

Transforming *In Vitro* Tissue & Disease Models with Precision Culture Scaling

Replicating human tissues *in vitro* requires cultivating cells under controlled conditions. Hydrogel-based three-dimensional (3D) cell cultures can realistically mimic various aspects of both healthy and diseased human tissues. However, the complexity of these models has made their adaptation to high-throughput applications a significant challenge.

To address this, Professor Carsten Werner's team at the Leibniz Institute of Polymer Research Dresden pioneered Precision Culture Scaling (PCS-X). By integrating statistical experiment planning, automation, advanced image analysis, and mathematical modelling, PCS-X streamlines the customisation of hydrogel-based 3D cell cultures, making true high-throughput research applications a reality.

Three-dimensional (3D) cell cultures have become indispensable tools in biomedical research, providing platforms that closely model human tissue structure and function *in vitro*. They significantly enhance our understanding of diseases, accelerate the discovery and testing of novel therapeutics,

and support the development of personalised treatments.

HYDROGELS: A LEAP FORWARD IN *IN VITRO* TISSUE MODELLING

Expanding the advantages of 3D cell cultures, hydrogels – 3D networks of hydrophilic polymers – have

emerged as powerful tools for *in vitro* tissue modelling. By recapitulating the structural and biochemical properties of the extracellular matrix, hydrogels enable cells to grow and interact, approximating *in vivo* conditions. Professor Carsten Werner and his team at the Leibniz Institute of Polymer Research Dresden have conducted seminal work in this field. They explored how specific hydrogel properties and the combination of different cell types influence tissue formation. Their work has propelled the use of hydrogels in biomedical research and paved the way for more complex, predictive *in vitro* models.

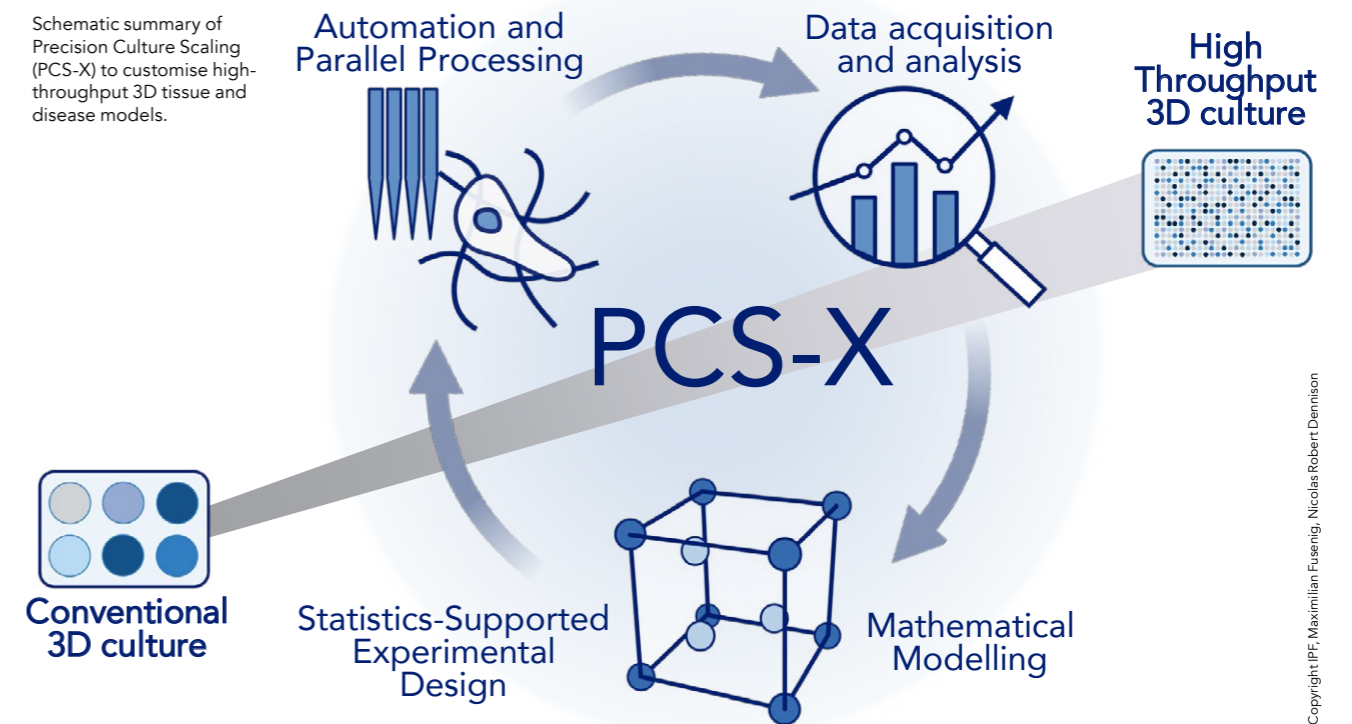
TACKLING THE CHALLENGE OF SCALING

Despite the promise of hydrogel-based 3D cultures, scaling *in vitro* models for high-throughput applications –



3D cell cultures have become indispensable in medical research, bridging the gap between traditional 2D models and *in vivo* systems.

Schematic summary of Precision Culture Scaling (PCS-X) to customise high-throughput 3D tissue and disease models.



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where numerous samples are tested simultaneously – remains a significant challenge. Their inherent complexity, smaller culture wells and nutrient diffusion limitations all hinder the adaptation of low-throughput protocols to large-scale setups. Achieving truly high-throughput 3D hydrogel-based models therefore necessitates careful optimisation of hydrogel composition, processing methods, cell seeding density, culture nutrients, and analytical techniques – all while preserving consistency and reliability. Recognising this need, Professor Werner and his team developed a coordinated method that makes hydrogel models suitable for both high-throughput studies and accurate tissue physiology modelling.

PRECISION CULTURE SCALING (PCS-X): A GAME-CHANGER IN HIGH-THROUGHPUT APPLICATIONS

This method, called Precision Culture Scaling (PCS-X), combines several key techniques to address the complexities of hydrogel-based 3D cell cultures in a streamlined and sustainable manner. The core components of PCS-X include:

- **Statistics-Supported Experimental Design:** Design of Experiments methodologies are used for effective planning and optimisation of experiments. By varying multiple parameters at once, they enable the

identification of the most influential factors and optimal conditions for cell growth and tissue formation.

- **Automation and Parallel Processing:** Automated liquid handling systems

and parallel processing techniques facilitate the production of numerous 3D culture samples at once, boosting throughput and minimising variability between samples.

By recapitulating the structural and biochemical properties of the extracellular matrix, hydrogels enable cells to grow and interact in three dimensions.



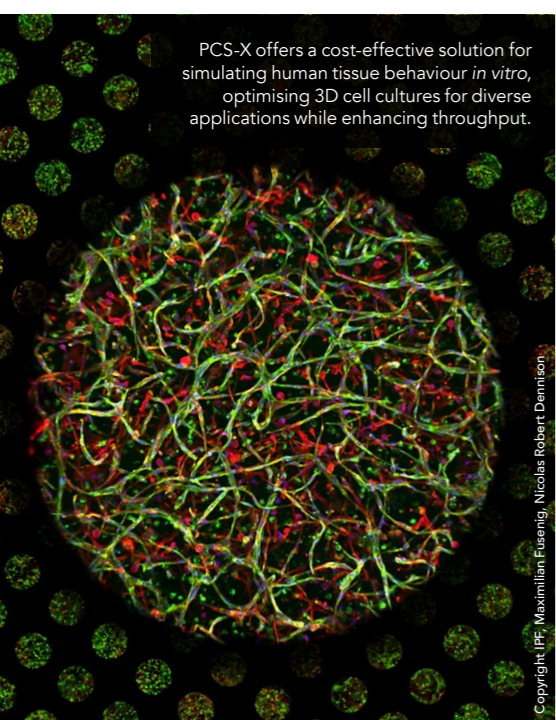
Automation streamlines the high-throughput production and analysis of 3D cell cultures, enabling scalable, standardised workflows and reducing manual effort.

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PCS-X enables the creation of realistic human tissue mimetics that accurately mirror the complexity of healthy and diseased states.



PCS-X offers a cost-effective solution for simulating human tissue behaviour *in vitro*, optimising 3D cell cultures for diverse applications while enhancing throughput.

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PCS-X streamlines the creation of high-throughput 3D culture models, thus benefitting multiple areas of research – particularly oncology, regenerative therapies, and personalised medicine.

not only improves the efficiency of experimental design but also speeds up the optimisation process.

PCS-X's potential was exemplified by customising hydrogel-based high-throughput 3D vasculogenesis models involving both highly proliferative umbilical cord-derived endothelial cells and fully differentiated ocular endothelial cells. These models were employed to simultaneously study the effects of multiple vasculogenesis inhibitors across a range of concentrations – showcasing PCS-X's potential for high-throughput drug screening and complex biological research.

PCS-X: PIONEERING ETHICAL AND PERSONALISED MEDICINE

PCS-X can transform the production of high-throughput, physiologically relevant 3D cell cultures by offering a more precise, cost-effective, and ethically responsible method for simulating human tissue behaviour *in vitro*. Its flexible approach to hydrogel composition allows

researchers to create tissue models that closely mimic the mechanical, structural, and biochemical characteristics of human tissues and organs. Incorporating patient-specific cells captures individual genetic and biological nuances, enabling more accurate drug testing, targeted treatment regimens, and advancements in regenerative medicine. Moreover, PCS-X streamlines large-scale drug screening by reducing both costs and development timelines, with broad potential applications in oncology, regenerative therapies, and personalised medicine.

As medical science advances, technologies like PCS-X will be pivotal in bridging the gap between *in vitro* studies and clinical applications, providing scalable, human-relevant testing environments that reduce reliance on animal models and deepen our understanding of disease complexity and therapeutic efficacy. Ultimately, by enhancing data quality and accelerating research, PCS-X paves the way toward improved patient outcomes.

- **Data Acquisition and Analysis:** Advanced imaging technologies and sophisticated image analysis tools enable real-time tracking and quantitative evaluation of cells within 3D cultures. This provides in-depth understanding of cell behaviour, morphology, and interactions.
- **Mathematical Modelling:** Mathematical models applied to experimental data can pinpoint optimal conditions for cell growth. This predictive modelling



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Behind the Research Professor Carsten Werner

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Research Objectives

The team of Professor Werner developed Precision Culture Scaling (PCS-X), a platform for the creation of realistic 3D tissue models.

Detail

Bio

Carsten Werner, a biochemist, is Scientific Director of the Leibniz Institute of Polymer Research Dresden and professor for Biofunctional Polymer Materials at the Dresden University of Technology. He established a biomaterials programme to explore functional living matter from a materials science perspective and develop bio-inspired polymer materials.

Collaborators

Peter D Westenskow (Roche Pharma Research and Early Development, Roche Innovation Center Basel)

Competing Interest Statement

The reported work was sponsored in part by F. Hoffmann La Roche, Basel, Switzerland. Carsten Werner is co-inventor of a patent (WO2010060485A1) covering the hydrogel materials referred to; he also holds shares in the spin-off company ZetaScience GmbH, Dresden, offering customised hydrogel precursors.



References

Nicholas Robert Dennison*, Maximilian Fusenig*, Lisa Grönnert*, et al, (2024) Precision culture scaling to establish high-throughput vasculogenesis models. *Advanced Healthcare Materials*, 13, 2400388. doi.org/10.1002/adhm.202400388

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Personal Response

How will the wide adoption of PCS-X change high-throughput drug discovery and tissue engineering, and what fields in the biological and medical sciences will benefit most from the use of this methodology?

“ The wide adoption of PCS-X will transform high-throughput drug discovery and tissue engineering by enabling efficient, scalable, and accurate 3D cell culture models that closely mimic human tissues. PCS-X streamlines the creation and optimisation of complex tissue models, facilitating the rapid screening of drug candidates in physiologically relevant environments. This methodology will significantly benefit fields such as cancer research, regenerative therapies, and personalised medicine, where understanding complex cell interactions and responses is crucial. By reducing reliance on animal models and enhancing predictive accuracy, PCS-X fosters more ethical and effective approaches in biomedical sciences. ”



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