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Thinking Nonlinearly about Brain Dynamics: A Neurocommentary

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Abstract

Despite significant progress over the past several decades in neural research there still remains an ingrained tendency to approach the field using overly reductionistic as well as linear theories and methods. We are just beginning to appreciate the complexity of the brain. A further shift in our "consciousness" about neural dynamics is needed to take the next steps in brain research. We need to use more reflexively what we have learned about the nonlinear dynamical and complex nature of the brain to attempt to "bootstrap" our own thinking processes about neural science itself.

1: Introduction

Significant progress has been made in recent decades in our understanding of the neural sciences. For example we now know that memory in the brain is distributed over neuronal networks that in many cases have appreciable spatial extent. We also know that the brain is much more plastic and adaptable than once thought – this has important implications for recovery and rehabilitation from insult to the brain. We have also made remarkable strides in development of new "windows" into brain structure and function including many exciting imaging modalities such as functional MRI, PET, MEG, and near-infrared to name a few. Yet, there remains an ingrained tendency toward the use of reductionistic tools as well as linear methods in neural research. To take the next bold steps in our understanding of the brain we must make more extensive use of what we've learned about the brain to help shape the direction of the research itself – we must bootstrap brain research by applying what we've learned about the brain to it - itself! This will require a subtle yet significant shift in mindset concerning how we approach such research over the next decade and beyond.

2: Bottom Up/Top Down Brain Research

There have been many advances in complexity theory and nonlinear dynamical systems research in general that have occurred over the last several decades. There are many examples of how these discoveries are now being applied to research in neuroscience (e.g. [1-3]). Yet the ingrained tendency toward reductionistic thinking still dominates brain science in general. For example the tendency to probe the neuron down to ever-increasingly smaller scales and to assume that the knowledge obtained generalizes to higher levels up the chain is very subtle and strong. While it is important to understand the molecular and cellular biology of neurons and glia we must overcome the inertia of the long-held belief on the part of some sectors of the neuroscience community that more probing into the machinery of the neuron will unlock all the secrets of the brain. It is clear from developments in neural network theory in general that we must develop and apply tools to the brain that allow us to understand how neurons interact with each other in small, intermediate, and large scale networks. At each of these levels different tools and strategies may be required. We need not only a bottom-up approach, but also a top-down one. New analysis tools remain to be developed that enable us to "see the forest for the trees" simultaneously without blinding ourselves to the details of the neuronal apparatus.

In psychiatry there has been a similarly disturbing trend toward "biologization" of the field – to reduce psychiatric conditions and illness almost completely to a physical level where it is assumed that medications will someday be the cure-all of such conditions. This implies that the software (mind) reduces and is equivalent to the hardware (brain). In the final analysis, this may turn out to be the case, but working now under this assumption is likely taking us down a blind alley.

3: Taking the Nonlinear Leap

These days engineers still spend a good deal of time studying linear systems, but now mainly to serve as a foundation for the study of nonlinear dynamical systems (NDS). Nowadays there is a significant trend teaching that linear systems are 1) crucially important in and of themselves (very true), and 2) a linear systems approach is not "the only game in town" and indeed is less of the norm in nature than nonlinear systems. In our linear system studies we learn about the law of proportionality (system outputs are proportional to their inputs) and about transformations (e.g., transformation of a summation of system inputs is equal to the sum of the transformed inputs). We learn the linear concepts of correlation, convolution and coherence, and about one-to-one structure/function relationships in various closed and open systems.

We also learn that systems scale linearly, that time runs the same forward or backward (second law of thermodynamics notwithstanding) and that reductionism is often the most sensible paradigmatic system analysis approach. The danger comes when we place an overemphasis on linearity and reductionism as the "most true" models of our world. For example, two sets of data may be highly related to each other by a U-shaped function (not uncommon in biology) even though their correlation coefficient is zero, the relationship between them in this case being nonlinear.

We appear to be slowly but steadily taking the leap toward making use of linear systems as a springboard for the study and understanding of NDSs (of which chaotic ones are a subset). However, it is the implications and consequences of NDS theory (not just knowledge of these systems in and of themselves) that are well worth cogitating upon [4]. One immediate and important implication of such systems is that they are "wholistic" – meaning that they are most properly viewed in terms of interacting units that yield more than the sum of their parts.

The use of the term "dynamical" in NDS also has important implications for our worldview. It relates to the evolutionary capacity of such systems – i.e, we must take into account their adaptability and their flexibility over time. These systems may also be self-referential which frequently leads to paradoxical and/or counter-intuitive behaviors. Fig. 1 is an example of such a system.

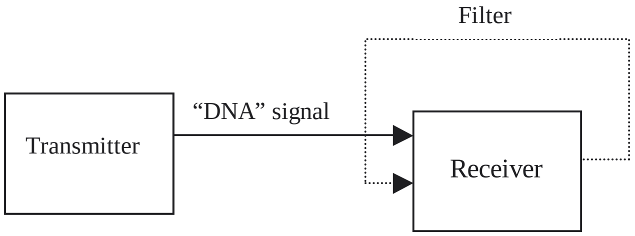

Fig. 1. A very powerful self-referential transmitter and a self-filtering receiver.

In the figure, the black box on the left is a very powerful transmitter that has a single function: it transmits ("gives") a special signal - one that is a pure essence of itself ("DNA" signal). This is a self-referential transmitter. The black box on the right is a powerful receiver: it can only receive a signal to varying degree. In this case the receiver is to receive a signal whose essence is one of pure transmission (giving). But there is a contradiction lurking here - if the receiver receives this particular signal it will take on the essence of the transmitter (to transmit or "give" only) and to that extent cease to be a receiver. One powerfully simple way to avoid the contradiction is for the receiver to self-limit. By filtering its own input it is performing a proactive rather than a reactive function – the only one it can. By performing this function the receiver in a sense mimics what the transmitter does thus receiving the transmitted signal via a paradoxical route. We see a similar principle embodied in self-feedback inhibition in many activities and functions of the nervous system in general.

Another simple example of the self-inhibition principle is an incandescent light bulb: if its positive and negative terminals make direct connect with each other, there is a short and the light bulb malfunctions (just prior to this there's a surge of light energy, then the bulb pops and goes out). The flow of electricity must be resisted or inhibited by a filament for a light bulb to function at its peak effectiveness over time. This is an example of the nonlinear principle that is colloquially expressed as "less is more." We see this principle at work in arguably its purest form in chaotic systems where small differences in initial conditions often lead to vastly different behavioral outcomes (sensitive dependence on initial conditions). It also has very important consequences for neural science. In functional neuroimaging for instance, a region of the brain that displays very low or even absent activity (bloodflow, metabolism, PET counts, etc.) may be just as important if not more so than another area of the brain that is actively "turned on."

The natural tendency for scientific and rational thinkers is to shy away from NDSs – such systems are not only (usually) analytically intractable, but they are mathematically messy, especially the chaotic ones which themselves lack long-term predictability. Part of this reticence is due to indoctrination in linear, analytical, and reductionistic, (left brain) modes of thinking. Underlying such thinking in the deep recesses is an assumption that we can "answer any question", that all is "knowable and solvable if we just apply ourselves hard enough." We are very uncomfortable with the notion that some things may simply be unknowable – at least on our current level. We are also uncomfortable with things that don't resolve themselves concretely and rationally.

As scientists we remain somewhat blind to the usefulness of not knowing all. This unknowingness paradoxically allows us to keep our jobs and brings more young people into the scientific fold! The right-brained, fuzzy, spatio-temporal pattern thinkers appear to have less trouble embracing some of the paradoxes that result from NDSs. They don't see themselves giving up any knowledge ground – rather they engage a different kind of knowing made possible by increasing their field of awareness – they recognize the inherent subjectivity in the scientific enterprise thus making room for the creative impulse. While taking a graduate class in biosignal processing about 20 years ago, one of my mentors (who shall remain nameless to protect the innocent) set off a light bulb in my head that remains lit: he said "signal processing is approximately 10% science, 90% art." Perhaps the percentages were exaggerated, but I for one have found the recognition of the inherent uncertainty of our world and subjective nature of the scientific enterprise useful in my own research.

4: Chaos on the Mind/Brain

As a subset of NDSs, chaotic systems in particular have far-reaching implications for neural science (as well as our worldview) that we're only just beginning to fathom. Although there is no universally accepted definition of chaos, it is fundamentally a paradox in that such systems manifest themselves in unpredictable ways while having an underlying deterministic basis. Chaotic systems are certain in and of their uncertainty! When we delve into such systems we should prepare our minds for entry into an "Alice in Wonderland"-like world! Yet there is a "method to their madness." We understand a number of important characteristics of such systems, even though they are for the most part unpredictable and analytically messy. For example they are characterized by "strange" attractors in phase space – a bounded region containing a large number of nonintersecting quasiperiodic trajectories characterized by fractal dimension [5]. It turns out that this characteristic of chaotic systems is actually useful in being able to manipulate their behavior without having to expend a great deal of energy (not usually easy to do in linear systems). We can cajole the system into behaving in a more orderly manner by applying small, properly timed "pushes" to move the system trajectory onto a particular quasiperiodic orbit in the phase space.

In 1992 this idea was used to attempt to control cardiac fibrillations in rabbit hearts [6] and since then "chaos control" methods for regularizing various bio- and other systems continue to undergo refinement and further development [7,8]. A reverse process to chaos control – known as "anticontrol of chaos" - that is inducing chaos in a system behaving in an orderly manner, was attempted with some success in 1994 in slices of rat brain (hippocampus) in which epileptiform EEG activity was chemically induced [9].

The very characteristics that make chaotic systems unruly and unpredictable also make them information-rich, flexible and adaptable – we *can* work with them! Walter Freeman and colleagues have utilized this concept in their study of the brain's olfactory system [10-12]. They recognized its implications for storage and retrieval of odor memories – chaotic attractors in the phase space make an excellent model of neural memory and learning in general. What we learn from these examples is that there is a new way of viewing NDSs – they can behave orderly and/or disorderly – but these are just flip sides of a story that can enhance our understanding of neural science and psychology if we utilize it properly [13].

5: EEG/Evoked Potential Brain Dynamics

Here we discuss some aspects of our own research into EEG/evoked potential dynamics that has implications for NDSs. Evoked potentials (EPs) are time-locked brain electromagnetic responses to presentation of discrete stimuli such as tones, light flashes, or touch. The magnitude of such responses measured at the scalp surface is very tiny (on the order of a few microvolts) and is usually considered to be "buried" within and independent of the ongoing background EEG (average amplitude of more than 100 microvolts). A simple linear model is often used to represent the EEG/EP relationship roughly as

$$y(t) = s(t) + n(t) \tag{1}$$

where $y(t)$ is the acquired response as measured usually from the scalp surface, $s(t)$ is the deterministic EP independent of the ongoing EEG "noise" $n(t)$. The usual procedure for measuring an evoked response is to apply the stimulus repeatedly (acquire many trials), then signal average the individual responses in order to estimate the brain's "true" underlying $s(t)$. In this way all time-locked brain activity will become signal enhanced while non time-locked activity will be reduced in the average. But the inherent assumptions of this linear model are not very realistic. These are that 1) the true underlying $s(t)$ is invariant from trial to trial, 2) the neural hardware that produces the EEG is truly independent of the generation mechanisms of the evoked potential (no EEG changes evoked by the stimulus), 3) the ongoing EEG is stationary from trial to trial, and 4) previous trial evoked responses do not influence later ones. We know that in real humans, evoked responses vary in time and that the EEG is not stationary, nor is it 100% independent of the evoked response. It is also far from clear that the generational mechanisms that produce the EEG and EPs are in fact independent.

This led us (and many others) to search for alternatives to the linear model by exploring other assumptions. One is that the neural systems that produce the EEG and EP are spatiotemporally the same. This leads to the hypothesis that when a stimulus is presented, the ongoing EEG undergoes a reorganization that may be mediated through a nonlinear transformation. In relationship form:

$$y(t) = f\,[e(t)] + n(t) \tag{2}$$

where $y(t)$ is the measured response, $e(t)$ is the ongoing EEG up to the moment of stimulus presentation, $n(t)$ is any non event-related activity, and $f\,[.]$ is the transformation function. The reorganization may reflect a timeshift in the neuronal responsiveness – in other words a phase reorganization of the ongoing EEG [14,15]. A related, alternative assumption is that only a portion of the neural apparatus undergoes this phase shift leading to a "hybrid" model:

$$y(t) = f\,[e(t)] + s(t) + n(t) \qquad (3)$$

where $s(t)$ is the activity from the portion of the neural apparatus that responds independently to the stimulus with respect to the ongoing EEG, $e(t)$. This is currently an active area of speculative research.

Fig. 2 shows averaged evoked potential responses of a neurologically normal adult male to repeated light flashes presented randomly and measured from a centro-occipital scalp electrode. EEG was measured starting 1 second before each flash and the responses to about 1000 flashes were digitally processed. The relative amount of power in the alpha EEG frequency band (8-13 Hz) was computed in each 1 sec. prestimulus epoch per trial. Then the single trials were sorted on this power measure and amplitude selective averaged visual EPs were computed for each 4% alpha power increase (from top trace to bottom). In the poststimulus 1second period, one sees a gradual increase in the amplitudes of the P1 and N1 VEP components (marked in Fig. 2) as a function of increasing relative prestimulus alpha power. This shows that the evoked response is sensitive to the amplitude of the ongoing EEG: VEP amplitude is increased with increased alpha activity present. These results at least argue that model (2) or model (3) better explain these data than model (1).

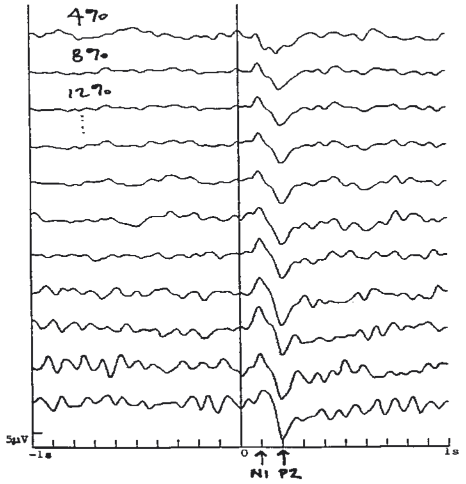

Fig. 2. Effect of increasing relative prestimulus alpha power on evoked response amplitude.

Fig. 3 shows a similar plot to Fig. 2 in another neurologically normal adult male. Here the trials have been sorted based on the phase angle of the EEG at the moment of stimulation for all those trials that had dominant ongoing alpha activity to be able to adequately measure a sinusoidal phase angle. Trials were sorted into eight 45° bins (totaling one sinusoidal cycle) and the trials contained in each bin were averaged to produce phase selective visual EPs. Fig. 3 shows the clear morphological differences in VEP shape as a function of phase angle at time of stimulus presentation. The timing as well as the amplitude of critical components of the VEP (e.g., the P1 and N1 peaks) are sensitive to brainstate at the moment of stimulation. This indicates that the activity of the brain (as reflected in the ongoing EEG) adapts or self-modifies partially by making use of what is happening in its environment. This phase sensitivity is somewhat analogous to a pendulum driven by an outside impulsive force. Its resultant motion is a function not only of the timing, direction and amplitude of the impulse, but of the pendulum's amplitude and phase angle at the moment when the impulse is applied.

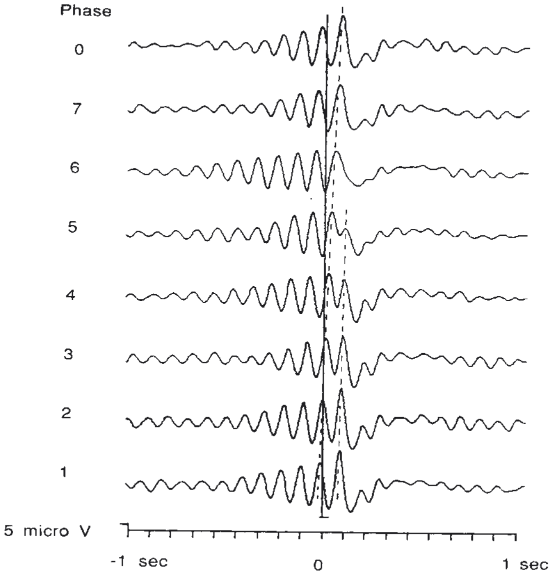

Fig. 3. Selective averaged EPs based on phase angle at the time of stimulus presentation. Trials with dominant ongoing alpha EEG rhythms.

6: Structure/Function Brain Relationships

Despite much progress in the field, there remains an ingrained tendency toward one-to-one structure/function relations in neural science (e.g., neuroimaging and functional localization studies such as MEG, PET, fMRI). The more we come to realize that we must adopt a "many-to-many" approach to understanding neural information processing the better off the field will be. We must use existing tools to explore patterns of interactivity in the brain and develop new ones. Trying to collocate the "me" in the brain (the seat of consciousness) may be another example of traversing a fruitless path. Localization studies themselves often imply that we can isolate a particular brain function from all others and put an address on it. This may not only be another disguised form of reductionistic, analytic thinking but may also be missing the forest for the trees. Clearly there are brain functions that can be teased apart from others. But in a functioning individual we can't do this exclusively, we must put the functions in context with one another and the whole individual. A related example is that an individual with psychiatric illness should not be diagnosed without taking into account his/her family situation and history, genetic predispositions, and the environment in which he/she both finds and puts him/herself in. Fig. 4 is a tongue-in-cheek illustration of the state of neuro-localization today, and Fig. 5 is the other extreme view of this. On the one hand we're looking for the seat of consciousness (or "me") in the brain (recall that the ancients thought it was not in the brain at all, but in the heart!), on the other hand (Fig. 5) we're dispersing it too widely across a large neural network.

One interesting example of the search for a happy medium between the depictions in Figs. 4 and 5 comes from the study of spatial cognition [16]. It is known that the posterior parietal cortex (PPC) is a major brain center for carrying out "where" functions that enable individuals to successfully navigate their environments.

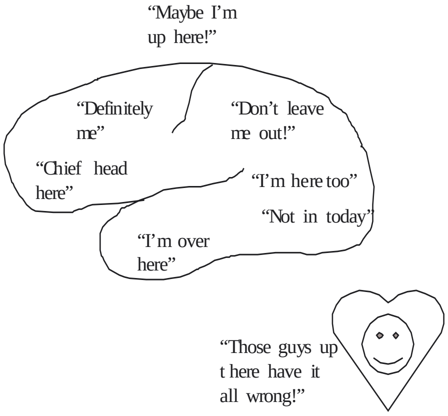

Fig. 4. One (extreme) view of the state of neural localization.

It receives multiple projections from primary visual, auditory and somatosensory cortices in addition to subcortical structures such as the superior colliculi. The PPC integrates these inputs to produce a space representation of an individual's environment that is predominantly ego-centered. That is, its frame of reference is with respect to the effectors of the body, such as the arms and legs. In some sense then, the PPC produces a space map for each of the bodies' effectors. Thus it has an integratory function of its inputs while at the same time being able to perform segmentation in order to produce multiple maps that allow the individual to interact with his/her environment.

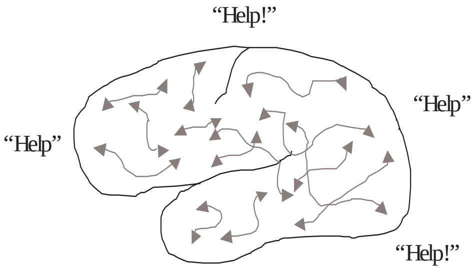

Fig. 5. The other extreme.

The hippocampus is also heavily involved in spatial information processing: it tends to produce a representation which can be thought of as "object-centered" as opposed to "body-centered" – it is concerned more with "what's out there" as opposed to "what's in here." Clearly, each individual must have both systems to get around in the world, but these are not the only neural systems involved with spatial cognition. They are also not unitary – they operate interdependently and it is understanding this interdependence that remains a major neuroscience challenge.

Another cautionary tale concerning how we view brain structure/function relations (Fig. 6) is an example and consequence of NDSs. The subsystems labeled TSICs represent "temporary systems in control." They are representative of thoughts, action plans, or neurofunctional subroutines that animate us from moment-to-moment. They become "up front", or command our attention at various points in time on a continual basis. These TSICs are dynamically changing, some may be spontaneously created while others disappear. They also may interact to some degree. Now we hypothesize the existence of an upper level black box which we refer to as the "true system." This system actually enables the TSIC subsystem to function. With respect to this "true system" then, the TSIC subsystem can be considered in some sense "less true" than itself. One can imagine one or more of these "true system" blocks, perhaps also interacting at this higher level (not shown in Fig. 6). An interesting consequence of such a system is that when one or more TSICs are "in process" in the foreground it produces a side-effect: it essentially inhibits or obscures the "true system" in the background – much like a whining child in the presence of his/her parent who is conversing with a friend. The role of the "true system" can effectively be rendered invisible to the outside world while the TSICs are active.

We acknowledge that the brain consists of neural networks consisting of many interacting parts. Reminiscent of Fig. 6 we also assume that the complexity of such networks is associated with emergent properties underlying them. Essentially, a virtual system, perhaps just as complex (if not more so) than the hardware itself, can exist with properties that are only constrained by the hardware (circuits, genes, molecules, synapses, neurons, etc.) rather than defined by it.

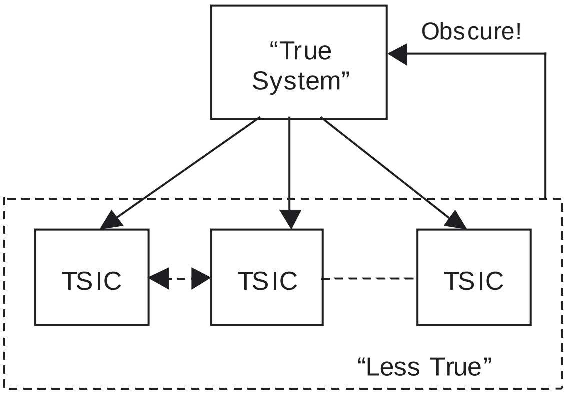

Fig. 6. Foreground/background system: when the TSICs are active the "True System" is effectively obscured.

One such system may be the mind itself or conscious experience, containing a whole new set of rules and organizing principles barely resembling those of the hardware. By analogy the operating principles of any TV program are independent of those governing the CRT that displays it. Furthermore, we often imagine that these virtual systems themselves arise from the hardware that produces them. But how do we know that Fig. 6 isn't a more accurate model: that the virtual system is the "more true" one? Or, perhaps it's not very useful to try to figure out which comes first, the chicken or the egg. Perhaps it would be more reasonable to assume the hardware and "software" are on an equal footing and see what path to discovery that takes us down.

7: Some Lessons from Physics

There are clear trends in physics away from materiality and toward wholism. In particle physics for example, the notion of fuzzy fields has pretty much replaced the idea that there are fundamental bounded particulates of matter with independent existences. In this way physics has already struck a significant anti-reductionistic blow. The concept of "interaction dynamics" replaces reductionism in particle physics, and system self-consistency moves ahead of causality in importance [17]. Nature appears to have a fractal character: it is self-referential and self-bootstrapping – further characteristics of NDSs. Functional correlation between widely separated particles/waves in spacetime speaks to the interdependence and connectivity underlying natural phenomena. The equivalence of energy and matter tells us that we better pay attention to the fully real, ethereal world, and not assume it is less real than the apparent, visible, matter-based world. One lesson of Heisenberg's Uncertainty Principle relates to the fact that we influence the measurements we take from nature – thus we cannot stand outside and distinct from what we observe, and argues that we explore our role within physics. Is our existence dependent on the universe, is it the other way around, or something in between? Are the very tight ranges of certain universal parameters in which the existence of life is critically dependent merely a coincidence or is there an underlying "virtual system" at work here?

8: Discussion

When I was a small boy the butterflies that inhabited the Catskill Mountains of New York State fascinated me. I would chase after them with my butterfly net to near-exhaustion. Then someone convinced me to take an alternative, right-brained approach that never occurred to me before: wait patiently and quietly for the butterflies to come near to me! Forcing myself on the butterflies was definitely less effective than letting them come near to me. Initially I ruled out this successful strategy as too simple-minded to ever be effective. I had to go after what I wanted directly. We are fundamentally discussing in this work taking into account the role of our own consciousness in the neural research we do. We tend to perform this work as if we have the ability to be completely objective (and rational) and stand outside the object of study. We tend to assume in our smugness that our path is the right one – that we <u>can</u> know all that we set out <u>to</u> know. We take a kind of imperialistic view of neural science in this way by believing that if we force ourselves hard enough upon the problems all their secrets will automatically yield to us. Maybe yes, maybe no. But by checking this attitude at the door and by "letting the butterflies come to us," I sense that more of those secrets will paradoxically open up to us. Reverse psychology has a scientific basis! Fact: we now have a much more powerful hand in our own re-creation and evolution – we are re-directing in a profound way the engineering of our own brains as well as our minds. If we're not careful we may delude ourselves into creating a new reality for ourselves in which we become the ultimate creators. There is great potential danger here. History has shown us time and again how our unchecked egos have led us to untold disasters visited upon ourselves.

Perhaps a shift in our own consciousness can help us here. The shift is toward a consciousness of self-bootstrapping by increasing our awareness of not only our own mental processes, but questioning our role (if any) in transforming our self-perceived universe. Opening up to the possibility that we may not simply place our brain/mind on a table and examine it as if it were totally disconnected from ourselves and the world may free us from a too-tight chain of causal reasoning. Opening up to the possibility that some avenues of our current drive toward knowledge are dead ends may paradoxically move us closer toward better avenues of knowledge. An example is the one I discussed in the Introduction – we must move closer to understanding patterns of interaction as opposed to isolating units (neurons, glia, etc.) atomistically – while at the same time learning how to incorporate what we've already learned about those units into the big picture.

If we are to know all there is to know we might just be sacrificing our own humanity. Not knowing has an important human purpose – it feeds our curiosity and maintains both our humility and our ability to remain in awe – all necessary scientific tools! We also need to develop a consciousness of openness to paradox – given what we now know about the brain in terms of complexity and nonlinear dynamics – this would be a more appropriate mode of scientific self-reflection – paradoxical thinking is becoming more the norm (perhaps a paradox in itself!).

Some may accuse me of trying to inject Eastern thinking, spirituality, and/or mysticism into neural science. We don't have to put labels on everything. Science is a dynamic, creative and evolving process. The physicists could justifiably be accused of a similar shift as was discussed above. If we take a judgmental stance on these matters it may be further injurious to progress. At the same time we must always maintain our healthy skepticism. We must be cognizant of our tendency to politicize science while appreciating how its history, developments and discoveries have brought us to the present moment.

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