Small Excitable Systems

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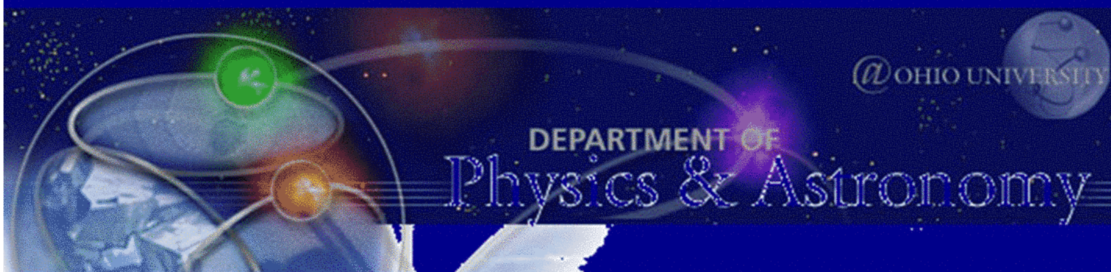

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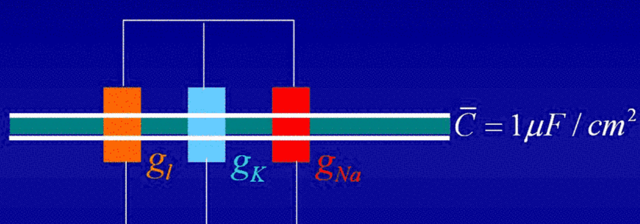
Thanks: NSF, Ghanim Ullah, J.W. Shuai (UC Irvine)

Conductance-based excitable systems



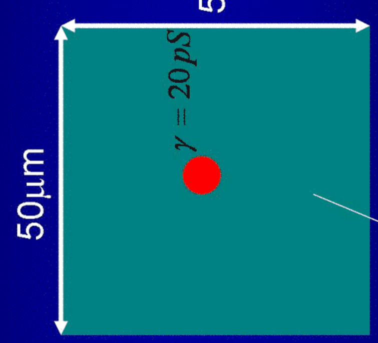
$$\bar{C}\dot{V} = \sum_i g_i(\{n\})(V_i - V) + j$$

continuous, fraction of open channels

Reality: discrete units

$\frac{N_{open}}{N}$ continuous if $N \to \infty$

Changing the system size



Channel opens for 1ms:

$$\Delta q = I \cdot 1ms$$

$$= \gamma \underbrace{V}_{voltage} \cdot \underbrace{1ms}_{\text{channel-open time}}$$

$$\approx 2 \cdot 10^{-15} C$$

Change of voltage:

$$\Delta V = \frac{\Delta q}{C} = 0.1 mV$$

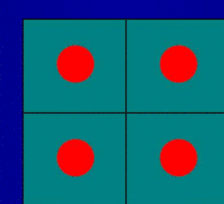
(Length-scale: ≈ 0.1-1.0mm)

Changing the system size (2)

Channel-density constant:

$$\rho_{sodium} = 60 / \mu m^2$$

$N \to \infty$: continuous model



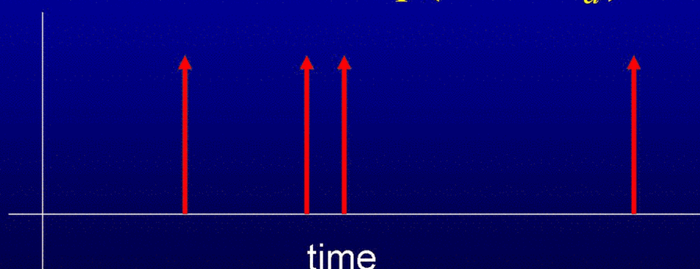
1 channel: area ≈100nm x 100nm

What do we expect?

Large size (but finite):

Small fluctuations 1/N, rare action potentials

$$rate \propto \exp(-N \cdot E_a)$$

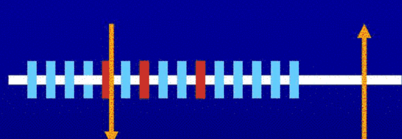


Hodgkin-Huxley model with sodium conductance

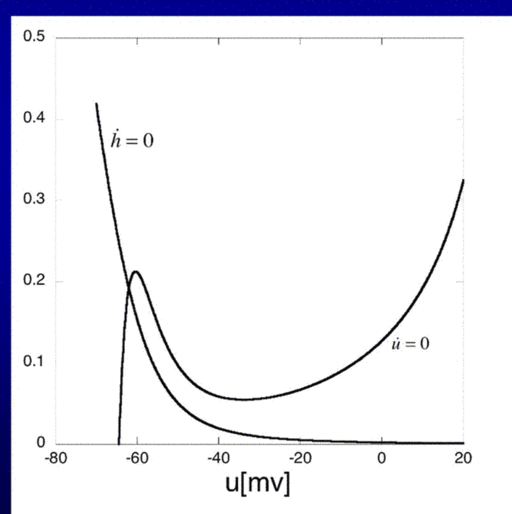
$$C\dot{u} = -g_{\mathrm{Na}} m_\infty^3(u) h \left(u - u_{\mathrm{Na}}\right) - g_{\mathrm{leak}} \left(u - u_{\mathrm{leak}}\right)$$

$$\dot{h} = \alpha_h (1-h) - \beta_h h$$

$$\dot{m} = \alpha_m (1-m) - \beta_m m$$



3 fast activation gates
1 slow inactivation gates



Stochastic modeling of inactivation

Single channel conductance: γ_0=20pS

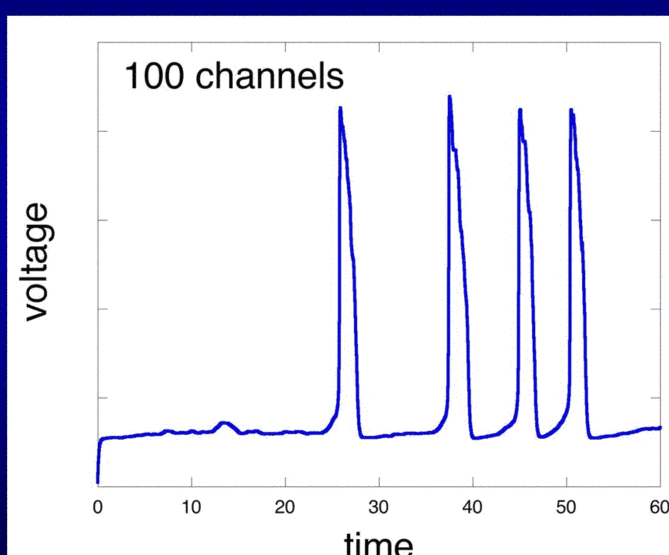
Channel density: ρ=N/Area=60/μm^2

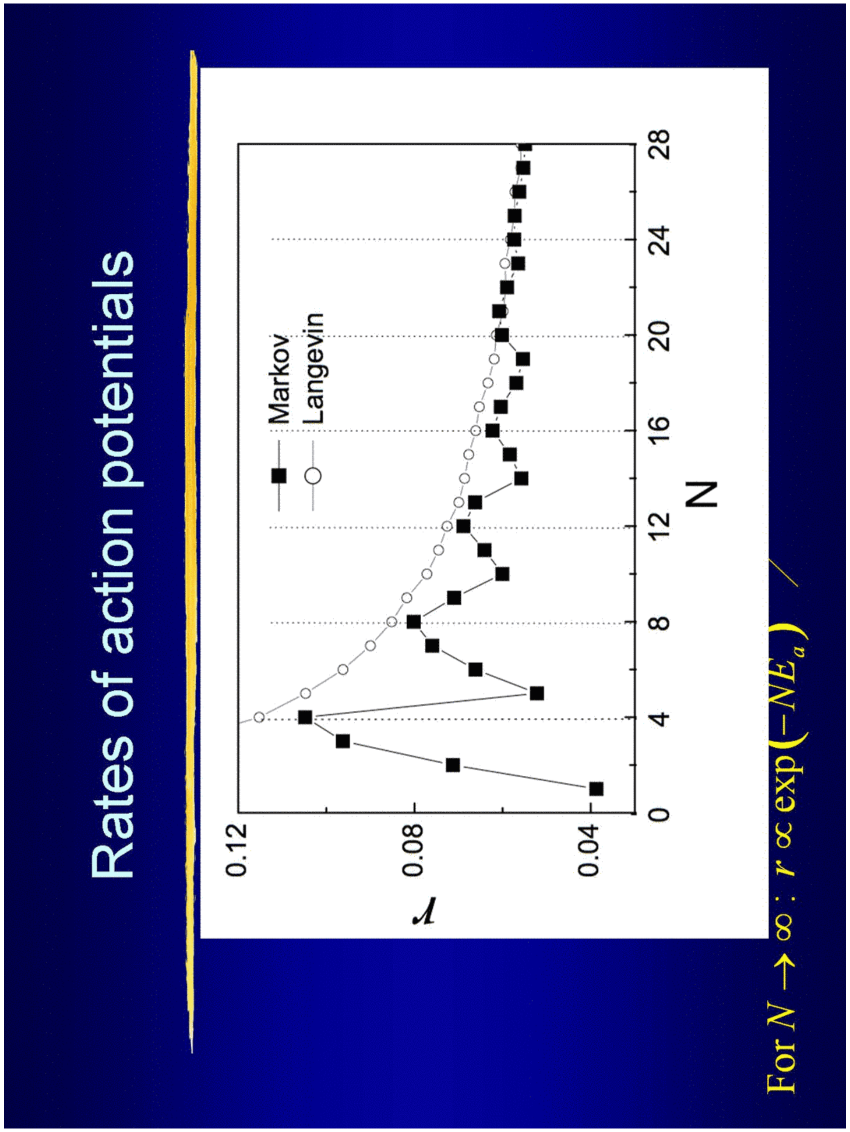
Conductance of cluster: $g_{Na} = N_{open}\gamma$

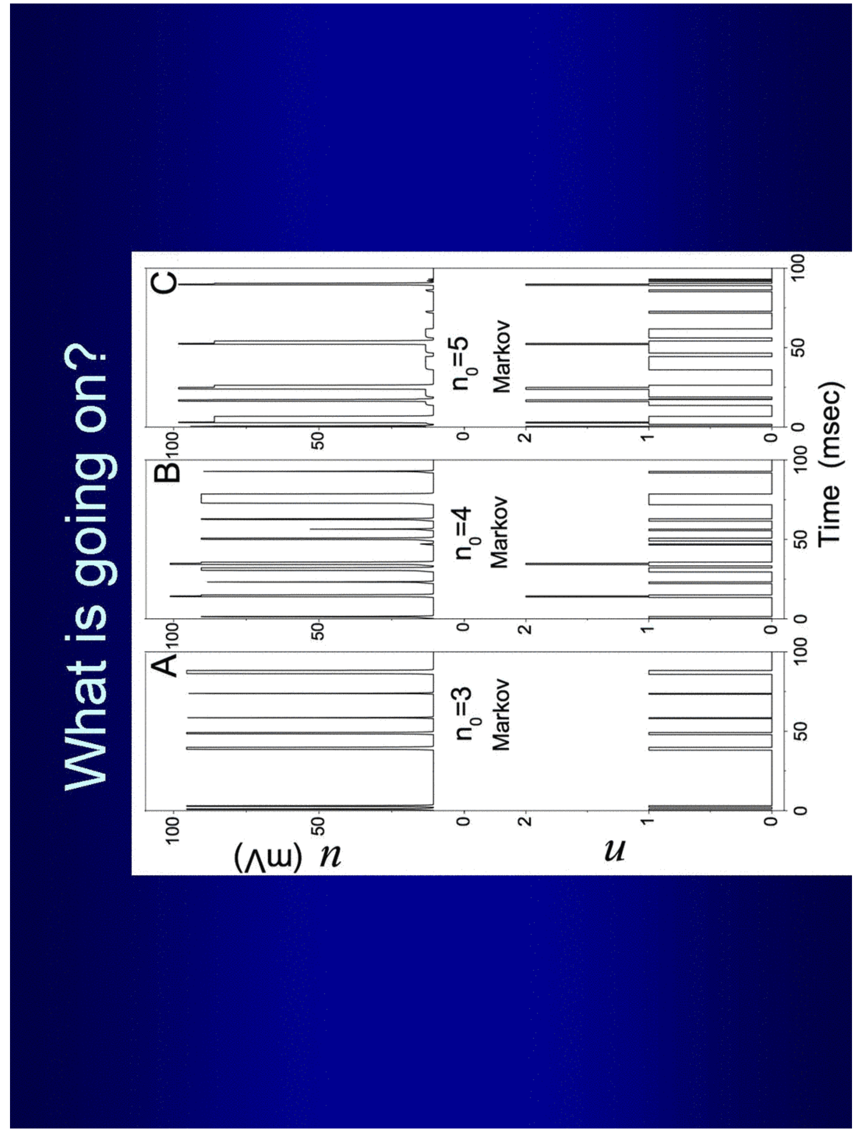
$$\dot{u} = \left(\frac{N_{\text{open}}}{\text{N}}\right) m_\infty^3 \frac{\gamma_{\text{Na}}\rho}{\bar{C}}\left(u - u_{\text{Na}}\right) + \frac{\bar{g}_{\text{leak}}}{\bar{C}}\left(u - u_{\text{leak}}\right)$$

$$N_{open} \underset{\left(N_{open}+1\right)\beta_h}{\overset{(N-N_{open})\alpha_h}{\rightleftarrows}} N_{open} + 1$$

Results




Rates of action potentials
r
0.12
0.08
0.04
0
4
8
12
16
20
24
28
N
Markov
Langevin
For $N \to \infty : r \propto \exp(-NE_a)$


What is going on?
A
B
C
u (mV)
v
100
50
0
2
1
n0=3
Markov
n0=4
Markov
n0=5
Markov
Time (msec)

Entropy density of firing state

Example: activation threshold: a=0.25 (25% open)

5 channels/cluster:

6 states in total (0 open, 1 open, …)

4 states firing (2 open , … , 5 open)

Entropy density: E=4/6=0.667

A little arithmetic

$N = 1 \Rightarrow f = 1/2 = 0.500$

$N = 2 \Rightarrow f = 2/3 = 0.666$

$N = 3 \Rightarrow f = 3/4 = 0.750$

$N = 4 \Rightarrow f = 4/5 = 0.800$

$N = 5 \Rightarrow f = 4/6 = 0.667$

$N = 6 \Rightarrow f = 5/7 = 0.714$

$N = 7 \Rightarrow f = 6/8 = 0.750$

$N = 8 \Rightarrow f = 7/9 = 0.777$

$N = 9 \Rightarrow f = 7/10 = 0.700$

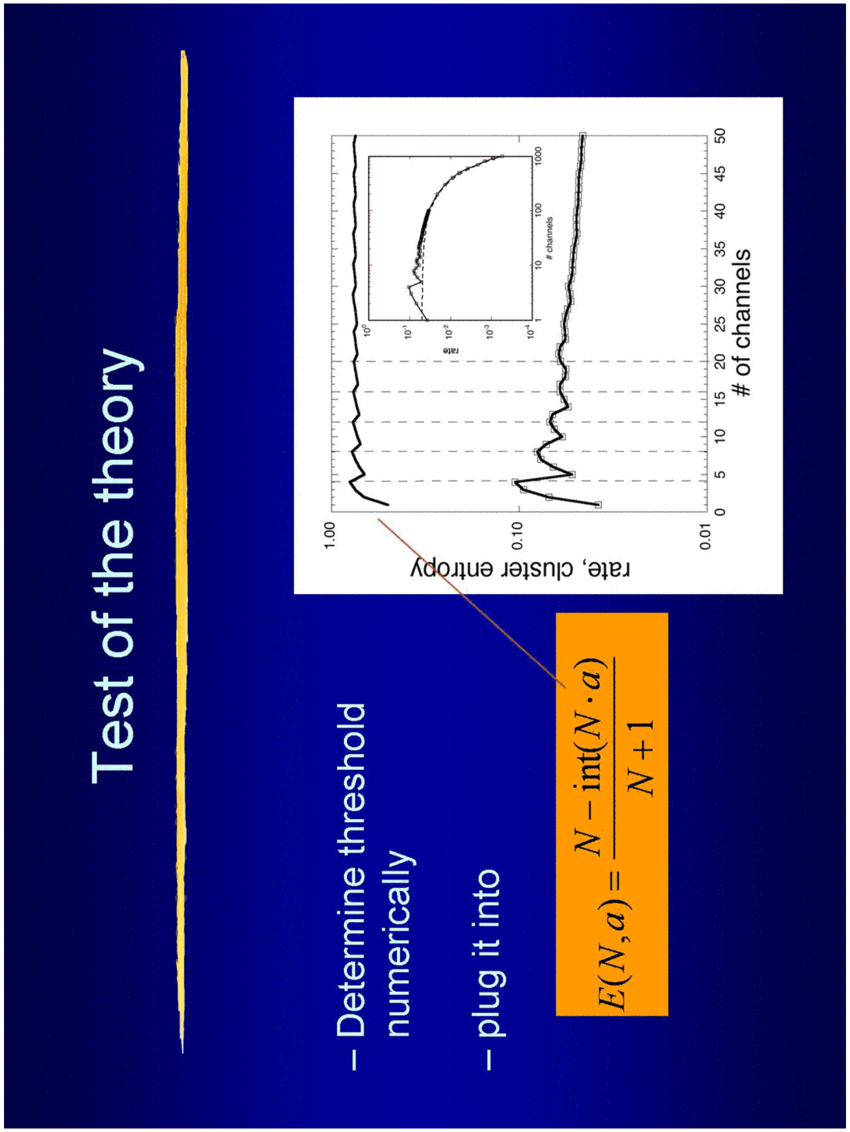
Number of fractions n/N with

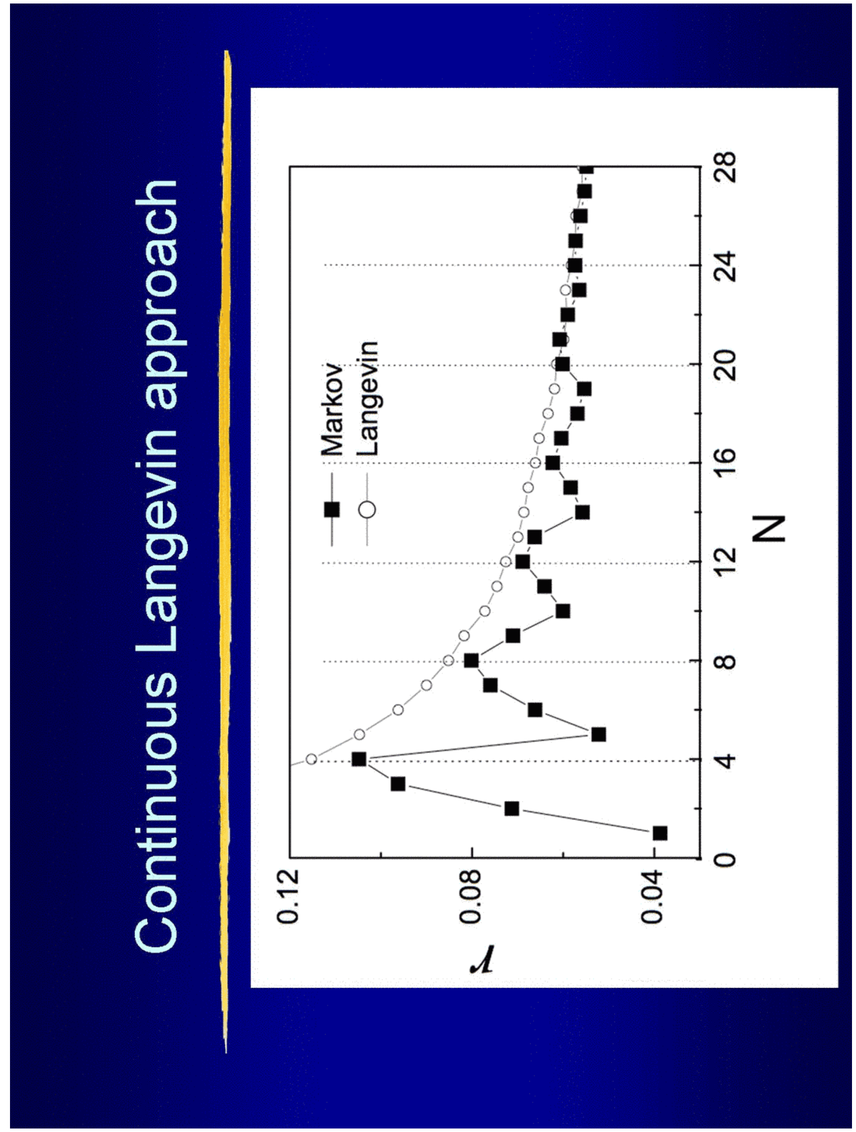
$$a \le \frac{n}{N} \le 1$$

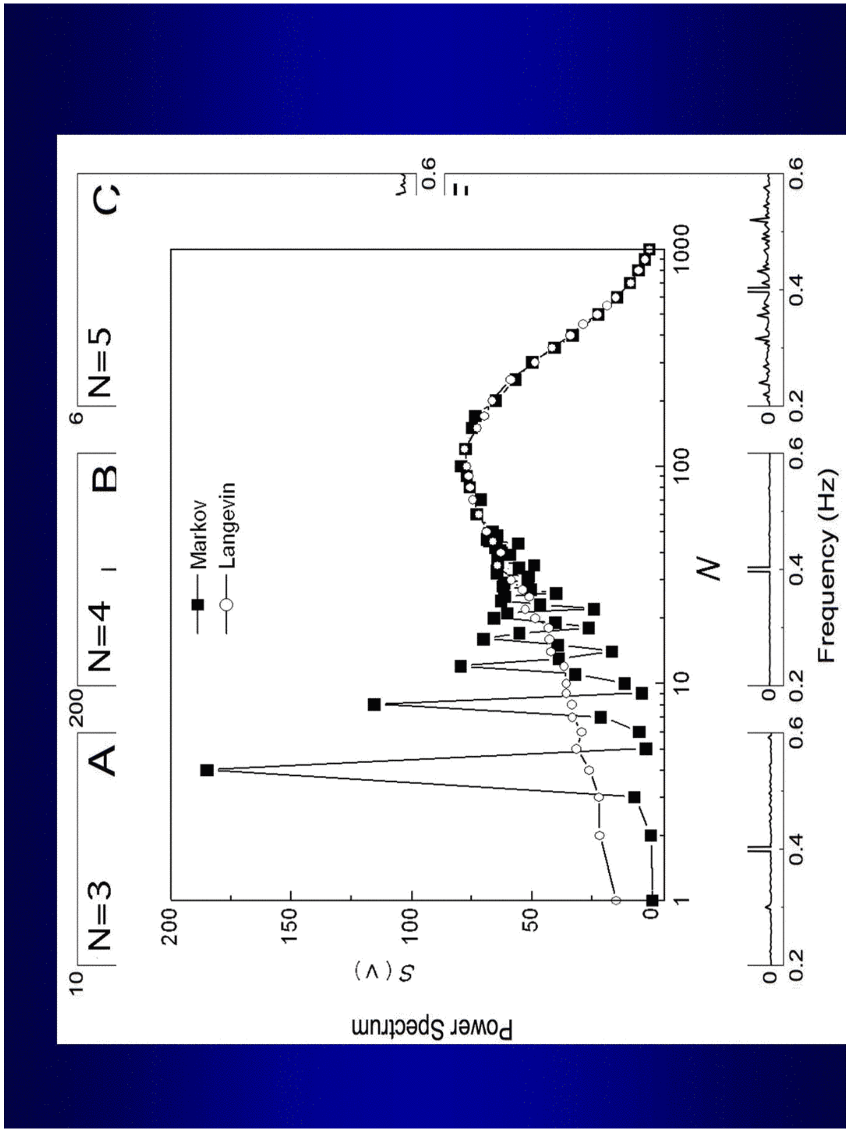
Answer:

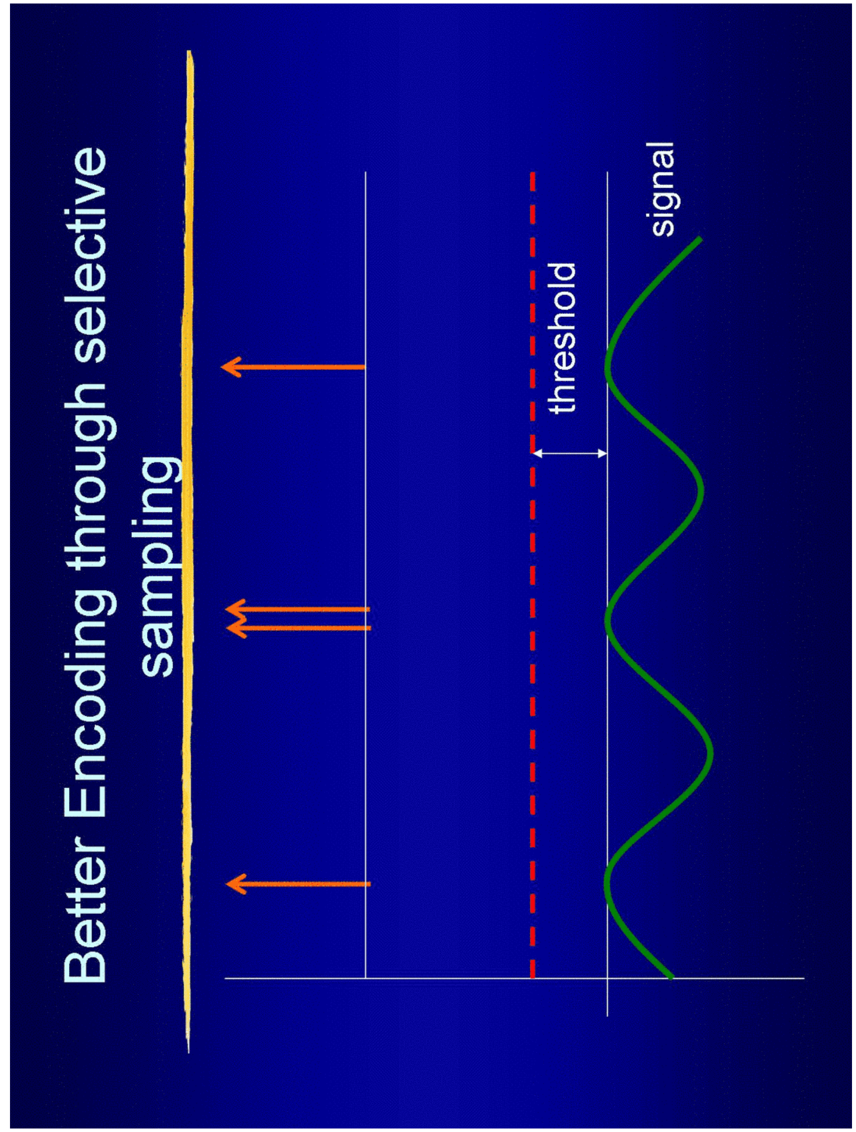
$$N + 1 - (1 + \mathrm{int}(N \cdot a))$$

$$E(N,a) = \frac{N - \mathrm{int}(N \cdot a)}{N + 1}$$


Test of the theory
– Determine threshold numerically
– plug it into
$E(N,a) = \frac{N - \mathrm{int}(N \cdot a)}{N+1}$
rate, cluster entropy
# of channels
1.00
0.10
0.01
0
5
10
15
20
25
30
35
40
45
50
rate
channels

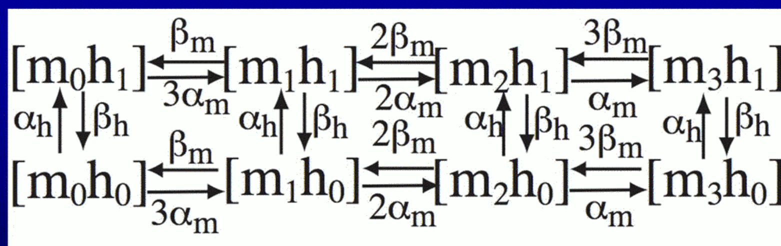

Continuous Langevin approach
Markov
Langevin
r
N
0.12
0.08
0.04
0
4
8
12
16
20
24
28


A
B
C
N=3
N=4
N=5
Markov
Langevin
Power Spectrum
S (ν)
N
Frequency (Hz)


Better Encoding through selective sampling
threshold
signal

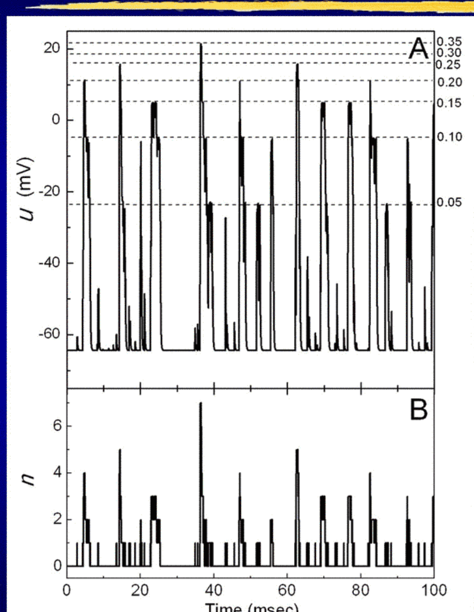
Fully stochastic sodium channels

$$\dot{u} = \left(\frac{N_{open}}{\mathrm{N}}\right)\frac{\gamma_{Na}\rho}{\bar{C}}\left(u - u_{Na}\right) + \frac{\bar{g}_{leak}}{\bar{C}}\left(u - u_{leak}\right)$$

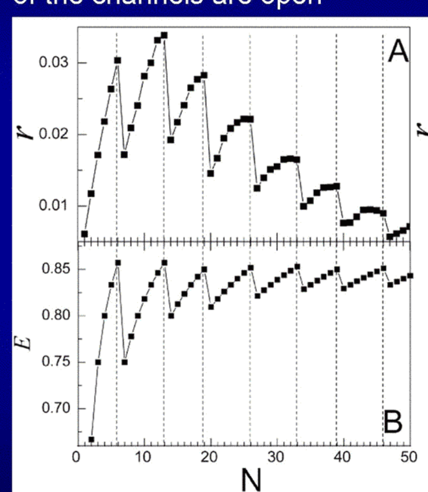


m_2h_1 : 2 actiavtion gates open, inactivated

Results

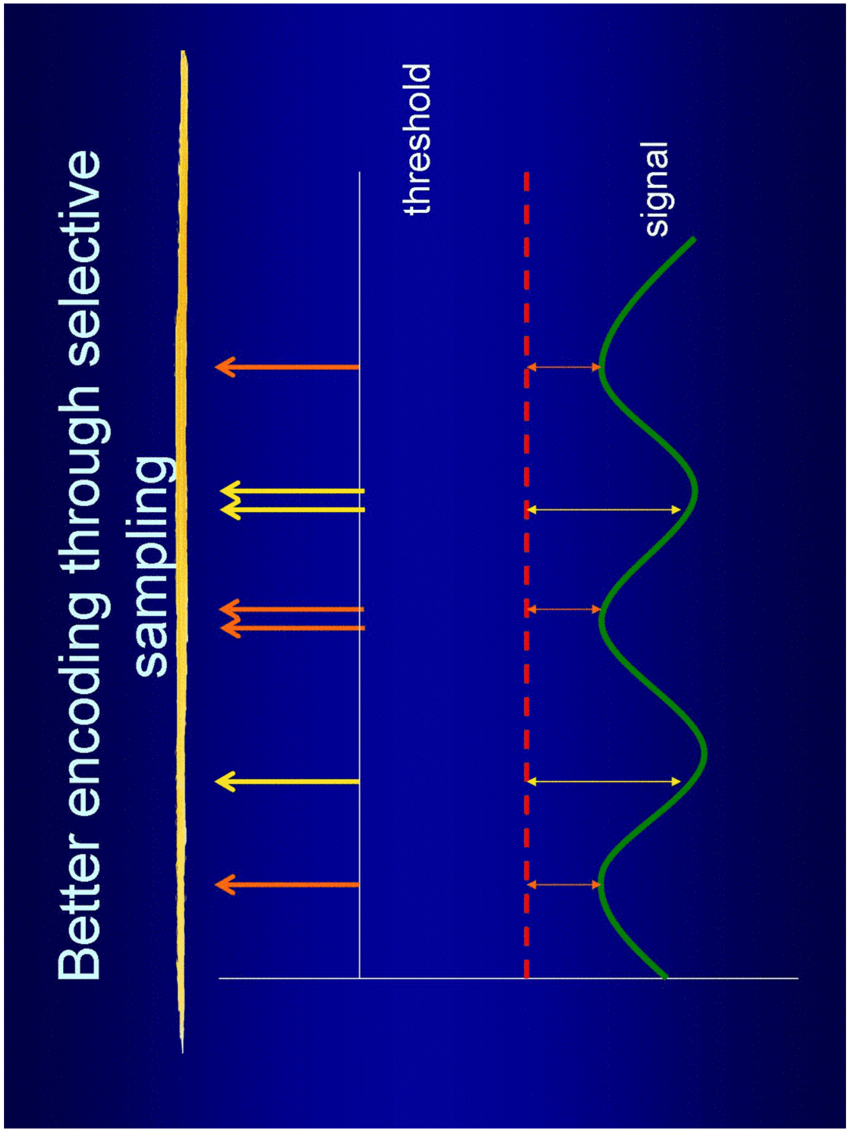


Steady-state voltage if 15% of the channels are open



20 channels

$$E(N, a = 0.15) = \frac{N - \mathrm{int}(N \cdot a)}{N + 1}$$



Summary

- Magic cluster sizes with large firing rates and enhanced signal encoding
- Requires homogenous cluster with simple gating structure and a unique quasi-discrete relation between fraction
- Fraction of firing states oscillate with cluster size but ONLY for small clusters
- Design optimal sensors for small signals with selective encoding capability

Key elements of excitability

- Inhibition:

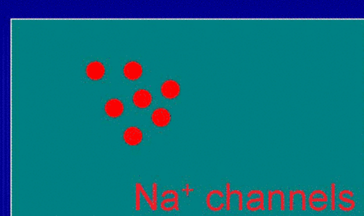
Neurons: Na^{+}-channels shut when depolarized

Ca^{2+}-release channels shut when Ca^{2+} is high

Key elements of excitability

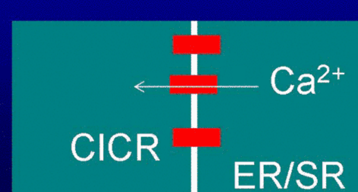
- positive feedback

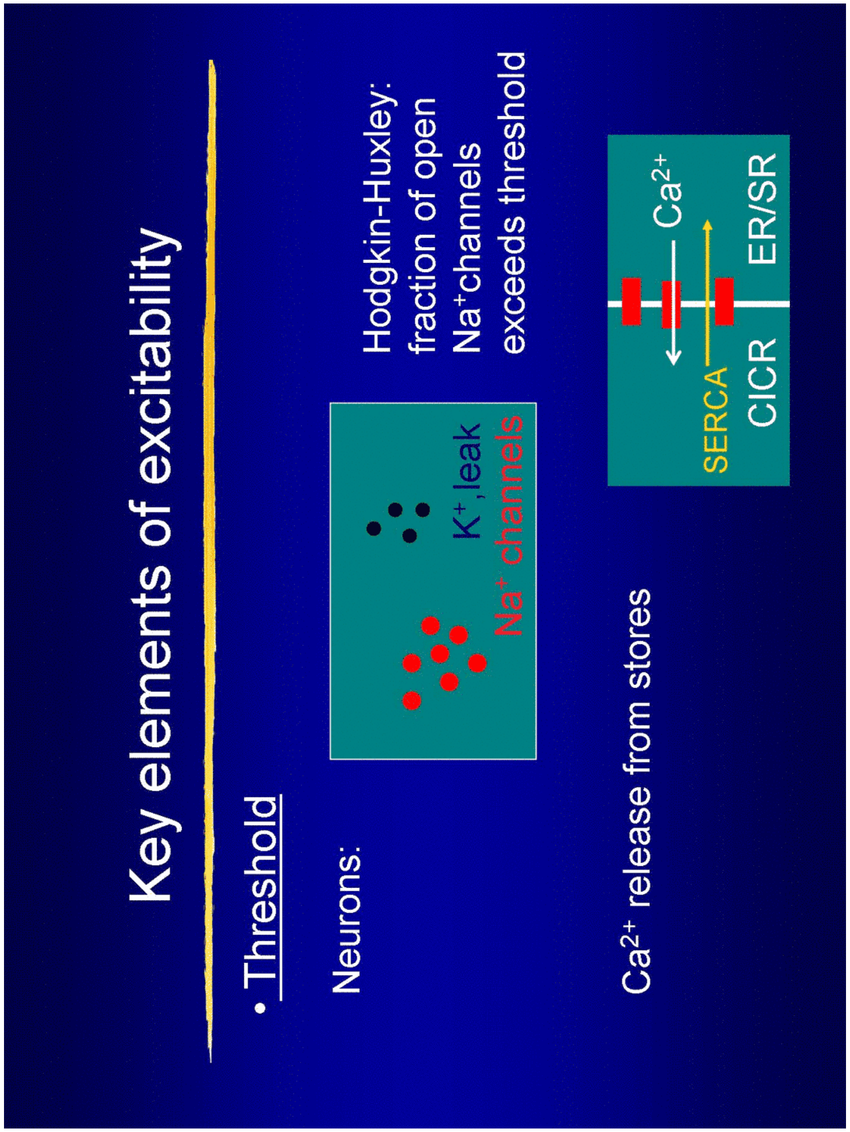
Neurons:



channel opens → depolarization → more channels open

Ca^{2+} release from stores:




Key elements of excitability
• Threshold
Neurons:
Na^+ channels
K^+,leak
Hodgkin-Huxley:
fraction of open
Na^+channels
exceeds threshold
Ca^{2+} release from stores
CICR
ER/SR
SERCA
Ca^{2+}