Neural Information Processing: Normal and Pathological

Péter Érdi

Center for Complex Systems Studies, Kalamazoo College,
Kalamazoo, MI 49006 and

Department of Biophysics, KFKI Research Institute for Particle and Nuclear Physics of the Hungarian Academy of Sciences
Budapest, Hungary

KALAMAZOO COLLEGE

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Center for Complex Systems Studies

K HOME

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web@kzoo.edu

Comments for CCSS specific pages

The Computational Neuroscience Group

Department of Biophysics
KFKI Research Institute for Particle and Nuclear Physics
of the Hungarian Academy of Sciences
Budapest, Hungary

H-1121 Budapest, Konkoly-Thege út 29-33
Mail address: P.O.Box 49, H-1525 Budapest, Hungary
Phone: +36 (1) 392-2222
Fax: +36 (1) 392-2742

Welcome to our homepage. We hope you will enjoy our pages and wish you good luck for navigating through them. Although we try to do our best to make this site as interesting, fascinating and up-to-date as possible and at the same time also easy to handle and hard to get lost in, still you must keep in mind that the contents are under construction, constant rewriting and reediting so you might meet some errors or signs of uncompleteness - for which we apologize.

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- BRAIN: Methods, Levels, Representations, Computation
- NEUROLOGICAL DISORDERS AS DYNAMICAL DISEASES
- ANXIETY
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BRAINS: Methods, levels, representations, computation

Brains

- Experimental methods and disciplines

- Levels

- Neural representation: cells, networks, modules

- Neural computation versus computational neuroscience

Experimental methods and disciplines

- Anatomy: discover the structure of the brain
- Electrophysiology
  - Single cell recording
  - Electroencephalography (EEG)
- Psychological experiments on people with brain damage, e.g. HM
- Brain imaging

Brain imaging

- EEG and MEG
- CT or CAT: Computerized axial tomography
- PET : Positron emission tomography
- fMRI: Functional magnetic resonance imaging

EEG and MEG

EEG is an acronym for Electroencephalograph

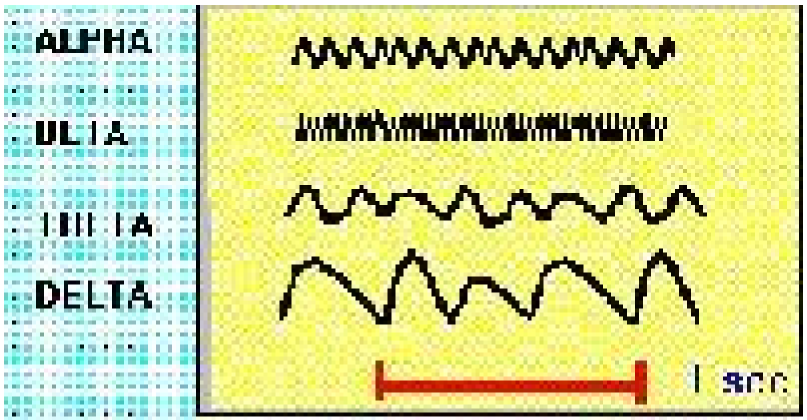
This is a recording (”graph”) of electrical signals (”electro”) from the brain (”encephalo”)

electroencephalographs from humans: Hans Berger (1929)

The skull has low conductivity to electric current but is transparent to magnetic fields, the measurement sensitivity of the magnetoencephalography (MEG)

in the brain region should be more concentrated than that of the electroencephalography (EEG).

BRAIN WAVES
normal, pathological



EEG and MEG: relatively good temporal resolution ($\sim$ms), poor spatial resolution

detection of lesions

Computerized axial tomography

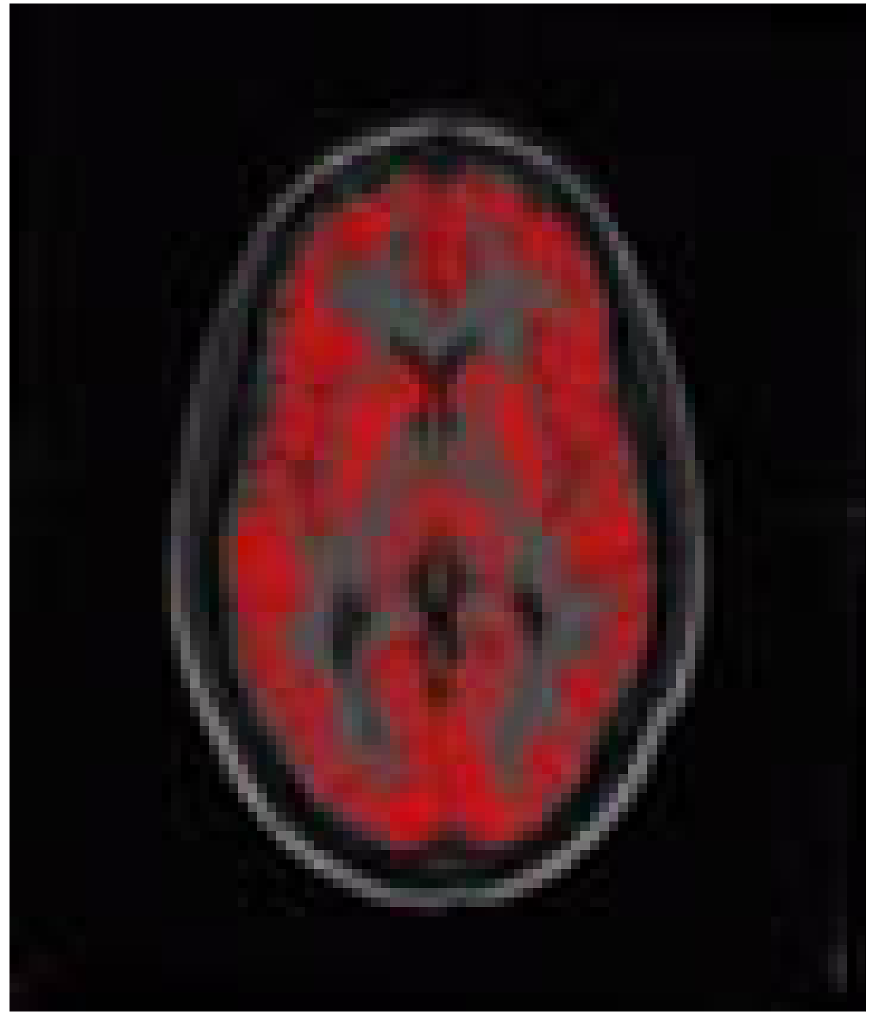
- A computerized axial tomography scan: CAT scan or CT scan
- It is an x-ray procedure which combines many x-ray images with the aid of a computer to generate cross-sectional views and
- 3D images of the internal organs and structures
- CAT scan is used to define normal and abnormal structures in the body
- Nobel prize in medicine: 1979
- Hounsfield and Cormack

Positron emission tomography

"hemodynamic" changes

first scanning method to give FUNCTIONAL information on the brain

measures the emission of positrons from the brain after a small amount of radioactive isotopes, or tracers, have been injected into the blood stream. A common example is a glucose-relative with embedded fluor-18. With this molecule, the activity of different regions of the brain can be measured. The result is a three-dimentional map with the brain activity represented by colors.



function

Functional magnetic resonance imaging

- Head is inserted into a giant circular magnet
- The magnet realigns atoms and protons
- Machine sends a radio pulse that causes atoms to release energy
- A computer detects energy release and produces an image
- Functional MRI measures brain function by measuring changes in blood volume
- Possible to map functions down to a few millimeters

Sample results: `http://www.fmrib.ox.ac.uk/`

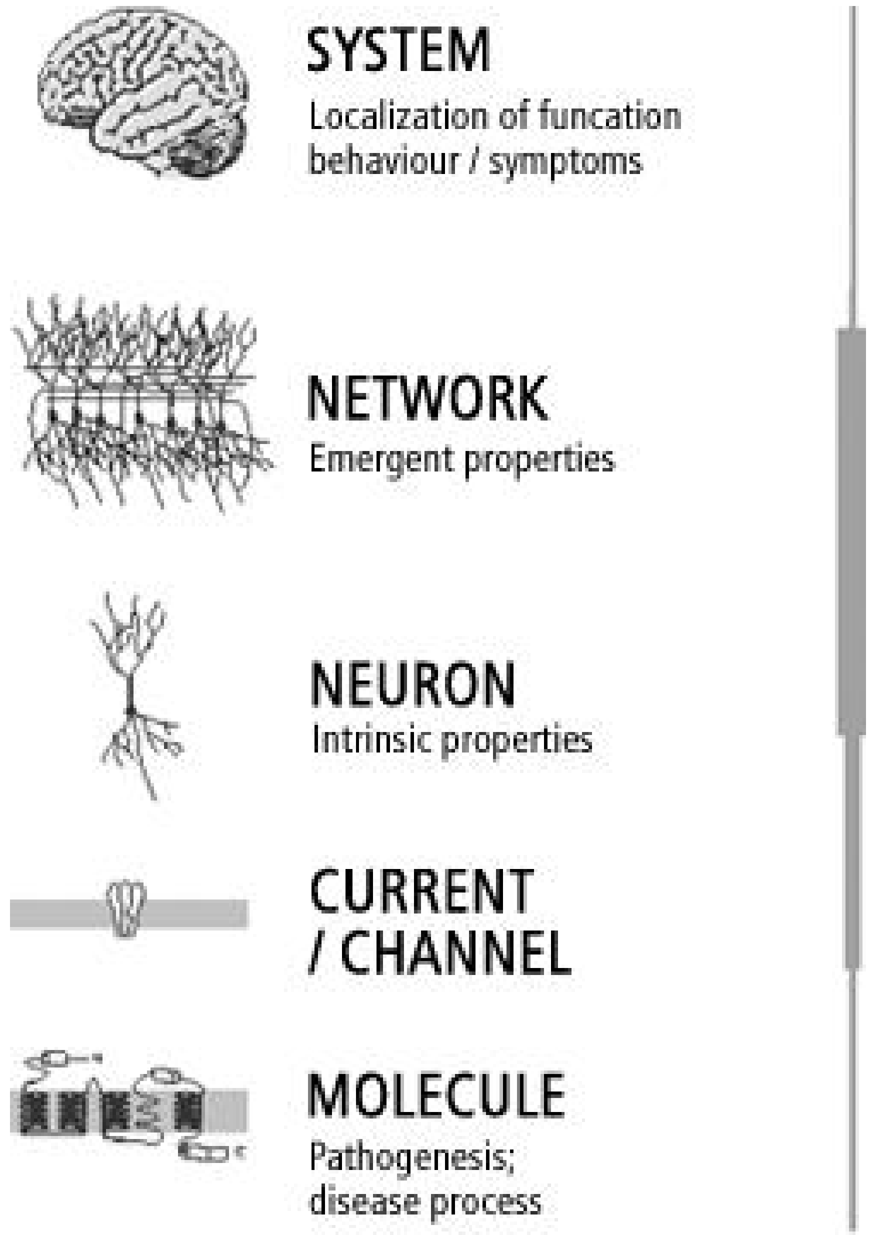
Functional magnetic resonance imaging

Limitations of fMRI

- Makes strong assumptions about relation between brain activity and blood flow
- Numerous calculations required
- Low temporal resolution because of sluggish metabolic response

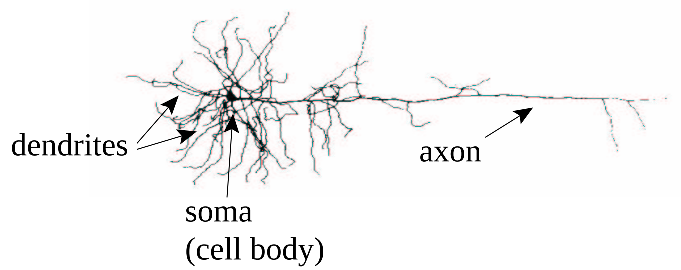
LEVELS

Levels

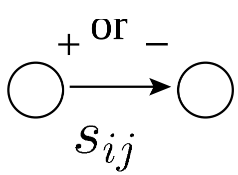

SYSTEM
Localization of funcation
behaviour / symptoms
NETWORK
Emergent properties
NEURON
Intrinsic properties
CURRENT
/ CHANNEL
MOLECULE
Pathogenesis;
disease process

Hierarchy of dynamics

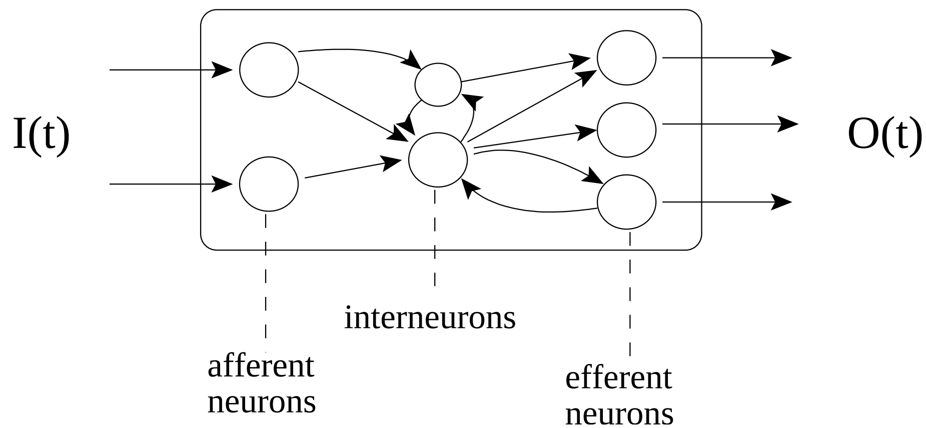
- Neuron



- Synapse



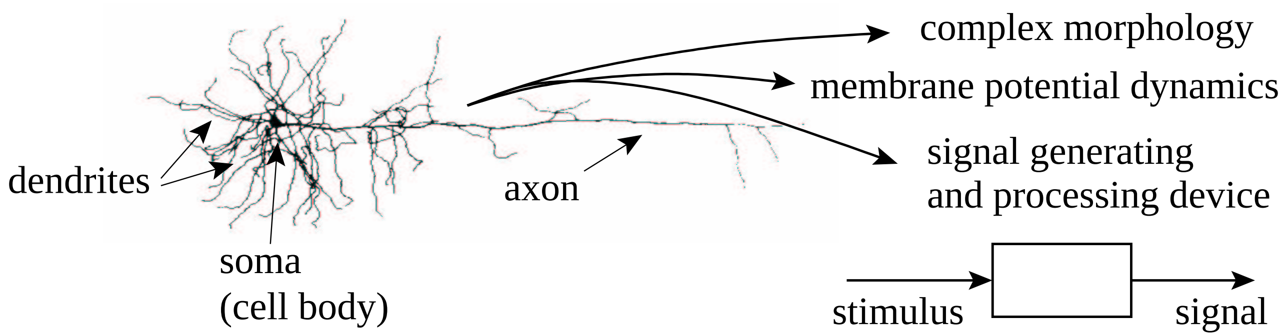
- Network



Hierarchy of dynamics

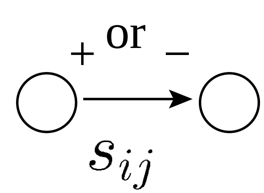
Neuron and synapse

Neuron



Synapse

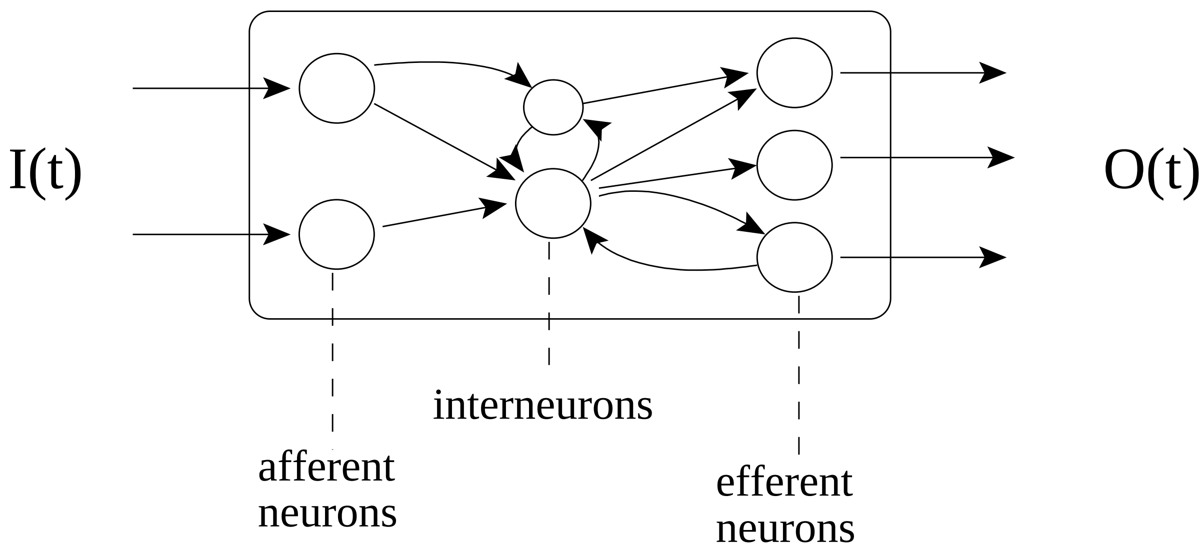
- structural and functional connection between cells specialized for trasferring information
- neurochemically mediated synapses (mostly)
- excitatory and inhibitory
- synaptic strength (synaptic weight, synaptic efficacy)
- $\frac{d}{dt} s_{ij}(t) \longleftrightarrow$ learning



Hierarchy of dynamics

Network

Network

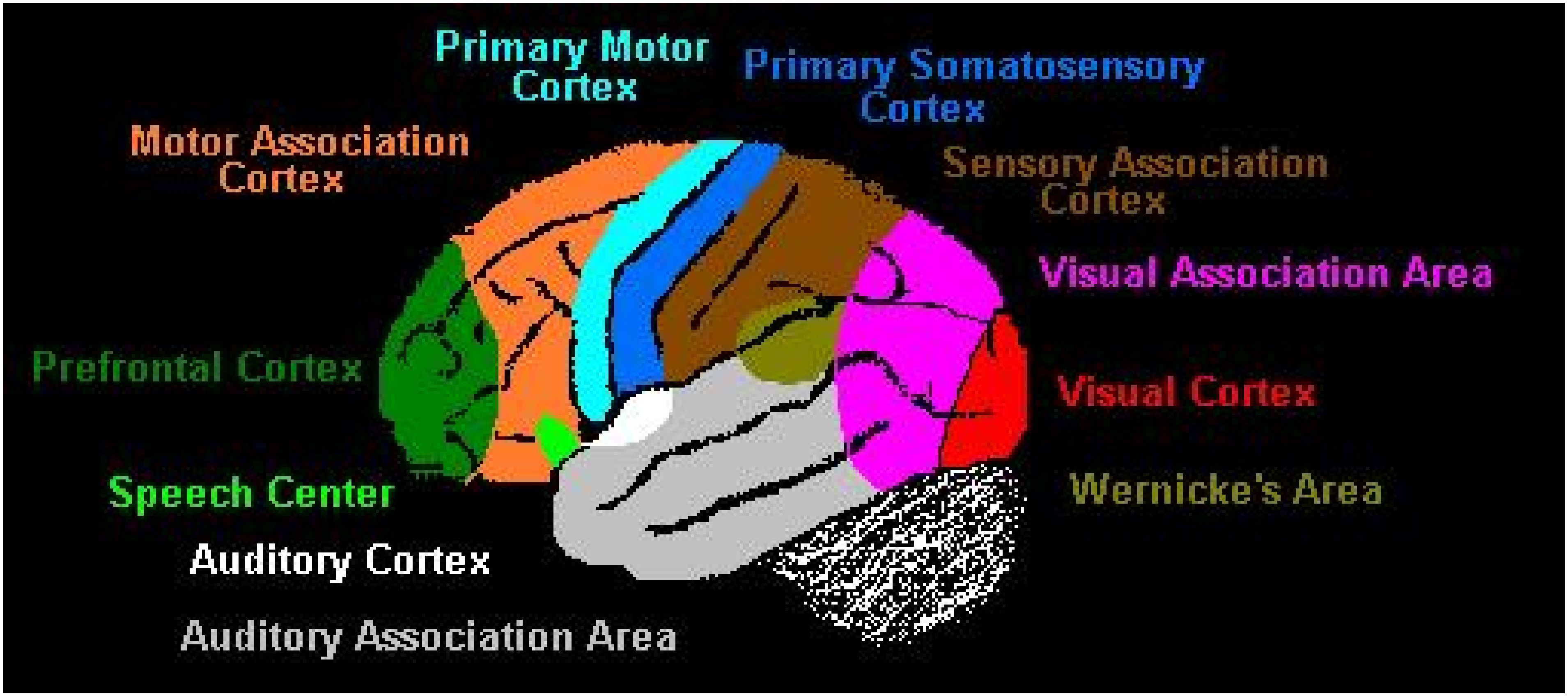


$\frac{d}{dt} s_{ij}(t) = 0 \longrightarrow$ fixed wiring

$\frac{d}{dt} s_{ij}(t) \neq 0$ → pattern formation problems

→ pattern recognition problems

Large-scale organization

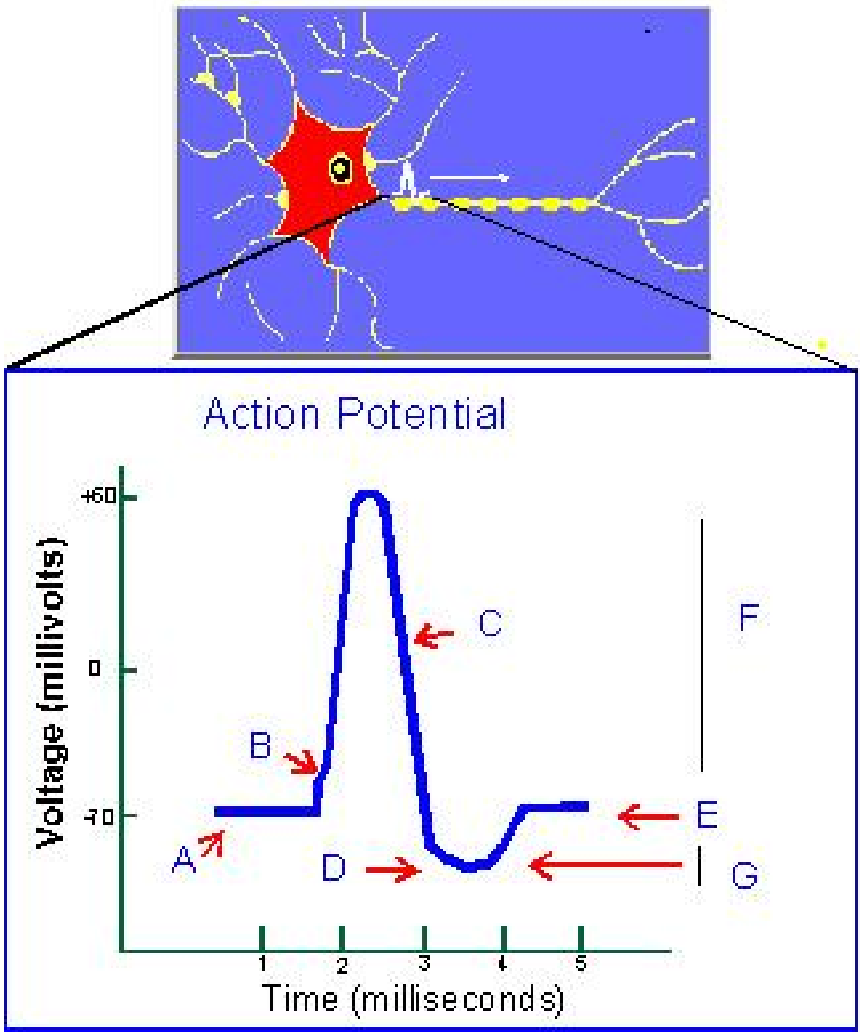


Large-scale organization

Cortical Area	Function
Prefrontal Cortex	Problem Solving, Emotion, Complex Thought
Motor Association Cortex	Coordination of complex movement
Primary Motor Cortex	Initiation of voluntary movement
Primary Somatosensory Cortex	Receives tactile information from the body
Sensory Association Area	Processing of multisensory information
Visual Association Area	Complex processing of visual information
Visual Cortex	Detection of simple visual stimuli
Wernicke's Area	Language comprehension
Auditory Association Area	Complex processing of auditory information
Auditory Cortex	Detection of sound quality (loudness, tone)
Speech Center (Broca's Area)	Speech production and articulation

Neural representation: cells, networks, modules

Representation with neurons and populations of neurons



A. Resting membrane potential.

B. If voltage change surpasses this value, the depolarization automatically goes to its maximum value.

C. If a stimulus arrives during this phase of the potential it can not stimulate the neuron.

D. Only a very strong stimulus can stimulate the neuron during this phase.

E. Resting potential.

F. Absolute refractory period.

G. Relative refractory period.

Neural representation: cells, networks, modules

Representation with neurons and populations of neurons

A typical neuron can fire as much as 100 times per second.

Spike train of a neuron: its pattern of firing or not firing over a period of time.

10100 and 00011: both involve a neuron with a firing rate of 2 times out of 5

”rate code” vs. ”temporal code”

Is there, at some high level, a cell so specialized that it only signals when viewing a particular object?

This is the idea of grandmother cells: a single cell might be responsible for signalling the presence of a single stimulus, for example, your grandmother.

sharp debate on ”grandmother cell”

Neural representation: cells, networks, modules

Representation with neurons and populations of neurons II.

Do we really have a certain nerve cell for recognising the concatenation of features representing our grandmother(s)?

Population (ensemble) code: Perception depends on the combined output of a group (ensemble) of cells

not on the ouput of any one cell in particular.

Both natural and most artificial neural networks use distributed representations

oncepts are encoded by a population of neurons: a group of neurons represents a concept by virtue of a pattern of firing rates in all of the neurons.

Thus a group of neurons, each with its own firing rate, can encode a large number of aspects of the world.

Neural representation: cells, networks, modules

Modules of the visual cortex

Different brain regions represent different kinds of sensory stimuli

visual cortex: has neurons that respond to different visual inputs

orientation selectivity, position selectivity, colour selectivity, direction selectivity

the response of each of these cells is dominated by one eye

binocular integration: ocular dominance columns

Neural computation

Is the brain a computer?

computation: transformation of representations

$2 + 3 = 5$

p-$>$q, p; so q

Brain: performs transformations of representations encoded by the firing patterns of neurons

Retinal cells:

respond to light reflected from objects into your eye, and send signals through a series of layers of neurons in the visual cortex.

Successive layers:

detect more and more complex aspects of the objects that originally sent light into the eye, as neurons in each layer abstract and transform the firing patterns of neurons in the preceding layer

Visual cortex:

progressively constructs representations of lines, patterns in two dimensions, and finally three-dimensional colored objects

GENETIC versus DYNAMICAL DISEASES

genetic disease:
caused by abnormalities in an individuals genetic material (genome).

There are four different types of genetic disorders:

- single-gene
- multifactorial
- chromosomal
- mitochondrial

even genetic disorders have dynamic aspects

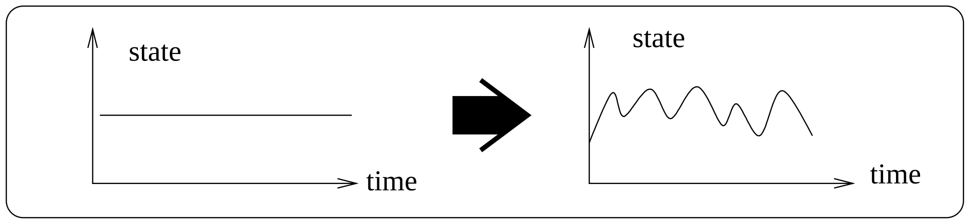
NEUROLOGICAL DISORDERS AS DYNAMICAL DISEASES I

Dynamical disease occurs due to the impairment of the control system: associated to ‘abnormal’ dynamics

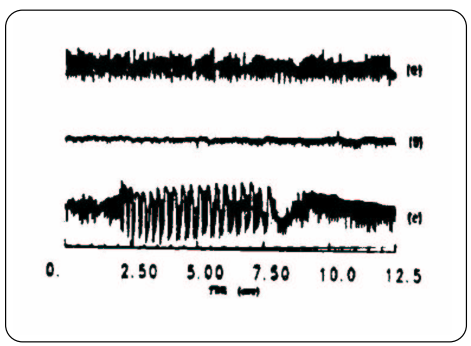
- Develop realistic mathematical models and study effects of parameter changes
- Neurobiological interpretation
- Integration of molecular, cellular and system neuroscience
- Therapeutic strategies

NEUROLOGICAL DISORDERS AS DYNAMICAL DISEASES II

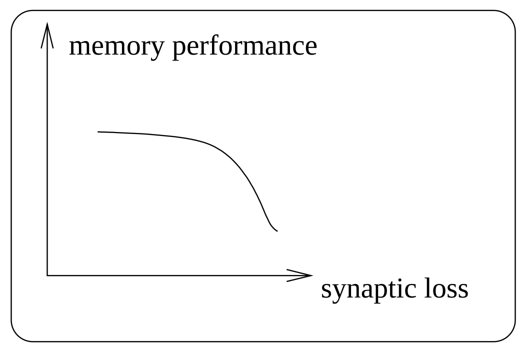
CHANGES in Qualitative Dynamic States



Parkinson disease



Epilepsy



Alzheimer disease

EPILEPSY

Cellular and Network Mechanisms of Epileptogenesis

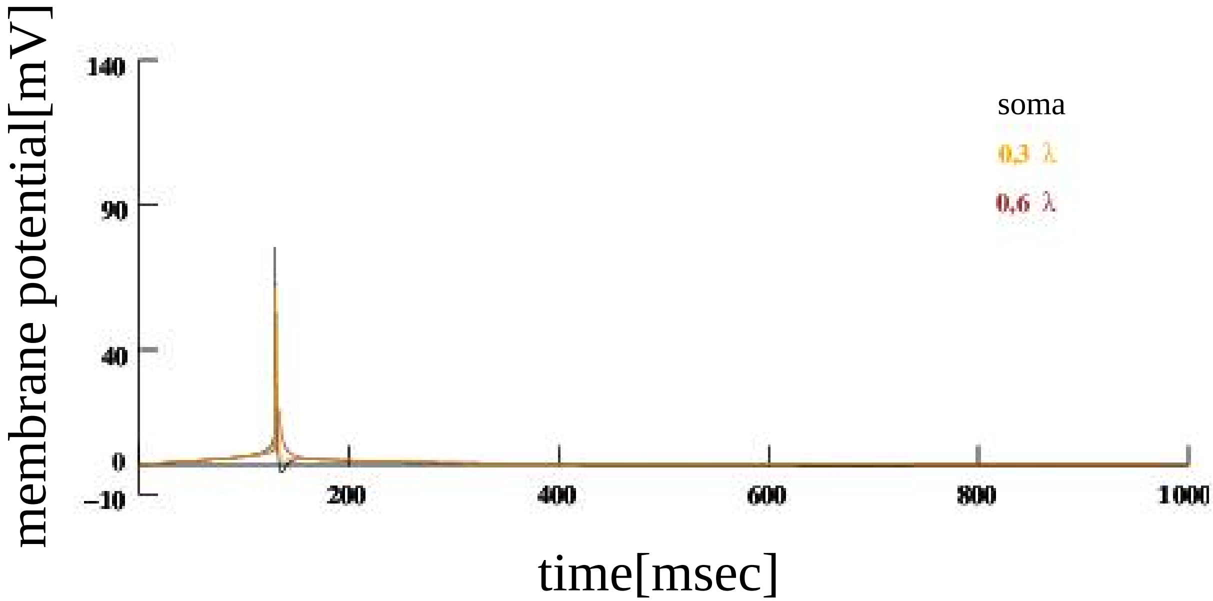
1. epileptic neuron hypothesis:
   - altered intrinsic firing properties
   - individual neurons
   - spontaneous bursting

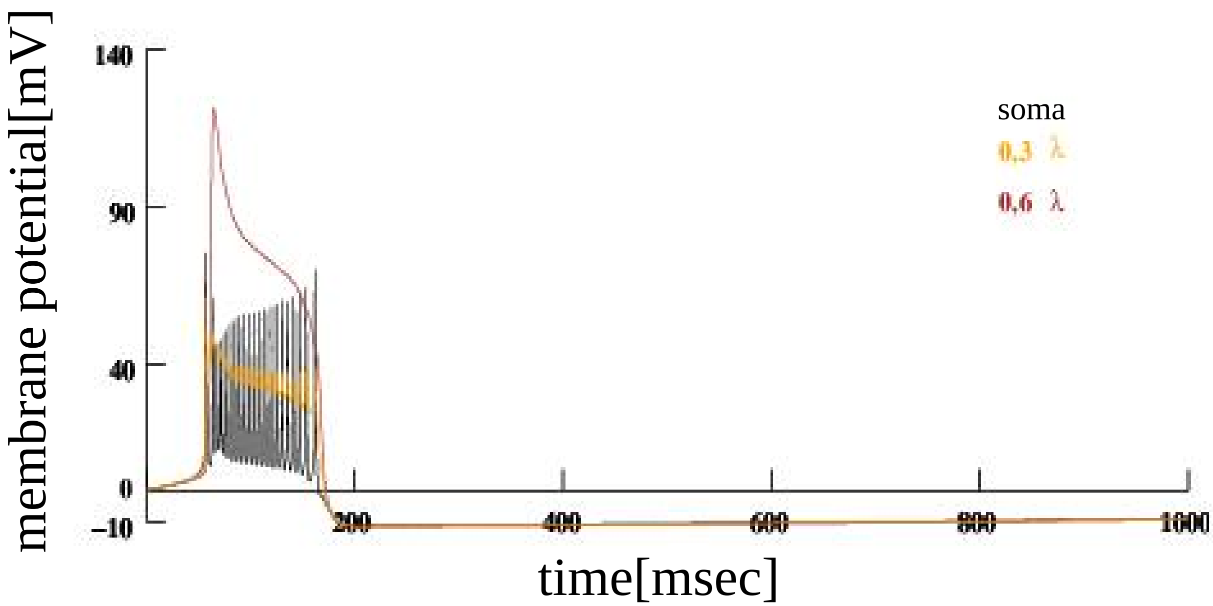
2. epileptic aggregate hypothesis:
   - aberrant connectivity
   - recurrent excitations
   - normal neurons are driven into burst

Probably both are true

EPILEPSY

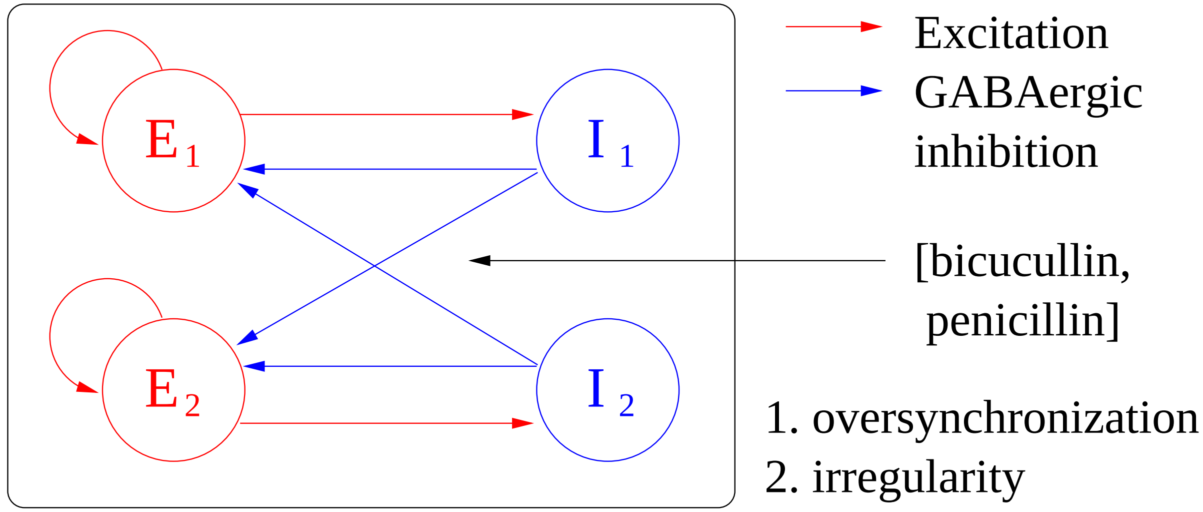
- Typical single cell effects: many possible changes in dynamics of ion-currents can result similar pathological activity.
- Increasing of Ca^{2+} conductance can transform a simple spiker cell to burster.

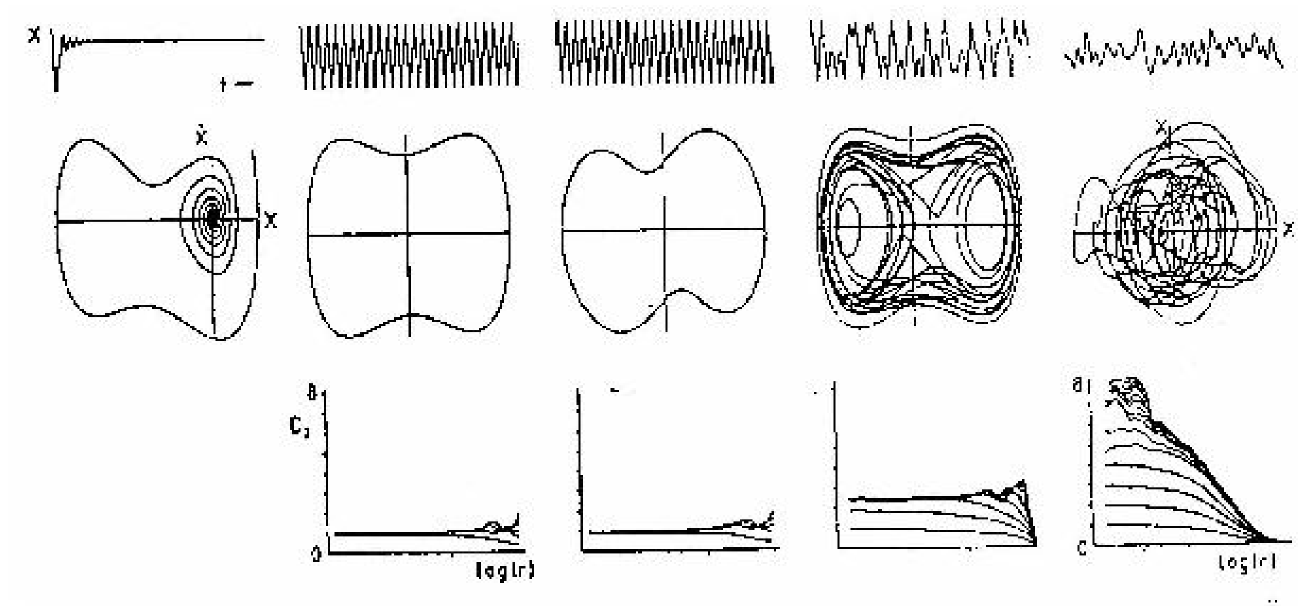




EPILEPSY

- Epileptic seizures in hippocampus and in certain cortical areas
- Large amplitide, quick waves in EEG records





Antiepyleptic drugs to influence $GABA_A$ transmission.

EPILEPSY

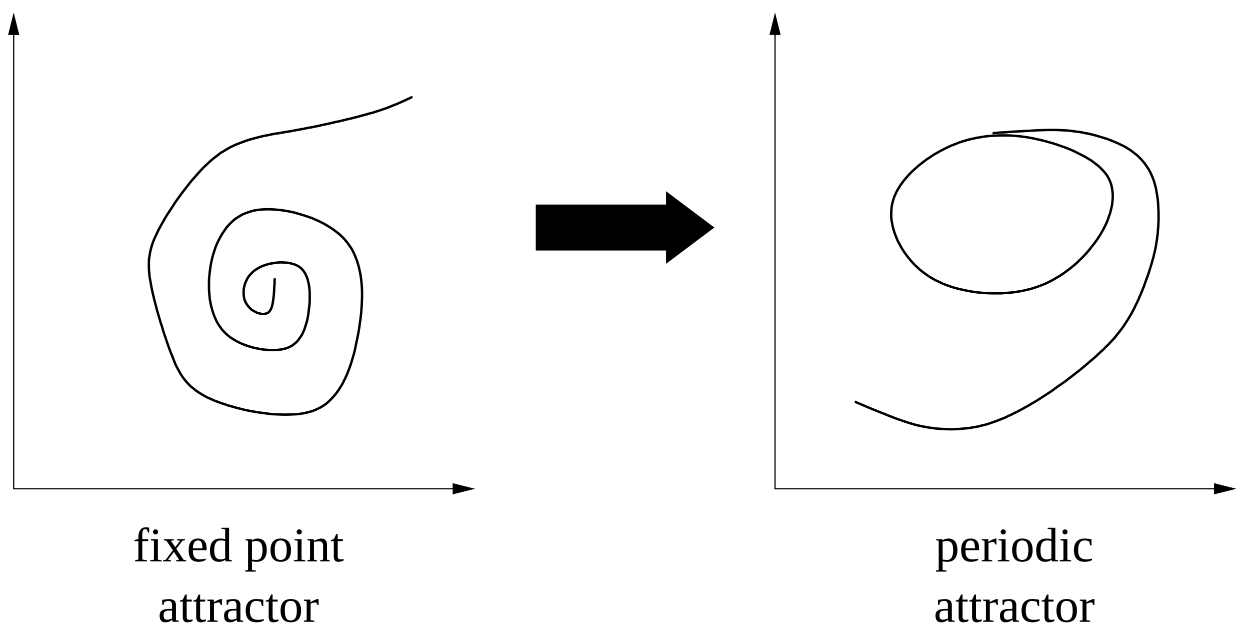
- predicting epileptic seizures (earthquakes, stock market crashes?)
- seizure control (feedback, electric fields: S. Schiff)
- general theory? (Milton and Jung)

PARKINSON DISEASE

(hypokinesia, dyskinesia)

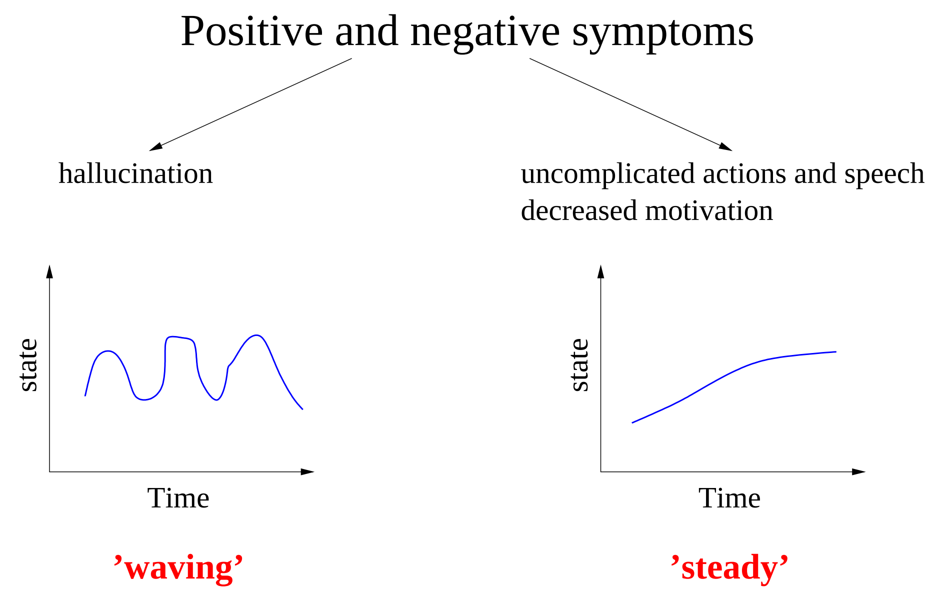
- Decrease of DOPA neuron's number (approx. 80%) in Substantia Nigra.
- Examination of the effect of DOPA using neuron network models.

$$\text{DOPA} \rightarrow \left\{ \begin{array}{l} \text{excitation} \\ \text{threshold} \end{array} \right. \quad \text{decrease}$$



- Modification of Central Pattern Generators

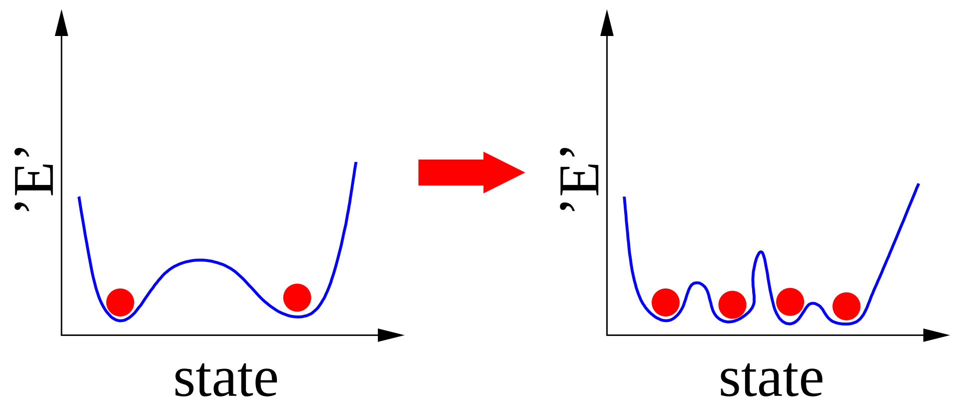
SCHIZOPHRENIA



Models:

- 'lesion models' does not explain waving
- neurotransmitter model (DOPA)
- disconnection hypothesis
- NMDA: delayed maturation of NMDA receptors
- cortical pruning (synaptic depression)

storage and recall of memory traces

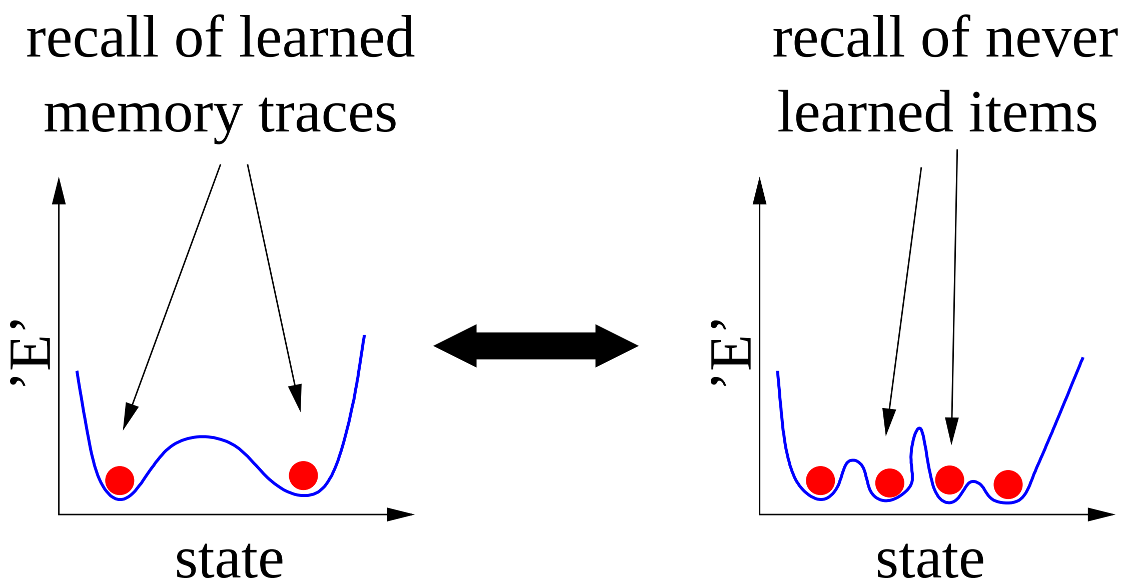


changes in attractor structure
pathological attractors

SCHIZOPHRENIA

THE NMDA RECEPTOR DELAYED MATURATION HYPOTHESIS

Pathological attractors appear

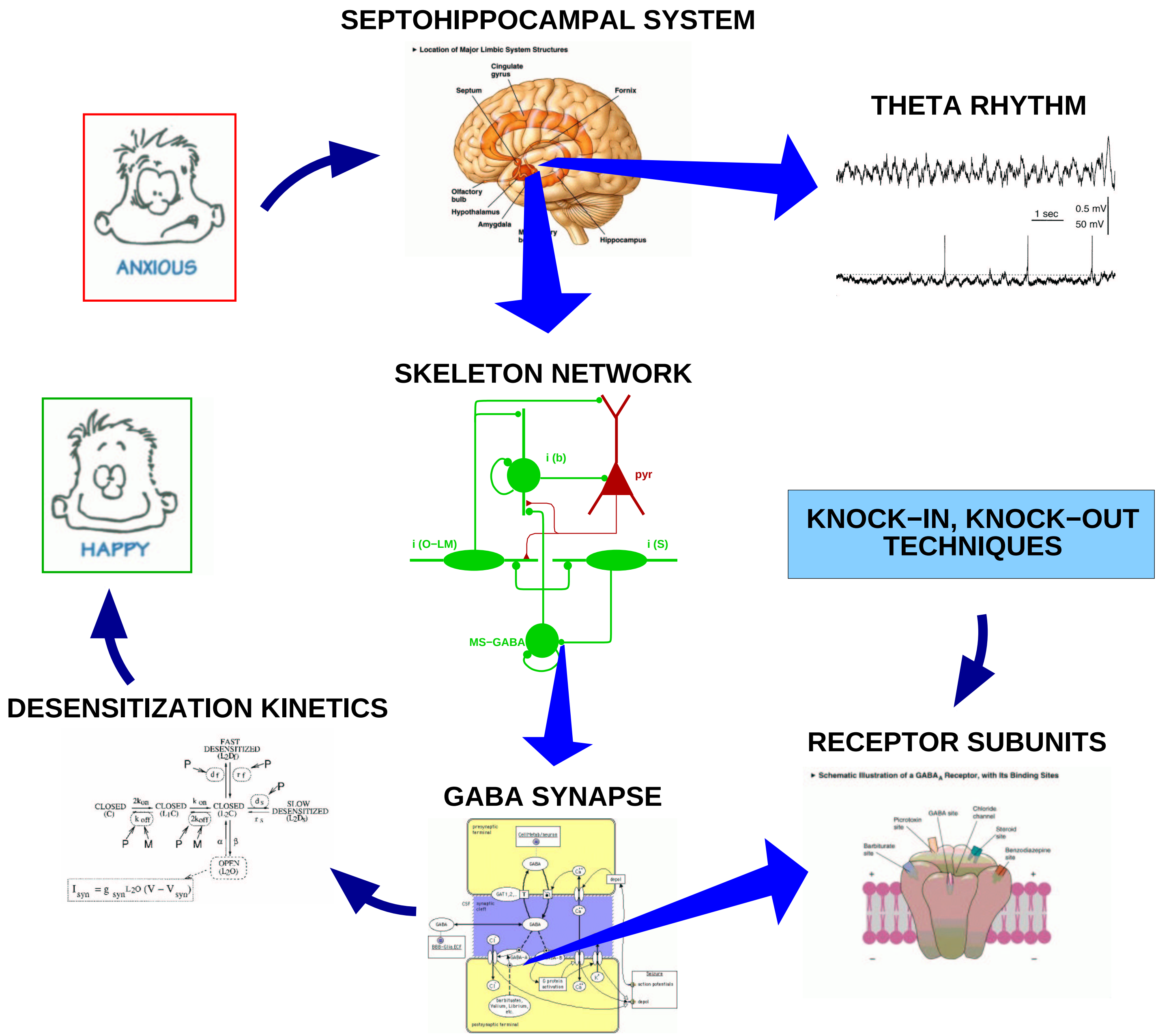


'delusion'
'hallucination'

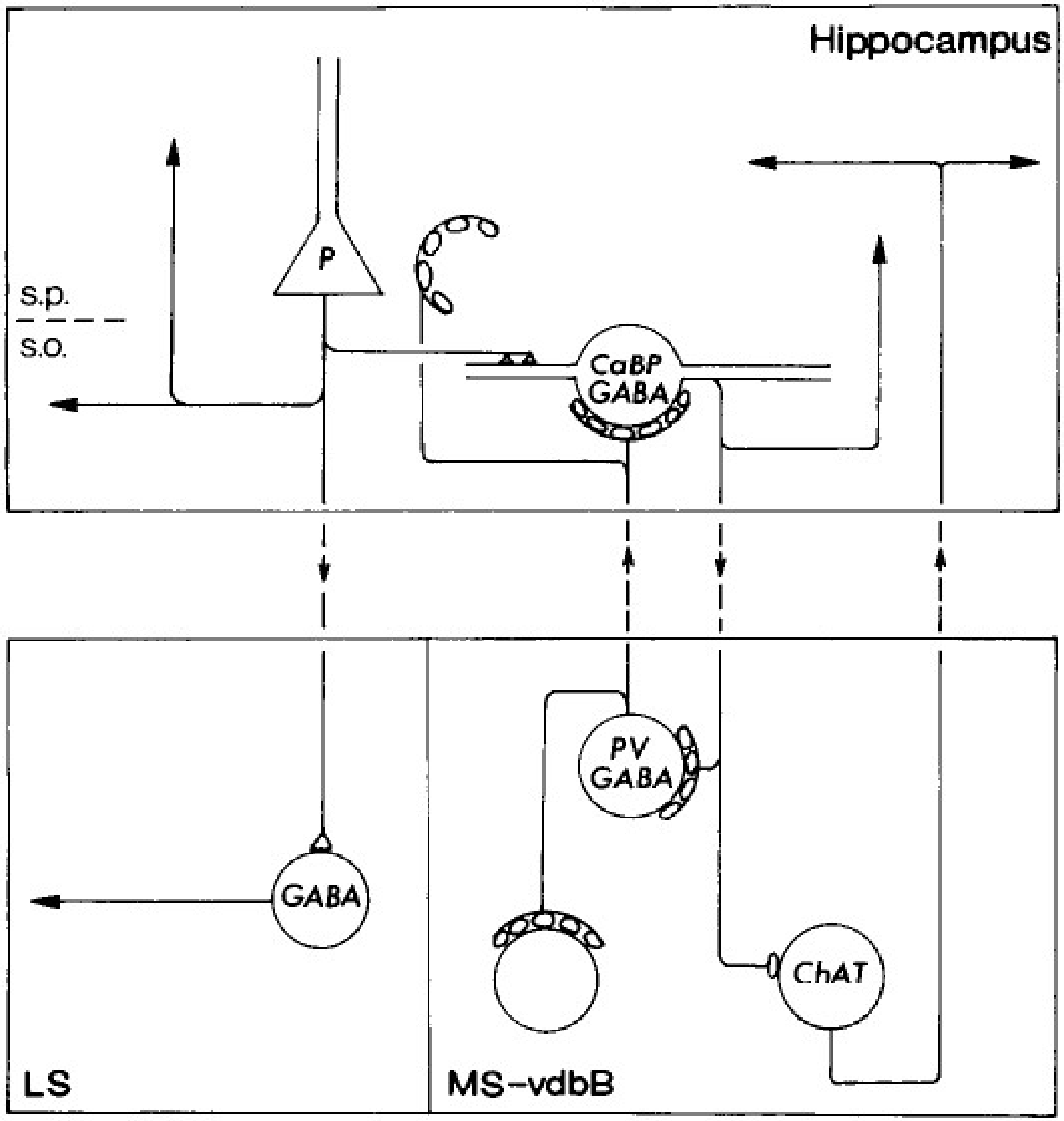
Anxiety

A disorder characterized by generalized and persistent free-floating anxiety (anxiety not restricted to any particular event or circumstance). The symptoms are variable, and can include muscle tension, continuous feelings of nervousness, trembling, sweating, lightheadedness, dizziness, palpitations. A variety of worries are often expressed, including the worry that the sufferer or a relative will have an accident or become ill. Sleep disturbance is common. Generalized Anxiety Disorder is more common in women than men. One factor in its development appears to be chronic stress. Its course varies, but tends to be fluctuating and chronic.

Overview


SEPTOHIPPOCAMPAL SYSTEM
Location of Major Limbic System Structures
Cingulate gyrus
Septum
Fornix
Olfactory bulb
Hypothalamus
Amygdala
Hippocampus
THETA RHYTHM
1 sec
0.5 mV
50 mV
ANXIOUS
SKELETON NETWORK
i (b)
pyr
i (O–LM)
i (S)
MS–GABA
HAPPY
KNOCK–IN, KNOCK–OUT TECHNIQUES
DESENSITIZATION KINETICS
FAST DESENSITIZED
SLOW DESENSITIZED
CLOSED (C)
CLOSED (L1C)
CLOSED (L2C)
OPEN (L2O)
GABA SYNAPSE
RECEPTOR SUBUNITS
Schematic Illustration of a GABAA Receptor, with Its Binding Sites
GABA site
Chloride channel
Picrotoxin site
Steroid site
Barbiturate site
Benzodiazepine site

The septohippocampal system



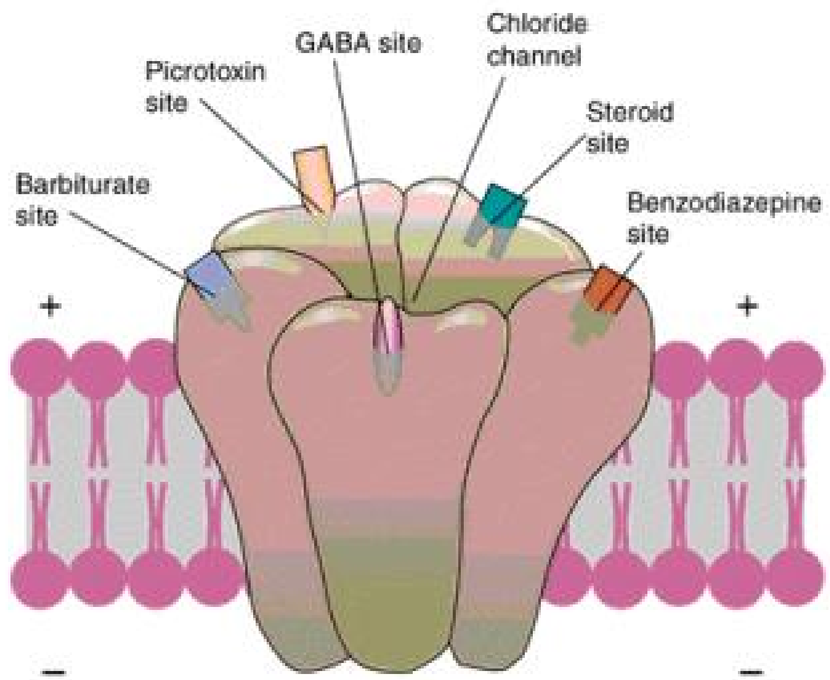
- the medial septal region and the hippocampus are connected reciprocally via GABAergic neurons,
- Toth K, Borhegyi Z, Freund TF. J Neurosci. 1993
- the physiological role of this loop is still not well understood

The $GABA_A$ receptor

Subunit composition

Subunit composition of synaptic $GABA_A$ receptors $GABA_A$ receptors are pentameric hetero-oligomers assembled from members of seven different subunit classes, some of which have multiple members: α(1-6), β(1-3), γ(1-3), δ, ϵ, θ and π.

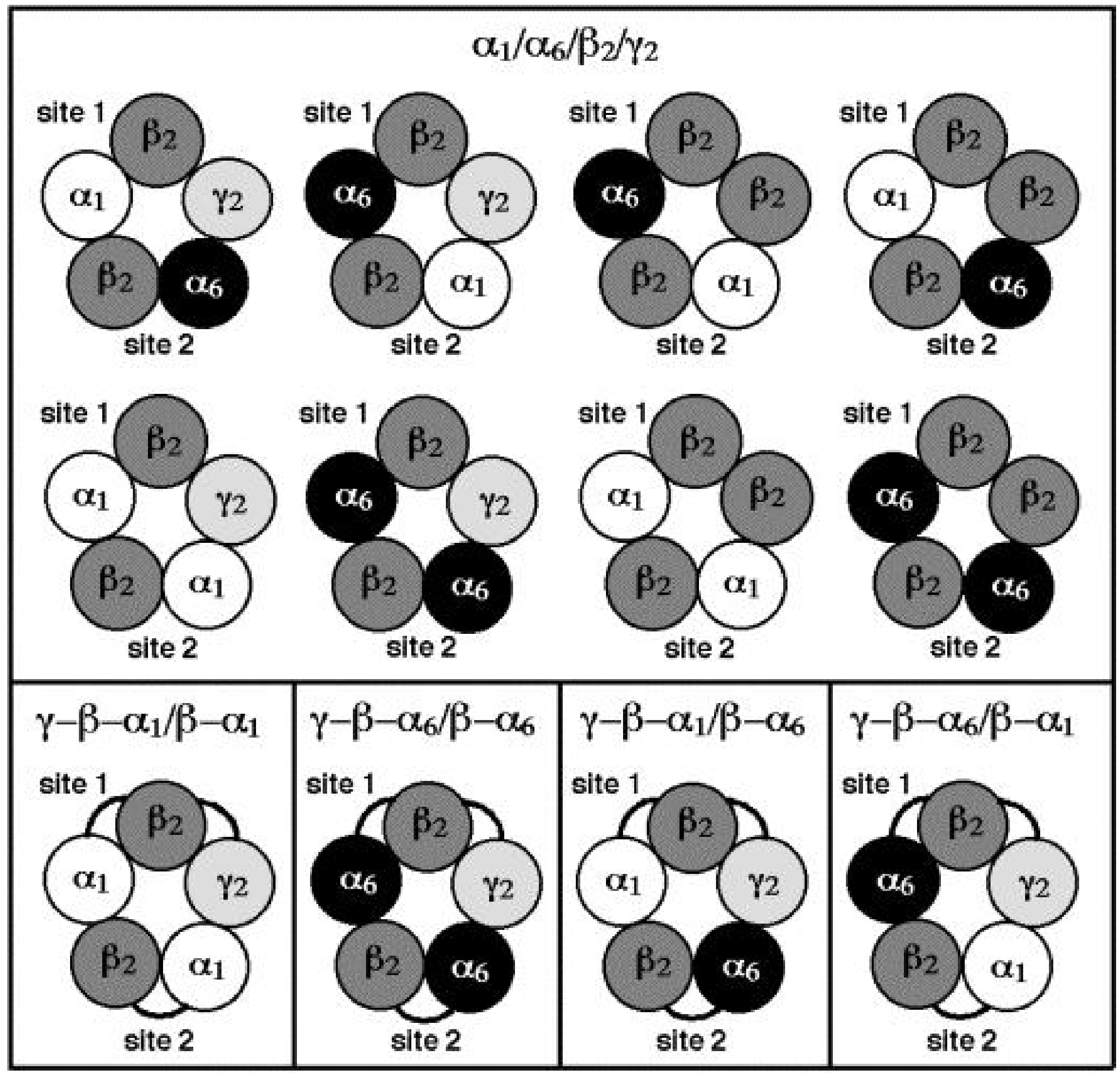
▸ Schematic Illustration of a $GABA_A$ Receptor, with Its Binding Sites



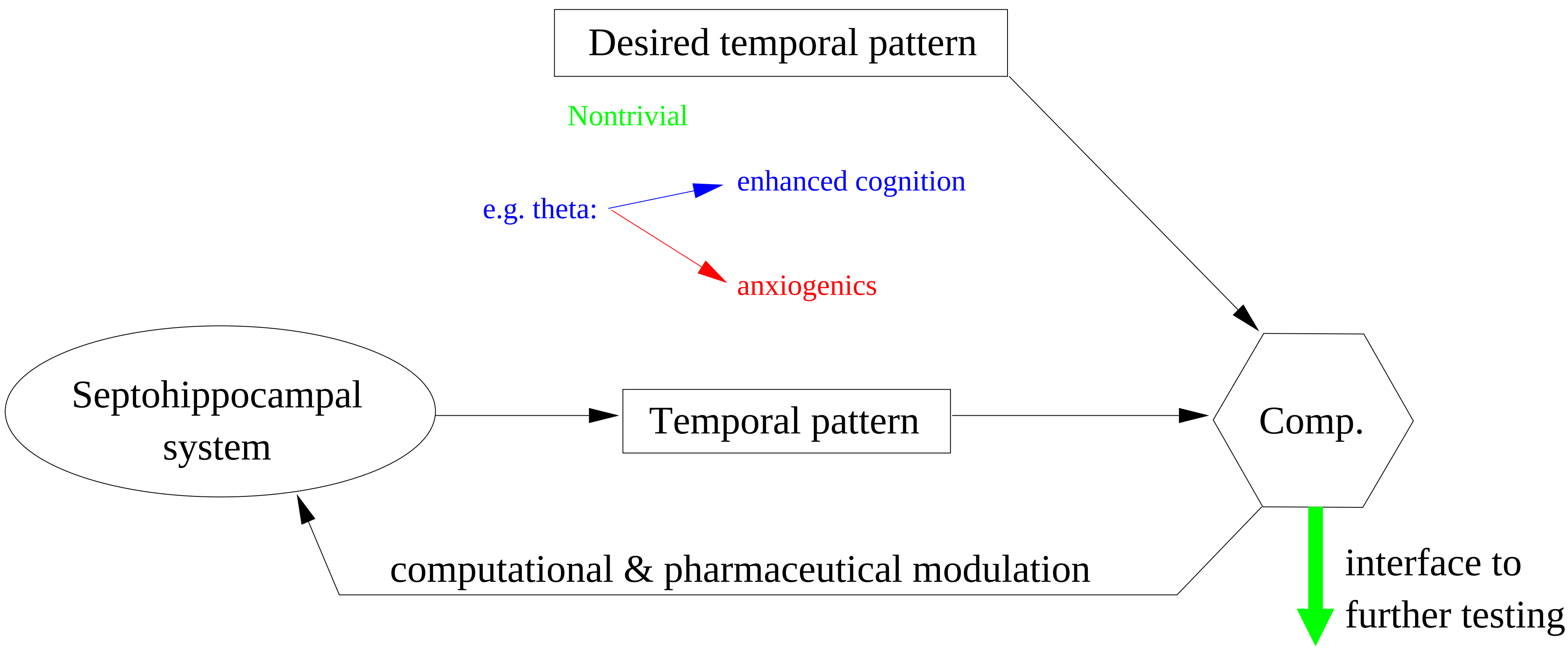
The GABA$_A$ receptor

Subunit composition

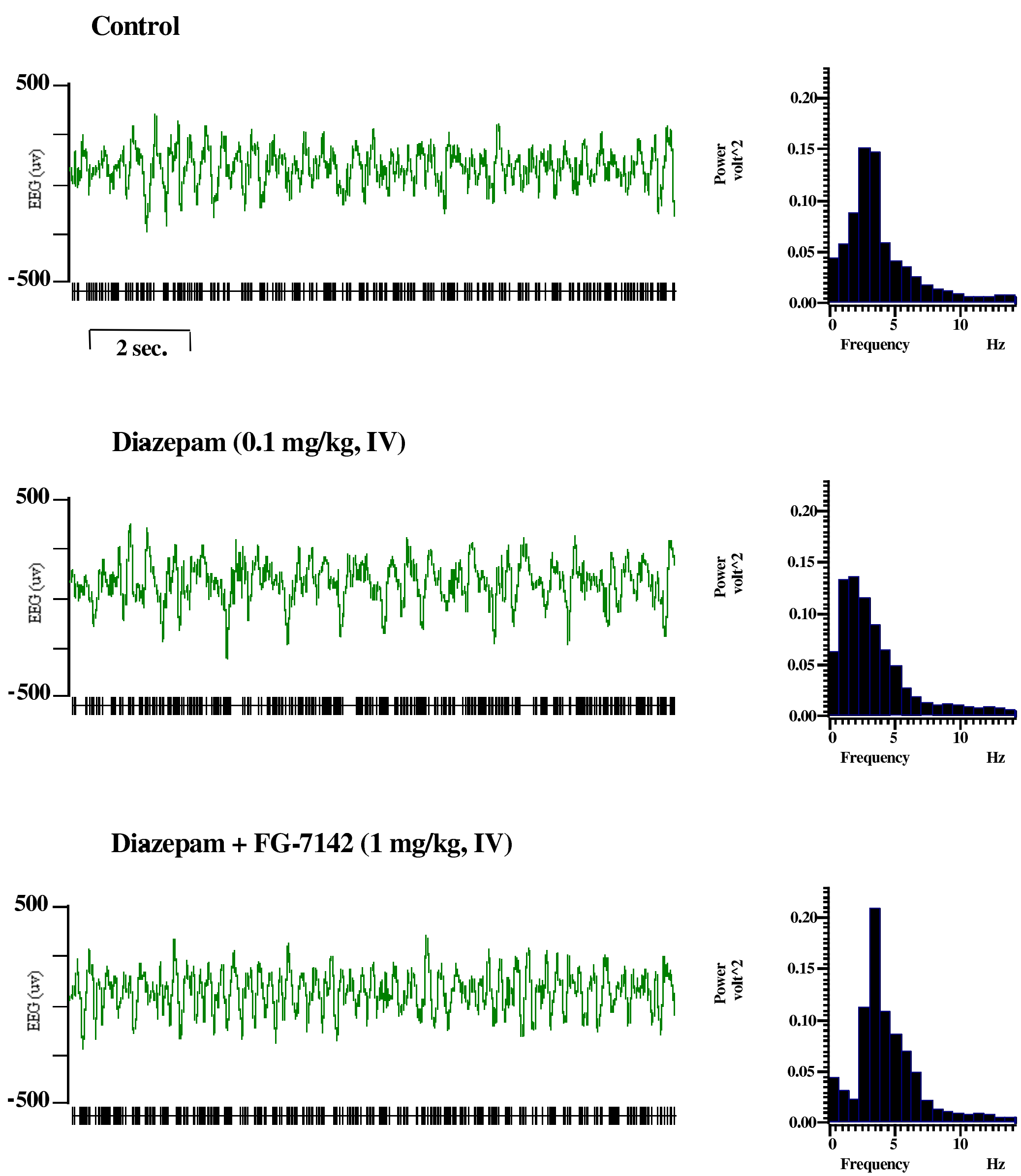
Complex patterns of subunit distribution in different brain regions and cell types support the view that dozens of GABA$_A$ receptor combinations are present in the brain.



TOWARDS A COMPUTATIONAL/PHYSIOLOGICAL MOLECULAR SCREENING (and DRUG DISCOVERY)



Physiological Experiments

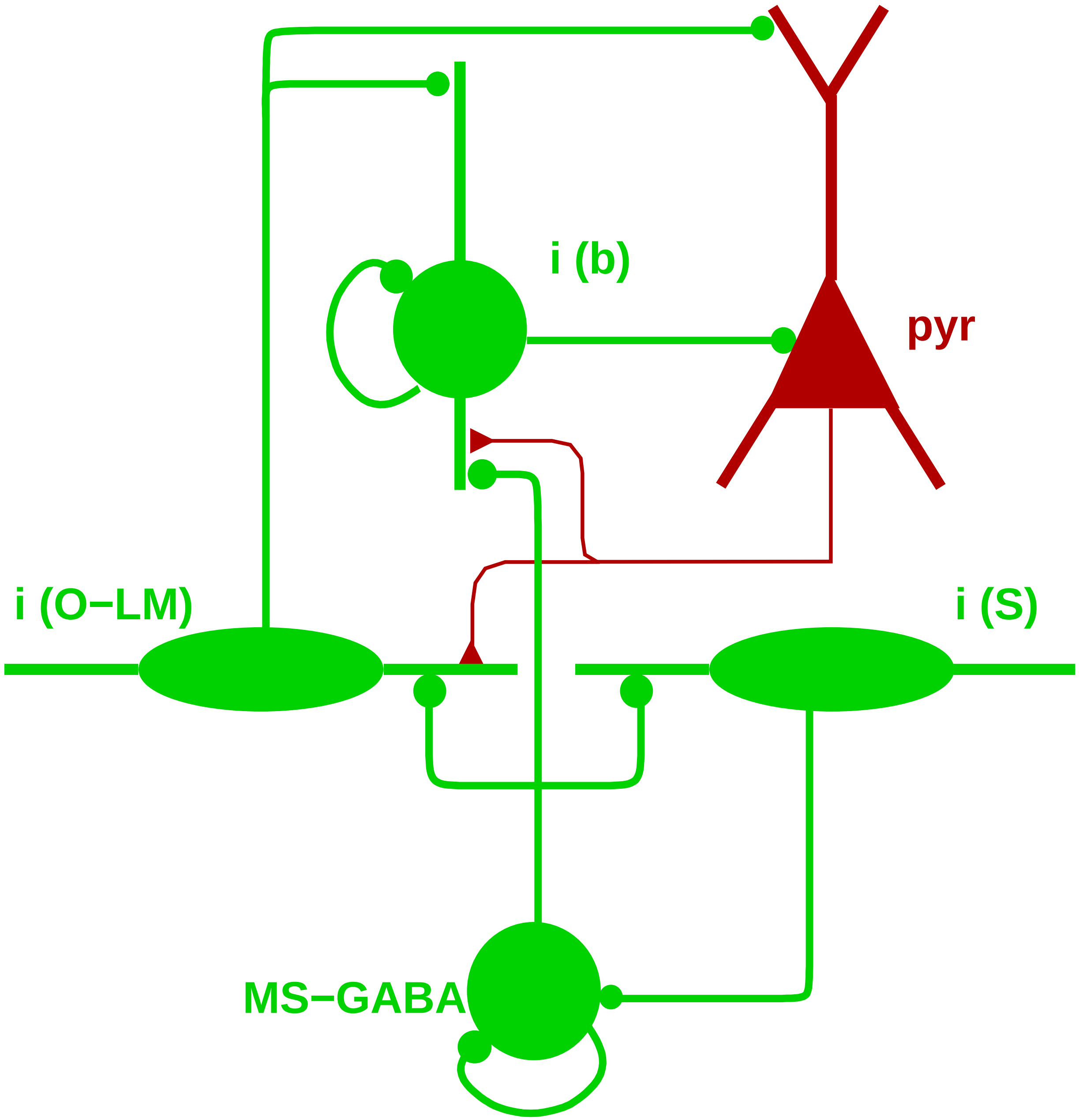


Theta activity can be depressed and induced in the hippocampal CA1 by GABA allosteric modulators

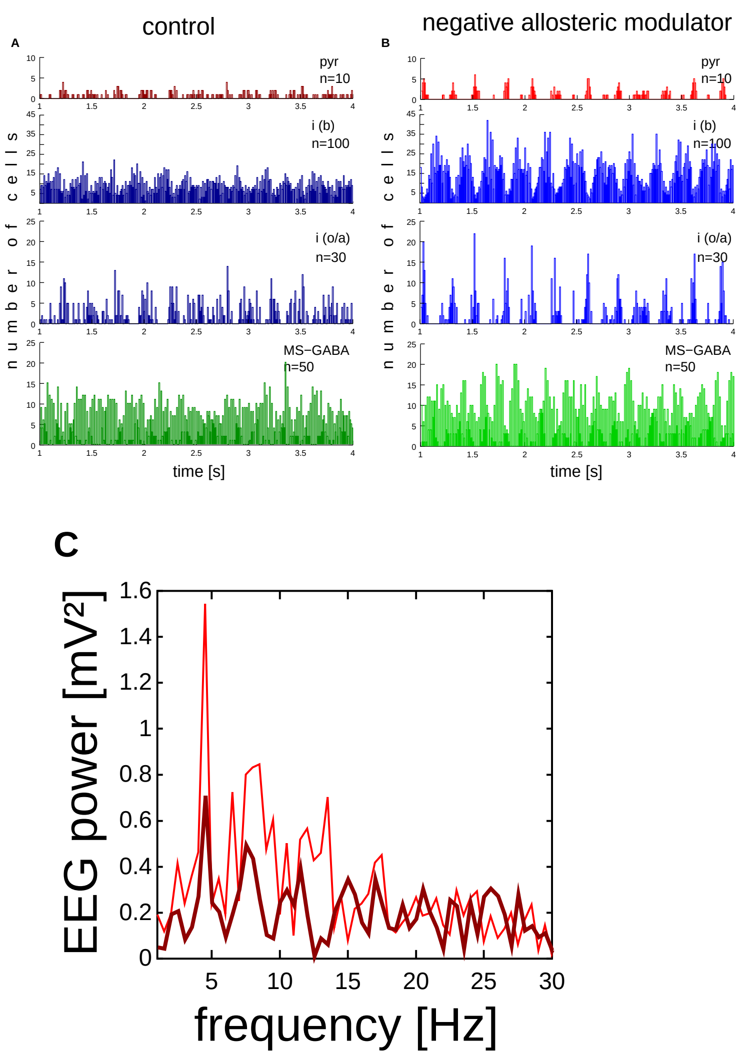
The positive allosteric modulator diazepam, which increases chloride conductance, suppresses theta activity

Negative allosteric modulator FG-7142, which reduces transmission at GABA-A synapses, reverses the effect of diazepam

The skeleton network



Theta modulation in the MS-CA1 system



Effect of negative allosteric modulator was taken into account by lower synaptic conductance at all pathways

In all neuron populations clustering of spikes occurs at lower synaptic conductance values

Timing of action potentials tends to have a well defined value

Theta power in EEG computed from the activity of pyramidal neurons shows a significant increase during simulated administration of the negative allosteric modulator

CONCLUSIONS

DYNAMICAL MODELS

HIERARCHICAL LEVELS

INTEGRATION of LEVELS

THERAPEUTIC STRATEGIES