Tonotopic regions have specialized potassium channel properties in the avian cochlear nucleus

Perla Ortiz Baca[1], Kristine McLellan[1,2], & Jason Tait Sanchez[1,2,3]

[1]Roxelyn and Richard Department of Communication Sciences and Disorders, [2]Department of Neurobiology, Northwestern University, [3]Knowles Hearing Research Center

Background

- The avian nucleus magnocellularis (NM) is an analogous structure to the mammalian anteroventral cochlear nucleus (AVCN) and has a specialized tonotopic gradient.
- Low-frequency NM neurons (denoted NMc) have distinct structural and functional differences compared to higher-frequency NM neurons (Hong et al., 2018).
- Low-frequency NMc neurons receive low-frequency auditory nerve inputs and high-frequency NM neurons receive high-frequency auditory nerve inputs.
- High- and low-frequency neurons have synaptic differences. High-frequency neurons are mostly adendritic, while low-frequency neurons retain profuse dendrites throughout development.
- Functionally, high- and low-frequency neurons respond differently to current input. High-frequency neurons are onset responders, while low-frequency neurons are sustained responders.
- Low- and high-frequency neurons express differing amounts of potassium channels, but it is unknown how this affects the magnitude and speed of potassium currents.
- Measuring the kinetics of potassium currents in these neuronal subtypes is essential to explain how and why low- and high-frequency neurons react differently to electrical input.
- Individuals with auditory deficits show adaptation in neural intrinsic properties so their neurons may change the amount and type of potassium current or channels that they have.
- CN refine inputs from the auditory nerve and allows us to accurately encode timing information which is essential for sound localization.
- Normal CN function will assist in understanding a dysfunctional system.

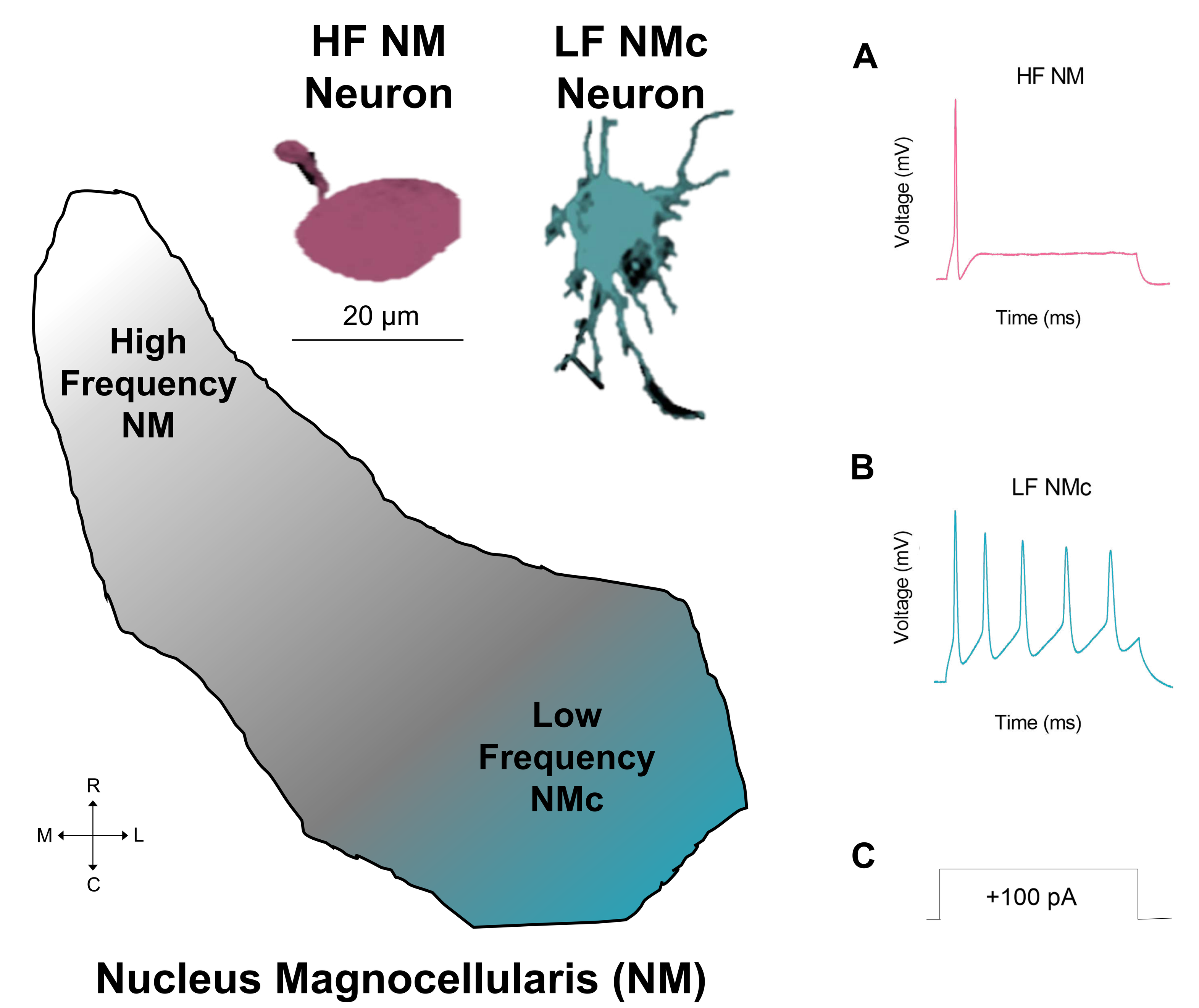

Figure 1: Low- versus high- frequency action potentials in response to current input. (A) High-frequency onset action potentials (B) low-frequency sustained action potentials in response to (C) 100 pA current input.

Methods

- Brainstem slices were prepared from White Leghorn chicken (*Gallus gallus domesticus*) at mature embryonic stages (embryonic days 19-21).
- Whole-cell current and voltage clamp recordings were obtained from LF neurons in the most caudal slices of NM.
- Low-frequency neurons were confirmed in current clamp recordings and potassium currents were isolated by adding 1μM TTX to the bath.
- Voltage commands of varying durations and strengths were activated in the soma of low-frequency and high-frequency NM neurons using an Axon Multiclamp 700B amplifier.
- Results were acquired and analyzed using Clampfit 11.0 analysis software.

Channel Opening

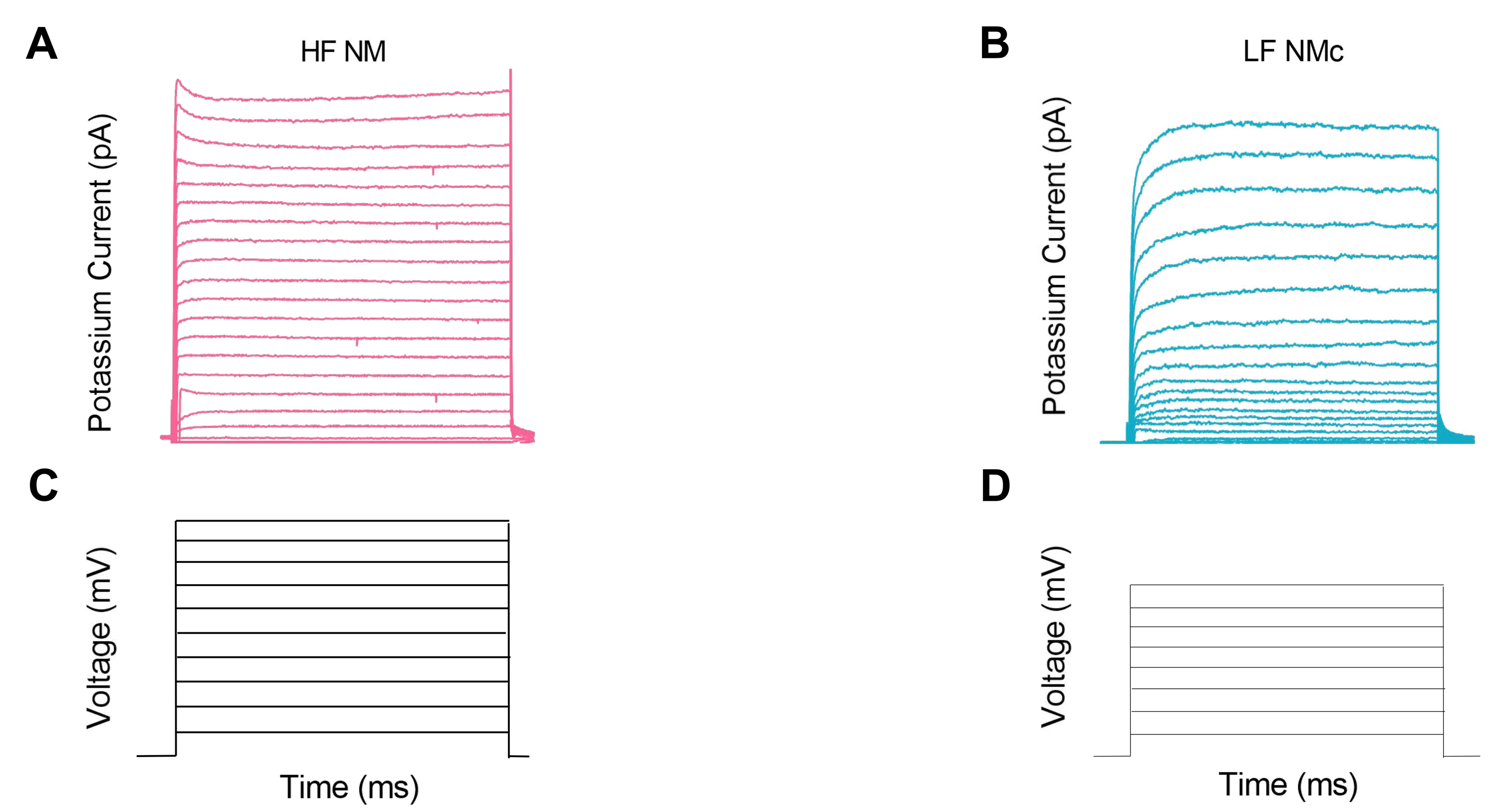

Figure 2: Current and voltage clamp recordings in high- versus low-frequency neurons. Examples of potassium current traces in response to voltage commands at different depolarizing voltages of 100 ms duration. (A) high-frequency and (B) low-frequency potassium currents and its associated voltage commands (C & D, respectively).

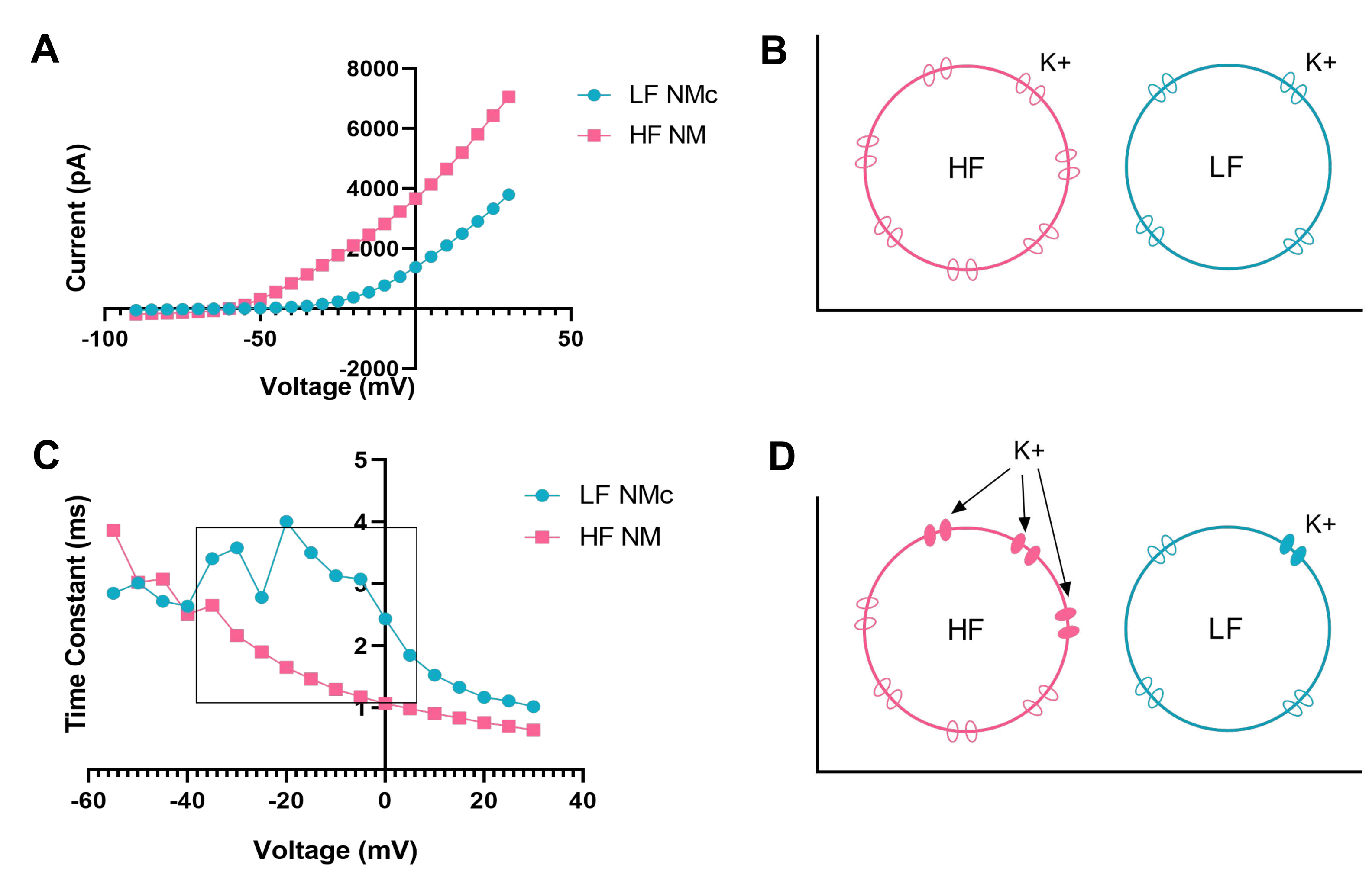

Figure 2: (A) Low- versus high-frequency potassium current. At depolarized voltages, high-frequency neurons have significantly more outward potassium current than low-frequency neurons. (B) Working theory: high-frequency neurons have more potassium channels and low frequency-neurons have fewer channels. (C) Low- versus high-frequency speed of potassium channel opening. High-frequency potassium channels have a faster opening speed compared to low-frequency potassium channels. (D) Working theory: difference suggest different types of channel potassium channels in low- versus high-frequency neurons.

Channel Closing

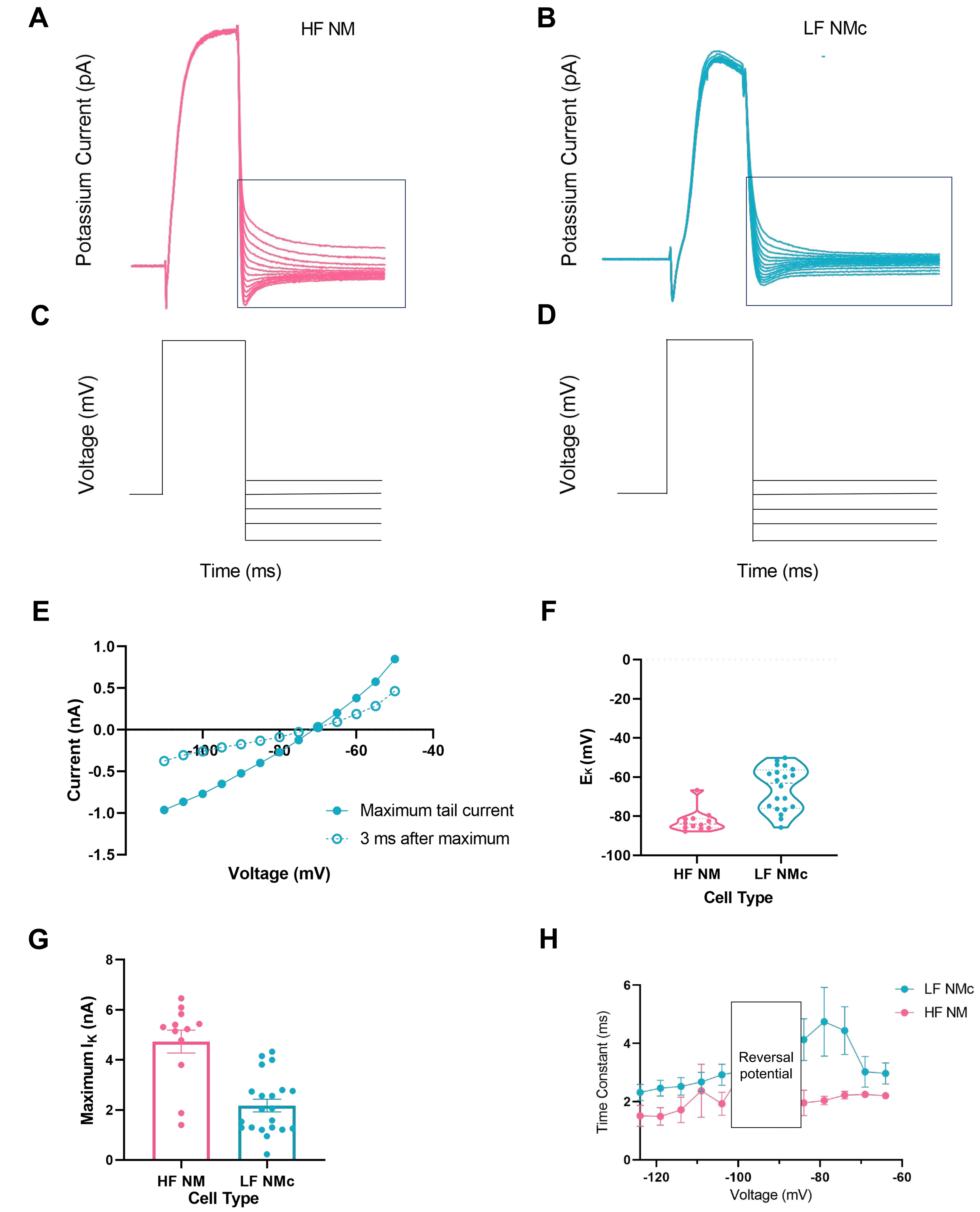

Figure 3: Potassium currents in high- versus low-frequency neurons. Representative currents from (A) high-frequency and (B) low-frequency neurons in response to voltage deactivation steps protocol (C & D, respectively) with a short, 5 ms depolarization. (E) Representative I-V curve with tail currents plotted at their maximum and at 3 ms after their maximum. These were used to measure reversal potential for potassium (E_K). (F) Measured reversal potentials for potassium (E_K) and (G) maximum potassium currents, and (H) time constants of potassium tail currents are all significantly different across tonotopic regions.

Conclusions

1. Potassium tail current analysis contributes to the rich characterization of low-frequency NMc neurons compared to high-frequency NM.
2. High- and low-frequency neurons exhibit unique potassium currents in response to voltage commands, as shown by their differences in current magnitude, time constant, and potassium reversal potential.
3. High-frequency neurons have more K+ current and faster kinetics at specific voltages compared to low-frequency neurons.
4. Neurons encode temporal information relevant to their frequency specific inputs.
5. People with auditory deficits show adaptation in their neural intrinsic properties, suggesting a role of specialized potassium channels.

Funding: NIH, NIDCD R01 DC017167 (JTS)

The School of Communication and The Knowles Hearing Research Center, Northwestern University