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Opinion

# Cultured fruit: growing fruit without plants

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**Dominant forms of agriculture burden our environment, and food production is threatened by climate change. In this opinion article we introduce a paradigm shift in food production by describing a method to cultivate fruit without having to grow plants, and outline remaining scientific challenges. 'Cultured fruit' is less vulnerable to climate change, and can drastically improve sustainability, but only if non-agricultural sources of sugar are used to fuel fruit growth. Lessons for industrial scaling can be drawn from the micropropagation industry. Equitable access to this technology should be promoted to prevent power imbalances that can result from the further industrialization of agriculture. A just adoption of cultured fruit technology can help build a fair and sustainable food system.**

## Highlights

Cultured fruit is a new food production modality in which edible fruits grow directly from plant cells or seeds, eliminating the need to cultivate whole plants.

Novel insights into molecular regulation of flowering allows production of flowers and subsequent fruits without production of vegetative tissues.

Cultured fruit systems decouple agriculture from land use, allowing indoor fruit cultivation that is less vulnerable to climate change and dramatically reduces the environmental footprint of farming.

The sustainability of cultured fruit hinges on sourcing non-agricultural sugars to fuel growth, ensuring that production gains are not offset by hidden land and resource demands.

## Towards fruit without plants

Since the beginning of agriculture, plants have been cultivated with the goal of harvesting their fruits. Herein we outline **cultured fruit** (see Glossary), a new paradigm in which botanical fruits (including berries, beans, seeds, nuts, and fruit-vegetables) are grown while producing (almost) no vegetative plant organs.

Current agricultural practices are the main driver of biodiversity loss, freshwater depletion and eutrophication, and they are a major source of other environmental impacts [1]. Moreover, in the coming decades, yields of important crops are predicted to decrease because of climate change [2]. Therefore, in parallel with reducing the impact of conventional agriculture and our diets, radical new approaches should be investigated to safeguard our food supply.

We argue that cultured fruit can shield food production from increasingly harsh climates, while reducing impacts on the environment by substantially uncoupling land use from food production. Cultured fruit derives its energy from an **exogenous carbohydrate** source instead of direct (sun)light, and thus can be produced indoors in **bioreactors** or tightly stacked shelves, instead of on agricultural land. Since these carbohydrates still need to be sourced, uncoupling can be achieved only if non-agricultural sources of carbohydrate are utilized to fuel fruit growth. We do warn that this disconnect between agriculture and land use can reinforce **power asymmetries** in food systems [3].

This opinion article introduces the scientific study of cultured fruit and traces what a just future for cultured fruit looks like. It looks back at its inception (Box 1) and forward to its challenges concerning technical implementation, food quality, environmental impact, economic impact, and societal concerns.

## Growing cultured fruit in four steps

The cultured fruit method can be conceptualized in four steps and results in a complete fruit (Figure 1). In step 1, shoot apical meristems are formed. Shoot apical meristems are self-maintaining organized

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### Box 1. History of cultured fruit

In the 1940s, La Rue observed the spontaneous development of fruits from detached flowers [60]. In 1953, Nitsch [61] cut pollinated tomato, cucumber, strawberry, and bean flowers from the plants. When placed in a solution containing solely minerals and sucrose, the flowers grew into fruits. Tomato fruits in these experiments ripened normally but remained small. In the 1980s and 1990s, detached tomato fruits and maize kernels were shown to grow to a similar size to that on the plant when some maternal tissue was left attached [30,31].

During the 1960s through the 1980s researchers demonstrated that *de novo* generation of floral buds and fruits is possible by culturing plant tissues with exogenous plant signaling molecules [54,55].

The mapping of the flowering gene network from the 1990s onwards offered a more rational method for *de novo* flower formation. Flowers formed reliably from seed or plant tissues after genetic overexpression of key flowering regulators [9].

At present, research into flower development is ongoing. There is also a strong focus on molecular and tissue culture tools, including CRISPR systems, cell-penetrating particles, and virally induced flowering.

populations of pluripotent cells that produce all above-ground organs, including flowers. *In vitro*, meristem formation can be initiated by applying the right balance of auxin and cytokinin phytohormones to small pieces of plant tissue. This results in dedifferentiation into a cell mass called **callus** from which new meristems can be grown multiple times. Many plants, however, are unable to produce callus or to regenerate meristems. To address this, exogenous expression of developmental regulator genes or hormone biosynthesis genes can be employed to cause meristem formation [4,5]. Instead of *in vitro* regeneration, meristems can also be obtained by simply letting seeds germinate. Seedlings contain a root and a shoot apical meristem. In this case the cultured fruit formed in subsequent steps can be thought of as an extremely dwarfed plant.

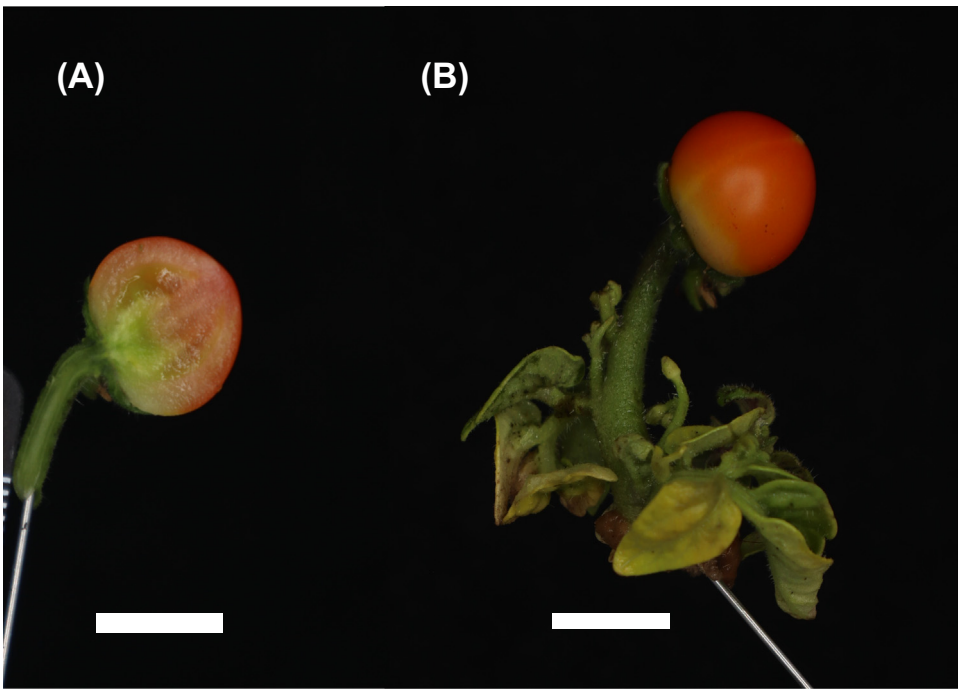


Figure 1. Cultured tomato fruits grown directly from plant tissue. (A) Longitudinal section of cultured tomato fruit. (B) A tomato fruit and its fruit-stalk growing directly from callus. Additionally, a few leaf-like structures grow from this callus. White scale bars represent 1 cm.

## Glossary

**Bioreactor:** vessel in which plant cells and organs can be grown.
**Callus:** a cluster of undifferentiated cells that forms when wounded tissue is supplemented with sugar and phytohormones.
**Cell-penetrating peptide:** peptide sequence that facilitates the entry of a macromolecule into the cell.
**Clustered regularly interspaced short palindromic repeats (CRISPR) activation system:** modified CRISPR-associated protein (Cas) fused with transcriptional activators that boosts expression of a target gene. It can bind to, but not cut, DNA and recognizes specific gene promoters using a guide RNA.
**Cultivar:** a variety of a plant intentionally created by humans for desired traits.
**Cultured fruit:** the fleshy or dry ripened ovary, potentially enclosing seeds, grown in the absence of – or with hardly any – supporting vegetative organs such as leaves and stems.
***De novo* flowering:** formation of flowers directly from plant tissue or seed without the prior formation of vegetative tissue.
**Exogenous carbohydrate:** carbohydrates supplied to developing cultured fruits from the growth medium instead of being produced by endogenous photosynthesis.
**Floral pathway integrator genes:** genes that control when a plant flowers by integrating environmental and endogenous signals.
**Fruit set:** the onset of fruit development from a mature flower.
**Functional conservation:** the preservation of a gene's or protein's biological role across different species despite potential evolutionary changes.
**Micropropagation:** large-scale clonal propagation of plants using tissue culture techniques.
**Plant cell suspension:** plant cells and cell clumps suspended in liquid growth medium.
**Power asymmetry:** the uneven distribution of power within society.
**Ribonucleoprotein complex:** a complex made up of RNA and protein. The CRISPR protein with its guide RNA is an example of such a complex. Since these complexes do not integrate into the DNA of the host, the host remains free of transgenes.
**Timmermann's dimensions of justice for agricultural innovations:** a

framework used to meet the demands of social justice by assessment and governance of innovation in the agricultural sector.

If left alone, induced shoot meristems will pass through several developmental stages before flowers are produced. The exact timing and control of these stages depend on the species and environmental conditions. In step 2, therefore, the meristem is induced to directly form a flower by activating **floral pathway integrator genes** [6]. These genes integrate environmental and endogenous signals and can be grouped into those repressing, enabling, and promoting the floral transition. High floral repressor levels render the vegetative meristem unresponsive to promoting signals [7]. Two key floral pathway integrator genes are *FLOWERING LOCUS T (FT)* and *LEAFY (LFY)* [6]. By activating floral pathway integrator gene expression, vegetative meristems can be transformed into flower-producing reproductive meristems regardless of developmental age or environmental cues, and without the formation of any leaves. Floral pathway integrator genes as well as genes that establish floral identity show high **functional conservation** across plant species [8].

Genetic induction of ***de novo* flowering** has been shown in a wide range of species. Notably, seed of transgenic *Arabidopsis* (*atFT* and *atLFY* overexpression [9]) and trifoliate orange (*CiFT* overexpression [10]) gives rise to flowers directly after forming two small cotyledons. Several studies aiming to reduce the length of plant breeding cycles report flowering of regenerated shoots after the formation of a few small, underdeveloped leaves. Reported species include cacao (*atFT* overexpression [11]), grape (*atFT* overexpression [12]), blueberry (*VcFT* overexpression [13]), apple (*bpMADS4* overexpression [14], or *mdFT1* overexpression [15]), wheat (*TaFT1-D* overexpression [16]), kiwi (*AcCEN* and *AcCEN4* mutation [17]), and pear (*bpMADS4* overexpression [18]). In the two studies that reported flowering efficiency, 100% of trifoliate orange seeds [10] and 69–100% of grapevine shoots across different **cultivars** [12] formed flowers. Transgenic apple [14], grape [12], trifoliate orange [10], kiwi [17], and pear [18] were grown until fruit was formed. In all cases, fruit was formed after rooting, transfer to greenhouse conditions, and formation of multiple leaves.

Non-genetically modified organism (GMO) alternatives to activate floral pathway integrator genes exist. For example, direct delivery to the plant of a **clustered regularly interspaced short palindromic repeats (CRISPR) activation system** as a **ribonucleoprotein complex** can activate genes in a transgene-free way [19], **cell-penetrating peptides** can deliver recombinant floral pathway proteins or mRNA directly into the cell [20], or viruses can induce transient expression of floral pathways [12].

Alternatively, *de novo* flowers can be induced in wild-type tissue by culturing reproductive or mature plant organs in the presence of cytokinin and auxin [21]. The floral identity of these tissues seems to be carried over into the regenerated organs. This leads to 100% flower generation in tobacco [22], 60% in arabidopsis [21], and 58% for the formation of lentil pods [23]. By contrast, tomato shows efficiencies of 0–50% depending on tissue, cultivar, and phytohormone treatment, with only 1% of explants forming a fruit [24]. While the phytohormonal approach lacked efficacy in the past, current knowledge of molecular biology can help optimize flower induction by measuring the effect of classic tissue culture techniques, such as phytohormone treatments, on the expression of flowering genes.

Within the developing flower, the ovary develops too. The ovary is triggered into fruit development during **fruit set** in step 3. On the plant, fruit set starts when pollen fertilizes the ovary, mediated by the signaling molecule auxin. *In vitro,* pollen produced by the *de novo* flowers can be transferred onto the stamens of other flowers to induce fruit set [25]. Alternatively, exogenous auxin can be applied to induce seedless fruit formation [26]. Finally, many cultivars exist that produce seedless fruit after flowering without the need for pollination or phytohormone application [27]. If fruits with seed are desired, more research is needed into effective means of *in vitro* fertilization.

Box 2. Quality of cultured fruit

In new food technologies, quality is often defined by the degree of similarity between the product and its conventional counterpart. Since cultured fruit production results in a whole fruit, fruits will be macroscopically identical to the plant-grown alternative. Research on *in vitro* tomatoes grown from excised flowers found that, on a molecular level, *in vitro* tomato fruits also resemble plant-grown fruits. Fructose and glucose, the dominant fruit sugars, were slightly elevated in cultured fruits, and the difference in color was small and insignificant [62]. When measuring flavor volatiles, seven compounds were within 25%, ten compounds were >25% elevated and eight compounds were >25% reduced compared to conventional fruits. Lycopene was roughly ten times as high in cultured fruit [63]. The production of flavor metabolites is dependent on the availability of sugars and environmental conditions. Both can be controlled *in vitro*. Indeed, soluble sugar and anthocyanin concentrations respond to the sucrose concentration of the growth medium of *in vitro* grown grapes [28]. However, vitamin C content is linked to light intensity and is lower for *in vitro* tomato fruits grown in darkness [64]. This nutritional deficit can be overcome by exposing fruits to light during the final ripening stage [65].

Exogenous phytohormones or proteins can be used to control fruit development in all three methods of cultured fruit production. These compounds will likely be absent or present only in trace amounts in the final product, as has been shown for **plant cell suspension** culture [30]. Still, the addition of these compounds at any step can influence the perception of quality. It is desirable to minimize the use of exogenous growth factors and use natural products where possible.

In general, cultured fruit will be a very tunable system since inputs to its metabolism and culture conditions are controllable to a degree that is impossible when a plant and its environment intervene. A perceived unnaturalness will be one of its largest drawbacks.

Finally, in step 4, the fruit is grown by feeding it water, minerals, and sugars. This step does not require any exogenous signaling molecules. Botanical fruits as distinct as grape [28], rice [29], maize [30], tomato [31], and strawberry [32] have been grown into mature fruits by cutting the fruits from the plant just after fruit set and placing them in a suitable growth medium. They share all anatomical features of *in planta* fruits. The few available reports show a highly similar organoleptic quality (Box 2). However, fruits often remain smaller than *in planta*. Leaving some maternal tissue attached to *in vitro* tomato fruits [31] and maize kernels [33] caused fruit size to approach *in planta* size. Slow growth in maize kernels has been attributed to insufficient uptake and transport of sugars [34]. However, future research needs to elucidate the roles of plant–fruit signaling and metabolism in maternal tissues.

This overview proves the technical feasibility of every step. However, some knowledge gaps remain: (i) the effect of artificial flowering induction on fruit developmental anomalies, (ii) efficient *in vitro* pollen transfer, (iii) the necessity for light during the cultivation (Box 3), and (iv) the growth rate and final size of *in vitro* fruits.

## Environmental sustainability

While the environmental performance of cultured fruit will evolve along with the maturation of this technology, an early qualitative comparison to conventional production will allow industry, academia, and governments to harness its strengths and avert its weaknesses (Figure 2).

### Production process impacts

Because cultured fruit production takes place indoors, nutrient runoff and pesticide use is eliminated. Production can occur on vertically stacked shelves as in a vertical farm or in fermentation-style bioreactors. In both cases, direct land use for production will be greatly reduced. Energy demand will depend on the necessity of light during the production process. There is evidence that light is not required, but more research is needed for conclusive proof of this (Box 3). Since plant tissues grow at ambient temperatures, no significant energy use is foreseen for heating of the cultures. In addition, in a well-insulated facility the energy demand for climatization will be low. Impacts from material use for equipment will depend on whether vertically stacked shelves or a fermentation-tank-style process will be chosen. Regardless,

the relative impact of material use is typically low for both vertical farms [35] and fermentation-style processes [36].

### Downstream and upstream impact

Cultured fruit, like vertical farming [35], can be produced year-round and close to consumers, reducing transport-related emissions. Its closed production environment minimizes water and nutrient losses, lowering both water use and eutrophication risk. However, the requirement of exogenous sugar presents a major environmental hotspot. We expect a sugar demand of 0.063 kg sucrose $kg^{-1}$ fresh weight for tomato fruit and 1.300 kg sucrose $kg^{-1}$ fresh weight for maize kernels [33,37–39] (Figure 3). The environmental impact of the required sugar alone is roughly in the same order of magnitude as the total impact of current field tomato or maize production. In locations where field production is (seasonally) impossible, cultured fruit could still produce major sustainability benefits since global warming potential is greatly reduced compared with fossil-fuel-heated greenhouse production (Figure 3). Still, to more completely disconnect food production from its environmental impacts, non-agricultural forms of sugar production must be developed.

Several non-agricultural sources of sugar can be considered. Side streams from the food industry can be used to replace sugars as well as macronutrients in the medium, as has been shown for plant cell cultures [40]. Non-crop lignocellulosic feedstocks can be used to produce glucose, but its sustainability depends on the feedstock and conversion method used [41]. Finally, electrolysis of $CO_2$ into acetate could provide a highly scalable and efficient source of carbohydrate, if plant metabolism is engineered for growth on acetate [42].

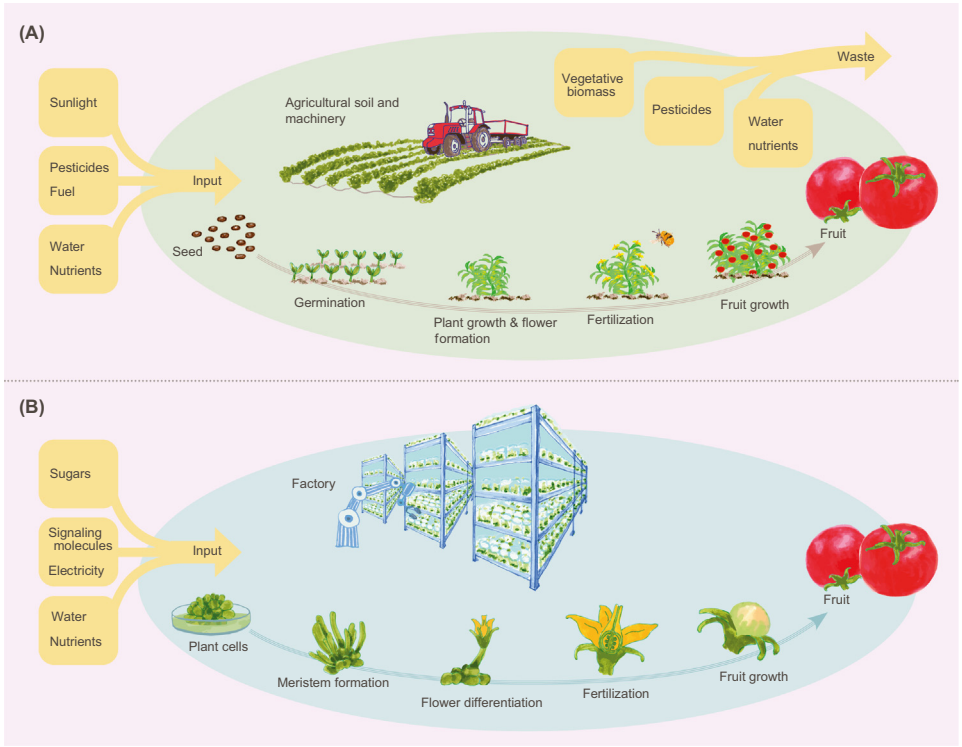


Figure 2. Conceptual models of field and cultured fruit production. Inputs and waste products are represented by yellow arrows. (A) Field production. (B) Cultured fruit production; in this representation nutrients and water are recycled within the factory and therefore not presented by a waste arrow.

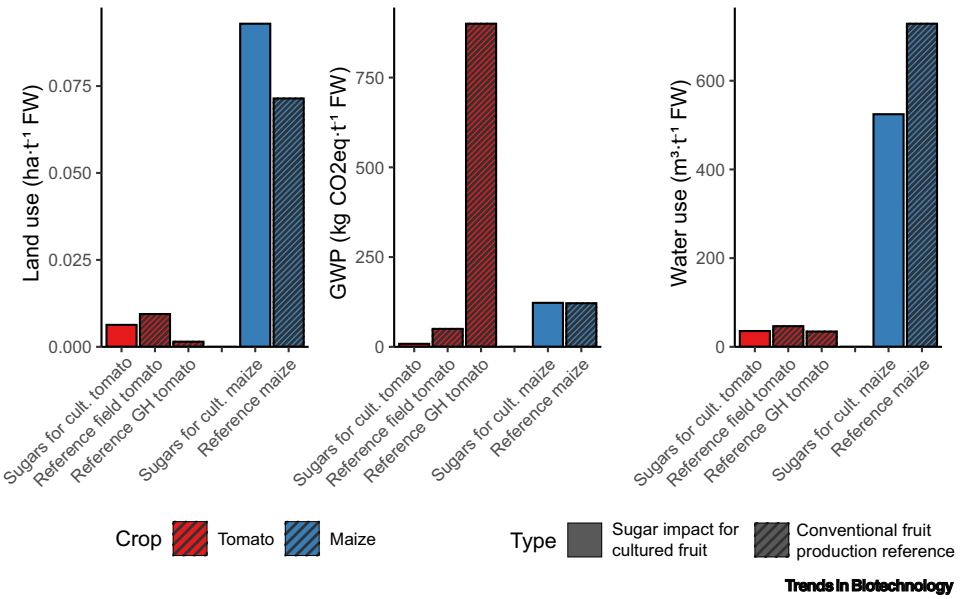


Figure 3. Environmental impact of sugar requirements for cultured tomato and maize compared with the total environmental impact of conventional production. If cane sugar is used to produce cultured fruits, the impact of the cane sugar alone is similar to the total impact of conventional fruit production. Based on carbon content – 0.024 g carbon $g^{-1}$ fresh weight (FW) for tomato fruit and 0.40 g carbon $g^{-1}$ FW for maize kernels [37,38] – and carbon use efficiency reported in the literature (0.75 g carbon incorporated $g^{-1}$ carbon taken up for tomato fruit and 0.84 g carbon incorporated $g^{-1}$ carbon taken up for maize kernels, 100% uptake assumed) [33,39], we expect a minimum sugar demand of 0.063 kg sucrose $kg^{-1}$ fresh weight for tomato fruit and 1.300 kg sucrose $kg^{-1}$ fresh weight for maize kernels. Abbreviations: cult., cultured; GH, greenhouse, GWP, global warming potential.

### Box 3. Light requirement

Because cultured fruit methods are fueled by exogenous sugars, they are independent of light for their energy needs. Still, apart from providing energy, light also has physiological functions. During multiplication, light stimulates meristem formation, although it is not strictly required [47,48]. Darkening tomato fruits on the plant does not affect final fruit size, but *in vitro* grown tomatoes are reportedly smaller when grown in darkness [66,67]. By contrast, darkness did not affect grain weight of *in vitro* rice panicles [29]. Darkness inhibits the outgrowth of flowers from the meristem and causes spindly stem growth. However, these typical dark adaptations can be partly overcome using plant signaling molecules or genetic modifications [68]. To summarize, fundamental research provides evidence that each of the four individual steps in cultured fruit production can occur without light. However, the complete light-free method has not yet been demonstrated. A mostly light-free method is desired for environmental and financial reasons and should be investigated in more detail.

## Scalability and economic bottlenecks

Lessons about the future scalability of cultured fruit can be drawn from the **micropropagation** industry which produces clonal plantlets. The two approaches are highly similar: both involve initiation of tissue in sterile culture followed by generation of shoot apical meristems. In both approaches growth media consist of inorganic nutrients, carbohydrates, phytohormones, and water. During micropropagation shoots are subsequentially rooted and acclimatized to *ex vitro* conditions, whereas cultured fruits are formed by inducing flower and fruit formation. Additionally, the biomass of a cultured fruit is one to three orders of magnitude greater than that of a plantlet. Duration of *in vitro* flower production is comparable with rooted plantlet production [10,13,14,43,44]. However, *in vitro* fruits develop at the same pace as *in planta* fruits [28,29,33]. For slow-developing fruit species this will add considerable time to the culture duration. Both micropropagation and cultured fruit conventionally use light, but light may not be a hard requirement (Box 3). In conclusion, cultured fruit and micropropagation are similar from a

manufacturing perspective, with their biomass output and, depending on the species, the process duration being the biggest differences.

The micropropagation industry has been successfully scaled, with large laboratories having capacity for ~10–50 million plants per year across low- to high-income countries; global production is estimated at 1.5–2.0 billion plants [45,46] (www.floraldaily.com/article/9281895/vitroplus-produces-record-amount-of-ferns-34-million/). The inflation-adjusted production costs reported in the literature are US$0.11–0.26 per plantlet [43,44,47]. Labor represents the highest fraction at 38–58% of the costs, infrastructure and equipment 7–24%, medium 4–14%, and electricity 1.3–8% of the costs [44,47,48]. If cultured fruit uses the same process as micropropagation, we expect labor costs to remain constant, medium costs to scale with produced biomass, and electricity, infrastructure, and equipment costs to scale relative to some combination of biomass and culture duration. For comparison, the production costs of a 15 g greenhouse cherry tomato are reported to be $0.02 [49].

Medium costs can be greatly reduced by switching from laboratory-grade to low-cost medium ingredients [50,51], and using a larger fraction of the available nutrients before discarding the medium [52]. Most of the electricity demand and considerable equipment cost comes from artificial light and heating, ventilation, and air conditioning (HVAC) for removing heat from the lamps [44,47]. This illustrates the necessity of designing a light-free system (Box 3).

Subculturing is the most labor-intensive task in micropropagation, because dense clusters of multiplied shoots are manually divided and placed on new medium. Robotization of this and other steps is starting to be adopted in high-income countries. We expect advances in AI to stimulate this trend and further bring down costs [53]. Obtaining meristems by simply germinating seeds in step 1 of the cultured fruit method will cut down on labor costs but add costs for seed.

Flower induction brings additional costs relative to micropropagation. Gene editing of flowering pathways results in flower formation without any external inputs, but it requires molecular breeding of every individual cultivar. By contrast, exogenous flowering agents must be supplied every production cycle but may be applicable across species. Finally, a phytohormonal approach can bypass the need for both gene editing and exogenous macromolecules, but will be viable only if its efficacy is increased [21–24,54,55].

If these challenges can be overcome, crops that suffer from supply-chain challenges will form the biggest opportunity. Cultured fruit is produced independently of climate and location. This allows for stable and local production during the off-season as well as under extreme weather events and political conflicts.

At least one company has been moving towards industrial scale. GALY produces cotton, the fruit of the cotton plant, by proliferating cotton cells in bioreactors, after which they are matured into cotton fibers [56]. As of September 2024, it was reported to have produced a few kilograms and has a contract in place for the large-scale production of medical grade cotton (www.bloomberg.com/news/newsletters/2024-09-03/fast-fashion-bets-on-greener-lab-grown-cotton).

## Social justice

Along with the promises of cultured fruit come issues that could worsen existing injustices in food systems [3]. Using **Timmermann's dimensions of justice for agricultural innovations**, we highlight three main issues [57].

First, conventional crop production is geographically constrained, whereas cultured fruit can be produced anywhere by actors with adequate resources. This could allow a few actors to dominate global food production, increasing inequality and reducing access to healthy food [3]. Additionally, optimized cultured fruit cultivars risk diminishing crop variety [57].

Second, cultured fruit builds on the historical work of farmers and other professionals [58]. Excluding them from the production process would lead to major problems like loss of farmers' livelihoods and loss of agricultural culture.

The third issue is the governance of food systems. While governance systems for food safety and environmental sustainability exist, the aforementioned justice issues are insufficiently addressed in current systems [59].

These risks should be addressed by (i) providing free access to developed knowledge, (ii) fostering an open innovation process that stakeholders like farmers and consumers can influence, and (iii) designing a low-tech and low-capital production process usable in both high-income and low-income economies.

## Concluding remarks

Cultured fruit can revolutionize food production by disconnecting food production from land use provided that non-agricultural sugars are used. It can eliminate direct emissions associated with field agriculture, while avoiding the high energy requirement of current indoor production systems such as greenhouses. The increasing pressure on supply chains will drive interest in these land-free systems. Innovations in cellular agriculture around bioreactors, signaling molecule production and aseptic workflows will also benefit cultured fruit technology. Research should focus on production of non-agricultural sugars, the effect of darkness on the cultured fruit production process, as well as fundamental understanding of fruit development (see Outstanding questions). Careful consideration should be given to a just implementation so that social, economic, and environmental aspects align with the needs of citizens.

### Outstanding questions

How can we overcome recalcitrance to shoot regeneration in different plant species?

What is the most effective way to transform regenerated shoots into flowers?

What factors limit the growth rate of cultured fruits?

What is the effect of steering flower development on fruit quality?

How can we produce non-agricultural sugars for cellular agriculture at scale?

How can we grow cultured fruit outside of sterile systems?

What design implementations lead to just and sustainable cultured fruit production?

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### Declaration of interests

R.J. is a co-founder of Chi Botanic and is its chief scientific advisor. He is an inventor on patent US20230104872A1 for a method for producing plants with minimized biomass by-product and associated plants thereof. The remaining authors have no interests to declare.

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