ION CHANNEL RETREAT 2016
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Regulation of Piezo2/mechanically-activated (MA) ion channel by static plasma membrane tension

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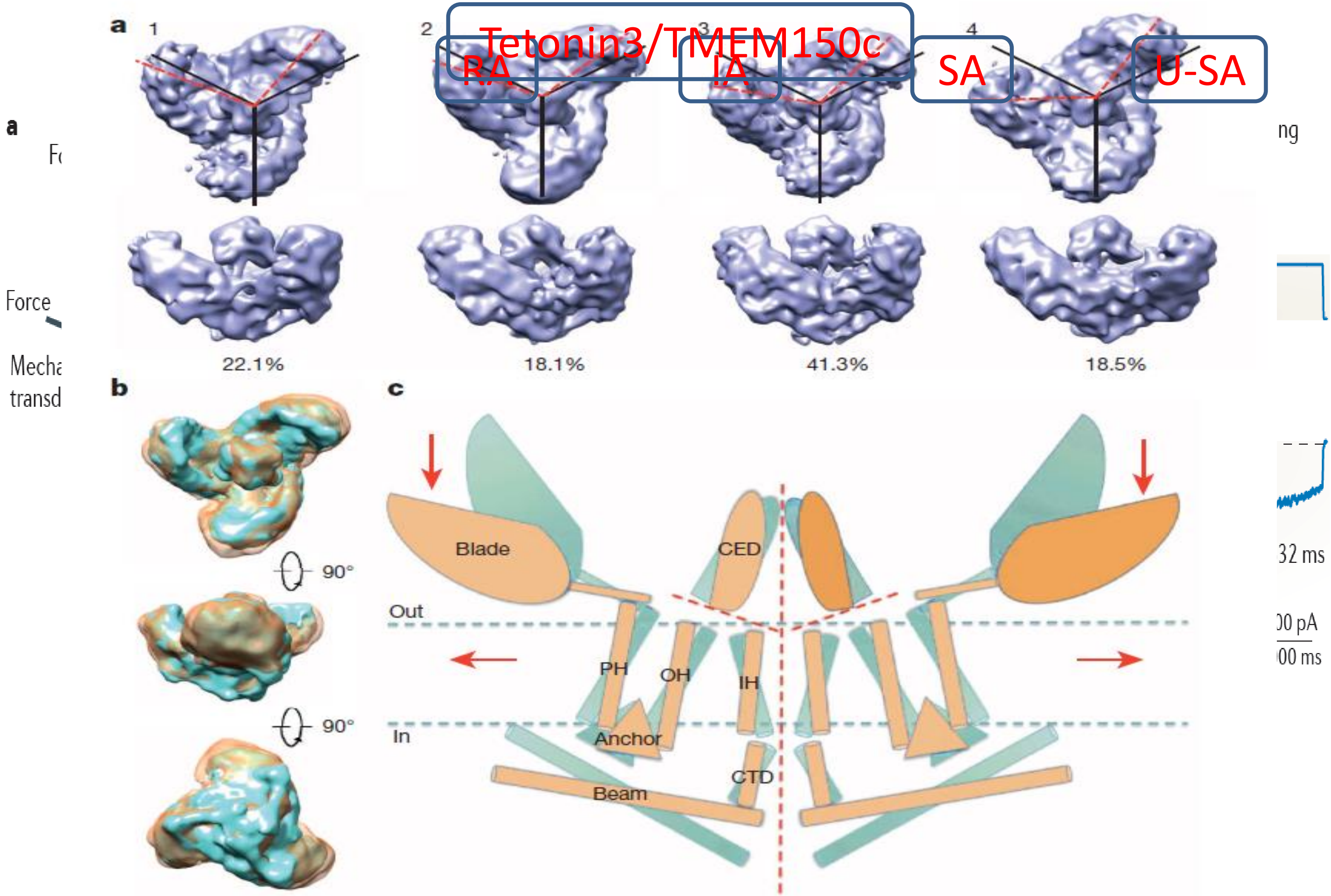
Hebei Medical University

Guangzhou, 2016-11-10



Gee,lnias, V, Coste, B, et al., Science. 2010

Function of PIEZO channel…

- Piezo1 is required for the development of the mouse vasculature.

Li, et al., *Nature*. 2014

- Piezo2 is required for the mechanosensitivity of Merkel cells that detect light touch.

Ikeda, et al., *Cell*. 2014

Woo, et al., *Nature*. 2014

- Deletion of Piezo2 in sensory neurons and Merkel cells led to loss of low threshold mechanosensation (LTM).

Ranade, et al., *Nature*. 2014

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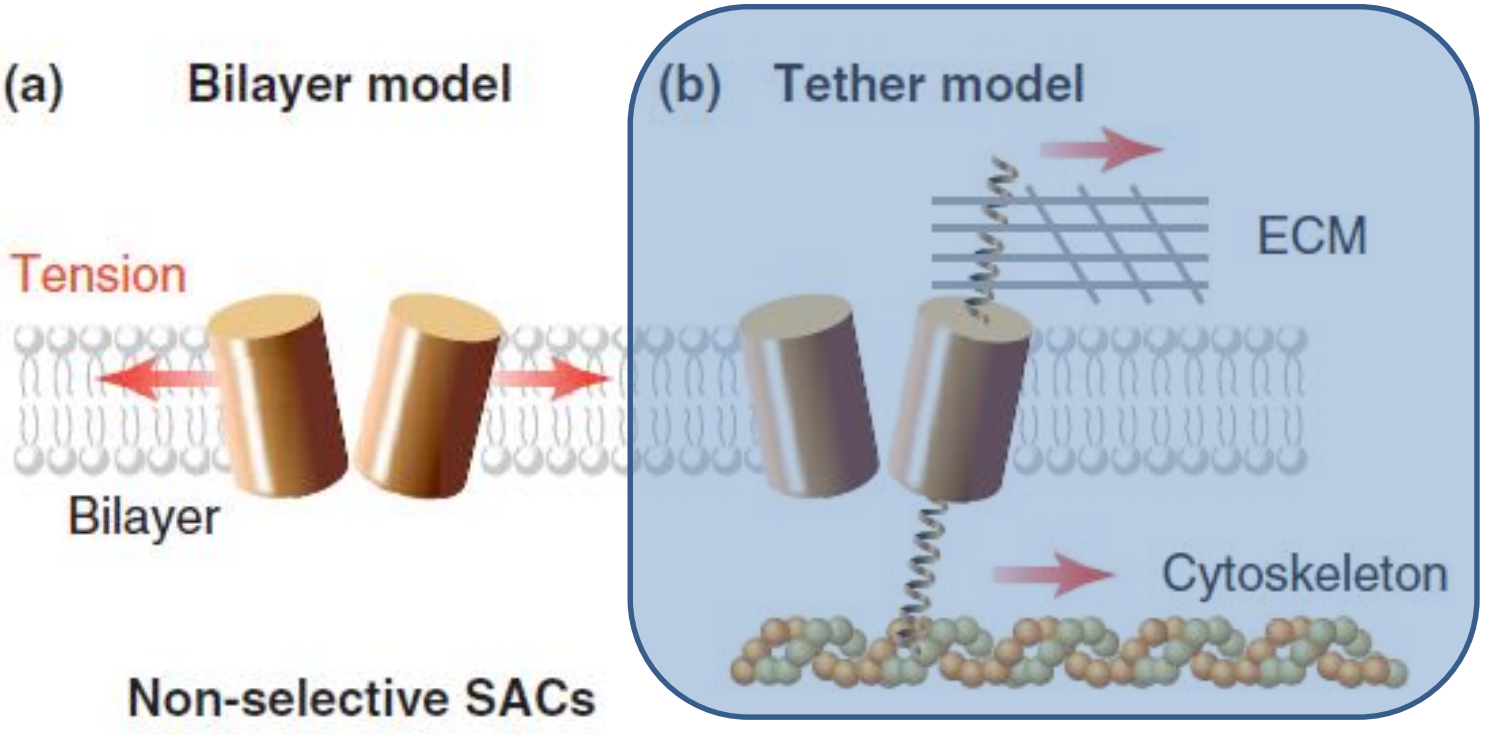
Qust. 1, Gating of mechanically activated (MA) channels.



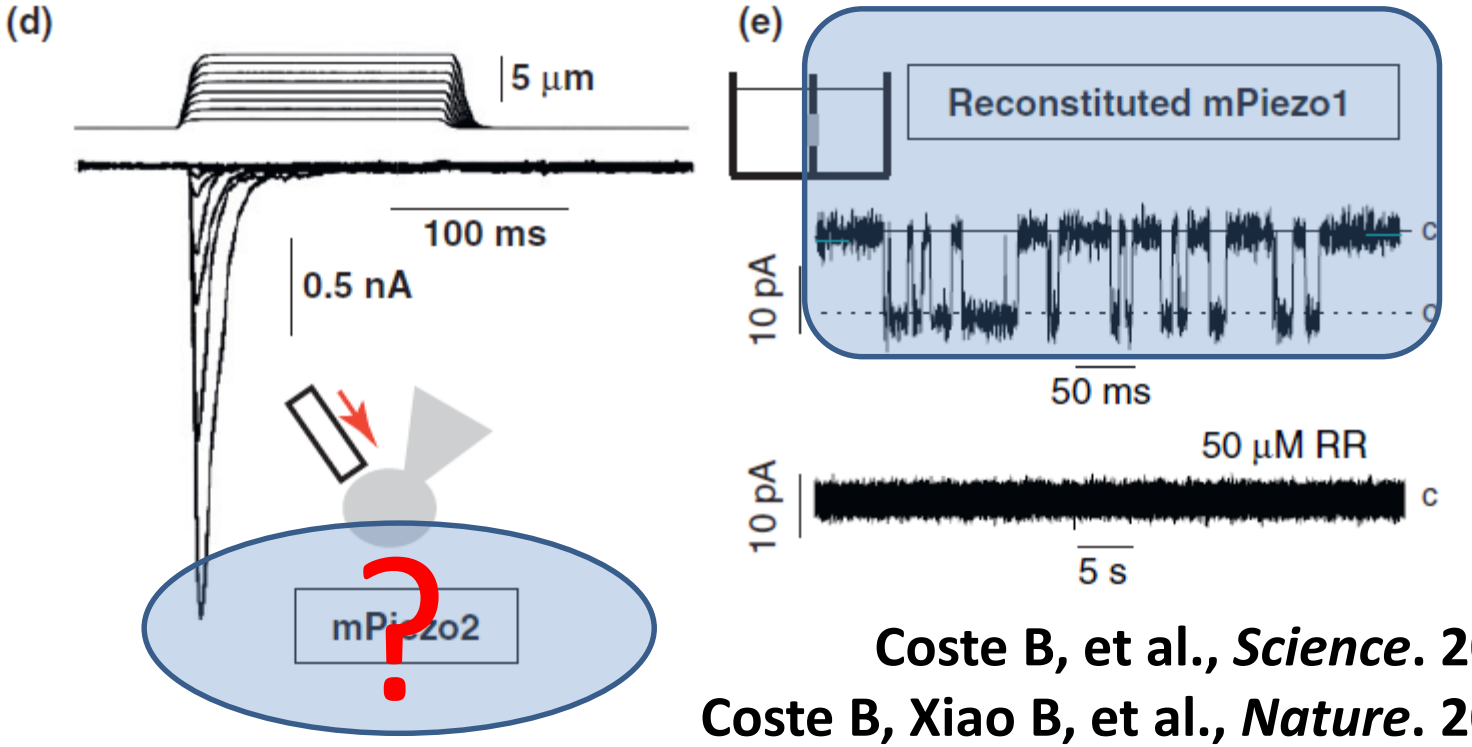
A laminin-like protein filament (~100 nm) may link RA-MA channel to ECM

Piezo 2 ?

Hu J, et al., *EMBO J*. 2010

Nilius B, et al., *Trends in neurocience*. 2012

Qust. 1, Gating of mechanically activated (MA) channels.



Coste B, et al., *Science*. 2010

Coste B, Xiao B, et al., *Nature*. 2012

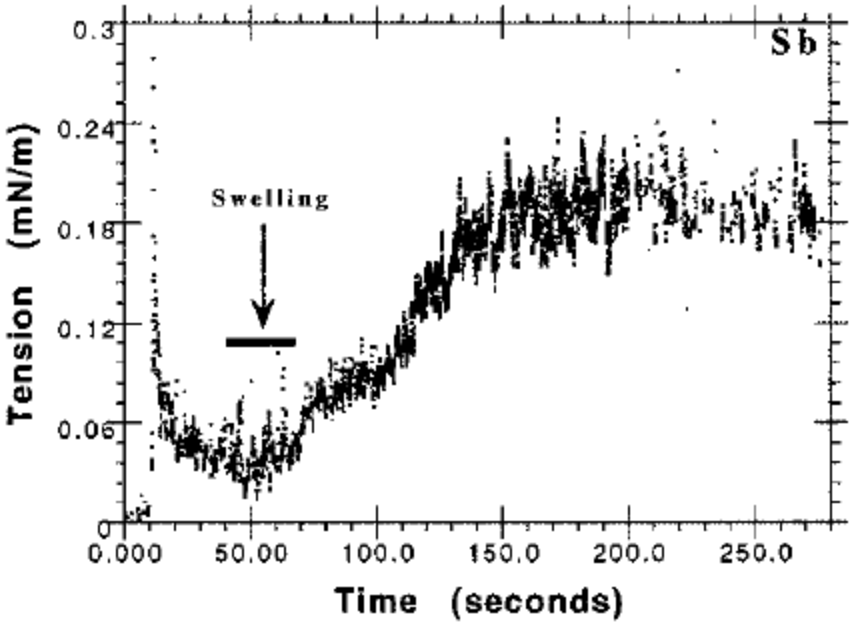
Mechanical sensitivity of Piezo1 ion channels can be tuned by cellular membrane tension.

Lewis AH, et al., *eLife*. 2015

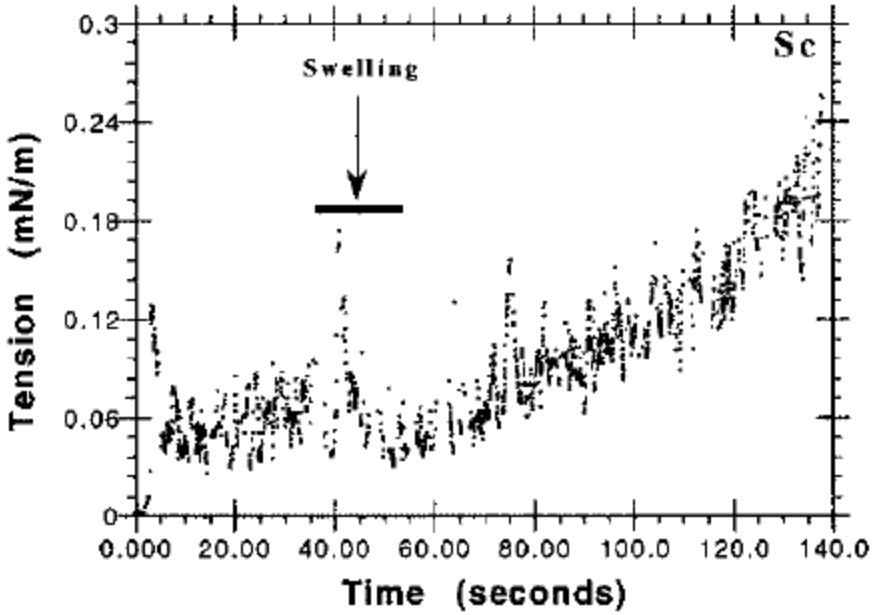
Removal of the mechanoprotective influence of the cytoskeleton reveals PIEZO1 is gated by bilayer tension

Cox CD, et al., *Nat commun*. 2016

Osmotic-induced cell swelling increase the membrane tension.



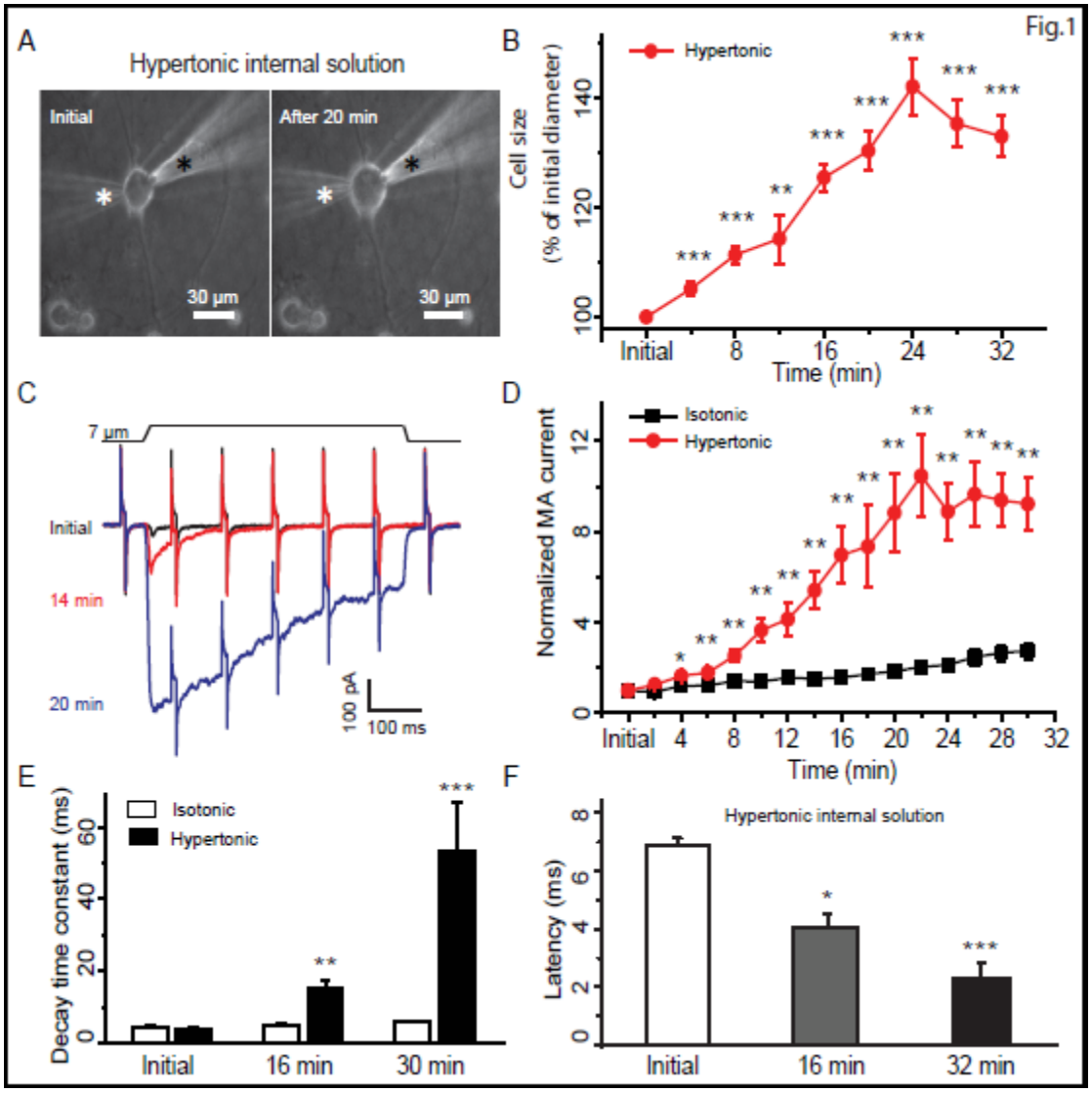
Static tension



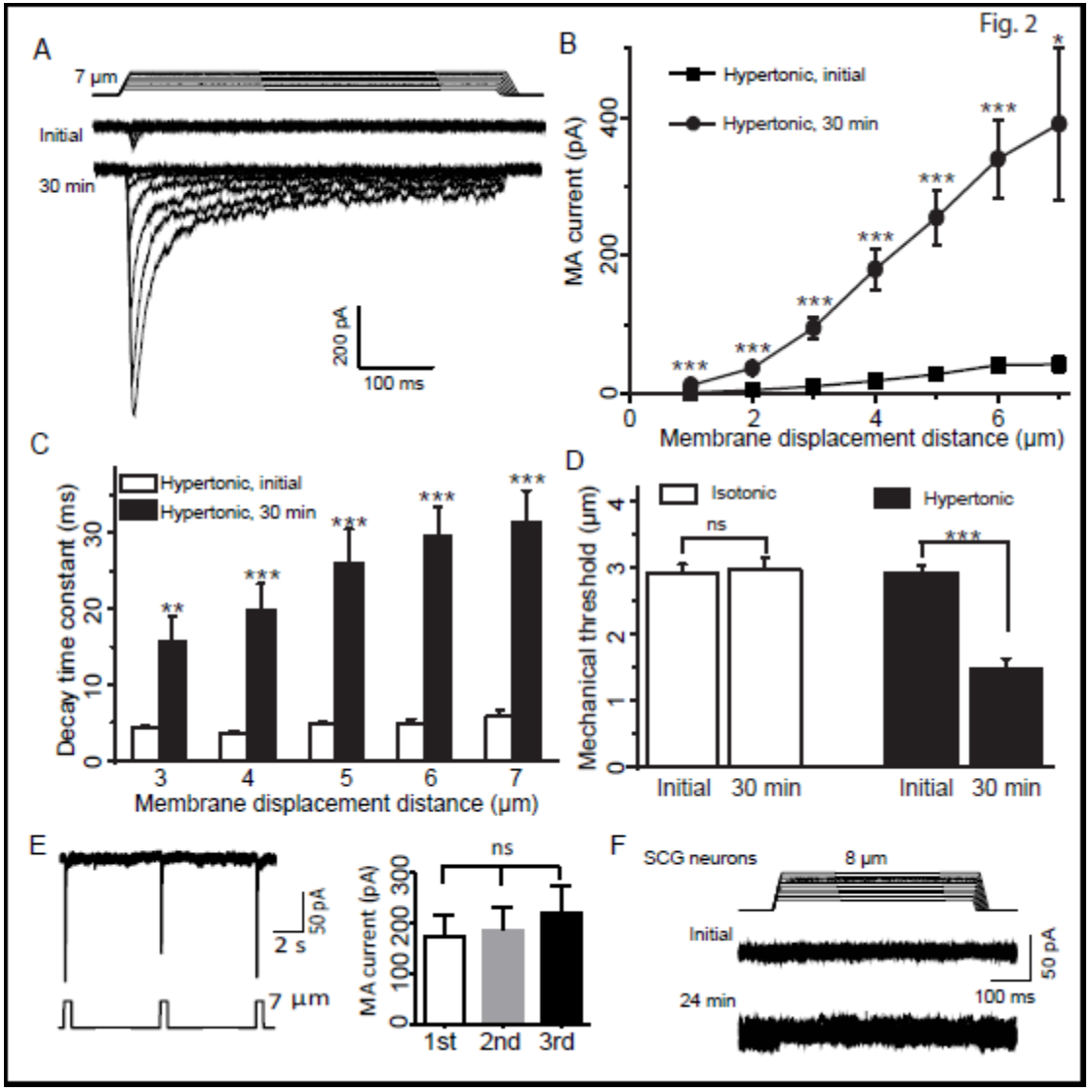
transient tension

Dai J, et al., *J Neurosci*. 1998

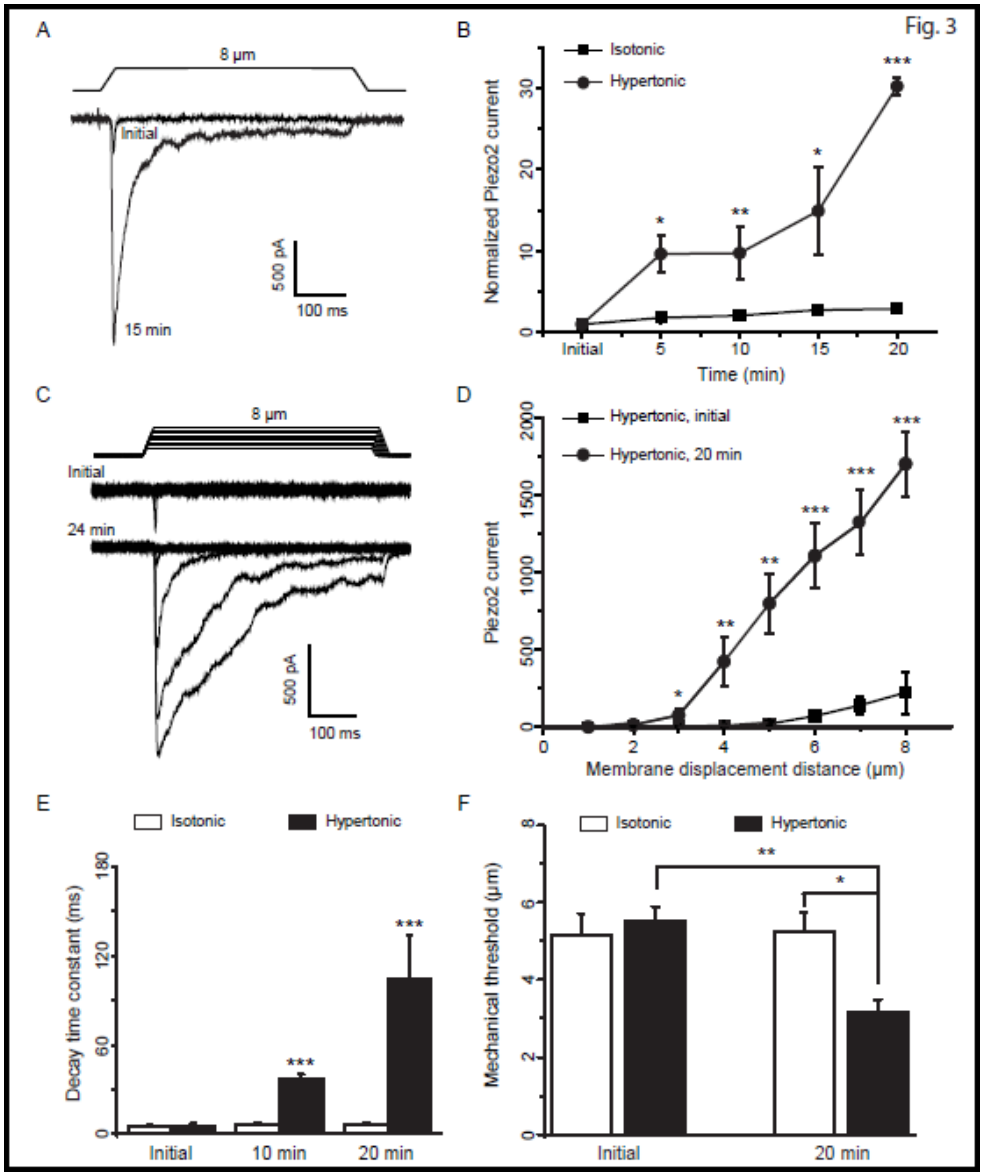
1. Osmotic swelling (420 mOsm) potentiates rapidly adapting mechanically activated (RA-MA) currents in rat DRG neurons.



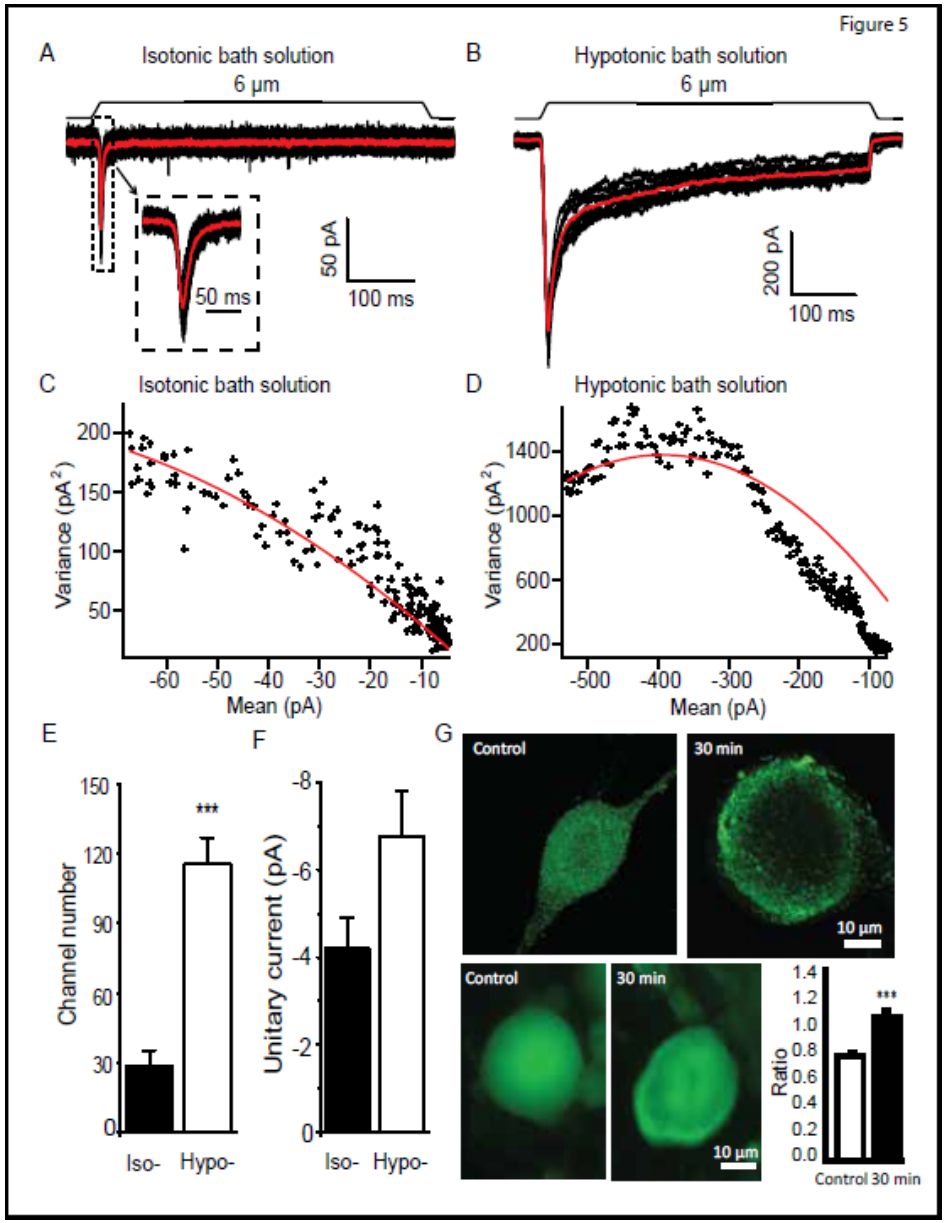
2. Osmotic swelling potentiates DRG neuronal RA-MA currents at different mechanical stimulation intensities.



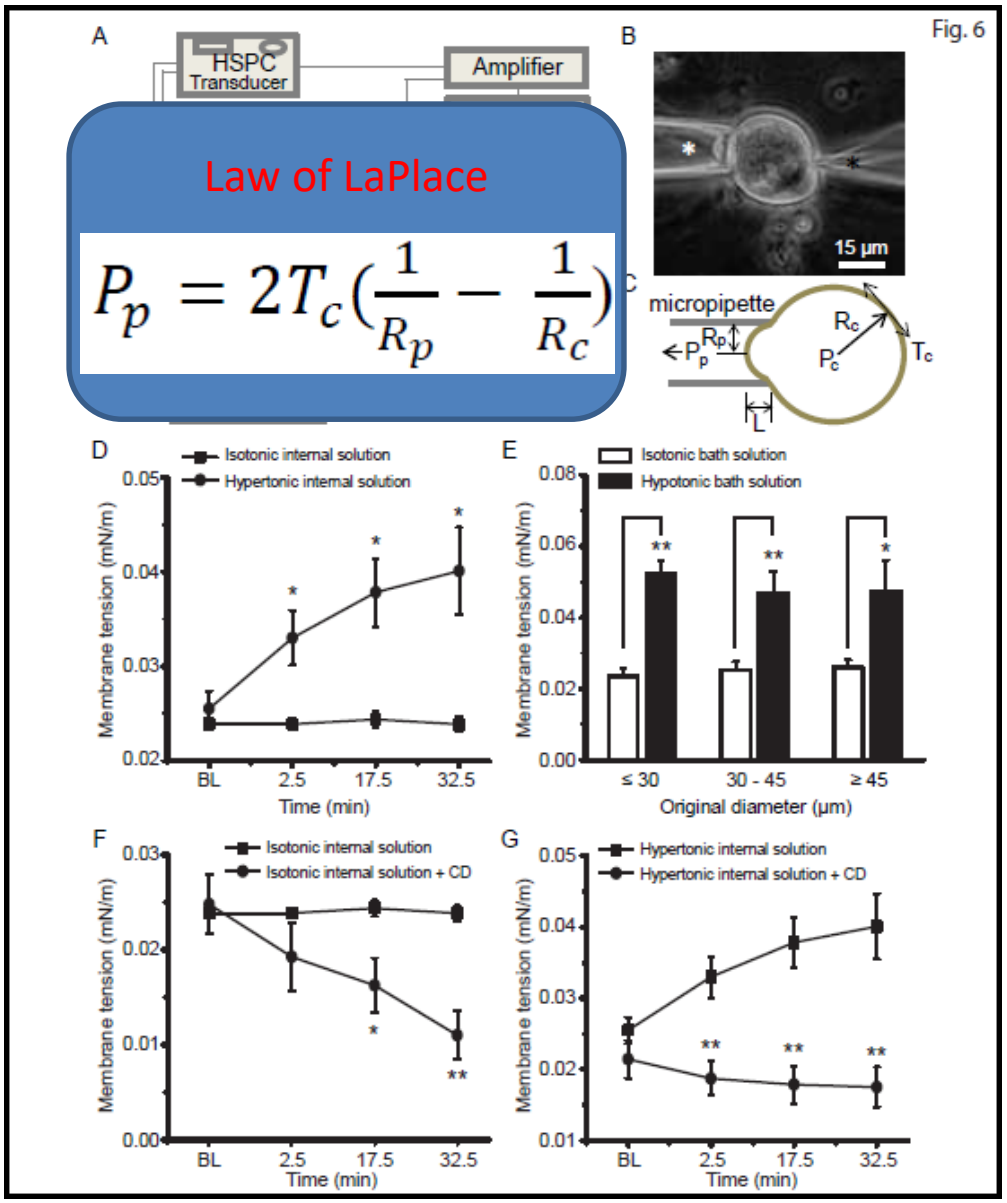
3. Osmotic swelling potentiates RA-MA currents in HEK293 cells expressing Piezo2 channels.



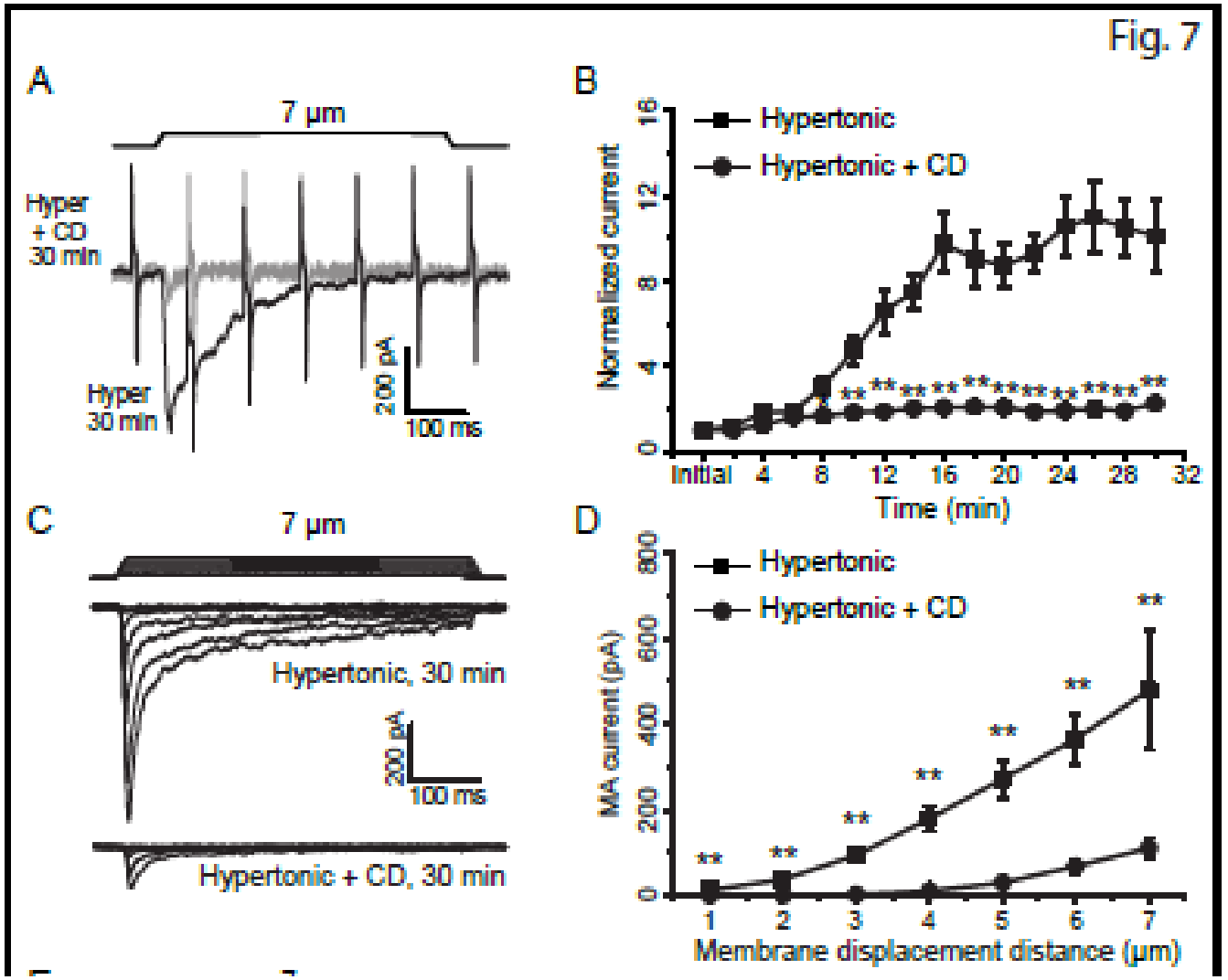
4. Assessment of channel numbers and unitary current sizes of RA-MA channels of rat DRG membranes. (hypo = 220 mOsm)



5. Static plasma membrane tension of primary afferent neurons is measured by the micropipette aspiration technique



6. Disruption of actin filaments by cytochalasin D (CD) abolishes osmotic swelling-induced potentiation of RA-MA currents.



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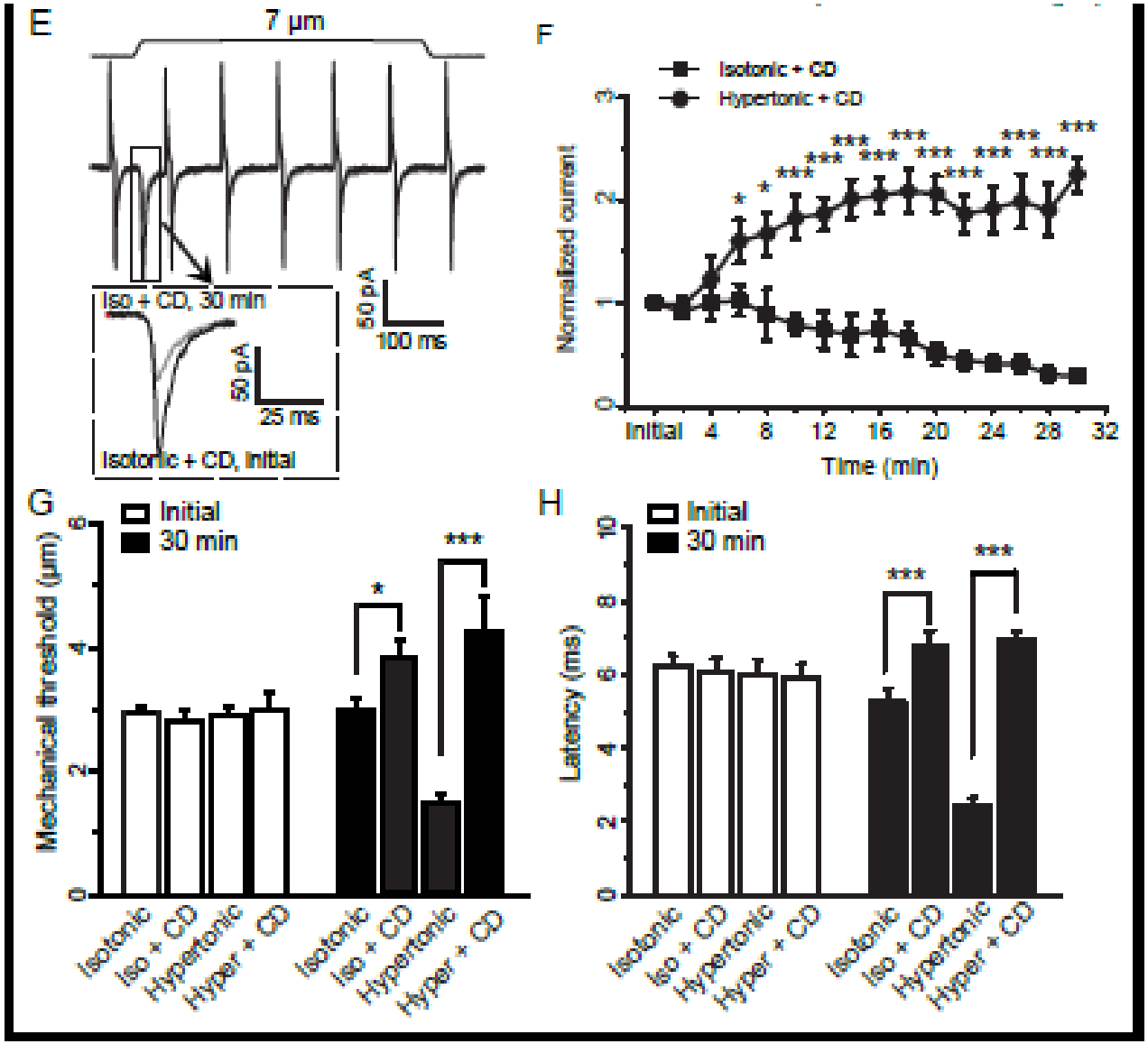
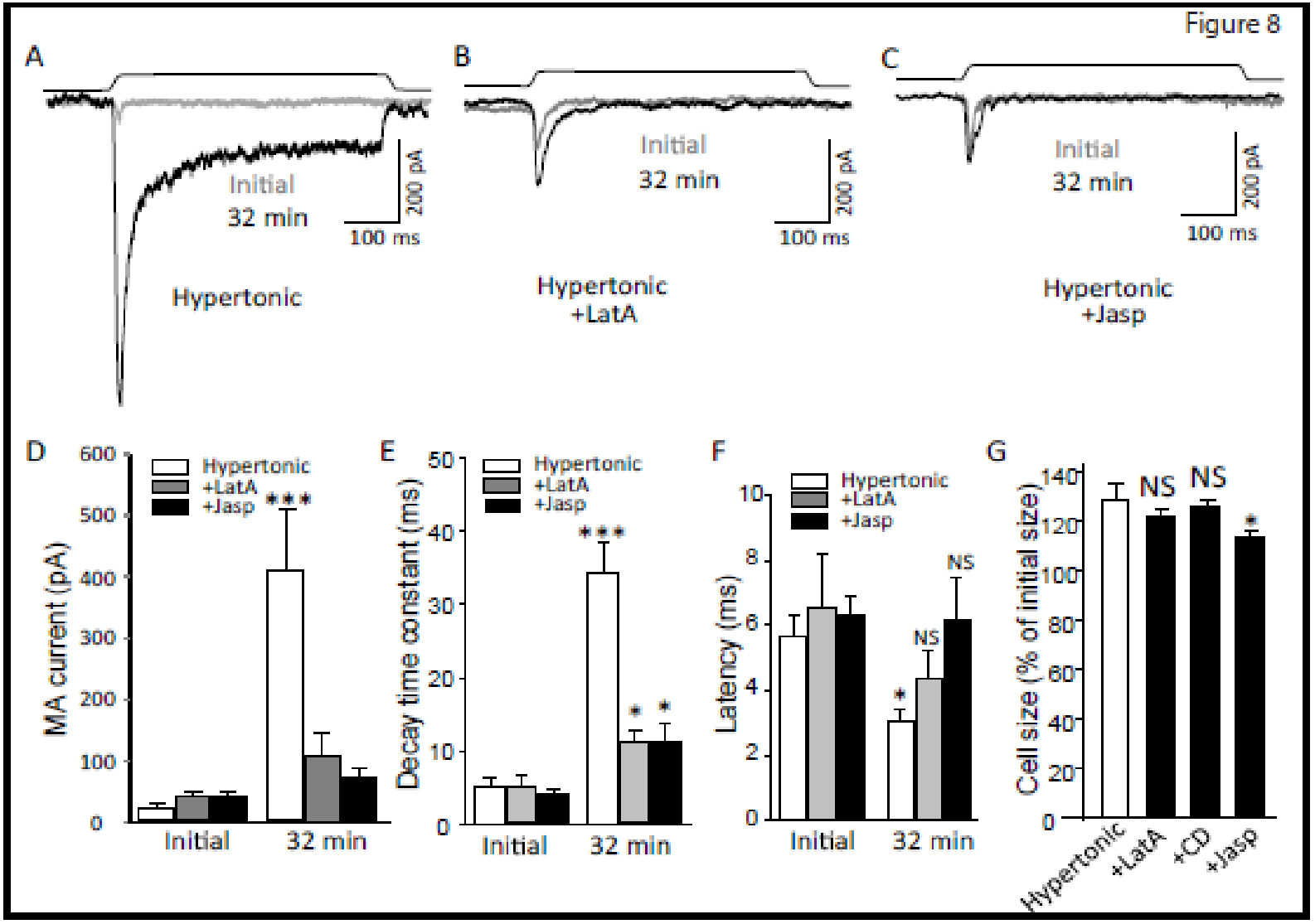
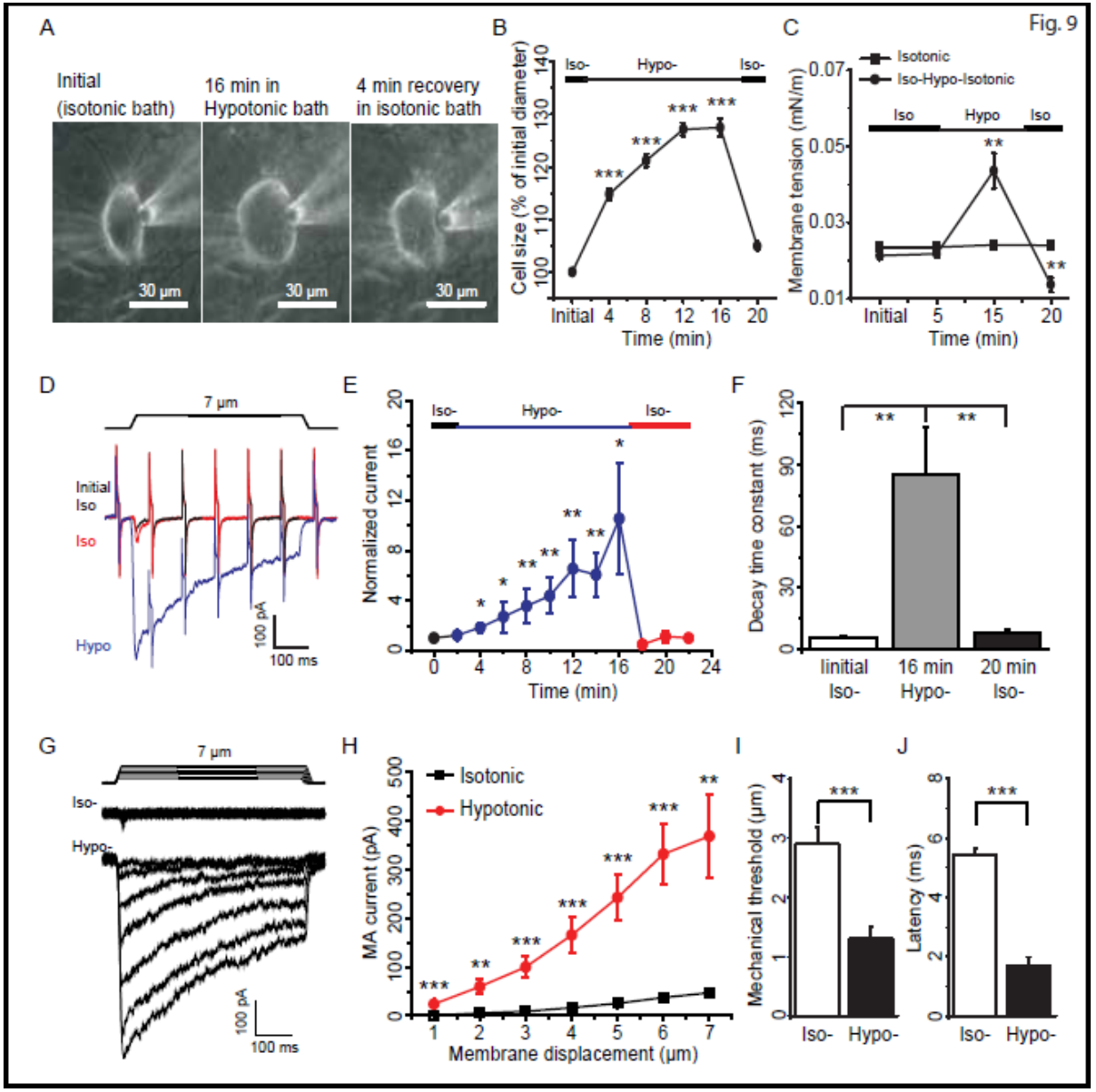


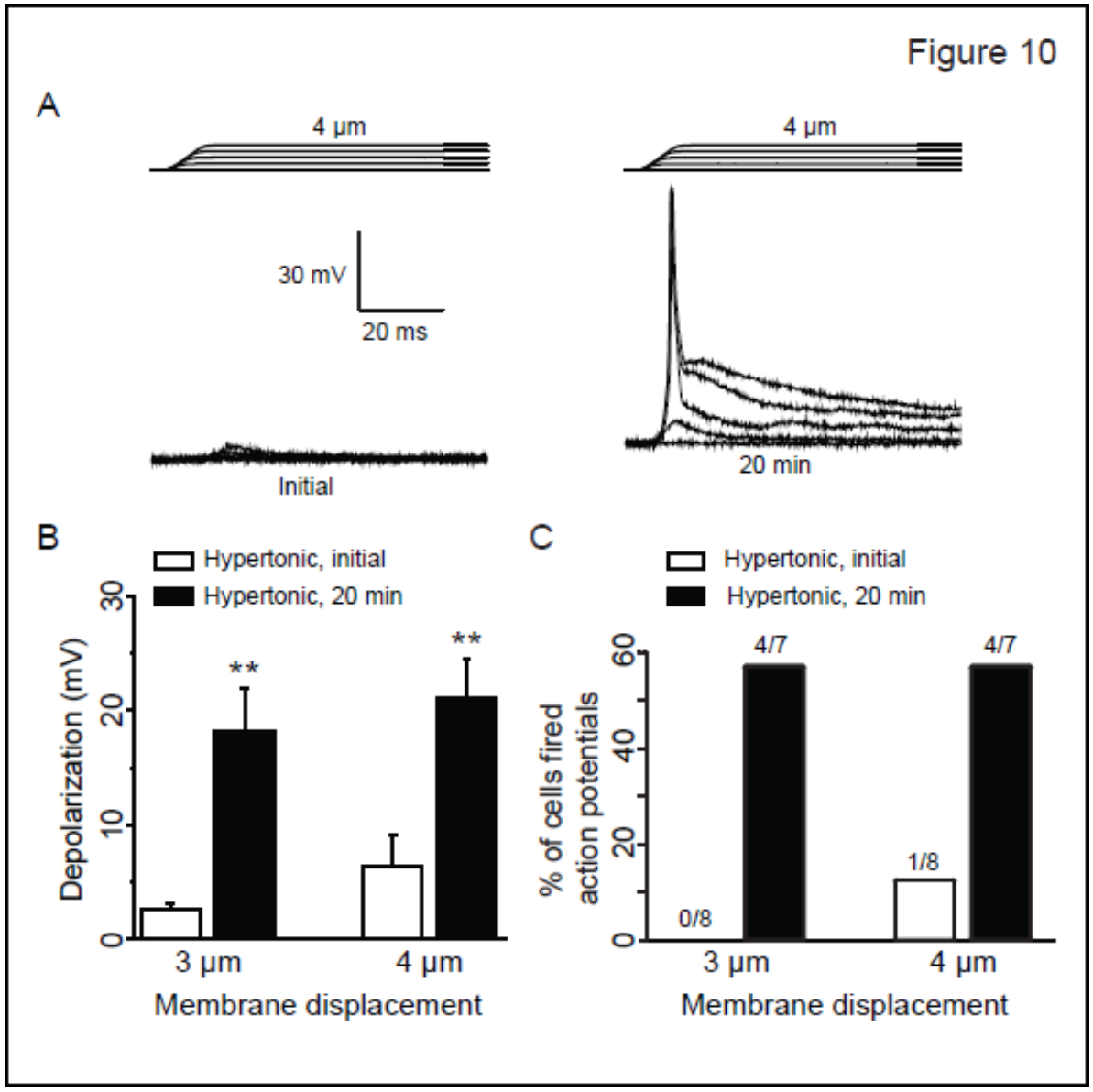
7. Osmotic swelling-induced potentiation of RA-MA currents is diminished by latrunculin A and jasplakinodide.



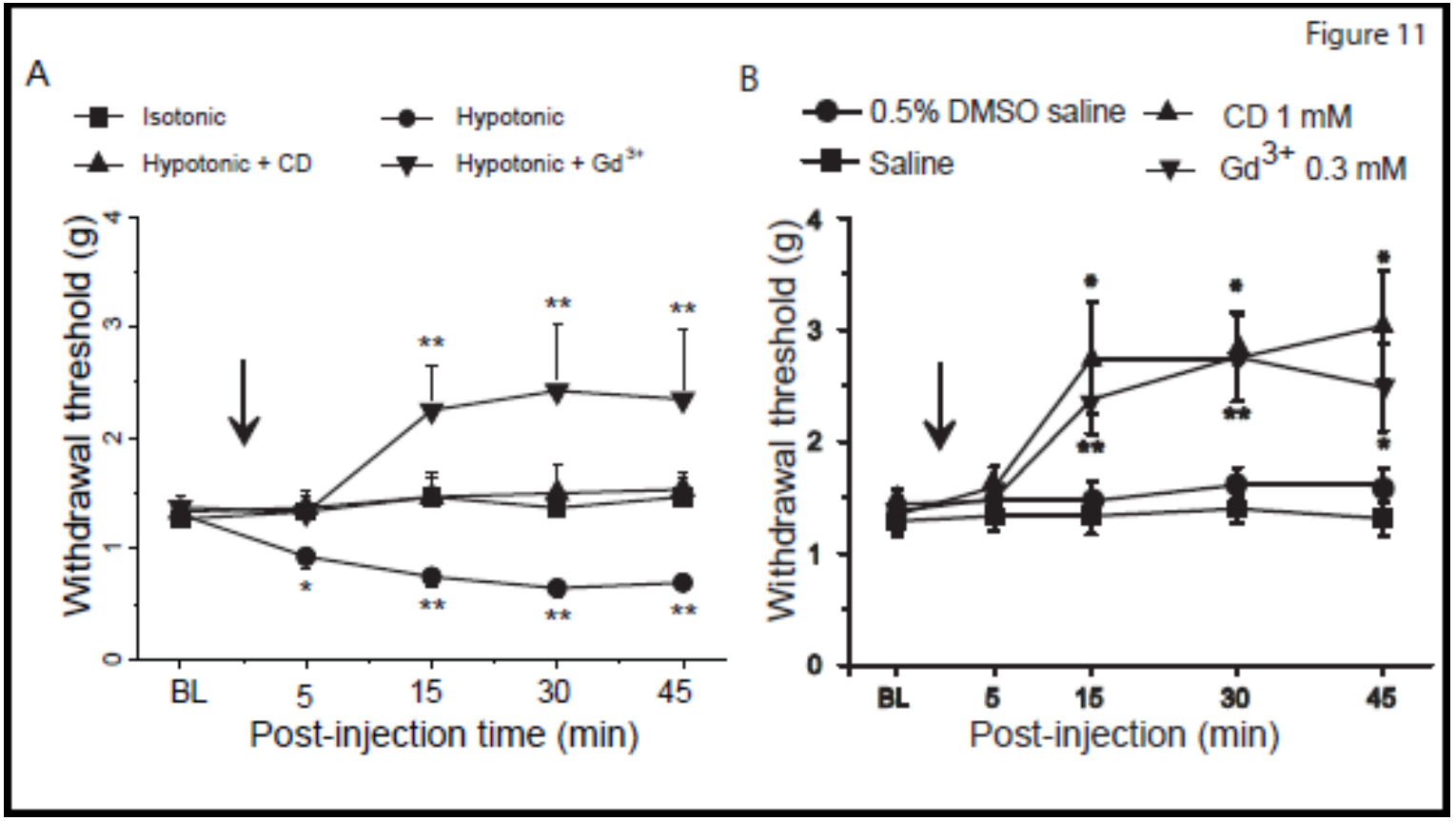
8. Osmotic swelling, static plasma membrane tension, and RA-MA currents can be rapidly reversed in isotonic condition.



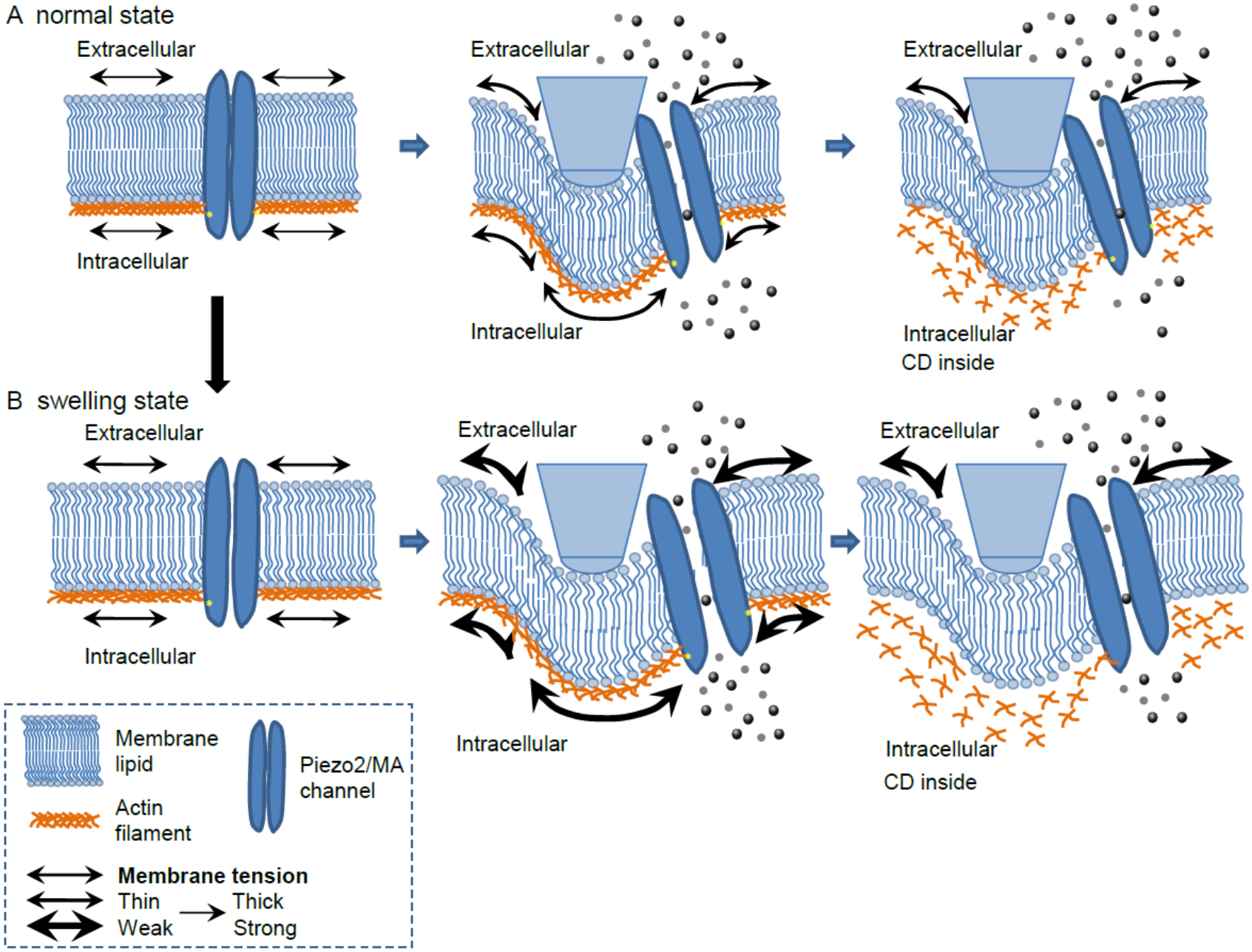
9. Osmotic swelling increases mechano-excitability rat DRG neurons.

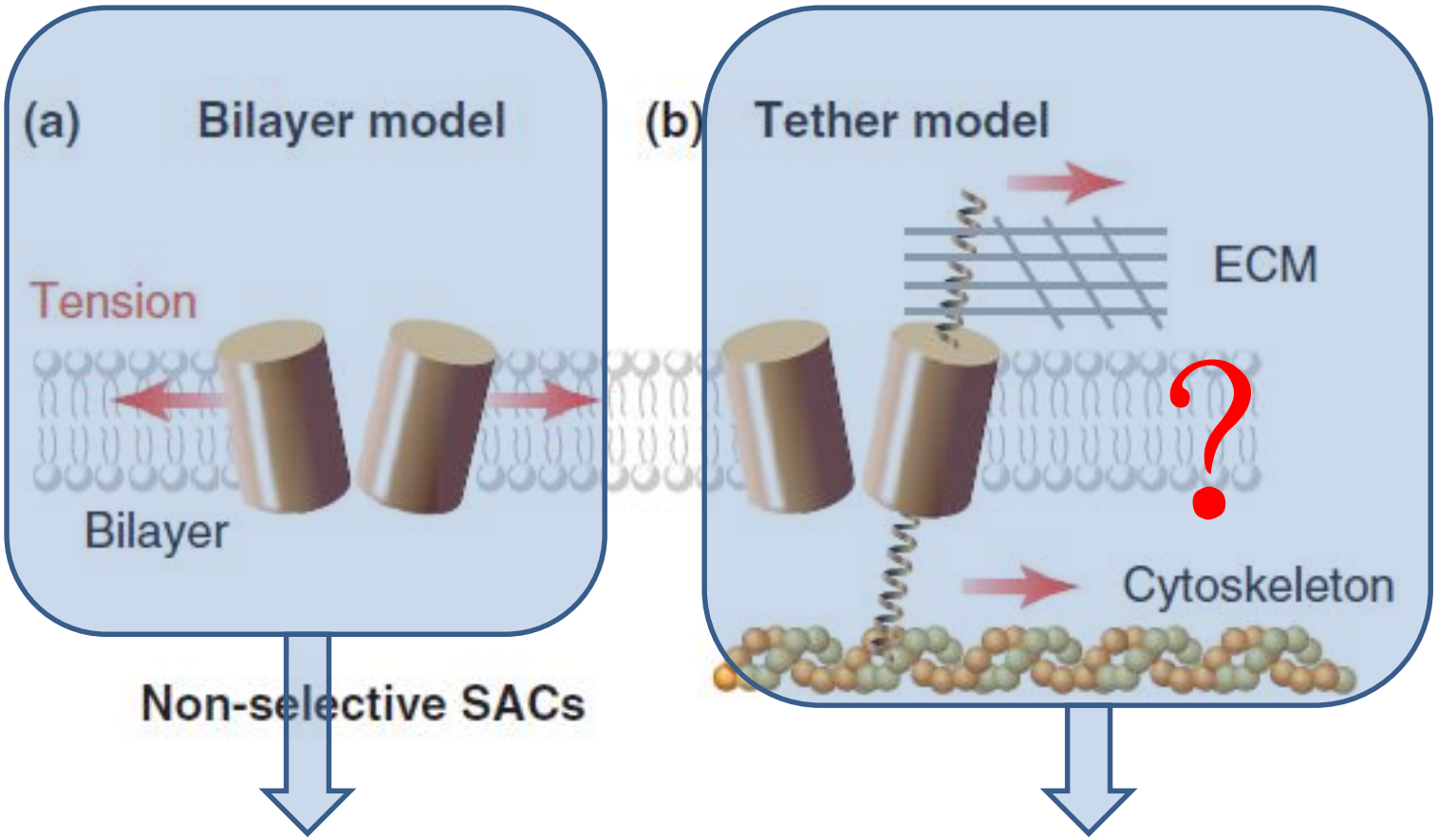


10. Extracellular hypotonicity induces behavioral mechanical hypersensitivity.



Jia Z, et al., *J Biol Chem*. 2016


A normal state
Extracellular
Intracellular
Extracellular
Intracellular
Extracellular
Intracellular
CD inside
B swelling state
Extracellular
Intracellular
Extracellular
Intracellular
Extracellular
Intracellular
CD inside
Membrane lipid
Piezo2/MA channel
Actin filament
Membrane tension
Thin
Weak
Thick
Strong



Piezo1/2 MA channel function positively modulated by membrane tension

Piezo1/2 MA channel function modulated by tether model?

Nilius B, et al., *Trends in neurocience*. 2012

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