Bursting (beta) rhythms

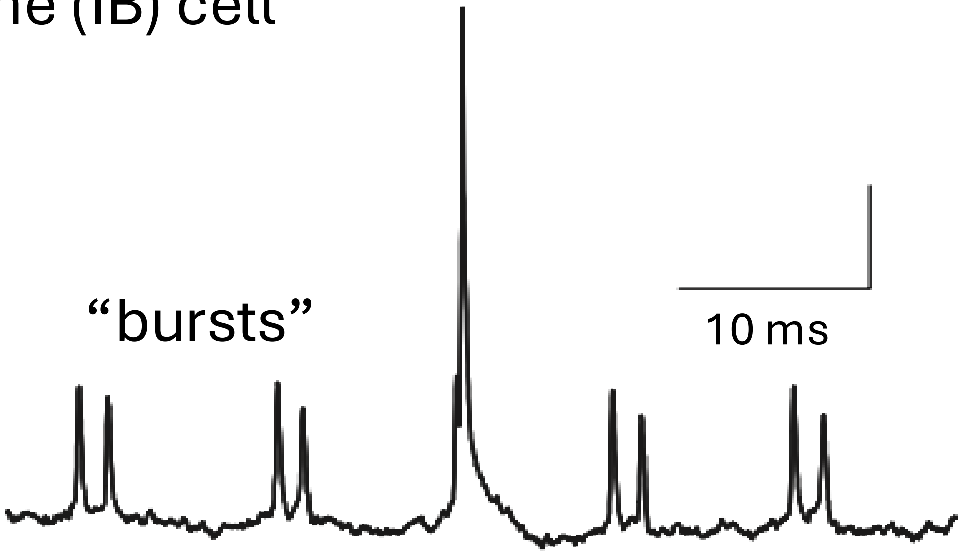
Instructor: Mark Kramer

Today

Model of the bursting (beta) rhythm

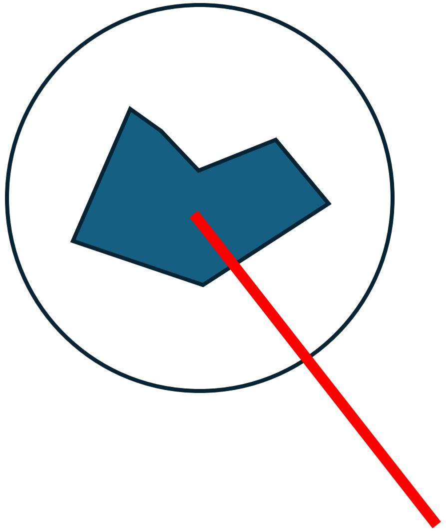
Beta rhythms

Record from one (IB) cell



20-30 Hz

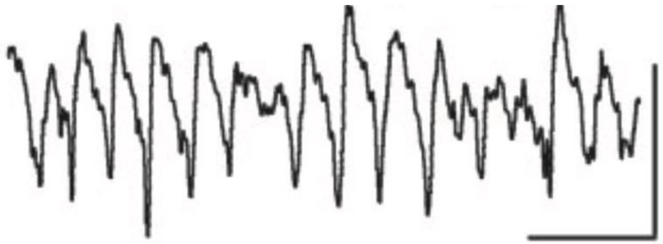
<u>experiment</u>



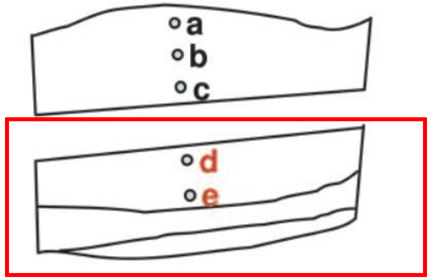
in vitro preparation

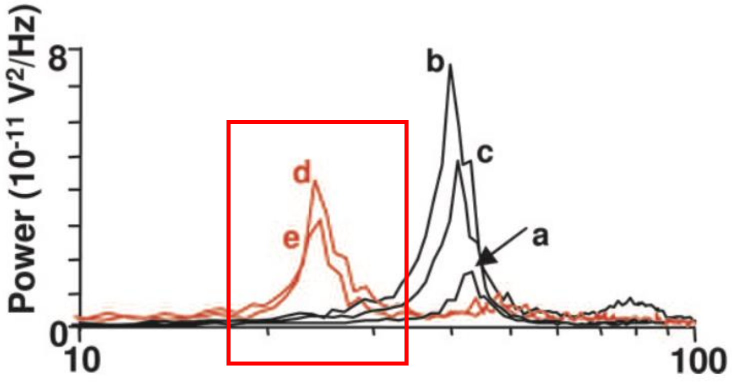
block synaptic transmission

record LFP



100 ms

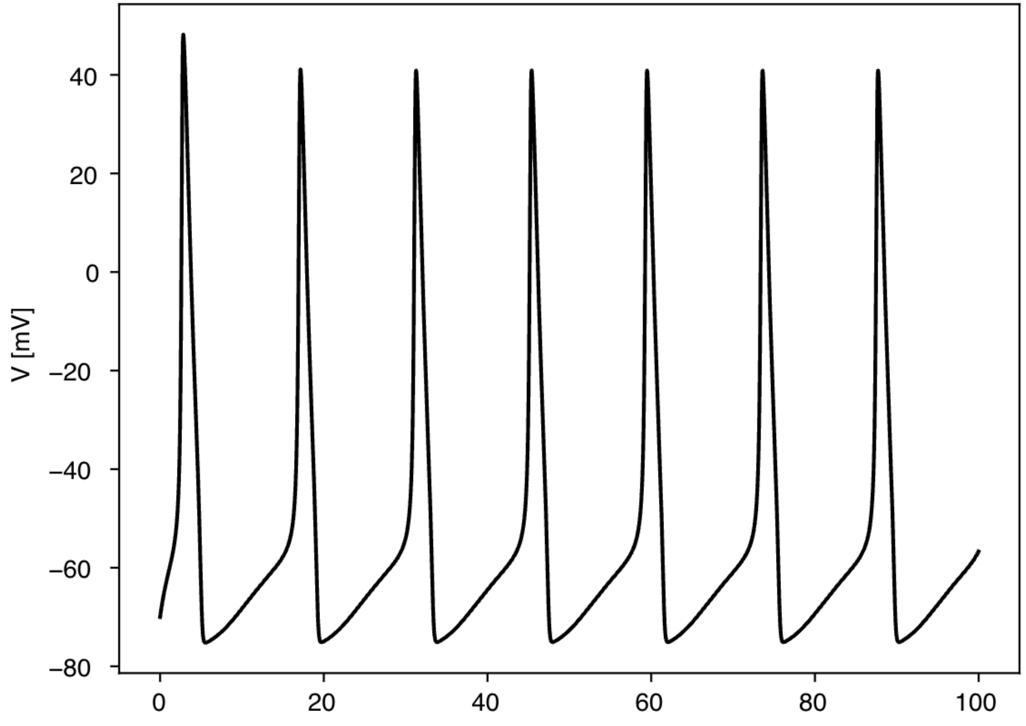




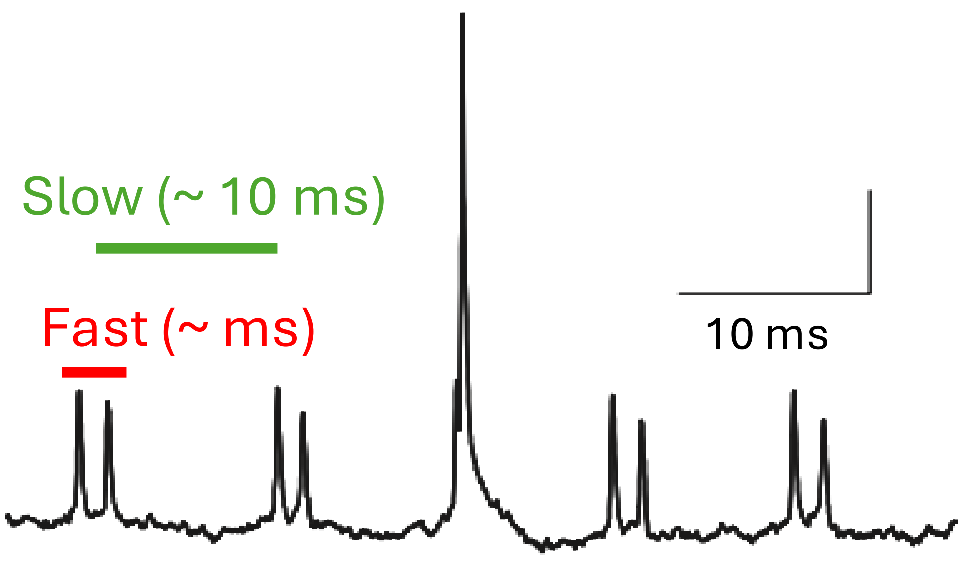
[Roopun et al., PNAS, 2006]

Beta rhythm model

Our existing models (LIF, HH, ING, PING) do **not** burst



one timescale



two timescales

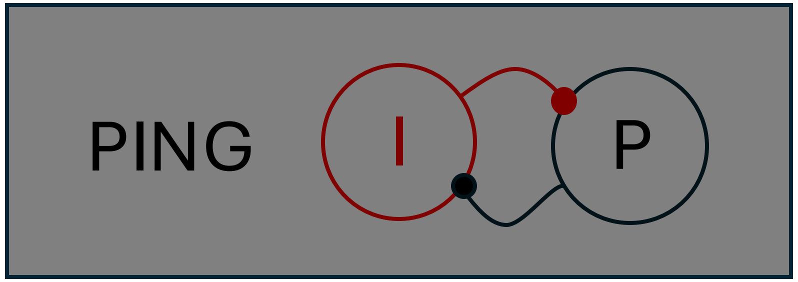
Q. Model this?

Beta rhythm model

Mechanisms

- not synaptic
- another ion current?

No



Intuition: imagine injecting a modulated current I_* to I&F model

bursting … I_* sets the slow timescale

Idea: update HH model with a new current that acts like I_*

Beta rhythm model

Remember HH

$$C\,\frac{dV}{dt} = I_{\text{input}}(t) - \bar{g}_{\text{K}}n^4(V - V_{\text{K}}) - \bar{g}_{\text{Na}}m^3h(V - V_{\text{Na}}) - \bar{g}_{\text{L}}(V - V_{\text{L}})$$

$$\frac{dn}{dt} = \boxed{-\frac{n - n_\infty(V)}{\tau_n(V)}}$$

$$\frac{dm}{dt} = \boxed{-\frac{m - m_\infty(V)}{\tau_m(V)}}$$

$$\frac{dh}{dt} = \boxed{-\frac{h - h_\infty(V)}{\tau_h(V)}}$$

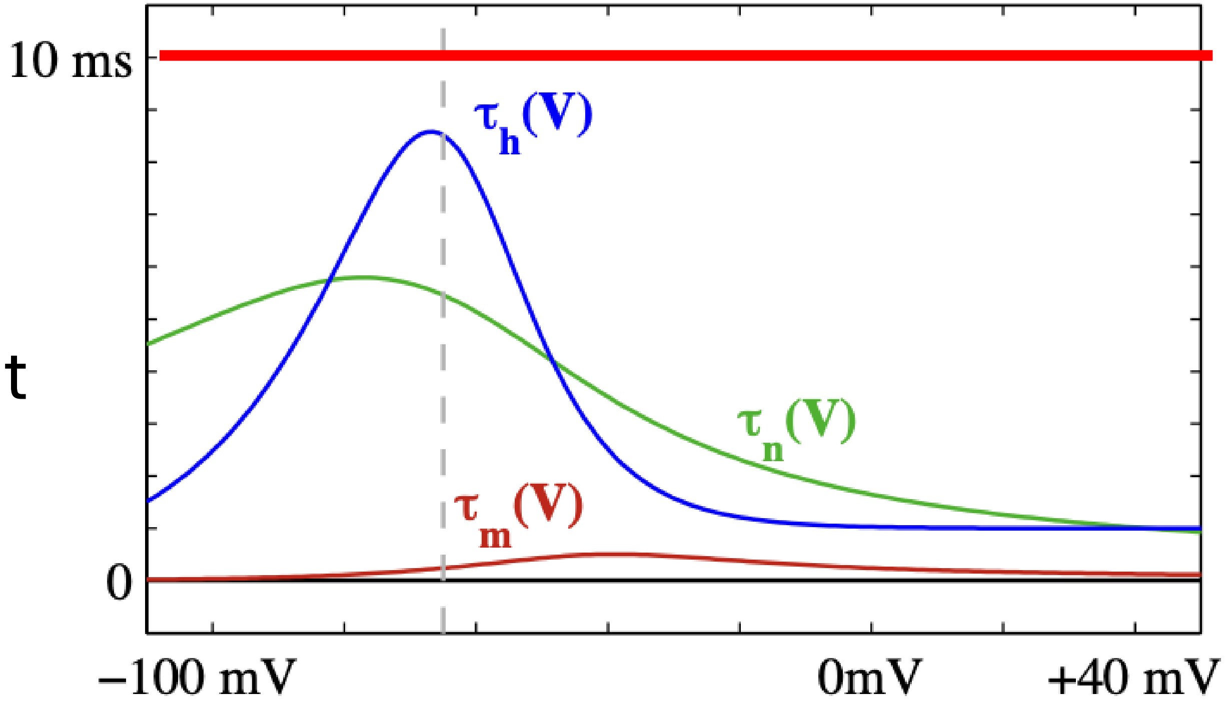
Time constants are voltage dependent

The gate dynamics {n,m,h} are **fast**

➔ V changes quickly (~ ms spike)

➔ No slow dynamics in HH model

Below 10 ms … FAST



Beta rhythm model

Q. How do we add the slow dynamics?

A. Add a new current

$$C\frac{dV}{dt} = \underbrace{\boxed{I_{Na} + I_K + I_L + I_{inj}}}_{\text{original HH (fast)}} + \underbrace{\boxed{I_{new}}}_{\text{new current (will set the slow timescale)}}$$

Q. What is I_{new}?

Beta rhythm model

Currents

- "fast" sodium & "fast" potassium → original HH model
- many others exist

… with V-dependent steady-states & time constants

TABLE A2. *Ionic conductance kinetic parameters*

Conductance Type	Steady-State Activation/Inactivation	Time Constant (ms)
g_{Na}-transient: activation	$1/\{1 + \exp[(-V - 34.5)/10]\}$;	$0.025 + 0.14 \exp[(V + 26.5)/10]$ $[V \leq -26.5]$ $0.02 + 0.145 \exp[(-V - 26.5)/10)]$ $[V \geq -26.5]$
g_{Na}-transient: inactivation	$1/\{1 + \exp[(V + 59.4)/10.7]\}$;	$0.15 + 1.15/\{1 + \exp[(V + 33.5)/15]\}$
g_{Na}-persistent: activation	$1/\{1 + \exp[(-V - 48)/10]\}$;	$0.025 + 0.14 \exp[(V + 40)/10]$ $[V \leq -40]$ $0.02 + 0.145 \exp[(-V - 40)/10]$ $[V \geq -40]$
g_K-delayed rectifier: activation	$1/\{1 + \exp[(-V - 29.5)/10]\}$;	$0.25 + 4.35 \exp[(V + 10)/10]$ $[V \leq -10]$ $0.25 + 4.35 \exp[(-V - 10)/10]$ $[V \geq -10]$
g_K-transient ("A"): activation	$1/\{1 + \exp[(-V - 60)/8.5]\}$;	$0.185 + 0.5/\{\exp[(V + 35.8)/19.7] + \exp[(-V - 79.7)/12.7]\}$
g_K-transient ("A"): inactivation	$1/\{1 + \exp[(V + 78)/6]\}$;	$0.5/$ $[V \leq -63]$ $\{\exp[(V + 46)/5)] + \exp[(-V - 238)/37.5]\}$ 9.5 $[V \geq -63]$
g_K-"K2": activation	$1/\{1 + \exp[(-V - 10)/17]\}$;	$4.95 + 0.5/\{\exp[(V - 81)/25.6] + \exp[(-V - 132)/18]\}$
g_K-"K2": inactivation	$1/\{1 + \exp[(V + 58)/10.6]\}$;	$60 + 0.5/\{\exp[(V - 1.33)/200] + \exp[(-V - 130)/7.1]\}$
g_{Ca}-low-threshold: activation	$1/\{1 + \exp[(-V - 56)/6.2]\}$;	$0.204 + 0.333/\{\exp[(V + 15.8)/18.2] + \exp[(-V - 131)/16.7]\}$
g_{Ca}-low-threshold: inactivation	$1/\{1 + \exp[(V + 80)/4]\}$;	$0.333 \exp[(V + 466)/66.6]$ $[V \leq -81]$ $9.32 + 0.333 \exp[(-V - 21)/10.5]$ $[V \geq -81]$
Anomalous rectifier	$1/\{1 + \exp[(V + 75)/5.5]\}$;	$1/[\exp(-14.6 - 0.086V) + \exp(-1.87 + 0.07V)]$

Conductance Type	Forward Rate Function (α)	Backward Rate Function (β)
g_K-Ca- & V-dependent ("C") (voltage-dependent term)	$0.053 \exp[(V + 50)/11 - (V + 53.5)/27]$ $[V \leq -10]$ $2 \exp[(-V - 53.5)/27]$ $[V \geq -10]$	$2 \exp[(V - 53.5)/27] - \alpha$ $[V \leq -10]$ 0 $[V \geq -10]$
g_K-"M"	$0.02/\{1 + \exp[(-V - 20)/5]\}$;	$0.01 \exp[(-V - 43)/18]$
g_K-AHP	$\min(10^{-4}\chi, 0.01)$;	0.01
g_{Ca}-high-threshold	$1.6/\{1 + \exp[-0.072(V - 5)]\}$;	$0.02 (V + 8.9)/\{\exp[(V + 8.9)/5] - 1\}$

[Traub et al., J Neurophysiol, 2003]

Beta rhythm model

Ignore details & assume 4 candidate currents

{A, B, C, D}

We know their steady-state functions $x_\infty[V]$ and time constants $\tau_x[V]$

<u>Note</u> voltage dependent

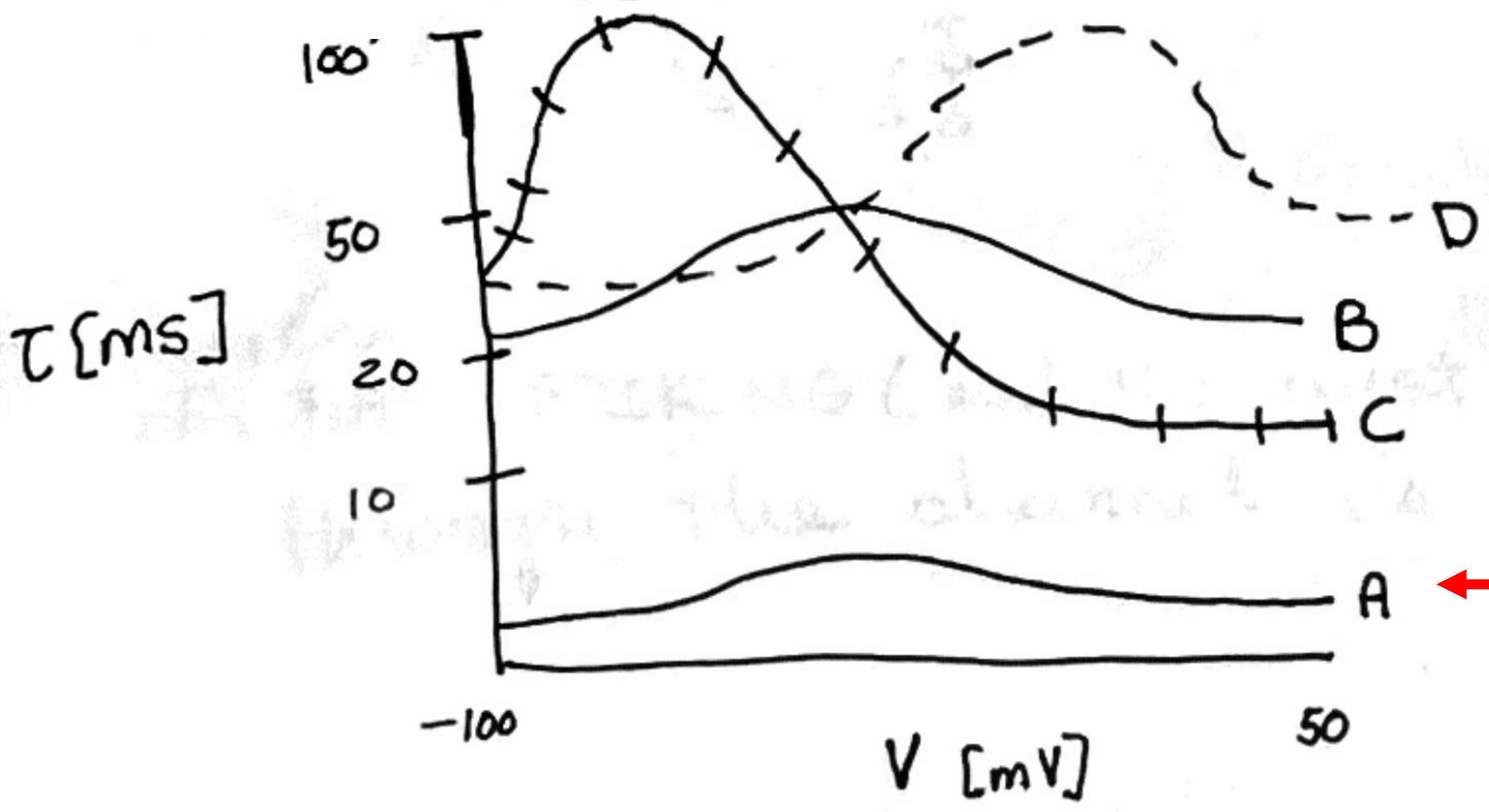
<u>Goal</u>: Determine <u>which current</u> could produce bursting we observe

A process of elimination ...

Beta rhythm model

{~~A~~, B, C, D}

Investigate the <u>time constants</u> $\tau_x[V]$



We want a <u>**slow**</u> current

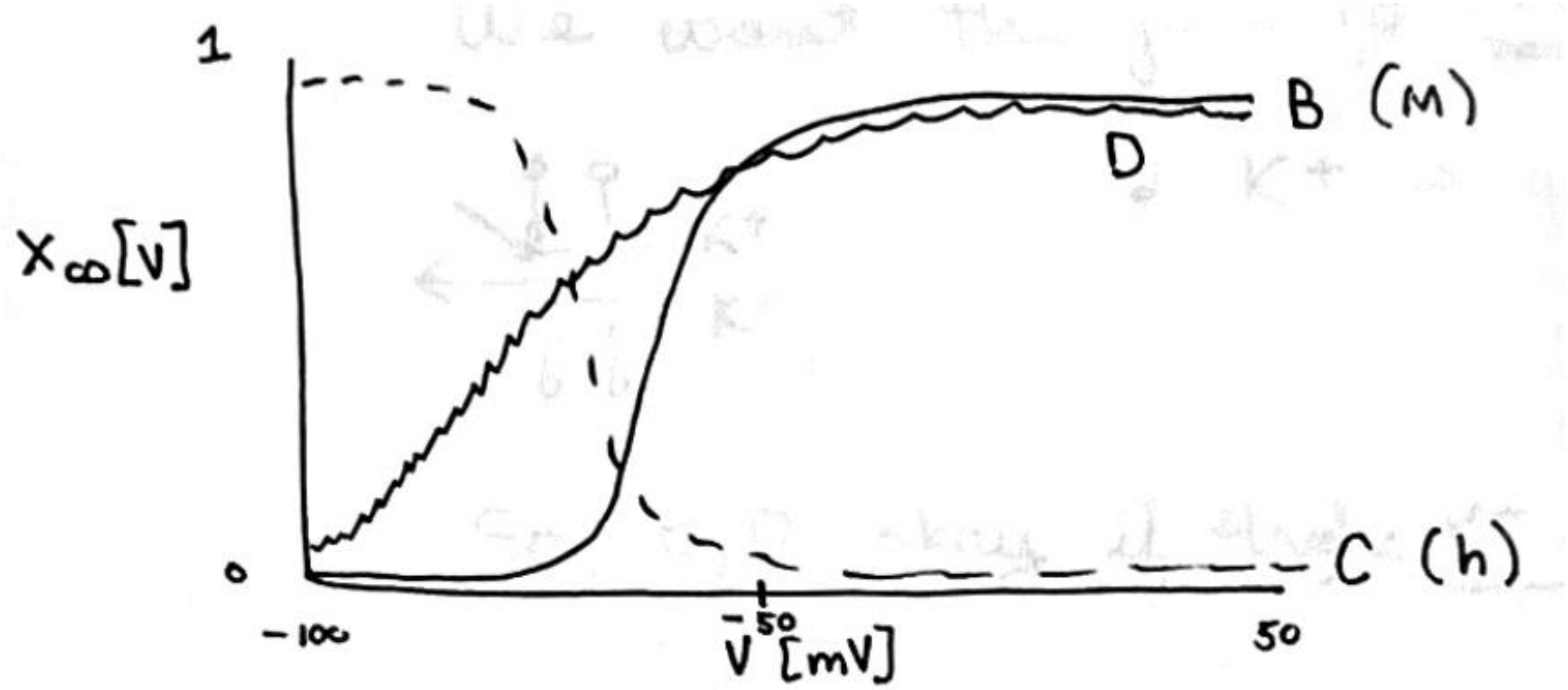
Eliminate A

- too fast for bursting

Beta rhythm model

{$\cancel{A}$, B, C, D}

Investigate the <u>steady-state functions</u> $x_\infty[V]$.

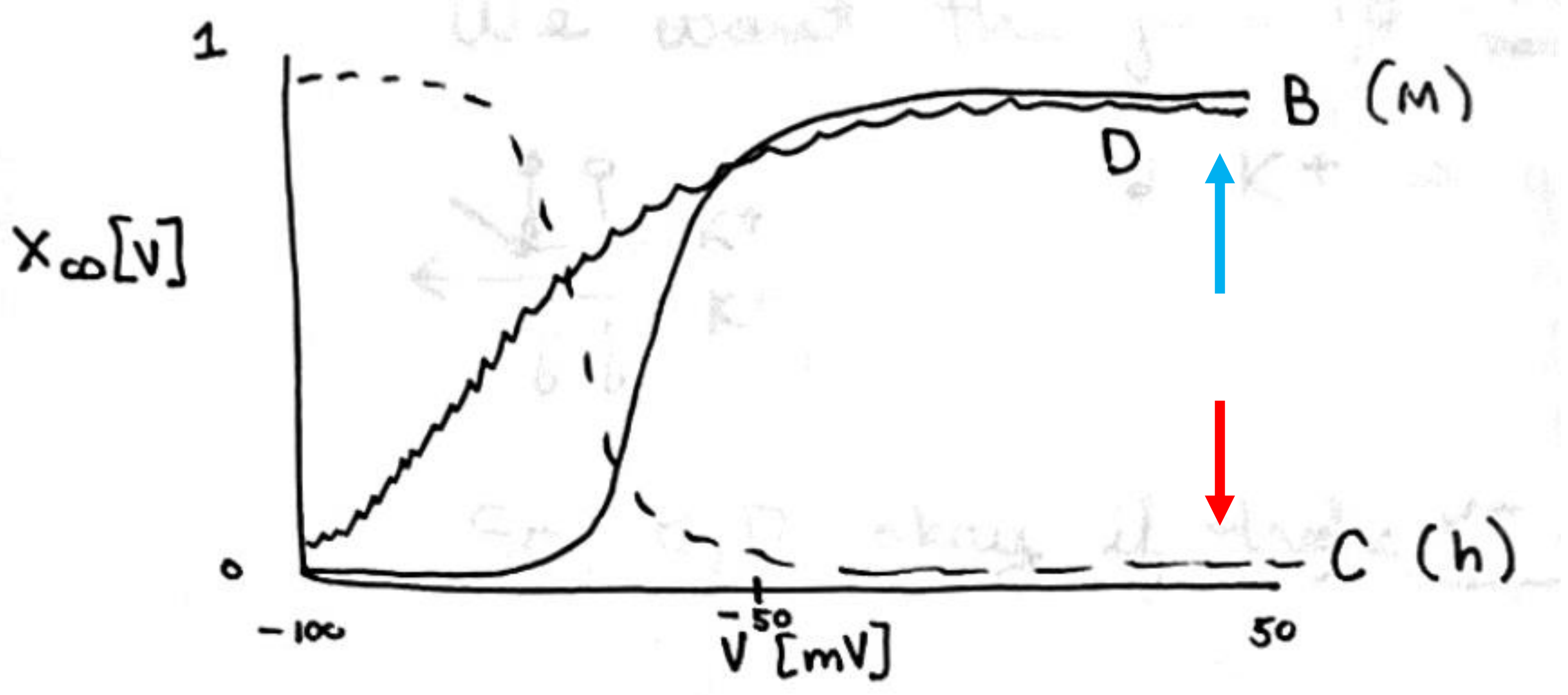


Q. Which one?

Beta rhythm model

{~~A~~, B, C, D}

Case 1: Gate changes (slowly) during the burst



burst → a depolarized state

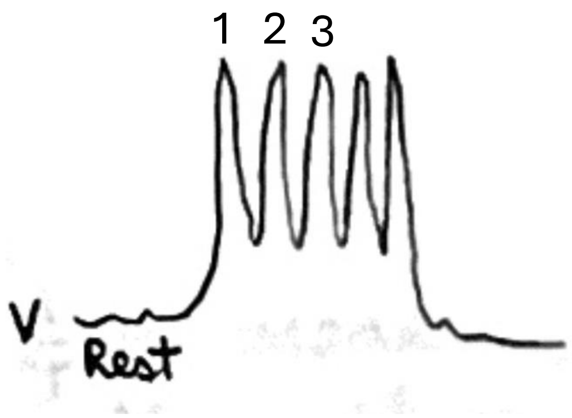
Gates: (B, D) "depolarization activated" gates **open** during burst

(C) "depolarization inactivated" gates **close** during burst

Beta rhythm model

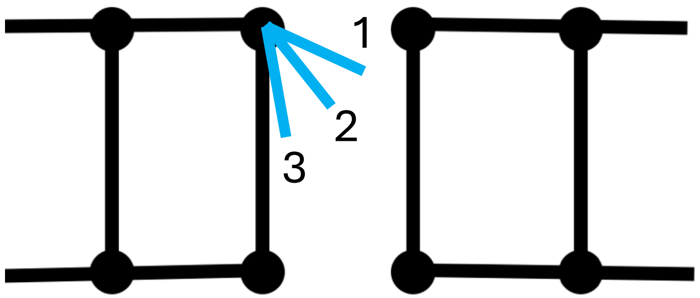
{~~A~~, B, C, D}

Case 1: Gate **opens** (slowly) during the burst (B,D)



burst → a depolarized state

Each spike opens the gate a little bit



when gate is open enough, this current halts the spiking

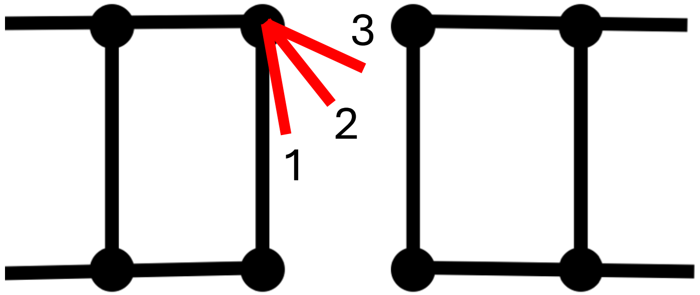
Beta rhythm model

{~~A~~, B, C, D}

Case 2: Gate **closes** (slowly) during the burst (C)

burst → a depolarized state

Each spike closes the gate a little bit



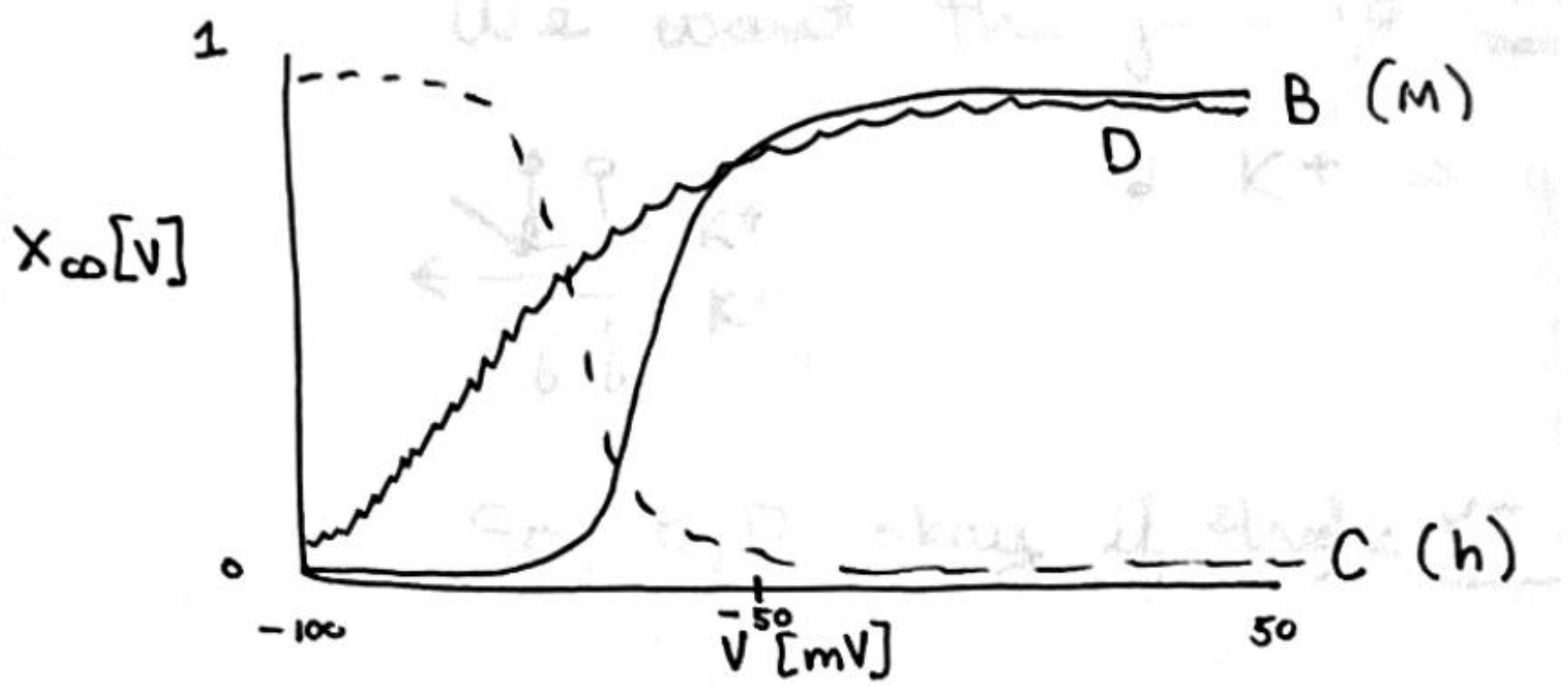
when gate is closed enough, this current halts the spiking

Beta rhythm model

{~~A~~, B, C, D}

Case 1: Gate **opens** (slowly) during the burst (B,D)

Case 2: Gate **closes** (slowly) during the burst (C)



In either case, to halt spiking (end the burst), the type of ion that flows through the channel is critical.

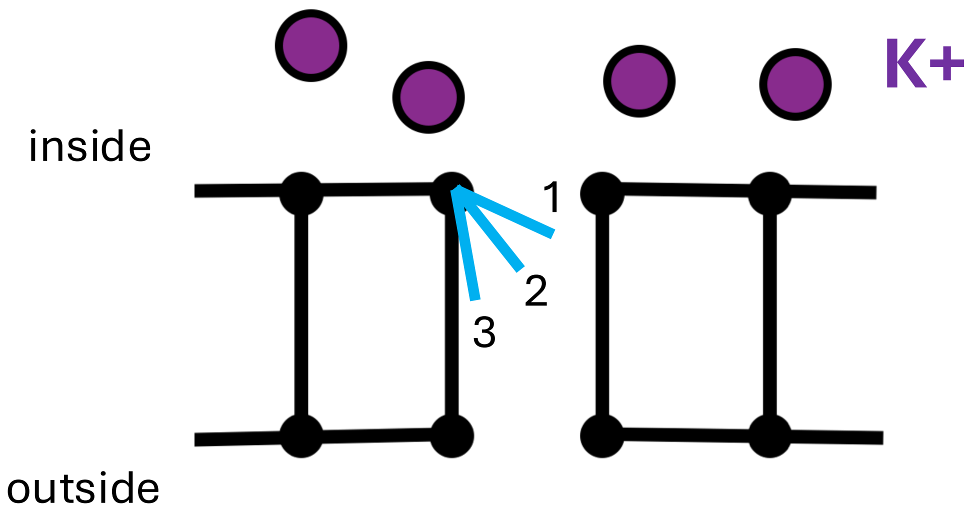
Beta rhythm model

{~~A~~, B, C, D}

Case 1: Gate **opens** (slowly) during the burst (B,D)

Q. What ion is gated?

We want the gate to open & halt bursting



Gate opens enough

K+ released from cell

hyperpolarize neuron

So (B,D) work if they're K+ currents

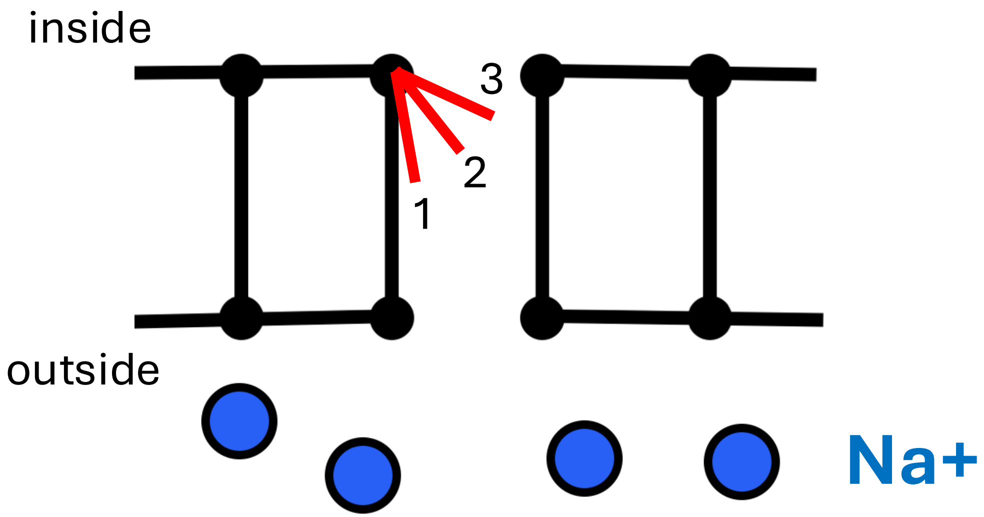
Beta rhythm model

{~~A~~, B, C, D}

Case 2: Gate **closes** (slowly) during the burst (C)

Q. What ion is gated?

We want the gate to close & halt bursting



Gate closes enough

Na+ cannot enter cell

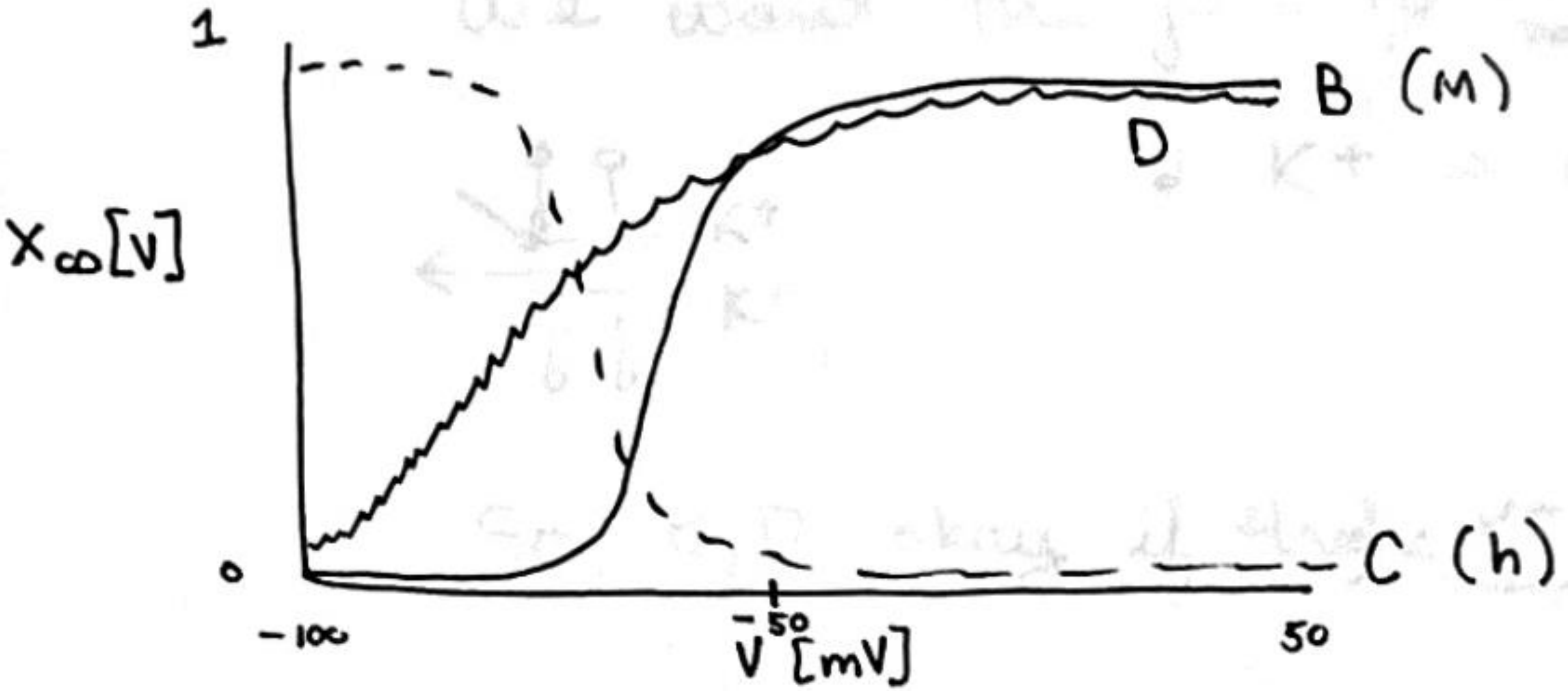
hyperpolarize neuron

So (C) works if it's Na+ (or Ca^{2+}) currents

Beta rhythm model

{~~A~~, B, C, ~~D~~}

Summary



(B,D)

okay if K+ current slowly open & halt burst

(C)

okay if Na+ current slowly close & halt burst

We learn: B gates K+ ☑ C gates Na+ ☑ D gates Na+ ✗

$\{\cancel{A}, \boxed{B}, C, \cancel{D}\}$

Beta rhythm model

Two options remain for I_{new}

B: slow, depolarization activated, outward K+ current

C: slow, depolarization inactivated, inward Na+ current

Sketch a model for B

Beta rhythm model

{$\cancel{A}$, $\boxed{B}$, C, $\cancel{D}$}

HH + B

$$C\,\frac{dV}{dt} = I_{\text{input}}(t) - \bar{g}_{\text{K}}n^4(V - V_{\text{K}}) - \bar{g}_{\text{Na}}m^3h(V - V_{\text{Na}}) - \bar{g}_{\text{L}}(V - V_{\text{L}})\ \boxed{-g_B B(V - E_K)}$$

linear (from lit.)

K+ current

$$\frac{dn}{dt} = -\frac{n - n_\infty(V)}{\tau_n(V)}$$

$$\frac{dm}{dt} = -\frac{m - m_\infty(V)}{\tau_m(V)}$$

$$\frac{dh}{dt} = -\frac{h - h_\infty(V)}{\tau_h(V)}$$

$$\boxed{\frac{dB}{dt} = \frac{B_\infty[V] - B}{\tau_B[V]}}$$

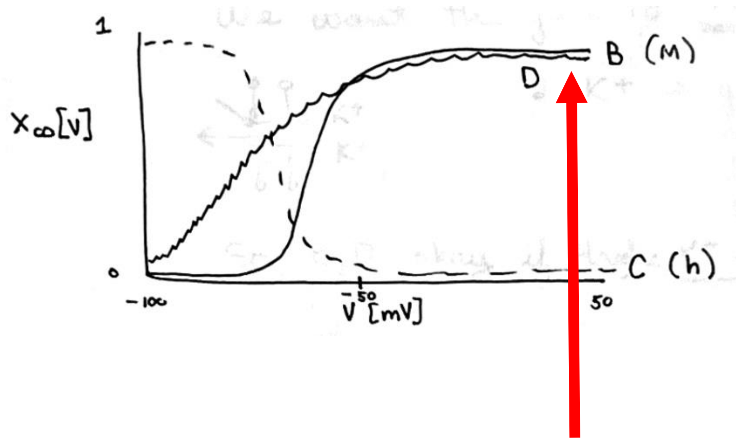
where $B_\infty[V]$ and $\tau_B[V]$ plotted above

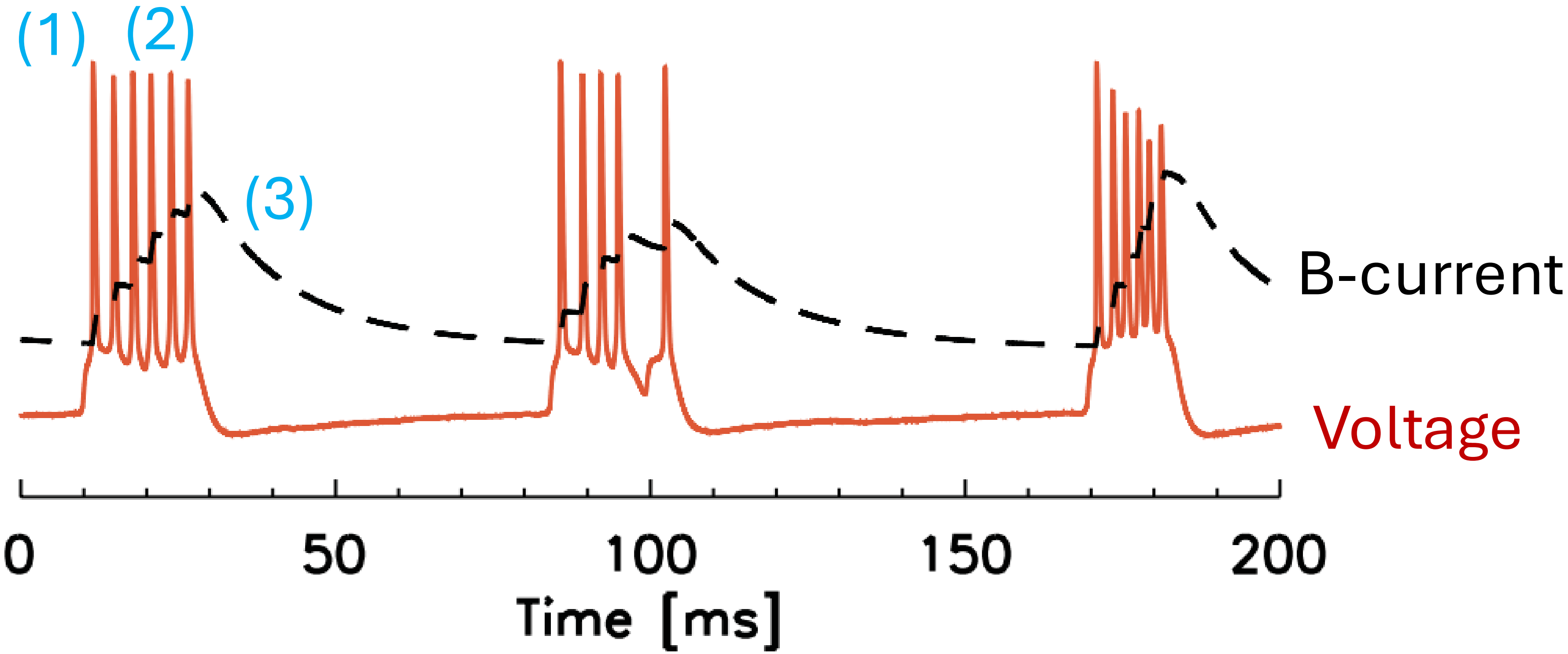
Note: model now has 5 variables {V, n, m, h, B}

Beta rhythm model

$\{\cancel{A}, \boxed{B}, C, \cancel{D}\}$

Illustration





(1) During spike, $B_\infty[V] \rightarrow 1$ so, B → 1 but slowly so, B increases a little

(2) repeat for multiple spikes B → 1 B opens enough to halt spiking

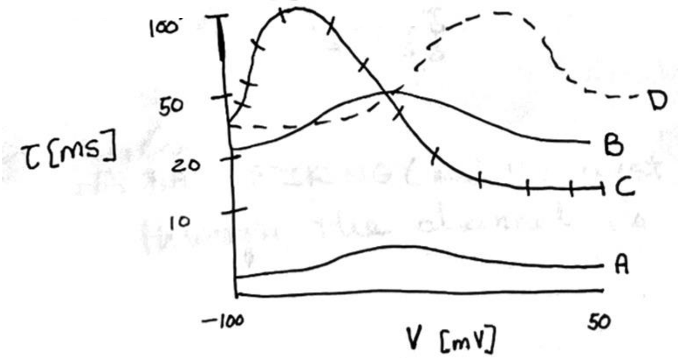
(3) B decays → 0 another burst starts

Summary

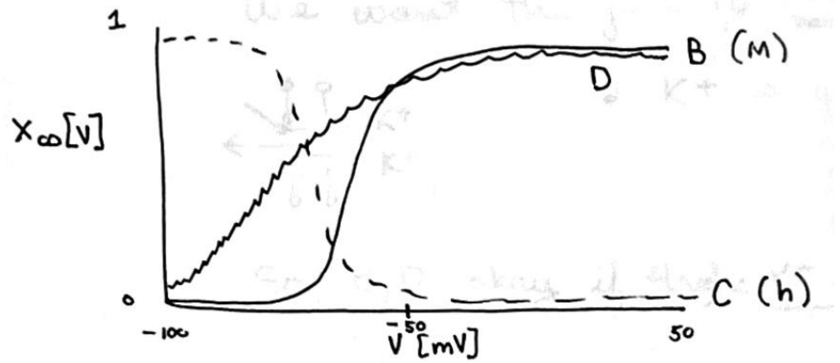
A procedure to classify the dynamic effects of a current on a neuron

<u>3 questions</u>

1. Is it fast or slow?



2. Is to depolarization activated or inactivated?



3. What ion is gated?

K+

Then, we know enough to predict dynamic behavior.

Beta rhythm model

Python ***Homework***