MACACC

Modeling the Activity in the Cortex and Analysing the Cortical neural Code

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Partenaires

ALCHEMY-INRIA

CORTEX-INRIA

Institut de Neurosciences Cognitives de la Méditerranée

Laboratoire Jean-Alexandre Dieudonné, Nice

ODYSSEE-INRIA

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Proposer une méthode **générique** de construction de **modèles statistiques optimaux** pour l'analyse de **trains de spikes** et produire de nouveaux **algorithmes de traitement** de ces données.

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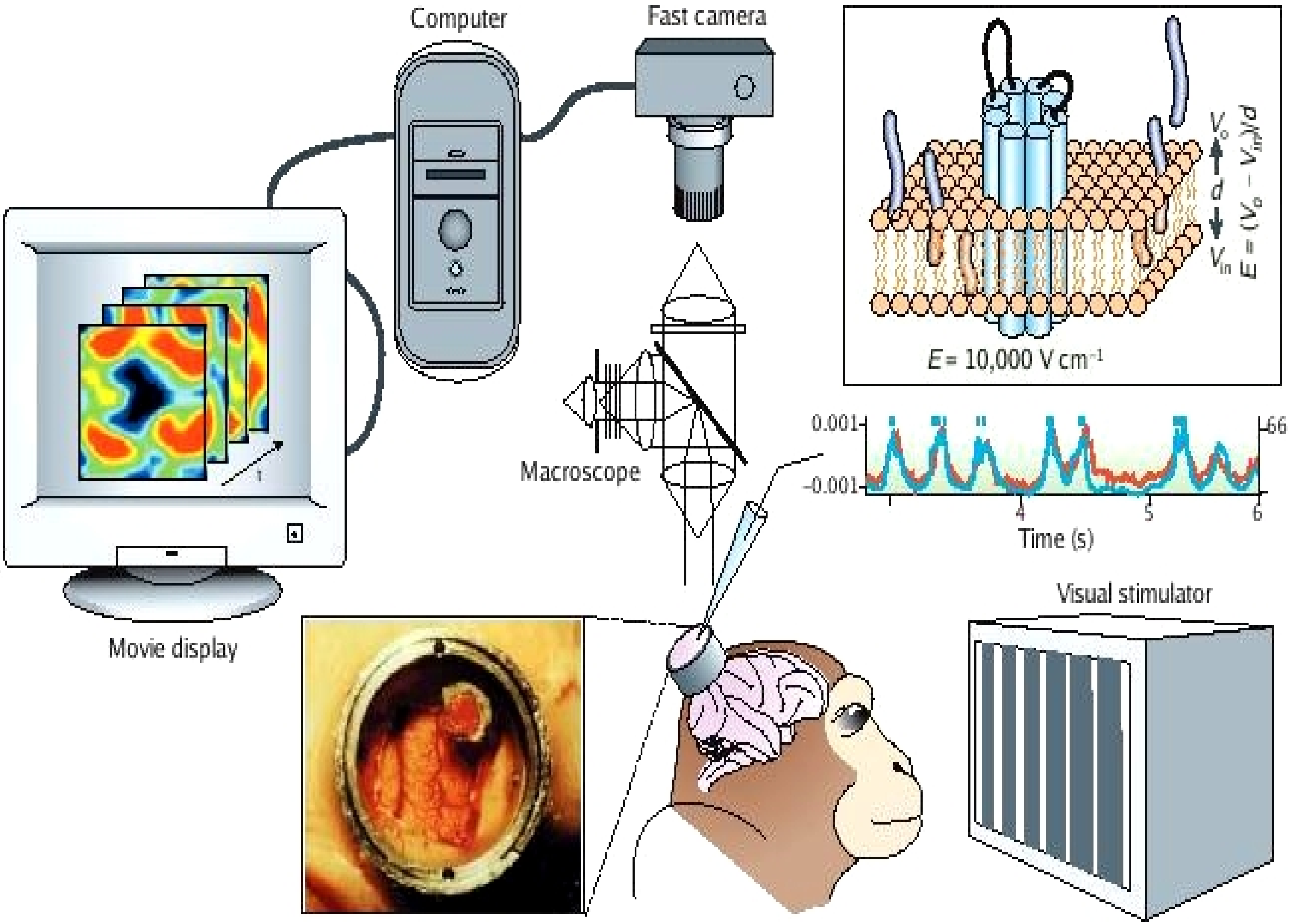
Modélisation mésoscopique de colonnes corticales et imagerie.

Proposer et analyser la **dynamique** d'un modèle **mesoscopique**, contraint par les **données expérimentales**, du **signal biologique** mesuré à l'échelle de la **colonne corticale** et comparer les prédictions théoriques à l'activité corticale du **système visuel** (aires V1-V2), mesurée par **imagerie optique** et **MEG-EEG**.

Modélisation mésoscopique de colonnes corticales et imagerie.

(Courtesy S. Chemla)



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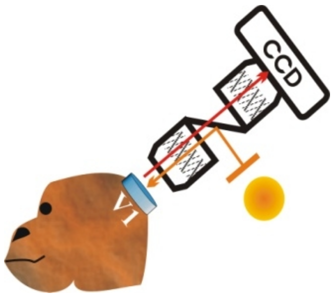
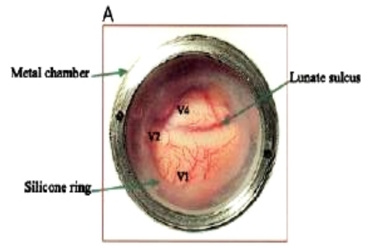
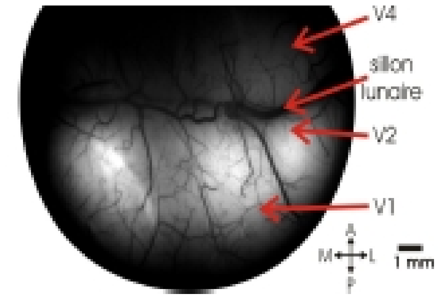




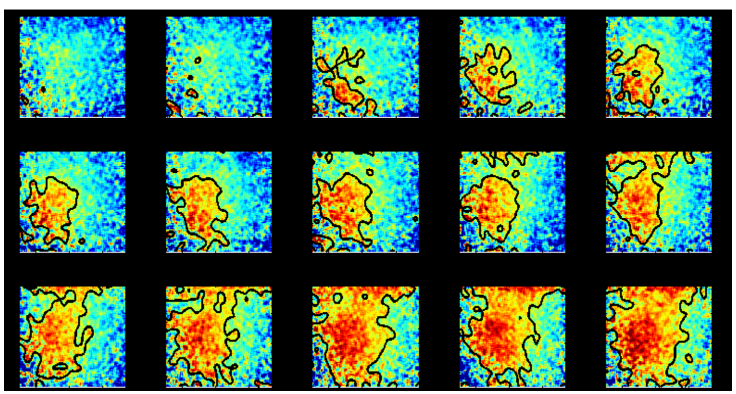


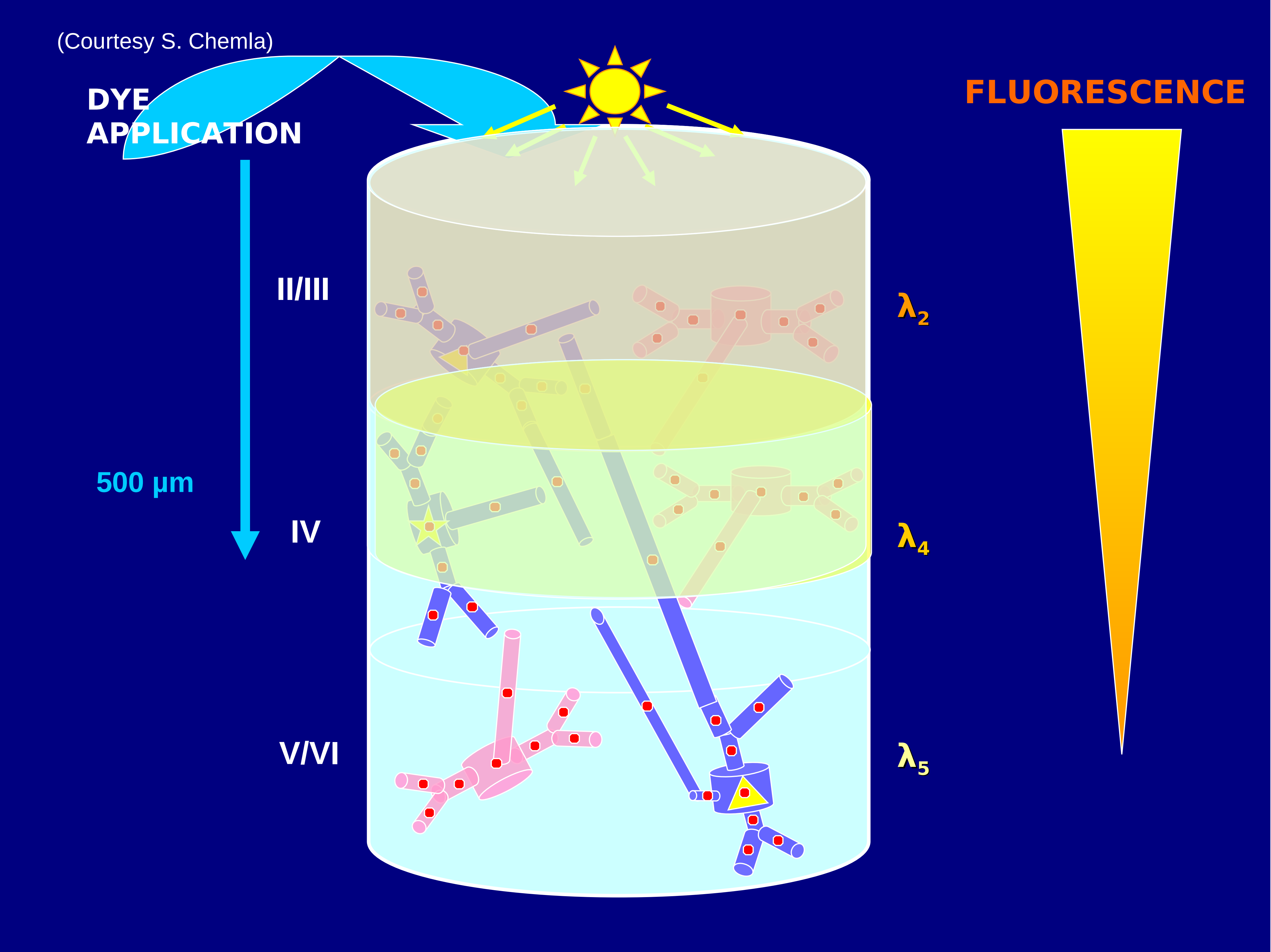
- The membrane potential can be measured optically using Voltage-Sensitive Dyes (VSDs)

- The dye molecules act as molecular transducer that transform changes in membrane potential into optical signals

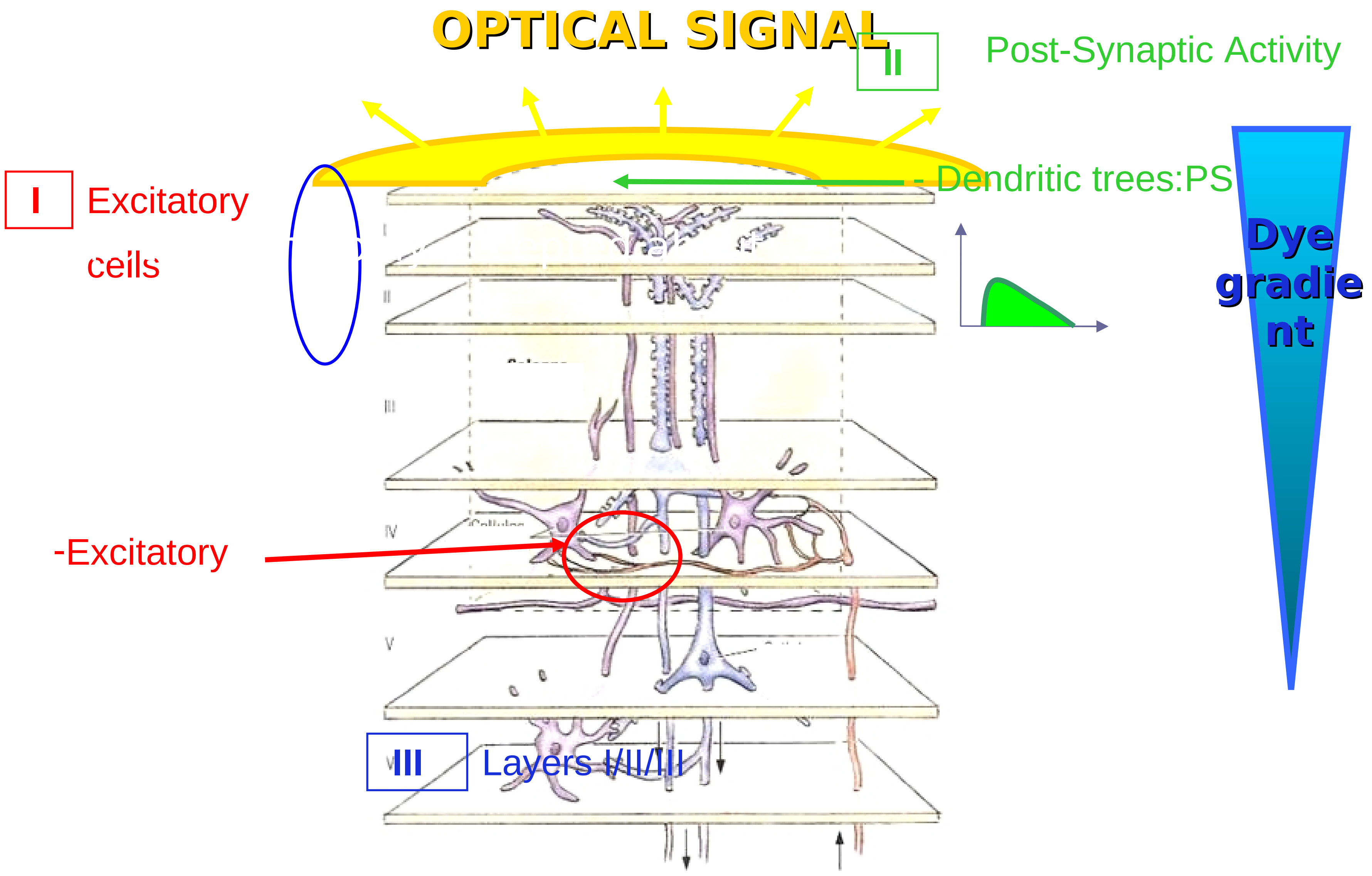
- High temporal resolution: < 1 ms

- High spatial resolution: ~ 50 µm




(Courtesy S. Chemla)
DYE APPLICATION
FLUORESCENCE
II/III
IV
V/VI
500 µm
λ2
λ4
λ5

(Courtesy S. Chemla)



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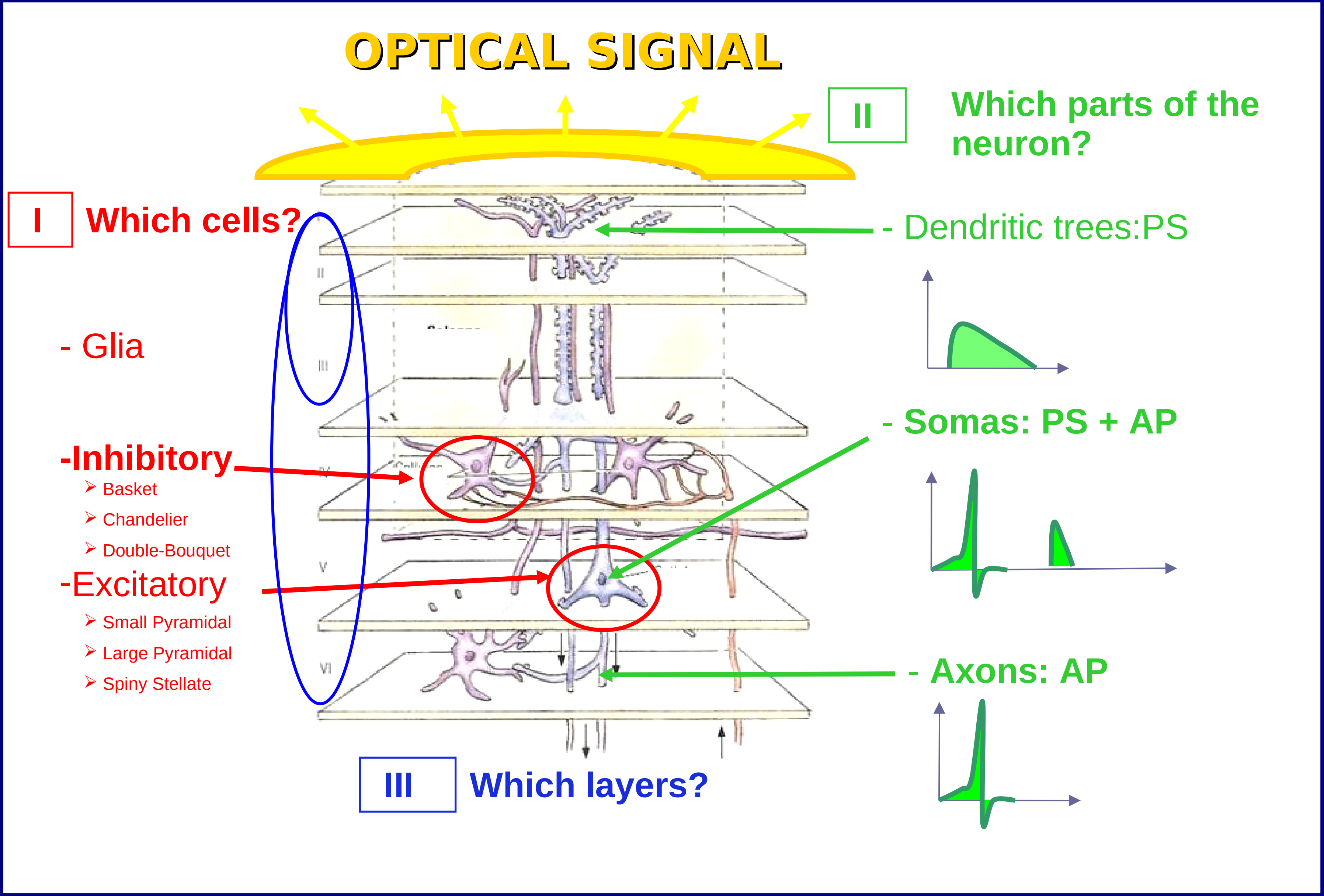
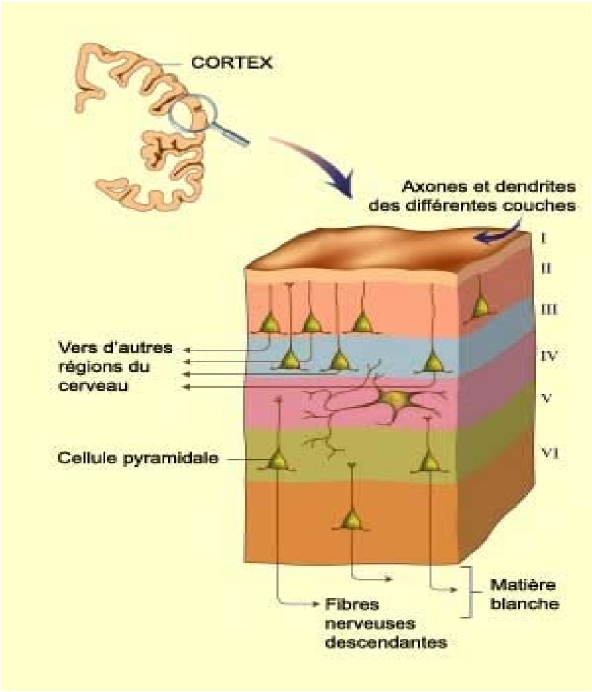


(Courtesy S. Chemla)

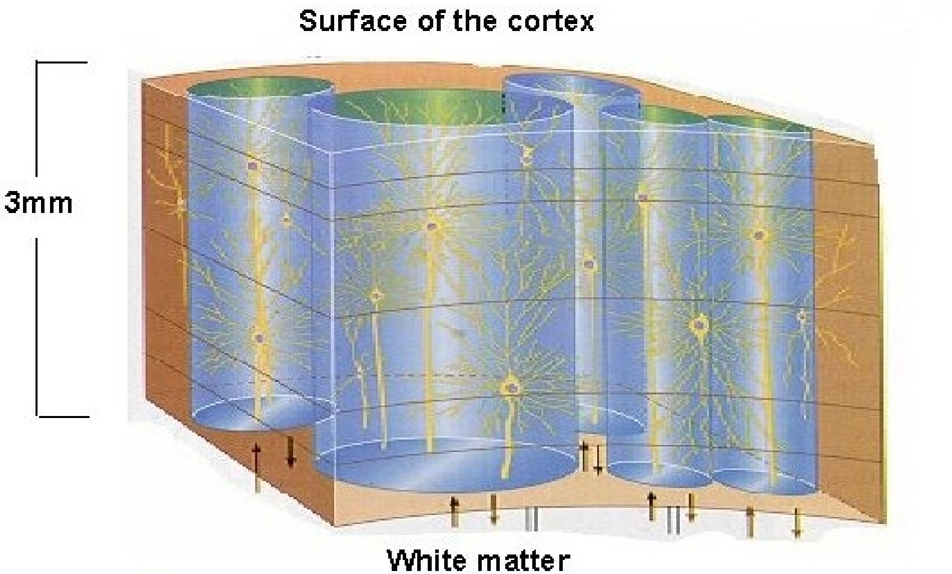
Nature of the signal

- Locally proportional to the membrane potential of all neuronal components
- Proportional to the excited membrane surface of all neuronal components
- A simple gradient of VSD fluorescence depending on depth

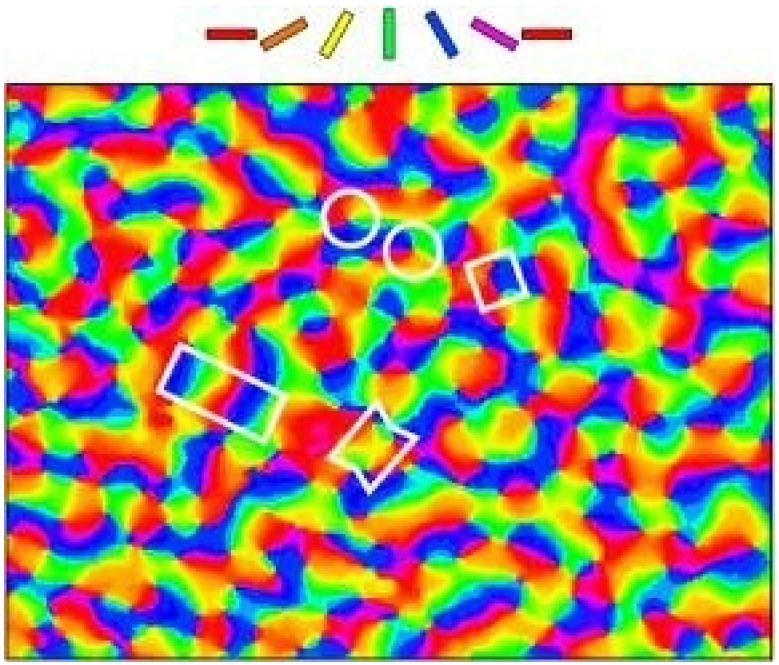
Colonnes corticales.



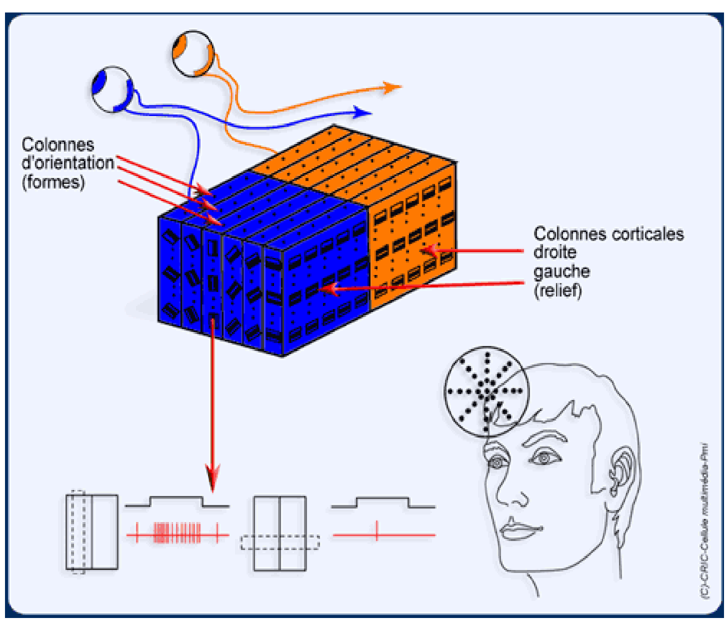
Petits cylindres, de diamètre 0.1~1mm, traversant les couches du cortex, contenant entre 10^3-10^4 neurones, de différents types, fortement connectés.

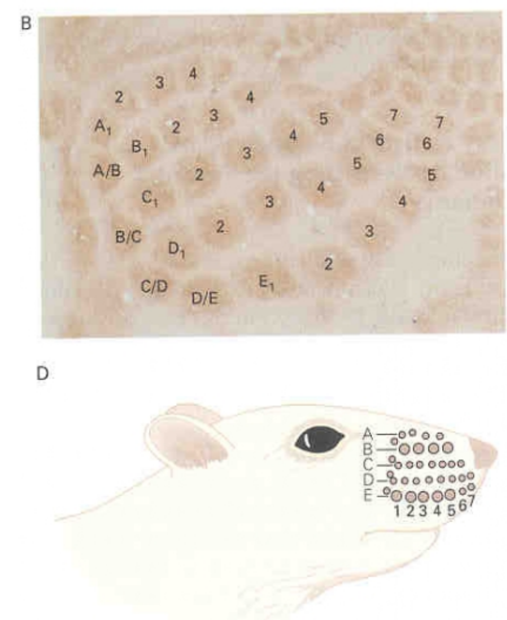


Colonnes corticales.



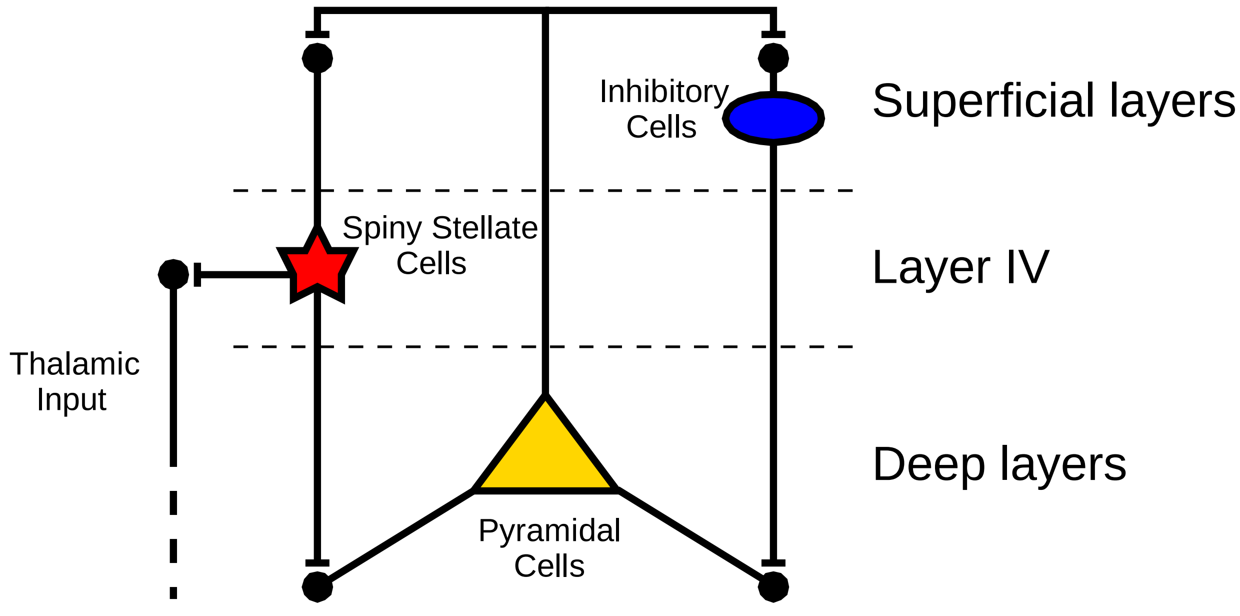
Les colonnes corticales sont impliquées dans des fonctions sensori-motrices élémentaires telles que la vision.





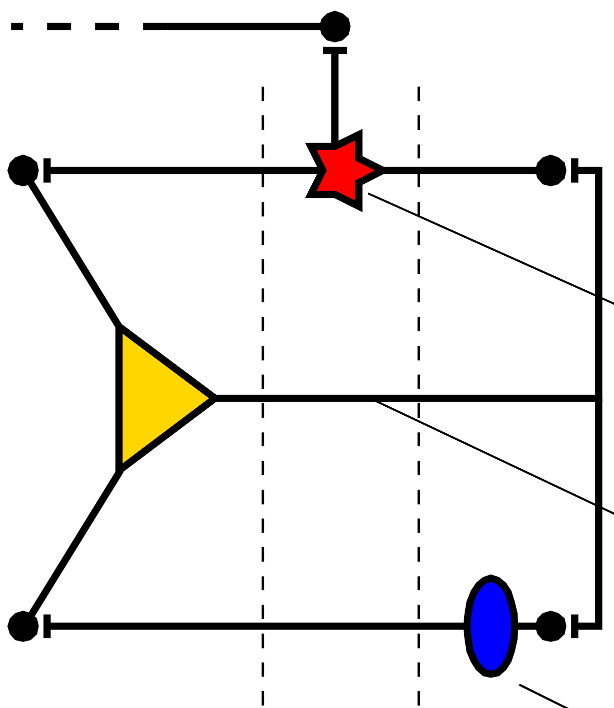
Colonnes corticales.

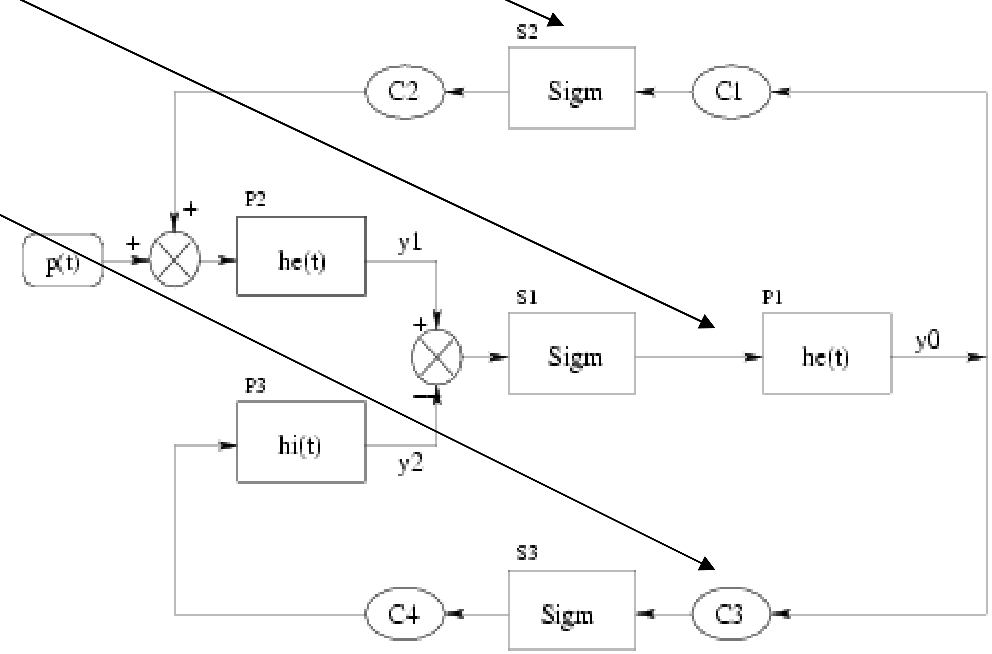
Les colonnes corticales sont composées de neurones appartenant à un petit nombre de populations différentes interagissant entre elles. Ces populations appartiennent à des couches différentes du cortex.



Colonnes corticales.

Il est possible et utile de proposer des modèles phénoménologiques rendant compte de l'activité mésoscopique de ces colonnes, en prédisant notamment le comportement du potentiel de champ local engendré par l'activité électrique des neurones, et en mettant ce comportement en relation avec mesures et observations cliniques.





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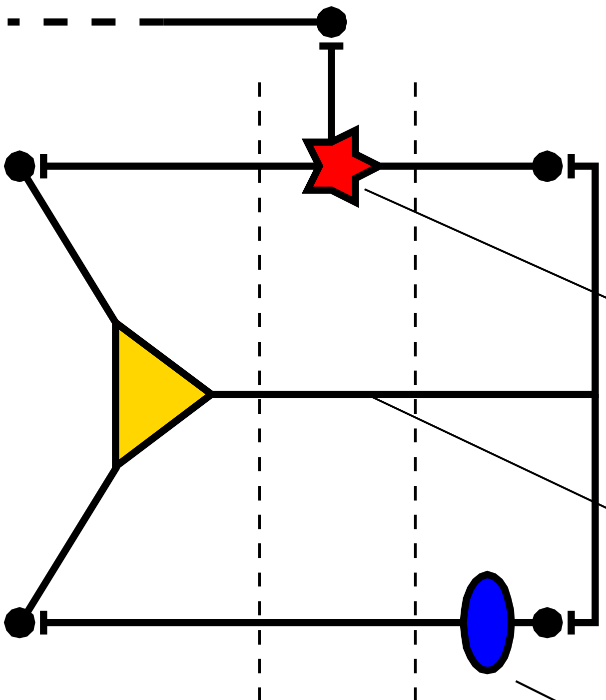

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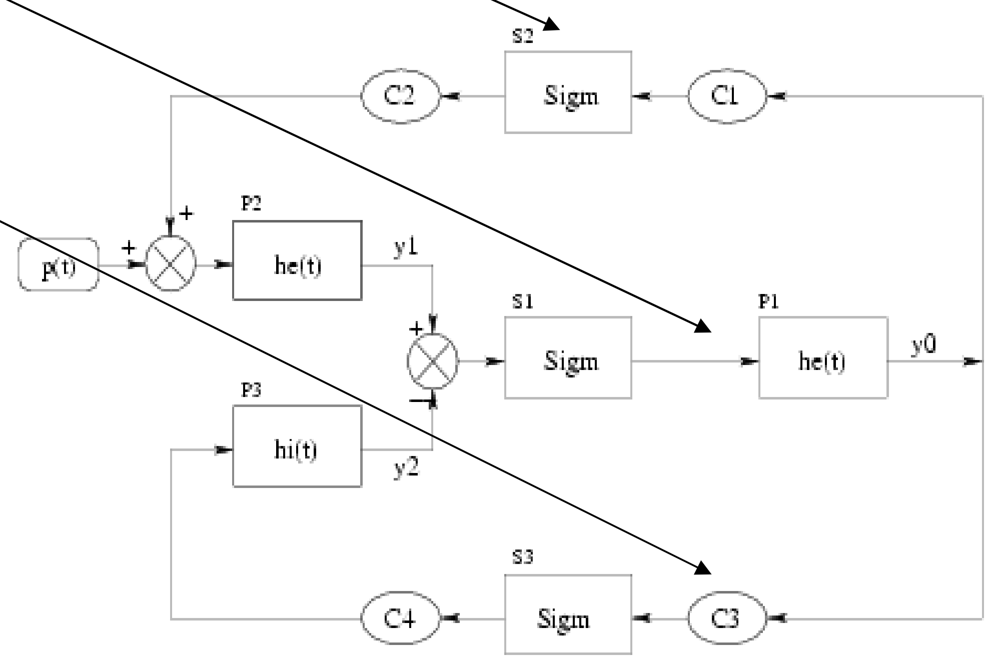


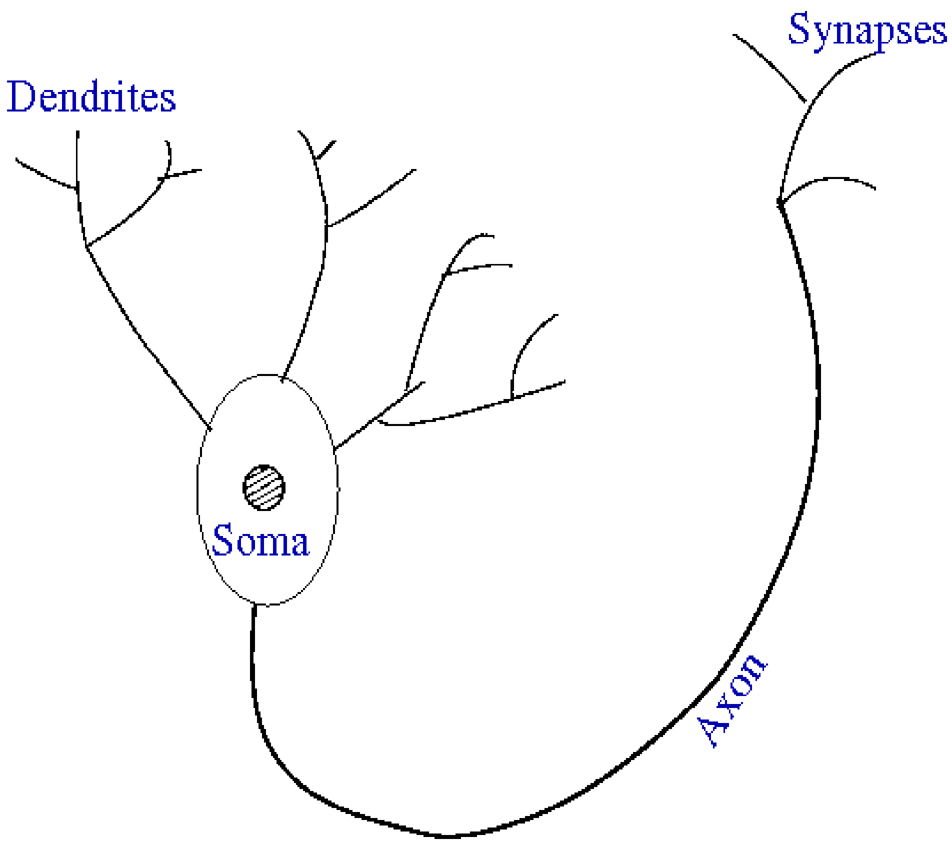
Ces modèles, tel le modèle de Jansen-Rit (**Biological Cybernetics, 73, 1995**) sont obtenus à partir d'**hypothèses ad hoc**.

Tâche n° 1.
(première année)

Obtenir les équations caractérisant la dynamique l'activité mésoscopique de plusieurs populations neuronales, à partir de la dynamique microscopique.

Neurons and synapses.

Neurons and synapses.



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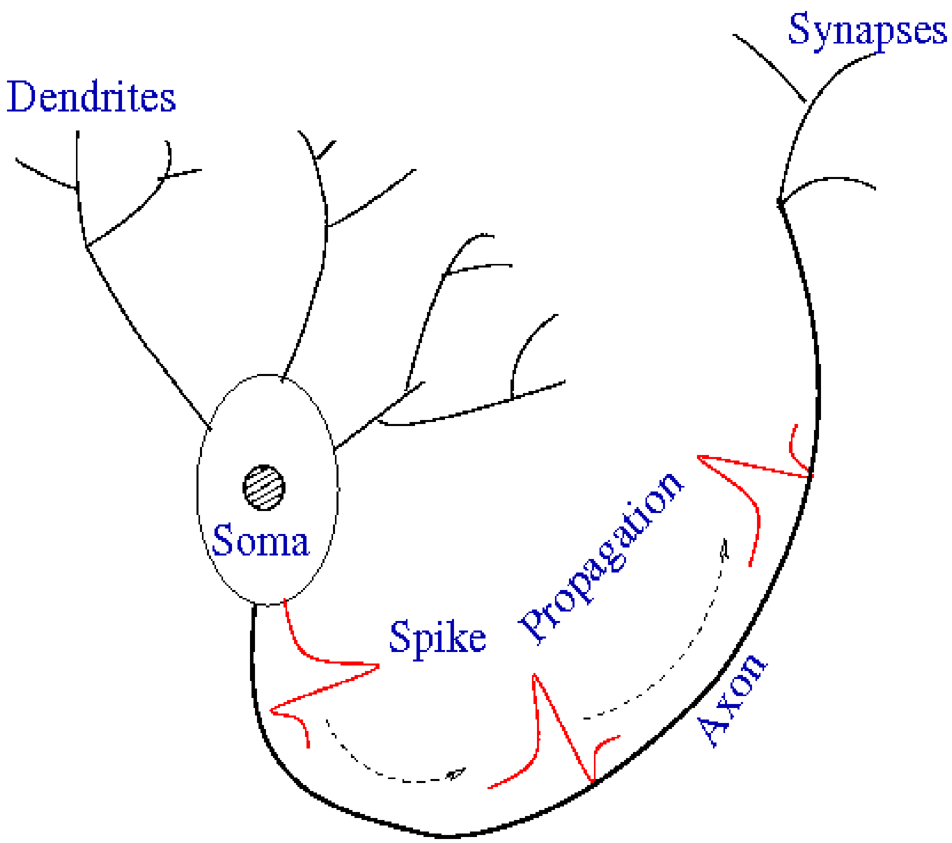

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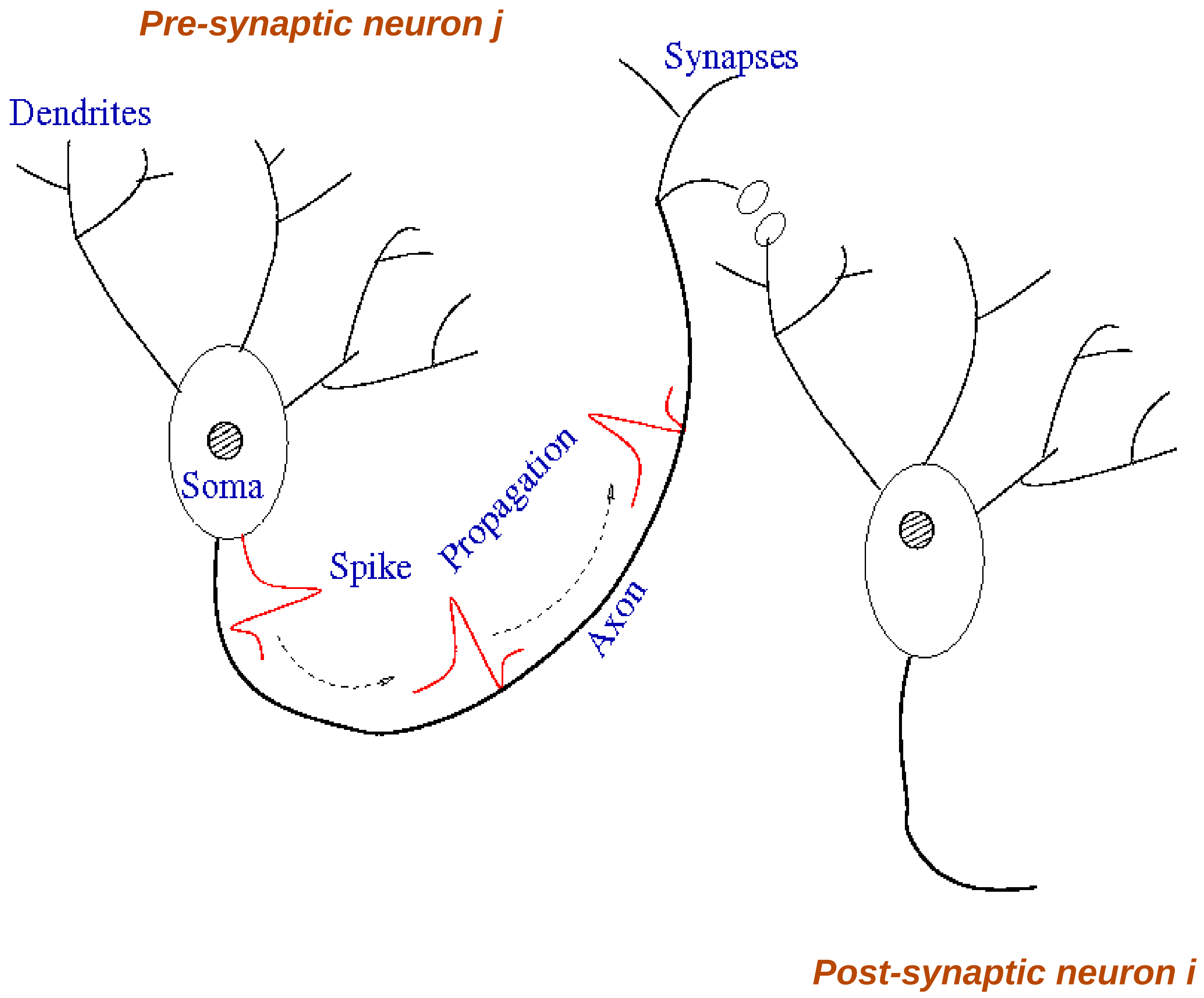

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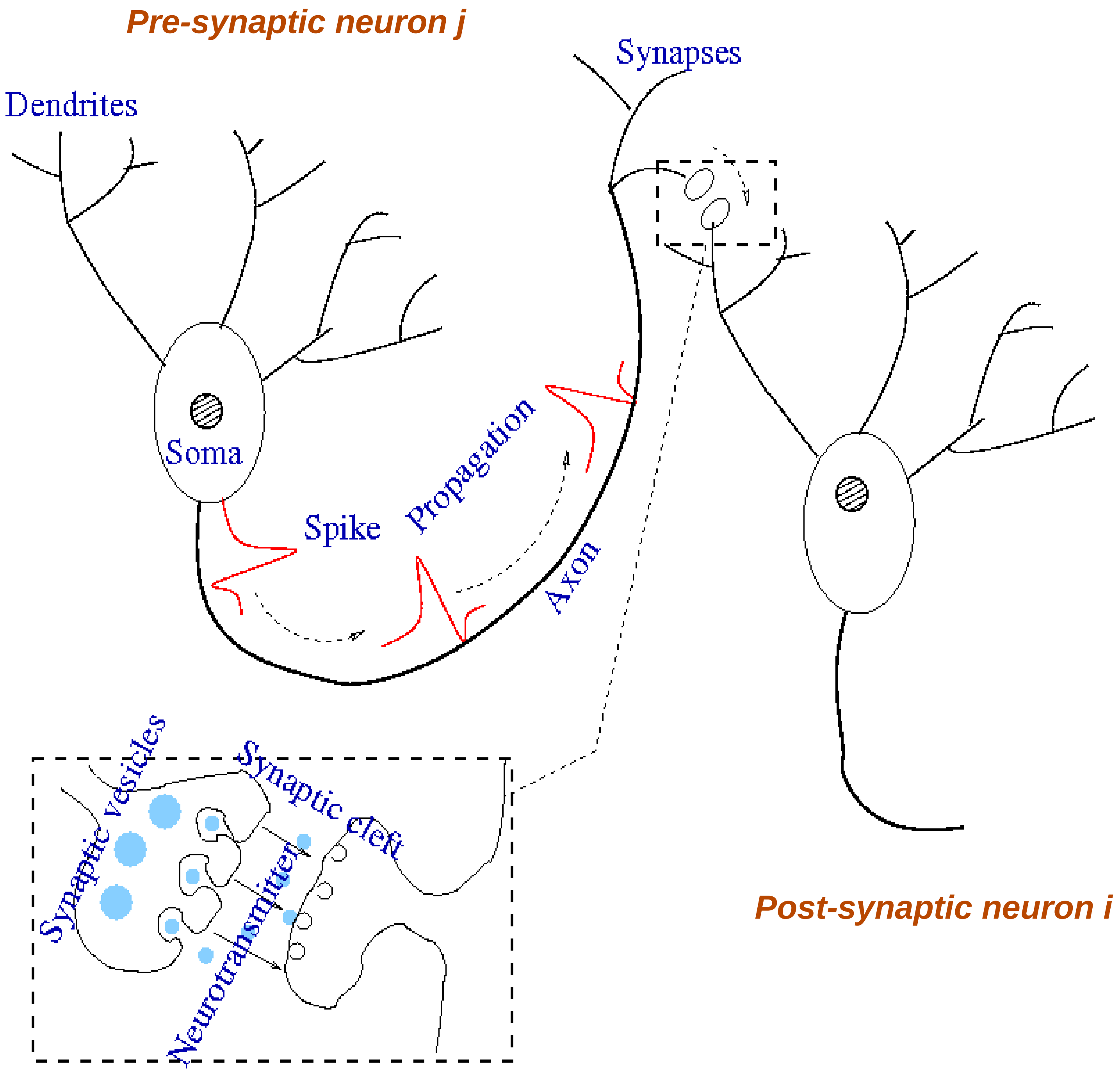

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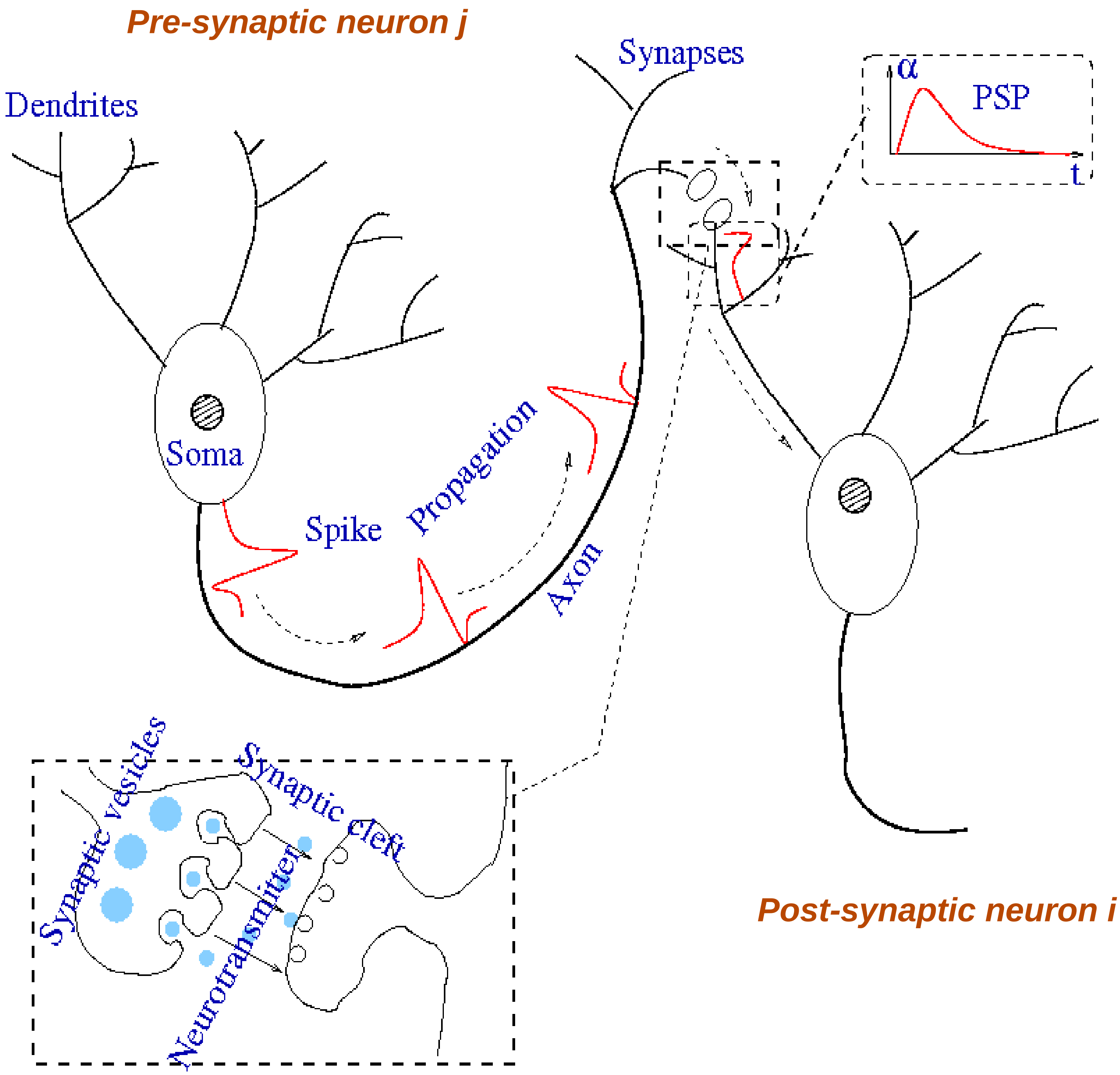

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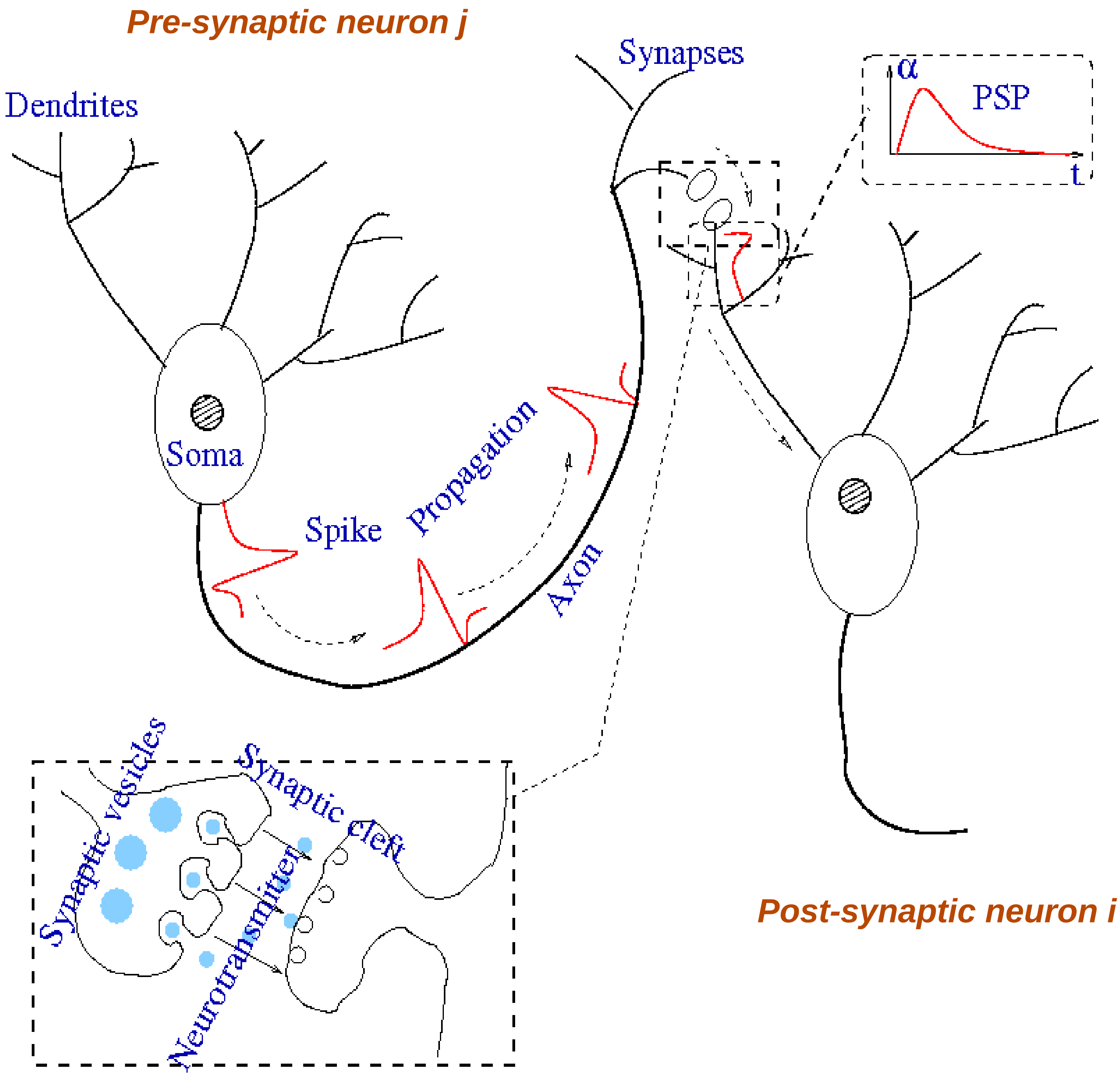

$$\sum_{l=0}^{k} a_i^{(l)} \frac{d^l \alpha_i}{dt^l}(t) = \delta(t)$$

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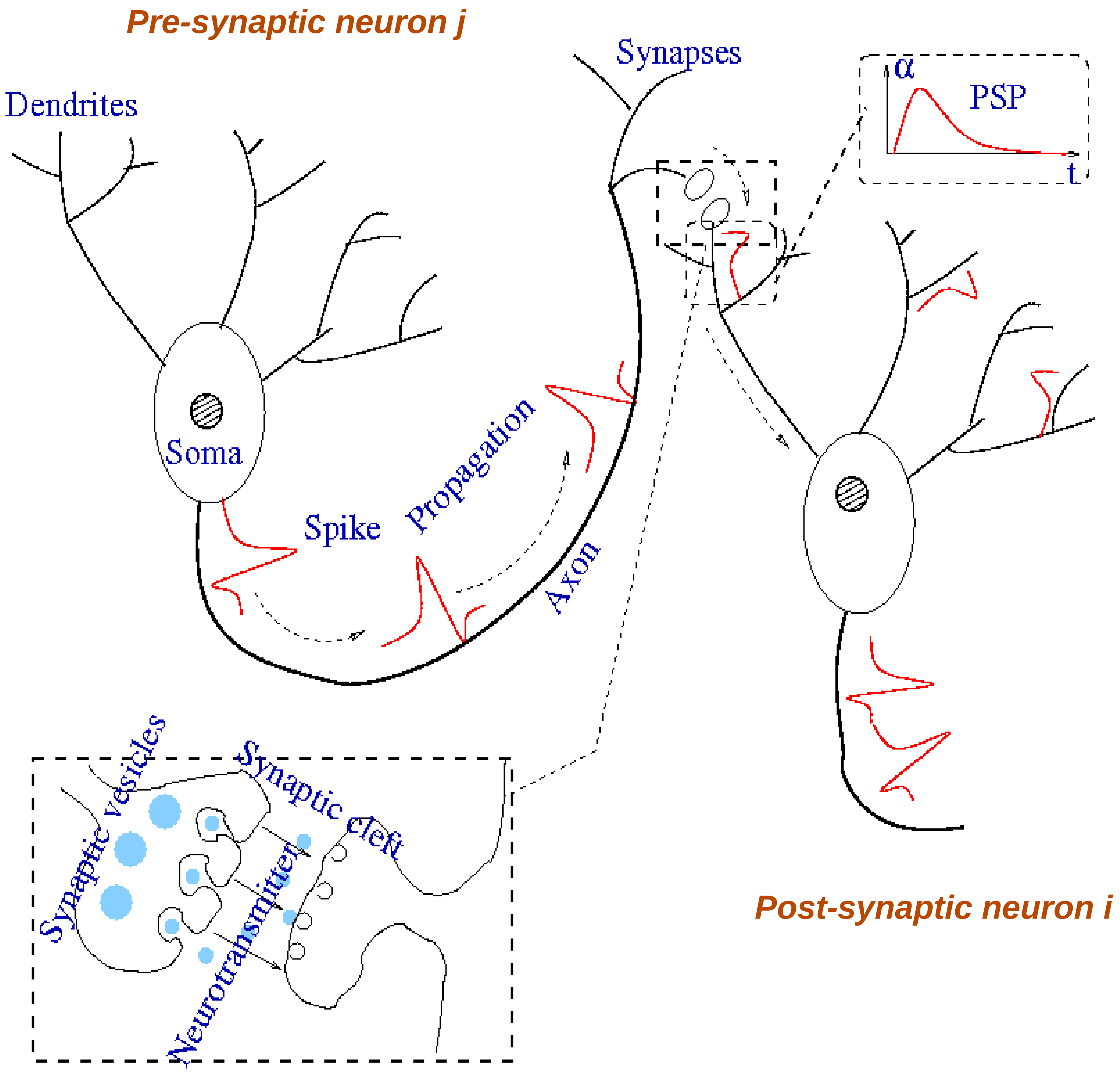

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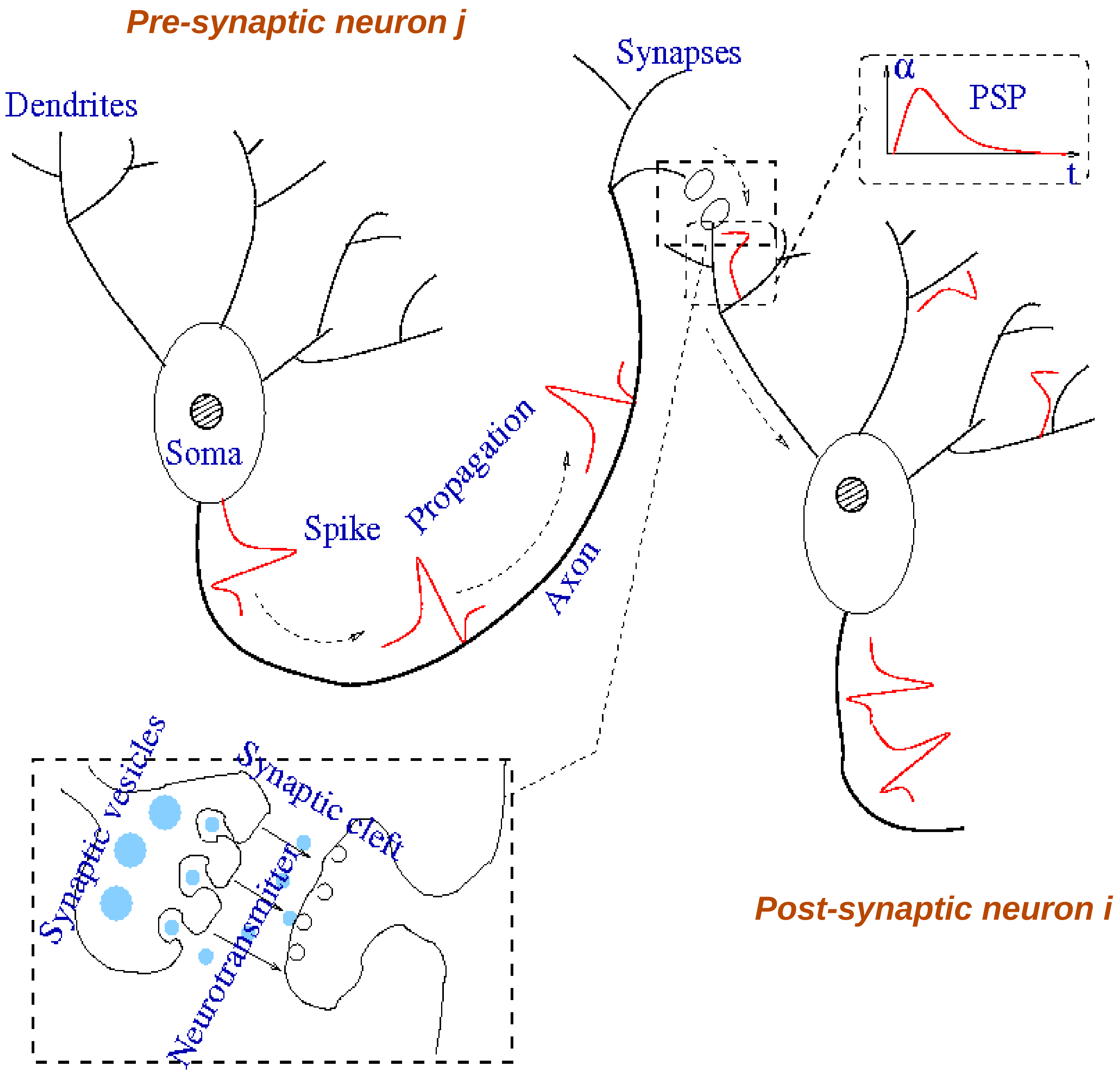

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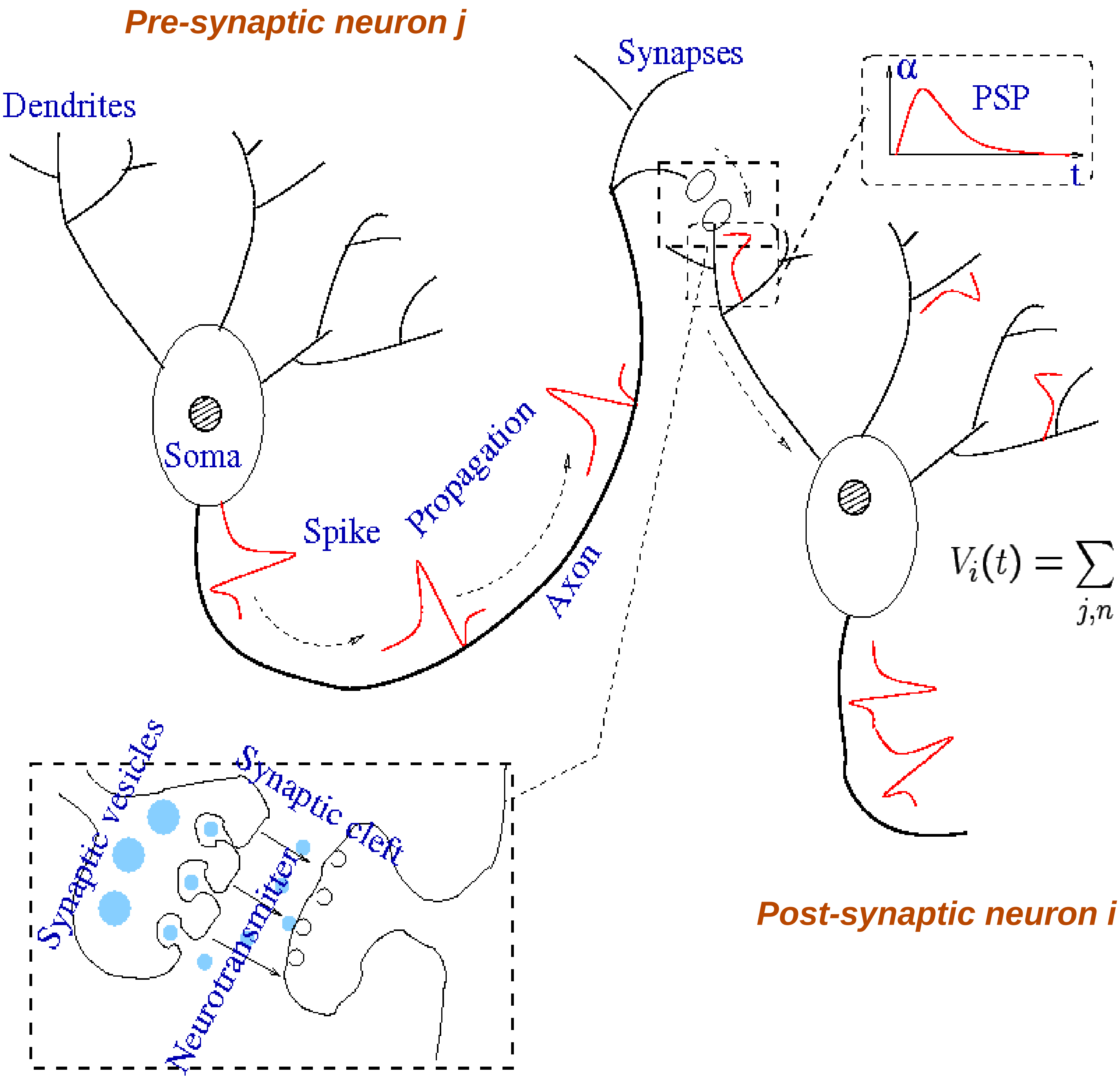

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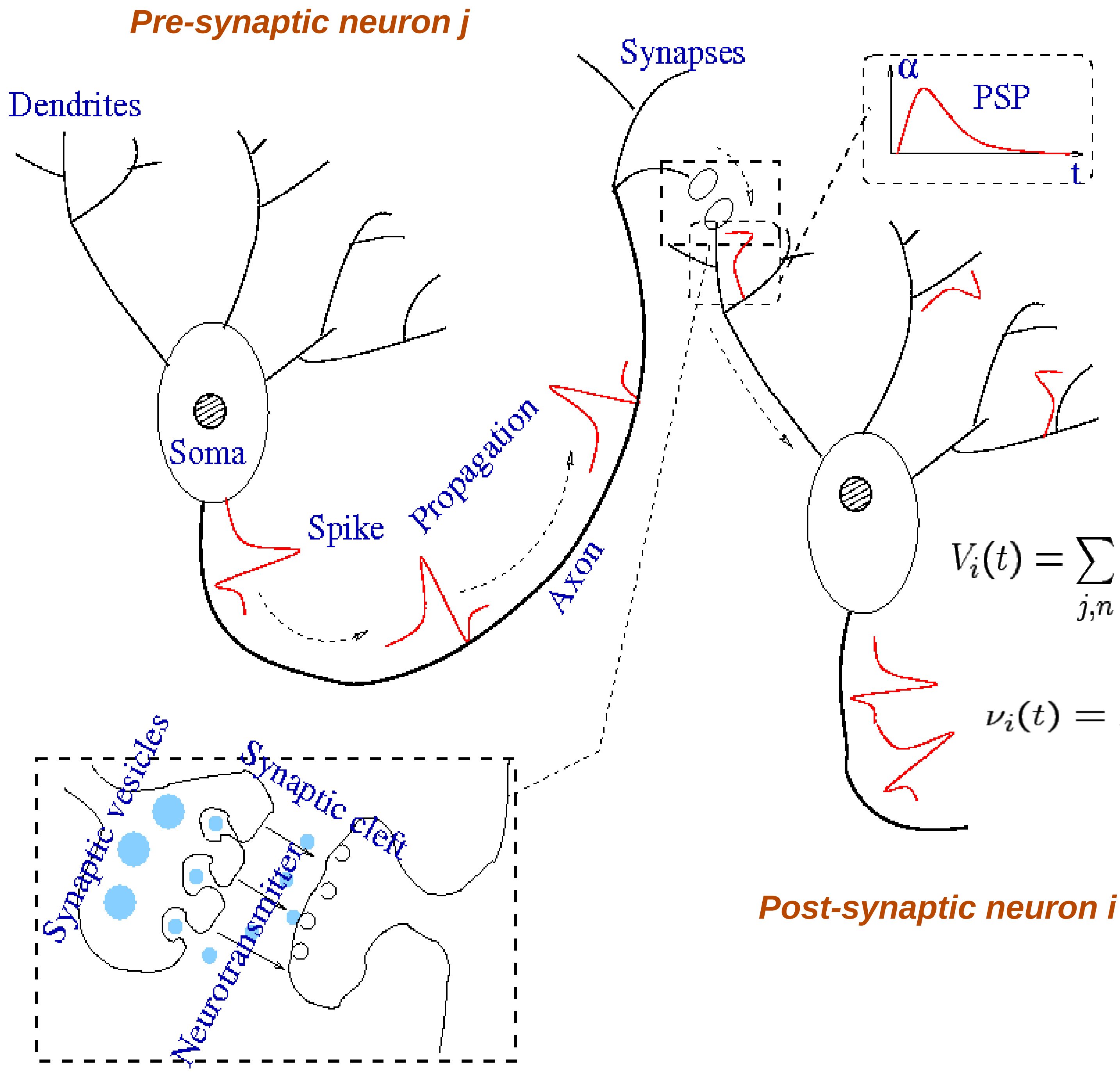

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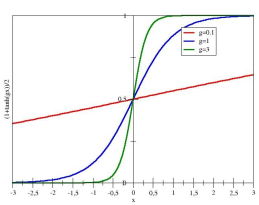
$$\nu_i(t) = S_i(V_i(t))$$



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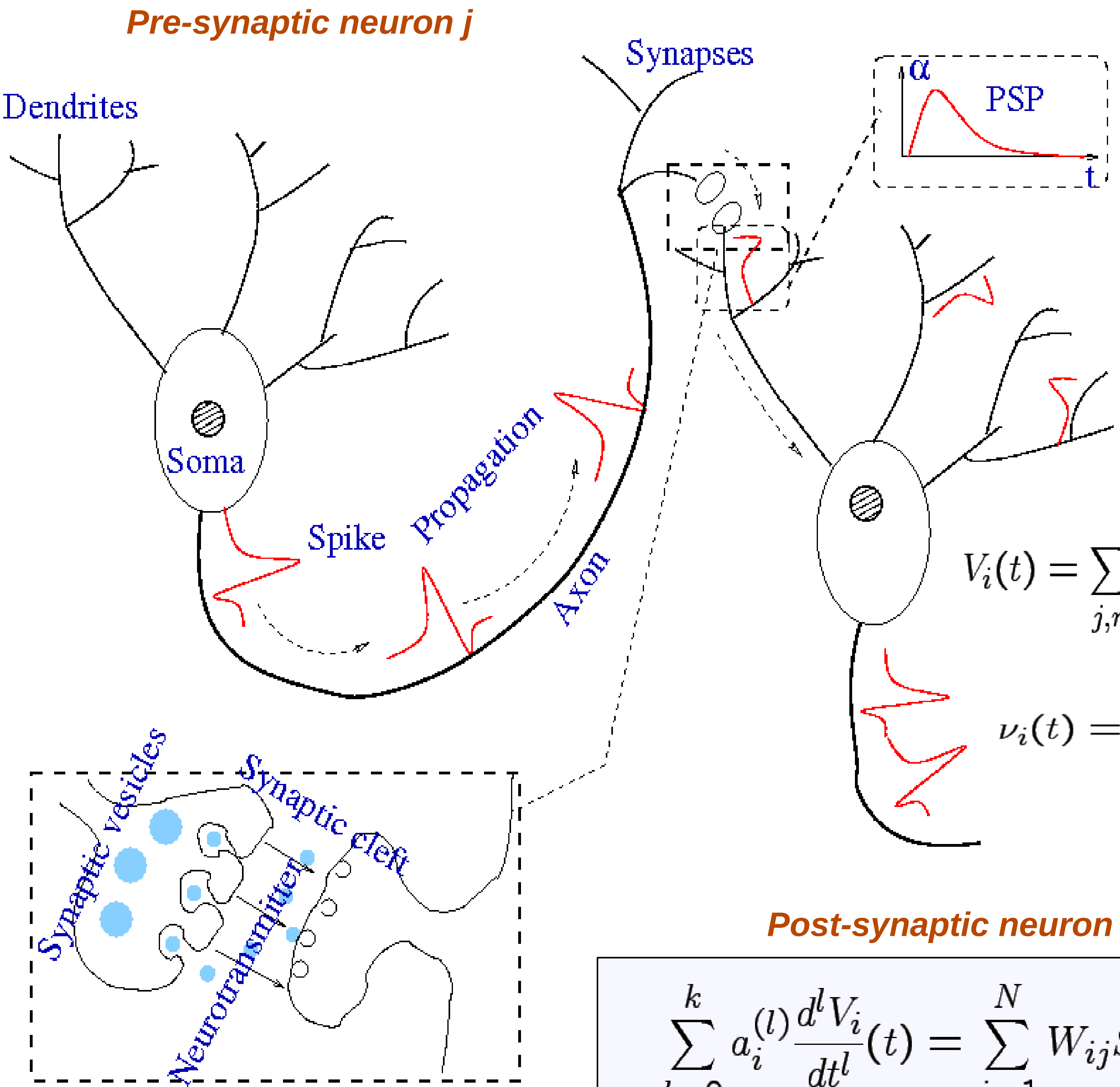

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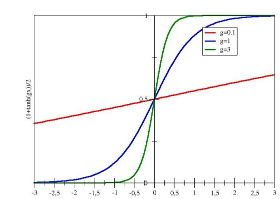

Post-synaptic neuron i

$$\sum_{l=0}^{k} a_i^{(l)} \frac{d^l V_i}{dt^l}(t) = \sum_{j=1}^{N} W_{ij} S_j(V_j(t)) + I_i(t) + B_i(t).$$

Neural mass model.

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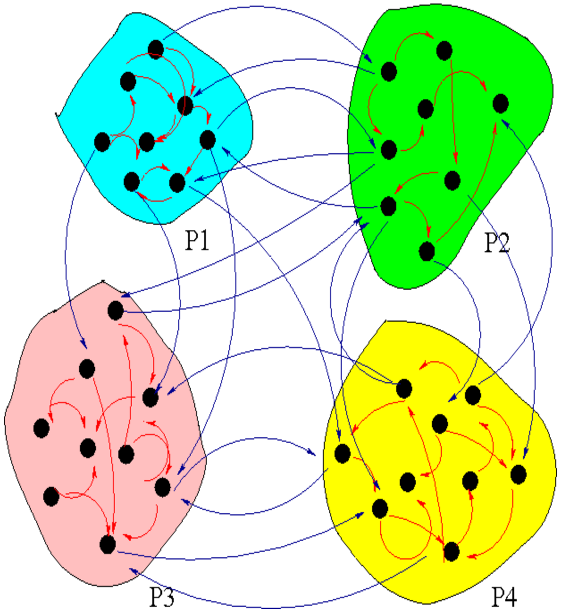
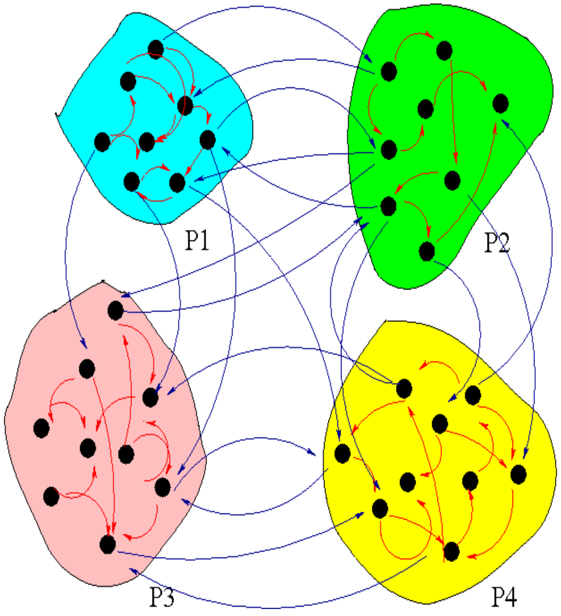


P populations of neurons, a =1 ... P

Neural mass model.



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Voltage-based model

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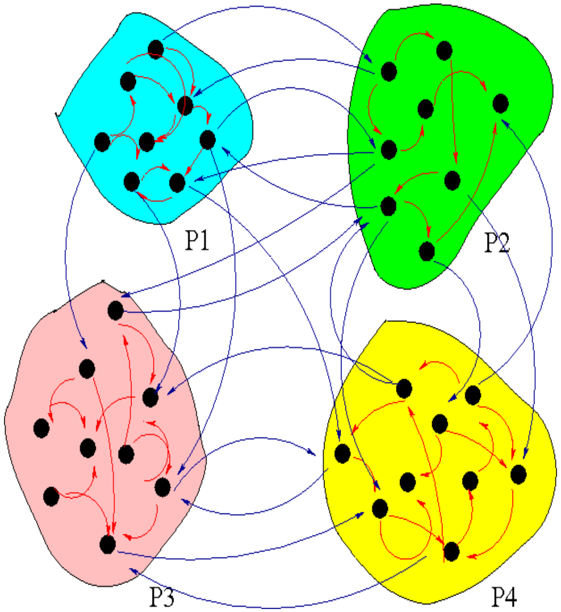

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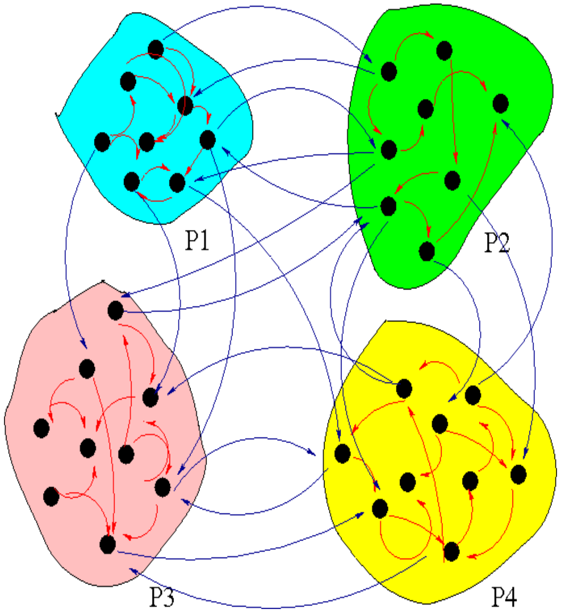

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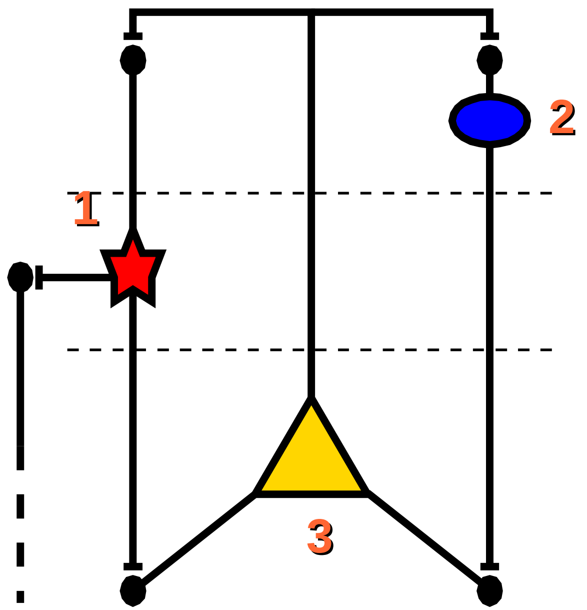
Assumptions:

- **Synapse response, current and noise depend only on the neuronal population.**

Neural mass model.



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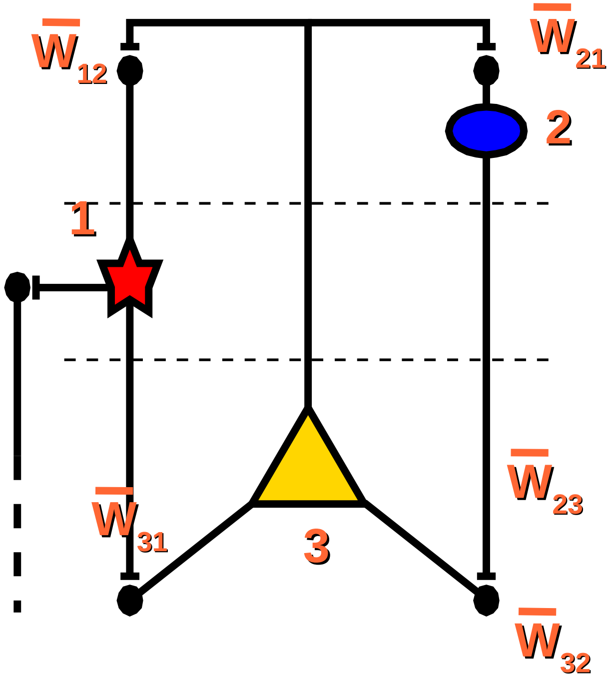

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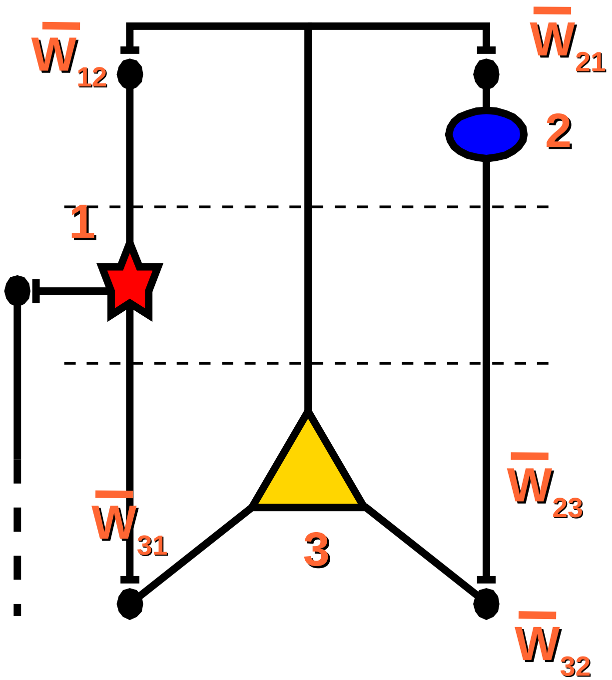

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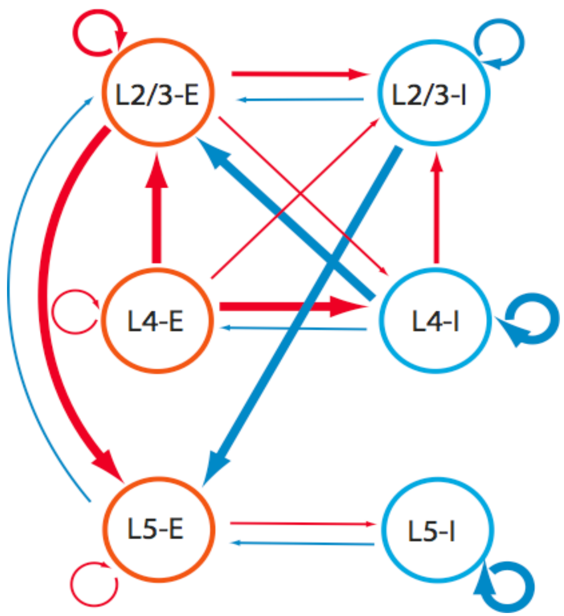
Synaptic efficacies

$$W_{ij} \sim \mathcal{N}\left(\frac{\bar{W}_{ab}}{N_b}, \frac{\sigma_{ab}^2}{N_b}\right)$$ (independent)

Assumptions:

- Synapse response, current and noise depend only on the neuronal population.
- The probability distribution of synaptic efficacies depend only on pre- and post synaptic neuron' population

Neural mass model.



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Random
(quenched)

Nonlinear

Stochastic
(annealed)

Dynamic mean-field theory.

Voltage-based model

$$\sum_{l=0}^{k} a_a^{(l)} \frac{d^l V_i}{dt^l}(t) = \sum_{b=1}^{P} \sum_{j=1}^{N_b} W_{ij} S_b(V_j(t)) + I_a(t) + B_a(t).$$

Dynamic mean-field theory.

Voltage-based model

$$\sum_{l=0}^{k} a_a^{(l)} \frac{d^l V_i}{dt^l}(t) = \eta_i(V,t) + I_a(t) + B_a(t).$$

Local interaction field.

$$\eta_i(V,t) = \sum_{b=1}^{P} \sum_{j=1}^{N_b} W_{ij} S_b(V_j(t))$$

Dynamic mean-field theory.

Voltage-based model

$$\sum_{l=0}^{k} a_a^{(l)} \frac{d^l V_i}{dt^l}(t) = \eta_i(V,t) + I_a(t) + B_a(t).$$

Non random synaptic weights.

$$W_{ij} = \frac{\bar{W}_{ab}}{N_b},\ i \in a, j \in b.$$

Local interaction field.

$$\eta_i(V,t) = \sum_{b=1}^{P} \sum_{j=1}^{N_b} W_{ij} S_b(V_j(t))$$

Dynamic mean-field theory.

Voltage-based model

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$$\frac{1}{N_b} \sum_{j=1}^{N_b} S_b(V_j(t)) \to \phi_b((t))$$

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Jansen-Ritt equations.

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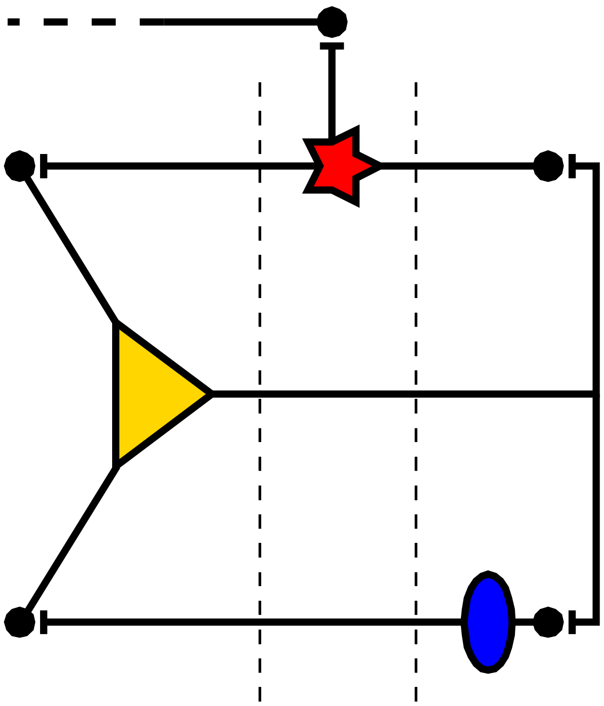
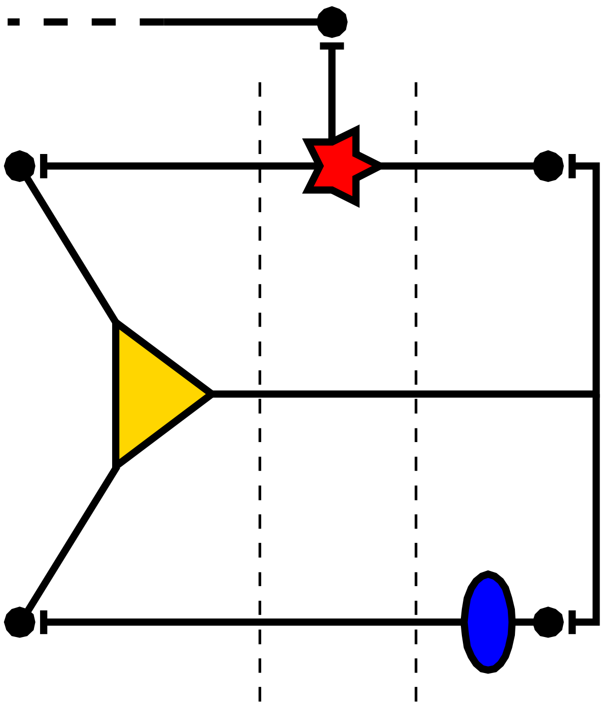


Jansen-Ritt equations.



Il est possible et utile de proposer des modèles phénoménologiques rendant compte de l'activité mésoscopique de ces colonnes, en prédisant notamment le comportement du potentiel de champ local engendré par l'activité électrique des neurones, et en mettant ce comportement en relation avec des mesures.

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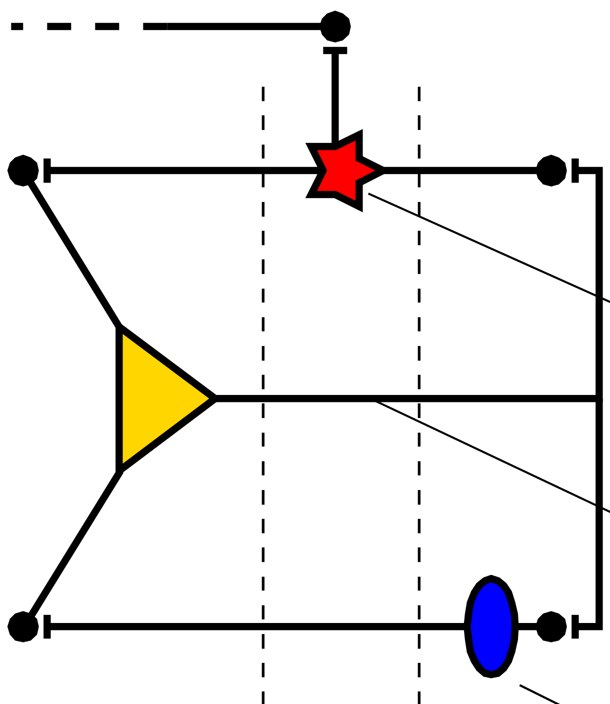

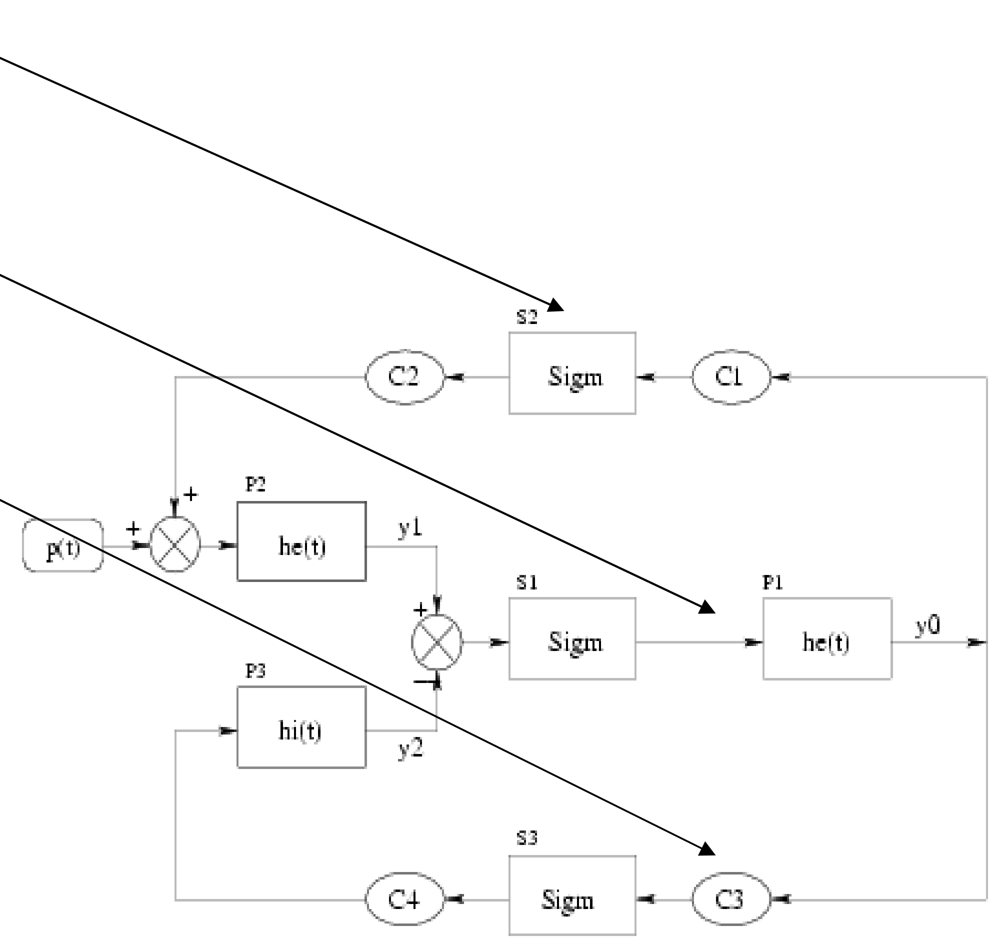

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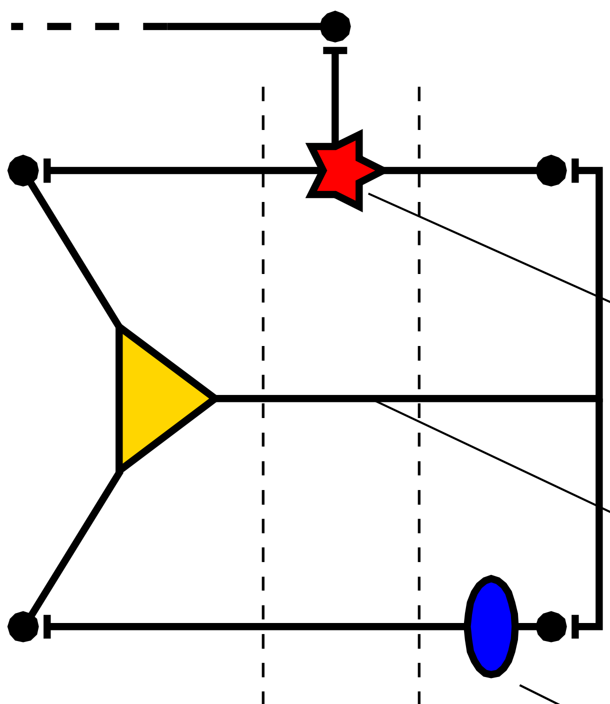

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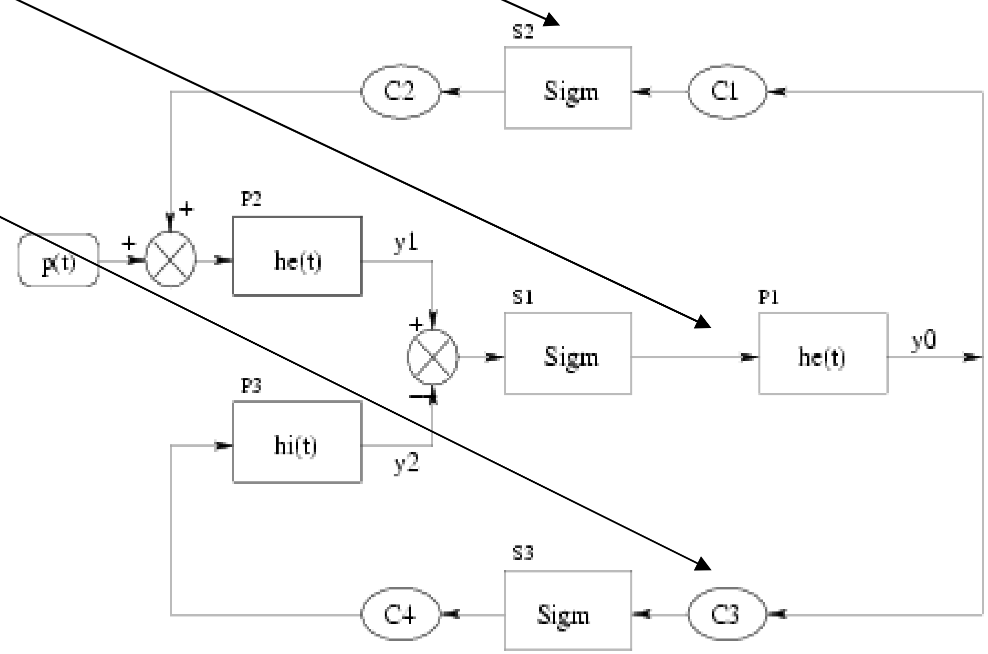

Modèle de Jansen et Rit (1995).

$$\begin{cases} \dot{y}_0 = -a y_0(t) + A f(y_1(t) - y_2(t)), \\ \dot{y}_1 = -a y_1(t) + A\left[p(t) + C_2 f(C_1 y_0(t))\right], \\ \dot{y}_2 = -b y_2(t) + B C_4 f(C_3 y_0(t)). \end{cases}$$

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Empirical measure.

$$\mathcal{F} = \mathbf{R}^{[0,T]} \qquad A \in \mathcal{F}^{N_b}$$

$$\pi_V^{(N_b)}(A) = \frac{1}{N_b} \sum_{j=1}^{N_b} \chi(V_i \in A)$$

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Dynamic mean-field theory.

Simple model

$$\frac{dV_i}{dt} = -\frac{V_i}{\tau_a} + \sum_{b=1}^{P} \sum_{j=1}^{N_b} W_{ij} S_b(V_j(t)) + I_a(t) + B_a(t), \quad i \in a$$

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$$v_a(t) = Var\left[V_a(t)\right]$$

$$\frac{d\mu_a}{dt} = -\frac{\mu_a}{\tau_a} + \sum_{b=1}^{P} \bar{W}_{ab} \int_{-\infty}^{+\infty} S_b\left(h\sqrt{v_b(t)} + \mu_b(t)\right) Dh + I_a(t)$$

$$Dh = \frac{e^{-\frac{h^2}{2}}}{\sqrt{2\pi}} dh$$

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$$C_{ab}(t,s) = \delta_{ab} e^{-(t+s)/\tau_a}\left[v_a(0) + \frac{\tau_a s_a^2}{2}\left(e^{\frac{2s}{\tau_a}} - 1\right) + \sum_{b=1}^{P} \sigma_{ab}^2 \int_0^t \int_0^s e^{(u+v)/\tau_a} \Delta_b(u,v)\, du\, dv\right]$$

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Dynamic mean-field theory.

Simple model

$$\frac{dV_i}{dt} = -\frac{V_i}{\tau_a} + \sum_{b=1}^{P}\sum_{j=1}^{N_b} W_{ij} S_b(V_j(t)) + I_a(t) + B_a(t), \quad i \in a$$

Non random synaptic weights.

$$W_{ij} = \frac{\bar{W}_{ab}}{N_b}, \; i \in a, j \in b.$$

Dynamic mean-field equations.

$$\mu_a(t) = E\left[V_a(t)\right]$$

$$v_a(t) = Var\left[V_a(t)\right]$$

$$\frac{d\mu_a}{dt} = -\frac{\mu_a}{\tau_a} + \sum_{b=1}^{P} \bar{W}_{ab} \int_{-\infty}^{+\infty} S_b\left(h\sqrt{v_b(t)} + \mu_b(t)\right) Dh + I_a(t)$$

$$Dh = \frac{e^{-\frac{h^2}{2}}}{\sqrt{2\pi}} dh$$

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Naive mean-field equations.

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Dynamic mean-field theory.

Simple model

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Evolution is not ruled anymore by EDOs but by a mapping on a space of trajectories.

$C_{ab}(t,s) = Cov\,[V_a$ [illegible] $C_{ab}(t,s) =$ [illegible] $\frac{\tau_a s_a^2}{2}\left(e^{\frac{2s}{\tau_a}} - 1\right) + \sum_{b=1}^{P}$ [illegible] $\int_0^t \int_0^s$ [illegible] $\Delta_b(u,v)\,du\,dv]$

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Dynamic mean-field theory.

Voltage-based model

$$\sum_{l=0}^{k} a_a^{(l)} \frac{d^l V_i}{dt^l}(t) = \eta_i(V,t) + I_a(t) + B_a(t).$$

Random synaptic weights.

$$W_{ij} \sim \mathcal{N}\left(\frac{\bar{W}_{ab}}{N_b}, \frac{\sigma_{ab}^2}{N_b}\right)$$

Local interaction field.

$$\eta_i(V,t) = \sum_{b=1}^{P} \sum_{j=1}^{N_b} W_{ij} S_b(V_j(t))$$

Th. (Faugeras, Touboul, Cessac, 2008)

Dynamic mean-field equations.

$$\sum_{l=0}^{k} a_a^{(l)} \frac{d^l V_a}{dt^l}(t) = \sum_{b=1}^{P} U_{ab}(t) + I_a(t) + B_a(t)$$

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Th. (Faugeras, Touboul, Cessac, 2008)

- Existence and uniqueness of solutions in finite time.
- Existence and uniqueness of stationary solutions in a specific region of the macroscopic parameters space.

Dynamic mean-field equations.

$$\sum_{l=0}^{k} a_a^{(l)} \frac{d^l V_a}{dt^l}(t) = \sum_{b=1}^{P} U_{ab}(t) + I_a(t) + B_a(t)$$

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Th. (Faugeras, Touboul, Cessac, 2008)

- Existence and uniqueness of solutions in finite time.
- Existence and uniqueness of stationary solutions in a specific region of the macroscopic parameters space.
- Constructive proof => Simulation algorithm.

Tâche n° 2.
(deuxième année)

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1) Etudier numériquement puis mathématiquement les régimes dynamiques exhibés par ces équations “non naïves”, dans le cas Jansen-Ritt .

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1) Etudier numériquement puis mathématiquement les régimes dynamiques exhibés par ces équations “non naïves”, dans le cas Jansen-Ritt .

2) Qu'apportent ces équations aux neurosciences ? (imagerie, phénoménologie).

Analyse statistique de trains de potentiels d'action.

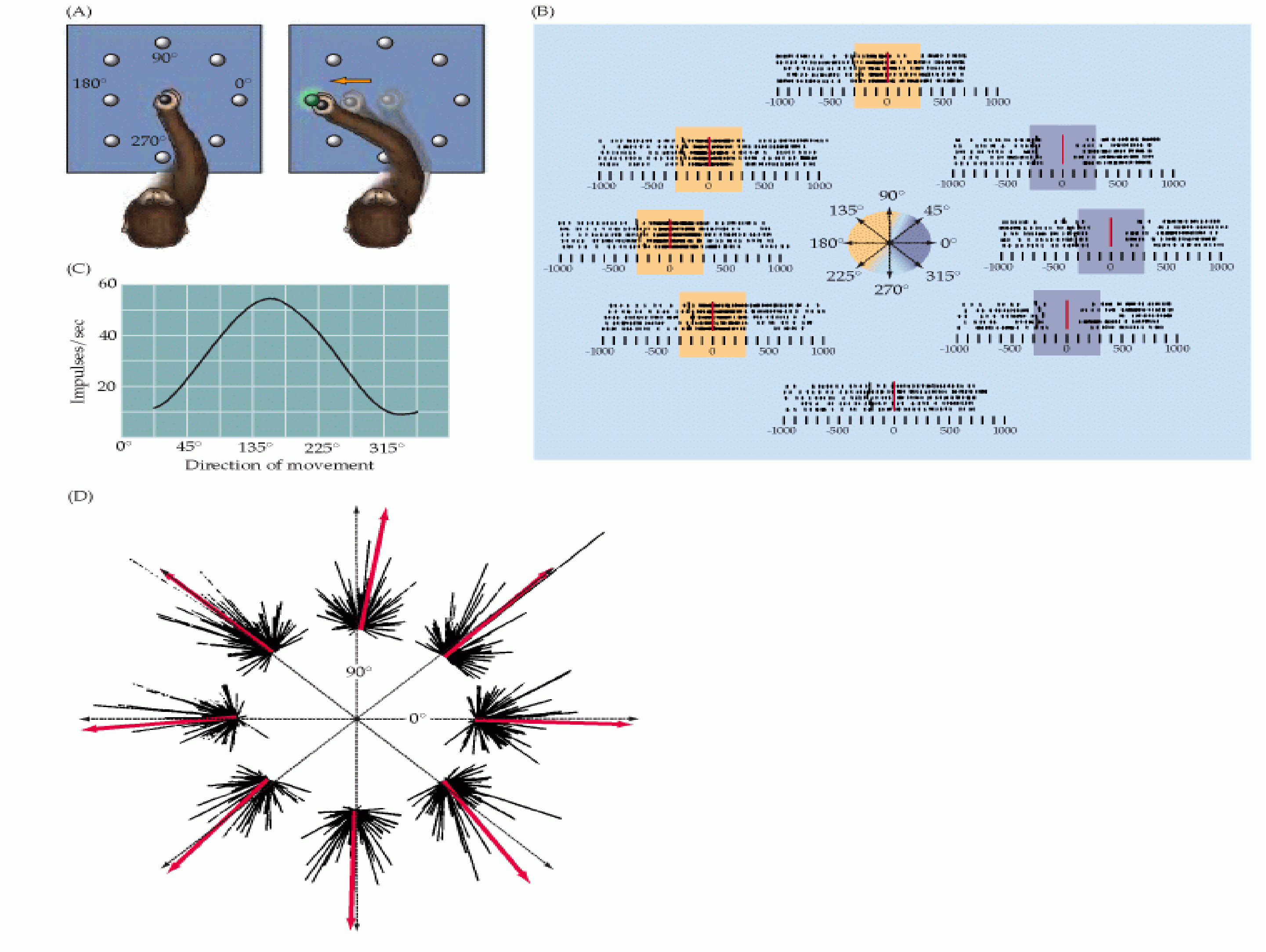
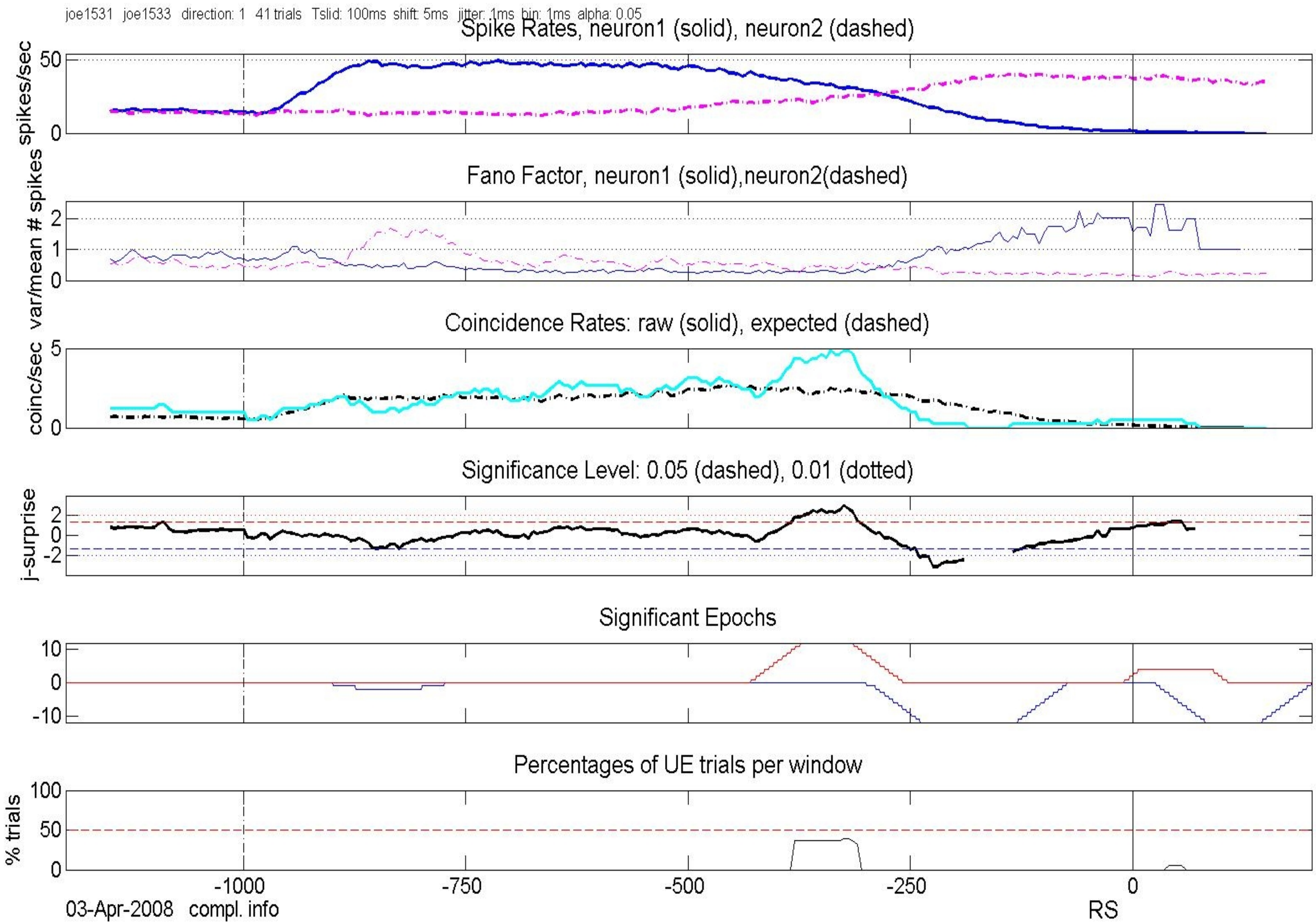
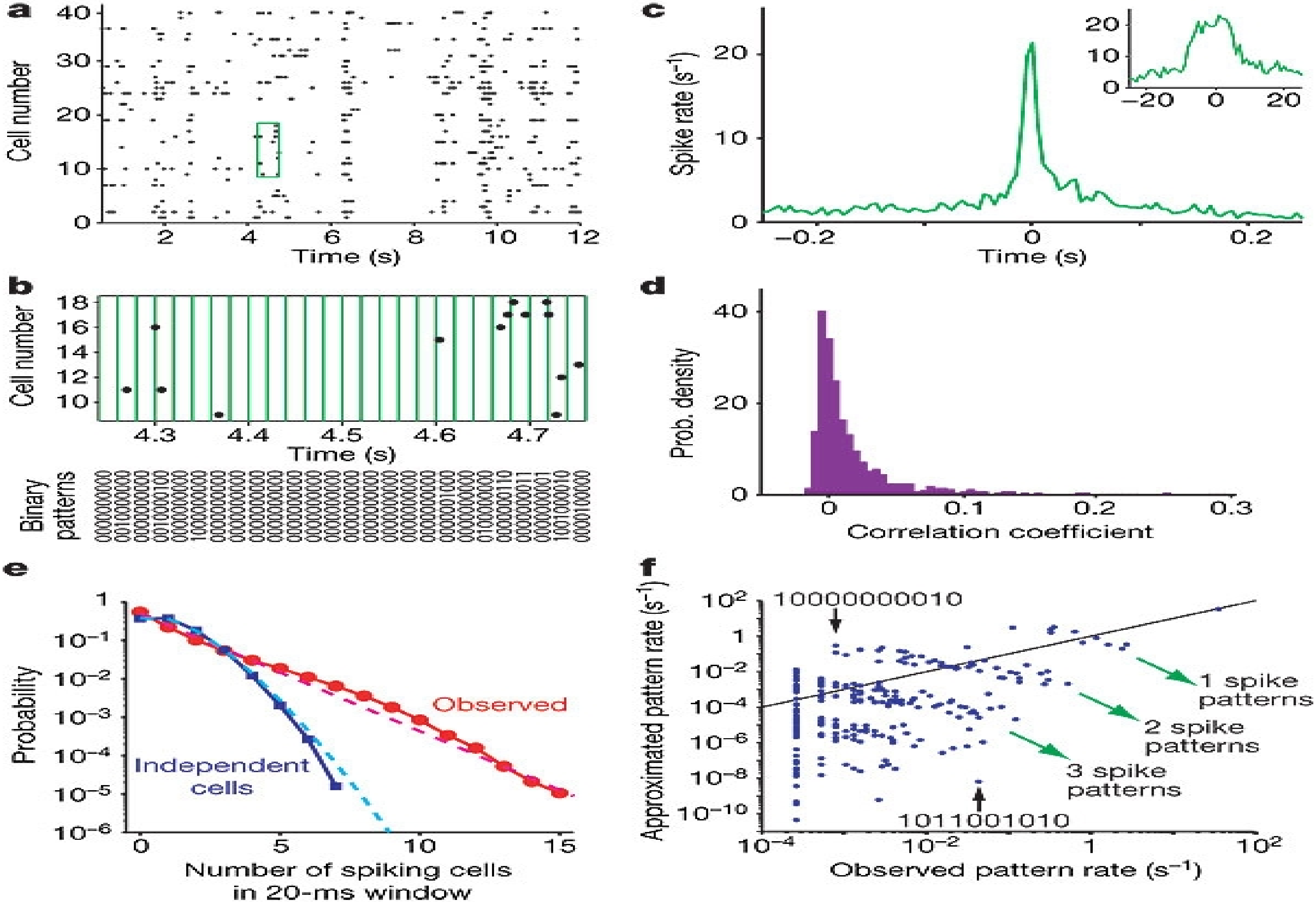


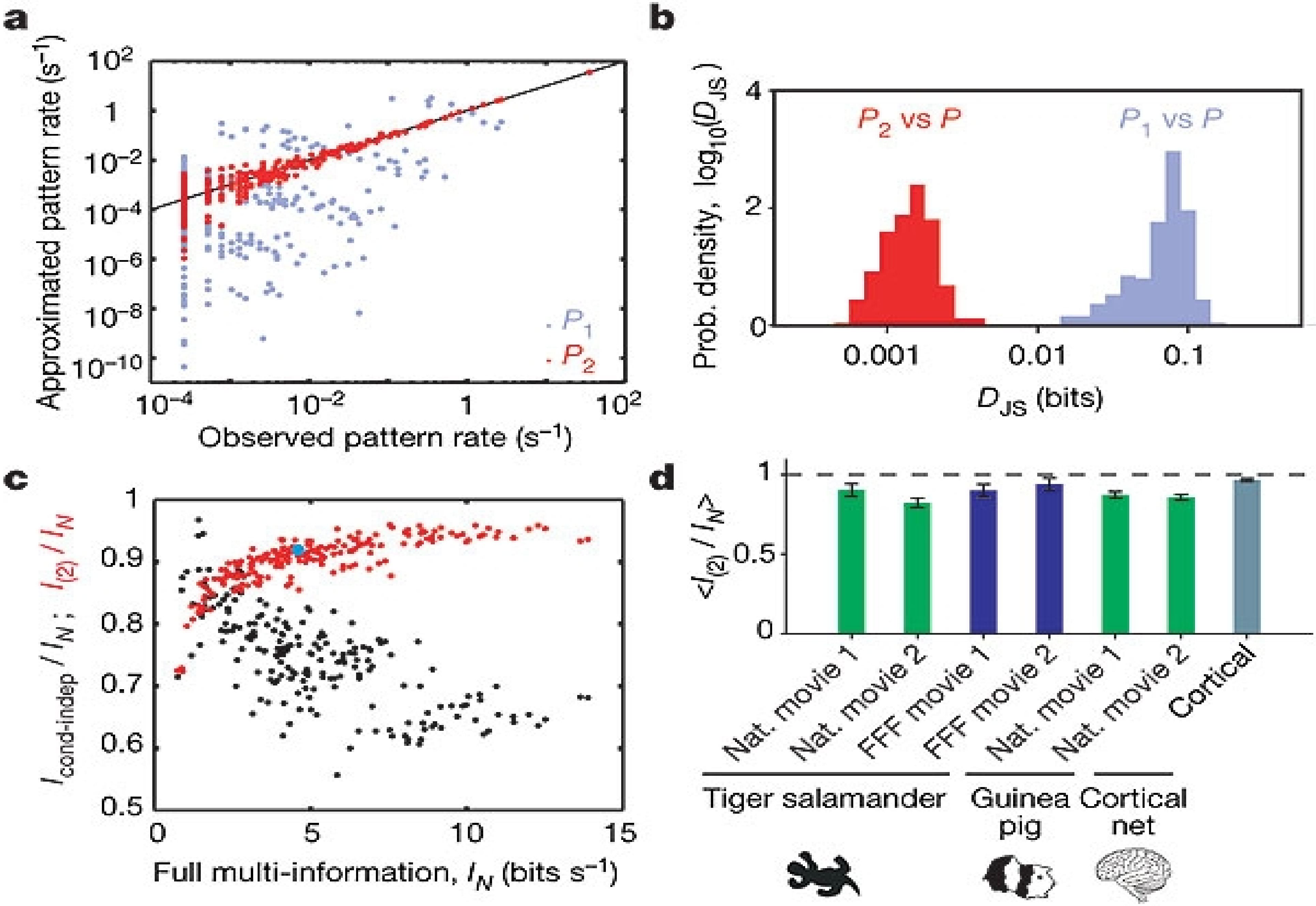
Figure 17.12. Directional tuning of an upper motor neuron in the primary motor cortex. (A) A monkey is trained to move a joystick in the direction indicated by a light. (B) The activity of a single neuron was recorded during arm movements in each of eight different directions (zero indicates the time of movement onset, and each short vertical line in this raster plot represents an action potential). The activity of the neuron increased before movements between 90 and 225 degrees (yellow zone), but decreased in anticipation of movements between 0 and 315 degrees (purple zone). (C) Plot showing that the neuron's discharge rate was greatest before movements in a particular direction, which defines the neuron's “preferred direction.” (D) The black lines indicate the discharge rate of individual upper motor neurons prior to each direction of movement. By combining the responses of all the neurons, a “population vector” can be derived that represents the movement direction encoded by the simultaneous activity of the entire population. (After Georgeopoulos et al., 1986.)

F. Grammont and A. Riehle, “Precise spike synchronization in monkey motor cortex involved in preparation for movement”, Exp Brain Res, 128, 1999.





E. Schneidman, M. J. Berry II, R. Segev, W. Bialek, Nature 440, 1007-1012



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Tâche n° 1.
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- Etudier la statistique de trains de spikes dans des ***modèles*** “suffisamment” réalistes.

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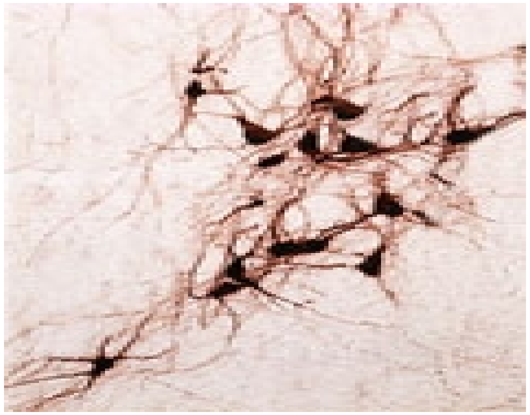
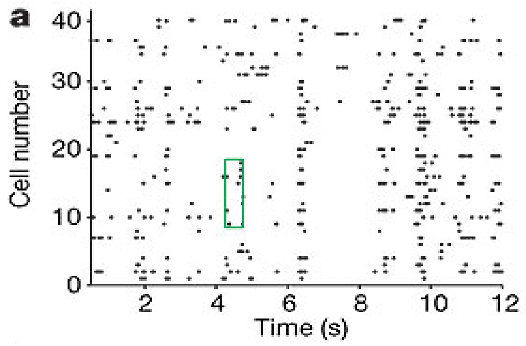
- Etudier la statistique de trains de spikes dans des ***modèles*** “suffisamment” réalistes.

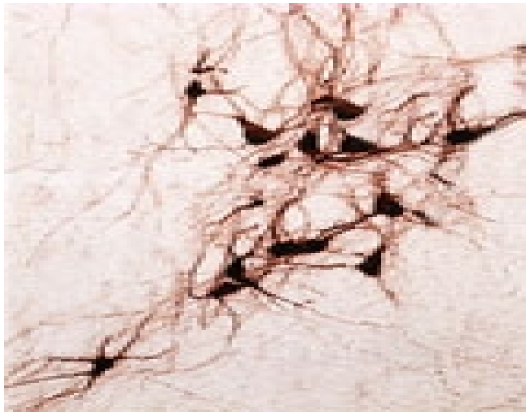
- En quoi les distributions de Gibbs sont-elles pertinentes dans le cadre de ces modèles?



- Multiples scales.
- Non linear and collective dynamics.
- Adaptation.
- Interwoven evolution.

Neural network activity.





- Spontaneous activity;
- Response to external stimuli ;
- Response to excitations from other neurons...

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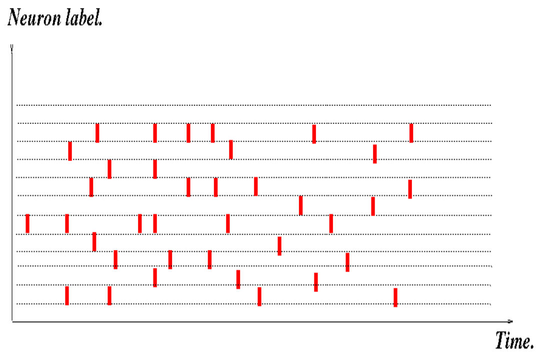

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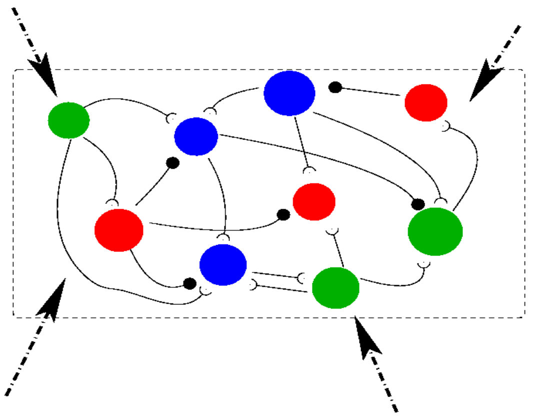

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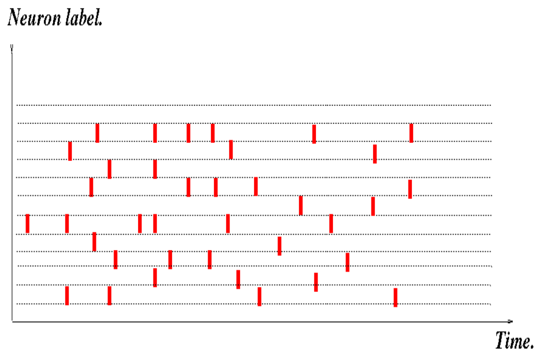

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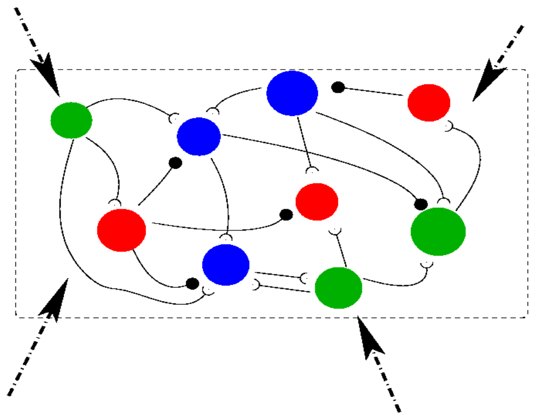
Spike generation.

$\omega_i(t)=1$ if i fires at t

$=0$ otherwise.

A raster plot is a sequence

$\tilde{\omega} = \{\omega_i(t)\}$, i=1...N, t=1...



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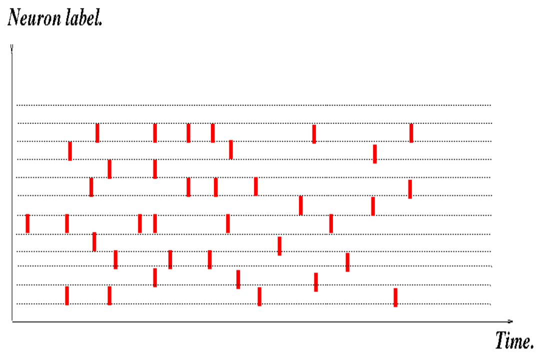

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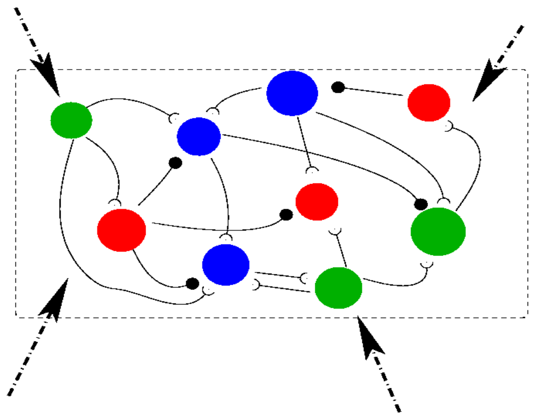

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neural response to some stimulus ?

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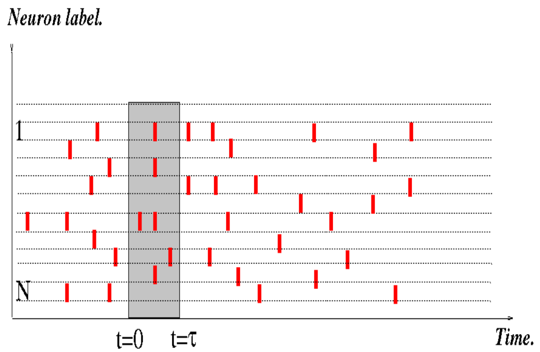

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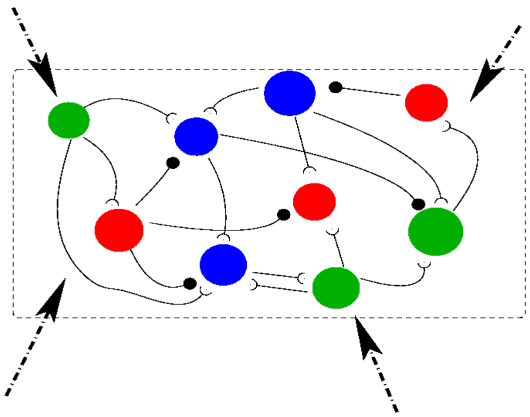

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neural response to some stimulus ?

- Definite succession of spikes during a definite time period.

$$R = [\omega(1) \dots \omega(\tau)]$$
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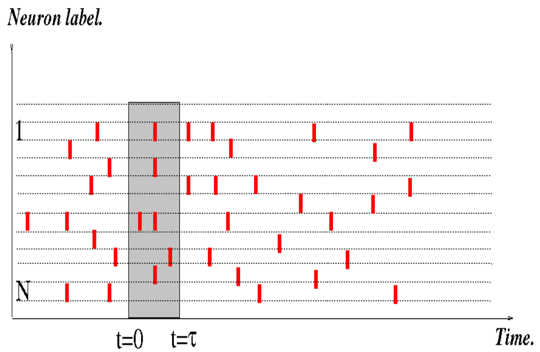
Neural network activity.



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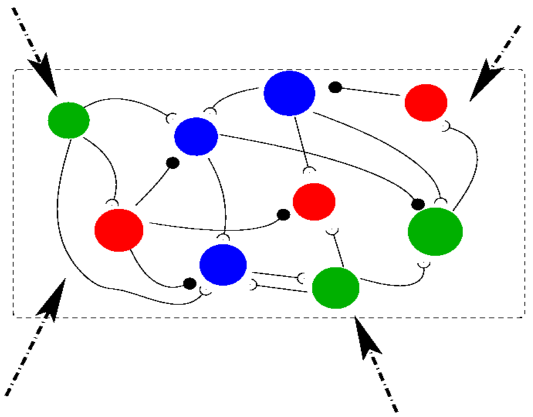

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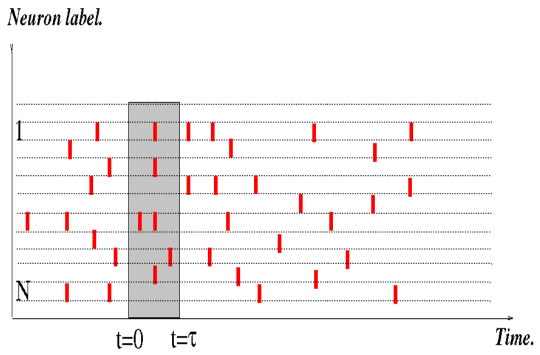
- Statistical coding.

Neural network activity.



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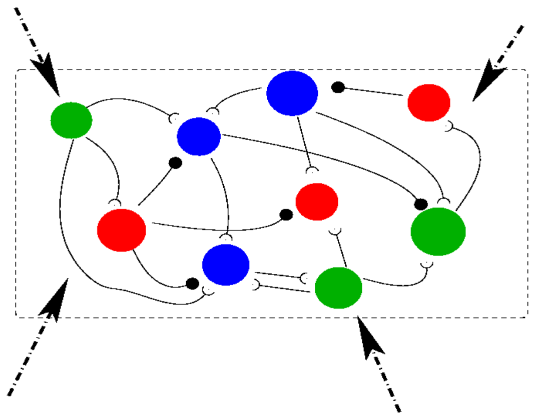

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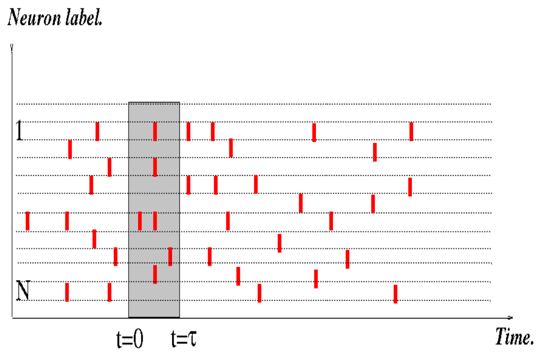
- Definite succession of spikes during a definite time period.

$$R = [\omega(1) \dots \omega(\tau)]$$
$$\omega(t) = [\omega_i(t)]_{i=1}^{N}$$

- Statistical coding.

$$P\left[R \middle| S\right]$$

Neural network activity.



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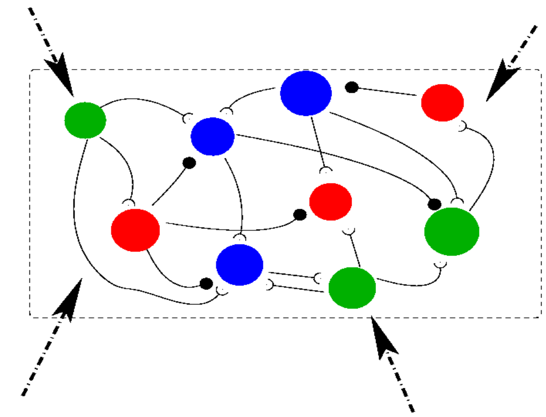

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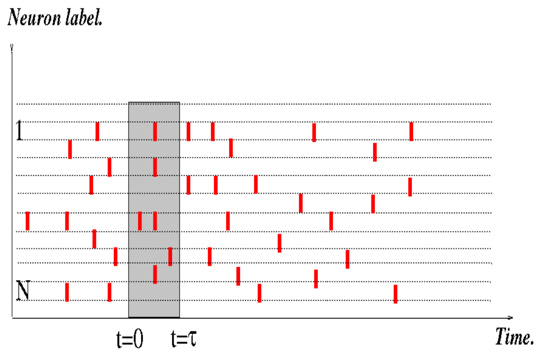

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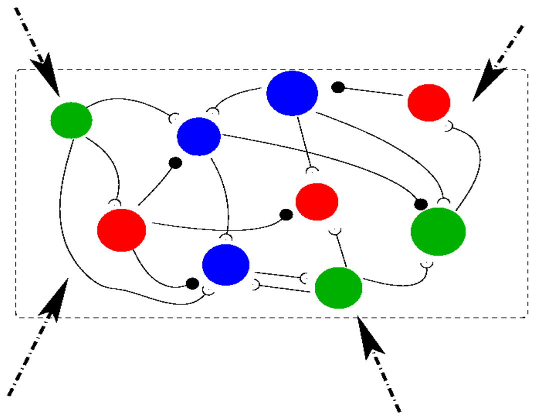

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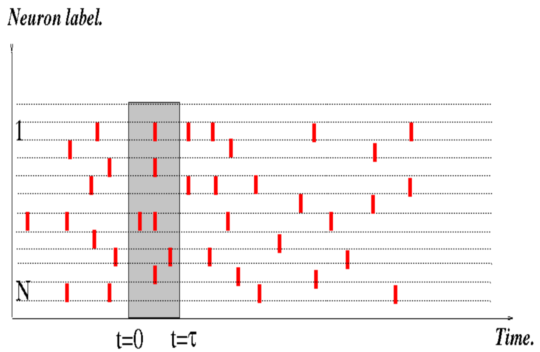

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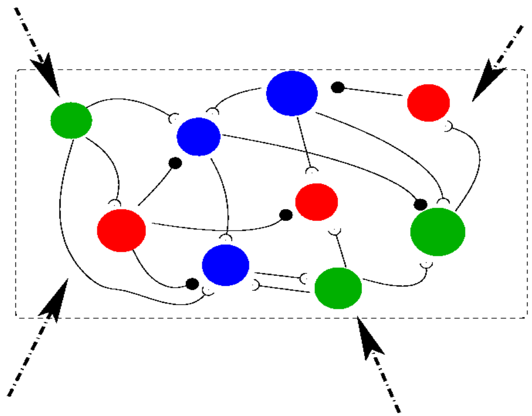

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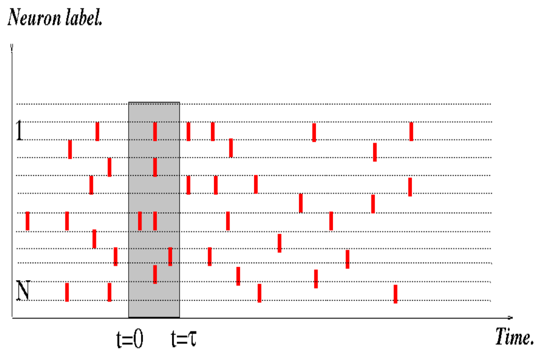

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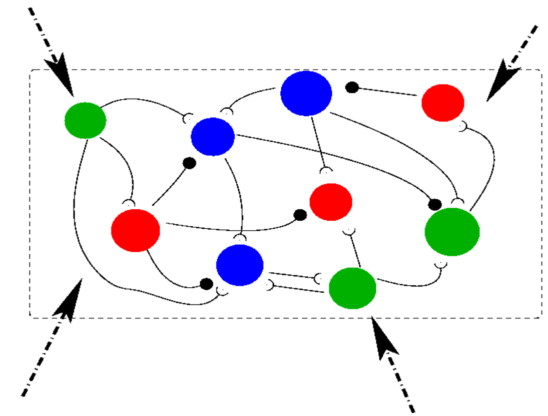

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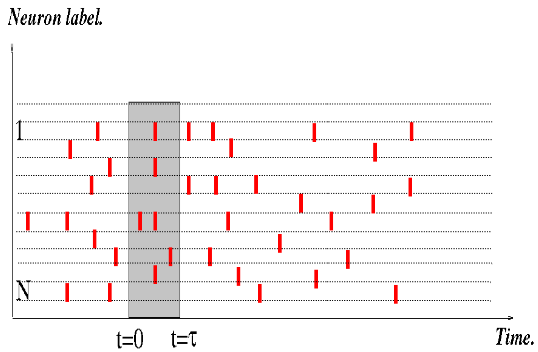

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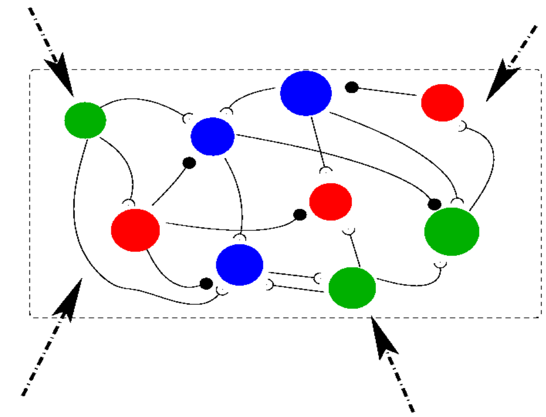

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Sample averaging.

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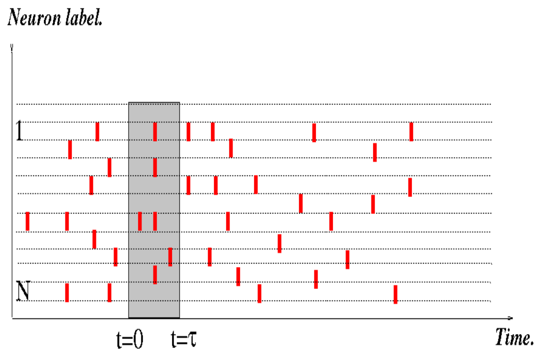

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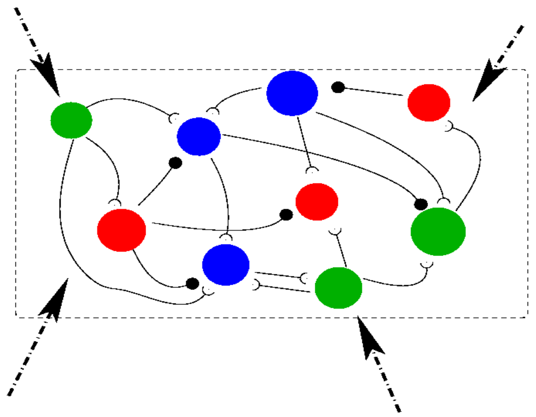

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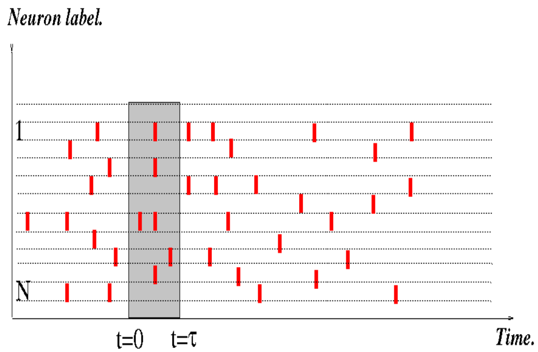

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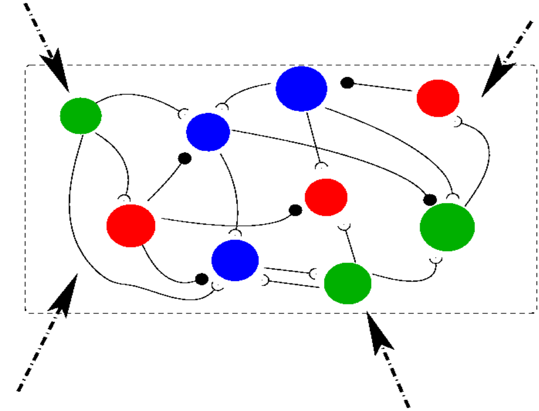

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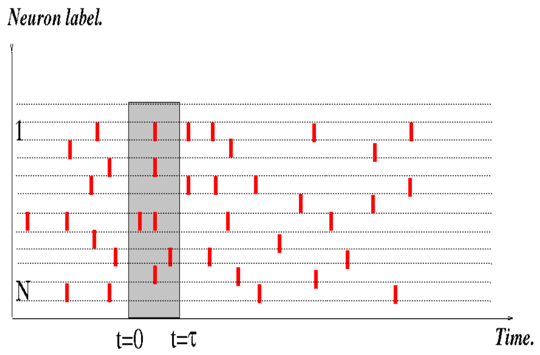

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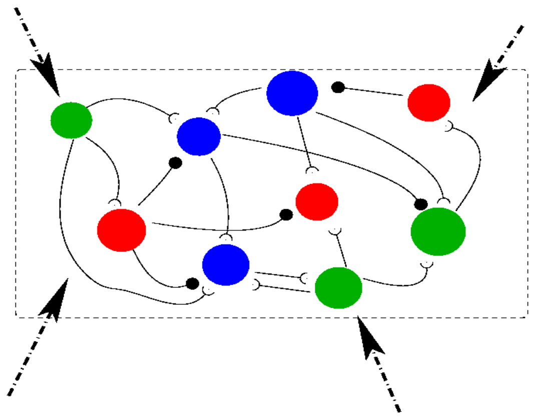

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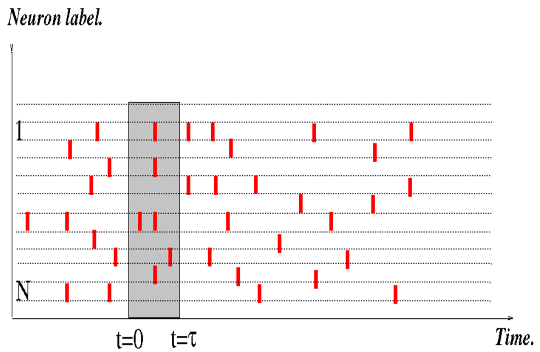

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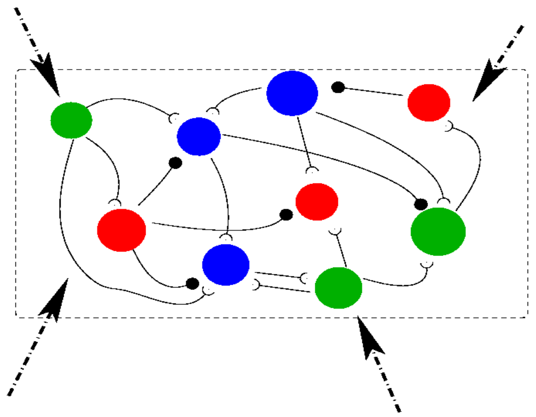

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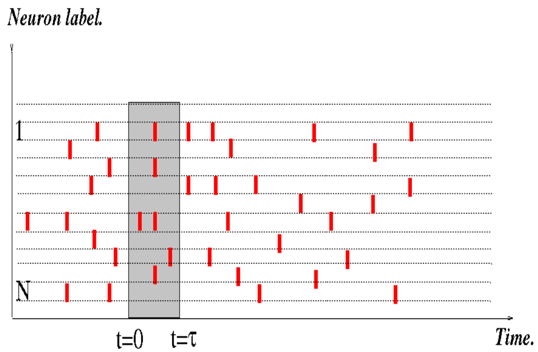

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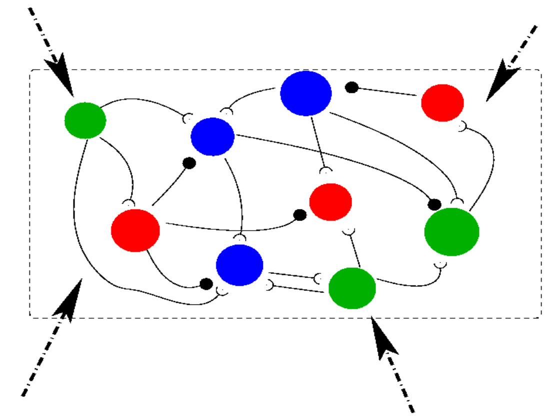
I-F models are (maybe) good enough.

Approximating real raster plots from orbits of IF models with suitable parameters.

R. Jolivet, T. J. Lewis, W. Gerstner (2004)J. Neurophysiology 92: 959-976



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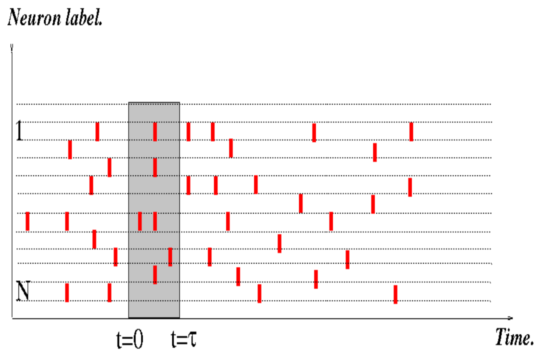

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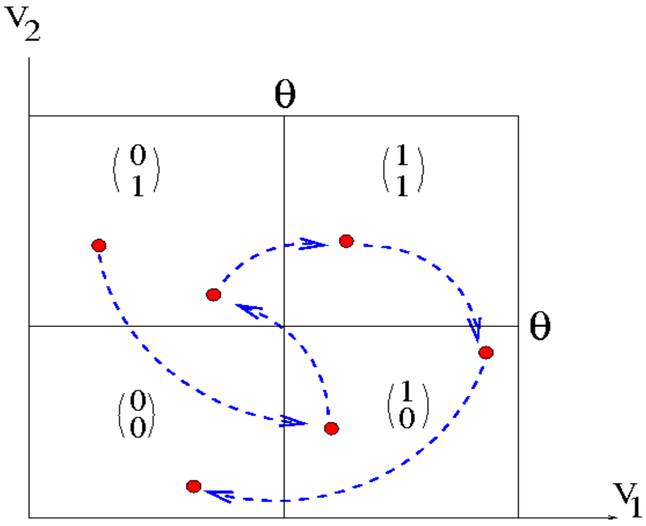

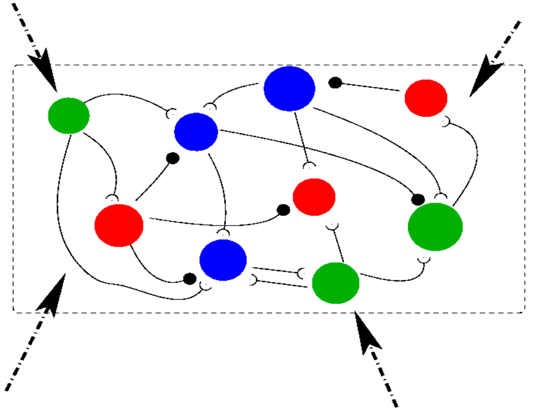

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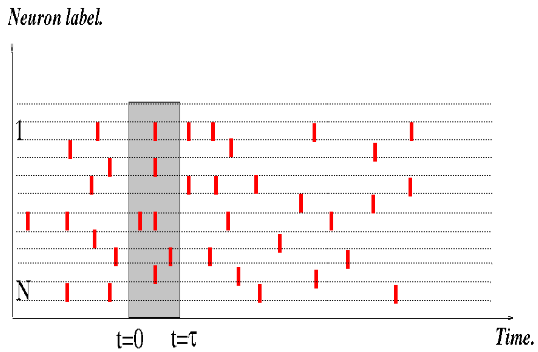

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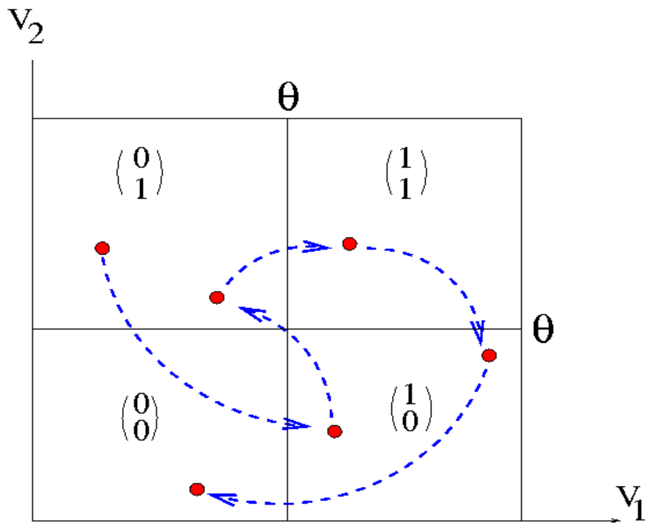
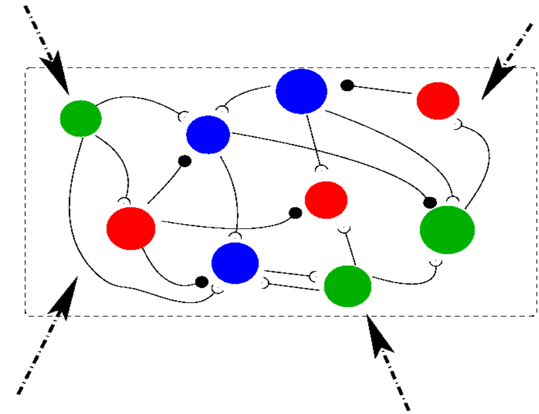


Raster plot. $\begin{pmatrix} 0\ 1\ 0\ 1\ 1\ 0 \ldots. \\ 1\ 0\ 1\ 1\ 0\ 0 \ldots. \end{pmatrix}$



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Conductances depend on past spikes over a finite time.

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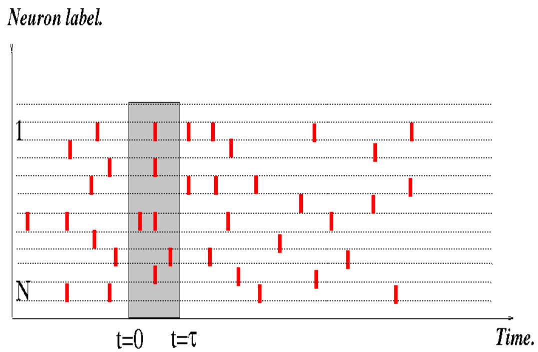

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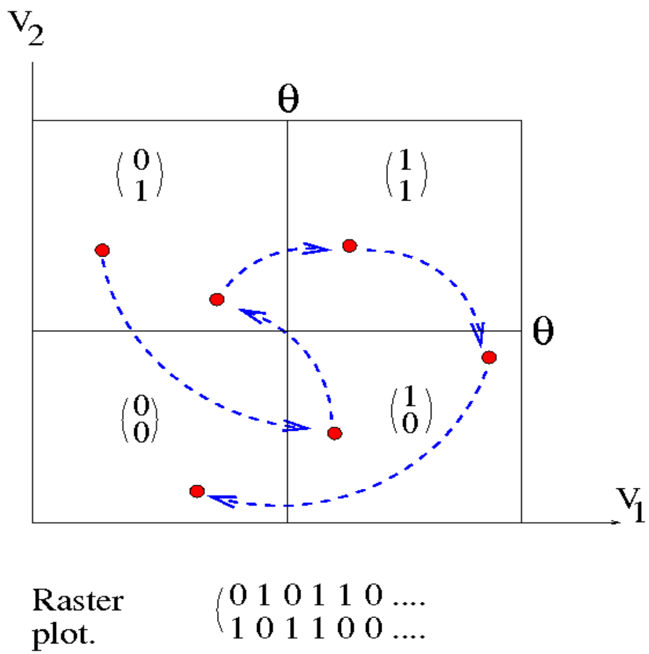

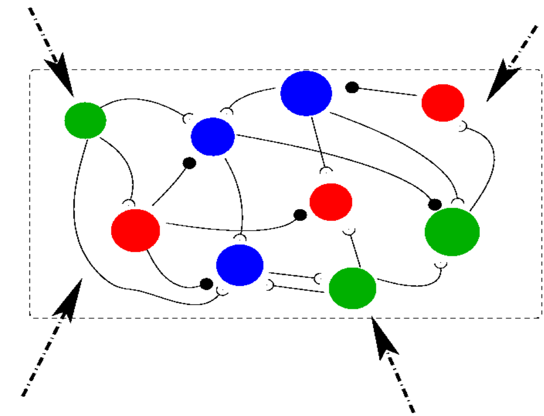

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Generic dynamics. **B. Cessac, T. Viéville, Front. Comput. Neurosci. 2:2 (2008).**

- There is a ***weak form of initial condition sensitivity***.
- Attractors are generically ***stable period orbits***.
- The number of stable periodic orbit ***diverges exponentially*** with the number of neurons.
- Depending on parameters (synaptic weights, input current), periods ***can be quite large*** (well beyond ***any accessible computational time***).

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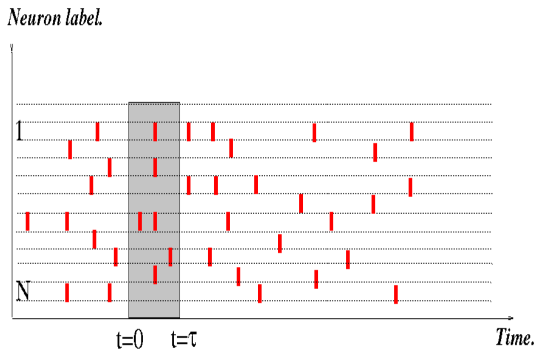

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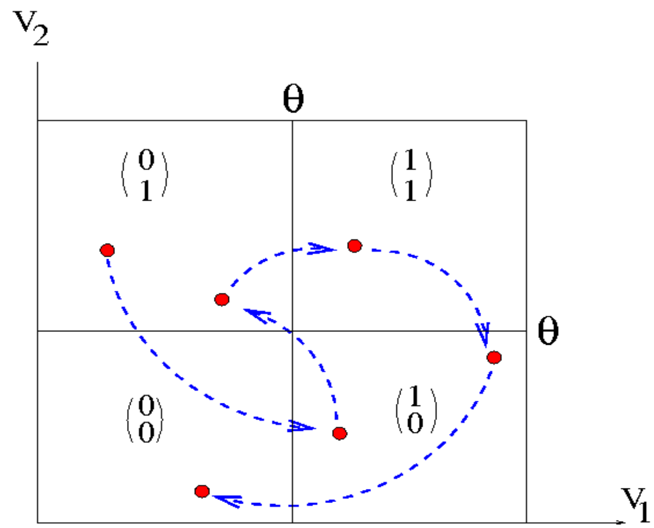

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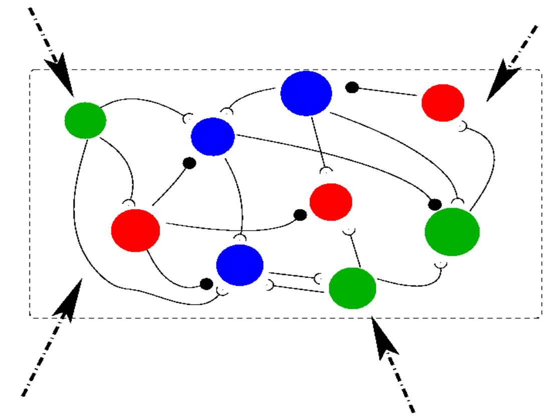

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Spikes trains provide a **symbolic coding**.

To a given "input" one can associate a **finite number** of **periodic orbits** (depending on the initial condition).

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Statistical model

Statistical model

Fix ϕ_α, $\alpha = 1 \ldots K$, a set of *observables* (prescribed quantities whose *time average* C_α has been *measured*).

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Examples

Firing rate of neuron i :

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$$\phi(\tilde{\omega}) = \omega_i(0)$$

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Prob[j fires at some time t and i fires at t+τ]

Statistical model

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An *ergodic* probability measure ν on the set of *admissible* raster plots is called a *statistical model* if, for all α:

$$\nu\left\{\tilde{\omega} \;\middle|\; |\pi_{\tilde{\omega}}^{(T)}(\phi_\alpha) - C_\alpha| \geq \epsilon\right\} \sim e^{-TI(\alpha,\epsilon)}$$

$$I(\alpha, y) = \sup_u \{uy - F(\alpha, u)\}$$

$$F(\alpha, u) = \lim_{T \to \infty} \frac{1}{T} \log \nu\left[e^{u\pi_{\tilde{\omega}}^{(T)}(\phi_\alpha)}\right]$$

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E. Schneidman, M.J. Berry, R. Segev, W. Bialek, Nature,440, (2006)

The knowledge of prescribed observables average fixes the statistical model.

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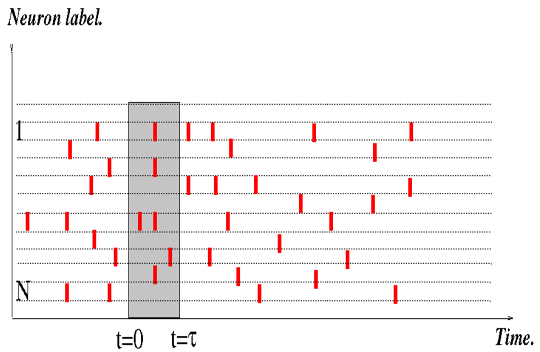
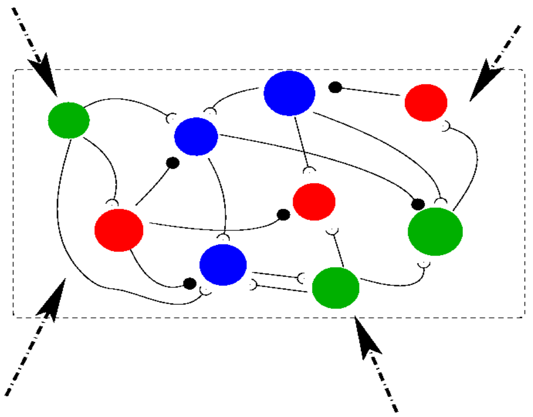
Which observables ?

Neural network activity.



- Spontaneous activity;
- Response to external stimuli ;
- Response to excitations from other neurons...



- Multiples scales.
- Non linear and collective dynamics.
- Adaptation.
- Interwoven evolution.

Synaptic weight evolution.

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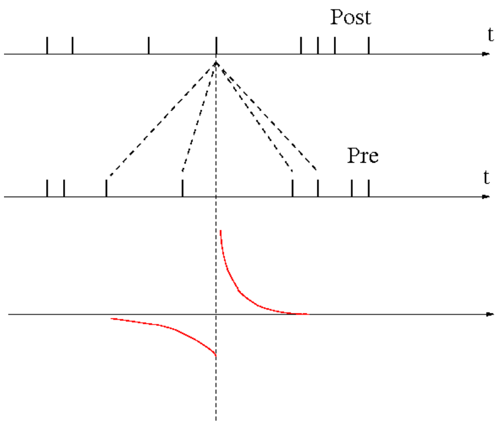

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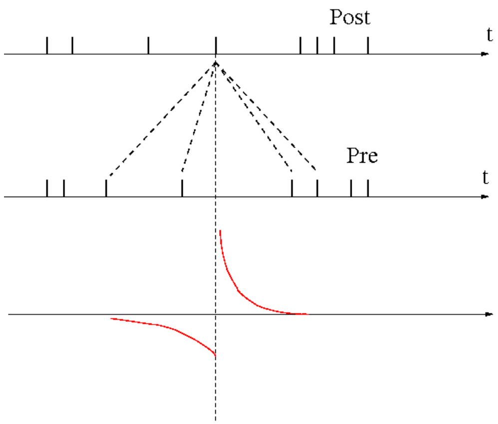

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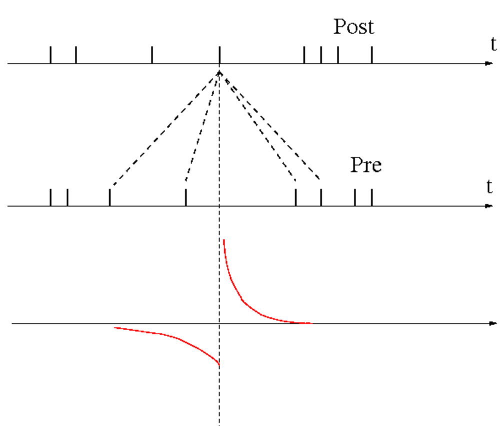

Dynamics and statistics evolution

Changing synaptic weights

changing membrane potential dynamics

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- **Check on numerical examples ?**

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Tâche n° 2.
(deuxième année)

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