Capillary action occurs when the cohesive forces that hold molecules together in a fluid work together with the adhesive forces that cause the fluid to cling to a solid surface (such as the wall of a tube), thereby pulling the liquid in a given direction. Gravitational forces act against capillary action when fluid rises vertically. Capillary flow in simple systems, such as tubes, can be described mathematically by considering the interplay between these various forces. The capillary rise in Dudukovic and colleagues' unit cells is more complex than that in tubes, and so the authors derived a theoretical model that describes how strut diameter and the number of cells coupled together influence the overall capillary action of a cellular fluidics system.

The fabrication of open structures, such as Dudukovic and co-workers' unit cells, can be difficult to achieve using many of the methods typically used in microfluidics. The authors therefore used 3D printing to build up their unit cells layer by layer. This is an attractive option because one can think of a design in the morning, then draw a model using computer-aided design programs, upload the file to a 3D printer and simply press 'start'. A working prototype can be ready by the end of the day. 3D printing is also appealing because of the range of materials that can be printed, from hard resins for prototypes of diagnostic devices to biocompatible gels for tissue engineering. However, in many applications it is necessary to produce structures that are fabricated from multiple materials.

Cellular fluidics provides a solution to this problem. Dudukovic *et al.* show that, by adjusting the size, shape and density of the unit cells in a 3D structure, fluid flow can be controlled and guided along a chosen path (Fig. 2). This provides a way to coat specific unit cells in a structure with metal: when solutions of appropriate catalysts and reagents were channelled along a particular pathway, only the cells in that pathway were metallized when the whole structure was subsequently immersed in a plating solution. The authors used this approach to coat selected regions of a cylinder-shaped structure with metal, producing concentric rings that alternated between being electrically conductive and non-conductive (see Fig. 6e of the paper[1]). The researchers also suggest that the ability to channel fluids to specific areas of a structure could be used to deliver fluids within artificial organs.

Fluidic systems based on unit cells have been developed previously[6,7], and a limitation of Dudukovic and colleagues' work is that it largely reports known physical phenomena. However, a key advance of the present study is that it considerably increases our understanding of fluid flow in coupled unit-cell structures. We look forward to future applications in which cellular fluidics is used to investigate unknown physical principles or to fabricate novel multi-material structures. This technological platform opens up many exciting opportunities for research and is a valuable addition to the open-microfluidics toolkit.

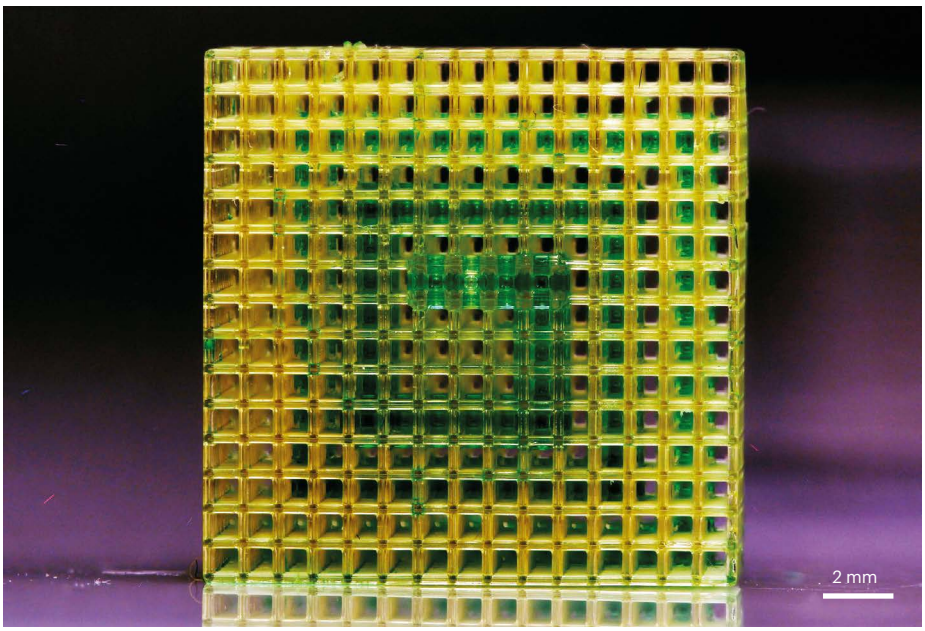

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Figure 2 | Selective fluid flow in 3D structures. Dudukovic *et al.*[1] demonstrate that the flow path of a fluid through 3D cellular fluidics structures can be precisely controlled by altering the size, shape and density of unit cells. Here, a green fluid passes along a spiral path.

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A.B.T. declares competing interests: see go.nature.com/3gwlr44 for details.

Microbiology

Designer fibre meals sway human gut microbes

Avner Leshem & Eran Elinav

Understanding how diet affects gut microbes and thereby influences human health might lead to targeted dietary strategies. A clinical trial now provides some steps on the path towards this goal. **See p.91**

There is growing evidence that our normal resident gut microorganisms, termed commensal microbes, can affect human health. Promoting beneficial commensal microbes through a type of nutritional supplement called a prebiotic is an area of intensive scientific and medical research. However, trying to harness a diet with the desired effect is challenging because the gut microbial community (also known as the microbiome) is highly complex, and because dietary responses are modulated by multiple hereditary and non-hereditary factors. On page 91, Delannoy-Bruno *et al.*[1] fill an essential gap in our mechanistic understanding of diet–microbiome interactions by focusing on dietary fibre, a family of substances of pronounced physiological virtues that are predominantly metabolized by commensal

microbes. This provides a sequel to the team's previous work on the development of microbiome-targeting foods[2–6].

To characterize the effect of dietary-fibre supplementation in overweight individuals, Delannoy-Bruno and colleagues used germ-free mice — animals raised and maintained in a sterile environment that are therefore devoid of the usual resident microbes of any sort. The team colonized the gut of each of nine mouse groups with the microbiome of one of nine women classed as obese. The mice were continuously fed a low-fibre, high-fat diet, coupled with periodic fibre supplementation (Fig. 1). Their microbiome was characterized to assess gene content (the level of particular genes present) before, during and after each episode of fibre supplementation. Building on previous work by this team[5], which identified fibres that promote the growth of certain intestinal bacteria (those of the genus *Bacteroides*, which are less prevalent than normal in obese individuals), Delannoy-Bruno *et al.* chose three types of fibre that were fed sequentially to the mice. Each supplementation cycle was followed by a 'washout' period to enable intestinal clearing of the fibres, thereby allowing the authors to discern the effect of every individual type of fibre as distinct from the other fibres.

Human-microbiome-inoculated mice showed pronounced compositional shifts in their gut microbes in response to fibre supplementation. To identify fibre–microbe interactions and subtract irrelevant 'noise' in the data arising from normal fluctuations in the microbiome profile, the authors used a feature-reduction approach termed higher-order singular value decomposition. This revealed that exposure of the microbial population to a particular fibre resulted in a greater presence of genes that encode proteins needed for the metabolism of that fibre. For example, consumption of cellulose-containing pea and orange fibre led to a higher representation of genes encoding the β-glucosidase enzymes that hydrolyse such fibre, probably owing to the proliferation of bacteria that can use cellulose as an energy source. Interestingly, in mice inoculated with human microbiomes, similar signatures of fibre-responsive genes became highly abundant through the expansion of various bacterial taxa including, but not limited to, *Bacteroides*. The bacterial taxa that rose to dominance shared a competitive advantage in their response to the presence of the respective fibre. This highlights that a shift in microbial gene abundance, rather than a shift to a particular community structure in terms of the species present, is a common denominator in the response pattern to dietary interventions across individuals.

The authors then examined whether these findings have relevance to human biology. They characterized the microbiome of 12 overweight or obese study participants before, during and after pea-fibre dietary supplementation. To minimize the effect of microbiome variations stemming from dietary differences between individuals, participants were given meals consisting of a uniform high-saturated-fat, low-fibre diet (equivalent to the type of diet the mice were placed on). The microbial gene responses to fibre supplementation in humans largely resembled those observed in mice.

The authors also tested whether consumption of multiple fibre types results in a greater microbiome shift than was observed upon consumption of pea fibre alone as a supplement. For this study, a group of 14 individuals received a diet supplemented with a combination of two and then four types of fibre. The results indicate that the more types of fibre an individual consumes, the greater the rise in the number of microbial genes present that are involved in fibre metabolism. Changes in fibre-responsive enzymes closely correlated with changes in the plasma levels of proteins that are associated with specific metabolic and immune functions, as revealed by the analysis of blood samples from participants.

The emerging concept of precision nutrition proposes that human dietary responses are specific to food components, and that these components might be tailored to the individual to optimize their dietary response. Such responses are quantifiable and driven by a number of variables, including features of the food components (such as protein, carbohydrate and fat), the individual's physiological traits, and gut microbiome composition and function. Indeed, it has been suggested that the gut microbiome is a key modulator of physiological food responses and associated differences in such responses between individuals[7,8]. Current US dietary guidelines recommend that healthy adults ingest at least 14 grams of fibre per 1,000 calories consumed[9], with no individualization specified in terms of the fibre type or intake in grams. Delannoy-Bruno and colleagues' findings provide a framework that paves the way for optimizing an individual's fibre consumption, based on fibre type and their microbiome fibre-degradation signatures.

The authors' results underscore the considerable plasticity of the gut microbiome and its amenability to manipulation by prebiotics. Fibre-degradation capacity in individuals with habitual low levels of fibre consumption is not necessarily irreversibly diminished, but rather might be recovered by increasing their fibre consumption through combinatorial fibre selection[10–13]. Furthermore, the findings by

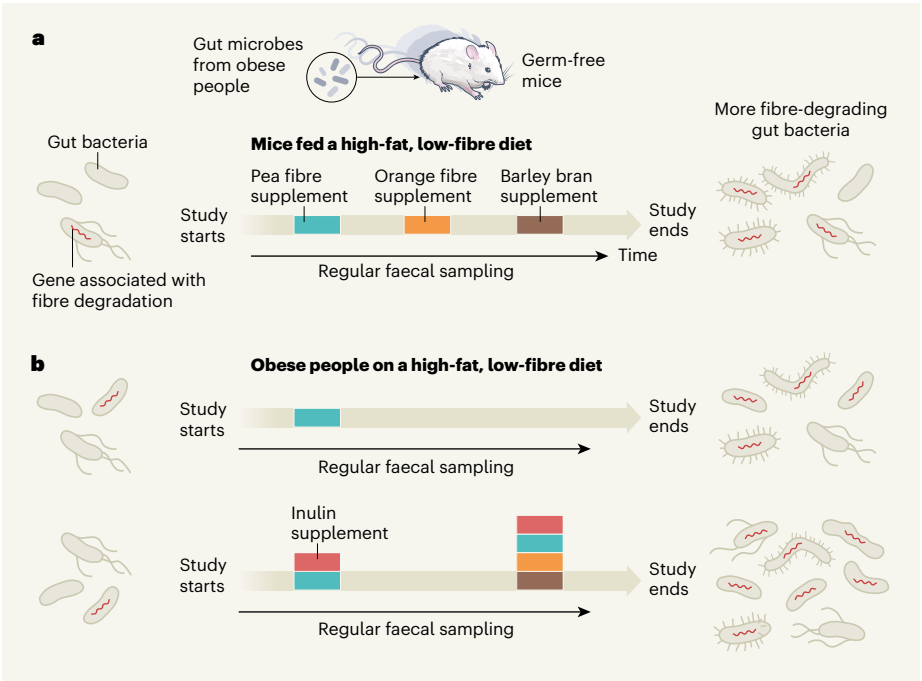

Figure 1 | Assessing the response to dietary fibres. Evidence-based dietary interventions to target gut microbes might offer a way to boost human health. **a**, Delannoy-Bruno *et al.*[1] analysed germ-free mice, which lack their natural gut microbes. These animals had their gut colonized with microbes from obese individuals. The animals received the type of diet associated with obesity, plus fibre snacks (pea fibre, orange fibre and barley bran) as indicated. The authors tracked the genes associated with intake of a particular type of dietary fibre by analysing microbial DNA in faecal samples. Each period of fibre supplementation resulted in an increase in the abundance of genes related to degradation of the fibre, presumably because the presence of the fibre gave a competitive advantage to bacterial species harbouring those genes. **b**, The authors carried out a similar type of experiment in a human clinical trial, which corroborated the results of pea-fibre consumption in mice. A dietary-supplement regime that combined multiple types of fibre (including inulin) led to a substantial increase in the number of genes present that were associated with fibre degradation.

Delannoy-Bruno *et al*. demonstrate that dietary responses might be mainly determined by the levels of relatively sparse microbiome genes (that become predominant after a dietary intervention), stressing the importance of studying diet–microbiome interactions at the level of genes. Different microbial communities in individuals contributed to these distinct functional capacities, highlighting the possibility that microbiome function (genes), rather than species composition, might correlate with personalized human physiological responses to food.

In some situations, the metabolic and immune-system characteristics of germ-free mice harbouring human microbiomes might affect the validity of using these animals as human surrogates in an experimental context[14,15]. Nevertheless, the fibre-degrading properties of the mice analysed by Delannoy-Bruno *et al*. were strikingly similar to those of humans. This suggests that human microbiome colonization in germ-free mice might be a relevant tool for studying the causal drivers of diet–microbiome interactions and their effect on the mammalian host.

Such studies would greatly benefit from the development of computational-analysis tools that can identify temporal trajectories of microbial genes in response to dietary interventions, in both human donors and mice who receive microbial transplants. In this study, the authors used one such tool, higher-order singular value decomposition, which uncovered a profound microbiome gene response to dietary-fibre supplementation despite the modest sample size. Further refinement of such analytical pipelines, by the expansion of microbiome genome-level databases of gene functions and the incorporation of protein-level features, will probably aid further decoding of the contributions of the dietary–microbiome axis to host physiology.

Delannoy-Bruno and colleagues' findings provide valuable mechanistic insights into the microbial contributions to human dietary responses. This will probably lead to long-term, randomized clinical trials that assess causal links between distinct food ingredients, microbiome modulation and downstream health-related outcomes for humans. Indeed, this research team recently reported[2] that a data-driven dietary intervention targeting the microbiome helped to promote growth in undernourished children. The advances made by Delannoy-Bruno *et al*. bring us closer to the integration of precise microbiome engineering with evidence-based dietary sciences.

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E.E. declares competing financial interests: see go.nature.com/3cgrukn for details.
This article was published online on 23 June 2021.

Ecology

Migratory birds distribute seeds to new climates

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Birds that travel long distances can disperse seeds far and wide. An assessment of the timing and direction of European bird migration reveals how these patterns might affect seed dispersal as the planet warms. **See p.75**

The rapid pace of global warming and its effects on habitats raise the question of whether species are able to keep up so that they remain in suitable living conditions. Some animals can move fast to adjust to a swiftly changing climate. Plants, being less mobile, rely on means such as seed dispersal by animals, wind or water to move to new areas, but this redistribution typically occurs within one kilometre of the original plant[1]. On page 75, González-Varo *et al*.[2] shed light on the potential capacity of migratory birds to aid seed dispersal.

When the climate in a plant's usual range becomes hotter than it can tolerate, it must colonize new, cooler areas that might lie many kilometres away. It is not fully clear how plants distribute their seeds across great distances, let alone how they cross geographical barriers. One explanation for long-distance seed dispersal is through transport by migratory birds. Such birds ingest viable seeds when eating fruit (Fig. 1) and can move them tens or hundreds of kilometres outside the range of a plant species[3]. In this mode of dispersal, the seeds pass through the bird's digestive tract unharmed[4,5] and are deposited in faeces, which provides fertilizer that aids plant growth. In the case of European migratory birds, for example, the direction of seed dispersal will depend on whether the timing of fruit production coincides with a bird's southward trip to warmer regions around the Equator, or northward to cooler regions. Many aspects of this process have been a mystery until now.

González-Varo and colleagues report how plants might be able to keep pace with rapid climate change through the help of migrating birds. The authors analysed the fruiting times of plants, patterns of bird migration and the interactions between fruit-eating birds and fleshy-fruited plants across Europe. Plants with fleshy fruits were chosen for this study because most of their seed transport is by migratory birds[6], and because fleshy-fruited plants are an important component of the woody-plant community in Europe. The common approach until now has been to predict plant dispersal and colonization using models fitted to abiotic factors, such as the current climate. González-Varo *et al*. instead analysed an impressive data set of 949 different seed-dispersal interactions between bird and plant communities, together with data on entire fruiting times and migratory patterns of birds across Europe. The researchers also analysed DNA traces from bird faeces to identify the plants and birds responsible for seed dispersal.

The authors hypothesized that the direction of seed migration depends on how the plants interact with migratory birds, the frequency of these interactions or the number of bird species that might transport seeds from each plant species. González-Varo and colleagues found that 86% of plant species studied might have seeds dispersed by birds during their southward trip towards drier and hotter equatorial regions in autumn, whereas only about one-third of the plant species might be dispersed by birds migrating north in spring. This dispersal trend was more pronounced in