Complex systems perspective in neuroscience - historical and current approaches

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http://www.bscs-us.org/
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1. Systems Neuroscience: Structure, Function and Dynamics

2. Brain Connectivities

3. Disconnection Syndromes

4. Schizophrenia - a broken hermeneutic circle

5. Dynamics, Causality and Criticality

6. Computational Neurology and Computational Psychiatry: two glimpses
Twenty years ago

Both structure-based "bottom-up" and function-based "top-down" models offer coherent concepts by which to evaluate the experimental data. The goal of this book is to point out the advantages of a multidisciplinary, multistrategied approach to the brain.
Brain Connectivities

Between determinism and randomness

“Whenever he is looking at any piece of neural tissue, the investigator becomes immediately confronted with the choice between two conflicting issues: the question of how intricate wiring of the neuropil is strictly **PREDETERMINED** by some genetically prescribed blueprint, and how much freedom is left to **CHANCE** within some framework of statistical probabilities or some secondary mechanism of trial and error, or selecting connections according to necessities or the individual history of the animal. Even on brief reflection one has to arrive at the conclusion that the case may not rest on either extreme...” (J. Szentágothai; my boldfaces: PE)

”Quasi-randomness”??
Noise-induced ordering
Brain Connectivities

Specificity Versus (Quasi-) Randomness in Cortical Connectivity

J. Szentágothai

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NEURAL CONNECTIVITIES: BETWEEN DETERMINISM AND RANDOMNESS

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RÉNYI ALFRED—SZENTÁGOTHAI JÁNOS
AZ INGERÜLETÁTVITEL VALÓSZÍNÜSÉGE EGY EGYSZERŰ KONVERGENS KAPCSOLÁSÚ INTERNEURONÁLIS SYNAPSYS MODELLBEN
(Előzetes közlemény)

Alfréd Rényi
Michael Arbib, János Szentágothai, Luigi Ricciardi (Capri, 1992)
Brain Connectivities

- **Random graph**: A graph with uniform connection probabilities and a binomial degree distribution. All nodes have roughly the same degree (‘single-scale’).

- **Small-world graph**: A small-world network is a type of mathematical graph in which most nodes are not neighbors of one another, but most nodes can be reached from every other by a small number of hops or steps.

- **Scale-free graph**: Graph with a power-law degree distribution. 'Scale-free' means that degrees are not grouped around one characteristic average degree (scale), but can spread over a very wide range of values, often spanning several orders of magnitude.
Modes of brain connectivity. Sketches at the top illustrate structural connectivity (fiber pathways), functional connectivity (correlations), and effective connectivity (information flow) among four brain regions in macaque cortex. Matrices at the bottom show binary structural connections (left), symmetric mutual information (middle) and non-symmetric transfer entropy (right). Data was obtained from a large-scale simulation of cortical dynamics ...(Olaf Sporns: http://www.scholarpedia.org/article/Brain Connectivity)
Disconnection syndromes

Disconnection syndromes

- Geschwind's (general) disconnection syndromes (1965)
- The pathways implicated in the principle syndromes described by Geschwind, classified into three types:
  - sensory-limbic disconnection syndromes (dotted lines)
  - sensory-motor disconnection syndromes (dashed lines)
  - sensory-Wernicke’s area disconnection syndromes (solid lines)
Disconnection syndromes

Griesinger argues that mental illnesses are brain disorders

Meynert works on cytoarchitectonic maps of the cortex and suggests brain disorders to be related to fiber pathology

Wernicke postulates ‘Sejunctionshypothese’

Wernicke’s Grundriss der Psychiatrie is published one year after his death from a bicycle accident

Kleist develops functional brain atlas based on lesions in veterans

The first PET evidence for disconnectivity in schizophrenia

Sporns and Hagmann introduce the ‘connectome’

1840

1845

1865

1899

1906

1934

1988

2005

1995

1952

1911

1899

1888

WW I

WW II

Discovery of chlorpromazine’s antipsychotic properties; return to neurobiological research

Bleuler coins the term ‘schizophrenia’ and postulates dissociation as the underlying mechanism

The 6th edition of Kraepelin’s textbook inspires a paradigm shift in psychiatry

Golgi, Ramón y Cajal, and Forel discover that the brain consists of interconnected neuronal cells

DISCONNECTION SYNDROMES

- Impairments in functional macro-networks in schizophrenia was suggested.

- Abnormal prefronto-hippocampal connectivity?

- Changes in effective connectivity: (i) intrinsic connectivity of the network, (ii) input-dependent changes.


Which connections are significantly impaired during schizophrenia? Quantitative estimation for the degree of impairment.
Schizophrenia - a broken hermeneutic circle

Understanding situations: needs hermeneutic interpretation

- logic, rule-based algorithms, and similar computational methods are too rigid to interpret ill-defined situations,
- hermeneutics, "the art of interpretation" can do it.
- hermeneutics: emphasize the necessity of self-reflexive interpretation and adopts circular causality

To understand other minds: i.e. to show empathy is to simulate other minds.

The neural basis of theory of mind related to mirror neurons, which is the key structure of imitation, and possibly language evolution (Michael Arbib).

A failure in interpreting self-generated action generated by the patient himself: (lack of ability to close the hermeneutic circle) can be characteristic for schizophrenic patients (Chris Firth). -> Neural basis: disconnection syndrome,
So far so good. But what is hermeneutics?

"A physicist friend of mine once said that in facing death, he drew some consolation from the reflection that he would never again have to look up the word "hermeneutic" in the dictionary."

(Steve Weinberg)

Hermeneutics: branch of continental (i.e. mainland European) philosophy which treats the understanding and interpretation of texts.

**Hermeneutic circle**: definition or understanding of something employs attributes which already presuppose a definition or understanding of that thing. The method is in strong opposition of the classical methods of science, which does not allow such kinds of circular explanations.
Schizophrenia fMRI study: experiment and methods

**Task:** learning of object-location associations over repeated encoding and retrieval periods

**Subjects:** 11 diagnosed with schizophrenia and 11 healthy controls

**DCM:** generative model of the BOLD signal, parameters estimated by Bayesian statistics

\[ x = (A + \sum_{j=1}^{N} u_j B^j) x + Cu \]
\[ y = \lambda(x, \theta_{\lambda}) \]
\[ p(\theta | y, M) = \frac{p(y | \theta, M) p(\theta | M)}{p(y | M)} \]

**Model space:** five areas involved, two sets defined by varying connections and the effects of conditions

**Model selection:** by the estimation of the Bayesian evidence
Schizophrenia fMRI study: results

Parameter level comparison: connections between PFC and HPC and HPC and IT are impaired

Slow learning: differentiated from the illness by model probability distribution

Model comparison: top-down information flow and the modulatory effects of conditions are less likely to be present in schizophrenia

Schizophrenia - a broken hermeneutic circle

the role of prefrontal cortex: interpretation of the incoming signal: new associative learning vs. recall

less accurate interpretation/control -> poorer performance:

if the PFC does not tell to the hippocampus when to learn and when to recall; -> poorer performance

the hermeneutic circle is broken

therapeutic strategy: towards a computational psycho-pharmacology: another story
Dynamics, Causality and Criticality

Hermenetutic circle can be implemented by circular and network causality
Systems with feedback connections and the systems of these connected loops can be understood based on the concepts of circular and network causality.

Neural implementation of circular causality
Functional macro-network for associative memory
Dynamics, Causality and Criticality

CIRCULAR CAUSALITY OF THE SELF

Figure 2. Circular causality expresses the interrelations between levels in a hierarchy; a top-down macroscopic state simultaneously influences microscopic particles that bottom-up create and sustain the macroscopic state. The state exists over a span of inner time in the system that can be collapsed to a point in external time. Events in real time are marked by changes in the state of the system, which are discrete. This conceptualization is widely used in the social and physical sciences. In an example used by Haken (1983), the excited atoms in a laser cause coherent light emission, and the light imposes order on the atoms. The laser was also used by Cartwright (1989) to exemplify levels of causality, by which she contrasted simple, direct cause-effect relations not having significant interactions or second-order perturbations with higher order “capacities” (according to her, closely related to Mill’s “tendencies”, but differing by “material abstraction”, p. 226), which by virtue of abstraction have an enlarged scope of forward action, but which lack the circular relation between microscopic and macroscopic entities that is essential for explaining lasers - and brains. The notion of an ‘agency’ does not enter, and multiple scales of time and space are required for the different levels.

Walter Freeman (1927-2016)
Correlation Vs Causation

- Correlation does not imply Causation

- Correlation only means that two events co-exist more often than ordinary chance.[2]
Is there any way to infer causality?
Dynamics, Causality and Criticality

- Granger causality: (Nobel prize in economics)
- A variable $X$ Granger-causes $Y$ if $Y$ can be better predicted using the histories of both $X$ and $Y$ than it can using the history of $Y$ alone.
- linear autoregression
- strong assumptions (linearity, stationarity, Gaussian noise etc.)

\[
X_1(t) = \sum_{j=1}^{p} A_{11,j} X_1(t - j) + \sum_{j=1}^{p} A_{12,j} X_2(t - j) + E_1(t) \quad (1)
\]

\[
X_2(t) = \sum_{j=1}^{p} A_{21,j} X_1(t - j) + \sum_{j=1}^{p} A_{22,j} X_2(t - j) + E_2(t) \quad (2)
\]
Cross Convergence Map: A new framework for causality analysis

Detecting Causality in Complex Ecosystems
George Sugihara,1* Robert May,2 Hao Ye,1 Chih-hao Hsieh,3* Ethan Deyle,1 Michael Fogarty,4 Stephan Munch5
Science 338, 496 (2012)

A new approach, promising
• Detection of circular causality
• Causality in nonlinear system
• Deterministic (chaotical) system
Dynamics, Causality and Criticality

• An ongoing project in Budapest (Zoltán Somogyvári): (Even circular) causality detection between brain regions
• based on Sugihara method:
• S. method uses the theory of nonlinear state space reconstruction (Taken’s theorem)
• nearby points on the manifold of one variable can be used to estimate nearby points on the manifold of another variable
Connection dynamics during seizure

This seizure appeared only on in the right hippocampus.

It is clear, that the right hippocampus has large effect to the Left hippocampus, while there is only mild effect in the backward direction.
Connection dynamics in seizure

The seizure was more pronounced in the left hippocampus.

Although,

The right hippocampus drove the left during the first period of the seizure, then a circular connection structure emerged.

May help in surgical preparation
Dynamics, Causality and Criticality

Critical states, metastable states, phase-transitions... etc

(From A. Hudetz et al: Front. Systems Neurosci. 2014 At the critical T, metastable states dominate and the diversity of brain states as measured by D is maximum. The high repertoire of states at critical T is consistent with the postulated condition to support conscious cognition.)
Activity patterns in lattices in the sub- and supercritical regimes, as well as in the window of phase transition. Notice the emergent giant cluster near the critical probability ($p_c$) similarly as it has been described in the evolution of random graphs. Lattice size is $N \times N = 128 \times 128$.

$p = 0.080$ $p = 0.120$ $p = 0.133$ $p = 0.134$ $p = 0.136$ $p = 0.140$

Subcritical regime
weak- /no clustering

Phase transition
prominent clustering

Supercritical regime
clustering / decreases

Mean activity
Time / Iteration step (total number of iterations is $5 \times 10^6$)

(Thanks to Robert Kozma)
Self-organized criticality

Turcotte (1999)

Earthquakes Cannot Be Predicted
Robert J. Geller, David D. Jackson, Yan Y. Kagan, Francesco Mulargia
Science 275, 1616-1617 (1997)

from Sornette: Power Laws and Dragon-kings Heavy Tails and Long Tails
from Sornette: Power Laws and Dragon-kings Heavy Tails and Long Tails

Theories:

self-organized criticality -> Black Swans -> no precursors -> unpredictable

intermittent criticality: -> Dragon Kings -> there are some precursors -> somewhat predictable
Black Swans and Dragon Kings
(N.N. Taleb vs. D. Sornette)

Types of rare events

- Extreme events are large in size and at the tail of the PDF.
- Black swans — observation from the same population distribution (power law)
- Dragon Kings — observation not related to the distribution of the majority of observations (too large and too many).
Black Swans and Dragon Kings

Neural avalanches

Fig. 3. Avalanche size distribution for 100 configurations of scale free networks with \( N = 4000 \) neurons and different percentage \( p_{\text{inh}} \) of inhibitory synapses under strong random drive.

L. de Arcangelis

disinhibiton induced DKs
Neuropercolation

(Kozma, Puljic, Balister, Bollobas, Freeman)

Consider d-dimensional discrete tori. There are two possible states: active and passive.

At a given time $t$, $x$ becomes active with probability $p$. $p$ is a function of the state of the closed neighborhood nodes $\Gamma_x$.

Governing rules vary in terms of connection types (range, probabilistic, directional), arousal functions, etc.
Simulation Results

a: ferromagnetic regime ("order")
b: critical state
c: paramagnetic regime ("disorder")
Simulation Results

Figure: self-organized criticality
Simulation Results

**Figure:** intermittent criticality. Jumps from the mostly inactive system to mostly active, and vice versa, take a relatively short time.
Computational Neurology and Computational Psychiatry: two glimpses

Anxiety

SEPTOHIPPOCAMPAL SYSTEM

THETA RHYTHM

SKELETON NETWORK

KNOCK–IN, KNOCK–OUT TECHNIQUES

DESENSITIZATION KINETICS

GABA SYNAPSE

RECEPTOR SUBUNITS

Typeset by FoilTEX
Alzheimer’s Disease and epilepsy: the big picture

Concentration-dependent plasticity

\[ \frac{dW_i}{dt} = \eta(C_a(t)) \theta(C_a) - \lambda W_i \]

\[ \frac{d[C_a(t)]}{dt} = J_{NMDA} - \frac{1}{\tau_{CN}} [C_a(t)] \]

\[ C_n V = \sum_i J_i(V) + J_{syn} \]

\[ I(t,V) = \theta(t) \cdot (V - V_m) \]

\[ g(t,V) = \theta(t) \cdot m(V)^3 \cdot h(V) \]

\[ n(t,V) = \alpha_n(V)^2 \cdot (1 - n) - \beta_n(V) \cdot n \]

Concentration-dependent rhythm generator

network dysfunction

Increased synchrony

pre- and postsynaptic positive feedback

memory deficit (mouse)

memory deficit (human)