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Scalable Processes for Culturing Meat Using Edible Scaffolds

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Abstract

There is increasing consumer demand for alternative animal protein products that are delicious and sustainably produced to address concerns about the impacts of mass-produced meat on human and planetary health. Cultured meat has the potential to provide a source of nutritious dietary protein that both is palatable and has reduced environmental impact. However, strategies to support the production of cultured meats at the scale required for food consumption will be critical. In this review, we discuss the current challenges and opportunities of using edible scaffolds for scaling up the production of cultured meat. We provide an overview of different types of edible scaffolds, scaffold fabrication techniques, and common scaffold materials. Finally, we highlight potential advantages of using edible scaffolds to advance cultured meat production by accelerating cell growth and differentiation,

providing structure to build complex 3D tissues, and enhancing the nutritional and sensory properties of cultured meat.

1. INTRODUCTION

Consumer demand for delicious and nutritious protein alternatives continues to rise alongside consumer concerns about the environmental impact of the mass production of animal food products (Aschemann-Witzel et al. 2021). The practice of growing animal-based meat ex vivo—or culturing meat—is emerging as a promising approach to producing animal protein. Cultured meat may improve the resiliency of food systems by diversifying protein production methods (Tzachor et al. 2021), which can help to ensure that nutritious, protein-rich food is accessible to everyone in the future. However, continued research and development are needed to advance processes to culture meat at the scale required for food production and to ensure that cultured meat is delicious, nutritious, and sustainable both economically and environmentally.

One major barrier to scaling up production of cultured meat is the technical challenge of engineering a complex tissue composed of multiple cell types and components ex vivo; this is amplified by the demands of commercial viability, including mass production, affordability, and, most importantly, consumer appeal (Pakseresht et al. 2022, Ruzgys & Pickering 2020, Tomiyama et al. 2020). Common cuts of commercially sold meat comprise skeletal muscle, which often contains intramuscular fat that contributes to meat texture and flavor (Aberle 2001, Listrat et al. 2016). Both muscle and fat cells naturally adhere to a surrounding matrix, enabling them to flex and exert biological tension; through cell–matrix interactions, cells sense mechanical cues, which can determine how quickly they grow and develop into tissue (Naqvi & McNamara 2020, Romani et al. 2021). For ex vivo culture, naturally adherent cells are commonly grown on Petri dishes (Butler 2003). To give a sense of scale, one 10-cm Petri dish can support the growth of ~1 mg of cells, which means that 1 kg (or 2.2 lb) of meat would require 453,592 Petri dishes! This is how the proof-of-concept cultured meat burger was produced in 2013 (Fountain 2013), but the excessive use of Petri dishes to culture the kilograms of tissue needed for food production would be costly and wasteful. Producing cultured meat at scale thus requires novel methods to increase the available surface area for culturing adherent cells while maintaining cost efficiency and sustainability.

Several scalable methods to culture mammalian cells and tissues have been developed for pharmaceutical and biomedical applications; however, supporting the scale-up of cultured meat production requires a different set of criteria, including edibility, sustainability, and affordability, to make products accessible to consumers. To scale up the culture of adherent cells, microcarriers—or bead-like particles—are commonly used in bioprocessing with suspension bioreactors (Li et al. 2015); bioreactor vessels are well established in the food industry (e.g., beverage fermentation) and pharmaceutical industry (e.g., drug and vaccine production). However, commercially available microcarriers are typically inedible and would need to be separated from cells for cultured meat upon harvesting, adding postprocessing steps and hindering the scalability of production. Another approach is to grow naturally adherent cells in a suspended state, which is compatible with large-scale suspension bioreactors. The development of suspension cell lines has been successful in the biomedical sciences (Shen et al. 2019) and for chicken fibroblasts (Pasitka et al. 2023); however, the development of suspension cell lines requires time-intensive adaptation or genetic modification, and consumer concerns about genetically modified cells may pose a challenge for larger-scale adoption of cultured meat products (Mohorcich & Reese 2019).

Edible scaffolds provide an attractive strategy to scale up the production of palatable and delicious cultured meat. Culturing cells on edible scaffolds obviates the need for postprocessing

separation of cells from microcarriers at harvest. For example, cell-laden edible microcarriers can be harvested directly from a suspension culture into a cultured meat product (Liu et al. 2022, Norris et al. 2022, Yen et al. 2023). Moreover, cells in skeletal meat are naturally adherent, and cell–matrix interactions can regulate cellular behaviors (**Figure 1**). Edible scaffolds can also support structural organization within a tissue, such as a structured cultured steak. However, producing structured cultured meat presents another unique set of challenges. Growing tissue with >1 mm thickness in the absence of vasculature does not allow for media and oxygen diffusion on timescales of cellular metabolic activity, which can impede tissue growth and survival (Jain et al. 2005). In addition, generating skeletal muscle that contains fat requires different cell types, which have varying scaffold requirements that are challenging to achieve in coculture. Generating edible scaffolds with customized physical properties for different types of cells—including muscle and fat cells—can present a solution to engineering multicomponent cultured meat with improved texture, tenderness, juiciness, and flavor.

In this review, we discuss edible scaffolds as a solution to scale up cultured meat production based on our knowledge of literature within the public domain. We provide an overview of different types of edible scaffolds, scaffold fabrication techniques, and common scaffold materials. Finally, we highlight potential advantages of using edible scaffolds to advance cultured meat production by accelerating cell growth and differentiation, providing structure to build complex 3D tissues, and enhancing the nutritional and sensory properties of cultured meat.

2. ENGINEERING EDIBLE SCAFFOLDS FOR SCALABLE CULTURED MEAT PRODUCTION

Edible scaffolds have the potential to increase the efficiency of cultured meat production and contribute nutrient-rich mass, texture, and mouthfeel to final cultured meat products. Scaffolds also provide opportunities to create cultured meats with different textures and structural features with defined length scales, such as the fibrous structure of natural skeletal muscle or the organized integration of intramuscular fat or marbling that is highly prized in meat across many cultures (Aberle 2001). Here, we review different methods to generate edible scaffolds and the opportunities and challenges of applying these scaffolds to cultured meat at scale.

2.1. Scaffold Fabrication Techniques for Cultured Meat

Scaffolds can be fabricated to have different shapes, geometries, and mechanical properties across micro- to macro-scales. Some scaffold fabrication techniques enable control of scaffold properties that can be harnessed to promote cell and tissue growth via cell–matrix interactions (**Figure 1**). The physical properties of scaffolds may also contribute to the overall texture and sensory properties of the resultant cultured tissues. Compatibility of fabrication techniques with existing industrial-scale processes may also be an important consideration in scaling up cultured meat production.

2.1.1. Edible three-dimensional porous scaffolds. Three-dimensional porous scaffolds (**Figure 2**) provide surface area on which cells for cultured meat can adhere and grow. Scaffold porosity also facilitates the exchange of oxygen and nutrients for cell growth.

2.1.1.1. Whole-tissue plant scaffolds by decellularization. One approach to making edible scaffolds is to decellularize or remove the cellular components from natural materials that have porous and veinous structures, for example, by using detergents or supercritical CO_2; this results in an intact, acellular structure that retains high levels of extracellular matrix (ECM) components (Gershlak et al. 2017, Seo et al. 2018) (**Figure 2**). Importantly, the natural structures and features

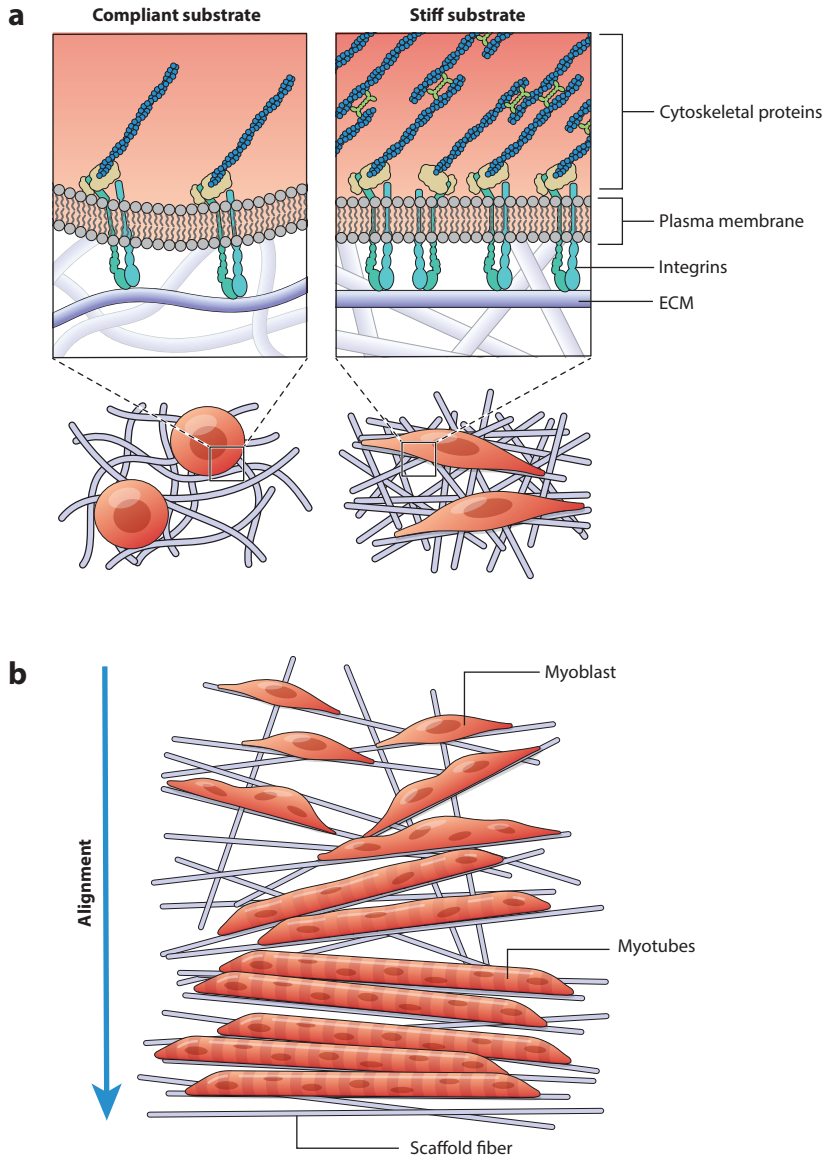


Figure 1

Scaffold mechanical and physical properties can regulate cell behaviors. Simplified schematic illustrations show two examples of matrix mechanical and physical properties that modulate cell behaviors. (*a*) On a compliant matrix, cells tend to have a lower density of integrin heterodimers (composed of α- and β-polypeptides) at the plasma membrane, which facilitate attachment to the extracellular matrix (ECM). By contrast, cells on a stiffer matrix tend to exhibit higher density and a larger number of integrins. Integrins interact with many ligands in the extracellular matrix including collagens, laminins, and fibronectins. Integrin-mediated mechanical signaling can drive cell behaviors such as proliferation and differentiation and is just one example of a mechanism that cells use to sense cues in their mechanical and physical environments. (*b*) Alignment of fibers in a scaffold can drive cell alignment and promote myoblast fusion and production of multinucleated myotubes. For more detailed descriptions of mechanisms involved in how cells sense and respond to mechanical and physical cues, we direct the reader to one of the many wonderful resources on cellular mechanobiology (e.g., Romani et al. 2021). Illustration by Yu-Ting Dingle.

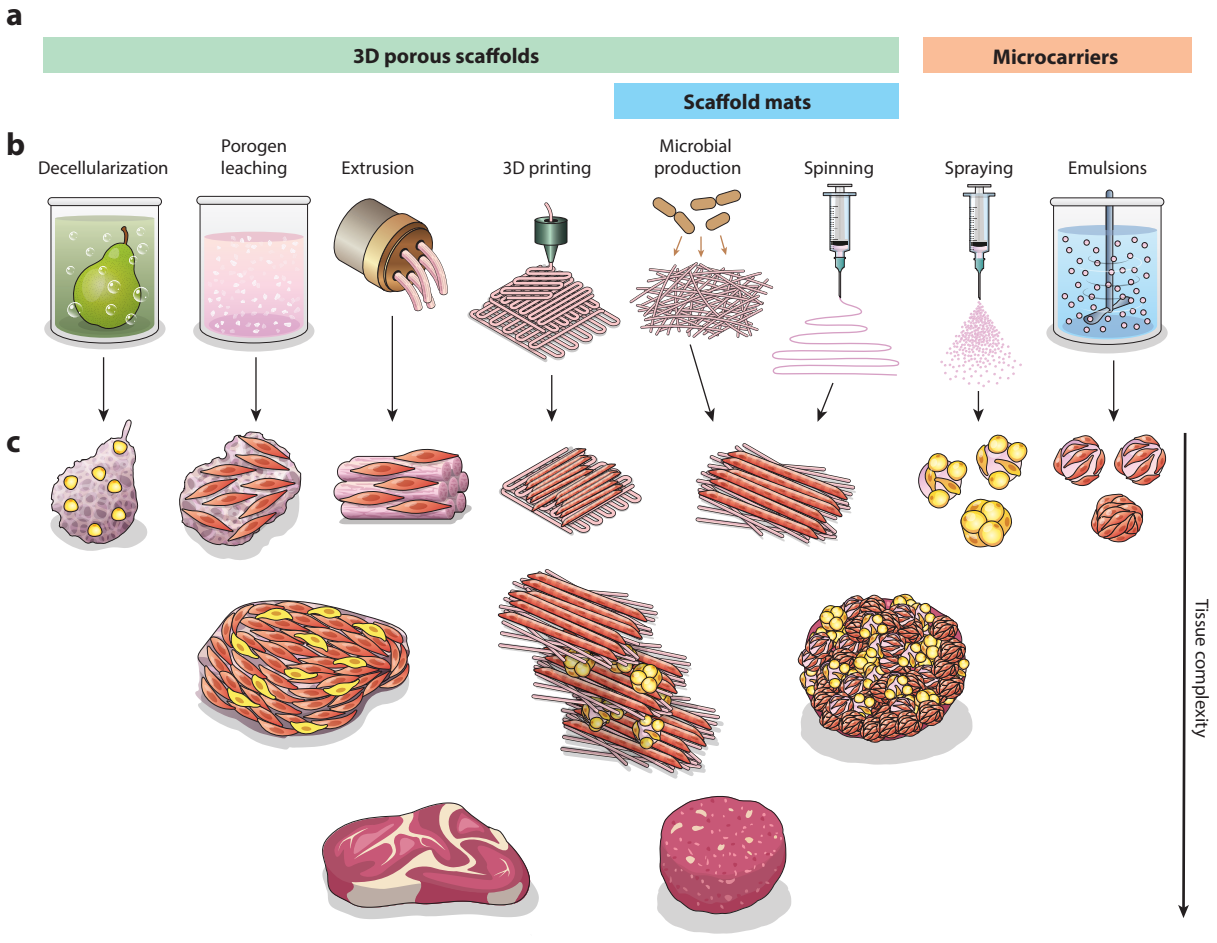


Figure 2

Overview of edible scaffold types and fabrication methods. (*a*) Major classes of edible scaffolds include 3D porous scaffolds, scaffold mats, and microcarriers. (*b*) Methods commonly used to fabricate scaffolds to support the growth and differentiation of mammalian cells. In some cases, aggregation of cells and scaffolds can occur in culture (as shown for the microcarriers), which results in cell-laden scaffolds that provide building blocks for the modular assembly of larger multicomponent tissues or cultured meat products. (*c*) Strategies for assembling tissue include seeding cells directly onto 3D scaffolds (top-down approach) and using cells or microtissues as building blocks to generate larger-scale tissue constructs (bottom-up approach). Images not to scale. Illustration by Yu-Ting Dingle.

from a wide variety of plant tissues can be harnessed to support tissue growth for cultured meat, from the highly aligned ~20-μm-wide vascular structures of celery stalks (Campuzano et al. 2020) to the ~100-μm-scale cell wall cavities of apple tissue (Modulevsky et al. 2014) and the ~2-mm-scale bead-like structures of broccoli florets that provide microcarriers with micron-scale porosity (Thyden et al. 2022).

Scaling up the production of decellularized scaffolds has potential given the ease of growing plants, but it will be critical to maintain optimal decellularization conditions, as excessive chemical treatment and mechanical agitation can result in scaffold degradation and/or the denature of ECM proteins (Adamski et al. 2018). A potential advantage is that decellularization can be achieved via other processes similar to industrial methods such as supercritical CO_2 (Seo et al. 2018), which is used to decaffeinate coffee beans (Chen et al. 2011). Decellularized scaffolds can also be fabricated

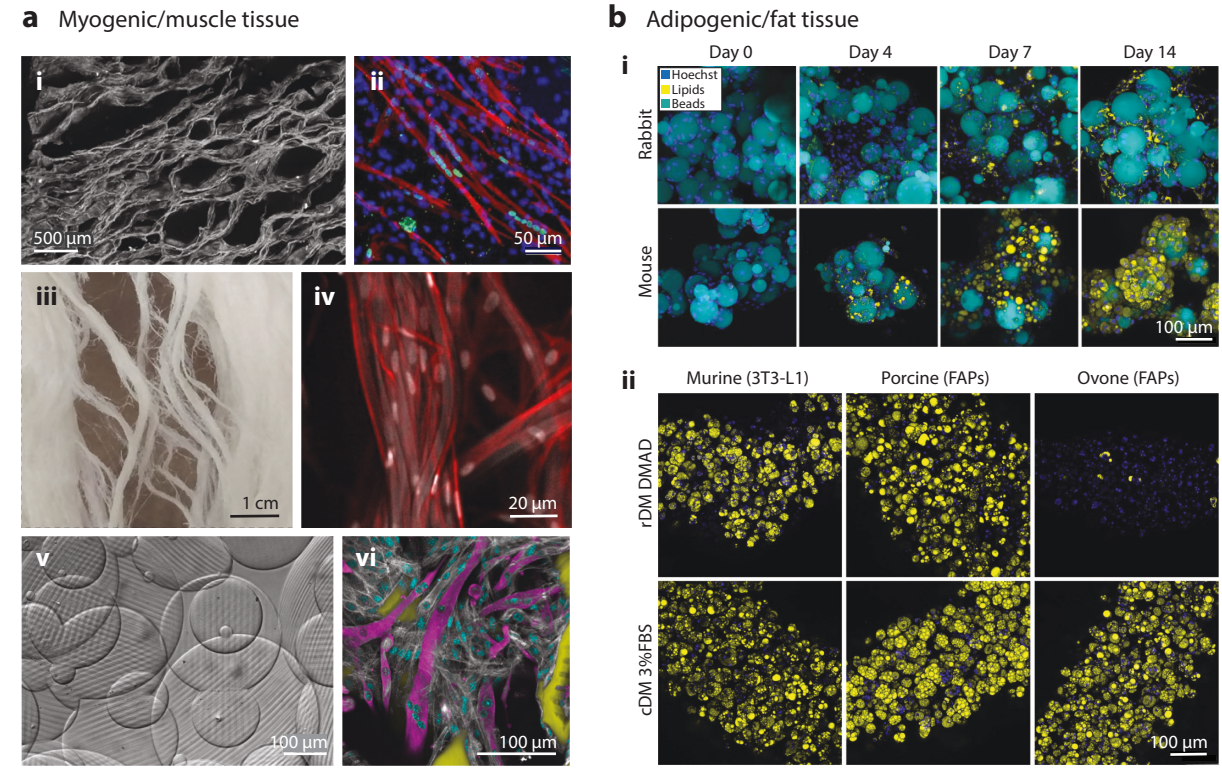
using ingredients upcycled from food waste (Perreault et al. 2023), which may contribute to a sustainable economy for cultured meat production. One downside is that decellularized scaffolds tend to require further treatment or functionalization to ensure adhesion of mammalian cells (Allan et al. 2021, Campuzano et al. 2020).

2.1.1.2. Porous scaffolds produced by fungi. The three-dimensional vegetative, thread-like structures called mycelia, which are produced by fungi, can also be harnessed as edible scaffolds (**Figure 2**). Composed primarily of natural polymers, including chitin and cellulose, the diameters of branching thread-like hyphae typically range between 1 and 30 μm depending on the fungal species; scaffold shape and size can be modulated by culturing mycelia using a growth substrate or vessel with defined geometries to generate scaffolds with varying 3D shapes and sizes such as pellets or mats (Dessi-Olive 2022, Letcher et al. 2022, Pereira et al. 2021). Mycelial scaffolds support the adhesion, growth, and differentiation of mammalian cells—such as primary human fibroblasts—after decellularization (Antinori et al. 2021, Letcher et al. 2022) or autoclaving to deactivate mycelial cells (Antinori et al. 2021). Such approaches have strong potential for scale-up, as harvesting products produced by microbes are commonly used in industrial fermentation.

2.1.1.3. Creating porous scaffolds using porogen leaching. Highly porous 3D scaffolds can be produced in a batch process by introducing a sacrificial material—or porogen particles—into a scaffold material, such as salt or sugars, which are then leached out to result in a porous scaffold structure (Wosek 2015) (**Figure 2**). By tuning the size of the porogen particles, pore size can be modulated from tens to hundreds of micrometers (Coogan et al. 2020), enabling scaffold customization for desired phenotypes of specific cell types (Zeltinger et al. 2001). Although porogen leaching has the potential to produce large volumes of scaffolds within a single batch and enables control over pore size, other scaffold features such as alignment are more challenging to control. Note that porogen leaching can be used in combination with other fabrication methods such as extrusion, spinning, or 3D printing to generate scaffolds with tunable porosity to promote cell growth and diffusion (Nguyen et al. 2021).

2.1.1.4. Extrusion for porous scaffolds. Widely used in the food industry from pasta to plant-based meats (Riaz 2000), extrusion can generate fibrous structures with a defined length scale from millimeters to centimeters by forcing a raw material to flow through an orifice. The structure and physical properties of the extruded material—or extrudate—can be tuned by adjusting the extrusion parameters such as the raw material composition (protein content, moisture), extrusion conditions (screw speed, temperature), and orifice diameter and shape (Alvarez-Martinez et al. 1988); the expansion of the material upon extrusion can introduce porosity into the resultant extrudate (Hu et al. 1996). The resultant fibrous structures that mimic muscle fibers—for example, by high-moisture extrusion of wheat gluten (Samard et al. 2019)—are valuable for plant-based meat analogs and could also provide scaffolds for cultured meat. Extrusion can also generate 3D-textured soy protein scaffolds with pores of ∼100 μm, which support the coculture of bovine satellite cells, smooth muscle cells, and endothelial cells (Ben-Arye et al. 2020) (**Figure 3*a*, subpanels *i,ii***). Extruded peanut protein scaffolds also support the adhesion and proliferation of porcine smooth muscle cells (Zheng et al. 2022). Extrusion methods can also be used to produce hydrogel fibers with larger ∼500–1,000 μm diameters, which can support the growth and differentiation of embedded cells (Mitic et al. 2023). Extrusion is already widely used in the food industry, so it has strong potential as a scalable process to generate edible scaffolds for cultured meat.

2.1.1.5. Three-dimensional printing of scaffolds. 3D printing relies on patterning extruded fibers with a diameter of ∼0.5–2 mm into scaffolds with intricate shapes and spatial organization (Dick et al. 2019, Kang et al. 2021) (**Figure 2**). The bioink can contain both cell and scaffold



(*Caption appears on following page*)

Figure 3 (*Figure appears on preceding page*)

Examples of current approaches using edible scaffolds to generate (*a*) myogenic (muscle) tissues; (*b*) adipogenic (fat) tissues; and (*c*) multicomponent tissues. (*a*, *i*) Confocal image of textured soy protein scaffolds. (*ii*) Representative confocal images of differentiated bovine satellite muscle cells on textured soy protein scaffolds after 4 d. Cells are stained to visualize desmin (*red*) and DNA (DAPI, *blue*). (*iii*) Gelatin fibers produced by wet spinning. (*iv*) Rabbit skeletal muscle myoblast cells cultured on gelatin fibers. Cells are stained to label nuclei (DAPI, *white*) and the cytoskeleton (F-actin, *red*). (*v*) Grooved gelatin microcarriers. (*vi*) C2C12 cells cultured and differentiated on grooved gelatin microcarriers (FITC, *yellow*), DNA (Hoechst, *cyan*), myosin heavy chain (Myh4, *magenta*), and F-actin (phalloidin, *gray*). Panel *a*, **subpanels *i*** and ***ii*** adapted with permission from Ben-Arye et al. (2020). Panel *a*, **subpanel *iii*** adapted from MacQueen et al. (2019) (CC BY 4.0). Panel *a*, **subpanels *v*** and ***vi*** adapted from Norris et al. (2022) (CC BY-NC-ND 4.0). (*b*, *i*) Primary rabbit subcutaneous adipocytes and 3T3-L1 murine adipocytes imaged at 0, 4, 7, and 14 days of differentiation. Images show DNA (Hoechst, *blue*), intracellular lipids (LipidTox, *yellow*), and gelatin microbeads (*cyan*). Panel adapted from Kawecki et al. (2023) (CC BY 4.0). (*ii*) Murine (3T3-L1), porcine, and ovine adipogenic tissue encapsulated in alginate hydrogel fibers and differentiated in serum (cDM 3% FBS) and serum-free media (rDM DMAD). Images show DNA (Hoechst, *blue*) and intracellular lipids (Nile Red, *yellow*). Panel adapted from Mitic et al. (2023) (CC BY 4.0). (*c*, *i*) Layer-by-layer assembly to generate rabbit multicomponent tissue. Shown here are cryosectioned samples stained for DNA (Hoechst, *blue*), Myh4 (*red*), intracellular lipids (Nile Red, *yellow*), and microbeads (*cyan*). False-colored images are used to visualize the organization and structure of myogenic (*red*) and adipogenic (*yellow*) microtissue layers. Panel adapted from Kawecki et al. (2023) (CC BY 4.0). (*ii*) Raw and cooked cultured meat prototypes generated using microtissues cultured using edible microcarriers. Panel adapted from Yen et al. (2023) (CC BY 4.0). (*iii*) Tendon–gel integrated bioprinting generates hydrogel fibers that contain different bovine cellular components. Whole fluorescence (*top*), optical (*inset*), and magnified (*bottom*) images of muscle on day 4 of differentiation stained for myosin heavy chain (MF20, *green*) and DNA (DAPI, *blue*), fat on day 14 of differentiation, stained for lipids (Nile Red, *red*) and DNA (DAPI, *blue*), and vascular on day 7 stained for CD31 (JC70A, *magenta*) and DNA (DAPI, *blue*). (*iv*) Images of cultured steak generated by assembling muscle, fat, and vascular cell fibers. View of the cross-section indicated by the dotted line. Muscle and vascular tissue labeled with carmine (*red*). Panel adapted from Kang et al. (2021) (CC BY 4.0). Abbreviations: cDM, control differentiation medium; CM, cultured meat; DAPI, 4′,6-diamidino-2-phenylindole; DMAD, defined animal component-free medium; FAPs, fibro-adipo-genic progenitor cells; FBS, fetal bovine serum; MHC, myosin heavy chain; Nu, nuclei; rDM, reduced differentiation medium.

materials to pattern complex tissues or even functional organs (Kang et al. 2021, Lee et al. 2019) (**Figure 3*c*, subpanels *iii*,*iv***). 3D-printing approaches are being explored to fabricate edible scaffolds for cultured meat applications (Handral et al. 2022), including using plant-based bioinks such as cereal prolamins (Su et al. 2023) and pea/soy protein isolates mixed with alginate conjugated with an arginine-glycine-aspartate (RGD) peptide (Ianovici et al. 2022).

The scalability of 3D printing for food applications remains a challenge. Producing large quantities of tissue required for cultured meat using 3D printing requires continuous extrusion without clogging. Moreover, although spatial patterning of multiple cell types into multicomponent tissues can be readily enabled by 3D printing, the higher extrusion pressures needed for print speed and spatial resolution of 3D tissue constructs may expose cells to shear stresses that reduce cell viability (Dong et al. 2023); this can be mitigated using lower pressures and larger nozzle sizes but compromises resolution and print speed (Murphy & Atala 2014). Further innovations to increase printing speed and resolution while remaining compatible with cell culture will be needed to scale up 3D printing for cultured meat.

2.1.1.6. Spinning techniques. Spinning of fibers involves extruding material through an orifice while applying an external force to manipulate fiber size and organization (**Figure 2**). Spinning can generate 3D scaffolds that mimic the naturally aligned structure of skeletal muscle by producing fibers with diameters from approximately 10 nm to 10 μm (Cramariuc et al. 2013); spinning techniques also allow for control over fiber alignment, the size of gaps or pores between fibers, and scaffold thickness (Cramariuc et al. 2013, He et al. 2018, MacQueen et al. 2019). Spinning can be categorized into different subtypes, including wet-spinning and electrospinning. Wet-spinning is the process of extruding material using rotational speed into a solution bath, enabling fabrication of ∼1–10-μm fibers. The wet-spinning approach can generate gelatin-based fibrous scaffolds that support the volumetric expansion and maturation of adherent muscle cells for meat analogs

(MacQueen et al. 2019) (**Figure 3*a***, **subpanels *iii,iv***). Electrospinning is widely used in tissue engineering to produce scaffolds with fibers approximately 10 nm to 1 μm in diameter by applying high voltage to the polymer solution during extrusion (Subbiah et al. 2005). Electrospinning is already being scaled for pharmaceutical and biomedical applications (Omer et al. 2021). However, electrospinning is sensitive to temperature and humidity, and needle nozzles are subject to clogging (Nieminen et al. 2018), which can be challenging to mitigate at a larger scale. The ability to fine-tune scaffold alignment while producing 3D structures makes it worthwhile to further explore the scalability of spinning techniques to make edible scaffolds.

2.1.2. Edible scaffold mats. Generating cultured meat by culturing cells on a 2D substrate—such as edible scaffold mats—can ensure a ready exchange of nutrients and gases, and the resultant cell-laden scaffolds can be layered to generate a 3D tissue construct with approximately centimeter thickness (Park et al. 2021) (**Figure 2**). Edible scaffold mats can be generated by electrospinning fibers into a layer with ∼100 μm thickness (Ahirwal et al. 2013). The secreted products of bacteria and fungi, such as bacterial cellulose (Chen et al. 2022) and filamentous mycelial mats (Narayanan et al. 2020), can also be harvested as scaffold mats. Other approaches to fabricating thin hydrogel mats for cell culture applications include templating hydrogels using elastomeric molds (Li et al. 2022) and extruding polymers through a micron-scale slot (Malladi et al. 2020).

The resultant cell-laden stacks of edible scaffold mats can be layered together to form a cohesive 3D tissue (**Figure 2**). Cross-linkers such as microbial transglutaminase—a.k.a. meat glue—can promote mechanical stability of the tissue construct (Yen et al. 2023). Cohesive, multilayered 3D tissues can also be achieved without the use of additional cross-linkers by relying on spontaneous adhesion that is mediated by cell–cell interactions (Furuhashi et al. 2021, Kawecki et al. 2023). Importantly, the resultant tissue constructs formed by layering myotube-laden gelatin scaffolds interspersed with fat-laden microcarriers show similar mechanical properties as conventional Wagyu beef steak (Kawecki et al. 2023). Scaffold-free tissue constructs can also be generated using cell monolayers detached from the culture surface (Tanaka et al. 2022). However, edible scaffold mats can enable customization of length scales of individual tissue components. For example, tuning the thickness of the scaffold mats can enable spatial patterning with ∼100–1,000-μm length scales of individual microtissue components in larger tissue structures, such as the thickness of muscle or fat features (**Figure 3*c***, **subpanels *i,ii***) (Kawecki et al. 2023, Yen et al. 2023). Further developments in automated tissue stacking will be necessary to make this approach amenable for cultured meat scale-up. Strategies to achieve spatial patterning using self-assembly of microtissues are particularly attractive to minimize energy inputs.

2.1.3. Edible microcarriers. The rich study of microcarriers as a substrate for culturing cells in suspension culture (Van Wezel 1967) provides a strong foundation for using microcarriers to culture meat. Importantly, culturing cells on microcarriers is compatible with suspension bioreactors, which presents the opportunity for edible microcarriers as a scalable process to culture meat. Edible microcarriers can be generated using varied approaches, including emulsions as templates and spraying techniques (Norris et al. 2022, Tokárová et al. 2013, Yuen et al. 2023) (**Figure 2**). Emulsion-templated gelatin microcarriers support the proliferation and differentiation of C2C12 muscle cells (Norris et al. 2022) (**Figure 3*a***, **subpanels *v,vi***). Although hydrogel microcarriers generated using bulk emulsions are polydisperse, the size distribution of particles can be tuned within a size range of 10–1,000 μm using filtration (Norris et al. 2022). Microcarriers can also be formed by depositing a suspension of scaffold material—such as collagen and/or eggshells—into a liquid nitrogen bath, which forms a solid microcarrier upon freezing (Andreassen et al. 2022). Electrospraying is commonly used to produce food-grade microparticles (Gómez-Mascaraque et al. 2015, Tomadoni et al. 2022). Edible chitosan-collagen microcarriers generated using

electrospraying support the adhesion and expansion of bovine mesenchymal stem cells (Yen et al. 2023). Spray drying is an industrial technique commonly used to convert liquid food products into powders (Piñón-Balderrama et al. 2020), but the use of spray-dried microcarriers to support cell culture is currently limited (Huang et al. 2018a). Compared to other types of scaffolds, microcarriers provide a scaffold with a high surface-area-to-volume ratio, which can have benefits for cell growth, including proximity to immobilized or encapsulated ingredients such as growth factors that promote cell proliferation. Encapsulating nutrients or flavor compounds in microcarriers could also boost cultured meat's nutritional properties or flavor.

There may be some limitations to using edible microcarriers for scaled-up cell culture. In reactors with agitation or sparging, hydrodynamic stresses can reduce cell growth (Chisti 2000, Humbird 2021). Cells may also be damaged by fluid shear stresses as well as microcarrier–impeller and microcarrier–microcarrier collisions (Cherry & Papoutsakis 1988, Humbird 2021). Yet edible microcarriers may hold benefits that streamline the downstream processing of cultured meat. Edible microcarriers can be harvested together with cells from a suspension bioreactor and incorporated directly into a blended cultured meat product, such as a burger or meatball (Liu et al. 2022, Norris et al. 2022, Yen et al. 2023), or even a structured 3D multicomponent tissue or cultured meat product akin to a steak (Kawecki et al. 2023, Yen et al. 2023) (**Figure 3*c***, **subpanels *i*,*ii***). Interestingly, microcarriers in suspension culture aggregate with cells to form larger-scale microtissues with ∼100–1,000 μm dimensions; this provides an opportunity to modulate the size of microtissues in a cultured meat product (**Figure 2**; **Figure 3*a***, **subpanel *vi***; **Figure 3*b***, **subpanel *i***). Microtissues can also be used to assemble macroscale tissues using a modular approach with other scaffold types, such as edible scaffold mats (Kawecki et al. 2023, Yen et al. 2023) (**Figure 3*c***, **subpanels *i*,*ii***).

2.1.4. Challenges and opportunities in methods for fabrication and application of different scaffold types for cultured meat. The different scaffold fabrication techniques we highlight here provide a toolbox to engineer scaffolds that can be customized to mimic the physiological environment of different cell types and/or achieve desired properties in cultured meat. Some considerations when deciding on a scalable fabrication method and scaffold type include:

- **Culture efficiency:** The ability to fabricate customized scaffolds has the potential to accelerate behaviors of specific cell types, which could ultimately improve the efficiency of cultured meat growth. For example, scaffold mechanics and topography could be customized to increase cell proliferation or promote myogenesis or adipogenesis. In other contexts, we anticipate that the same scaffolds could be used for culturing different types of cells; the integrin adhesome is largely conserved across mammalian cell types (Zaidel-Bar 2009), so the same scaffolds could be used to support myocytes, adipocytes, and even endothelial cells (**Figure 3**).
- **Tissue structure:** Scaffolds with different geometries, shapes, and structural features could be used to generate cultured meat with specific length scales, translating to advantages for the texture and organization of cultured meat products. The surface-area-to-volume ratio of different scaffold types has implications for both cell growth and the volume of scaffolding material in the final cultured meat product. For example, scaffold mats can support the culture of cells in 2D layers, which facilitates the diffusion-mediated exchange of nutrients and metabolites but may introduce a larger volume of scaffold into the final tissue construct. On the other hand, microcarriers have a high surface-area-to-volume ratio, which provides an optimal solution to increase culture area in suspension culture and minimize the volume of scaffold in the final cultured meat product. The physical properties of scaffolds can also determine the extent of ECM production and matrix remodeling by cells (Zeltinger et al.

2001), which will be important for the final structure, texture, and, potentially, regulatory approval of cultured meat.

- **Compatibility with industrial-scale processes:** The compatibility of different types of scaffolds with current bioreactor technologies is another consideration for scale-up. Some scaffolds—such as edible microcarriers—are compatible with stirred tank bioreactors, whereas other scaffold types may necessitate the design of new bioreactors for larger-scale culture. Some fabrication methods for generating scaffolds—such as electrospinning and emulsion templating—are already operational at an industrial scale and may be more easily adapted for larger-scale production of cultured meat. However, it remains to be seen how the production of scaffolds and/or cultured meats could be sustained at larger culture volumes.

2.2. Scaffold Materials for Cultured Meat

The choice of materials for scaffolds has impacts across length scales from the attachment and growth of cells to the sensory and textural properties of the final cultured meat product; the sourcing, sustainability, and availability of scaffold materials are also important considerations. To generate scaffolds for cultured meat, natural polymers commonly found in the foods we eat, such as collagen, cellulose, and alginate, are promising candidates, as they are generally recognized as safe for consumption (Biswas et al. 2022) and can form hydrogels, which are cross-linked polymer networks with similar structure to the ECM (Drury & Mooney 2003). The physical properties of hydrogels can be modulated to define scaffold mechanical properties by adjusting total polymer content or cross-linking density or even the choice of polymer to generate a linear or nonlinear elastic material.

2.2.1. Animal-derived molecules for scaffolds. Animal-derived biomaterials are attractive as scaffold materials, as they tend to be derived from the ECM and thus naturally promote cell adhesion. For example, gelatin provides an edible scaffold material for muscle and fat cells (MacQueen et al. 2019, Negrini et al. 2019, Norris et al. 2022); collagen (Antoine et al. 2014), hyaluronic acid (Collins & Birkinshaw 2013), and fibrin (Janmey et al. 2009) are widely used in biomedical tissue engineering applications. The use of animal by-products in cultured meat can contribute to a sustainable circular economy (Jurgilevich et al. 2016), but sourcing scaffold materials that are not reliant on livestock agriculture could diversify supply chains for cultured meat production. To assess the true cost of scaffolds generated using animal by-products, further evaluation of process efficiency and environmental impact is needed. Further, some consumers may prefer products that do not rely on animal-derived materials (Pakseresht et al. 2022).

2.2.2. Molecules from plants and microbes for scaffolds. Plant- and microbially derived biopolymers provide attractive sustainable materials for scaffolds; such scaffold polymers will also be critical for creating meat analogs for consumers who prefer cultured meat products that do not contain scaffold ingredients sourced from animals. Cellulose, fungi-derived chitin, and lignin are the three most abundant natural polymers on Earth (Banwell et al. 2021). Plant-derived products, such as textured soy protein, zein, and glutenin, can also be used to fabricate scaffolds that support the growth of muscle cells (Ben-Arye et al. 2020, Wei et al. 2023, Xiang et al. 2022). Existing food-grade production methods for many of these ingredients could provide abundant and reliable sources of scaffold materials to support a cultured meat supply chain. Decellularization of plant tissues provides another source of cellulose-rich scaffolds (Allan et al. 2021, Campuzano et al. 2020, Modulevsky et al. 2014). Polysaccharide networks produced by bacteria—such as cellulose mats (Chen et al. 2022)—or the chitin-rich fungal networks of mycelia (Dessi-Olive 2022)

can also support the growth of relevant cells for cultured meat (Letcher et al. 2022, Wang et al. 2018).

One challenge with plant-derived scaffolds is that mammalian cells do not readily adhere to plant-derived polymers (Samir et al. 2022). Chemical modifications, such as conjugating cell adhesion ligands (e.g., with RGD and/or dopamine) onto the polymers or altering surface charge, can promote cell adhesion, proliferation, and differentiation (Courtenay et al. 2017, Custódio et al. 2010, Kummala et al. 2020, Rowley & Mooney 2002). However, chemical modifications require additional processing, which can raise concerns for food safety and may face additional regulatory hurdles (Gu et al. 2023). Pre-soaking naturally textured scaffolds in cell media containing fetal bovine serum (Allan et al. 2021, Campuzano et al. 2020) or coating plant scaffolds with gelatin (Lee et al. 2022) can also promote cell attachment and growth. It will be valuable to explore other avenues to promote cell adhesion—for example, by generating topography (Ranucci & Moghe 2001)—to ensure compatibility of abundant plant-derived materials for cultured meat.

2.2.3. Harnessing host organisms to produce proteins for animal-free scaffolds. Efforts to produce animal proteins for scaffolds without animal inputs are underway, relying on host organisms that genetically encode for the protein of interest and then purifying through downstream processes (Huang et al. 2018b). Precision fermentation uses microbial hosts, for example, to produce the heme protein that is used in commercially available plant-based meat products (Shao et al. 2022). Scaffold proteins such as collagen, gelatin, and hyaluronic acid can also be produced using precision fermentation (Báez et al. 2005, Chong et al. 2005). Producing animal proteins for scaffolds using plants, or molecular farming, is another strategy with high potential for scale-up (Buyel et al. 2017, Stein et al. 2009, Twyman et al. 2003). Although plants and prokaryotic hosts provide a promising approach to producing animal-free scaffold proteins, strategies for post-translational modifications will be important to achieve the higher-order protein structures, which are important for mediating cell–matrix adhesion (Bansode et al. 2020). Additional downstream processing is also required to harvest proteins generated using heterologous expression technologies; however, such approaches nonetheless provide exciting potential to support the scalable production of scaffolds for cultured meat.

2.2.4. Challenges and opportunities in materials for scalable scaffolds. The choice of materials for fabricating scaffolds will have direct impacts on the scalability of cultured meat. Important considerations in material choice include:

- **Sourcing scaffold ingredients:** To meet the demands for protein-rich foods in extreme environments and during societal instabilities, scaffold ingredients should come from stable supply chains. Upcycling food processing by-products or food waste products, such as pectin, presents a potential opportunity for sustainable production of scaffolds.
- **Sustainability:** Plant-based scaffold materials may be desired by consumers for environmental or ethical reasons (Tomiyama et al. 2020), but a major challenge is to develop scalable strategies to promote cell adhesion. Rigorous evaluations, including techno-economic assessment (TEA) and life-cycle analysis, will be needed to assess the true economic feasibility and environmental impact of any scaffold ingredient.
- **Compatibility with industrial-scale processes:** The compatibility of materials with existing industrial processes can be leveraged for scaling cultured meat production. For example, there are well-established industrial processes for manufacturing foods with soy protein (Rakosky 1970). Utilizing raw materials for scaffolds that are already found in existing supply chains (Jurgilevich et al. 2016), such as soy or cellulose from agricultural crop waste (Humbird 2021, Kumar Sarangi et al. 2023), could also support scale-up.

3. ADVANTAGES AND CHALLENGES OF SCAFFOLDS FOR SCALED-UP PRODUCTION OF CULTURED MEAT

Although several challenges remain, edible scaffolds can provide benefits for scaling up cultured meat production from cellular to macroscale levels.

3.1. Scaffolds to Promote Tissue Growth and Development

The central challenge in culturing meat is upscaling tissue growth using processes that are efficient and cost-effective. Scaffolds have the potential to enable mechanical, chemical, and electrical cues to accelerate cell growth and tissue development for cultured meat production.

3.1.1. Scaffolds to accelerate growth and differentiation through mechanical cues. Producing cultured meat requires the expansion of cells in culture and their differentiation into the desired tissue. Cell proliferation and differentiation can be stimulated by exogenous soluble factors as well as by physical and mechanical cues (**Figure 1**). For example, substrate stiffness regulates the proliferation and differentiation of muscle and fat cells through multiple mechanisms, including integrin-mediated signaling (Bachmann et al. 2019). In culturing muscle tissue, substrates with a Young's modulus of ∼12–14 kPa are ideal for promoting expansion of satellite muscle cells and myogenic differentiation (Ansari et al. 2016, Engler et al. 2004, Gilbert et al. 2010). In culturing fat tissue, substrates with similar ∼12 kPa stiffness accelerate preadipocyte proliferation (Chandler et al. 2011), whereas more compliant ∼2–3 kPa substrates promote adipogenesis compared to stiffer substrates (Young et al. 2013). Other physical cues can also drive differentiation: Substrates with aligned topology promote myotube formation (Huang et al. 2006, Norris et al. 2022, Yeo & Kim 2019), whereas adipogenesis can be enhanced with circular or cubic micropatterns (Ferlin et al. 2016, Muneekaew et al. 2022, Peng et al. 2011).

Tuning scaffold mechanics may also provide a strategy to reduce dependence on exogenous growth factors—contained in serum—one of the most expensive components of growth media for cell culture (Humbird 2021). For example, stiffer substrates (66 kPa versus 1.1 kPa) activate extracellular signal-regulated kinase (ERK) in 3T3-L1 preadipocytes even in the absence of fibroblast growth factor (FGF) and epidermal growth factor (Paszek et al. 2005); ERK activation promotes the proliferation of muscle precursor cells (Jones et al. 2001) and the differentiation of fat cells (Prusty et al. 2002). Further work should examine how harnessing mechanical cues provided by scaffolds could supplement or even replace growth factors used in cultured meat cell media.

Determining how cells respond to multiple simultaneous physical and mechanical cues will also be important in designing effective scaffolds in the future. High cell densities and cell–cell contact can override the effects of substrate stiffness on cellular behaviors such as adipogenesis (Ye et al. 2016), and cells may experience additional fluid shear stresses in suspension culture. Understanding mediators that regulate how cells sense and respond to mechanical and physical cues could also be important to identify new strategies to accelerate desired cell behaviors for cultured meat by genetically modifying cells and/or using small molecule enhancers as media additives.

3.1.2. Scaffolds to immobilize or encapsulate growth factors. Scaffolds provide the opportunity to localize growth factors in close proximity to cells. Growth factors are rapidly internalized by cells (Chen et al. 1997) and have low stability in their soluble form. For example, FGF-2, a key regulator of adipogenic differentiation (Kakudo et al. 2007), has a half-life of only 10 hours at 37°C (Benington et al. 2020). Thus, to support cell growth in culture, growth factors must be regularly replenished (Enriquez-Ochoa et al. 2020), which further increases cost. Physical and chemical conjugation strategies to immobilize growth factors on biomaterials for tissue engineering are reviewed elsewhere (Enriquez-Ochoa et al. 2020); here, we highlight some examples that

illustrate the potential benefits of cultured meat. The immobilization of FGF-2, transforming growth factor-β (TGF-β), and platelet-derived growth factor on gelatin scaffolds can support proliferation of human mesenchymal stem cells in serum-free media to a similar degree as media that contains serum (Mao et al. 2017). Epidermal growth factors chemically conjugated to a dextrin scaffold promote the proliferation of keratinocytes to a similar extent as soluble factors and show increased stability to enzymatic degradation (Hardwicke et al. 2008). Entrapping growth factors in a hydrogel meshwork shows promise for sustaining cell growth; greater than 80% reductions in growth factor usage compared to conventional methods can be achieved (Khalil et al. 2020, Lotz et al. 2013). Localizing growth factors on edible scaffolds could enable potential increases in efficiency for cultured meat production; however, the safety of consuming such products needs to be considered.

3.1.3. Scaffolds to facilitate electrical stimulation to promote tissue growth and maturation. Skeletal muscle is a highly innervated tissue; in vivo, electrical stimulation induces muscle contractility (Mukund & Subramaniam 2020). Ex vivo, electrical stimulation can enhance the growth of myoblasts, promote differentiation into myotubes, and induce myotube hypertrophy (Khodabukus et al. 2019, Pedrotty et al. 2005). Scaffolds could enhance the efficacy of electrical stimulation, as they provide a substrate for cell attachment and contractility. Electrical stimulation of cells on scaffolds may also be a potential strategy to reduce reliance on exogenous growth factors. Pulsing electromagnetic fields induce C2C12 myoblasts to secrete extracellular vesicles containing myogenic regulator proteins, which promote myoblast proliferation (Wong et al. 2022). However, applying electrical stimulation can increase the complexity of bioreactor designs needed for cultured meat processing (Montorsi et al. 2022).

Piezoelectric scaffolds have the potential to deliver electrical stimulation without any external power input (Montorsi et al. 2022), as they can generate an electrical charge in response to deformations induced by the traction forces of cells themselves (Liu et al. 2021). Importantly, edible polymers—including silk, collagen, and gelatin—exhibit piezoelectric properties (Sharova et al. 2021), and piezoelectric substrates can support the in vitro regeneration of skeletal muscle (Yoon et al. 2017). These findings suggest there may be valuable opportunities to develop edible, exercise-mimetic scaffolds for cultured meat.

3.2. Scaffolds to Address Challenges with Diffusion-Limited Growth

A major challenge in engineering tissues ex vivo is mass transfer. Diffusion-mediated exchange of small molecules is fast across small length scales of ∼1–10 μm, but a ribeye steak thickness is on the order of centimeters. Cells require the exchange of nutrients on timescales of hours, so diffusion-mediated exchange of nutrients limits the in vitro growth of cells into larger, viable tissue structures with thicknesses up to ∼1,000 μm (McMurtrey 2016). Biology solves the challenge of diffusion limitations by vasculature, which enables the exchange of oxygen, nutrients, and metabolites to support and maintain viable tissue in plants and animals. However, engineering vasculature requires an additional cell component to be patterned into cultured tissue. Here, we discuss solutions to address diffusion limitations using scaffolds.

3.2.1. Tuning porosity of scaffolds for increased diffusion. To maintain cell viability in ex vivo tissues for cultured meat, scaffolds fabricated with high porosity can support a more rapid exchange of oxygen and nutrients by diffusion. Although larger pores can increase the diffusion-mediated transport of small molecules through scaffolds, increasing pore size can compromise scaffold mechanical properties and reduce the available surface area for cell attachment, leading to a lower cell-to-scaffold ratio. One example of a scaffold design that addresses the need for high cell density and increased diffusion is a dual pore scaffold, which contains larger pores (243 ± 14 μm)

that allow diffusion as well as cell infiltration and attachment and smaller pores (42 ± 3 μm) that provide additional surface area for cell attachment (Rasoulianboroujeni et al. 2018).

3.2.2. Harnessing natural vasculature using decellularized scaffolds. The natural structures of plants can also be used to address diffusion-limited growth of tissues. Decellularization preserves the micron-scale vasculature of tissues, which can promote the infiltration of cells into decellularized scaffolds together with enhanced oxygen, nutrient, and waste exchange (Uygun et al. 2010). It will be important to screen a variety of decellularized scaffolds to identify which plant or fungal species provide the ideal growth environment for food-relevant cell types.

3.2.3. Engineering microtissues as building blocks. Another approach to address diffusion-limited growth of larger macroscale tissues is to engineer tissues with ~100–1,000 μm length scales—or microtissues—to be used as building blocks for larger structures (**Figure 2**). Such a modular approach also enables generation of multicomponent tissues, which include different cell types, using layer-by-layer assembly. After microtissue harvesting and assembly, an intact >1,000 μm tissue can be generated within timescales of hours, either by spontaneous adhesion (Kawecki et al. 2023) or chemical cross-linking (Kang et al. 2021, Yen et al. 2023); this approach can avoid culture across timescales longer than diffusion-mediated exchange into the core of the tissue, which can reduce cell viability within a tissue construct.

3.3. Scaffolds to Provide Structure for Cultured Meat

Scaffolds can achieve structure and texture for organized cuts of cultured meat like a marbled steak; scaffolds can also create structure in ground cultured meat mimics, which can be shaped into a burger patty, sausage, or meatball.

3.3.1. Modular approaches to create structure in multicomponent tissue. Using microtissues as building blocks is a promising approach to scale the assembly of larger tissue structures with different cell types. Tuning the size and physical properties of scaffolds as well as culture conditions provides a strategy to produce microtissues with defined dimensions (Kawecki et al. 2023, Norris et al. 2022), which could be valuable to tune the length scale of fat microtissues that could be integrated into ground cultured meat mimics or even structured cuts of meat. Tuning of fat content can be achieved by blending a measured ratio of lean muscle to fat. To achieve desired texture, fillers or binders such as gelatin and alginate and/or cross-linkers such as microbial transglutaminase can be added to stabilize tissues in a ground meat mimic post-harvest (Norris et al. 2022, Yen et al. 2023, Yuen et al. 2023); such additives are commonly used in the meat industry (Kieliszek & Misiewicz 2014, Pirsa & Hafezi 2023). Fillers, binders, or cross-linkers can also be used to stabilize microtissues into larger structured 3D tissues such as a cohesive marbled cultured "steak" that contains layers of microtissue derived from primary bovine mesenchymal stem cells and plant-based oleogels (Yen et al. 2023) (**Figure 3*c***, **subpanel *ii***). Myogenic and adipogenic microtissues can also spontaneously adhere into mechanically stable multicomponent tissue without the use of additional cross-linkers or additives (Kawecki et al. 2023) (**Figure 3*c***, **subpanel *i***); strategies to minimize additional ingredients needed to produce cohesive multicomponent tissues may be especially attractive for scale-up. Importantly, microtissues with defined dimensions can determine length scales of microtissue features, such as ~100–500-μm-thick fat layers in cultured meat that are similar to intramuscular fat in Wagyu beef steak (Kawecki et al. 2023) (**Figure 3*c***, **subpanel *i***).

3.3.2. Printing cuts of meat with defined spatial structure. Marbled cultured meat can be created by directly depositing different tissue components into complex structures across length

scales using 3D printing. For example, collagen fibers embedded with different cell types, including myocytes, preadipocytes, or endothelial cells, can be printed and subsequently cross-linked into a macroscale tissue construct (Kang et al. 2021) (**Figure 3*c***, **subpanels *iii,iv***). Although 3D printing can successfully regenerate functional organs—such as a contractile heart (Lee et al. 2019)—the level of skeletal muscle function required for desired cultured meat palatability remains to be determined.

3.4. Scaffolds to Enhance the Palatability and Nutritional Quality of Cultured Meat Products

Scaffolds provide opportunities to engineer cultured meat products that are delicious, nutritious, and meet consumer demand.

3.4.1. Enhancing nutritional properties of cultured meat. Edible scaffolds have the potential to supplement protein and dietary fiber in cultured meat. Scaffolds engineered from gelatin, soy, or textured vegetable protein could increase cultured meat protein content. Indeed, soy protein isolates increase total protein content in processed meats (Rakosky 1970). Scaffold materials such as pectin, cellulose, and lignin could fortify cultured meat products with dietary fiber; in fact, pulse flour and vegetable pulps are added during the processing of conventional meat products (Talukder 2015). Edible scaffolds provide further opportunities to create cultured meat superfoods that contain nutritional additives, extra antioxidants, or even probiotics that are not typically present in meat.

3.4.2. Tuning sensory properties of cultured meat. Strategies to enhance food sensory properties can also be used for cultured meat products. Scaffold materials such as gelatin, pectin, and alginate are commonly used as gelling or thickening agents, which can improve the mouthfeel and structural integrity of products (Pirsa & Hafezi 2023). Many scaffold polymers also retain water after cooking, which can enhance juiciness (Rakosky 1970). Pectin is a natural thickening, gelling, binding, and emulsifying agent that increases miscibility between fat and water and is commonly used in sausages to retain fat-associated flavor and juiciness (Ngouémazong et al. 2015). Taken together, scaffolds can support cultured meat products with nutritional, sensory, and flavor profiles that mimic or could even surpass existing food products.

3.5. Impact of Scaffolds on Cultured Meat Production Costs

The predicted costs of cultured meat present a major challenge for consumer appeal (Humbird 2021, Tomiyama et al. 2020).

3.5.1. Scaffolds to increase bioprocess efficiency. Preliminary TEAs of different cultured meat production scenarios indicate that low bioreactor cell mass yields will be a significant driver of cultured meat costs (Humbird 2021, Negulescu et al. 2023). Scaffolds have potential to address this challenge by increasing the growth efficiency of cultured meat and reducing the dependence on growth factors. Using scaffolds also provides a potential opportunity to utilize existing industrial-scale bioreactors that could support the suspension growth of mammalian cells (Humbird 2021). However, this approach may be limited as bioreactor processes designed for microbial cell culture may need modifications to support the more complex needs of mammalian cells (Humbird 2021, Negulescu et al. 2023).

3.5.2. Scaffold sterilization for large-scale tissue culture. Viral and bacterial contamination of meat cell cultures are expected to be major challenges, which could severely impact production yields and pose a threat to human health and consumer perceptions (Barone et al. 2020, Malik et al.

2023). To minimize contaminations, one strategy is to sterilize cell culture ingredients, but this is projected to be a major cost in cultured meat (Humbird 2021). A variety of techniques can be used to sterilize scaffolds at the lab scale (Dai et al. 2016, Hanga et al. 2020, Yang et al. 2019)—including UV, gamma irradiation, autoclaving, and chemical sterilization; however, few studies have examined the scalability of these techniques. It also remains to be determined what level of scaffold sterilization may be necessary for the viable production of cultured meat, as real-time monitoring can provide some control over contamination. Analyses examining the costs of sterilization necessary for cultured meat production will be instrumental in guiding future developments of scaffolds.

4. SUMMARY AND FUTURE OUTLOOK

Scaffolds have the potential to advance cultured meat by accelerating cell growth and differentiation, providing structure to build complex 3D tissues, and enhancing its nutritional and sensory properties. These potential benefits will need to be balanced with the projected costs and challenges of integrating scaffolds into cultured meat production.

4.1. Making Cultured Meat that Consumers Demand

Concerns of future consumers include cultured meat palatability, nutrition, cost, and sustainability (Pakseresht et al. 2022, Ruzgys & Pickering 2020, Tomiyama et al. 2020). Advances in cultured meat using scaffolds can address some of these concerns by contributing to cultured meat's nutritional quality, flavor, and sensory properties, including juiciness and tenderness. The ability to customize scaffolds and generate precision cultured meats could open the possibility of designing tailored cultured meats to meet individual tastes and/or health needs. To meet consumer demand for environmentally friendly food options (Pakseresht et al. 2022, Ruzgys & Pickering 2020), scaffolds could reduce the mass of cultured animal cells required for an individual portion of cultured meat and/or make use of upcycled materials; pectin scaffolds could make use of discarded citrus peels, whereas soy or gelatin scaffolds could utilize by-products of existing food supply chains. The impact of scaffolds on the economic and environmental feasibility of cultured meat production continues to be explored and balanced with potential opportunities for scaffolds to reduce the environmental impact of cultured meat.

4.2. Cost Efficiency and Footprint

The use of scaffolds for cell culture can require additional ingredients and processing steps (e.g., sterilization). However, there is also potential to leverage scaffolds to increase culture efficiency by enhancing cell proliferation, reducing the need for costly exogenous growth factors, and increasing cellular metabolic rates as well as myogenic and adipogenic potential. Scaffolds may also reduce the total number of cells and thus culture time needed to produce cultured meat, as scaffolds contribute to the volume, texture, and nutritional composition of cultured meat. The cost and scale at which we can produce cultured meat will determine the extent to which cultured meat is a niche product to meet the needs of people in extreme or extraterrestrial environments versus an option on the menu of a fast-food restaurant.

4.3. Trust in the Technology

Public perception and trust in technology will be major factors in the successful scaling and commercialization of cultured meat. The science behind the development of cultured meat is complex and far beyond the average education level of the general public. The addition of scaffold materials into cultured meat will add ingredients that may not be familiar to consumers, which may increase their reluctance to consume such products. Cultured meat companies will need to work

with experts in science communication to ensure marketing and communications around cultured meat products are transparent and understandable by the general public to establish public trust and acceptance of cultured meat products. Academic experts can also play an important role in leading dialogue around cultured meat to general audiences.

CONCLUDING REMARKS

Humans are faced with global demands to reduce antibiotic use, conserve water, restore soil health, reduce anthropogenic carbon emissions, and provide everyone with access to nutritious food. Cultured meat production is an exciting and fast-growing area of agricultural and food science, and successful scale-up will depend on our ability to make cultured meat that consumers demand.

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