
KITP July 31 2006

Stochastic Aspects of Cardiac Arrhythmias



Trine Krogh-Madsen

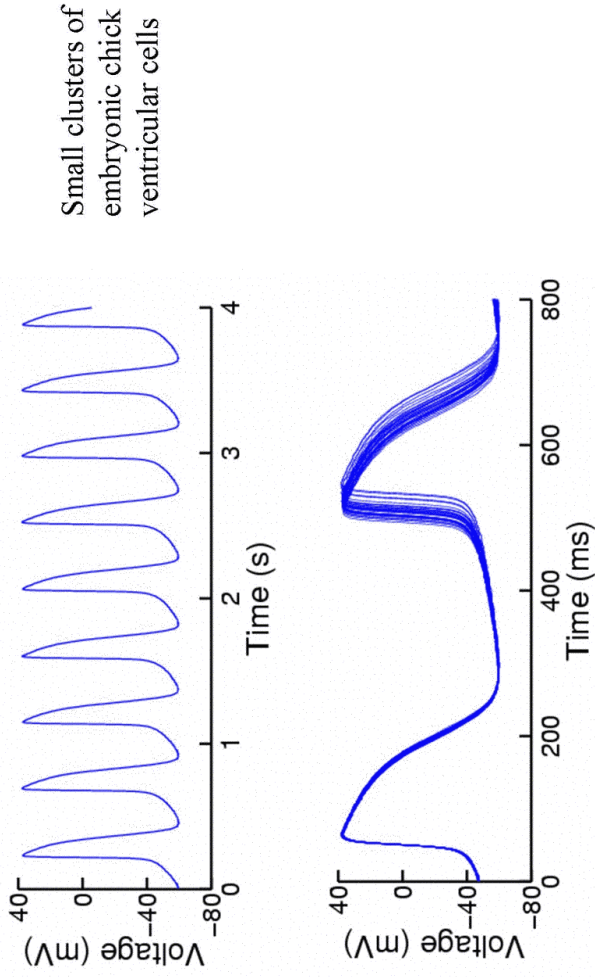
Weill Medical College of Cornell University
Dept. Medicine, Div. Cardiology

Single channel noise



- 1) Effects on regularity of beating of cells
- 2) Effects on phase resetting of cells
- 3) Effects on generation of EADs

Beat-to-beat variability



HH-type model \Leftrightarrow single-channel model

HH-type model

$$I_x(V, t) = g_x \gamma(V - E_x)$$

Krogh-Madsen et al.
AJP Heart & Circ. 2005

Single-channel model

$$g_x = \gamma_x N_x$$

Find γ in literature, compute N

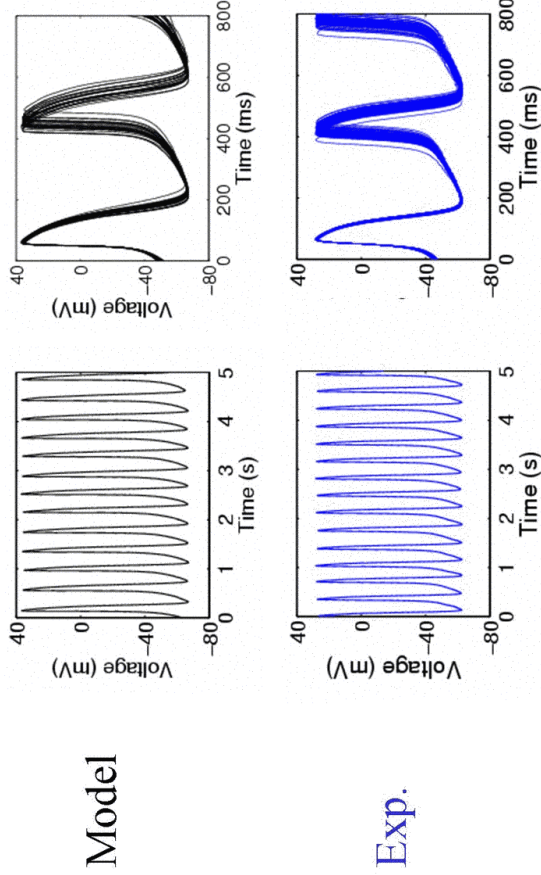
$$N_{Ca} = 15,000; \quad N_{Ks} = 520;$$

I_b and I_{seal} kept deterministic

$$N_{Kr} = 2,700; \quad N_{K1} = 450;$$

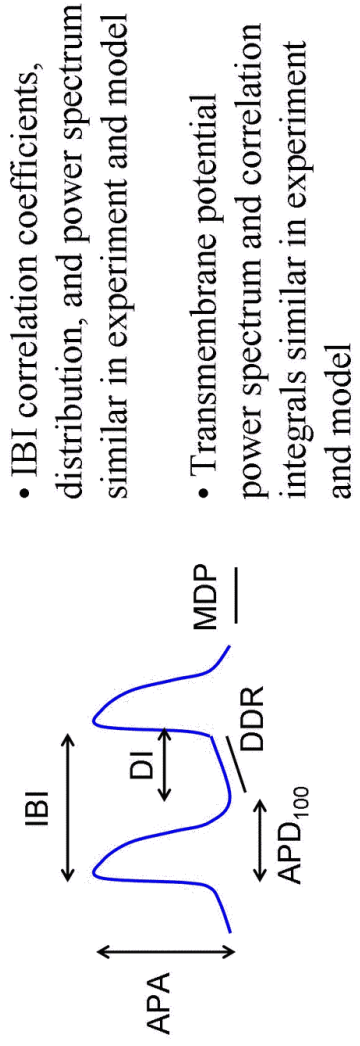
Compute current $I_x(V, t) = \gamma_x N_{x,open}(V - E_x)$

Experiment vs. single-channel model

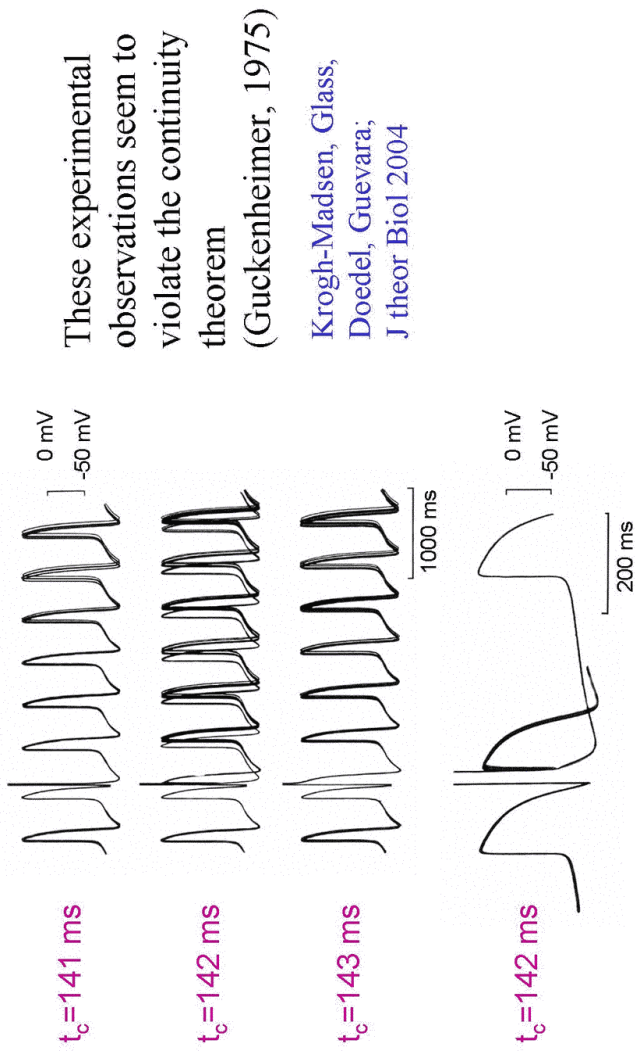


Experiment vs. single-channel model

| | IBI (ms) | APD ₁₀₀ (ms) | DI (ms) | APA (mV) | MDP (mV) | DDR (V/s) | dV/dt _{max} (V/s) |
|-------|----------|-------------------------|---------|----------|----------|-----------|----------------------------|
| Model | 4.4% | 5.4% | 8.1% | 0.7% | 0.6% | 12.2% | 4.0% |
| Exp. | 3.9% | 3.3% | 7.7% | 1.3% | 1.2% | 10.8% | 6.2% |



Single-channel noise in phase-resetting

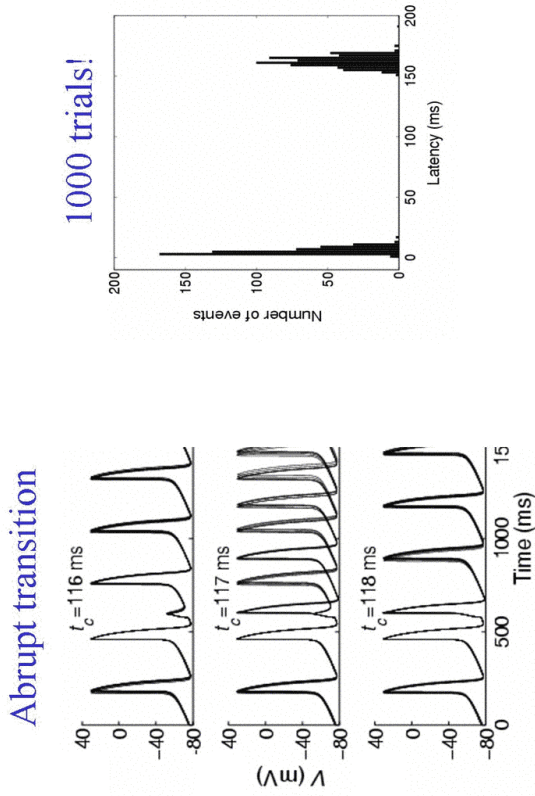


These experimental observations seem to violate the continuity theorem (Guckenheimer, 1975)

Krogh-Madsen, Glass, Doedel, Guevara, J theor Biol 2004

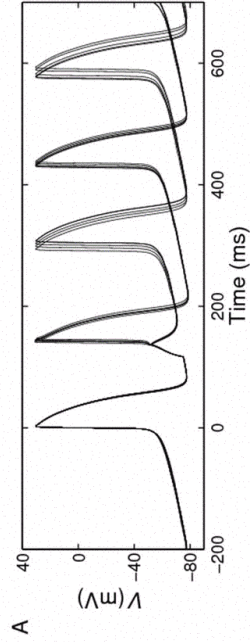
Guevara, Shrier, Glass, 1986

Single-channel model simulations

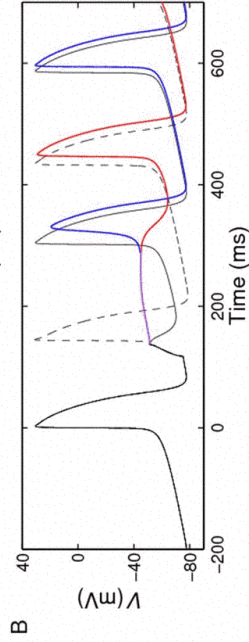


Ionic model: modified Irisawa & Noma

Single-channel vs. HH-type

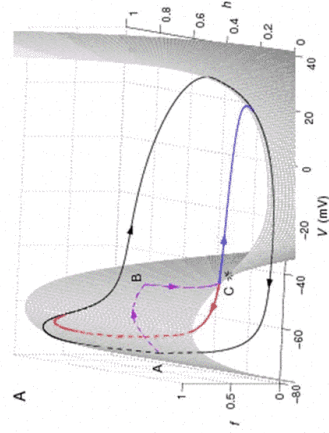


Single-channel model
 $t_c = 117$ ms

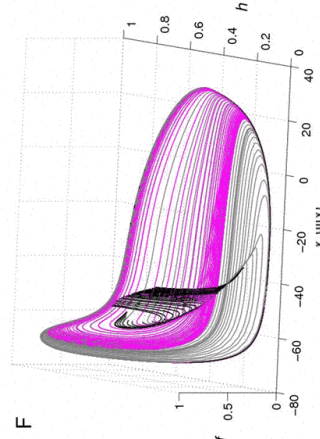


HH-type model
 $t_c = 117.158751189269$ ms
 $t_c = 117.158751189270$ ms

Mechanism of separation



Slow manifold
 $dV/dt = 0 \Rightarrow$ canards

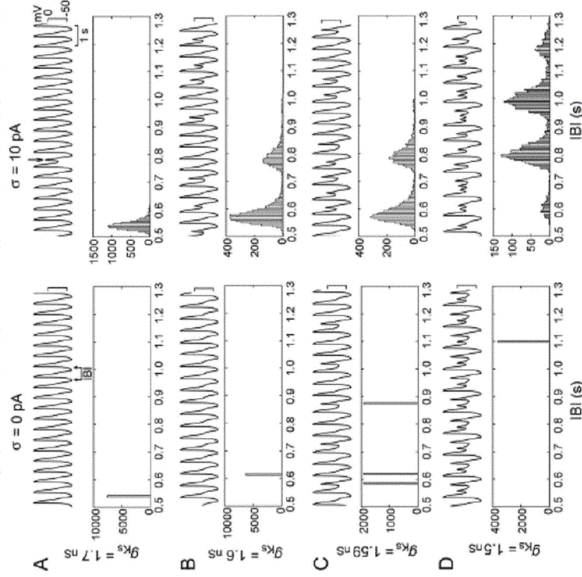


Stable manifold of the
weak unstable manifold

Canard solutions are notoriously unstable – the opening of one Na channel for a typical duration may change the response

Effects of noise on EAD generation

Noise-free model Stochastic model



Lerma, Krogh-Madsen, Guevara, Glass;
in print J Stat Phys.

Main points

The bifurcation between normal and abnormal dynamics might be traversed slowly with respect to the time between heart beats. In such a situation, stochastic effects will become prominent.

Noise-free vs. stochastic mathematical models:
Important qualitative differences in dynamics

Collaborators

McGill University

- Michael Guevara
- Leon Glass
- Claudia Lerma

Concordia University

- Eusebius Doedel
-

Chick experiments:

Medical University Graz

- Peter Schaffer
- Brigitte Pelzmann
- Bernard Koidl