The Roles Potassium Currents Play in Regulating the Electrical Activity of Ventral Cochlear Nucleus Neurons

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Paper Used:

Name: The Roles Potassium Currents Play in Regulating the Electrical Activity of Ventral Cochlear Nucleus Neurons.
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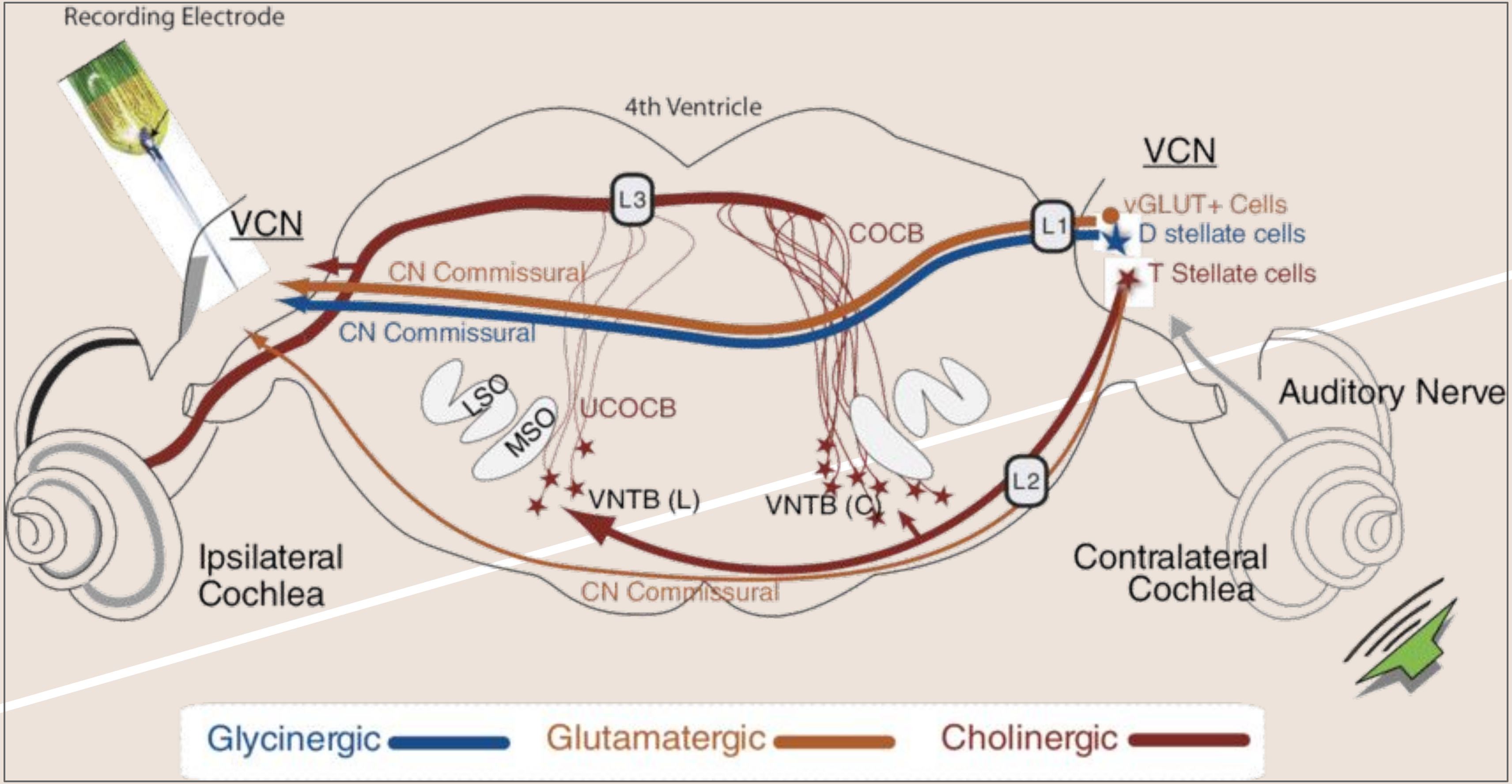
Colab Notebook:

Link:
https://colab.research.google.com/drive/13MfGEDeTwzL8ROGJgayhKPVpR7TgkLAS?usp=sharing



Recording Electrode
4th Ventricle
VCN
VCN
L3
L1
L2
vGLUT+ Cells
D stellate cells
T Stellate cells
COCB
CN Commissural
CN Commissural
CN Commissural
LSO
MSO
UCOCB
VNTB (L)
VNTB (C)
Auditory Nerve
Ipsilateral Cochlea
Contralateral Cochlea
Glycinergic
Glutamatergic
Cholinergic

The Goal Of The Study

Voltage-gated ionic currents introduce strong nonlinearities into a cell's electrical behavior. Computational models are often necessary to provide the appropriate predictive power.

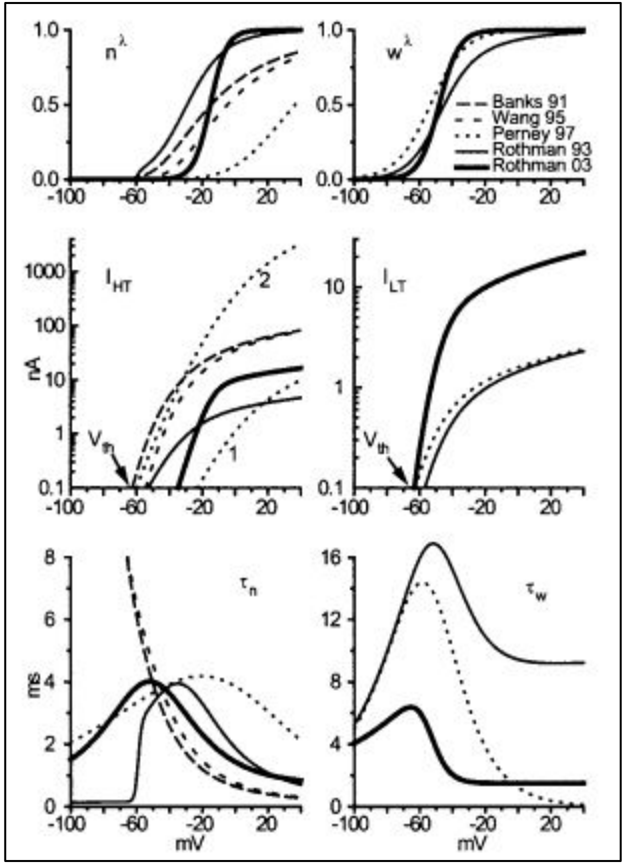
These models were created using limited knowledge of the K+ channels, despite the fact that they have generally proven successful at simulating the response characteristics of stellate and bushy cells.

We considered it relevant and necessary to theoretically reevaluate the functions K currents play in controlling the electrical activity of VCN neurons in light of the numerous differences between the prior theories and our new experimental evidence.

The models are represented by the thin lines. Bold lines represent average experimental data from earlier investigations.

We notice several discrepancies such as:

1. Because they have shallow voltage dependence and activate over several voltage ranges, the activation functions of the model high-threshold currents (n^4) all significantly deviate from the actual data.
2. The model current magnitudes are roughly 10 times less than what the new experimental data suggest. Therefore, the earlier models did not fully explore the potential of the I_{LT} to minimise the membrane time constant.



The membrane potential V is described by the following first-order differential equation:

$$C_m \frac{dV}{dt} = I_A + I_{LT} + I_{HT} + I_{Na} + I_h + I_{lk} + I_E - I_{ext}$$

Where,

1. I_A: Fast inactivating A-type current.
2. I_{LT}: Fast-activating slow-inactivating low threshold current.
3. I_{HT}: High threshold current.
4. I_{NA}: Fast-inactivating TTX-sensitive Na^+ current.
5. I_h: Hyperpolarization activated cation current.
6. I_{lk}: Leak current.
7. I_E: Excitatory synaptic current.
8. I_{ext}: External current source.

TABLE 1. *Model parameters and properties*

	Model Type				
	I-c	I-t	I-II	II-I	II
$\bar{g}_{Na}$, nS	1000	1000	1000	1000	1000
$\bar{g}_{HT}$, nS	150	80	150	150	150
$\bar{g}_{LT}$, nS	0	0	20	35	200
$\bar{g}_{A}$, nS	0	65	0	0	0
$\bar{g}_{h}$, nS	0.5	0.5	2	3.5	20
$\bar{g}_{lk}$, nS	2	2	2	2	2
V_{rest}, mV	−63.9	−64.2	−64.1	−63.8	−63.6
R_{rest}, MΩ	473	453	312	244	71
τ_m, ms	7.0	4.0	3.7	2.9	0.9
V_{th}, mV	−38.3	−34.9	−51.2	−58.0	−62.2
$S_{-50/-70}$, nS	0.3	0.3	5.0	12.6	49.5
$\bar{g}_{E\theta}$ @ 22°C, nS	2.0	2.2	2.8	3.2	8.6
$\bar{g}_{E\theta}$ @ 38°C, nS	11	12	15	17	34

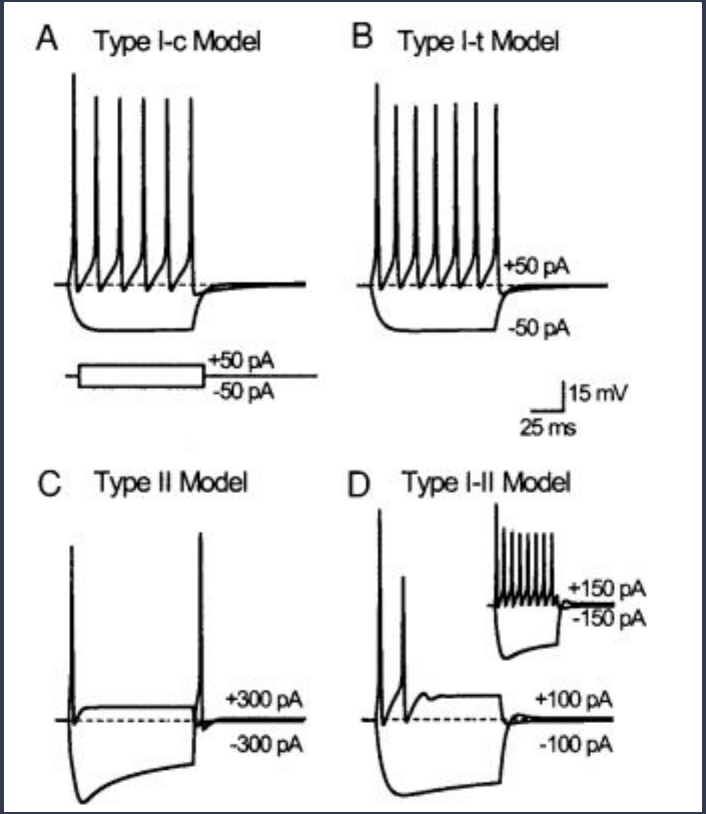
```
maximal_conductances = dict(
type1c=(1000, 150, 0, 0, 0.5, 0, 2),
type1t=(1000, 80, 0, 65, 0.5, 0, 2),
type12=(1000, 150, 20, 0, 2, 0, 2),
type21=(1000, 150, 35, 0, 3.5, 0, 2),
type2=(1000, 150, 200, 0, 20, 0, 2),
)
```

Current Clamp Responses Of Model Types

We considered it relevant and necessary to theoretically re-evaluate the functions K^+ currents play in controlling the electrical activity of VCN neurons in light of the numerous differences between the prior theories and our new experimental evidence.

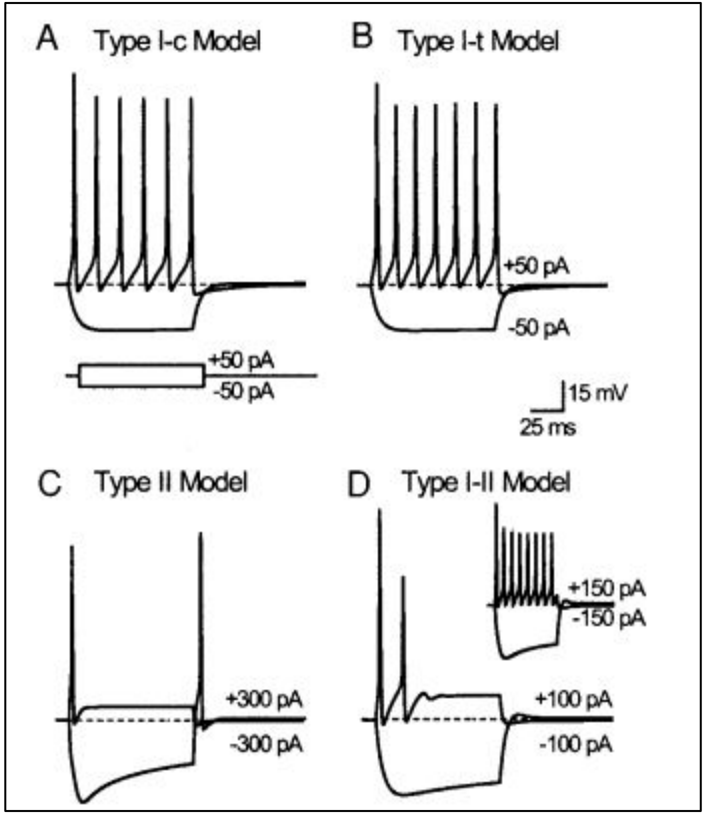
The size of the low-threshold current and the voltage dependence of the high-threshold K^+ current (I^{HT}) are the most significant differences between the models (I^{LT}). The interpretation of the relative functions of the currents, particularly with regard to VCN bushy cells, was constrained by the confounding of these two currents in the majority of earlier models, which caused I^{HT} to behave more like I^{LT}.

Since our characterizations of these two currents were acquired from other neurons, it will be crucial to define the activity of I_{Na} and I_h in VCN neurons in the future.

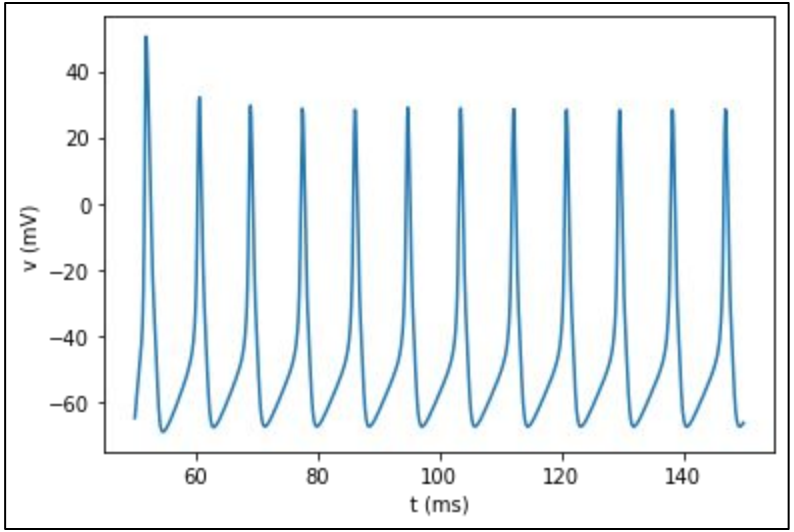


Two different models - Type I-c and Type I-t - respond to small current injections in a similar way. Both models respond to a small depolarizing current pulse with a train of regularly spaced APs, and both respond to a small hyperpolarizing current pulse with an exponential decay of the membrane potential. The only difference is that the Type I-t model shows a higher discharge rate than the Type I-c model during the same current step.

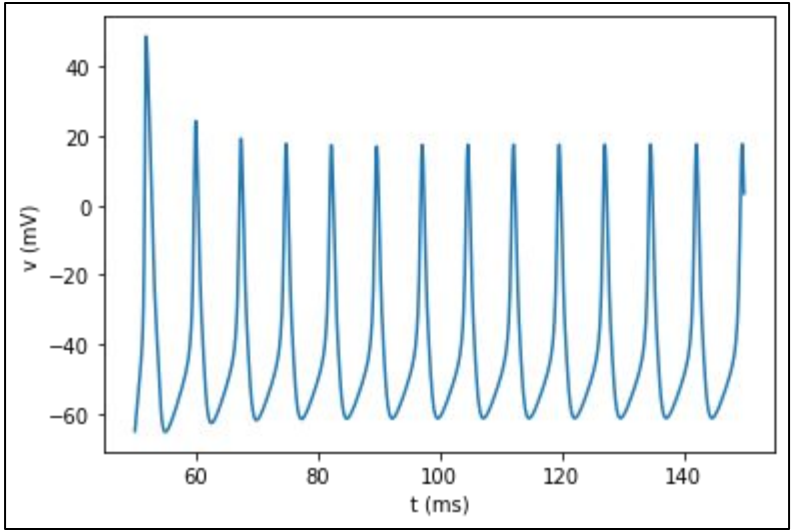
Type I-c and Type II models differ in the magnitude of I_{LT} and I_h. When I_h is blocked, the Type II model no longer displays inward rectification during a hyperpolarizing current pulse, but still displays the characteristic Type II response of a single AP at the onset of a depolarizing current pulse. When I_{LT} is blocked, on the other hand, the Type II model displays a regular discharge of APs in response to a depolarizing current pulse, similar to the canonical Type I current-clamp response. This means that I_{LT} is responsible for the phasic discharge pattern of the Type II model.



Type 1c

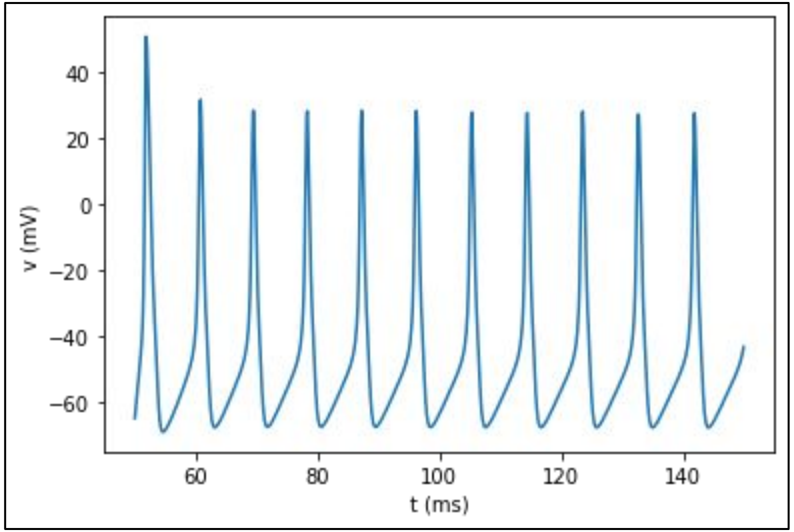


Type 1t

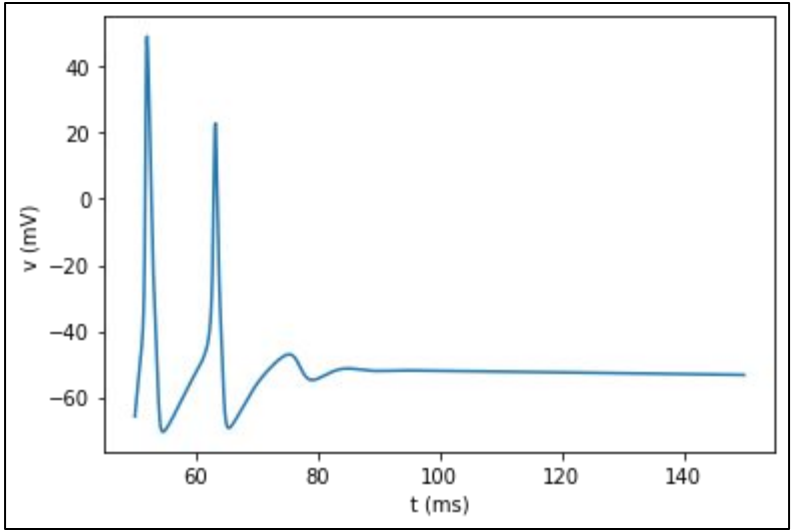


. . . replicating the current clamp results

Type 12

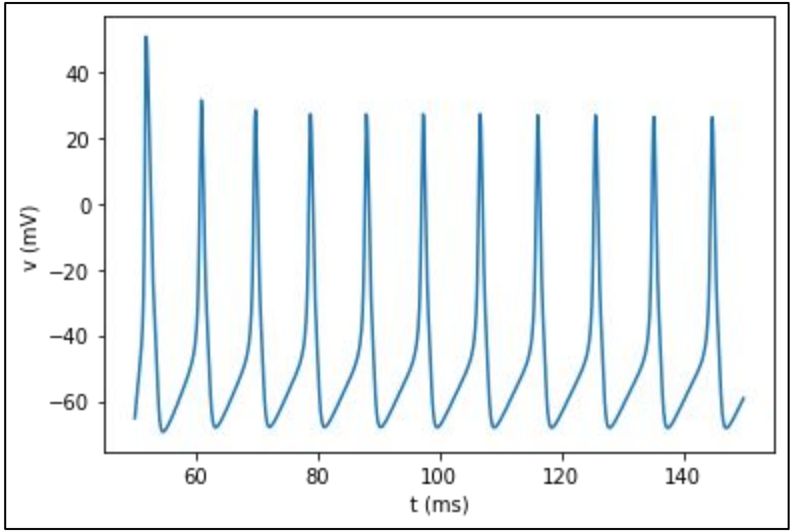


Type 2



. . . replicating the current clamp results

Type 2



(BONUS) . . . replicating the current clamp results

Thank You!