Innate oscillations and signal propagation in engineered neuronal circuits

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Wednesday, Poster session
Collective activation and activity propagation in engineered networks of neuronal clusters

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TAU

Neuro-Engineering
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• Giora Beit-Ya’akov
• Assaf Shoval
• Raya Sorkin
• Alon Greenbaum
• Tamir Gabay
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CNT MEMS
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• Gabi Karp
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nanoRectna
• Inbal Friedler,

Collaborators
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• Andreas Griner (IMTEK, Germany)
• Jan Korvink (IMTEK, Germany)
• David Kauzlari’c
• Amir Boag (EE, TAU)
• Koby Scheuer (EE, TAU)
Engineered neuronal circuits

How do they form? How do they function?
Outline

• Motivation
• How self-engineering takes place?
  – Nano-topography (CNT)
• How does the activity of such systems look like?

• CNT based neuro-prosthetic devices
Motivation

- See the whole picture
- Function follows form
- Clusters are biologically relevant
Patterning

CNT electrodes

PDL patterns on TiN electrodes

Gabay et al. Nanotechnology, 2007
Self-assembled engineering

Clustered network development
First 7 DIV
PDL clusters on MCS electrode
Inter-cluster distance = 500μm
Cluster diameter = 200μm
cultured 05/11/09, Electrode 11953
Locust neurons on CNTs

Scale bar = 60 \mu m

Greenbaum et al., J NeuroSci Method 2009
Axonal Growth – Mechanics in Action
Double Clamped Beam Model

\[ kC = T_0 \]
\[ 0.5(mN / m) \times 10^{-5} m = 5nN \]

Average value
The Axon and the Growth cone

- Axons: 1 μm thick and some are more than 1 m long
- Extensive growth, especially during developmental stages
- Extremely sensitive chemical sensors
- Mechanical tension
Mechanical Properties of Axons

\( \kappa \), Main spring constant \( \sim 0.05-0.7 \) mN/m > stiff \( E \sim 12 \) kPa (microtubules)

\( \kappa \), Secondary spring constant \( \sim 10^{-3} \) mN/m

\( \gamma \), neurite dissipation

\( M \), Molecular motors mechanical response

\( T_0 \), Neurite initial tension \( \sim 0-2 \) nN

\( T_{\text{max}} \), tension applied by Molecular Motors \( \sim 0-2 \) nN

Bernal PRL 2007, BioPhys J 2010
Role of Tension

- Tension and Network Wiring
- Tension and Cellular Mobility
- Tension and Cell Shape
- Tension and Adhesion
Axons and Tension

Anava et al, Biophysical Journal 2009
Neurite Pruning

Anava et al, Biophysical Journal 2009
“Synapses” with CNTs (antisynapsin)
Cell Mobility
Tension and Mobility

\[ T_0 d_{up} = 2T_0 d_{down} \cos \theta \]
Tension, mobility & Clustering

Model
Actin, Mobility and Shape
Clustering
Preferred Adhesion to Rough Surfaces

Sorkin et al., Nanotechnology 2009

Greenbaum et al., J NeuroSci Method 2009
Twining – Thin Processes

Sorkin et al., Nanotechnology 2009
Twining and Scale

Sorkin et al., Nanotechnology 2009
Length Scales

Sorkin et al., Nanotechnology 2009
Tendrils and processes; Not Just a CNT Effect

Sorkin et al., Nanotechnology 2009
Entanglement

Neurons

Glia

Fluorescence confocal

HRSEM

Sorkin et al., Nanotechnology 2009
CNT Multi electrode array

SiO₂  TiN  Si₃N₄

Si substrate

Ni+CNTs

Gabay et al. Nanotechnology, 2007
3D electrodes
Neuro Chips

- In vitro: Brain-on-a-chip
- In vivo: Neuroprosthetic Devices
Recordings with CNT MEA from Engineered Neural Circuits

Shein et al., Bio Med micro devices, 2009
Networks

Uniform

Engineered Clusters

Shein et al. 2009
Uniform networks

- Recruitment of the entire network (tens – hundreds of ms).
- All the neurons act as one unitary network – if the threshold for SB activation is reached, all the neurons in the network exhibit firing.
- High correlations are found both between adjacent as well as distant neurons.
Clusters;
Isolated and Connected
Isolated Cluster Activity
Onset of Bursting Activity
Isolated clusters

- Fast recruitment (tens of ms).
- All the neurons act as one unitary network.
- Persistent oscillations
Population Level Activity
Frequency range
Coupled clusters

- Restricted directionality
- Long delays between the activation of connected clusters
- Gating in the propagation of activity between clusters - not all initiated SBs propagate to the next cluster.
Clustered network

- Restricted directionality.
- Slow recruitment (hundreds of ms)
- Sequential activation of connected clusters.
- Correlations are high within each cluster and decrease in accordance with the topological distance between neurons.
- The SB is not necessarily activated in all the clusters in the network.
Neurons and CNTs
Flexible CNT Devices

After three months in the eye of a rat, Arie Solomon (TAU)
Summary

• Neuronal mechanics is very important in determining network structure
• Engineered networks are a very rich system for the investigation of neuronal systems
  – Oscillations
  – Asymmetry (gating)
• Three open questions:
  – How significant is the role of cellular mechanics in neuronal development and activity?
  – Are the precise details of neural networks matter?
  – Does spontaneous activity in developing networks determines their function?