Electroencephalographic (EEG) Influence on Ca²⁺ Waves

Lester Ingber*, Marco Pappalepore, Ronald R. Stesiak * ingber@alumni.caltech.edu

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Neuronal Scales of Neocortical Interactions



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SMNI

- Statistical Mechanics of Neocortical Interactions (SMNI)
 - Progression of aggregation of probability distributions
- Synaptic interactions via quantal transmissions
- Neuron-neuron interactions across minicolumns & macrocolumns
 - Minicolumn of hundreds of neurons
 - Macrocolumn of thousands of minicolumns
- Macrocolumnar aggregation to regions (scalp EEG scales)
 - Region of thousands of macrocolumns
 - About 15-20 billion neurons in cerebral cortex

SMNI Successes

- Short-term memory (STM)
- STM duration and stability
- STM capacity rules of 7 ± 2 (auditory) and 4 ± 2 (visual)
- STM primacy versus recency rule (first > last > middle)
- Hick's law: g-factor linear time to access sets of STM
- Rate of minicolumnar information diffusion (nearest neighbors)
 - Short-ranged unmyelinated within epochs of long-ranged myelinated fibers
- Scaled up to fit scalp EEG data

Interactions Among Scales

- Include molecular and quantum scales
 - Ca²⁺ ions
- Research into interactions across multiple scales
 - Interactions between the largest scalp EEG scale and the smallest Ca^{2+} scale?

Tripartite Neuron-Astrocyte-Neuron

- Astrocyte
 - Important class of glial cells
 - Nourish neurons
 - Major source of Ca²⁺ waves (includes "free" unbuffered ions)
 - Up to tens of thousands of free ions/wave
 - Concentrations up to 5 μ M (μ M = 10⁻³ mol/m³)
 - Range up to 250 µm
 - speed 50-100 µm/s
 - Influence Glutamate quantal (integral units) concentrations in synaptic gaps
 - Primary excitatory neurotransmitter depolarizes and excites neurons

Regional Magnetic Vector Potential A

Regional Scales

- Neocortical current I due to coherent synchronized firings
 - Observed values \rightarrow includes all theoretical screening, etc.
- Wire model of minicolumns fit to \mathbf{I} has log dependence on r

$$\mathbf{A} = \frac{\mu}{4\pi} \mathbf{I} \log\left(\frac{r}{r_0}\right)$$
$$\mathbf{E} = \frac{ic}{\omega} \nabla \times \mathbf{B} = \frac{ic}{\omega} \nabla \times \nabla \times \mathbf{A}$$

• Magnetic vector potential $\mathbf{A} \propto \mathbf{I}$

Molecular Ca²⁺ Wave

- Consider only sources from regenerative processes from internal stores
 - Process involves Ca^{2+} released from IP_3R acting on other IP_3R sites
 - Process requires or affects other processes, e.g., IP₃, mGluR, mAChR, etc.
- Momentum of Ca²⁺ ions in wave with mean **p**
- $|\mathbf{p}| = 10^{-30} \text{ kg-m/s}$
 - $|\mathbf{p}| < |q\mathbf{A}| = 10^{-28} \text{ kg-m/s}$
 - q = -2 e where $e = -1.6 \ 10^{-19}$ C (charge of electron)
- Duration of a wave up to 500 ms

$\mathbf{p} + q\mathbf{A}$ Interaction

- Canonical momentum $\mathbf{\Pi} = \mathbf{p} + q \mathbf{A}$
 - Established in both classical and quantum physics
- Classical comparison of magnitudes of molecular \mathbf{p} and regional $q\mathbf{A}$
- Quantum treatment of $\mathbf{p} + q\mathbf{A}$ for wave packet in \mathbf{p} -space
 - SI units ($\mathbf{p} + q/c \mathbf{A}$ in Gaussian units, c =light speed)
 - Many-body **p** effects not yet considered

$\mathbf{p} + q\mathbf{A} \mathbf{p}$ -Space Wave Function

 $\phi(p,0) = (2\pi(\Delta \mathbf{p})^2)^{-3/4} e^{-(\mathbf{p}-\mathbf{p}_0)^2/(4(\Delta \mathbf{p})^2)}$

 $U(p,t) = e^{-i((\mathbf{p}+q\mathbf{A})^2t)/(2m\hbar)}$

 $\phi(p,t)=\phi(p,0)U(p,t)$

$\mathbf{p} + q\mathbf{A} \mathbf{r}$ -Space Wave Function

 δ

$$\begin{split} \varphi(r,t) &= (2\pi\hbar)^{-3/2} \int_{-\infty}^{\infty} d^3 \mathbf{p} \phi(p,t) e^{i\mathbf{p}\cdot\mathbf{r}/\hbar} = \alpha^{-1} e^{-\beta/\gamma} \\ \alpha &= (2\hbar)^{3/2} (2\pi(\Delta \mathbf{p})^2)^{3/4} \left(\frac{it}{2m\hbar} - \frac{1}{4(\Delta \mathbf{p})^2}\right)^{3/2} \\ \beta &= \left(\mathbf{r} - \frac{q\mathbf{A}t}{m} - \frac{i\hbar \mathbf{p}_0}{2(\Delta \mathbf{p})^2}\right)^2 \\ \gamma &= 4 \left(\frac{it\hbar}{2m} + \frac{\hbar^2}{4(\Delta \mathbf{p})^2}\right) \\ \delta &= \frac{\mathbf{p}_0^2}{4(\Delta \mathbf{p})^2} + \frac{iq^2\mathbf{A}^2t}{2m\hbar} \end{split}$$

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Possible Long Time Quantum Coherence

- Several examples of extended quantum coherence in "wet" media
- Bang-bang (BB) kicks or quantum Zeno effect (QZE)

 $U_n(p,t) = [U_k U(p,t/n)]^n$

• A mechanism sometimes used in quantum computation

Classical and/or Quantum Effects

• Alignment of Ca^{2+} waves along $A \parallel I$

 $\mathbf{\Pi} = p_x \mathbf{\hat{x}} + p_y \mathbf{\hat{y}} + (p_z + qA_z) \mathbf{\hat{z}}$

- A influence on regional-averaged synaptic quantal transmissions
 - Ca^{2+} waves influence quantal transmissions influencing background *B*
 - A affects **p** of Ca²⁺ waves
 - A therefore affects background synaptic activity

Fits to EEG to Test A Influences

- SMNI conditional probability of firing P
 - SMNI Lagrangian L function of firings M(t)
 - All parameters taken within experimentally observed ranges
 - SMNI "threshold factor" F argument of nonlinear means and covariance
 - Minicolumnar-averaged quantal means and variances of synaptic interactions
- Scales of application of Lagrangian
 - STM mesocolumn (converge to minicolumn; diverge to macrocolumn)
 - Mesocolumn of excitatory *E* and inhibitory *I* firings
 - Trough of minima permit "centering mechanism" (CM)
 - Scaling SMNI to scale of scalp EEG

SMNI Lagrangian

$$P = \frac{1}{\sqrt{(2\pi dtg)}} \exp(-Ldt)$$

$$L = \sum_{G,G'} (2N)^{-1} (\dot{M}^G - g^G) g_{GG'} (\dot{M}^{G'} - g^{G'}) / (2N\tau) - V$$

$$g^G = -\tau^{-1}(M^G + N^G \tanh F^G)$$

$$g^{GG'} = (g_{GG'})^{-1} = \delta_G^{G'} \tau^{-1} N^G \operatorname{sech}^2 F^G$$

 $g = \det(g_{GG'})$

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SMNI Threshold Factor $F^{G} = \sum_{G'} \frac{\nu^{G} + \nu^{\ddagger E'}}{\left((\pi/2)[(v_{G'}^{G})^{2} + (\phi_{G'}^{G})^{2}](\delta^{G} + \delta^{\ddagger E'})\right)^{1/2}}$ $\nu^{G} = V^{G} - a^{G}_{G'} v^{G}_{G'} N^{G'} - \frac{1}{2} A^{G}_{G'} v^{G}_{G'} M^{G'}$ $\nu^{\ddagger E'} = -a_{E'}^{\ddagger E} v_{E'}^E N^{\ddagger E'} - \frac{1}{2} A_{E'}^{\ddagger E} v_{E'}^E M^{\ddagger E'}$ $\delta^{G} = a_{G'}^{G} N^{G'} + \frac{1}{2} A_{G'}^{G} M^{G'}$ $\delta^{\ddagger E'} = a_{E'}^{\ddagger E} N^{\ddagger E'} + \frac{1}{2} A_{E'}^{\ddagger E} M^{\ddagger E'}$ $a_{G'}^G = \frac{1}{2}A_{G'}^G + B_{G'}^G, \ a_{E'}^{\ddagger E} = \frac{1}{2}A_{E'}^{\ddagger E} + B_{E'}^{\ddagger E}$

Intuitive Lagrangian L of Firings M

 $Mass = g_{GG'} = \frac{\partial^2 L}{\partial(\partial M^G/\partial t)\partial(\partial M^{G'}/\partial t)}$ (Canonical) Momentum = $\Pi^G = \frac{\partial L}{\partial (\partial M^G / \partial t)}$ Force = $\frac{\partial L}{\partial M^G}$ $\delta L = 0 = \frac{\partial L}{\partial M^G} - \frac{\partial}{\partial t} \frac{\partial L}{\partial (\partial M^G / \partial t)}$ F - ma = 0

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Centering Mechanism (CM)

- Shift background noise B in synaptic interactions
 - Shifts are consistent with experimental observations of selective attention
- Shift *B* to keep $F \propto M$ (no constant offset)
 - Minima typically driven to small values of $A_E^E M^E A_I^E M^I$
 - Defines "trough" along line in *M* firing space
 - Maximizes number of minima within firing boundaries
 - STM firing patterns appear within a sea of "noise"

Dependence of Synaptic Background B on A

- Quantal mean of mesocolumnar average
 - $a = \frac{1}{2}A + B$
 - A is coefficient of firings
 - *B* is background "noise"
 - Influenced by astrocytes Ca²⁺ waves
 - Model **A** influence as $B = B_0 + B_1 |\mathbf{A}|$
 - $\mathbf{A} \propto \mathbf{I} \propto \mathbf{\Phi}$
 - Φ is EEG electric potential at previous *t* for these fits
 - A model requires Dynamic Centering Mechanism (DCM) at each t

Preliminary Results

- EEG Data: http://kdd.ics.uci.edu/databases/eeg/
 - Collected by Henri Begleiter in large NIH alcoholism study
 - Entered into KDD database by Lester Ingber in 1997
 - Knowledge Discovery in Databases
 - merged with http://archive.ics.uci.edu/ml/
 - Paradigms to test attentional states during P300 events
- Train in-sample to L and test out-of-sample
 - Sensitive Canonical Momenta Indicators (CMI)
- A model has stronger signal than no-A model
 - similar to aggregated data over 11,075 runs

Adaptive Simulated Annealing (ASA)

- <u>http://www.ingber.com</u>
 - <u>http://alumni.caltech.edu/~ingber</u>
 - <u>http://asa-caltech.sourceforge.net</u>
 - <u>https://code.google.com/p/adaptive-simulated-annealing</u>
- C-language importance-sampling for global fit over *D*-dimensional space.
- ASA annealing temperature exponentially decreasing T schedule
 - Faster than fast Cauchy annealing with polynomial decreasing T schedule
 - Much faster than Boltzmann annealing with logarithmic decreasing schedule
- Over 100 OPTIONS provide robust tuning since 1989 (VFSR \rightarrow ASA)
- ASA_PARALLEL OPTIONS hooks developed as PI 1994 NSF PSC project
- ASA currently used as PI of NSF XSEDE projects.

A Versus No-A Models

A model



No-A model



Supplementary Analysis

Marco Pappalepore and Ronald Stesiak

Overall, mixed results were demonstrated when evaluating the efficacy or improvements of the CMI when comparing to the EEG data.

However, many definitively positive improvements with the A model were observed, both when comparing to the EEG data and the no-A model.

See http://ingber.com/smni14_eeg_ca_supp.zip

Calculations on XSEDE.org

- Adaptive Simulated Annealing (ASA) fit SMNI to EEG data
 - 6 CPU-hrs for each of 120 train-test runs = cumulative CPU-month+
 - 6 CPU-hrs for all runs on XSEDE in parallel
 - NSF Extreme Science & Engineering Discovery Environment

Tentative Conclusions

- Top-down interactions
 - Regional coherent firings \Leftrightarrow Selective Attention
 - Attention ⊂ Consciousness
 - Attention influences molecular scales via $\mathbf{p} + q\mathbf{A}$
 - Certainly in domain of classical physics
 - Possibly in domain of quantum physics
- SMNI support for $\mathbf{p} + q\mathbf{A}$ interactions at tripartite synapses
 - DCM control of background synaptic activity B
 - Control of STM during states of selective attention