

Bladder Volume Sensation and Sensory Processing

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Disclosures

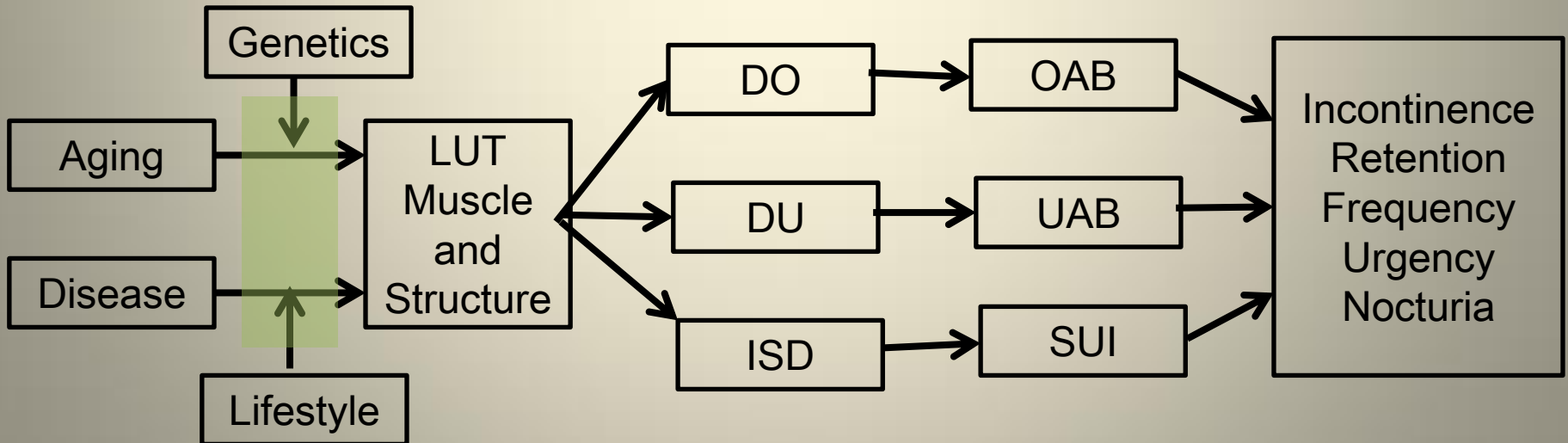
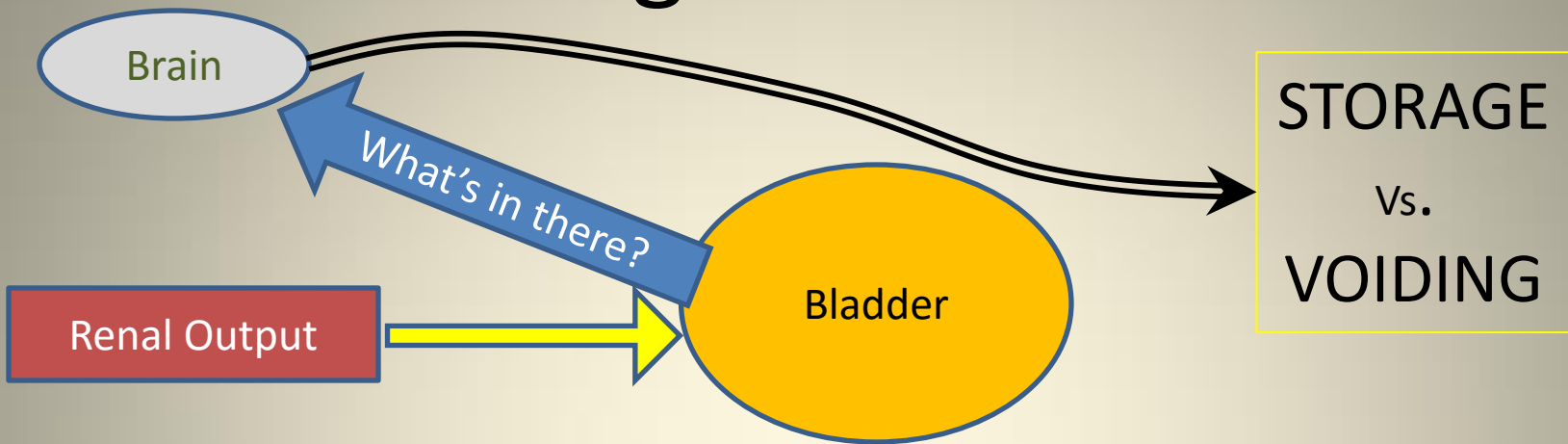
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- Financial Relationships - none

- Conflicts of Interest - none

Significance



Significance

Mature Adult

Old Adult

Frail Adult

SUI

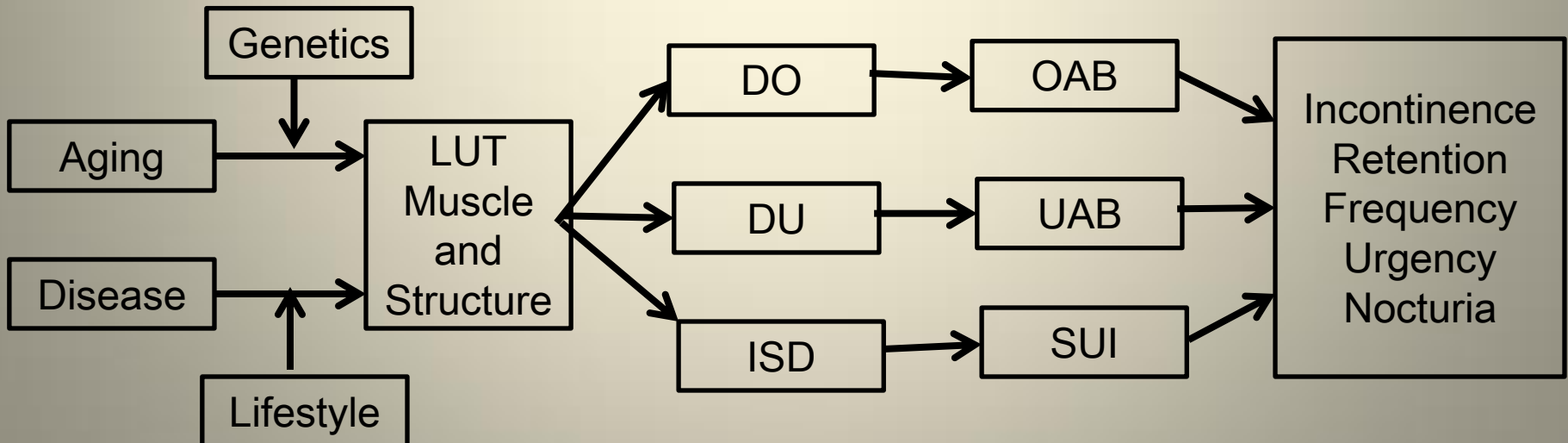
Richter et al., J Urol. 2008 Mar;179(3):1024-30

OAB

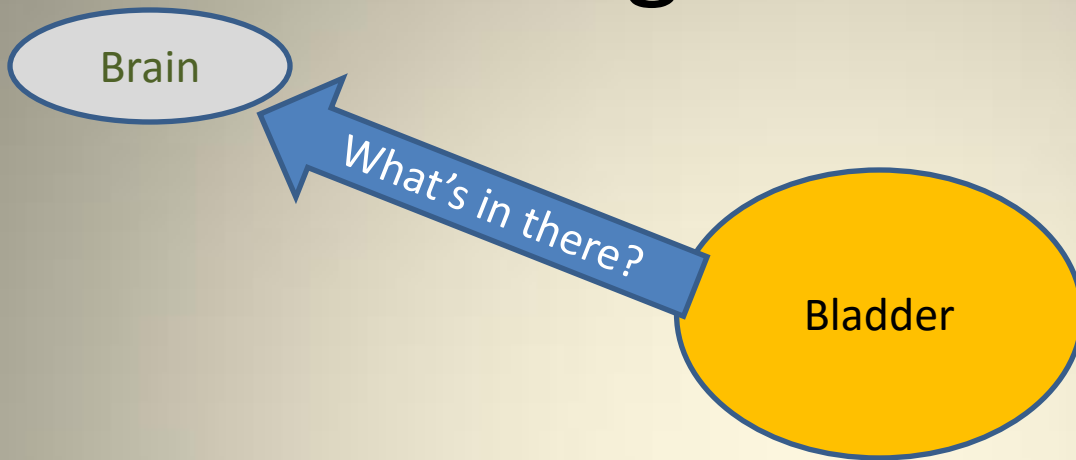
Krause, et al., Drugs Aging. 2010 Sep 1;27(9):697-713

UAB

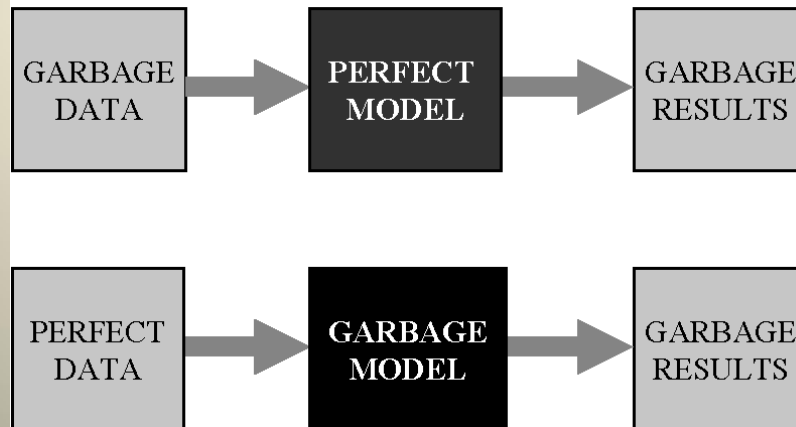
Smith et al., Int Urol Nephrol. 2014 Sep;46 Suppl 1:S35-44.



Significance



MODEL CALCULATIONS "Garbage In-garbage Out" Paradigm



Knowledge

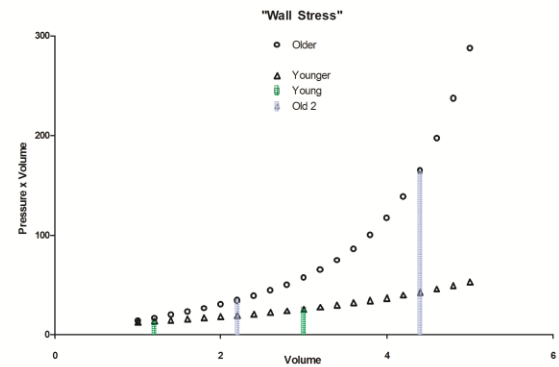
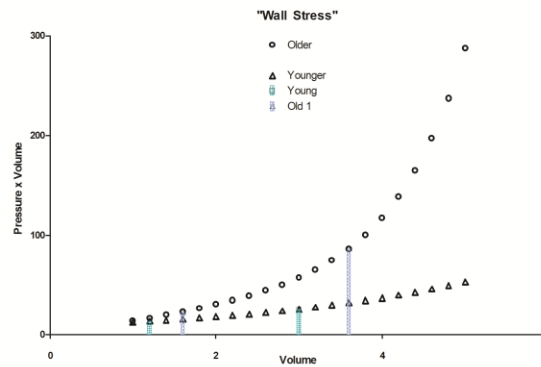
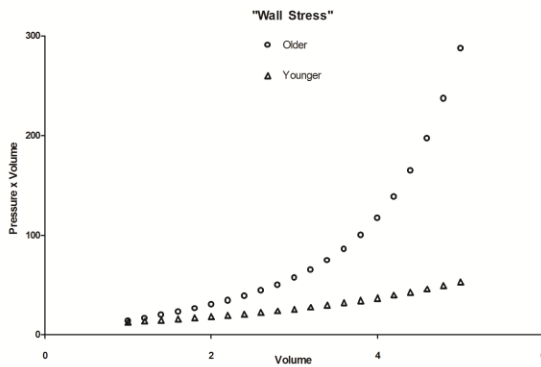
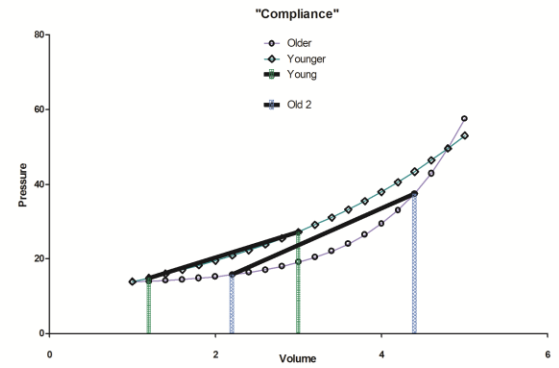
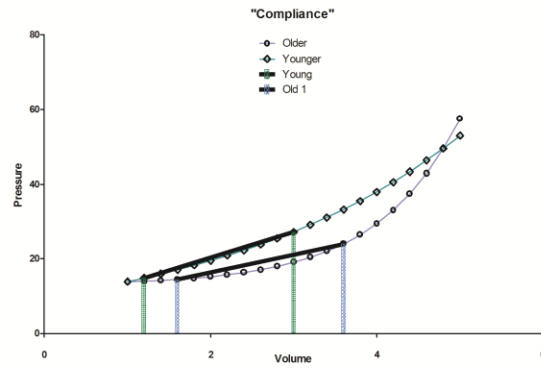
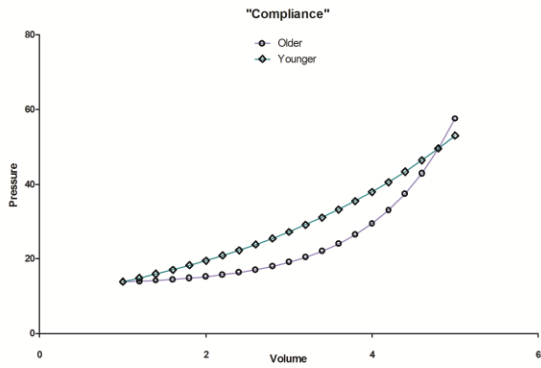
- Older asymptomatic patients less sensitive to bladder content
Pfisterer et al. J Am Geriatr Soc 2006;54:405-412.
- Ex-Vivo bladder sensitivity to volume might increase with aging
Daly et al., J Physiol 2013.
- Brain areas relevant to sensory signaling become less responsive to bladder volume
Griffiths et al., NeuroImage 2009;47:981-986.
- OAB can be considered as a syndrome of impaired volume perception
- UAB is a syndrome of volume hyposensitivity
Smith et al., Bladder 2015;2:e17.
- Incontinence can also be viewed as an impaired content response
Deffieux et al., Neurourol Urodyn 2008;27:291-296.

Knowledge

Bladder afferent activity is a function of bladder wall stiffness *le Feber J et al., Urological Research 2004;32:395-405.*

Bladder wall stiffness vs. volume is the result of diffuse smooth muscle activity interacting with the extracellular matrix *Coolsaet B, Neurourol Urodyn 1985; 4, 263-273.*

Bladder collagen content and form change with aging *Shueth A, et al; Age (Dordr) 2015; 38(1), 17.; Zhao et al, J Urol 2010; 184, 378-385; Lepor et al., J Urol 1992; 148, 414-417; Lluel P. et al., AJP Int Comp Phys 2000; 278, R964-972*



Hypothetical curves illustrating aging and the relationship of pressure/volume, The Problem of "Compliance", and how the P/V relationship can affect volume sensitivity

Knowledge

“micromotional” activity of bladder wall creates
“afferent noise” *Gillespie et al., BJU International 2009;103:1324-1333.*

Micromotions are modulated by autonomic
transmitters *Gillespie JI. BJU Int 2004;93:393-400; Gillespie et al., BJU Int 2012;110:E132-142; Gillespie et al., Naunyn-Schmiedeberg's archives of pharmacology 2015;388:719-726.*

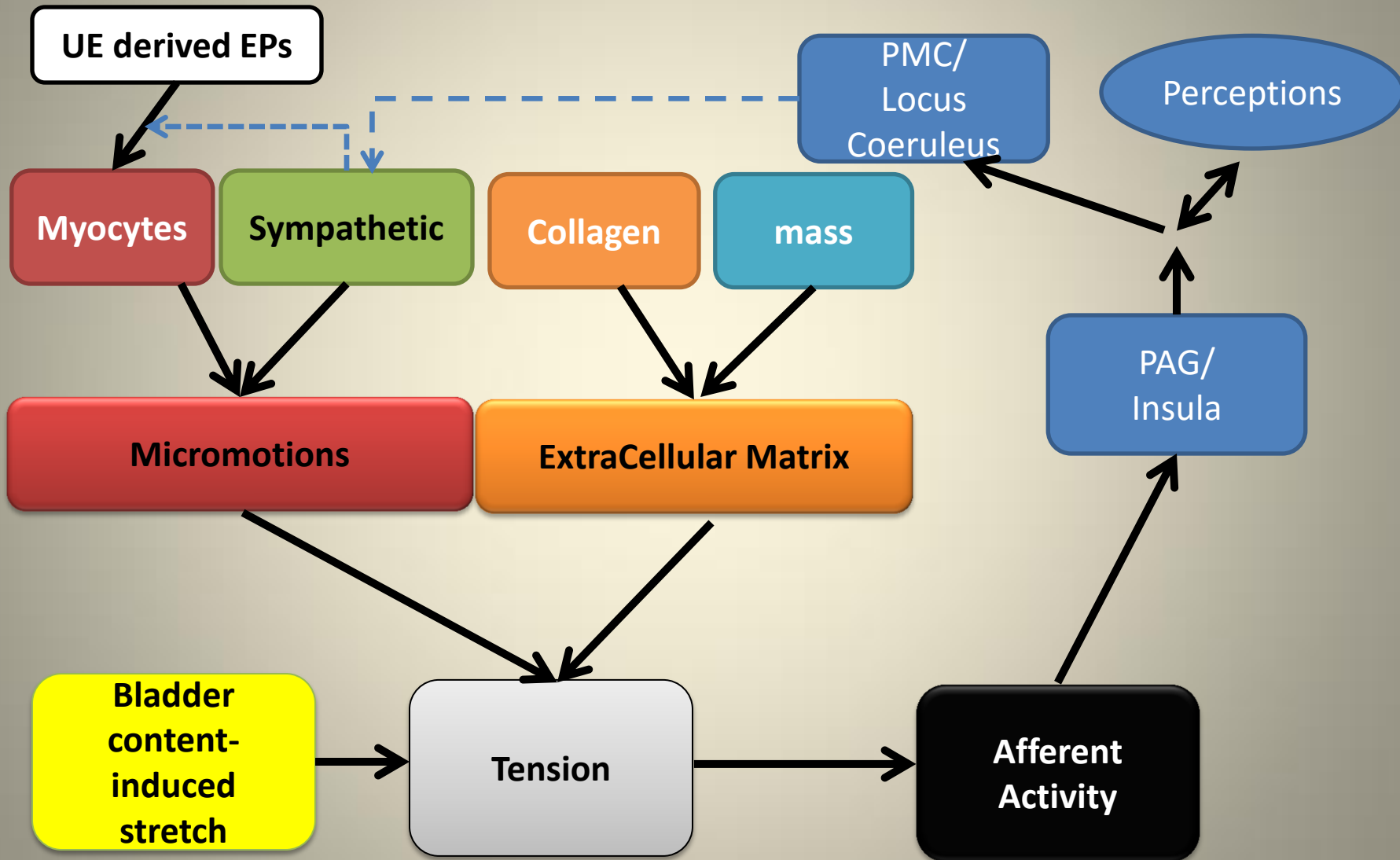
Modulation of micromotions drives changes in afferent
activity *Heppner et al., J Gen Physiol. 2016 Apr;147(4):323-35*

Concept of adjustable volume sensitivity *Eastham JE, Gillespie JI. Organogenesis 2013;9:224-233.*

Knowledge

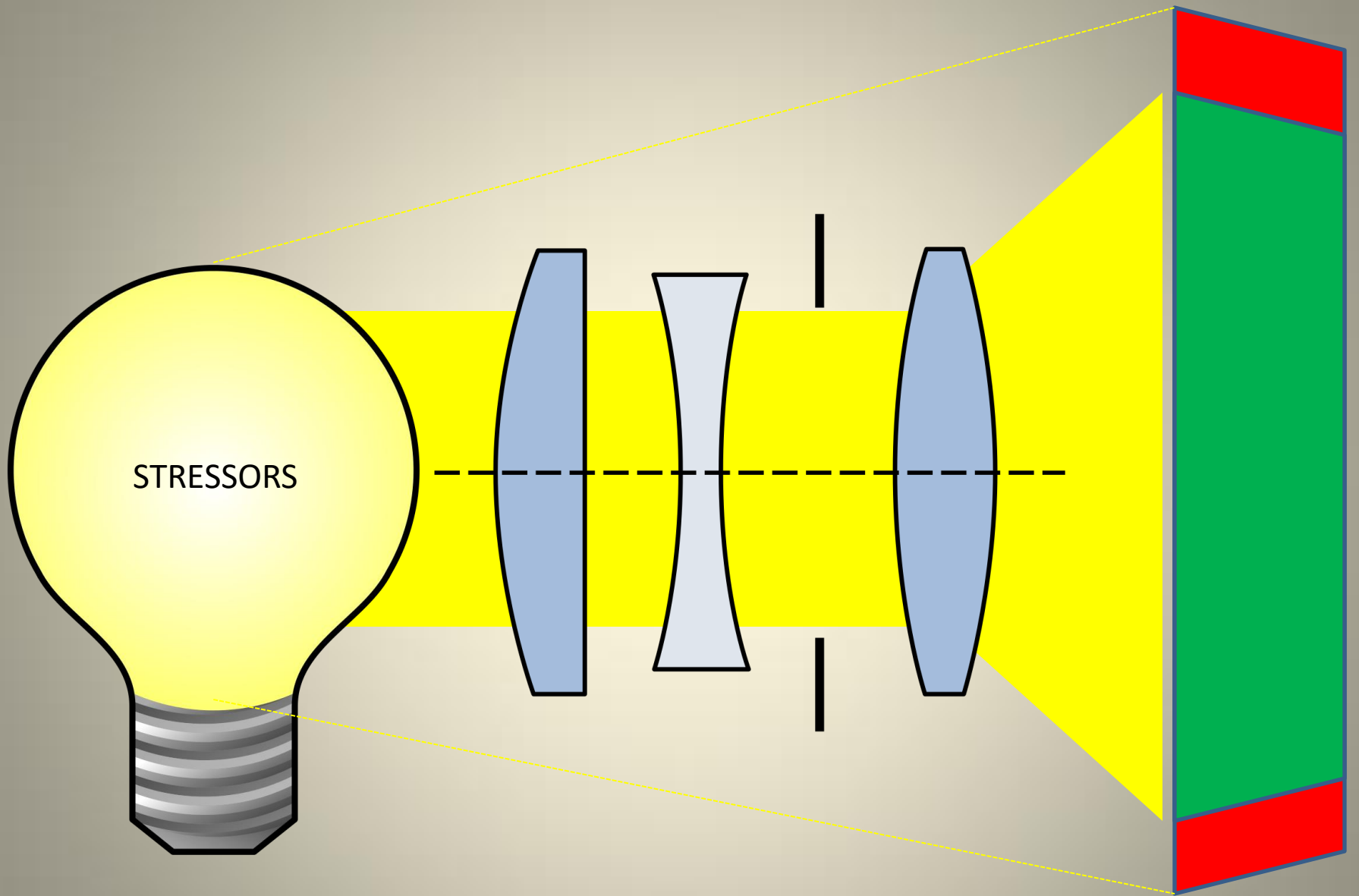
- Suppression of adrenoceptors diminishes bladder capacity (dogs) *Wein et al., Urology 1974;4:27-32.*
- Sympathetic innervation increase compliance and increases threshold volumes for voiding (cats) *Floyd et al, J Physiol 1982;323:65-75.; McGuire et al., Investigative urology 1979;17:9-15.*
- Suppression of the voiding reflex increases bladder stiffness and reduces spectral content (mouse) *Smith et al., Neurourol Urodyn 2012;31:30-35.*
- Spectral content and stiffening effect of voiding suppression increase with aging (mouse) *Smith et al., BJU Int 2015;115:322-329.*

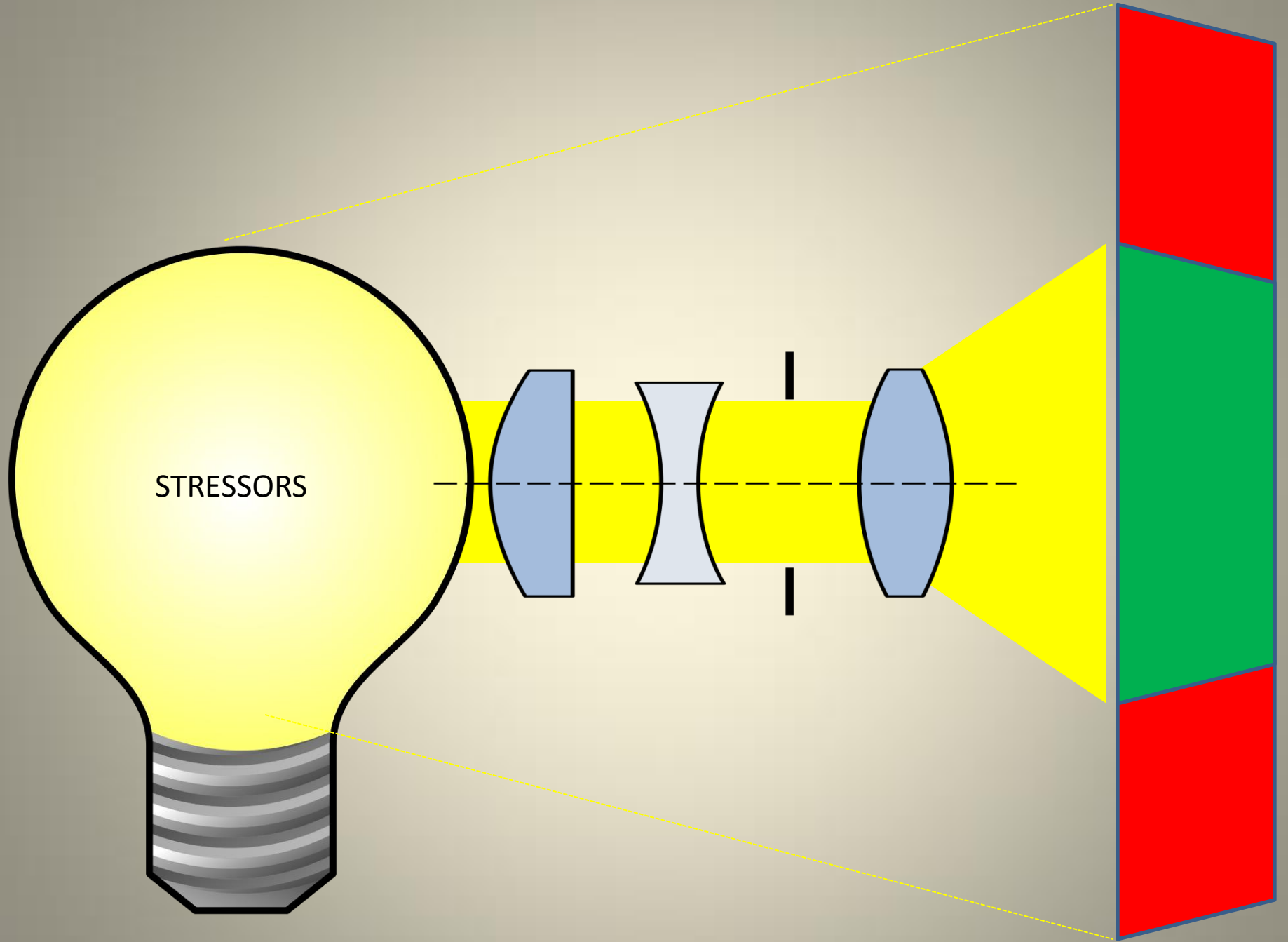
Bladder Volume Transduction



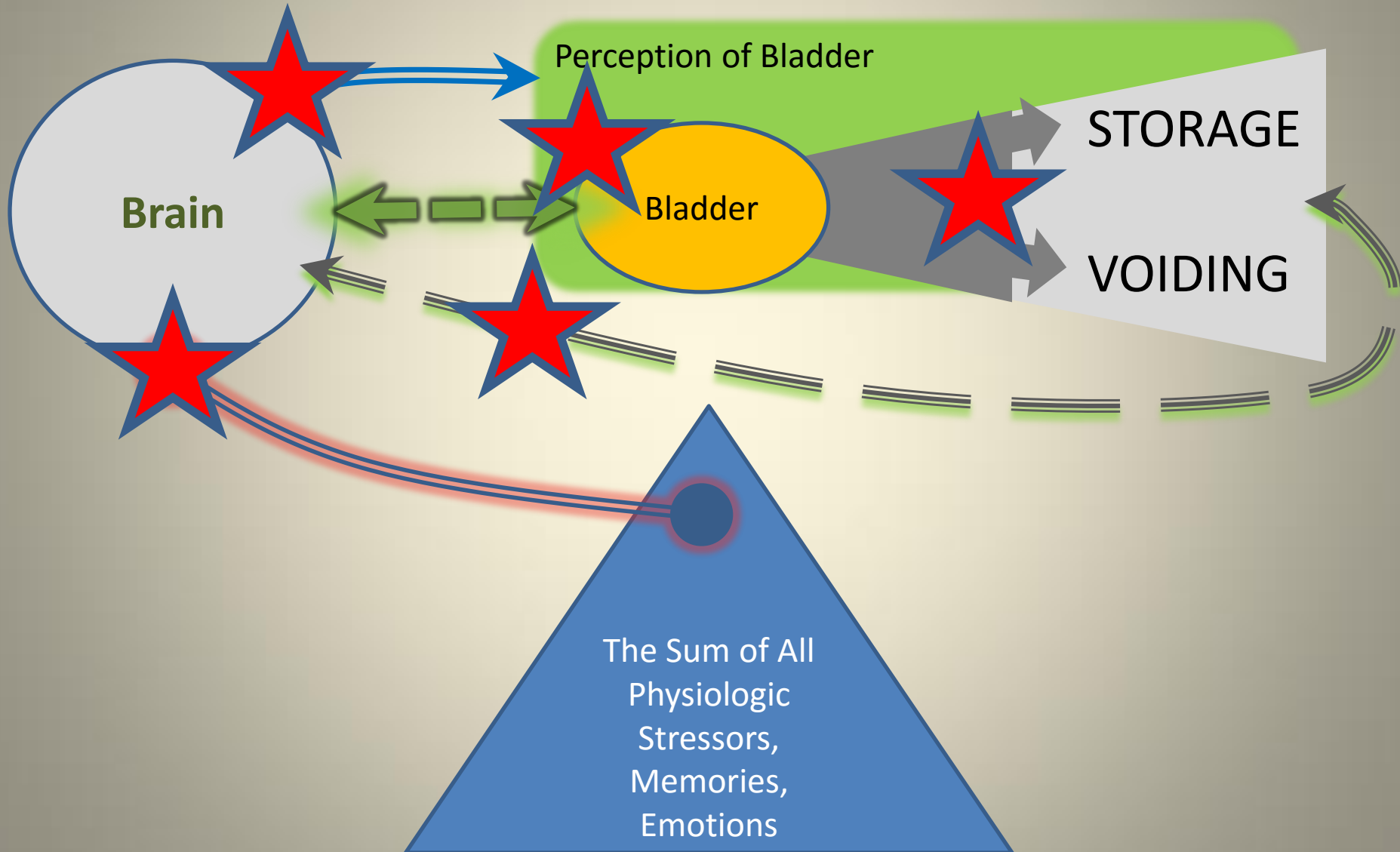
Knowledge

- The outer hair cells of the organ of Corti are the target of abundant efferent projections from the olivocochlear system.
- Thought to be modulated by central activity via corticofugal descending auditory system, and to modulate active cochlear micromechanics.
- May be involved in ear protection against noise damage and auditory perception, especially in the presence of background noise.
- Mounting evidence that its activity is modulated by auditory *and visual* attention.
- Differences in olivocochlear function might reflect differences in peripheral auditory function, or in more central factors such as top-down attentional modulation.





Research Opportunities



Research Opportunities

- What is “normal adaptive response” vs pathology (phenotyping)?
- How do adjustable sensors function and what is the impact of aging and disease?
- What are the mechanisms of central control over centrifugal processing?
- What is the impact of aging on central (integrative) mechanisms?
- Where are potential points of intervention ?

Gratitude to my mentors

- George Kuchel MD,
- Eric Levine PhD
- Laura Haynes PhD
- Lori Birder PhD

And -

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- NIA / NIH
- CT Institute for the Brain and
Cognitive Sciences
- UConn/JAX Institute for
Systems Genomics
- And others

