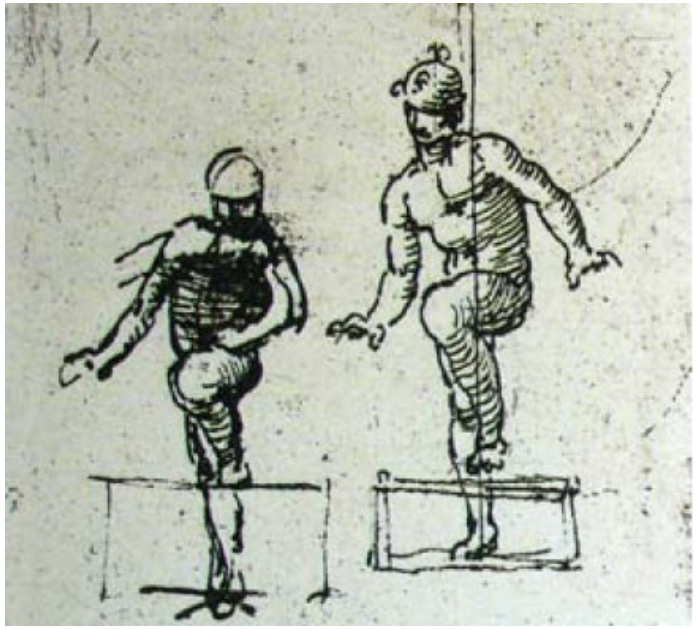
# Action Systems - neural circuits for motor control





Andy Murray
SWC Room 284 (L2 West)

# Lecture overview

| | | |
|---|---|---|
| Motor systems overview | Mon 12th | Andy Murray |
| Pattern generation | Tues 13th | Peter Latham |
| Computational control | Fri 16th | Maneesh Sahani |
| Cerebellum | Mon 9th | Tom Otis |
| Basal Ganglia | Tues 20th | Marcus Stephenson-Jones |
| Neocortex/Discussion | Fri Nov 23rd | Andy Murray/Maneesh Sahani |

# Practical overview

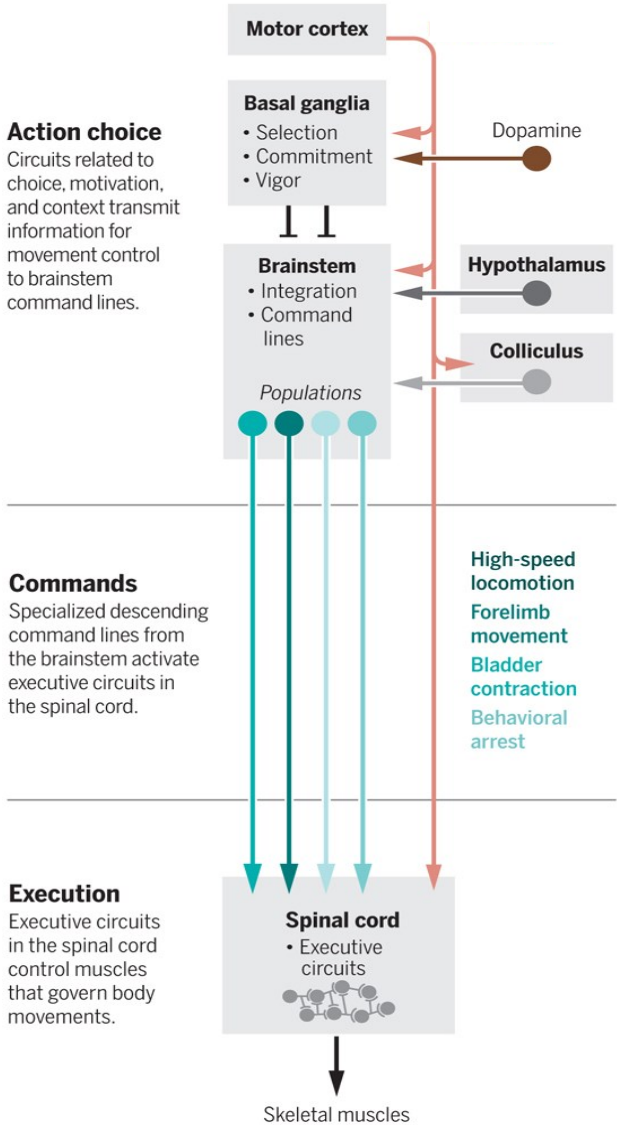
Week 1
- Build a fiber photometry rig (lecture/tutorial this afternoon)
- Surgery – virus injection and fiber optic implant tutorial (tomorrow)

Week 2
- Design experiments to test motor control in mice
- Use you photometry rig to record from the mice injected in week 1

# Motor control is our only means to interact with the environment

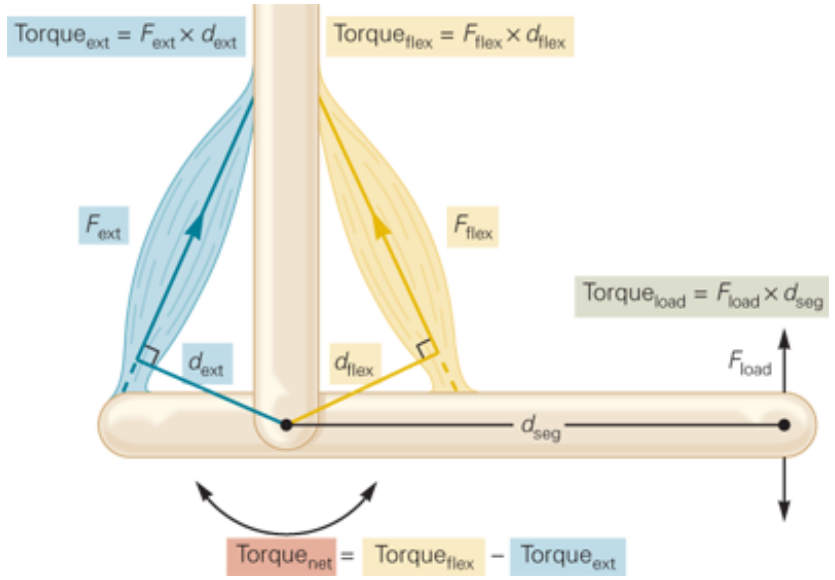
# We are surprisingly bad at recreating natural movement

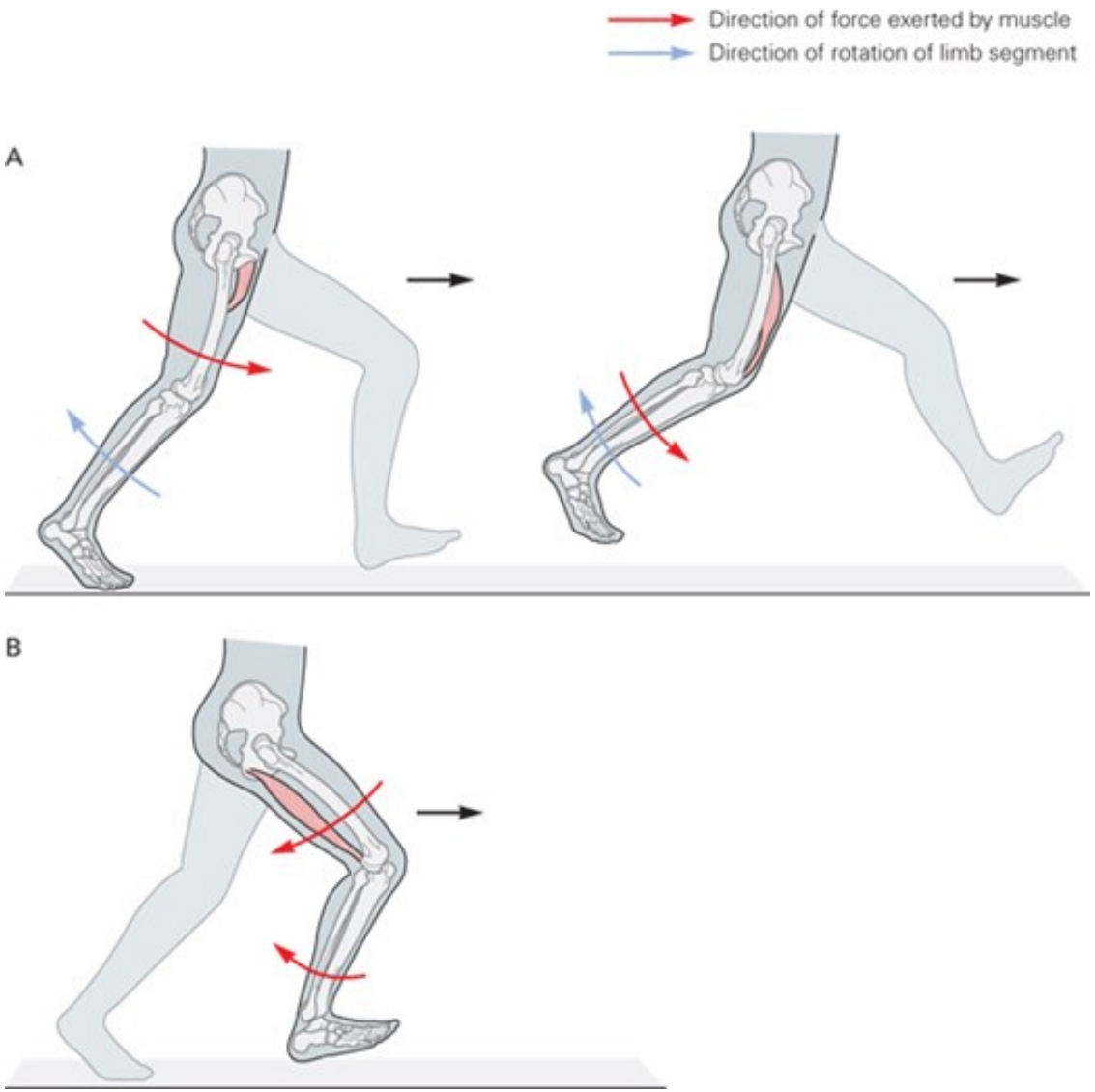
# Which parts of the nervous system are involved in motor control?



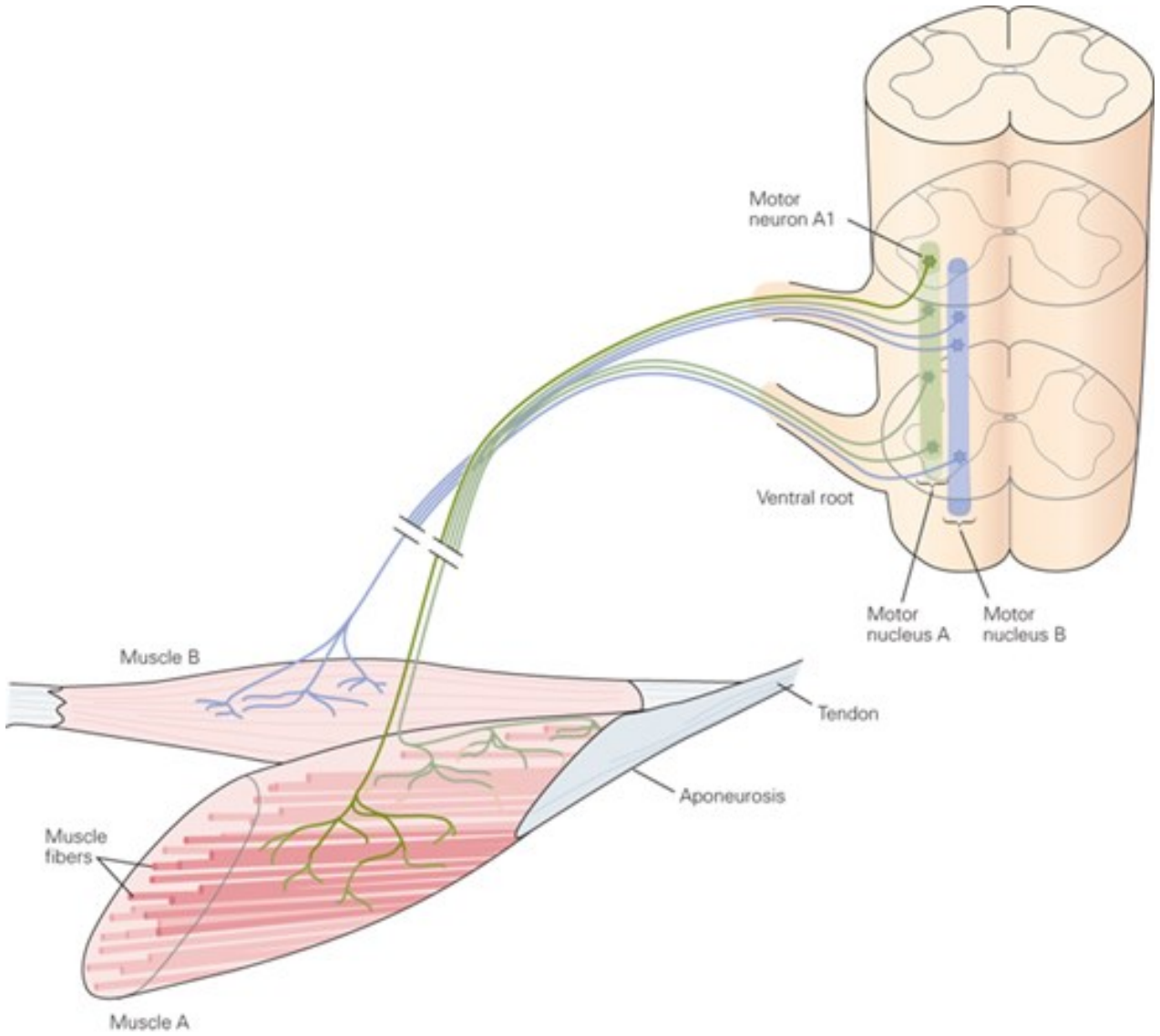

**Reading:**
Connecting neuronal circuits for movement
Arber & Costa, Science 2018
Vol. 360, Issue 6396, pp. 1403-1404

# Muscles and motor neurons

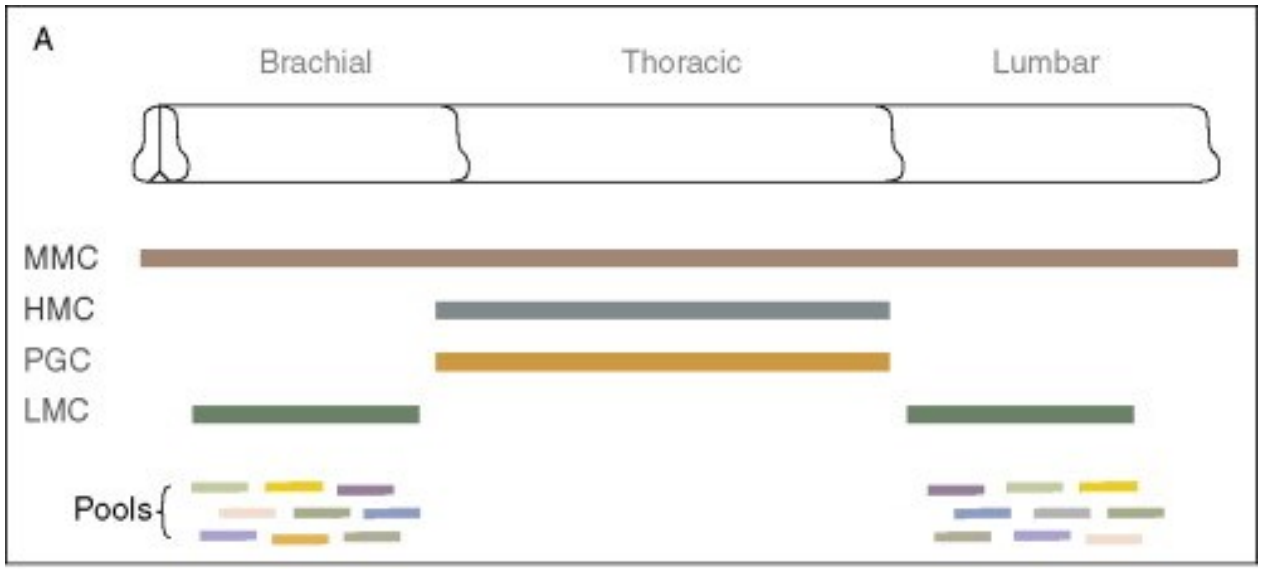


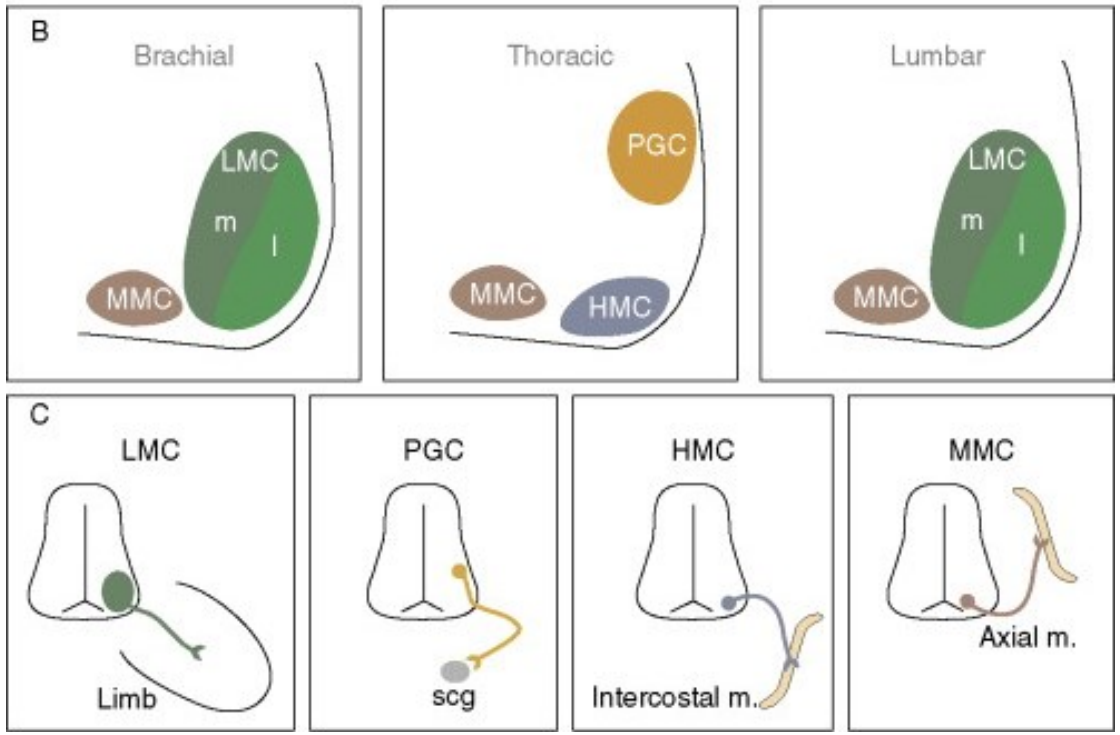



# Muscles and motor neurons



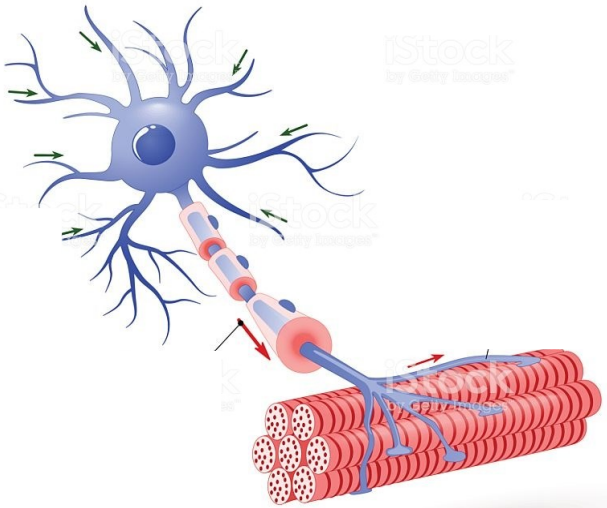
# Spinal circuitry – organisation of motor neurons



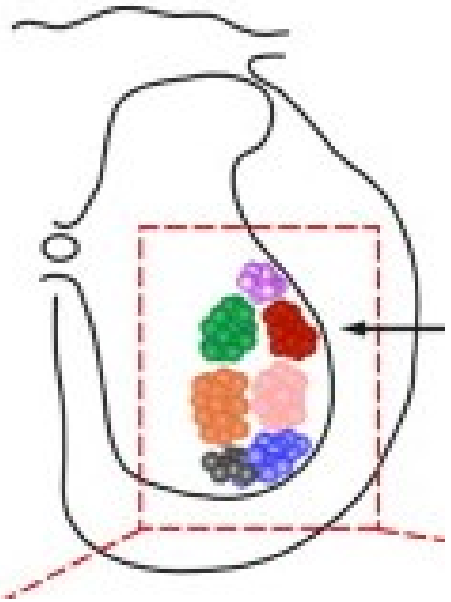



# Spinal circuitry – organisation of limb motor neurons

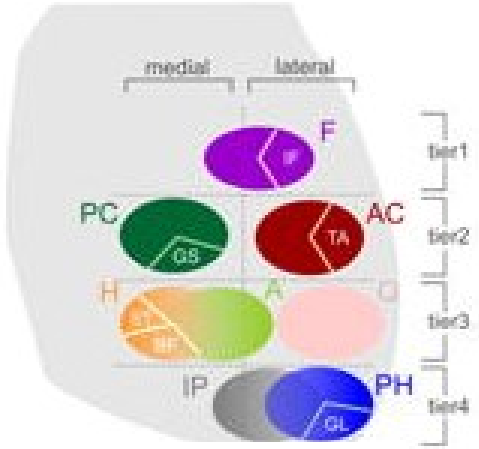
Motor unit

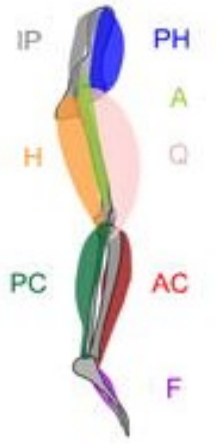


Motor pool

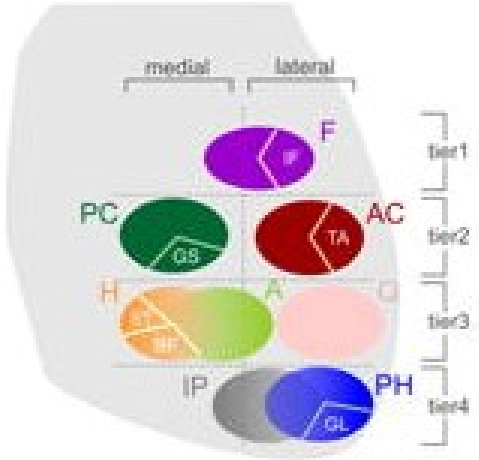


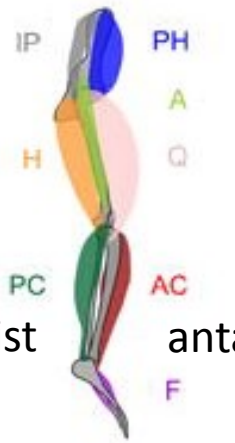
Motor columels




Motor columns

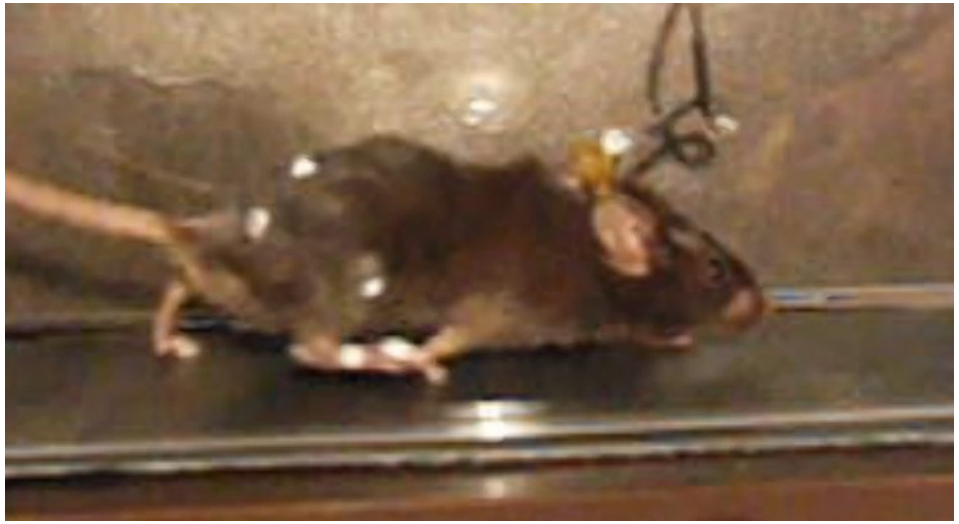


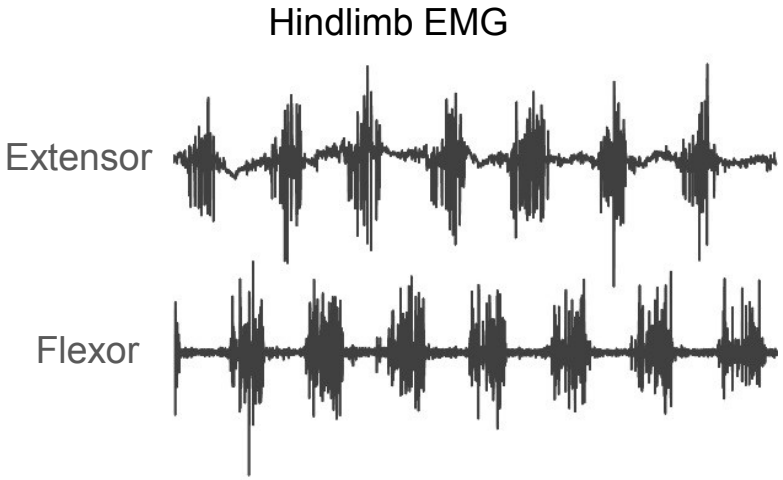



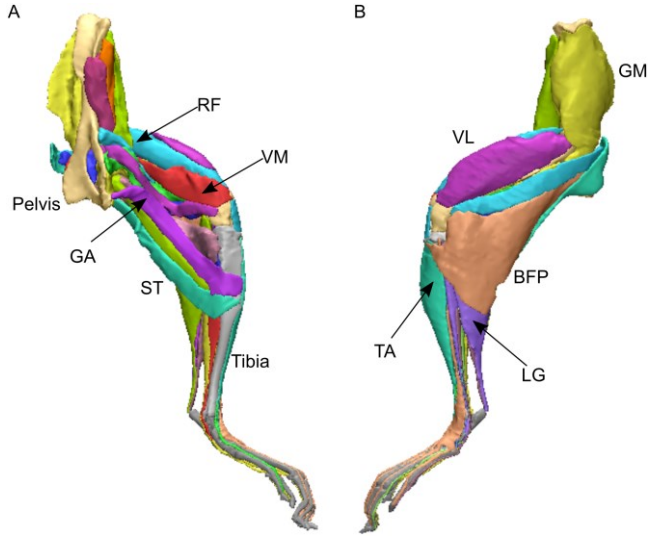

agonist antagonist

Sainsbury Wellcome Centre

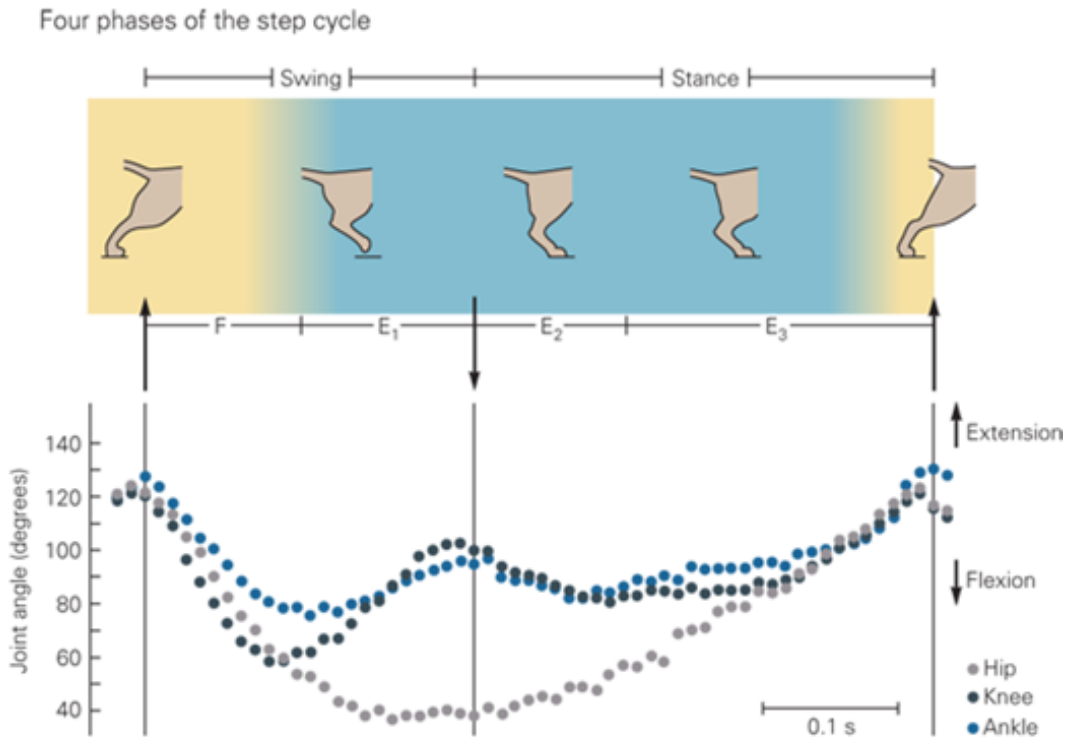
# Simple motor control is based on rhythmic movements

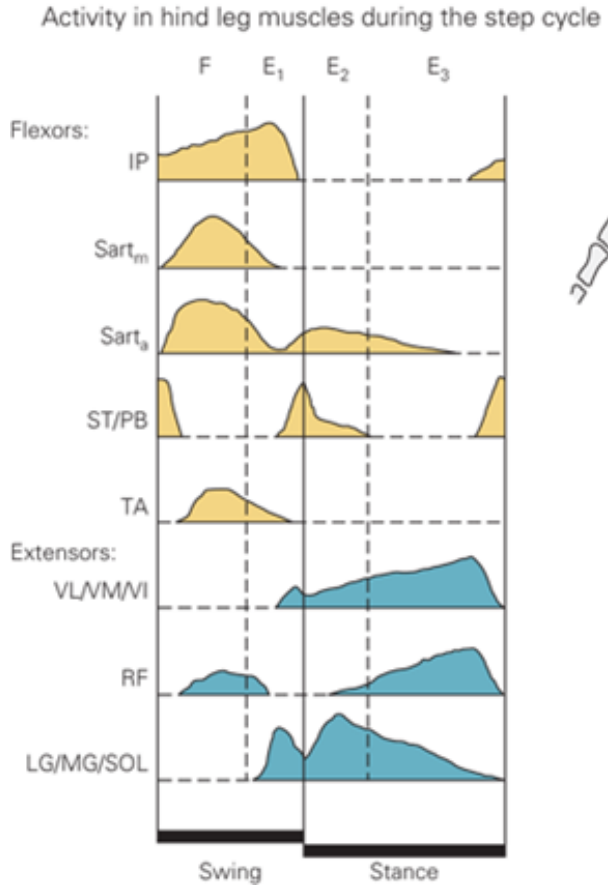


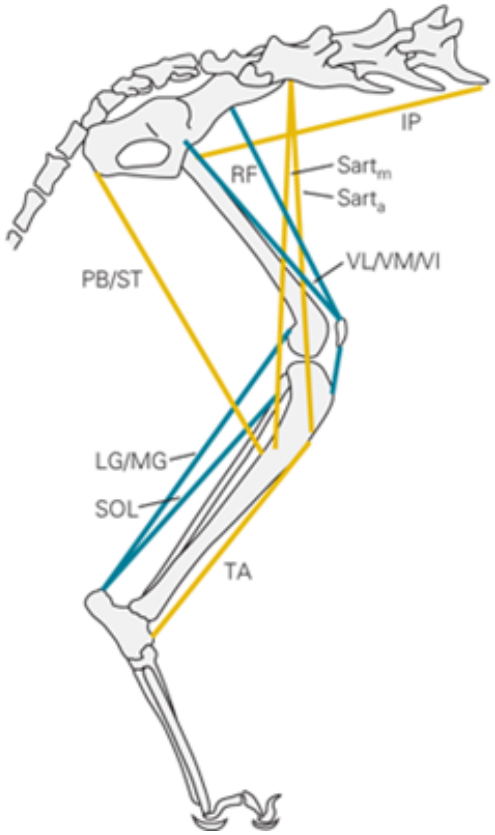


# The locomotor step cycle



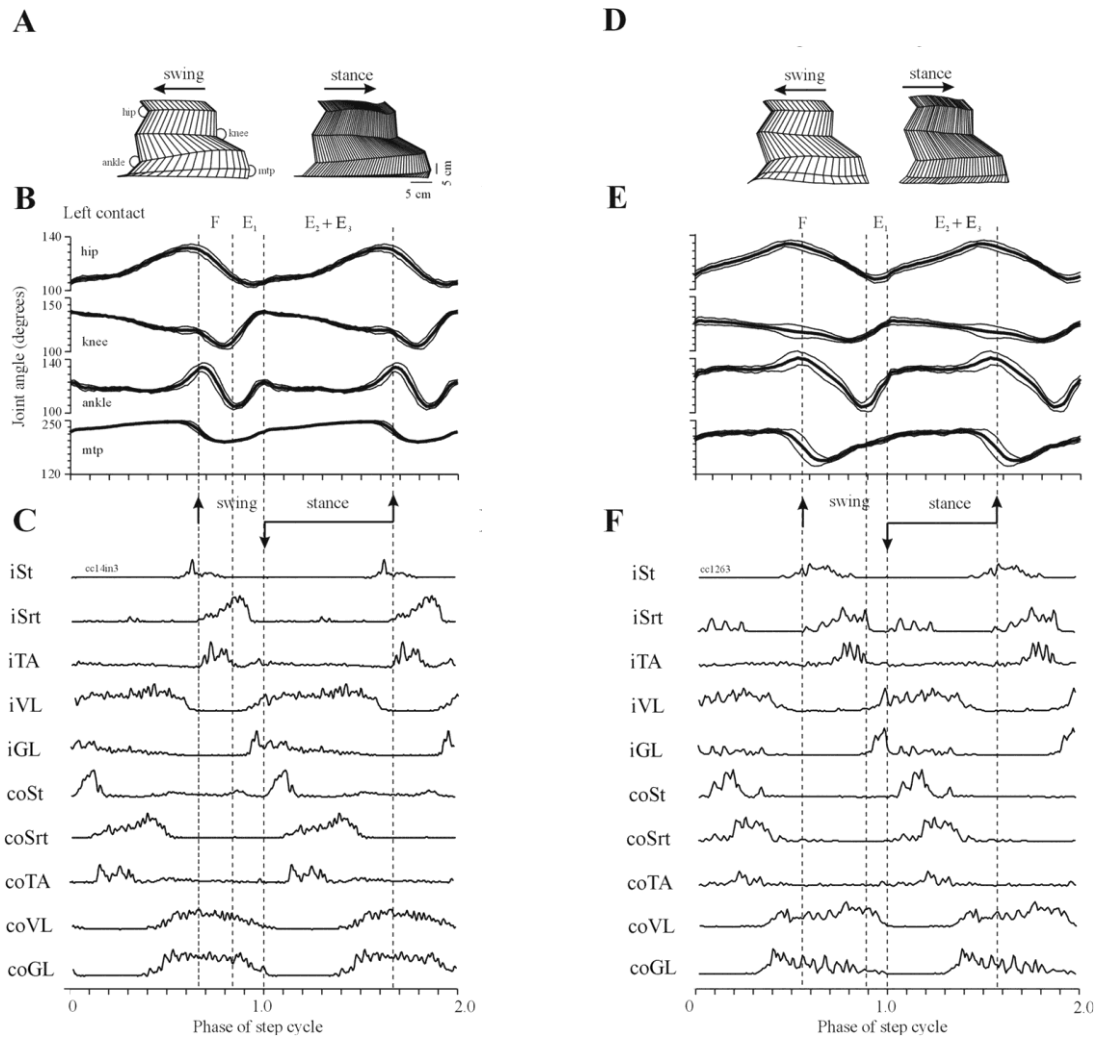



# The spinal cord can generate rhythmic locomotion

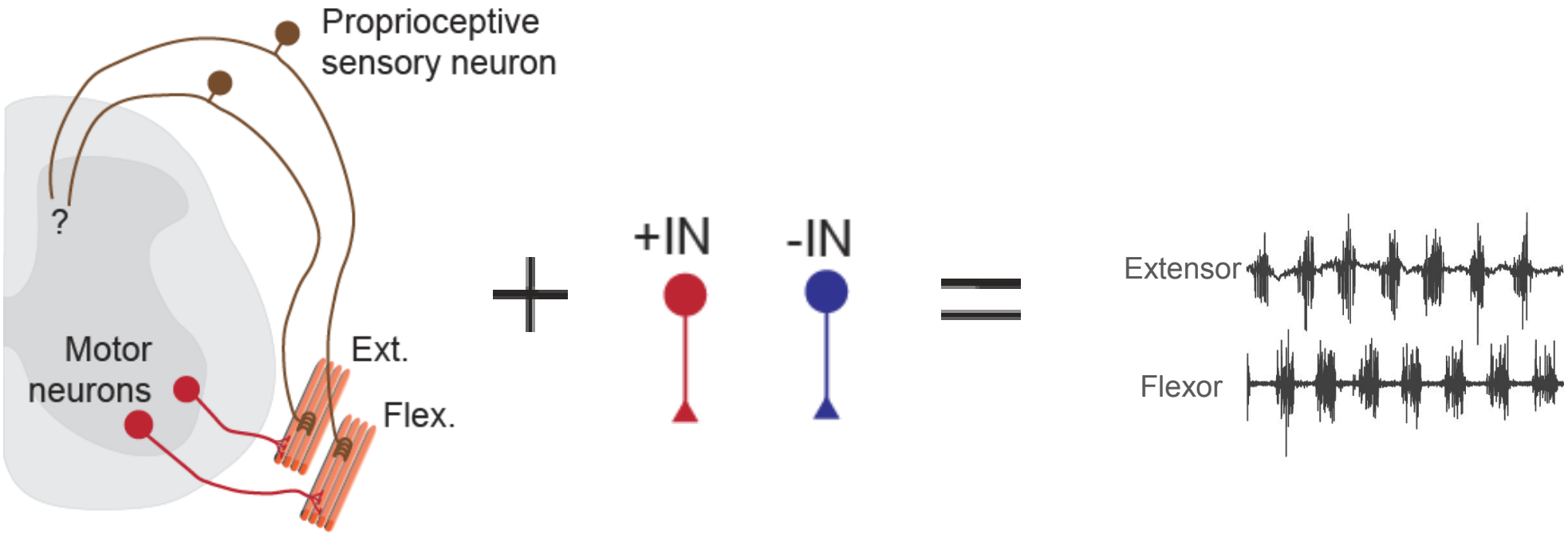
Intact

Spinalised (T13; 38 days)

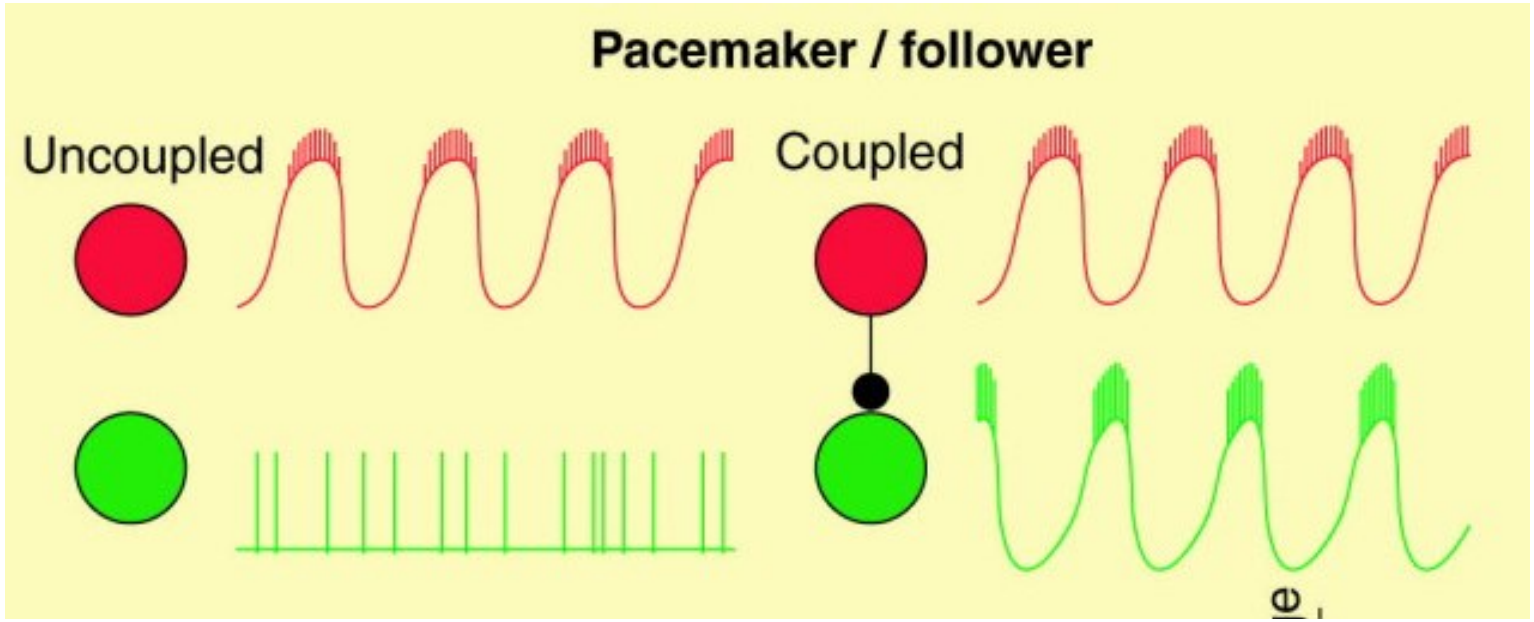



Rossignol and Bouyer, 2004

# Build a rhythmic spinal circuit…..



# 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

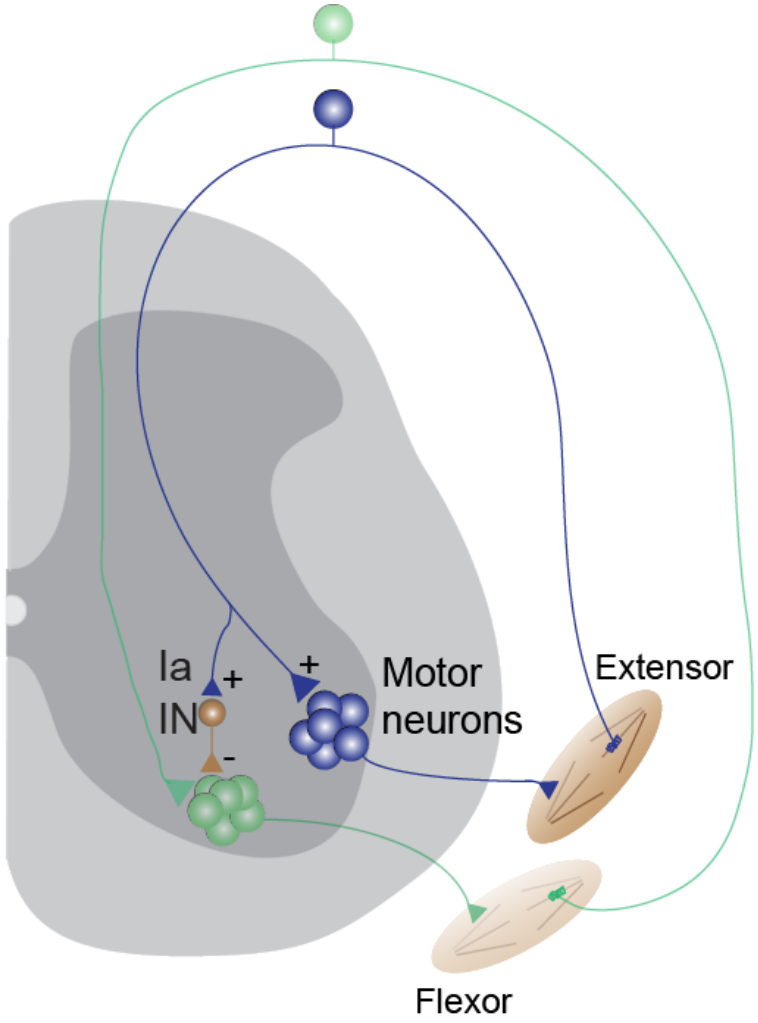


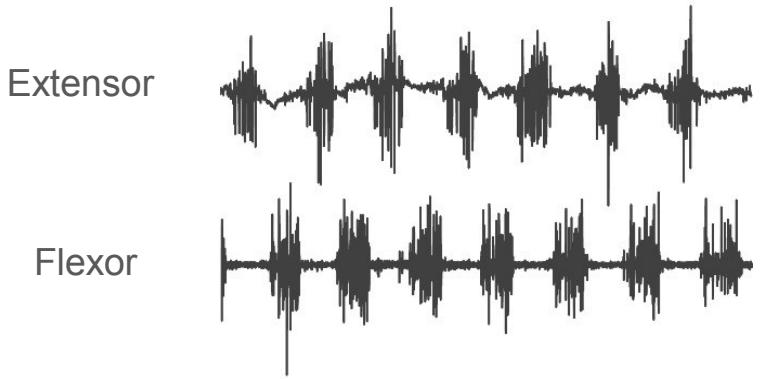
Eve Marder, Dirk Bucher

Show more

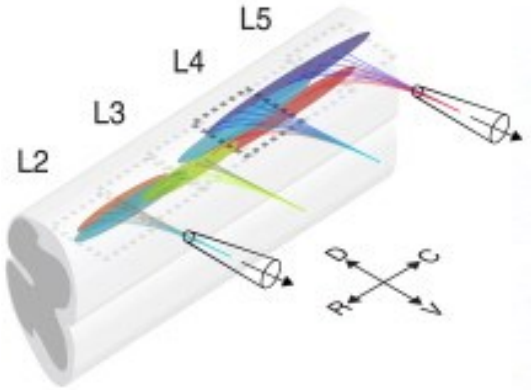
http://dx.doi.org/10.1016/S0960-9822(01)00581-4

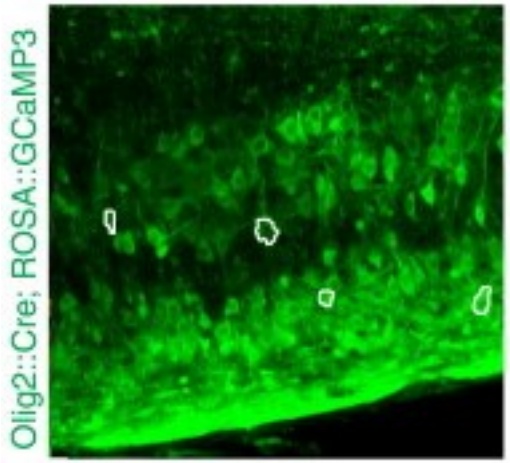
# Sensory pathways could drive rhythmic firing in the spinal cord

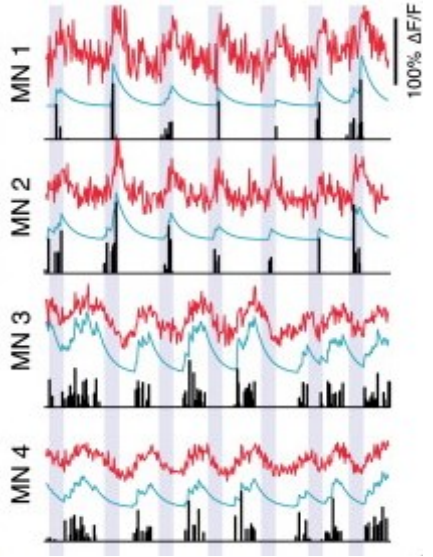


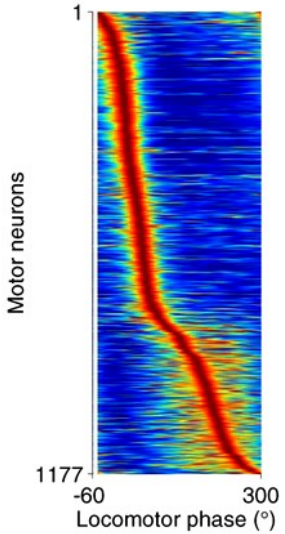



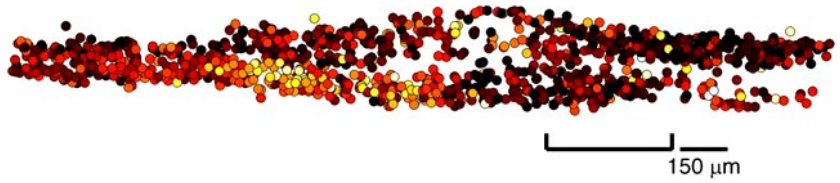
# The spinal cord can generate rhythmic firing of motor neurons (in the absence of sensory feedback)

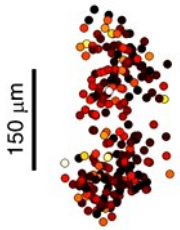



Sainsbury Wellcome Centre

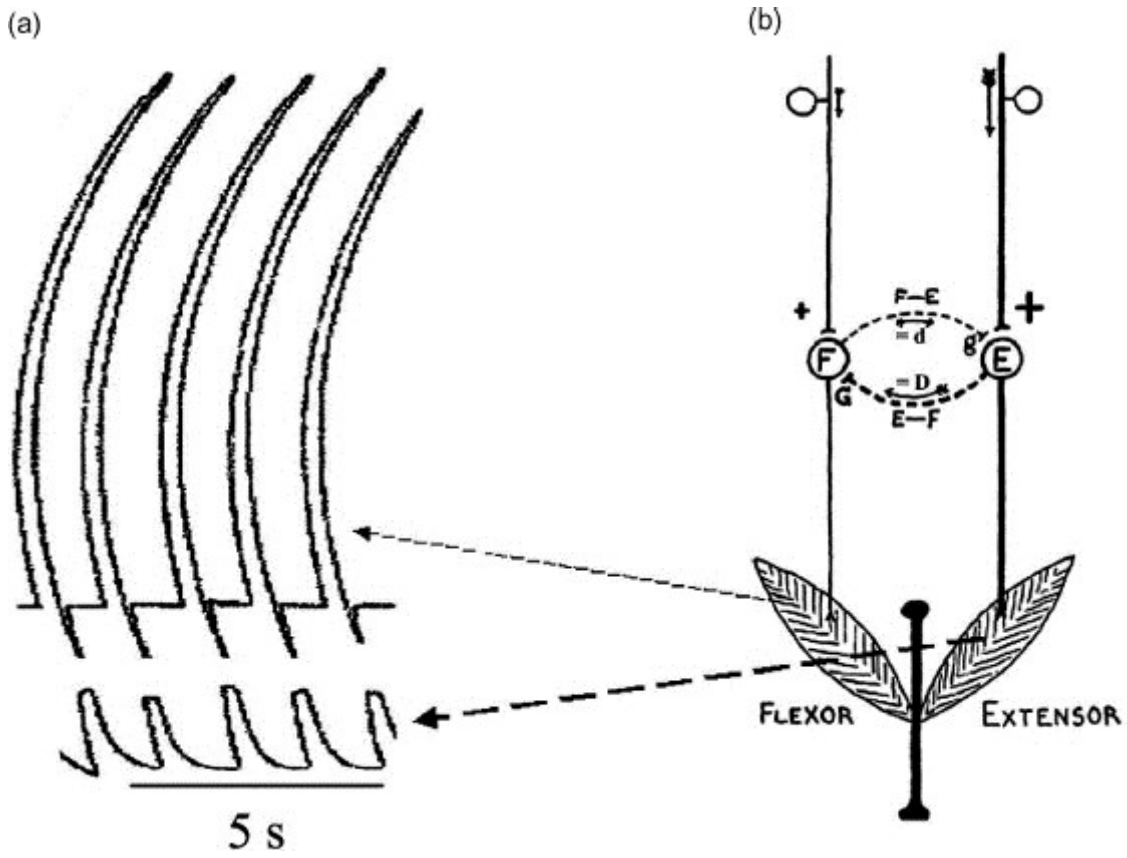
Machado et al., 2015

# Locomotion is based on rhythmic movements generated in the spinal cord

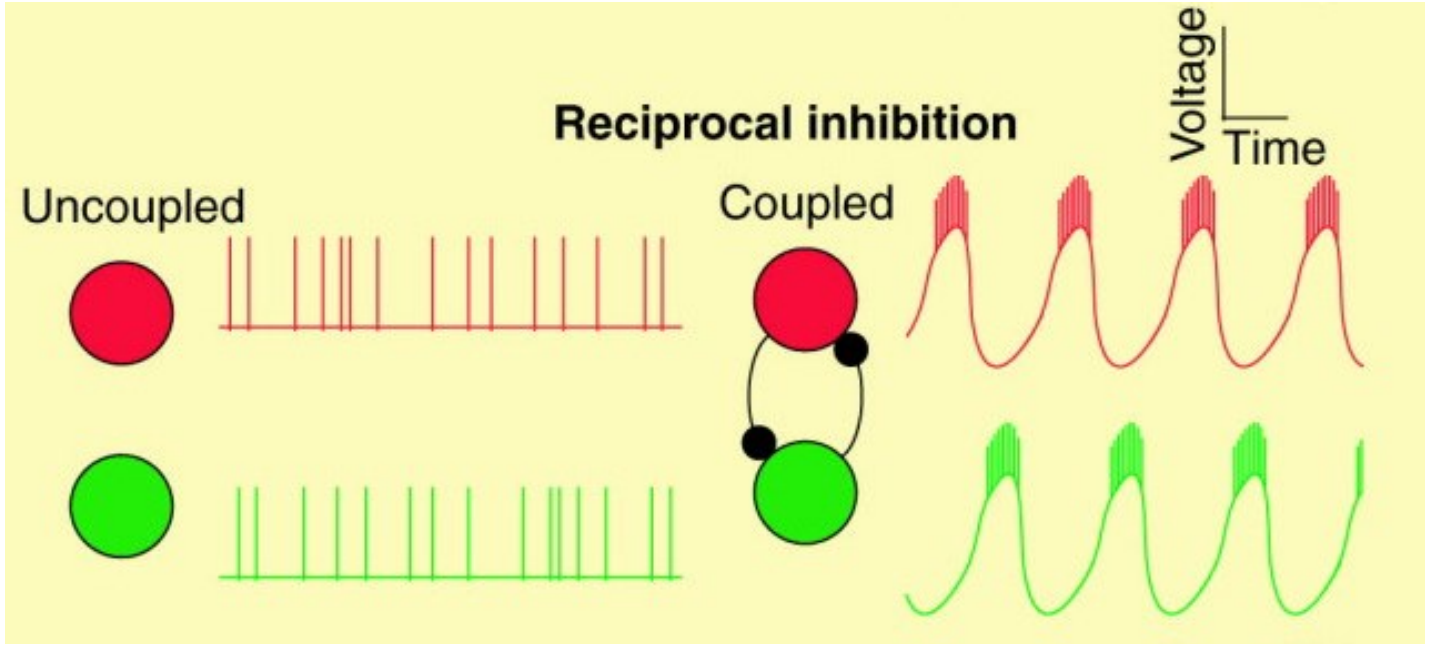
T. Graham Brown

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




Current Biology

Volume 11, Issue 23, 27 November 2001, Pages R986–R996

Review Article

Central pattern generators and the control of rhythmic movements

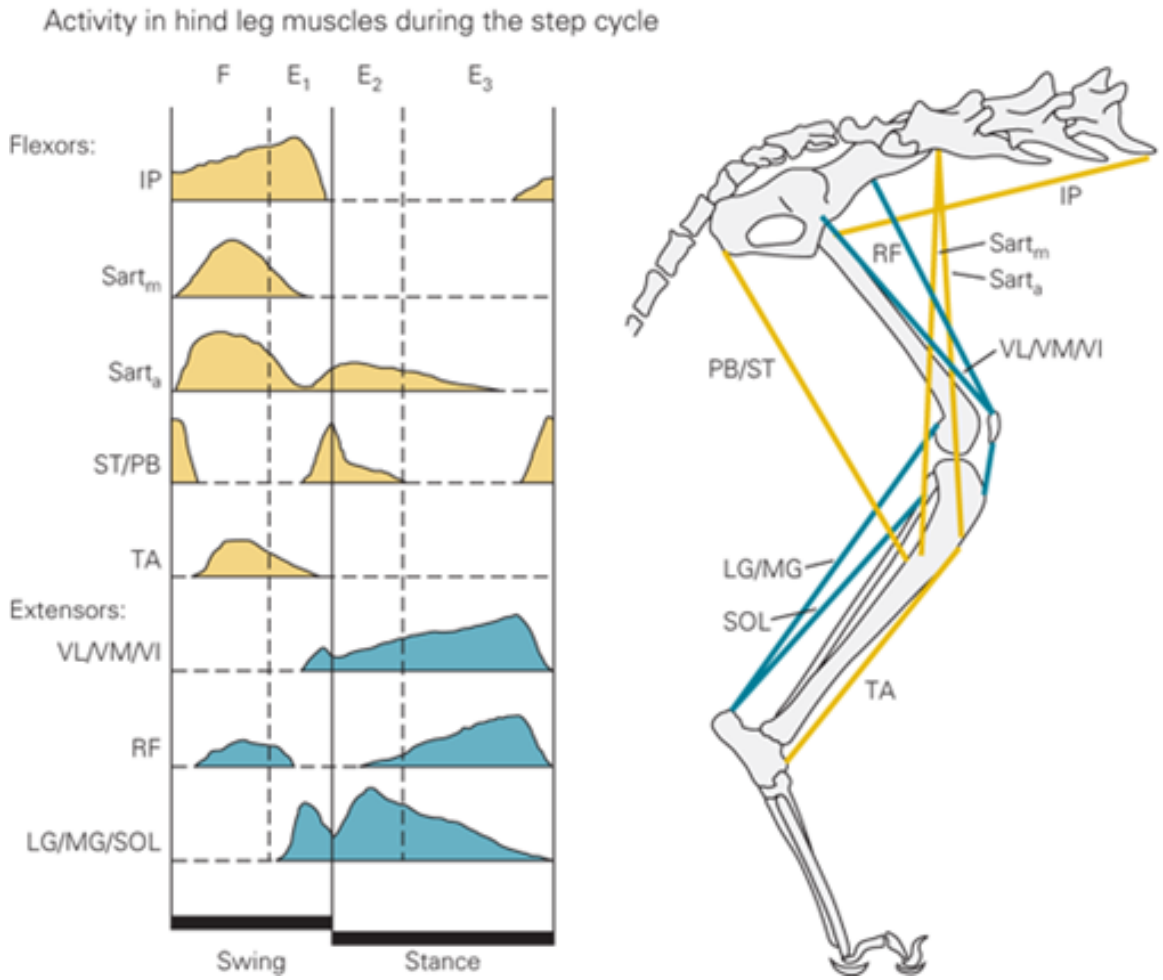


Eve Marder, Dirk Bucher

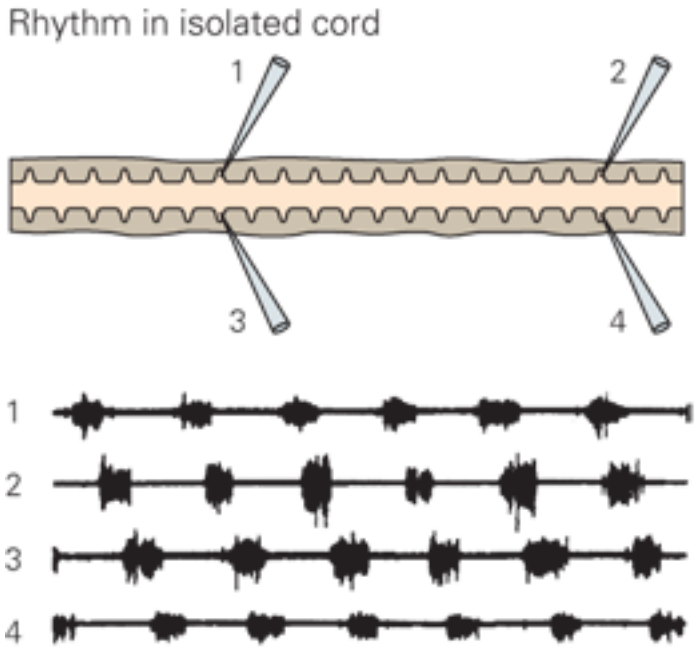
Show more

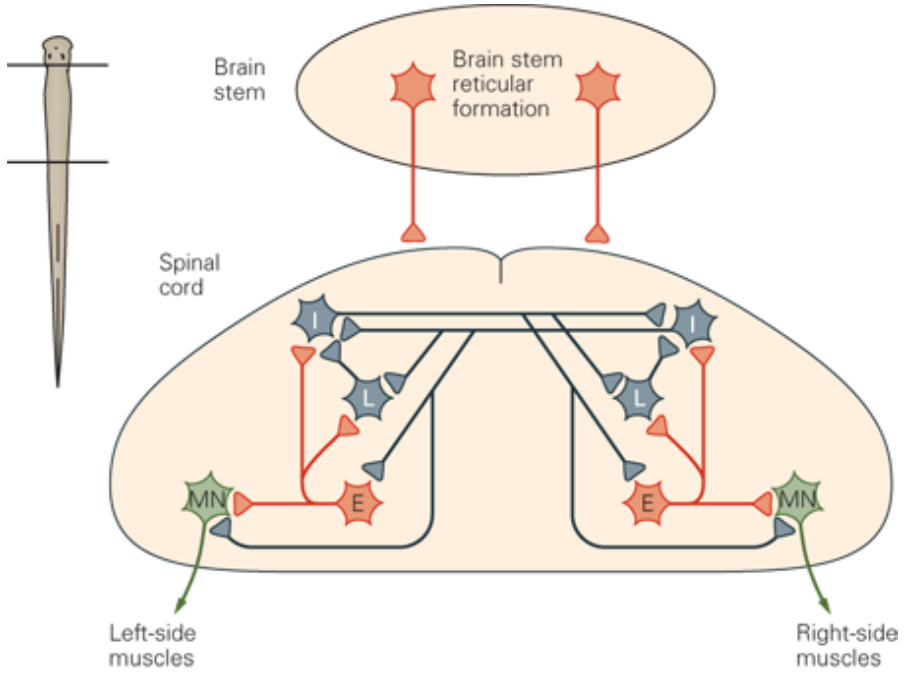
http://dx.doi.org/10.1016/S0960-9822(01)00581-4

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

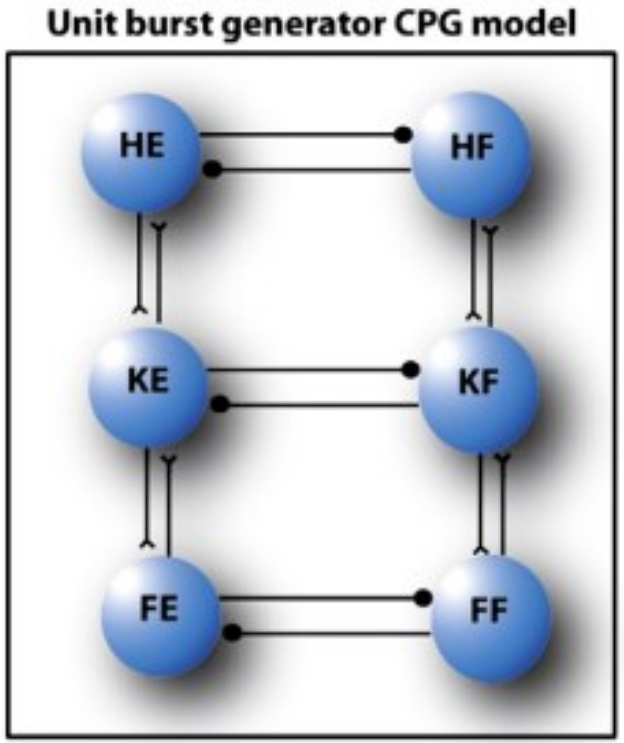


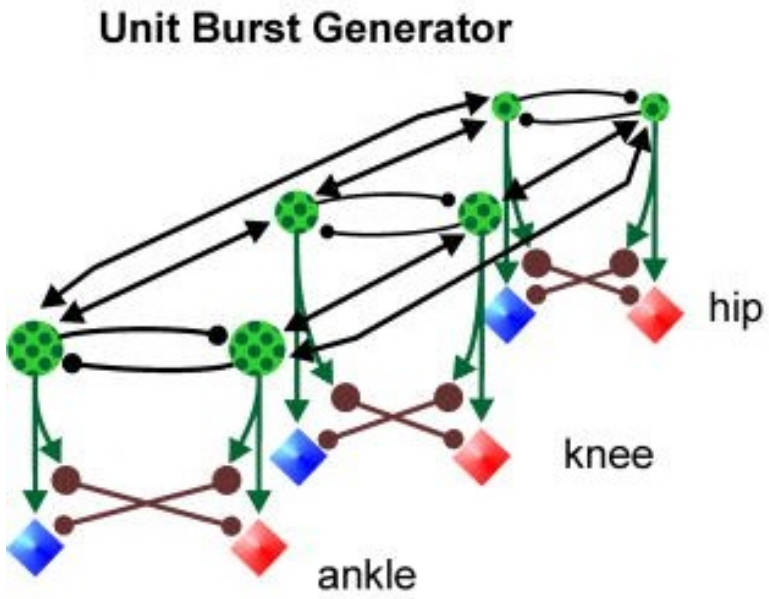
# The unit burst generator as an alternative to the half-centre model



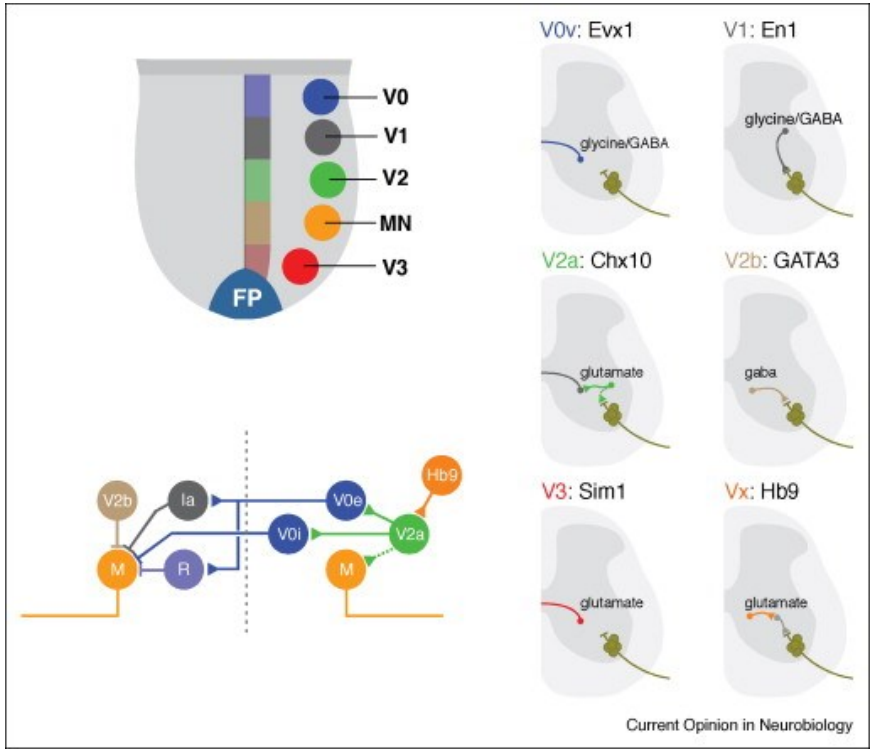



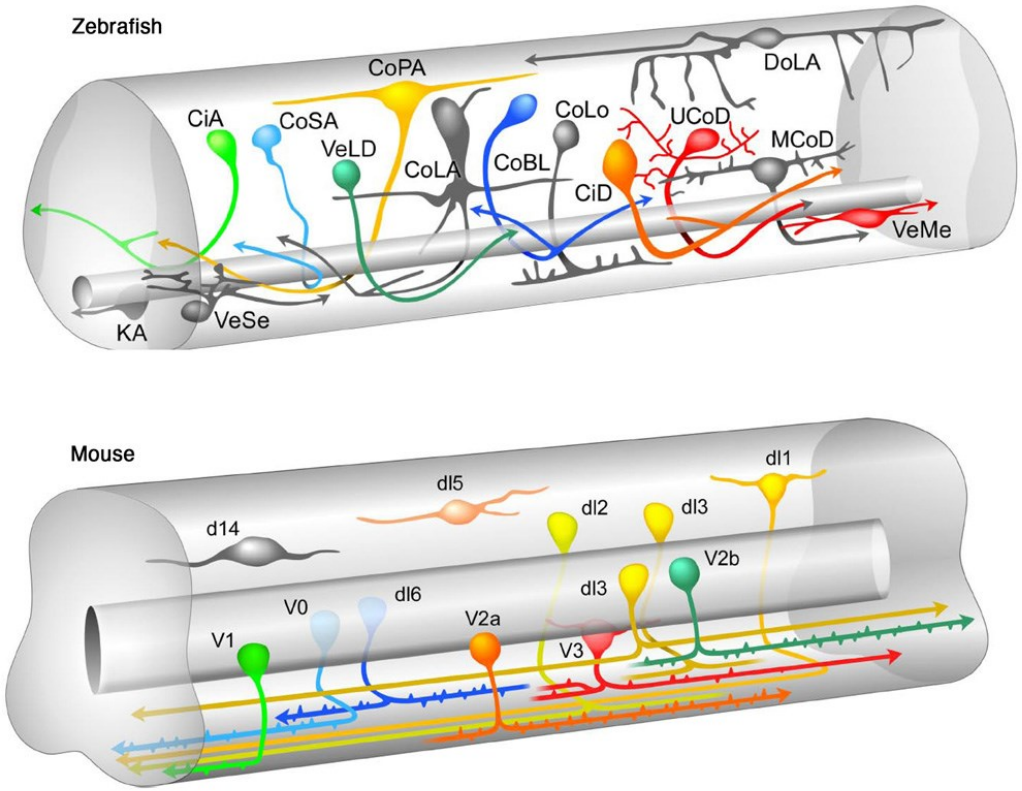
# The unit burst generator as an alternative to the half-centre model



# The diversity of spinal interneurons

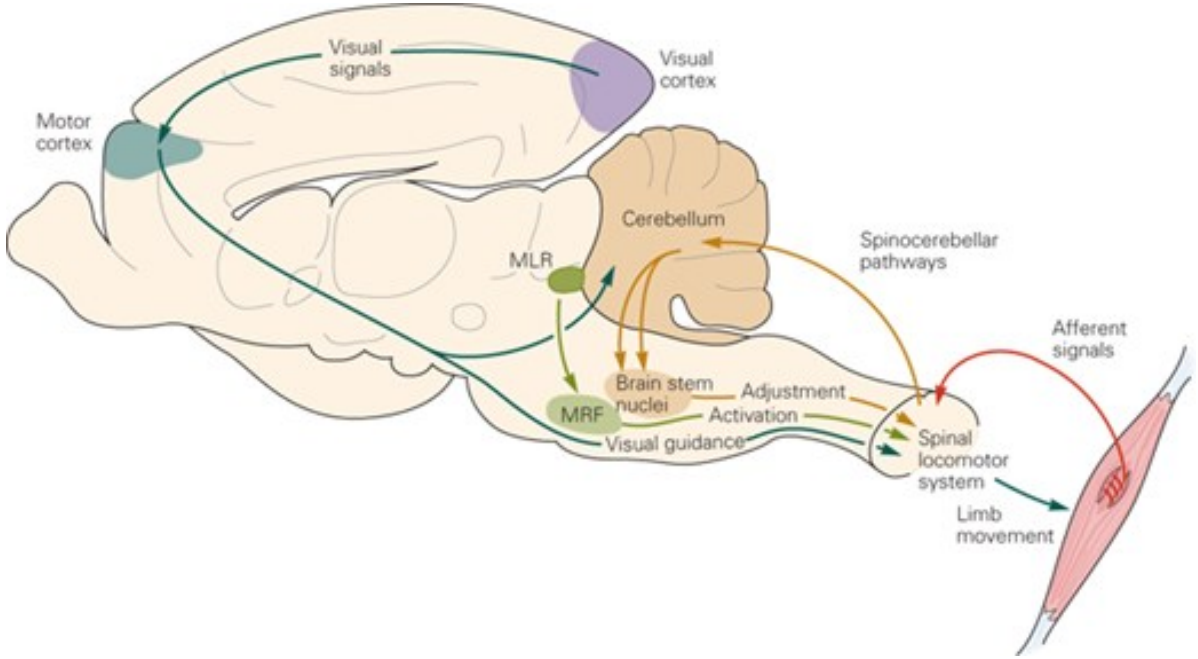


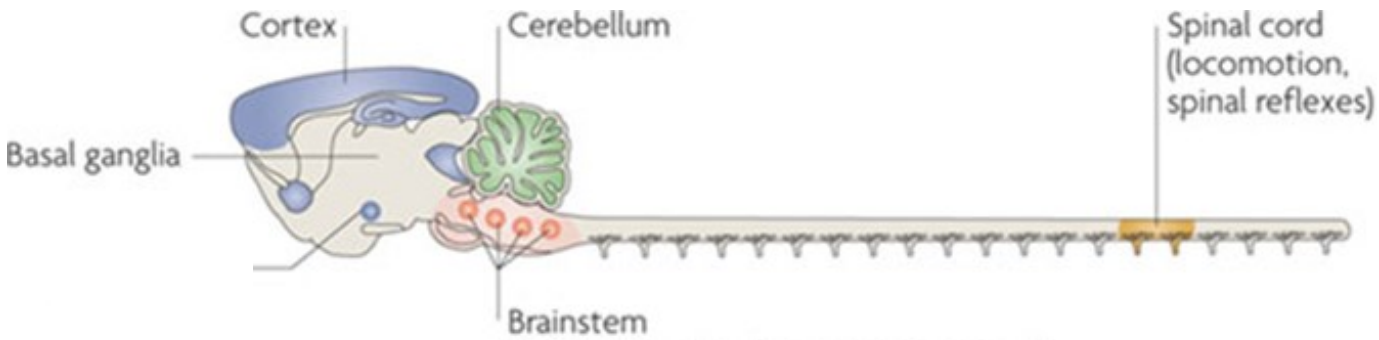

**Reading:** Goulding, 2009. Nat. Rev. Neurosci.
Circuits controlling vertebrate locomotion: moving in a new direction.

# Why do we need a brain?

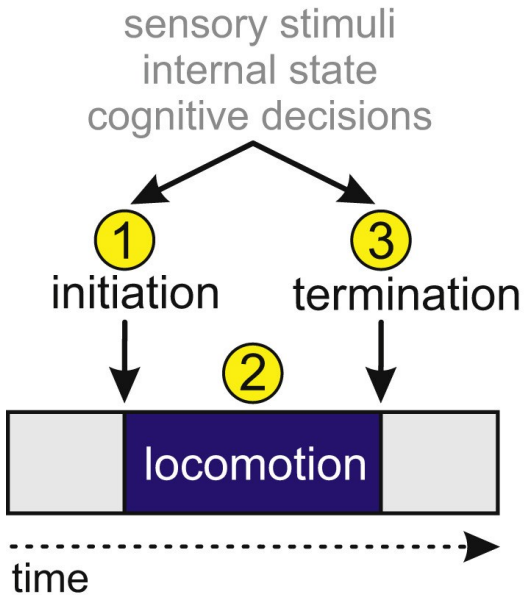
1. To start/stop locomotion
2. To adjust ongoing motor commands
3. When we want conscious control over our movements



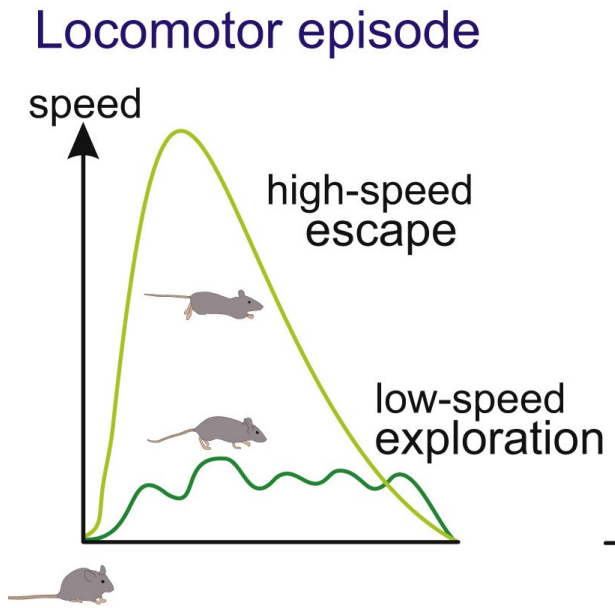
# Starting locomotion– the MLR



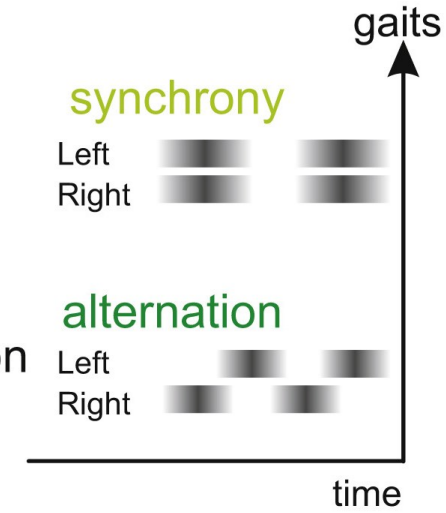
# Locomotor transitions and choosing a gait



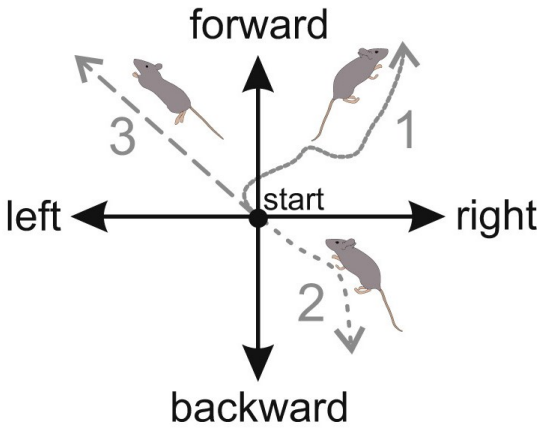

Behavioral phases




Speed

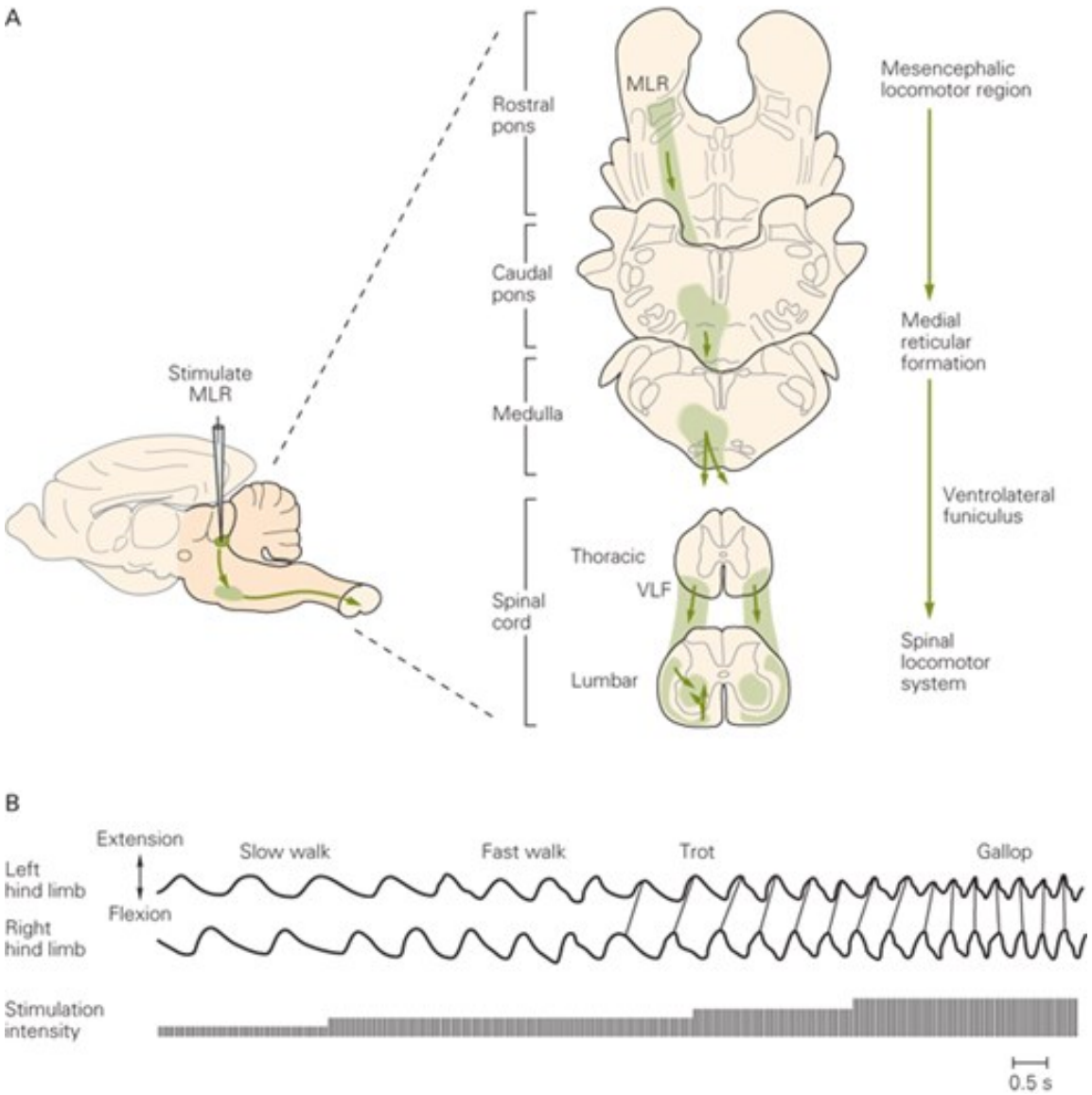



Limb positioning

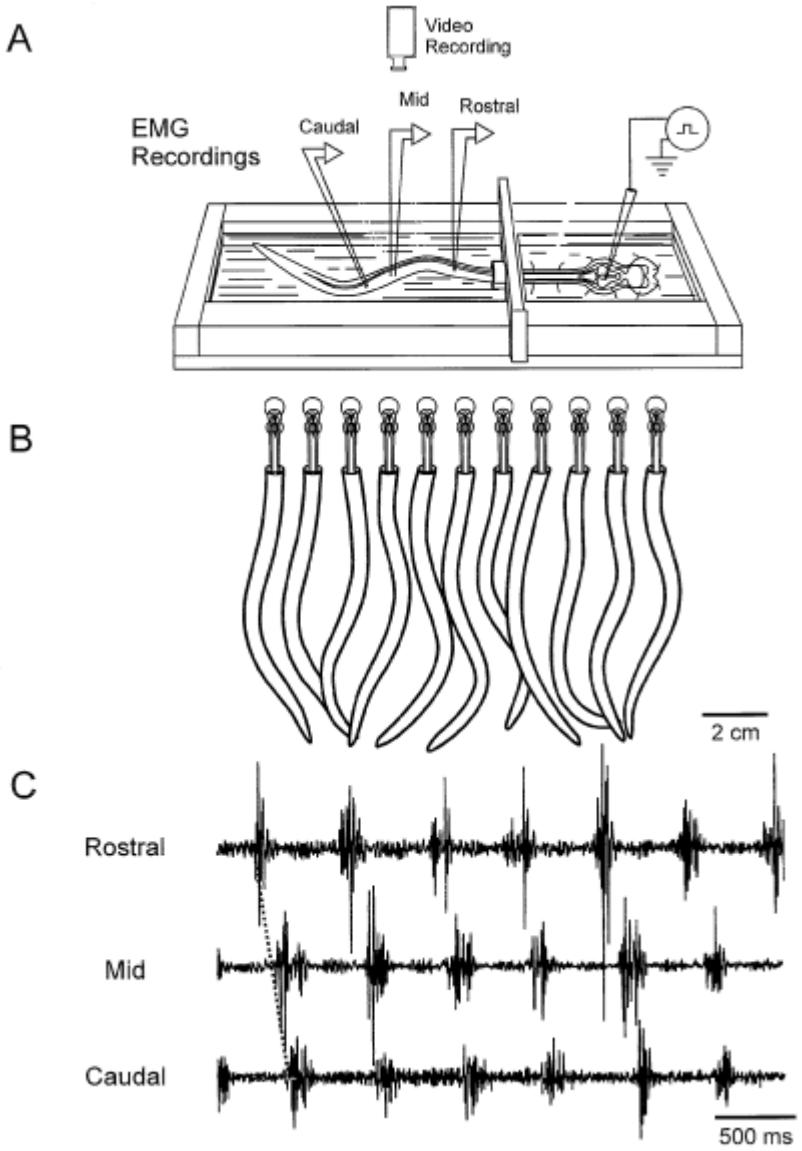


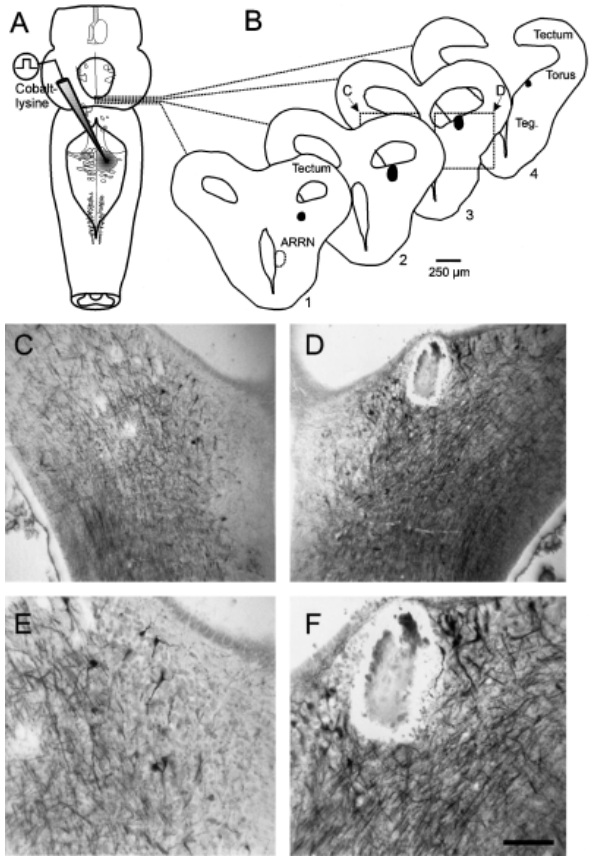

Direction

# Activation of spinal CPGs – the mesencephalic locomotor region



# The MLR is conserved across species




Sainsbury Wellcome Centre

Sirota et al., 2000

# Tomorrow's practical – stimulating and recording from the MLR in mice

nature
International journal of science

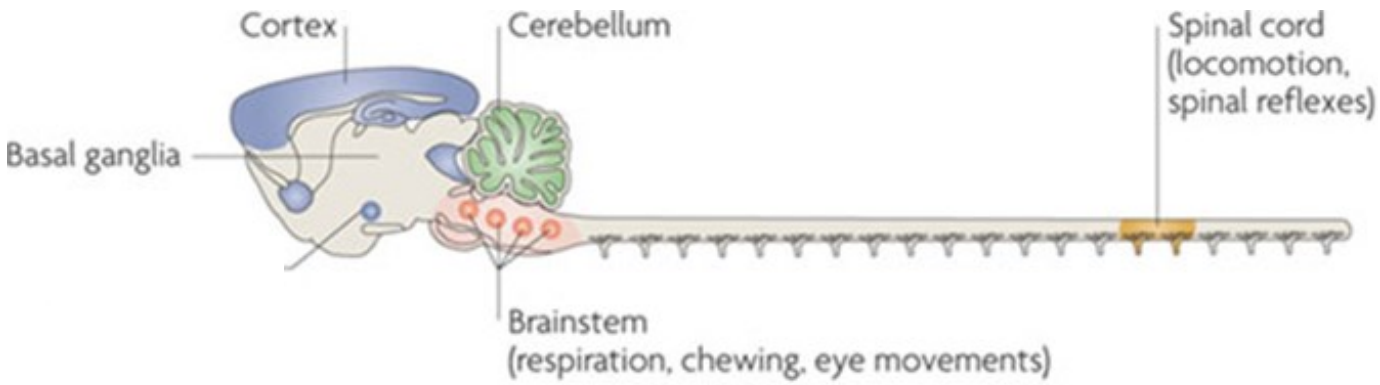
Article | Published: 17 January 2018

## Midbrain circuits that set locomotor speed and gait selection

V. Caggiano ✉, R. Leiras ✉, H. Goñi-Erro, D. Masini, C. Bellardita, J. Bouvier, V. Caldeira, G. Fisone & O. Kiehn ✉

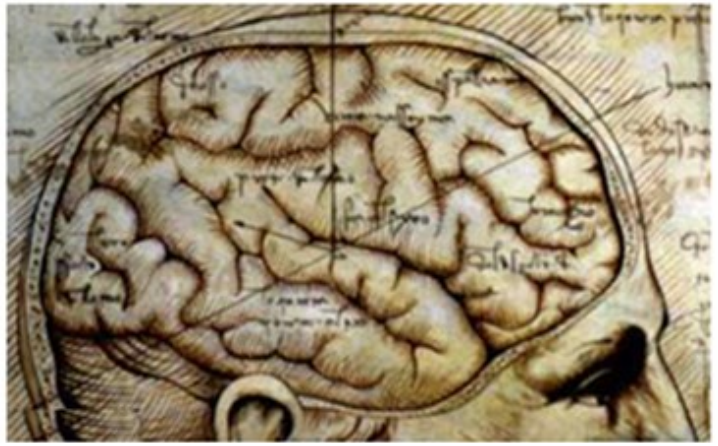
*Nature* **553**, 455–460 (25 January 2018) | Download Citation ↓

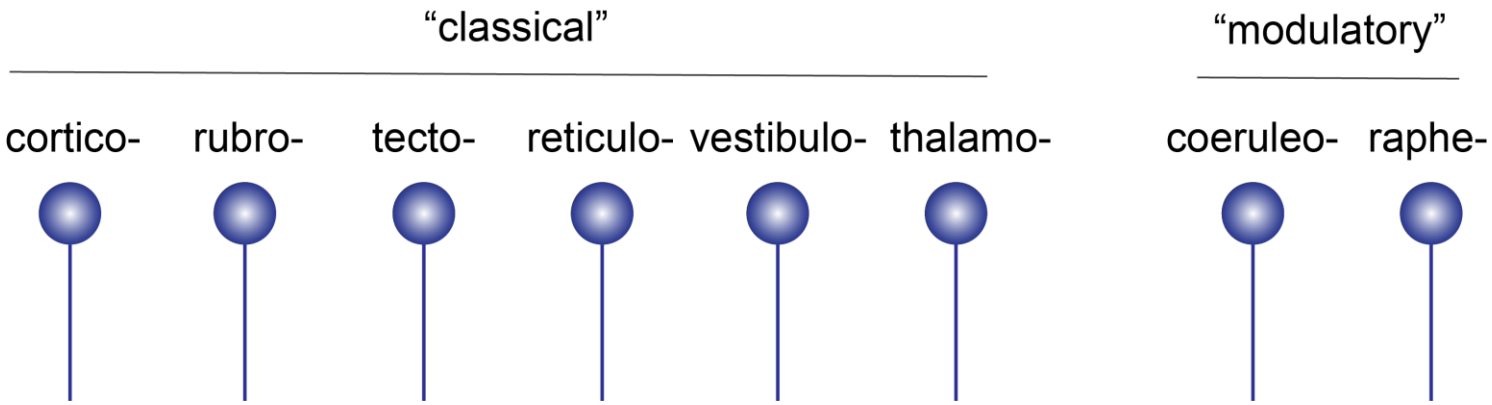
# Adapting the spinal rhythm via descending brainstem pathways



# Descending pathways modify and modulate spinal circuits

a snapshot of 27 descending tracts….

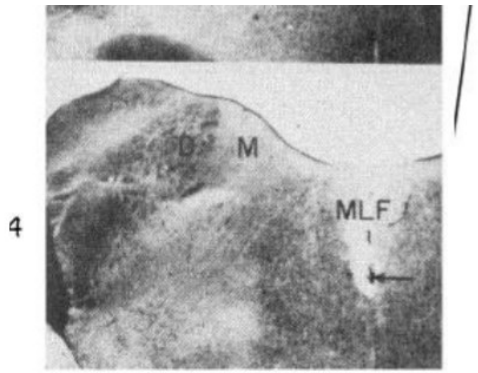


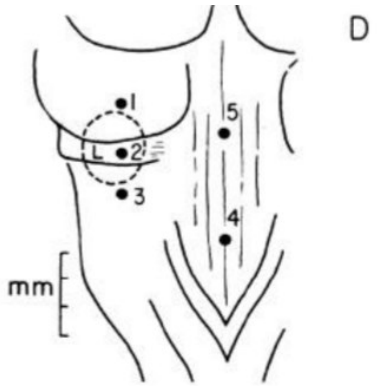



**Reading:** Ferreira-Pinto et al., 2018. Neuron. Connecting circuits for supraspinal control of locomotion.

# Reticulospinal pathways

excite both extensors and flexor motor neurons



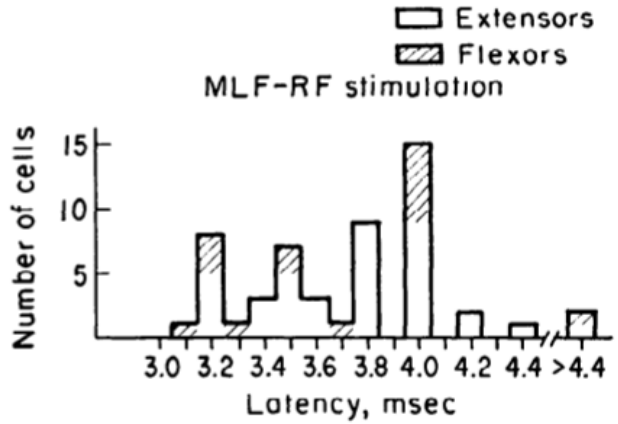



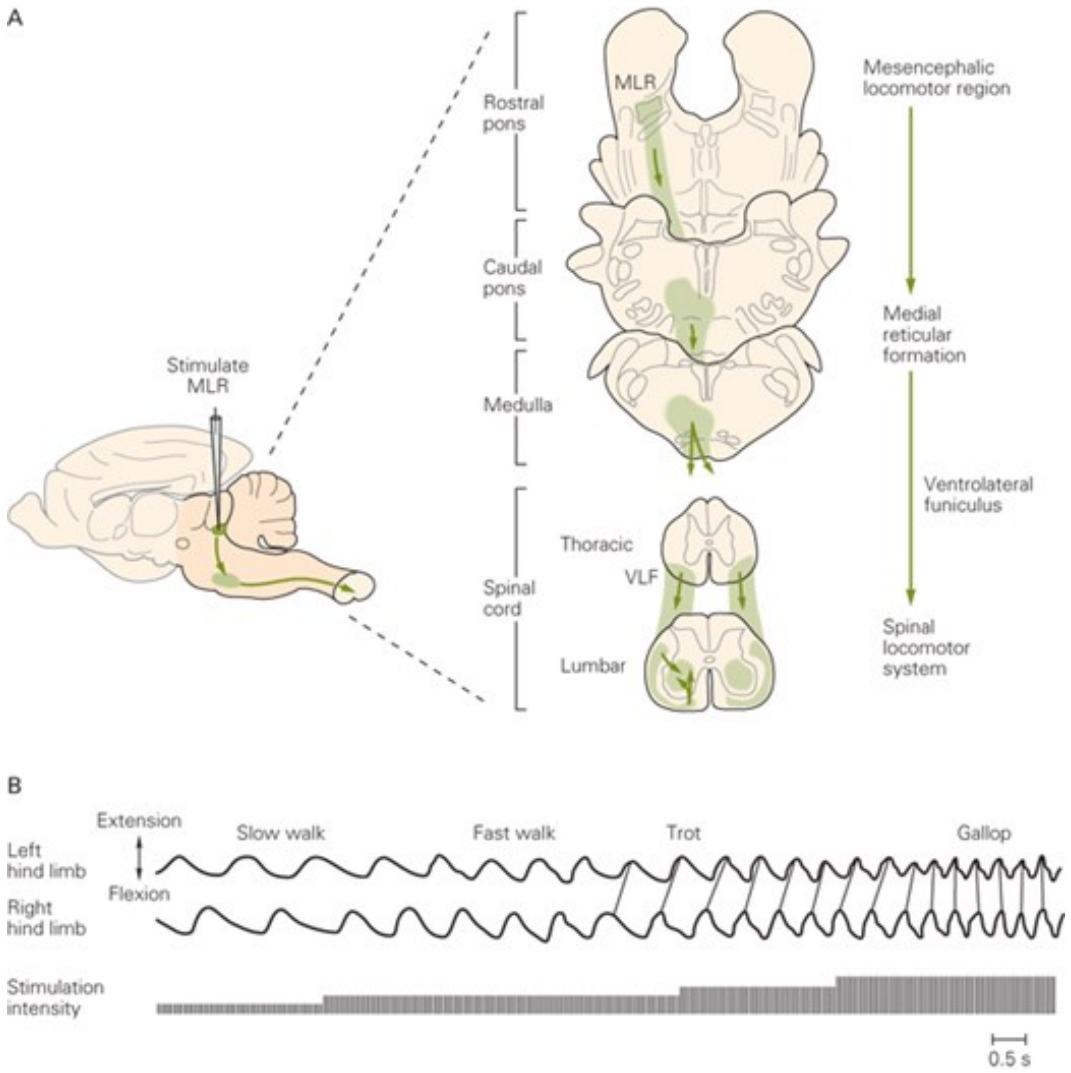

TABLE 1. *Effect of stimulation of Deiters' nucleus and medial longitudinal fasciculus (MLF-RF) on hindlimb motoneurons*

| | 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 |



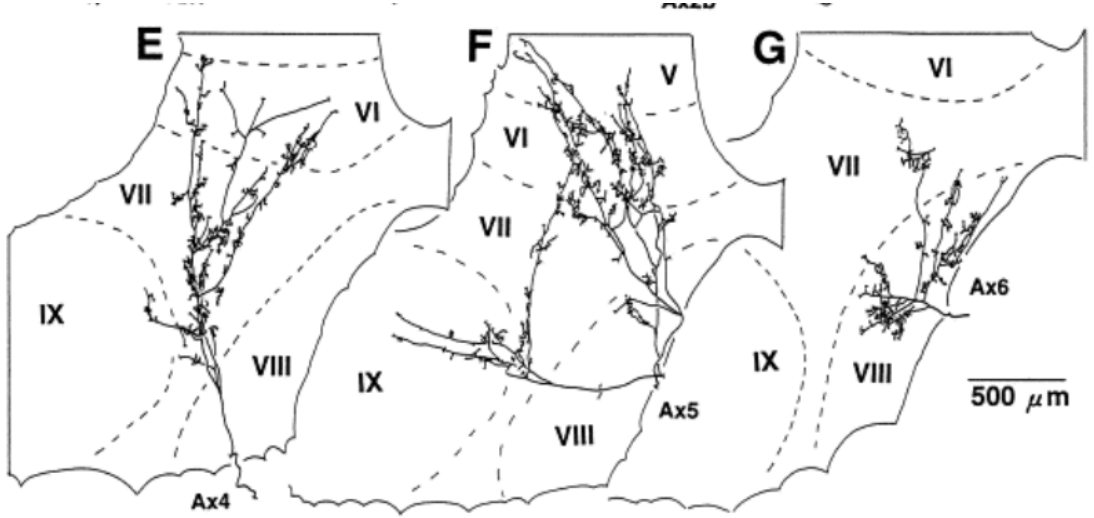
Wilson and Yoshida, 1969

# Reticulospinal pathways – the command neurons for movement (?)

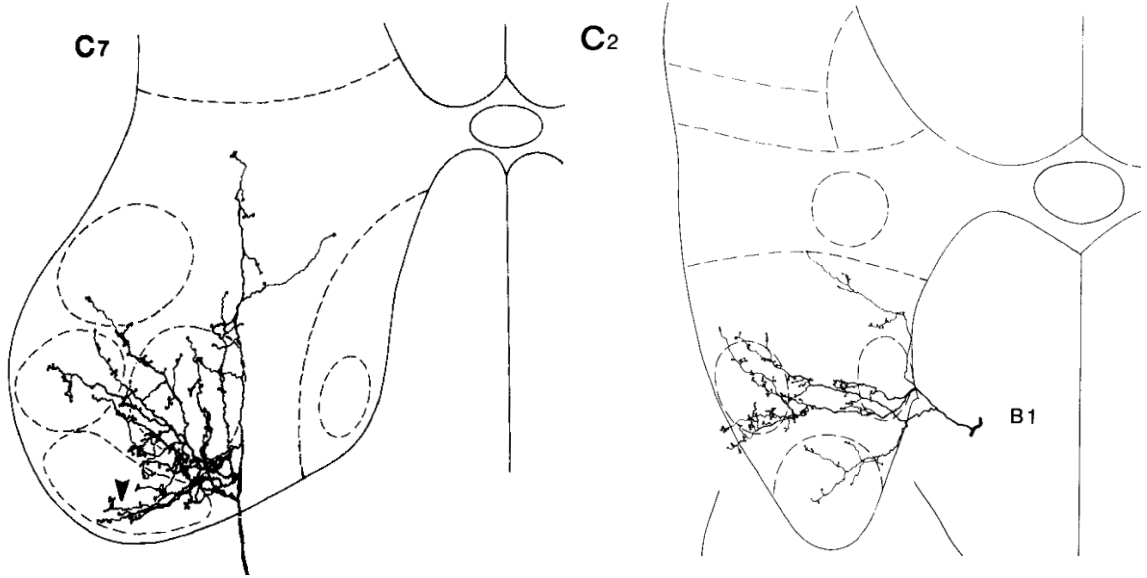


# Individual descending axons can influence multiple spinal circuits

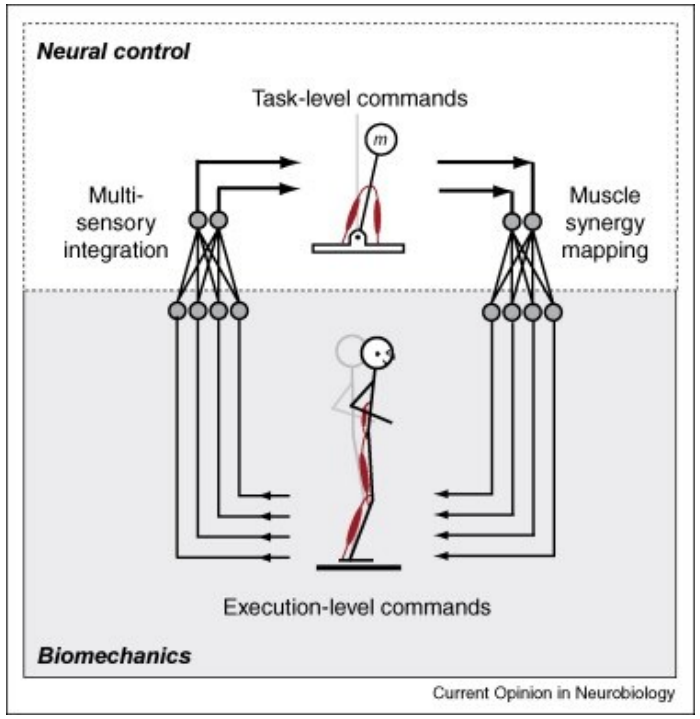
## Reticulospinal

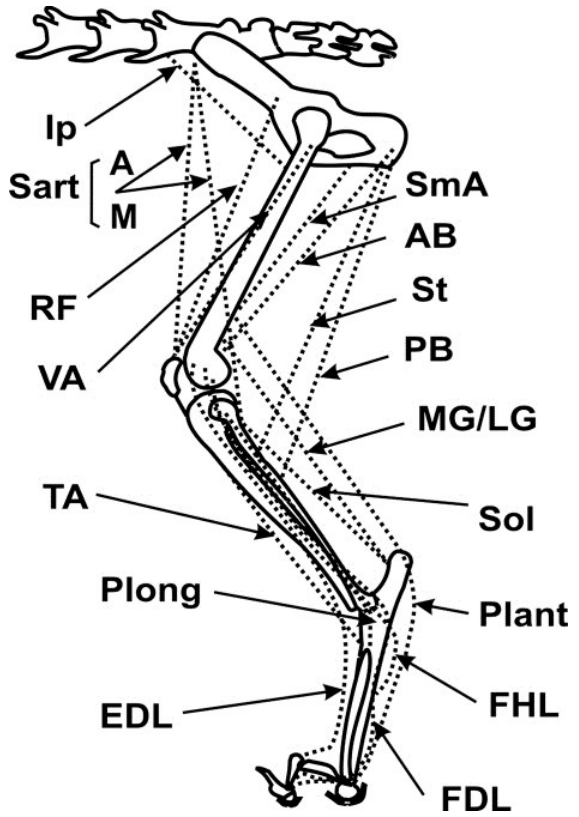


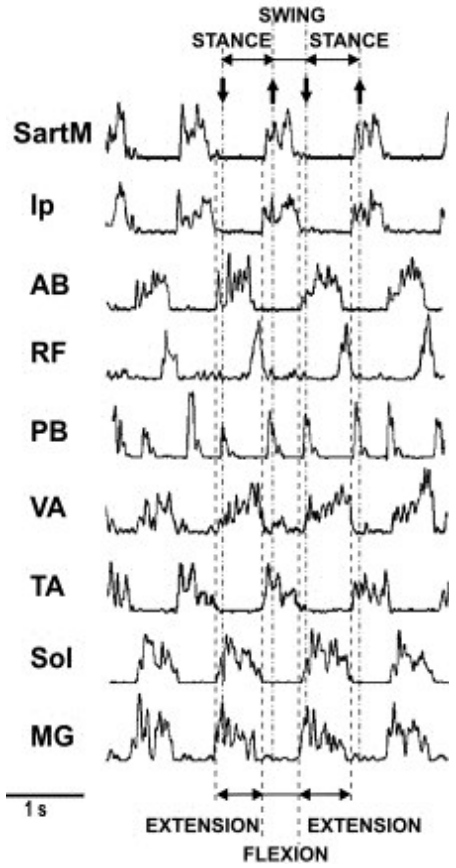

## Vestibulospinal



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



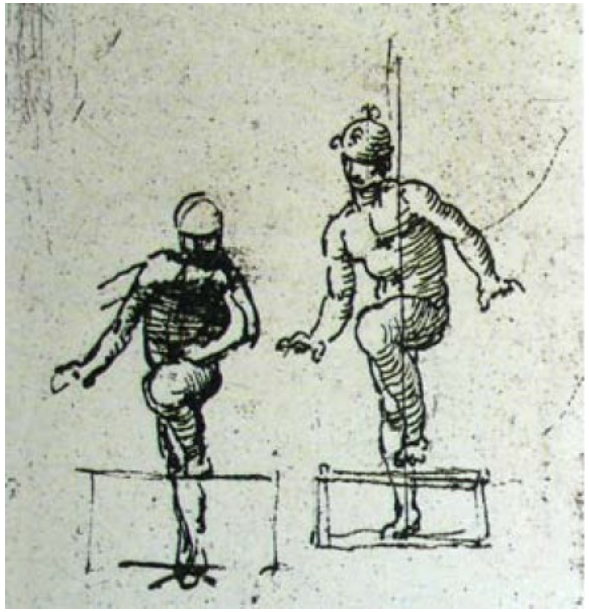




Markin et al., 2012; Ting and McKay, 2007

# Adaptable movement

# Movement must be flexible

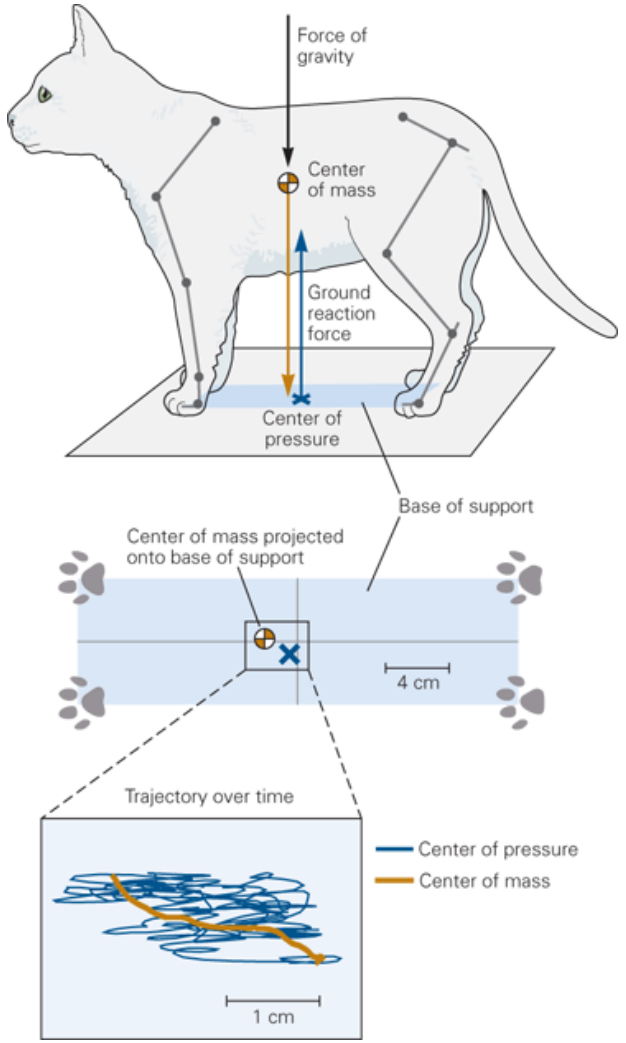


Da Vinci, ~1500

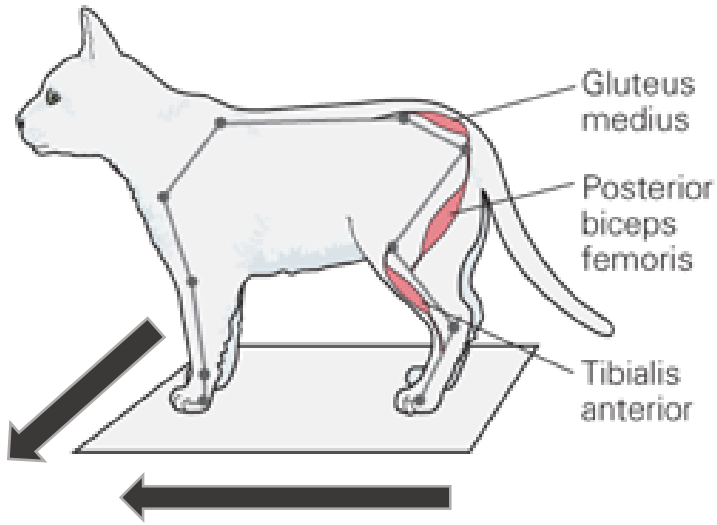

Borelli, 1681

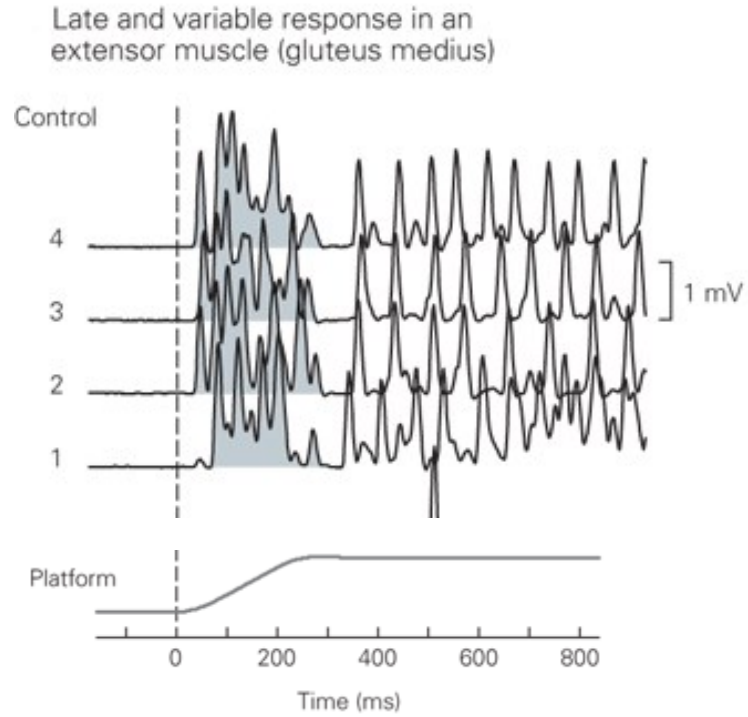
Marey, 1873

# Postural control is an active process that requires descending commands



# Postural control is an active process that requires descending commands

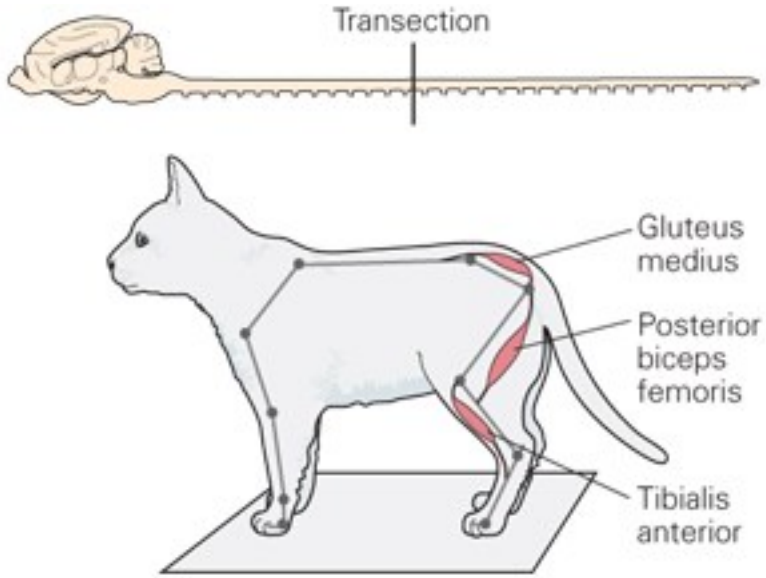


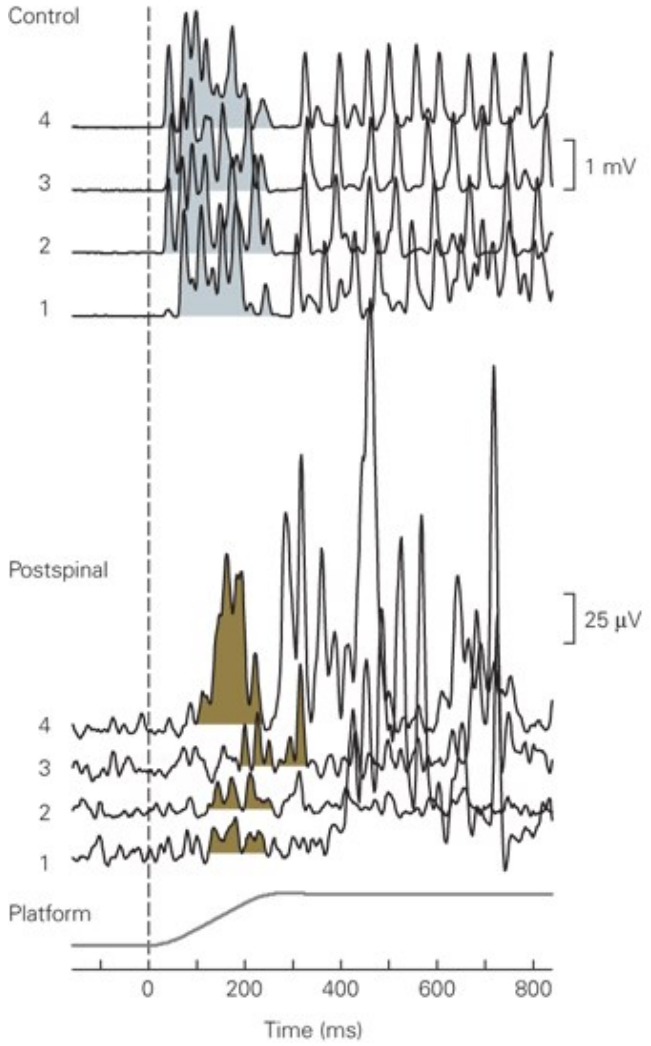






Macpherson and Fung, 1999

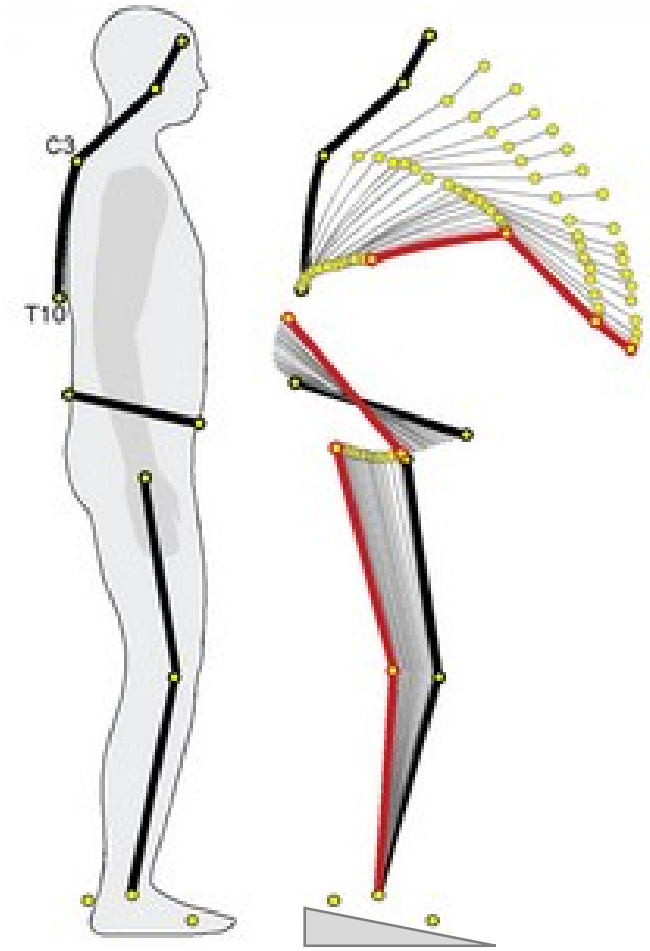
# Postural control is an active process that requires descending commands



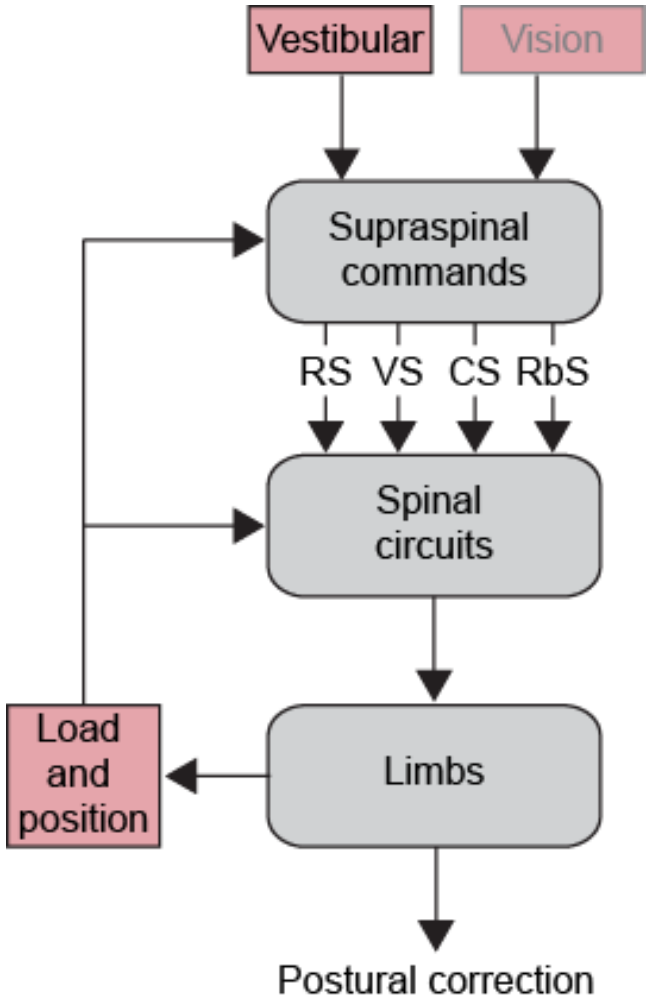



# Postural control and balance – you only notice when it's not there


Courtesy of Prof. Fay Horak, OHSU



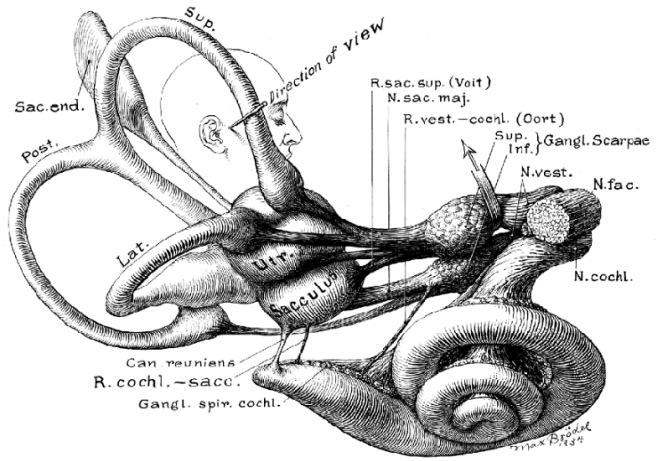
# Postural pathways

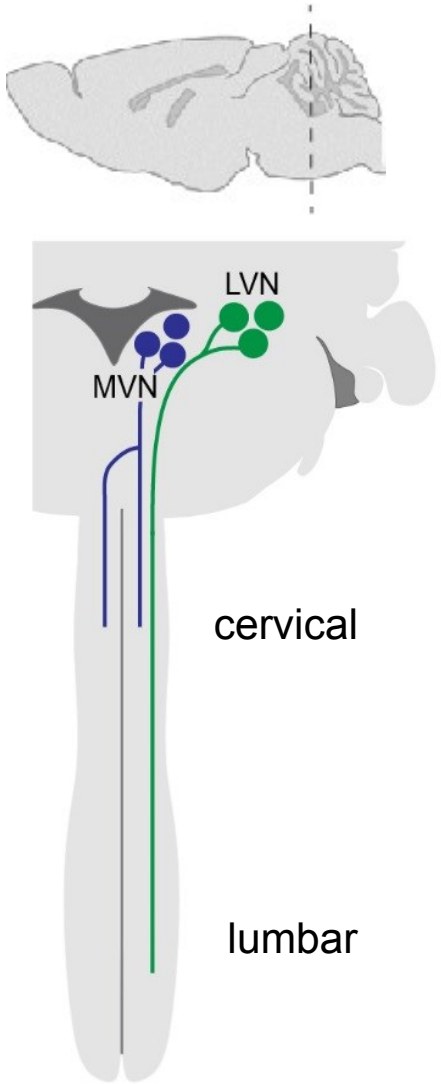



Deliagina et al., 2014

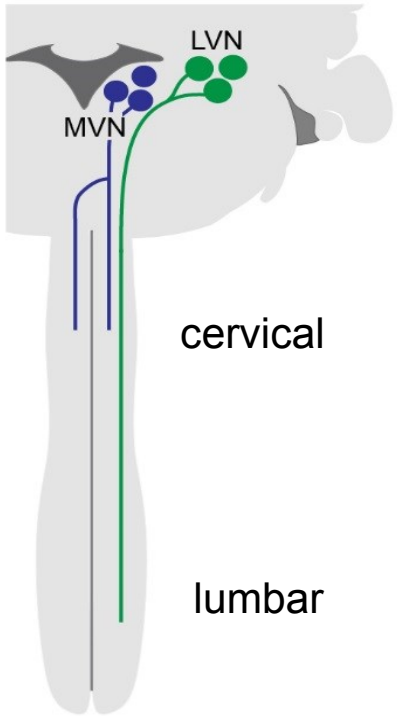
# Vestibulospinal tracts

Maintain balance and posture using rotation and acceleration of the head



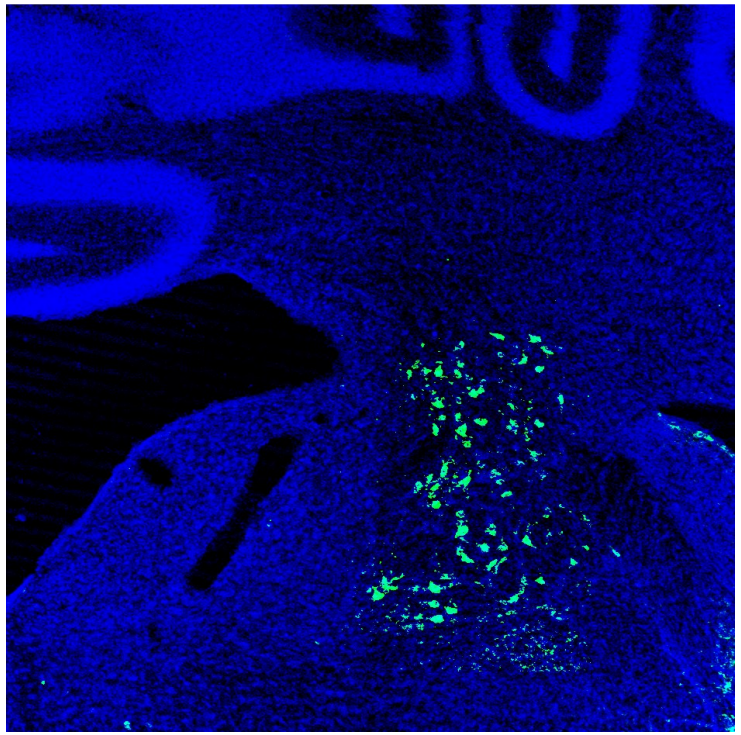



# The lateral vestibular nucleus projects to all spinal levels

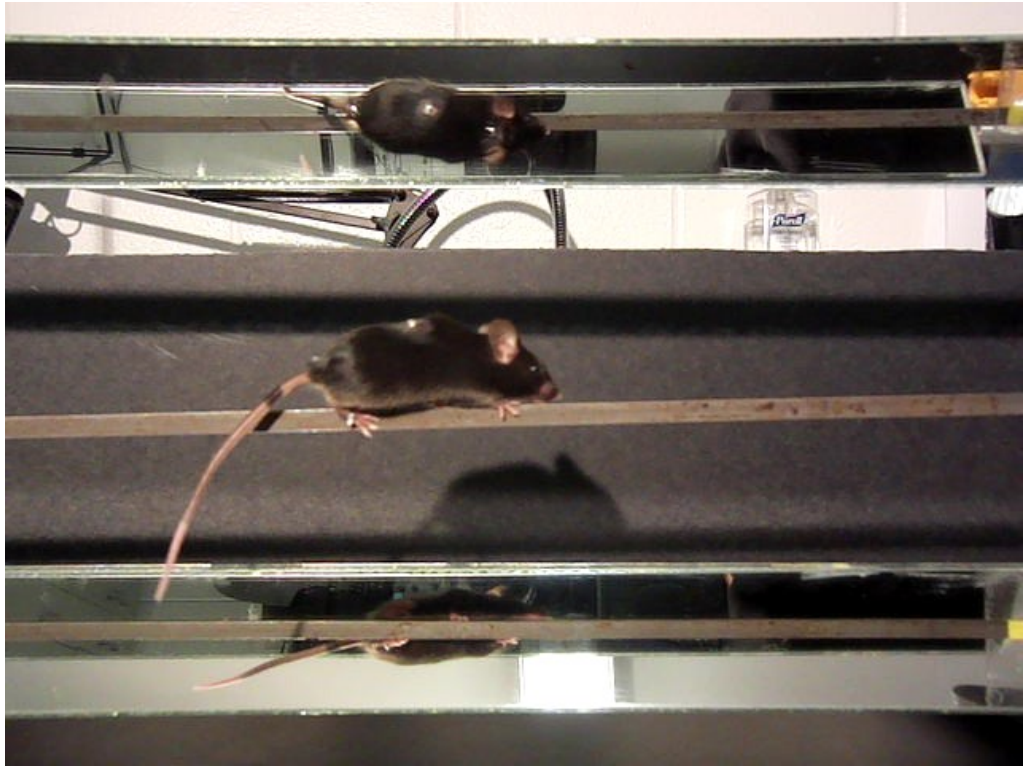


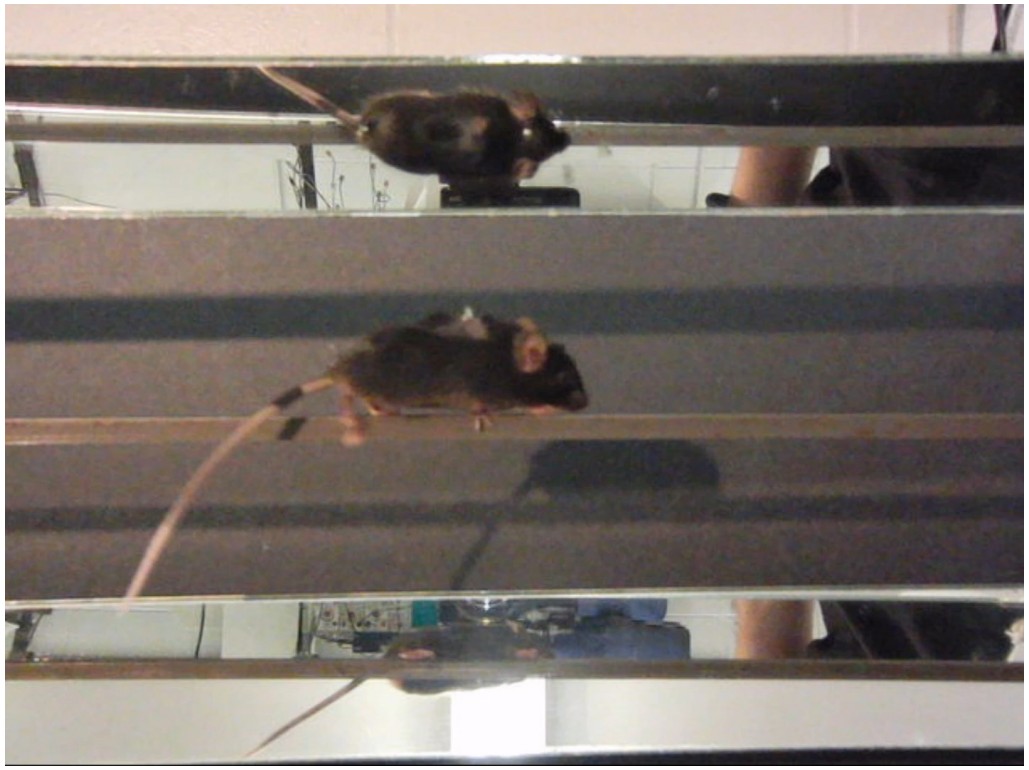

Fluorogold (lumbar SC)

Nissl



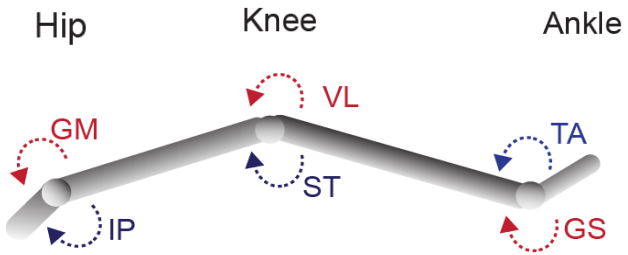
# Vestibulospinal pathways are required for reflexive balance control

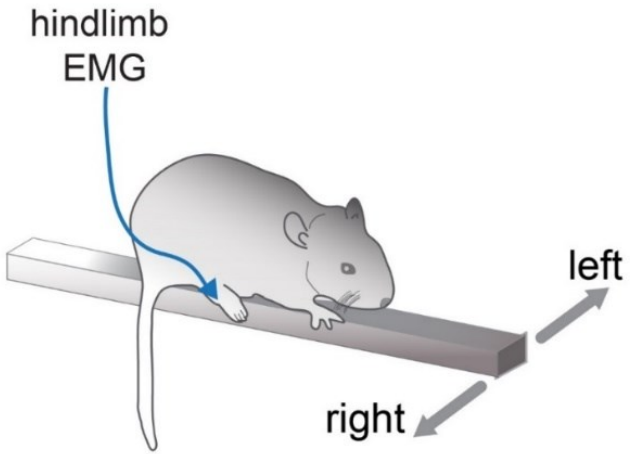




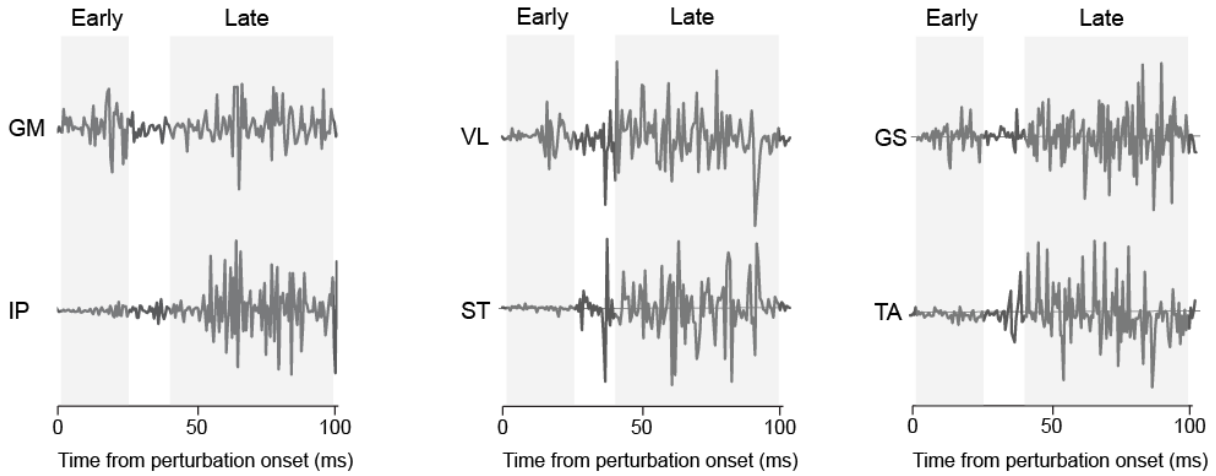
# Vestibulospinal pathways generate a contextually appropriate motor program to maintain balance

Extensors
Flexors

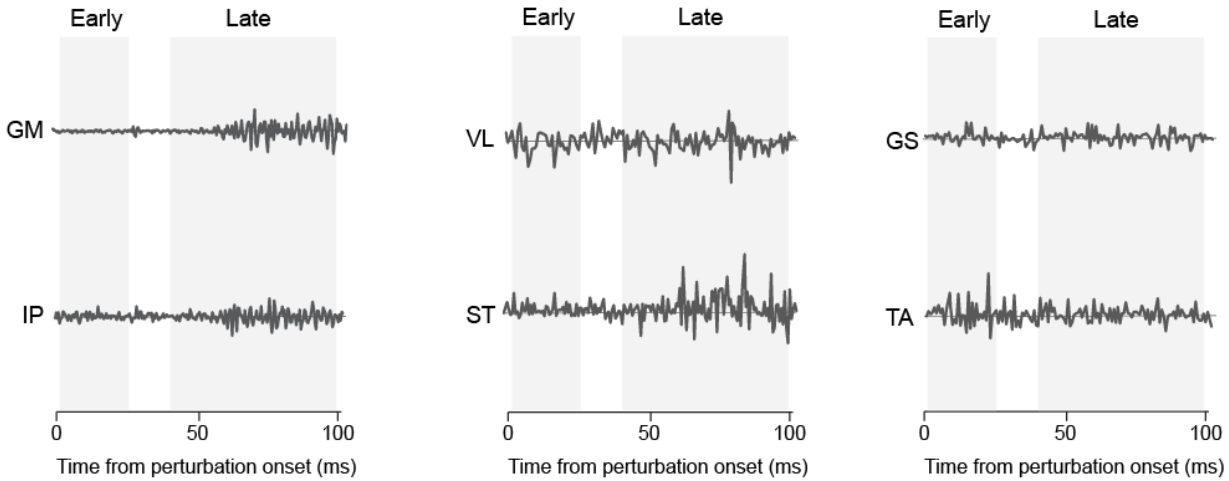



## With lateral vestibulospinal pathway

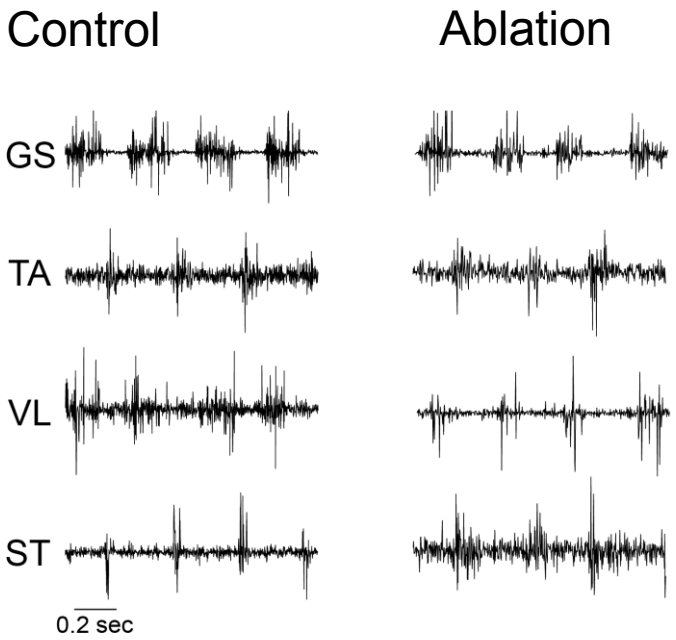


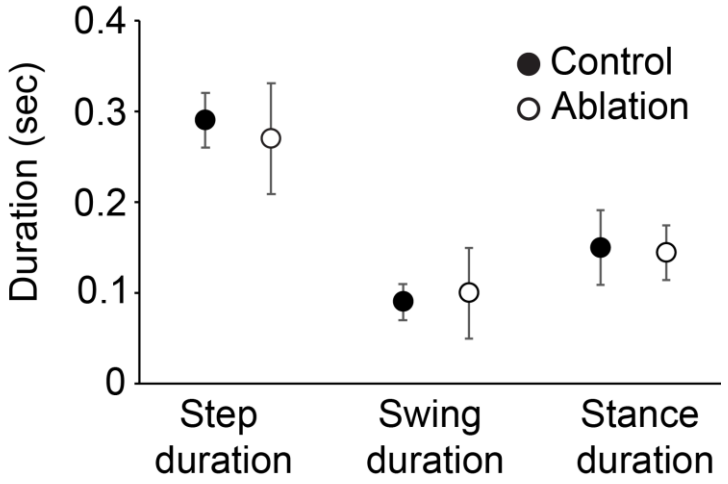

## Without lateral vestibulospinal pathway

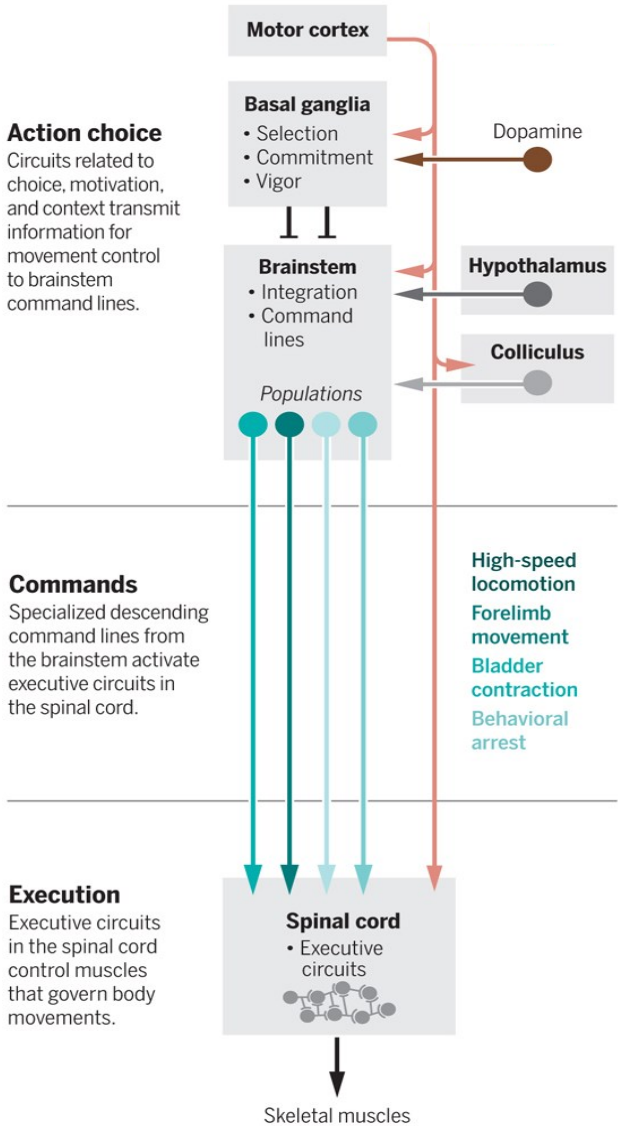



Sainsbury Wellcome Centre

# Vestibulospinal neurons are not required for treadmill locomotion

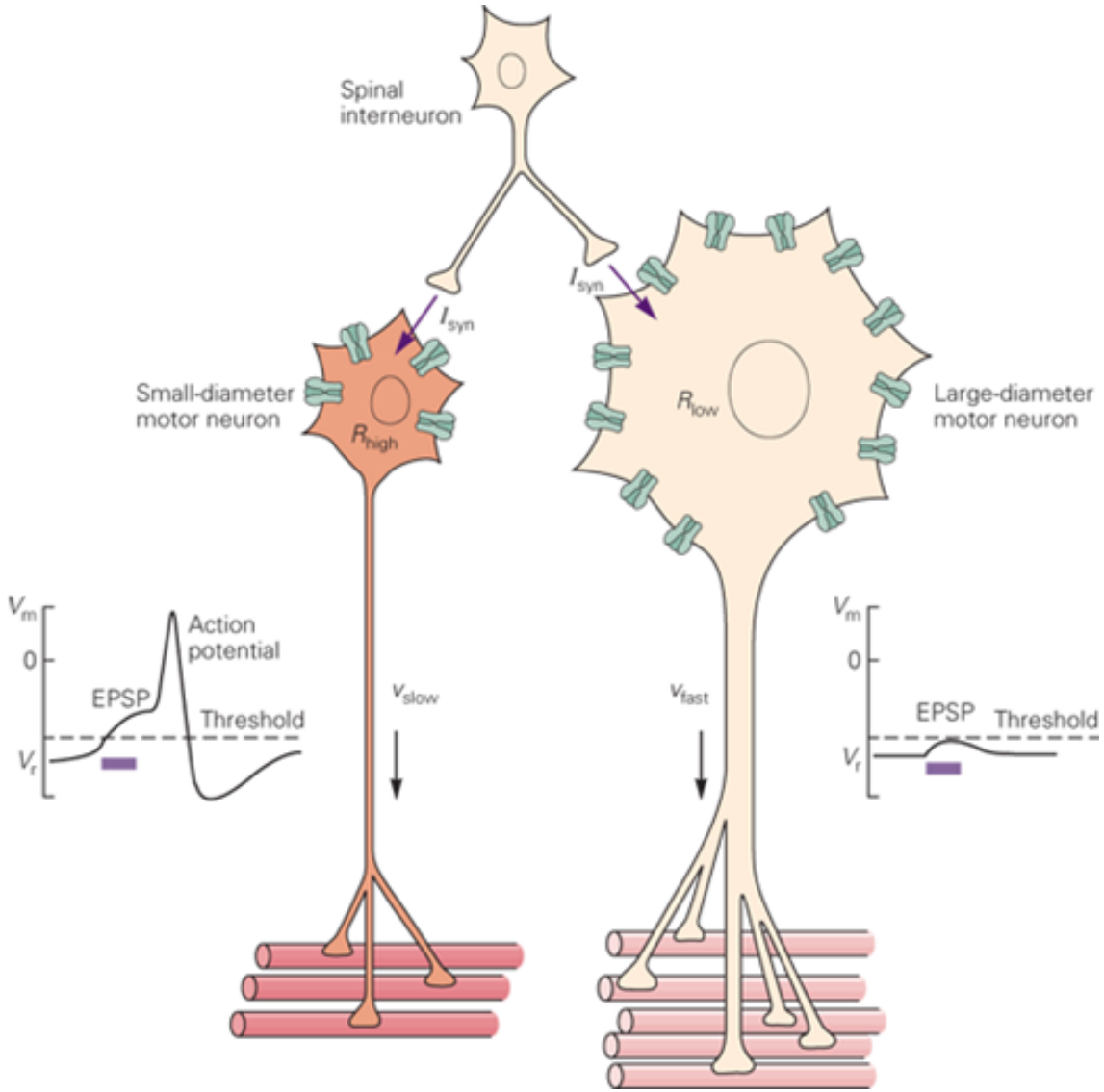




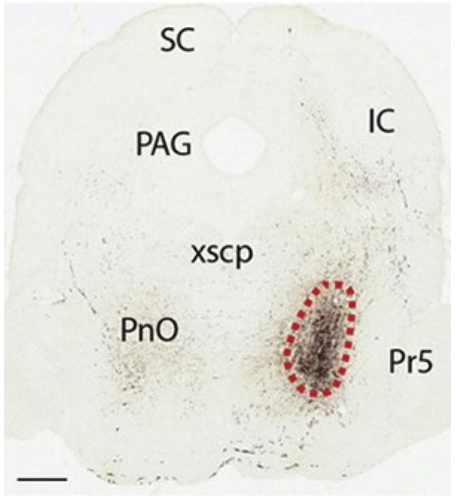

| | |
|---|---|
| Motor systems overview | Mon 12th |
| Pattern generation | Tues 13th |
| Computational control | Fri 16th |
| Cerebellum | Mon 9th |
| Basal Ganglia | Tues 20th |
| Neocortex/Discussion | Fri Nov 23rd |

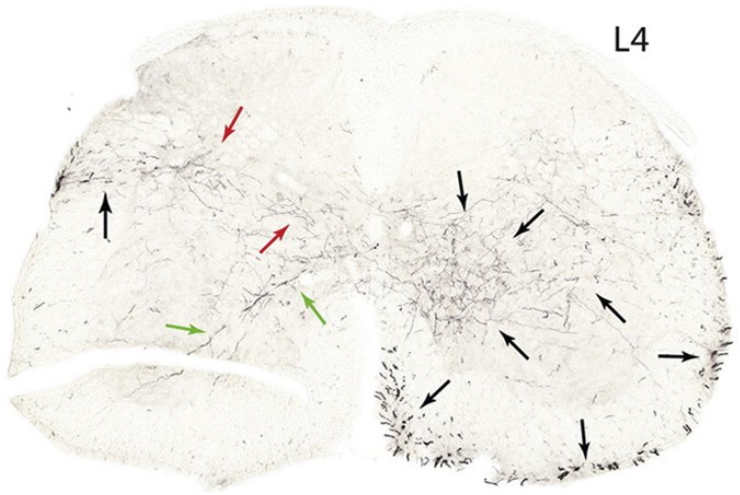
# Muscles and motor neurons

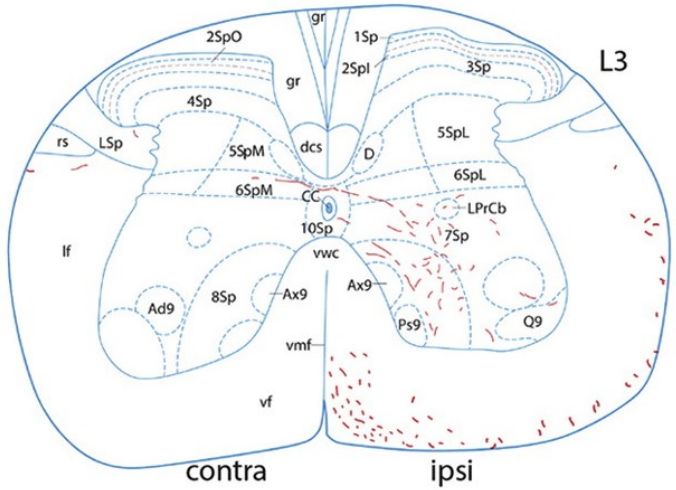


# Reticulospinal pathways

have diffuse projections into the spinal cord




Liang et al., 2015