

## Observations During the Study of Hair Cell Mechanotransduction

ARO Virtual Seminar Series  
October 15, 2020  
*Anthony W. Peng*

 University of Colorado  
Anschutz Medical Campus

1

---



---



---



---



---



---



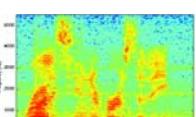
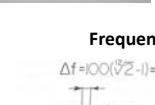
---



---

### The remarkable hearing system



<b>Dynamic Range</b>  	<b>Complex processes</b>  
<b>Frequency Selectivity</b> $\Delta f = 100(\frac{f_2 - f_1}{f_2}) = 6\%$ $\Delta f = 0.2\%$  	

Dallos & Fay, 1996  <http://www.ee.utoronto.ca/object/crossed-party-effect>

2

---



---



---



---



---



---



---



---

### Outline



- Introduction to hearing and mechanotransduction mechanisms
- 2 Major Observations
  - Regarding fast adaptation
  - Regarding slow adaptation
- Summary and speculation of mechanotransduction mechanisms

3

3

---



---



---



---



---



---

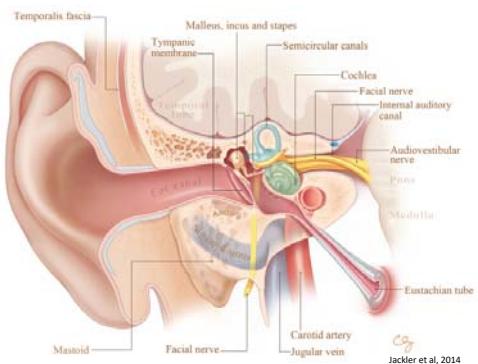


---



---

## How does the ear detect sound?



4

---

---

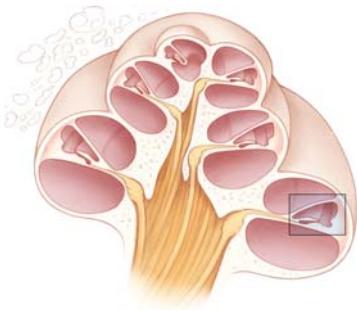
---

---

---

---

## Cochlea



5

---

---

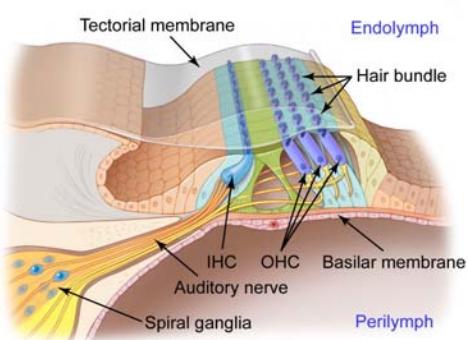
---

---

---

---

## Organ of Corti



6

---

---

---

---

---

---

6



---

---

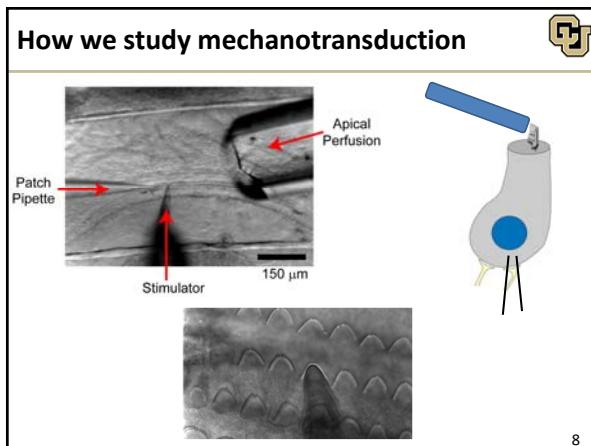
---

---

---

---

7



---

---

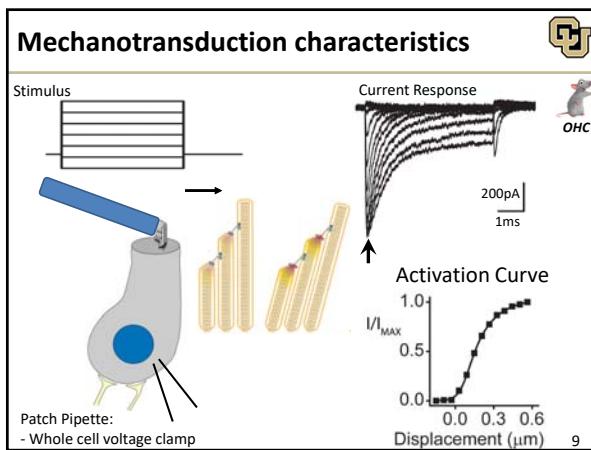
---

---

---

---

8



---

---

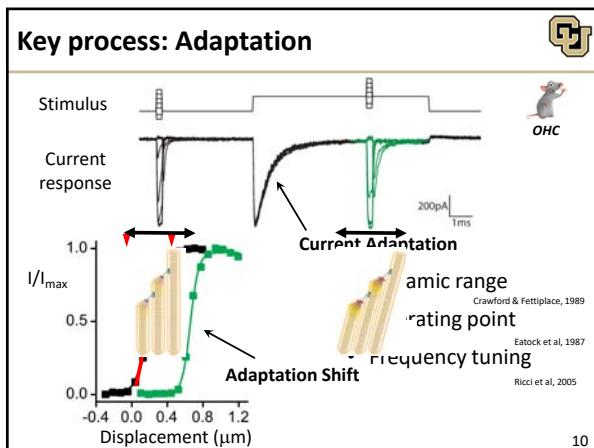
---

---

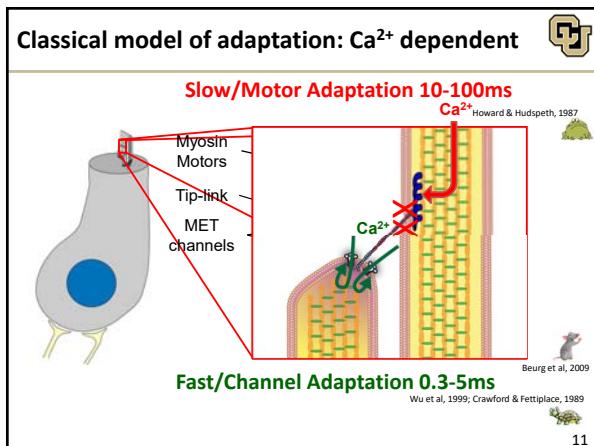
---

---

9



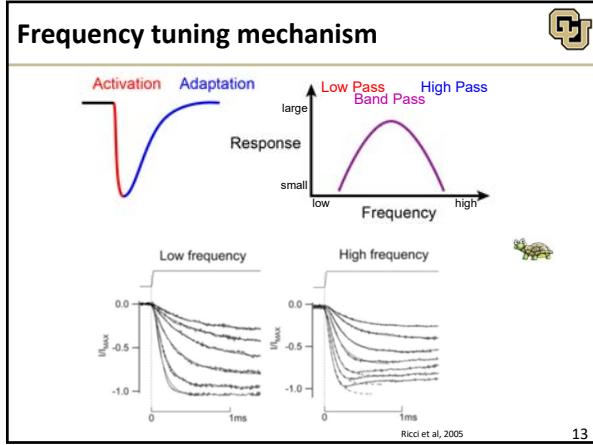
10



11

- Outline**
- Introduction to hearing and mechanotransduction mechanisms
  - 2 Major Observations
    - Regarding fast adaptation
    - Regarding slow adaptation
  - Summary and speculation of mechanotransduction mechanisms
- 12

12



13

---

---

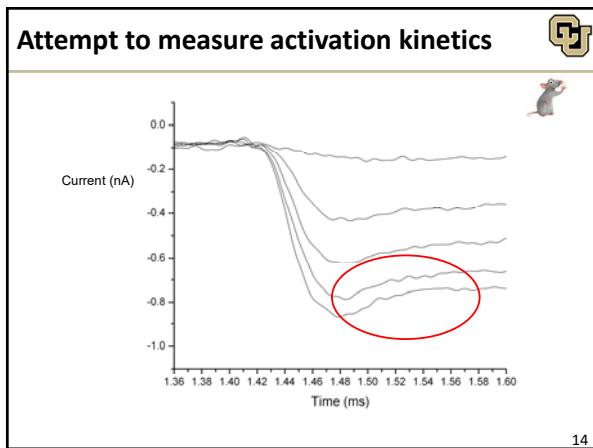
---

---

---

---

---



14

---

---

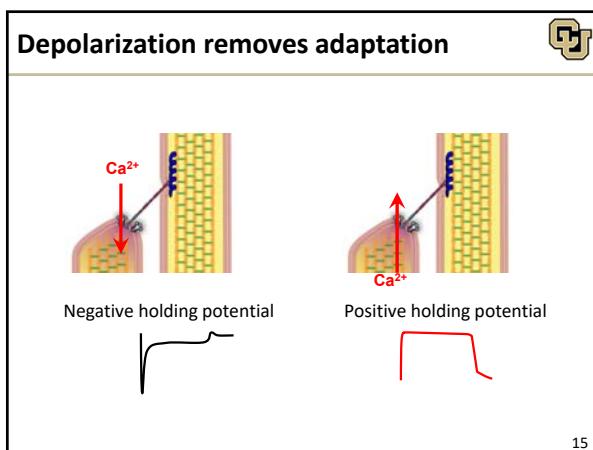
---

---

---

---

---



15

---

---

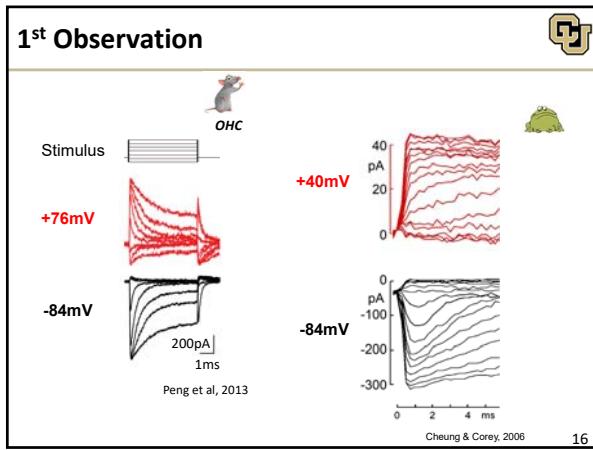
---

---

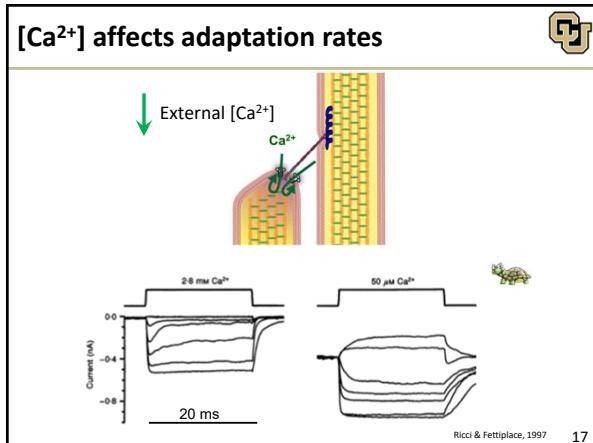
---

---

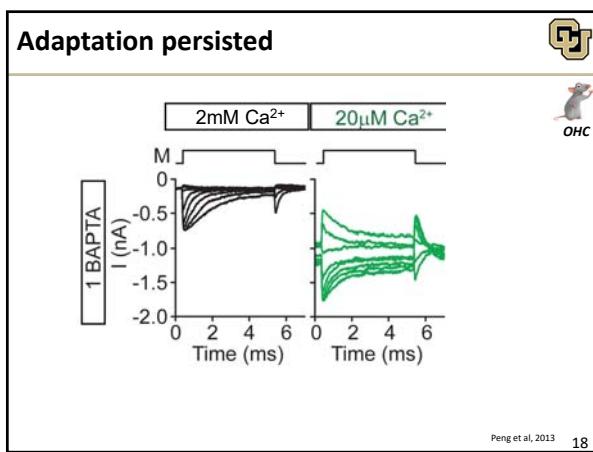
---



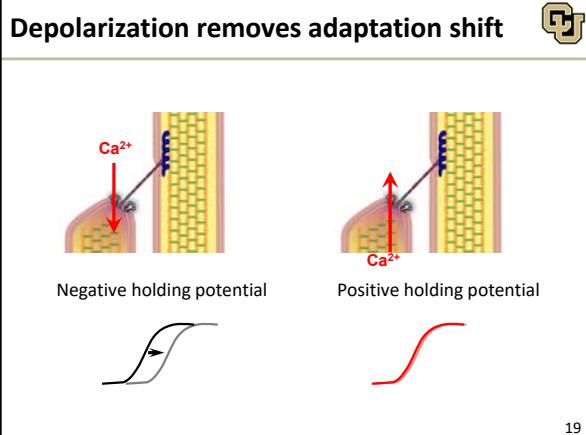
16



17



18




---

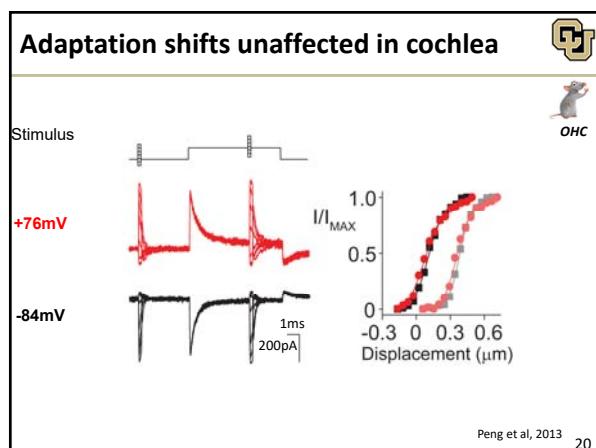
---

---

---

---

---




---

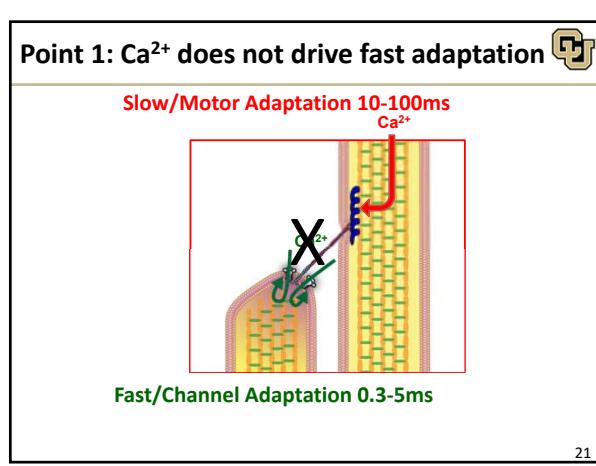
---

---

---

---

---




---

---

---

---

---

---

## Outline

- Introduction to hearing and mechanotransduction mechanisms
- 2 Major Observations
  - Regarding fast adaptation
  - Regarding slow adaptation
- Summary and speculation of mechanotransduction mechanisms

22

---



---



---



---



---



---



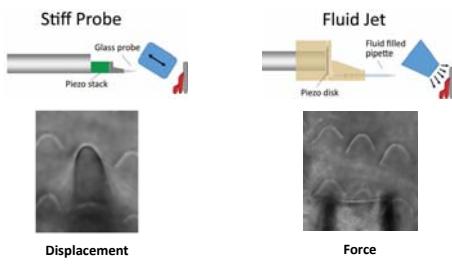
---



---

22

## Most common stimulators used



$$F = kx$$

23

---



---



---



---



---



---



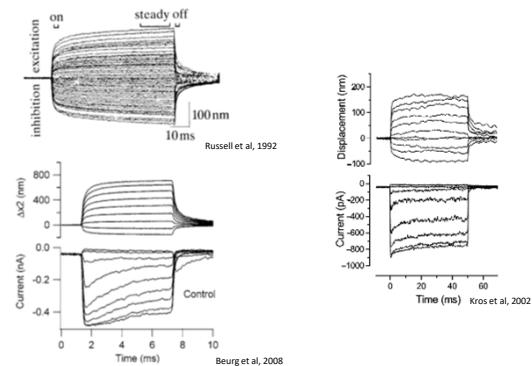
---



---

23

## Known that hair bundle stiffness changes



24

---



---



---



---



---



---



---

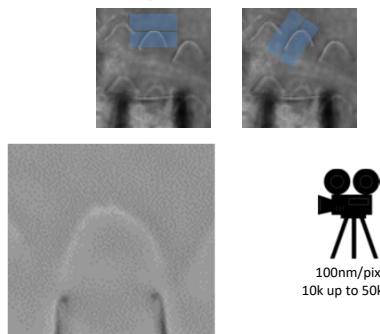


---

24

### New method to measure bundle motion

Original Photodiode method



25

---

---

---

---

---

---

---

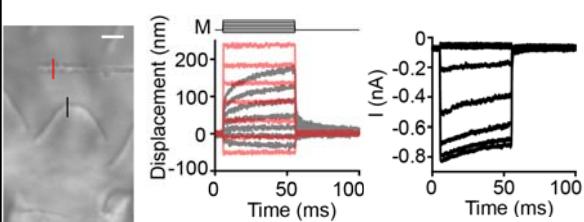
---

---

---

25

### FJ stimulus accentuates slow adaptation in the receptor current



Caprara et al., 2019

26

---

---

---

---

---

---

---

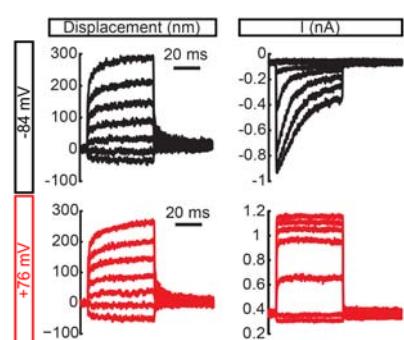
---

---

---

26

### 2<sup>nd</sup> Observation



27

---

---

---

---

---

---

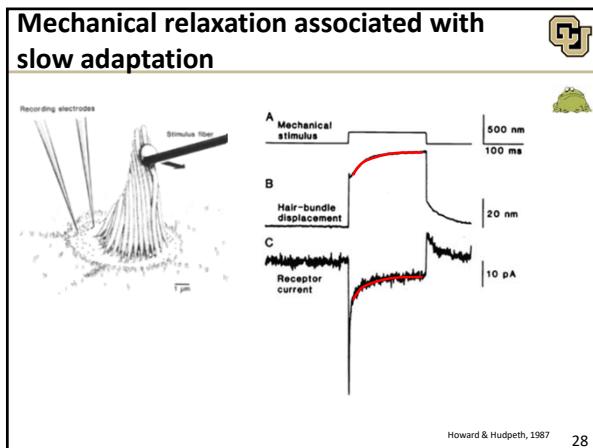
---

---

---

---

27



28

---

---

---

---

---

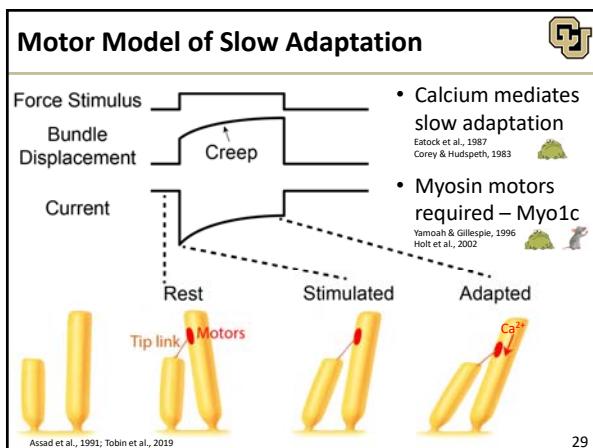
---

---

---

---

---



29

---

---

---

---

---

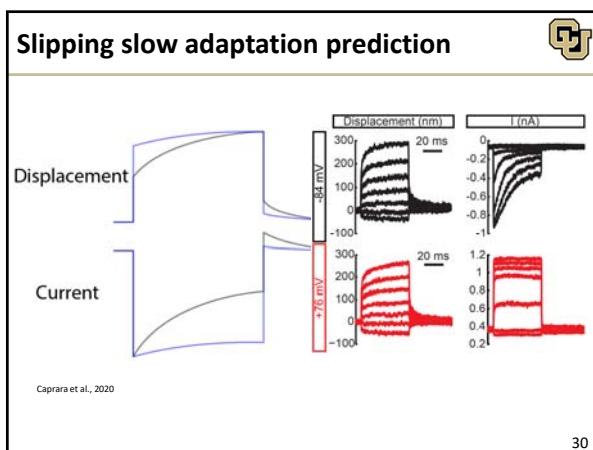
---

---

---

---

---



30

---

---

---

---

---

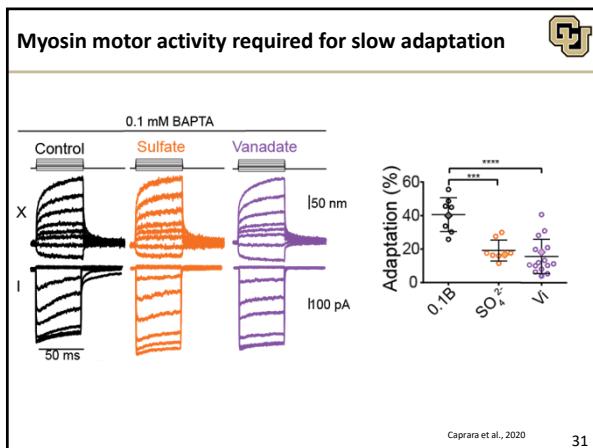
---

---

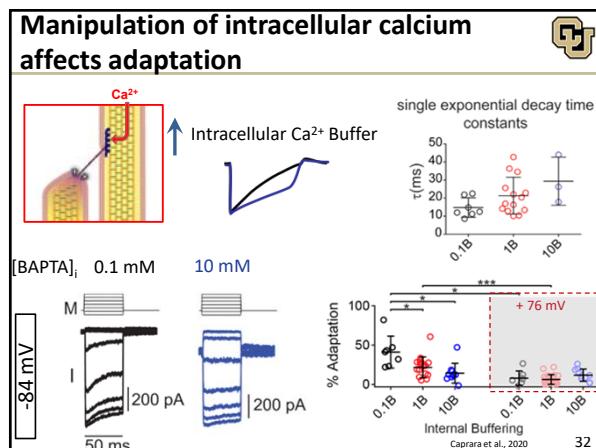
---

---

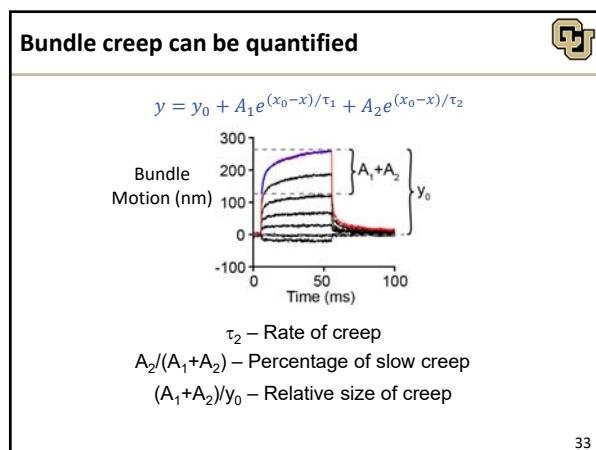
---



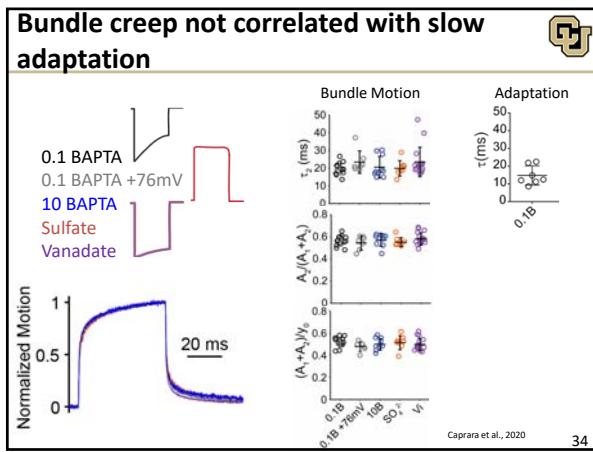
31



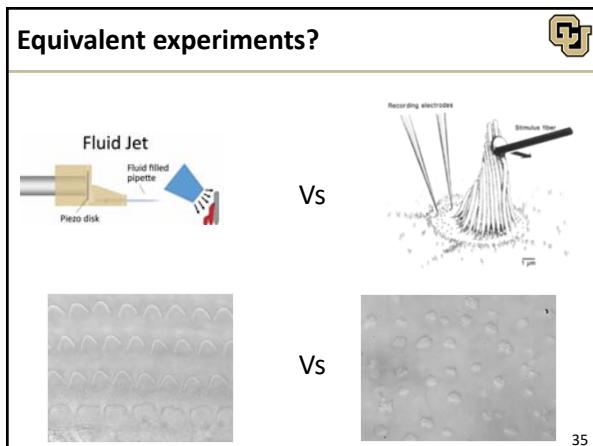
32



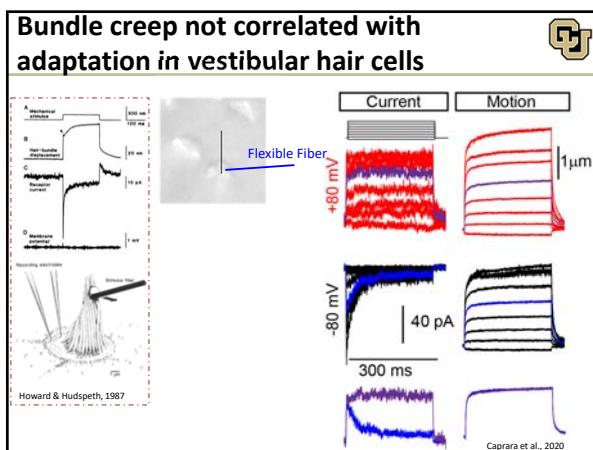
33



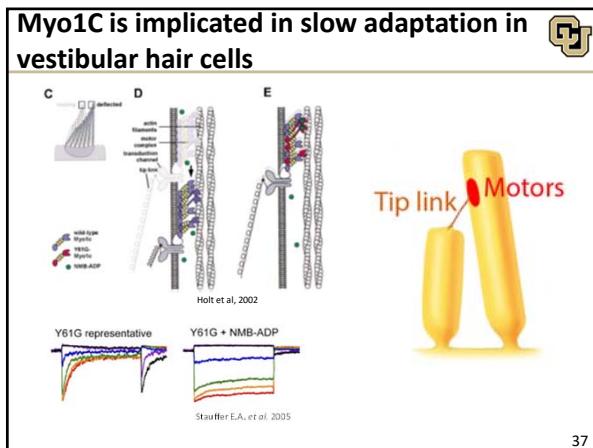
34



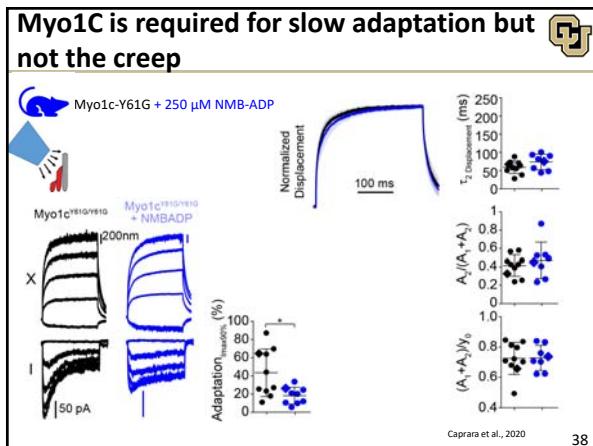
35



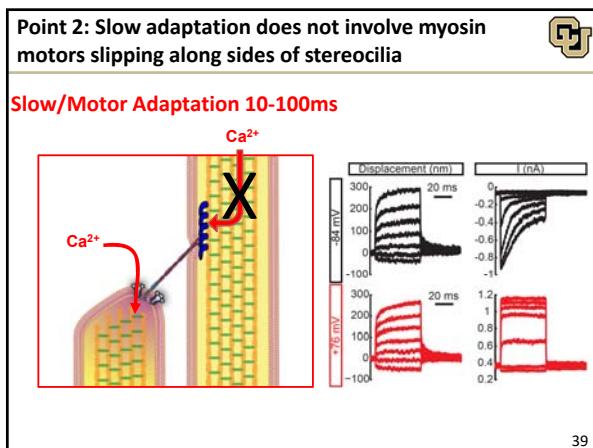
36



37



38



39

## Outline

- Introduction to hearing and mechanotransduction mechanisms
- 2 Major Observations
  - Regarding fast adaptation
  - Regarding slow adaptation
- Summary and speculation of mechanotransduction mechanisms



40

40

---



---



---



---



---



---

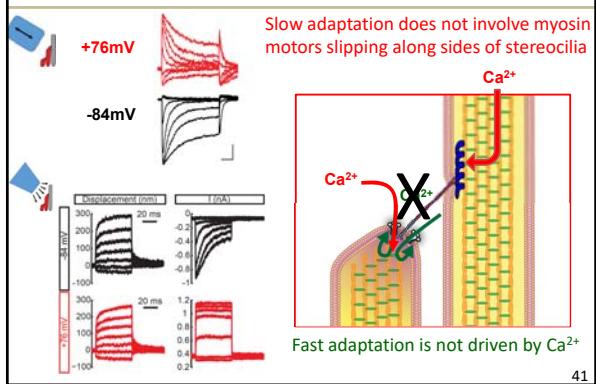


---



---

## Summary



41

41

---



---



---



---



---



---



---

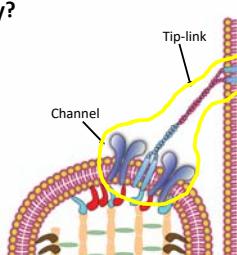


---

## Future Directions – Fast adaptation



- Not calcium-dependent
- Viscoelasticity?



42

42

---



---



---



---



---



---



---



---

**Future Directions – Slow adaptation**

The diagram illustrates two models of slow adaptation:

- Previous Motor Model:** Shows myosins at the tip link interacting with actin filaments. Calcium ions ( $\text{Ca}^{2+}$ ) are shown activating the myosins. A double-headed arrow indicates the resulting movement.
- New Lipid Model:** Shows myosins interacting with a lipid bilayer. Calcium ions ( $\text{Ca}^{2+}$ ) and inositol triphosphate ( $\text{IP}_3$ ) are shown activating the myosins. The model is based on Myo7a – Li et al., 2020.

Cited references: Hirono et al., 2004; Effertz et al., 2017; Cunningham et al., 2020.

43

43

**Acknowledgments**

UVA:  
Jung-bum Shin  
Sihan Li  
Tingting Du

Peng Lab:  
Andrew Mecca  
Giusy Caprara

Stanford:  
Anthony Thomas  
Beth Pr  
Joseph Doll  
Tom Larsen

SUNY Buffalo:  
Fred Sachs  
Krishnan Gnanasambandam

"Science is a method for asking awkward questions and subjecting them to reality-check, thus avoid the human tendency to believe whatever makes us feel good"

Terry Pratchett

**Postdoc opening in the lab!**  
Email: anthony.peng@cuanschutz.edu

OHSU:  
Peter Barr-Gillespie

NIDCD:

R01 DC013299  
R01 DC016868 to AWP

44

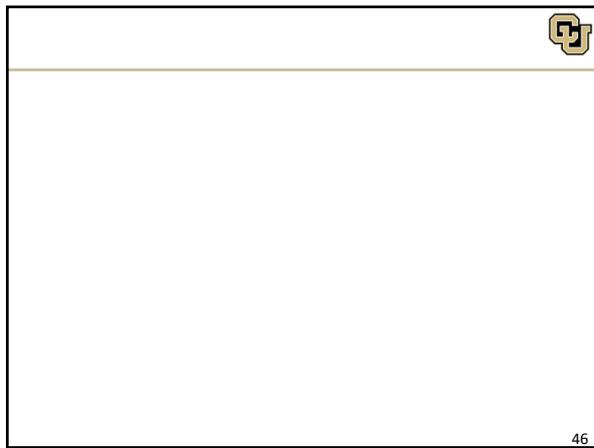
44

**Thank you for your attention!**

**Questions?**

45

45



---

---

---

---

---

---

---