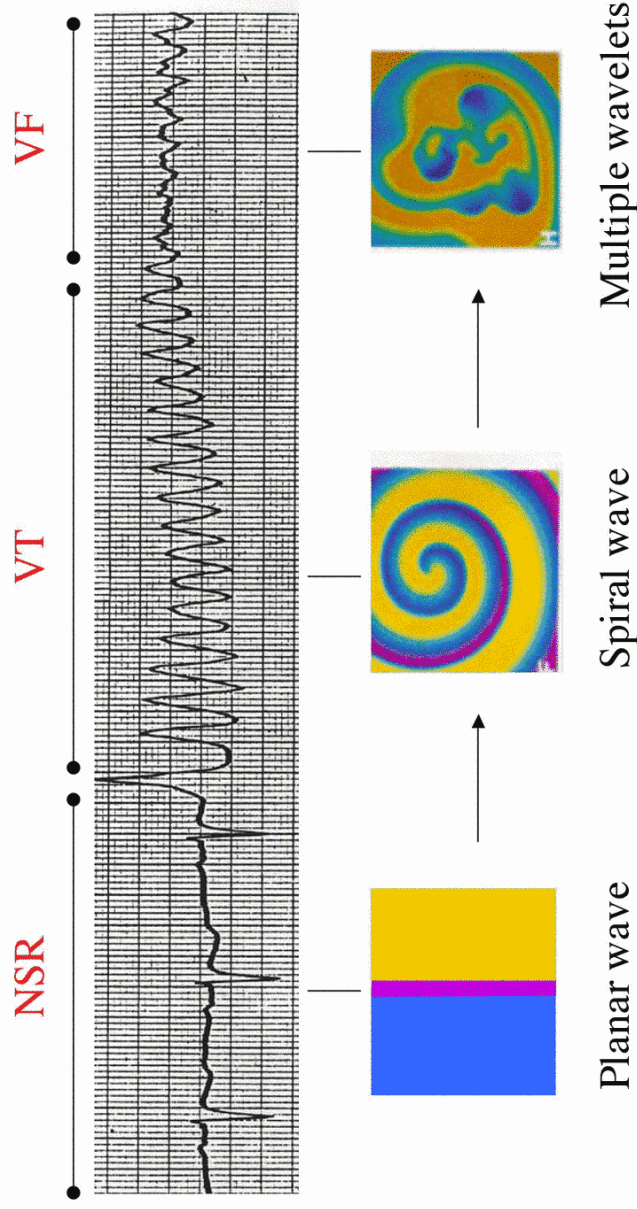
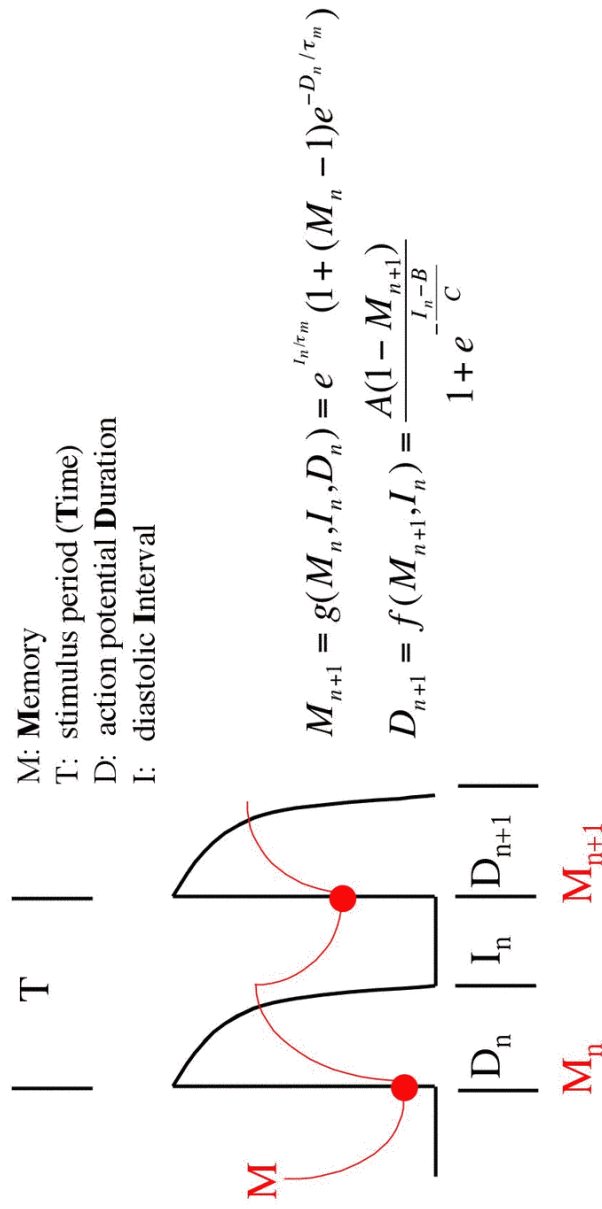


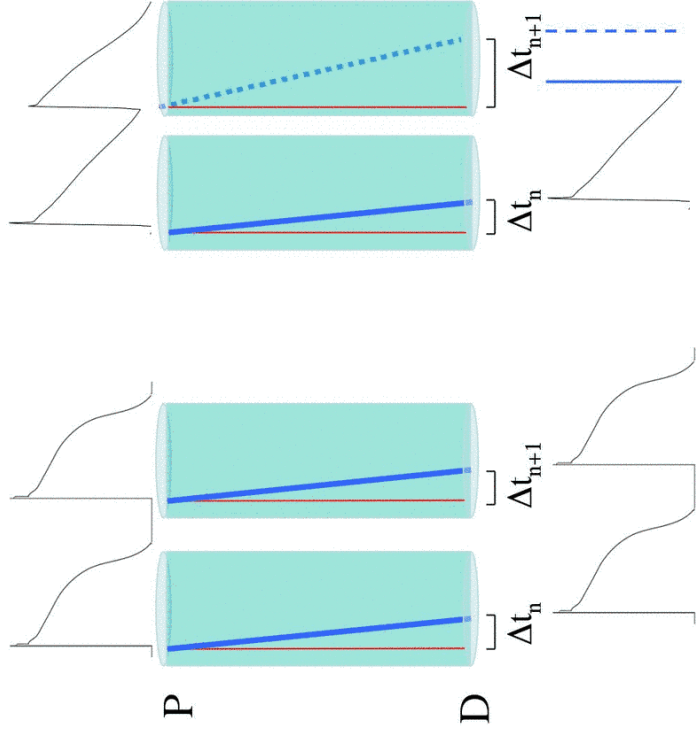
Progression from normal sinus rhythm to VF



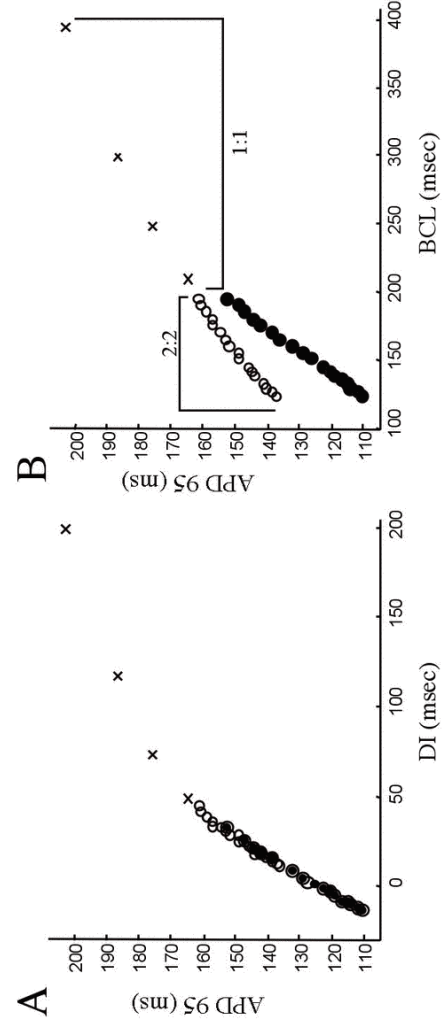
Return map memory model for APD restitution



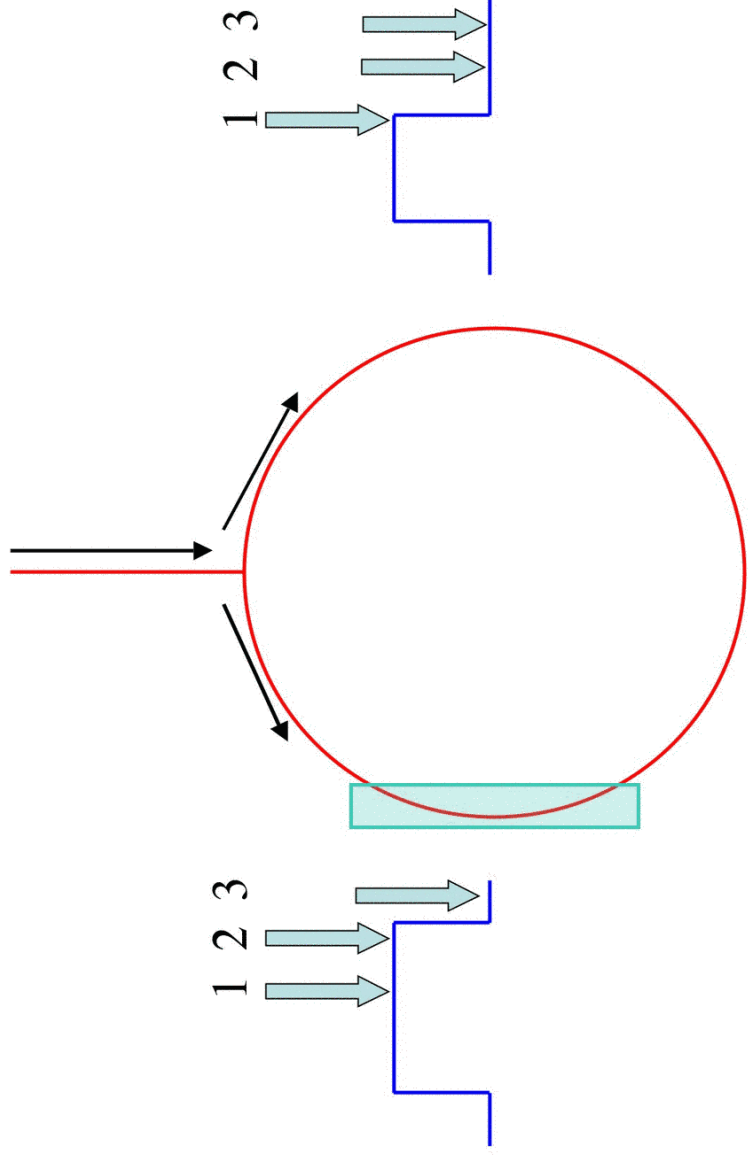
### Conduction velocity restitution



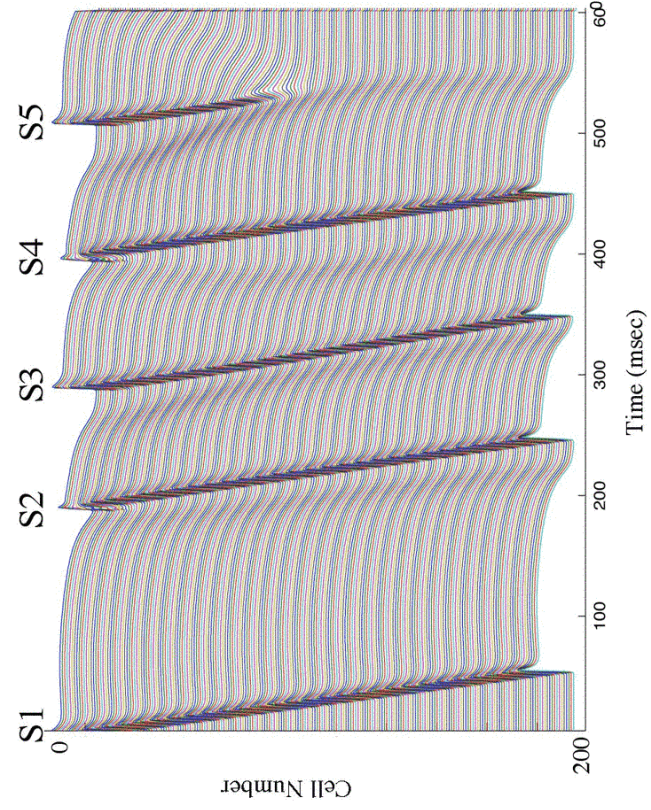
### APD alternans and restitution during rapid pacing



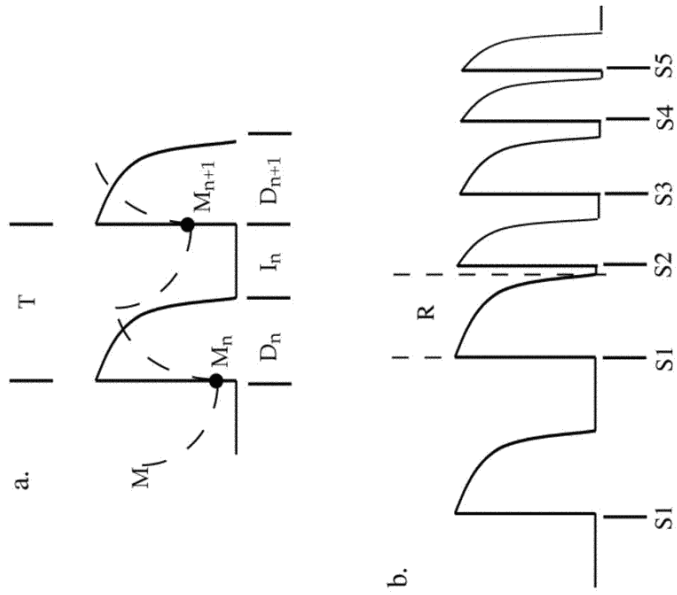
### Schematic for circus movement reentry



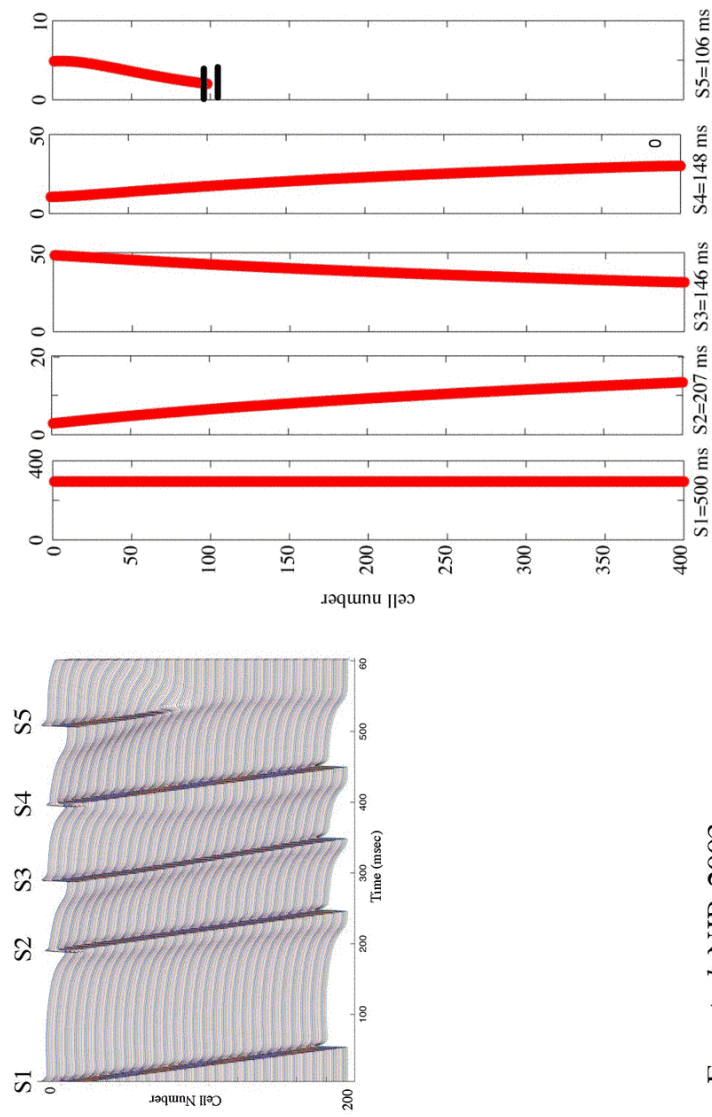
### Discordant APD alternans to conduction block



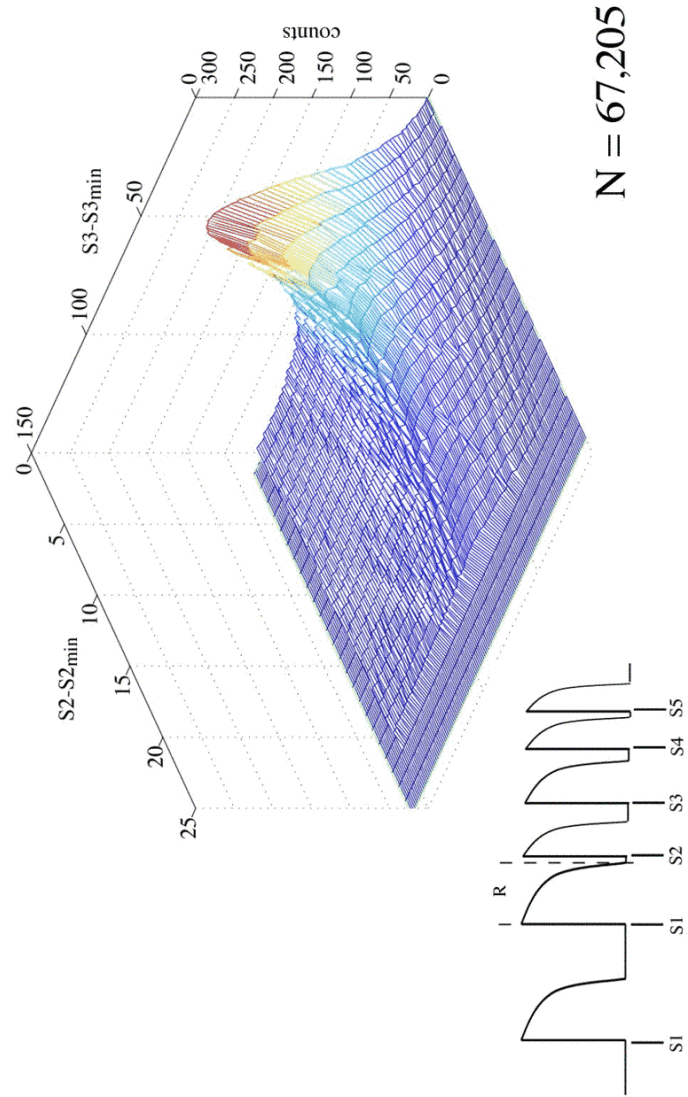
## Induction of conduction block by premature stimulation



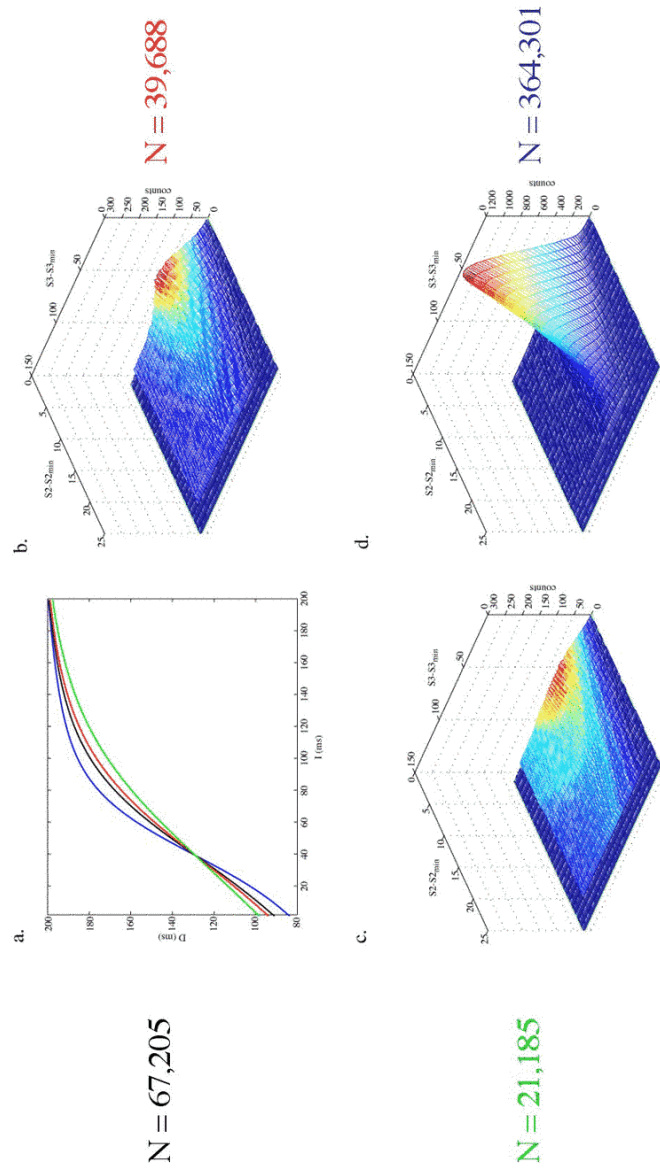
## Induction of conduction block by premature stimulation



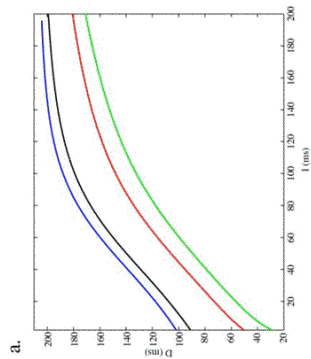
### Incidence of conduction block for different patterns of premature stimulation



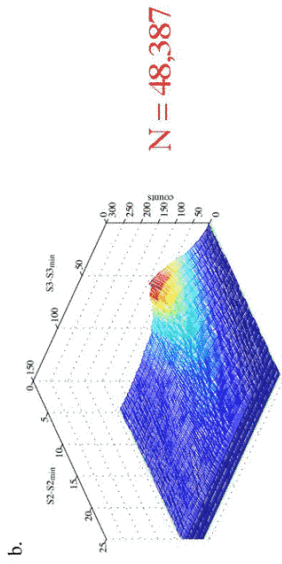
### Effects of altering APD restitution on the incidence of conduction block



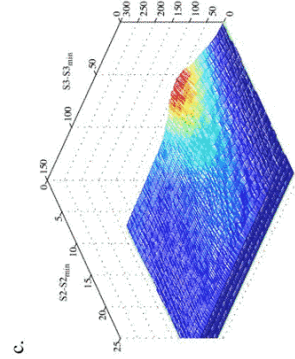
## Effects of altering memory on the incidence of conduction block



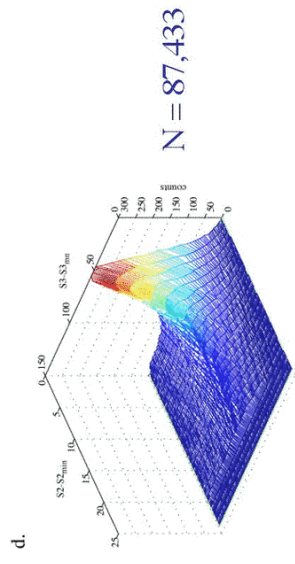
N = 67,205



N = 48,387

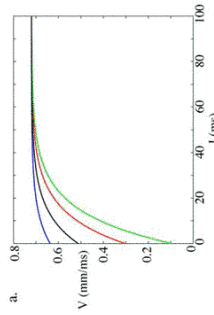


N = 43,715



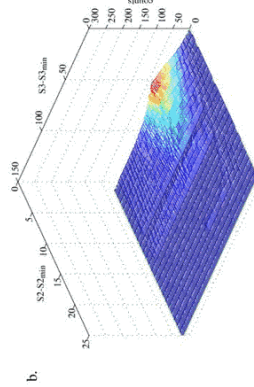
N = 87,433

## Effects of altering CV restitution on the incidence of conduction block

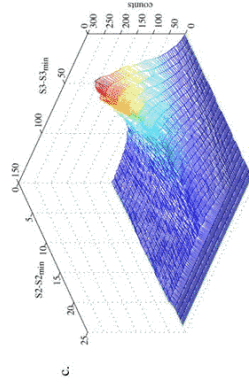


N = 67,205

N = 0



N = 8,879

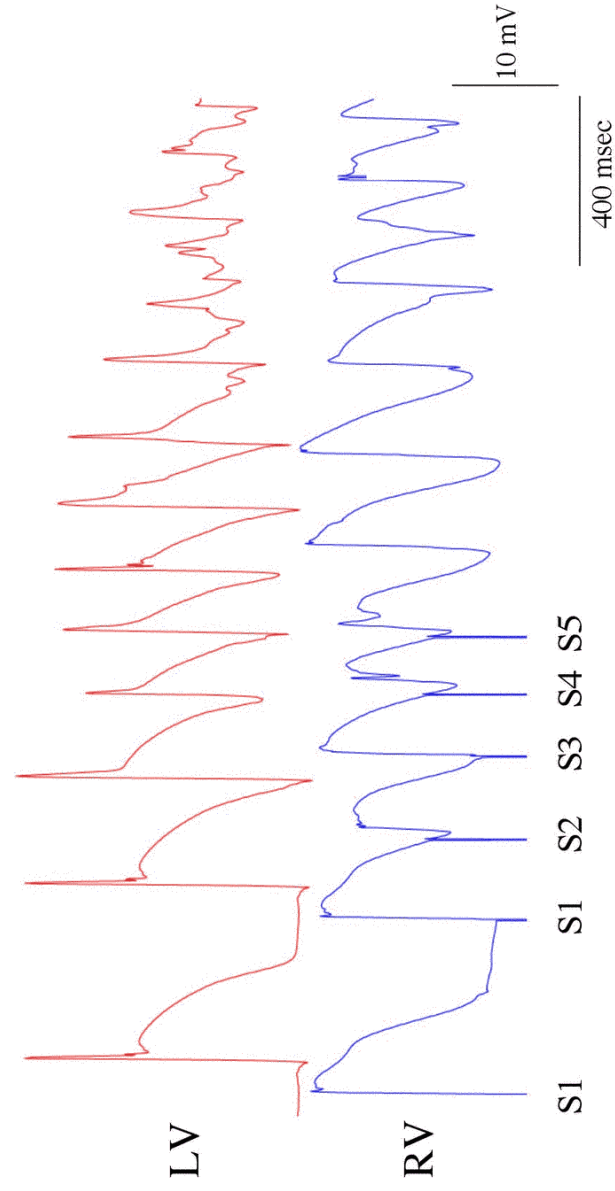


N = 86,032

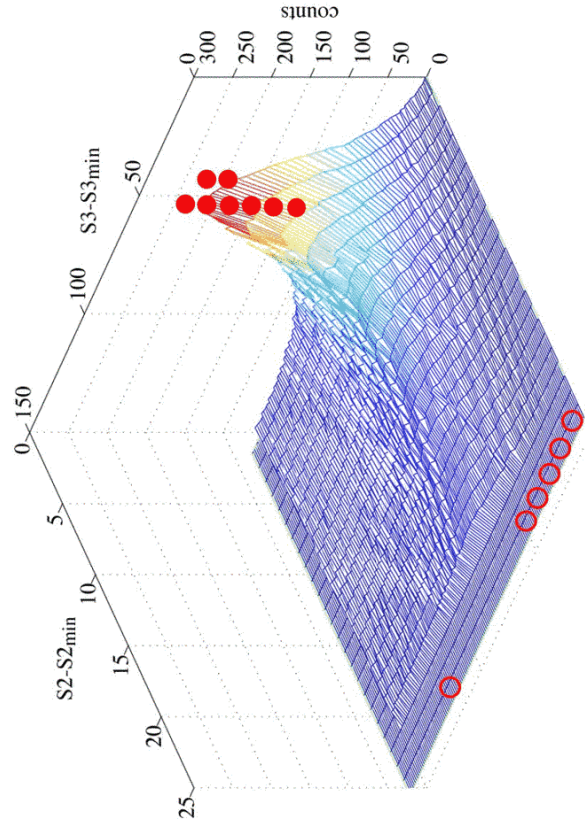
## VF induction in normal beagles

- Pentobarbital anesthesia
- Closed chest, artificially ventilated
- Measurements of arterial blood pressure, surface ECG, RV and LV endocardial MAP
- MAP duration restitution determined using standard protocol for S1-S4 and “dynamic” protocol
- VF induction attempted using standard premature protocol, dynamic protocol and ICB protocol

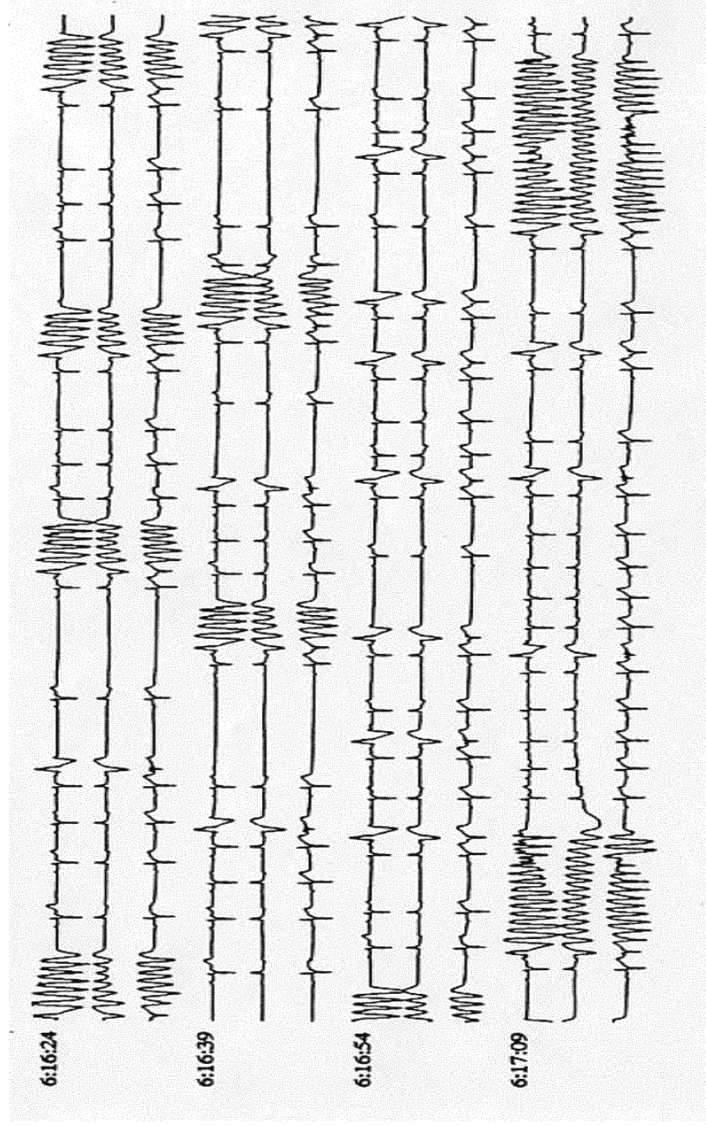
## Induction of VF using ICB protocol



### Incidence of conduction block for different patterns of premature stimulation

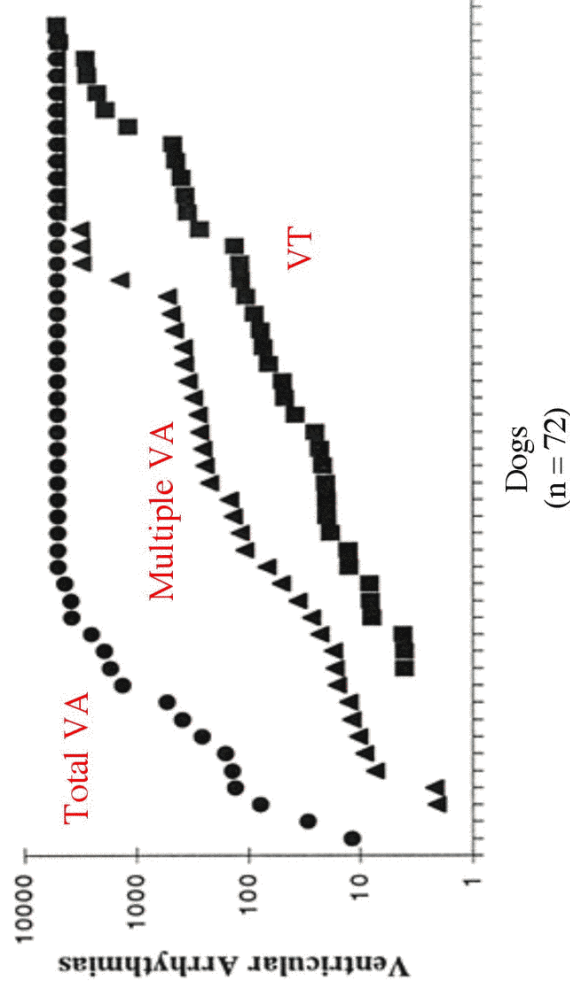


### Spontaneous VT in German shepherd dogs





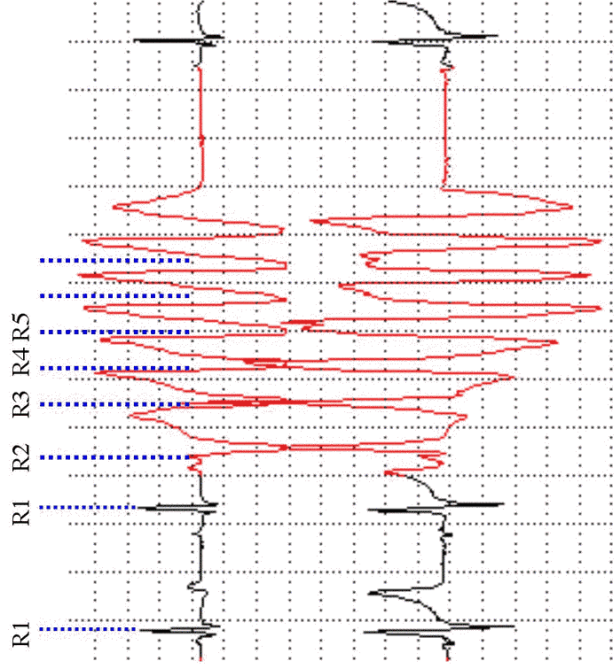
## Phenotypic spectrum of ventricular arrhythmias



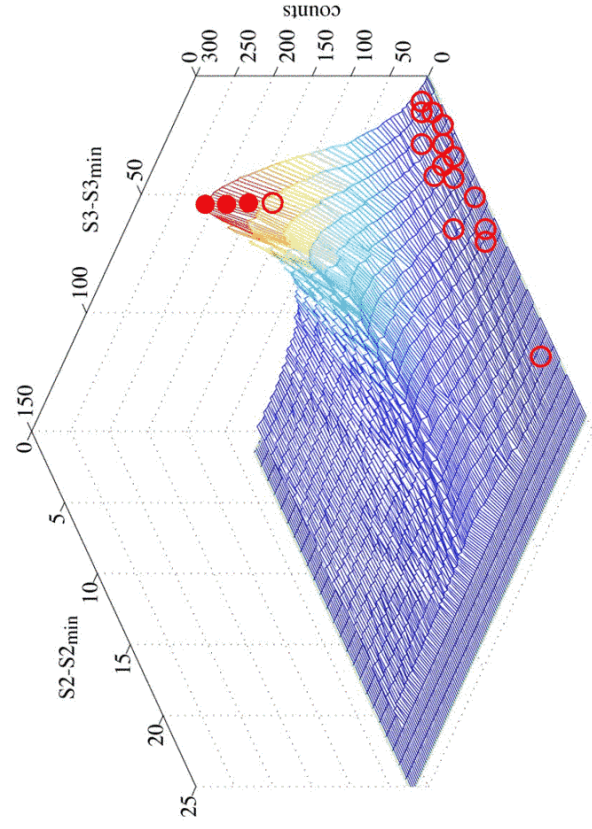
## VF induction in affected German shepherds

- Pentobarbital and fentanyl anesthesia
- Closed chest, artificially ventilated
- Measurements of arterial blood pressure, surface ECG, RV and LV endocardial MAP
- MAP duration restitution determined using standard protocol for S1-S4
- VF induction attempted using spontaneously occurring VT cycle lengths and ICB protocol

### Spontaneous VT in German shepherd dogs



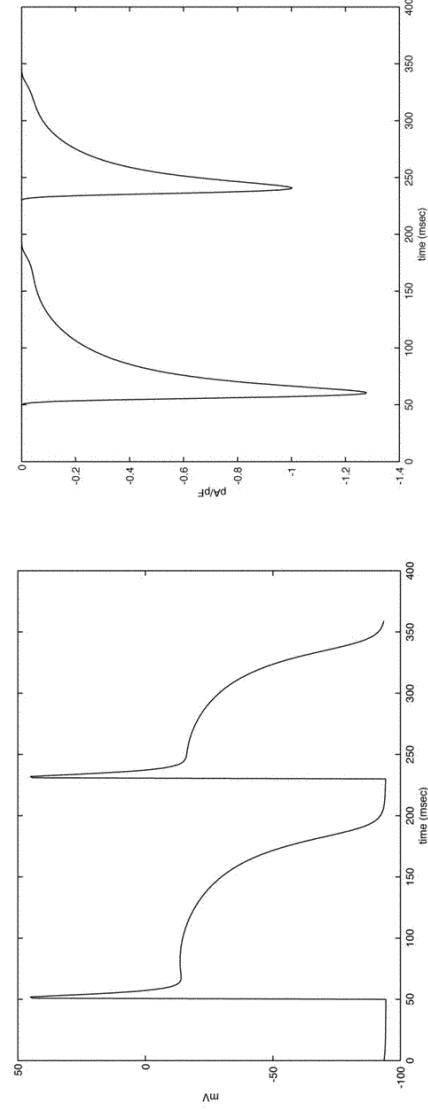
### Incidence of conduction block for different patterns of premature stimulation



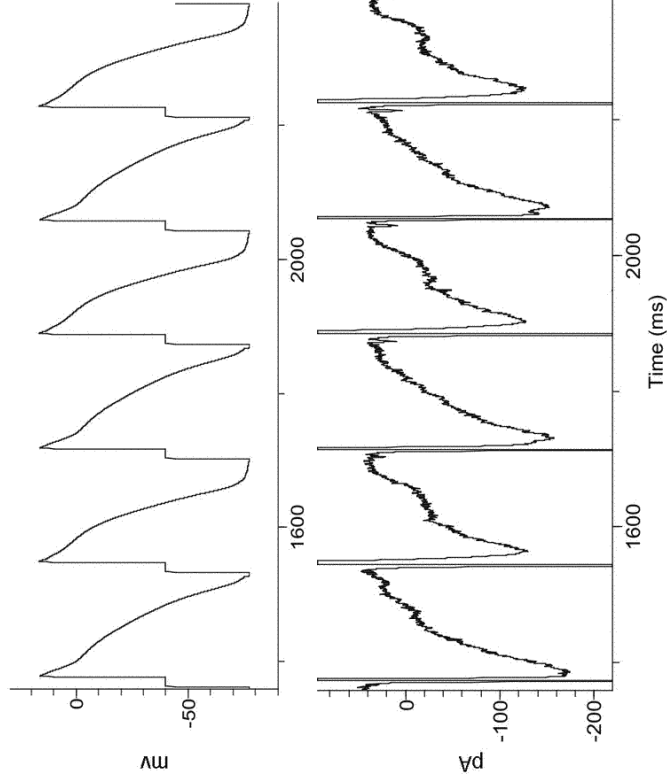
## Alternans control

- Drugs
  - Ca<sup>2+</sup> channel antagonists
  - K<sup>+</sup> channel agonists
- Gene modification
  - enhanced HERG expression
- Programmed electrical stimulation
  - chaos control

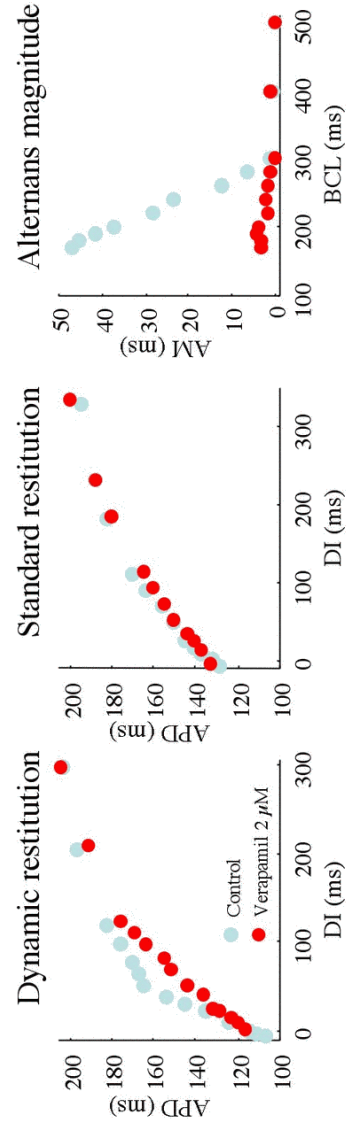
## Alternans of APD and I<sub>Ca</sub>: model

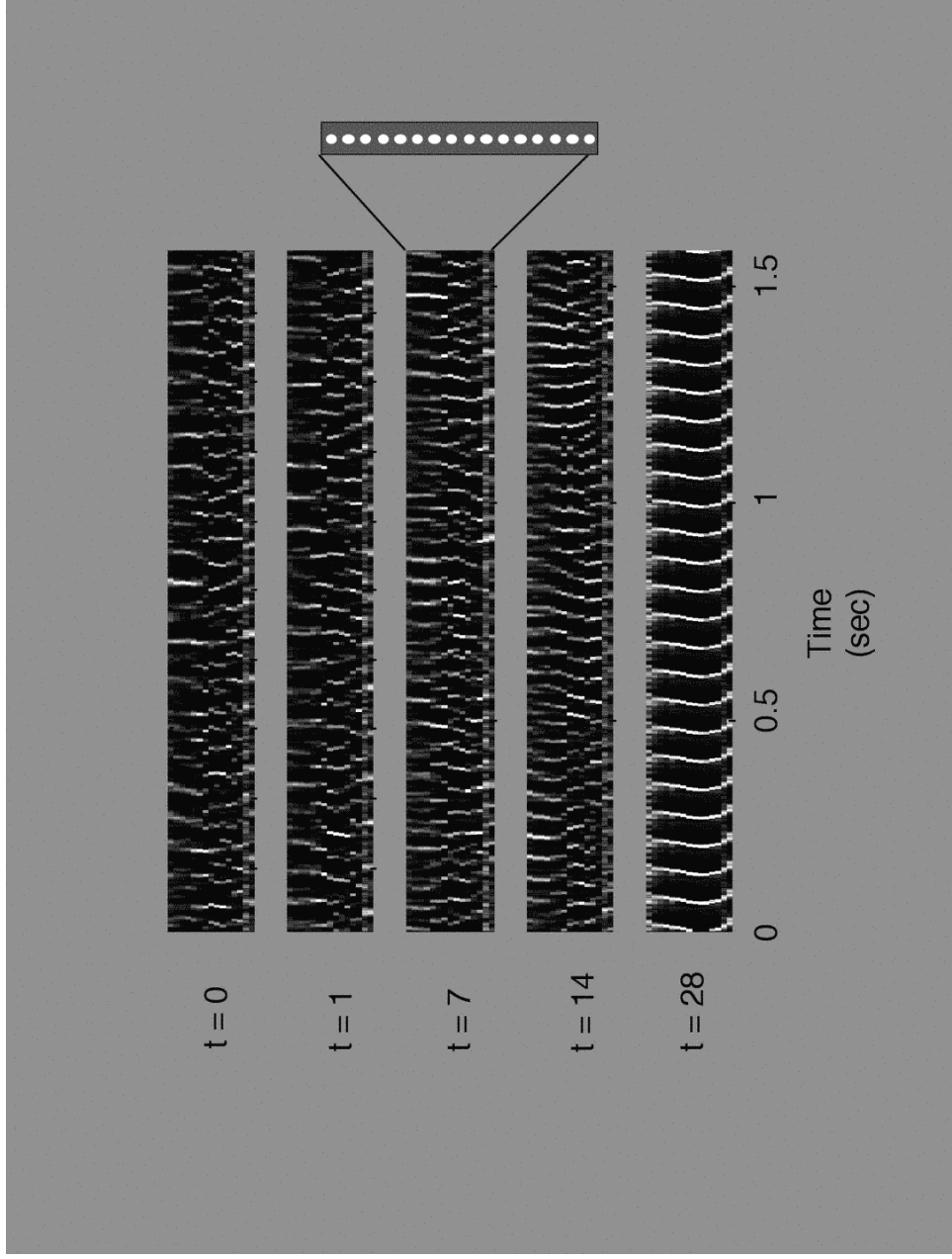


### Alternans of APD and $I_{Ca}$ : experiment

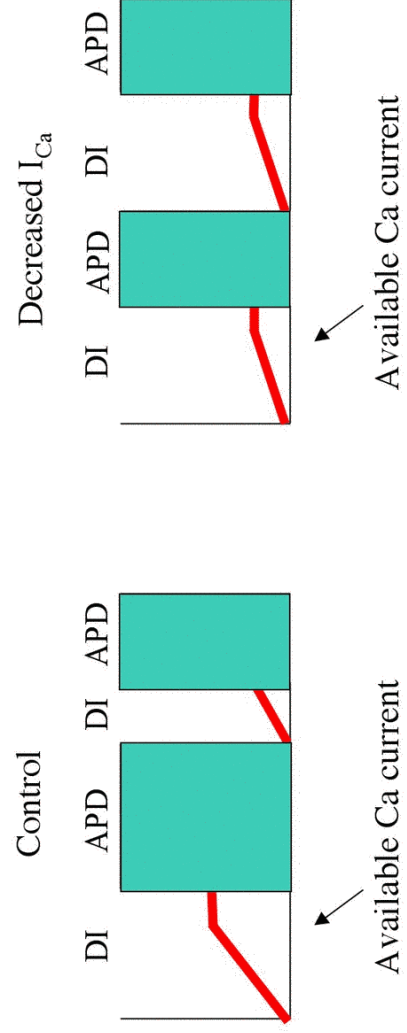


### Effects of verapamil on APD restitution

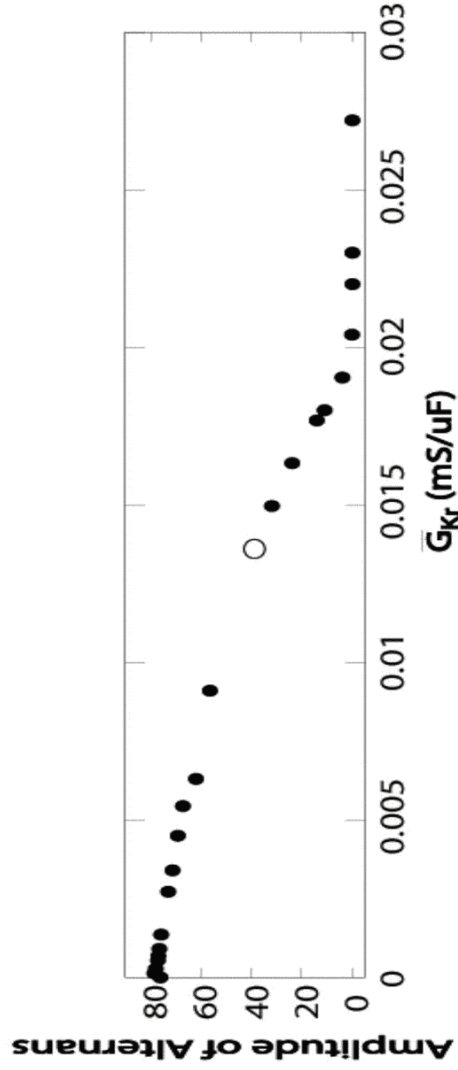




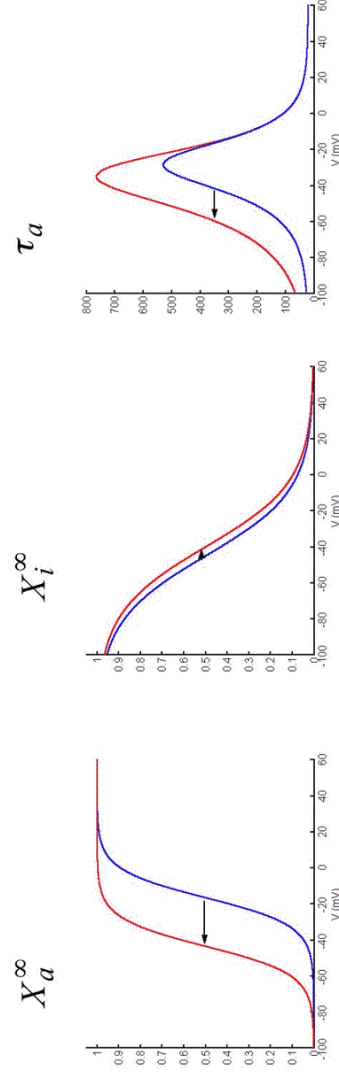
### Suppression of alternans by decreasing $I_{Ca}$



Suppression of alternans by increasing  $I_{Kr}$

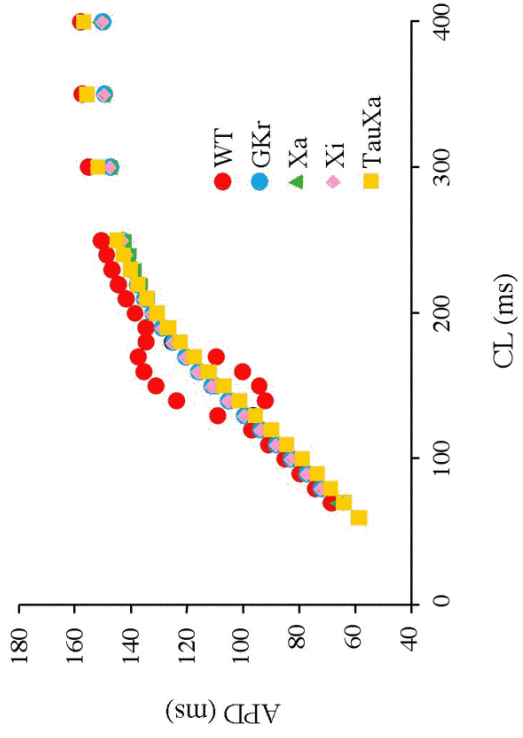


Increasing  $I_{Kr}$  in the ionic model

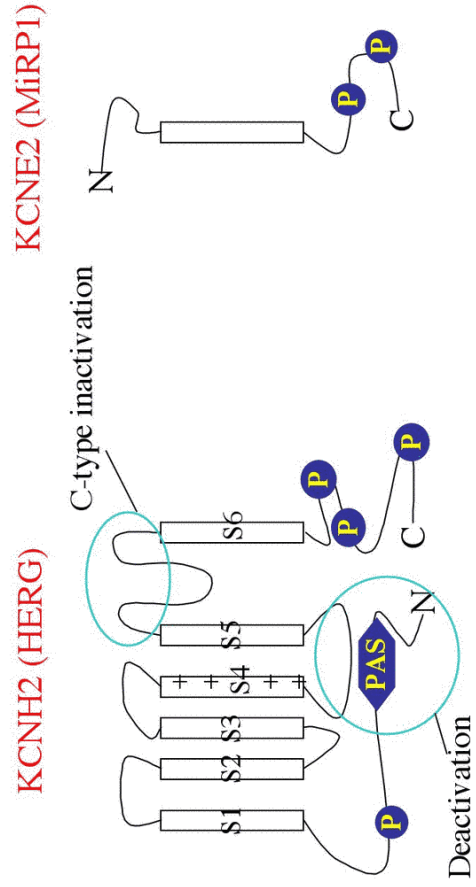


$$\bar{G}_{Kr} = 0.0541 \longrightarrow 0.068$$

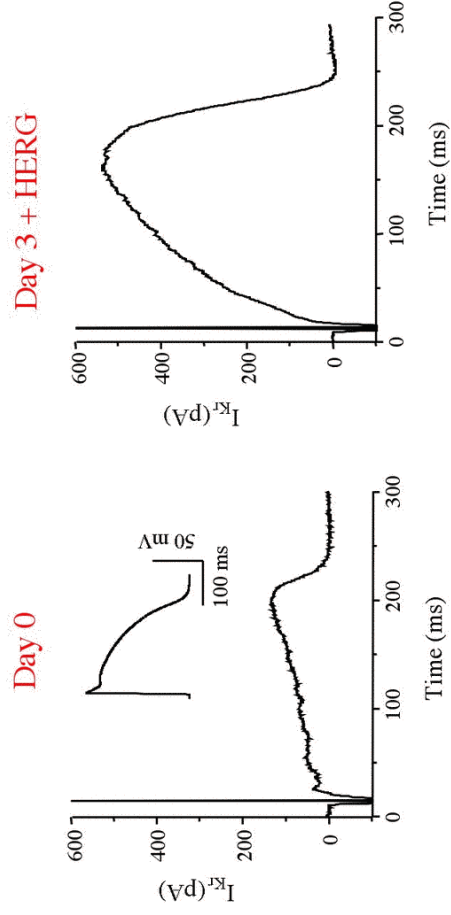
### Effects of increasing $I_{Kr}$ on APD alternans



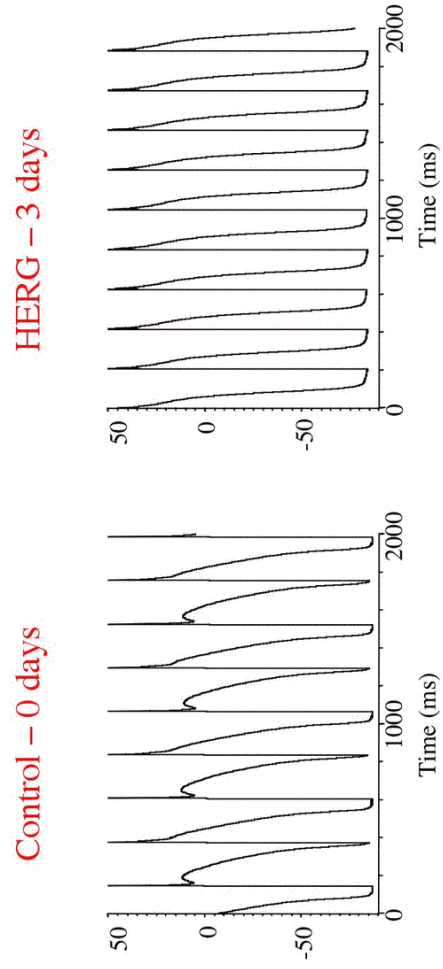
### Genes encoding $I_{Kr}$



### HERG overexpression increases $I_{Kr}$

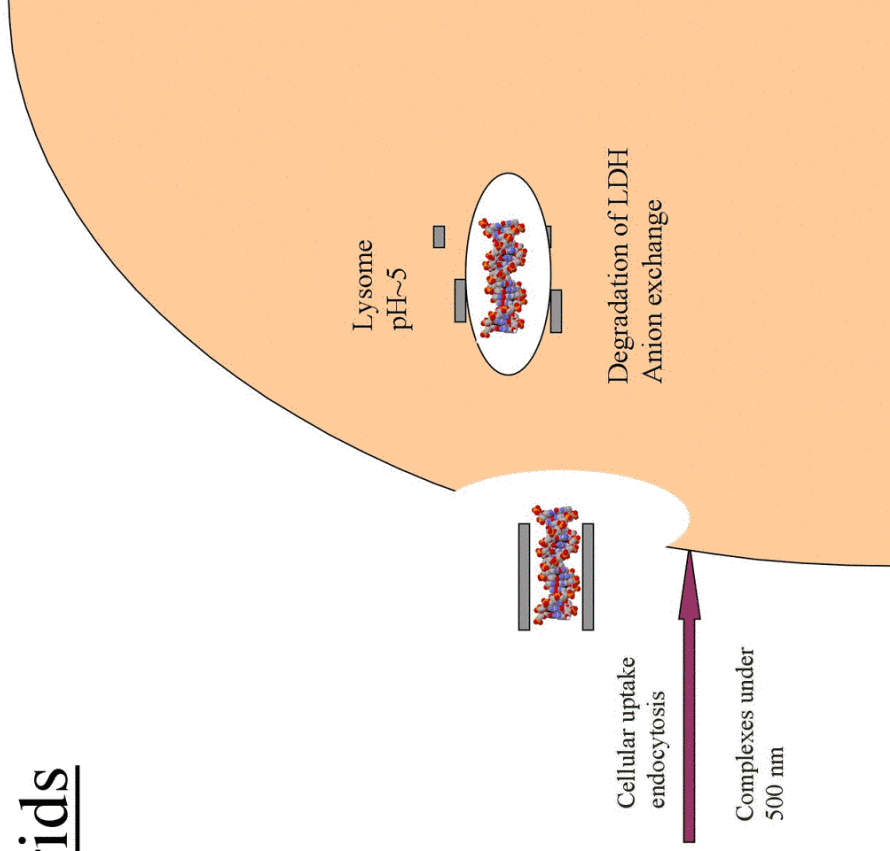
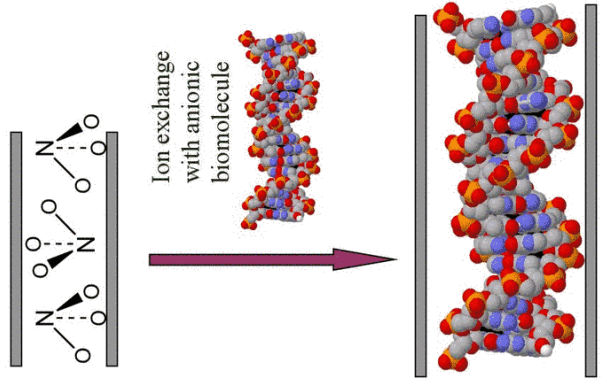


### Increasing $I_{Kr}$ suppresses APD alternans

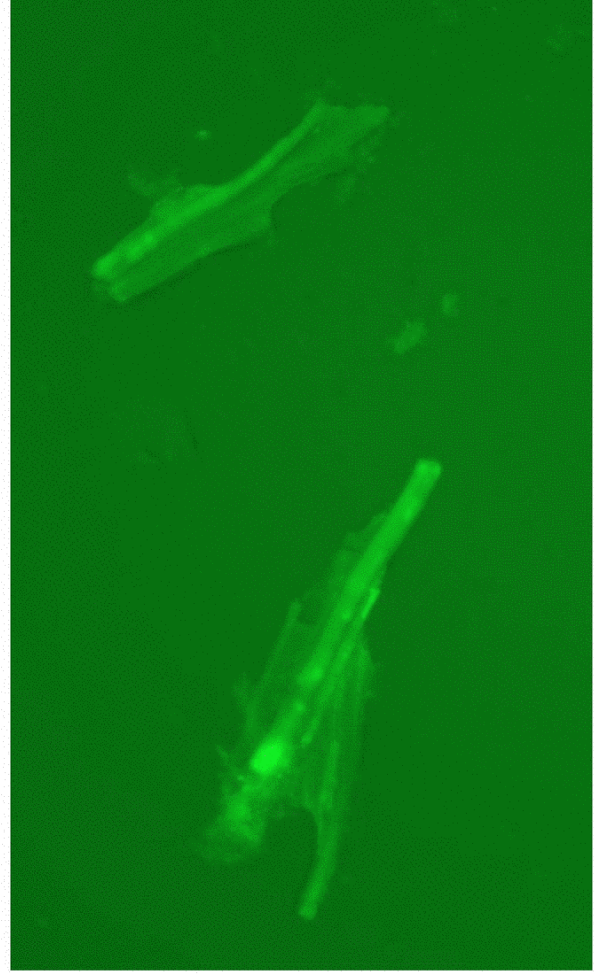




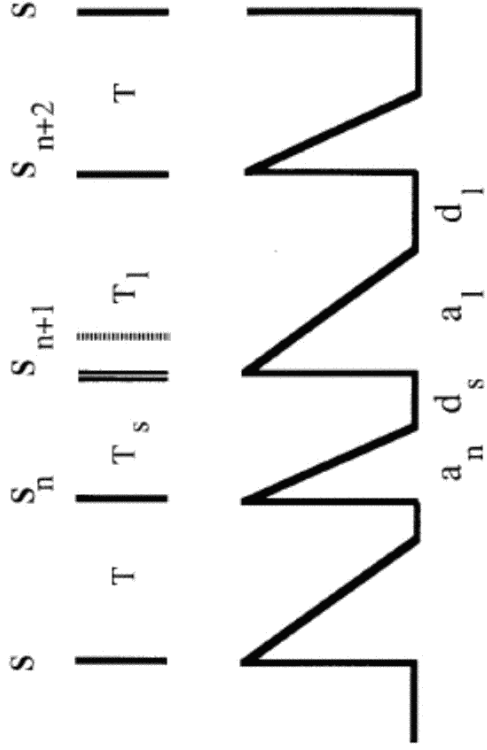
# Nanobiohybrids



Expression of GFP cDNA after uptake  
via nanobiohybrids

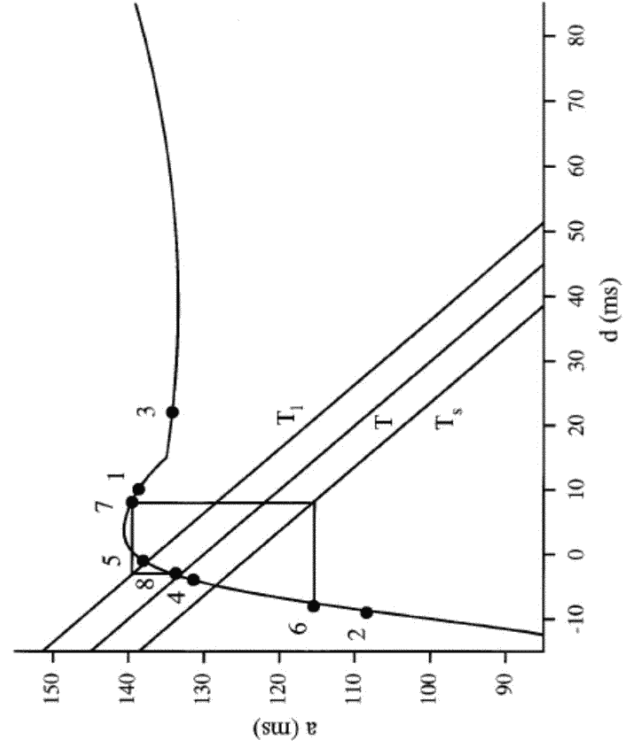


### Control of chaotic dynamics

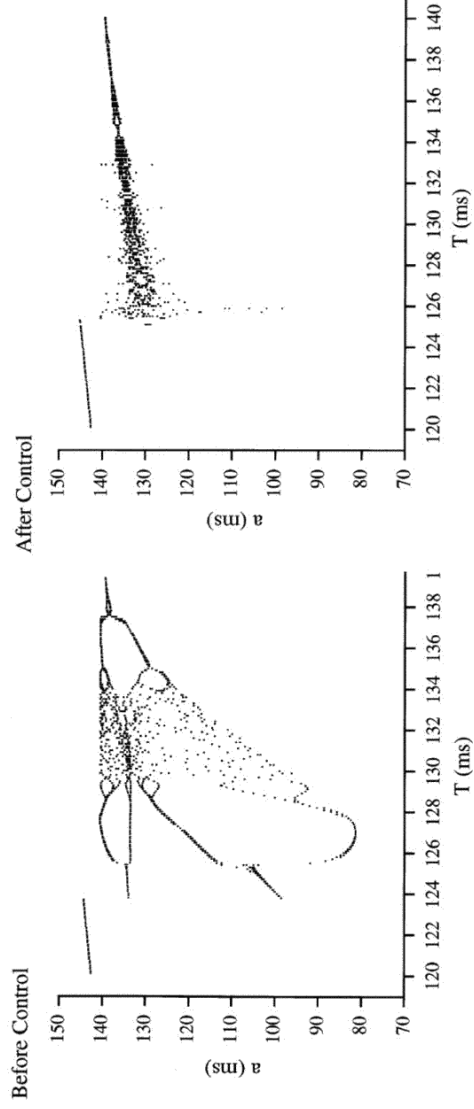


Watanabe and Gilmour, J. Math. Biol., 1996

### Control of chaotic dynamics

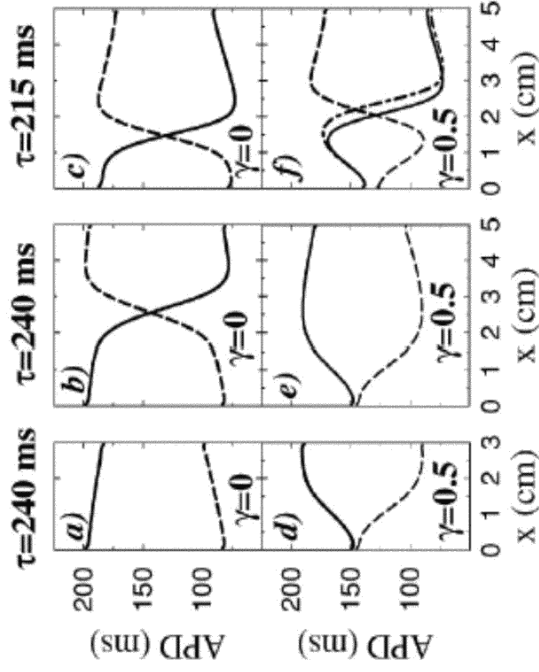


## Control of chaotic dynamics

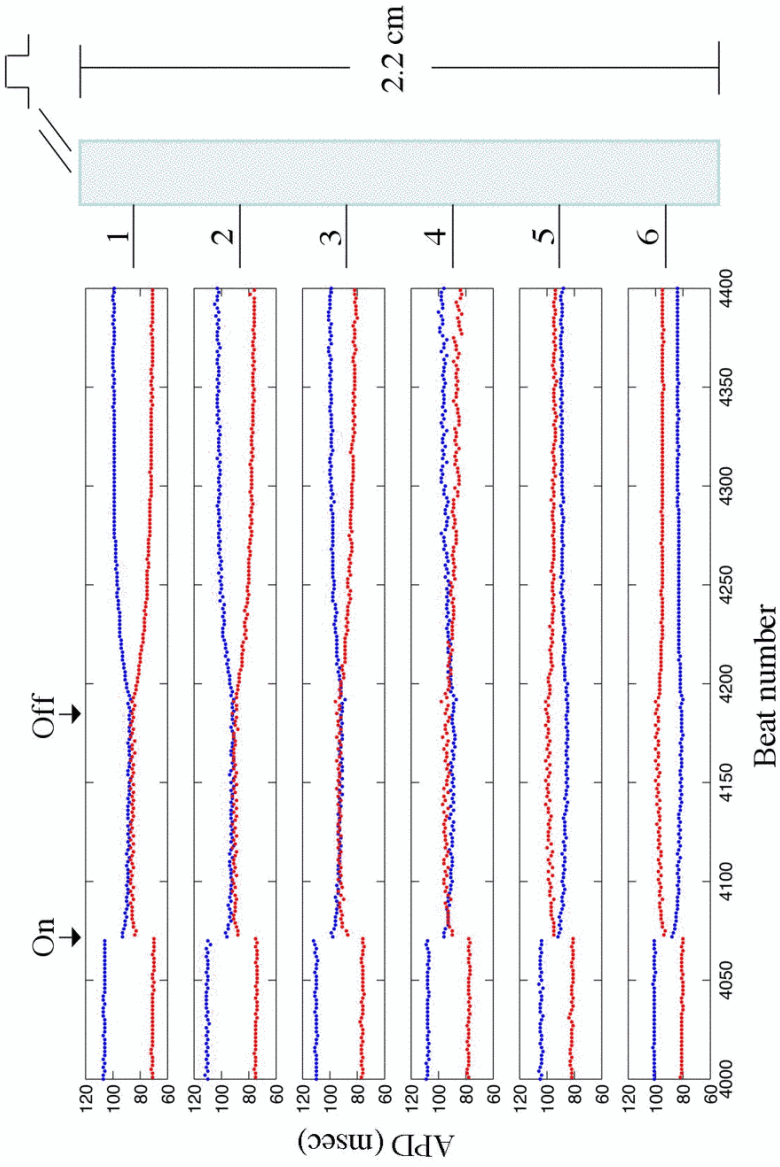


## Alternans control: theory

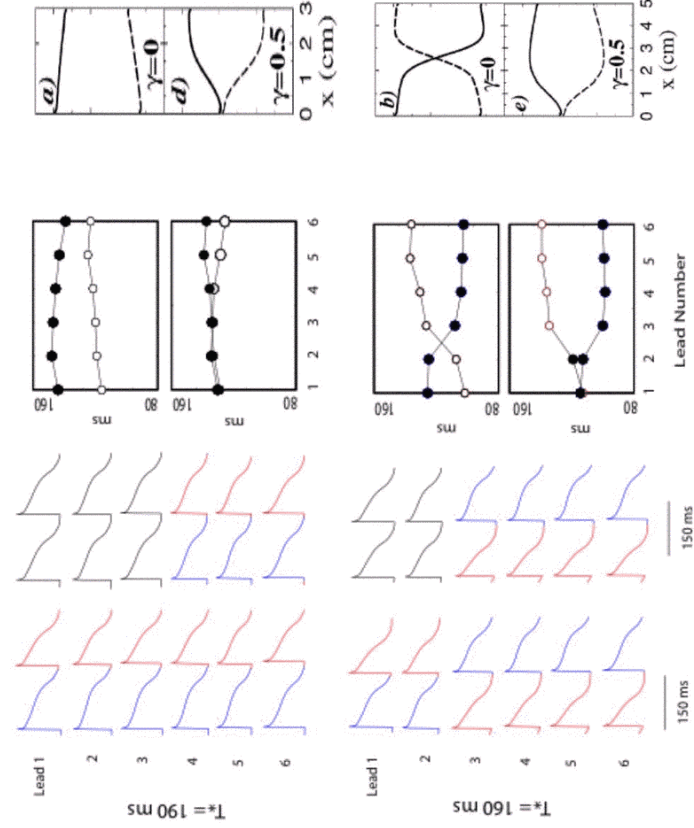
$$\text{Control equation: } T^n = \tau + \frac{\gamma}{2} (\text{APD}^n - \text{APD}^{n-1})$$



### Alternans control: experiment



### Alternans control: experiment vs theory





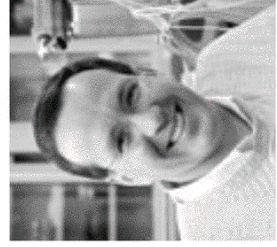
Sydney Moise  
Cornell



Mark Riccio  
Cornell



Jeff Fox  
GNS



Eberhard Bodenschatz  
Cornell



Marcus Koller  
Würzburg



Niels Otani  
Case Western



Dante Chialvo  
UCLA



David Christini  
Cornell Med



Anna Gelzer  
Cornell