4pPP41

Testing Phenomenological Auditory-Nerve Model Predictions for Selective Inner-Hair Cell Dysfunction

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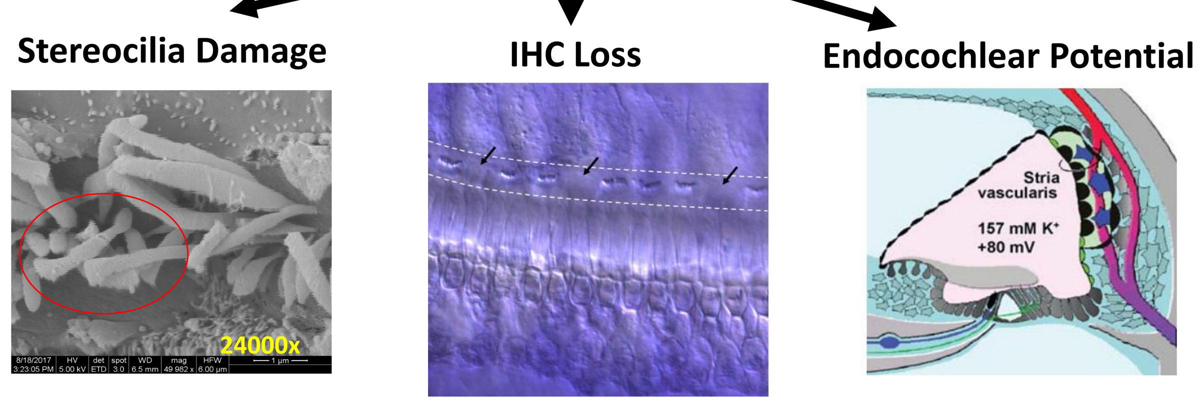
Introduction

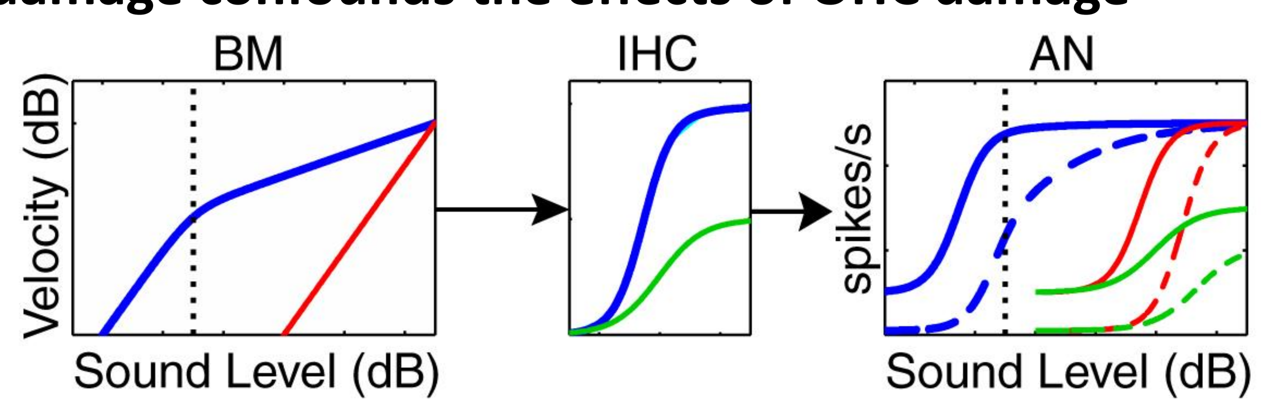
- **Sensorineural hearing loss is a downstream result of (at least) OHC and IHC-related dysfunction**

- **IHC dysfunction stems from various pathophysiologies**

dB Hearing Loss = **HL_ihc** + HL_ohc



- **IHC damage confounds the effects of OHC damage**

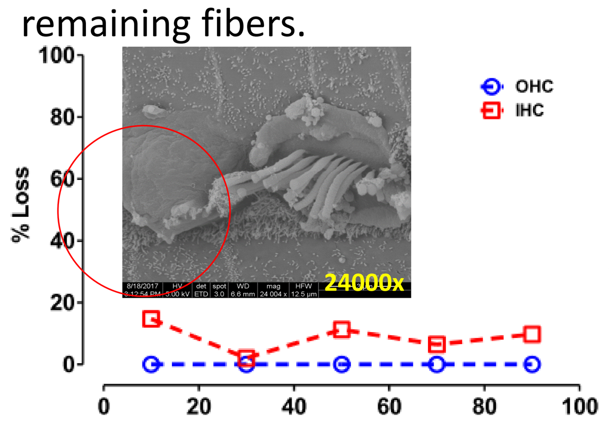


- **There is a significant need to accurately model how neural function is altered after IHC damage**

Methods

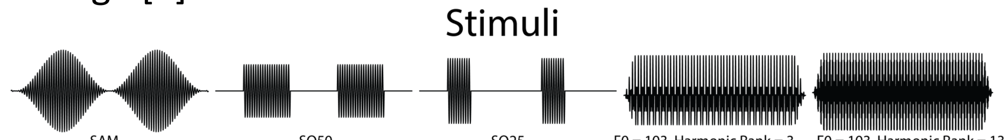
Physiology:

-**IHC Damage** induced using 38mg/kg carboplatin (CA) in chinchillas
Histologically determined : ~0% OHC loss, ~10% IHC loss with **stereocilia loss** in remaining fibers.



-**Single Unit AN characterization:** Effects on temporal coding deficits after CA exposure quantified using spontaneous rates , driven rates and vector strength [1]

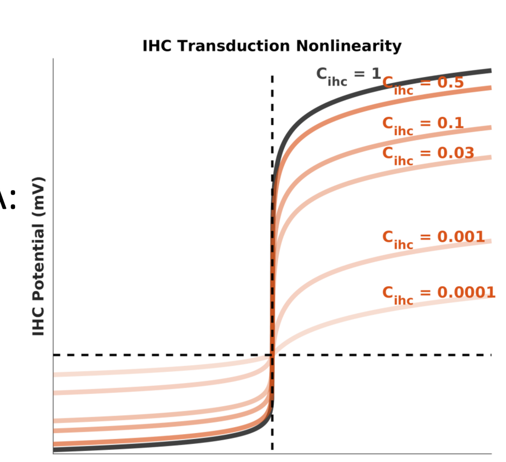
-**Evoked potential data (EFRs):** Used to study deficits in modulation and tone complex coding in presence of IHC damage [2]



Modeling (BEZ2018 [3]):

-**Single Unit responses** :
-For rate level curves, CF range distribution matched to in-vivo data.
-For VSpp, SAM stimulus F_c set at fiber CF
-Spont. rate matched to mean of physiological data (NH: 55, CA: 40)

-**Evoked potential responses** to stimuli presented in-vivo:
- SAM, sq25, and tone complex
- CFs spaced in half increments of modulation frequency
- alternating-polarity PSTHs summed and normalized across CF



-**Simulated a wide range of** cihc **values (0.0001 to 0.9 [HI]; 1.0 [NH])**

Single-Unit

ANF model used to simulate rate level curves (RLVs) and phase-projected vector strength (VSpp) to compare physiological and model responses

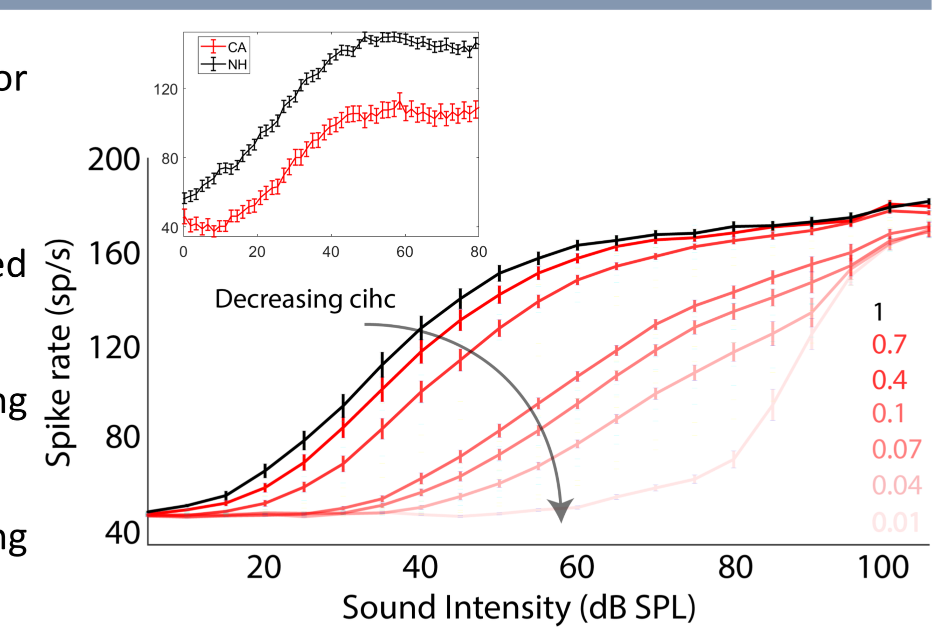
Rate level curves

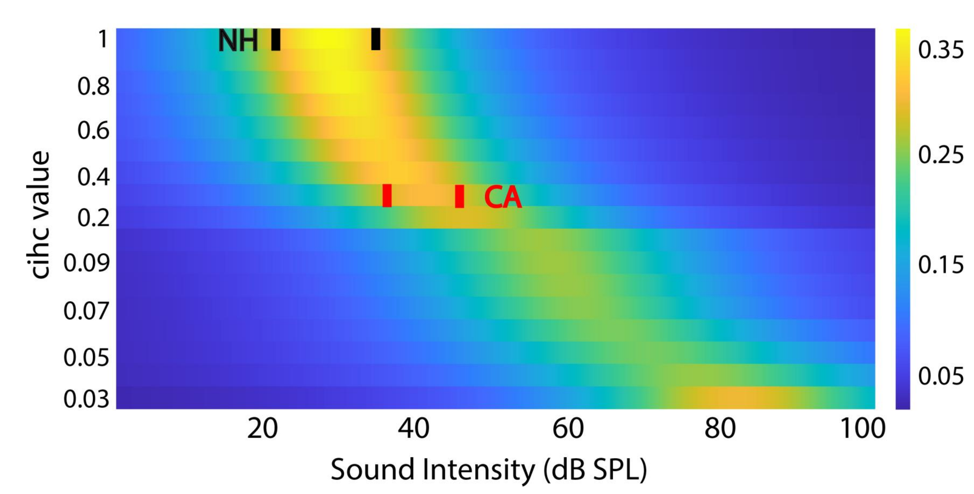
- **Driven rates** were compared for physiological data (inset) and model responses for varying cihc values

- Arctan sigmoid estimate computed for each of the RLVs

- Dynamic range width calculated using threshold on slope of sigmoid fit

- Saturation rate calculated using sigmoid parameters as x→∞

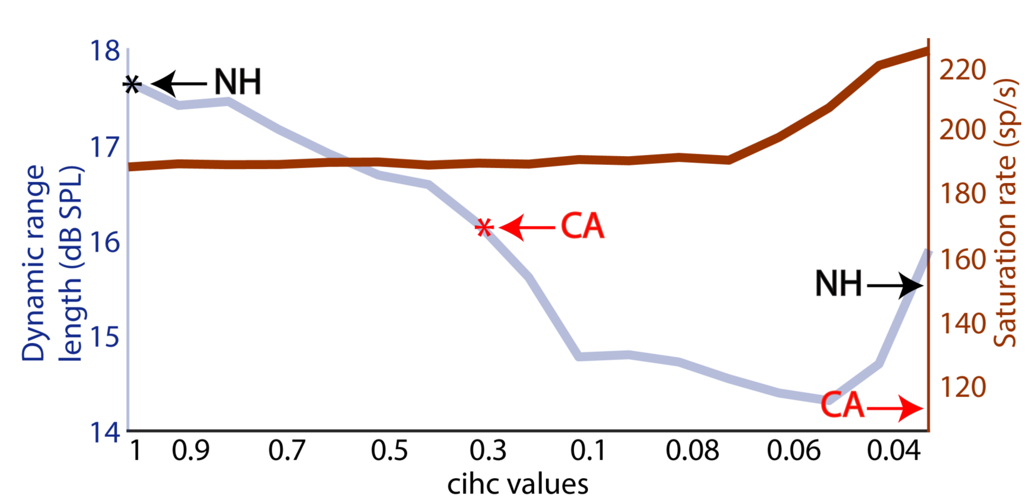




- RLVs for decreasing cihc values show a reduced slope translating to reduced dynamic range width

- cihc~=0.3 **most closely matches physiological ANF data**

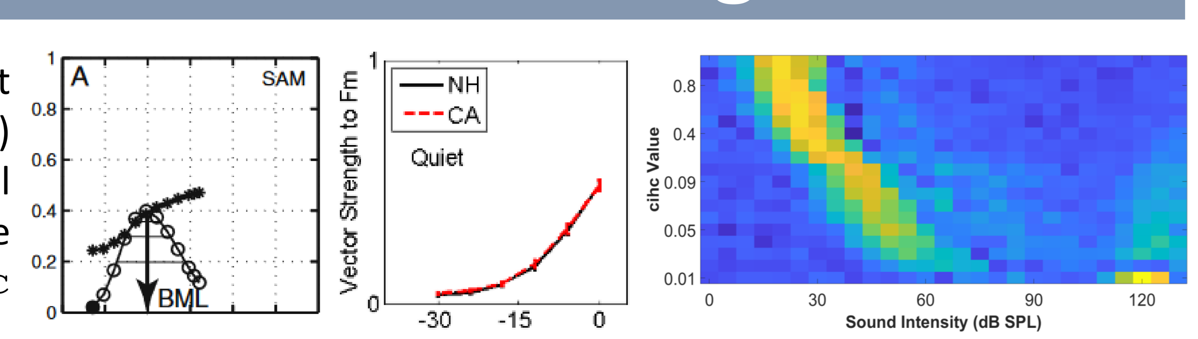
- ANF physiological saturation rate drops after CA, **but model saturated rates do not account for this drop for any cihc**



Measure	Best cihc
Dynamic Range	**0.3**
Saturation Rate	**NO MATCH**

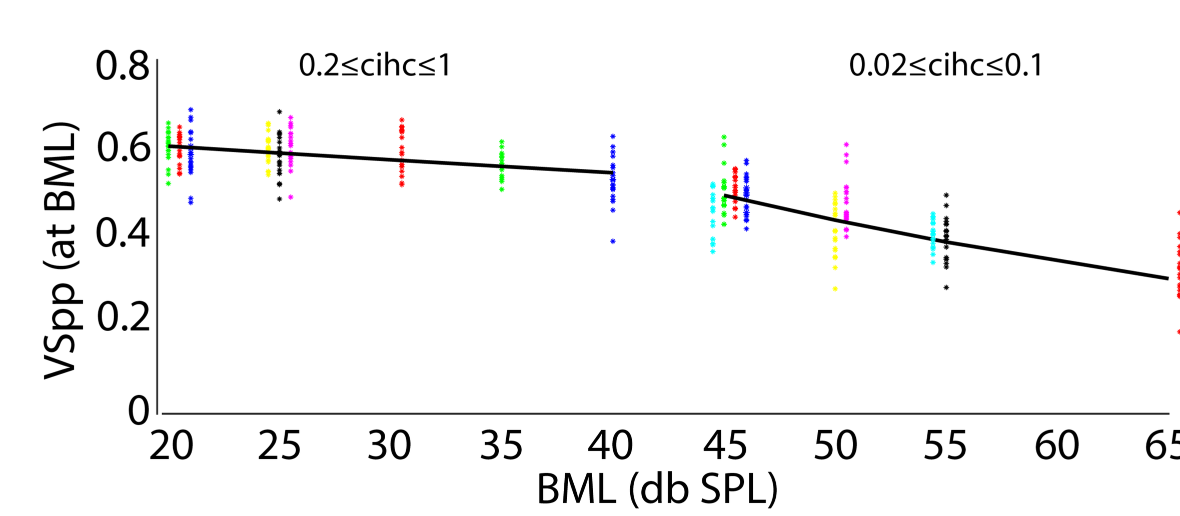
Modulation coding

- VSpp at Best Modulation Level (BML) shows a gradual decrease in amplitude with reducing cihc down to 0.2



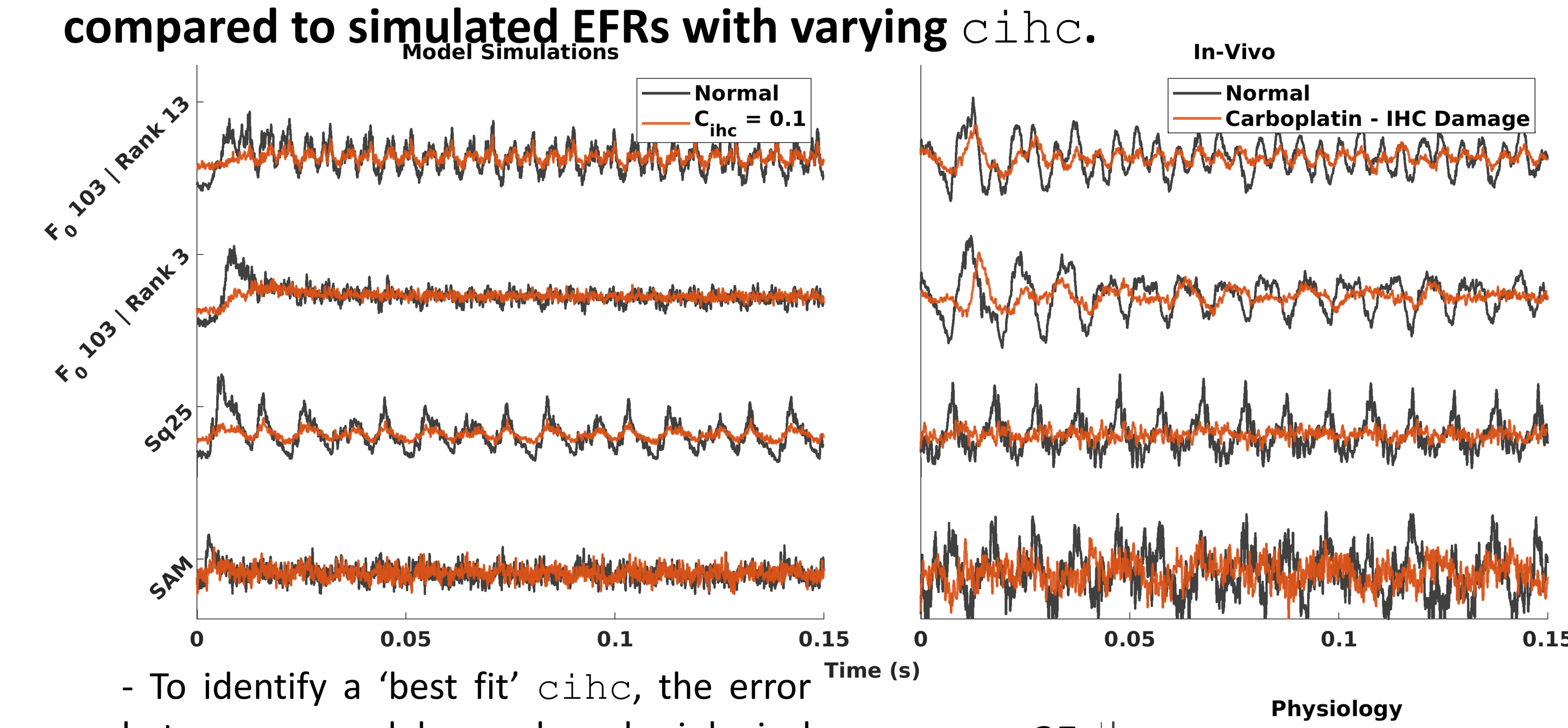
- Exponential fit shows steeper reduction in lower cihc regime, **inconsistent with ANF physiology**

- This suggests that this best-fit model cihc needs to be > 0.2



Evoked Potentials

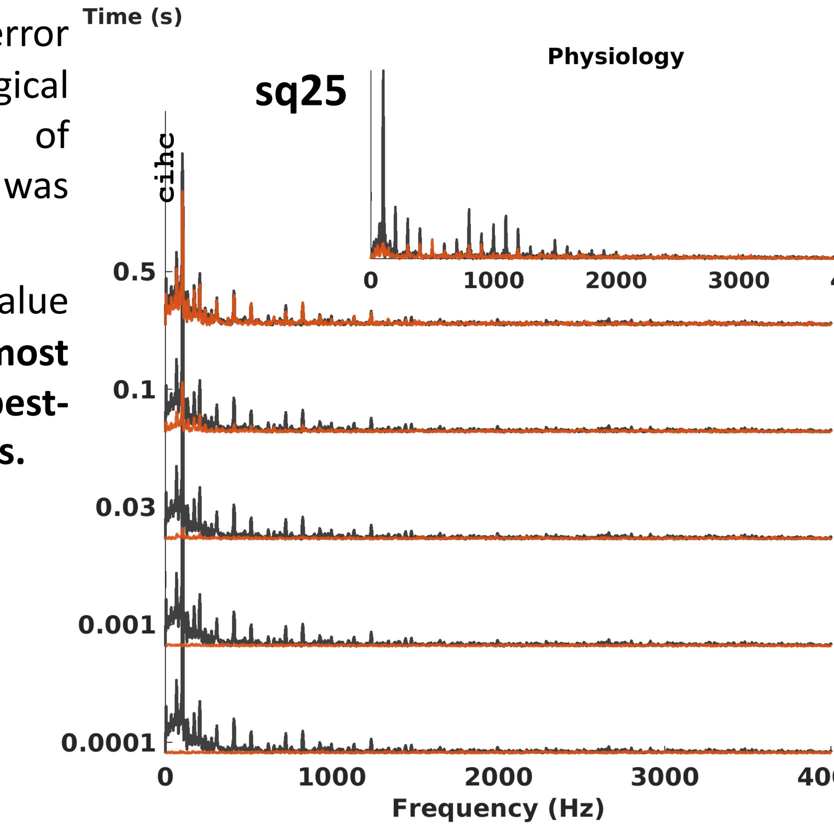
In-vivo evoked potentials to four stimuli after CA exposure were compared to simulated EFRs with varying cihc**.**



- To identify a 'best fit' cihc, the error between model and physiological magnitude squared coherence of impaired vs normal waveforms was minimized.

- Interestingly, the best-fit cihc value appears **stimulus-dependent** and **almost an order of magnitude lower than best-fit** cihc **from single-unit comparisons.**

Stimulus	Best cihc
F_0 103 |Rank 13	0.01
F_0 103 |Rank 3	0.09
Sq25	0.08
SAM	1.0



Conclusions

A single unifying parameter cihc **may not fully encapsulate the wide array of underlying pathophysiology behind IHC impairment**

- The model **does not match** our in-vivo saturation rate values, despite matched spontaneous rate statistics and CF distribution

- Our varied best-fit cihc values for the same animal model highlights that IHC dysfunction is a key area for model improvement

Future Directions:

- Refine our optimization framework to improve best-fit cihc resolution

- Propose refinements to current AN model to better represent biophysical damage properties (e.g., ionic current reduction with stereocilia damage or EP reduction), i.e., to link DR, SR, and transduction-slope effects

- Apply framework to physiological data with OHC damage (e.g. PTS, Gentamicin) to identify matching cohc parameters

Check out our code!!

Acknowledgements:

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References:

[1] Axe, D., Thesis, Purdue University 2017
[2] Sivaprakasam, A., Schweinzger, I., Bharadwaj, H., Heinz, M., 46th Annual ARO MidWinter Meeting, 2023
[3] Bruce, I., et al., Hearing Research, 2017