Understanding an Unfolded Border-Collision Bifurcation in Paced Cardiac Tissue

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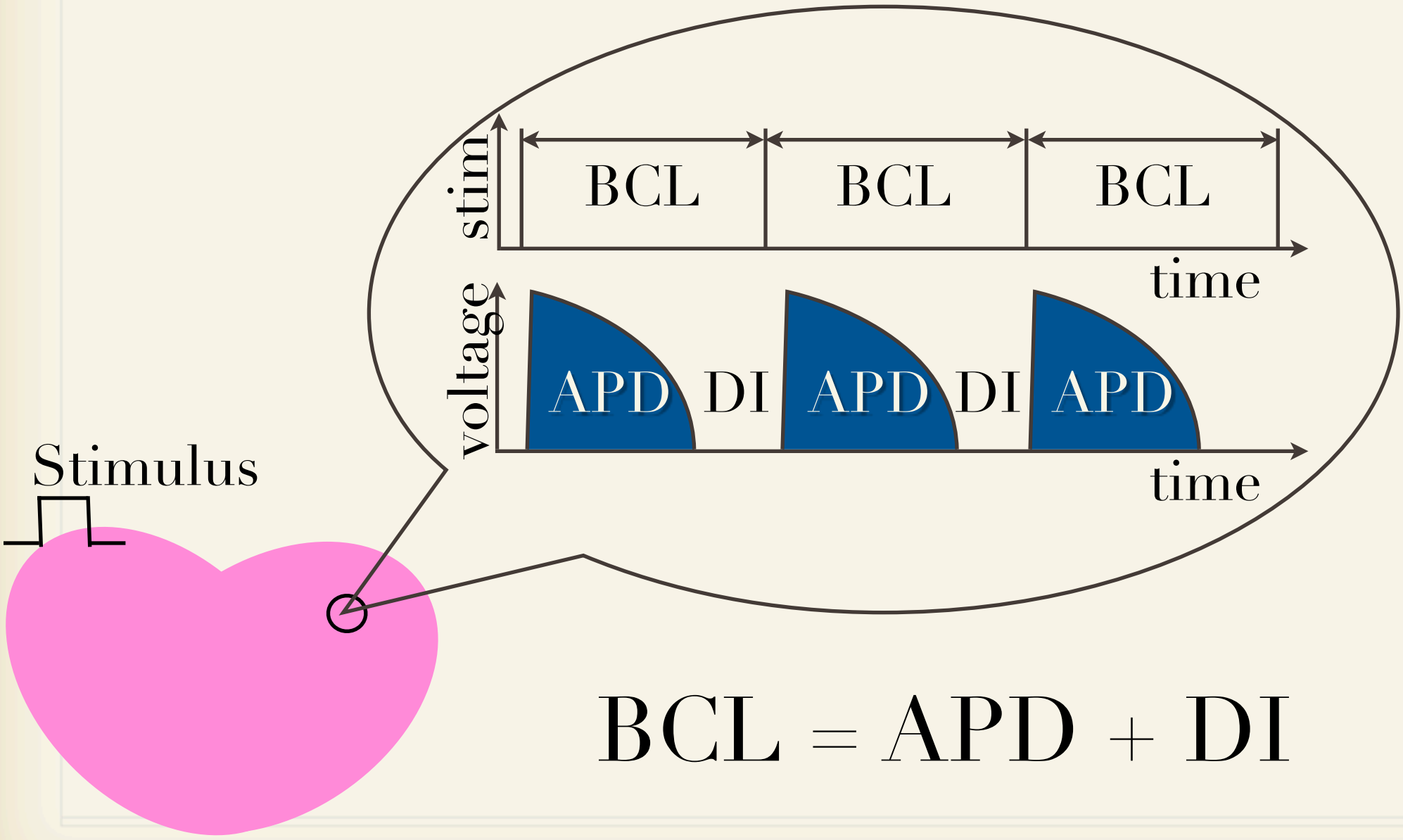
Outline

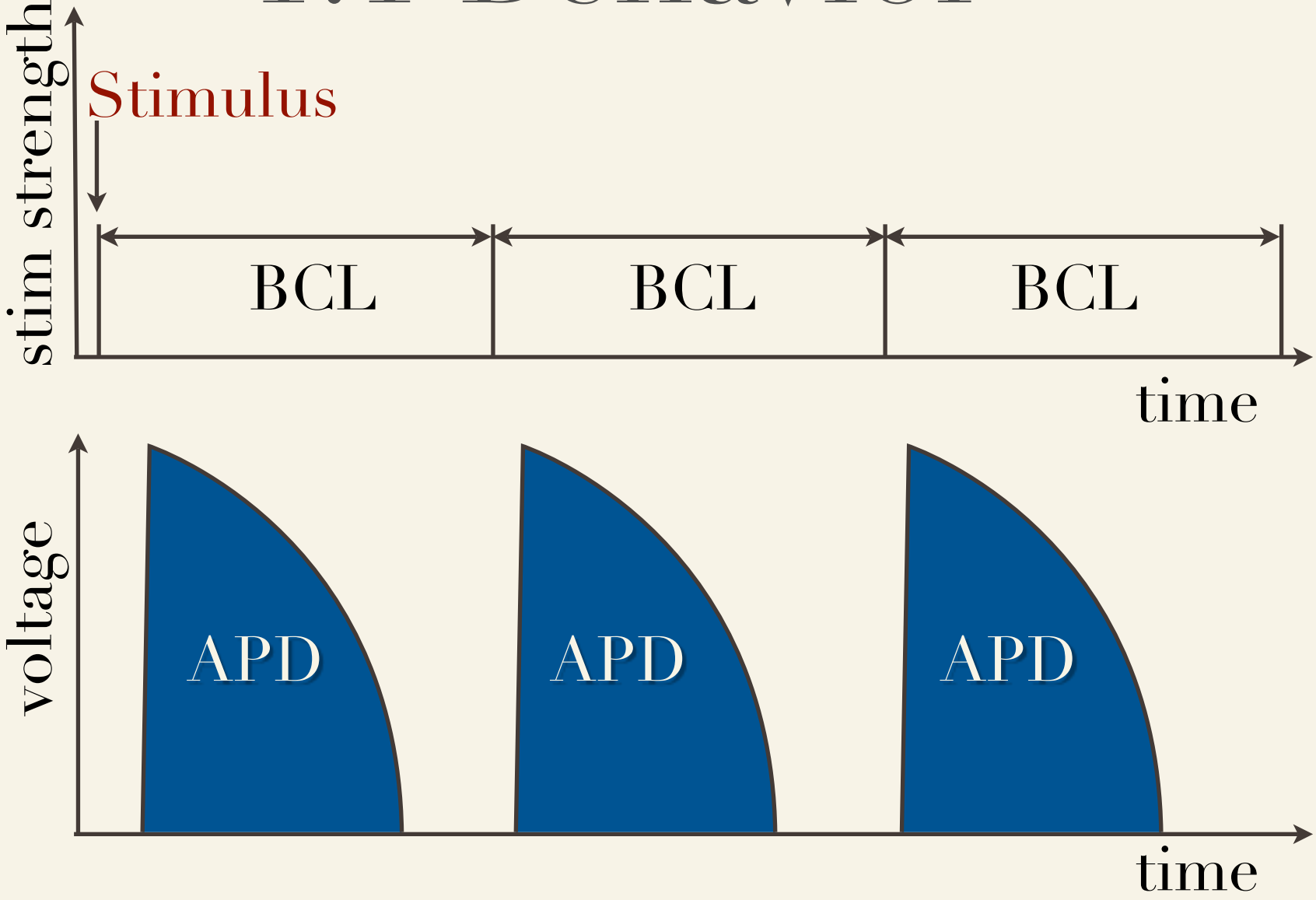
- Bifurcation in Cardiac Tissue
- Technique to Uncover Bifurcation Type
- Experimental Results
- New Model

Cardiac Dynamics

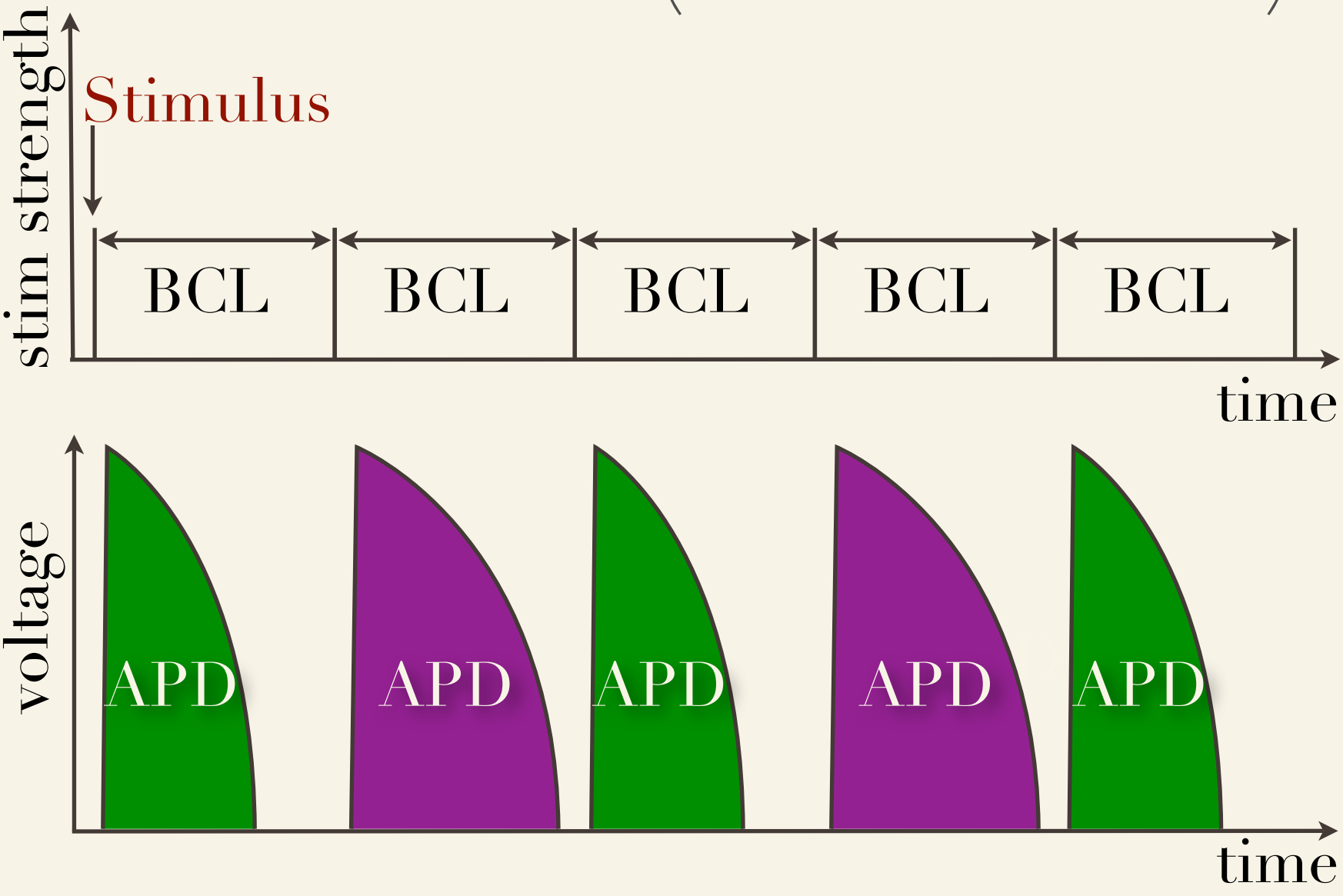


$$BCL = APD + DI$$

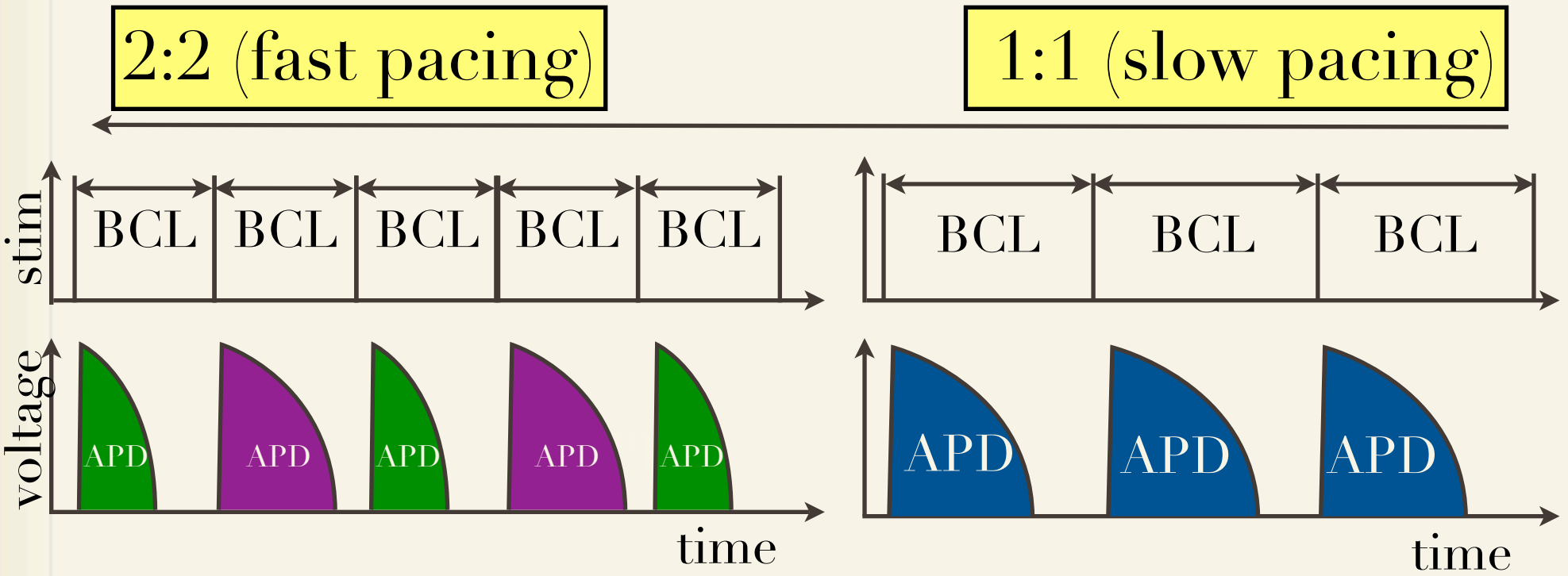
1:1 Behavior


stim strength
Stimulus
BCL
BCL
BCL
time
voltage
APD
APD
APD
time

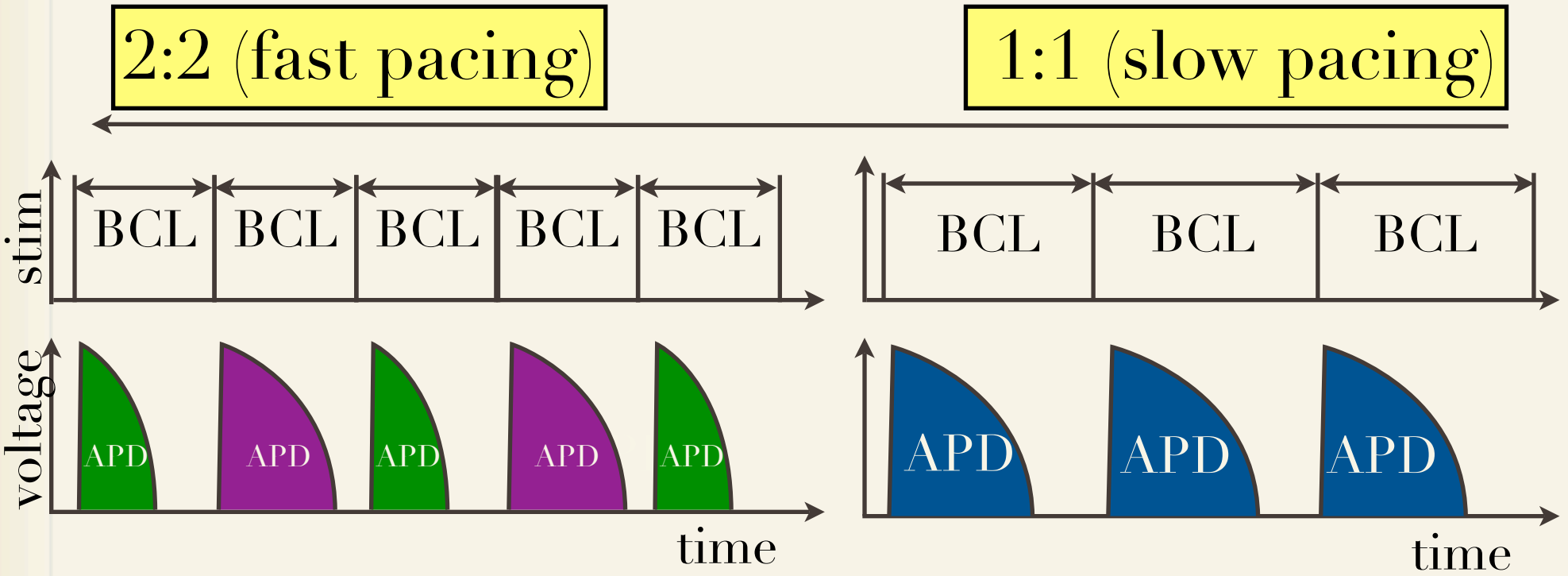
2:2 Behavior(Alternans)



Transition

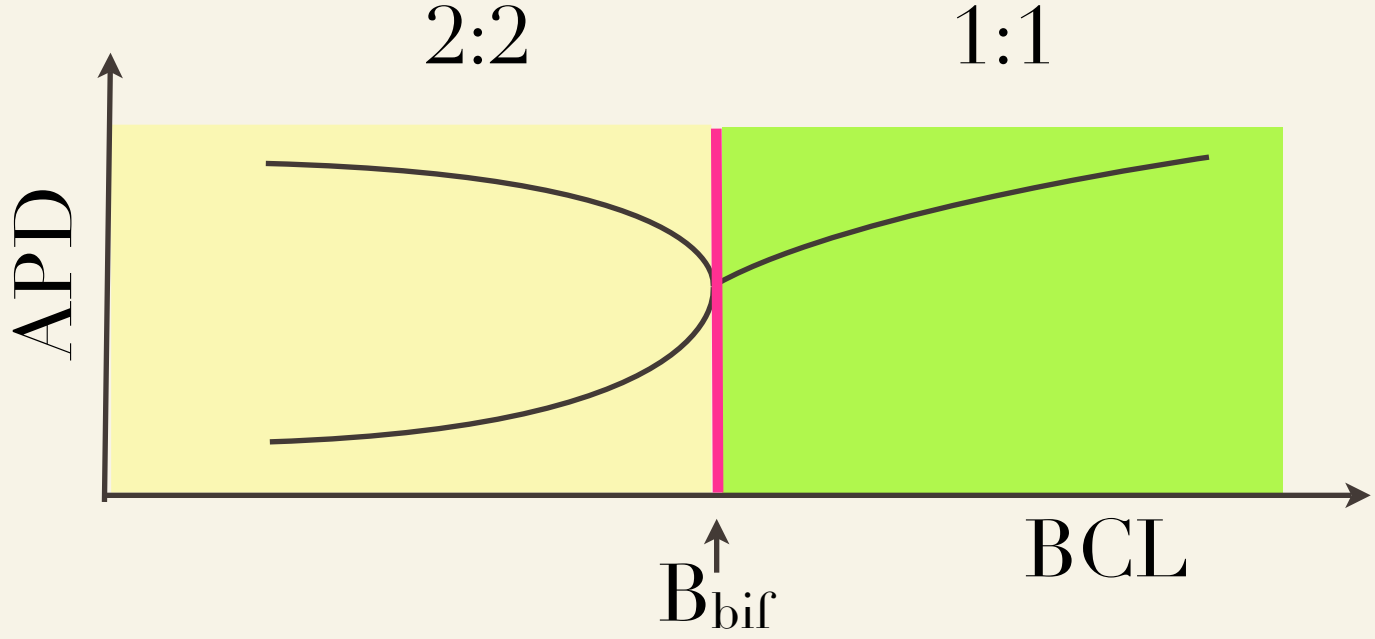

2:2 (fast pacing)
1:1 (slow pacing)
stim
BCL
BCL
BCL
BCL
BCL
BCL
BCL
BCL
voltage
APD
APD
APD
APD
APD
APD
APD
APD
time
time

Transition

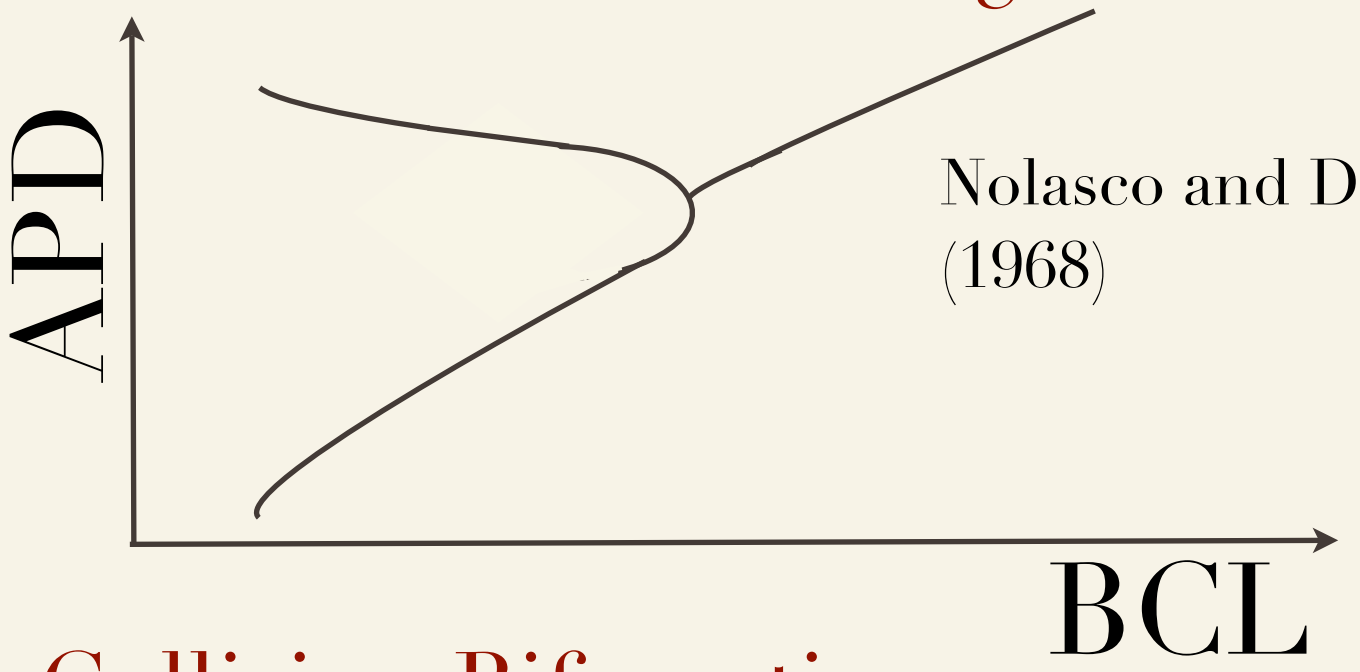


~ 2:2 (alternans) linked to ventricular arrhythmias and sudden cardiac death

Bifurcation Diagram

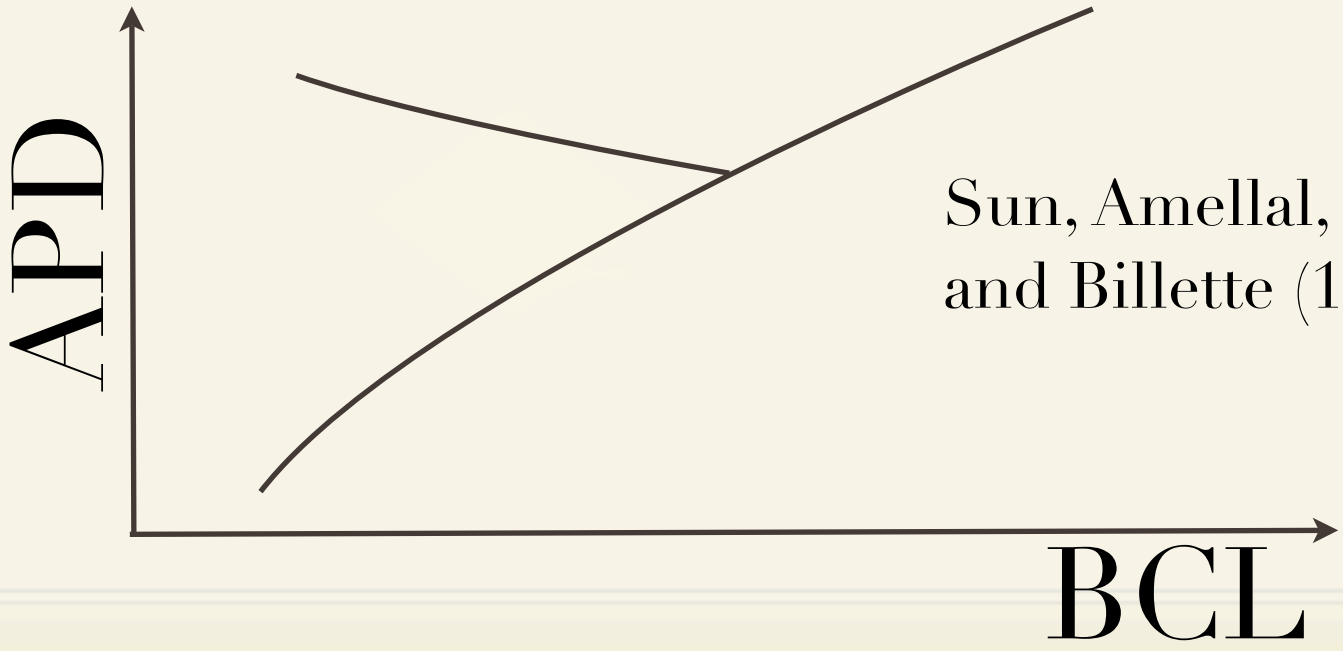


Supercritical Period-Doubling Bifurcation

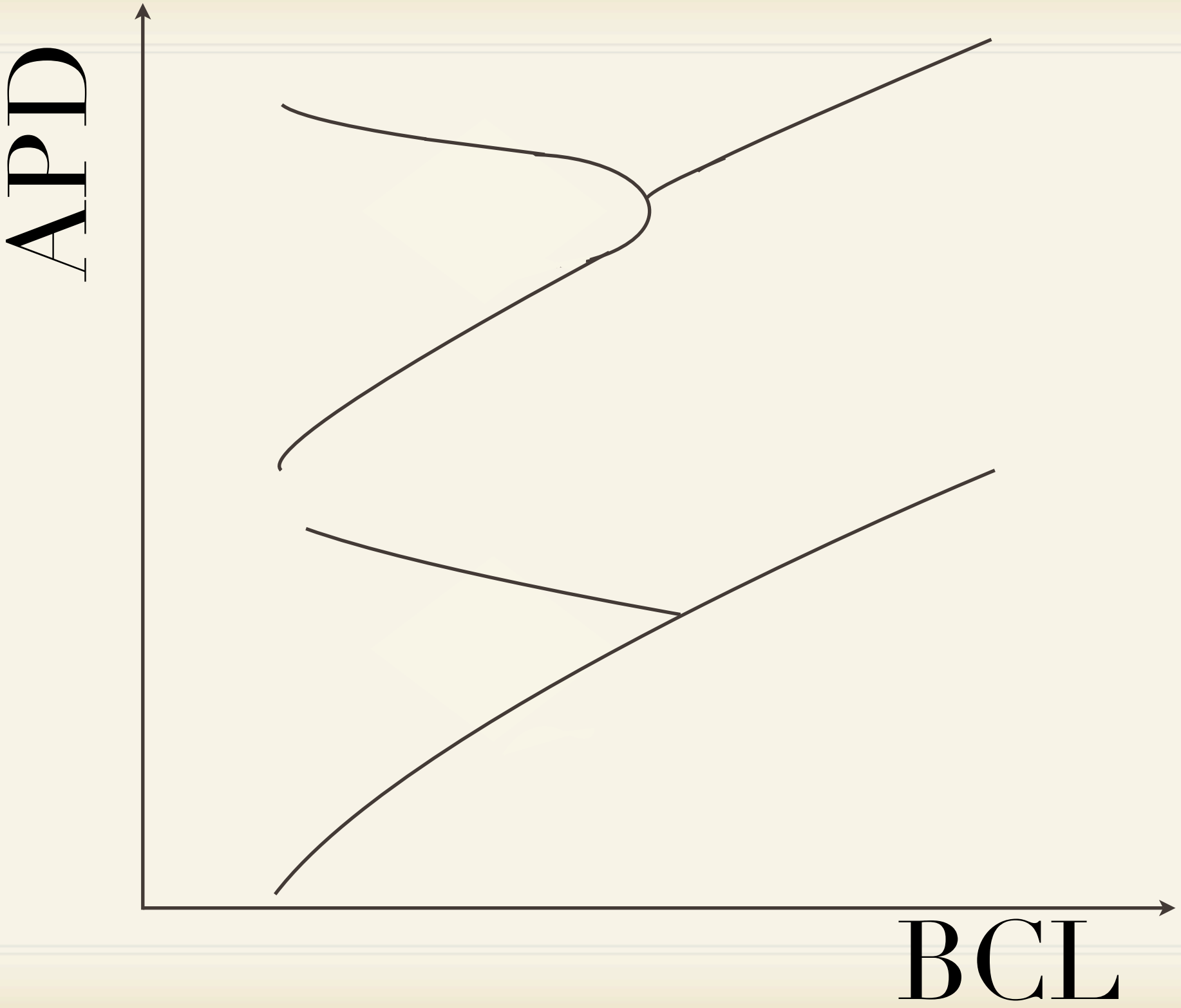


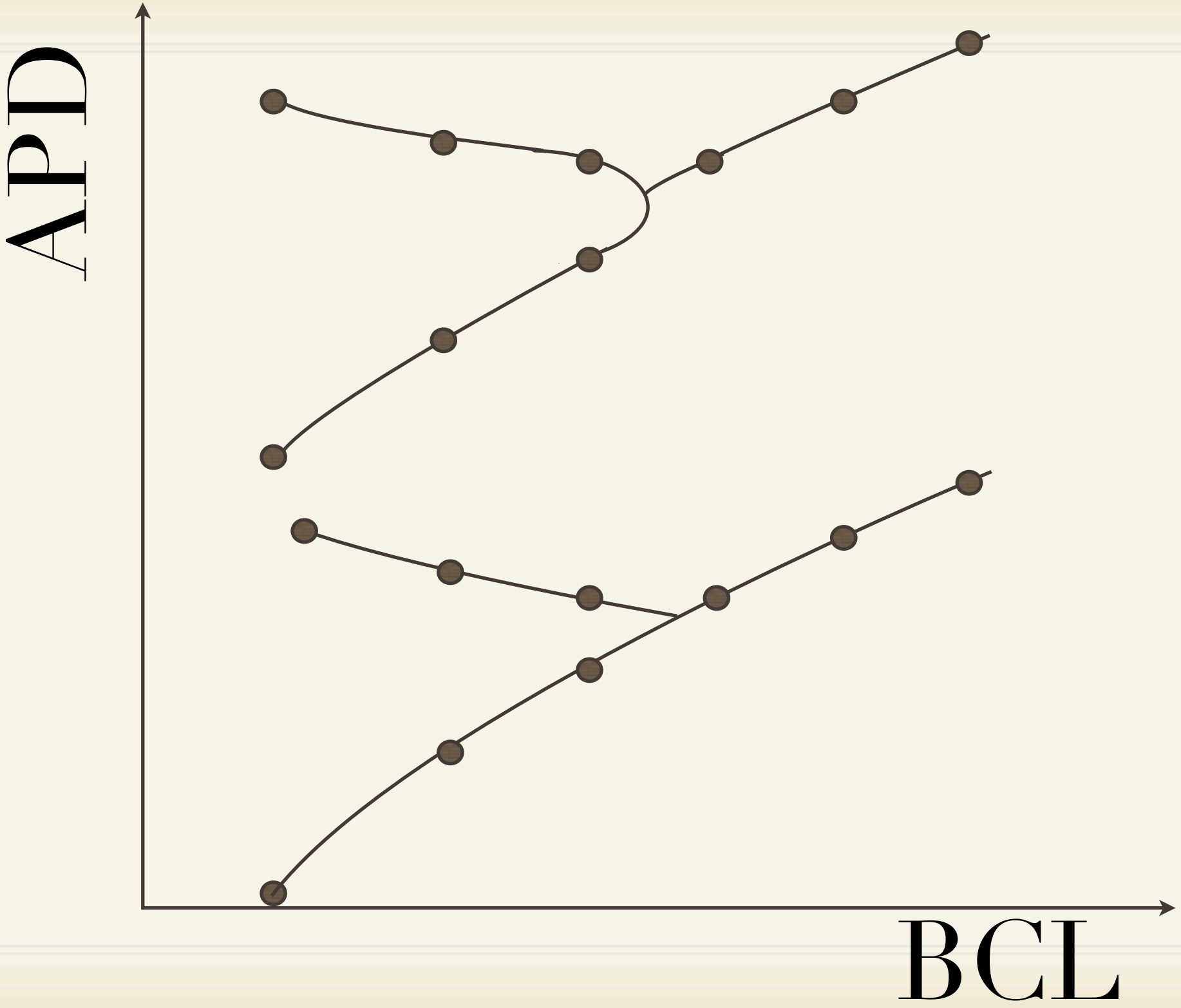
Nolasco and Dahlen (1968)

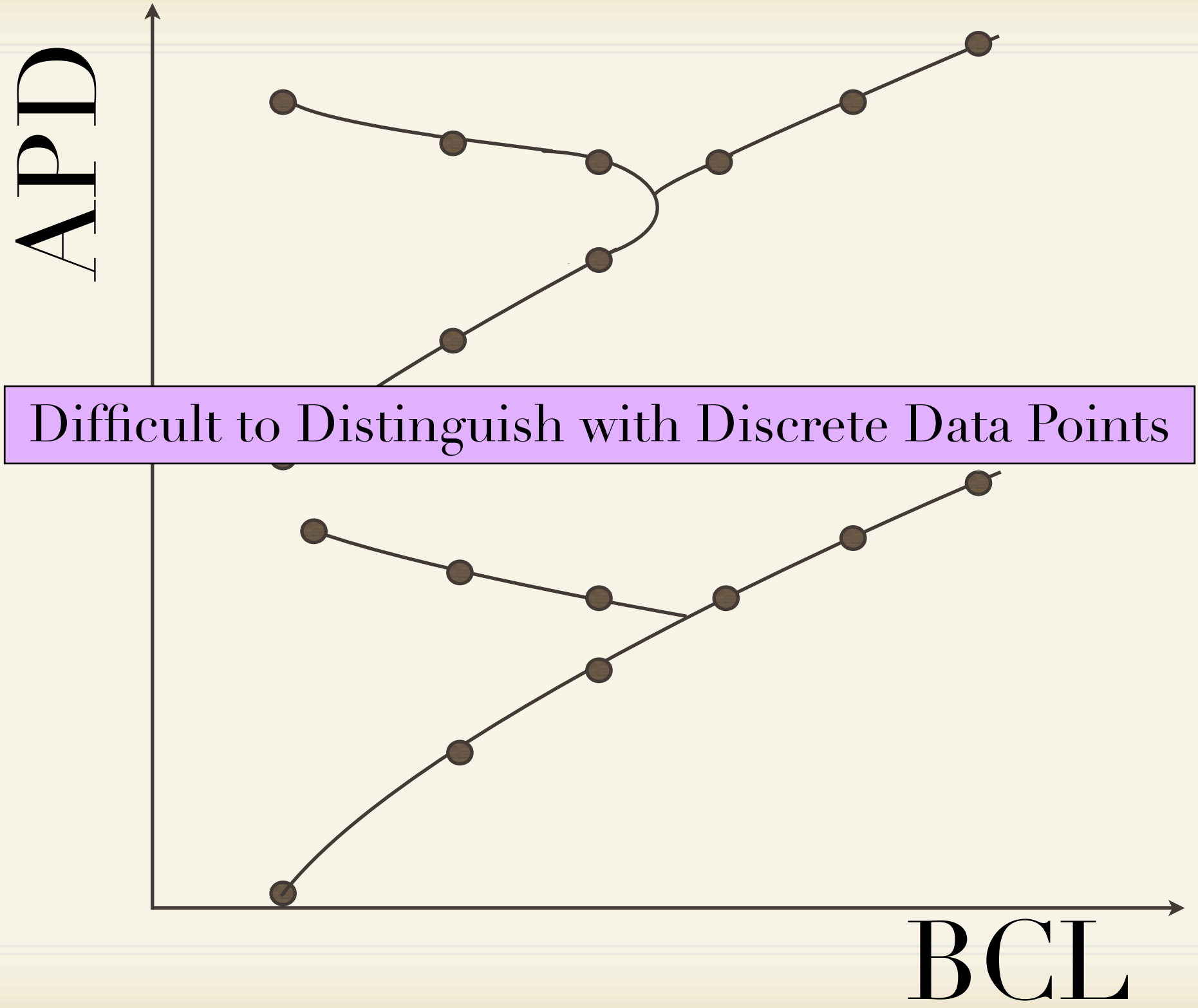
Border-Collision Bifurcation

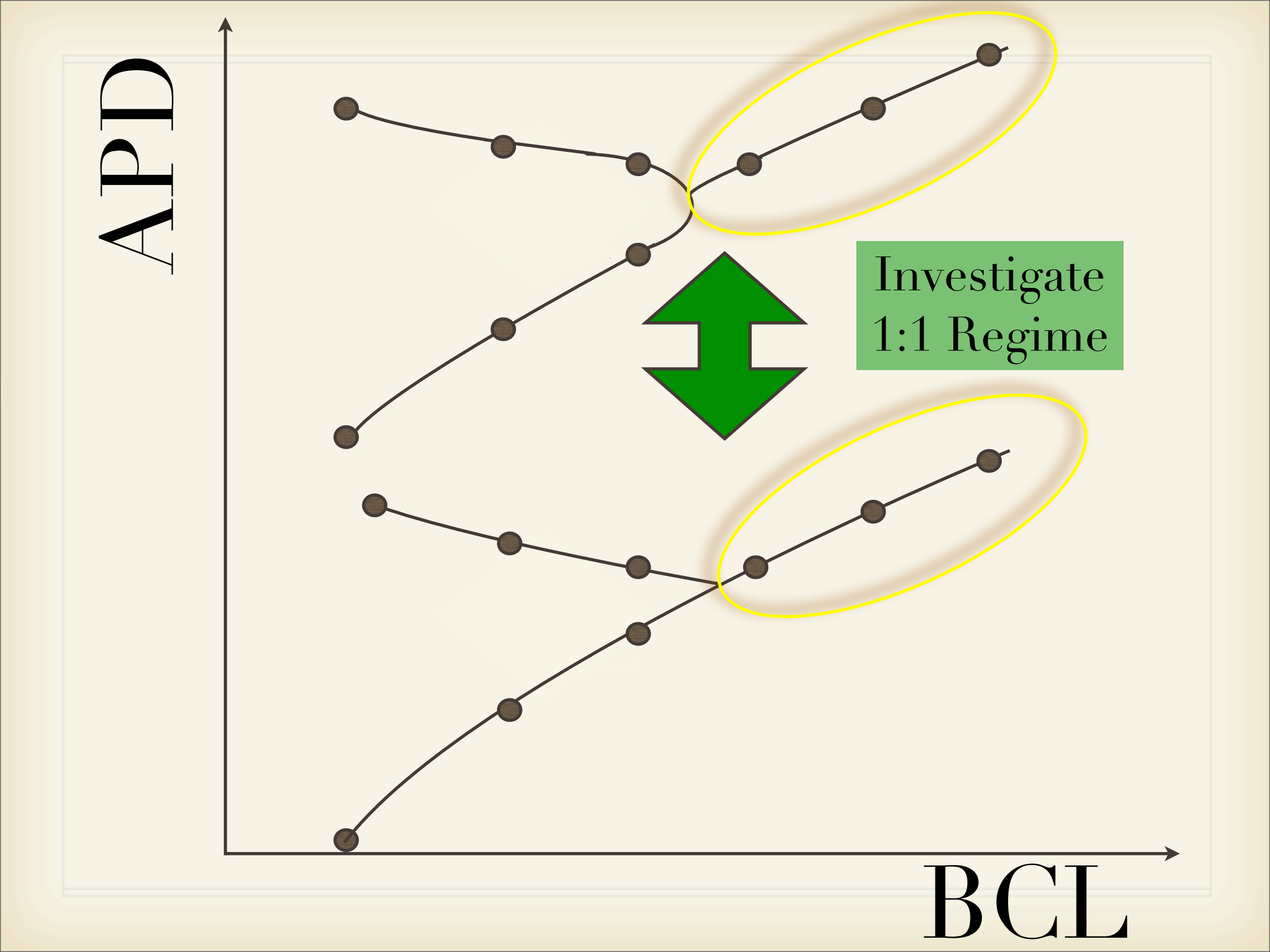


Sun, Amellal, Glass, and Billette (1995)


APD
BCL

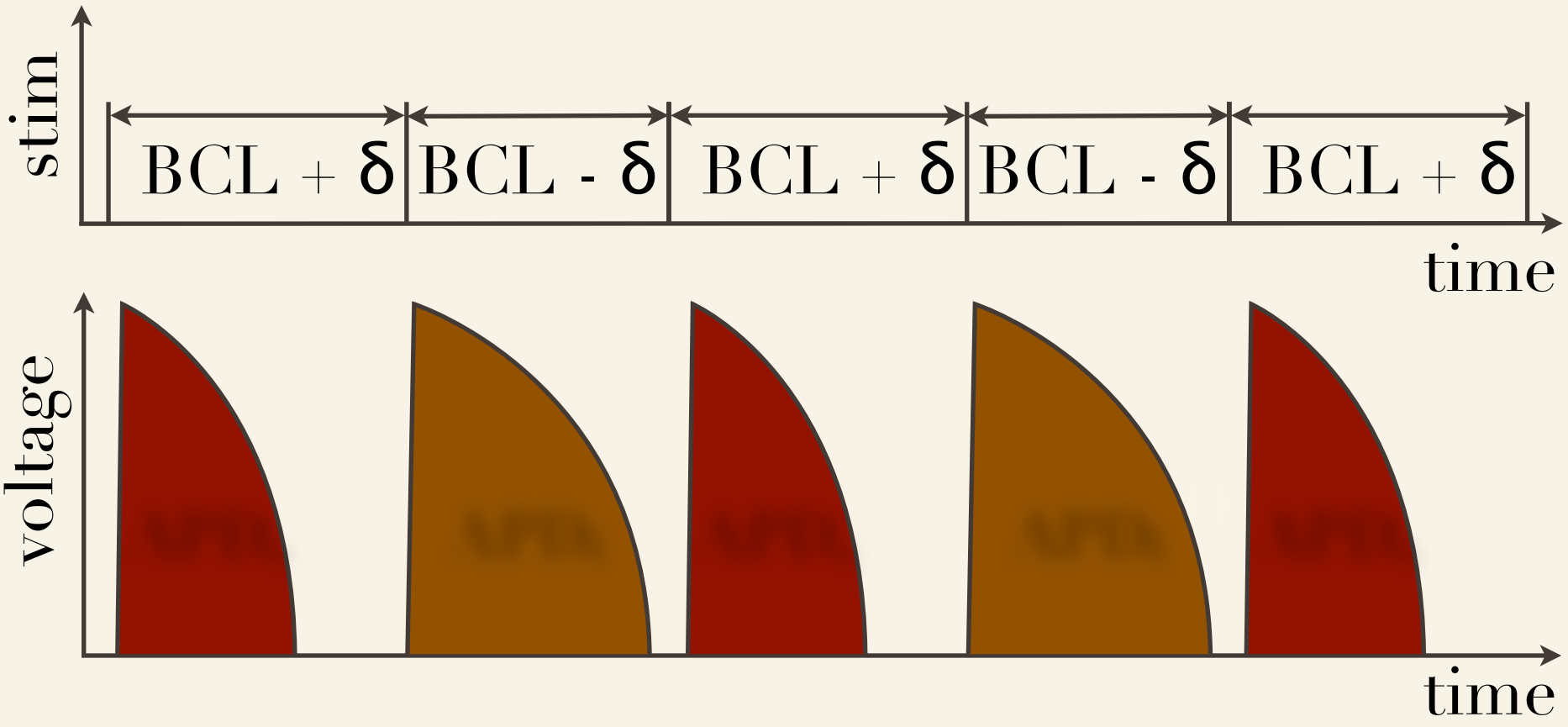

APD
BCL


APD
Difficult to Distinguish with Discrete Data Points
BCL


APD
Investigate
1:1 Regime
BCL

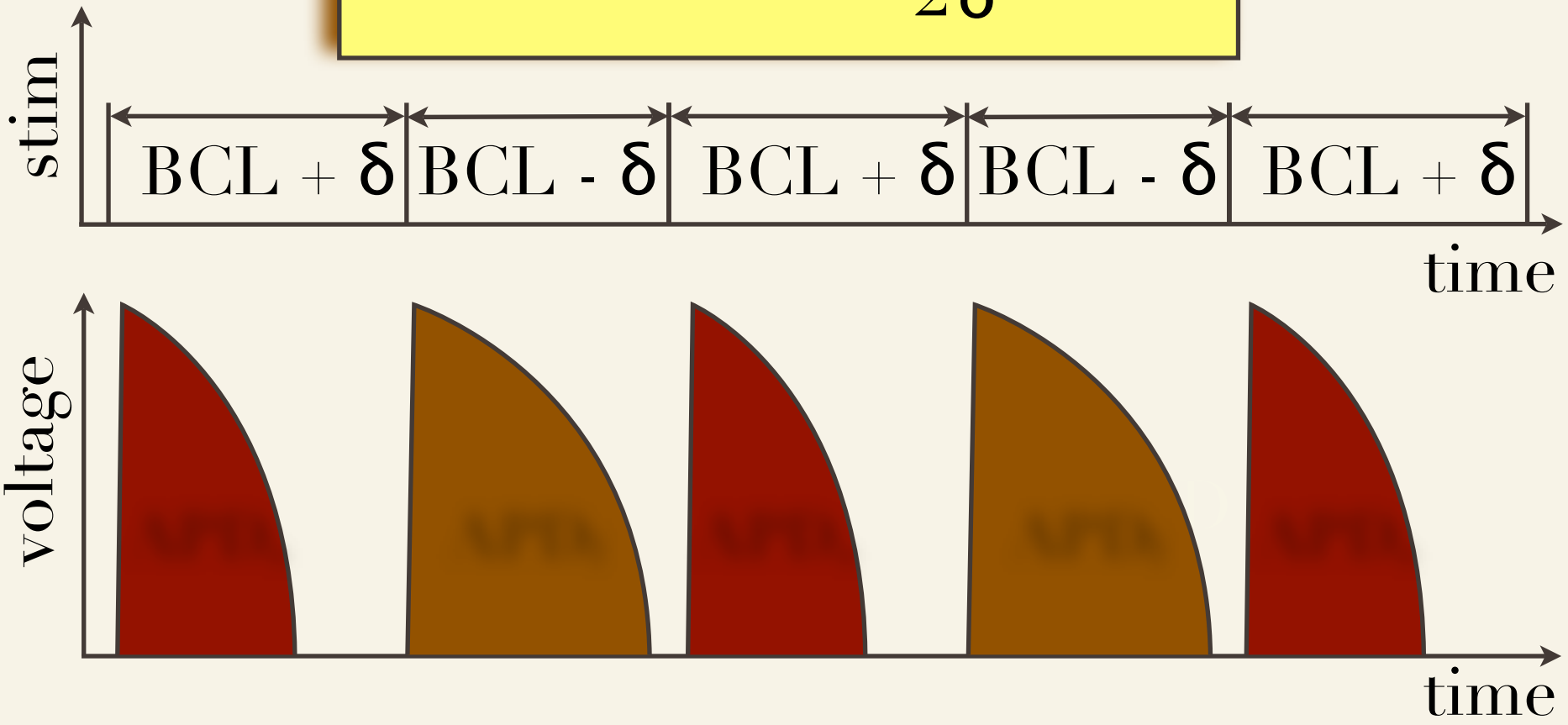
Alternate Pacing

- vary BCL by δ in 1:1 regime



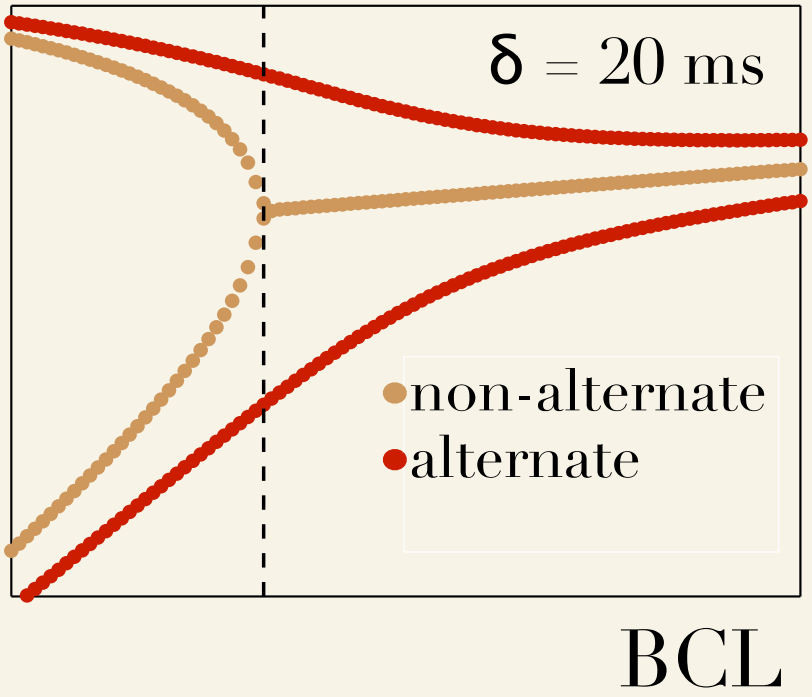
Alternate Pacing

$$\text{Gain} = \frac{APD_l - APD_s}{2\delta}$$

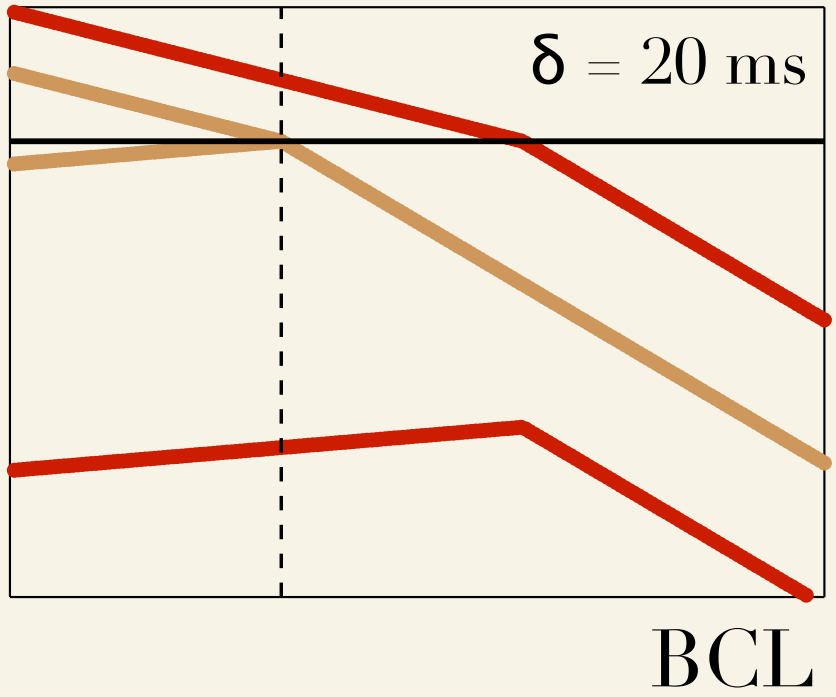


Alternate Pacing Simulations

Smooth

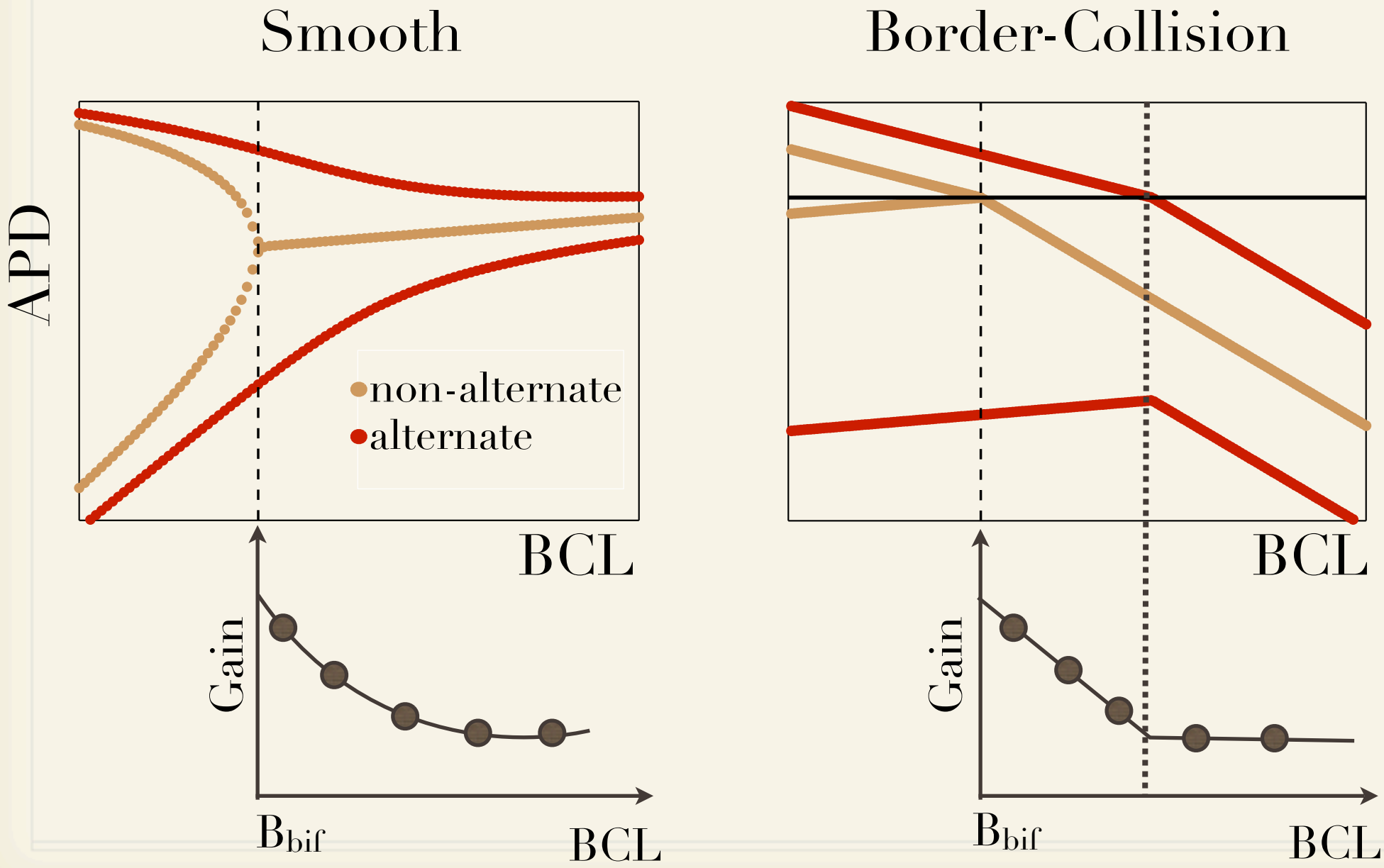


Border-Collision



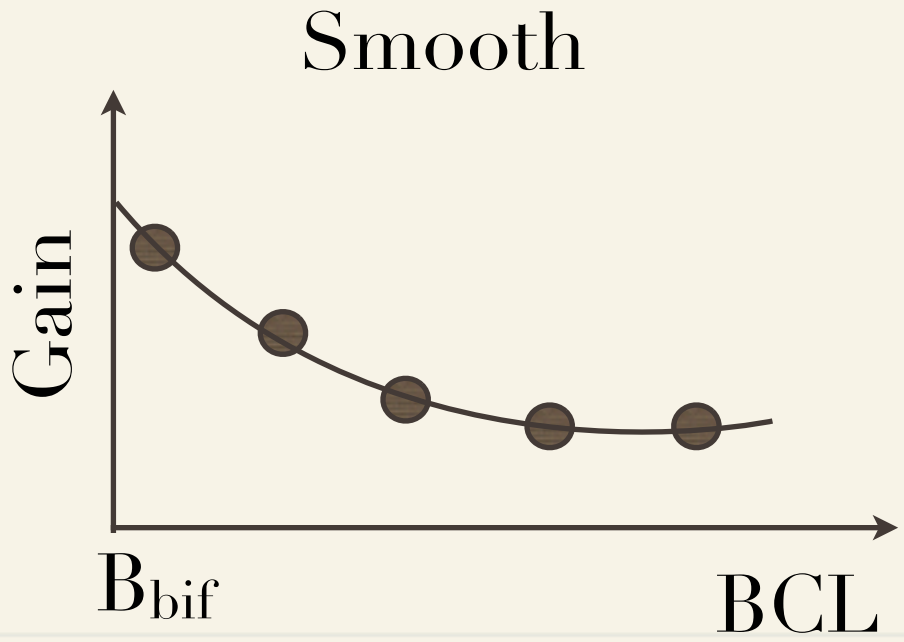
$$\text{Gain} = \frac{APD_l - APD_s}{2\delta}$$

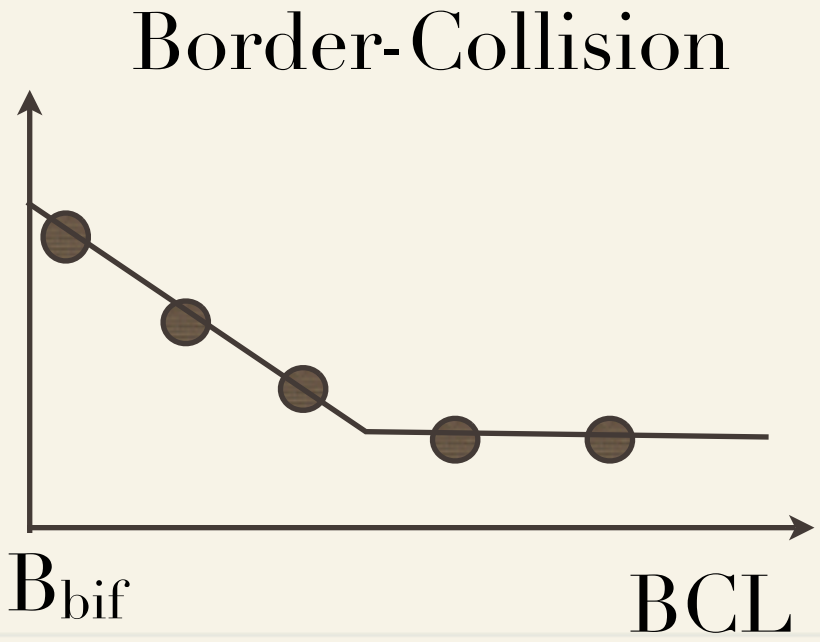
Alternate Pacing Simulations



Alternate Pacing Trends

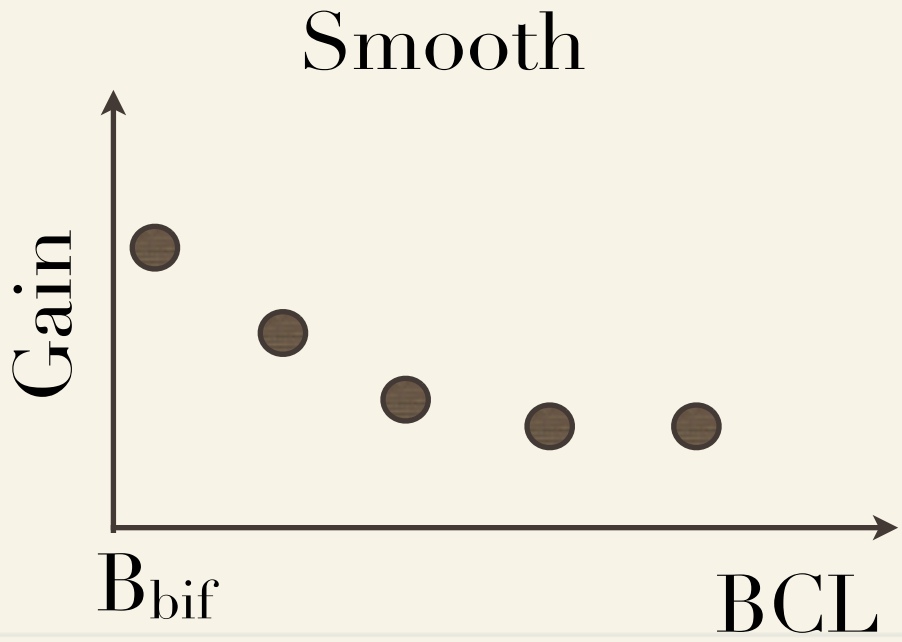
Difficult to Distinguish with Discrete Data Points

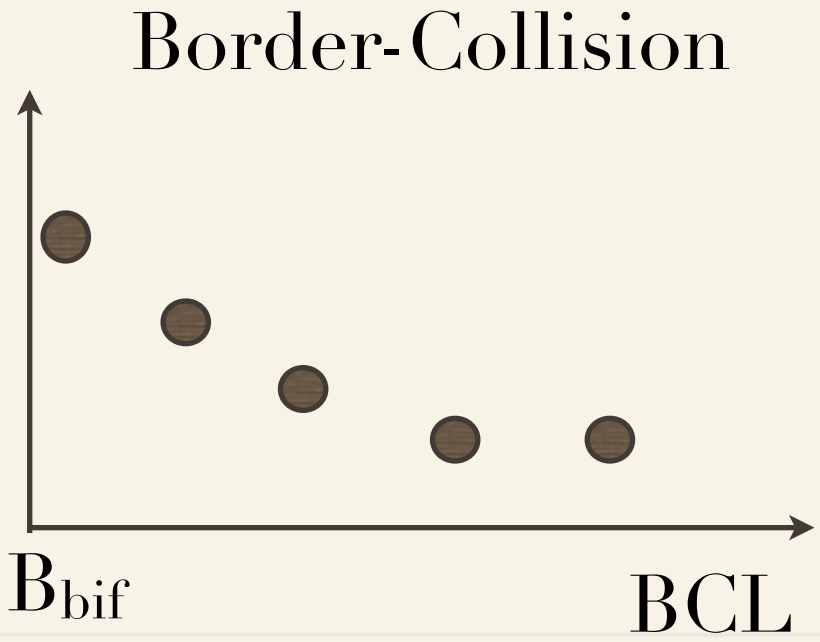




Alternate Pacing Trends

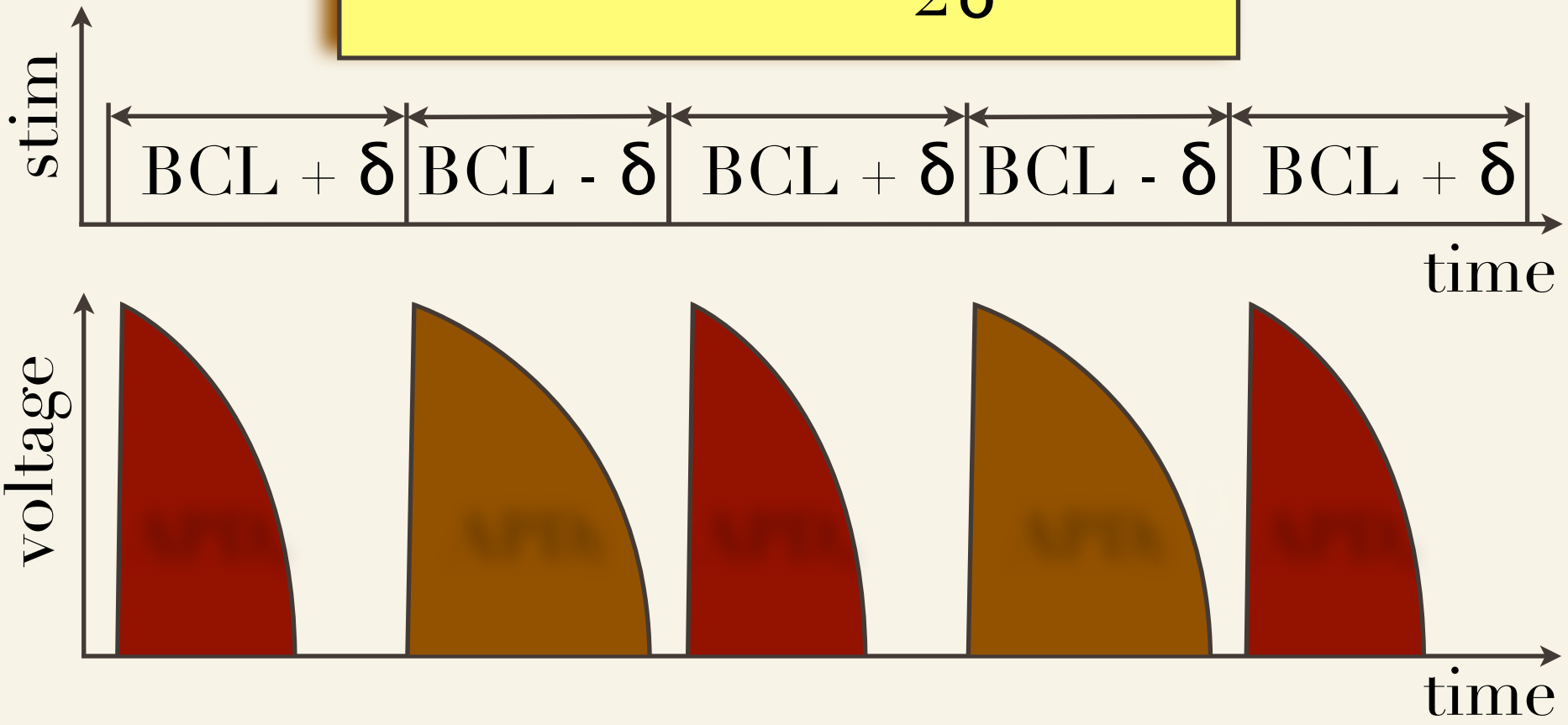
Difficult to Distinguish with Discrete Data Points



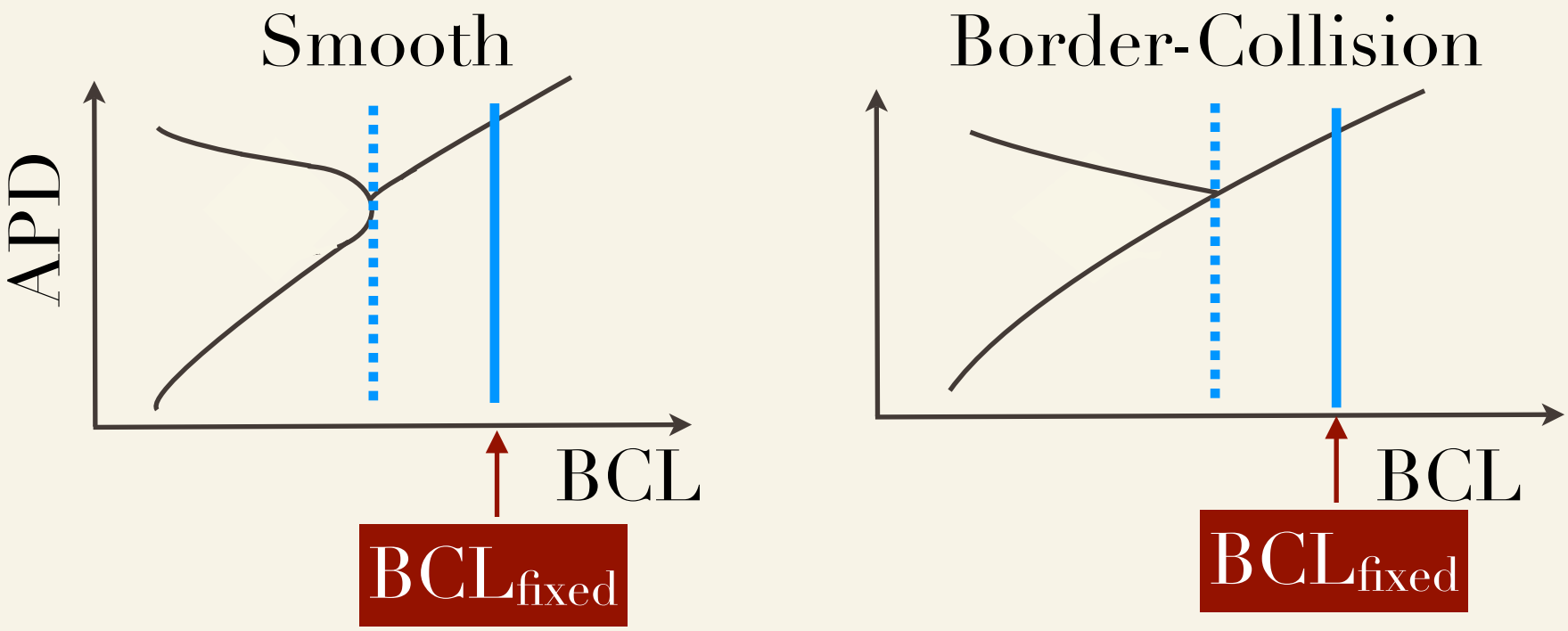


Alternate Pacing

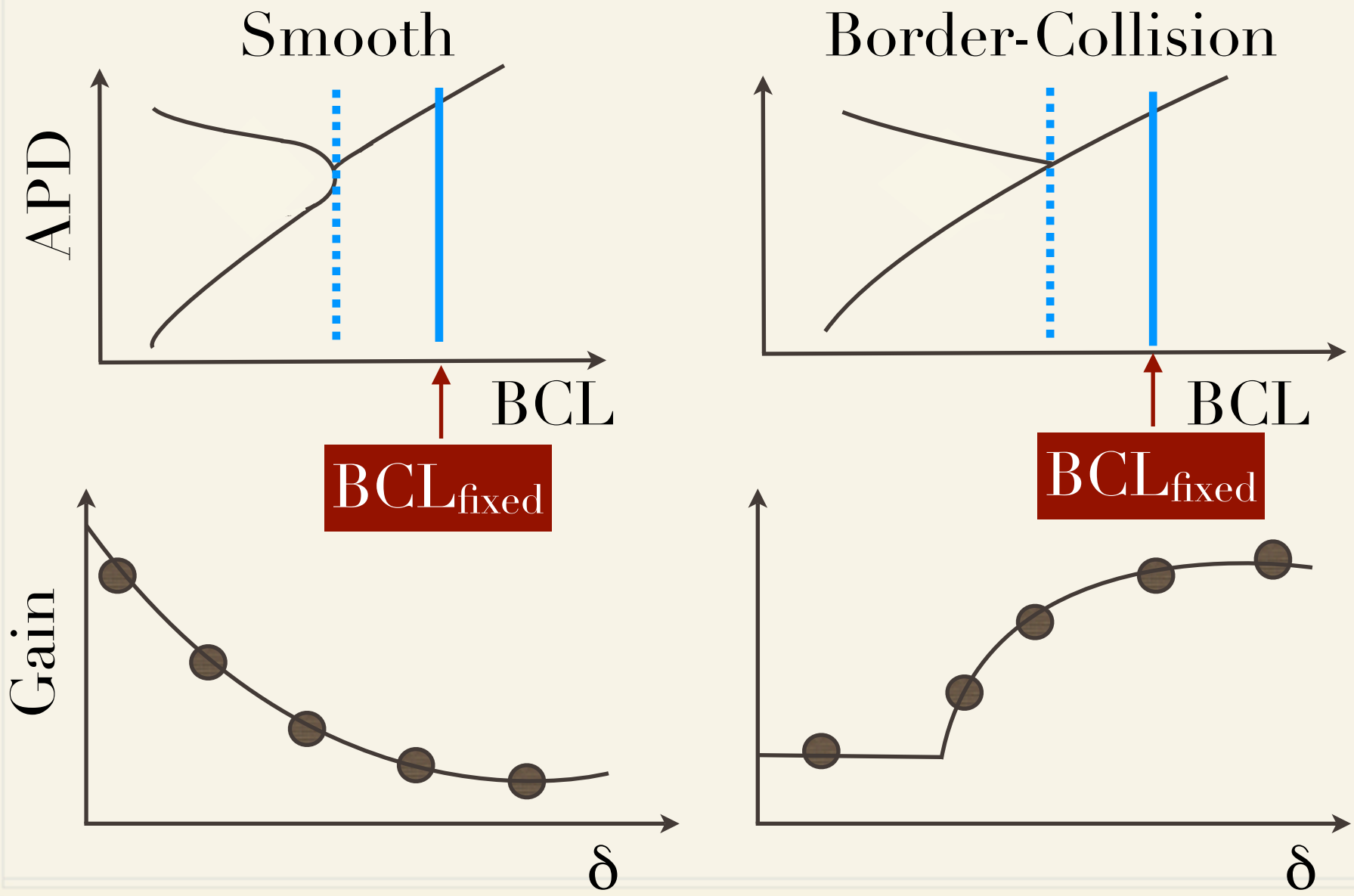
$$\text{Gain} = \frac{APD_l - APD_s}{2\delta}$$



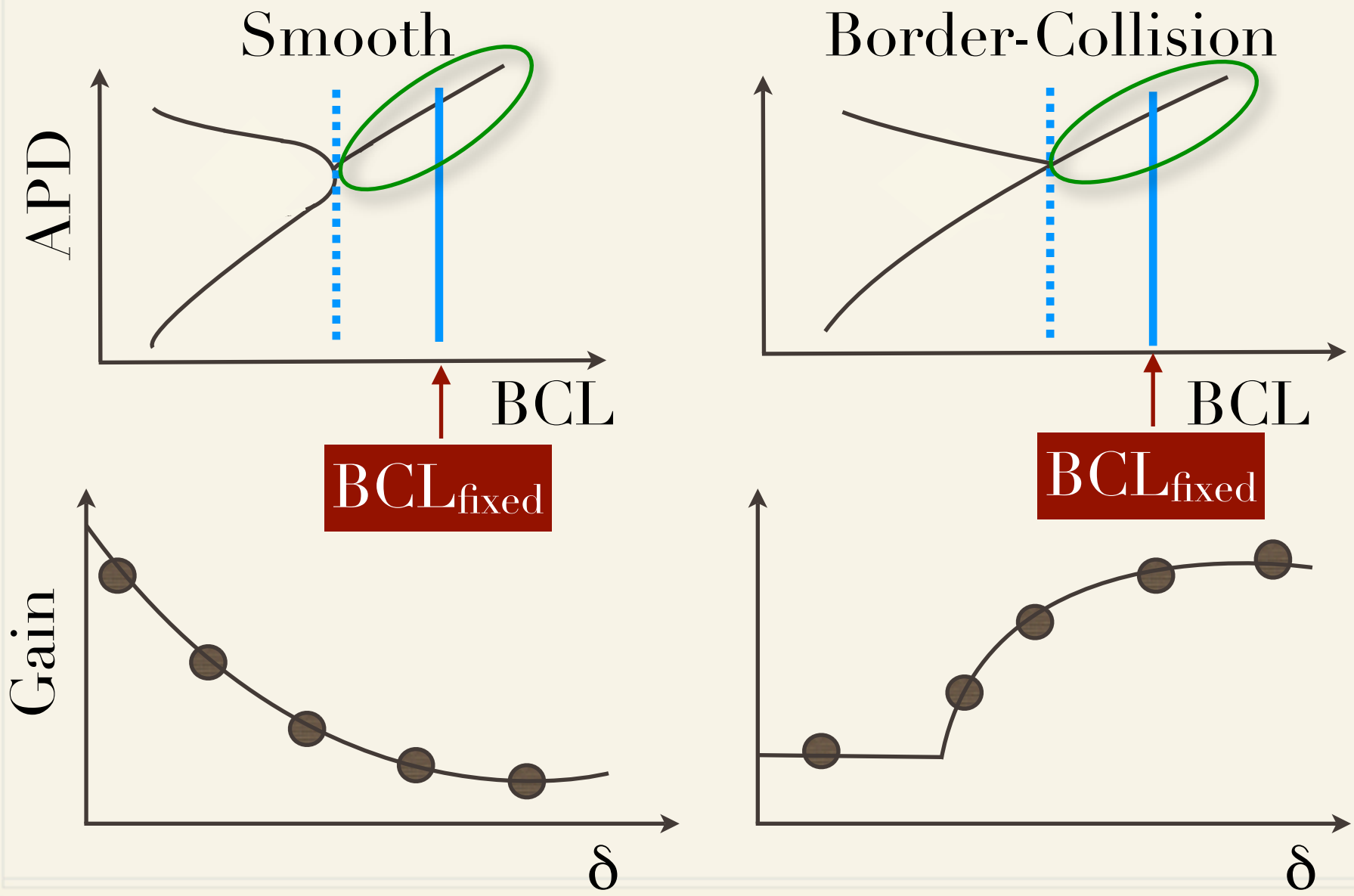
Vary δ Size



Alternate Pacing Trends

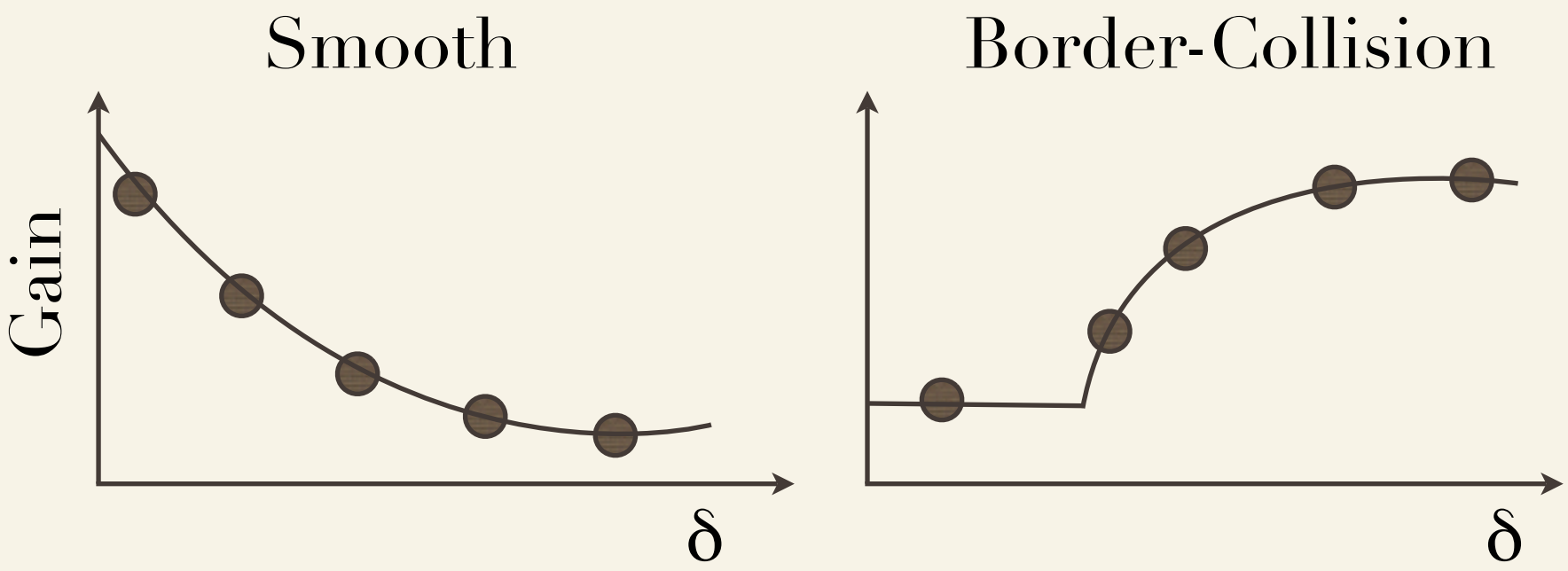


Alternate Pacing Trends

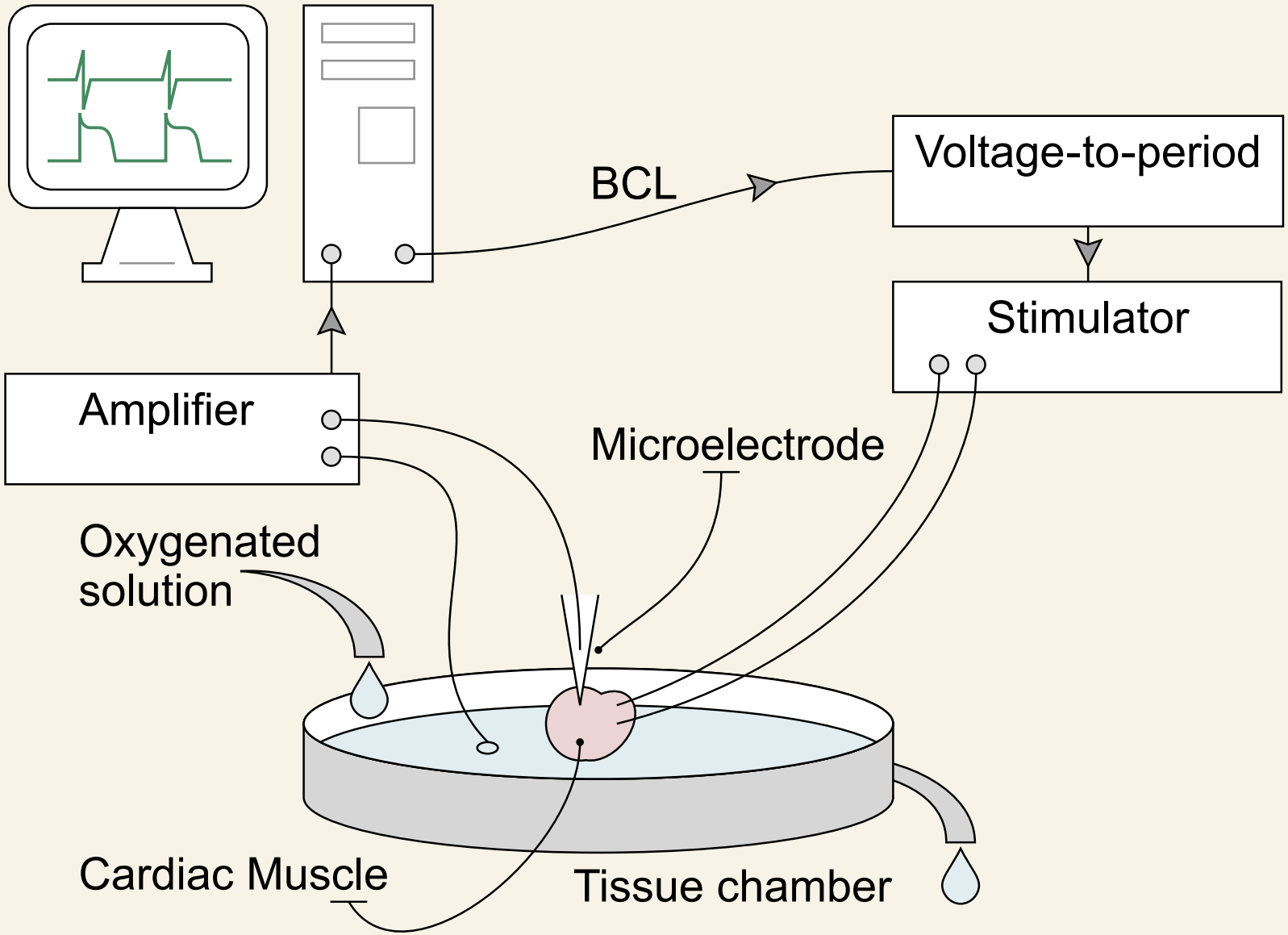


Alternate Pacing Trends

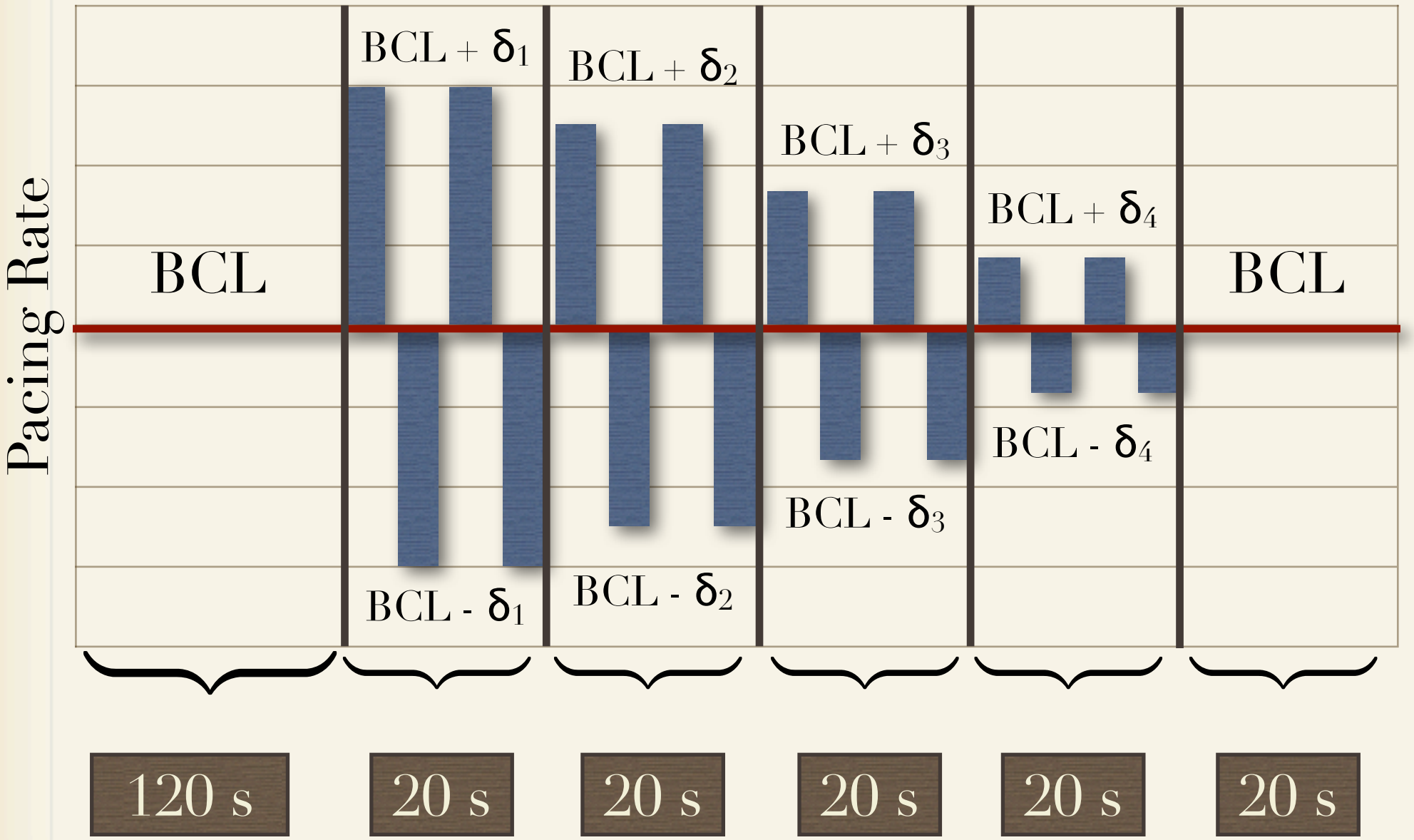
Different Trends with Discrete Data Points



Experimental Setup

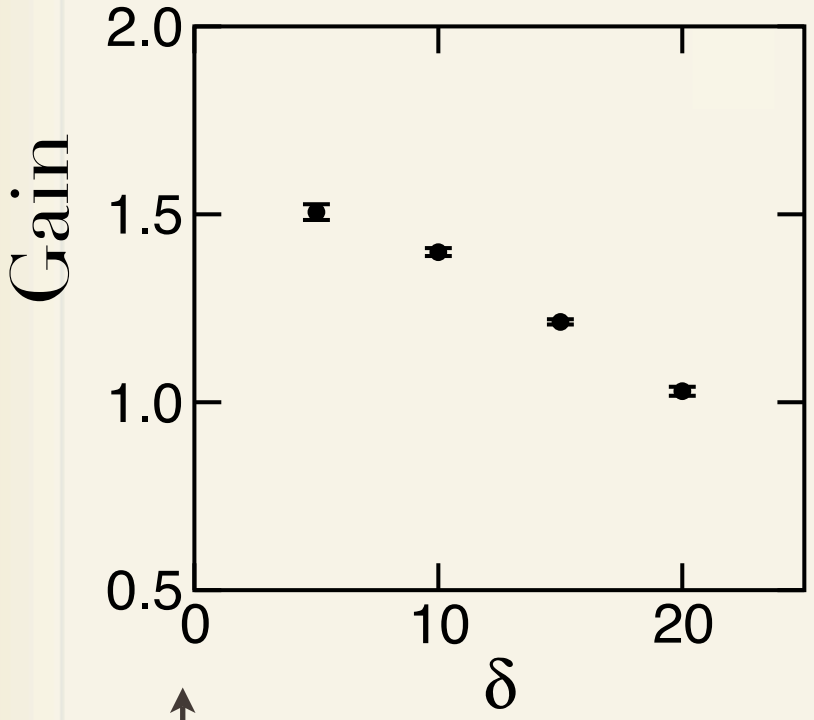


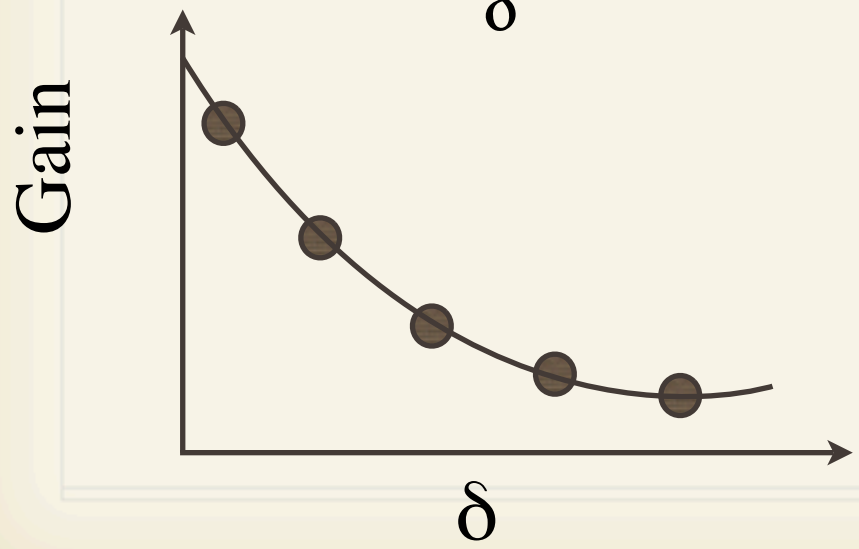
Alternate Pacing Protocol



Experimental Trends in One Frog

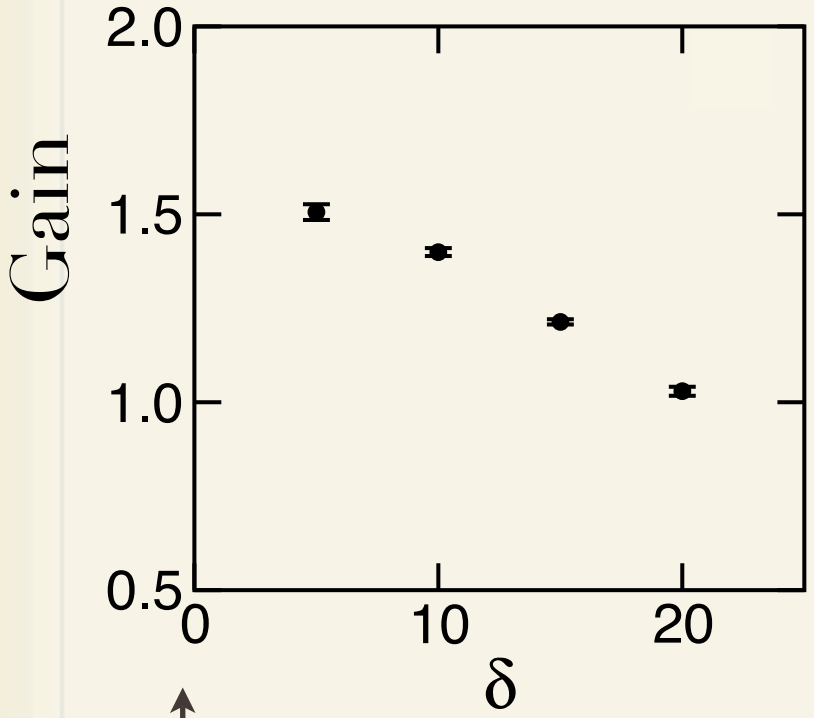
Smooth

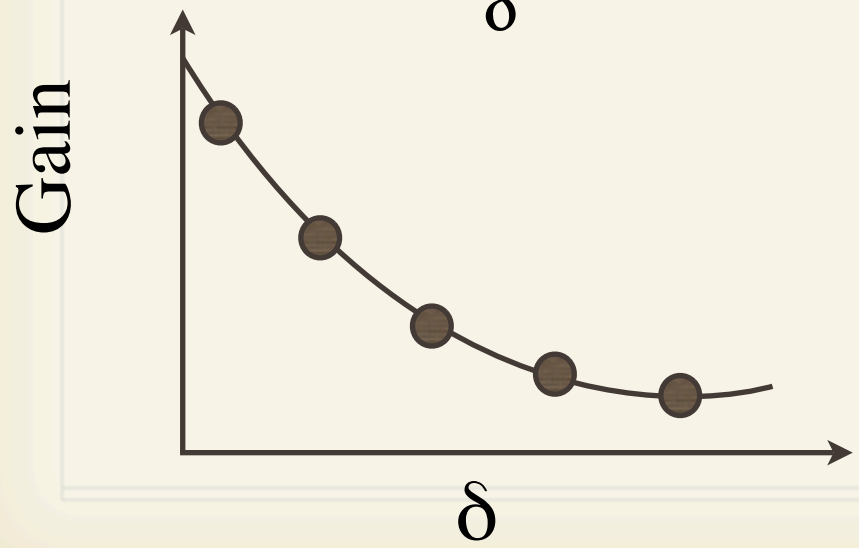




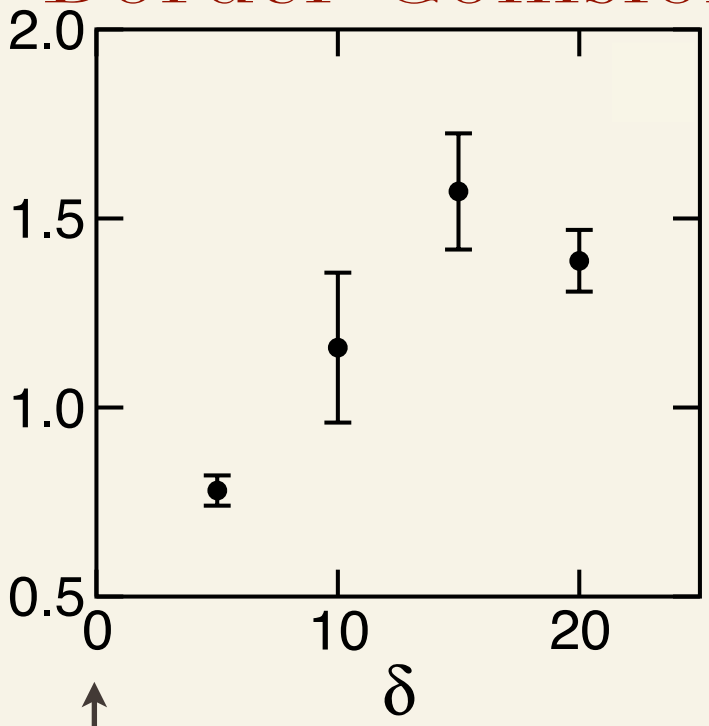
Experimental Trends in Two Frogs

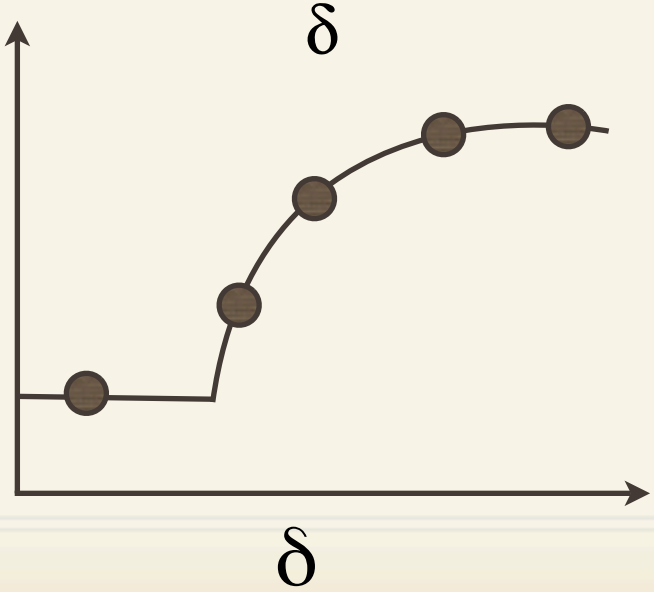
Smooth





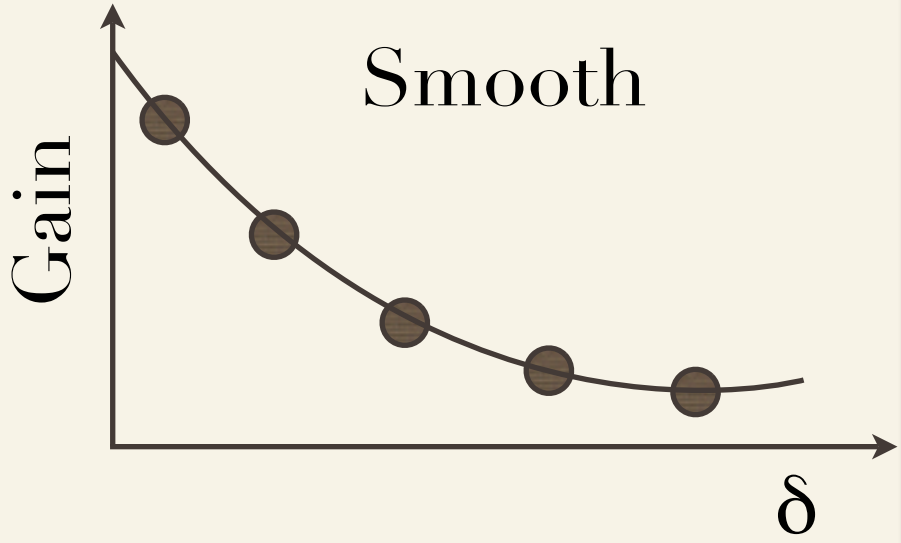
Border-Collision

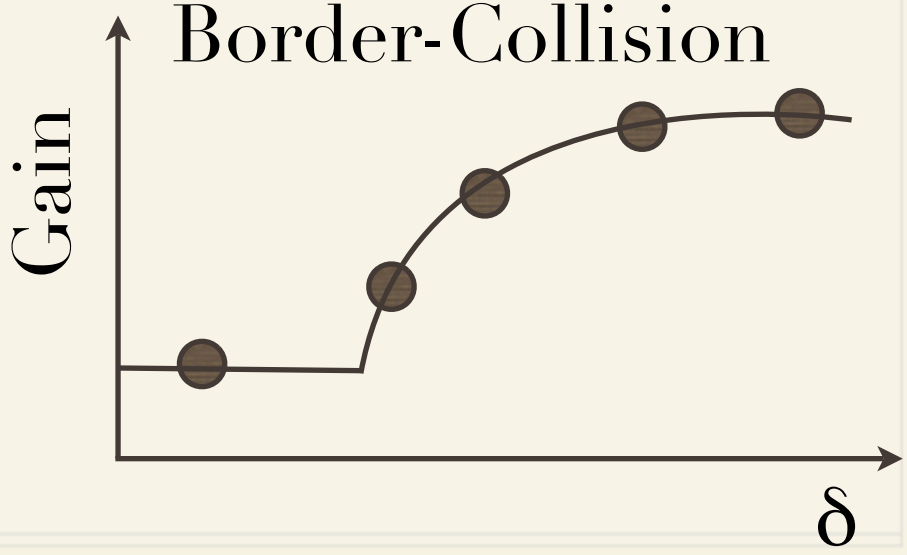




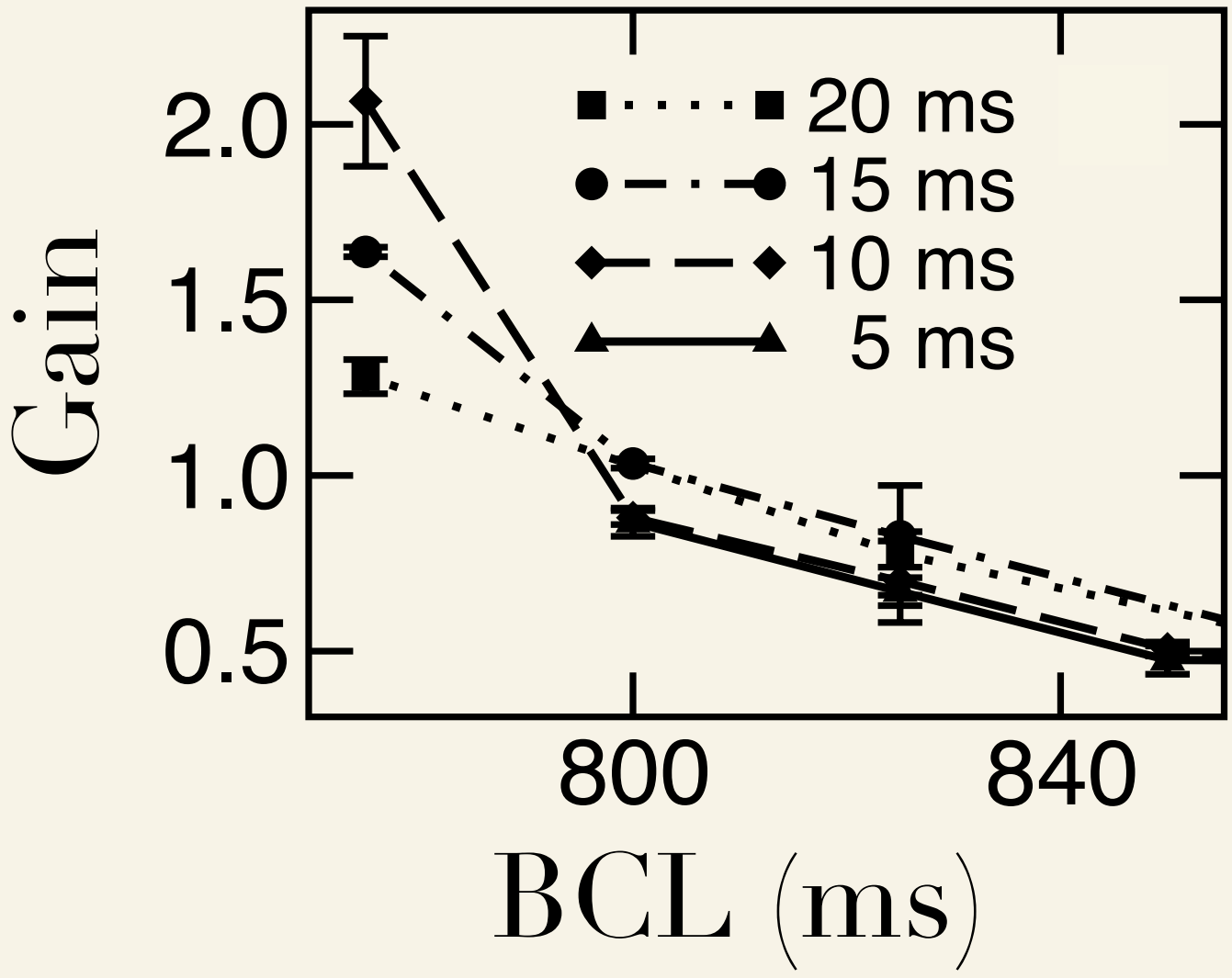
Experiment Trends

# of trials	Behavior	# of frogs
4	Smooth	3
4	Border-Collision	2
3	Flat	3
1	Combo	1

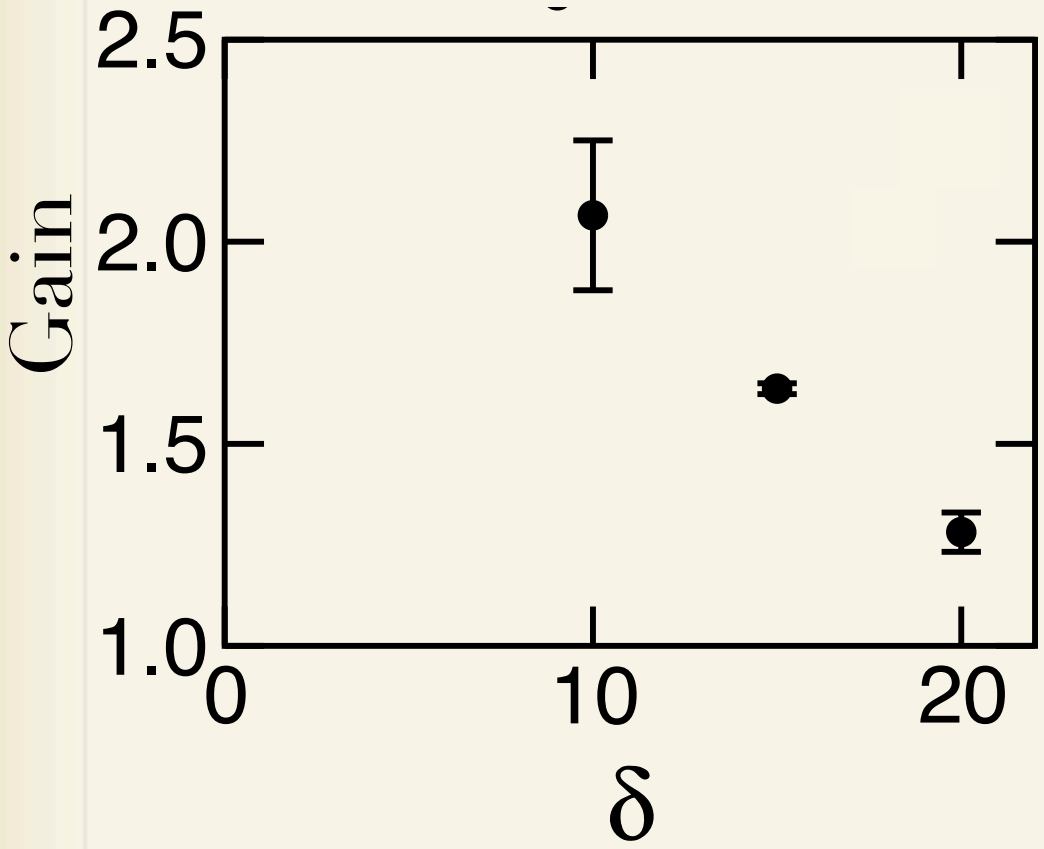


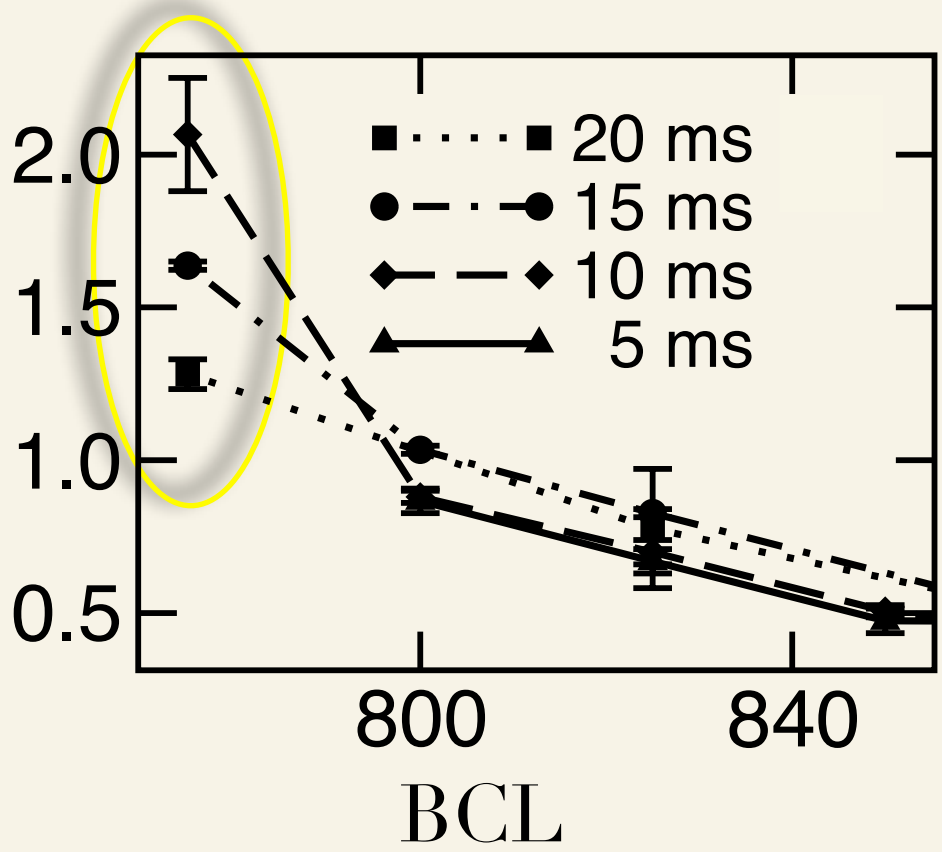


Combination



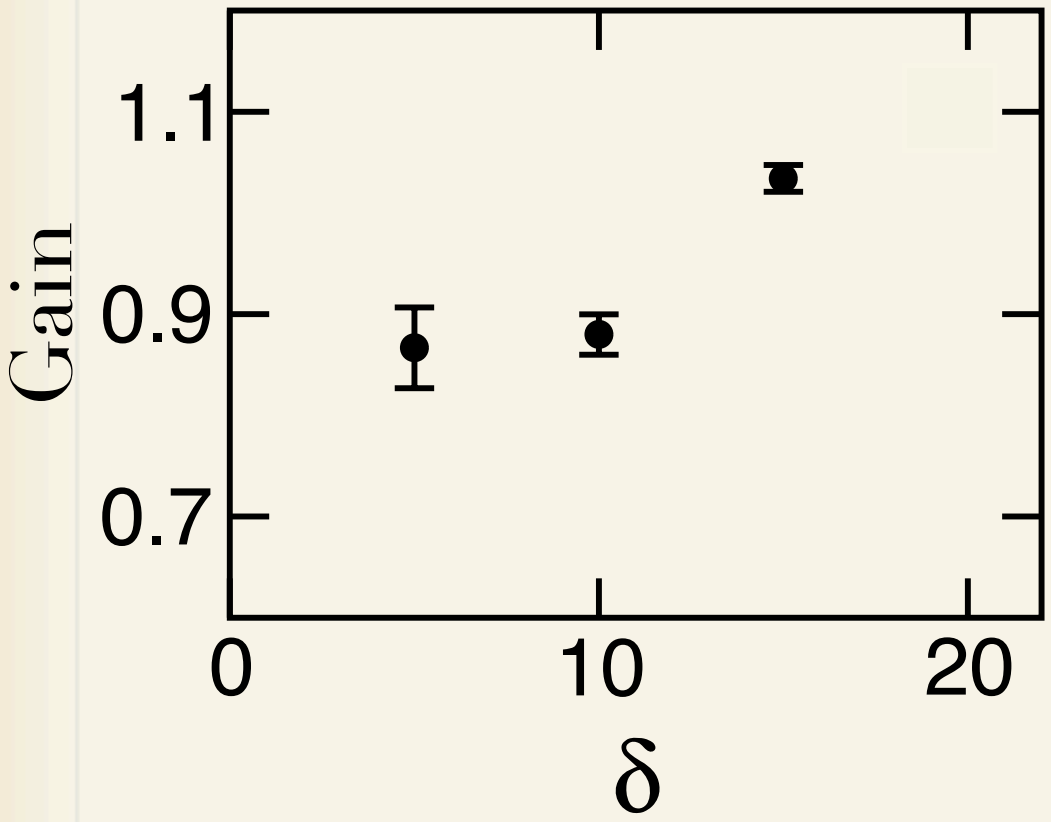
Single Trial in One Frog

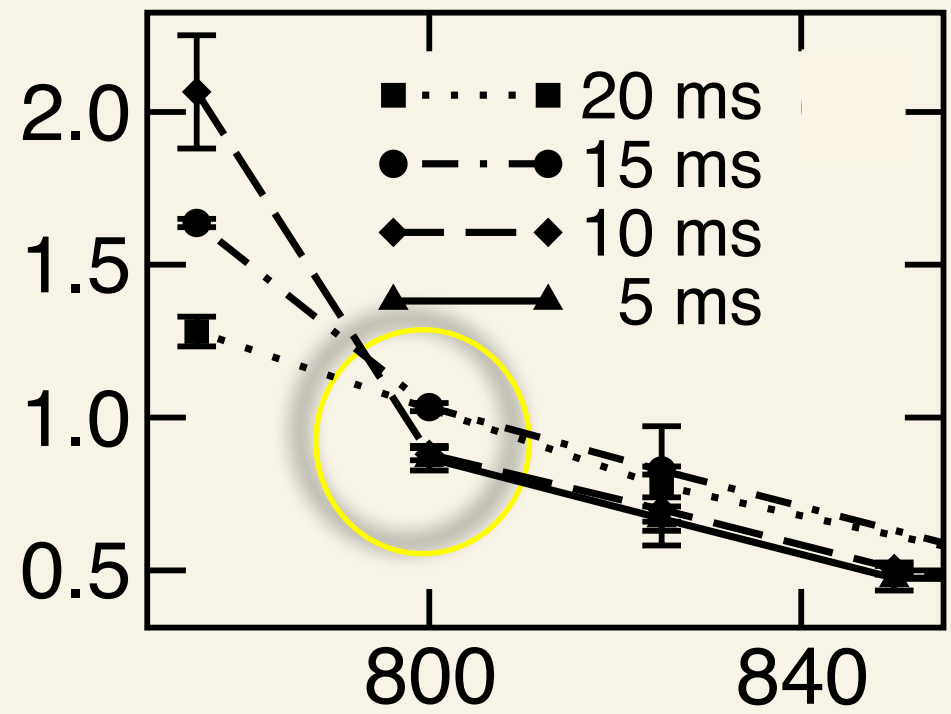




Smooth Trend Close to Bifurcation

Single Trial in One Frog





Border-Collision Trend Far from Bifurcation

Unfold Border-Collision Bifurcation

$$APD_{n+1} = f(D_n)$$

- where D_n=BCL – APD_n

Unfold Border-Collision Bifurcation

$$APD_{n+1} = f(D_n)$$

❇ where D_n=BCL – APD_n

$$APD_{n+1} = A_0 + \alpha\,(D_n - D_{th}) + \beta\,|(D_n - D_{th})|$$

Unfold Border-Collision Bifurcation

$$APD_{n+1} = f(D_n)$$

❇ where D_n=BCL – APD_n

$$APD_{n+1} = A_0 + \alpha\,(D_n - D_{th}) + \beta\,|(D_n - D_{th})|$$

Recall BCL is the bifurcation parameter

Unfold Border-Collision Bifurcation

$$APD_{n+1} = A_0 + \alpha(D_n - D_{th}) + \beta\,|(D_n - D_{th})|$$

- parameters

Unfold Border-Collision Bifurcation

$$APD_{n+1} = A_0 + \alpha(D_n - D_{th}) + \beta|(D_n - D_{th})|$$

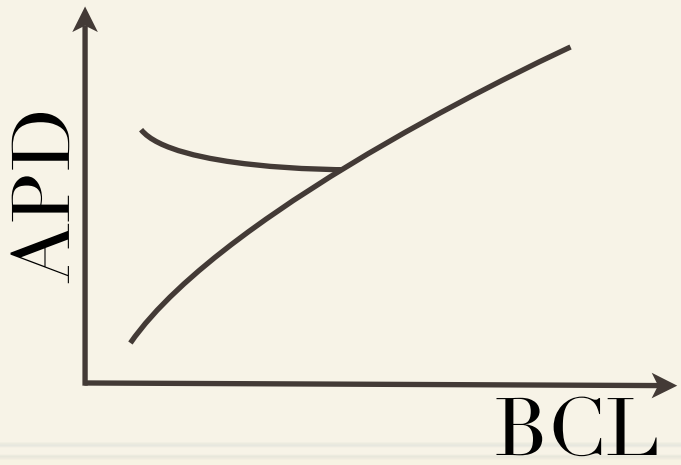
- parameters

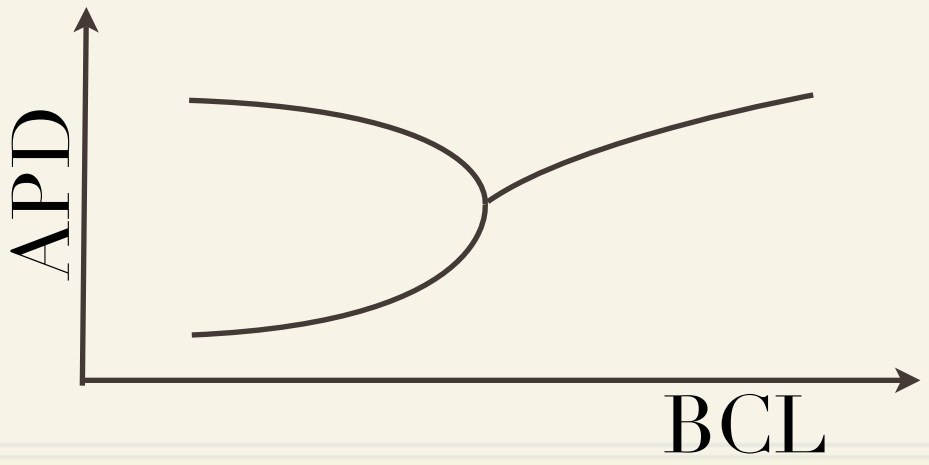
Unfold Border-Collision Bifurcation

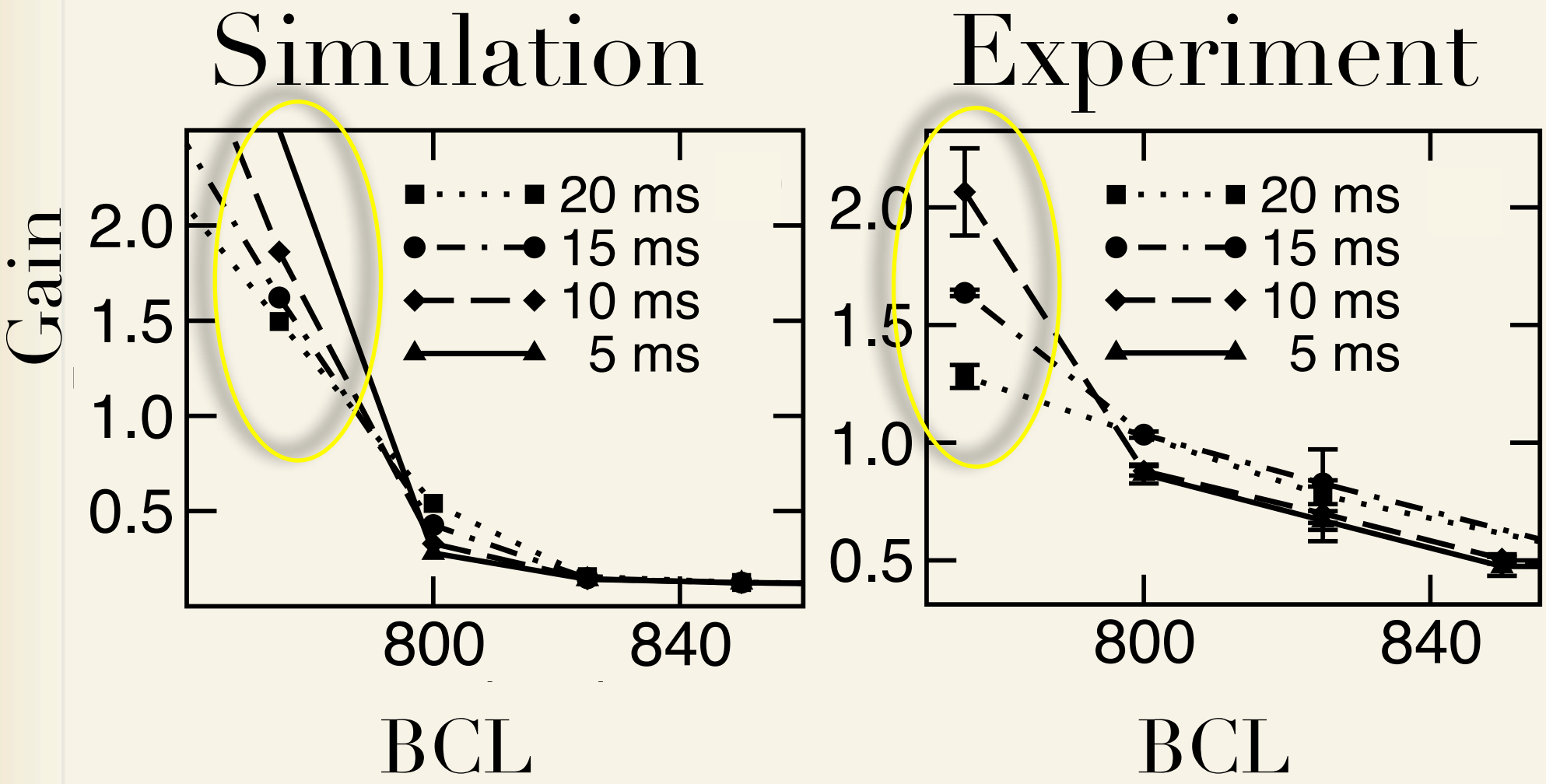
$$APD_{n+1} = A_0 + \alpha(D_n - D_{th}) + \beta|(D_n - D_{th})|$$

- parameters

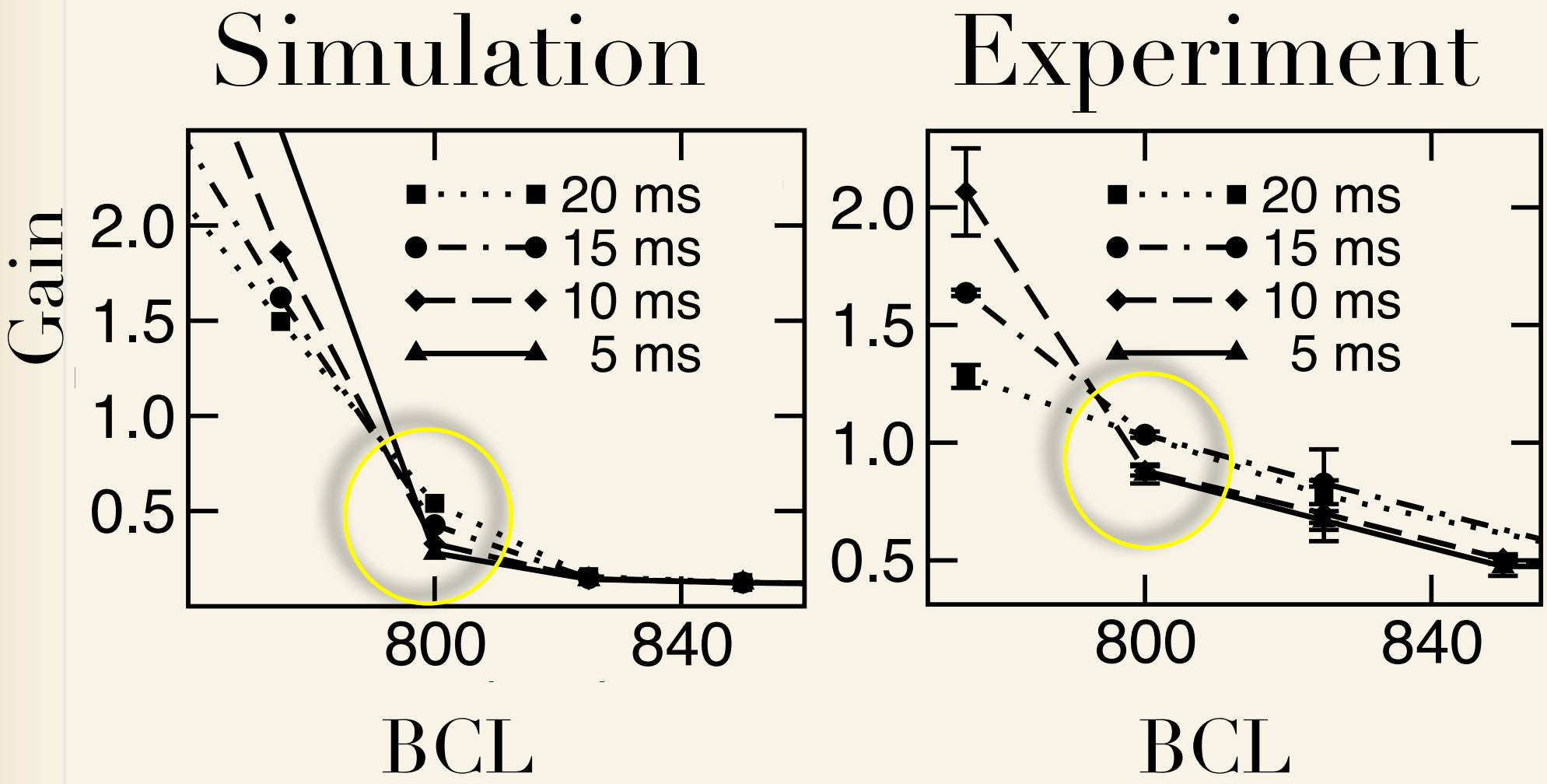
$$|(D_n - D_{th})| \Rightarrow \sqrt{(D_n - D_{th})^2 + D_s^2}$$







Smooth Trend Close to Bifurcation



Border-Collision Trend Far from Bifurcation

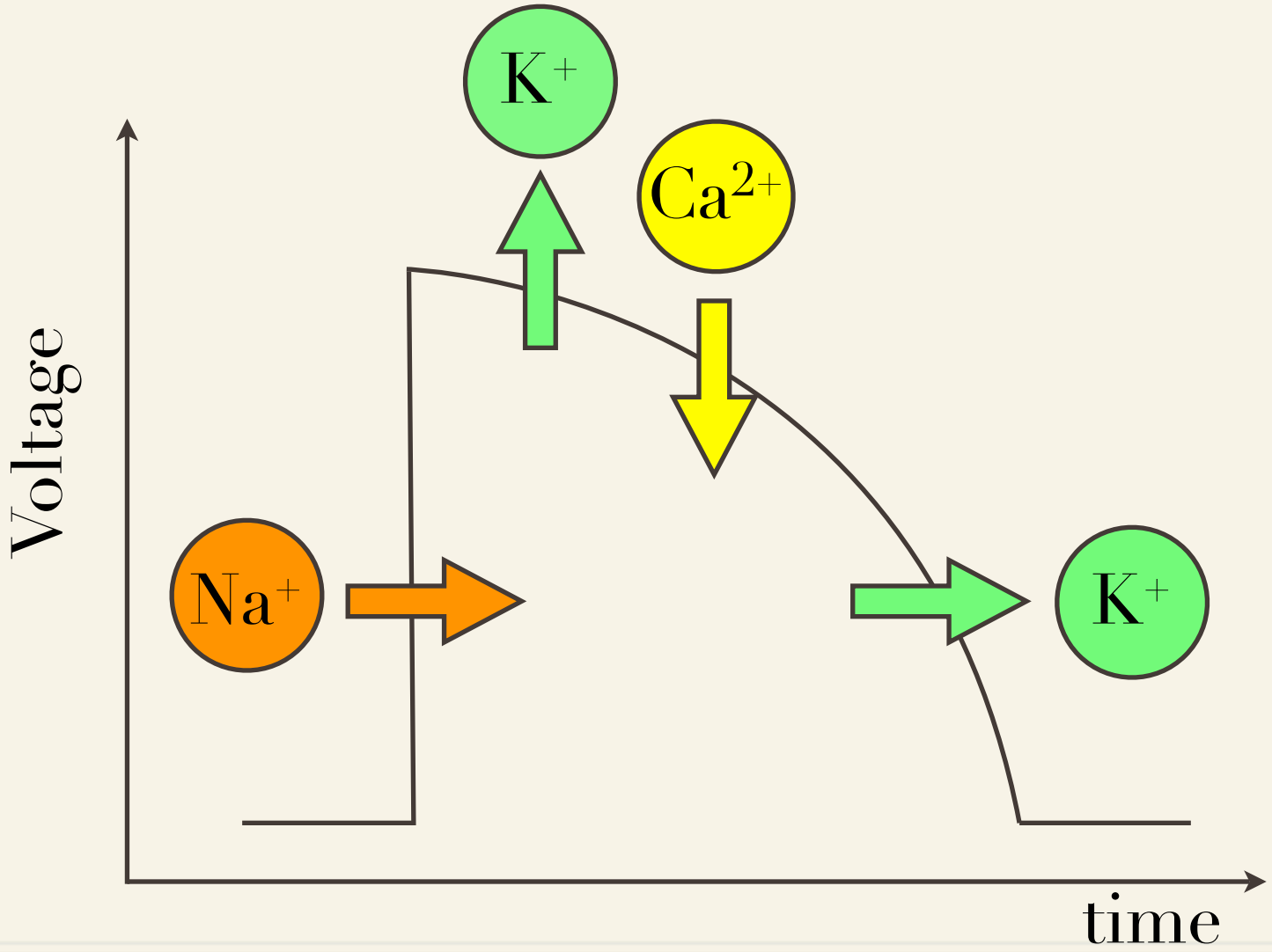
Conclusions

- Bifurcation to Alternans exhibits BOTH smooth and border-collision-like features
- Far from bifurcation $\longrightarrow$ Insensitive to δ
- Close to bifurcation $\longrightarrow$ Sensitive to δ
- Unfolded Border-Collision Bifurcation

So What...

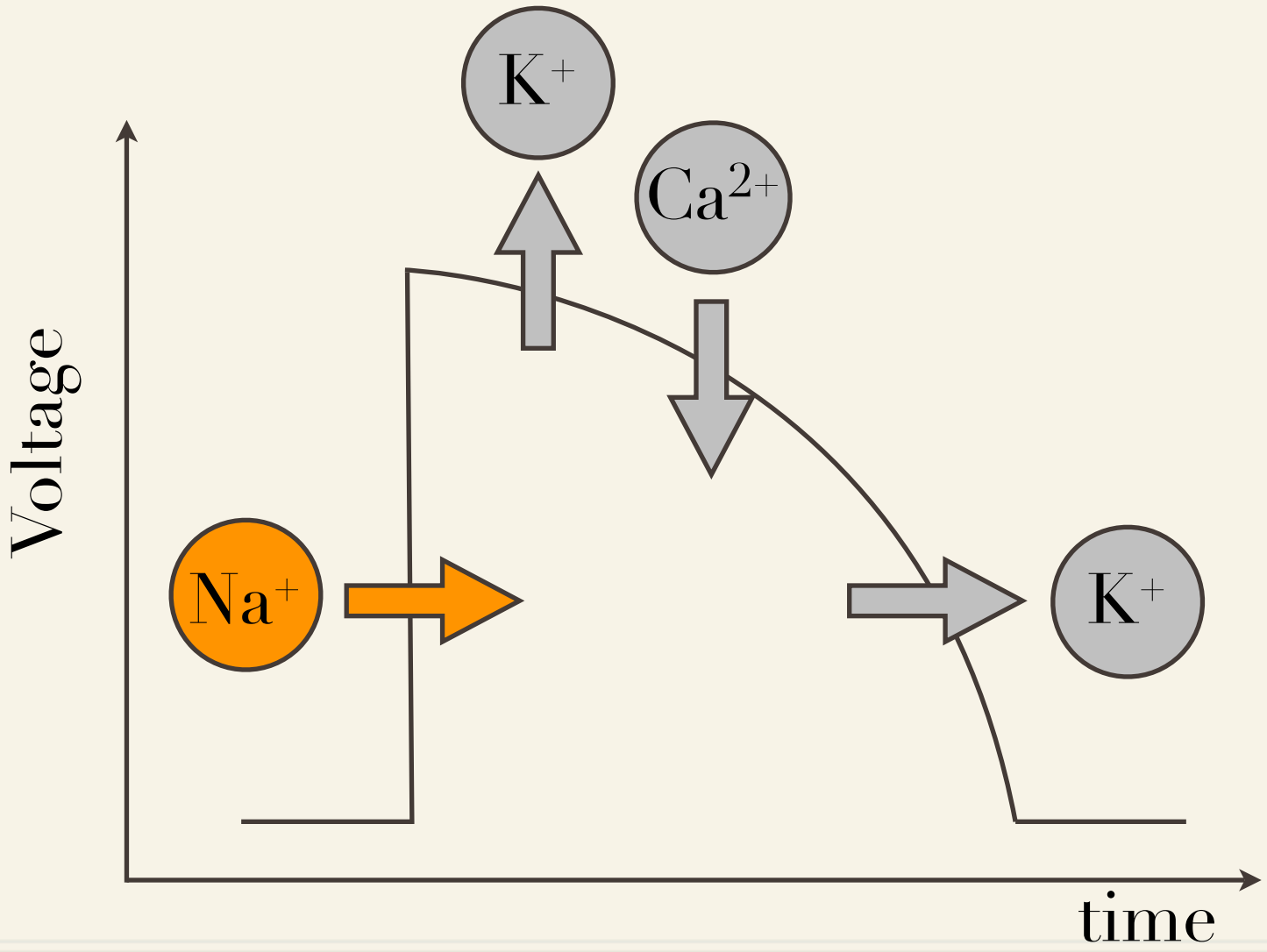
- Fundamentally still Smooth Bifurcation
- Importance: Connection to other dynamical processes occurring in cardiac cells
- Identify the “border”

Main Players

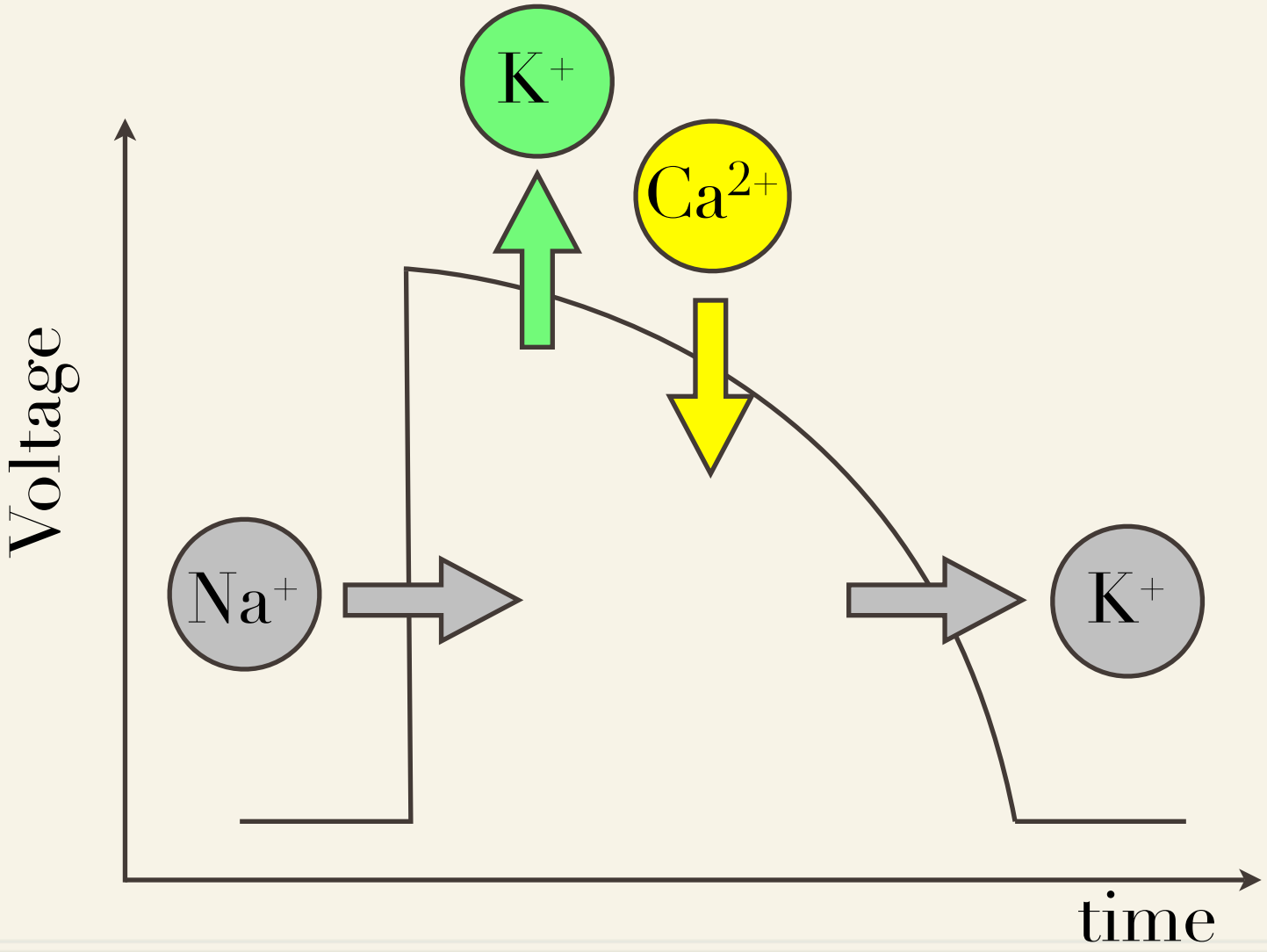


Dubin, D., Ion Adventures in the Heartland. (2003)

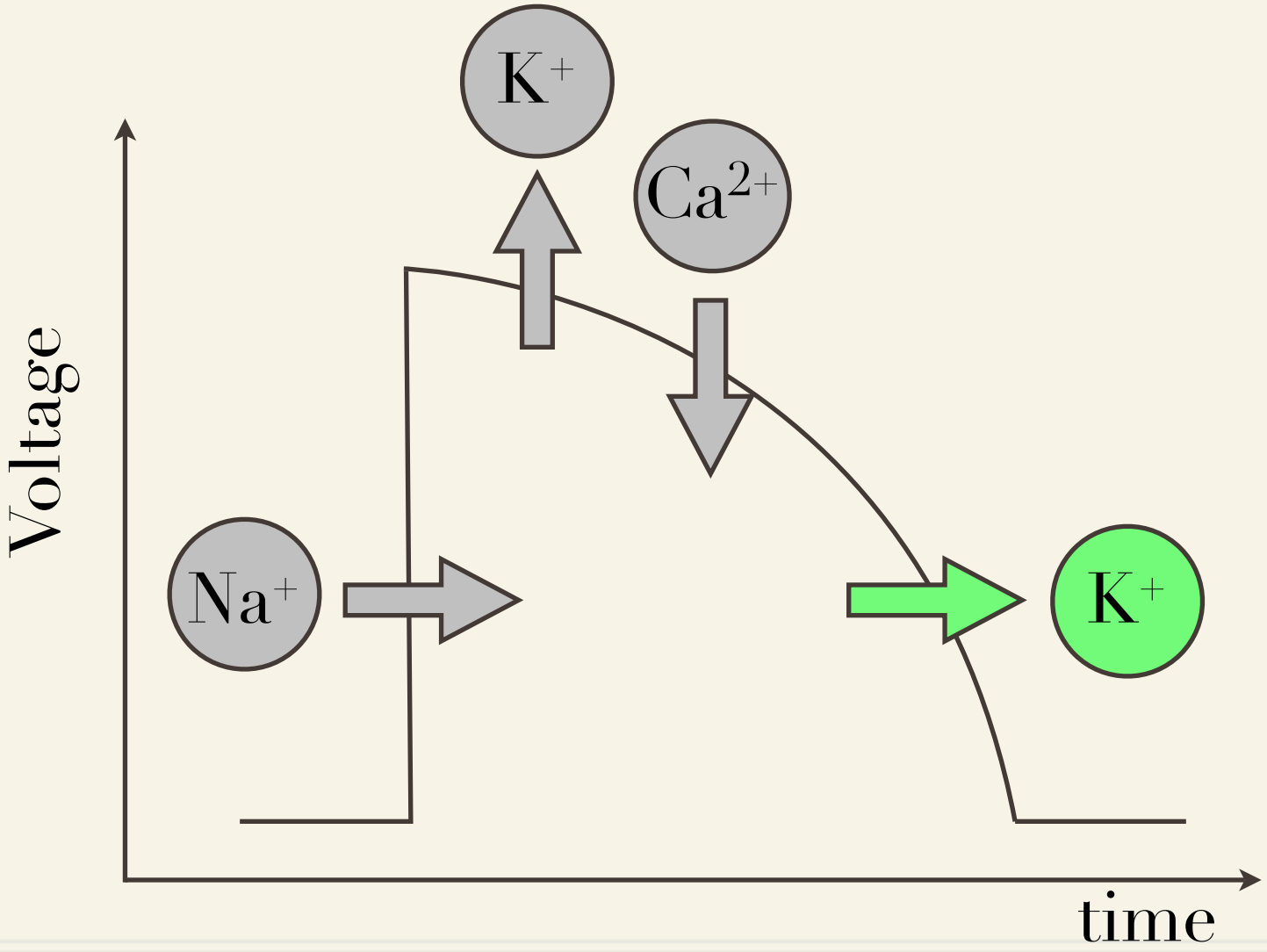
Main Players



Main Players

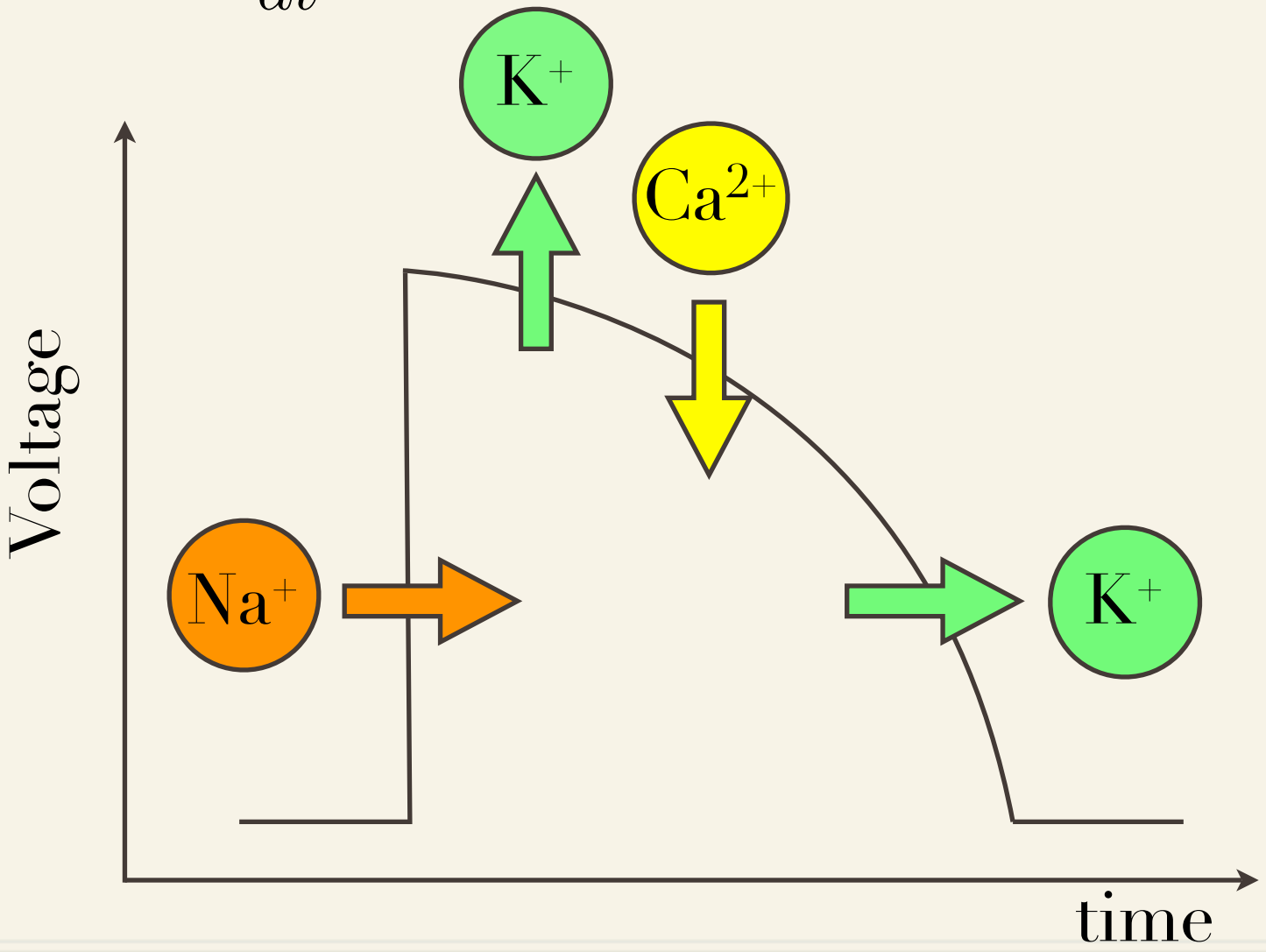


Main Players



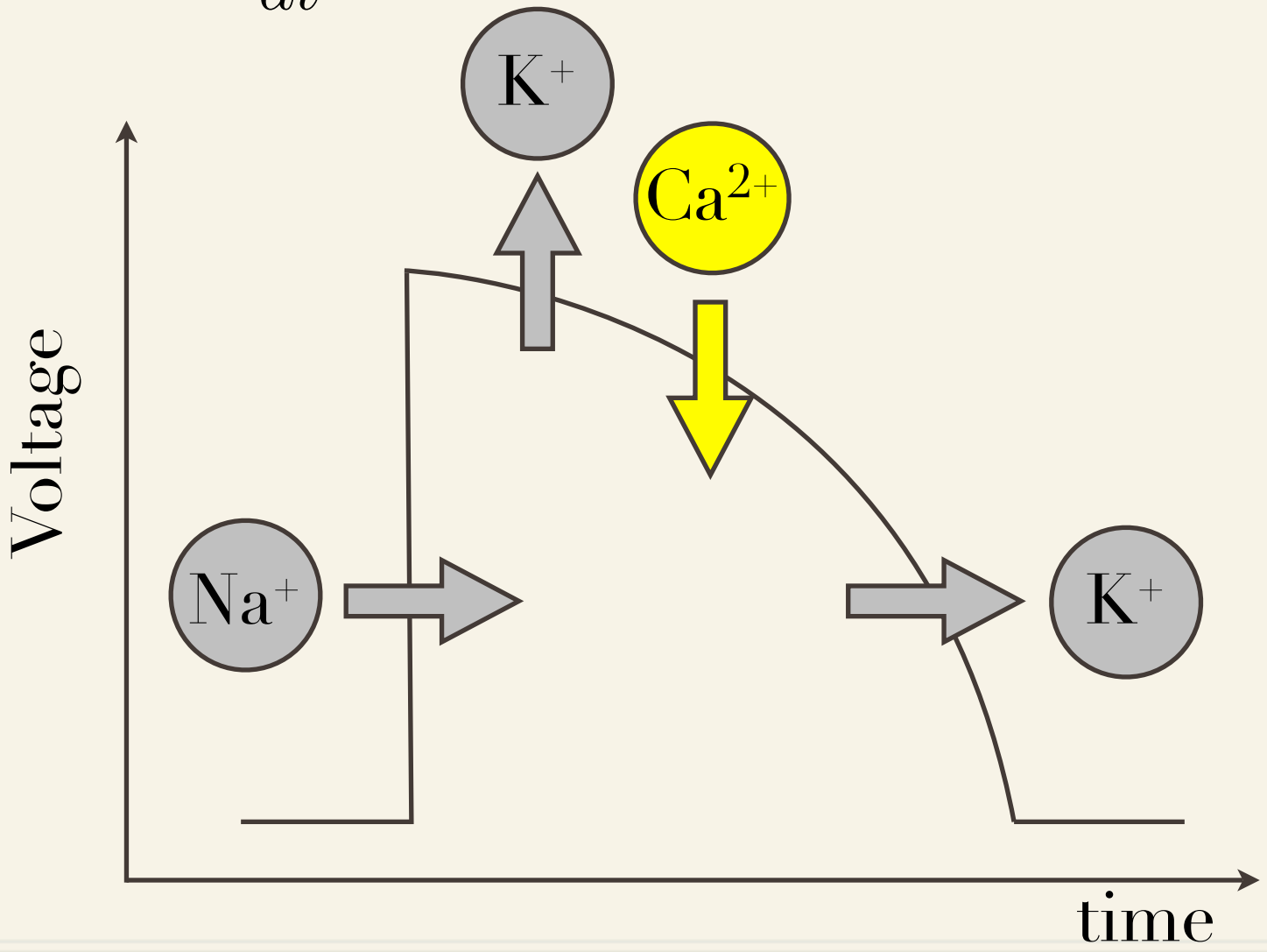
Calcium Effects Plateau

$$C_m \frac{dV}{dt} = I_{Na} + I_K + I_{Ca} + I_{stim}$$



Calcium Effects Plateau

$$C_m \frac{dV}{dt} = I_{Na} + I_K + I_{Ca} + I_{stim}$$



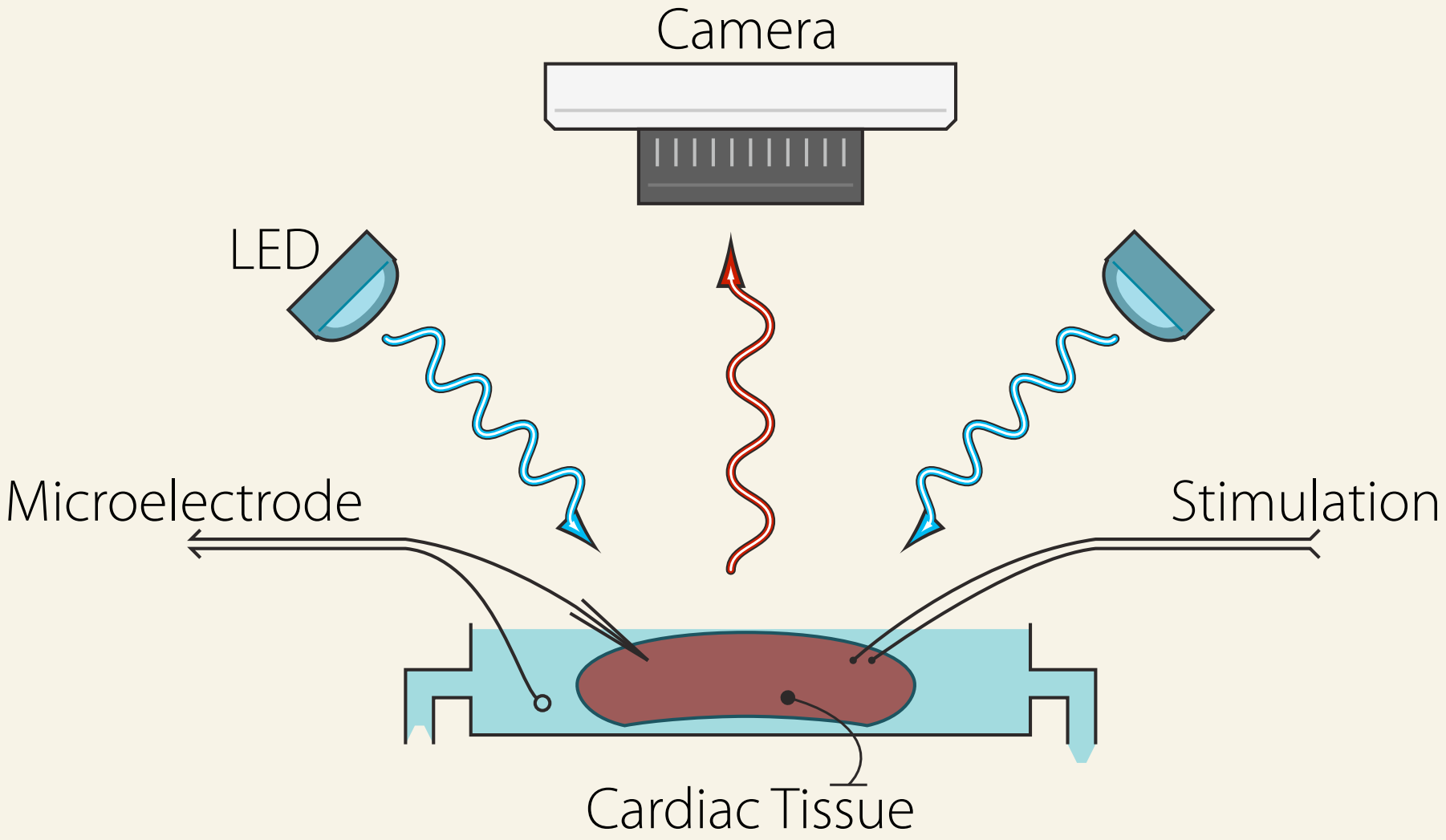
Chudin, E. J. et al. Biophys. J. 77, 2930 (1999)

Calcium's Role

- Calcium responsible for contraction
- Stores of Calcium in the cell get "stuffed" and then release
- Study Store or Intracellular Space

Karin R. Sipido, Understanding Cardiac Alternans: The Answer Lies in the Ca^{2+} Store, Circulation Res., 94: 570-572 2004.

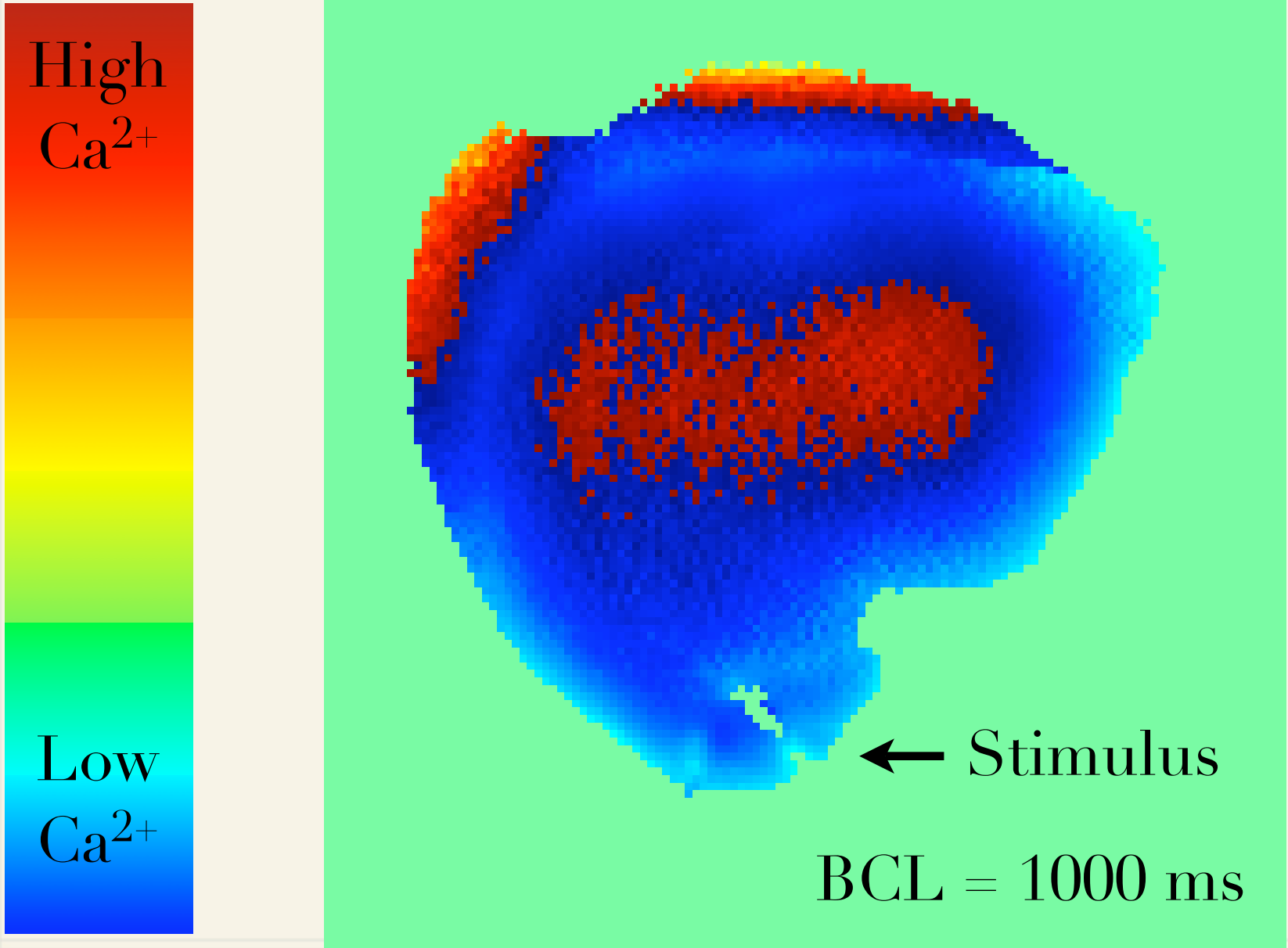
Experimental Setup



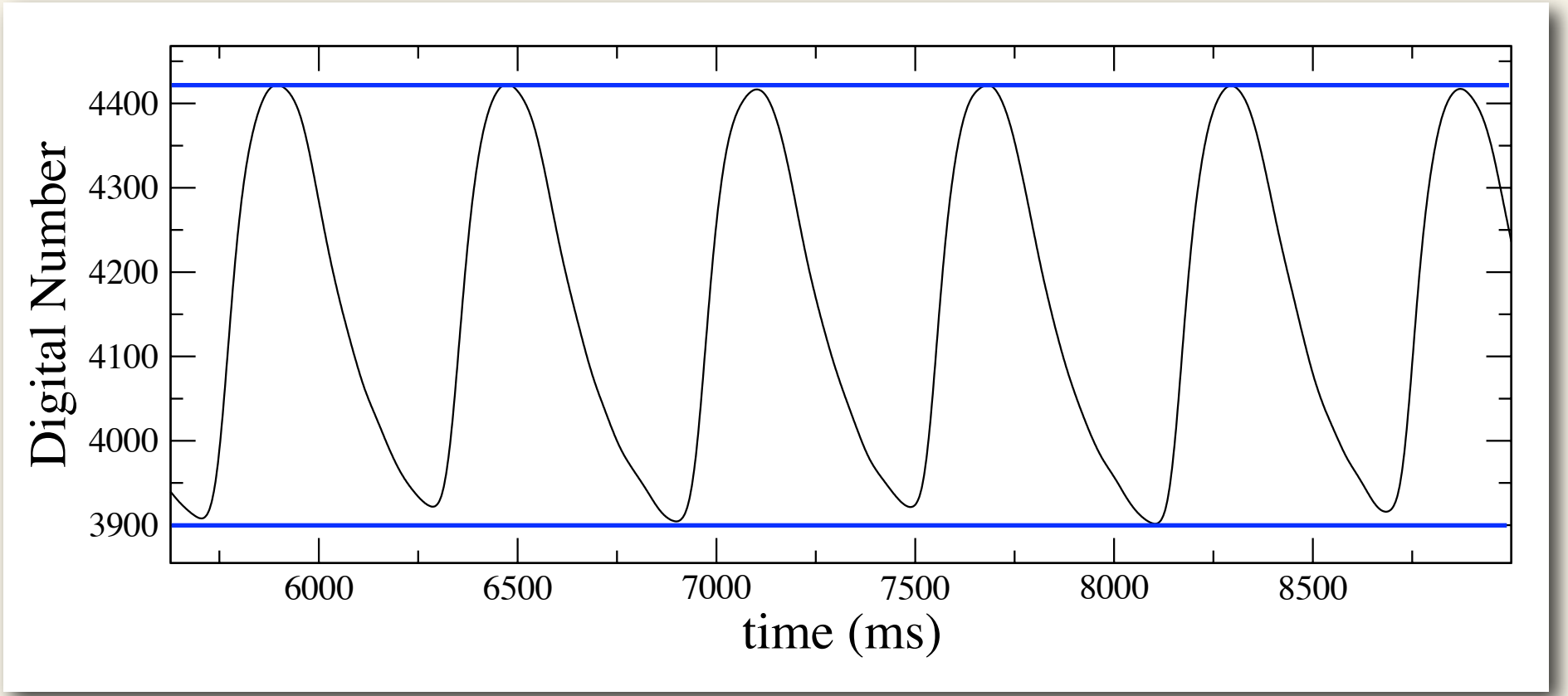
Pacing Scheme

- Pace for 150 s at constant BCL
- Alternate pace for 20 s (δ = 20 ms)
- Repeat with a new BCL

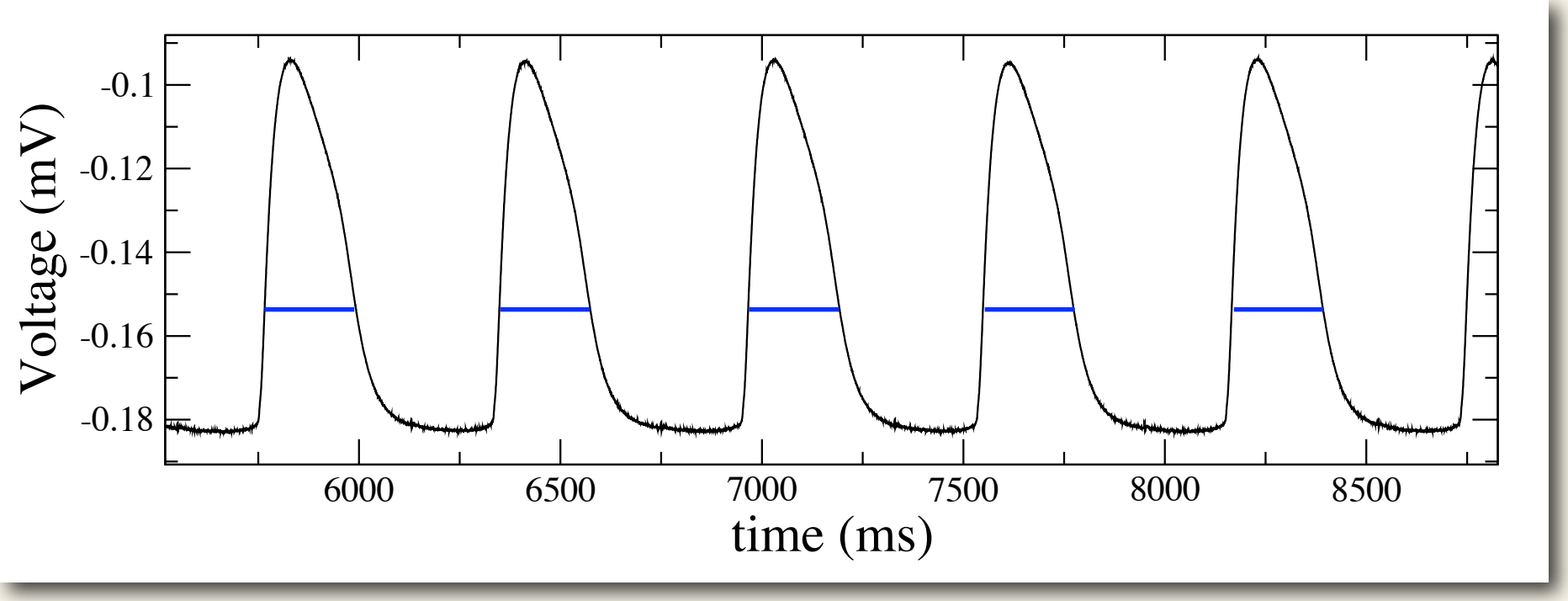
Calcium Waves

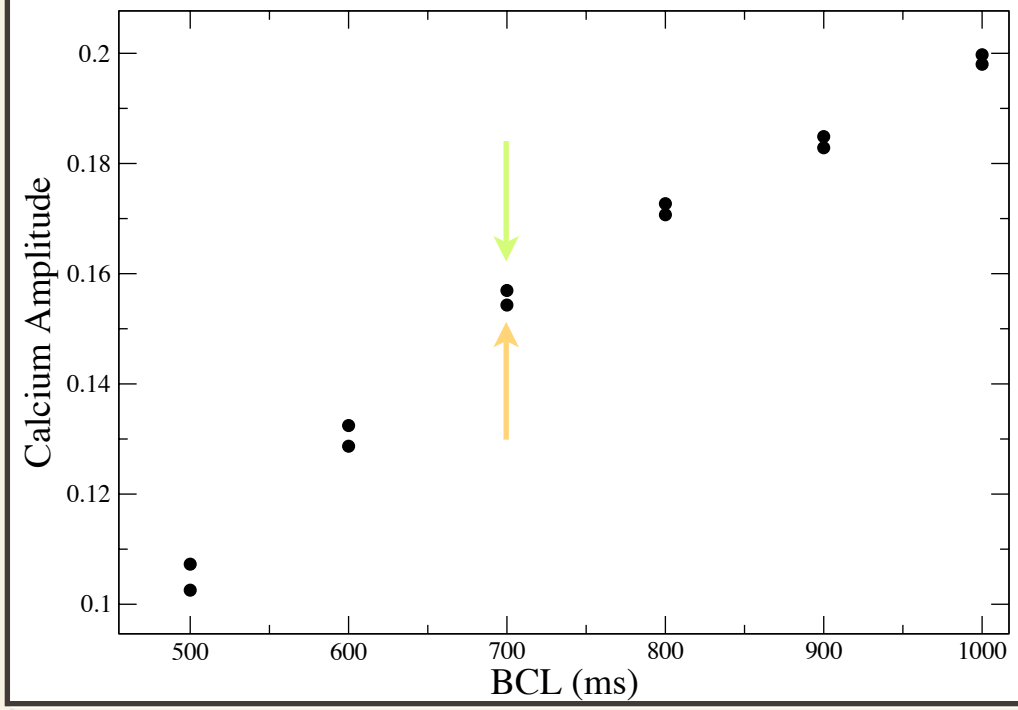


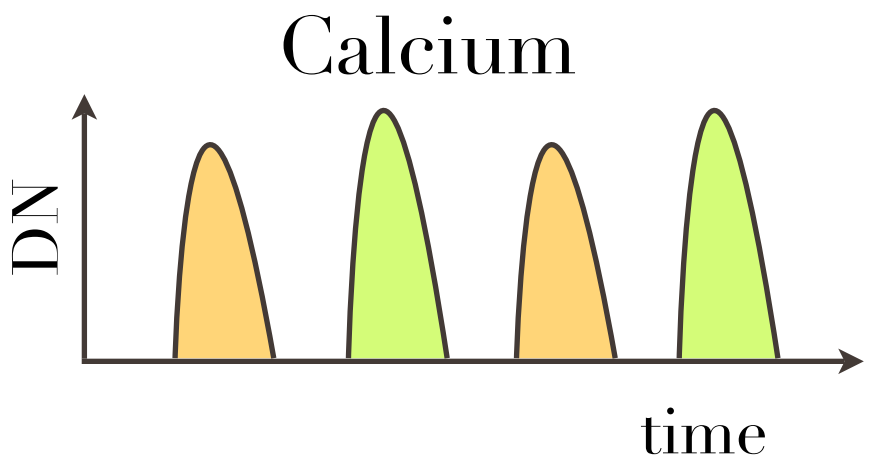
Alternate Pacing

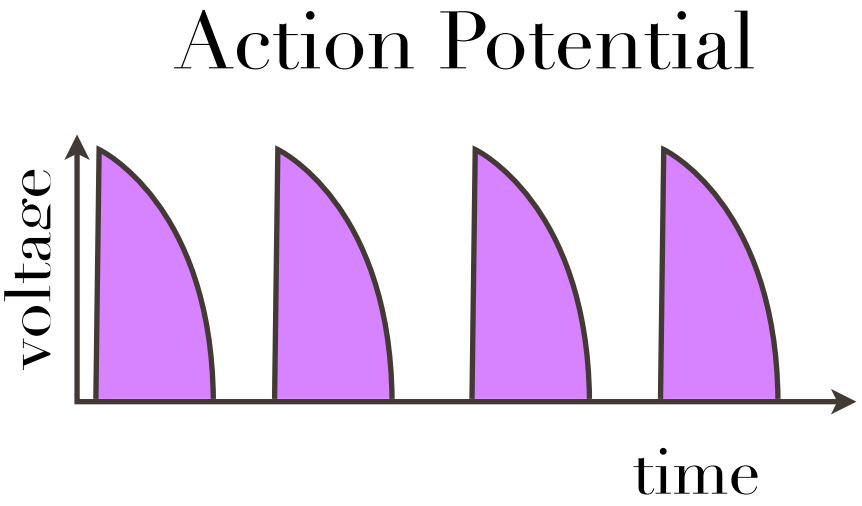


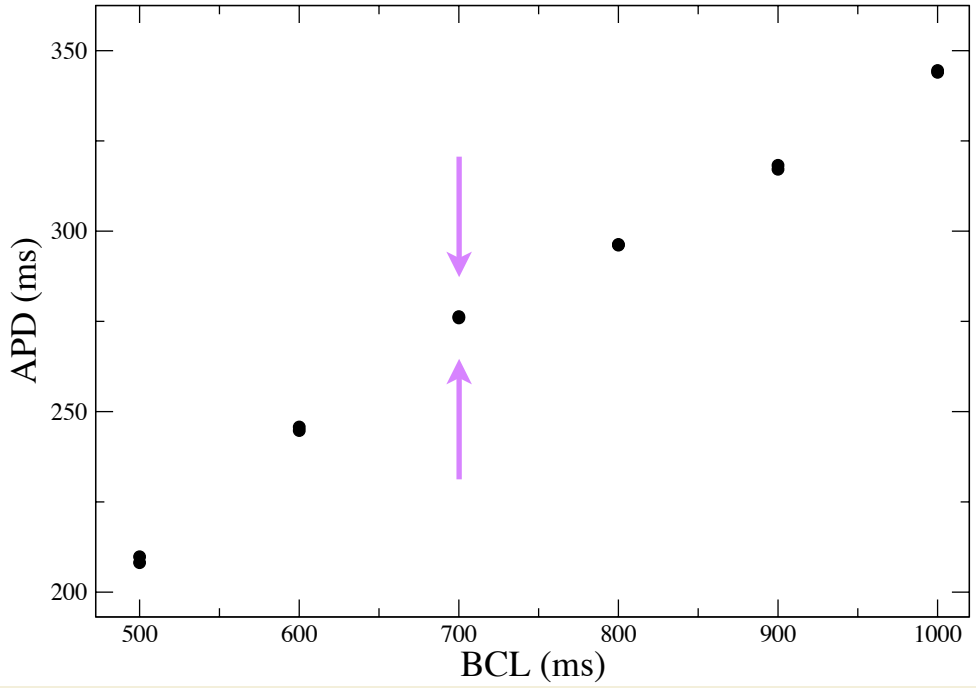
Perturbative Pacing




Calcium Amplitude
0.2
0.18
0.16
0.14
0.12
0.1
500
600
700
800
900
1000
BCL (ms)

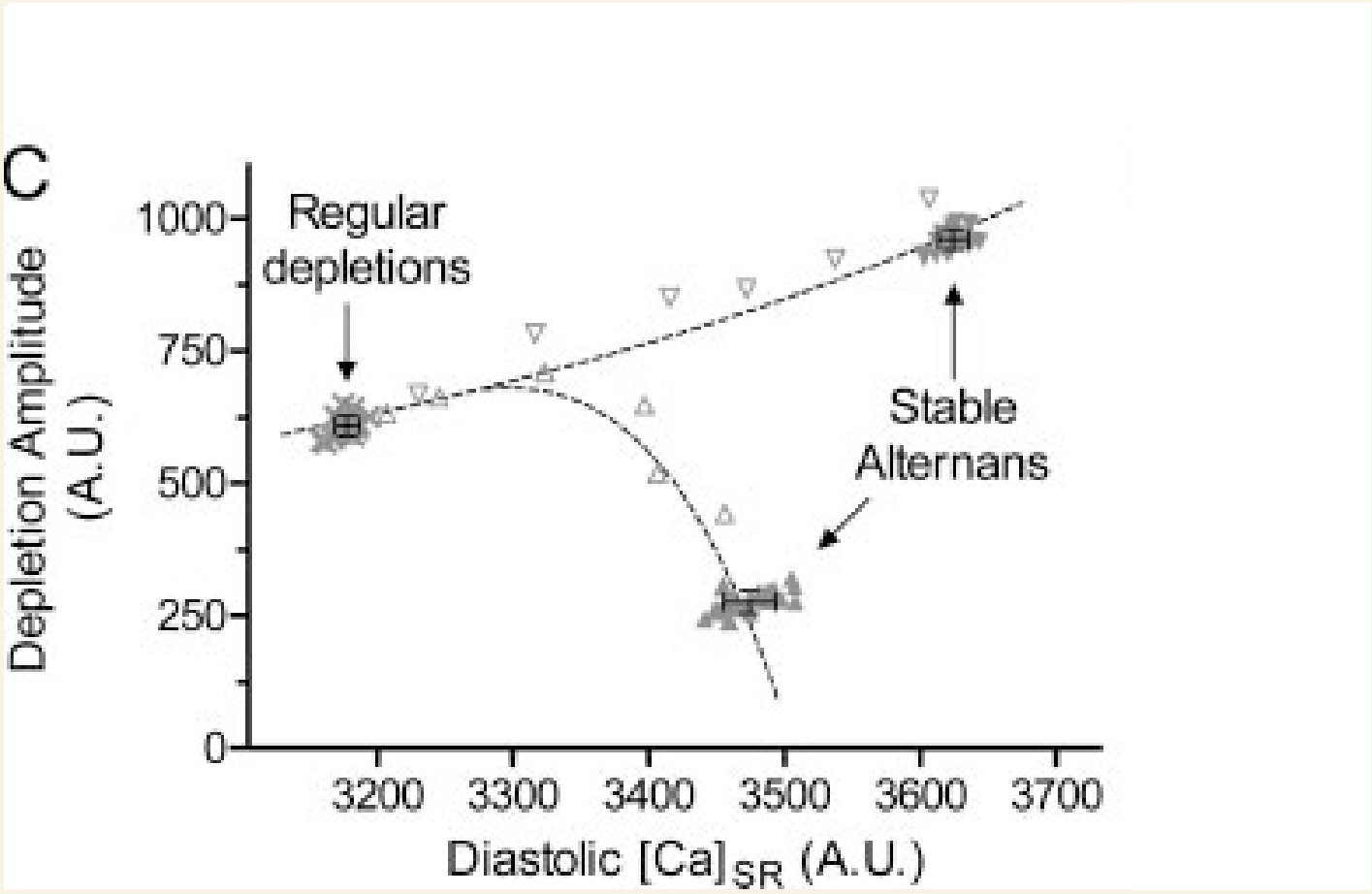

Calcium
DN
time


Action Potential
voltage
time


APD (ms)
350
300
250
200
500
600
700
800
900
1000
BCL (ms)

Conclusion

- Previous result: APD relatively insensitive to perturbations in BCL
- Initial Result: Calcium more sensitive to perturbations
- Hypothesis: Calcium instability in cardiac cells drives electrical instability


C
Depletion Amplitude (A.U.)
1000
750
500
250
0
Regular depletions
Stable Alternans
3200
3300
3400
3500
3600
3700
Diastolic [Ca]SR (A.U.)