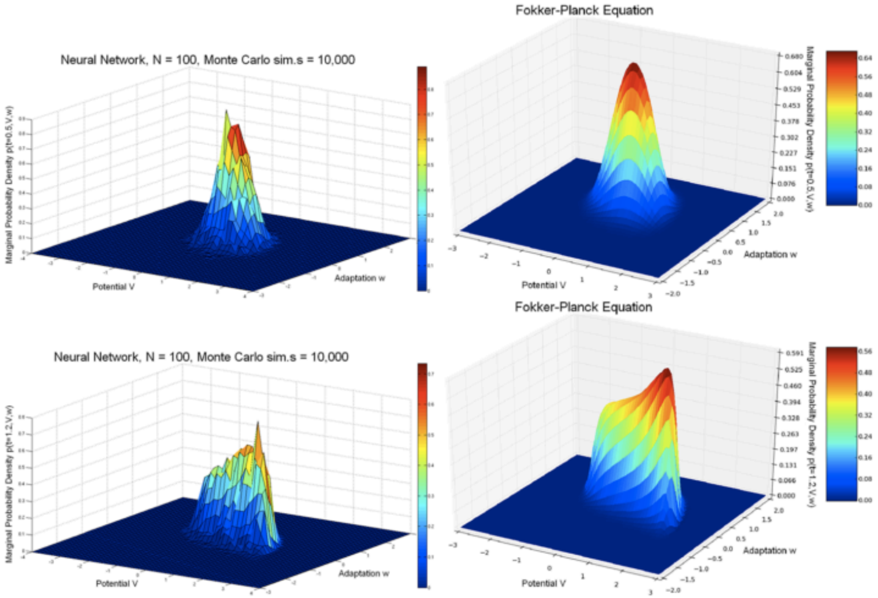
MULTISCALE MODELING



NEURONAL ANALYSIS AND MODELING

WINTER SEMESTER 2013

ING. ERNESTO GONZALEZ TREJO, M. SC.

Systems Neuroscience &
Neurotechnology Unit
Neurocenter, Saarland University Hospital

UNIVERSITÄT
DES
SAARLANDES

Hochschule für
Technik und Wirtschaft
des Saarlandes
HTW

INDEX

THEORETICAL BACKGROUND

- Physiological background of APs, synapses, neurons
- Non- linear dynamics in modeling
- Integrate and Fire model.
- Hodgkin & Huxley model
- H&H-Based models (FitzHugh-Nagumo, Izhikevich).
- Kuramoto model of synchronization (oscillators)
- H&H Simulator.
- Dif. Between single neurons – neuronal masses – neuronal fields.

DESCRIPTION OF NEURONAL DYNAMICS

- **Why modeling?** Phenomena not directly observable. Generate data, study emergent behaviors, or observation models (inverted giving empirical data)

-**Action Potential (AP):** Units of information transmission <u>at inter-neuronal level.</u>

- Information encoded through firing rate / temporal coding.

- Neuronal networks: embedded stochastic processes = difficult to analyze and solve mathematically. Populations are analyzed as “tending to infinity”.

- Dimensional reduction is desired in every case. For example: Reduction of a population to a function, a “**probability distribution**” describing its activity at a given time.

-Probability distribution > reduced to a single variable describing the evolution of the system (its dynamics):

“MEAN FIELDS” - “FIRING RATE (FR)”

MEAN-FIELD MODELS

- Spatiotemporal spike patterns from AP (input). Temporal evolution given by the single-cell model, e.g (sub-treshold):

$$\tau \frac{dV_i(t)}{dt} = -[V_i(t) - V_L] + RI_i(t), \qquad (1)$$

- Each neuron i described through Vi (t) . Total synaptic input from other neurons is Ii (synaptic current flow) and can be described for N neurons as the contribution of their spikes δ:

$$RI_i(t) = \tau \sum_{j=1}^{N} J_{ij} \sum_{k} \delta\left(t - t_j^{(k)}\right), \qquad (2)$$

If we integrate (1), given (2)…

Systems Neuroscience & Neurotechnology Unit
Neurocenter, Saarland University Hospital

UNIVERSITÄT DES SAARLANDES

Hochschule für Technik und Wirtschaft des Saarlandes

HTW

MEAN-FIELD MODELS

$$\begin{aligned} V_i(t) &= V_L + \sum_{j=1}^{N} J_{ij} \int_0^t e^{-s/\tau} \sum_k \delta\left(t - s - t_j^{(k)}\right) ds, \\ &= V_L + \sum_{j=1}^{N} J_{ij} e^{-\left(t - t_j^{(k)}\right)/\tau} \sum_k H\left(t - t_j^{(k)}\right), \end{aligned} \qquad (3,4)$$

Non-linear: stochastic spike generation, defined by sub-threshold dynamics.

Moreover:

- IF each neuron is explicitly modeled in such fashion (1-4) and
- We are talking of neuronal networks on the order of 10^16…

Processing costs too high and impractical (but possible..)

MEAN-FIELD MODELS

Alternative: Population (ensemble) density approach, using Fokker-Planck:

- Create a phase space for each neuron; attributes of the neuron (V, I, t) are the dimensions of the space e.g. $v = \{V, I, T\} \in \Re^3$ called a point or particle in the phase space; then the space is 3D and the density is given by $p(v,t)$, , a scalar function. It evolves to a steady state.

$$\dot{p} = -\nabla \cdot (f - D\nabla)p \equiv \frac{\partial p}{\partial t} = tr\left(-\frac{\partial (fp)}{\partial v} + \frac{\partial}{\partial v}\left(D\frac{\partial p}{\partial v} \right) \right). \quad (5)$$

(Fokker-Planck equation)

MEAN-FIELD MODELS

$$\dot{p} = -\nabla\cdot(f - D\nabla)p \equiv \frac{\partial p}{\partial t} = tr\left(-\frac{\partial(fp)}{\partial v} + \frac{\partial}{\partial v}\left(D\frac{\partial p}{\partial v}\right)\right).$$

Dynamics (phase flow, f(v,t)) and random fluctuations (dispersion, D(v,t)) describe the model at neuronal level, and is considered a stochastic differential equation.

Resuming: the Fokker-Planck equation summarizes the flow and dispersion of the states over the given phase space, as a natural summary of population dynamics.

But which dynamics are being used to describe the population?

MEAN-FIELD MODELS

- Individual IF neurons are grouped into populations of statistically similar neurons, based on **V(t).**
- The probability density function expresses the distribution of neuronal states (membrane potential) over the population. But neurons with the same V(t) at a given t are different due to fluctuations in I(t) (stochastic element).
- Population density approach assumes: I(t)s in neurons are uncorrelated, so neurons with same V(t) are uncorrelated.
- For its evolution in time, if currents are uncorrelated, they share the same statistics. So we can replace discharge rate of individual cells with a common time-dependent population activity (ensemble average). = NO SINGLE NEURONS

(good news!)

MEAN-FIELD MODELS

- We can talk now of the change of the membrane potential in time, for all neurons as:

$$dV(t) = \langle J \rangle_J N Q(t) dt - \frac{V(t) - V_L}{\tau} dt, \qquad (6)$$

N = # of neurons; Q(t) = mean firing rate;

$$Q(t) = \lim_{dt \to 0} \frac{n_{spikes}(t, t+dt)}{N dt}.$$

<J>j = average of synaptic weights.

The so-called "mean-field approximation"

Systems Neuroscience & Neurotechnology Unit
Neurocenter, Saarland University Hospital

UNIVERSITÄT DES SAARLANDES

Hochschule für Technik und Wirtschaft des Saarlandes

HTW

MEAN-FIELD MODELS

Synaptic weights / connectivity kernels (examples)

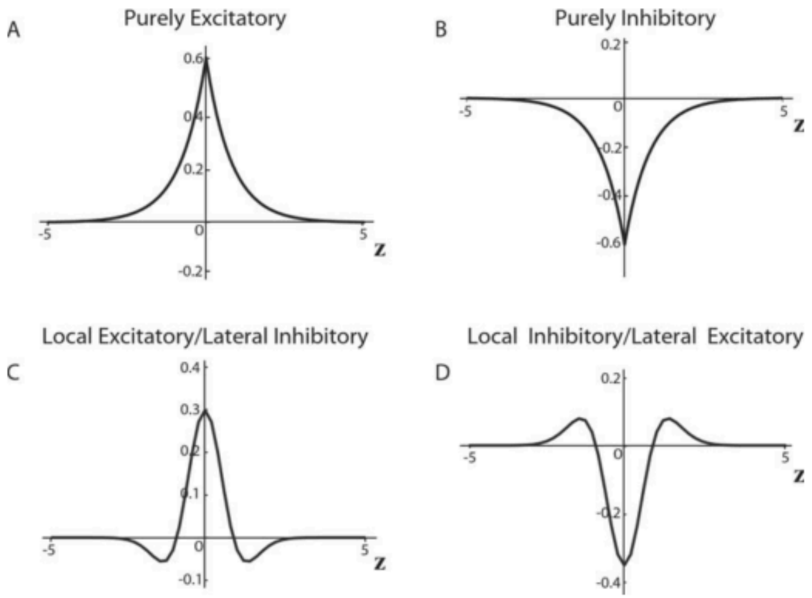


Figure 2. Typical homogeneous connectivity kernels, $W_{hom}(z)$, used for local architectures plotted as a function of spatial distance z. Purely excitatory connectivity is plotted in (A); purely inhibitory in (B); center-on, surround-off in (C); and center-off, surround-on in (D). The connectivity kernel in (C) is the most widely used in computational neuroscience.
doi:10.1371/journal.pcbi.1000092.g002

Systems Neuroscience & Neurotechnology Unit
Neurocenter, Saarland University Hospital

UNIVERSITÄT DES SAARLANDES

Hochschule für Technik und Wirtschaft des Saarlandes

MEAN-FIELD MODELS

Until now:

- Simulation of a network of neurons allows the study of firing rates;
- The Fokker-Planck equation describes the dynamical behavior and evolution of the network, including the original neurons.

But can we simplify it even more?

- If the population has many states (features) the equations needed will increase.
- We can reduce the number of states (i.e. the dimension of the phase space), for example 1D PDEs in terms of refractory density.

MEAN-FIELD MODELS

NEURAL MASS MODELS

- Special case of ensemble density models, which describe the ensemble density with a scalar.
- Description in terms of expected values for the neural states under the assumption that the equilibrium density has a point mass (a δ).
- This means: We replace the density with a mass at a particular point and we describe the dynamics based on the location of that mass.

MEAN-FIELD MODELS

NEURAL MASS MODELS

- We lose resolution compared to a full Focker-Planck equation; different phase functions could couple to each other, e.g. average depolarization in one ensemble could be affected by the dispersion or variance of another.
- Only coupling the expectations (mean) between such ensembles.

MEAN-FIELD MODELS

NEURAL MASS MODELS

Example: depolarization = convolution of the input signal (firing rate) with an impulse response kernel

$$\mu_v(t) = \int W(t-t')\varsigma[\mu_v(t)]dt', \qquad (7)$$

$$W(t) = \gamma^2 t \exp(-\gamma t).$$

Summary: Neural mass models ignore all but the mean of the ensemble density.

But what happens if we consider the states being a function of the position of our ensemble in the cortex?

…NEURAL FIELD MODELS

NEURAL FIELD MODELS

- Until now the models have covered point processes (useful for EEG sources, neurons or neuronal networks).
- E.g., depolarisation of the ensemble not as a point process but as a continuum or field (funcion of time AND space).
- Modeled through wave equations dealing with lateral interactions.

$$\begin{aligned} \mu_v(x,t) &= \int W(x-x',t-t')\varsigma[\mu_v(x',t')]dx'dt', \\ W(x-x',t-t') &= \delta\left(t-t'-\frac{|x-x'|}{c}\right)\frac{\exp\left(\frac{-|x-x'|}{\gamma}\right)}{2\gamma}, \end{aligned} \tag{8}$$

- spatiotemporal convolution; in generic form as:

NEURAL FIELD MODELS

$$\dot{\mu} = f(\mu) + \alpha \int_{\Gamma} W(|x - x'|)\varsigma[\mu(x', T_c)]dx' + h, \tag{9}$$

Where:

- $\mu = \mu(x,t)$ = neural field (neural mass activity at x,t).
- $f(\mu)$ = local dynamics of neural field
- $T_c = t - |x - x'| / c$ = delay due to signal propagation
- h = threshold value
- Γ = spatial domain
- $W(|x - x'|)$ = connectivity function

Systems Neuroscience & Neurotechnology Unit
Neurocenter, Saarland University Hospital

UNIVERSITÄT DES SAARLANDES

Hochschule für Technik und Wirtschaft des Saarlandes
HTW

NEURAL FIELD MODELS

If our firing rate is a Heaviside function we can simplify as:

$$\mu(x) = \int_0^a W(|x - x'|)dx', \quad \mu(0) = h = \mu(a), \tag{10}$$

the so-called “one bump solution”.

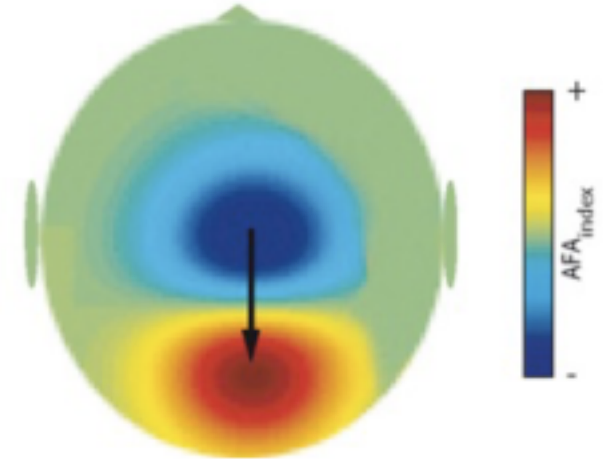
Features can be added to the model such as separate exc/inh neural populations, nonlinear neural responses, corticothalamic feedback among others.

Parameters significant for EEG generation (synaptic time constants, neurotransmitter release/uptake, speed of signal propagation along dendrites . . .) [balanced parameters!]

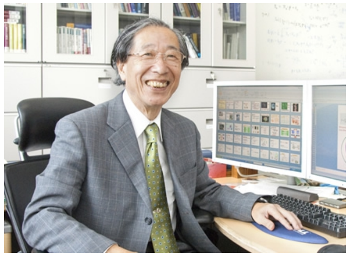
NEURAL FIELD MODELS

Recent development using neural field models:

- Predictions about brain electrical activity (EEG timeseries, spectra, coherence and correlations, ERPs, seizure dynamics, among others…)



AMARI MODEL



(1977) Neural tissue as neural field which form and propagate non-homogeneous excitation patterns in an homogeneous field. Their dynamics play a role in information processing.

Starting on a field equation, derived from statistical considerations. Study of pattern formation in 1D homogeneous fields of lateral inhibition. Defined independent neurons and split into small homogeneous random subnets.

Arranged a field with m type of neurons, in m layers.

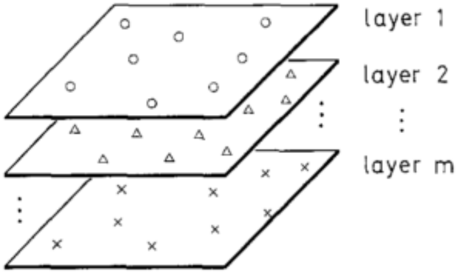


Fig. 1. Neural field

AMARI MODEL

Average activity (firing rate) of the neurons at x, at t:

$$Z_i(x,t)=f_i[u_i(x,t)]\,, \tag{11}$$

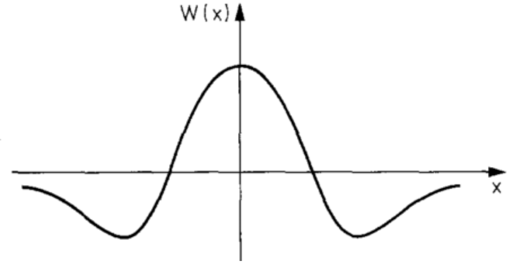
Starting from the field equation:

$$\tau_i \frac{\partial u_i(x,t)}{\partial t} = -u_i + \sum_{j=1}^{m} \int w_{ij}(x,x';t-t')\,Z_j(x',t')\,dx'\,dt' + h_i + s_i(x,t)\,, \tag{12}$$

Wij = intensity of connection between layers (i-j)
si = intensity of stimulus (avg stimulation level)

For no time lag, we can drop t completely.

AMARI MODEL



Specific cases:

- 1 D field
  Homogeneous
  Negligible lag
  One layer with both exc/inh neurons (lateral inhib f(dist) weight function)
  Output function: step function (fires or not at all, instead of sigmoid).

$$\tau \frac{\partial u(x,t)}{\partial t} = -u + \int w(x-y)\, f[u(y)]\, dy + h + s(x,t), \quad (13)$$

"Basic equation of simplified 1-layer Amari fields"

$$R[u]=\{x|u(x)>0\}$$

$$f(u)=\begin{cases}0, & u\leqq 0\\ 1, & u>1\,.\end{cases}$$

AMARI MODEL

Specific cases:

In the absence of input s(x,t)=0:

In equilibrium, $\partial u/\partial t=0$ and therefore

$$u(x)=\int_{-\infty}^{\infty} w(x-y)\,f[u(y)]\,dy+h\,. \qquad (14)$$

For a localized excitation, the excited region of the field $R[u]=(a_1,a_2)$

and therefore

$$u(x)=\int_{R[u]} w(x-y)\,dy+h\,. \qquad (15)$$

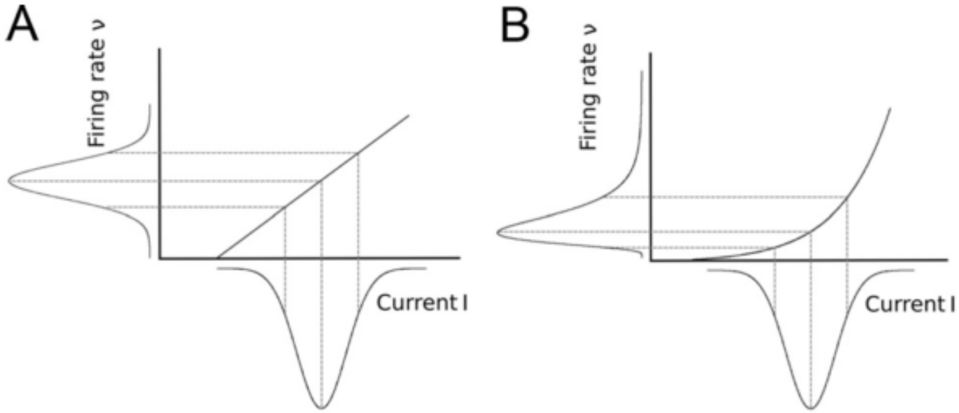
Systems Neuroscience & Neurotechnology Unit
Neurocenter, Saarland University Hospital

$$R[u] = \{x | u(x) > 0\}$$

FIRING RATE MODELS

Firing rate = highly non-linear. In vivo, in vitro, in silico (both conductance and IF models) due to noise. Only if a linear input is present, will the output be linear (e.g. currents being injected).

Assumed that interactions in populations are mediated by firing rates instead of spikes per-se



$$R[u] = \{x \mid u(x) > 0\}$$

FIRING RATE MODELS

If we observe one of the most common firing-rate functions (sigmoid):

$$f(g) = \frac{1}{1 + \exp(-\beta(g - h))},$$

It saturates to 1 for large values of g. Therefore, firing rate is a function of conductance of the presynaptic neuron (which is directly proportional to the drive in the postsynaptic neuron). If we express the conductance as:

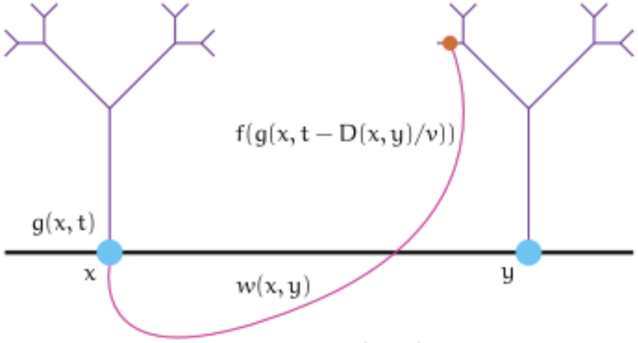
$$Qg = w_0 f(g),$$

And then we introduce a coupling function, integrate over a domain for a tissue level in 1D, we obtain:

$$R[u] = \{x | u(x) > 0\}$$

FIRING RATE MODELS

$$Qg = \int_{-\infty}^{\infty} w(x,y) f(g(y, t - D(x,y)/v)) \mathrm{d}y.$$



And for the special case when $v \to \infty,\ Q = (1 + \mathrm{d}/\mathrm{d}t),$

We can start to reconstruct the Amari model:

$$u(x) = \int_{-\infty}^{\infty} w(x-y) f[u(y)] dy + h.$$

$$R[u] = \{x \mid u(x) > 0\}$$

FIRING RATE MODELS

Amari, Wilson & Cowan, among others described the population-averaged firing-rate.

The mean field equations are not always easy to interpret and to relate to physical observable quantities.

Considering:

- P populations composed of N neurons (N tending to infinity, “mean field limit”).
- Each neuron described by its membrane potential and a d-dimensional variable Z dependent on the model employed to represent single neuron dynamics:

Systems Neuroscience & Neurotechnology Unit
Neurocenter, Saarland University Hospital

UNIVERSITÄT DES SAARLANDES

Hochschule für Technik und Wirtschaft des Saarlandes

$R[u] = \{x | u(x) > 0\}$

FIRING RATE MODELS

$$\left\{\begin{aligned} dv_t^i &= \left(F_\alpha(v^i, Z^i) + I^\alpha(t) + \sum_{j=1}^{N} J_{ij} v_t^j * h\right) dt + \sigma_\alpha dW_t^i \\ dZ_t^i &= G_\alpha(v_t^i, Z_t^i)\, dt + \Gamma_\alpha dB_t^i \end{aligned}\right.$$

Stochastic differential equation to describe dynamics in the population. Describing specific neuron models through stochastic differential equations:

$$\left\{\begin{aligned} C dv_t^i &= \Big(I^i - g_K (n^i)^4 (v_t^i - E_K) - g_{Na} (m^i)^3 h^i (v_t^i - E_{Na}) \\ &\qquad - g_L (v_t^i - E_L) + \textstyle\sum_j J_{ij}\ (v_t^j * h)\Big) dt + \sigma^i dW_t^i \\ dn_t^i &= \big(\alpha_n(v_t^i)(1 - n^i) - \beta_n(v_t^i) n^i\big) dt \\ dm_t^i &= \big(\alpha_m(v_t^i)(1 - m^i) - \beta_m(v_t^i) m^i\big) dt \\ dh_t^i &= \big(\alpha_h(v_t^i)(1 - h^i) - \beta_h(v_t^i) h^i\big) dt \end{aligned}\right.$$

H&H

$$\left\{\begin{aligned} dv_t^i &= \left(v_t^i - \frac{(v_t^i)^3}{3} - w_t^i + I^i + \textstyle\sum_j J_{ij}\ (v_t^j * h)\right) dt + \sigma^i dW_t^i \\ dw_t^i &= \epsilon_w (v_t^i - a w_t^i + b) dt \end{aligned}\right.$$

FitzHugh-Nagumo

Very complex to analyze and simulate!

$$R[u] = \{x | u(x) > 0\}$$

FIRING RATE MODELS

Firing rate as macroscopic descriptor as seen before: $Q(t) = \lim_{dt \to 0} \frac{n_{spikes}(t, t+dt)}{N dt}$.

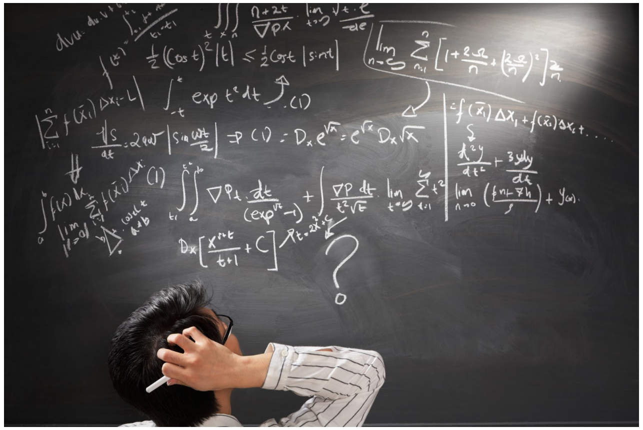
Other way to see it: Integrating the value of the membrane potential during a time window and dividing by the area under a spike. This means, the membrane potential is a lineal transformation of the firing rate!

Then, one can use the average of the membrane potential, within a population and for a certain time as a definition of macroscopic activity.

Sub-threshold activity has an impact in membrane potential but not in firing rates.

TIME FOR QUESTIONS

None? Hmm…



$$R[u]=\{x|u(x)>0\}$$

REFERENCES

Deco, G. et al., “The dynamic brain: from spiking neurons to neural masses and cortical fields”, *PLoS Computational Biology*, Vol. 4, No. 8, 2008.

Amari, S., “Dynamics of Pattern Formation in Lateral-Inhibition Type Neural Fields*”, Biol. Cybernetics*, Vol. 27, pp. 77-87, 1977.

Galtier, M. and Touboul, J., “Macroscopic equations governing noisy spiking neuronal populations”, *PLoS One,* in Press.

Baladron, J. et al., “Mean-field description and propagation of chaos in networks of Hodgkin-Huxley and FitzHugh-Nagumo neurons”, *Journal of Mathematical Neuroscience,* Vol. 2, No. 10, 2012.

Roxin, A. et al., “On the Distribution of Firing Rates in Networks of Cortical Neurons”, *The Journal of Neuroscience,* Vol. 31, No. 45, 2011.

Coombes, S., “Neural Field Modelling”, Lectures, 2011.