Dynamic Causal Modeling for EEG

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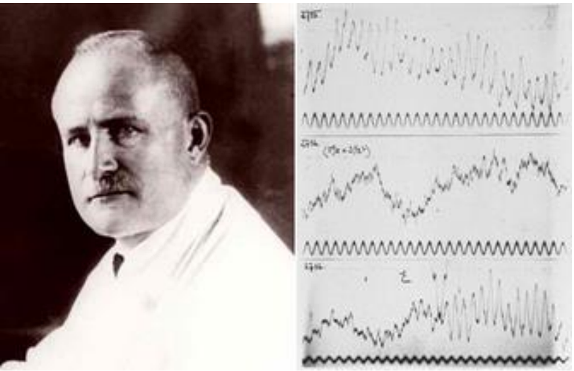
Computational Psychiatry Course 2019

Chapter 1

Story Time

1924

2006



Invention of the EEG
(Hans Berger 1873-1941 [1])

- Non-invasive measure of brain activity
- Electrical signals due to the flow of charged Ions

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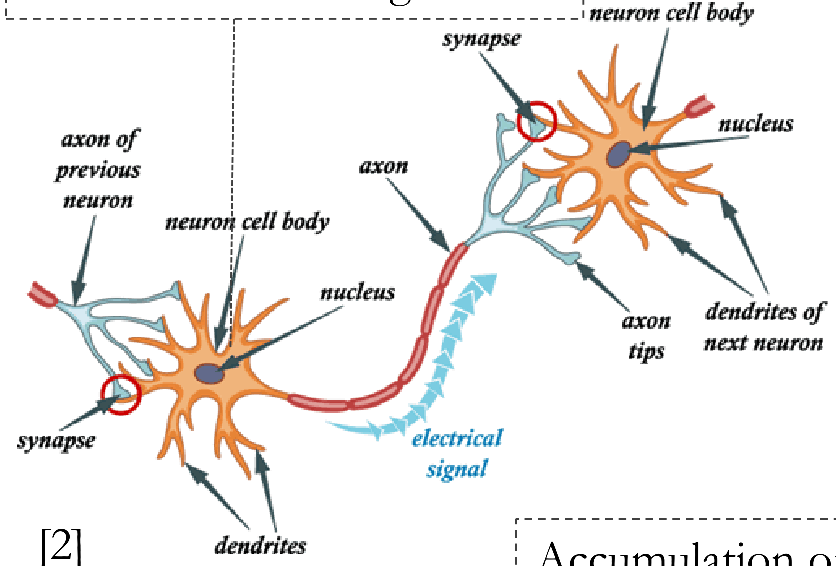
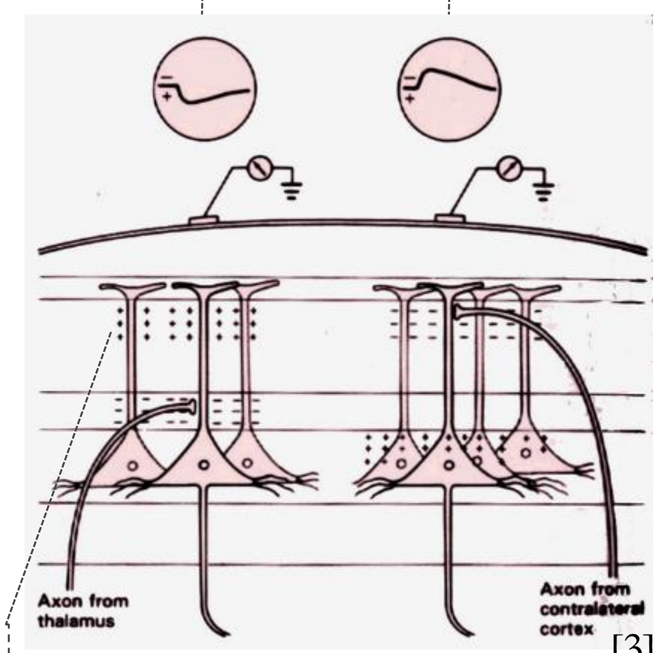
Depolarization of cell membrane due to change in distribution of charged Ions.



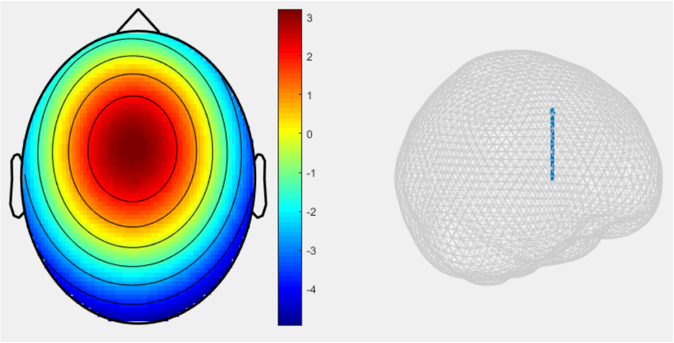
[2]

Dipole fields manifest as differences of electrical potentials on the scalp.



[3]

Accumulation of charge leads to dipole field.



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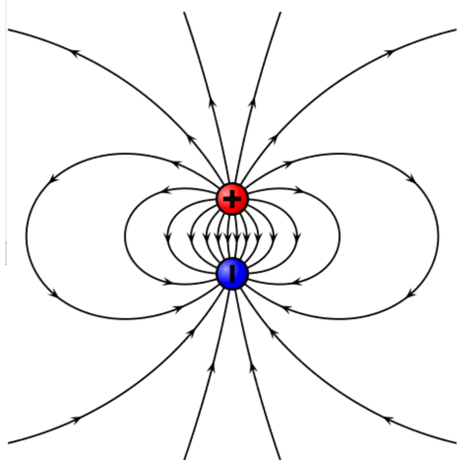

Figure | Electric dipole field [4]

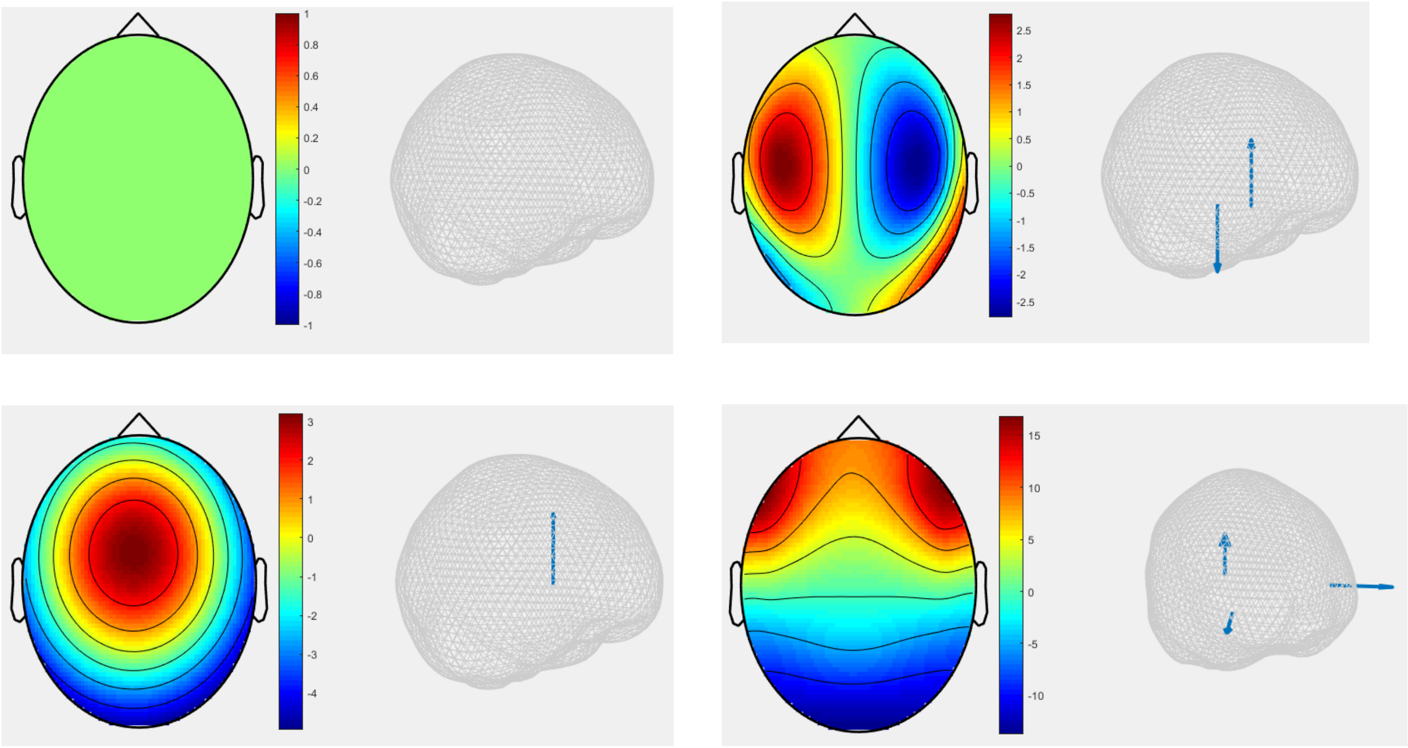

Figure | Different possible dipole configurations that lead to different scalp potentials.

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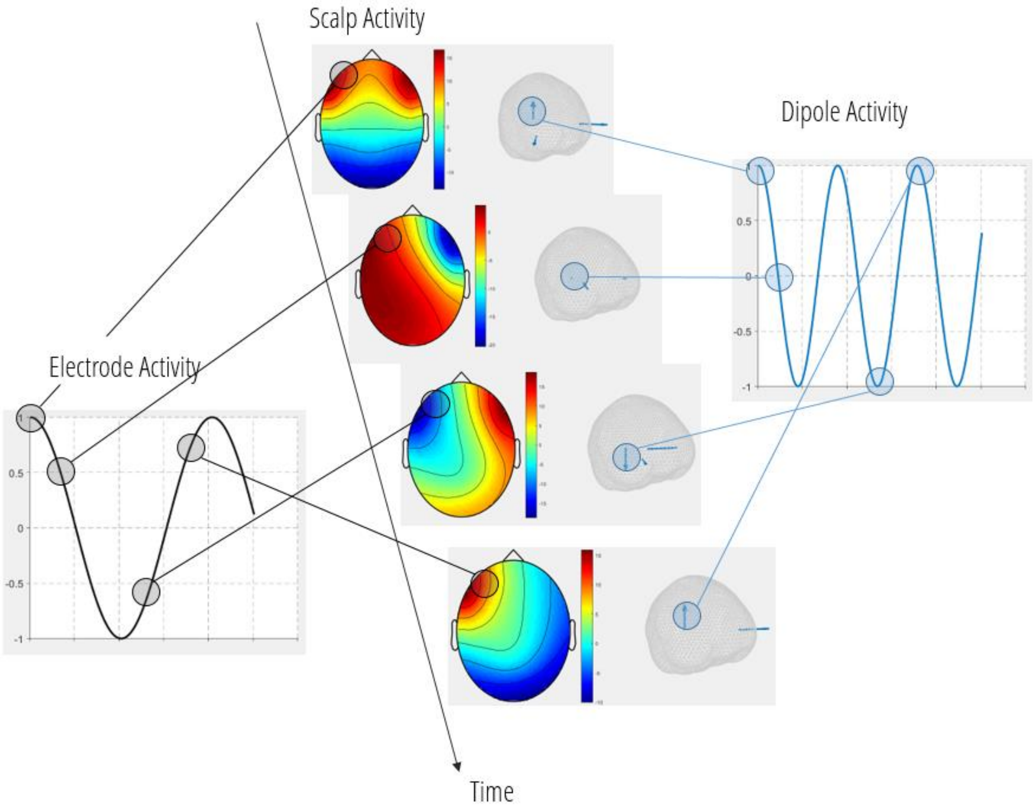

Figure | Changes in the scalp and electrode potential, as the dipole moments change over time.

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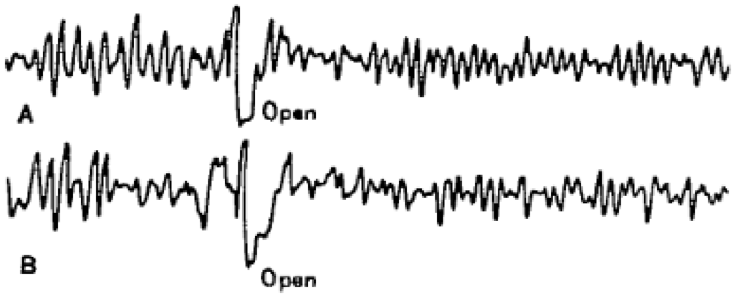

Discovery of Evoked Response Potentials (ERP) across multiple modalities

- Somatosensory (SEP)
- Visual
- Auditory

[5]

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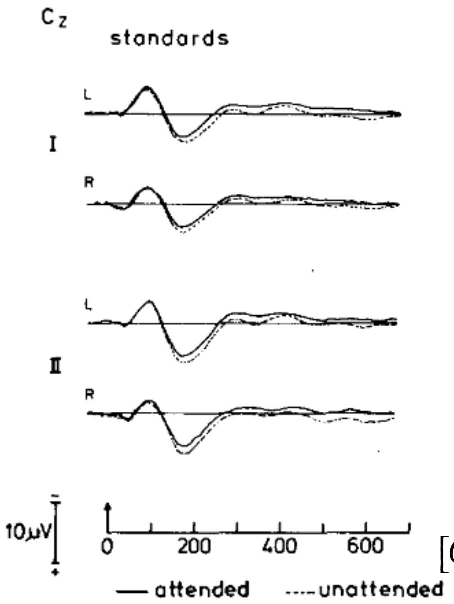

[6]

Change in the average evoked response to attended and unattended stimuli (Mismatch Negativity, MMN)

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Role of cortical *N*-methyl-D-aspartate receptors in auditory sensory memory and mismatch negativity generation: Implications for schizophrenia

line/monkey/intracortical/cognitive/event-related potential)

VITT*†, MITCHELL STEINSCHNEIDER†‡, CHARLES E. SCHROEDER†‡, AND JOSEPH C. AREZZO†‡

Visual Evoked Response in Diagnosis of Multiple Sclerosis

A. M. HALLIDAY, W. I. McDONALD, JOAN MUSHIN

Errors in reward prediction are reflected in the elated brain potential

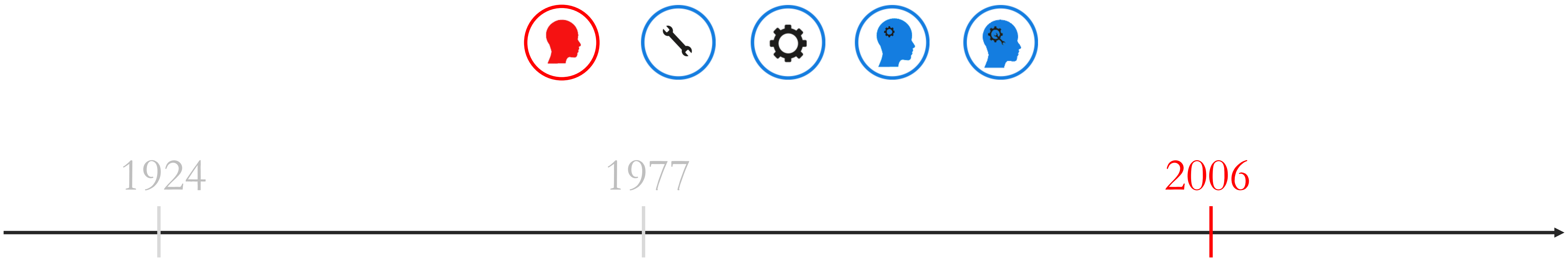
er Nieuwenhuis, Nick Yeung and Jonathan D. Cohen

Acetylcholine modulates averaged sensory evoked responses and perforant path evoked field potentials in the rat dentate gyrus

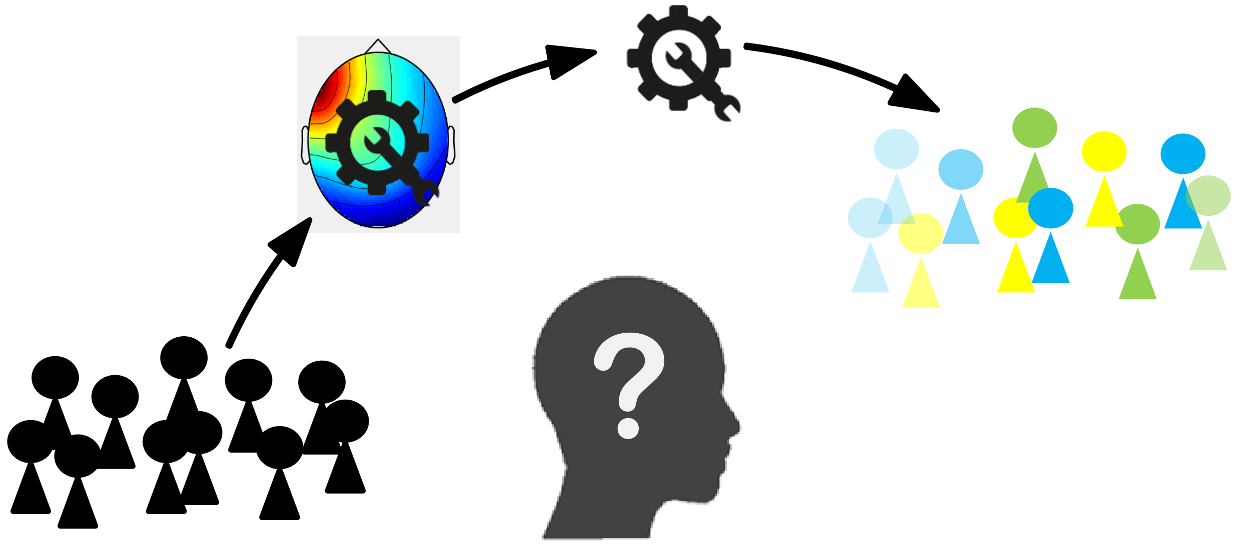
Tom C. Foster [a] and Sam A. Deadwyler [b]

DIFFERENTIAL EFFECTS OF ASCENDING NEURONS CONTAINING DOPAMINE AND NORADRENALINE IN THE CONTROL OF SPONTANEOUS ACTIVITY AND OF EVOKED RESPONSES IN THE RAT PREFRONTAL CORTEX

J. MANTZ, C. MILLA, J. GLOWINSKI and A. M. THIERRY*



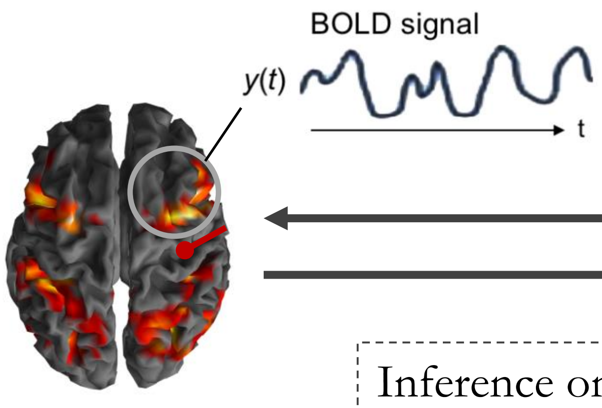
- Heterogenous, clinical population
- EEG contains information about neuromodulatory processes
- Having a model with the power to estimate these hidden processes from peripheral measures could give a mechanistics understanding …
- … And potentially allowing for the identification of clinical subgroups, treatment outcome, disease or relapse risks, etc.



1924 1977 **2003** 2006

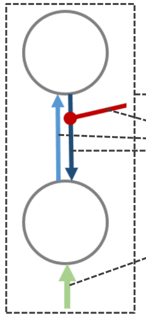
Dynamic causal modelling

K.J. Friston,* L. Harrison, and W. Penny



Prediction of measured data

Inference on parameters and (causal) network structure



- Differences in network structures
- Differences in neuronal parameters
- Changes in connectivity strength through experimental manipulation

$$y = g(x, \Theta_g) + \epsilon$$

Forward Equation describing the transformation of hidden activity to measurable data

$$\frac{dx}{dt} = f(x, u, \theta)$$

Equations describing (hidden) neural activity

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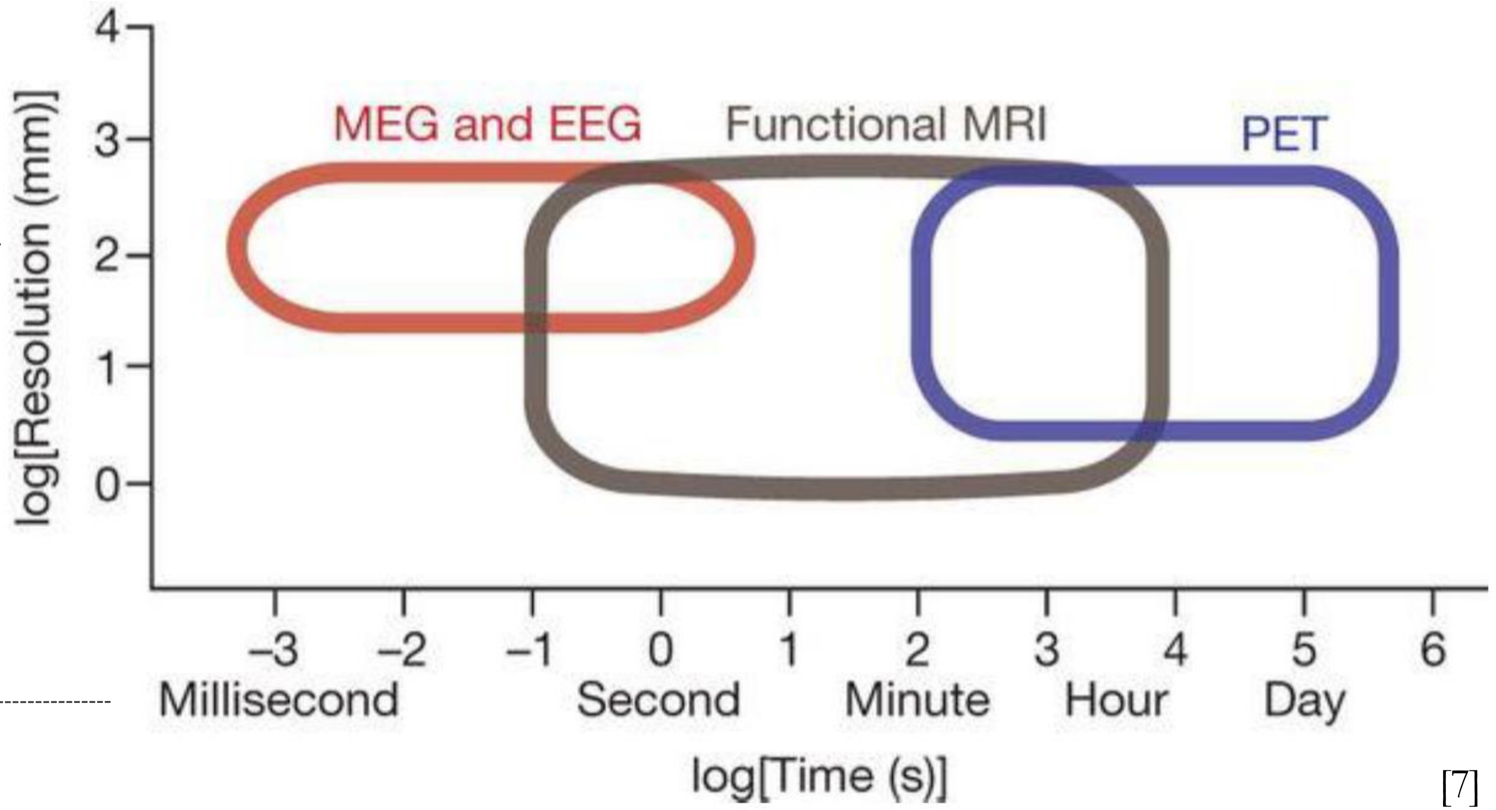
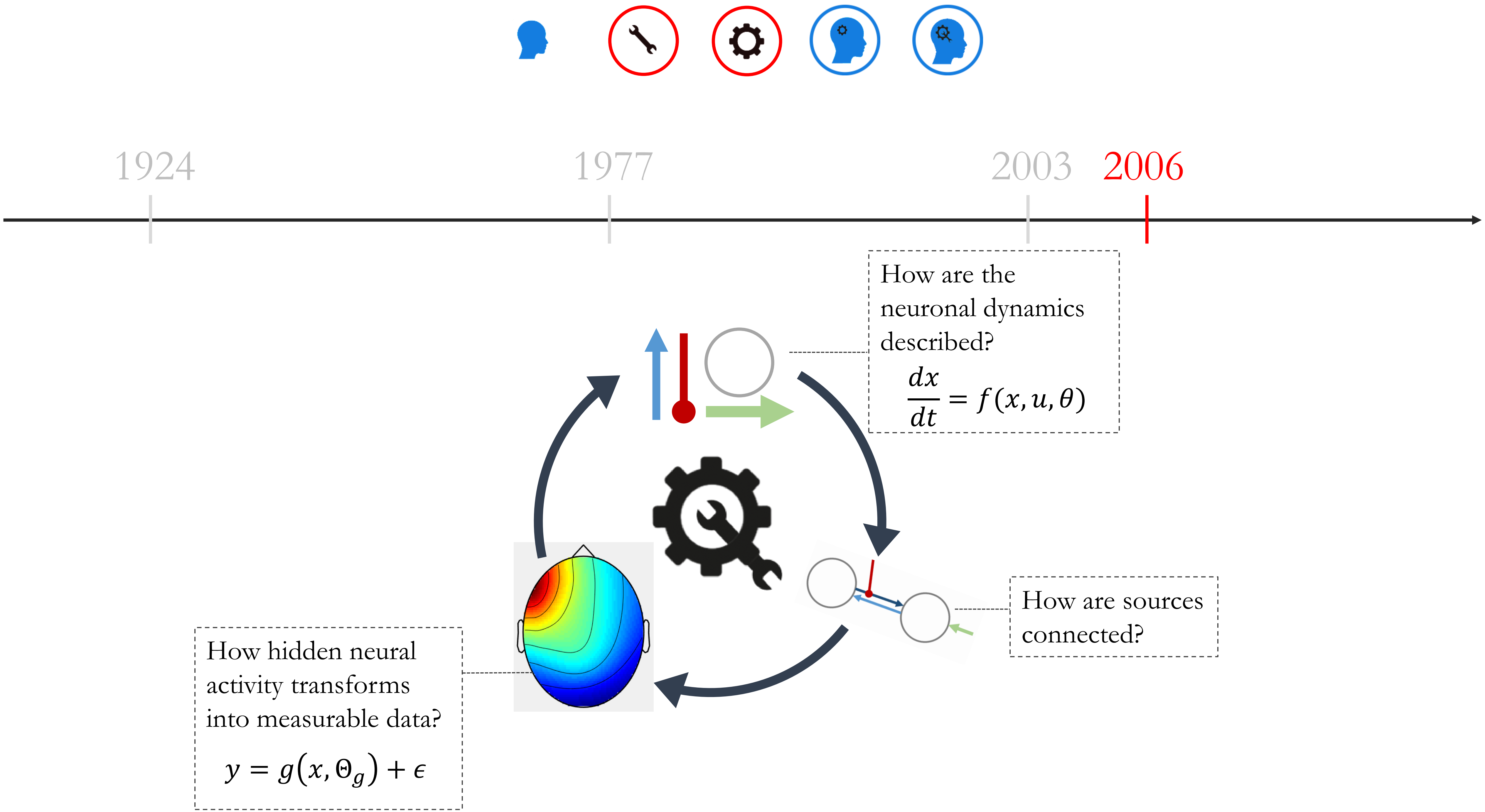
Much worse spatial resolution than fMRI. Need to know, **where** the signal is coming from!

Much better temporal resolution than fMRI. Modeling of synaptic processes possible.



[7]



1924
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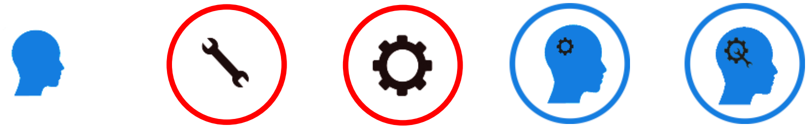
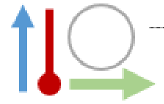
How are the neuronal dynamics described?
$$\frac{dx}{dt} = f(x, u, \theta)$$
How are sources connected?
How hidden neural activity transforms into measurable data?
$$y = g(x, \Theta_g) + \epsilon$$



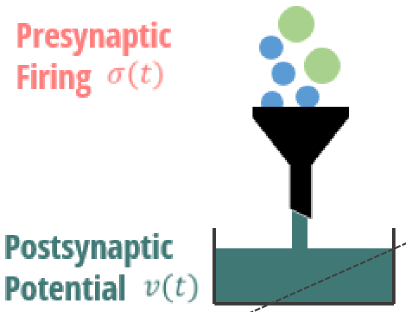


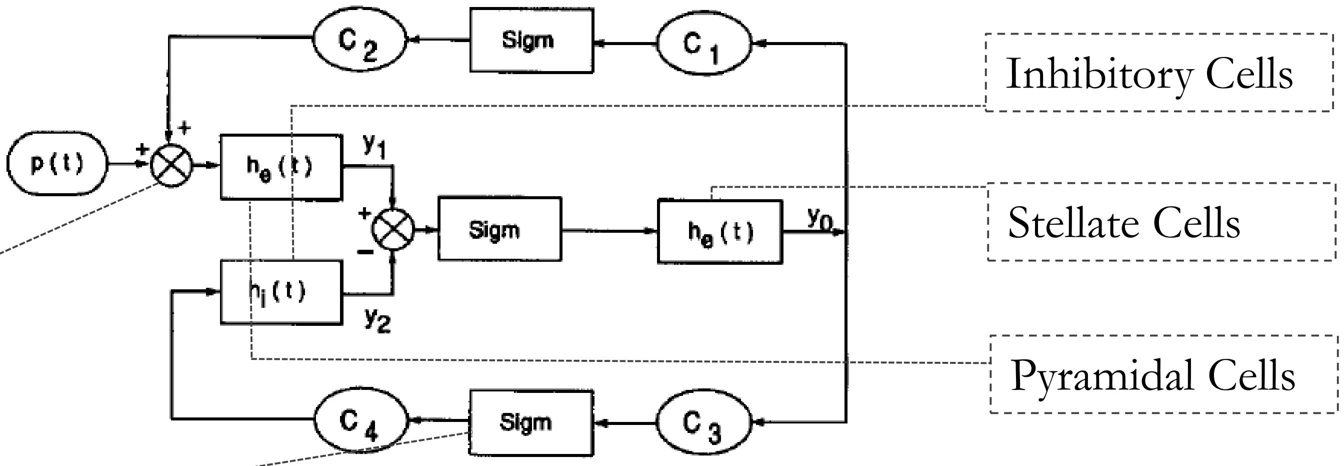
How are the neuronal dynamics described?

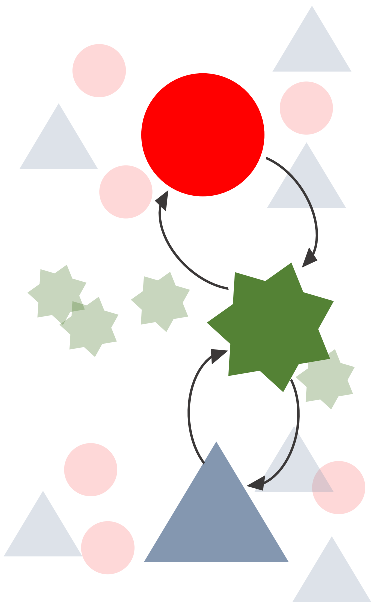
$$\frac{dx}{dt} = f(x, u, \theta)$$

Electroencephalogram and visual evoked potential generation in a mathematical model of coupled cortical columns

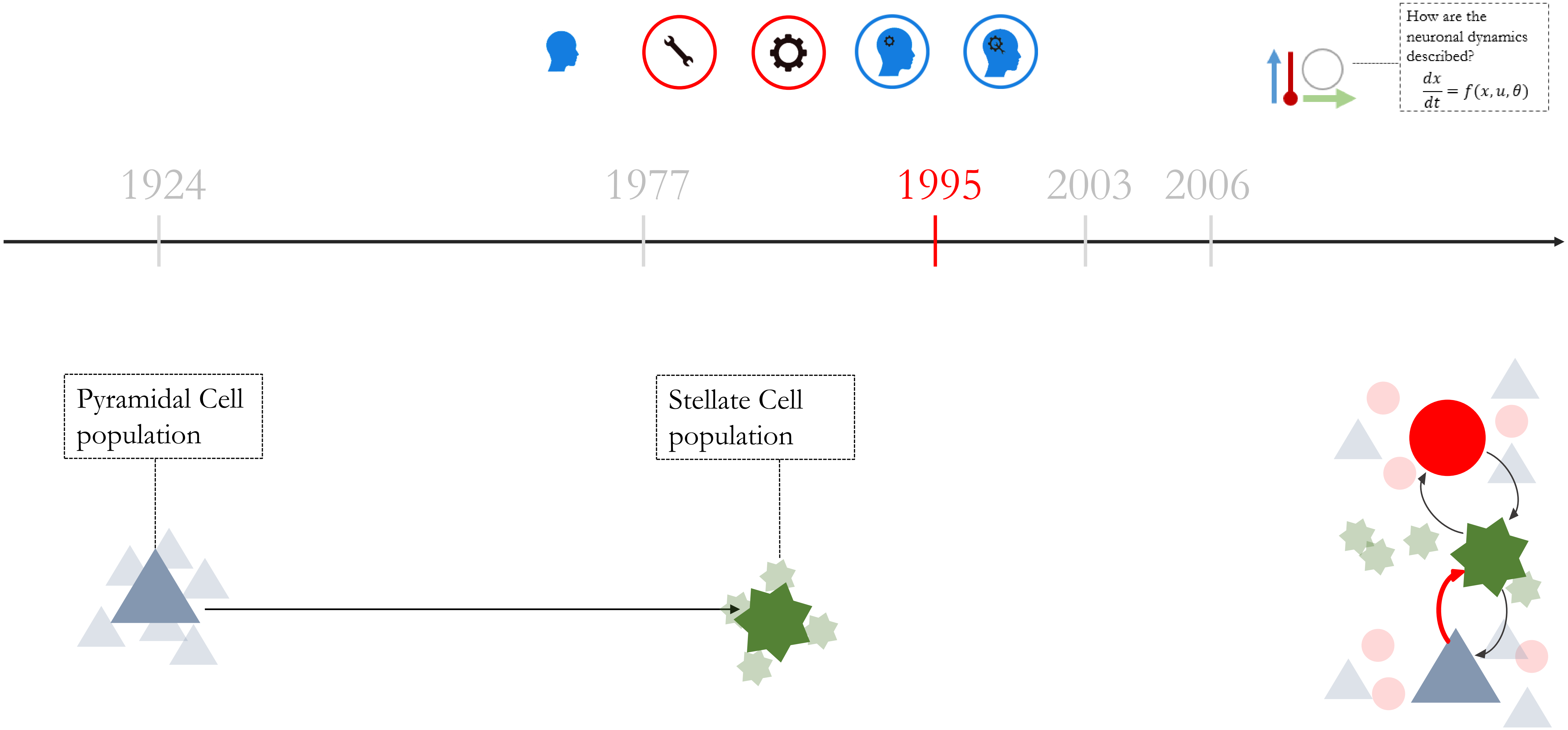
Ben H. Jansen, Vincent G. Rit







$$v(t) = \int_{-\infty}^{t} h(t-\tau, H, \kappa)\sigma(\tau)d\tau$$


How are the neuronal dynamics described?
$\frac{dx}{dt} = f(x, u, \theta)$
1924
1977
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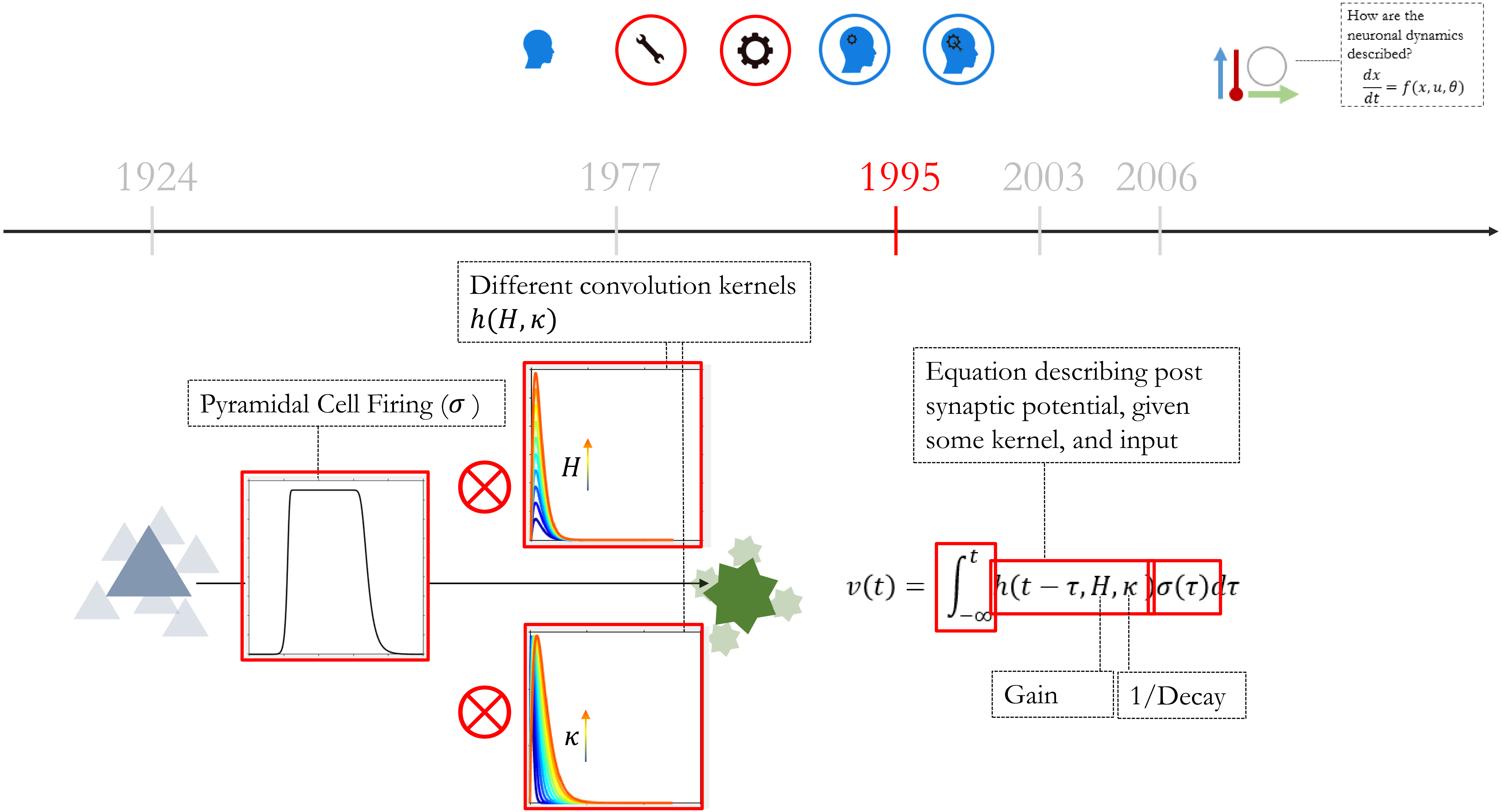
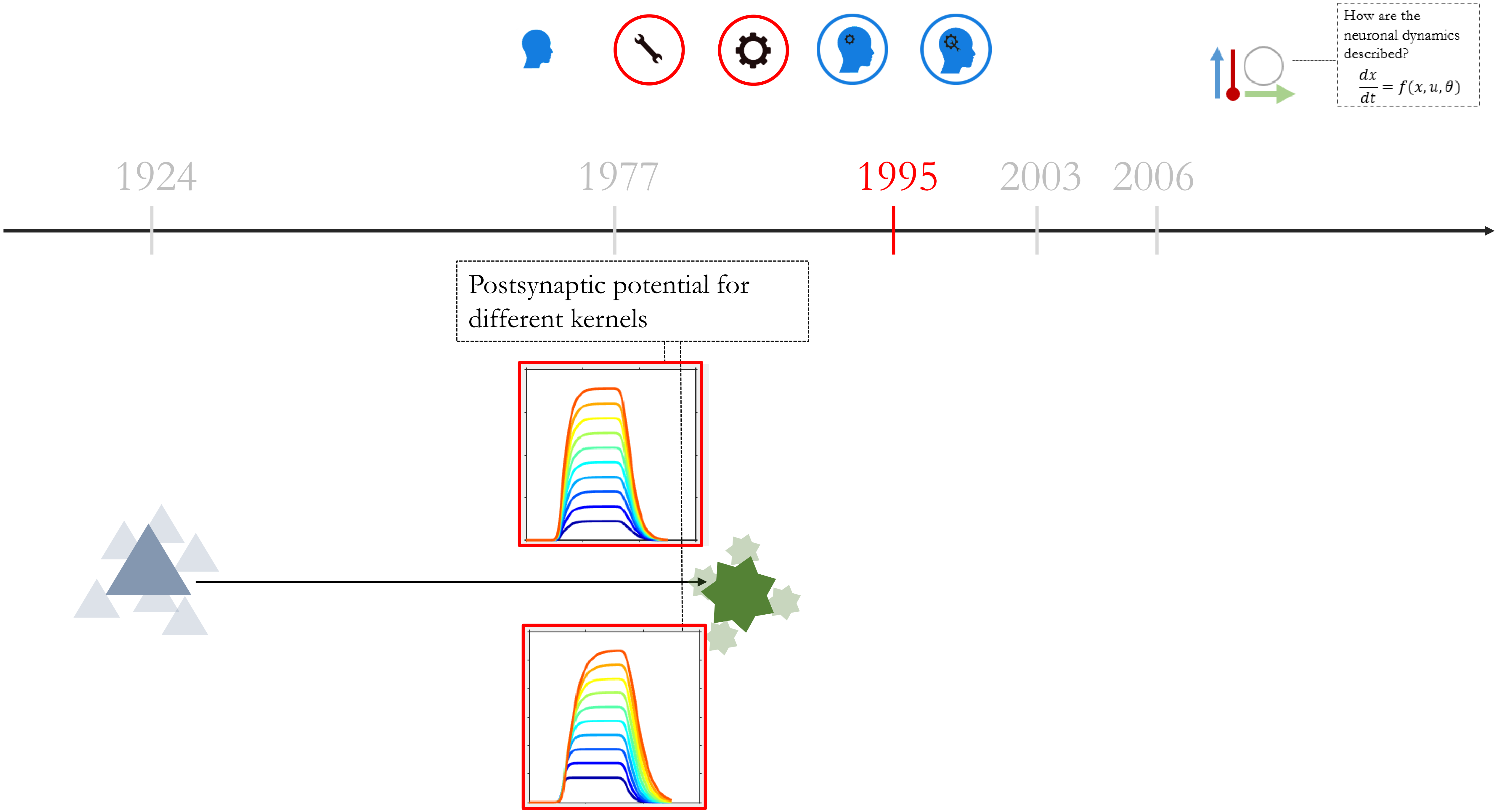
Pyramidal Cell population
Stellate Cell population



How are the neuronal dynamics described?
$\frac{dx}{dt} = f(x,u,\theta)$
1924
1977
1995
2003
2006
Different convolution kernels $h(H,\kappa)$
Pyramidal Cell Firing (σ)
H
κ
Equation describing post synaptic potential, given some kernel, and input
$v(t) = \int_{-\infty}^{t} h(t-\tau, H, \kappa)\sigma(\tau)d\tau$
Gain
1/Decay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1924
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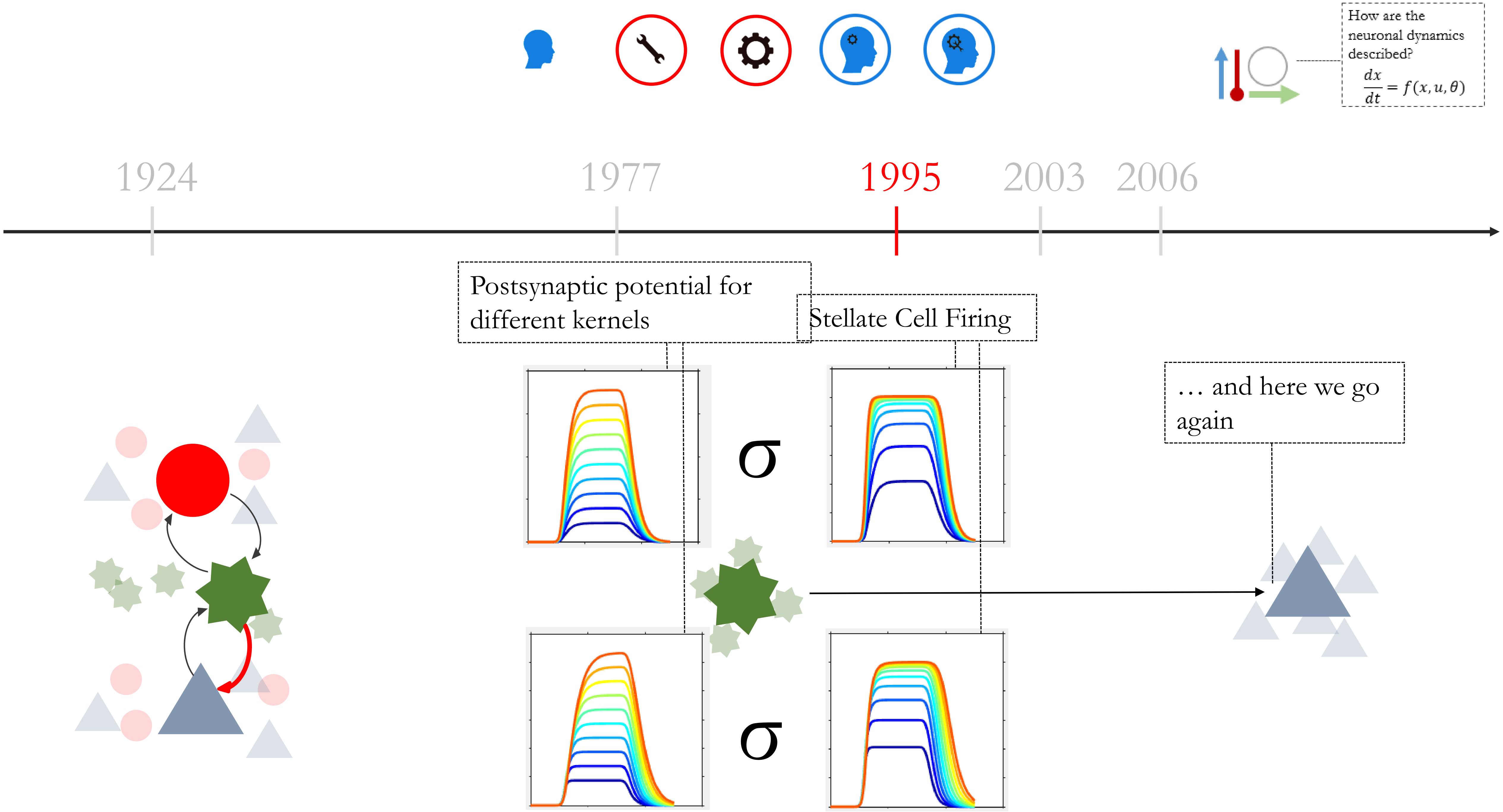
Postsynaptic potential for different kernels

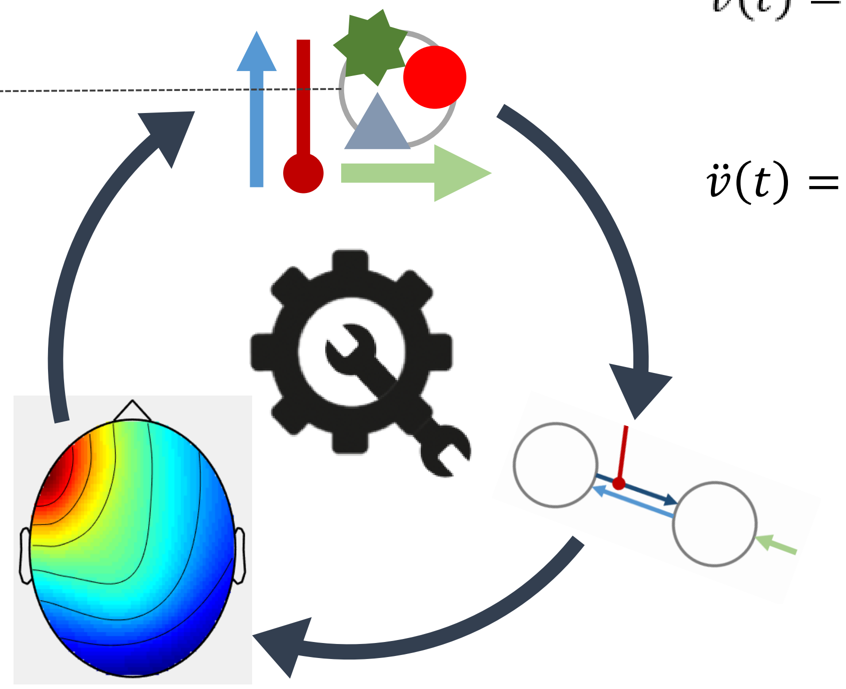


How are the neuronal dynamics described?
$\frac{dx}{dt} = f(x, u, \theta)$
1924
1977
1995
2003
2006
Postsynaptic potential for different kernels
Stellate Cell Firing
σ
σ
… and here we go again

1924 1977 1995 2003 2006

Each source comprises of a triplet of neuronal populations:

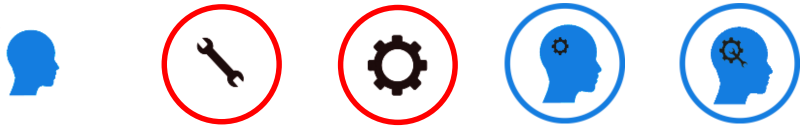
- Stellate Cells
- Inhibitory Interneurons
- Pyramidal Cells



$$v(t) = \int_{-\infty}^{t} h(t-\tau, H, \kappa)\sigma(\tau)d\tau$$

$$\ddot{v}(t) = \frac{H}{\kappa}\cdot\sigma(t) - \frac{2}{\kappa}\cdot\dot{v}(t) - \frac{1}{\kappa^2}v(t)$$

Second derivative of the post synaptic potential of a population is a function of the current state of depolarization, it's first derivative and the input.



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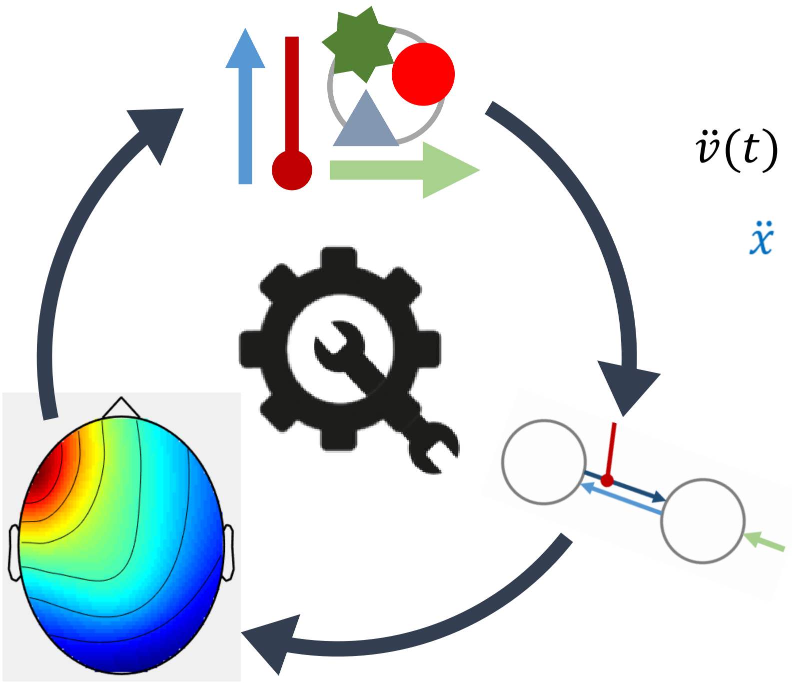
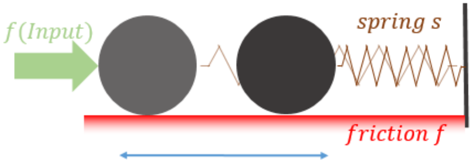
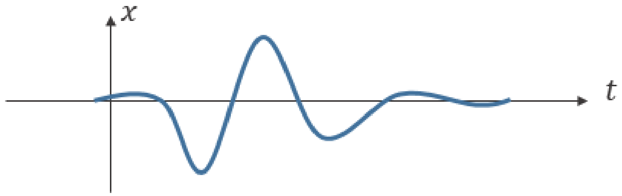


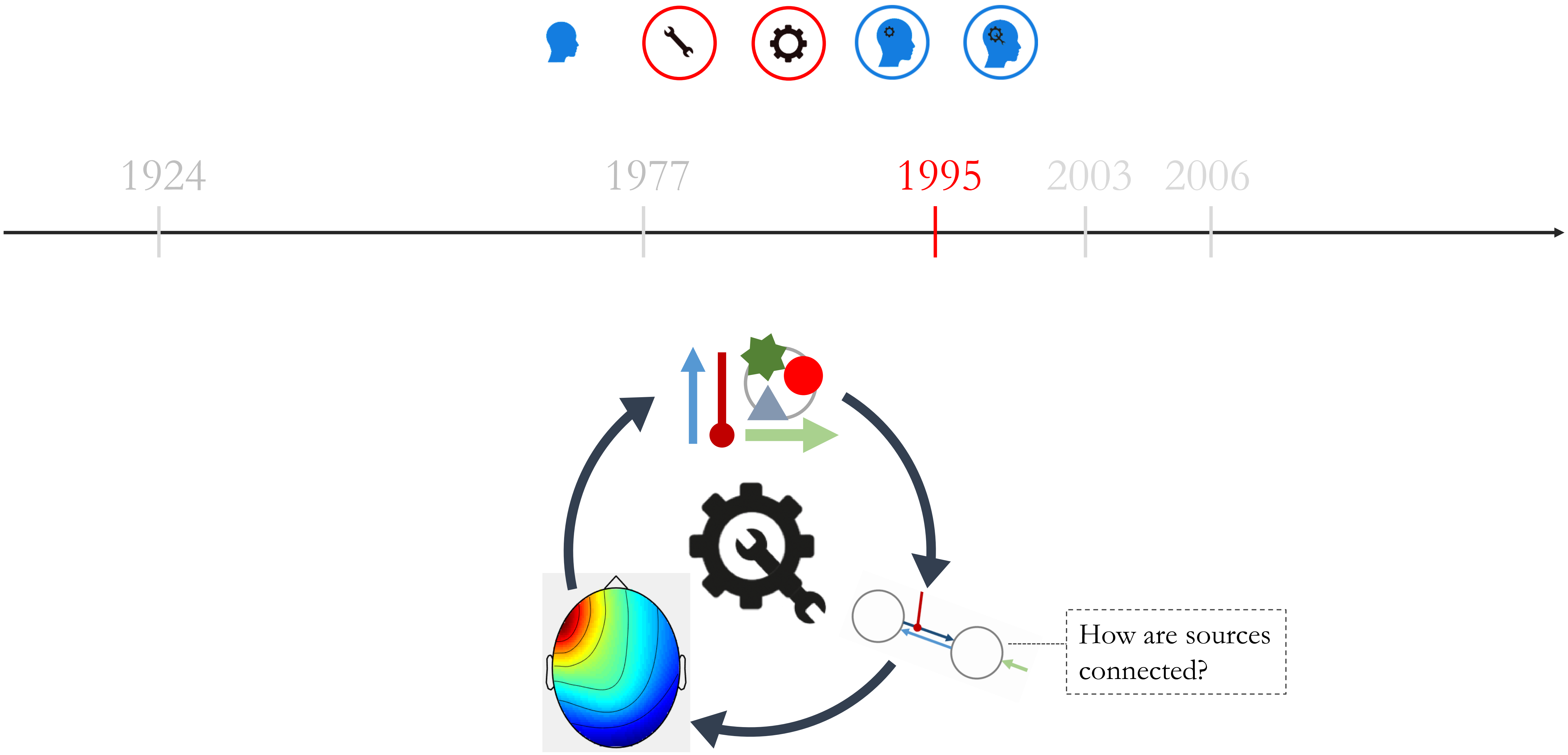
$$\ddot{v}(t) = H \cdot a \cdot \sigma(t) - 2 \cdot a \cdot \dot{v}(t) - a^2 v(t)$$

$$\ddot{x} = f(Input) - f\dot{x} - sx$$

Equation describing the behavior of a mass attached to a spring







1924
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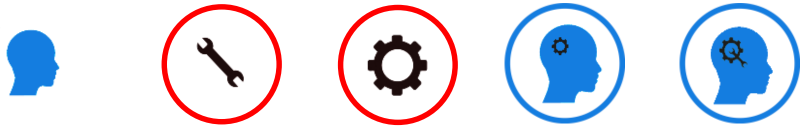
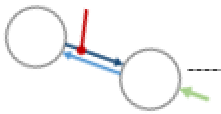
How are sources connected?



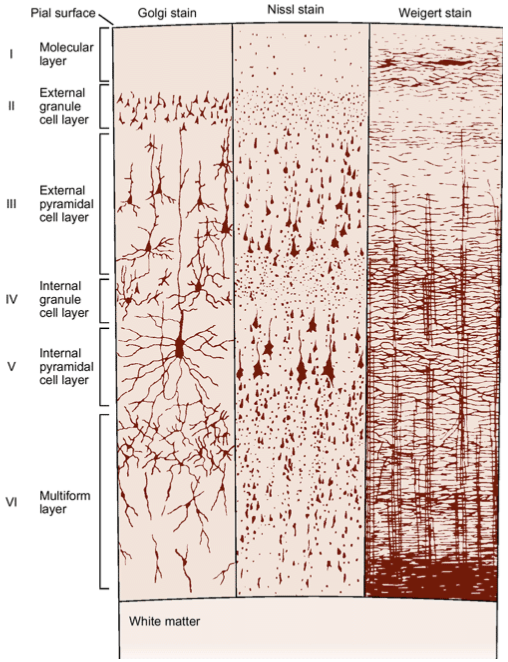


1924 1977 1991 1995 2003 2006

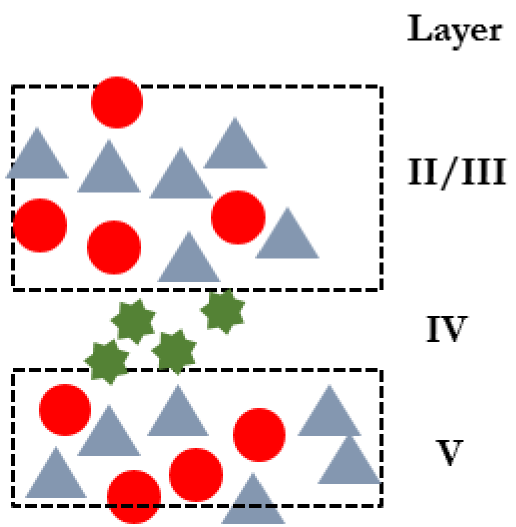
Distributed Hierarchical Processing in the Primate Cerebral Cortex

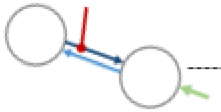
Daniel J. Felleman[1] and David C. Van Essen[2]

[1] Department of Neurobiology and Anatomy, University of Texas Medical School, Houston, Texas 77030, and [2] Division of Biology, California Institute of Technology, Pasadena, California 91125



[8]





How are sources connected?

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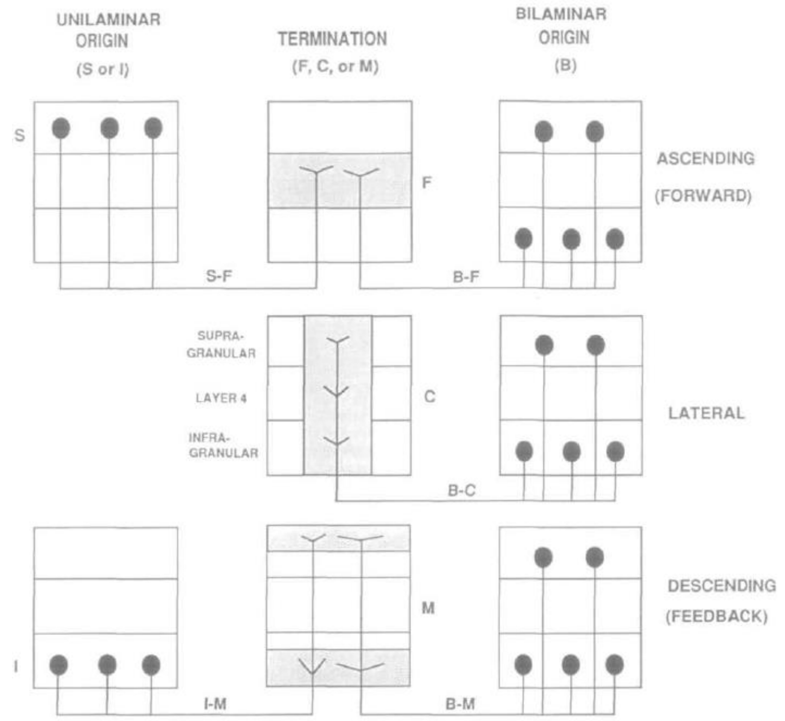

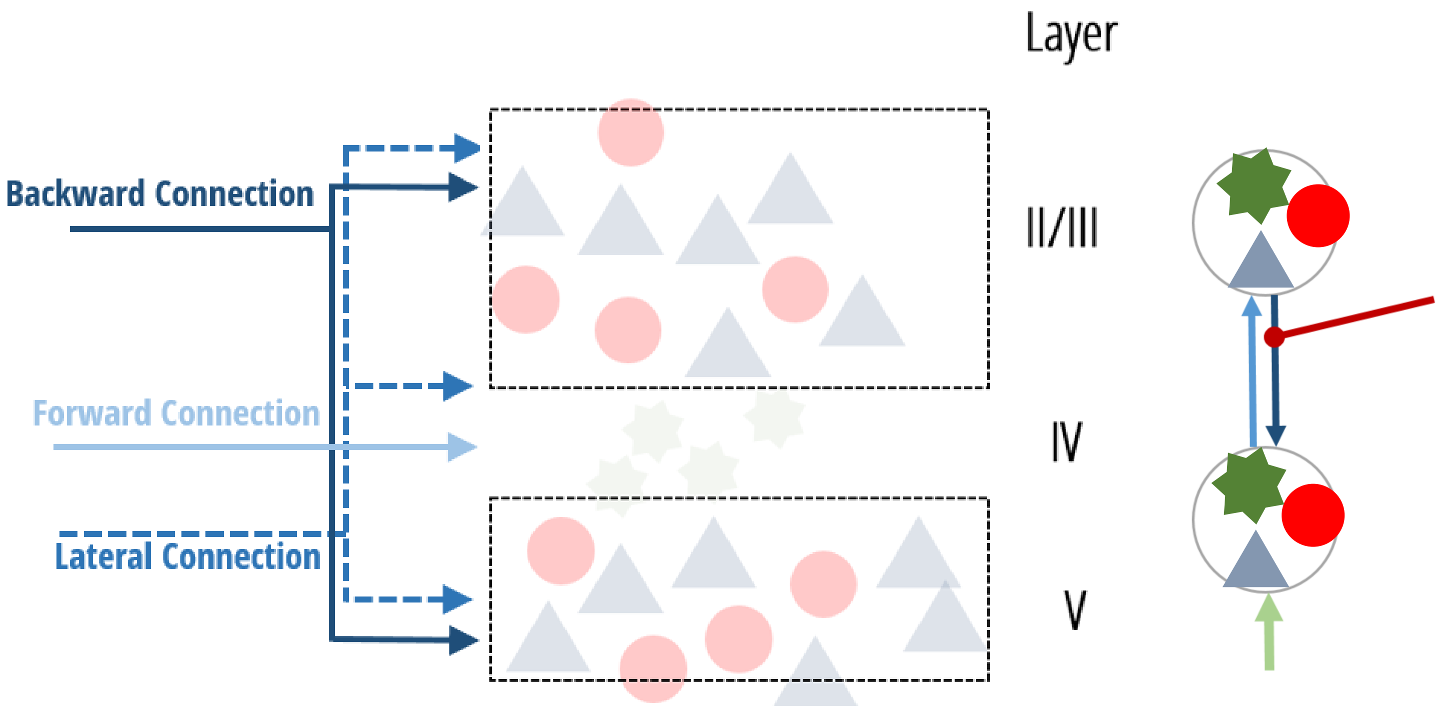

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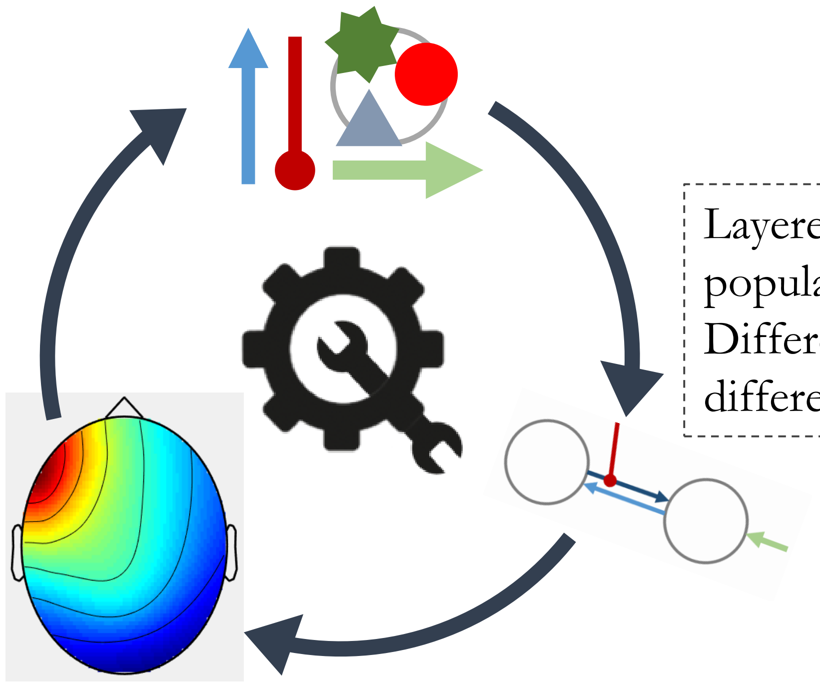
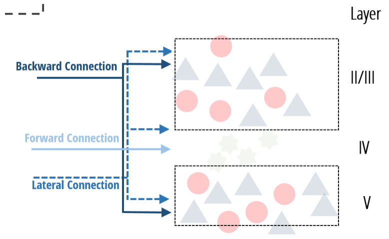


Layered organization of the populations within a source. Different layers receive different kinds of input.



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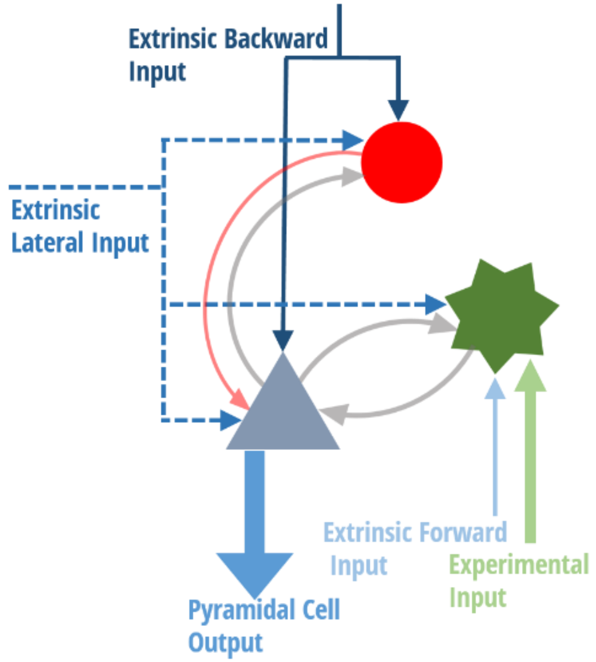
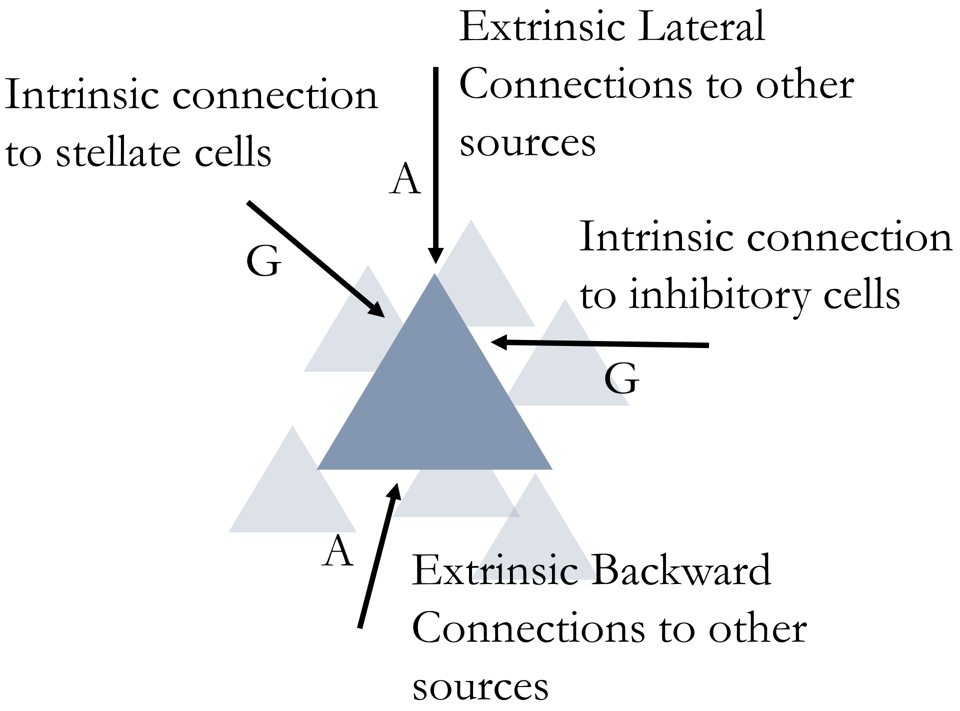
A slightly different view on the parameters





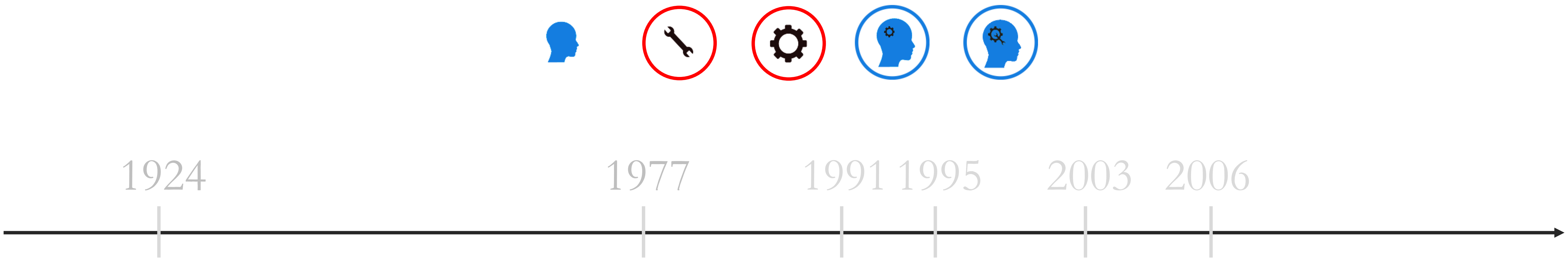
Current state of the population.

How much firing arrives.

$$\frac{dx}{dt} = f(x, A, H, C, \sigma, f_s(\theta_{kernel}))$$

What the cell population is connected to.

The size of the kernel.



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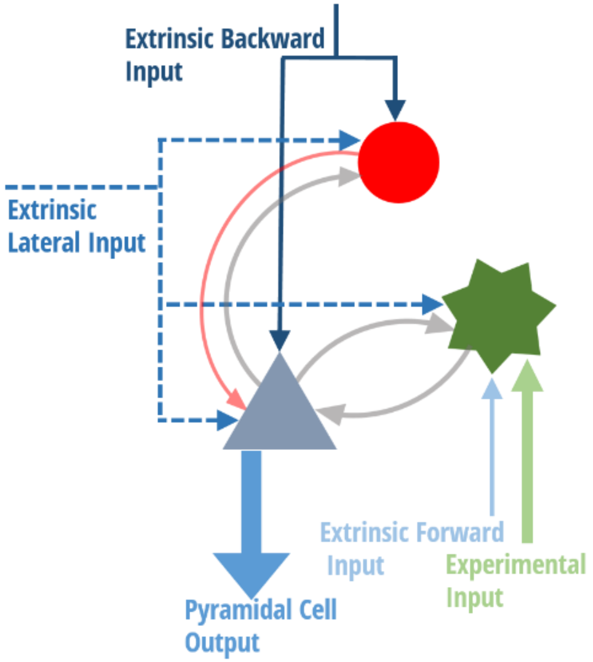
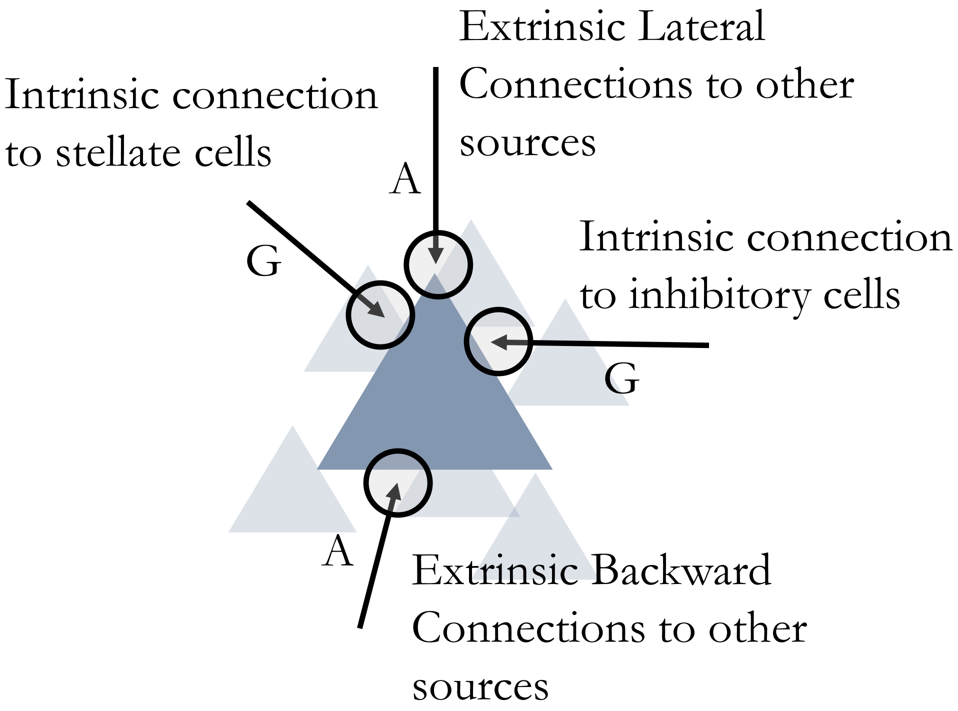




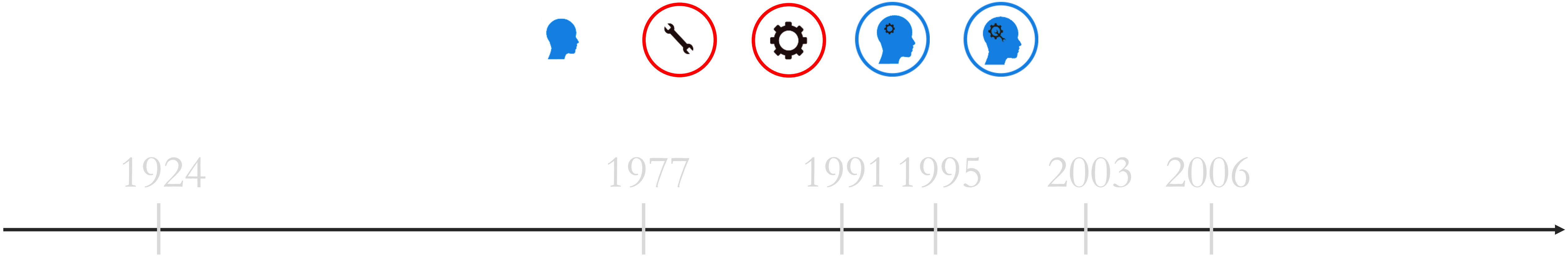
Current state of the population.

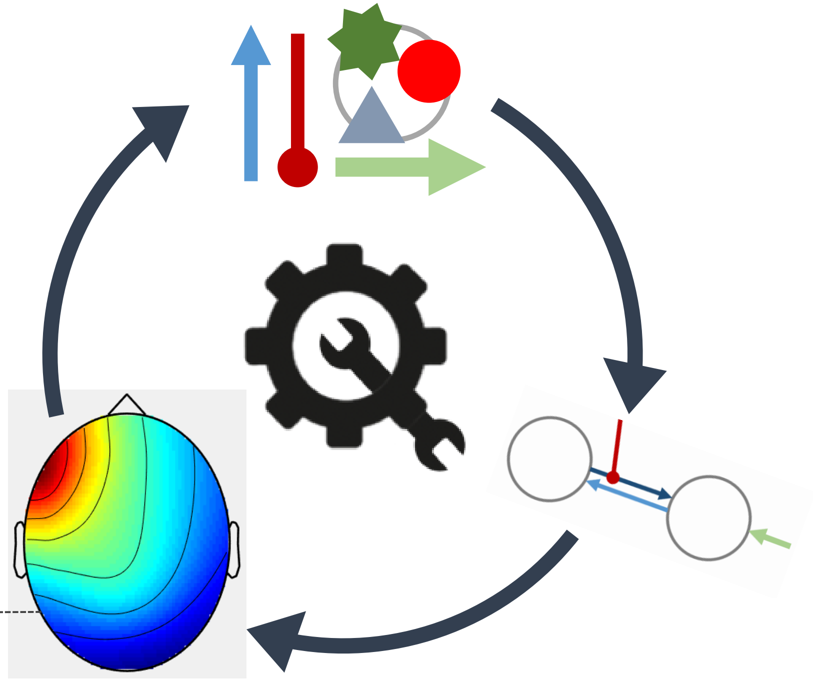
How much firing arrives.

$$\frac{dx}{dt} = f(x, a, H_{A,G,C}, \sigma, K, f_s(\theta_{kernel}))$$

What the cell population is connected to.

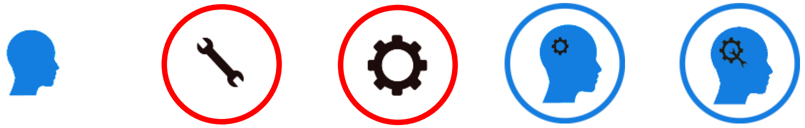
The size of the kernel.





How hidden neural activity transforms into measurable data?

$$y = g(x, \Theta_g) + \epsilon$$



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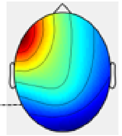

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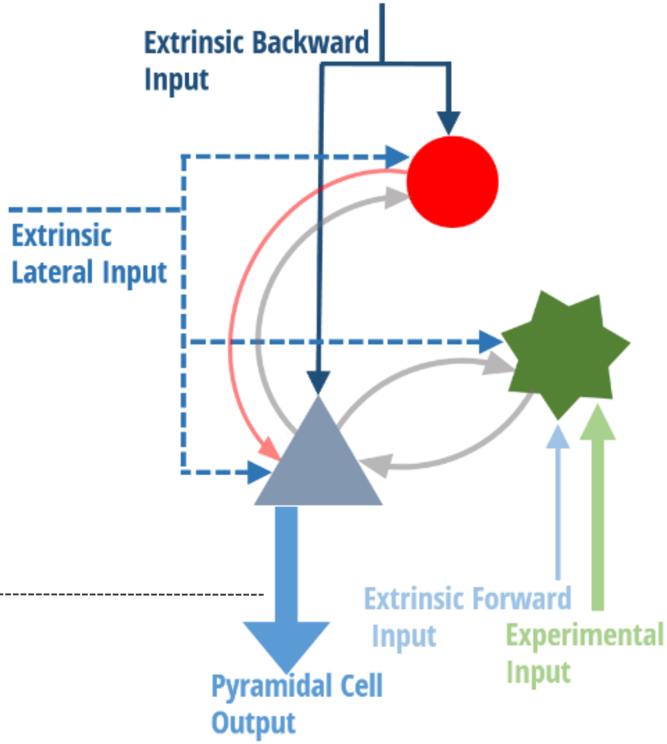
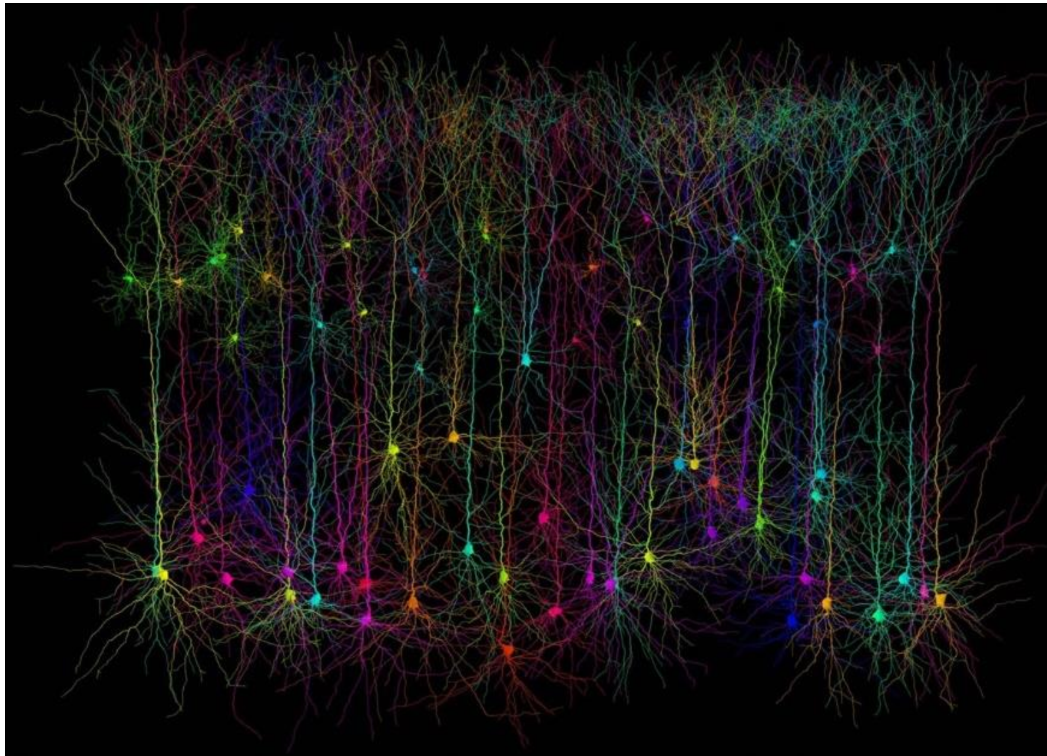
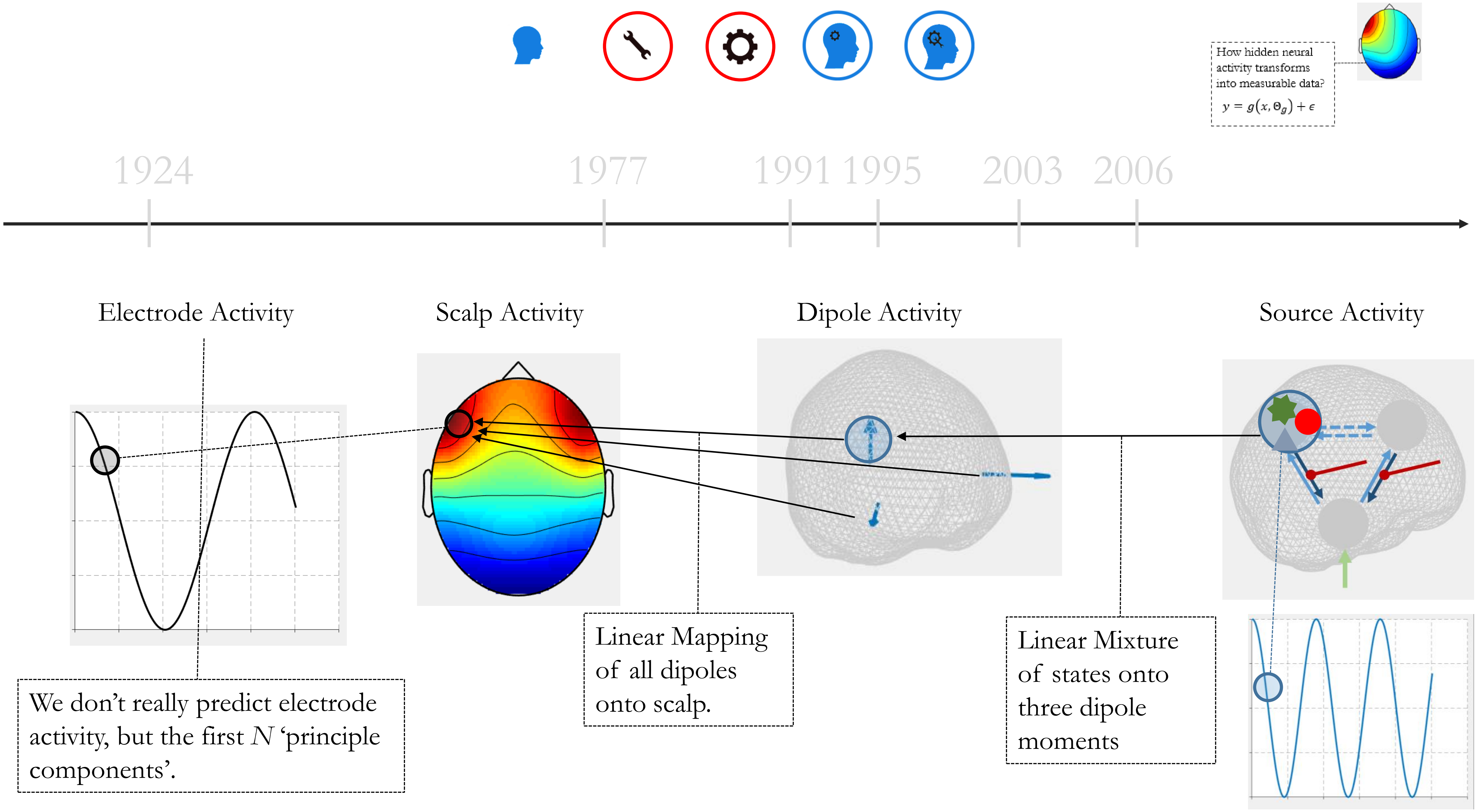


Due to their special alignment, pyramidal cells contribute most to the measured signal.



[9]

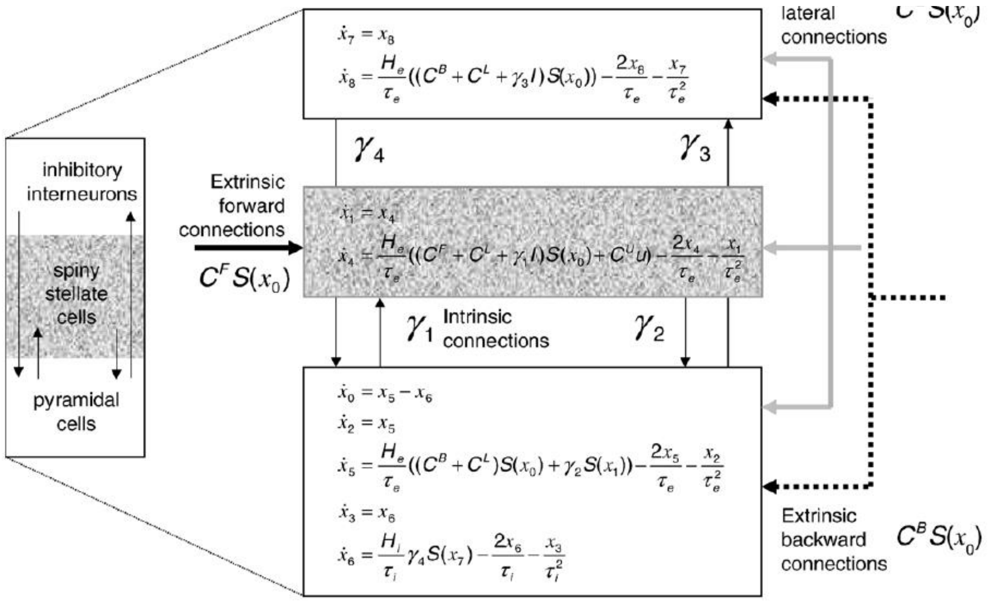


How hidden neural activity transforms into measurable data?
$y = g(x, \Theta_g) + \epsilon$
1924
1977
1991
1995
2003
2006
Electrode Activity
Scalp Activity
Dipole Activity
Source Activity
We don't really predict electrode activity, but the first N 'principle components'.
Linear Mapping of all dipoles onto scalp.
Linear Mixture of states onto three dipole moments

1924 1977 1991 1995 2003 2006

Dynamic causal modeling of evoked responses in EEG and MEG☆

Olivier David,[1] Stefan J. Kiebel,* Lee M. Harrison, Jérémie Mattout,
James M. Kilner, and Karl J. Friston



Single source model

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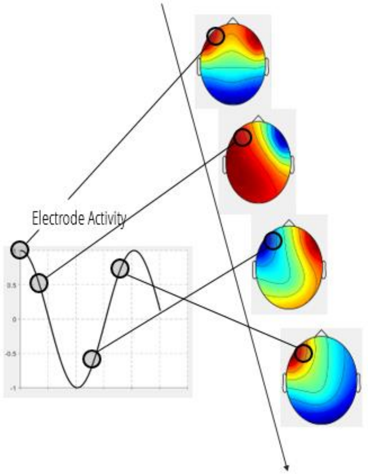
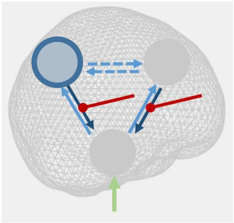
Prediction of measured data





Inference on parameters and (causal) network structure

$$y = g(x, \Theta_g) + \epsilon$$

$$\frac{dx}{dt} = f(x, u, \theta)$$

Linear forward mapping describing the transformation of hidden source activity to measurable data

Equations describing (hidden) post synaptic potentials of the neuronal populations.

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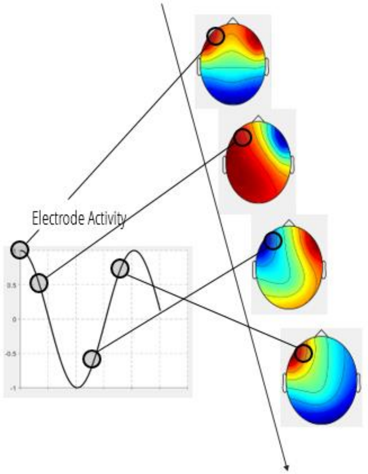
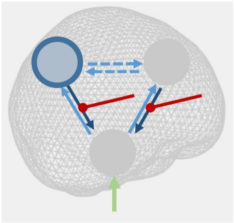
EEG



$$y = g(x, \Theta_g) + \epsilon$$

simple

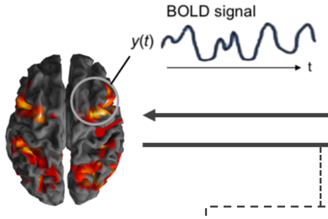
Tough (at least parameter inference)



$$\frac{dx}{dt} = f(x, u, \theta)$$

complicated

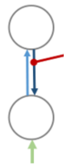
fMRI



$$y = g(x, \Theta_g) + \epsilon$$

complicated

Probably better behaved

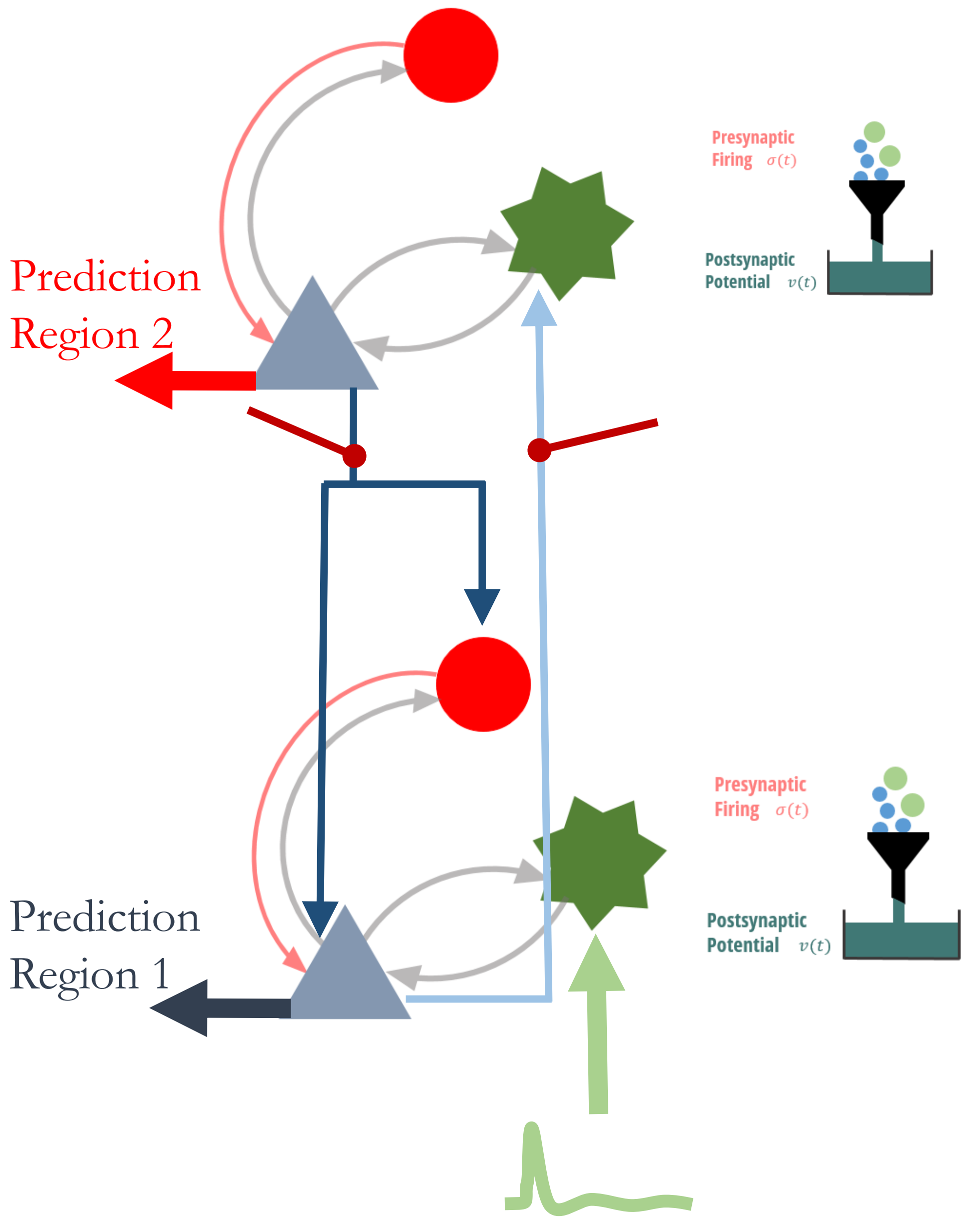


$$\frac{dx}{dt} = f(x, u, \theta)$$

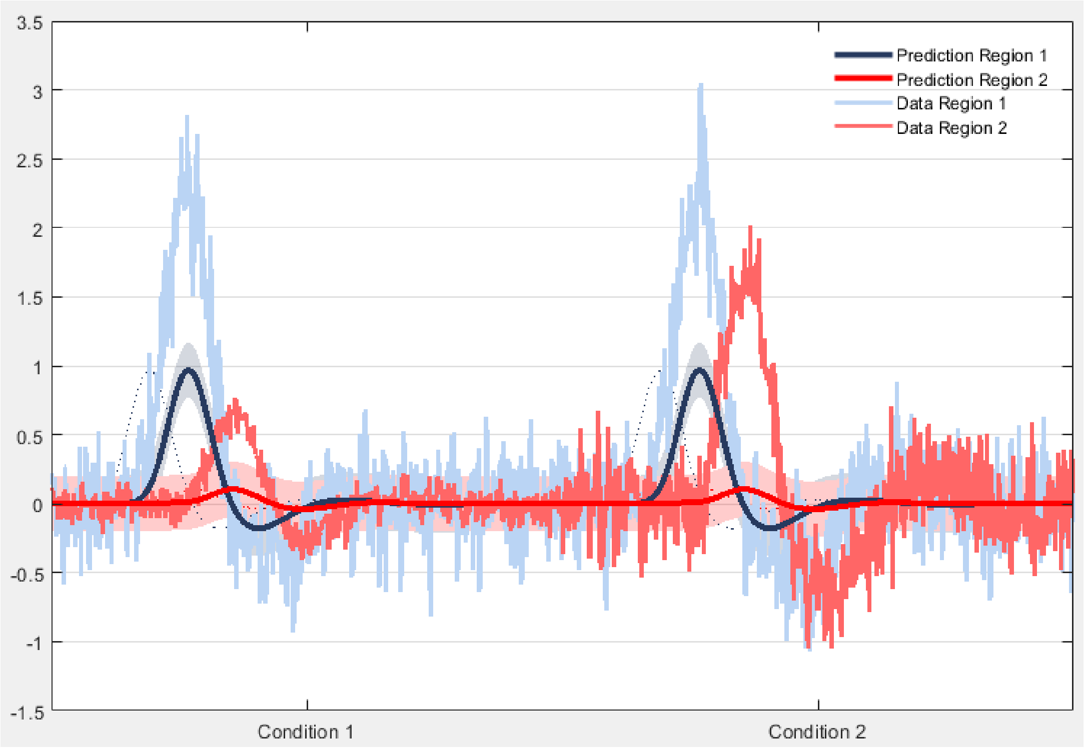
simple

Chapter 2

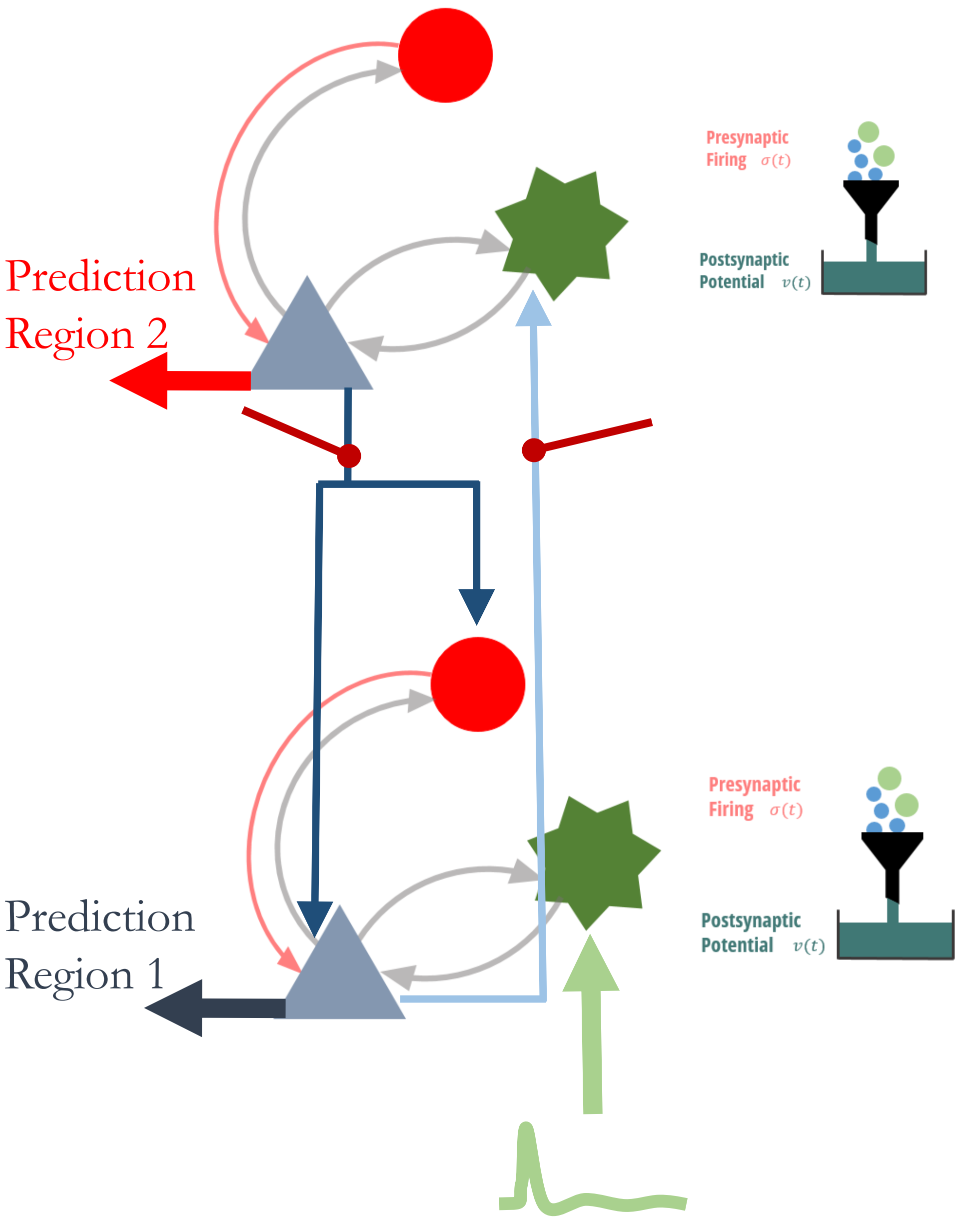
Getting a feel for the equations



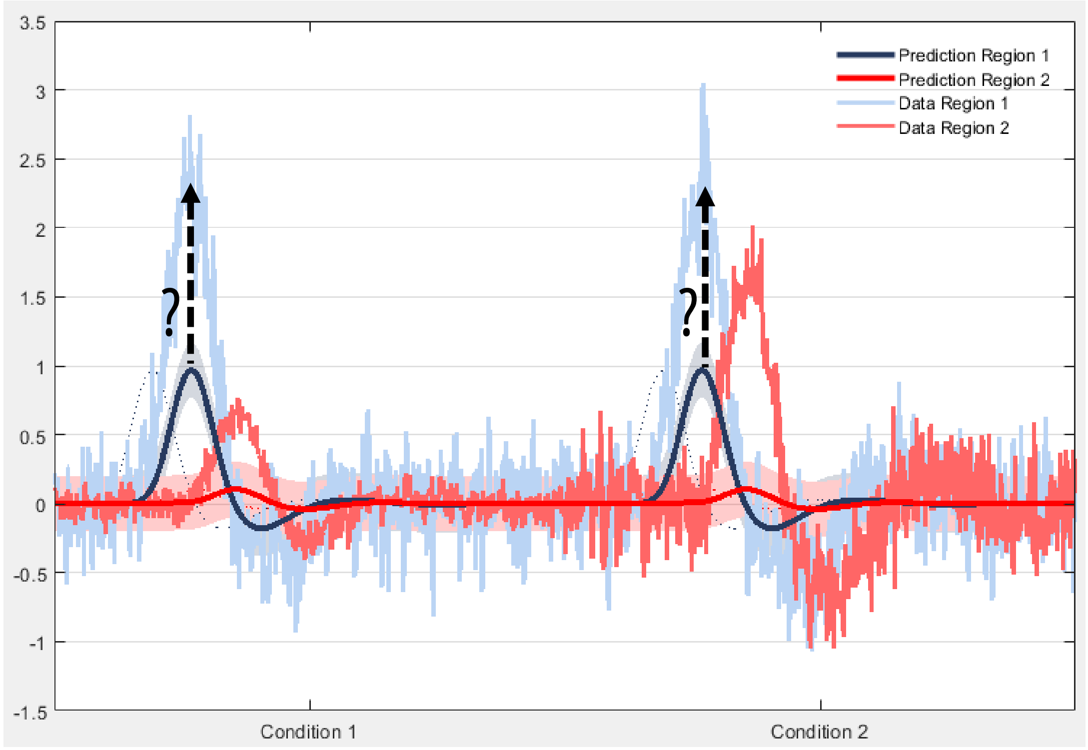
Prediction Region 2
Presynaptic Firing $\sigma(t)$
Postsynaptic Potential $v(t)$
Prediction Region 1
Presynaptic Firing $\sigma(t)$
Postsynaptic Potential $v(t)$



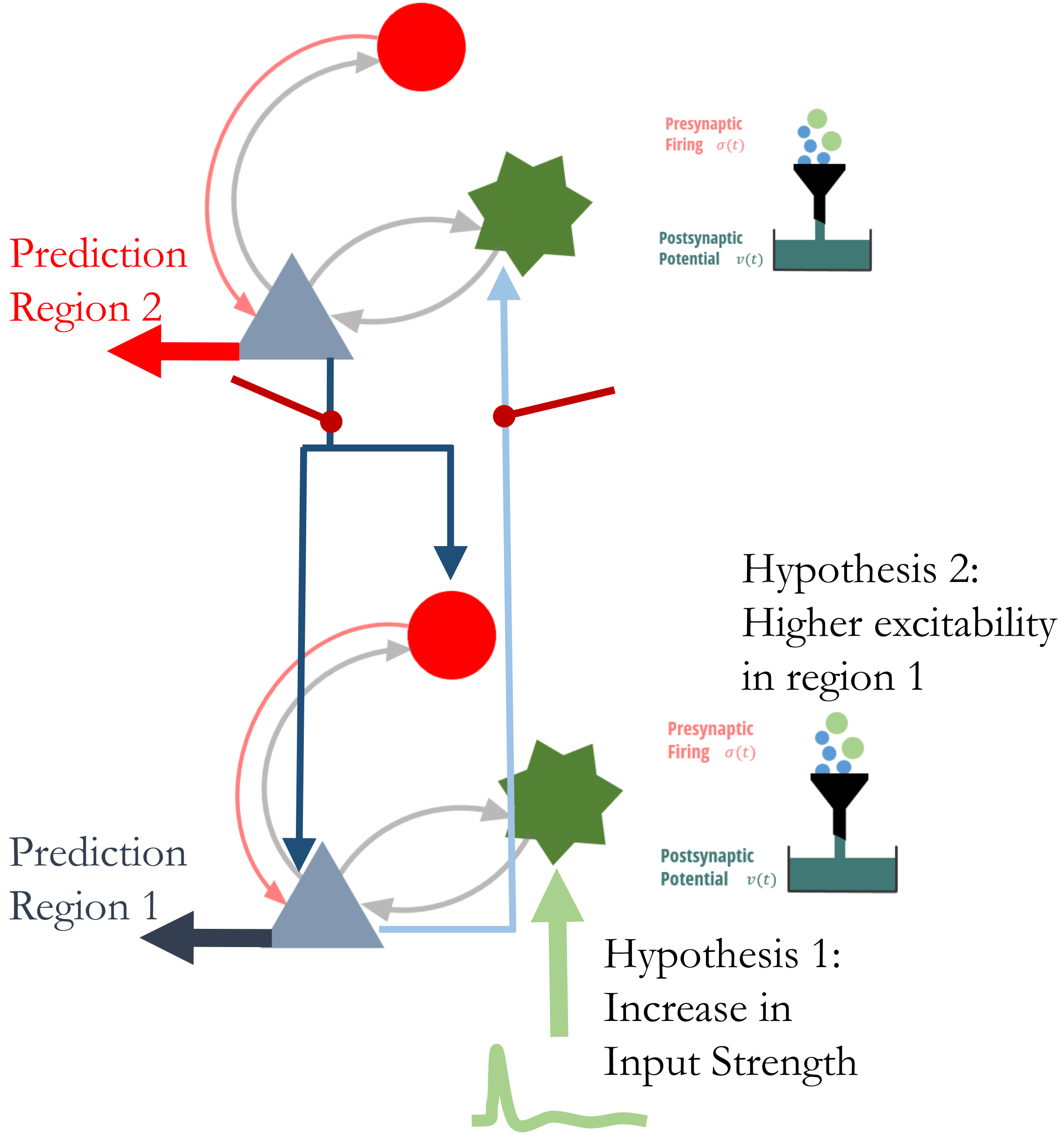
Prediction Region 1
Prediction Region 2
Data Region 1
Data Region 2
3.5
3
2.5
2
1.5
1
0.5
0
-0.5
-1
-1.5
Condition 1
Condition 2

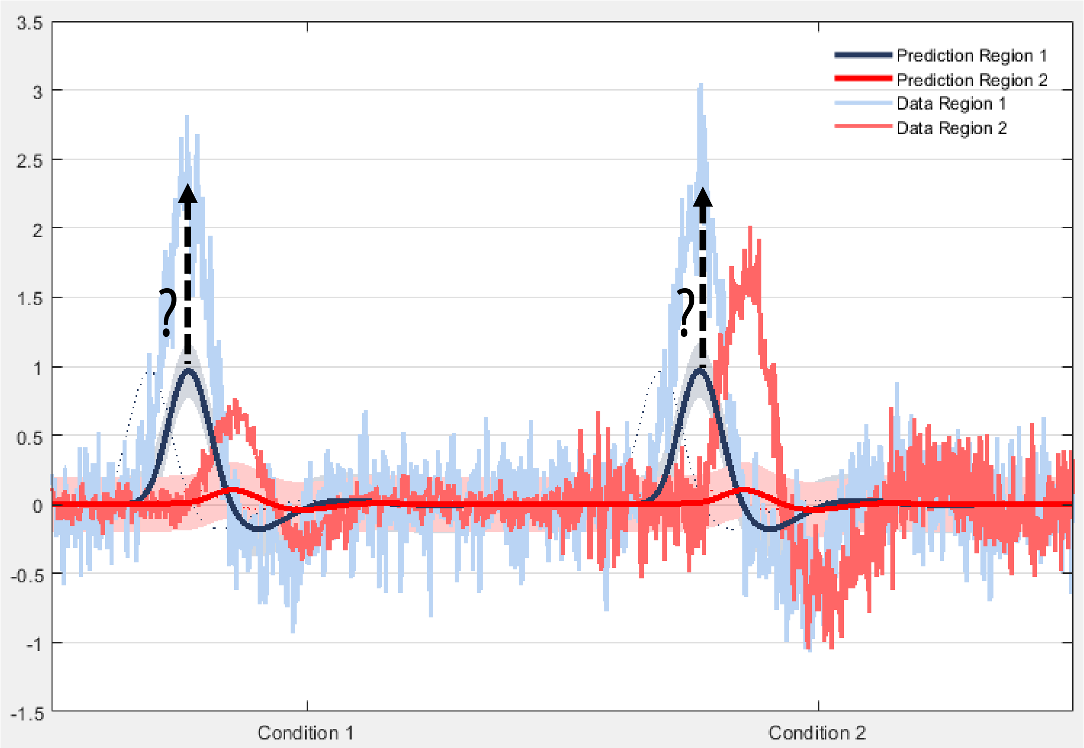


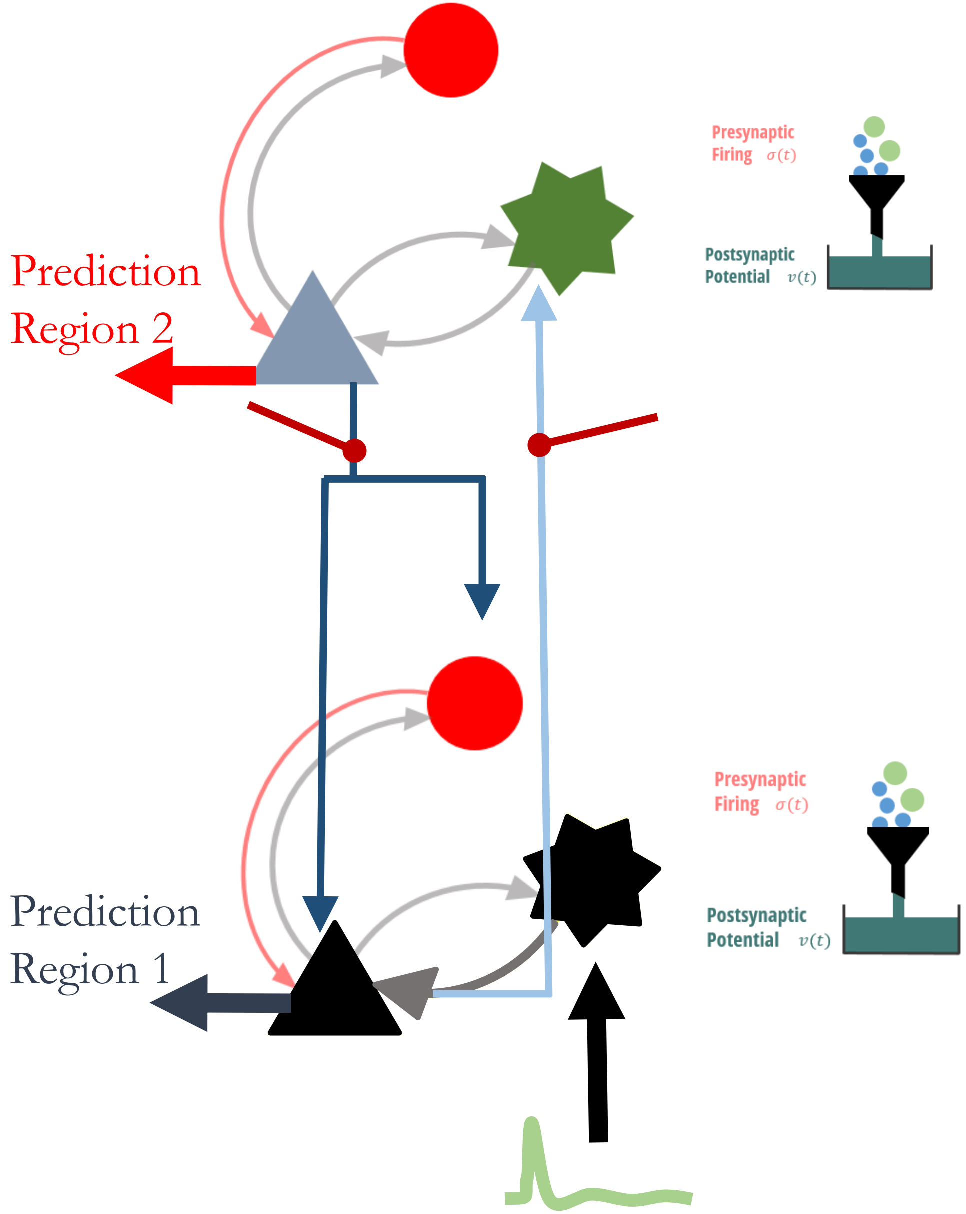
Prediction
Region 2
Presynaptic
Firing $\sigma(t)$
Postsynaptic
Potential $v(t)$
Prediction
Region 1
Presynaptic
Firing $\sigma(t)$
Postsynaptic
Potential $v(t)$

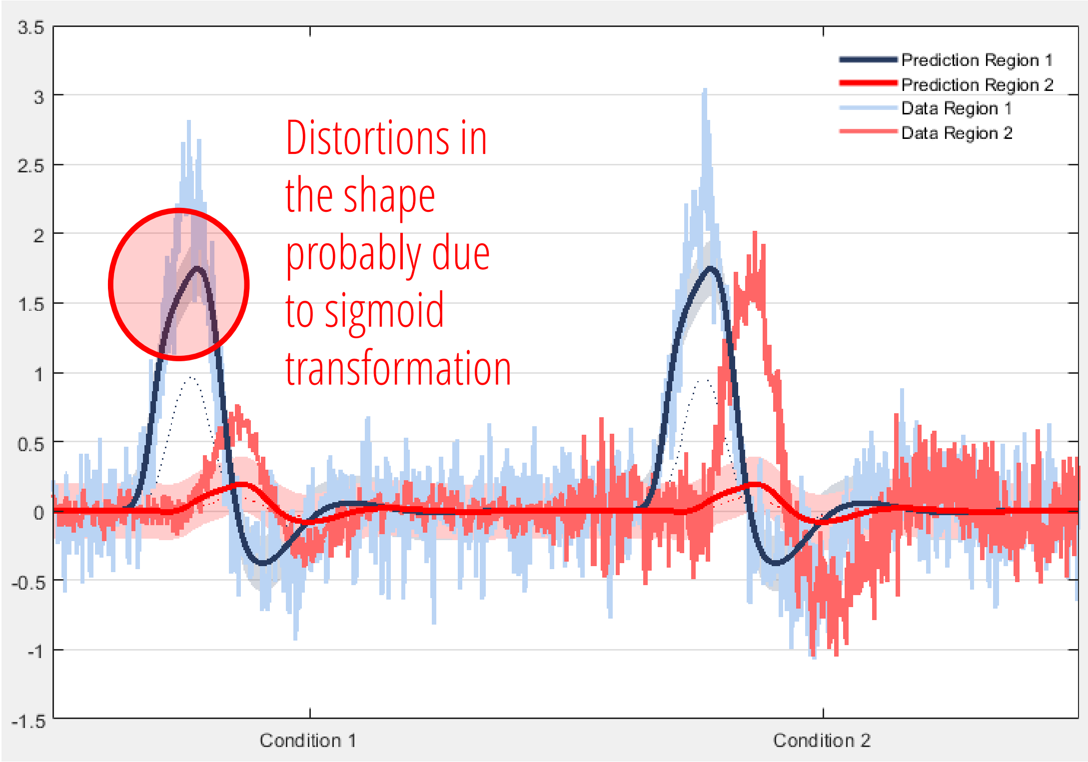


Prediction Region 1
Prediction Region 2
Data Region 1
Data Region 2
3.5
3
2.5
2
1.5
1
0.5
0
-0.5
-1
-1.5
?
?
Condition 1
Condition 2

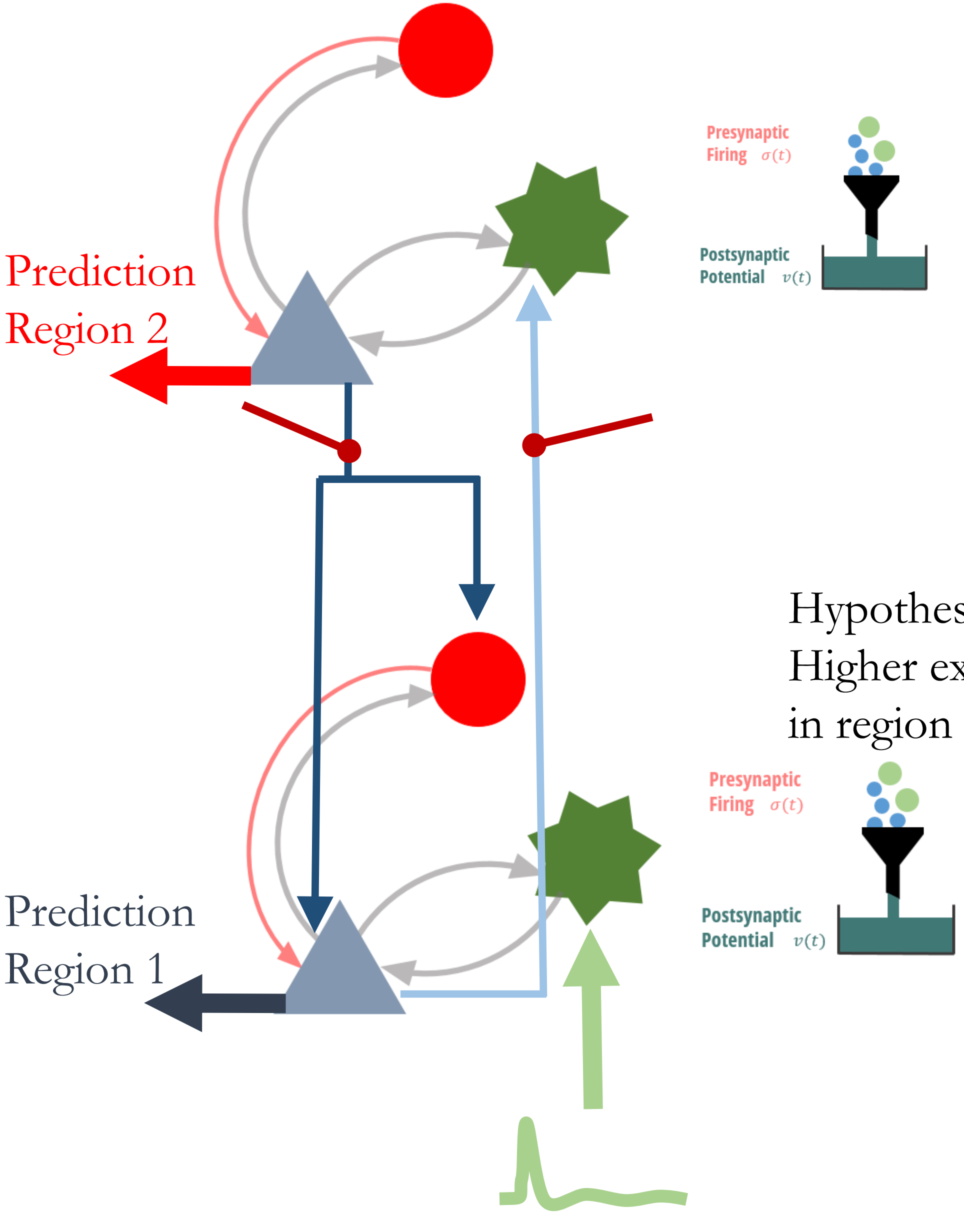

Prediction
Region 2
Presynaptic
Firing $\sigma(t)$
Postsynaptic
Potential $v(t)$
Hypothesis 2:
Higher excitability
in region 1
Presynaptic
Firing $\sigma(t)$
Postsynaptic
Potential $v(t)$
Prediction
Region 1
Hypothesis 1:
Increase in
Input Strength

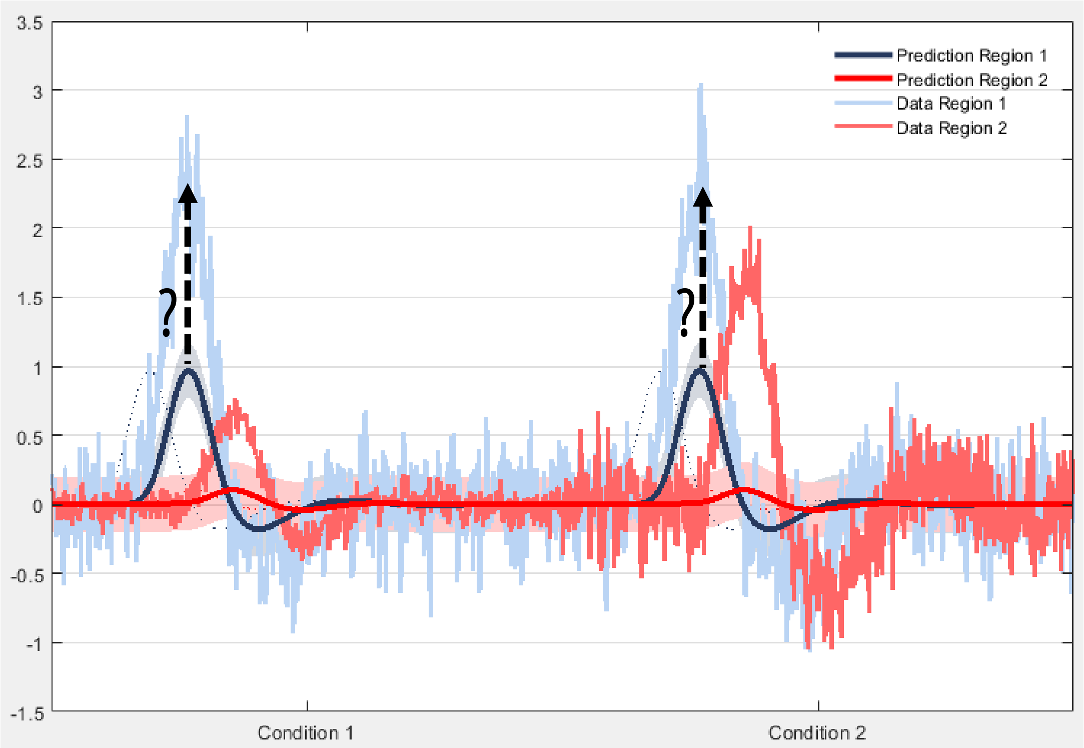

Prediction Region 1
Prediction Region 2
Data Region 1
Data Region 2
3.5
3
2.5
2
1.5
1
0.5
0
-0.5
-1
-1.5
?
?
Condition 1
Condition 2

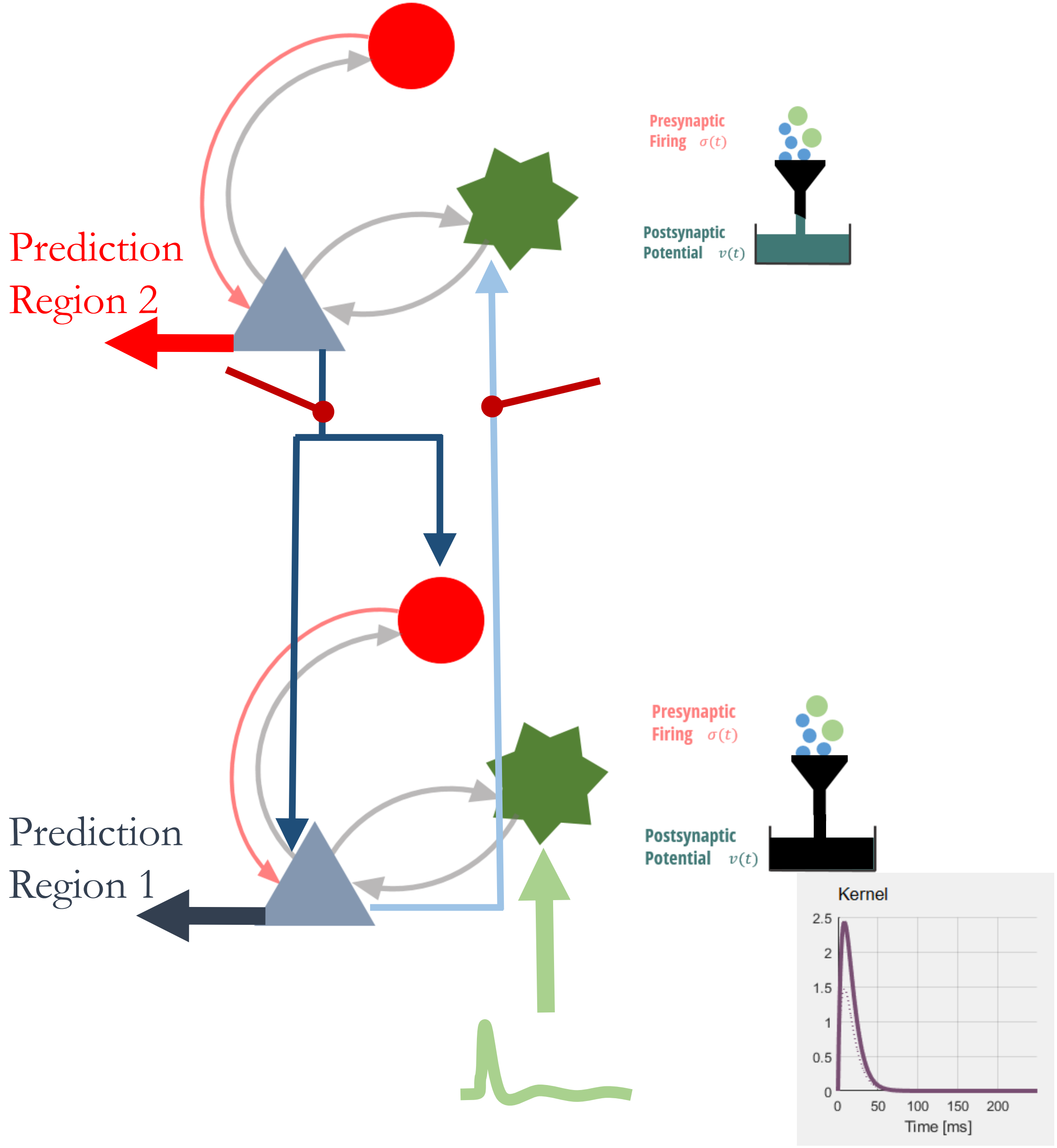

Prediction Region 2
Presynaptic Firing $\sigma(t)$
Postsynaptic Potential $v(t)$
Presynaptic Firing $\sigma(t)$
Postsynaptic Potential $v(t)$
Prediction Region 1

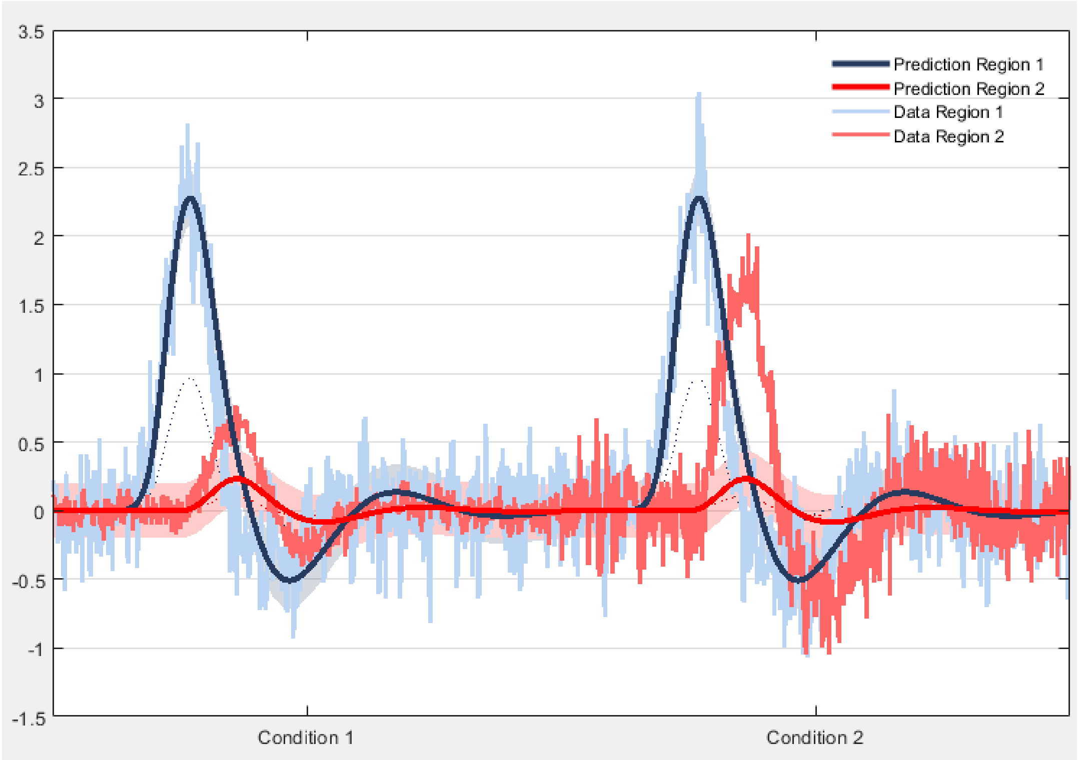

3.5
3
2.5
2
1.5
1
0.5
0
-0.5
-1
-1.5
Prediction Region 1
Prediction Region 2
Data Region 1
Data Region 2
Distortions in the shape probably due to sigmoid transformation
Condition 1
Condition 2

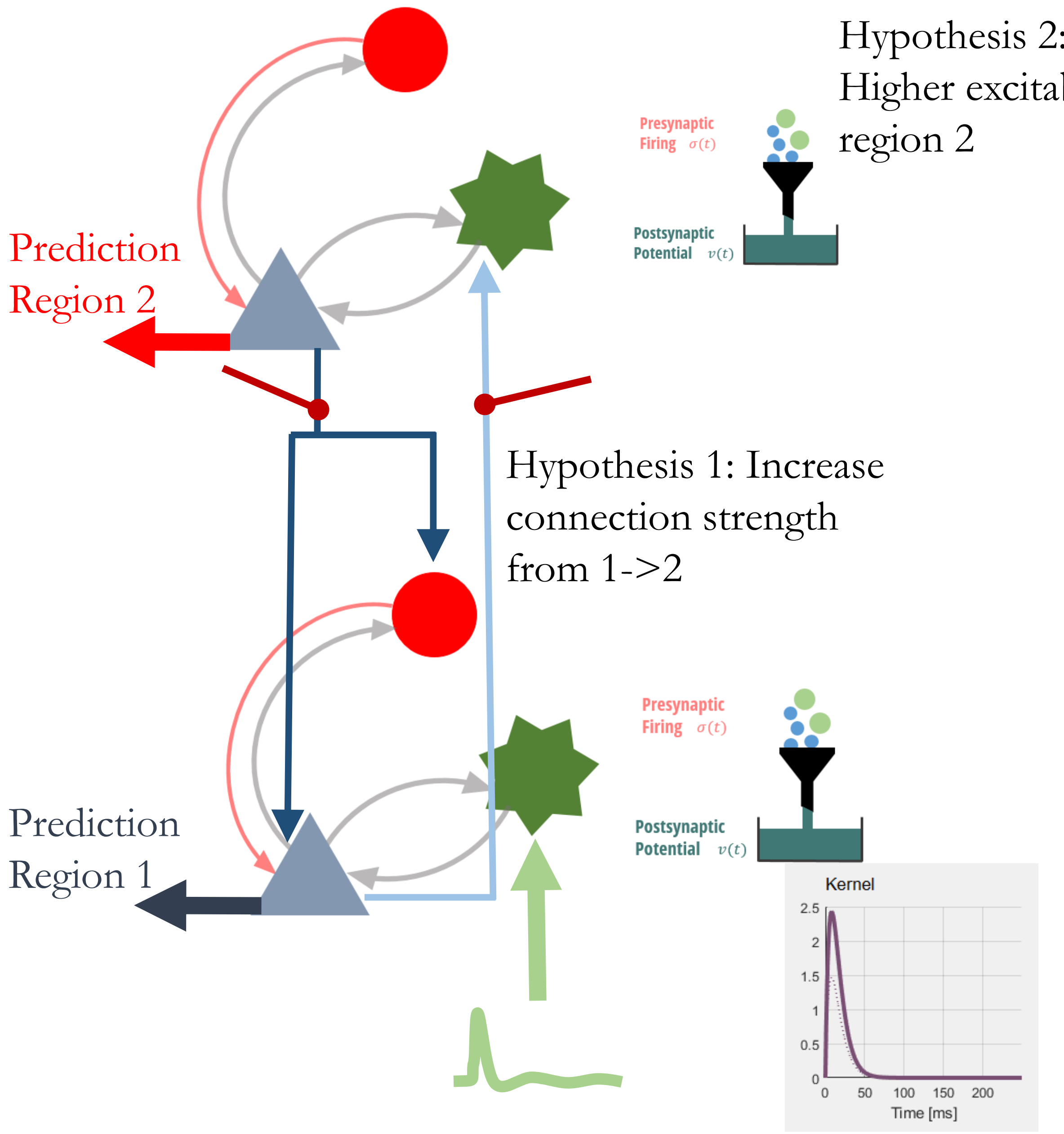
Hypothesis 2: Higher excitability in region 1





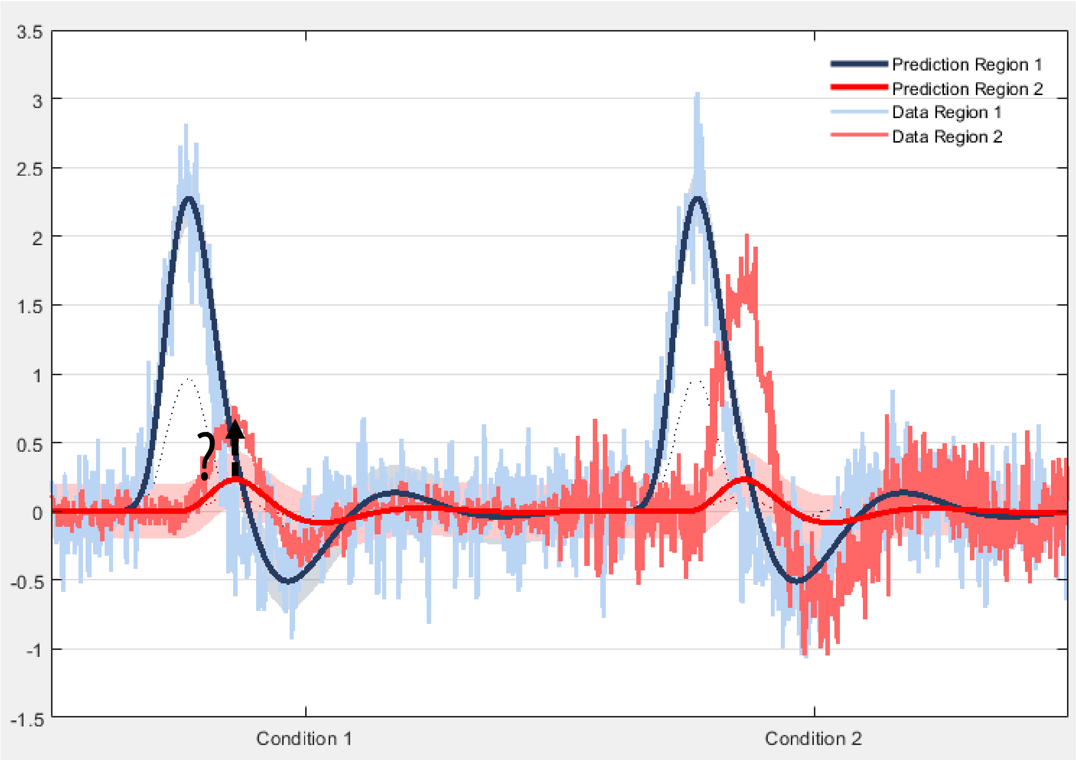

Prediction Region 2
Presynaptic Firing σ(t)
Postsynaptic Potential v(t)
Presynaptic Firing σ(t)
Postsynaptic Potential v(t)
Prediction Region 1
Kernel
2.5
2
1.5
1
0.5
0
0 50 100 150 200
Time [ms]

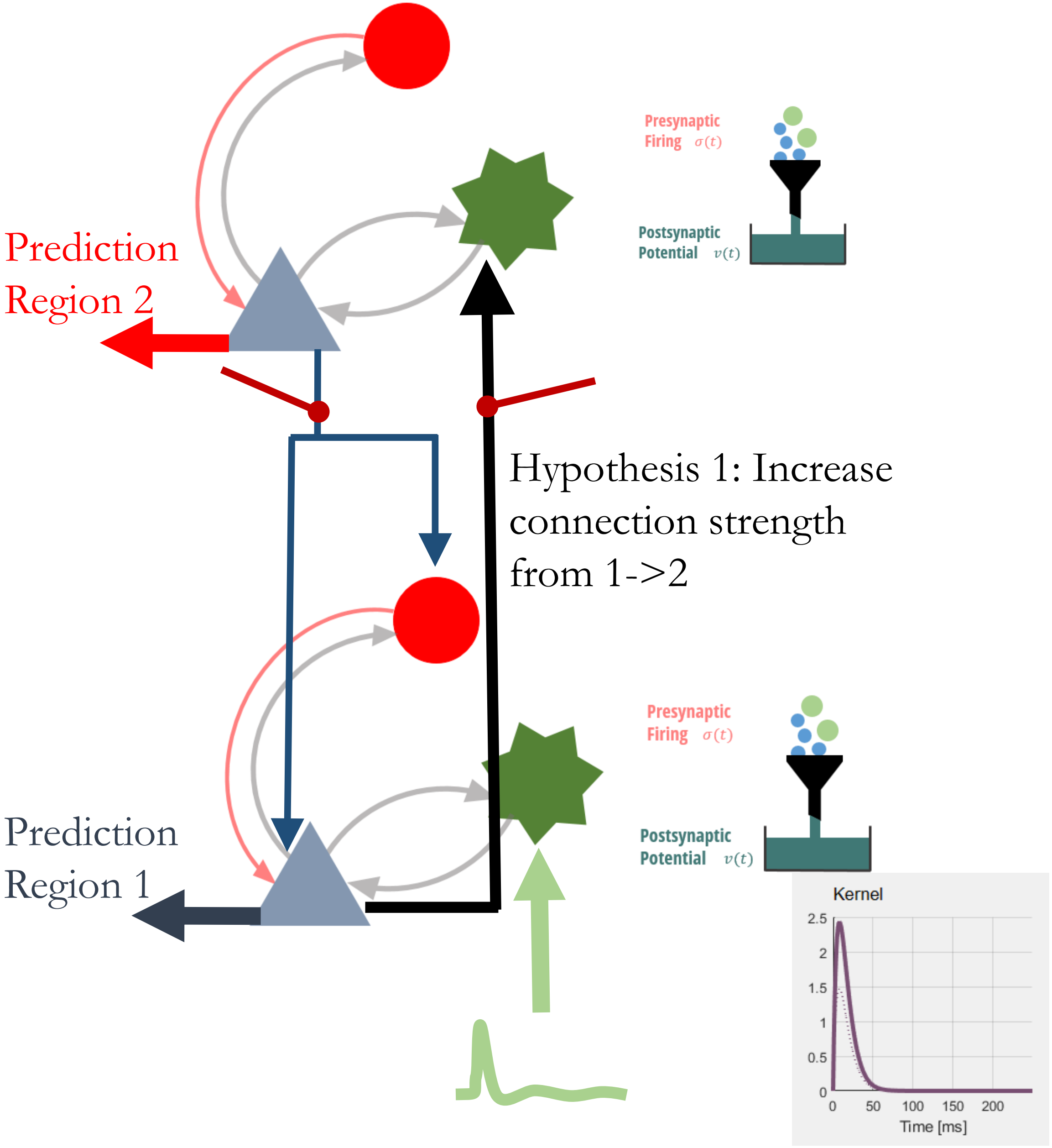

Prediction Region 1
Prediction Region 2
Data Region 1
Data Region 2
3.5
3
2.5
2
1.5
1
0.5
0
-0.5
-1
-1.5
Condition 1
Condition 2

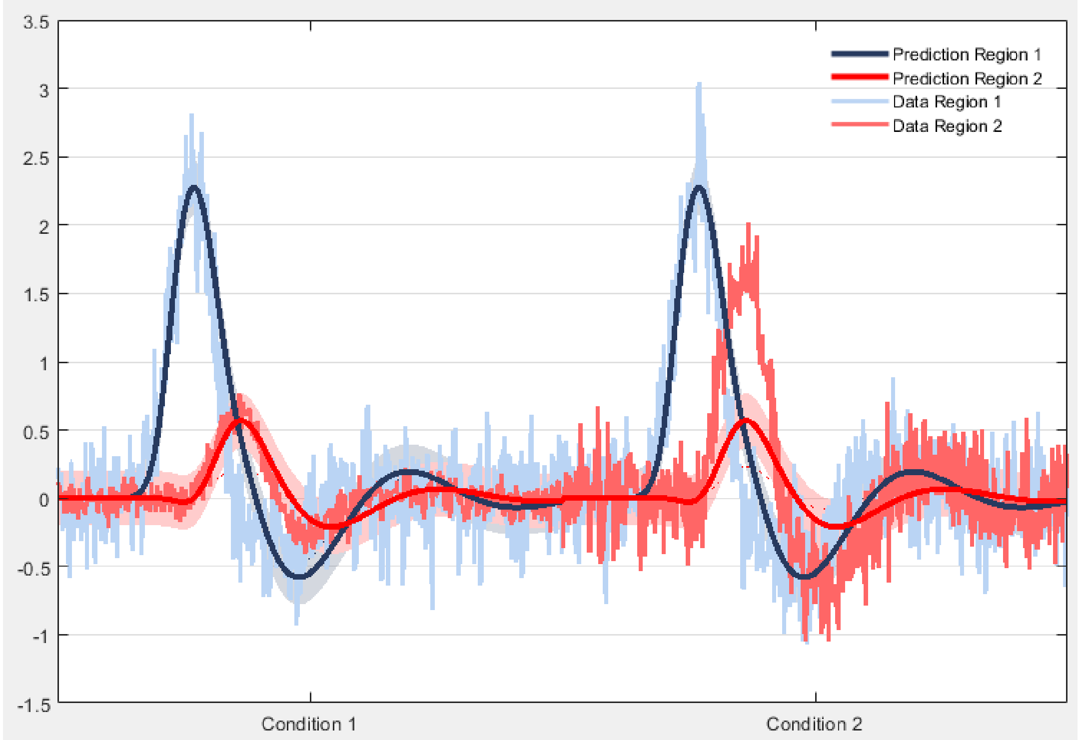


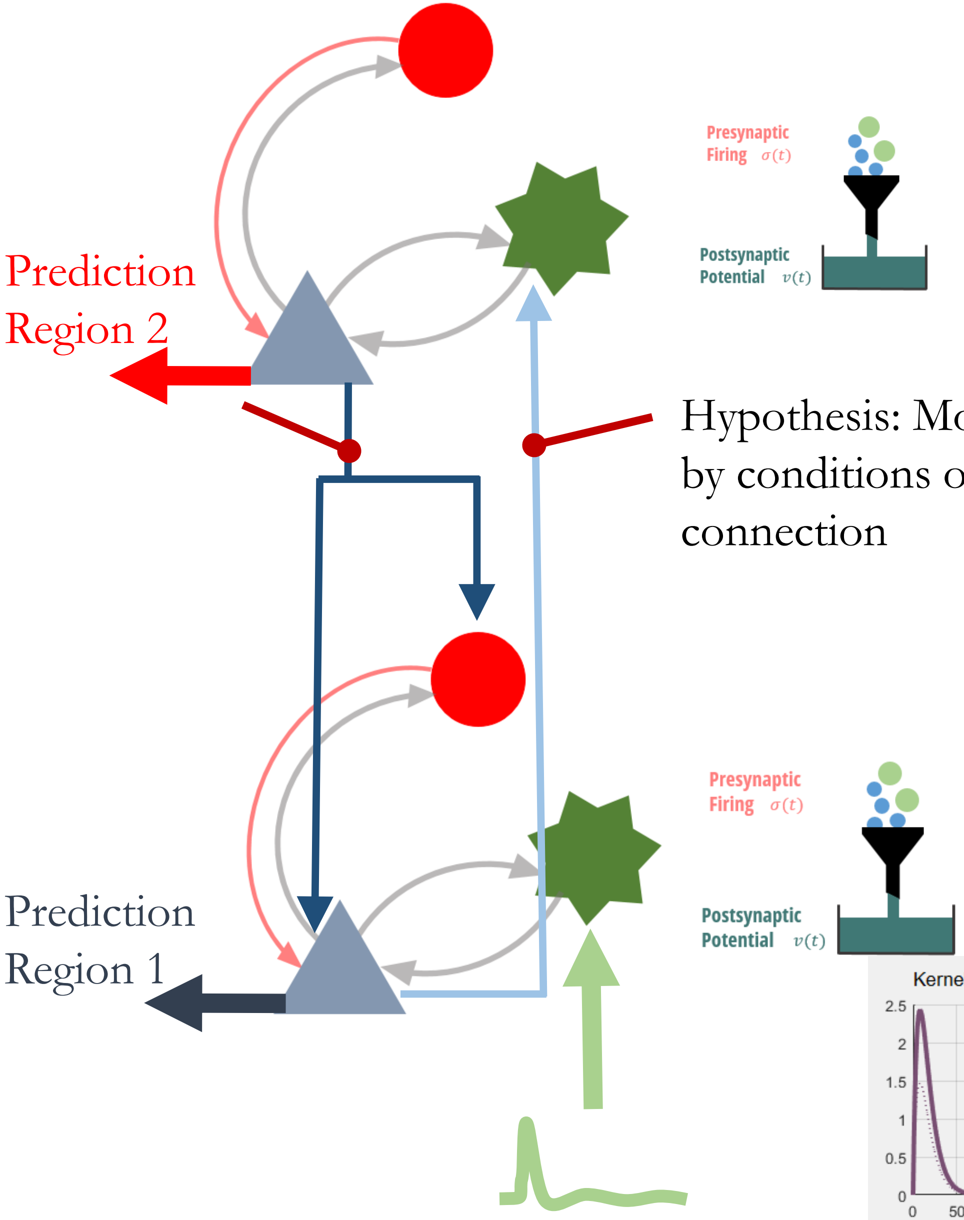
Hypothesis 2: Higher excitability in region 2

Hypothesis 1: Increase connection strength from 1->2

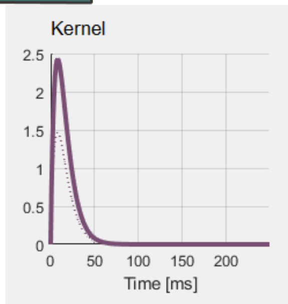


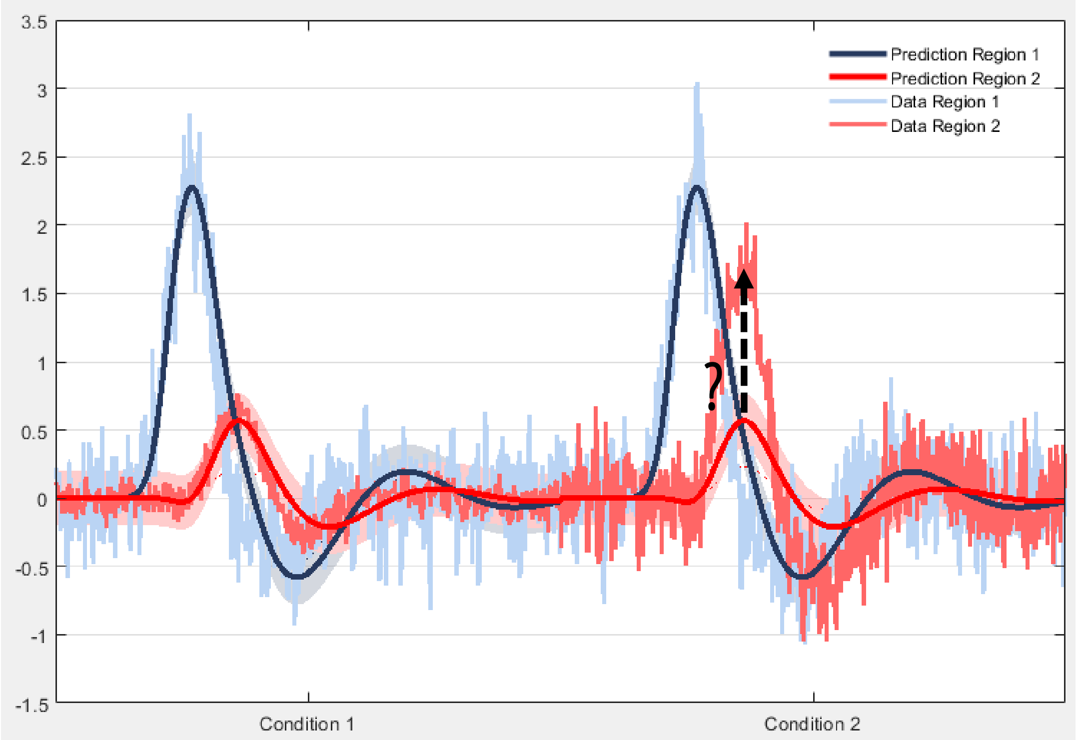

Prediction
Region 2
Presynaptic
Firing $\sigma(t)$
Postsynaptic
Potential $v(t)$
Hypothesis 1: Increase
connection strength
from 1->2
Presynaptic
Firing $\sigma(t)$
Postsynaptic
Potential $v(t)$
Prediction
Region 1
Kernel
Time [ms]

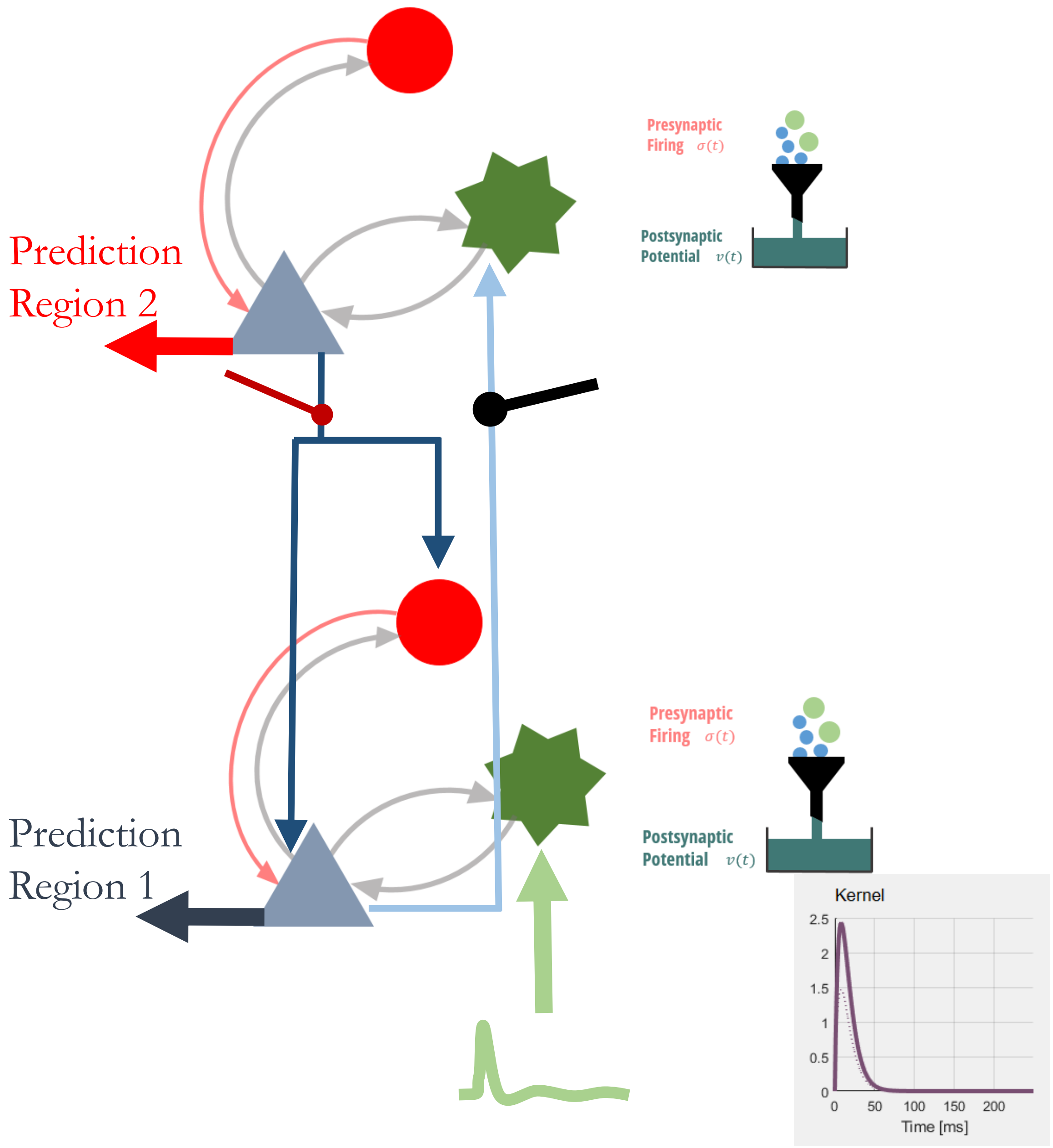

Prediction Region 1
Prediction Region 2
Data Region 1
Data Region 2
Condition 1
Condition 2

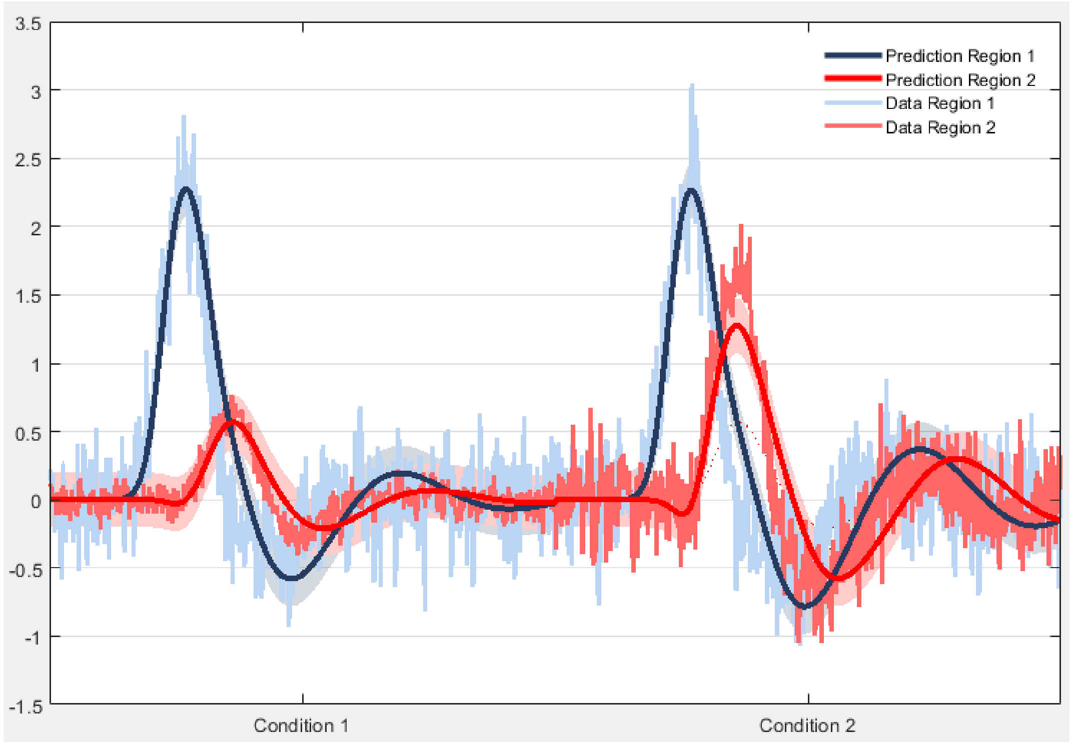


Hypothesis: Modulation by conditions of forward connection





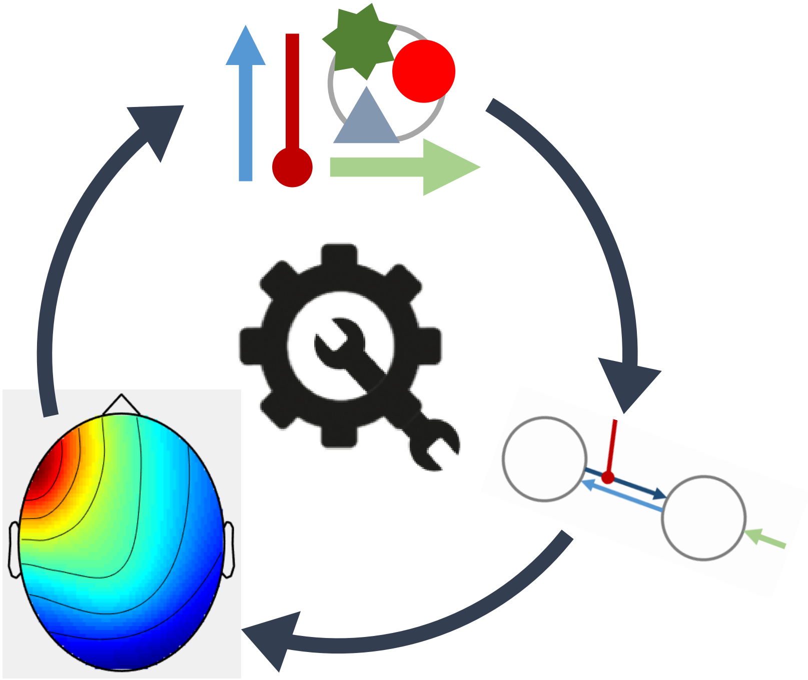

Prediction Region 2
Presynaptic Firing σ(t)
Postsynaptic Potential v(t)
Presynaptic Firing σ(t)
Postsynaptic Potential v(t)
Prediction Region 1
Kernel
2.5
2
1.5
1
0.5
0
0 50 100 150 200
Time [ms]

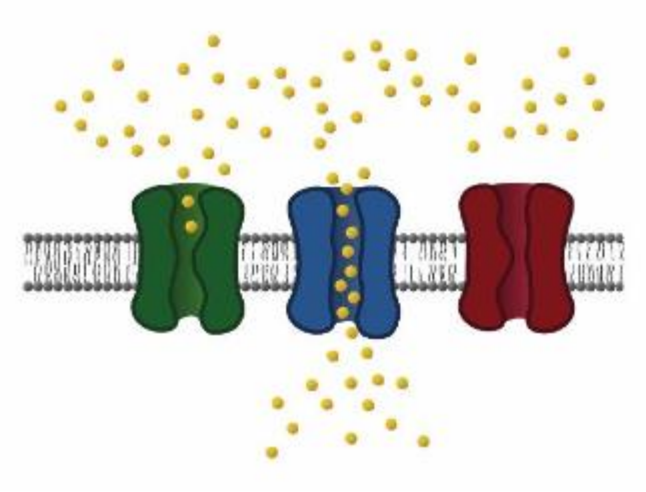

Prediction Region 1
Prediction Region 2
Data Region 1
Data Region 2
3.5
3
2.5
2
1.5
1
0.5
0
-0.5
-1
-1.5
Condition 1
Condition 2

Chapter 3

Application

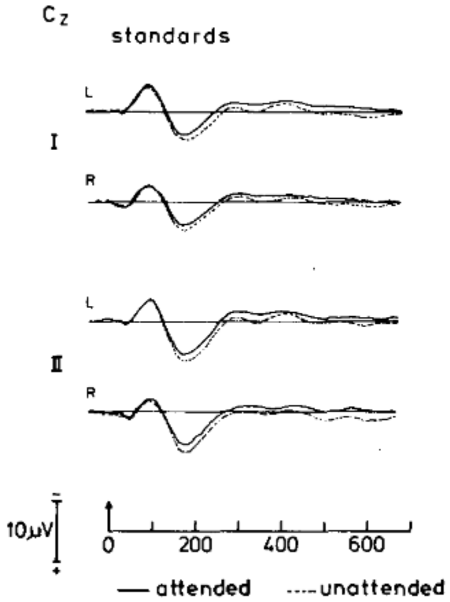
data macroscale mesoscale microscale





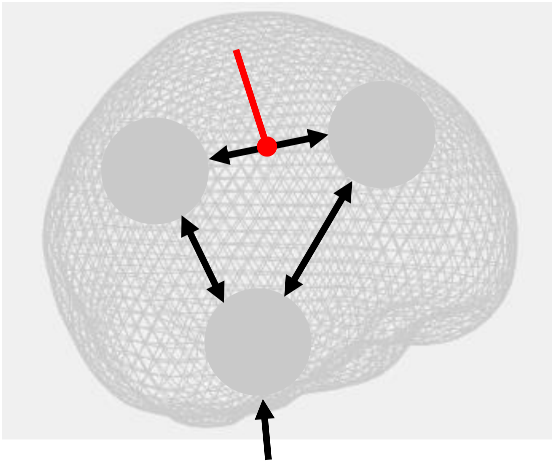
Mechanisms governing generation of average post-synaptic potentials:

data



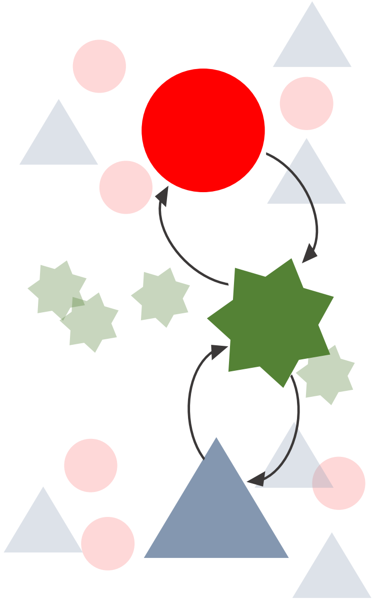
Averaged Evoked Responses

macroscale



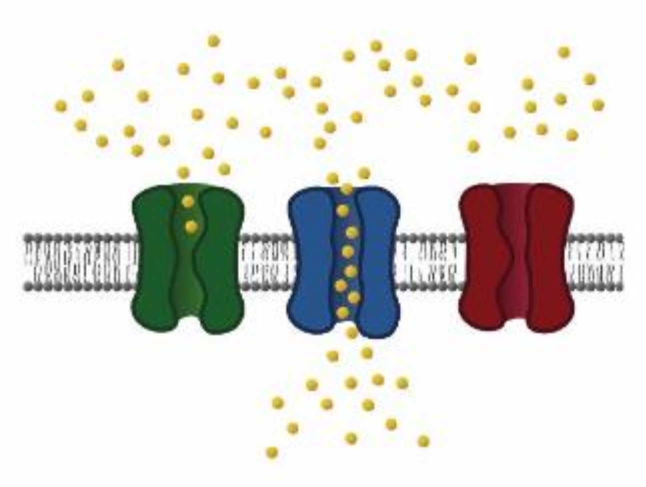
Network and modulation structure

mesoscale



Layered Structure of the cortical column

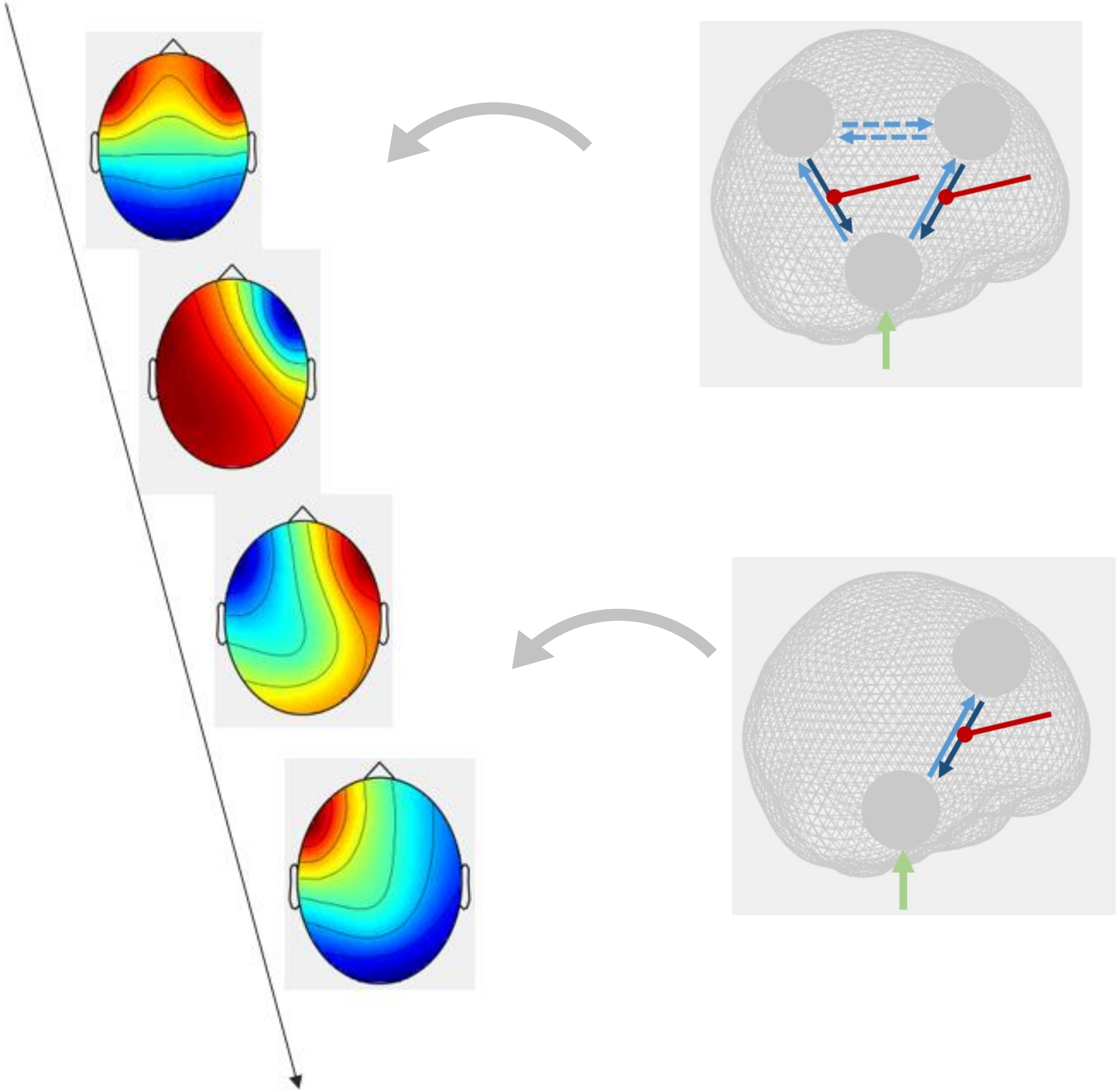
microscale



Mechanisms governing generation of average post-synaptic potentials

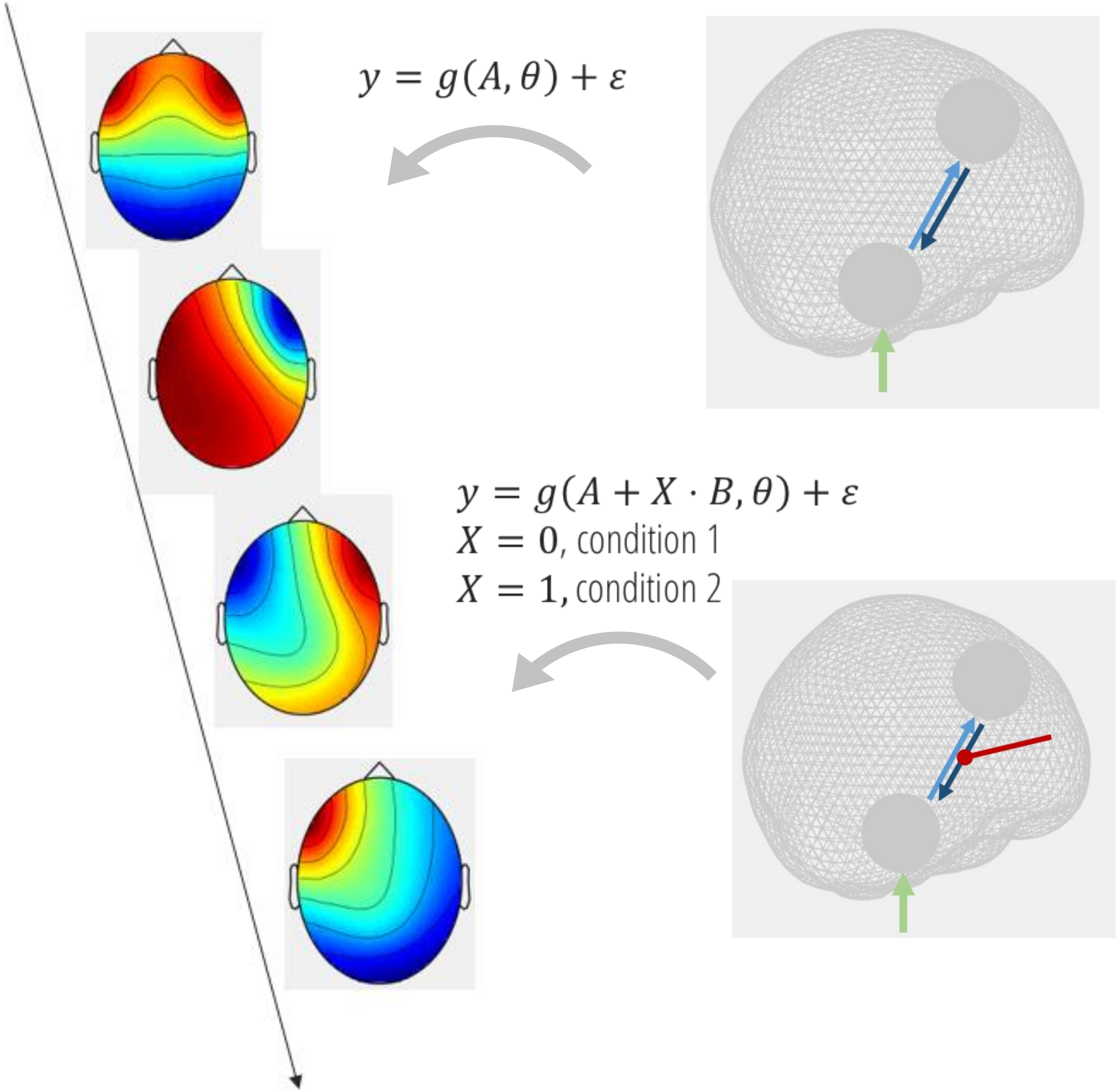
Hypothesis Testing

- Macroscale view (similar to DCM for fMRI)
- Framework to test multiple hypotheses as Bayesian Model Selection (BMS -> Lionel Rigoux) questions:
  - Does a model including regions A, B and C explain the data better than a model including only A and B.
    Only possible for scalp data (not LFP or fMRI)

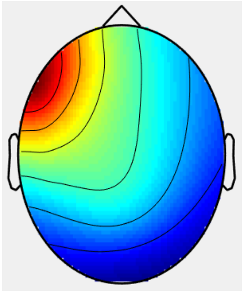


Hypothesis Testing

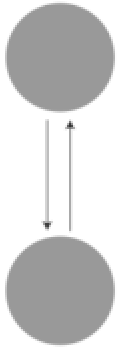
- Macroscale view (similar to DCM for fMRI)
- Framework to test multiple hypotheses as Bayesian Model Selection (BMS -> Lionel Rigoux) questions:
    - Does a model including regions A, B and C explain the data better than a model including only A and B.
      Only possible for scalp data (not LFP or fMRI)
    - Can we explain a difference in activation between conditions as a condition specific modulation of one of the connections?



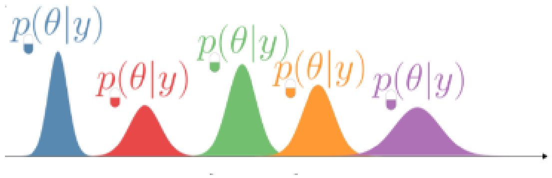
Inferring on parameters



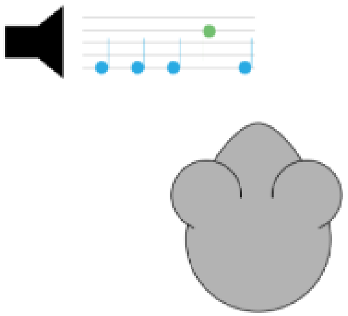
Inference



$$\frac{dx}{dt} = f(x, u, \theta)$$

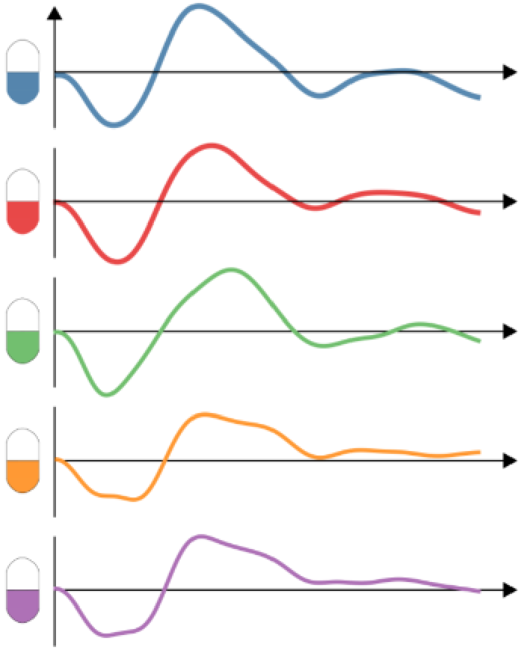


- Differences (across groups, manipulations, interventions, …)
- Relationships
- Features for classification
- …

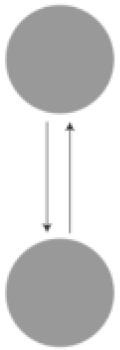


N = 10

- Auditory MMN
- 10 black hooded rats
- Epidural recordings (bilaterally) from A1 and PAF

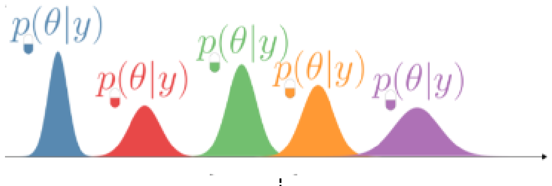


- Five levels of muscarinic manipulations
- Can we detect drug effects in the ERPs?



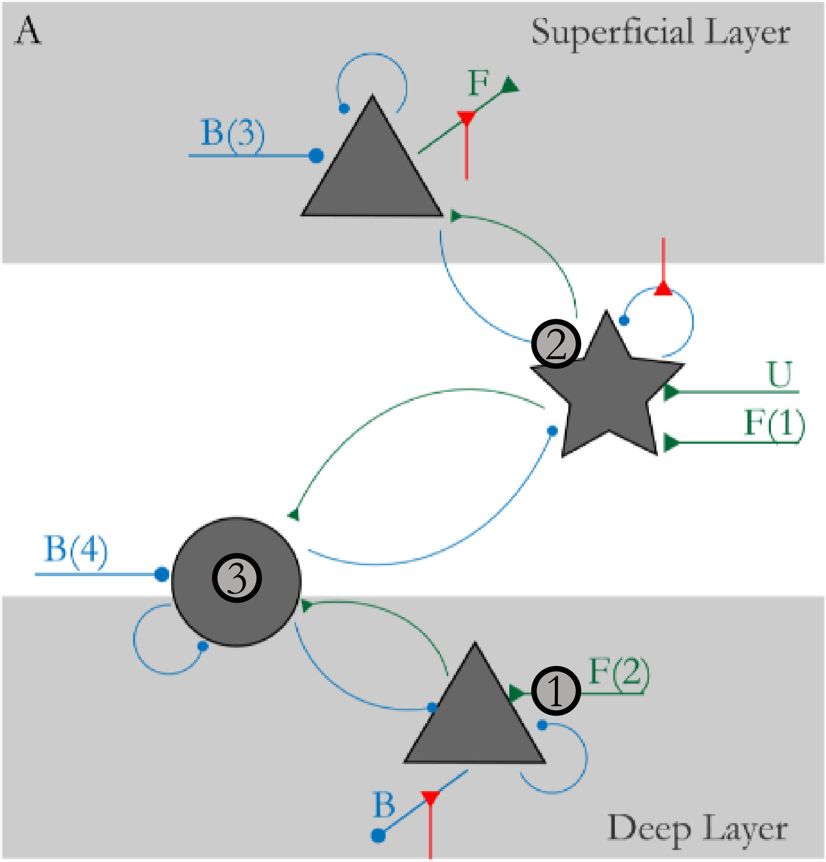
$$\frac{dx}{dt} = f(x, u, \theta)$$

DCM for ERPs
1000 datapoints reduced to ~20-30 Parameters

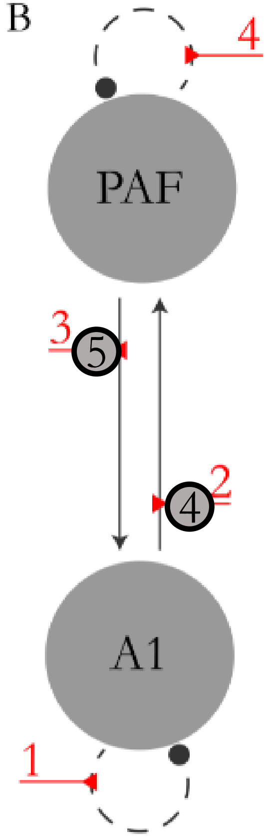


- Are there model parameters showing a drug effect?
- What is the dose response relationship?
- Can we predict the drug label of a left out rat in a classification?

Schöbi et al. (in prep)



Convolution based DCM with CMC



Single hemisphere DCM with full factorial modulation structure

Linear Effect of drug:

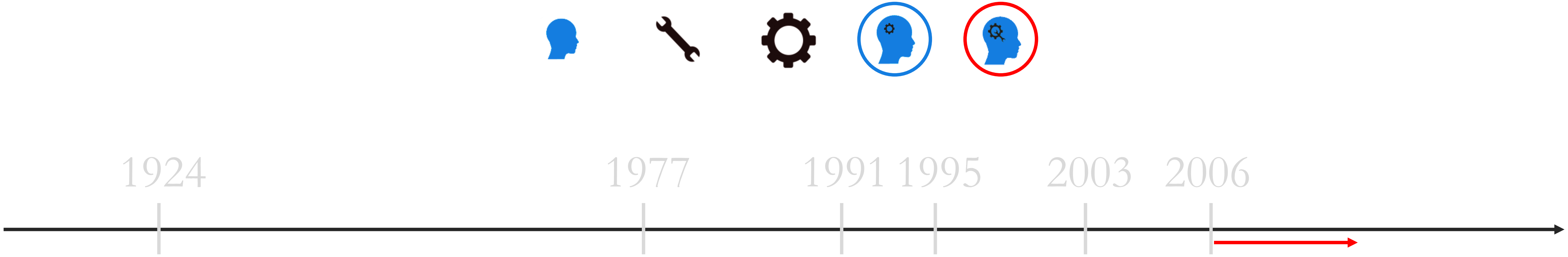
1. Forward connection (decrease)
2. Kernel Gain (increase)
3. Kernel decay (decrease)
4. Forward Modulation (increase)
5. Backward Modulation (increase)

Prediction of left out dataset:

We could significantly* predict the drug label of all classification involving the muscarinic agonist with up to 92.9% (Chance 50%).

* Significance was assessed with a permutation test

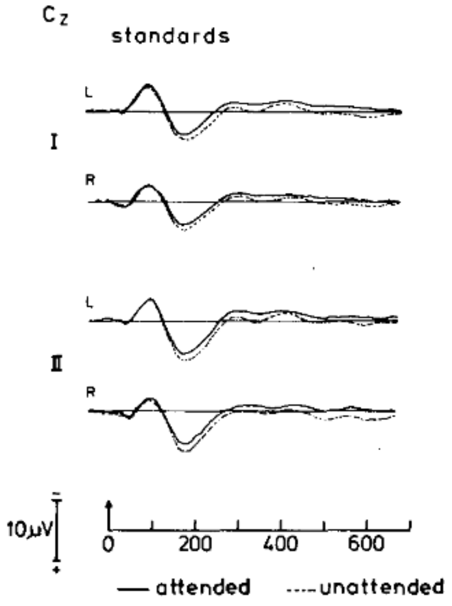
Schöbi et al. (in prep)

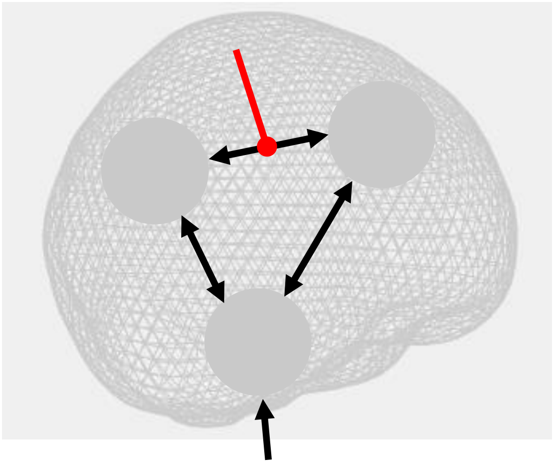


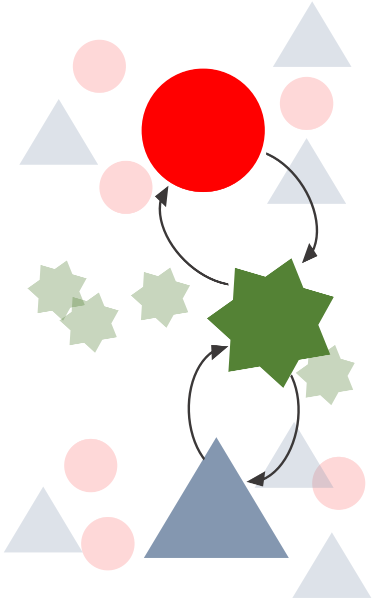
Chapter 4

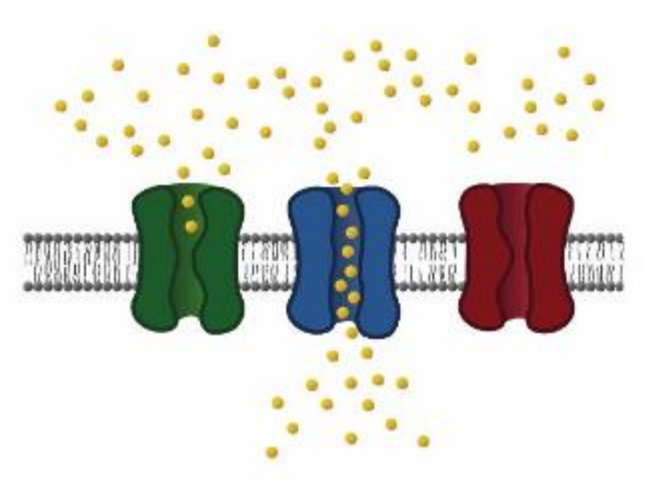
What happened next …

data macroscale mesoscale microscale

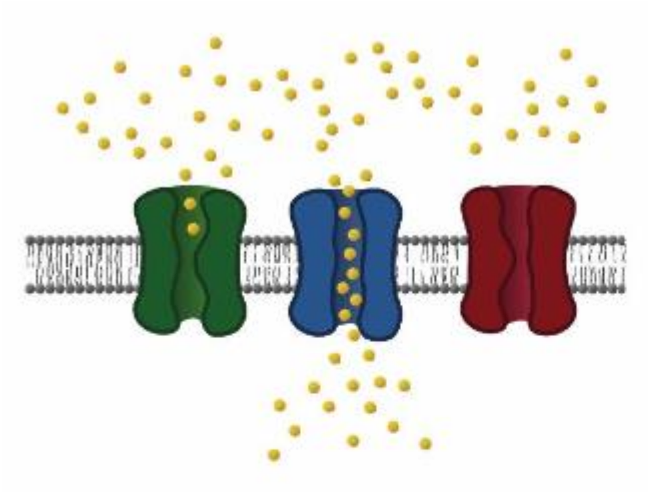






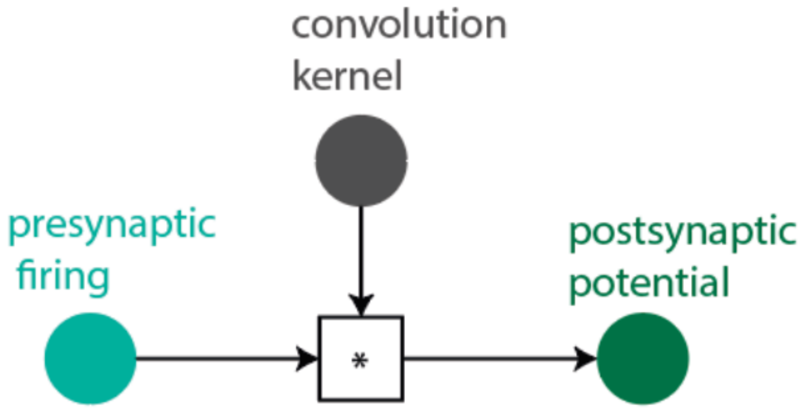


microscale



Transformation of presynaptic firing into post synaptic potential.

microscale



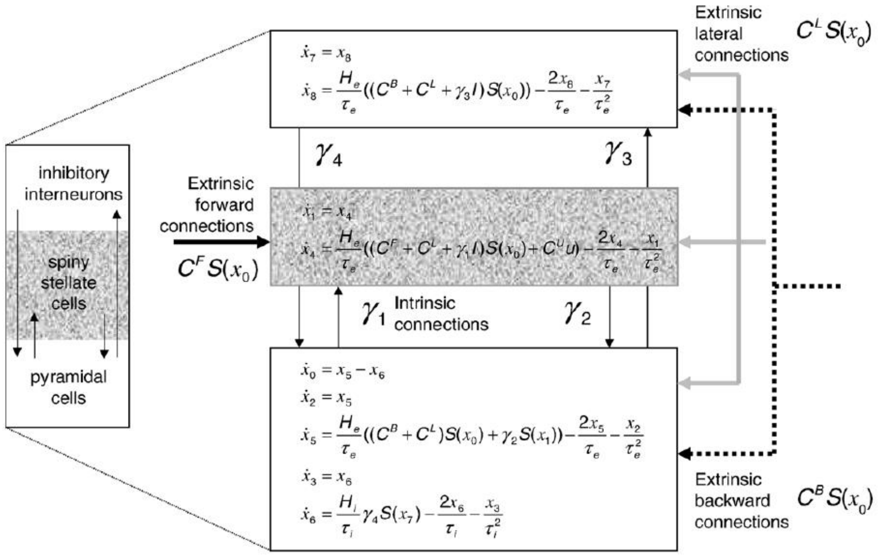
Current state of the population.

How much firing arrives.

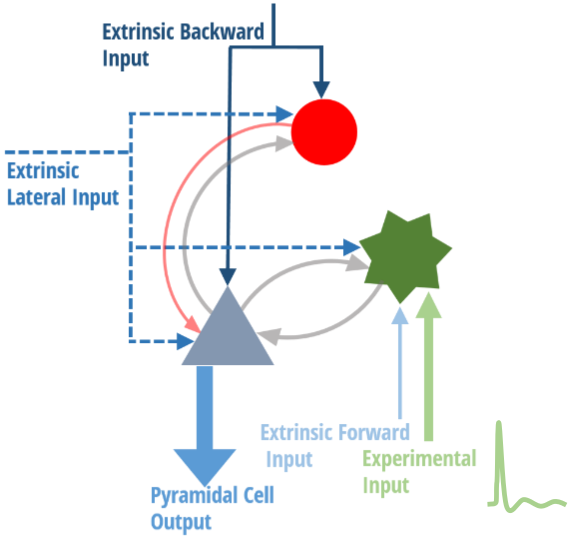
$$\frac{dx}{dt} = f(x, A, H, C, \sigma, f_s(\theta_{kernel}))$$

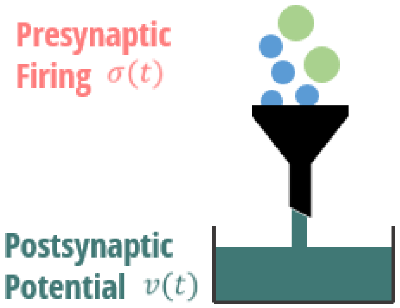
What the cell population is connected to.

The size of the kernel.

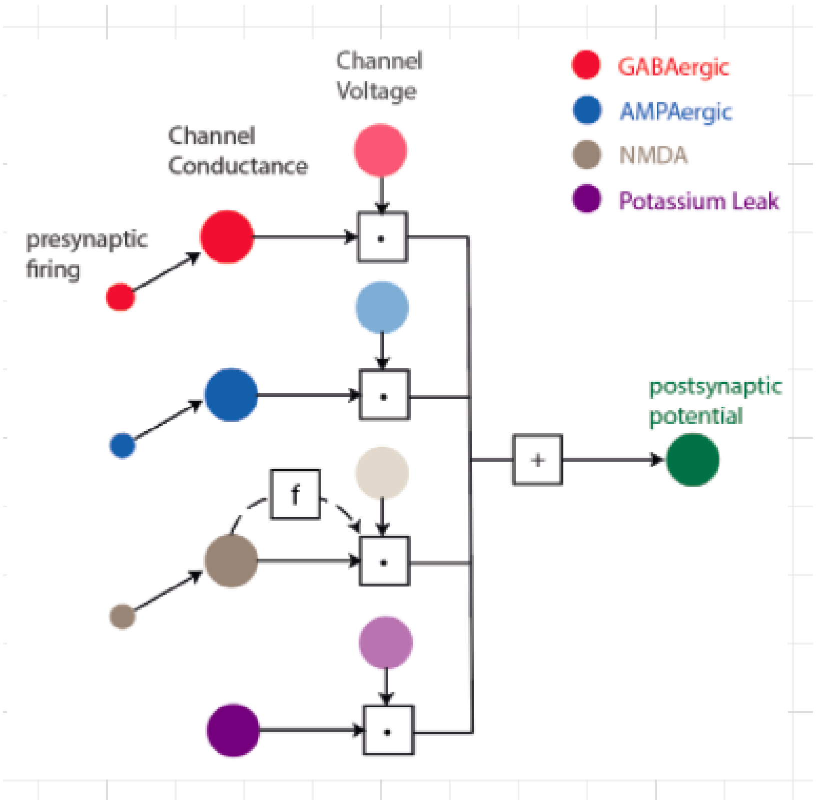


Single source model





microscale



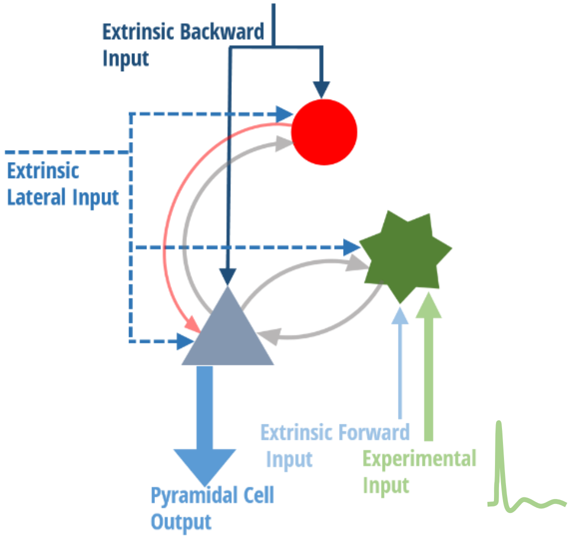
Current state of the population.

How much firing arrives.

$$\frac{dx}{dt} = f(x, A, H, C, \sigma, f_s(\theta_{conductance}))$$

Connection strengths

Channel resistance



S1

Extrinsic Cortical Input (u)

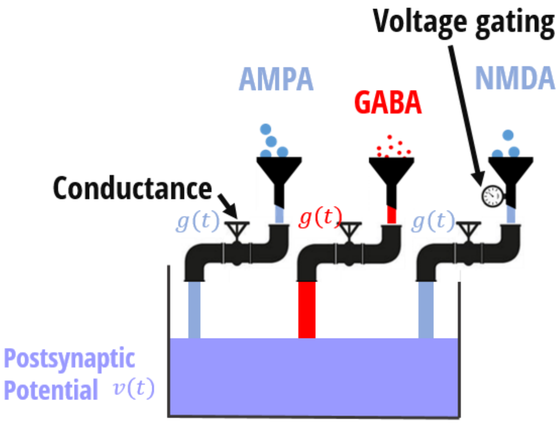
$$C\dot{V}^{(2)} = g_L(V_L - V^{(2)}) + g^{(2)}_{AMPA}(V_E - V^{(2)}) + g^{(2)}_{NMDA} f_{Mg}(V^{(2)})(V_E - V^{(2)}) + \Gamma_V$$
$$\dot{g}^{(2)}_{AMPA} = \kappa_{AMPA}(\gamma_{2,3}\sigma(\mu^{(3)}_V - V_R, \Sigma^{(3)}) - g^{(2)}_{AMPA}) + \Gamma_{AMPA}$$
$$\dot{g}^{(2)}_{NMDA} = \kappa_{NMDA}(\gamma_{2,3}\sigma(\mu^{(3)}_V - V_R, \Sigma^{(3)}) - g^{(2)}_{NMDA}) + \Gamma_{NMDA}$$

$\gamma_{3,2}$ $\gamma_{1,2}$ $\gamma_{2,3}$

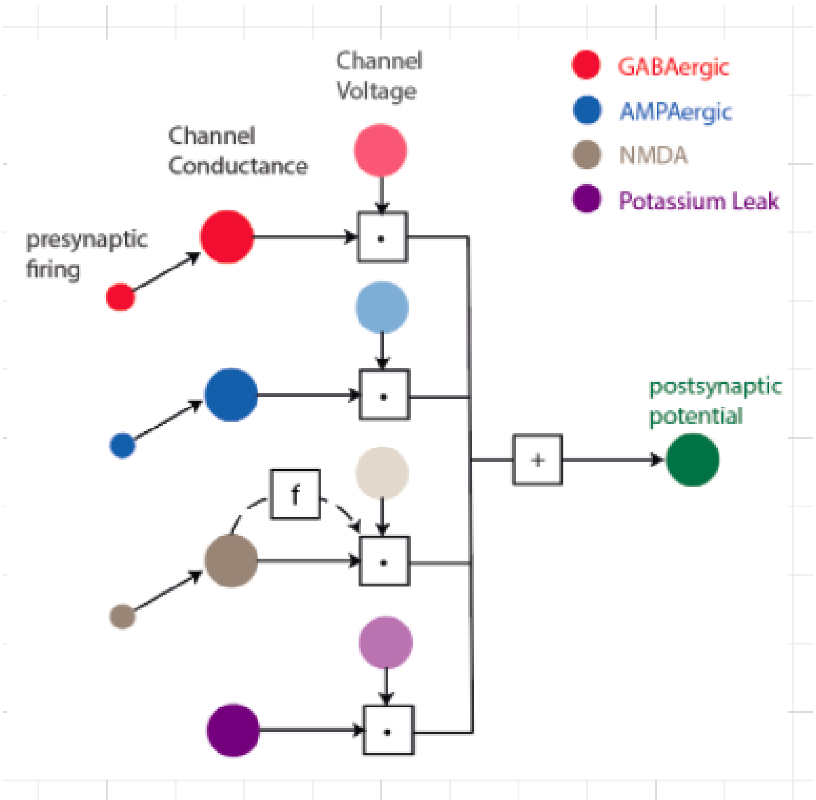
$$C\dot{V}^{(1)} = g_L(V_L - V^{(1)}) + g^{(1)}_{AMPA}(V_E - V^{(1)}) + g^{(1)}_{GABAa}(V_I - V^{(1)}) + u + \Gamma_V$$
$$\dot{g}^{(1)}_{AMPA} = \kappa_{AMPA}(\gamma_{1,3}\sigma(\mu^{(3)}_V - V_R, \Sigma^{(3)}) - g^{(1)}_{AMPA}) + \Gamma_{AMPA}$$
$$\dot{g}^{(1)}_{GABAa} = \kappa_{GABAa}(\gamma_{1,2}\sigma(\mu^{(2)}_V - V_R, \Sigma^{(2)}) - g^{(1)}_{GABAa}) + \Gamma_{GABAa}$$

$\gamma_{1,3}$ $\gamma_{3,1}$ $\gamma_{3,3}$

$$C\dot{V}^{(3)} = g_L(V_L - V^{(3)}) + g^{(3)}_{AMPA}(V_E - V^{(3)}) + g^{(3)}_{NMDA} f_{Mg}(V^{(3)})(V_E - V^{(3)}) + g^{(3)}_{GABAa}(V_I - V^{(3)}) + \Gamma_V$$
$$\dot{g}^{(3)}_{AMPA} = \kappa_{AMPA}([\gamma_{3,1}\sigma(\mu^{(1)}_V - V_R, \Sigma^{(1)}) + \gamma_{3,3}\sigma(\mu^{(3)}_V - V_R, \Sigma^{(3)})] - g^{(3)}_{AMPA}) + \Gamma_{AMPA}$$
$$\dot{g}^{(3)}_{NMDA} = \kappa_{NMDA}([\gamma_{3,1}\sigma(\mu^{(1)}_V - V_R, \Sigma^{(1)}) + \gamma_{3,3}\sigma(\mu^{(3)}_V - V_R, \Sigma^{(3)})] - g^{(3)}_{NMDA}) + \Gamma_{NMDA}$$
$$\dot{g}^{(3)}_{GABAa} = \kappa_{GABAa}(\gamma_{3,2}\sigma(\mu^{(2)}_V - V_R, \Sigma^{(2)}) - g^{(3)}_{GABAa}) + \Gamma_{GABAa}$$



microscale



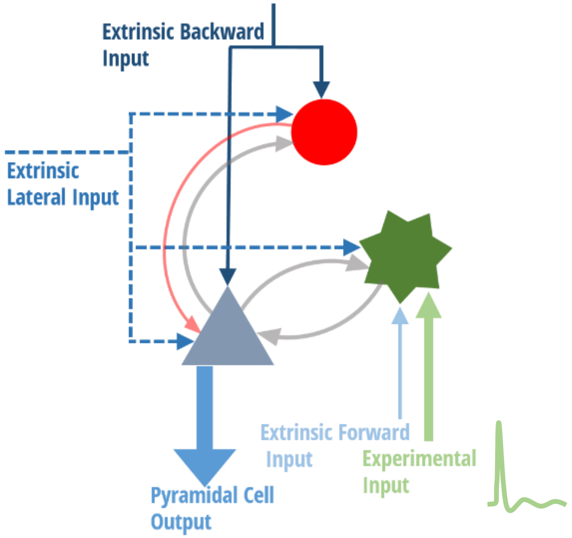
Current state of the population.

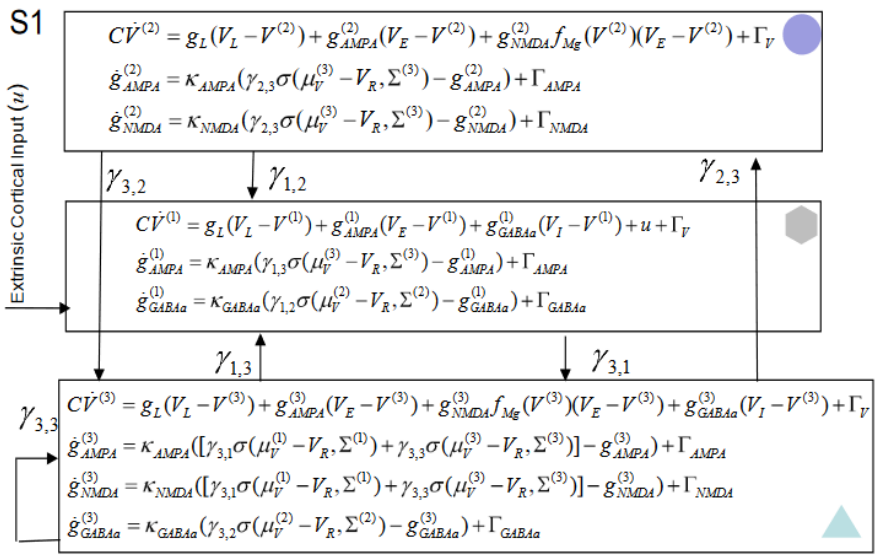
How much firing arrives.

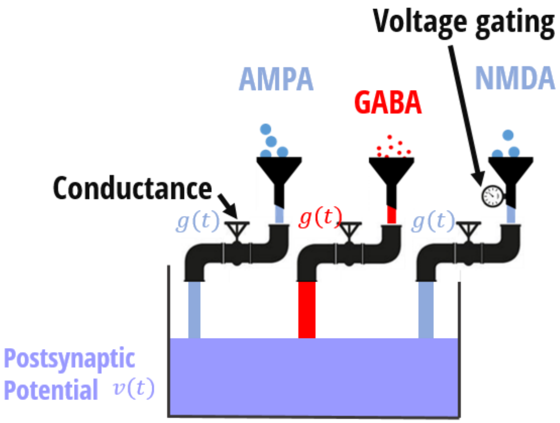
$$\frac{dx}{dt} = f(x, A, H, C, \sigma, f_s(\theta_{conductance}))$$

Connection strengths

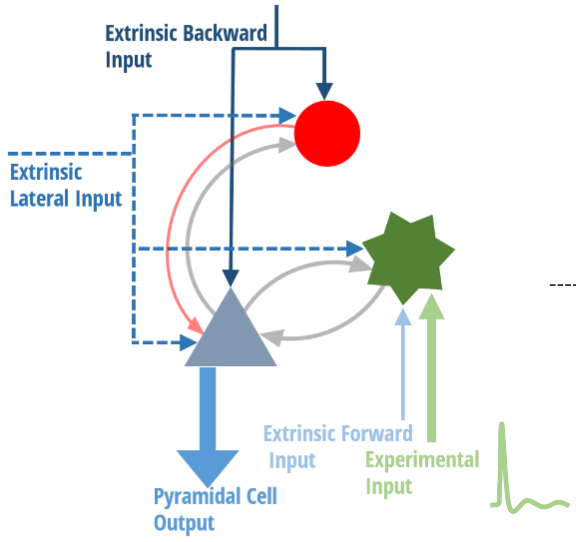
Channel resistance





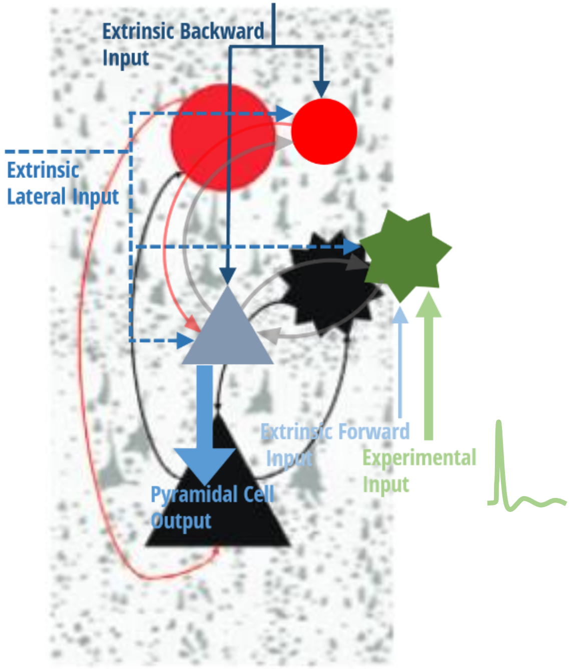


mesoscale



Structure of the cortical column

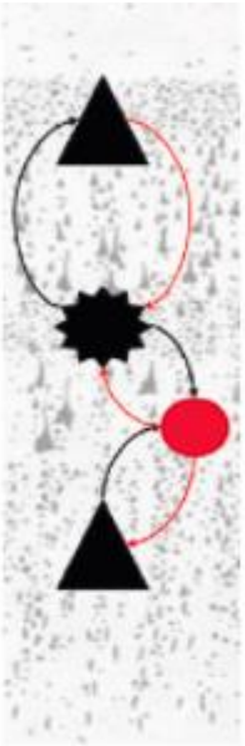
mesoscale



ERP model:

- Inhibitory Population
- Stellate Population
- Pyramidal Population

mesoscale



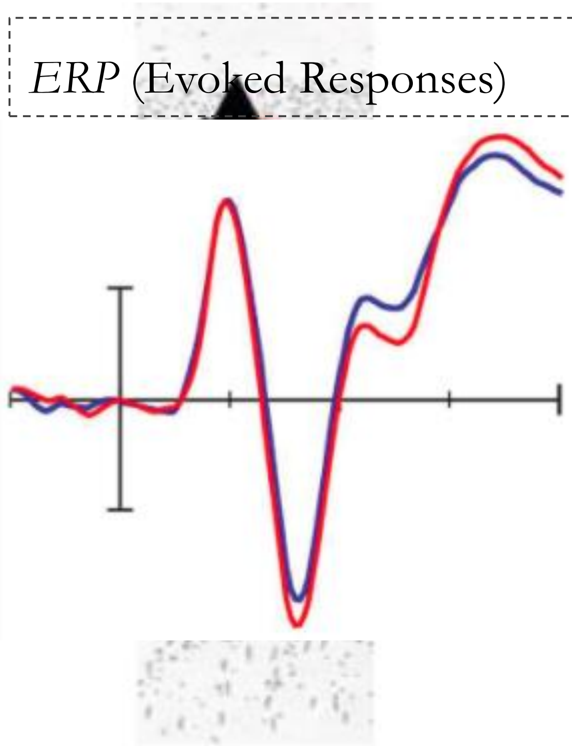
CMC (Canonical Microcircuit Model)

- Inhibitory Population
- Stellate Population
- 2 x Pyramidal Population:
    - Predictive Coding

mesoscale

data

ERP (Evoked Responses)

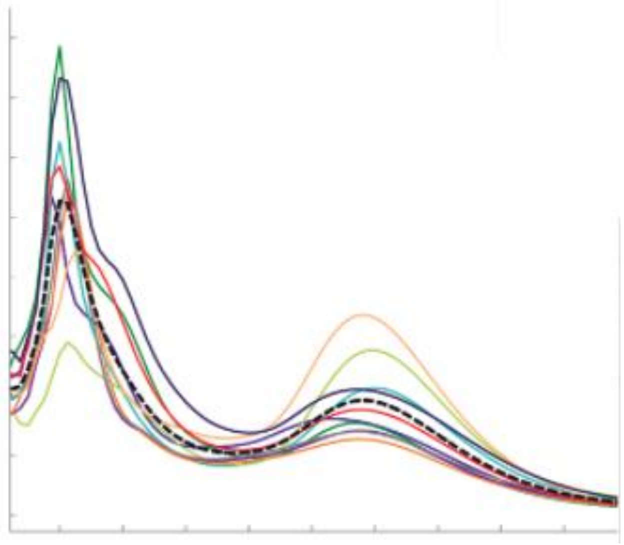


CMC (Canonical Microcircuit Model)

- Inhibitory Population
- Stellate Population
- 2 x Pyramidal Population:
    - Predictive Coding

data

CSD Cross spectral densities

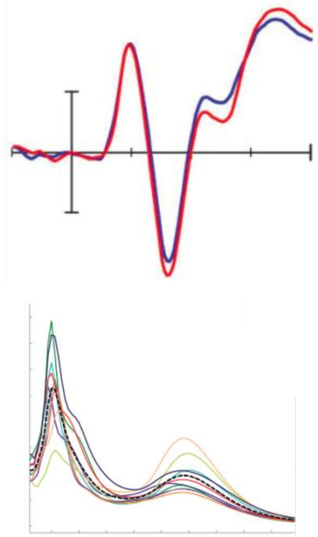


Inverse Problem: Inference

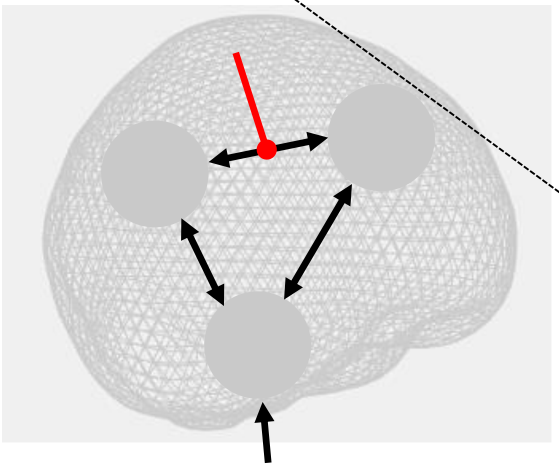
$p(\theta, \Sigma | y)$

One can only infer on mechanisms, that have actually been modeled.

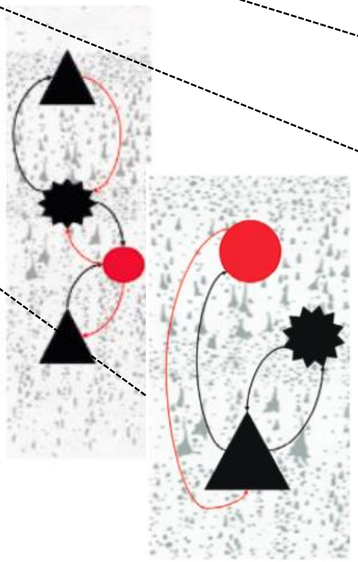
data	macroscale	mesoscale	microscale



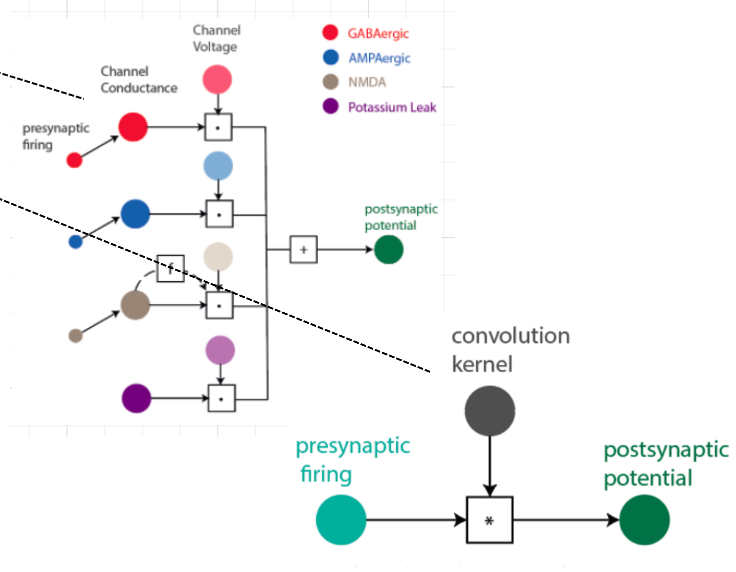
Data features



Network and modulation structure



Layered Structure of the cortical column



Mechanisms governing generation of average post-synaptic potentials:

Many thanks Cao Tri Do for some of the slides!

Citations

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