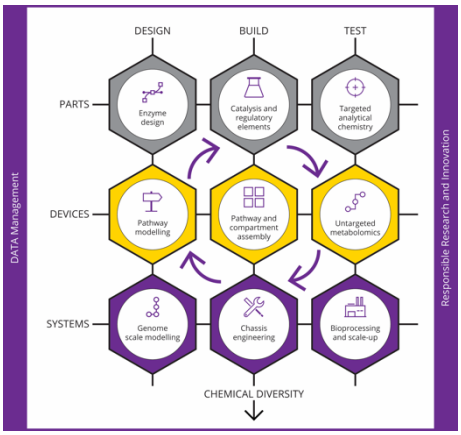
SYNBIOCHEM Manchester Synthetic Biology Research Centre

SYNBIOCHEM
Manchester Synthetic Biology Research Centre
for Fine and Speciality Chemicals

The Manchester Synthetic Biology Research Centre SYNBIOCHEM is a globally significant BioFoundry for the biosynthesis and sustainable production of fine and speciality chemicals.

The Centre's integrated technology platforms provide a powerful capability that facilitates predictable engineering of microbial bio-factories for chemicals production. By harnessing the power of predictive synthetic biology, SYNBIOCHEM is driving next-generation sustainable manufacturing processes for scale-up across many industrial sectors (e.g. healthcare, energy, agrichemicals, green chemistry pharmaceuticals, novel materials and bioremediation).

In 2014 SYNBIOCHEM set out an ambitious vision of harnessing predictive methods of synthetic biology for the microbial production of diverse families of high-value chemicals. Modelled on the Bio-Foundry concept the Centre has successfully brought together an interdisciplinary core research team with a broad academic community in a collaborative environment to tackle grand challenge projects.



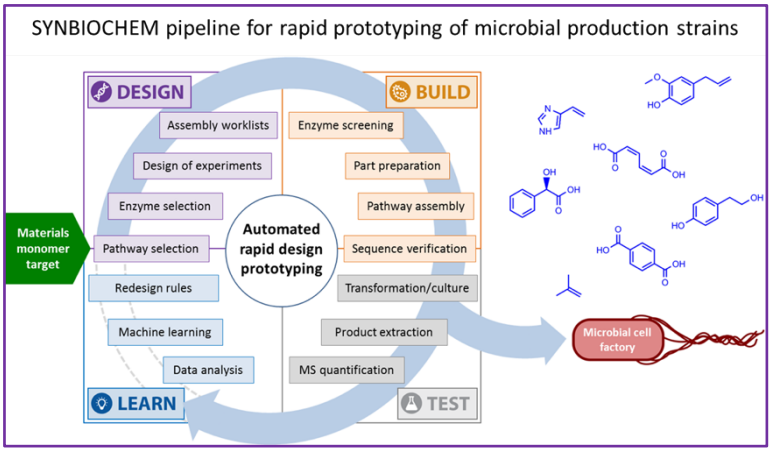
Over the past 5 years, SYNBIOCHEM has benefited from extensive and continued investment in a range of state-of-the art equipment that has been underpinned by chemical, enzyme engineering, systems biology (computational) and microbial research expertise within the Manchester Institute of Biotechnology (MIB).

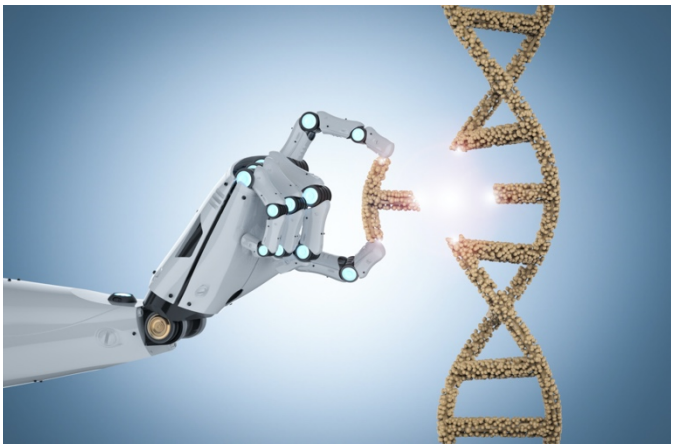
The Centre has developed an innovative suite of Design/Build/Test/Learn tools and technologies which it has integrated into an **automated compound-agnostic biomanufacturing pipeline** for *E. coli.* [1]

This significant capability integrates new Design software tools for pathway (RetroPath2.0) and enzyme selection (Selenzyme), part design (PartsGenie), Design of Experiments and *in-silico* work-list generation for automated Build protocols. Build workflows have been developed for prompt enzyme screening, pathway assembly, sequence verification, chassis engineering, product extraction and scale-up fermentation. New rapidly optimised Test mass spectrometry analytical methods support the screening of a wide range of target compounds and include protocols for enantiomer separation. Finally Learn protocols have been applied to inform re-design and improved production titres.

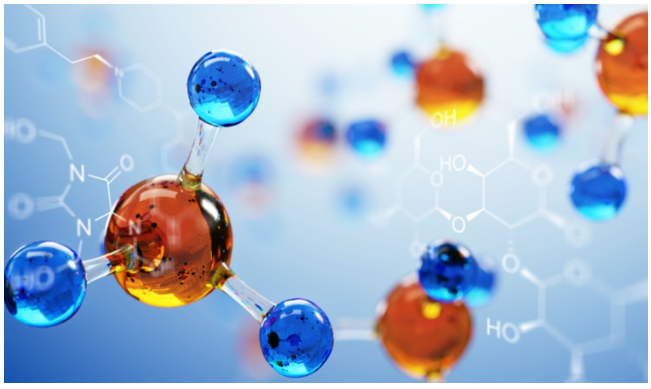
Automation and multiplexing of pipeline protocols now allows rapid prototyping for transformative on-demand microbial production of diverse chemicals. The Centre recently showcased its capability to rapidly prototype, optimize and scale-up production of chemically diverse industrially relevant materials building blocks (monomers).[2] In 85 days, by combining >160 genetic parts into 115 unique biosynthetic pathways, the Centre produced 17 materials monomers and went on to deliver g/L enantio-selective production of selected targets.

1) Comms. Biol. 2018, 1: 66. 2) Met.Eng. 2020, 60: 168-182.



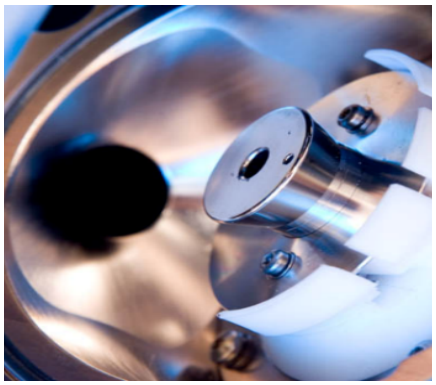


Diverse chemical targets have been produced using the Centre's pipeline including alkaloids, flavonoids and terpenoids. SYNBIOCHEM has also supported a broader portfolio of projects for the microbial production of diverse compounds (e.g. polyketides and cannabinoids). In addition, projects on the discovery of new bio-based advanced materials (co-sponsored by Dstl) with self-healing or tuneable optical properties (e.g. reflectins) and high-tensile strength (e.g. polymers based on aramid fibres). SYNBIOCHEM is working with the Royce Institute to engineer *advanced materials from biology* supported by new equipment infrastructure (automation platforms and next generation sequencing) in the MIB.

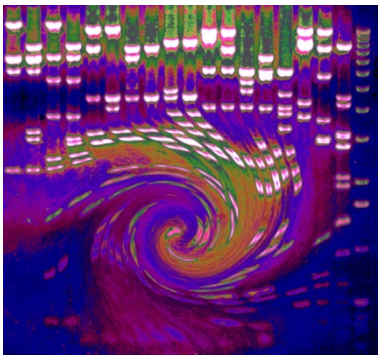


Through national leadership in **Responsible Research and Innovation** the Centre has also undertaken a range of anticipation, engagement, focal end-to-end studies and dialogue activities. Recent work has included socio-techno economic analysis and constructive sustainability assessments for our chemical targets, and international horizon scans whilst working with industry partners to incorporate ideas into working practices.

Globally connected for a sustainable future: The Centre engages in national and international collaborations across with current EU programmes and projects in US, China, India and Brazil, and is a member of the Global BioFoundries Alliance which connects >25 non-commercial biofoundries. To expand its research portfolio and instrument capabilities, SYNBIOCHEM academics secured further Synthetic Biology related research awards worth >£20M in Y5 with a further £17M worth of applications submitted.



Policy and Engagement: An important activity of the Centre has been to nationally and internationally raise the profile and impact of synthetic biology. By working on international working groups, it has contributed to policy papers on biosecurity, ethics and horizon scans. Whilst nationally it has contributed to the Synthetic Biology Leadership Council and supported the delivery of national roadmaps and position papers to ensure input into a cohesive national agenda for synthetic biology and the engineering of biology towards sustainable production process and delivery of a bio-based economy. The Centre has also engaged directly with Members of Parliament, the Department for Business Energy and Industrial Strategy, Innovate UK and the UKRI.



Translation and Industrial engagement: Whilst focused on fundamental research, the Centre has also paid attention to the translation of its science and technologies to maximise innovation impact. 10 patents have been filed which include routes for the microbial biosynthesis of aromatic polyketides, monoterpenoids, propane gas, and ethanol from CO_2.

The Centre has also seen the formation of 2 spin out companies. C3 Biotechnologies is using synthetic biology to design new routes to the bioproduction of fuels, working across the biomanufacturing and distribution supply chains to deliver next-generation fuels that are sustainable, renewable and cost effective. A new company, Manchester BioFactory was founded by SYNBIOCHEM researchers to provide rapid discovery and engineering of high value proteins and enzymes for the biotechnology industry.

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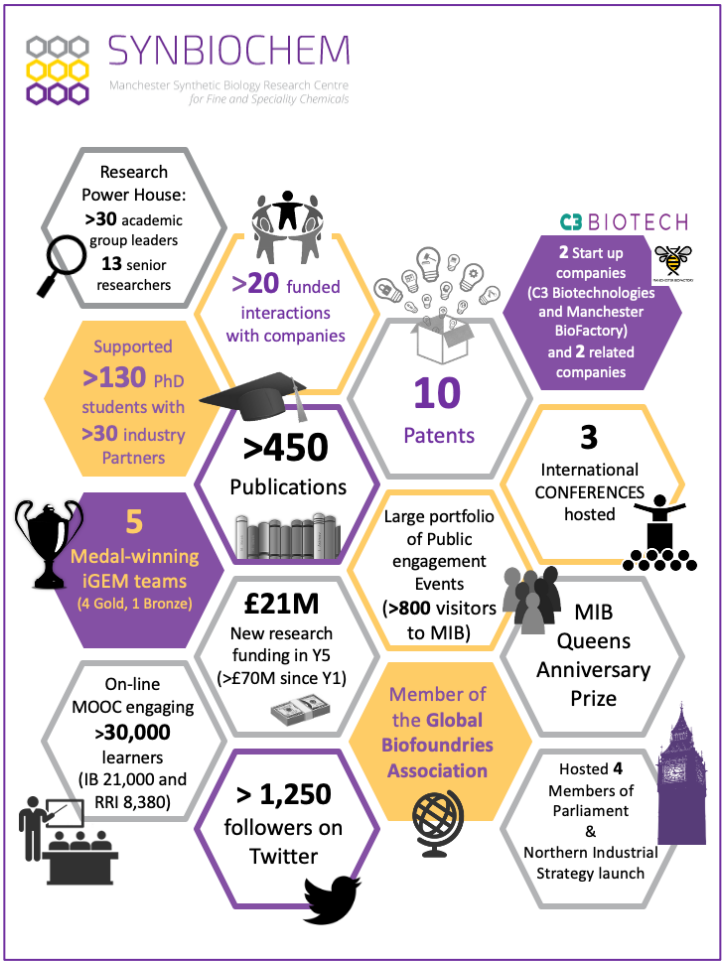
Forward strategy and industrial engagement: Current Centre priorities include further pipeline optimisation and application, the engineering of new industrial host strains and the development of new design and learn tools that will further support new intelligent design. SYNBIOCHEM is working closely with other UKRI investments to support delivery of the Synthetic Biology Roadmap and the translation of discovery science. As an example the Centre is using its engineering biology expertise to support the EPSRC Future Biomanufacturing Research Hub (www.futurebrh.com) and provide a link between enzyme discovery and engineering, and industrial scale-up production, bringing synthetic biology expertise to industrial projects.

The Centre is now identifying new grand challenge programmes that will address the barriers that remain to scale-up and adoption of industrial scale biomanufacturing processes. Foresight and understanding of these challenges will enable the Centre to develop the necessary tools and technology required to deliver transformative innovation in microbial strain engineering.

We encourage industry to work with the Centre, to bring industrial insight into these challenge problems as we move forward.



In 2019 the Manchester Institute of Biotechnology (MIB), where the Hub for the Future BRH is based, received the Queen's Anniversary Prize for Higher and Further Education, the most prestigious award in the sector. It recognised the MIB as "*a leader in the UK's strategic development of biotechnology and biomanufacturing, through innovative technologies in partnerships with industry*". SYNBIOCHEM activities contributed significantly to this award.

THE QUEEN'S ANNIVERSARY PRIZES
FOR HIGHER AND FURTHER EDUCATION
2019

In 2020 SYNBIOCHEM Directors Prof Nigel Scrutton and Prof Nicholas Turner were both elected as Fellows of the Royal Society. The highly prestigious award is thanks to their pioneering contributions to scientific discovery in the field of industrial biotechnology.

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