

Institution: BRUNEL UNIVERSITY (H0113)
Unit of Assessment: 11 – Computer Science and Informatics
Title of case study: Algorithms to support faster, cheaper and more accurate diagnosis of specific medical conditions
<p>1. Summary of the impact (indicative maximum 100 words)</p> <p>Innovative algorithms to support the evaluation of gold immunochromatographic assays have been applied in a test strip as part of medical devices to test for Down's syndrome and Acute Myocardial Infarction (AMI). The device has been used in China, with a total of over 4500 patients having used it in two city hospitals and in five county hospitals. The impact of the research has been to allow faster, cheaper and more accurate diagnosis. This has led to estimated savings of £10 per patient per test and improved accuracy of 9% across the period 2009-2012, compared to the use of the previously applied tests.</p>
<p>2. Underpinning research (indicative maximum 500 words)</p> <p>In the past few years, the rapid immunochromatographic test strip, also called lateral flow immunoassay (LFIA), has been under especially intensive investigation because of its advantages such as ease of use, short analysis time, low cost, high sensitivity, good specificity, and satisfactory stability when applied to a wide variety of point-of-care (POC) tests. Owing to these attractive properties, the lateral flow immunoassay has been widely used in many fields, including clinical diagnostics, food safety testing, environmental health and safety, agriculture, as well as some emerging areas, such as molecular diagnostics and theranostics.</p> <p>Although the lateral flow immunoassay technology is widely used in a variety of areas, the format suffers from certain shortcomings including that most gold immunochromatographic assays (GICA) can at present only provide qualitative or semi-quantitative results, observed directly with the naked eye, which limits the applications of these assays. For example, the positive or negative result of female human chorionic gonadotropin (hCG) can only indicate pregnancy status, but the quantitative tracking result of serum hCG can provide more useful information in ectopic pregnancy differentiation and in fetal Down syndrome screening tests. Thus, gold immunochromatographic quantitative assay has been paid a great deal of research attention, the outcomes of which will have an important clinical value.</p> <p>During 2009-2012, Prof Zidong Wang and Prof Xiaohui Liu (both at Brunel University across all of the eligible period) conducted collaborative research with Dr Nianyin Zeng, Prof Yurong Li and Prof Min Du of the Fujian Key Laboratory of Medical Instrumentation and Pharmaceutical Technology at Fuzhou University, China, sponsored by an international joint project from the Chinese Science and Technology Ministry. Within the collaboration, the Brunel researchers developed a series of effective algorithms for helping with the quantitative evaluation of the gold immunochromatographic assay based on image processing techniques. Since GICA images directly taken from sensors contain a great deal of non-Gaussian noise that will influence the accuracy of the GICA, significant effort was made by the Brunel team in analysing, modelling and filtering for GICA images (viewed as time-series) by employing a number of the state-of-the-art evolutionary/statistical algorithms in a more robust and more adaptive way. As a result, the Brunel team's research successfully dealt with the technical bottlenecks for GICA quantitative determination, and also improved the measurement results in terms of stability and accuracy.</p> <p>In addition to the developed algorithms, the Brunel team also investigated the algorithms' integration into relevant medical devices used for testing and screening. It is important to note that the R&D issues associated with medical instruments have been largely ignored in China, which has in turn limited the improvement of the performance of such instruments. This is a common problem in China's medical equipment industry. The effective and efficient algorithms developed by the Brunel team have helped to develop/improve specific medical devices used to test for Down's syndrome and Acute Myocardial Infarction (AMI). The devices have been trialled in China with 468 patients having used them in two city hospitals. Furthermore, the devices are being used in five other county hospitals with approximately 1000 patients for each hospital per year and 10 pounds saving per patient per test.</p>

3. References to the research (indicative maximum of six references)

Patent: A detection device of biochemical strips, Invention patent of China, No.ZL 200710008476.X

Registration of computer software: Embedded software V1.0 of the intelligent instruments for gold immunochromatography strip of Fuzhou University, National Copyright Administration of the People's Republic of China, No.: 2010SR012071

N. Zeng, Z. Wang, Y. Li, M. Du, J. Cao and X. Liu, Time series modelling of nano-gold immunochromatographic assay via expectation maximization algorithm, IEEE Transactions on Biomedical Engineering (ISSN 0018-9294) <http://dx.doi.org/10.1109/TBME.2013.2260160>

N. Zeng, Z. Wang, Y. Li, M. Du and X. Liu, A hybrid EKF and switching PSO algorithm for joint state and parameter estimation of lateral flow immunoassay models, IEEE/ACM Transactions on Computational Biology and Bioinformatics, (ISSN 1545-5963) Vol. 9, No. 2, Mar./Apr. 2012, pp. 321-329. <http://dx.doi.org/10.1109/TCBB.2011.140>

N. Zeng, Z. Wang, Y. Li, M. Du and X. Liu, Identification of nonlinear lateral flow immunoassay state-space models via particle filter approach, IEEE Transactions on Nanotechnology, (ISSN 1536-125X) Vol. 11, No. 2, Mar. 2012, pp. 321-327. <http://dx.doi.org/10.1109/TNANO.2011.2171193>

N. Zeng, Z. Wang, Y. Li, M. Du and X. Liu, Inference of nonlinear state-space models for sandwich-type lateral flow immunoassay using extended Kalman filtering, IEEE Transactions on Biomedical Engineering, (ISSN 0018-9294) Vol. 58, No. 7, Jul. 2011, pp. 1959-1966. <http://dx.doi.org/10.1109/TBME.2011.2106502>

4. Details of the impact (indicative maximum 750 words)

The developed quantitative instrument is suitable, among other things, for use in: (i) township, county and community primary hospitals for use in birth defect screening of the large-scale population; and (ii) grass-roots hospitals, the emergency rooms of large hospitals, and by patients' families to conduct the rapid detection and efficacy tracking of Acute Myocardial Infarction (AMI).

The importance of each of the two application areas – screening for birth defects and for detection and tracking of AMI – will now be presented, before the overall impacts of the Brunel research in terms of cost and savings are summarised.

Birth defects screening (see corroborating source [S1]): There are about 26,600 Down's syndrome children born in China every year, resulting in an added social burden of up to 6.5 billion RMB, and tremendous mental anguish for, as well as economic pressure on, many families. Neural tube defect is the most common congenital malformation in China, and it is the most frequently occurring birth defect. There are about 8 to 10 million children born in China with neural tube defects each year, accounting for 1/3 to 1/4 of the world's children with neural tube defects, and representing the highest country-based incidence in the world. The economic burden in China per year of neural tube defects is up to 200 million RMB arising from associated birth qualities that threaten the mental and physical health of affected children and their mothers. The social burden is, however, much higher (estimated at 6.5 billion RMB). As such, this is a serious public health issue. Rapid, early prediction and diagnosis of neural tube birth defects across a wide range of populations will greatly reduce the incidence of birth defects and also have great significance for the social and economic benefits. The impact of the research has been to improve the speed and accuracy of diagnosis in the hospitals across the five Chinese provinces where the medical device which uses the algorithms has been adopted, reducing the economic and alleviating the social burden to parents, families and the provinces involved.

Cardiovascular disease screening (see corroborating source [S1]): Currently, about 17 million people die of cardiovascular disease each year, of which more than half die of AMI. In the past few years, the incidence of AMI has significantly increased and more than 1 million people now die of AMI and its complications each year. However, about 1/3 of patients pass away outside hospital since they have not had the opportunity for timely diagnosis. Thus, early diagnosis and correct

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handling can not only reduce incidences of mortality, but also play a vital role in the future of rehabilitation. According to relevant statistics, two out of three patients have prodromal symptoms a week before the onset of AMI. In these cases, most patients can avoid death by using affordable, convenient and accurate pre-screening offered by simple, cheap, reliable and easily-accessible medical devices instead of the sophisticated and expensive instruments available in hospitals (which are usually accessible only by appointment).

The device developed as a result of the research reported in this impact case offers an improved method to carry out the prediction of *birth defects* and *AMI* via the Brunel team's innovative image processing algorithms. The usage of the device is simple, rapid and inexpensive, which is appropriate for developing countries such as China. Most similar products available in the market are very much related to qualitative and semi-quantitative results, requiring expert interpretation which can be costly and error-prone. The product developed as a result of this research, however, takes the lead in achieving rapid quantitative testing by the improvement of the strip and instrument. Taking into account the high occurrence of AMI as well as China's existing types of hospitals and clinics, even if just 1% of the hospitals in China adopt the product, the impact will continue to grow and be significant. The impact is reflected in the product being approved for sale by the Chinese health authorities and adopted by five Chinese hospitals outside the trial sites, representing penetration into 14% of China's administrative areas.

Before being approved by the Chinese state and adopted by hospitals, we conducted four clinical trials on 448 patients in Fujian Province Hospital and Fuzhou General Hospital in China in 2012 (see corroborating sources [S2,S3]). All trials demonstrated that there was no significant difference between our devices and currently commonly used instruments (e.g., ASCCESS-type automated chemiluminescence analyzer of Beckman Coulter, Inc.). As a result of the trials, the product has been commercialised and is currently used in the following county hospitals in China:

- Tingzhou Hospital, Changting County, Fujian Province.
- Mashan County People's Hospital, Guangxi Province.
- Jinxiang County People's Hospital, Shandong Province.
- Linquan County People's Hospital, Anhui Province.
- Tanghe County People's Hospital, Henan Province.

Conservative estimates are that there are approximately 1000 patients for each hospital per year currently using the device. Based on the current costs for using the traditional instruments and our developed devices, a patient should be able to save at least 100 RMB (approximately £10) per test with improved test accuracy of 9% on previous tests and with faster turnaround times for test results.

5. Sources to corroborate the impact (indicative maximum of 10 references)

[S1] Letter received from Professor from Fujian Key Laboratory of Medical Instrumentation and Pharmaceutical Technology, Fuzhou University, 523 Gong Ye Road, Fuzhou 350002, China (for corroboration on the joint project).

Contactable:

[S2] Doctor at Fujian Province Hospital, China (for corroboration on the clinical trials)

[S3] Doctor at Fuzhou General Hospital, China (for corroboration on the clinical trials)