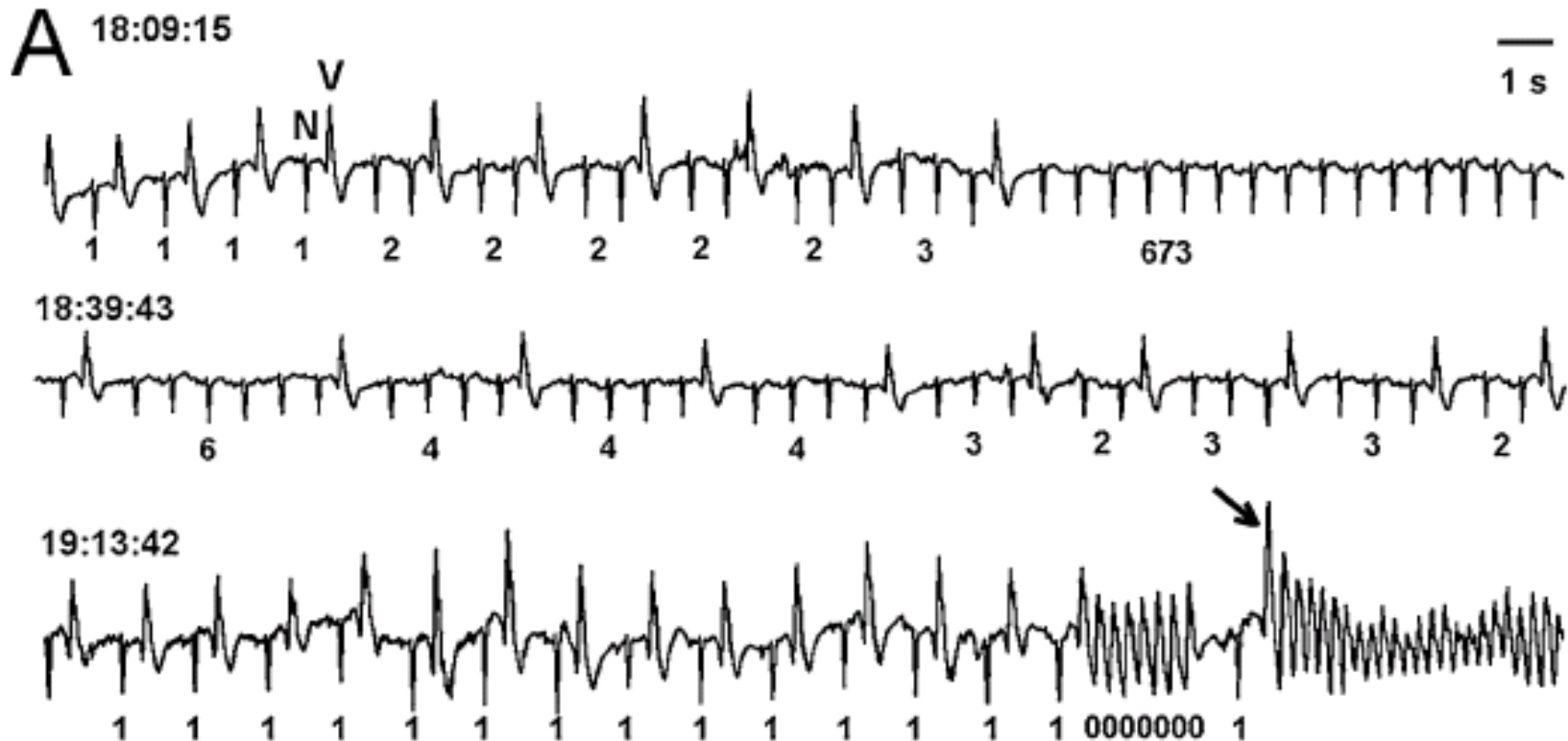


Simple Models for Cardiac Oscillations and Arrhythmias

Leon Glass

Isadore Rosenfeld Chair in
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Montreal, Quebec

Sudden death. Why did this 82 yr old woman die at 19:13:42 and not at 18:09:15 ?



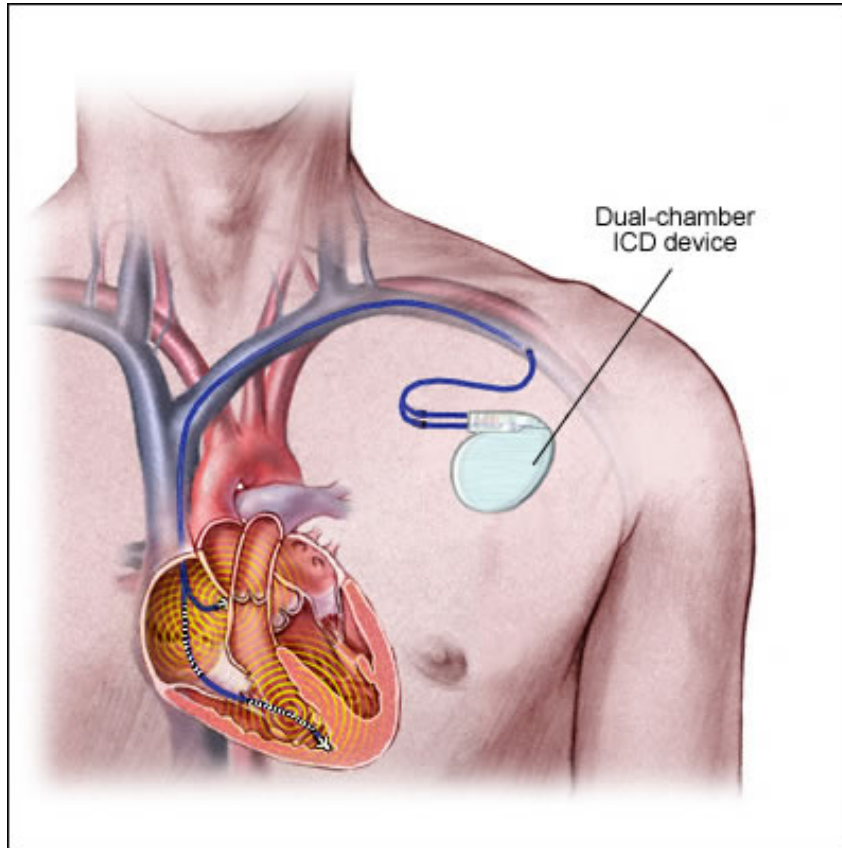
Sequence of NIB values

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2	2	2	2	2	2	2	2	2	2	1318	5	3	1	2	1	3	1	1	2	1	1	1	1
1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
1	1	1	1	1	0	1	1	1	1	1	1	1	0	0	1	0	2	2	1	1	1	1	1
1	1	1	1	1	1	1	1	1	1	1	2	1	2	1	1	2	2	2	2	2	2	2	2
2	2	2	2	2	2	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	0	2	2	
2	2	2	2	2	2	2	2	2	3	4	4	4	3	4	5	4	4	5	4	4	4	3	4
4	3	3	2	5	4	3	4	3	4	3	4	3	4	4	2	3	3	3	2	3	4	4	4
6	4	6	5	4	4	4	5	4	4	4	4	4	8	2	5	4	4	8	6	7	6	6	6
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4	4	6	4	4	4	3	2	3	3	2	4	4	4	4	4	4	4	4	4	4	5	4	4
5	6	6	4	5	4	6	4	8	6	4	4	4	5	5	6	4	5	4	4	4	4	4	4
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1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	1	1

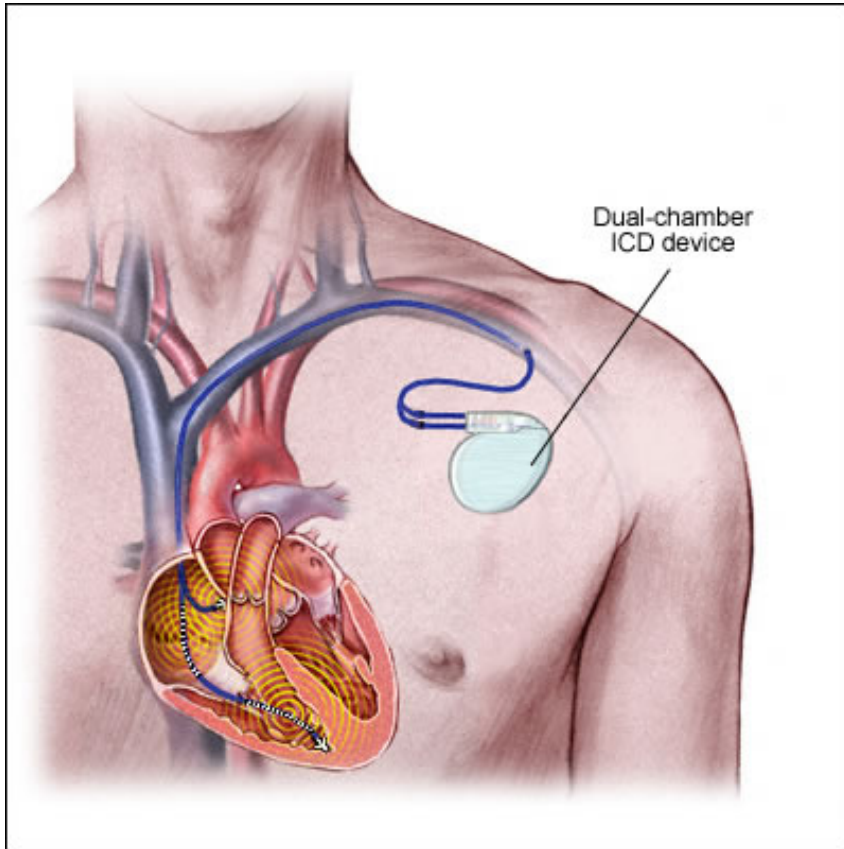
Challenge – A practical problem facing cardiologists

- (To understand the transition from sinus rhythm to ventricular tachycardia/fibrillation in individual patients in order) To better assess the risk for sudden cardiac death

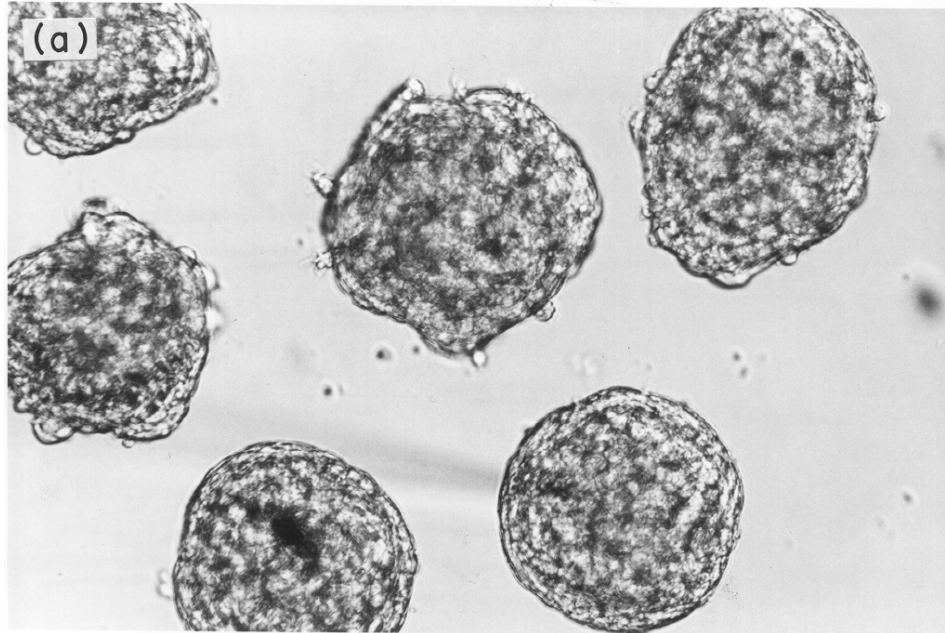
Implantable Cardiac Defibrillators (ICD) reduce the incidence of sudden death



Implantable Cardioverter Defibrillators (ICD) reduce the incidence of sudden death



Model System – Embryonic chick heart tissue culture (Guevara, Shrier, Glass 1980s)

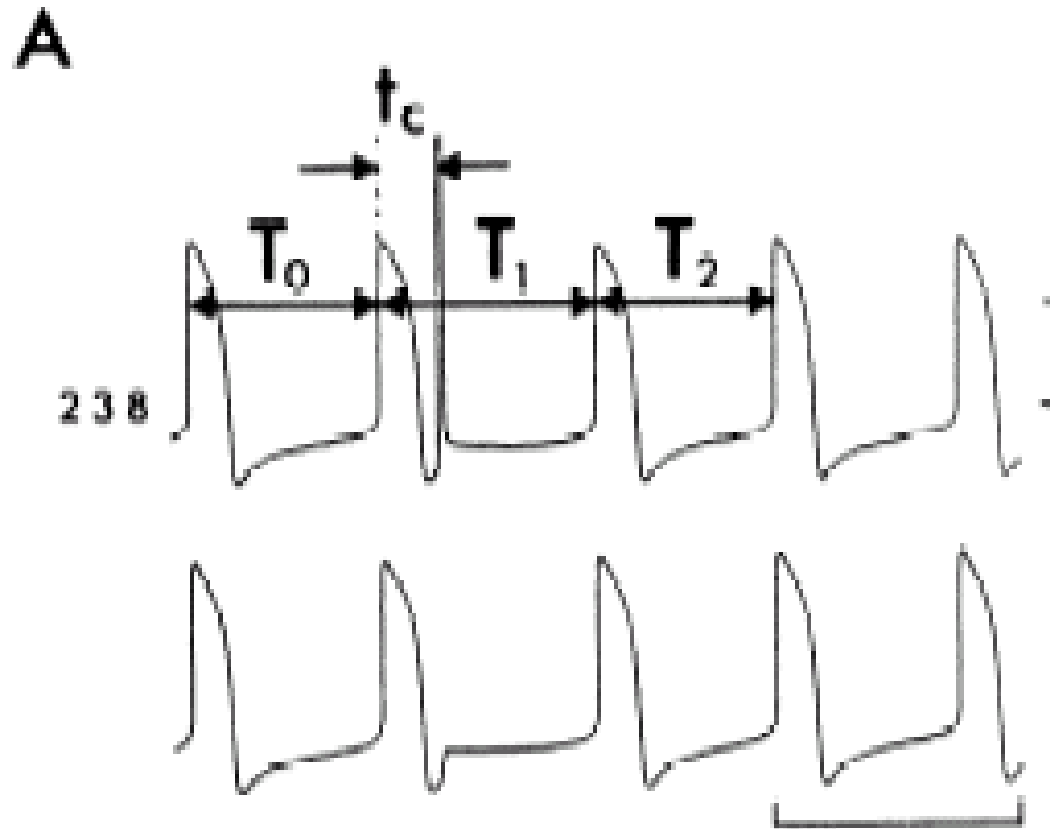


What experiments can be done?

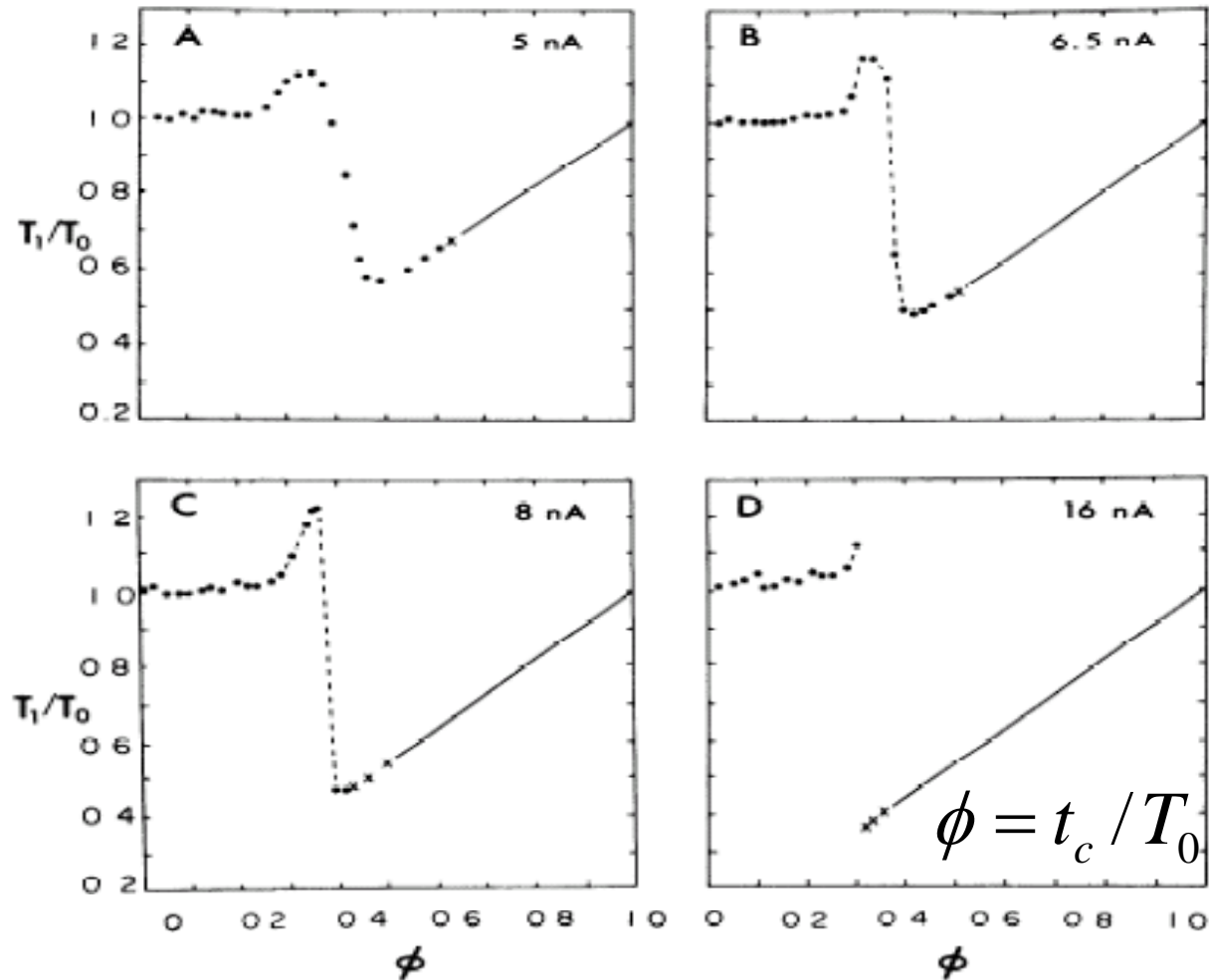
What experiments can be done?

- Phase resetting (model of a clinical test – sinus node recovery test)
- Periodic stimulation (model of interacting pacemakers in the heart)
- Fixed delay stimulation (model of reentrant rhythms in the heart)
- Grow cells in different geometries
- Add drugs (model of drug effects on the heart and some mutations)

A Resetting Experiment (in chicken heart)

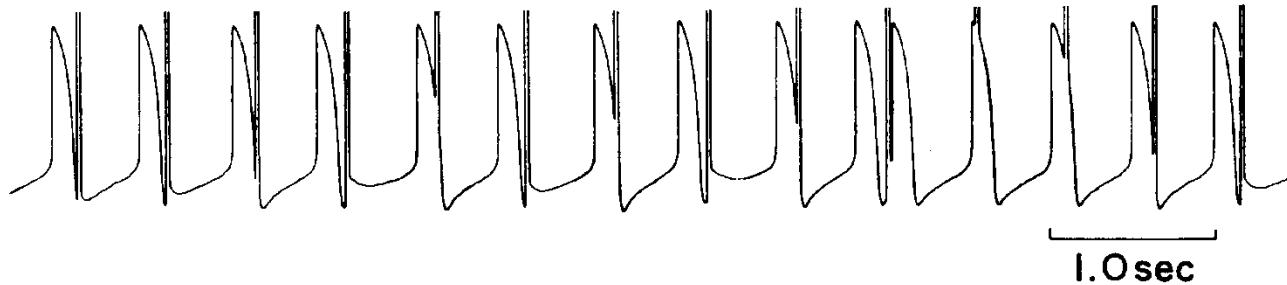


Perturbed Cycle Length Curves



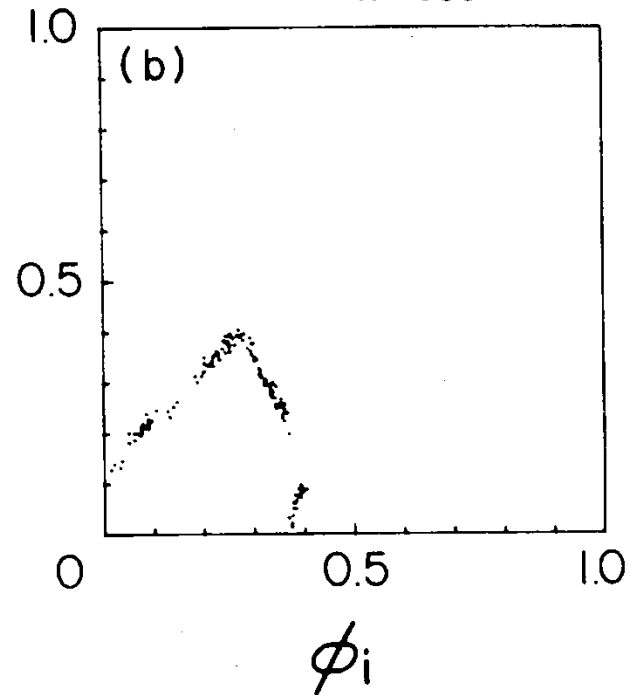
Chaos in periodically stimulated heart cells

(a)



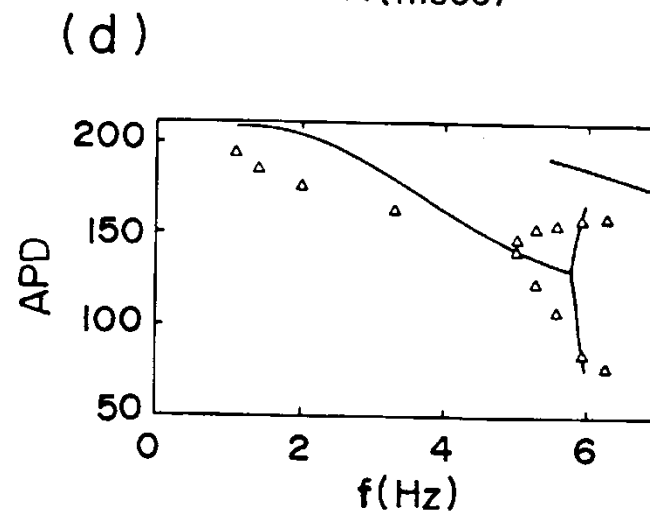
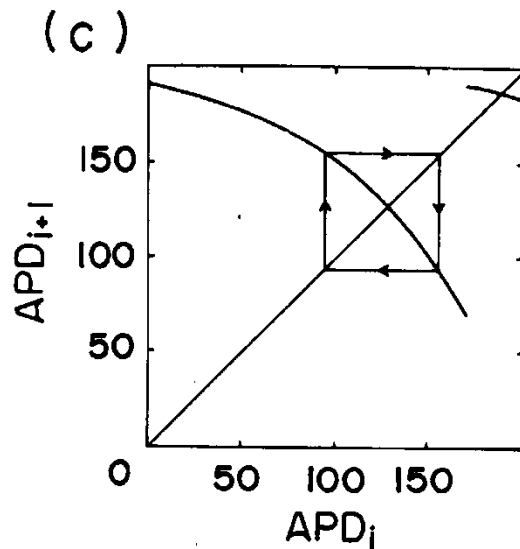
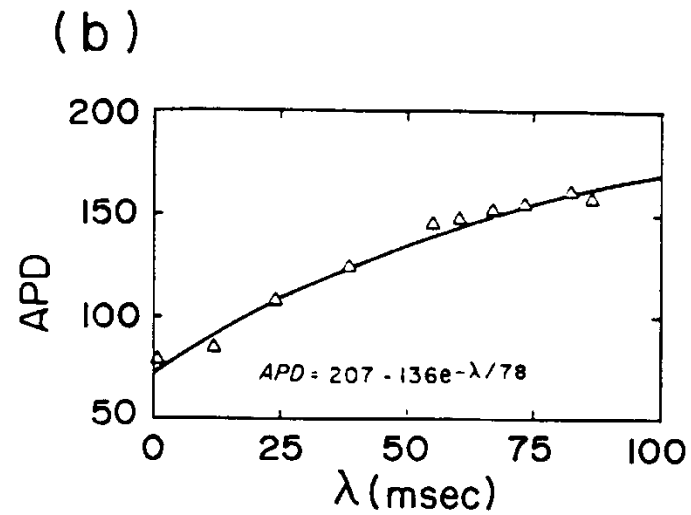
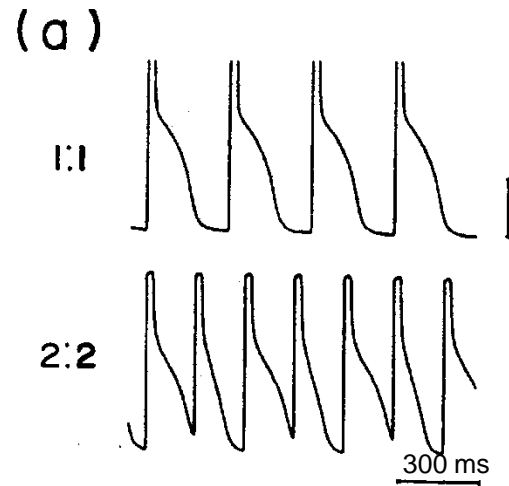
Predict chaos based on
1D circle maps determined
from resetting experiments.
Resetting depends on phase
of stimulus.

$$\phi_{i+1}$$



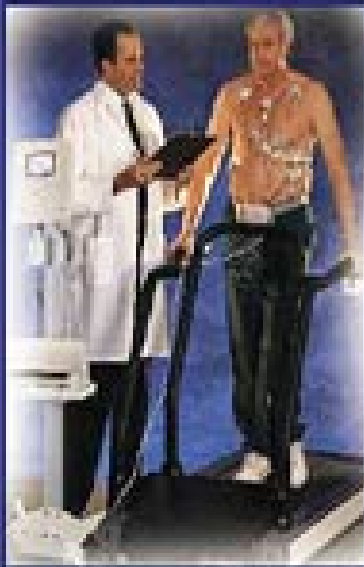
(Guevara, Glass, Shrier 1981)

Alternans in chick hearts



Measure T wave alternans to predict SCD (Cambridge Heart)

Unique Proprietary Technology



HearTwave™



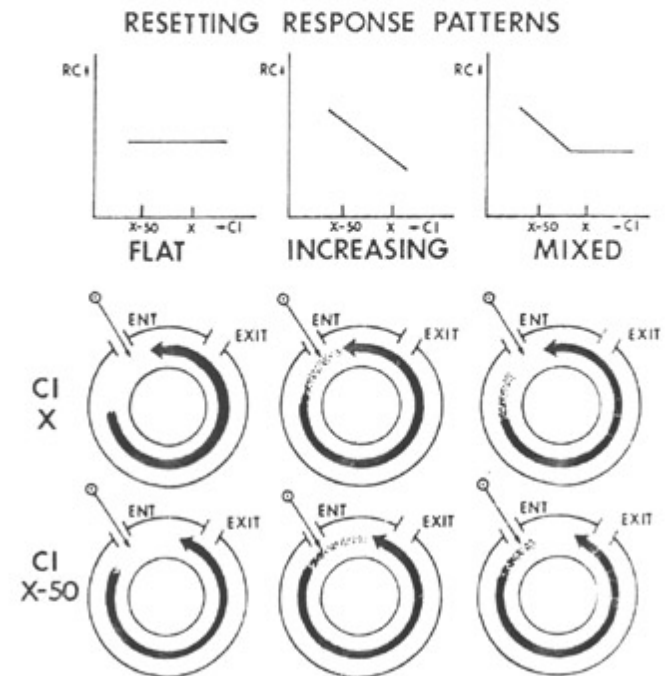
- Microvolt T-Wave Alternans
- Stand alone or simple addition to existing stress test or EP test
- Predicts SCD equal to or better than invasive EP test
- Patent protection

**Reentrant
arrhythmias:
period of oscillation
is set by a reentrant
circuit NOT a
pacemaker**

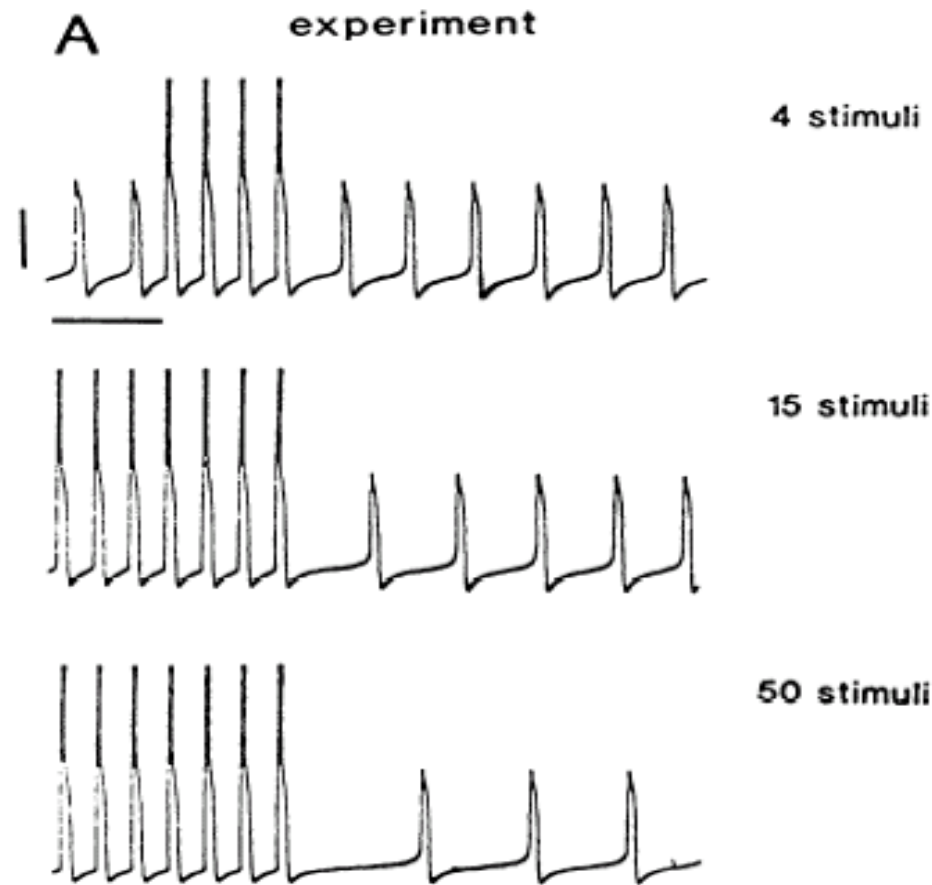


Resetting and Entrainment of Ventricular Tachycardia Associated with Infarction: *Clinical and Experimental Studies*

M. E. JOSEPHSON, D. CALLANS, J. M. ALMENDRAL,
B. G. HOOK, R. B. KLEIMAN

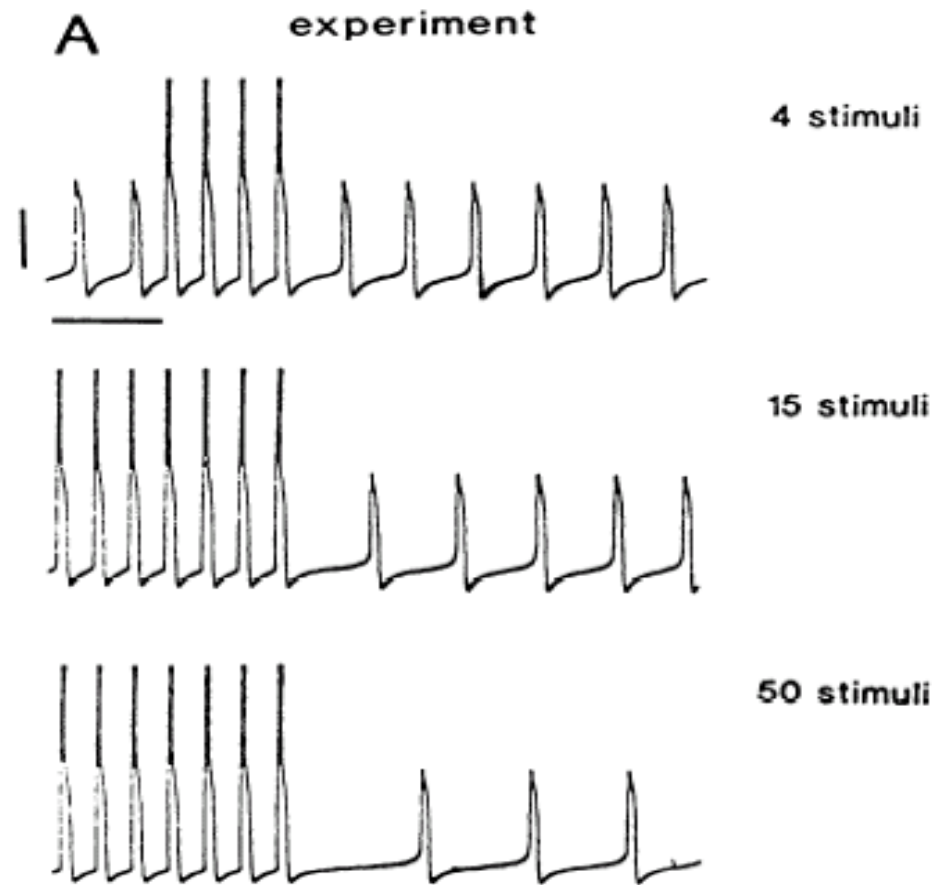


Rapid Stimulation of Chick Heart Cell Aggregates Leads to a Slower Rhythm (Overdrive Suppression)



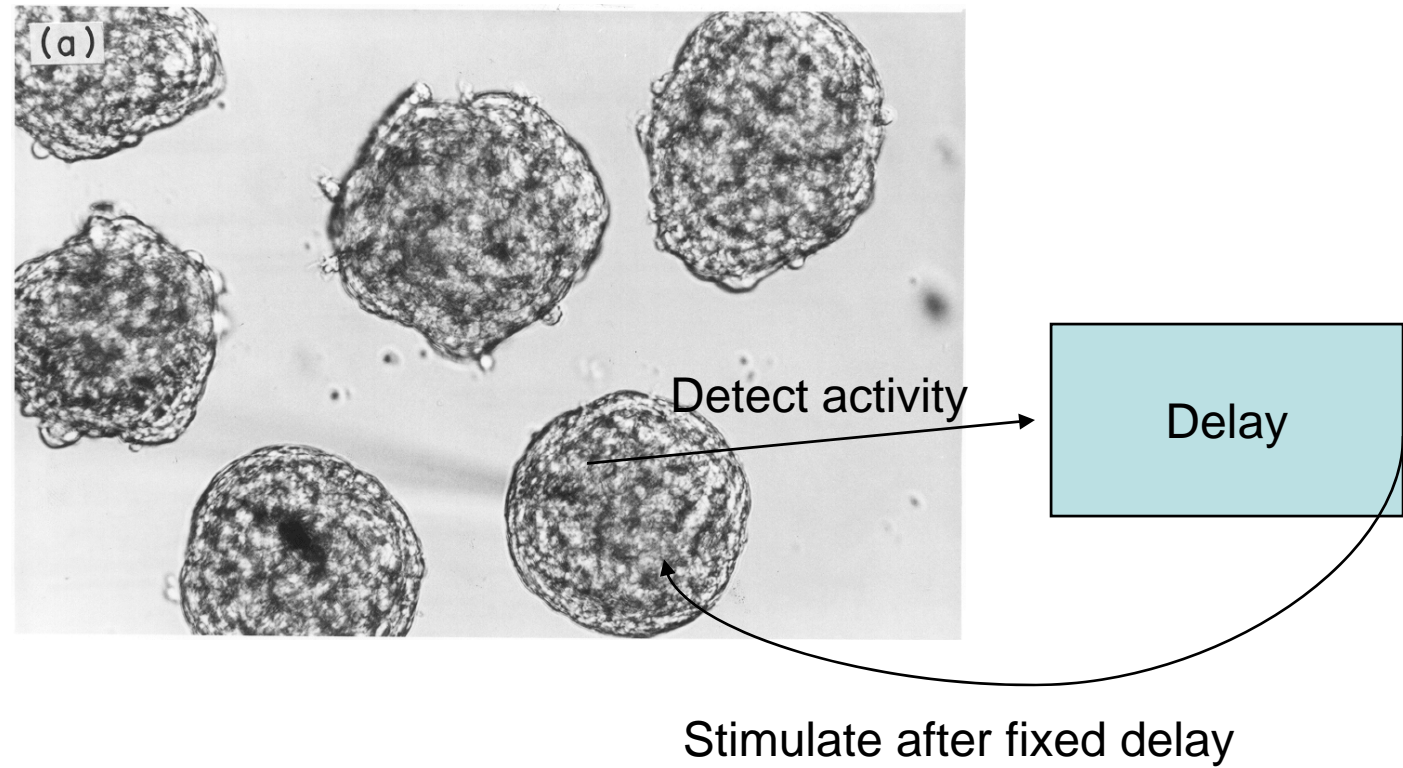
(Kunysz, Glass, Shrier 1995)

Rapid Stimulation of Chick Heart Cell Aggregates Leads to a Slower Rhythm (Overdrive Suppression)

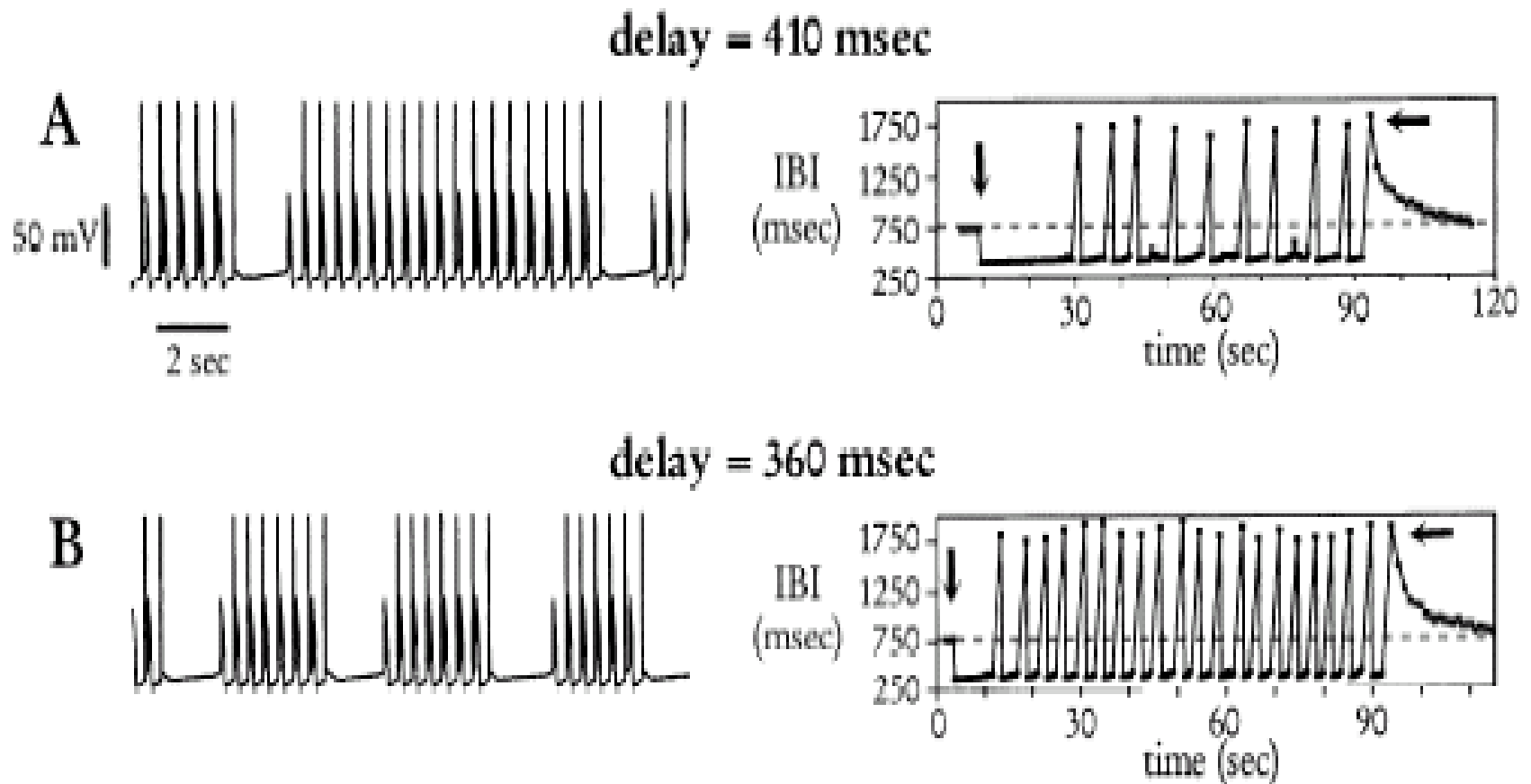


(Kunysz, Glass, Shrier 1995)

Fixed Delay Stimulation



Fixed Delay Stimulation of Cardiac Aggregates Leads to Bursting



...

(Kunysz, Shrier, Glass 1997)