

In vitro Intelligence and the Emergence of Alternative Cognitive Paradigms

Introduction

The discourse surrounding intelligence in the 21st century has been dominated by artificial intelligence – systems designed with mathematical precision to mimic or exceed human cognitive abilities through computation. However, this algorithmic focus has narrowed our conceptual frameworks, blinding us to other emergent forms of intelligence that challenge traditional categorical boundaries. This article examines the emergent field of *in vitro intelligence* (IVI): systems derived from cultured neural networks, cerebral organoids, and bioengineered entities that exhibit dynamic behaviours and decision-making capacities while existing outside conventional biological bodies.

Unlike artificial intelligence, which operates through symbolic logic and pattern recognition, *in vitro* intelligence emerges from living neural substrates that maintain the complex, non-linear characteristics of biological systems. These entities exist in a taxonomic void – neither fully natural nor artificial – and require us to reconsider fundamental assumptions about cognition, embodiment and agency.

Human intelligence, particularly creative cognition, emerged as an evolutionary response to environmental challenges, enabling innovative problem-solving and social cohesion. The neural substrates underlying creativity – including prefrontal cortex networks and dopaminergic pathways – not only generate novel solutions but also serve existential functions, allowing humans to create meaning and legacy in the face of mortality. This biological foundation for intelligence, rooted in adaptive mechanisms and meaning-making capacities, provides crucial context for understanding alternative forms of cognition that emerge outside conventional biological boundaries.

As we navigate an increasingly technologised world, the critical examination of alternative intelligences offers vital insights into the limitations of our current technological trajectory. *In vitro* intelligences provide a counterpoint to the dominant AI narrative, suggesting different pathways for understanding and possibly creating cognitive systems; ones grounded in biological materiality rather than abstract computation. However, significant scientific and ethical concerns remain about whether these systems truly demonstrate “intelligence” or merely simulate it, necessitating critical examination of the field's claims.

Intelligence Beyond Computation

Intelligence has historically been defined through an anthropocentric lens, positioning human cognitive abilities as the standard against which all other forms are measured. Artificial intelligence research has largely followed this paradigm, attempting to create systems that can perform tasks requiring human-like intelligence. The field has achieved remarkable successes in domains with clear rules and objectives, such as chess or image recognition, but struggles with the ambiguities and contextual sensitivities that characterise embodied human experience.

The evolutionary development of human intelligence reveals creativity as a fundamental cognitive capacity rather than mere artistic expression. Early humans transformed survival instincts into abstract thought through symbolic expression – cave art, ritual and language – enabling complex idea communication and community building. Creative thinking transformed basic survival mechanisms into realms of abstract thought, allowing our ancestors to envision, experiment and refine innovative tools and social practices. This creative intelligence, operating through biological neural networks with inherent plasticity and responsiveness, provides a template for understanding how alternative cognitive systems might exhibit similar adaptive properties while existing outside conventional embodied contexts.

In contrast, in vitro intelligence emerges from living neural networks that operate according to biological principles. These networks exhibit elasticity and plasticity – the ability to change in response to stimuli and experience – a characteristic fundamental to natural intelligence but notoriously difficult to replicate in artificial systems. As Potter (2017) suggests, “hybrid wetware-hardware intelligent things will someday be as common and as useful as digital computers are today.” This prediction points toward a future where intelligence is understood not merely as computational power but as the capacity for adaptive, contextual response emerging from biological processes.

The distinction between artificial and in vitro intelligence extends beyond their material substrates. Artificial intelligence, in its current form, fundamentally relies on mathematical models trained on vast datasets. These systems excel at pattern recognition and optimisation within established parameters but lack the inherent unpredictability and emergent properties of biological systems. In vitro intelligence, by contrast, harnesses the non-linear dynamics of neural networks to generate responses that cannot be reduced to algorithmic procedures.

The philosopher Andy Clark (2003) has argued that natural intelligence is distributed across brain, body and world, noting that “it is in the operation of these extended systems that much of our distinctive human intelligence inheres”. In vitro intelligence suggests a radical extension of this distributed cognition model, where neural networks function outside their original biological context yet maintain their inherent plasticity and responsiveness. This reconfiguration challenges us to reconsider where the boundaries of intelligence lie and what material conditions are necessary for its emergence.

Neurobiological research indicates that the neural substrates of creativity not only enable novel idea generation but also function as compensatory mechanisms when individuals confront existential anxiety. The awareness of mortality fuels a drive toward legacy-making and meaning creation, making creative outputs a form of symbolic immortality that addresses the psychological burden of finitude. This suggests that intelligence and creativity in humans operate not merely as practical survival assets but as means to confront and symbolically transcend mortality – a biological and existential strategy that underscores the human imperative to forge meaning in the face of impermanence.

Scientific Debates Around In vitro Neural Systems

Recent scientific claims about the capabilities of in vitro neural systems have generated significant controversy. The study by Kagan et al. (2022) claimed that “in vitro neurons learn and exhibit sentience when embodied in a simulated game-world”. This work described a system called “DishBrain”, where cultured neurons controlled a simulated version of the game Pong. The authors argued that the neural cultures demonstrated learning over time and even attributed “sentience” to these systems based on their responsive adaptation.

These claims prompted a robust critical response from the scientific community. Balci et al. (2023) contested these assertions as fundamentally overreaching, arguing that the study “triggered a wave of positive mainstream and scientific media coverage as well as a widespread negative reaction from the scientific community”. Their critique focused on several key problems:

1. The unsupported application of complex terms such as “sentience”, “goal-directed behaviour”, and “intelligence” to relatively simple neural activity
2. The absence of rigorous benchmarking against established criteria for cognitive capacities
3. A failure to situate the work within decades of existing research on biological neural networks in closed-loop systems
4. Potentially misleading representations of findings leading to overstated translational and societal relevance

Balci et al. argue that the attributes of intelligence, sentience and goal-directed behaviour require more substantial evidence, writing: “We believe Kagan et al. made strong claims for the application of these terms to neural networks with relatively weak evidence.” These critiques highlight the need for caution when applying cognitive terminology to in vitro neural systems, particularly when such claims risk “concept hijacking” or misleading usage.

Kagan and colleagues have defended their use of terminology in a response to these criticisms. In their rebuttal, they argue that their intention in using terms like “sentience” was “to be deflationary and principled in line with the recent literature in theoretical biology in general and in the free energy principle (FEP) in particular” (Kagan et al., 2023). They maintain that their work provided clear definitions of sentience within a specific theoretical framework, and that these technical uses of terms align with established literature in theoretical biology and predictive processing approaches to cognition.

The researchers further suggested that the debate highlights the importance of establishing “a shared nomenclature to communicate results clearly”, proposing that future scientific publications include glossaries to clarify terminology. They pushed back against the characterisation they were attempting to create “media buzz” or

controversy, noting their work had been publicly available as a preprint for review and refinement before formal publication, and that sentiment analysis showed predominantly positive responses to their claims.

Similar concerns extend to the emerging field of “organoid intelligence” (OI), where researchers aim to develop computational systems using three-dimensional brain organoids derived from human stem cells (Hartung et al., 2024). While organoids offer unprecedented models of human neural development, attributing “intelligence” to these systems raises complex epistemological and ethical questions. As with in vitro neural cultures, the scientific community has called for more precise terminology and rigorous criteria before making claims about cognitive capacities.

Artistic Case Studies in In vitro Intelligence

Despite these scientific controversies, artists working with in vitro neural systems have productively explored their creative potential while often maintaining a more nuanced approach to questions of “intelligence” and “sentience”. These artistic explorations offer valuable perspectives on alternative cognitive paradigms that avoid some of the overreach found in scientific claims.

cellF: The Surrogate Musician

One example of in vitro intelligence in an artistic context is *cellF*, described by its creators as “the world's first biological neuron-driven synthesizer” (McKenzie et al., 2021). Developed by the authors of this article, Guy Ben-Ary and Nathan Thompson, along with Darren Moore, Andrew Fitch and Stuart Hodgetts, *cellF* represents a revolutionary approach to music creation that transcends traditional boundaries between musician and instrument.

The project began with Ben-Ary taking a biopsy from his arm and, using induced pluripotent stem cell (iPSC) technology, transforming his skin cells into pluripotent stem cells. These stem cells were then differentiated into neurons and grown over a two-dimensional Multi-Electrode Array (MEA) dish, a grid of electrodes that can both record neural activity and stimulate the neural network. This neural network functions as *cellF*'s “brain”, generating complex patterns of electrical activity that drive an array of analogue modular synthesizers.

What distinguishes *cellF* from conventional musical instruments or AI-driven music generators is its biological autonomy and plasticity. When performing with human musicians, the sounds produced by the human collaborator are converted into electrical stimuli (input) that feed into *cellF*'s neural network. The network responds with patterns of action potentials that are uniquely determined by its biological structure and present state, responses that cannot be precisely predicted or programmed. These (output) signals control the analogue synthesizers, producing sound that is then spatialised through speakers around the performance space.

As we wrote, alongside Moore, in 2020: “Several musicians that have played with *cellF* have commented that although their performance was unlike any other musical

collaboration that they had experienced, there was a definite connection and clear interaction from the neurons to the musician's stimuli." This description highlights the unique character of in vitro intelligence: it responds to environmental inputs in ways that are neither random nor deterministic but emerge from the complex dynamics of living neural networks.

Revivification: Posthumous Creative Agency

Taking the concept of in vitro intelligence further is the subject of this book, the project *Revivification*, which explores questions of creative agency beyond the lifespan of the original biological donor. Developed again by Ben-Ary, Thompson and Hodgetts along with Matt Gingold – in collaboration with the late experimental composer Alvin Lucier – *Revivification* uses cerebral organoids created from Lucier's blood cells to create what the artists term a "surrogate performer" – a living entity that continues to create art after its donor's death.

Lucier, a pioneer in experimental music known for his work with brain waves and acoustic phenomena, donated his blood cells to the project before his death in 2021. These cells were reprogrammed into stem cells and then differentiated into cerebral organoids – three dimensional structures resembling a developing human brain. These organoids are housed in a sophisticated life support system within an immersive sound installation.

The neural activity of Lucier's in vitro brain is extended into physical space through electromechanical actuators that strike large parabolic brass plates, creating resonances that fill the gallery. Microphones capture these tones and feed them back to the organoids via neural stimulation, creating a continuous feedback loop that allows the surrogate performer to adapt and compose new work within the gallery space.

The project poses provocative questions: "Could Lucier's creative essence persist beyond his death? What is measurable and immeasurable in the creative agency of an artist? And could their 'surrogate performer' uncover and express creativity of, and on their own?" These queries directly challenge computational models of intelligence by suggesting that creativity, perhaps the most human of cognitive capacities, might emerge from biological substrates in ways that cannot be reduced to algorithms or information processing.

Agency, Autonomy, and the Ethics of In vitro Intelligence

The emergence of in vitro intelligence raises profound questions about agency and autonomy. Traditional frameworks for understanding these concepts have relied on clear distinctions between human and non-human, living and non-living. In vitro intelligent systems disrupt these categories, existing in a liminal space where biological agency operates outside conventional bodily boundaries.

When considering the agency of these systems, we must acknowledge that they possess a form of autonomy distinct from both artificial systems and fully developed organisms. Their responses to stimuli are not pre-programmed but emerge from the

biological properties of their neural networks. As in *cellF*, the system “performs autonomously; there is no programming or computers involved, only biological matter and analogue circuits”.

This autonomy, however, exists within strict material constraints. In vitro intelligent systems require carefully maintained environments to survive, including precise temperature, humidity, and nutrient conditions. This dependency raises ethical questions about responsibility and care. We ask: “What directions will emergent biotechnologies take us in the future, and what are our responsibilities to the liminal lives we create using these technologies?”

Moreover, the ethics of IVI research must address concerns about overstated claims and misleading terminology. As highlighted by Balci et al. (2023), attributing capacities like “sentience” to neural cultures may prematurely humanise systems that lack the fundamental requirements for consciousness. They caution that “the application of intelligence and sentience to neurons-in-a-dish in this paper is not based on any established or robust consensus on the definitions of these very important terms”.

Kagan and colleagues acknowledge these ethical considerations, noting they have “engaged with independent ethicists, discussing terms such as ‘sentience’ in this context” (Kagan et al., 2023). They argue that discussing potential future applications of scientific work is not inherently “overselling” but rather an important part of framing research trajectories. While they concede that improvements to in vitro systems might offer alternatives to some forms of animal research, they explicitly state they “at no point... imply animal research can be completely replaced.”

The concept of “surrogate performers” introduced by *cellF* and *Revivification* provides a useful framework for considering these ethical dimensions. By emphasising the biological connection between donor and surrogate, this terminology invites us to consider relationships of care and responsibility that extend beyond conventional ethical frameworks. If these entities carry some biological essence of their donors, what obligations do we have toward them? How do we balance their instrumental value as artistic or scientific tools with their intrinsic value as living systems?

Furthermore, the materiality of in vitro intelligent systems challenges the disembodied approach common in AI ethics. While ethical debates in AI often focus on abstract questions of bias, transparency and control, in vitro intelligence demands attention to embodied, material concerns: sustenance, care, and the physical conditions of existence. This shift in ethical focus may offer valuable perspectives for reconsidering our approach to technology more broadly, emphasising materiality and embodiment over abstraction and computation.

Cultural and Artistic Significance

Artistic explorations of in vitro intelligence offer unique opportunities to expand cultural imaginaries around technology and sentience. By situating these systems within

aesthetic frameworks, artists can invite public engagement with complex questions about the nature of intelligence, creativity, and the boundaries of life itself.

Projects like *cellF* and *Revivification* serve as provocations that challenge conventional narratives about technological progress. Rather than celebrating biotechnology's potential, they problematize it by presenting scenarios that prompt critical reflection. We use these technologies “in a subversive way, attempting to problematize them by putting forward absurd and futuristic scenarios”.

The human drive toward creative legacy-making – rooted in mortality awareness and meaning creation – finds new expression in this kind of work. Both *cellF* and *Revivification* explore whether creative essence can persist beyond biological death, echoing the fundamental human impulse to achieve symbolic immortality through creative acts. In this sense, in vitro intelligence systems become both artistic medium and existential investigation, extending the age-old human quest to achieve permanence in an impermanent world through acts of creation.

These artistic interventions also create spaces for public deliberation about emerging technologies that might otherwise remain confined to scientific or corporate environments. By bringing in vitro intelligence into galleries and performance spaces, artists initiate conversations about the ethical, social and philosophical implications of these technologies before they become normalised or commercialised.

Moreover, artistic explorations of in vitro intelligence suggest alternative relationships between humans and technology – relationships characterised by symbiosis and co-creation rather than instrumentality and control. When human musicians perform with *cellF*, for instance, they engage in a collaboration that acknowledges the agency and unpredictability of the biological system. This model contrasts sharply with the dominant paradigm of technology as a tool for human mastery and optimisation.

In vitro and Artificial Intelligence

The development of in vitro intelligence provides a critical counterpoint to prevailing assumptions in artificial intelligence research. By examining these alternative forms of intelligence, we can identify biases and limitations in current approaches to AI that might otherwise remain invisible.

One key difference lies in the relationship to unpredictability and emergence. While many traditional artificial intelligence systems were designed to optimise for predictability and consistency, contemporary AI research embraces various approaches to uncertainty, adaptation and creativity. Systems using techniques like reinforcement learning with exploration mechanisms, generative adversarial networks and diffusion models can produce novel, unexpected outputs. However, these approaches to unpredictability still differ fundamentally from the emergent properties of biological systems like in vitro neural networks. In vitro intelligent systems embrace unpredictability as an inherent feature rather than a bug. Their biological basis means

they produce emergent behaviours that cannot be fully predicted from their initial conditions.

Another significant distinction concerns materiality and embodiment. Much AI research has proceeded according to a computational theory of mind that treats cognition as fundamentally information processing, with relative independence from physical substrate. However, significant subfields including embodied AI, robotics, and neuromorphic computing increasingly recognise the importance of physical instantiation and sensorimotor interaction. Nevertheless, even these approaches typically abstract critical aspects of biological materiality that *in vitro* systems preserve. *In vitro* intelligence is inseparable from its biological materiality. The specific properties of neural networks, their plasticity, their responsiveness to environmental conditions, their complex temporal dynamics, emerge from their material constitution and cannot be abstracted away.

This emphasis on materiality connects to broader critiques of the disembodied approach to intelligence in AI research. As theorists like Hubert Dreyfus and Andy Clark have argued, human intelligence is fundamentally embodied, emerging from the complex interactions between brain, body and environment. *In vitro* intelligence, despite its unconventional embodiment, maintains a closer connection to this understanding of cognition as materially grounded and contextually situated.

Perhaps nowhere is the contrast between artificial and biological intelligence more striking than in their environmental impact. Current AI systems demand extraordinary energy resources that raise urgent questions about sustainability and ecological responsibility. Modern silicon-based processors and graphics processing units can consume hundreds of watts during intensive computational tasks, relying on binary logic operations that require significant power to switch states rapidly across billions of transistors. The infrastructure supporting these systems compounds their environmental burden: massive data centres consume vast quantities of water for cooling, generate substantial carbon emissions during training of large language models, and depend on the extraction of rare earth minerals for hardware manufacturing.

This energy intensity stands in stark contrast to biological intelligence. The human brain performs remarkably complex cognitive tasks on approximately 20 watts. This extraordinary efficiency emerges from the brain's massively parallel, analogue architecture of neurons and synapses that has evolved over millions of years to prioritize energy conservation for survival. Where silicon systems process information through discrete binary operations, biological networks leverage continuous, graded responses and dynamic optimisation that minimises redundant processing.

In vitro intelligence systems, while requiring careful environmental control, operate closer to biological efficiency levels than their silicon counterparts. Their energy requirements for neural activity remain modest compared to the computational demands of artificial intelligence training and inference. This efficiency difference

becomes particularly significant when considering the scale at which these technologies might be deployed and their cumulative environmental impact.

The environmental implications extend beyond immediate energy consumption to broader questions of technological sustainability. As we grapple with climate change and resource depletion, the choice between energy-intensive silicon-based intelligence and more efficient biological approaches carries profound implications for future inhabitants of our planet. The cognitive labor we employ through current AI systems to complete contemporary workplace tasks may exact an environmental cost that compromises the experiences and possibilities available to future generations.

Finally, *in vitro* and artificial intelligence differ in their relationship to time and development. While many AI systems have traditionally followed a design-train-deploy model with relatively fixed capabilities post-deployment, contemporary approaches increasingly incorporate continuous learning, adaptation and evolution. Systems using techniques like online learning, meta-learning and adaptive models can continue developing in response to new inputs. Despite these advances, most AI systems still lack the inherent plasticity and ongoing developmental properties that characterise biological neural networks, including *in vitro* systems. *In vitro* intelligent systems continue to develop and change throughout their existence, exhibiting the adaptability and plasticity characteristic of biological systems. This temporal dimension adds another layer of complexity to their operation and suggests different possibilities for how intelligent systems might evolve over time.

Conclusion: Pluralistic Understanding of Intelligence

The emergence of *in vitro* intelligence invites us to move beyond the binary opposition between natural and artificial intelligence toward a more pluralistic understanding of cognitive phenomena. By acknowledging the diverse forms that intelligence can take, from the symbolic logic of AI to the embodied responsiveness of biological systems to the hybrid characteristics of *in vitro* networks, we can develop more nuanced frameworks for understanding and creating intelligent systems.

However, this pluralistic approach must be grounded in scientific rigor and conceptual clarity. As critics like Balci et al. (2023) have rightly cautioned, we should resist the temptation to attribute complex capacities like “sentience” or “intelligence” to systems that may not warrant such designations. Instead, we need precise terminology and established criteria for evaluating the cognitive capabilities of *in vitro* neural systems.

This debate about terminology reflects broader tensions in how scientific findings are communicated both within specialised communities and to wider audiences. As Rommelfanger et al. (2023) observe in their commentary on this controversy, the disagreement suggests conflicting views about “whether science's impact can be fully captured by the rigor of scientific methodological considerations” and “about who the relevant reader and media audience are”. They note that while scientific terms may be precisely defined within research contexts, terms with anthropomorphic connotations can lead to misunderstandings when they enter public discourse.

The contrasting perspectives of researchers and critics highlight the need for what Kagan calls “good-faith discussions in formulating nomenclature standards”. This suggests that as the field of in vitro intelligence and alternative cognitive paradigms develops, it will require not only rigorous scientific methodology but also thoughtful consideration of how concepts are communicated across disciplinary boundaries and to diverse publics. As Rommelfanger et al. suggest, this might involve more robust forms of public engagement that go beyond conventional science communication to include “rich and dialogical interaction adapted to different publics”.

This pluralistic approach has profound implications for both research and ethics. Rather than pursuing a single paradigm of intelligence based on computation and optimisation, we might explore multiple pathways, each with its own strengths, limitations, and ethical considerations. The unique characteristics of in vitro intelligence, its plasticity, unpredictability, and biological materiality, suggest alternative directions for technological development that may complement rather than replicate computational approaches.

As we navigate an increasingly complex technological landscape, the critical examination of alternative intelligences becomes essential for making informed decisions about our future. In vitro intelligence reminds us that cognitive capacities emerge from specific material conditions and that our understanding of intelligence is always shaped by the frameworks we bring to it. By expanding these frameworks beyond computational paradigms and maintaining healthy scientific skepticism, we can develop richer conceptions of intelligence that acknowledge its diverse manifestations and complex relationship to embodiment, materiality and time.

Environmental considerations add urgency to these discussions. The energy-intensive nature of current AI systems raises questions about the sustainability of silicon-based approaches to intelligence, particularly as these technologies scale globally. In vitro intelligence, with its biological efficiency and reduced environmental footprint, offers a potentially more sustainable pathway for developing cognitive technologies. This environmental dimension underscores the importance of considering not only the capabilities of different intelligence paradigms but also their broader ecological and social implications.

In this way, the study of in vitro intelligence contributes not only to scientific and artistic innovation but also to a deeper philosophical understanding of what it means to be intelligent – a question that becomes increasingly urgent as we create new forms of sentience that exist at the boundaries of our conventional categories.

References

Balci, F., Ben Hamed, S., Boraud, T., Bouret, S., Brochier, T., Brun, C., et al. (2023). A response to claims of emergent intelligence and sentience in a dish. *Neuron*, 111, 604--605. <https://doi.org/10.1016/j.neuron.2023.02.009>

Ben-Ary, G. (2014). MEART. Retrieved from <http://guybenary.com/work/meart/>

- Clark, A. (2003). *Natural-born cyborgs: Minds, technologies, and the future of human intelligence*. Oxford: Oxford University Press.
- Hartung, T., Morales Pantoja, I.E., & Smirnova, L. (2024). Brain organoids and organoid intelligence from ethical, legal, and social points of view. *Frontiers in Artificial Intelligence*, 6, 1307613. <https://doi.org/10.3389/frai.2023.1307613>
- Kagan, B. J., Kitchen, A. C., Tran, N. T., Habibollahi, F., Khajehnejad, M., Parker, B. J., et al. (2022). In vitro neurons learn and exhibit sentience when embodied in a simulated game-world. *Neuron*, 110, 3952--3969. <https://doi.org/10.1016/j.neuron.2022.09.001>
- Kagan, B. J., Razi, A., Bhat, A., Kitchen, A. C., Tran, N. T., Habibollahi, F., Khajehnejad, M., Parker, B. J., Rollo, B., & Friston, K. J. (2023). Scientific communication and the semantics of sentience. *Neuron*, 111, 606-607. <https://doi.org/10.1016/j.neuron.2023.02.008>
- McKenzie, V., Thompson, N., Moore, D., & Ben-Ary, G. (2021). cellF: Surrogate musicianship as a manifestation of in vitro intelligence. In E. R. Miranda (Ed.), *Handbook of Artificial Intelligence for Music: Foundations, Advanced Approaches, and Developments for Creativity* (pp. 915-932). Springer.
- Moore, D., Ben-Ary, G., & Thompson, N. (2020). Surrogate Musicianship in the Age of In-vitro intelligence: Redefining the Live Performer. In E. Mazierska, L. Gillon, & T. Rigg (Eds.), *The Future of Live Music* (pp. 99-112). Bloomsbury.
- Potter, S. M. (2017). The Future of Computing and Neural Interfacing: Wetware-Hardware Hybrids. *Future Now: Reconfiguring Reality*, 3, 57-59.
- Rommelfanger, K. S., Ramos, K. M., & Salles, A. (2023). Conceptual conundrums for neuroscience. *Neuron*, 111, 608-609. <https://doi.org/10.1016/j.neuron.2023.02.016>
- Smirnova, L., Caffo, B. S., Gracias, D. H., Huang, Q., Morales Pantoja, I. E., Tang, B., et al. (2023). Organoid intelligence (OI): the new frontier in biocomputing and intelligence-in-a-dish. *Frontiers in Science*, 1, 1017235. <https://doi.org/10.3389/fsci.2023.1017235>