Properties of locomotion: Coordinated and Rhythmic.

Coordination: can be L/R alternative or synchronous

- Basic locomotion pattern can be generated in the spinal cord:
    - **Experiment shows cat can walkon treadmill following transection of the spinal cord.**
    - **Experiment recording firing from a rat spinal cord segment shows flexor-extensor coordinated firing.**
    - Spinal cord network act as a central pattern generator (CPG): generate rhythmic motor output.
- Basic spinal cord circuitry layout: based on reciprocal inhibition
    - Excitatory ipsilateral interneuron (IINe) stimulate motor neurons (MN), stimulate inhibitory contralateral interneurons (CINi).
    - Inhibitory contalateral interneuron (CINi) inhibit motor activity on the other side, generates L/R coordination
    - **Optogenetic experiment: expression of channelrhodopsin in glutamatergic neurons with light activation recreates swim-like movement in lamprey.**
    - Development of the spinal cord circuitry occur early in development: **Switching thoracic with lumbar spinal segment lead to synchronous leg movment (hopping) and alternating wing movement.**

- Mammalian spinal circuitry: more complex than the Lamprey, 3 regulatory pathways:
    - Indirect inhibitory: excitatory commissural interneuron (CINei) excites the inhibitory interneuron on the contralateral side, inhibiting motor neuron (Glutamatergic)
    - Direct inhibitory: inhibitory commissural interneuron (CINi) inhibits the contralateral motor neuron, same as in Lamprey (GABA-nergic)
    - Direct excitatory: excitatory commissural interneuron stimulates the contralateral motor neuron, result in synchrony. (Glutamatergic)

- Development of mammalian interneuron network is a result of transcription factor patterning.
    - Reciprocal inhibition pathway is a result of Dbx1 transcription factor inducing V0 interneuron formation. **Dbx1 KO mice lead to loss of alternating pattern**
    - Alternation pattern is developed from L/R synchrony, mediated through the ventral white commissure. **Cutting of ventral white commissure lead to loss of synchrony.**
        - Early synchrony is due to excitatory signals generated by CINi, later converted to inhibitory signal
        - During early development, intracellular chloride ion concentration is high, cell is hyperpolarised, and the opening of anionic channel leads to efflux of chloride ions, causes depolarisation.
        - High NKCC1 expression during early development (Na + Cl import), high KCC2 expression later in development, export of chloride ions. The expression pattern of 2 transporters — reverse flow of chloride ions. L/R synchrony to L/R alternation.

- Descending control
    - At the spinal cord central pattern generator, it receives sensory feedback and integrate into movement. **Obstacle will cause extended limb lifting to step over obstacle**.
    - The basal ganglia determines the goal of the action, initiate rhythmic pattern generated by CPG
    - Selected locomotion programme is then initiated in the midbrain locomotion region (MLR), control the speed of locomotion
    - Steering and posture of the action is controlled by the reticulospinal tract.
    - MLR controlling the speed can lead to change in locomotion pattern (e.g. walking to galloping alternation-

synchrony)

- Posture control development:
    - Descending input is required before locomotion can occur in both zebrafish and mice
        - In mice, control of the hindlimb is acquired after P14
        - Synapse formation of the reticulospinal tract allow stimulation of anti-gravity muscles for posture maintainence.
        - In zebrafish, development of dopaminergic neurons into the spinal cord lead to CPG activation, shown by decapitation + DA rescue

- Muscle type development:
    - Fast and slow fibre development depend on type of innervation.
        - **Switching of phasic/tonic nervous input lead to changes in muscle type**