# Thermodynamics, entropy and information processing in the basal ganglia

Mandar S. Jog, MD, FRCPC
Associate Professor
Canadian Foundation for Innovation Scientist
Director, Movement Disorders Program
London, Ontario, Canada

**“ it is not easy to be continuously active in solitude; but with others and towards others it is easier” Aristotle.**

**This journey made possible and enjoyable through fruitful collaboration with colleagues and research associates and funding from CIHR, NSERC, PSC, MMO, IRAP and others.**

# Acknowledgements

- Dr. Dorian Aur
- Dr. Mircea Chelaru
- Anca Chelaru
- Dr. Christopher Connolly - SRI International

# Facts and Hypothesis

- Neurons receive charge in terms of voltage transfer from many sources
- They change their firing threshold and spike
- This leads to flow of charge in intra- and extracellular space that propagates
- We record this charge as an EC spike
- This charge flow/spiking occurs over time

# Facts and Hypothesis

- The charge flow may be occurring spatially
- It may be possible to understand the dynamics of the charge flow
- Using these flux and spike based spatiotemporal aspects, neurons in networks store information and communicate it between each other

# The task is not easy

- Can we understand the concept of spatial charge flux and voltage spread that occurs in space in the network
- Along with temporal aspects of spiking
- In the context of learning and behaviour
- And understand this in terms of information encoding within neurons and networks

# Coding in Spikes

- Since a spike was considered as a stereotyped waveform, the information was only carried by the occurrence of AP at particular times
- The spike itself is felt to be a passive event that does not itself represent information
- Indeed physiologists often reduce the spike to a discrete scalar event in time and analyze behavior in the context of spike timing alone

# Lets look at the levels of analysis

- **Fundamental level**

  - setting the stage within ionic fluxes

- **Second level**

  -scalar dimension of the time of spiking

- **Final level**

  - groups of neurons encode for complex behavior

---

- **A framework that ties the fundamental machinery to function is currently missing**

# In this context of coding

- What does the spike represent?
  - Represents information within the spike itself
  - Occurs with some timing that allows transfer of information
- In order to study the former, charge flux or flow is possibly an important method
- Since multiple charges contribute to this charge flux, in what may appear a random fashion, concepts of thermodynamic entropy and mutual dependence of variables can reveal a better understanding of changes in information
- The temporal occurrence of spikes can be understood as a transfer of information entropy due to a change in the thermodynamic entropy.

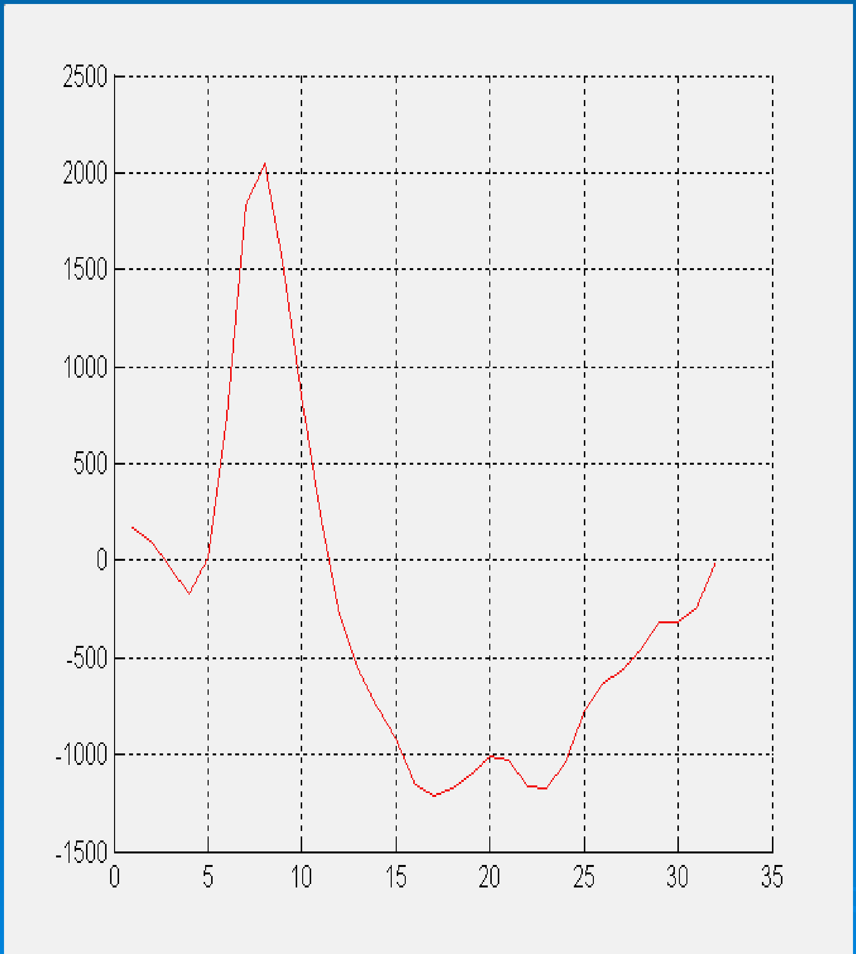
# What we will talk about today

- State properties we have described of charge flow
- Show that charge flux during spiking has information content
- The temporal interdependencies that result between spikes enrich the neuronal information network
- These and possibly other observations extend the bandwidth of operation of the neural network

# Premise – Information Processing

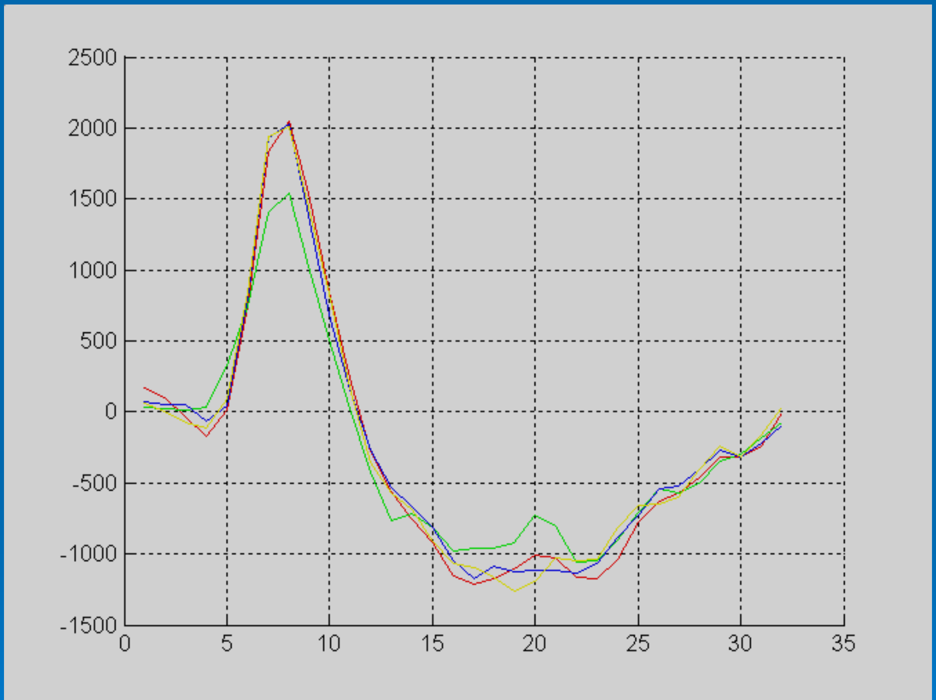
- The thermodynamic entropy of the neurons determines the informational state of the neuron
- A change in the thermodynamic entropy of the neuron represents information
- Between spikes, a neuron is gathering information and hence altering its thermodynamic entropy
- Extracellular charge flow can be analysed in order to understand these thermodynamic changes
- These changes of thermodynamic entropy can then be related to information entropy

# The SPIKE



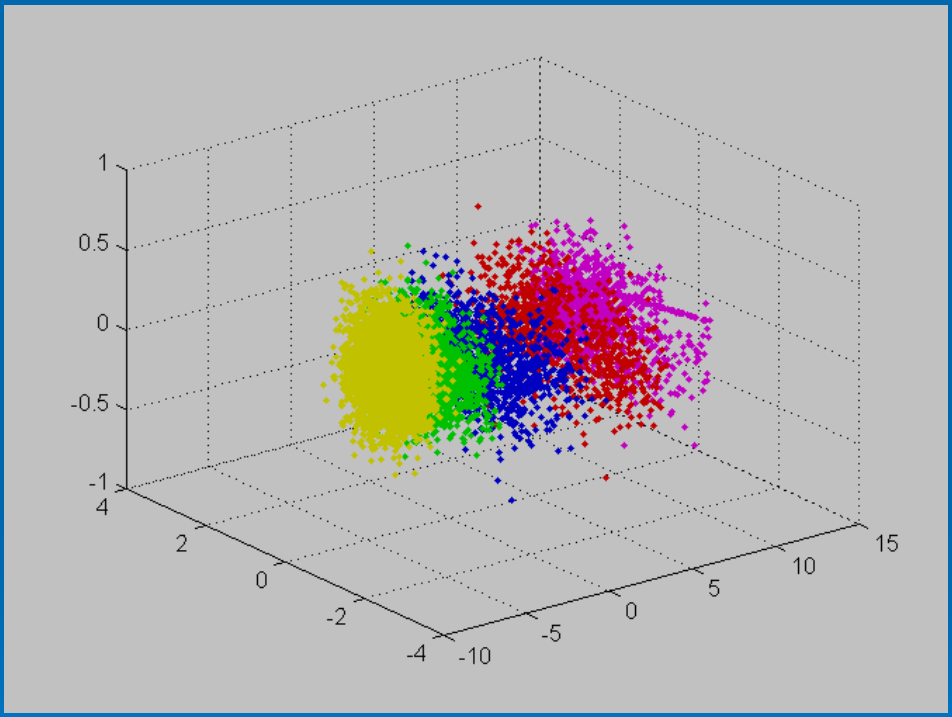

- Stereotyped waveform
- Signals  appear to be identical to a single electrode
- Spike sorting by maneuvering the electrode tip

# Tetrode recordings



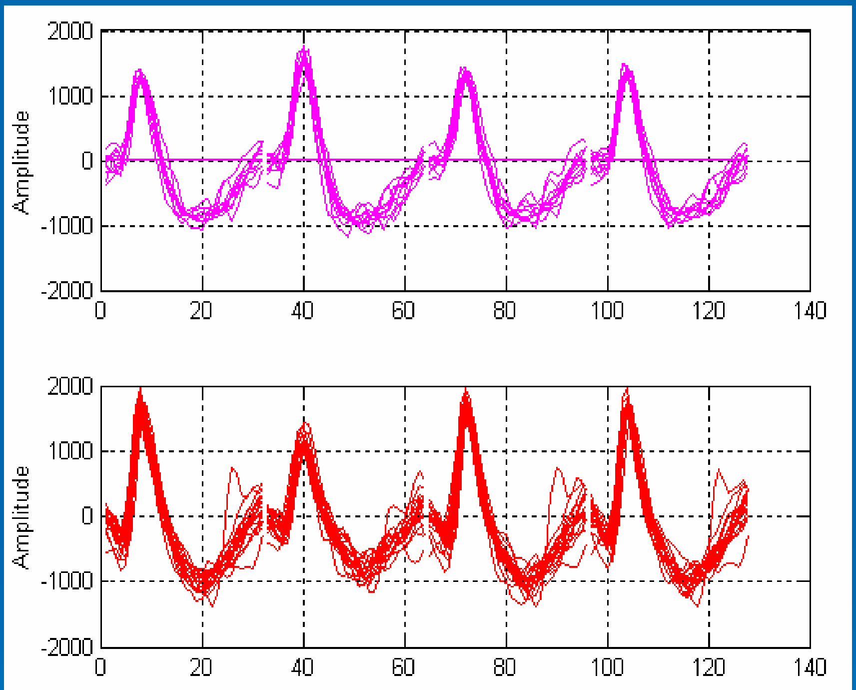

- Tetrodes are four channel wires
- Are able to grab a four dimensional image of spikes
- Spike sorting – four views
- Spike has 3D spatial profile

# Spike sorting




- No need for electrode movement for spike sorting
- Spike sorting is based on algorithms (Jog et al J. Neuroscience Methods 2002 and 2004)
- An example of clusters for waveforms measured by the four channels of tetrode

# Clustered waveforms




- An example of clustered waveforms measured by the four channels of a tetrode for two different neurons

Our first series of papers looked at flux flow and directionality

# Moving on to Fluxes

- The questions are….
  - How do neurons receive and code information
  - How do they communicate this information
  - What does the spike actually mean?
  - Can we perform an analysis over and above time series analysis?

# PREMISE 1

SPIKING AND FLUX FLOW

We started with the basics: Single charge movement in space

ELSEVIER

Journal of Neuroscience Methods 149 (2005) 57–63

JOURNAL OF NEUROSCIENCE METHODS

www.elsevier.com/locate/jneumeth

# Computing spike directivity with tetrodes

Dorian Aur[a,*], Christoper I. Connolly[b], Mandar S. Jog[a]

[a] *Department of Clinical Neurological Sciences, Movement Disorders Program, London Health Sciences Centre, 339 Windermere Rd., London, Ont., Canada N6A 5A5*

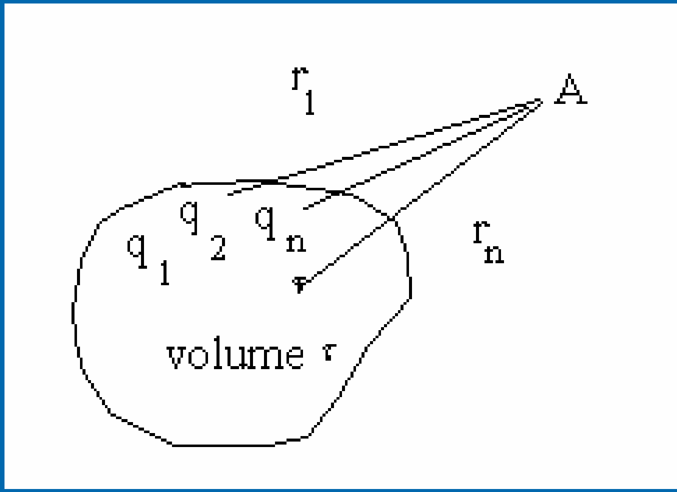
[b] *SRI International, Menlo Park, CA, USA*

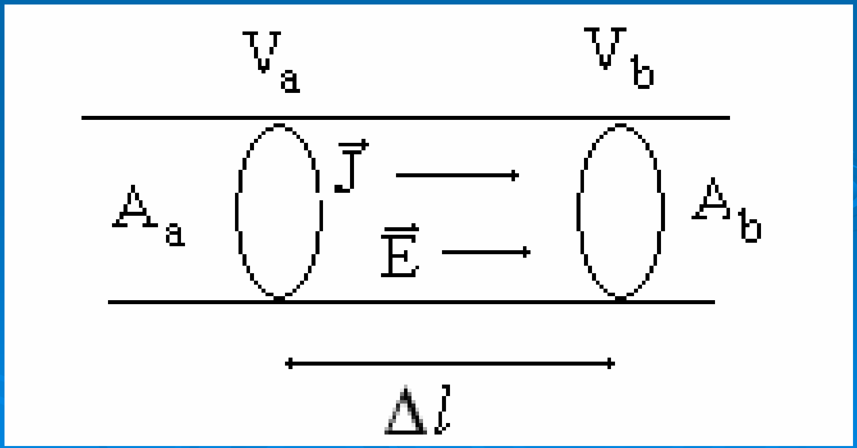
Received 6 January 2005; received in revised form 4 May 2005; accepted 5 May 2005

# Ionic flux

- If these charges are moving in space and if a conductor is in the field the drop of potential in a length of conductor can be computed by:

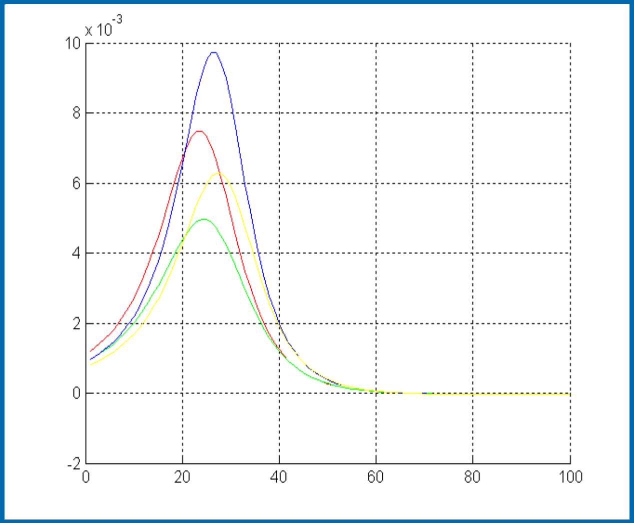
$$V_b(t) - V_a(t) = \frac{I(t)\Delta l}{\sigma A}$$

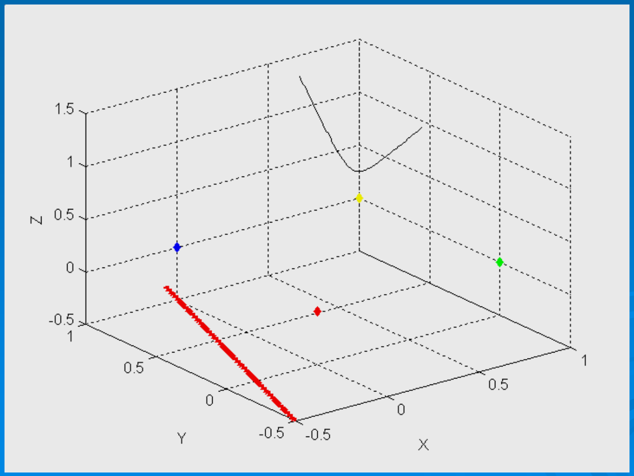


If I were an electrode watching I would see…

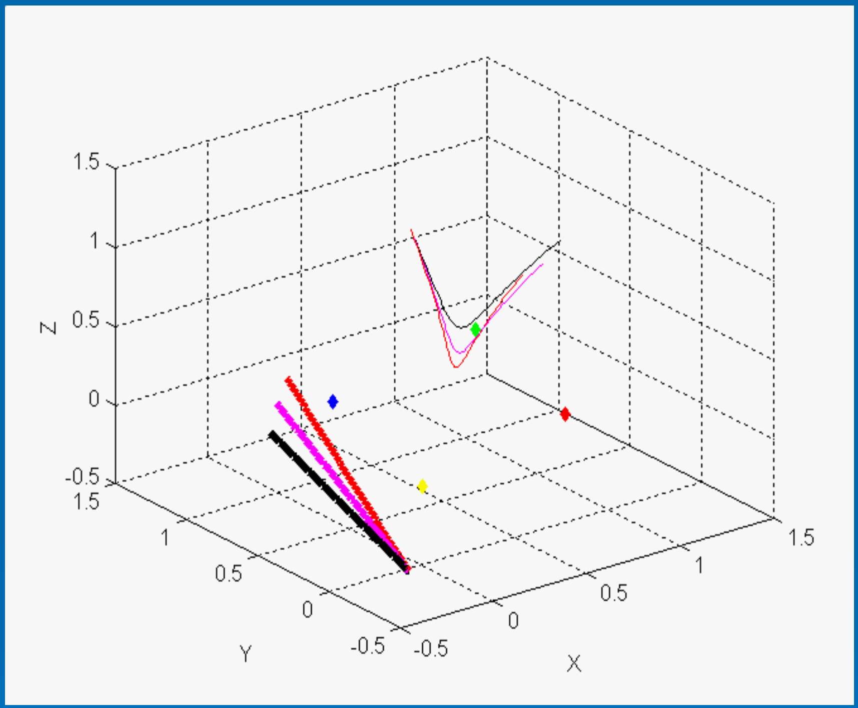
# Artificial Spike and Computed trajectory



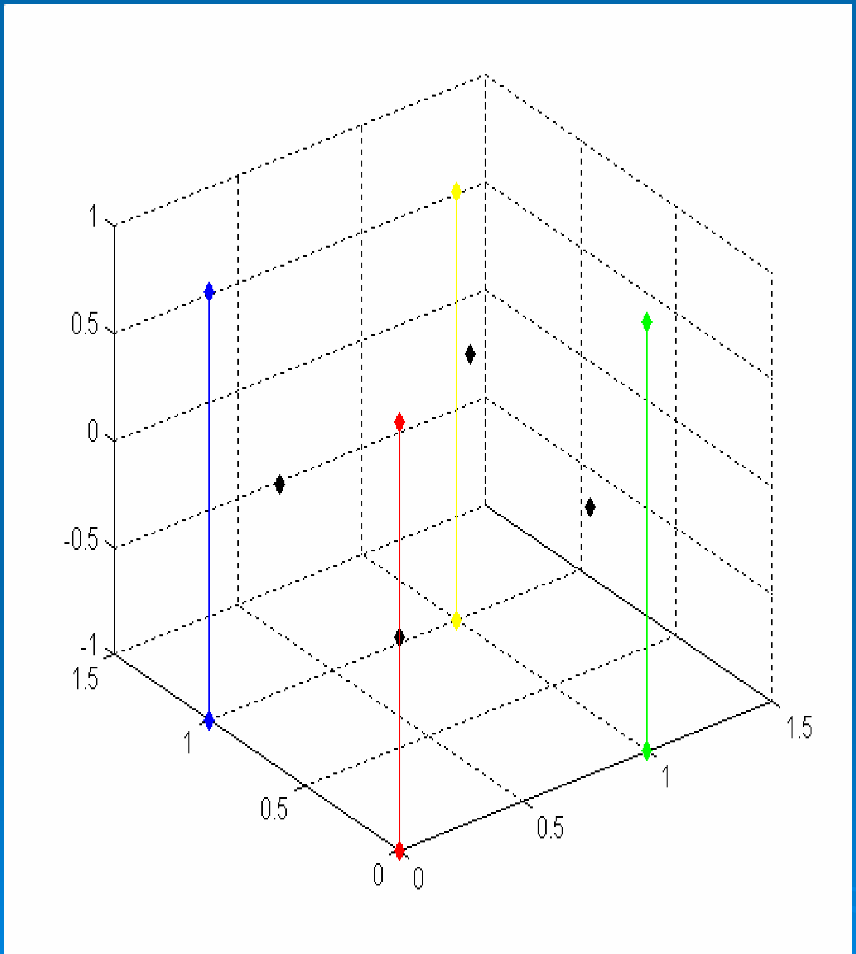

- Four view of action potential;
- Linear charge trajectory (bold red line)
- Computed trajectory from spike (black curve)

# Multiple charge trajectories




- Trajectory of charges (bold red, magenta and black lines)
- Surprise - Computed trajectories are not lines but are curves
- Tetrode properties determine the curvature

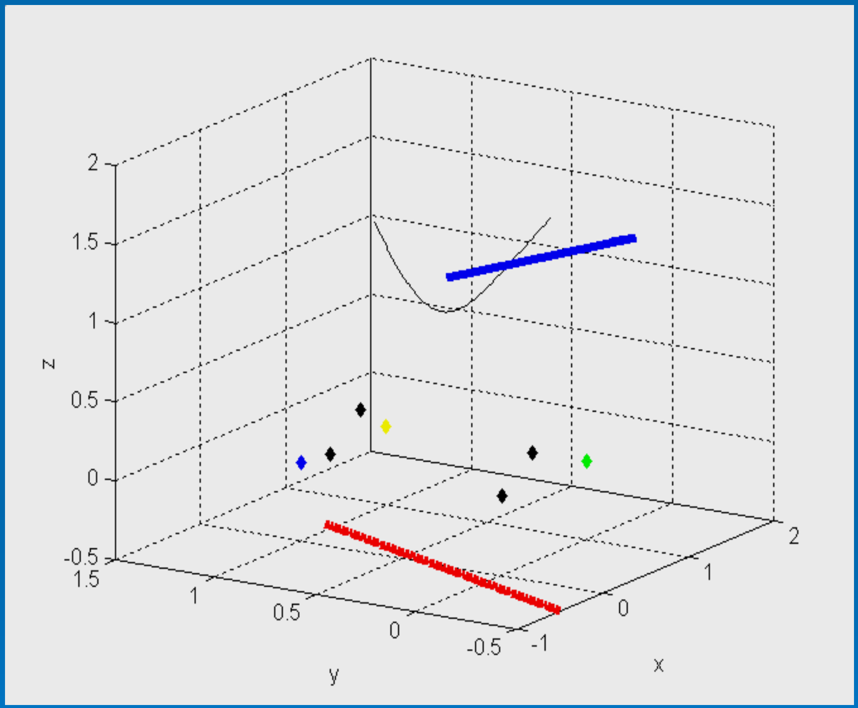
# A Problem -- Two references systems




- Avoid unknown tips positions;
- Rr reference system for charge movement;
- Pr reference system for trajectory computation

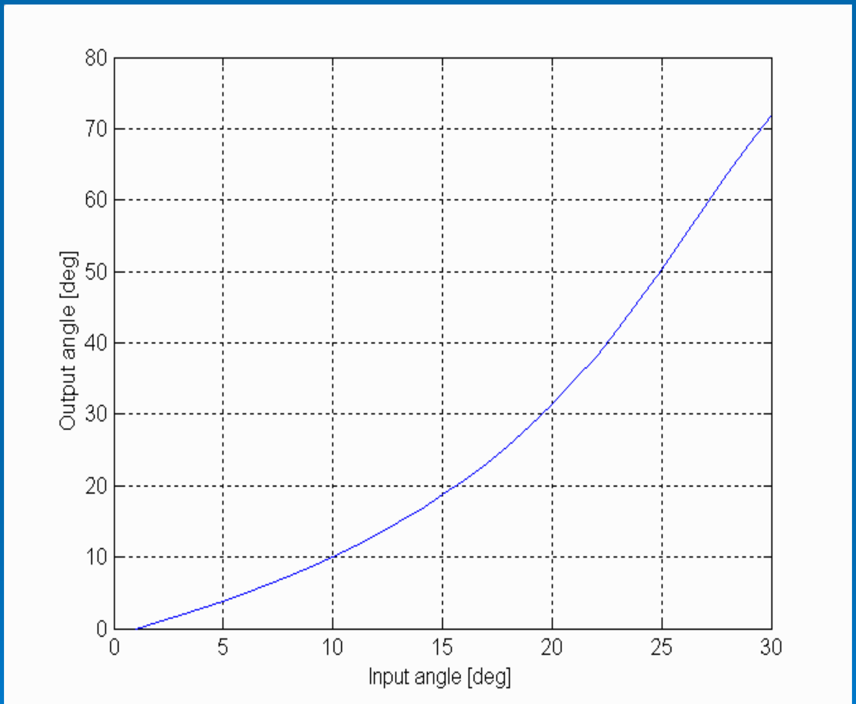
# Now computing directivity

# Computing directivity – singular value decomposition (SVD)



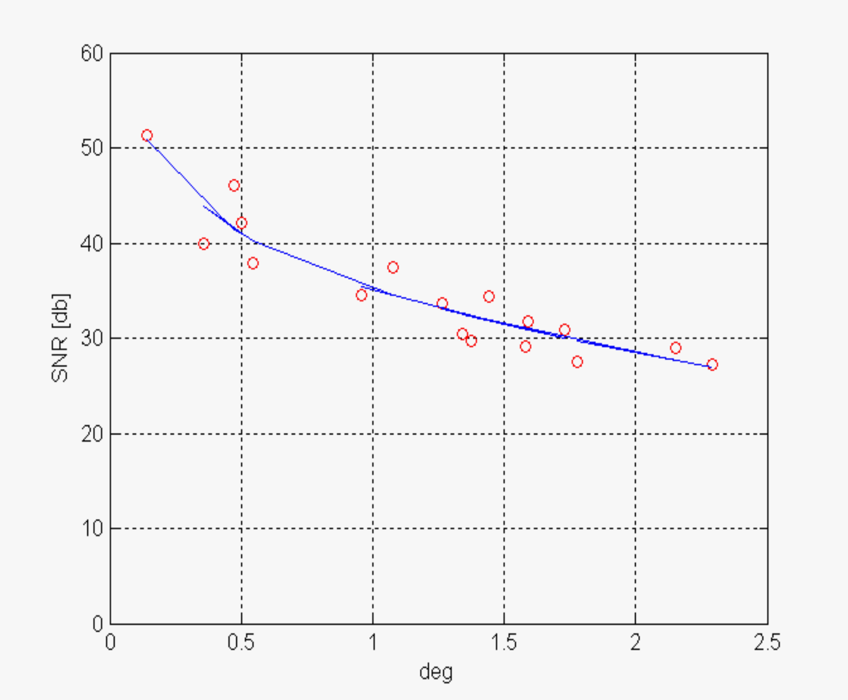

- Example of charge linear trajectory (bold, red line)
- Computed trajectory (black trajectory)
- Estimated directivity (blue line) in the tetrode reference system.

# Computed charge deviation



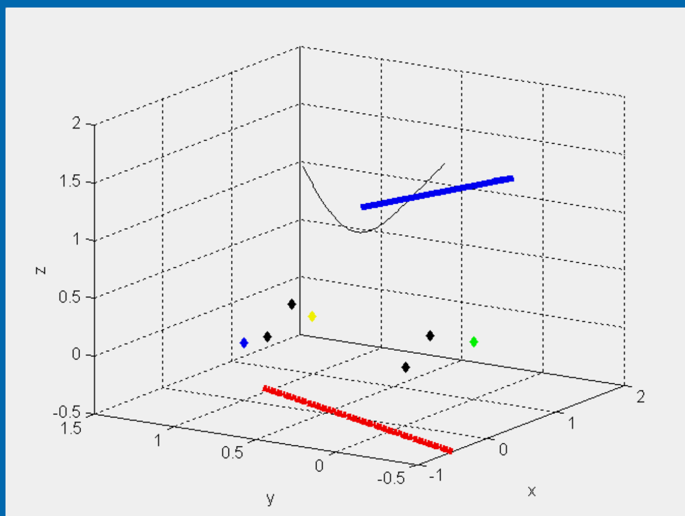

- Dependence between charge movement deviation (input angle) and computed charge deviation angle (output angle)
- Nonlinear dependence

# Noise errors



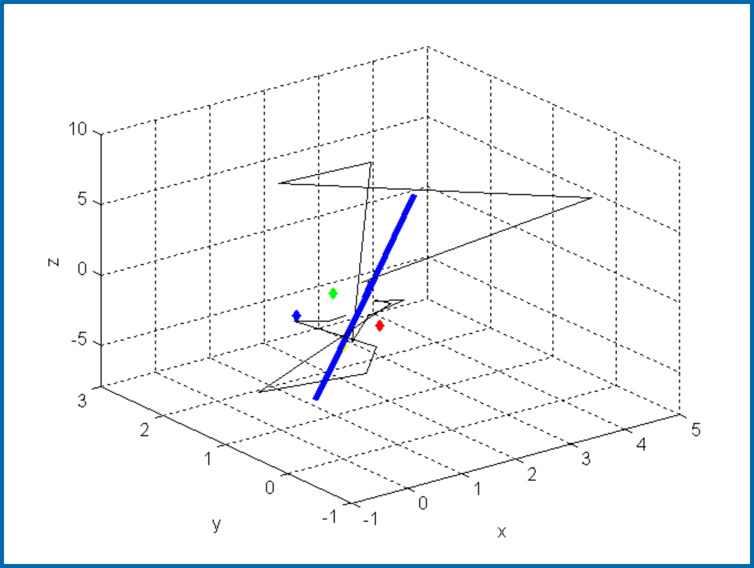

- SNR and error in computing deviation angle.
- For high SNR the error is under $3^0$

# Several charges in movement



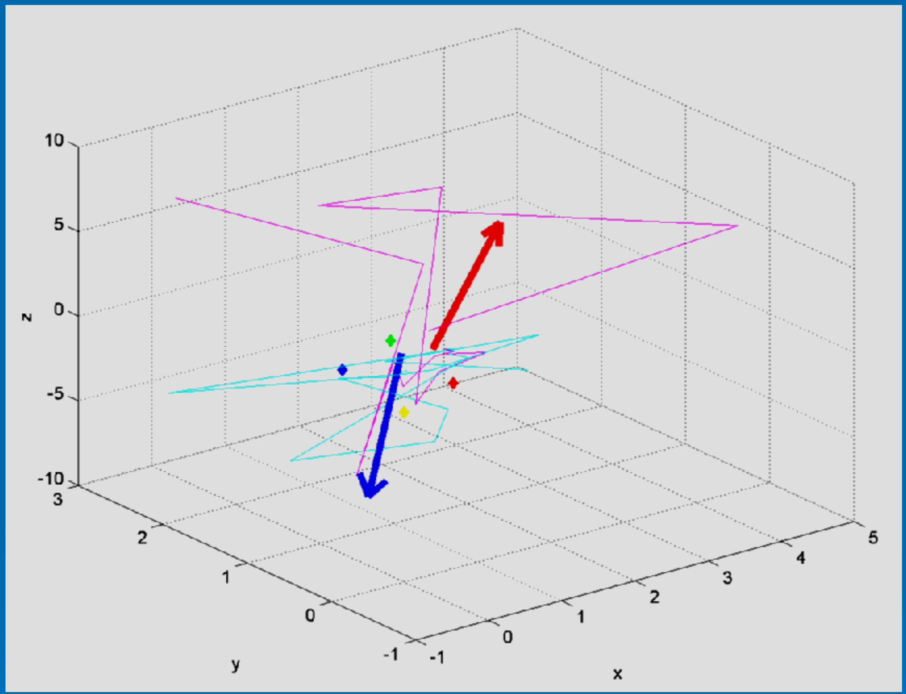

- Three charges in movement and computed directivity
- This is similar to what is expected when we register an AP

# Real spike trajectory




- real spike trajectory - black curve
- computed directivity - bold blue line

# Two different spikes and their directivity




- Directivity analysis of the action potentials from the same neuron shows preferred spatial direction for different spikes

# So What did we do?

- We analysed spikes from many neurons during tetrode recordings during free walk and after training animals on a T-maze task
- We calculated the directionality of charge flow over time for each neuron recorded

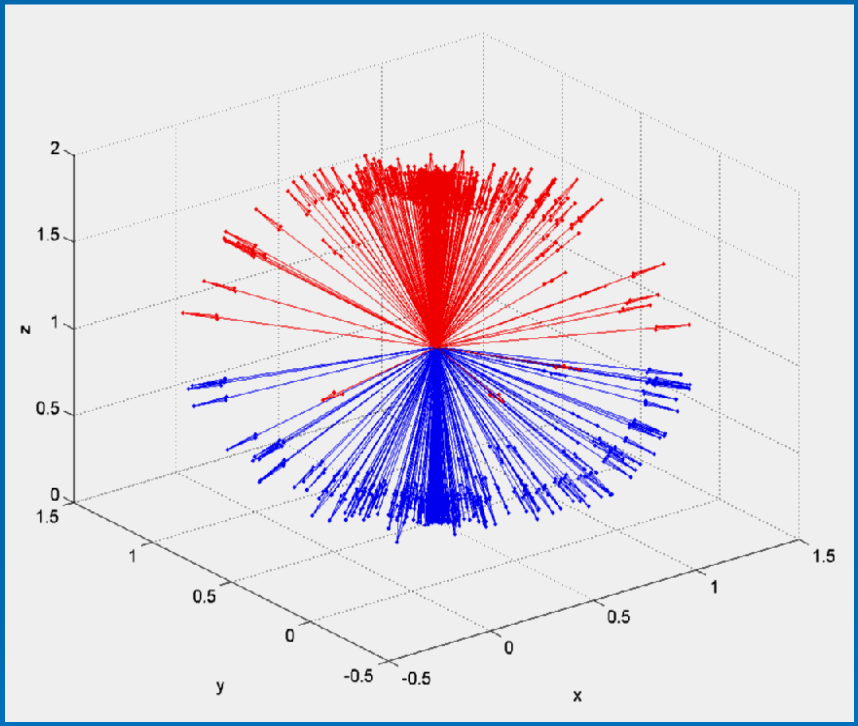
Neural Processing Letters (2006)
DOI 10.1007/s11063-006-9029-2



# Neuronal spatial learning

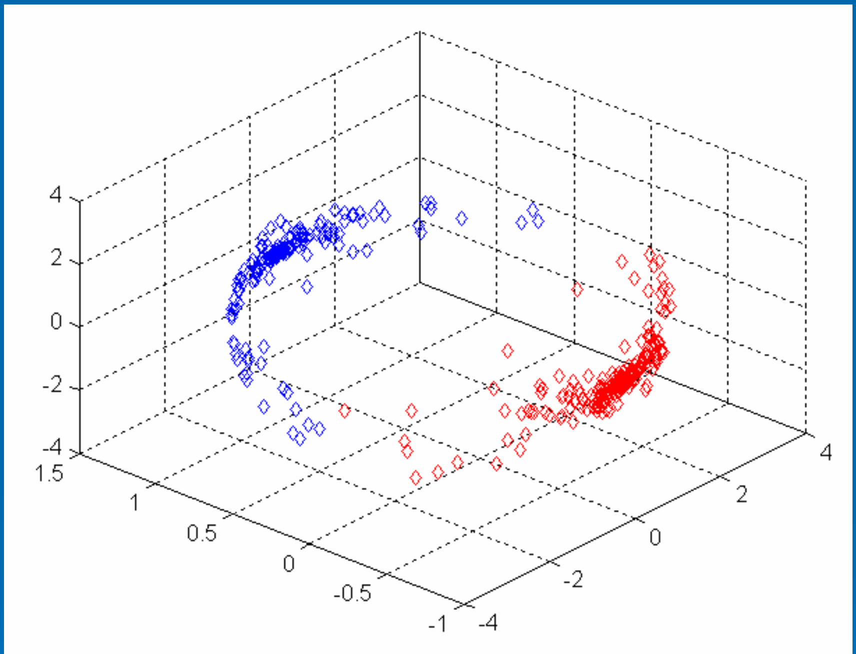
DORIAN AUR* and MANDAR S. JOG
*Department of Clinical Neurological Sciences, Movement Disorders Program, London, ON, Canada e-mail: daur2@uwo.ca*

# Multiple spikes from the same neuron



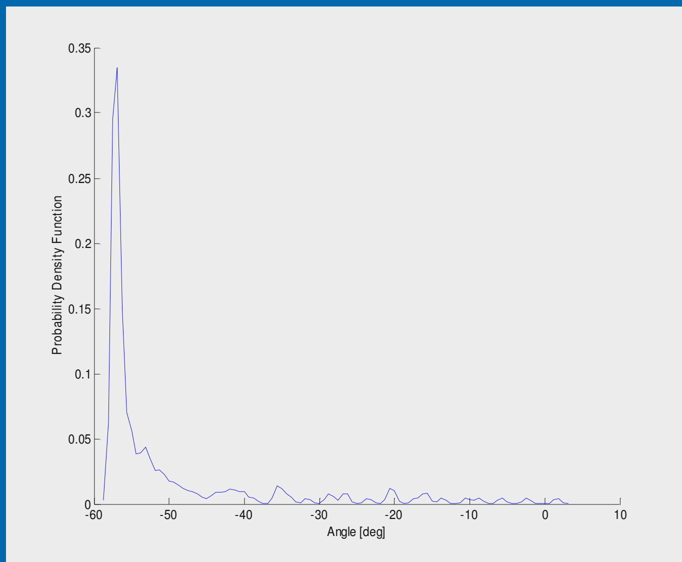

- For four hundred spikes, in real space the directionality of charge flow appears to be random

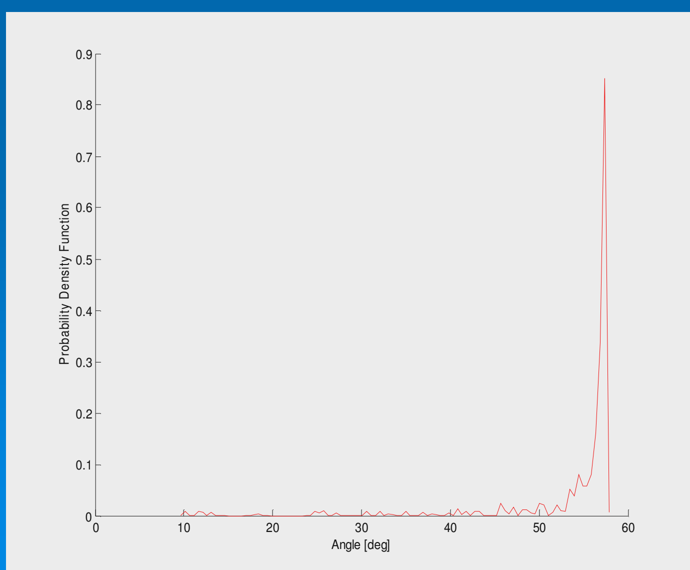
# Predominance of directivity




- In PCA space, the cosines on the angles are distributed
- Three angles are generated for each
- This is followed by computation of the probability density matrix for each distribution for every angle

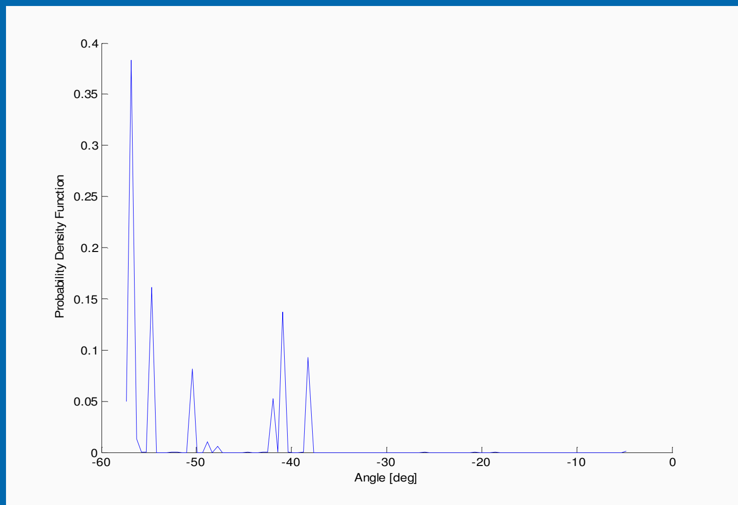
# Before Learning

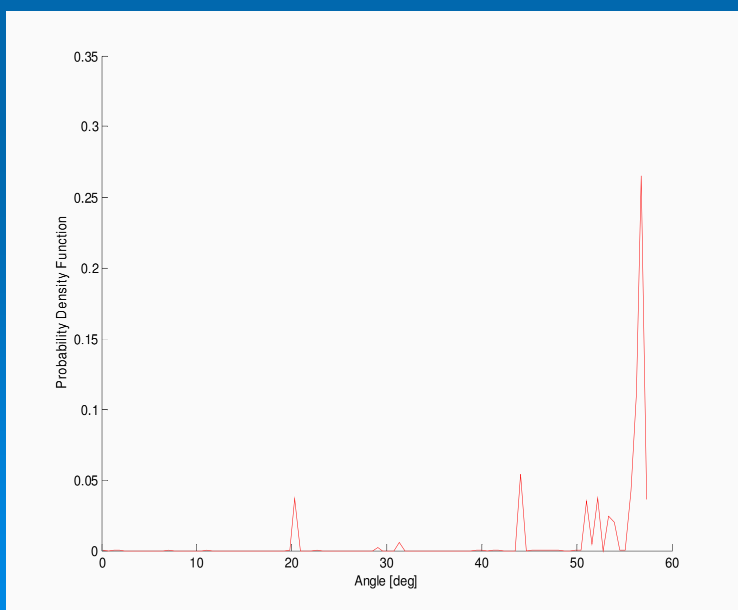



- Directivity is characterized by three cosines angle $v_1, v_2, v_3$
- A global maximum for each cosine angle is perceived in probability distribution function (pdf) before learning
- Only the pdf for cosine angle $v_3$ is shown

# After Learning

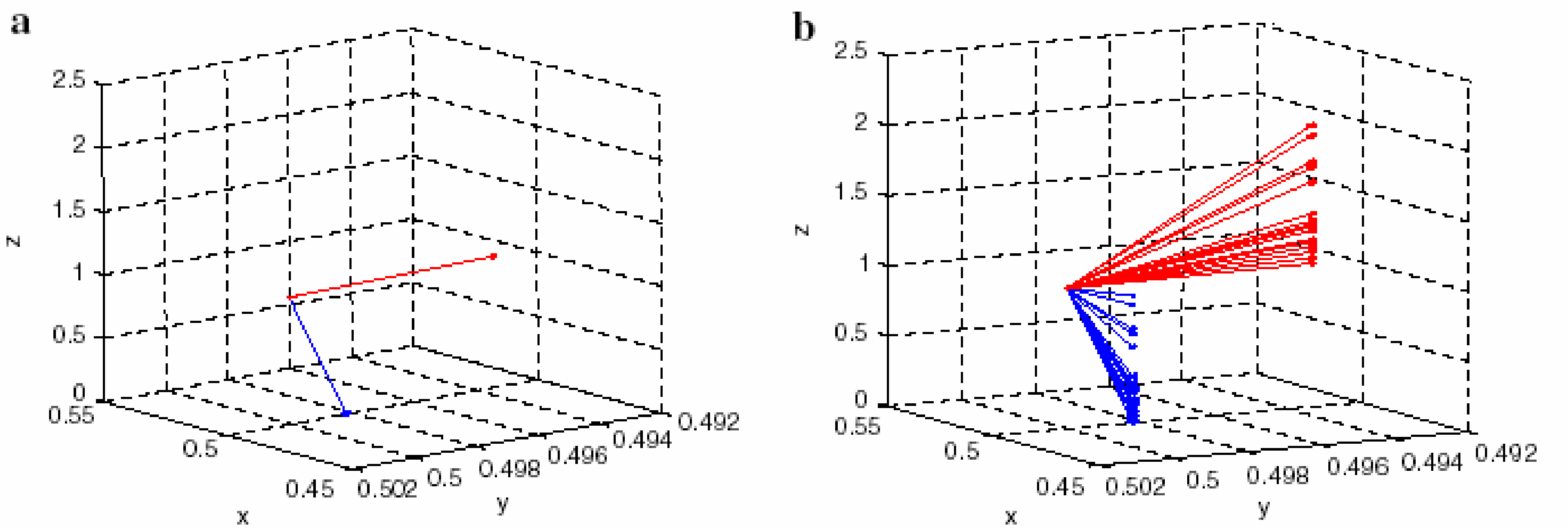


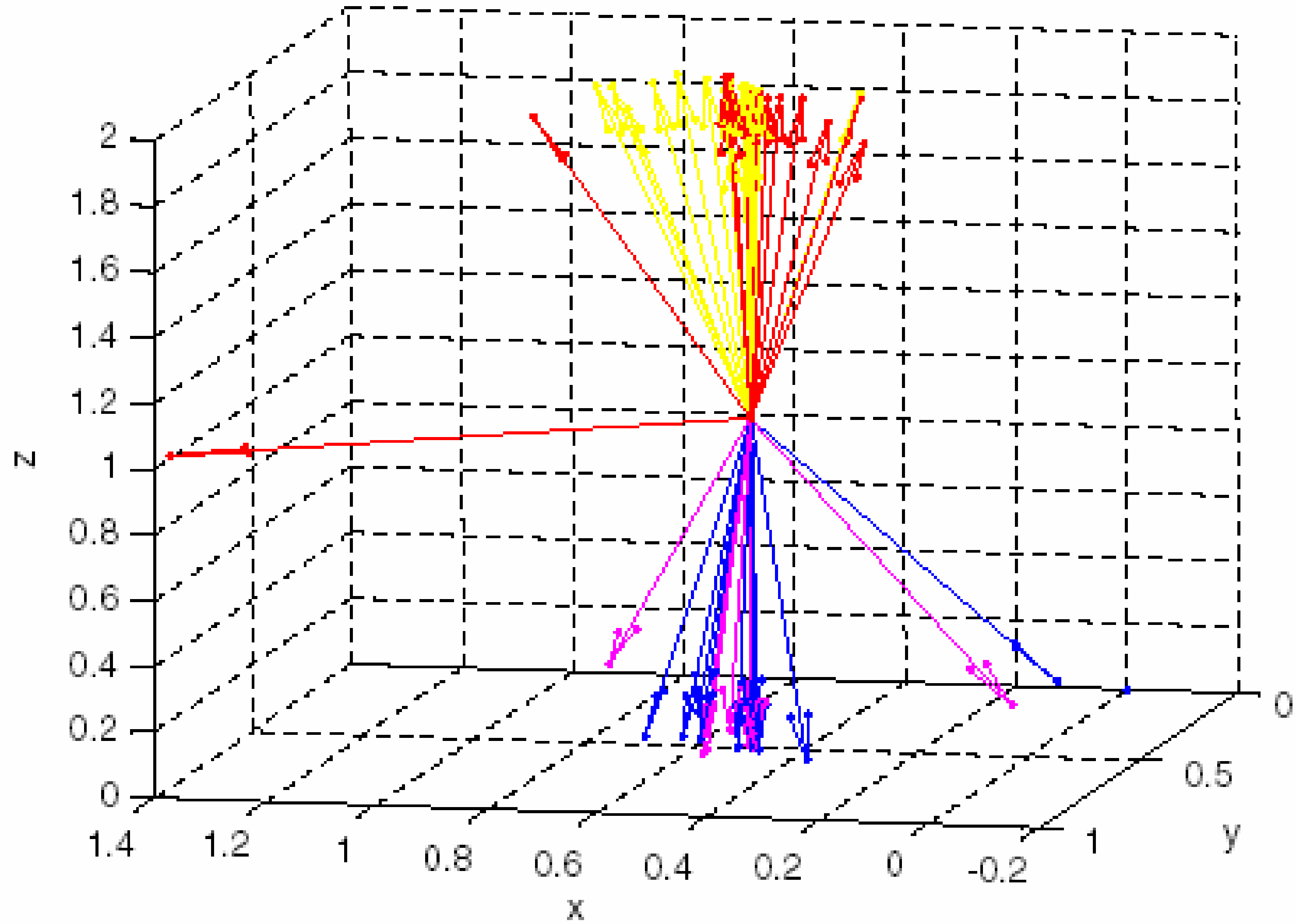




- A global maximum in pdf for each cosine angle

**+**

- Several visible local maxima are present after learning


a
b
x
y
z
2.5
2
1.5
1
0.5
0
0.55
0.5
0.45
0.502
0.5
0.498
0.496
0.494
0.492



z
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
x
1.4
1.2
1
0.8
0.6
0.4
0.2
0
-0.2
y
0
0.5
1

# Can we quantify this in terms of entropy?

- Mean estimated entropy for cosine angle is 4.2 bits before learning, while after learning the entropy decreases substantially around the mean of 2.7 bits
- This implies that the direction of charge flow becomes much more organized as the change above is logarithmic

# What we observed

- The directed charge flow becomes less random with preferred directions during learning
- Every neuron after local learning shows a slightly better “selection” of direction for spike propagation than the initial “random guessing”
- Neurons within a neuronal group will provide their own preferential directional charge flow for the dataset they receive
- “Weak learning” within each neuron while in the network these are equivalent to “strong learning”

# This analysis of charge flow showed

- When charges move in space local voltage effects are created
- These effects can be recorded in extracellular medium as spikes
- Spikes are a reflection of the electrical state of the neighboring neurons
- Using tetrodes, spikes appear to have directivity in space

# This analysis of charge flow showed

- During learning spatial directivity organization (SDO) of charge flow within spikes occurs for each analyzed neuron
- This organization seen in each neuron supports group's cooperation that engages neighbor neurons to generate electrical waves with preferred directionality sustaining a strong learning phase  that can achieve any level of performance in the probably approximately correct sense (Valiant, L. G. 1984).

# So what ????

- Does directionality tell us anything more than that it exists?
- Does it really matter?
- Is it surprising that ions moving along a conductor should do this?
- If not what else can this mean

# We can conclude

- Ionic fluxes (charges) are responsible for building this directionality;
- Depending on the direction of the AP and hence the associated ionic fluxes in the extracellular space, structures are influenced
- Therefore each spike, spreading charge in space in a particular direction, may influence different neighboring cells.

# What can we conclude from this?

- Neurons then "see" inputs from many directions and effectively sum them before producing their own response.
- This method is an efficient way of information gathering and transfer

# SPIKES, FLUX, ENTROPY AND INFORMATION

# The Charge Flux Hypothesis

- That neurons exist in an electrochemical flux
- This flux is determined by a balance between the intrinsic condition of the neuron and the milieu it is functioning in
- Information encoding and transmission is a dynamic within this system

# Premise 1

- Spikes communicate information through the network directly at the synapse and indirectly through an alteration of the extracellular space
- This charge flow has directivity in extracellular space
- Learning may be reflected as a change in the spatiotemporal properties of neuronal firing and extracellular charge flow

Imagine a milieu

As these fluxes occur, what happens to the neuron?

ELSEVIER

Journal of Neuroscience Methods 157 (2006) 364–373

JOURNAL OF NEUROSCIENCE METHODS

www.elsevier.com/locate/jneumeth

# Building spike representation in tetrodes

Dorian Aur *, Mandar S. Jog

*Department of Clinical Neurological Sciences, Movement Disorders Program, London, Ont., Canada*

Received 2 March 2006; received in revised form 12 April 2006; accepted 1 May 2006

- Showed spike-spike variability contributed by ionic fluxes
- Intrinsically represents information computation

Neural Processing Letters (2006) 23:183–199
DOI 10.1007/s11063-006-6266-3


# Computing Information in Neuronal Spikes

DORIAN AUR[1,*], CHRISTOPHER I. CONNOLLY[2] and MANDAR S. JOG[1]
[1] *Department of Clinical Neurological Sciences, Movement Disorders Program, London, Ontario, Canada. e-mail: daur2@uwo.ca*
[2] *SRI International, Menlo Park, California, USA.*

# Entropy within a neuron

- Entropy is a measure of randomness
- It is determined by the existing state of the component processes within the system and its input/output
- Changes in entropy can be viewed as a method of altering "information"

# Variability of Neuron's Entropy

- Entropy changes equal to the sum of:
  - entropy transfer by heat;
  - entropy transfer by mass flow;
  - entropy generated by irreversible processes.

$$\Delta H = \Sigma \frac{Q_k}{Tk} + \left( \Sigma m_i h_i - \Sigma m_o h_o \right) + \Delta \mathrm{H}_\mathrm{i}$$

- A change in entropy by an alteration of these variables could be seen as an alteration of information (Shannon Information)

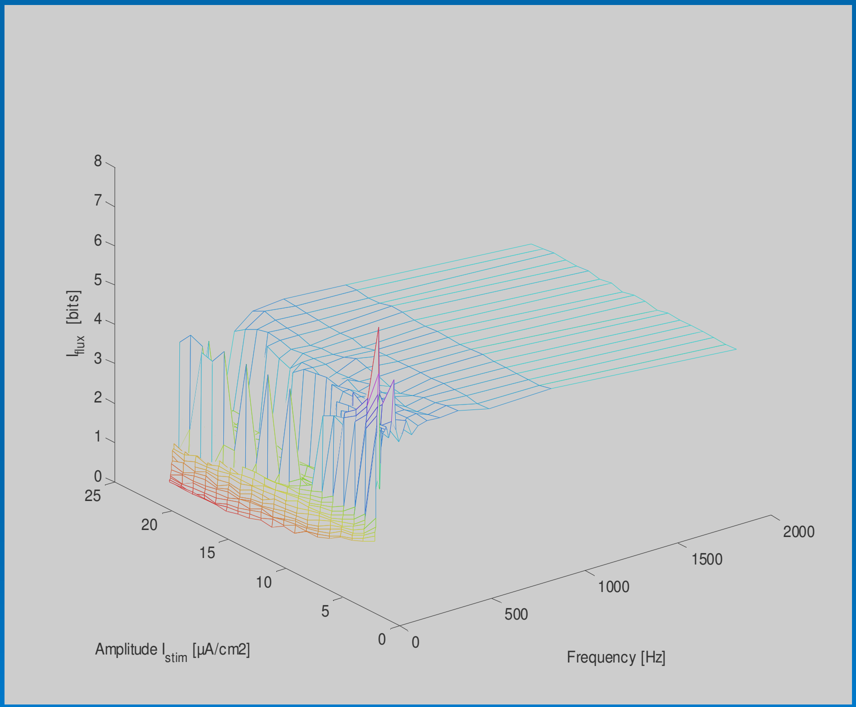
# Entropy and Fluxes

- Ionic fluxes represent the random variables
- These ionic fluxes, that appear to have directionality induce signals by the motion of charges at the tetrode tips
- This equates to what is seen by neurons at their membrane

# We next studied the HH model

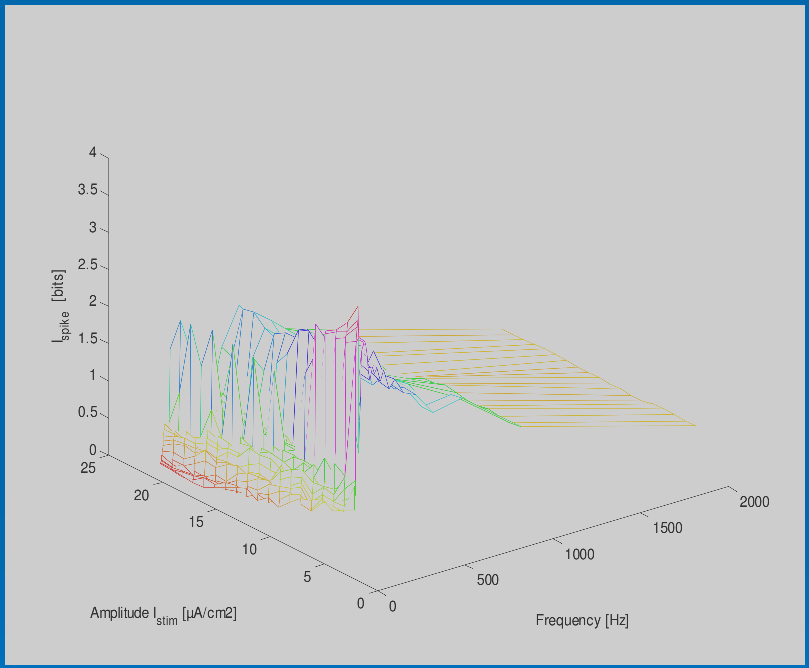
- Can we compute information content from the entropy of charge flow itself?
- How does this compare to the information that is flowing through the spike?
- Are we looking at a temporally shifted slower learning process?
- Can we understand it?

# Estimation of I(Na+, K+) from Hodgkin Huxley model




- Estimated values of mutual information $I_{flux}$ across amplitudes and frequencies for sinusoidal stimulus $I_{stim}$ (μA/cm2) computed over 30 ms

# Estimated information in spike, based on membrane potential




- The 3D dependence of estimated $I_{spike}$ over $I_{stim}$ frequency and amplitude for Hodgkin Huxley model

# Simulation

- We then used the HH model to generate simulations to look at
  - How much information is carried by the spike as an event
  - How much information is buried inside the charge fluxes themselves.

# Low information values

- Theoretical estimations based on spike timing for the fly H1 visual cells predicted a value of 1.80 bits/spike (Strong et al., 1998).
- Panzeri S. showed recently that neurons in somatosensory cortex of rat are transmitting on average $1.59 \pm 0.1$ bits/spike.

# High Information Value

- The maximum value of MI per spike attained $I_{spike}$= 3.5 ± 0.2 bits while the maximum values for $I_{Na}$ fluxes is 7 ± 0.2 bits based on HH model.
- Mutual information between input signal and sodium flux is about two times that between input signal and output spikes during each spike within a millisecond-level time domain
- This higher transfer of information provided by ionic fluxes extends the working frequency domain of neural cells beyond those accessible to information transfer within spikes alone

# What does it mean?

- Ionic fluxes provide richer information and spatial directivity
- Information stands at another level above that has been mainly studied in the last sixty years
- Information is encoded within ionic fluxes

# Physical Representation of Information

- Information in neurons can thus be shown to have *physical representation*, and is related to charge flow during electrochemical events
- This charge flow is influenced by synaptic and non-synaptic events
- The changes in the constituents within the neuron that result from these fluxes may cause an entropy change or gradient that represents information

# Going back to the entropy

- For removing 1bit of information entropy in each neuron an ionic efflux of required is:

$$\frac{\Sigma m_o h_o}{k_B}$$

- For adding 1bit of information entropy an ionic influx of is necessary :

$$\frac{\sum m_i h_i}{k_B}$$

# But ionic fluxes are linked

- We can now analyze the dependencies in information entropies of several ionic fluxes--a way to find the encoding information in spike
- Different ionic fluxes convey information mutually because they are correlated.
- Several related fluxes of $Na^{+}$, $K^{+}$,$Ca^{2+}$, or $Cl^{-}$ ions are contributing in changing the information entropy during AP.

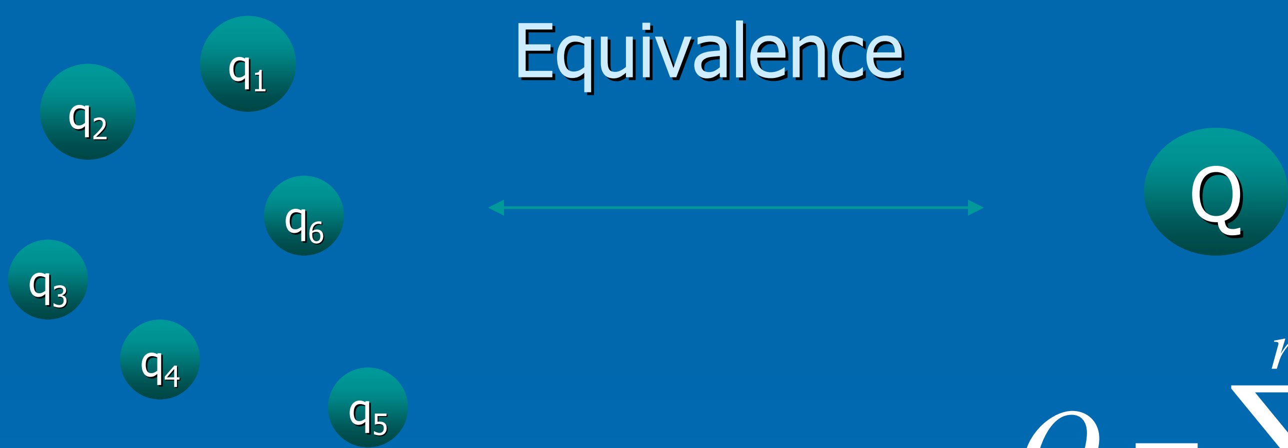
# In This Context

- Example:

  $I(Na^+, K^+)$ measures the reduction in uncertainty about the $Na^+$ flux due to the knowledge $K^+$ flux.

$$I(Na^+, K^+) = H(Na^+) - H(Na^+ / K^+)$$

# Using multiple charges




$$Q = \sum_{i=1}^{n} q_i$$

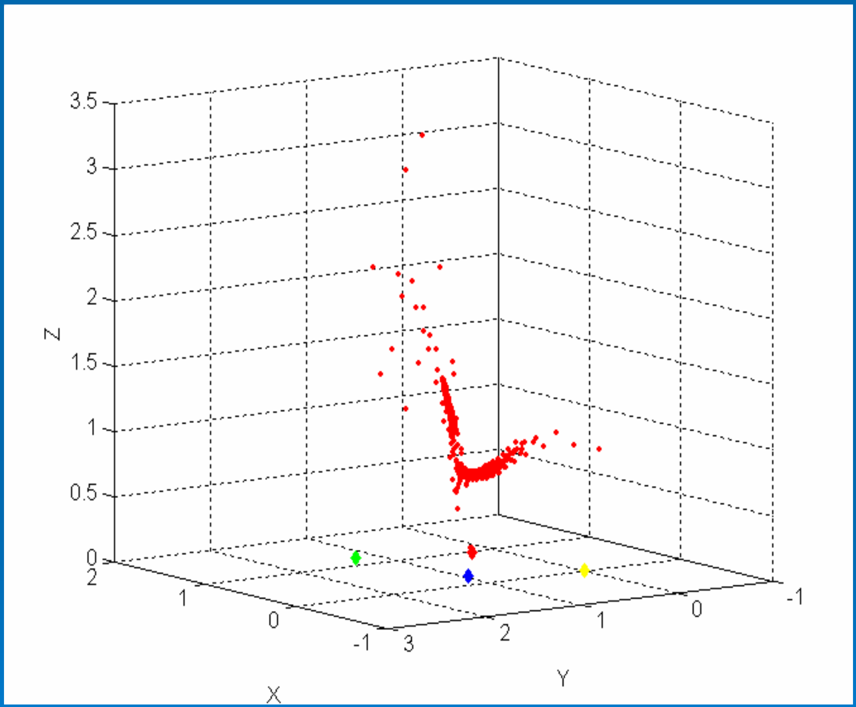
# Quantized Information in Spike

$$I_{spike} = H(Na^+) + H(K^+) + H(Cl^-) + \ldots\ldots - H(Na^+, K^+, Cl^- + \ldots)$$

$$I(p^+; n^-) = H_{p^+} + H_{n^-} - H(p^+, n^-)$$

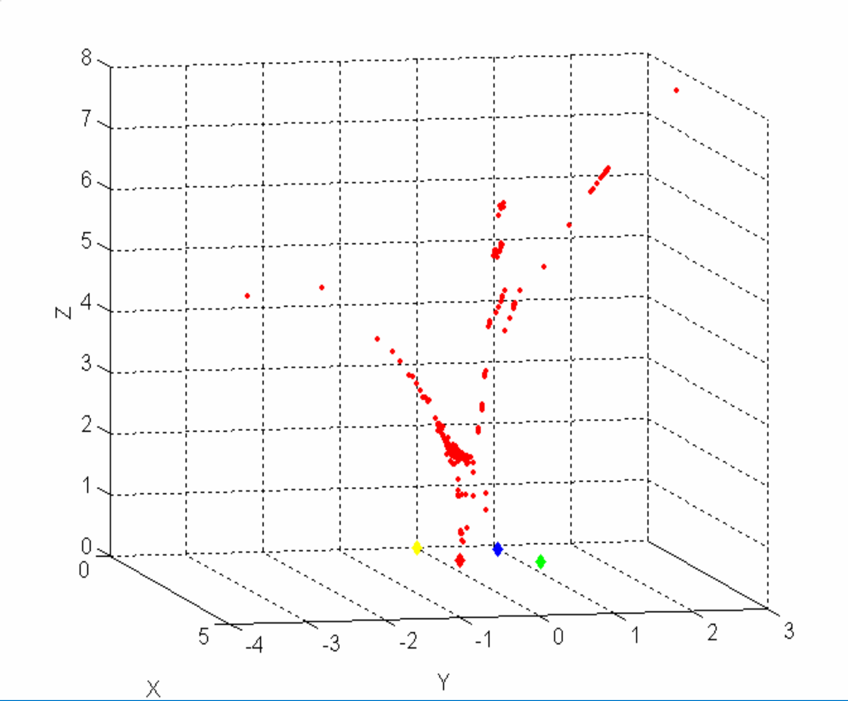
- Ionic fluxes are correlated therefore they convey information mutually
- Our estimation is based on ICA components

# Simulated ions trajectory



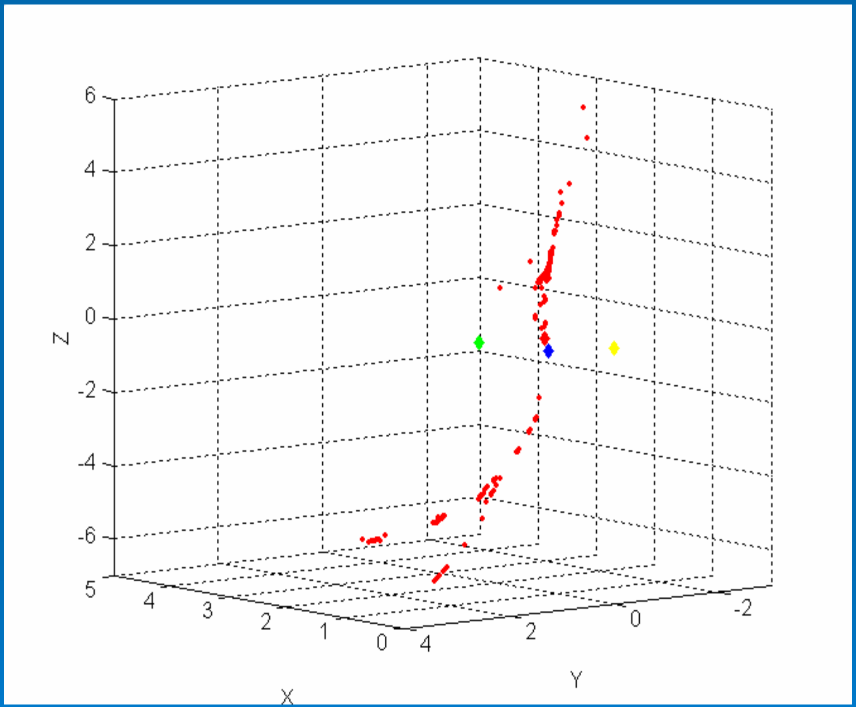

- Trajectory based on ICA and Newton-Raphson for a single charge in movement
- Noise was added to simulate recorded signals from measurements

# Actual ionic trajectories




- Neuron electrical image is constructed based on the points that represent the position of charges in movement during the AP
- Bending is caused by several factors including the nonlinearity of the recorded spike.

# 3-D spike representation




- De-bended image of spike. Electrical image is constructed based on the points that represent the position of group of charges in movement.
- Each division on the axes is approximately 20 microns