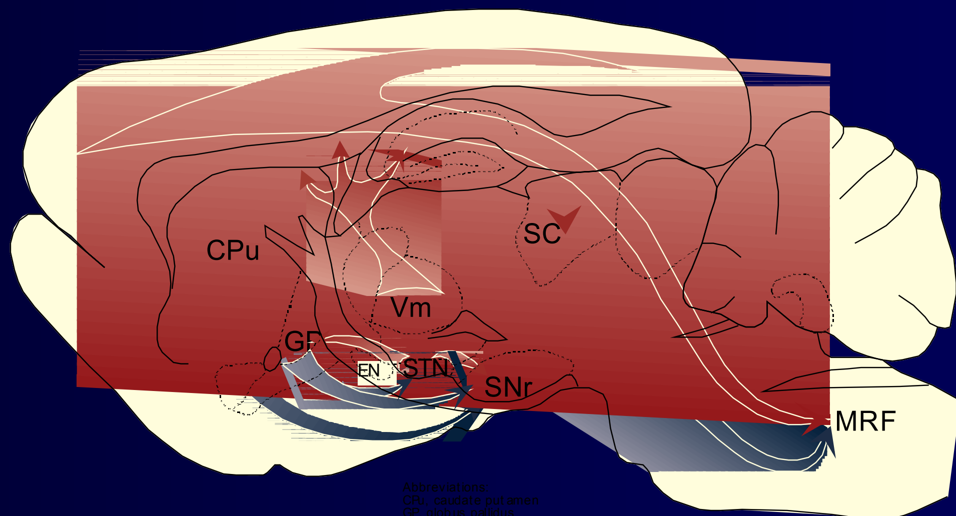
Is it just a question of priority ?

Inspiration from the vertebrate basal ganglia



Abbreviations:
CPu, caudate putamen
GP, globus pallidus
MRF, medullary reticular formation
SC, superior colliculus
SNr, substantia nigra pars reticulata
STN, subthalamic nucleus

wellcome trust

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EPSRC

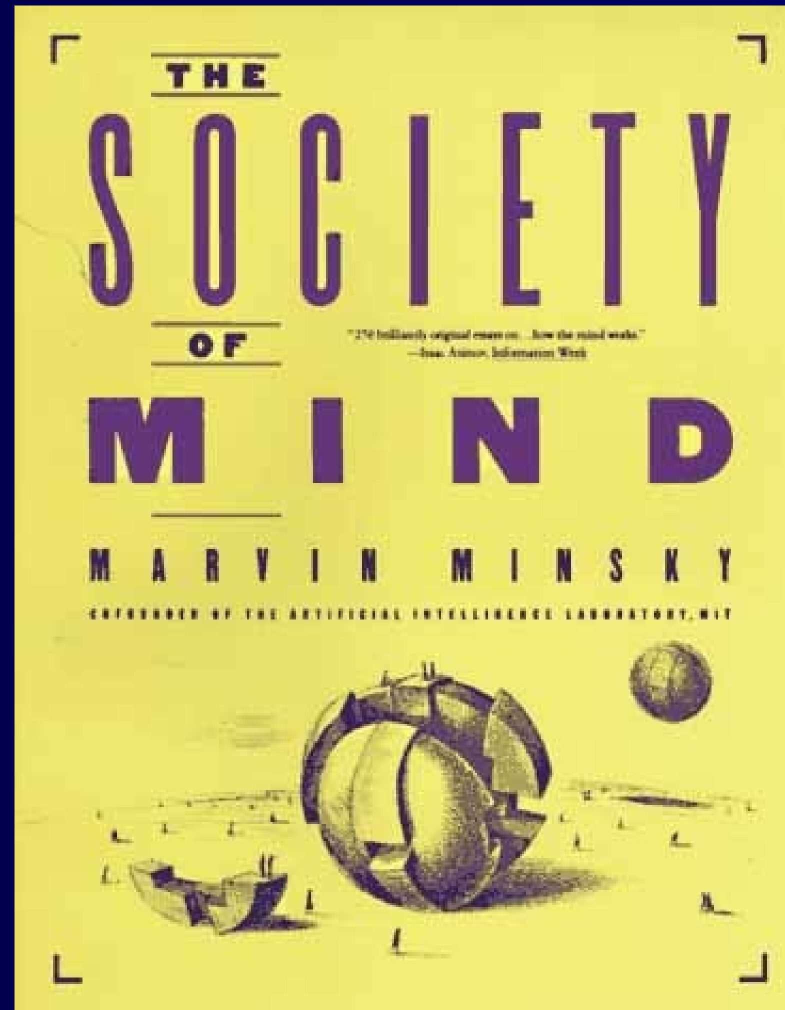
Overview

- Selection - a fundamental computational problem
- Basal ganglia as a biological solution – looped architecture
- Evolution of competing functional systems – layered architecture
- Subcortical loops through the basal ganglia
- Cortical/subcortical competitions – a basis for irrational behaviour
- Adaptive function(s) of the basal ganglia

A general architecture for a multifunctional system

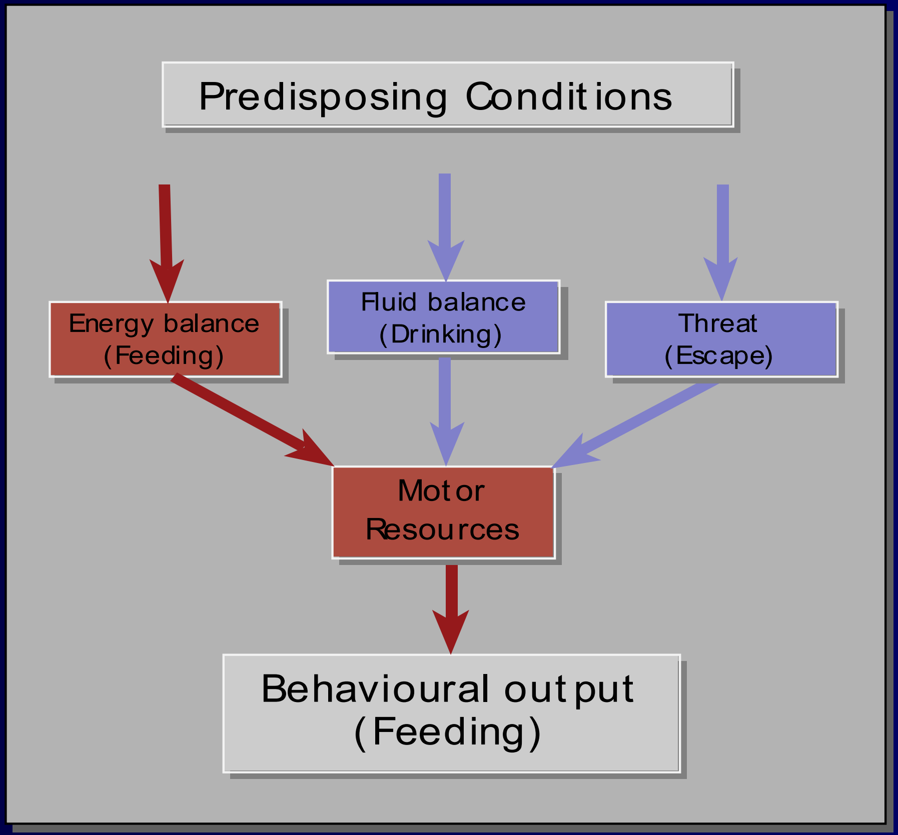
…including the brain

- Largely independent parallel processing functional units
- Each with:
  - specialised sensory input
  - specific functional objectives
  - specialised physiological and behavioural output



The Selection Problem

- Multiple functional systems
- Spatially distributed
- Processing in parallel
- All act through final common motor path



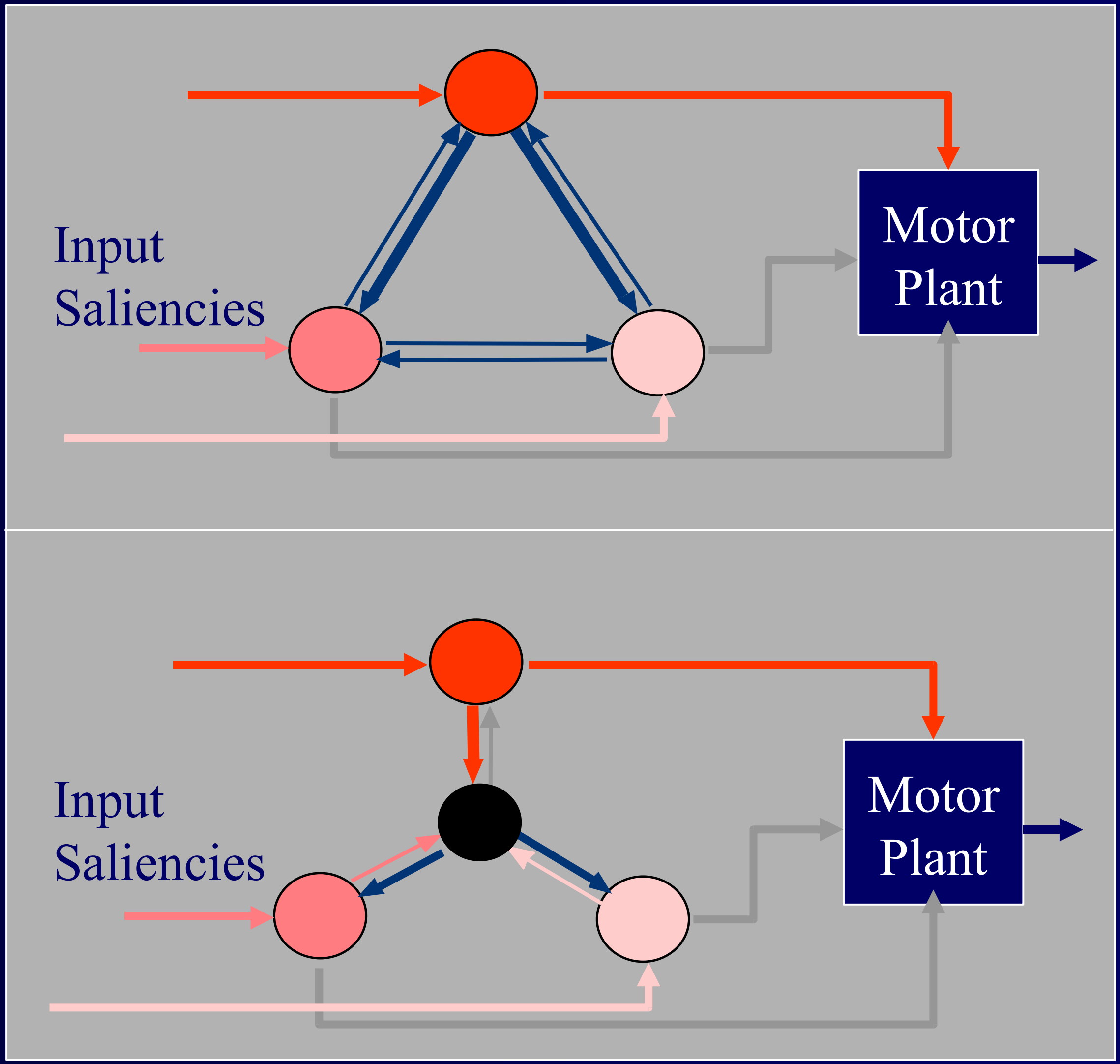
At any point in time which system should be permitted to guide motor output (behaviour)?

Parallel processing within sensory representations

Theoretical Solutions

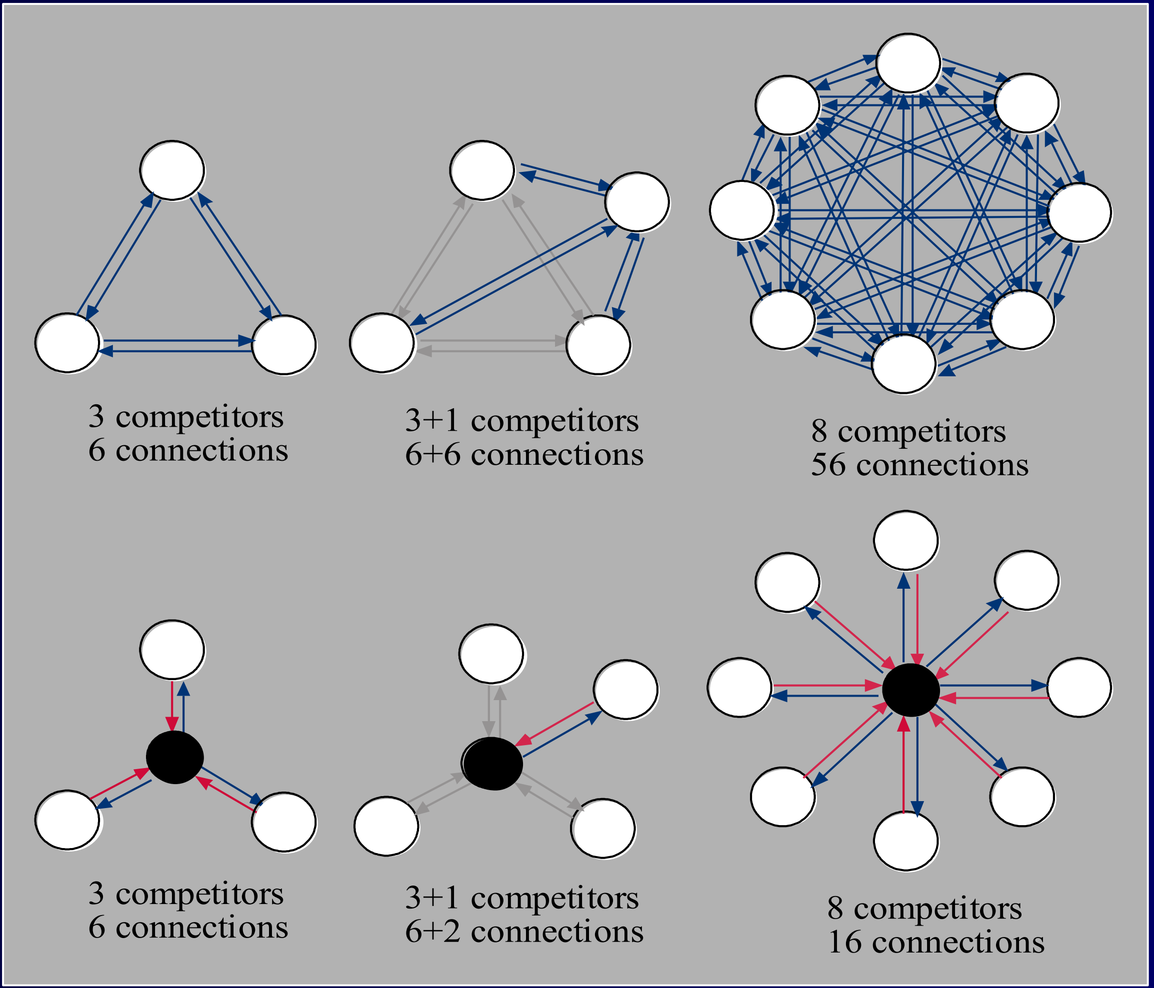
- Recurrent reciprocal inhibition
  - Selection an emergent property
  - Positive feedback
  - Winner-take-all

- Centralised selection
  - Localised switching
  - Dissociates selection from perception and motor control

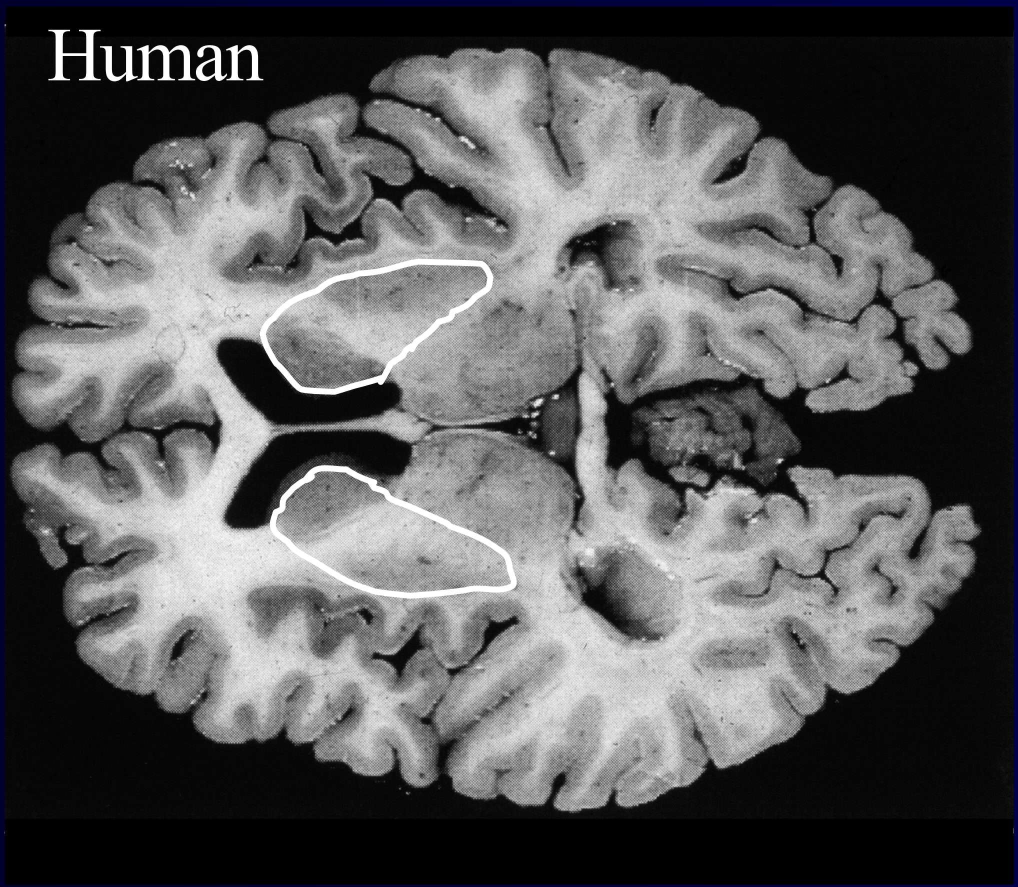


Problems of Scale

- Recurrent reciprocal inhibition
  - Each additional competitor increases connections by n(n-1)
- Centralised selection
  - Each additional competitor adds 2 further connections



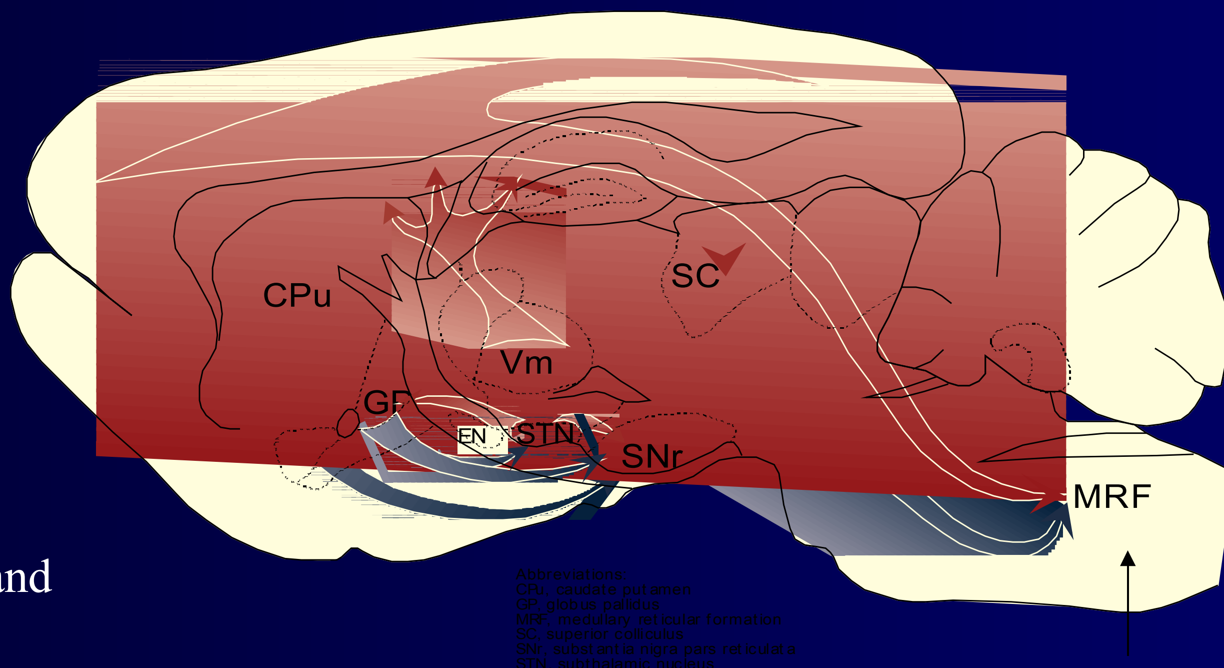
Basal Ganglia: a biological solution to the selection problem



Rat

External command systems and the basal ganglia

- External command systems
  - Cortical
  - Limbic
  - Midbrain
- Command inputs
  - Sensory
  - Cognitive
  - Affective
- Command outputs
  - Converge on brainstem and spinal motor generators
- Links with basal ganglia
  - Phasic excitatory inputs
  - Tonic inhibitory outpus



Motor plant

Redgrave P, Prescott T, Gurney KN. 1999. The basal ganglia: A vertebrate solution to the selection problem? Neuroscience 89:1009-1023.

Evolutionary conservatism

"The basal ganglia in modern mammals, birds and reptiles (i.e. modern amniotes) are very similar in connections and neurotransmitters, suggesting that the evolution of the basal ganglia in amniotes has been very conservative."

Medina, L and Reiner, A.

Neurotransmitter organization and connectivity of the basal ganglia in vertebrates: Implications for the evolution of basal ganglia. Brain Behaviour and Evolution (1995) **46**, 235-258

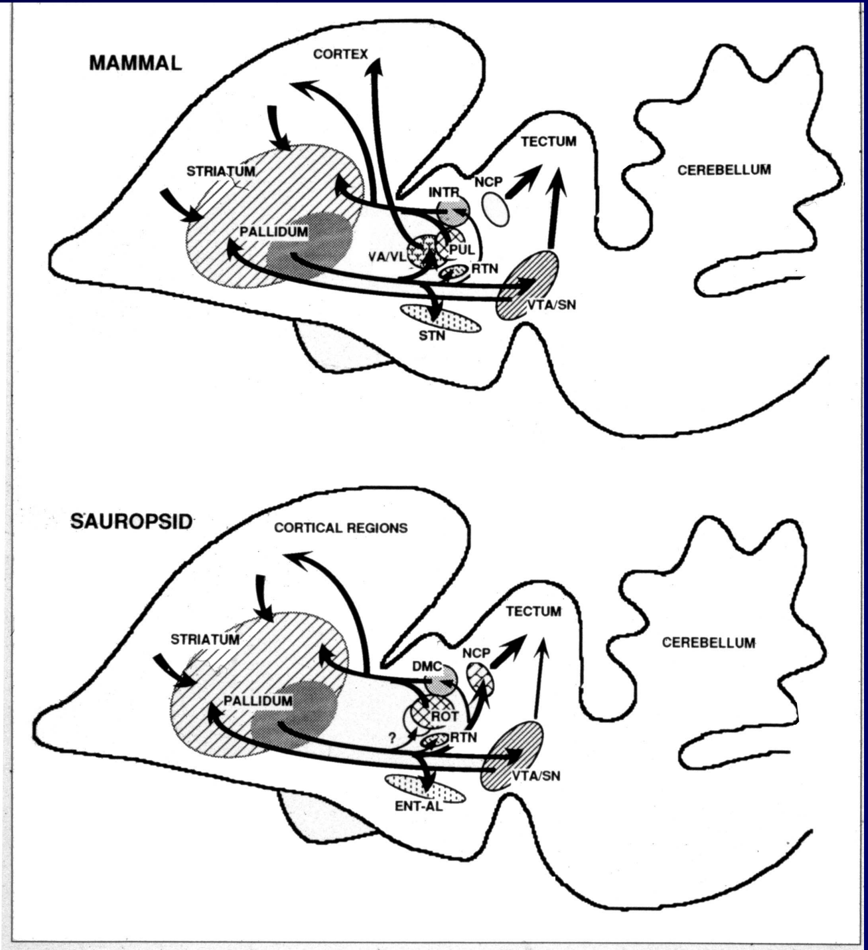
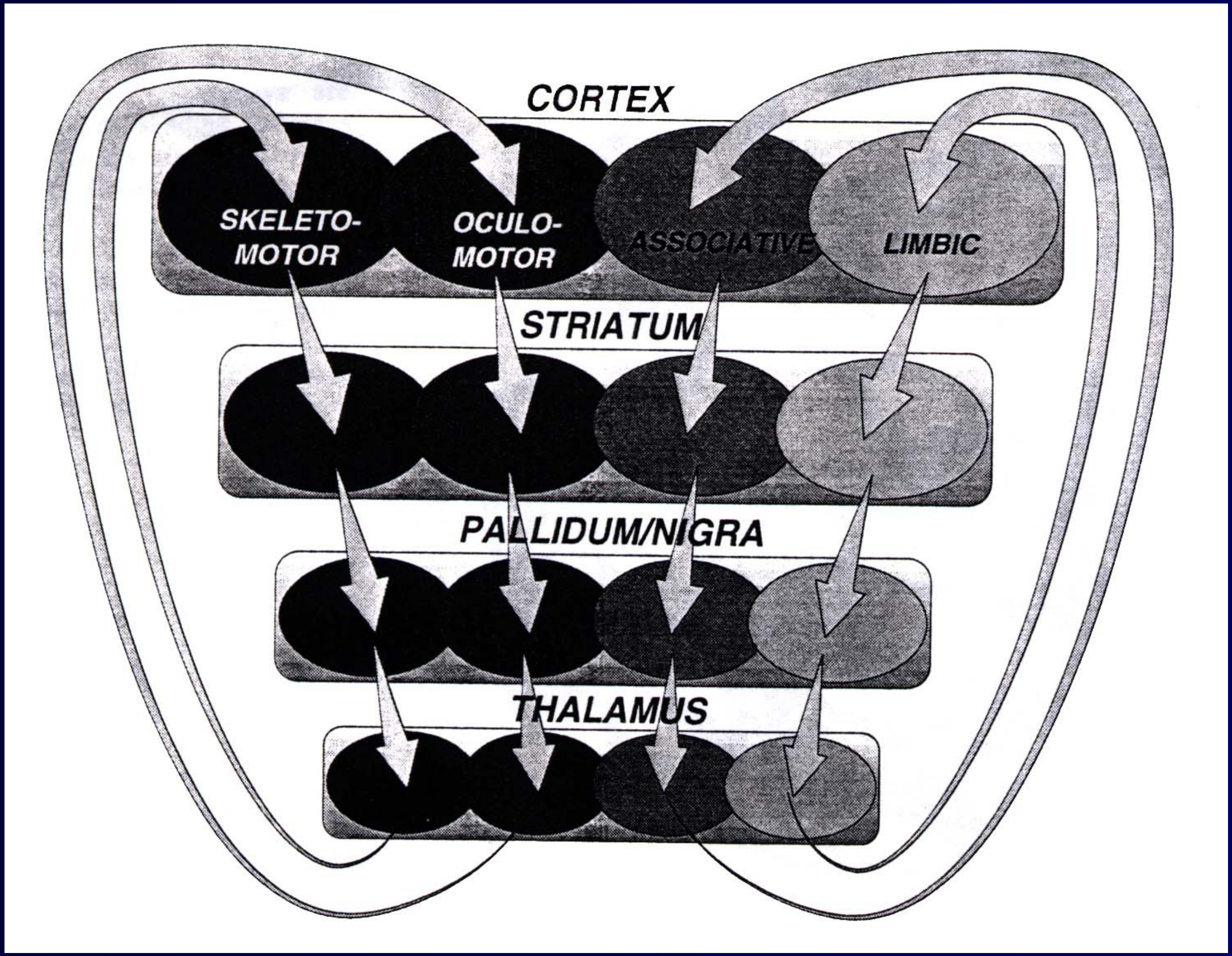


Fig. 5. Schematic drawings of sagittal sections through the brains of a mammal and a sauropsid (i.e. birds and reptiles), showing the basic connections involved in the circuitry of the basal ganglia in both amniotic groups. Abbreviations: DMC = Avian and reptilian dorsomedial thalamic complex; ENT-AL = reptilian entopeduncular nucleus, and avian anterior nucleus of the ansa lenticularis; INTR = mammalian midline-intralaminar nuclei; NCP = nucleus of the posterior commissure in reptiles and mammals, and lateral spiriform nucleus in birds; PUL = mammalian laterodorsal-pulvinar complex and medial geniculate nucleus; ROT = avian and reptilian nucleus rotundus and avian nucleus ovoidalis/reptilian nucleus medialis; RTN = reticular thalamic nucleus; STN = subthalamic nucleus; VA/VL = ventral anterior and ventral lateral nuclei; VTA/SN = ventral tegmental area and substantia nigra.

Basal Ganglia Architecture :Cortically based loops

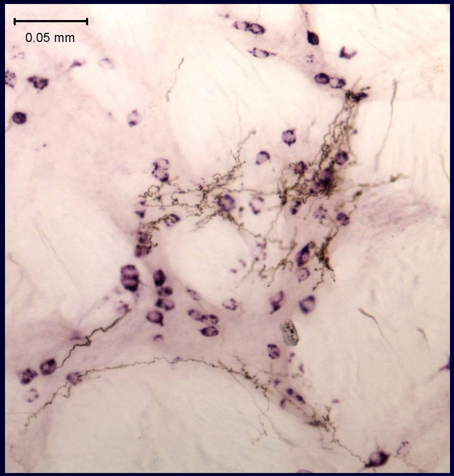


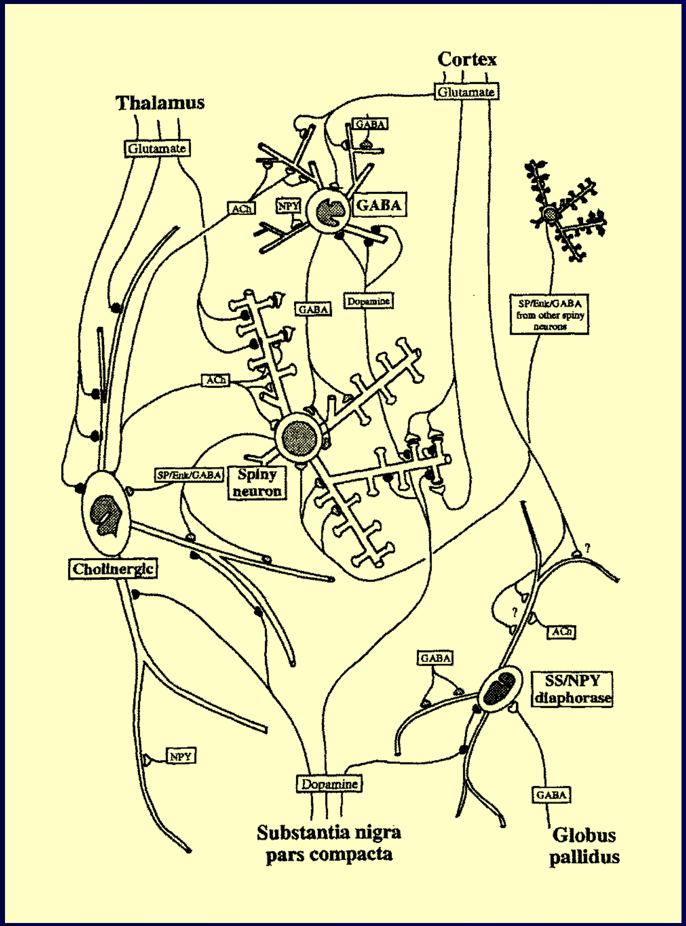
Alexander, G. E., M. R. DeLong, et al. (1986). "Parallel organization of functionally segregated circuits linking basal ganglia and cortex." Ann. Rev. Neurosci. **9**: 357-381.

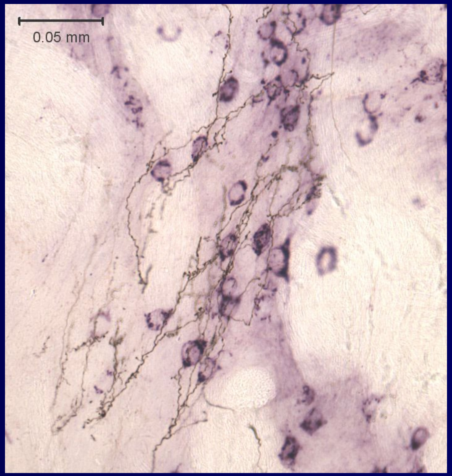
Repeating microcircuitry across territories

- External inputs
  - Cerebral cortex
  - Limbic system
  - Brainstem via thalamus

- Input functions
  - Cognitive
  - Affective
  - Sensorimotor







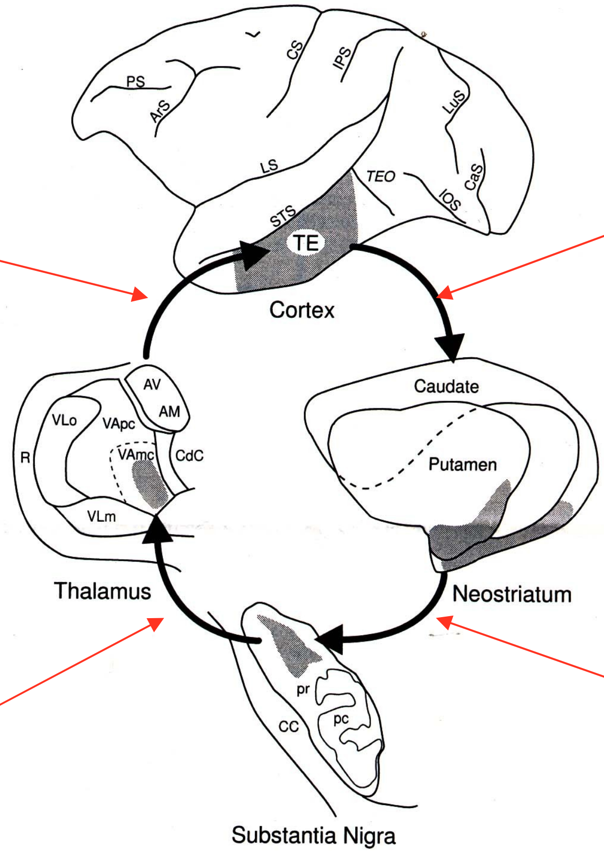
Bolam JP, Bennett BD. 1995. Microcircuitry of the neostriatum. In: Ariano MA, Surmeier DJ, editors. Molecular and cellular mechanims of neostriatal function. Austin, TX.: R.G. Landes Co. p 1-19.

Cortical loop: a specific example

Proc. Natl. Acad. Sci. USA 93 (1996) 8685

Phasic/
Disinhibitory
(Positive
Feedback)

Phasic/
excitatory



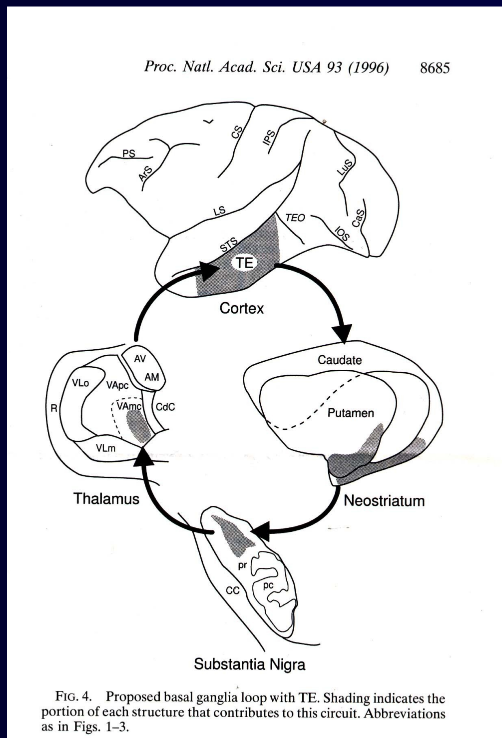
Tonic/
inhibitory

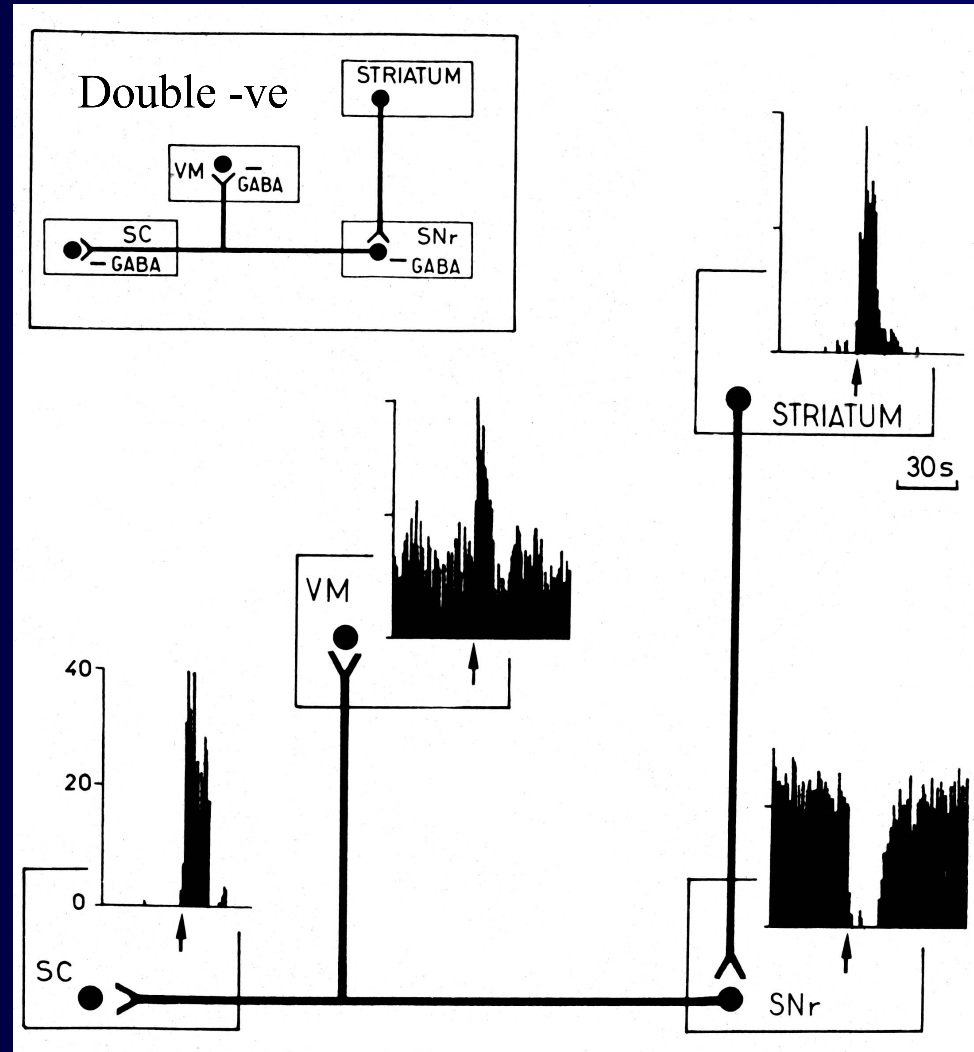
Phasic/
inhibitory

FIG. 4. Proposed basal ganglia loop with TE. Shading indicates the portion of each structure that contributes to this circuit. Abbreviations as in Figs. 1–3.

Middleton, F. A. and P. L. Strick (1996). "The temporal lobe is a target of output from the basal ganglia." Proc Natl Acad Sci USA **93**(16): 8683-8687.

Disinhibitory output

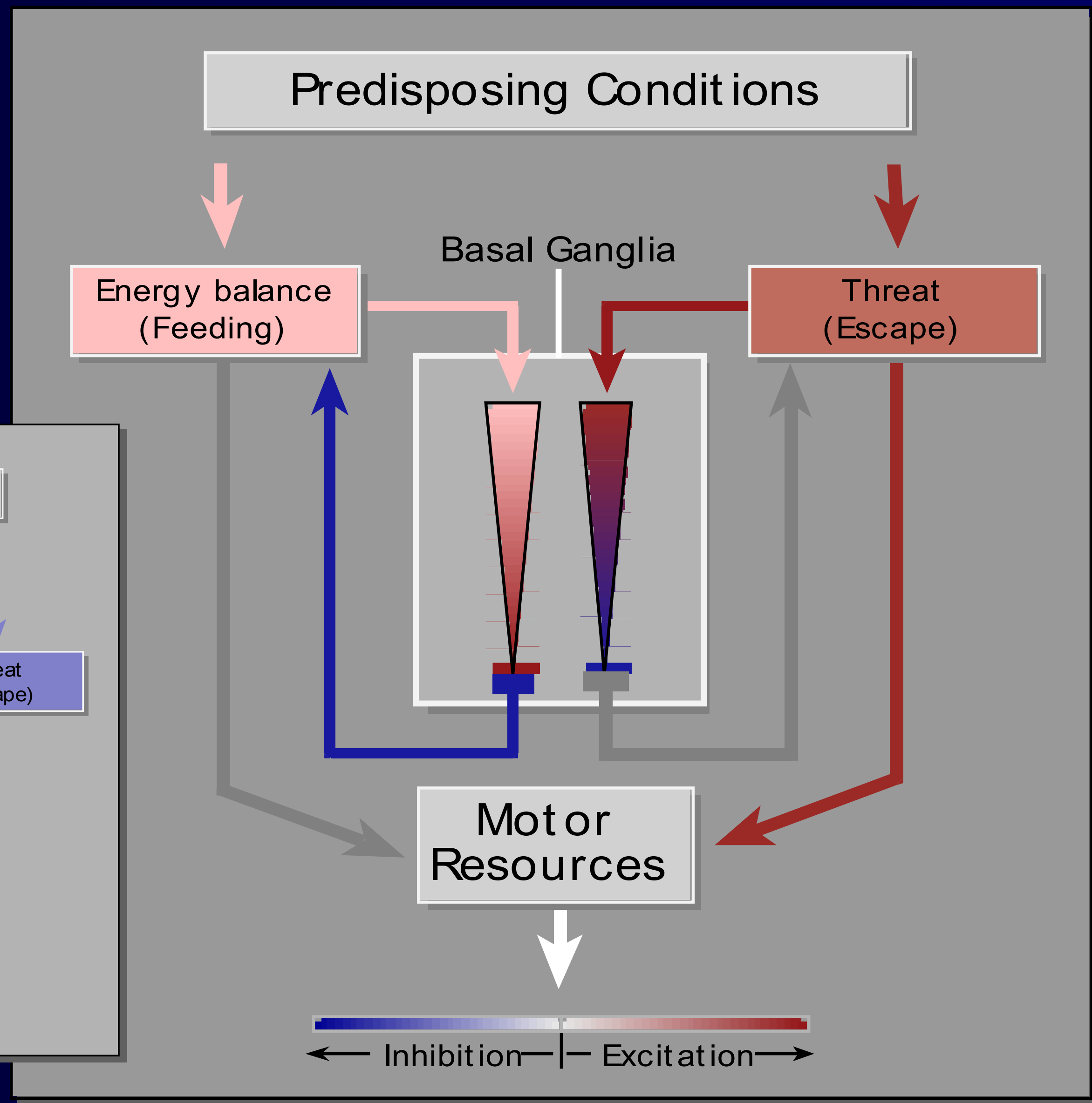




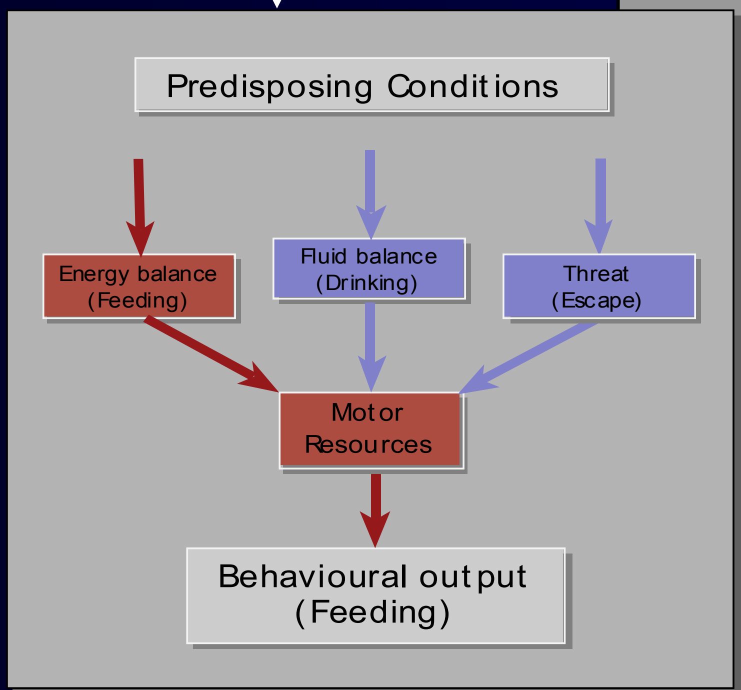
Chevalier, G. and J. M. Deniau (1990). "Disinhibition as a basic process in the expression of striatal functions." Trends Neurosci. **13**: 277-281.

Selection by inhibition and disinhibition

Potential resolution →



The Selection Problem



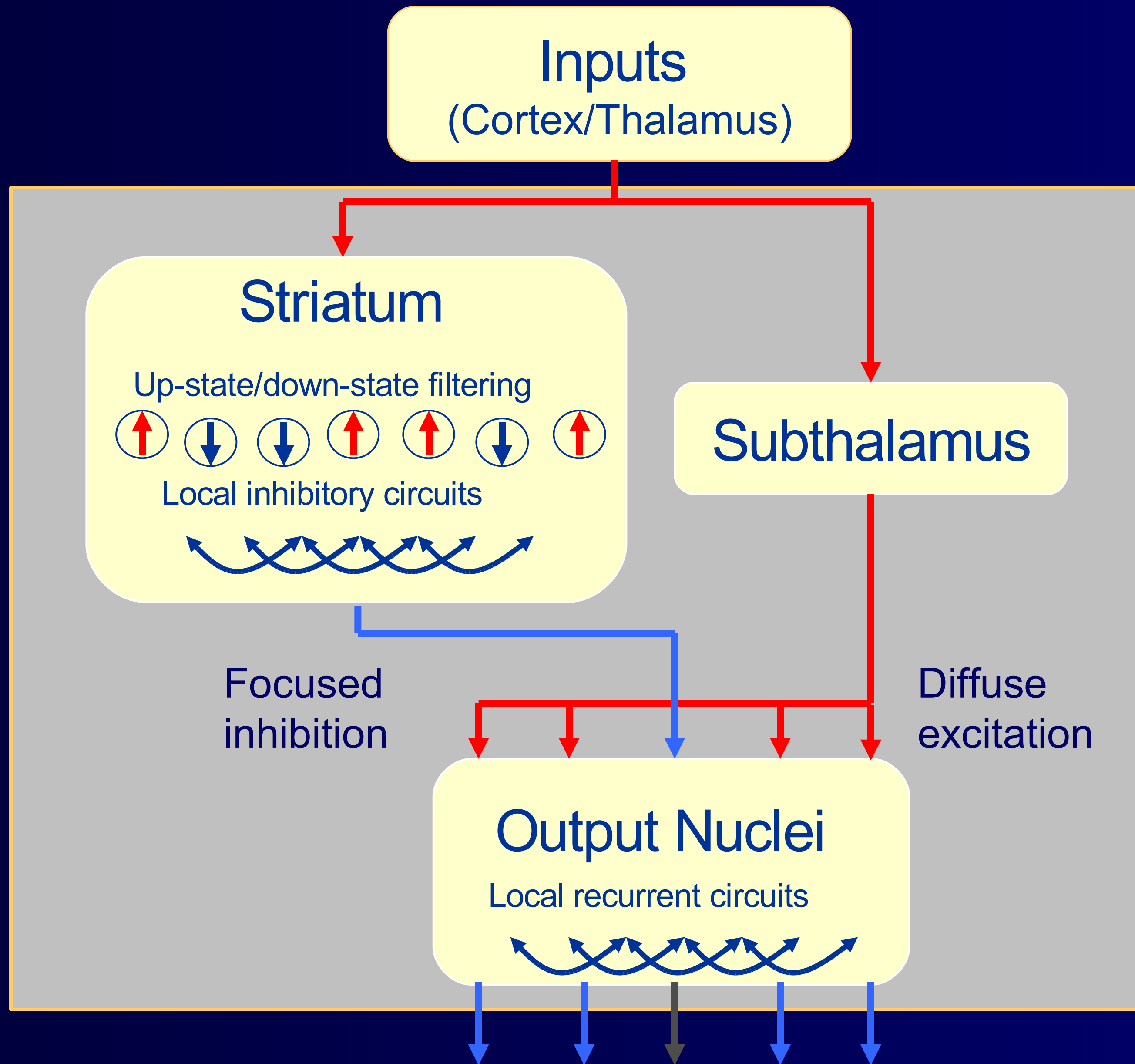
Serial Selection in the Basal Ganglia

1) Up-down states of medium spiny neurones

2) Local inhibition in striatum

3) Diffuse/focused projection onto output nuclei

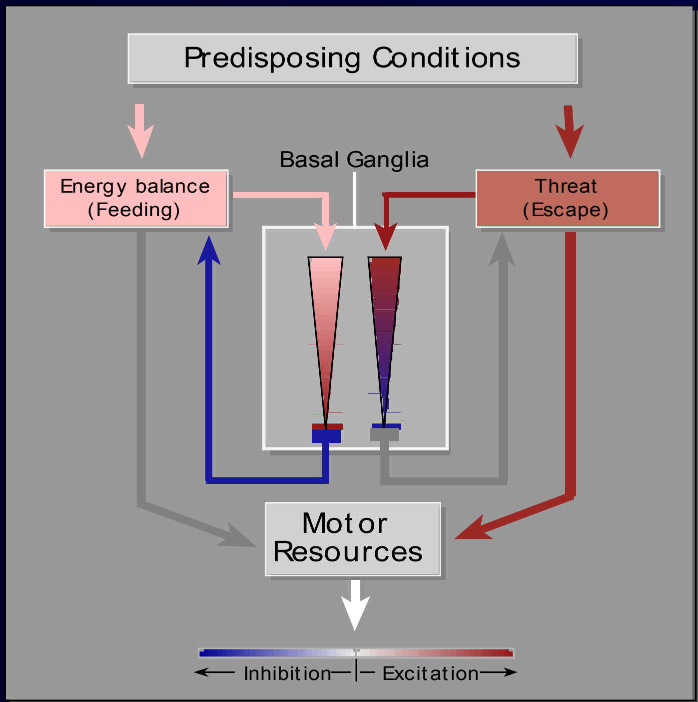
4) Recurrent inhibition in output nuclei



Basis for selection

- Relative levels of input salience in competing channels
  - Common currency for evaluating priority
- Determined by
  - Evolution…inputs from different command modules varies across species
  - Individual experience…reinforcement learning
- Implemented by
  - Differences in relative levels of afferent activity
  - Different weights of contact in different channels

Qualitative model:



Gurney, K., T. J. Prescott, et al. (2001). "A computational model of action selection in the basal ganglia. I. A new functional anatomy." Biol Cybern **84**: 401-410.

Analysis

Analytic equilibrium solution

(Kevin Gurney)

Model neurons - leaky integrators with piecewise linear output

striatum - control pathway

$$H[c_i - \epsilon/w_s(1-\lambda)] \equiv H_i^{\uparrow}(\lambda)$$

$$x_i^{e-} = m^-[w_s(1-\lambda_e)c_i - \epsilon]H_i^{\uparrow}(\lambda_e)$$

striatum - selection pathway

$$x_i^{g-} = m^-[w_s(1+\lambda_g)c_i - \epsilon]H_i^{\uparrow}(-\lambda_g)$$

STN

$$\begin{aligned} x_i^+ &= m^+(w_t c_i + \epsilon' - w_g y_i^e)H_i^{+\uparrow} \\ H_i^{+\uparrow} &= H(w_t c_i + \epsilon' - w_g y_i^e) \end{aligned}$$

GPe

$$\begin{aligned} \tilde{a}_i^e &= w^-(\delta X^+ - x_i^{e-}) + \epsilon_e \\ y_i^e &= m^e \tilde{a}_i^e H(a_i^e) \end{aligned}$$

GPi/SNr

$$\begin{aligned} \tilde{a}_i^g &= w^-(\delta X^+ - x_i^{g-}) - w_e y_i^e + \epsilon_g \\ y_i^g &= m^g \tilde{a}_i^g H(a_i^g) \end{aligned}$$

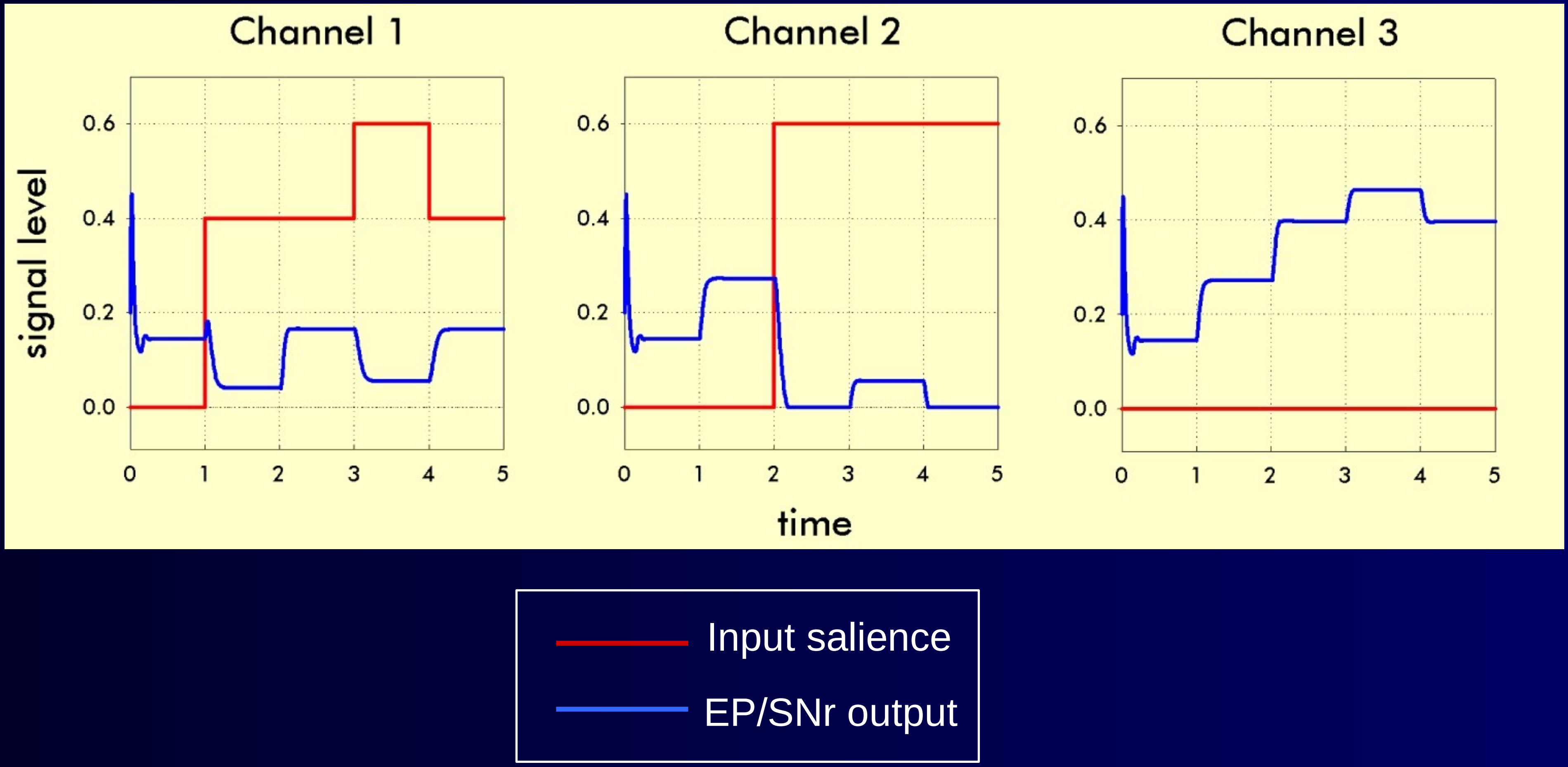
Solving for STN excitation

$$X^+ = \frac{n}{1 + \delta w_g w^- n \phi_{m,s}} \{w_t \phi_{*,s} \langle c \rangle_*^s + \phi^s \epsilon' + \phi_{q,s} w_g w^- [(1-\lambda_e) w_s \langle c \rangle_{q,s} - \epsilon] - w_g \phi^s \epsilon_e\}$$

....

Network and spiking model simulations

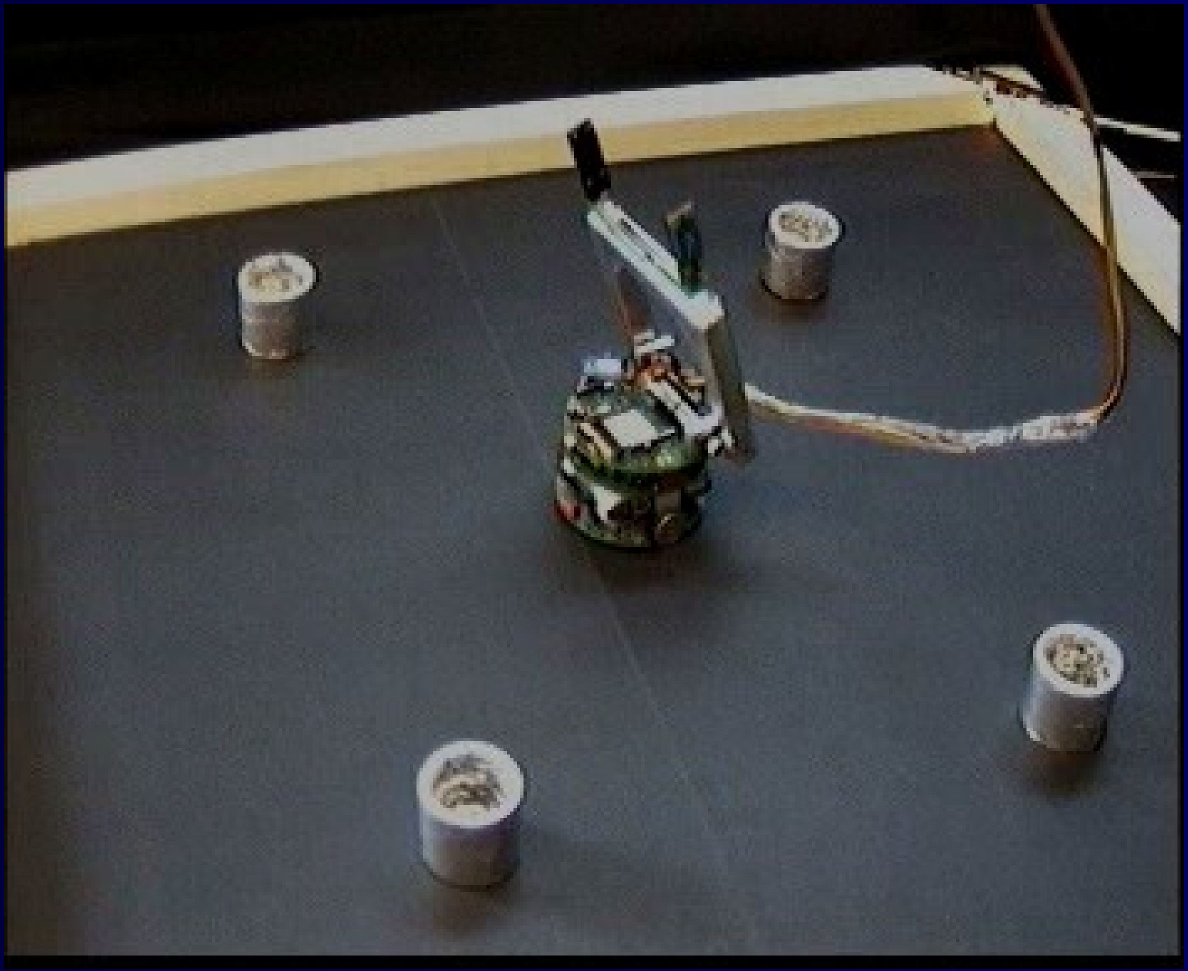
Dynamic switching between channels on basis of changes in input salience



Gurney, K., T. J. Prescott, et al. (2001). "A computational model of action selection in the basal ganglia. I. A new functional anatomy." Biol Cybern **84**: 401-410.

Robot Action Selection

- Motivations
  - Hunger
  - Fear
- 5 behavioural sub-systems
  - Wall seek
  - Wall follow
  - Can seek
  - Can pick-up
  - Can deposit
- 8 Infra-red sensors detect
  - Walls
  - Corners
  - Cans
- Gripper sensors detect
  - Presence/absence of can



Prescott TJ, Gonzalez FMM, Gurney K, Humphries MD, Redgrave P. 2006. A robot model of the basal ganglia: Behavior and intrinsic processing. Neural Networks 19(1):31-61.

Conclusions

- Uniquely, selection hypothesis of basal ganglia architecture confirmed in analysis, simulation and control of robot action selection
- Represents a generic task performed in all functionally segregated territories of the basal ganglia
  - Selection of overall behavioural goal (limbic)
  - Selection of actions to achieve selected goal (associative)
  - Selection of movements to achieve selected actions (sensorimotor)
- Consistent with early development and evolutionary conservation
- Explains basal ganglia ‘involvement’ in so many tasks

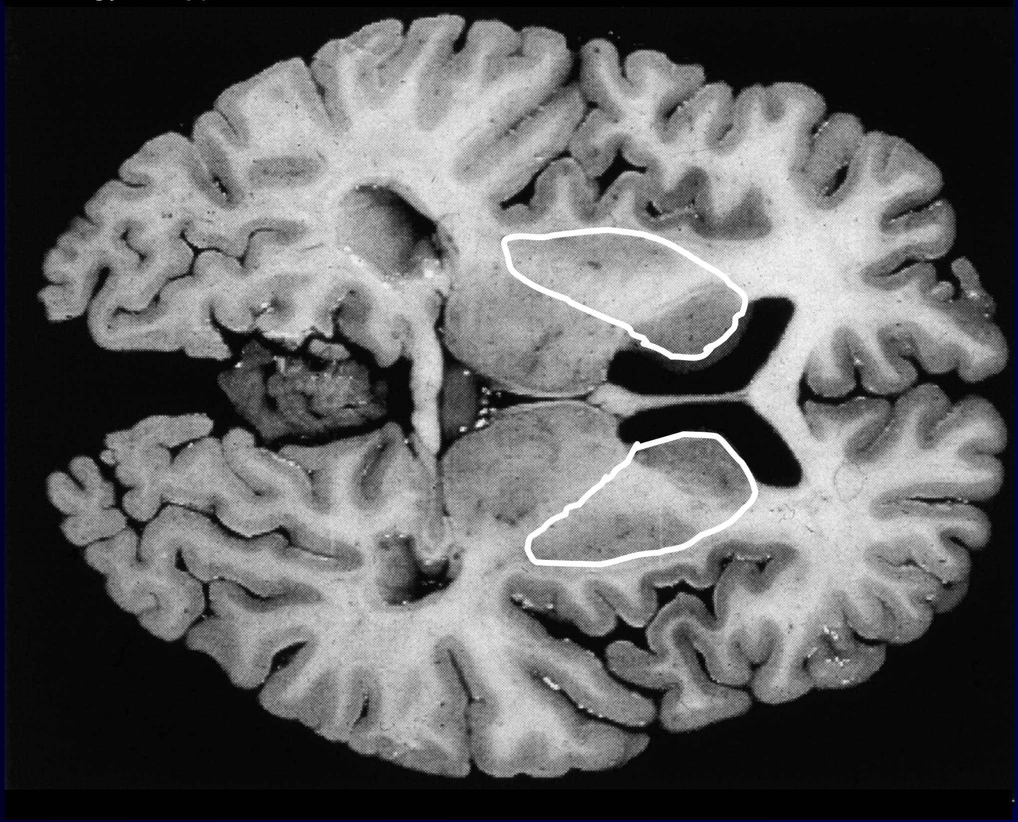
Implications

- If the basal ganglia are operating as a central selection mechanism, what follows ?
  - Is “selective attention” a higher level description of currently selected (winning) channels ?
  - How does the evolutionary status of external command systems affect selection ?
  - What is the role of the central selector in adaptive behaviour ?

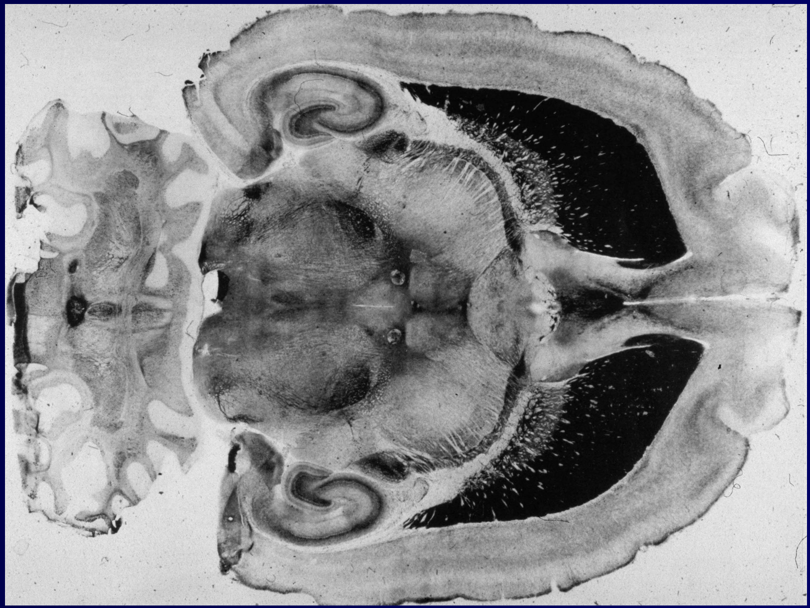
The basal ganglia may have be conserved

…. unlike cerebral cortex and cerebellum the basal ganglia have not increased in relative size with brain development

Human

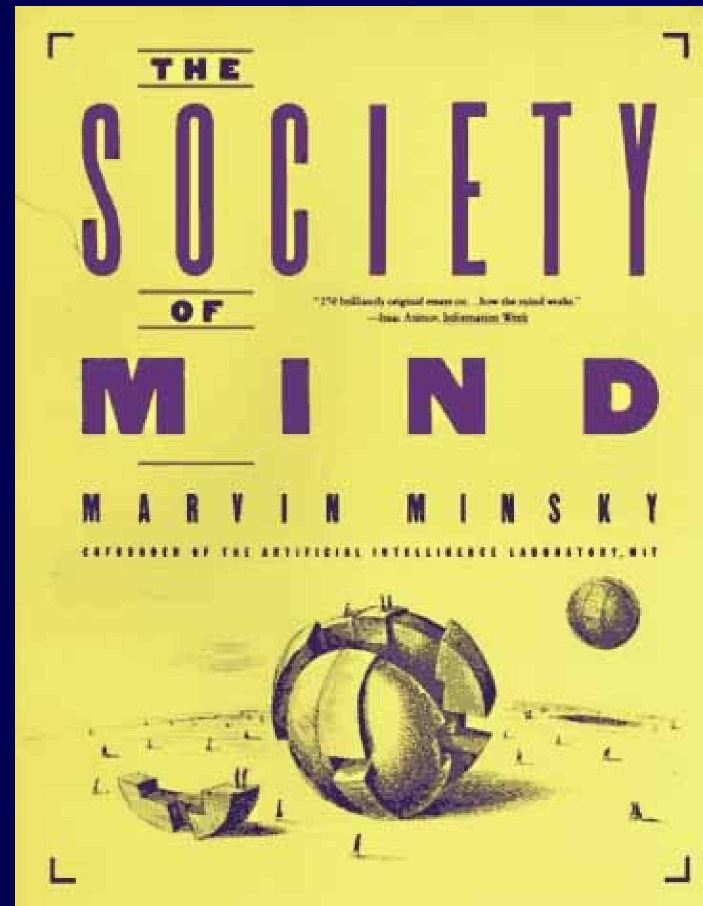


Rat



…but the competing systems certainly haven't

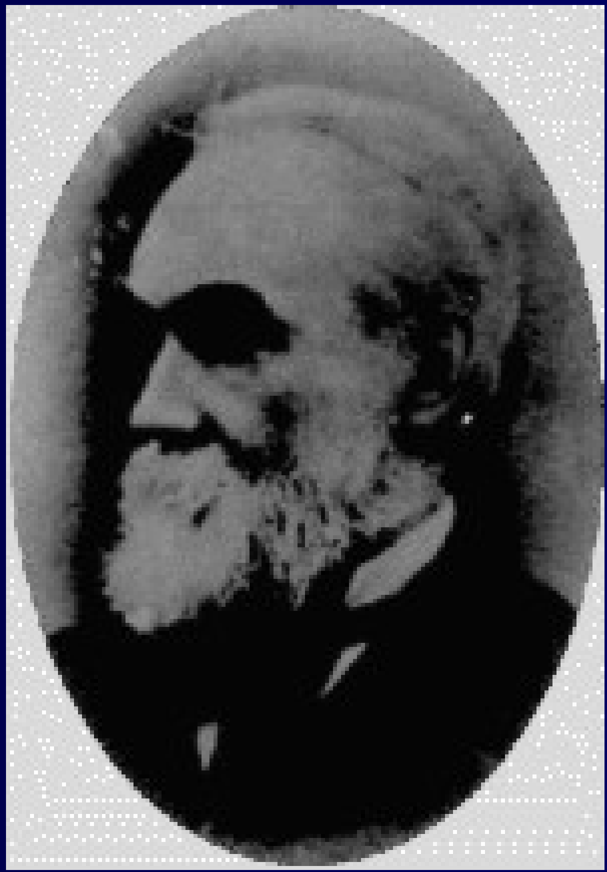
- How have functional units developed during evolution ?
  - Early systems simple solutions
  - Later components added to provide increasingly sophisticated solutions
  - ….to the same problems



Layered architecture: not a new idea

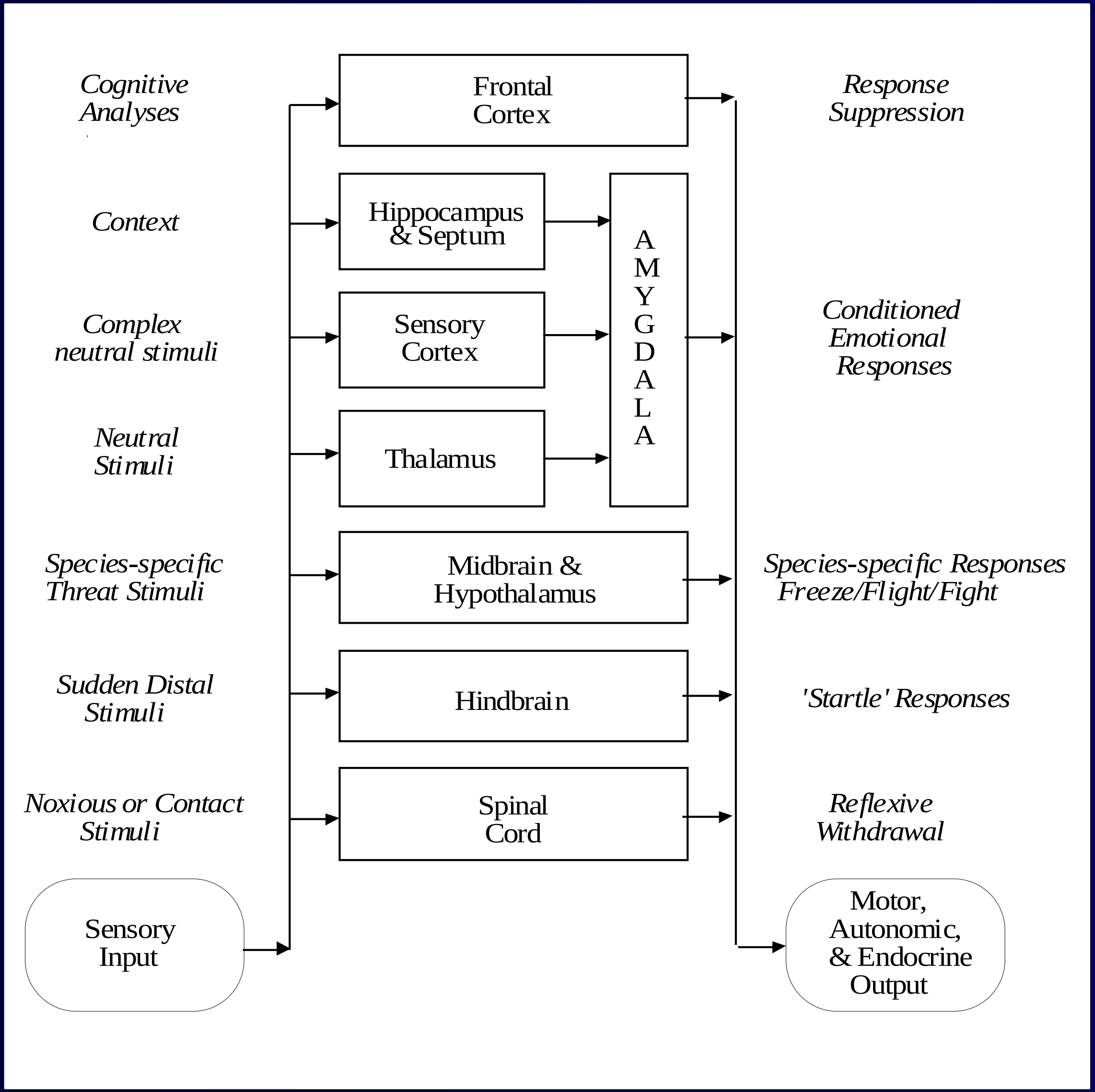
"That the middle motor centers represent over again what all the lowest motor centers have represented, will be disputed by few. I go further, and say that the highest motor centers (frontal lobes) represent over again, in more complex combinations, what the middle motor centers represent."

From "The evolution and dissolution of the nervous system" (1884)



John Hughlings Jackson
1835-1911

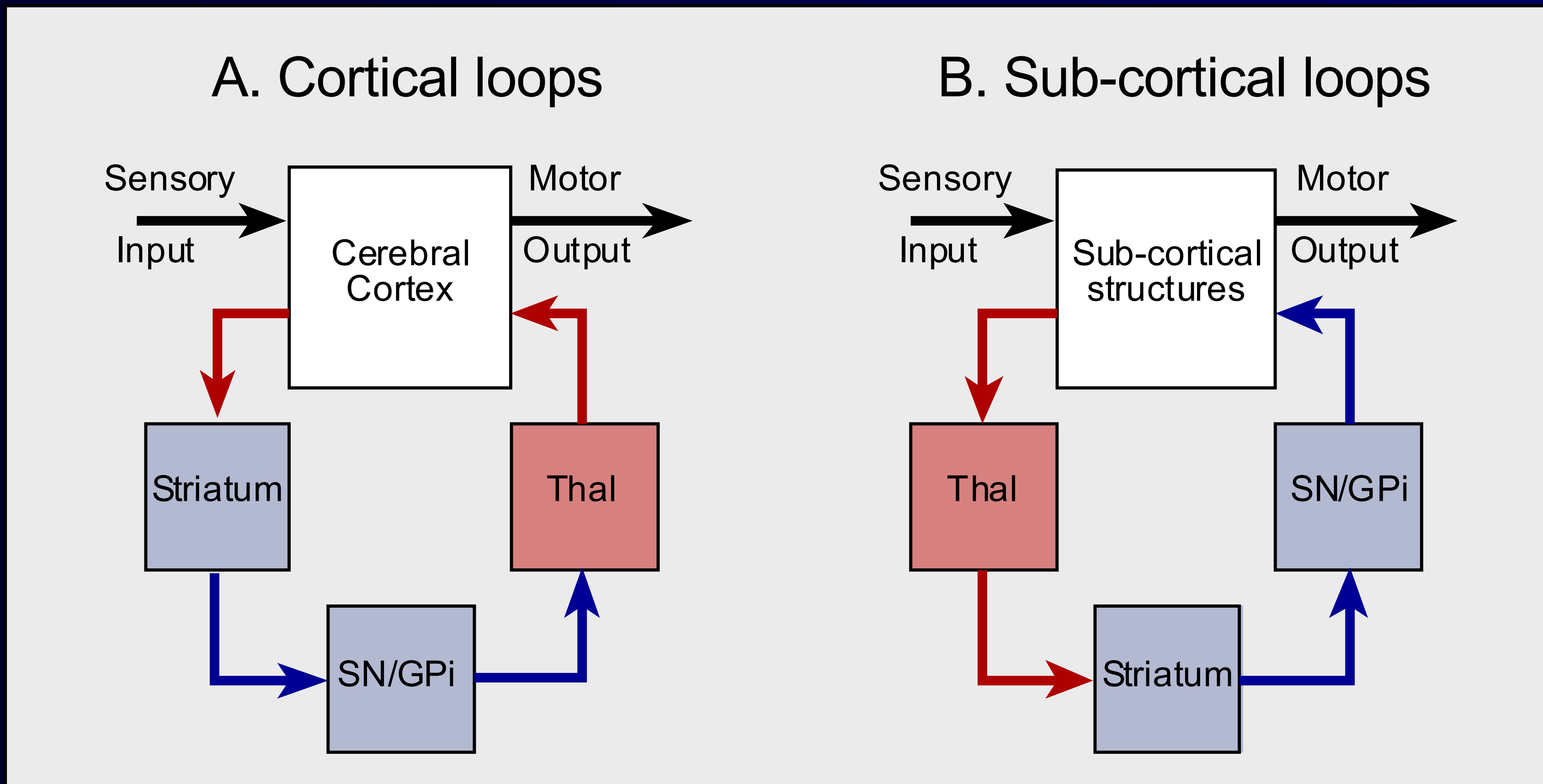
Increasing sophistication across the neuraxis



Prescott TJ, Redgrave P, Gurney KN. 1999. Layered control architectures in robots and vertebrates. Adaptive Behavior 7:99-127.

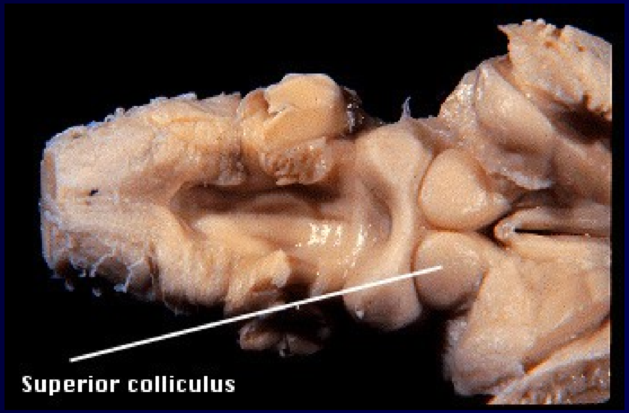
How was selection done before cortical loops ?

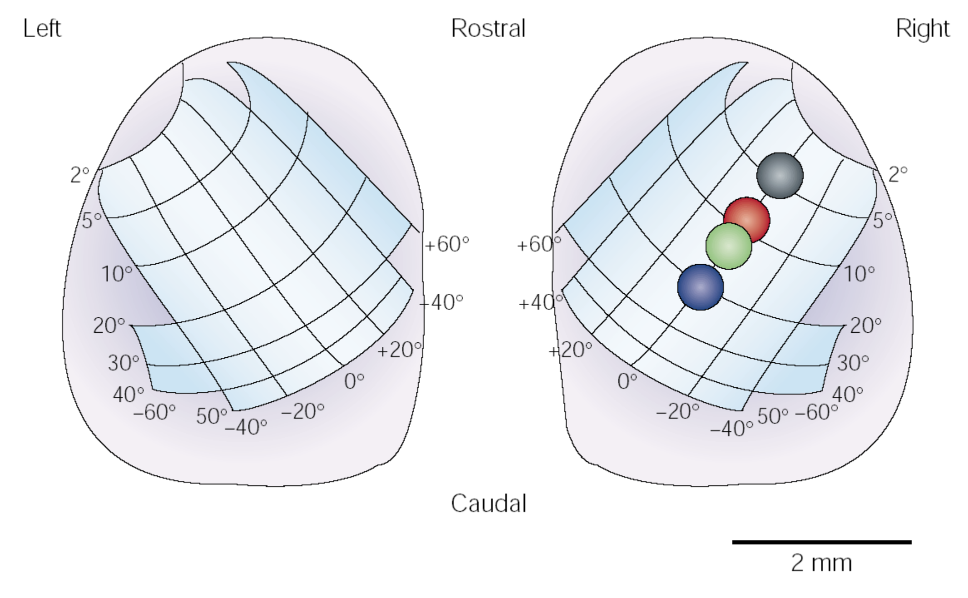
Subcortical loops through the basal ganglia

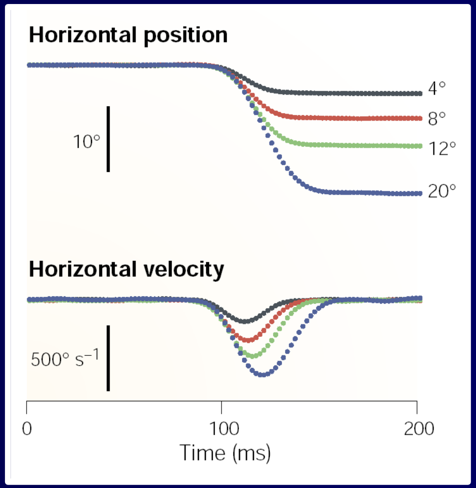


McHaffie JG, Stanford TR, Stein BE, Coizet V, Redgrave P. 2005. Subcortical loops through the basal ganglia. Trends Neurosci 28(8):401-407.

Midbrain superior colliculus

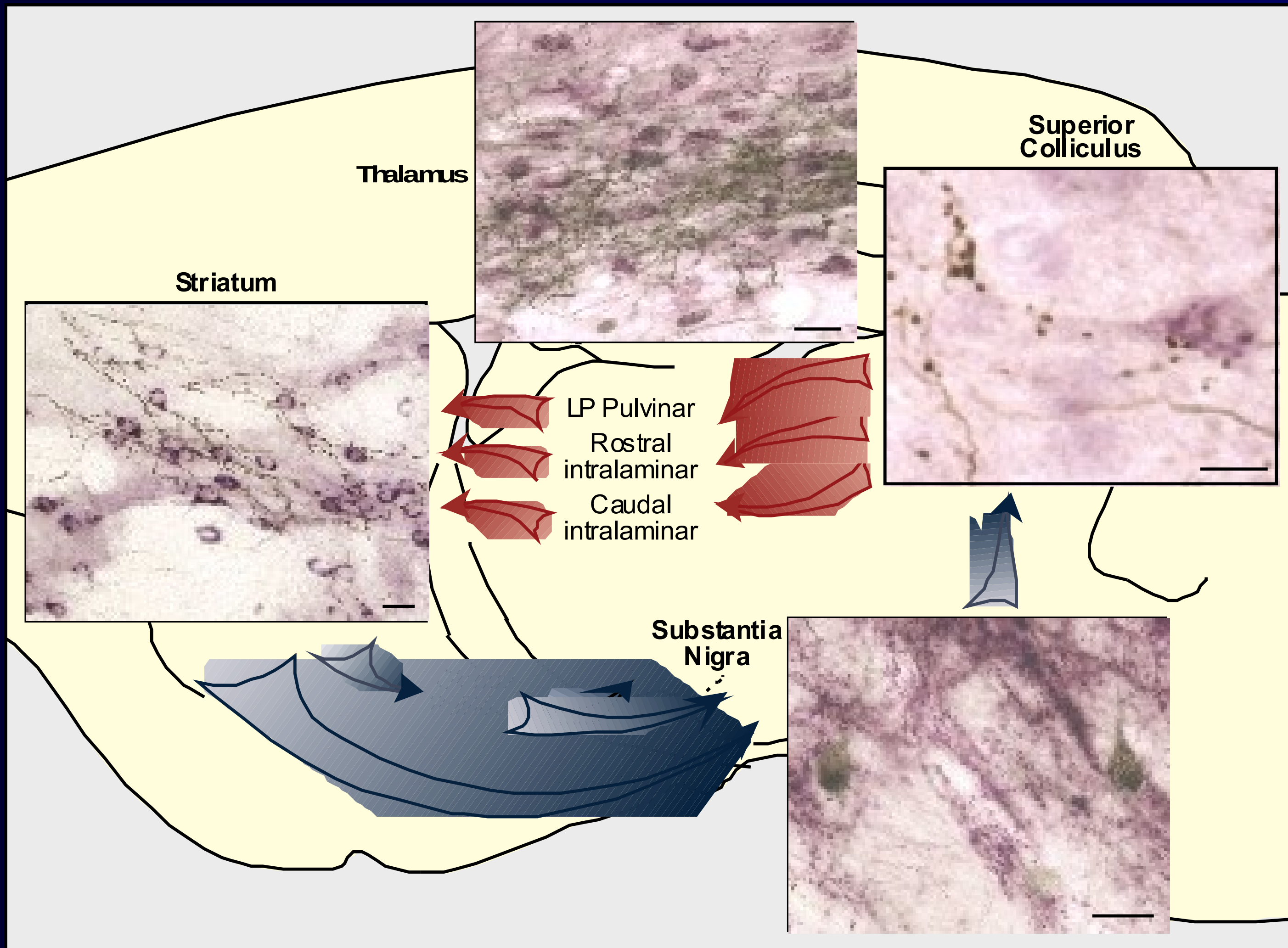






Sparks DL. 2002. The brainstem control of saccadic eye movements. Nature Reviews Neuroscience 3:952-964.

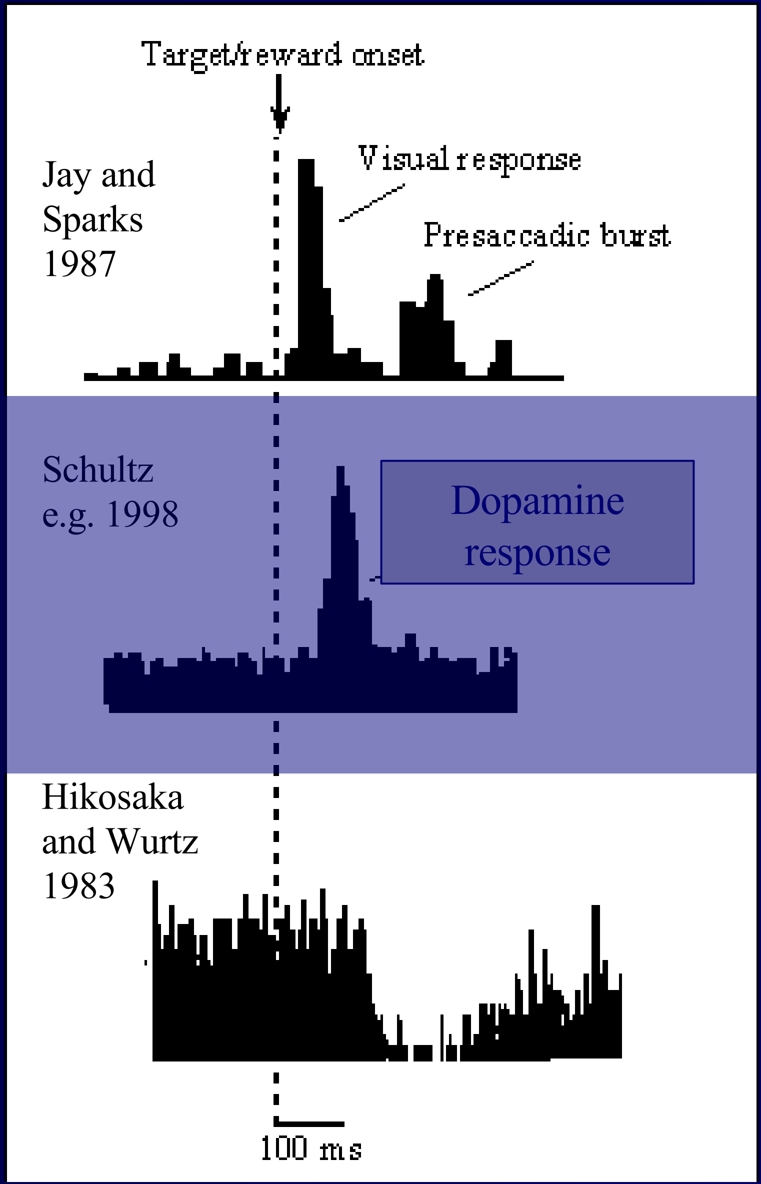
Subcortical loops from the superior colliculus



Parallel processing sensory representations

Signal timing in the superior colliculus

- Unexpected visual stimuli elicit sensory and motor responses in the superior colliculus:
  - short latency sensory reaction (~40 ms)
  - longer latency (<150 ms) pre-saccadic motor burst temporally associated with orienting



- Activity in basal ganglia output nuclei :
  - at 120ms+ nigrotectal disinhibition releases the orienting motor response in the colliculus

Cortical and subcortical command systems

Architecture for rational/irrational behaviour

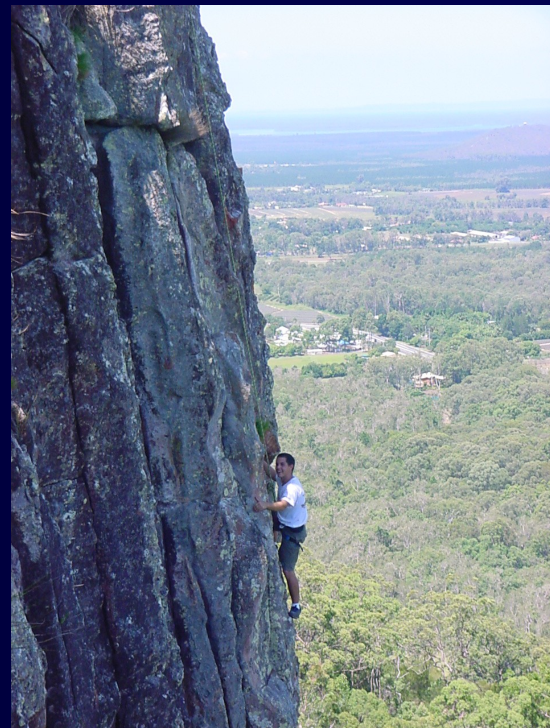
- Cortical representations (bids) often based on more sophisticated sensory analyses and models of action consequences

- Subcortical representations heavily dependent on immediate sensory events

- What happens when they go head-to-head in the basal ganglia ?

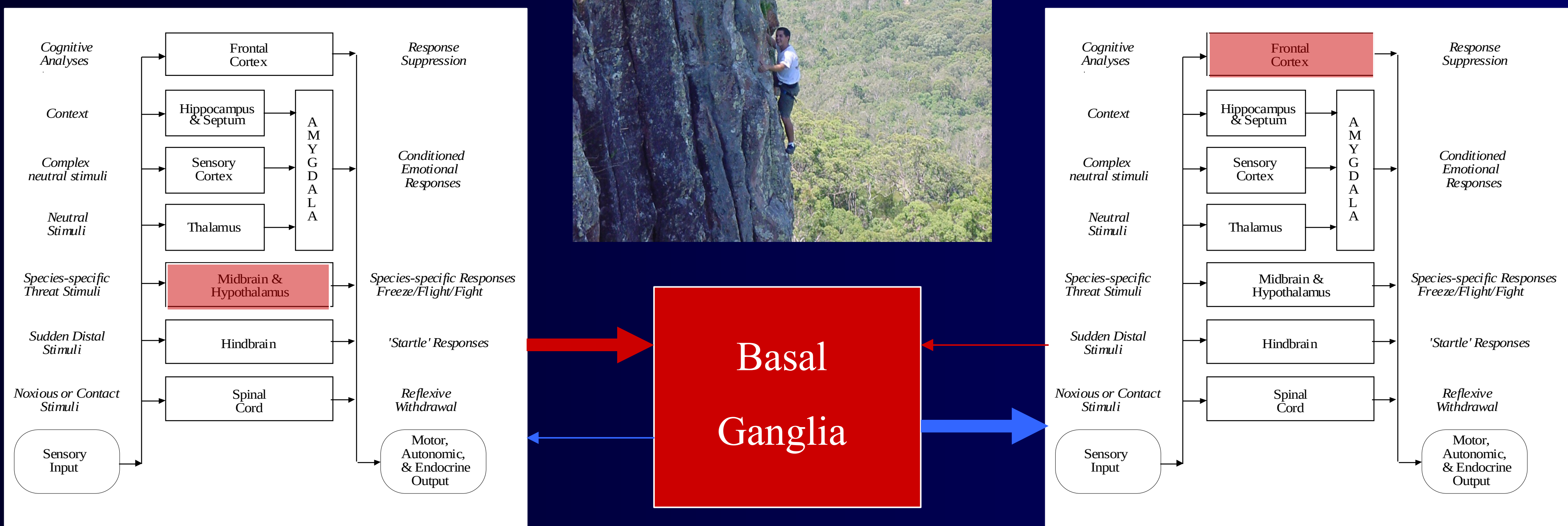
…depends on relative input salience

Cortical/subcortical competition ?



- Subcortical system
  - Slow optic flow in lower visual field
  - Defense reaction

- Cortical system
  - Knowledge of rope strength
  - …go for it !

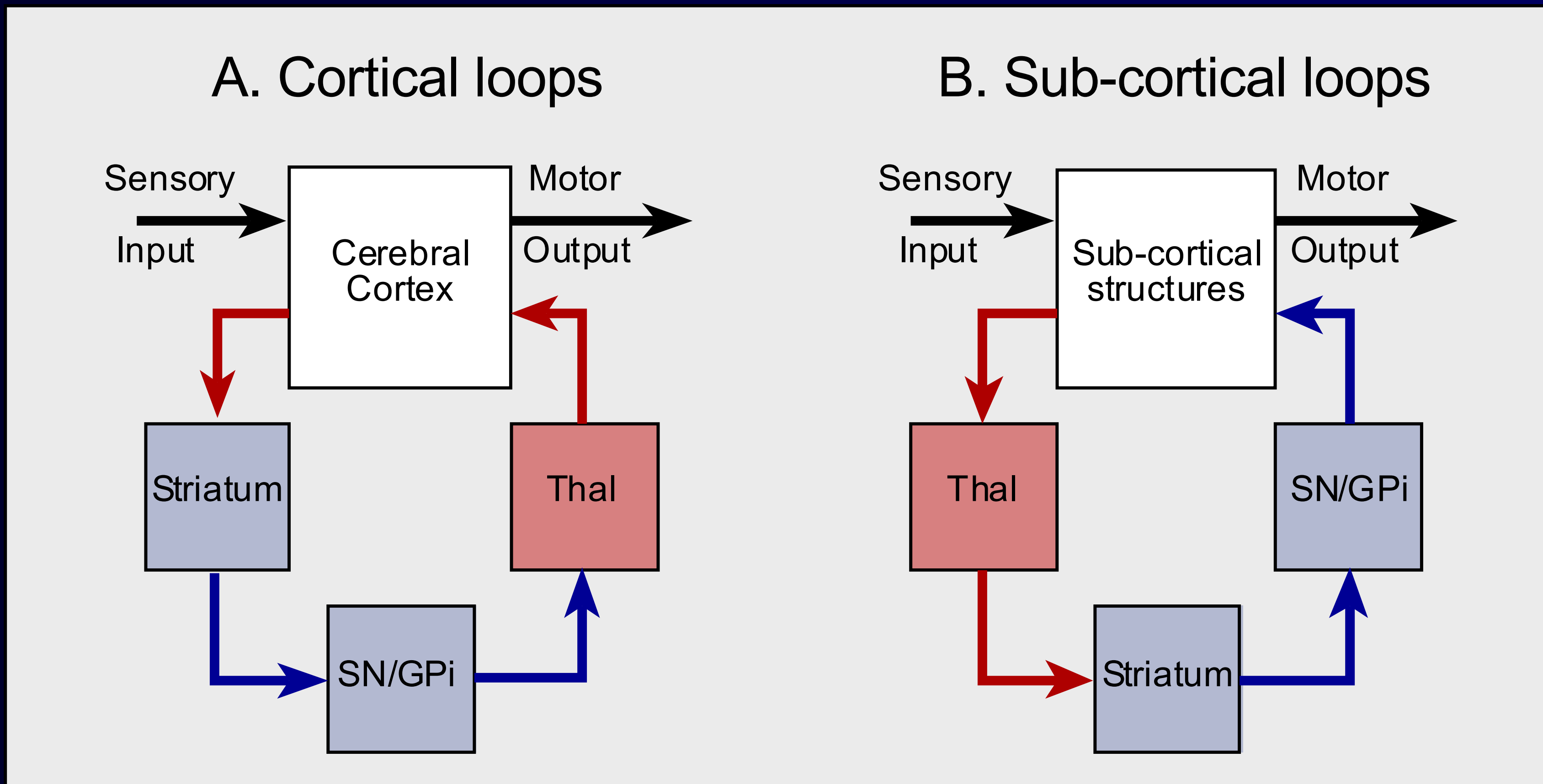


Examples of (cortical) loosers

- Phobias
  - Specific trigger stimuli known to be harmless
  - Elicit uncontrollable fear and defensive reactions
- Anxiety-panic attacks
  - Situations known not to be dangerous
  - Incapacitating anxiety in absence of specific triggers
- Post-traumatic stress disorders
  - Current circumstances unrelated to traumatic event
  - Irrelevant stimuli evoked flash-backs which elicit uncontrollable fear and defensive reactions
- Addictions
  - Knowledge of detrimental effects of drug dependence explicit
  - Often powerless in the face of drug/food/sex related sensory stimuli
- Head versus heart
  - Situations where we should know better

Cortical and subcortical loops

An architecture for understanding such conflicts



McHaffie JG, Stanford TR, Stein BE, Coizet V, Redgrave P. 2005. Subcortical loops through the basal ganglia. Trends Neurosci 28(8):401-407.

Adaptive selection

For action selection to adapt with experience, must be responsive to reinforcement consequences of action-outcome contingencies

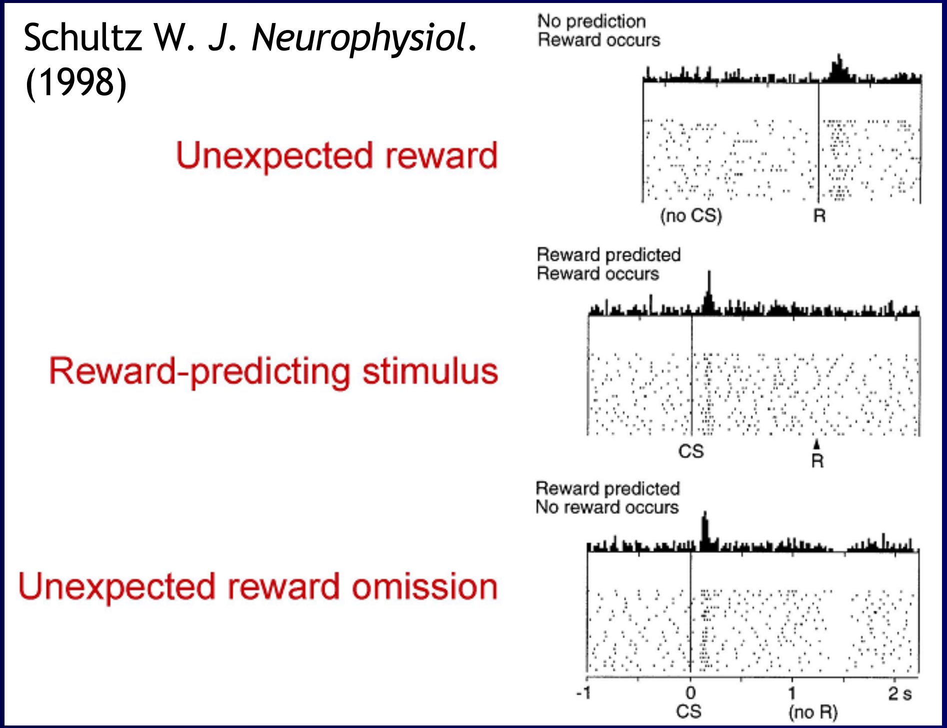
- Selective adjustment of afferent signals by reinforcement outcome
- and/or adjustment of input weights of reinforced channels
- The role of dopamine in reinforcement learning

Ascending dopaminergic systems in rat brain

Picture by Wes Chang
(Gallo center San Francisco)

Dopaminergic neurones sensitive to reward

- Phasic short-latency sensory response
  - Short latency (70-100ms)
  - Short duration (~ 100ms) burst of impulses



- Schultz (1998) – signals reward prediction error
  - Shares many characteristics of ‘r’ in Temporal Difference algorithms
  - Used to adjust response probabilities in associative learning

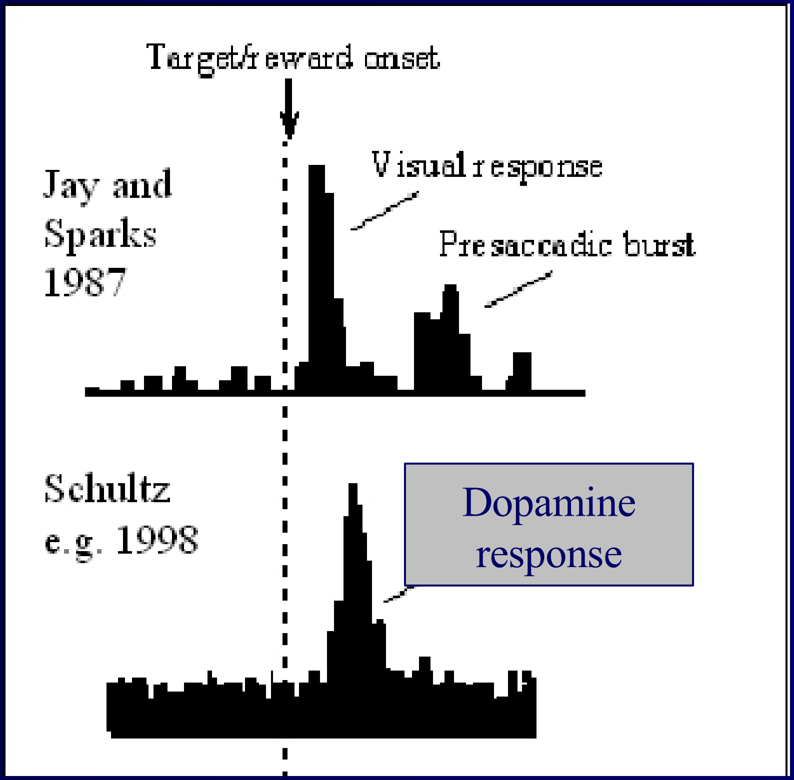
Phasic dopamine unlikely to signal reward prediction error

- Elicited by unpredicted biologically salient stimuli
  - Salient by virtue of:
    - novelty (independent of reward value)
    - association with reward
    - intensity
    - physical resemblance to reward related stimuli
- Response homogeneity
  - 100ms latency 100ms duration response constant across:
    - species
    - experimental paradigms
    - sensory modality
    - perceptual complexity of eliciting events
- Response latency (~100ms)
  - Precedes gaze shift that brings event onto fovea…

The latency constraint

Unexpected visual stimuli elicit sensory and motor responses in superior colliculus:

- sensory response (~40 ms)
- motor response (<150 ms)



Phasic DA responses occur before foveating eye-movements

70-100ms after stimulus onset

- **Conclusion:** anomaly of having brain's main reinforcement learning systems relying on reward identification done by pre-attentive, pre-saccadic stimulus processing

Redgrave P, Prescott TJ and Gurney K (1999). TINS 22(4): 146-151

So how was it for you ?

"We also noticed that DA neurons typically responded to a visual or auditory stimulus when it was presented unexpectedly, but stopped responding if the stimulus was repeated; a subtle sound outside the monkey's view was particularly effective."

Takikawa Y, Kawagoe R, Hikosaka O. 2004. A possible role of midbrain dopamine neurons in short- and long-term adaptation of saccades to position-reward mapping. J Neurophysiol 92(4):2520-2529.

If phasic dopamine isn’t signaling reward prediction error….
what is it signaling ?

Essential characteristics of the phasic dopamine signal

- A striking resemblance to the Temporal Difference reinforcement error term

  ….suggests it is critically associated with reinforcement learning

- It is precisely timed

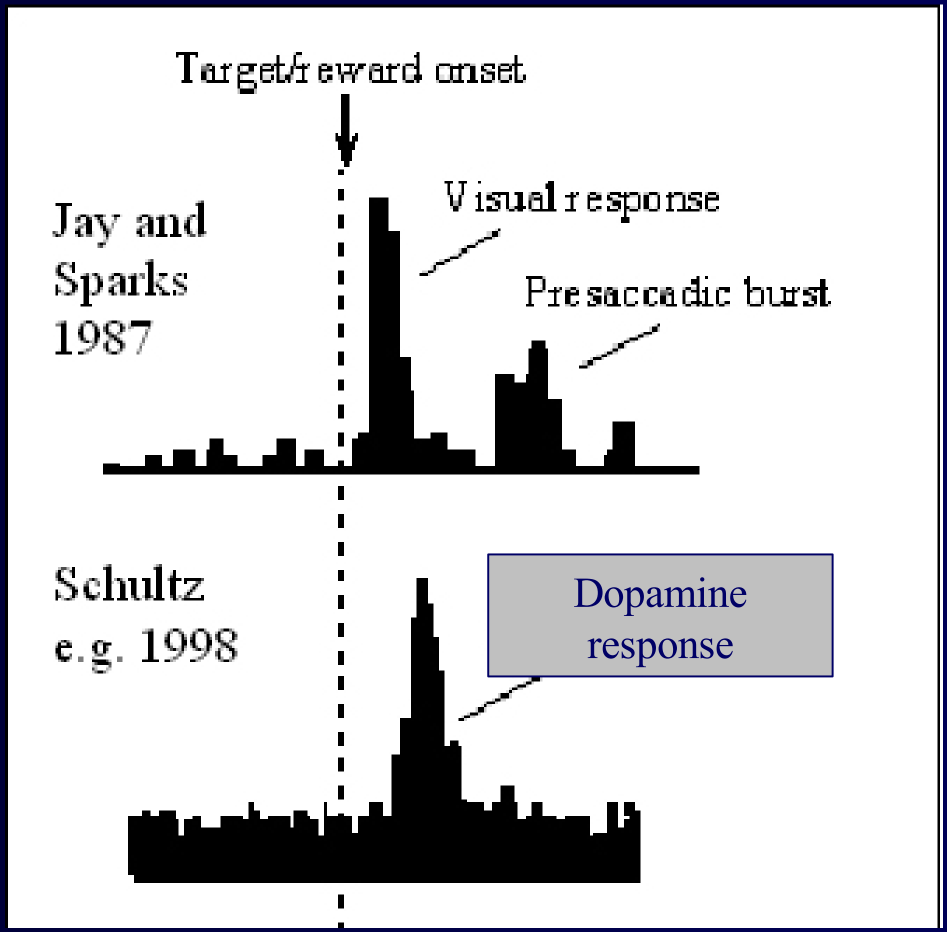
  …..involved in a process where the timing of the reinforcement signal is critical

But more information needed

Prior Questions

- What is the source of the short latency sensory (visual) input to dopamine neurones ?
- What signals does the timed dopamine response interact with in target regions of the basal ganglia ?

Response latencies suggest the superior colliculus



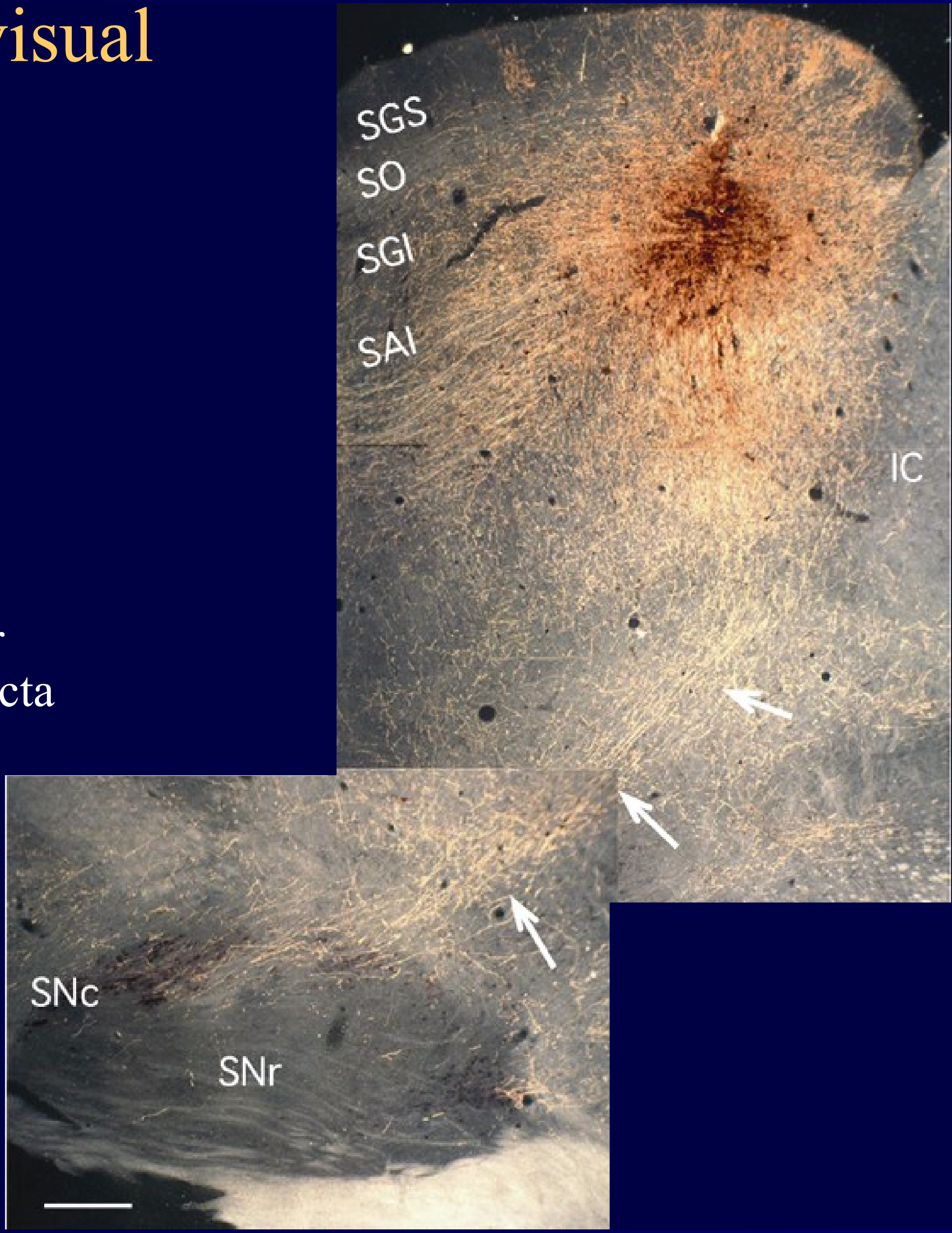
Redgrave P, Prescott TJ and Gurney K (1999). TINS 22(4): 146-151

Colliculus as the source of visual input: I

Anatomical Evidence

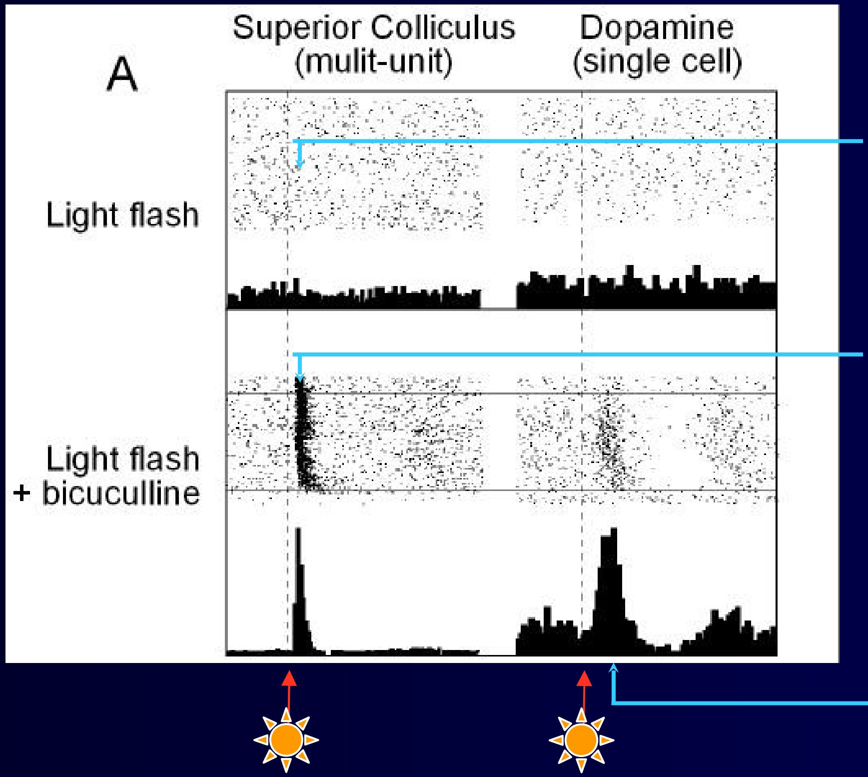
- The Tectonigral projection
- Direct pathway discovered from superior colliculus to substantia nigra pars compacta

Comoli, et al. (2003). Nature Neurosci **6**: 974-980.



Colliculus as <u>the</u> source of visual input: II

Electrophysiological Evidence



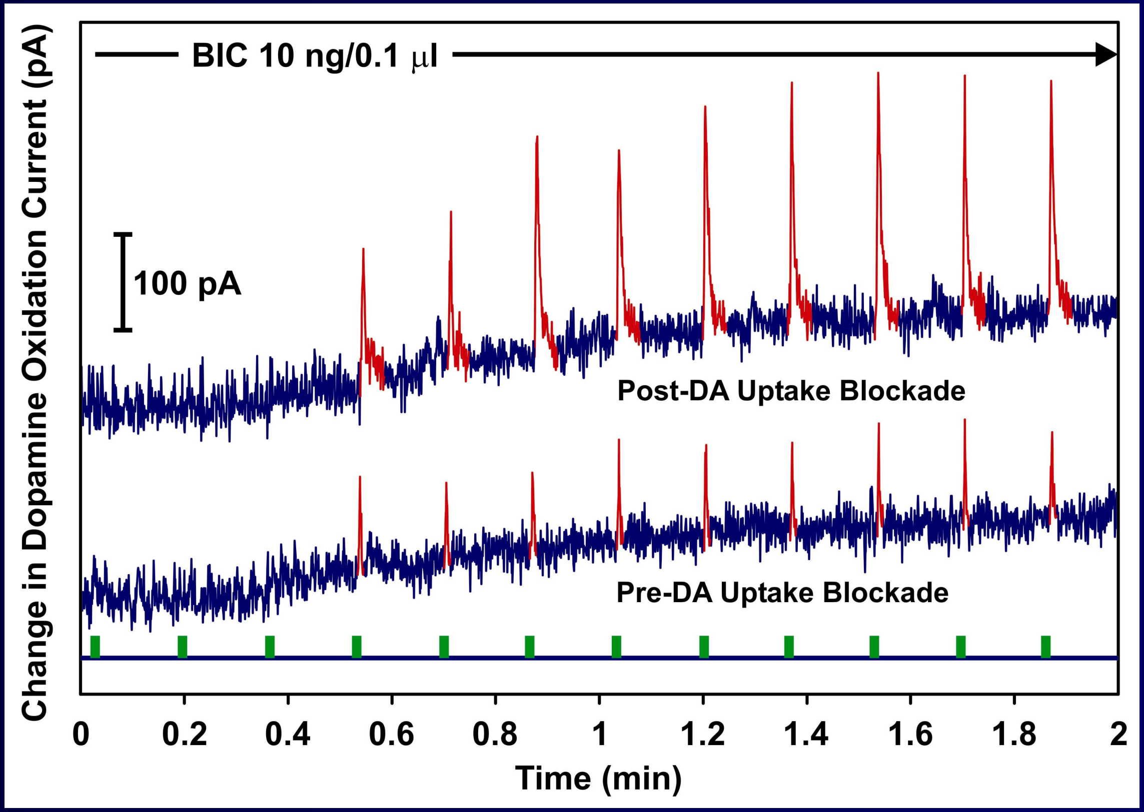
- Pre-drug baseline
  - No flash-evoked response in deep SC or DA cells
- After BIC into deep SC
  - local neurones responsive to light
- When SC cells ‘see’ so do DA cells
  - Excitatory responses: 17/30 (56.6%)

Dommett E, Coizet V, Blaha CD, Martindale J, Lefebvre V, Walton N, Mayhew JE, Overton PG, Redgrave P. 2005. How visual stimuli activate dopaminergic neurons at short latency. Science 307(5714):1476-1479.

Colliculus as the source of visual input: III

Electrochemical Evidence

- No release to light without collicular bicuculline
- 10-40ng bicuculline in 100-400nl into colliculus elicited light response
- Amplitude and duration of response increased by selective DA re-uptake blocker *Nomifensin*

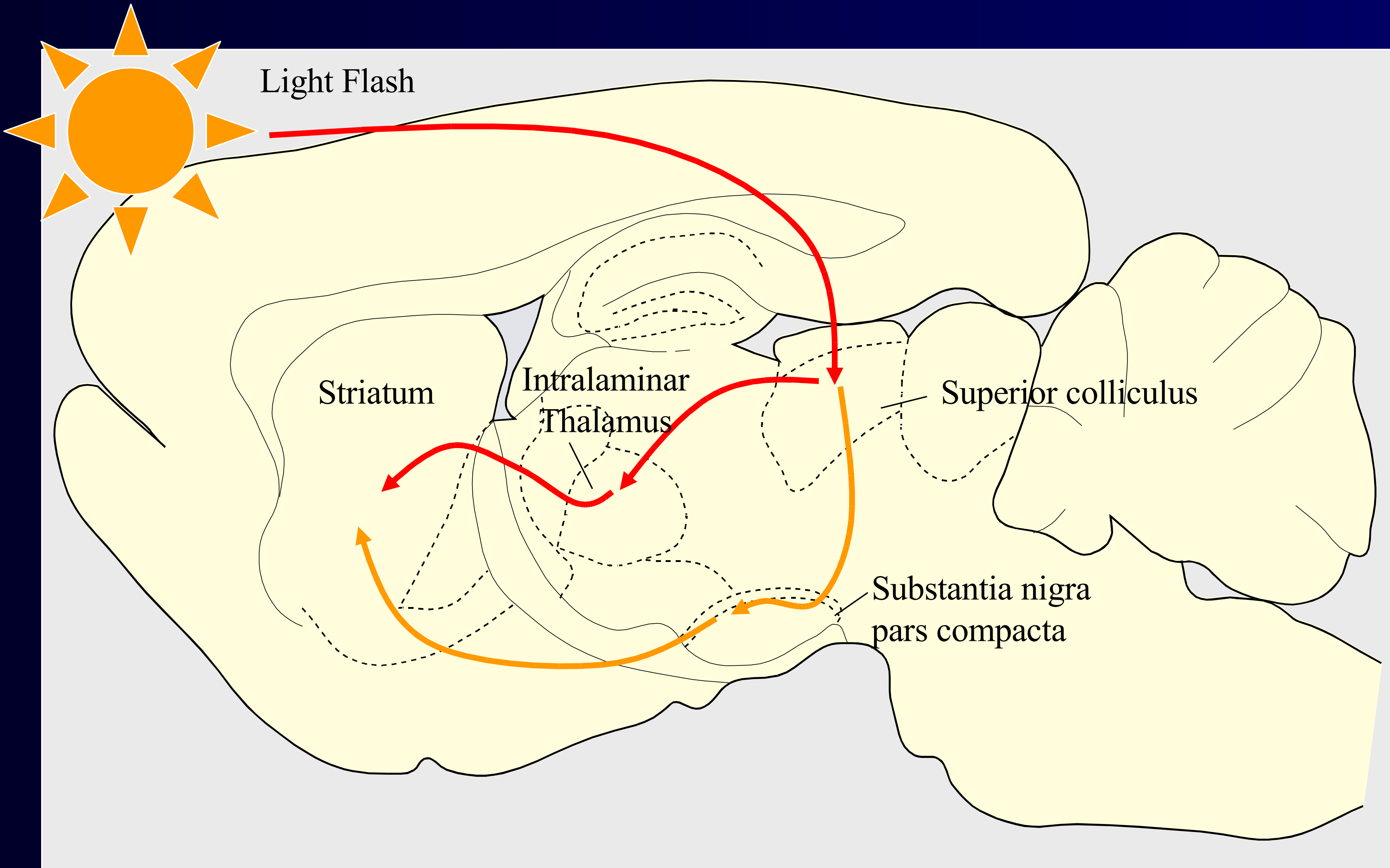


Dommett E, Coizet V, Blaha CD, Martindale J, Lefebvre V, Walton N, Mayhew JE, Overton PG, Redgrave P. 2005. How visual stimuli activate dopaminergic neurons at short latency. Science 307(5714):1476-1479.

Question:
What signals are present in the target regions at the time of the phasic dopamine input ?

- 1st Signal – a separate representation of the sensory event that fired off the dopamine signal

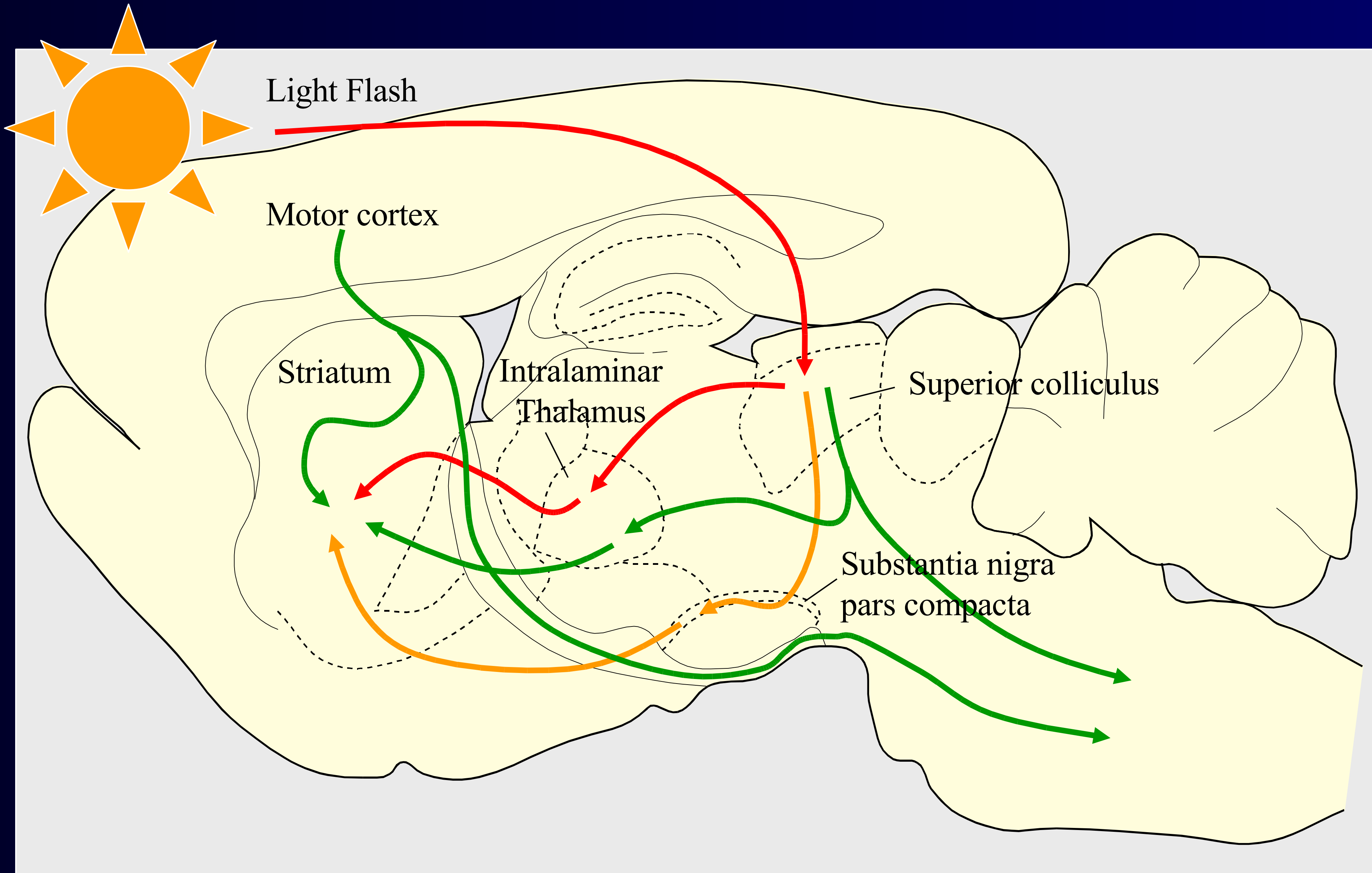
Sensory inputs to the striatum



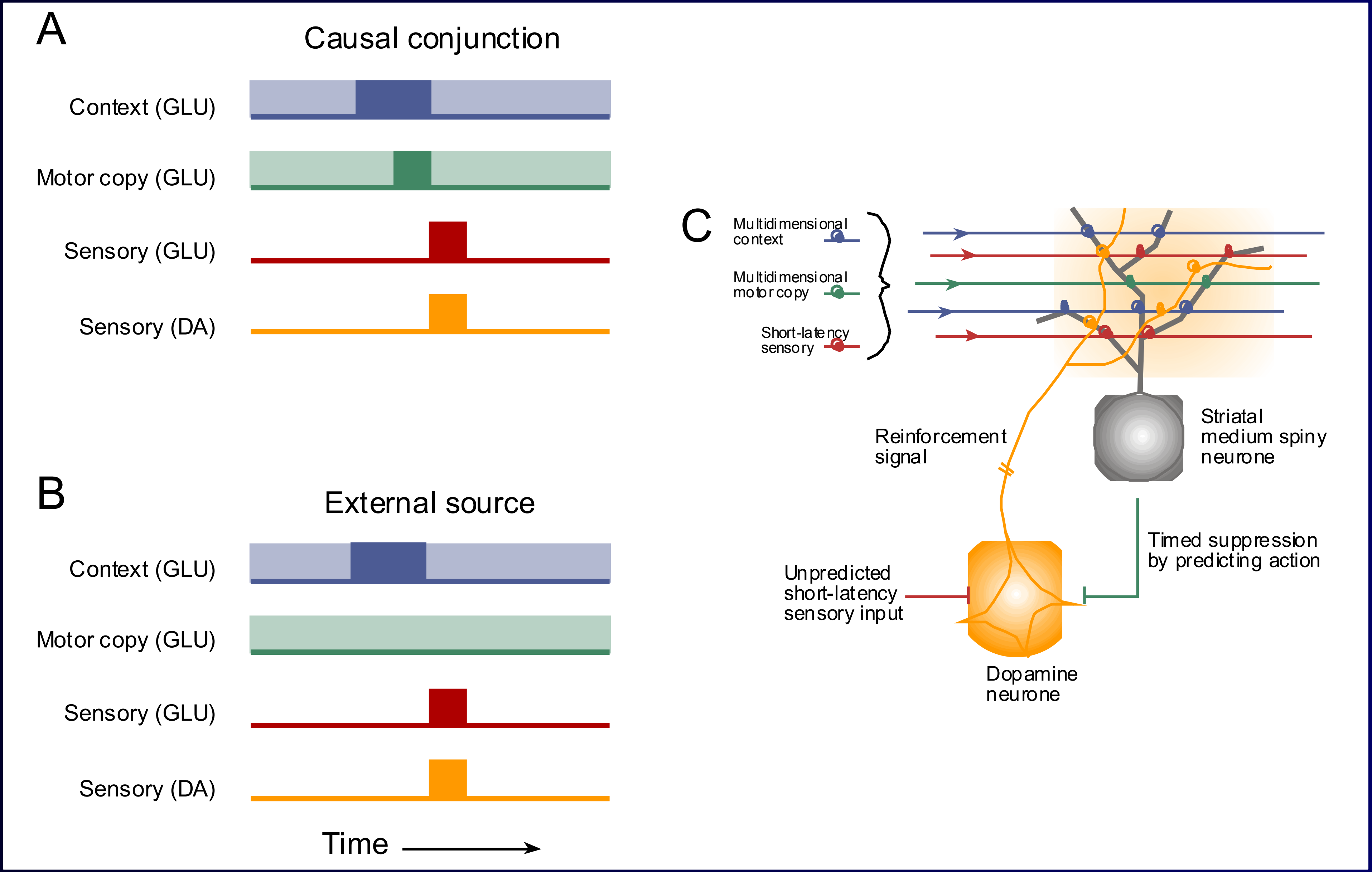
McHaffie et al *TINS* , Aug. 2005, Sub-cortical loops through the basal ganglia

- 2nd Signal – a running efference copy or corollary discharge of ongoing motor commands

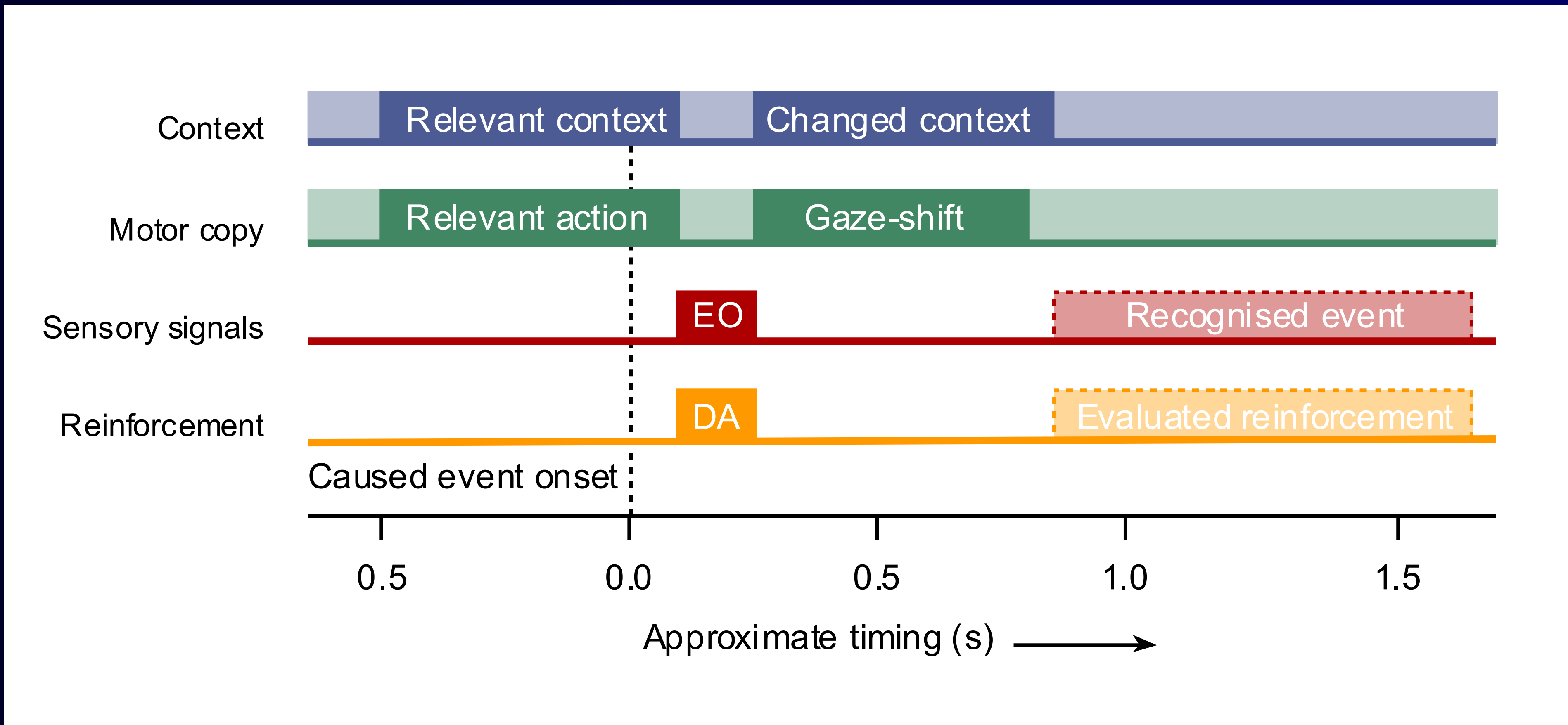
Motor inputs to the striatum: Efference copy



Causal Contingencies



Why a short latency reinforcement signal is essential



What-action-caused-the-event learning

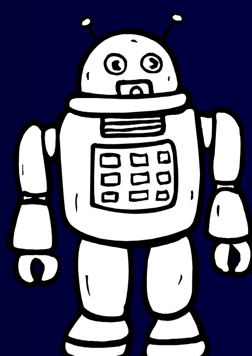
Conclusions

- Multifunctional systems must have effective solution(s) to the selection problem
- The basal ganglia appear to provide a biological solution deemed adequate for > 400M years
- Distribution of competitors across different levels of the neuraxis can lead to competition between systems of different evolutionary status
- Analysis of basal ganglia functional architecture suggests intrinsic reinforcement properties could operate to determine agency

The Team

- Biology
  - Veronique Coizet
  - Eliane Comoli
  - Ellie Dommett
  - Paul Overton

- Computation
  - Kev Gurney
  - Mark Humphries



- Robotics
  - Tony Prescott
  - Jon Chambers