



Effects of Wall Heterogeneity in an Anatomically Realistic Model of Canine Ventricles: A Simulation Study

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Abstract

Background. To date, simulations of cardiac tissue in anatomically realistic structures have assumed homogeneous cell types¹. However, variations in cell properties throughout the ventricular wall are essential for reproducing ECGs without inverted T-waves. **Methods.** Using published experimental data², variations in action potential shape and rate adaptation were developed for an ionic cell model and incorporated for the first time into a computer model of the canine ventricles. **Results.** Simulated activation and recovery patterns and ECGs using homogeneous cell types, an apex-base gradient in action potential duration (APD), wall cell types, and the combination of the apex-base gradient and wall cell types were generated and compared. For the simulations to closely match experiments, it was imperative that wall heterogeneities in cell types be included. **Conclusions.** Incorporating transmural heterogeneities in simulated canine ventricles resulted in normal ECGs for V4-V6 leads, while the apex-base gradient was necessary for proper ECGs in V1-V3 leads.

Cell Models

The model consists of 3 currents and 4 variables:

Currents: $I_p(V, v) = -v^p(V - V_p)(V_m - V)/\tau_p$
 $I_{to}(V) = (V - V_{to})(1 - p)/\tau_{to} + p(X_{so11} + X_{so12}(1 + \tanh((V - X_{so2})/X_{so3}))/2)$
 $I_{tr}(w, d) = -w d / \tau_{tr}$

Gate Variables: $q_1 w(x, t) = (1 - p)(1 - v)/\tau_1(V) - pv/\tau_1^*$
 $q_2 w(x, t) = (1 - r)(1 - w)/\tau_w - rv/\tau_w^*$
 $q_3 d(x, t) = ((1 + \tanh((V - V_{d1})/k))/2 - d) / \tau_d$

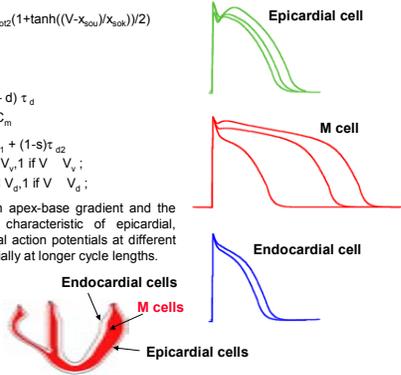
Voltage: $q_4 v(x, t) = \nabla \cdot (D\nabla V) - (I_p + I_{to} + I_{tr}) / C_m$

where $\tau_1(V) = (1 - q) \tau_{11} + q \tau_{12}$; $\tau_d = s \tau_{d1} + (1 - s) \tau_{d2}$
 $p=0$ if $V < V_p$, 1 if $V > V_p$; $q=0$ if $V < V_{d1}$, 1 if $V > V_{d1}$
 $r=0$ if $V < V_r$, 1 if $V > V_r$; $s=0$ if $V < V_{d1}$, 1 if $V > V_{d1}$

The model parameters are varied to produce an apex-base gradient and the variations in cellular currents for activations characteristic of epicardial, endocardial, and M cells, following Ref. 2. Several action potentials at different rates are shown, with M cells prolonging preferentially at longer cycle lengths.

The outer 2 mm of tissue are assigned as epicardial cells and the inner 3-6 mm are assigned as endocardial. The remaining tissue, which consists of M cells and transitional cells, are modeled here as M cells, pictured in red.

Model action potentials for different cell types

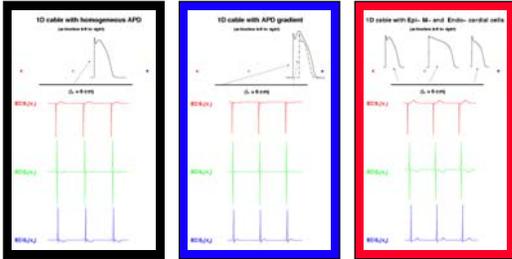


ECGs for 1D Cables

ECGs generated using 1D cables with various combinations of cell types:

- Identical cell types (homogeneous cable).
- Endocardial-epicardial gradient, without M cells.
- Endocardial, epicardial, and M cells.

See similar cable ECGs with cell types in Ref. 3.



Results

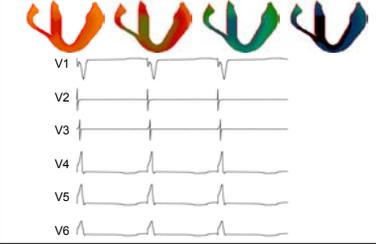
Activation



Following Ref. 4, activation began endocardially along the septum, proceeded towards the apex, and finished towards the base and epicardium. Both ventricles were fully activated within 70 ms.

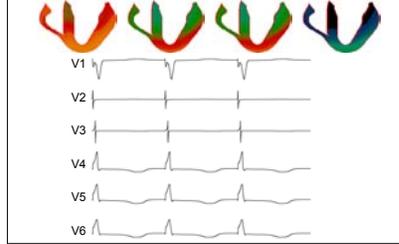
Repolarization: Homogeneous

The repolarization pattern is identical to the activation pattern. T-waves are small and inverted.



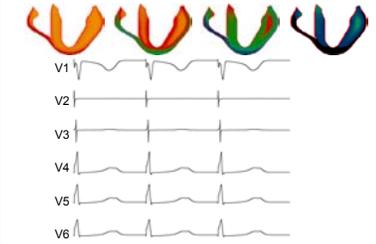
Repolarization: Apex-Base Gradient

The base repolarizes faster than the apex. T-waves are larger but still inverted.



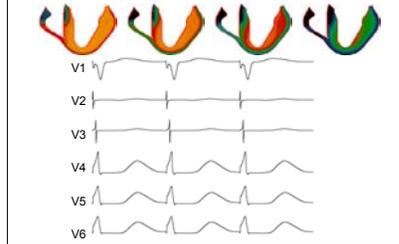
Repolarization: Transmural Heterogeneity

Repolarization starts at the epicardium, then endocardium, and then M cells. T-waves are up for leads V3-V6



Repolarization: Apex-Base + Transmural

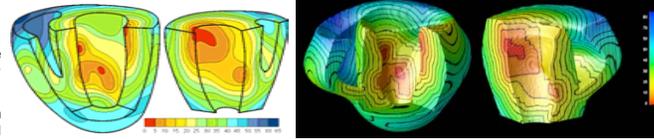
Epicardial cells repolarize first, M cells last, and the base before the apex. T-waves were larger with proper polarity.



Ongoing Work

Reproduce ECGs accurately in 3D:

- Step 1. Activation sequence from experimental data.⁴ **Accomplished.**
- Step 2. Repolarization sequence from experimental data. **In progress.**



Activation sequence from Ref. 4.

Our reproduction of the activation sequence from Ref. 4.

Conclusions

Simulated activation and recovery patterns and ECGs using homogeneous cell types; an apex-base gradient in APD; transmural epicardial, endocardial, and M cell types; and the combination of the apex-base gradient and wall cell types were generated and compared.

- In **homogeneous** ventricular tissue, T-waves were small and inverted.
- Using only the **apex-base gradient increased the magnitude of the T-wave** but did not change its polarity.
- When **epicardial, endocardial, and M cell types** through the ventricular wall were included, **T-waves of proper polarity** were produced.
- The **combination of the apex-base gradient and transmural heterogeneity** amplified differences in repolarization and resulted in **larger T-waves with proper polarity.**

References

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