Introduction à la dynamique des ensembles neuronaux

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CNRS UPR 640

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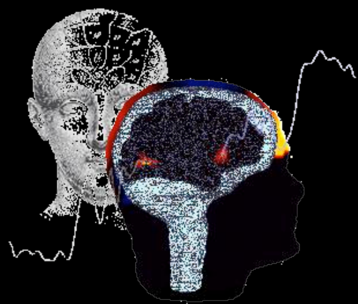
PARIS



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a research program for a neurodynamics at the large-scale.
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Methodological advances.
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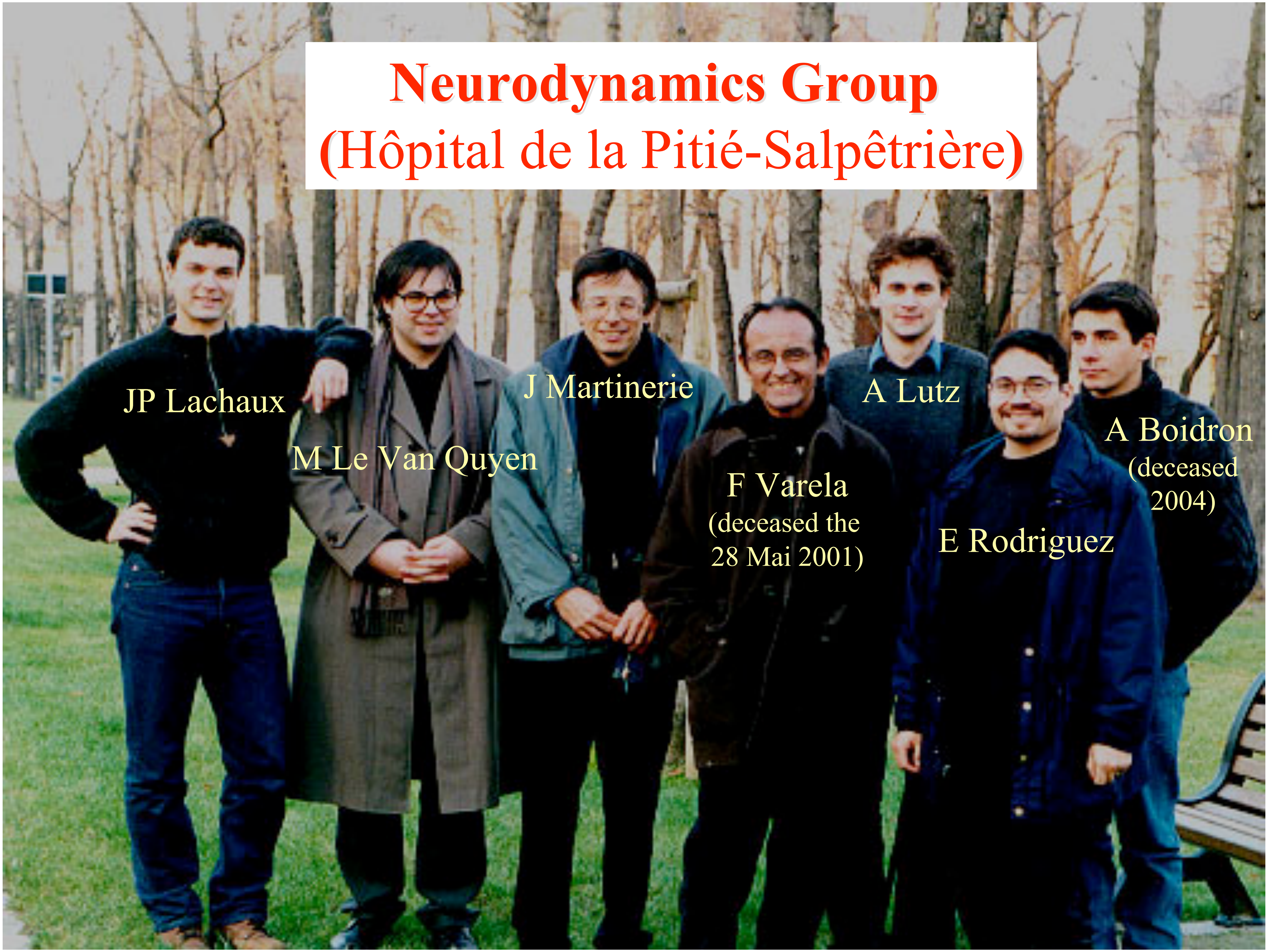
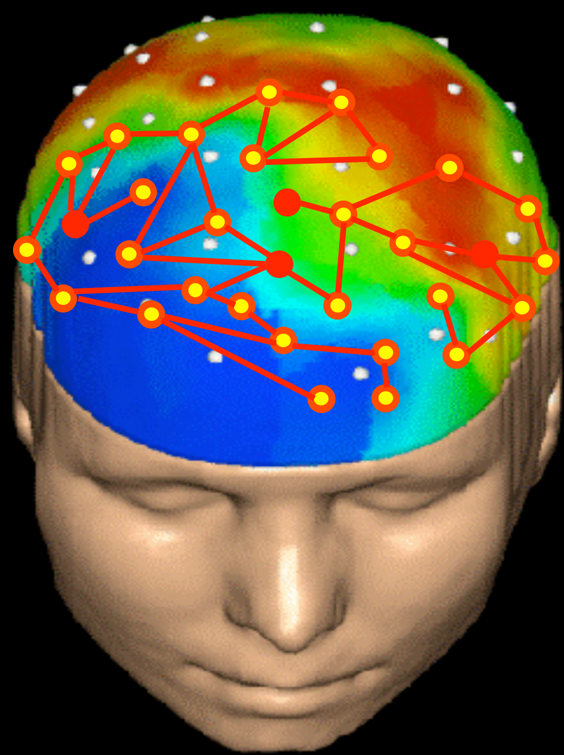

Neurodynamics Group
(Hôpital de la Pitié-Salpêtrière)
JP Lachaux
M Le Van Quyen
J Martinerie
F Varela
(deceased the
28 Mai 2001)
A Lutz
E Rodriguez
A Boidron
(deceased
2004)

How can we study large-scale brain phenomena?



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The multi-scale nervous system

Microscopic scale

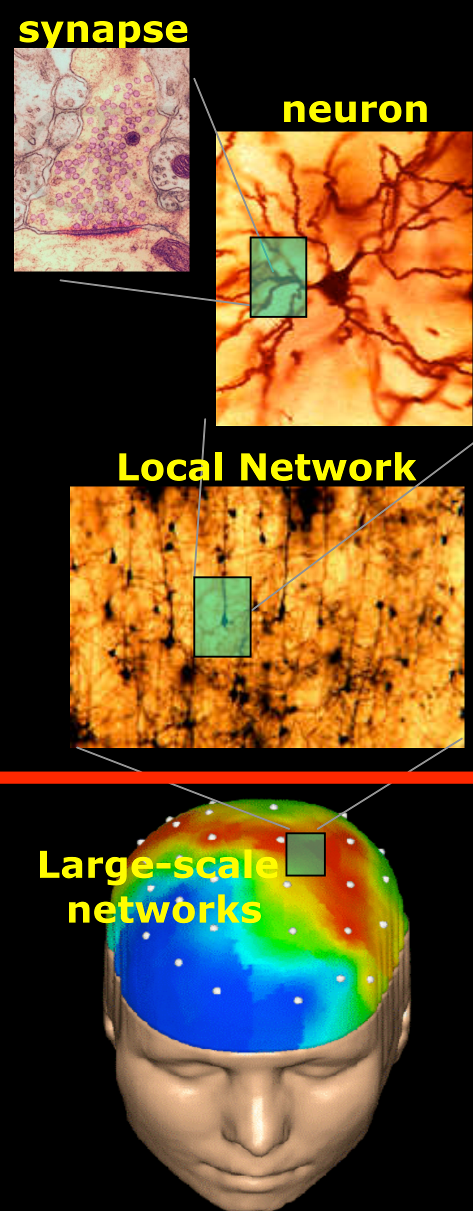
Mesoscopic scale

Cells in a macrocolumn ~ (80)(100) = 8000

Macroscopic scale

Cortical region, cm3

> 100 000-1 million

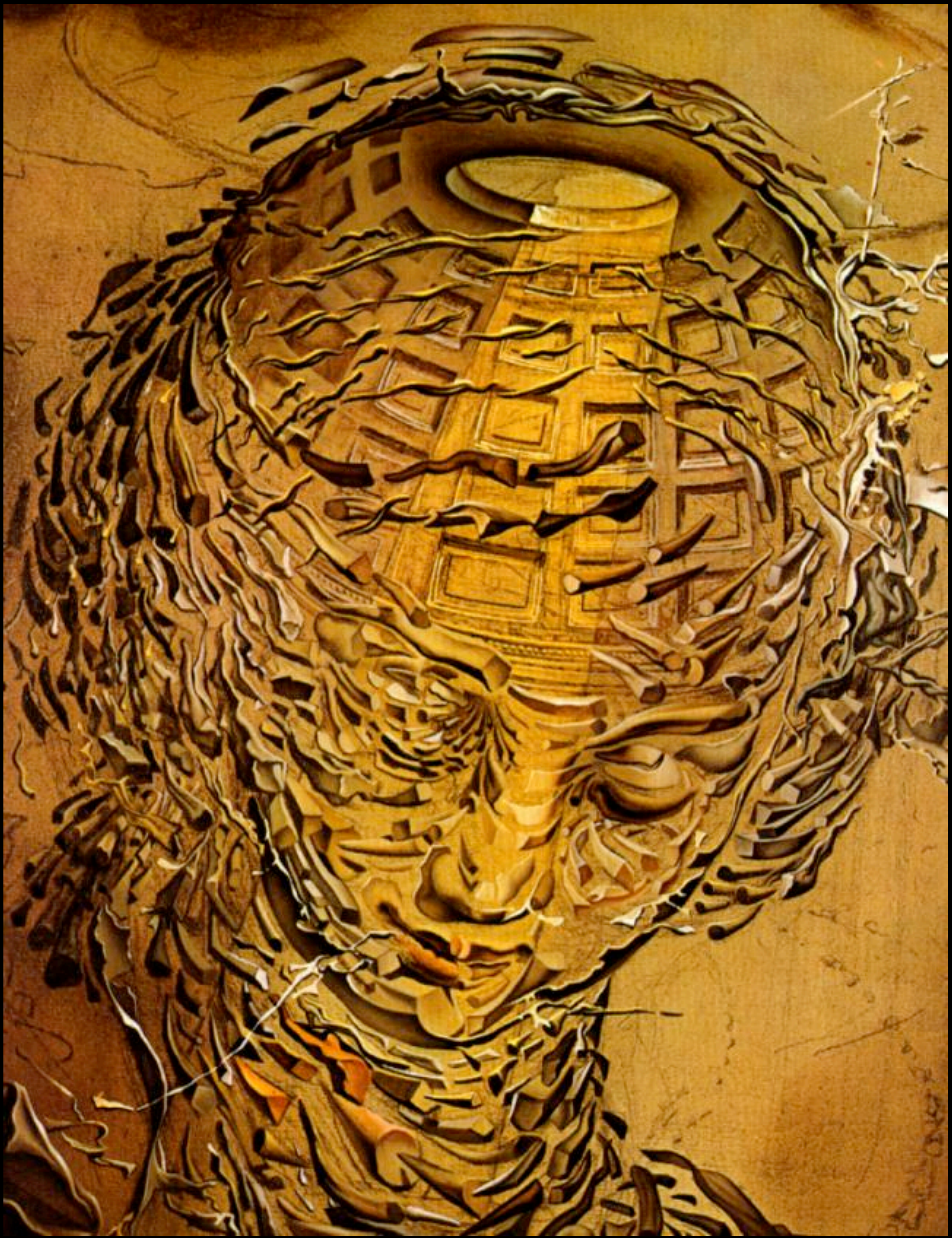


Dynamique des ensembles neuronaux

- **Le cerveau en action « in vivo »**

- **échelle macroscopique**

- **étude de phénomènes coopératifs complexes**



Gray cortical matter is found in the *cerebral neocortex*, a thin layered sheet of ca. 20^9 neurons lying just underneath the surface of the cerebrum.

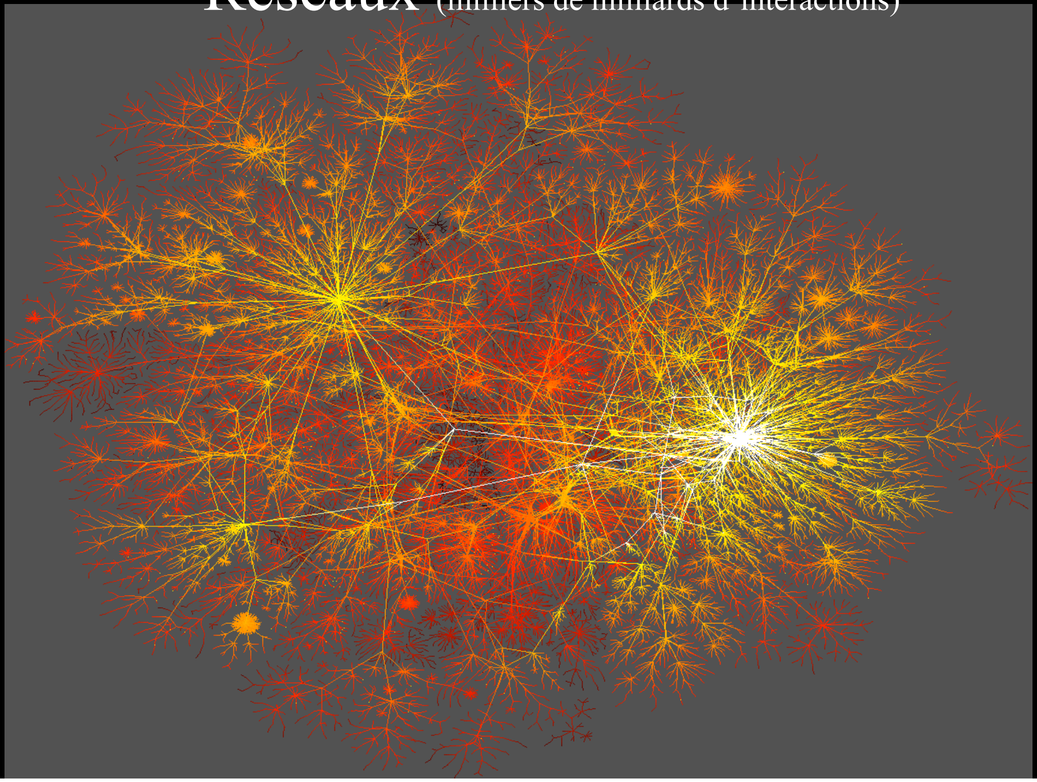
Parameter	Value
number of neurons	ca.130^9
number of cortical neurons	ca.20^9 (*)
surface of neocortex	ca.11 m²
connections per neuron	ca.1000
cortical synapses	ca.240 trillion (*)

(*) Koch, C : Biophysics of Computation, Oxford University Press - New York, 1999, p.87.

Neurones (10 milliard de cellules)

synapses

Réseaux (milliers de milliards d'interactions)



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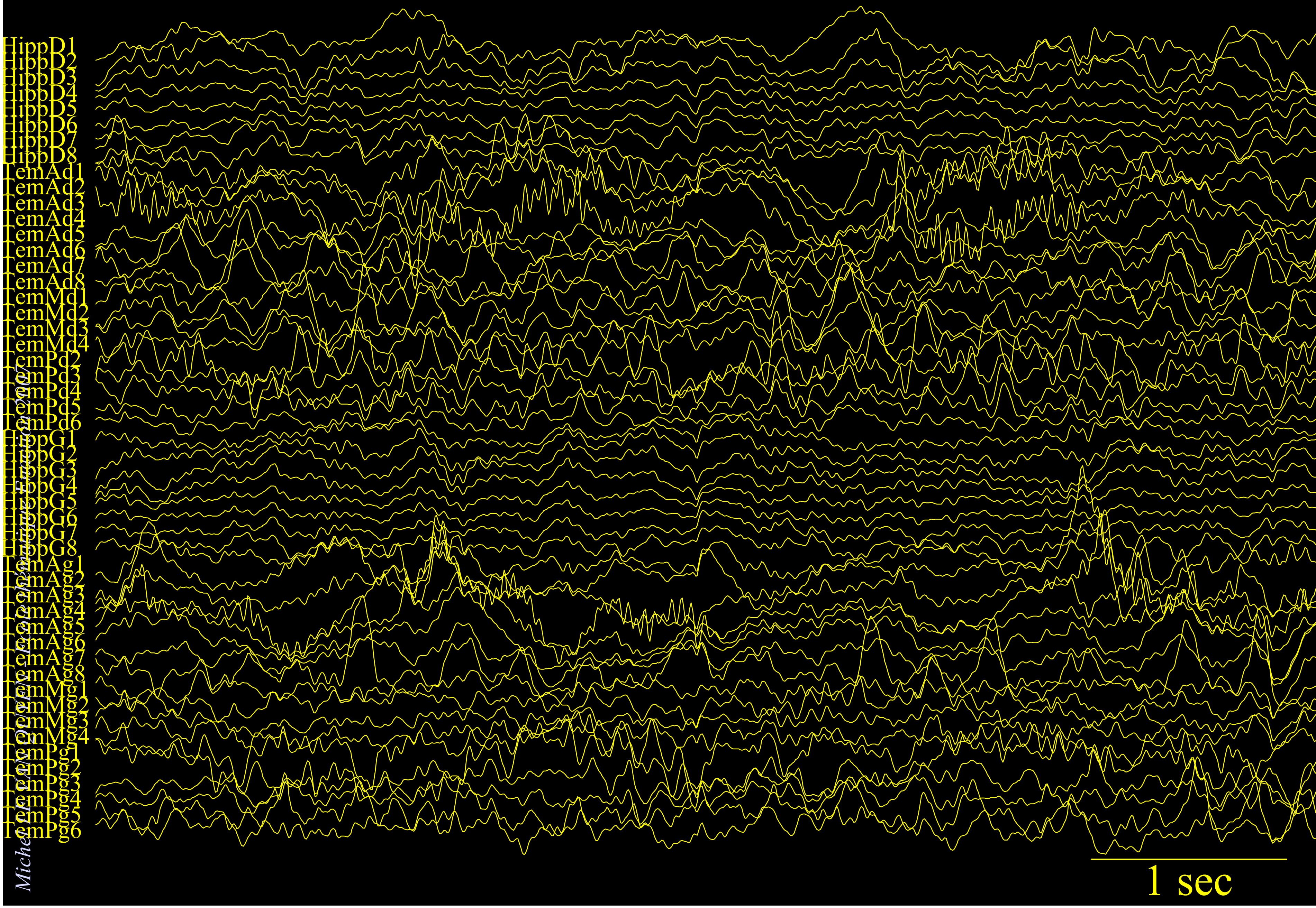
100 milliard d‘étoiles

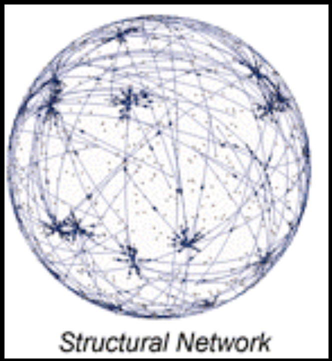
Le cerveau engendre du chaos et de l'ordre

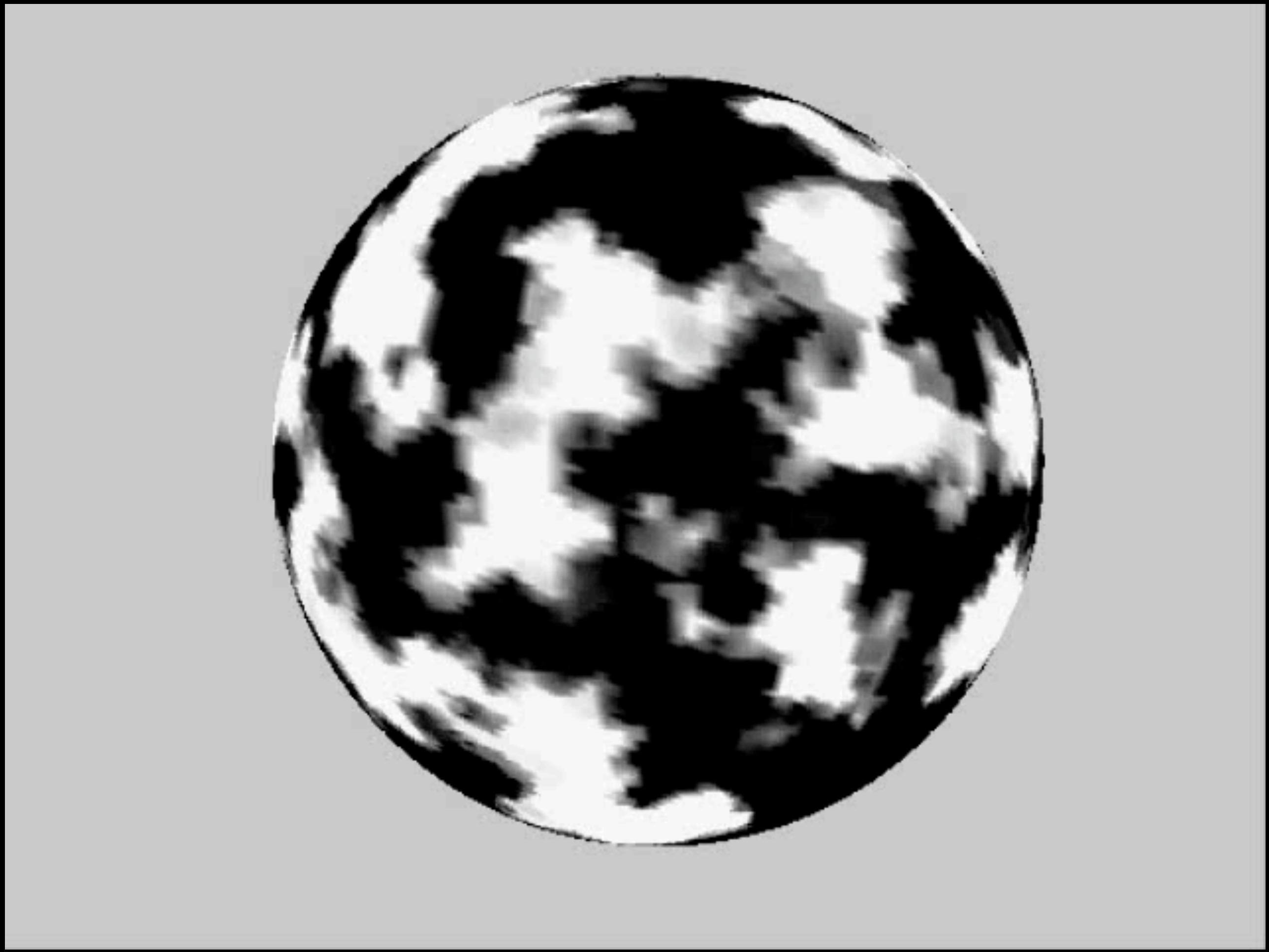


PNAS |**2006** | vol. 103 | **19219-19220**

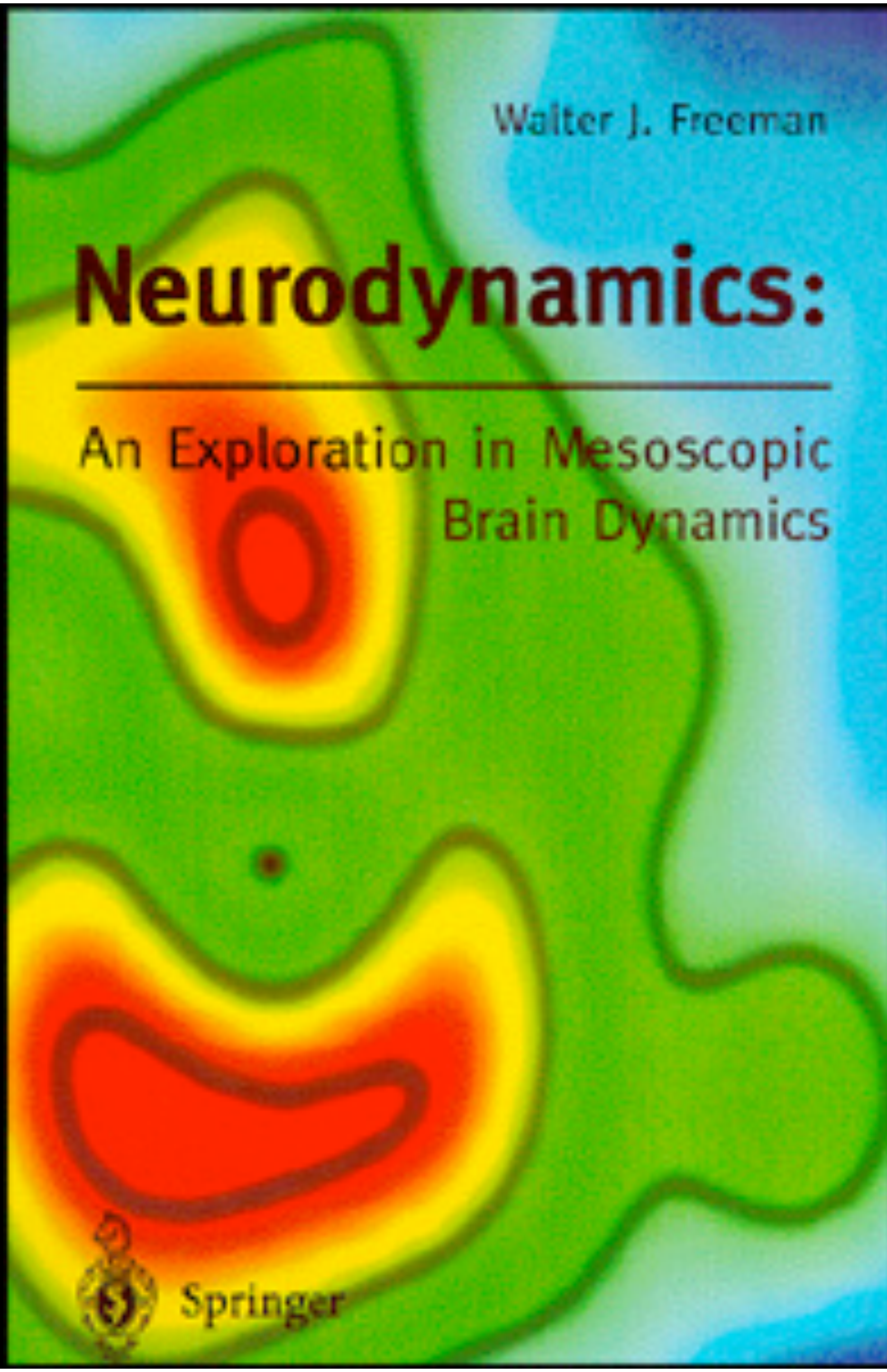
Small worlds inside big brains

Olaf Sporns and Christopher J. Honey






Nature ondulatoire (liquide)
des activités cérébrales

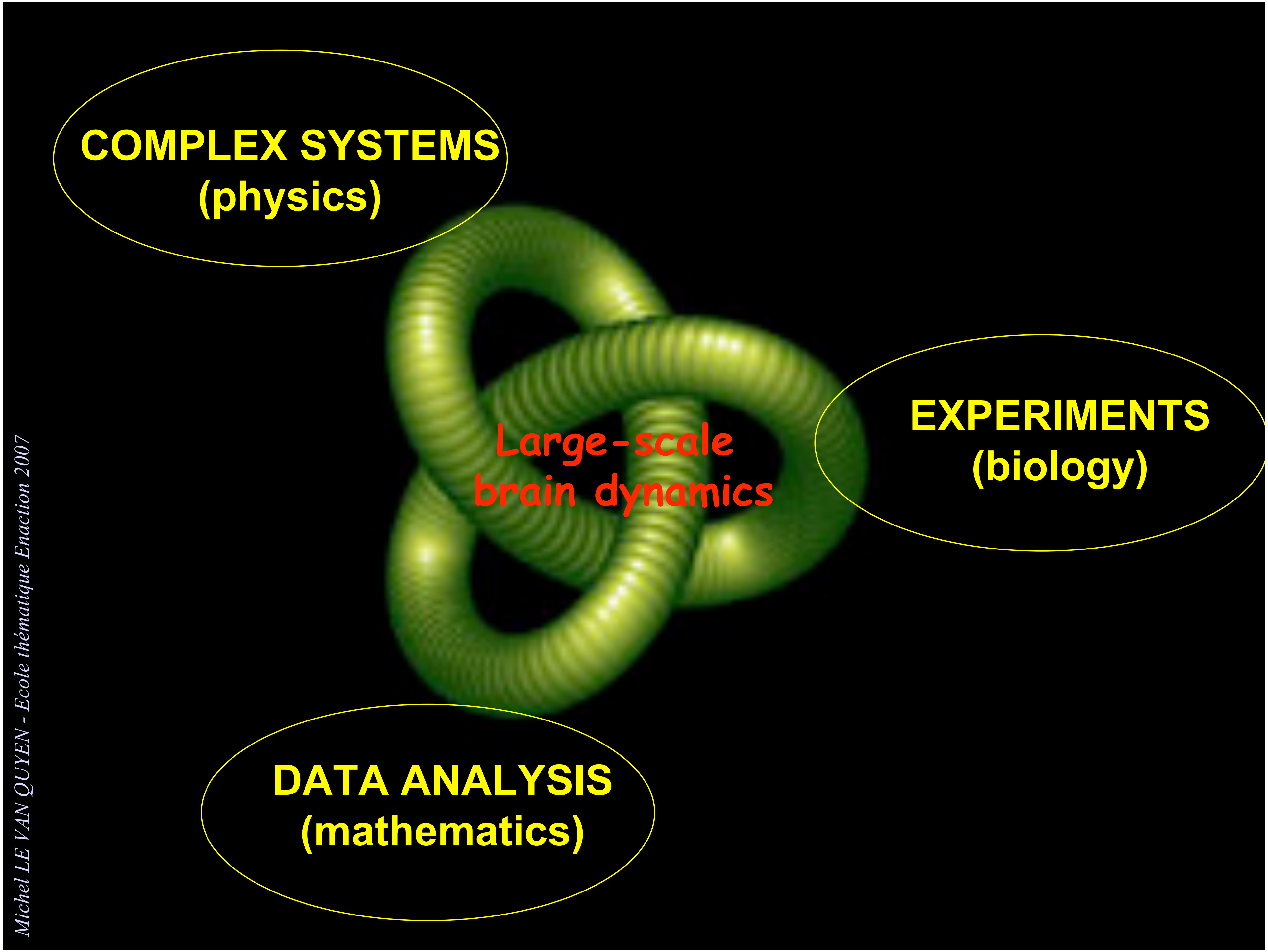

Walter J. Freeman
Neurodynamics:
An Exploration in Mesoscopic Brain Dynamics
Springer

UN INTERET POUR L'INSTABILITE

1. Fluctuations, chaos, désordre / Auto-organisation

2. Coordination transitoire, spatiale et temporelle (e.g. oscillations, synchronisation locale et à large-échelle)

3. Lois cachées dans le désordre (1/f, chaos déterministe, ect.)


COMPLEX SYSTEMS
(physics)
Large-scale
brain dynamics
EXPERIMENTS
(biology)
DATA ANALYSIS
(mathematics)
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PLAN DU COURS

1. Introduction: Dynamique des ensembles neuronaux- hypothèses de travail

2. Physique: Auto-organisation des systèmes complexes

3. Biologie: Signaux EEG

4. Analyses mathématiques: oscillations et synchronisations longue-distance

5. Questions pour l'avenir: Analyses multiniveaux

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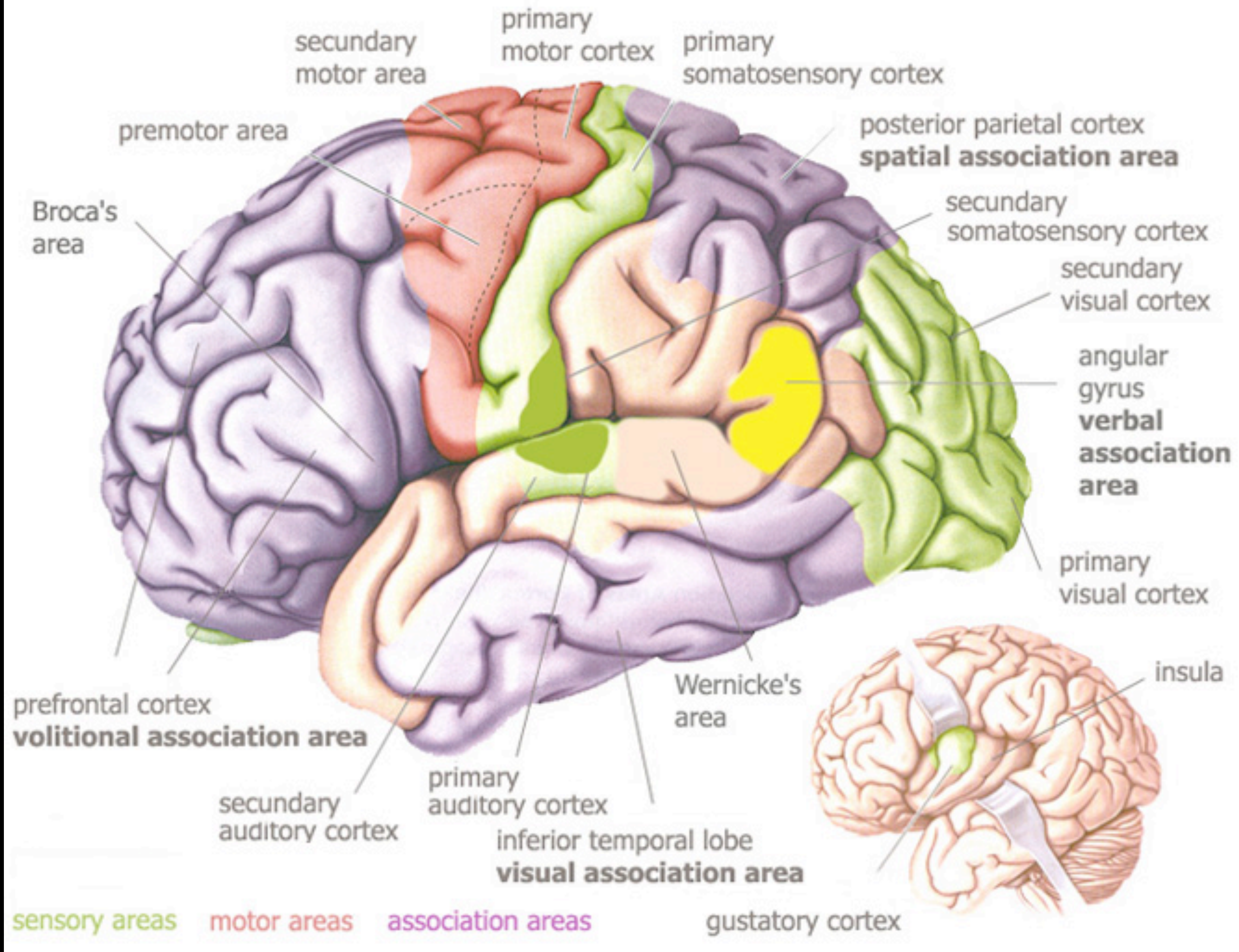
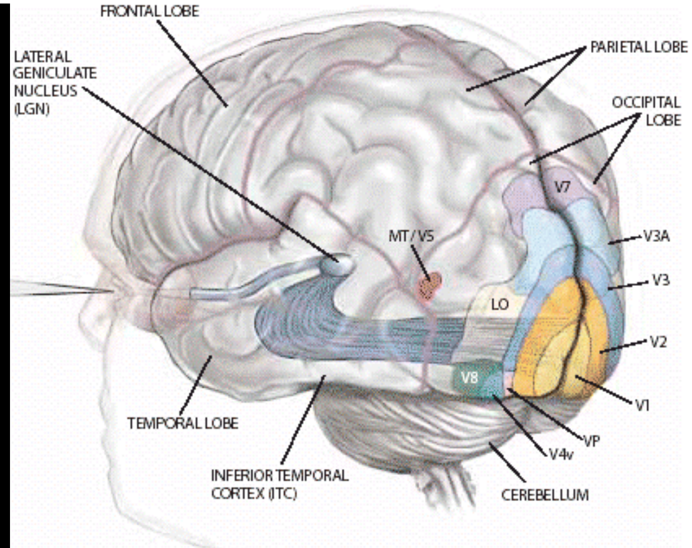
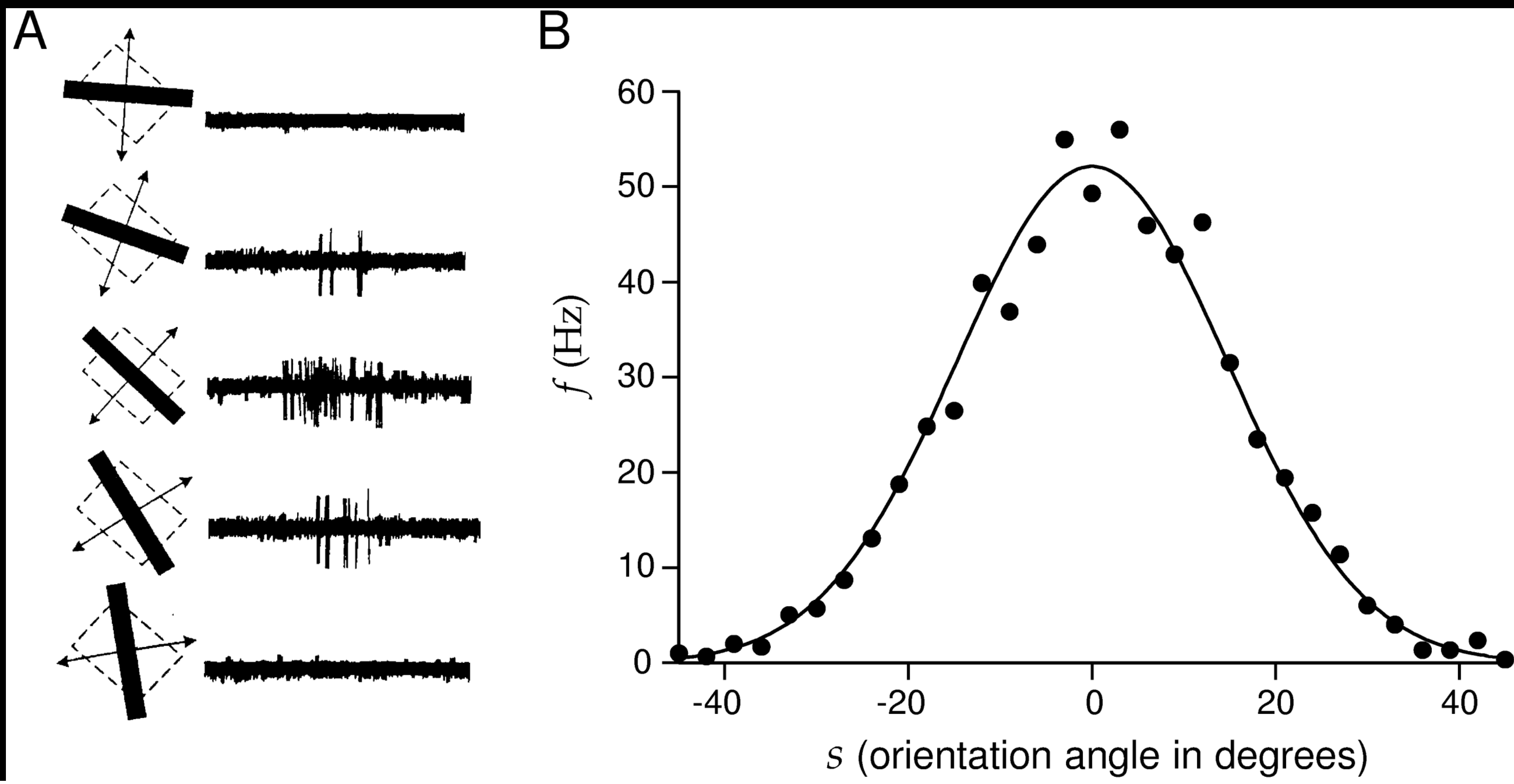



FRONTAL LOBE
LATERAL GENICULATE NUCLEUS (LGN)
PARIETAL LOBE
OCCIPITAL LOBE
V7
V3A
V3
V2
V1
VP
V4v
V8
LO
MT / V5
TEMPORAL LOBE
INFERIOR TEMPORAL CORTEX (ITC)
CEREBELLUM

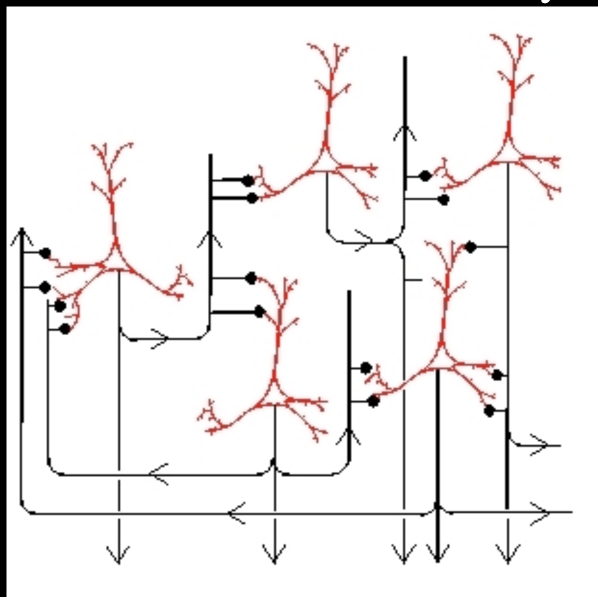

A
B
60
50
40
30
20
10
0
-40
-20
0
20
40
f (Hz)
s (orientation angle in degrees)

How are these myriads of parallel,distributed processes grouped and bound together in a meaningful way?

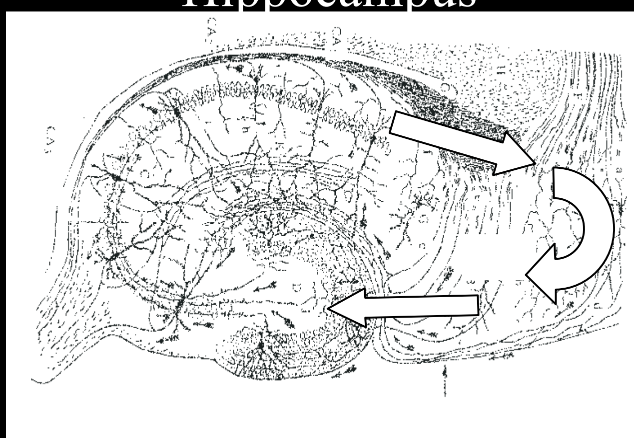
Anatomical Reentrant loops

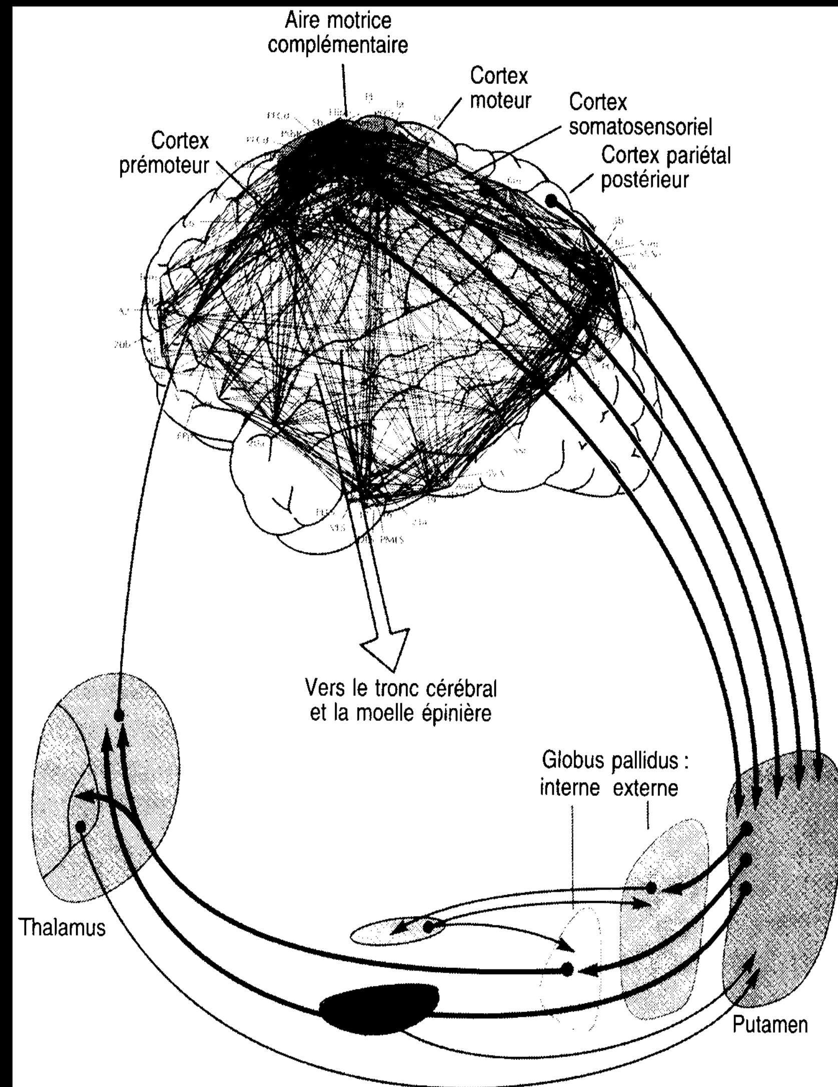
There can be no input or output from such system…

Lorente de Nó's reverberatory circuit



Hippocampus





Edelman & Tononi, O. Jacob, 2000

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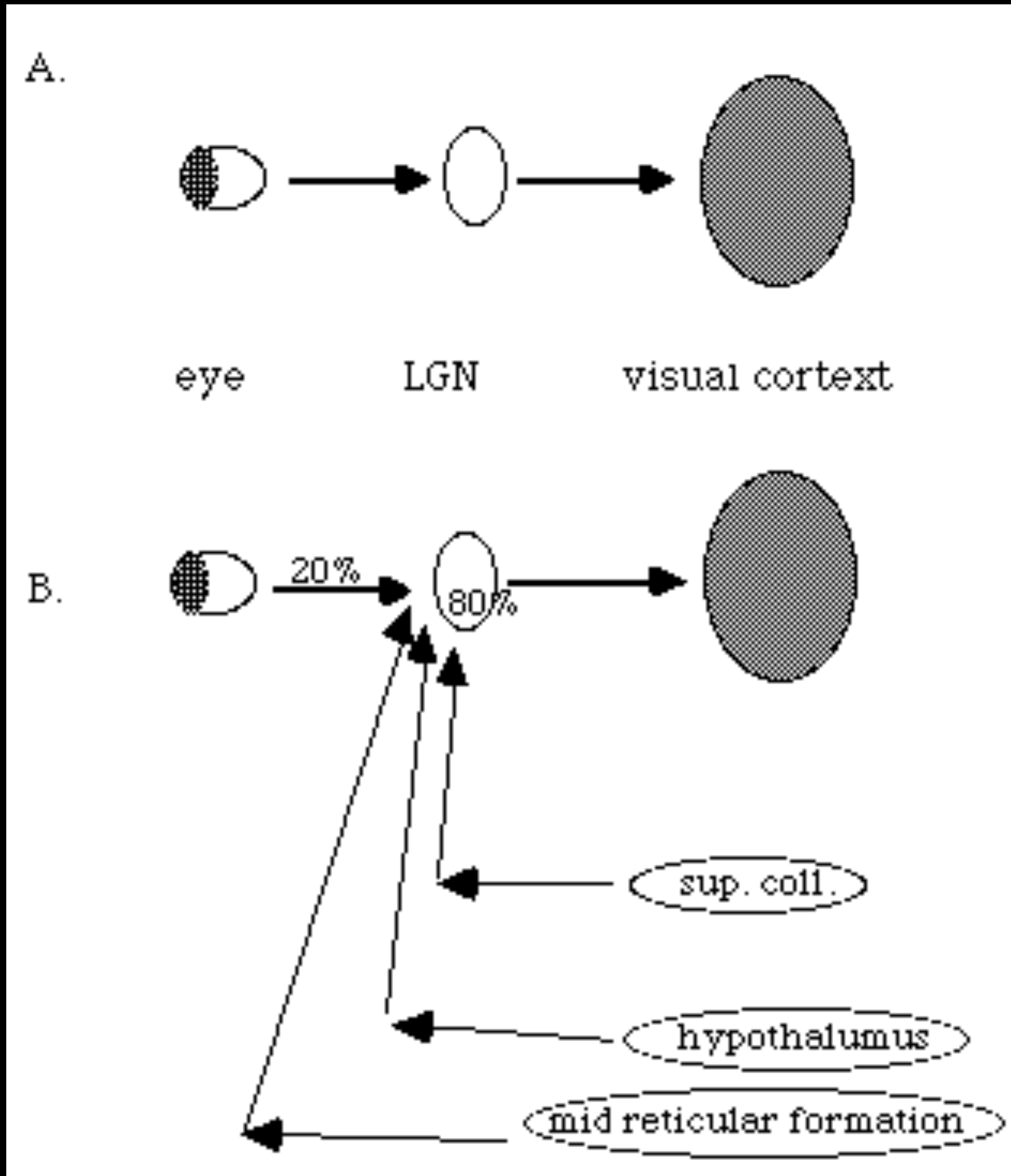
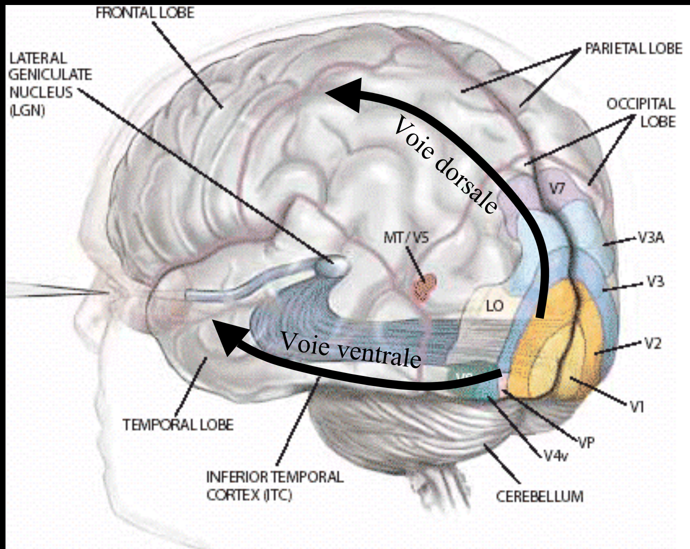
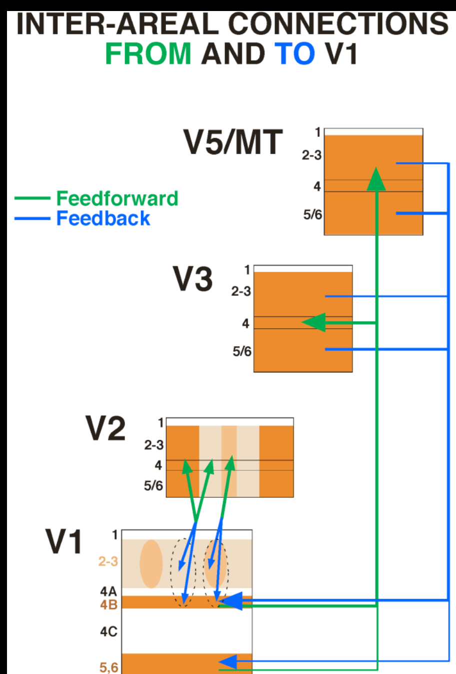

A.
eye
LGN
visual cortext
B.
20%
80%
sup. coll.
hypothalumus
mid reticular formation

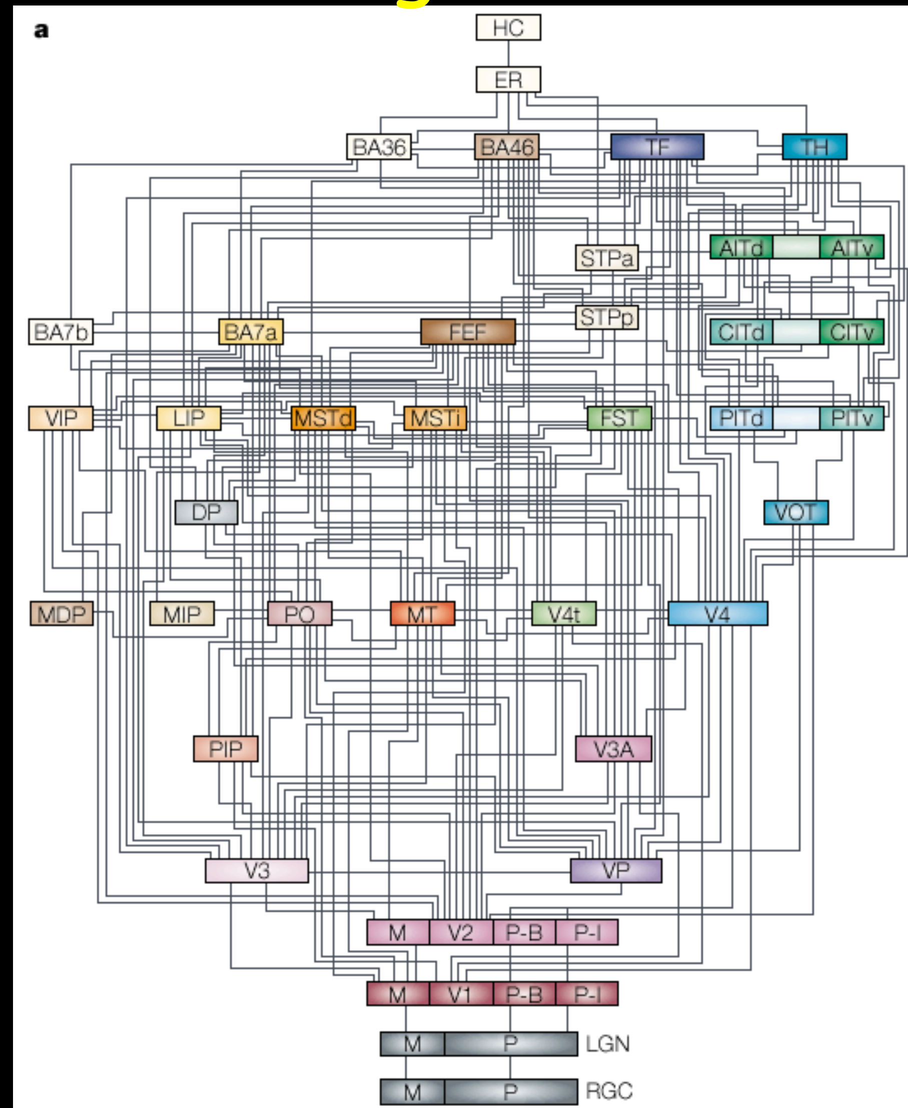
Varela, 1993

Ségrégation fonctionnelle:
couleur, forme, mouvement, …





intégration



Van Essen, 1990

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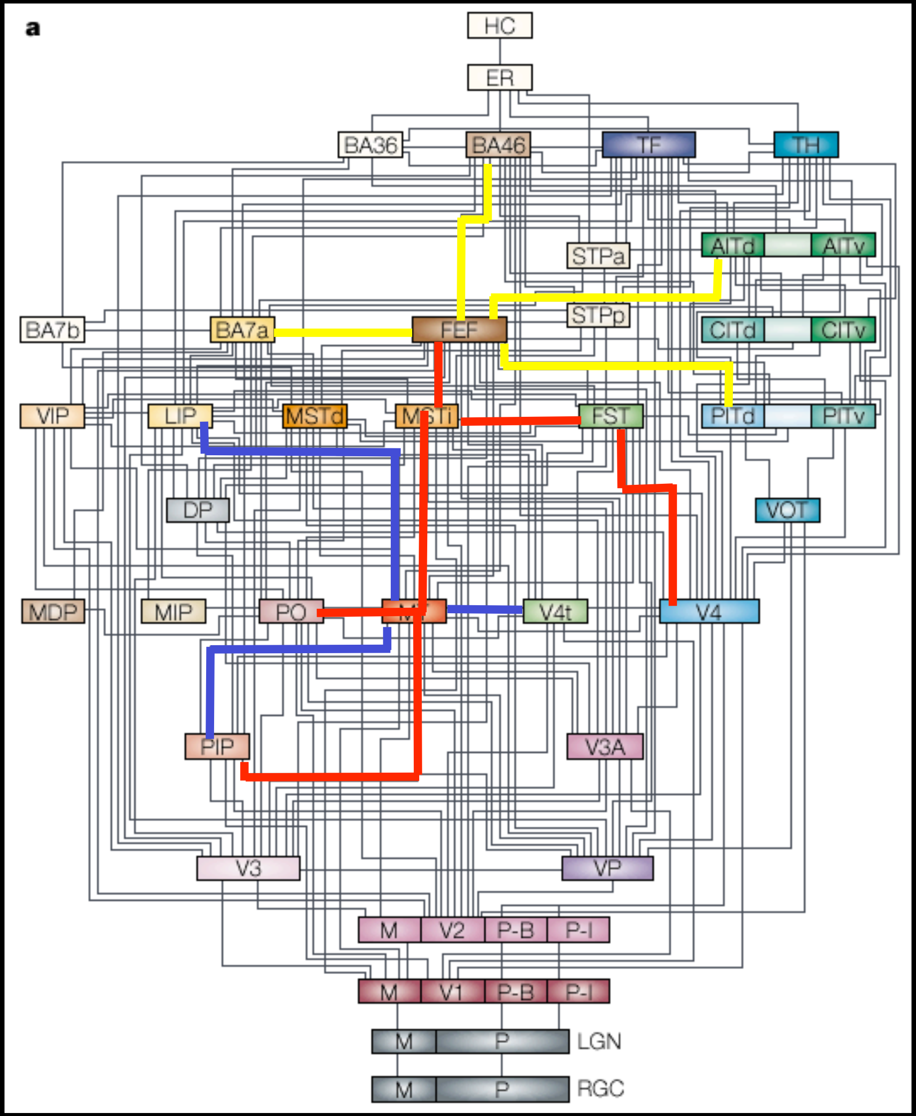
Deux principes d’organisation fondamentaux du cerveau sur une large échelle:

Segrégation (anatomique/dynamique)

Intégration (anatomique/dynamique)

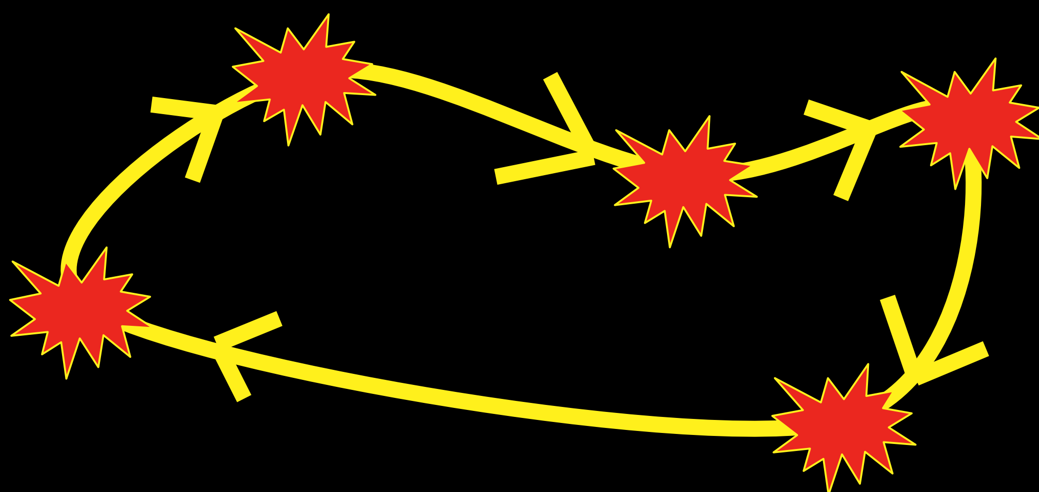
Ces principes sont complémentaires!

La circuiterie seule ne permet pas de comprendre la fonction du réseau:
D'où l' importance d'un point de vue dynamique…



Tâche cognitive = formation transitoire d 'une assemblée distribuée de neurones, coopération temporelle des activités

- Hebb's proposal (1949): “Thoughts are produced by neurons functioning within CELL ASSEMBLIES”
  - Sets of neurons whose interconnections have been strengthened and specified through experience



Brain connectivity

Anatomical connectivity

- the set of all physical (structural) connections between neuronal units (brain regions) at a given time
- relative static in the short-time scales
- major determinant of functional properties

Functional (dynamic) connectivity

- describes the interdependence of neuronal units that are dynamically related
- time-dependent
- can contribute to the changes in the anatomical connections

Small worlds inside big brains
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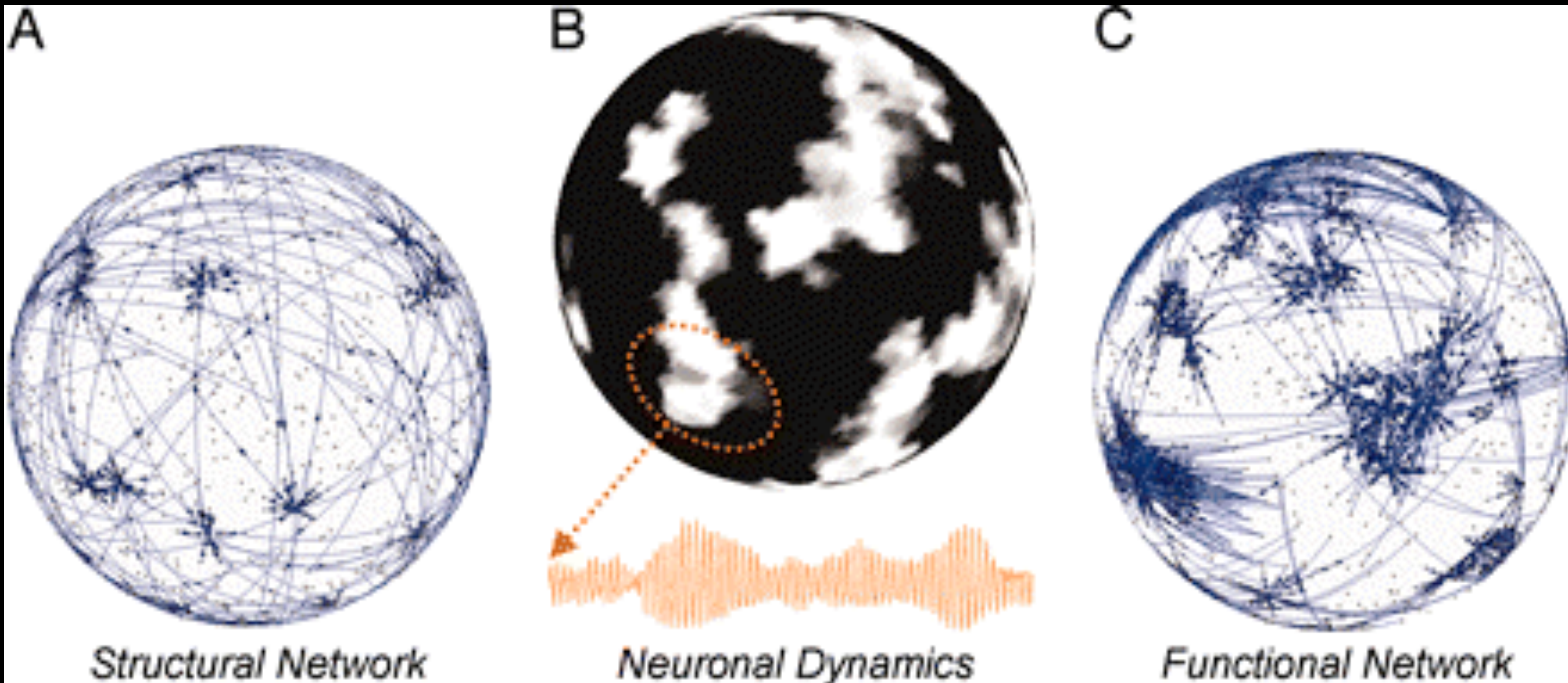

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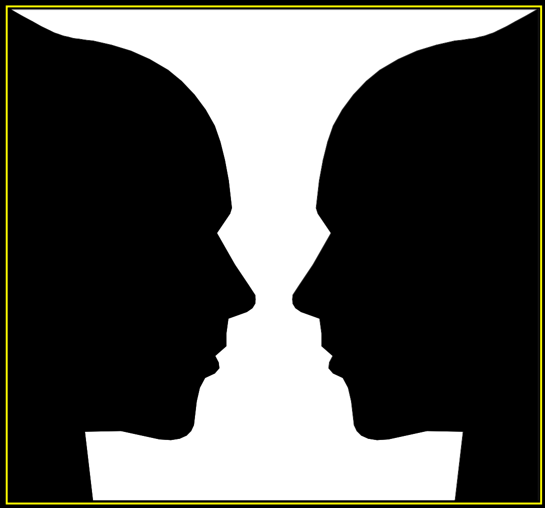
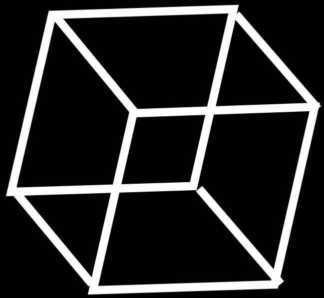
Cognition

- Integrated cognitive experiences

  – we experience everything as one cognitive event, e.g. sound, sight, our feelings and reactions



- Cognition appears to us as a continuous flow - Constant change between successive states

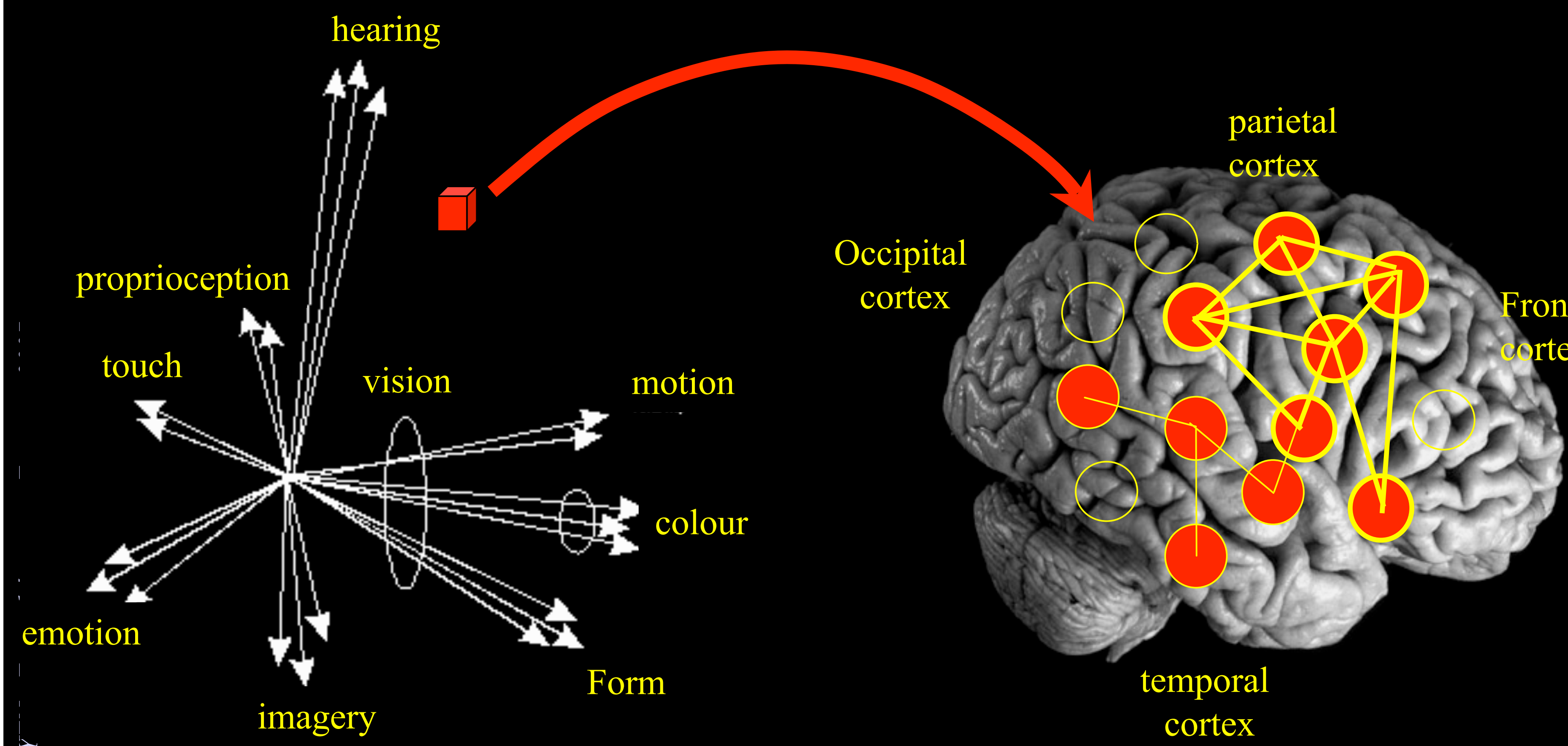


The Principles of Psychology, **William James** (1890)

James illustrates the ever-changing stream of thoughts like a rotating kaleidoscope where each momentarily stable pattern is a thought. Similarly, consciousness is always changing, but it presents us with a series of substantive thoughts that are themselves momentarily stable.

Thus, James considered that consciousness has a composite structure: it contains stable nuclei (or images) and transitive fringes (or periods).

Hypothesis 1: Large cell assemblies underlie the emergence of cognitive complexity



Phenomenal states

Web of interaction

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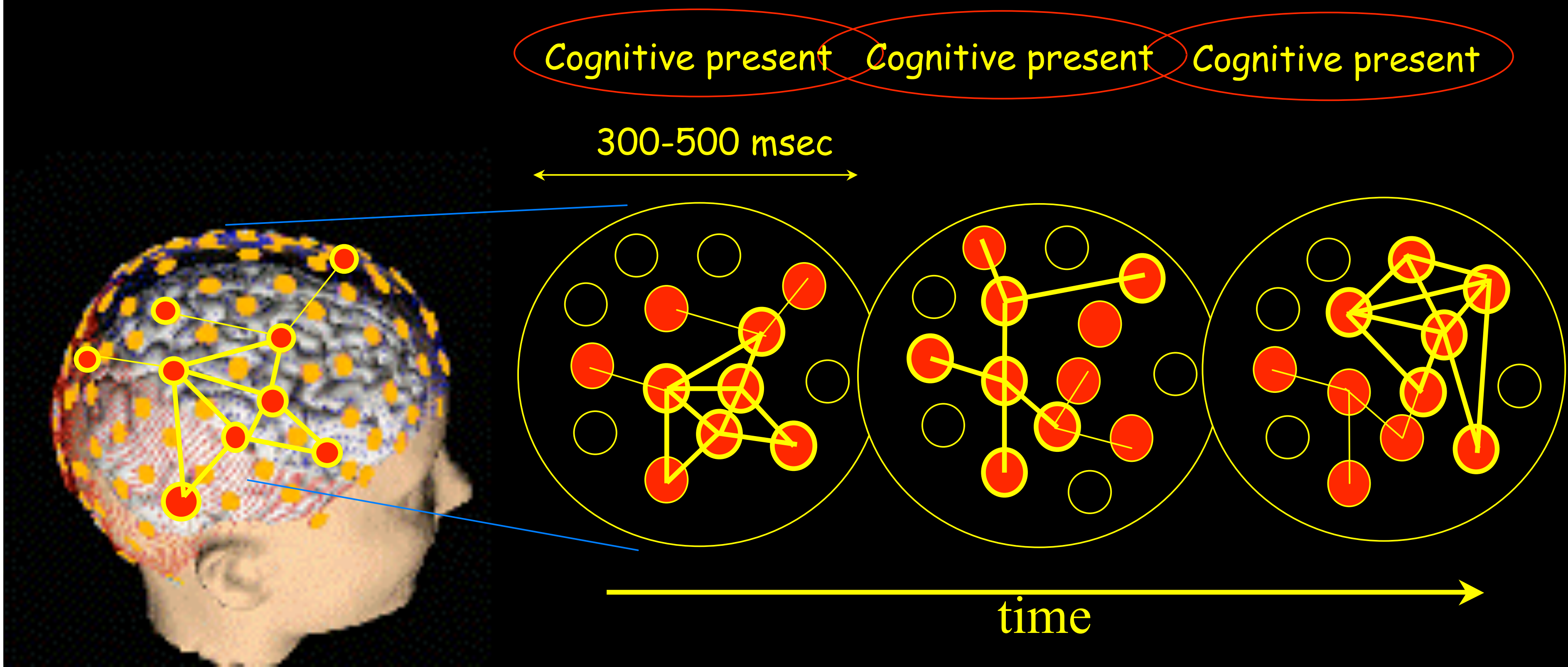
Hypothesis 2: The dynamic core_

« ...a large functional cluster of neuronal groups that together constitute, on a time scale of hundred of milliseconds, a unified neuronal process of high complexity » (Tononi & Edelman, 1998; Varela, 1999)

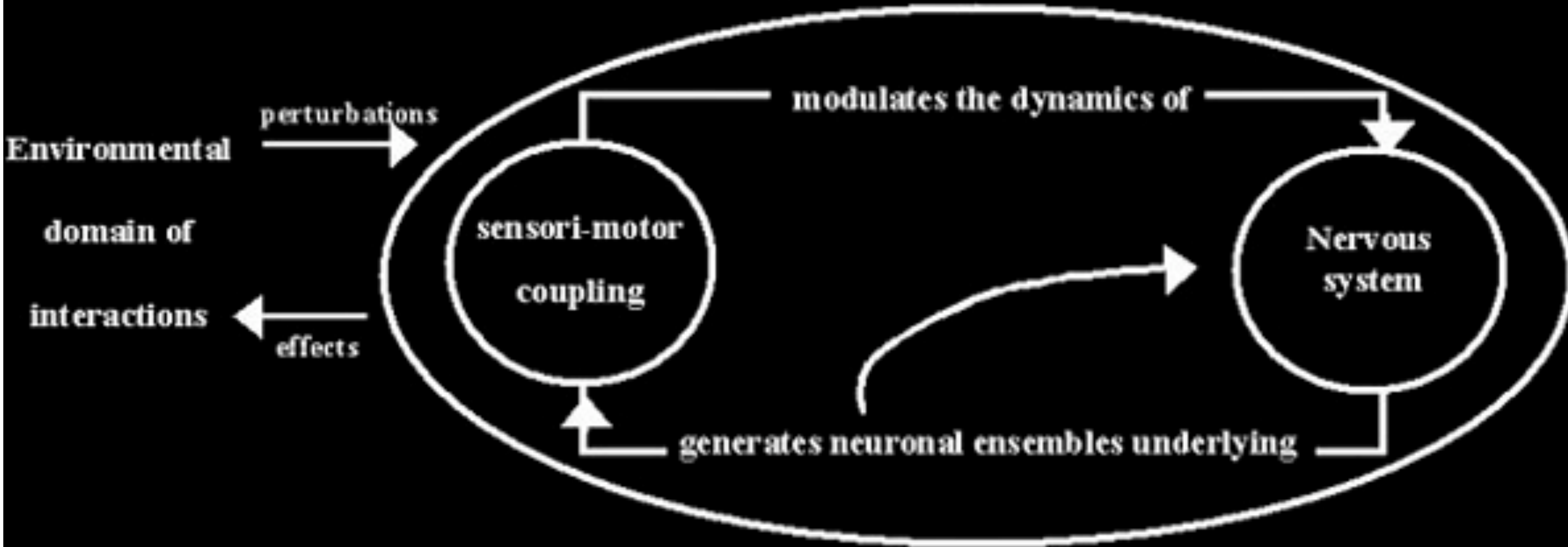


3 Properties: Meta-stability, Reference pole, Fast integration

Enactive point of vue:

It does not follow that the internal neural characteristics of such assemblies are sufficient for their correlative mental states. On the contrary, the somatic and dynamic sensorimotor context of neural activity is also crucial. According to the enactive approach, mental states depend crucially on the manner in which neural processes are embedded in the somatic and environmental context of the organism's life and hence it is doubtful that there is such a thing as a minimal internal neural correlate, even a complex dynamical one, whose intrinsic properties are sufficient for conscious experience
(Lutz et al., 1999).

Ces assemblées de neurones sont à la fois la source et le résultat de l'activité des aires sensorielles et motrices.



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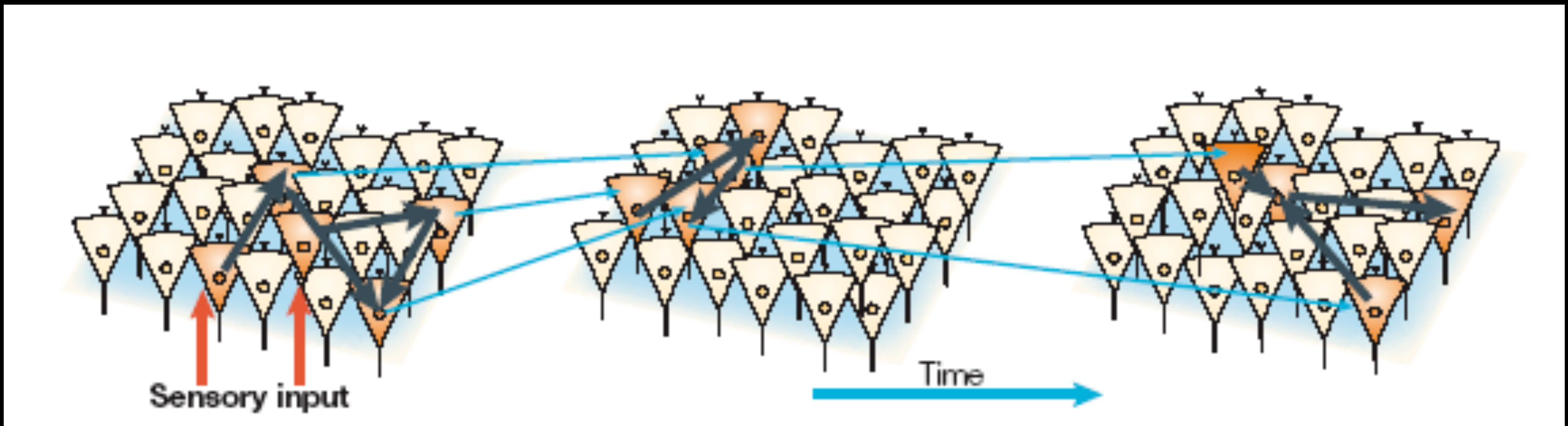
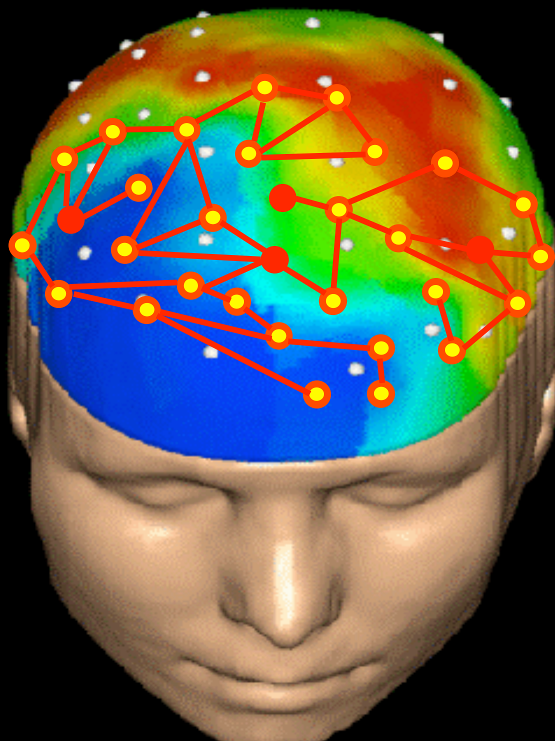
No neuronal code…

Classical theories of sensory processing view the brain as a passive, stimulus-driven device. By contrast, more recent approaches emphasize the contructive nature of perception, viewing it as an active and highly selective process.
(Engel et al., 2001)



Ongoing activity that precedes sensory stimulation plays an important part in shaping neural activity during stimulus presentation, which indicates that it might be more accurate to regard sensory stimuli as modulating ongoing neural dynamics, rather than deterministically controlling firing patterns.

How can we study large-scale brain phenomena?



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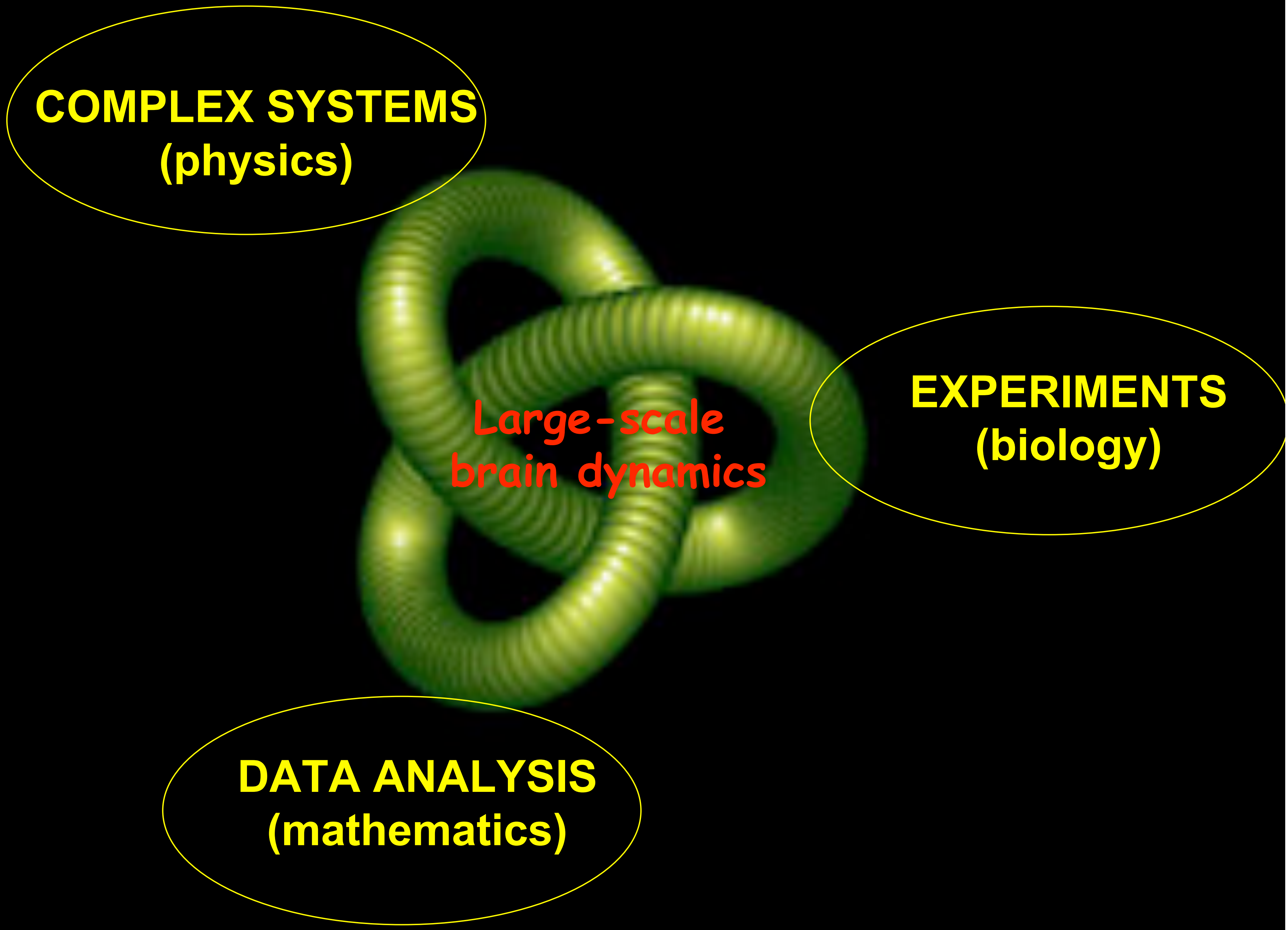
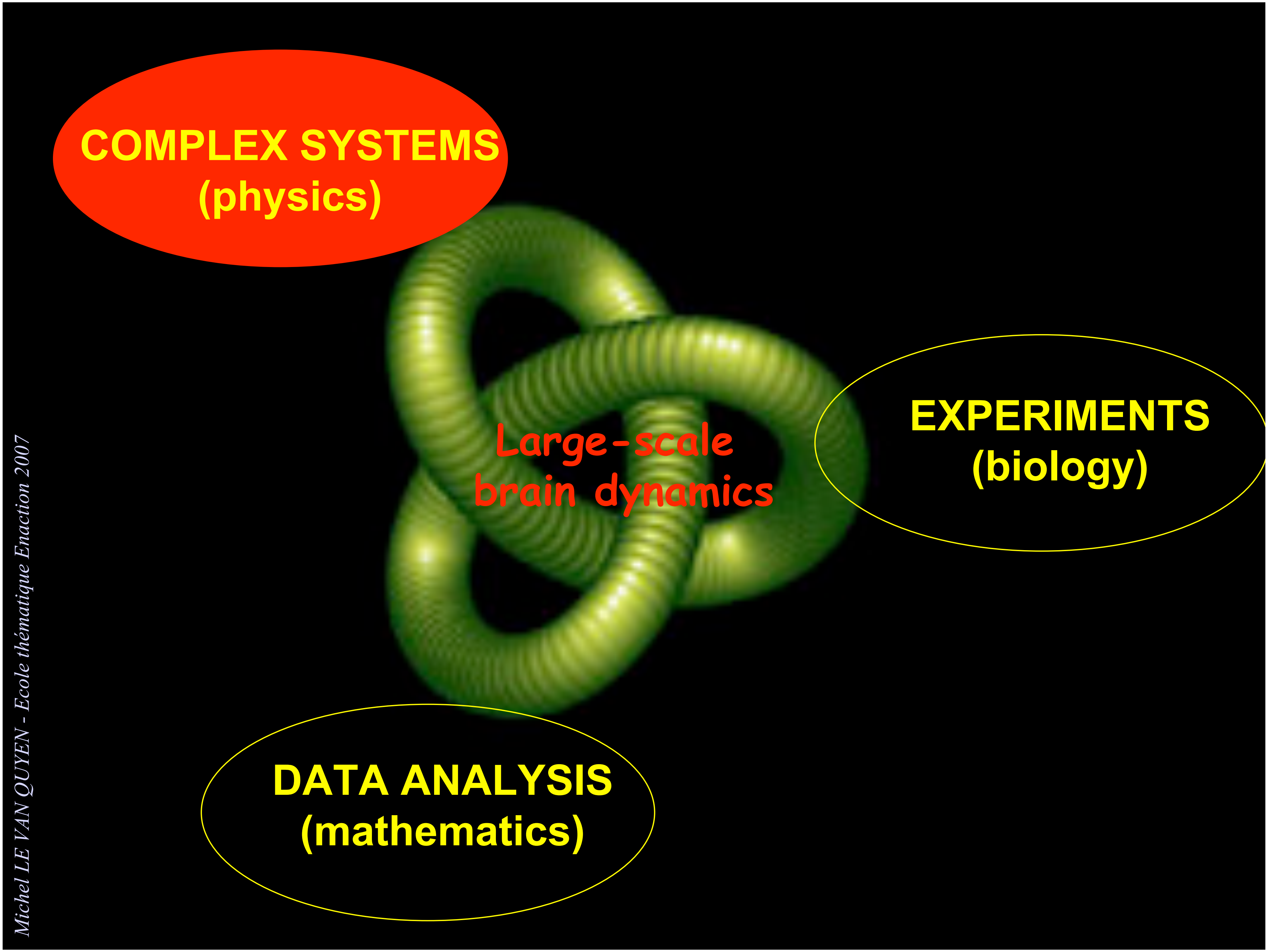

COMPLEX SYSTEMS
(physics)
Large-scale
brain dynamics
EXPERIMENTS
(biology)
DATA ANALYSIS
(mathematics)


COMPLEX SYSTEMS
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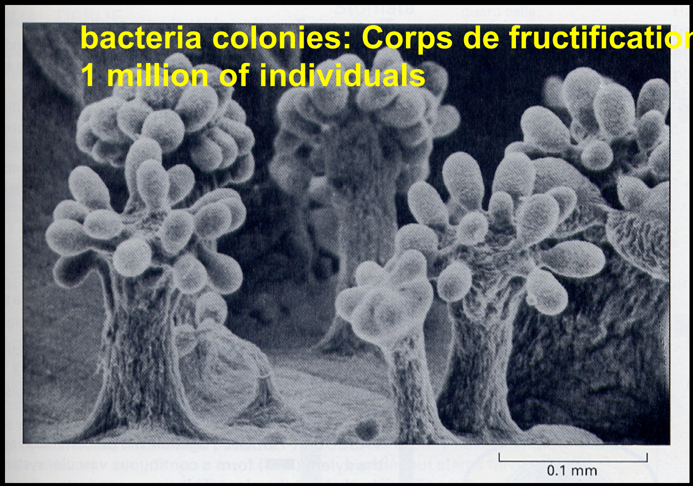
Self-organisation in natural systems



Green algae: from Chlamydomonas to Volvox

Parrish and Edelstein-Keshet 1999. Picture by Norbert Wu (1999)

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DIE NATURWISSENSCHAFTEN

28. Jahrgang 16. August 1940 Heft 33

Der Organismus als physikalisches System betrachtet.

Von Ludwig von Bertalanffy, Wien[1]).

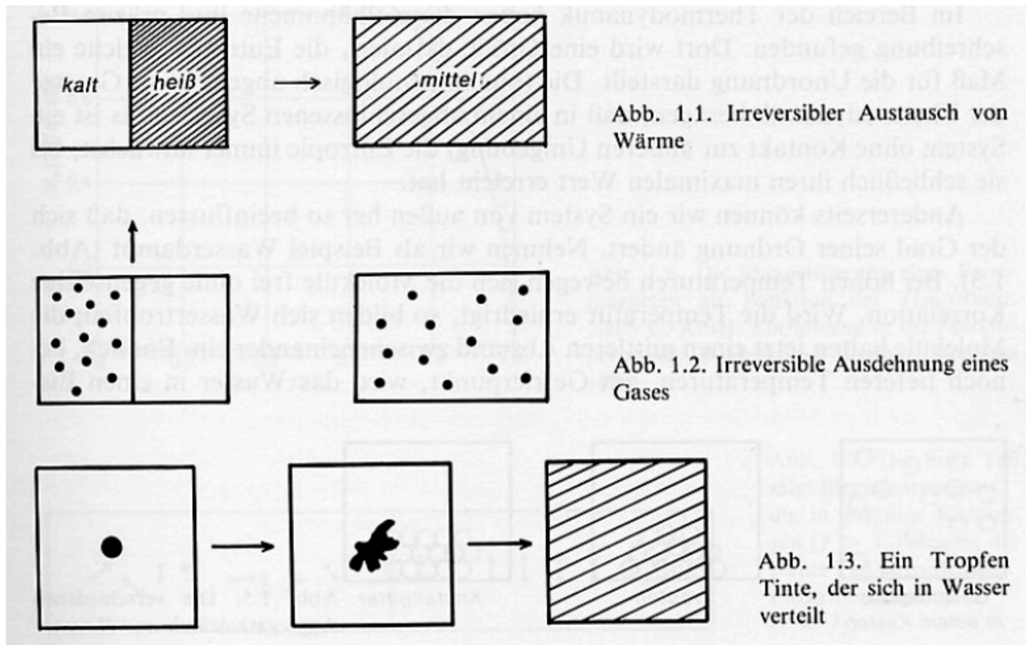
- ✓ Organism is open, not closed (chemical or physical) system
- ✓ Dynamic (quasi-) steady state, as opposed to static equilibrium
- ✓ Fine-tuned coordination of all process rates for steady state
- ✓ Processes nonlinear
- ✓ Perturbations and stability
- ✓ "…even after a full explanation of all individual processes are we as far away from a total understanding of metabolism as the sky is wide."

Self-organisation in non-living systems?

heat exchange

expansion of a gas

diffusion of ink drop



H. Haken

Typically, macroscopic structure vanishes:
thermodynamics: entropy (disorder) always increases,
no self-organization

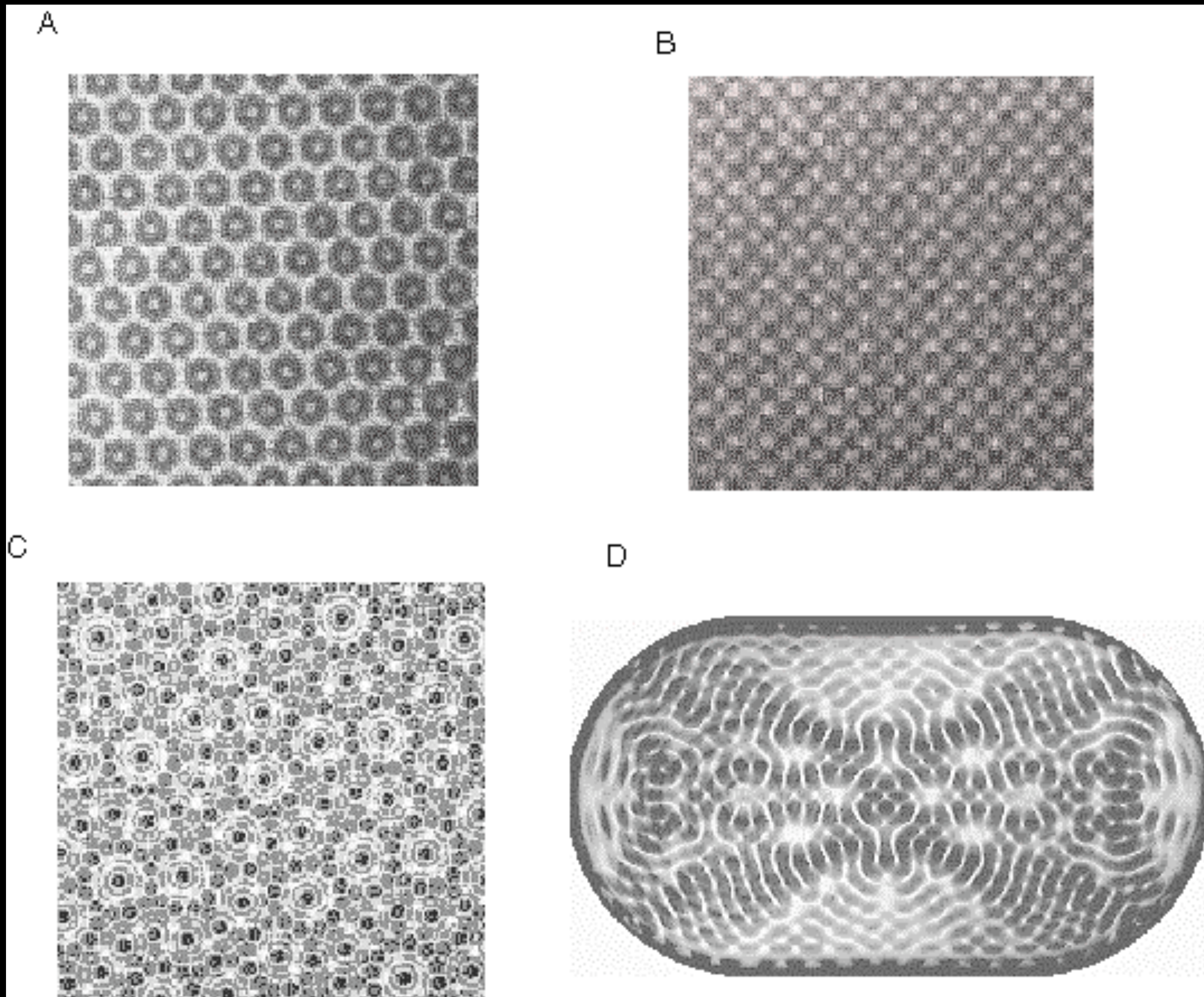
NEWTON

PRIGOGINE

Ordre,
loi de l'équilibre

Désordre,
Structures dissipatives
hors de l'équilibre

Harmonic Resonance, Chladni (1787)



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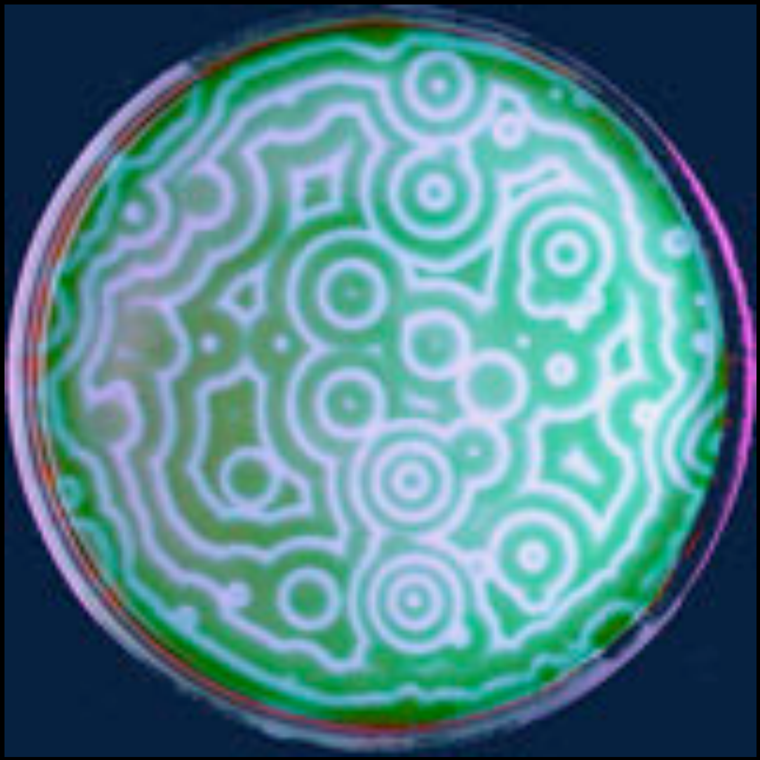
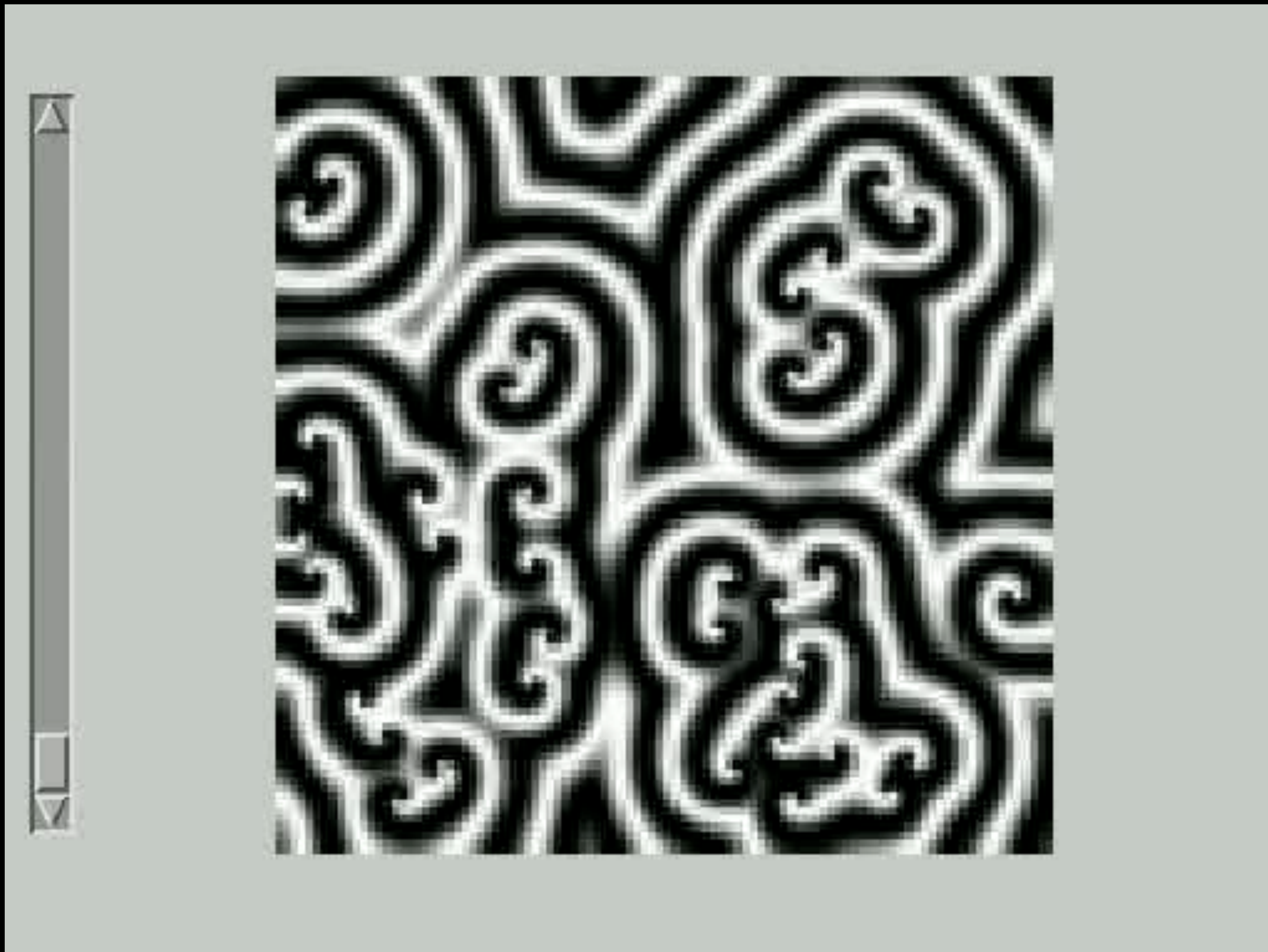
Non-living pattern formation

- Based on physical and chemical properties
  - Belousov-Zhabotinsky reaction
  - Bénard convection cells
  - Sand dune ripples



horloge chimique



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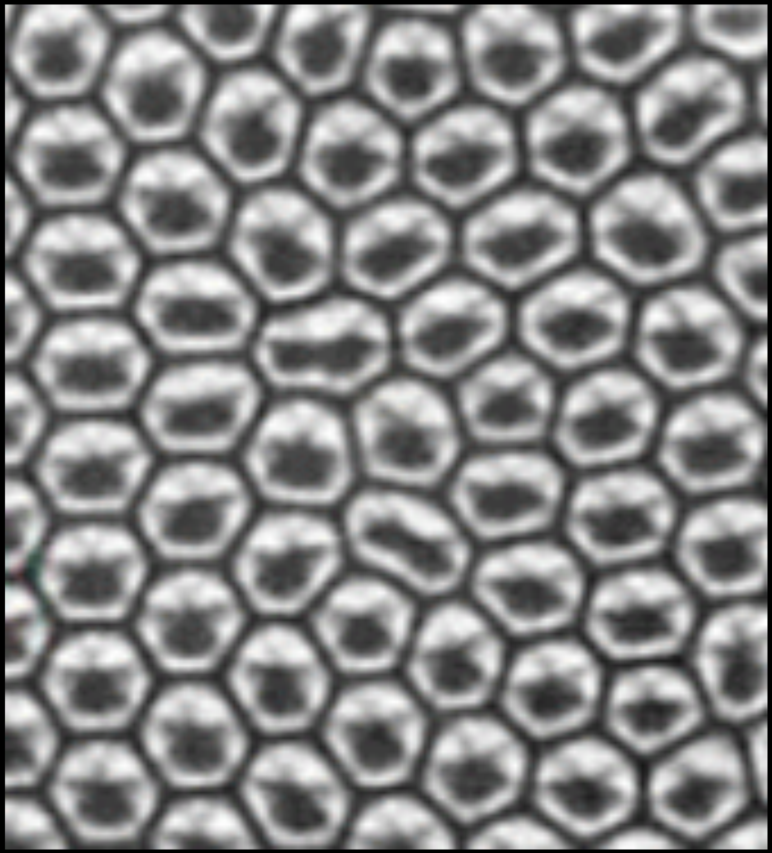

Non-living pattern formation

- Based on physical and chemical properties
  - Belousov-Zhabotinsky reaction
  - Bénard convection cells
  - Sand dune ripples

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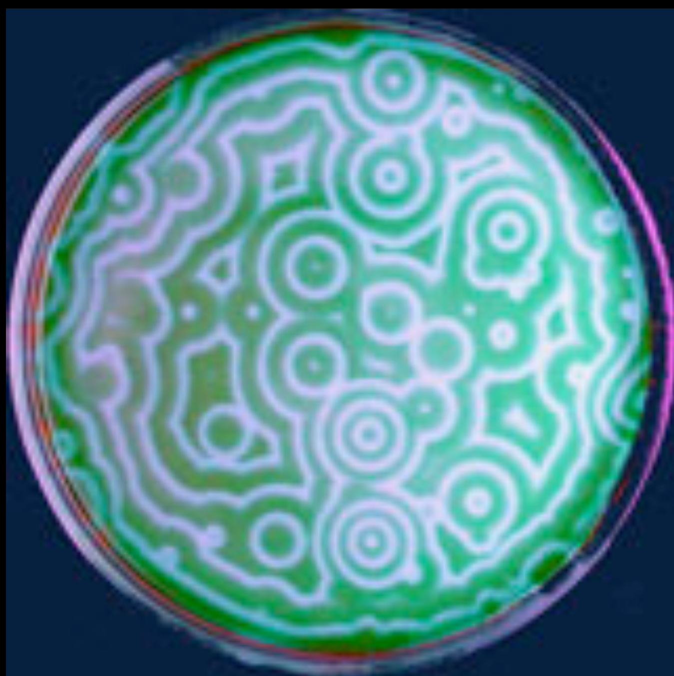
Système dynamique complexe

Coexistence d'ordre et de désordre

Le système manifeste une dynamique nonlinéaire:
une petite perturbation peut entrainer
une cascades d'évenements imprévisibles
(i.e sensibilité aux conditions initiales)

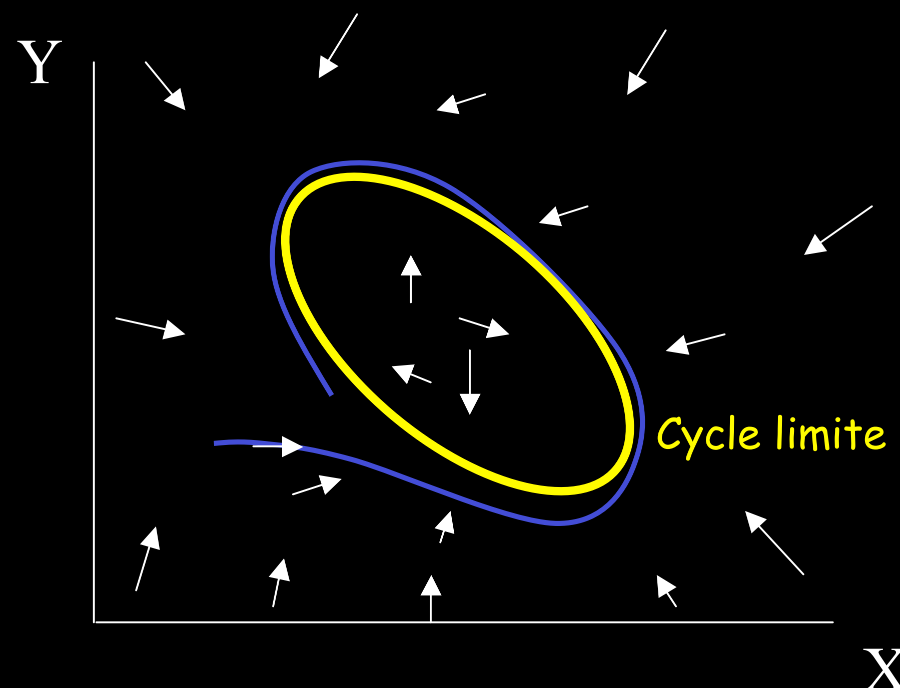
Le système s'auto-organise en une dynamique d'ensemble
contrainte et controlée des états "attracteurs"

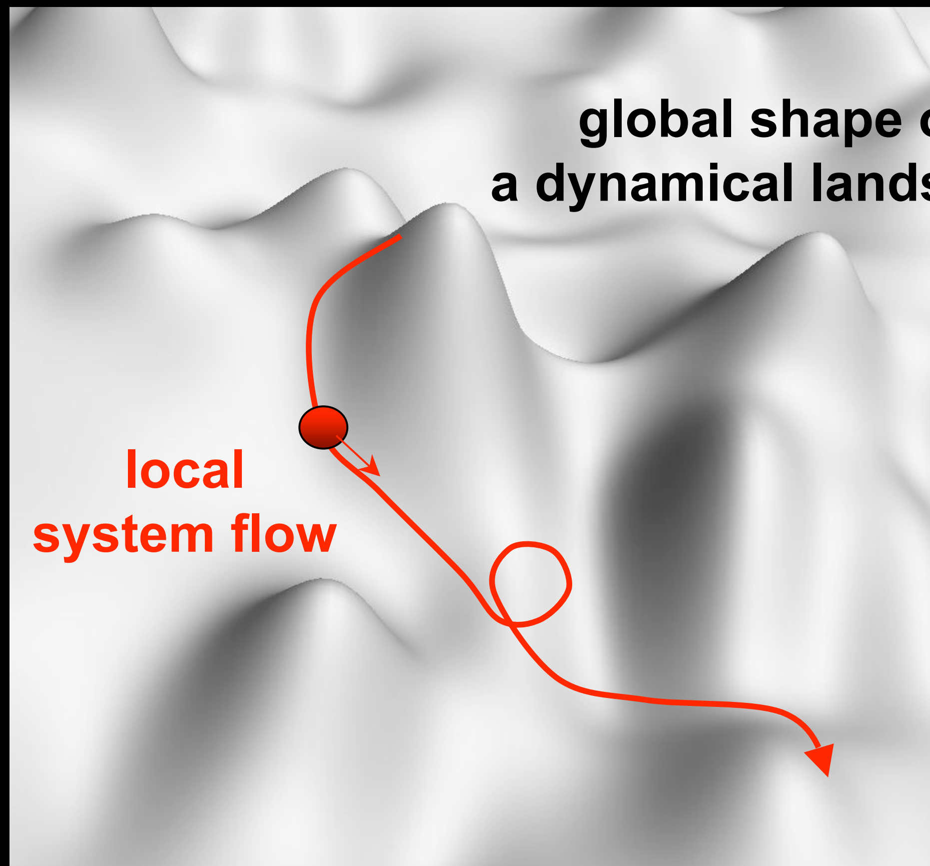
Lois d'organisation globale: Etat attracteur

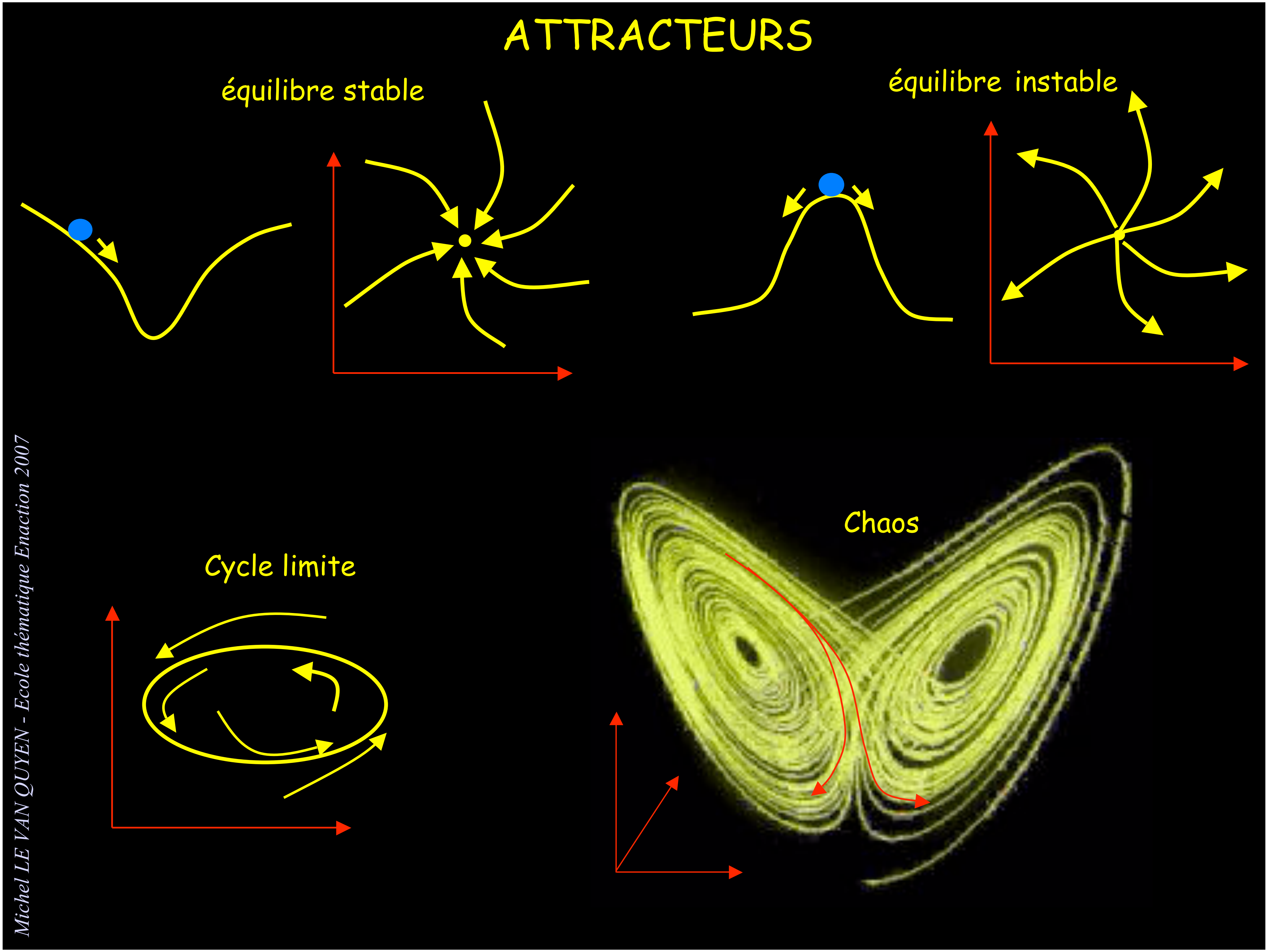


$$\dot{X} = r - X - \frac{4XY}{1+X^2}$$

$$\dot{Y} = bX\left(1 - \frac{Y}{1+X^2}\right)$$




global shape
a dynamical lands
local
system flow


ATTRACTEURS
équilibre stable
équilibre instable
Cycle limite
Chaos
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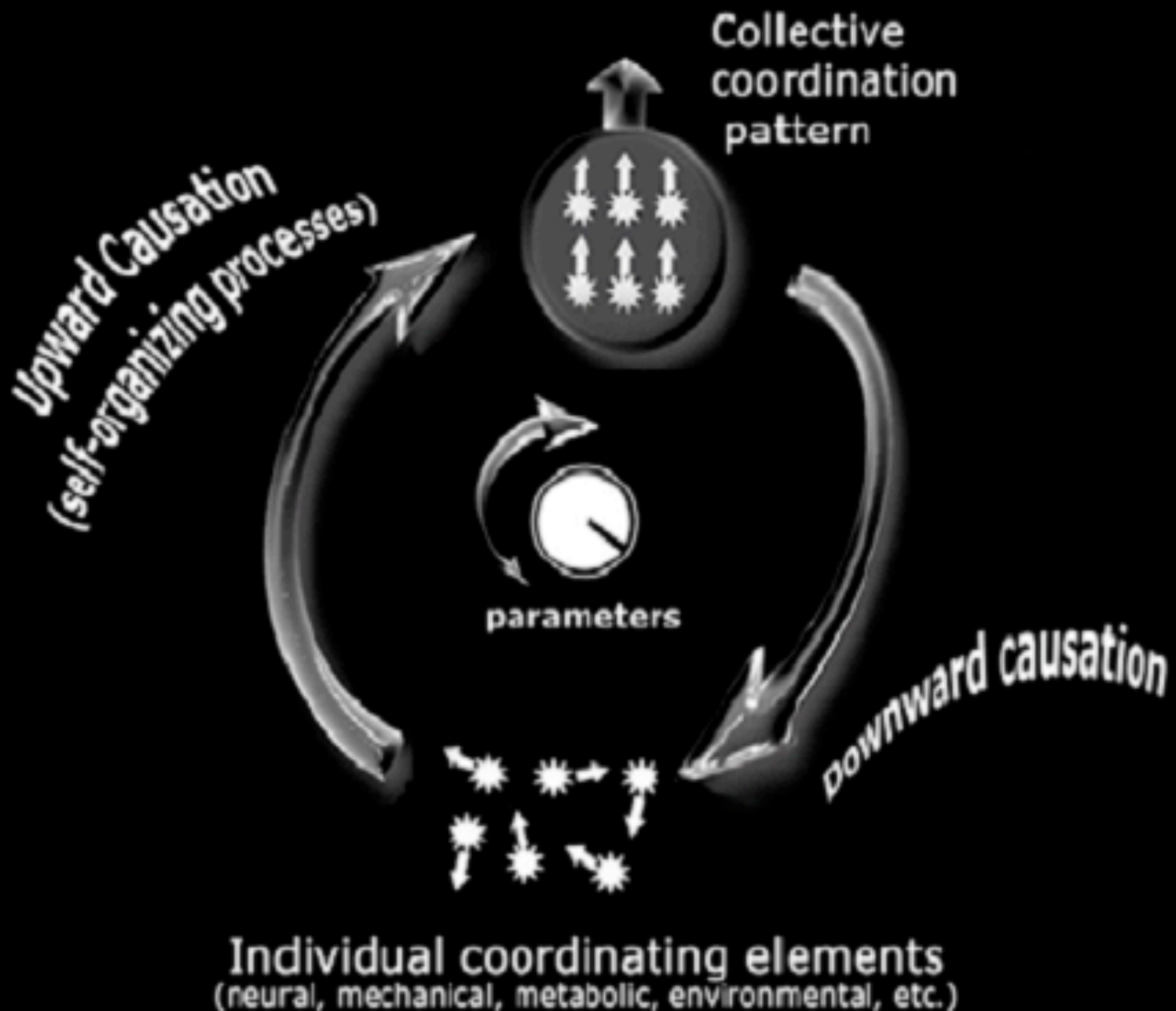
Reciprocal causality of coordination dynamics



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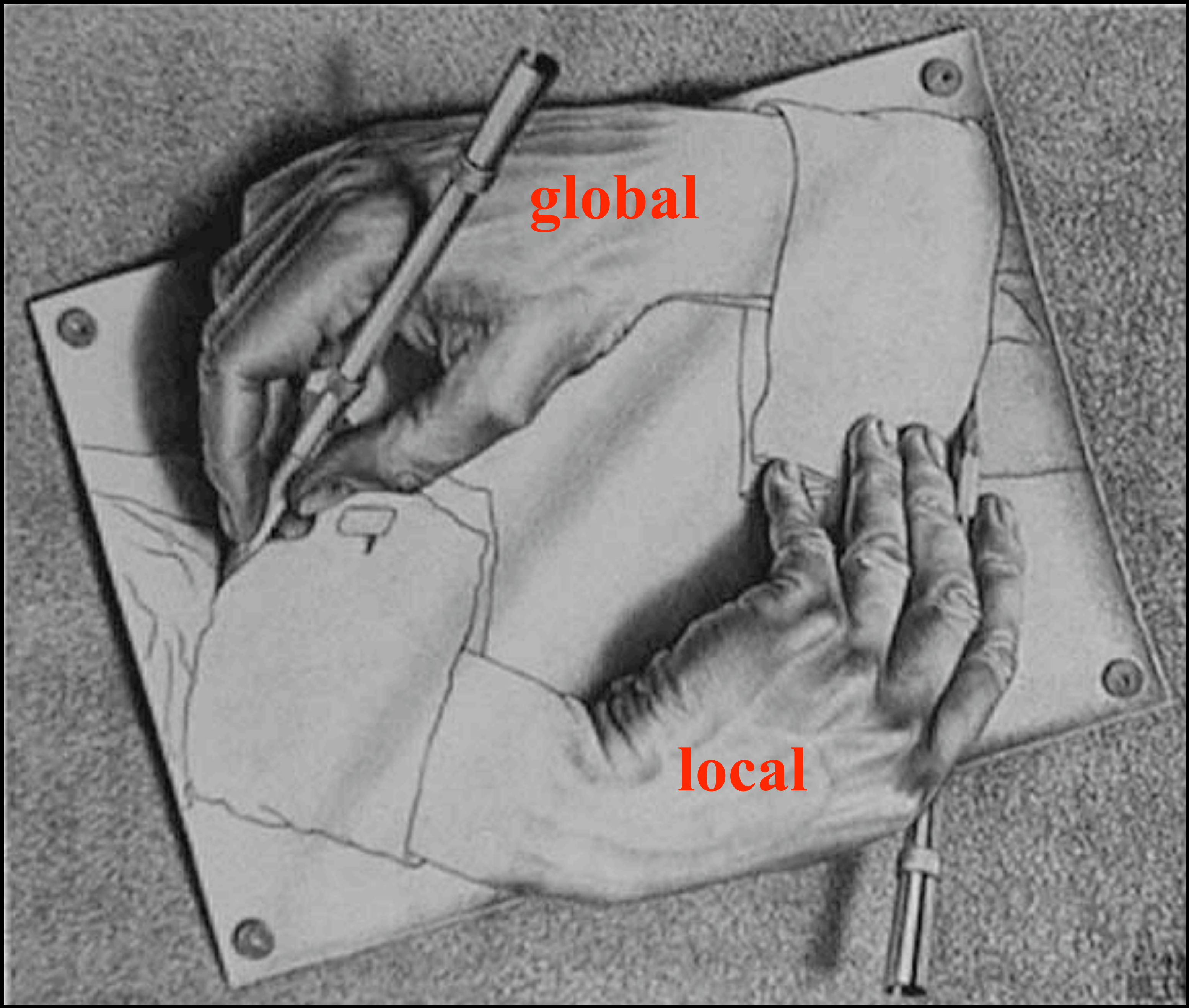
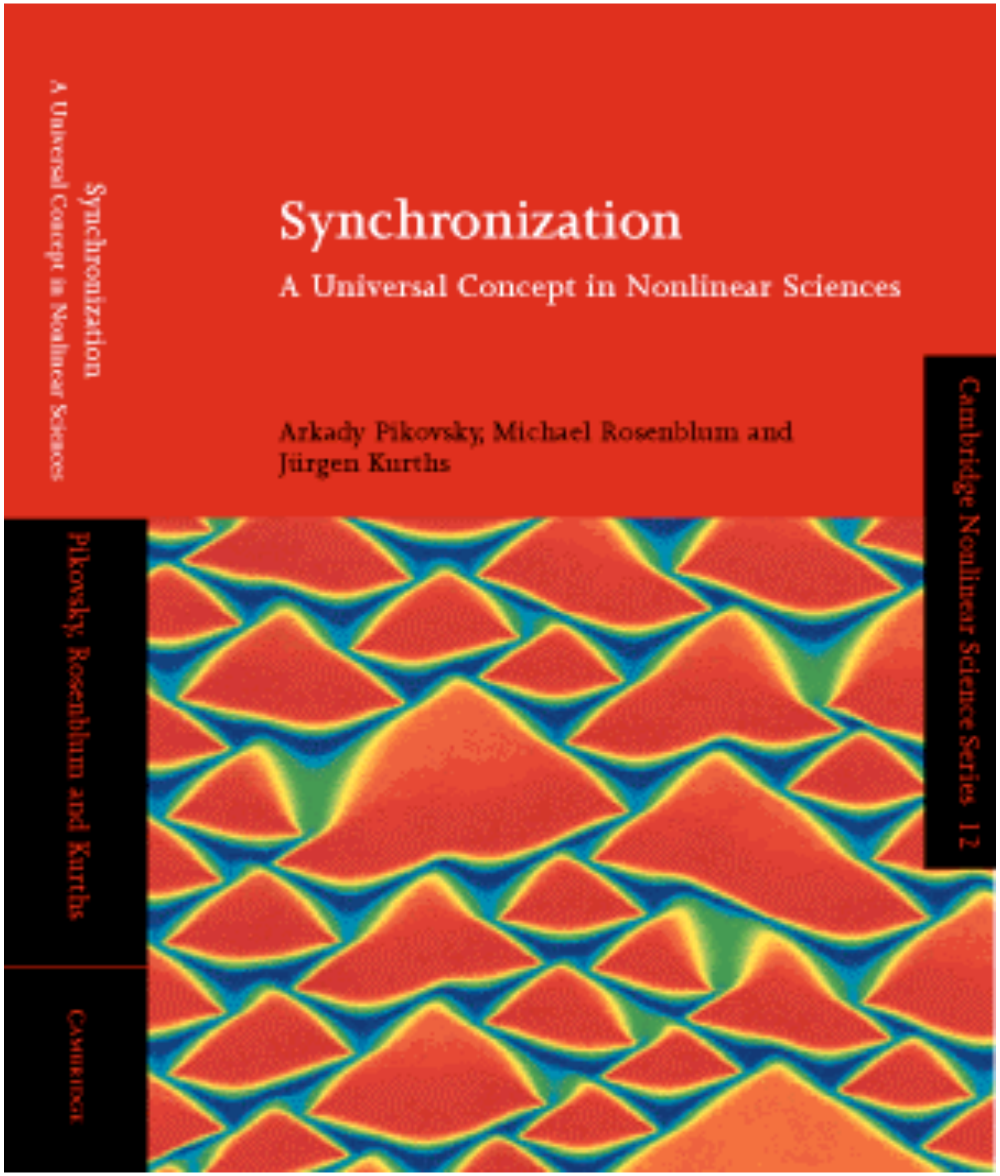

global
local

Synchronization is one of the most pervasive phenomena in the Universe.

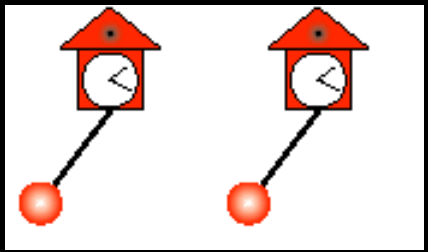


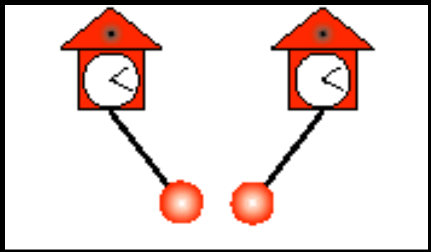
Synchronization of Clocks

In 1665, Dutch physicist Christiaan Huygens observed the motions of two pendulum clocks he had built.

He detected an “odd kind of sympathy” between the clocks: regardless of their initial state, the two pendulums soon adopted the same rhythm, one moving left as the other swung right.

This synchrony to tiny forces transmitted between the clocks by the wooden beam from which they were suspended.





- A group of fireflies in Asia (Pteroptyx Malacae, Pteroptyx Cribellata) can synchronously flash.
  - A firefly flashes independently at its own rate when it is apart from others.
  - When a firefly meets a group, their flashes stimulate it, and this firefly adjusts an internal timer to flash at the same rate as its neighbors.
- The synchronization mechanism is fully-distributed and self-organizing.

Kuramoto Model-A Crucial Breakthrough

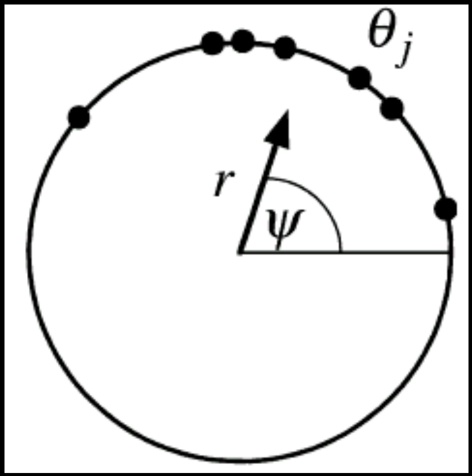
- It corresponds to the simplest possible case of equally weighted, all-to-all, purely sinusoidal coupling:

$$\dot{\theta}_i = \omega_i + \frac{K}{N} \sum_{j=1}^{N} \sin(\theta_j - \theta_i)$$

- **where K is the coupling strength and the factor 1/N ensures that the model is well behaved as $N \rightarrow \infty$.**
- **The frequencies ω_i are distributed according to some probability density g(ω). For simplicity, Kuramoto assumed that g(ω) is unimodal and symmetric about its mean frequency.,**

Order Parameter

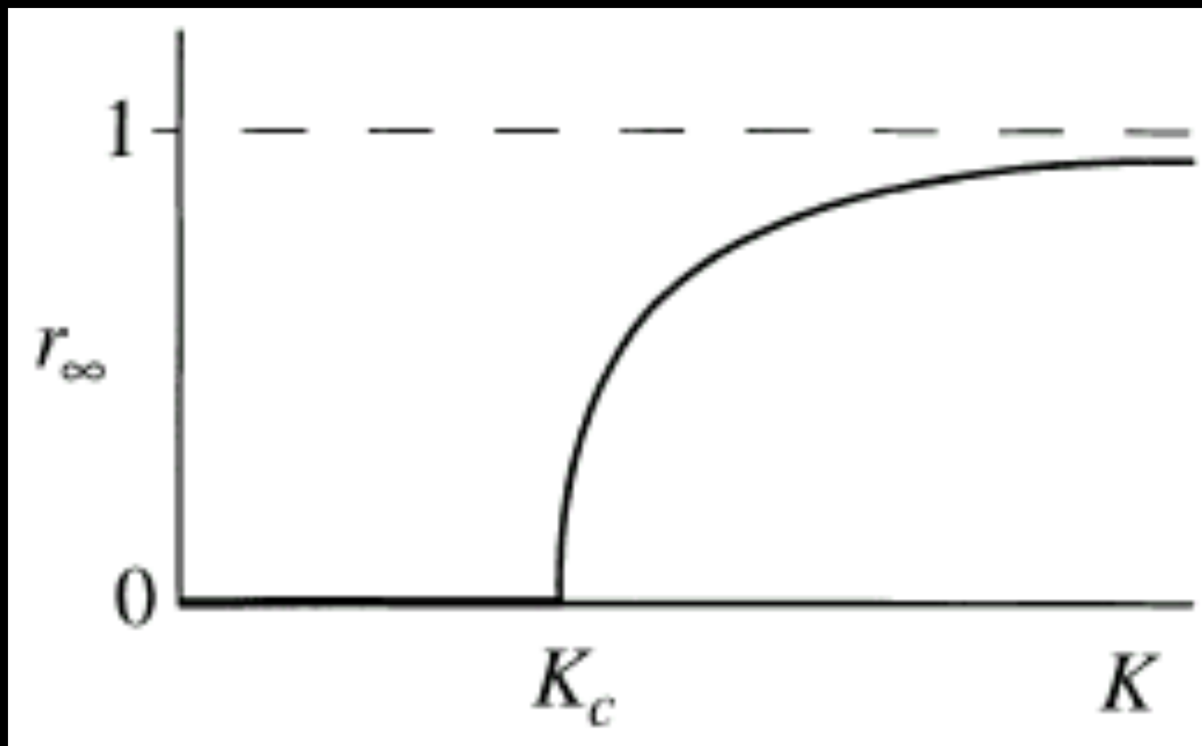
- To visualize the dynamics of the phases, it is convenient to imagine a swarm of points running around the unit circle in the complex plane.



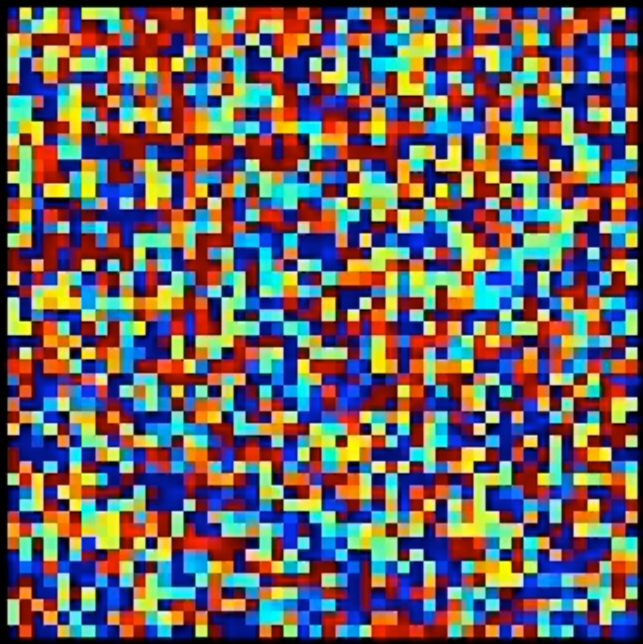
$$re^{i\psi} = \frac{1}{N}\sum_{j=1}^{N} e^{i\theta_j}$$

◆ **The parameter is a macroscopic quantity that can be interpreted as the collective rhythm produced by the whole population. It corresponds to the centroid of the phases. The radius r(t) measures the phase coherence, and ψ(t) is the average phase.**

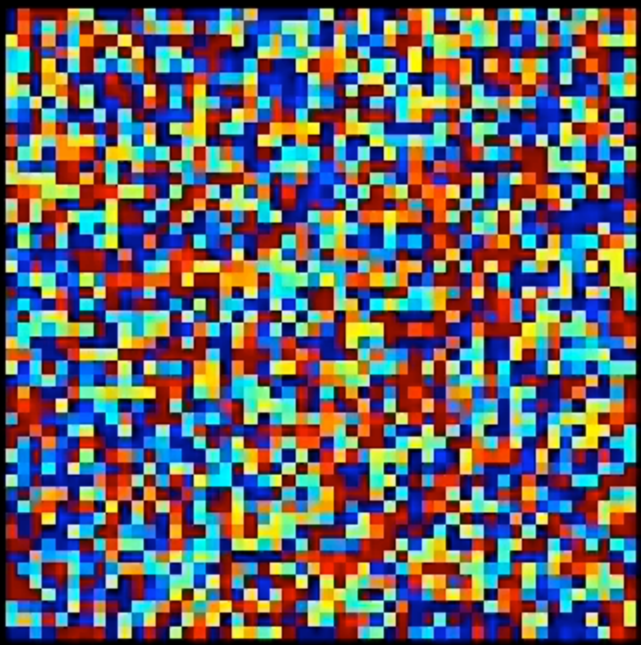
Synchronization threshold



Dynamique d'un réseau d'oscillateurs couplés



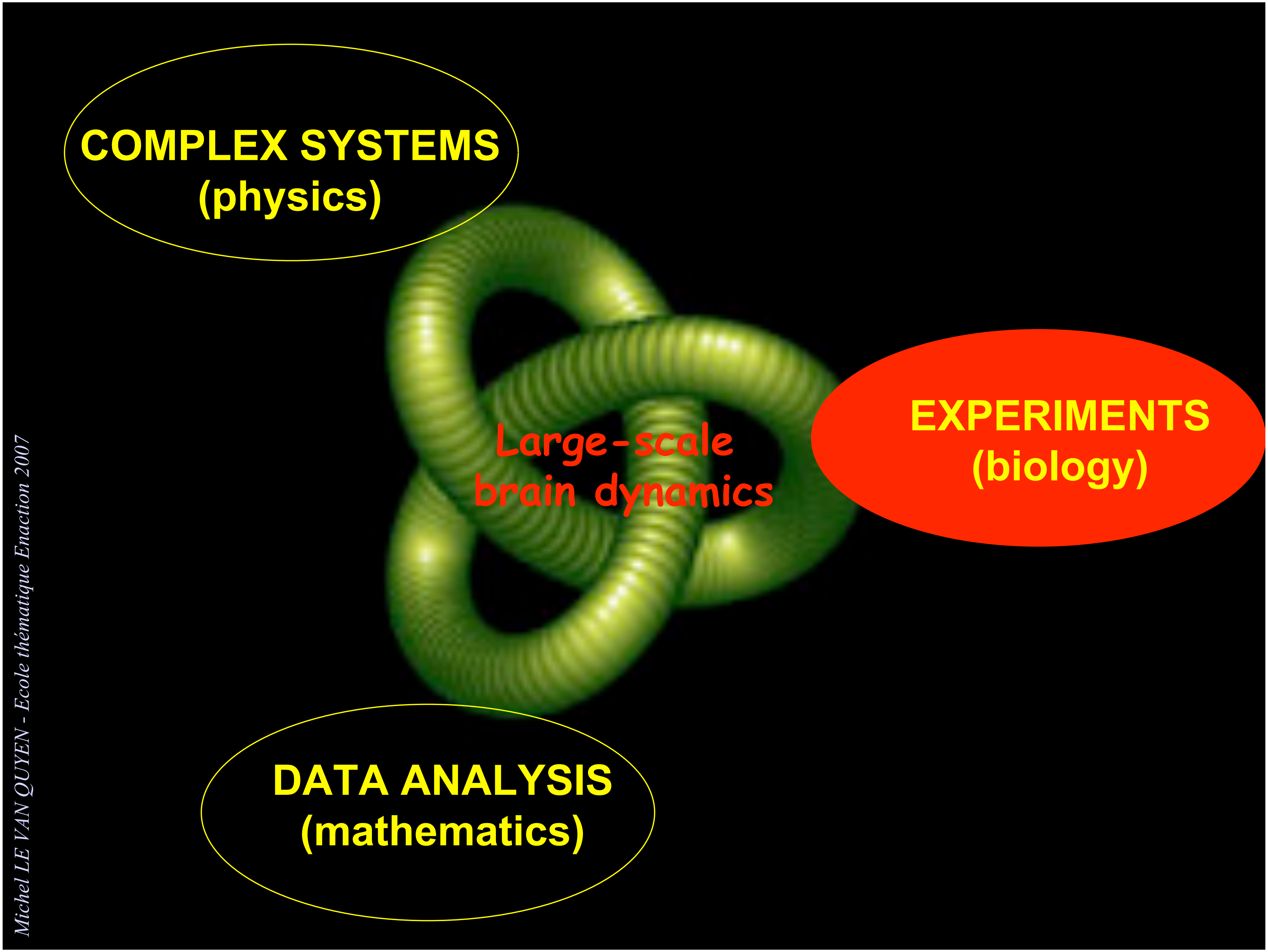
C<C*



C>C*

Michel LE VAN QU

LE VAN QUYEN M., SCHUSTER H.G., VARELA F (1996) International Journal of Bifurcation and Chaos 6


COMPLEX SYSTEMS
(physics)
EXPERIMENTS
(biology)
DATA ANALYSIS
(mathematics)
Large-scale
brain dynamics
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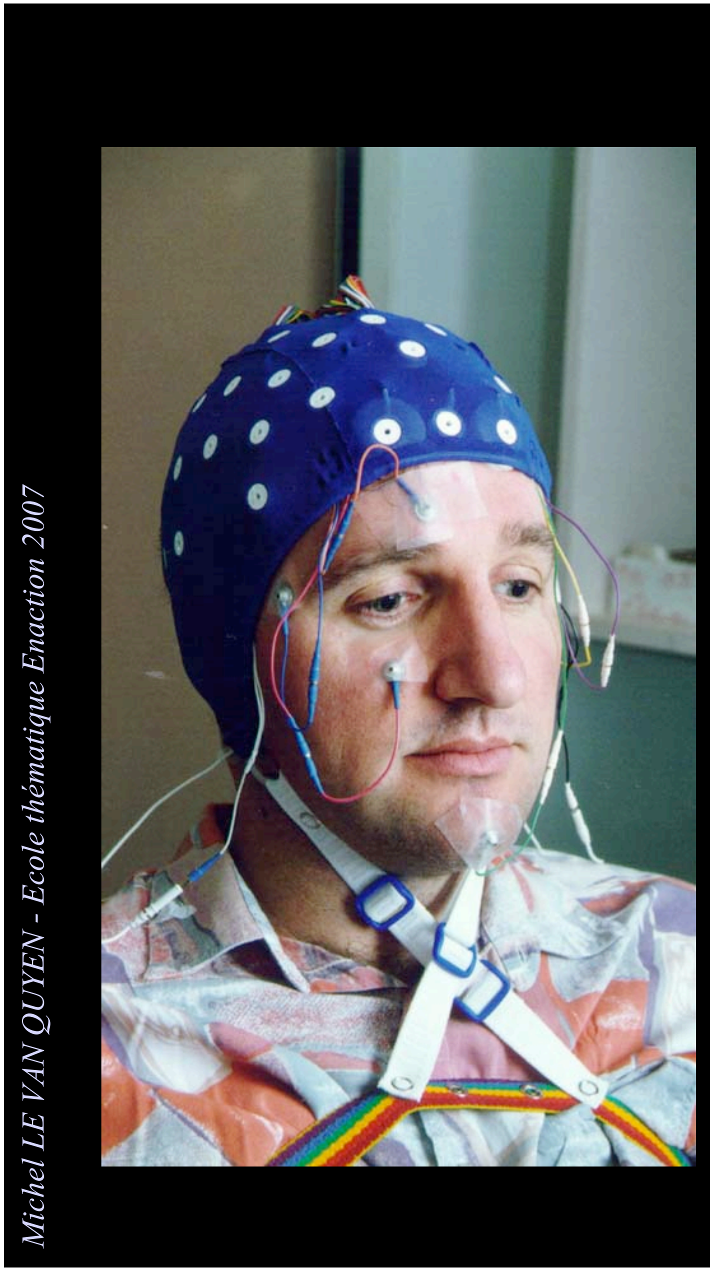
EEG (Elec



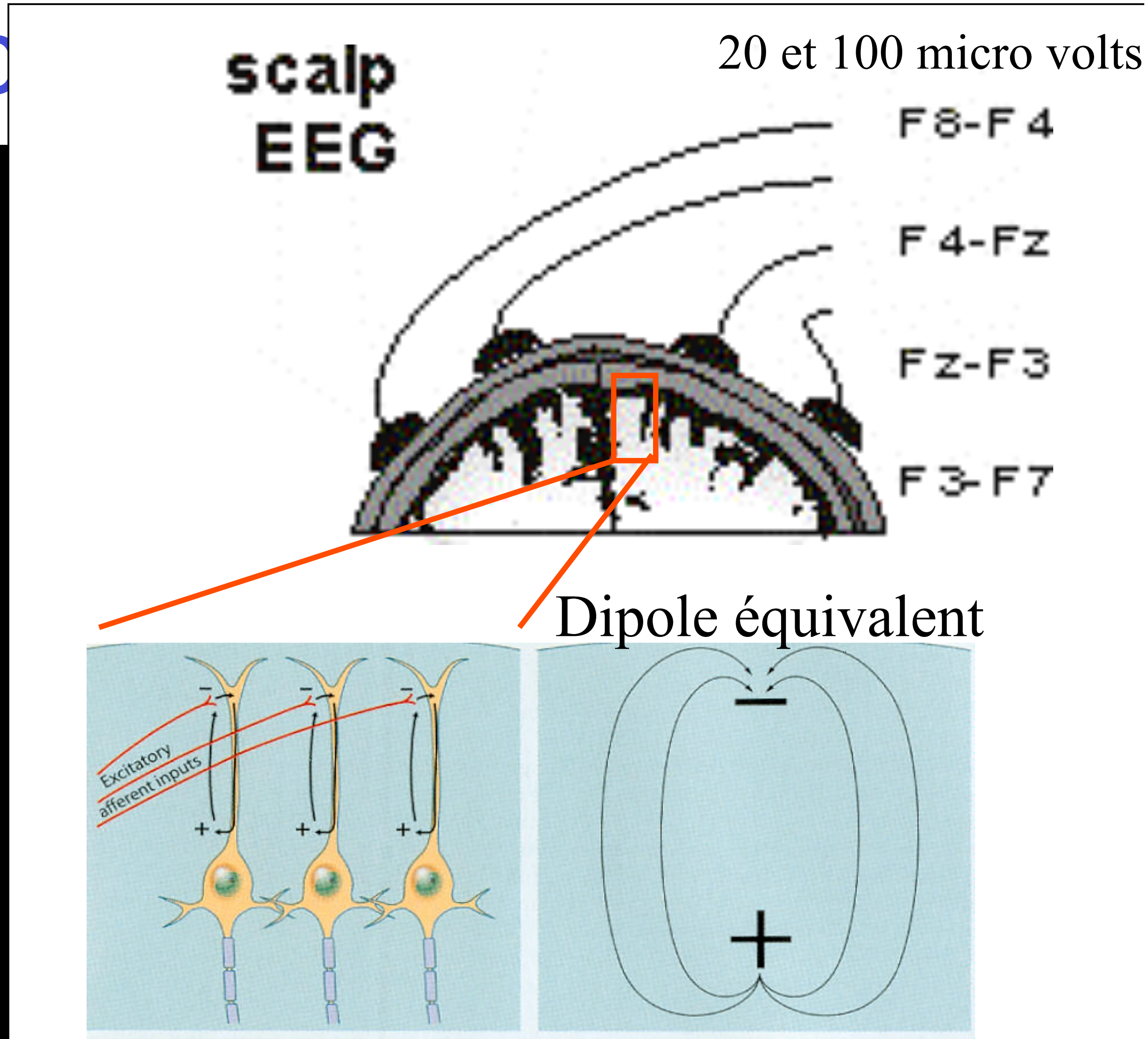
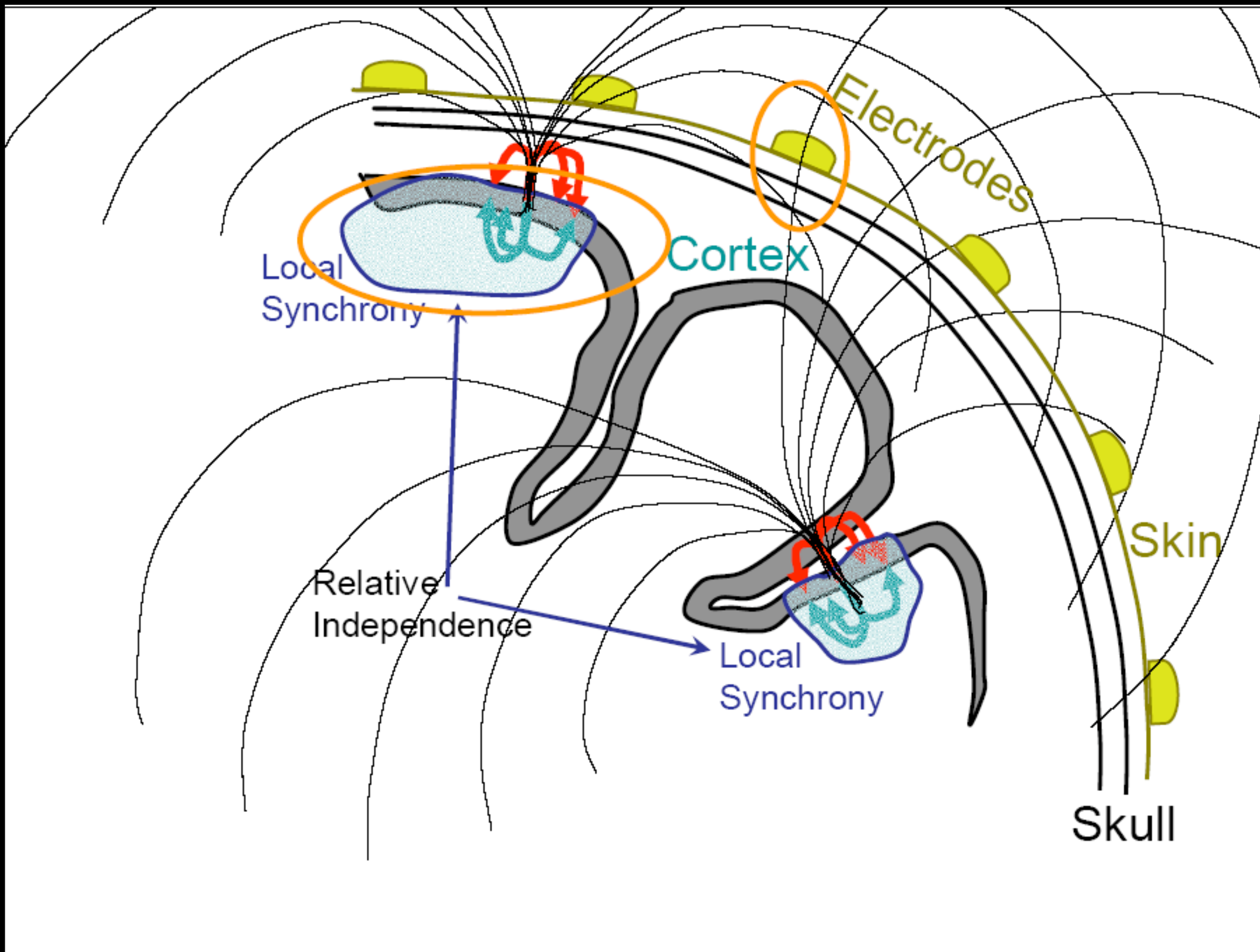
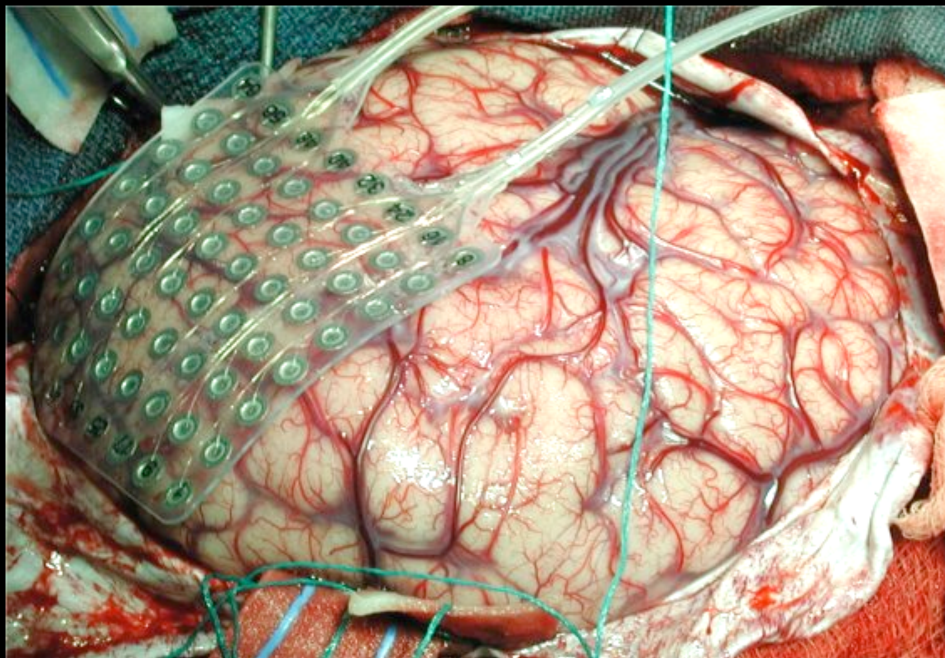


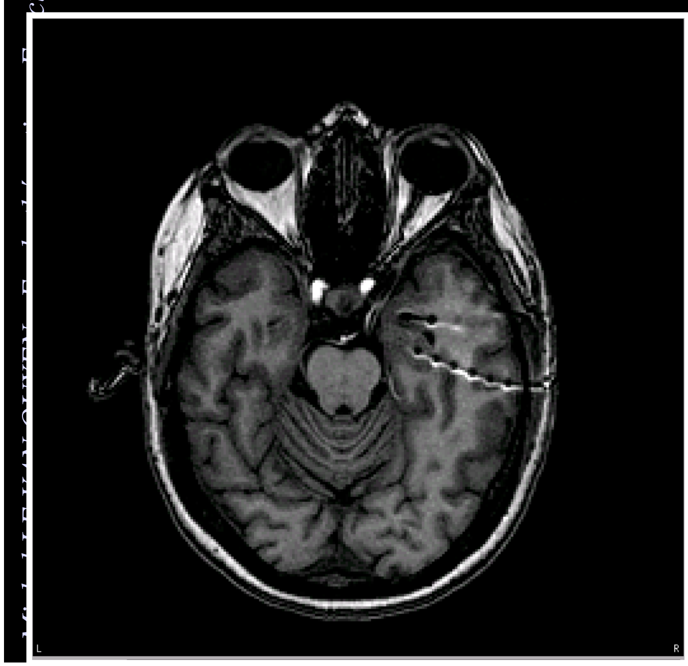
Figure 3.36 Gazzaniga et al 1998

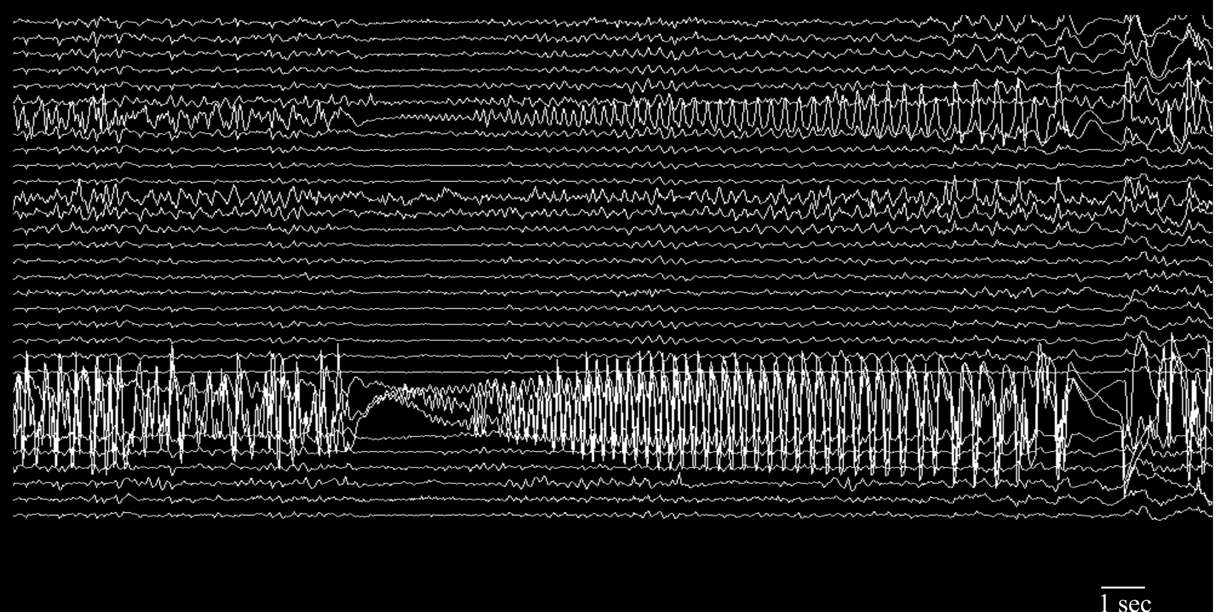
- A positive-negative pair of electrical charges
- Summed *post-synaptic potentials*
- *Synchronous* activity
- *Aligned* neurones
- Conducted to scalp
- Decaying strength: most EEG produced by underlying *cortex*


Electrodes
Cortex
Local
Synchrony
Skin
Relative
Independence
Local
Synchrony
Skull

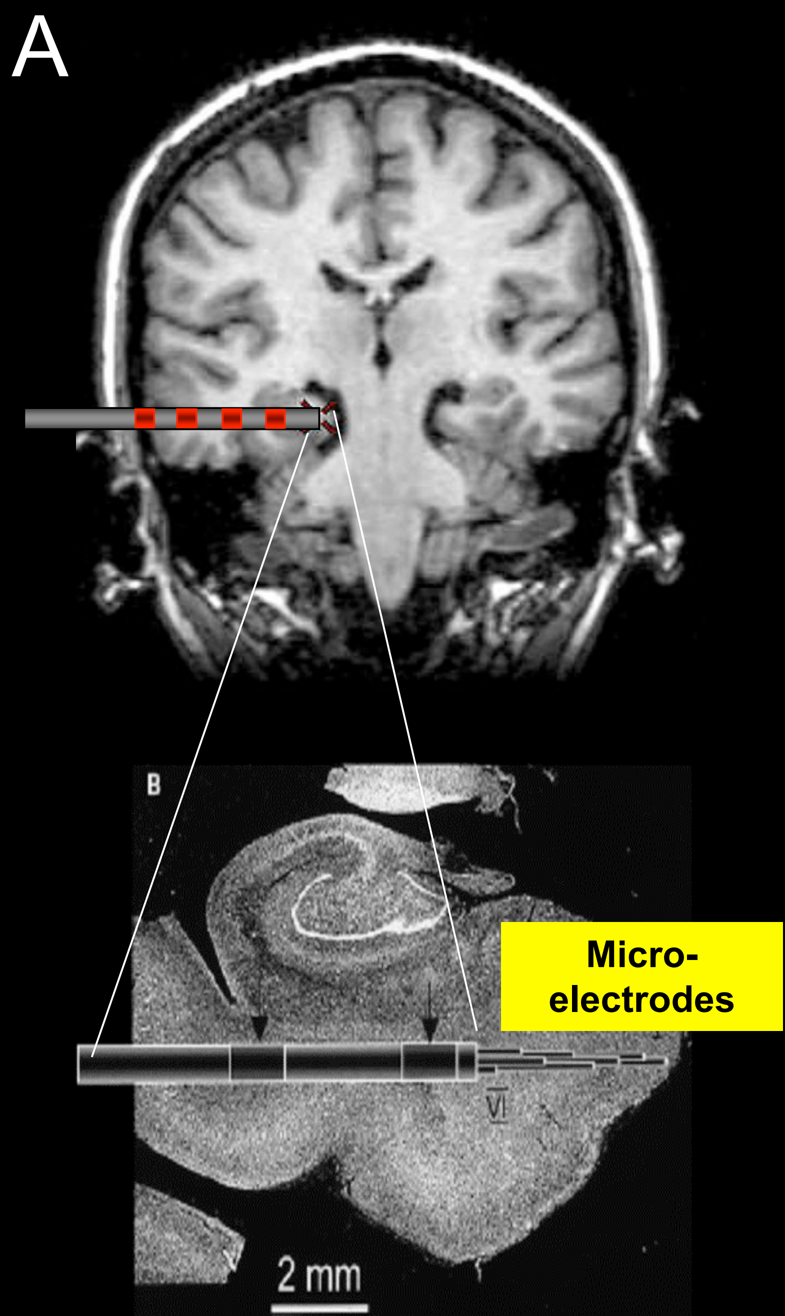


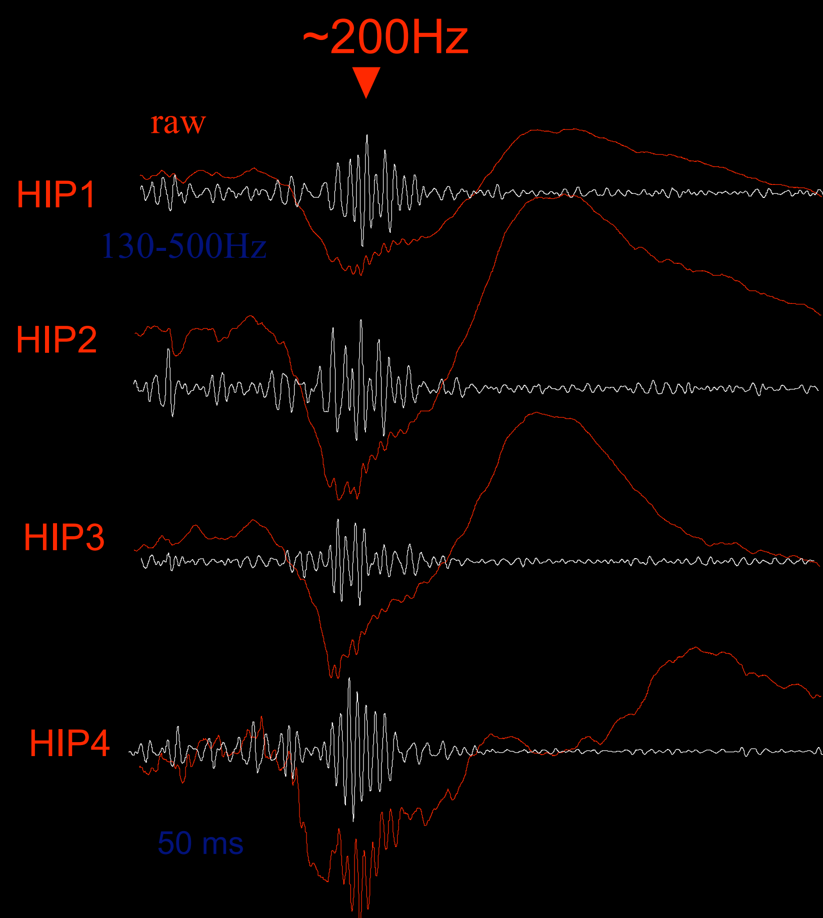
Intracranial recordings in epileptic patients

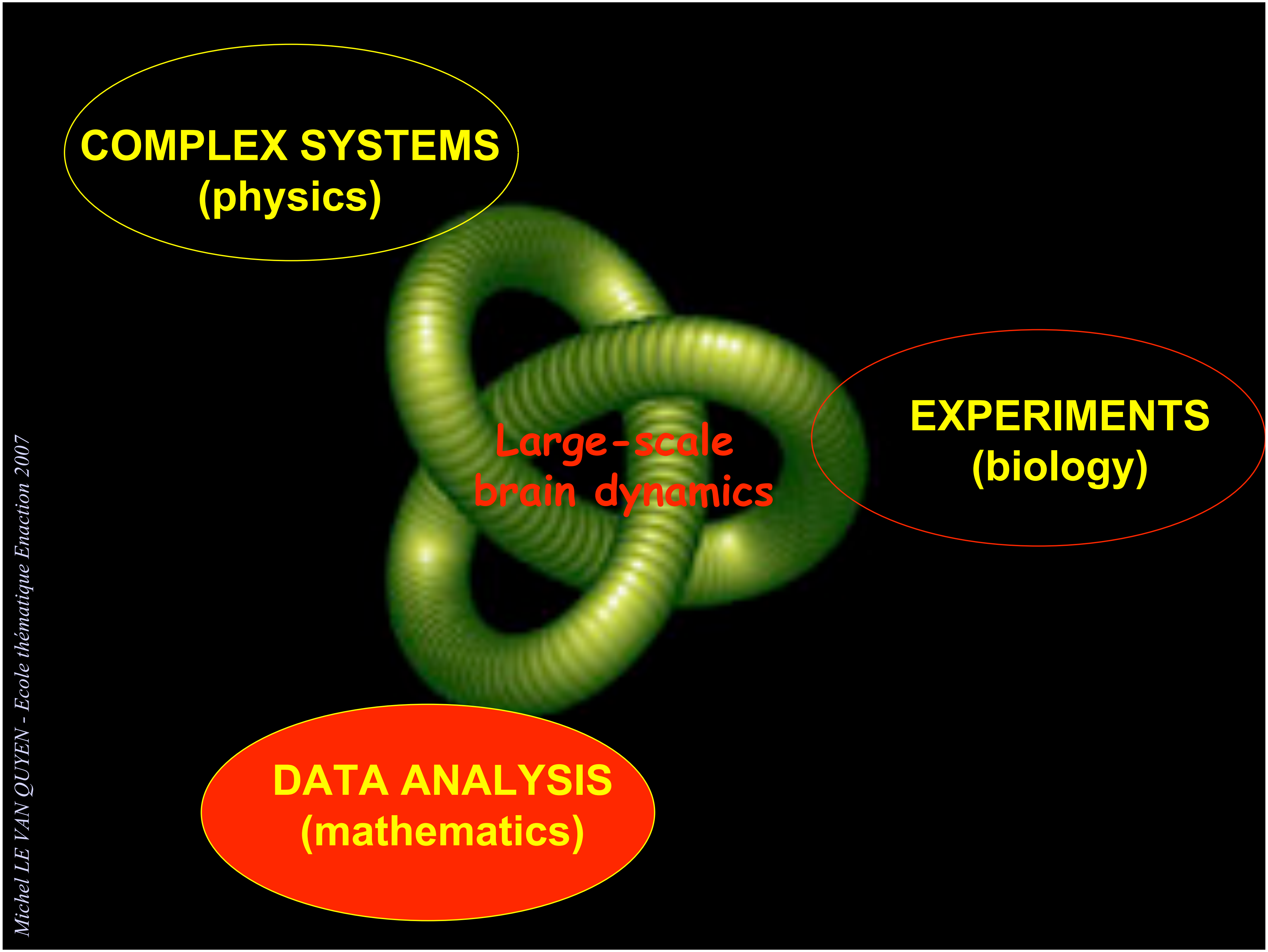




Projet microelectrodes
Hop. Salpétrière






COMPLEX SYSTEMS
(physics)
EXPERIMENTS
(biology)
DATA ANALYSIS
(mathematics)
Large-scale
brain dynamics
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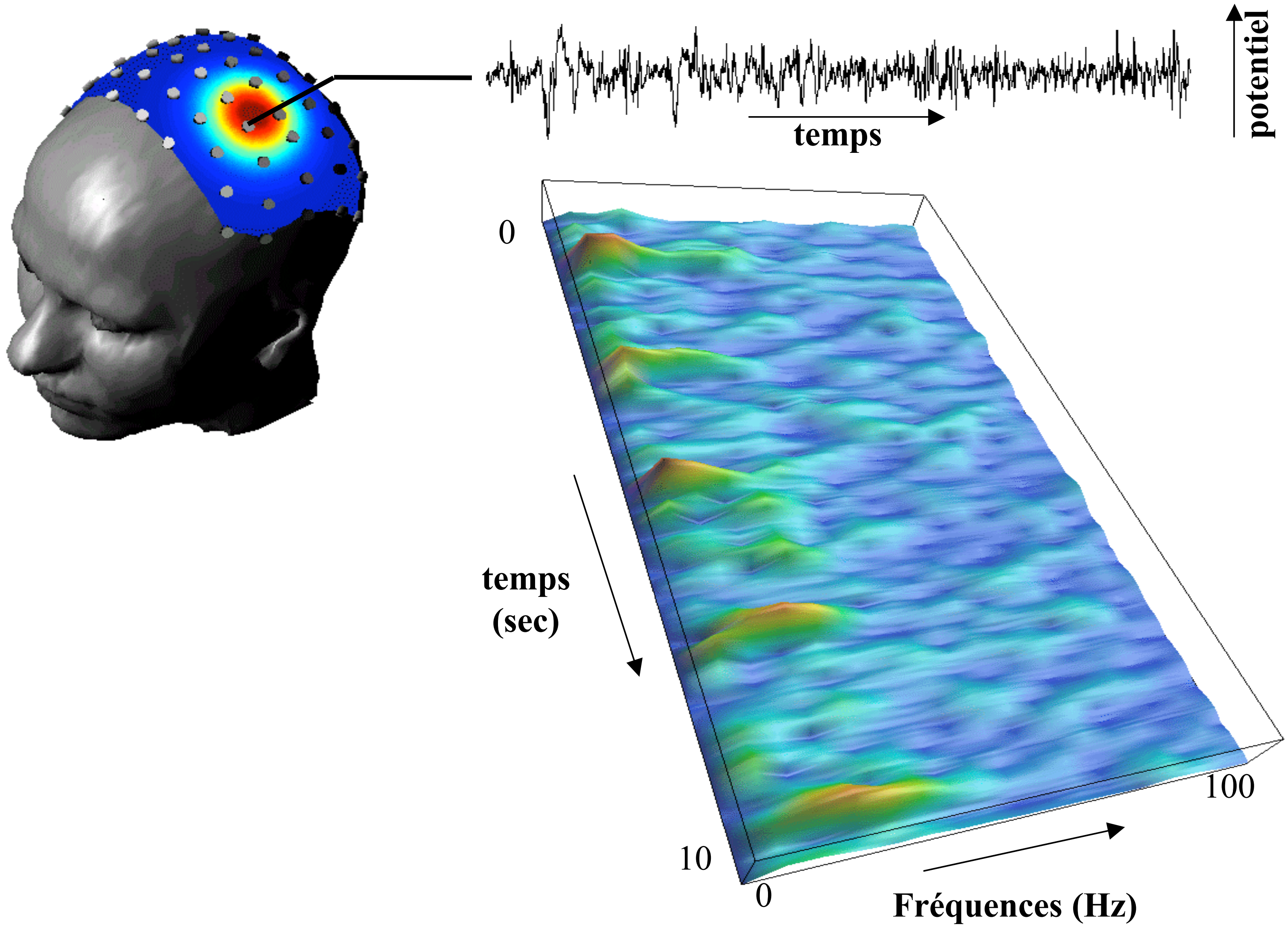
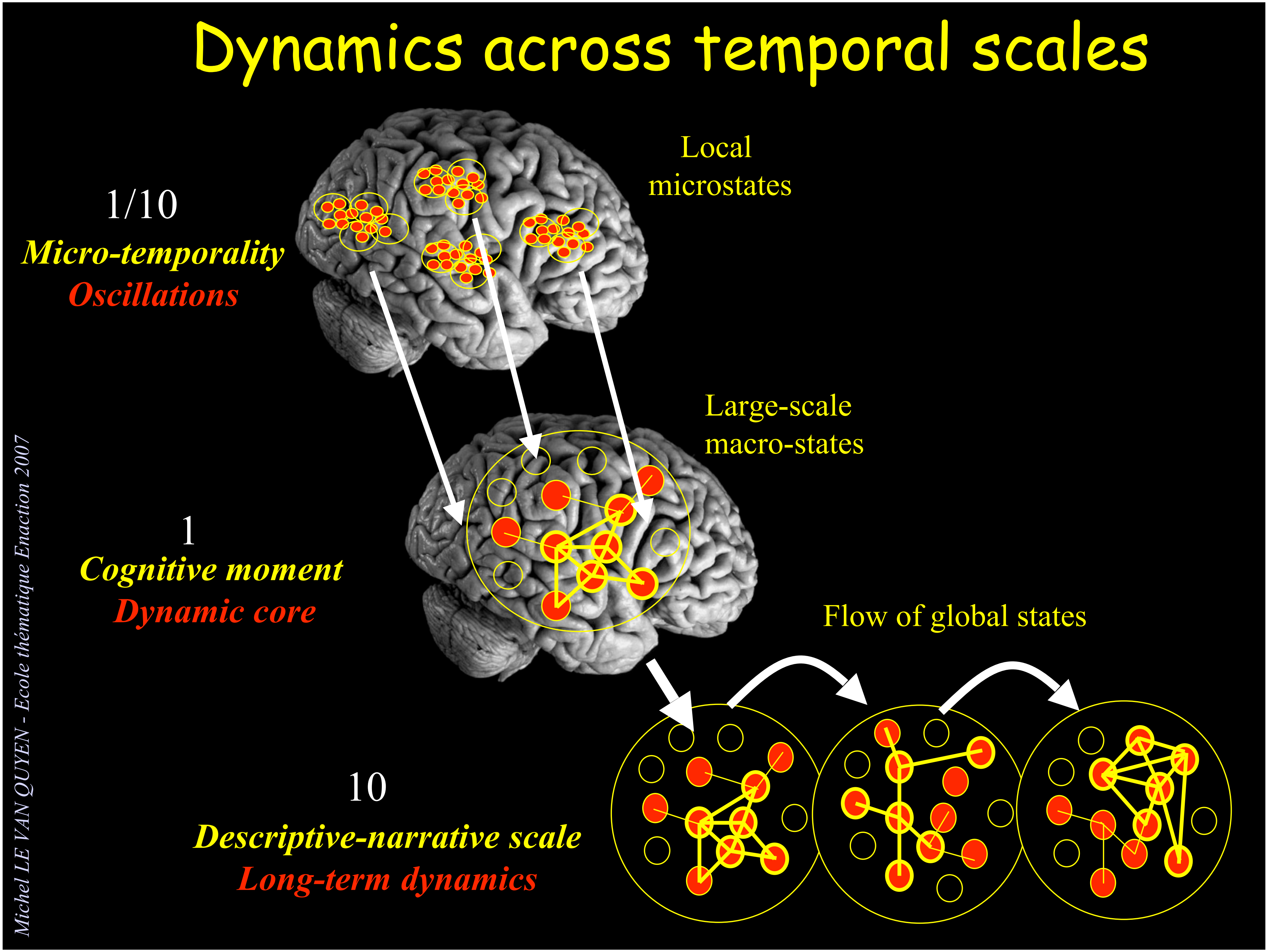


Signaux complexes dans le temps et l'espace

…les méthodes traditionnelles sont insuffisantes pour caractériser ces phénomènes



Dynamics across temporal scales
Local microstates
1/10
Micro-temporality
Oscillations
Large-scale macro-states
1
Cognitive moment
Dynamic core
Flow of global states
10
Descriptive-narrative scale
Long-term dynamics
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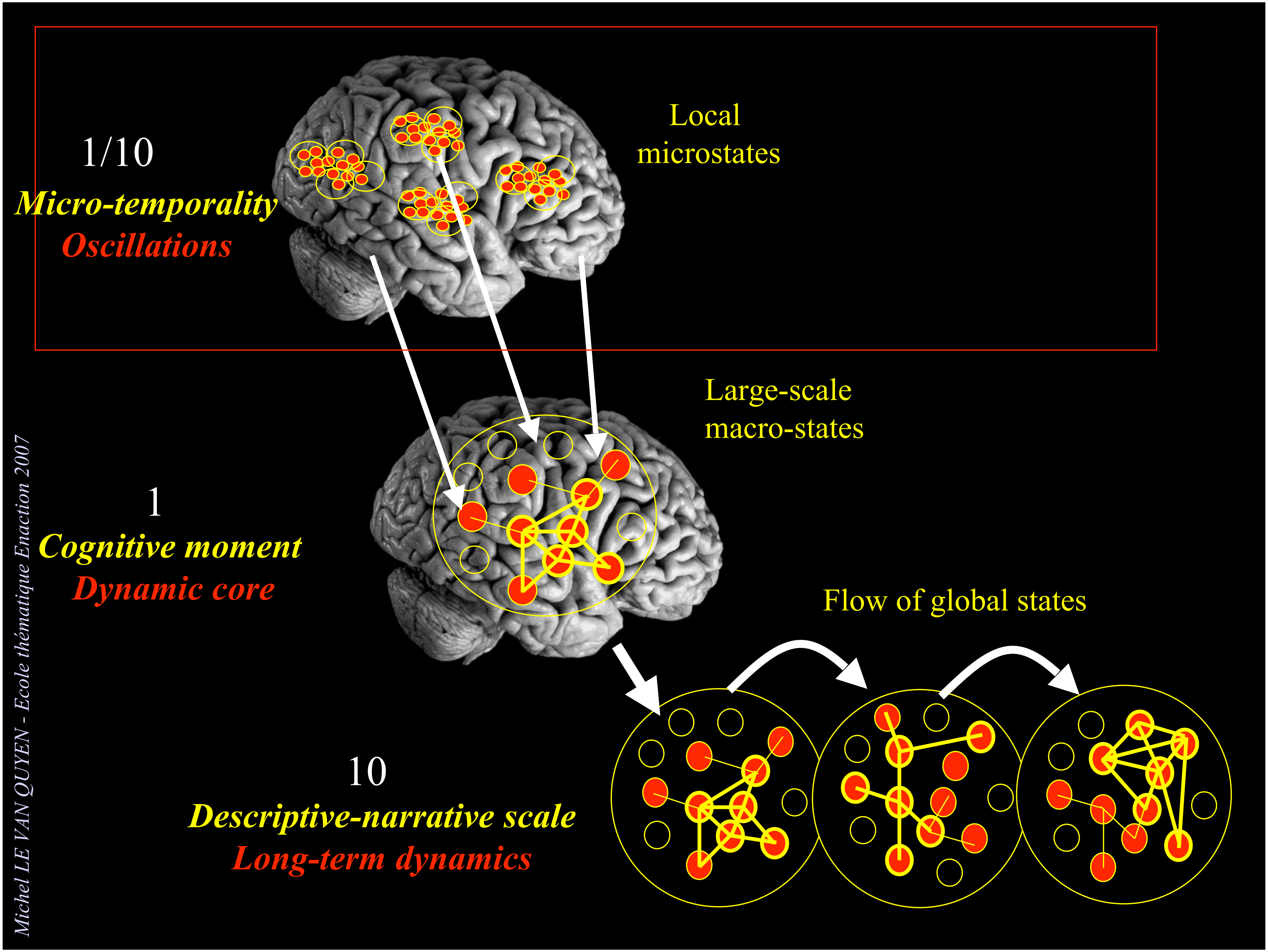
1/10
Micro-temporality
Oscillations
Local
microstates
Large-scale
macro-states
1
Cognitive moment
Dynamic core
Flow of global states
10
Descriptive-narrative scale
Long-term dynamics
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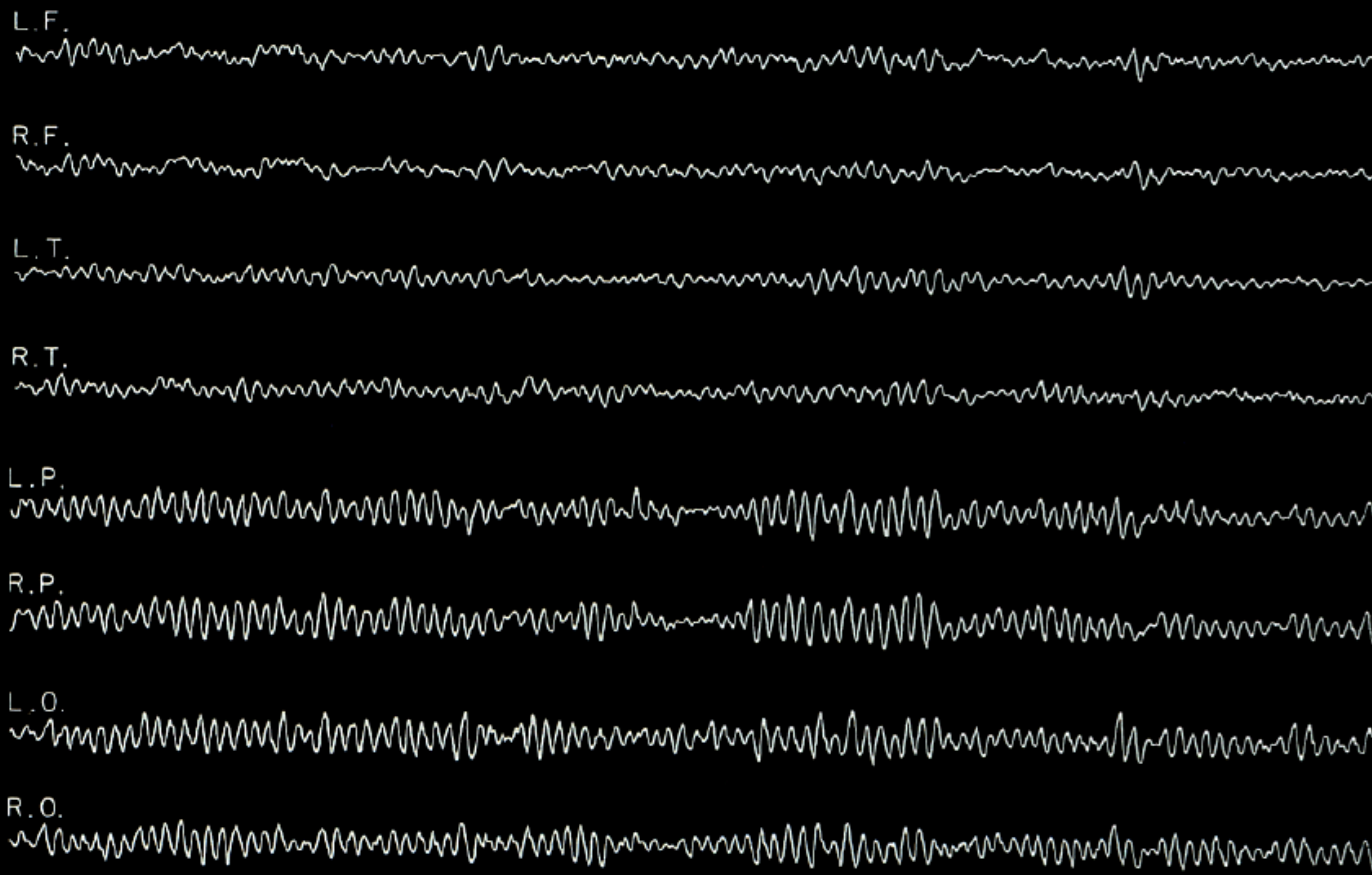
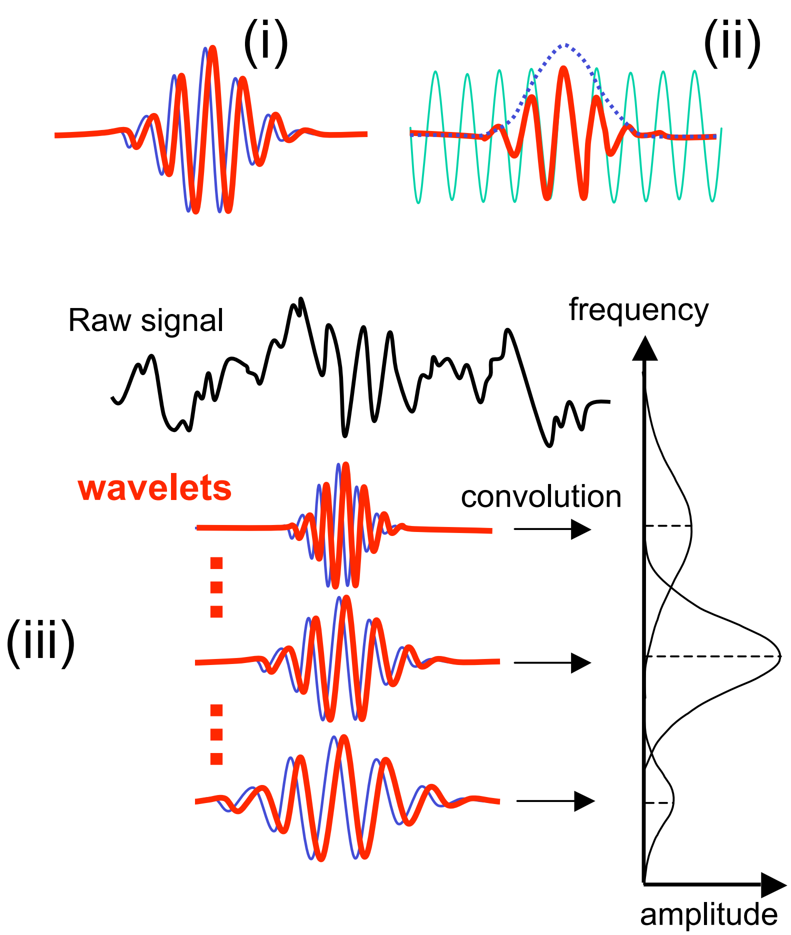
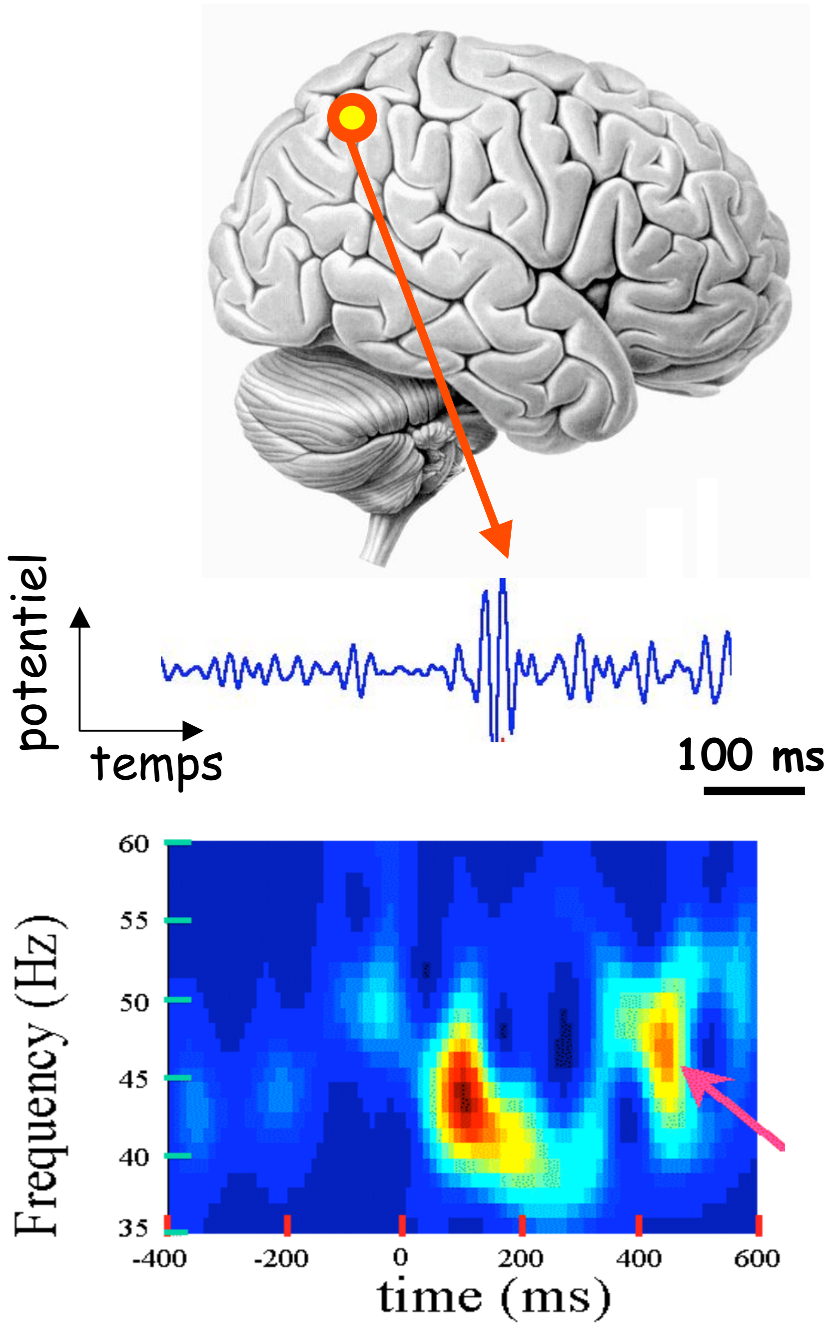
Brain Oscillations



Gibbs and Gibbs, 1950

Detection of transient oscillations





Brain Oscillations during the perception of visual objects

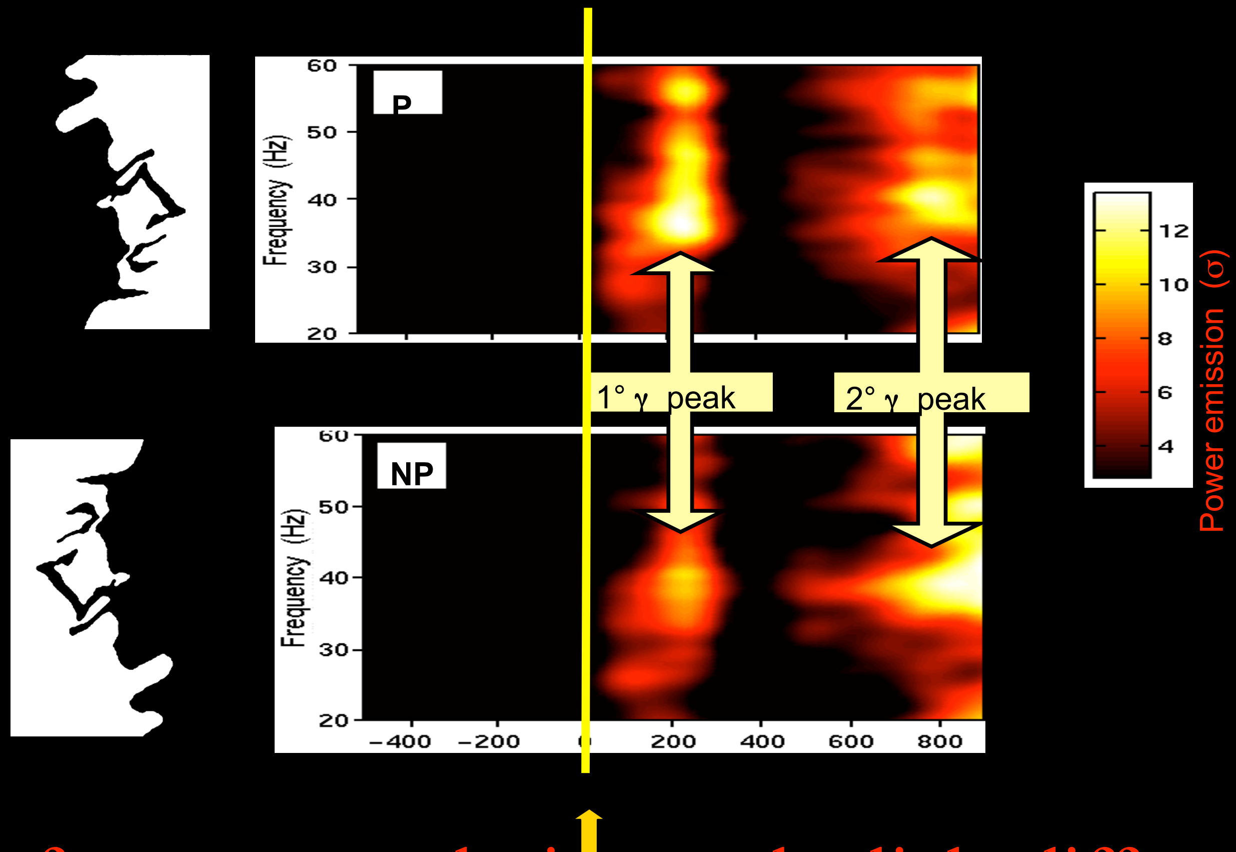
Stimuli: 'Mooney' faces

Readily recognized when presented in upright orientation

Usually seen as meaningless black and white spots when presented upside-down.

Rodriguez et al., Nature 2001:

Task: recognition of 320 Mooney faces presented to a group of 10 subjects reporting whether they had seen a face or not by pressing two different keys under right and left indexes.



Time-frequency analysis reveals slight difference between perception and no-perception

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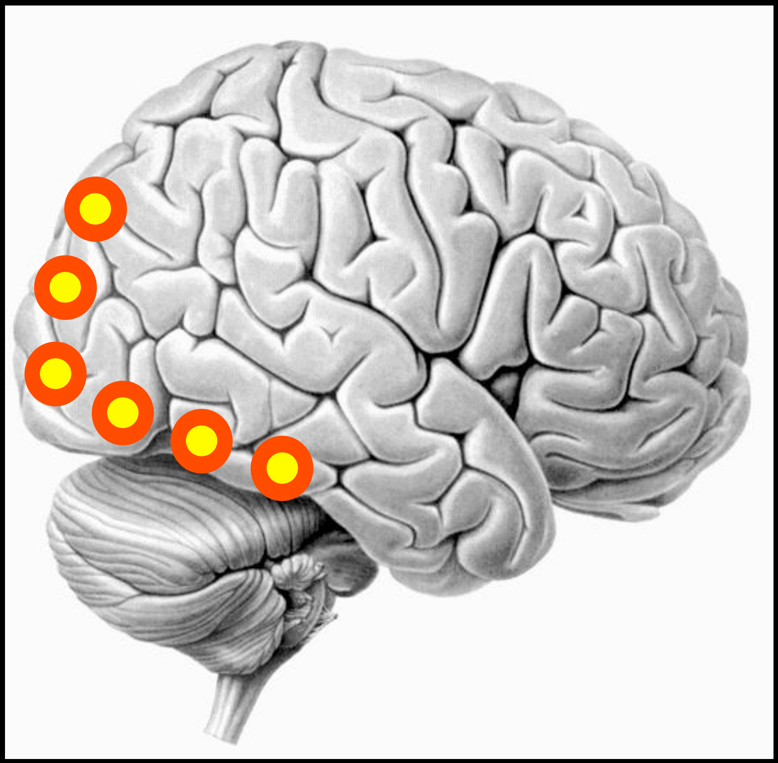
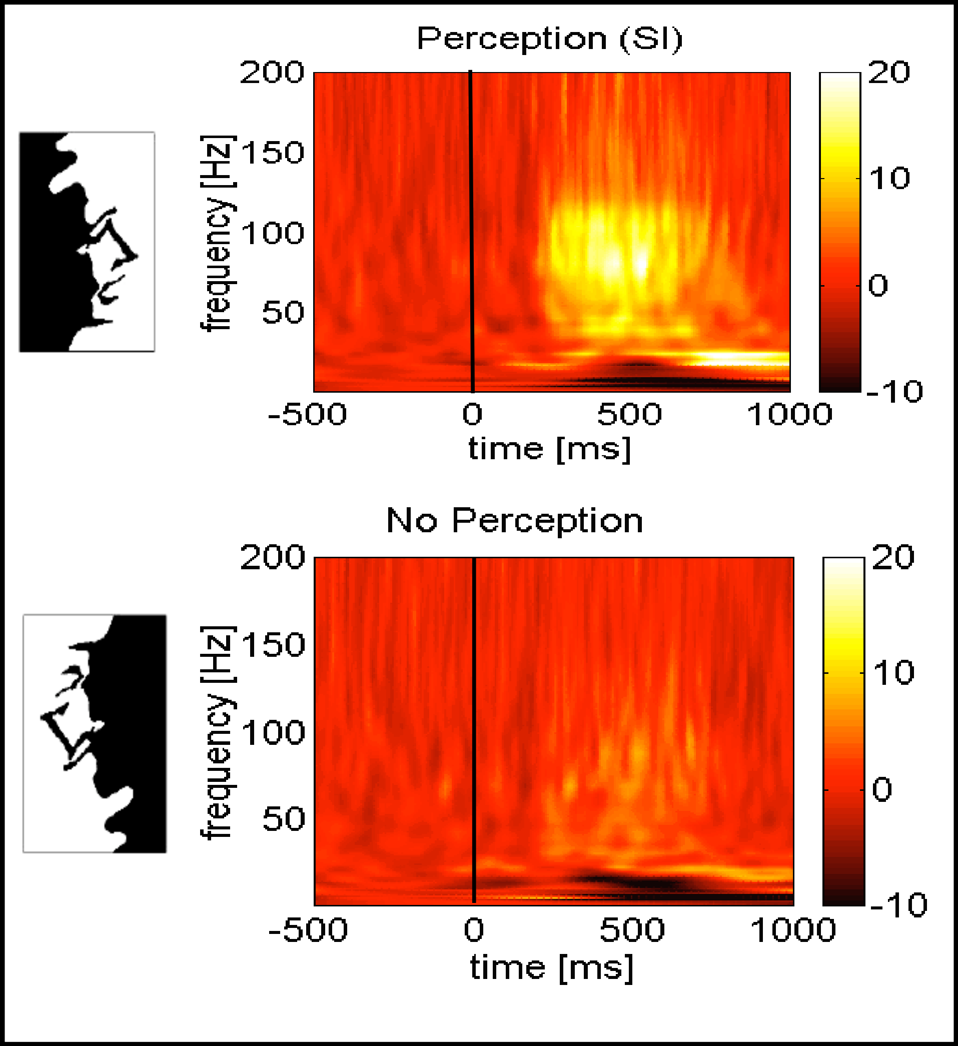
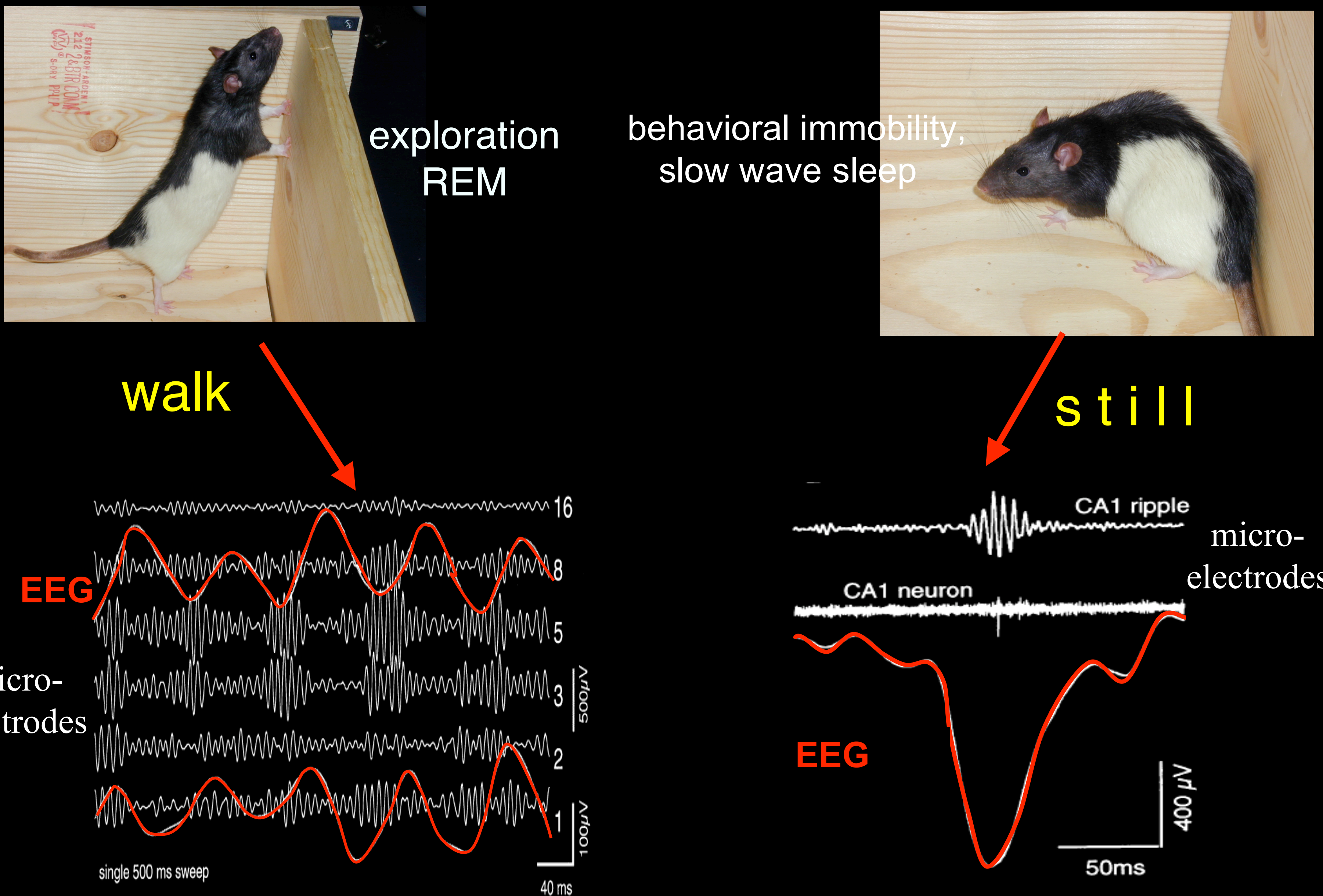
Lachaux et al., NeuroImage 2004





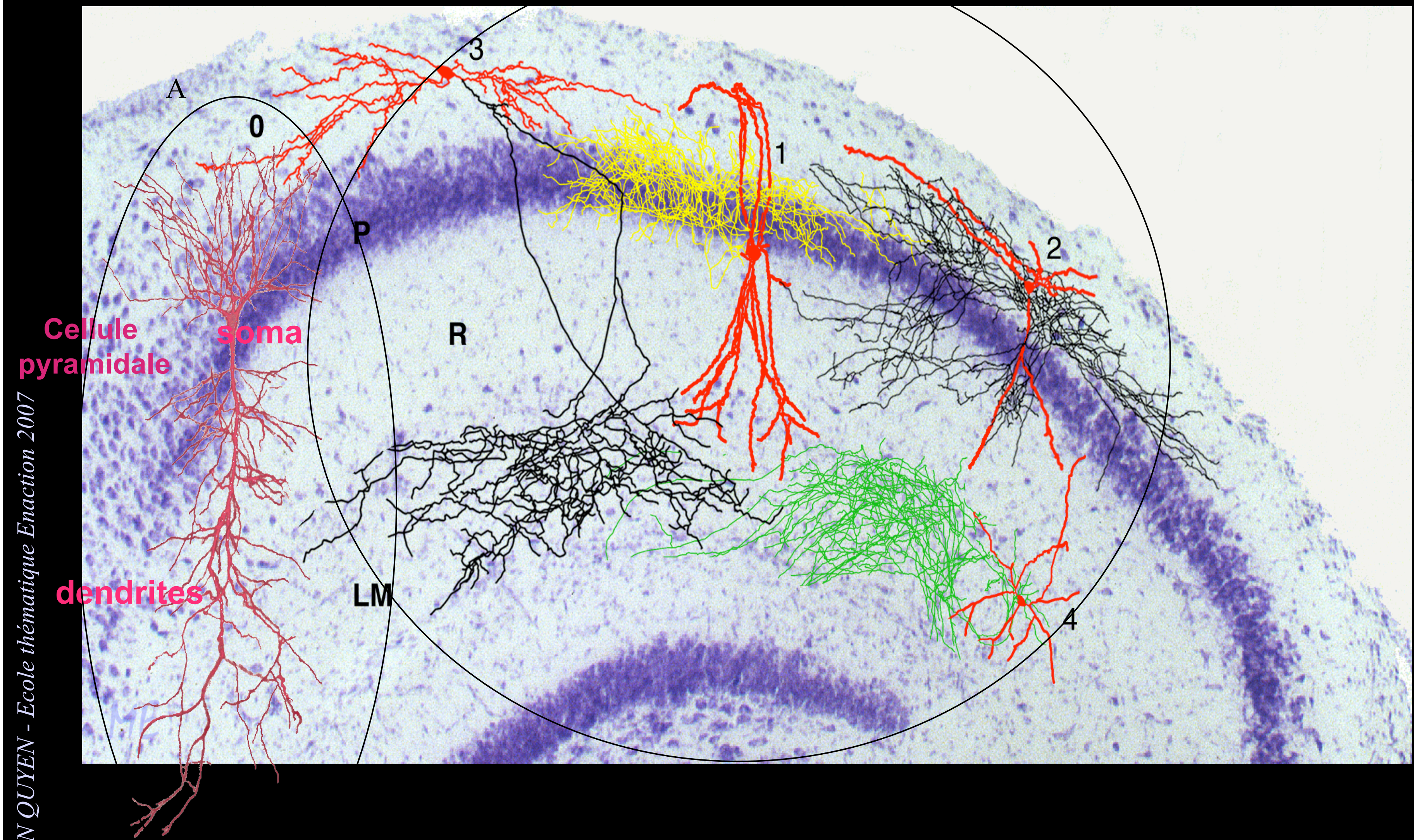
Physiological fast oscillations in the hippocampus



Gamma oscillations (40-100Hz)

Ripples (140-200Hz)

Morphological complexity



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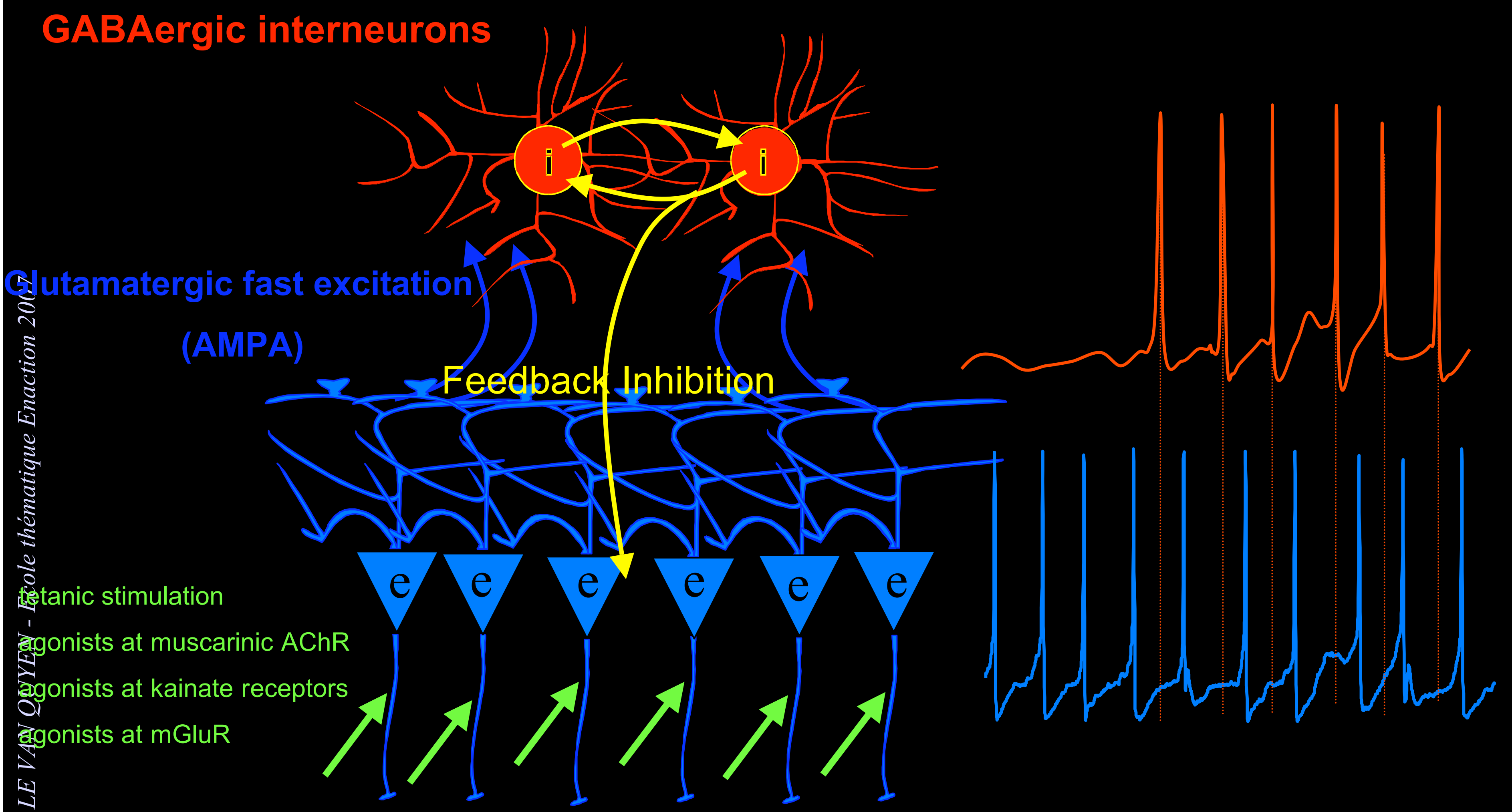
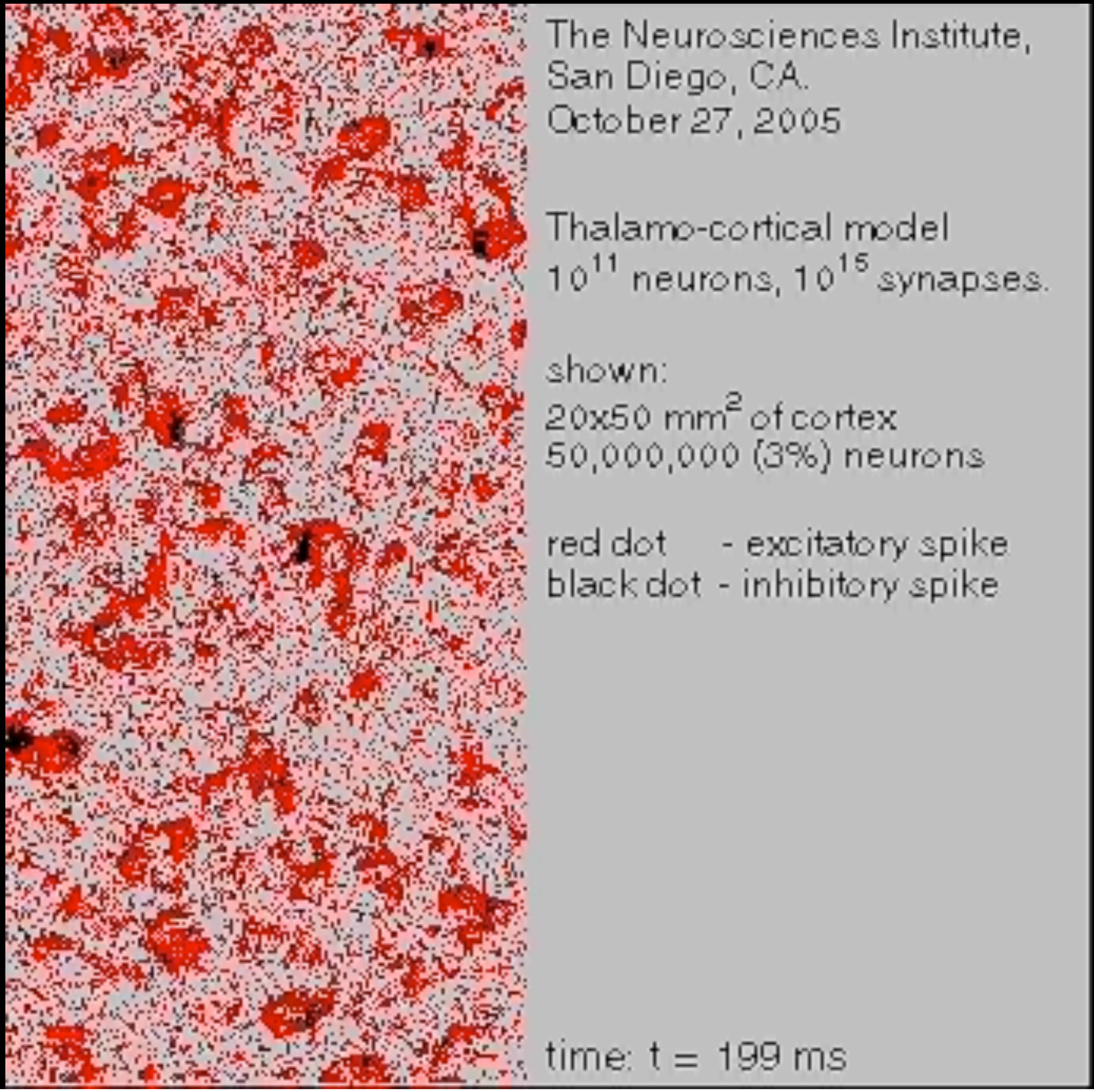
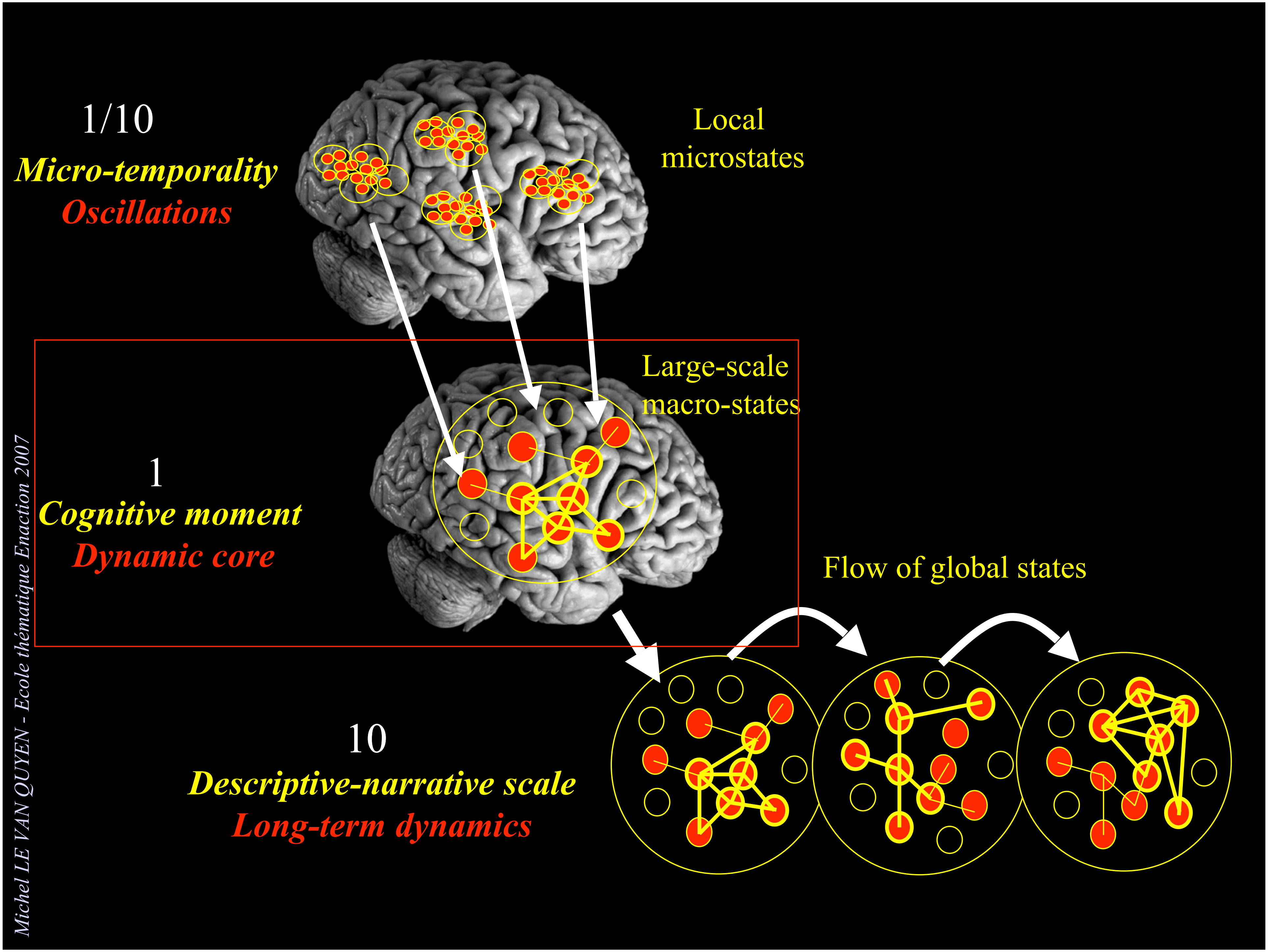
Physiological gamma oscillations (in vitro) require both fast excitatory and fast inhibitory transmission…



(Fisahn et al., Nature 1998)

Simulation of large-scale brain models (2005)
Eugene M. IZHIKEVICH — The Neuroscience Institute, San Diego, Californie




1/10
Micro-temporality
Oscillations
Local
microstates
Large-scale
macro-states
1
Cognitive moment
Dynamic core
Flow of global states
10
Descriptive-narrative scale
Long-term dynamics
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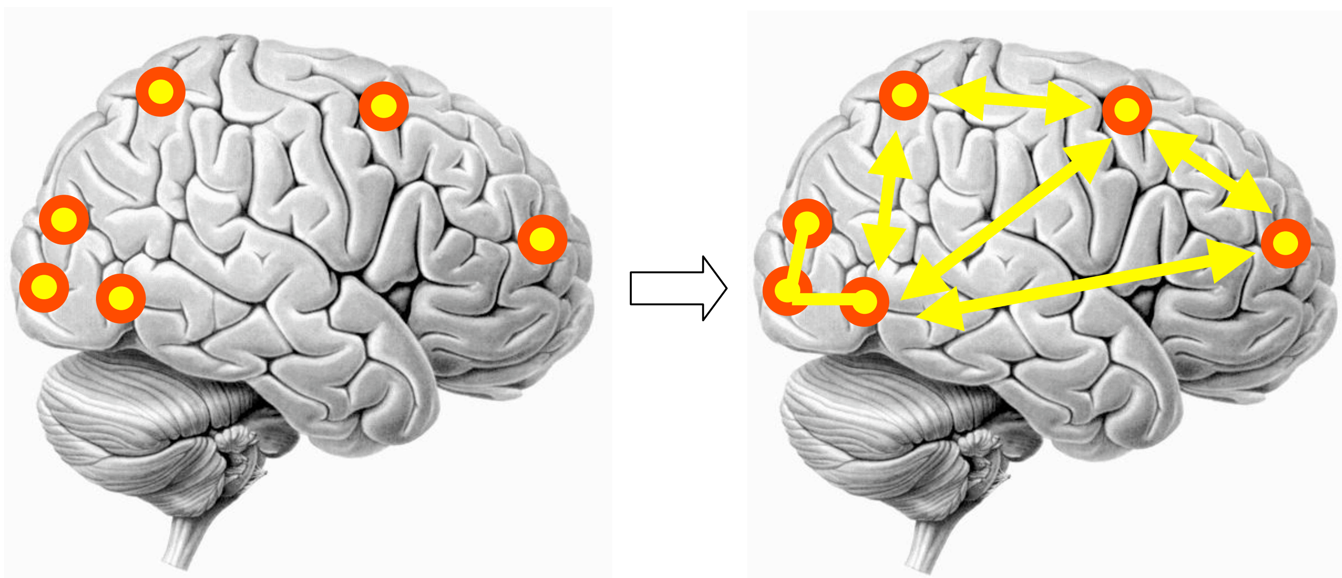
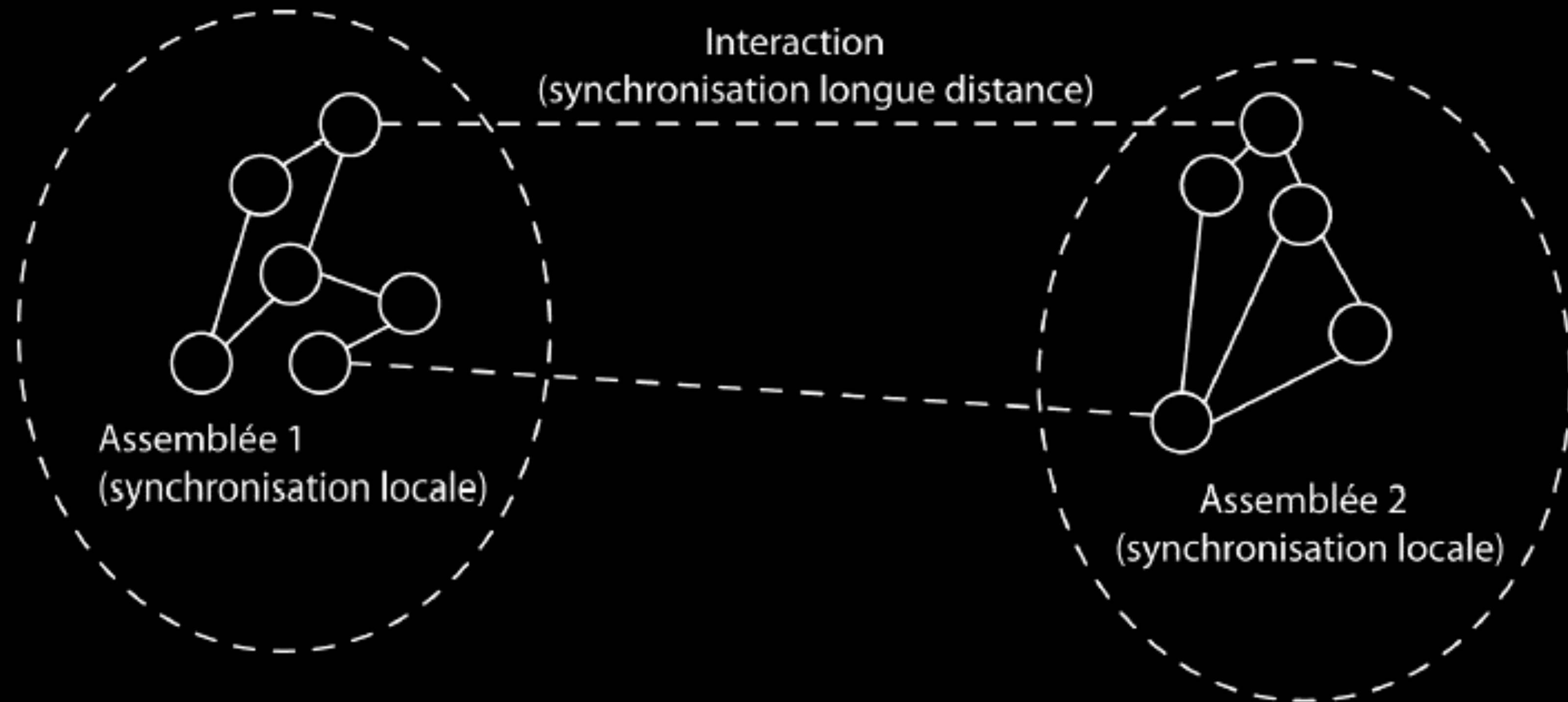
D’une cartographie
des **Activations** ...

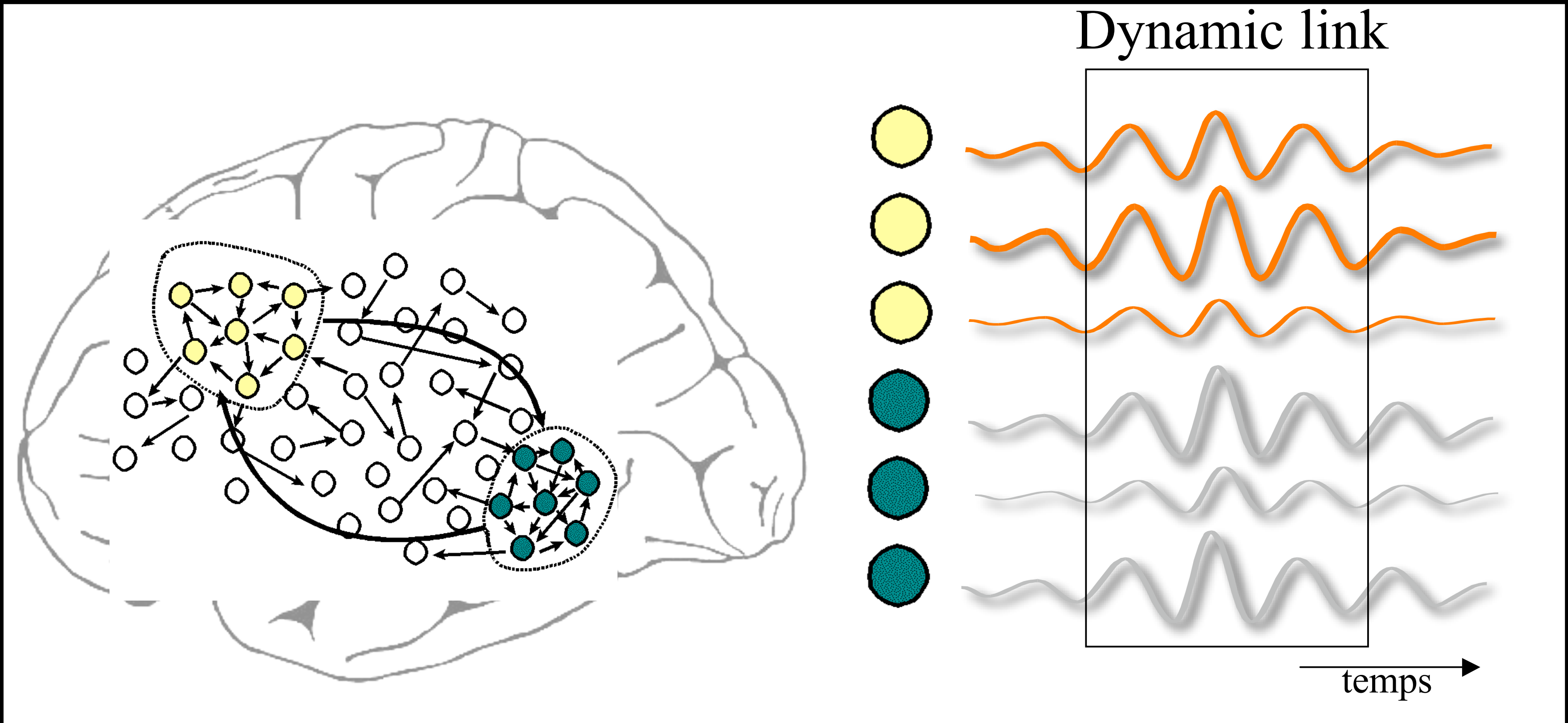
… à une cartographie
des Liens Dynamiques



ANALYSE DES SYNCHRONISATIONS


Interaction
(synchronisation longue distance)
Assemblée 1
(synchronisation locale)
Assemblée 2
(synchronisation locale)

Binding between two distant neuronal populations through the phase synchronization of local oscillations



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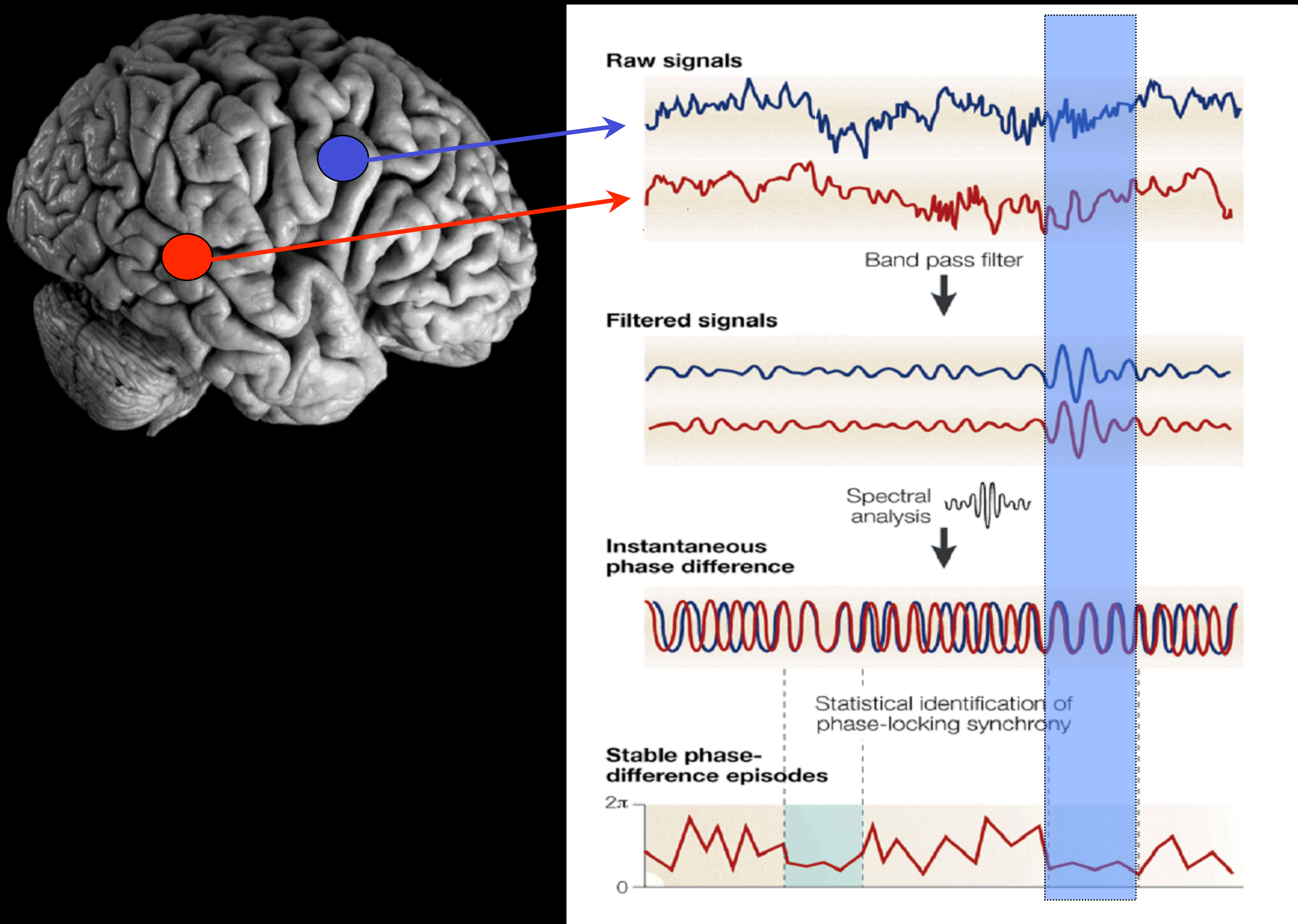
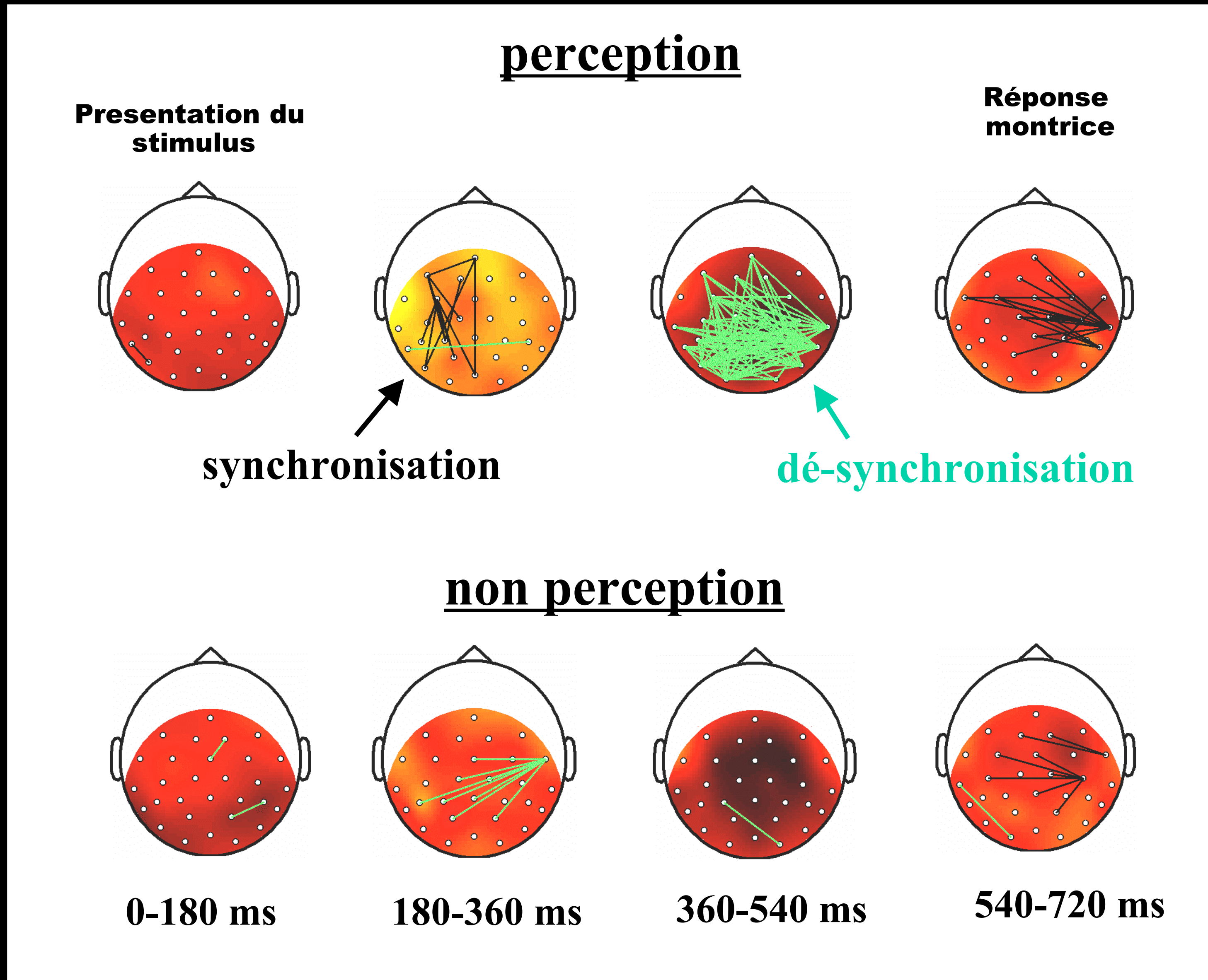
Phase-locking of oscillations



Varela, Nature Review Neuroscience 2001



Rodriguez, George, Lachaux, Martinerie, Renault, Varela (Nature, 1999)

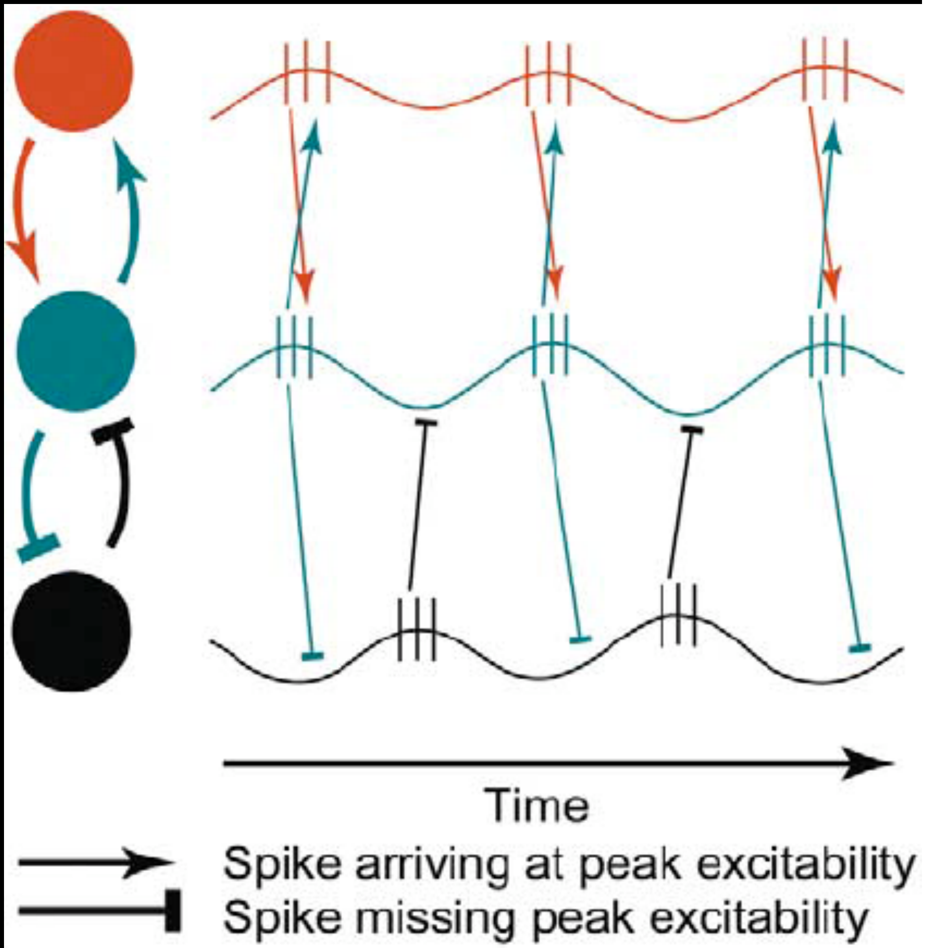
Fries, Trends Cog. Sci., 2005

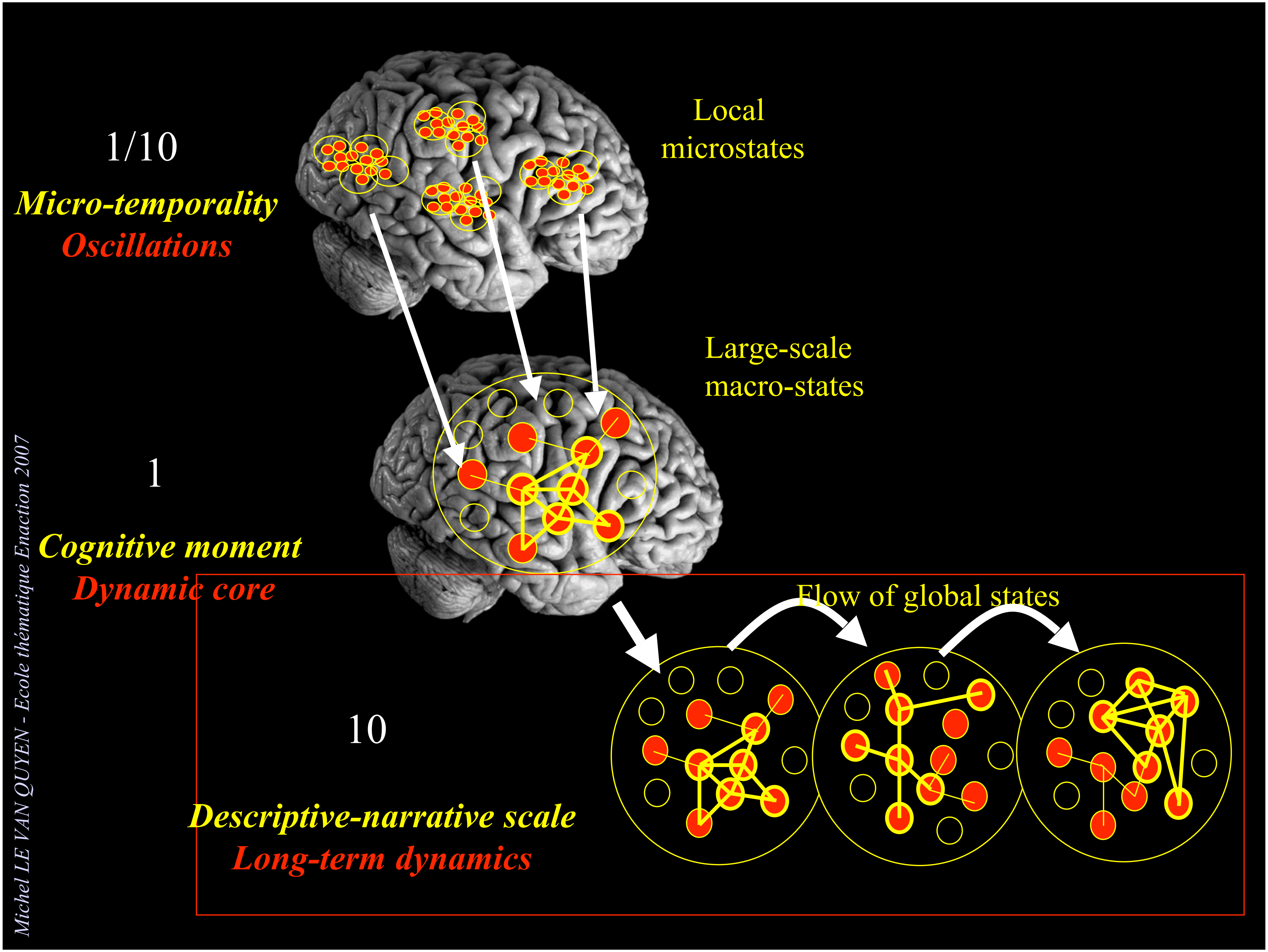
Communication hypothesis

Communication structure is mechanistically implemented by the pattern of coherence

Coherent oscillations could provide:

- Predictivity
- Temporal windows for communicating




1/10
Micro-temporality
Oscillations
Local
microstates
Large-scale
macro-states
1
Cognitive moment
Dynamic core
Flow of global states
10
Descriptive-narrative scale
Long-term dynamics
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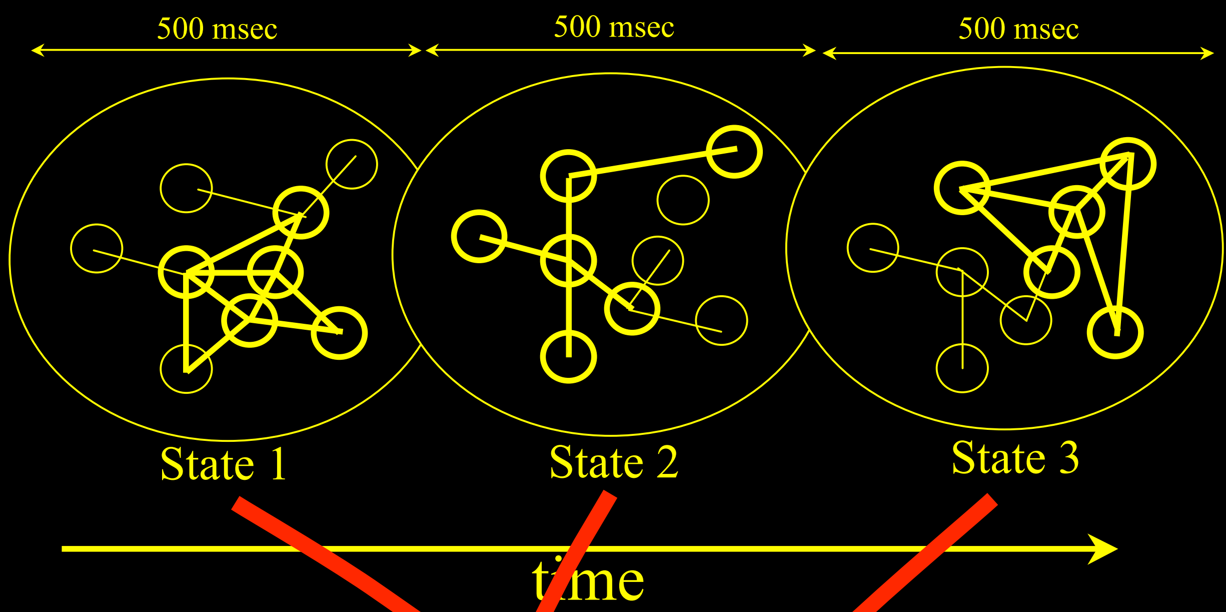
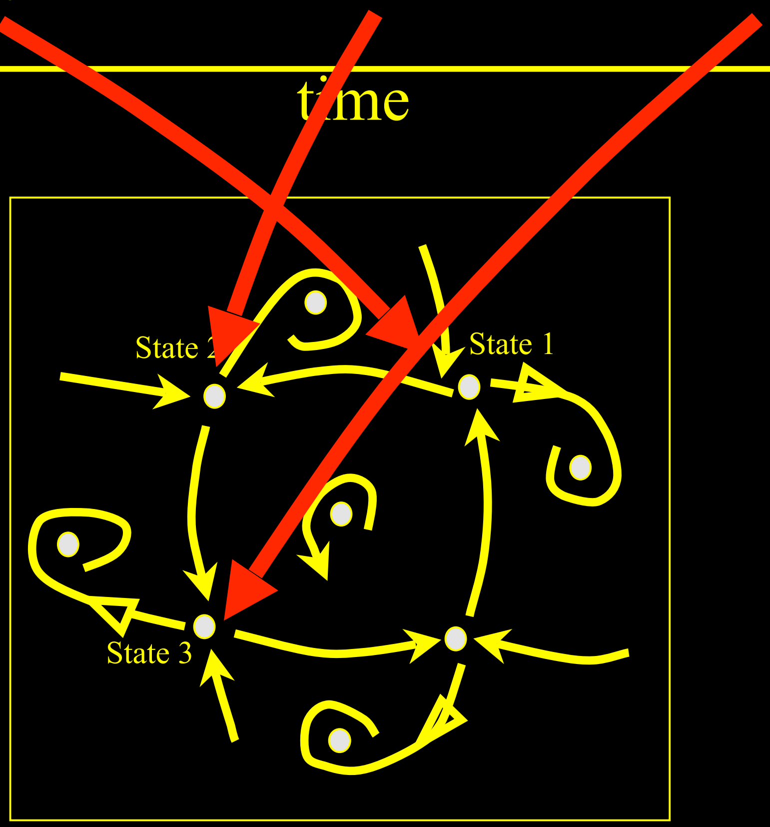
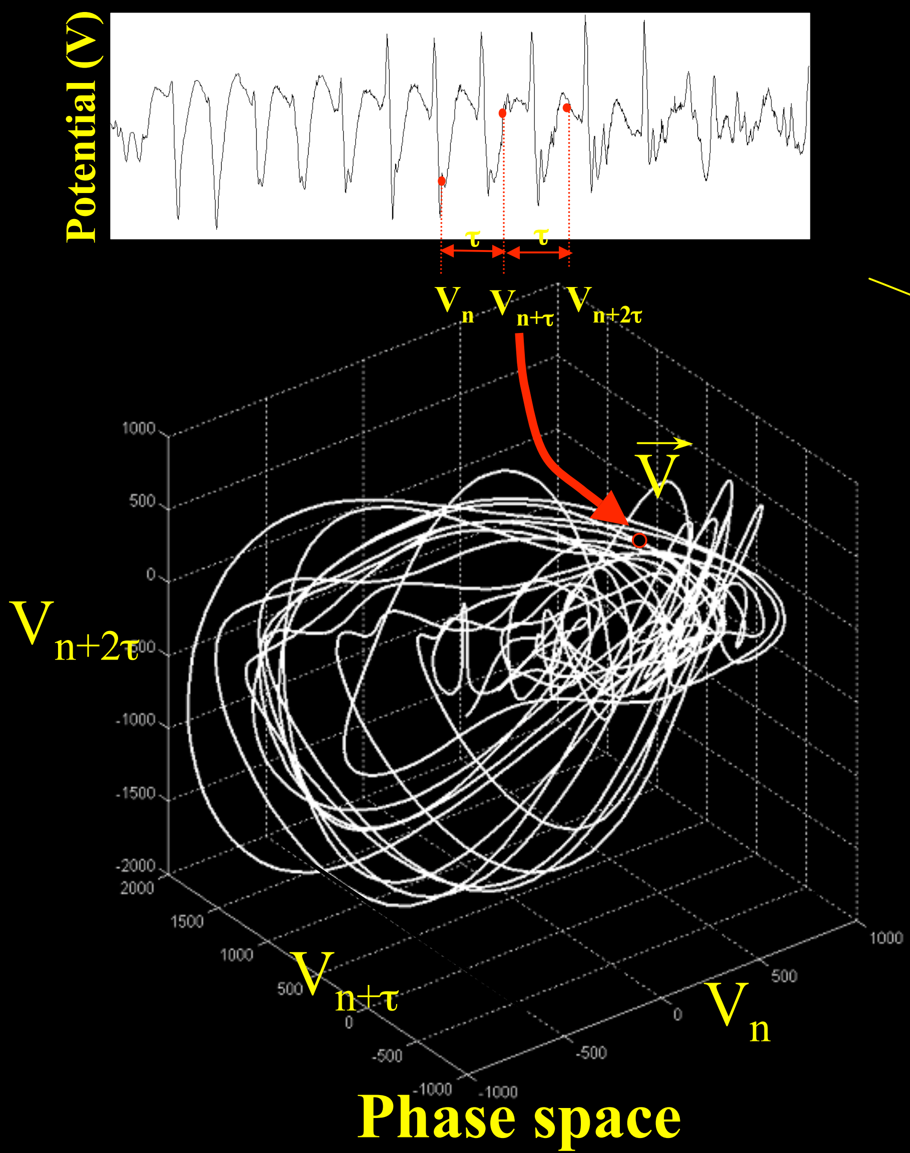
Noyau dynamique

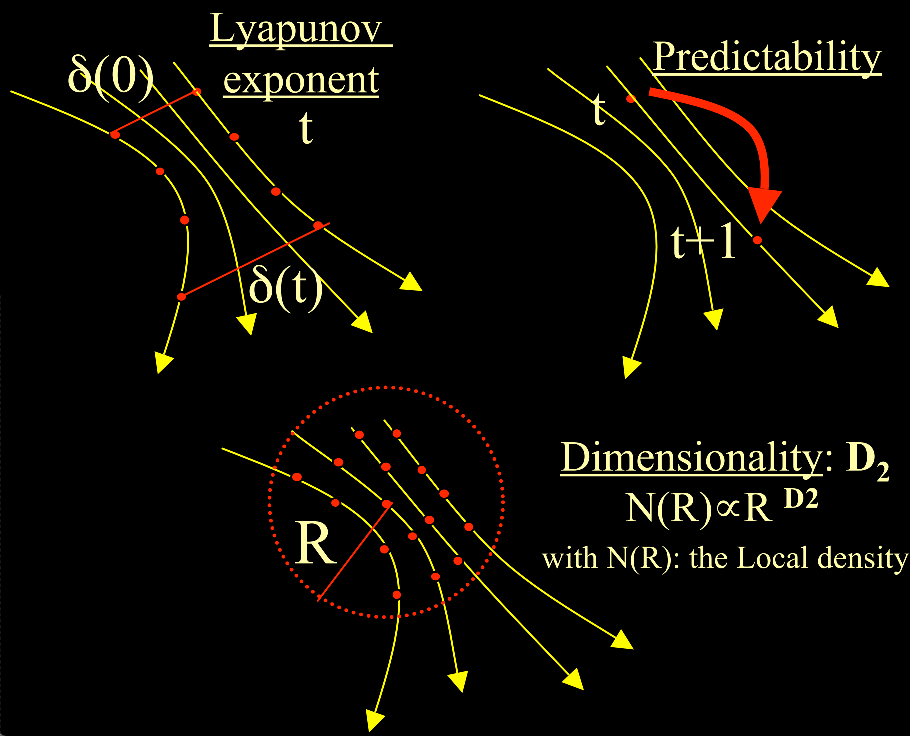


Paysage dynamique du flux des états



Detection of nonlinear temporal correlations





Nonlinear measures

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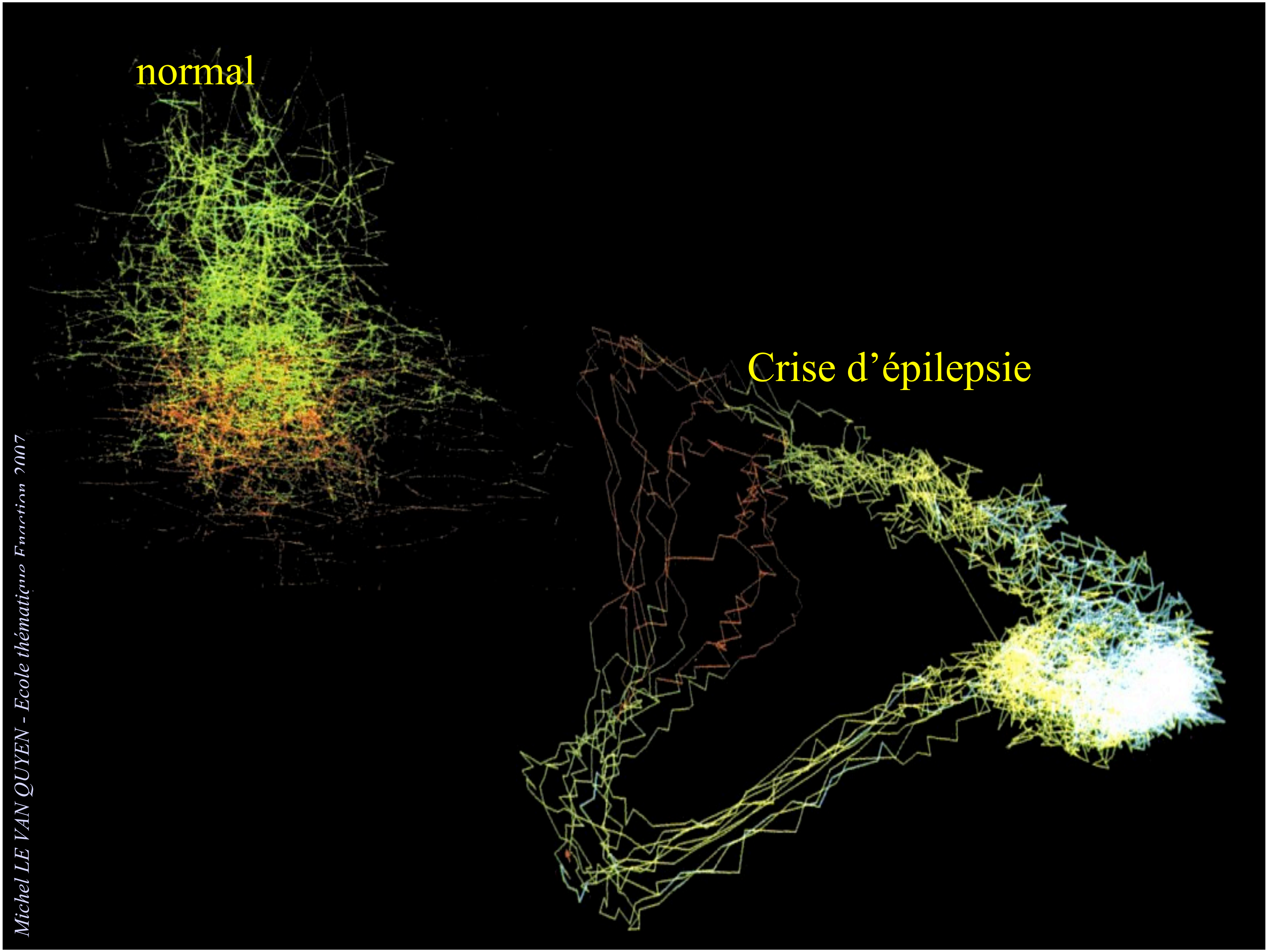
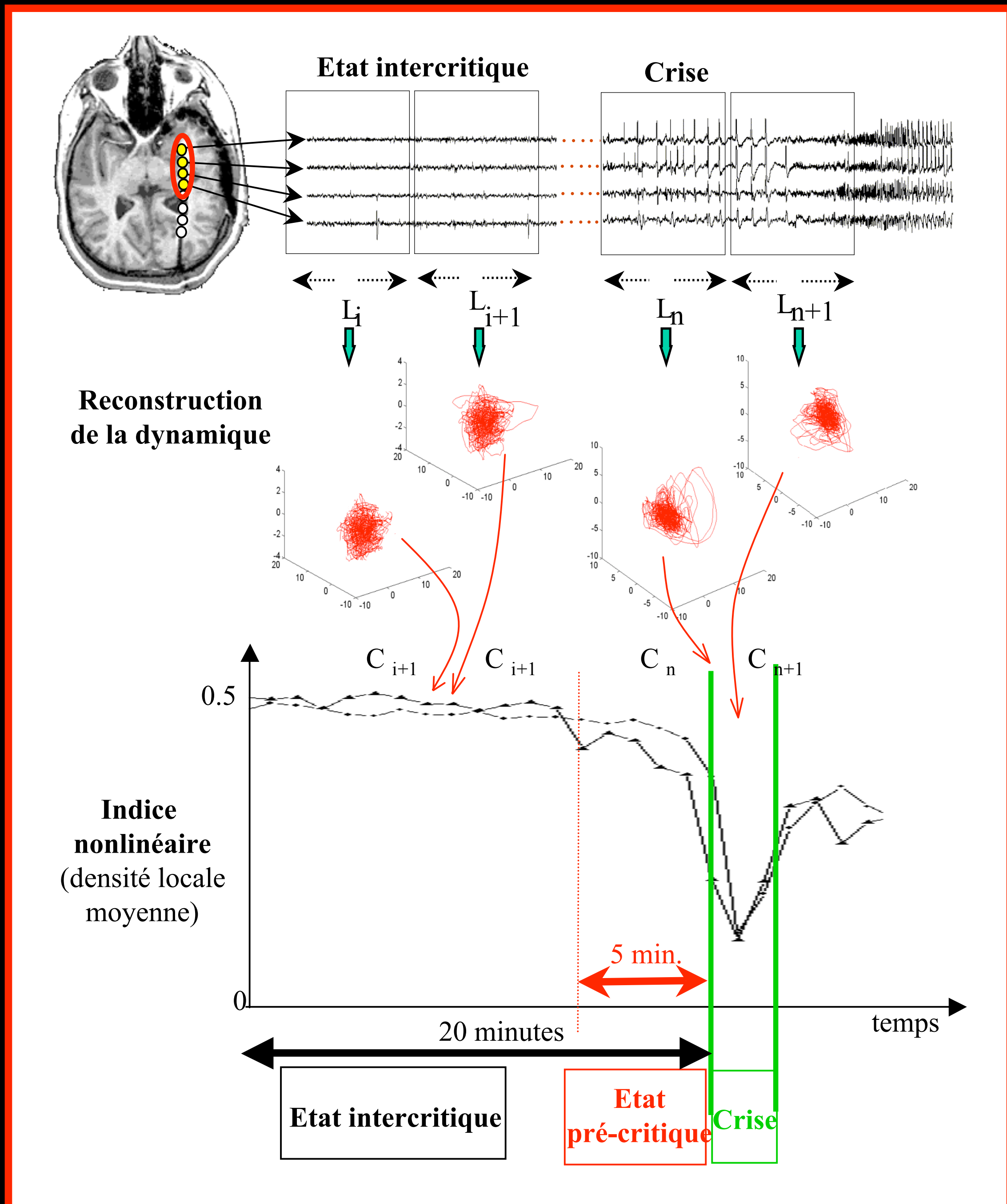

normal
Crise d'épilepsie



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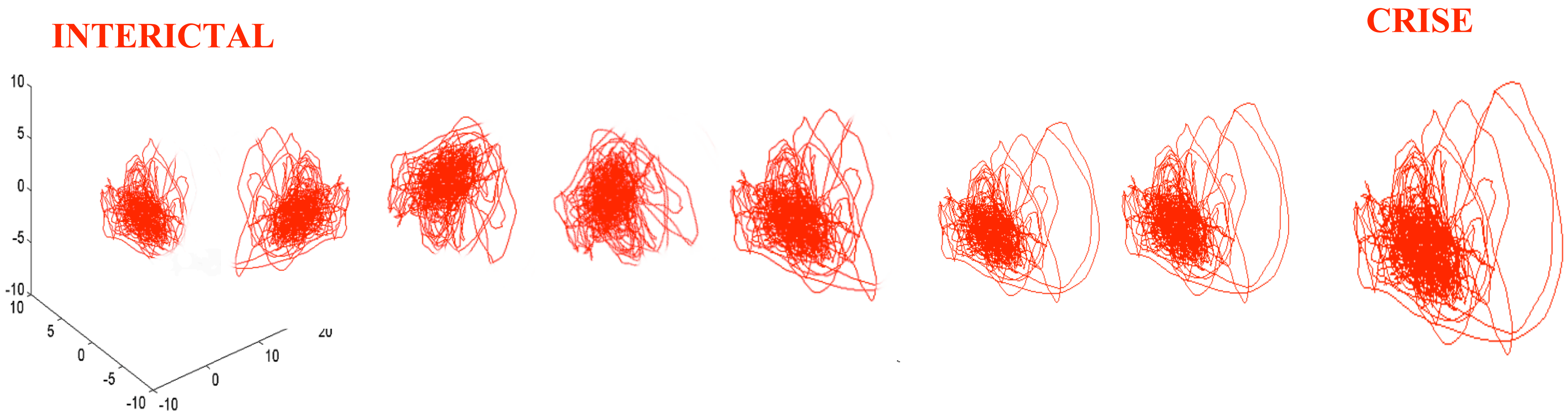
Une route vers la crise

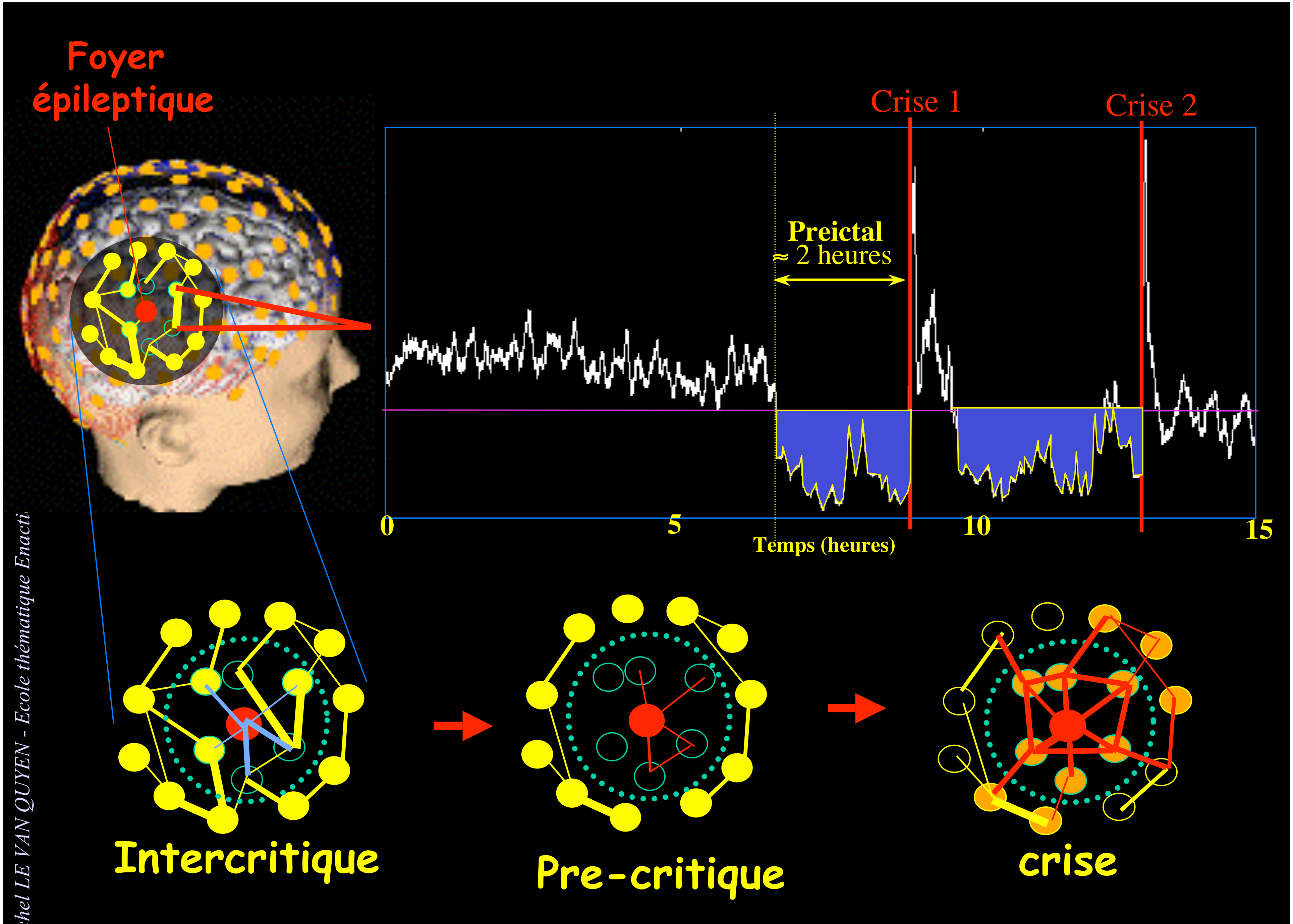


<u>État normal</u>, fonctionnement cérébral chaotique

Perte de complexité →

<u>État pathologique</u> , fonctionnement cérébral trop ordonné

Michel LE VAN QUYEN - Ecole thém

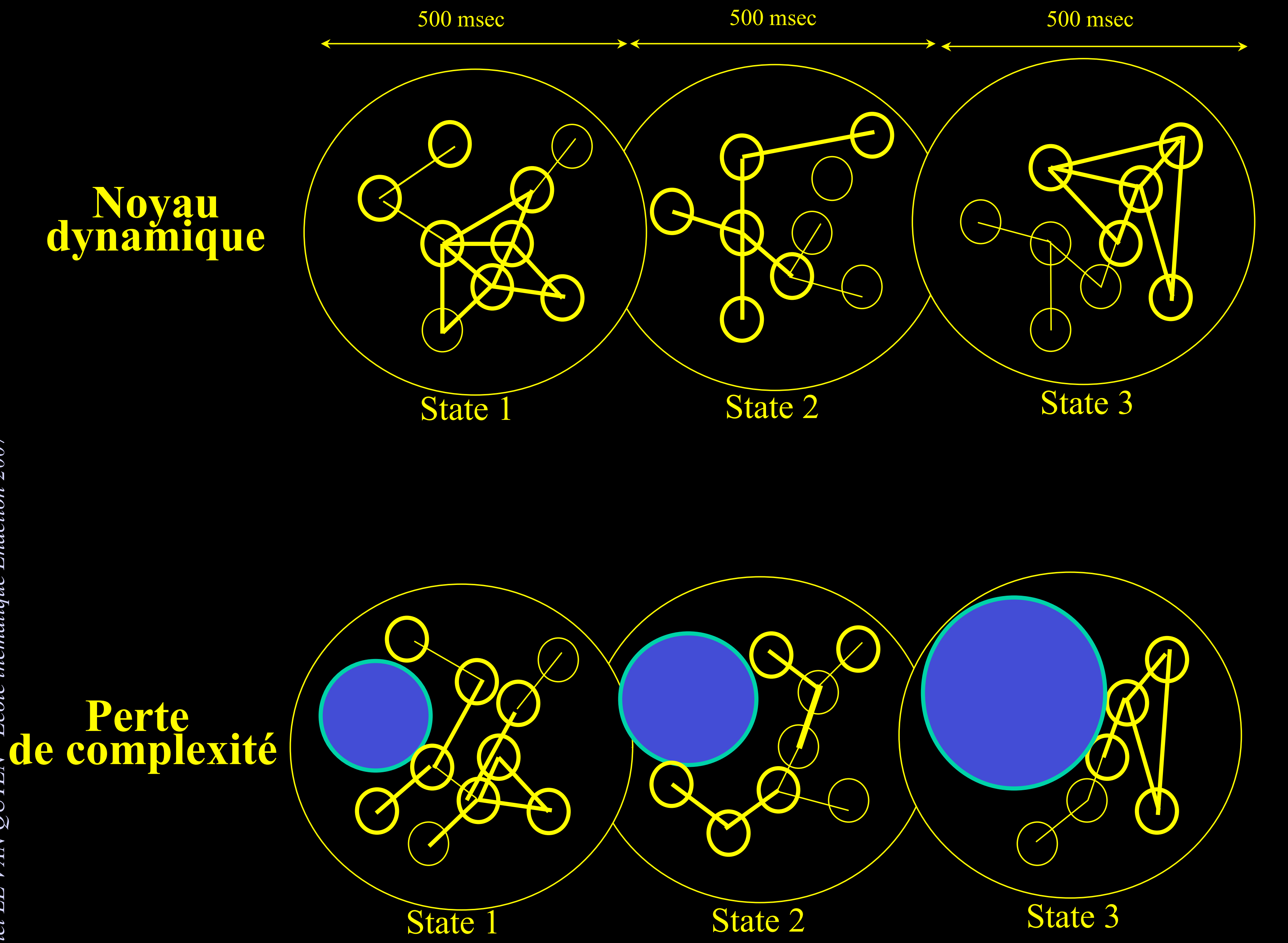


LE VAN QUYEN M., MARTINERIE J., NAVARRO V., BAULAC M., VARELA F. (2001) **J Clinical Neurophysiology** 18: 191.

PRODROMES:

Période de comportement ou de sensation anormal précédant la crise d'épilepsie et qui progresse lentement durant des heures ou des jours. Elle est caractérisée par des changements de l’humeur, fatigue, agitation, trouble de l'appétit, etc.

«…le patient perd le sentiment de sa propre réalité et ressent son corps comme irréel. Cet état s’accompagne souvent d’anxiété, d’impression d’étrangeté du monde extérieur. Le patient qui souffre de ce mal être se sent différent de ce qu’il était jusque là, même les personnes qui lui sont habituellement proches ont perdues pour lui tout caractère de familiarité… »



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Quelques questions pour l'avenir ...

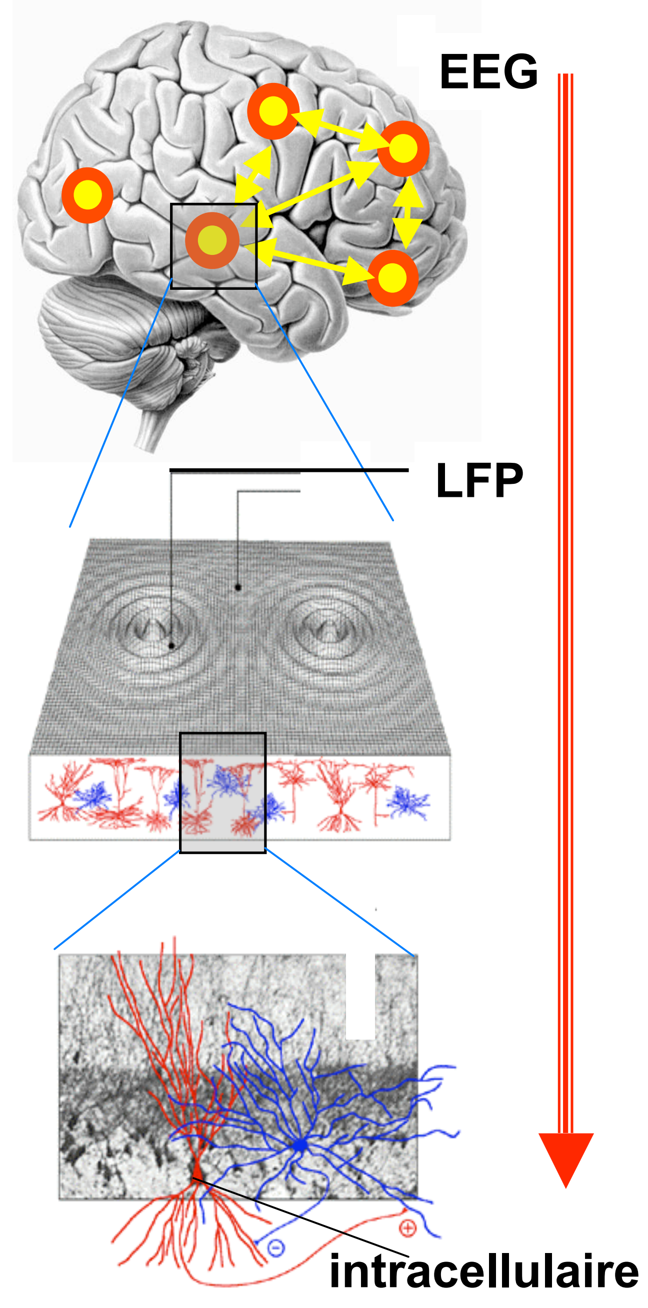
Relations entre niveaux d'intégration?

Échelles spatiales

Macroscopique:
Régions distantes

Mesocopique:
Population locale
de neurones

Microscopique:
Neurones
individuels



Causalité descendante
un rôle causal de la dynamique de large échelle sur une dynamique locale

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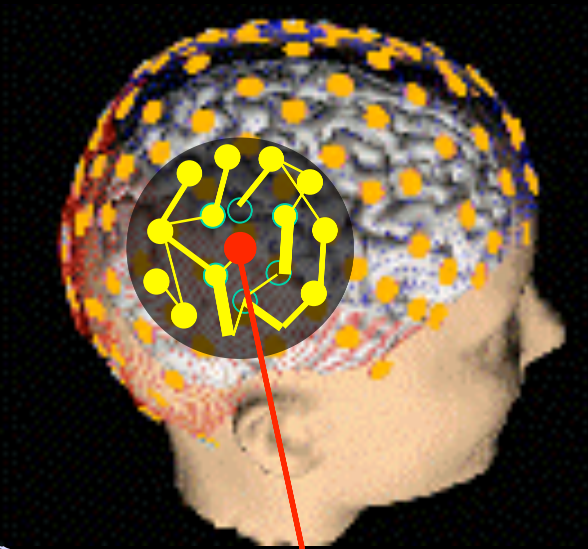
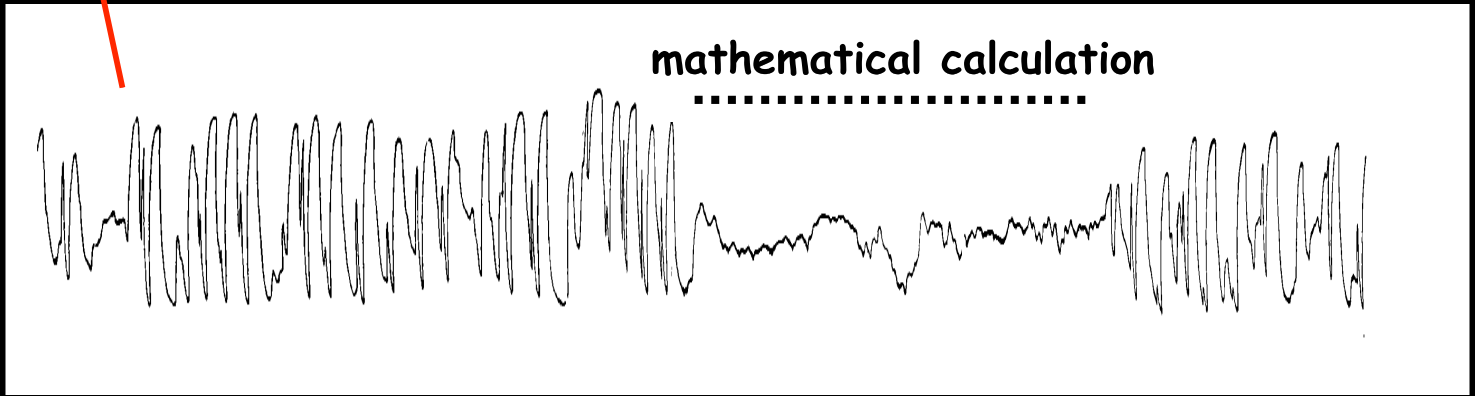
Seizure control through downward causality



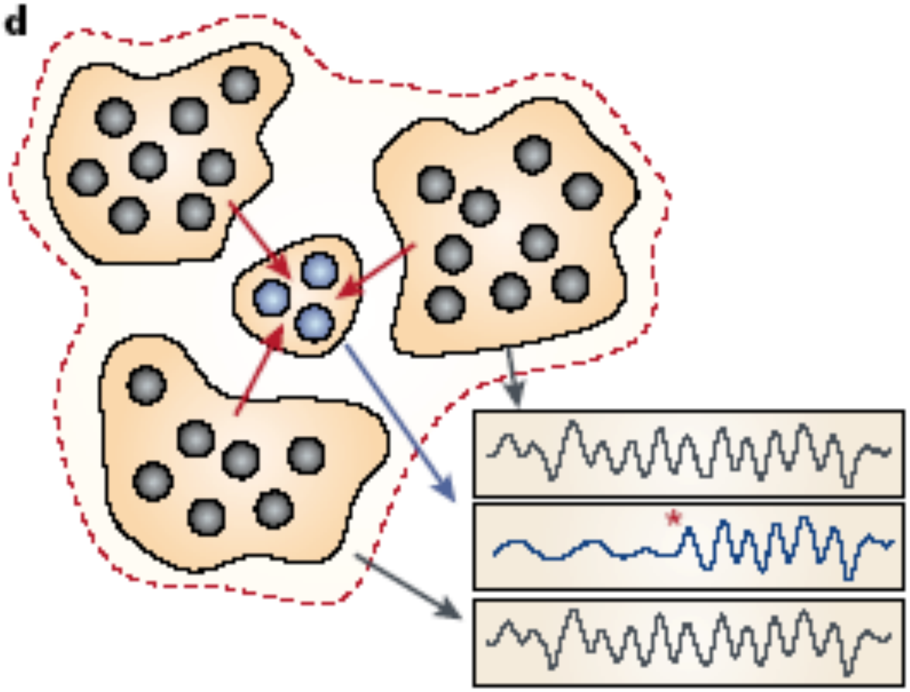


<u>W. Penfield and H. Jasper</u>, Epilepsy and the functional anatomy of the human brain (1954)

TOP-DOWN PROCESSES :

Large-scale dynamics can have a predominant influence on a local scale by enslaving local neuronal elements.

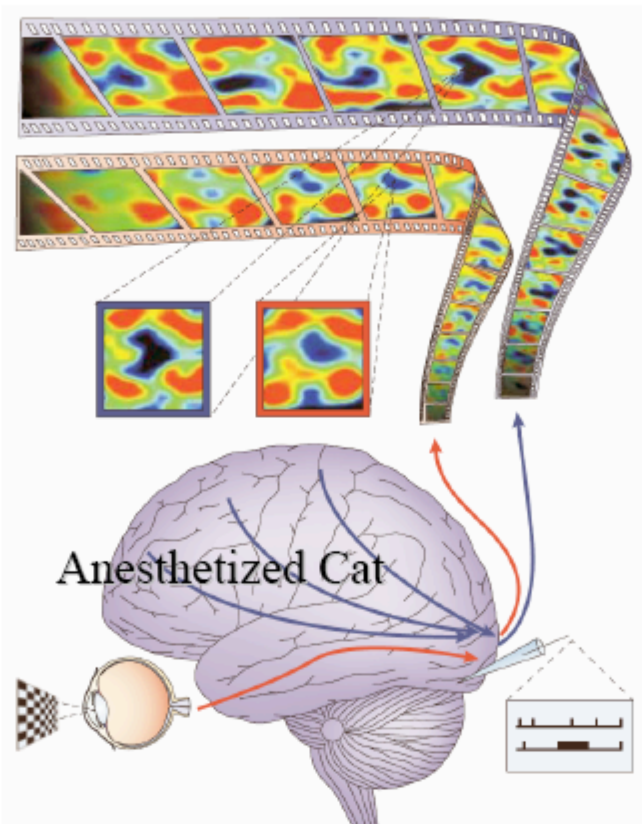
d



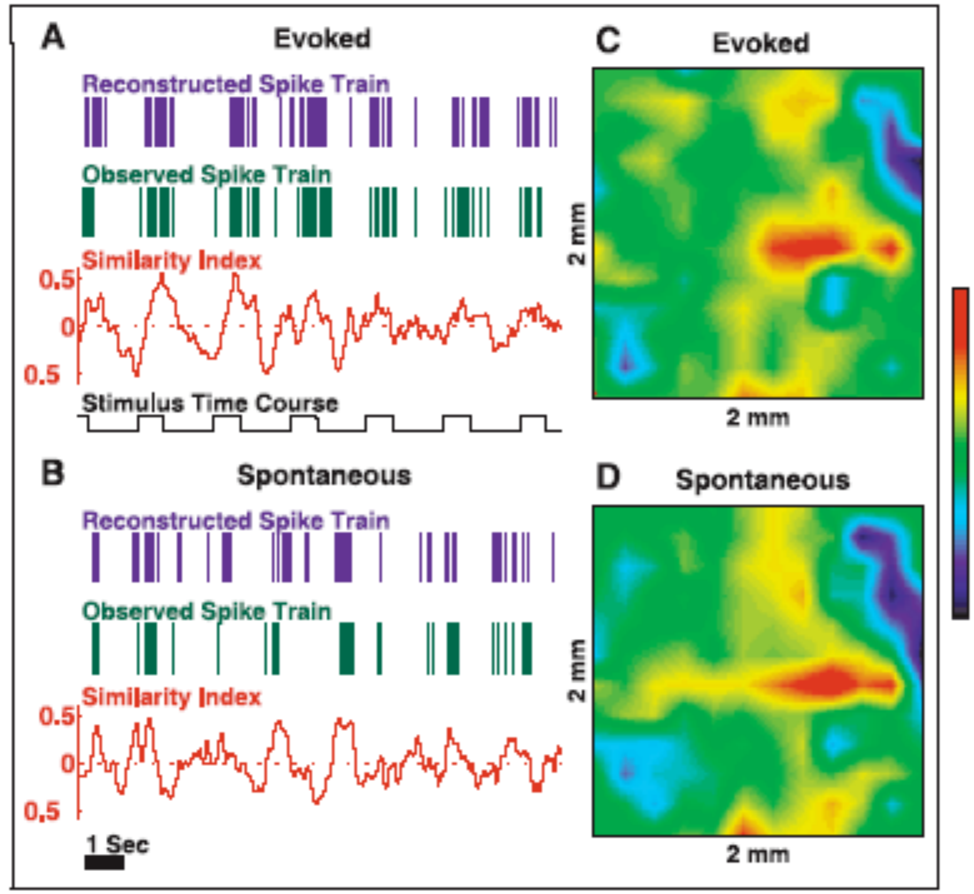
Top-down influences lead to « dynamic prediction » adopting the form of sub-threshold oscillations in neuronal modules

Matching of the expected spatiotemporal pattern leads to resonance and broadcasting of the signal to other centers

The firing rate of a single neuron strongly depends on the instantaneous spatial pattern of ongoing population activity in a large cortical area.



Optical imaging in combinaison with single unit recording



Tsodyks, et al., Science 1999

There are difficulties in experimental assessments of these processes (in particular in animals) because internal cognitive processes look like background fluctuations for an external observer.

Neurophenomenology:

Three ingredients have turned out to play an equally important role (Varela, 1999):

(1) the neurobiological basis

(2) the formal mathematical/descriptive tools mostly derived from nonlinear dynamics

(3) the structure of lived experience studied under a particular methodological approach (reduction)

What is local ? What is global?

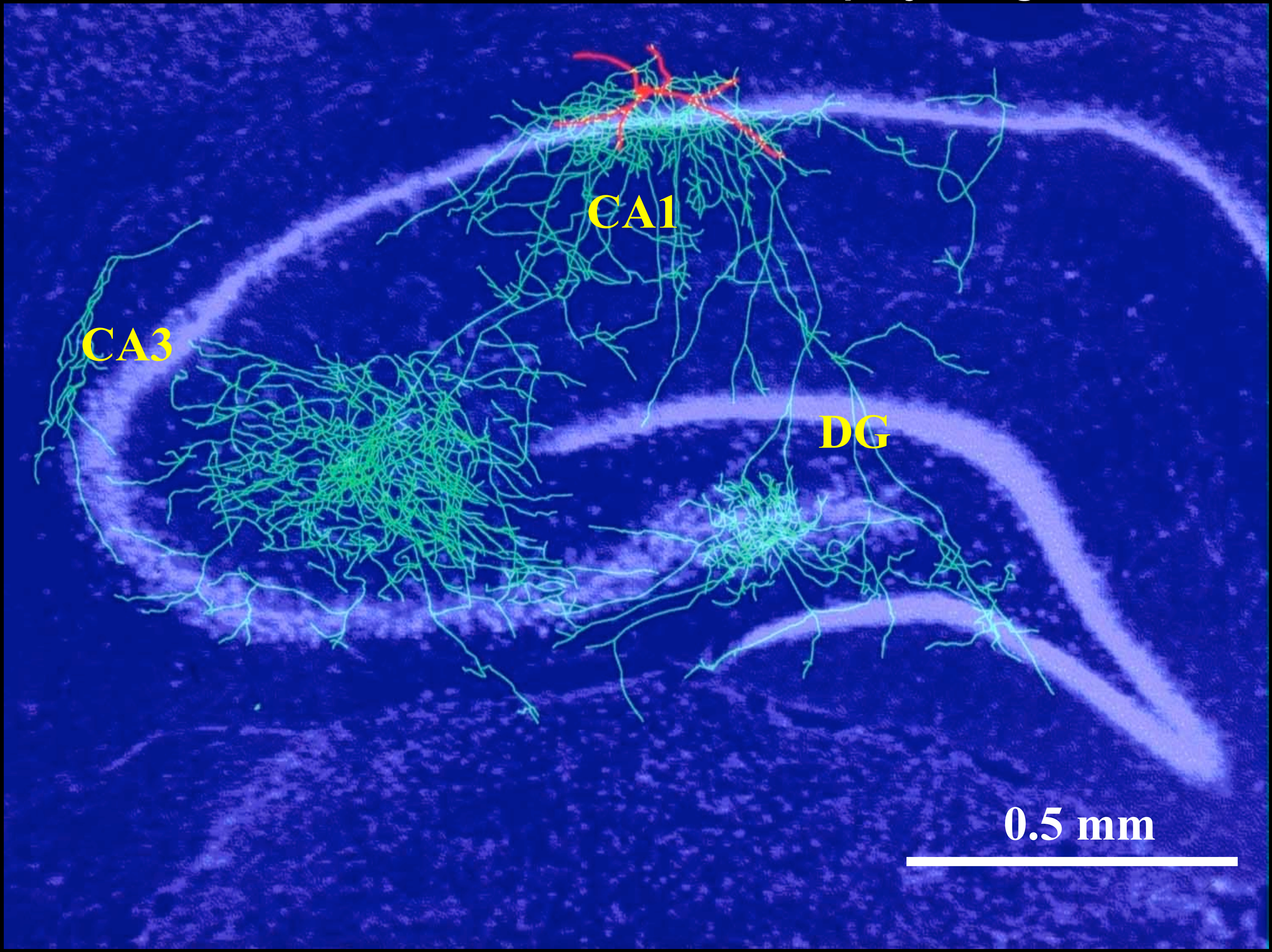
the local-global paradigm

(e.g. Upwards-downwards causation; Synergetics; Catastrophe theory)

... is only characterized by a mere two-level structure: a "microscopic" level (e.g. neurons, local networks) interact with a"macroscopic" emergent whole (e.g. large-scale integration).

…often leads to a hierarchy between "higher" and "lower" levels, and creates an adherence to either a top-down or bottom-up approache, generating therefore a false dichotomy.

3D reconstructed axon collaterals of a 'backprojecting' interneuron



Sik et al. Science 265, 1994

…the brain as an irreducible multi-level « architecture » of spatial and temporal scales that are are braided together in an extremely complex web of interactions

Until now, the most popular paradigms used for explaining cross-scale interactions in the brain (e.g. *upwards-downwards causality, synergetics, catastrophe theory*) are characterized by a mere two-level approach (local/global, outside/inside, upwards/downwards)

...A refined and more general framework for the description of multi-scale brain dynamics has still to be developed.

Varela's explanatory pluralism:

Multiple, distinct and interrelated levels of explanation are needed in neurosciences…

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