regular spiking

spike frequency accommodation

bursting
Tonic firing mode

Oscillatory mode

One burst of 2-5 action potentials at high frequency (up to 200 Hz)

Leresche et al. 1991
Thalamic Relay Neuron

Burst Tonic firing

Rebound Burst

Deschenes et al. 1984
Cd$^{++}$ blocks all V-gated Ca$^{++}$ channels
Ni$^{++}$ blocks T-type V-gated Ca$^{++}$ channels
The transient (T-type) Ca\(^{++}\) current \(I_T\)

Activation protocol: Hold the neuron at -90 mV and then step to different potentials

Inactivation protocol: Hold the neuron for a “long time” (\(t \gg \tau_h\)) at different potentials and then step to -30 mV

Hernandez-Cruz & Pape 1989
Kim et al 2001

A

\[ V_m = -70 \text{mV} \]

\[ +/+ \]

T-type Ca\(^{++}\) channel KO

\[ -/- \]

(pA) -200 -400 -500 -600 -800 -1000

B

\[ V_m = -80 \text{mV} \]

\[ +/+ \]

T-type Ca\(^{++}\) channel KO

\[ -/- \]

(pA) 200 400 500 600 700 800 900 1200 1400

Kim et al 2001
The T-type Ca\(^{++}\) channel

**Channel name** Cav3.1  
**Description** voltage-gated calcium channel 1 subunit  
**Other names** T-type, 1G, CavT.1  
**Molecular information** human: 2171aa, O43497, NP_061496, chr. 17q22, CACNA1G (ref. 1)  
rat: 2254aa, O54898, AAC67372,  
mouse: 2288aa, Q9WUB8, NP_033913  
(see Comments)  
**Associated subunits** no biochemical evidence, small changes induced by 21 (ref. 2) and 22 (refs. 3,4)  
**Functional assays** voltage clamp, calcium imaging  
**Current** ICa,T  
**Conductance** 7.5pS (ref. 1)  
**Ion selectivity** Sr\(^{2+}\) > Ba\(^{2+}\) = Ca\(^{2+}\) (ref. 5)  
**Activation** Va = 46mV; τa = 1ms at 10mV (ref. 6)  
**Inactivation** Vh = 73mV; τh = 11ms at 10mV (ref. 6)  
**Channel distribution** brain, especially soma and dendrites of neurones in olfactory bulb, amygdala, cerebral cortex, hippocampus, thalamus, hypothalamus, cerebellum, brain stem, heart  
**Physiological functions** thalamic oscillations18,19, possibly cardiac pacemaking
Cs+ blocks the mixed cationic current $I_h$
The channel underlying $I_h$ in thalamic neurons is called HCN4.
HCN4 is permeable to both Na$^+$ and K$^+$ ions with a preference for K$^+$ ions.
Under physiological ionic conditions the reversal potential of $I_h$ is -40 mV, i.e. somewhere in between $E_K$ and $E_{Na}$.
Hence, when HCN4 is open but $V_m$ is -40 mV no net current flows through the channel.
Generally, however, HCN4 is closed at -40mV.
The hyperpolarization activated current $I_h$

HCN4 opens at hyperpolarized potentials

HCN4 does not inactivate; i.e. at hyperpolarized potentials it remains open.
HCN4 de-activates, i.e. closes, at depolarized potentials.
Activation of HCN4 is slow

McCormick&Pape1990
**Channel name**: HCN4 (refs. 1–4)

**Description**: hyperpolarisation-activated, (cyclic nucleotide-gated) cation channel

**Other names**: HAC4, BCNG3

**Molecular information**
- **human**: 1203aa, Q9Y3Q4, AJ132429, chr. 15q24-q25, \( HCN4 \)
- **rat**: 1198aa, Q9JKA7, AF247453, chromosomal location not established
- **mouse**: AF064874, chromosomal location not established

**Associated subunits**: not established

**Functional assays**: voltage clamp

**Current**: \( I_h \) or \( I_f \) or \( I_q \)

**Conductance**: not established

**Ion selectivity**: \( K^+ \), \( Na^+ \) (\( pNa/pK \approx 0.2 \)); divalents do not permeate

**Activation**: \( V_{0.5} = 65mV \) to \( 100mV \); \( \tau_a = 260ms–30s \) at \( 140mV \) to \( 70mV \)

(values are strongly influenced by experimental parameters such as temperature, pH, pulse protocol)

**Inactivation**: no inactivation

**Activators**: \( cAMP > cGMP \) (both induce a positive shift of \( V_{0.5} \) in the range \( +10mV \) to \( +25mV \))

**Gating inhibitors**: ZD7288

**Blockers**: Cs+, ZD7288, ivabradine, zatebradine, alinidine

**Radioligands**: none

**Channel distribution**: thalamus, retina, olfactory bulb, sinus node, taste cells, testis

**Physiological functions**: pacemaker activity, resting potential, rebound depolarisations, control of synaptic transmission, transduction of sour taste

**Mutations and pathophysiology**: homozygous deletion of HCN4 is lethal at embryonic day 10 in mouse
The temporal sequence of conductances underlying a burst:
Activation of $I_h$;
Activation of $I_t$;
$\text{Na}^+/\text{K}^+$ Action potentials;
Inactivation of $I_t$ and de-activation of $I_h$;
Removal of $I_i$ inactivation (de-inactivation);
The temporal sequence of conductances underlying a burst:
Activation of $I_h$;
Activation of $I_t$;
$\text{Na}^+/\text{K}^+$ Action potentials;
Inactivation of $I_t$ and de-activation of $I_h$;
Removal of $I_i$ inactivation (de-inactivation);