ANALYSIS OF NEURONAL INTERACTIONS USING INFORMATION- THEORETICAL MODELS

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ICFAS21

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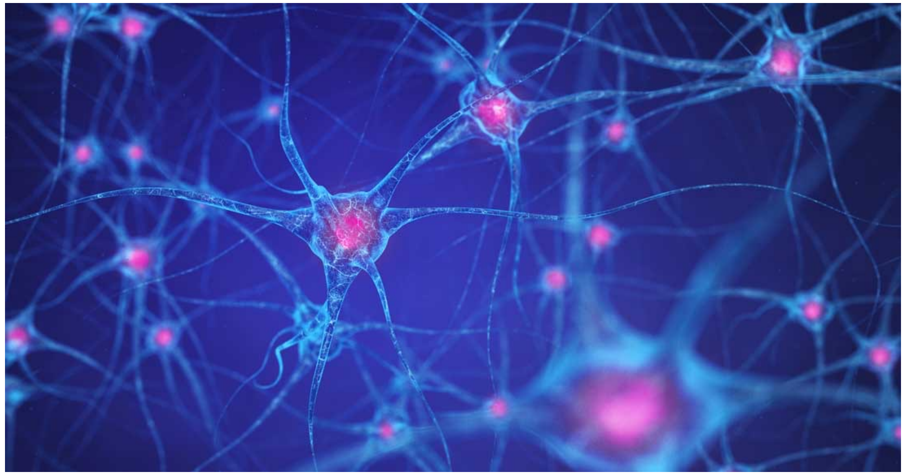
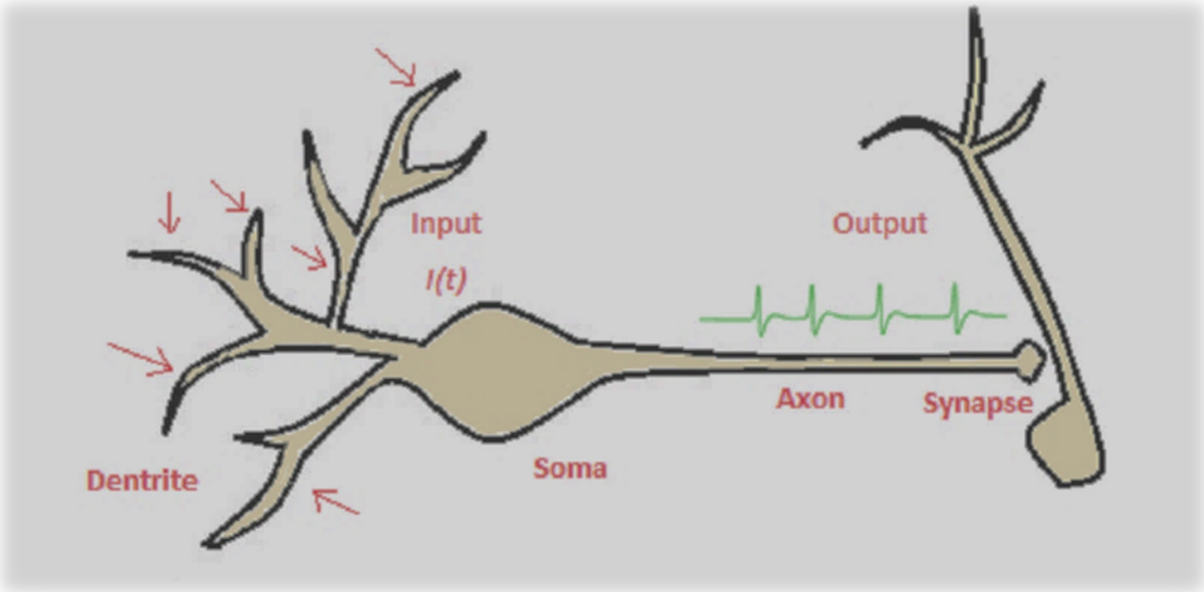
EXCITABLE CELLS AND NEURONS

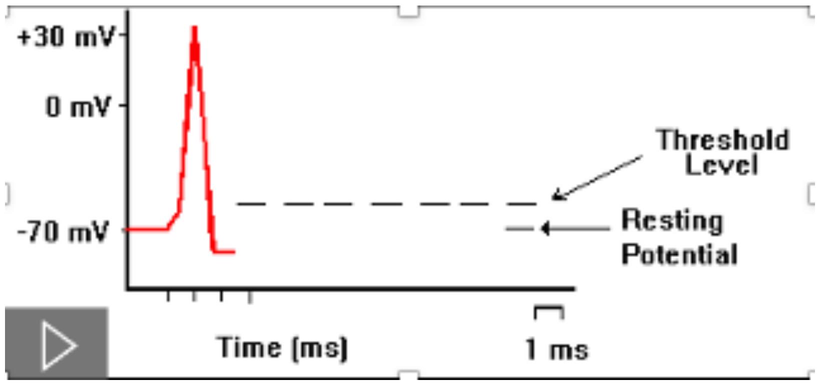


Example: Nerve cells, muscle cells, heart cells and secretary cells such as pituitary cell, pancreatic beta cells.

The signals circulating neurons forms the basis of memories, thoughts and emotions.

NEURON ACTION POTENTIAL

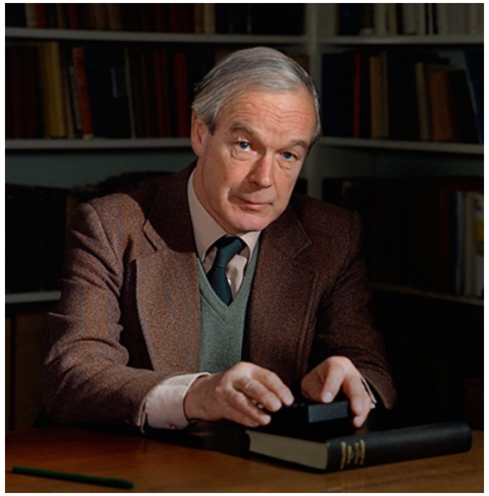




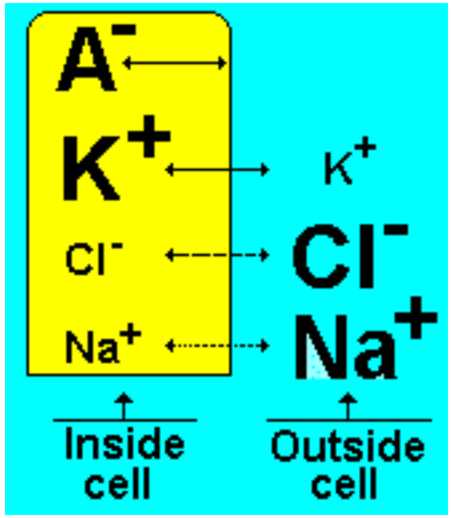
Neurons sends messages electrochemically. It means that chemical cause an electrical signal.

MODELLING ACTION POTENTIAL IN NEURONS

HODGKIN HUXLEY MODEL



$$C\frac{dV}{dt} = \bar{g}_{Na}\, m^3 h\,(V_{Na} - V) + \bar{g}_K\, n^4\,(V_K - V) + g_L(V_L - V) + I_{ext}$$



Alan Hodgkin and Andrew Huxley conducted experiment to understand the movement of ions in a nerve cell during an action potential

MORRIS LECAR MODEL

The Morris–Lecar neuron model is a 2-D nonlinear differential system.
In comparison to the four-dimensional Hodgkin–Huxley model, it is considered a simpler model.

$$C\frac{dV}{dt} = I - g_{\mathrm{L}}(V - V_{\mathrm{L}}) - g_{\mathrm{Ca}} M_{\mathrm{ss}}(V - V_{\mathrm{Ca}}) - g_{\mathrm{K}} N(V - V_{\mathrm{K}})$$

$$\frac{dN}{dt} = \frac{N_{\mathrm{ss}} - N}{\tau_N}$$

where

$$M_{\mathrm{ss}} = \frac{1}{2} \cdot \left(1 + \tanh\left[\frac{V - V_1}{V_2}\right]\right)$$

$$N_{\mathrm{ss}} = \frac{1}{2} \cdot \left(1 + \tanh\left[\frac{V - V_3}{V_4}\right]\right)$$

$$\tau_N = 1/\left(\varphi \cosh\left[\frac{V - V_3}{2V_4}\right]\right)$$

I : applied current
C : membrane capacitance
gL, gCa, gK : leak, Ca++, and
K+ conductances through membranes channel
VL, VCa, VK : equilibrium potential of relevant ion channels
V1, V2, V3, V4: tuning parameters for steady state and time constant
ϕ: reference frequency

HINDMARSH ROSE MODEL

This is non-conductance model

In experiments, Hindmarsh and Rose observed Spiking behaviour of the membrane potential

Membrane potential: Electic potential between the interior and the exterior of a biological cell.

x(t)=Membrane potential
y(t)=Spiking variable
z(t)=Adaption current

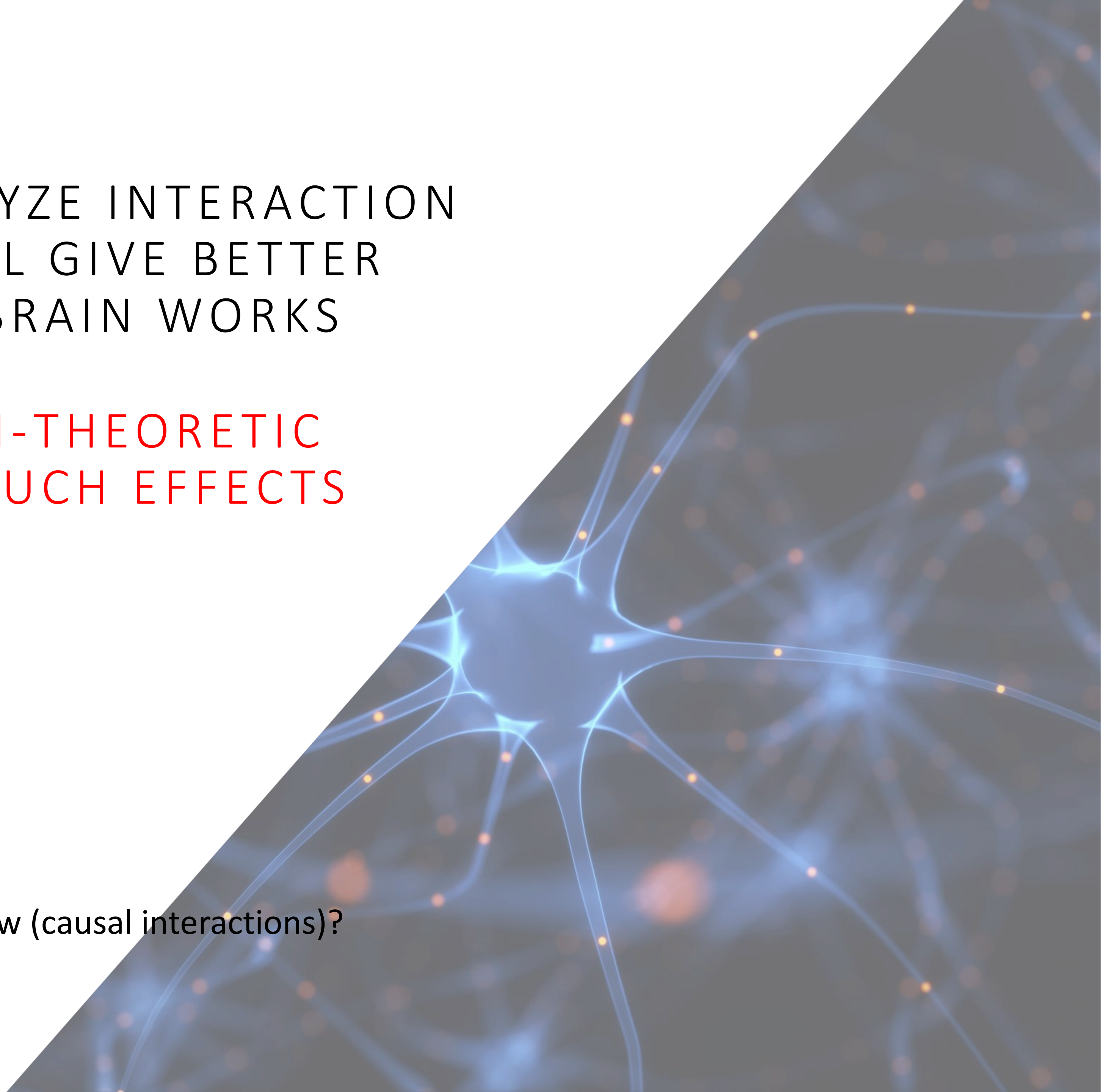
$$\dot{x} = y - ax^3 + bx^2 + I - z$$

$$\dot{y} = c - dx^2 - y$$

$$\dot{z} = r\left(s\left(x - x_1\right) - z\right),$$

UNDERSTAND AND ANALYZE INTERACTION BETWEEN NEURONS WILL GIVE BETTER UNDERSTANDING HOW BRAIN WORKS

WE APPLY INFORMATION-THEORETIC METHODS TO ANALYZE SUCH EFFECTS

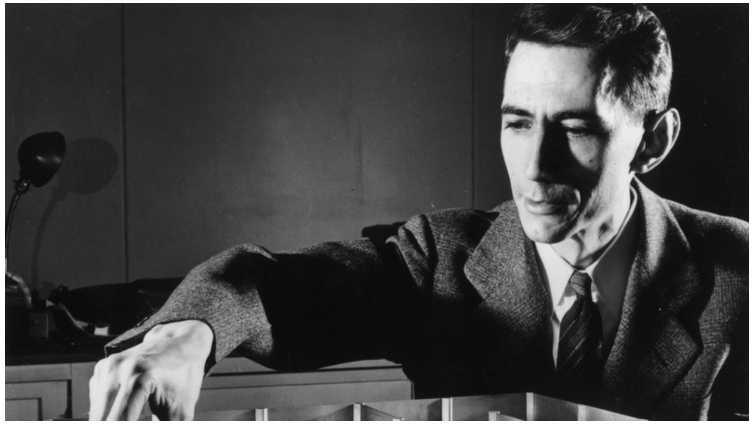


Which neurons are related?
What is the direction of the information flow (causal interactions)?

INFORMATION THEORY

Entropy: Fundamental information theoretical quantity to describe the average uncertainty of a system.

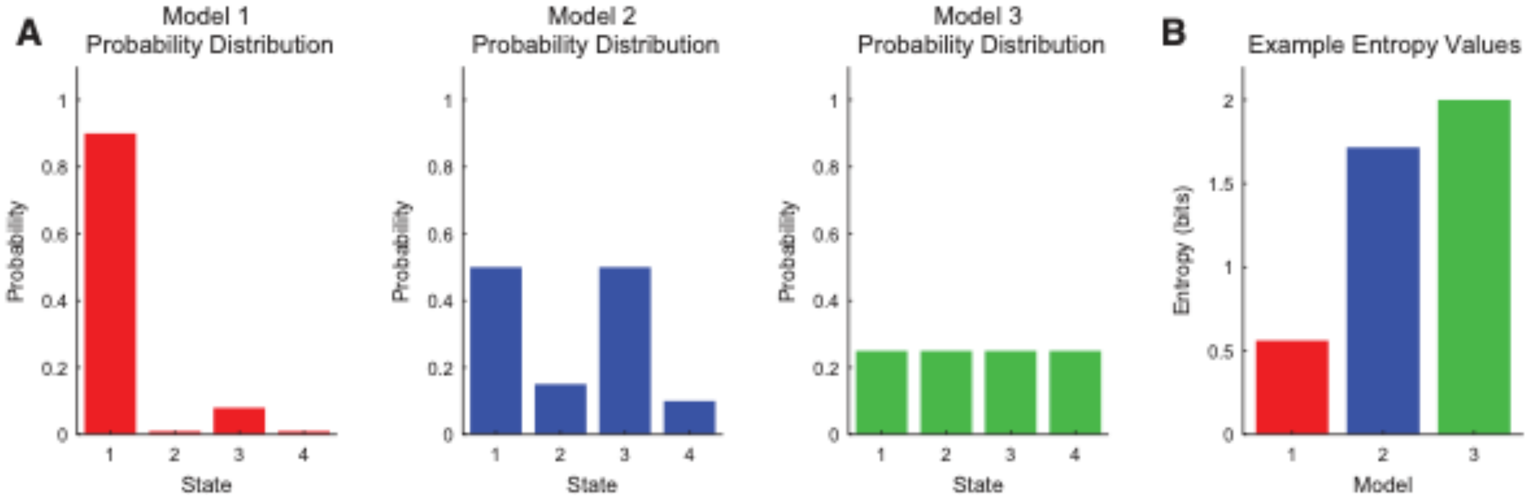
Claude Shannon



$$H(X) = -\sum_{x \in X} p(x) \log\big(p(x)\big)$$

where H denotes the entropy of a random variable "X" and p(x) represents its probability density function (pdf).

INFORMATION is reduction in uncertainty



Systems with varied distribution , the entropy is lower
Systems with uniform distributions, the entropy is higher

Timme, Nicholas & Lapish, Christopher. (2018). A Tutorial for Information Theory in Neuroscience. eneuro. 5. ENEURO.0052-18.2018. 10.1523/ENEURO.0052-18.2018.

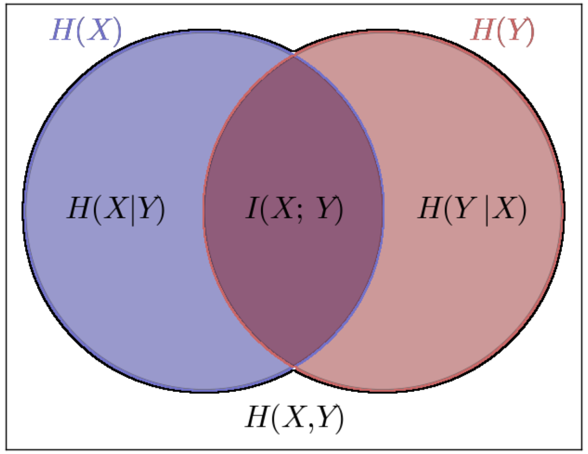
MUTUAL INFORMATION (MI)

- Conditional Entropy which quantifies the uncertainty in a variable given the state of another variable.

$$\mathrm{H}(Y|X) = -\sum_{x\in\mathcal{X},y\in\mathcal{Y}} p(x,y)\log\frac{p(x,y)}{p(x)}$$

$$I(X;Y) = H(X) - H(X|Y) = \sum_{x\in X, y\in Y} p(x,y) log_2\left(\frac{p(x,y)}{p(x)p(y)}\right)$$

- MI (I(X;Y)):



We can quantity reduction in uncertainty so we can quantity information

TRANSFER ENTROPY(TE)

To identify the direction of information flow from one variable to another, we use Transfer Entropy which is capable of detecting the direction.

Information Flow: Information we learn from the past state of one variable about the current state of the other

The TE in two directions are calculated from data by using the following equations

$$\boldsymbol{TE_{V_1V_2}} = T\left(V_{2(i+1)} \middle| \boldsymbol{V_2}_{(i)}^{(k)}, \boldsymbol{V_1}_{(i)}^{(l)}\right) = \sum_{v_{2(i+1)}, \boldsymbol{v_2}_{(i)}^{(k)}, \boldsymbol{v_1}_{(i)}^{(l)}} p\left(v_{2(i+1)}, \boldsymbol{v_2}_{(i)}^{(k)}, \boldsymbol{v_1}_{(i)}^{(l)}\right) \log_2 \frac{p\left(v_{2(i+1)} | \boldsymbol{v_2}_{(i)}^{(k)}, \boldsymbol{v_1}_{(i)}^{(l)}\right)}{p\left(v_{2(i+1)} | \boldsymbol{v_2}_{(i)}^{(k)}\right)},$$

$$\boldsymbol{TE_{V_2V_1}} = T\left(V_{1(i+1)} \middle| \boldsymbol{V_1}_{(i)}^{(k)}, \boldsymbol{V_2}_{(i)}^{(l)}\right) = \sum_{v_{1(i+1)}, \boldsymbol{v_1}_{(i)}^{(k)}, \boldsymbol{v_2}_{(i)}^{(l)}} p\left(v_{1(i+1)}, \boldsymbol{v_1}_{(i)}^{(k)}, \boldsymbol{v_2}_{(i)}^{(l)}\right) \log_2 \frac{p\left(v_{1(i+1)} | \boldsymbol{v_1}_{(i)}^{(k)}, \boldsymbol{v_2}_{(i)}^{(l)}\right)}{p\left(v_{1(i+1)} | \boldsymbol{v_1}_{(i)}^{(k)}\right)},$$

Gencaga, Deniz & Sengul Ayan, Sevgi & Farnoudkia, Hajar & Okuyucu, Serdar. (2020). Statistical Approaches for the Analysis of Dependency Among Neurons Under Noise. Entropy. 22. 387. 10.3390/e22040387.

$$TE_{V_1V_2} = T\left(V_{2\,(i+1)}\middle|\boldsymbol{V_2}_{(i)}^{(k)}, \boldsymbol{V_1}_{(i)}^{(l)}\right) = \sum_{v_{2\,(i+1)}, \boldsymbol{v_2}_{(i)}^{(k)}, \boldsymbol{v_1}_{(i)}^{(l)}} p\left(v_{2\,(i+1)}, \boldsymbol{v_2}_{(i)}^{(k)}, \boldsymbol{v_1}_{(i)}^{(l)}\right) \log_2 \frac{p\left(v_{2\,(i+1)}|\boldsymbol{v_2}_{(i)}^{(k)}, \boldsymbol{v_1}_{(i)}^{(l)}\right)}{p\left(v_{2\,(i+1)}|\boldsymbol{v_2}_{(i)}^{(k)}\right)},$$

$$TE_{V_2V_1} = T\left(V_{1\,(i+1)}\middle|\boldsymbol{V_1}_{(i)}^{(k)}, \boldsymbol{V_2}_{(i)}^{(l)}\right) = \sum_{v_{1\,(i+1)}, \boldsymbol{v_1}_{(i)}^{(k)}, \boldsymbol{v_2}_{(i)}^{(l)}} p\left(v_{1\,(i+1)}, \boldsymbol{v_1}_{(i)}^{(k)}, \boldsymbol{v_2}_{(i)}^{(l)}\right) \log_2 \frac{p\left(v_{1\,(i+1)}|\boldsymbol{v_1}_{(i)}^{(k)}, \boldsymbol{v_2}_{(i)}^{(l)}\right)}{p\left(v_{1\,(i+1)}|\boldsymbol{v_1}_{(i)}^{(k)}\right)},$$

$$\boldsymbol{v_1}_{(i+1)}^{(k)} = \left\{v_{1\,(i)}, v_{1(i-1)} \dots, v_{1\,(i-k)}\right\}$$
$$\boldsymbol{v_2}_{(i+1)}^{(l)} = \left\{v_{2\,(i)}, v_{2(i-1)} \dots, v_{2\,(i-l)}\right\}$$

Gencaga, Deniz & Sengul Ayan, Sevgi & Farnoudkia, Hajar & Okuyucu, Serdar. (2020). Statistical Approaches for the Analysis of Dependency Among Neurons Under Noise. Entropy. 22. 387. 10.3390/e22040387.

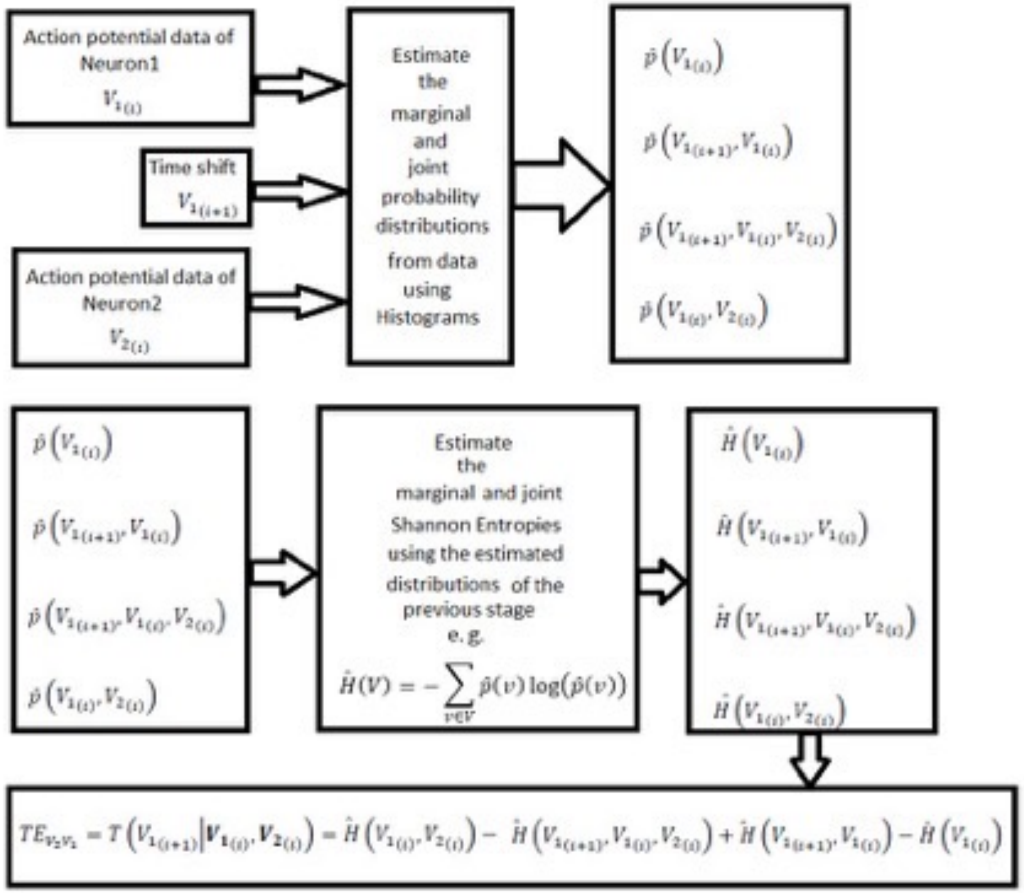
NetTE

$$NetTE_{XY} = \max(TE_{YX}, TE_{XY}) - \min(TE_{YX}, TE_{XY})$$

- The NetTE allows us to compare the relative values of information flow in both directions giving a sense of main interaction direction between the two variables X and Y.

Estimation Of TE From Data

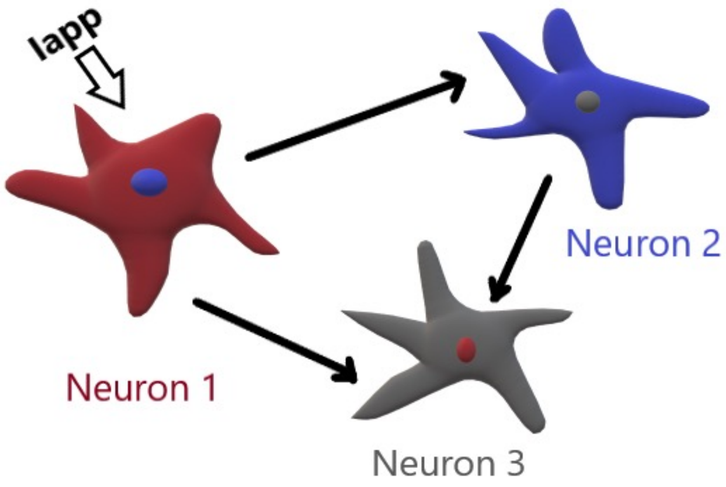
$$H\left(V_{1_{(i)}}, V_{2_{(i)}}\right), H\left(V_{1_{(i+1)}}, V_{1_{(i)}}, V_{2_{(i)}}\right), H\left(V_{1_{(i+1)}}, V_{1_{(i)}}\right), H\left(V_{1_{(i)}}\right).$$



Finally, TE from V_2 *to* V_1 is computed

SIMULATIONS

Coupling For All 3 Neuron Model



HH Model Simulation

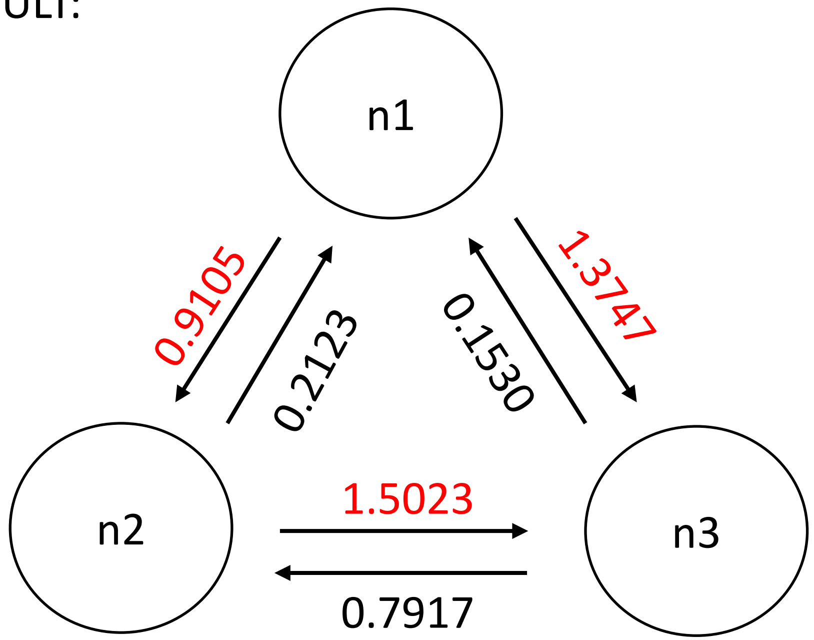
$$C_m \frac{dV_1}{dt} = I_{app} - I_{Na,1} - I_{K,1} - I_{L,1}$$

$$C_m \frac{dV_2}{dt} = -I_{Na,2} - I_{K,2} - I_{L,2} - I_{Syn_{1-2}}$$

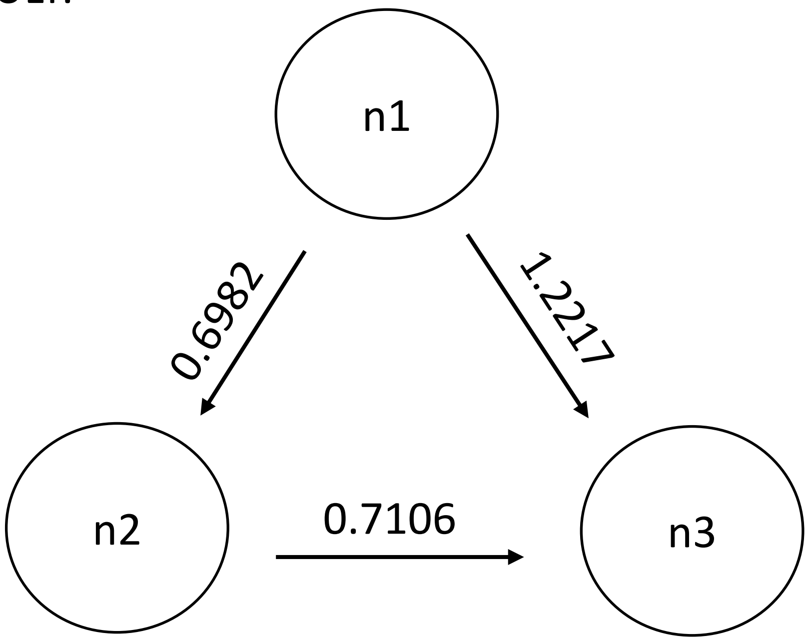
$$C_m \frac{dV_3}{dt} = -I_{Na,3} - I_{K,3} - I_{L,3} - I_{Syn_{1-3}} - I_{Syn_{2-3}}$$

$I_{Syn_{i-j}} = k_x(V_i - V_j)$ is the synaptic current defined from pre-synaptic neuron i to post-synaptic neuron j.

TE RESULT:



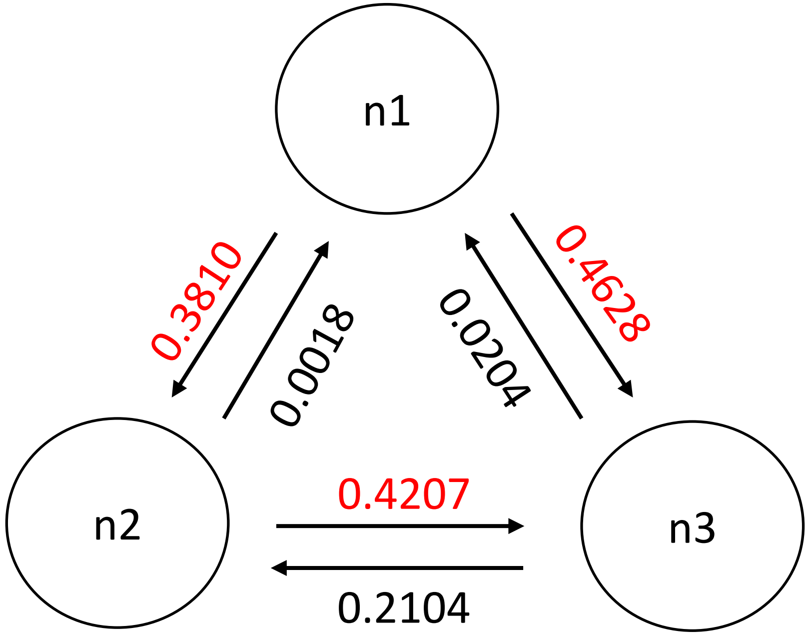
NETTE RESULT:



n1:Neuron1 n2:Neuron2 n3:Neuron3

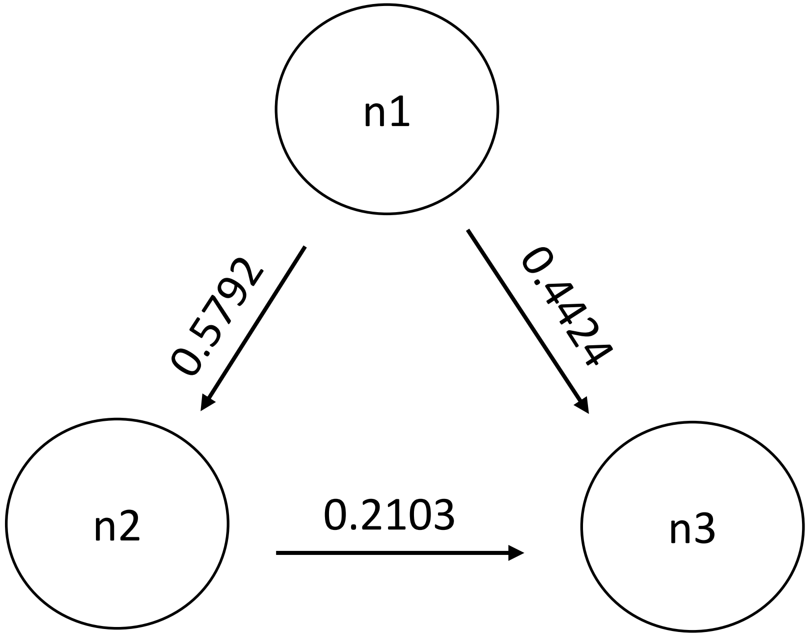
ML 3 Neuron Model Simulation

TE RESULT:



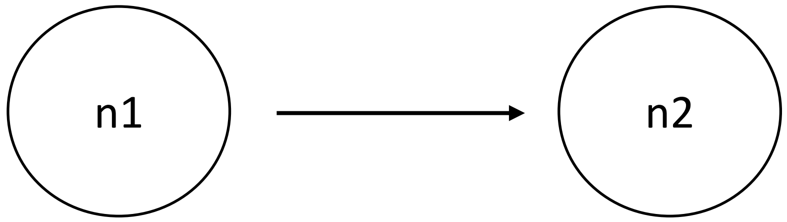
n1:Neuron1 n2:Neuron2 n3:Neuron3

NETTE RESULT:

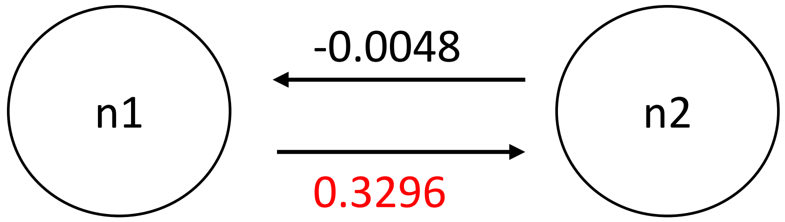


ML 2 Neuron Model Simulation

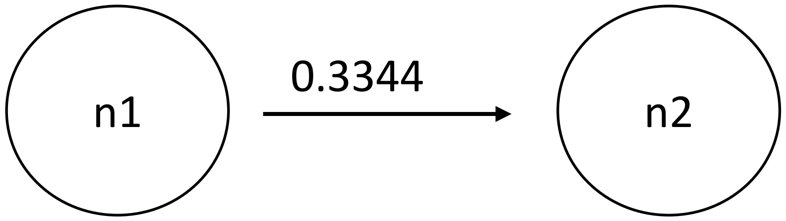
Model Simulation Copuling:



TE RESULT:



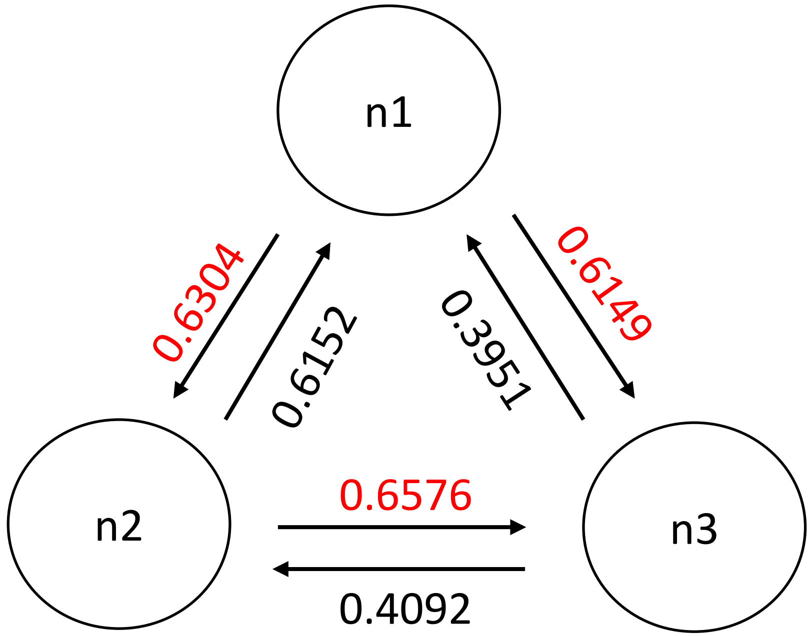
NETTE RESULT:



n1:Neuron1   n2:Neuron2

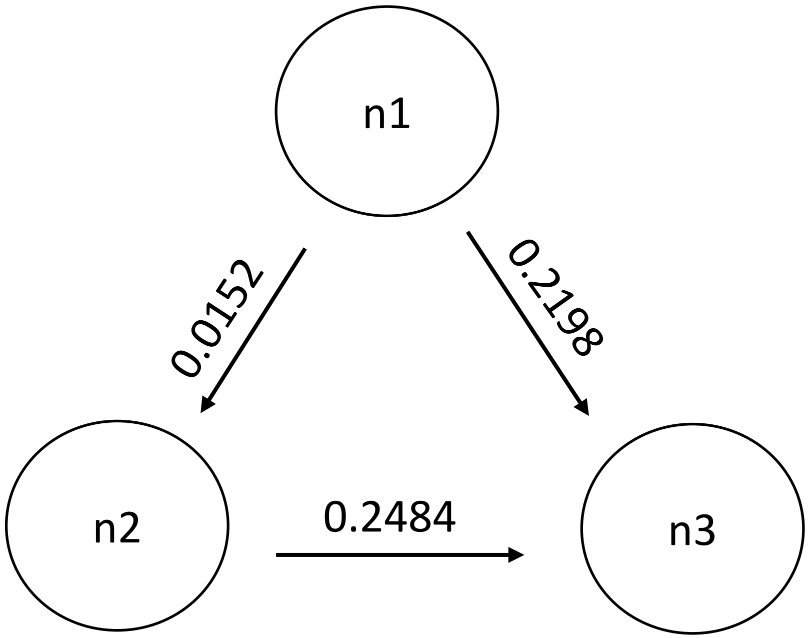
HR 3 Neuron Model Simulation

TE RESULT:



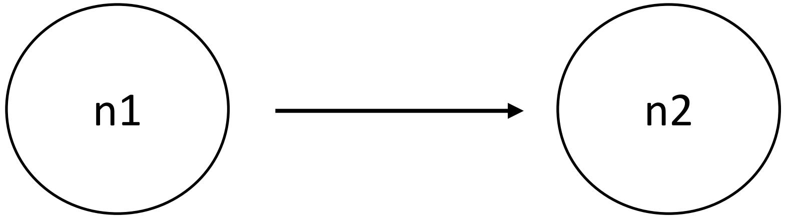
n1:Neuron1   n2:Neuron2   n3:Neuron3

NETTE RESULT:

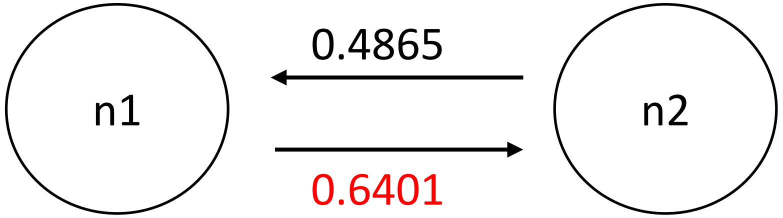


HR 2 Neuron Model Simulation

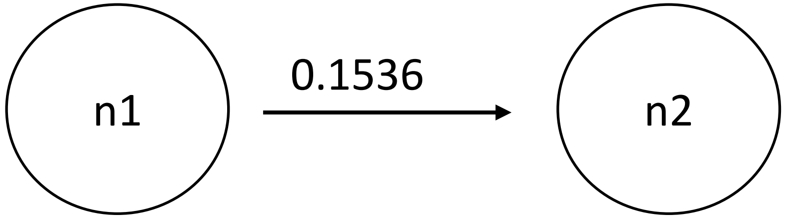
Model Simulation Copuling:



TE RESULT:



NETTE RESULT:



n1:Neuron1 n2:Neuron2

Summary

- Neuronal interactions were analyzed by information-theoretic methods
- Different neural interaction models have been considered
- Cause and effect between neurons have been analyzed using these models
- Successful interaction modelling for each case

THANK YOU

Acknowledgment

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RESEARCH TEAM

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$$TE_{V_1V_2} = T\left(V_{2(i+1)} \middle| \boldsymbol{V_2}_{(i)}^{(k)}, \boldsymbol{V_1}_{(i)}^{(l)}\right) = \sum_{v_{2(i+1)}, \boldsymbol{v_2}_{(i)}^{(k)}, \boldsymbol{v_1}_{(i)}^{(l)}} p\left(v_{2(i+1)}, \boldsymbol{v_2}_{(i)}^{(k)}, \boldsymbol{v_1}_{(i)}^{(l)}\right) \log_2 \frac{p\left(v_{2(i+1)} \middle| \boldsymbol{v_2}_{(i)}^{(k)}, \boldsymbol{v_1}_{(i)}^{(l)}\right)}{p\left(v_{2(i+1)} \middle| \boldsymbol{v_2}_{(i)}^{(k)}\right)},$$

$$TE_{V_2V_1} = T\left(V_{1(i+1)} \middle| \boldsymbol{V_1}_{(i)}^{(k)}, \boldsymbol{V_2}_{(i)}^{(l)}\right) = \sum_{v_{1(i+1)}, \boldsymbol{v_1}_{(i)}^{(k)}, \boldsymbol{v_2}_{(i)}^{(l)}} p\left(v_{1(i+1)}, \boldsymbol{v_1}_{(i)}^{(k)}, \boldsymbol{v_2}_{(i)}^{(l)}\right) \log_2 \frac{p\left(v_{1(i+1)} \middle| \boldsymbol{v_1}_{(i)}^{(k)}, \boldsymbol{v_2}_{(i)}^{(l)}\right)}{p\left(v_{1(i+1)} \middle| \boldsymbol{v_1}_{(i)}^{(k)}\right)},$$

BACKUP **

where $(i + 1)$ is an indice for the leading time instant and (i) is an indice for the current time. Above, $\boldsymbol{v_1}_{(i)}^{(k)} = \left\{v_{1(i)}, \ldots, v_{1(i-k+1)}\right\}$ shows the vector including the value of V_1 at time instant (i) and its values at $(k-1)$ preceeding time instants. Similarly, $\boldsymbol{v_2}_{(i)}^{(l)} = \left\{v_{2(i)}, \ldots, v_{2(i-l+1)}\right\}$ denotes the vector including the value of V_2 at time instant (i) and its values at $(l-1)$ leading time instants. Here, V_1 shows the k-th order and V_2 shows the l-th order Markov processes. In the literature, k and l are also referred as the embedding dimensions.

In our simulations, one past value of each signal is taken into consideration by assuming $k = l = 1$ during TE analysis

$$TE_{V_2V_1} = T\left(V_{1(i+1)} \middle| \boldsymbol{V}_{1(i)}, \boldsymbol{V}_{2(i)}\right)$$
$$= H\left(V_{1(i)}, V_{2(i)}\right) - H\left(V_{1(i+1)}, V_{1(i)}, V_{2(i)}\right) + H\left(V_{1(i+1)}, V_{1(i)}\right) - H\left(V_{1(i)}\right)$$

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