CyberCardia Project: Modeling, Verification and Validation of Implantable Cardiac Devices

A Collaborative Project of the NSF Cyber-Physical Systems Frontier Program

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The Story of David [1]

- Pacemaker implanted with baseline HR of 60 bpm
- Well-conditioned with avg HR of $<$ 60 bpm
- Resulted in pacemaker sensing bradycardia and continuously pacing
- At 2-month checkup, cardiologist discovered mistake and realized that pacemaker had not been necessary
- His heart, however, had remodeled and pacemaker now required!

[1] Actual patient story

Lessons Learned

His case highlights the need for:

- Heart modeling and simulation from patient data to evaluate patient-specific conditions
- Automated selection of 8,000+ parameter combinations to guide cardiologists to choose most appropriate settings
- Heart model as part of patient electronic health records

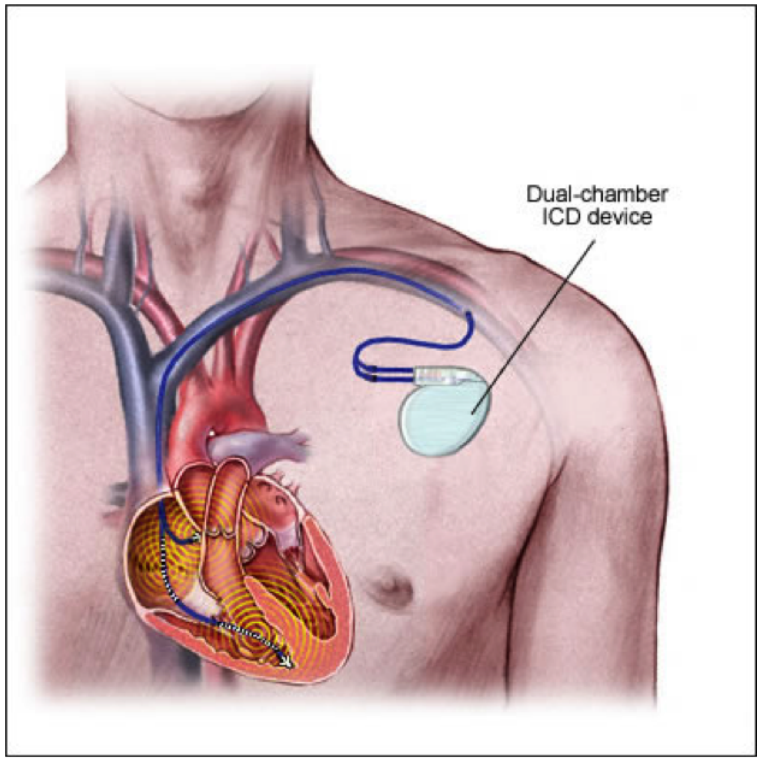
CyberCardia Verification and Validation for Medical CPSs

Goal:

- Accurate & detailed cardiac models needed for patient-specific
- Formal analysis: closed-loop V&V

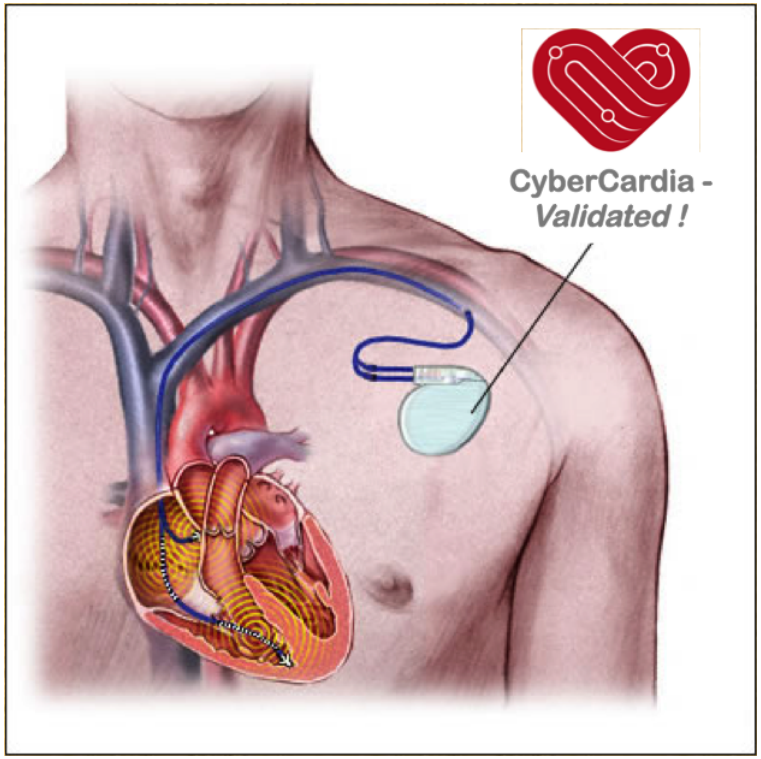
Current Practice:

- Safety & efficacy of medical devices established largely by clinical trials
- Difficulties in programming devices with patient-specific settings



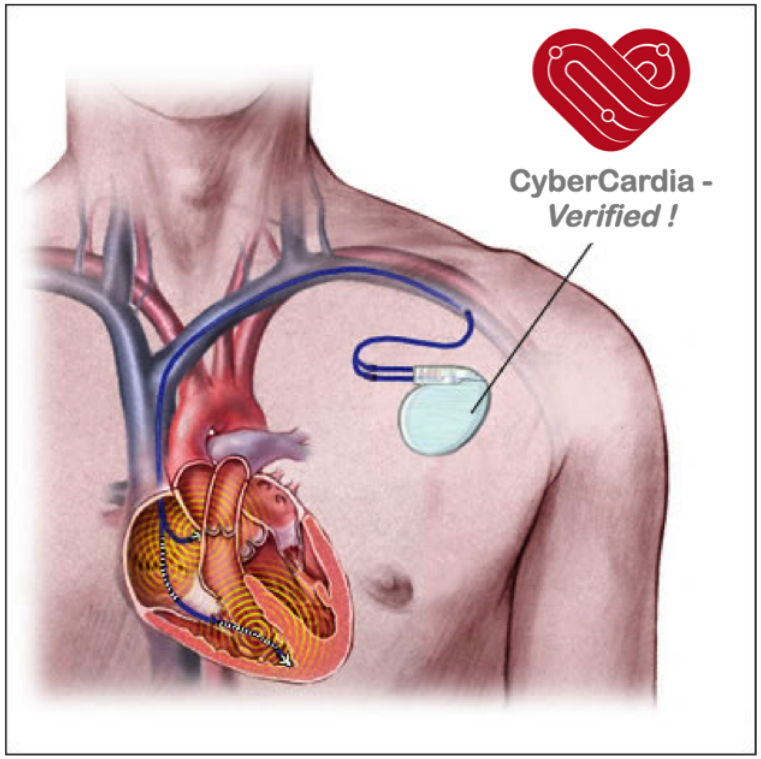
Our Vision

- Closed-loop CyberCardia-V&V of devices!
- With patient-specific settings
- Streamlined regulatory process
- Shorter Time-To-Market
- Fewer Device Recalls

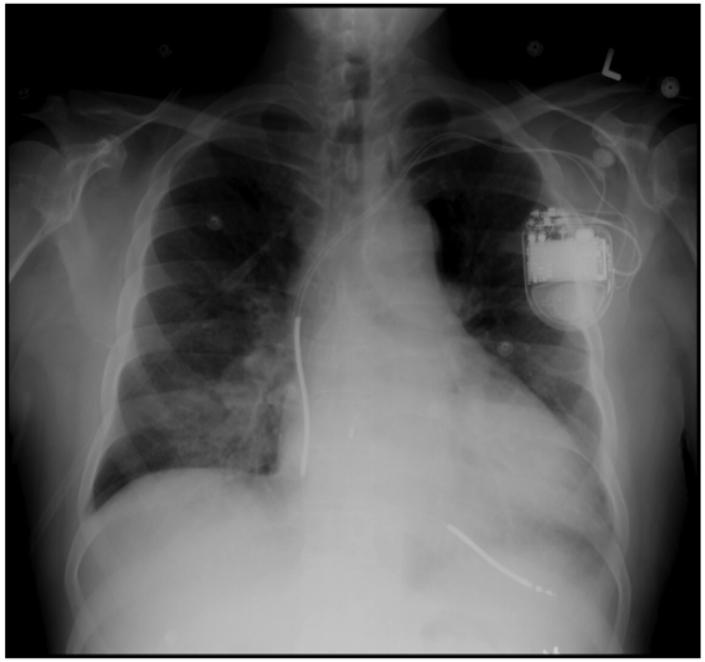


Closed-loop CyberCardia-V&V

- **Virtualize** (in silico) patient's heart and/or device
- Perform **verification** in each of 4 scenarios
- Each with its own attendant benefits!

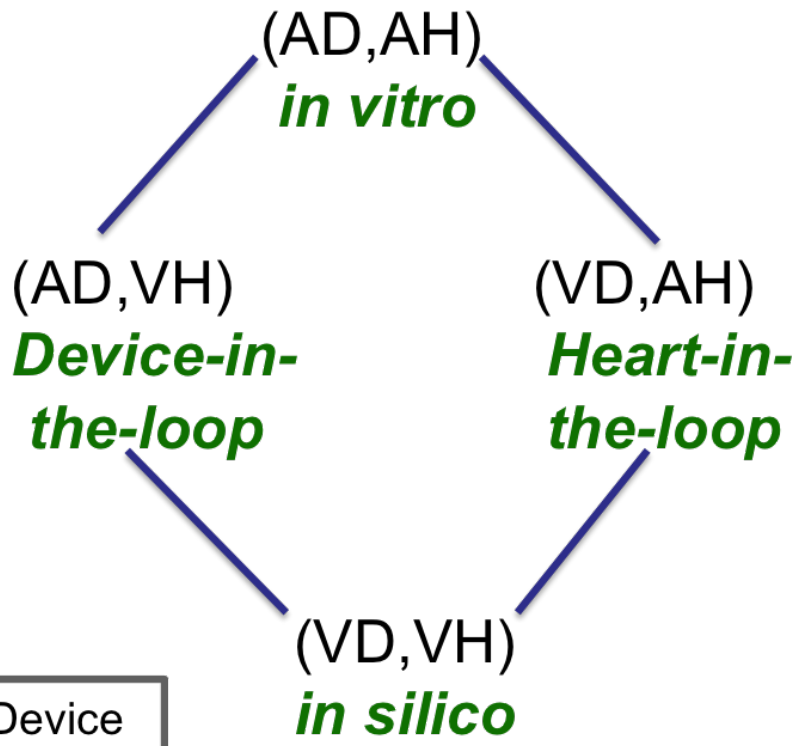


Closed-loop CyberCardia-V&V (contd.)



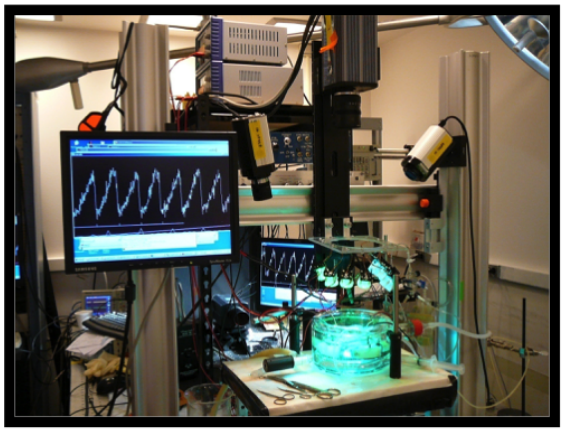
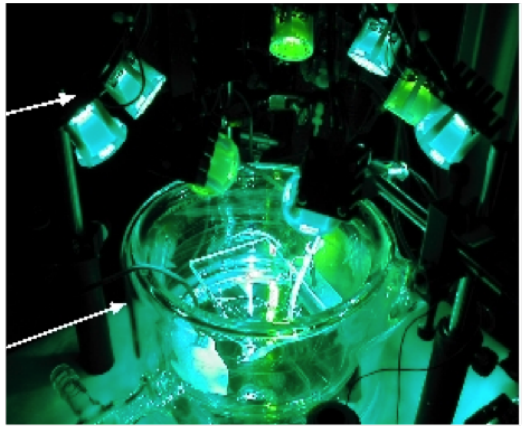
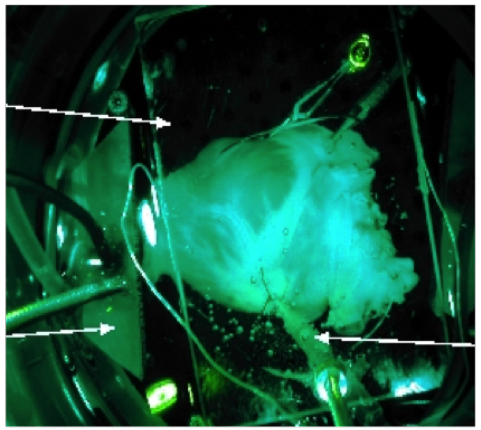
in vivo

What is Closed-Loop V&V?



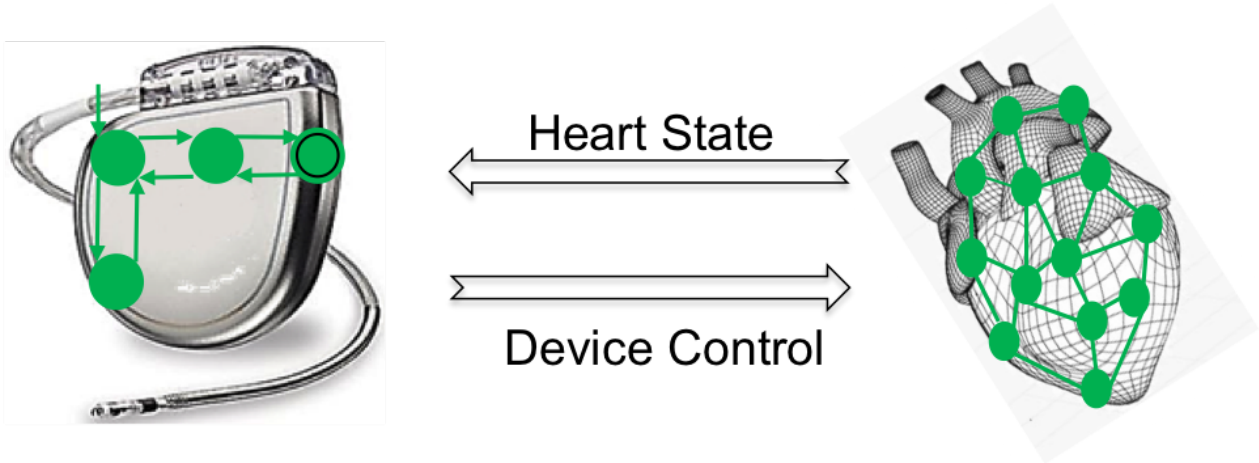
AD=Actual Device	VD=Virtual Device
AH=Actual Heart	VH=Virtual Heart

In Vitro: Actual Heart, Actual Device

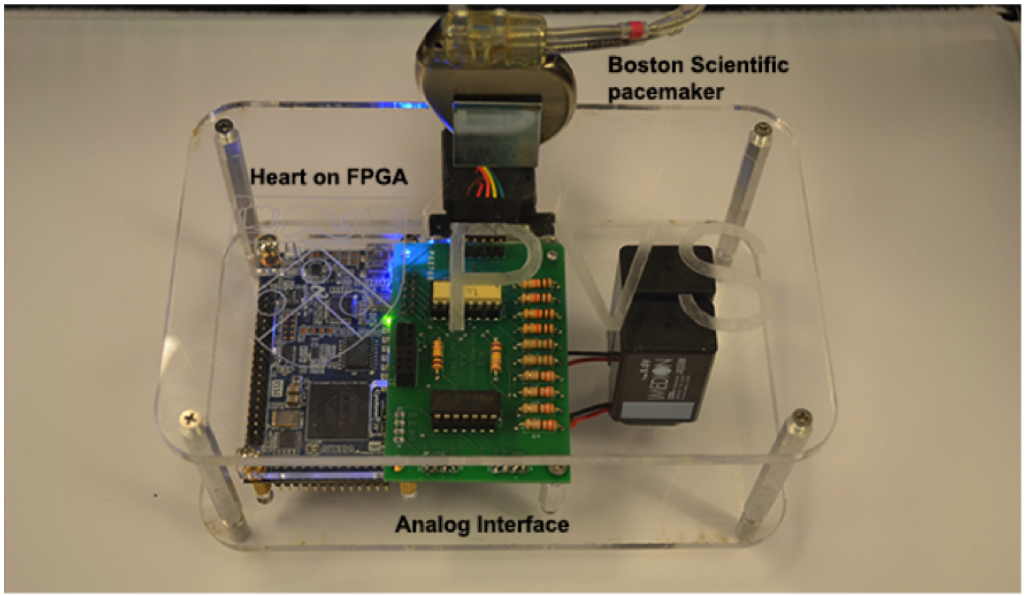
- **Optical-mapping** wet-lab setup (Flavio Fenton, GT) where:
- **Surgically removed heart** *will be* in the loop with actual device
- **V&V possible** in this setup by repeatedly running experiments

In Silico: Virtual Heart, Virtual Device



- Will develop detailed & accurate **patient-specific** heart & device models
- In this fully ***in silico*** setup, we can perform **exhaustive** or semi-exhaustive verification
- **Compositional, approximate** and **quantitative** reasoning will be essential here!

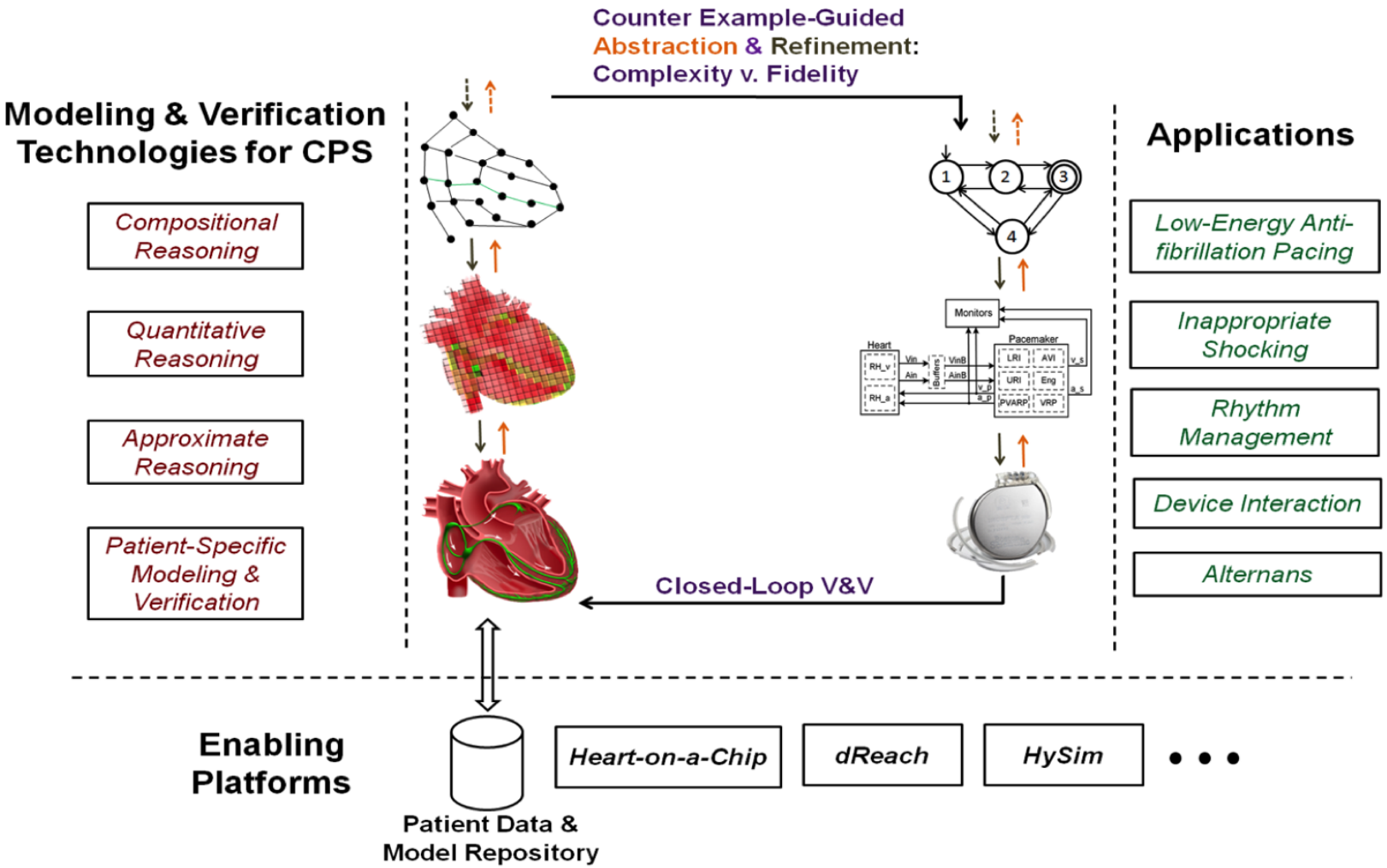
Device-in-the-Loop: Virtual Heart, Actual Device



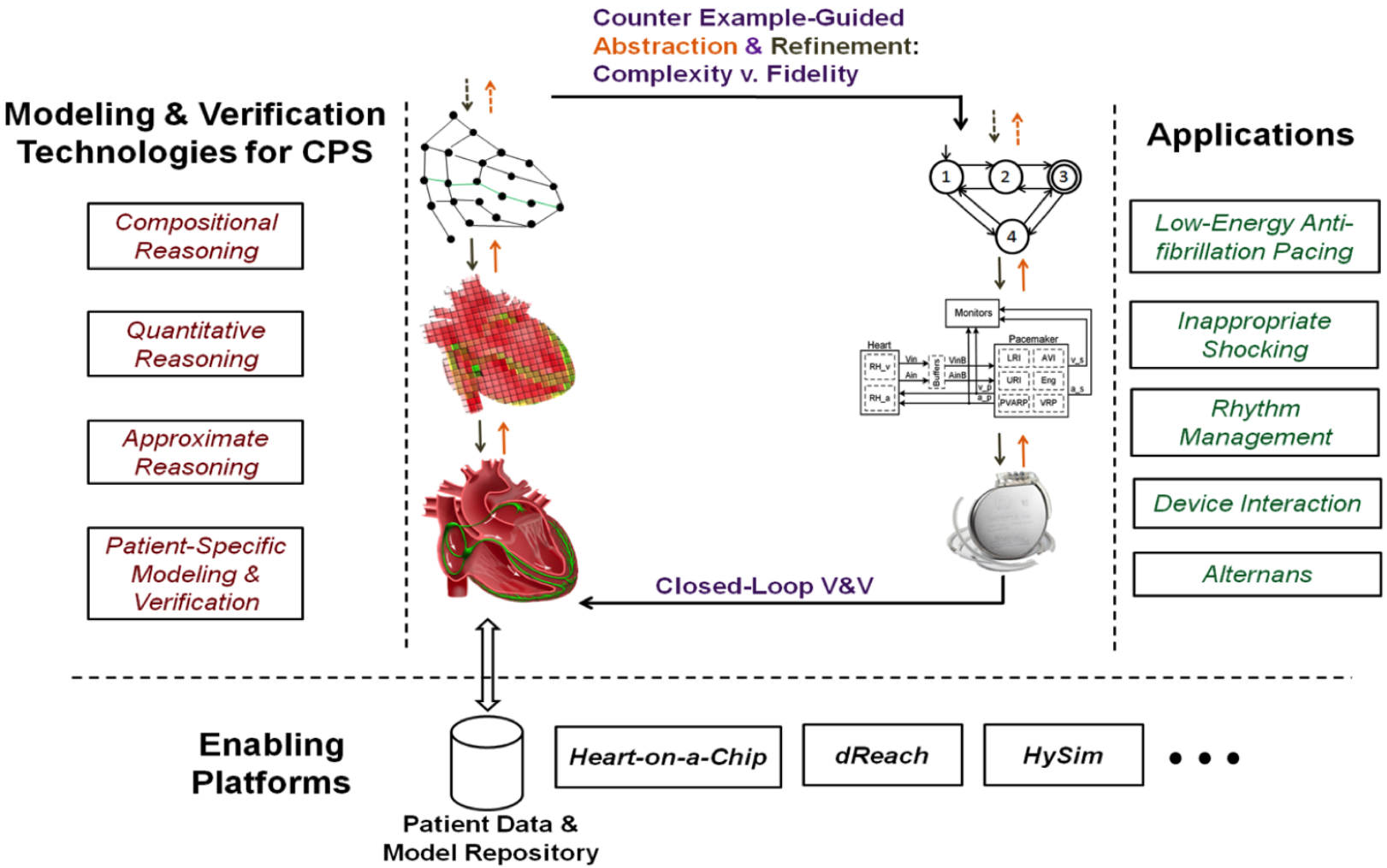
Adds a CPS dimension!

- **Heart-on-a-Chip** model, with interface to actual device. Pioneered by Co-PI Mangharam et al.
- Beyond hardware-in-the-loop testing via **Statistical Model Checking** verification

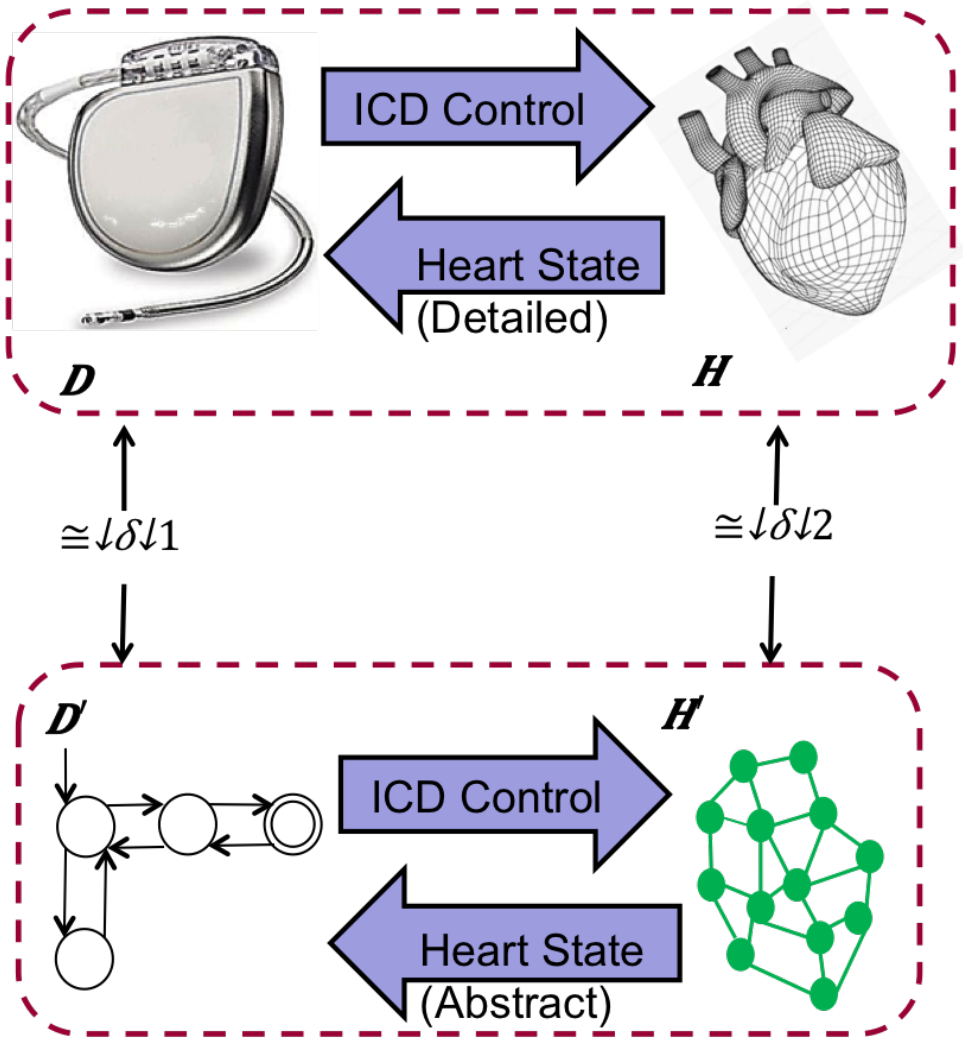
The CyberCardia Framework



The CyberCardia Framework



Compositional & Approximate Verification



$D \times H$: Difficult to verify

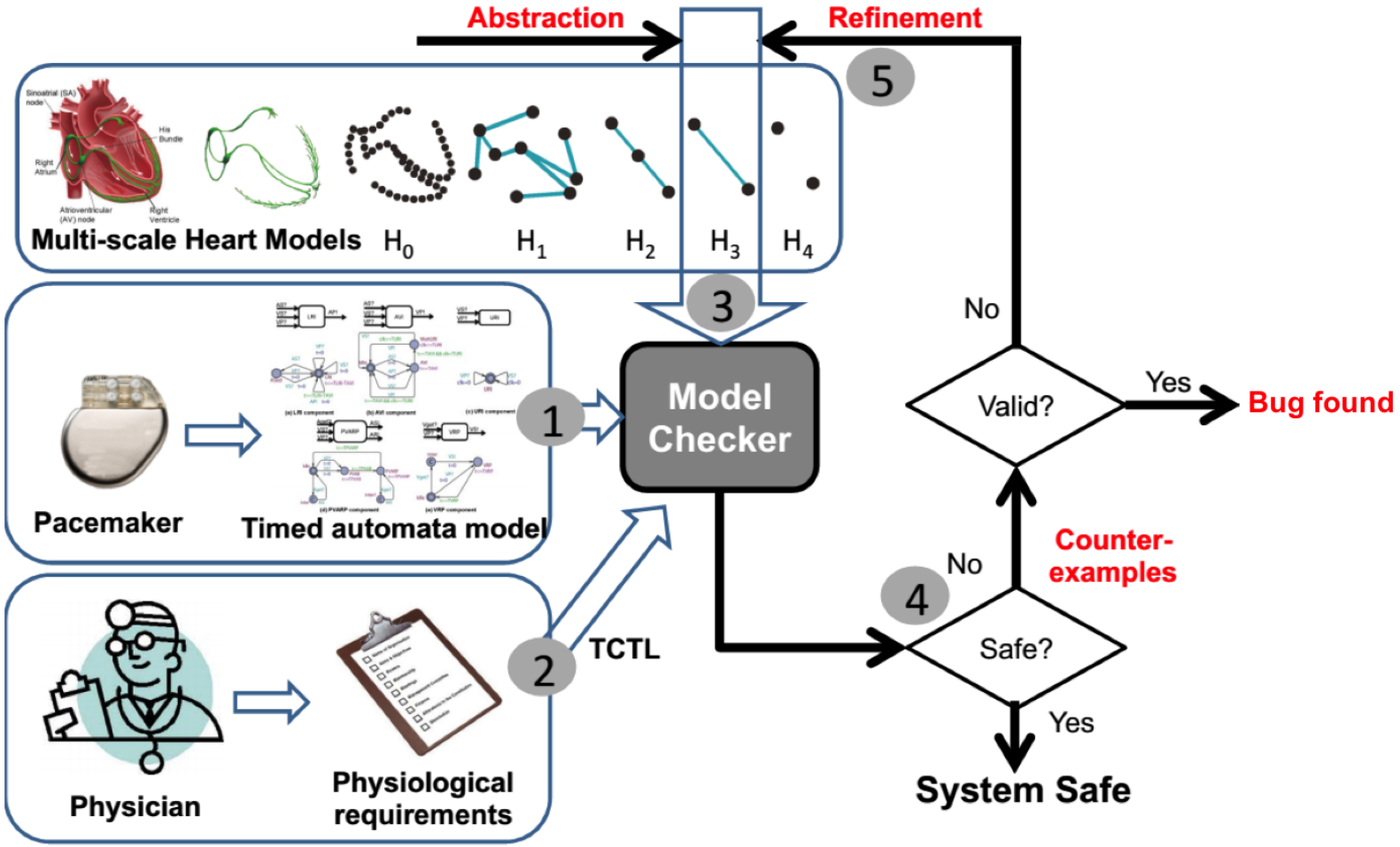
Detailed feedback-composed closed-loop model of device (D) & heart (H)

$\cong \downarrow\alpha\downarrow 1$
$\delta\downarrow 1 + \alpha\downarrow 2$
$\delta\downarrow 2 \ \alpha\downarrow 1, \alpha\downarrow 2 \geq 1$

$D' \times H'$: Easier to verify

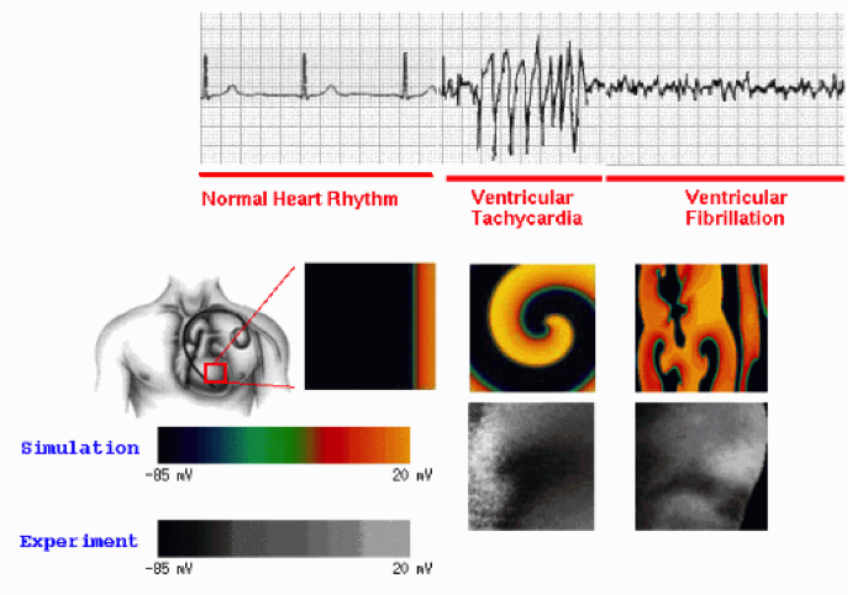
Abstract feedback-composed closed-loop model of device (D') & heart (H')

Compositional & Approximate Verification (contd.)



Reduced Model for Cardiac Action Potential

- Models are used to explain cardiac arrhythmia
- Existing models are complex and not amenable for formal verification
- Our collaborators developed a reduced model of cardiac action potential that can reproduces
  - Cellular excitability and its recovery
  - Beat-to-beat cellular alterations
  - Unstable spiral waves and spiral wave breakup



Electrocardiac Defibrillation Modeling

Goal: Study the effect of defibrillating shock on fibrillation

- Existing model (Chaste model by Oxford Univ.) cannot reproduce experimental results accurately
- We improve Chaste model by adding electroplating current (CyberCardiac model, SBU)
- CyberCardiac model can reproduce experimental results more accurately

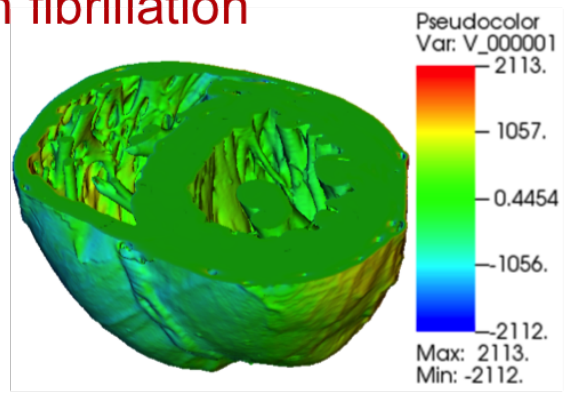


Fig. Simulation of Chaste Model

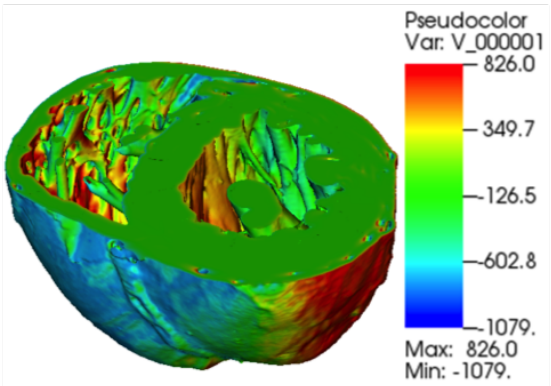


Fig. Simulation of CyberCardiac Model

Regular Expression for Irregular Rhythm

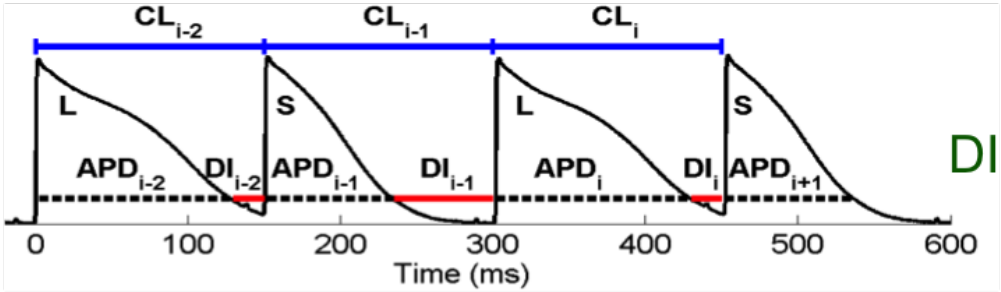
- Peak Detection: Implantable cardioverter-defibrillator (ICD) detects peaks in ECG
- Discriminator: Detected peaks are used to discriminate fatal and no-fatal rhythms
- Decision Error:
  - Over-sensing (too many false peaks detected)
  - under-sensing (too many true peaks missed)
  - Accounted for 10% decision error (Swerdlow et al.)

Our Contribution:

- Wavelet-based characterization of peak
- Propose the use of Quantitative Regular Expression (QRE) to describe wavelet-based peak detection
- Formalize commercial peak detection algorithm (Medtronic) as a QRE
- Study accuracy and sensitivity of QRE-based peak detection algorithm

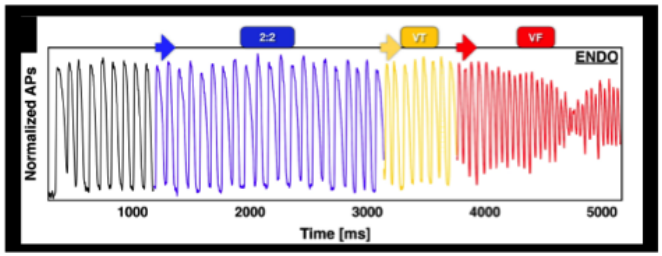
Formal Verification of Alternans

- Cardiac alternans appears as a beat-to-beat long-short alternation of action potential duration (APD)



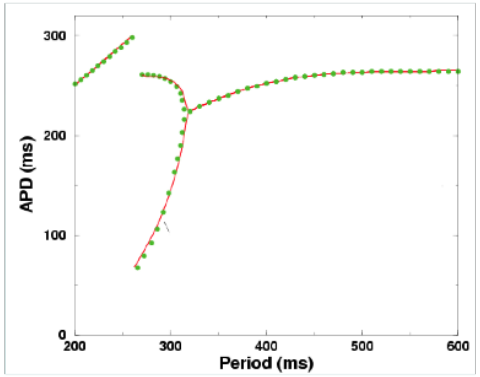
DI: Diastolic Interval

- Often leads to fibrillation

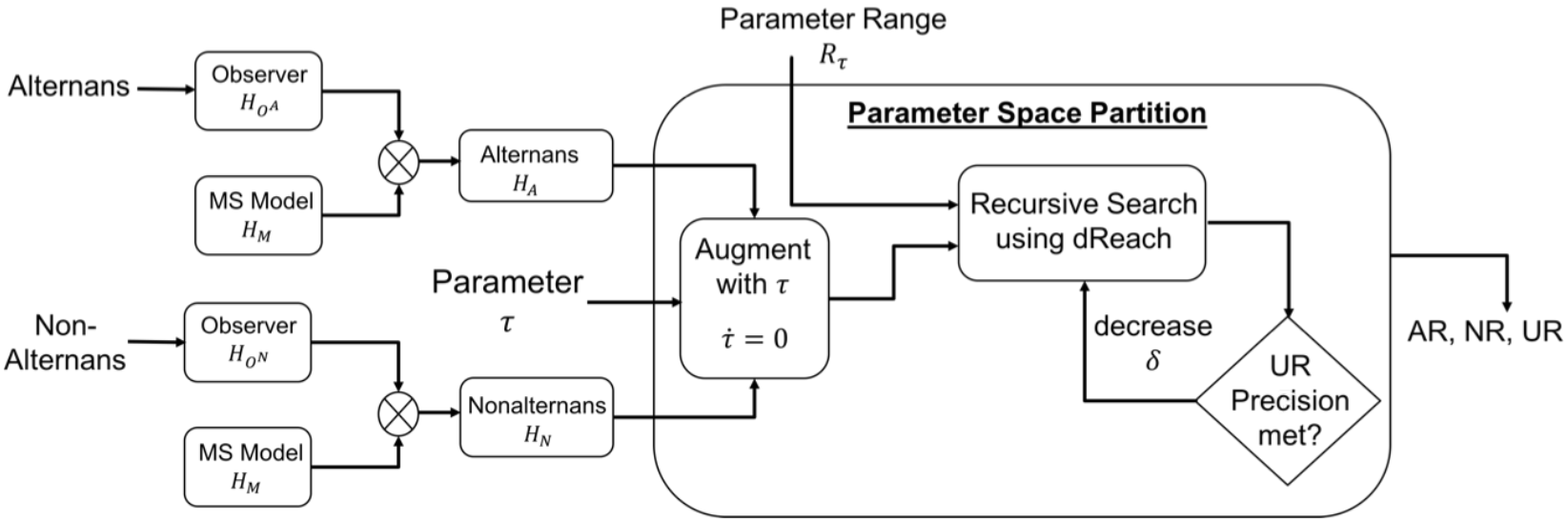


Bifurcation Analysis of Alternans

- Finding bifurcation points (BP) that split the parameter space into alternans and non-alternans regions



Bifurcation Analysis



Ongoing Work

- Model-based clinical trial
- Personalized patient heart model
- Integration of research with education for cross-disciplinary projects

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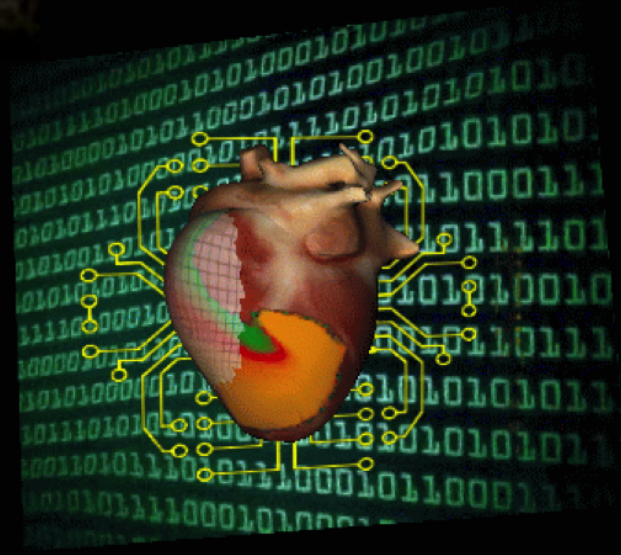

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