup is  
 380 shown in Fig. 5(a), with a closer view of the sensors adhered to  
 381 a participant in Fig. 5(b).

382 The sensors were fixed to the participant using 75 mm ×  
 383 100 mm surgical dressings, modified by cutting to allow the  
 384 right-angled SMA connectors to protrude. Cables were secured  
 385 to the limbs of the participant using a surgical tape, primarily  
 386 for mechanical strength. Prior to placement, the sensor and area  
 387 under test was cleansed with an alcohol wipe. No shaving or  
 388 other preparation of the skin was undertaken.

## 389 V. RESULTS AND DISCUSSION

390 With 34 participants and a total of 367 blood lactate mea-  
 391 surements, on average there were 11 blood samples taken per  
 392 participant. Naturally, this varied depending on the fitness level  
 393 of participants, and thus their ability to maintain a steady ca-  
 394 dence despite the increasing work rate. Fig. 6 gives an indicative

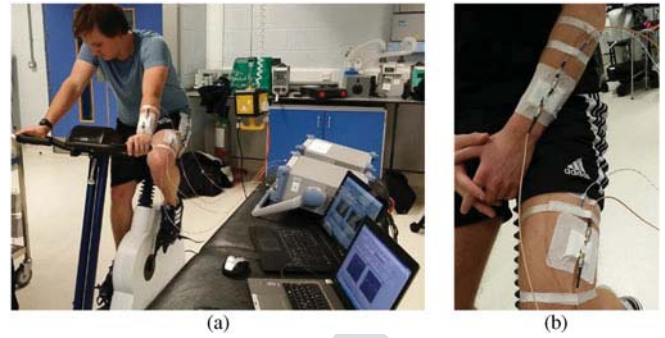


Fig. 5. (a) Experimental setup, with participant on ergometer and sensors attached to data acquisition hardware; (b) illustrates placement of sensors on both arm and leg with another participant.

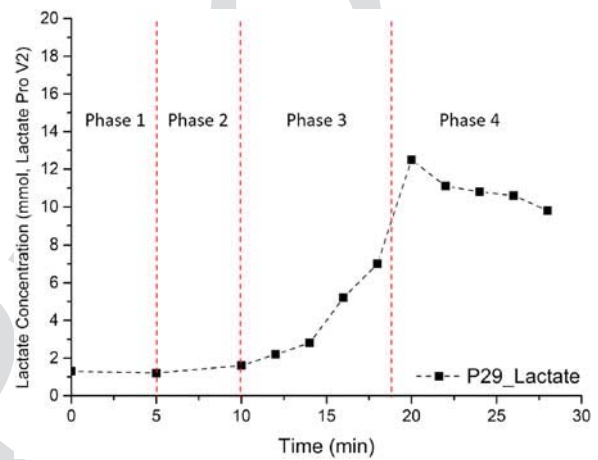


Fig. 6. Illustrating the test regime implemented, as described in Section IV.

lactate profile, with markers denoting the four phases discussed 395  
 in the methodology section. 396

397 Separating the collected data into the groups 0–5 (48.2%),  
 398 6–10 (22.1%), 11–15 (26.3%) and >16 (5.8%) by lactate con-  
 399 centration (in mmol/L) gave an indication of data distribution.  
 400 The majority of data collected is in the range of 0–5 mmol/L,  
 401 with an approximately even split then between the 6–10 and  
 402 11–15 mmol/L groups. This is reasonable given participants  
 403 would spend 5 minutes resting at the beginning and end of the  
 404 resting regime, and a further 5 minutes warming up with little  
 405 exertion (for most) experienced in this period. Few participants  
 406 were able to raise their lactate level above 15 mmol/L, and so  
 407 the data availability > 15 mmol/L for the purposes of creating  
 408 relevant models linking EM sensor output with actual lactate  
 409 level is limited.

410 A number of techniques were considered for providing robust  
 411 analysis and models to test the correlation between EM wave  
 412 sensor outputs and lactate level measured via Lactate Pro V2.  
 413 Typical linear models, which have proven successful for in-vitro  
 414 laboratory based tests (for example, see previous work of the  
 415 authors in this field [5]–[9]) yielded relatively low correlation  
 416 across the complete data set.

417 Therefore, for this work, the authors applied the approach  
 418 of Pointwise Mutual Information (PMI), combined with Neural

419 Networks (NNs). PMI is a useful method for establishing the re-  
 420 lationship between datasets and their supposed target data, and  
 421 producing rankings that indicate the prominence of relation-  
 422 ships. In this work, PMI was used to consider the relationship  
 423 between the lactate value measured with the Lactate Pro V2,  
 424 and the corresponding spectral data captured using the EM wave  
 425 sensor. By doing this, it was possible to rank the spectral data  
 426 by frequency in order of its relevance, and therefore reduce the  
 427 spectral dataset being provided to the NN. This has significance  
 428 for two reasons since: 1) it reduces the amount of irrelevant  
 429 information being provided to the NN, thereby improving the  
 430 likelihood of a suitable model being generated and; 2) it assists  
 431 in the commercial objectives of the work since limiting the fre-  
 432 quency of operation reduces cost, size and power requirements,  
 433 all of which are barriers to implementing a wearable system.

434 A number of reduced datasets were produced using the PMI  
 435 method, based on the top 10, 20, 50, 100, 250 and 500 frequen-  
 436 cies of interest per measurement with the EM sensor, where  
 437 originally data was acquired at 4000 discrete frequencies be-  
 438 tween 10 MHz and 4 GHz. This was replicated for data collected  
 439 from both the arm and leg of each participant, as well as for each  
 440 measurement mode, i.e.,  $S_{11}$  and  $S_{21}$ .

441 The NN approach was applied in Mathworks MatLab soft-  
 442 ware for each dataset. The data was split into a training set  
 443 (225 values, 65%), validation set (75 values, 22%) and test set  
 444 (45 values, 13%). Splitting of the data was performed at random  
 445 and 10-fold cross validation was performed. It is noted that the  
 446 volume of data available for lactate levels exceeding 15 mmol/L  
 447 is limited and so this part of the dataset was excluded from  
 448 this machine learning exercise. Thus, the total number of lactate  
 449 measurements available was reduced from 367 to 345. Results  
 450 corresponding to each mode of measurement (i.e.,  $S_{11}$  or  $S_{21}$ ),  
 451 each location (i.e., arm or leg) and each frequency ranking (i.e.,  
 452 10, 20, 50, 100, 250 and 500) were recorded, and are shown  
 453 in Table I. On average, the best performing measurement was  
 454 achieved with the sensor located on the arm, and with the  $S_{11}$   
 455 mode of measurement; this consistently achieves an  $R_{test} >$   
 456 0.75 once the number of discrete frequencies used for training  
 457 approaches or exceeds 100. Typically speaking, the results pro-  
 458 duced from the NN modelling indicate that once 100 frequencies  
 459 of interest are exceeded, there is a little relative improvement  
 460 in model performance with further increase in the number of  
 461 frequencies—this is evident in the plateau effect for both R and  
 462 RMSE shown in Fig. 7.

463 The measurements conducted on the leg, also in the  $S_{11}$  mode,  
 464 tend to give next best performance, achieving an R-value of ap-  
 465 prox. 0.7 with 100 frequencies of interest fed into the training  
 466 model. It is noted that the error in this case is reported to be  
 467 higher, which is thought to be a result of the sensor (and par-  
 468 ticularly the cables) moving during the exercise, which increase  
 469 noise apparent in the acquired data. A better mechanical fit of  
 470 the sensor to the skin might resolve such issues, as might the  
 471 future integration of the electronics into an all-in-one wearable  
 472 device, which would completely remove the need for cables.

473 Fig. 8(a) illustrates the training model created for the top 100  
 474 ranked frequencies of interest using the  $S_{11}$  arm combina-  
 475 tion, which tended to be most significantly concentrated in the

TABLE I

NEURAL NETWORK TRAINING AND TEST R AND RMSE VALUES FOR EACH MODEL CREATED ACROSS THE MEASUREMENT MODES, LOCATIONS AND NUMBER OF TOP RANKED FREQUENCIES FROM THE INPUT DATASET

No. Freq	Data Type	$S_{11}$ Arm	$S_{21}$ Arm	$S_{11}$ Leg	$S_{21}$ Leg	Ave.
10	$R_{training}$	0.8719	0.7191	0.7669	0.7252	0.7708
	$R_{test}$	0.5543	0.4268	0.5936	0.3682	0.4857
	$RMSE_{training}$	2.0721	2.9301	2.7149	2.9213	2.6596
	$RMSE_{test}$	4.4068	4.1791	3.7223	4.7677	4.2690
20	$R_{training}$	0.8311	0.8897	0.8140	0.7998	0.8337
	$R_{test}$	0.5267	0.2213	0.6107	0.2734	0.4080
	$RMSE_{training}$	2.3543	1.9321	2.4589	2.5413	2.3217
	$RMSE_{test}$	4.775	5.6949	3.7047	5.4118	4.8966
50	$R_{training}$	0.9529	0.8424	0.9245	0.8016	0.8804
	$R_{test}$	0.6456	0.50900	0.7060	0.5160	0.5942
	$RMSE_{training}$	1.2949	2.2721	1.6149	2.5297	1.9279
	$RMSE_{test}$	4.0165	4.0477	3.8603	4.278	4.0506
100	$R_{training}$	0.9653	0.9225	0.8571	0.9469	0.9230
	$R_{test}$	0.7827	0.3274	0.7270	0.2575	0.5237
	$RMSE_{training}$	1.1087	1.6316	2.1857	1.3698	1.5740
	$RMSE_{test}$	2.8786	5.1848	3.081	8.7872	4.9829
250	$R_{training}$	0.9486	0.9607	0.9247	0.9765	0.9526
	$R_{test}$	0.8047	0.4747	0.5700	0.3718	0.5553
	$RMSE_{training}$	1.3589	1.1724	1.625	0.9148	1.2678
	$RMSE_{test}$	2.7426	4.8635	4.6707	5.4387	4.4289
500	$R_{training}$	0.9163	0.9589	0.7968	0.9606	0.9082
	$R_{test}$	0.7632	0.5449	0.6871	0.3945	0.5974
	$RMSE_{training}$	1.7621	1.228	2.5578	1.2061	1.6885
	$RMSE_{test}$	3.242	5.0805	3.2657	5.743	4.3328
Ave.	$R_{training}$	0.9144	0.8822	0.8473	0.8684	-
	$R_{test}$	0.6795	0.4174	0.6491	0.3636	-
	$RMSE_{training}$	1.6585	1.8611	2.1929	1.9138	-
	$RMSE_{test}$	3.6769	4.8418	3.7175	5.7377	-

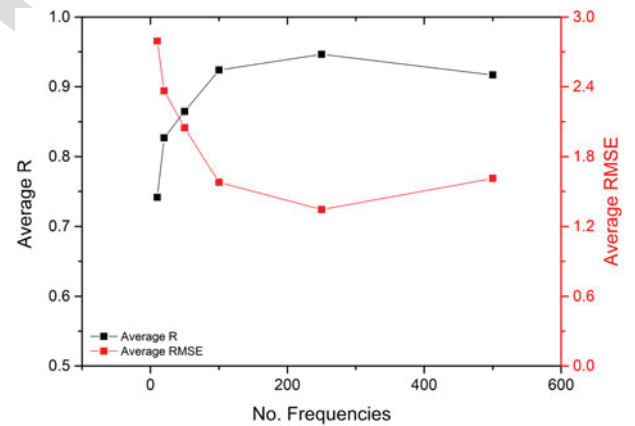


Fig. 7. Average R and RMSE values for all modes of measurement vs. number of frequencies used to create a prediction model.

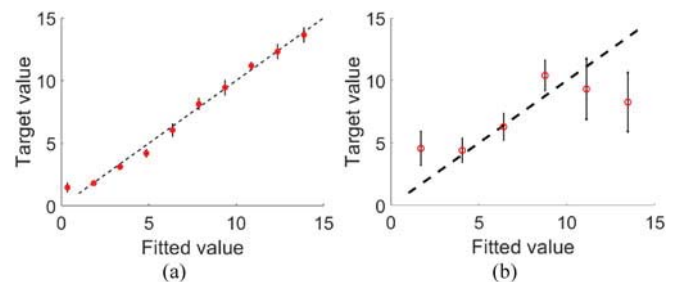


Fig. 8. Correlation for the top 100 frequencies selected via the PMI method for  $S_{11}$  arm; (a) training model and (b) test data fit in the range 0-15 mmol/L

3.4–3.6 GHz region of the measured spectra. It is noted that the RMSE reported for the test data (see Table I) is typically higher than that for the training mode, which is to be expected with NN methods.

The data contained in Table I is relevant for the range 0–15 mmol/L, based upon the categories used to represent the distribution of lactate values collected. The best performing combination of sensor position and measurement mode in this study was the  $S_{11}$  arm combination, which in part is thought to be a result of the arm location having little movement during the experimentation. Using the top 100 ranked frequencies, the training model error is 7.4%, and the test error 19.2% in the range 0–15 mmol/L. However, Fig. 8(b) demonstrates that the NN model does not perform well at lactate levels >12 mmol/L; in the range 0–12 mmol/L the test error is reduced to 13.4%.

It is planned to conduct further trials to augment the current collected data, which it is hoped will reduce the sensor error at higher lactate levels. Trial of the sensor on athletes for example will assist in this, since they will be able to maintain high lactate levels for longer and therefore provide more data in the range >12 mmol/L. Ideally this additional data collection should be coupled with the earlier suggestions regarding improved mechanical fit of the sensor to the skin.

A parallel study, conducted by the authors at Alder Hey Children’s Hospital to assess the expected levels of blood lactate in patients undergoing intensive care, found that only 0.87% of blood samples reported a lactate concentration >12 mmol/L. This was based on 1,000 blood samples taken over a 3 month period and measured using the standard BGA method. This therefore suggests that the sensor, even in its current form, can report clinically relevant information.

A major benefit of real-time on-patient monitoring noted earlier was the potential to be able to monitor live patient information. Current blood sampling does not give enough resolution to understand whether a patient’s lactate level is rising or falling, and therefore deciding on an intervention strategy can be challenging. Thus, being able to track the direction of lactate change is perhaps as important as knowing its absolute value. The capability of the sensor to do this is illustrated in Fig. 9, where all of the collected data from the 34 participants is overlaid with the predicted data from the NN model, trained using 100 discrete frequencies.

Temperature and heart rate were measured in this study to understand if they influenced the sensor output. It is known that temperature is crucial in the use of EM wave devices, particularly due to the resultant change in  $\epsilon_r$  [46]. During this study, it was noted that the average absolute skin temperature variation between the end of phase 1 and beginning of phase 4 was 2.28 °C (min 0.92 °C, max 4.30 °C). It was also noted that the temperature recorded by the thermocouple sensors tended to fall during exercise, most likely due to participant perspiration [47].

Heart rate on the other hand, tended to rise as work output increased from a resting average of 85 bpm to a maximum of 172 bpm. Notably however, whereas heart rate tended to fall almost immediately post-exercise, lactate level would continue to rise due to the latency inherent in lactate metabolism. As a result,

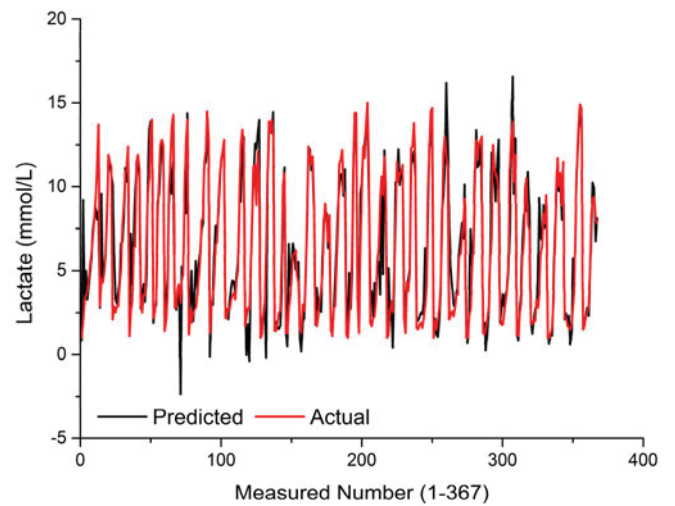


Fig. 9. Actual data measured vs. neural network model, highlighting the capability of the model to predict the lactate profile, not only absolute value.

both temperature and heart rate failed to yield a significant correlation with the EM wave sensor measurements, with  $R < 0.4$  in both cases. This adds further weight to the previously discussed correlation between the EM wave sensor and blood lactate, as it shows that other parameters such as temperature and heart rate do not significantly influence the sensor.

## VI. CONCLUSION

This work has demonstrated the novel application of an EM wave sensor for the non-invasive real-time monitoring of blood lactate, as correlated with the well-known Lactate Pro V2 electrochemical analyser. In total 34 participants, generating a dataset of 367 blood lactate measurements, took part in the study through a static cycling test regime designed to promote a traceable blood lactate profile. Using a PMI method to reduce the necessary dataset acquired from the sensor, and a NN machine learning algorithm to create a predictive model, it was demonstrated that a reliable correlation ( $R = 0.78$ ) could be obtained when the sensor was configured in the  $S_{11}$  measurement mode, and located on the arm of the test subjects. In the range 0–12 mmol/L lactate, the sensor was shown to have an error of 13.4%. In addition, it was demonstrated that this model has relevance in not only predicting absolute lactate values, but also tracking their direction for the purposes of, for example, prescribing patient interventions. Furthermore, it was shown that participant temperature and heart rate did not have a significant influence on the results. This work therefore shows the potential for EM wave sensors as PoC systems. Future work in this area will focus on two areas: (1) the collection of further data to improve the predictive model and; (2) the improvement of the sensor design toward an “all-in-one” wearable solution. The present study has provided useful information in this regard, since the best performance was noted in the  $S_{11}$  measurement mode, and in the range of 3.4–3.6 GHz. This information will enable reduction of the number of cables (and the associated electronics) required for a commercial solution, in addition to focusing ef-



568 forts to enhance the sensor design in the noted frequency range  
569 for improved sensitivity and robustness of measurement, as well  
570 as a reduction in sensor size.

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