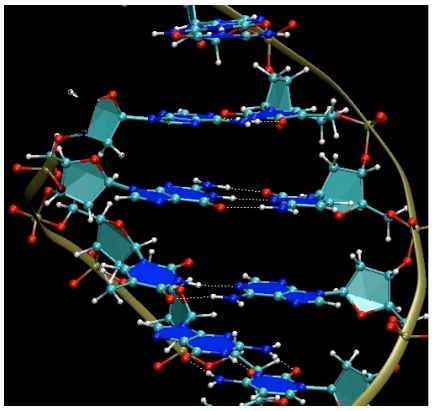
Institution: PHYESTA (Physics at Edinburgh and St Andrews)

Unit of Assessment: UoA 9 - Physics

Title of case study: Novel molecular diagnostics, leading to fast detection of infection biomarkers, creates a new business venture for Mölnlycke Health Care

1. Summary of the impact



Impact: altered business practice / new business venture created
Research into biophysical detection methods undertaken within PHYESTA has resulted in a Gothenburg-based multi-national, Mölnlycke Health Care, establishing a Scottish subsidiary (MHC Scotland) to exploit a commercial (exclusive license) partnership involving PHYESTA and Scottish Enterprise. This represents (i) creation of a new business sector for the company, and (ii) adoption of a new technology into its portfolio.

Significance:
Mölnlycke Health Care has used its access to PHYESTA's IP portfolio, via license arrangements, as the primary vehicle for creating a new business venture enabling its entry into the diagnostics market for the first time.

Reach:
Mölnlycke Health Care is a leading innovator in infection control in hospitals with employees in 30 countries worldwide. Its entry into the diagnostics market has implications for the entire company.

Beneficiaries:
Impact in 2011-2013 pertains primarily to Mölnlycke Health Care and to the Scottish economy.

Attribution: This work was led by Professor Jason Crain, in collaboration with Professor Andrew Mount (Chemistry), Professor Peter Ghazal (Medicine), and Professor Anthony Walton (Engineering).

2. Underpinning research

The underpinning research was highly interdisciplinary involving several research Centres in Edinburgh: the COSMIC research facility (Physics - Crain), Genomic Technology and Informatics (Medical School - Ghazal), the Scottish Microelectronics Centre (SMC - Walton) and the School of Chemistry (Mount). It addressed major limits on detection capabilities of infections in situations relevant to a clinical context. Initial work on novel molecular detection methods included the development and subsequent patenting of a novel class of DNA bio-switches [R1, R2, R3]. These were demonstrated to be highly discriminating sensors of nucleic acids. The devices employ a unique method of molecular recognition in which the optically detected switch characteristics are modified in the presence of an unlabelled target. Subsequent work led to several novel modes of detection and signal amplification in complex biological matrices.

Subsequently the same collaboration developed a method for label-free electrochemical impedance immunosensing and demonstrated application of this method to the detection of infection biomarkers directly from biological matrices [R4]. The results showed that there was sufficient sensitivity for rapid and clinically relevant wound infection detection. A method for label-free, electrochemical impedance immunosensing for the detection and quantification of several infection biomarkers was demonstrated. Triggering of Receptor-1 Expressed on Myeloid cells (TREM-1) and Matrix MetalloPeptidase 9 (MMP-9) were detected via direct assay. Other compounds relevant in bacterial quorum sensing were detected using competition assays.

Detection was achieved in less than 1 hour straight from mock wound fluid without any extensive sample preparation steps. The sensitivity of detection was already near or above the level required for reliable diagnosis of infection. Subsequently, an MRSA (hospital superbug) assay requiring neither labelling nor amplification of target DNA was reported [R5]. Sequence-specific binding of bacterial genomic DNA fragments could be detected at femto-molar concentration using electrochemical impedance spectroscopy (EIS). Observed detection levels fully met the clinical requirements, where the usual definition of an infected wound is 10^5 cells/mL.

Personnel:
Key PHYESTA researchers involved were Professor Jason Crain (1993-present) and Gerard Giraud (PDRA 2009-2011).

3. References to the research

The quality of the underpinning research is best illustrated by R1, R4 and R5. *[Number of citations]*

[R1]	Giraud, G; Schulze, H; Bachmann, TT, Crain J et al., *"Solution state hybridizatio detection using time-resolved fluorescence anisotropy of quantum dot-DNA bioconjugates"* , Chemical Physics Letters **484**, p. 309-314 (2010) DoI: 10.1016/j.cplett.2009.11.032, *[10]*
[R2]	Campbell, CJ; Mountford, CP; Stoquert, HC and J. Crain, *"A DNA nanoswitch incorporating the fluorescent base analogue 2-aminopurine detects single nucleotide mismatches in unlabelled targets",* Analyst **134**, p.1873-1879 (2009) DOI: 10.1039/b900325h, *[2]*
[R3]	Buck, AH; Campbell, CJ; Dickinson, J. Crain et al., *"DNA nanoswitch as a biosensor",* Analytical Chemistry **79,** p. 4724-4728 (2007) DOI: 10.1021/ac070251r, *[14]*
[R4]	Ciani, Ilenia; Schulze, Holger; Corrigan, Damion K.; Crain Jason, et al., *"Development of immunosensors for direct detection of three wound infection biomarkers at point of care using electrochemical impedance spectroscopy",* Biosensors & Bioelectronics **31** p. 413-418 (2012), DOI: 10.1016/j.bios.2011.11.004, *[8]*
[R5]	Corrigan, Damion K.; Schulze, Holger; Henihan, Grace; Crain, Jason et al., "*Impedimetric detection of single-stranded PCR products derived from methicillin resistant Staphylococcus aureus (MRSA) isolates",* Biosensors & Bioelectronics **34**, p.178-184 (2012), DOI: 10.1016/j.bios.2012.01.040, *[3]*

4. Details of the impact

Mölnlycke Health Care is a world-leading manufacturer of wound care products and a major service provider to the healthcare sector. Its annual sales have grown rapidly from EUR 770M in Q4 2007 to EUR 1,120M in 2012 of which approximately 40% derives from its Wound Care Division with the remainder coming from its Surgical Division. Mölnlycke Health Care has sales operations in 30 countries and 7400 employees worldwide. In wound care management, the company has recognised (a) the pressing requirement for the development of rapid and sensitive technologies for portable medical diagnostics, and (b) that disruptive technologies can arise from research at the physical/life science interface. The company's current estimates suggest that automated platforms for chronic wound diagnosis will address a global market opportunity of between £1.4bn and £2.8bn by 2017. In many cases, accurate and rapid diagnosis of wound infection can inform treatment and guide isolation measures. Related to this, bacterial resistance to antibiotics is a public health issue of increasing significance, and there is growing urgency not only for new treatments, but also for improved diagnostics of often-lethal infections such as MRSA (the hospital "super-bug"). Reduced efficacy of antibiotics, and the increasing emergence of resistant strains, present serious problems for the healthcare industry generally. They represent a key target area for Mölnlycke Health Care across its wound-care operations.

Against the backdrop described above, Mölnlycke has, as a matter of priority, sought a route to establishing a competitive presence in the diagnostics market for wound infection to complement and enhance its sector-leading business in wound-care treatments. This has now been made possible as a direct result of underpinning research conducted by the PHYESTA-led team. PHYESTA's research on electrochemical impedance spectroscopy (EIS) has created a particularly attractive and sensitive detection mode which can be readily incorporated into point-of-care platforms. This meets the requirements of Mölnlycke Health Care for a clinically deployable solution with improved performance over existing methods, which is compatible with rapid clinical response in infection control. Demonstrator experiments have illustrated the performance of the methodology for specific biomarkers of interest. The elimination of the PCR (polymerase chain reaction) amplification step, which forms the basis of many biomarker assays but usually takes several hours and/or skilled sample preparation, represents an IP-protected disruptive technology; it is a key aspect of the attractiveness of PHYESTA's diagnostic methodologies to Mölnlycke [F1].

The direct detection by EIS of wound-infection biomarkers emerged as particularly well aligned to Mölnlycke Health Care's core business interests, and was chosen as the primary focus for discussions between PHYESTA researchers, their Edinburgh collaborators, and MHC that were brokered initially by Scottish Enterprise – Scotland's national economic development and investment agency. In August 2011, Scotland's Finance Minister announced the completion of a business partnership with Mölnlycke Health Care whereby the company has taken an exclusive licence to IP from the Edinburgh team's research project portfolio and established a new Scottish subsidiary company: MHC Scotland Ltd. The subsidiary commenced operations on 3rd September 2012 and is located in Building 9 BioQuarter, within Scotland's flagship life science incubator.

The establishment of MHC Scotland, and in particular its role in the fight against MRSA, has generated significant press coverage [S1]. Scottish Enterprise has assisted Mölnlycke Health Care in setting up its facility at the BioQuarter, culminating in the creation of a new Diagnostic Division of MHC which is led from its new Edinburgh subsidiary. The impact in 2011-2013, deriving from the underpinning research, is primarily on Mölnlycke itself and on the Scottish economy, as evidenced by (i) the formation of a significant new business venture and (ii) an alteration of business practice through the adoption of a new technology and the creation of a new Diagnostic Division.

As of 2013, MHC Scotland employs 8 full time staff members. Expansion is expected, and while the direct economic and healthcare impacts will occur only after the current REF period, these developments already establish substantial impact by changing the business plans of a major multinational company. Indeed, Mölnlycke's primary reason for starting inward investment to the UK has been to exploit the results of the PHYESTA-led Edinburgh research team. In a recent press statement [S2] the CEO of Mölnlycke Health Care comments *"We are delighted to be expanding our capabilities and product offering in close collaboration with Scottish Enterprise and the University of Edinburgh. This initiative marks our entry into the diagnostic market. We are very proud to be extending our offering of efficient infection control and prevention solutions that make life easier and safer for health care professionals and patients."*

Formation of MHC Scotland also represents the first (and so far only) international inward investment to the BioQuarter which is an important part of Scottish Enterprise's delivery plan for economic benefit from the life sciences. The Senior Director of Scottish Enterprise, said that [F2]: *"Scotland's life sciences industry contributes over £3 billion a year to the Scottish economy. [It is] our role to ensure that this continues and Scottish Enterprise is committed to encouraging more ambitious life sciences companies at all stages of development, from new spin-out firms to major international corporations to locate at the world-leading Edinburgh BioQuarter."*

5. Sources to corroborate the impact

[F1]	Factual statement by the Managing Director, MHC Scotland Ltd. *Corroborates the claims made in the case study .*
[F2]	Factual statement by the Senior Director Life and Chemical Sciences at Scottish Enterprise. *Corroborates the directness of the link between underpinning research and impact*
[S1]	UK STV News news.stv.tv/east-central/301912-new-mrsa-swab-test-could-allow-detection-of-super-bug-straight-away/ Scottish Development International www.sdi.co.uk/news/2012/12/in-fight-against-superbugs.aspx *Corroborate the media interest in diagnostic tests for MRSA*
[S2]	Mölnlycke Healthcare Press Release www.molnlycke.com/com/About/Media/News--press-releases/Molnlycke-Health-Care-joins-up-with-Scottish-Enterprise-and-University-of-Edinburgh-in-fight-against-superbugs-/ *Corroborates establishment of MHC Scotland with line of sight to underpinning research*