

# Decoding Cardiomyocyte Ageing Through AI: Tracking Functional Decline via Temporal Motion Signatures

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Code and data links:  
<https://github.com/borisveytsman/acmart>  
<https://zenodo.org/link>

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BT and GKMT designed the study; LT, VB, and AP conducted the experiments, BR, HC, CP and JS analyzed the results, JPK developed analytical predictions, all authors participated in writing the manuscript.

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## Problem statement

Cardiomyocyte ageing and injury are essential contributors to cardiac dysfunction and heart failure, yet early detection remains a challenge due to the severe limitations of traditional assessment techniques. Existing methods, such as mechanosensory tracking and calcium imaging, are expensive, labour-intensive, and not readily adaptable for efficiently analysing large volumes of cardiomyocyte data. Additionally, conventional motion analysis approaches often fail to capture localised contraction variations, leading to an inaccurate classification of cardiomyocyte health. To address these pressing challenges, we propose an advanced AI-driven framework that leverages Transformer-based motion analysis for automated cardiomyocyte classification into Healthy, Aged, or Damaged states. It provides a comprehensive strategy and a high-accuracy classification system. The proposed method improves cardiomyocyte phenotyping by effectively differentiating contraction intensity patterns, enabling early identification of functional decline with superior accuracy and resilience over traditional motion tracking techniques [1–3].

## Methods

The novel dataset, a unique creation, was generated in a controlled biosafety environment at the University of East London. Induced Pluripotent Stem cell-derived cardiomyocytes were thawed, counted (700,000–1M cells), and seeded in 96-well plates. Over 8 days, cells differentiated into beating heart cells, with their contractile motion recorded daily using high-resolution Vitro Imaging data and microscopy at 30–87 FPS. Motion tracking was performed from Day 1 (first visible contraction) to Day 8 (cessation of contractions), allowing temporal phenotyping of cardiomyocyte function.

Motion tracking [4–6] was performed using Optical Flow Farneback tracking to extract systolic ( $M_{\text{systolic}}$ ) and diastolic ( $M_{\text{diastolic}}$ ) motion intensities. Cells were classified as:

- **Healthy:**  $M_{\text{systolic}} \geq 0.7$ ,  $M_{\text{diastolic}} \geq 0.5$
- **Aged:**  $0.3 \leq M_{\text{systolic}} < 0.7$ ,  $0.3 \leq M_{\text{diastolic}} < 0.5$
- **Damaged:**  $M_{\text{systolic}} < 0.3$ ,  $M_{\text{diastolic}} < 0.3$

A Transformer-based Spatio-Temporal AI Model was trained alongside CNN-LSTM networks, improving classification accuracy. Manual bounding box annotations were applied using Roboflow open-source automation tools. and SHAP, LIME, GradCAM, Integrated gradient, DeepLift and attention maps enhanced model interpretability for

clinical right decisions. Kruskal-Wallis and Dunn's post-hoc tests verified statistical significance.

## Results

The novel findings suggest a biological and experimental cardiomyocyte maturation and degradation timeline. The logical explanation behind this variation is rooted in the stages of differentiation, functional maturation, and cellular stress over time. Biological Processes Underlying Cardiomyocyte Ageing and Functional Decline are given below:

- Days 1–3: Aged and Few Healthy Cells During the initial days following differentiation, ipsc-derived cardiomyocytes do not immediately exhibit complete contraction-relaxation cycles. The cells are still developing sarcomeric structures, the fundamental contractile units within cardiomyocytes. Calcium signalling pathways remain suboptimal, resulting in irregular and uncoordinated contractions. As a result, a mix of aged and underdeveloped but potentially healthy cells is observed during this early phase.
- Day 4–6: Healthy Phase By Day 5, the cardiomyocytes typically develop fully formed **sarcomeres**, enabling efficient and stable **contraction–relaxation dynamics**. This phase is characterised by improved **calcium handling**, due to the functional expression of key regulatory proteins such as **ryanodine receptors (RyR)** and **sarcoplasmic/endoplasmic reticulum  $Ca^{2+}$ -ATPase (SERCA2a)**. As a result, the cells exhibit **synchronous and rhythmic beating** – a hallmark of cellular maturity and optimal contractile function during this developmental window.
- Day 7–8: Damaged Phase Several signs of cellular damage and dysfunction emerge in the later days of culture. Prolonged incubation without adequate growth factor replenishment leads to cellular ageing and senescence. There is increased accumulation of oxidative stress, with reactive oxygen species (ROS) damaging cellular membranes and reducing structural integrity. Calcium dysregulation becomes more pronounced, resulting in spontaneous arrhythmic contractions, cellular fragmentation, and in some cases, necrosis. Additionally, some cardiomyocytes detach or undergo apoptosis, contributing to debris and noise observed in microscopy images. This phase is indicative of a transition to a damaged or degenerative state.

The TimeFormer model achieved 94% accuracy, outperforming CNN-LSTM (89.6%) and traditional motion tracking (78.3%). Self-attention mechanisms improved differentiation between Aged and Damaged cardiomyocytes. Segmentation performance, evaluated via Dice Score (0.91) and IoU (0.87), demonstrated high agreement with expert labels. LIME and gradient attention Explainable AI mechanism regarding Novel transformer analysis confirmed that localised contraction intensity predicts cell health more than global motion magnitude.

## Conclusion

This study establishes Transformer-based motion phenotyping as a precise tool for early cardiomyocyte dysfunction detection, enabling scalable and interpretable AI-driven assessment for cardiac disease research. All experimental procedures adhered to institutional biosafety protocols; no patient data or ethical approval was required due to using commercially sourced ipsc-derived cardiomyocytes.

## Significance

This study introduces a Transformer-based AI framework that enables accurate, early detection of cardiomyocyte ageing and injury using motion phenotyping. Unlike traditional

methods, the proposed system captures localised contraction-relaxation abnormalities over time, improving phenotypic resolution. Achieving 94% classification accuracy, the model outperforms CNN-LSTM and conventional tracking approaches. Its integration of explainable AI tools enhances interpretability, supporting precise functional assessment. This framework offers a scalable, non-invasive solution for cardiomyocyte evaluation, with implications for preclinical screening, ageing research, and regenerative medicine.

### Blockdiagram of Cardiomyocyte Ageing and Injury Using Motion Phenotyping

The block diagram of an advanced Transformer-based AI framework for the early detection and prediction of cardiomyocyte ageing and injury using motion phenotyping is shown in Figure 1.

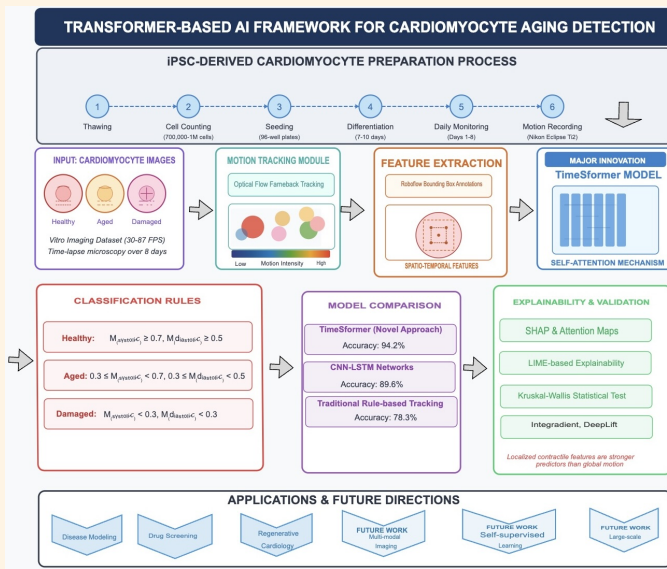


Fig. 1. Proposed AI Framework for Cardiomyocyte Phenotyping

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