ADVERTISEMENT FEATURE

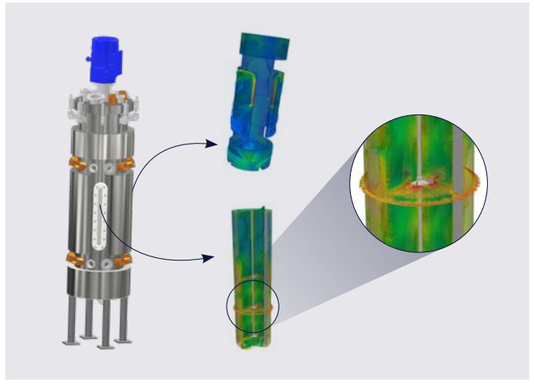
BIOREACTORS FOR THE FACTORY FLOOR

In an era of cultivated meats and rapidly evolving pharmaceuticals, biomanufacturing is facing a capacity crunch. WHO'S REACTING TO THE PROBLEM?

Cultivated meat substitutes, medicines and mass-produced proteins for food hold vast market potential, and environmental benefits, while addressing ethical concerns presented by livestock farming. The basic science of animal and plant cell cultivation is now well developed, with many companies around the world intent on moving from the laboratory into manufacturing. But scaling up will be challenging.

"Bioreactors in which living cells grow will play a crucial role, but there is currently a capacity crunch," says Hamid Noori, CEO of Germany-based bioengineering company The Cultivated B (TCB).

To scale up, biomanufacturers need to reduce the level of expertise needed to operate a bioreactor. "Large scale manufacturing plants predominately employ workers who would be considered non-experts, operators, not process engineers," says Kristala Prather, department executive officer of Chemical Engineering at MIT. The industry needs simpler, more adaptable, reusable and sustainable bioreactor technology, and this has driven TCB to develop bioreactors that they say anyone could use.



▲ TCB optimizes the bioreactor design using computational fluid dynamics, and compares the simulation with experimental results. Exploratory technical illustration shows a bioreactor vessel (left), a high-efficiency temperature control system, or 'jacket', for heating/cooling (top right) and an optimized propeller design to reduce shear stress on the cells when mixing (bottom right)

CAUSING A STIR

Cathy Ye, director of the Oxford Centre for Tissue Engineering and Bioprocessing, is well placed to assess the challenges of scaling up cellular agriculture, with a research background in mammalian cell culture and a recent move into the marketplace as co-founder of cultivated meat start-up, Ivy Farm.

"A major technical issue is controlling the disruptive shear forces on large volumes of fragile mammalian cells, while maintaining the necessary stirring of the cells in their sustaining fluid," Ye says. Moving from the lab to a factory requires larger bioreactors, but these have higher shear forces than smaller, lab-based ones. This excessive pressure can cause cell damage if not controlled properly.

Prather also sees hurdles in the crucial issue of costs, both operational and capital. "While the science for making cultivated meat products might be ready, the cost of doing so has to meet the parameters for a feasible business model."

A bioreactor is essentially a vat, usually made of stainless steel, allowing living cells to multiply in an environment that can nourish them and keep them healthy. The cells must be steadily but gently mixed within their growth medium, generally by a series of rotating paddles. Suitable plumbing is needed to deliver nutrients and to extract the cells that are the product. Some options allow continuous extraction, while others operate in batch production — where all the cells are harvested at specific time intervals. In addition to suitable nutrient levels and a bubbling oxygen supply, the crucial environmental factors that must be monitored and controlled are temperature, pH and carbon dioxide levels.

These are considerations that TCB took on board when designing their bioreactors, which allow efficient scalability and are optimized for accelerated cell proliferation. However, "the major differentiating factor of our new bioreactors is their ease of use," says Noori, likening this to the difference between first generation computers — massive, costly and complicated — and the modern graphical user interface systems. "We are taking a complicated specialist technology and transforming it into a system that can be used by anyone."

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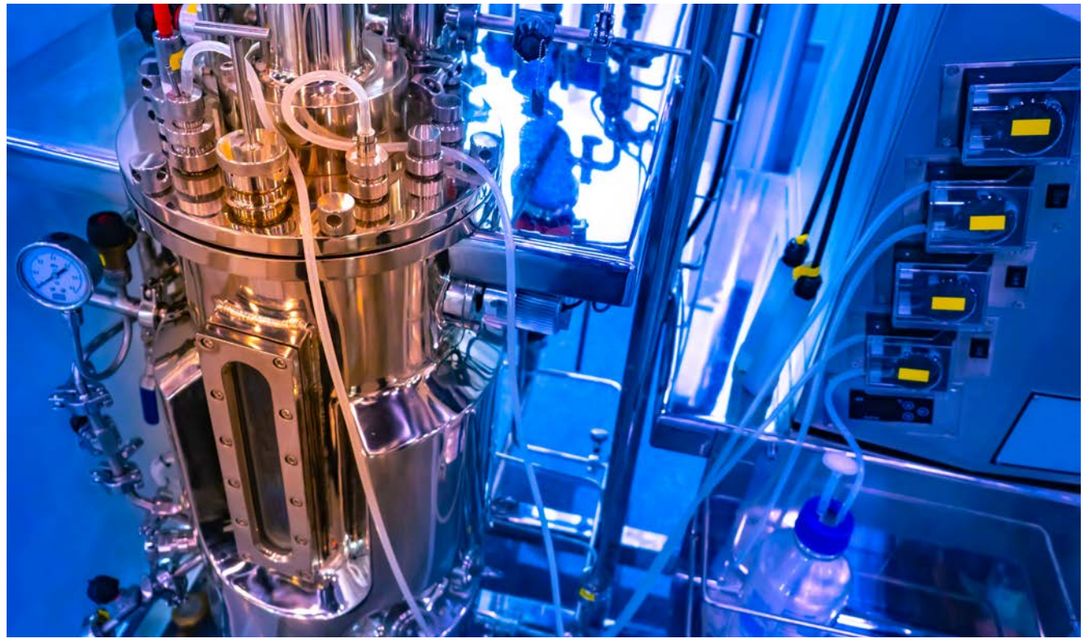
VERSATILE AND SUSTAINABLE

The main customers of traditional bioreactors are research labs and the pharmaceutical industry, both populated with highly qualified operators who have PhDs and years of experience. "Our bioreactors can change all that," says Noori. "The demand for large-scale cell and protein production is clearly growing and the market is ready to vastly expand." It makes sense to develop products that are usable by many different people, he adds.



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▲ Scale up of cell cultivation needs advanced biomanufacturing technology.

But what are the key innovations needed to achieve these market advances? Wolfgang Kühnl, co-CEO of InFamily Foods, Germany's second largest meat processing company, highlights that these lie in the control systems and intuitive control panels, which TCB have made considerably more straightforward than other models. "These adopt the level of automation, together with pre-programming, to allow operators to nurture the growing cells without any knowledge of the biological details involved," he says. The aspect of automation also helps to control the shear force, reducing cellular damage. But Ye warns that even larger vats may be required for expanding cultivated meat production.

Another advantage of TCB's new bioreactor is modularity, meaning that a single bioreactor can be readily adapted to differing needs, cells and products — not only for cultivated meat and food production but also for the pharma, cosmetic and personal care industry. It is easy to switch these devices from producing bacterial or plant cells to coping with the gentler care necessary for fragile mammalian cells, for example. The operator simply requests the necessary pre-programmed adjustments, which proceed automatically. This avoids the expense of buying different bioreactors for different product streams. And it allows TCB to be able to fulfil an order for a new bioreactor within a few weeks, as opposed to a year or more for conventional units.

In the interests of sustainability and cost-reduction, TCB has also explored innovative ways to recycle and reuse as many components of the growth medium as possible. "We don't want users to throw away very expensive materials when they could be purified and fed back into the process, which also saves energy," says Noori. "We can guide clients towards a much more efficient and sustainable eco-system approach, using substantially less electricity per batch."

One aspect of the improved sustainability comes from extracting cellular by-products: biochemicals that are produced by cells but are not the primary product of the manufacturing process. This allows these useful materials to become nutrients for other batches of cells.

SUPPORTING SCIENCE INNOVATION

The TCB bioreactors are already available for researchers and government agencies, who Noori says will provide valuable feedback. The full product range — with volumes from 1 to 1000 litres — will be launched in late 2023.

With modular design, ease of use and sustainability, the bioreactors are suitable for start-ups and smaller companies, Noori says. Many firms are making strides in scientific innovation but can struggle with moving these products from the lab to market. With new developments in bioreactor technology, this can be made easier.

"To work in food-processing surroundings without specialized clean rooms, the bioreactors have to be simple to operate and the processes must be robust and highly automated," says Kühnl. That is the essential task that TCB is set to tackle. ■

Cultivated B

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