Neurodynamics of expectancy that underlie the placebo effect

Walter J Freeman
Department of Molecular & Cell Biology

http://soma.berkeley.edu
The placebo effect stems from the dynamics by which sensations are transformed into perceptions.

The seamless fabric of the dynamics of mind, brain and behavior is revealed by the ECoG.

- Perception is **intentional** – self-organizing.
- Perception is **categorical** – attractor landscapes.
- Perception is **cinematic** – phase transitions.
"... the tiger salamander ... is appropriately named, for within the obscurity of its contracted world it is a predaceous and voracious terror to all humbler inhabitants."

C. Judson Herrick (1948), p. 3

The Brain of the Tiger Salamander

Herrick concluded that the salamander brain is the best surviving example of the primitive vertebrate brain from which we evolved.
Perception is the act of creating the meaning of sensations. All sensory systems have the same perceptual code.
Intentional dynamics creates knowledge from information by meaningful interactions between brains.

Low energy
sensory categories
information
motor signs

High energy
coyote brain [knowledge]
“eat”
meaning
“die”
rabbit [knowledge]

Low energy
motor signs
information
sensory categories

(basins of attraction)

Prepyriform EEG, hungry cat smelling fish.

An hour later, fed to satiety.

Freeman, 1958
Single-shock electrical stimulation of the input axons to the olfactory bulb causes a brief increase in activity, which is followed by an exponential return to the background level.

The rate of return increases with increased stimulus intensity. The mechanism is saturation by refractory periods of axons.
With decreasing stimulus intensity, response amplitude extrapolates to zero at threshold.

With decreasing amplitude the rate of return to baseline slows to zero rate at threshold.

The results prove that cortical background activity is governed by a non-zero point attractor. It is self-regulated.
Intentionality (intendere) was conceived by Aquinas as analogous to bow string (tendon) driving an arrow. Dynamics conceives it as non-zero point attractors.
An example of intentionality
First Law of Thermodynamics

“[My] approach is derived from clinical observations of ‘excessively intense’ ideas in hysteria. … I have in mind the principle of neuronic inertia. It finds expression in a current passing from dendrites to axon. … Memory is in contacts between the neurons that function as barriers.”


[Three years later, Foster and Sherrington named the ‘synapse’.]
The placebo effect accrues from the dynamics by which sensations are transformed into perceptions.

The seamless fabric of the dynamics of mind, brain and behavior is revealed by the ECoG.

• Perception is intentional – self-organizing. The energy of intention comes from mutual excitation.
• Perception is categorical – attractor landscapes.
• Perception is cinematic – phase transitions
A state transition is induced in the olfactory system by each inhalation that signals a new sensory input.

Freeman, 1972
Left hemisphere of the rabbit brain with size and location of 8x8 electrode arrays. The circles show modal diameters of gamma (smaller) and beta (larger) activity domains.
Each new pattern of neural activity occupies the whole bulb. It is formed and continually updated by learning.
Each frame gives a point in 64-space. Multiple frames are projected into 2-space for classification, here by stepwise discriminant analysis. Similar patterns give clusters of points.
Correct classification depends on the number of channels, not their locations. No channel is more or less important than any other. The spatial density of information is uniform, despite variation in content.
Pattern classification under serial conditioning.

Patterns are unique to subjects. Every pattern embodies the life-long experience of each individual.
The state space contains an attractor landscape that emerges with each new sensory stimulation, and embodies a set of Bayesian prior probabilities of expected stimuli.
Partial complex seizures disrupt normal behavior.

- Each inhalation opens the landscape realizing limit cycle attractors by a phase transition.

- Expectancy creates a landscape of attractors that is governed by a non-zero point attractor.

- Flat EEG is due to a zero point attractor.

From Freeman (1987)
Meaning vs. Information

- ECoG patterns represent meaning, not sensory information. They result from tests of hypotheses.

- Hypotheses are tested by chaotic dynamics whenever cortex is destabilized by input.

  - All that a brain can know is the hypotheses it has created and tested in itself by brain chaos.

- Great quantities of irrelevant sensory information are deleted by convergence to an attractor.

- Convergence enacts generalization and abstraction.
Lashley’s Dilemma
‘Generalization is one of the most primitive basic functions of organized nervous tissue.’ …
‘Here is the dilemma. Nerve impulses are transmitted through definite cell-to-cell connections. Yet all behavior seems to be determined by masses of excitation. … The problem is almost universal in activities of the nervous system.’ [p 306]

His dilemma was resolved by chaotic dynamics.
The placebo effect accrues from the dynamics by which sensations are transformed into perceptions.

The seamless fabric of the dynamics of mind, brain and behavior is revealed by the ECoG.

- Perception is intentional – self-organizing. The energy of intention comes from mutual excitation.
- Perception is categorical – attractor landscapes. Categories come from basins of attraction.
- Perception is cinematic – phase transitions
Cognitive-related EEG information is in the spatial domain.

Left hemisphere of the rabbit brain.
Squares show 8x8 electrode arrays.
Circles show modal and 95% half-power diameters of domains of gamma activity; beta domains are larger.
EEGs simultaneously from limbic and sensory cortices
A. gamma activity: 30 - 80 Hz

\[ N = 40 \]
\[ \text{window} = 128 \text{ ms} \]
\[ \text{step} = 64 \text{ ms} \]
\[ p < .01 \]
\[ p < .05 \]

B. beta activity: 12 - 40 Hz

\[ N = 40 \]
\[ \text{window} = 128 \text{ ms} \]
\[ \text{step} = 64 \text{ ms} \]

C. gamma activity: 30 - 80 Hz

20 trials, CS+

D. Beta activity: 12 - 40 Hz

20 trials, CS+
EEG amplitudes from visual, auditory, somatic, olfactory, and entorhinal cortex formed a feature vector to classify. Removal of any component reduced classification.

From Freeman & Burke, 2003
Rayleigh noise
From Kozma and Freeman, 2011
The placebo effect accrues from the dynamics by which sensations are transformed into perceptions.

The seamless fabric of the dynamics of mind, brain and behavior is revealed by the ECoG.

• Perception is intentional – self-organizing. The energy of intention comes from mutual excitation.
• Perception is categorical – attractor landscapes. Categories come from basins of attraction.
• Perception is cinematic – phase transitions

Knowledge is created by neural condensations.
“A movie, with its taut stream of thematically connected images, its visual narrative integrated by the viewpoint and values of its director, is not at all a bad metaphor for the stream of consciousness itself. .... The mechanism of our ordinary knowledge is of a cinematographical kind.”

New York Review, 2004
In the garden of the Villa Borghese

<table>
<thead>
<tr>
<th>Aquinas</th>
<th>Neurodynamics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensatio</td>
<td>Sensory receptors</td>
</tr>
<tr>
<td>Phantasmata</td>
<td>Action potentials, “raw sense data”</td>
</tr>
<tr>
<td>Abstractio</td>
<td>Local wave packet generalization categorization</td>
</tr>
<tr>
<td>Sensus Communis</td>
<td>Gestalt, multisensory percept</td>
</tr>
<tr>
<td>Imaginatio</td>
<td>Global wave packets</td>
</tr>
<tr>
<td>Intellectio</td>
<td>Speech, cognition</td>
</tr>
</tbody>
</table>

Thomas Aquinas 1225-1274
Avicenna  980-1037
(Abu Ali Hussein)

Rabbi Moshe ben Maimon
Maimonides 1135-1204
Elizabeth called Descartes on the mind-body problem.
Sir Thomas Willis 1621-1675 coined "voluntary" vs. "reflex"

Basal view of a human brain drawn by Sir Christopher Wren

"animal spirits" vs. "the soul"
Helmholtz, an army surgeon, became a neuroscientist, discovered and proved the First Law of Thermodynamics: the Conservation of Energy.

He measured the conduction velocity of the action potential, and thereby demonstrated that the nerve impulse is an electrochemical wave and not a flux of animal spirits.
“The involuntary transmission of nerve-force may or may not be accompanied by consciousness. Why the irritation of nerve-cells should generate or liberate nerve-force is not known; but that this is the case seems to be the conclusion arrived at by all the greatest physiologists such as Müller, Virchow, Bernard, and so on.”

The Expression of Emotions in Man and Animals (1863) p. 70
Conservation of Nerve Energy

[It is] “… an unquestionable truth that, at any moment, the existing quantity of liberated nerve-force, which in an inscrutable way produces in us the state we call feeling, must expend itself in some direction. … An overflow of nerve-force, undirected by any motive, will manifestly take the most habitual routes.”

Essays: Scientific and Political (1893) p. 109

Herbert Spencer 1820-1903
“A epileptic fit is an excess of a normal process during what is called voluntary action. ...

“We have, in the case of ‘discharging lesions’, to consider not only the quantity of energy liberated, but the rate of its liberation.”

”Resistances will be considered later.” (1882)

“No more of this was published.”
(Note in margin, “Selected Writings” 1912)
Letter to Fliess on 25 May 1895:

"Actually, a satisfactory general conception of neuropsychotic disturbances is impossible if one cannot link it with clear assumptions about normal mental processes."

Wilhelm Fliess 1858-1928  Sigmund Freud 1856-1939
Letter to Fliess
22 September 1898:

“I do not know how to go on, neither theoretically nor therapeutically, and therefore must behave as if only the psychological were under consideration. Why I cannot fit it together [the organic and the psychological] I have not even begun to fathom.”
At the beginning of the 20th century, brain theory collapsed.

Psychiatry and neurology disintegrated.

The reason: ‘nerve energy’ is not conserved; brains are open, dissipative systems for energy, but closed with respect to form and meaning.

A corollary: mind was again split from brain.
Freud’s Legacy of Deterministic Equilibrium Thermodynamics

“In his attempt to be scientific, Freud made what philosophers call a category mistake. He substituted a uniform, impersonal concept for the idiosyncratic, highly variable experience of the individual. …

“Freud’s category error was perpetuated by ego psychologists who enshrined the term defense mechanisms.”

Arnold Modell, Division 9 Lecture, p. 9.
“Freud radically altered his initial vision of the unconscious … not as an area in which knowledge is processed, but as a place of conflict between instincts seeking discharge and the forces of repression.

The primary function of the revised unconscious was not to process knowledge but to prevent unacceptable impulses, wishes and fantasies from becoming conscious.”
Regression to animism
Regression to mechanism and materialism
Regression to taxonomy, leading to DSM
The neurochemistry of affiliation:

- Learning
- Unlearning

Neuroamines
- Norepinephrine
- Dopamine
- Acetylcholine
- Serotonin
- Histamine

Neuropeptides
- Oxytocin
- Vasopressin
- Endorphins
- Cholecystokinin
- Substance P

Create connections, dissolve them

Regression to neurochemistry
Cognitive Neurobiologists failed to recognize or correct the category error.

In the 1950s upon the emergence of computational neural science, neuroscientists replaced the failed quantity of “nerve energy” with the new quantity of “neural information”: new wine in an old bottle.

They adapted the metaphor of the flow of energy: sources and sinks information flow rates channel capacities information = negentropy.
Likewise by Shannon:

“The fundamental problem of communication is to reproduce a message. … Frequently the messages have meaning. … These semantic aspects are irrelevant to the engineering problem.”


Claude Shannon 1916-2001
• This step completes my summary description of how the world and other people are internalized by the action-perception cycle, so that in Merleau-Ponty’s terms, the mind is the structure of behavior.

• The process has been described repeatedly in terms other than those of neurodynamics for 700 years.

• The question arises, what is the barrier that impedes widespread understanding and use of this conception of human nature in a materialist society?
• My answer is that a broadly accepted theory of brain science and psychiatry must be based soundly in the prevailing science of the era.

• The history of Western civilization shows that oncordance has been achieved in three eras: that of Aristotle, that of Aquinas, and the era of 19th century thermodynamics.

• I believe that interpersonal psychiatry can flourish only when grounded in nonlinear, nonequilibrium dissipative thermodynamics.
Carnot founded thermodynamics in 1824. His theory enabled engineers to design workable steam engines.
“Once or twice I have been provoked and have asked the company how many of them could describe the Second Law of Thermodynamics. The response was cold; it was also negative. Yet I was asking something which is about the scientific equivalent of: 'Have you read a work of Shakespeare's?' ” Charles Percy Snow, The Two Cultures. 7 May 1959.