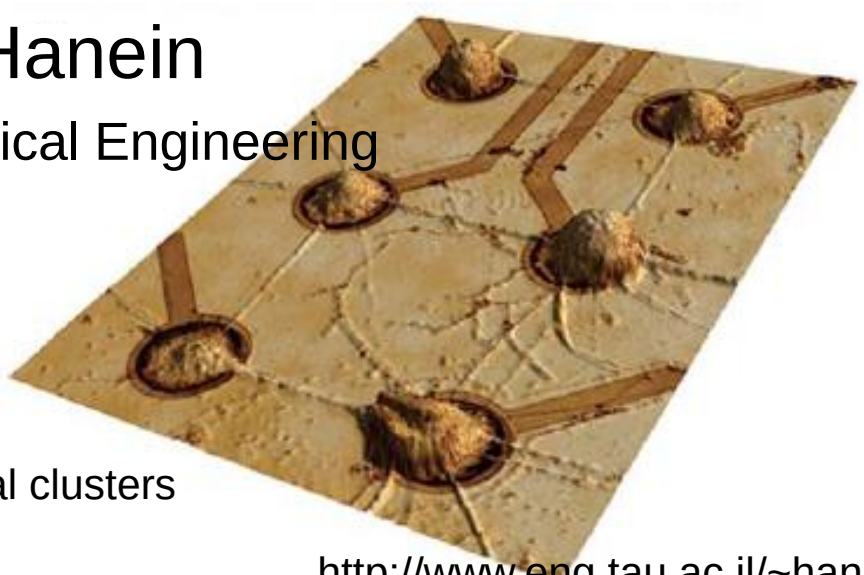
Innate oscillations and signal propagation in engineered neuronal circuits

Yael Hanein

School of Electrical Engineering



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

http://www.eng.tau.ac.il/~hanein




TAU

Neuro-Engineering

- **Mark Shein**
- Nitzan Herzog
- **Moshe David Pur**
- Lilach Bareket
- Giora Beit-Ya'akov
- Assaf Shoval
- **Raya Sorkin**
- **Alon Greenbaum**
- Tamir Gabay
- Moti Ben-David

CNT MEMS

- Assaf Ya'akobovitz (ME),
- Gabi Karp
- Orly Levy
- Ze'ev Abrams

nanoRectna

- Inbal Friedler,

Collaborators

- Eshel Ben-Jacob (Physics, TAU)

- Amir Ayali (Zoology, TAU)
- Sarit Anava

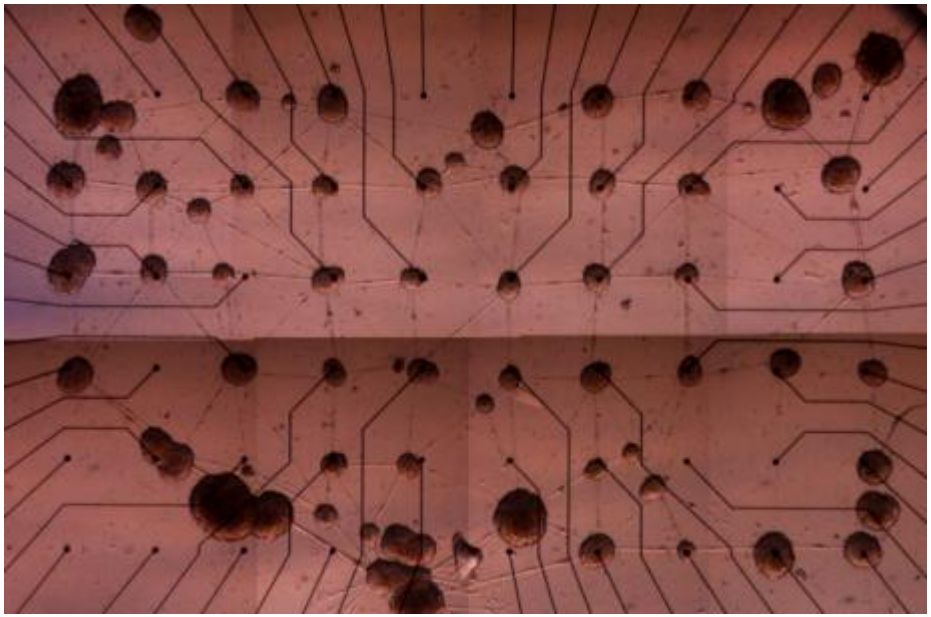
- Evelyne Sernagor (Neuro, UN)
- Christopher Adams

- Ori Cheshnovsky, Zvi Ioffe (Chem, TAU)
- Shlomo Yitzchaik (Chem, HUJI)
- Uri Banin (Chem, HUJI)

- Slava Krylov (ME, TAU)
- 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**

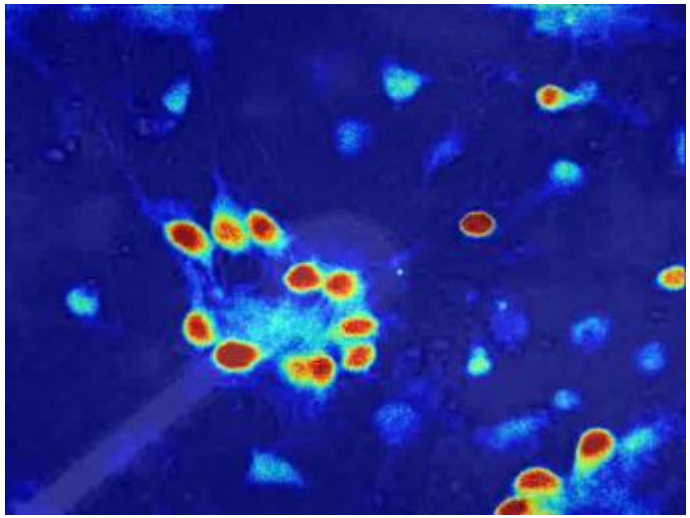
Outline

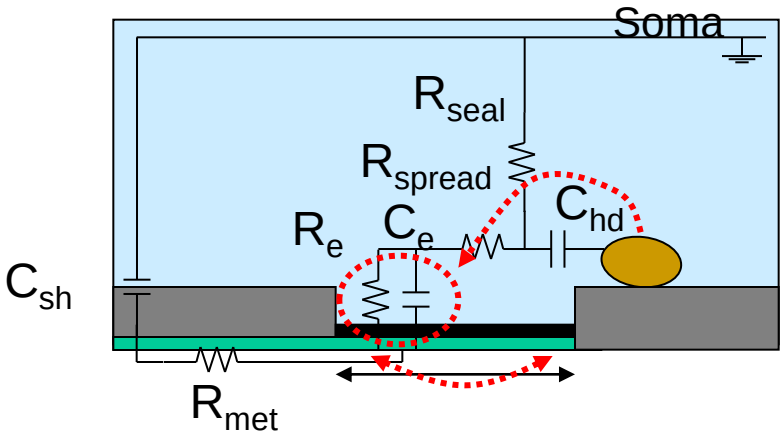
- Motivation
- How self-engineering takes place?
  - Nano-topography (CNT)
- How does the activity of such systems look like?

- CNT based neuro-prosthetic devices

Motivation

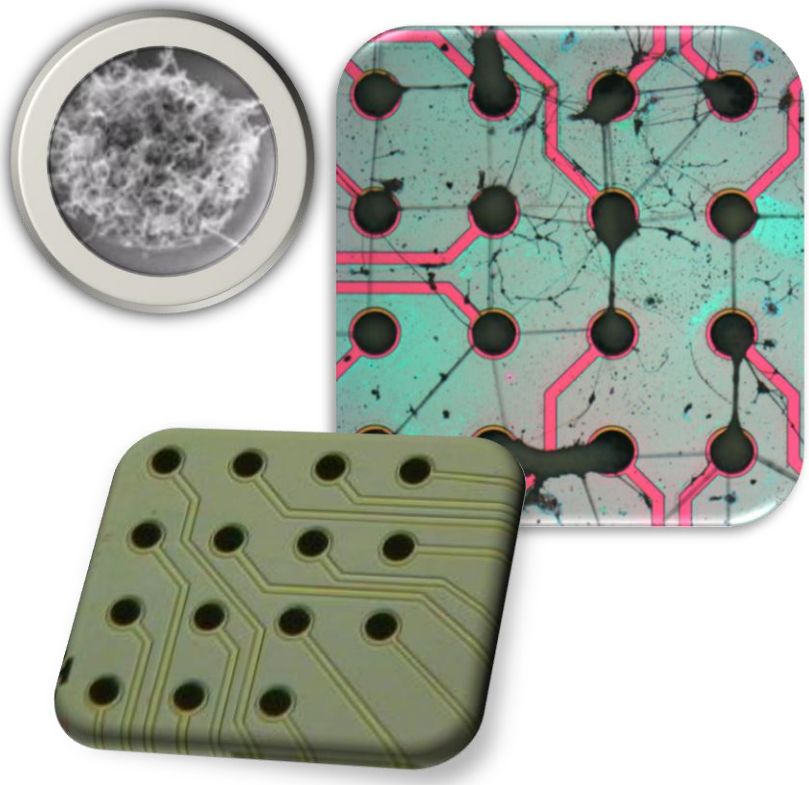
- See the whole picture
- Function follows form
- Clusters are biologically relevant



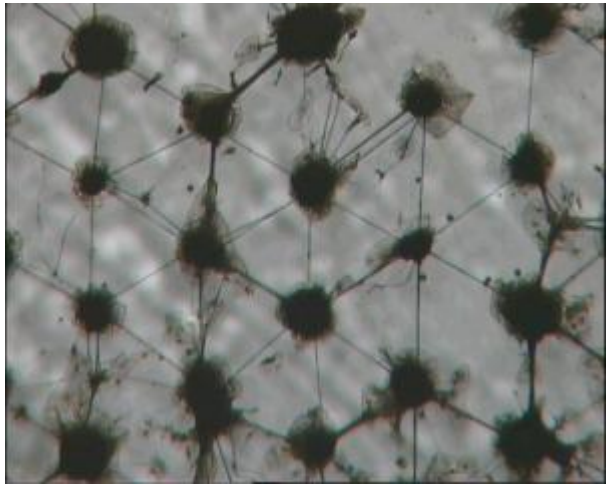


Patterning

CNT electrodes



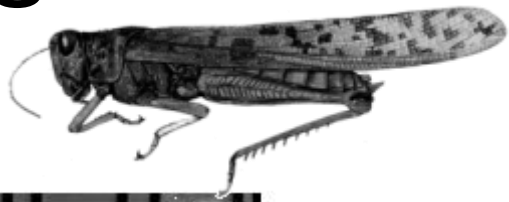
PDL patterns on TiN electrodes



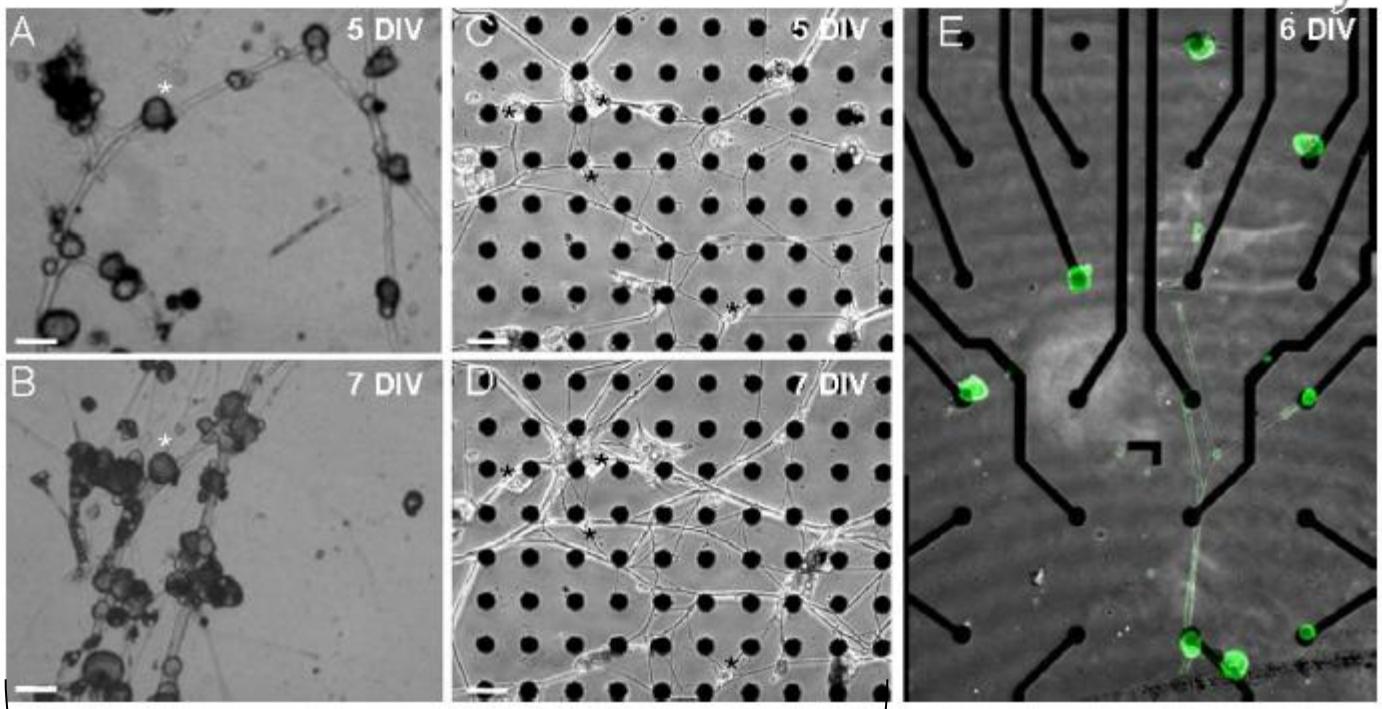
Gabay et al. Nanotechnology, 2007

Self-assembled engineering

Locust neurons on CNTs



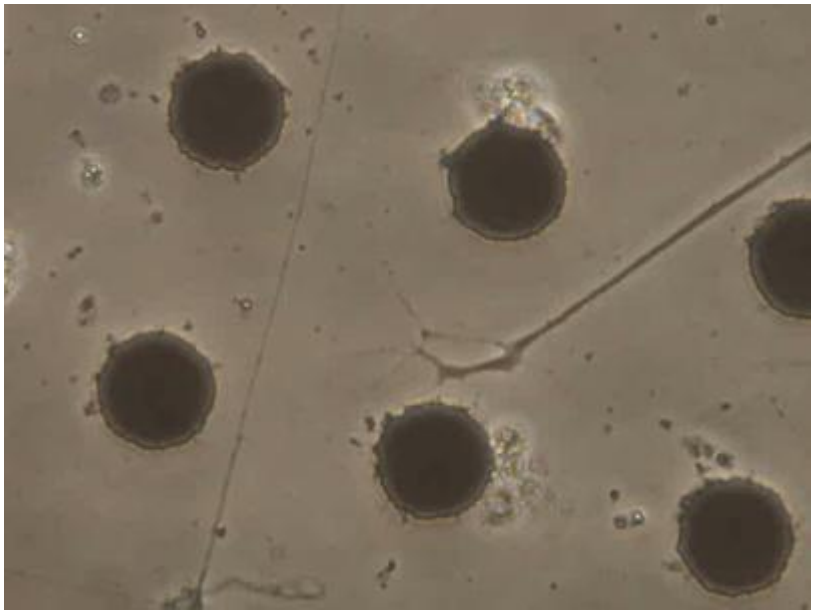
ConA CNTs

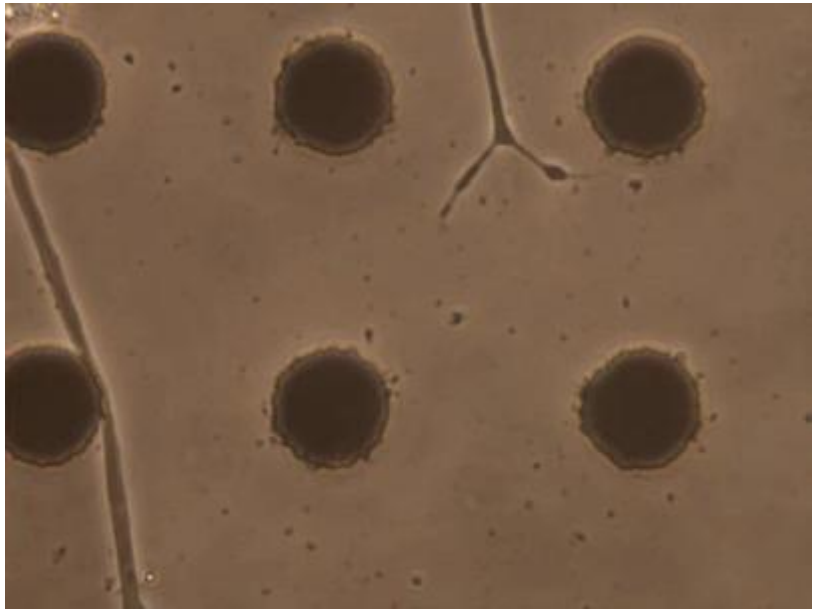


Scale bar = 60 μm

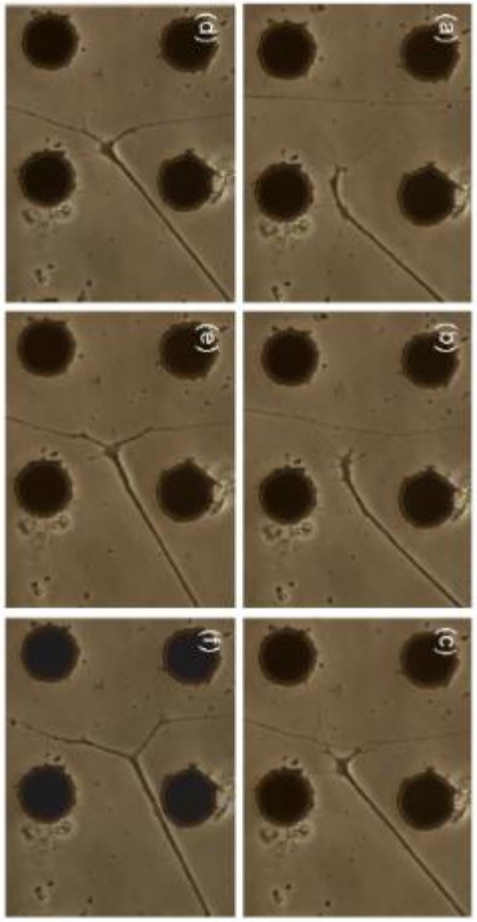
Greenbaum et al., J NeuroSci Method 2009

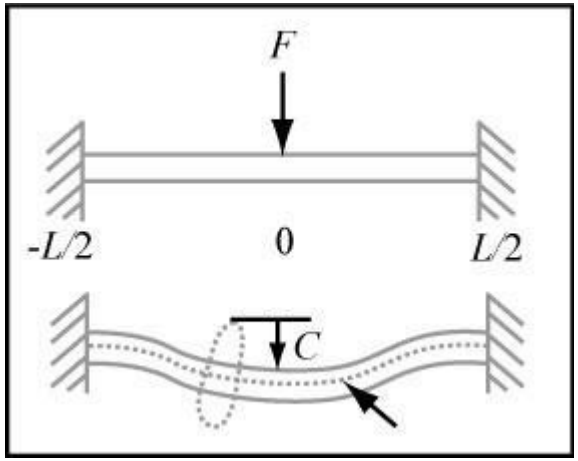
Axonal Growth – Mechanics in Action





Double Clamped Beam Model



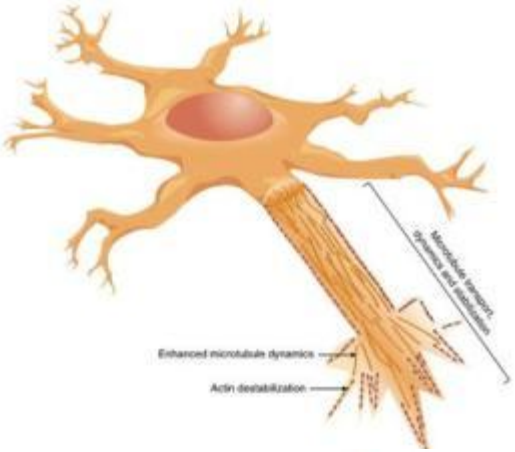


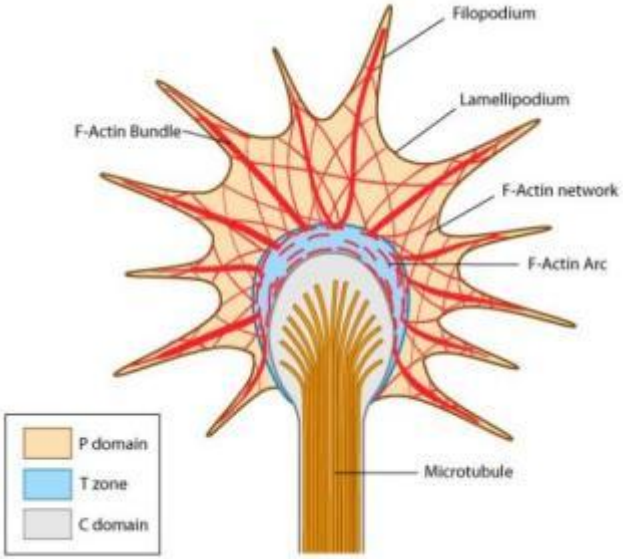
$$kC = T_0$$

$$\underbrace{0.5(mN/m)}_{\text{Average value}} \times 10^{-5} m = 5nN$$

The Axon and the Growth cone

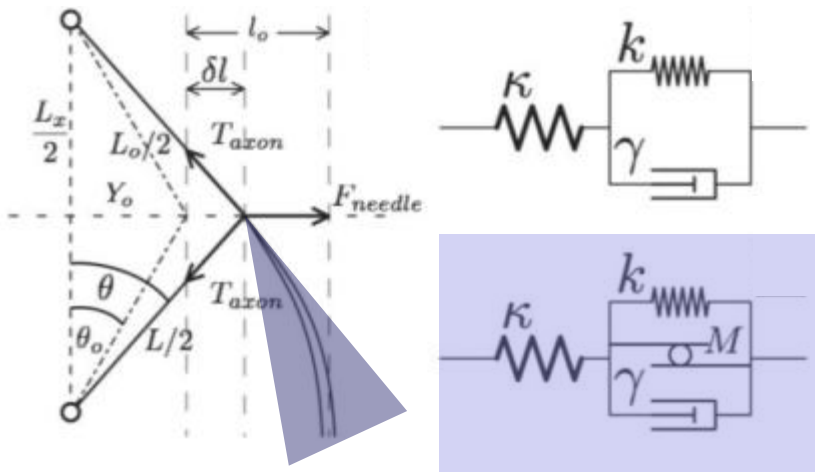
- Axons: 1 μm thick and some are more than 1 m long
- Extensive growth, especially during developmental stages
- Extremely sensitive chemical sensors
- Mechanical tension



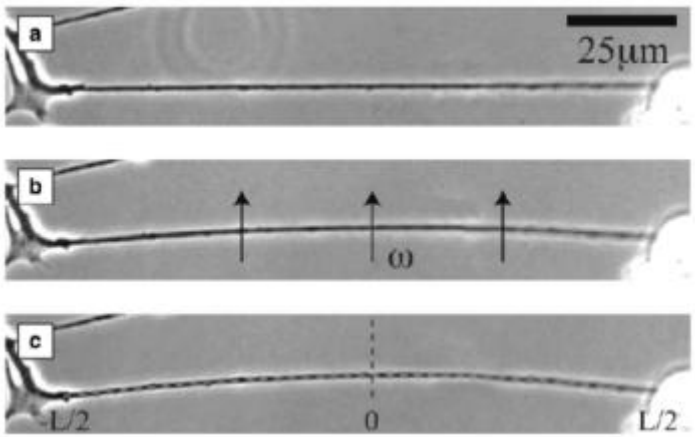


Mechanical Properties of Axons

Needle



Flow



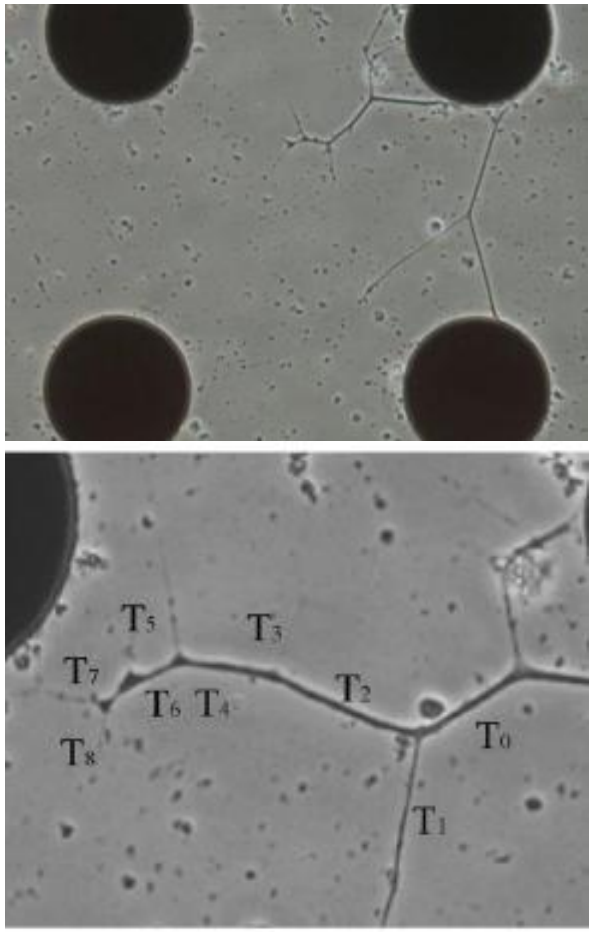
κ, Main spring constant ~ 0.05-0.7 mN/m > stiff E ~ 12 kPa (microtubules)
κ, Secondary spring constant ~ 10^{-3} mN/m
γ, neurite dissipation
M, Molecular motors mechanical response
T_0, Neurite initial tension ~ 0-2 nN
T_{max} tension applied by Molecular Motors ~ 0-2 nN

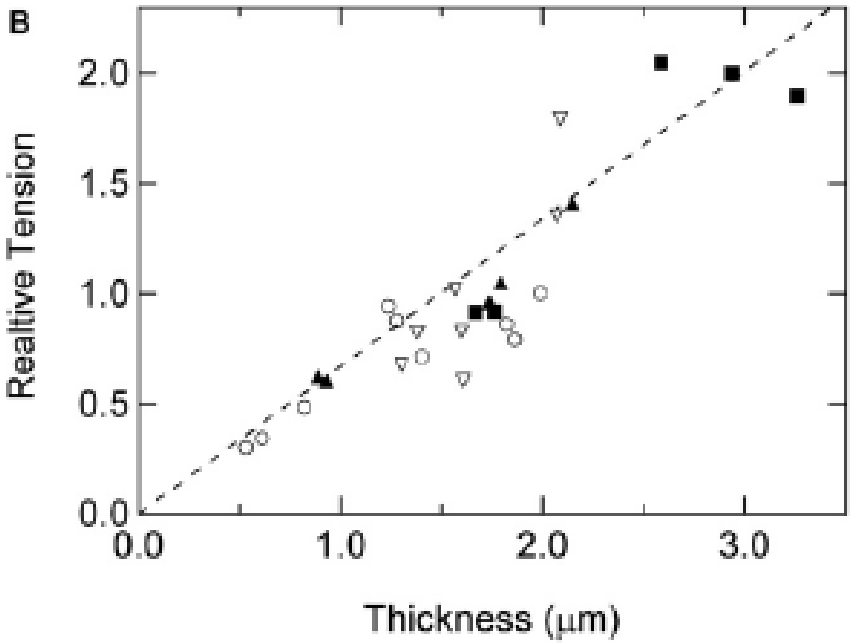
Bernal PRL 2007, BioPhys J 2010

Role of Tension

- Tension and Network Wiring
- Tension and Cellular Mobility
- Tension and Cell Shape
- Tension and Adehsion

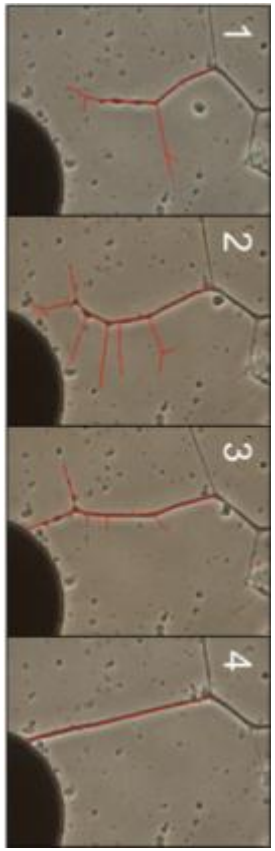
Axons and Tension

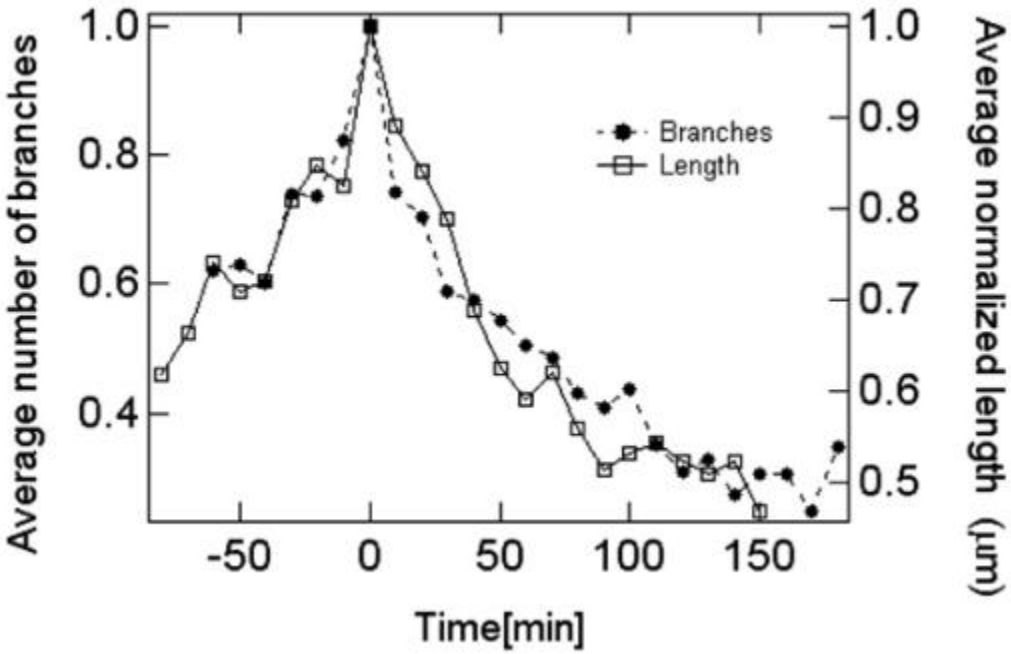




Anava et al, Biophysical Journal 2009

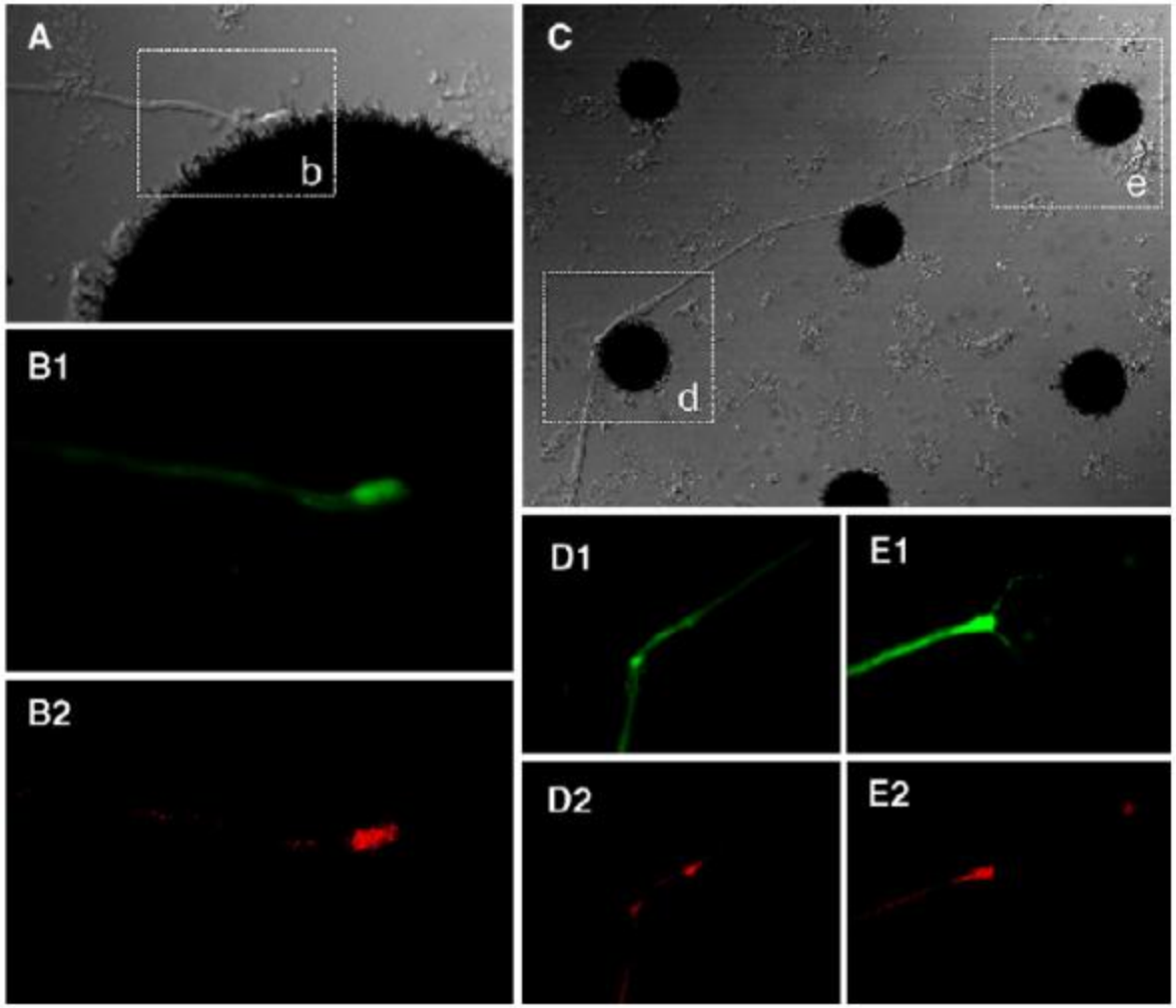
Neurite Pruning



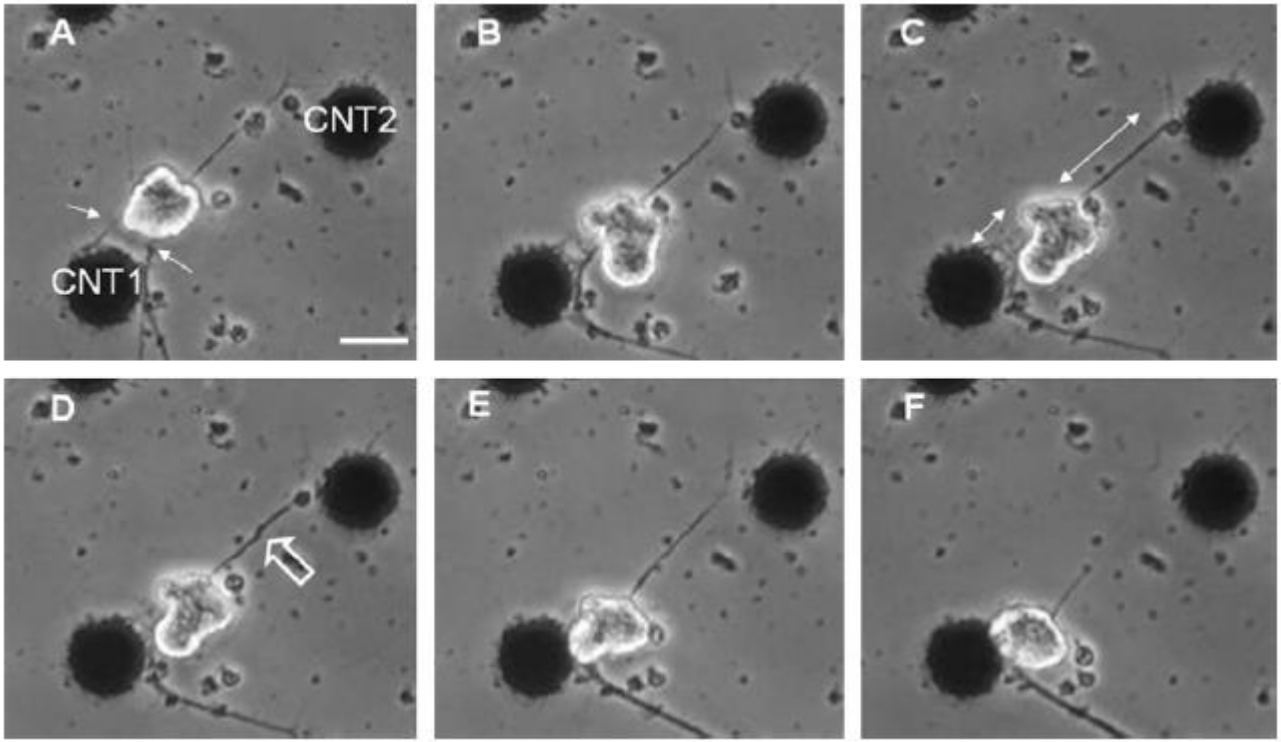


Anava et al, Biophysical Journal 2009

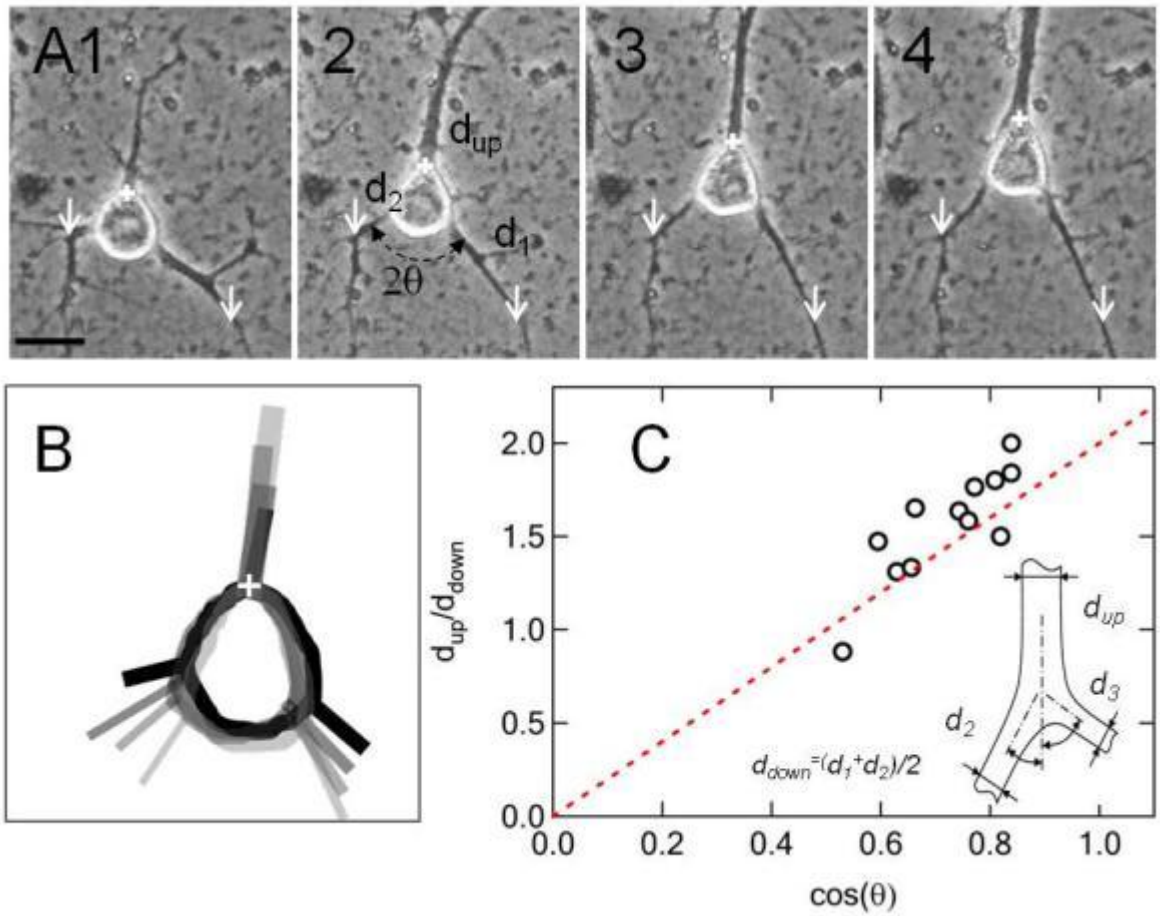
“Synapses” with CNTs (antisynapsin)



Cell Mobility

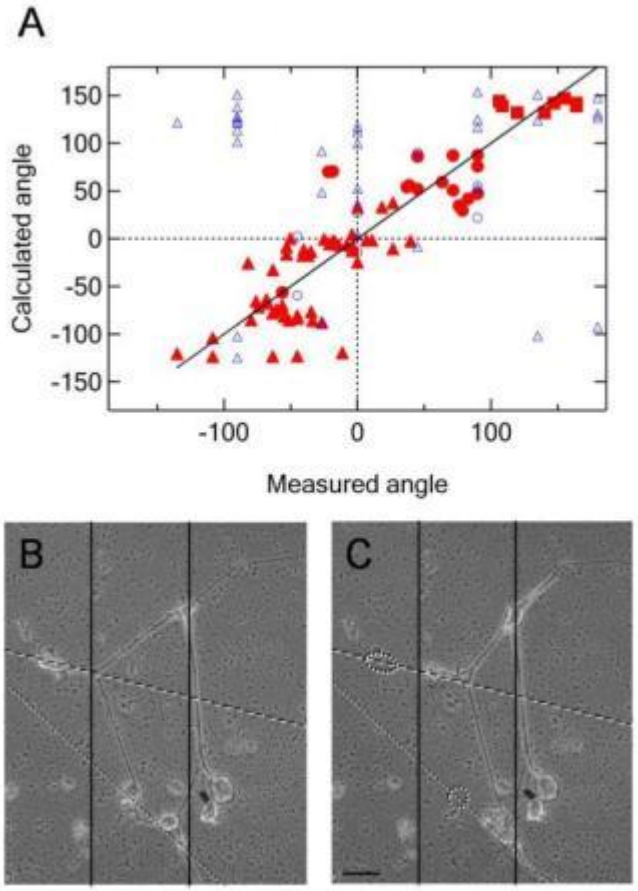


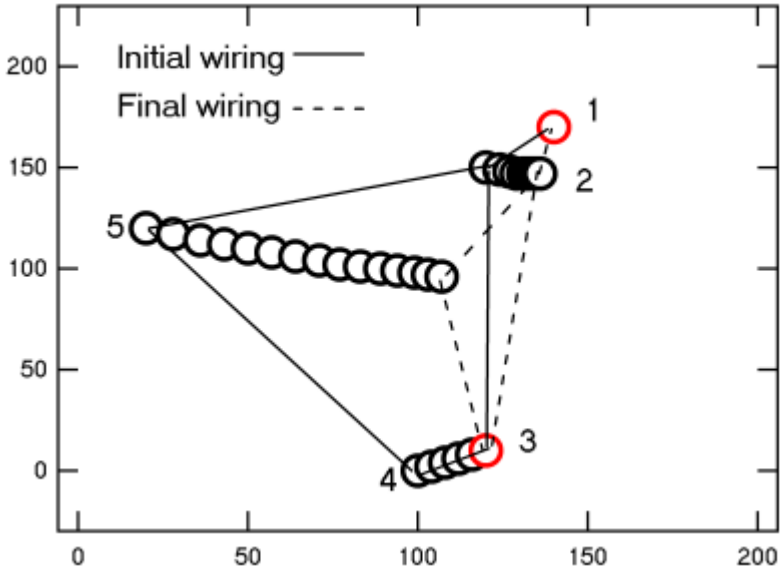
Tension and Mobility



$$T_0 d_{up} = 2T_0 d_{down} \cos\theta$$

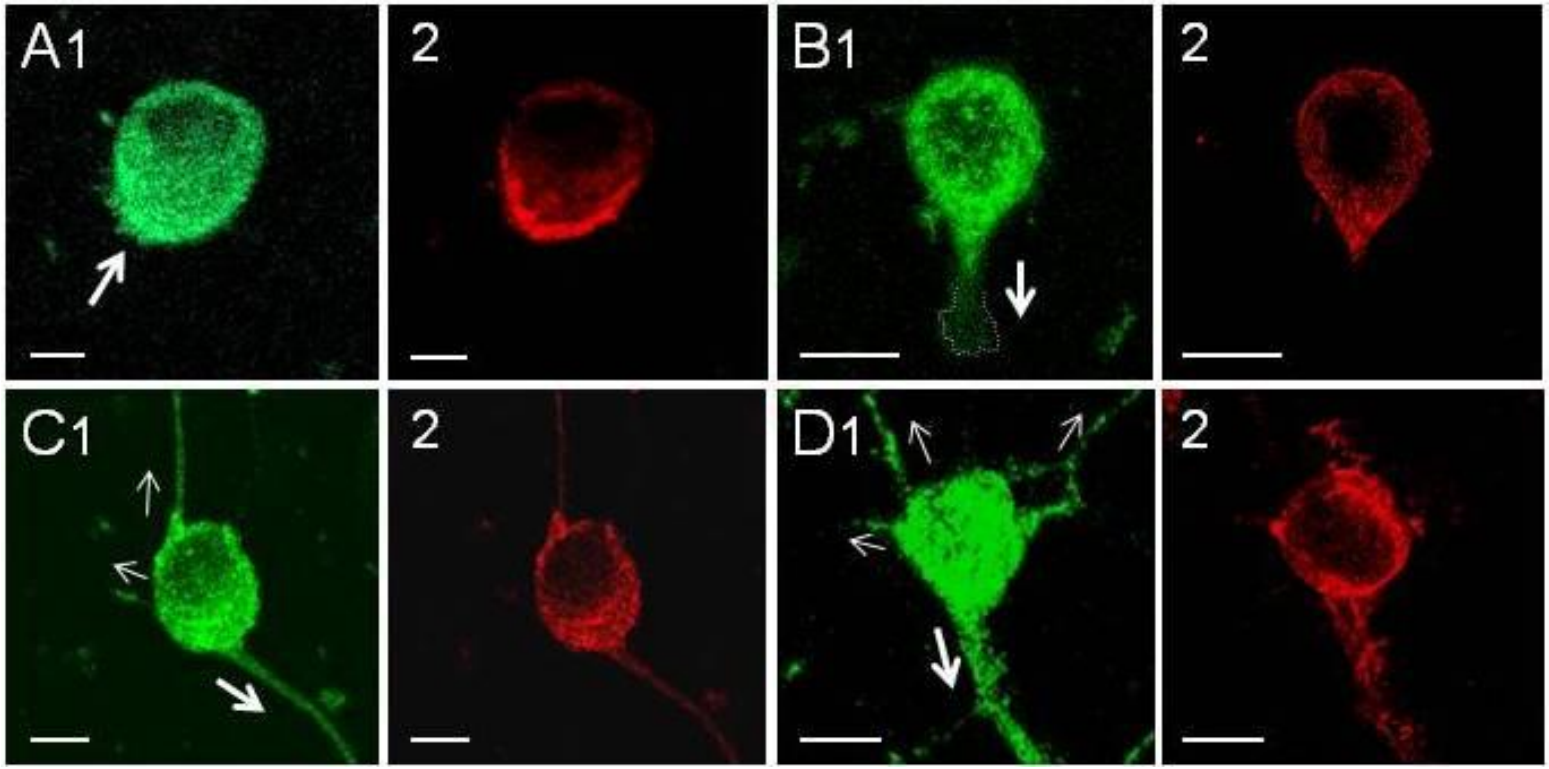
Tension, mobility & Clustering



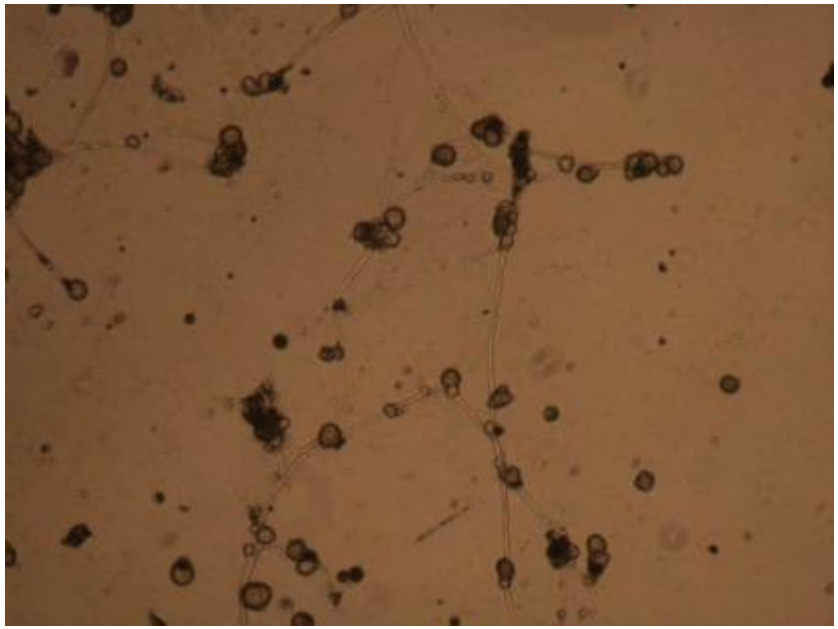


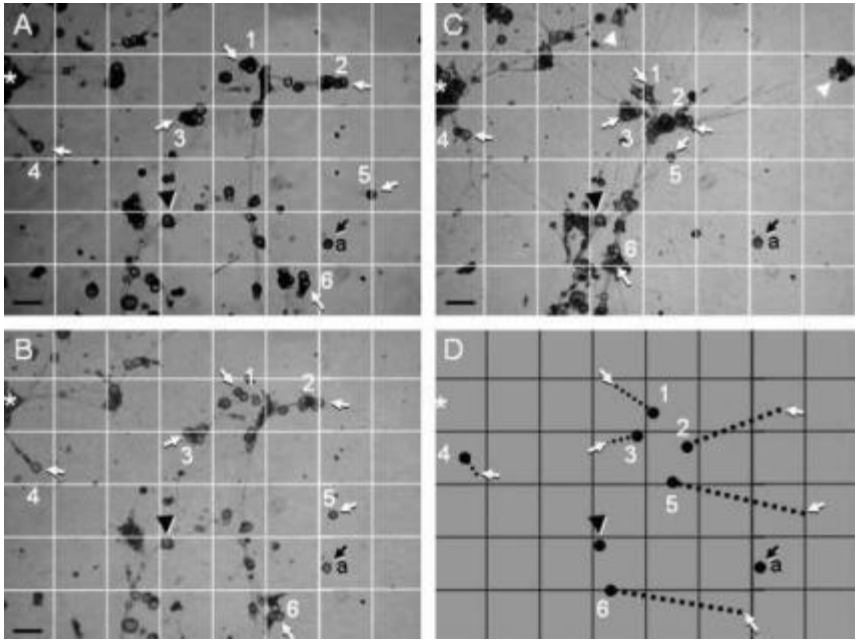
Model

Actin, Mobility and Shape

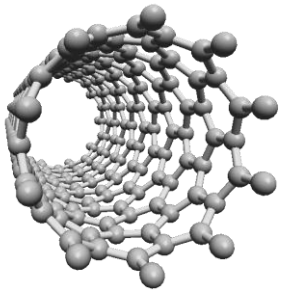


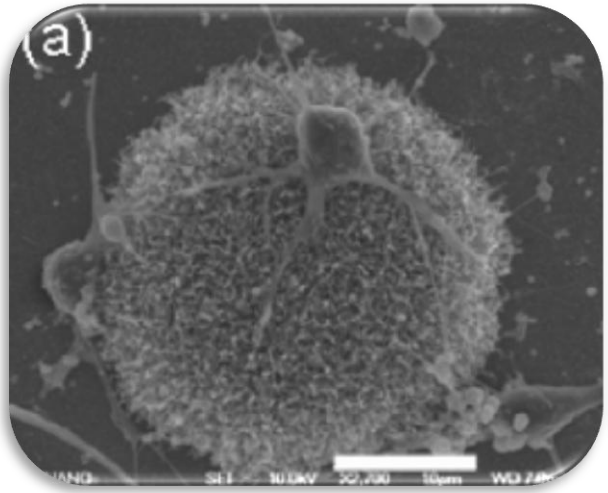
Clustering

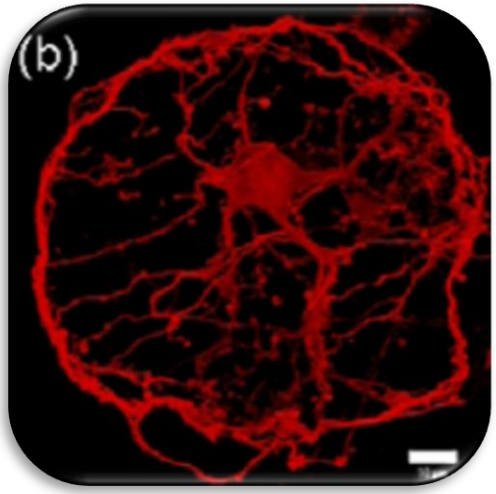




Preferred Adhesion to Rough Surfaces



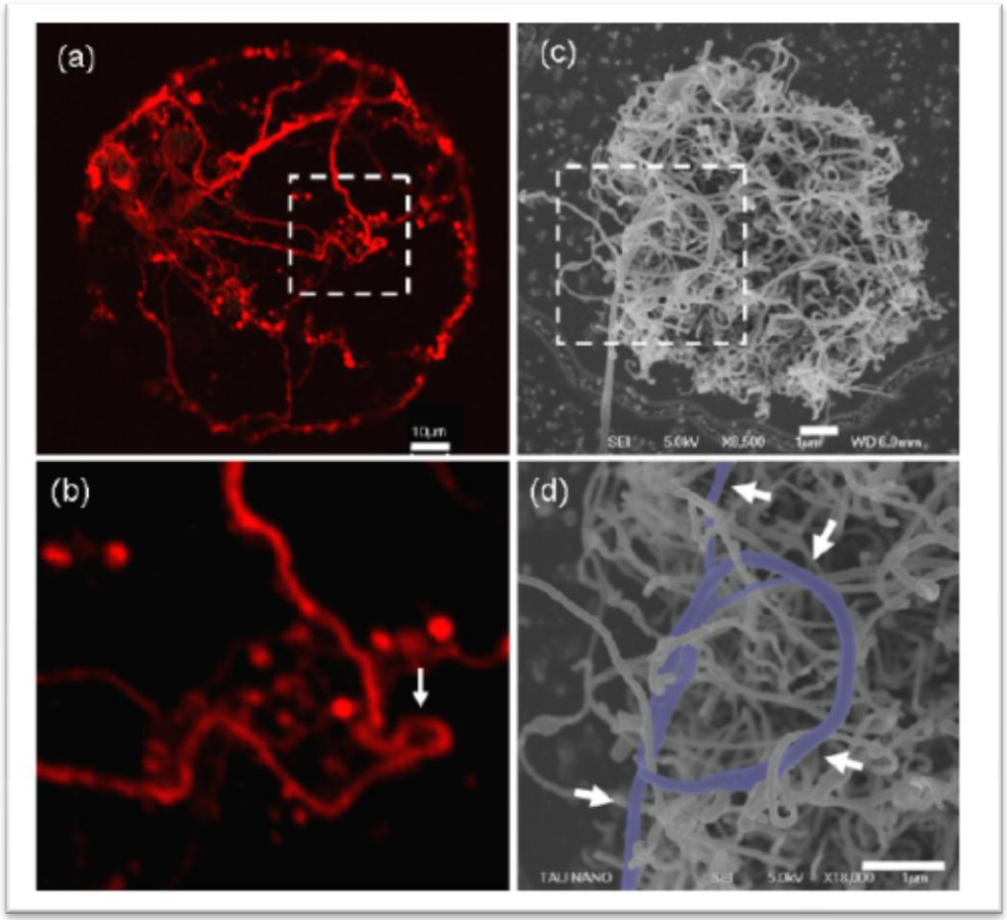




Sorkin et al., Nanotechnology 2009

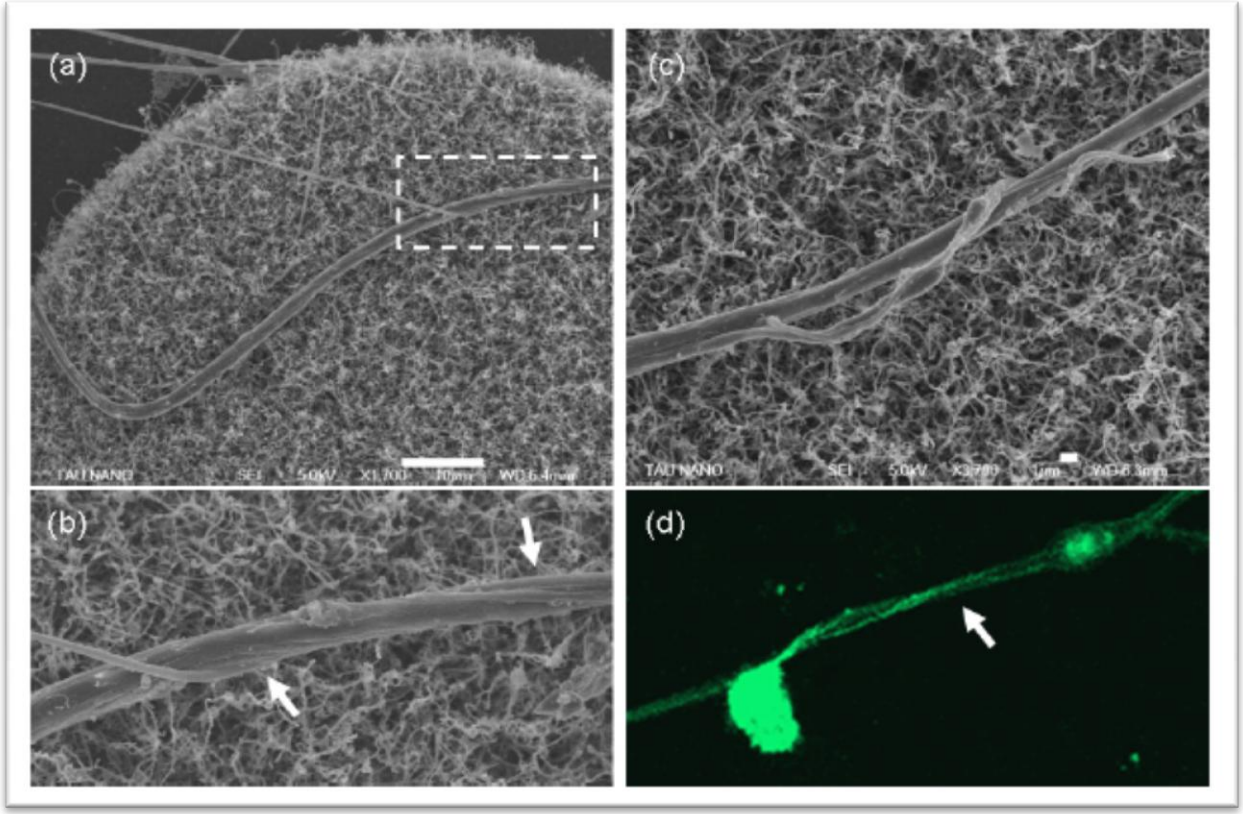
Greenbaum et al., J NeuroSci Method 2009

Twining – Thin Processes



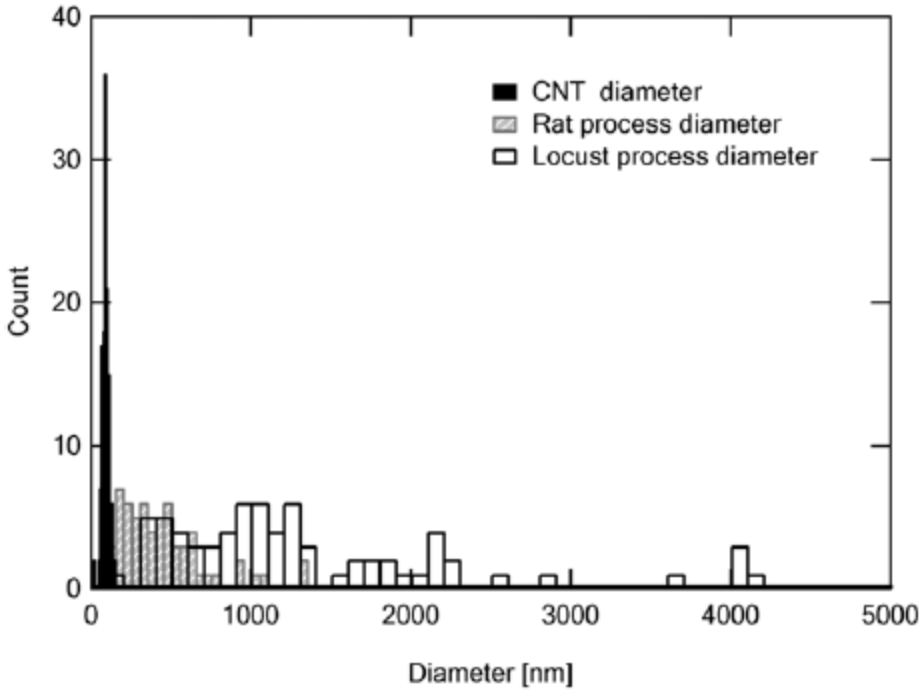
Sorkin et al., Nanotechnology 2009

Twining and Scale



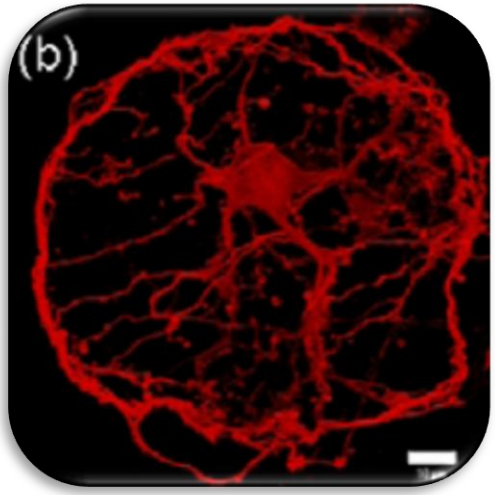
Sorkin et al., Nanotechnology 2009

Length Scales



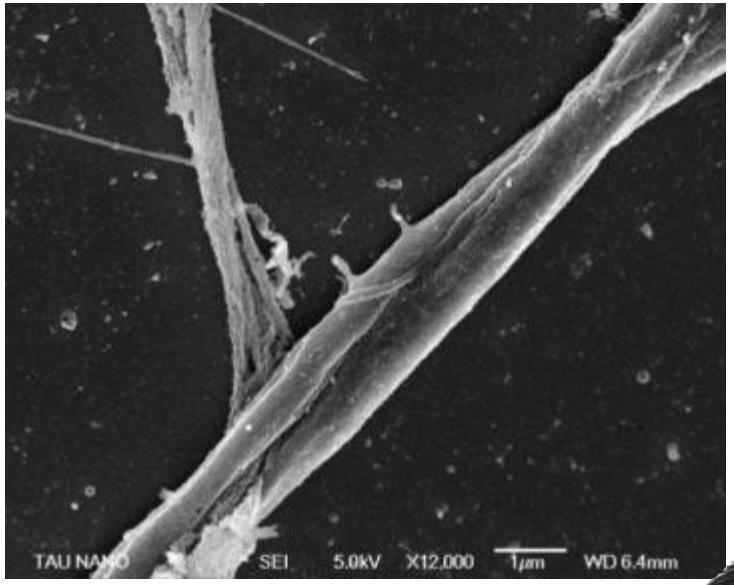
Sorkin et al., Nanotechnology 2009

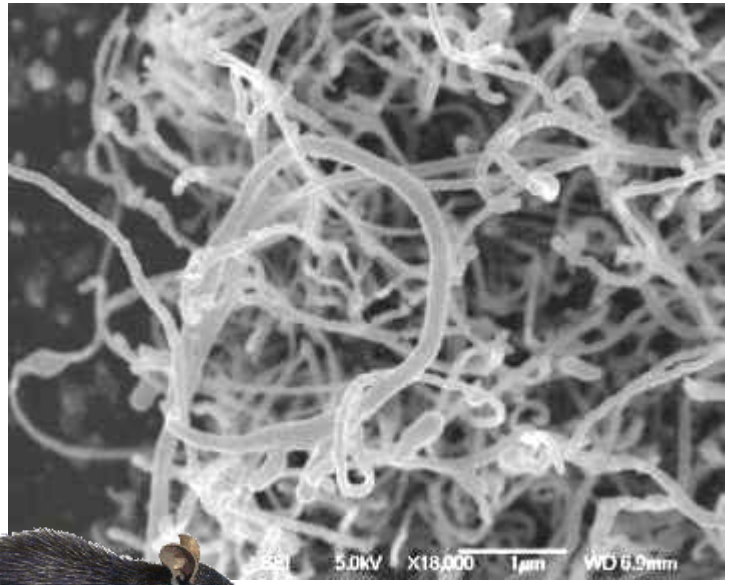
Rat Neuron

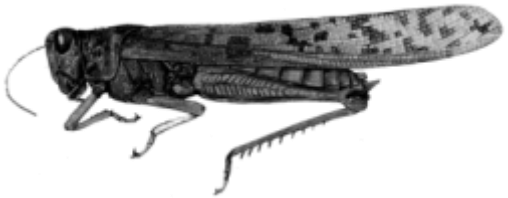


Locust Neuron

Tendrils and processes; Not Just a CNT Effect

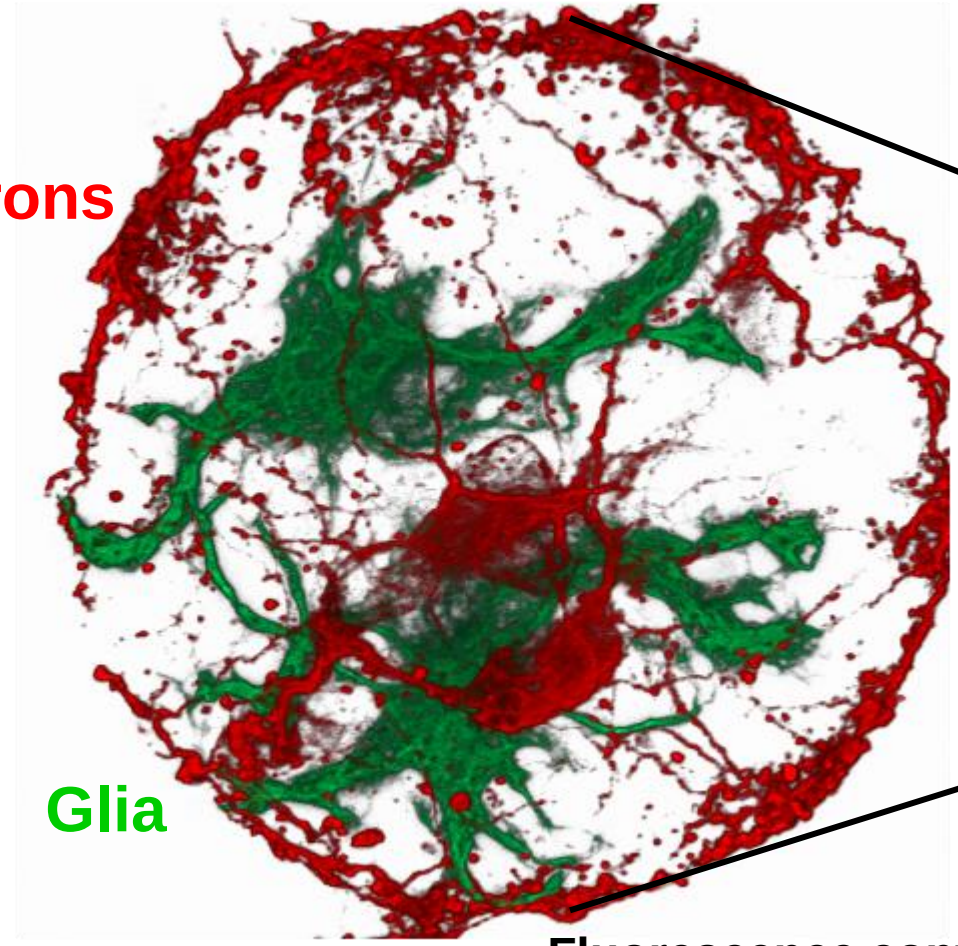


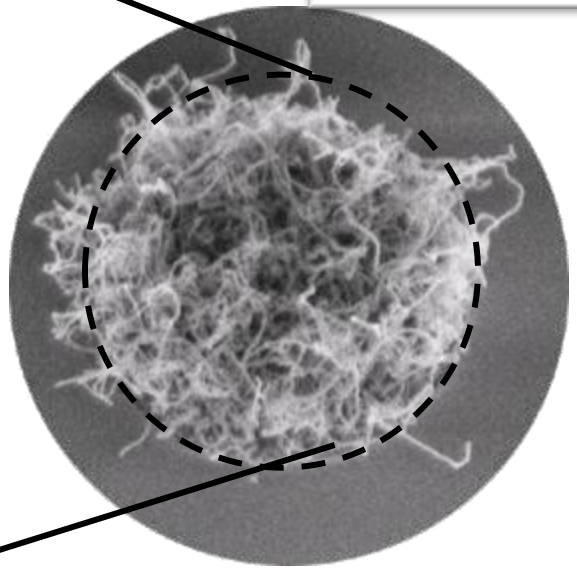




Sorkin et al., Nanotechnology 2009

Entanglement

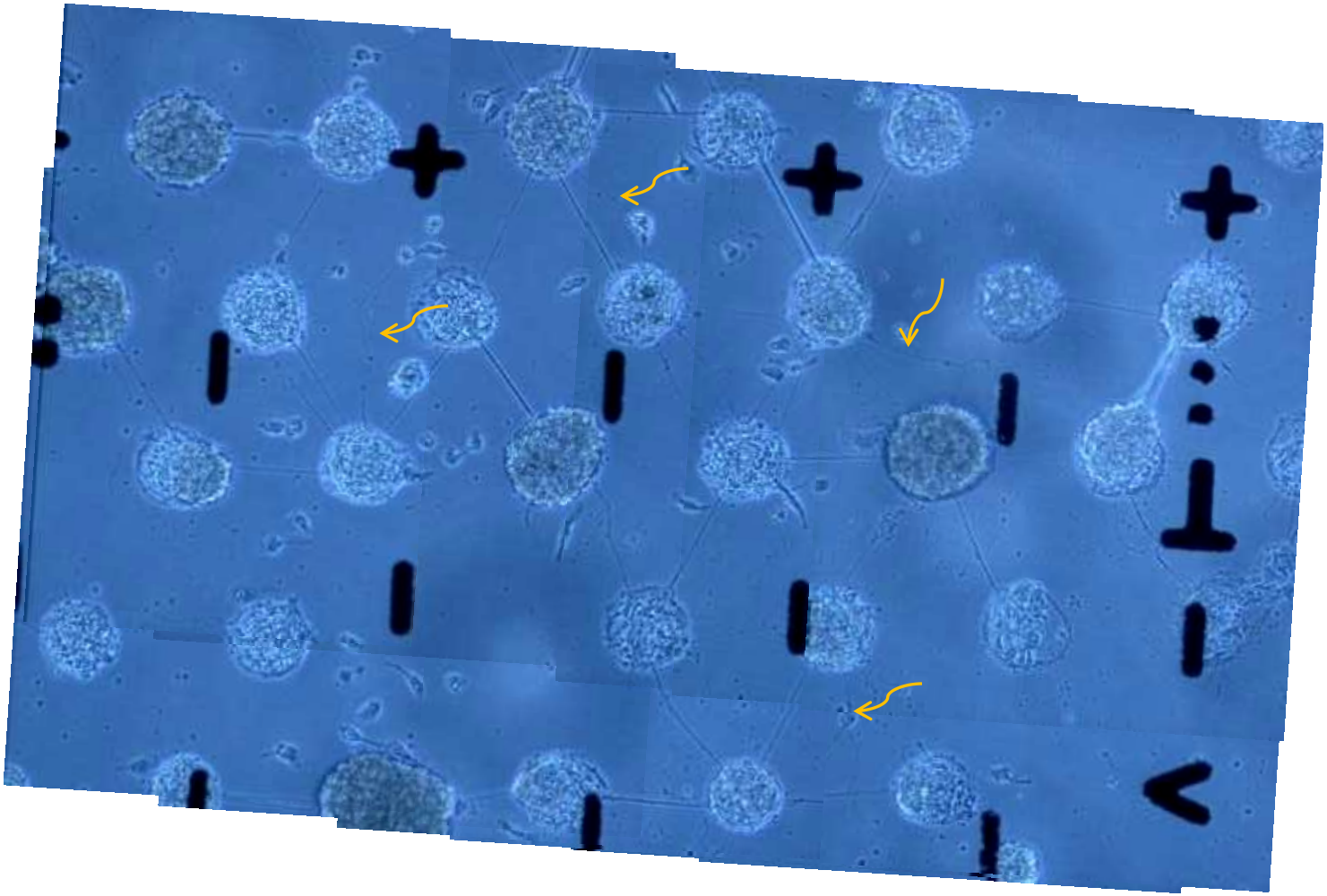




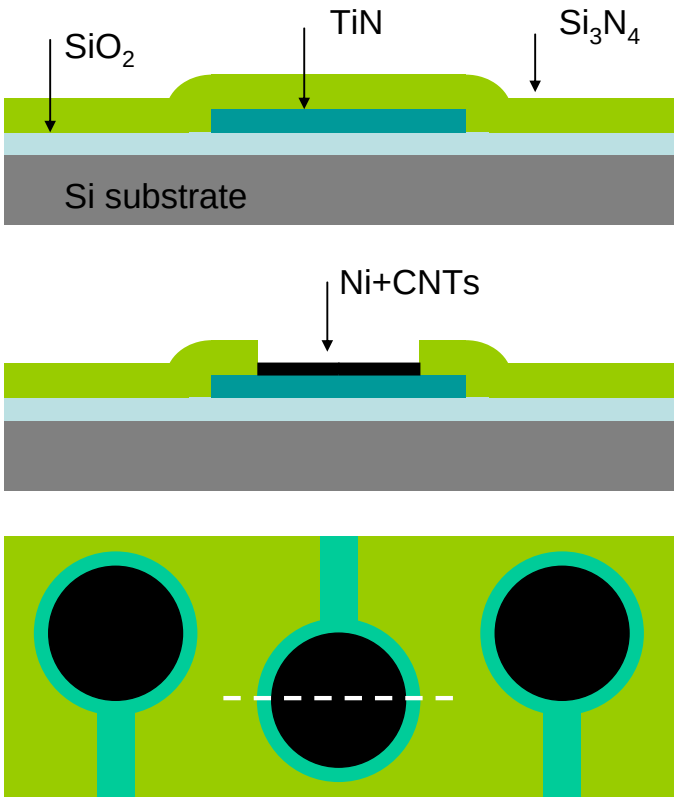
HRSEM

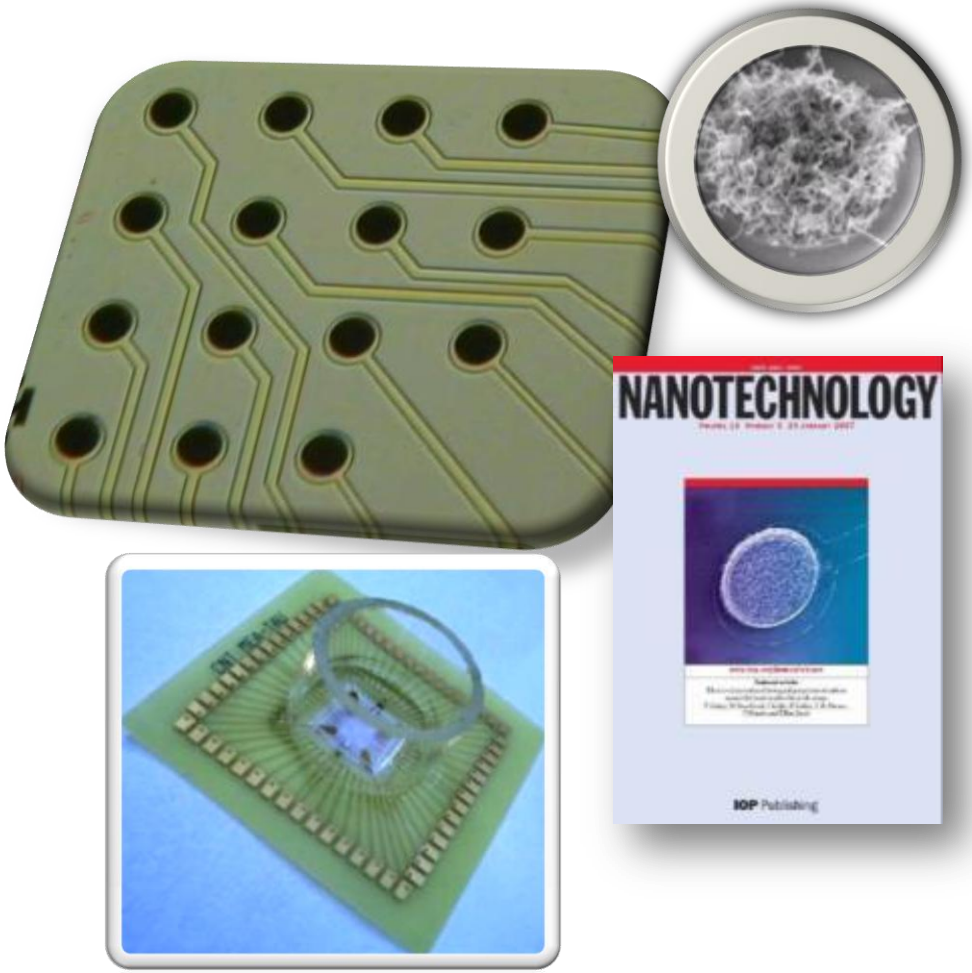
Fluorescence confocal

Sorkin et al., Nanotechnology 2009



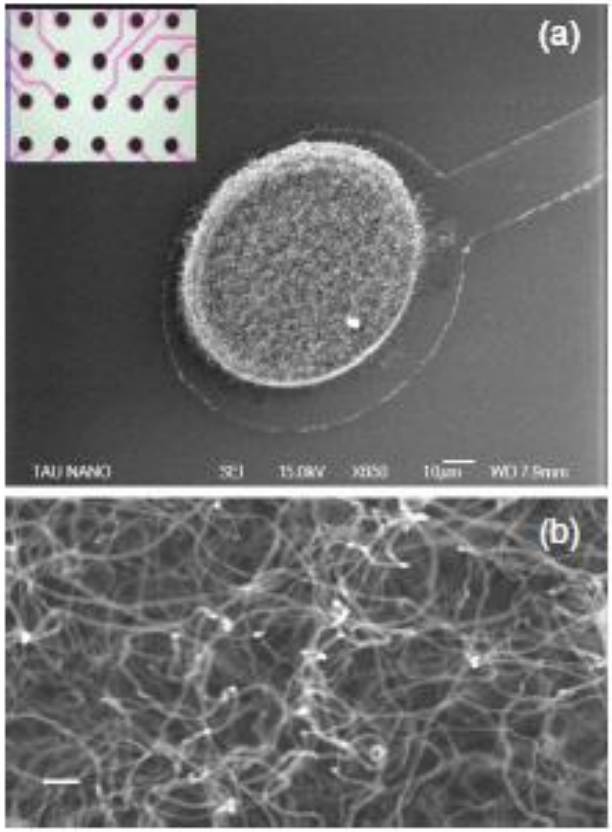
CNT Multi electrode array

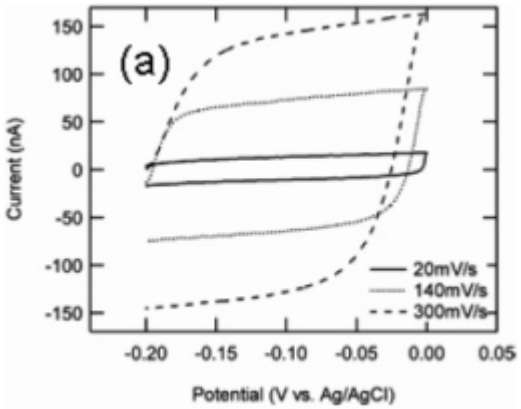


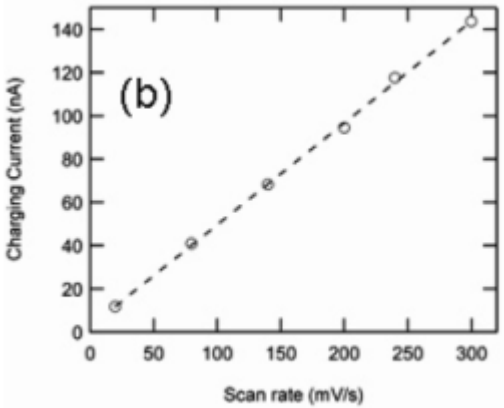


Gabay et al. Nanotechnology, 2007

3D electrodes



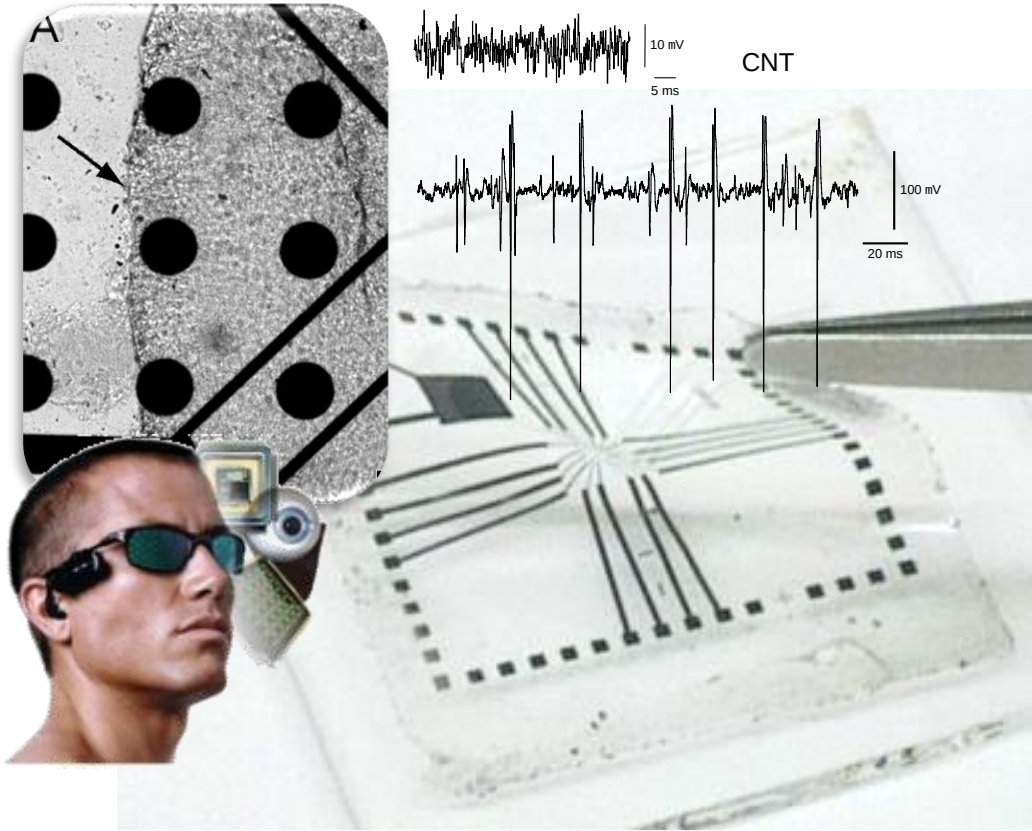




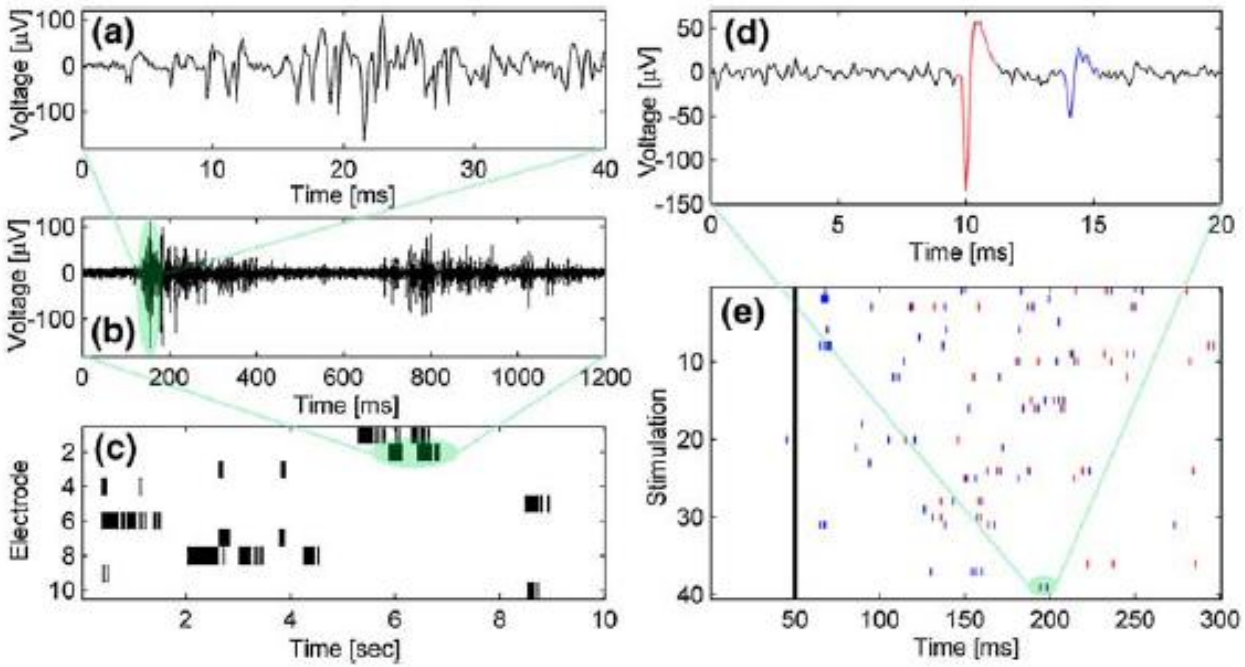
Neuro Chips

- In vitro: Brain-on a chip

- In vivo: Neuroprosthetic Devices



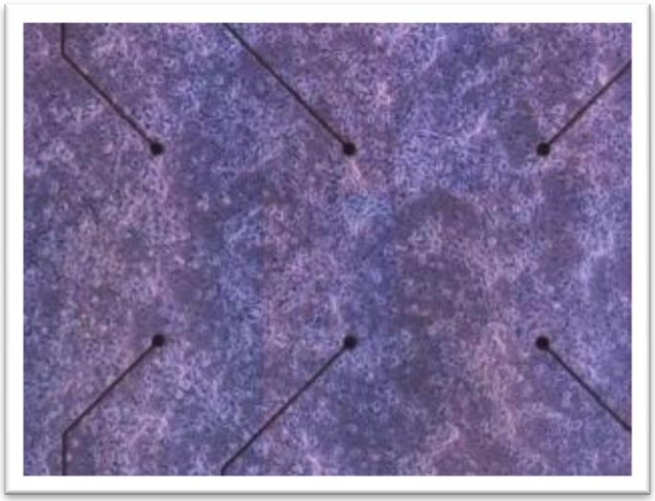
Recordings with CNT MEA from Engineered Neural Circuits



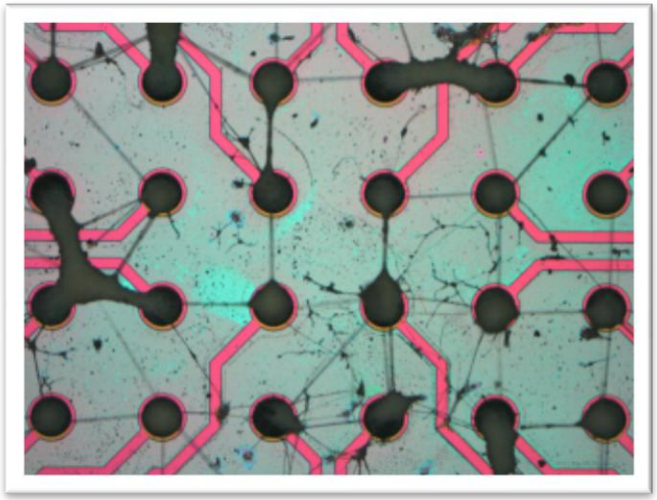
Shein et al., Bio Med micro devices, 2009

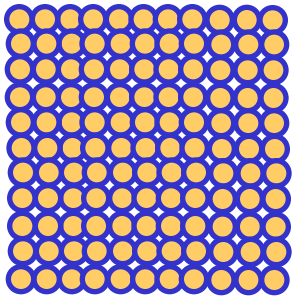
Networks

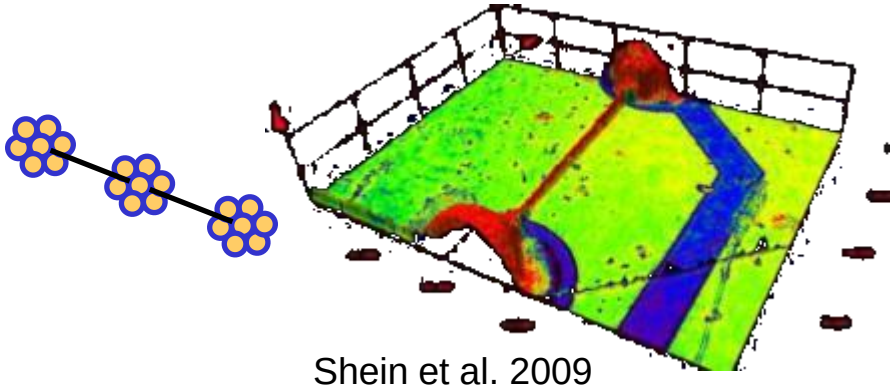
Uniform



Engineered Clusters

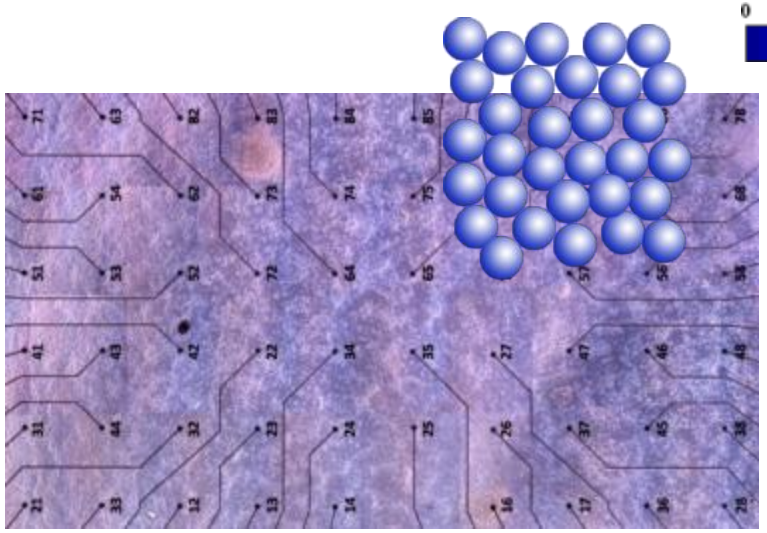


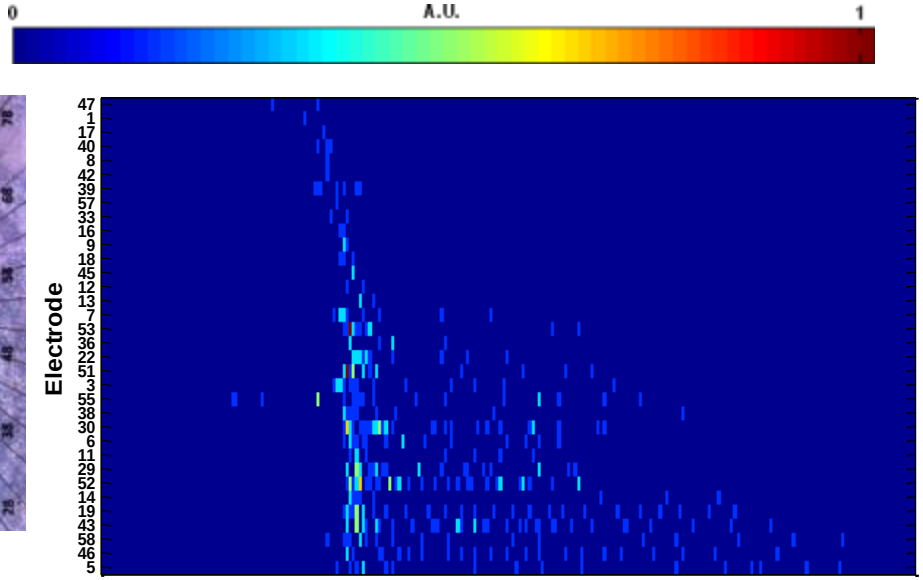




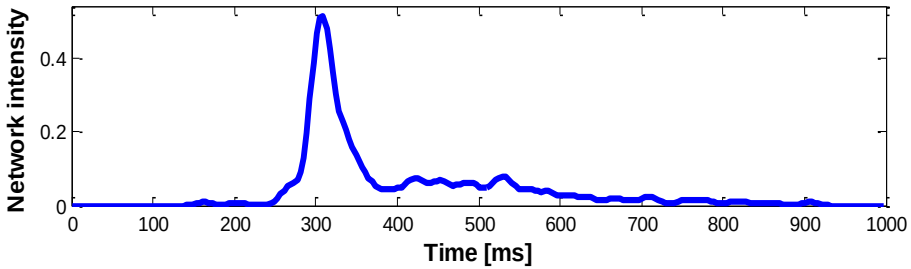
Shein et al. 2009

Uniform networks

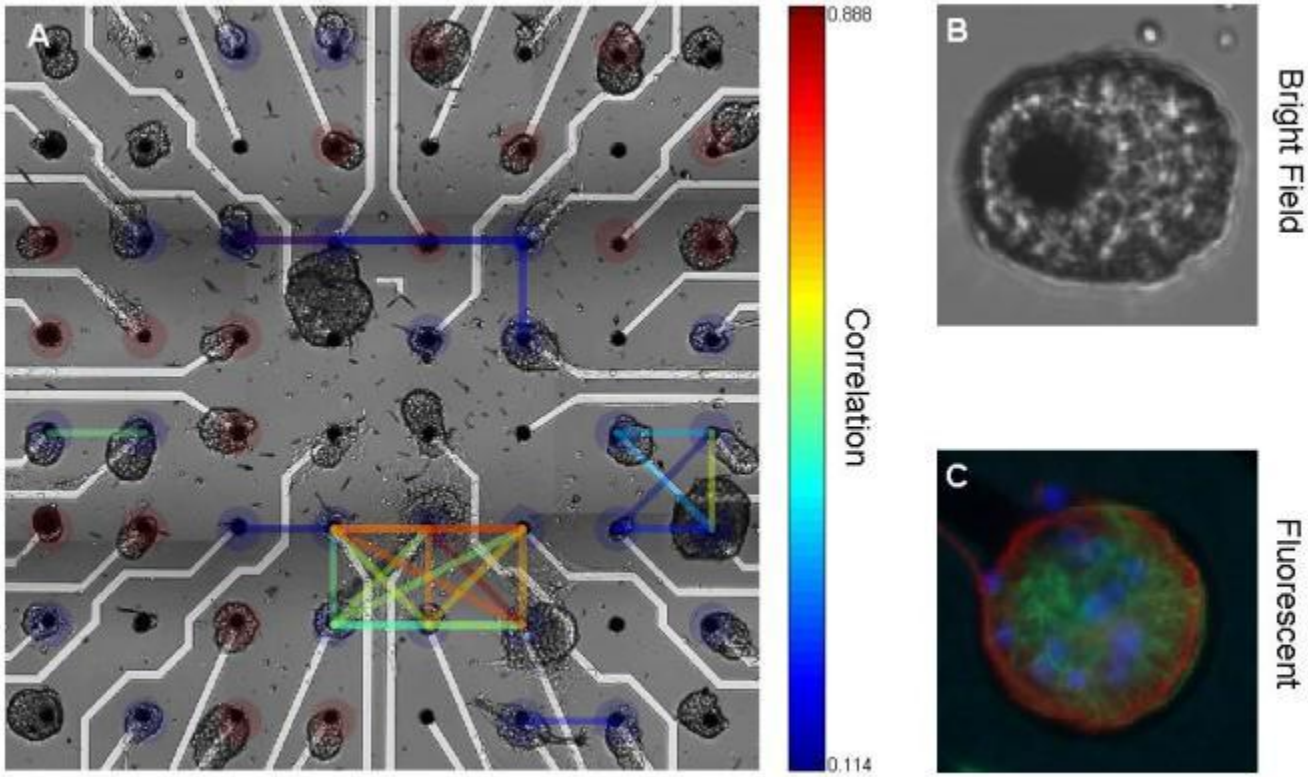




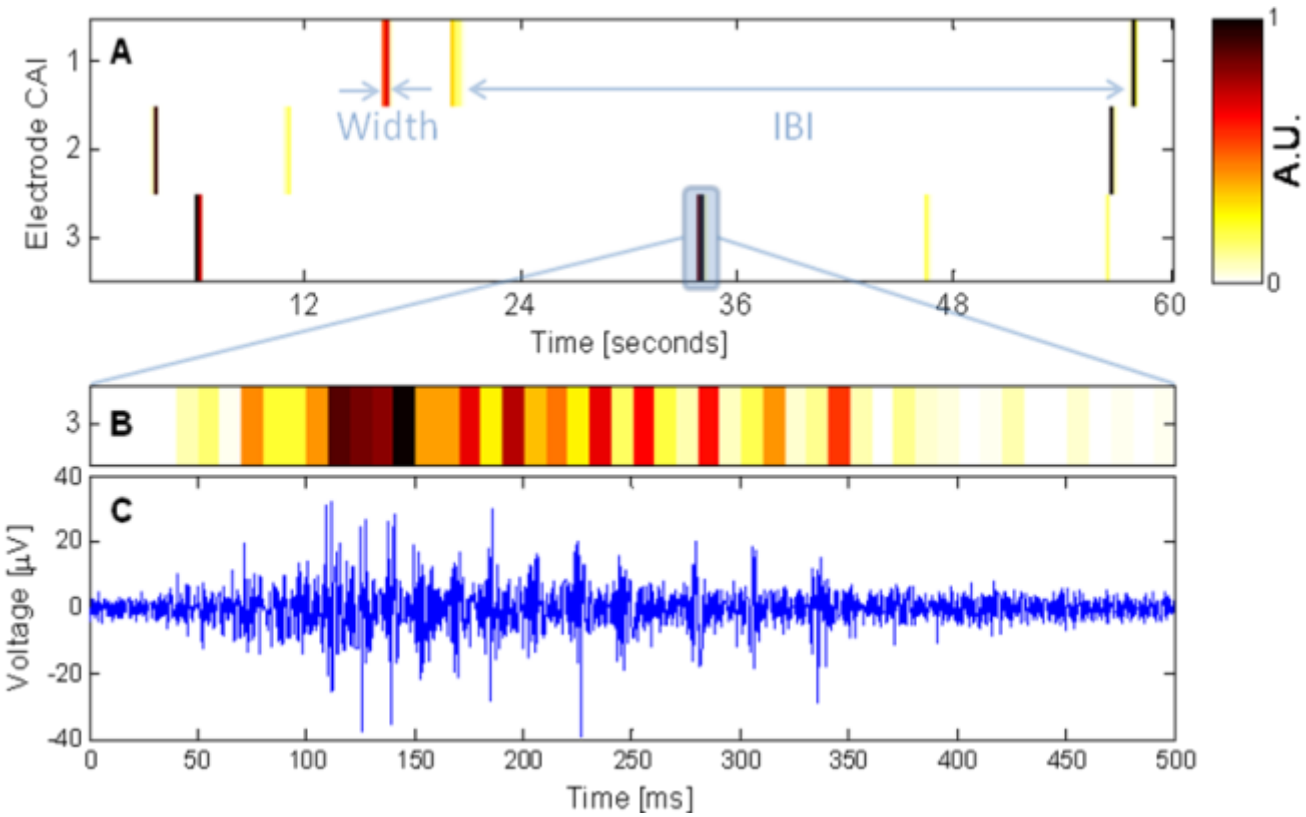
- Recruitment of the entire network (tens – hundreds of ms).
- All the neurons act as one unitary network – if the threshold for SB activation is reached, all the neurons in the network exhibit firing.
- High correlations are found both between adjacent as well as distant neurons.



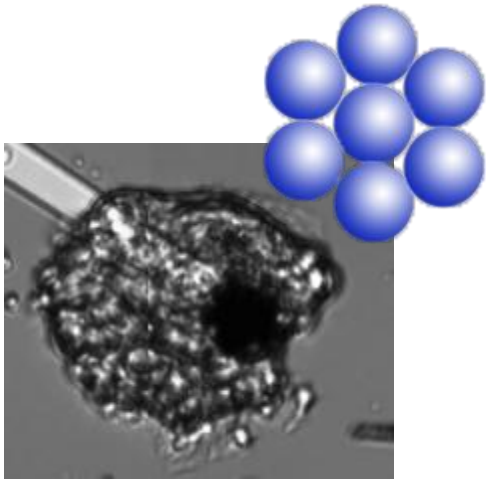
Clusters;
Isolated and Connected

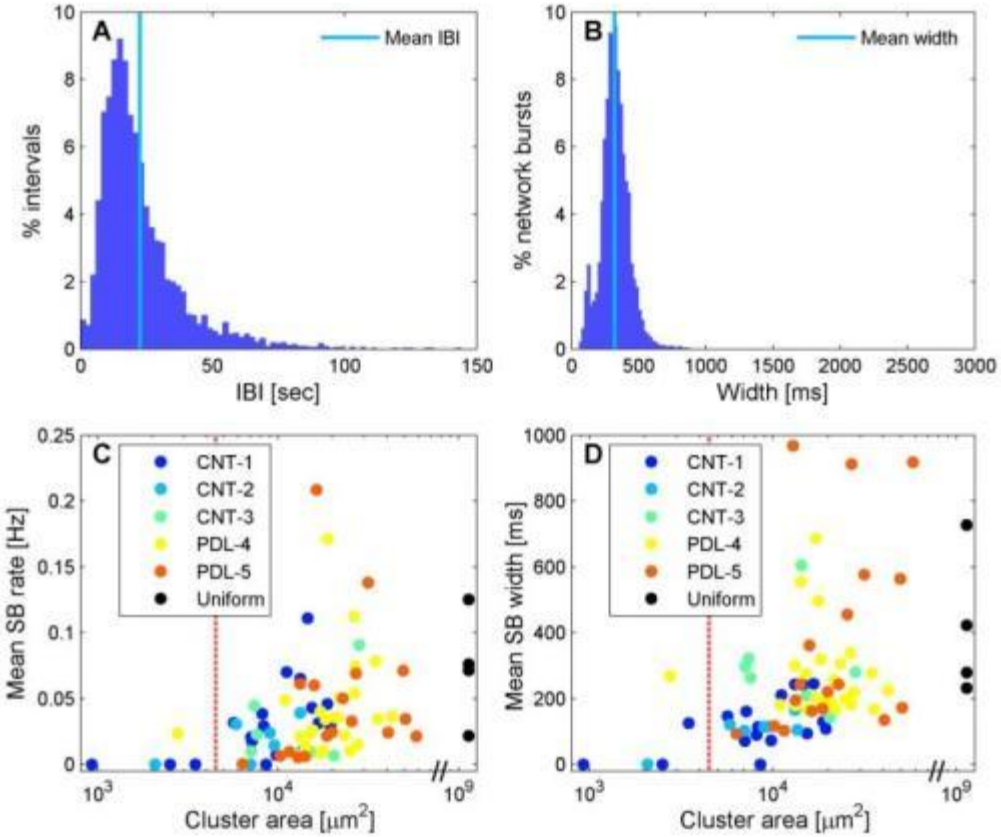


Isolated Cluster Activity

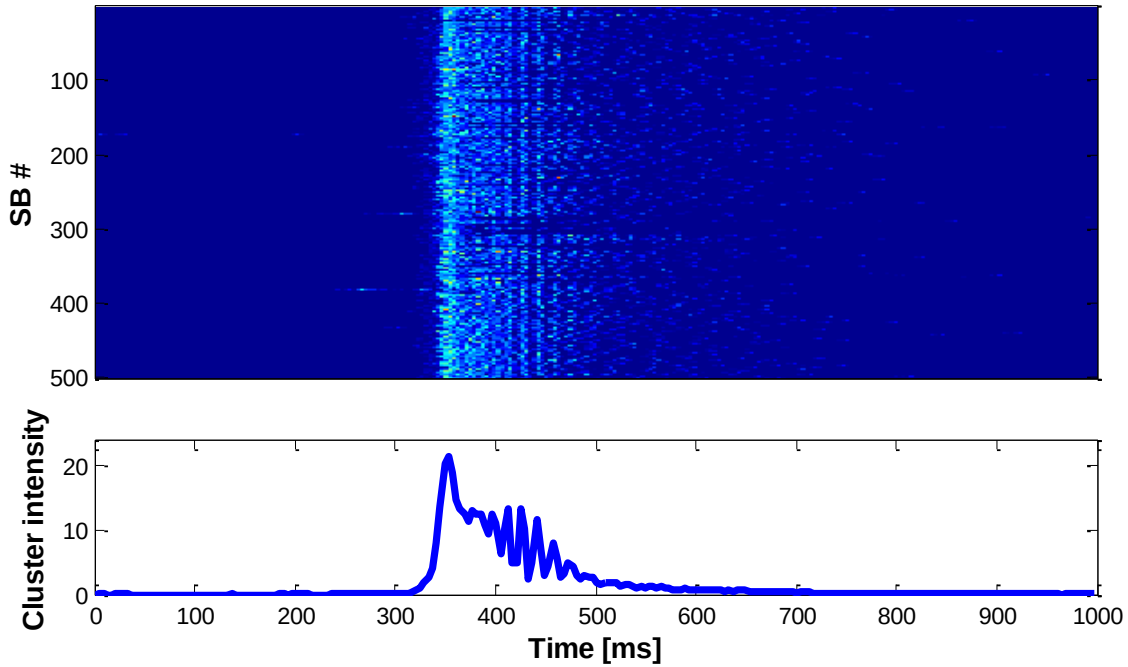


Onset of Bursting Activity



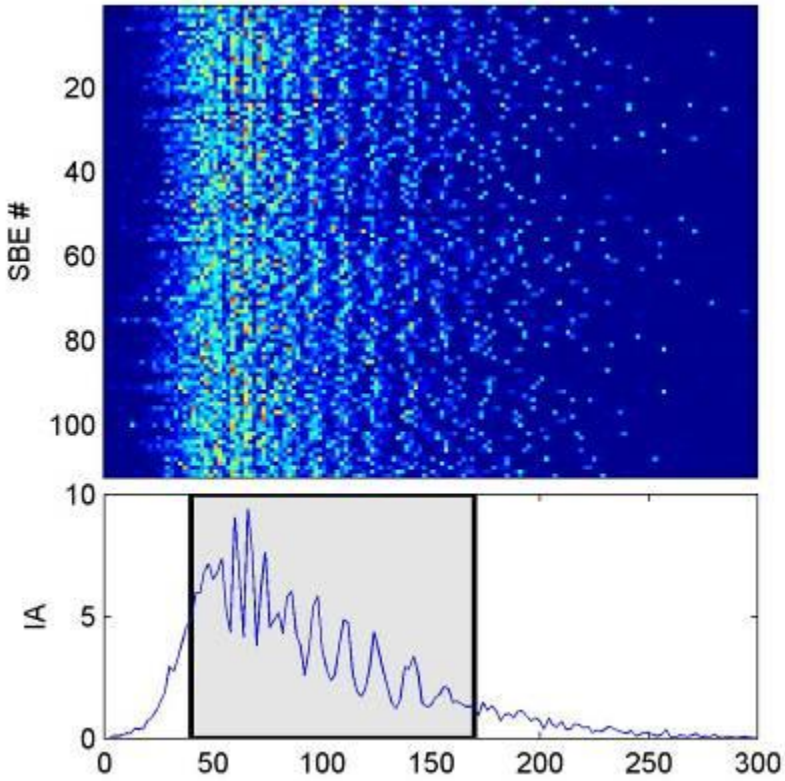


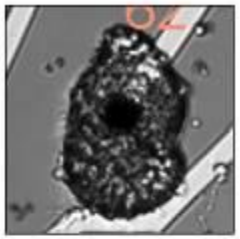
Isolated clusters

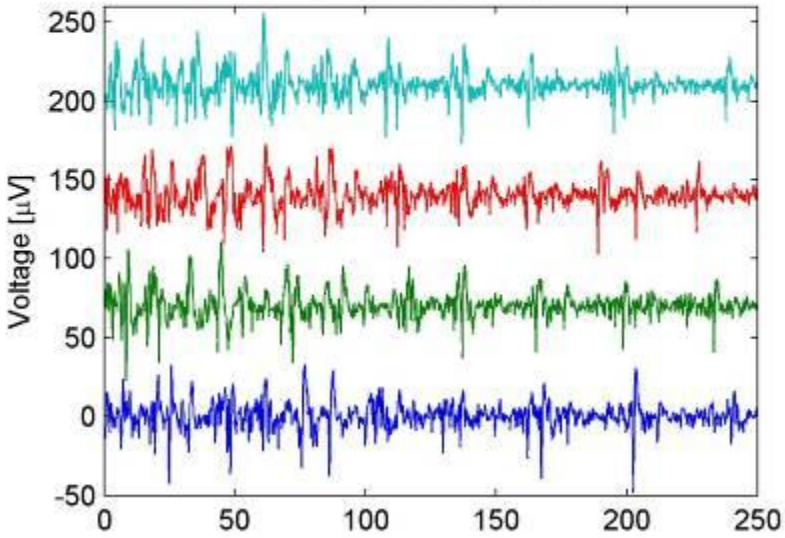


- Fast recruitment (tens of ms).
- All the neurons act as one unitary network.
- Persistent oscillations

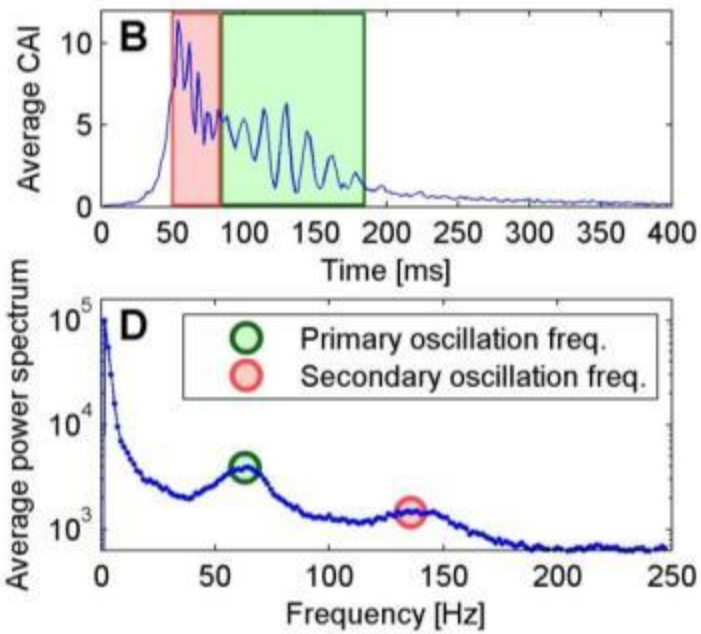
Population Level Activity

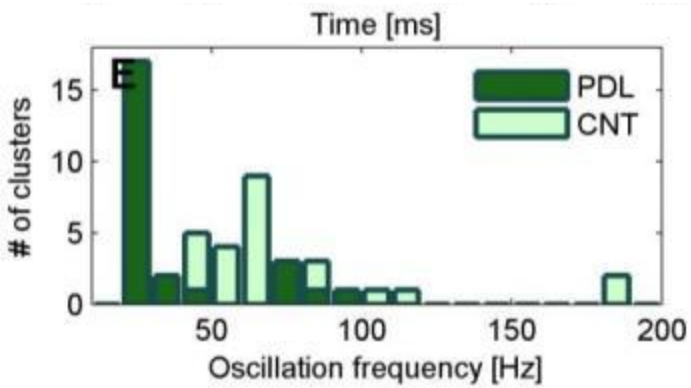




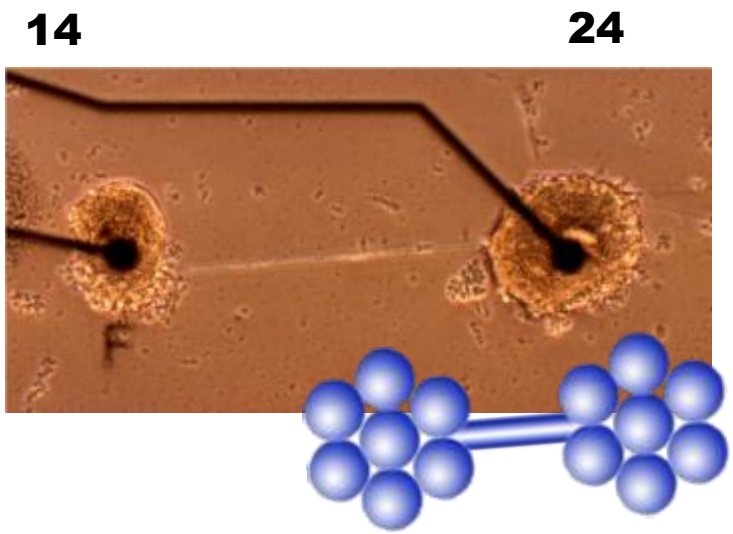


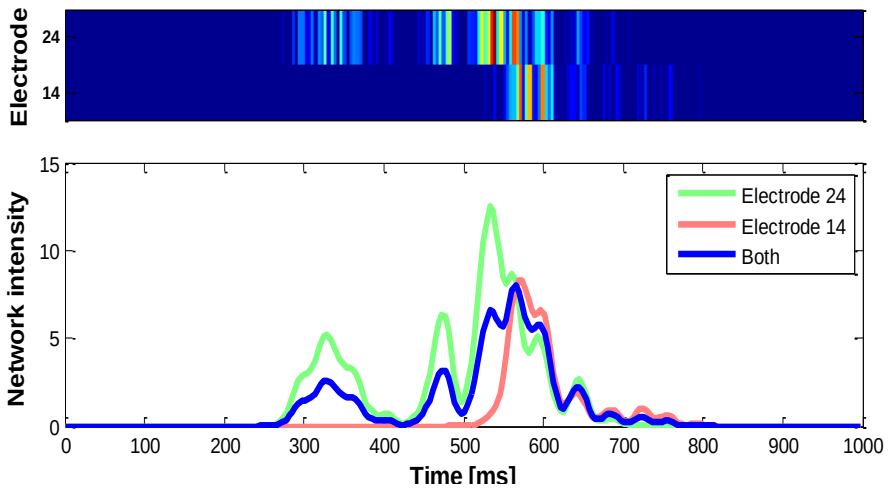
Frequency range





Coupled clusters

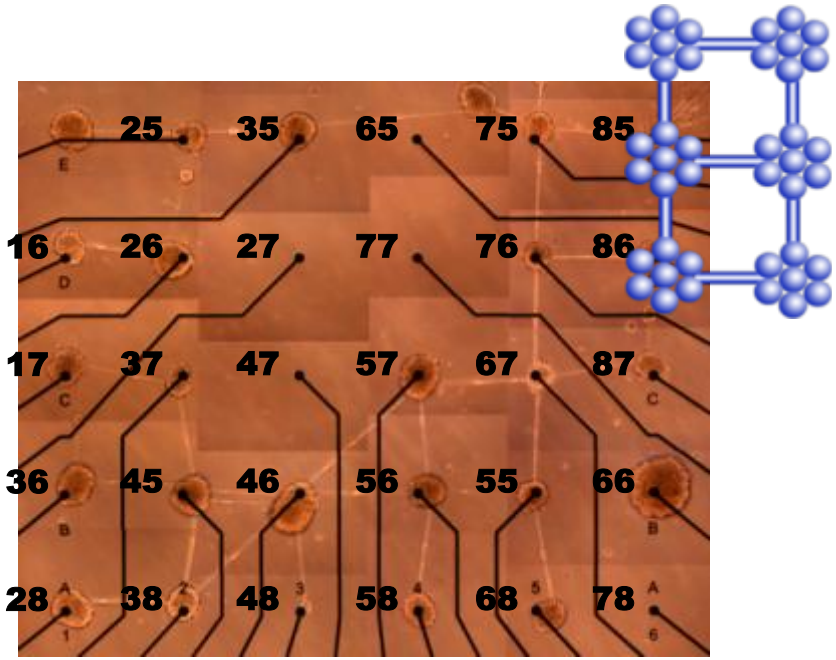


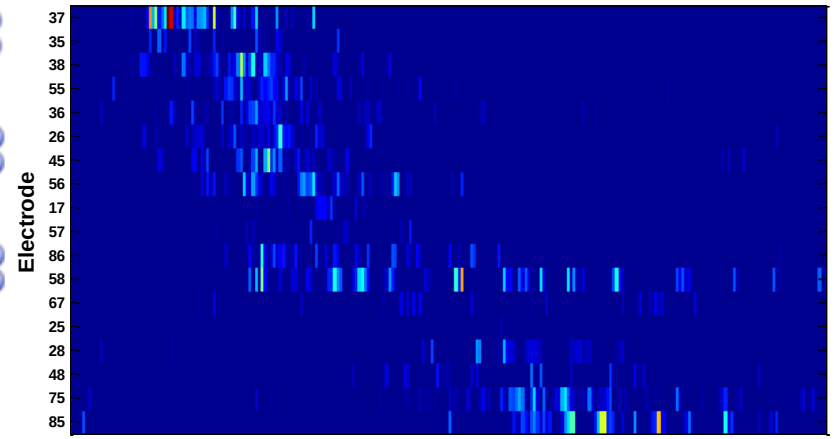


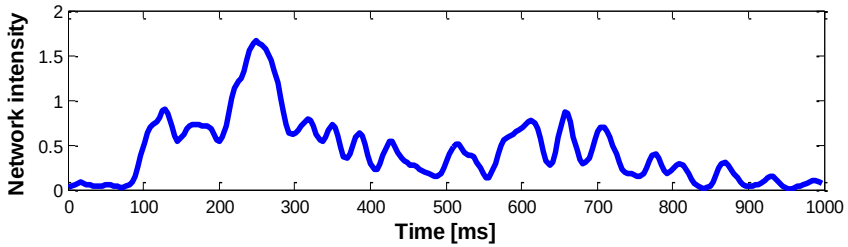
- Restricted directionality
- Long delays between the activation of connected clusters
- Gating in the propagation of activity between clusters - not all initiated SBs propagate to the next cluster.


x 10^-6

Clustered network

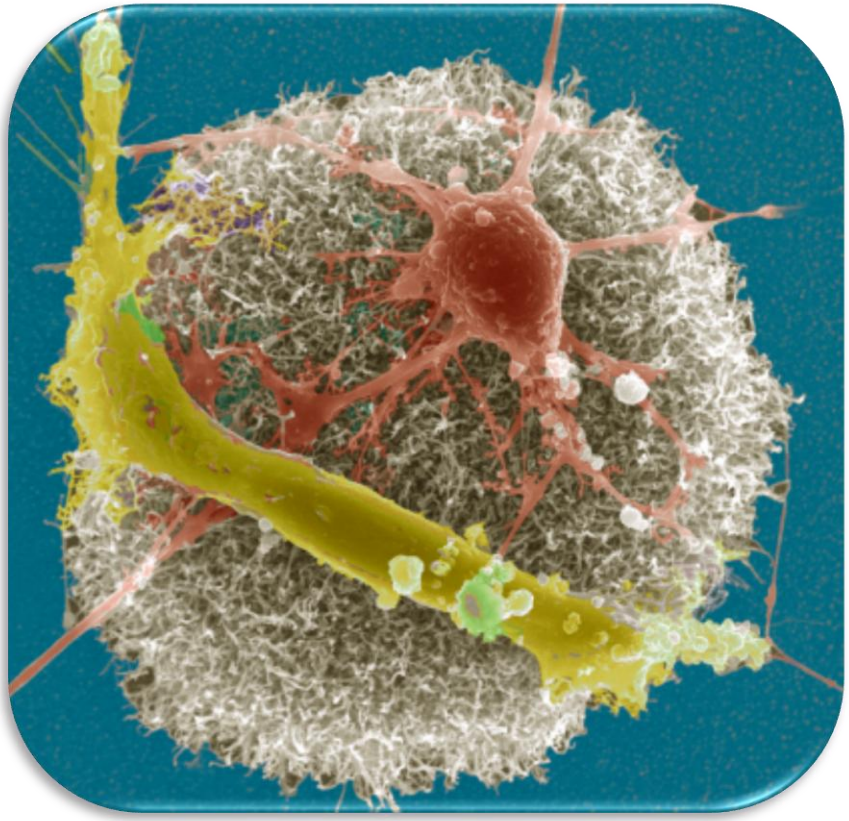




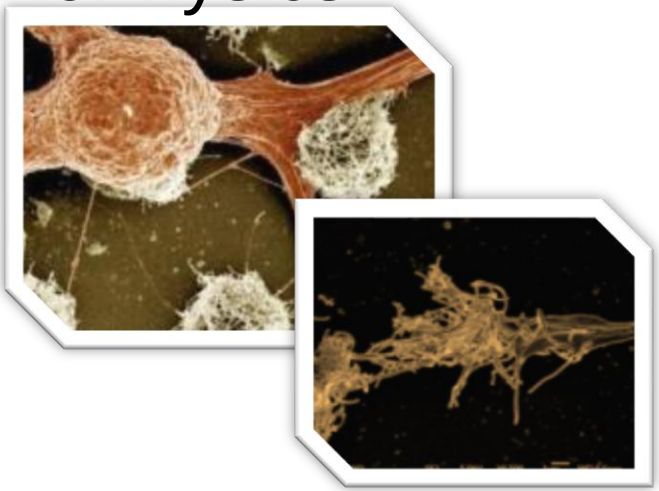


- Restricted directionality.
- Slow recruitment (hundreds of ms)
- Sequential activation of connected clusters.
- Correlations are high within each cluster and decrease in accordance with the topological distance between neurons.
- The SB is not necessarily activated in all the clusters in the network.

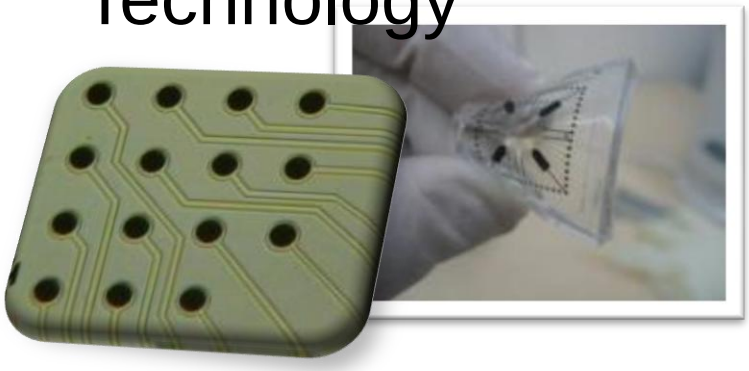
Neurons and CNTs



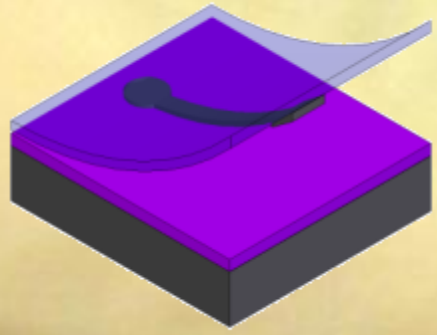
BioPhysics

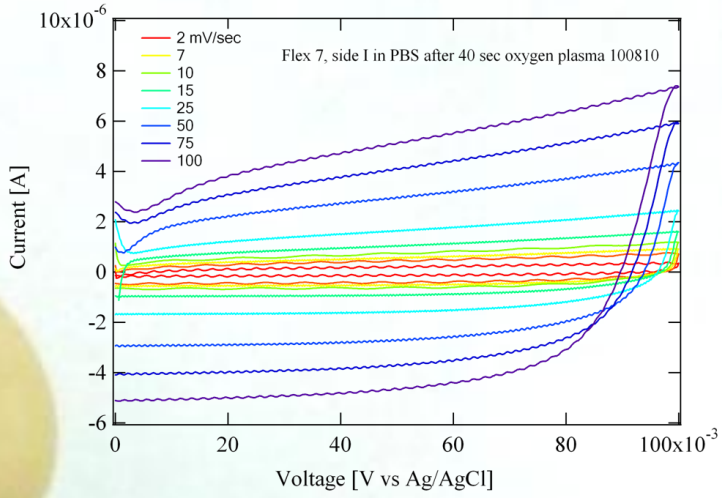


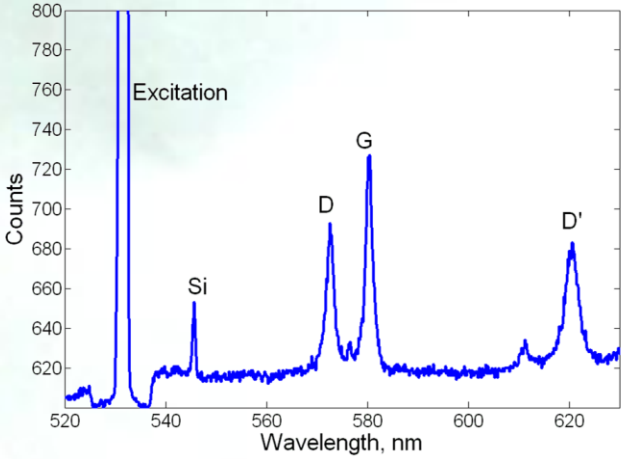
Technology



Flexible CNT Devices



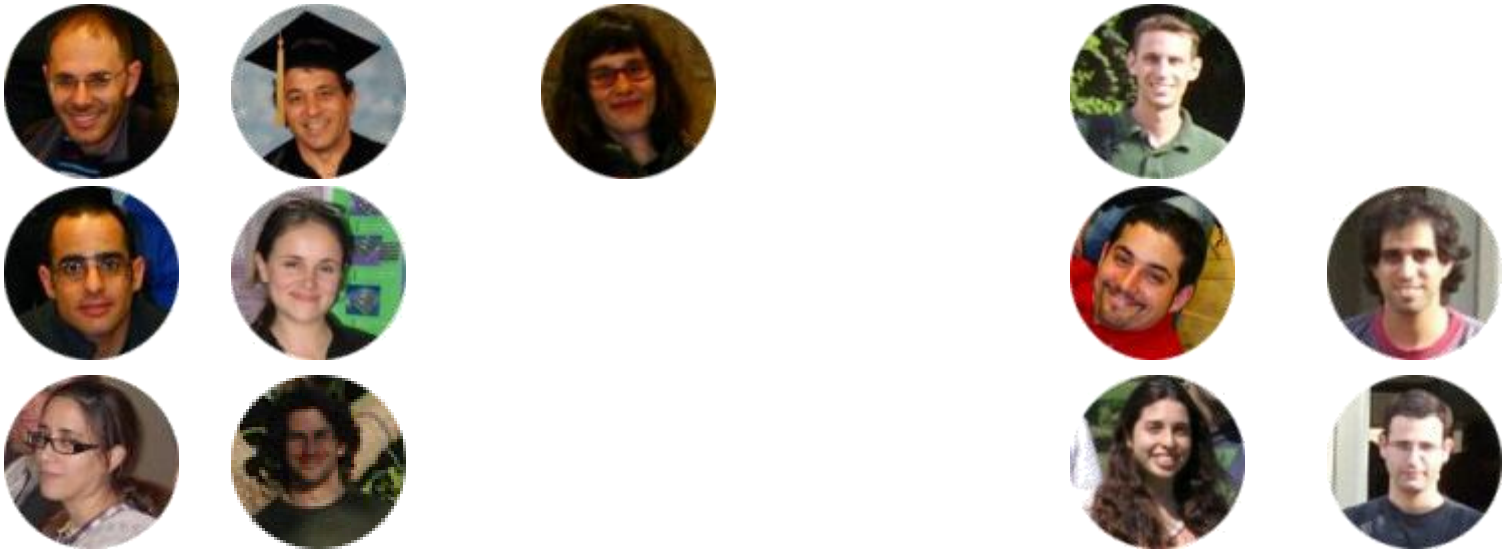




After three months in the eye of a rat, Arie Solomon (TAU)

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)
- <u>Three open questions:</u>
  - 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?



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