The University of Nottingham

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Sustainable Chemical and Biological Processing at Nottingham

www.nottingham.ac.uk/go/sustainablecbp

Contents

Sustainability at Nottingham

The University of Nottingham has committed itself to becoming a leading green university, making sustainability one of its nine guiding principles in the University's 2010-2015 strategic plan.

Sustainability is embedded in teaching and research programmes and manifests itself through our award winning campuses in the UK, China and Malaysia. This commitment extends to the design of our new buildings, which meet the highest levels of energy efficiency, waste minimisation and sustainable construction. Examples include the Centre for Sustainable Chemistry (see page 9), the BioEnergy and Brewing Science Building and the Energy Technology Building.

We carry out world-leading research into new, green chemical, biological and engineering technologies. By working together with the chemical-using industries we wish to embed sustainability within manufacturing processes, minimise energy usage and adopt new types of renewable feedstocks and catalysts, including biocatalysts. Our aim is to transfer new technologies and approaches from academia into industry, in order to create real, global impacts.

We work across a broad range of manufacturing sectors including pharmaceuticals, agrochemicals, energy and advanced materials, food science and FMCG, industrial biotechnology and synthetic biology and bioenergy and biofuels. Our approach encompasses feasibility and pre-competitive scoping projects through to more focussed, near market opportunities and defining new supply chains.

We welcome industrial partners across all manufacturing and chemical-using sectors to work on large-scale collaborative projects to help take sustainable concepts and ideas to commercial reality.

Contact

Professor Steve Howdle
t: +44 (0)115 951 3486
e: steve.howdle@nottingham.ac.uk

w: **www.nottingham.ac.uk/go/sustainablecbp**

Supercritical fluids

Supercritical fluids (SCFs) are compressed gases, heated and pressurised above their critical point, which combine the properties of both liquids and gases.

At Nottingham we have primarily investigated supercritical carbon dioxide (scCO_2) and water (scH_2O) as solvents for chemical reactions. Many organic compounds are soluble in scCO_2 and scH_2O, and SCFs are miscible with other gases including oxygen, hydrogen and nitrogen. The compressibility of SCFs means they can be easily pumped, making them ideal media for reactions in continuous flow. They can also be used for extraction and purification, treatment of biomass and synthesis and processing of polymers.

Nottingham has a strong record in developing commercial processes using supercritical fluids; we have worked in collaboration with major chemical companies across the sector and we continue to seek new partners. We have employed heterogeneous and homogeneous catalysis to synthesise industrially important commodity and pharmaceutical chemicals in continuous flow. A wide range of reactions have been optimised, including hydrogenations, oxidations and photochemical reactions and we have also developed a suite of real-time analytical methods which contribute to greater fundamental understanding. We have also developed a wide range of new approaches to polymer synthesis that are energy efficient, and could open up new polymeric materials not accessible through conventional routes. Through our industrial partners and spin-out companies (see case studies), we have taken processes developed in our laboratories to pilot plant scale and beyond.

Case Study: Critical Pharmaceuticals

Critical Pharmaceuticals is a spin-out of The University of Nottingham that offers new approaches to the controlled drug delivery of modern therapeutics; from small molecules to large peptides.

The company's core technology is based upon the discovery at Nottingham that polymers, such as PLGA and PLA, are liquefied (plasticised) by scCO_2. When the CO_2 is removed, the polymer can foam or can be sprayed to form particles that encapsulate the drugs molecules uniformly throughout the polymer matrix. The mild process temperature available using scCO_2 (ca. 35°C) means that temperature-sensitive molecules, e.g. biologics such as human growth hormone (hGH), can be incorporated into the polymer without any loss of activity.

Critical Pharmaceuticals is developing new drug delivery approaches based upon this technology for the controlled release of biotherapeutics. The slow release of the bioactive compounds from the polymer matrix in vivo significantly reduces the number of painful and invasive procedures patients have to undergo.

w: **www.criticalpharmaceuticals.com/**

Case Study: Promethean Particles

Promethean Particles is a company spun-out from The University of Nottingham to commercialise the continuous flow hydrothermal synthesis of nanoparticles.

Using a proprietary reactor design developed at Nottingham, streams of scH_2O and cold aqueous metal salt solutions are mixed and the subsequent reaction produces nanoparticles suspended in solution. Bespoke products can be manufactured by altering the compositions of the salt solution and reaction conditions. This allows Promethean Particles to rapidly screen materials and develop processes in partnership with its customers.

Promethean Particles has won several innovation awards in recognition of its unique scH_2O technology and is a lead partner in the EU FP7 SHYMAN project, enabling it to reach full manufacturing plant capacity.

w: **www.prometheanparticles.co.uk/**

Contacts

Professor Steve Howdle
t: +44 (0)115 951 3486
e: steve.howdle@nottingham.ac.uk

Professor Ed Lester
t: +44 (0)115 951 4974
e: edward.lester@nottingham.ac.uk

CRITICAL PHARMACEUTICALS
Delivering Advanced Therapeutics

PrometheanParticles
Formulating solutions with nanomaterials

Ionic liquids

The unusual physical and chemical properties of ionic liquids make them potential replacement solvents in a number of industrial processes, from biomass treatment to carbon capture.

The large number of available ionic liquids is both an advantage and a disadvantage as choosing which one is the best solvent for a reaction or process can be challenging. At Nottingham we are committed to understanding how the fundamental properties of ionic liquids relate to reaction outcomes and process performance. This will enable the development of predictive toolkits that will greatly enhance the industrial applicability of this exciting class of solvents.

Nottingham employs a number of approaches to investigate the properties of ionic liquids, including surface science techniques, electroanalysis, simulations and solution-phase spectroscopy. We realised that the low volatility of ionic liquids opens up the possibility of studying them using ultrahigh vacuum approaches such as X-ray Photoelectron Spectroscopy (XPS) and synchrotron-based techniques. Nottingham is building upon its ionic liquid expertise and recently installed a unique Liquid Phase Photoelectron Spectroscopy machine (LiPPS), the first in the world dedicated solely to studying liquid surfaces.

Our investigations have focused on transition metal catalysis, polymer science, biomass conversion, gas storage and separation and hydrogen fuel cells. We have uncovered how the interactions between the cations, anions and solutes affect the rates of reactions in ionic liquid. Already this is helping to explain why many reactions are faster in ionic liquids than in conventional organic solvents.

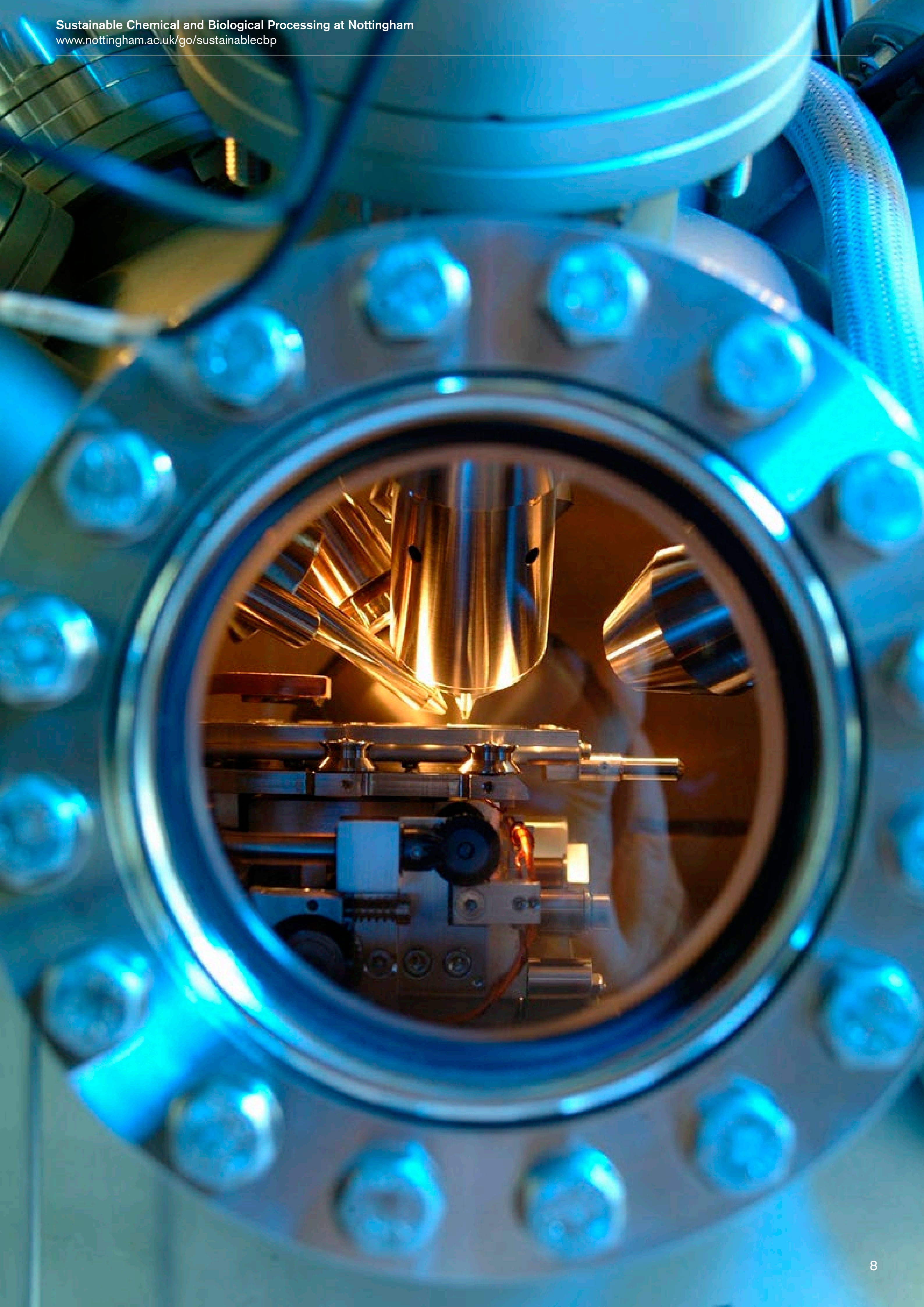
We are also world leaders in the study of the ionic liquid vapour phase, which we identified as consisting of neutral ion pairs. Our measurements provide key physical data that will improve the validation of computer simulations and models and help design better industrial processes.

Contacts

Professor Pete Licence
t: +44 (0)115 846 6176
e: pete.licence@nottingham.ac.uk

Professor Jairton Dupont
t: +44 (0)115 748 4613
e: Jairton.Dupont@nottingham.ac.uk

w: **www.nottingham.ac.uk/ionicliquids**



Centre for Sustainable Chemistry

Chemistry, although central to the scientific advances essential to secure our future, is often viewed as energy demanding, hazardous and polluting. At Nottingham we are challenging these assumptions with our new Centre for Sustainable Chemistry.

The centre will be housed in a brand new carbon neutral laboratory, the first of its kind in the UK. Part funded by a very generous gift from GlaxoSmithKline, the building will serve as a hub to catalyse new collaborations with industry.

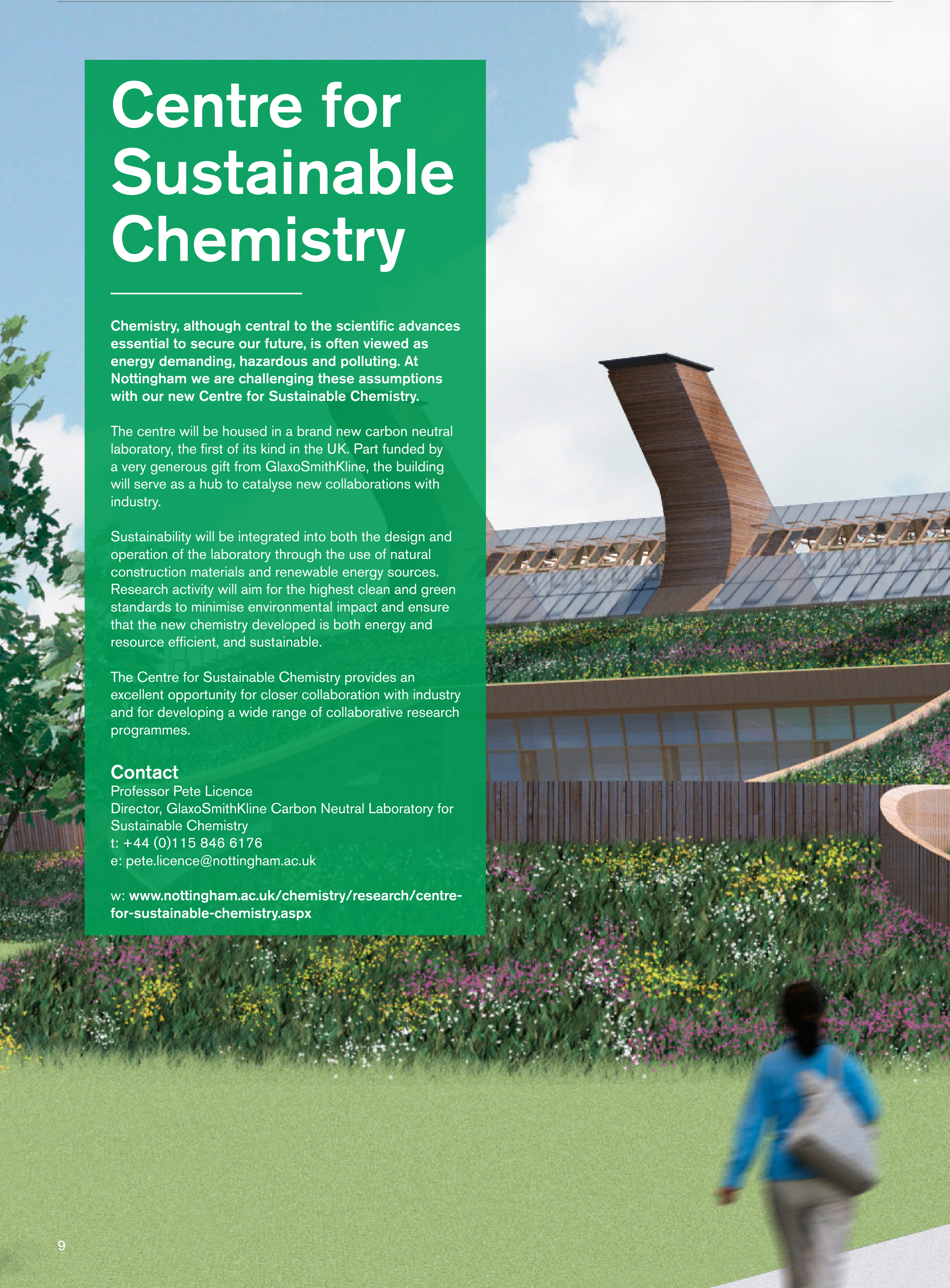
Sustainability will be integrated into both the design and operation of the laboratory through the use of natural construction materials and renewable energy sources. Research activity will aim for the highest clean and green standards to minimise environmental impact and ensure that the new chemistry developed is both energy and resource efficient, and sustainable.

The Centre for Sustainable Chemistry provides an excellent opportunity for closer collaboration with industry and for developing a wide range of collaborative research programmes.

Contact

Professor Pete Licence
Director, GlaxoSmithKline Carbon Neutral Laboratory for Sustainable Chemistry
t: +44 (0)115 846 6176
e: pete.licence@nottingham.ac.uk

w: **www.nottingham.ac.uk/chemistry/research/centre-for-sustainable-chemistry.aspx**



Green and sustainable synthetic chemistry

The new Centre for Sustainable Chemistry reflects the importance that sustainability has in the research and teaching programmes at The University of Nottingham.

Research in synthetic chemistry at Nottingham focuses on achieving difficult chemical transformations and synthesising complex natural products. Traditionally, synthetic chemistry has received negative attention for the use of large quantities of toxic solvents and reagents and the production of large volumes of waste. By applying the principles of green chemistry, researchers at Nottingham are creating new ways to minimise solvent use, increase atom efficiency and replace hazardous reagents with benign ones.

Approaches include the use of supercritical fluids and ionic liquids as solvents, enzymatic catalysis, continuous flow and microwave chemistry, using air as an oxidant in place of toxic metal reagents, and converting biorenewable feedstocks into useful chemicals.

Contact

Professor Chris Moody
t: +44 (0)115 846 8500
e: c.j.moody@nottingham.ac.uk

Case Study: DABAL-Me_3 – An Air stable Alkyl Aluminium Reagent

Synthetically useful alkyl aluminium reagents are pyrophoric and therefore require control measures for safe handling. Researchers at Nottingham have developed DABAL-Me_3: a solid, easy-to-handle alternative alkyl aluminium reagent for use in a range of commercially important pharmaceutical transformations including alkylations and amide bond formation. This new reagent is being commercialised with Sigma-Aldrich, Key Organics and to Aesica who are investigating the potential of DABAL-Me_3 in industrial scale processes.

Demonstration of the stability of DABAL

Microwave Process Engineering

The Microwave Process Engineering Research Group (MPE) at the University of Nottingham conducts multi-disciplinary research, development and commercialisation studies into microwave heating and processing technologies which deliver economic and technical benefits across fields as diverse as chemicals, fuels, mineral processing, biotechnology, food, pharmaceuticals and recycling.

The MPE focuses on the interaction of microwaves with materials and in the scale-up of microwave heating processes. Effective robust scale-up methodologies are central to successful process design and have been well proven at Nottingham across a wide range of applications including within the mineral processing, oil and gas, bulk minerals, and chemical sectors.

Our work with industry sponsors is always based on mutual understanding and genuine shared interest, with a focus on the highest quality delivery to commercial timescales. In collaboration with our industrial partners, we have led teams to successfully design, build and license 4 industrial microwave processing systems, including the world's largest microwave processing facility (TRL6) capable of treating some 150 tonnes of solids per hour.

Case Study: Vermiculite

Vermiculite is a commercially valuable mineral used in applications including fire-proofing, insulation and packing. To convert the raw material into the commercial product involves "exfoliation", in which the mineral is expanded by heating to over 1000 °C. The current process is inefficient and inflexible and an alternative is needed that reduces energy and space usage while improving quality and control.

MPE have developed microwave technology to process vermiculite, significantly reducing energy consumption and generating significant health and safety benefits over the existing industrial method. Using a multi-disciplinary approach allowed the team to overcome previous hurdles in scale up, addressing fundamental issues through better understanding, metrology and modelling. The microwave process is now at pilot plant stage and provides energy savings of 1000 kWh/t, smaller plant footprint and highly controllable product specification.

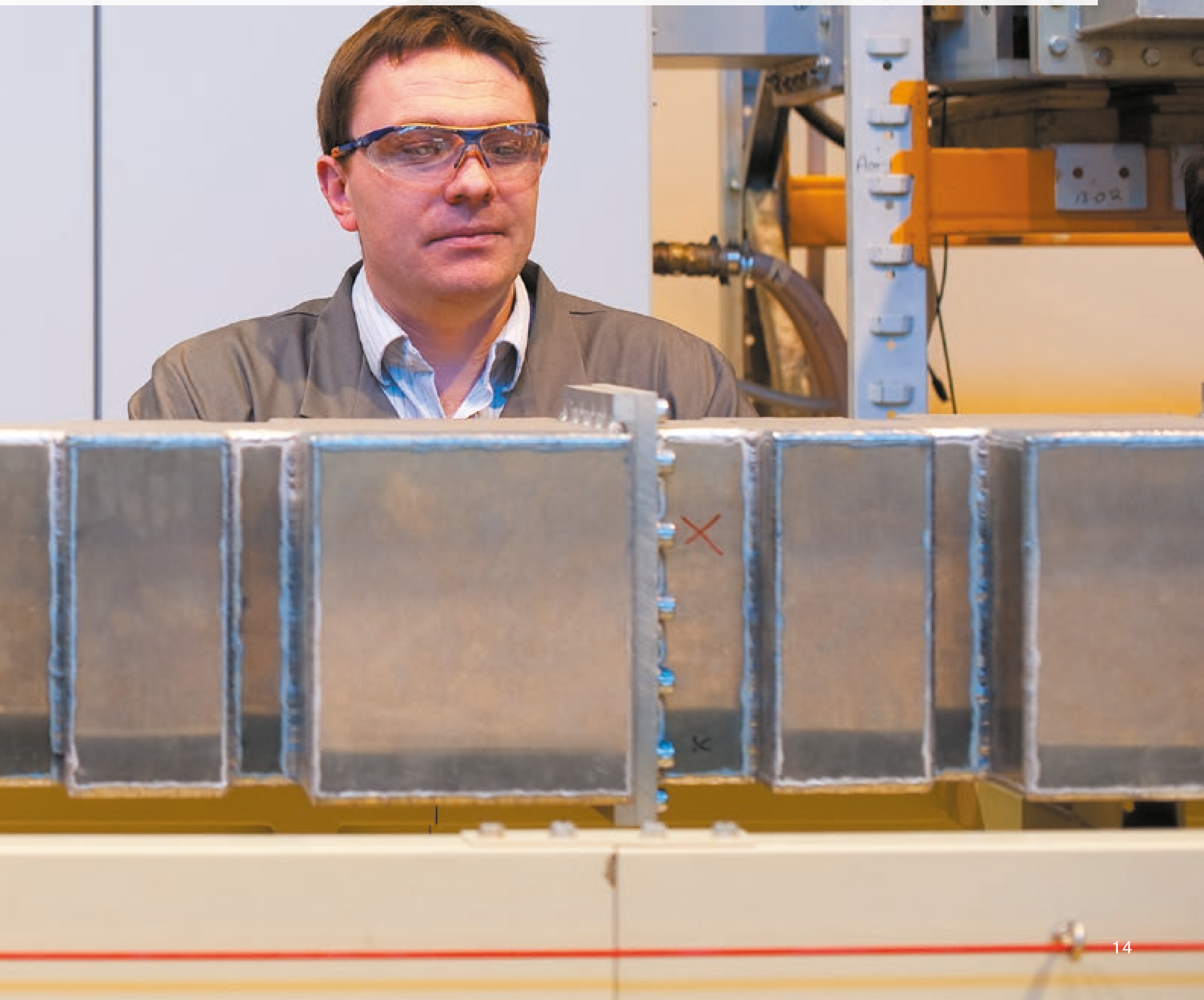
Contacts

Microwave Process Engineering Research Group (MPE)

Dr Stephen Ison
t: +44 (0)7773 252394
e: stephen.ison@nottingham.ac.uk

Dr Paula Palade
t: +44 (0)7964 864818
e: paula.palade@nottingham.ac.uk

w: **http://www.nottingham.ac.uk/research/groups/industrial-microwave-processing/index.aspx**



Industrial biotechnology: biorenewables and bioprocessing

At the University of Nottingham, we specialise in the sustainable manufacturing of chemicals and materials from renewable resources. Our approach integrates fundamental discoveries in biological science, chemistry and engineering to deliver innovative products and processes.

Research is truly interdisciplinary and includes groups in biology, chemistry, engineering and molecular science with global collaborators in industry and academia.

Research interests include:

- Metabolic engineering to produce bulk chemicals, e.g. monomers, amines, from renewable feedstocks
- Improving substrate delivery and product recovery in biocatalytic processes
- Theoretical and computational investigations of reaction pathways in biological systems.
- Understanding the fate of pharmaceuticals and steroids in wastewater and mitigating their effects
- The design of enzymes for non-natural transformation and the combination of proteins with chemical catalysts
- Manufacturing new materials from renewable feedstocks, e.g. cellulose aerogels, which can be used in commercial applications.

The University hosts state-of-the-art, newly equipped synthetic, engineering and analytical laboratories. Facilities include equipment for aerobic and anaerobic microbiology, enzymology, molecular biology, synthetic chemistry and bioreactors. We have a strong record of working with industry on projects involving biorenewables and bioprocessing.

Contact

Professor Gill Stephens
t: +44 (0)115 514002
e: gill.stephens@nottingham.ac.uk

w: **www.nottingham.ac.uk/go/biorenewables**

Bioenergy and biofuels

Nottingham was part of the UK's BBSRC Sustainable Bioenergy Centre (BSBEC), which ran from 2009 to 2015 and which funded two of our research programmes focusing on the conversion of lignocellulose to ethanol and the development of new bacterial strains to produce biobutanol. The programmes brought together world-class researchers spanning the bioenergy pipeline from growing biomass to fermentation of biofuels.

The Lignocellulose to Ethanol (LACE) programme focused on three technical challenges of converting waste biomass into ethanol: the deconstruction of cell walls, hydrolysis of cell wall sugars and fermentation to ethanol. Pre-treatment is essential to allow enzymes access to cell-wall sugars and the methods assessed at LACE included microwaves, extrusion and ionic liquids. Fungal enzymes are then used to hydrolyse cell wall polymers and yeasts are responsible for fermentation of the resultant sugars. We are developing new enzyme cocktails by investigating the response of fungi to novel feed stocks, and developing improved strains of yeast with enhanced tolerance to the inhibitors generated during the pre-treatment and stresses encountered during the fermentation. Doing so will ensure that these processes can occur more efficiently and economically. LACE focussed on the use of agricultural residues such as wheat straw but more recently the interest has moved towards the use of the organic fraction of municipal solid waste. Other interests include the identification, and manipulation, of the plant traits conferring recalcitrance to processing. This research is carried out in state-of-the-art facilities, including the Food and Biofuel Innovation Centre at Sutton Bonington.

The conversion of biomass to biobutanol is part of a wider research programme at Nottingham aimed to develop Clostridia strains for the production of bulk chemicals. Through a synthetic biology approach, the Clostridia Research Group utilise beneficial strains of this genus of bacteria to convert biomass and biorenewables into chemicals. The group receives substantial industrial funding, nearly £3m in 2013 alone, from companies including Evonik, LonzaTech, Merck and INVISTA. This programme is now closely related to the new BBSRC Synthetic Biology Centre (see page 19).

Contacts

Professor Greg Tucker
LACE
t: +44 (0)115 951 6126
e: gregory.tucker@nottingham.ac.uk

Professor Nigel Minton
Clostridia Research Group
t: +44 (0)115 84 67458
e: nigel.minton@nottingham.ac.uk

Synthetic Biology Research Centre

The University of Nottingham has been awarded a £14.3m grant to create a new Synthetic Biology Research Centre (SBRC). The SBRC-Nottingham will use a synthetic biology approach to develop microorganisms than can make the chemicals and fuels that our modern society needs. A key aim of the SBRC-Nottingham is to demonstrate that we can break our reliance on fossil fuels and make chemicals and biofuels in a sustainable, cleaner and greener way.

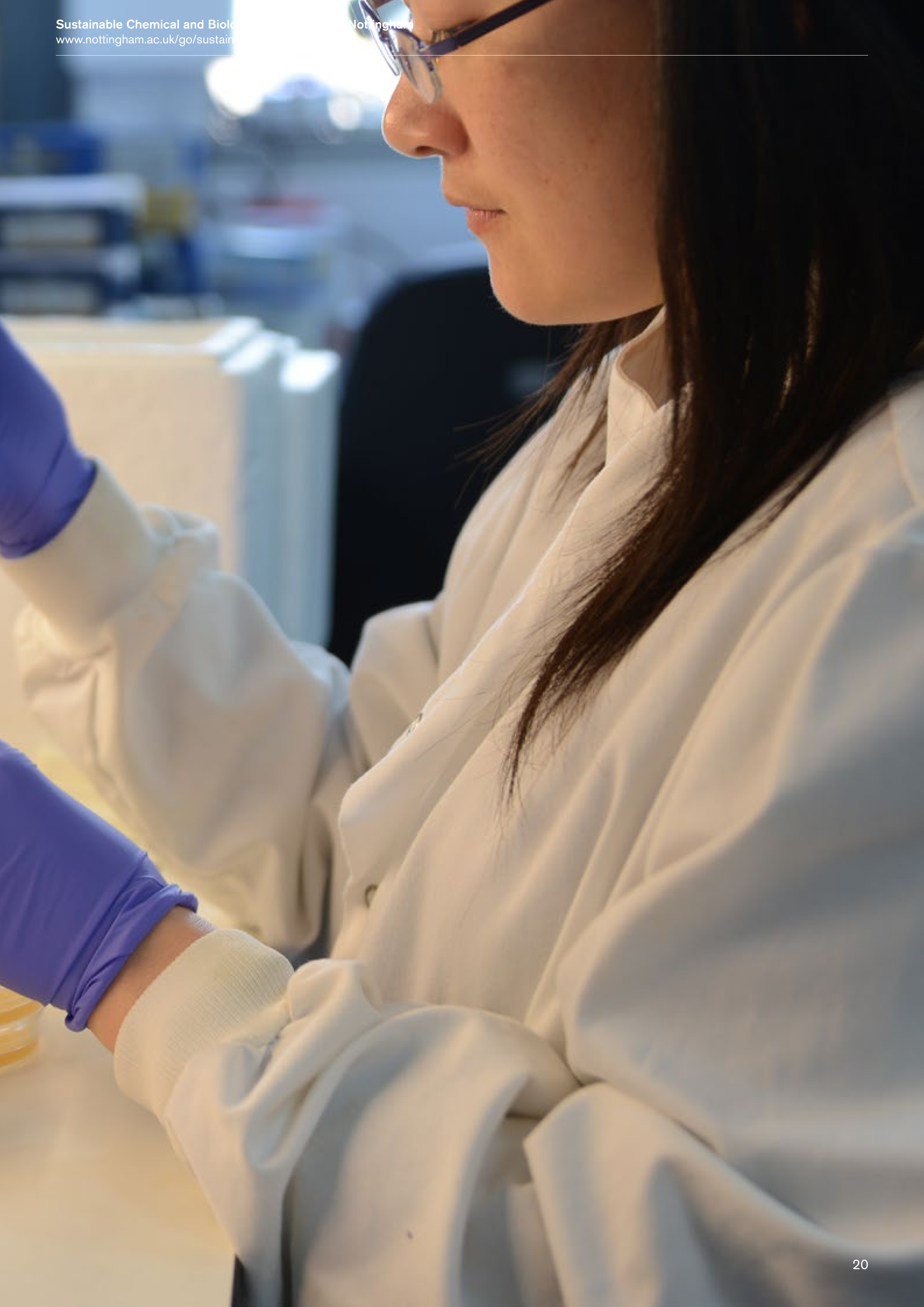
These organisms will convert simple gases, such as carbon dioxide and carbon monoxide into valuable chemicals. Carbon monoxide in particular is a waste gas from many industries such as steel mills. It can also be produced by converting waste biomass e.g. from the forestry and agriculture industries into "syngas". By using waste biomass and greenhouse gases we aim to remove competition between fuel and food production and open the way to having positive impacts on climate change.

Contacts

Dr Alan Burbidge
t: +44 (0) 115 74 84094
e: alan.burbidge@nottingham.ac.uk

Professor Nigel P Minton
t: +44 (0)115 84 67458
e: nigel.minton@nottingham.ac.uk

w: www.sbrc-nottingham.ac.uk



Food science

Food Sciences research at Nottingham is committed to fundamental and applied research associated with food and beverage production. We undertake research at all levels of the food production process with expertise and interests ranging from the quality of food raw materials from the farm right though food and beverage processing to consumer preference and choice.

Our research programmes are strongly aligned to the needs of industrial sponsors, who contribute half of our £8m research budget. We have collaborators who extend across the globe, including large multinational companies such as Mars, Cargill, Unilever, Nestle, Kelloggs and SAB Miller, as well as SMEs from Europe, North America and Asia.

The University has invested time in developing a Food and Drink Capability Statement to capture our expertise throughout this sector and highlight the ways our research works within and aligns to the ten key pre-competitive research areas, as determined by industry itself. This has resulted in the creation of a matrix to enable industry to navigate and better access our skills and knowledge. The Food and Drink Capability Statement can be found at: http://www.nottingham.ac.uk/servicesforbusiness/documents1/fdbrochure.pdf

Centre for Innovative Manufacturing in Food

Nottingham is the lead partner in a new £4.5m Centre for Innovative Manufacturing in Food, which will bring together academic institutions and companies to work on solutions to the major challenges facing the food industry.

Research themes will include

- new processing and manufacturing technologies, e.g. microwave-vacuum-drying and distributed manufacture
- improved resource utilisation and sustainable supply chains, e.g. valorisation of natural materials and waste streams
- eco-food manufacturing to create new strategies and tools for the food industry to measure and maximise resource efficiency in production

Contact

Professor Tim Foster
Director, Centre for Innovative Manufacturing in Food
t: +44 (0) 115 951 6246
e: tim.foster@nottingham.ac.uk

Dr Ian Fisk
t: +44 (0) 115 951 6037
e: ian.fisk@nottingham.ac.uk

Innovation and ingenuity

The University of Nottingham presents not only a vibrant blend of scientific and engineering expertise, but also close collaboration with the University's Haydn Green Institute of Innovation and Entrepreneurship.

The institute's mission is to be a centre of excellence in the development of enterprise and entrepreneurial skills, innovation and understanding the commercialisation of research. Its approaches to innovation are now being employed to help our scientists and engineers develop sustainable solutions with existing and new industrial partners. Our researchers take a holistic view of developing new processes and we employ stage-gate strategies and life-cycle assessments to evaluate commercial viability at an early stage. This ensures we identify failures early, saving time and investment, and increasing the likelihood of successful innovation.

Industry Challenge Days

Supported by academics from the Haydn Green Institute of Innovation and Entrepreneurship our scientists and engineers are pioneering new approaches to working with industry. We are developing Industry Challenge Days as a means to inspire collaboration and communication between academic and industrial researchers.

We have successfully trialled this approach with a leading speciality chemical company. Company managers addressed a team of academics about the major research and development challenges they faced and then in mixed teams explored the root causes for the problem and developed radical new approaches. Not only did discussions create exciting new scientific ideas, they led to a better understanding of the business and supply chain challenges faced by the company.

The challenge day concept is already coming to fruition with Nottingham and the company exploring a number of collaborative research projects around ideas generated during the meeting.

Contacts

Professor Simon Mosey
Haydn Green Institute of Innovation and Entrepreneurship
t: +44 (0)115 951 3763
e: simon.mosey@nottingham.ac.uk

Dr Jon McKechnie
Life cycle assessment
t: +44 (0)115 748 4435
e: jon.mcKechnie@nottingham.ac.uk

The University of Nottingham and Britest

The University of Nottingham is also a member of Britest Ltd. Britest is a global leader in the development of innovative process design solutions for the chemical processing sector. Britest members include global businesses drawn from a diverse set of industry sectors, including pharmaceuticals, fine chemicals and FMCG together with a number of internationally recognised academic institutions.

As a member of Britest, the University is contributing to the development of Britest's proprietary tools and methodologies from which all members can derive business benefit. As part of their commitment to Britest, Nottingham researchers are members of the Britest Board and Innovation Committee and participate in working groups on a range of research topics.

For more information about Britest, visit **www.britest.co.uk** or contact Mark Talford at mark.talford@britest.co.uk.

For more information on Nottingham's role within Britest, contact steve.howdle@nottingham.ac.uk.

Britest

Contacts

To discuss opportunities to collaborate with The University of Nottingham, please contact:

Professor Steve Howdle
t: +44 (0)115 951 3486
e: steve.howdle@nottingham.ac.uk
w: **www.nottingham.ac.uk/go/sustainablecbp**

More information about the University's approach to sustainability can be found at **www.nottingham.ac.uk/sustainability**

Other contact details

Supercritical fluids
Professor Steve Howdle
t: +44 (0)115 951 3486
e: steve.howdle@nottingham.ac.uk

Professor Ed Lester
t: +44 (0)115 951 4974
e: edward.lester@nottingham.ac.uk

Professor Mike George
t: +44 (0)115 951 3512
e: mike.george@nottingham.ac.uk

Professor Martyn Poliakoff
t: +44 (0)115 951 3520
e: martyn.poliakoff@nottingham.ac.uk

w: **www.nottingham.ac.uk/chemistry**

Ionic Liquids
Professor Pete Licence
t: +44 (0)115 846 6176
e: pete.licence@nottingham.ac.uk

Professor Jairton Dupont
t: +44 (0)115 748 4613
e: Jairton.Dupont@nottingham.ac.uk

Professor Robert Jones
t: +44 (0)115 95 13468
e: robert.g.jones@nottingham.ac.uk

Dr. Darren Walsh
t: +44 (0)115 846 7495
e: darren.walsh@nottingham.ac.uk

w: **www.nottingham.ac.uk/ionicliquids**

Synthetic and pharmaceutical chemistry
Professor Chris Moody
t: +44 (0)115 846 8500
e: c.j.moody@nottingham.ac.uk

Professor Simon Woodward
t: +44 (0)115 951 3541
e: simon.woodward@nottingham.ac.uk

Dr John Moses
t: +44 (0)115 951 3533
e: john.moses@nottingham.ac.uk

w: **www.nottingham.ac.uk/chemistry**

Microwave Process Engineering Research Group (MPE)
Dr. Derek Irvine
t: +44 (0) 115 95 14088
e: derek.irvine@nottingham.ac.uk

Dr. Chris Dodds
t: +44 (0) 115 95 14172
e: chris.dodds@nottingham.ac.uk

Dr Stephen Ison
t: +44 (0)7773 252394
e: stephen.ison@nottingham.ac.uk

Dr Paula Palade
t: +44 (0)7964 864818
e: paula.palade@nottingham.ac.uk

w: **www.nottingham.ac.uk/research/groups/industrial-microwave-processing/index.aspx**

Biorenewables and Bioprocessing
Professor Gill Stephens
t: +44 (0)115 951 4002
e: gill.stephens@nottingham.ac.uk

Dr Anna Croft
t: +44 (0)115 846 6391
e: anna.croft@nottingham.ac.uk

Dr Anca Pordea
t: +44 (0)115 951 4087
e: anca.pordea@nottingham.ac.uk

Dr Rachel Gomes
t: +44 (0)115 846 8883
e: rachel.gomes@nottingham.ac.uk

w: **www.nottingham.ac.uk/go/biorenewables**

Food science
Professor Tim Foster
t: +44 (0)115 951 6246
e: tim.foster@nottingham.ac.uk

Dr Ian Fisk
t: +44 (0)115 951 6037
e: ian.fisk@nottingham.ac.uk

w: **www.nottingham.ac.uk/go/food**

Bioenergy and Biofuels
LACE Programme
e: bioenergy@nottingham.ac.uk

Professor Greg Tucker
t: +44 (0)115 951 6126
e: gregory.tucker@nottingham.ac.uk

Professor Nigel Minton
t: +44 (0)115 84 67458
e: nigel.minton@nottingham.ac.uk

w: **www.nottingham.ac.uk/bioenergy/**

Synthetic Biology Research Centre
Professor Nigel Minton
t: +44 (0)115 84 67458
e: nigel.minton@nottingham.ac.uk

Dr Alan Burbidge
t: +44 (0) 115 74 84094
e: alan.burbidge@nottingham.ac.uk

w: **www.sbrc-nottingham.ac.uk**

Haydn Green Institute of Innovation and Entrepreneurship
Professor Simon Mosey
t: +44 (0)115 951 3763
e: simon.mosey@nottingham.ac.uk

w: **www.nottingham.ac.uk/uniei**

Life cycle assessment
Dr Jon McKechnie
t: +44 (0)115 748 4435
e: jon.mcKechnie@nottingham.ac.uk

w: **www.nottingham.ac.uk/engineering/people/jon.mckechnie**

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