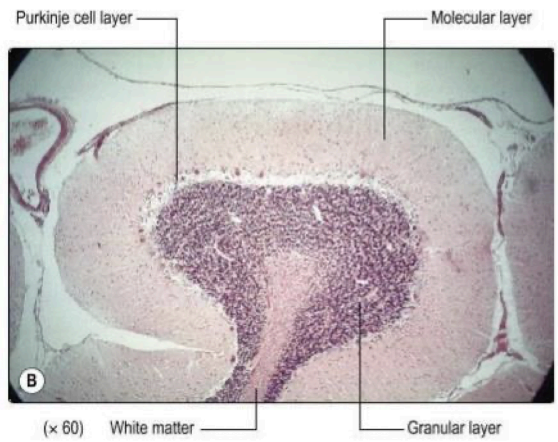
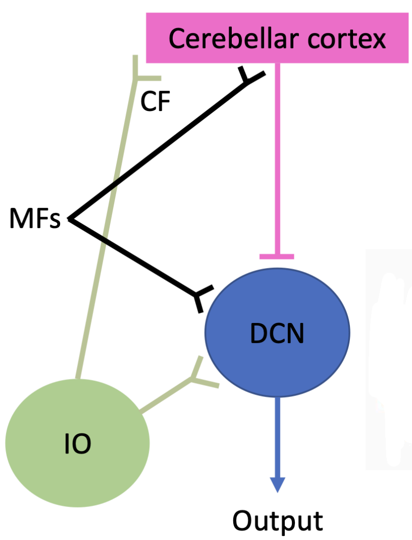
- Cerebellar cortex
  - 

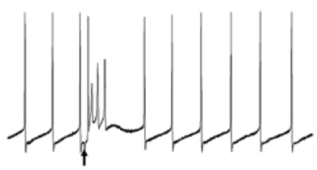
  - Major circuit elements:
    - Granule cells
    - Golgi cells
      - Input from mossy fibers and parallel fibers
      - Porvide inhibition to surrounding granular cells
      - Can contact up to thousands of granular cells
      - Gate information coming through granular layer
      - Affect timing of information coming through
      - Controlling volume of info coming through
    - Molecular layer
    - Purkinje cells
  - Outputs: Purkinje cell
  - Inputs: Mossy fibers & climbing fibers

Cerebellar Cortex

- Major inputs to the cerebellar cortex:
  - 

- Mossy fibers (target **granule cells** which send out **parallel fibers**, which then contact Purkinje cells)
  - Sensory input (e.g tactile, position and movement of the joint) and copies of motor command (e.g. basal ganglia) to the granular layer of cerebellar cortex
    - Spinal cord → sensory info about touch, pain, temperature, proprioception
    - Vestibular nuclei in the medulla and pons → movement of head
    - Via pontine nuclei in the pons which branch off to the cerebellum, the cerebellum receives:
      - Descending information from visual, auditory and other cortical regions
      - **Efference copies** of descending motor instructions going to the spinal cord
  - Main output and input cells in the cerebellum
    - Input integrated by granule cells
      - Bifurcate into parallel fiber
      - Receive 3 or 4 mossy fiber inputs per cell
      - Excite Purkinje cells as they are gutamintergic, but can also inhibit Purkinje cells as they synapse with molecular layer interneurons (which inhibit Purkinje cells)
    - Ouput via Purkinje cell
      - Dendrites spread in transverse plane
      - All parallel fibers connect Purkinje cells
      - Able to sample inputs from thousands of parallel fibres
      - Parallel cells make excitatory connections with Purkinje cells
      - Certain patterns of inputs affect spiking
- Climbing fibers (from inferior olive, target Purkinje cell mostly)
  - Target both cerebellar cortex and deep cerebellar nuclei
  - Strong control over Purkinje cells (wraps around Purkinje cells)
    - Potent connections

- Major output of cerebellar cortex: Purkinje cells
  - Purkinje cells target deep cerebellar nuclei and vestibular nuclei
  - Output is inhibitory, but often causes disinhibition of target
  - Fire 2 types of AP:
    - Simple Spikes
      - Depends on parallel fiber (from granule cell) inputs and molecular layer interneurons inputs modulates the rate of spikes
    - Complex Spikes
      - Climbing fibers (from inferior olive) fire causes complex spikes
      - Very stong depolarisation
        - Parallel fibers (from granule cells) and climbing fibers active at the same time = plasticity
          - Long-term depression (LTD) of parallel fiber

                ■ Parallel fiber becomes silent/shut off when climbing fiber active → cannot drive Purkinje cell
                    - Climbing fiber input can be seen as correcting error / learning signal
                ■ Apps R, Hawkes R. (2009)
                    - Studies indicate that different molecules expressed in Purkinje cell stripes could affect how LTD is regulated.
                    - For example, certain molecules like mGluR1b and neuroplastin are restricted to specific Purkinje cell subpopulations, while others like protein kinase Cδ, GABAB2 receptor, and EAAT4 are preferentially expressed in different Purkinje cell subpopulations. This suggests that the mechanisms and manifestations of long-term depression might vary between these subpopulations.
        - 

          Purkinje cell simple and complex spikes. IO stimulation is indicated with an arrow.

- Vestibulo-ocular reflex (VOR)
    - A reflex that helps to stabilize images on the retina during head movement
        - Produces an eye movement in the direction opposite to the head movement
    - Head movement detected by horizontal canals
    - They send inputs to vestibular nuclei and cerebellum (in particular the flocculus)
        - Input into cerebellum is via mossy fibres (which target granule cells which sends out parallel fibers)
        - Flocculus is responsible for adjusting gain of VOR (as vestibular nuclei is excited by horizontal canals)
            - Flocculus has 5 zones with 5 separate groupings of Purkinje cells that project to other areas
    - Direct excitatory input to vestibular nuclei and indirect inhibitory input from cerebellumm to vestibular nuclei
    - Balance of excitation and inhibition on the vestibular nuclei
    - Balanced outpu from vestibular nuclei to oculomotor nuclei
    - Eyes offset changes in position by amount equal and opposite to amount of head movement
    - Feedback and Error correction
        - Error signals are sent to inferior olives which send inputs via climbing fibers to the cerebellum → causes LTD of the parallel fiber inputs → corrects errors
        - Blocking LTD prevents adaptation

Learning

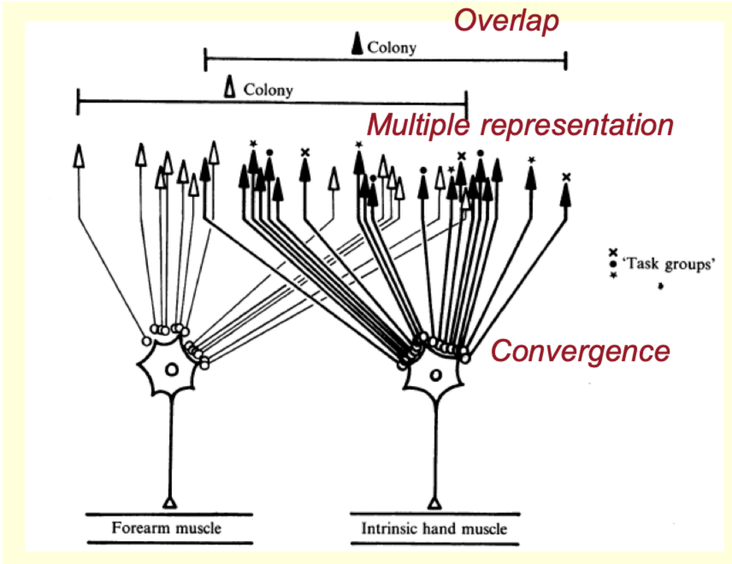
- Motor commands are sent by a controller (brain structures) to an effector (muscles)
- Feedback on the effectiveness of the resulting movement can facilitate improved motor commands through learning
- Learning is more effective when sensory feedback can be compared to copy of the initial motor command
- **Cerebellum** receives information from both feedforward/feedback models → involved in learning
    - Feedforward → copy of initial motor command
    - Feedback → copy of the sensory info from actual result
    - It can then compare the 2 copies

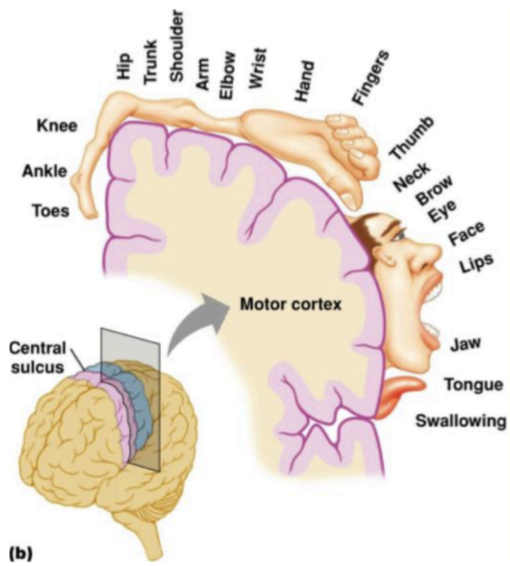
Cerebral Cortex

- Motor control involves a distributed network system with parallel processing
- The cerebral cortex is a part of the system that is the major route to enable other parts of the network to access the spinal cord
    - It consists of various projections to the spinal cord

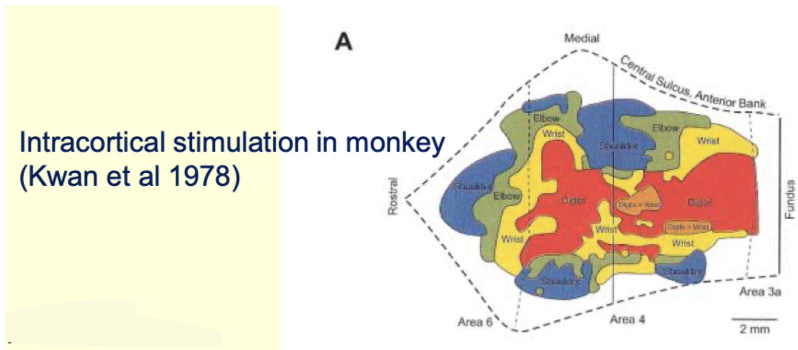
- Structure of Cerebral Cortex:
    - Lobes are divided into:
        - Frontal → motor function (e.g. primary motor cortex)
        - Parietal → Process sensory inputs
        - Occipital → visual processing
        - Temporal → language processing
    - Lobes are subdivided into Brodmann's functional areas
    - Gyri and Sulci
        - Increase surface area
    - Neurons of the cerebral cortex are organized in:
        - Columns
            - Combo of different columns of neurons activating →
            - Lateral connections
        - Layers
            - 6 layers
- **3 key aspects of cortical structure:**
    - Gyri and sulci
    - Thickness
        - Cortical thickness (represents number of cortical neurons) may be linked to Alzheimer's Disease

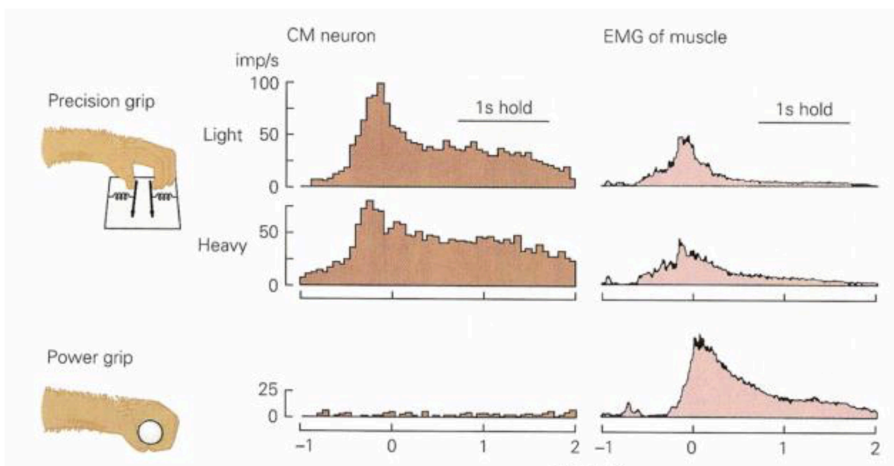
- Neurons organised in columns and layers

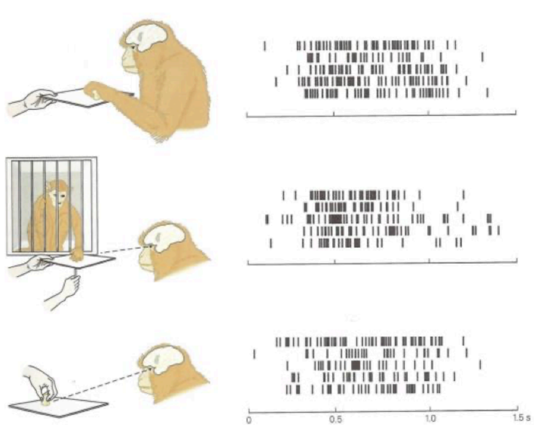
- Neurons convergence
  - 

  - Neurons are organised by tasks
  - Convergence: Many cortical neurons converging on 1 motor neuron
    - They perform the same task
- Somatotopical organization in the primary motor cortex
  - 

  - Neuron organisation is task-dependent (neurons controlling similar / same areas are grouped)
  - Multiple areas of representation for muscles and movements (same muscles may be controlled by different areas of the cortex)
    - Multiple representation → important for adaptability
    - Damage to 1 part of cortex, other parts can take on role of that part

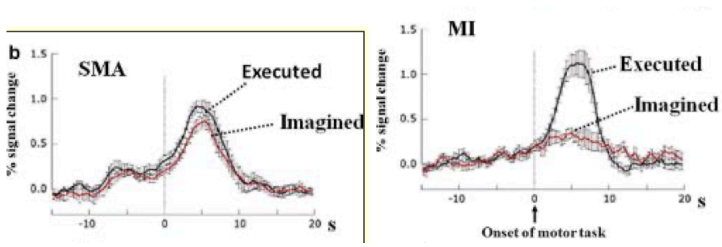
- 

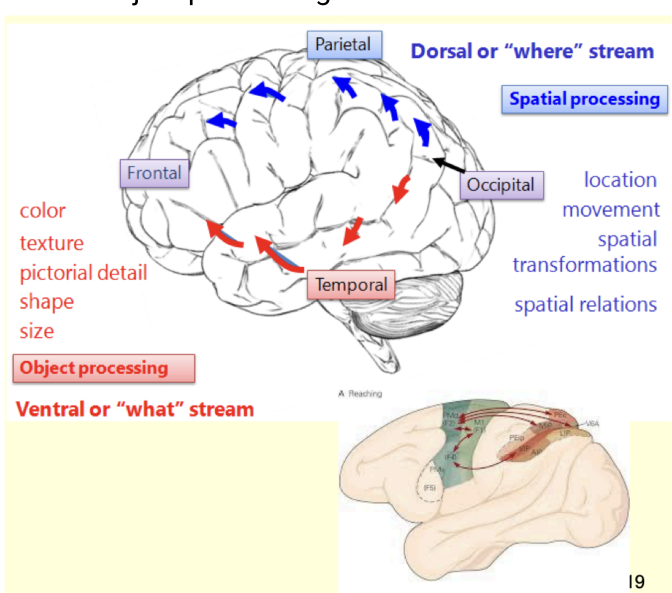
    - Mapped out representation of different muscles
- Cortical neurons are active before movement begins and firing corresponds to the direction of movement (preference for direction of movement)
  - Neurons are task-dependent
- 

  - The firing of neurons correlates with EMG
  - Precision grip ⇒ firing of neurons + EMG of muscle
  - Power grip ⇒ no firing of neuron, but lots of EMG, thus this particular neuron is responsible for precision rather than power
- Mirror neurons → role in observational learning and mental imagery
  - Firing of similar patterns of neurons when doing the task as well as observing the same task
  - Recorded from F5 region (premotor areas) of macaques
  - 

        - (Rizzolatti et al 1996)
    - Autism ⇒ defects in mirror neurons

Motor cortical areas

- Supplementary motor area (SMA)
    - Motor planning for learned **sequences** of movement (rather than specific movements)
        - 

        - SMA active when imagining and executing movement, but the motor cortex isn't
        - Motor initiation (intention to move = readiness potential)
    - Bilaterally active
    - Receives inputs from prefrontal cortex and basal ganglia via thalamus
        - Reciprocal connections with basal ganglia as well
- Premotor Area (PM)
    - Ventral and dorsal parts
        - Dorsal → Processes where the object is in space
            - Spatial processing
        - Ventral → Processes features of the object (e.g. weight, size, colour)
            - Object processing
        - 

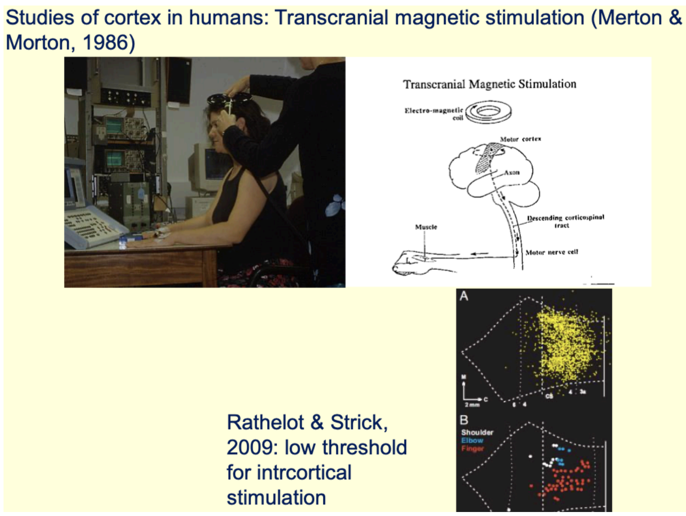
            - Demonstrates what information travels to which part of the PM
    - Important for visually guided movements and bilateral hand movements associated with visual cues
        - Uses sensory information to plan motor commands
    - Strong inputs from cerebellum
    - Links to the primary motor cortex to send out motor commands
- Cingulate motor area (CMA)
    - Active during imagined movements and signal trigged movements (e.g. in response to someone saying "go")
        - fMRI study finds that internally simulated movements during motor imagery activate cortical motor areas (CMA, SMA) and the cerebellum (Naito et al., 2002)
    - Anterior and posterior cingulate cortex may be important for action monitoring in task adaptation (e.g. detecting errors, such as what is the error magnitude) in feedback driven decision making (Li et al 2019)
- Primary motor cortex (M1)
    - Has somatotopic representations
    - Controls output to various systems and subsystems
    - Inputs to M1:
        - Mainly from sensory cortex
        - From ventral lateral nucleus of thalamus which relays info from PMC
        - From areas of thalamus that receive inputs from cerebellum
        - Some from basal ganglia
    - Outputs from M1
        - 50% of corticospinal neurons to spinal cord
            - ⅓ corticospinal tracts devoted to hand
            - Some directly to the motor neurons (corticomotoneuronal) others via spinal interneurons
        - Brain stem
    - Convergence of inputs on the primary motor cortex, which then determines output to the spinal cord
    - Division:
        - New M1 → indirect projections via interneurons (CST) + direct projections to motor neuron (CM) + area 3a
            - Corticomotor neuronal projection (CM, the direct projection) is unique to primates
            - Importat for dexterity of finger movements in particular
        - Old M1 → indirect projections to motor neurons via interneurons

Corticospinal Tract

- Corticospinal tract main output from M1 for voluntary movement

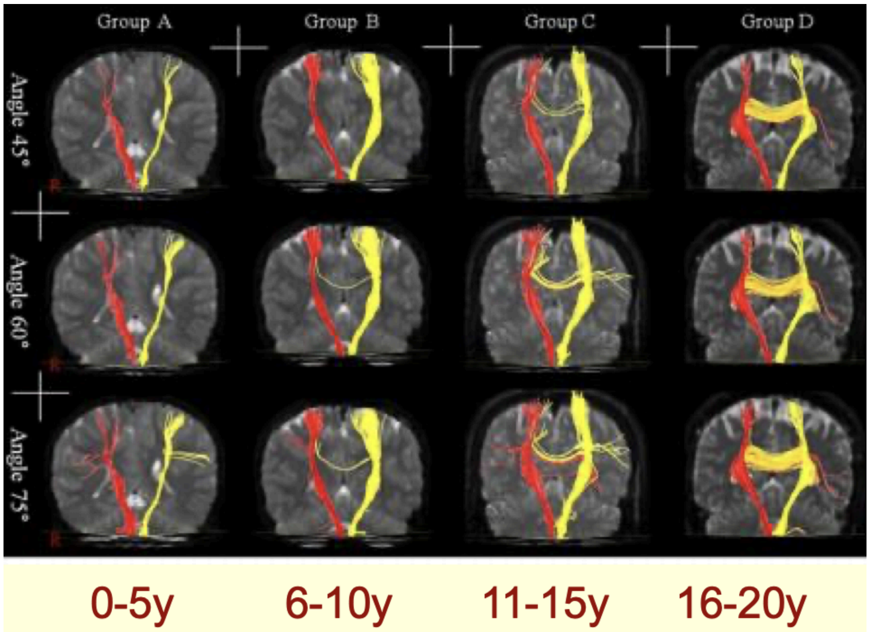
- Lateral - Predominant in humans
  - Innervates motor neuron pools via interneurons for distal muscles mostly
  - Crosses at the pyramids of the medulla
    - Has small ipsilateral (same side of the body) projection
    - 80% - 90% cross in the medulla to form the **lateral tract**
- Anterior
  - Innervates proximal / medial / truncal muscles
  - Cross over in spinal cord before synapsing with MN
- Direct corticomotor neurons (CM)
  - Synapse directly with motor neurons instead of through interneurons
  - 5% to 25%
  - Strong task specific effects
    - CM cell and target muscle were active during precision grip but not during power grip
  - Mostly to distal muscles but also to some proximal and truncal
  - CM activity can be dissociated from their target muscles
    - CM cell deactivated while muscle still active, indicating there are other inputs to the muscle than the CM tested
  - CM cells facilitate multiple muscles at once → have a muscle field
    - Muscle field includes multiple functional synergists
    - Relatively uncommon for CM to exhibit activity similar to its target muscle if it is just a simple agonist
  - Important for skilled hand movements, independent finger movements
    - Split-hand syndrome → greater weakness and muscle wasting in thumb and index, less for ulnar side of hand
    - Largest monosynaptic excitation following CST activation found in thumb and index finger muscles → these 2 are innervated by CM
    - Syndrom caused by TDP43 pathogen acting on CM projection
- Brain stem (some)
  - Pontine nuclei (which innervate the cerebellum) → provide copy of motor commands to cerebellum to allow for movement updates
- Ascending sensory systems → control sensory flow

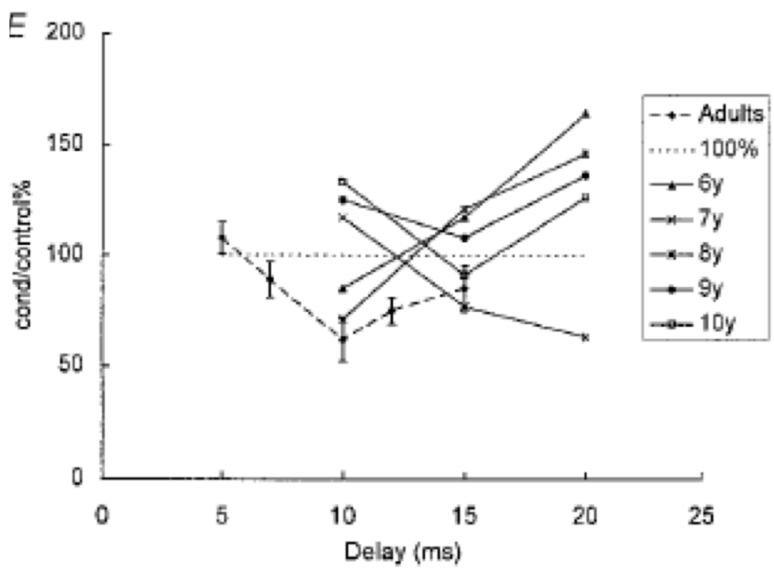
- Originates from neurons in layer 5
  - From several cortical areas, not just M1:
    - M1 (37.3%)
    - S1 (21%)
    - SMA (20.5%)
    - dPMC (10.2%)
      - (Seo and Jang, 2013)
    - Parietal cortex
      - CST is not purely motor in function (data from Rothwell)
- CM originates from caudal region of M1 and area 3a (part of S1)
- Involved in all body movements (direct and indirect excitation of motor neurons), but especially important for:

    - Fractionated movements → relatively independent finger movements
        - Particularly important for dexterity
    - Selective limb movements → Intralimb coordination
- Functions of CST (perfroms multiple functions but a common feature is **cortical modulation of spinal cord activity**):
    - Selection and gating of spinal reflexes
    - Facilitates inhibition via innervation of 1a inhibitory interneuron in the spinal cord
        - Impairment of CST linked with increased co-contraction (aka extensor less inhibited)
- Low threshold for intracortical stimulation → easy to activate
    - Transcranial Magnetic Stimulation
    - 

- Increased corticalisation = increased dexterity of primate hand
- Humans have the greatest density of corticospinal tracts
    - More reliant on corticospinal tracts for precise movements
    - Reticulospinal and rubrospinal tracts less involved in movements in humans

- Pyramidal neuron (in cerebral cortex) activates agonist and antagonist
    - Reciprocal conversation via cortical neuron
- Inhibitory connections between 2 hemispheres via **corpus callosum** → enable **interhemispheric inhibition**

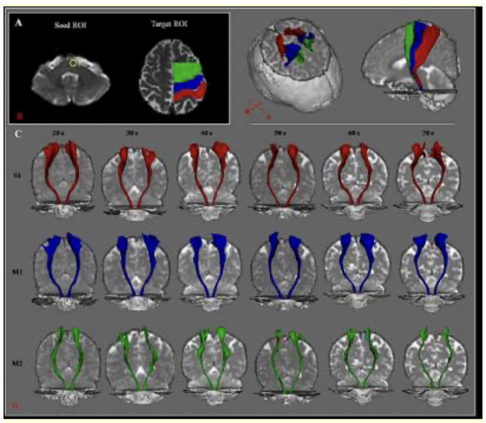
- 

- Corpus callosum fully myelinated in late teenage years and able to lateralise function
- 

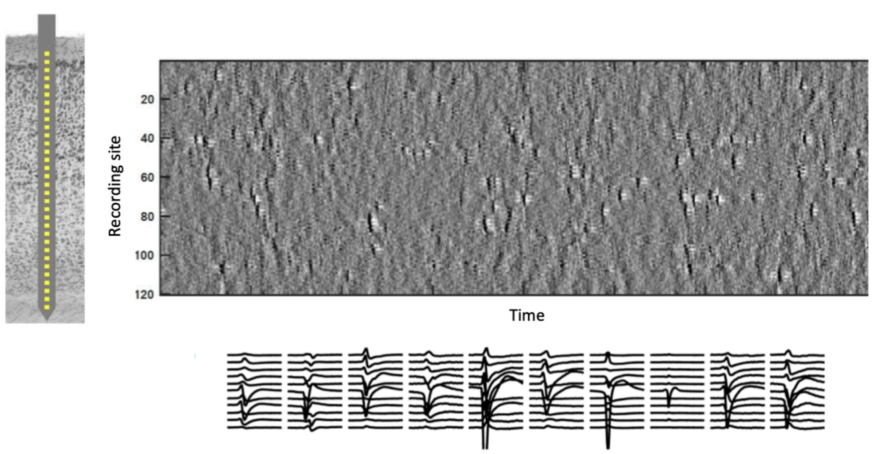
Mayston et al 1999 I-H inhibition
- Myelination (speed of conduction) are important in affecting callosal inhibition

- Storke results in loss of selective and fractionated movement due to damage to corticospinal tract
  - CST is important for dexterity
  - Recovery can consider complementary pathways to corticospinal tracts:
    - Reticulospinal pathway (more developed in non-human primates)
      - Brain stem origin
      - Elbow movements, reticular cells activated during flexion of joint in monkeys (Soteropoulos et al., 2012)

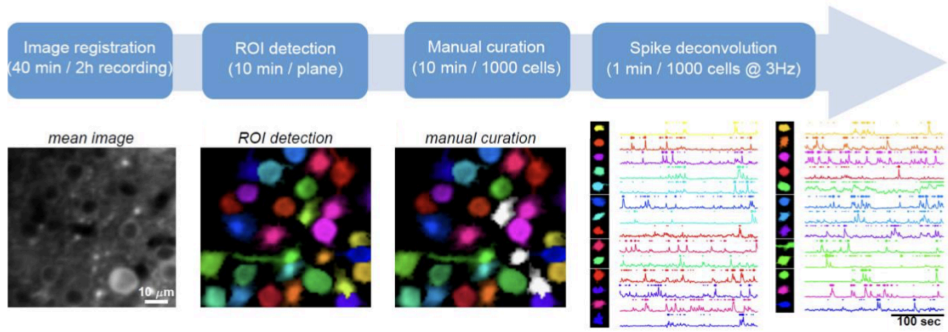
        - Propriospinal pathways
            - Spinal cord origin
                - Connections between different levels of spinal cord
            - Role in reaching

- Nervous systems adapt as we age
    - There is activation of other cortical areas for production of hand movement
    - Both sides of cortex activated for unimanual movement for older people
        - Similarities between activated areas when you impair system and when you age
    - No significant difference in corticospinal tract structure with aging, its more the activation pattern that results in this lack of lateralisation
        - 
          Jang & Seo 2014
- Control of movement is distributed and adaptable

Computational Neuroscience

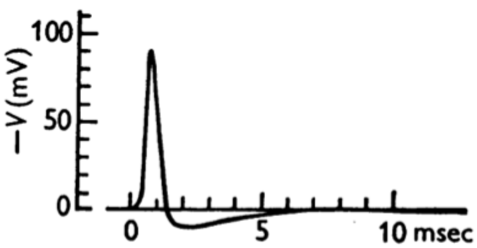
- Computational neuroscience:
    - Using computers to make sense of neural data
        - 

- Spike sorting in multielectrode recordings
- Repetition of firing pattern



- 2 photon imaging

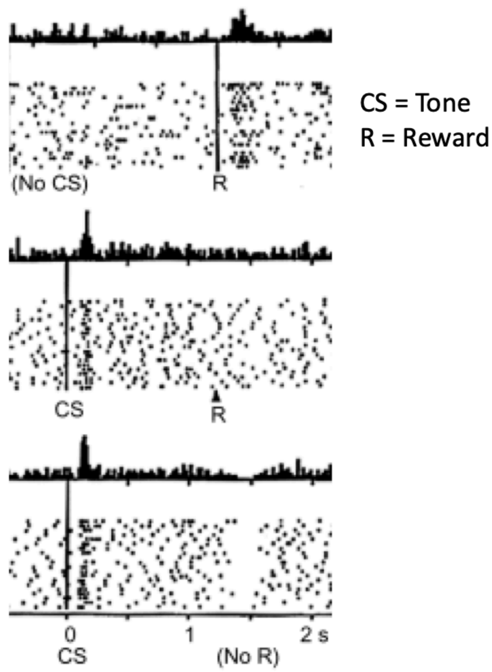
- Applying equations to describe neural phenomena
  - Action potential



- The shape very similar to an action potential
- Predict biological phenomena

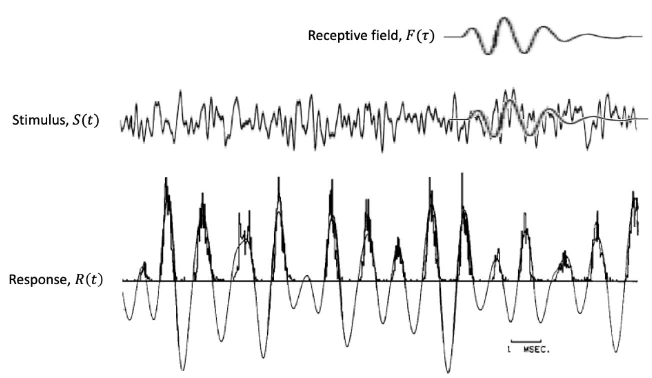
Studying computations performed by the brain

- Prediction error
  - Basis of reinforcement learning
    - Key equation maps to neuron activity
  - Prediction error = actual reward - expected reward
    - $$\delta(t) = r(t) - V(t)$$
    - Actual reward could be negative to indicate a punishment
    - Makes prediction about world



- Neuron firing increases after reward (histogram spikes) and then returns to normal
- Neuron firing increases with reward after tone
  - Tone is predictive of reward
- Neuron firing decrease with no reward after tone
  - Expected reward is higher than actual reward

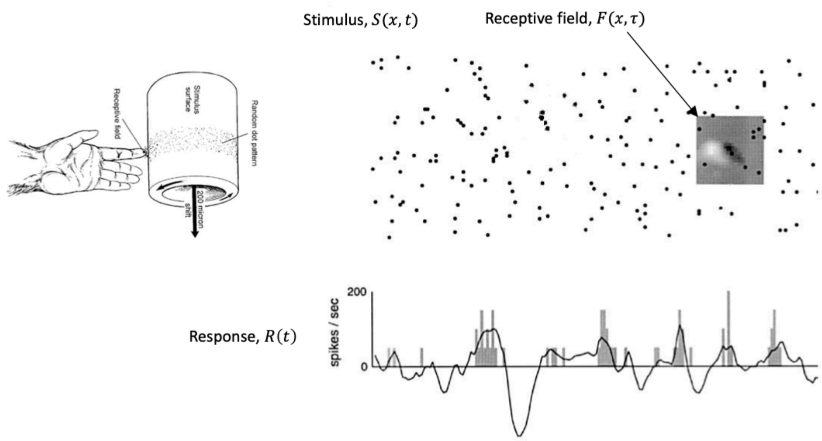
- Filtering

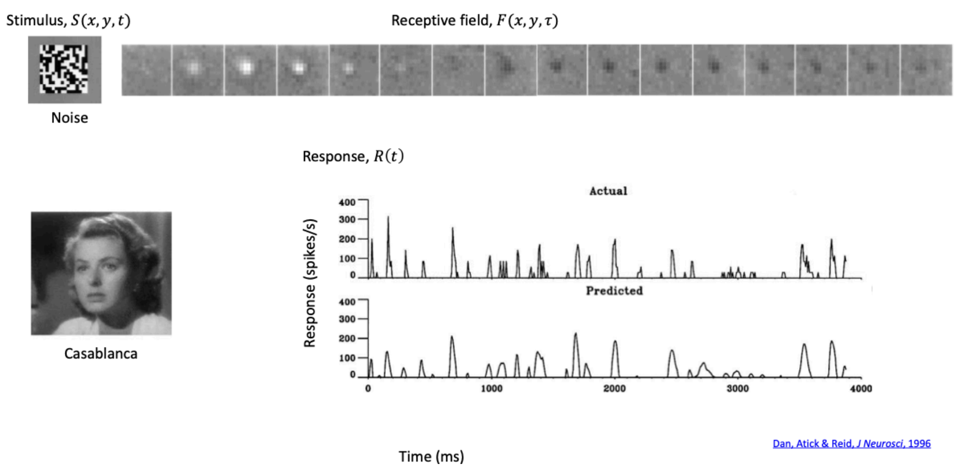


- 1 dimensional
- Noisy stimulus applied
- Neuron produces response when the stimulus maps to the receptive field shape

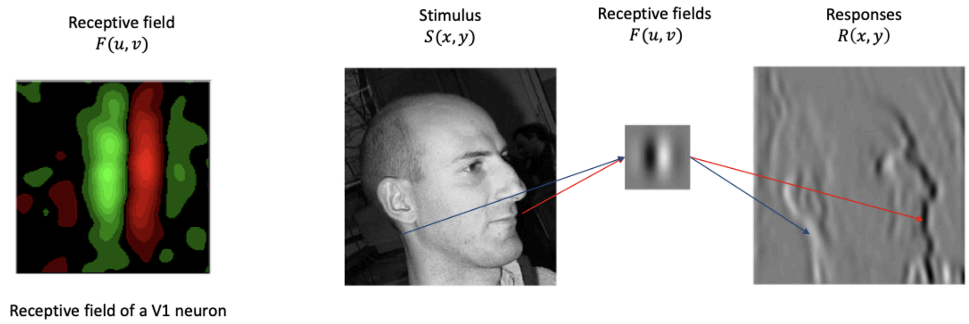
$$R(t) = \sum_{\tau} S(t-\tau)\, F(\tau)$$

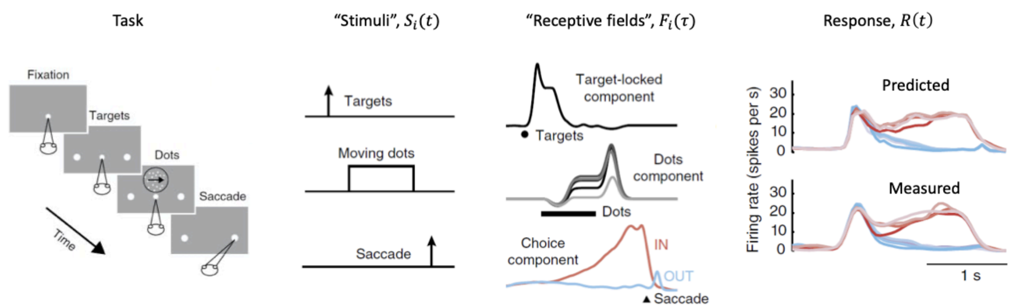
- t = time

- 

  - 2 dimensional
  - Neurons receptive fields are small per neuron in hand
    - Precision
  - $$R(t) = \sum_{x,\tau} S(x, t-\tau)\, F(x,\tau)$$
  - Model predicted neuron response in somatosensory cortex very well, equation / graph mapped onto the responses recorded
- 

  - 3 dimensional
  - Presented noisy stimulus to cat and recorded receptive field
    - Neurons fired when white light is shown
    - Neurons fired when black areas are shown
  - $$R(t) = \sum_{x,y,\tau} S(x, y, t-\tau)\, F(x,y,\tau)$$
  - Prediction of responses by the equation mapped to actual responses

- 

    - The neuron receptive field responds to white on the right and black on the left
    - The image shows an edge which has black on the right and white on the left
    - Neuron will fire “negatively”
        - Neurons cannot fire negatively, it may be that a twin of this neuron will fire
- 

    - Filtering in the parietal cortex

Locomotion

Locomotion is the ability of an organism to move in space in purposeful ways under its own power by efficient mechanisms

Locomotion reqruies precise rhythm (frequency of cyclic activity) and pattern (spatiotemporal activation of muscle groups within a cycle)

3 basic elements:

- Basic locomotor pattern
- Maintenance of equilibrium
- Adaptation to environment and personal goals

Characteristics:

- Progress through space
- Adaptability to different terrains and obstacle