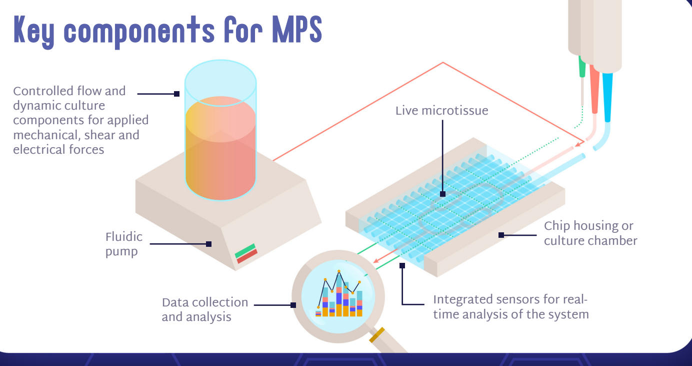
TECHNOLOGY NETWORKS

MICROPHYSIOLOGICAL SYSTEMS

Microphysiological systems (MPS) are two- or three-dimensional cellular platforms that are designed to recapitulate the physiology and function of the human body *in vitro*.[1,2] These systems are also sometimes referred to as organ-on-a-chip technologies or *in vitro* organ constructs. MPS are helping to broaden our mechanistic understanding of disease and have numerous applications in biology and medicine. In this infographic, we take a closer look at these systems, how they came to be and discuss key applications, advantages and challenges.

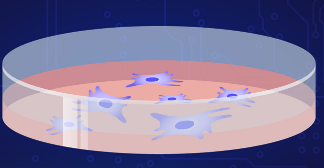
Key components for MPS



Evolution of MPS – Key milestones

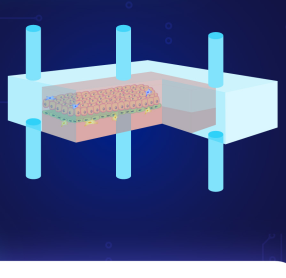
The development of MPS has been driven by advances in several technologies, including microfluidics, tissue engineering, bioprinting and human cell culture.[3,4,5,6]

2-D CULTURES



3-D ORGANOIDS

MICROPHYSIOLOGICAL SYSTEMS (MPS)



- 2010 – Lung-on-a-chip[7]
- 2011 – Liver-on-a-chip[8]
- 2012 – Blood vessels-on-a-chip[9]
- 2014 – Brain-on-a-chip[10]
- 2016 – 3D-printed organ-on-a-chip with integrated sensing[11]
- 2018 – Body-on-a-chip[12]

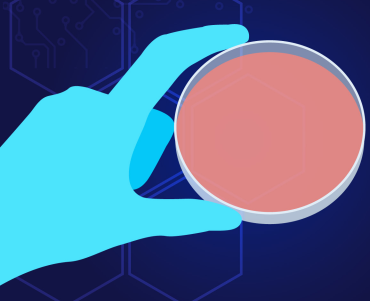
MODEL MULTI-ORGAN PHYSIOLOGY

Why are MPS so attractive?

Interest in MPS is growing for several reasons, largely it is driven by the need for improved predictive models to address the increasing costs and high attrition rates seen in drug discovery.[4,13]

Most notably, MPS can closely recapitulate aspects of human physiology and organ function.[14]

They can overcome many shortcomings associated with traditional *in vitro* cell culture models such as:[1]



- Difficulties maintaining concentration gradients
- Inefficient diffusion
- Difficulties incorporating mechanical and shear forces
- Insufficient interstitial flow
- Perfusion challenges
- Cyclic changes of nutrients, metabolites and pH
- Inability to replicate the heterogeneous tissue microenvironment

In addition, they can reduce the need for animal models[15] and address associated challenges, including:

- Cross-species specificity
- Lack of relevant animal models for some rare diseases
- Ethical concerns

Together, these factors make MPS attractive tools for a range of applications.

MPS challenges

However, despite the attraction, creating and using MPS can present several challenges.[1,16,17,18]

- How to reproduce the complexity of human organs
- How to connect the organs
- How to control the organs
- Developing a blood surrogate
- Adsorption and absorption to platform materials
- Managing liquid-to-cell ratios
- Low sample volumes, extended sampling intervals
- Sourcing enough high-quality cells
- Regulatory considerations, validation
- Lack of standardization guidelines
- Encouraging adoption of MPS
- Costs

Key applications

DRUG SCREENING

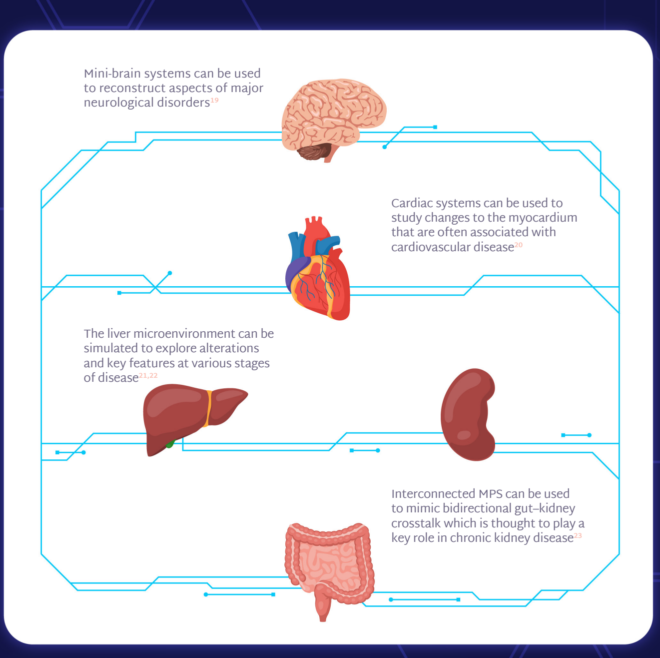
MPS are an ideal platform for testing the safety of drug compounds. They can produce a precisely controlled geometrical, physical and biochemical microenvironment that simulates drug response,[14] providing researchers with pharmacokinetic and pharmacodynamic information.

These systems can be used during drug discovery stages of development to identify from several promising "high-quality" leads, which ones warrant further investigation and optimization. MPS can also be used as preclinical models to further scrutinize the properties of the drug candidate to ensure its efficacy and safety before it is tested in human subjects.

Drugs can either be tested using single-organ chips, or culture chambers within multi-well plates, to investigate their effects in a particular tissue or they can be tested in multi-organ MPS to predict a drug's effects in a wider system that more accurately represents the interconnected nature of the human body.

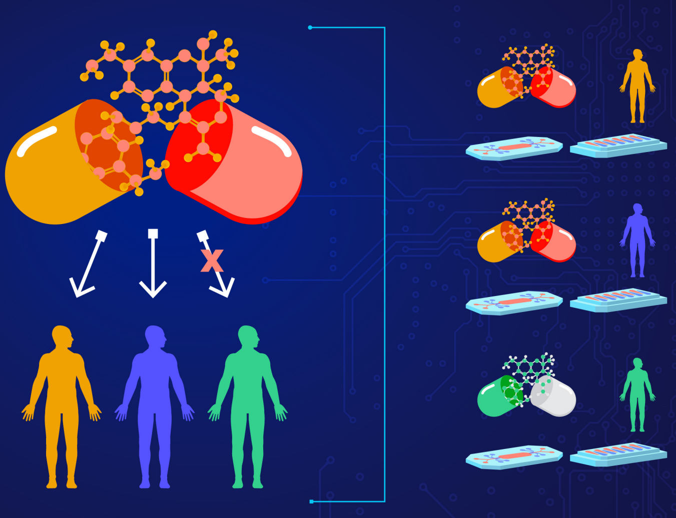
DISEASE MODELING

MPS can be used to help to unravel the mechanistic understanding of a particular disease and identify potential therapeutic targets. Multi-organ MPS can be created by interconnecting single-organ models to reproduce complex multi-organ interactions.



PERSONALIZED MEDICINE

MPS can be used to explore the effects of drugs using patient-derived tissue. These systems can help to identify targeted therapies for specific individuals or subgroups of patients to ensure the best response and highest safety margin.[24,25]



MICROBIOME

The microbiota living within the human body have been shown to play key roles in human health and disease. This understanding has driven research into deciphering host–microbiome interactions.[26]

MPS are being designed to mimic interactions between microorganisms and host tissue in the human gut, liver and brain.[27]

Other emerging applications include the use of MPS to investigate infectious diseases, reproduction and development, and environmental contaminants and toxins.[28]

Sponsored by CN-BIO

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