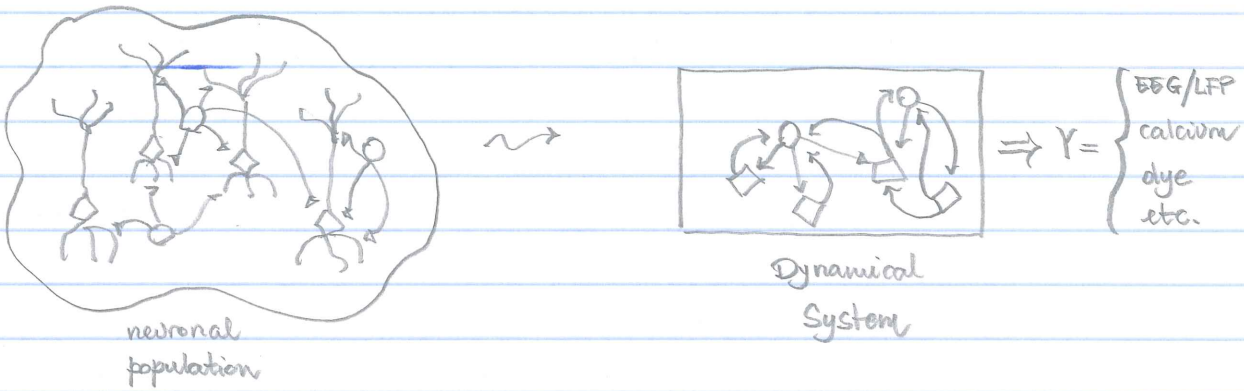
LECTURE 6

* Mean Field Models and Cortical Dynamics

Let us consider a population of neurons with synapses and projections
⇒ It can be represented as a whole system made by a network of nodes (neurons) and edges (synapses and projections):



In the representation of the neural population, there are a few issues:

- Complexity: The number of neurons is typically too big to be handled. The network topology is only partly known. The exchange between neurons is organized through multiple (redundant) connections.

- Nonlinearity: While in a network of linear systems, coupled linearly, the macroscopic behavior is accounted for by the sum of the output of individual systems, in a nonlinear network the whole behavior is NOT the sum of the individual systems' behaviors

⇓

The output measurements Y collected at the macroscopic level have no easy link to the measurements that may be collected at the level of single neurons

- Redundancy and Locality: The particular organization of the neuronal

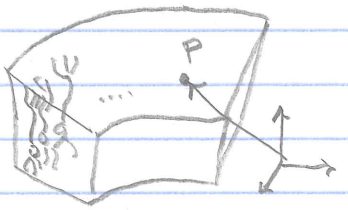
networks is such that the estimation of synaptic gains and links is theoretically impossible (i.e., over parameterization)

Based on these issues, we aim to build models that are TOPOLOGICALLY EQUIVALENT to the global behavior captured by measurements Y WITHOUT explicitly modeling the individual neurons

⇓

One way to obtain this is by using the mean-field theory:

1)



Volume of cortical tissue

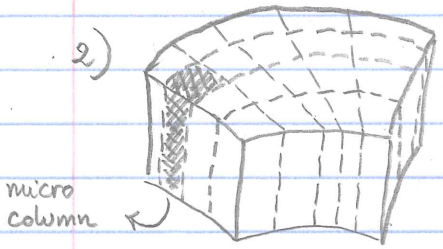
Given the high number of neurons and synapses even in small tissue samples, let us approximate the volume as a continuum of activity:

$Y(t,P) \triangleq$ measure of activity at position P and time t

⇓

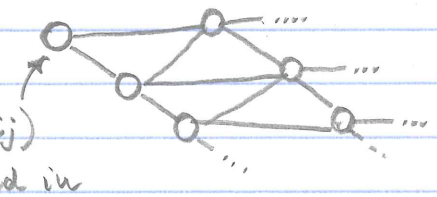
$Y(t,P)$ is now a FIELD and, for each position P, $Y(\cdot)$ must reflect the mean activity (e.g., firing rate) of an ensemble of uniformly distributed neurons around P

2)



continuum field

Partition the continuum into micro-columns and average $Y(t,\cdot)$ across all the points in a column ⇒ We have a coarse-grained 2D or 3D network



(a)

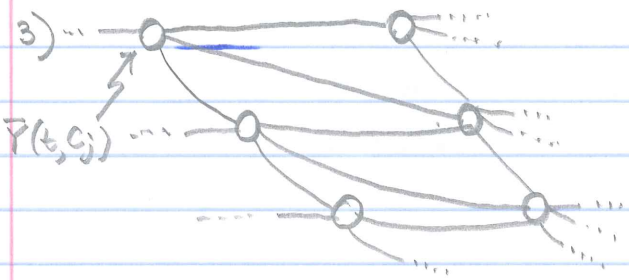
$\bar{Y}(t, C_j)$ mean field in micro-column C_j

Note: In the passage from the continuum to the network (a), one must decide how to set the edges in the network ⇒ A locality principle is

usually followed and each micro-column is mainly connected to proximal (i.e., neighbor) micro-columns

⇓

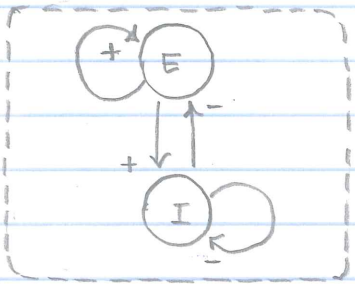
This modeling premises are reasonable if the model focuses on large cortical areas (e.g., primary sensory) but may not be valid for subcortical areas (e.g., thalamus)



The resultant coarse-grained structure is a lattice network and generative models must be defined for:

- $\bar{Y}(t, C_j)$ → How is it generated?
- $C_j \leftrightarrow C_k$ → How the activity of one column affects another column?

One approach to these two questions is provided by Wilson and Cowan (1972; 1973) under the following assumptions:



Individual Node

- All nervous processes depend on the interaction of excitatory and inhibitory neurons

- Every node includes both excitatory and inhibitory neurons with all the potential connections

- It does not matter how many excitatory or inhibitory neurons are in the node, but what proportion of them vary from an inactive state to an active state ⇒ Note: this assumption depends on the fact that, at rest, some neurons will be active (statistical assumption)

Let us define:

$E(t) \triangleq$ fraction of excitatory neurons that get activated at time t beyond the average value ($\Rightarrow$ In this way, $E<0$ means "depressions")

$I(t) \triangleq$ fraction of inhibitory neurons that get activated at time t beyond the average value

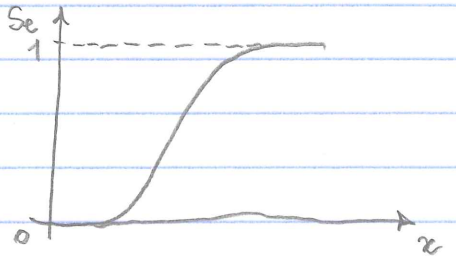
Everything is expressed in terms of variation from the resting state and normalized between -1 and $+1$ $\Rightarrow$ The model is NOT expected to fit physiol. variables (i.e., it is like the F-N model we saw before)

Let us use the fundamental relationship:

$E(t+\tau) =$ fraction of excitatory cells that are NOT in refractory $\times$ fraction of non-refractory excitatory cells that receive a supra-threshold stimulus

$$1 - \int_{t-r}^{t} E(u)\,du$$

$S_e(x)$ - to be chosen



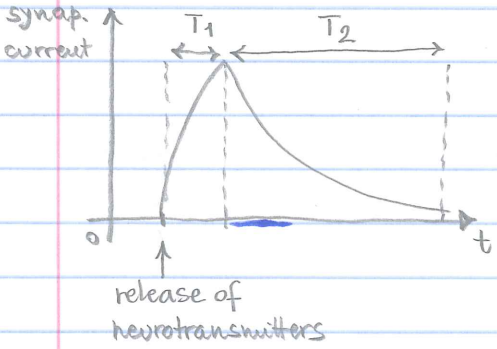
where $r \triangleq$ refractory period

$\tau \triangleq$ interval (arbitrary for now) between assessments of $E(\cdot)$

The sigmoidal shape reflects the important fact that neurons may differ for number and amount of synaptic currents but the higher these currents (on average across neurons) the larger the fraction of cells that will fire in response

- What is x? $\Rightarrow x = x(t)$ represents the amount of excitation (either due to synapses or external currents) received by the E cells

But synaptic currents are not instantaneous (the chemical processes of release of neurotransmitters in the cleft and post-synaptic opening of ion channels are longer than an action potential)



- $T_1 \ll T_2$
- T_2 can last several tens of ms
- The current is decaying exponentially

One way to model these aspects is:

$$x(t) = \int_{-\infty}^{t} \alpha(t-u)\left[\omega_1 E(u) - \omega_2 I(u) + P(u)\right] du$$

$\alpha(t-u) \triangleq e^{-a(t-u)}$ - decaying factor
$\omega_1 E(u) \triangleq$ excitatory currents due to synapses from E cells
$\omega_2 I(u) \triangleq$ inhibitory currents due to synapses from I cells
$P(u) \triangleq$ exogenous input (e.g., noise, DBS, etc.)

Note that we are preserving a linear template and we are keeping a door open for plasticity via ω_1 and ω_2

The resultant equations are quite complicated but can be easily modified to accommodate numerical integration:

$$E(t+\tau) = \left[1 - \int_{t-r}^{t} E(u)\,du\right] S_e\left(\int_{-\infty}^{t} \alpha(t-u)\left[\omega_1 E(u) - \omega_2 I(u) + P(u)\right] du\right)$$

(**) Let us define: $\overline{E}(t) \triangleq \frac{1}{r}\int_{t-r}^{t} E(u)\,du$ - moving average with window r
$\Rightarrow$ It averages out fast variations of E that takes less than r ms

Similarly, note the following:

$$\int_{-\infty}^{t} \alpha(t-u)\, E(u)\, du = \int_{-\infty}^{t-r} + \int_{t-r}^{t} \cong k_1 \bar{E}(t)$$

if $\alpha(t-u) \cong 0$ for $u < t-r$
$\alpha(t-u) \cong \bar{\alpha}$ for $t-r \le u \le t$

with k_1 appropriate constant to be determined

Finally, by using the Taylor series expansion, we can write:

$$E(t+\tau) \cong E(t) + \frac{dE}{dt}(t)\,\tau$$

$$\Downarrow$$

$$(*) \quad \tau \frac{dE}{dt} = -E(t) + \left(1 - r\bar{E}(t)\right) S_e\left(k_1\left[\omega_1 \bar{E}(t) - \omega_2 \bar{I}(t) + \bar{P}(t)\right]\right)$$

where $\bar{I}(t)$ and $\bar{P}(t)$ are defined as in (**). The problem with (*), though, is that here we have both $E(t)$ and its moving average $\bar{E}(t)$
⇒ In case we are only interested to slow dynamics, we can apply the moving average to (*) and obtain:

$$(1) \quad \tau \frac{d\bar{E}}{dt} = -\bar{E}(t) + \left(1 - r\bar{E}(t)\right) S_e\left(k_1\left[\omega_1 \bar{E}(t) - \omega_2 \bar{I}(t) + \bar{P}(t)\right]\right)$$

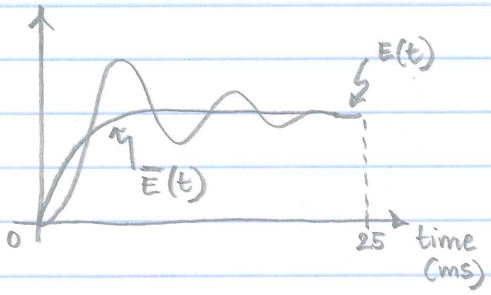
Analogously, we can follow the same steps for $I(t)$ and obtain:

$$(2) \quad \tau \frac{d\bar{I}}{dt} = -\bar{I}(t) + \left(1 - r\bar{I}(t)\right) S_i\left(k_2\left[\omega_3 \bar{E}(t) - \omega_4 \bar{I}(t) + \bar{Q}(t)\right]\right)$$

with: $S_i(x) \triangleq$ sigmoidal function to be chosen
$\bar{Q}(t) \triangleq$ moving average of exogenous input $Q(t)$ to I cells
$k_2 \triangleq$ parameter to be estimated

Equations (1)-(2) are the W-C mean field model

The main mathematical passage to get (1)-(2) is the moving average
⇒ It is appropriate if we focus on dynamics that are not excessively fast (e.g., EEG, dye staining, calcium imaging, fMRI, etc.)

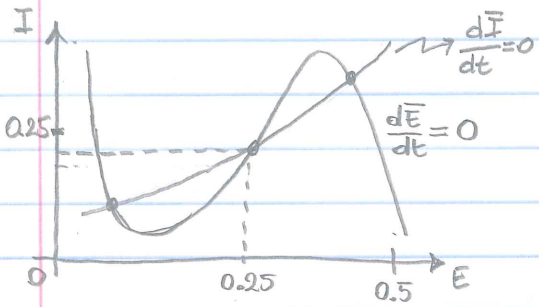


The main appeal of eq. (1)-(2) is that we can now use a phase portrait to study the dynamics of a single node (as we did for the F-N model) and determine whether oscillations are stable or not:

- For $\bar{P}(t)=0 \ \forall t$: $\frac{d\bar{E}}{dt}=0 \Leftrightarrow \frac{\bar{E}}{1-r\bar{E}} = S_e\left(k_1\left[\omega_1\bar{E}-\omega_2\bar{I}\right]\right)$

$$\Leftrightarrow \bar{I} = \frac{1}{\omega_2 k_1}\left[k_1\omega_1\bar{E} - S_e^{-1}\left(\frac{\bar{E}}{1-r\bar{E}}\right)\right]$$

- For $\bar{Q}(t)=0 \ \forall t$: $\frac{d\bar{I}}{dt}=0 \Leftrightarrow \bar{E} = \frac{1}{\omega_3 k_2}\left[k_2\omega_4\bar{I} + S_i^{-1}\left(\frac{\bar{I}}{1-r\bar{I}}\right)\right]$



Phase portrait for typical values of parameters ω_i, k_i estimated from cortical recordings

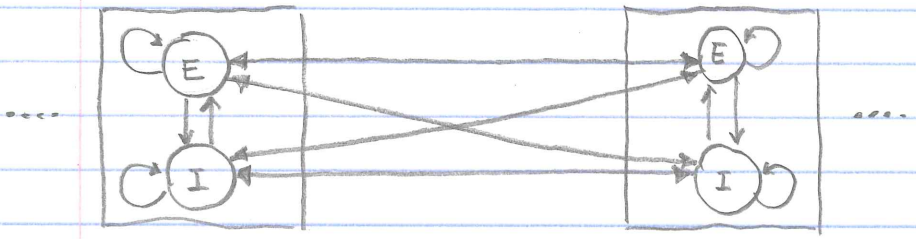
⇓

Three combinations $(\bar{E},\bar{I})$ correspond to equilibrium conditions

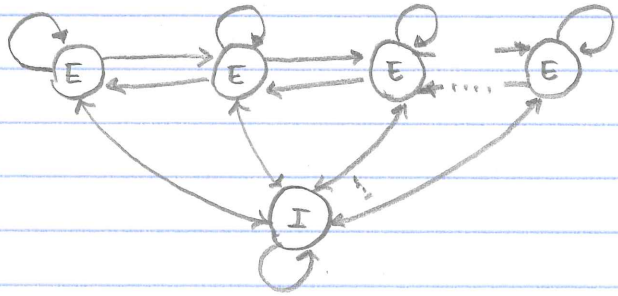
We can also determine the effects of constant currents P and Q on the node dynamics and under what conditions a limit cycle can emerge or be quenched ⇒ See Slides.

* How to interconnect nodes?

In order to move from the dynamics of a single node to the interaction among nodes, the following general template is followed:



or, if the disproportionality between E cells and I cells must be captured, the following hybrid template is considered:



For the first model, the equations become dependent on both time t and position x of the node:

$$(3)\quad \tau \frac{\partial \bar{E}(t,x)}{\partial t} = -\bar{E}(t,x) + \left(1 - r\bar{E}(t,x)\right) S_e\left(k_1\left[w_1 \sum_s \bar{E}(t,x-s) - w_2 \sum_s \bar{I}(t,x-s) + \bar{P}(t,x)\right]\right)$$

where the summation is for s spanning the neighbor nodes (left and right side of the node at position x). A similar model can be written for $\bar{I}(t,x)$:

$$(4)\quad \tau \frac{\partial \bar{I}(t,x)}{\partial t} = -\bar{I}(t,x) + \left(1 - r\bar{I}(t,x)\right) S_i\left(k_2\left[w_3 \sum_s \bar{E} - w_4 \sum_s \bar{I} + \bar{Q}(t,x)\right]\right)$$

The importance of model (3)-(4) is that, through a lattice structure (hence, spatially discrete) we are able to reproduce the migration of oscillations and other perturbations from one cortical area to one another

⇓

The keys for having travelling perturbations are:

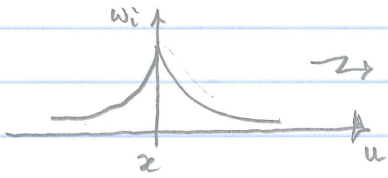
- The nodes must be insensitive to small perturbations when at rest (otherwise, they would constantly excited)

- The inhibitory connections must be longer range than the excitatory connections (otherwise, the perturbations would spread homogeneously)

↓

This condition can be satisfied by choosing: $w_i = b_i\, e^{-\frac{|x-u|}{\sigma_i}}$ $i=1,2,3,4$ in (3)-(4)

and imposing: $\omega_2, \omega_3 > \omega_1$



→ The synaptic gains are varied continuously along the x direction

- What about spirals and chaotic waves? ⇒ The W-C model (3)-(4) defines a general template that allows to replicate a large repertoire of macroscopic brain dynamics. However, when used in 2D lattice structures, it fails to reproduce complex wavefront shapes and patterns ⇒ See slides.

↙ The model needs anisotropy (i.e., a preferred direction of propagation of the waves)

↘ The model needs a more various array of behaviors for $\overline{E}(\cdot, x)$ and $\overline{I}(\cdot, x)$, i.e., we cannot simply rely on the interaction $\overline{E} \leftrightarrow \overline{I}$

An evolution of the W-C model that addresses these issues is:

$$(5)\quad \begin{cases} \dfrac{d\bar{E}}{dt}(t,x,y) = -\bar{E}(t,x,y) - a(t,x,y) + S_e(\dots) \\ \tau \dfrac{da}{dt}(t,x,y) = -a(t,x,y) + \beta_1 \bar{E}(t,x,y) \end{cases}$$

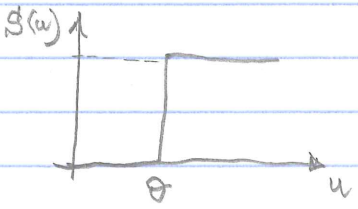
$$(6)\quad \begin{cases} \dfrac{d\bar{I}}{dt}(t,x,y) = -\bar{I}(t,x,y) - b(t,x,y) + S_i(\dots) \\ \tau \dfrac{db}{dt}(t,x,y) = -b(t,x,y) + \beta_2 \bar{I}(t,x,y) \end{cases}$$

The combination (5)-(6) introduces 2 auxiliary variables (a, b) to regulate the evolution of $\bar{E}$ and $\bar{I}$ ⇒ They have NO physiological meaning but allow to reduce the activity of E and I cells, respectively, in presence of weak inhibitory input (as it is the case in cortex)

Functions $S_i(\cdot)$ and $S_e(\cdot)$ are also modified from sigmoidal to non-monotonic to accommodate the anisotropy:

$$S_e(\dots) = k_1 \left[\sum_{s,h} w_1 S\left(\bar{E}(t, x-s, y-h) - \theta\right) - \sum_{s,h} w_2 S\left(\bar{I}(t, x-s, y-h) - \theta\right) \right]$$

where: $S(\cdot)$ is a sigmoidal or step function with threshold θ



s, h loops along the x- and y-direction, respectively

$$w_i = e^{-\gamma_i\left((x-s)^2 + (y-h)^2\right)} \quad i = 1,2 \quad \text{(for isotropic diffusion) or}$$

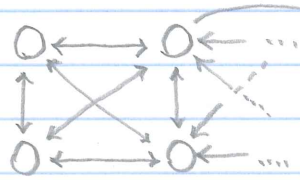
$$w_i = e^{-\gamma_i (x-s)^2} e^{-\delta_i (y-h)^2} \quad i = 1,2 \quad \text{(for anisotropic diffusion)}$$

Results are reported in the slides.

□

* Mean Field Models and Control

Let us now consider a lattice structure with one node for each probe we can acquire measurements from:



Each node is given by the W-C model (5)-(6) and each ODE can be discretized in time according to:

$$\frac{d\bar{E}}{dt}(t,x,y) \cong \left[\bar{E}(t+\Delta t, x, y) - \bar{E}(t,x,y)\right] / \Delta t$$

$$\Rightarrow \text{If we call: } \left.\begin{array}{l} t_k \triangleq t \\ t_{k+1} \triangleq t + \Delta t \end{array}\right\} \Rightarrow \bar{E}(t_{k+1}, x, y) = \bar{E}(t_k, x, y) + \Delta t\,(\ldots.)$$

($\ldots.$ ↑ from (5))

And similarly:

$$\bar{I}(t_{k+1}, x, y) = \bar{I}(t_k, x, y) + \Delta t\,(\ldots.)$$

($\ldots.$ ↓ from (6))

If we list the variables $\bar{E}, \bar{I}, a, b$ estimated at the same time t_k across the lattice structure in one vector:

$$X_k \triangleq \left[\bar{E}(t_k, x_1, y_1)\ \bar{I}(t_k, x_1, y_1) \ldots \bar{E}(t_k, x_2, y_1) \ldots \bar{E}(t_k, x_n, y_m) \ldots\right]^T$$

where n and m is the number of columns and rows in the structure, we have:

- X_k is a $(4 \cdot n \cdot m) \times 1$ vector
- $X_{k+1} = X_k + \Delta t \underbrace{[\ldots.]}_{\text{right side of (5)-(6)}} \Rightarrow X_{k+1} = F(X_k)$

} i.e., we can represent (5)-(6) as a state-space model

Also note that, given the nature of $\bar{E}$ and $\bar{I}$ at any point (x,y), it is expected that the measure $Y(t_k, x, y)$ given by the probe is related

to the net activation at that position, i.e.:

$$Y(t_k, x, y) = \bar{E}(t_k, x, y) + \varepsilon_k \quad \text{or}$$

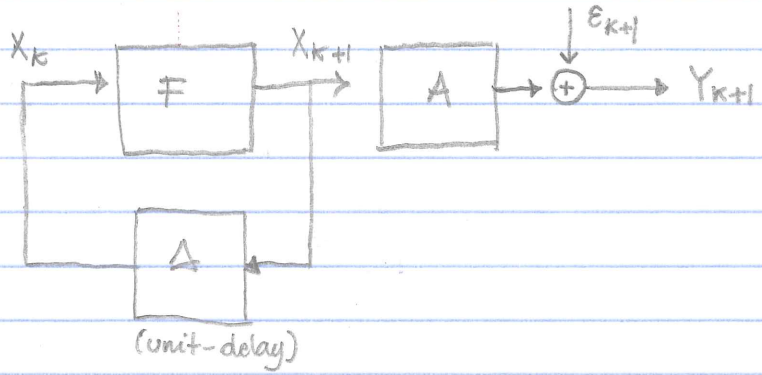
$$Y(t_k, x, y) = \bar{E}(t_k, x, y) - \bar{I}(t_k, x, y) + \varepsilon_k$$

where ε_k is white noise $\Rightarrow$ We can gather the measurements into one vector:

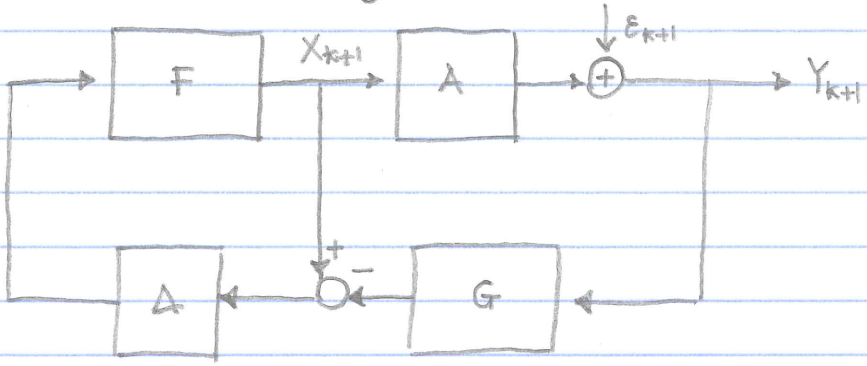
$$Y_k \triangleq \left[Y(t_k, x_1, y_1) \quad Y(t_k, x_2, y_1) \cdots Y(t_k, x_n, y_m) \right]^T \quad \text{and}$$

$$Y_k = A X_k + \varepsilon_k$$

with A being a $(4 \cdot n \cdot m) \times (n \cdot m)$ matrix $\Rightarrow$ Graphically:



With this setup, one may use Y_k to steer the dynamics of F:

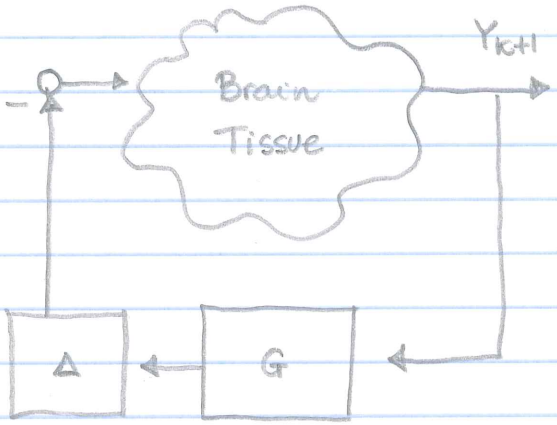


(ΔV)

$G \triangleq$ controller to be chosen

Note :

(F, A, X_K) - is just a model $\Rightarrow$ Scheme $(\Delta\nabla)$ implies that we will apply $-GY_K$ directly to the brain tissue and we use the model to design G and predict the most likely effect of stimulation



See slides.

□