AGNES

A Digital Model Transfer Proof of Concept

Can a published wet lab assay become a reusable digital model?

KEY IDEA

• A published angiogenesis assay was transferred into a digital model.
• Built using publicly available information from the original study.
• Explores whether biological models can continue evolving after publication.

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125 Digital Replicates

< 5 Minutes

WHAT WE FOUND

• Reproduced key biological trends from the original assay.
• Demonstrates one possible path for extending biological models digitally.

Proof-of-Concept Study

Estimated reading time: 5 minutes

AvatarsBio

AGNES:

A proof of concept in digitising an organ-on-chip angiogenesis assay

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Drug discovery is one of the most resource-intensive endeavours in science. Bringing a single compound to approval costs nearly $2.9 billion (in 2013 dollars) on average and takes over a decade [1]. Every experiment that contributes to that journey takes months to years of preparation, skilled operator time, carefully controlled conditions, and biological variability that no protocol can fully tame.

In an open survey we conducted on LinkedIn, seven in ten scientists reported difficulty using historical data in their current work. Many well-characterised, validated assay data exist — the question is whether they can be reused, put to work in a new context, for a new purpose, to test ideas before the lab.

> ***If we're so confident in our models — why don't we digitise them?***

That is what this proof of concept sets out to answer. If a cell or organ-on-chip model or microphysiological system is robust enough to publish, peer-review, and screen compounds on — can we digitise it? Can we transfer that model into a digital framework that preserves its biological logic and reproduces its outputs?

1,537	5/5	25	< 5 min
kinase inhibitors screened (source assay)	conditions — direction match	digital replicates per condition	to run 125 simulations

DIGITISING AN ASSAY

In a companion concept white paper, we explored what it would mean for organ-on-chip models to have a digital twin counterpart — faster iterations, focused experimental planning, and the ability to test ideas before committing physical resources [2]. AGNES puts that concept into practice on a specific, published assay.

AGNES is a browser-based digital model of endothelial sprouting. Individual endothelial cells are represented as agents that follow a VEGF gradient, push through ECM resistance, and extend sprouts behind migrating tip cells — in a simulation domain that mirrors the geometry of the original microfluidic chip. The source is entirely public. No proprietary data was used to build it. Everything in AGNES comes from the published record.

The goal here is explicit and bounded: to test whether a published, established assay can be transferred into a digital model that reproduces the direction of compound effects, the inhibition ranking, and the readout logic of the original screen. In this paper, model transfer refers to recreating the biological logic and experimental readouts of a published assay within a

computational framework. Not to replace the experiment. To digitise it, test ideas, and focus decisions before the resource-heavy and time-consuming wet lab.

THE PHYSICAL ASSAY BEHIND THE DIGITAL MODEL

The physical assay is described in Soragni et al. (2024), a large-scale phenotypic screen of 1,537 kinase inhibitors on a 3D angiogenesis model [3]. Endothelial cells were cultured as perfused micro-vessels in microfluidic chips, exposed to a pro-angiogenic cocktail, and treated with kinase inhibitors at 10 µM for 48 hours. Sprouting was quantified as the mean travel distance of the ten furthest nuclei into the ECM gel zone, and classified by robust Z* score into four inhibition levels: None, Mild, Moderate, and High.

The screen was the largest organ-on-chip phenotypic screen reported at the time — over 4,000 chips, 65 plates, four batches. AGNES implements five conditions from that screen: Vehicle Control, Sunitinib, PD0325901, Brivanib, and Butein — all at 10 µM. The readout mirrors the paper directly. In this version, AGNES focuses on sprouting behaviour; the main vessel integrity readout and morphological phenotype classifications from the paper represent a natural next layer of fidelity. All parameters and reference values used are drawn exclusively from this published, openly licensed source. Figure 1 shows the model running under Vehicle Control conditions at the end of the 48-hour simulation window.

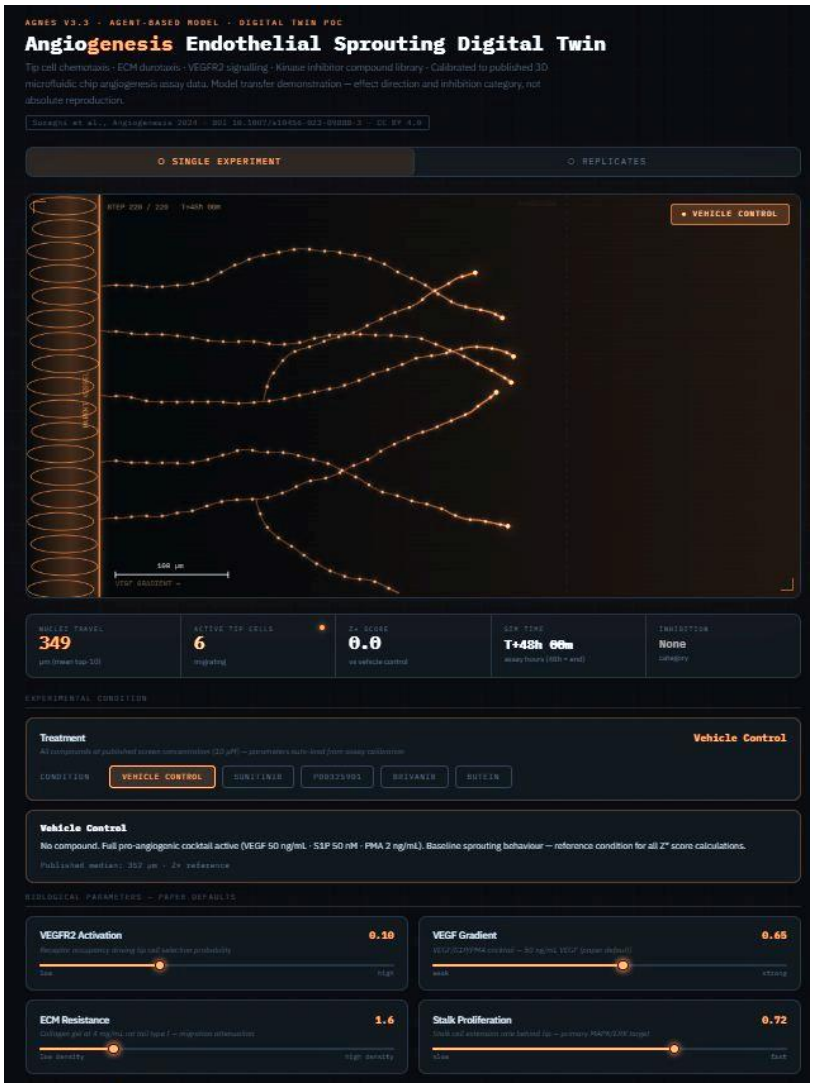

Figure 1. AGNES v3.3 — Vehicle Control condition at T+48h. Tip cells (orange) extend from the vessel wall (left) across the ECM gel zone toward the VEGF gradient source (right). Sprout morphology is deliberately simplified — the model prioritises computational efficiency and quantitative readout fidelity over visual realism. Parameter panel and compound selector shown below the canvas. Scale bar 100 µm.

WHAT THE DIGITAL MODEL PRODUCES

The model was initially calibrated against a single inhibitor compound. In this version, four named compounds from the published screen are implemented. The direction of compound effect is correct across all five conditions, and rank ordering is fully preserved.

Condition (10 µM)	Published reference	Digital mean (µm)	Z* (digital)	Inhibition category	Direction match
Vehicle Control	352 µm (median)	352 µm	0.0	None	Ref
Sunitinib	62 µm (median)	61 µm	−10.3	Moderate	✓ Yes
PD0325901	Z* −17.9 (High)	5 µm	−12.3	Moderate	✓ Yes
Brivanib	Z* −7.2 (Mild–Mod)	141 µm	−7.5	Mild	✓ Yes
Butein	Z* −4.9 (Mild)	217 µm	−4.8	Mild	✓ Yes

Model transfer POC — concordance evaluated at effect direction and inhibition category level, not absolute values. Published Z scores from primary screen at 10 µM.*

Sunitinib and PD0325901 produce strong inhibition. Brivanib sits in the middle. Butein is mild. Vehicle control reproduces the published median exactly. The rank ordering originally established through thousands of physical chips can be reproduced digitally in minutes once the model has been constructed.

That contrast matters. The replicates panel (Figure 2) represents 25 runs per condition — 125 simulation runs completed in under five minutes. Generating equivalent replicate distributions physically would require substantial time and resource. Here, the distributional output — mean, standard deviation, Z* spread across conditions — is immediate.

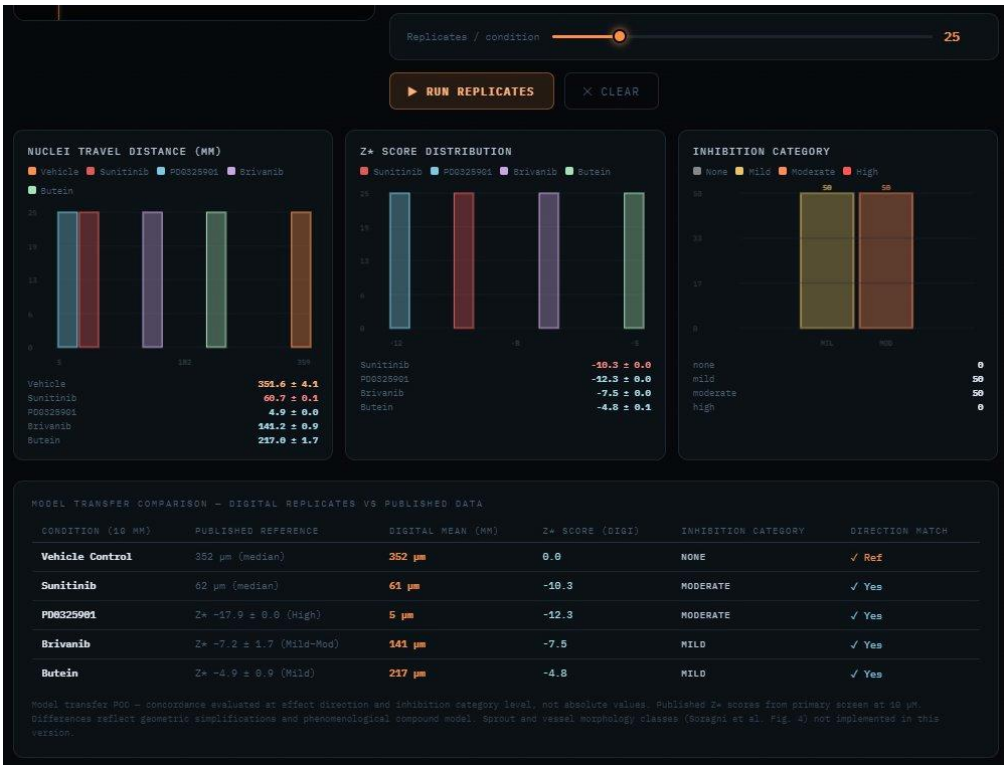

Figure 2. AGNES v3.3 Replicates tab — 25 replicates per condition (adjustable up to 100). Left: nuclei travel distance distributions (mean ± SD). Centre: Z score distributions. Right: inhibition category counts. Bottom: Model Transfer Comparison table with published reference values and direction match across all five conditions.*

PD0325901 warrants a brief note. The model correctly reproduces near-complete suppression of sprouting, consistent with the published High inhibition result. The digital score falls one category lower than the experimental reference, likely because a digital system contains less biological noise than a physical assay. The important observation remains unchanged: sprouting is effectively shut down. Additional experimental data could help calibrate this behaviour more closely.

WHAT THIS MEANS

AGNES demonstrates that a published organ-on-chip assay can be digitised. The biological logic of an established screen — its geometry, its compound mechanisms, its readout definitions — can be transferred into a digital model that reproduces its qualitative outputs from public data alone.

The model can be made more powerful still. Just as large language models are grounded with domain-specific knowledge to sharpen their outputs, a digital assay model can be grounded with internal experimental notebooks, unpublished historical data, and proprietary compound characterisation — giving it the biological context needed to move from reproducing known results toward anticipating new ones.

Unlike physical chips, a digital model can be not constrained by standard labware formats — dimensions, densities, and geometries can be explored freely, allowing possibilities to explore biology more freely, including configurations that better approximate in vivo anatomy.

It shows that historical assay data can be reused, transferred, and put to work — to orient experimental thinking, focus physical resources, and test ideas before we step into the wet lab. This is what we envision the future of cell-based research to look like. Digital models that make every physical experiment count.

REFERENCES

1. DiMasi JA, Grabowski HG, Hansen RW. Innovation in the pharmaceutical industry: new estimates of R&D costs. J Health Econ. 2016;47:20–33. https://doi.org/10.1016/j.jhealeco.2016.01.012

2. Ng CP. What if organ-on-chip were digital? Exploring biology before the lab. AvatarsBio White Paper. 2026. https://avatarsbio.com/research/pdfs/digital-organ-on-chip.pdf

3. Soragni C, Queiroz K, Ng CP, et al. Phenotypic screening in Organ-on-a-Chip systems: a 1537 kinase inhibitor library screen on a 3D angiogenesis assay. Angiogenesis. 2024;27:37–49. https://doi.org/10.1007/s10456-023-09888-3