BIOMECHANICALLY REALISTIC PHYSICAL HEAD MODELS

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Physical head models are essential for studying traumatic brain injuries (TBI) due to ethical and biological limitations of animal studies, the limitations of Finite element models (FE,) and the inability to examine human brains after concussive events.

This document provides a comprehensive technical review of creating realistic physical models for studying TBI, focusing on four critical components, the neck, the brain, the skull, and cerebrospinal fluid.

Current helmet impact testing protocols are based on the most frequent instantaneous impact forces athletes experience, from accelerometer data in athletic helmets. Without baseline data about brain tissue response to a wide variety of impact scenarios, a helmet system cannot be evaluated for reducing impact response that may cause brain tissue damage.

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SUMMARY

The Neck

Current limitations: Existing neck models like Hybrid III and Thor use simplified materials (metal discs with rubber) that don't accurately represent human muscle behavior. Hybrid III models are stiffer and biased toward specific bending directions, whereas Thor models more closely simulate human intervertebral discs using silicone foam rubber.

Key findings:
Real neck muscles contract reflexively or voluntarily to resist impact forces.

- Muscle activation significantly affects head injury outcomes. People who anticipate impacts experience significantly less rotational acceleration.
- Anticipation generally involves visual awareness of incoming impacts.

Guidance:
Mimicking muscle activation is not practical. Instead, adjust neck model flexibility given the impact direction's location in peripheral vision: the more peripheral, the more flexible.

The Brain

Material challenges: Brain tissue has two distinct types:

- **Gray matter**: Responds isotropically (uniform in all directions) to impacts, softer.
- **White matter**: Responds anisotropically (directionally-dependent) to impacts, contains aligned fiber tracts that are vulnerable to damage when strained along their length.
- **Interfaces:** Damage most often occurs where gray and white matter meet, as each responds differently to mechanical loads, causing mechanical mismatch.

Current approaches:

- **Silicones & Gels**: Used in blast and medical studies, models respond isotropically (unrealistic for white matter).

Hydrogel Innovation: Newer materials can be engineered to respond anisotropically to mimic white matter behavior. Recent advances create anisotropic hydrogels using magnetic fields, electrical orientation, or freeze-casting to realistically model white matter's directional vulnerabilities.

Guidance:

- Use anisotropic hydrogels for white matter regions
- Use isotropic materials for gray matter
- Assemble model brains in layers, ensuring white and gray matter interfaces are accurate.
- Accomplished manually, using servo systems, with 3D printing, or cast in place.

The Skull

Structure: Real skulls have a sandwich design - two dense cortical bone layers surrounding spongy trabecular bone (diploe). This provides both rigidity and shock absorption.

Modeling solutions: 3D-printed materials like PLA can approximate skull mechanical properties. The elastic modulus of skull bones varies widely (1.7-15.5 GPa), but PLA composites can be tuned to match these ranges.

Guidance: Material heterogeneity and layered structures, feasible with programmed 3D printers, can enhance biomechanical accuracy.

Cerebrospinal Fluid (CSF):

- CSF cushions the brain, reducing rotational and shear strain during impacts.
- CSF is contained by membranous meninges: pia, arachnoid, and dura.
- A TBI head model filled fluid around an artificial brain to replicate the CSF, and found it important in response to impacts.

Guidance: Thin membranes forming sealed cavities, filled with fluid and positioned next to the skull, mimic biological meninges, and are more practical and realistic than saturating a model with fluid.

In summary, these approaches will provide more accurate predictions of brain injury mechanisms than current simplified head models, particularly for rotational impacts common in sports and vehicle accidents.

RESULTS

THE NECK

Real-world experimental studies of TBI are challenging. Animal use involves ethical and technical issues, and tested animals have brain properties that significantly differ from human brains. This leaves physical head models, that simulate the properties of human brains, as the way to conduct experimental studies of human brain response to impacts and blasts. A realistic head model sits on a realistic neck. Muscles are not static structures like bones and brains. Muscles contract and relax, sometimes reflexively, often due to voluntary effort. Neck muscles play a critical role in head movements.

Hybrid III neck models used in crash, blast and helmet tests use four or five metal discs interconnected by four incompressible butyl rubber discs. A single fissure in the rubber reduces neck stiffness. This, however, biases the neckform to bend directly backwards and forwards, a biased response for impact testing. Such necks showed significantly slower rotational acceleration from angular impacts compared to a NOCSAE neckform.[1]

Wayne State's THOR neck model uses six metal discs and twelve silicone foam rubber rings to simulate intervertebral disks. Its design simulates ligaments and musculature, as well as vertebrae, with multi-axis joints. This better represents rotational dynamics caused by oblique impacts. Humanetics Inc., affiliated with Wayne State, developed a more sophisticated neck (and head) dummy called THOR-AV. It has greater structural biofidelity, incorporating neck curvature, with vertebrae offset at different distances and angles.

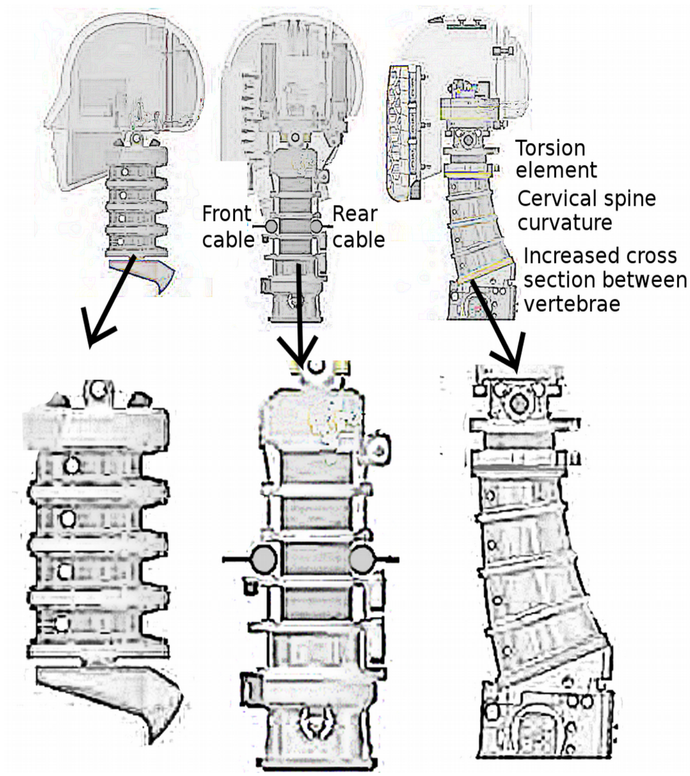

Figure 1 Drawn by author

Physical principles infer that shorter, thicker necks will respond more stiffly to angular impacts. For a vertical mass, a larger diameter increases I, the second moment of area (proportional to r^4, where r is radius) $I = \pi r^4 / 4$. Shorter, thicker columns resist buckling under compressive or angled loads. In

1 Walsh, E.S., Kendall, M., Post, A. et al. (2018) "Comparative analysis of Hybrid III neckform and an unbiased neckform" Sports Eng. 21, 479–85

Euler's buckling formula the critical force $F_{cr} = \pi^2 EI / (KL)^2$ where E is modulus, L is height, and K is how supported the column is. This is analogous to the logic that athletes with shorter, thicker necks resist angular impacts better than people with thinner, longer necks. However, there is an important factor in humans that such models do not incorporate: real neck response to impacts is governed by muscle activity as much as muscle area.

Humm et al. compared the Hybrid III and Thor systems with cadavers, and found Thor systems were somewhat more accurate in representing actual injury under impact accelerations found in vehicle crashes.[2] Wang et al. crashed the three different systems at angles (oblique impacts) to see how well their neck movements compared to real human necks during collisions. Several different testing devices were used. Overall, THOR-AV was marginal to good, THOR marginal, and Hybrid III poor, in terms of human-like rotation responses. None allow attached heads to twist sideways like real people do in angled crashes. The THOR-AV actually spun too much in some of the tests, presumably because of a special rotating part in its design.[3]

The greater biofidelity of THOR systems may be due to the arrangements of component structures. For example, Awad et al.'s 2015 paper assessed a modified THOR neck, along with brain, skull, and skin components. The neck incorporated 6 steel discs, with silicone foam rubber rings on either side of each. From the top, 4 steel cables were run to each of 4 steel disks. The cable ends were attached to springs, either to one of 4 springs, or cables grouped to fewer or all at a single spring. The authors compared neck flexion and found using one spring per each cable (which they compared to neck tendons) mimicked human neck flexion best, 15° - 30°.[4] Flexion and extension of the neck refer to back and forth movements. The authors did not report rotational movement. Bogduk & Mercer reviewed human neck structural motion. In seven studies flexural motion ranged from 10° to 21°. In normal individuals neck axial rotation from CT scans averaged 43° to either side.[5]

Neck model materials may not be biofidelic. In humans, cervical vertebra are not flat disks. The top disks, which are critical for head motion, have highly convex shapes formed by thick cartilage tissue. The first disk (the atlas) moves down into the second disk (the axis) during head rotations. The atlas and head rotate from side to side as one unit. Other cervical vertebrae respond to different impacts in complex ways, often with some having the reverse motion of others.[6]

Cadaver tests find that the effective modulus of human intervertebral discs ranges from ~5 to 50 MPa.[7] Hybrid III uses butyl rubber discs. Different butyl rubber suppliers report variable modulus rates, but

2 Humm, J. & N. Yoganandan (2021) "Lower Neck Injury Assessment Risk Curves Based on Matched-Pair Human Data for Anthropomorphic Test Devices" Military Medicine; 186(Sup 1): 639–44

3 Wang, Z.J. et al. (2022) "Neck Biofidelity Comparison of THOR-AV, THOR and Hybrid III 50th Dummies" Proc. 2021 IRCOBI; 395, 136–56

4 Awad, N, El-Dakhakhni, W.W. & A.A.Gilani (2015) "A Physical Head and Neck Surrogate Model to Investigate Blast-Induced Mild Traumatic Brain Injury" Arab J. Sci. Eng.; 40:945–58

5 Bogduk, N. & S. Mercer (2000) "Biomechanics of the cervical spine. I: Normal kinematics" Clin. Biomech.; 15(9):633–48

6 Swartz, E.E., Floyd, R.T. & M. Cendoma (2005) "Cervical spine functional anatomy and the biomechanics of injury due to compressive loading" J. Athl. Train.; 40(3):155-61

7 Yang, H. et al. (2016) "Effective Modulus of the Human Intervertebral Disc and its Effect on Vertebral Bone Stress" J. Biomech.;49(7):1134–4

these include the range of human tissue. THOR systems' silicone foam rubber has a lower Young's modulus than human discs, below 5 MPa.

Neither Hybrid III, Thor, nor other neckforms use biomimetic materials for neck muscles. Differences in muscle material properties can change tissue stress and strain by up to 70%. There's little data on the mechanical properties of such muscles. Arnold, Scott & Bush reviewed, in 2023, studies of soft tissue mechanical properties of humans, including muscles. No study focused on neck muscles. Overall, *in vivo* studies of muscles report higher Young's modulus than cadavers. This isn't surprising, since muscle tone presumably weakens without metabolic inputs or exercise.[8]

Cadavers (and current model necks) cannot activate muscles. Muscle activation is important in resisting head movements after impacts. Computer models suggest muscle activation plays an important role in responding to impacts that induce head movement.[9] Nasim & Galvanetto assembled a complex FE neck model that incorporated various muscles, and ran a simulation under 15g frontal impact loading. This was compared to similar data of young male volunteers engaged in sled tests. Two FE models were used, one with muscles activated during impact, and one with muscles passive. The FE active muscle model was somewhat better at predicting subject responses. The experimental data showed that active muscles of the lower neck play an important role in response to impact forces. Muscle activation increases neck strength to resist head motion.[10]

The difference between both FE models and experimental evidence was large. Fig. 2 shows 15g frontal impacts, with passive and active neck models compared to volunteer experiments with volunteers, from Nightingale et al. FE models exag-gerated acceleration in the X-axis, failed to predict Z-axis acceleration, and modestly correlated with volunteer response in the Y-axis.

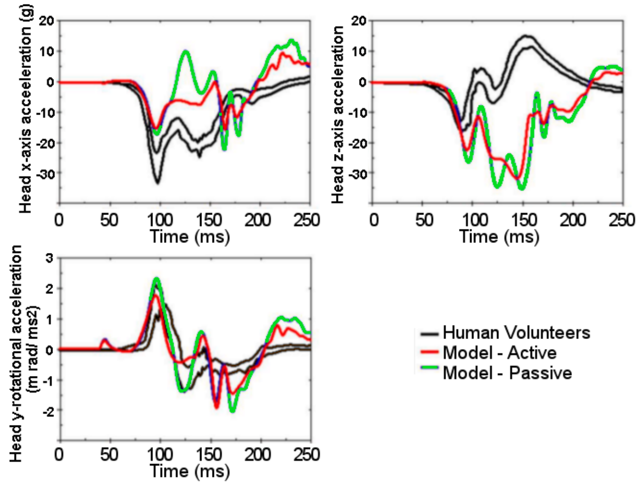

Figure 2 Redrawn from Nightingale et al.[9]

Houdini Motif

Harry Houdini died of a burst appendix, which before antibiotics was usually a death sentence. Nine days earlier he had been punched hard in the stomach, unexpectedly, by a student who believed Houdini capable of withstanding such blows. Houdini was hurt. Because it coincided with the later appendicitis, an inaccurate story emerged that the punch killed him. Regardless, unlike many blows that

8 Arnold, N., Scott, J. & T.R. Bush (2023) "A review of the characterizations of soft tissues used in human body modeling: Scope, limitations, and the path forward" J. Tissue Viability; 32(2):286-304

9 Nightingale, R.W. et al. (2016) "Impact responses of the cervical spine: A computational study of the effects of muscle activity, torso constraint, and pre-flexion" J. Biomechanics; 49(4), 558–64

10 Nasim, M. & U. Galvanetto (2023) "Muscle activity on head-first compression responses of a finite element neck model" Forces in Mechanics; 10, 100163

Houdini expected and sustained, the student's unanticipated punch did injure him.[11] It highlights how preparatory muscle activation ahead of an expected perturbation is a whole-body, feedforward process.

Evidence about neck muscle strength and increased neck stability during impacts is mixed. Neck muscle strength training for eight weeks did not enhance head-neck stabilization during force application in collegiate soccer players.[12] But evidence for muscle activation and reduced head movement is abundant. Although activation may be reflexive, it often requires a person's awareness of an imminent impact. Awareness helps to protect, being struck without expectation is more damaging.

The key neck muscles in neck stabilization are the sternocleidomastoid (SCM) and trapezius muscles. They help control head–neck flexion and extension. Ito et al. found that reflexive response of the SCM begins to decelerate head velocity before voluntary movement takes effect.[13] Bauer et al. monitored activity of the left and right SCM and trapezius muscles with electrodes attached to female soccer player's skins, over the muscles. They analyzed muscle activation during heading. The SCM became active earlier than the trapezius and showed greater activity before ball contact. The trapezius became active just before ball contact and showed greater activity after ball contact. The combination stabilized the head-neck complex.[14]

Muscle activation is only partly reflexive; athletes activate muscles differently depending on their expectation of impacts. Kumar et al. seated subjects in chairs, and these chairs were impacted with a pneumatic device that caused sudden movement at speeds of about 10 to 25 mph, then were abruptly stopped. Subjects were either informed of the impending impact, or blindfolded. Peak shoulder and head acceleration was more significantly correlated with whether the impact was expected, than with muscle mass or gender.[15] Tierney et al. put electrodes on SCM and trapezius muscles on 40 subjects, who were seated and had a 1 kg ball dropped 15 cm on their heads. Subjects were either warned 3 seconds prior a ball drop, or told that sometime in the next 30 seconds a ball would drop. Males had 25% less rotational acceleration when expecting the ball drop. Females did not differ between the two conditions, but may have been more vigilant in both.[16]

A real-world study of impact anticipation and muscle activation showed it had an effect for medium-intensity impacts. Mihalik et al. placed HITS accelerometers in helmets of 16 male hockey players aged 14, and videotaped the players for 54 games. 666 collisions were both detected and observed. The authors determined whether players anticipated impacts or not. For the most severe linear and rotational acceleration-causing impacts, anticipation did not matter. But in medium-intensity impacts there was a significant, 20% reduction in rotational acceleration when the impact was anticipated.

11 Begley, A. (2020) Houdini: The Elusive American, Yale
12 Mansell, J. et al. (2005) "Resistance training and head-neck segment dynamic stabilization in male and female collegiate soccer players" J. Athl. Train.;40(4):310-9
13 Ito Y. et al. (1997) "The functional effectiveness of neck muscle reflexes for head-righting in response to sudden fall" Exp. Brain Res.; 117:266–72
14 Bauer J.A. et al. (2001) "Impact forces and neck muscle activity in heading by collegiate female soccer players" J. Sports Sci. 19:171–9
15 Kumar S., Narayan, Y. & T. Amell (2000) "Role of awareness in head-neck acceleration in low velocity rear-end impacts" Accid. Anal. Prev.; 32:233–41
16 Tierney, R.T. et al. (2005) "Gender differences in head-neck segment dynamic stabilization during head acceleration" Med. Sci. Sports Exerc.;37(2):272-9

Anticipation meant the athlete saw the collision coming. The authors hypothesize that when an impact is anticipated, cervical musculature is contracted, and the head accelerates less.[17]

Mihalik et al.'s results resemble what is found in results of freefall in humans. A person who falls responds with rapid neck and limb activation, and the response is protective. As fall height increases, however, the same activation contributes proportionally less, and beyond some height it serves no protective purpose, and may become counterproductive.[18] A braced limb transmits load rather than absorbing it, which is why parachutists and stunt performers are trained to land loose. The same logic may apply to the neck. If in response to severe loads cervical activation still resists some head motion, it transmits load. Whether this causes greater brain rotational acceleration than a neck overwhelmed by an impact that causes the head to rotate rapidly is an open question. Resolving it requires an instrument that reports regional tissue response rather than headform kinematics.

Another combination telemetry and video study, this one of American high school football players, found player stance most correlated with concussion. The authors tried to determine if players were looking in the direction of collision, but rater reliability was low and anticipation level was absent.[19]

Anticipation generally requires visual sighting of the entity that will be collided with. Visual fixation or tracking is closely associated with neck muscle activity. Coordination between eye and neck movement is important in posture stability, especially during impacts that can cause head movements.[20] The link between visual stimulus and neck muscles is tight. Research with monkeys showed that visual cues induced neck muscle activity before further eye movement occurred.[21] However, periods of extreme muscle activity reduce neuromuscular control of the body. Neck muscle activation should remain reduced unless impacts are expected.[22]

People respond to cues more slowly, and with less accuracy, to visual stimulus in their peripheral vision, problems that significantly increase with the degree of peripheral location. Impacts that approach in the visual periphery, or from outside the visual field, are associated with slower muscle activation.[23] This is illustrated in Figure 3.

17 Mihalik, J.P. et al. (2010) "Collision type and player anticipation affect head impact severity among youth ice hockey players" Pediatrics;125(6):e1394-e1401
18 Sanders, O.P. et al. (2015) “Protective balance and startle responses to sudden freefall in standing humans” Neuroscience letters, 586, 8–12
19 Schmidt J.D. et al. (2016) "Head impact magnitude in American high school football" Pediatrics; 138(2):e20154231
20 Bexander, C.S.M. & P.W. Hodges (2019) "Cervical rotator muscle activity with eye movement at different speeds is distorted in whiplash" Phys. Med. Rehabil.;11(9):944-53
21 Rungta, S. et al. (2021) "Preparatory activity links the frontal eye field response with small amplitude motor unit recruitment of neck muscles during gaze planning" J. Neurophys.; 126(2):451-63
22 Cholewicki, J., Panjabi, M.M. & A. Khachatryan (1997) "Stabilizing function of trunk flexor-extensor muscles around a neutral spine posture" Spine; 22,2207-12
23 Stevenson, R.A. et al. (2012) "Interactions between the spatial and temporal stimulus factors that influence multisensory integration in human performance" Exp. Brain Res.;219(1):121-37

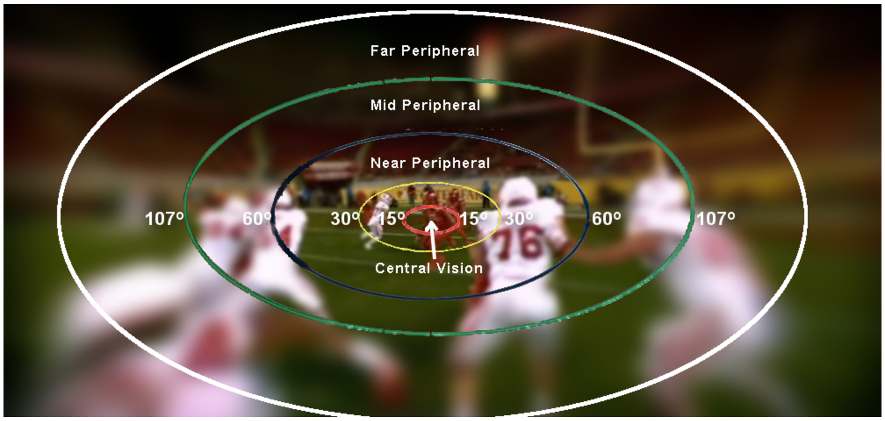

Figure 3 Redrawn from Younis et al.[24]

Contemporary large football helmets reduce player peripheral vision, and a study found this impaired player reaction time to peripheral visual stimuli. The authors suggested larger helmets and eye shields intended to mitigate head impacts may have the unanticipated consequences of decreasing player safety and performance. Enhanced peripheral vision acuity reduces reaction time and accelerates target detection; diminished peripheral acuity correlated with slower response to lateral targets.[25]

15 high school male hockey athletes were put through oculomotor tasks, tracking rapidly moving and peripheral objects. They were scored by oculomotor performance. During the following competitive ice hockey season, players with higher oculomotor scores had fewer head impacts; players with less efficient oculomotor performance were associated with increased incidence of head impacts.[26]

Clark et al reported that in U.S. high school soccer athletic population, female athletes incur a higher concussion rate than males. No consensus has been established to explain this high incidence rate, but many mechanisms are proposed, including cervical spinal musculature, skull thickness, hair length, and psychological factors. Women are assumed to report injuries more than men. Heading the soccer ball is one of the primary conditions that lead to player-to-player head contact in soccer, and many young players close their eyes during heading. The authors analyzed photographs of high school players heading soccer balls, and found women were more likely than men to have eyes closed. This correlation with higher injury suggests visual anticipation reduces concussion risk.[27]

Guidance:
<u>A neck model is optimized by having increased flexibility for impacts from directions in a model head's periphery or outside its predicted view field.</u> Neck models are usually configured as if for active muscle condition, accurate for impacts within the core visual field. <u>As impacts are programmed to come from</u>

24 Younis, O. et al. (2019) "A Hazard Detection and Tracking System for People with Peripheral Vision Loss using Smart Glasses and Augmented Reality" Int. J. Adv. Comput. Sci. Appl.; 10(2):1-9
25 Miller, R.A. et al. (2019) "Effects of protective American football headgear on peripheral vision reaction time and visual target detection in Division I NCAA football players" Sports (Basel); 7(9):231–38
26 Kiefer, A.W. et al. (2018) "Less efficient oculomotor performance is associated with increased incidence of head impacts in high school ice hockey" J. Sci. Med. Sport.;21(1):4–9
27 Clark, J.F. et al. (2017) "Lack of eye discipline during headers in high school girls soccer: a possible mechanism for increased concussion rates" Medical hypotheses, 100, 10-14

more peripheral directions, the configuration can be modified for increased flexibility, and head movement will increase. When testing helmets, the range of potential vision can be determined, and neck flexibility modified for specific impact directions that correspond to targets that may or may not be seen. For example, the Hybrid III neck model has a nut that can be loosened to raise the head, increasing the neck's flexibility.

THE BRAIN

Gray and White Matter

Gray matter consists of neuronal cell bodies and is considered isotropic. White matter consists of aligned axonal fibers and is considered to be anisotropic.[28] Gray matter contains the majority of neurons in the brain, and their dendrites, axons, and interneuron synapses, supported by glial cells and capillaries. White matter is composed of mostly long-distance axons that transport information for inter-brain coordinated activity. The white color is due to white myelin protecting these axons.

White matter axons are organized into tracts, like cables running in a specific direction through the brain. White matter has been further divided into groups based on the alignment of these fibers. For example, the superior longitudinal fasciculus (SLF) connects frontal lobes to parietal and occipital lobes at the rear of the brain. Its axon tracts are aligned horizontally, from front to back. The corticospinal tract axons run from the brain to spinal cord, its fibers aligned vertically. The uncinate fasciculus involves long axon fibers that bend from the orbital frontal cortex around to the anterior temporal lobe and back to the amygdala. Brain tissue deformation has consistently been shown to occur when white matter axon tracts are strained along their alignment direction.[29]

This directional strain is anisotropic, meaning that axon tracts respond differently depending on the direction of impact force. Rotational TBI is associated with anisotropic orientations of axonal fibers. As impacts extend a fiber along its pathway it thins, and if bent or twisted can fail. Impacts perpendicular to a tract compress fibers, which does not greatly heighten failure risk.[30] For a data set of mild TBI from the National Football League, strain in the axonal direction was found to be a better injury predictor than maximum strain, averaged strain, or cumulative strain.[31]

The reliability of axonal strain models has been questioned by studies showing white matter tract alignment orientation, and the degree of strain they may suffer, varies between individuals. Veenith et al. found the SLF and corticospinal tracts had around a 3.5% interindividual variance, the uncinate fasciculus a 6.0% variance.[32] Another study, based on white matter axonal tract patterns of 485 subjects

28 Carlsen, R.W. et al. (2021) "A quantitative relationship between rotational head kinematics and brain tissue strain from a 2-D parametric finite element analysis" Brain Multiphysics; 2,100024
29 Giordano, C. et al. (2014) "The influence of anisotropy on brain injury prediction" J. Biomech.; 47:1052–9
30 Maslo, A. et al. (2023) "Mechanical Reliability and Lifetime of Optical Fibers After 20 Years of Use," 2023 International Workshop on FOAN, Gent; pp.61-6
31 Giordano, C. & S. Kleiven (2014) "Evaluation of Axonal Strain as a Predictor for Mild Traumatic Brain Injuries Using Finite Element Modeling" Stapp Car Crash J.; 58:29-62
32 Veenith, T. et al. (2013) "Inter subject variability and reproducibility of diffusion tensor imaging within and between different imaging sessions" PLoS ONE;8(6):e65,941

aged 22–35 years, modeled predicted strain for these. This found a coefficient of variation between subjects of nearly 12% for maximum axonal strain.

However, despite interindividual variance in strain levels, the brain areas where maximum axonal strain occurs did not vary.[33] There is a relative uniformity of gray and white matter regions within primate species, including humans.[34] Human gray and white matter volume, cortical area, and architecture are consistent at primate population levels. Variation in the fine-grained level of the depth or shape of brain foldings may occur between subjects, but not overall structural organization.[35] The parts of human brains that vary least in relative size are gray areas with the most white matter connections to other parts of the brain.[36] White matter brain tissue is anisotropic and deforms according to impact orientation. Gray matter is largely composed of dispersed neuronal cell bodies and non-aligned dendritic projections, all of which are isotropic in orientation.[37] Given their brain locations, areas with gray and white matter can have extensive surface contact where biomechanical interactions occur.

The angular momentum of a brain around its mass center imposes strain between white and gray matter due to their different biomechanical responses. Strain concentrations occur at their interfaces. This mechanical mismatch increases white matter anisotropic strain. From a purely physical perspective, the main factors that govern strain propagation at an interface between two materials is the degree of mismatch in the elastic properties of the materials.[38] Computation models predict gray-white matter interfaces, which axons intersect and where each matter has mechanical differences, impose amplified stress on axons. The long, thin architecture of axons, bundled in extensive organized tracts, and their viscoelastic nature, increases damage from shear and tensile forces as the brain is rapidly deformed.[39]

Chan et al. placed subjects 33 male and female subjects in an MRI machine with a head cradle. Subject heads were mildly rotated using the cradle, repeated up to 52 times for 13 images at successive tissue depths. This imaged most of each brain during rotations. The rate of head motion was ~200 rad/s2, only 10-15% of the angular accelerations experienced by soccer players heading a ball. They superimposed grid patterns onto brain tissue, each voxel in the grid moving with the tissue as it deformed. For each voxel they calculated a displacement vector that showed how far and in what direction it moved. A Lagrangian strain tensor was applied to voxels grouped by brain tissue, to show how tissue stretched, compressed, or sheared. The maximum shear strain measured the maximum amount of deformation that occurred when tissue materials slid past each other while remaining in contact. Cortical gray matter strains were highest, followed by white matter (much of it directly below the outer cortex) followed by

33 Giordano, C., Zappalà, S. & S. Kleiven (2017) "Anisotropic finite element models for brain injury prediction: the sensitivity of axonal strain to white matter tract inter-subject variability" Biomech. Model. Mechanobiol.;16(4):1269-93

34 Zikopoulos, B., García-Cabezas, M.Á. & H. Barbas (2018) "Parallel trends in cortical gray and white matter architecture and connections in primates allow fine study of pathways in humans and reveal network disruptions in autism" PLOS Biology; 16(2): e2004559

35 Barbas, H. & N. Rempel-Clower (1997) "Cortical structure predicts the pattern of corticocortical connections" Cerebral Cortex; 7(7): 635-46

36 Smith, S. et al. (2019) "Structural Variability in the Human Brain Reflects Fine-Grained Functional Architecture at the Population Level" J. Neurosci.;39(31):6136-49

37 Nazeri, A. et al. (2020) "In Vivo Imaging of Gray Matter Microstructure in Major Psychiatric Disorders: Opportunities for Clinical Translation" Biol. Psych.: Cogn. Neurosci. Neuroimag.; 5(9):855-64

38 Pribe, J.D., Siegmund, T. & J.J. Kruzic (2020) "The roles of yield strength mismatch, interface strength, and plastic strain gradients in fatigue crack growth across interfaces" Engin. Fract. Mech.; 235, 107072

39 Alisafaei, F. et al. (2020) "Mechanisms of Local Stress Amplification in Axons near the Gray-White Matter Interface" Biophys. J.; 119(7), 1290–1300

deeper gray matter. Cortical gray matter changed shape more than the white matter it covers, which changed shape more than gray matter embedded in it.[40]

More severe local injury occurs near white and gray matter boundaries. In one example, the corpus callosum followed the skull's motion more closely than more compliant gray matter that readily deforms around it, straining axonic connections.[41]

As will be seen, blast studies with physical models generally use silicones as artificial brain materials. Medical studies with physical brain models often use hydrogels. Silicones are stiffer than hydrogels; superficially, this aspect makes the former resemble white matter and the latter gray. But there are other important variables, the most important of which is their behavior when suddenly loaded. In the past both silicones and hydrogels responded isotropically. It is critical that any material representing white matter respond anisotropically, in particular stressing in the direction of impact. This is the condition that causes axons to deform.

Contemporary silicones can be made as soft as hydrogels, but they remain isotropic. On the other hand, hydrogels have been developed that respond anisotropically in ways that mimic white matter. Silicones are isotropic; hydrogels can exhibit anisotropy.

Blast Studies, Silicones and Siloxanes

Because of the many service members with TBI from Improvised Explosive Devices (IEDs), researchers have examined the effects of powerful blasts on brains. Head forms with model brains are placed in shock tubes. Analysis is made of powerful blast waves on the brain models.

Blast studies converged on silicone gels as the optimal material for brains. Further, different silicone formulations may represent different brain materials. Wayne State University has developed brain injury models since the 1960s. In the post 9/11 period they focus on blast impacts.

In a 2010 Wayne State thesis, Hossain prepared different experimental models of human heads incorporating model brains. Materials simulating skin, skull and brain were tested. The brain material tested included water gels, oil based compounds, and silicone gels. Their viscoelastic properties were tested under different stress levels. Silicone gel had the most promising results for brain models. Because silicone dynamic modulus was higher than human brains, thinner was added to soften it up. Gelled in a mold with accurate geometry, the author put the brain in an artificial skull, covered in simulated skin, then made preliminary blast tests on the model.[42]

40 Chan, D.D. et al. (2018) "Statistical characterization of human brain deformation during mild angular acceleration measured in vivo by tagged magnetic resonance imaging" J. Biomech Eng.; 140(10): 101005
41 Bayly, P.V. et al. (2005) "Deformation of the human brain induced by mild acceleration" J Neurotrauma; 22(8):845–56
42 Hossain, S.G.M. (2010) "Material modeling and analysis for the development of a realistic blast headform" Mechanical (And Materials) Engineering – Dissertation; Wayne State University

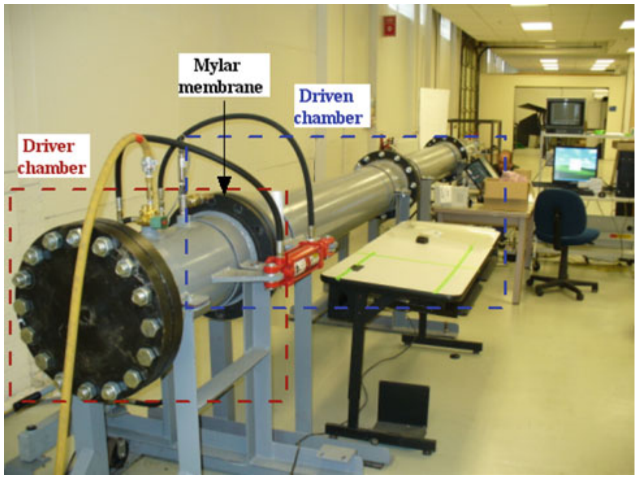

Figure 4 Shock Tube System at Wayne State, from Zhang[43] shared under CC BY 4.0

The author's conclusion was that for brain simulant material in blast tests, appropriately thinned silicone gels are better than water-based gels or oil-based compounds.

Surrogate brains in head forms can record rotational data that FE simulations can have difficulty predicting. In a 2012 paper Zhu et al., at Wayne State, reviewed research, and carried out their own, on blast-induced TBI. Animal experiments required great effort to conduct experiments, and even more resources to examine resulting biological tissues. This limited the number and scale of these studies. The authors found that FE simulations had found localized stress-caused axon injuries, but none were validated against experimental data.

The authors made a physical head surrogate, then based an FE model on experimental results. The FE tests were validated with more head experiments. The surrogate was an egg-shaped deformable object. The simplified geometry reduced the FE complexity. A more realistic head with a multilayered skull and inhomogeneous brain tissues was too difficult to computationally model and interpret.

The surrogate skull was a polyethylene shell; the brain was a silicone gel brain simulant, Sylgard 527 A&B (Dow Corning.) Sylgard's mechanical properties, under strain, are reported to be similar to those of brain tissues during car crashes. A fiber optic sensor in the brain recorded internal pressure. The FE model was modestly validated with surrogate results, but even the simplified surrogate generated more complexity than the FE could process. This was despite the single blast being more or less uniformly distributed over the surrogate’s frontal surface, and the homogeneity of surrogate materials.

The authors did examine how the surrogate's orientation altered pressure responses, and FE predictions. They turned the surrogate so blast waves struck it off-axis, but fixed the surrogate in place. Otherwise the blast would rotate it. Although the surrogate could record rotational data, the FE model did not have the capacity to simulate rotational acceleration.

43 Zhang, J. (2019) "Blast-induced tinnitus: Animal models" J. Acoustic. Soc. Am.; 146(5): 3811-31

Zhu et al. reported the following material properties of their Sylgard 527 silicone gel brain model, and I compare these to typical material properties of real brains (bovine, porcine, and human.) Values vary according to age, anatomical region, temperature, etc.

Properties	Sylgard Silicone Gel	Brain (averaged)
Density	950 kg/m^3	~1040 – 1060 kg/m^3
Bulk modulus	1.0 Gpa	2.1 GPa
Short-term shear modulus	3,600 Pa	~1500 – 3000 Pa
Long-term shear modulus	586 Pa	~100 – 500 Pa
Decay constant[44]	0.05 ms	~10–100 ms

The large difference between the Sylgard and brain decay constants is problematic, because decay times are associated with injury-level brain deformations. Non-lethal, sports-related shear brain injury involve movement that is not instantaneous. Nicolle et al.'s study of shear on porcine brains, from which the decay constant data above is drawn, recorded from 10^{-5} s to 270 s, although based on linear head acceleration only.[45] Hrapko et al. found that friction between a porcine brain and the plate on which it is positioned had a significant effect on shear measurements over time. Frictional influence increased linearly. This is an important consideration, because a brain's attachment in a head leads to friction, and modifies decay of movement over time.[46]

In a 2018 paper Chanda et al. addressed the significantly different biomechanical properties of the cerebrum's white and gray matter. The authors suggested the different matter types must be considered in any brain injury test, including blast studies. The suggested such data cannot be recovered in cadaver tests, where brains have mechanical behavior changes due to tissue dehydration and death. The authors developed patented silicone-based materials that mimic some of the mechanical behavior of gray and white matter tissues. They began with five different silicone ratio blends, each with different stress and strain rates. The softest silicone simulation material corresponded to gray matter properties, and the hardest material corresponded to white matter. The nonlinear stress versus stretch responses of the brain tissue surrogates were characterized by different models, and Yeoh's hyperelastic model, which models incompressible materials like rubber most accurately, predicted the behavior of both.

The silicones are low-cost, and can be used for experiments and practicing surgeries. However they respond isotropically to loads. Under uniaxial tension in blast tests, this may be realistic. But helmeted collisions in sports cause angular forces, which cause anisotropic, not isotropic, brain effects. The authors do not report decay constants, which may be similar to Sylgard.[47]

Chanda et al. filed and obtained a patent for crosslinked siloxanes, a type of silicone material, that exhibits "non-linear" behavior. This means the material's stiffness changes as it is loaded or deformed.

44 Darvish, K.K. & J.R. Crandall (2001) "Nonlinear viscoelastic effects in oscillatory shear deformation of brain tissue" Med. Eng. Phys.; 23(9):633-45
45 Nicolle, S., Lounis, M., Willinger, R. & J.F. Palierne (2005) "Shear linear behavior of brain tissue over a large range of frequencies" Biorheology; 42(3): 209–23
46 Hrapko, M. et al. (2008) "Characterisation of the mechanical behaviour of brain tissue in compression and shear" Biorheology; 45(6): 663–76
47 Chanda, A. et al. (2018) "Biofidelic human brain tissue surrogates" Mech. Adv. Mat. Struct.; 25(15-16):1335-41

It may go into plastic deformation after a certain stress level. Mammal skins are nonlinear-elastic material, which promotes tear resistance.[48] Chanda et al.'s patent described siloxanes that mimic human skin, in particular vaginal skin.[49] In a later paper reviewing the siloxanes they had developed, the authors noted the limitation that these materials, being isotropic, do not model angular forces well.[50]

The anisotropy of several different brain tissue areas was estimated:

Brain region	Anisotropic fraction
occipital lobes (gray)	0.0 – 0.2
frontal, parietal lobes (gray & white)	0.2 – 0.3
thalamus (gray)	0.3 – 0.4
corona radiata (white)	0.4 – 0.6
corpus callosum (white)	0.6 – 1.0

The most significant difference in anisotropy in brain areas is between gray and white matter.[51]

Gray matter is soft. Gray matter under load has a 1 to 1.4 kPa modulus.[52] Silicones, in the past, were not particularly soft. However Chandra et al. and other researchers have found siloxane elastomers that are very soft, by varying the crosslink density of elastomers. Vatankhah-Varnoosfaderan et al. developed polysiloxane elastomers with multiple, covalently-linked side chains that have Young's moduli below 1.2 kPa. The ultrasoft moldable elastomers expand and extend isotropically.[53] Material like this is suited for models of gray matter, though not white.

Brain models for Medical Research and Hydrogels

A number of researchers have used hydrogels in models of whole brains, without differentiating white and gray matter. Ray et al. sought a method to assess particle movement through brains. They started with on MRI scans, from which they designed, in CAD, the outer pial surface of a brain in a mesh surface. This was 3D printed, and a mold was made from it. 0.6% agarose was inserted into the mold, gelled, then removed. Agarose forms a porous hydrogel that allows molecules to migrate through it. The gelled brain included an accurate model of gyri, the folded structures on the cerebral cortex. It used to test different particle diffusion models. The model's structural accuracy, involving the visible shape of the brain, better represented interference patterns in particle movement, compared to just using a block of gel. Material costs were <$100.[54]

48 Yang, W. et al. (2015) "On the tear resistance of skin" Nat. Commun.; 6, 6649
49 Chanda, A., Unnikrishnan, V. & Z. Flynn (2021) US Patent 10,954,383, filed March 3, 2018, and issued March 23, 2021
50 Singh, G., Yadav, P. & A. Chanda (2024) "Development of Biofidelic Skin Simulants Based on Fresh Cadaveric Skin Tests" Eur. Burn J.;5(4):454-63
51 Giordano, C. & S. Kleiven (2013) "Connecting fractional anisotropy from medical images with mechanical anisotropy of a hyperviscoelastic fibre-reinforced constitutive model for brain tissue" J. Royal Society Interface, 11(91), 20130914
52 Budday, S. et al. (2020) "Fifty Shades of Brain: A Review on the Mechanical Testing and Modeling of Brain Tissue" Arch. Computat. Methods Eng.; 27, 1187–1230
53 Vatankhah-Varnoosfaderani, M. et al. (2017) "Bottlebrush Elastomers: A New Platform for Freestanding Electroactuation" Adv. Mater.; 29, 1604209
54 Ray, L.A. et al. (2019) "MRI-to-Synthetic 3D Gel Brain: Proof-of-Concept Fabrication For Intra-Parenchymal Diffusion Studies" "Fluid Flow and Mass Transport in Brain Tissue" bioRxiv doi: 10.1101/2022.10.27.514134

0.6% agarose mimics the poroelastic properties of the brain. Formal models of brains tend to be either poroelastic or viscoelastic. Poroelasticity describes porous semi-solid matrices saturated with fluid flows. Stress and strain in the porous material affect fluid pressure. Poroelastic models are best for studying the interaction of fluids and tissue. Viscoelastic models, instead, are best for studying tissue under loads. A brain's viscoelastic material parameters may predict the response of brain tissue under uniaxial and multiaxial loading conditions. Viscoelastic properties are examined in blast tests.

Hydrogels made with agarose and acrylamide can be prepared in concentrations other than 0.6%. This changes their viscosity. Composite structures made with hydrogels having different viscosities may better represent different types of brain tissues, and show both poroelastic and viscoelastic response to nonlinear impacts.[55]

A composite hydrogel consisting of a rigid polysaccharide network (sodium alginate and pectin) and a flexible polyacrylamide network, exhibited brain tissue-like mechanical properties under various solution environments and strain rates. The hydrogel brain model behaved similarly to a porcine brain under different loading conditions. The intrinsic shear modulus of the hydrogel and brain tissues were similar. Both had similar magnitudes of modulus increase as strain rate increased. The hydrogel cost was <$100.[56]

Kainz et al. synthesized a hydrogel with polyvinyl alcohol and Phytagel that mimicked a porcine brain, and examined its viscoelastic properties. The hydrogel was able to match several material responses, including a porcine brain's characteristic relaxation rate, its adhesive behavior, and structural features resulting from a brain's porous nature.[57] The same authors later provided a computational analysis, based on a cadaver brain, that modeled the brain as a combined poro-viscoelastic material. They found that that gray and white matter had different viscous and porous effects. This explained large variations in measured properties of brains that did not differentiate between them. At small, common loading rates, more fluid flows through white matter, and gets squeezed out of it, than in gray matter. Under these loading conditions, white matter appears softer than gray. But at fast loading rates, such as in collisions, white matter stiffens as fluid is trapped in it, becoming stiffer than gray matter.[58]

Compared to complex brain tissues, hydrogels are simple structures. Biological soft tissues contain 50−85% of water by weight, which serves as a medium for dynamic biological processes. At the same time they have elaborate structures, with multiple components in hierarchies from molecular to macroscopic scales. This combination of squishiness and structure permits sophisticated functions to evolve. Hydrogels are squishy, but in the past, like silicones, there were isotropic structures. However the use of hydrogels in reconstruction and rehabilitation medicine has led to the recent development of

55 Cacopardo, L. et al. (2019) "Engineering hydrogel viscoelasticity" J. Mech. Behav. Biomed. Mater.; 89, 162-7
56 Wang J. et al. (2023) "Hydrogels with brain tissue-like mechanical properties in complex environments" Materials & Design, 234, 112338
57 Kainz et al. (2023) "Poro-viscoelastic material parameter identification of brain tissue-mimicking hydrogels" Front. Bioeng. Biotechnol.; 11:1143304
58 Alexander, G. et al. (2024) "Model-driven exploration of poro-viscoelasticity in human brain tissue: be careful with the parameters!" Interface Focus.; 1420240026

hydrogels with anisotropic structures.[59] Many metazoan tissues possess anisotropic structure, from molecular to macroscopic levels. With hydrogels often explored as scaffolds for dynamic living tissues, numerous efforts try to fabricate anisotropic gels that can move accordingly. This usually requires managing hydrogel synthesis with some type of external force. The hydrogel contains components that can be directed into position with external stimuli, such as mechanical forces, magnetic and electric fields, and gradients of temperature and ions.

Shear forces can be applied to orient nanofibers and nanofillers during their situ polymerization in a dispersion. Manually applied shear forces tend to vary inconsistently. Dispersions with electrical nanofillers can be electrically oriented, often into thin hydrogel films. These require care in the arrangements of electrical contacts, to avoid electrochemical decomposition. Magnetic nanofillers form anisotropic hydrogels under applied magnetic fields. Magnetic forces are applied in a noncontact, nondestructive, consistent manner, and penetrate homogeneously into samples. This can synthesize anisotropic hydrogels with various dimensions, thicknesses, and shapes.[60] Erb et al. mixed microparticles coated with superparamagnetic iron oxide nanoparticles into fluid polymer solutions that were gelled in the presence of a magnetic field. The resulting composites had microparticles aligned by the magnetic dipole axis. Composites containing 7.5 vol% of aligned microparticles had 250% higher swelling and 200% higher shrinkage in the direction perpendicular to the alignment axis. With microparticles aligned horizontally in a long thin gel rod, the rod thinned and lengthened when swelled with water.[61]

Liu et al. also used magnetic fields to make a composite hydrogel with anisotropic mechanical properties. They made a positively-charged gel with negatively charged unilamellar titanate nanosheets embedded. Fabrication involved aligning the nanosheets in an aqueous colloidal dispersion with a magnetic field. The dispersion was then transformed into a composite hydrogel using light-triggered *in situ* polymerization. The resulting hydrogel behaves like white matter, deforming under shear forces applied along the direction of the embedded nanosheets, yet resisting compressive forces applied orthogonally. Shearing parallel to the nanostructures has a modulus of 0.6 kPa, while perpendicular shearing gave a modulus of 2.2 kPa. A higher perpendicular modulus means the material resists sideways squeeze. However the gel's shear anisotropy doesn't establish its tensile anisotropy, which is probably the mode where axon bundles fail.[62]

Anisotropic hydrogels have been fabricated with light energy. Qin et al. mixed a water-soluble surface ligand into an aqueous solution with silver nanoparticles (NPs.) The ligands cleaved and bound to the silver NPs. Under UV radiation these ligand-silver nanocomposites aggregated into long 2D lamellar assemblies, only a single NP thick. These were put in polyacrylamid solution that formed dense,

59 Fan, H., and Gong, J. P. (2020). Fabrication of bioinspired hydrogels: Challenges and opportunities. Macromolecules 53, 2769–2782. doi:10.1021/acs.macromol.0c00238
60 Sano, K., Ishida, Y. & T. Aida (2018) "Synthesis of anisotropic hydrogels and their applications" Angew. Chem. Int. Ed.; 57, 2532–43
61 Erb, R.M. et al. (2013) "Self-shaping composites with programmable bioinspired microstructures" Nat. Commun.; 4, 1712
62 Liu, M. et al. (2015) "An anisotropic hydrogel with electrostatic repulsion between cofacially aligned nanosheets" Nature; 517, 68−72

entangled cross-link chains with the lamellar assemblies. The resulting hydrogel could be stretched 20 times in the direction of lamellar assemblies without breaking, twice that of perpendicular stretch.[63]

While hydrogels can be tuned with compounds to mimic overall white matter behavior, another approach uses various materials that actually mimic white matter structure. Winter and colleagues did a series of studies that incorporated electrospun fiber mats in hydrogels to replicate features of parts of the occipital region responsible for vision.[64] Aligned electrospun nanofibers are topographically similar to white matter tracts. These composites were used to study the pathway of tumor migration, not mechanical response.[65] Calhoun et al. found that the gray and white matter tissues differ in relaxation time, the duration needed to reduce internal stress after a sudden stretch or impact. White matter takes about three times as long to relax under a held strain. Its fibrous elements do not slide past one another as easily as the rounder gray matter elements.[66] The authors suggested that, in making a white matter surrogate material, increasing the aspect ratio and surface area of electrospun fibrous elements would limit their movement past one another, and restrict their flexible response to forces in the alignment directions. This could create a structural response to mechanical load similar to white matter

Zhang et al. found a different method to align supramolecular fibrils over macroscopic scales. Isotropic solutions of peptide-containing molecules group into long filaments of bundled nanofibres under heating. By manually dragging these liquid crystals into salty media, they generated noodle-shaped viscoelastic gel strings that extended for centimeters. [67]

These studies of structure-mimicking gels report no mechanical data, and the gel fibers may have little mechanical strength. A very different hydrogel pathway was developed for connective (bone, tendon) and muscle tissue. These animal tissues have highly defined hierarchical structures that respond anisotropically to mechanical forces. Bai et al. tried to mimic the internal structure of such tissue by freeze casting poly N-isopropylacrylamide (monomer) and clay platelets together. Anisotropic ice crystals grow along a temperature gradient and expel the monomer and clay platelets from the freezing water, creating oriented voids. The authors cryo-polymerized the composite into a hydrogel. It had a highly aligned porous structure at micrometer scale and a nacre-like layered structure at nanoscale. These hydrogels are stretchable, with greater tensile strength in mechanical impacts along their alignment direction than perpendicular impacts. Importantly, while many hydrogels used as scaffolds in medical tissue regeneration have poor mechanical properties, freeze-cast clay hydrogels have a fracture energy in the range of cartilage.[68]

63 Qin, H. et al. (2019) "Anisotropic and self-healing hydrogels with multi-responsive actuating capability" Nat. Comm.; 10, 2202
64 Rao, S.S. et al. (2013) "Glioblastoma behaviors in three-dimensional collagen-hyaluronan composite hydrogels" ACS Appl. Mater. Interfaces; 5(19): 9276−84
65 Rao, S.S. et al. (2013) "Mimicking white matter tract topography using core-shell electrospun nanofibers to examine migration of malignant brain tumors" Biomaterials; 34(21): 5181−90
66 Calhoun, M. et al. (2019) "Beyond Linear Elastic Modulus: Viscoelastic Models for Brain and Brain Mimetic Hydrogels" ACS Biomat. Sci. Eng.
67 Zhang, S. et al. (2010) "A self-assembly pathway to aligned monodomain gels" Nat. Mater.;9(7):594-601
68 Bai, H. et al. (2013) "Thermoresponsive composite hydrogels with aligned macroporous structure by ice-templated assembly" Chem. Mater.; 25(22):4551-6

The white matter modulus at rest is different from its modulus during rotational acceleration. Indentation tests of bovine brains found that between a rate of 1 μm/s to 160 μm/s, white matter modulus increased from 1.26 kPa to 2.51 kPa. However 160 um/s is vastly slower than the result of a sports impact, by orders of magnitude (a typical ant walks 8300 μm/s.)[69] If modulus increases with acceleration rates, then white matter becomes very stiff during some impacts.[70] One way to directly mimic this with hydrogels is through water loss, which increases their elastic modulus. The highest elastic modulus occurs in a nearly dry state.[71]

However a model brain used in an impact test may have a high elastic modulus in its resting state because it represents the brain during impacts. The modulus can be tuned to the head rotation velocity predictably caused by the mechanical instrument.

Guidance: Brain Models with Materials as in Brains

Gray matter and white matter share brain volume somewhat equally, although with major shifts throughout the lifespan. Gray matter makes up the outermost layer of the brain, the cerebral cortex and the cerebellar cortex. It is also in the inner sections of the brain.[72]

The architecture of brain matter is a significant factor in impact studies. The gray-white matter interface represents an area where mechanical mismatch of adjoining tissues occurs, and where there is the greatest risk of white matter damage. Soft and hard materials respond differently to mechanical stress, and mechanical instability occurs at their interface. The mismatched stress moduli can take a long distance (up to centimeters) to reach equilibrium, during which material damage occurs.[73]

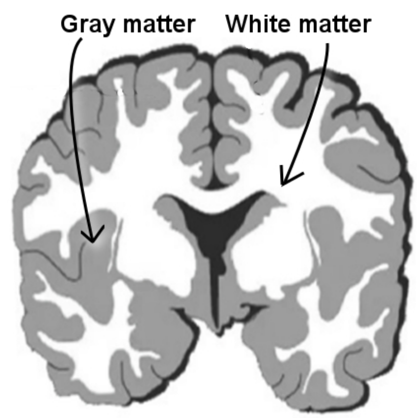

Figure 5 redrawn from Alkan, A. et al.[74]

As brain tissue deforms under rotational acceleration, softer gray matter pulls the stiffer white matter along. This stiffness, while preventing axon deformation, imposes higher tensile stress on axons. Gray matter pulling the white matter causes greater tensile elongation of axons, compared to areas of white matter more isolated from gray matter.[75]

69 Budday S., Nay R. & E. Kuhl (2015) "Mechanical properties of gray and white matter brain tissue by indentation" J. Mech. Behav. Biomed. Mater.; 46:318–30
70 Moss W.C., King M.J. & E.G. Blackman (2009) "Skull flexure from blast waves: a mechanism for brain injury with implications for helmet design" Phys. Rev. Lett.; 103:108702
71 Li, Z. et al. (2019) "The effect of water content on the elastic modulus and fracture energy of hydrogel" Extreme Mech. Let.; 100617
72 Narvacan, K. et al. (2017) “Evolution of deep gray matter volume across the human lifespan” Human brain mapping, 38(8), 3771–90
73 Fang, Y. et al. (2022) "Dissecting Biological and Synthetic Soft-Hard Interfaces for Tissue-Like Systems" Chem. Rev.; 122(5):5233-76
74 Alkan, A. et al. (2023) "Investigation of the effect of “Nicotiana rustica/Maraş Otu” use on gray matter using image processing techniques from brain MRI images" SIViP; 17(7):348593
75 Alisafaei, F. et al. (2020) "Mechanisms of Local Stress Amplification in Axons near the Gray-White Matter Interface" Biophys. J.; 119(7):1290-1300

To make a biomechanically realistic brain model for angular impact tests requires casting anisotropic hydrogels for white matter, and isotropic hydrogels or siloxanes for gray matter. These have to be cheek by jowl, with interfaces like real brains, so that impacts have realistic results. The molding process must be fairly easy to perform and inexpensive, because model brains may be sacrificed in impact tests. Material should be recyclable and be quickly reformed.

The following is based on the author's process of prototype development of a model brain as described in the author's allowed patent at the U.S. Patent and Trademark Office, and the author's published patent application at the World Intellectual Property Organization (see "Competing Interests" section.) This approach utilized axial brain scan layers from Subject 100206 in the Human Connectome Project database. The layers were processed to display four distinct brain tissue components: gray matter and white matter with three cardinal directions of anisotropy (anterior-posterior, left-right, and superior-inferior). Each axial layer measures approximately 1 mm in thickness and presents unique anatomical features. Importantly, gray and white matter images exhibit dimensional discrepancies and do not align precisely. Gray matter imaging is considered more anatomically accurate, while white matter imaging, which relies on water diffusion to assess axonal organization, is subject to greater geometric distortion. Gray matter serves as the reference structure, to which directional-dependent (in each of the 3 cardinal directions) white matter is aligned and iteratively refined and averaged to reinforce correct anatomical features. Casting molds were designed at 8 mm height (z-dimension), with each mold incorporating multiple axial brain layers. This scaling provides manageable physical models while preserving essential anatomical relationships.

White matter molds are filled with hydrogel precursors and a suspension of magnetic nanoparticles. A magnetic field emitter is positioned to enforce directionality on the hydrogel, the dipole establishing one of three cardinal directions. The gelation process produces a material with directional-dependent anisotropy. Once cast, a sliding layer is removed, and the white matter falls in place into the negative area of the gray matter material. In this way, hydrogels with different anisotropic and isotropic directionalities can be configured together, as they are in a real brain.

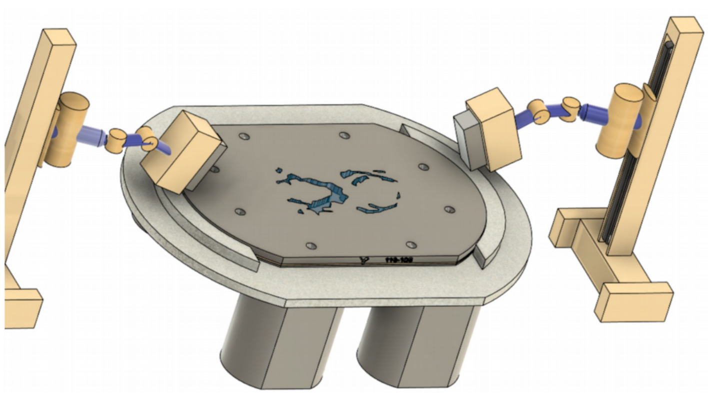

Figure 6 Mold Positioned with Magnetic Microparticle-Loaded Liquid Hydrogel Poured and Gelling with Magnet Devices Positioned to Apply Y-axis Magnetic Field

Bio-mimicking gels can be assembled by hand. To form models in a reproducible and fast manner, a CAD program guiding servo driven injectors, or 3D printers, can be used. A single printer may alternate printing material and density during the printing process. Alternatively, material can be printed that serves as support for material later inserted in internal void.[76]

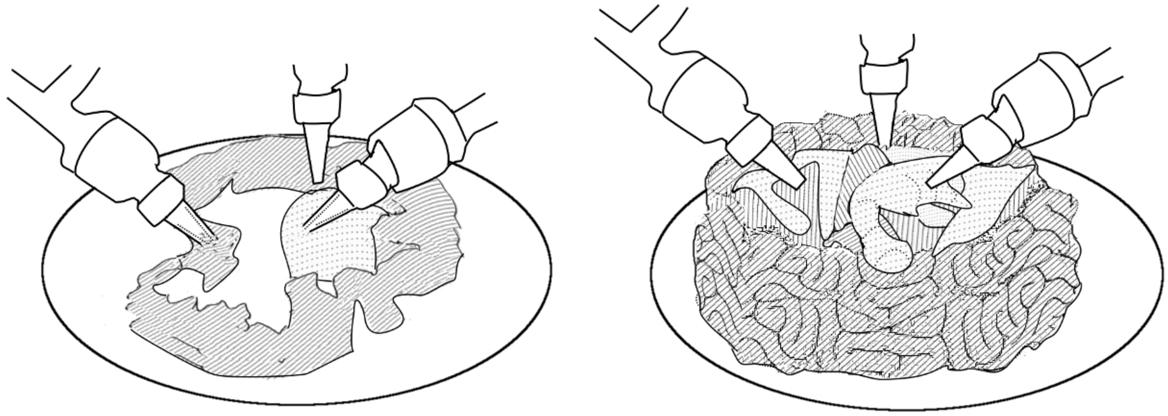

Figure 7 Methods to deliver hydrogels in place

Figure 7 illustrates an automated system that uses servo motors to drive injectors to deposit white and gray matter simulant materials in place. Figure 8 illustrates a 3D printer and a robotic arm with an articulated arm that moves a "force" emitter, such as a magnetic force, to different positions. When the printer extrudes liquid or flexible white matter simulant material, the robotic arms moves into a position to apply the correct force to influence the white matter as its gels. This causes the hydrogel's anisotropy to accurately resemble the real brain component it serves to represent.

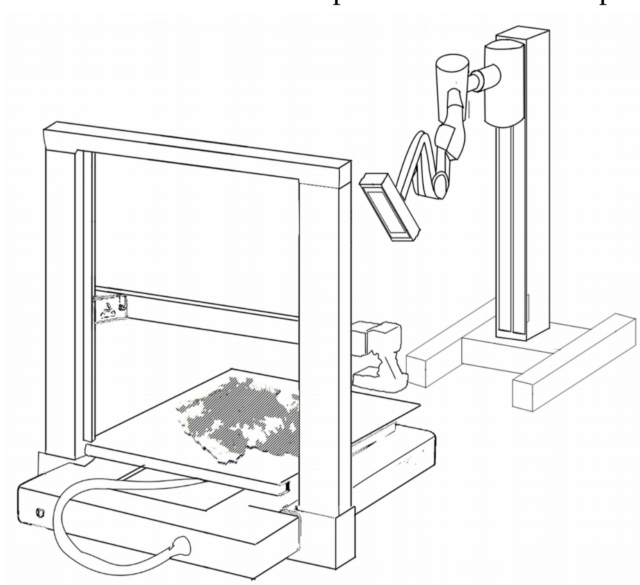

Figure 8

76 Lima, T.d.P.L. et al. (2022) "3D Bioprinting Technology and Hydrogels Used in the Process" J. Funct. Biomater.; 13(4): 214

The model brain may have different materials cast simultaneously, in place. Polyvinyl alcohol (PVA) can be 3D printed as the mold. Because it is water soluble, PVA molds can be dissolved away, leaving behind the cast material. Different complex brain architectures can be 3D printing this way. White and gray matter hydrogels or other materials are funneled, piped, or injected in mold components. Once the materials have taken shape, the PVA mold is dissolved.[77]

THE SKULL

The skull is composed of two types of bone, trabecular and cortical. Trabecular is porous, spongy, and lightweight. Cortical bone is denser, with an organized microstructure for stability and rigidity. In skull bones, two layers of cortical bone sandwich a layer of trabecular; this inner layer is called diploe in the skull. The bones that encase the brain are cranial, and others are considered facial. The cranial bones exist as separate structures because they cannot be fused for a baby to pass through a birth canal. After birth bones fuse, with the border areas called sutures. There are 22 cranial and facial bones of different shapes and thicknesses.[78] Figure 9 shows 5 of them in the skull.

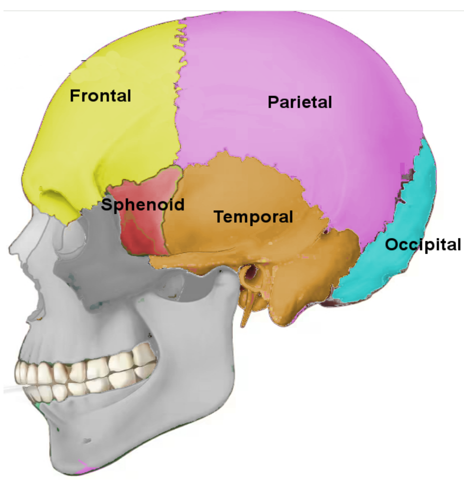

Figure 9 redrawn from LoPresti[79]

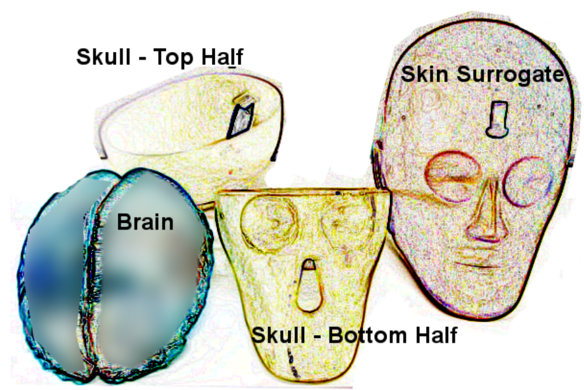

Figure 10 BIPED redrawn from Ouellet & Philippens[80]

The bone sandwich system provides outer stiffness to respond to sharp, sudden linear impacts. The diploe provides cushioning and shear strength, and by separating the cortical plates increases the bending strength of skull bones.[81]

Standardized headforms, such as ISO/DIS 6220, use a urethane or metal head-like shell. The Hybrid III headform has a hollow aluminum shell and vinyl scalp (the scalp is less stiff than a human scalp to offset the aluminum stiffness.) A NOCSAE headform uses a polyethylene skull. A blast injury

77 Brooks-Richards, T.L. et al. (2022) "Dissolvable 3D printed PVA moulds for melt electrowriting tubular scaffolds with patient-specific geometry" Materials & Design; 215, 110466
78 Henwood, B.J. & G. Appleby-Thomas (2020) "The suitability of Synbone® as a tissue analogue in ballistic impacts" J. Mater. Sci.; 55(7): 3022-33
79 LoPresti, L. (2025) "Head and Neck Anatomy: Part I – Bony Structures" www.dentalcare.com/en-us/ce-courses/ce591
80 Ouellet, S. & M. Philippens (2017) " The multi-modal responses of a physical head model subjected to various blast exposure conditions" Shock Waves; 1-21
81 Zapata, U. & Q. Wang (2020) "Material properties of the skull layers of the primate parietal bone: A single-subject study" PLoS One; 15(3):e0229244

protection evaluation device (BIPED) developed by Defense Research and Development of Canada has polyurethane skull material 6.35 mm thick. A study of the BIPED that modified this thickness found it was a significant variable in head acceleration for impacts tested.[82] The BIPED also has surrogate brain tissue, silicone Sylgard 527, and water is used as cerebrospinal fluid. The head is covered with a skin of tough urethane rubber. Clearly, none of these headforms are biofidelic.

Skull bone thickness and density are the main factors that influence the mechanical properties of skull bone. A strong positive correlation between skull bone thickness and stiffness is often observed. Temporal bones are stiffer than parietal bones, that are stiffer than the frontal bone. Trabecular bone typically accounts for 20% of total skull mass, but varies depending on location. Lee et al. found a correlation of bending modulus and trabecular volume ratio. Their study examined skulls from cadavers, geriatric osseous tissues. Trabecular bone composition looks like very thin struts of a bridge. This distributes compressive forces through spaces between the struts filled with fluid and fat. These fillings do not survive death unchanged. The elastic modulus of two examined skulls varied from 1.7 to 2.7 GPa. Different skull bones in the same subject varied by as much as 1.3 GPa. Overall tensile strength varied from 42 to 53 MPa, with within individual strength varying up to 14 MPa.[83]

The elastic modulus of skull bones, which defines their resistance to deformation, is not consistent in published studies. Falland-Cheung et al. calculated the mean for six studies was 8.51 GPa, but varied from 1.23 to 15.54. The authors tested five skull simulant materials to assess their elastic moduli and flexural strength. The materials were epoxy resin, fibre filled epoxy resin, PETG, polylactic acid (PLA), and self-cure acrylic denture base resin. The elastic modulus of epoxy resin, 6.65 GPa, was closest to the mean 8.51. PLA flexural strength was closest to the mean for real bone, but its elastic modulus was less, 3.03 GPa. However given the variance in studies, this is not conclusive.[84]

Since skull bones are combinations of trabecular and cortical, it may be important to determine the mechanics of each, and how they interact. Skull simulations may benefit from exploiting similar combinations, which is functionally straight-forward using 3D printing.

Trabecular skull bone elastic modulus varies by study, the difference in reported modulus of trabecular bone varies even more. Wu et al. examined 110 articles, and found assessment methods influence trabecular moduli results. Compression tests report elastic modulus around 10 GPa; ultrasonic test results are generally higher, in the teens, and nanoindentation is higher still, around 20 GPa. FE models report generally much lower elastic moduli, below 10 GPa. One study of trabecular elastic moduli in the same bones in 20 humans found a range of 2.7-9.1 GPa in mandibular condyle, the jaw's hinge

82 Azar, A. et al. (2020) "Protective Headgear Attenuates Forces on the Inner Table and Pressure in the Brain Parenchyma During Blast and Impact" J. Biomech. Eng.; 142(4)
83 Lee, J.H.C. et al. (2019) "An Investigation on the Correlation between the Mechanical Properties of Human Skull Bone, Its Geometry, Microarchitectural Properties, and Water Content" J. Healthc. Eng.; 6515797
84 Falland-Cheung, L. et al. (2017) "Investigation of the elastic modulus, tensile and flexural strength of five skull simulant materials for impact testing of a forensic skin/skull/brain model" J. Mech. Behav. Biomed. Mater.; 68, 303–7

bone. The same study found the T12 vertebra, near the base of the spine, varied between 8.5-15.6 GPa. None of Wu et al.'s studies examined skull trabecular and cortical bones separately.[85]

Hunt et al. analyzed elastic modulus of cortical bone in femurs and tibias, of 19 individuals, using ultrasound. The mean tibia modulus was 34.11 GPa, the mean for femurs was 32.52 GPa. These were around 20% higher than some previous ultrasound results for cortical bone elastic modulus. Previous compression tests for cortical bones were around 20 Gpa.[86] Rho et al. found that microspecimens of cortical bone measured ultrasonically 20.7 GPa (S.D. 1.9) and mechanically 18.6 GPa (S.D. 3.5). Average trabecular Young's modulus measured ultrasonically 14.8 GPa (S.D. 1.4) and mechanically 10.4 (S.D. 3.5). The authors concluded that when considered mechanically, cortical and trabecular bone are not the same material.

Studies find cortical bone modulus 1.5–2 times larger than trabecular in magnitude. Wang et al. tested trabecular and cortical bone moduli, using nanoindentation, in several rabbit skulls. Trabecular skull bones clustered around 10 GPa. Cortical bones in rabbit skulls had modulus around 17 Gpa.[87] These are half the GPa reported for nanoindentation tests of non-skull trabecular bones in humans, but are larger than the elastic modulus reported for overall skull bones. However two materials in tight configuration with each other will combine for a different modulus.

Material combinations are most studied in composites, usually with fibers embedded in a matrix. Their combination leads to modulus that may be anisotropic, with some load directions causing high modulus, and others low. Plywood-like fiber laminates, with many fiber directions crossing, obtain a isotropic higher modulus. However the cortical-trabecular sandwich is not a blend, but two materials layered. When materials with different elastic moduli are aligned over each other, the overall structure's flexibility can increase, and its elastic modulus decrease. Material with lower modulus, such as trabecular bone, absorbs and redistributes stresses to the more rigid cortical bone. This can reduce the elastic modulus of the overall structure.[88]

Because of the ubiquity of PLA in 3D printing, its ease of use, and its relative similarity to several to skull features, it is favored by researchers. Mantecón et al. compared the flexural properties of 3D printed samples to Lee's results, for four different skull bone thicknesses. Bending strength was different between the PLA samples and skull bones of the same thickness. Bending strength of flat PLA specimens was between 92 and 123 MPa. Bending strength of skull bone was between 42 and 99 MPa. Bending modulus of PLA and skull bones also differed for samples of the same thickness, except for PLA and skull bones 7.83 mm thick. The PLA modulus was between 1.81 and 2.71 GPa. The modulus of actual bone was between 1.7 and 3.95 GPa. The printed samples did not have different layers; they

85 Wu, D. et al. (2018) "Young’s modulus of trabecular bone at the tissue level: A review" Acta Biomaterialia
86 Hunt, K.D. et al. (1998) "Ultrasonic determination of the elastic modulus of human cortical bone" Medical & Bio. Eng. & Comp.; 36, 51-6
87 Wang, L, et al. (2024) "Regional variation of the cortical and trabecular bone material properties in the rabbit skull" PLoS One;19(2):e0298621
88 Ashby, M.F. & D.R.H. Jones (2013) "Properties of Composites and Foams" Engin. Mater.; 2, 477–92

were homogeneous. The role of trabecular bone was absent. But the overall similarity of PLA and skull bones is striking.[89]

Similar mechanical result for PLA have been found in other studies. Zhao, Chen & Zhou tested PLA'S elastic properties and tensile strength. It's elastic modulus varied between 2.5 and 2.8 GPa when printed flat. Its tensile strength was close to 50 MPa when printed flat. Increased values for both elasticity and strength were associated with thinner layers.[90] PLA strength and elasticity modulus can be modified in several ways. Greater infill density increases strength and stiffness, as does increasing PLA crystallinity. Blending PLA with other polymers, such as masticated natural rubber, poly(ε-caprolactone), or poly(butylene adipate-co-terephthalate) (PBAT) can increase or decrease its flexibility and strength.[91] PLA/PBAT blends have much greater flexibility than PLA alone, but reduced tensile strength. PLA/PBAT blends further modified with organic clays (and gum or stearic acid rosins) recover most of the lost strength, without increasing elastic modulus. Different percentages of clay alter mechanical properties in predictable ways.[92,93]

Lee et al.'s results for one sample was that skull bones had a mean bending modulus of 1.7 GPa.[94] Ludwiczak, Frąckowiak & Leluk found that a PLA/PBAT combination with 5% clay had a 1.86 modulus. Given the linear relationship between clay and flexibility, increasing clay percentage could produce a 1.7 modulus.[95] Lee et al.'s other sample had a mean skull bone bending modulus of 2.7 GPa. PLA alone can have that modulus.

Guidance: While various composites can accurately mimic skull bones, it may be interesting to develop models that use a sandwich-like system of materials. The density of any 3D material can be altered during printing. The skull could be printed with a narrow dense surface, on top of which is printed a more sparse surface, on top of which is a thicker, dense surface. Because different print densities correlate with different mechanical response, this could reproduce accurate skull bone dynamics. Alternatively, different materials could be assembled together. Some 3D printers have the capacity to switch materials on-the-fly. This allows both materials and print density to change, like actual skull bone internal structure.

Because 3D printed skulls are generally produced in several parts, they need to be bonded together. Hanna et al. determined the glue line was a weak spot in skull models, and tested a number of

89 R. Mantecón, R. et al. (2022) "Additive manufacturing and mechanical characterization of PLA-based skull surrogates" Polymers; 15(1):58
90 Yu Zhao, Y., Chen, Y & Y. Zhou (2019) "Novel mechanical models of tensile strength and elastic property of FDM AM PLA materials: Experimental and theoretical analyses" Materials & Design; 181:108089
91 Huang Y. et al. (2021) "A new strategy to improve viscoelasticity, crystallization and mechanical properties of polylactide" Polymer Testing; 107160
92 Ludwiczak, J., Frąckowiak, S. & K. Leluk (2021) "Study of Thermal, Mechanical and Barrier Properties of Biodegradable PLA/PBAT Films with Highly Oriented MMT" Materials (Basel); 14(23):7189
93 Moustafa, H. et al. (2017) "PLA/PBAT Bionanocomposites with Antimicrobial Natural Rosin for Green Packaging" ACS App. Mater. & Interfac.; 9(23):20132-41
94 Lee, J.H.C. et al. (2019) "An Investigation on the Correlation between the Mechanical Properties of Human Skull Bone, Its Geometry, Microarchitectural Properties, and Water Content" J. Healthc. Eng.; 6515797
95 Ludwiczak, J., Frąckowiak, S. & K. Leluk (2021) "Study of Thermal, Mechanical and Barrier Properties of Biodegradable PLA/PBAT Films with Highly Oriented MMT" Materials (Basel); 14(23):7189

adhesives for suitability in withstanding the strains of ballistic tests. They found Pro-Flex 50, a 50 Shore A liquid polyurethane system, to be the best performer.

CEREBROSPINAL FLUID

Hanna et al. made a head surrogate with an ABS skull and a homogeneous "ballistics gel" as a brain. But they also scaled down the brain slightly so there was a 2 mm space between it and the inner skull. After they ensured the brain and skull were water-tight, they injected water into the area, as a proxy for CSF. They placed surrogate head models in a drop tower and tested "front" and "crown" impacts. The frontal impact orientation was used to test the model with CSF, because it led to the most rotational motion. With the addition of a CSF layer, maximum shear strain was on average 2.7 times lower compared to a brain that pressed against the skull. The average strain rate was 6.8 times lower. The water layer was causing the brain gel to experience less deformation. The water layer a larger effect on surrogate brain deformation than the brain or skull material properties. Note that the simplicity of the brain gel, and the use of very flexible ABS as a skull material, may have elevated the water layer's influence on rotational responses.[96] Also, the brain's CSF layer is not a simple fluid, but is contained within subarachnoid space's complex geometry. Also the most distal part of the dura mater is connected to the inner skull surface. Still, CSF may be a very important variable.

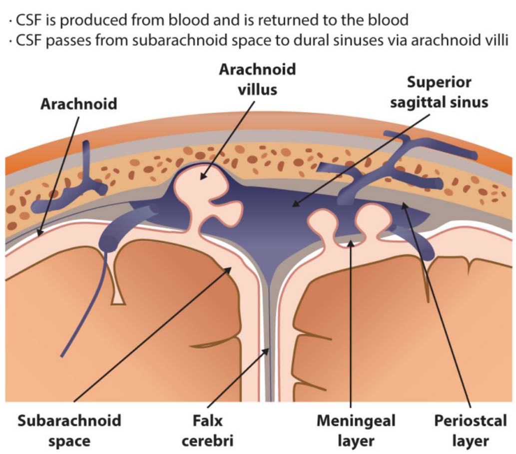

Fig. 11 CSF Circulation, StatPearls[97] reproduced under CC BY-NC-ND 4.0

CSF is a protective fluid that cushions the brain and spinal cord from mechanical injury. It also reduces the brain's effective weight from its normal 1,500 grams to a much lower 50 grams. This weight reduction reduces impact force during mechanical injury. To achieve this , the brain has to be completely enveloped in CSF. [98] The CSF clearly protects the brain from fast and abrupt head movements. Membrane barriers, above the arachnoid and dura maters, below the pia mater, contain the CSF.[99] The pia mater is a thin, delicate membrane, averaging 0.1 mm thick, that forms the innermost

96 Hanna, M. et al. (2024) "Anatomical Features and Material Properties of Human Surrogate Head Models Affect Spatial and Temporal Brain Motion under Blunt Impact" Bioengin (Basel); 11(7):650
97 Sehgal, I. & J.M. Das (2026) "Anatomy, Back, Spinal Meninges updated 2023" In: StatPearls [Internet] www.ncbi.nlm.nih.gov/books/NBK547755/
98 Adigun, O.O. & M.A. Al-Dhahir (2021) "Anatomy, head and neck, cerebrospinal fluid" StatPearls [Internet],(Treasure Island, FL: StatPearls)
99 Tumani, H., Huss, A. & F. Bachhuber (2018) "The cerebrospinal fluid and barriers – anatomic and physiologic considerations" Handbook of Clinical Neurology, Vol. 146, 21–32

layer of the meninges and is closest to the brain. The dura mater has an average thickness of 1.11 mm. The arachnoid mater is 0.2 mm thick.

Rather than try to seal the brain model and inject water into it, a set of membranes, each membrane perhaps 1 mm thick, can be used, that form a sealed cavity between them. Fluid, perhaps water, can be injected into the sealed cavity. The membranes can then be positioned over the brain, next to the skull.

CONCLUSION

There is a need for multi-material brain models that combine:

- **Anisotropic hydrogels for white matter regions**
- **Isotropic materials for gray matter**
- **Realistic interfaces between materials (where most damage occurs)**
- **Dummy neck flexibility based on the head's optical field**
- **Cerebrospinal fluid simulation in membranes**
- **Skull surrogates tuned to accurately model skull bones**

INSTRUMENTATION

The choice of instrumentation depends on the specific research questions, the nature of the impacts studied, and whether the focus is on pressure, deformation, and/or acceleration.

Internal Pressure Sensors

- **Fiber optic sensors** embedded within the brain simulant material record internal pressure changes during impact
- **Pressure transducers** placed at specific brain regions to measure intracranial pressure
- Multiple sensors can map pressure distribution across different brain areas

Acceleration Measurement

- **Accelerometers** mounted in the skull or brain material to measure linear acceleration.
- **Gyroscopes** for measuring instantaneous angular velocity.
- **Rotation-tracking sensor (author's invention)** that uses a Hall-effects sensor and a surface magnetic array to measure the distance and velocity of head rotation.

Strain and Deformation Sensors

- **Measurement arrays** distributed throughout the model to create 3D maps of:
- Pressure distribution
- Strain fields
- Acceleration patterns

COMPETING INTERESTS

The author submitted U.S. patent 19/264,598 for biomechanically realistic brain models, which has been allowed. The author submitted an International Application for biomechanically realistic brain models at WIPO, PCT/IB2025/062404, published at www.patentscope.wipo.int/search/en/detail.jsf?docId=WO2026042059&_cid=P22-MSFSC4-11840-1. The author was previously awarded U.S. patents 11,464,270 and 12,433,362 for helmet systems that reduce rotational acceleration under tangential impacts. The author has refined the helmet system in response to prototype testing, in U.S. patent submission 19/757,298. The author was awarded U.S. patent 12,702,180 for a magnetic sensor that measures rotational and tangential motion of a helmet. The author submitted U.S. patent 19/291,259 for a helmet system that triggers an airbag to rapidly inflate around a player's neck when impact thresholds are exceeded.

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