4Dcell
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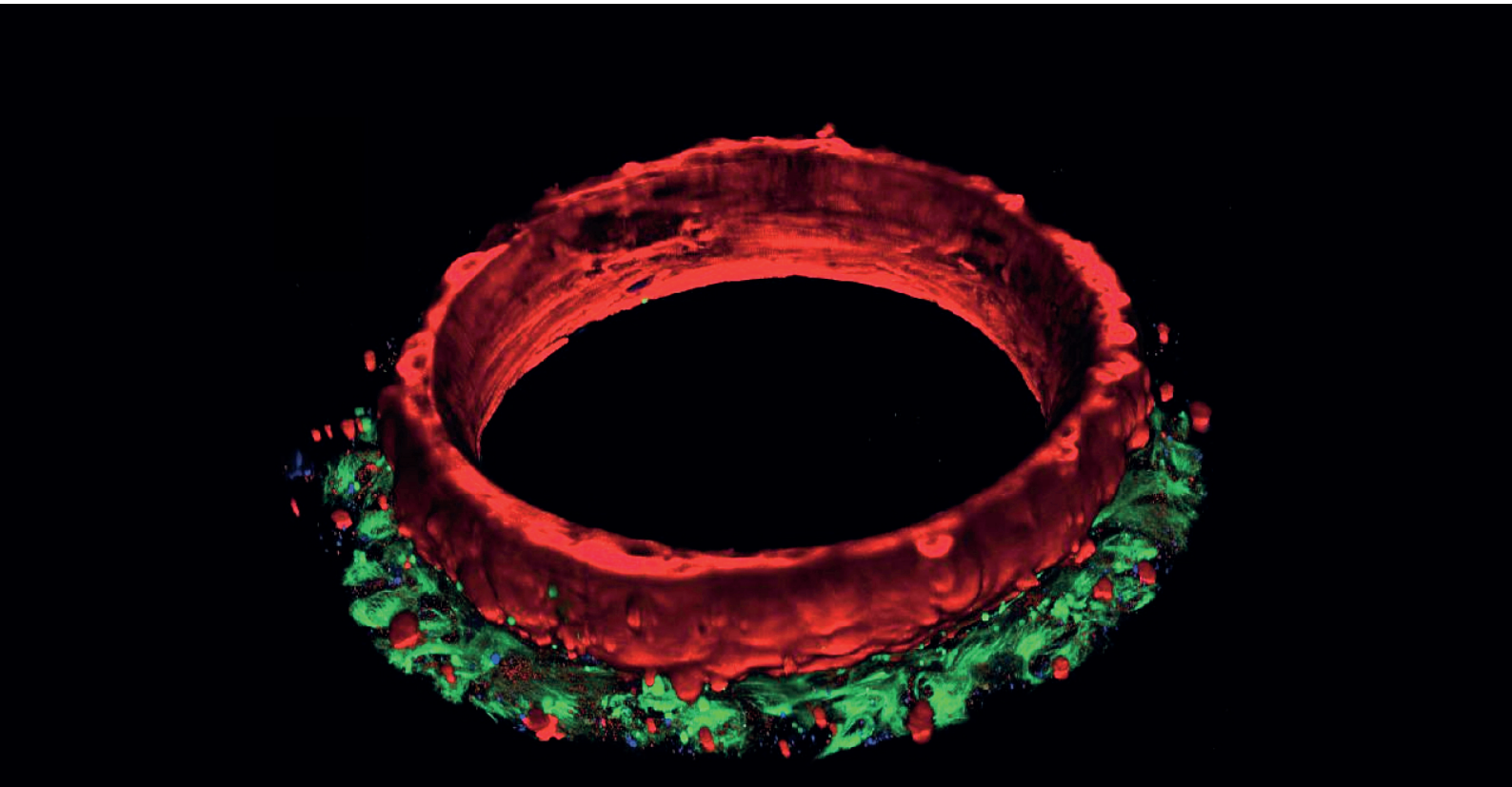
SmartHeart® Platform

Self-assembled human cardiac tissues under mechanical load for drug efficacy testing, cardiac safety assessment and disease modeling.

- **SmartHeart® plate**
- **Biological protocol**
- **SmartX 3.0 analysis software**



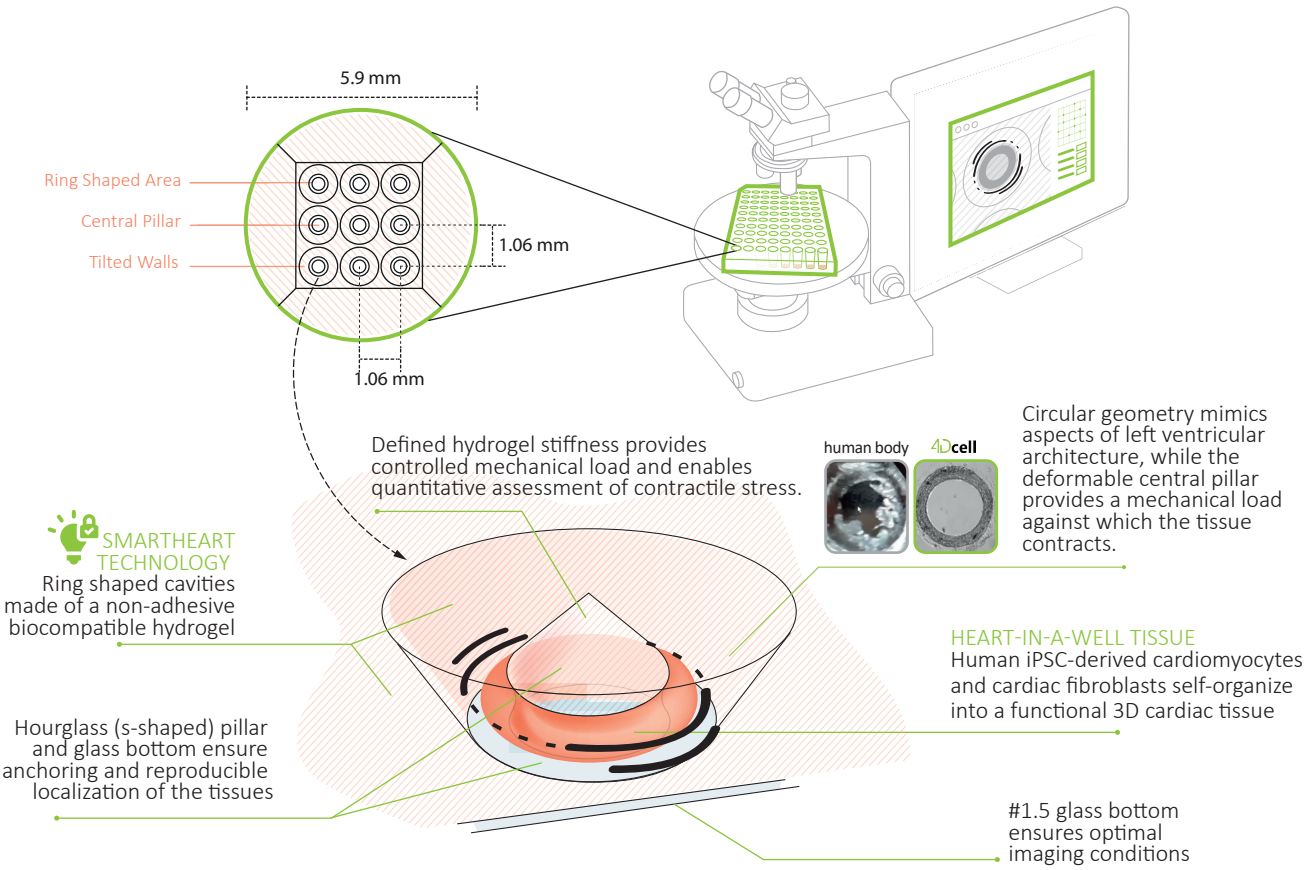
HOW SMARTHEART® WORKS

- **Guided tissue formation**
Sloped microwells guide cells to self-assemble into ring-shaped cardiac tissues around a central pillar.

- **Controlled mechanical load**
Deformable pillars anchor the tissues and resist contraction. PEG hydrogel stiffness can be tailored to the cell model (~5–20 kPa).

- **Quantitative contractility**
Tracking tissue and pillar deformation enables measurement of contraction strain, contractile stress, beating frequency, and contraction and relaxation kinetics.

- **Complementary functional readouts**
Optically transparent hydrogel enables brightfield and fluorescence imaging to assess contractility, electrical activity and calcium dynamics directly in the plate.



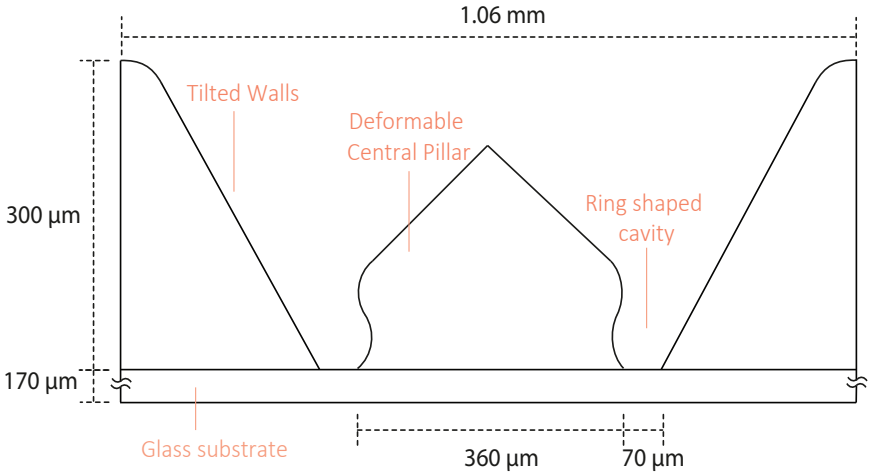
96 wells

9 tissues/well

7200 cells/tissue

FLASH TO SEE THE SMARTHEART BEATING

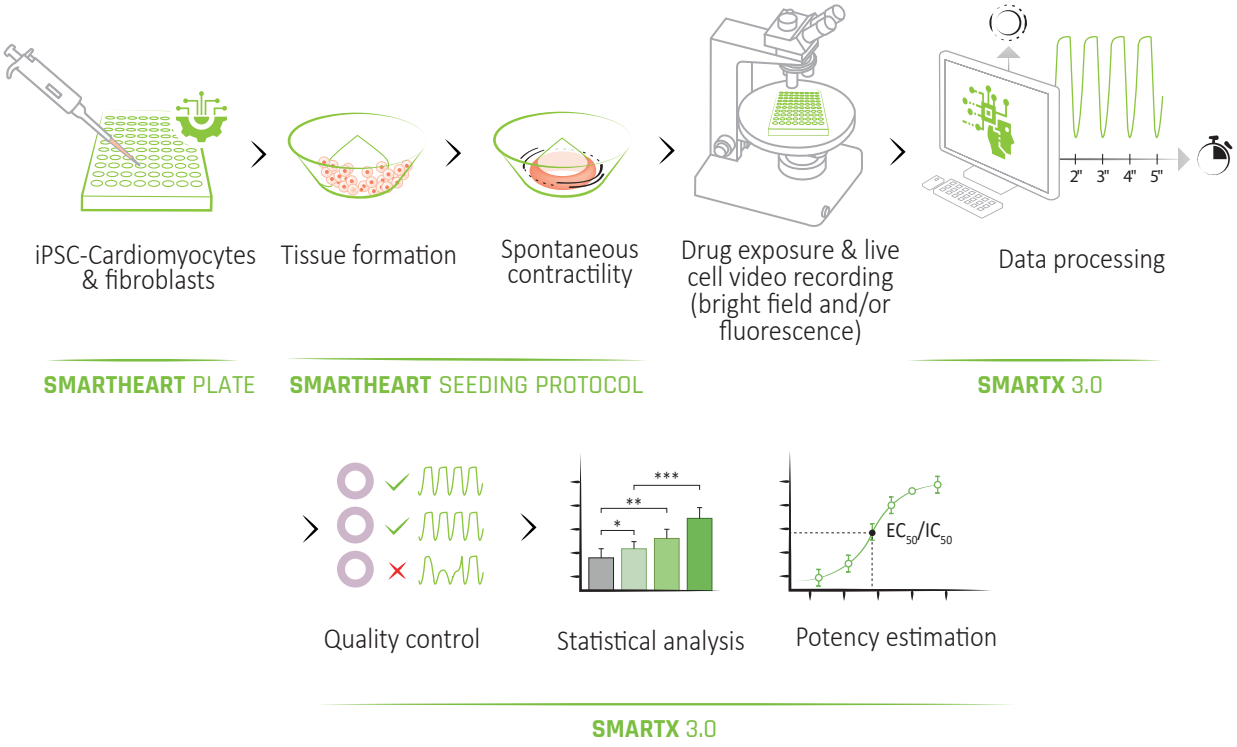
SMARTHEART® MICROWELL DIMENSIONS



The industry-standard 96-well format is compatible with automated liquid-handling and imaging platforms, enabling integration into high-throughput screening (HTS) and high-content screening (HCS) workflows for drug efficacy testing, cardiac safety assessment and disease modeling.

SMARTHEART® WORKFLOW

SmartHeart® provides an integrated workflow to characterize how compounds affect human 3D cardiac contractility. Tissue self-assembly, in situ imaging and SmartX 3.0 analysis connect biological responses with quantitative measurements. Quality control and statistical evaluation support concentration–response profiling and potency estimation where appropriate.



DEFINED CELLULAR COMPOSITION

SmartHeart® tissues combine human iPSC-derived cardiomyocytes and primary human ventricular cardiac fibroblasts at a 3:1 ratio. Cardiomyocytes provide the contractile component, while fibroblasts support tissue organization and structural stability.

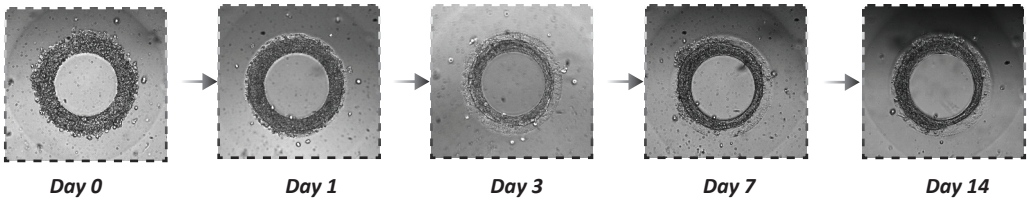
- **75% cardiomyocytes / 25% cardiac fibroblasts**
- **Approximately 7,200 cells per microtissue**, corresponding to 65,000 cells per well across nine tissue-forming cavities
- **Culture at 37°C and 5% CO_2**

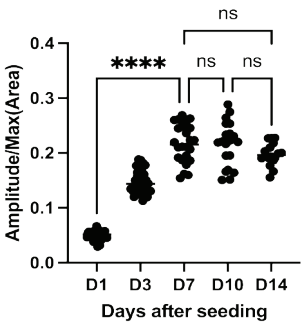
SELF ASSEMBLY & FUNCTIONAL DEVELOPMENT IN CULTURE

Over 14 days of culture, cells formed connections and became elongated as the cardiac tissues organized and developed contractile function.

Contraction amplitude:
- Increased during the first week.
- Remained broadly stable through D14.

Tissue formation is illustrated through D14; pharmacological qualification was performed at D21.

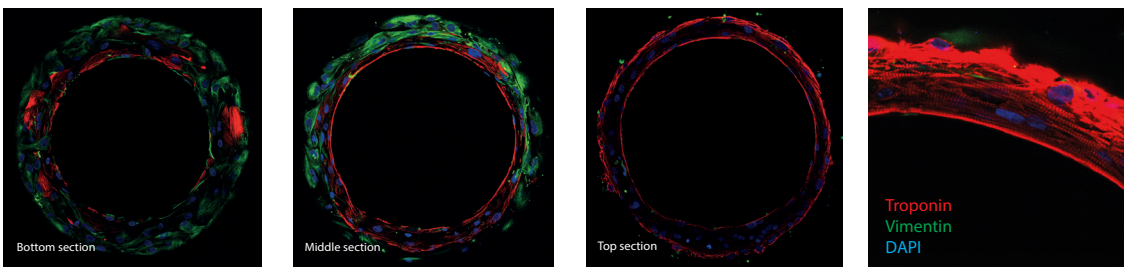




Images and data from Seguret et al. eLife 12:RP87739 (2023).

TISSUE MORPHOLOGY & STRUCTURAL ORGANIZATION

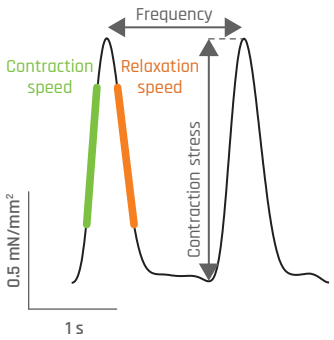
Confocal immunofluorescence imaging after 14 days of culture reveals organized troponin-positive contractile fibers above a fibroblast-rich basal layer that provides structural support. These structural observations complement contractility, electrophysiology and calcium-handling measurements when assessing tissue maturation.

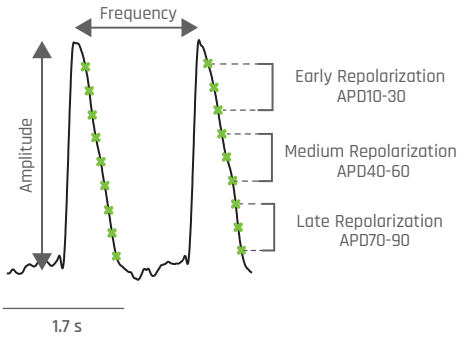


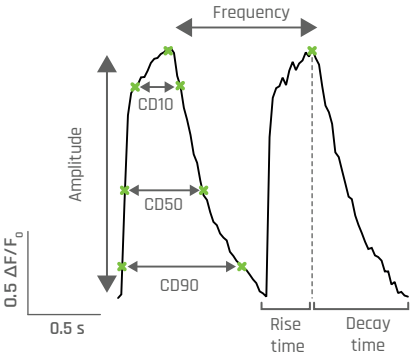
Images from Seguret et al. eLife 12:RP87739 (2023).

3-IN-1 CARDIAC PLATFORM

SmartHeart® measures three interconnected components of cardiac function: electrical excitation, intracellular calcium dynamics and mechanical contraction. Together, these readouts help characterize how compounds affect excitation–contraction coupling in human 3D cardiac microtissues.







CONTRACTILITY METRICS

Contraction stress
Contraction strain
Beating frequency
Contraction & relaxation speed

ELECTROPHYSIOLOGY METRICS

Frequency
Interpeak duration STD
Rise time, upstroke velocity
Triangulation & plateau duration
APD10-90

CALCIUM METRICS

Frequency
Area under curve
Rise & decay duration & velocity
CD10, 50, 90

EXCITATION-CONTRACTION COUPLING

Why an integrated system matters

Cardiac contraction emerges from interacting ion channels, intracellular calcium cycling and the contractile machinery within a loaded tissue. Calcium entry can trigger sarcoplasmic-reticulum calcium release. Calcium binding to troponin enables contraction. Calcium removal supports relaxation.

Electrical excitation → ***Calcium dynamics*** → ***Mechanical response***

Membrane potential and ion-channel activity

Ca^{2+} release, transient and removal

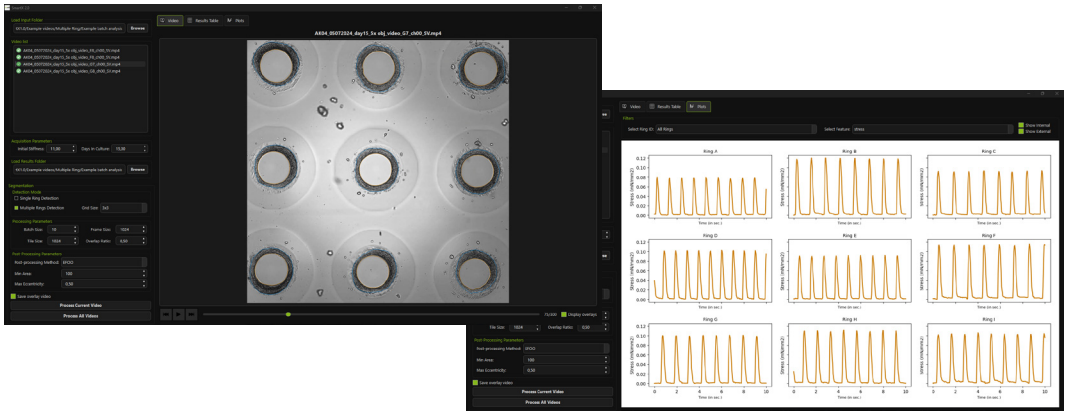
Myofilament activation, contraction and relaxation

Optical action potential ***Calcium transient*** ***Tissue strain & kinetics***

SMARTX 3.0

Deep-learning contractility analysis

SmartX 3.0 analyzes brightfield videos to quantify cardiac tissue contraction. Its deep-learning algorithm detects individual ring contours and tracks their deformation over time.



- **Quantifying contractile function**

  SmartX 3.0 extracts 22 metrics describing tissue morphology and contractile activity, including contraction strain, beating frequency, rhythm regularity, and contraction and relaxation speeds.

  Contraction strain measures the relative change in tissue radius: **ε(t) = [Rmax – R(t)] / Rmax**
  Contractile stress is estimated using the hydrogel pillar's batch-measured Young's modulus: **σ(t) = E × ε(t)**
  Rmax: relaxed radius · **R(t)**: instantaneous radius · **E**: pillar Young's modulus.

- **Automated data curation**

  Automated quality-control criteria to assess segmentation, tissue morphology and baseline activity, supported by visual review. Technical artifacts are identified to retain evaluable recordings for downstream analysis. Drug-induced loss of beating or rhythm irregularity is preserved as a biological response when recordings remain technically evaluable.

- **Post-processing and pharmacological analysis**

  SmartX 3.0 supports baseline normalization, concentration–response plotting and statistical analysis. Each evaluable ring is normalized to its own vehicle baseline to quantify compound-induced changes.

HOW TO WORK WITH 4DCELL

To integrate our platform into your lab or have our expert manage your project in our facilities, feel free to contact us at: contact@4dcell.com

Explore SmartHeart for your cardiac research