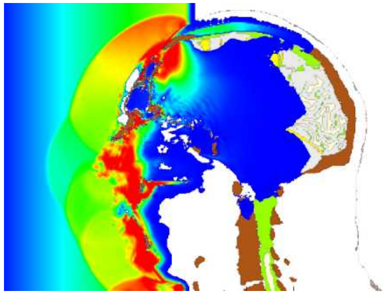

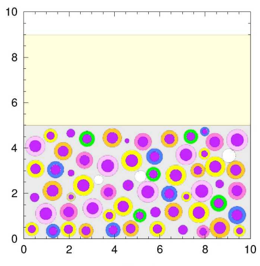

SAND2017-1193C

A Computational Study of Intracranial Cavitation in White Matter Axon Fiber Bundles as it Relates to Blast-Induced Traumatic Brain Injury

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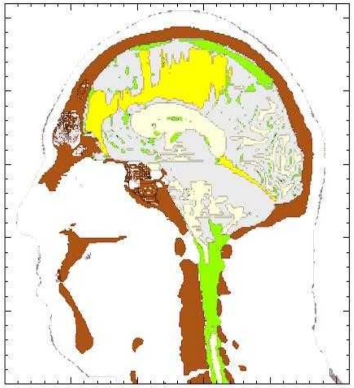
Blast-Induced Traumatic Brain Injury (TBI) Background

- Closed-Head Blast Injuries are leading cause of traumatic brain injury (TBI) in military personnel returning from combat [1]
  - Latest statistics show 352,000 US warfighters sustained TBI since 2000
- Objective: Primary Blast Injury (caused by direct blast exposure)
  - Investigate early-time wave intracranial wave mechanics leading to cavitation and traumatic brain injury
  - Previous work suggests shear stress and deviatoric shear energy correlate with localized brain injury identified in clinical TBI study
  - Separate work suggests intracranial cavitation may also cause brain injury
- Hypotheses: (1) Blast exposure induces intracranial fluid cavitation, (2) fluid cavitation, if it occurs, causes localized brain injury (3) the mechanisms of tissue damage, caused by cavitation bubble collapse, can be investigated on a microscale using a modeling & simulation approach
- Significance: Prediction, investigation, and identification of a new brain injury mechanism

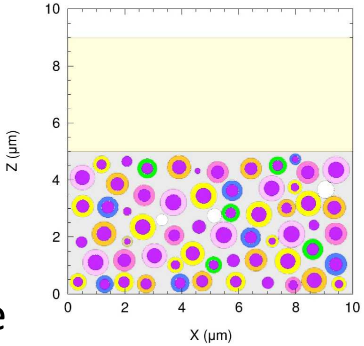
[1] Defense & Veterans Brain Injury Center TBI numbers: DoD numbers for traumatic brain injury, 2015.

Modeling Approach

- Simulate blast exposure to a macroscale model of the head to identify regions of the brain exposed to cavitation [2]
  - Blast waves directed to the front, side and rear
  - Simulations predicted cavitation occurring in areas with high concentrations of CSF

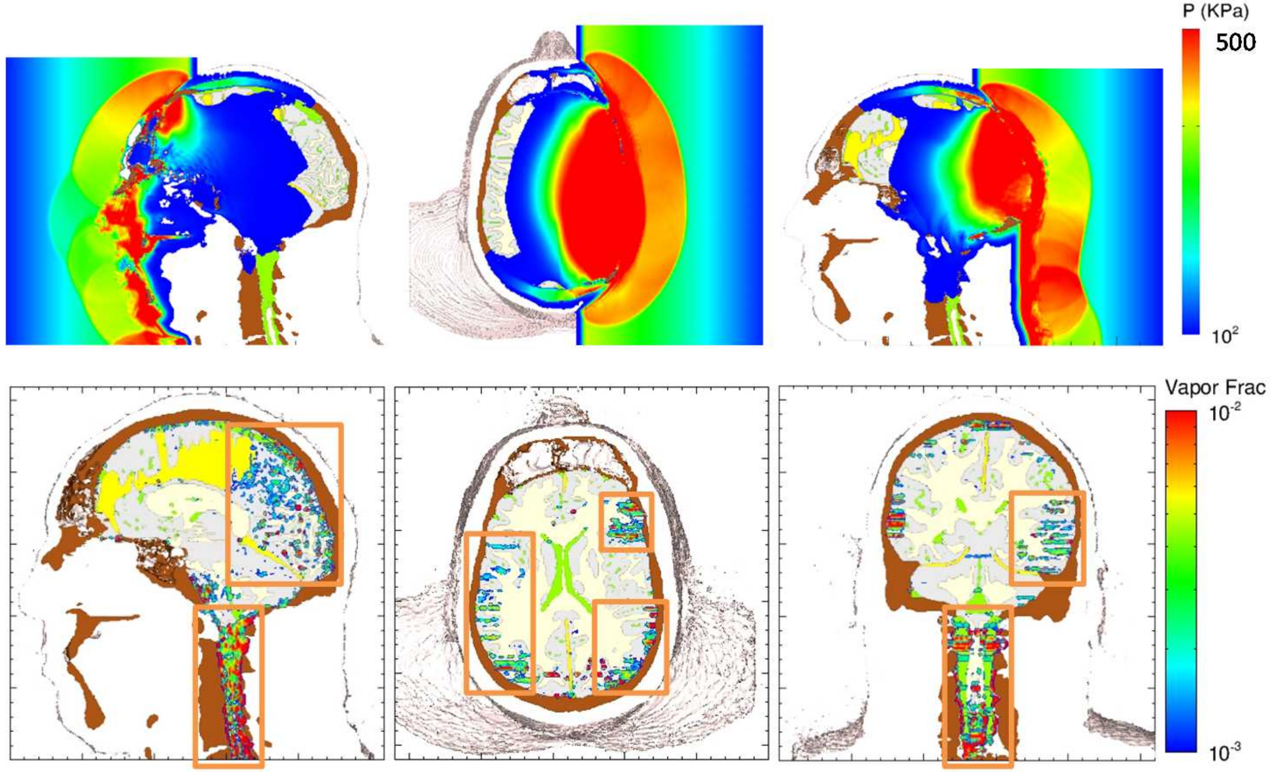


- Guided by the macroscale studies, conduct microscale investigations into the details of cavitation bubble collapse
  - Simulations assume the existence of cavitation bubbles
  - Investigate the tissue damaging mechanisms caused by bubble collapse within the white matter axon fiber bundle tracts
    - Examine the effects of the compressive wave strength and bubble size



[2] Taylor, P. A., Ludwigsen, J. S., and Ford, C. C., 2014, "Investigation of blast-induced traumatic brain injury," Brain Inj., **28**(7), pp. 879–895

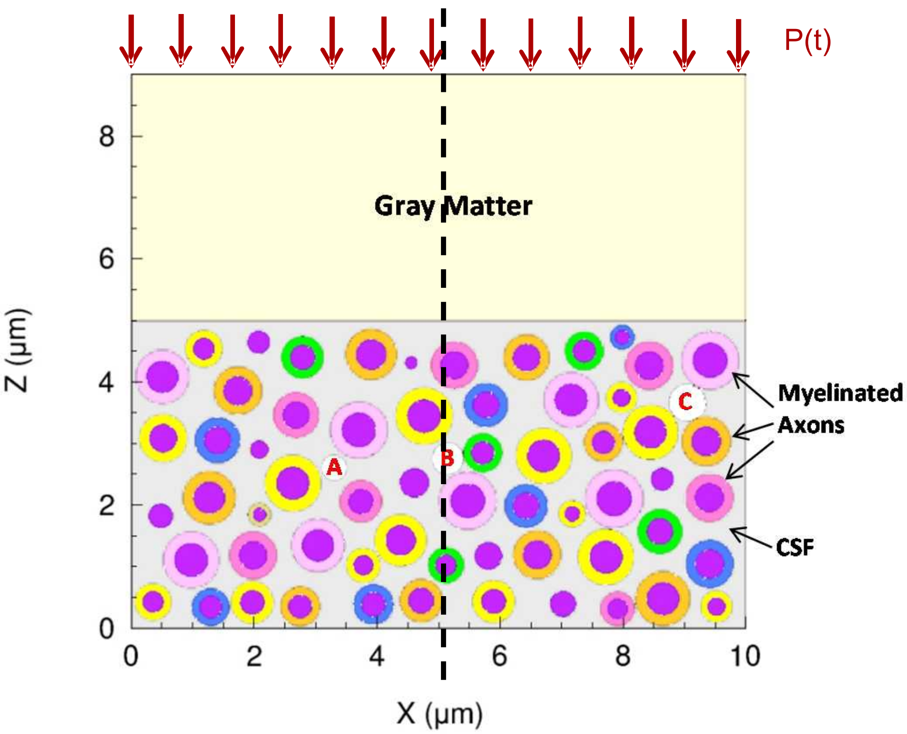
TBI Macroscale Modeling
260 KPa Blast Exposure: Cavitation Vapor Volume Fraction



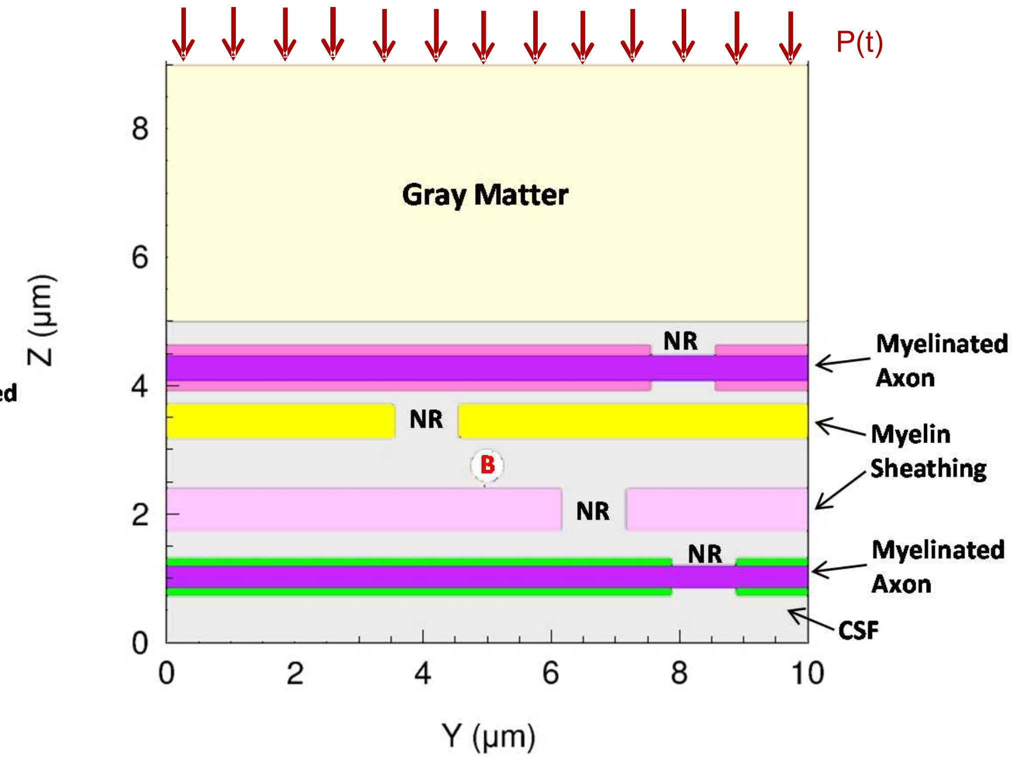
Note cavitation occurrence in white matter regions of the corpus callosum, cerebellum and brain stem

Microscale Model of the White Matter Axon Fiber Bundle

Axial View



Longitudinal View



10 µm x 10 µm x 9 µm, 0.02 µm cell size
52% volume fraction of randomly distributed axons
axon+myelin sheath diameter = 0.72 $\pm$ 0.15 µm

Initial pressures:
Bubbles: 5 kPa
100 kPa for all other materials

Bubble Radii:
A: 0.2 µm
B: 0.25 µm
C: 0.3 µm

Material Model

- EOS (volumetric response)
  - Equations relating pressure, volume, and temperature
  - Use Tillotson-Brundage for CSF, axon, myelin sheath, gray matter
  - Use sesame (tabular data table) for air

- Constitutive model (deviatoric response)
  - Use Swanson hyperelastic model for axon, myelin, and gray matter [3]

$$Damage, D = \begin{cases} 0, & for\ \varepsilon_{max} < \varepsilon_f \\ 1, & for\ \varepsilon_{max} \geq \varepsilon_f \end{cases}$$

ε_f = 0.435 for axon and myelin [4]

[3] Swanson, S. R., 1985, "A constitutive model for high elongation elastic materials," Trans. Am. Soc. Mech. Eng., **107**, pp. 110–114.

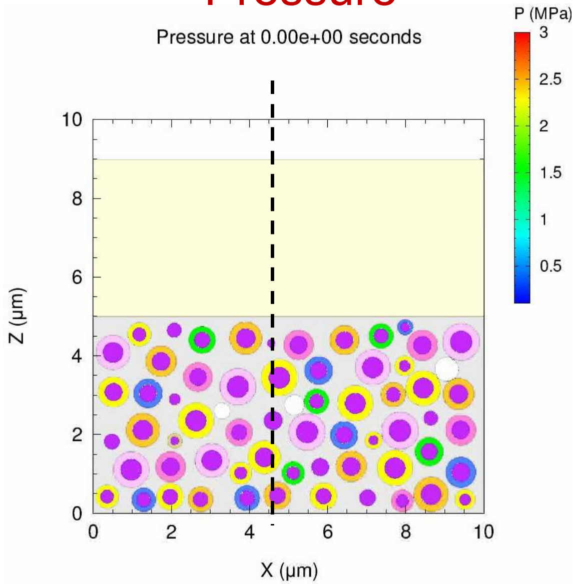
[4] Shreiber, D. I., Hao, H., and Elias, R. A. I., 2009, "Probing the influence of myelin and glia on the tensile properties of the spinal cord," Biomech. Model. Mechanobiol., **8**, pp. 311–321.

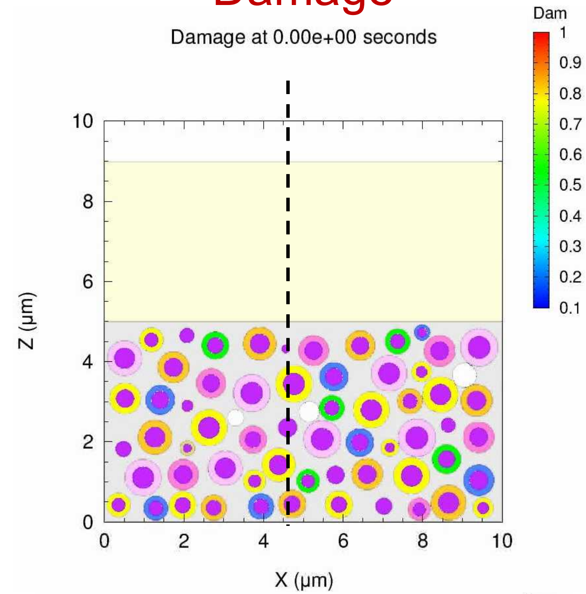
400 kPa Compressive Wave

Pressure

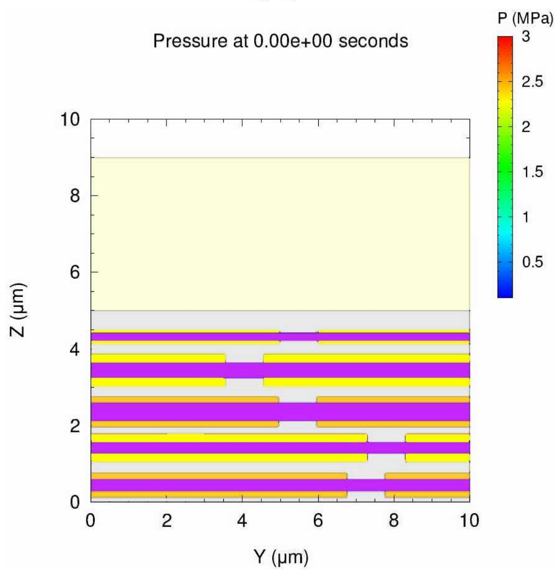
Damage

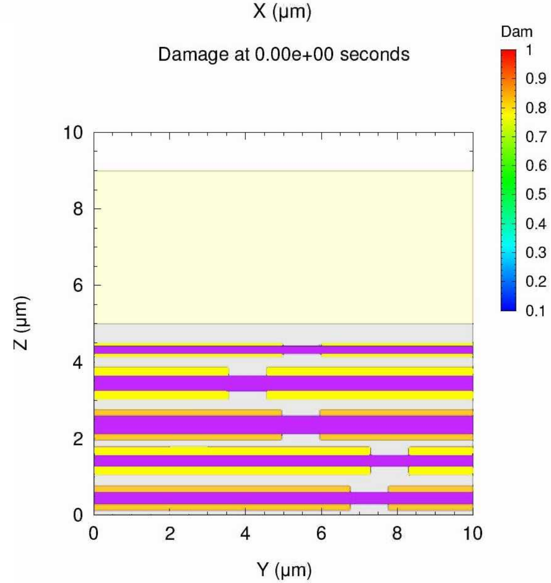
Axial





Longitudinal



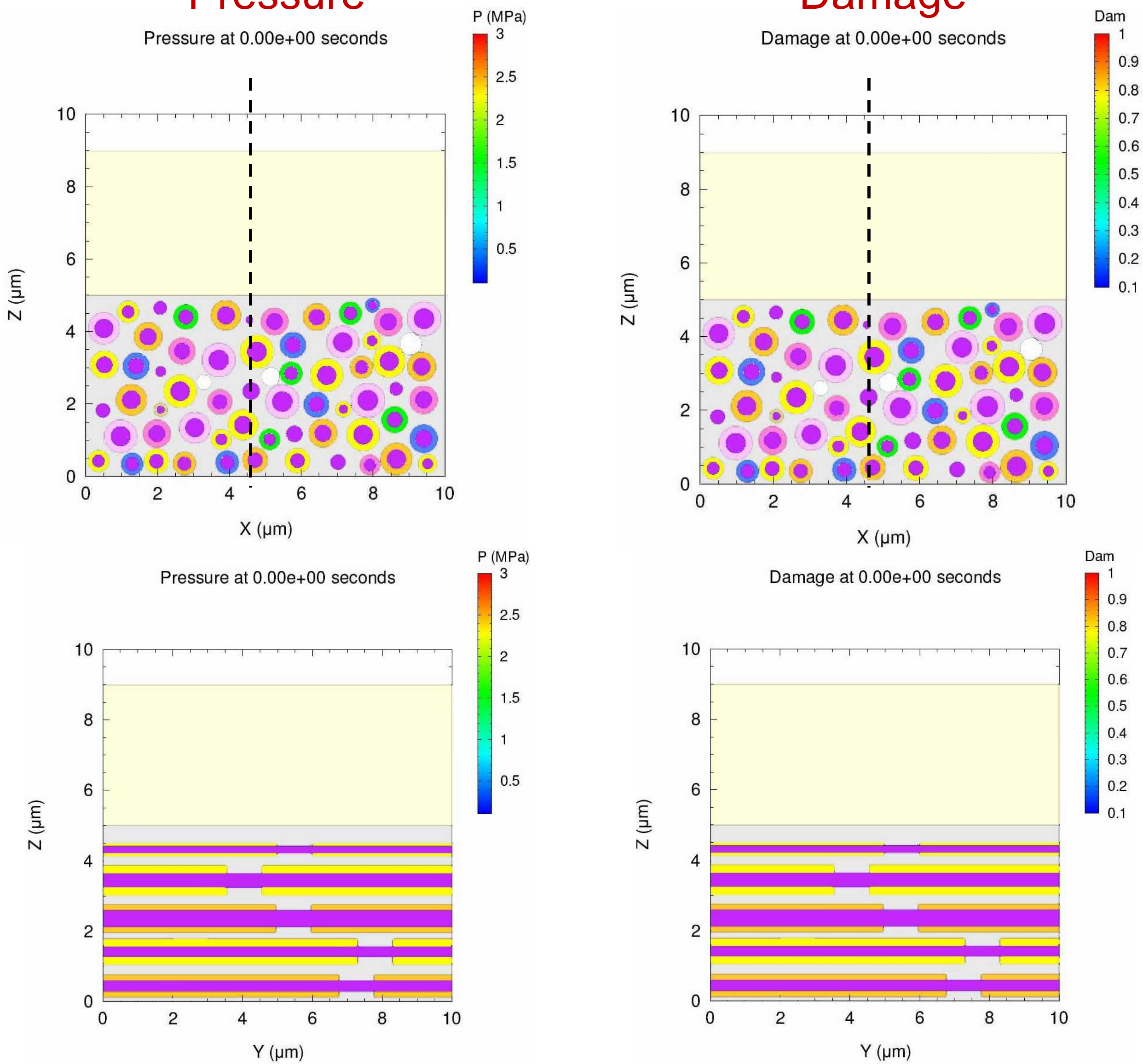


400 kPa Compressive Wave

Pressure | Damage

Axial

Longitudinal

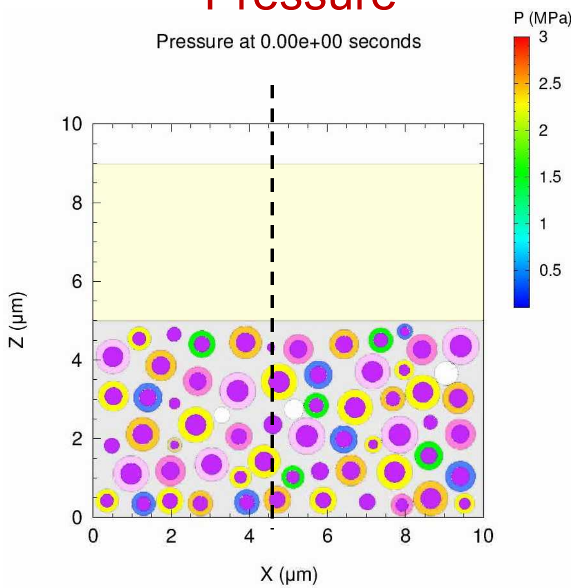


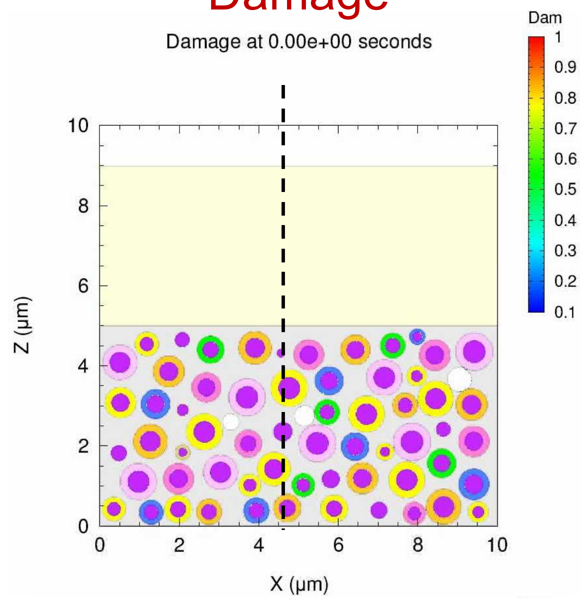
400 kPa Compressive Wave

Pressure

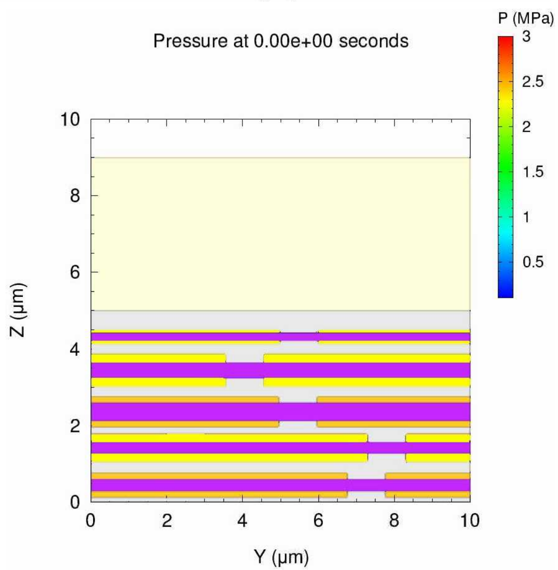
Damage

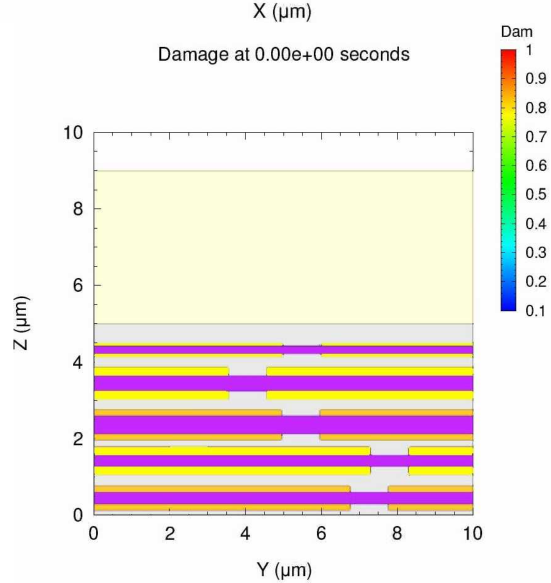
Axial



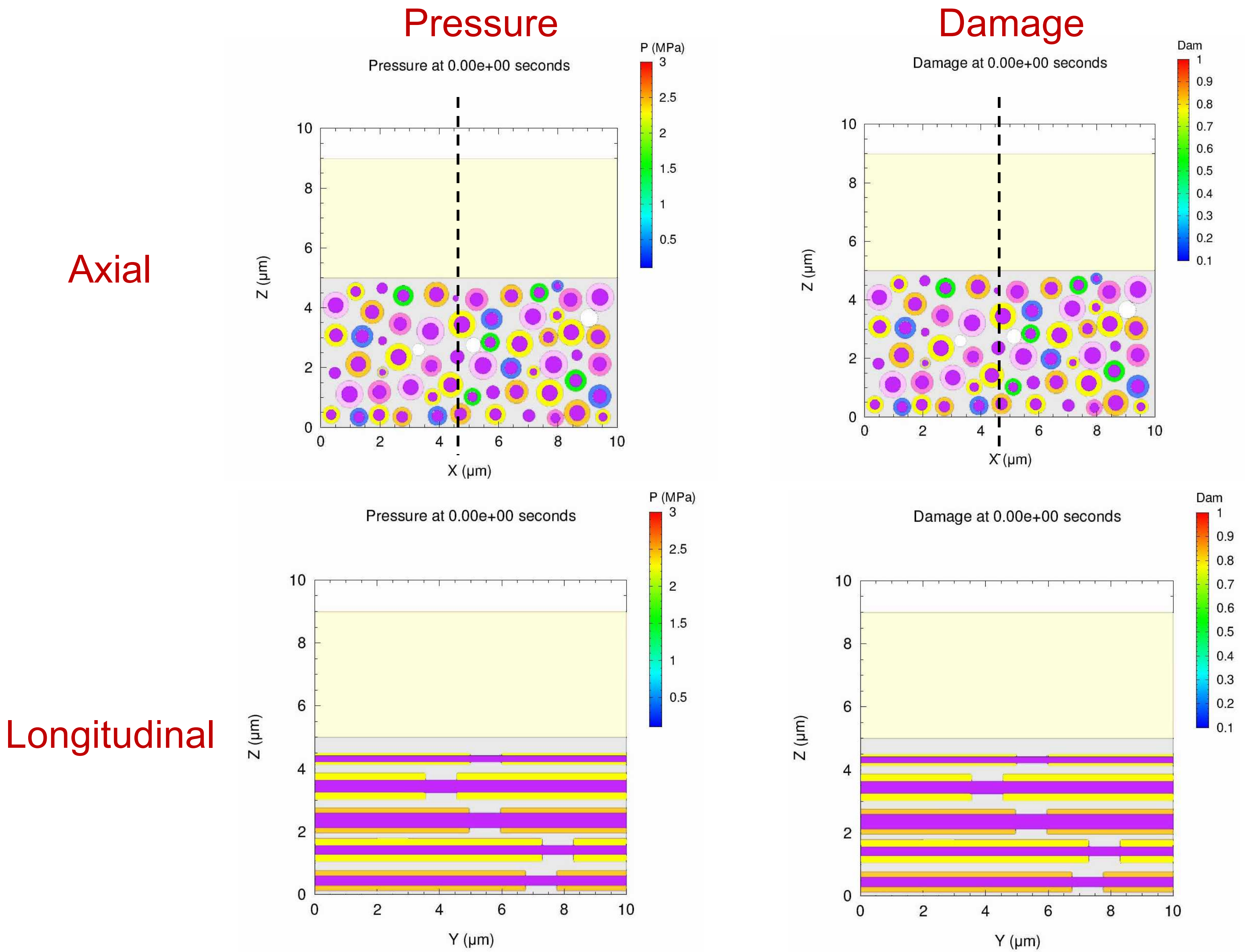


Longitudinal





700 kPa Compressive Wave



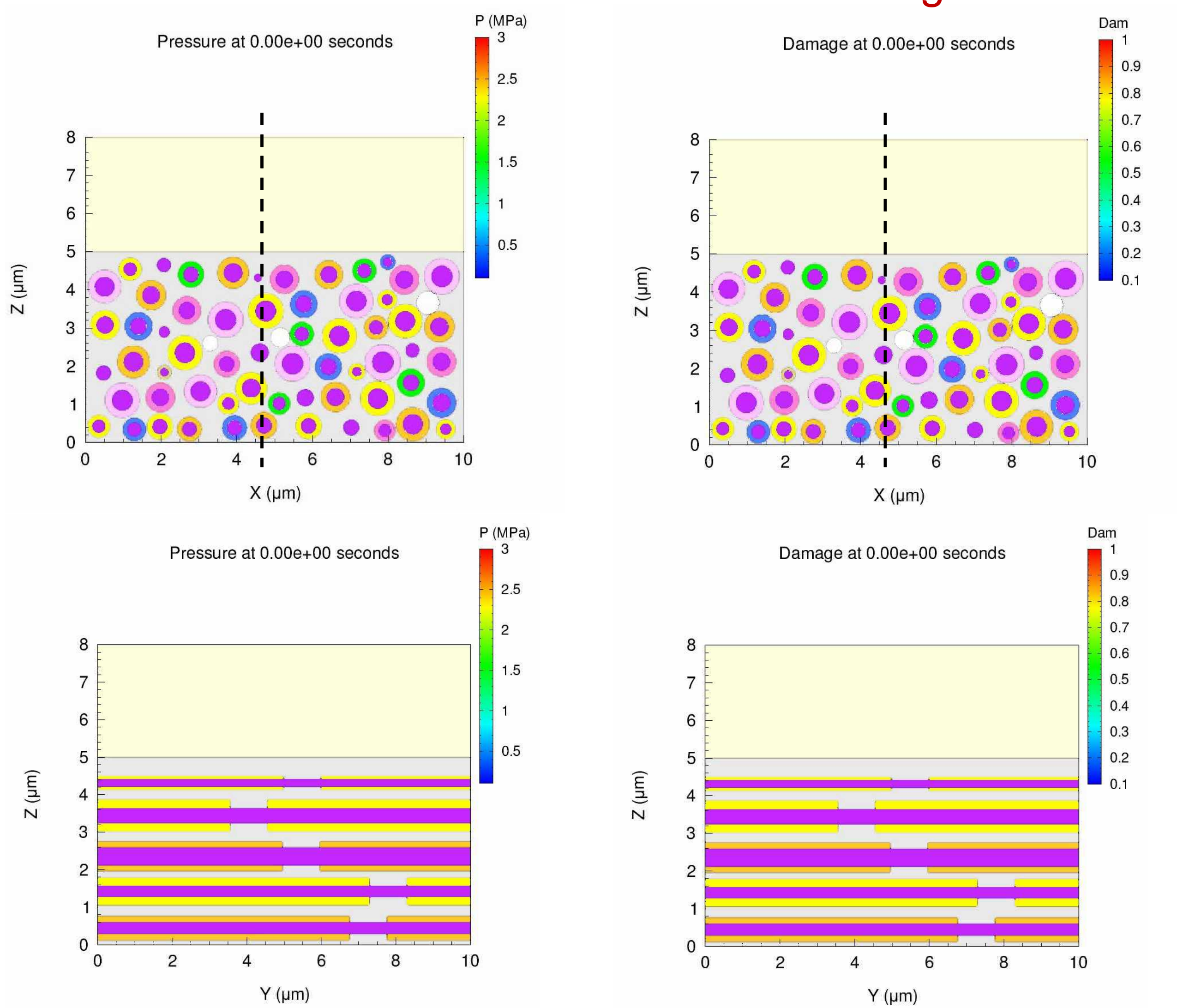
Spontaneous Bubble Collapse (Baseline result)

Pressure

Damage

Axial

Longitudinal



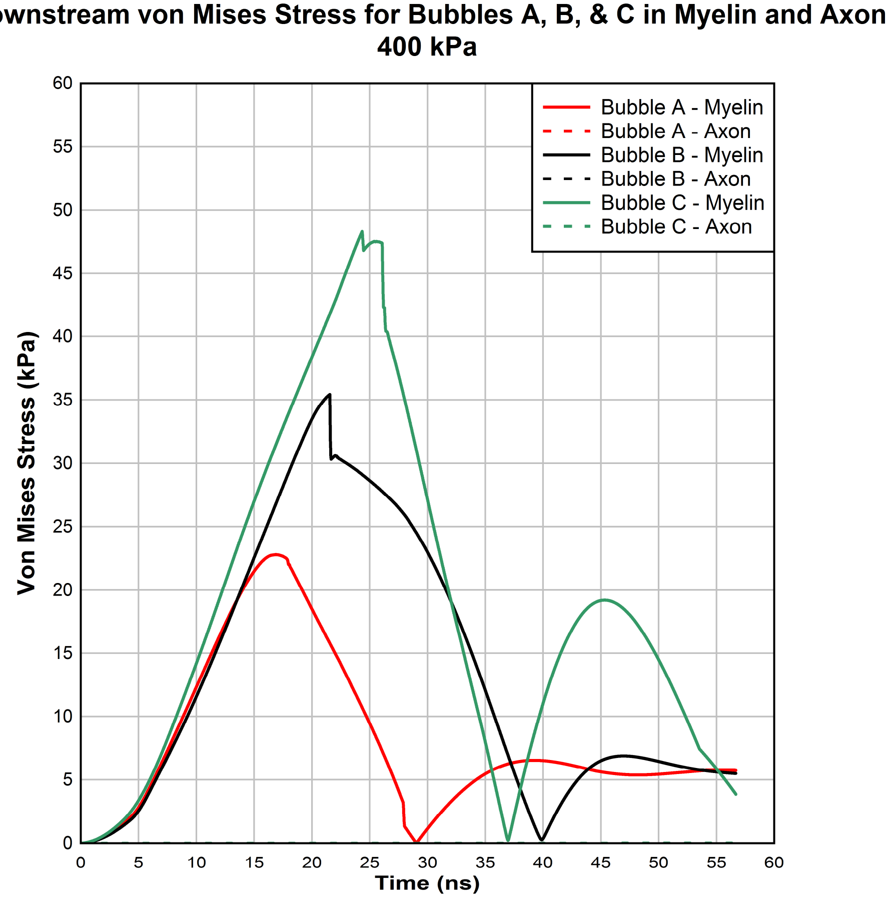
WM Microscale Model

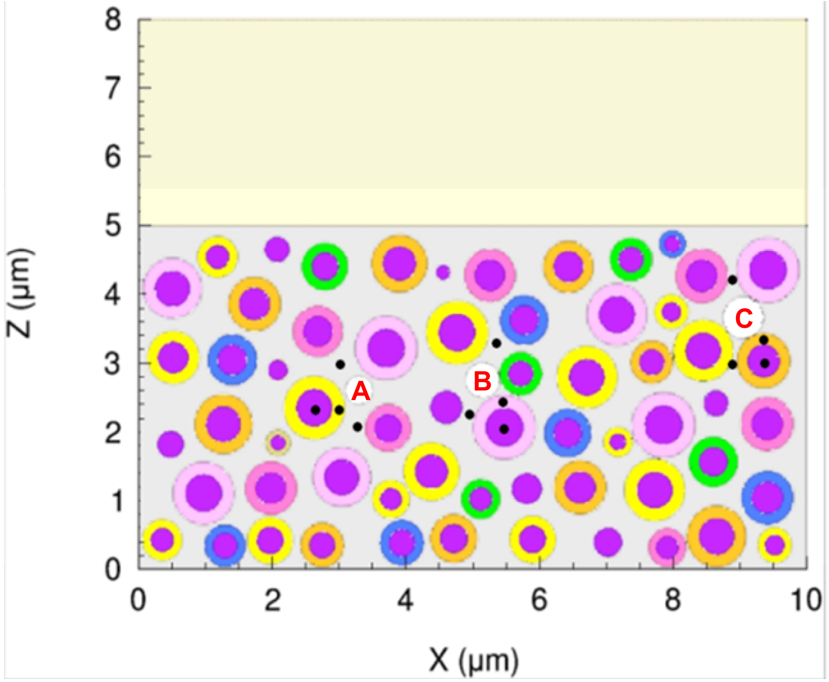
Hypotheses:

- Cavitation bubble collapse dependent on:
  - Bubble diameter
  - Strength of intracranial stress wave (related to blast strength)
- Effects of cavitation bubble collapse:
  - Microjetting of fluid surrounding bubble in downstream direction for scenarios with a follow-on compressive wave of 400 or 700 kPa
  - Increase in pressure and von Mises stress in axons downstream of the bubbles after collapse
  - Axon cores suffer significantly lower shear stresses from proximal bubble collapse than does their myelin sheathing

Microscale simulation results – 400 kPa

Myelin Sheathing and Axon





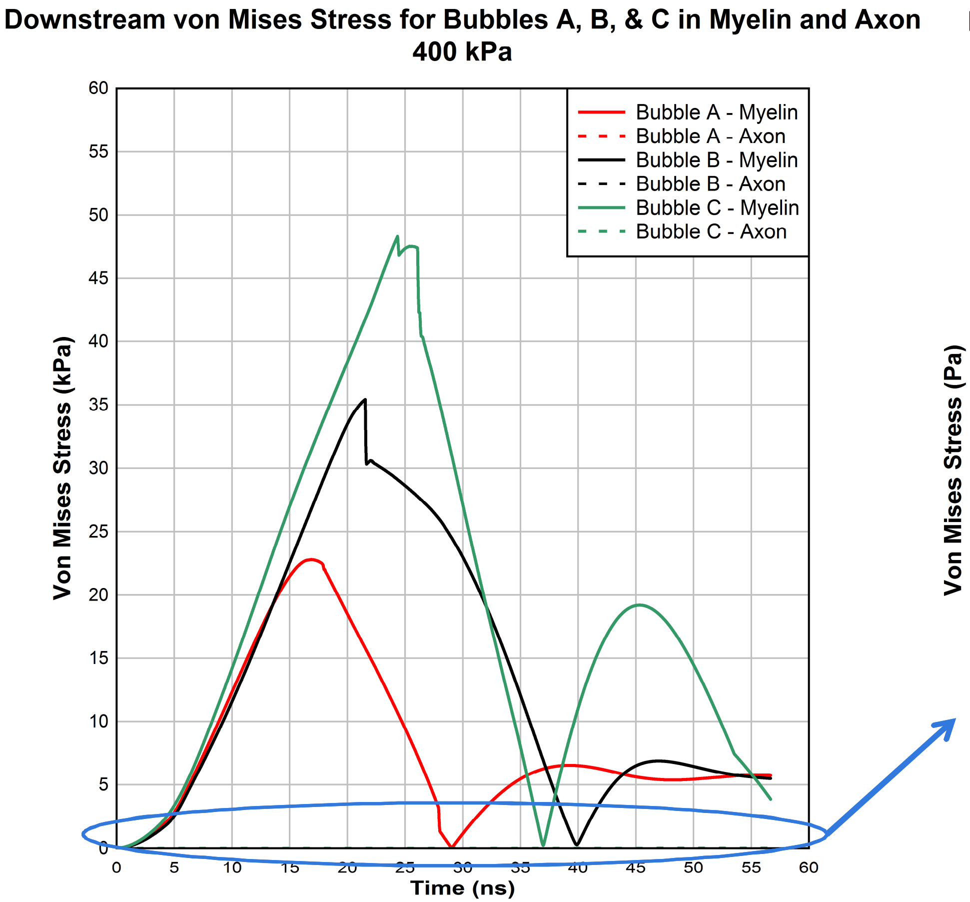
Diameter of bubble:
Bubble C > Bubble B > Bubble A

Relevant tracer locations denoted by black dot

Increase bubble size -> increase von Mises Stress in bundle -> impair myelin sheathing

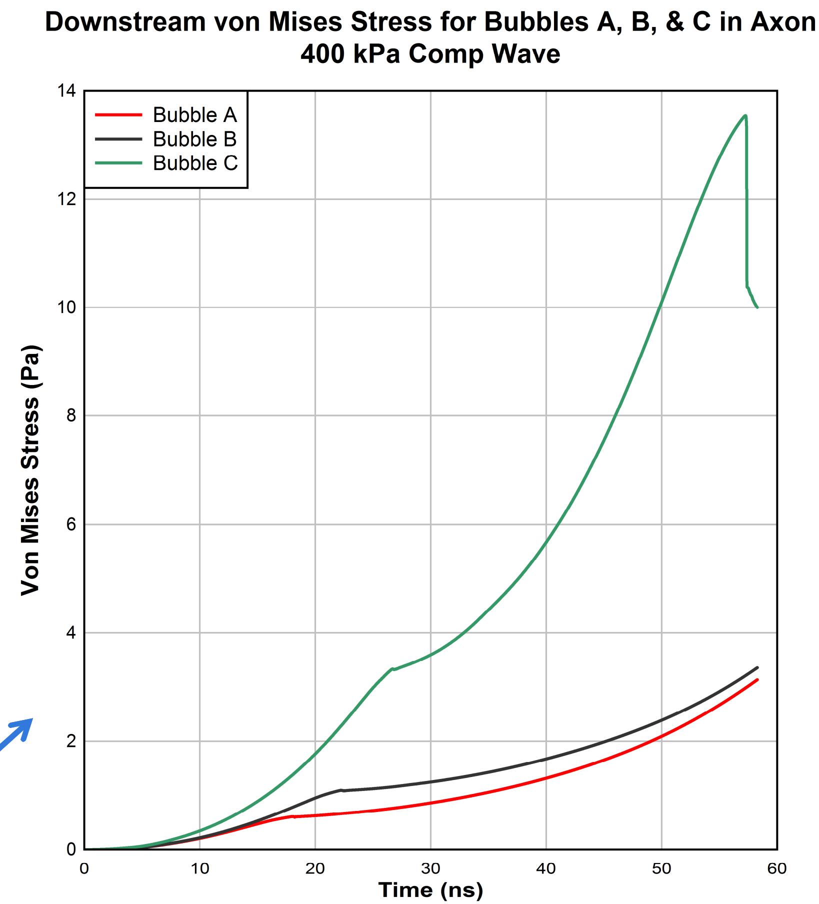
Microscale simulation results – 400 kPa

Myelin Sheathing and Axon



kPa

Axon

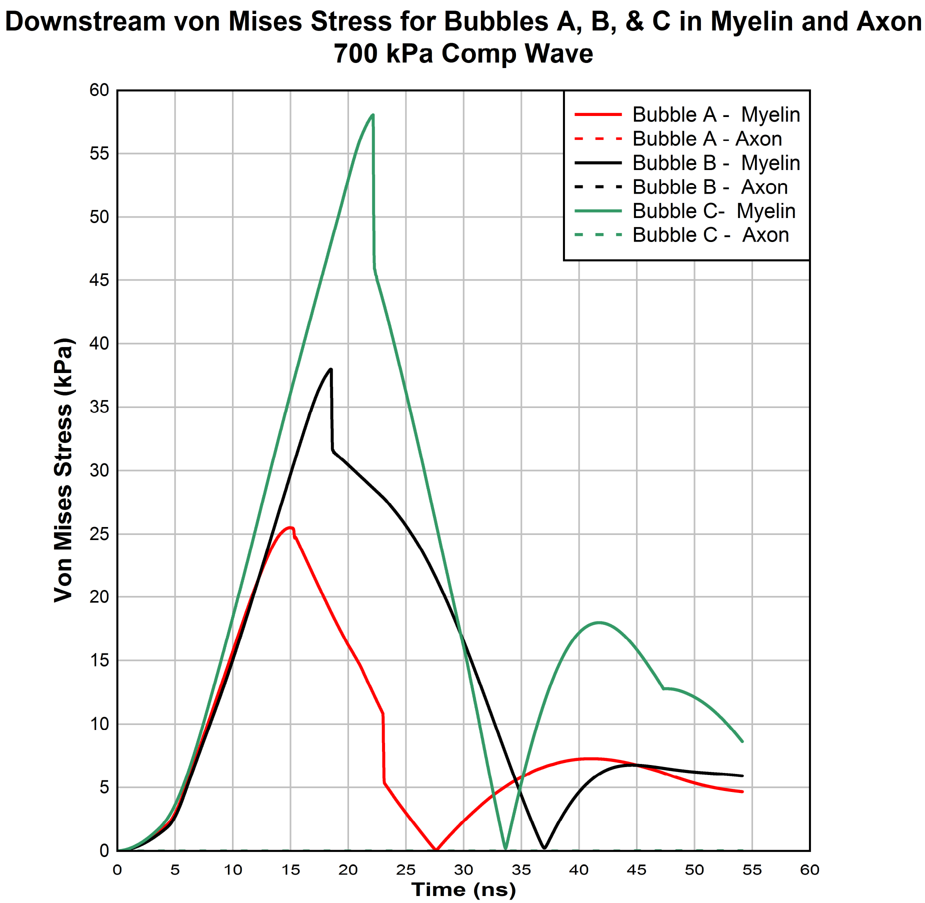


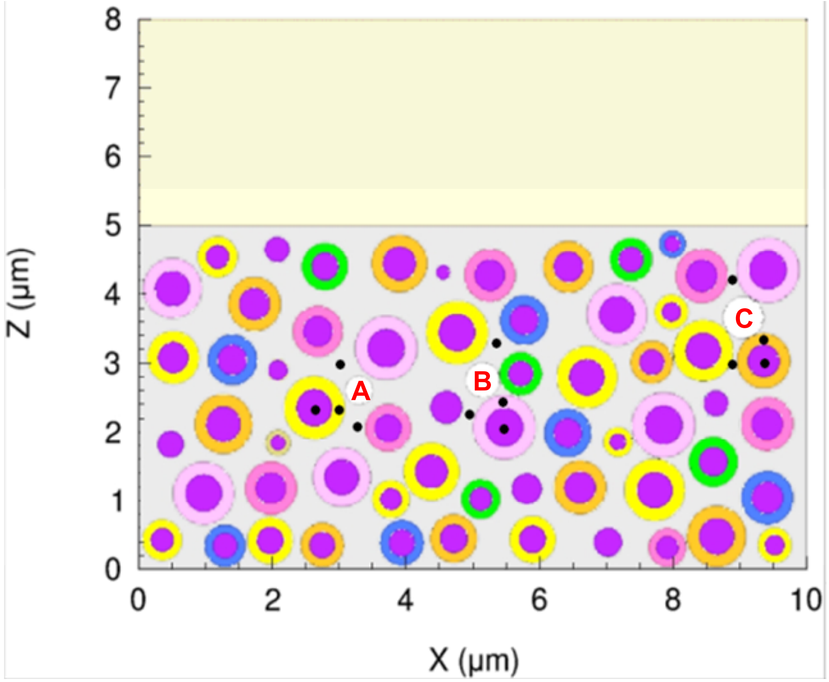
Pa

3 orders of magnitude difference

Microscale simulation results – 700 kPa

Myelin Sheathing and Axon





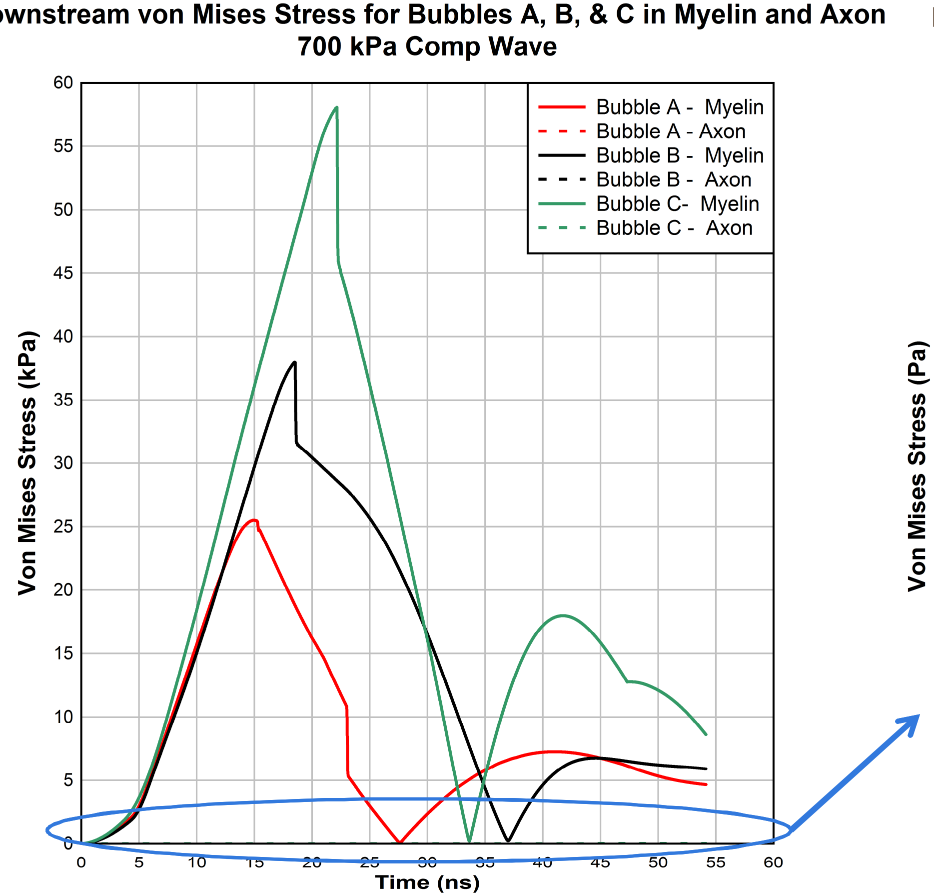
Diameter of bubble:
Bubble C > Bubble B > Bubble A

Relevant tracer locations denoted by black dot

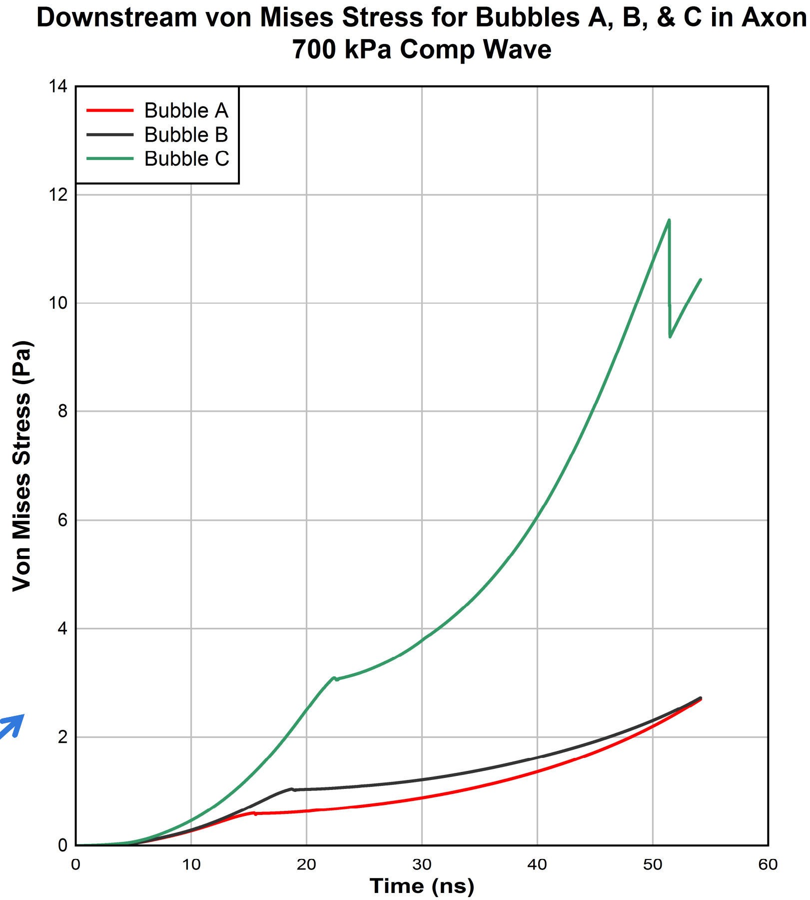
Increase bubble size -> increase von Mises Stress in bundle -> impair myelin sheathing

Microscale simulation results – 700 kPa

Myelin Sheathing and Axon



Axon



kPa

Pa

3 orders of magnitude difference

Microscale simulation results – 0 kPa

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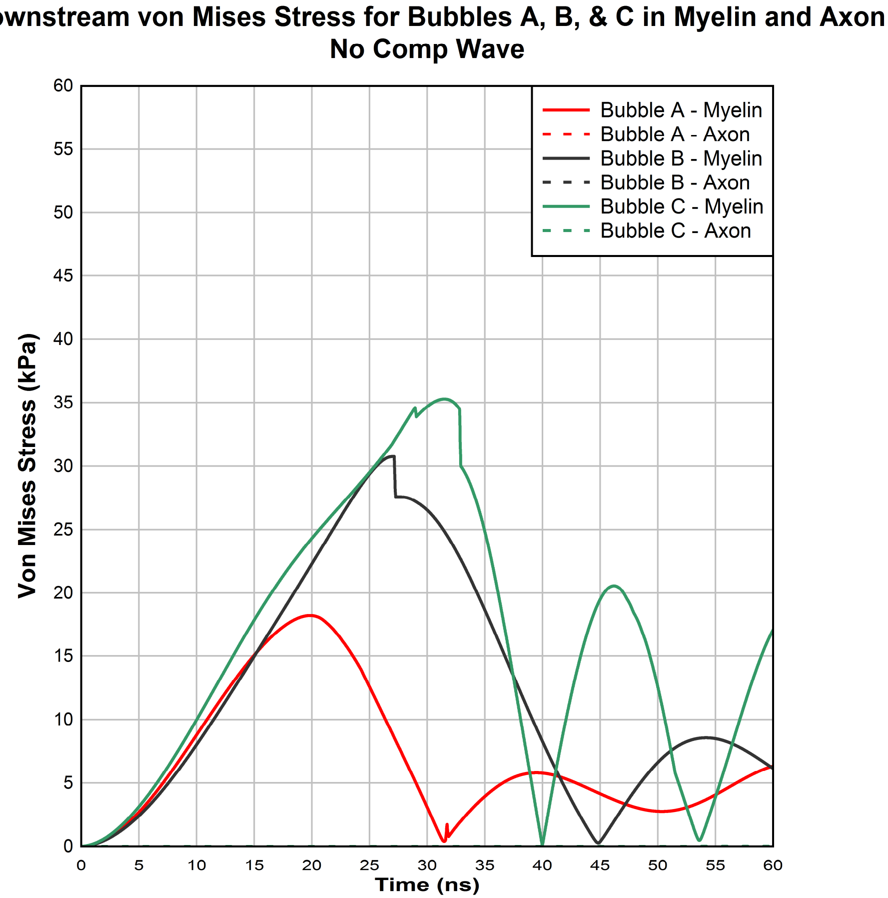
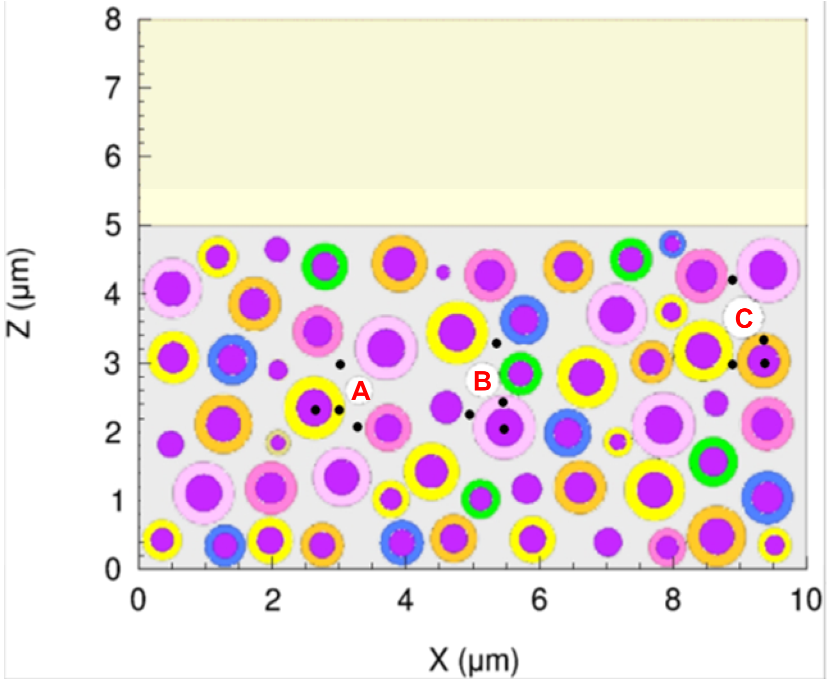
Myelin Sheathing and Axon





Increase bubble size -> increase von Mises Stress in bundle -> impair myelin sheathing

Diameter of bubble:
Bubble C > Bubble B > Bubble A

Relevant tracer locations denoted by black dot

Microscale simulation results – 0 kPa

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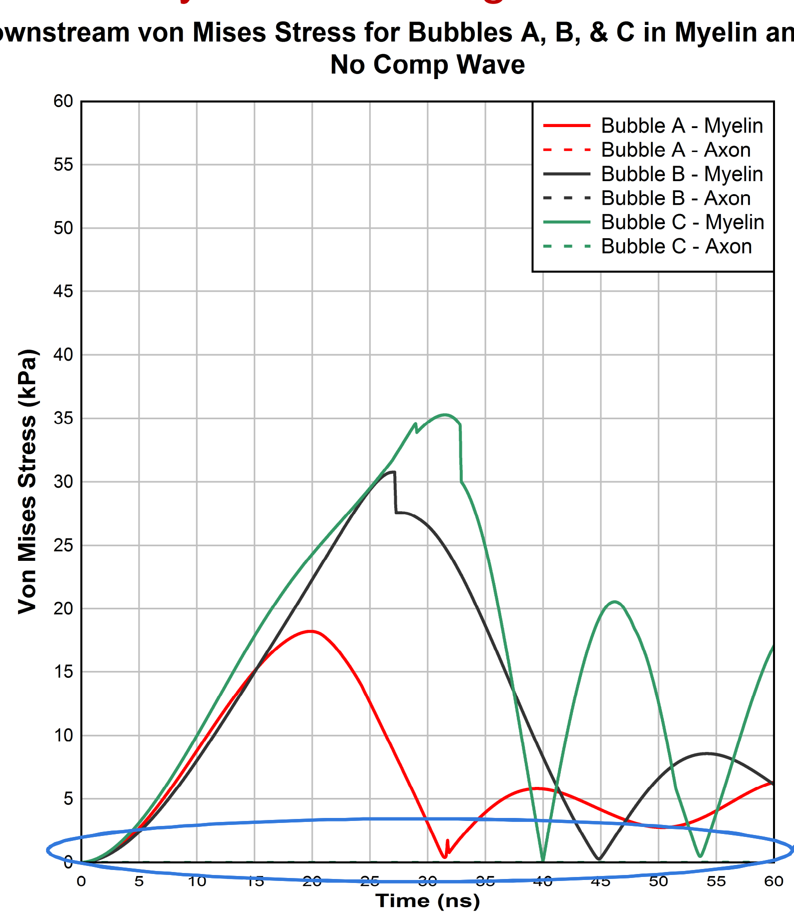
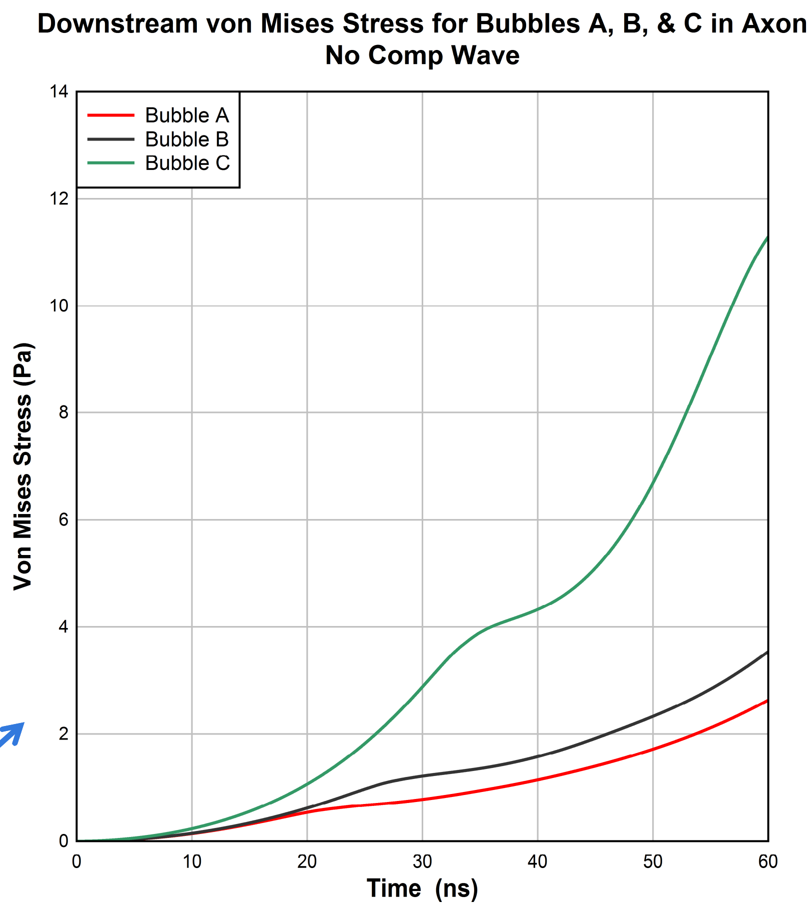
Myelin Sheathing and Axon



Axon



kPa

Pa

3 orders of magnitude difference

Microscale simulation results
Effect of Compressive Wave Amplitude

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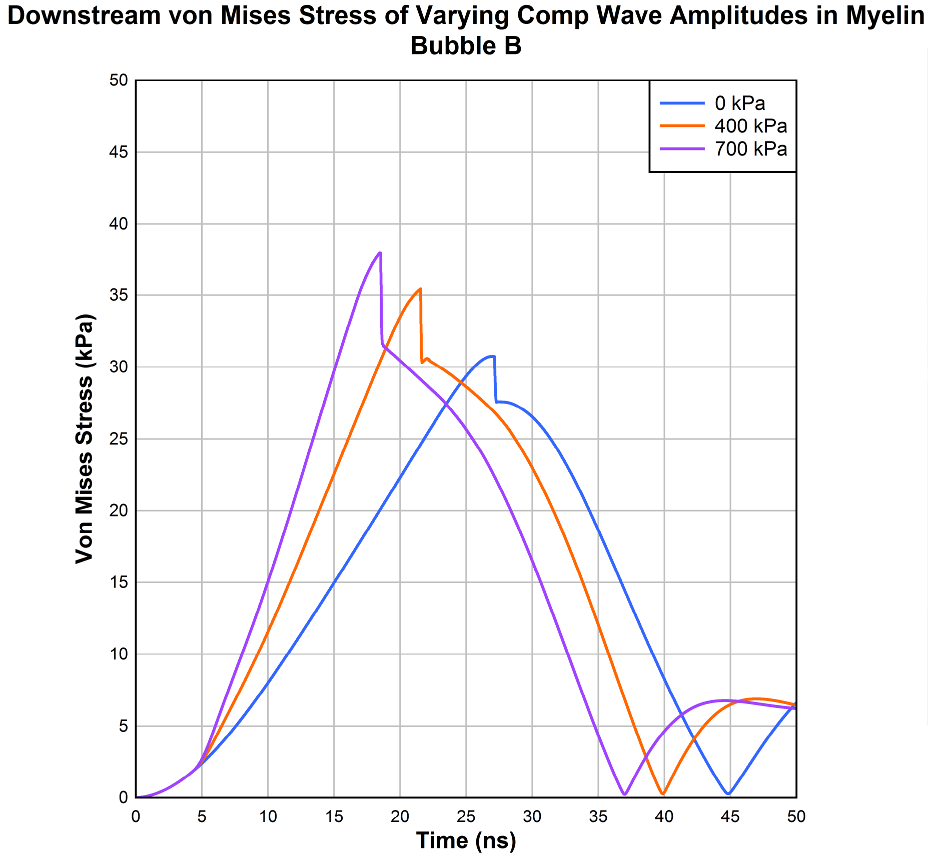
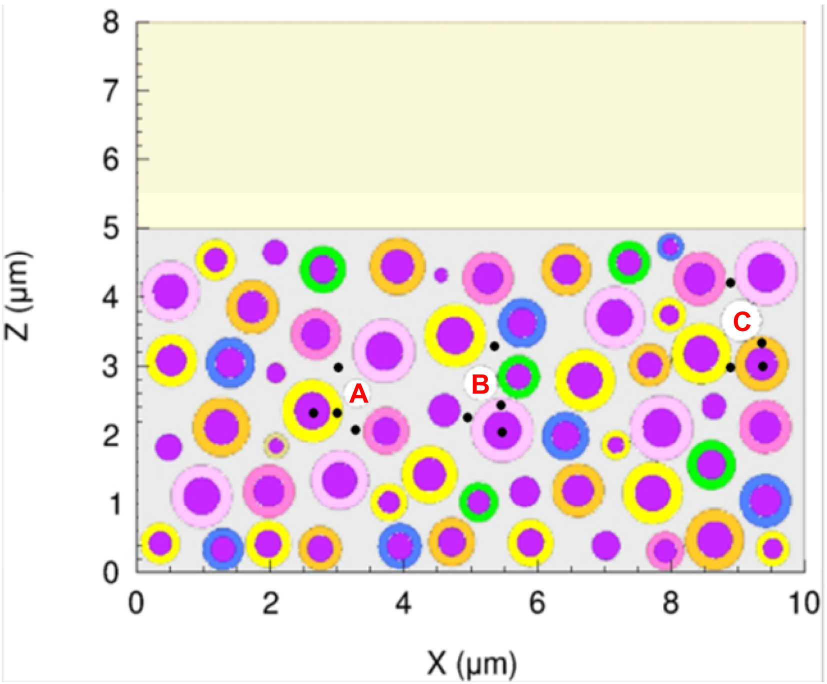
Myelin Sheathing





Diameter of bubble:
Bubble C > Bubble B > Bubble A

Relevant tracer locations denoted by black dot

Increase of compressive wave amplitude -> increase von Mises Stress in myelin sheathing -> impair myelin

Concluding Remarks

- Modeled 3 microscale scenarios within the white matter axonal fiber bundles to investigate effects of cavitation bubble size in the presence of intracranial compressive waves of various magnitudes: 1) bubbles at ambient pressure and the passage of a compressive wave of 2) 400 kPa or 3) 700 kPa
  - Measured von Mises stress experienced by axons adjacent to bubble
  - Observed damage experienced by axons adjacent to bubble
- Simulations predict an increase in downstream von Mises stress with increasing bubble size and compressive wave amplitude
- Von Mises stresses experienced by axon are about 3 orders of magnitude less than those it its myelin sheathing
  - Myelin sheath acts as a defense barrier against mechanical insult
- Predicted damage to both the myelin sheathing and the underlying axon
  - Damage to the myelin sheathing has the potential to degrade nerve conduction [5]
  - Damage to the axon core can lead to symptoms associated with concussion and/or coma
- This work was submitted to the bTBI Thematic Issue of *Shock Waves*

[5] Medana, I. M., and Esiri, M. M., 2003, "Axonal damage: a key predictor of outcome in human CNS diseases," Brain, **126**, pp. 515–530.

Questions?