# Short Communication:
# Synergy among multiple scales of neocortical interactions

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Abstract
A lot of what we consider Consciousness ($\mathbf{C}$) is conscious attention to short-term memories (STM). At least some STM memories are actively processed by highly synchronized patterns of neuronal firings, with enough synchrony to be able to be easily measured by scalp electroencephalographic recordings (EEG). Large-scale synchronous macrocolumnar EEG firings is a top-down process developed by a statistical mechanics of neocortical interactions (SMNI), depending on the associated magnetic vector potential $\mathbf{A}$. Molecular-scale $\mathrm{Ca}^{2+}$ waves are the affected bottom-up process that influence neuronal firings, depending on the wave momentum $\mathbf{p}$. $\mathbf{A}$ directly influences $\mathbf{p}$ via the canonical momentum $\mathbf{\Pi} = \mathbf{p} + q\mathbf{A}$ (SI units), where the charge of $\mathrm{Ca}^{2+}$ is $q = -2e$, $e$ is the magnitude of the charge of an electron. Calculations in both classical and quantum mechanics are consistent with this effect. This approach also suggests some nanosystem-pharmaceutical applications. Results give strong confirmation of the SMNI model of STM, but only weak statistical consistency of $\mathbf{\Pi} = \mathbf{p} + q\mathbf{A}$ influences on scalp EEG.

## 1. “Mind over matter”

This short paper is intended to be primarily an Executive Summary of previous papers, “Electroencephalographic field influence on calcium momentum waves” (Ingber et al., 2014) and “Calculating consciousness correlates at multiple scales of neocortical interactions” with a minimum of technical math and physics (Ingber, 2015).

“Mind Over Matter” is a stretch, but not an inaccurate, context for this project. The logic of this metaphor is based in calculations on specific processes that have specific experimental confirmation, and that have been demonstrated to have support for viable models to support this study. While results presented here show only that these processes are statistically consistent with current experimental and theoretical evidence, the importance of this study is to at least demonstrate ingredients of analysis that can be considered reasonable to approach this subject.

(1) A lot of what we consider Consciousness ($\mathbf{C}$) and “mind” is conscious attention to short-term memories (STM), which can develop by (a) external stimuli directly, (b) internal long-term storage, (c) new ideas=memories developed in abstract regions of the brain, etc.

(2) It is now accepted by some neuroscientists and confirmed by some experiments (Asher, 2012; Salazar et al., 2012), that at least some such memories in (1) are actively processed by highly synchronized patterns of neuronal firings, with enough synchrony to be able to be easily measured by scalp electroencephalographic recordings (EEG) during activity of processing such patterns, e.g., P300 waves, etc. These minicolumnar currents giving rise to measurable EEG also give rise to magnetic vector potentials $\mathbf{A}$, for brevity commonly referred to as vector potentials. The $\mathbf{A}$ fields have a logarithmic range insensitivity and are additive over larger distances than electric $\mathbf{E}$ or magnetic $\mathbf{B}$ fields.

Only for brevity, unless otherwise stated, dependent on the context, “EEG” will refer to either the measurement of synchronous firings large enough to measurable on the scalp, or to the firings themselves.

(3) Previous papers (Ingber, 2011, 2012a, 2015; Ingber et al., 2014) calculate the influence of such synchronous EEG at molecular scales of $\mathrm{Ca}^{2+}$ ionic waves, a process which is present in the brain as well as in other organs, but particularly as astrocyte influences

at synaptic gaps, thereby affecting background synaptic activity, which in turn can be synchronized by other processes to give rise to the large-scale activity discussed in (1). The $\mathrm{Ca}^{2+}$ wave have a duration of momentum $\mathbf{p}$ which is observed to be rather large, on the order of STM duration.

(4) These papers connect the influence of (1) over (3) directly via a specific interaction, $\mathbf{p} + q\mathbf{A}$, where $q$ for a $\mathrm{Ca}^{2+}$ ion = $-2e$, where $e$ is the magnitude of the charge of an electron. The $\mathbf{p} + q\mathbf{A}$ interaction is well established in both classical and quantum physics.

The direct $\mathbf{p} + q\mathbf{A}$ influence of (1) over (3) can reasonably be discussed as a "mind over matter" process. E.g., just thinking about thinking can give rise to this effect.

These SMNI models (Ingber, 1982, 1983) assume that STM responses to internal or external stimuli evoke such background-noise control to maintain maximal numbers of information states as calculated and detailed in multiple previous papers (Ingber, 1984, 1985, 1994).

## 2. Scope of research

This work is not designed to be a review of research in $\mathbf{C}$. Certainly $\mathbf{C}$ is an important component of many disciplines, not just Science. However, within the realm of Science, there still is a quite unscientific immediate negative reaction from many people focused within their particular disciplines, ranging from neuroscience to physics, to exclude the study, even mention, of $\mathbf{C}$ from their own disciplines and journals. Within the realm of Science, there are other projects that also examine specific microscopic and quantum processes that may influence $\mathbf{C}$ (Clark, 2014; Hameroff and Penrose, 2013; Kouider, 2009; McFadden, 2007; Nunez and Srinivasan, 2006; Pereira and Furlan, 2009; Quiroga et al., 2013; Stiefel et al., 2014), as well as neural correlates of reasonable models of $\mathbf{C}$ (Nacia et al., 2014; Nunez and Srinivasan, 2010), but this work is focused on a particular $\mathbf{p} + q\mathbf{A}$ mechanism.

However, by necessity, this project requires interdisciplinary contributions from neuroscience, physics, biomedical engineering, optimization, and similar disciplines. This work addresses the importance of considering topics usually focused within physics, e.g., the vector potential $\mathbf{A}$ (Jackson, 1962), and of a specific interaction between $\mathrm{Ca}^{2+}$ ions and $\mathbf{A}$ developed by highly synchronous neocortical EEG. The necessity of addressing multiple scales of neuroscience has required a mathematical physics of multivariate nonlinear nonequilibrium statistical mechanics to develop aggregation of these scales (Ingber, 1982, 1983). The algebra presented by this development and the stochastic nature of EEG data has required the development of sophisticated importance-sampling algorithms like Adaptive Simulated Annealing (ASA) (Ingber, 1989, 1993), and other algorithms like PATHINT (Ingber, 1994, 2000; Ingber and Nunez, 1995) to evolve the fitted probability distributions.

### 2.1. $\mathbf{C}$ and Dark $\mathbf{C}$

It would be simply hubris to assume that we are even on the verge of knowing everything about our physical and human existence, including $\mathbf{C}$. Indeed, similar to current concepts of "Dark Energy" and "Dark Matter", it is possible there are aspects of $\mathbf{C}$ that we may only be able to infer existence or possibly prove we cannot know. These latter possibilities can be considered as belonging to a "Dark $\mathbf{C}$" ($\mathbf{DC}$) category, and $\mathbf{DC}$ should be researched as well as **C**. However, here we are definitely examining **C** within the realm of Science, looking for viable experimental data and viable theoretical understandings of such data.

## 3. Summary of approach

### 3.1. Neurology

Astrocytes are considered to influence glutamate (the main excitatory excitatory neurotransmitter in neocortex) production across synaptic gaps, by taking in some glutamate released by presynaptic neurons and converting it back into glutamate via conversion into glutamine which can enter presynaptic neurons where it can be converted into glutamine via interaction with glutaminase. In the context of SMNI calculations here, GABA (the main inhibitory neurotransmitter in neocortex) can be produced by inhibitory neurons by also utilizing glutamic acid (which when stripped of a hydrogen atom is glutamate) from astrocytes (Patel et al., 2001; Walls et al., 2014).

The $\mathrm{Ca}^{2+}$ waves considered specifically belong to a class arising from nonlinear cooperative regenerative processes from internal stores, complementary to $\mathrm{Ca}^{2+}$ released through classic endoplasmic reticulum channels and voltage-gated and ligand-gated $\mathrm{Ca}^{2+}$ transients. This class includes $\mathrm{Ca}^{2+}$ released from an inositol triphosphate receptor ($\mathrm{IP_3R}$), requiring the presence of $\mathrm{IP_3}$, acts on the same or other $\mathrm{IP_3R}$ to release more $\mathrm{Ca}^{2+}$ while $\mathrm{IP_3}$ is still present. This requires or affects additional processes, e.g., as metabotropic glutamate receptors (mGluR), muscarinic acetycholine receptors (mAChR) (Goldberg et al., 2010; Pitta et al., 2012; Ross, 2012). A fire-diffuse-fire model is often used to describe these waves (Coombes et al., 2004; Dawson et al., 1999; Keener, 2006).

### 3.2. Vector potential

Columnar EEG firings develop electromagnetic fields as described by a magnetic vector potential, referred to here as the SMNI vector potential (SMNI-VP). Early discussions of SMNI-VP were suggested, including the "Smoking Gun" that implicates top-down interactions at molecular scales (Ingber, 2011, 2012a). Previous papers outlined the approach in a classical physics context (Ingber, 2012b). Other papers have described detailed interactions of SMNI-VP firing states with $\mathrm{Ca}^{2+}$ waves, in both classical (Ingber, 2011, 2012a) and quantum contexts (Ingber, 2015; Ingber et al., 2014).

A columnar firing state is modeled as a wire/neuron with current $\mathbf{I}$ along a length $z$ observed from a perpendicular distance $r$ from a line of thickness $r_0$. The integral of $\mathbf{I}$ over $r$ defines the vector potential $\mathbf{A}$ (Jackson, 1962). This yields an insensitive log dependence on distance. The oscillatory time dependence of The contribution to $\mathbf{A}$ includes many minicolumnar lines of current from 100's to 1000's of macrocolumns, within a region not large enough to include many convolutions, but contributing to large synchronous bursts of EEG (Srinivasan et al., 2007). $\mathbf{E}$ and $\mathbf{B}$, derivatives of $\mathbf{A}$ with respect to $r$, do not possess this logarithmic insensitivity to distance, and therefore they do not linearly accumulate strength within and across macrocolumns.

### 3.3. Classical physics

Classical physics calculates $q\mathbf{A}$ from macroscopic EEG to be on the order of $10^{-28}$ kg-m/s, while the momentum $\mathbf{p}$ of a $\mathrm{Ca}^{2+}$ ion is on the order of $10^{-30}$ kg-m/s (Ingber, 2011, 2012a, 2015; Ingber et al., 2014). This numerical comparison illustrates the importance of the influence of $\mathbf{A}$ on $\mathbf{p}$ at classical scales.

### 3.4. Quantum physics

During a duration of 100 ms, there is a displacement of the $\mathbf{r}$ coordinate in the real part of the $\psi$ quantum wave function of $qAt/m = 1.5 \times 10^{-2} t$ m, on the order of $1.5 \times 10^{-3}$ m, the range of a macrocolumn (Ingber, 2015; Ingber et al., 2014). If $\Delta\mathbf{r}$ can be on the order of a synapse of a few nm (Stapp, 1993), then this spatial extent is on the order of about $\mu$m $= 10^4$ Å(Å= Angstrom $= 10^{-10}$ m). The displacement of $\mathbf{r}$ by the $\mathbf{A}$ term is much larger than $\Delta\mathbf{r}$. If the uncertainty principle is close to saturation, $\Delta\mathbf{p} \geq \hbar(2\Delta\mathbf{r})$ = $1.054 \times 10^{-34}/(2 \times 10^{-6}) = 5 \times 10 - 29$ kg-m/s. This would make $\Delta\mathbf{p}$ on the order of $\mathbf{p}$.

There may be specific interactions between $\mathbf{A}$ and $\mathbf{p}$ within neocortex, e.g., perhaps requiring explicit frequency dependence of $\mathbf{A}$. For example, processing speeds of information at quantum scales may be influenced by $\mathrm{Ca}^{2+}$ waves, e.g., via Grover's algorithm giving a quantum square-root versus a classical linear search (wherein the search is processed by the wave function instead of its square, the associated probability function) (Clark, 2014; Mukherjee and Chakrabarti, 2014), in turn influenced by $\mathbf{A}$, providing a feedback loop between states of attention at regional scales and control of STM information at molecular scales.

$\mathrm{Ca}^{2+}$ waves of coherent free ions (Pereira and Furlan, 2009), may develop pulsed-dynamical decoupling, generalizing the quantum Zeno effect (QZE) and "bang-bang" (BB) decoupling of ions from their environment, promoting long coherence times (Facchi et al., 2004; Facchi and Pascazio, 2008; Wu et al., 2012) as the system receives $n$ "kicks" during time $t$. The kicks may come from other quantum systems, e.g., other $\mathrm{Ca}^{2+}$ ions in the same wave developed in the regenerative processes discussed previously. Similar phenomena are investigated in quantum computation (Rego et al., 2009; Yu et al., 2012). These systems include distinguishable particles which can exhibit quantum coherence and entanglement via collisions (Benedict et al., 2012; Harshman and Singh, 2008). Other studies calculate how environment noise may lead to extended entanglement (Zhang1xz and Fan, 2013).

Recent work has clarified differences between continuous QZE and BB effects, the latter typically causing a collapse/decoherence of the wave-function at each short time kick into a sub-space of the original state, but ultimately also often greatly extending coherence times of the basic original state (Giacosa and Pagliara, 2014). The regenerative processes $\mathrm{Ca}^{2+}$ wave processes are in the class of BB models, wherein kicks from new individual/few ions at time $t_n$ are "weak measurements" projecting the previous wave-packet onto a sub-space of a weakly modified wave-packet. Each projection starts a new wave-packet at $t_n$ that starts its own evolution from the previous wave-packet $\phi(\mathbf{p}_{n-1}, t_{n-1})$ in momentum space or $\psi(\mathbf{r}_{n-1}, t_{n-1})$ in coordinate space, thereby prolonging the effective coherence time of the physical system into a new wave-packet $\phi(\mathbf{p}_n, t_n)$ in momentum space or $\psi(\mathbf{r}_n, t_n)$ in coordinate space.

Simple calculations of overlap wave functions from the effect of BB kicks on $\mathrm{Ca}^{2+}$ wave functions suggest that long coherence times are possible, and also suggests that $\mathbf{A}$ effects on $\mathrm{Ca}^{2+}$ wave functions may maximize their influence on STM at frequencies consistent with synchronous EEG during STM (Ingber, 2015). These calculations of survival times, $A(t) = < \phi^*(\mathbf{p} + \delta\mathbf{p}, t) | \phi(\mathbf{p}, t) >$ (Facchi and Pascazio, 2008), show that even many repeated kicks do not appreciably affect the real part of $A$, and these projections do not appreciably destroy the original wave packet, giving a survival probability $p(t) = |A(t)|^2$ per kick as $p(t) \approx \exp(-2.5 \times 10^{-7}) \approx 1 - 2.5 \times 10^{-7}$. Also, time-dependent phase terms in the exponent of the survival time $A$ are sensitive to time scales on the order of 1/10 sec (Ingber, 2015), the same scales prominent in STM and in synchronous neural firings measured by EEG. This suggests that $\mathbf{A}$ effects on $\mathrm{Ca}^{2+}$ wave functions may maximize their influence on STM at frequencies consistent with synchronous EEG during STM. Recent research suggests frequency modulation (FM), as well as amplitude and frequency modulation (AFM), dependence of the role of astrocyte influences on synaptic interactions via $\mathrm{Ca}^{2+}$ waves (just one of a few prominent $\mathrm{Ca}^{2+}$ processes) (Allam et al., 2012; Pitta et al., 2012; Volterra et al., 2014).

More detailed calculations likely will utilize PATHINT (Ingber and Nunez, 1995) or PATHTREE (Ingber et al., 2001) to take into account repeated BB kicks to sustain survival times. The use of these codes for path-integral calculations, in contrast to Monte Carlo codes, permits a time step-wise propagation of quite general time-dependent nonlinear multivariate propagators, during which new events may enter the propagation, e.g., simulating weak decoupling from interacting ions in $\mathrm{Ca}^{2+}$ waves, promoting long coherence times. However, here the propagator may not be easily defined, and it likely will live in complex $(x + \hat{\mathbf{i}}y)$ space which makes numerical details quite harder, unless a good model for the survival probability, defined above, is obtained and suffices.

Models still must consider interactions of $\mathrm{Ca}^{2+}$ ions in the wave packet with its immediate surroundings. Any degree of quantum coherence among ions in $\mathrm{Ca}^{2+}$ waves can only be resolved by experiment, but as yet there is no such evidence.

### 3.5. Coupling calcium waves with SMNI Lagrangian

SMNI develops time-dependent and nonlinear multivariate drifts and diffusions. This was calculated in the mid-point (Stratonovich or Feynman) representation, and all Riemannian contributions were calculated and numerically estimated for neocortex, as the nonlinear multivariate diffusions present a curved space (Ingber, 1982, 1983). Derivations of the mathematical physics are in texts (Langouche et al., 1982) and compact derivations have been given in several papers (Ingber, 1991).

EEG data is fit to SMNI, using data collected at several centers in the United States, sponsored by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) project. that the author made public in 1997 (Ingber, 1997; Zhang et al., 1997a,b, 1995), This project examines the influence of $\mathbf{A}$ on the background-noise synaptic parameters in the SMNI Lagrangian $L$, using ASA to fit 28 parameters across a circuitry underlying 6 electrode sites (Ingber, 2015; Ingber et al., 2014).

## 4. Conclusion

An SMNI model has been developed to calculate coupling of molecular scales of $\mathrm{Ca}^{2+}$ wave dynamics with $\mathbf{A}$ fields developed at macroscopic regional scales measured by coherent neuronal firing activity measured by scalp EEG, during tests of STM. This requires crosses molecular, microscopic (synaptic and neuronal), mesoscopic (minicolumns and macrocolumns), and macroscopic regional scales.

Over the past three decades, the SMNI approach has yielded specific details of STM and LTM phenomena, likely components of other phenomena like attention and $\mathbf{C}$, not present in molecular approaches (Ingber, 2012a).

More recently, SMNI calculations detail information processing of patterns of columnar firings, e.g., as observed in scalp EEG (Salazar et al., 2012), in terms of an SMNI vector potential $\mathbf{A}$ that influences molecular $\mathrm{Ca}^{2+}$ momentum $\mathbf{p}$, in turn influencing synaptic interactions. Explicit Lagrangians serve as cost/objective functions that are fit to EEG data (Ingber, 2015; Ingber et al., 2014).

Considerations of both classical and quantum physics give predictions of the influence of $\mathbf{A}$ on the momenta of $\mathrm{Ca}^{2+}$ waves during STM processing as measured by scalp EEG. Since the spatial scales of $\mathrm{Ca}^{2+}$ wave and macro-EEG are quite disparate, an experiment would have to be able to correlate both scales in time scales on the order of tens of milliseconds.

This study is robust against much theoretical modeling, as experimental data is used wherever possible. The theoretical construct of the canonical momentum $\mathbf{\Pi} = \mathbf{p} + q\mathbf{A}$ is firmly entrenched in classical and quantum mechanics at scales of both classical and quantum physics.

The SMNI model supports a process of $\mathbf{p}+q\mathbf{A}$ interaction at tripartite synapses, via the Dynamic Centering Mechanism (DCM) to control background synaptic activity, which acts to maintain STM during states of selective attention. Results of fits to EEG data presented here only demonstrate that fits to an $\mathbf{A}$ model are within reasonable statistical ranges of fits to a no-$\mathbf{A}$ model. While these fits are not conclusive for the importance of the $\mathbf{A}$ model, this study presents a testing methodology and code to further test the $\mathbf{p} + q\mathbf{A}$ interaction with future better EEG data.

However, other fits do demonstrate the importance of the Centering Mechanism (CM) for the no-$\mathbf{A}$ model and the importance of the DCM for the $\mathbf{A}$ model, giving further support to SMNI detailing STM (Ingber, 2015).

This study likely sheds some light on the multiple scales of neocortical interactions underlying $\mathbf{C}$, and how models can be developed faithful to experimental data. The scientific focus on computational models that include experimental data opens these ideas to testable hypotheses. This approach also suggests some nanosystem-pharmaceutical applications (Ingber, 2015). Results give strong confirmation of the SMNI model of STM, but only weak statistical consistency of $\mathbf{\Pi} = \mathbf{p} + q\mathbf{A}$ influences on scalp EEG.

This project investigates a synergy of interactions across otherwise disparate scales, i.e., the SMNI model is used to explore “top-down” influences of highly synchronous neuronal firings on “bottom-up” ionic processes that influence these firings.

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