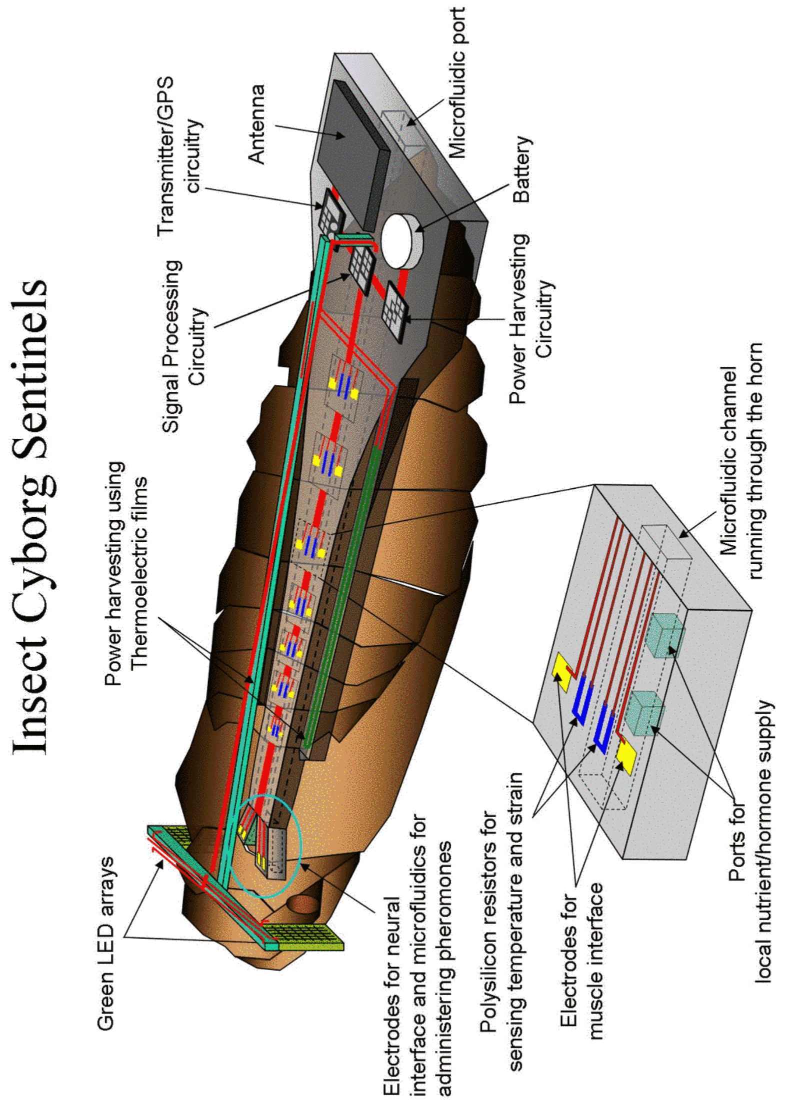
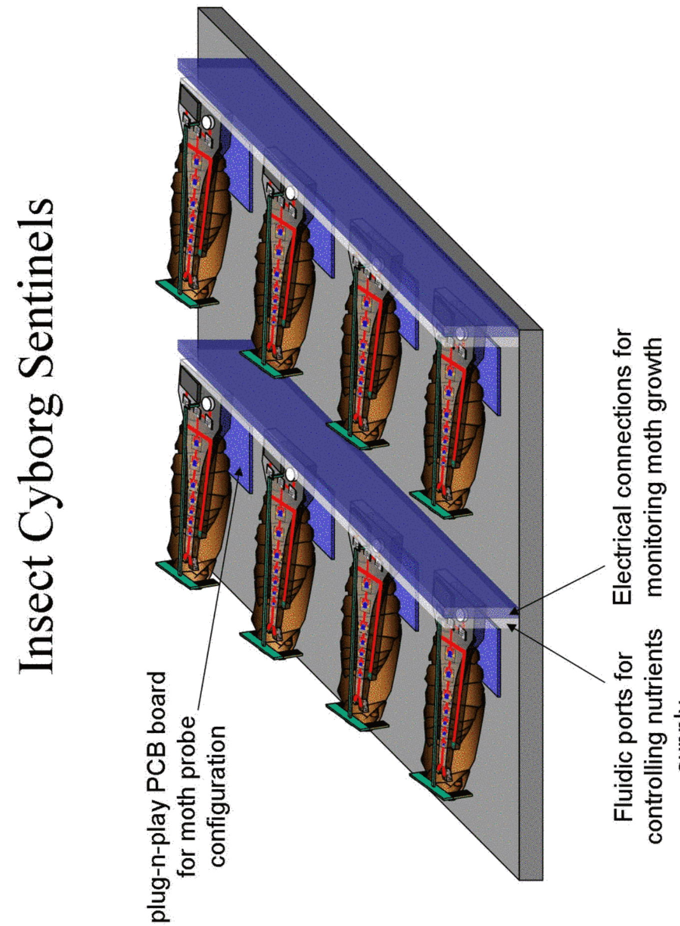
Projects

- Maximizing dynamically induced heterogeneity of refractoriness to facilitate the induction of conduction block and reentry
- Using virtual electrodes to pace cardiac tissue at multiple sites and suppress tachycardia and fibrillation
- Locating and tracking phase singularities during ventricular fibrillation
- Building ionic models of ventricular myocardium
- Controlling local action potential duration dynamics
- Investigating the role of APD and CV restitution in the development of ventricular tachyarrhythmias
- Engineering insect cyborg sentinels

Projects

- Maximizing dynamically induced heterogeneity of refractoriness to facilitate the induction of conduction block and reentry
  - **Niels Otani**
- Using virtual electrodes to pace cardiac tissue at multiple sites and suppress tachycardia and fibrillation
  - **Valentin Krinski** (theory)
  - **Stefan Luther** (experiments)
- Locating and tracking phase singularities during ventricular fibrillation
  - **Eberhard Bodenschatz**
- Building ionic models of ventricular myocardium
  - **Elizabeth Cherry**
- Controlling local action potential duration dynamics
  - **Alain Karma** (theory)
  - **Dave Christini** (experiment)
- Investigating the role of APD and CV restitution in the development of ventricular tachyarrhythmias
  - **Flavio Fenton**
- Engineering insect cyborg sentinels


Insect Cyborg Sentinels
Transmitter/GPS circuitry
Antenna
Microfluidic port
Battery
Signal Processing Circuitry
Power Harvesting Circuitry
Power harvesting using Thermoelectric films
Microfluidic channel running through the horn
Green LED arrays
Electrodes for neural interface and microfluidics for administering pheromones
Polysilicon resistors for sensing temperature and strain
Electrodes for muscle interface
Ports for local nutrient/hormone supply


Insect Cyborg Sentinels
plug-n-play PCB board for moth probe configuration
Electrical connections for monitoring moth growth
Fluidic ports for controlling nutrients supply

So what’s left?

So what’s left?

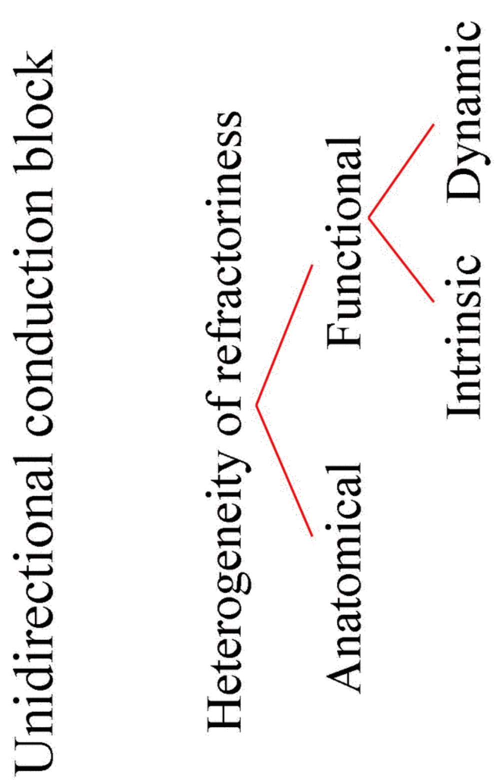
Lunch

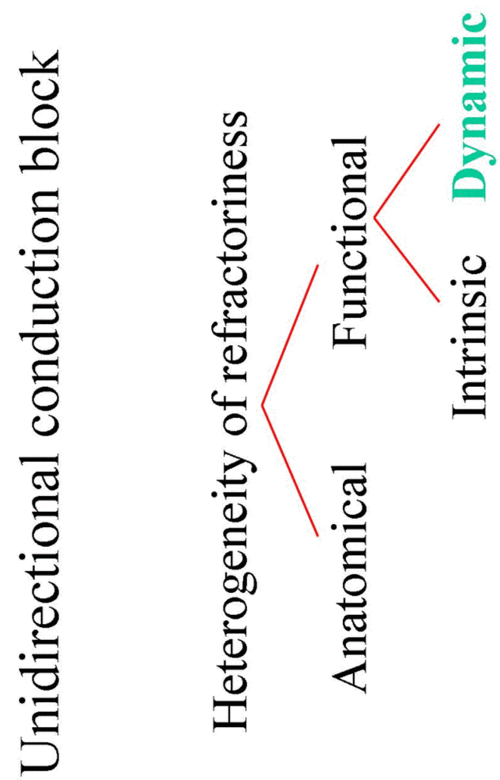
Induction of reentry

- Unidirectional conduction block
- Slow conduction
- Re-excitation of previously blocked region

Induction of reentry

- **Unidirectional conduction block**
- Slow conduction
- Re-excitation of previously blocked region


Unidirectional conduction block
Heterogeneity of refractoriness
Anatomical
Functional
Intrinsic
Dynamic

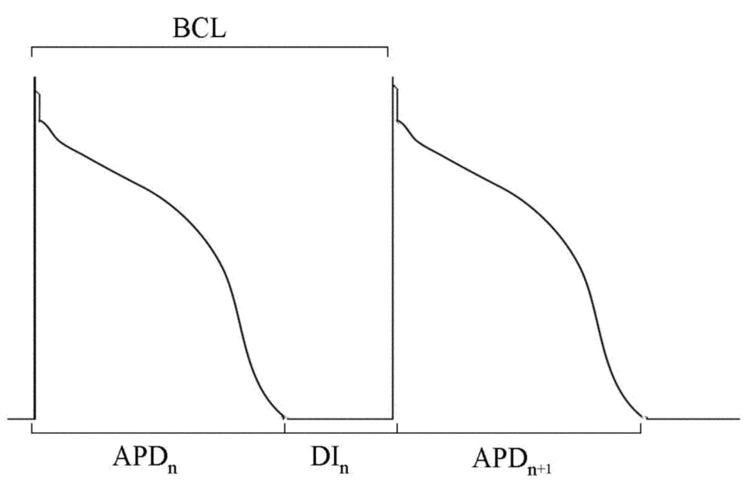

Unidirectional conduction block
Heterogeneity of refractoriness
Anatomical
Functional
Intrinsic
Dynamic

Dynamic heterogeneity

Restitution of:

- Action potential duration (APD)
- Conduction velocity (CV)

APD restitution



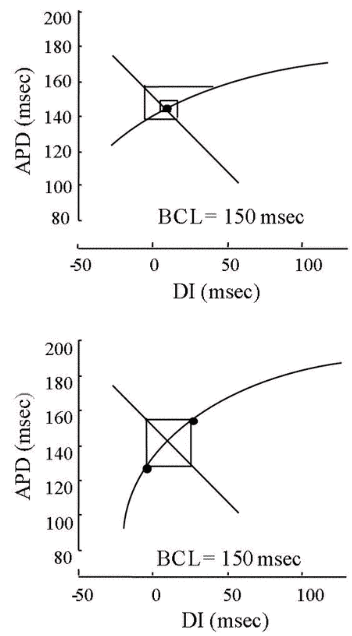
$BCL = APD + DI$

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

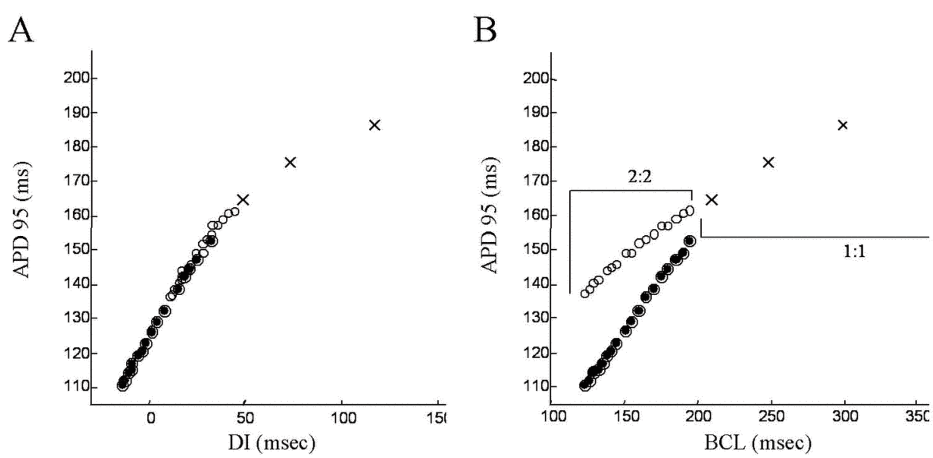
Restitution and APD dynamics

Slope < 1

Slope > 1

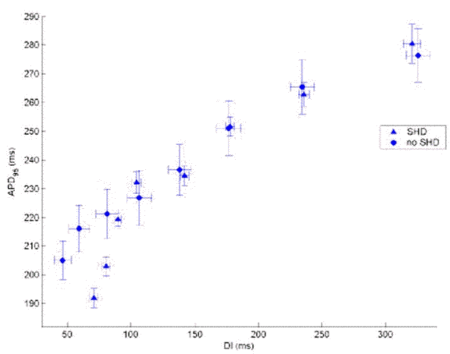


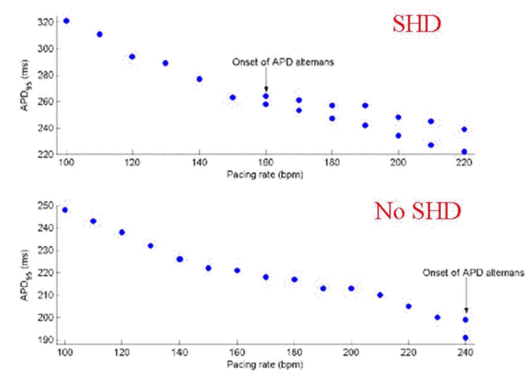
APD alternans: dog



Koller *et al*, AJP, 1998

APD alternans: human

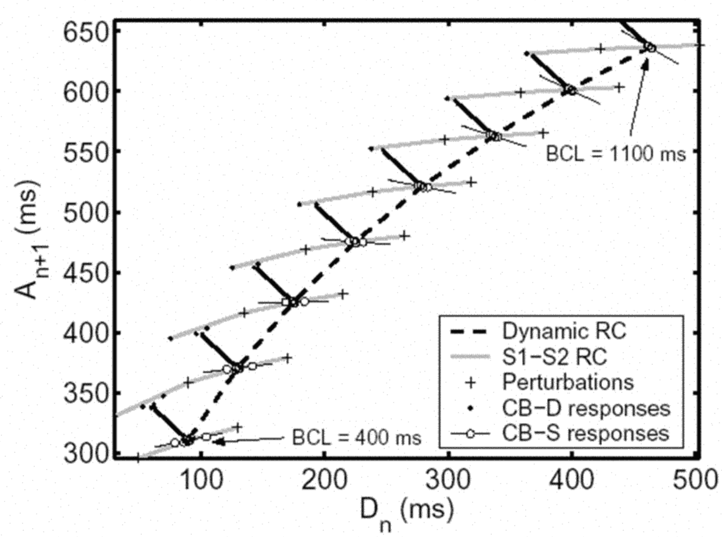




Koller *et al*, Circulation, 2005

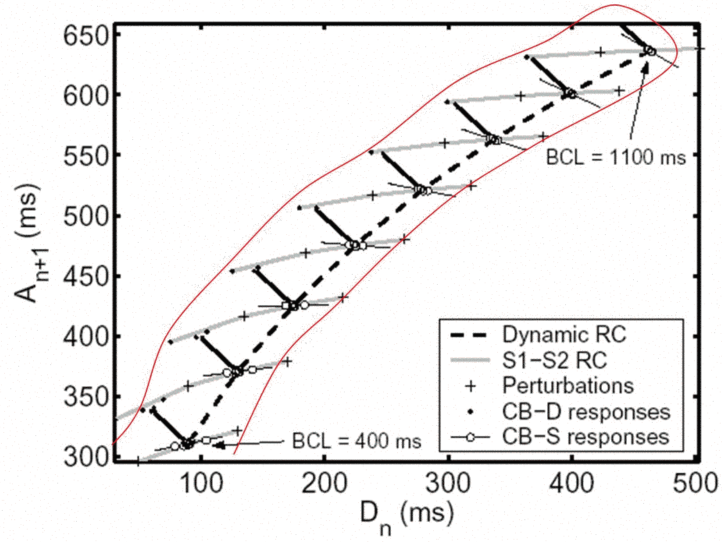
No SHD = 12
SHD = 24 (17 ICM)

Restitution and APD dynamics (for real)



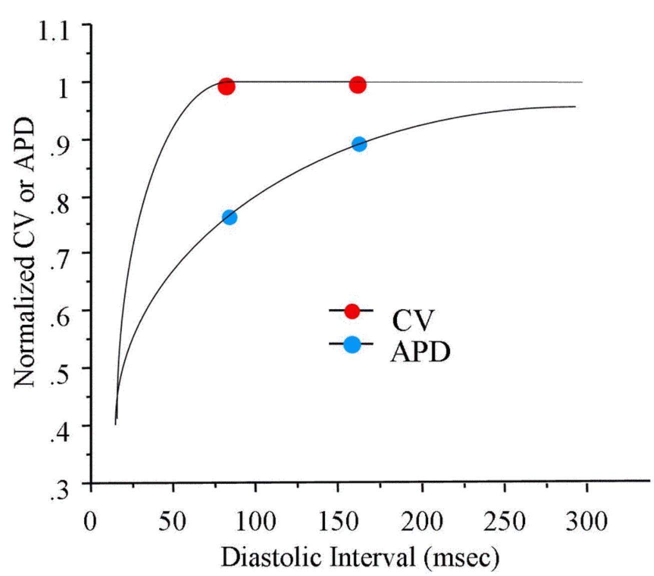
Kalb *et al*, JCE, 2004

Restitution and APD dynamics (for real)

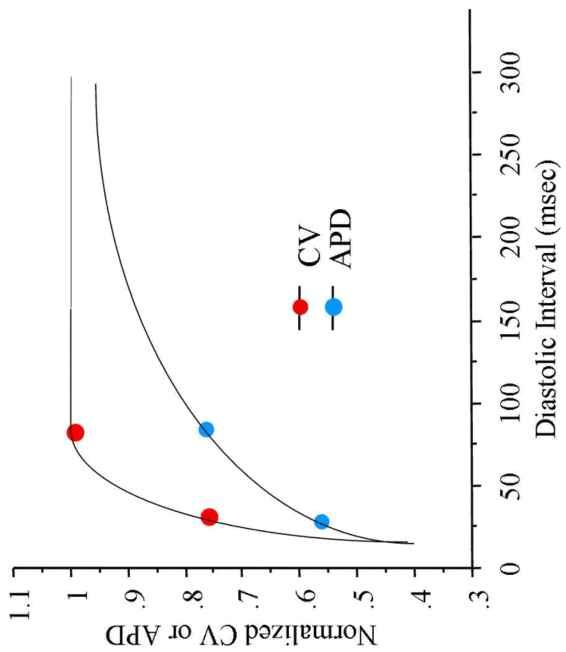


Kalb *et al*, JCE, 2004

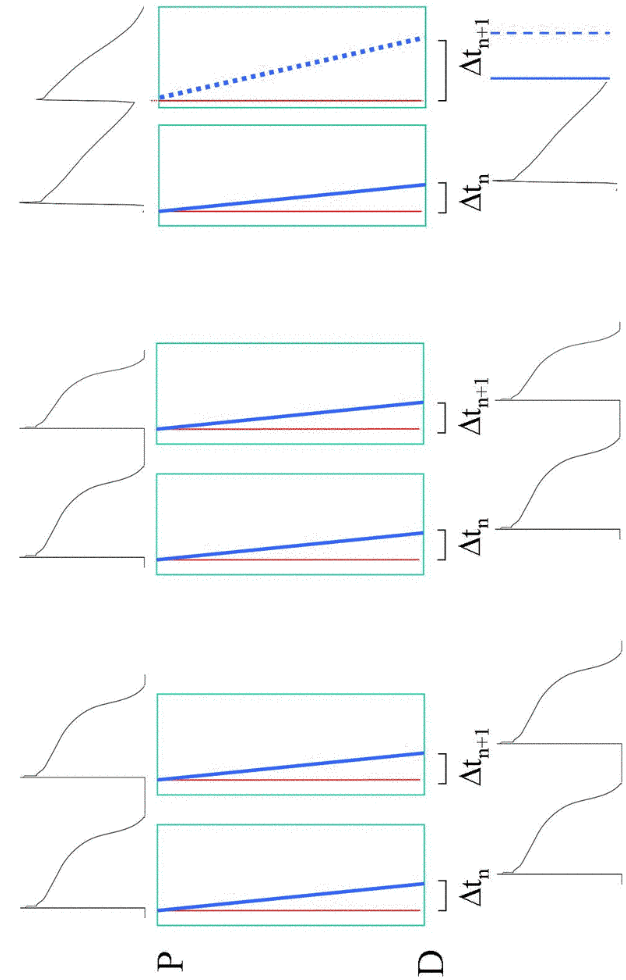
APD and CV restitution



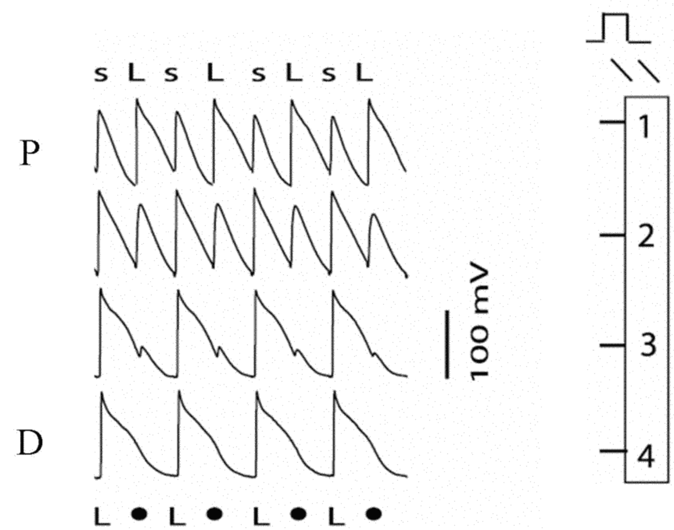
APD and CV restitution



CV Restitution

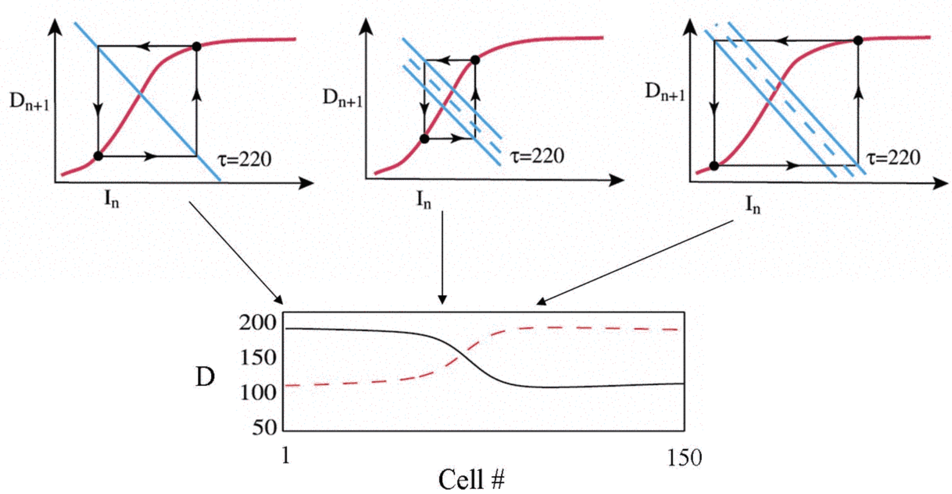


Discordant APD alternans and conduction block

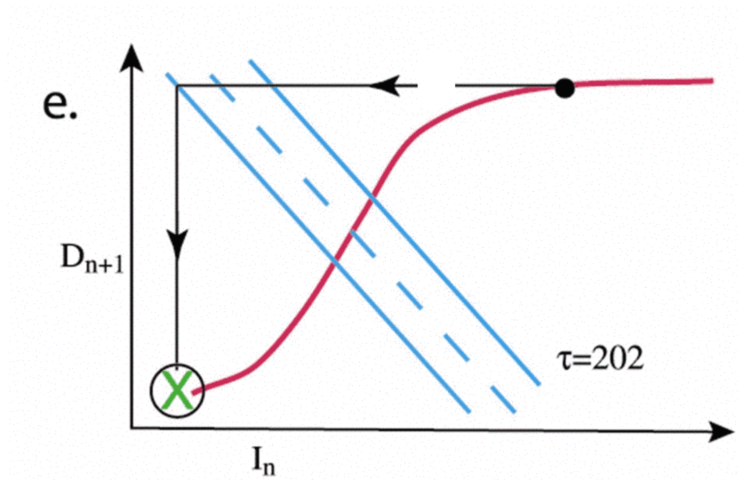


Fox *et al*, Circ Res, 2002

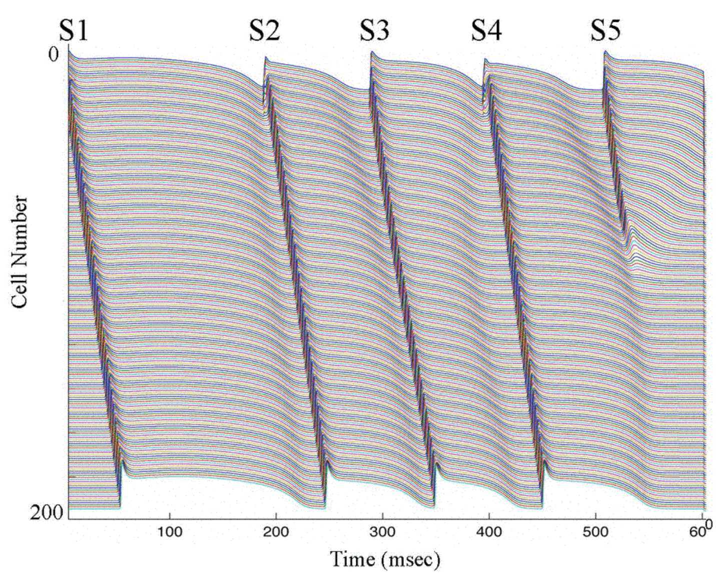
Mechanism for transition from concordant to discordant APD alternans



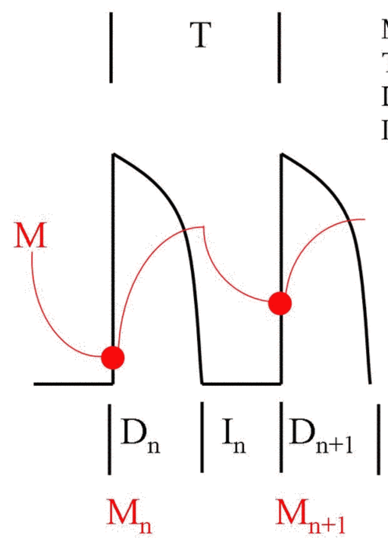
Mechanism for transition from discordant APD alternans to conduction block



Discordant APD pattern leading to conduction block



Return map memory model



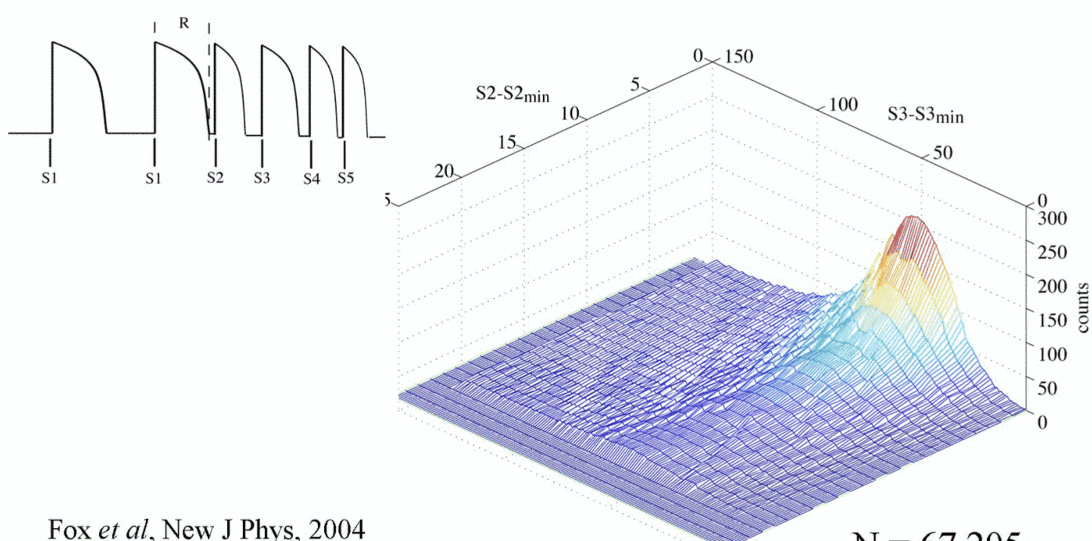
M: **M**emory
T: stimulus period (**T**ime)
D: action potential **D**uration
I: diastolic **I**nterval

$$M_{n+1} = g(M_n, I_n, D_n) = e^{I_n/\tau_m}(1 + (M_n - 1)e^{-D_n/\tau_m})$$

$$D_{n+1} = f(M_{n+1}, I_n) = \frac{A(1 - M_{n+1})}{1 + e^{-\frac{I_n - B}{C}}}$$

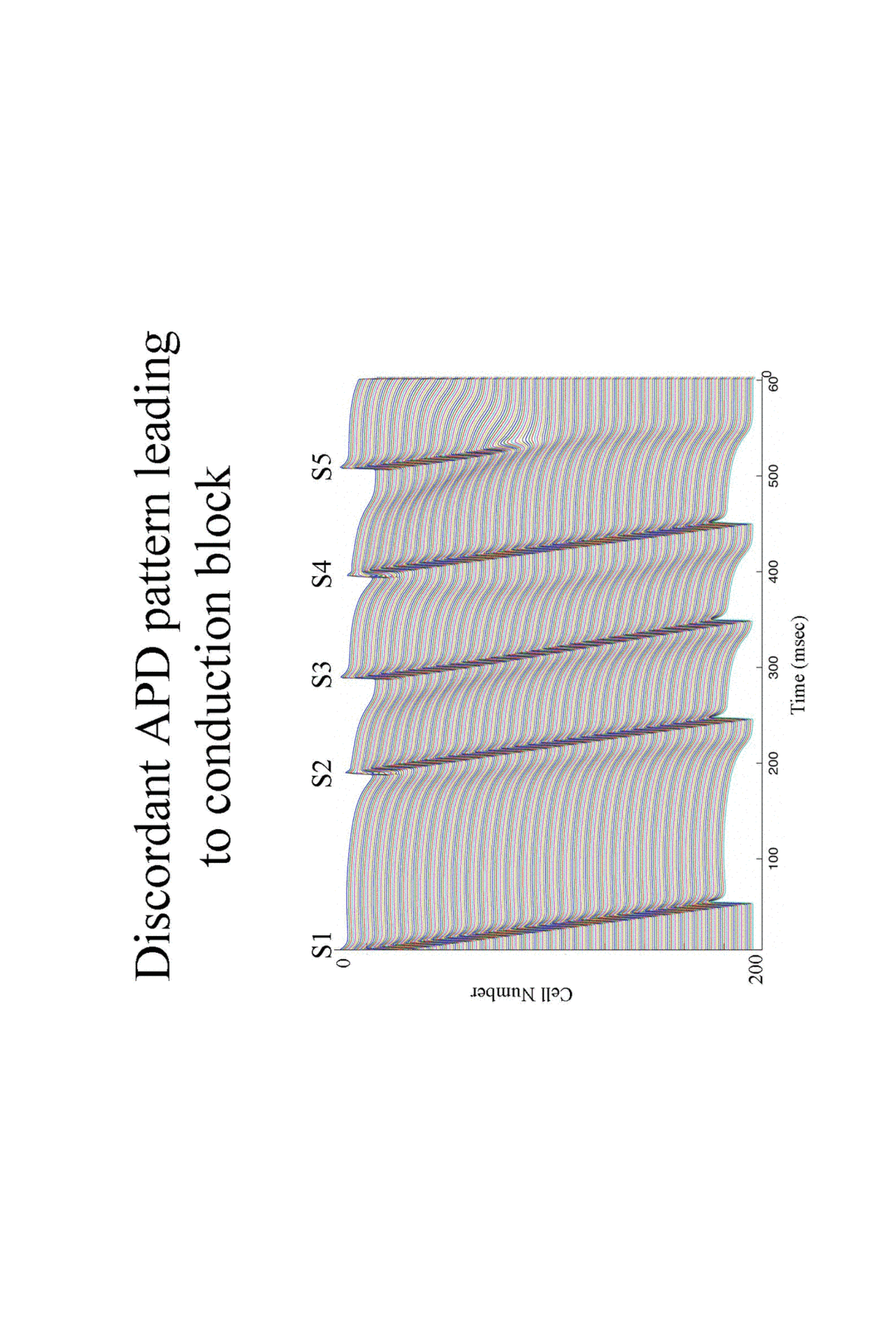
Fox *et al*, PRL, 2002

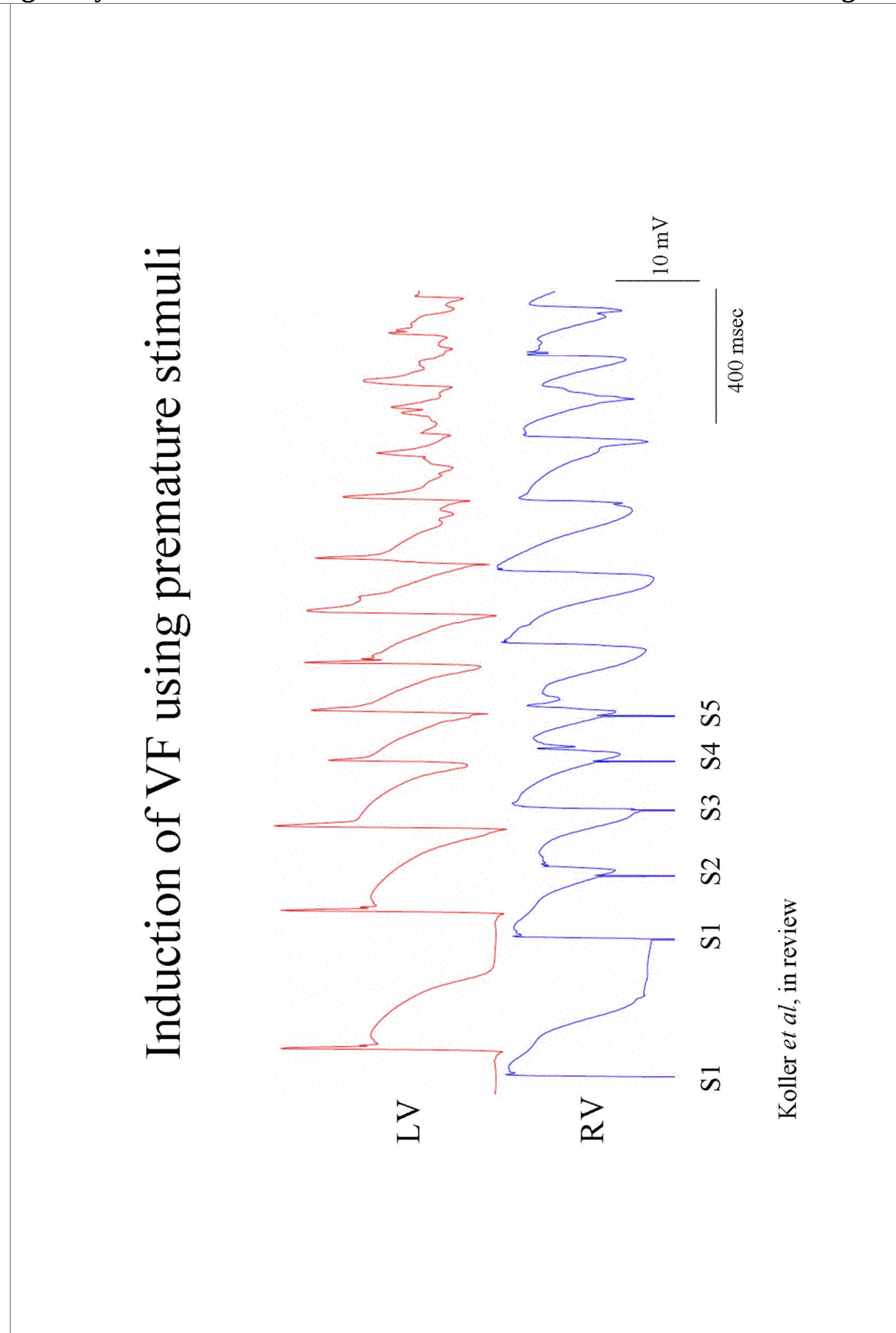
Conduction block for different patterns of premature stimulation: theory



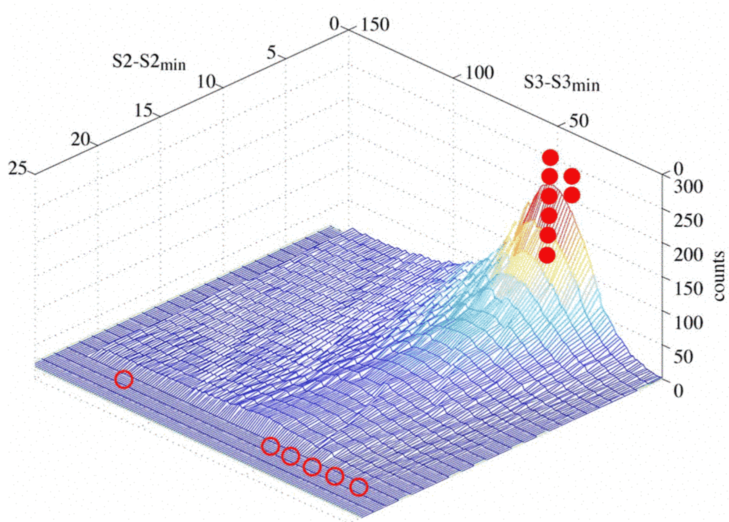
Fox *et al*, New J Phys, 2004

N = 67,205

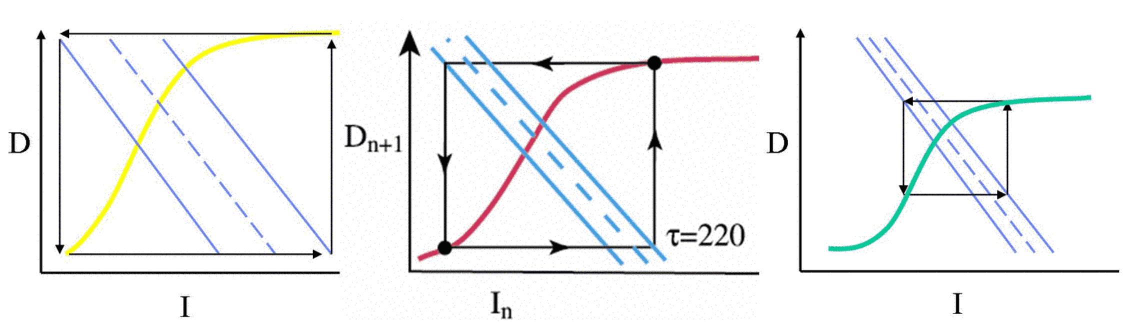

Discordant APD pattern leading to conduction block
S1
S2
S3
S4
S5
Cell Number
0
200
Time (msec)
0
100
200
300
400
500
600


Induction of VF using premature stimuli
LV
RV
10 mV
400 msec
S1
S1
S2
S3
S4
S5
Koller *et al*, in review

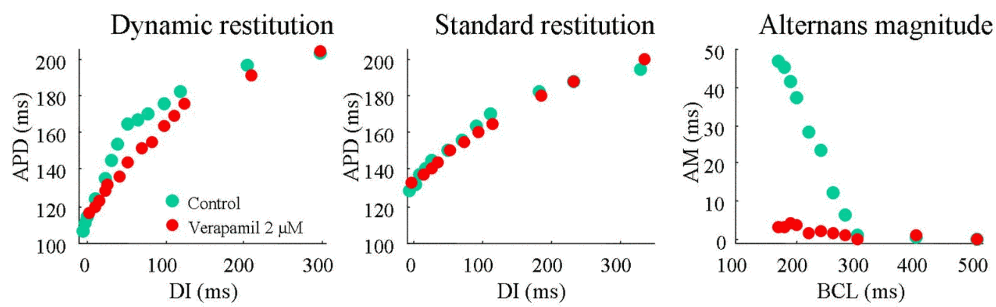
Conduction block for different patterns of premature stimulation: experiment



Role of APD heterogeneity for transition from concordant to discordant alternans

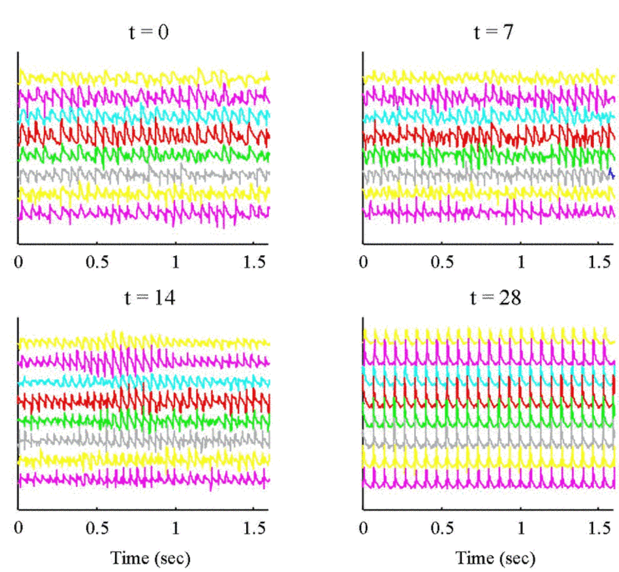


Effects of verapamil on APD restitution



Riccio *et al*, Circ Res, 1999

Effects of verapamil on VF



Effects of verapamil on electrophysiologic and hemodynamic parameters

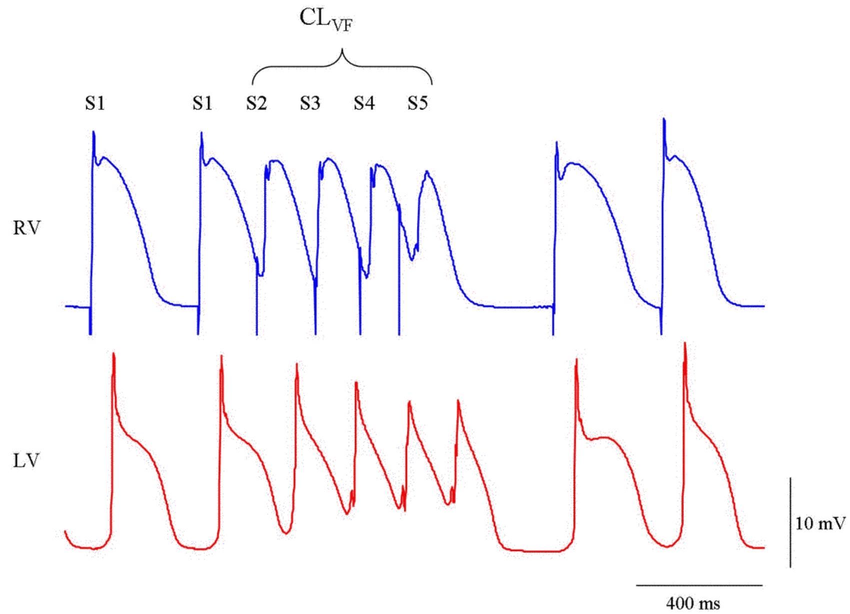
	Control	Vera_lo	Vera_med	Vera_hi
BP_{syst} (mmHg)	164 ± 8	142 ± 7	131 ± 9 *	129 ± 10 *
BP_{diast} (mmHg)	98 ± 8	82 ± 8	71 ± 5 *	59 ± 7 ¶
BP_{mean} (mmHg)	127 ± 6	105 ± 8	96 ± 6 ¶	93 ± 7 ¶
HR (bpm)	140 ± 6	105 ± 4 ¶	97 ± 5 ¶	83 ± 5 ¶
PR (ms)	94 ± 8	119 ± 7 *	147 ± 9 ¶	207 ± 10 ¶
APD_{95} RV (ms)	214 ± 4	223 ± 9	238 ± 9 *	238 ± 8 *
APD_{95} LV (ms)	220 ± 4	241 ± 10	240 ± 8 *	245 ± 10 *

V_{lo} = 0.1 mg/kg/h
V_{med} = 0.3 mg/kg/h
V_{hi} = 1.0 mg/kg/h
each dose preceded by a bolus dose of 0.1 mg/kg.

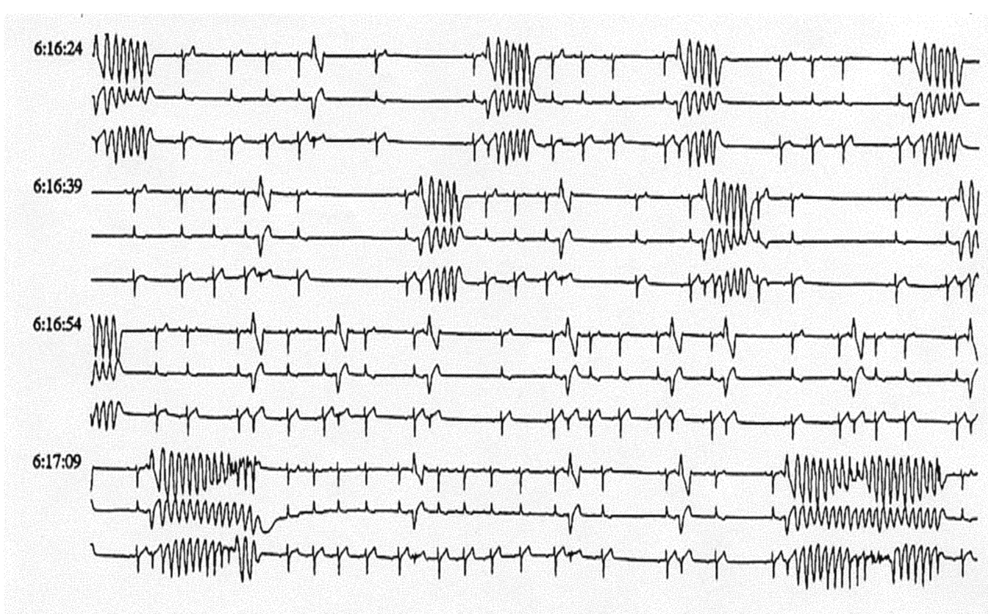
Effects of verapamil on electrophysiologic parameters and VF induction

	Control	V_{lo}	V_{med}	V_{hi}
APDR	**1.44 ± 0.13**	1.22 ± 0.07 *	1.07 ± 0.06 *	**1.06 ± 0.06 ***
ΔCT (ms)	**19.6 ± 2.6**	17.2 ± 2.4	11.5 ± 2.0 *	**6.1 ± 1.2** ¶
APD_{diff} (ms)	**99 ± 16**	94 ± 12	82 ± 15	**66 ± 13 ***
VF induction	**8 of 8**	6 of 8	4 of 8	**1 of 8**

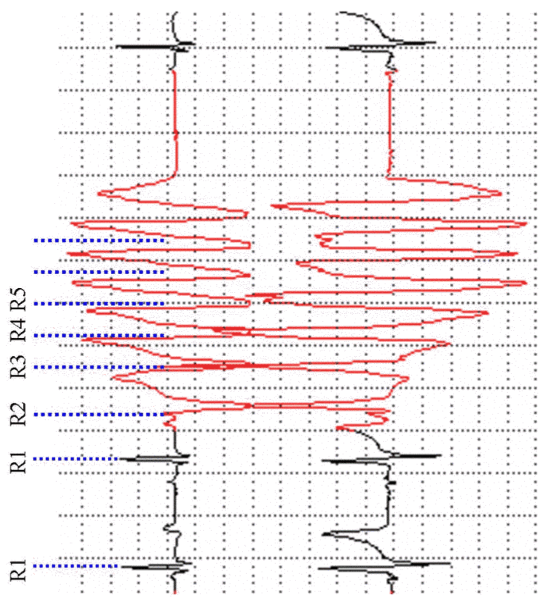
Non-induction of VF using premature stimuli after verapamil



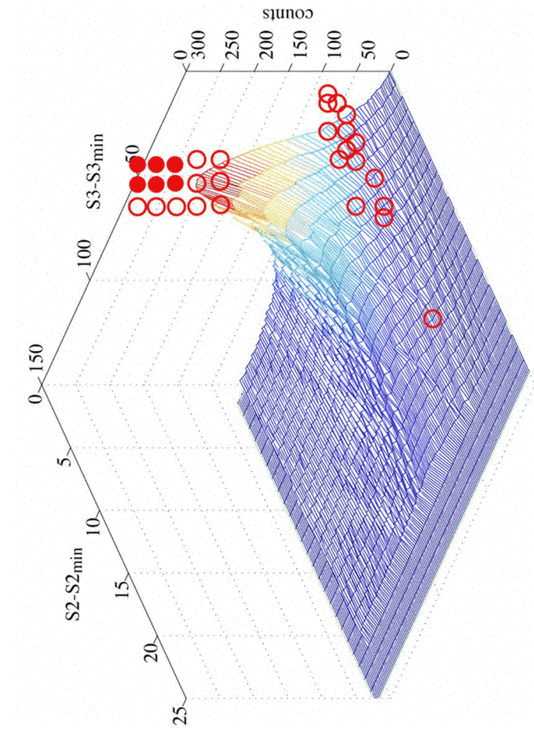
Spontaneous VT in German shepherd dogs



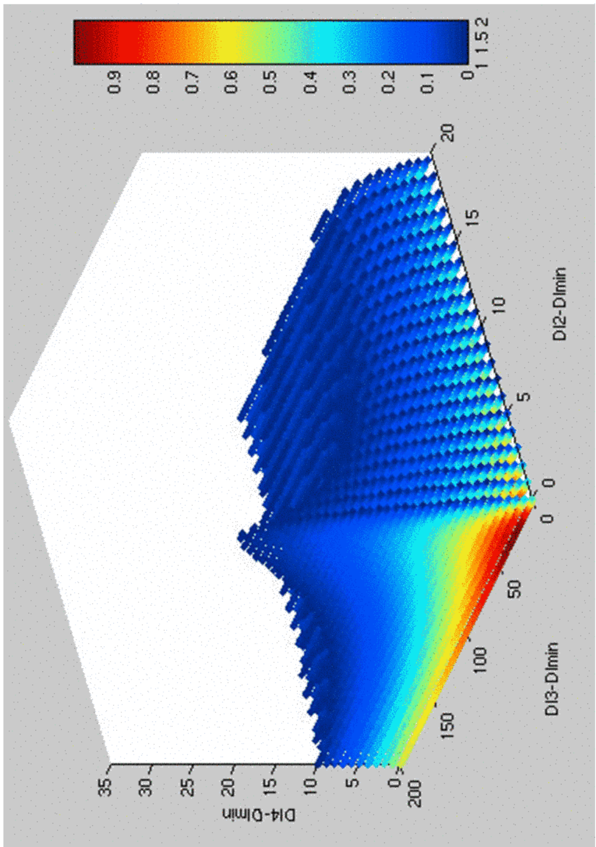
Spontaneous VT in a German shepherd dog



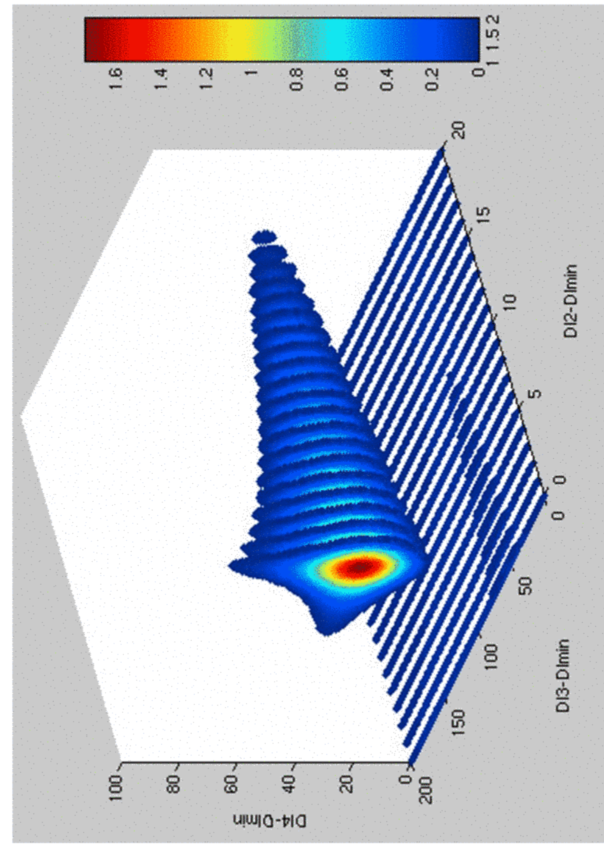
Incidence of conduction block in German shepherds



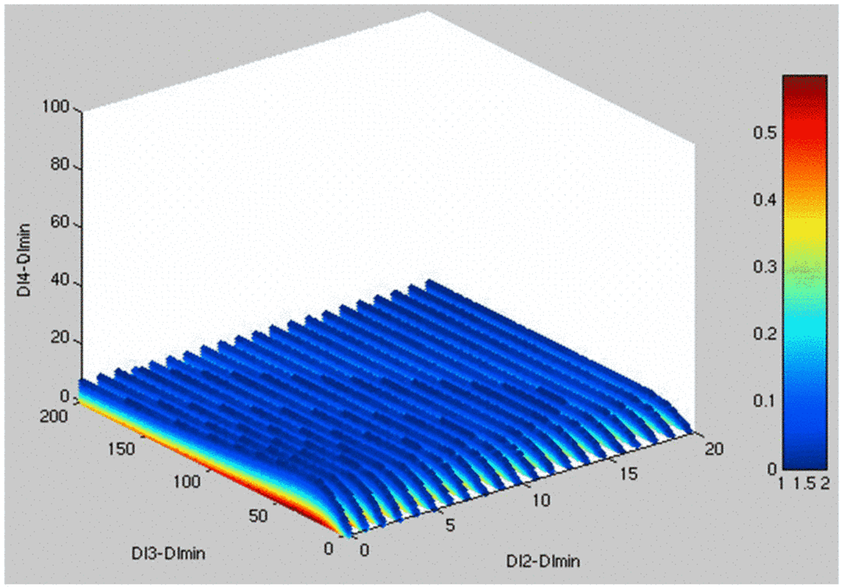
Predicted incidence of conduction block in German shepherd ventricle



Predicted incidence of conduction block in German shepherd ventricle



Predicted incidence of conduction block in German shepherd ventricle

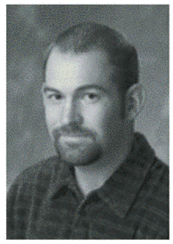


Potential Implication

If the form of the APD and CV restitution relations are known, predictions can be made with respect to which sequences of premature stimuli will precipitate conduction block and, perhaps, VF.

Sydney Moïse
Cornell

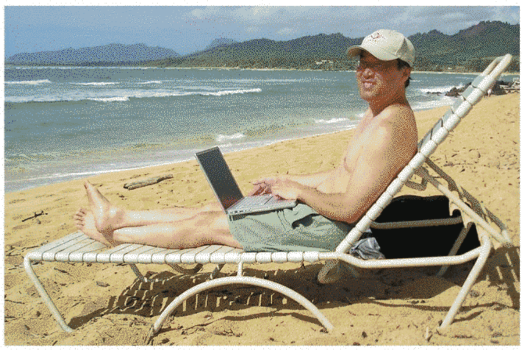
Mark Riccio
Cornell



Jeff Fox
GNS

Marcus Koller
Würzburg

Anna Gelzer
Cornell



Niels Otani
Cornell