MiGut

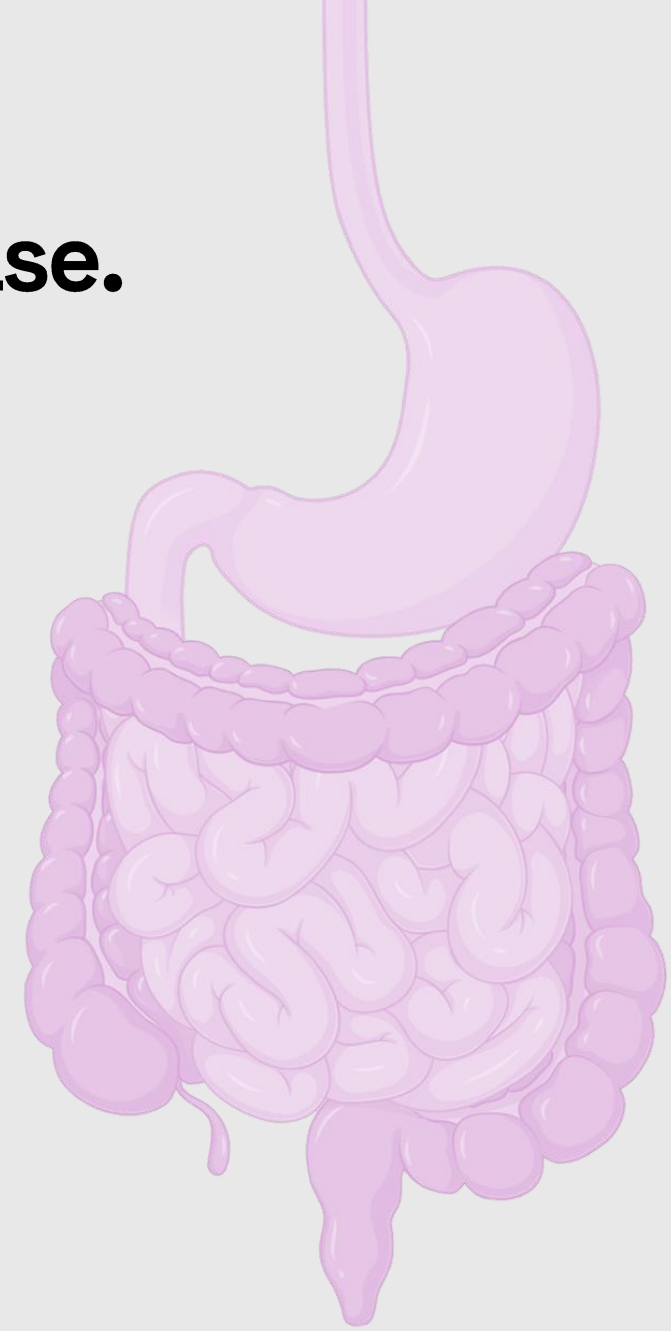
Taking gut microbiome research from bench to business.

Dr William Davis Birch (W.A.DavisBirch@leeds.ac.uk)

The gut microbiome in health & disease.

- The gut microbiome plays a central role in immunity, metabolism, and disease.
- Microbiome modulations is an emerging therapeutic frontier (dietary interventions, FMTs, targeted antimicrobials).
- Studying the microbiome requires specialist systems – the gut is anaerobic, regionally distinct, and many key taxa are difficult to culture in isolation.

Meaningful microbiome research requires models that capture this complexity – reliably, reproducibly, and at scale.

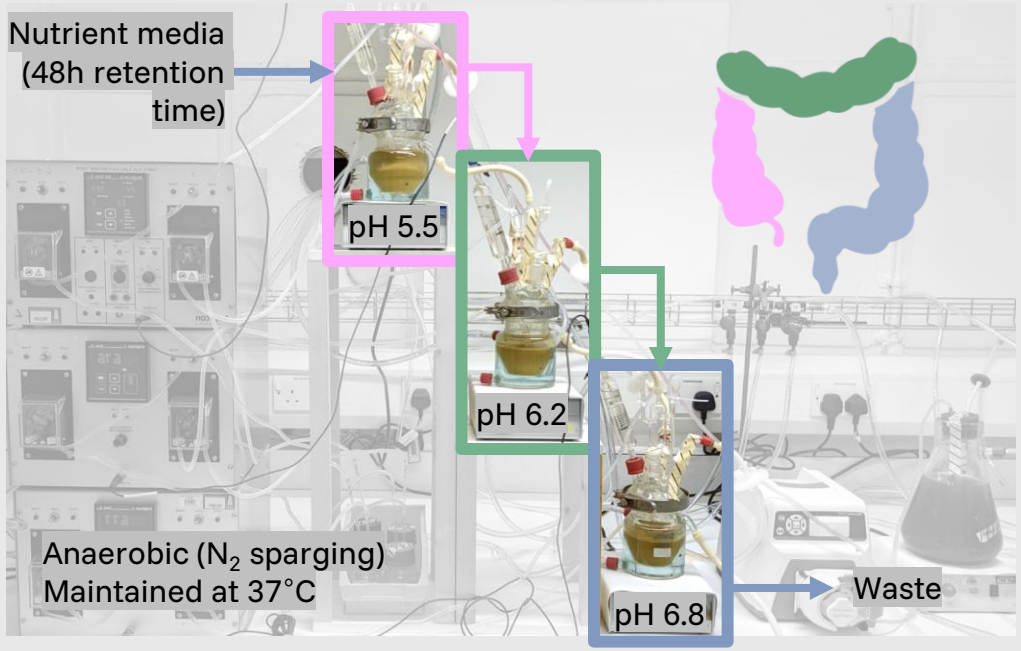


The gut as an engineered system.

Springwell Brewery, North Bar, Leeds
Copyright: Amy Heycock Photography

- Sequential processing
- Precise pH control
- Temperature control
- Anaerobic environment
- Residence time management
- Contamination control

In vitro models of the gut microbiome.

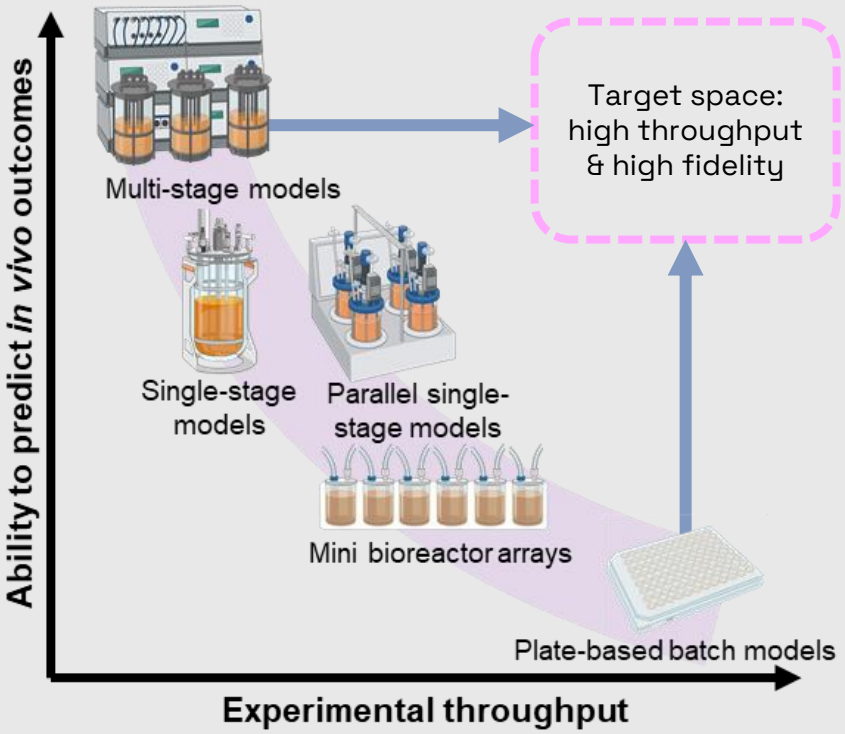


The **triple-stage gut model**

- High-fidelity tool for in vitro microbiome research
- Three vessels to simulate different colonic regions
- pH gradient from 5.5 proximally to 6.8 distally
- Continuous flow of nutrient medium
- Used extensively at Leeds, Reading, and other Universities

… Limitations around scalability!

The engineering/biology challenge.



In vitro models compromise between fidelity and throughput – can this be overcome with **a high-fidelity model that can be run at scale?**

The interdisciplinary team.

Interdisciplinary team from across the University of Leeds, with expertise in:

- Molecular microbiology
- Infectious diseases (CDI)
- In vitro systems & methods
- Bioreactor & fermentation systems design
- Mechatronics, instrumentation & process engineering

PhD project developing MiGut 2019-2023.


Dr William Davis Birch


Dr Anthony Buckley

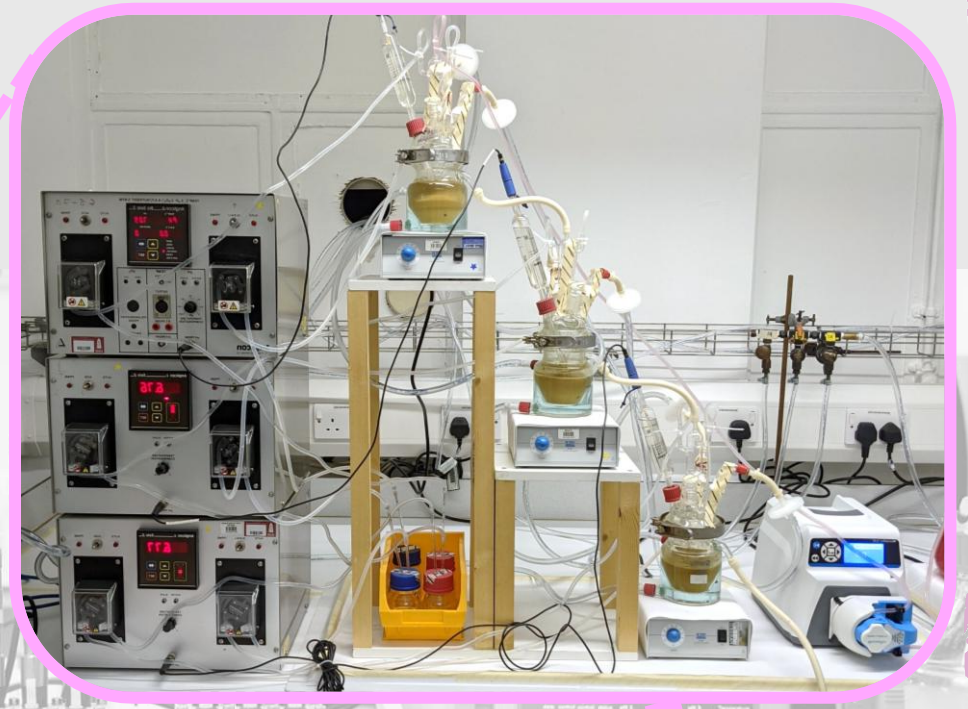

Dr Ines Moura


Prof Nik Kapur


Prof Pete Culmer

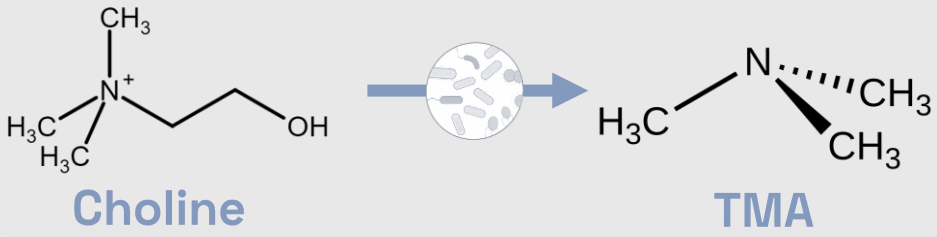
The MiGut system.

- Biologically identical to triple-stage model
- Miniaturised culture volume
- Improved automation, reliability, control
- Integration with IoT
- Modular and adaptable



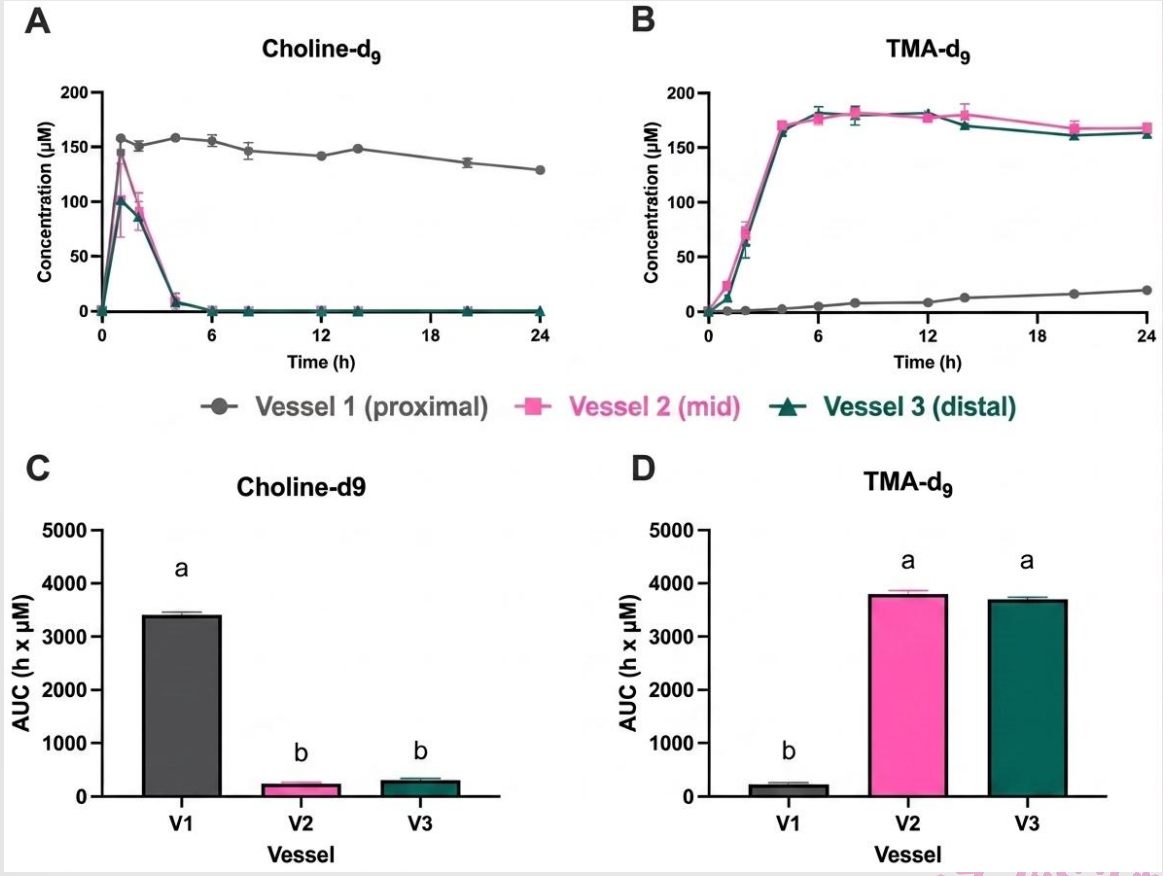
Why triple stage models?

Choline is metabolised into TMA in the colon → links with cardiovascular disease via TMAO formation in the liver.



Choline metabolism happens only in the medial and distal colon, with very little metabolism proximally. cutC gene found throughout the colon.

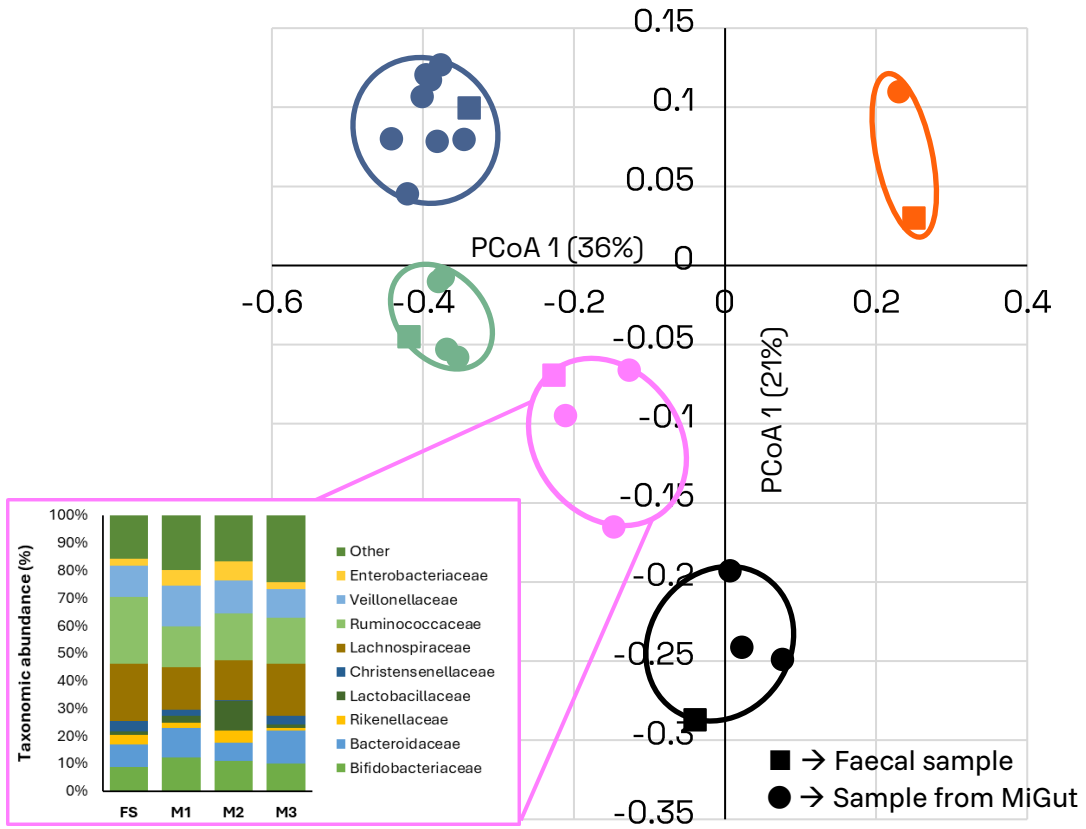
Dr A. Buckley and Prof A. Neilson
https://doi.org/10.3390/metabo15080552



Dr Anthony Buckley

Prof Andrew Neilson

PCoA plot comparing faecal sample to MiGut.



Recapturing faecal ecologies in MiGut.

Different faecal ecologies are recaptured in MiGut after stabilisation period. Differences between original microbiomes are retained – what you put into the models is what you get out of them.

This makes it possible to study specific population groups (e.g. elderly).

Data generated from 16S rRNA sequencing of samples taken from the distal colon vessel of MiGut.

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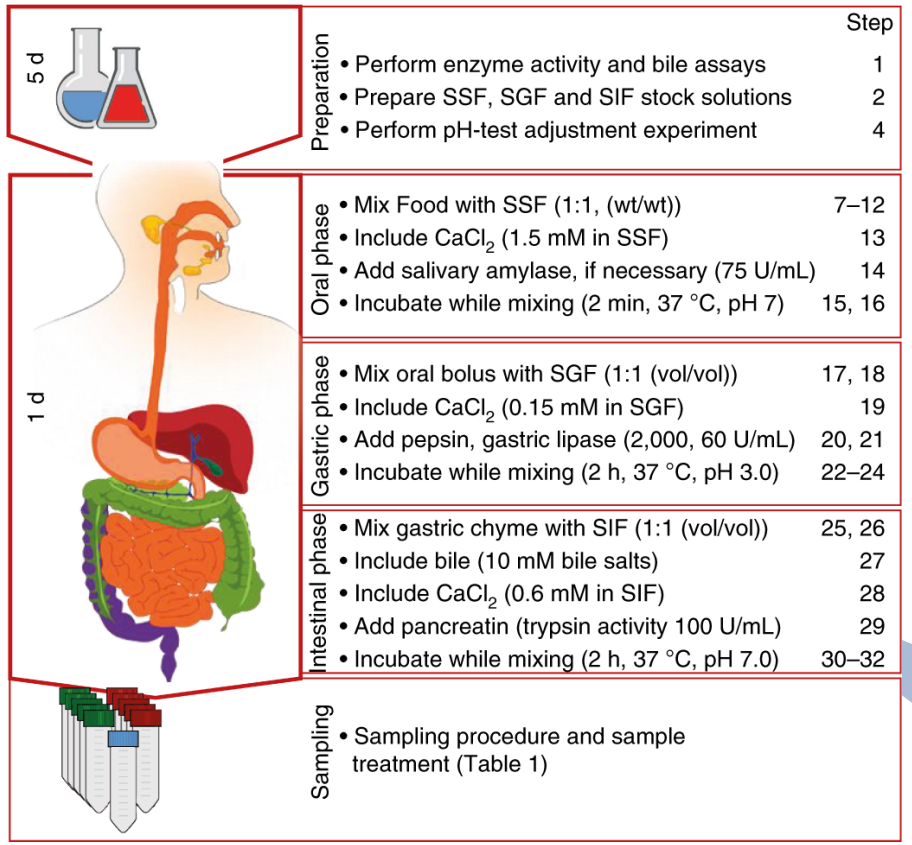


Brodkorb et al. INFOGEST static in vitro simulation [...]

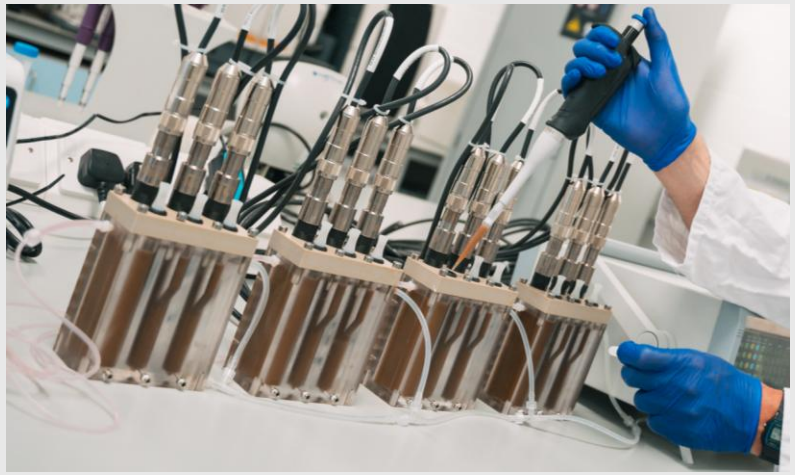
Simulating the upper GI tract.

INFOGEST is a consensus methodology widely used in the literature to simulate the oral, gastric, and small intestine digestion.

We take the output of INFOGEST, separate the digested and undigested fractions via centrifugation and use it as an input for MiGut – **replicating complete transit through the GI tract**.

Engineering unlocks new Biology.

MiGut allows researchers to ask new scientific questions and robustly test hypotheses.



Therapeutic development.

Development/testing of novel antimicrobials, live biotherapeutics, FMT.

Infectious disease & dysbiosis.

Simulating C. difficile infection, AMR gene transfer, antibiotic-associated dysbiosis.

Food, nutrition, and supplements.

Ingredient and/or whole food testing coupled with INFOGEST, pre/probiotics, dietary supplementation.

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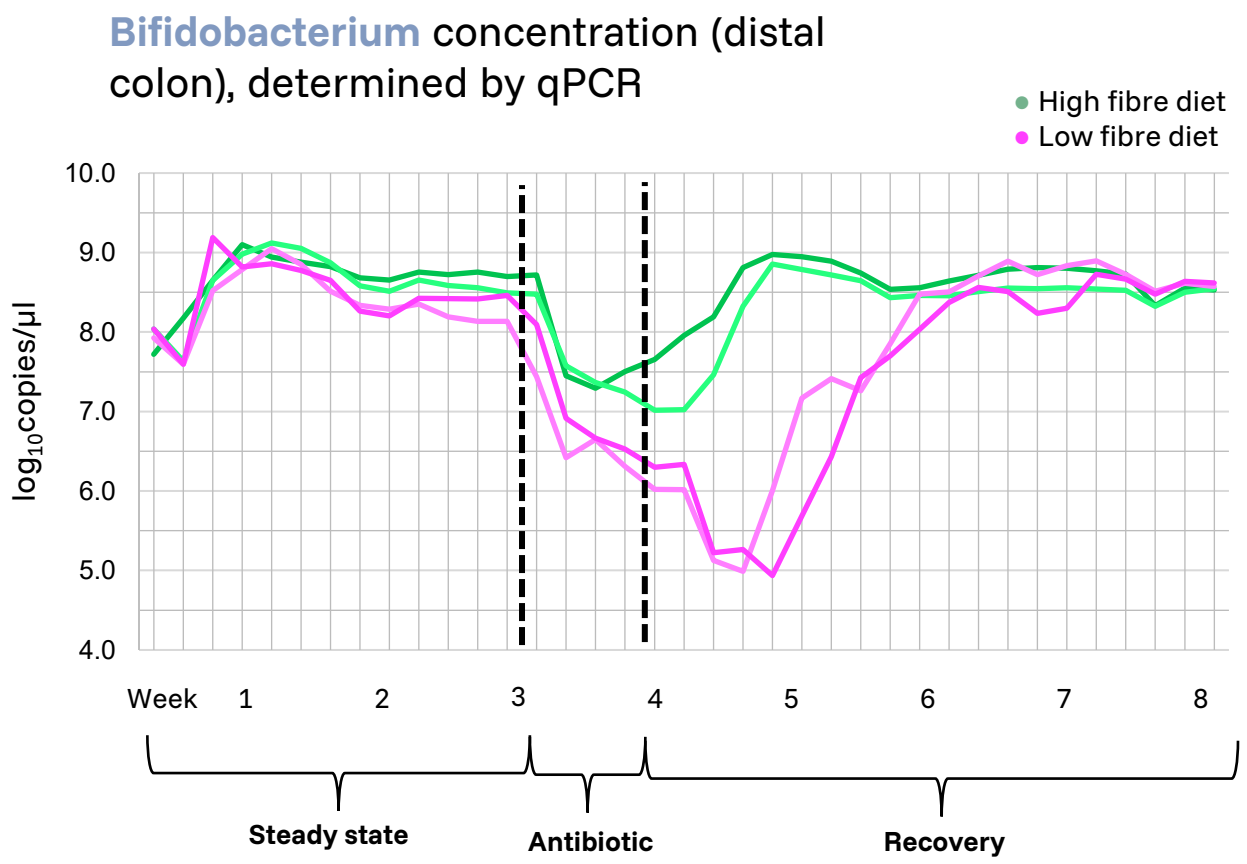


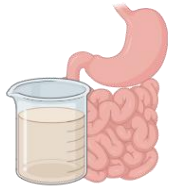
Case study 1: Fibre & antibiotics.

Antibiotics can have a detrimental effect on the gut microbiome, which can provide opportunistic pathogens a niche for expansion.

Prebiotic supplementation may help alleviate the effects of antibiotics on the gut microbiota.

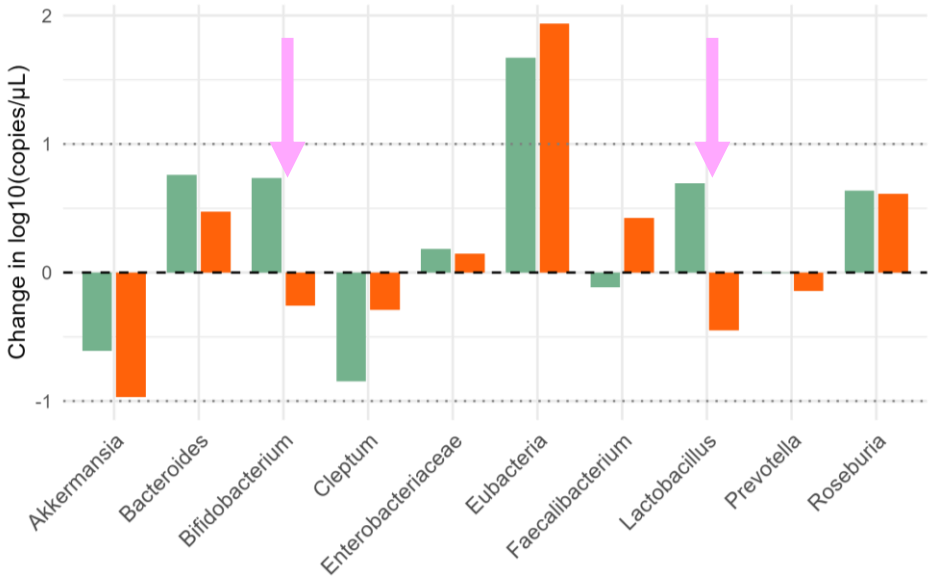
Work carried out by **Dr Ines Moura**.

Pea protein & whey protein



INFOGEST digestion

MiGut models:
- 6 models
- 3 donors



Compositional changes

qPCR of key taxa shown as log_{10} change in concentration from baseline to the end of the dosing period.

- Pea protein
- Whey protein

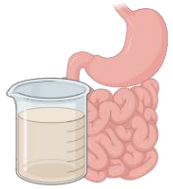
Case study 2: Pea vs whey protein.

Plant-based proteins are increasingly being used instead of animal-derived sources.

Pea protein (84% protein) was compared with whey protein (90% protein) for microbiome effects.

Work carried out by **Megan Pott** and **Kai Yang**.

Pea protein &
whey protein



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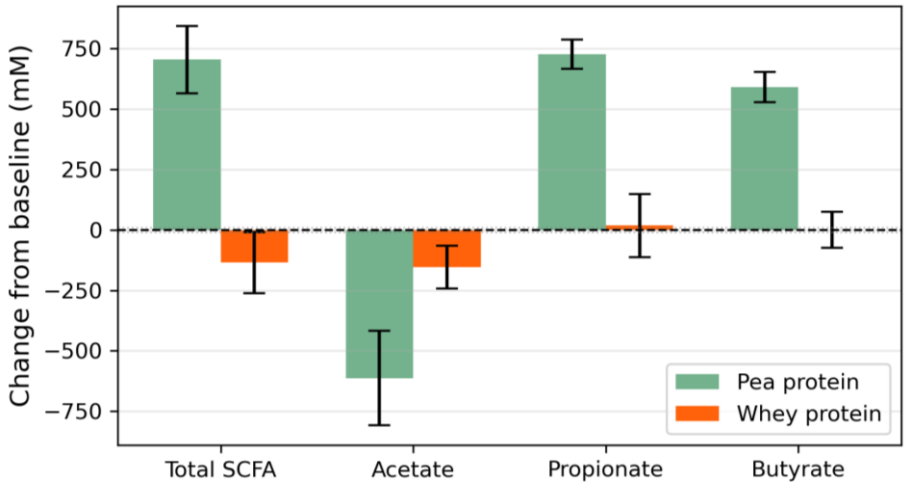

Functional changes

GCMS quantification of change in short-chain fatty acid concentration from baseline to end of dosing period

- Pea protein
- Whey protein

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Biology defines new Engineering.

Biologist's needs are continually changing, creating new engineering demands.

Animal models

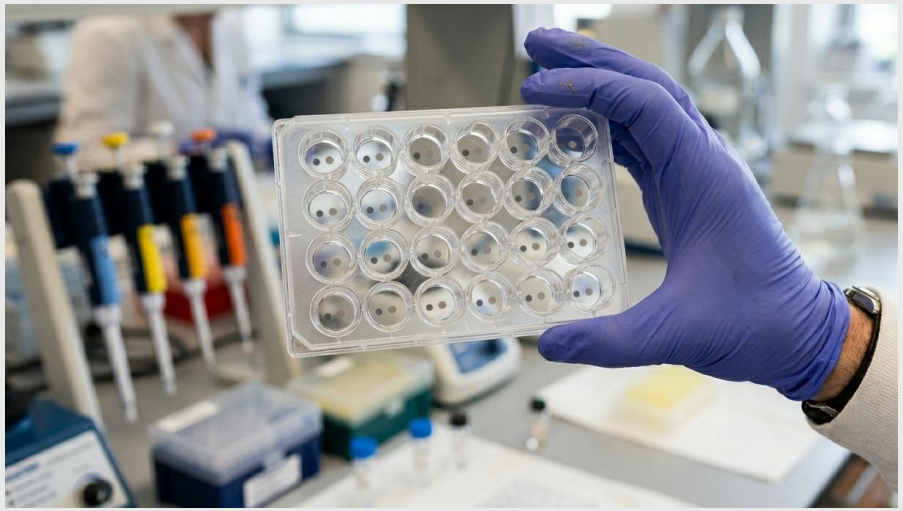
Adapting MiGut to simulate animal microbiomes, starting with pigs (RoboHog).

Simulating disease

Adapting MiGut conditions to replicate disease-specific environment: modified flow rate, pH, oxygen.

Batch culture system.

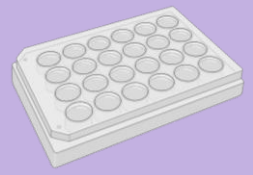
Developments in rapid screening and early-stage product development through a plate-based batch culture system.



What's next: screening at scale.

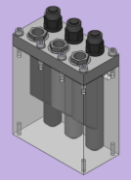
MiGut delivers fidelity, but throughput and cost are still restrictions for high-throughput early-stage screening studies.

Lessons learned from MiGut, applied to a scalable batch culture.



Batch culture.

Screen extensive list of candidates in simple model, taking days not weeks.



MiGut.

Validate results and demonstrate mechanisms of action.

One platform, two scales.

Shared culture conditions and cross-validation ensure results translate between platforms.

End-to-end microbiome research service.

Plan.

Define objectives, design study, agree scope and costs.

Run.

MiGut studies executed in our laboratories to client-defined design.

Analyse.

Targeted qPCR, 16S, metabolomics – in-house or via partners.

Deliver.

Custom report, raw data files, publication support.

Modular engagements from single-arm pilots to multi-donor, multi-intervention studies.

Scientific input throughout – not just bench time.

MicroMimetics

MicroMimetics is a commercially-operated research services unit at the University of Leeds, offering access to MiGut and associated microbiome analytics on a flexible, project-by-project basis.

We work with food, pharma, and biotech partners and welcome academic and industry collaborations. If you have a research question that need in vitro models, please get in touch.

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