Supporting Information

The networking brain: how extracellular matrix, cellular networks, and vasculature shape the in vivo mechanical properties of the brain

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**Table S1.** Brain networks, their macro-organization, involved structures and connections with other networks.

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| **Network** | **Macro-organization** | **Structures and their mechanical functions** | **Inter-network connections** |
| Neurons | **Total brain**Weight: 1509 ± 299 g[1]67-86 billion neurons [1-3] **Cerebral cortex** Weight: 1233 ± 234 g[1]81.8% of brain mass, contains 19.0% of brain neurons[1]10-20 billion neurons[1],[2]**Grey matter** Weight: 316 ± 53 g[1]15 ± 2 billion neurons[1]Neuron density per mm2:Layer III: 419, layer V: 454, layer VI: 458[4]**White matter** Weight: 294 ± 60 g[1]1.29 ± 0.54 billion neurons[1]Neuron density (not uniformly distributed): 250-1000 per mm3 [5]Fiber (myelinated axons) diameters ranging from 0.16-9µm[6]**Cerebellum**154 ± 19 g[1]10.3% of brain mass, 80.2% of brain neurons[1]54-105 billion neurons[1,2]Density: 721 ± 69 cells (neurons + glial cells + pericytes) per 0,001 mm³ in cerebellar cortex[7] | * Myelin: extracellular support
* Cytoskeleton: intracellular scaffold and support, cell movement
* Cytoplasm: intracellular pressure, cell viscosity, (in)compressibility
* Organelles: scaffold
 | * Other neurons – through synapses
* Glial cells – through myelin (oligodendrocytes), perisynaptic astrocytic processes (astrocytes)
* ECM through via filopodia and glycocalyx
* Vasculature
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| Glial cells | **Total brain**Estimated 40-50 billion glial cells[2]:* Oligodendrocytes 29-75%[2]
* Astrocytes 19-40%[2]
* Microglia ≤ 10%[2]

**Cerebral cortex**18.2-100 billion non-neuronal cells (including glial and endothelial cells), of which around 70% are estimated to be glial cells[2]**Grey matter**18.2-39 billion[2]Density: 100,000 per mm3 [2]**White matter**20,000-200,000 per mm3, mostly oligodendrocytes[2]**Cerebellum**3 billion[2] | * Cytoskeleton: intracellular scaffold and support, cell movement
* Cytoplasm: intracellular pressure, cell viscosity, (in)compressibility
* Organelles: scaffold
 | * Neurons – through myelin (oligodendrocytes), perisynaptic astrocytic processes (astrocytes)
* Other glial cells
* ECM – through glycocalyx
* Vasculature - through endfeet via ECM and cell-adhesion molecules
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| Extracellular space (ECS) | **Extracellular/ interstitial space (ECS/ ISS) = interstitial fluid + extracellular matrix (ISF + ECM)**15-20% of brain volume[8], about 250-300 ml[9]During sleep increased to 22-24%[10]ECM includes:* Interstitial ECM
* Perineuronal ECM (perineuronal nets, PNNs)
* Perivascular ECM (basal lamina)

**Cerebrospinal fluid (CSF) + interstitial fluid (ISF)**8.7% for grey matter (GM)[11]5.9% for white matter (WM)[11]**CSF**150 mL, 25mL in ventricles and 100 mL in subarachnoid spaces[12]<2% (0.57 ml) for WM[13]7.5% (10.8 ml) for GM with some older subjects 25% in GM[13]3.7% (15.3 ml) for mixed brain tissue[13] | * Scaffold for RGC migration (CNS development)
* Reservoir for ions and nutrients
* Hydrophilic interactions: water binding, elasticity
* Hydrophobic interactions: mechanical attenuation, viscosity, fluidity
* ISF and CSF are interchanging via glymphatic system: clearance of metabolites (active flow)
* Marginal intracranial pressure (ICP) regulation (fluid excess expelled via CSF)
 | * Neurons – glycocalyx, cell adhesion molecules (e.g. integrins)
* Glial cells – glycocalyx, cell adhesion molecules e.g. integrins)
* Other ECM components
* Vasculature – glycocalyx, cell adhesion molecules (e.g. integrins), tight junctions, primary cilia
* Basal lamina – radial glial cells (RGCs) through endfeet
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| Vasculature | **Vascular system:** 3-5% of brain volume[8]**Arterial cererebral blood volume (CBVa)**20-30% of intravascular space occupied by all blood vessels (CBVtot), can increase by up to 80% of its baseline values during functional or physiological stimulation[14]*whole brain*0.70 - 1.00 mL/ 100 mL (MRI)[14,15] and 2.60 mL/ 100 mL (PET)[14,16]*GM* 0.67-1.4 mL/ 100 mL (MRI) and 3.21 mL/ 100 mL (PET)*WM* 0.46 - 0.64 mL / 100 mL (MRI) or 1.87 mL/ 100 mL (PET)[14]**Venous blood volume***Whole brain*2.46 - 3.77 mL/ 100 mL (MRI)*GM*1.75 – 5.5 mL / 100 mL (MRI)*WM*0.58 – 3.9 mL / 100 mL (MRI)[14]**Diameters***arteries* Central arteries: 260 – 280 µm[17]Peripheral arteries: 150 – 180 µm[17]Penetrating arteries: 40 µm[17]*Arterioles*Anastomoses: 25 – 90 µm[17]Small straight arterioles: 10 µm[17]*Veins*Central veins: 280-380 µm[17]Peripheral veins: 130 µm[17]Anastomoses: up to 180 µm[17]*Capillaries*3-7 µm[18]**Endothelial cells***Whole brain*25%-30% of non-neuronal cells ([2])*white matter*10-20% of non-neuronal cells[2]*Cerebellum*~13 billion endothelial cells[2]**Densities**Vascular density (pre-frontal + basal forebrain + motor/sensory + hippocampus): 89.8 per mm2 [19]Cerebral arteries: 1.378 g/cm3 [20]Cerebral venous sinuses: 1.130 g/ cm3 [20] | * Providing of brain parenchyma with nutrients, physiological regulation: vascular walls, vessel diameter, vessel density, branching, tortuosity, arterial pulsation, blood pressure, osmotic pressure, vascular constriction / dilatation
 | * Astrocytes - through endfeet via ECM and cell-adhesion molecules
* ECM – through vascular basement membrane
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