

BRAIN ENERGY: Why Lactate Protects the Brain

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BRAIN ENERGY:

Why Lactate Protects the Brain

- What is an oligodendrocyte?
- Brain energy and lactate
- Lactate uptake in oligodendrocytes
- Lactate effect on myelination



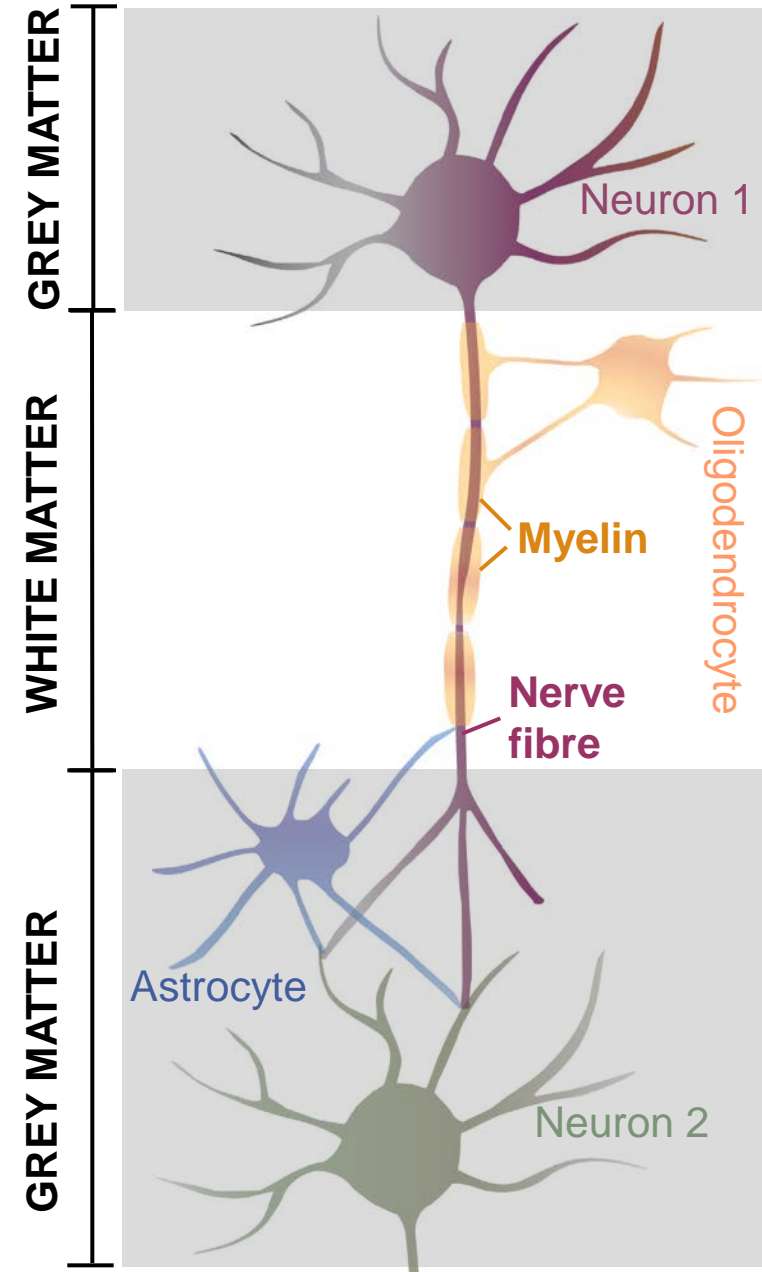
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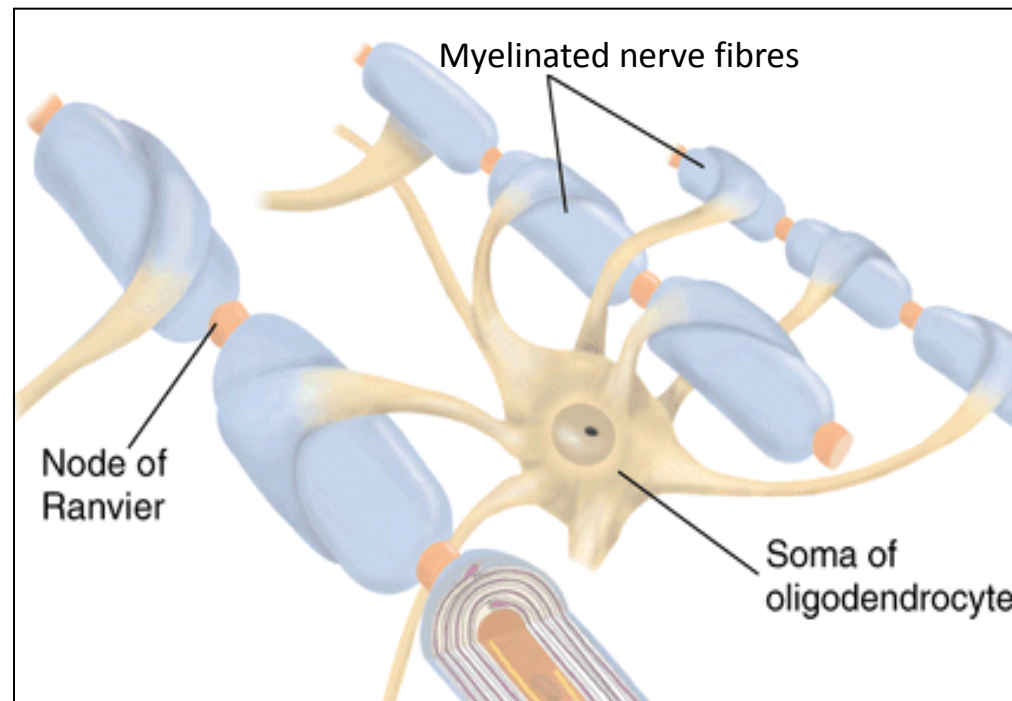
Oligodendrocytes and White Matter

- White matter: Myelinated nerve fibres
- Oligodendrocytes are the cells that myelinate nerve fibres

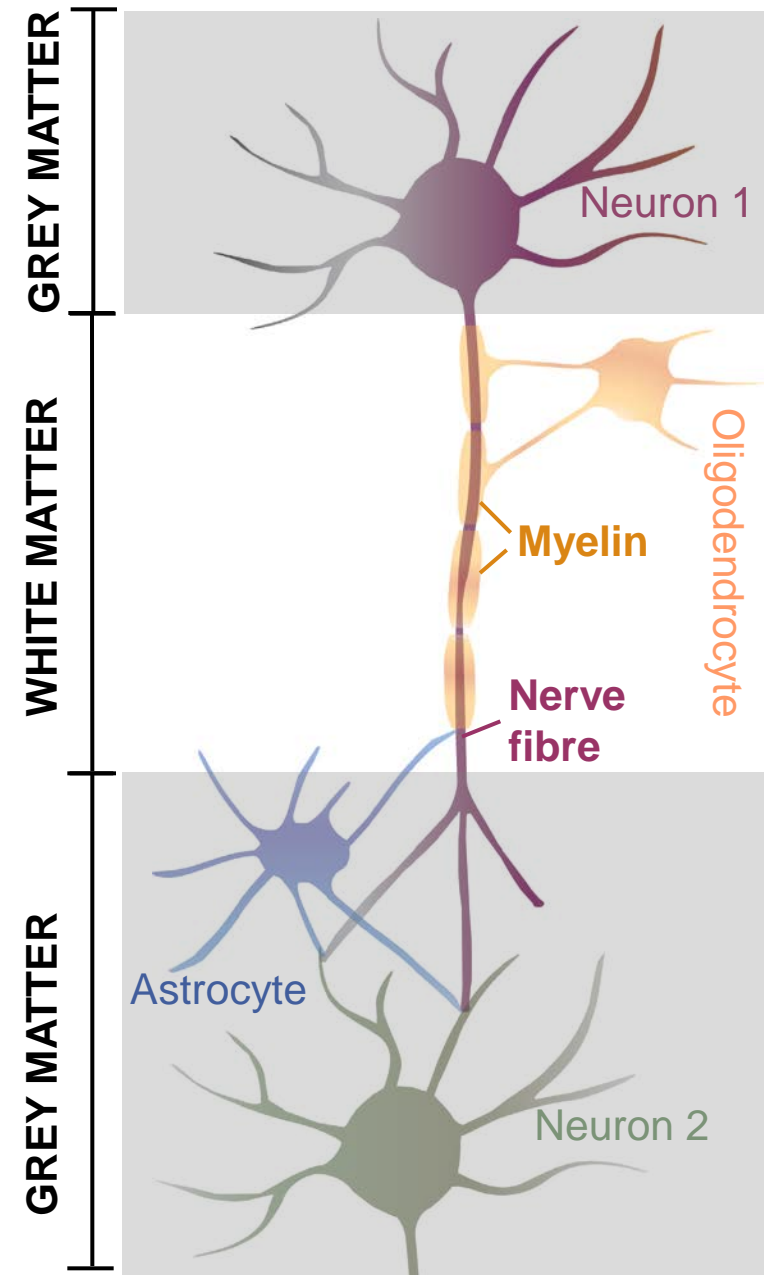


Oligodendrocytes and White Matter

- Increase the speed of action potentials
- Vulnerable to energy deprivation (*Pantoni et al., 1996*)



<http://homepage.psy.utexas.edu/homepage/class/Psy332/Salinas/Cells/Cells.html>





Loss of myelin

As in cerebral palsy or stroke

Impaired blood flow

Inflammation

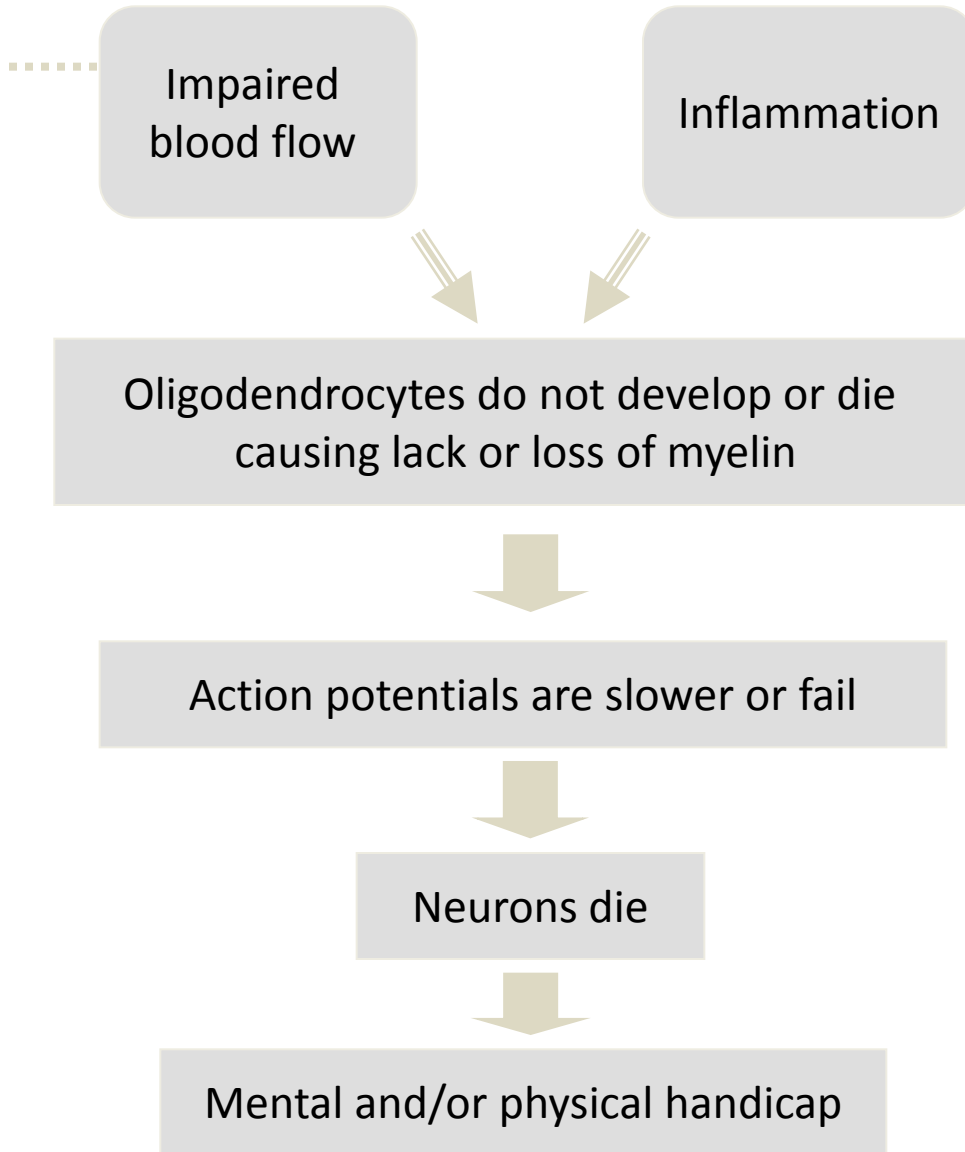
As in multiple sclerosis

Oligodendrocytes do not develop or die causing lack or loss of myelin

Action potentials are slower or fail

Neurons die

Mental and/or physical handicap





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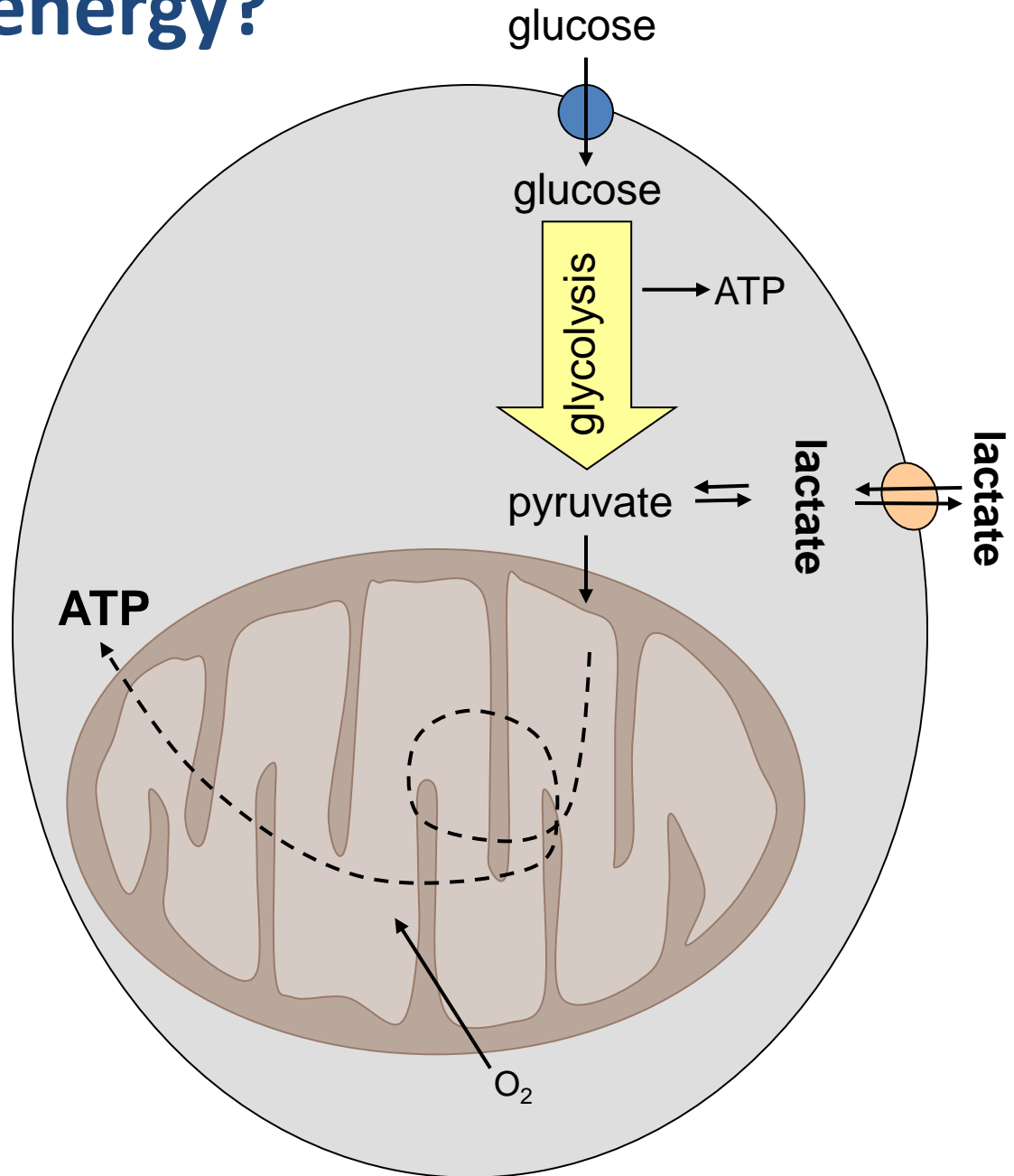
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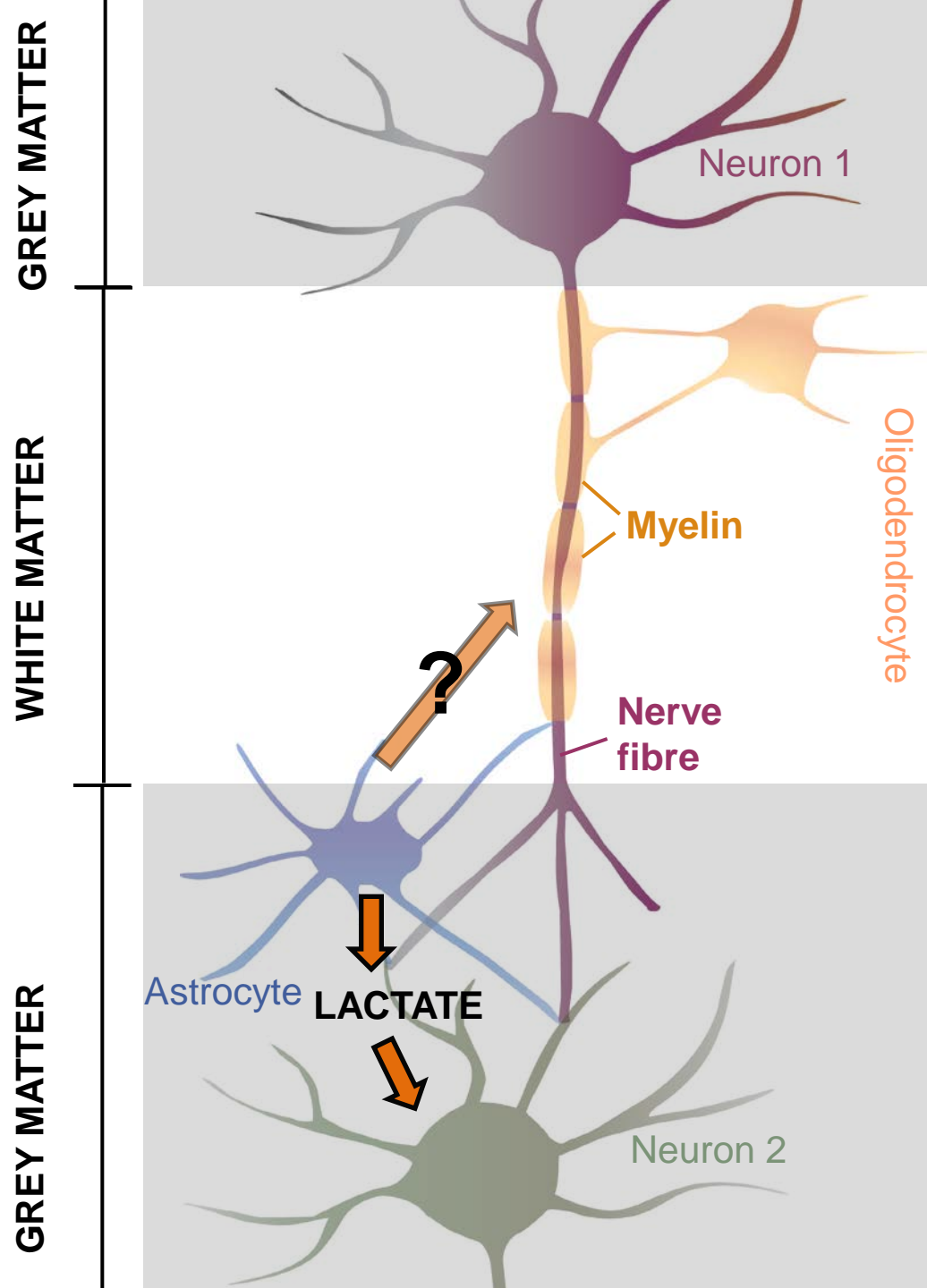
What is brain energy?

- Glucose is the most important energy substrate
- Must be converted to ATP, the cell's energy currency
- Lactate is an alternative energy substrate





- Astrocytes release lactate
- Neurons take up lactate
- Important for neuronal survival when glucose levels are low (Pellerin et al., 1998; Brown et al., 2004; Aubert et al., 2005)
- In culture: Oligodendrocytes are the most avid consumers of lactate in the CNS (Sanchez-Abarca et al., 2005)





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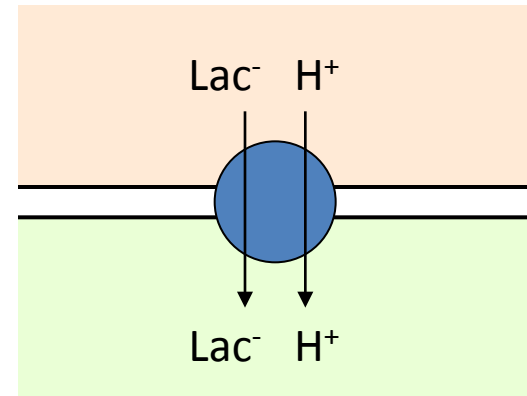
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Lactate transport across membranes

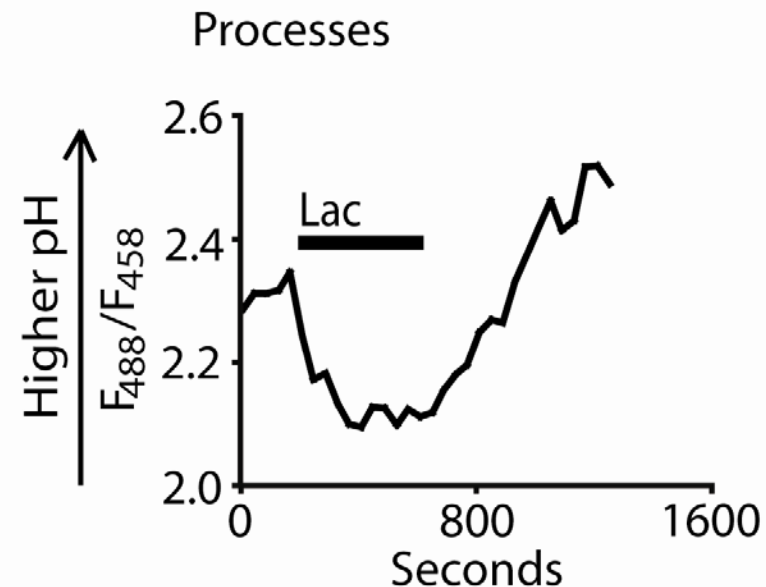
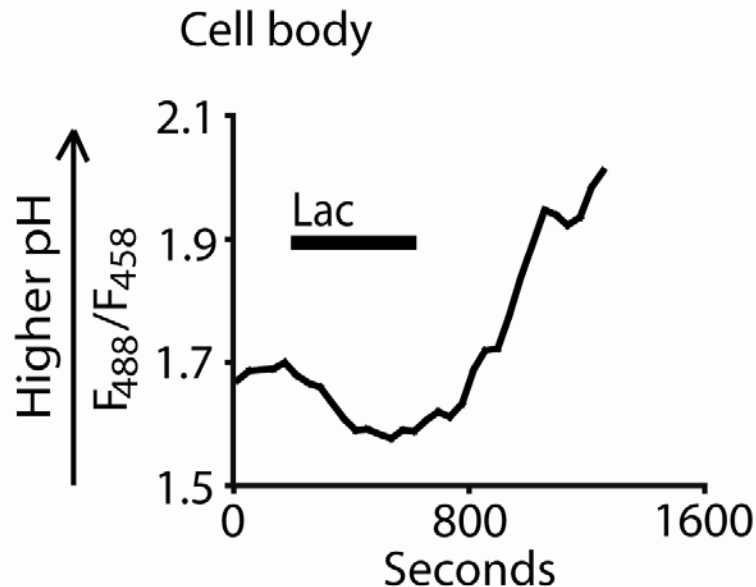
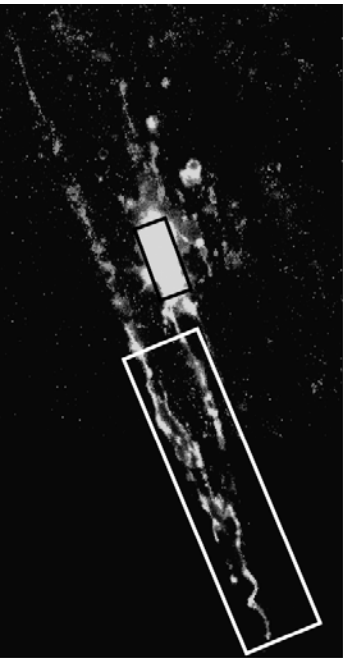
- Happens via monocarboxylate transporters (MCTs)
- MCT1, 2 and 4 located in the brain
- Cotransport of 1 lactate⁻ and 1 H⁺
- Produces a pH change
- We can measure this with a pH-sensitive dye, BCECF





Lactate uptake in Oligodendrocytes

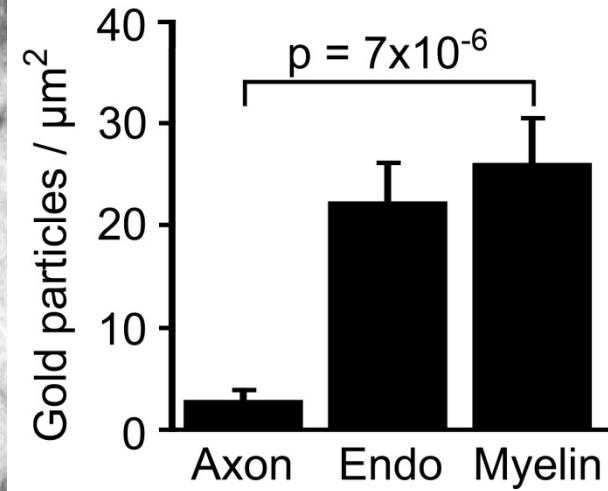
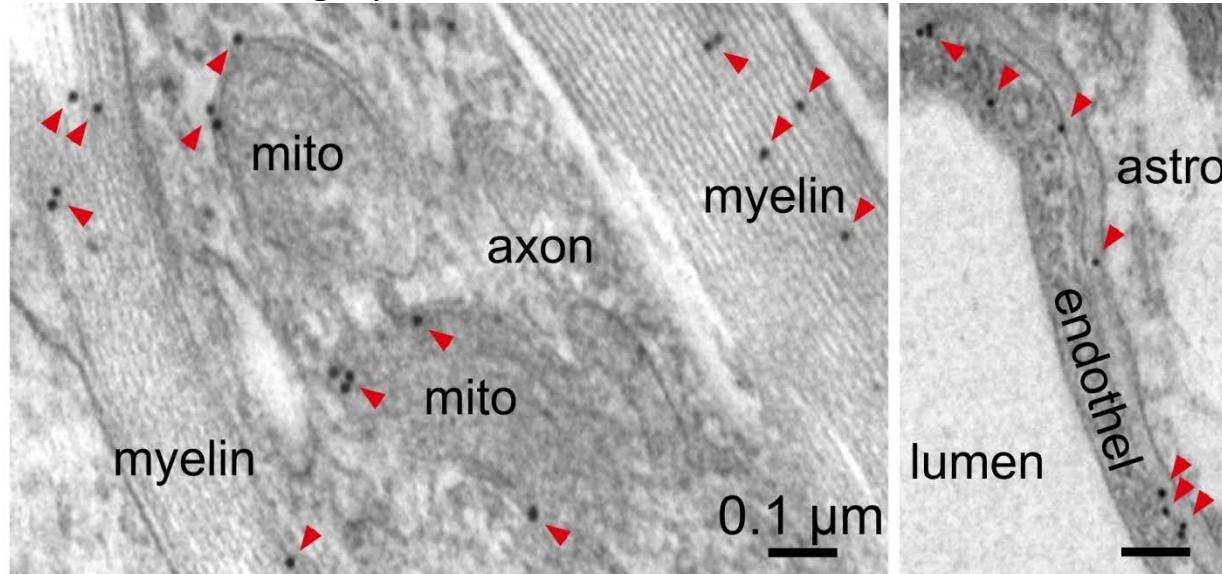
- Oligodendrocytes filled with pH-dye (BCECF) through patch-pipette
- Application of 10mM lactate produces a pH change
- Lactate (and H⁺) is transported into cells via MCTs





MCT1 is Expressed in Myelin

Electron micrographs from the cerebellar white matter





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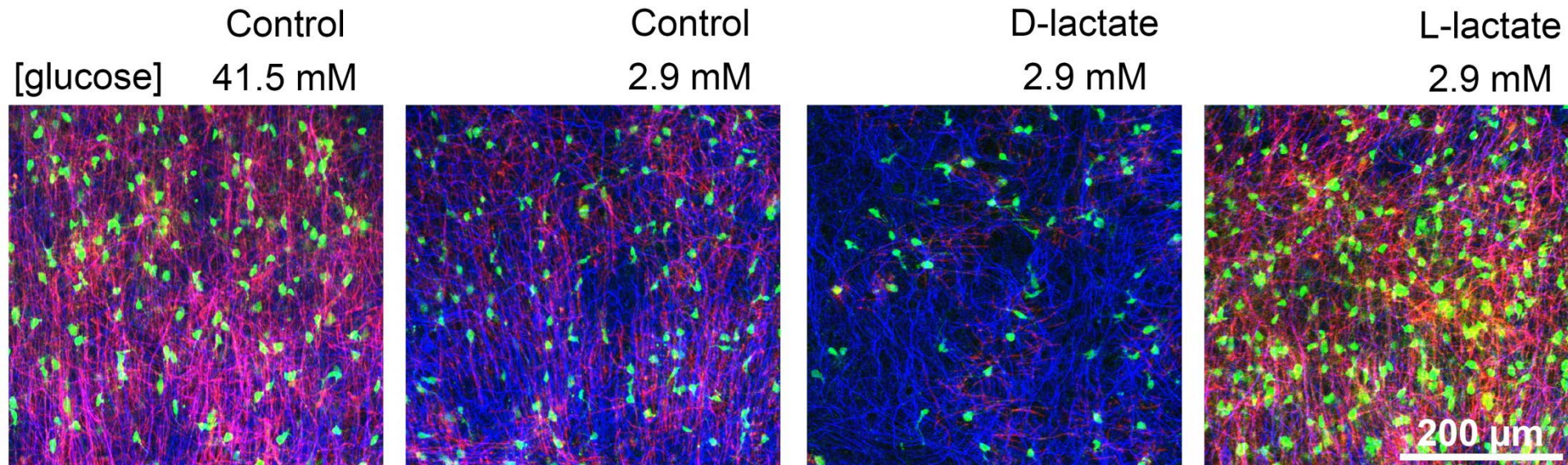
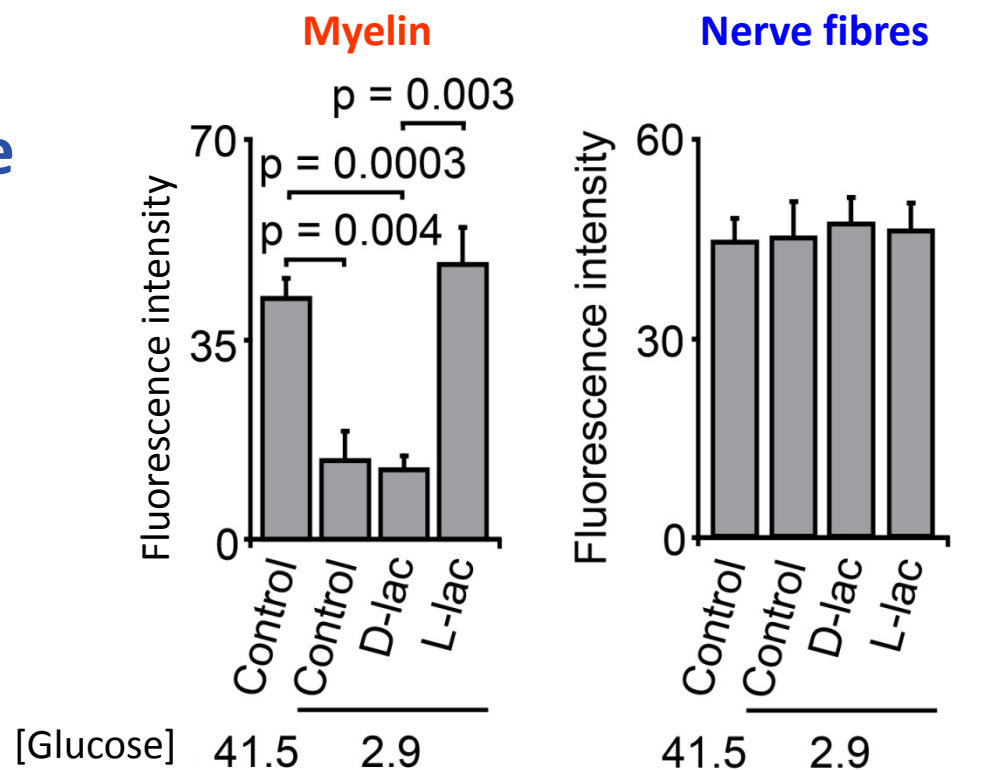
Lactate rescues myelination in low glucose

- Organotypic slices cultured for 2 weeks, looked at myelination
- Tested effect of glucose concentration and lactate (20 mM) on myelination

Myelin (Myelin Basic Protein)

Nerve fibres (Neurofilament)

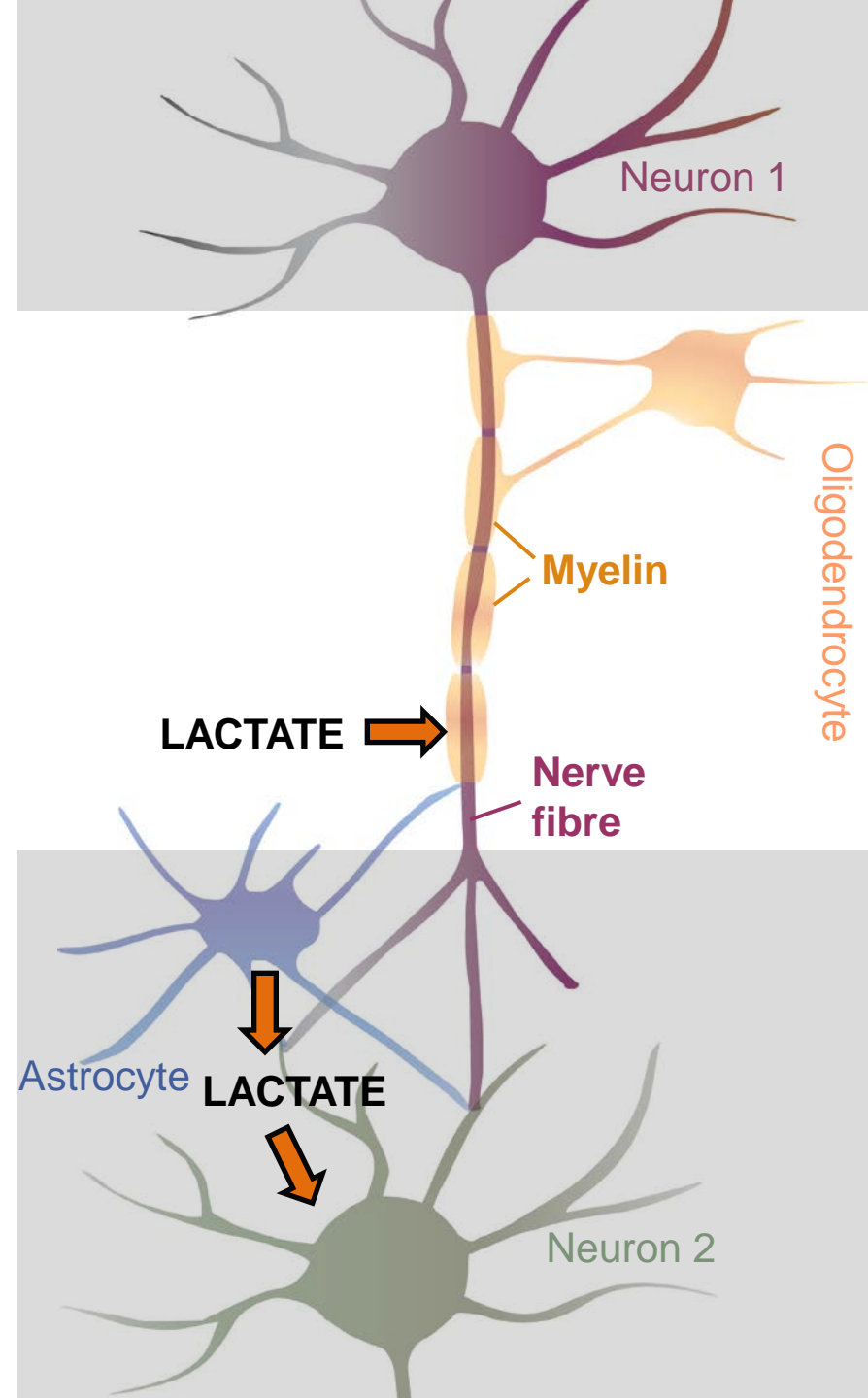
Oligodendrocyte lineage cells





Conclusion

- Lactate
 - Energy substrate
 - Shuttle from one cell type to another
- Oligodendrocytes can take up lactate
- Important for the formation of myelin when glucose levels are low
 - Cerebral palsy, stroke, spinal cord injury





CENTRE FOR
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