Model-Based Hypothesis Testing (with System ID) for Neural Systems

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Systems I Have Studied

- Human
  - Sensory reweighting in posture control
  - Stabilizing running
- Weakly Electric Fish
  - Direction selectivity in electro-sensation

OUTLINE

- Introduction to system identification
- Research problems for an undergraduate class
- Application to diagnosis of balance deficits
- Previous work
- Research goals

Analogy: Flying a Plane

Like balance, flying is a sensorimotor stabilization task.

Modeling Approach

Use a flight simulator with an autopilot
that mimics the brain of a real pilot.

Model Complexity Varies

Most autopilots ... trivialize human controller

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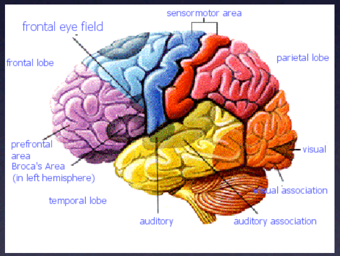

Autopilot behaving human ... trivializes variability in pilot population

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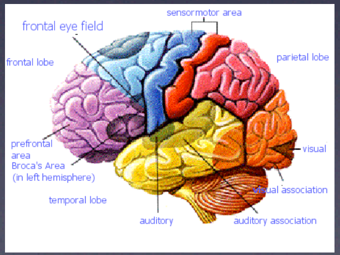

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Good model

For each pilot, want to know states of knobs and switches.

Need #1: Simple Behavior

Yes!

No!

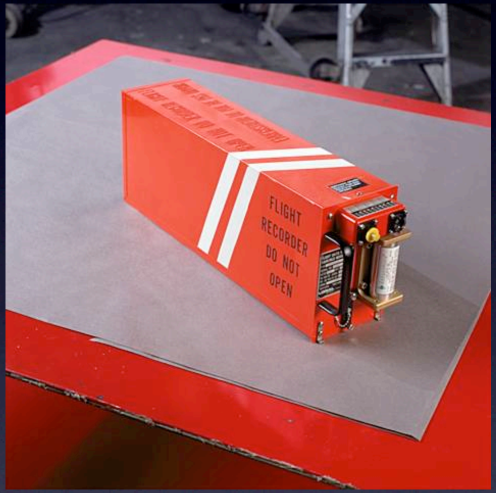
“Need” #2: Input

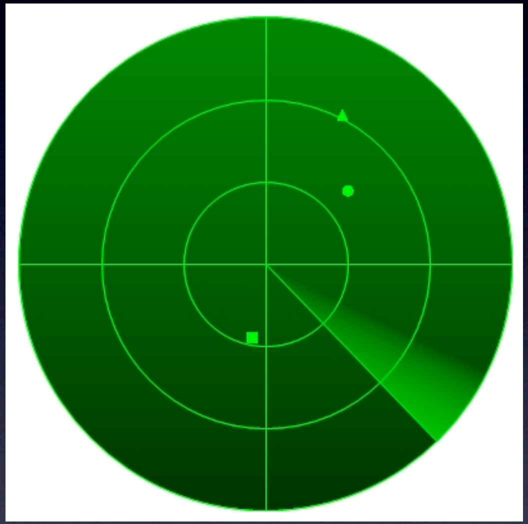
Balance: Move platform & visual surround

Flight: Change the wind

Need #3: Data

Flight:





Balance:

Need #4: Parameterized Model

Flight:

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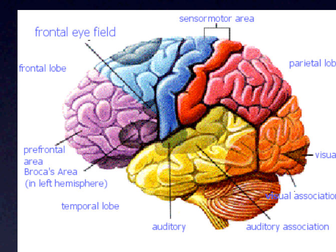

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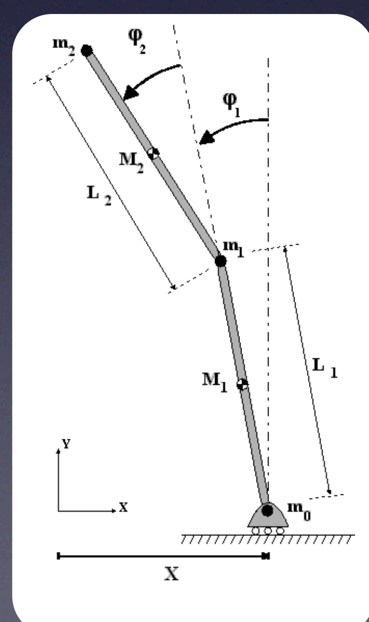
Balance:



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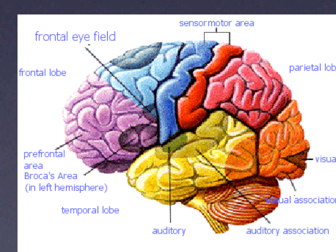

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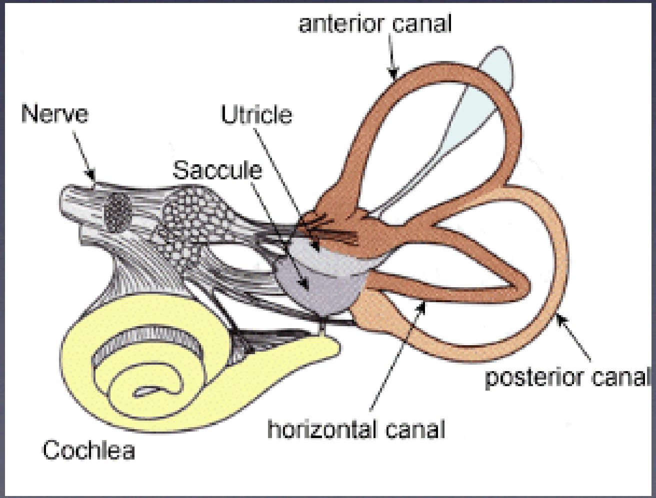
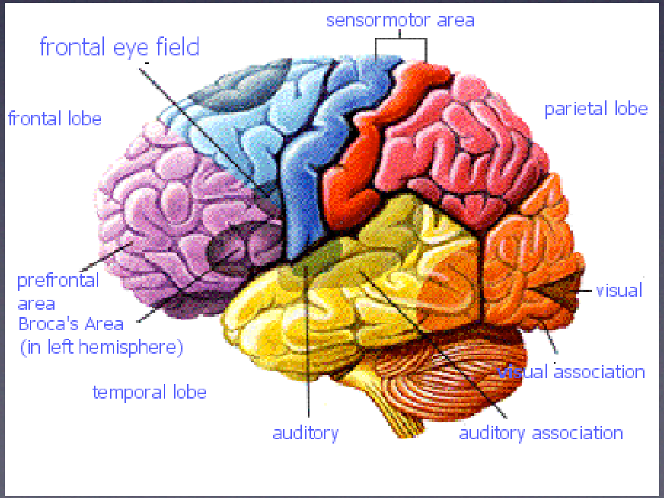
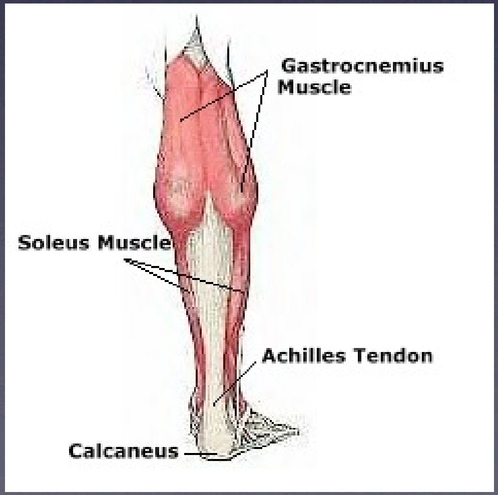
Need #5: Statistics of Noise

Noise is any input you do not know.







Needs

1. Simple Behavior to Be Studied
2. Known Inputs to System During Behavior
3. Data Collected During Behavior
4. Parameterized Model of System ...
5. Including Statistics of Noise (Unknown inputs)

System Identification: Infers the Values of Parameters (Knobs & Switches) and/or Decides If the Model Fits the Data

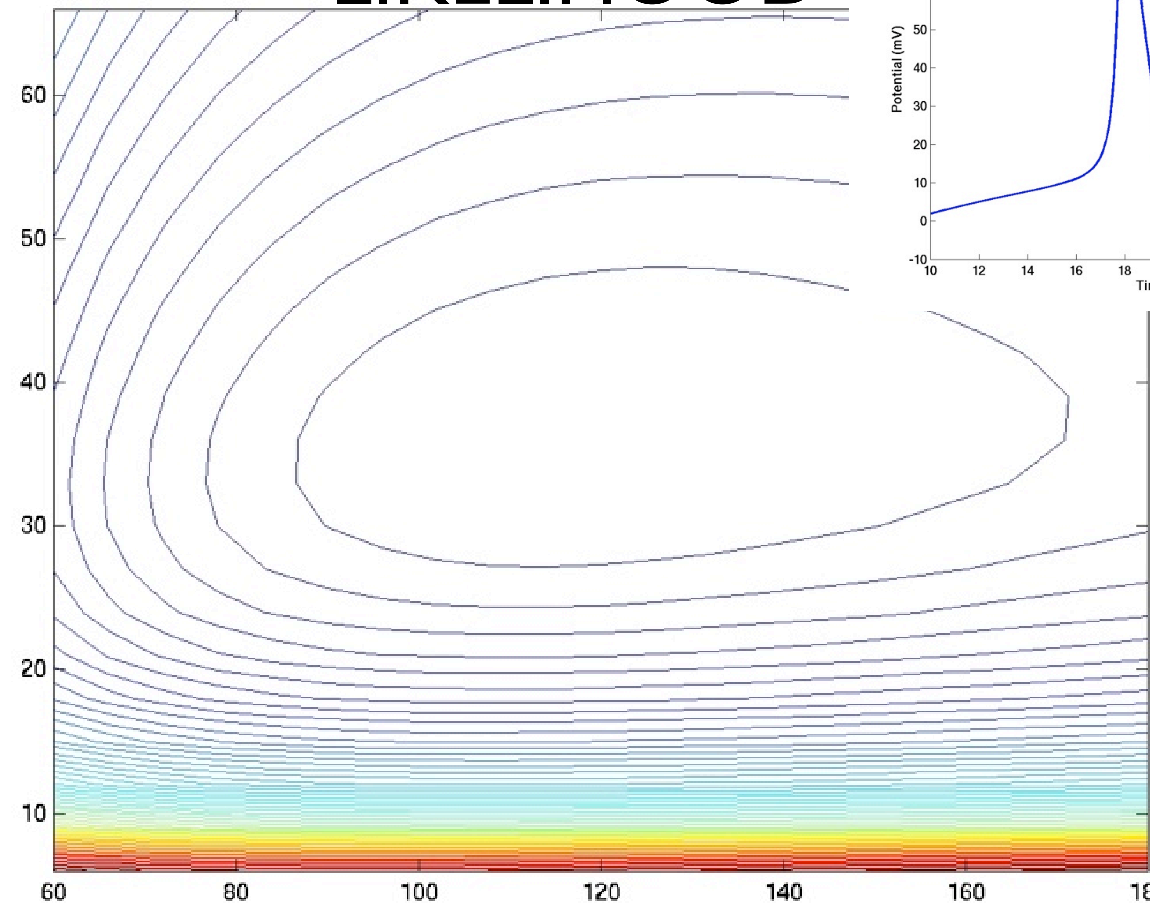
System ID Terminology

- Infer Position of Knobs: Parameter Estimation
- Infer Position of Switches: Model Selection
- Decide if Model Fits Data: Model Validation

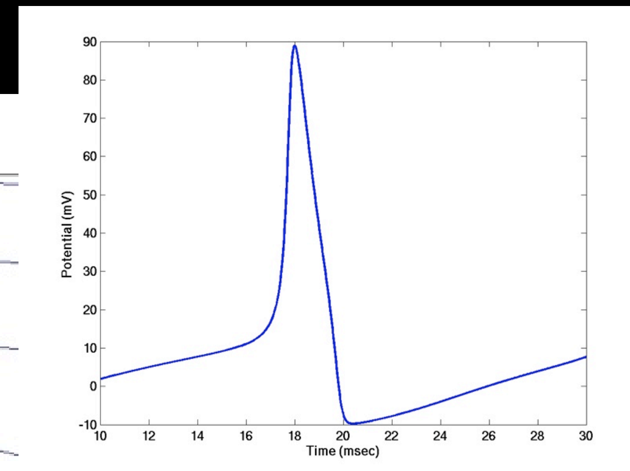
Parameter Estimation

LIKELIHOOD

K+
Maximal
Conductance
mS/cm^2

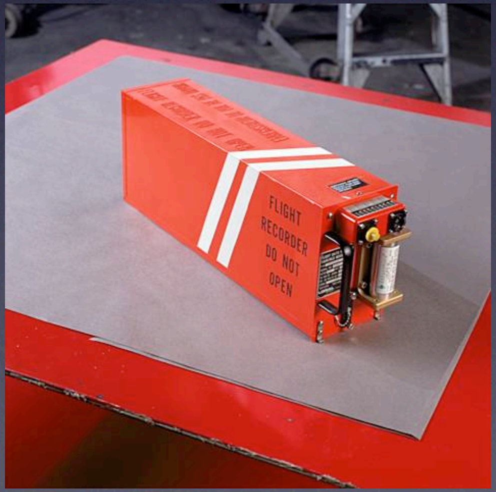


Sodium Maximal Conductance, mS/cm^2



Objective Function Quantifying How Well Model Fits Data (As Two Knobs Vary)

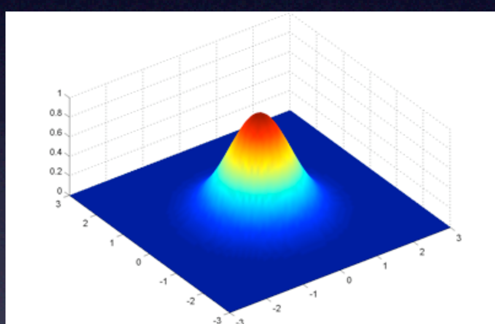
Hidden Variables Confound Likelihood Computation



Versus

Infer Hidden Variables With Bayesian Filtering

Prediction Step:



Start with an initial PDF for the hidden variables

Put it through the first time step of the model

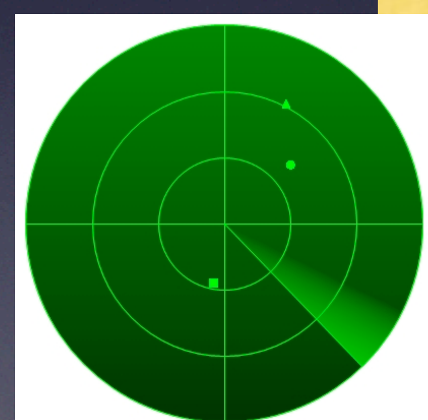
Get a new PDF for hidden variables at next time

Infer Hidden Variables With Bayesian Filtering

Update Step

Combine the prior PDF (from last step) ...

... with whatever information you get from the measurement



Get a new PDF (for the hidden variables)

Mathematical Model of The System

The model is written as a discrete mapping between the times when data is collected.

$$x_k = a(x_{k-1}, i_{k-1}, q_{k-1}, p)$$ State Equation

$$y_k = h(x_k, i_k, r_k, p)$$ Measurement Equation

$\{y_k\}$ models the data collected.

Bayesian Filtering

$Y_k = \{y_i, i = 1, \ldots, k\}$ First k measurements

$Y_0 = \{\}$ No measurements

$p(x_k|x_{k-1})$ Transition density (partly from function a)

$p(y_k|x_k)$ Measurement density (partly from function h)

Prediction (Chapman-Kolmogorov Equation):

$$p(x_k|Y_{k-1}) = \int p(x_k|x_{k-1})p(x_{k-1}|Y_{k-1})dx_{k-1}$$

Update (Bayes Rule, Simplified by the Markov Property):

$$p(x_k|Y_k) = \frac{p(y_k|x_k)p(x_k|Y_{k-1})}{p(y_k|Y_{k-1})}$$

The Denominator in The Update Step

$$p(y_k|Y_{k-1}) = \int p(y_k|x_k)p(x_k|Y_{k-1})dx_k$$

Called the "Marginal Measurement Likelihood"

The LIKELIHOOD of interest is the product of all marginal measurement likelihoods.

Log-likelihood computed as a sum then optimized.

Performing Bayesian Filtering

- If the functions a and h are linear and the noise is Gaussian, use a KALMAN FILTER.
- If the state space of x is finite, use a HIDDEN MARKOV MODEL.
- For general nonlinear a and h, use one of SEVERAL KNOWN APPROXIMATIONS.

Approximate Methods For Nonlinear Filtering

- Extended Kalman Filter: Linearize a and h around the means of the distributions.
- Unscented Kalman Filter: Similar except uses a "secant" rather than "tangent" approximation.
- Particle Filters: Use Monte Carlo Simulations to evaluate the Bayesian filtering integrals.
- Fancier methods, e.g. treat parameters as state variables.

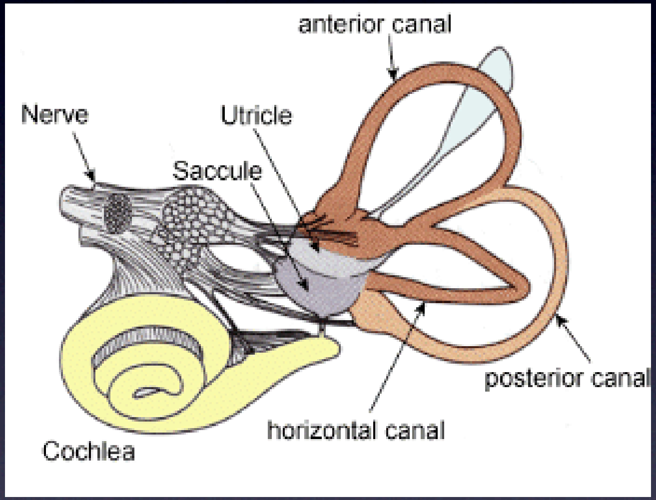
Research Problems Planned For An Undergraduate Class

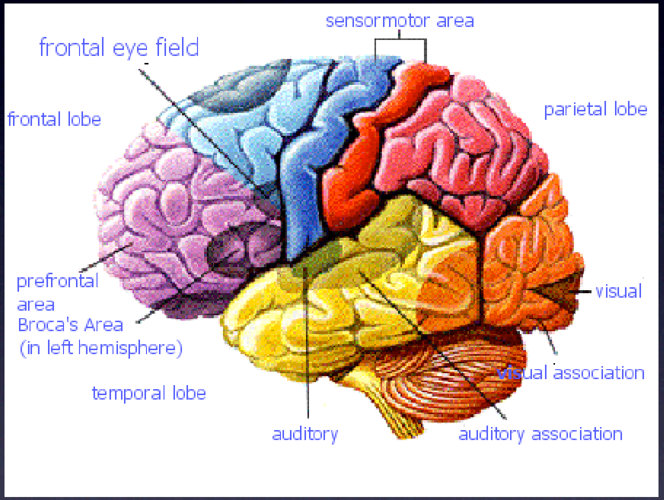
- Would Bayesian filtering have allowed Hodgkin & Huxley to understand the action potential without a voltage clamp?
- When is Bayesian filtering helpful for detecting ionic currents in single cells?
- When is Bayesian filtering helpful for detecting backpropagation from a somatic voltage trace in the “Ghostburster,” a two compartment model cell exhibiting chaos?

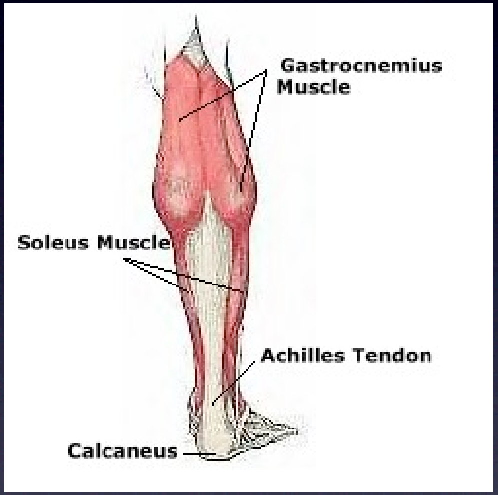
Diagnosis of Balance Deficits

Important problem impacting many lives

What Can Go Wrong With Balance?







Sensory

Central

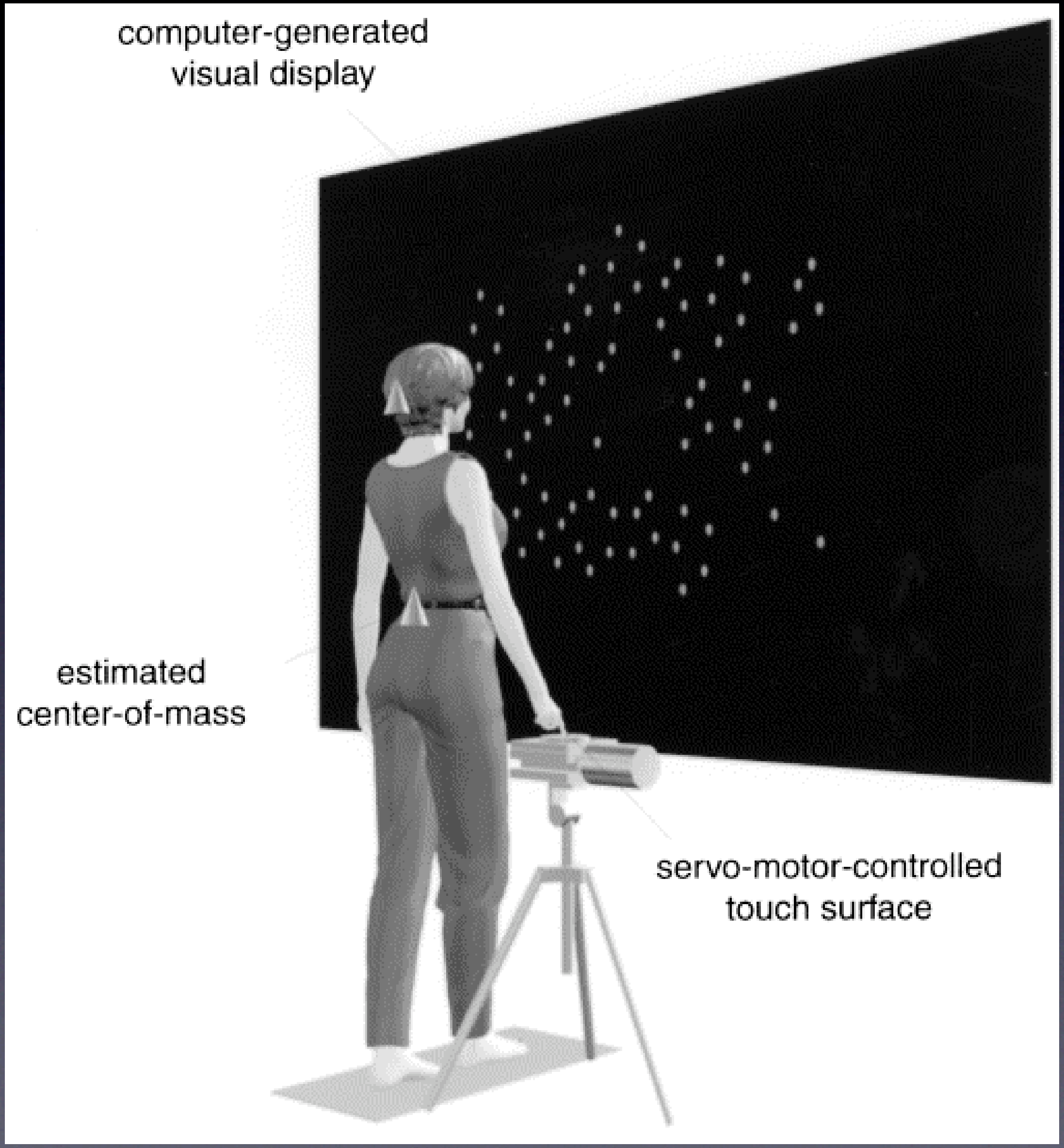
Motor

Patient populations are heterogeneous!

Want Clinical Data

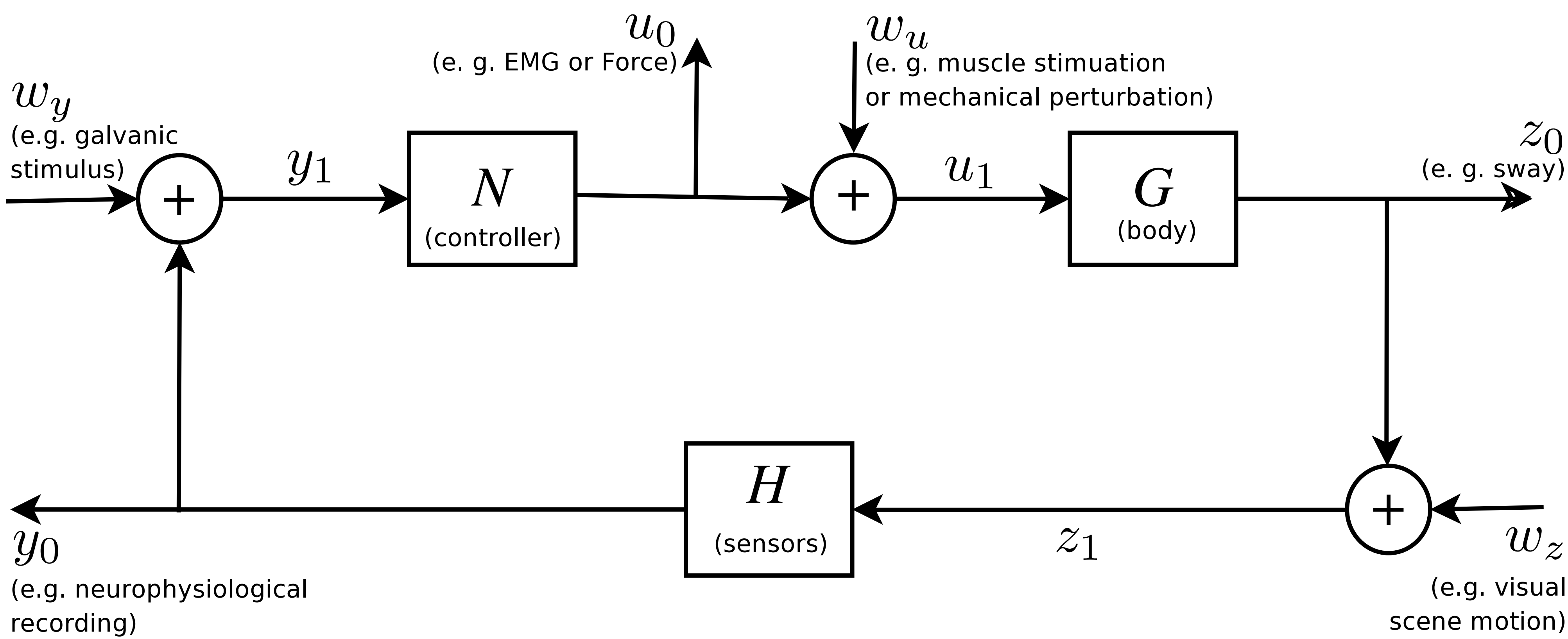
Useful for designing interventions
and monitoring progress

Previous Work



Carver et al, 2005
Jeka, Carver, et al 2005
Carver et al, 2006
Jeka, Carver et al, 2006

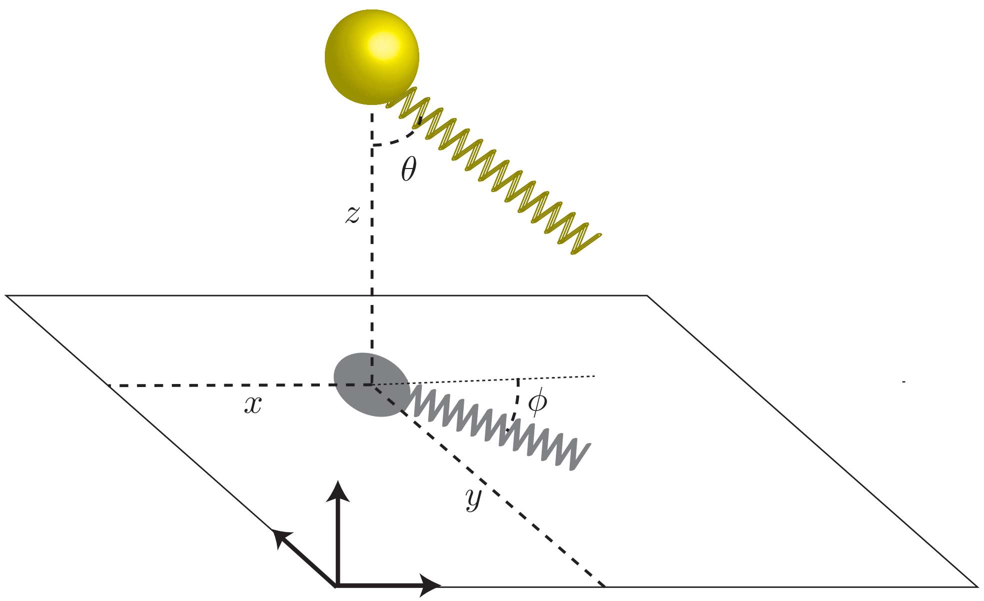
Previous Work

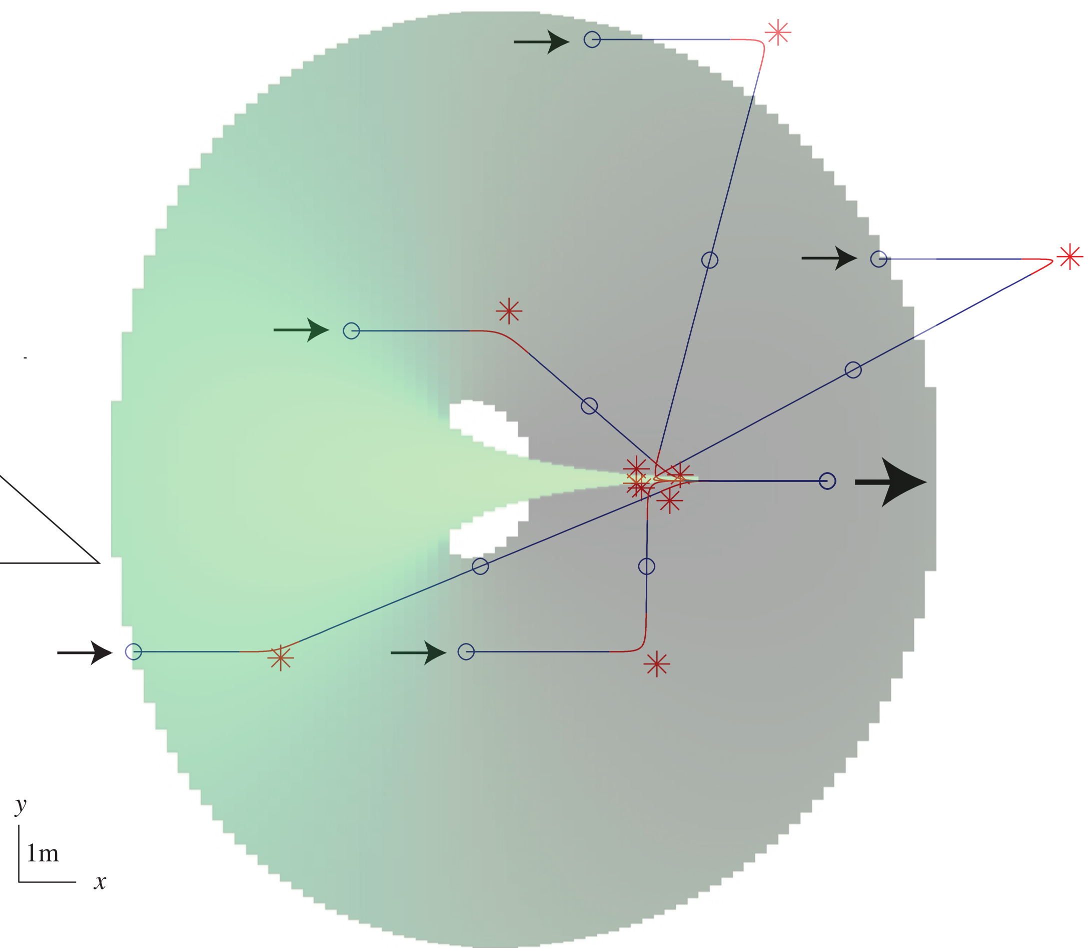


Under common hypotheses, N cancels dynamics of H.

Carver et al., Biological Cybernetics, Submitted.

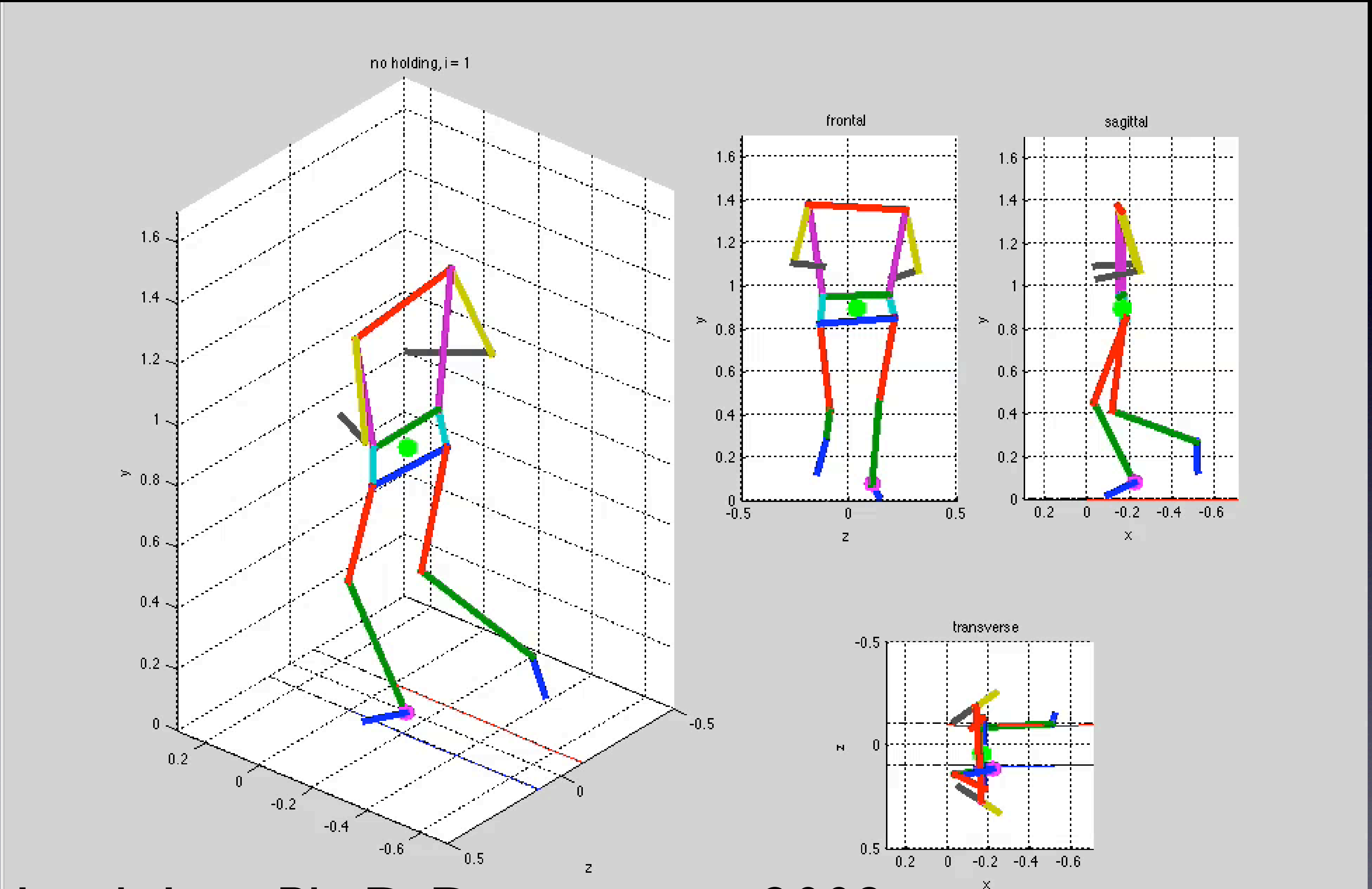
Previous Work





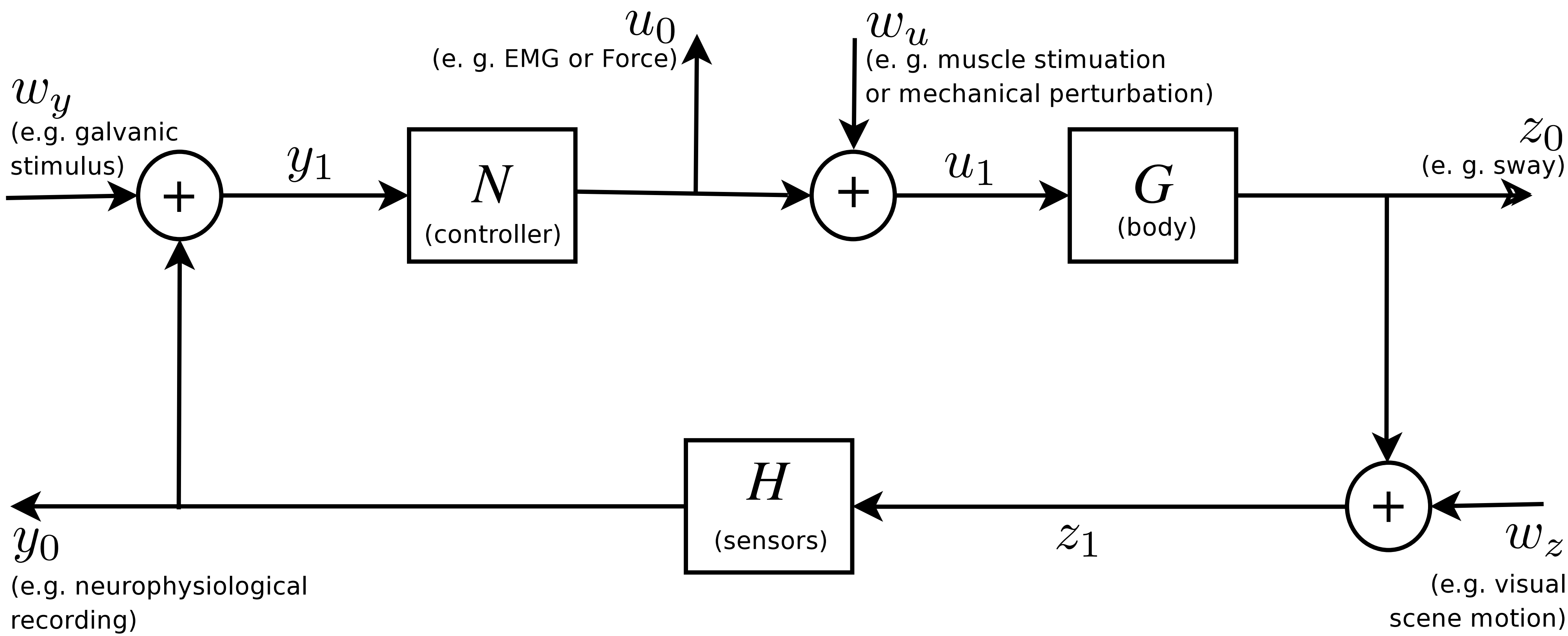
Carver et al.
Chaos, Accepted.

Testing The Hypothesis



Jusuk Lee, Ph. D. Dissertation, 2009.

Avoiding the Cancellation



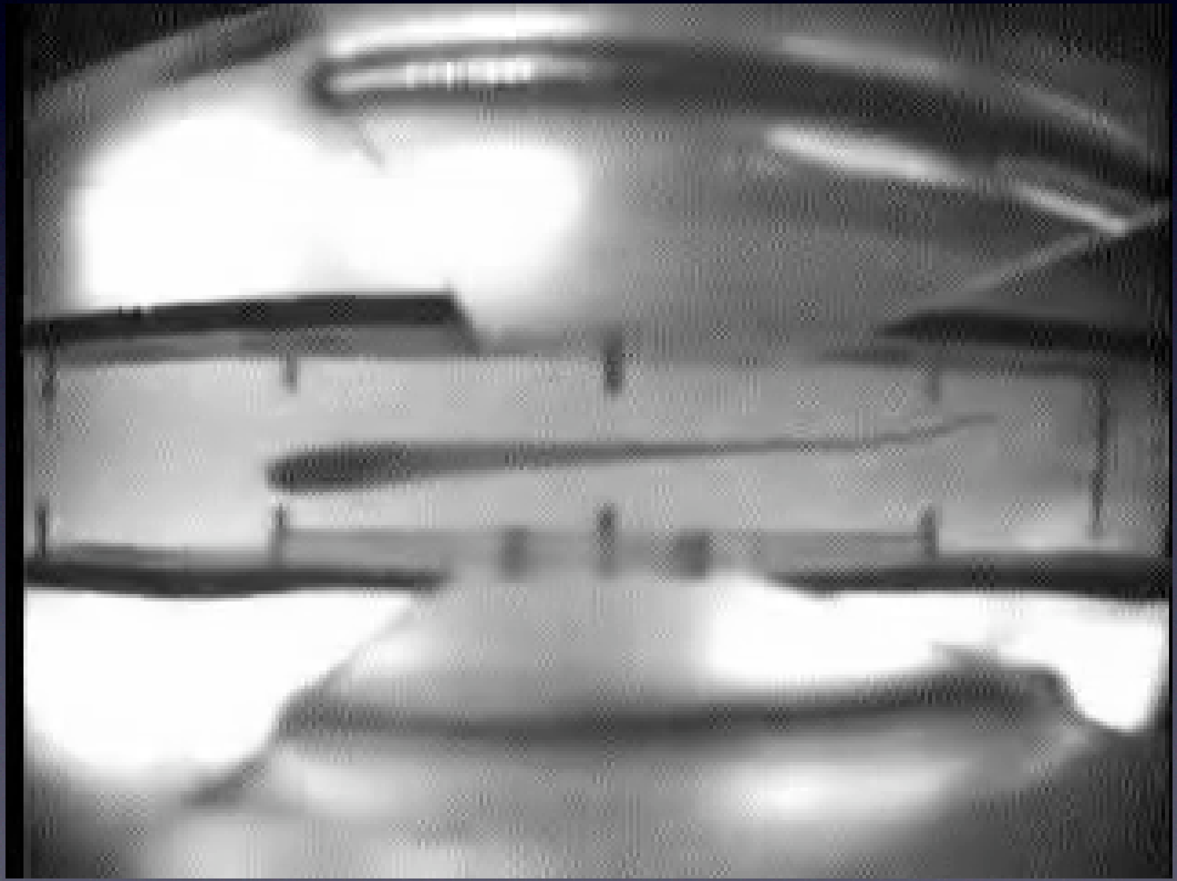
Under common hypotheses, N cancels dynamics of H.

So measure and/or perturb between H and N.

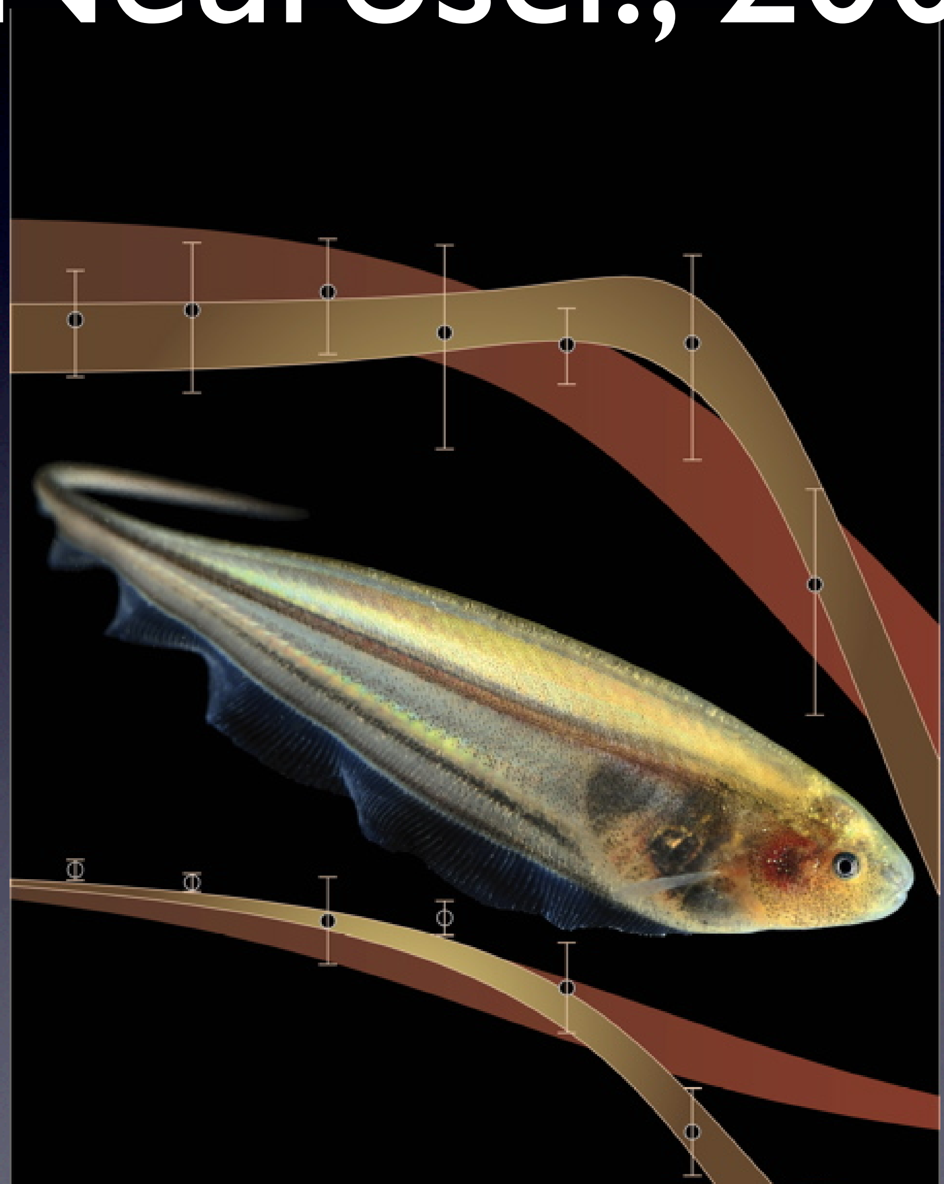
Enter Weakly Electric Fish

One Simple Behavior

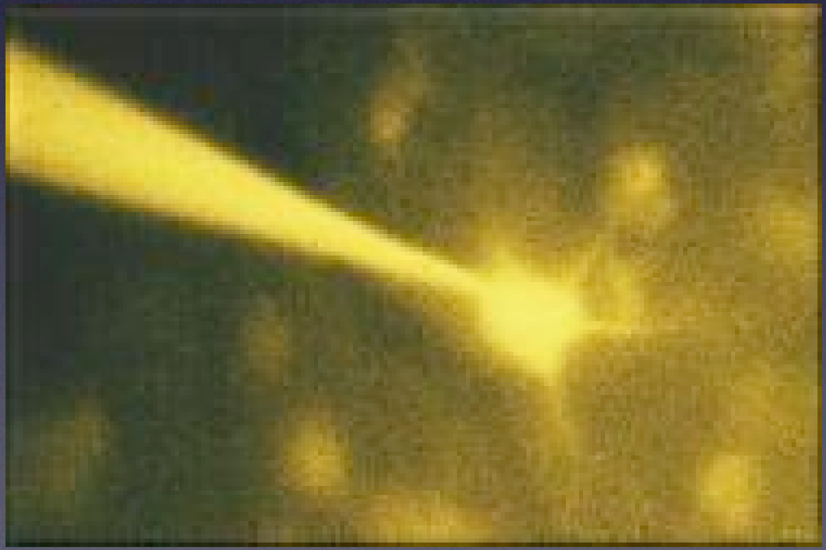
Experimental Apparatus

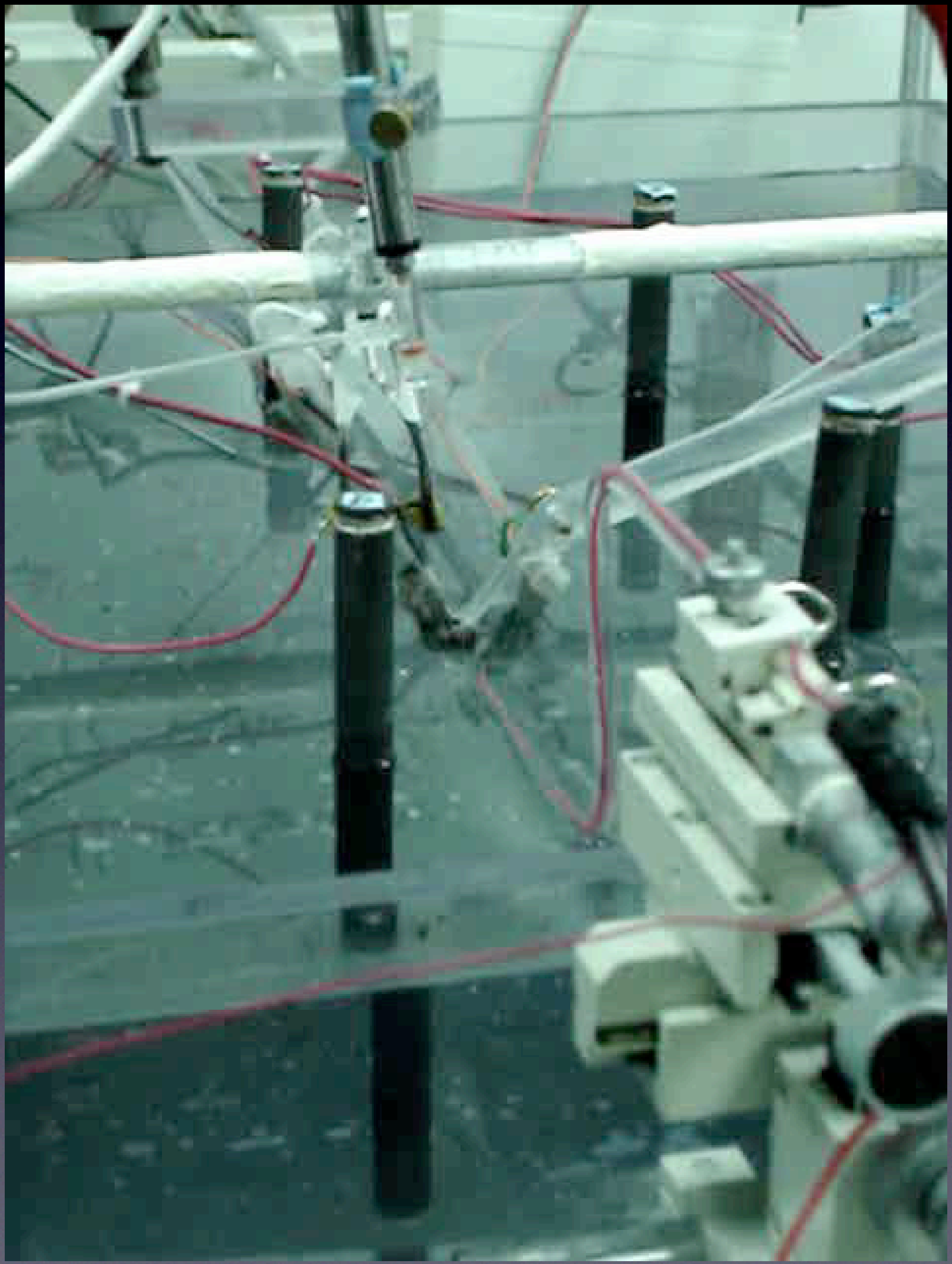


Cowan & Fortune, J.Neurosci., 2007



Neurophysiology



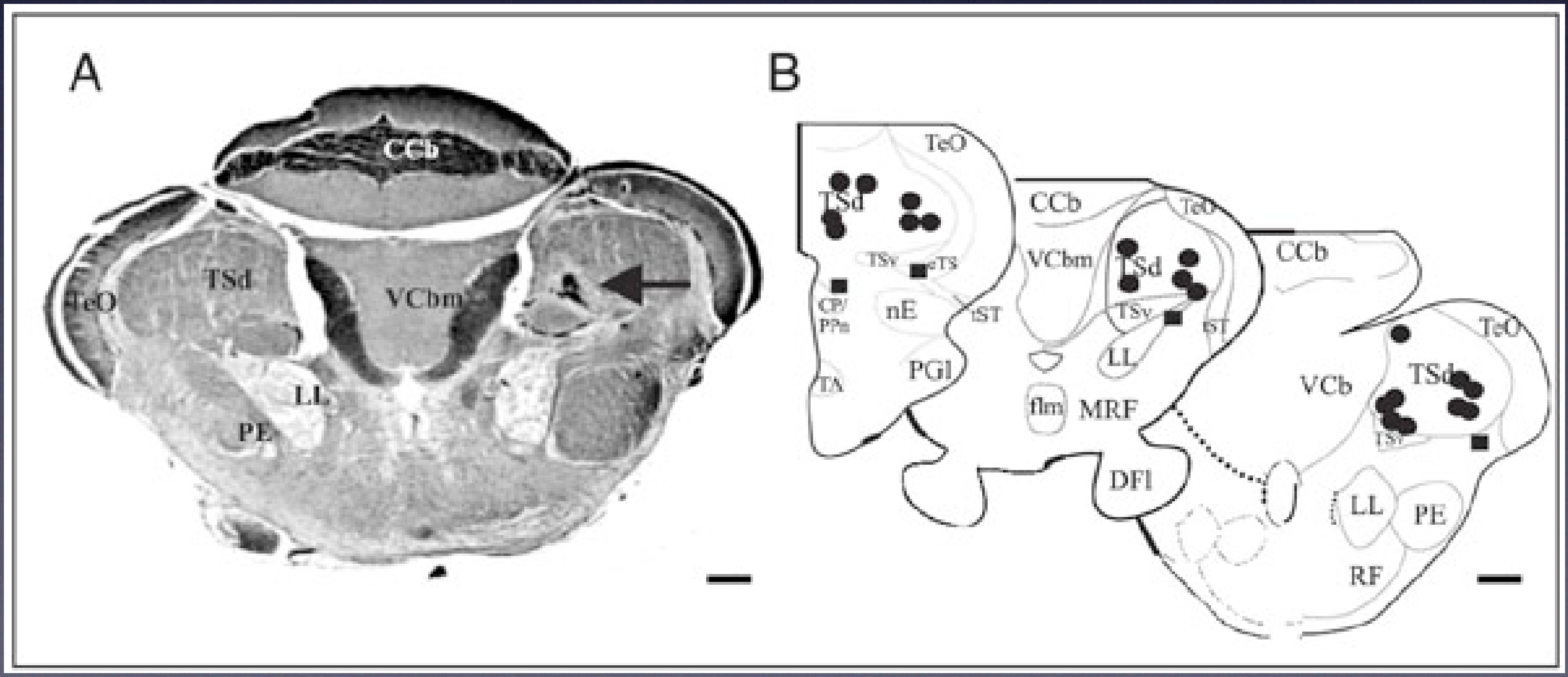


Direction Selectivity

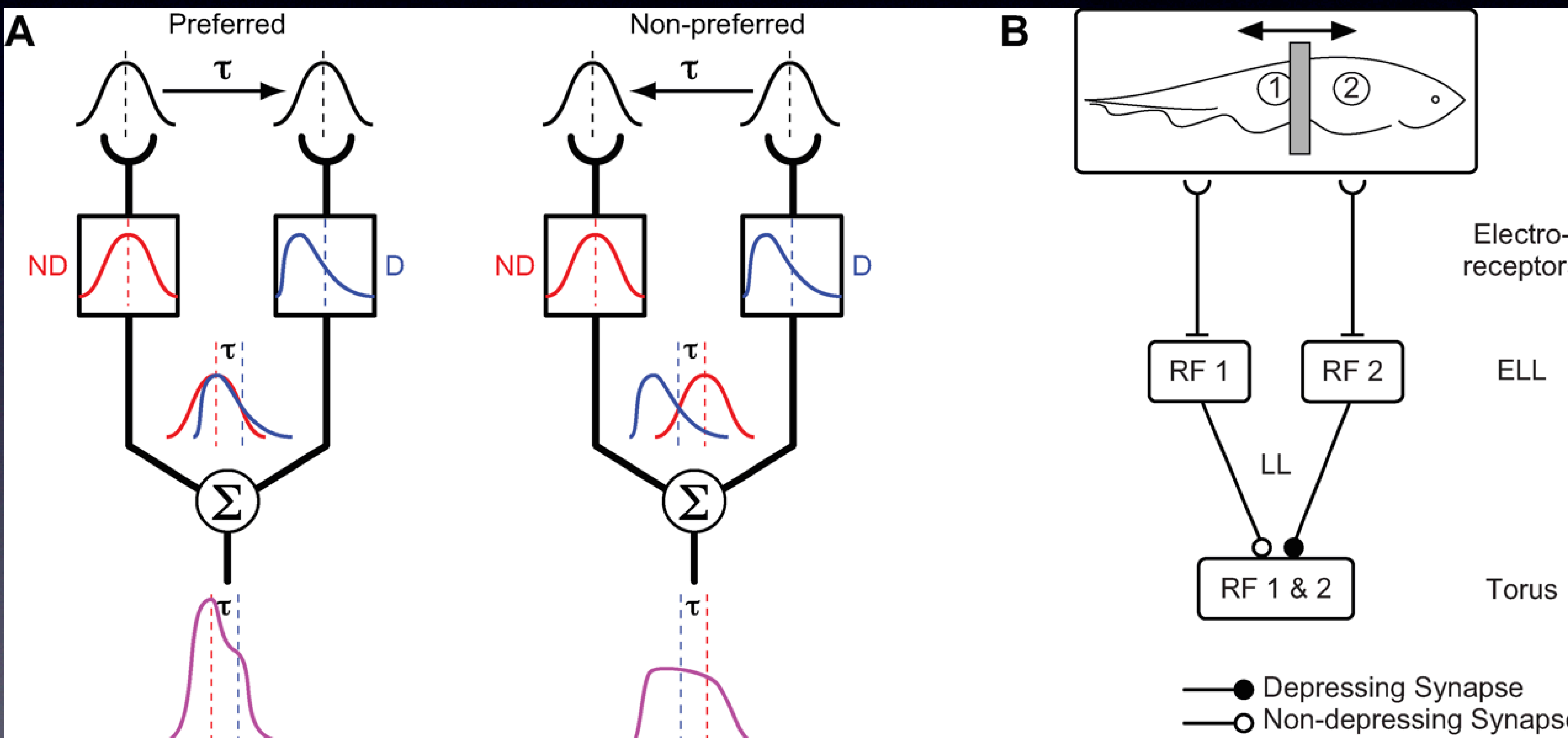
Video

Hubel & Wiesel ca. 1950

Many Neurons in the Electric Fish Torus Semicircularis are Directionally Selective

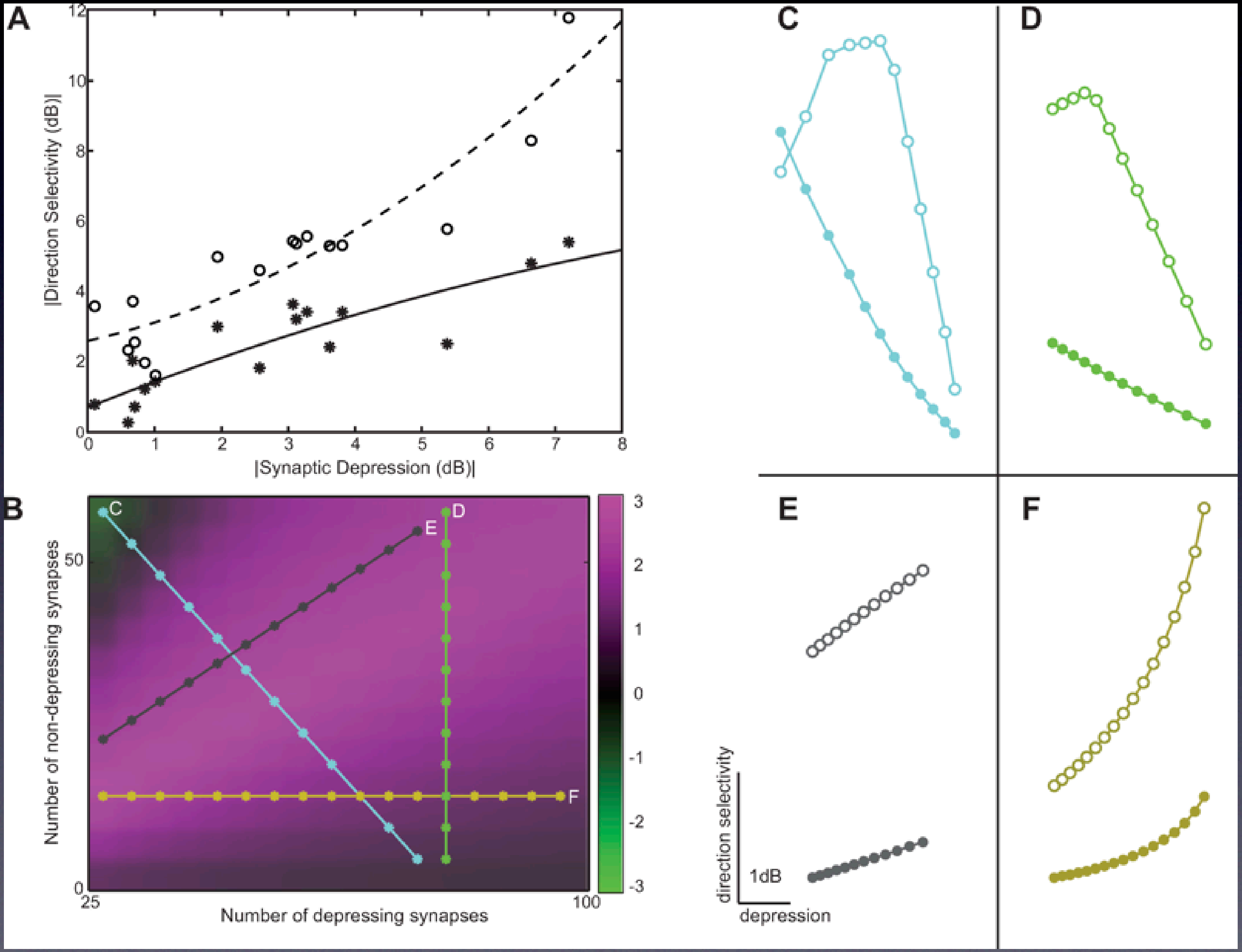


Direction Selectivity Hypothesis (Chance et al.)



Carver et al., PLoS Computational Biology, 2008.

Turning Knobs To Reproduce Population

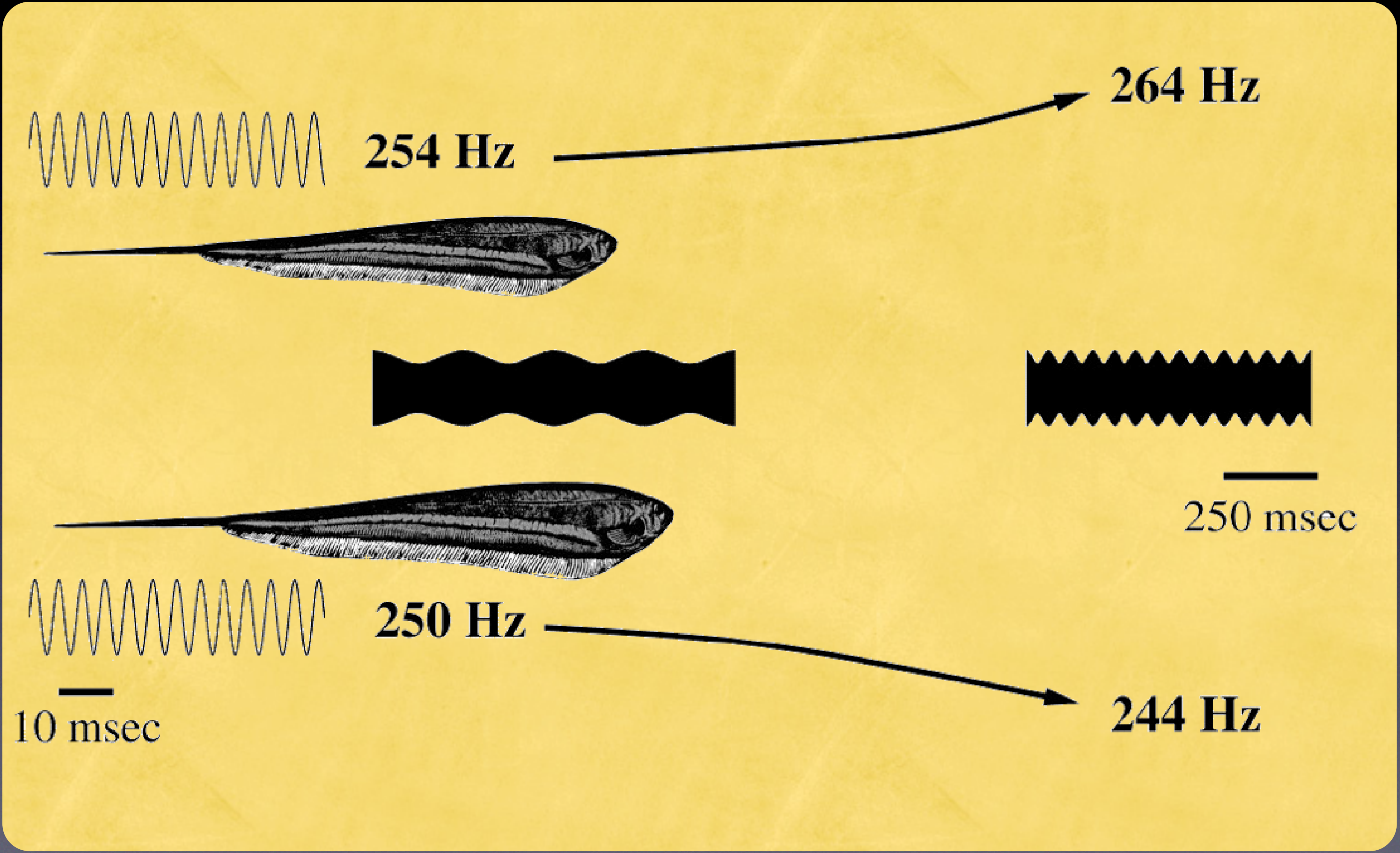


Carver et al., PLoS Computational Biology, 2008.

Prey Capture:

Courtesy Malcolm MacIver
Northwestern University

Jamming Avoidance

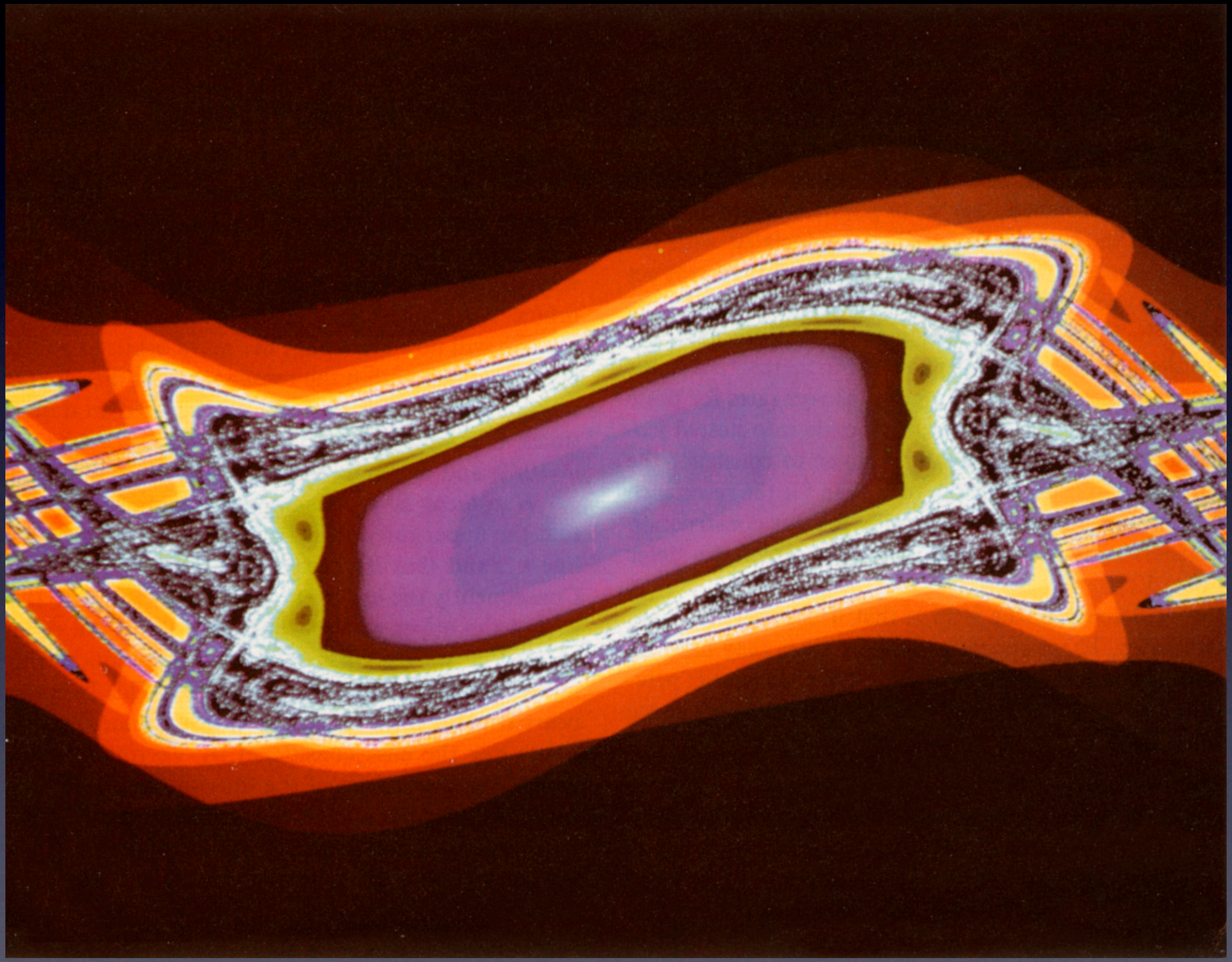


Research Goals

- Develop theory (guided by numerical experiments) to understand the usefulness of system ID to science.
- Develop software tools useful to scientists.
- Apply system ID to understand the mechanisms of sensorimotor processing in weakly electric fish ... leading to testable hypotheses in humans and tools that benefit the clinic.

Thank You!!

Previous Work



Easton, Meiss, Carver. Chaos, 1993

Software Project Plan

- Button in NEURON: You give data sampling frequency (i.e. 100 Hz) and name (i.e. 'foo'); it produces C++ code:
  - foo_a.c & foo_h.c, which when compiled produces discrete map.
- Modular programs: Objective functions and optimization routines, automatic differentiation.
- Graphical User Interfaces