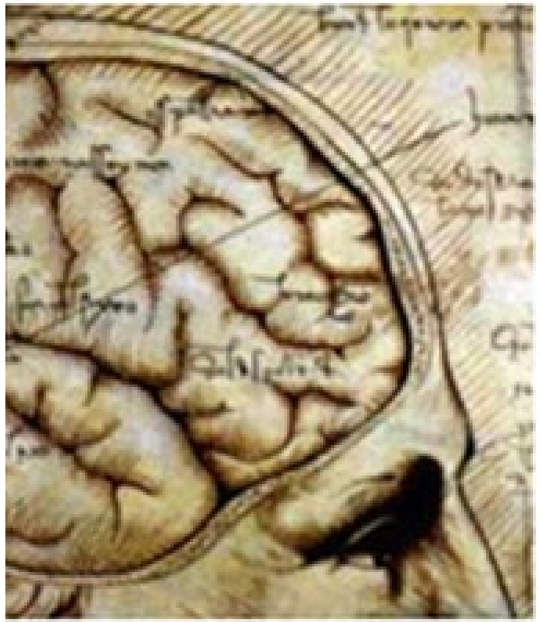
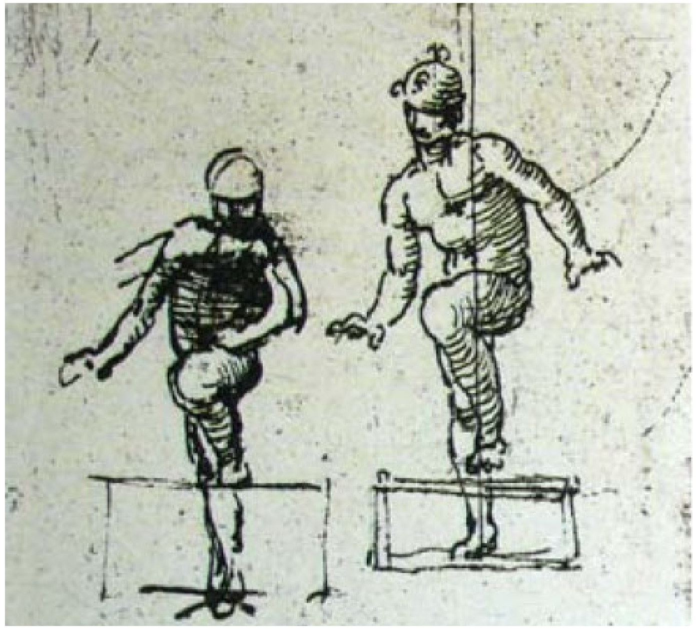
Action Systems - neural circuits for motor control





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Andy Murray
SWC Room 284 (L2 West)

Action Systems Overview

Lectures

Motor systems overview	Andy Murray
Pattern generation	Peter Latham
Computational control	Maneesh Sahani
Cerebellum	Tom Otis
Basal Ganglia	Marcus Stephenson-Jones
Neocortex/Discussion	Andy Murray/Maneesh Sahani

Practical

Build fiber photometry setup and perform behaviour

Journal Club I

Cregg et al., Brainstem Neurons that Command Left/Right Locomotor Asymmetries. BioRxiv

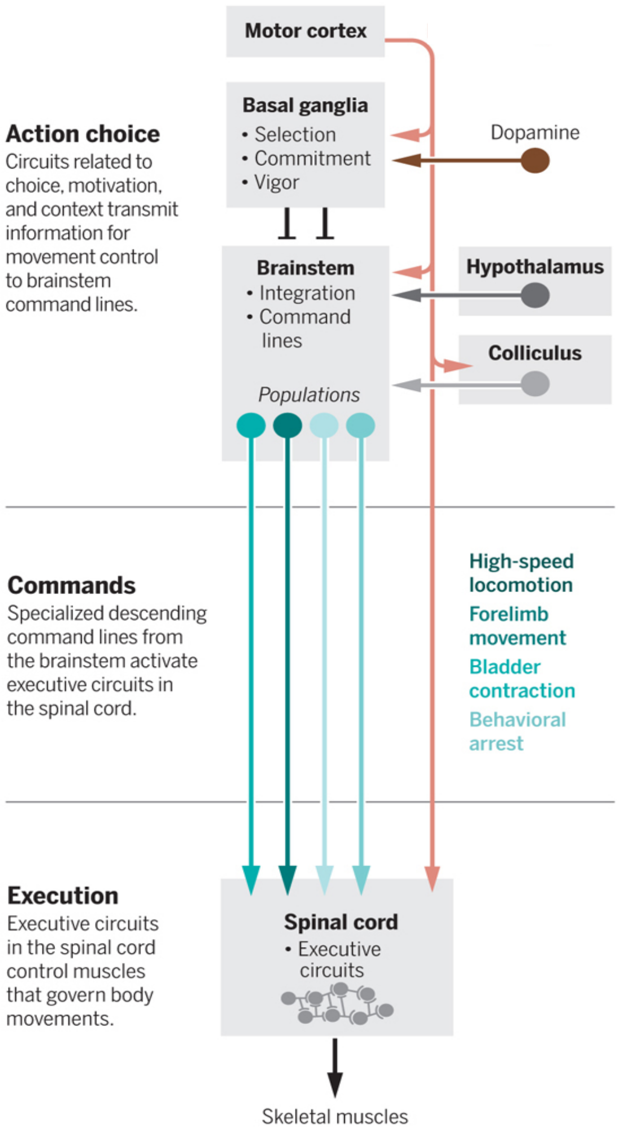
Journal Club II

Yang and Lisberger, Purkinje-cell plasticity and cerebellar motor learning are graded by complex-spike duration. Nature 2014.

Motor control is our only means to interact with the environment

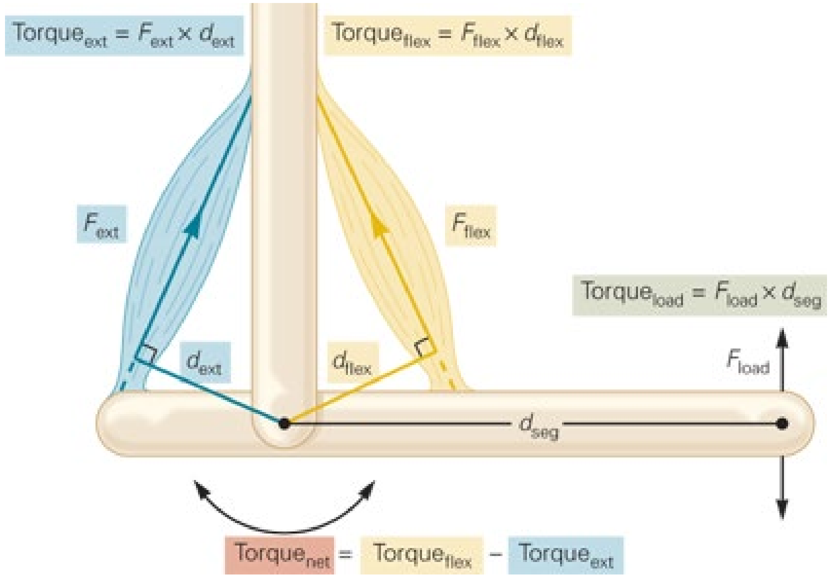
We are surprisingly bad at recreating natural movement

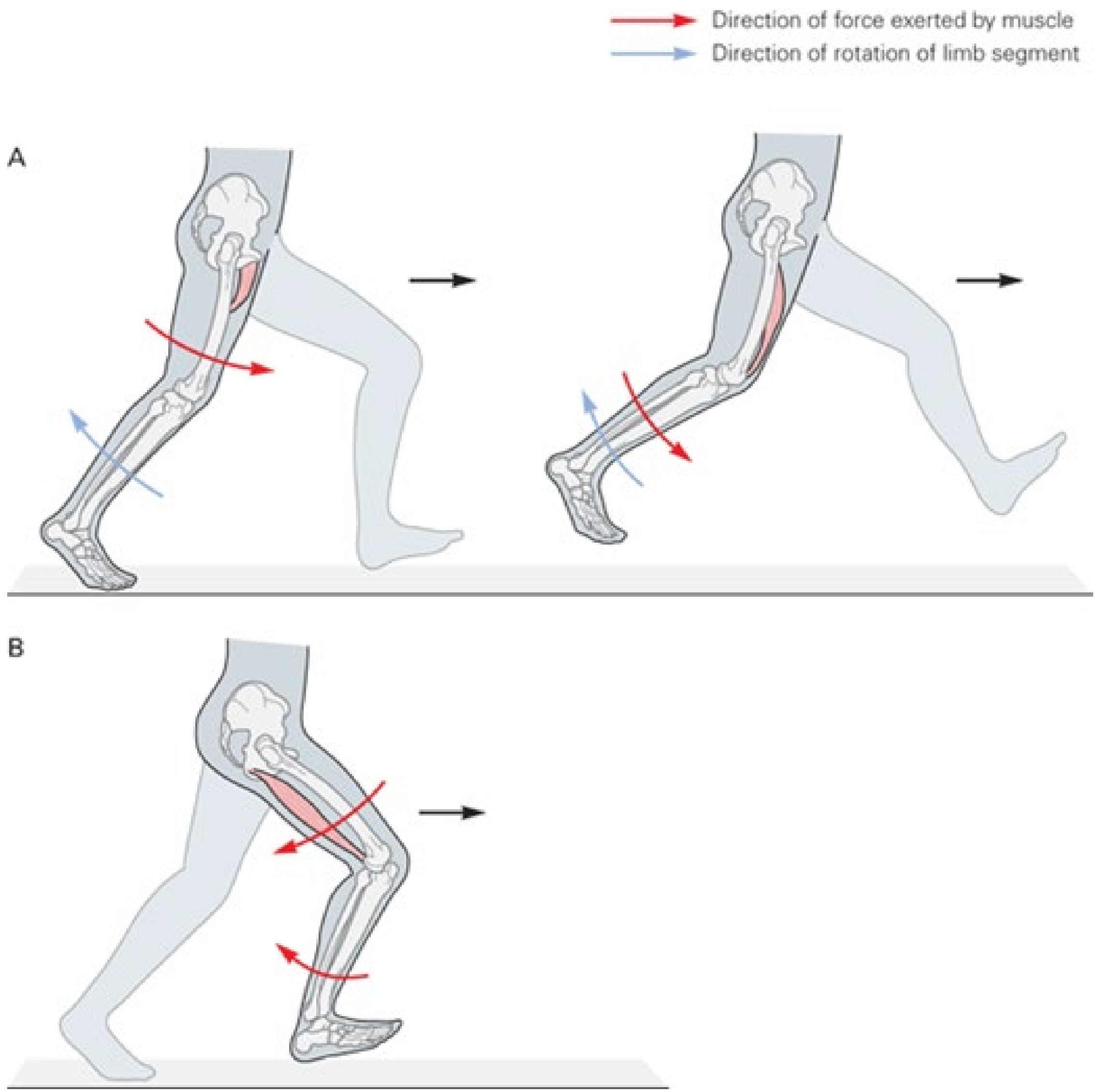
Which parts of the nervous system are involved in motor control?



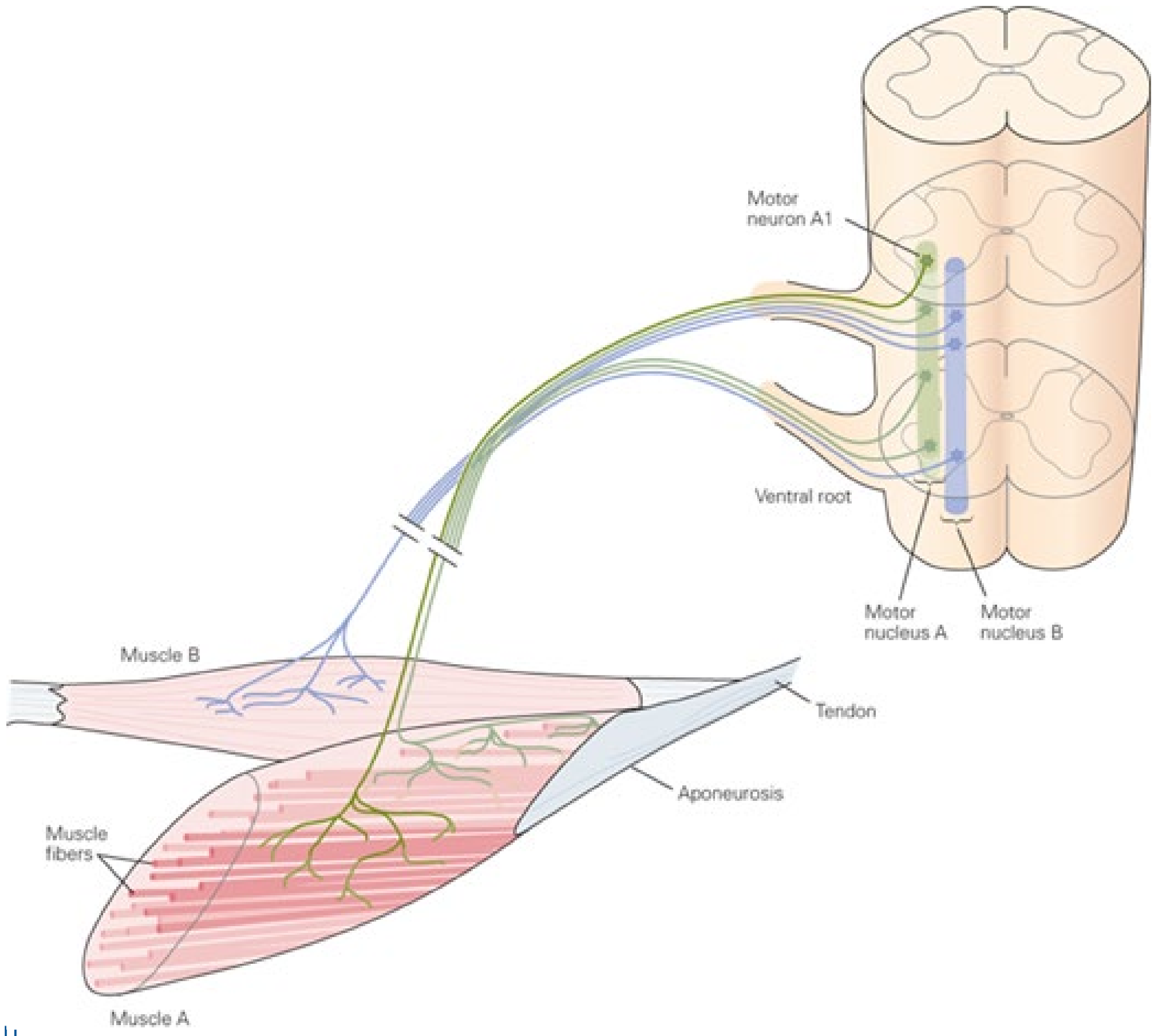
Reading:
Connecting neuronal circuits for movement
Arber & Costa, Science 2018
Vol. 360, Issue 6396, pp. 1403-1404

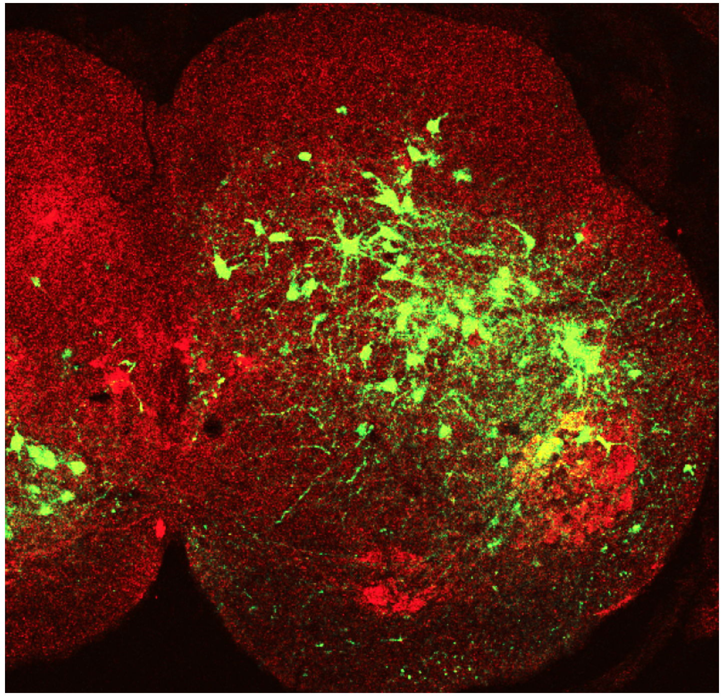
Muscles and motor neurons





Muscles and motor neurons





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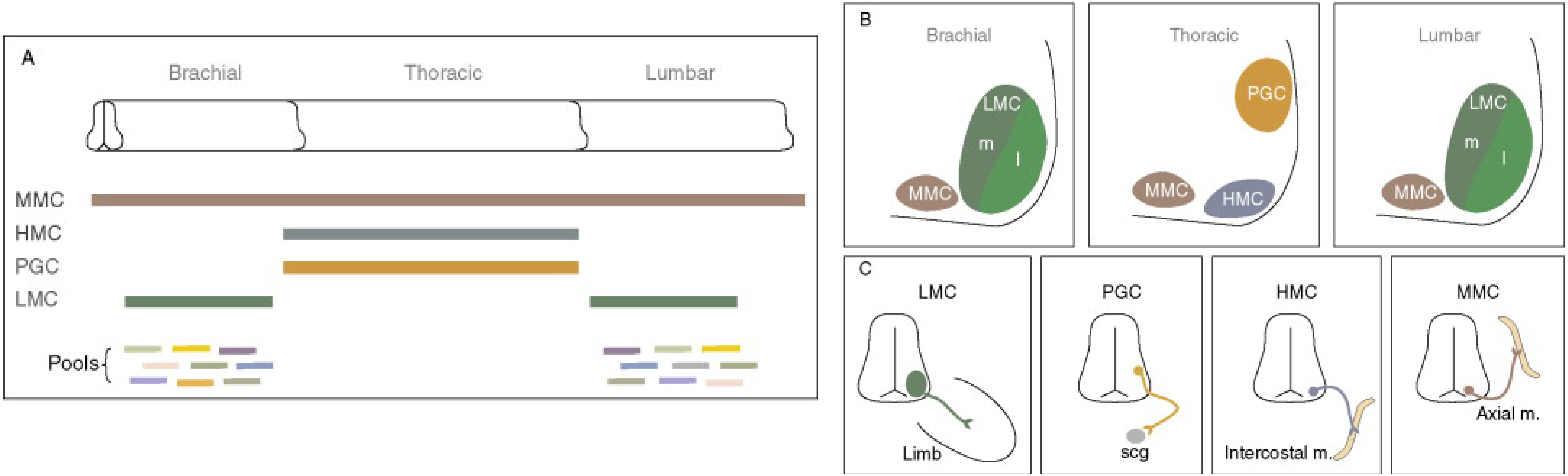
Spinal circuitry – organisation of motor neurons



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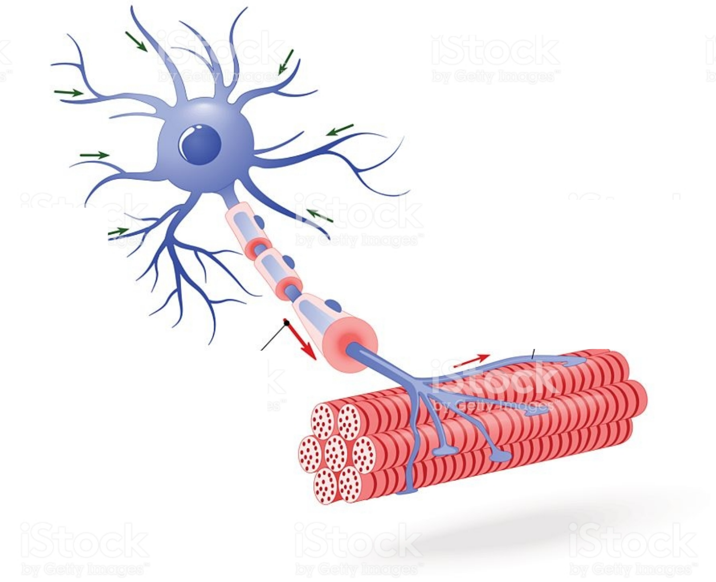
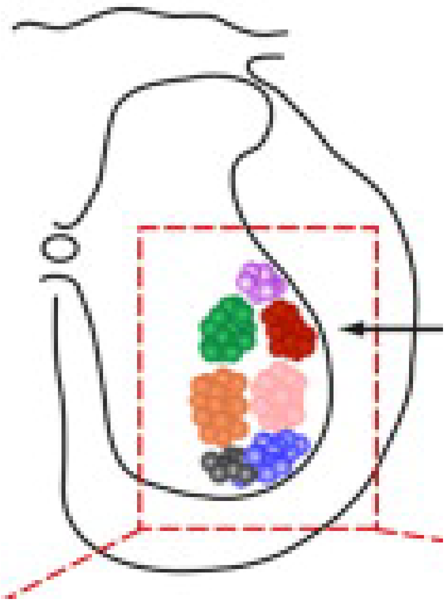
Spinal circuitry – organisation of limb motor neurons

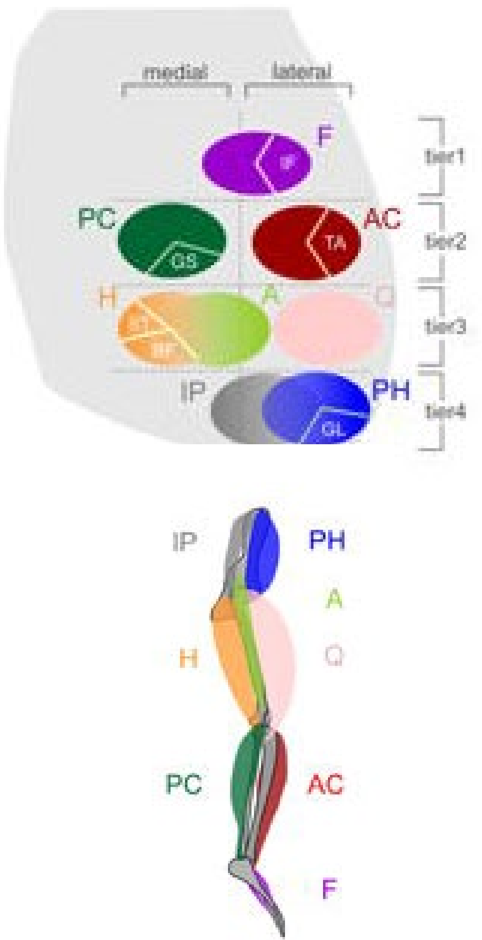
Motor unit



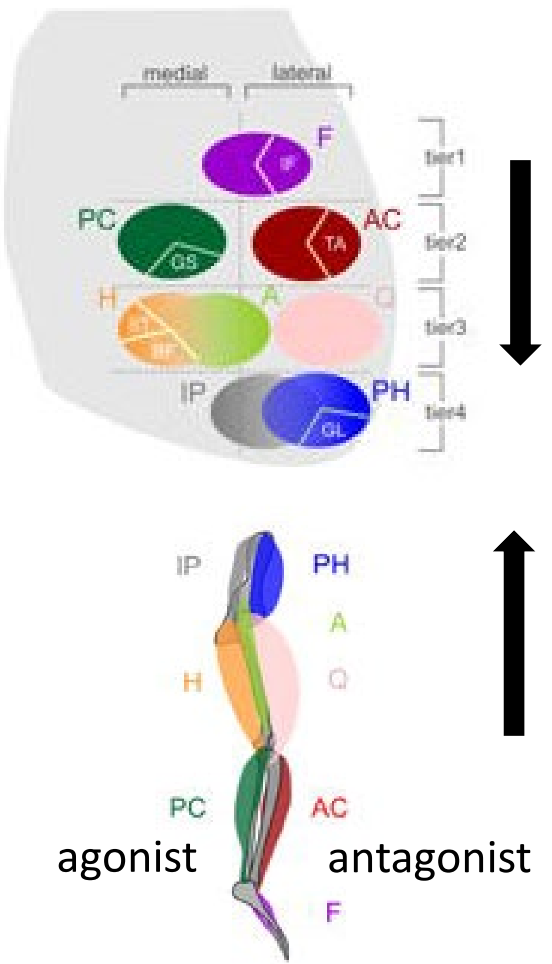
Motor pool



Motor columels



Motor columns



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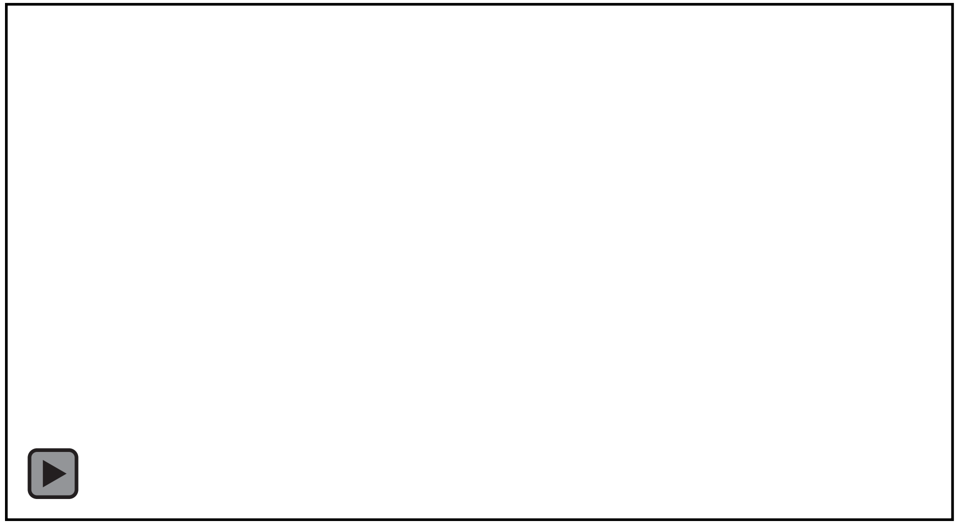
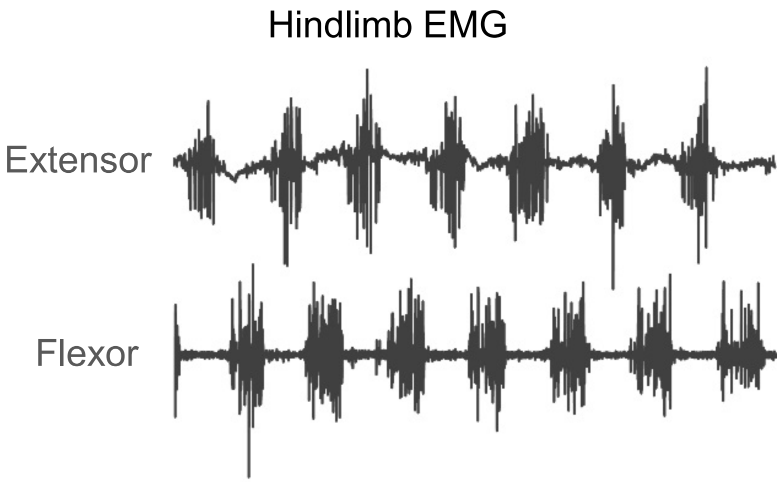
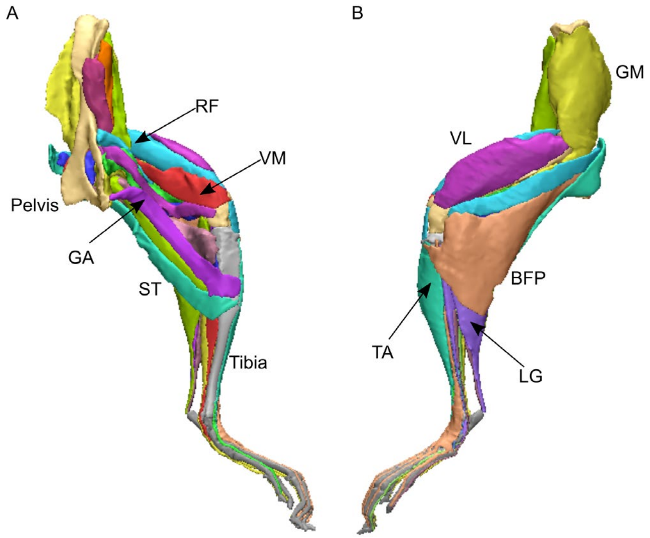
Simple motor control is based on rhythmic movements







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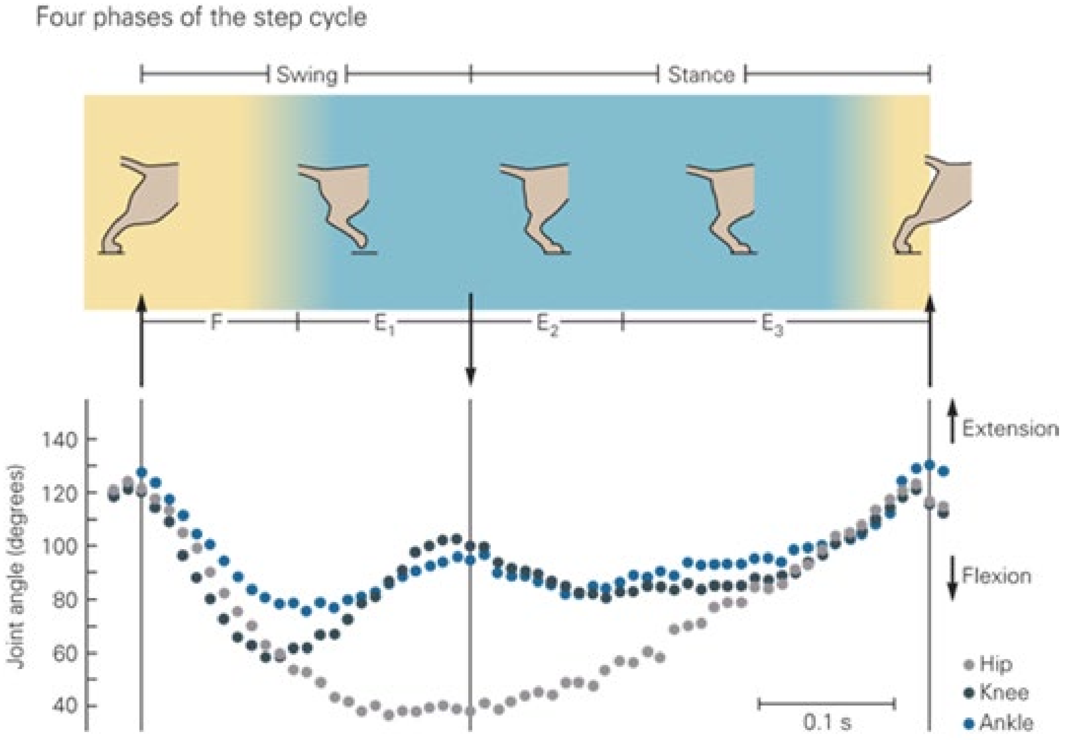
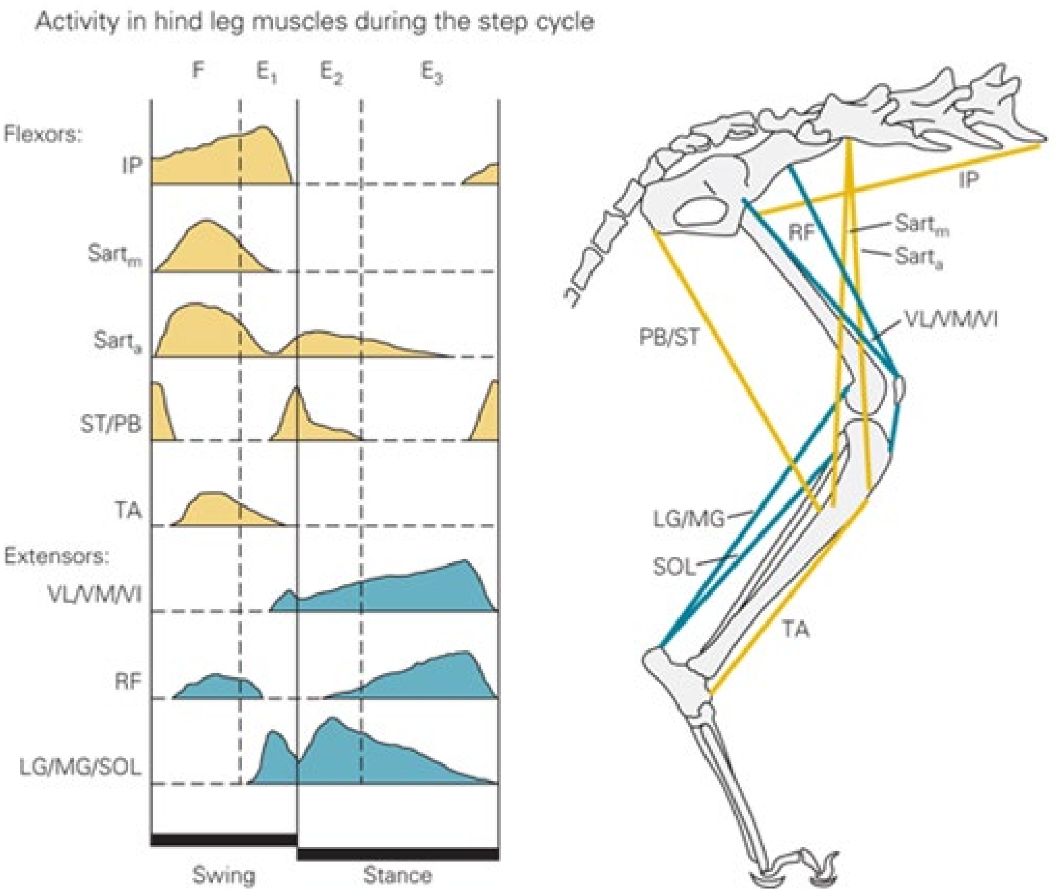
The locomotor step cycle





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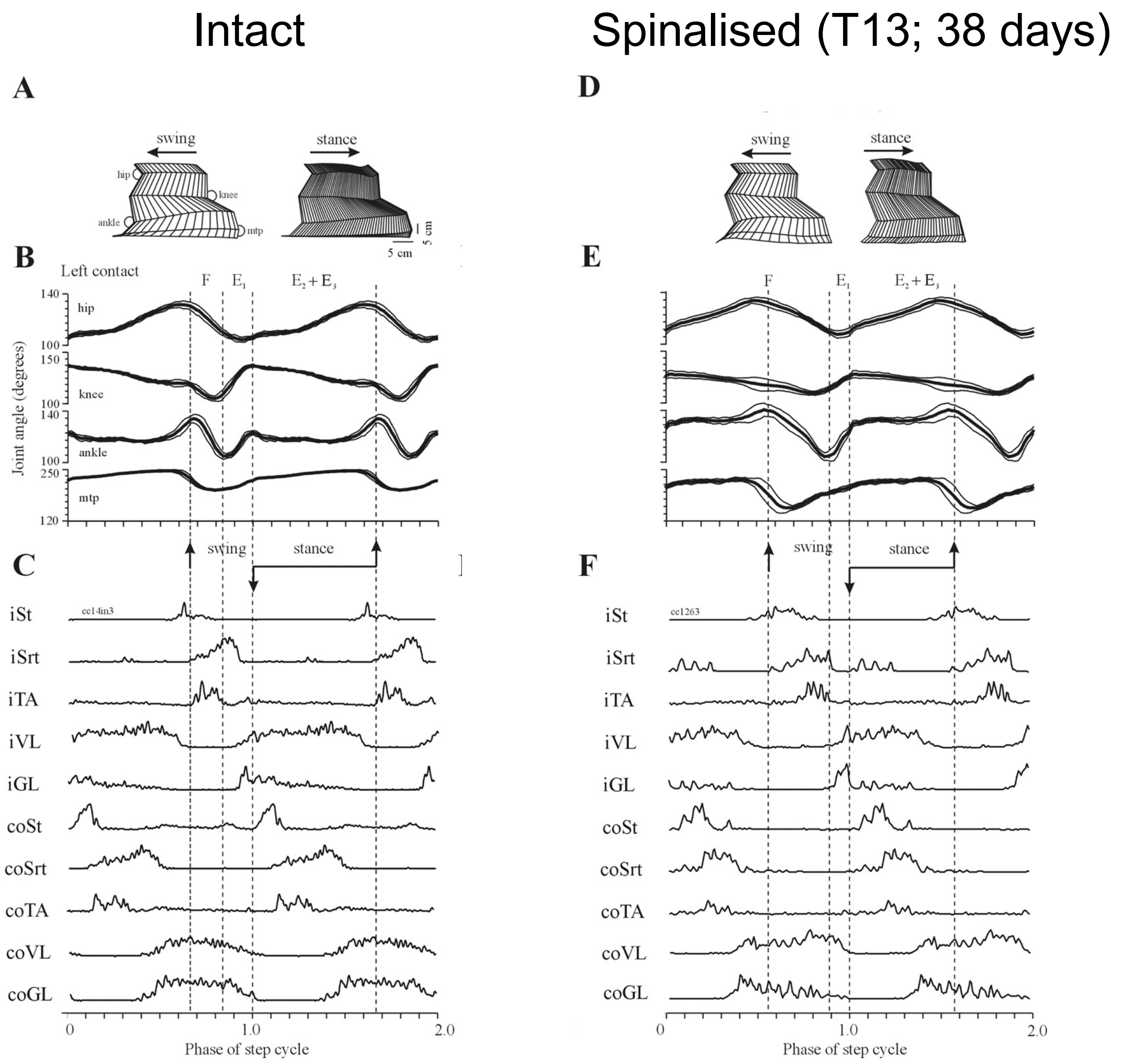
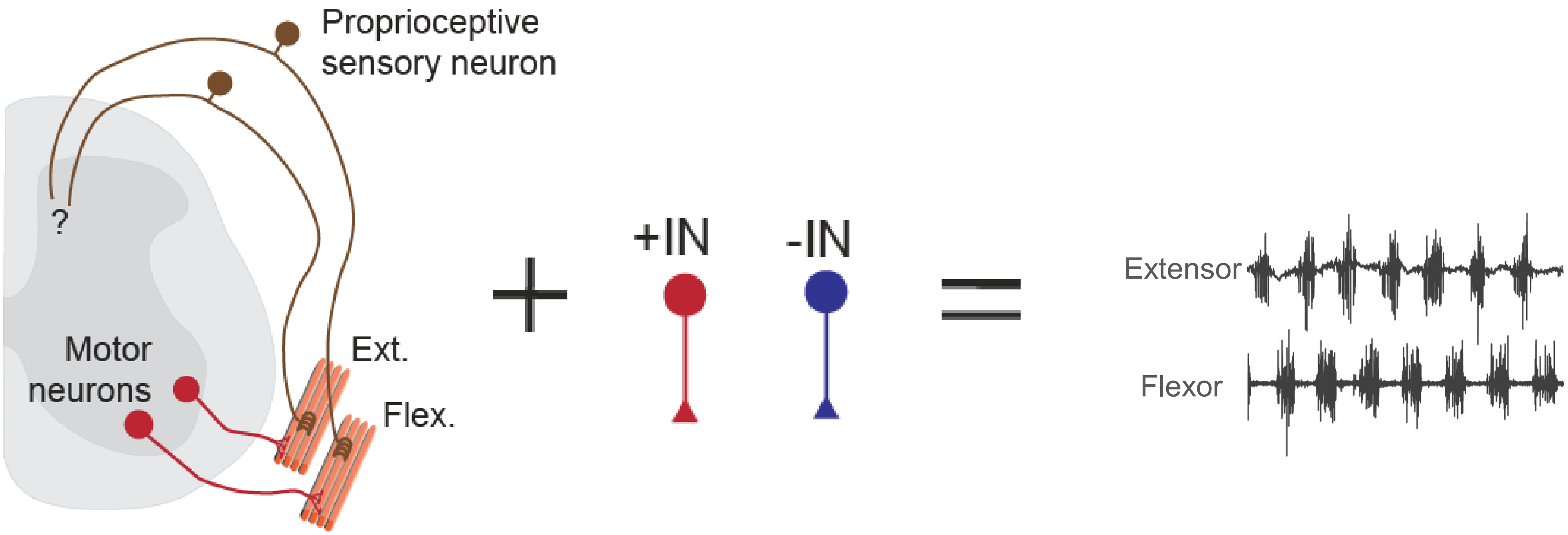
The spinal cord can generate rhythmic locomotion

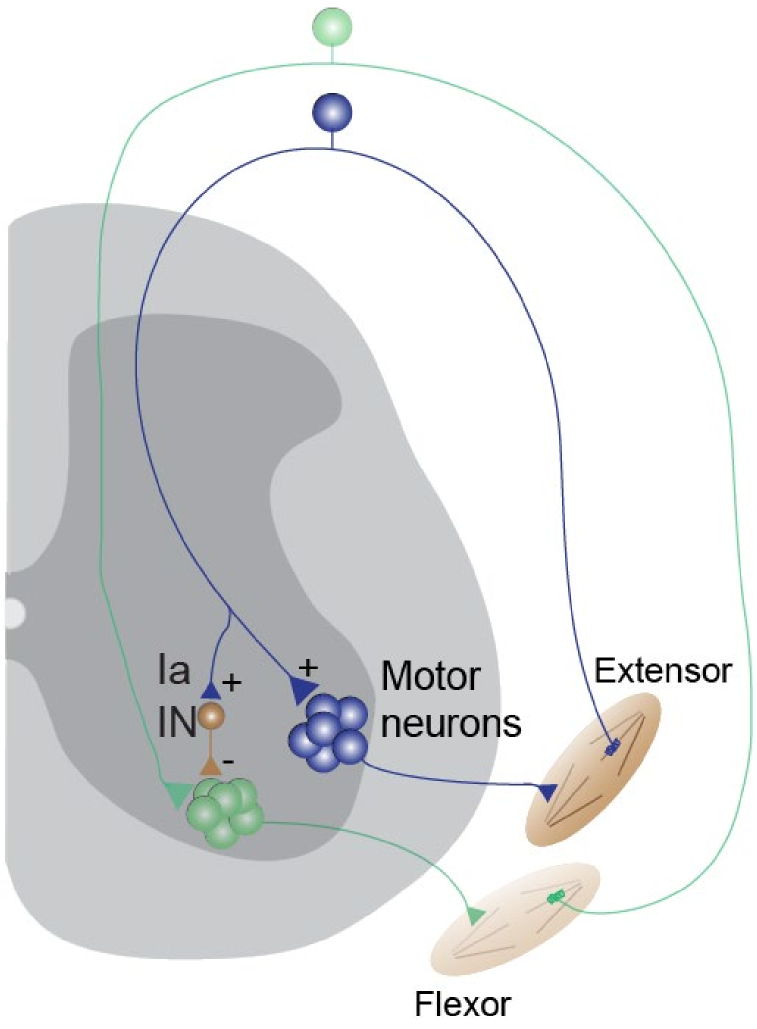


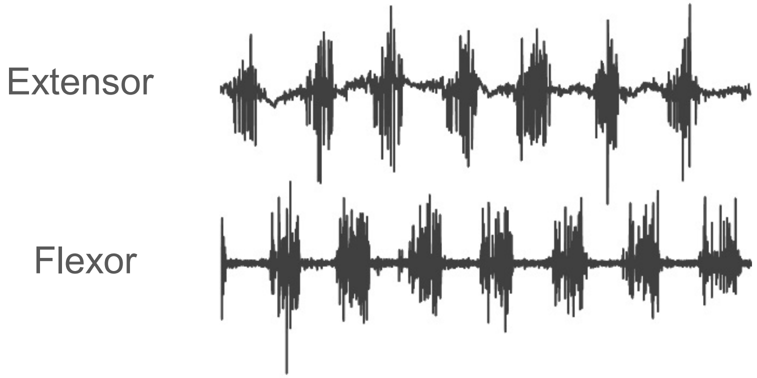
Rossignol and Bouyer, 2004

Build a rhythmic spinal circuit.....

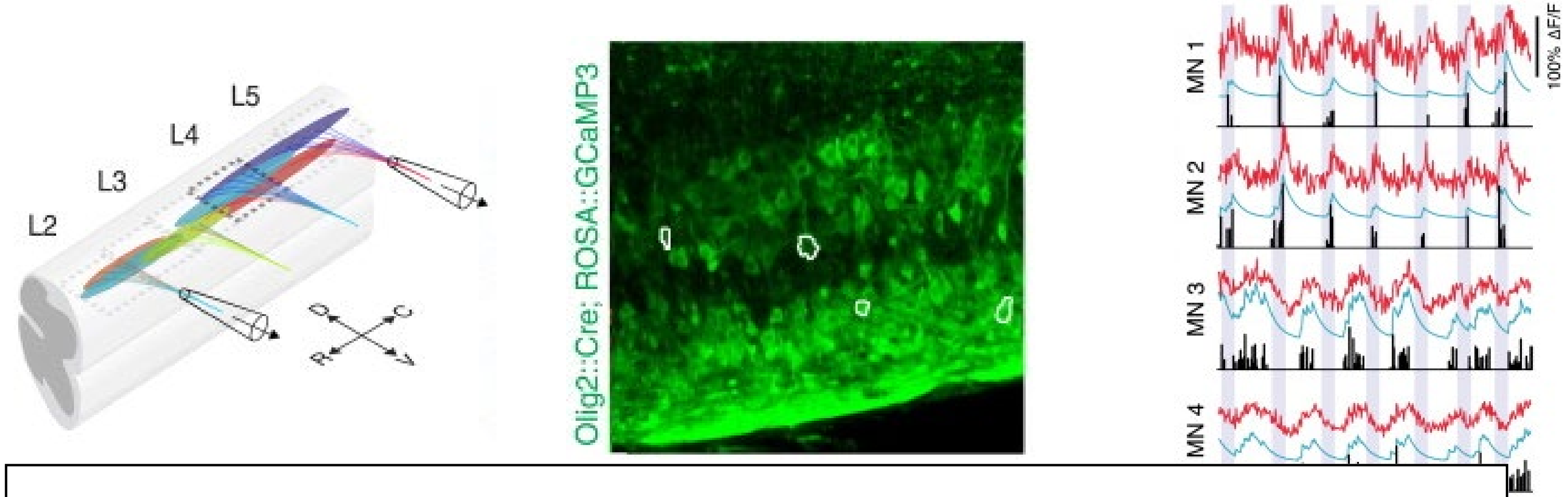


Sensory pathways could drive rhythmic firing in the spinal cord



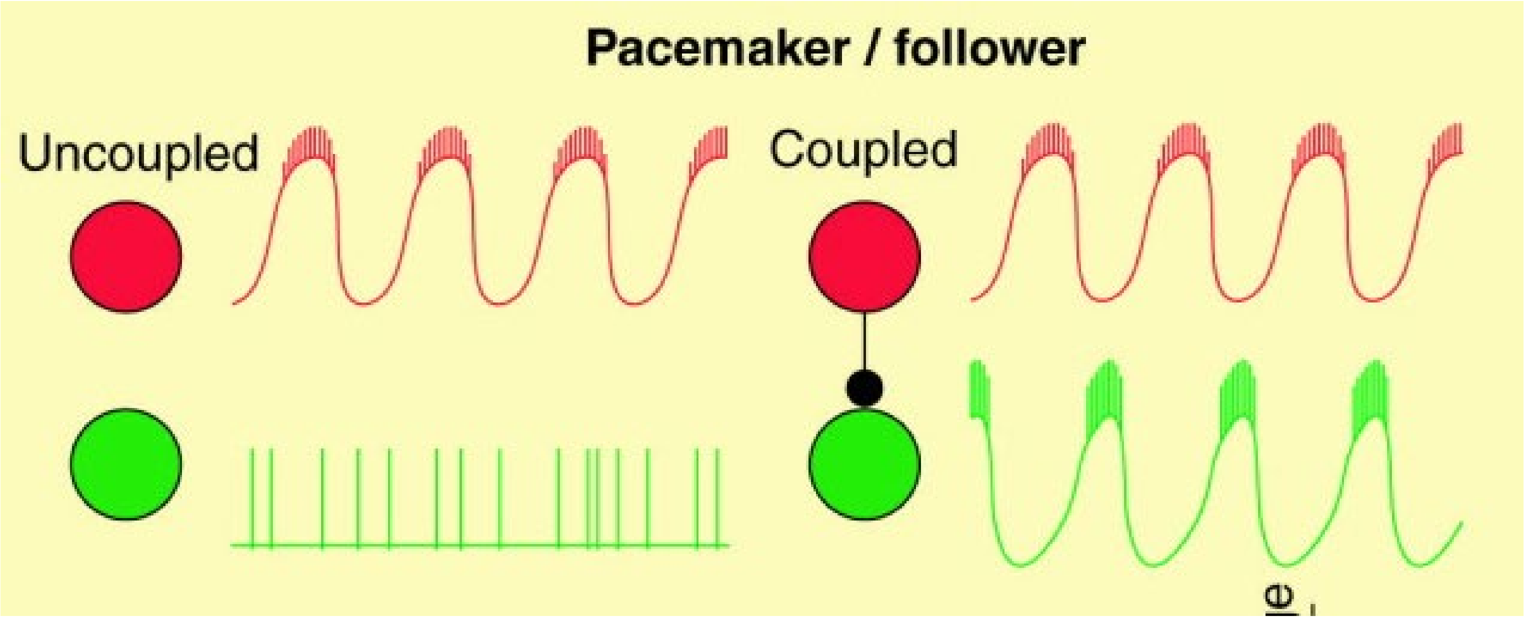


The spinal cord can generate rhythmic firing of motor neurons (in the absence of sensory feedback)



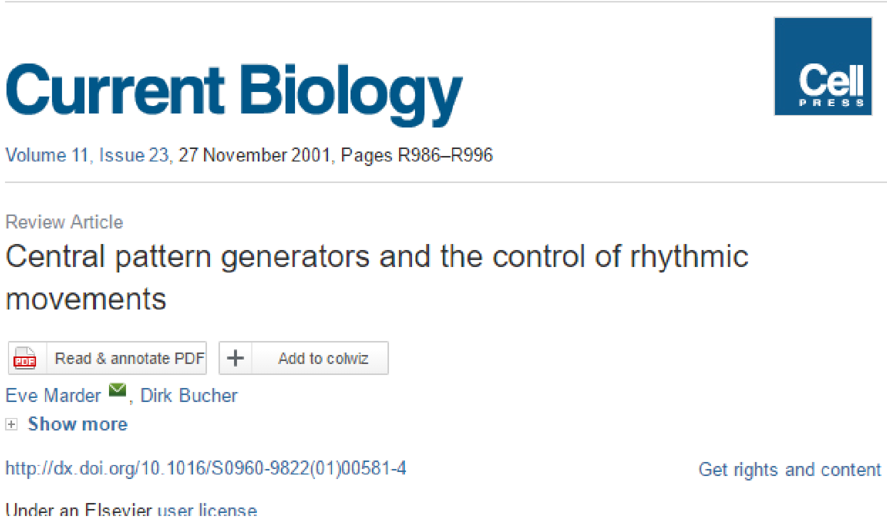
Machado et al., 2015

Pacemaker neurons



Crustacean stomatogastric ganglion

Respiratory centres



Current Biology
Volume 11, Issue 23, 27 November 2001, Pages R986–R996
Review Article

Central pattern generators and the control of rhythmic movements

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Eve Marder, Dirk Bucher

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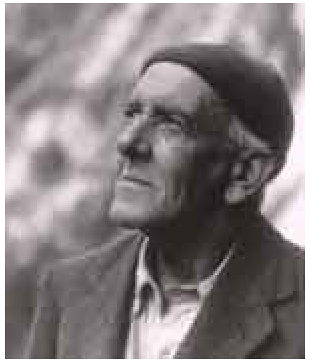
http://dx.doi.org/10.1016/S0960-9822(01)00581-4

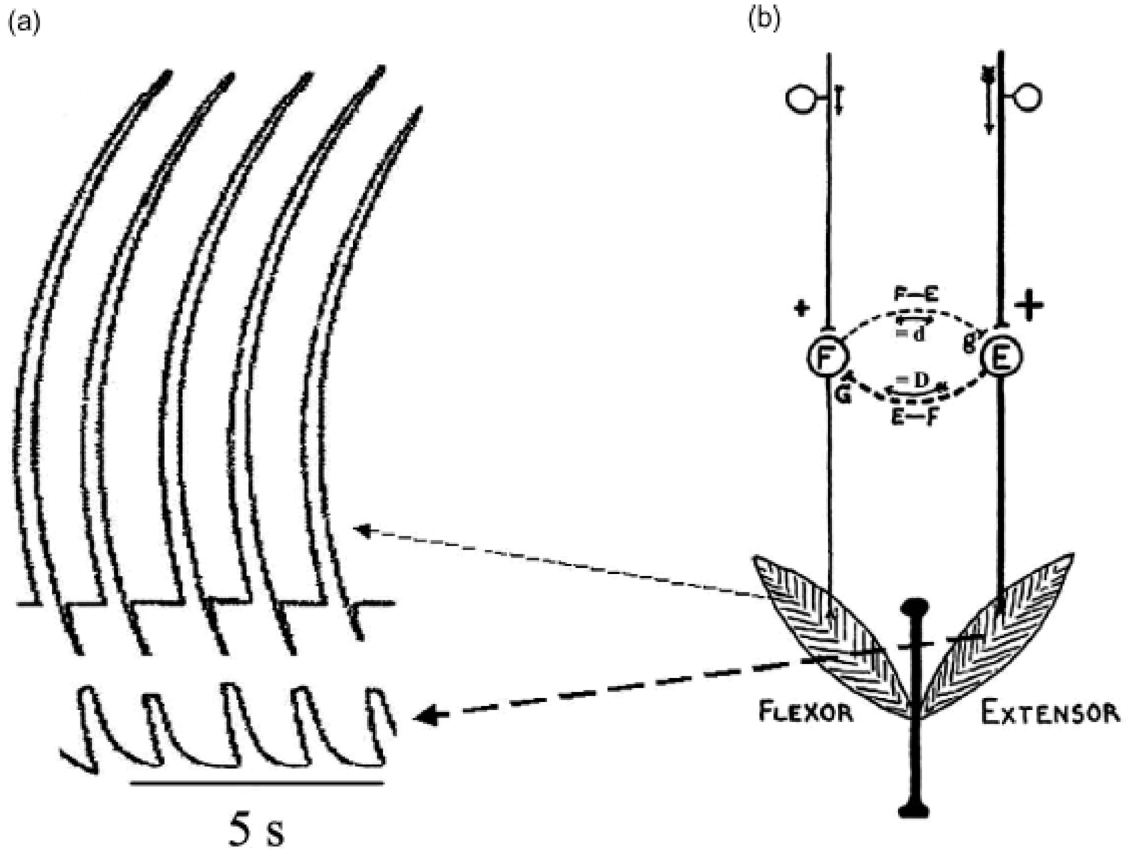
Locomotion is based on rhythmic movements generated in the spinal cord



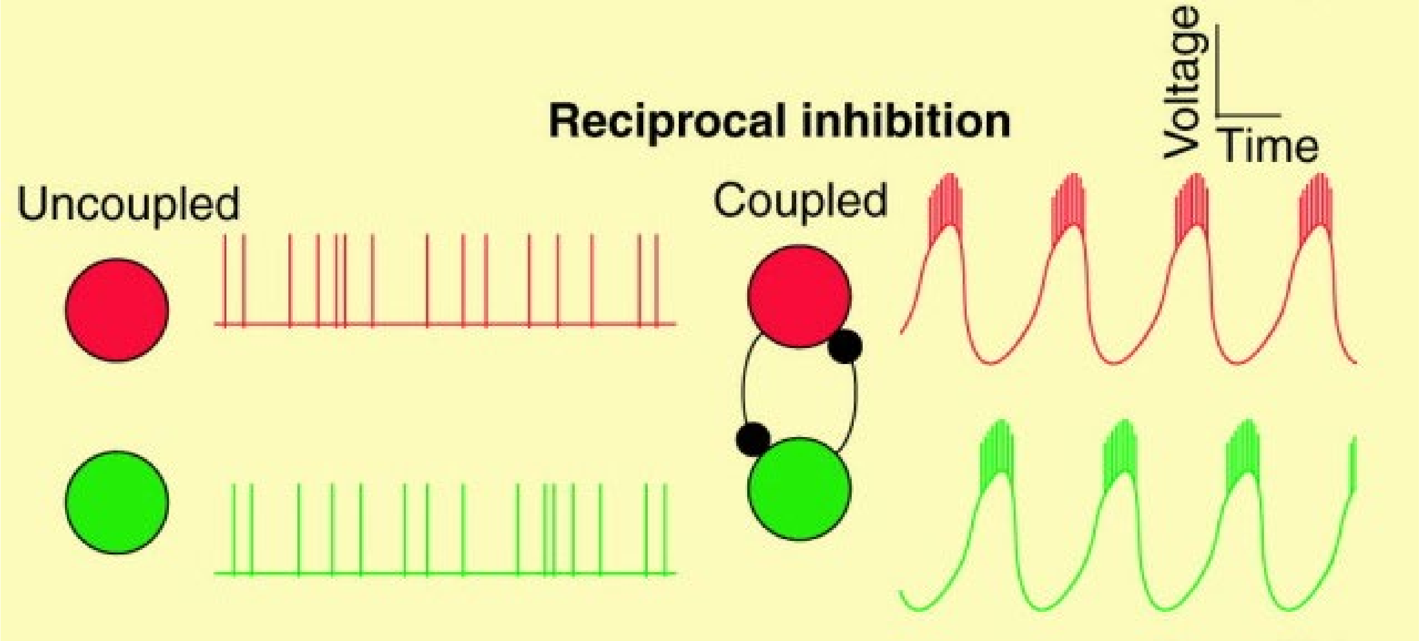
T. Graham Brown

8. The experiments seem to show that the fundamental unit of activity in the nervous system is not that which we term the spinal reflex. They show the independence of the efferent neurone, and suggest that the functional unit is the activity of the independent efferent neurone; or rather, that it is the mutually conditioned activity of the linked antagonistic efferent neurones ("half-centres") which together form the "centre": and they also suggest that the primitive activity of the nervous system is seen in such rhythmic acts as progression and respiration.

Brown, 1914



Reciprocal inhibition



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Eve Marder, Dirk Bucher
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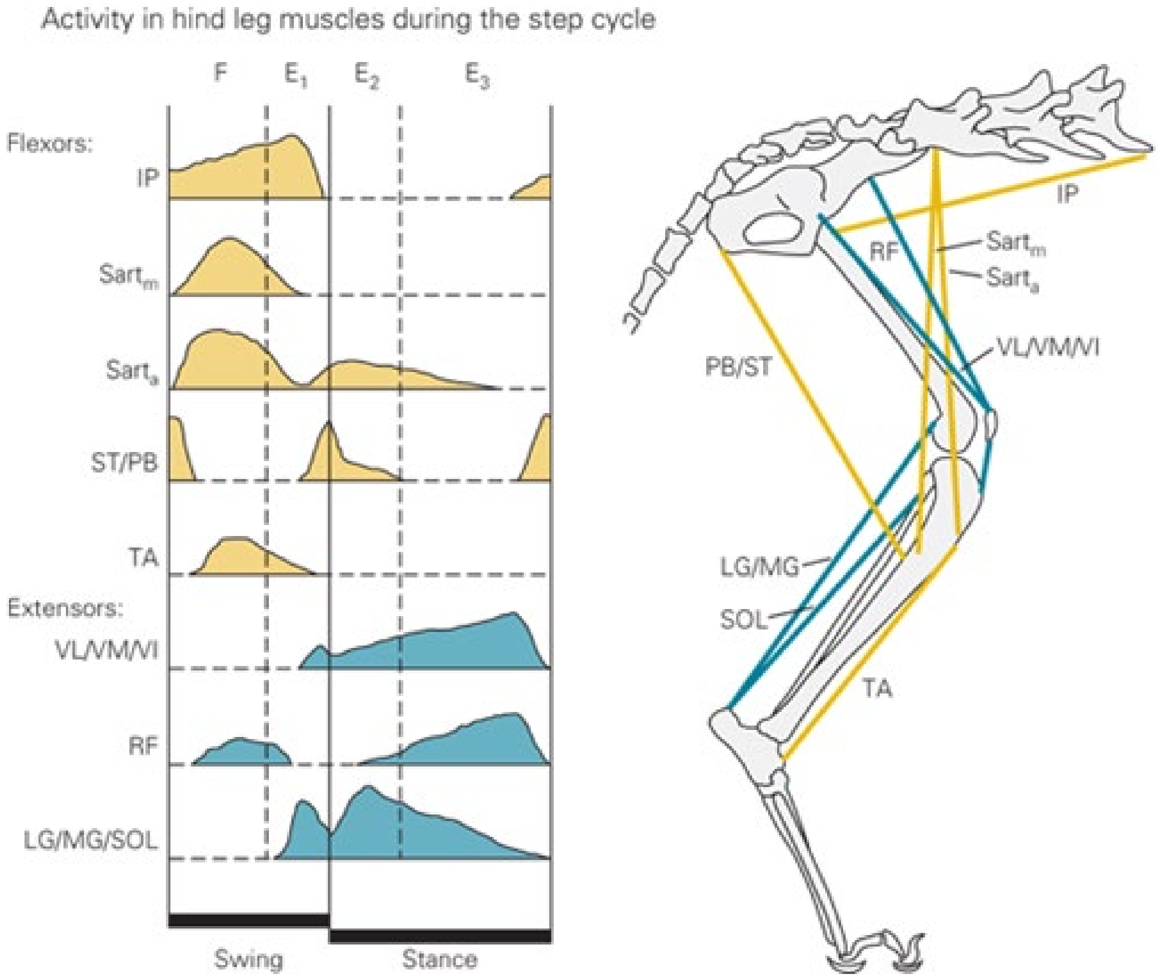
The unit burst generator as an alternative to the half-centre model



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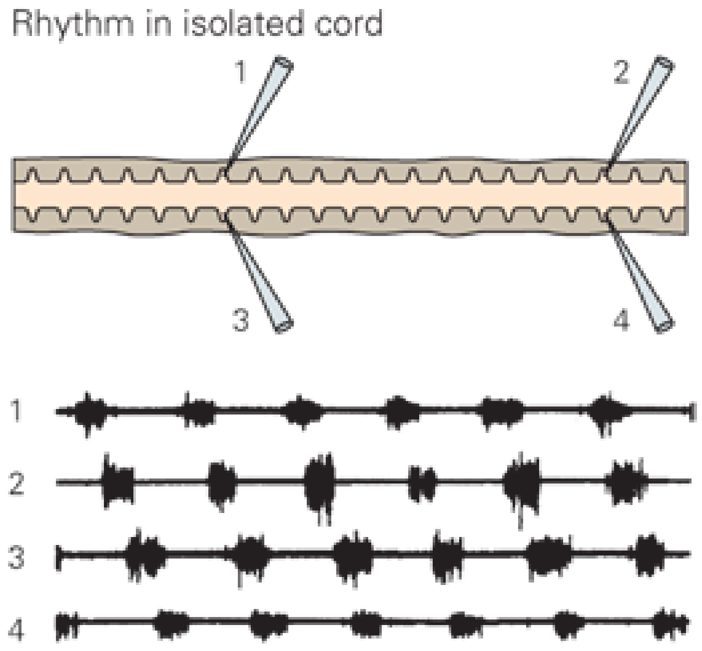
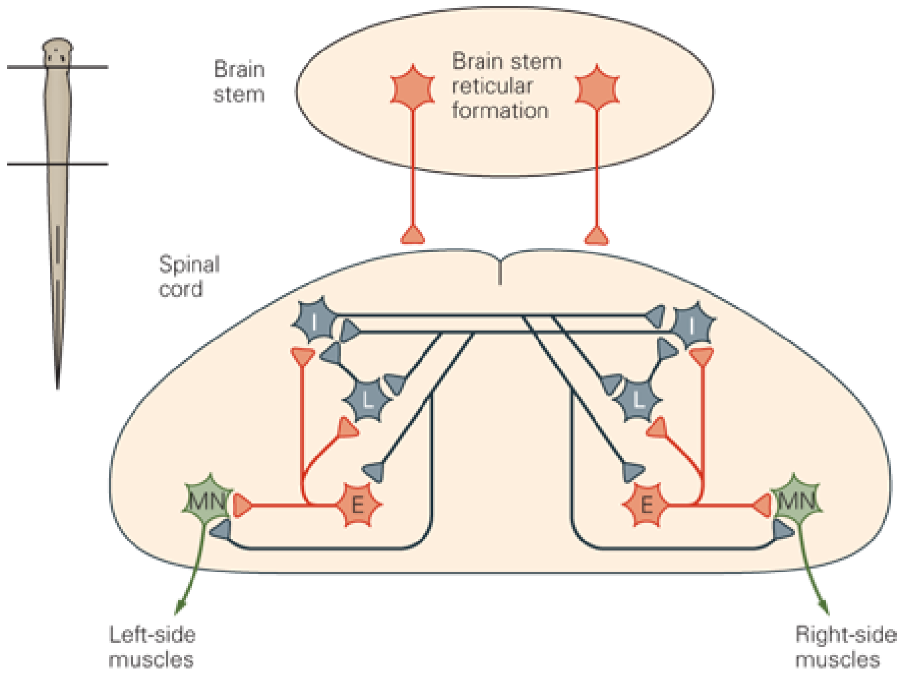
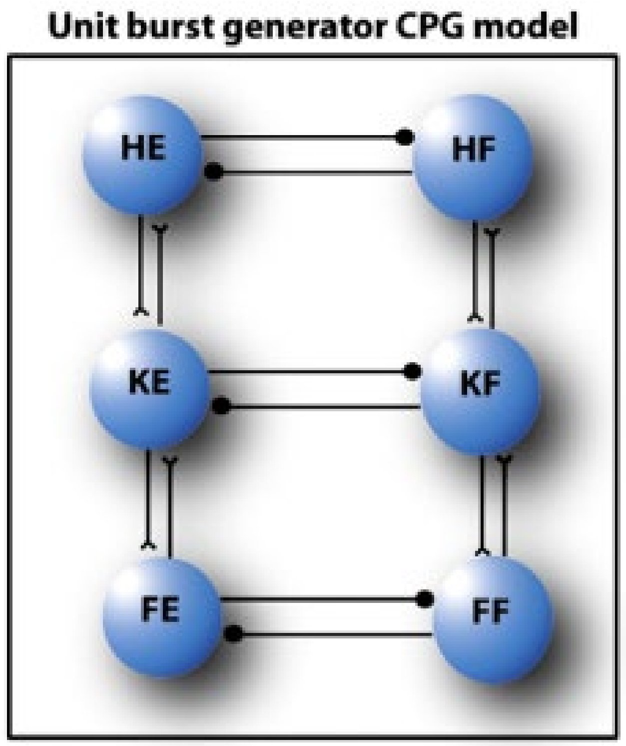
The unit burst generator as an alternative to the half-centre model

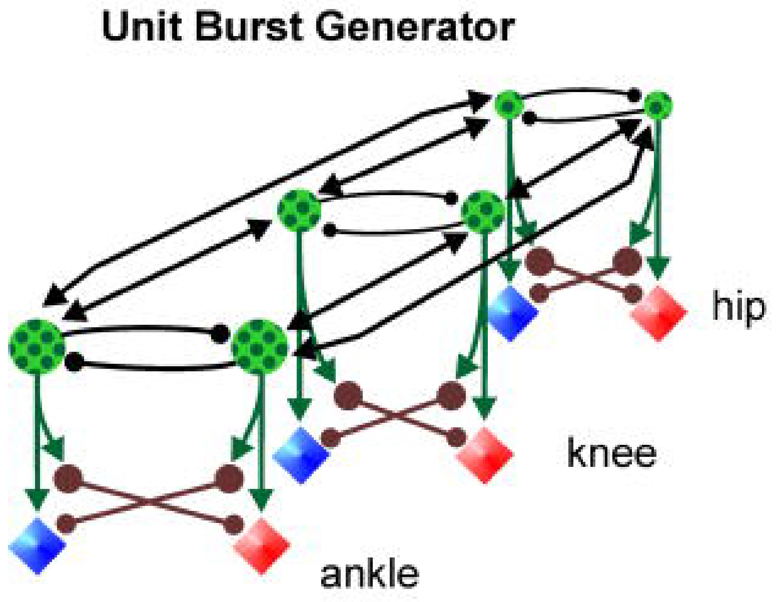




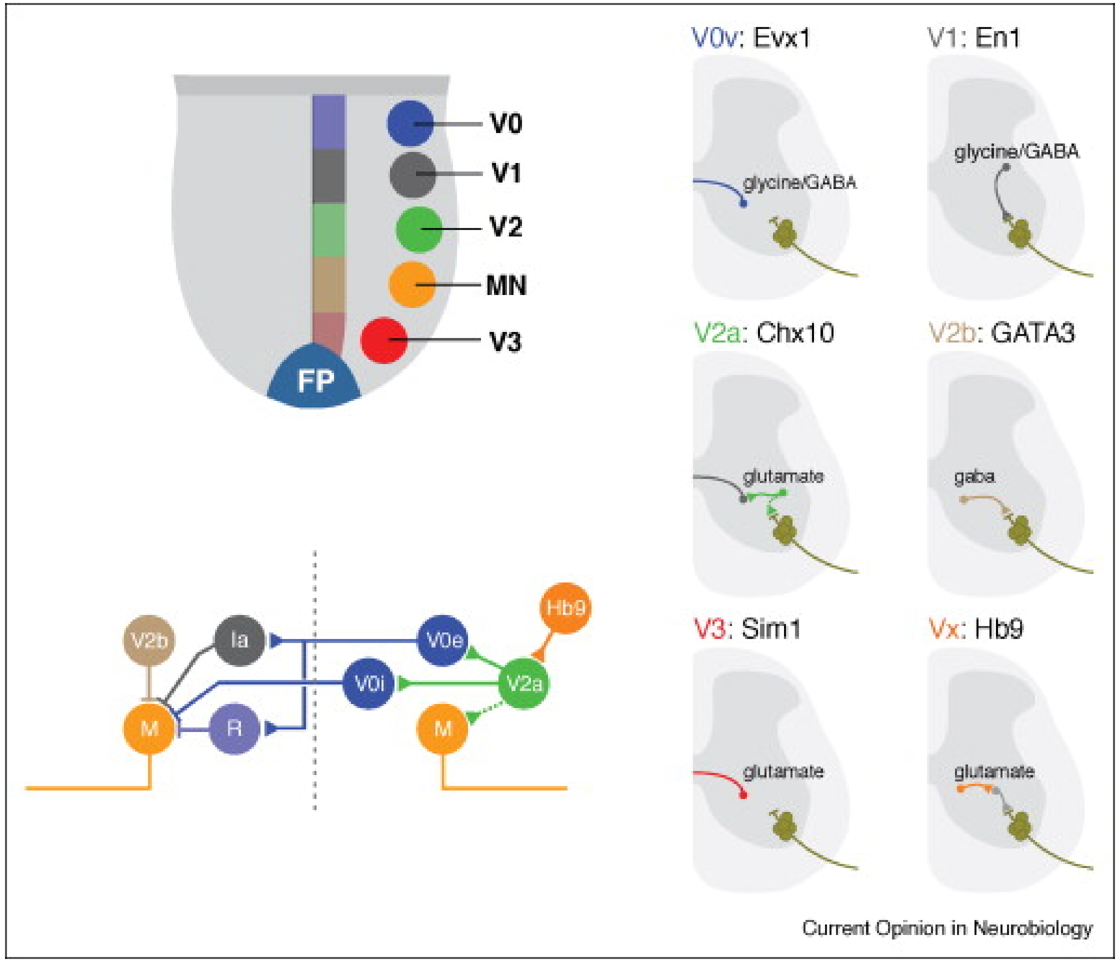
Grillner

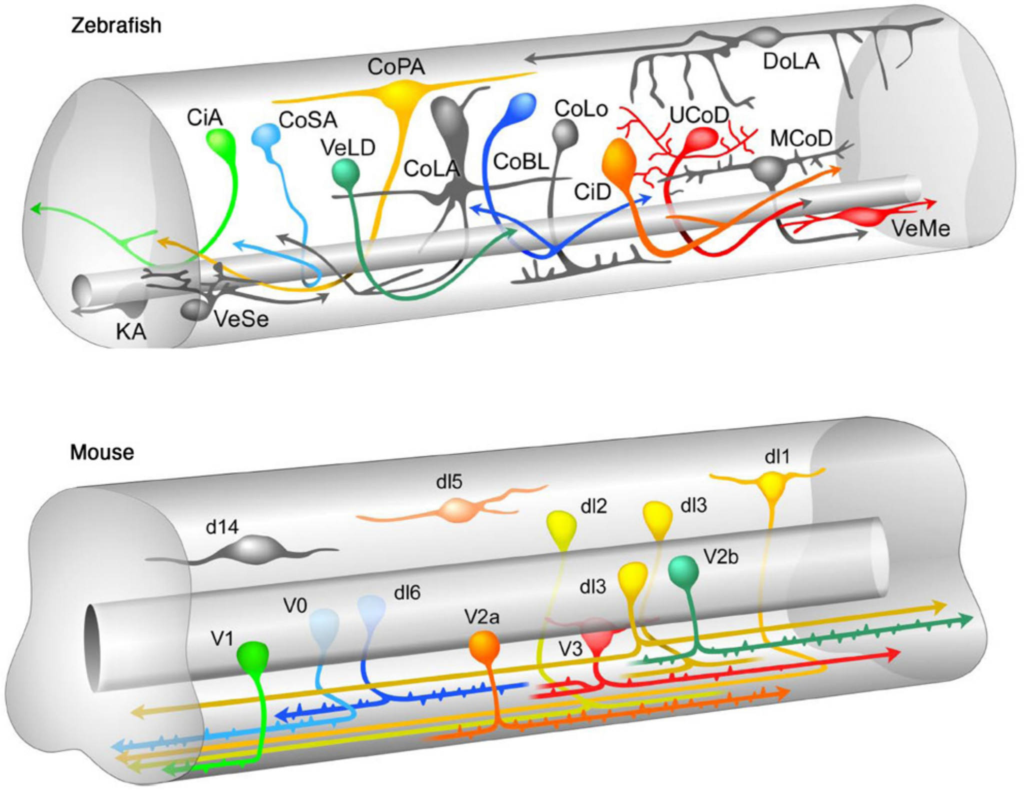
The unit burst generator as an alternative to the half-centre model





The diversity of spinal interneurons – how many types are there?





Reading: Goulding, 2009. Nat. Rev. Neurosci.
Circuits controlling vertebrate locomotion: moving in a new direction.

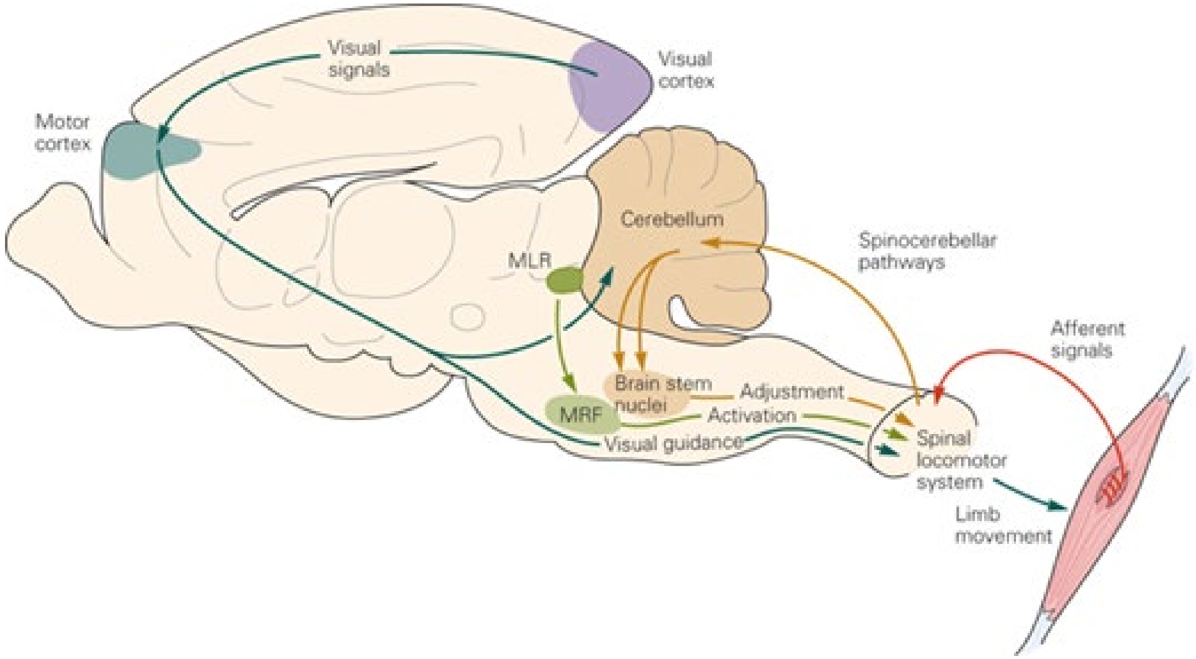
Bikoff et al., 2016. Spinal Inhibitory Interneuron Diversity Delineates Variant Motor Microcircuits. Cell. 165: 207-219

Why do we need a brain?

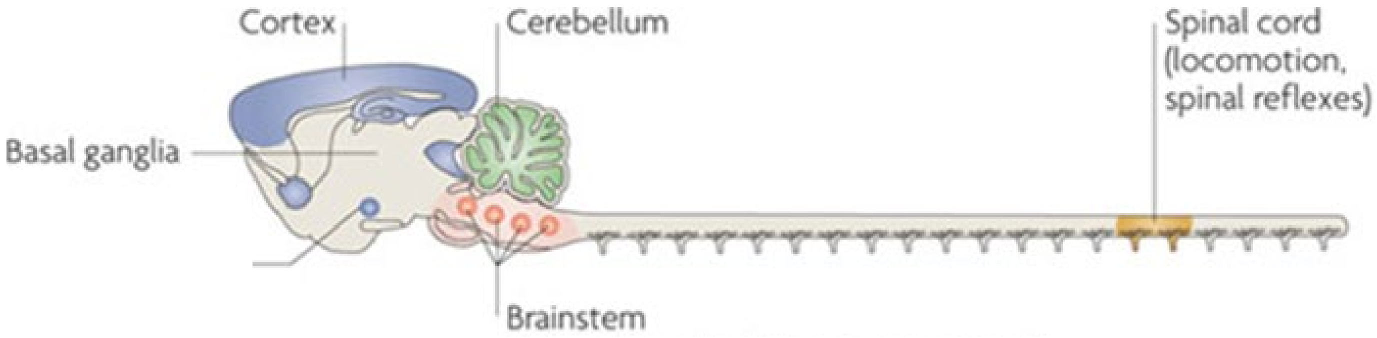
1. To start/stop locomotion

2. To adjust ongoing motor commands

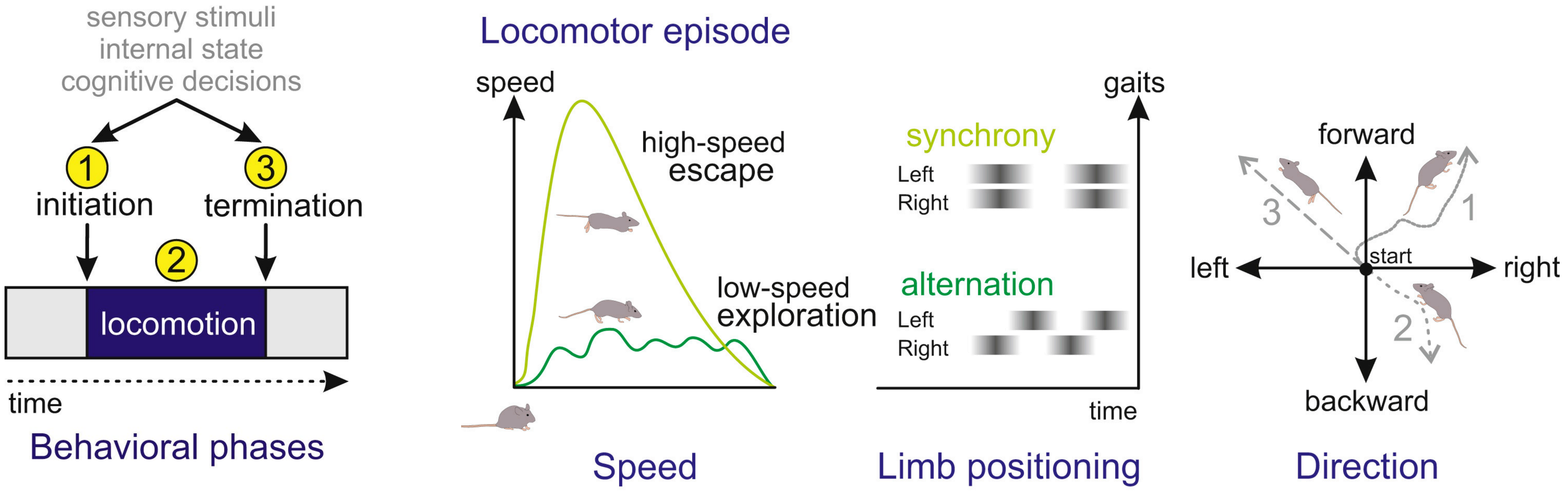
3. When we want conscious control over our movements



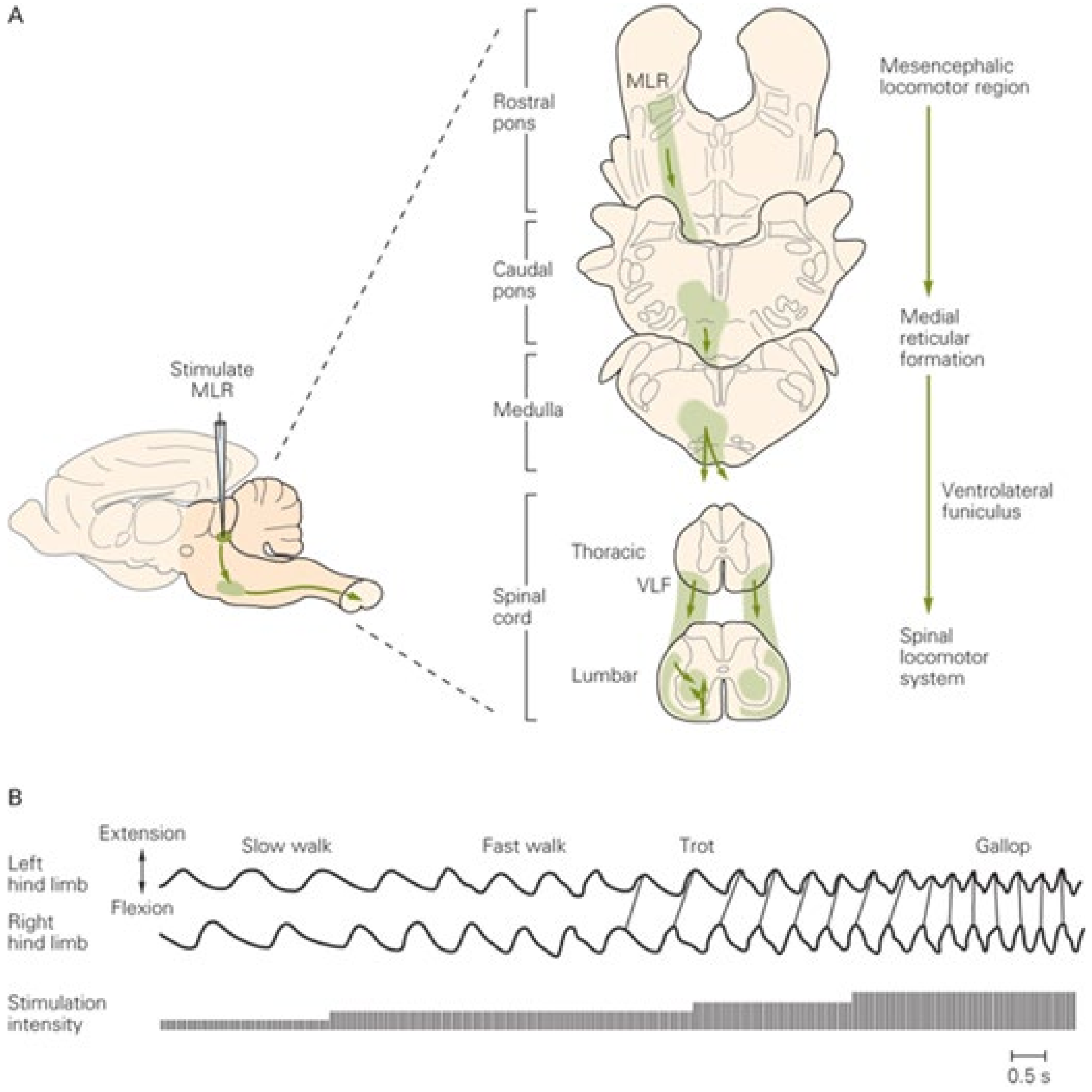
Starting locomotion– the MLR



Locomotor transitions and choosing a gait



Activation of spinal CPGs – the mesencephalic locomotor region



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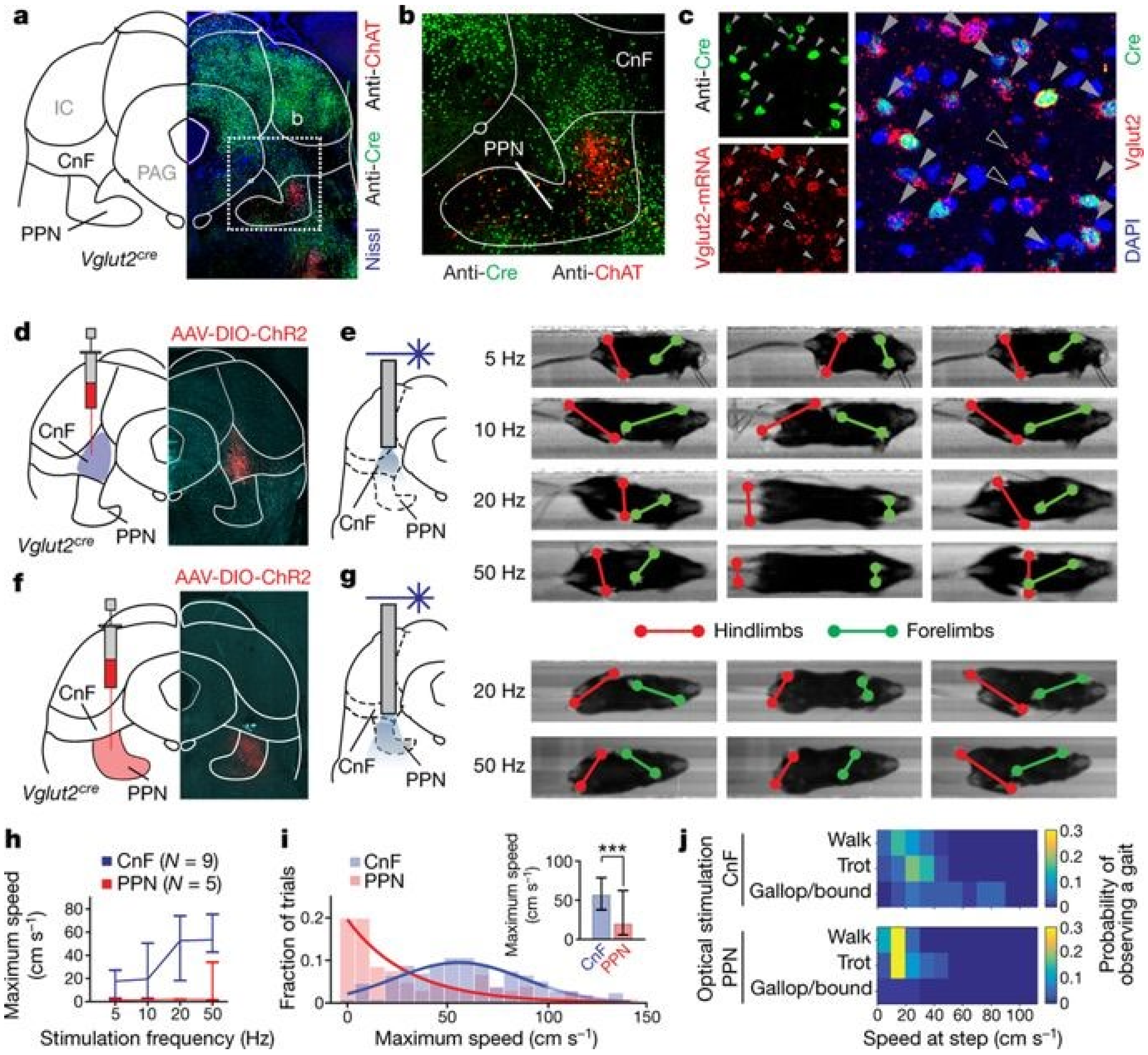
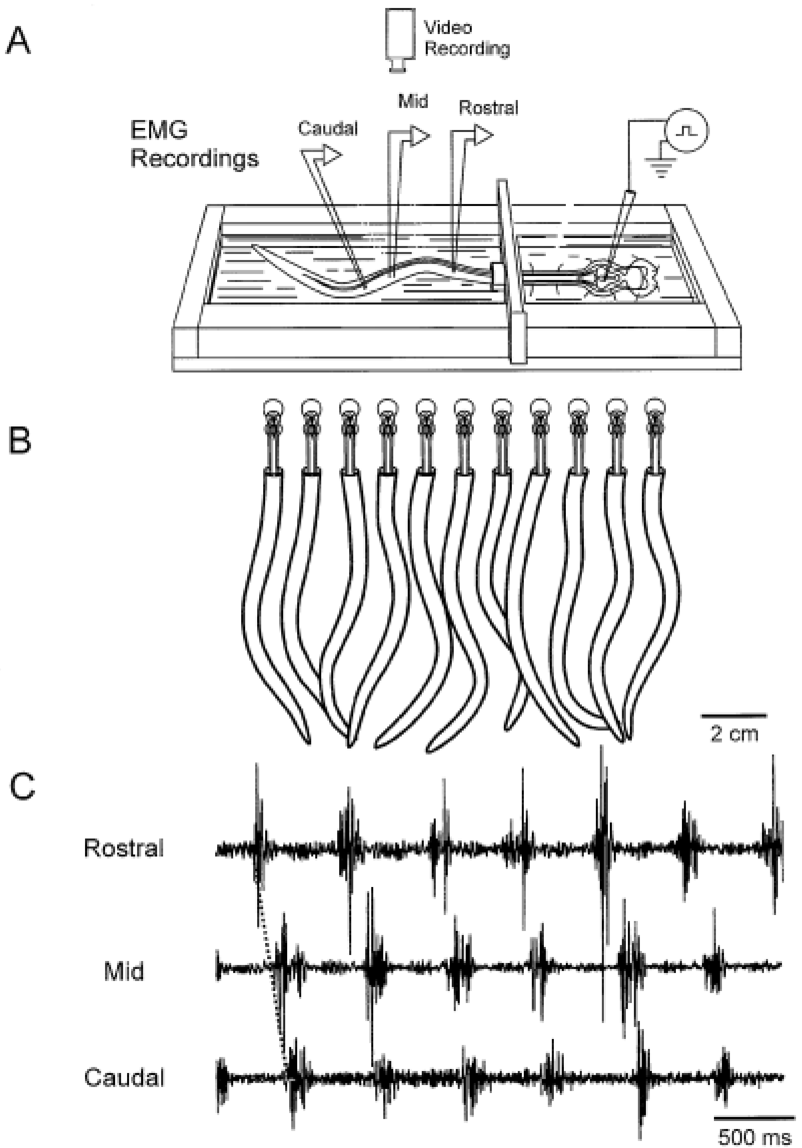
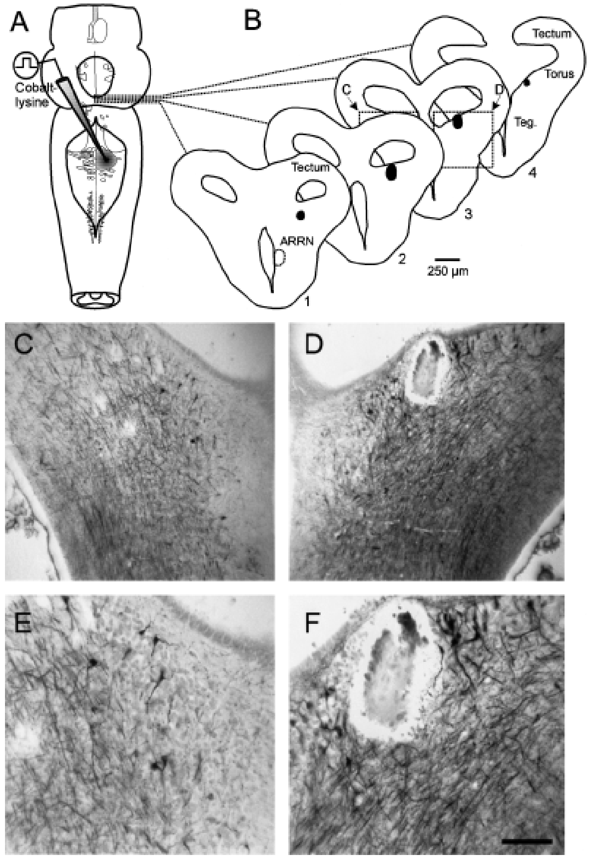


Reading:
Caggiano et al., 2018
Nature 553:445-460

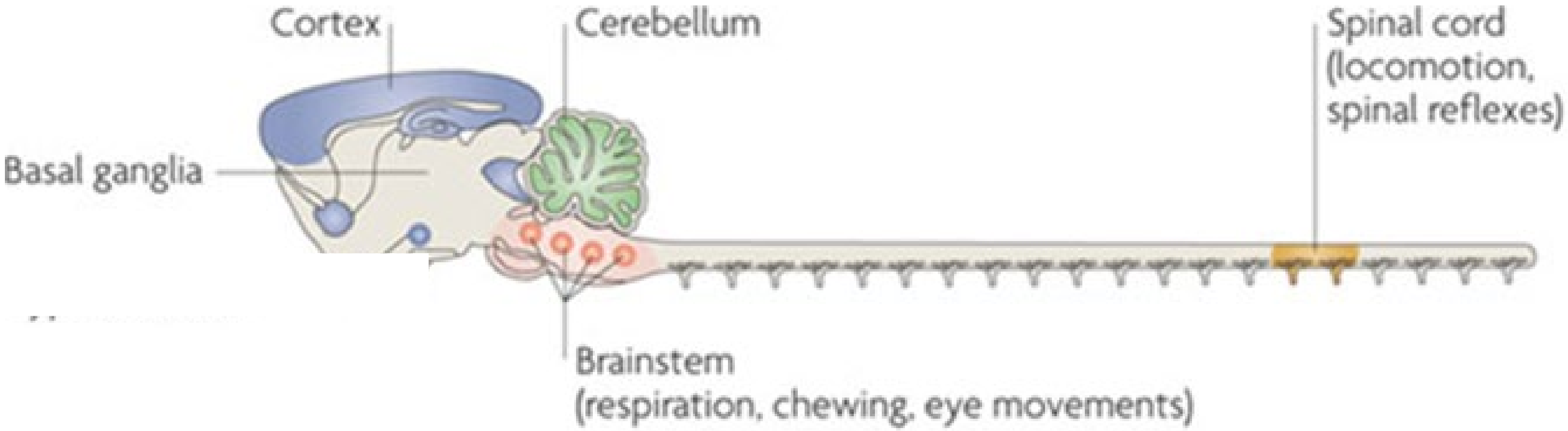
The MLR is conserved across species





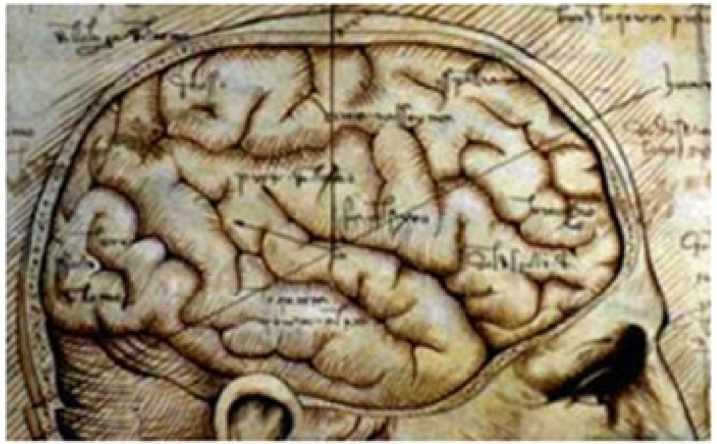
Sirota et al., 2000

Adapting the spinal rhythm via descending brainstem pathways



Descending pathways modify and modulate spinal circuits

a snapshot of 27 descending tracts….



“classical”

cortico- rubro- tecto- reticulo- vestibulo- thalamo-

“modulatory”

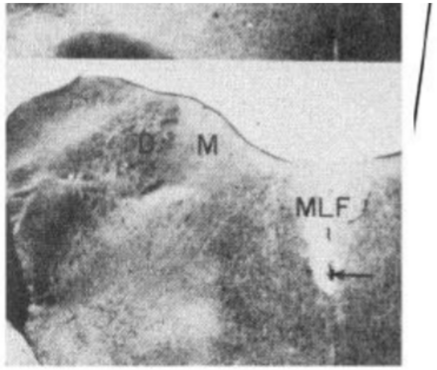
coeruleo- raphe-

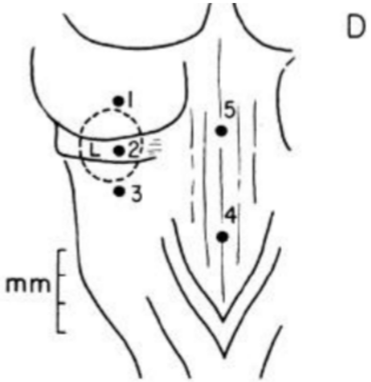
Reading: Ferreira-Pinto et al., 2018. Neuron. Connecting circuits for supraspinal control of locomotion.

Reticulospinal pathways

excite both extensors and flexor motor neurons

4





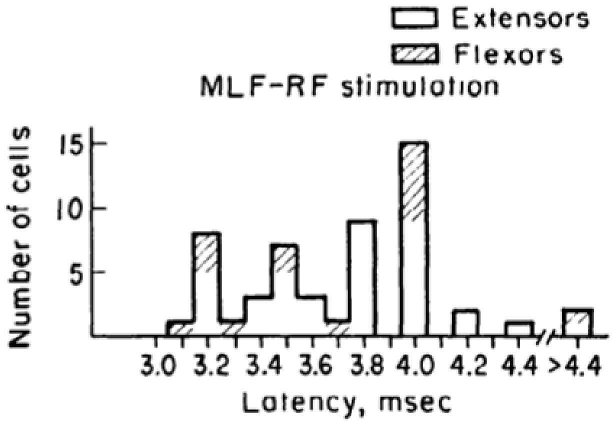


TABLE 1. *Effect of stimulation of Deiters' nucleus and medial longitudinal fasciculus (MLF-RF) on hindlimb motoneurons*

	Extensors				Flexors	
	GS	FDL-PL	BASM	PLANT	BST	PER
Monosynaptic EPSP						
Deiters' only	14/38	1/25	0/10	1/5	0/13	0/10
MLF-RF only	10/38	16/25	10/10	2/5	10/13	9/10

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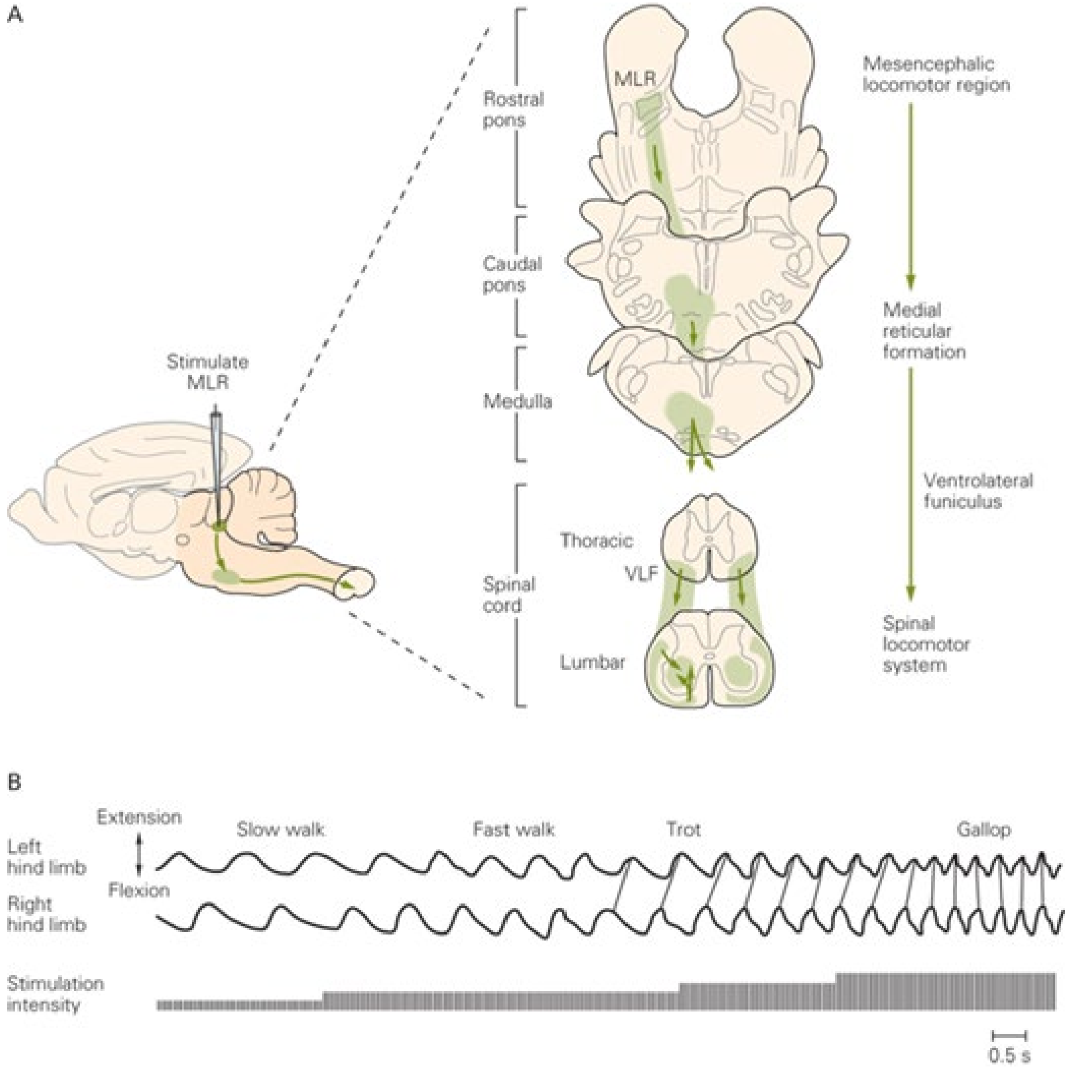
Wilson and Yoshida, 1969

Reticulospinal pathways – the command neurons for movement (?)



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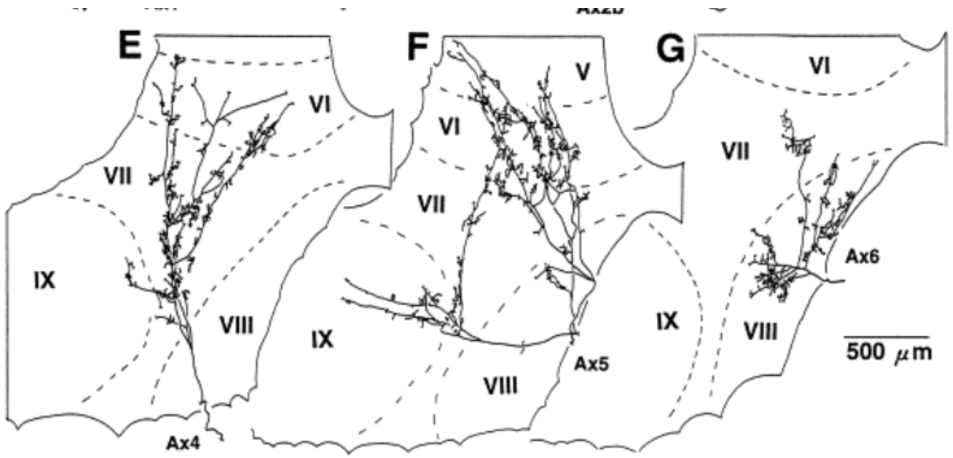
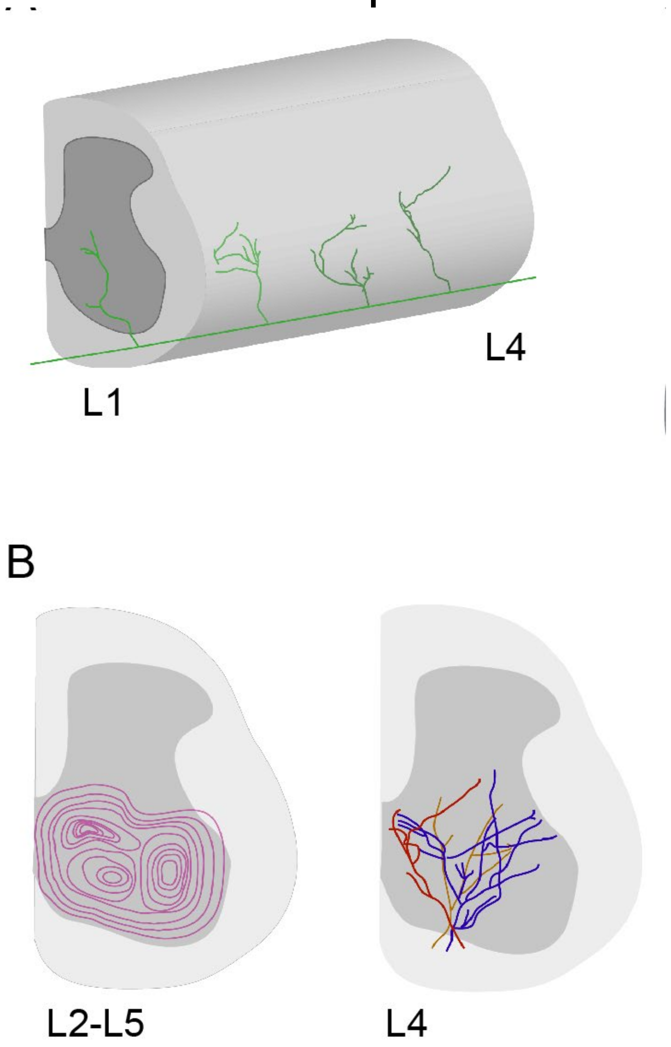
Individual descending axons can influence multiple spinal circuits

Reticulospinal



Peterson et al., 1975

Vestibulospinal



Witts and Murray, 2019

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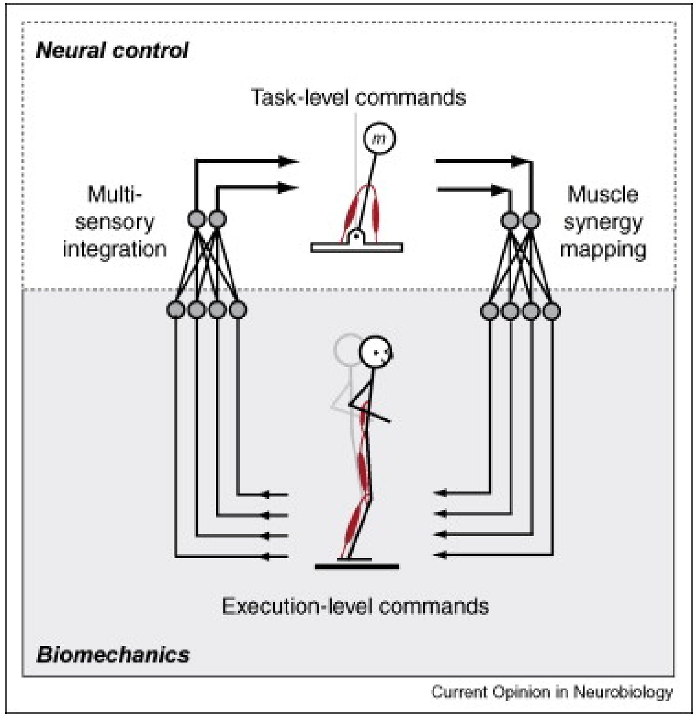
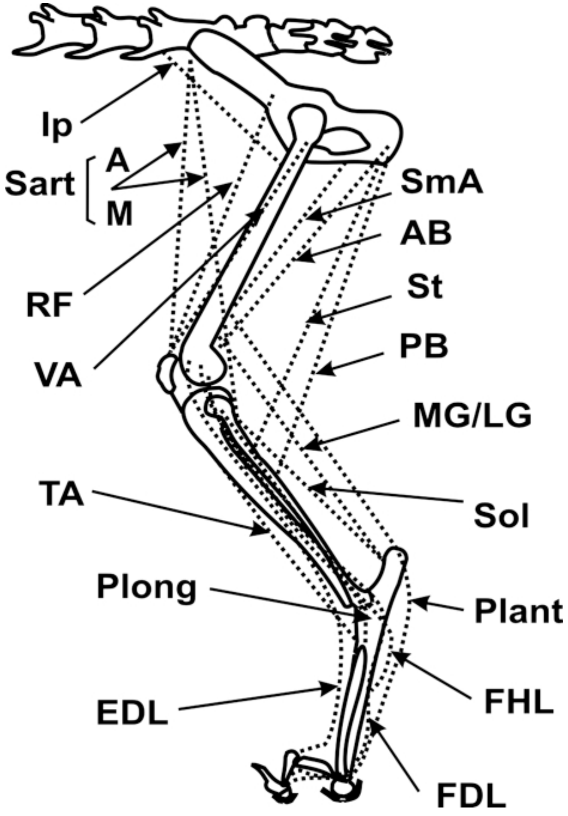
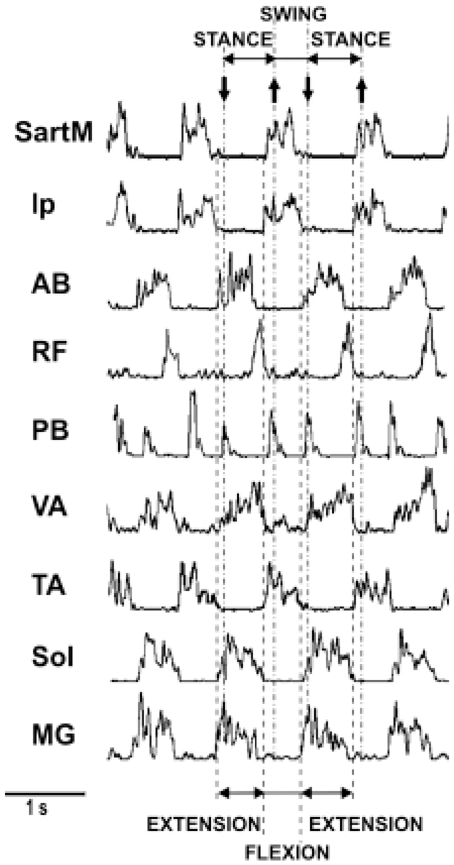
The nervous system (probably) doesn't care about individual muscles







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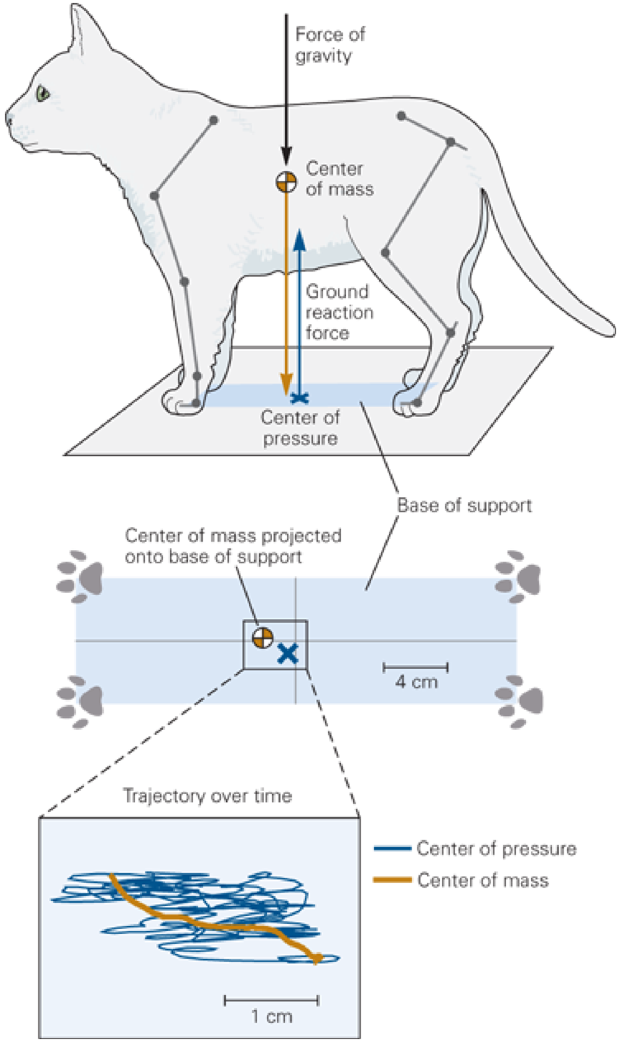
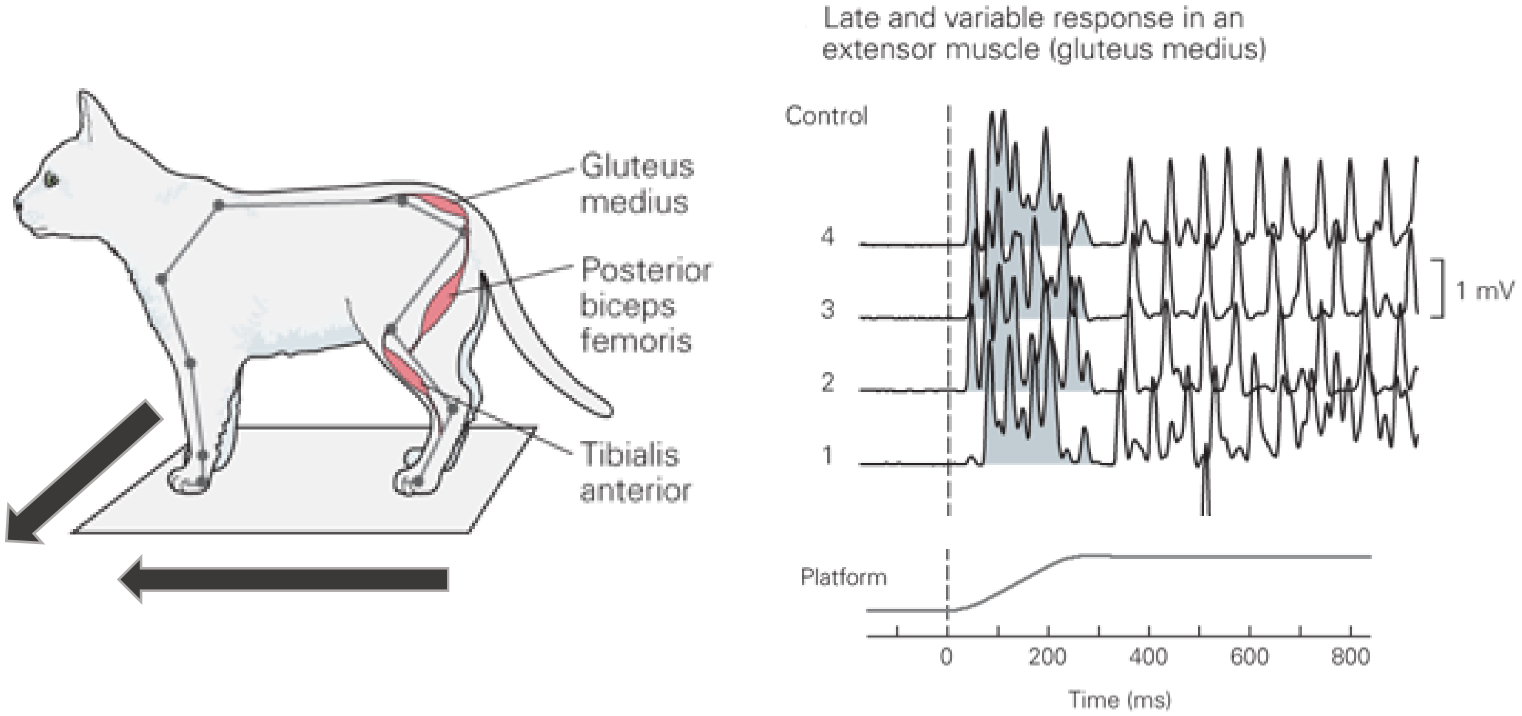
Markin et al., 2012; Ting and McKay, 2007

Adaptable movement

Postural control is an active process that requires descending commands

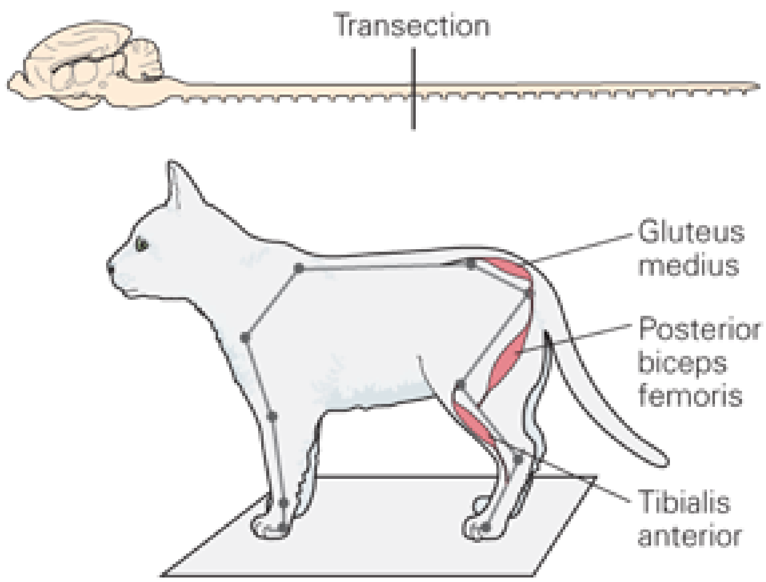


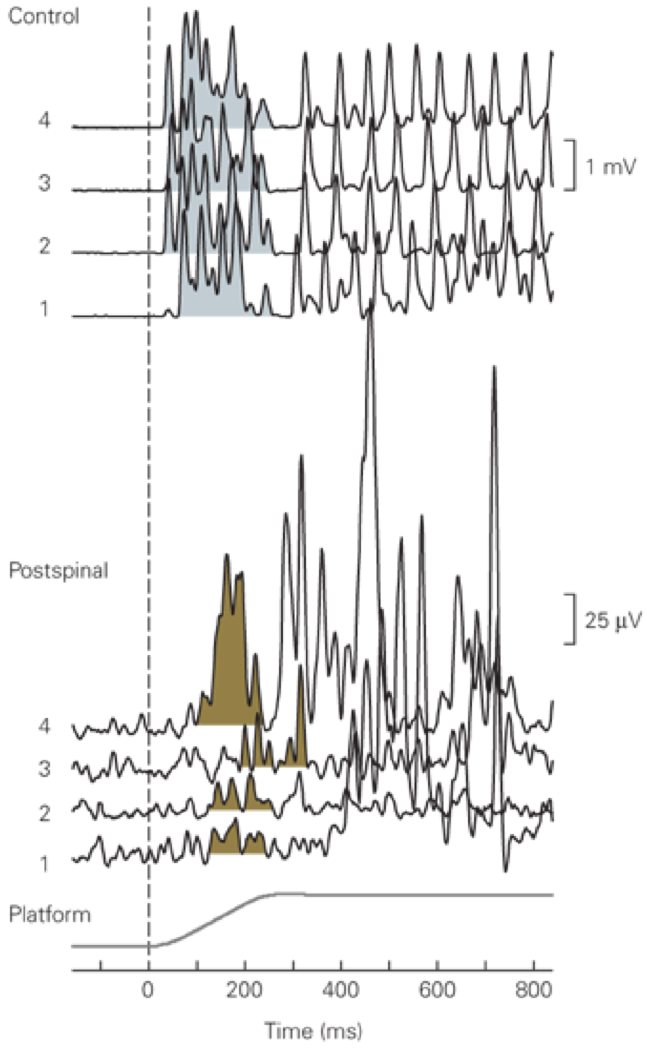
Postural control is an active process that requires descending commands



Macpherson and Fung, 1999

Postural control is an active process that requires descending commands





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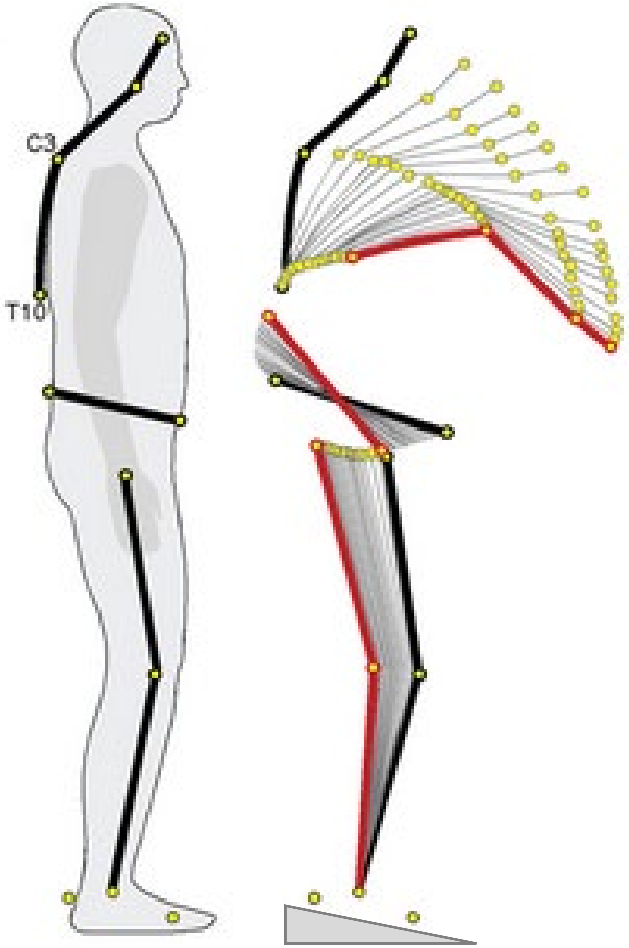
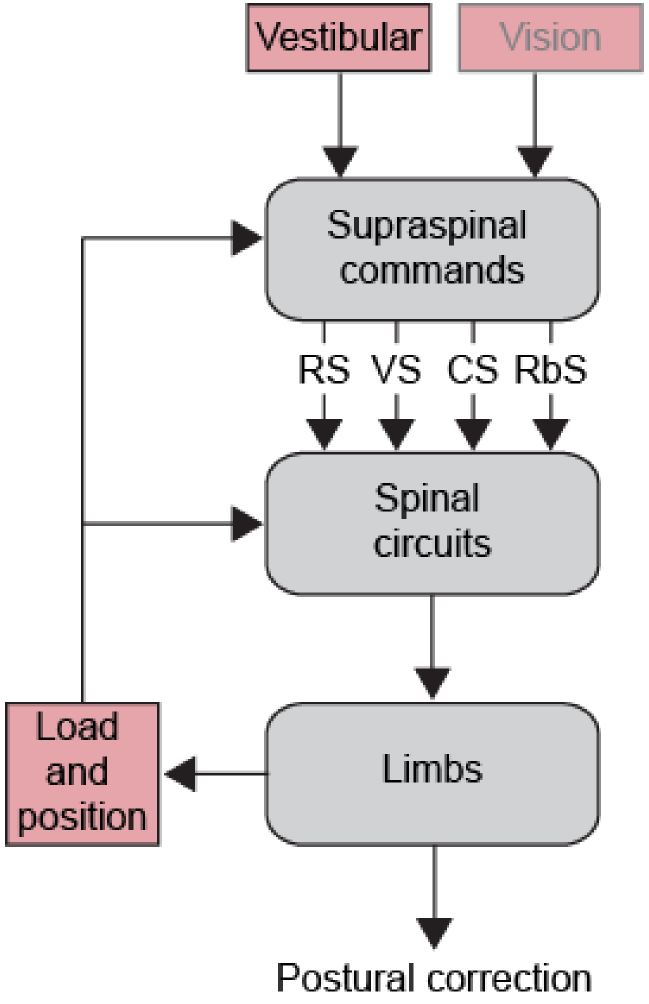
Postural control and balance – you only notice when it's not there

Courtesy of Prof. Fay Horak, OHSU

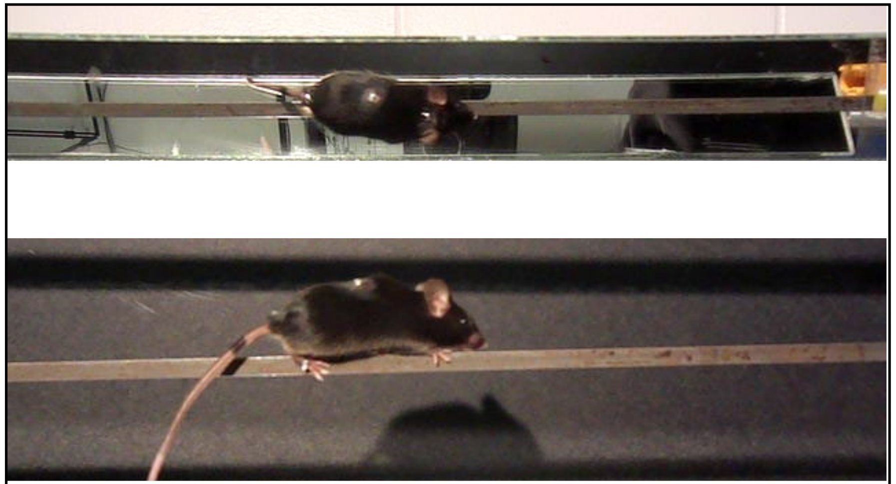


Postural pathways

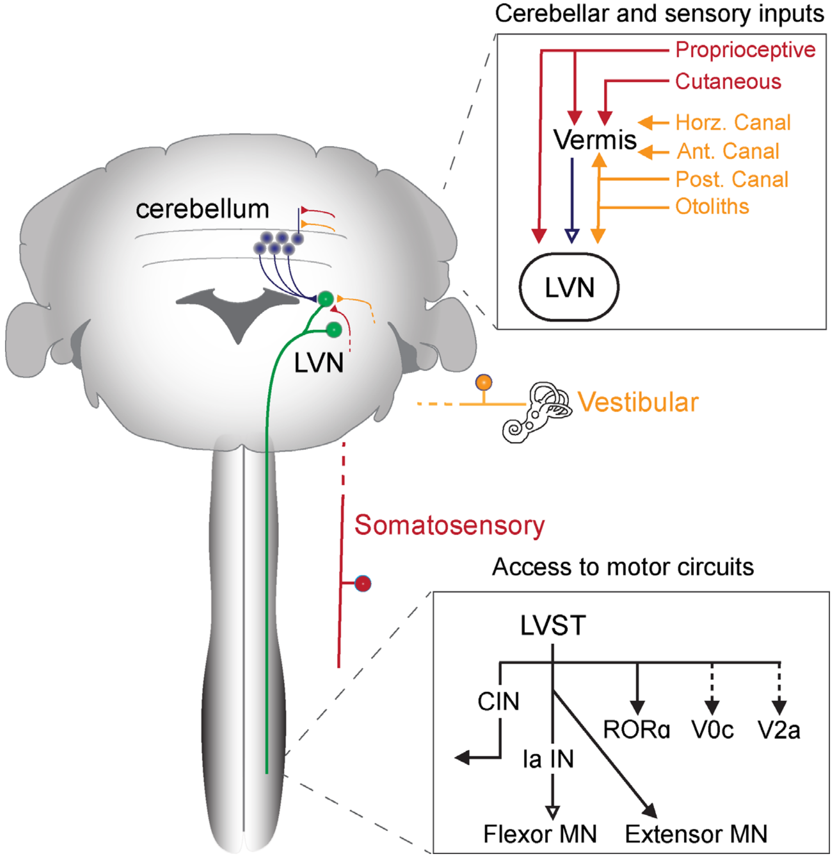


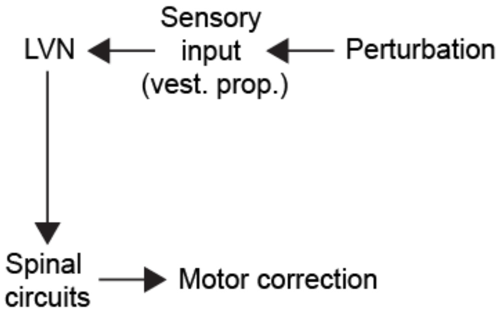
Deliagina et al., 2014

Responding to unexpected perturbations – the lateral vestibular nucleus



Control



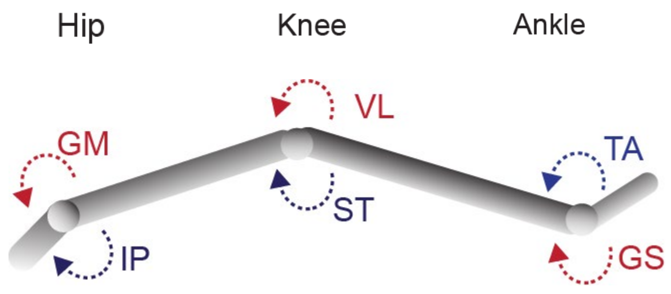


Mu

Witts and Murray, 2019

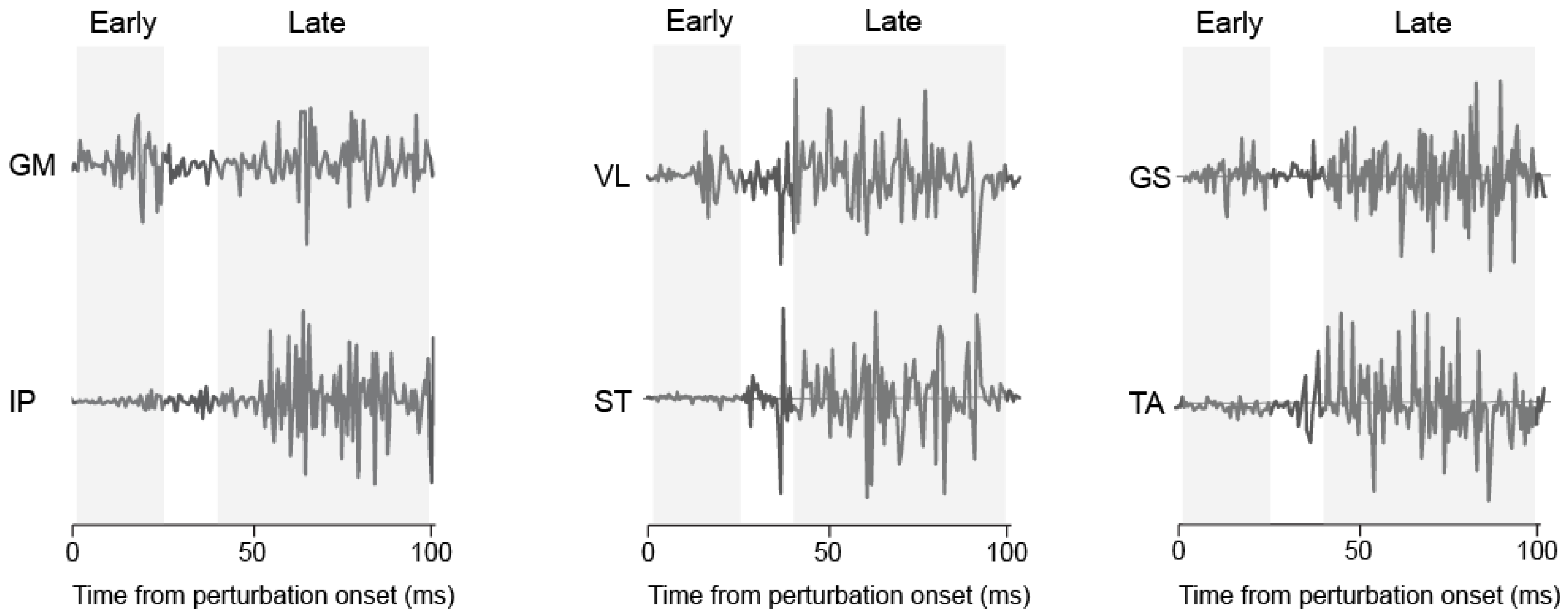
Behaviourally relevant motor programmes maintain posture

Hindlimb muscles

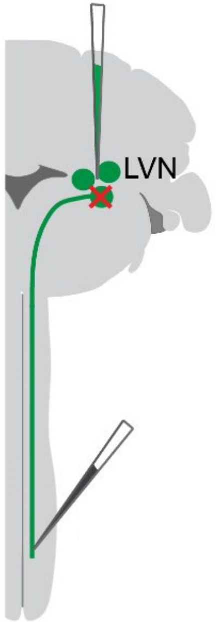


Extensors Flexors

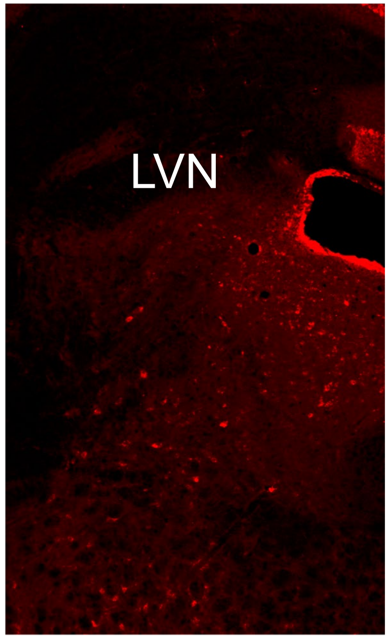
EMG response to perturbation



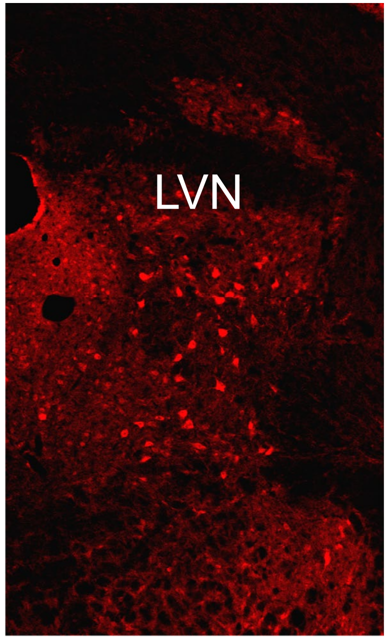
LVST-neurons are required for postural corrections after a perturbation



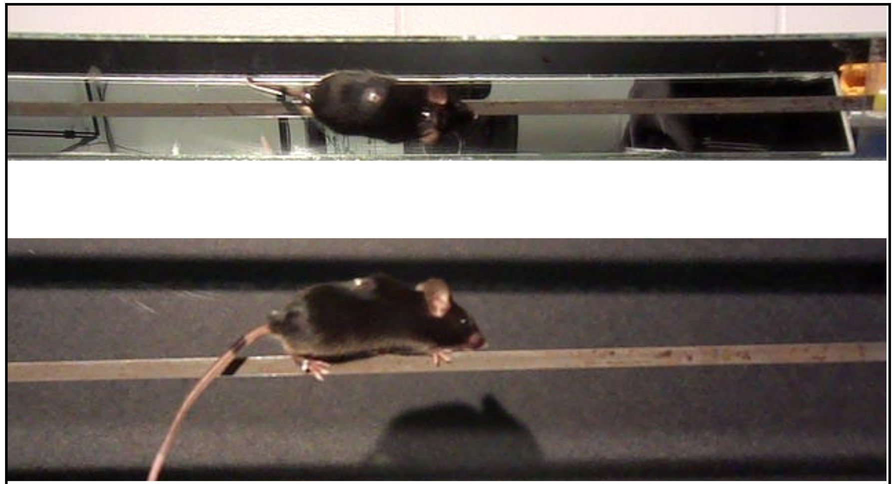
Fluorogold (lumbar SC)



Ipsilateral



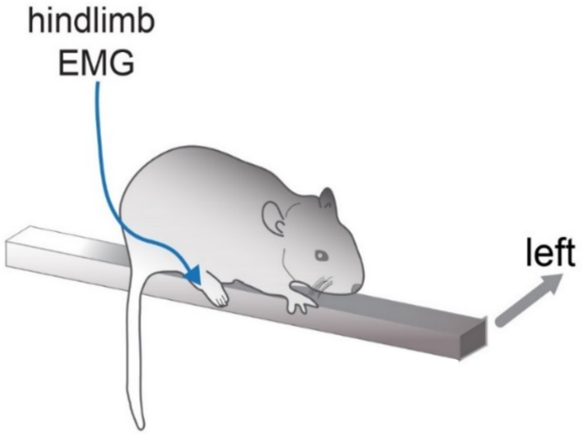
Contralateral



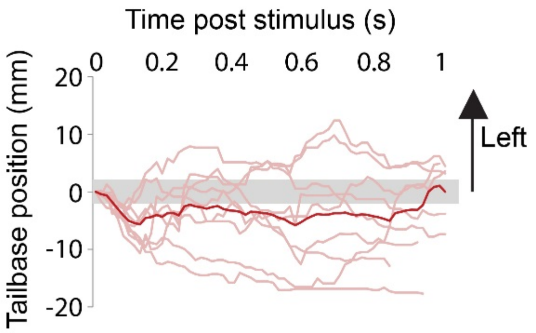
Control

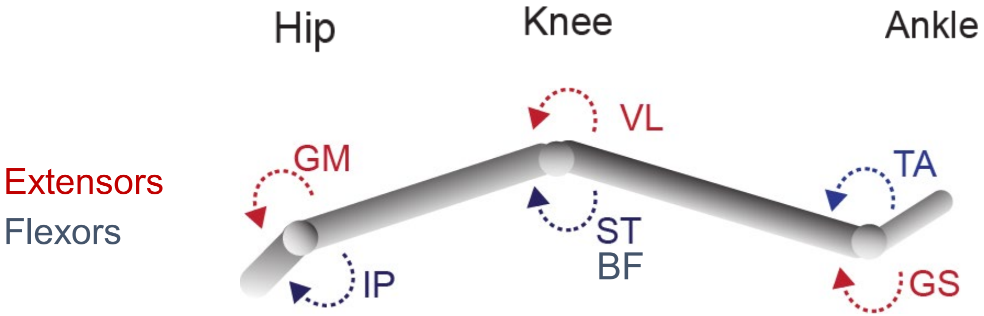
Mu

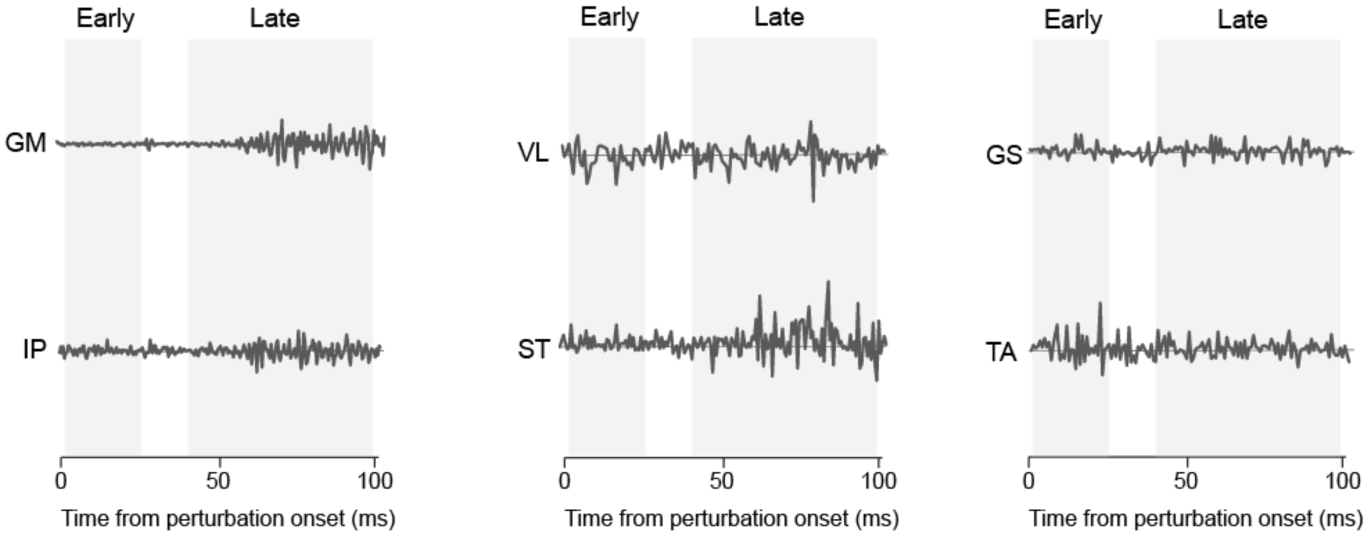
LVST-neurons are required for postural corrections after a perturbation



LVN^{lumbar} ablation (right)

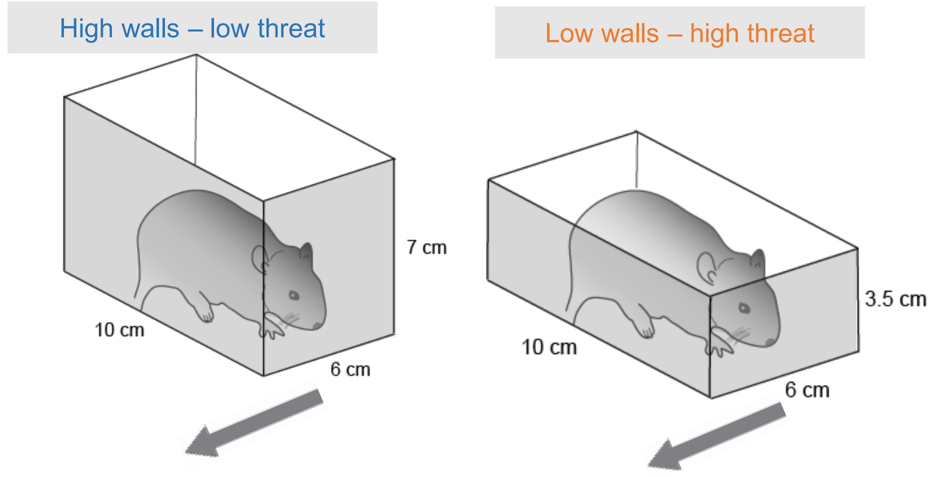




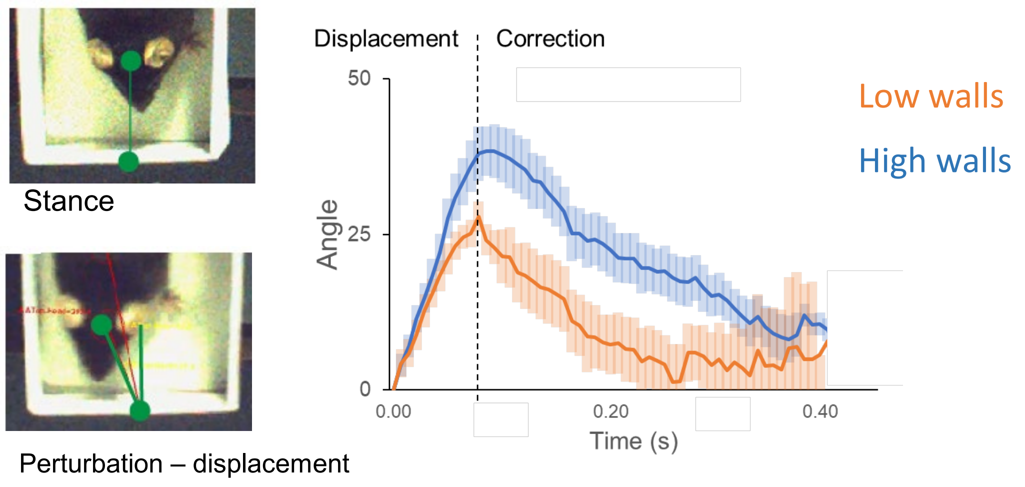


Postural reflexes are not simple sensory-motor transformations – they are altered by environmental context

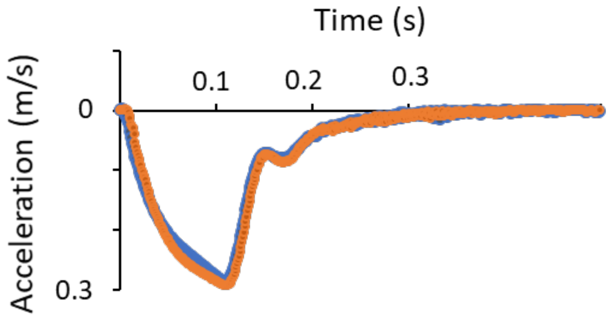
Environment



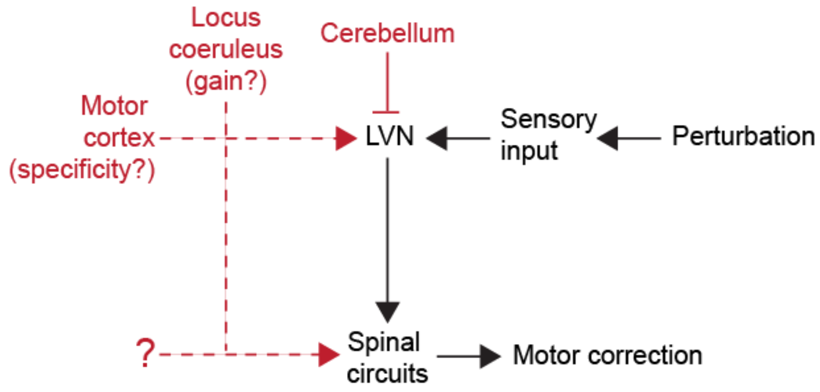
Altered motor output gain



Perturbation (acceleration)

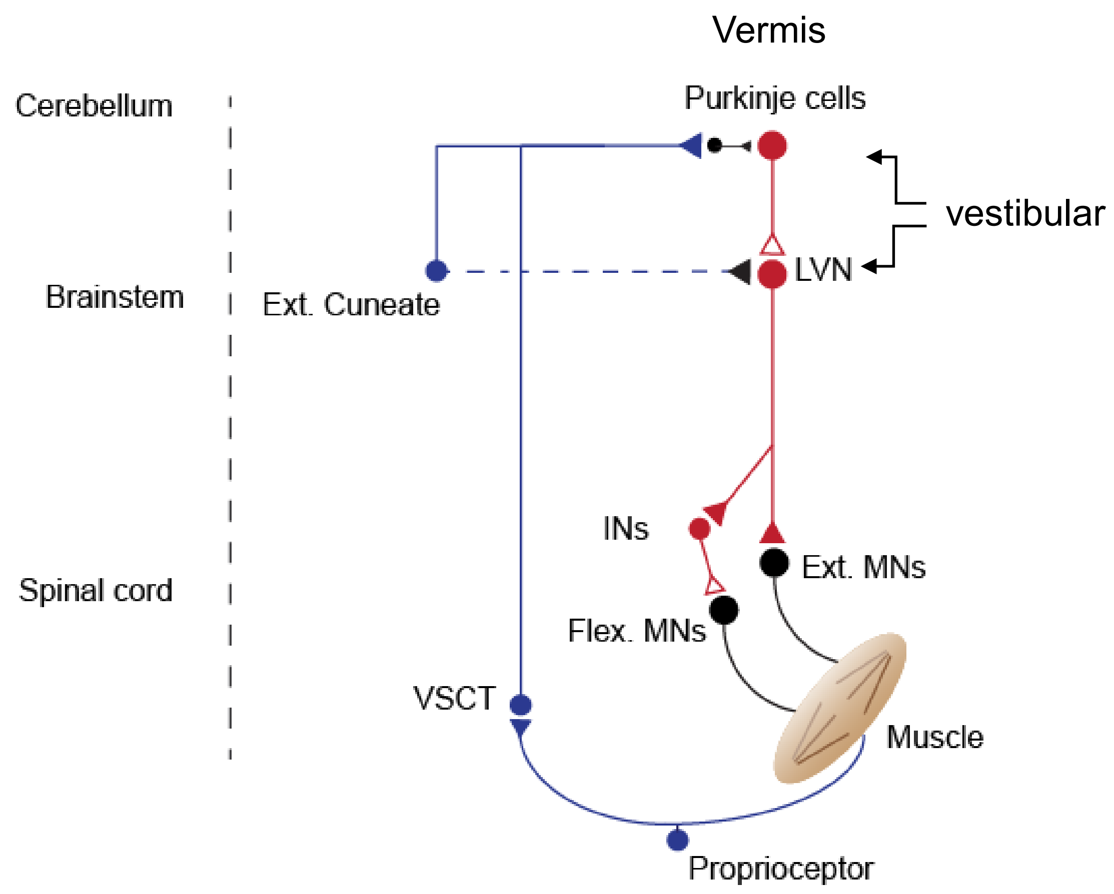


Mechanism?



Emily Reader-Harris

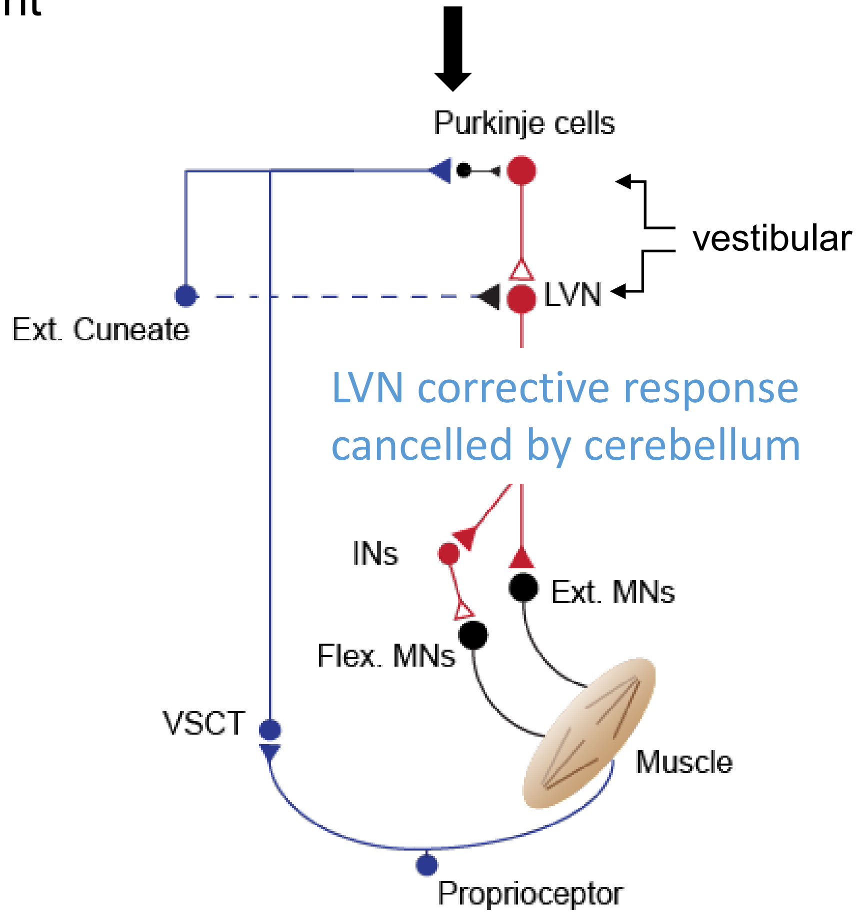
Simplified circuit for the generation of postural reflexes



The predominant input to LVST-neurons is cerebellar in origin

Self-generated movement

Motor command copy

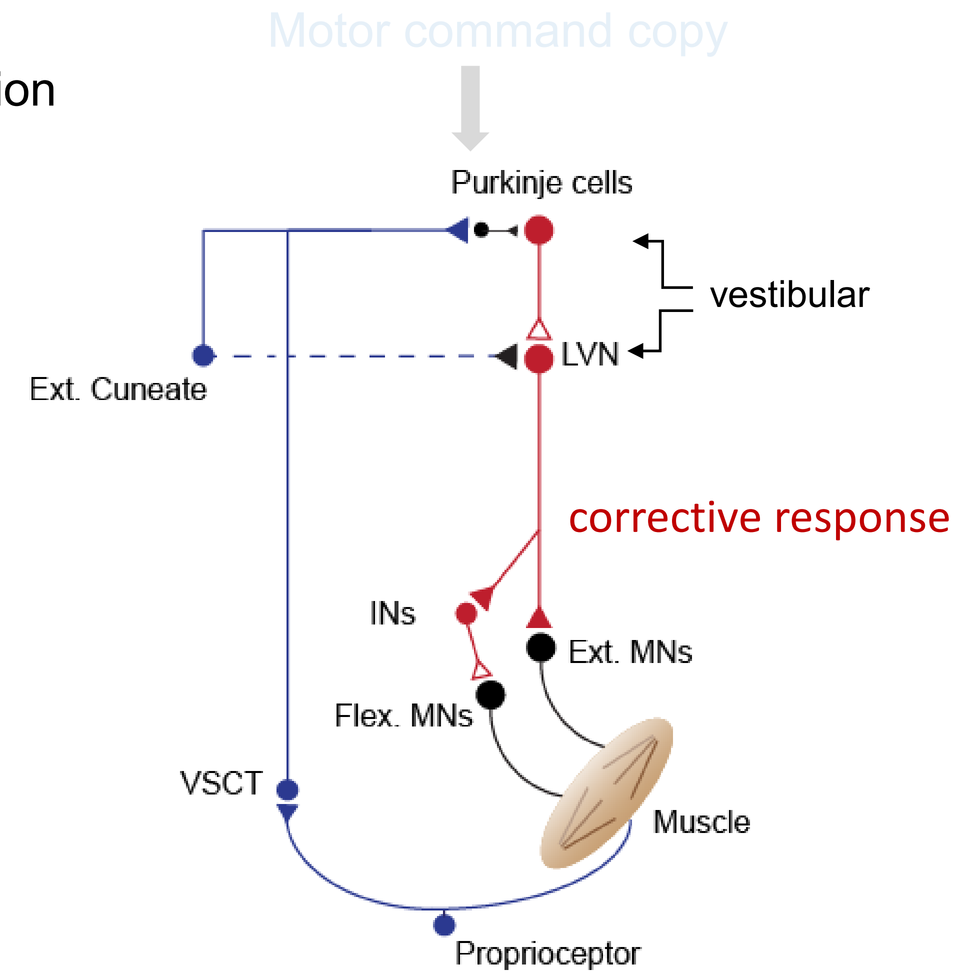


Predicted acceleration

Predicted muscle stretch

The predominant input to LVST-neurons is cerebellar in origin

Unexpected perturbation

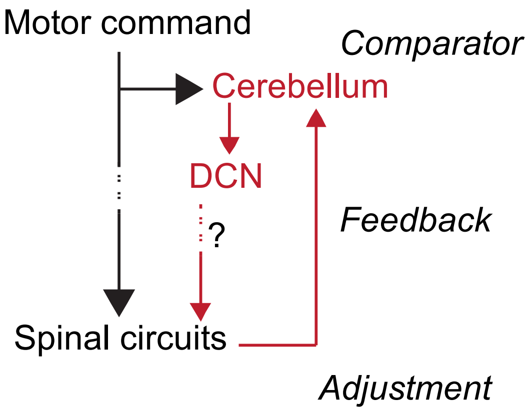


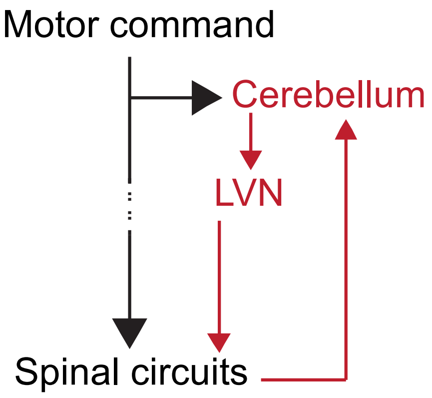
unpredicted acceleration

unpredicted muscle stretch

Cerebellar-LVST circuits for tuning locomotor output

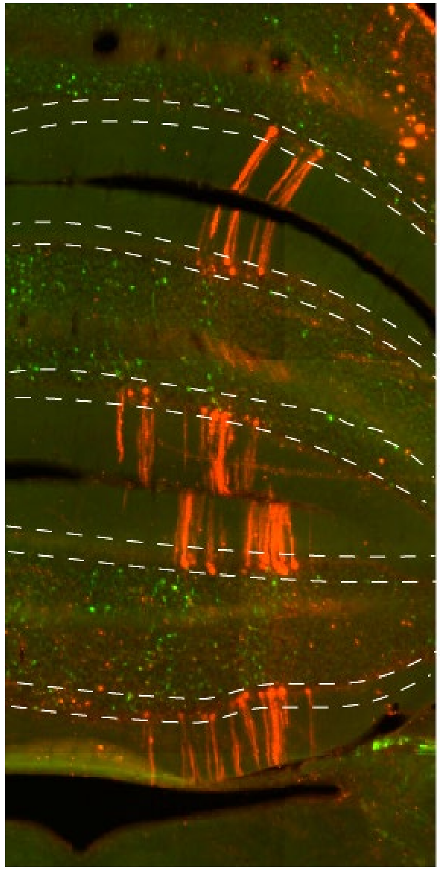
Circuits for online adjustments of motor output



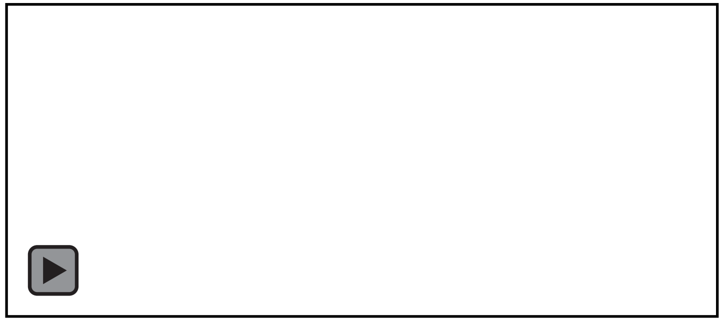


The LVN as a spinal-projecting deep cerebellar nucleus

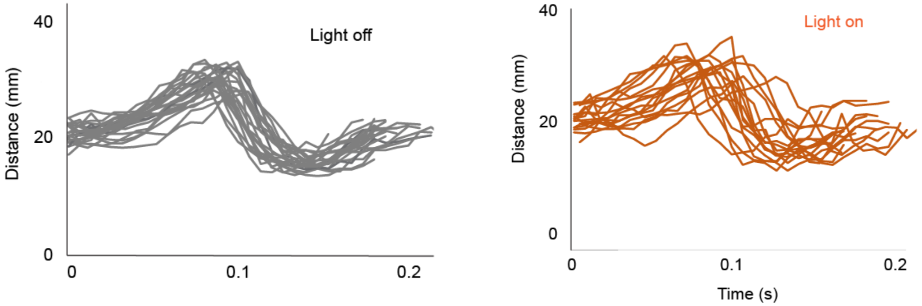
RABVdG-N2c-tdTom
(from LVST neurons)



Degradation of locomotor precision with LVN inhibition



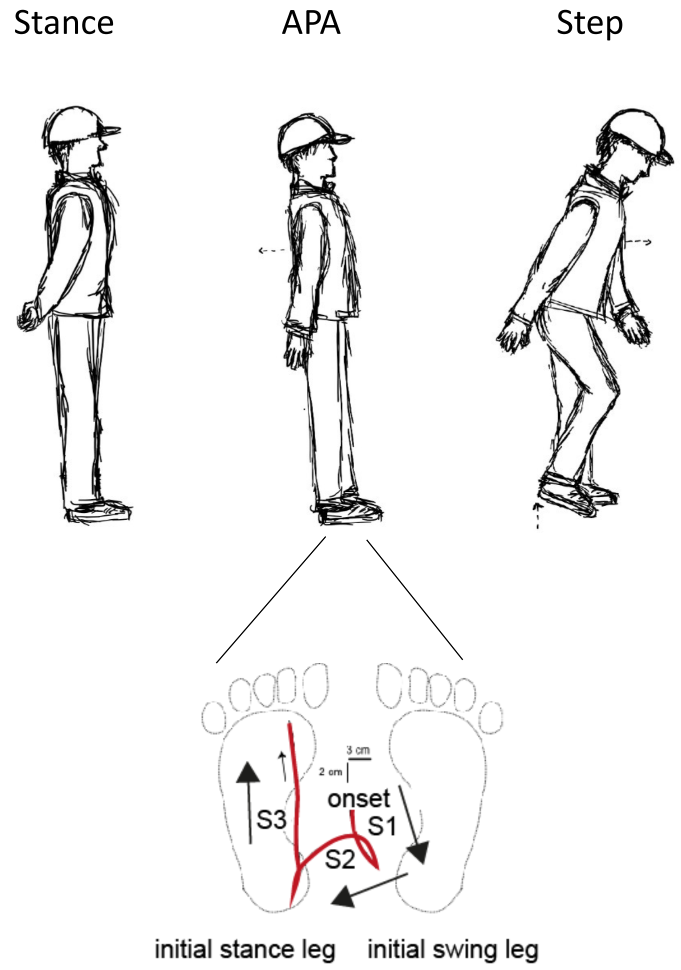
Forelimb kinematics



Emily Reader-Harris & Miranda Mathews

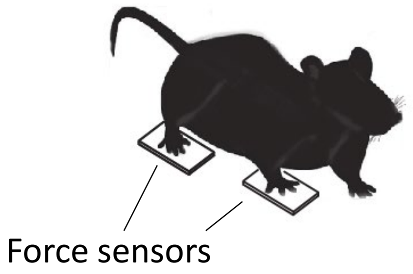
Preparing the dynamics of movement – anticipatory postural adjustments

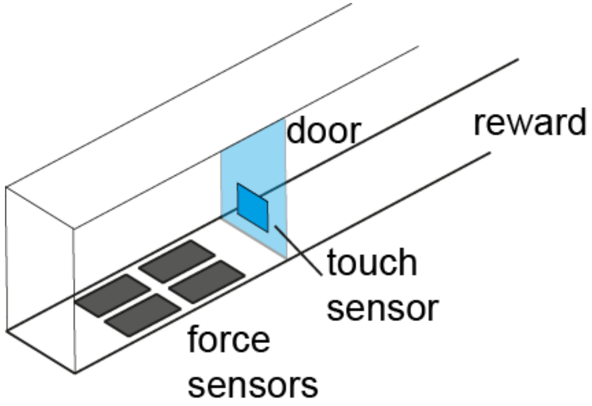
Locomotor initiation APA

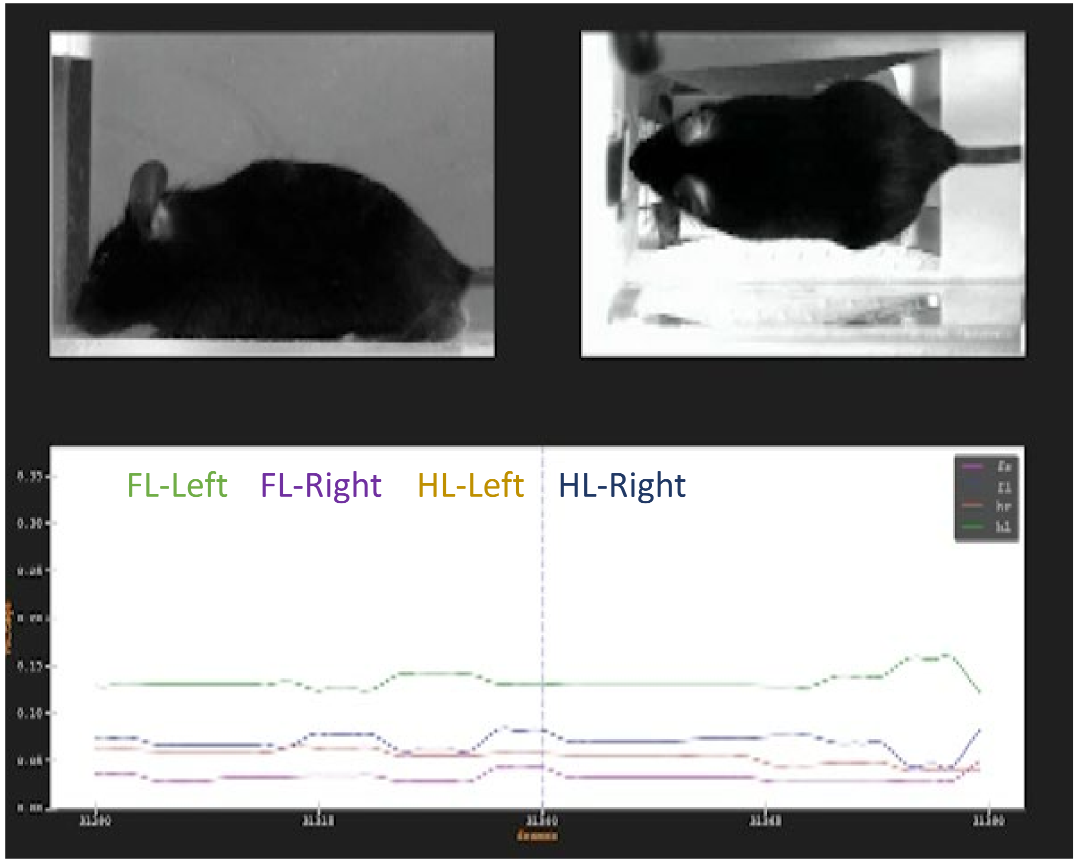


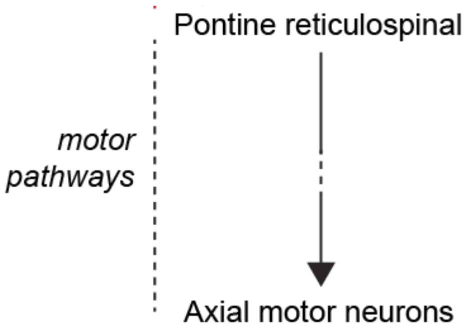
Egzona Morina
Holly Morley

Measuring anticipatory postural adjustments in mice



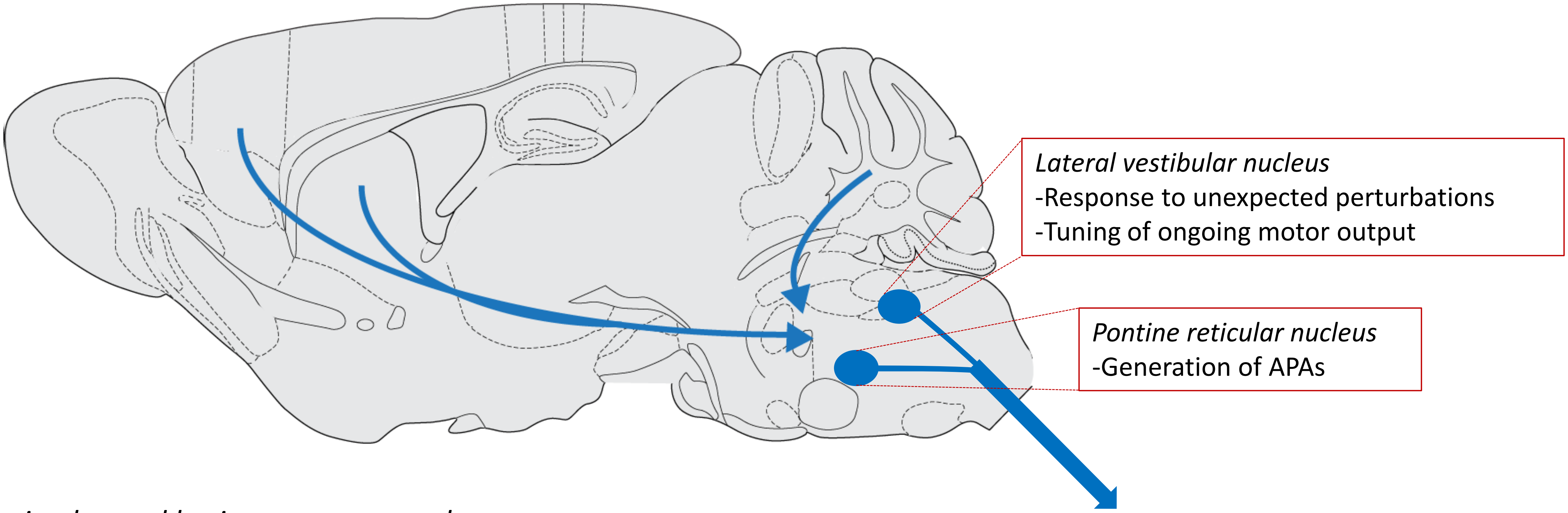






Egzona Morina in collaboration with SWC FabLabs

Adaptive motor control - Summary and future plans



Moving beyond brainstem motor pathways

-How do cerebellar-LVN interactions ensure smooth motor output?

-How do higher order circuits generate contextually appropriate APAs?