

Investigating a Period-Doubling Bifurcation in Cardiac Tissue Using Alternate Pacing

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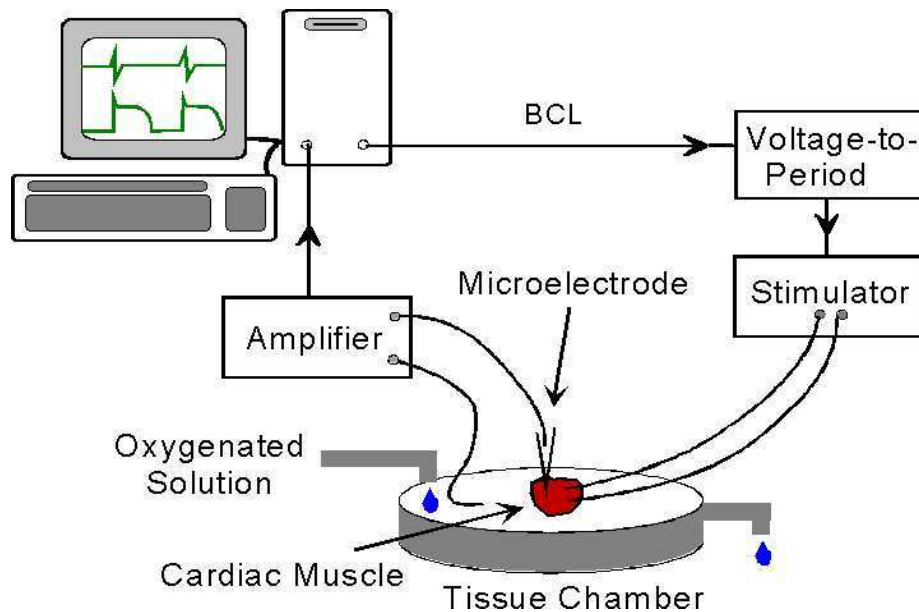
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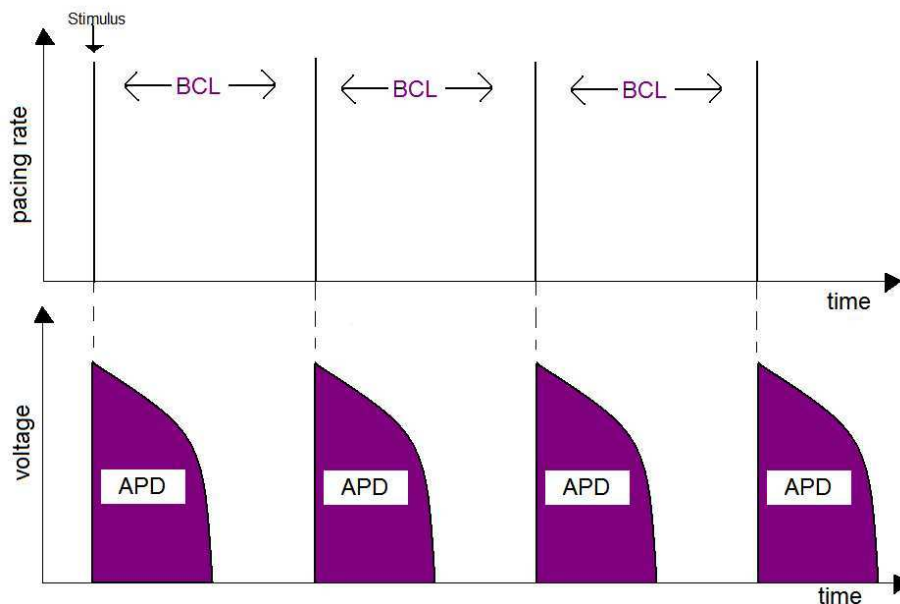
^ePediatric Cardiology

Introduction to Cardiac Dynamics

Experimental Setup

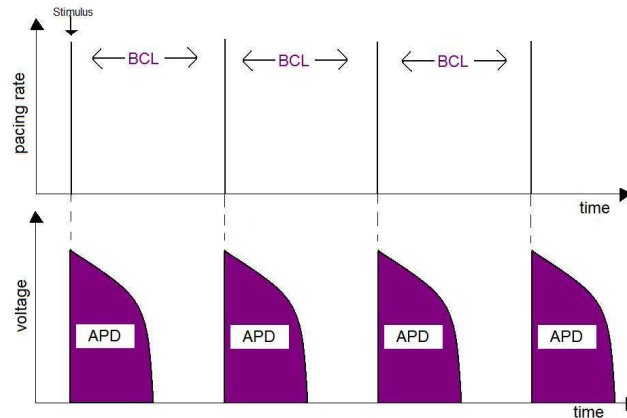


Single Cell Cardiac Dynamics

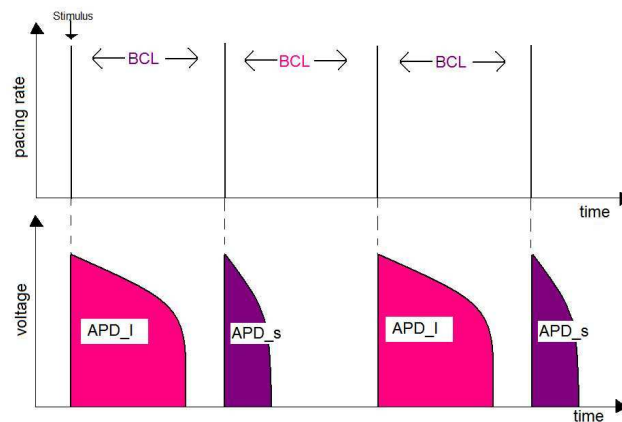


1:1 \Rightarrow 2:2 Transition

● 1:1



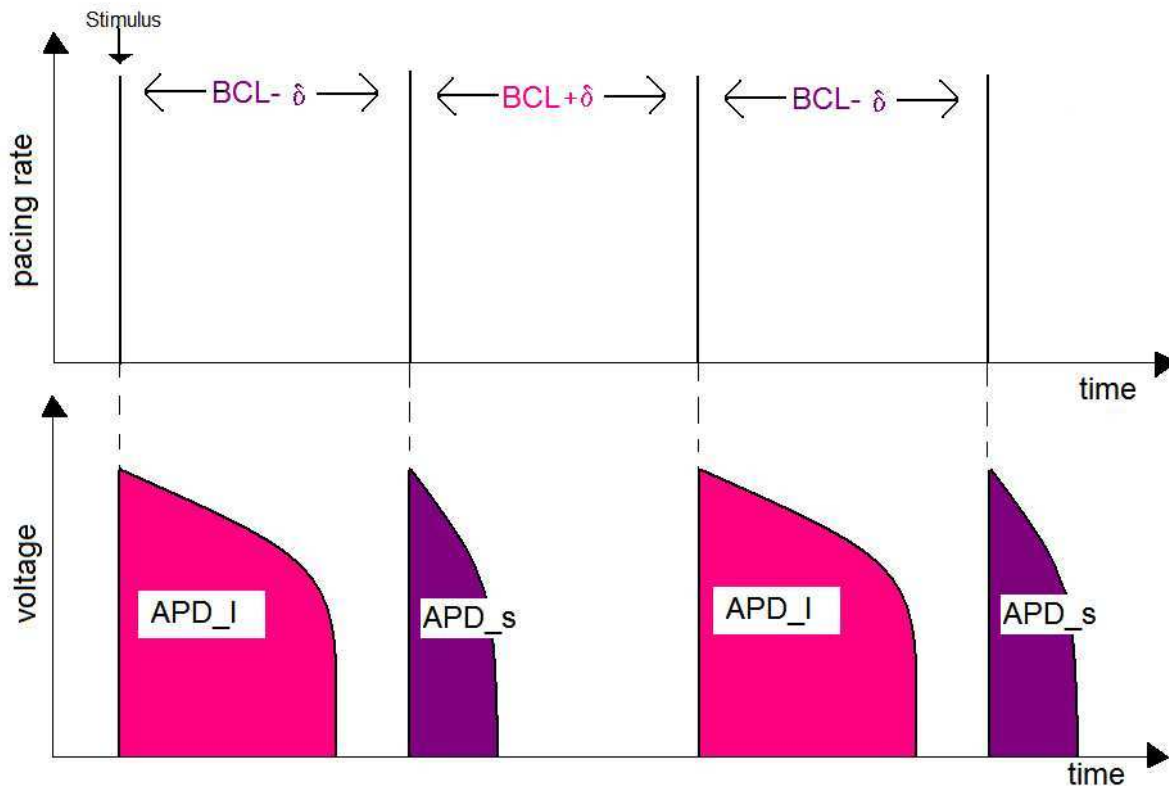
● 2:2 (alternans)



- Increase Pacing Rate \Rightarrow bifurcation to 2:2
- 2:2 behavior linked to ventricular arrhythmias and sudden cardiac death
- We are interested in the 1:1 \Rightarrow 2:2 transition

New Technique: Alternate Pacing Protocol (APP)

- alternate **pacing** induces alternate response



- Measure the gain, defined as

$$\text{Gain} = \frac{\text{APD}_l - \text{APD}_s}{2\delta}$$

Purpose of the APP

- **Small** beat-to-beat changes in the BCL, 2δ , will induce a **large** difference between APD_l and APD_s
- **Hypothesis**: APD variations will be more prominent in tissue susceptible to alternans
- **Goal**: identify the tissue's propensity towards alternans before the actual onset

Simple Mathematical Explanation

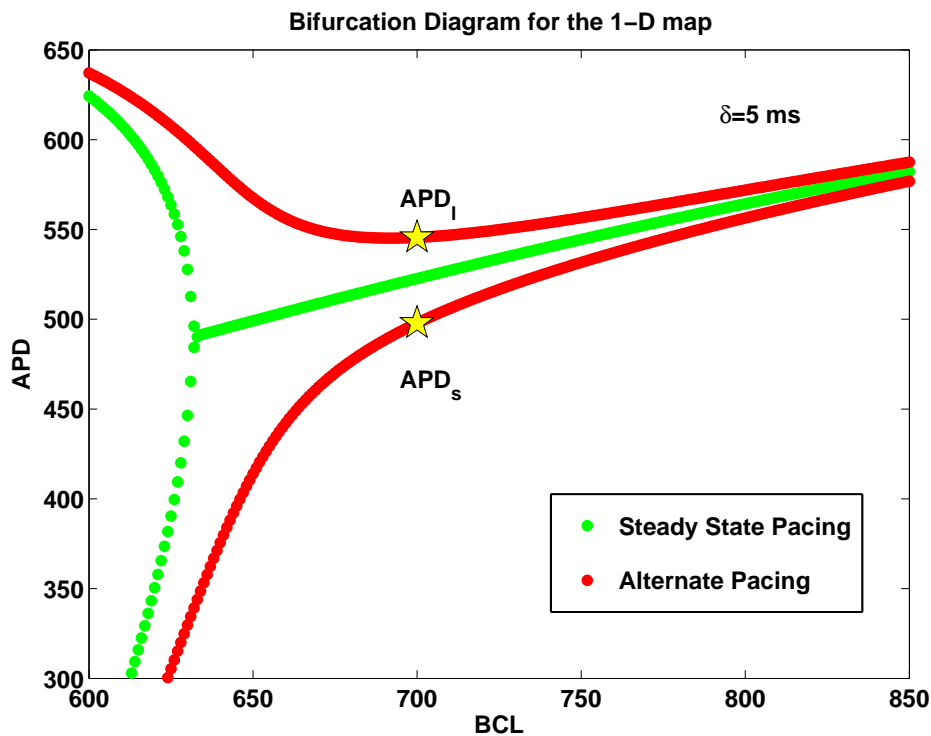
- $APD_{n+1} = f(DI_n)$
 - where $DI_n = BCL - APD_n$
- APPLY Alternate Pacing Protocol
- Linear approximation to 1-D map

$$\text{Gain} = \frac{f'(DI_n)|_{DI^*}}{1 - f'(DI_n)|_{DI^*}}$$

- $f'(DI_n)|_{DI^*} = 1$ condition for bifurcation
- DIVERGENCE $f'(DI_n)|_{DI^*} \Rightarrow 1$

1-D Map Simulation

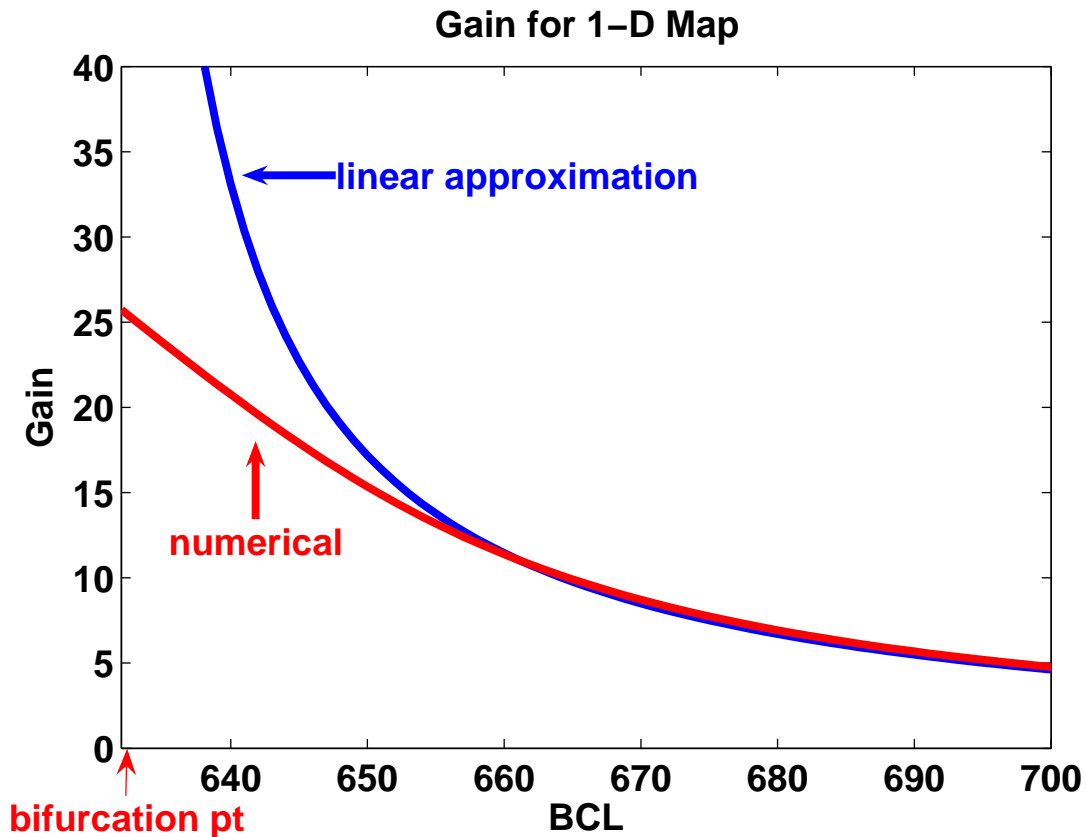
- $APD_{n+1} = f(DI_n) = A_{max} - Ae^{-DI_n/\tau}$
(Nolasco, Dahlen. *J. Appl. Physio.* (1968))



- $Gain = \frac{APD_l - APD_s}{2\delta}$
- at BCL = 700ms \Rightarrow Gain \sim 4.78

The Theoretical Gain

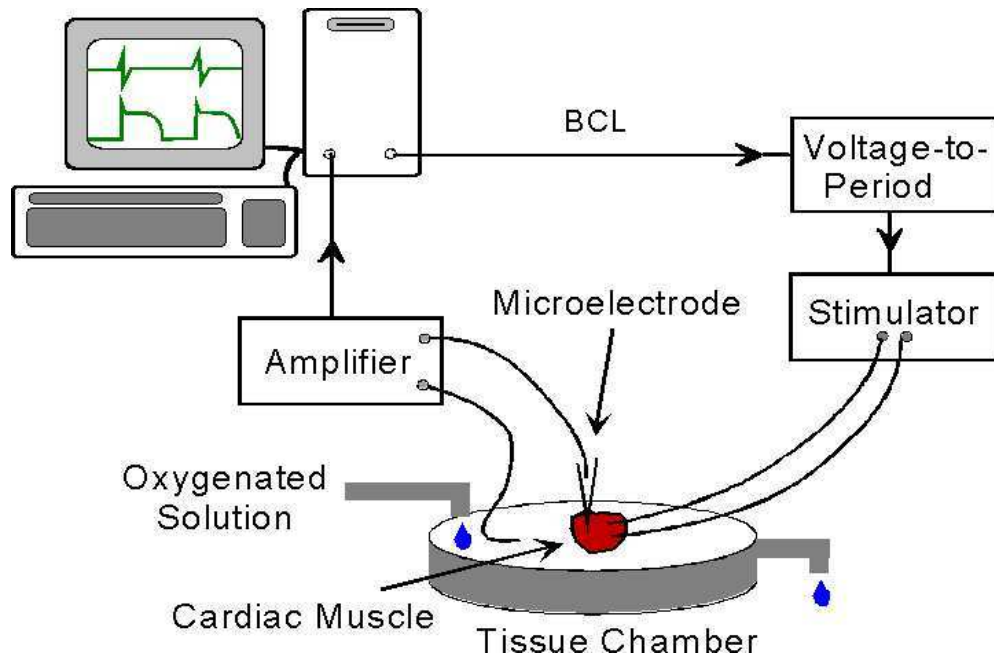
- for $APD_{n+1} = f(DI_n)$



- For linear approximation \Rightarrow gain diverges
- generic result for other mapping models
 - $APD_{n+1} = f(APD_n, DI_n)$
 - $APD_{n+1} = f(APD_n, DI_n, DI_{n-1})$

APP in Experiment


- Experimental Setup

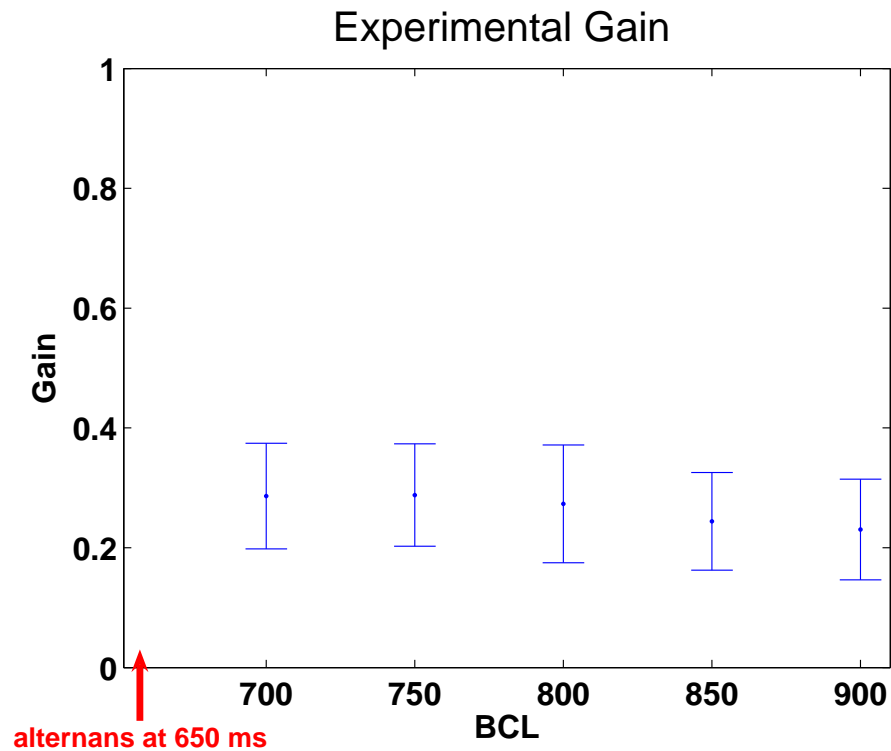
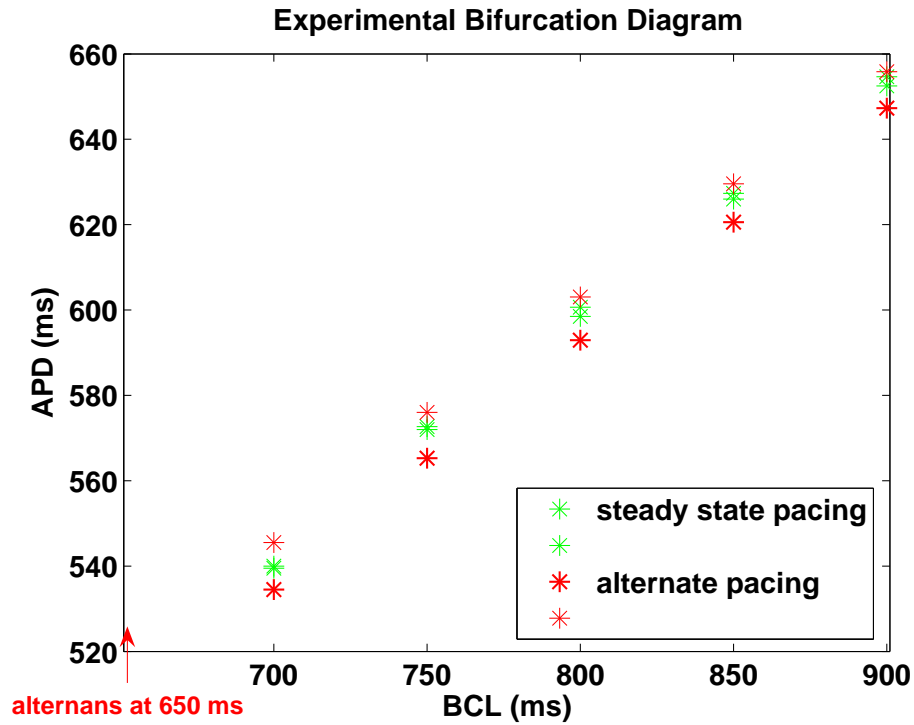


- Number of Animals: **13**

- Number of Trials: **50**

Data from One Trial

 $\delta = 20\text{ms}$



Summary

- Mapping models show gain becoming large near the bifurcation
- Fox Ionic Model (implemented by Dr. Kalb) also shows large gain near the bifurcation
- theoretically we expect the gain to become large near the bifurcation point; experimentally we find the gain does not exceed one
- APP serves as another protocol that can validate new map and ionic models
- Study calcium and voltage dynamics together