Institution: University of Birmingham		
Unit of Assessment: UoA 9, Physics		
Title of case study: Positron Emission Particle Tracking (PEPT) transforms manufacturing process design and operation		
Period when the underpinning research was undertaken: 2000–2016		
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:**
Prof. David J. Parker	Professor of Physics	1989–present
Prof. Jonathan P. K. Seville	Professor of Formulation Engineering	1994–2008; 2017–present
Dr Andrew Ingram	Senior Lecturer in Chemical Engineering	2000–present
Dr Thomas Leadbeater	Research Fellow in Physics	2000–2015
Dr Xianfeng Fan	Research Fellow in Physics	2001–2009
Dr Zhufang Yang	Research Fellow in Physics	2004–2008
Period when the claimed impact occurred: 1 August 2013–present		
Is this case study continued from a case study submitted in 2014? Yes		

1. Summary of the impact

Positron emission particle tracking (PEPT) — conceived and developed at the University of Birmingham — has been used to investigate, **redesign and improve manufacturing processes and technology** at over 20 leading international companies. This impact on **production** and on **commerce and the economy** led to **gains in productivity because of research-led changes in practice, improved products, more efficient processes and less waste**. PEPT has reduced energy use and production time in the manufacture of [text removed for publication]. It has improved design for pharmaceutical manufacturing equipment that has been adopted by global companies (GSK, Pfizer, AstraZeneca). This led to £100M in sales for GEA Pharma Systems and to reductions in the environmental footprint of pharmaceutical production. PEPT also enabled new and improved catalyst production processes, driving new sales and projects worth over £300M at Johnson Matthey.

2. Underpinning research

Background

Most continuous industrial manufacturing processes involve the **flow** of materials, examples being the production of chemicals, pharmaceuticals, home and personal care products, and food. However, such materials are typically opaque and real processes take place within the walls of vessels or pipes. Understanding and improving these processes therefore requires a measuring technique which can 'see inside' opaque materials and map their flow behaviour. Conceived by Parker and colleagues at Birmingham's interdisciplinary Positron Imaging Centre in the 1990s, Positron Emission Particle Tracking (PEPT) is a tool for studying the fundamentals of flow in physics and engineering. **PEPT is the most — and frequently *only* — effective way to follow motion in opaque systems**, particularly within metal-walled vessels.

Since 2001, PEPT at Birmingham has been funded by the EPSRC (notably three successive Platform Grants 1998–2014 and a Programme Grant running until 2024) and by industry. It is a novel adaptation of the medical imaging technique positron emission tomography (PET). Both rely on detecting the pairs of back-to-back gamma-rays emitted during positron/electron annihilation as a first step in locating a positron-emitting radioactive tracer. Whereas in PET the concentration of a radioactively labelled fluid tracer is mapped in 3D, in PEPT a single radioactively labelled particle is accurately tracked at high speed — making the technique suitable for studying high-speed flows (1–10 m/s). PEPT can be used to study flow in granular material (labelling and tracking a single grain) or fluid flow (using a neutrally buoyant tracer particle). Because gamma-rays are highly penetrating, measurements can be made through metallic walls (up to ~5cm thickness of steel, for example). This **enables non-invasive studies to be performed on realistic engineering systems under pressure and/or temperature, and brings a wide range of industrial processes within investigative reach**.

Key findings

PEPT is an innovation in measurement that was initially limited in application by the nature of both the hardware and analysis techniques. Improvements since 2000 — particularly the reduced size of the tracer particle and the adaption of the detector array to the process of interest — have enabled many more industrial processes to be studied. Significant developments in research underpinning PEPT since 2000 include:

- **KF1.** Developing and commissioning a new positron camera, for which we have **demonstrated 20x increase in sensitivity** (R1) widening the range of the industrial processes which can be studied.
- **KF2.** Increasing the range of tracer types and **reducing the minimum size of the tracer entity which can be tracked by an order of magnitude** (from 500μm to 50μm; R2), in keeping with the need to use a tracer which is identical, or closely similar to, the material of interest. This again widens the range of application, particularly in the manufacture of consumer goods such as detergent powders and pharmaceuticals.
- **KF3.** Improving and extending the range of detector arrays which can be used; constructing transportable **modular cameras with flexible geometries**, allowing application of PEPT on larger systems and investigation of **industrial equipment *in situ*** (R3, R4).

These underpinning improvements in measurement capability have been augmented by developments in analysis techniques which have been successfully applied to the investigation of flow processes in industrial equipment:

- **KF4.** Complex processes, such as agglomeration, can now be followed by **substantially better tracking and extraction of information from the data** (R5).
- **KF5.** Constructing **techniques to allow the use of PEPT trajectories for the determination of dispersion in mixing** and rates of shear in three dimensions (R6; fig. 1).

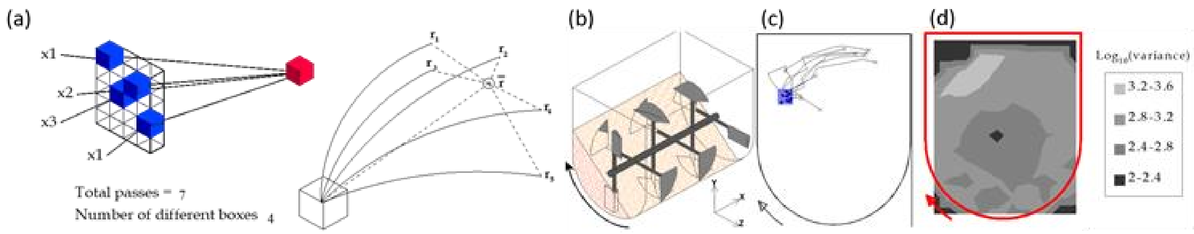

Fig. 1. (a) Measuring the dispersion of a series of particles originating from the same point (or, in the case of PEPT, the same voxel). (b) Schematic diagram of a bladed mixer imaged using PEPT. (c) A series of individual PEPT tracks within the mixer originating from the same voxel. (d) Spatial distribution of the mixing intensity.

3. References to the research

R1. D. J. Parker, R. N. Forster, P. Fowles and P. S. Takhar, Positron emission particle tracking using the new Birmingham positron camera, *Nuclear Instruments and Methods in Physics Research* A477 (2002) 540–545. DOI: 10.1016/S268-9002(01)01919-2.

R2. X. Fan, D. J. Parker and M. D. Smith, Enhancing F-18 uptake in a single particle for positron emission particle tracking through modification of solid surface chemistry, *Nuclear Instruments and Methods in Physics Research* A558 (2006) 542–546. DOI: 10.1016/j.nima.2005.12.186.

R3. T. W. Leadbeater and D. J. Parker, A modular positron camera for the study of industrial processes, *Nuclear Instruments and Methods in Physics Research* A652 (2011) 646–649. DOI: 10.1016/j.nima.2010.08.085.

R4. A. Ingram, M. Hausard, X. Fan, D. J. Parker, J. P. K. Seville, N. Finn, R. Kilvington and M. Evans, Portable positron emission particle tracking (PEPT) for industrial scale use, in *Fluidization XII*, F. Berruti, X. Bi, and T. Pugsley (eds.), Engineering Conferences International (2007) 497–504.

R5. Z. Yang, P. Fryer, S. Bakalis, X. Fan, D. J. Parker and J. Seville. An improved algorithm for tracking multiple, freely moving particles in a positron emission particle tracking system. *Nuclear Instruments and Methods in Physics Research* A577 (2007) 585–94. DOI: 10.1016/j.nima.2007.01.089.

R6. T. W. Martin, J. P. K. Seville and D. J. Parker. A general method for quantifying dispersion in multiscale systems using trajectory analysis. *Chemical Engineering Science* 62 (2007) 3419–3428. DOI: 10.1016/j.ces.2007.02.050.

4. Details of the impact

Over 20 industrial companies globally (from multinationals to SMEs), across a wide range of industry sectors, including oil and chemical, pharmaceuticals, minerals, and home and personal care, have adopted PEPT. We focus on three examples, [text removed for publication], GEA Pharma Systems and Johnson Matthey (JM).

[text removed for publication]

2. Pharma companies have adopted a new manufacturing technology, with considerable savings

PEPT enabled **improved machine design and the development of a new tablet manufacturing process**, ConsiGma, produced by GEA Pharma Systems [S3; KF4 and KF5]. Most pharmaceuticals are sold as tablets manufactured using a process called wet granulation, in which particles of the active drug substance are combined with other components to form free-flowing granules which can be fed to a tablet press. Using PEPT, GEA developed ConsiGma as a radically different continuous granulation system consisting of a twin-screw powder conveyor to which a binding liquid is added and in which screw elements perform different functions in the granulation process. GEA confirmed that this process is a more effective and efficient method stating, “in addition to the advantages of better process control and enclosed operation, adoption of ConsiGma results on average in a 40% reduction in labour costs, 60% reduction in manufacturing space compared with current industry standards and 50% energy savings resulting from reduced power requirement and heat recovery” [S3].

In 2012, GEA sold the ConsiGma continuous production line to GlaxoSmithKline (GSK), as an experimental tablet manufacturing process for its plant at Ware. This was the first of over 50 installations around the world at an average sale price of £2M each. GSK, Pfizer and AstraZeneca have all adopted the technology. The VP of GSK highlighted “some of the fantastic benefits and savings that GSK has experienced since investing in the GEA ConsiGma continuous tableting line. Savings included an 85% reduction in the amount of API [active pharmaceutical ingredient] that would normally have been used [. . .], and being able to carry out 90 experiments in one day, which would normally have taken between 3–6 months with conventional batch based development!” [S4]. Total sales of ConsiGma are in excess of £100M to date [S3]. ConsiGma is now used globally to manufacture drugs for a range of treatments including Cystic Fibrosis (Orkambi and Symdeko from Vertex Pharmaceuticals) and Acute Myeloid Leukaemia (Daurisimo, Pfizer Inc.), “with consequent benefits to the health of thousands of patients” [S3].

This new technology has **environmental benefits** as it replaces traditional discrete batch operations (typically crystallisation, milling, mixing, granulation, drying and tableting) — “all of which involve significant risk of failure, as well as environmental cost and risk of personal exposure to the active drug” [S3]. In contrast, ConsiGma produces “fast, continuous operation in enclosed machines with a high degree of automatic monitoring and control, a smaller physical footprint and a reduced environmental burden” [S3].

3. Enhancing JM’s business performance by creating new and improved products

PEPT has been used in developing new **products and processes** with JM, a world-leading catalytic materials technology company with annual sales of £4.2B, in four key areas.

- PEPT **enabled improvements in the design and operation of the multiphase catalytic reactors** operated by JM’s customers in the fine chemicals and pharmaceutical industries [KF1–KF5]. This enhanced the company’s technical support for its customers and generated new sales. JM’s Scientific Consultant (lead chemical engineer) confirmed that “learning and data derived from PEPT were widely used internally, to coach technical sales personnel” and that “retained and new sales were directly attributed to the PEPT data-based service” [S5].
- Models are being used to design two major capital projects worth in excess of £300M, which rely on the improvements in modelling and scale-up of precipitation processes based on KF4 and KF5. PEPT’s work “allowed Johnson Matthey to provide improved guidelines for precipitator design, resulting in product improvements or, in one case through design improvement, allowing introduction of a new product that could otherwise not have been manufactured at scale” [S5]. In addition, the PEPT data were used to validate a reduced order Zonal Model, which is much simpler to use than computational fluid dynamics models. This “formed the basis for several new product precipitations from pilot to production scale. Without the PEPT data, JM would not have had the confidence to use these models” [S5].
- PEPT informed operational problem diagnosis and validation of models and measurement techniques in blending of precursors for vehicle Emission Control catalysts (a £2.5B sales generator for JM [S5]), based on KF4 and KF5. JM confirmed that “[t]he combined output of the PEPT study enabled a step change in the process analysis and design of washcoat and ink manufacture in JM” [S5]. It has been applied to the manufacture of inks for fuel cells and automotive glazes “to improve manufacturing performance globally and led to significant improvements” [S5].

PEPT data [KF4 and KF5] were used to validate models for processing of particulate products. Discrete Element Method (DEM) modelling is a key company capability now deployed in support of several critical manufacturing process development projects: “JM is currently using DEM as a key development and design tool for key future manufacturing technologies, and has the confidence to do so in large part due to the validation data obtained using PEPT” [S5].

5. Sources to corroborate the impact

[text removed for publication]
S3. Testimony from the Head of Technology Management, Pharma Solids, GEA (dated 18 December 2020).
S4. ‘Continuous manufacturing continues to make inroads in improving tablet manufacturing efficiency’, *S3 Process website* [accessed 7 January 2021].
S5**.** Testimony from Scientific Consultant, Johnson Matthey (dated 22 December 2020).