- **HEALTH-2007-2.2.1-2: Coding in neuronal assemblies.** Research should focus on mechanisms of coding at the level of neuronal assemblies or microcircuits, aimed at understanding the interface between neuronal activity and behavioural performance. The project should develop interaction between experimentation and modelling, and therefore include a strong neuroinformatics dimension."

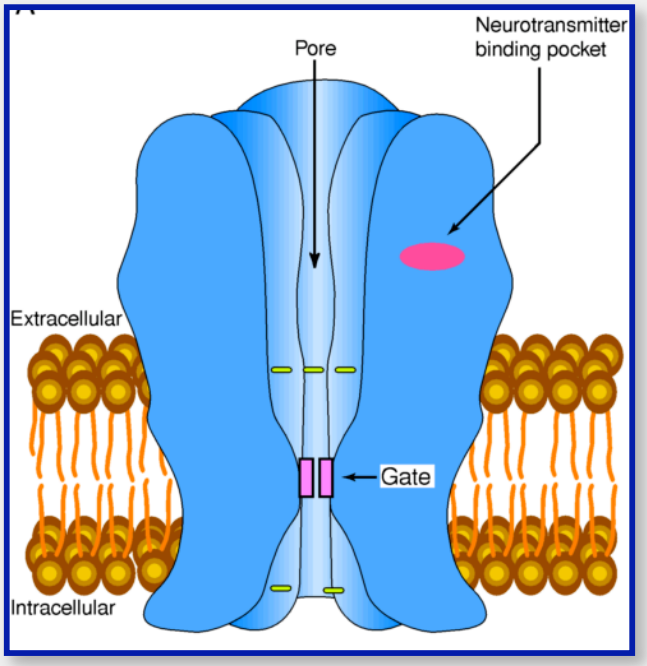
Neuronal networks the interface between the cellular level and global brain function

Sten Grillner

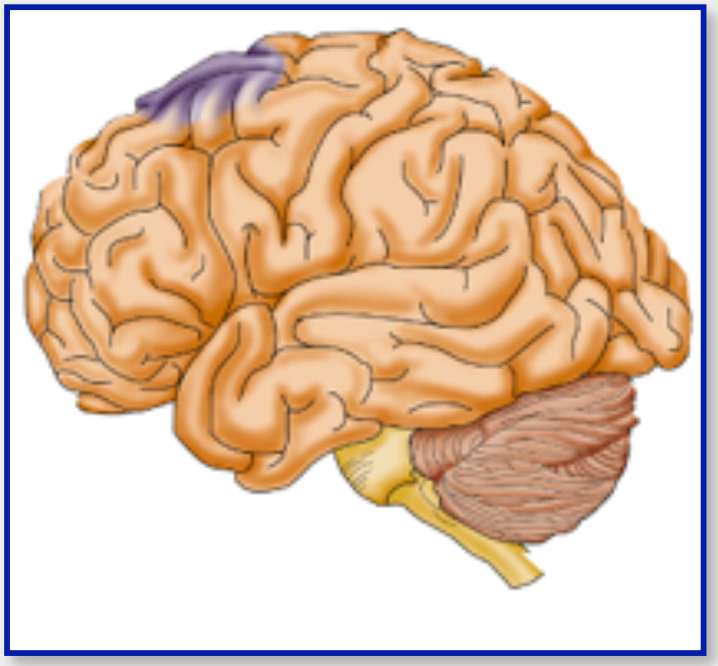
Karolinska institute

Stockholm

the great challenge of current neuroscience
the interface between
the cellular level and global brain function -



?



Behaviour is produced by networks/microcircuits of interacting nerve cells

molecule/gene - cell - synapse - network – behaviour - cognition

Modelling in interaction with experimentation needed to understand the Brain

- large number of dynamically interacting processes -

Ion channels

Synapses

Networks

Behaviour

Mental states

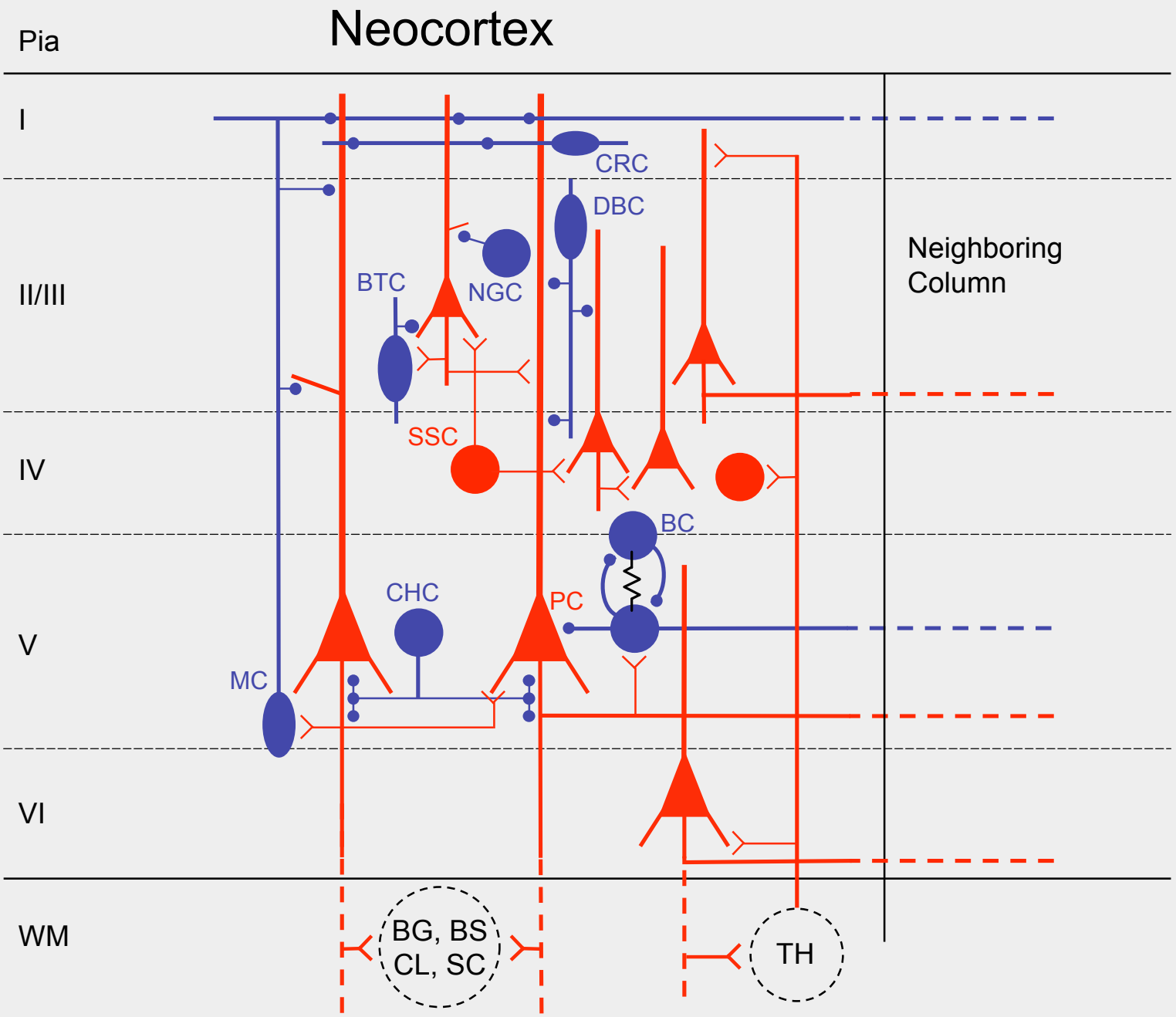
Diseases

Örjan Ekeberg

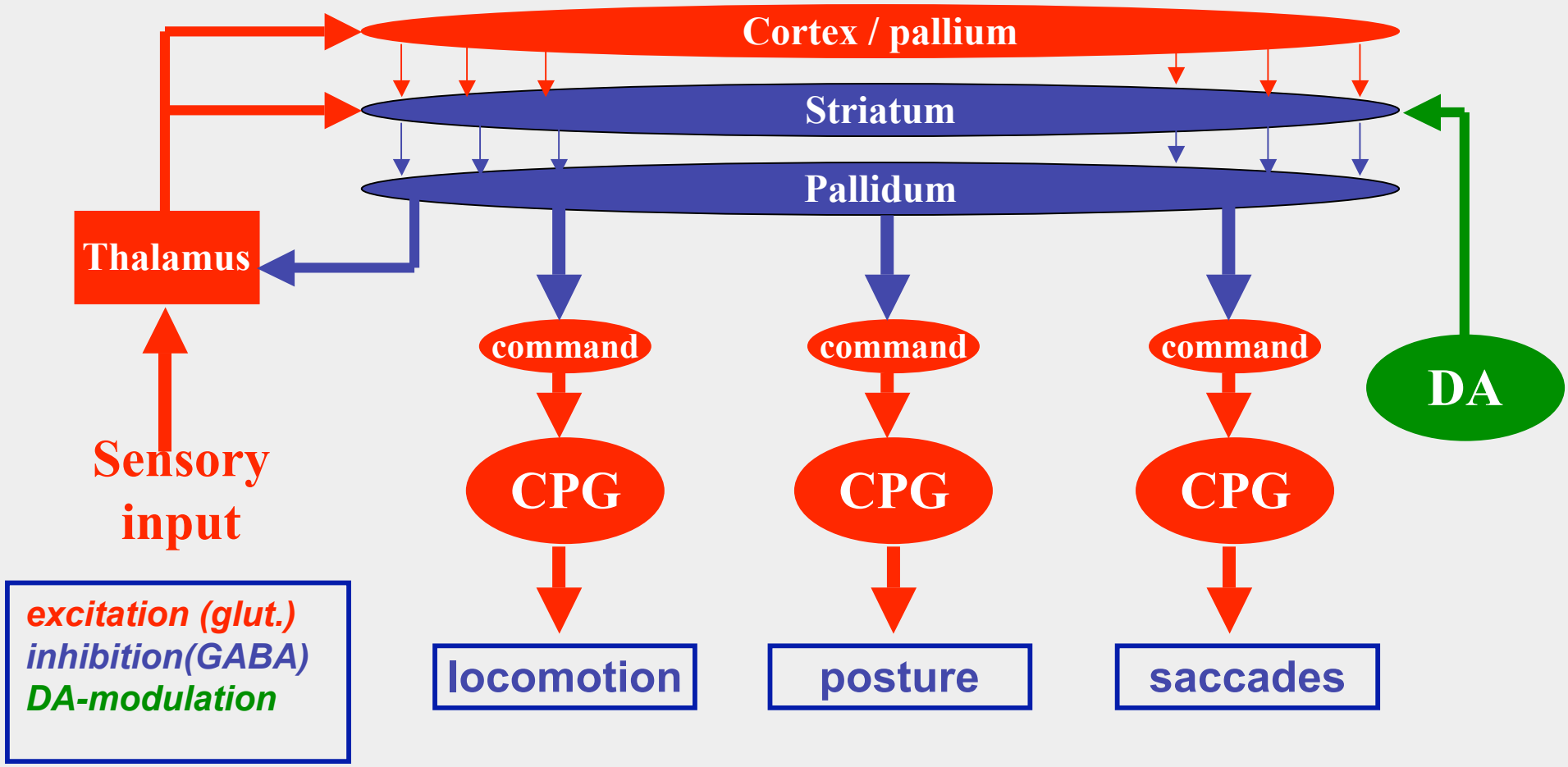
Neocortex

PC pyramidal cell
MC Martinotti cell
BC basket cell
SSC spiny stellate
CRC Cajal Rezius
BTC bitufted cell
CHC chandelier cell
DBC double-bouquet cell
NGC neurogliaform cell

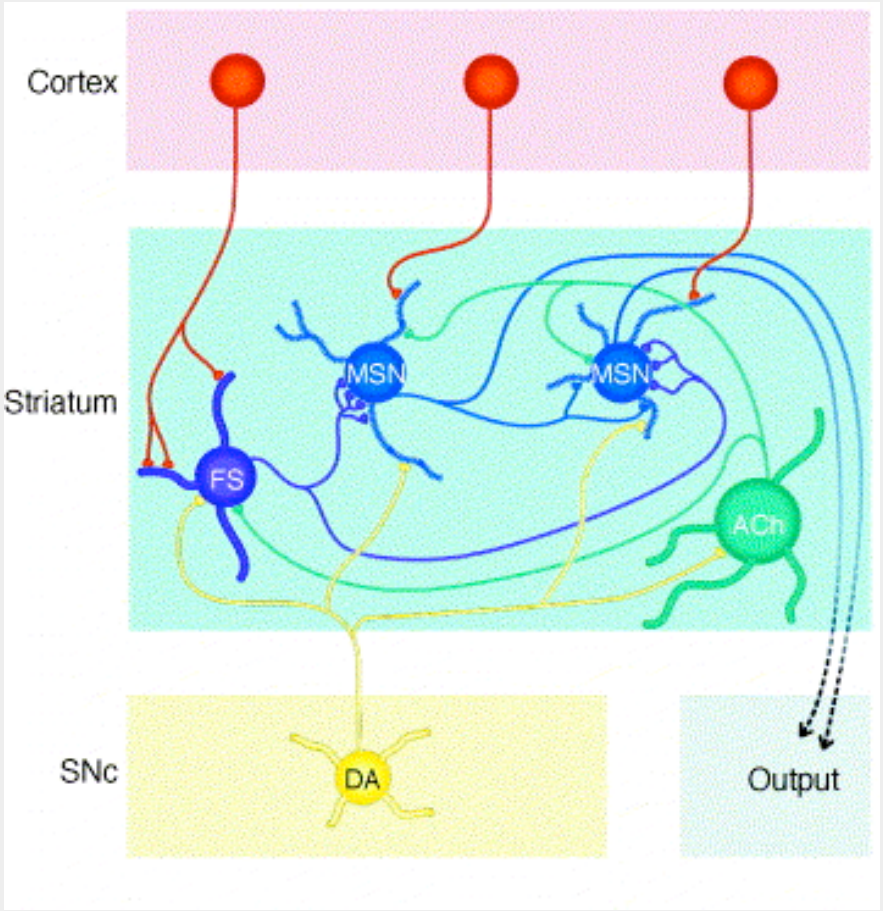
TH thalamus
BG basal ganglia
BS brainstem
CL contralateral cortex
SC spinal cord

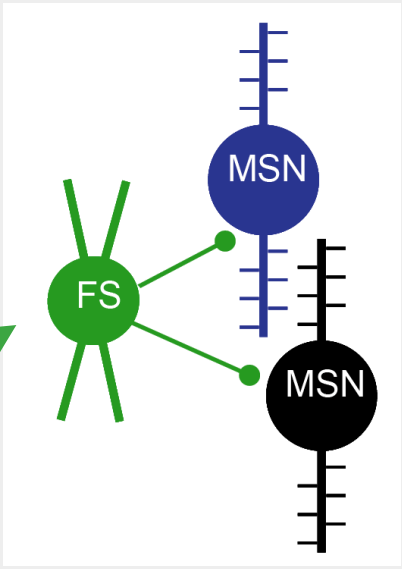


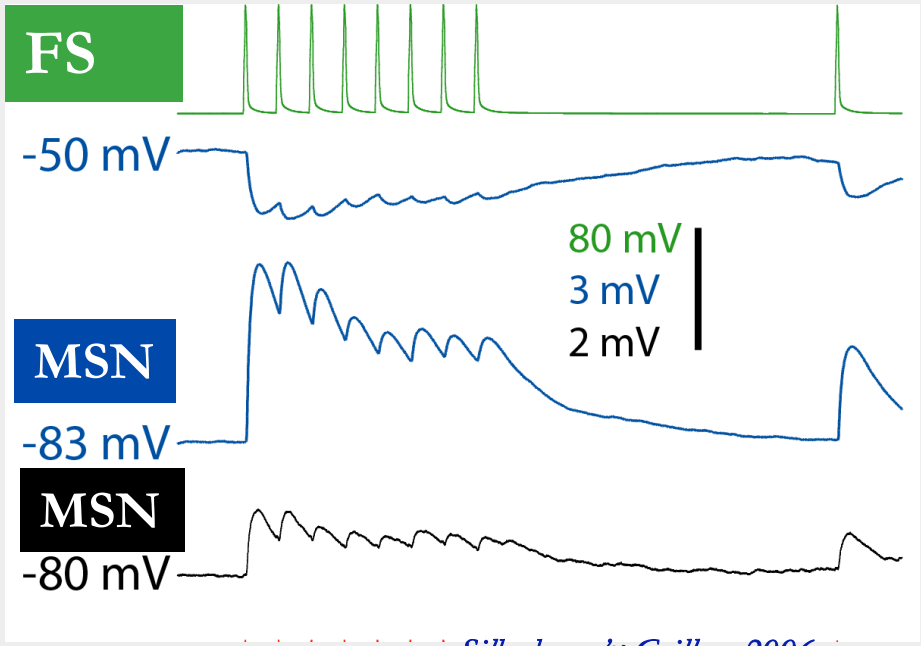
Selection of behaviour



Microcircuits in the basal ganglia





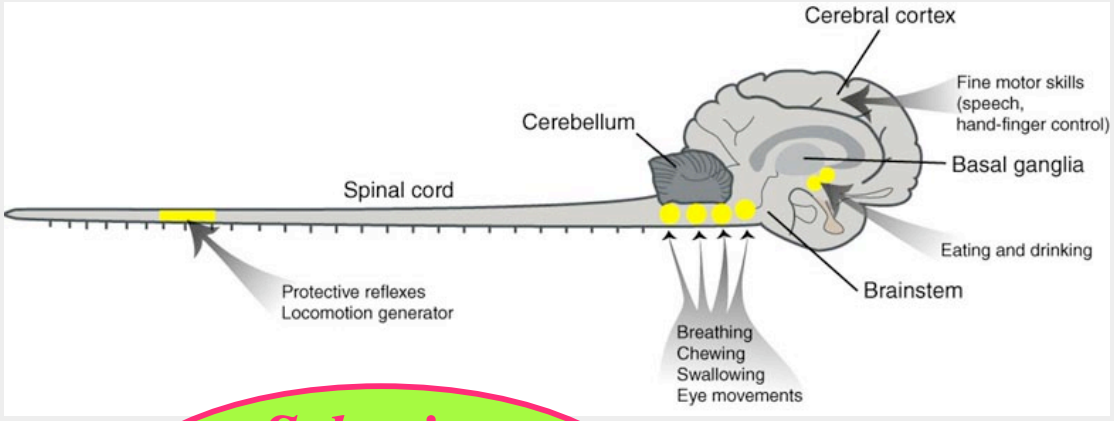


Projection neurons (MSN ~ 95%)
FS and Ach – types of interneurons
DA dopamine neuron

Silberberg & Grillner 2006

MOTOR INFRASTRUCTURE

Neuronal networks that co-ordinate different movements

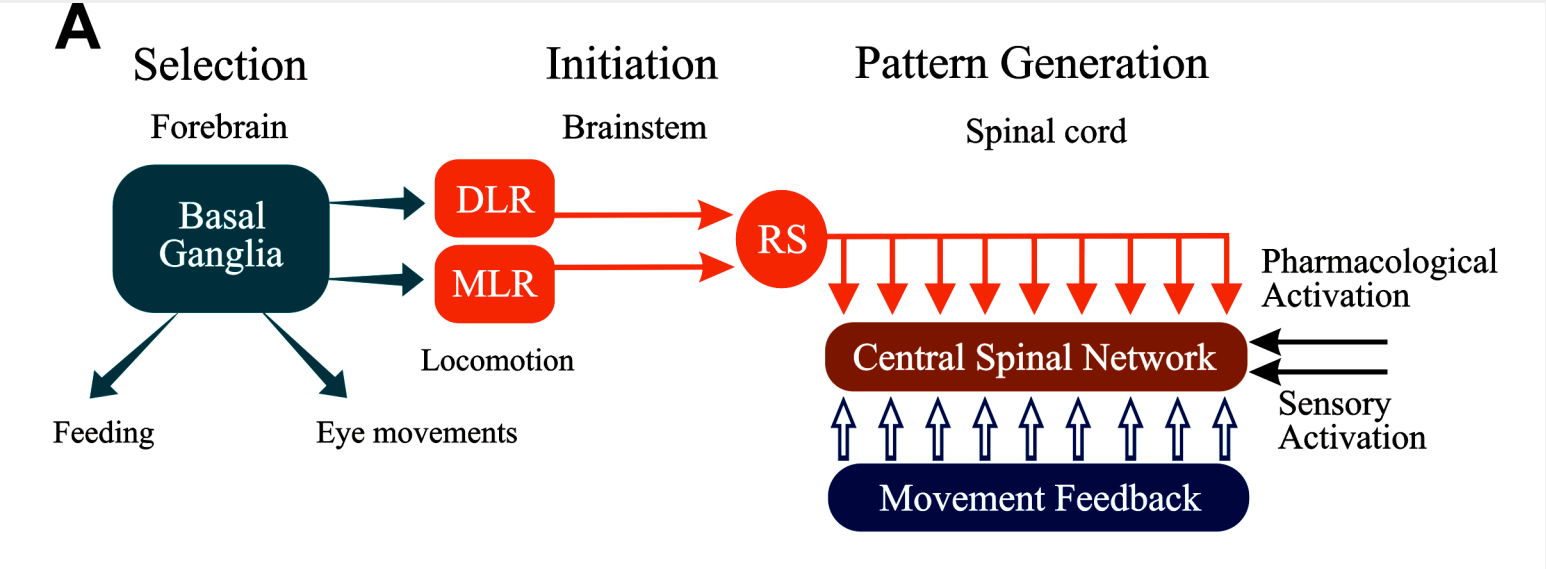


Protective reflexes
Swallowing CPG
Respiratory CPG
Locomotor CPGs
Postural networks
Chewing CPG
Express. of emotions
Saccadic motor map
Reaching

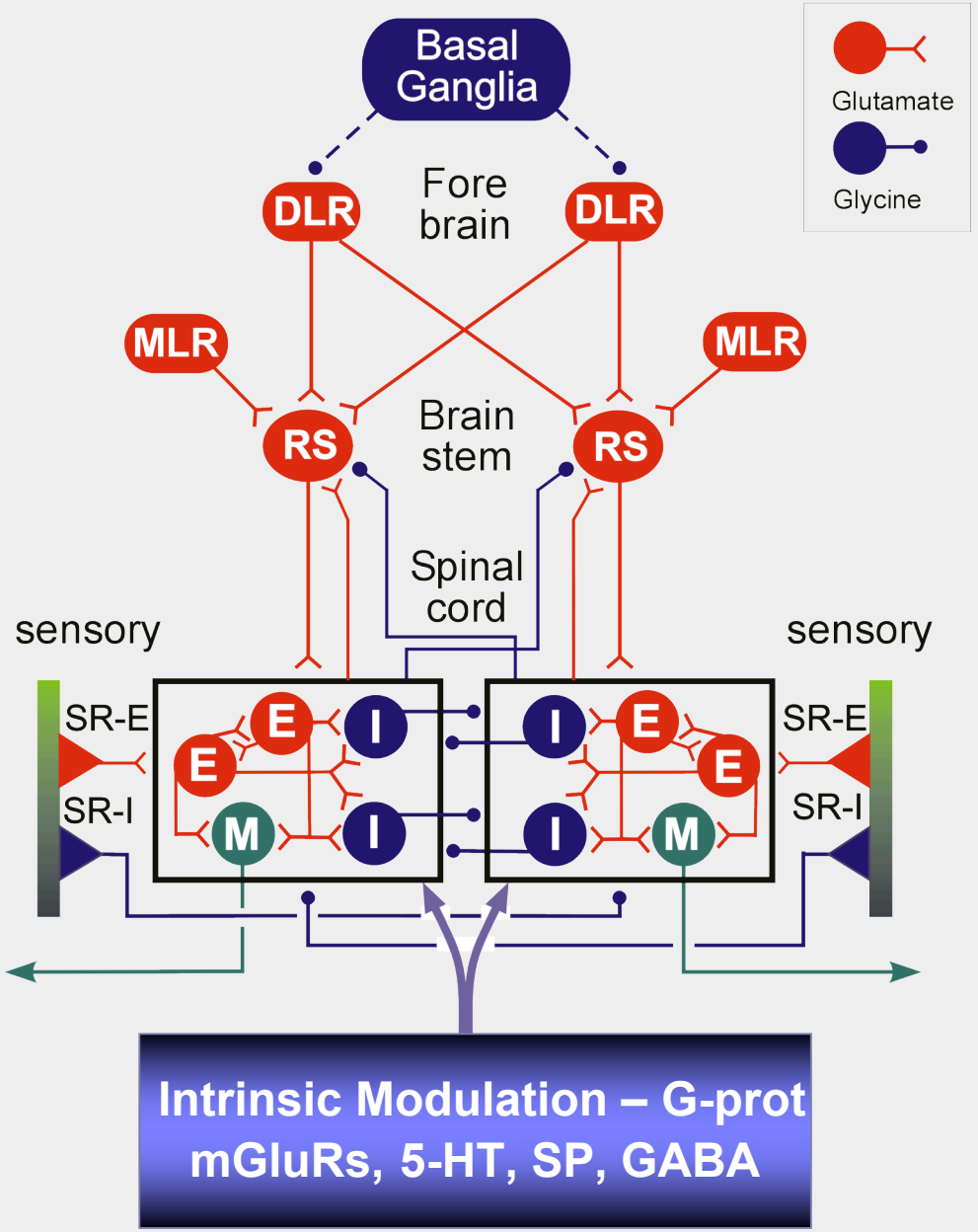
Selection
Sequencing
timing

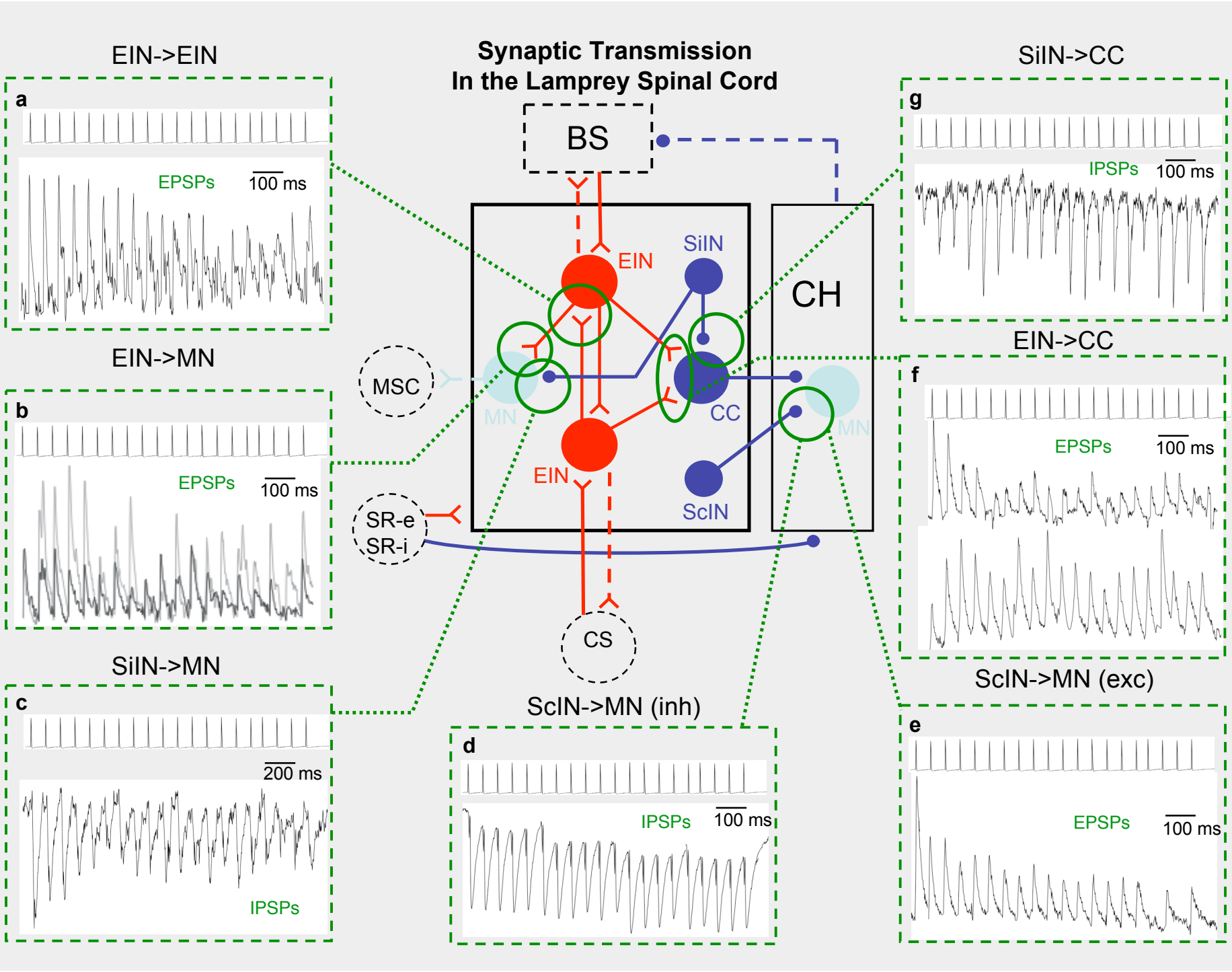
General vertebrate scheme - propulsion

From Fish to Mammals: Similar Neural Control System

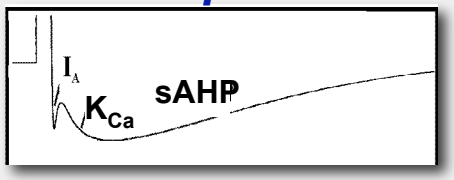


Lamprey Locomotor Network

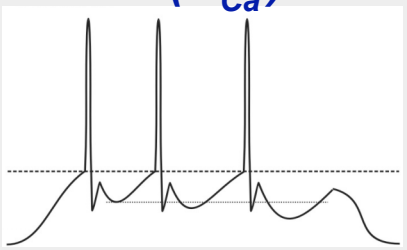



Synaptic Transmission
In the Lamprey Spinal Cord
BS
CH
EIN
SiIN
CC
ScIN
MN
MN
MSC
SR-e
SR-i
CS
EIN->EIN
a
EPSPs
100 ms
EIN->MN
b
EPSPs
100 ms
SiIN->MN
c
200 ms
IPSPs
ScIN->MN (inh)
d
IPSPs
100 ms
SiIN->CC
g
IPSPs
100 ms
EIN->CC
f
EPSPs
100 ms
ScIN->MN (exc)
e
EPSPs
100 ms

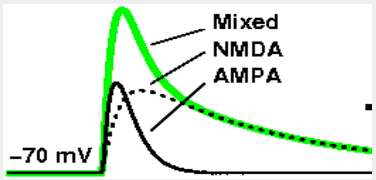
A *Action potential*



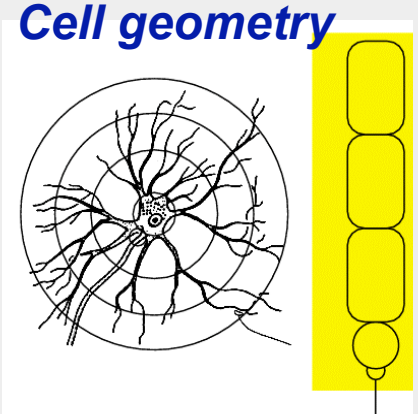
B *AHP (K_{Ca}) summation*



C *Mixed EPSP*

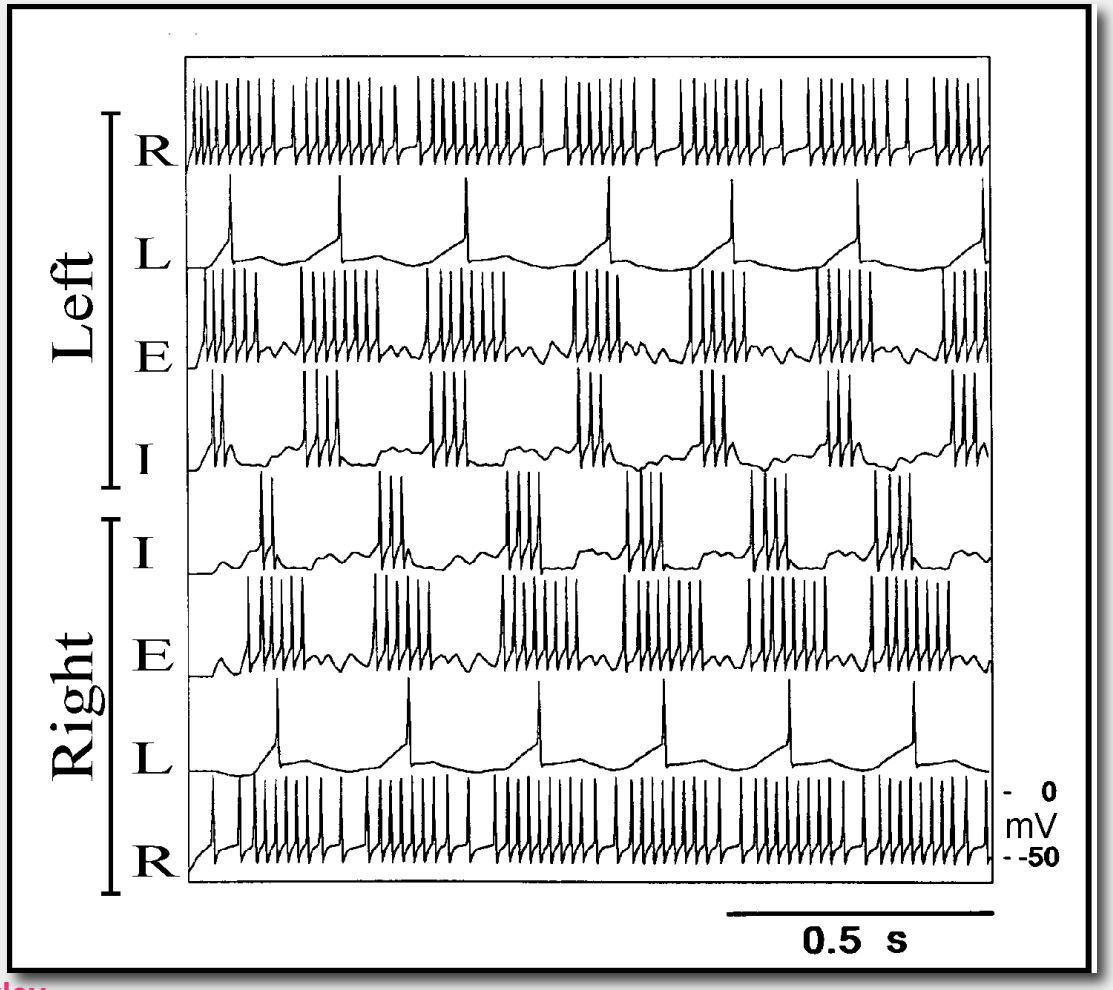


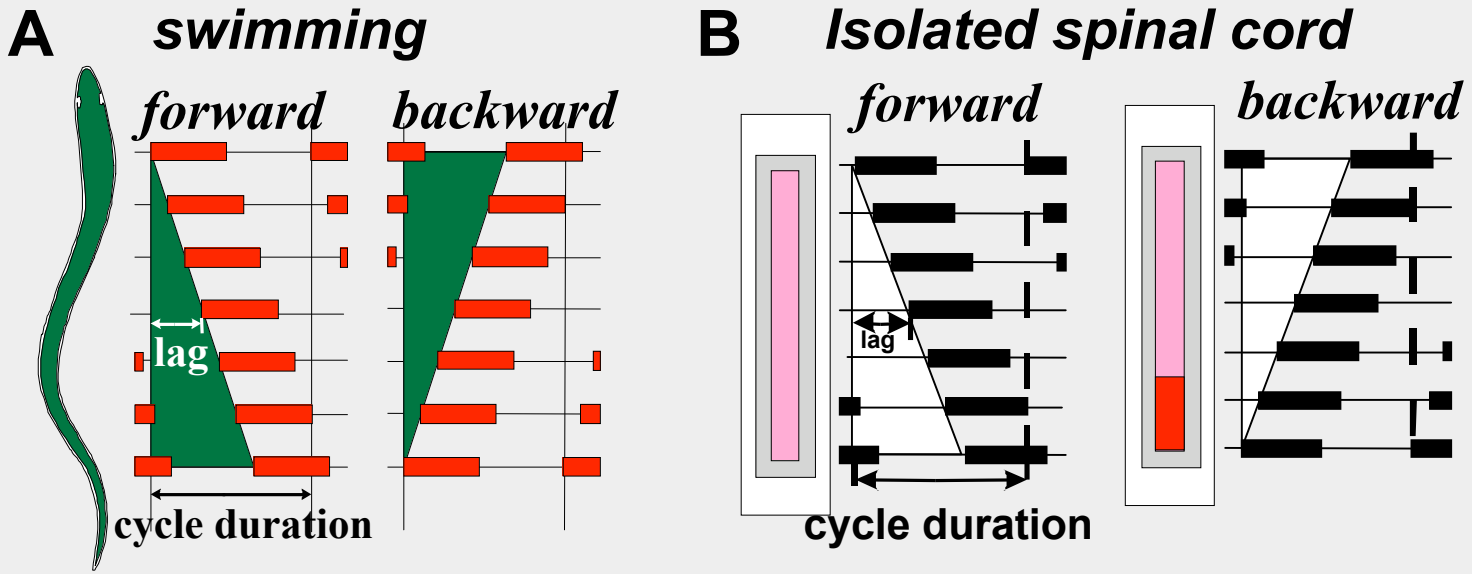
D *Cell geometry*



Hodgkin-Huxley formalism:
Na, K (IA, DR), KCa,KNa,Ca (N,T)-channels,

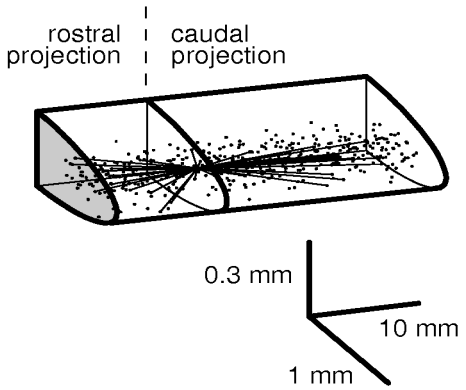
E. Segmental network



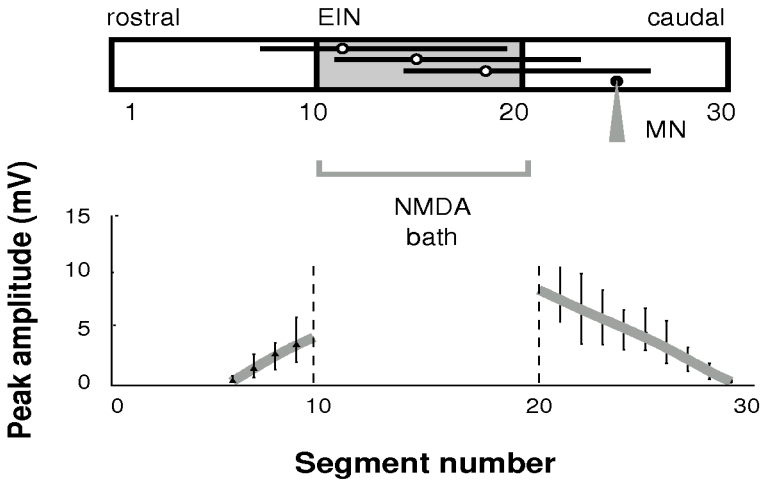

A
swimming
forward
backward
lag
cycle duration
B
Isolated spinal cord
forward
backward
lag
cycle duration

E-network: Hemicord

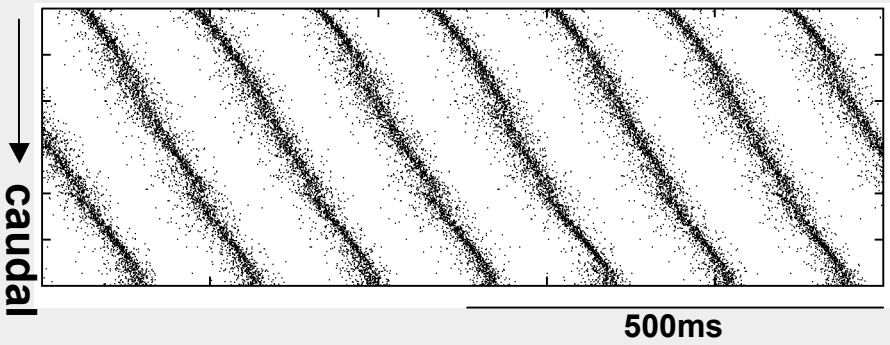
A



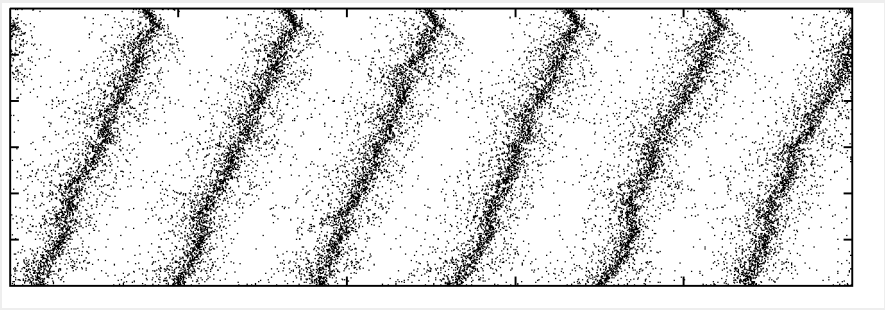
B



C1 **Forward swimming**

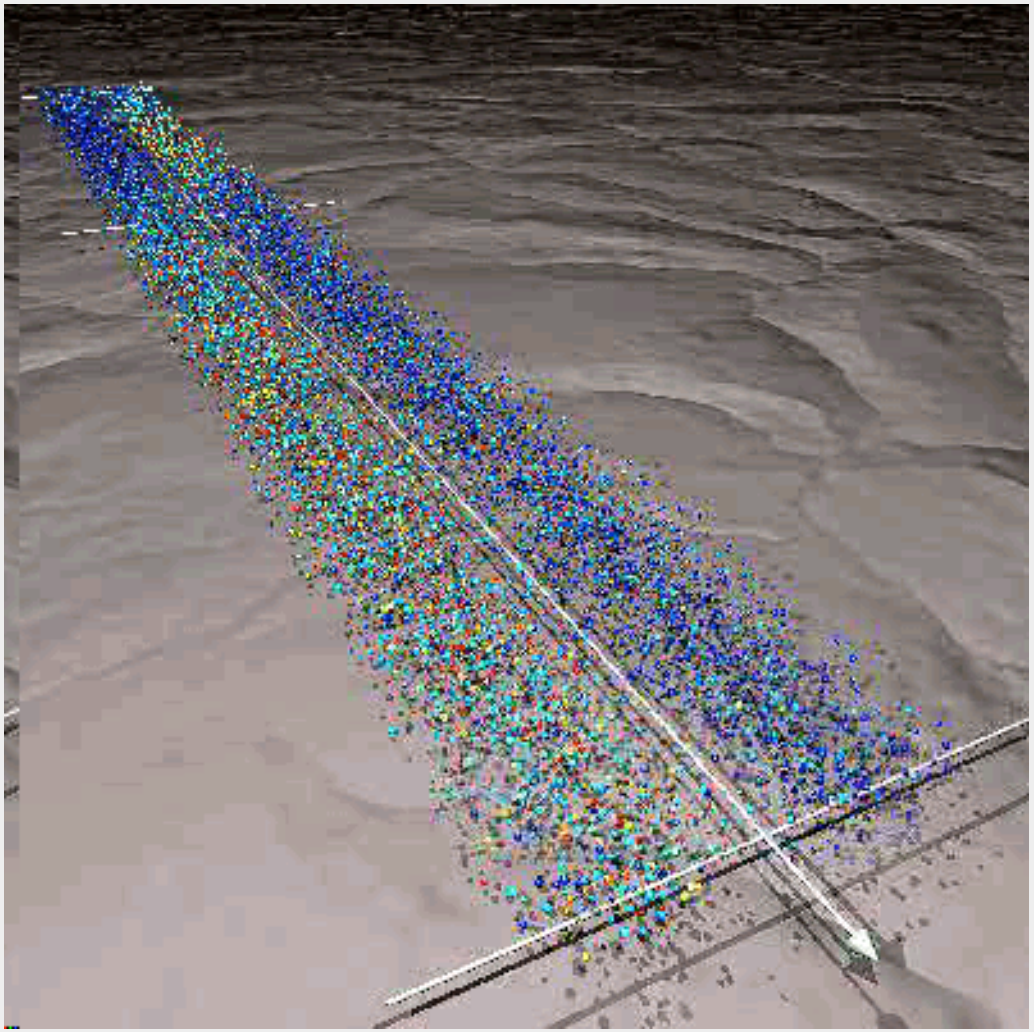


C2 **Backward swimming**

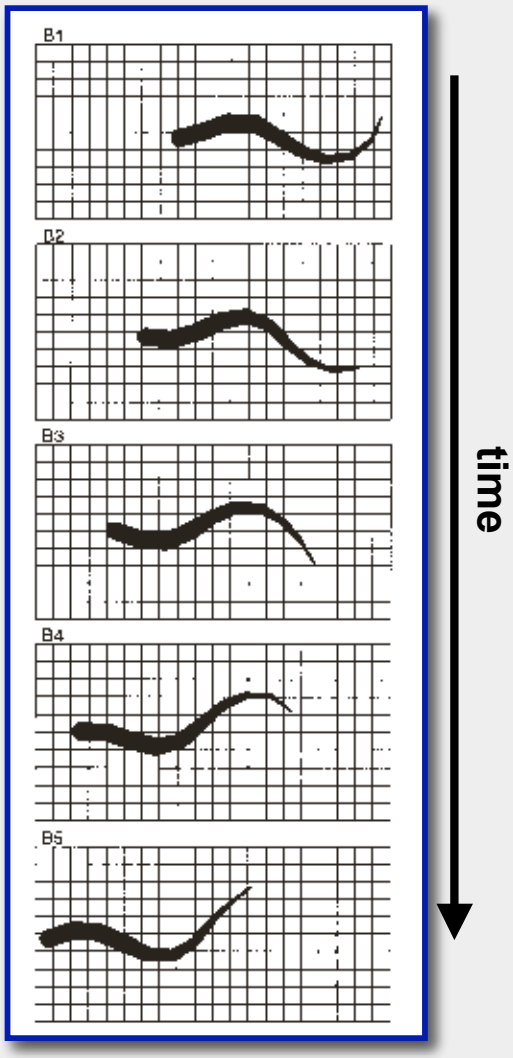


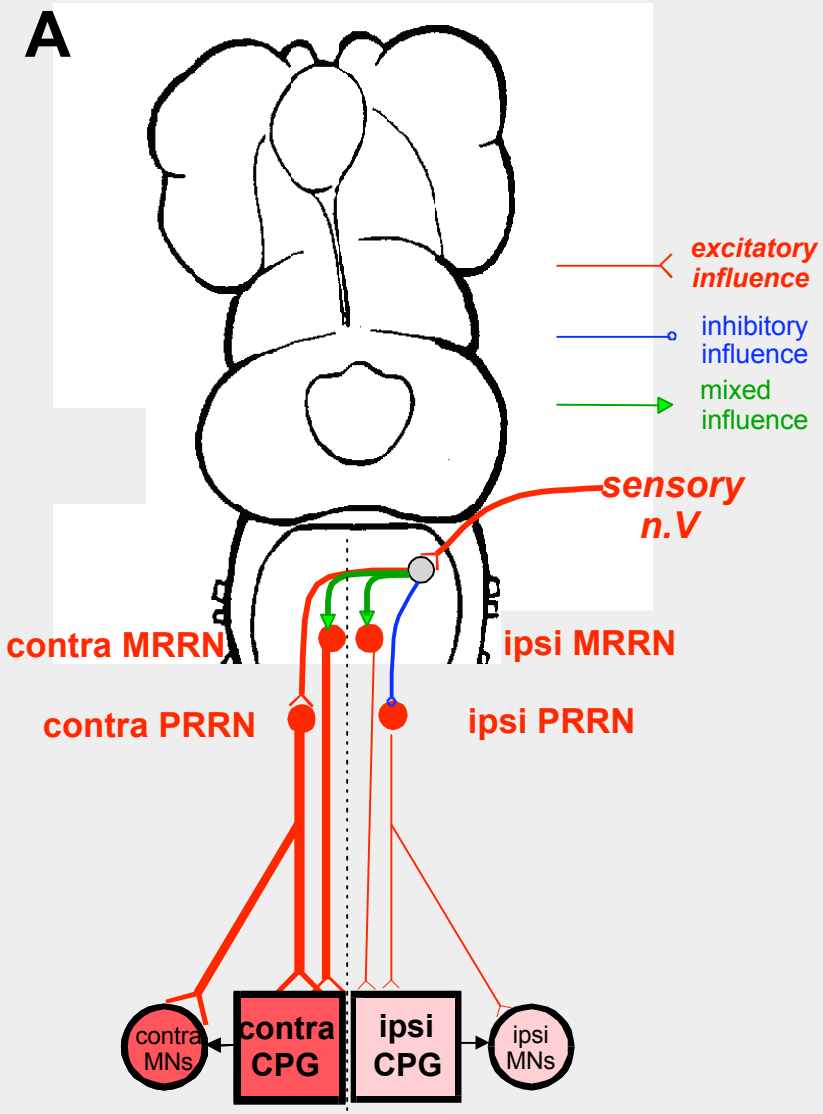
Lamprey intersegmental network

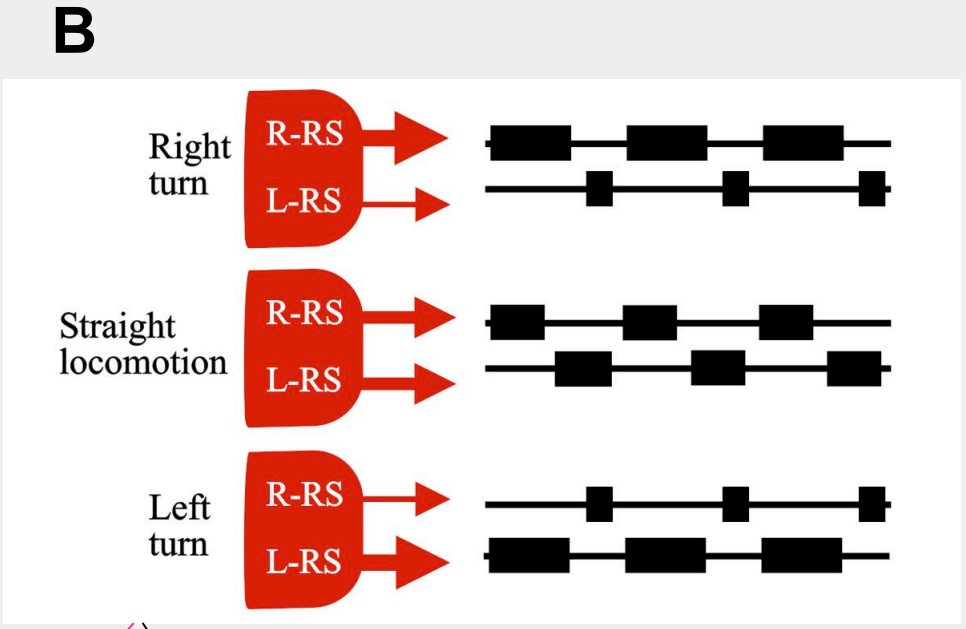
A

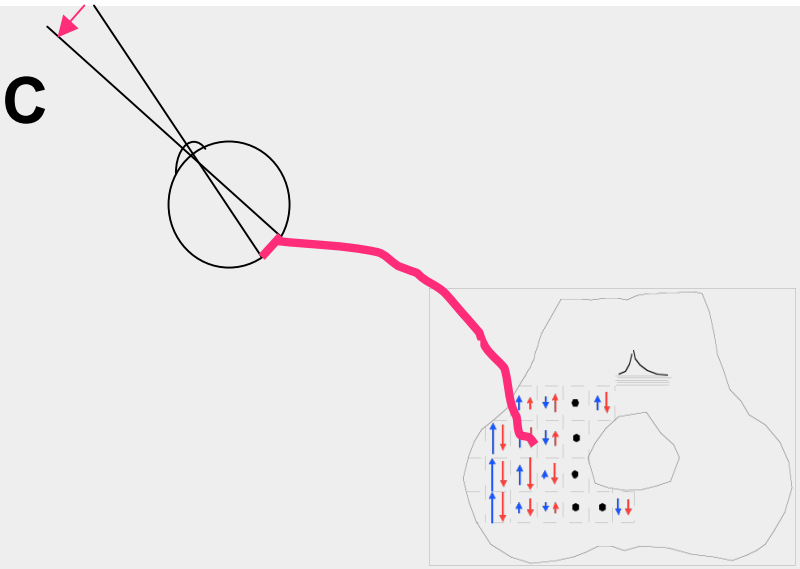


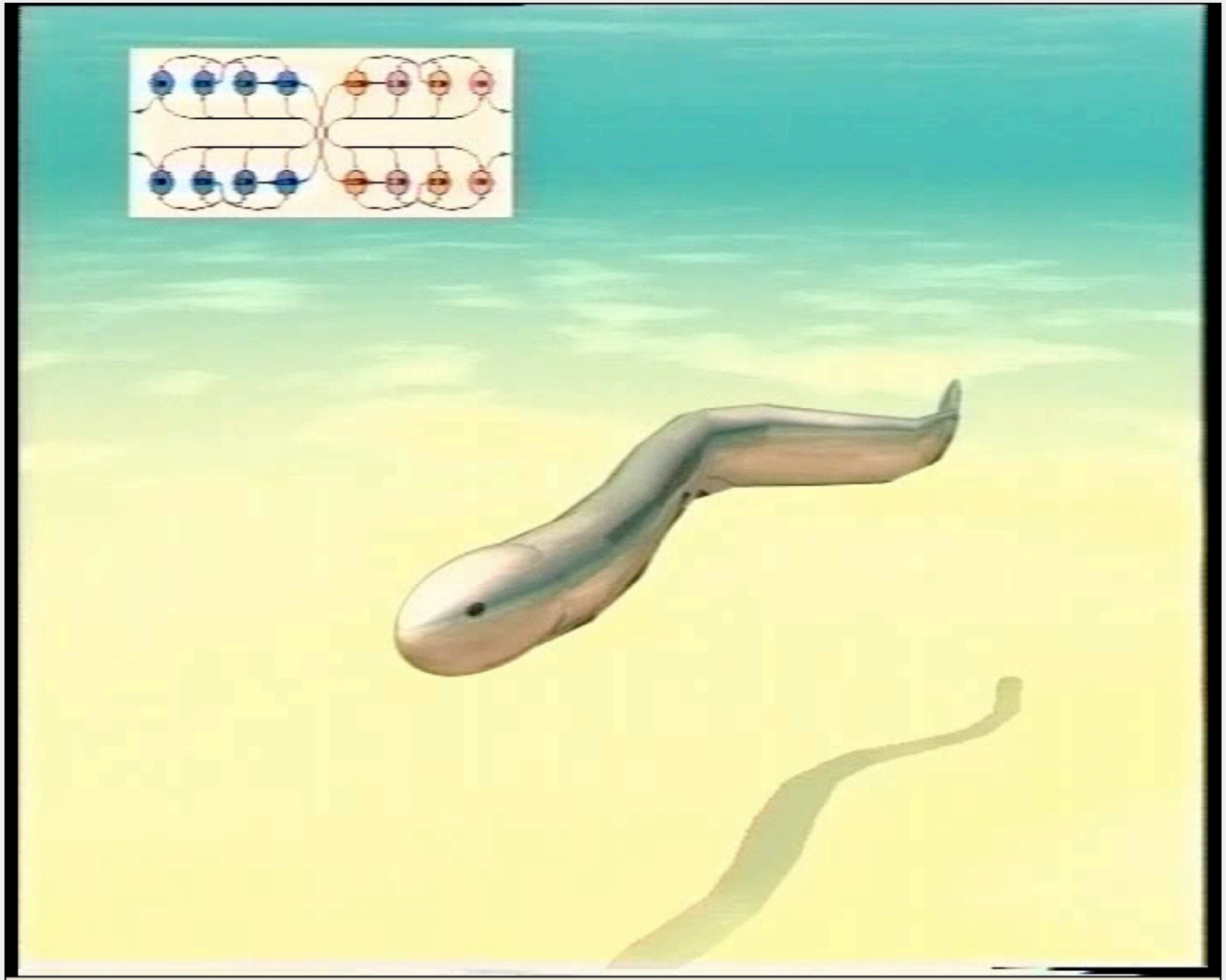
B



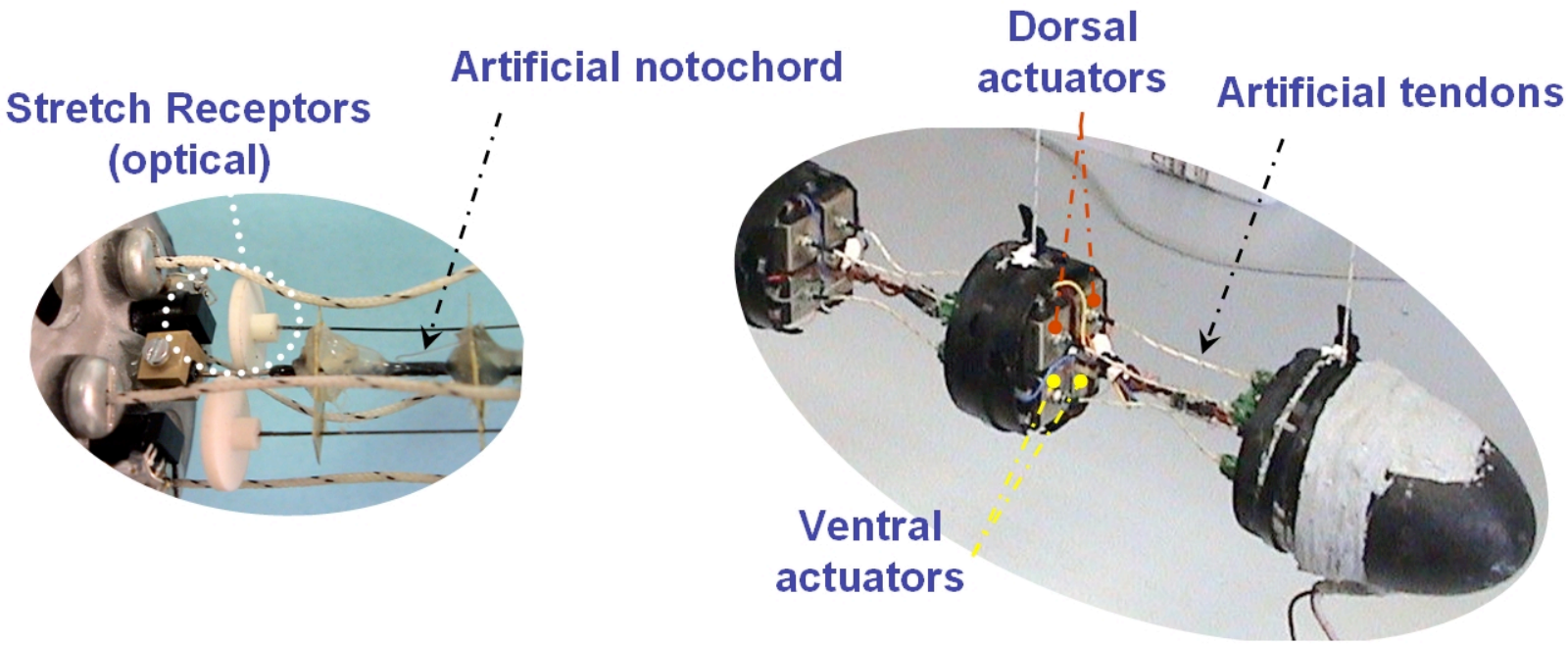

A
excitatory influence
inhibitory influence
mixed influence
sensory n.V
contra MRRN
ipsi MRRN
contra PRRN
ipsi PRRN
contra MNs
contra CPG
ipsi CPG
ipsi MNs


B
Right turn
R-RS
L-RS
Straight locomotion
R-RS
L-RS
Left turn
R-RS
L-RS


C



Ekeberg and Grillner



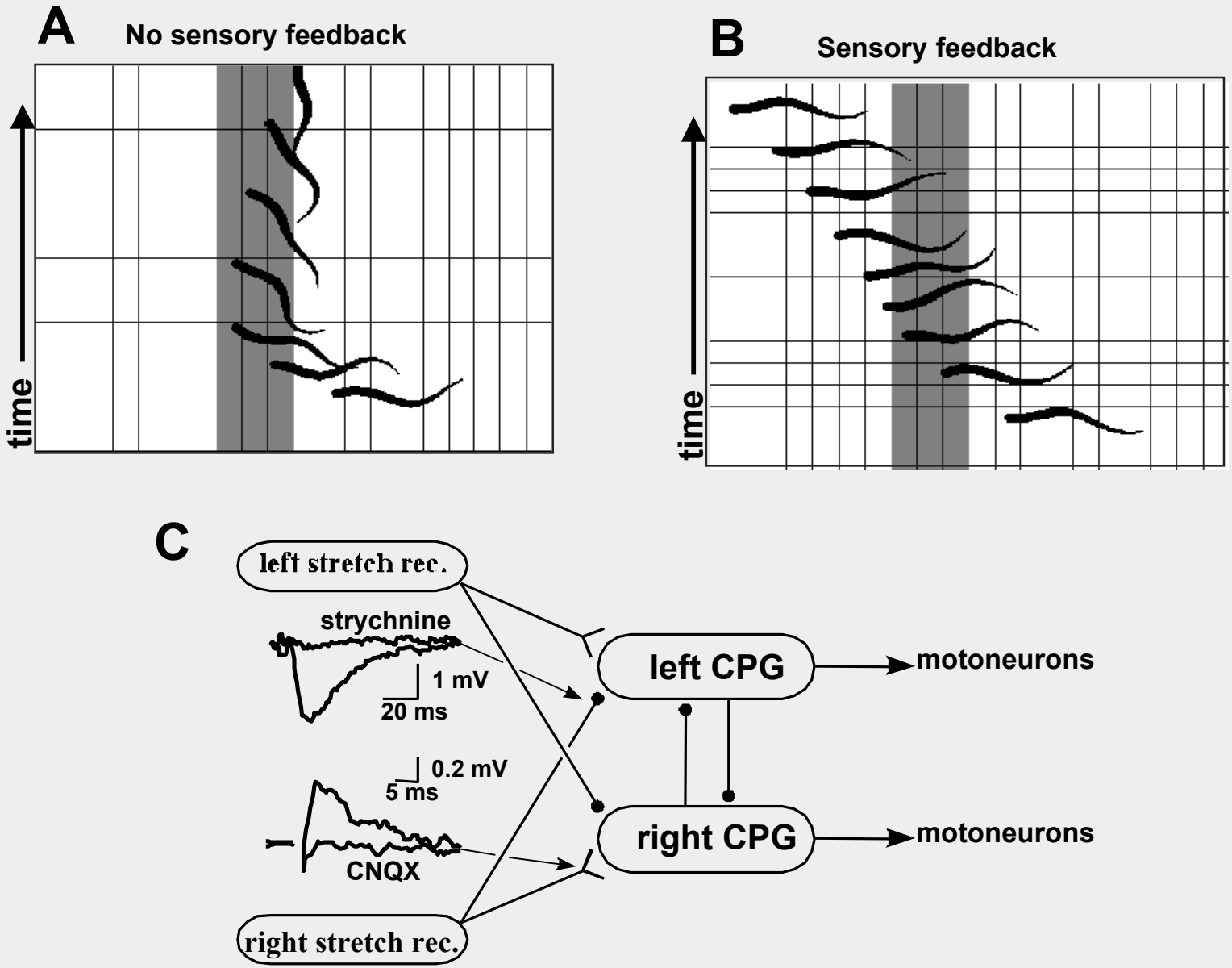
Stefanini, Dario, Menciassi , Grillner et al

CRIM Lab
Scuola Superiore Sant' Anna
Pisa, Italy

The Nobel Institute for
Neurophysiology
Karolinska Institutet, Sweden

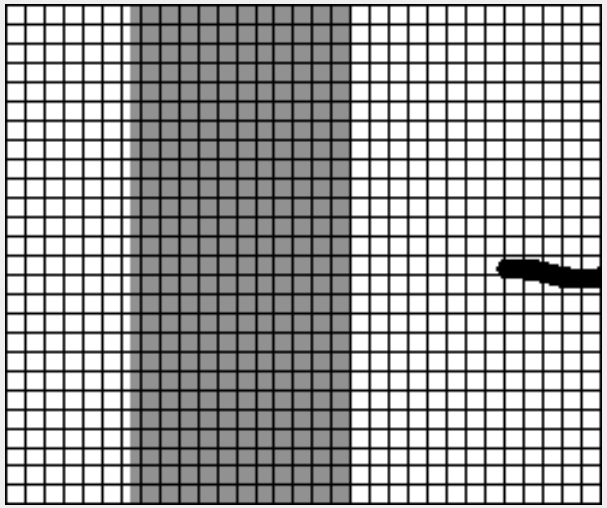
A Lamprey-like Robot for studying neuromuscular models of locomotion

August 2006 Experiments - Pontedera

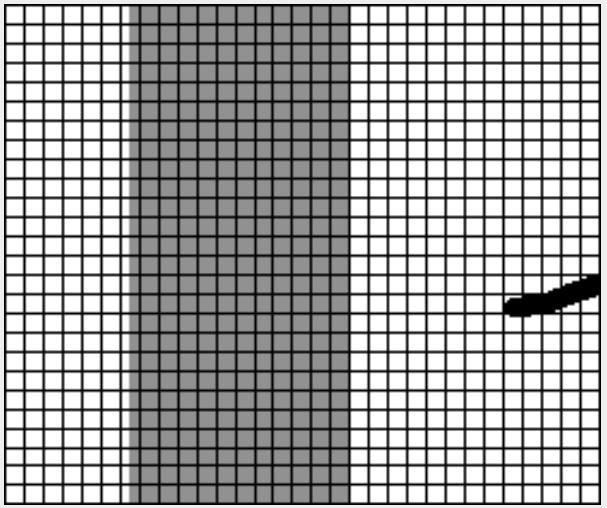

A
No sensory feedback
time
B
Sensory feedback
time
C
left stretch rec.
strychnine
1 mV
20 ms
0.2 mV
5 ms
CNQX
right stretch rec.
left CPG
right CPG
motoneurons
motoneurons

Neuromechanical model simulation - role of sensory feedback

1: No sensory feedback

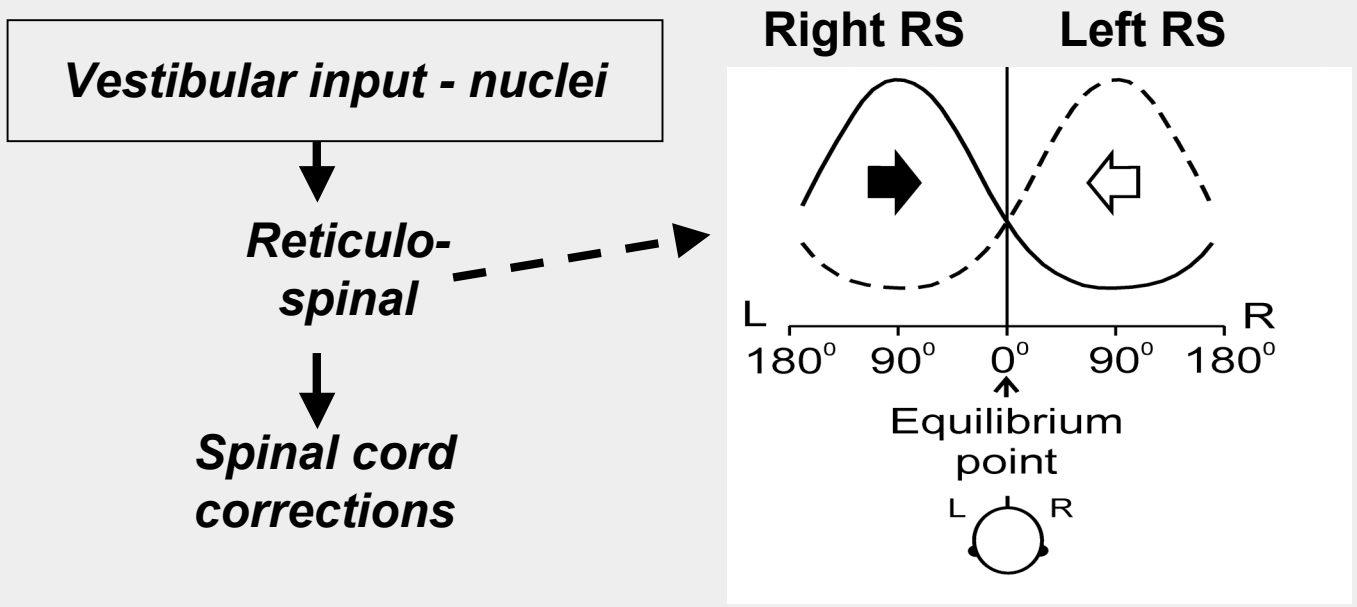


2: Sensory feedback to I-interneurons

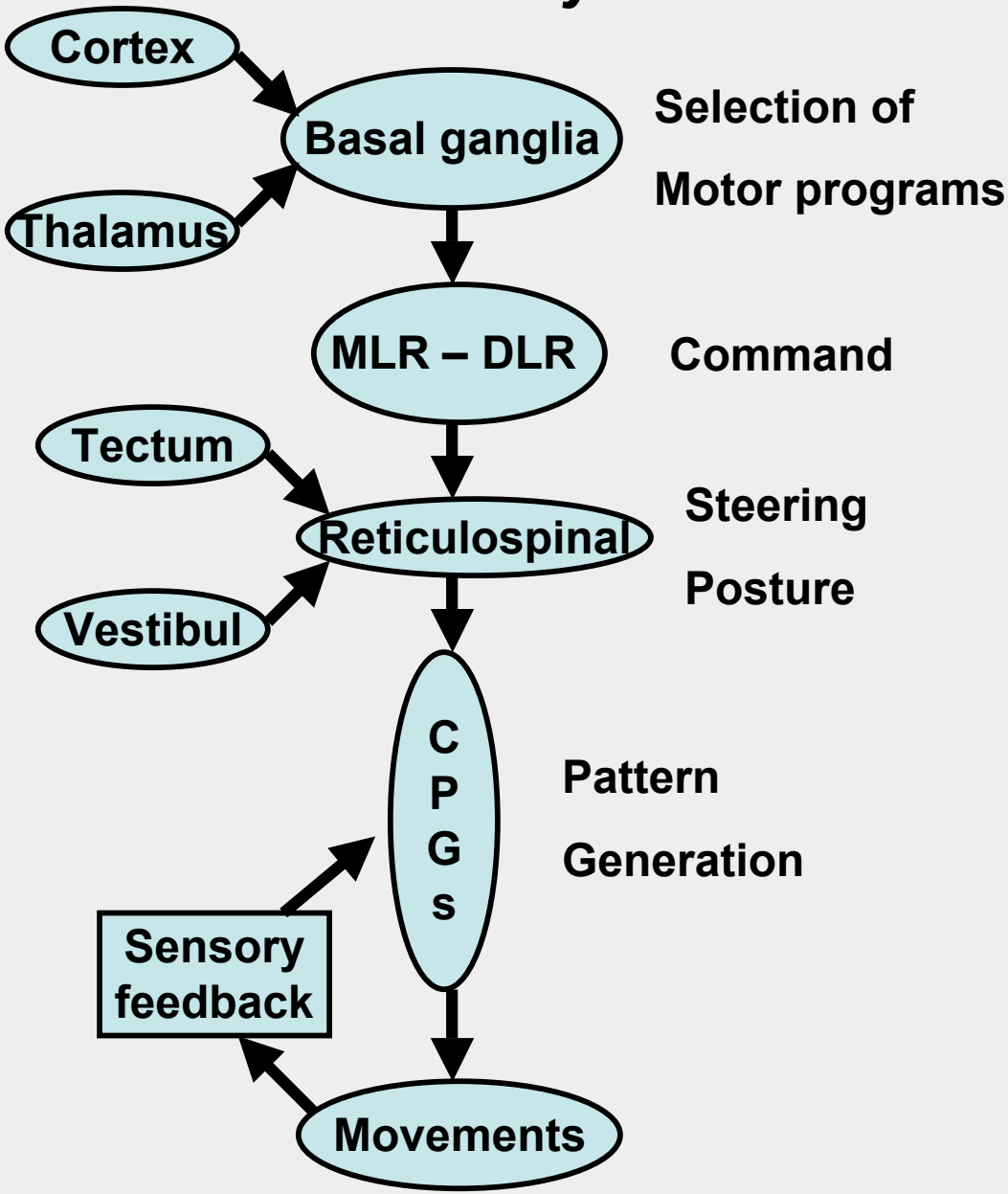


(Ekeberg)

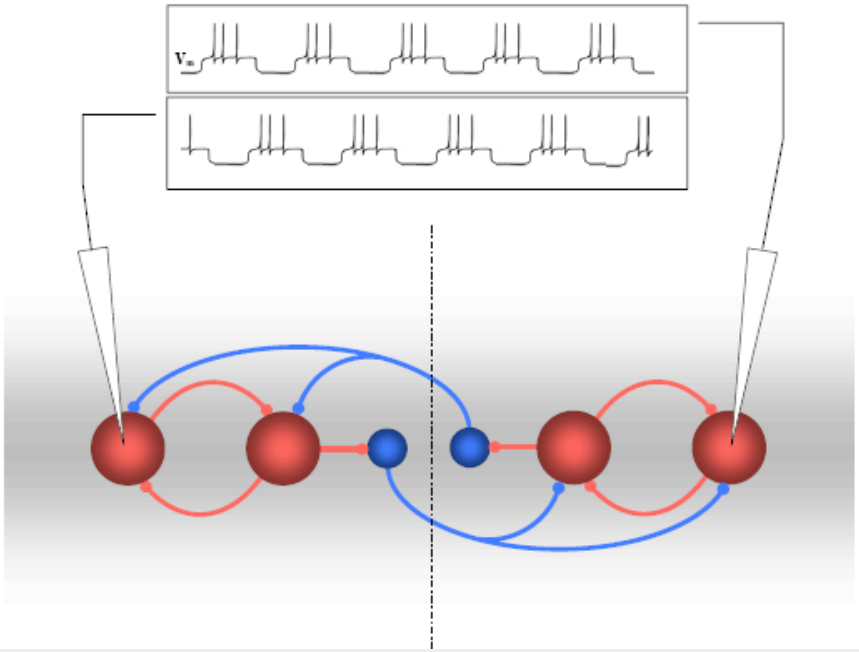
Control of Body Orientation



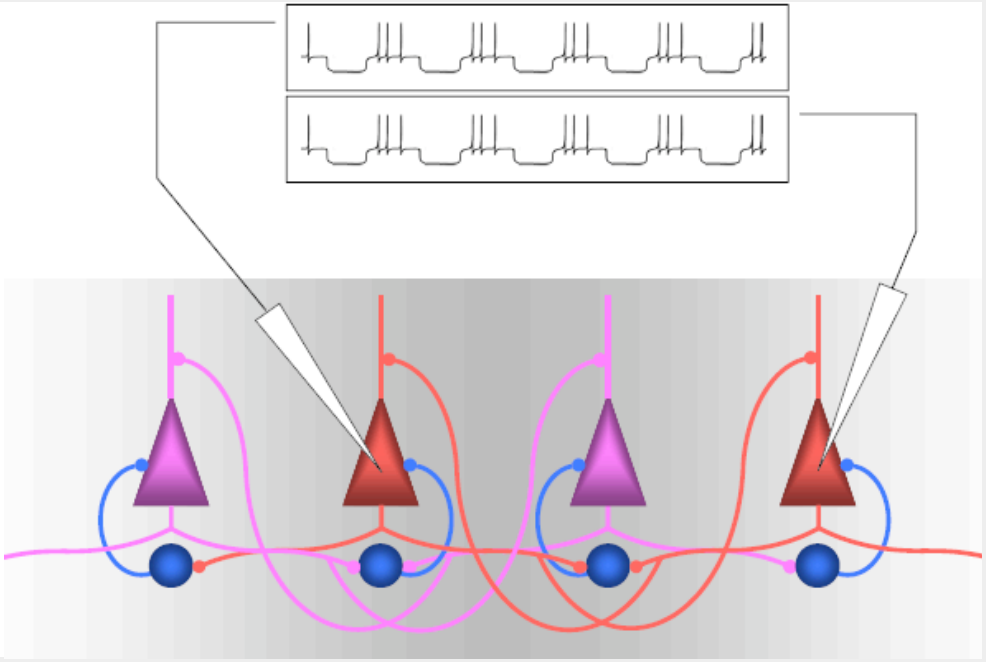
Control Systems for Locomotion



Lamprey CPG

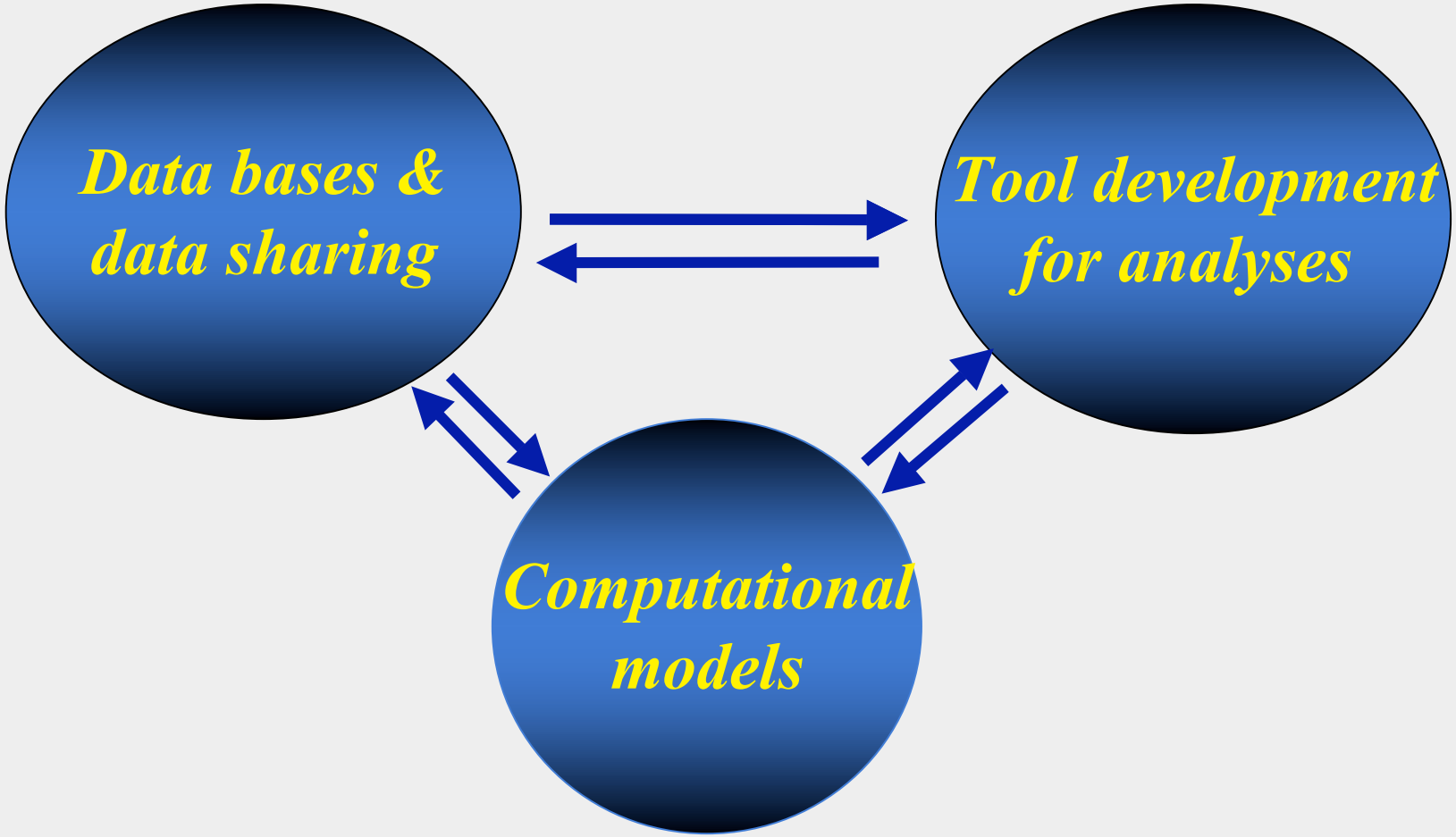


Cortical microcircuit

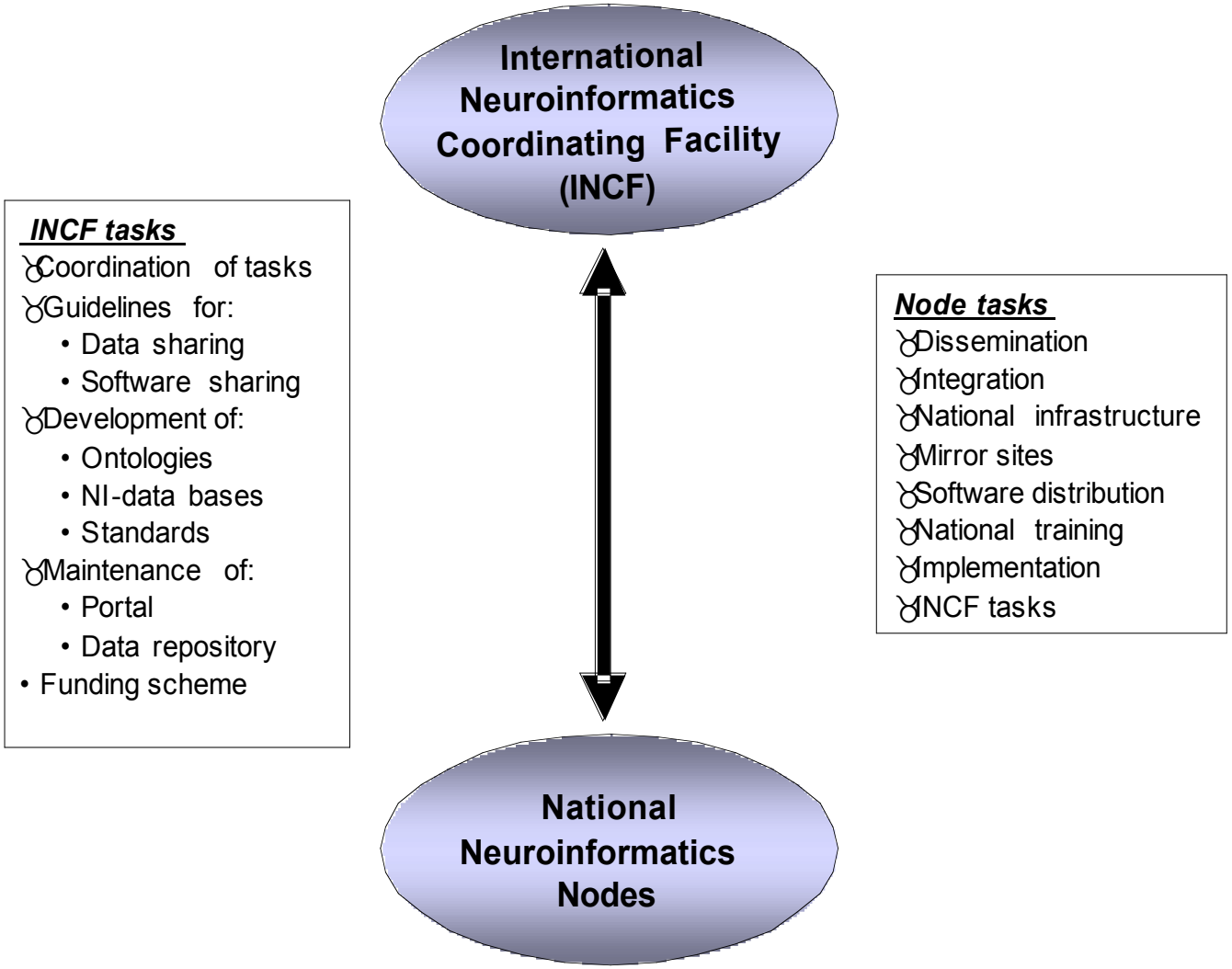


From "Neocortex as a central pattern generator"
Yuste, ... Lansner
Nature Neurosci. Rev (2005)

Neuroinformatics

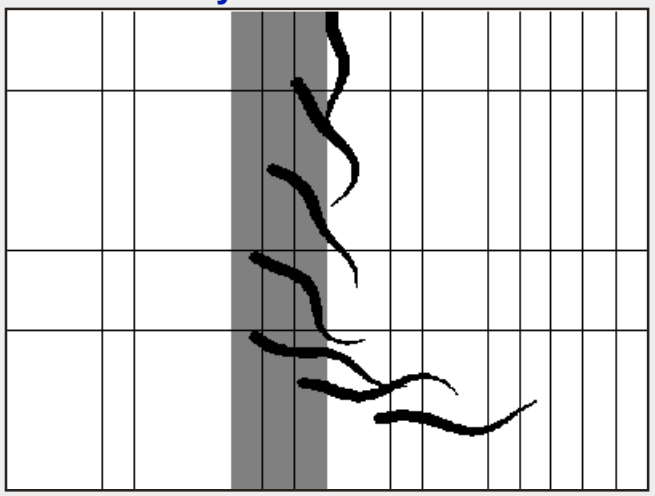


Global Neuroinformatics Coordination

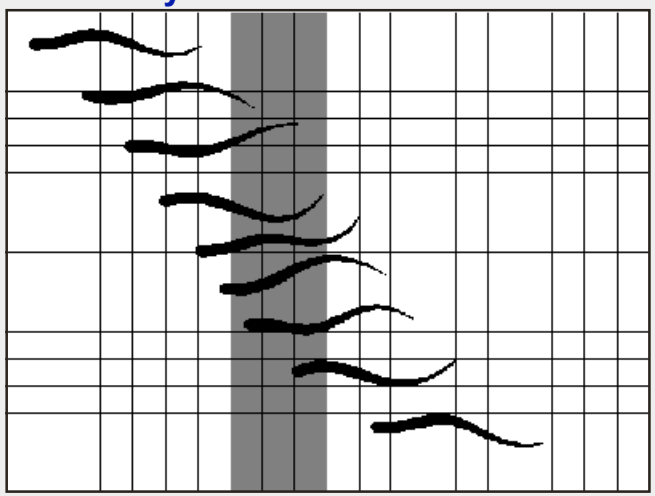


Neuromechanical model simulation of role of sensory feedback

1: No sensory feedback

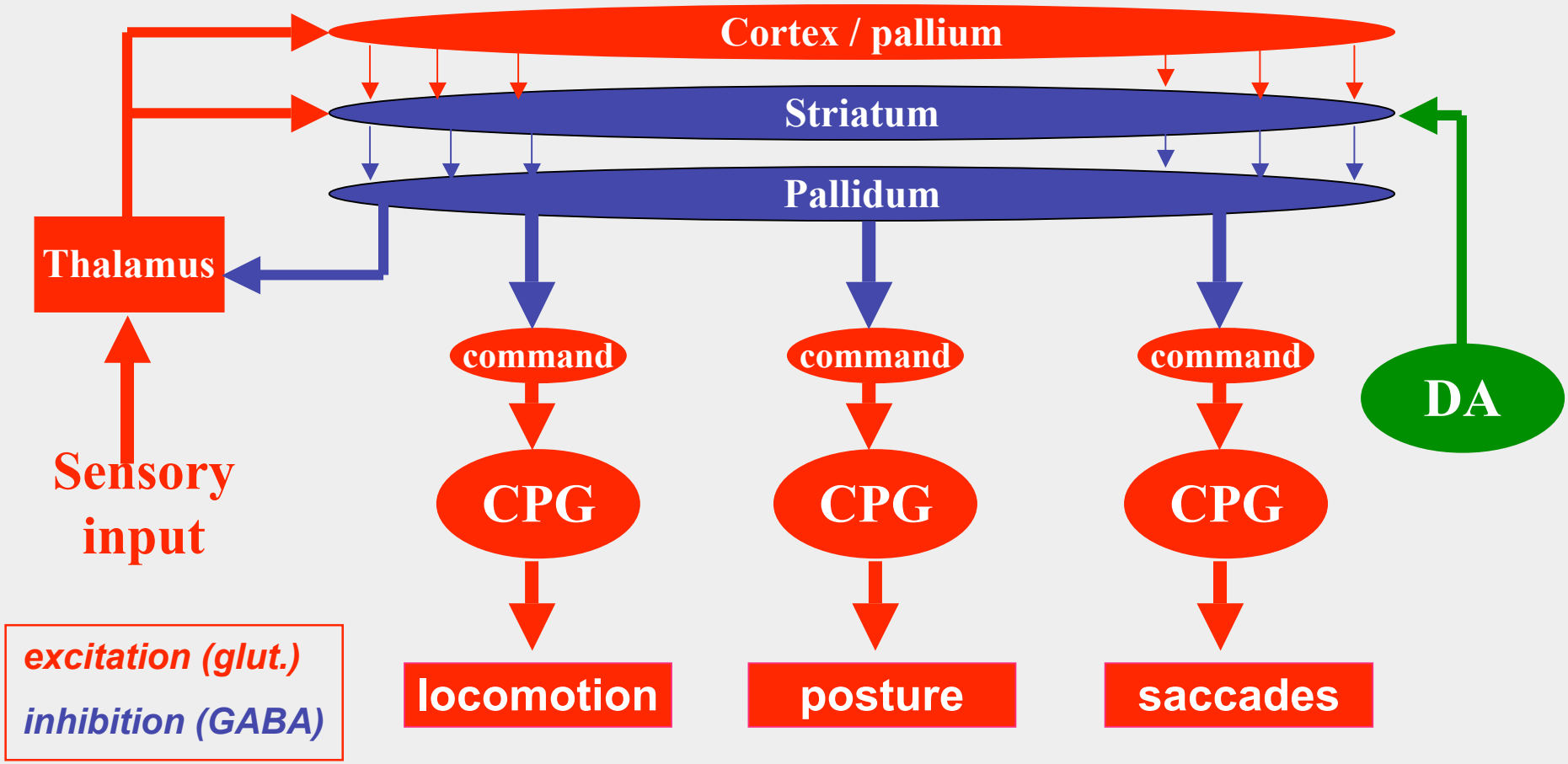


2: Sensory feedback to I-interneurons

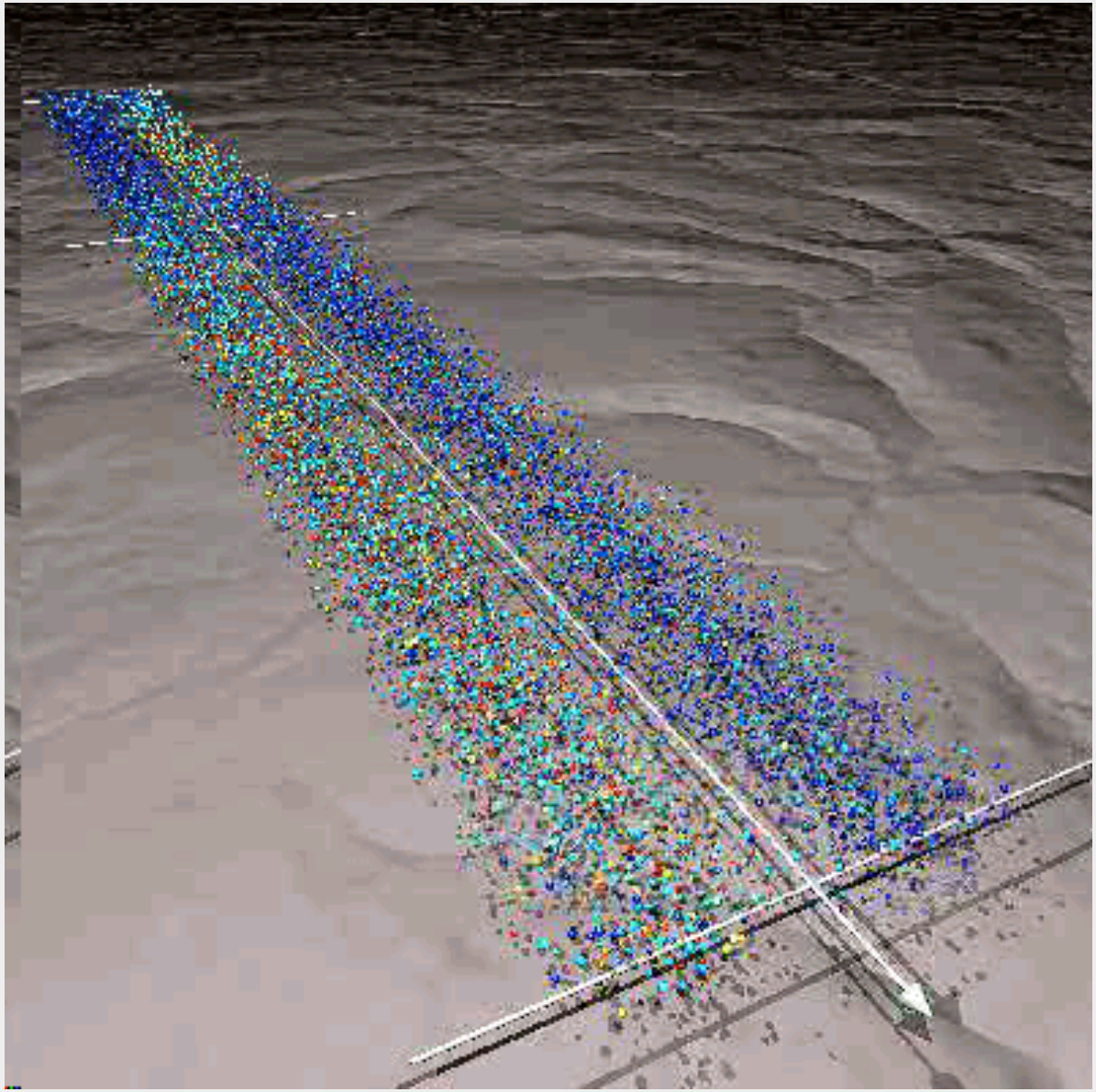


(Ekeberg and Grillner)

Selection of behaviour



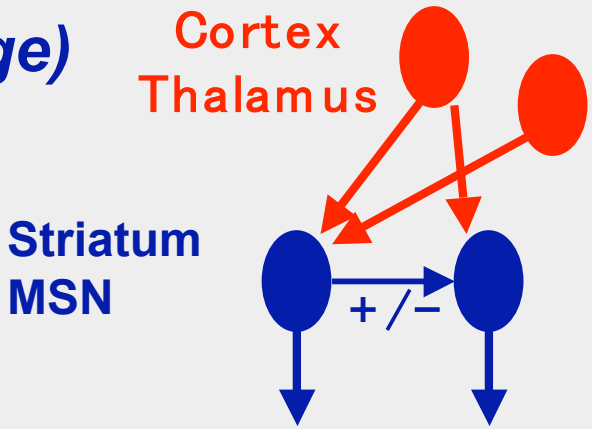
Model of lamprey intersegmental network

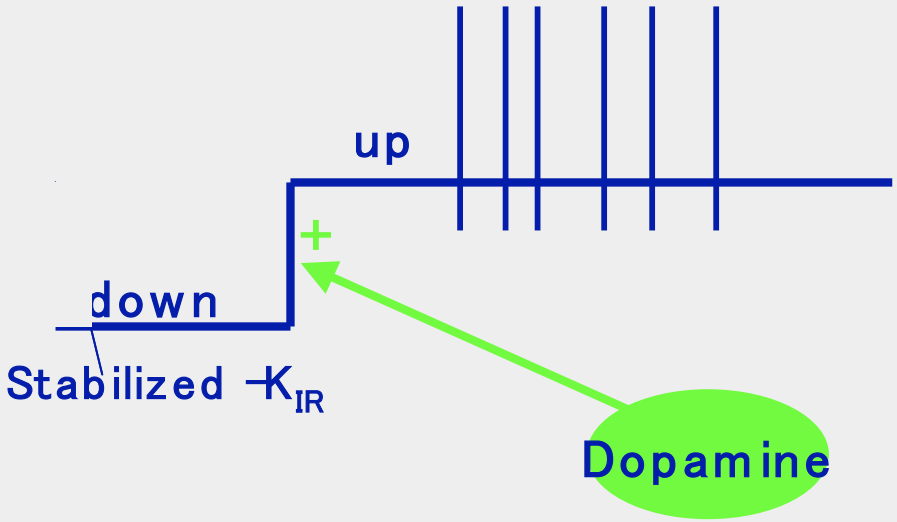


Kozlov, Lansner and Grillner

Medium spiny striatal cells (input stage)

- *High threshold for activation from cortex or thalamus*
- *Filter function*

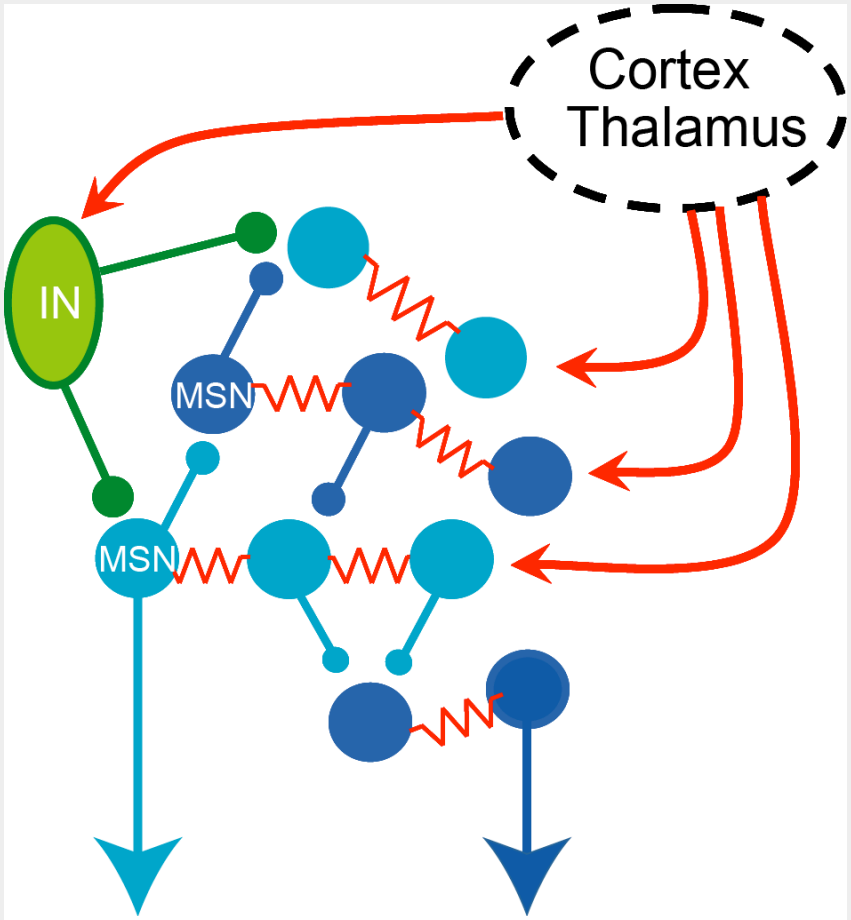




Pallidal neurones (output stage)

- *keep motor programs under tonic inhibition*

Suggested model for striatal functional organization

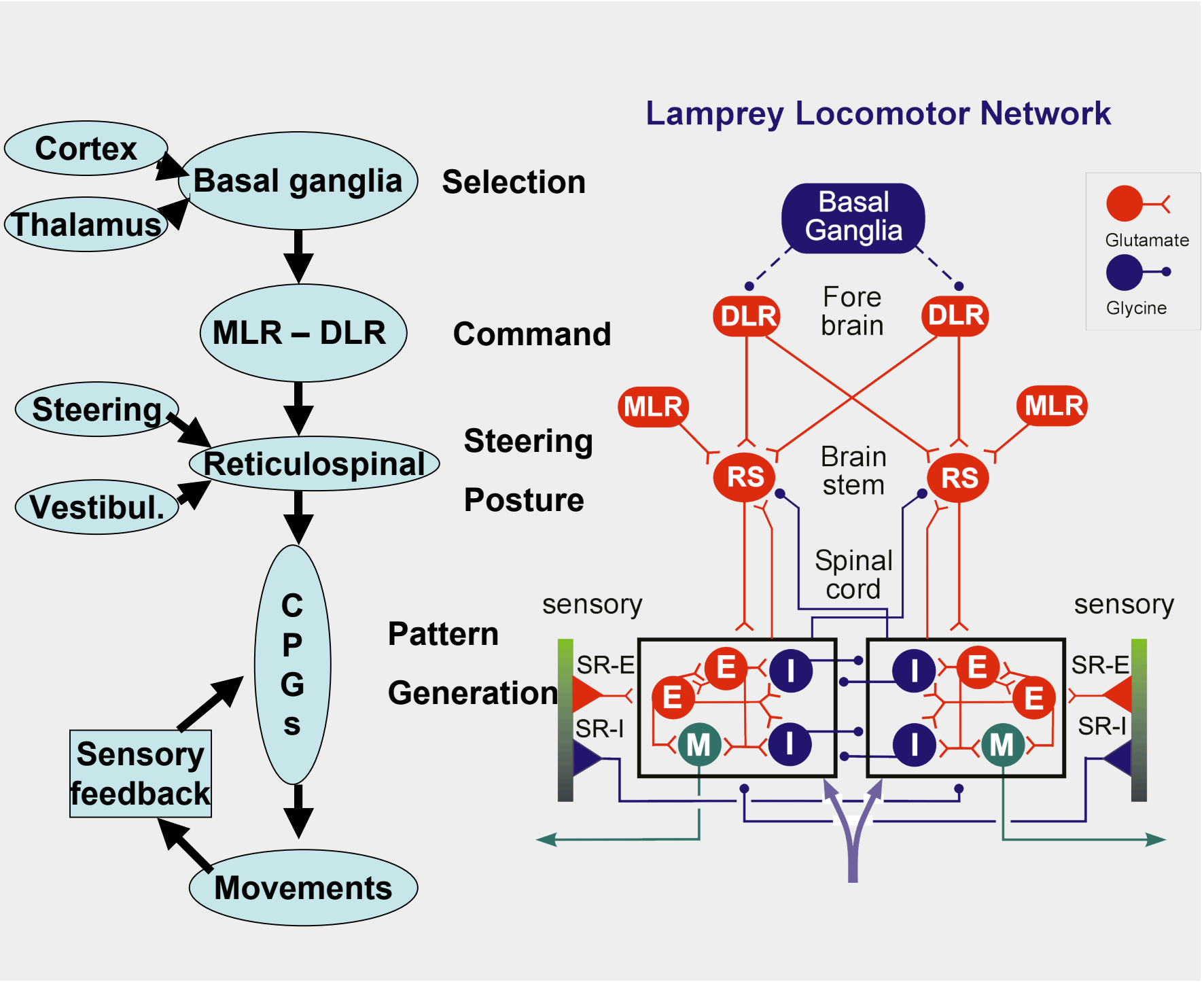


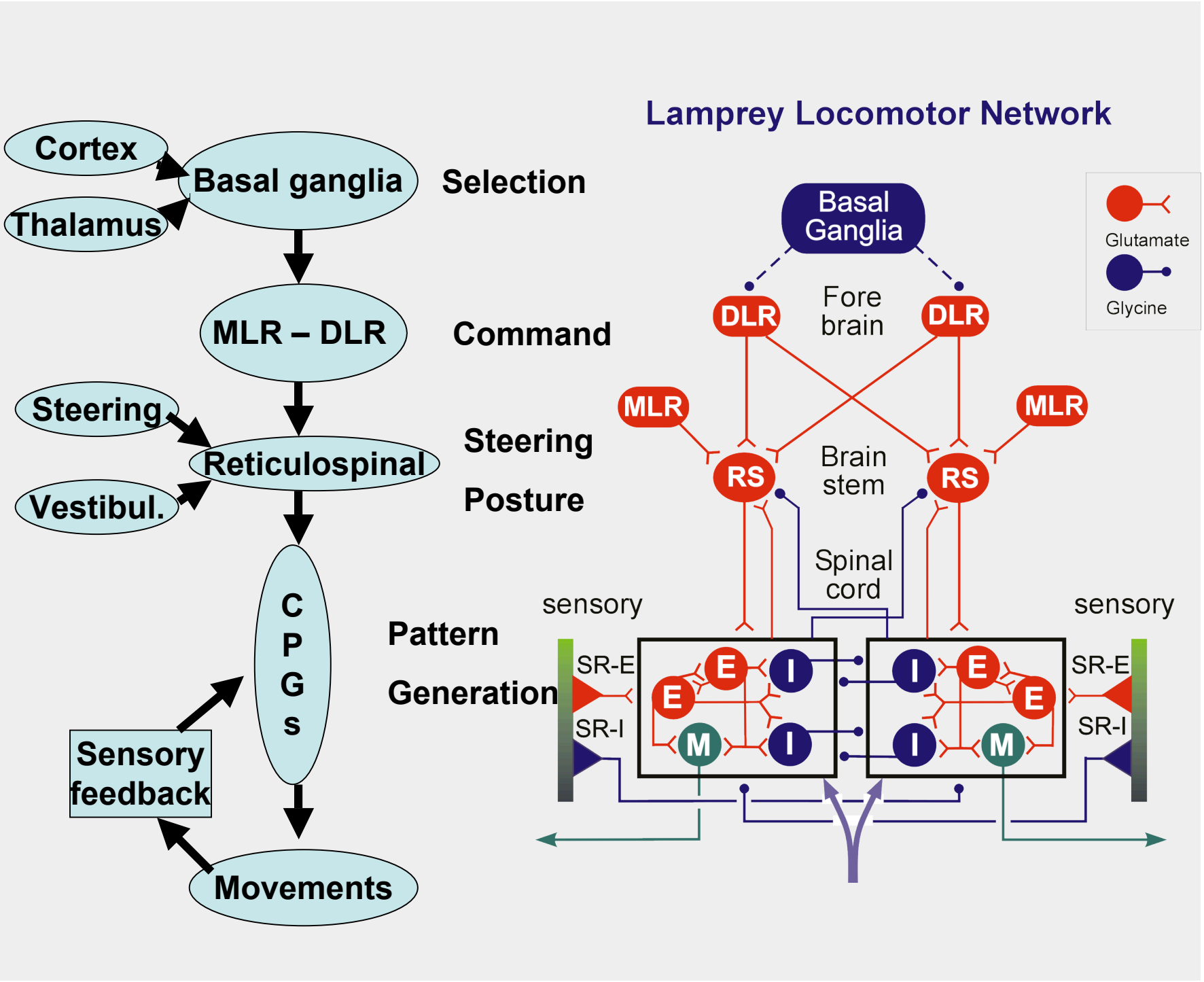
Different target cell subpopulations

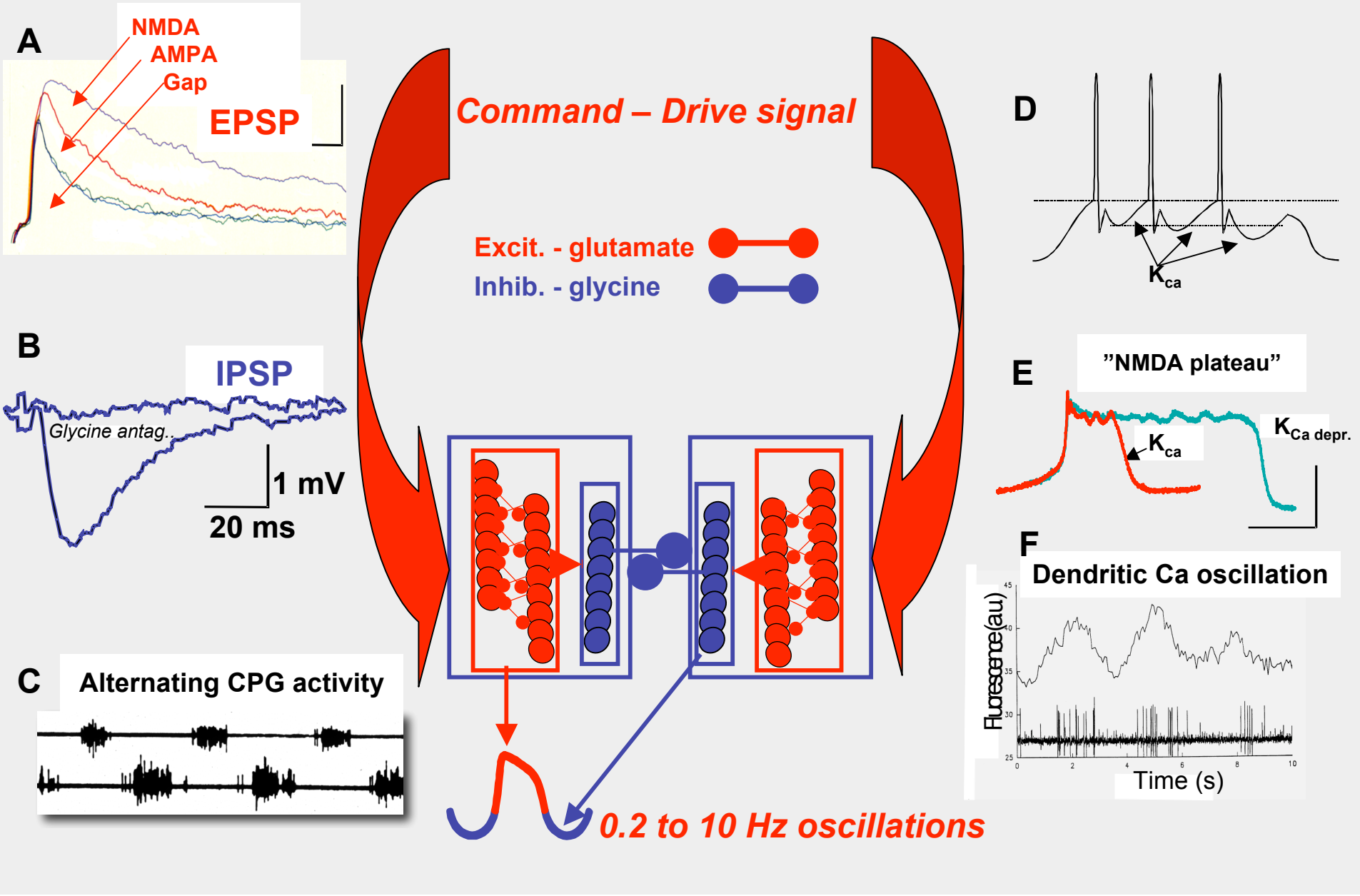
Next steps:

- Compare MSN connectivity pattern with biochemical identity (D1, D2, SP, ENK).

- Compare MSN connectivity with corticostriatal (Glu) input, and nigro-striatal (DA).

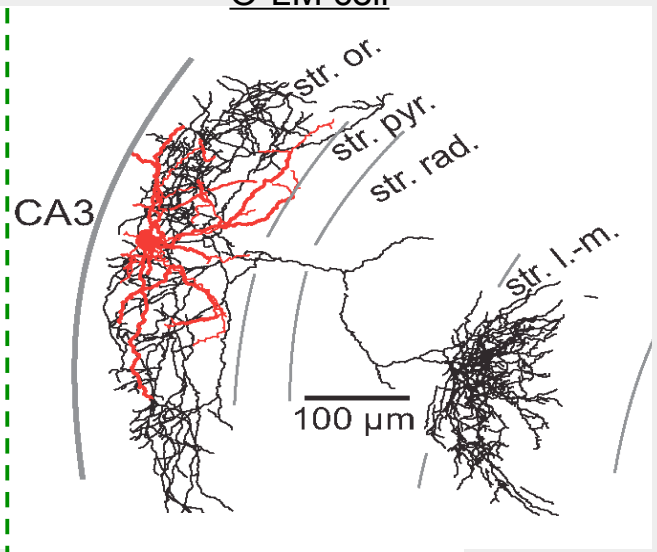

Cortex
Basal ganglia
Thalamus
Selection
MLR – DLR
Command
Steering
Reticulospinal
Vestibul.
Steering
Posture
C
P
G
s
Pattern
Generation
Sensory feedback
Movements
Lamprey Locomotor Network
Basal Ganglia
Glutamate
Glycine
Fore brain
DLR
DLR
MLR
MLR
RS
RS
Brain stem
Spinal cord
sensory
sensory
SR-E
SR-I
SR-E
SR-I
E
I
E
I
I
E
E
M
I
I
M

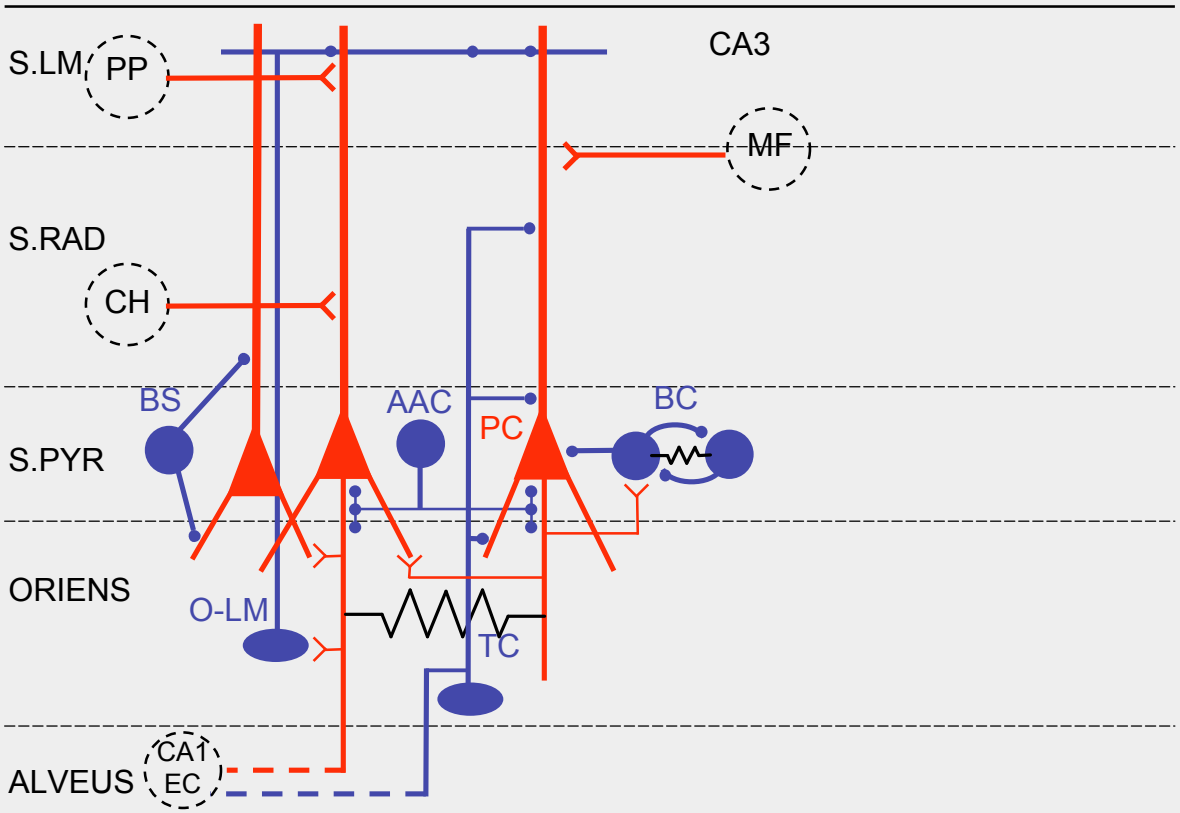

Cortex
Basal ganglia
Thalamus
Selection
MLR – DLR
Command
Steering
Reticulospinal
Vestibul.
Steering
Posture
C
P
G
s
Pattern
Generation
Sensory feedback
Movements
Lamprey Locomotor Network
Basal Ganglia
Glutamate
Glycine
Fore brain
DLR
DLR
MLR
MLR
RS
RS
Brain stem
Spinal cord
sensory
sensory
SR-E
SR-I
SR-E
SR-I
E
I
E
I
I
E
E
M
I
I
M


A
NMDA
AMPA
Gap
EPSP
B
IPSP
Glycine antag.
1 mV
20 ms
C
Alternating CPG activity
Command – Drive signal
Excit. - glutamate
Inhib. - glycine
0.2 to 10 Hz oscillations
D
K ca
E
"NMDA plateau"
K ca
K Ca depr.
F
Dendritic Ca oscillation
Fluorescence (au)
Time (s)

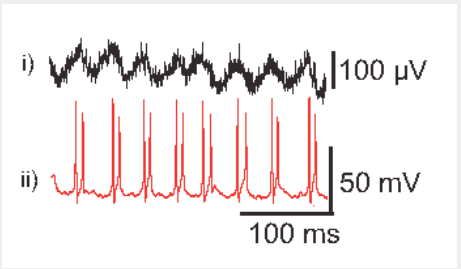
Hippocampus

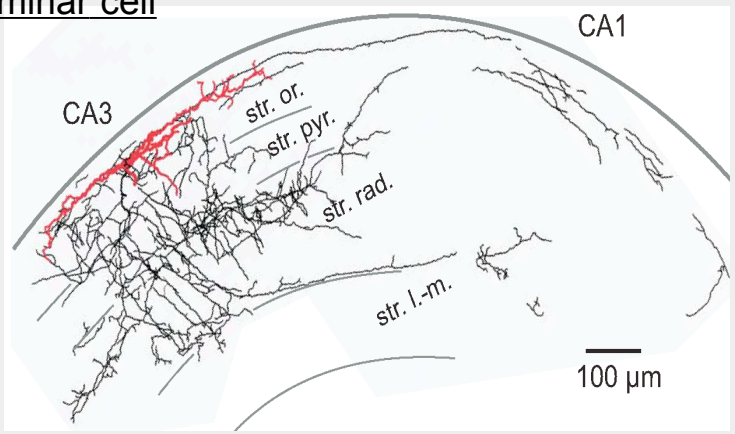
O-LM cell





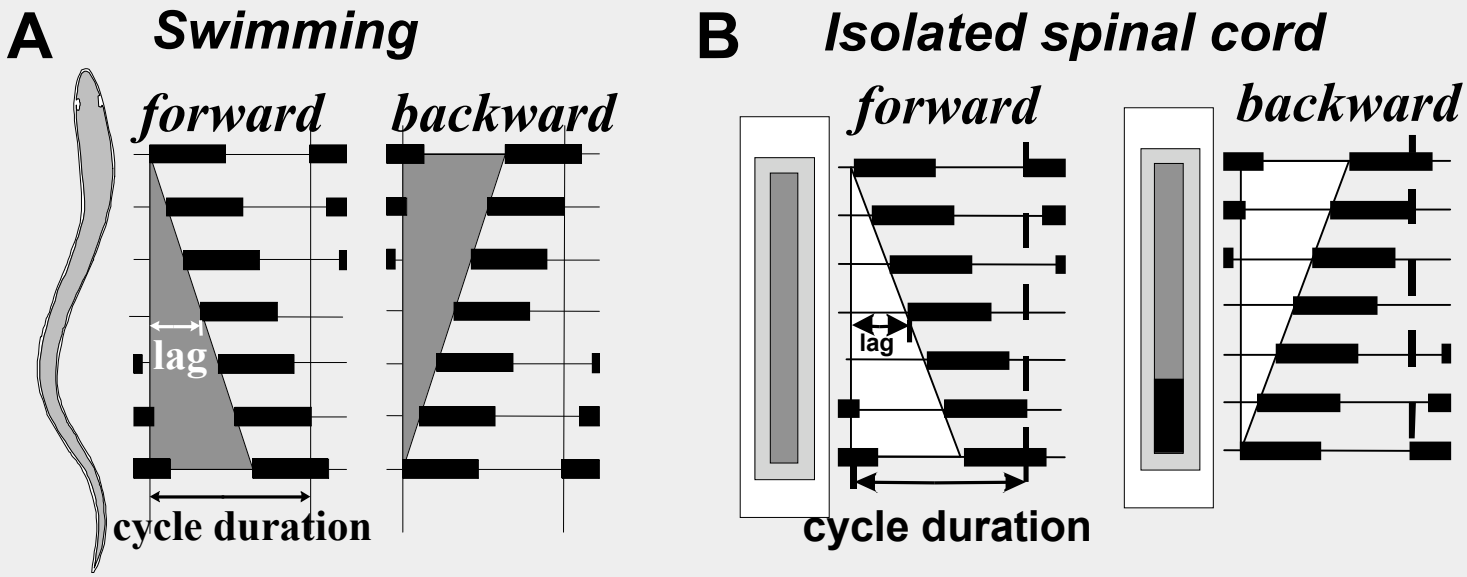
trilaminar cell





BS: bistratified cell
AAC: axo-axonic cell
PC: pyramidal cell
BC: basket cell
OLM: o-lm cell
TC: trilaminar cell

MF: mossy fiber
PP: perforant path
CH: contralateral hemisphere
SB: subiculum
EC: entorhinal cortex


A
Swimming
forward
backward
lag
cycle duration
B
Isolated spinal cord
forward
backward
lag
cycle duration

Selection of behaviour