Tracking Neuronal Dynamics During Seizures And Alzheimer's Disease

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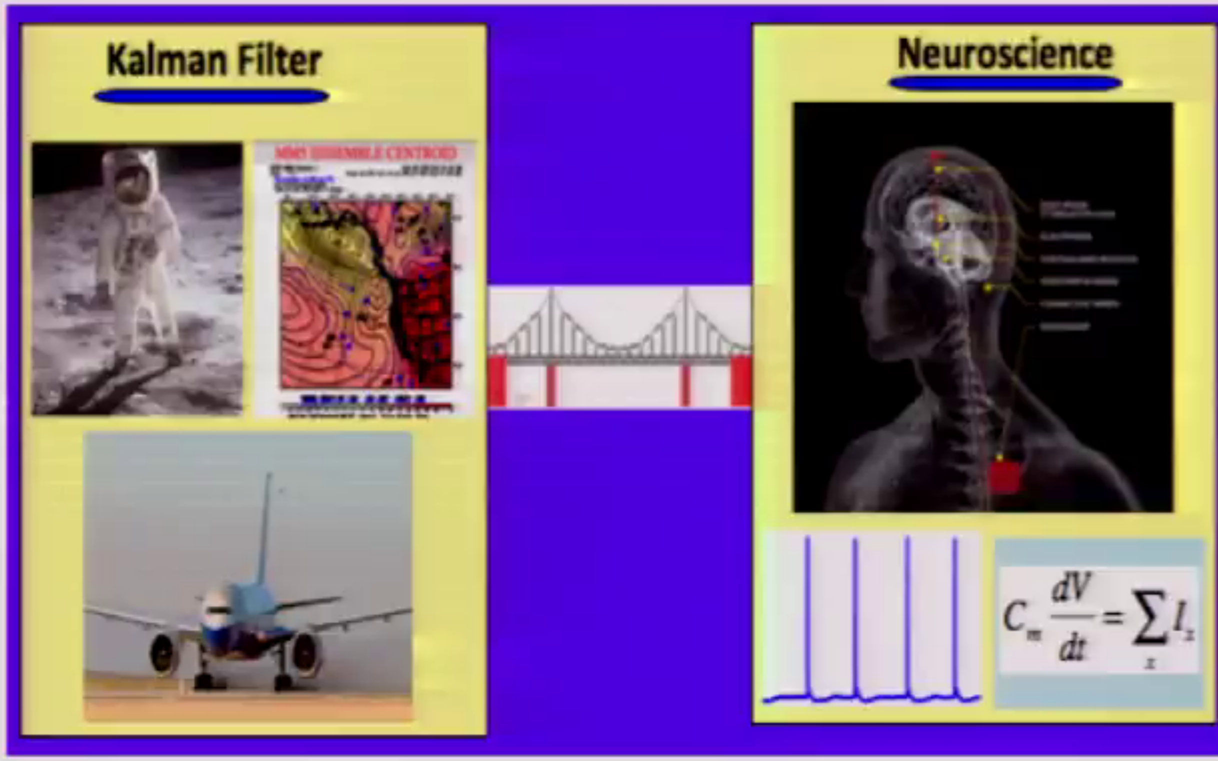
Tampa, Florida



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Motivation

A lot of work has been done in computational epilepsy –
(Ullah and Schiff, Models of Epilepsy, Scholarpedia)

Computational models need to be fused with neuronal networks

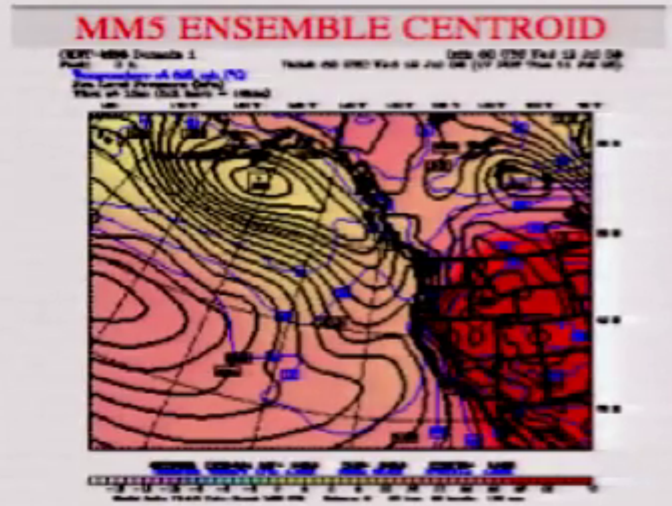
No one has attempted model-based tracking and control

Why Model-Based Control?

Control Engineering: Space ship control, airframe control, robotics etc.

Meteorology: Weather forecasting

Airframe control



Weather forecasting

Weather forecasting involves estimation and prediction
Airframe control involves estimation, prediction, and controlling

We wish to do the same with seizures and other neurological disorders

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So What Do We Need?

Fundamental models: that not only fit the data but also track and control the system

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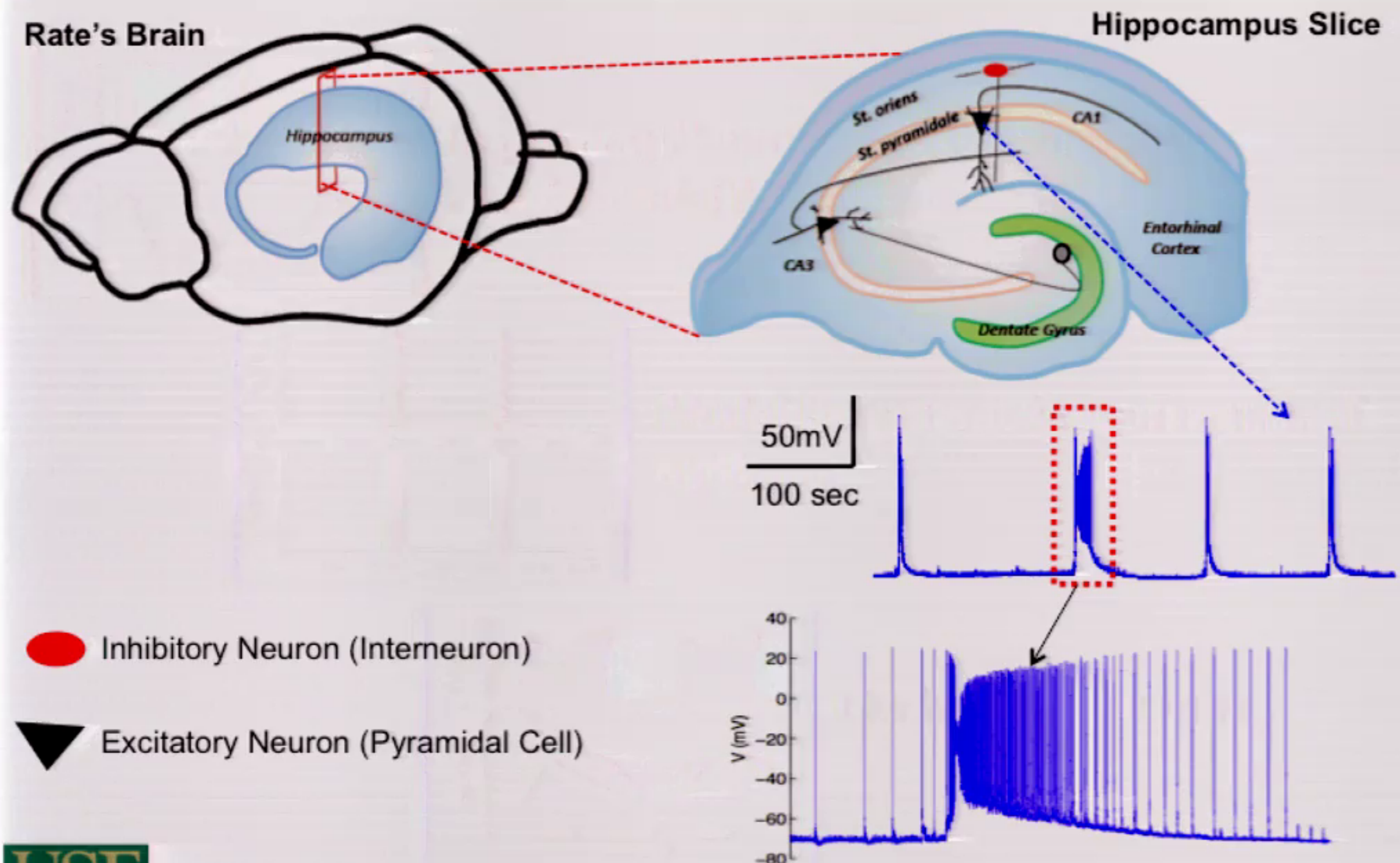
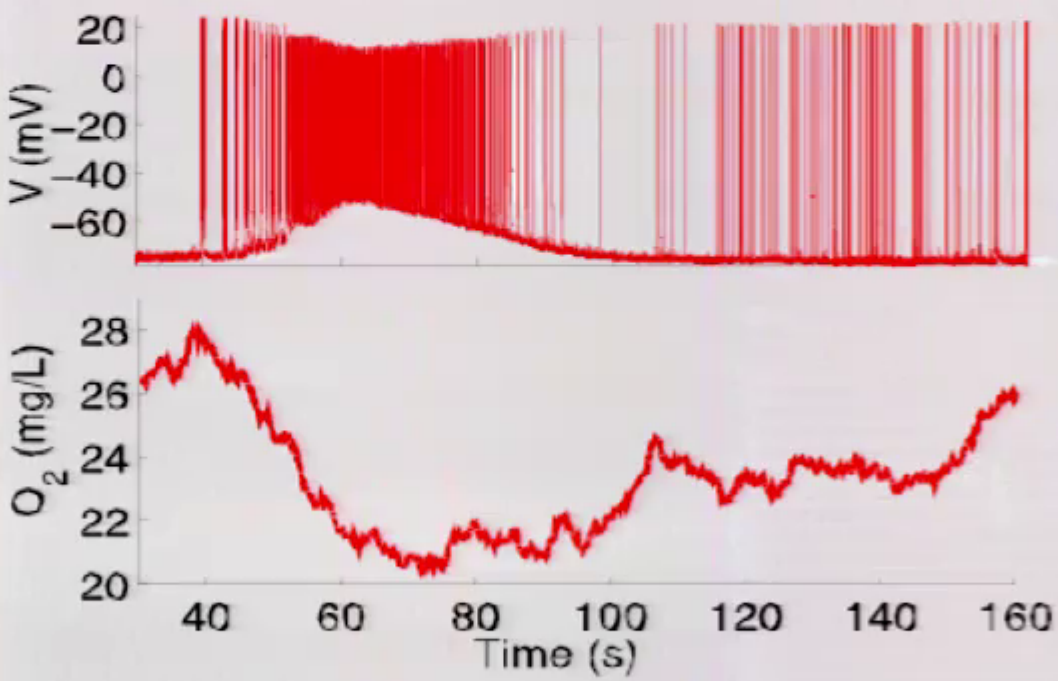
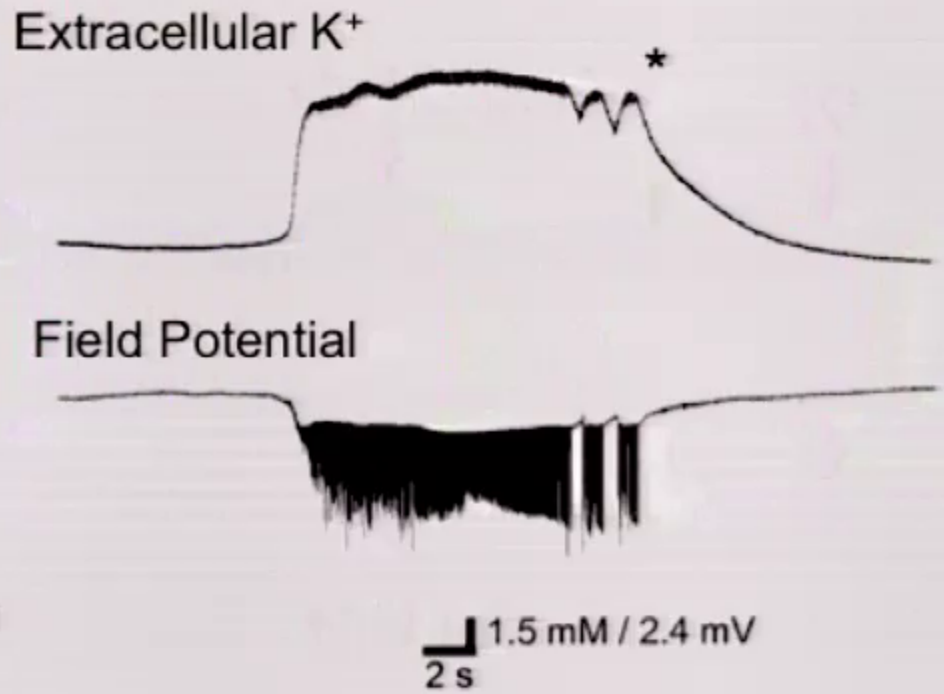
Seizures at the Single Cell Level



Ziburkus, et al, J. Neurophysiol. (2006)

But There Are Other Important Variables





Sodium, Calcium, Chloride, ATP, Glucose.....

(1) Need to take these factors into account
(2) Estimate the variables that are experimentally inaccessible

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Ingram, et al, J. Neurophysiol. (2014); Bikson, et al, J. Neurophysiol. (2003)

We Need More Than Electricity

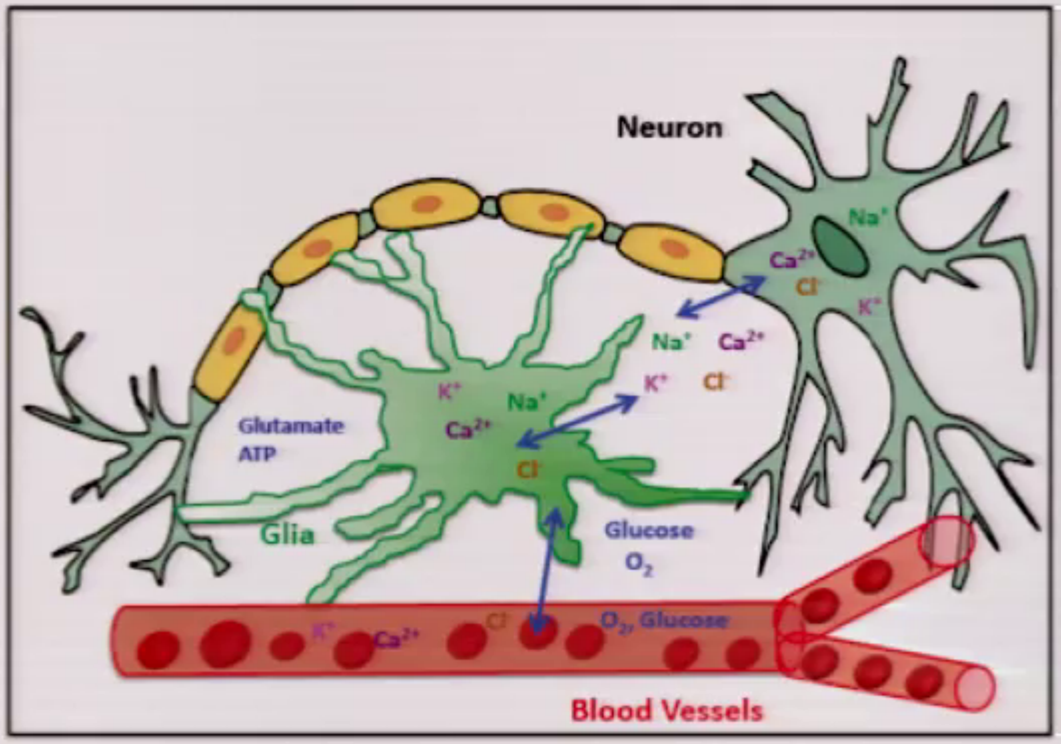
$$C_m \frac{dV}{dt} = I_{stim} + I_{na} - I_k - I_{pump} - I_{Cl} + I_{Ca}$$

$$\frac{\partial[ion]_o}{\partial t} = \frac{I_{ion}A}{FVol_o} + I_{diff}$$

$$\frac{d[ion]_i}{dt} = \frac{I_{ion}A}{FVol_i}$$

$$\frac{d[ion]_g}{dt} = \frac{I_{ion}A_g}{FVol_g}$$

$$\frac{\partial[O_2]}{\partial t} = I_{blood} - I_{pump} + I_{diff}$$



Modeling details in
Cressman, Ullah et al, J. Comp. Neurosci. (2009)
Ullah et al. J. Comp. Neurosci. (2009)
Ullah & Schiff, Phys. Rev. E. (2009)
Ullah & Schiff, PLoS Comp. Biol. (2010)
Wei, Ullah, Ingram, Schiff, J. Neurophysiol. (2014)
Wei, Ullah, Schiff, J. Neurosci. (2014)

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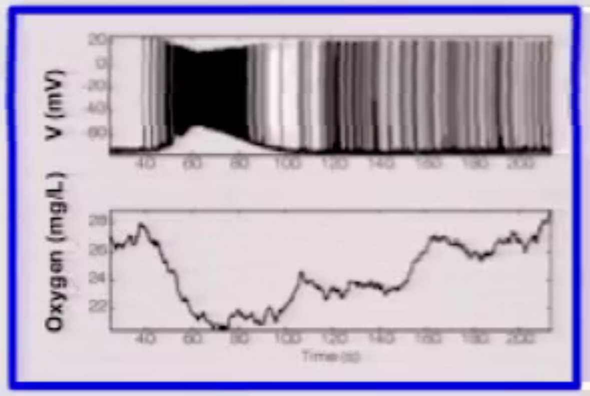
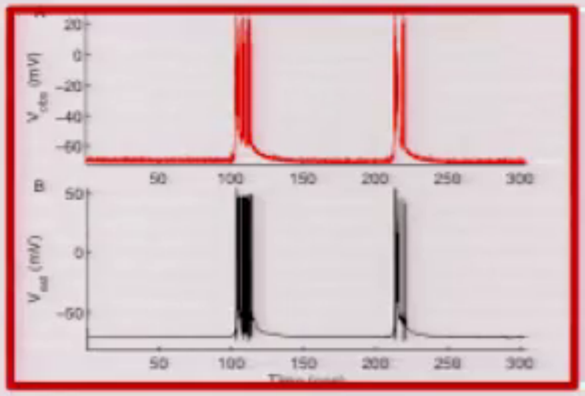
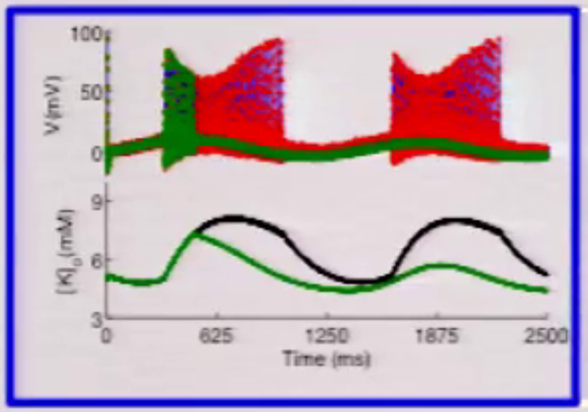
This Presentation Focuses on...



Improving Neuronal Models: Towards Fundamental Models



Model-based tracking of neuronal systems



Controlling Neurons

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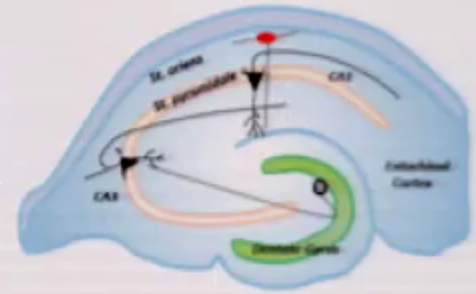
How Does Model-Based Framework Work?



Model

Partial Measurements
e.g. potential

Kalman filter: synchronizes the model with the data

"Full" estimate of the system dynamics (all variables and parameters)

Use Model to Predict

Control?

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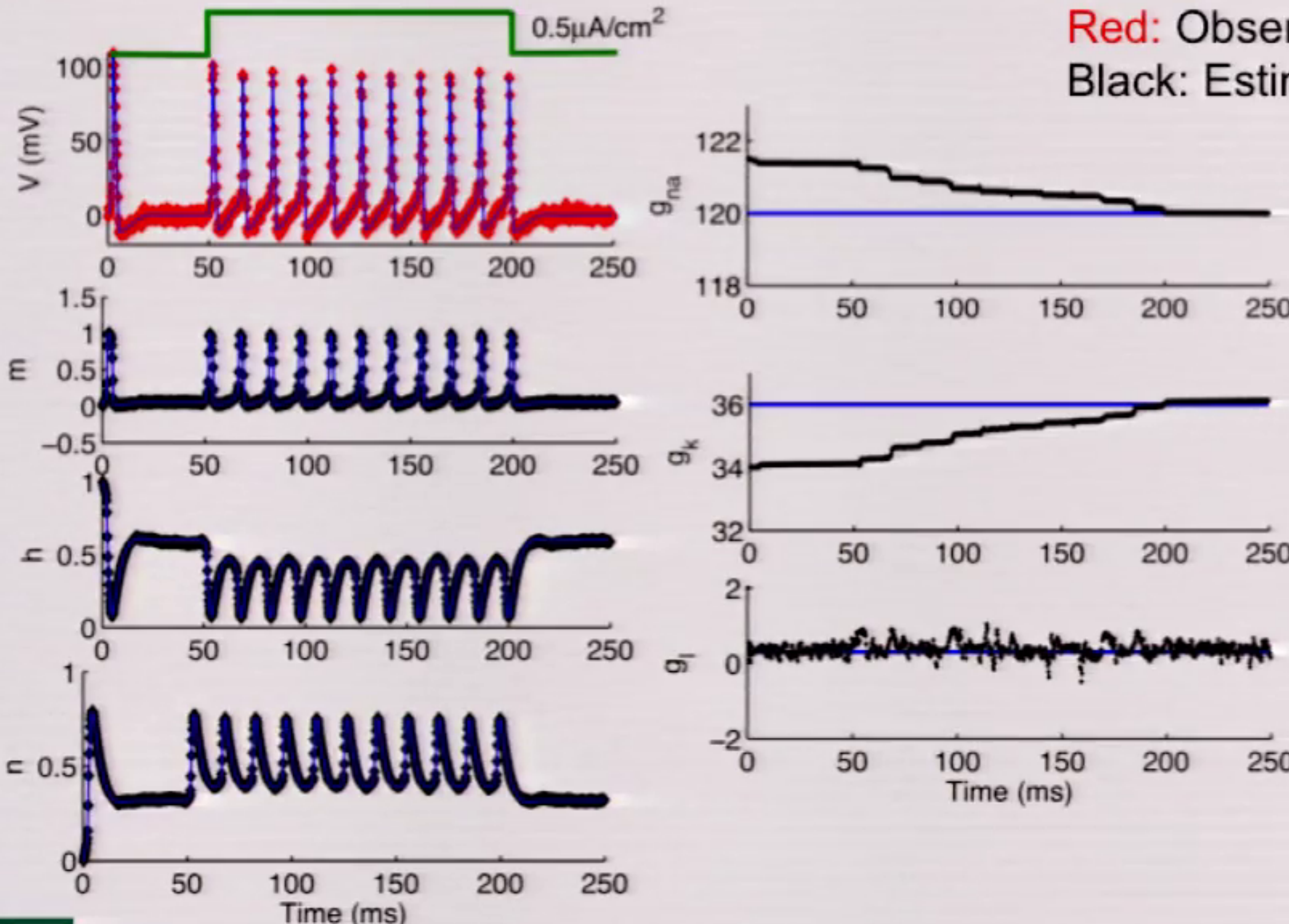
Julier & Uhlmann, Proc. SPIE (1997)

Tracking Hodgkin-Huxley Dynamics – No Microenvironment

Simulated data

Blue: True state
Red: Observed state
Black: Estimated state



Ullah & Schiff, PRE (2009)

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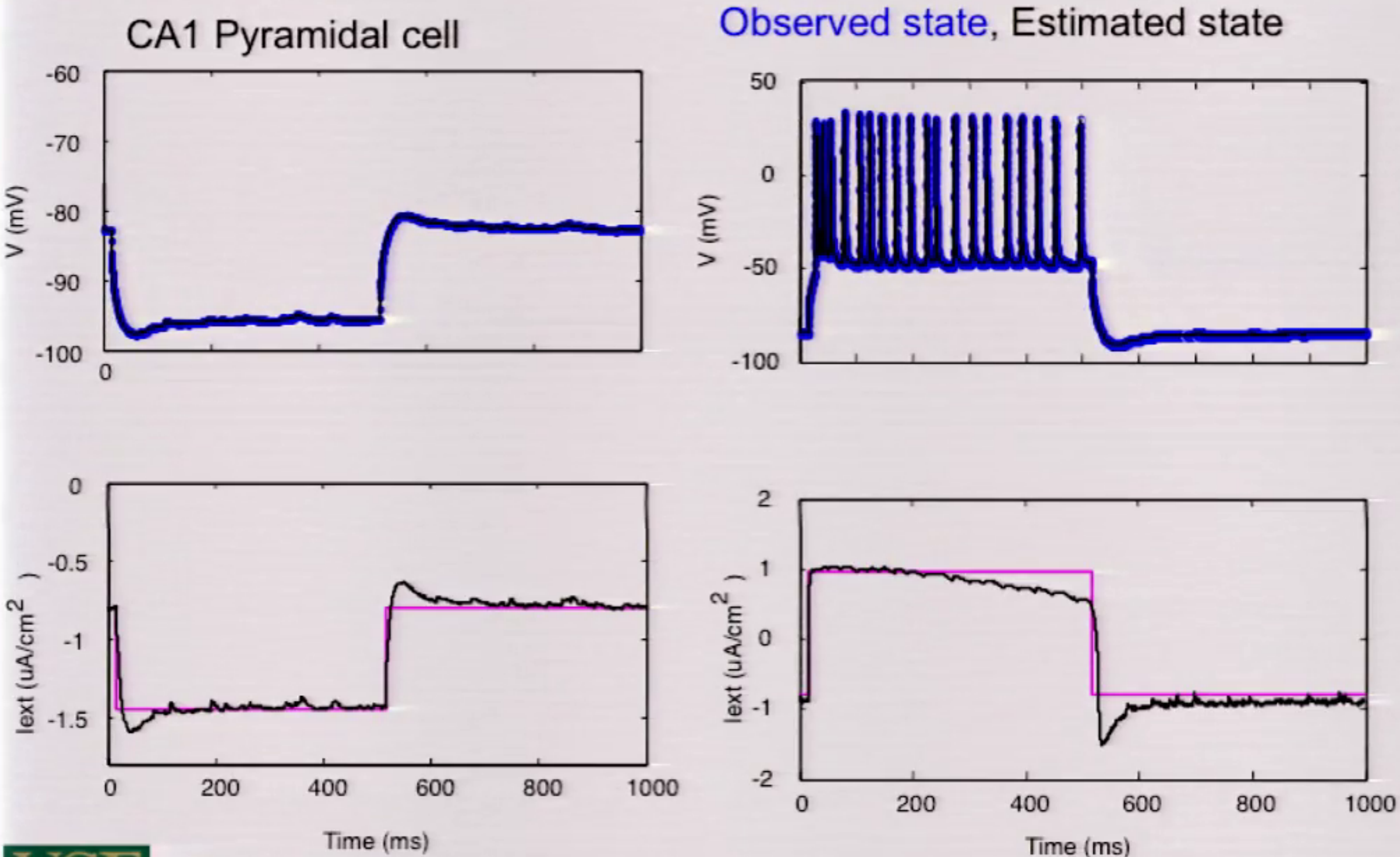
Verifying the Tracking



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Wei, Ullah et al, IEEE Decis. Cont. (2011)

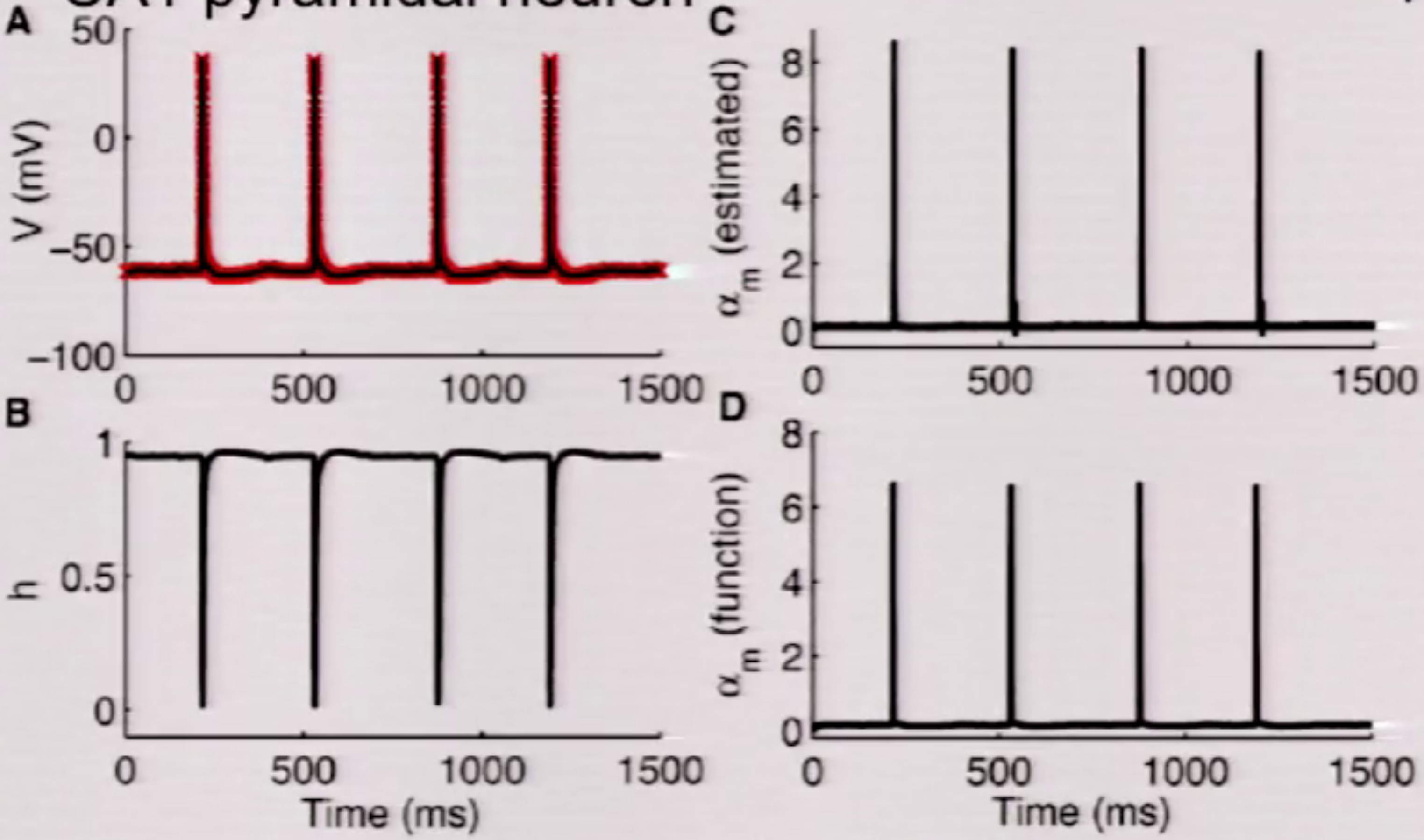
Improving Model With Tracked Data

$$\frac{dm}{dt} = \alpha_m(1-m) - \beta_m m$$

Observed state
Estimated state

CA1 pyramidal neuron

Treat α_m as unknown parameter



$$\alpha_m = \frac{0.1(V+30)}{1-exp(-0.1(V+30))}$$

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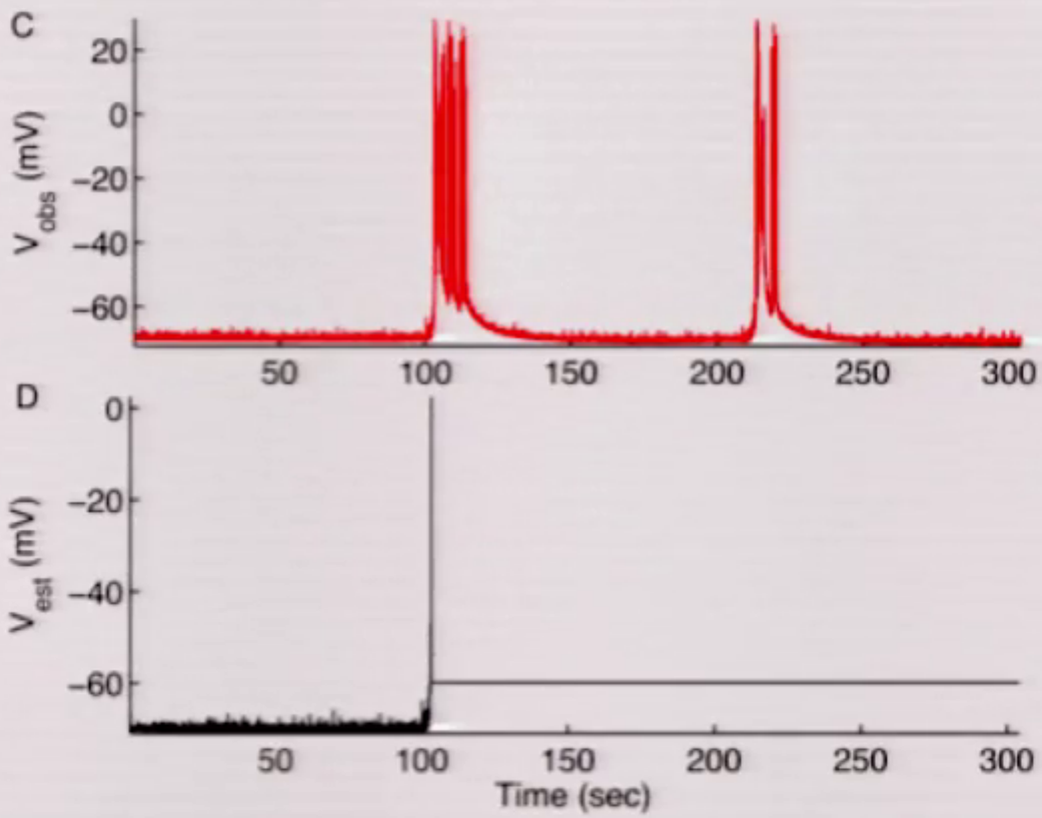
Ullah & Schiff, PLoS Comp. Biol. (2010)

But We Can't Track Seizures With This Model

Observed
Tracked

Hodgkin-Huxley Formulism - Model without ion concentrations



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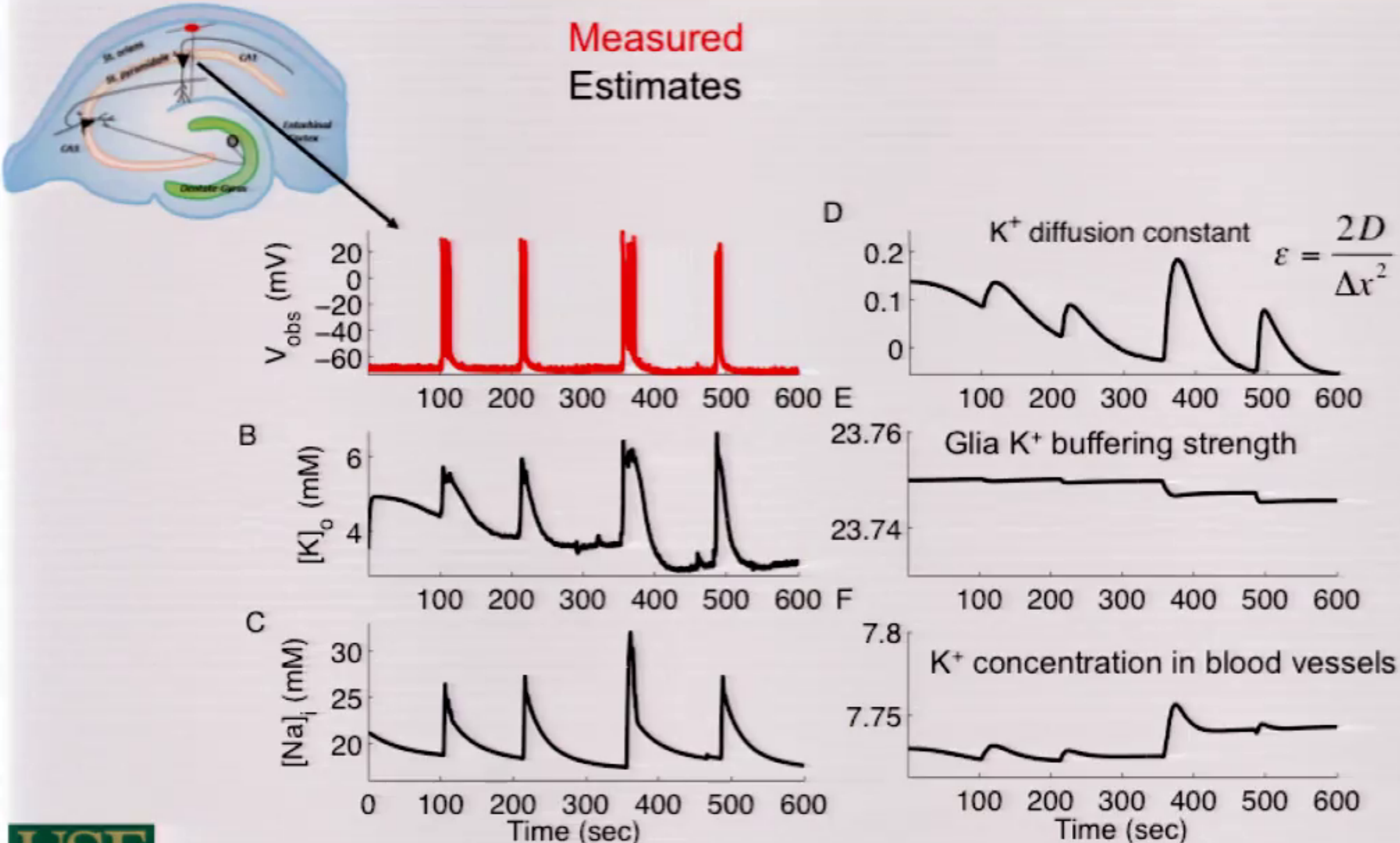
Ullah & Schiff, PLoS Comp Biol (2010)

Tracking Seizure Dynamics

Model (Cressman, et al. 2009; Ullah et al. 2009):
Membrane potential: V, m, n, h - Hodgkin-Huxley model
Ion concentrations: K^+, Na^+

Tracking Pyramidal Cell During Seizures



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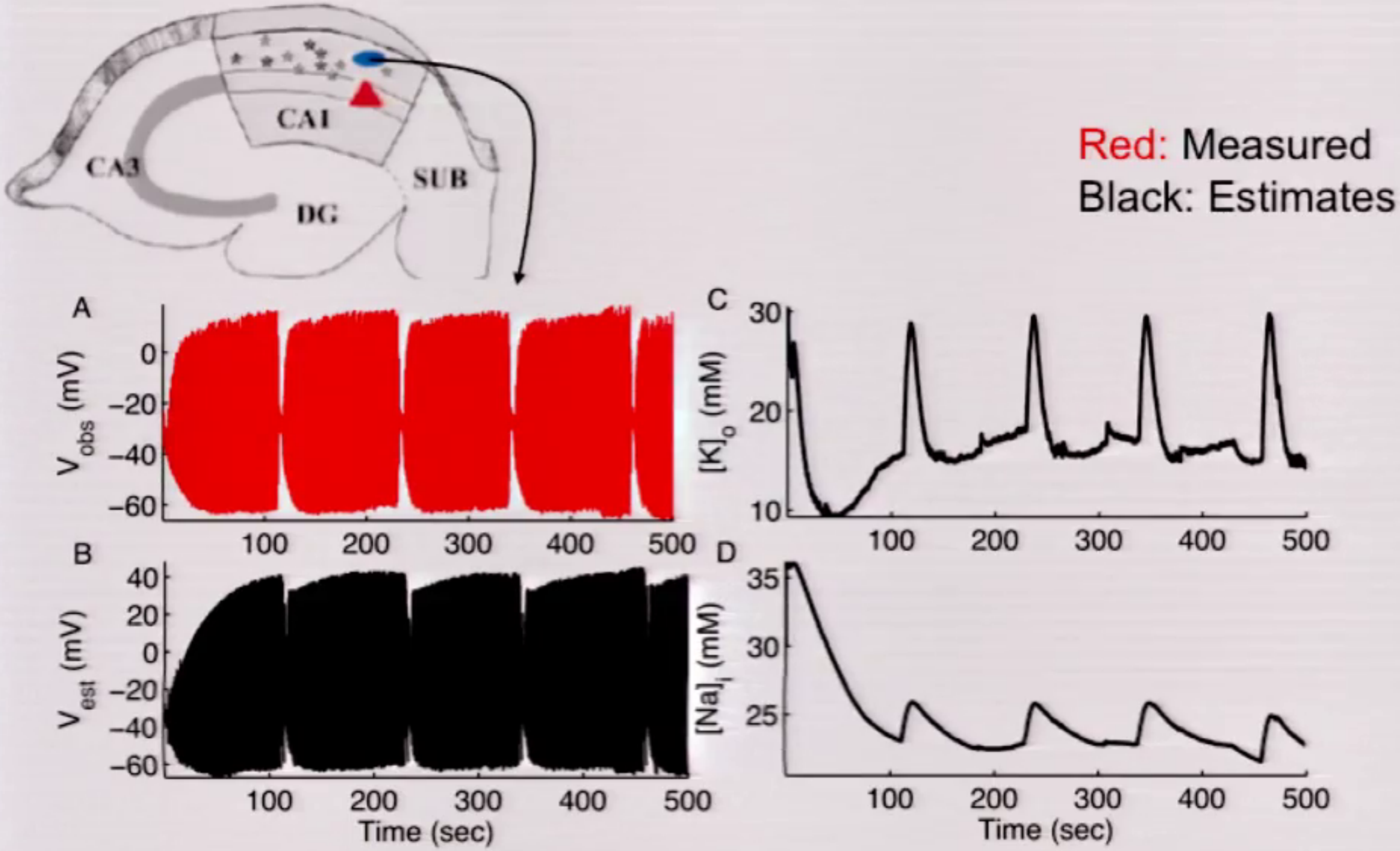
Ullah & Schiff, PLoS Comp. Biol. (2010)

Tracking Interneuron During Seizures



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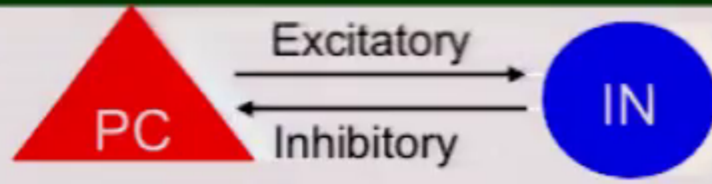
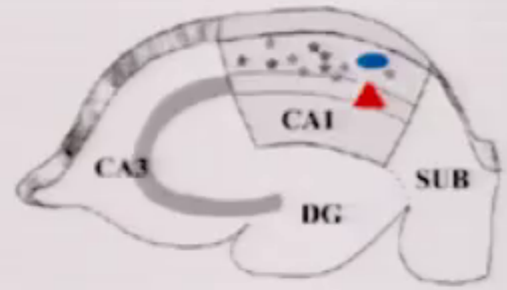
Ullah & Schiff, PLoS Comp Biol (2010)

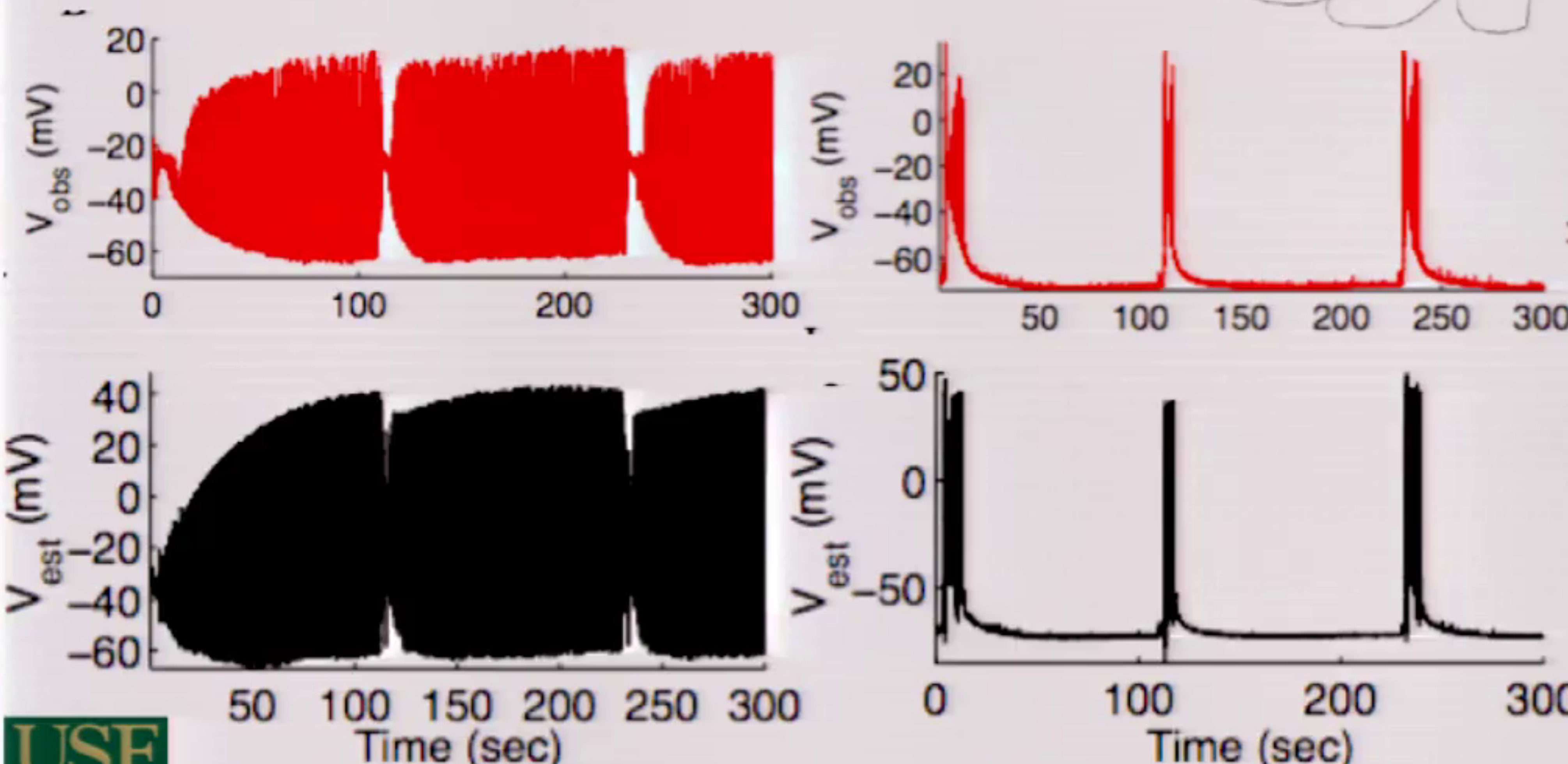
Verifying the Tracking

Observed

Estimates







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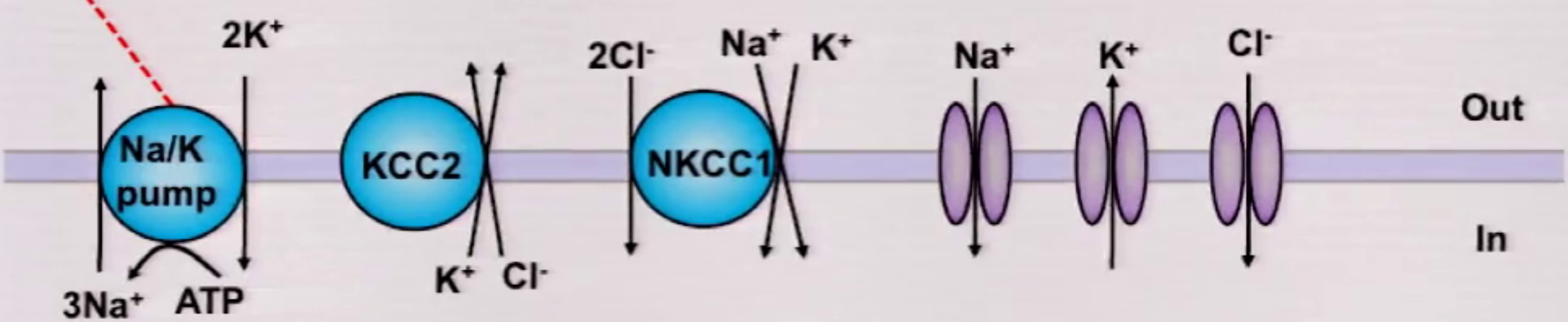
Ullah & Schiff, PLoS Comp. Biol. (2010)

Including Oxygen and Chloride Homeostasis

Model (Wei et al. 2014a, 2014b):
Membrane potential: V, m, n, h
Ion concentrations: K^+, Na^+, Cl^-, O_2

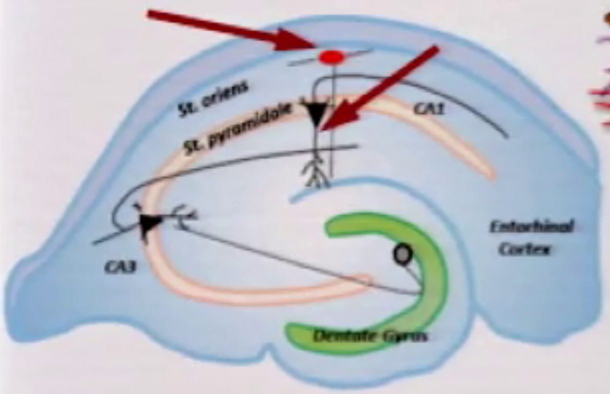
Pumps are fueled by ATP

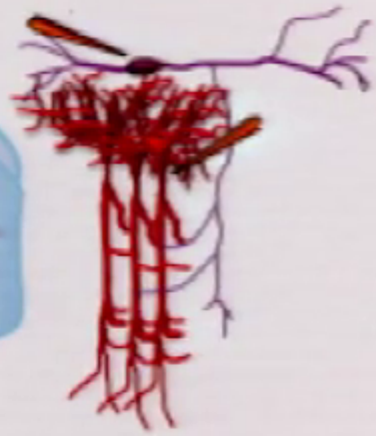
$$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O + 36ATP$$

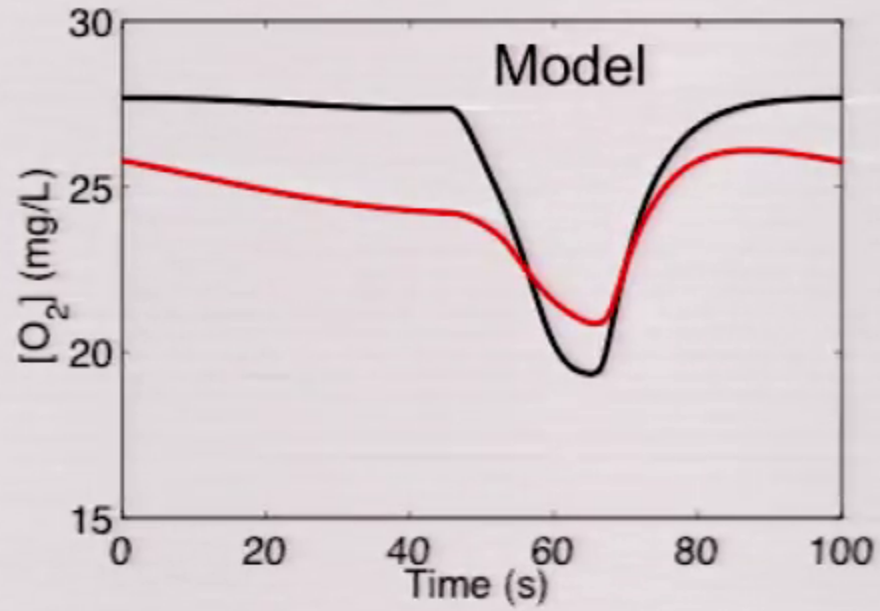


Wei, Ullah, Ingram, Schiff, J. Neurophysiol. (2014a); Wei, Ullah, Schiff, J. Neurosci. (2014b)

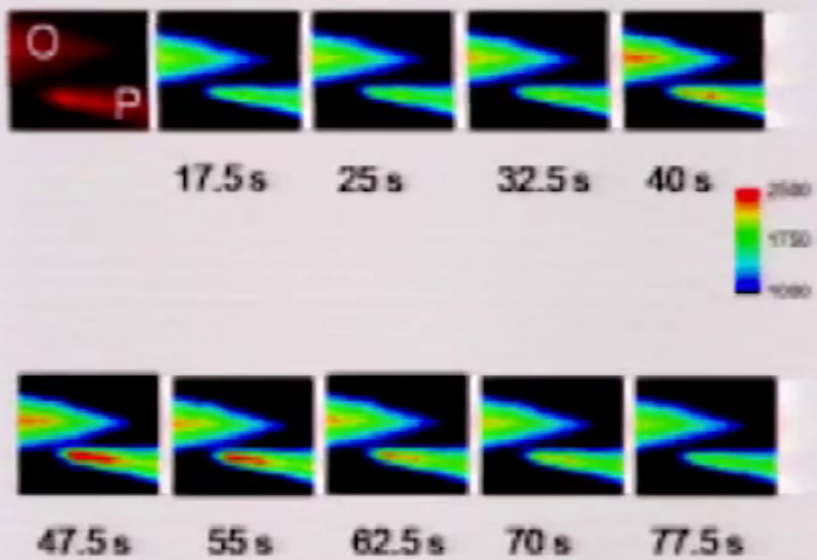
Oxygen Consumption During Seizure

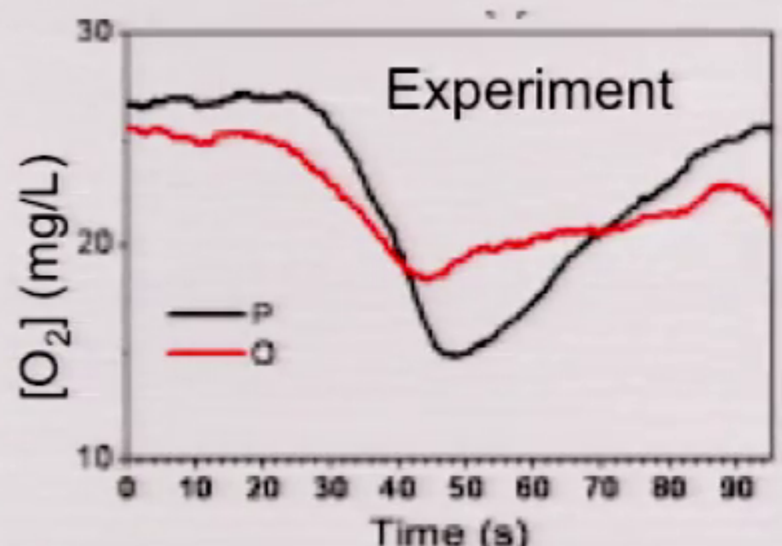






Optode tips during a seizure event





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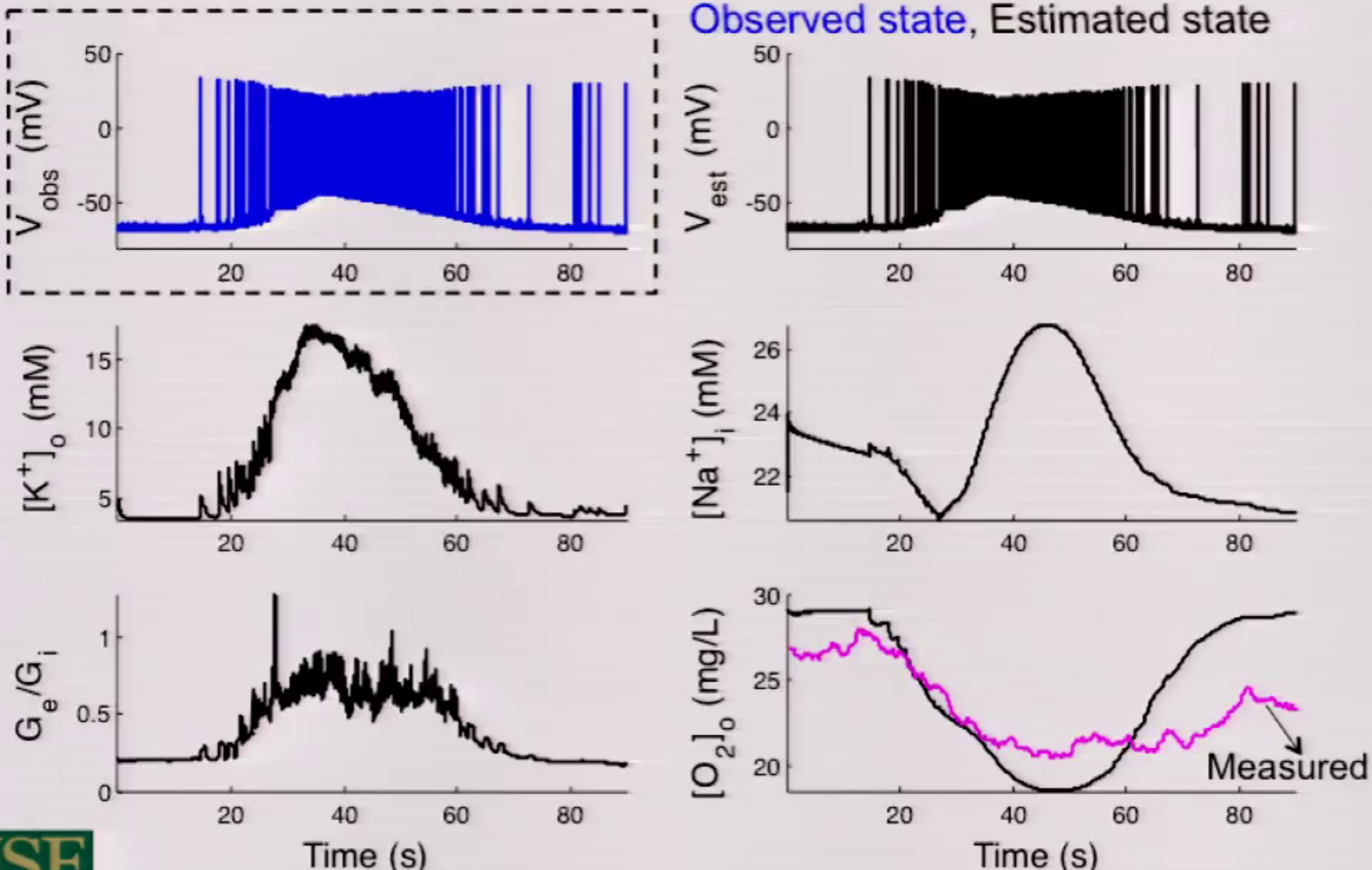
Ingram, et al, J Neurophysiol. 2014; Wei, Ullah, Ingram, Schiff, J. Neurophysiol. 2014.

Reconstructing Oxygen Dynamics



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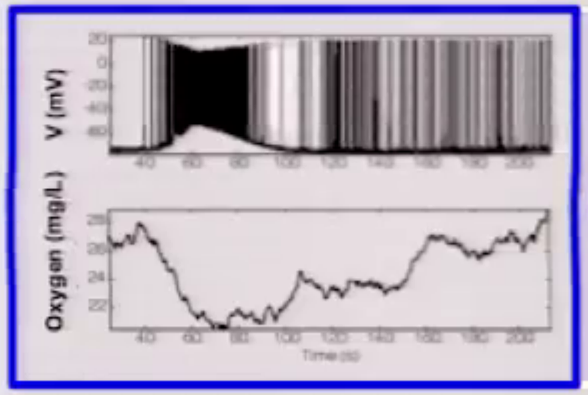

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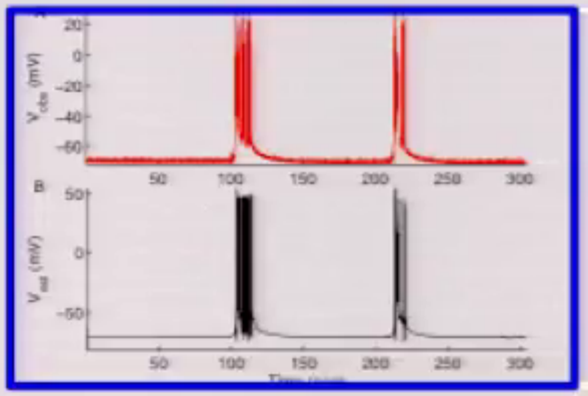

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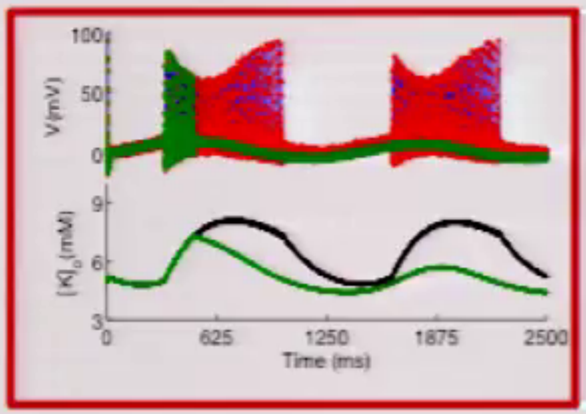

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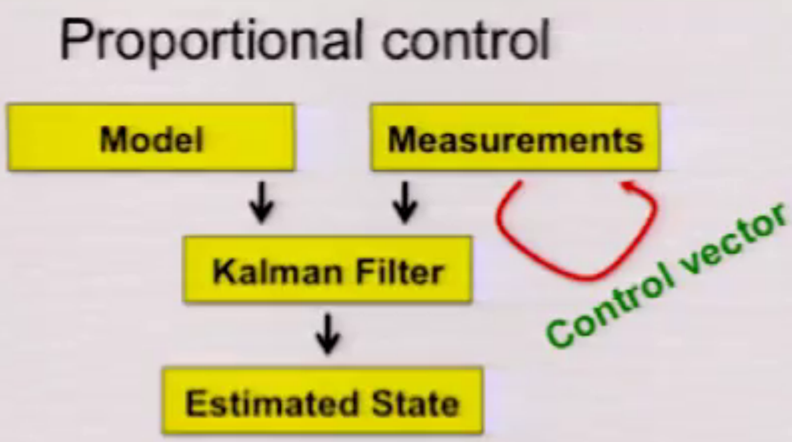
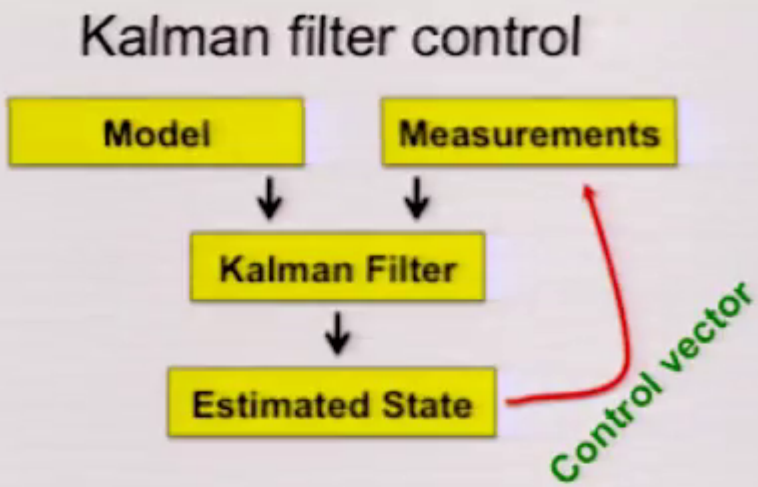
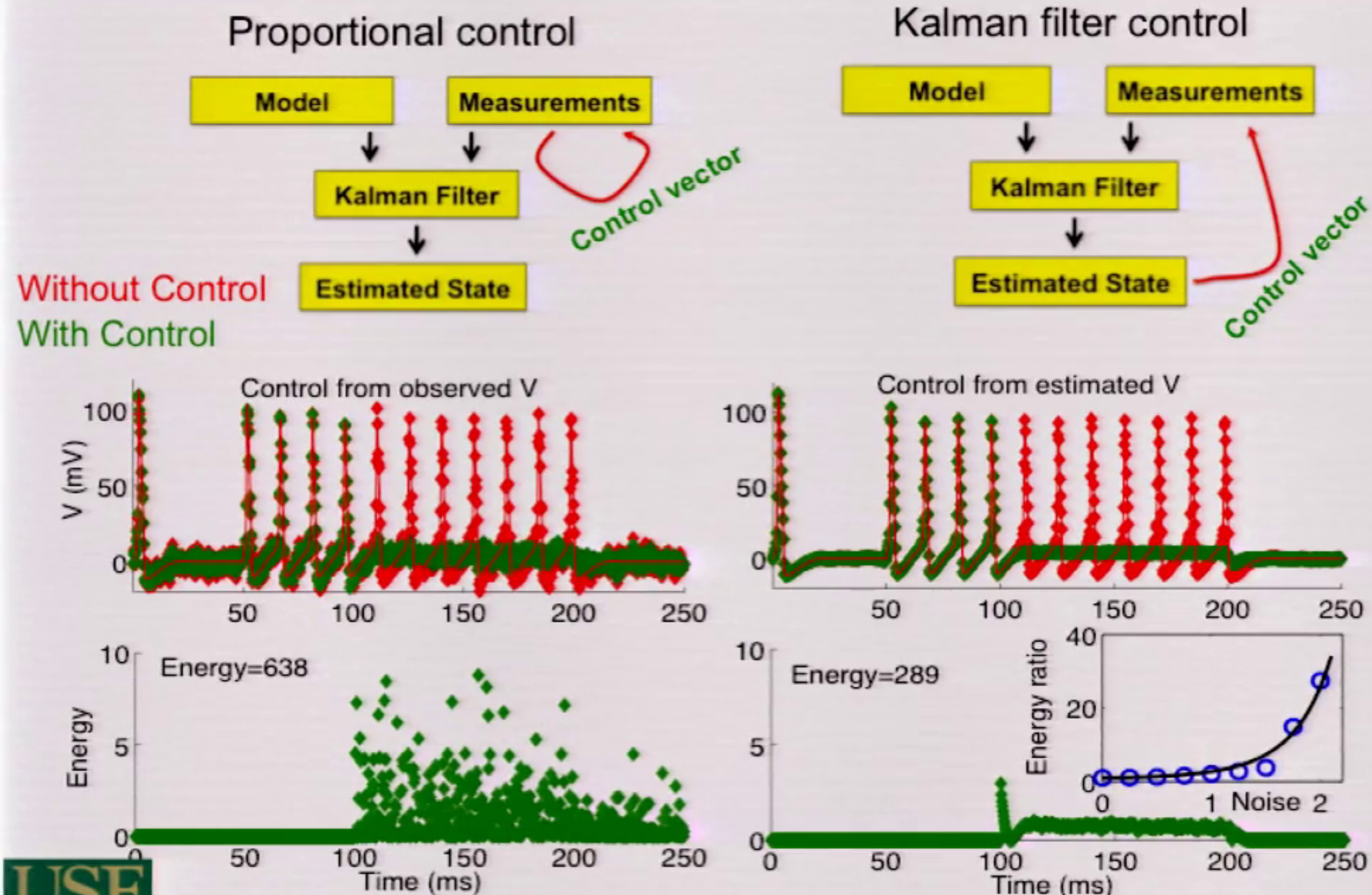
Better Control With Model-Based Approach





Ullah & Schiff, Phys. Rev. E (2009)

Better Control With Model-Based Approach



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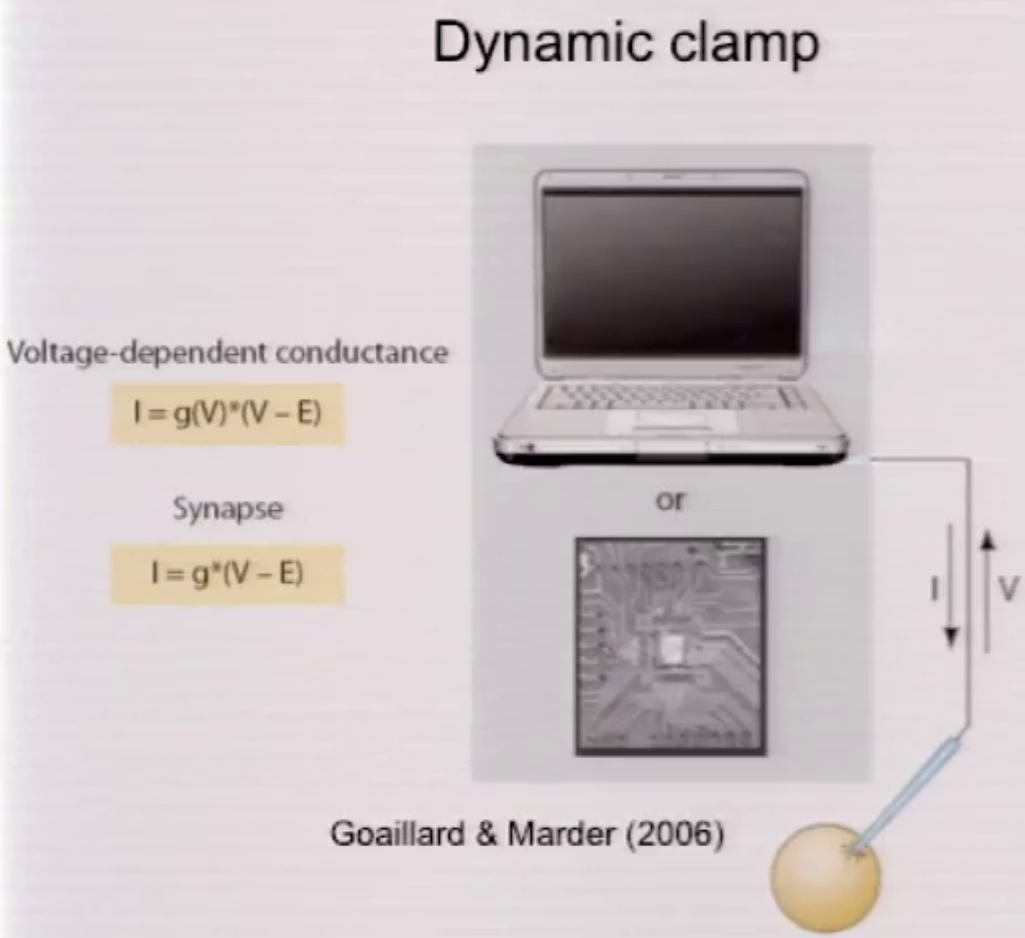
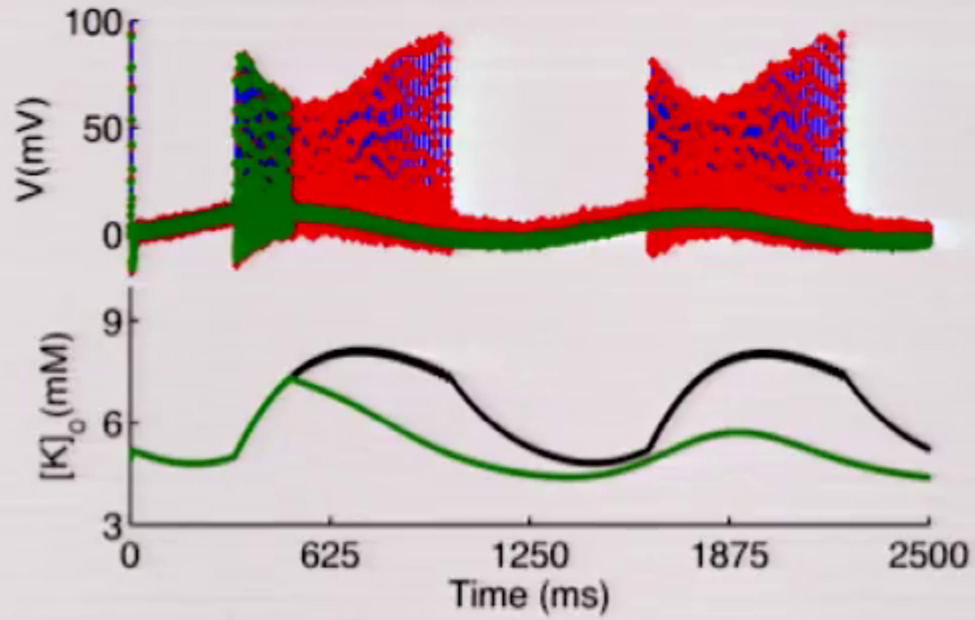
Ullah & Schiff, Phys. Rev. E (2009)

Dynamic Clamp





Ullah & Schiff, PRE (2009)

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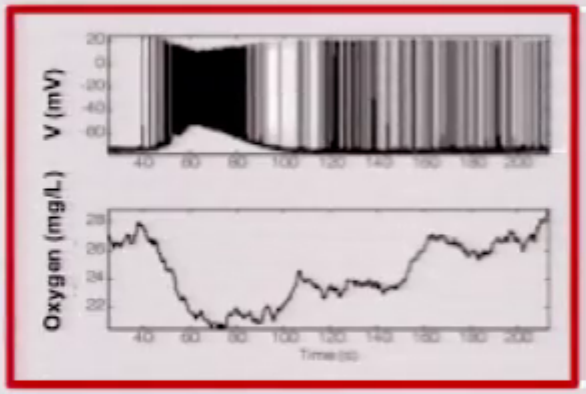

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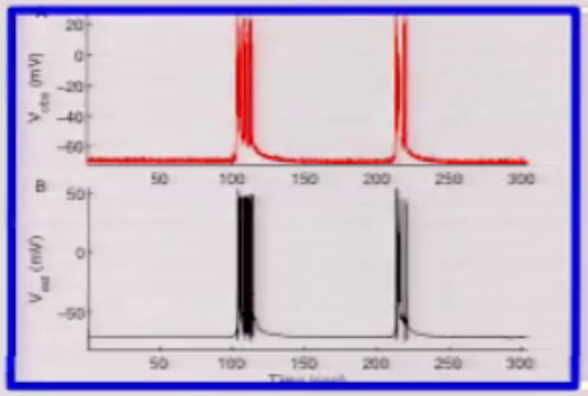
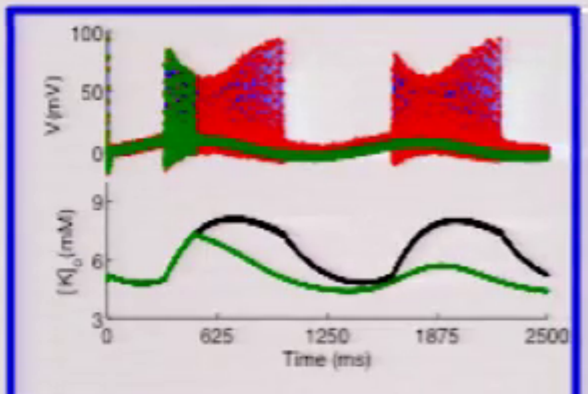


Model-based tracking of neuronal systems



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Cell Swells Too (e.g. Ischemic Stroke)

$$C_m \frac{dV}{dt} = I_{stim} + I_{na} - I_k - I_{pump} - I_{Cl} + I_{Ca}$$

$$\frac{\partial [ion]_o}{\partial t} = \frac{I_{ion} A}{F Vol_o} + I_{diff}$$

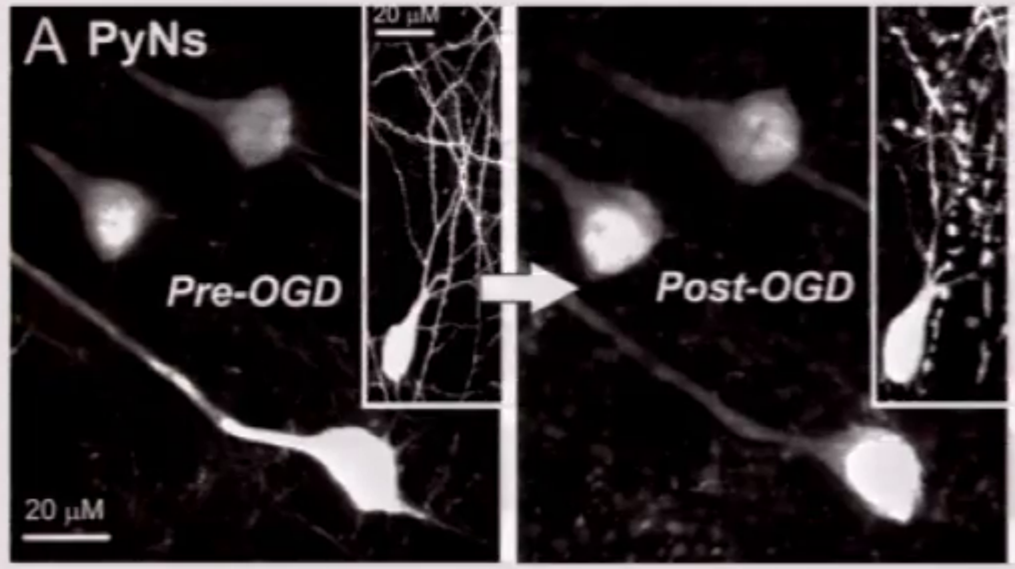
$$\frac{d[ion]_i}{dt} = \frac{I_{ion} A}{F Vol_i}$$

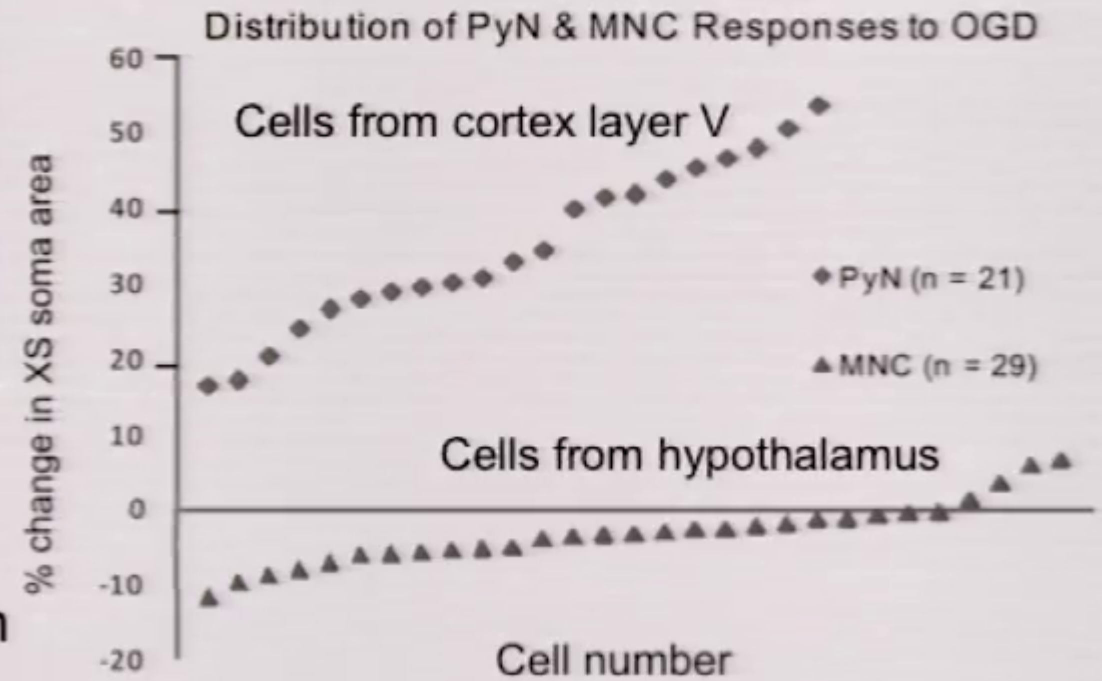
$$\frac{d[ion]_g}{dt} = \frac{I_{ion} A_g}{F Vol_g}$$

$$\frac{\partial [O_2]}{\partial t} = I_{blood} - I_{pump} + I_{diff}$$

$$\frac{dVol}{dt} = \frac{1}{\tau_v}\left(\widehat{Vol} - Vol\right)$$

Volume is a function of ion concentrations





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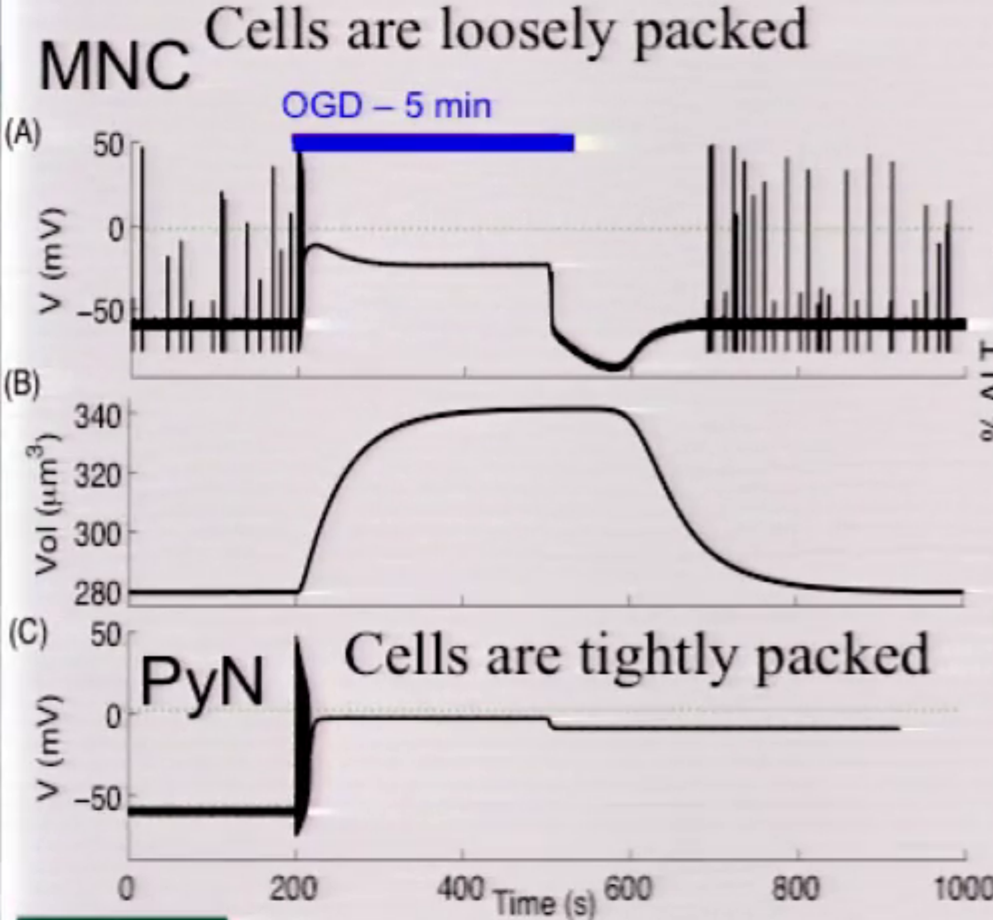
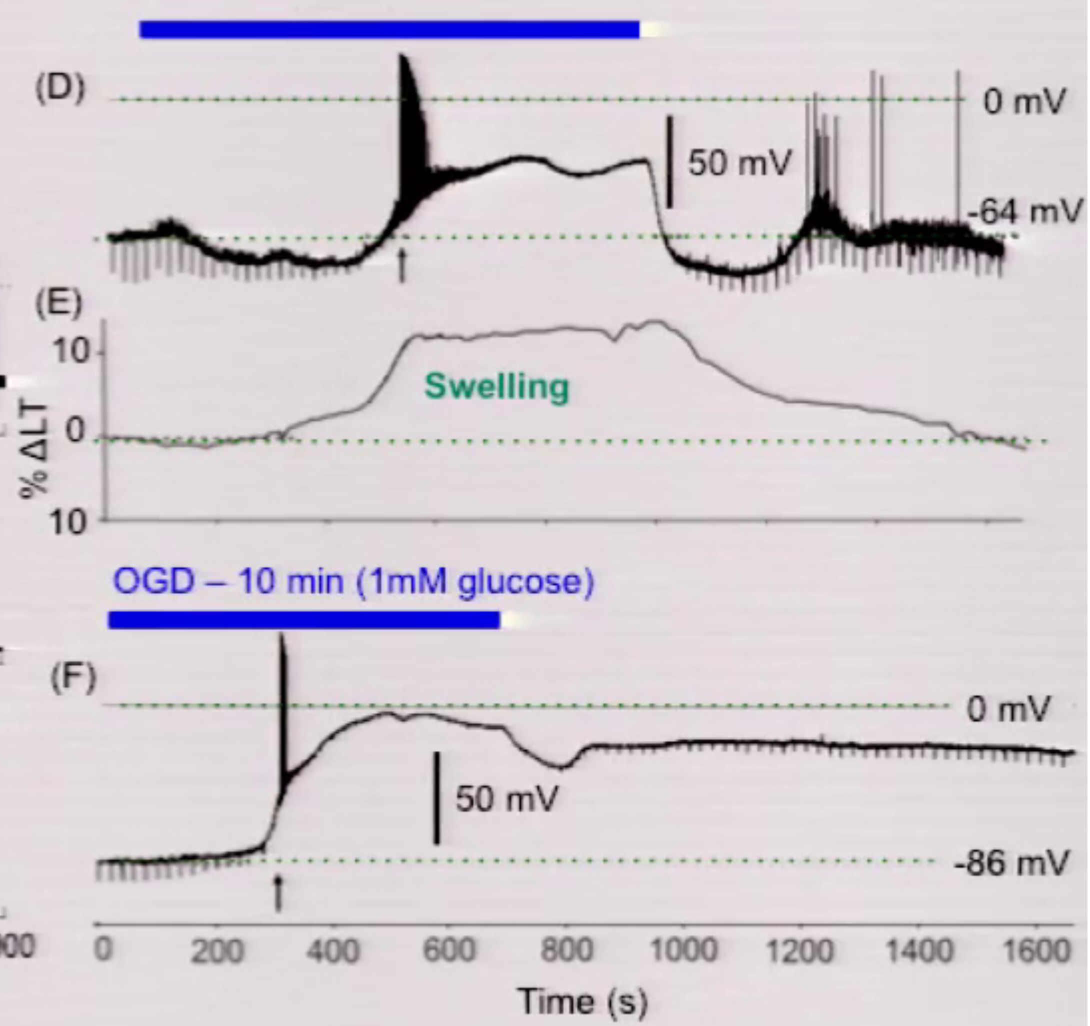
Ullah, et al. in review (2015), Brisson & Andrew, J. Neurophysiol. (2012)

Cell Swelling And Selective Neuronal Damage During Stroke

Model



Experiment



Ullah, et al, in review (2015); Brisson & Andrew, J. Neurophysiol. (2012).

Incorporating Microenvironment Leads To a Unified Framework For Several Neuronal Behaviors

Talk by Steven J Schiff

4.30PM Wednesday (Room Primrose B)

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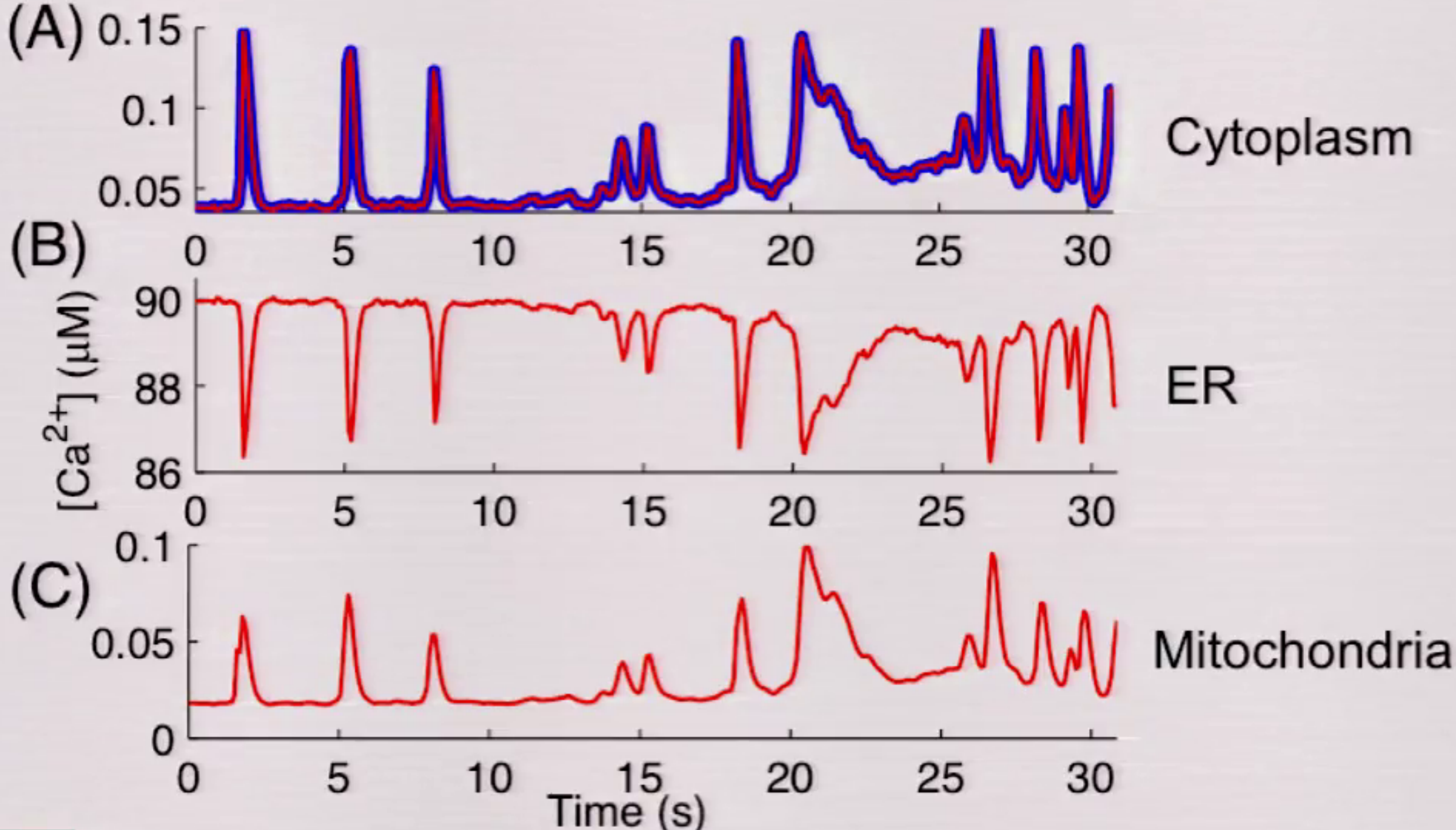
Wei, Ullah, Schiff, J. Neurosci. (2014).

Mitochondrial and Endoplasmic Reticulum Dynamic in Control and Alzheimer's Disease Cells



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Summary

Model-based approach can be used to

(1) Reconstruct inaccessible parameters and variables from a single measured variable

(2) Improve models by using tracked data

(3) Design efficient feedback control strategies

(4) Incorporating microenvironment into neuronal models leads to a unified framework for a range of neuronal behaviors