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Quantum stochasticity and neuronal computations

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Definition

A **stochastic** system is one whose behavior is **indeterministic** in that its inputs and initial state do not fully determine its next state (output)

- The only **intrinsically** (objectively) **stochastic** (indeterministic) processes in physical world are **quantum processes**
- Does **quantum indeterminism** affect the **dynamics of neuronal networks**? Is our brain a deterministic machine or an indeterministic system?

1. Criticism of quantum brain hypothesis

2. Two ways of taking advantage of quantum events in biology

3. Quantum neurophysiology – putative mechanisms of quantum computations in neuronal networks

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1. Criticism of quantum brain hypothesis

Two main arguments:

A. neurons and neural networks are **too large** for quantum phenomena to play a significant role in their functioning.

→ all quantum events are **self-averaging**, so that fluctuations among quantum particles are not important

“Most biologists think that quantum effects all just **cancel out** in the brain.”
Daniel Dennett

B. interaction of neurons/neuronal networks with their (noisy and warm) **environment** will **destroy** any **coherent** quantum states

1. Criticism of quantum brain hypothesis

NATURE|Vol 440|30 March 2006 ESSAY

Quantum mechanics in the brain

Christof Koch and Klaus Hepp

“Molecular machines, such as ... pre- and post-synaptic receptors and the voltage- and ligand-gated channel proteins that ...underpin neuronal excitability, are **so large** that they can be treated as **classical objects**.”

“The critical question...is whether any components of the nervous system - a **300-degrees Kelvin** tissue **strongly coupled to its environment** - display macroscopic quantum behaviours, such as quantum *entanglement*“

“A neuron either spikes ...or it does not, but is not in a *superposition* of spike and nonspike states.”

1. **Criticism of quantum brain hypothesis**

2. **Two ways of taking advantage of quantum events in biology**

3. **Quantum neurophysiology – putative mechanisms of quantum computations in neuronal networks**

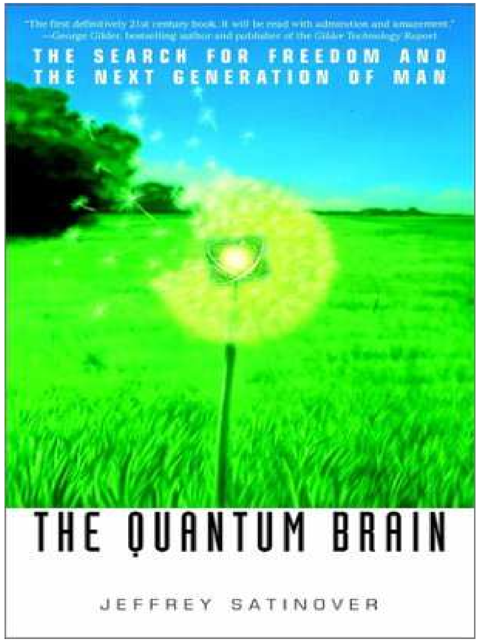
2. Two ways of quantum biological computations

• nervous system probably cannot display macroscopic quantum (classically impossible) behaviours such as quantum entanglement, superposition or tunnelling

however:

• there are two alternative (mutually related) ways in which quantum events might influence the brain activity

2. Two ways of quantum biological computations



1. quantum dynamics speeds up and modulates the computational processes at **microscopic** and **mesoscopic** levels for which **quantum effects** are **directly present**

   (biomolecules, e.g. enzymes, have **intrinsic, classically impossible, quantum properties** which are necessary for life to be possible at all)

2. because the brain is a **complex nonlinear** system, capable of **chaotic** dynamics, it can **amplify** lowest scale **quantum** fluctuations upward, modulating larger-scale **macroscopic** activity patterns

Quantum enzymology

NATURE | VOL 399 | 3 JUNE 1999 |

Quantum enzymology

Tunnel vision

Dagmar Ringe and Gregory A. Petsko

NATURE | VOL 399 | 3 JUNE 1999 |

Enzyme dynamics and hydrogen tunnelling in a thermophilic alcohol dehydrogenase

Amnon Kohen*, Raffaele Cannio†, Simonetta Bartolucci‡ & Judith P. Klinman*§

• empirical evidence shows that biomolecules (proteins, DNA) take **direct advantage of quantum effects** (in particular of **tunneling**)

• **protein folding** (into its functional three-dimensional structure) is a *minimization problem*

→ quantum tunneling of electrons and protons speeds up proper protein folding (even in a warm and noisy intracellular environment!)

→ quantum tunneling effects are involved in the **conformational changes** required for enzyme-mediated catalysis

NATURE|Vol 446|12 April 2007

BIOPHYSICS

Quantum path to photosynthesis

Roseanne J. Sension

Photosynthesis:

1. *light excites* electrons in pigment molecules (chlorophyll)

2. *electronic excitation moves downhill* from higher energy level to lower energy level through the pigment molecules

3. the excitation is *trapped in a reaction centre*, where its remaining energy is used *to produce energy-rich carbohydrates*

Computing problem: to establish the easiest route for the electronic excitation (which transfers the energy downhill) to the reaction complex

NATURE|Vol 446|12 April 2007

BIOPHYSICS

Quantum path to photosynthesis

Roseanne J. Sension

Evidence for wavelike energy transfer through quantum coherence in photosynthetic systems

Gregory S. Engel[1,2], Tessa R. Calhoun[1,2], Elizabeth L. Read[1,2], Tae-Kyu Ahn[1,2], Tomáš Mančal[1,2]†, Yuan-Chung Cheng[1,2], Robert E. Blankenship[3,4] & Graham R. Fleming[1,2]

Solution:

- a clever quantum computation built into the photosynthetic algorithm
- (quantum) coherent energy transfer allows the 'wavelike' sampling of the energy landscape to find the easiest route for the electronic excitation
- the electronic excitation samples two or more states simultaneously
- much faster than the semi-classical (incoherent) mechanism
- the process is analogous to Grover's algorithm in quantum computing

Conclusion: it is possible that evolution selected inherently quantum-mechanical process for the fast and efficient mechanism of light energy harvesting

EMBO *reports* VOL 7 | NO 10 | 2006

A quantum leap in biology

Philip Hunter

deterministic molecular mechanics vs. quantum molecular ‚mechanics'
(Density functional theory)

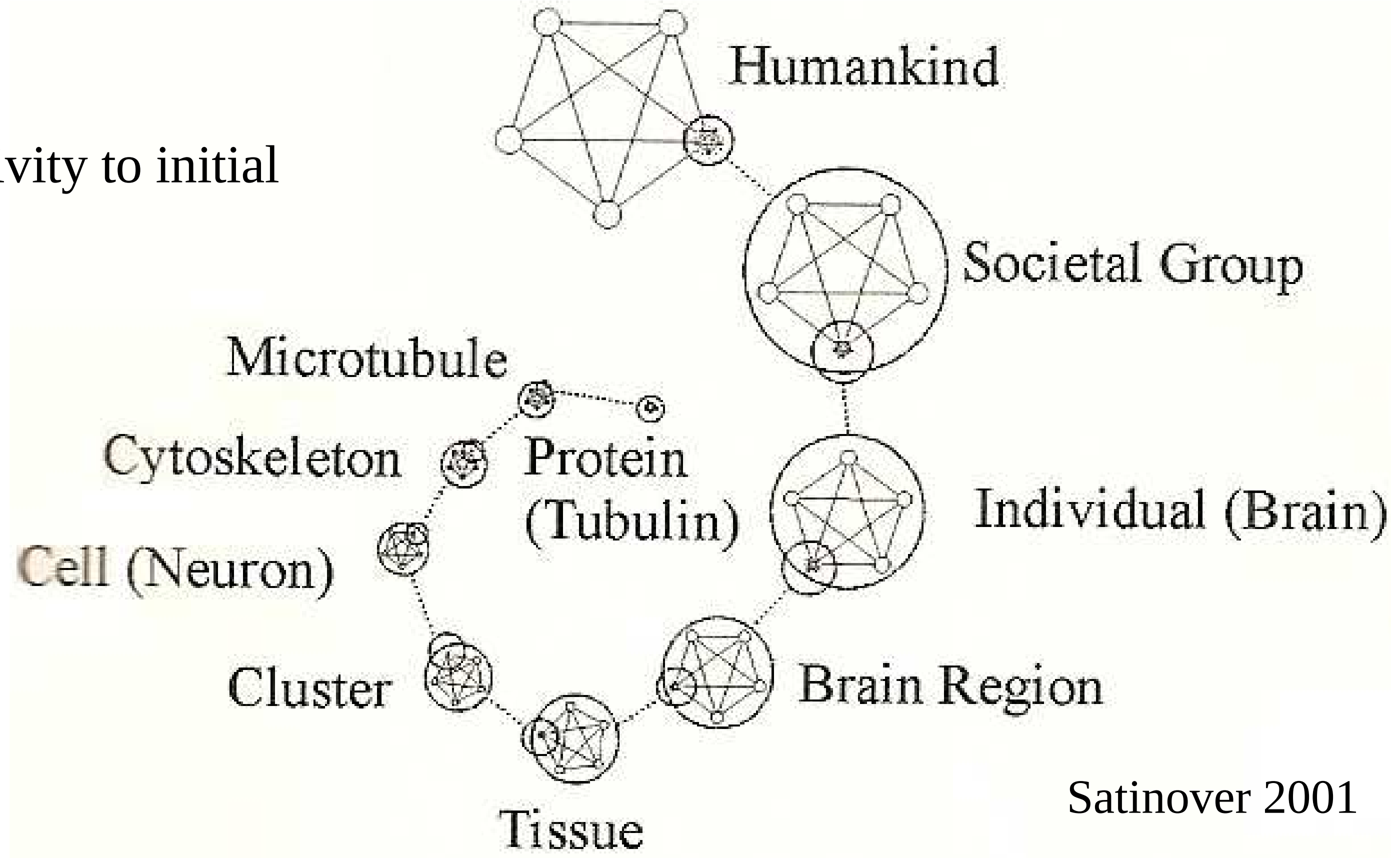
• whenever electrons and their associated energies need to be considered explicitly, quantum physics steps in (→ Schrödinger's equation)

• DFT replaces the individual electrons of a molecule with a single electronic density function

• examples: enzymatic reactions, photoreception, molecular motor proteins

Nested hierarchy of nonlinear complex networks

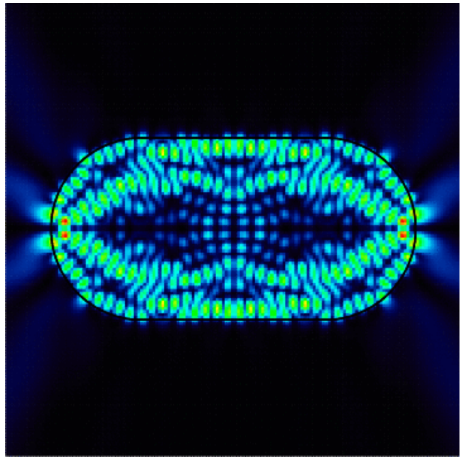
Extreme sensitivity to initial conditions



• In **iterative** hierarchies with **nonlinear** dynamics (prone to chaos), small (even infinitesimal) **fluctuations** are **not averaged away**, they can be **amplified**!

• Brain structure is iterative and its activity is prone to chaos

Quantum nonlinear (chaotic) systems



- 4 kinds of dynamic systems:

1. nonchaotic: a) classical – regular, objectively predictable

   b) quantum – irregular, objectively unpredictable

2. **chaotic** a) classical – irregular, subjectively unpredictable

   b) quantum – probabilistic and regular, upredictable

- Paradoxically, quantum effects **stabilize** the behavior of (classically) **chaotic systems**
- At finite temperatures, **quantum coherence** can create **new patterns at a mesoscopic scale**
- Quantum chaotic systems can exhibit **persistent „fuzzy" regular patterns**

Summary I

1. **Quantum effects** are **directly present** at **microscopic** and **mesoscopic** levels speeding up biological processes (protein folding, enzymatic reactions, etc.)

2. Lowest scale quantum effects influence the initial state of the next scale, while the higher levels shape the boundary conditions of the lower scales. This **hierarchy of nested networks** with many feedback loops **amplifies the quantum events**

Conclusion: quantum dynamics influences the computation at all levels (proteins, metabolic pathways, cells, cellular networks, etc.) – not by producing classically impossible solutions but by having a profound effect on which of many possible solutions are selected (Satinover 2001)

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Neuronal signaling:	1. electric	2. biochemical

A. transmembrane: synaptic transmission (receptors)
intrinsic excitability (ion channels)

B. cytoplasmic: biochemical networks (kinases, phosphatases)

C. nuclear: genetic networks (gene expression)

Where can we find stochastic processes?

Everywhere…

Small number of molecules (vesicles for release, postsynaptic receptors, signaling molecules in spines) → stochastic nature of synaptic plasticity regulation

3. Quantum neurophysiology – putative mechanisms of quantum computations in neuronal networks

TINS Vol. 23, No. 3, 2000

Channel noise in neurons

John A. White, Jay T. Rubinstein and Alan R. Kay

Neural Computation **10, 1679–1703** (1998)

Ion Channel Stochasticity May Be Critical in Determining the Reliability and Precision of Spike Timing

Elad Schneidman, Barry Freedman, and Idan Segev

• probabilistic gating of voltage-dependent ion channels is a source of electrical 'channel noise' in neurons

• channel noise limits the reliability (repeatability) of neuronal responses

• channel stochasticity increases the range of spiking behaviors

• channel noise enhances information coding abilities of neurons

3. Quantum neurophysiology – putative mechanisms of quantum computations in neuronal networks

Synaptic transmission in the central nervous system has a **stochastic character**:

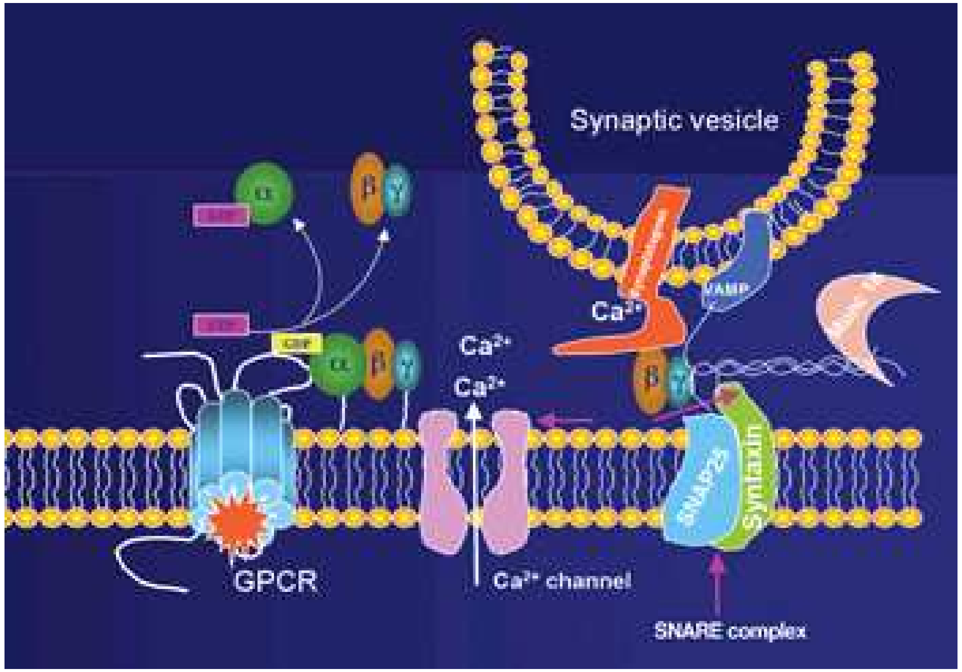
- when an action potential invades the presynaptic terminal there is a low release probability (20%)

  → vesicular **neurotransmitter release** as a random **Poisson-like process**

- some synapses possess a small number of **postsynaptic receptors**, receptor fluctuations can influence postsynaptic responses

3. Quantum neurophysiology – putative mechanisms of quantum computations in neuronal networks

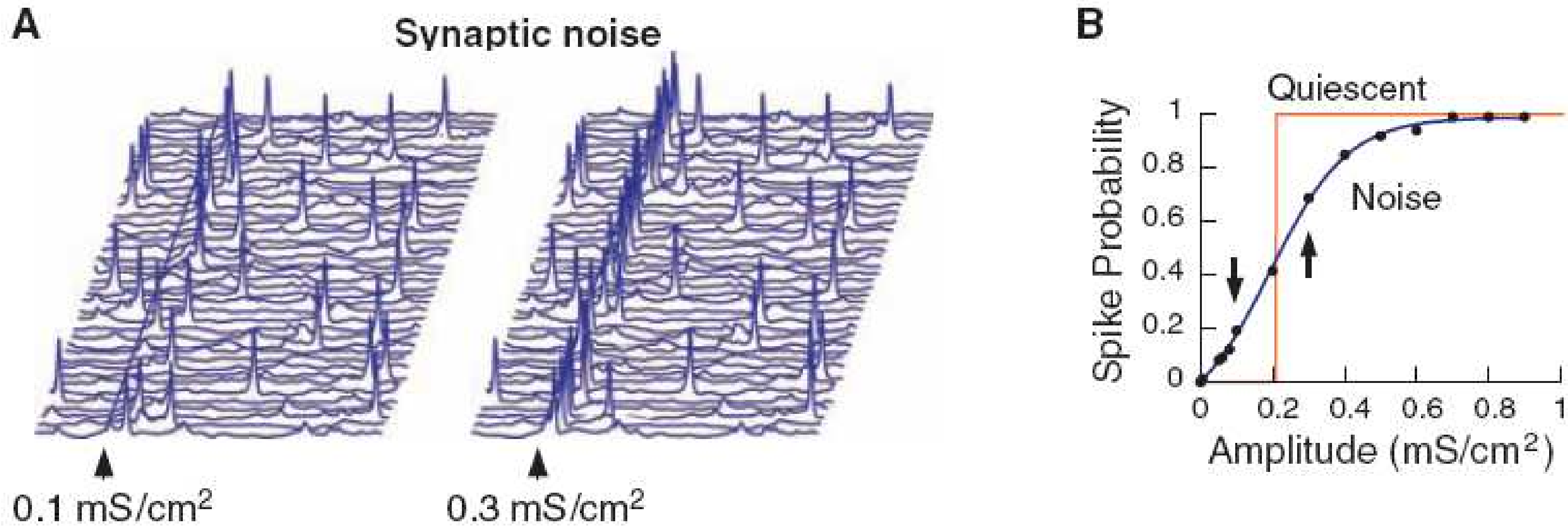
Stochastic neurotransmitter release



• Stochastic modeling of transmitter release can account for the synaptic plasticity data better than a deterministic model (Cai et al. J Neurophysiol 2007)

3. Quantum neurophysiology – putative mechanisms of quantum computations in neuronal networks

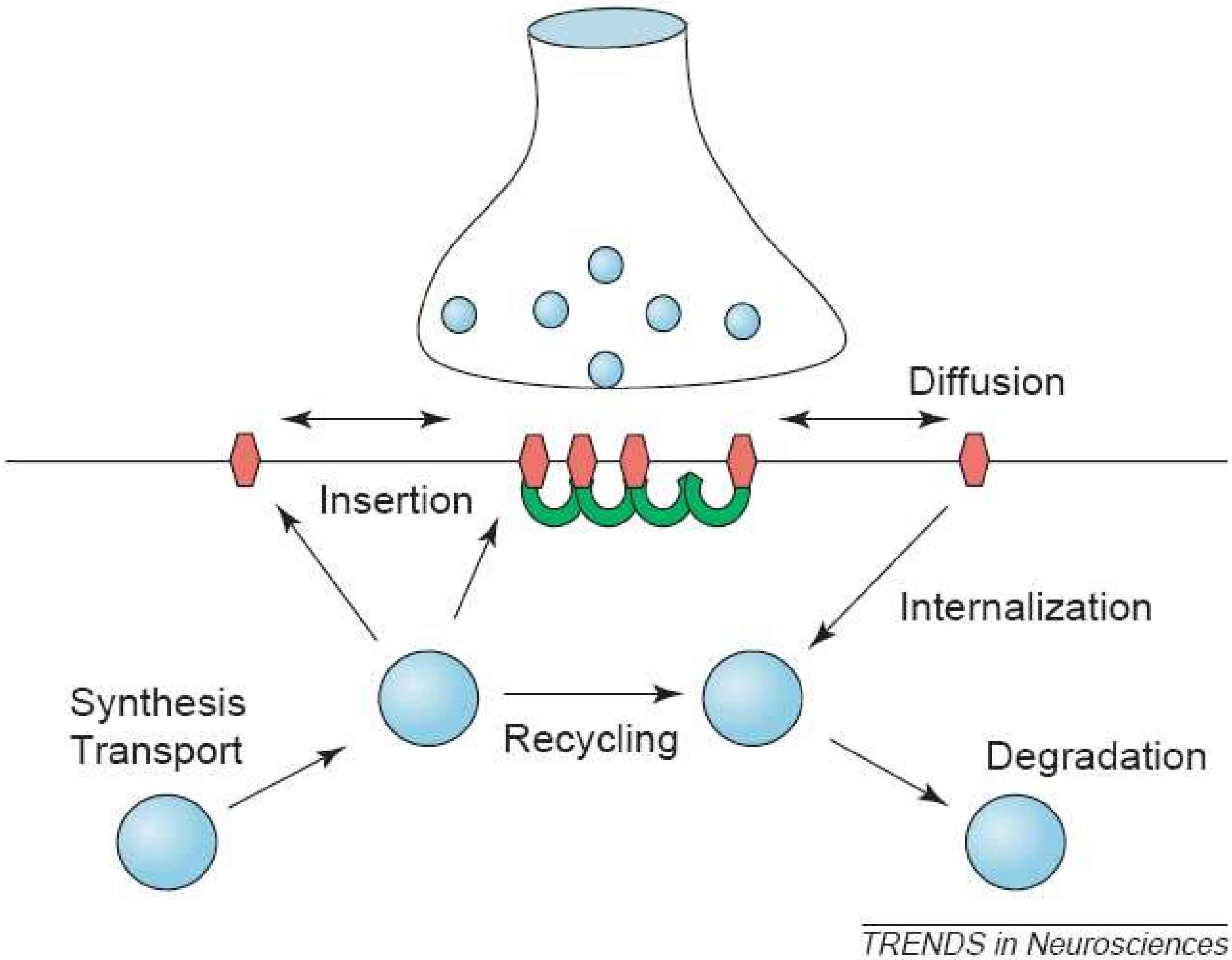
Impact of synaptic noise on input-output relationships of single neurons



Destexhe and Contreras Science 2006

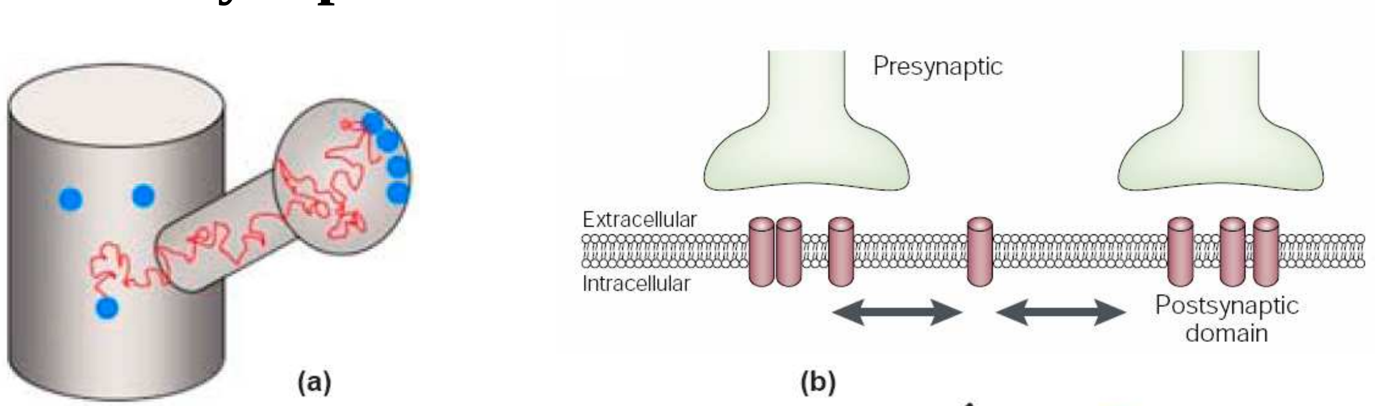
- in quiescent conditions: input-output curve is all-or-none
- with synaptic noise, subthreshold stimuli are boosted, while suprathreshold stimuli are attenuated

Postsynaptic trafficking of receptors

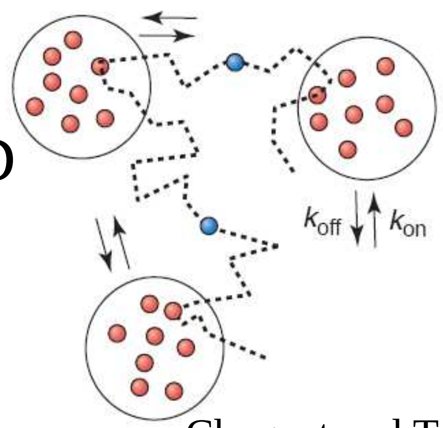


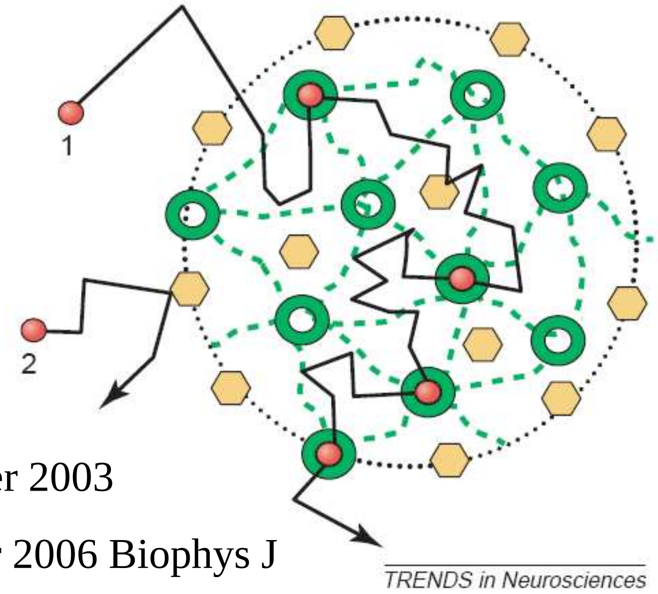
Choquet and Triller 2003

Postsynaptic membrane as a stochastic nanomachine



PSD



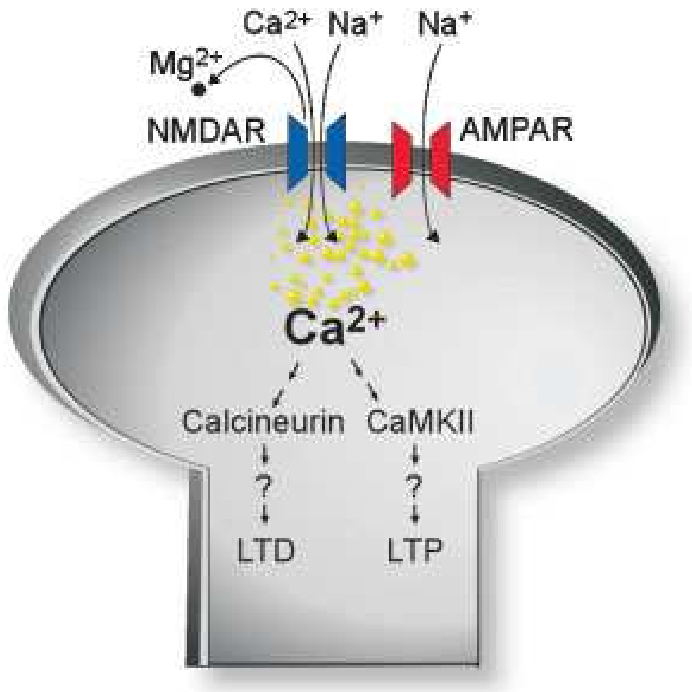


Choquet and Triller 2003

Holcman & Triller 2006 Biophys J

- Receptors traffic by random motion in and out from the PSD
- In the PSD they can be stabilized by binding to scaffolding proteins
- When a few (<15) receptors are involved, a stochastic model is necessary

Stochastic calcium signaling in synaptic spines



Franks & Sejnowski, Bioessays 2002

- Stochastic nature of signaling becomes important when the number of molecules is small
- E.g., a 50 nm calcium concentration in a dendritic spine → 3 free calcium ions;

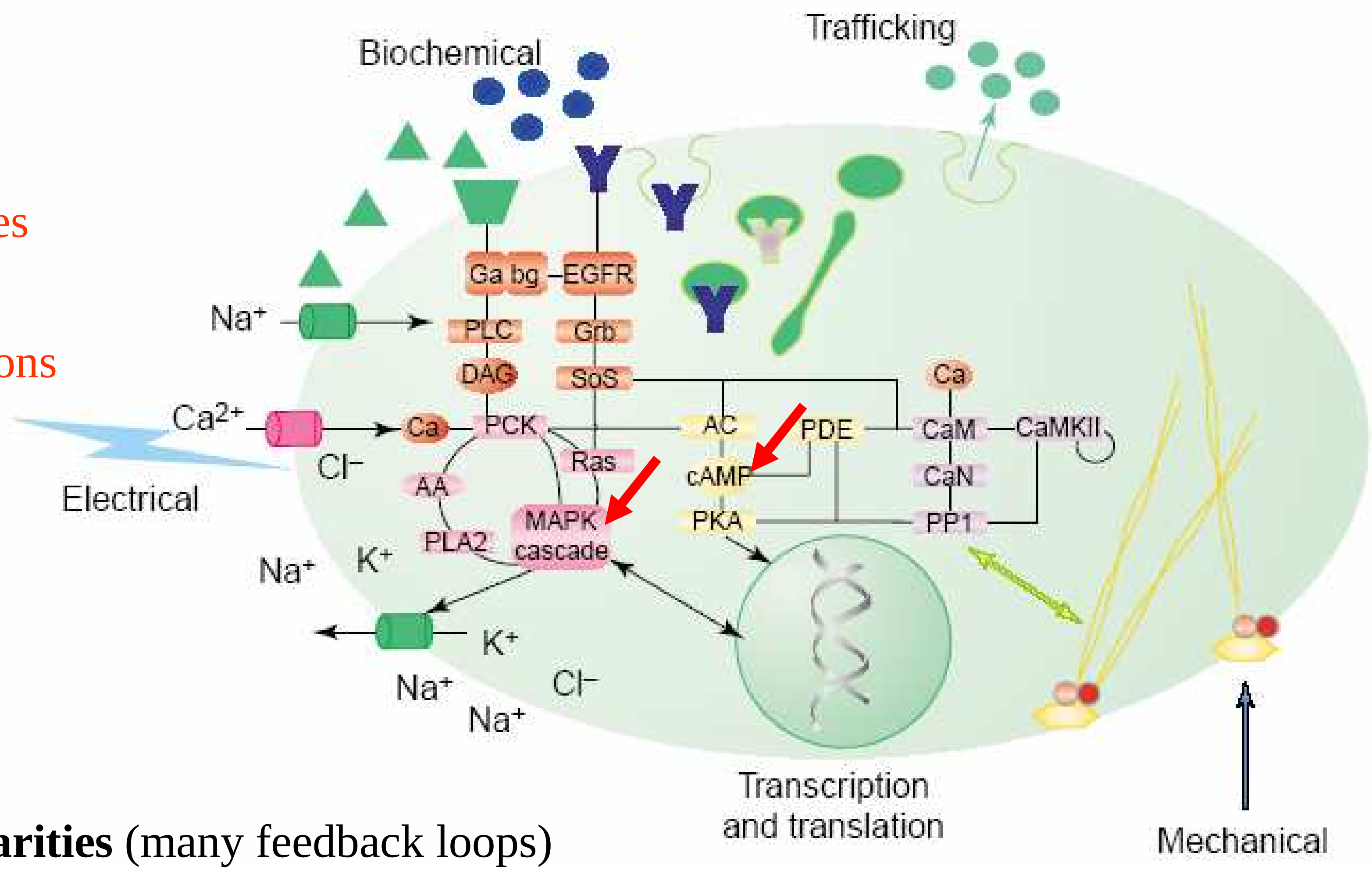
  1 mM (calcium able to induce biochemical changes) → 60 free ions

→ Stochastic modeling (Monte-Carlo simulations) is needed to represent the postsynaptic calcium signaling realistically

Stochastic signaling in biochemical intraneuronal networks

Nodes:
molecules

Links:
interactions



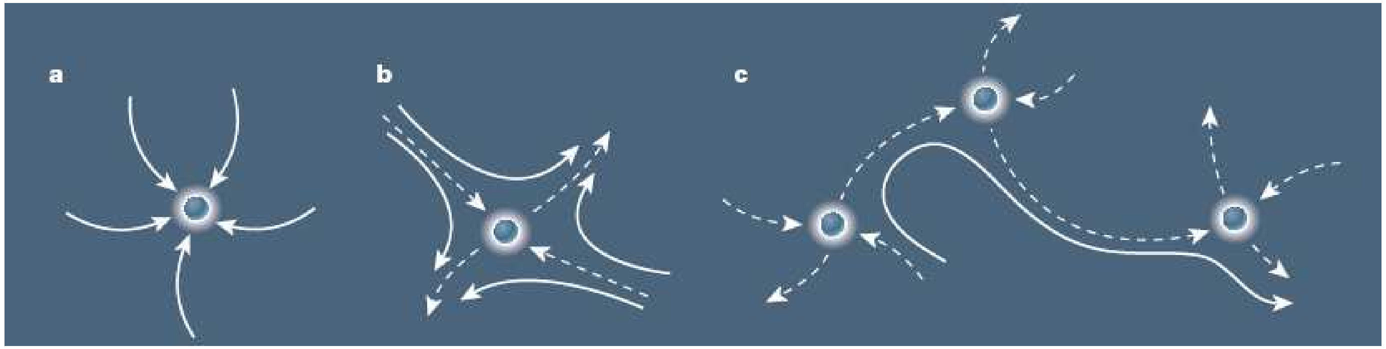
modified after Bhalla, Curr Op Genet Develop 2004

- **nonlinearities** (many feedback loops)
- **self-similar**, **scale-free** structure
- functional **modules** (amplifiers, filters, switches, oscillators, etc.)
- **stochastic events**

NONLINEAR DYNAMICS NATURE|Vol 436|7 July 2005

When instability makes sense

Peter Ashwin and Marc Timme



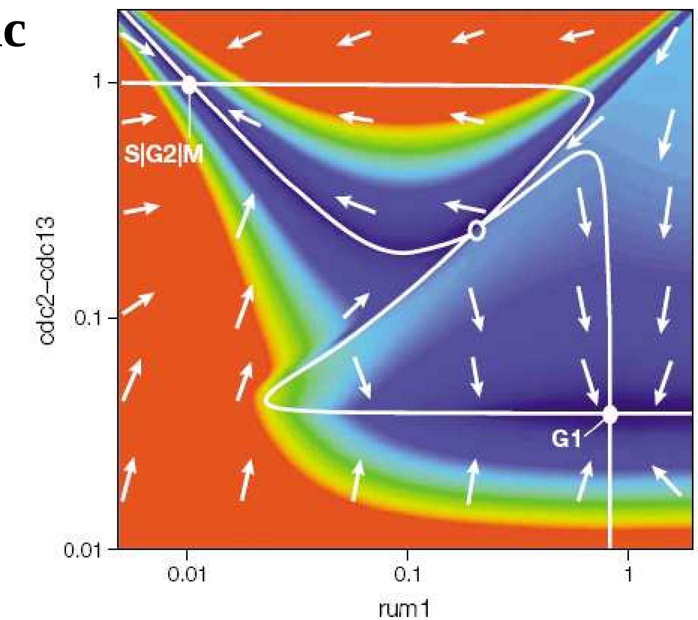
Network of interacting **proteins/genes** is a **dynamic system**

State: a point in a multidimensional system

Change: **vectors** defined by kinetic equations

Bifurcation points: thresholds

Feedback loops → instabilities → **state transitions**



Tyson et al. Nat Rev Mol Biol 2001

Stochastic kinetic equations: **quantum phase transitions**? (Coleman, Nature 2007)

Biochemical regulation at the nanomolar scale: it‘s a noisy business!

- Stochastic **genetic** expression has been observed directly (intrinsic vs. extrinsic noise)

- Molecular stochastic **fluctuations** play an important role in determining cellular functions by inducing spontaneous **state transitions** (e.g. in a **bistable** molecular **LTP/LTD switch** in **synaptic plasticity**)

- A theory combining cellular regulatory **modules** and **stochastic dynamics** is emerging

- **Nonintuitive** cellular/organismal **responses** driven by **molecular fluctuations** → **powerful new signaling** and regulatory **modes**

McAdams and Arkin, Trends in Genet 1999

Goutsias, Biophys J 2007

Samoilov, Price & Arkin, Sci. STKE 2006

Song et al. Biophys J 2006

Biological benefits of stochastic mechanisms

- Increase of **variability**, diversity, flexibility, novelty → **increase of survival**

  (unpredictabile behavior in a competitive environment,
  better adaptation over a wide range of environments,
  broader spectrum of internal states)

- Interaction of **stochasticity** with **nonlinearities** leads to **novel and even paradoxical neuronal dynamics**! (Swain and Longtin, Chaos 2006, Destexhe and Contreras 2006):

  - boosts the propagation of complex waves of activity
  - enhances input detection abilities
  - benefitial to associative memories by avoiding convergence to spurious states

Summary II

Neuronal computations are **inherently stochastic** at all levels:
transmembrane (ion channel noise and synaptic noise)

cytoplasmic (stochastic protein interactions)

nuclear (stochastic gene expression)

↓

„**Membrane voltage** is the product of interactions at the atomic level, many of which are **governed by quantum physics**.

… interactions between **action potentials** and **transmitter release** as well as interactions between transmitter molecules and **postsynaptic receptors** … seem likely to be **fundamentally indeterminate**."

Glimcher Annu. Rev. Psychol. 2005

Thank you for your attention