Big Idea Workshop Summaries

Mathematical Modelling for Next Generation Formulated Products

Summary of Virtual Workshops Held Between

25 – 27 Nov 2020

This document details the outputs of three sessions held between the 25th – 27th November 2020. The sessions were to engage more widely researchers and industrialists in the Big Idea submitted by PepsiCo to EPSRC on mathematical modelling for next generation formulated products. The sessions aimed to answer three specific pieces of feedback, namely to:

- Broaden engagement from a range of academic disciplines and industries
- Target the applications and what the bid would enable in various sectors
- Articulate excitement for the lay audience. Why should BEIS be interested in this? How can this idea appeal to the public?

The following report is in the form of unattributed comments collected during the workshop which have been subsequently clustered and order by KTN. The salient points have been fed into the proposal resubmission.

Table of Contents

Introduction

The drive towards rapid, smarter, greener and personalised formulation requires the development of innovative mathematical approaches which are predictive. Understanding microstructure, complex processes, perception and how these can be linked, will unlock productivity gains in formulation sector.

Sessions held between the 25th and 27th November focused on pharmaceuticals, food & drink and FMCG & speciality chemicals. KTN and EPSRC are grateful to all participants, in particular Gavin Reynolds, Ian Noble, and Jonathan Booth for chairing each session and providing sector specific context. Additionally, we would like to thank Helen Wilson, Rosemary Dyson, John and Hilary Ockendon for their invaluable support throughout the process.

The Big Ideas Framework aims to identify and prioritise new "Big Ideas" from the research community. Big Ideas should be be ambitious and have the ability to transform the research landscape. They should be able to attract public, industry and government enthusiasm and excitement. Big Ideas provide a mechanism which enables EPSRC to respond to a changing environment. They are assessed by EPSRCs Science, Engineering and Technology Board (SETB).

Members of the mathematical sciences community met in Cambridge in February 2020 to develop thoughts around what a Big Idea in physical modelling for formulation science might look like. KTN and PepsiCo developed this into a bid in April 2020 which was assessed over the Summer.

The workshops in November, and this document overview the reaction from as wider a community as possible to the proposal strengths, weaknesses, and valuable input on how to refine the bid for resubmission in December 2020 / January 2021.

Letters of support which have been gratefully received during the proposal preparation are added at the end of this document.

Initial Reactions

Delegates were provided the original proposal in advance to review, in addition, PepsiCo provided an introduction to the proposal by video. To highlight the mathematical elements, the academic organisers of the Cambridge meeting in February (which initiated the proposal) gave an overview on what the mathematical innovation involved might look like. The below three subsections provide a snapshot reaction to the proposal from the delegates Wordclouds generated live during the sessions using menti.com. Delegates listed on page 17.

Proposal strengths

Figure 1. Strengths from pharma session

Figure 2. Strengths from food & drink session

Figure 3. Strengths from FMCG & speciality chemicals session

Recurring themes across the sessions include; multidisciplinary, ambitious, cross-cutting, distinctive, original and relevant as highlighted strengths.

Proposal weaknesses

Figure 4. Weaknesses from pharma session

Figure 5. Weaknesses from food & drink session

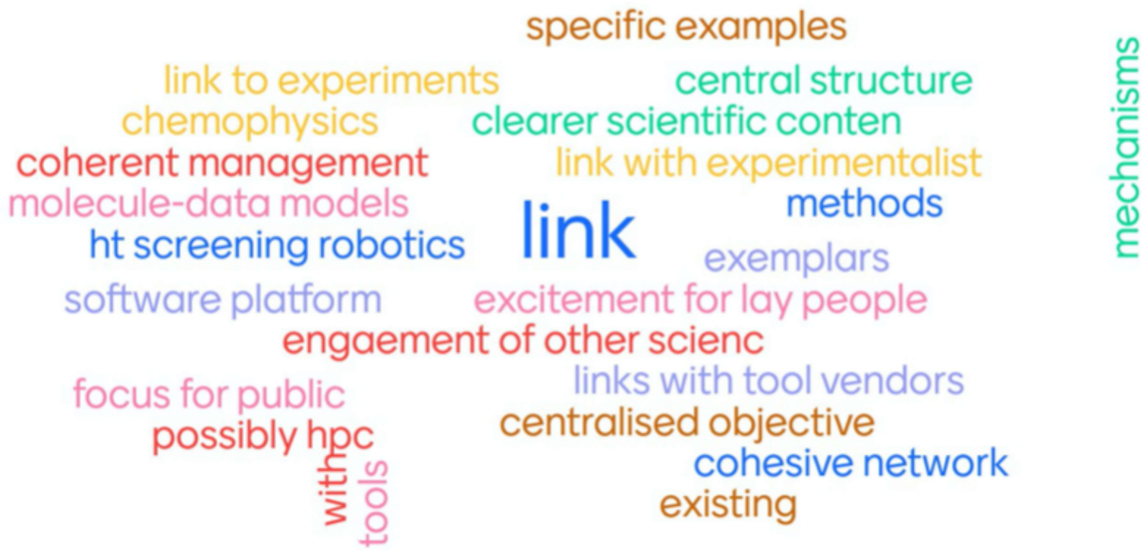

Figure 6. Weaknesses from FMCG & speciality chemicals session

There were a number of recurring themes the delegates identified as weaknesses including, engagement with experimentalists, links with other sciences, data. The rest of this report aims to address these perceived weaknesses.

How much support is there for the proposal?

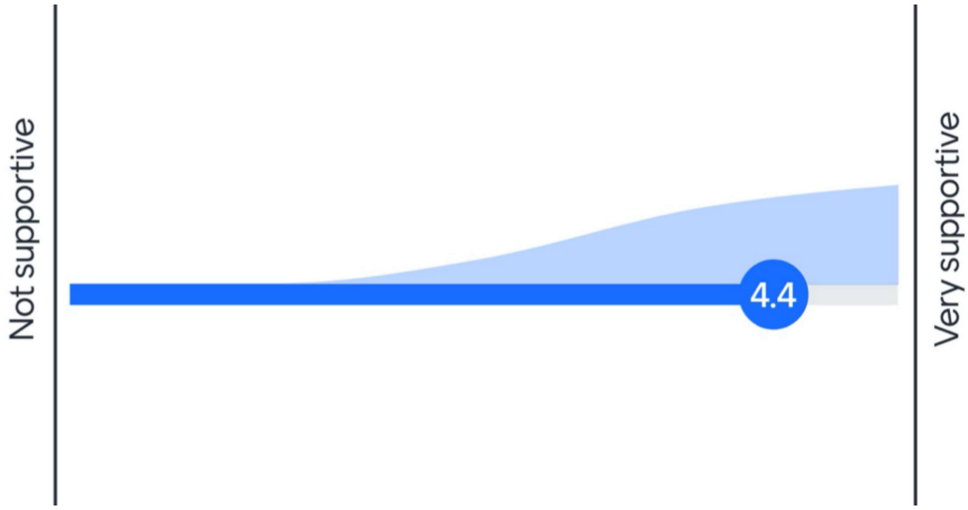

Figure 7. Support from the pharma session

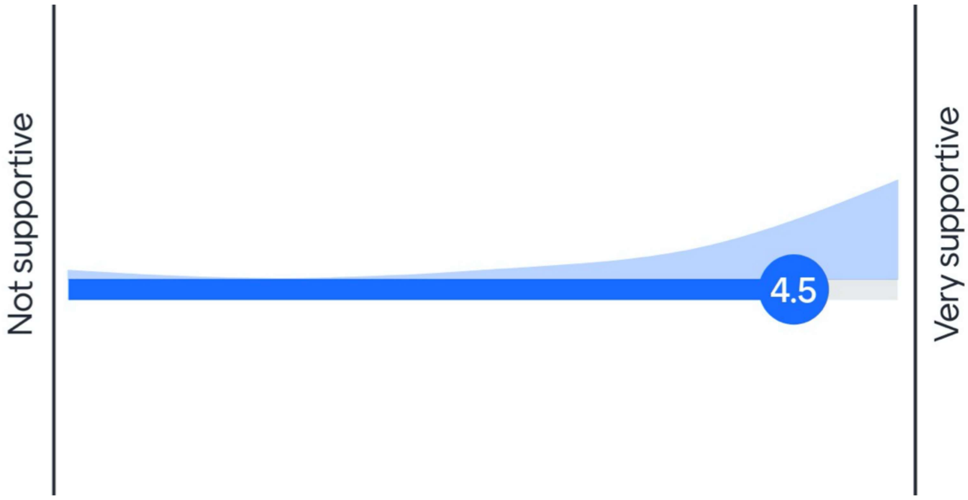

Figure 8. Support from the food & drink session

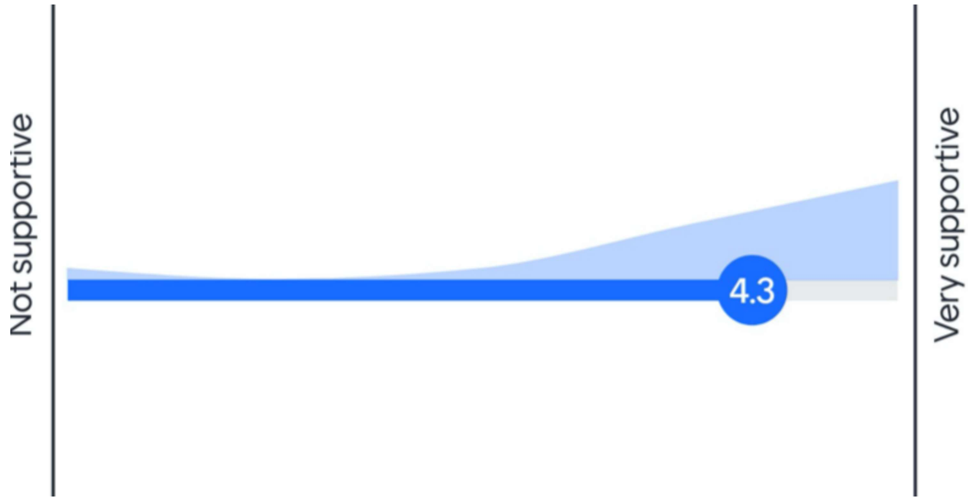

Figure 9. Support from the FMCG & speciality chemicals session

Articulating the Excitement

This section addresses the SETB feedback; *"articulate excitement for the lay audience. Why should BEIS be interested in this? How can this idea appeal to the public?*'. Participants across the three sessions were asked to comment on how to articulate the excitement of the economic, social and environmental opportunity.

It was highlighted by many participants that relevant case studies which demonstrate the benefit and impact of mathematical sciences to this sector would be beneficial to the bid. Whilst the participants were aware of many examples of engagement, many were proprietary. The MIIS Eprints Archive [1] overviews many relevant and interested examples. We list here but one relevant Impact Case Study from the 2014 REF exercise, and two from 2004 European Study Group with Industry to demonstrate the broad applicability of these methodologies..

Mathematics in the design and manufacture of novel glass products

https://impact.ref.ac.uk/casestudies/CaseStudy.aspx?Id=20200

The glass industry uses theoretical modelling to control, improve, and reduce the cost of designing and manufacturing novel glass products. Market-leaders [text removed for publication], Schott AG and Pilkington have developed modelling software which is underpinned by equations stemming from research at the University of Oxford.

[text removed for publication]. The same modelling approach is used in software developed by Schott which is now used in all of its modelling of drawing processes to reduce both development costs and the incidence of faults. Pilkington have implemented research performed at the University of Oxford to decrease the risk associated with manufacturing processes.

1 http://miis.maths.ox.ac.uk/miis/view/companyname/

Two-phase modelling of air bubbles in ice cream

http://miis.maths.ox.ac.uk/miis/24/

Ice cream is essentially a foam consisting of air bubbles dispersed in a mixture of fat, water and ice crystals. The air fraction is typically around 50% by volume, and this is crucial for the product to have the consistency and texture desired by customers. A common manufacturing method involves mixing the air and other ingredients under high pressure before discharging the product to atmospheric pressure for further processing. As the pressure is released, air may escape from the foam into the atmosphere. The Study Group was asked to quantify this air loss and to predict how it might depend on, for example, the rheological properties of the foam mixture, the bubble size distribution and the rate at which the pressure is released.

'Mud-cracking' in a latex paint film

http://miis.maths.ox.ac.uk/miis/406/1/ici.ps

Decorative latex paints consist mainly of polymer latex, titanium dioxide pigment (TiO2) and water. In the past, coalescing solvents were used which plasticise the latex and improve its flow, but nowadays the pressure us on to produce paints free of such organic solvents. Mineral extenders such as chalk, clay and talc are frequently added. As well as reducing the price of production the extenders alter the colour and the opacity of the paint, in particular since their inclusion ensures that air will be incorporated during drying. At the so-called critical pigment volume concentration (CPVC) there is just enough latex to encapsulate fully the TiO2 and extender. Beyond CPVC air is entrained, and failure in terms of cracking is observed in the drying film […] we discuss possible models for the stress build-up in the paint layer.

The below sets out broader areas which frame the exciting opportunities this bid would unlock. The below are KTN interpreted notes from the workshop sessions

- **COVID19 related opportunities.** In the early onset of the pandemic, there was a rapid need for alcoholic gel thickener, and formulation organisations were required to pivot to produce at scale. There was lots of trial and error for regulatory hurdles and customer acceptance. A more rigorous approach could speed this process up. Additionally, vaccines must be correctly formulated for them to be developed quickly, and work at room temperature.

- **Excitement around the scale, scope, and diversity of market.** Pharma, FMCG, food products are huge to the UK economy - far more than aerospace and automotive. In 2016, the formulated product industry contributed in excess of £ 149 bn to UK GVA [2]. The spill over economic impact is harder to measure, however advances in nutrition and drug design (expanded below) and manufacture will have a direct impact on the NHS and the economy. The business ecosystem is diverse, comprised of large and small companies. A programme in this space which democratises the outputs could bring benefit to small, local businesses as well as multinationals.

- **What could this proposal do for a patient, consumer, or customer?** Linking the bid to the consumer, patient, or customer was a recurring theme. As well as the personalisation aspect described below, the groups discussed the opportunity of more affordable, accessible medication with an improved efficacy of drug use. With a better understanding of mechanistic formulation processes, the bid could unlock opportunities around creating products which are nutritious, as well as pleasurable. There is also a direct link with the public in engaging them in projects around sensory perception.

- **Opportunities to personalise nutrition, and medication.** An end-to-end modelling capability could lead to personalised products to help different age or health groups, e.g. personalised products for diabetics. This was felt to be a very exciting area which could be delivered, turning individual preferences in the full spectrum of formulated products into consumer products with reduced, costly design cycles.

- **Responding to consumer trends and regulations.** The delegates felt that the direct link with consumer trends, and changing habits was an important one to convey in the bid. There is an increasing demand for plant-based products which could be supported by this bid. Foods which have as few ingredients and processing steps as possible - clean

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2 https://admin.ktn-uk.co.uk/app/uploads/2018/07/Formulated-Products-Sector-Strategic-Priorities-2018-Final.pdf

label – are particularly attractive. Wider than food, this bid can engage society in a conversation around more sustainable, green products.

- **A healthier society.** Wider than at the consumer-level, diet is essential for long term health and healthcare costs in the UK. Formulation for healthier ingredients that the consumer will eat – i.e. still tastes good – is essential. Removal of salt and fat and increasing use of vegetables as example drivers could position the UK in leading the world in the development of safe, high quality, inexpensive food, that could even shift population behaviour to a more nutritious, sustainable diet.

- **Formulating with new ingredients.** For a variety of reasons, formulations need to be adaptable to new ingredients additions. This may be due to regulatory changes, supply chain disruptions which lead to substitutions, a broader range of plant-based raw materials being introduced to increase biodiversity etc. These new ingredients will come with a lack of historical data and expertise when used in new formulations. The quality of the product shouldn't be compromised. A mechanistic modelling capability which is agile and adaptable, whilst capturing the intrinsic uncertainty in these novel ingredients is required to handle these dynamically.

- **Waste and sustainability opportunities.** Cutting down waste in the formulation design, manufacture and use stages could be seen as an enabler to the Governments Net Zero strategy. In the design phase, effective models could create less waste from the fewer experiments (often with valuable raw ingredients). Manufacturing processes which are optimised with mathematical models will also drive waste down. When considering end of life, models which better predict ingredient shelf life would reduce waste. The knock-on effect would be valuable virgin resource not being lost. Linking these phases, a better understanding of material behaviour could be an enable to the circular economy; can we use waste products from one process to develop new / replacement products in another? Can we model what effect this would have on performance?

- **Economic advantage for UK manufacturing.** Reducing expensive modelling / experimental / evaluation cycles would have a knock-on effect on productivity in this vast UK manufacturing sector. Predicting the correct formulation will reduce iterative research costs, and bring new products to market quicker, the link to vaccines and therapeutics was felt to be a compelling example. Proper understanding and modelling of formulation will help the UK do well in high-quality manufacturing, as we must be high quality to compete with other countries.

- **Excitement around multidisciplinary.** A final opportunity which should be conveyed is the academic opportunity regarding the sheer size of the multidisciplinary research effort required. There is a huge opportunity related to the applicability of these advances, the potential of high impact academic journals and patents.

Targeting Applications in the Formulation Space

This section addresses the feedback *"target the applications and what the bid would enable in various sectors"* from SETB. Participants across the three sessions were asked to comment where the limitations in current approaches are as a way to address what the programme would deliver. The below text is taken from the workshop delegates without attribution.

Without wishing to be prescriptive, below are three specific applications this bid could support. Broader areas are then introduced as areas the bid should address and why they are important to various sectors.

Powder compaction and fusion

Powder compaction and fusion are common processes across the formulated product sector. Take for example, the forming of paracetamol into tablets. An important task is to predict macroscale material properties after compaction of a powder to form a solid. How does this vary with changes in the input materials? What is the evolution of microstructure through compaction? It is vital to understand these processes and the variables which determine them to reduce tablet failure and achieve the required dissolution processes in the mouth and body.

Bubble growth in complex heterogeneous materials

Bubble nucleation and growth occur in many formulated product sectors. In many cases, the control of these bubbles ultimately determines the final performance of the product. Take for example the growth of bubbles in a material which is being flash fried. An important task is to model the final microstructure of a solid foam through expansion, solidification and shrinkage to predict the texture, wall crust formation etc. which ultimately is the USP of the fried product.

Chewing and swallowing

Chewing is an important process for the breakdown of food and pharmaceutical products within the mouth. Although saliva can chemically break down carbohydrates within the mouth, the timescales on which this occurs are unlikely to be important over then timescale the products spend within the mouth. A project could take existing models of the mechanoreceptor, and develop improved mechanoreceptor models for wet, in-mouth environment and development of models for taste and olfactory receptors. Development and analysis of the sensory networks based on known locations of the receptors. Additionally, the modelling of the breakdown of the material in mouth is also required.

The formulation industry lags behind other industries in terms of using computer modelling to help, due in part to mathematical limitations and experience in modelling by formulators. In some formulation industries, there is a dependence on one expert who knows what to do when something goes wrong, but this often limits progress to local parameter spaces. This results in current formulation being more of an art than a science. This is fine until something changes (new ingredients for example) and the formulation no longer works. The sectors reliance on a trial-and-error development of novel formulations acts as inertia against fast moving development.

- **Variability and uncertainty.** There was a common theme across the sessions around limitations in capturing the variability of real materials; input uncertainties and a lack of standardised methods for recording them. Often this is dealt with conventionally in design of experiments, but without a more mechanistic understanding. The opportunities around bio-based raw materials, often more variable quantities, make the need for methods which capture and propagate uncertainty pressing. Model based uncertainty; on process equipment modelling for example is also often not captured and quantified making comparisons, and reproducibility hard.

- **Understanding consumer needs.** The delegates discussed the need for methods which can robustly measure peoples reporting of sensory perceptions and other non-quantitative measures both across people and across time. The measures need to be transferable and ideally standardised. These measures are variable across consumers, one size does not fit all, how to accommodate in computer models?

- **Complexity.** The intrinsic complexity of the challenges create limitations in the current industrial practice. There is a need for programmes and mechanisms which are truly multi-disciplinary. The problems of interest here are messy, and not always of academic interest. Often there is a lack of understanding in the fundamental science to a level which is good enough to model. Modelling programmes are often too focussed on separate parts of a problem, which never get reassembled to provide more general insight, for example, microstructure does not explain everything; multi-component formulations may have multiple chemical interactions going on at the same time. Often, the mindset in industry is that the more you include in a simulation the better the results, there is a challenge / need to cut through this complexity, without becoming so coarse as to not provide value.

- **Coarse-graining models.** Building on the complexity points above, complex molecular dynamics simulations must be turned into empirical models to provide an input into mesoscale models. This coarse graining into empirical models is required so that the systems can be looked at properly. However, this coarseness inhibits progress in fundamental understanding of first principles.

- **Limitations in multiscale modelling.** Formulation processes are complex and require many approaches at different scales. There is a tradition of isolated modelling approaches which focus on one scale with very little interface between them. Formulation processes (and experimentation) are long-timescale, simulations are short timescale. There is a huge gap between low-level intuitive, simple models and huge “model everything” approaches with limited insight being gained. Being able to connect different models across different length-scales and insight into how to bridge problems which are too big for discrete models, and too small for continuum methods.

- **Difficulties with linking to real world experiments.** Experiments are sometimes performed on length-scales that are not the same as length-scales that capture the physics, can this bid unify the two? Models / simulations are too complex / cumbersome for many industrial experimentalists

- **Intellectual property barriers.** Particularly in the pharma session, it was felt that there are limitations in sharing pre-competitive modelling approaches due to IP issue. What is needed are reference cases which new tools could be standardised against to be maximal use to other sectors.

- **Lack of data.** There is a lack of experimental data for comparison hampered by the lack of standardised data collection which can be shared across platforms. Data in needed from industry on products which comes with commercial sensitivities. This industrial data can also have issues with ‘quality’.

Broadening Engagement

This section addresses the feedback *“broaden engagement from a range of academic disciplines and industries”* from SETB. Participants across the three sessions were asked to comment where the multi-disciplinary elements of the proposal are.

We feel this response is well-informed as we were represented by many disciplines; shown in the **People consulted** section of this report. These participants included mathematical scientists, industrialists and other academic disciplines in a nearly equal split. Across all the sessions we had representation from, mathematicians, chemical engineers, data scientists, food scientists, physicists, and engineers.

Because of funding constraints historically, projects look at one small aspect of the challenge. The problems in these sectors are extremely complex and need lots of different skills, so it is a perfect candidate for Big Ideas type of funding. Broadening engagement is vital for how to deliver the aims of the bid. Below we highlight a number of the areas a cross-discipline programme need to address to achieve the ambition:

- **Encoding complexity into the language of mathematics.** Using mathematics as the core discipline across the bid, we can identify overlaps between industries and develop a common language, making the translation more efficient.

There is a continuum of length and time scales which underpin the formulation sector. The delegates felt it important to link together the different scales; from molecule to manufacture to performance. How to establish a universal framework requires collaboration to understand the underpinning science and also what needs to be passed from one scale to another. What is the correct length scale to be thinking about in each problem? How should this be linked to the performance assessment?

- **Links with atomistic modellers.** There is a wealth of research in UK universities and industry on atomistic models; density functional theory, molecular dynamics and quantum simulations which would form part of the programme.

- **Links across industry using microstructure.** At a larger scale, the microstructure is of vital importance. Additionally, the microstructure is a great unifying concept as applications of the microstructure are very similar across pharma, healthcare, foods, paints, creams, soft solids atc.

- **Links with continuum modelling.** There are a wealth of problems to be studied regarding phase change of materials heat transfer, material and fluid flows and mixing, multiphase non-equilibrium systems, powders and granular flow, soft matter and rheology, coalescence and breakup. All these areas have expertise within physics, chemistry and engineering who could provide valuable insight into the programme.

- **Links within the mathematical sciences.** It should be noted that it was felt this proposal could develop strong links with other areas of the mathematical sciences, e.g. modelling, optimisation, numerical analysis, geometry, topology, graph theory, set theory etc.

- **Links to the biological sciences.** As many of the discussed applications have links with the human body, the delegates felt a strong link with biological sciences would be made. For example, models which predict adsorption of chemicals into the skin for pharmaceutical applications. Oral adsorption modelling for pharmaceutical and nutritional applications. For dysphagia and oral processing, the bid could involve psychologist-speech therapists, sensory scientists, and odontologists to support. Redesigning processes biomimetically to handle a greater degree of plant material variability could enable the UK to build biodiversity through market pull.

- **Links to the social sciences.** Perception is a vital aspect to the bid, and methods to provide a mathematical parametrisation and framework for this could be explored. People consume / engage with products differently. These differences could be due to their culture, past experience, exposure, etc. This bid could understand how these perceptions manifest, and provide tools to model products to cater to them,

- **Links with experimentalists (Imaging, sensing and characterisation).** The ability to parameterise models with experimental results and characterisation whilst providing insight into areas which are not directly measurable. For example, models could inform experimentalists in biology, chemistry, food chemistry based on results from mathematical models and simulations

- **Link with computation and simulation.** The bid would enable a connection with the state of the art in computational physics and simulation. The bid considers how to turn the models into effective simulations by using fast and effective computational methods.

- **Link with IT and programming skills.** The participants felt there was an important enabler required for adoption which could be in the form of an automated pipeline / platform for the mathematical models. The bid could provide a plug and play modelling environment, where new mathematical models could be implemented in an accessible reproducible open framework.

People consulted

Last Name	First Name	Title	Company Name
Abrahams	David	Director, Isaac Newton Institute	University of Cambridge
Aitken	Mungo	Student	University of Cambridge
Alberini	Federico	Lecturer	University of Birmingham
Amador	Carlos	Principle Scientist	Proctor & Gamble
Ang	Caroline	Manager of the Institute for Mathematical Innovation	University of Bath
Babasola	Oluwatosin	PhD Student	University of Bath
Bayly	Andrew	Chair of Chemical Engineering	University of Leeds
Beverly	David	Process Scientist	Diageo
Booth	Jonathan	Lead Technical Scientist	Croda
Bows	John	R&D Director and Global R&D Fellow	PepsiCo
Breward	Chris	Academic	University of Oxford
Budd	Chris	Professor of Applied Mathematics	University of Bath
Bugg	Dean	Formulated Materials Development Manager	Scott Bader Co LTD
Butchers	Matt	Industrial Mathematics	KTN
Charalambides	Maria	Professor	Imperial College London
Chen	Tao	Reader	University of Surrey
Cowley	Stephen	Senior Lecturer	DAMTP, University of Cambridge
Deacon	Benjamin	PhD Student	University of Surrey
Denmark	Willem	Principal Researcher	CPI
Donaldson	Joe	Computational Physicist	Unilever

Last Name	First Name	Title	Company Name
Drakopoulos	Alexis	Research Engineer	Intellegens
Drap	Oliver	Business Development	Pfizer
Dyson	Rosemary	Reader in Applied Mathematics	University of Birmingham
Engmann	Jan	R&D Expert	Nestlé Research
Field	Jamie	Product Innovation Technologist	Britvic
Findlay	Rachel	Senior Data Scientist	CPI
Finney	Karen	MRC Programme Manager	Medical Research Council as part of UKRI
Gibbon	Simon	CoP Leader	AkzoNobel
Goddard	Ben	Reader in Applied Mathematics	University of Edinburgh
Hardalupas	Yannis	Professor of Multiphase Flows	Imperial College London
Hodgson	Daniel	Director of Edinburgh Complex Fluids Partnership	University of Edinburgh
Holland	Sonia	Research Scientist	Diageo
Icardi	Matteo	Assistant Professor	University of Nottingham
Ilg	Patrick	Associate Professor in Theory of Soft Matter	University of Reading
Ingmire	Tim	Head of Research, Development and Quality	Quorn Foods
Ioannou	Phivos	Principal Engineer - Modelling & Simulation	The MTC
Kalogirou	Anna	Assistant Professor in Applied Mathematics	University of Nottingham
King	John	Professor	University of Nottingham
Koumakis	Nick	Post-doctoral researcher	University of Edinburgh
Kowalski	Adam	Modelling and Analytics	Unilever
Kusumaatmaja	Halim	Associate Professor	Durham University

Last Name	First Name	Title	Company Name
Kyprianou	Andreas	Professor of Mathematics, Director of the Institute of Mathematical Innovation	University of Bath
Lacey	Andrew	Professor of Applied Mathematics	Heriot-Watt University
Lee	William	Professor of Industrial Mathematics	University of Huddersfield
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Lopez Quiroga	Estefania	Lecturer	University of Birmingham - CDT in Formulation Engineering
Mottram	Nigel	Professor	University of Glasgow
Murray	Brent	Professor of Food Colloids	University of Leeds
Noble	Ian	Senior Research, Development & Quality Director	Mondelez International
O Conchuir	Breanndan	Research Staff Member	IBM Research
Ockendon	John	Retired	Oxford University
Owen	Jade	Senior Scientist	Johnson Matthey
Parker	Ritchie	Process Modelling Group Manager	Nestlé
Parr	Andrea	Business Development Manager	CPI
Pelan	Eddie	Professor of Formulation Engineering	University of Birmingham
Perry	Richard	Head of Data	Sterling
Please	Colin	Prof of Applied Mathematics	University of Oxford
Powell	Hugh	Academic & Research Partnerships Lead	Nestec York Ltd
Reynolds	Gavin	Principle Scientist	AstraZeneca
Rodriguez Garcia	Julia	Lecturer in Food Science and Technology	University of Reading

Last Name	First Name	Title	Company Name
Shah	Nilay	Professor	Imperial College London
Shendruk	Tyler	Reader	University of Edinburgh
Singleton	Colin	Technical Director	CountingLab Limited
Tayeb	Tariq	Business Development Manager	CPI
Thijssen	Job	Reader	ECFP
Thoukididou	Lia	Innovation Executive	FDF
Titmuss	Simon	University Lecturer	University of Edinburgh
von Gerichten	Johanna	PostDoc	University of Surrey
Watson	Nicholas	Associate Professor of Chemical Engineering	University of Nottingham
Westwood	Joseph	Senior Portfolio Manager	UKRI EPSRC
Whitehead	Tom	Head of Machine Learning	Intellegens
Wildman	Ricky	Professor	University of Nottingham
Williams	Rebecca	Senior Portfolio Manager	EPSRC
Wilson	Stephen	Professor of Applied Mathematics	University of Strathclyde
Wilson	Helen	Professor of Applied Mathematics	University College London
Wolf	Bettina	Professor of Microstructure Engineering	University of Birmingham
Zhang	Jason	Senior Lecturer	University of Birmingham
Zillmer	Ruediger	Senior Data Scientist	Unilever R&D

Letters of Support removed for publication

Connecting for
Positive Change

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