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MINI-REVIEW

Artificial Intelligence Virtual Organoid Laboratories (AIVO-Labs)

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Abstract

Organoids reproduce important tissue features, but variability in biomaterials and culture, labor-intensive workflows, limited standardization, and predominantly endpoint readouts constrain reproducibility and longitudinal interpretation. We propose Artificial Intelligence Virtual Organoid Laboratories (AIVO-Labs), a closed-loop experimental paradigm that couples physical organoid experiments with Artificial Intelligence Virtual Organoids (AIVOs) as continuously updated digital twins. Unlike an AIVO, which represents an individual organoid-scale computational counterpart, an AIVO-Lab is a laboratory-level, cross-experimental platform that coordinates data acquisition, model calibration, experiment selection, and prospective wet-lab validation across repeated cycles. In this bidirectional workflow, each physical result updates the AIVO, while model predictions prioritize the next experiment, directly addressing slow iteration, variable protocols, and endpoint-focused analysis. The framework builds on Artificial Intelligence Virtual Cells (AIVCs), which encode multimodal cell states as universal representations that can be interrogated by virtual instruments, and extends them to organoid scale through models of cell-cell and cell-matrix interactions. We outline a three-layer architecture comprising data, model, and interaction layers and discuss applications in drug screening, mechanism and resistance mapping, developmental and disease trajectories, and toxicology. AIVO-Labs are presented as a research framework whose predictions require prospective validation, transparent uncertainty estimates, and appropriate governance.

Keywords: Artificial intelligence; Organoid; AIVOs; AIVCs; AIVO-Labs

1. Introduction

Organoids are three-dimensional, miniaturized tissue models derived from stem or progenitor cells that reproduce selected anatomical and functional features of native organs[1] Compared with conventional two-dimensional cultures and many animal models, organoids can better preserve human-relevant cellular diversity and tissue organization[2]; however, critical limitations remain. Matrigel and other animal-derived extracellular matrices have complex, ill-defined, and batch-variable biochemical and mechanical properties, which can compromise the reproducibility of organoid culture[3] Manual culture, passaging, and readout procedures introduce operator-

dependent variability, and many assays still rely on destructive endpoint measurements rather than continuous monitoring. These constraints reduce reproducibility and make it difficult to compare results across experiments and laboratories.

In parallel, life-science research is adopting digital-twin concepts. Early virtual-cell models represented selected pathways or processes, whereas Artificial Intelligence Virtual Cells (AIVCs) aim to learn broader cell-state representations from heterogeneous biological data.[4,5] In this framework, multimodal measurements are encoded as universal representations (URs), which are compact numerical descriptions of cell state. Virtual instruments (VIs) operate on URs to predict responses, simulate perturbations, or decode model states into interpretable readouts. An AIVC is therefore an AI-enabled *in silico* counterpart of a living cell rather than a single fixed mechanistic model.

Virtual Organoids (VOs) extend computational modeling to multicellular, organoid-scale systems. The term 'VO' can include mechanistic, data-driven, or hybrid simulations of organoid structure and function. We use Artificial Intelligence Virtual Organoid (AIVO) for the AI-enabled subset of VOs that integrates multimodal data, models cell-cell and cell-matrix interactions, and can be updated from physical-organoid measurements.[6,7] An AIVO may predict multicellular growth, differentiation, spatial organization, or treatment response. When calibrated and prospectively tested, it can serve as a dynamic digital twin of a specific organoid system.

AIVO-Labs operate at a different level from individual AIVOs. An AIVO is the computational counterpart of an organoid system; an AIVO-Lab is the laboratory-level infrastructure and workflow that connects one or more AIVOs with physical experiments, data pipelines, experiment-selection algorithms, and validation procedures. Its defining contribution is a persistent closed loop across experiments: physical results update the models, and model outputs guide the next wet-lab tests. This cross-experimental integration turns AIVOs from standalone analytical models into active components of an iterative research platform. This mini-review defines the concept, describes its architecture, and examines representative applications and implementation challenges.

2. Conceptual framework

2.1. Key definitions and scope

2.1.1. Physical organoids

Organoids are three-dimensional cell-culture systems that self-organize into structures resembling selected cellular compositions and functions of native organs. They can model development, disease processes, and treatment responses, but their behavior remains sensitive to biological variability, matrix composition, culture conditions, and operator-dependent procedures.

2.1.2. Artificial Intelligence Virtual Cells (AIVCs)

An AIVC is an AI-enabled computational model of cell state and behavior. Traditional virtual-cell models often encode specific processes with mechanistic equations. AIVCs instead learn URs from large, heterogeneous datasets and use VIs to predict, perturb, or decode those representations.[4,5] This architecture can connect molecular measurements with cellular and multicellular phenotypes while retaining interfaces through which mechanistic constraints can be added.

2.1.3. Artificial Intelligence Virtual Organoids (AIVOs)

A Virtual Organoid (VO) is any computational representation of an organoid-scale system; an AIVO is the AI-enabled subset of that broader class. AIVOs combine virtual cells, models of cell-cell and cell-matrix interactions, and a simulated microenvironment to reconstruct selected organoid dynamics.[6,7] They integrate data-driven learning with mechanistic or physics-based components and are designed for iterative calibration against physical measurements. Thus, an AIVO is a model or digital twin, not a laboratory platform.

2.1.4. Artificial Intelligence Virtual Organoid Laboratories (AIVO-Labs)

An AIVO-Lab is an integrated experimental environment that links physical organoid studies with one or more AIVOs through a closed-loop workflow. Experimental data update the computational models; the models then rank perturbations, propose informative measurements, and guide the next physical experiments. The platform can connect successive experiments, organoid lines, assay modalities, and validation stages. Its purpose is to support hypothesis generation, treatment screening, and individualized modeling while preserving prospective wet-lab validation as the decision gate.

2.2. Physical and virtual systems: Differences and synergy

Physical organoids and AIVOs have different strengths. Physical organoids preserve biological complexity and provide the measurements needed to train and test computational models. AIVOs offer speed, controllability, and scalability after they have been calibrated for a defined use. They can evaluate large perturbation spaces and counterfactual scenarios that would be impractical to test exhaustively in culture. Their value depends on a feedback loop in which new measurements update the AIVO and model predictions guide subsequent experiments. This

exchange supports synchronization between the physical system and its computational counterpart without treating the model as a substitute for empirical evidence.

This complementarity allows an AIVO-Lab to address questions that neither component can resolve efficiently alone. Iterative simulation and wet-lab validation can prioritize drug doses, distinguish technical artifacts from reproducible biological signals, and expose model failures early. Shared data models and explicit calibration procedures may also improve comparisons across experiments and laboratories. Physical organoids provide empirical constraints, whereas AIVOs expand the space of testable hypotheses; the AIVO-Lab organizes their interaction into a closed-loop discovery process (Figure 1).

2.3. From AI-enabled organoids to closed-loop digital twin laboratories

AIVO-Labs build on, but extend beyond, current AI-enabled organoid research. Machine-learning systems already optimize culture conditions, analyze microscopy images, segment three-dimensional structures, and integrate omics measurements.[6,8] Engineered coculture platforms can also generate richer spatial and functional data from organoid-immune interactions.[9] In most current workflows, however, AI is applied to a single dataset or used after an experiment. The analysis does not automatically update a persistent digital twin or select and validate the next experiment.

The AIVO-Lab paradigm closes this gap by maintaining an AIVO as a continuously updated counterpart of the physical system. New measurements refine the model; researchers then query the model to identify informative perturbations, measurements, or culture conditions. Selected predictions are tested in physical organoids, and the observed outcomes become the next calibration data. The distinctive innovation is therefore the laboratory-scale orchestration of repeated model-experiment cycles across assays, time points, and experimental batches, rather than the existence of an isolated virtual organoid model.

3. Architecture of an AIVO-Lab

An AIVO-Lab can be organized into three interacting layers for data acquisition, model construction, and experimental coordination. The data layer converts quality-controlled multimodal measurements into model-ready inputs. The model layer combines AI with mechanistic and hybrid simulations. The interaction layer selects virtual and physical experiments and returns their outcomes to the data and model layers. Although described separately, the layers operate concurrently within a repeated data-model-experiment loop (Figure 2).

3.1. Data layer

The data layer includes the acquisition, quality control, integration, and governance needed to build and update an AIVO. The data layer should retain machine-readable metadata describing sample identity, experimental conditions, batches, time points, processing steps, and links to the corresponding physical organoids, consistent with FAIR principles for data provenance and reuse.[10] Its principal components are described below.

3.1.1. Multi-omics data including spatial transcriptomics

High-throughput molecular profiling provides a major part of the biological input. Spatial transcriptomics is particularly valuable because it locates gene-expression programs within a three-dimensional tissue context.[11] Combining single-cell sequencing with spatial omics allows an AIVO to represent both cell-state heterogeneity and

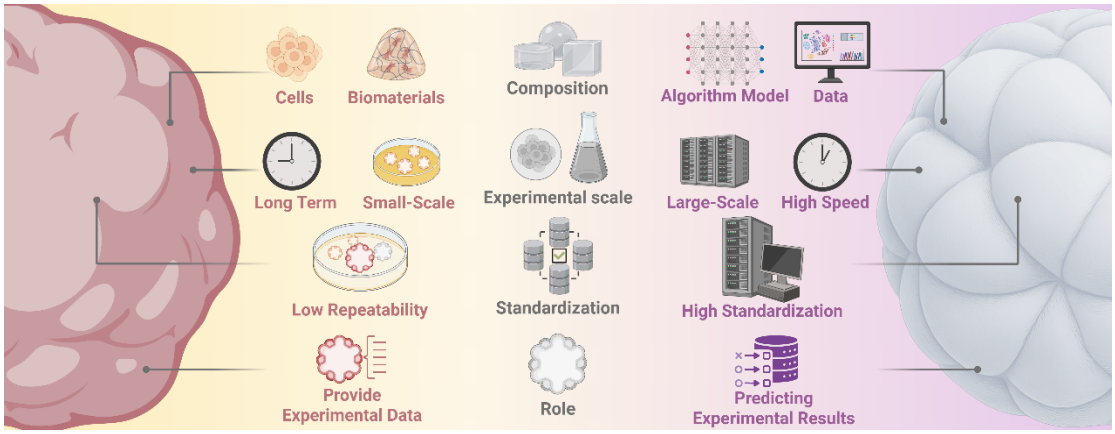


Figure 1. Complementary roles of physical organoids and Artificial Intelligence Virtual Organoids (AIVOs)

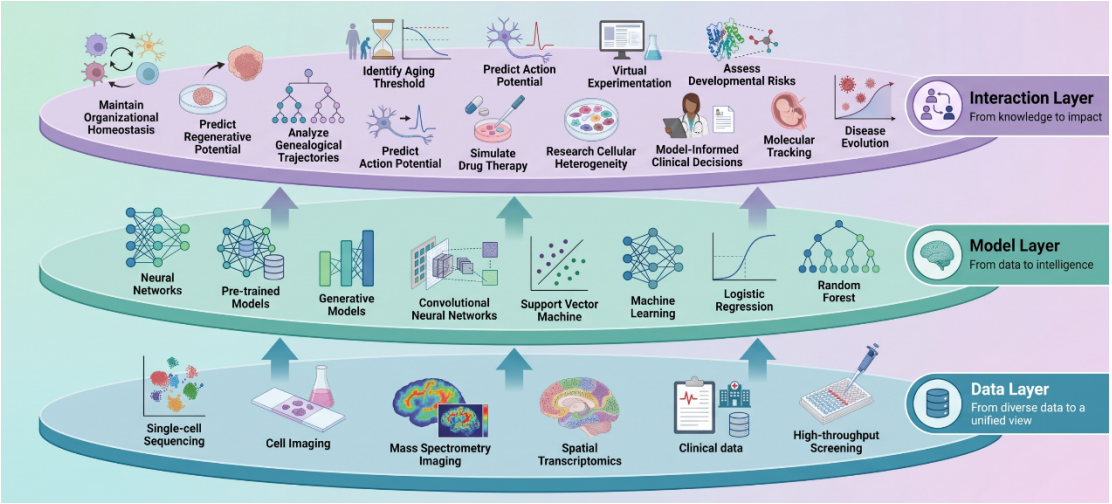


Figure 2. Three-layer architecture of an Artificial Intelligence Virtual Organoid Laboratory (AIVO-Lab)

spatial relationships. Proteomic, metabolomic, epigenomic, and functional measurements can add complementary constraints when available.[12]

3.1.2. Imaging and dynamic monitoring

Imaging supplies structural and functional phenotypes that molecular profiles alone cannot provide. Bright-field, fluorescence, and label-free three-dimensional imaging can quantify morphology, cell organization, and dynamic behavior. Automated segmentation and cellular-topology analysis can accelerate these measurements.[8] Time-lapse and sensor-based monitoring add longitudinal information, allowing model states to be updated from trajectories rather than from endpoint snapshots alone.

3.1.3. Clinical metadata and environmental parameters

For patient-derived organoids, clinical context is essential for individualized modeling.[13] The data layer should link each organoid to de-identified clinical variables, treatment history, and relevant outcomes under appropriate consent and governance. It should also record extracellular matrix composition, culture medium, oxygenation, mechanical conditions, passage number, and perturbation exposure. These variables help distinguish biological differences from culture-induced or batch-related effects.

3.1.4. Data integration

Heterogeneous measurements require explicit integration strategies. Multimodal measurements may be integrated using weighted-nearest-neighbor or related representation-learning approaches, whereas ligand-receptor inference and network-based methods can be used to investigate cell-cell communication across cell populations.[14,15] No single technique is preferred for every dataset; the method should match the sampling design and produce uncertainty estimates that can be tested experimentally. The integrated measurements are then encoded as universal representations (URs), defined here as compact numerical descriptions of organoid state that provide a common interface for predictive models and virtual instruments.

3.2. Model layer

The model layer converts integrated data into simulations, predictions, and uncertainty estimates. It combines data-driven learning with mechanistic knowledge so that performance and interpretability can be evaluated for a defined task. The principal model classes are outlined below.

3.2.1. Machine learning and AI models

Machine-learning methods support three-dimensional organoid image segmentation and topology analysis, while diffusion- and transformer-based models have been developed for predicting cell-state trajectories or treatment responses.[8,16,17] Convolutional neural networks can extract imaging features, whereas transformer and graph-based architectures can integrate long-range, multimodal, or relational information. Model selection should reflect the available sample size, data structure, and intended use rather than assume that a larger architecture is always better.

3.2.2. Mechanistic and hybrid simulations

Mechanistic simulations encode known biological or physical processes directly. In agent-based models, individual virtual cells follow defined rules and interact locally; platforms such as PhysiCell can simulate

multicellular dynamics.[18] Continuum and transport models can represent diffusion, mechanics, nutrient limitation, and flow. Hybrid models connect these components with machine learning, using biological constraints to improve extrapolation and interpretability while allowing data-driven modules to capture relationships that are difficult to specify analytically.

3.2.3. AIVC framework and universal representations

AIVCs provide a modular interface for the model layer. They map multimodal observations to URs at one or more biological scales. Mechanistic modules can constrain or update these representations, and VIs can operate on them to simulate interventions or generate predicted readouts. For example, a perturbation VI may transform a UR to represent a drug exposure, whereas a decoder may convert the resulting state into a predicted image, expression profile, or functional measurement. Throughout this review, we use only the term universal representation for this concept.

3.2.4. Generative models and state-space expansion

Generative models can expand the set of states considered by an AIVO, but generated outputs should be treated as hypotheses rather than replacement data. Diffusion and related models can predict cell-state trajectories and responses to perturbations from longitudinal or single-cell measurements.[16] They may also impute missing modalities or propose plausible intermediate states. These uses require calibration, uncertainty assessment, and external validation, particularly when the model is asked to extrapolate beyond the conditions represented in its training data.

Together, these methods transform multimodal inputs into task-specific predictions. The model layer should report both predicted outcomes and uncertainty, document the domain in which a model has been validated, and expose interfaces for biological constraints. Its outputs become experimentally useful only when the interaction layer converts them into testable actions and returns the resulting evidence to the model.

3.3. Interaction Layer

The interaction layer connects AIVOs with physical experiments. It manages experiment selection, virtual-assay execution, prospective validation, and feedback. Its central function is to ensure that model outputs lead to traceable tests and that observed outcomes update the model rather than remain as disconnected results.

3.3.1. Lab-in-the-Loop Workflows and Active Experimental Design

An AIVO-Lab alternates between measurement, modeling, and testing. After new data update the AIVO, active-learning or Bayesian-optimization methods can rank candidate experiments by expected information gain, predicted utility, feasibility, and uncertainty. Researchers retain control over safety constraints and the final experimental choice. The selected experiment is performed, and its outcome is compared with the prediction before the next cycle begins.

3.3.2. Virtual assay execution and perturbation planning

The interaction layer also supports virtual assays that mirror planned wet-lab experiments. A drug-screening model, for example, can apply a library of computational perturbations to an AIVO, rank candidate compounds, and identify predictions with high uncertainty. A small, informative subset is then tested in physical organoids. Figure 3 shows how prediction, prioritization, validation, and model updating form a closed loop.

3.3.3. Real-time feedback and continuous model updating

Synchronization requires explicit update rules. New measurements may trigger parameter recalibration, model retraining, or revision of the modeled mechanism. The physical outcome is compared with the predicted distribution, not only with a point estimate, so that disagreement can reveal model error, experimental noise, or previously unmodeled biology. Version control, audit trails, and predefined autonomy limits are necessary when experiment selection is partly automated.

The interaction layer therefore changes a static simulation into an experimentally accountable partner. It does not allow the model to replace physical evidence; it organizes repeated prediction-test-update cycles so that computational and empirical results improve one another. The following use cases illustrate how that closed-loop design could be applied.

4. Use-case scenarios

AIVO-Labs could support several areas of biomedical research and treatment development. The following examples specify the experimental problem, the role of the three-layer architecture, and the benefit expected from closing the model-experiment loop.

4.1. High-throughput drug screening and optimization

Scenario: A pharmaceutical team evaluates candidate compounds in patient-derived organoids (PDOs). Comprehensive physical screening may be limited by culture time, sample availability, and assay cost.

AIVO-Lab approach: The data layer combines molecular profiles, imaging, and measured drug responses. The model layer predicts dose-response relationships and associated uncertainty. ODFormer, for example, is a preprint

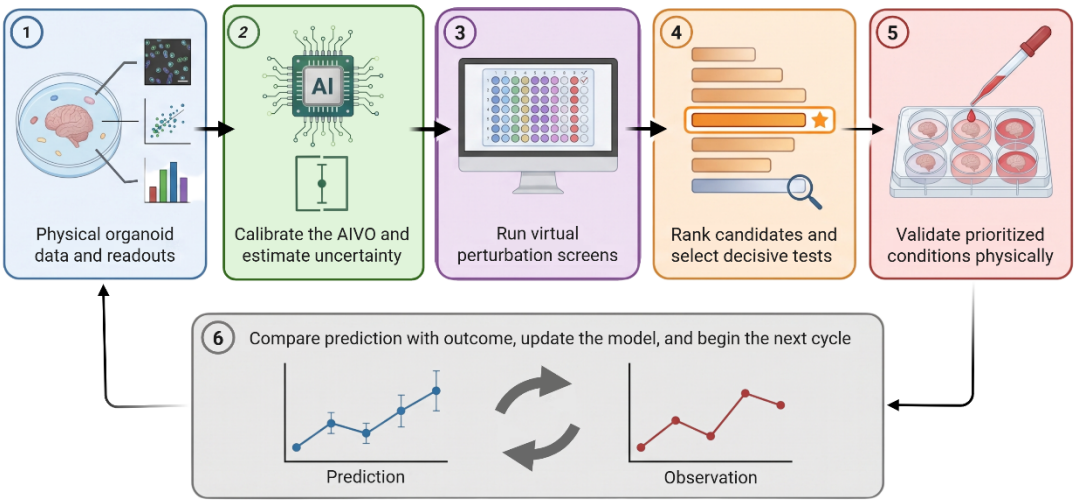


Figure 3. Closed-loop virtual assay and perturbation workflow
Abbreviation: AIVO: Artificial Intelligence Virtual Organoid.

framework that integrates transcriptomic, mutational, and drug information to predict responses in pancreatic-cancer PDOs.[17] Within an AIVO-Lab, such predictions would be used to prioritize a smaller set of compounds and doses for prospective physical testing. The measured responses would then update and re-evaluate the model.

Benefit: Virtual prioritization can reduce the number of low-information physical tests and allocate scarce organoid material to the most informative candidates. The gain depends on prospective performance, calibration, and the cost of false-negative predictions; it should not be inferred from retrospective accuracy alone.

4.2. Mechanism-of-action inference and resistance mapping

Scenario: Researchers observe drug resistance or heterogeneous responses among organoids and need to identify pathways that distinguish responders from non-responders.

AIVO-Lab approach: The model layer can combine causal-inference methods, pathway models, and interpretable machine learning to simulate gene knockouts, receptor inhibition, or changes in the microenvironment. Organoid-immune coculture systems can provide direct measurements of multicellular interactions[9], while experimentally established mechanisms such as regulation of ferroptosis sensitivity provide testable pathway-level hypotheses.[19] Predictions that a perturbation will restore sensitivity are then evaluated in physical organoids, and discordant results are used to revise the model.

Benefit: This workflow can prioritize mechanistic hypotheses and focus wet-lab resources on perturbations that distinguish competing explanations. Interpretation remains conditional on the model and training data, so causal claims require targeted experimental validation.

4.3. Developmental, regenerative, and pathological trajectories

Scenario: Developmental, regenerative, and pathological processes unfold over time, but organoid cultures often provide sparse snapshots and limited nondestructive measurements.

AIVO-Lab approach: Longitudinal imaging and molecular snapshots can calibrate state-space, recurrent, or diffusion models that predict alternative trajectories.[16] Researchers can simulate changes in signaling, mutation, stress, or intervention timing and then select time points that best discriminate among predicted mechanisms. Functional neural networks in brain organoids illustrate the type of multiscale phenotype that may require coordinated structural, molecular, and electrophysiological measurements.[20]

Benefit: The AIVO can help identify informative sampling times and compare intervention schedules before committing to long culture experiments. Accelerated simulation does not guarantee biological fidelity; physical validation at multiple time points remains necessary.

4.4. Toxicology and environmental health

Scenario: Liver and other metabolically active organoids are used to study repeated-dose toxicity and environmental exposures, but long culture periods and limited tissue

availability constrain the number of dose-time combinations that can be tested.

AIVO-Lab approach: The data layer combines longitudinal imaging, metabolic measurements, and multi-omics profiles. The AIVO screens exposure concentrations, schedules, and recovery periods, then identifies high-risk or high-uncertainty conditions for physical validation. Liver-organoid platforms provide a practical setting for integrating three-dimensional culture, bioprinting, and organ-on-chip measurements.[21]

Benefit: The workflow broadens AIVO-Lab applications beyond oncology and developmental biology. It can support preclinical toxicology and environmental-health studies while retaining physical assays for confirmation of safety-relevant predictions.

Together, these scenarios show that the value of an AIVO-Lab lies in disciplined iteration: models narrow the experimental search space, physical tests establish which predictions are reliable, and each outcome improves the next cycle.

5. Benefits and challenges

AIVO-Labs may increase experimental efficiency and integrate evidence across scales, but their value depends on data quality, model validity, transparent uncertainty, and governance. The following sections separate anticipated benefits from the technical and institutional conditions required to realize them.

5.1. Key benefits

5.1.1. Speed and throughput

AIVO-Labs can move selected exploratory experiments into computational space. Once a model has been calibrated for a defined task, virtual screens can evaluate more conditions than can be tested physically and return a prioritized set for validation. The resulting speed advantage should be reported for the specific model, hardware, and assay rather than assumed to generalize across applications.

5.1.2. Cost reduction and reproducibility

In silico experiments may reduce the use of reagents and scarce biological material by filtering candidate conditions before physical testing. Reproducibility can also improve when model versions, inputs, random seeds, and analysis pipelines are preserved. Simulations are not inherently deterministic or transportable across laboratories, however; comparable results require controlled software environments, standardized inputs, and external validation.

5.1.3. Multiscale insight and data integration

AIVOs can connect molecular, cellular, spatial, imaging, and functional data within a shared representation. This integration may reveal associations between a molecular alteration and a tissue-level phenotype that are difficult to detect in separate analyses. Virtual perturbations can then generate candidate causal explanations, which must be tested experimentally before they are treated as mechanisms.

5.1.4. Ethical and safety advantages

Virtual screening may reduce some animal experiments and support the replacement, reduction, and refinement principles when a model is sufficiently validated for the intended question.[22] It may also identify potential toxicity before a living system is exposed. In sensitive areas such as brain-organoid research, computational studies can limit unnecessary experiments, but they do not remove the ethical questions associated with the source material, physical organoids, or downstream clinical use.[23]

5.1.5. Data reuse and continuous learning

A closed-loop platform preserves information from both successful and unsuccessful experiments. Each result can update the AIVO, refine uncertainty estimates, or define conditions under which the model should not be used. This cumulative value depends on rigorous metadata, negative-result reporting, and versioned datasets rather than on continuous learning alone.

5.2. Technical challenges

5.2.1. Data integration and quality

High-fidelity AIVOs require large, well-annotated multimodal datasets, often sampled over time. Many studies omit relevant modalities, culture variables, or longitudinal measurements. Technical noise and batch effects can confound learning, and models trained in a single laboratory may fail under biological, technical, or protocol-related distribution shifts. Data integration must therefore preserve provenance and quantify missingness. External validation and explicit identification of out-of-distribution inputs are needed before model-guided decisions are generalized beyond the conditions represented in the training data.[24]

5.2.2. Computational complexity and scalability

Detailed organoid simulations can be computationally demanding, particularly when they represent thousands of interacting cells, immune cocultures, fluid flow, or multiple spatial scales. Real-time operation may require specialized accelerators and simplified surrogate models. Complex AI architectures may also be difficult to interpret. Explainability methods such as feature attribution can support analysis, but mechanistic constraints, ablation studies, and prospective tests are needed to establish whether a prediction is biologically meaningful.

5.2.3. Model validation and fidelity

Validation must match the intended use. Historical test sets can assess discrimination and calibration, but prospective experiments are needed to determine whether model-guided choices improve decisions. Agreement with an endpoint is insufficient if the model reaches the correct result for the wrong biological reason. Modular validation, challenge datasets, sensitivity analysis, and prespecified failure criteria can help distinguish model error from experimental noise or new biology. When model outputs are intended to guide clinical decisions, evaluation should additionally address the target population, human-AI interaction, clinically relevant performance, and prospective assessment in real-world workflows.[25]

5.3. Governance, ethics, and reproducibility

5.3.1. Regulatory and clinical oversight

AIVO-Labs that influence clinical decisions will require substantially stronger evidence and oversight than research-use systems. Depending on function and jurisdiction, associated software may be regulated as a medical device. Clinical AIVO-Labs should be governed across the total product lifecycle, with representative datasets, a clearly specified intended use, clinically relevant testing, transparent information for users, and post-deployment monitoring for changes in model performance.[26] Algorithmic fairness should also be evaluated across relevant patient subgroups.[27]

5.3.2. Privacy and data security

Patient-derived organoid programs must protect clinical and genomic data through appropriate consent, de-identification, access controls, and secure data pipelines. Federated learning may allow institutions to train shared models without pooling raw data, although privacy leakage and site heterogeneity still require evaluation. Cybersecurity is part of model safety because unauthorized access or model tampering could affect experimental or clinical recommendations.

5.3.3. Standardization and reproducibility

Common data formats, assay protocols, model cards, benchmark datasets, and reporting standards will be necessary for cross-laboratory comparison. Continuous models also require version control that links every prediction to the corresponding data, code, parameters, and validation record. Open sharing can improve scrutiny and reuse, but it must be balanced with consent, privacy, intellectual-property obligations, and restrictions on clinical data.

5.3.4. Ethical considerations and public trust

AIVO-Labs should supplement physical testing until evidence supports a narrower validated use. Human oversight is required to prevent automation bias and to review high-impact or out-of-distribution recommendations. Trustworthy deployment requires fairness, universality, traceability, usability, robustness, and explainability, together with transparent reporting of model limitations, uncertainty, and conditions of use.[28] Governance should include relevant scientific, clinical, ethical, and patient perspectives.[23]

These challenges are not secondary implementation details. They determine whether an AIVO-Lab produces reproducible knowledge and whether its predictions can be used responsibly. Technical development should therefore proceed together with validation standards, data governance, and clear limits on model autonomy.

6. Future outlook

AIVO-Labs may converge with organ-on-chip systems, bioprinting, clinical decision support, and collaborative data platforms. Progress will depend on whether these integrations produce measurable improvements in prediction, reproducibility, and experimental decisions. The following outlook identifies plausible development stages and open questions.

6.1. Convergence with organ-on-chip and biomanufacturing technologies

6.1.1. Integration with organ-on-a-chip

Organ-on-chip devices expose organoids to controlled flow, mechanical forces, and multicellular interactions. An AIVO-Lab could maintain digital twins of both the organoids and the device conditions, allowing flow rates, exposure schedules, and multi-organ interactions to be explored computationally before physical testing. A virtual body-on-chip linking liver, gut, and kidney compartments is one possible long-term application, but reliable coupling will require standardized transport models and cross-platform validation.

6.1.2. Synergy with bioprinting

Bioprinting provides controlled placement of cells and biomaterials. An AIVO-Lab could support a design-build-test-update cycle in which candidate structures are simulated, selected designs are printed, and measured outcomes refine the next design. Liver-organoid research already illustrates the convergence of organoids, bioprinting, and organ-on-chip technologies.[21] At scale, the same framework could support quality control by comparing each construct with a versioned digital counterpart.

A staged timeline is more realistic than a single translation date. Over approximately the next 3–5 years, integrated systems are most likely to remain as research-

use platforms for assay optimization, toxicology, and preclinical prioritization. Narrow, prospectively validated decision-support pilots may emerge over 5–10 years in standardized organoid production settings with clearly defined endpoints. Routine clinical use will probably require more than a decade and will depend on multicenter validation, manufacturing controls, regulatory pathways, and evidence of patient benefit. These intervals are scenario-based estimates rather than firm forecasts.

6.2. Integration with clinical AI and decision support

A longer-term goal is to use AIVO-Labs for individualized decision support. A patient sample could generate a physical organoid and an AIVO that jointly compare candidate treatments. Model predictions would prioritize tests, and physical responses would provide patient-specific evidence before a recommendation is considered. Early computational frameworks such as ODFormer illustrate the direction but remain to be independently and prospectively validated.[17] Clinical use will require predefined endpoints, representative cohorts, workflow integration, and regulatory review; the AIVO should support, not replace, clinical judgment.

6.3. Virtual laboratory ecosystems and collaboration platforms

A virtual-laboratory ecosystem could allow laboratories and hospitals to contribute versioned data, models, and validation results to shared platforms. General AIVC or AIVO models might be adapted locally and evaluated against common benchmarks. Linking organoid twins with pharmacokinetic or virtual-patient models could extend prediction across biological scales. Such collaboration may also support education and access, but governance must address data quality, privacy, model ownership, and unequal representation among participating sites.

6.4. Open questions and path forward

6.4.1. How complete must the models be

Model scope should be determined by the decision it must support. A reduced model may be adequate for ranking a defined drug panel, whereas developmental prediction may require single-cell, spatial, and temporal resolution. Future work should identify the simplest representation that retains prospective predictive value and state explicitly which mechanisms and scales are omitted.

6.4.2. How should mechanistic knowledge and AI be integrated

Hybrid models can incorporate conservation laws, transport processes, pathway structure, and other mechanistic constraints while using AI to learn unresolved relationships. Physics-informed and biology-informed approaches may improve extrapolation, but their assumptions must be testable. Interpretability should be evaluated by whether the model generates correct, discriminating predictions rather than by visualization alone.

6.4.3. Data sharing and privacy

Federated learning may support multi-institutional model development without centralizing raw patient data, but it does not eliminate privacy, harmonization, or governance problems. FAIR data principles, shared metadata, and interoperable reporting standards will be needed so that datasets and validation results can be compared across AIVO-Labs.

6.4.4. Validation at scale

Virtual Organoids (VOs) should be evaluated through prospective, task-specific challenges. Performance records should include calibration, robustness, external validity, and failure modes. A model may be useful for prioritizing short-term drug responses but unreliable for long-term stability or rare states. Identifying these boundaries early will direct resources toward applications with defensible evidence.

6.4.5. Human factors and adoption

AIVO-Labs require teams that can connect organoid biology, quantitative modeling, software engineering, and experimental design. Interfaces should expose uncertainty, provenance, and recommended tests without concealing model limitations. Training and workflow design will be as important as visualization technology for adoption.

AIVO-Labs provide a framework for linking organoid experiments with AI-enabled digital twins through repeated prediction, validation, and updating. Their near-term value is likely to be in research-use applications that prioritize experiments and integrate multimodal evidence. Broader clinical use will require prospective validation, standardized workflows, regulatory oversight, and evidence that model-guided decisions improve patient-relevant outcomes. Progress will depend on sustained collaboration among organoid scientists, computational researchers, engineers, clinicians, and governance experts.

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Conflict of interest

The authors declare they have no competing interests.

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Ethics approval and consent to participate

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Consent for publication

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Availability of data

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