SHORT-TERM SYNAPTIC PLASTICITY IN THE DETERMINISTIC TSODYKS-MARKRAM MODEL LEADS TO UNPREDICTABLE NETWORK DYNAMICS

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09/14/2015

BACKGROUND

PNAS

Short-term synaptic plasticity in the deterministic Tsodyks–Markram model leads to unpredictable network dynamics

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Contributed by Terrence J. Sejnowski, August 28, 2013 (sent for review April 13, 2013)

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AUTHOR INFORMATION

- HENRY MARKRAM
  - Spike timing dependent synaptic plasticity (1997)
  - Professor in EPFL
  - Head of Blue Brain Project
    - Simulated rat brain (100,000 columns of in the order of 10,000 neurons each)

The human brain — a spongy, three-pound mass of tissue — is the most complex living structure in the known universe.

Society for Neuroscience

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SIGNIFICANCE

- With increasing life expectancy, neurological disorders drastically increase. (WHO)
- 1000+ diseases related to brain result in hospitalization and loss in productivity. (SFN)
- Storage capacity of brain is larger than any supercomputer and the complexity of network is way larger than a social network. (SFN)

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BACKGROUND

- STSP : Temporal adjustment of synaptic strength in time-scales of ms to mins.
- STSP affects:
  - Network dynamics and brain function
  - Depression acts as activity regulator mechanism.
  - Facilitation is a way of implementing working memory.

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BACKGROUND

- **Synaptic enhancement (facilitation, augmentation, potentiation)**
  - ALL presynaptic mechanisms
  - Increase in mean number of transmitter quanta without change in quantal size or postsynaptic effectiveness

    Increased probability of release and perhaps an increased number of release sites
  - Crucial role of calcium

    Residual presynaptic intracellular calcium

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BACKGROUND

- **Synaptic depression**
    - MOSTLY presynaptic
    - Depletion of pool of vesicles
    - Decrease in number of transmitter quanta

      Decrease in probability of release and perhaps a reduced release efficacy

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MOTIVATION

- Prove the existence of highly irregular and chaotic-like dynamics in the TM model.
- Identifying Shilnikov Chaos to account irregularities in the overall network activity.

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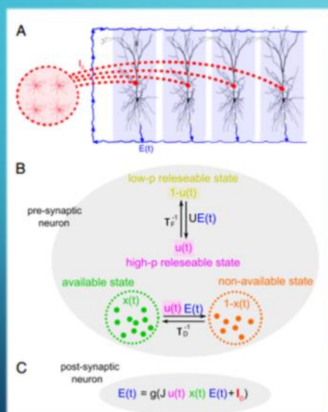
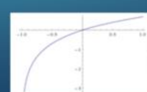
MODEL



$$\begin{cases} \tau\dot{E}(t) = -E(t) + g\big(Ju(t)x(t)E(t) + I_0\big) \\ \dot{x}(t) = \tau_D^{-1}\big(1 - x(t)\big) - u(t)E(t)x(t) \\ \dot{u}(t) = UE(t)\big(1 - u(t)\big) - \tau_F^{-1}\big(u(t) - U\big). \end{cases}$$

Symbol	Description	Value
τ	Time constant for rate dynamics	13 ms
τ_F	Time constant for synaptic facilitation	1,500 ms
τ_D	Time constant for synaptic depression	200 ms
U	Baseline for facilitation variable	0.3
J	Strength of recurrent connections	3.07
I_0	External inhibitory input	[−2,−1]
α	Normalization factor in the gain function	1.5



$$g(z) = \alpha\log(1 + \exp(\frac{z}{\alpha}))$$

METHODS

- XPPAUT AUTO
  - XPPAUT (freeware, simulation and analysis of differential equation models)
  - AUTO feature is used to obtain bifurcation diagram of the system.
  - Uses continuation techniques to numerically analyze sets of differential equations in an efficient manner

METHODS

- Gillespie Algorithm
  - Generates a statistically correct trajectory of a stochastic equation
  - Uses two random numbers to generate long trajectories, one for timestep and one for next state.

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METHODS

- Gillespie Algorithm
  - EXAMPLE

$$A + A \xrightarrow{k_1} \emptyset \qquad A + B \xrightarrow{k_2} \emptyset$$

$$\emptyset \xrightarrow{k_3} A \qquad \emptyset \xrightarrow{k_4} B.$$

METHODS

- Gillespie Algorithm
  - EXAMPLE

- Step 1: Generate two random numbers r_1 and r_2 in the range (0, 1)

- Step 2: Compute the following variables
  - $\alpha_1 = A(t)\ (A(t)-1)\ k_1$
  - $\alpha_2 = A(t)\ B(t)\ k_2$
  - $\alpha_3 = k_3$
  - $\alpha_4 = k_4$
  - $\alpha_0 = \alpha_1 + \alpha_2 + \alpha_3 + \alpha_4$

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METHODS

- Gillespie Algorithm
  - EXAMPLE

$$\tau = \frac{1}{\alpha_0} \ln \left[\frac{1}{r_1} \right]$$

METHODS

- Gillespie Algorithm
  - EXAMPLE

$$A(t+\tau) = \begin{cases} A(t)-2 & \text{if } 0 \le r_2 < \alpha_1/\alpha_0; \\ A(t)-1 & \text{if } \alpha_1/\alpha_0 \le r_2 < (\alpha_1+\alpha_2)/\alpha_0; \\ A(t)+1 & \text{if } (\alpha_1+\alpha_2)/\alpha_0 \le r_2 < (\alpha_1+\alpha_2+\alpha_3)/\alpha_0; \\ A(t) & \text{if } (\alpha_1+\alpha_2+\alpha_3)/\alpha_0 \le r_2 < 1; \end{cases}$$

$$B(t+\tau) = \begin{cases} B(t) & \text{if } 0 \le r_2 < \alpha_1/\alpha_0; \\ B(t)-1 & \text{if } \alpha_1/\alpha_0 \le r_2 < (\alpha_1+\alpha_2)/\alpha_0; \\ B(t) & \text{if } (\alpha_1+\alpha_2)/\alpha_0 \le r_2 < (\alpha_1+\alpha_2+\alpha_3)/\alpha_0; \\ B(t)+1 & \text{if } (\alpha_1+\alpha_2+\alpha_3)/\alpha_0 \le r_2 < 1; \end{cases}$$

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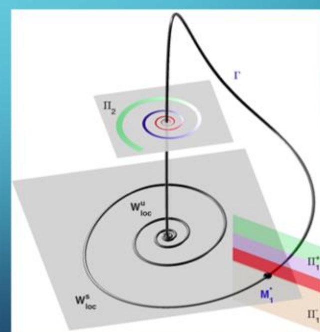
METHODS

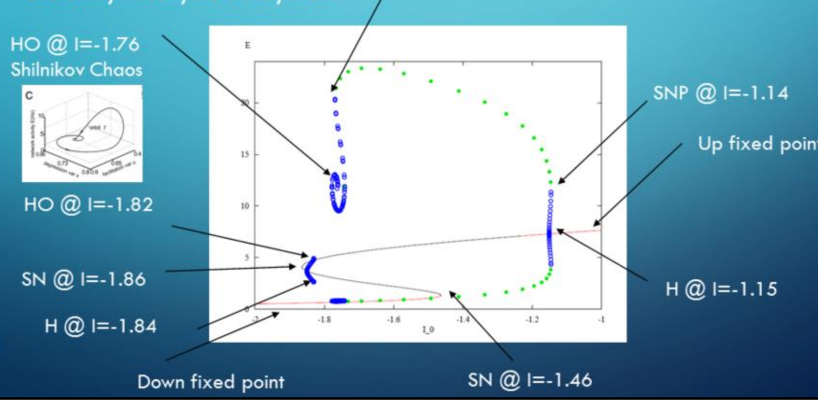
- Shilnikov Homoclinic Chaos

$$
\begin{aligned}
\dot{x} &= -\rho x - \omega y &+ \; F_1(x, y, z),\\
\dot{y} &= \omega x - \rho y &+ \; F_2(x, y, z),\\
\dot{z} &= \gamma z &+ \; F_3(x, y, z),
\end{aligned}
$$



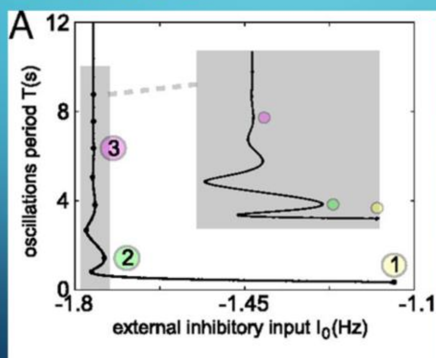
RESULTS

- Stability Analysis of System



RESULTS

- Shilnikov Homoclinic Bifurcation



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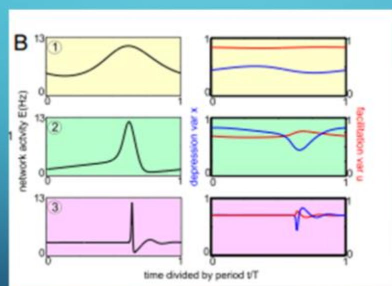
RESULTS

- Shilnikov Homoclinic Bifurcation

Far from homoclinic bifurcation

Closer to homoclinic bifurcation

At homoclinic bifurcation



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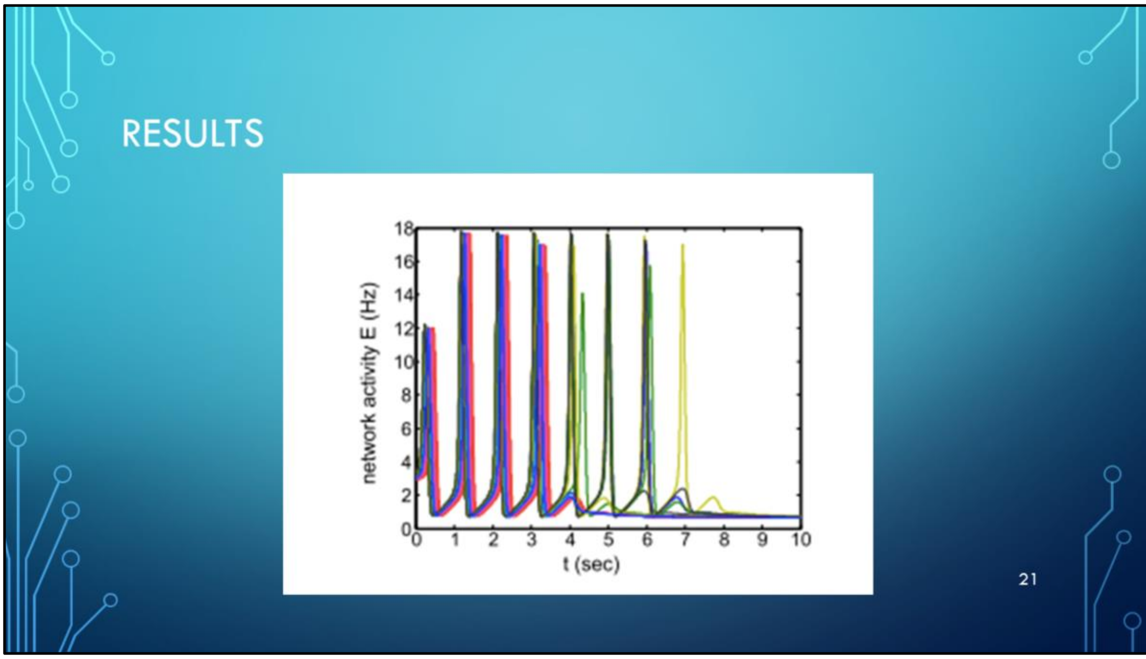
RESULTS
network activity E (Hz)
t (sec)
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RESULTS

- Influence of Noise on Network Dynamics near Shilnikov Homoclinic Bifurcation

$$T_+(n,t) = NS\left(Ju(t)x(t)\frac{n}{N} + I_0\right)\Big/\tau, \quad T_-(n) = -n/\tau,$$

$$\begin{cases} \dot{x}(t) = \tau_D^{-1}\left(1 - x(t)\right) - u(t)x(t)n(t)/N \\ \dot{u}(t) = -\tau_F^{-1}\left(u(t) - U\right) + U\left(1 - u(t)\right)n(t)/N. \end{cases}$$

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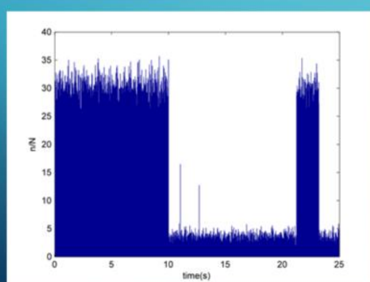
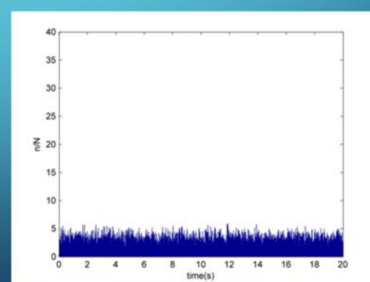
RESULTS

- Influence of Noise on Network Dynamics near Shilnikov Homoclinic Bifurcation

I=-1.77



I=-1.9



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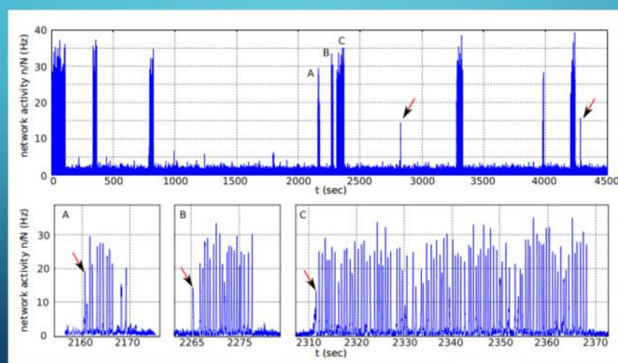
RESULTS

- Influence of Noise on Network Dynamics near Shilnikov Homoclinic Bifurcation



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Spring board like dynamics

RESULTS

- Derivation of mean field description in large N limit

$$\frac{d}{dt}P(n,t) = T_+(n-1)P(n-1,t) + T_-(n+1,t)P(n+1,t) - \left[T_+(n) + T_+(n,t)\right]P(n,t).$$

$$\frac{d}{dt}P(z,t) = N(T_+(z-1/N)P(z-1/N,t) + T_-(z+1/N,t)P(z+1/N,t) - [T_+(z) + T_+(z,t)]P(z,t)).$$

$$T_+(n,t) = NS\left(Ju(t)x(t)\frac{n}{N} + I_0\right)\Big/\tau, \quad T_-(n) = -n/\tau,$$

RESULTS

- Derivation of mean field description in large N limit:
  - Kramers-Moyal expansion of the master equation

$$\begin{cases} \tau dz = A(z,x,u)dt + \frac{1}{\sqrt{N}} B(z,x,u)dW(t) \\ dx = \left(\tau_D^{-1}(1-x(t)) - u\,x\,z\right)dt \\ du = \left(-\tau_F^{-1}(u(t)-U) + U(1-u)z\right)dt \end{cases}$$

$$\begin{cases} A(z,x,u) = S(Ju\,x\,z + I_0) - z \\ B(z,x,u) = S(Ju\,x\,z + I_0) + z, \end{cases}$$

RESULTS

- Derivation of mean field description in large N limit:
  - N →∞

$$\begin{cases} \tau \dot{E}(t) = -E(t) + S\big(Ju(t)x(t)E(t) + I_0\big) \\ \dot{x}(t) = \tau_D^{-1}\big(1 - x(t)\big) - u(t)x(t)E(t) \\ \dot{u}(t) = -\tau_F^{-1}\big(u(t) - U\big) + U\big(1 - u(t)\big)E(t). \end{cases}$$

CONCLUSION

- Chaos is existing in the simple TM model for STSP dynamics.
- The chaos explains the irregularities in large scale brain dynamics.
- Effects of periodic or balanced inputs can be investigated.
- Feedback loop between inhibition and excitation is a reasonable candidate for self organizing tuning mechanism to the edge of chaos.