Institution: University of York

Unit of Assessment: 13, Electrical and Electronic Engineering, Metallurgy and Materials

Title of case study: Automatic Diagnosis and Monitoring of Neurodegenerative Diseases

1. Summary of the impact (indicative maximum 100 words)

Bio-inspired computer algorithms, developed by Dr Stephen Smith at the University of York, have been integrated with commercially available hardware that analyse patients' movements to diagnose and monitor a range of neurodegenerative conditions including Parkinson's disease and Alzheimer's disease. Clinical studies undertaken in the UK and USA report a diagnostic accuracy exceeding 90% - a 15% improvement on current clinical practice. A new spinout company, ClearSky Medical Diagnostics Ltd, has licenced four products exploiting this technology to nine health centres in the UK, USA, Singapore, Australia and UAE, transforming clinical testing with improved diagnosis and monitoring of patients in hospitals and their own homes.

2. Underpinning research (indicative maximum 500 words)

Existing approaches to the diagnosis and monitoring of neurodegenerative (brain) disorders are very subjective, relying on a clinician's measurement against a rating scale and, occasionally, costly brain scans. Research undertaken by Dr Smith seeks to overcome these problems by employing a novel non-invasive task-based approach.

The underpinning research comprises two biologically inspired algorithms: Implicit Context Representation Cartesian Genetic Program (IRCGP) and Artificial Biochemical Networks (ABNs).

IRCGP is an evolutionary algorithm developed in 2005 by Smith (Senior Lecturer in Electronics since 2003). Its advantages over traditional forms of evolutionary algorithms, based around its implicit context representation, have been reported in a series of investigations conducted by Smith's group [1]. The use of these algorithms to reliably diagnose Parkinson's Disease patients demonstrated by Smith in clinical studies undertaken at the Royal Liverpool and Broadgreen Hospitals in 2007 [2-3] and at Leeds General Infirmary in 2011[4], has transformed the conventional clinical "finger-tapping test", revealing microscopic movements in Parkinson's patients that are invisible to the naked eye.

ABNs are a class of computational architectures inspired by the function and organisation of biochemical networks. ABNs were developed at York from 2008-13 as part of the EPSRC AlBiNo project [5] and can be coupled to complex dynamical systems, performing difficult computational behaviors such as control and classification [5]. When combined with IRCGP these algorithms can discriminate between Parkinson's disease patients and age-matched controls with accuracies exceeding 90% - a significant improvement on existing diagnosis of 75% [6].

These biologically inspired algorithms have been integrated with commercially available hardware such as electromagnetic tracking sensors, accelerometers, high performance data gloves and digitizing tablets to record over 100 patients' movements in detail as they perform a variety of conventional clinical tasks. The result is a technology that facilitates measurement of a host of patient groups, including Parkinson's disease, Alzheimer's disease, Progressive Supranuclear Palsy, Multiple System Atrophy and Frontal Temporal Dementia.

This research improves on previous technologies in two important ways:

(i) The biologically inspired algorithms have been trained to differentiate between neurodegenerative conditions with a higher degree of accuracy than can be achieved using traditional signal processing algorithms or conventional clinical evaluation and are less susceptible to variations in patients' motor function ability.

(ii) Integrating low cost, commercially available wireless sensors, permits diagnosis and monitoring to be taken out of the laboratory and into conventional clinical settings such as hospital day clinics and the patient's home, exploiting telemedicine to facilitate reliable and immediate communication.

These advancements have made the technology particularly suitable for use in routine diagnosis and monitoring of patients, the evaluation of new drugs and therapies. It led to the award of a Royal Academy of Engineering Enterprise Fellowship to Smith in April 2013 to launch ClearSky Medical Diagnostics Ltd. and commercialise the technology.

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

[1] "Benefits of Employing an Implicit Context Representation on Hardware Geometry of CGP," X. Cai[1], S. L. Smith[1] and A. M. Tyrrell[1], Lecture Notes in Computer Science. Vol. 3637, 143-154, 2005. *(Available on request)*

[2] "Diagnosis of Parkinson's Disease using Evolutionary Algorithms," S. L. Smith[1], P. Guaghan[1], Q. Du, N. M. Aly[2], J. R., Playfer[2], D. M. Halliday[1], Genetic Programming and Evolvable Machines, Vol.8, 433-447, 2007. DOI: 10.1007/s10710-007-9043-9

[3] "An Immune Network Inspired Evolutionary Algorithm for the Diagnosis of Parkinson's Disease," S. L. Smith[1] and J. Timmis[1], BioSystems, Vol. 94, Nos.1-2, 2008. DOI: 10.1016/j.biosystems.2008.05.024

[4] "How Slow is Too Slow? Objective Measurement of Bradykinesia in Parkinson's Disease using Novel Non-invasive Devices," J. E. Alty[2], D. R. S. Jamieson[2], M. A. Lones[1] and S. L. Smith[1], Proc. Int. Congress on Parkinson's Disease and Movement Disorders, Mov disord 27, Suppl. 1, S91-S92, 2012. *(Available on request)*

[5] "Artificial Biochemical Networks: Evolving Dynamical Systems to Control Dynamical Systems," M. A. Lones[1], L. A. Fuente[1], A. P. Turner[1], L. S. D. Caves[1], S. Stepney[1], S. L. Smith[1] and A. M. Tyrrell[1], IEEE Transactions on Evolutionary Computation, doi: 10.1109/TEVC.2013.2243732, 2013. DOI: 10.1109/tevc.2013.2243732

[6] "Evolving Classifiers to Recognise the Movement Characteristics of Parkinson's Disease Patients," M. A. Lones[1], S. L. Smith[1], J. E. Alty[2], S. Lacy[1], K. L. Possin[2], D. R. S. Jamieson[2] and A. M. Tyrrell[1], IEEE Transactions on Evolutionary Computation, doi:10.1109/TEVC.2013.2281532, 2013. DOI: 10.1109/TEVC.2013.2281532

[1]University of York, [2]Clinical collaborators

J. E. Alty and D. R. S. Jamieson are consultant neurologists at Leeds General infirmary.

N. M. Aly and J. R., Playfer were formerly consultant geriatricians at the Royal Liverpool and Broadgreen Hospitals.

K. L. Possin is a clinical psychologist at the University of California San Francisco Memory and Aging Center.

IEEE Transactions on Evolutionary Computation is the preeminent journal for evolutional computation with an impact factor of 4.81.

The International Congress on Parkinson's Disease and Movement Disorders is the leading medical conference in this area.

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

The biologically inspired computer algorithms, developed by Smith and colleagues at the University of York, have led to the creation of four products for the medical devices market.

PDMD - Objective Diagnosis of Parkinson's Disease

(Protected by patent application PCT/GB12/050093)

This novel non-invasive device, currently installed in hospitals in the UK [7], USA [8,9], UAE [10] and Australia [11], confirms diagnosis of Parkinson's Disease by digitally measuring patients performing a simple finger tapping test used in conventional clinical evaluation. This allows microscopic movements, invisible to the human eye, to be identified that characterise the symptoms of Parkinson's disease

in a way that has not previously been possible.

NDMD - A Unified Test for Neurodegenerative Disorders

(Protected by patent application PCT/GB12/050093)

This technology provides the means by which Parkinson's disease can be differentiated from other neurodegenerative conditions, such as Alzheimer's disease and Lewy Body Dementia, at a stage when symptoms are often confused and a conventional diagnosis is difficult to obtain. The test, which is currently in use in hospitals in the UK [7], USA [8,9] and UAE [10], can be undertaken quickly and safely, providing instantaneous feedback to health staff.

LIDMD - Recognition and Monitoring of Levodopa-induced Dyskinesia

(Protected by patent application PCT/GB13/051888)

This system is being used by Leeds General Infirmary [7] to monitor Parkinson's disease patients in their own homes and inform administration of their medication. The most effective form of treatment for Parkinson's Disease symptoms is a drug called levodopa, but approximately 90% of patients who take it for ten years or more develop severe side effects including involuntary movements called dyskinesia, a major source of disability severely affecting the patient's quality of life. In conventional practice, physicians rely on patients' own descriptions or, in severe cases, patients are admitted to hospital for several days, to monitor symptoms and adjust their medication accordingly. This system provides an objective measure of dyskinesia over extended time periods permitting a better informed course of medication, thereby reducing unplanned hospital admissions, consultations and greatly improving the patient's quality of life.

CFMD - Computer-Assisted Marking of the Benson Figure Test

(Protected by patent application PCT/GB13/051889)

The Benson Figure Test is used throughout the United States to asses decline in visuo-spatial ability, an important symptom of Alzheimer's disease. However, conventional scoring of patients' responses is subjective and therefore lacks sensitivity. Biologically inspired algorithms have been used at the UCSF [8] and VA Medical Centers [9] to analyze the dynamic characteristics of patients' pen movements during the drawing process. This provides additional objective measures that are better able to detect mild impairment than the conventional scoring systems, permitting an earlier and more secure diagnosis.

These products have had significant impacts in the following areas:

i) Routine clinical assessment of neurodegenerative (brain) disorders

Clinical studies at the Royal Liverpool and Broadgreen Hospitals in 2007, Leeds General Infirmary in 2010 (NHRES 08/H0903/36) and 2012 (NHRES 10/H1308/5) demonstrated PDMD improves diagnostic accuracy for Parkinson's Disease from 75% to over 90% [7]. Further studies at the University of California, San Francisco, Memory and Aging Center (UCSF MAC) in 2012 (NIH/NIA K23 AG037566-01A1) [8] and the Veteran's Affairs Medical Center in San Francisco (SFVA) in 2012 (Michael J. Fox Foundation) [9] demonstrated that NDMD can be used to monitor other neurological conditions such as Huntington's disease and Progressive Supranuclear Palsy, "The methods of assessment enabled by this technology are unique and provide an unrivaled means to investigate these conditions" said Dr Schuff, Professor of Radiology, Veterans Affairs Medical Center, San Francisco [9].

In 2013 the technology was licensed for use in additional hospitals worldwide including the Rashid Hospital, Dubai [10], Monash Medical Centre, Melbourne, Australia [11], the University of Washington School of Medicine and the National Neuroscience Institute in Singapore.

ii) Monitoring the effectiveness and side effects of prescribed medication

Following a successful clinical study at Leeds General Infirmary in 2011 and 2012 (NRES 11/NW/0541), the technology is now being used to monitor Parkinson's disease patients in their own homes [7]. Parkinson's UK has estimated savings of £270,000 per year for each specialist nurse employed to oversee home care for patients [12] and introduction of this technology enables these nurses to undertake objective measurements which can be instantly relayed to consultants, freeing up their time whilst maintaining close monitoring of their patients' condition. "For the first time, this technology provides objective, reliable measurements that can be easily assessed by health professionals to inform management of patients with Parkinson's disease. Real benefits, such as reducing specialist consultations, hospital admissions and time spent in hospital can now be realised" says Dr Jamieson, consultant neurologist at Leeds General Infirmary [7].

iii) Commercialization through a spinout company

ClearSky Medical Diagnostics Ltd. [13] is a new (2013) University of York spinout company set up to exploit this technology through four products described above, providing quick, safe and reliable means of diagnosis and monitoring of patients in the hospital clinic and their own homes. Currently employing one full time and five part-time staff, the company is in the process of fully commercialising the products ready for worldwide sale.

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

[7] Dr Stuart Jamieson MA, MBChB, PhD, FRCP - Consultant Neurologist, Leeds General Infirmary, UK.
[8] Dr Katherine L. Possin, Ph.D. - Clinical Psychologist, Memory and Aging Center, University of California San Francisco, USA.
[9] Dr Norbert Schuff, Ph.D. - Professor of Radiology, Veterans Affairs Medical Center, San Francisco, USA.
[10] Dr Yasir Mehmood Malik - Neurologist, Rashid Hospital, Dubai.
[11] Dr Peter Kempster MD, MRCP(UK), FRACP - Consultant Neurologist, Melbourne, Australia.
[12] Parkinson's UK - Parkinson's nurses: a guide for commissioners in England - http://www.parkinsons.org.uk/content/parkinsons-nurses-guide-commissioners-england
[13] ClearSky Medical Diagnostics Ltd. Web Site - www.clearskymd.com