Why 3D?

Stripping Complexity Out of Multi-Dimensional Cell Models

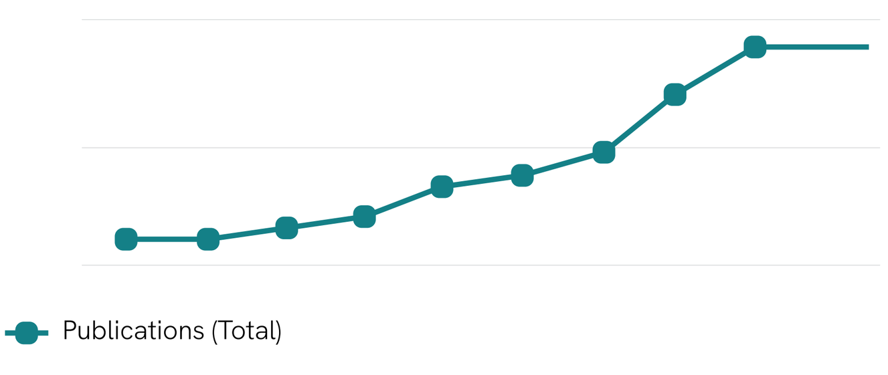
More than ever, researchers are looking to 3D cell cultures, microtissues, and organoids to bridge the translational gap between 2D cell cultures and *in vivo* conditions.

Advantages

- More physiologically relevant
- Closely mimic cell-cell and cell-extracellular matrix interactions
- Help for a better understanding of biology and thus to identify new targets
- Improved lead validation and characterization for effective and safe drugs

Landscape

The need for more biologically relevant disease models has spurred a steady **8% annual growth in research** on 3D cell models since 2013*.



* Source: Google Scholar

Applications

3D cell models can improve and accelerate different steps along the drug discovery workflow.

Model disease *in vitro* to better understand the underlying biology → Identify new targets using more physiologically relevant models → Screen drug candidates in high-throughput format → Perform efficacy and toxicity profiling *in vitro* for lead optimization & selection → Preclinical use of 3D models for
- Regenerative Medicine
- Transplantation
- Precision medicine

A precise distinction

The difference between 2D and 3D

2D Cell Model	3D Cell Model
Lacks *in vivo* imitation Doesn't mimic *in vivo* - like structures or molecular mechanisms	***In vivo* imitation** *In vivo* - like architecture and stable expression of relevant genes and proteins
Limited cell interactions Limited cell-cell interactions or cell-extracellular environment interactions	**Cell interactions** Interactions of cell-cell and cell-extracellular microenvironment
Simple culture High performance and reproducibility, short culturing times	**Complex culture** Challenging to define proper seeding methods and conditions, lower reproducibility, long culture formation times
Changed & uniform characteristics Changed morphology, loss of diverse phenotype, and polarity	**Preserved & diverse characteristics** Preserved morphology, diverse phenotypes, and polarity

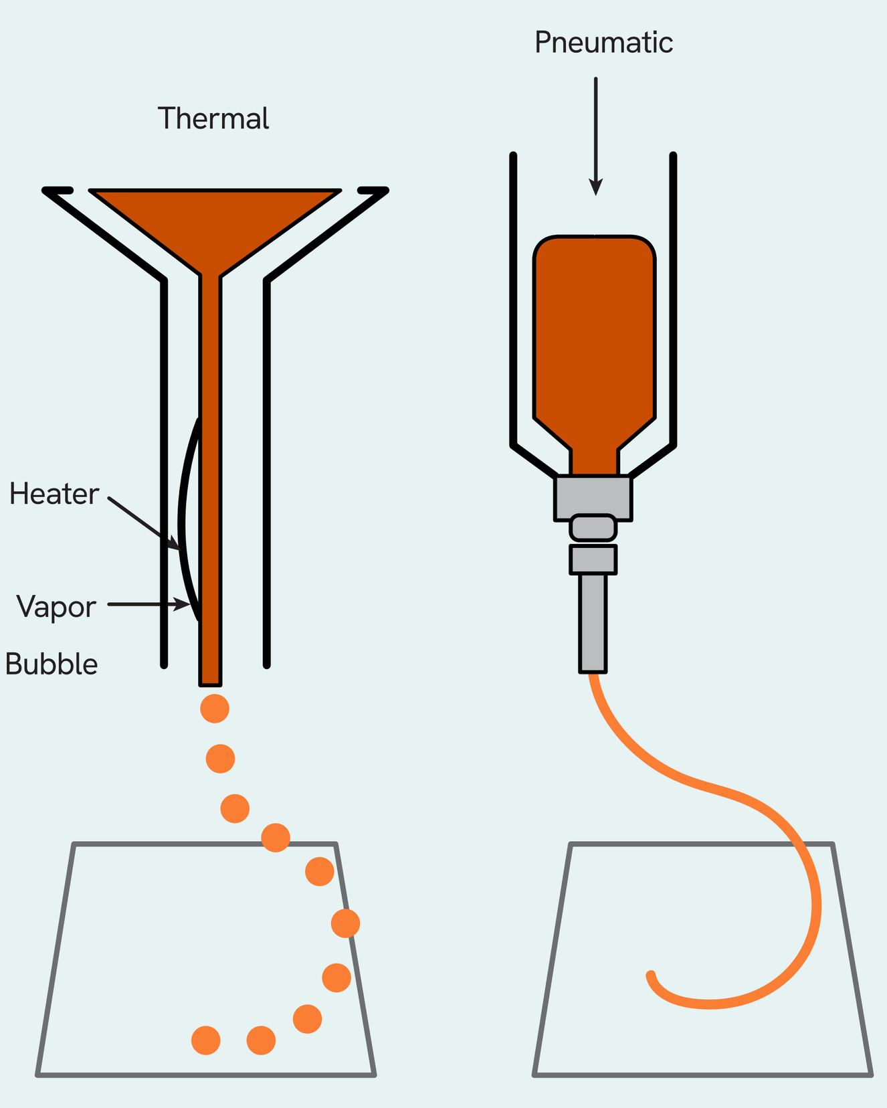
Types of cell models

Structure	Spheroid	Organoids	Organ-on-a-chip
Cell Type	▪ Cell line monoculture or co-culture	▪ Multiple organ-specific cell types (ESC, iPSC or patient derived)	▪ Multiple organ-specific cell types (primary cells, iPSCs)
Assembly method	▪ Cell aggregation	▪ Self-assembly ▪ Differentiation	▪ Self-assembly ▪ Differentiation
Advantages	▪ Easy-to-use protocol ▪ High reproducibility ▪ Co-culture ability	▪ Multiple cell lineages ▪ *In vivo* – like complexity and architecture	▪ *In vivo* – like architecture, microenvironment, and flow ▪ Transport of soluble factors, nutrients, and oxygen ▪ Good imaging compatibility
Disadvantages	▪ Simplified architecture ▪ Lack vasculature ▪ Only partial tissue components ▪ Limited imaging depth	▪ High variability ▪ Potential lack of vasculature ▪ Limited imaging depth	▪ High variability ▪ Lower throughput ▪ Careful handling is required, e.g. air bubbles

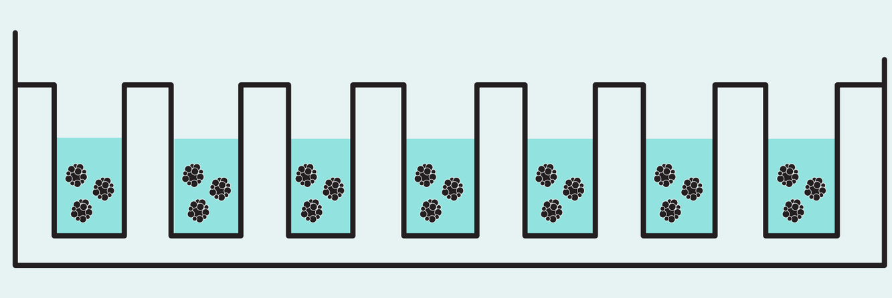
Common seeding methods

Different seeding methods, each with unique characteristics, must be selected based on the assay type and research questions at hand.

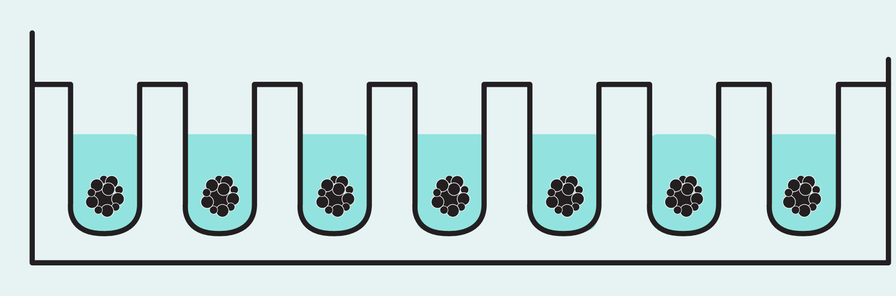
Bioprinter



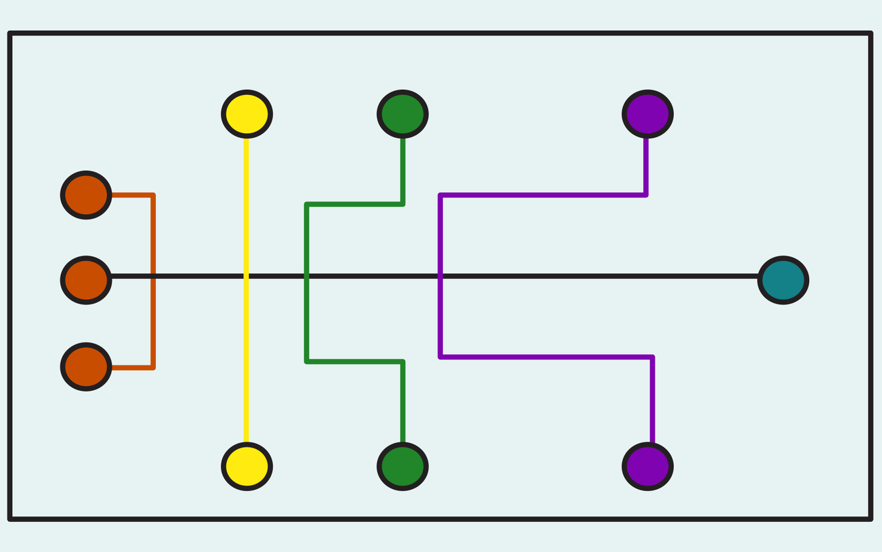
Biological hydrogels



Ultra low attachment plate



Organ-on-a-chip



The 3D cell culture workflow

1. **Selection of cell model and growth method**
2. **Grow 3D cell model**
3. **Treatment**
4. **Sample preparation**
   - Staining and Clearing
   - Preparing Detection Assay
   - Nucleic Acid Isolation & NGS Library Prep
5. **Read out**
   - High Content Imaging
   - Multimode Plate Readers
   - NGS
6. **Analysis**

Providing confidence and ease in 3D cell models

What to look for in technologies to help make it a seamless workflow.

- Reliability
- Reproducibility
- Speed
- Biologically relevant results
- Analyze data in context

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