Institution: University of Birmingham

Unit of Assessment: UoA 5, Biological Sciences

Title of case study: Commercialisation of synthetic biology technologies

Period when the underpinning research was undertaken: 2006–2020

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
Professor T. Dafforn	Professor of Biotechnology	December 2003 to present
Dr Matthew Hicks	Postdoctoral Researcher and Chief Technical Officer	August 2009 to October 2015
Professor James Tucker	Professor of Supramolecular Chemistry	July 2005 to present

Period when the claimed impact occurred: January 2014–December 2020

Is this case study continued from a case study submitted in 2014? No

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

Pioneering work by Dafforn and team resulted in numerous **commercially licensed** patents in synthetic biology. **New products** derived from these patents have made **a synthetic biology start-up company viable**, with nearly £2m in investment raised to refine a point-of-care test for sexually transmitted infections. Dafforn's success at commercialising excellent research in synthetic biology led to his appointment and secondment as Entrepreneur in Residence for Synthetic Biology at the Department of Business Innovation and Skills to champion the emerging discipline of synthetic biology. His influence has **impacted on public policy** resulting in **better access to finance opportunities** for synthetic biology start-ups across the country which has raised £1.8bn (starting at £0).

2. Underpinning research (indicative maximum 500 words)

In the last 10 years, synthetic biology has emerged as a discipline which uses an engineering approach to redesign organisms for a range of useful applications.

Dafforn and his team were the first to show that the **emerging discipline of synthetic biology could provide a solution to the problem of detecting infections**. Using synthetic biology, a novel reagent based on a virus (M13 Bacteriophage) was produced that could be specifically modified to generate an optical signal in the presence of that specific pathogen (R1, R2). This approach was applied to *E. coli* (O157) (R3), where the team developed, and patented, a hand-held instrument for such detection (Patent WO/2008/059280: Granted 2008) which was subsequently licensed by the University of Birmingham in 2012.

Based on this early scientific success, the team used the technology to assist in the **rapid and early detection of the sexually transmitted infections** (STIs) chlamydia and gonorrhoea. Together, these two infections are responsible for >50% of STIs in the UK. Dafforn and his team showed that organic dyes could be used to provide unique signals for each pathogen in the same test, which allowed both chlamydia and gonorrhoea to be investigated at the same time resulting in none, one or both pathogens detected (R4).

Regulators require that gonorrhoea and chlamydia tests have the specific capability of detecting DNA directly from the pathogen. This was achieved by developing a method that linked the pathogen DNA to the viral scaffold thereby allowing its direct detection (R5). It was also demonstrated that **polymerase chain reaction (PCR) could be used to increase the sensitivity** of the test. Initially the test took >30 minutes to produce a result, but Dafforn and his team

overcame this with a new patented method using a DNA amplification system (EXPAR) to reduce the **time to result to <5 minutes**. This improvement meant that the direct DNA test fitted within the requirements for point-of-care testing in the NHS**.**

Key Findings:

KF1. Organic dyes can be used to provide unique signals for different infection tests in the same system, meaning that a range of infections can be detected at the same time. Patent filed 2015, Granted 2019 (EP3149451B1)

KF2. Direct detection of DNA from pathogens can be achieved using viral scaffolding and the sensitivity of tests increased by using PCR. Patent filed 2015, Granted 2019 (US10329599B2)

KF3. The use of an EXPAR DNA amplification system can reduce time to result to <5 minutes. Patent Filed 2019 (PB158379GB).

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

R1. Hicks, M.R., Rodger, A., Thomas, C.M., Batt, S.M., Dafforn, T.R. (2006) . *Biochemistry*. 45(29): 8912–7. DOI: 10.1021/bi0601712

R2. Dicko, C., Hicks, M.R., Dafforn, T.R., Vollrath, F., Rodger, A., Hoffmann, S.V. (2008) Breaking the 200 nm limit for routine flow linear dichroism measurements using UV synchrotron radiation. *Biophysical Journal.* 95(12): 5974–7. DOI: 10.1529/biophysj.108.139964

R3. Pacheco-Gómez, R., Kraemer, J., Stokoe, S., England, H.J., Penn, C.W., Stanley, E., Rodger, A., Ward, J., Hicks, M.R., Dafforn, T.R. (2012) Detection of pathogenic bacteria using a homogeneous immunoassay based on shear alignment of virus particles and linear dichroism. *Analytical Chemistry.* 84(1): 91–7. DOI: 10.1021/ac201544h

R4. Tridgett, M., Lloyd, J.R., Kennefick, J., Moore-Kelly, C., Dafforn, T.R. (2018) Mutation of M13 Bacteriophage Major Coat Protein for Increased Conjugation to Exogenous Compounds. *Bioconjugate Chemistry.* 29(6): 1872–1875 DOI: 10.1021/acs.bioconjchem.8b00307

R5. Carr-Smith, J., Pacheco-Gómez, R., Little, H.A., Hicks, M.R., Sandhu, S., Steinke, N., Smith, D.J., Rodger, A., Goodchild, S.A., Lukaszewski, R.A., Tucker, J.H., Dafforn, T.R. (2015) Polymerase Chain Reaction on a Viral Nanoparticle. *ACS Synthetic Biology.* 4(12): 1316–25. DOI: 10.1021/acssynbio.5b00034

R6: Reverse Transcriptase free detection Patent (PB158379GB)

Research Grants:

T. Dafforn (01/03/11–29/02/12) Enhanced detection of drugs of abuse using linear dichroism and high extinction dyes. EPSRC (And Sirigen Ltd). £104,736

J. Tucker (16/03/09–31/03/14) Functional DNA-based assemblies. EPSRC. £1,727,391

T. Dafforn (17/11/08–16/11/09) Rapid and simple clinical assays using nanoscale phage-based detectors and linear dichroism spectroscopy. BBSRC. £102,376

T. Dafforn (01/08/2012–31/07/2013) A homogenous bimodal (immuno/PCR) pathogen detection system based on a bio-nanoparticle. BBSRC. £119,898

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

Dafforn and his team have pioneered a body of work on synthetic biology which has led to two key impacts: first, commercial impact, by attracting significant **venture capital investment** into an ailing start-up company. Second, Dafforn's reputation as a synthetic biologist producing commercially important results led to his appointment to champion the sector to policy-makers. This has resulted in increased recognition of the importance of synthetic biology and a transformation in funding streams which laid the foundations for **better access to finance opportunities** for the sector nationally.

Transforming the viability of an existing business through the design and delivery of new products

Dafforn's patented approaches (KF1, KF2 and KF3) featured in a series of **exclusive licensing deals** with a Biotech SME Linear Diagnostics Ltd (LDL) in order to **significantly diversify its commercial product offering** by entering into the STI market**.** The licensing agreements have proved to be a crucial lifeline for the company, **transforming the viability of the business by attracting two rounds of significant investment funding**:

1. The rapid DNA detection highlighted in KF1 and KF2 unlocked £400,000 for LDL, including £200,000 from Venture Capitalists I2S whose "investment in Linear Diagnostics is substantially based on [the] technical developments made by Professor Dafforn" (S2).
2. The reduced turnaround time for an STI point-of-care test (KF3) resulted in an additional £560,000 for LDL. The new assay capability "significantly changed our view of the market opportunity for the company and therefore it's suitability as an investment proposition." (S3)

Brendan Farrell, the CEO of Linear Diagnostics testified to the importance of the advances made in synthetic biology by Dafforn to the business:

> [the] Global exclusive licensing agreement with the university […] formed the foundations for a funding round that raised £2million and allowed us to increase the size of the research team at LDL. I would say that the inclusion of the technical development from Professor Dafforn was a key element for our success in this investment round and is certainly responsible for LDL still being a going concern today. (S1)

Taken together, the investments have enabled LDL to enter into a period of **unparallelled growth, stimulating foreign investment** from Denka-Seika Ltd, Japan, to develop a new test for Chlamydia (S4). This, along with a further £300,000 leveraged from Innovate UK, has led to the **creation of four new jobs** at the company. Two of these staff were co-opted from the University of Birmingham further underlining the continued collaboration with the University.

Impacts on public policy by influencing investment decisions

In 2013, the Government identified synthetic biology to be one of the country's "8 great technologies" and started to mobilise significant financial resource to support its growth as a sector. As a result of his body of scientific work in synthetic biology (e.g. R1, R2 and R3) and his track record in commercialising research, Dafforn was **appointed to two significant Government advisory committees**. In 2015, he became Entrepreneur in Residence for Synthetic Biology at the Department of Business Innovation and Skills (BIS) as well as a member of the UK Synthetic Biology Leadership Council. Dafforn used his positions to champion the sector and to enable policy-makers to recognise the importance of the sector to the UK and to support it going forward.

During his tenure at BIS, Dafforn was commissioned by the Minister of Life Sciences (George Freeman MP) to co-author the UK's second Synthetic Biology Roadmap (S5). The roadmap focused on infrastructure requirements for **accelerating commercialisation investment in synthetic biology** in all guises from bio-nanodesign applied to individual biomolecules through to synthetic biology approaches to engineering whole organisms (e.g. genetic modification). The contribution of Dafforn was attested by the Co-Chairman of the UK Engineering Biology Leadership Council:

> Your work in commercialising your Synthetic Biology research provided a unique insight into the challenges of translating this form of science. […] The Roadmap had significant impact on the UK Synthetic Biology Sector, with more than 150 synthetic biology start-ups now established in the UK, the top seventy of which attracting over £1.8bn private investment to mid 2019. […]. I would say that your work has had a significant impact on the development and growth of the Synthetic Biology sector in the UK. (S6)

Further underpinning the roadmap was "the development of a new national programme for engineering biology that links academia, industry and defence, from basic research to translation." (S7). Dafforn "played a significant role in the task initiation group which brought together the Chief

Executive of BBSRC, Chief Scientific Advisor of MoD and Head of Research at DSTL who agreed to a combined effort to support synthetic biology in the UK in the future." (S7)

As an additional example of the broad and far-reaching nature of his work, Dafforn was invited to give oral evidence to the House of Lords, Science Select Committee Genetically Modified Insects Enquiry on the scale and quality of basic research and commercialisation in this area. Dafforn "clearly helped to ensure regulation was proportionate in the UK ensuring that this industry continues within the UK" (S6), leading the Committee to recommend:

> investment in infrastructure and the skills pipeline must at least be preserved, and preferably enhanced, in order to maintain the UK's position as a world-leader in GM insect technology development. (S8)

Overall, the routes to market for synthetic biology technology are long and arduous, but the transformative impact for the UK of Dafforn's contributions is already evident in current investments and will become increasingly significant as synthetic biology technologies continue to mature. As stated by the Co-Chair of the UK Engineering (synthetic) Biology Leadership Council:

> [Dafforn has] played a significant role in helping shape our direction of progress and in establishing the UK's current global standing in synthetic biology and prospects for engineering biology innovation in years to come. (S6)

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

S1. Testimonial from the CEO of Linear Diagnostics Ltd [Dated 22 October 2020]

S2. Testimonial from I2S fund manager

S3. Testimonial from the Director of Midven

S4. Contract with Denka-Seika

S5. Biodesign for the Economy – UK Synthetic Biology Strategic Plan 2016, Synthetic Biology Leadership Council [Published December 2015]

S6. Testimonial from the Co-Chair of the UK Engineering (synthetic) Biology Leadership Council [Dated 21 December 2020]

S7. Testimonial from the Synthetic Biology lead at DSTL [Dated 16 December 2020]

S8. Science and Technology Select Committee, *Genetically Modified Insects*, 17 December 2015, HL 68, 2015-16.