What if organ-on-chip were digital?

Exploring biology before the lab.

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Organ-on-chip platforms were developed to bring physiologically relevant biology closer to reality. By combining microfluidics with living cells, they recreate the physical and mechanical conditions of human tissue — shear stress, dynamic flow, three-dimensional cell architecture. The result is a model that behaves more like the organ it represents than conventional cell culture ever could.

But physical organ-on-chip experiments are demanding to run, slow to iterate, and difficult to scale. What if the same biological logic could be run digitally — before a single chip is prepared or a single cell is seeded?

That is what a digital organ-on-chip is built to do.

WHAT IS ORGAN-ON-CHIP AND WHERE DOES IT STAND IN CELL MODELS?

The core idea behind organ-on-chip is straightforward. Take a small chip — typically the size of a USB drive — engineer channels through it, line those channels with living human cells, and flow fluid through at physiologically relevant rates. The cells experience the kind of mechanical environment they would encounter in the body: pressure, flow, and stretch. They organise themselves accordingly. This is what sets organ-on-chip apart from conventional two-dimensional cell culture — not just the biology, but the physical context in which that biology operates.

The approach has demonstrated real utility. A study by Soragni et al. screened over 1,500 kinase inhibitors on a three-dimensional vascular organ-on-chip model — notable because it demonstrated a level of throughput rarely achieved in organ-on-chip systems, using a 48-well plate format rather than individual chips [1, 2, 3].

However, physical organ-on-chip experiments are technically demanding. The setup alone requires specialised equipment — pumps, tubing, and flow control systems to maintain physiologically relevant conditions. Chips must be fabricated to tight tolerances, surfaces prepared and coated consistently, cells seeded at the right density and allowed to establish before any experiment begins. From preparation to result, experiments can take weeks to months. Each of these steps introduces variability. Results can differ between chip batches, between operators, and sometimes between runs on the same platform under nominally identical conditions. The materials themselves can interfere — any surface in contact with the experimental system, including those marketed as low-adsorption, can interact with small molecules and silently alter the concentration and profile a cell actually experiences.

Scaling adds further pressure. Running multiple doses, time points, or conditions in parallel requires multiple chips and significant operator time. And with small sample sizes comes a statistical reality: in a noisy biological system, low *n* means low power. Even a real effect may not be detectable, and what appears significant may not hold up.

Organ-on-chip is a more realistic model than what came before it. But like all models, it captures an aspect of biology — not the whole. Understanding that boundary is what motivates the next step.

THE DIGITAL TRANSLATION — WHAT IT IS AND WHAT IT ISN'T

The phrase "digital twin" gets used broadly, and it is worth being precise about what it means here.

In engineering, digital twins are well established. A chemical plant has a digital counterpart that mirrors its real-time behaviour. An aircraft is modelled computationally before it is ever built. Formula 1 teams run thousands of simulated race scenarios before a car turns a wheel on track. In each case, the digital model does not replace the physical system — it informs decisions about it. The question for biology is not whether this approach is valid, but why it has taken so long to arrive.

A digital organ-on-chip is not a theoretical simulation of how cells ought to behave. It is built from three inputs: experimental data from physical organ-on-chip systems, the underlying biology, physics, and chemistry that govern cell behaviour, and increasingly, machine learning to identify patterns that are difficult to capture by hand. The parameters in the model are not assumed — they are mapped from real measurements [4, 5].

The purpose is equally specific. A digital organ-on-chip is a planning instrument. It is built to explore conditions, test hypotheses, and narrow the experimental space before physical resources are committed. It does not claim to predict clinical outcomes. It does not replace the physical experiment. It answers a more modest and more useful question: given what we know, which experiments are most worth running?

It is also worth acknowledging what the digital model cannot do. It cannot capture the full complexity of biology. No model can — physical or digital. As the statistician George Box observed, all models are wrong, but some are useful. The physical organ-on-chip is itself a model: it captures an aspect of human tissue, not the whole. The digital version captures an aspect of the physical system. Both are approximations. The difference is that in a digital model, every assumption is explicit and every parameter is visible. When something is wrong, it can be identified and corrected. In a physical system, the sources of error are often harder to isolate.

Because biological systems are complex and variable, that is precisely the argument for digital tools — not against them. The noisier the system, the more value there is in structured exploration before committing to it.

> ***"All models are wrong, but some are useful." — George Box***

A PROTOTYPE IN PRACTICE — THE ENDOTHELIAL SPROUTING MODEL

Endothelial sprouting — the process by which new blood vessels grow from existing ones — is a well-studied biological system. It is driven by chemical signals, shaped by the surrounding tissue matrix, and modulated by the mechanical forces that blood flow imposes on vessel walls. It is directly relevant to drug development: angiogenesis plays a central role in tumour growth, wound healing, and cardiovascular disease.

It is, for these reasons, a good candidate for a first digital organ-on-chip prototype. The biology is well characterised enough to build from, and the process is visually and mechanistically rich enough to make the model meaningful.

The prototype is an agent-based model — meaning individual cells are represented as autonomous agents that respond to their local environment according to defined rules. Four parameters are experimentally mapped and adjustable: cell count, sprouting rate, VEGF gradient strength, and migration speed.

Figure 1. The endothelial sprouting digital model, showing active sprout formation with visible parameter controls — cell count, sprouting rate, VEGF gradient, and migration speed. Each parameter can be adjusted individually or swept across a defined range automatically.

Running the model takes minutes — what would take days or weeks to set up, execute, and image in a physical organ-on-chip experiment can be observed and iterated in a single sitting. A user can adjust a parameter, observe how the sprouting pattern changes, and build intuition about which conditions are worth pursuing in the physical system. Parameters can be added or removed depending on what is being investigated — the model adapts to the question, not the other way around. But the real power is in automation. Parameter ranges can be defined and the model left to run through combinations systematically — set the conditions, walk away, and return to a structured readout of which experiments showed meaningful behaviour and which did not. Running thousands of iterations also makes it possible to stress-test experimental designs statistically — understanding whether a planned physical experiment has sufficient power to detect a real effect before a single cell is touched. Conditions that produce no response can be deprioritised. Conditions that show interesting behaviour can be brought forward for physical validation.

The same modelling approach can be extended to other organ-on-chip contexts. A gut epithelial barrier model, a neuron model and a hepatotoxicity model exist as further prototypes, each grounded in the same framework. The endothelial sprouting model is the most developed, but the architecture is designed to grow.

PHYSICAL VS DIGITAL — A DIRECT COMPARISON

The table below sets out the practical differences between running an experiment on a physical organ-on-chip system versus a digital one. Neither column represents a better system in absolute

terms — they are tools for different purposes. What the table makes clear is that the two approaches are complementary rather than competitive.

Dimension	Physical	Digital
Scalability	Limited by chips, staff	Scales computationally
Iteration speed	Days–weeks	Minutes–hours
Cost per run	High	Very low
Data reuse	Difficult, siloed	Easy, cumulative
Variability	Biological noise	Controlled, tunable
Exploration space	Narrow, constrained	Broad, hypothetical
Failure mode	Expensive	Low-cost learning
What it can't do	Predict untested space	Capture full biology

Table 1. Physical vs digital organ-on-chip — a practical comparison. The last row is the most important: each system has a ceiling, and those ceilings are different.

The last row is the most important. A physical organ-on-chip cannot easily explore conditions it has never been run under — each new condition requires a new experiment. A digital model cannot capture the full complexity of living biology. Acknowledged honestly, these limitations define how the two systems should be used together: digital first to map the space, physical to validate what matters.

WHERE THIS IS HEADING

What is described here is a beginning.

The endothelial sprouting model demonstrates that the approach is technically feasible — that biological systems with well-characterised parameters can be translated into digital models that are useful for planning and exploration. The extension to gut epithelial barrier and hepatotoxicity models shows that this is not a single use case but a framework that can grow across biological contexts.

The broader ambition is a platform: a library of digital organ-on-chip models, each grounded in experimental data, each designed to work alongside its physical counterpart. Beyond single cell-type models, the same framework can be extended to co-cultures — systems where multiple cell types interact, communicate, and respond to each other. Vascular-parenchymal interactions, immune cell recruitment, and multi-tissue interfaces are all within scope as the platform matures. Not to replace the wet lab, but to make every decision that goes into it more deliberate. To reduce the number of experiments run on intuition alone, and increase the number run on historical evidence and grounded reasoning.

Other industries reached this point years ago. Chemical plants, aircraft, and racing cars all have digital counterparts that are consulted before physical resources are committed. Biology is more complex and less fully characterised than any of those systems — but that is an argument for investing in digital tools, not for waiting until the biology is simpler.

There are also contexts where a physical wet lab is simply not an option. Space travel is one of them. As human presence beyond Earth becomes a serious planning horizon, the ability to run biological experiments digitally — without reagents, chips, incubators, or operators — moves from a convenience to a necessity. A digital organ-on-chip model could, in principle, support health monitoring, drug testing, and physiological research in environments where no physical laboratory could fit.

This is the direction we are building toward. We believe the combination of organ-on-chip biology, mechanistic modelling, and AI represents a meaningful step forward in how preclinical research is designed and executed. The question is no longer whether biology can be modelled digitally. It is how far that model can take us. What begins with digitising sprouting vessels may be, in principle, a new way of doing biology.

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