Leaders of Activity in Dissociated Neural Cultures

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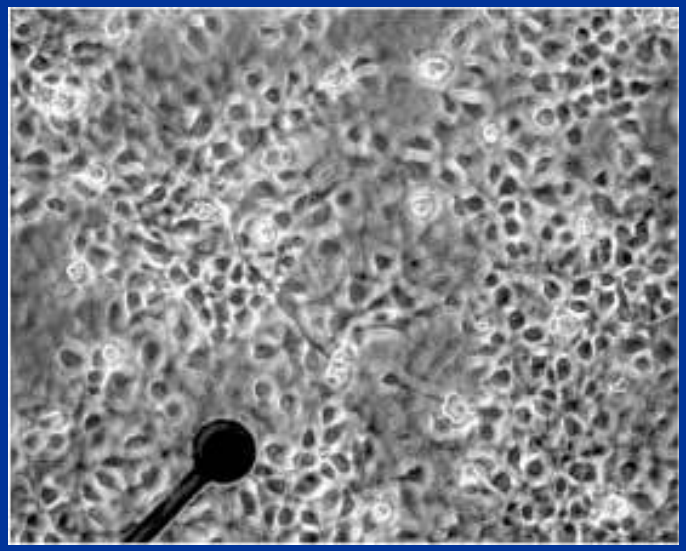

Thanks:

Steve Potter, *GeorgiaTech*

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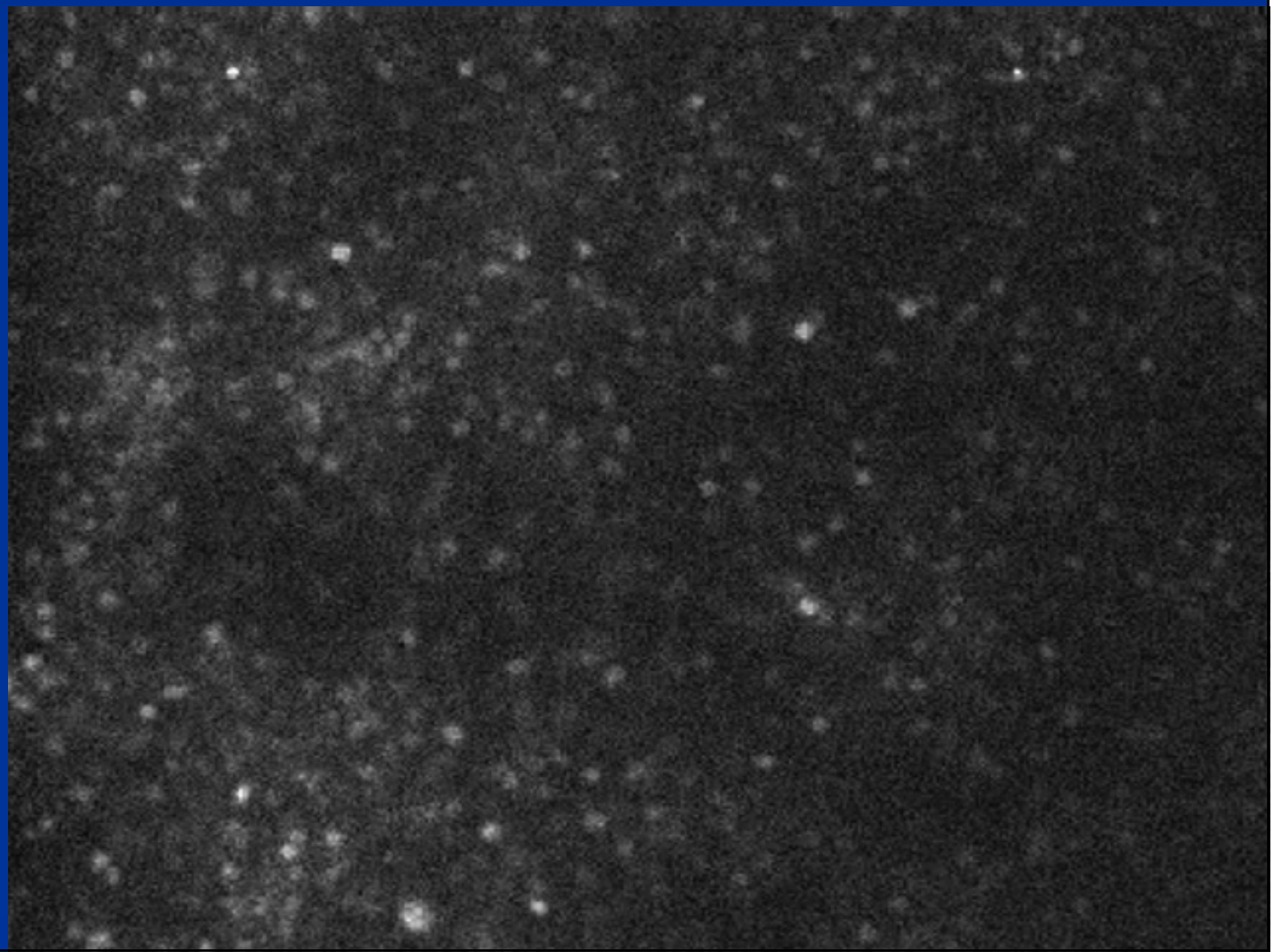
Spontaneous Activity

- Dissociated neurons in culture self-organize into a living network
- Spontaneous activity occurs in population bursts
- 1D shows centers,

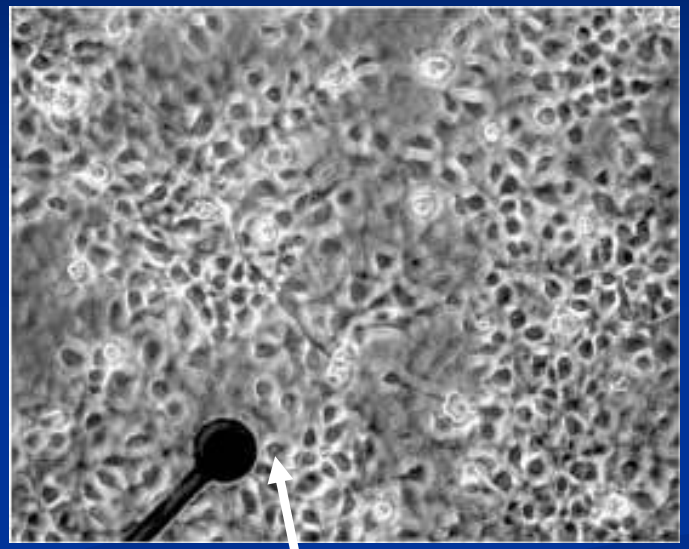
  2D …



Role of First-to-Fire Neurons

- Eytan and Marom found that specific neurons fire *>100msec earlier* than the majority of neurons
- What is their role ?
  - *Leaders* that cause the burst

  or
  - *Sniffers* that better sense the average activity



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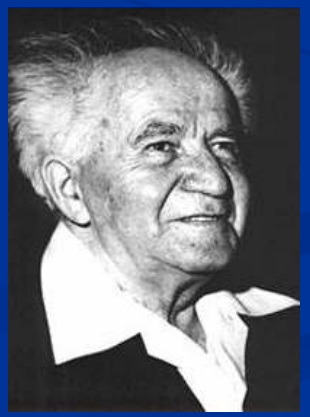
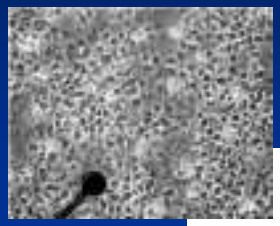
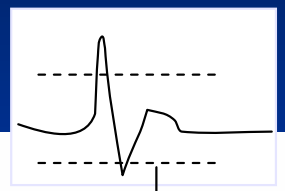
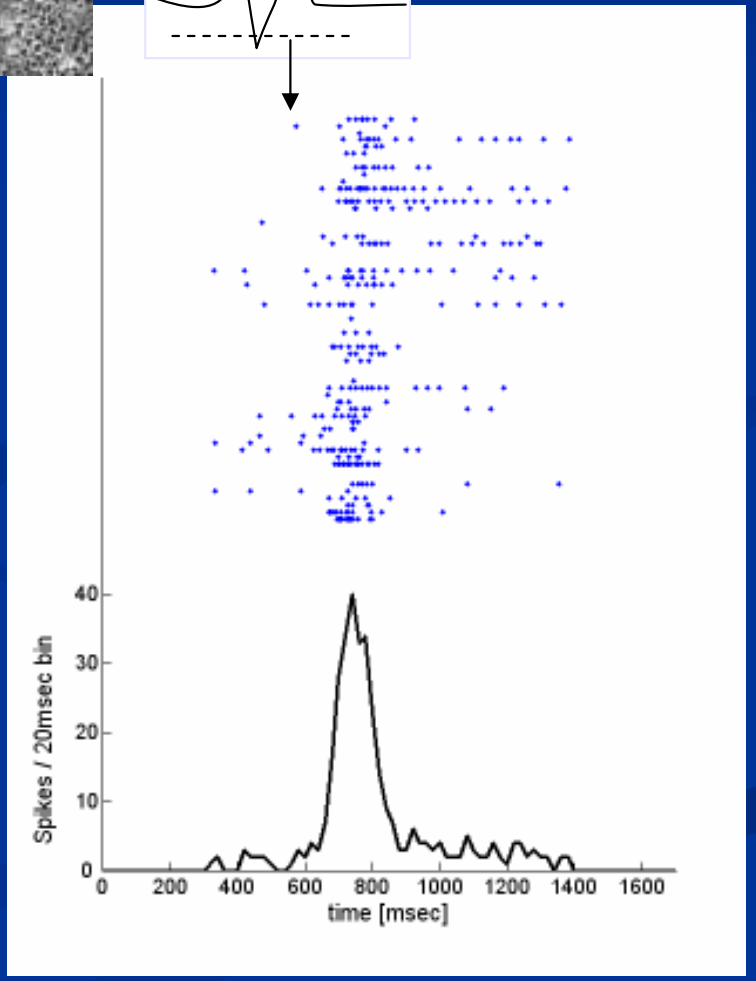


Recording Spontaneous Activity

- Spontaneous activity measurements from **3** labs
  - Potter Lab: rat cortical, pre-natal (E18)
  - Moses Lab: rat hippocampal, pre-natal (E19)
  - Marom Lab: rat cortical, post-natal (P1)
- Multi-electrode arrays (60 electrodes)
- Recording duration
  - Daily recording in ages of 5-40 days
  - ~1000 bursts (~30 minutes) / day





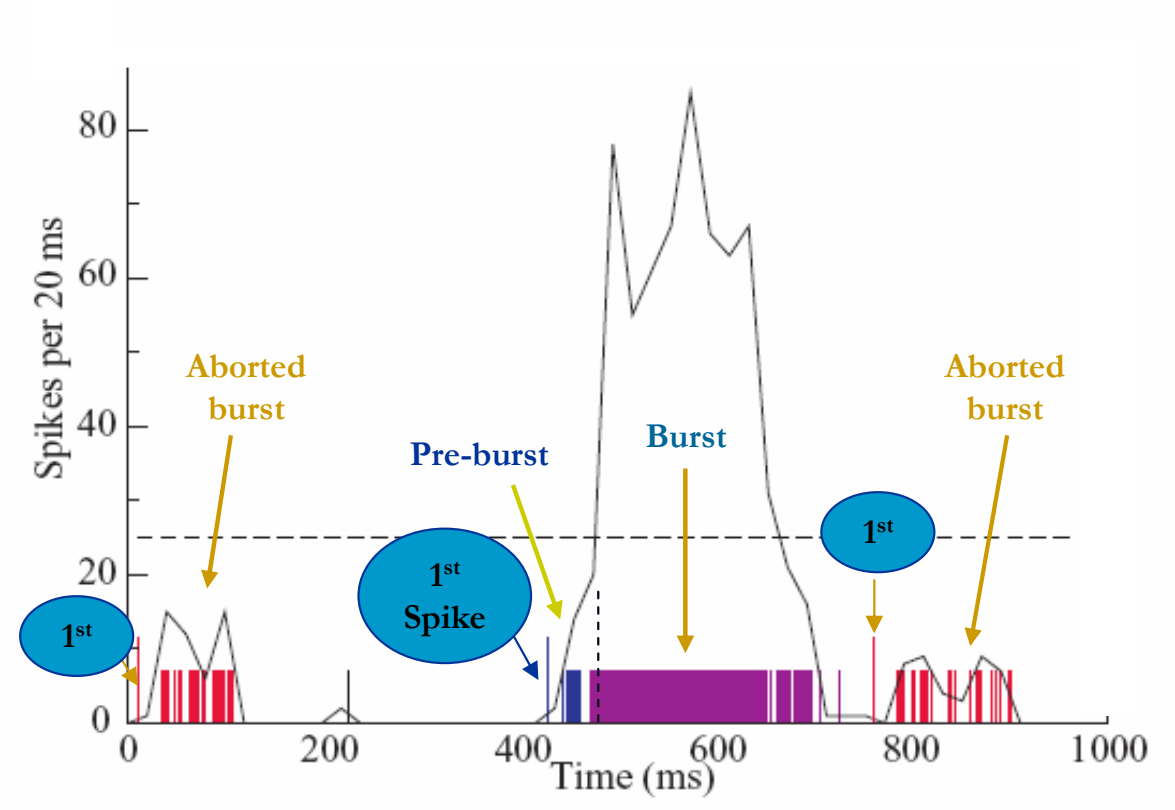


Burst Evolution is Gradual

- First-to-fire electrodes are detected after quiet periods
- Activity increase before the burst is gradual

Terms

- *1st spike*
- *'pre-burst'* → burst
- *'aborted burst'*

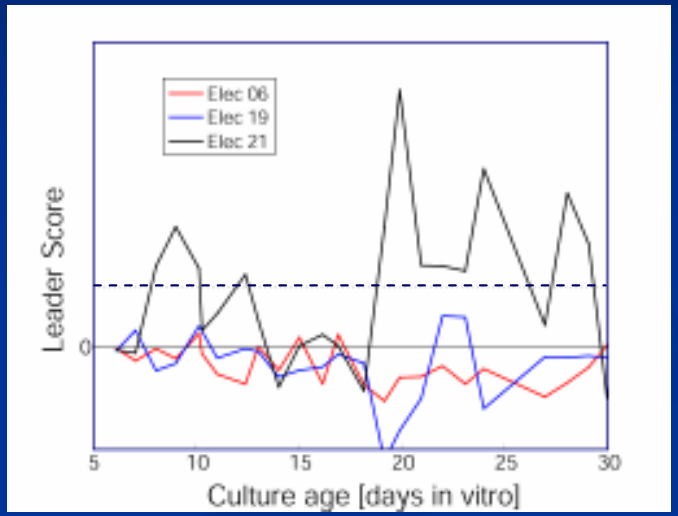


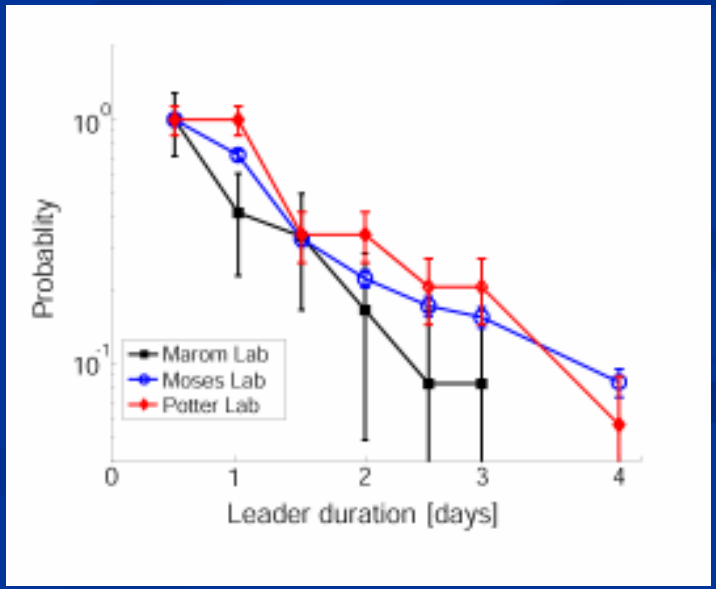
Leader Dynamics

- *Leader* electrodes are persistent & significant first-to-fire electrodes:

$$\text{Score} = \frac{n_{first} - n_{predicted}}{\sigma_{predicted}}$$

- In all cultures (Marom, Moses, Potter)
  - 2-5 Leaders electrodes (of 60)
  - Stable over few days





Position of the leaders

- We measure only ~0.1% of the neurons, but still, leaders show up in all cultures measured
- Sources of the activity
  - 10% of the bursts arrive from outside the array
  - 90% of the bursts are preceded with Pre-bursts that are ~100msec long
- Where is the initiation zone ???

Hence

➔ Leaders are **everywhere**

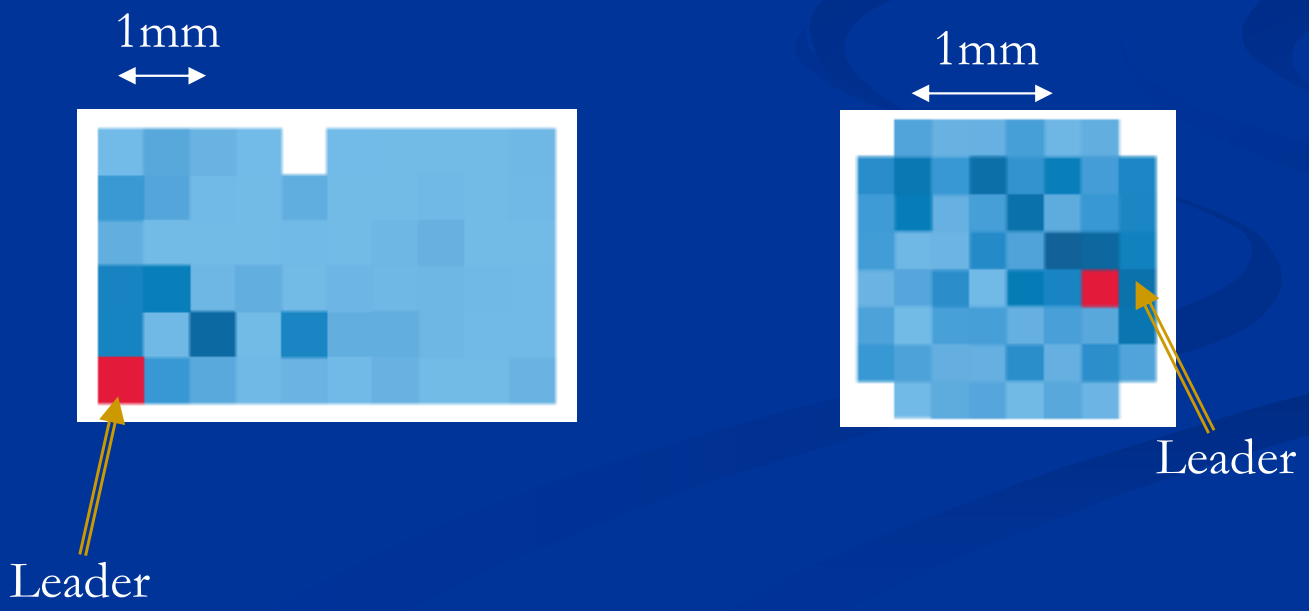
Are These Real Leaders ?

- Sniffers
  - Hyper sensitive neurons
  - Global activity wakes them up first
  - Have no impact on burst structure

- Leaders
  - Centers for nucleation of activity
  - Activity recruits around them
  - Have impact on the probability to burst and burst structure

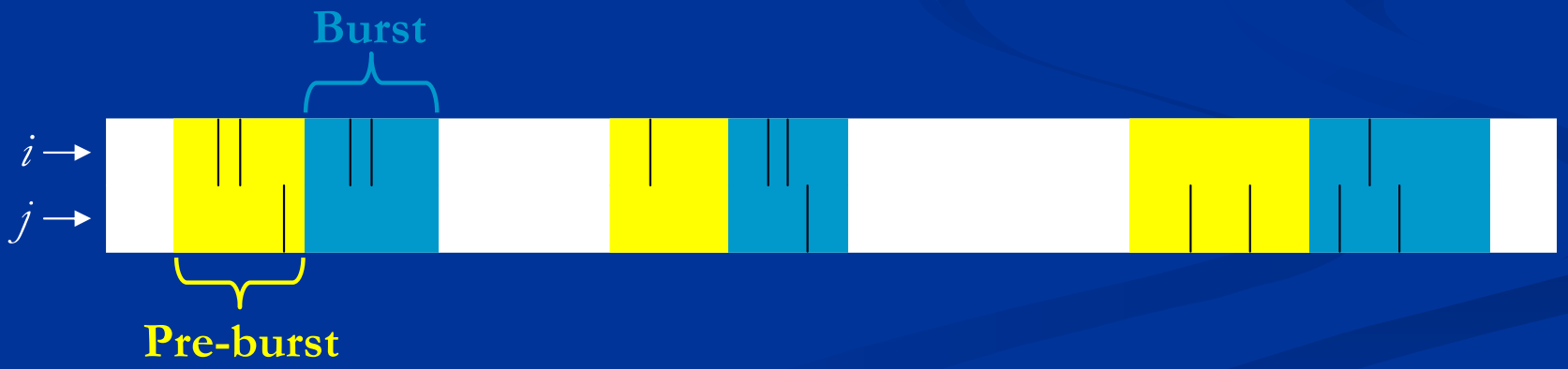
Evidence I
Pre-burst Firing Occurs Near the Leader

Pre-burst averaging reveals a length scale of ~1 mm



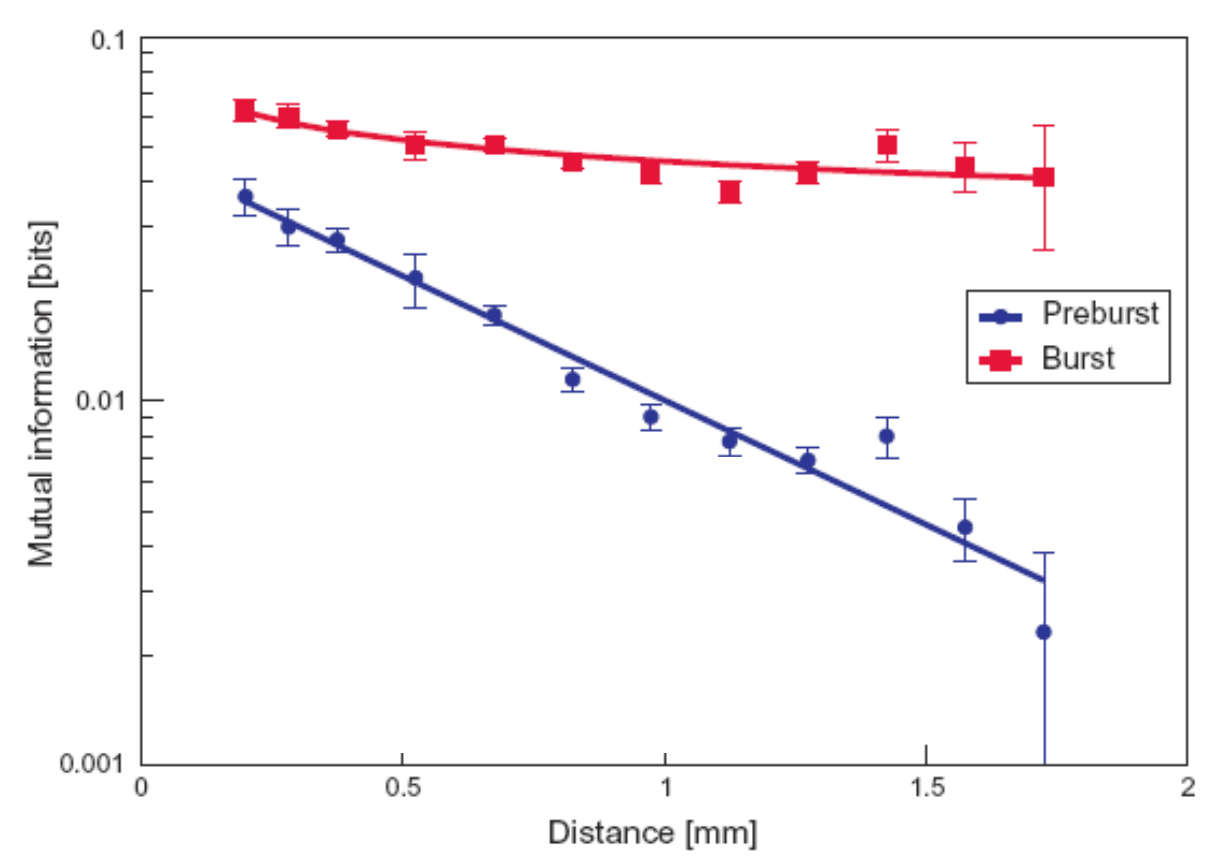
Pre-burst Firing is Local, Burst Firing is Global

- Mutual information was used to measure co-firing within pre-bursts and bursts



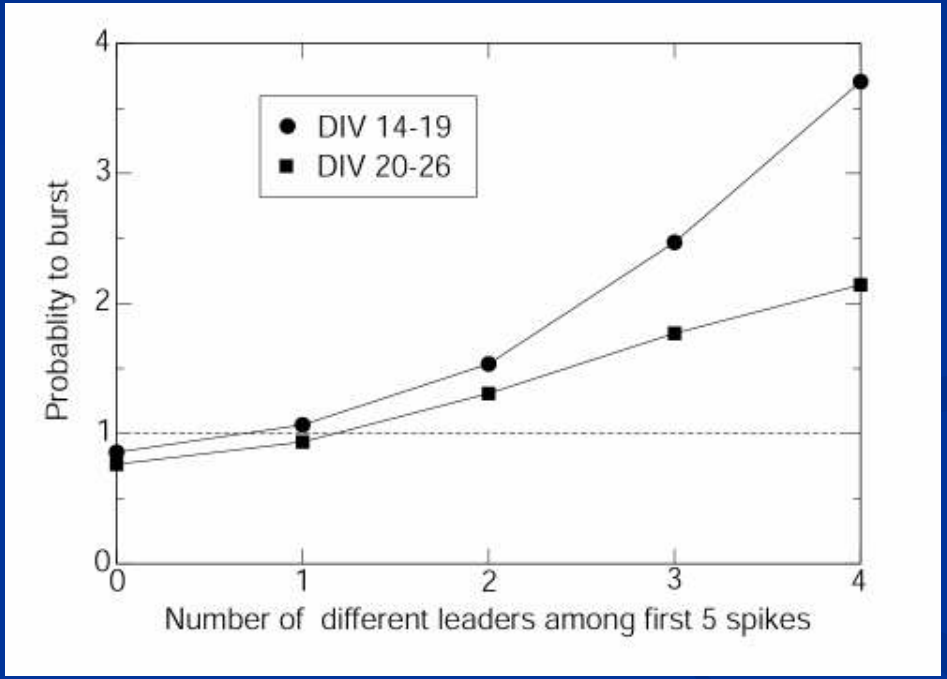
Pre-burst Firing is Local, Burst Firing is Global

- Mutual information is high when electrodes fire together and are quiet together



Evidence II
To burst or not to burst ?
Ask the leaders...

- An event may develop into a burst or abort
- The probability to burst depends on leader firing in the first spikes
- Younger cultures require less leaders to burst

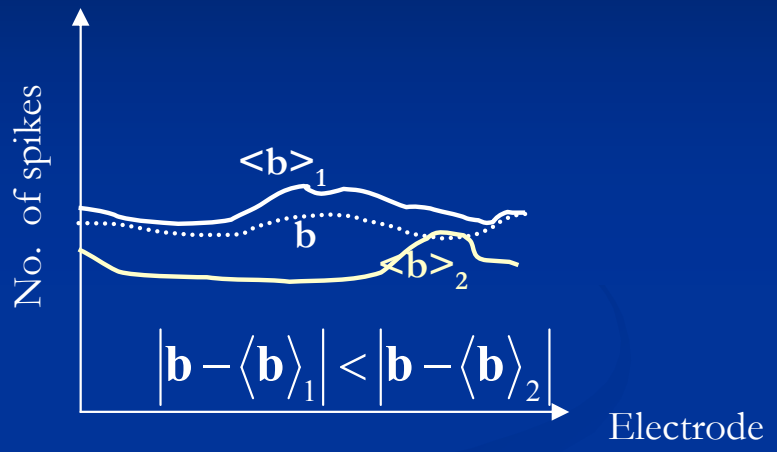


➔ **Early leader firing increases the probability to burst**

Evidence III
Leader Identity Implies Burst Profile

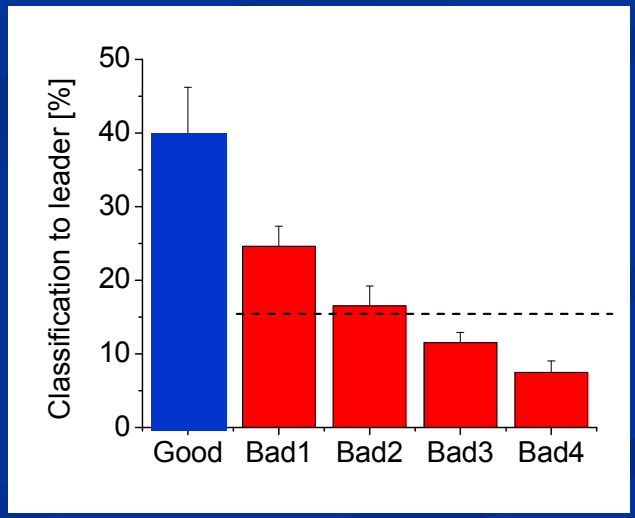
- Quantify burst profile - **b**
- Average profiles from same leader

$$\langle \mathbf{b} \rangle_{leader}$$



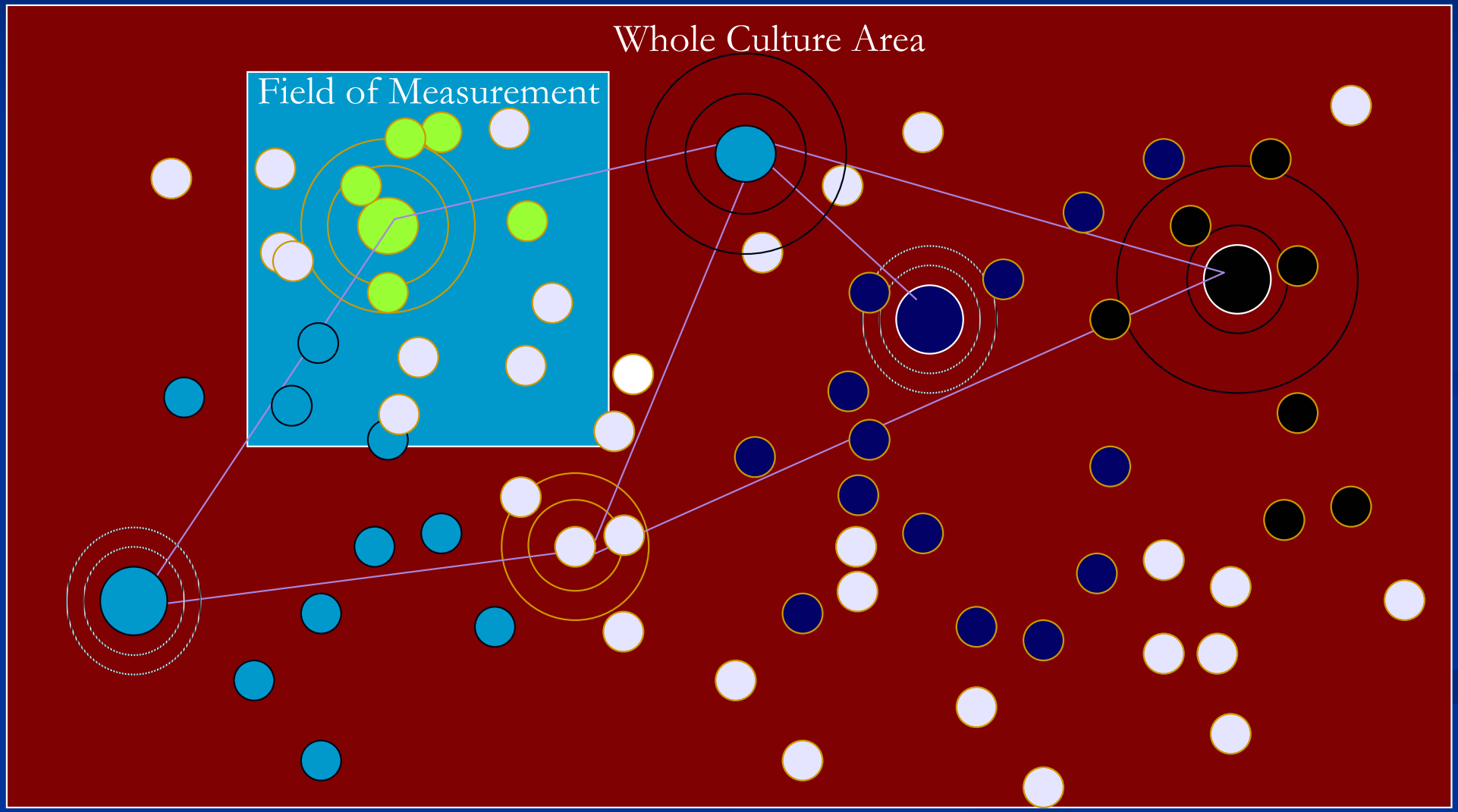
- Cluster bursts by proximity to leader group

$$\min_j \left| \mathbf{b} - \langle \mathbf{b} \rangle_j \right|$$



➔ **Leader identity correlates with burst profile**

Burst Initiation: Leader Sub-network Recruits the Whole Network



Conclusions

- *Conjecture:*
  First-to-fire neurons *lead* burst initiation
  - Pre-burst locality & near leader
  - Prediction of burst
  - Leader sets burst profile
- Leader neuron sub-network is culture-wide
- Open questions: physiological properties, role of connectivity