Building the algorithmic foundations for interfacing, understanding and exploiting neural systems

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Networks: Circuits, Cells, & Genes

Georgia Tech Neuro

Technology: Computation, Devices, & Molecular Tools

Systems: Cognition, Sensing, & Movement

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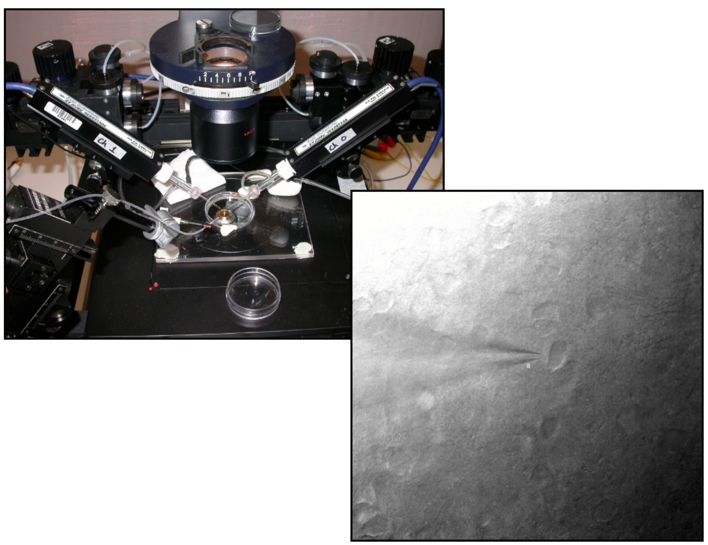
"I not only use all the brains I have, but all I can borrow."

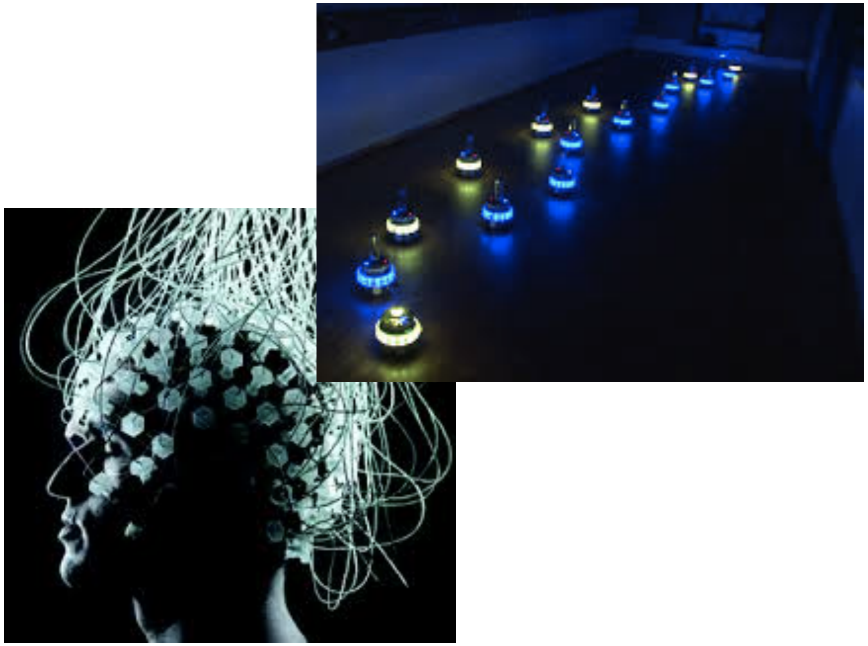
-Woodrow Wilson

Today

- Delay embeddings for nonlinear dynamics (math)
- Closed loop optogenetic stimulation (electrophysiology)
- Denoising and speech intelligibility (psychophysics)
- Later on request:



Real time computer vision for automated patch clamping in slices



EEG BMIs for controlling complex behavior in robot swarms

Today

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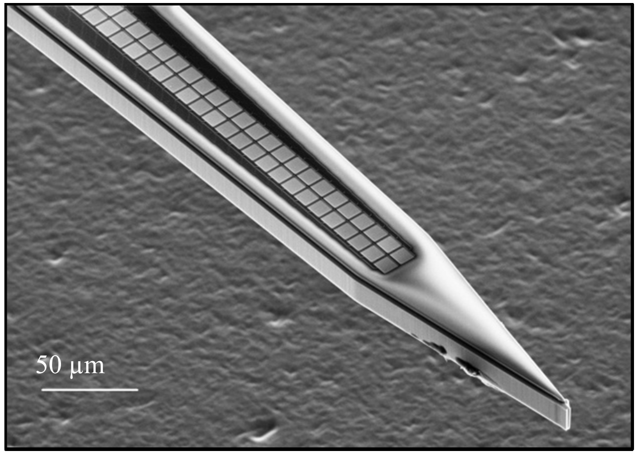
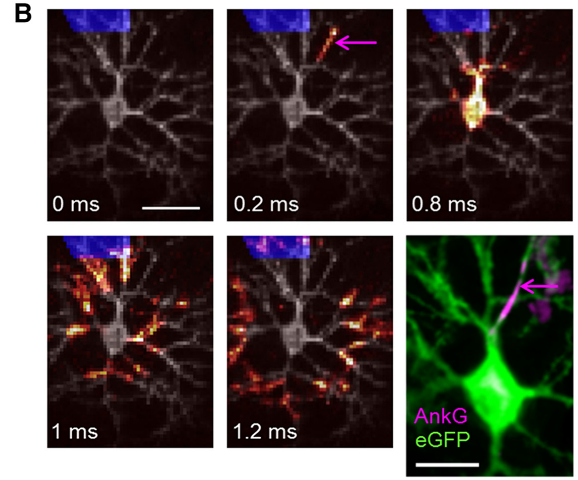
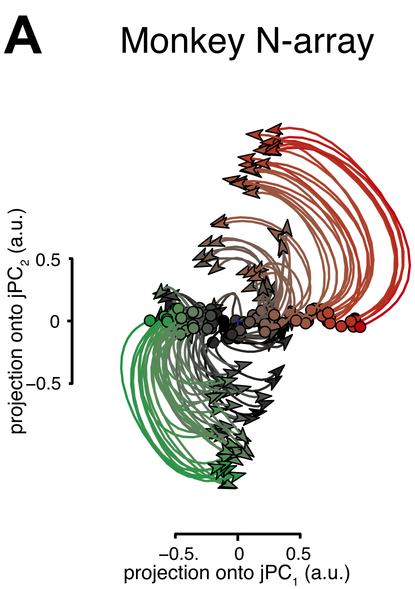
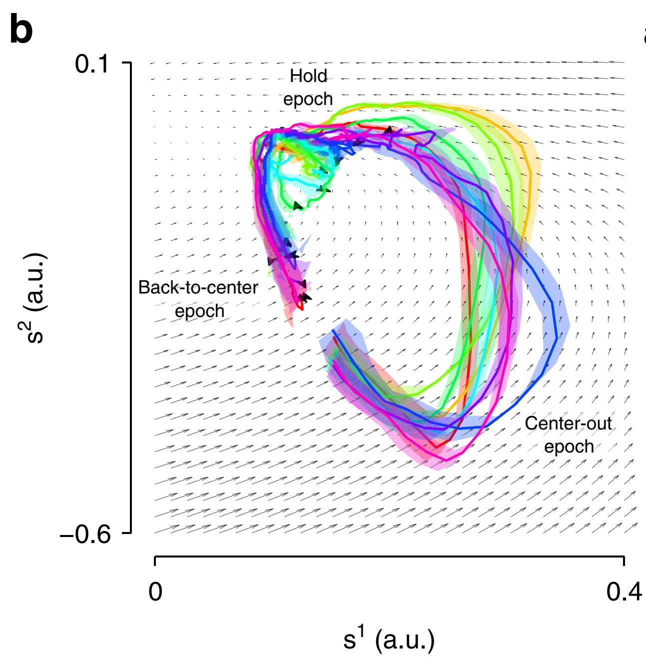
Observing dynamical systems: neural systems

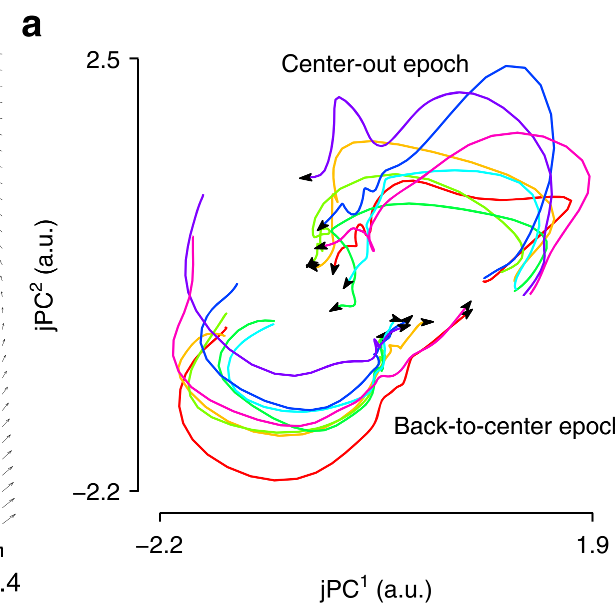




(Scholvin et al. 2015; Emiliani et al. 2015)







(Churchland et al. 2012; Kao et al. 2015; Pandarinath et al. 2015)

Setup

- Hidden state *x(t)* exists in *N* dimensional space
- Deterministic dynamics observable at interval T_s
- Evolution captured according to invertible flow:

$$\phi_T(x(t)) = x(t+T) \implies \phi_T^{-1}(x(t)) = x(t-T)$$

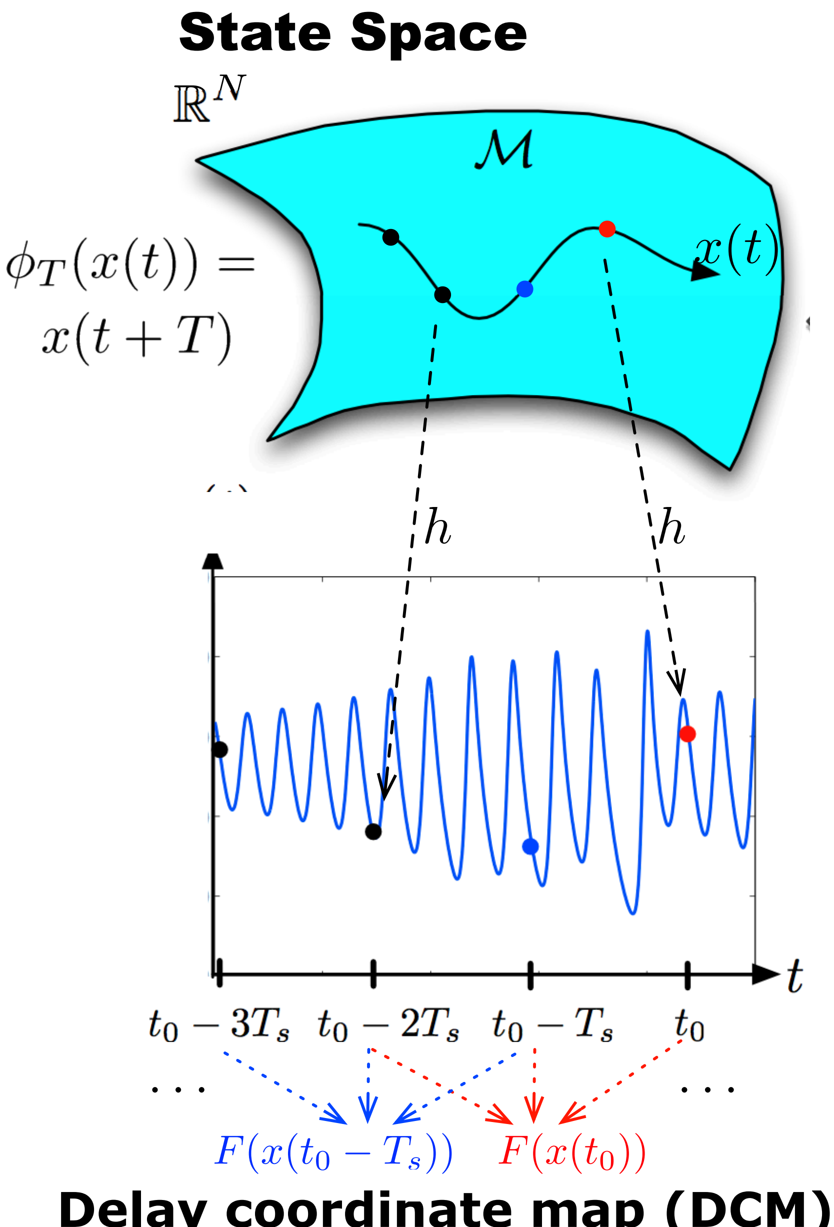
- Contained within a low-dimensional attractor that we (for now) assume to be smooth submanifold:

$$x(t) \in \mathcal{M} \subset R^N \text{ with } \dim(\mathcal{M}) \ll N$$

- State is only observed through scalar function $h(x(t))$
- Past *M* time-series observations: *delay coordinate map*

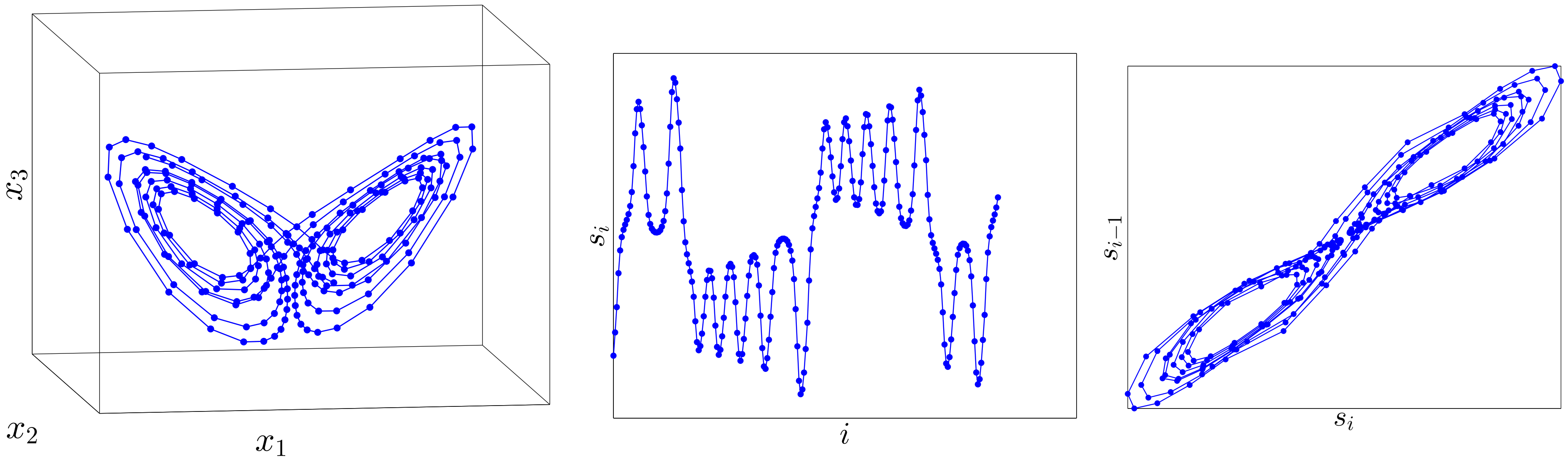
$$F(x(t)) = \begin{bmatrix} h(x(t)) \\ h(\phi_T^{-1}(x(t))) \\ \vdots \\ h(\phi_T^{-(M-1)}(x(t))) \end{bmatrix}$$

Embedology: Takens' Embedding Theorem



Reconstruction problems

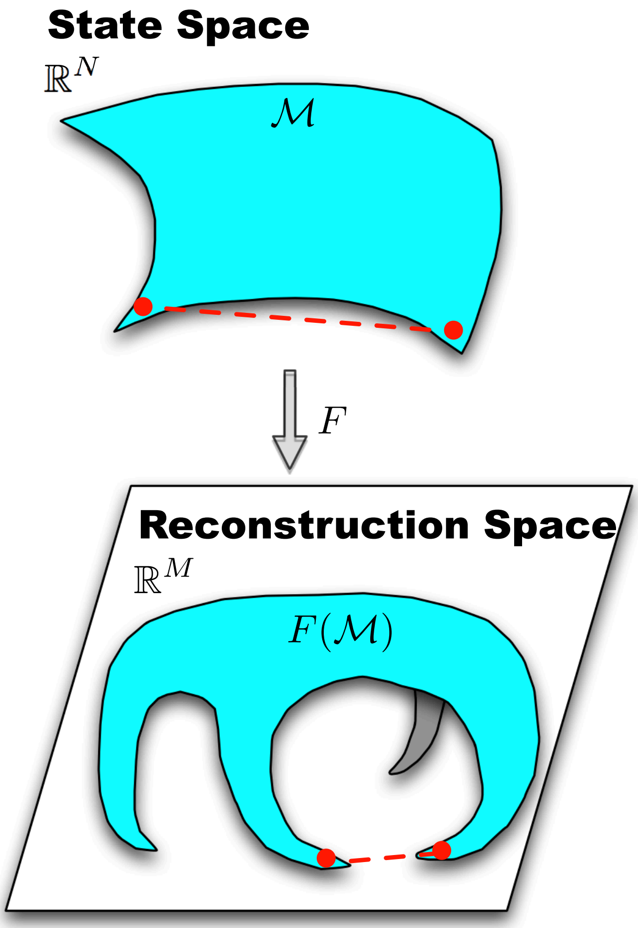
- Widely used: time-series prediction, dimensionality estimation



Original state Measurement Reconstruction

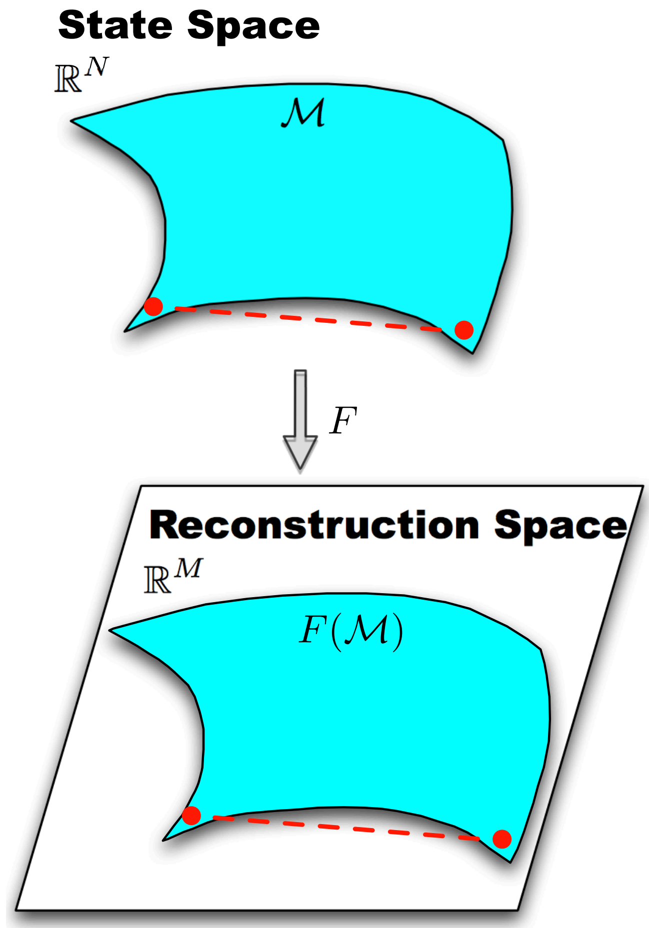
- Practical problems:
  - Concern about embedding sensitivity to noise, etc.
  - Heuristic methods for choosing parameters (e.g., *h*,*T*,*M*)
  - Effect of parameters on embedding quality unclear

One-to-one vs. Stable Embedding



One-to-one =>
topology preservation

$$x_1 \neq x_2 \implies F(x_1) \neq F(x_2)$$



Stable embedding =>
geometry preservation

$$\|F(x_1) - F(x_2)\|_2 \propto \|x_1 - x_2\|_2$$

Stable Takens' Embedding: Result

Theorem (Eftekhari, Yap, Wakin, R., 2017):

Under some regularity assumptions, if

$$R(\mathcal{M}_{H,T,M}) > \dim(\mathcal{M}) \cdot \log\left(\frac{\mathrm{vol}(\mathcal{M})^{\frac{1}{\dim(\mathcal{M})}}}{\mathrm{rch}(\mathcal{M})}\right)$$

Stable rank:
May scale like *M*?

linear in dimension

geometric regularity

then with high probability over measurement functions,

$$\epsilon_l(M) \leq \frac{\|F(x_1) - F(x_2)\|_2^2}{M\|x_1 - x_2\|_2^2} \leq \epsilon_u(M)$$

for all $x_1, x_2 \in \mathcal{M}$.

Depends on regularity of flow, attractor curvature and measurement operator.
Monotonic functions of *M* that may plateau.

Irrelevancy vs. Redundancy

- This result helps justify design rules that are commonly employed in constructing DCMs.
  - (e.g., Casdagli et al., 1991; Kugiumtzis, 1996; Uzal et al., 2011)

- Irrelevancy
  - If T is too large the rows of the stable rank matrix may have widely differing lengths, especially for chaotic systems.

- Redundancy
  - If T is too small, the rows of the stable rank matrix may not span a diverse set of directions.

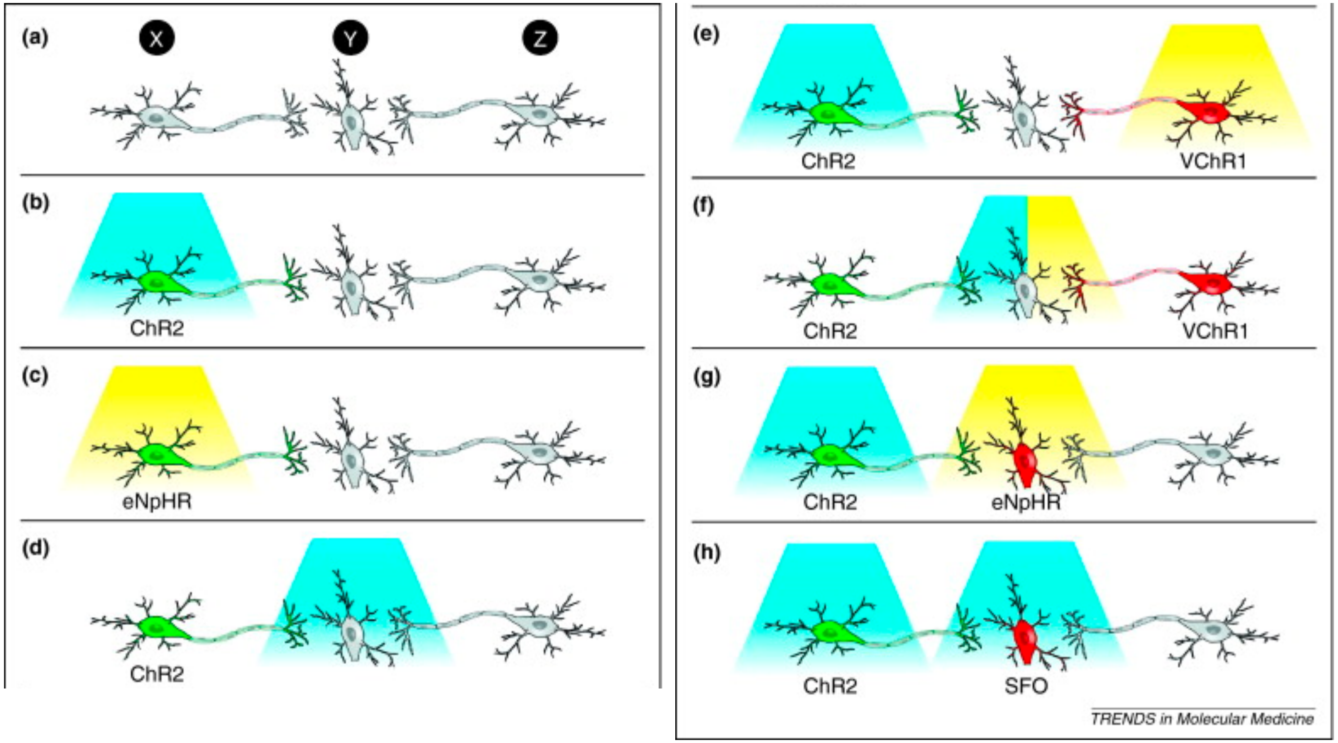
- Both situations can cause the stable rank to plateau when M is increased, leading to a poor embedding.

Today

- Delay embeddings for nonlinear dynamics (math)
- Closed loop optogenetic stimulation (electrophysiology)
- Denoising and speech intelligibility (psychophysics)

Stimulation for functional dissection

- All-or-nothing inputs with uncertain input-output map

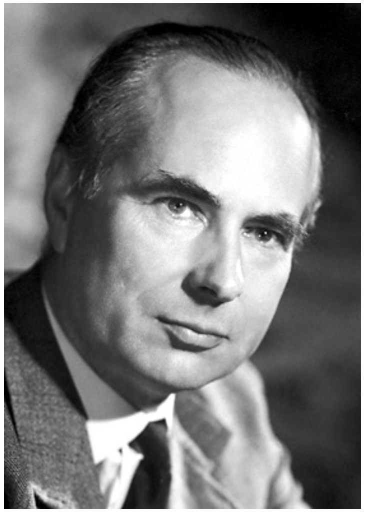


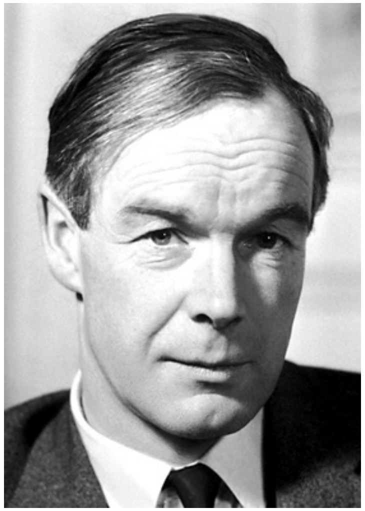
(Carter & de Lecea, 2011)

- How do we disentangle neural coding in coupled circuits?
- Proposal: use *closed-loop optogenetic control (CLOC)* to fix one subsystem **output** to study another in isolation

An old problem

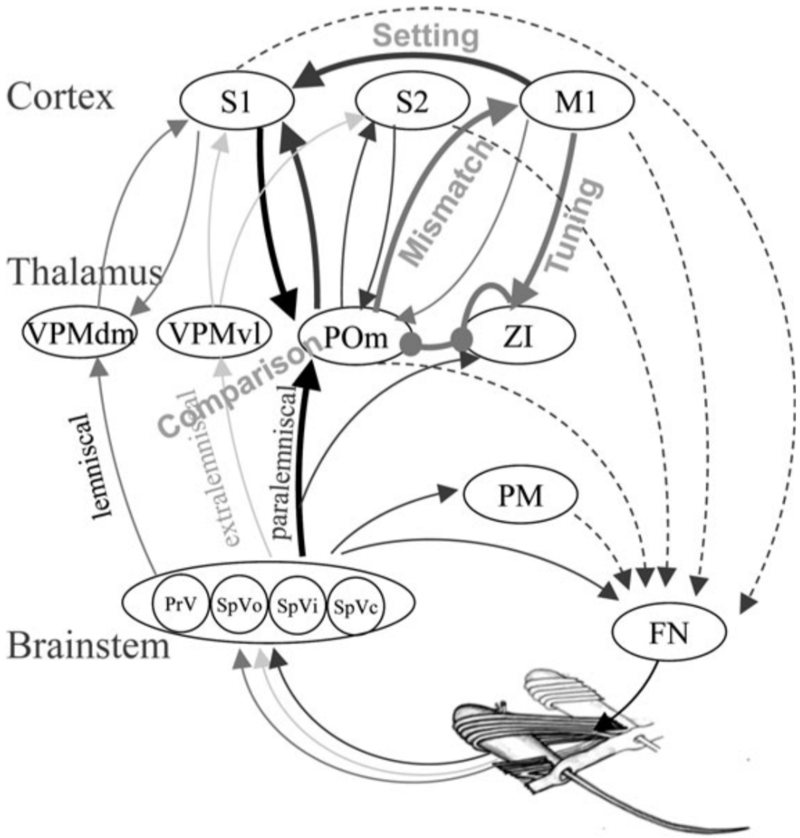
- Hodgkin & Huxley investigated action potential generation
- Problem: coupled ionic and capacitive currents
- Solution: use feedback control to clamp membrane potential and decouple current sources

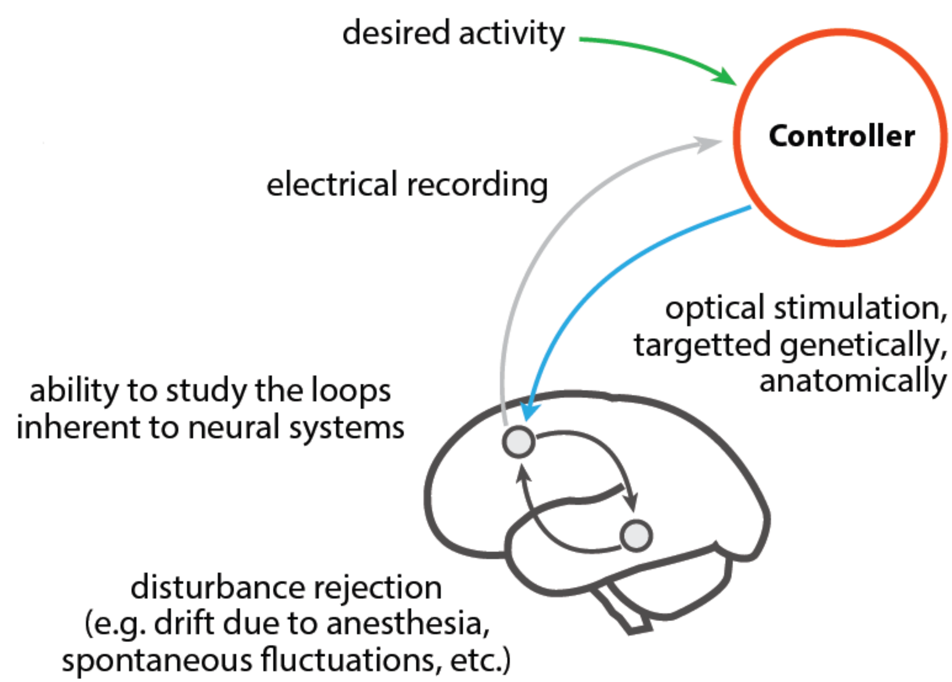




A new light: *loop de-loop*

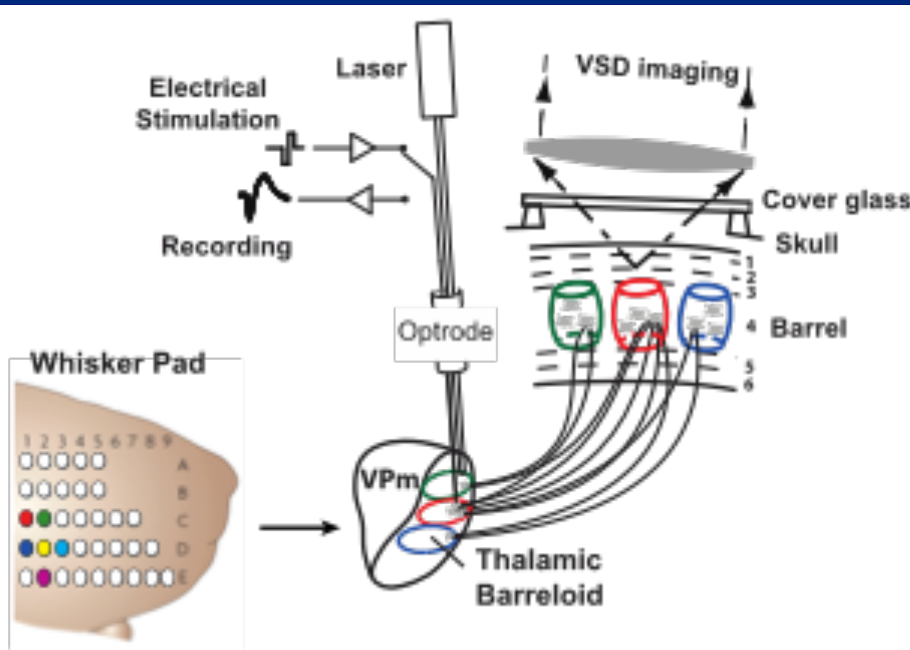
- Can we disentangle circuits at the systems level?
- Example: active sensing in a somatosensory pathway
  - Combines sensory drive, self-motion, and motor efferents

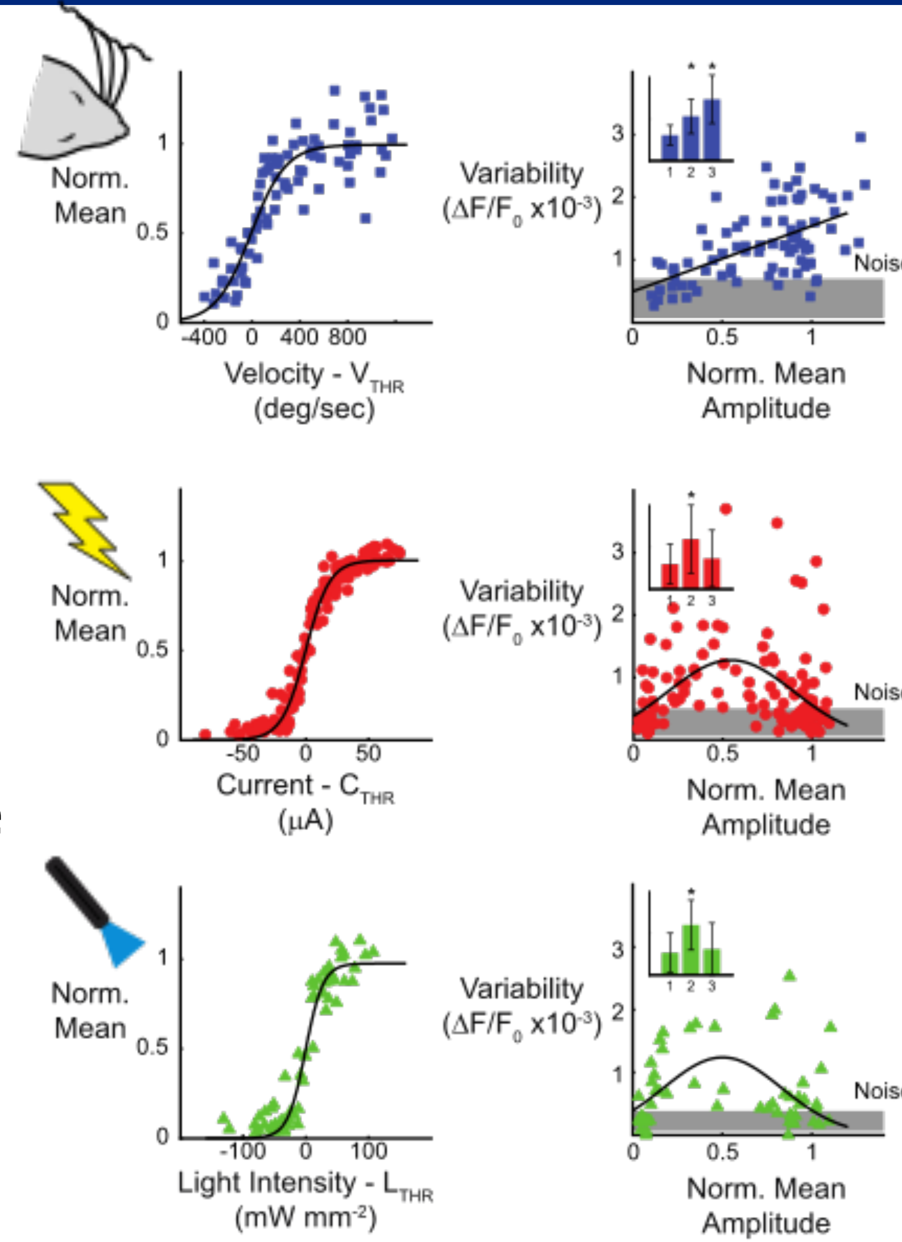




(Ahissar et al., 2013)

Why not open-loop stimulation?

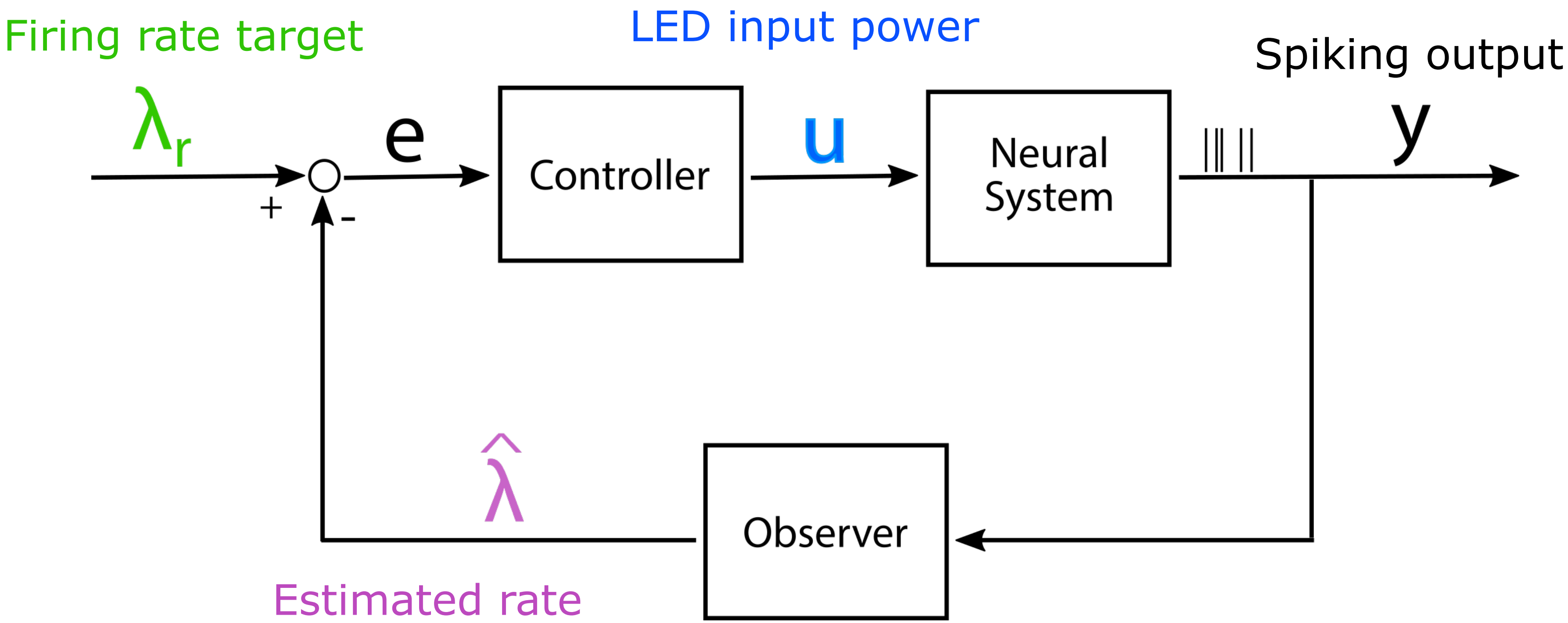




- Artificial stimulation yields high variance in critical range due to bimodal response
- Single trials unpredictable due to varying system state

(Millard, Whitmire, Gollnick, R., & Stanley, 2015)

CLOC of firing rate

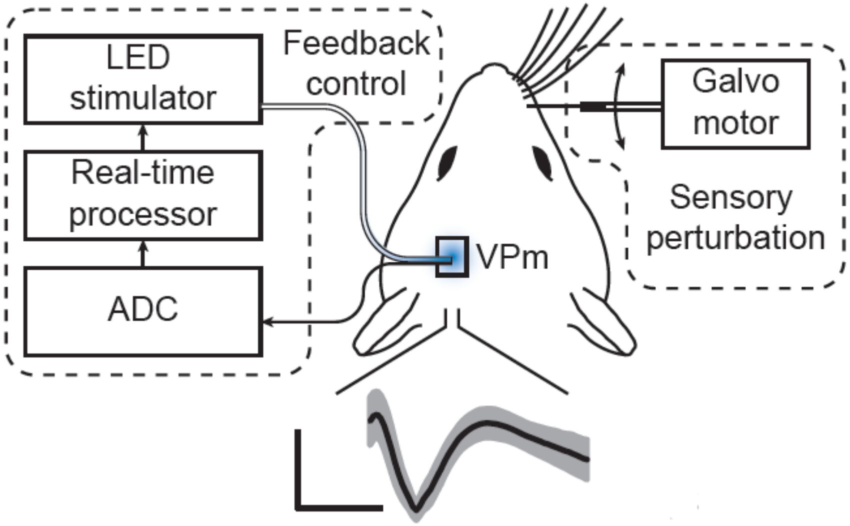


- Major steps:
  - Design observer → causal exponential filter
  - Model neural system → linear-nonlinear-Poisson model
  - Design controller → proportional-integral controller

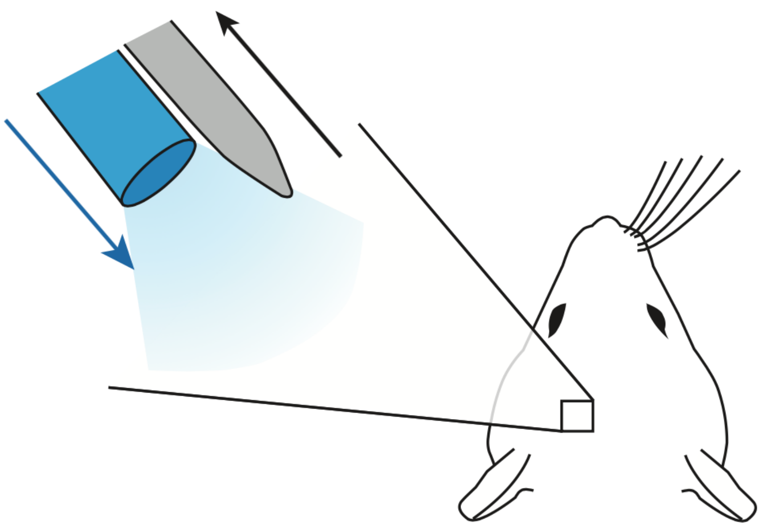
(Bolus, Willats, Whitmire, R. & Stanley. in prep)

In vivo experimental preparation

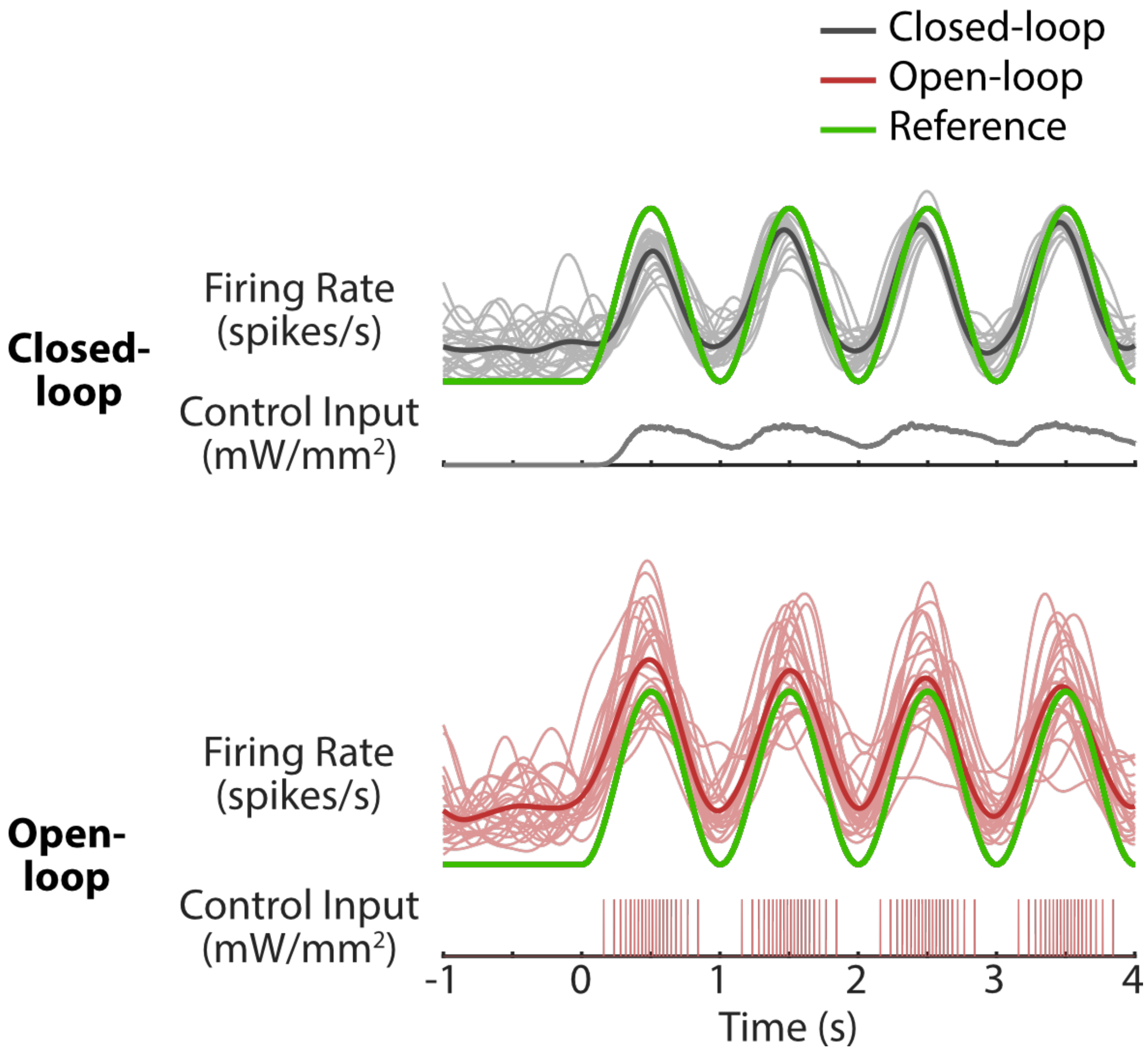
- Somatosensory thalamus of anesthetized rat (fentanyl cocktail)
- Expression of channelrhodopsin in excitatory neurons via viral injection (ChR2-CaMKII)
- Graded optical stimulation of population (200 μm optic fiber)
- Extracellular recording of single units (80 μm tungsten electrode)
- Tucker Davis Technologies (TDT) system for real-time processing



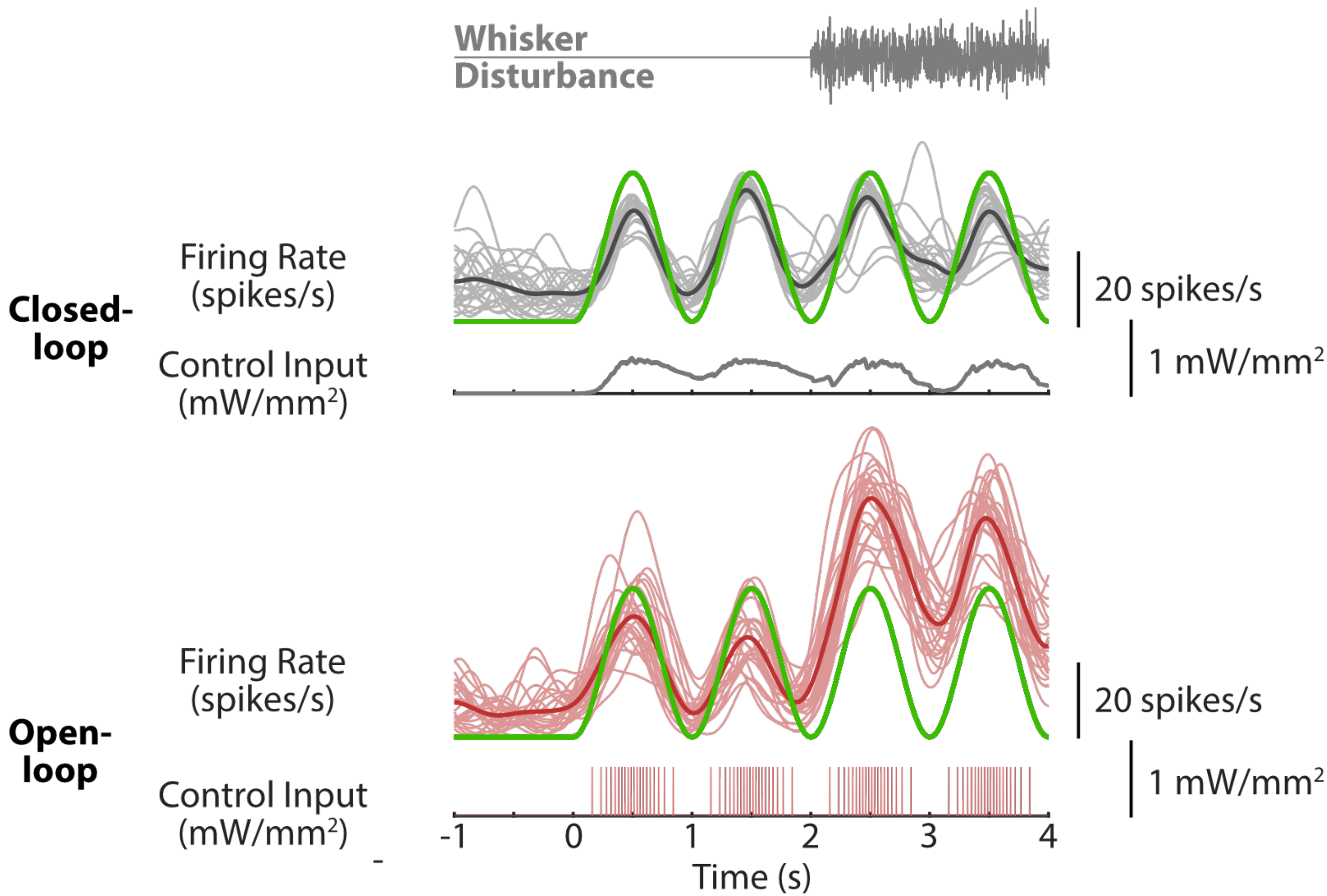
(Newman et al. 2015)



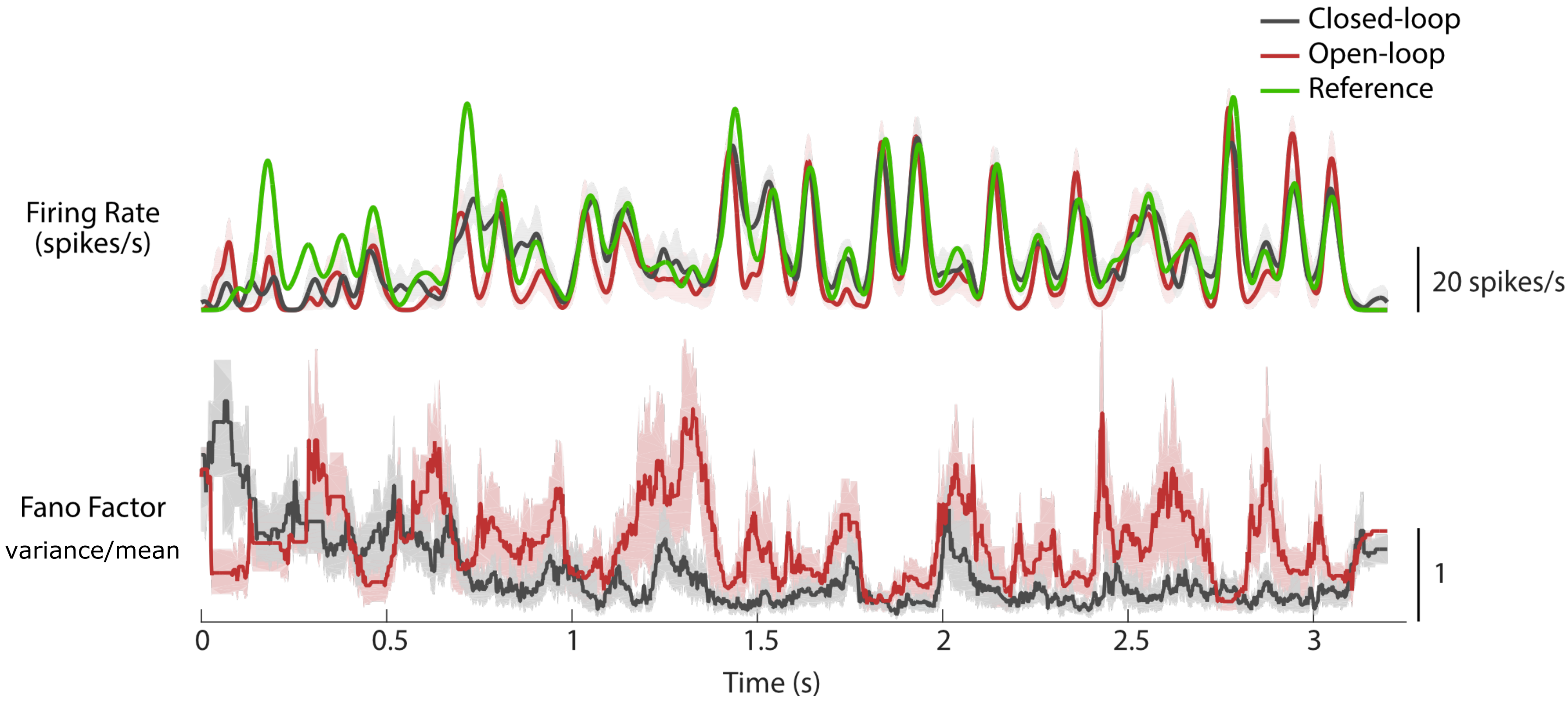
Tracking a simple 1Hz modulation



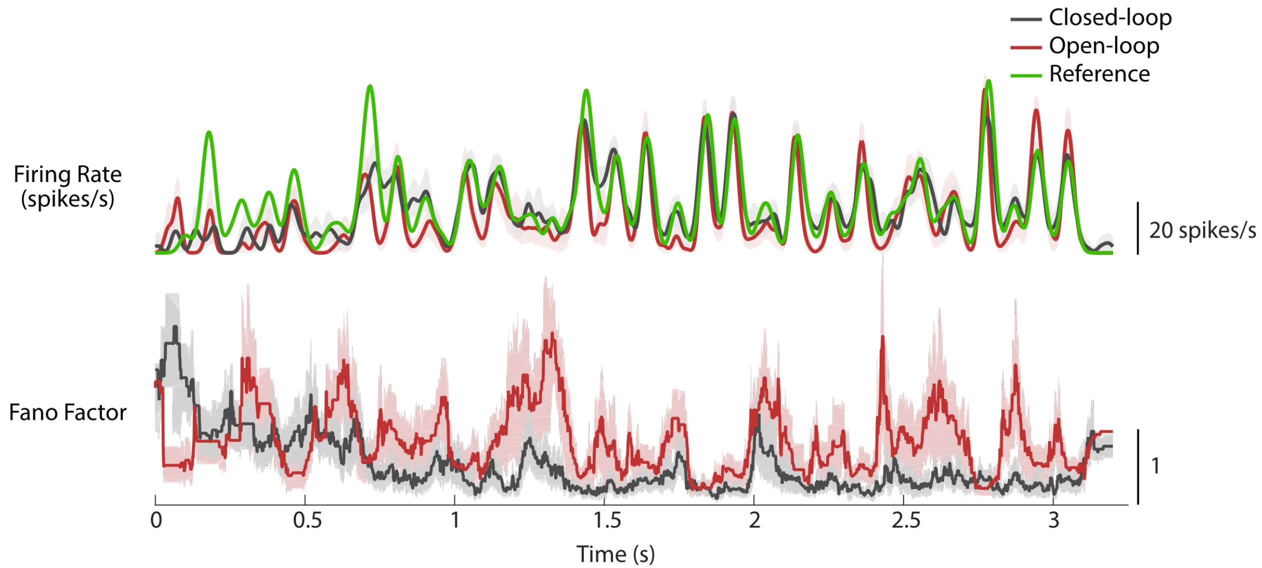
Disturbance Rejection

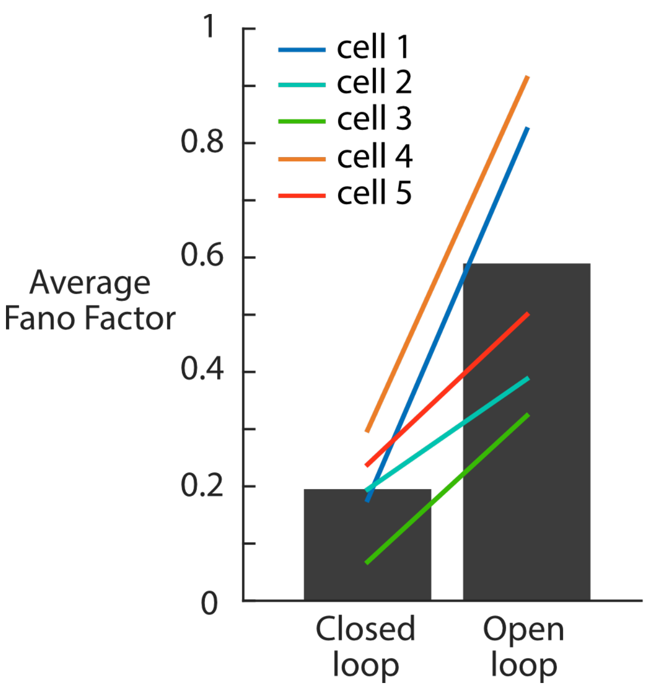


Tracking Complex Desired Trajectories



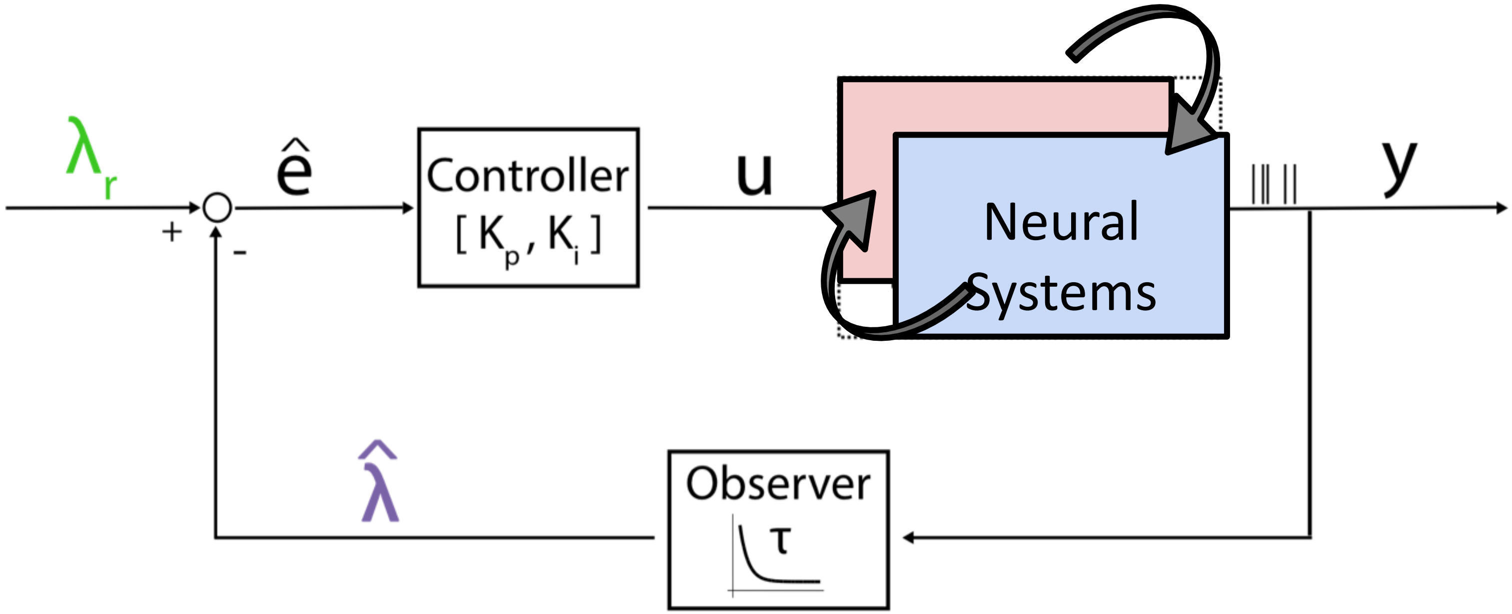
Reduced Response Variability





CLOC with Neural State-switching

- How to maintain control during state changes?
  - NOT pretend it's one system and design single controller
  - Switch between multiple models inferred with HMMs
  - Design controllers with robustness to multiple models



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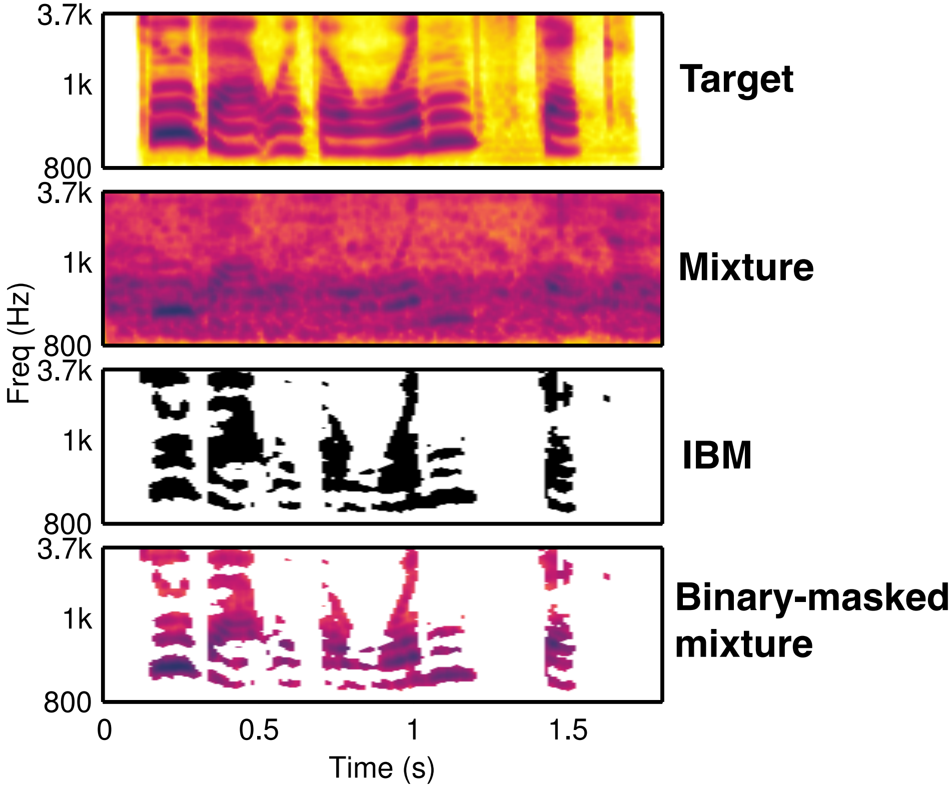
My Ulysses contract: auditory research

Ulysses and the Sirens, JW Waterhouse (1891)

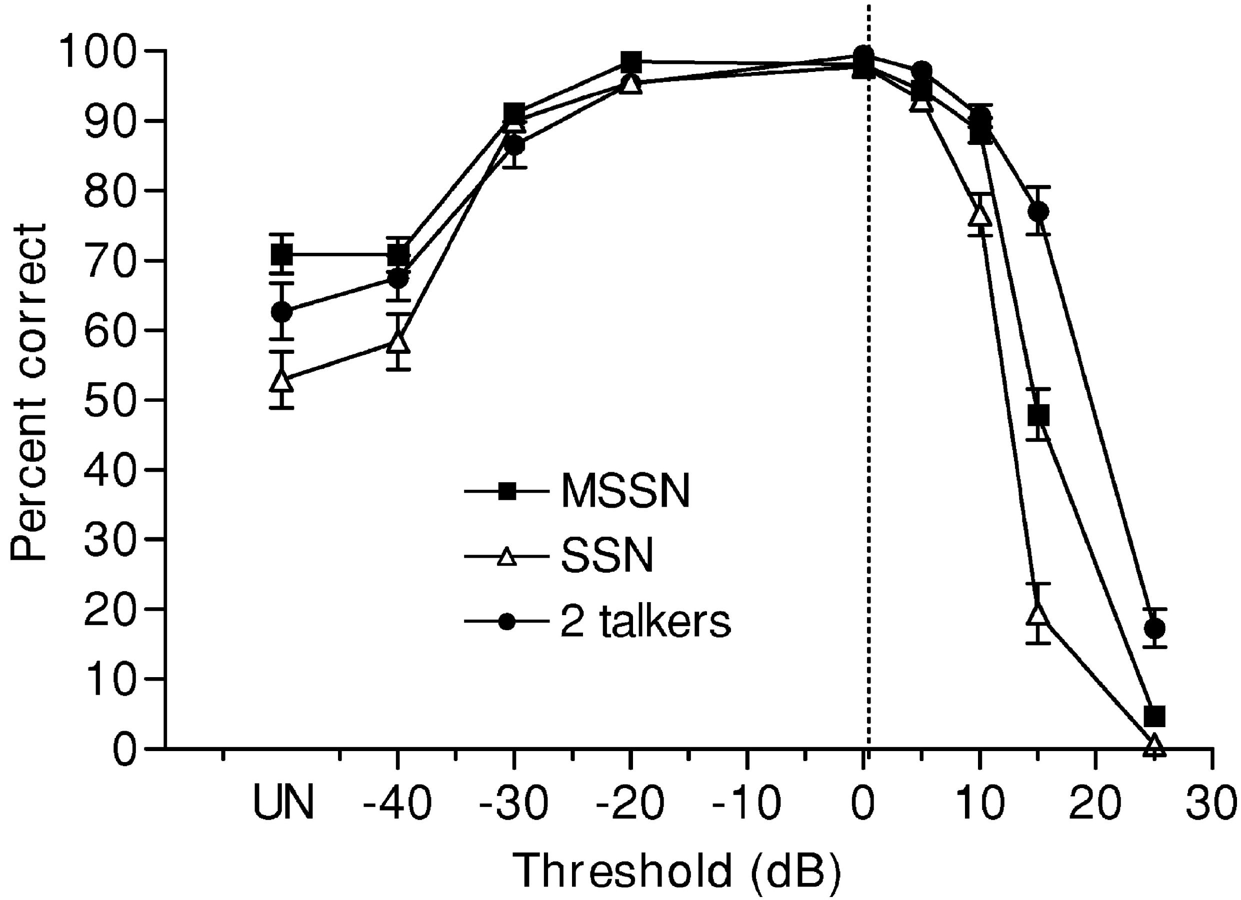
Speech intelligibility in noise

- Speech in noise is difficult to understand, especially for impaired listeners
- Traditional single channel speech denoising can improve quality but do not improve intelligibility
- Ideal binary mask (IBM)
  - Threshold noise-dominated TF bins; keep target-dominated
  - Requires oracle knowledge



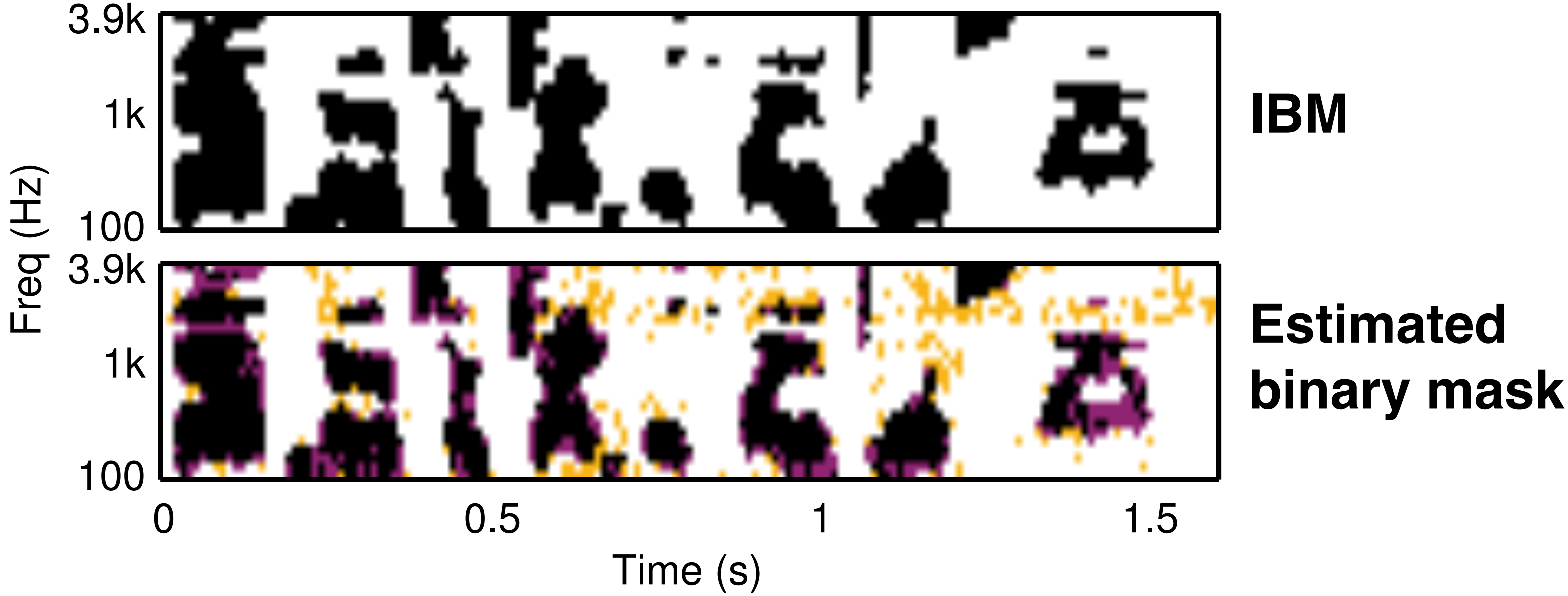
(Roman, Wang & Brown 2003)

IBM intelligibility benefits



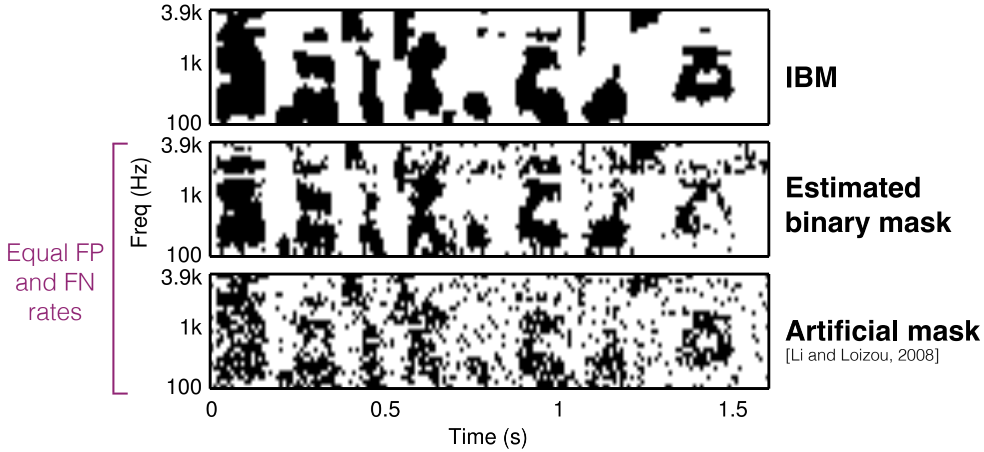
(Li & Loizou 2008)

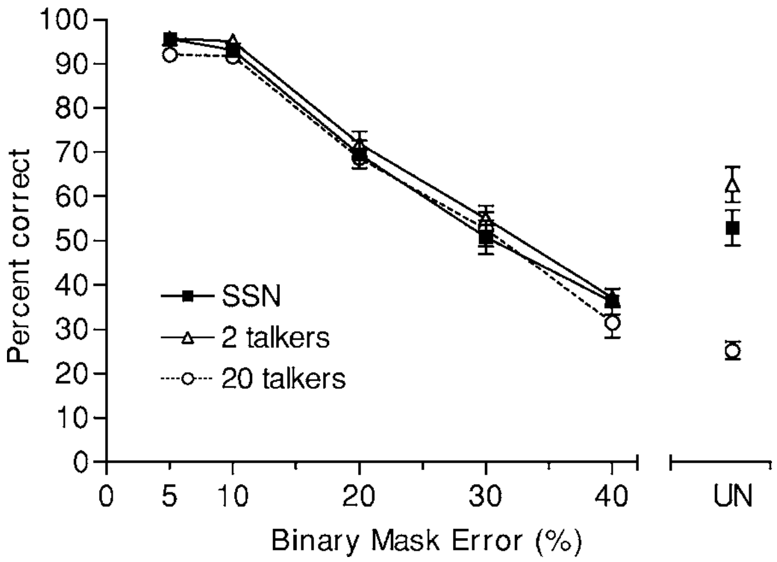
Binary mask estimation



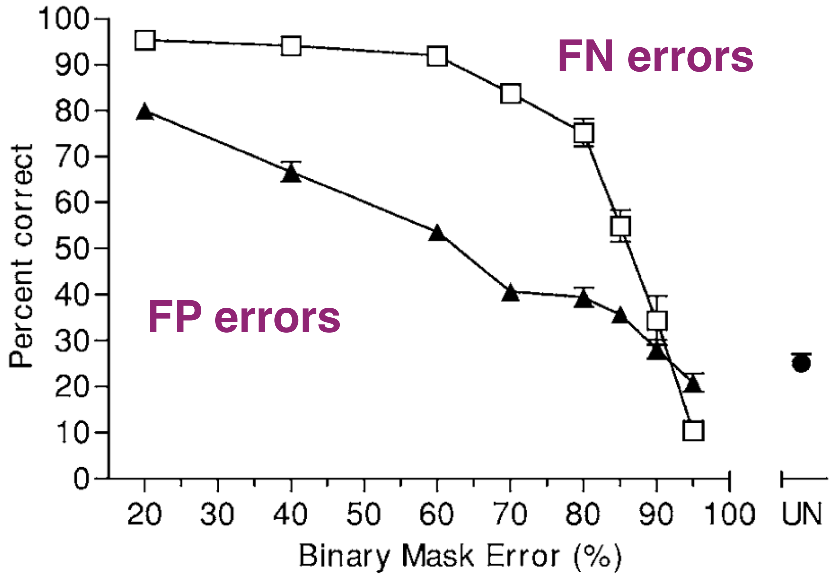
CLASSIFICATION PROBLEM		ideal mask 1	ideal mask 0
estimated mask	1	true positive	false positive (FP)
	0	false negative (FN)	true negative

How accurate is necessary?



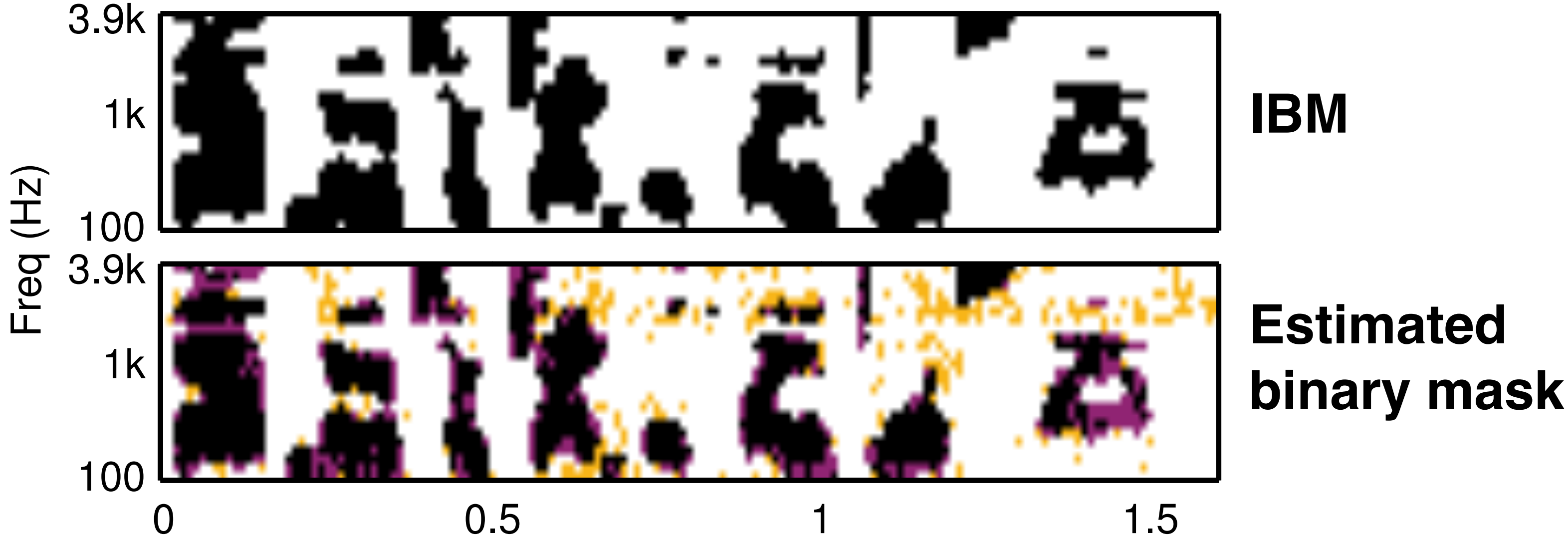


Conclusions:
FP rate < 20% when FN=0
FN rate < 60% when FP=0
Overall rate < 10%



(Li & Loizou, 2008)

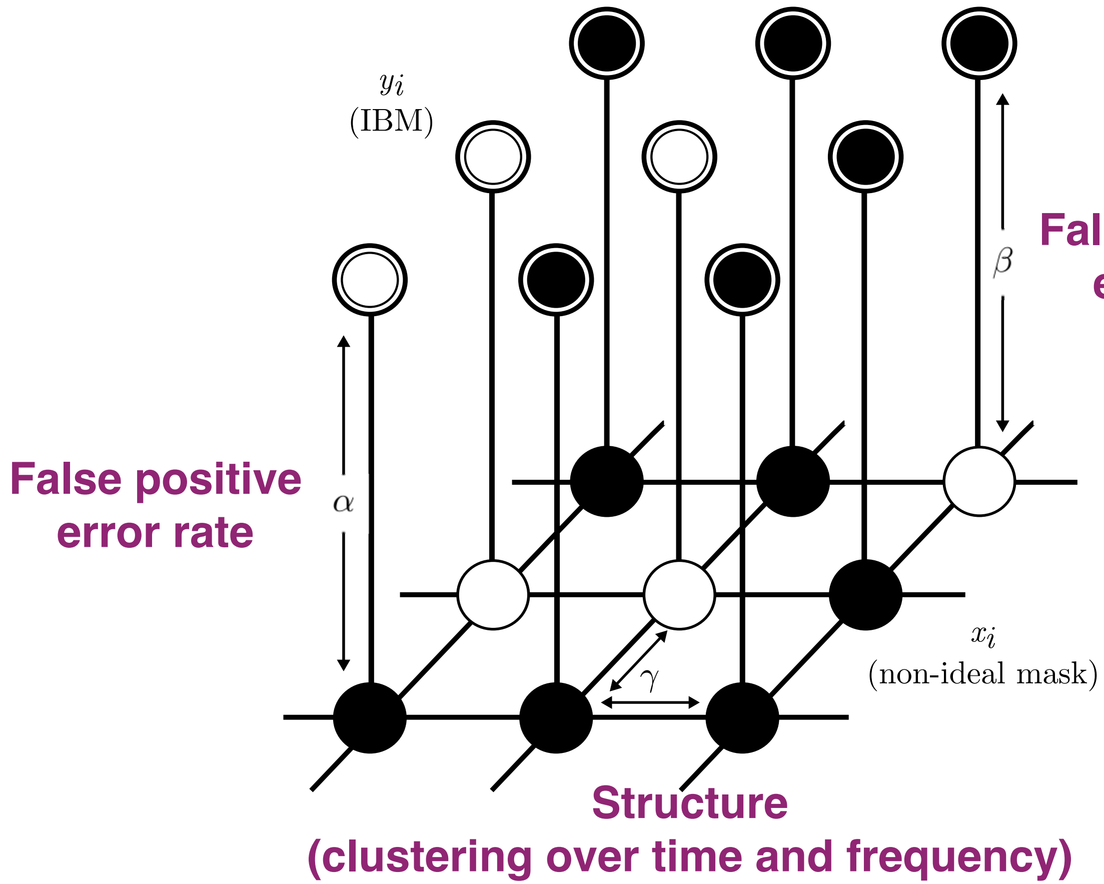
Binary mask estimation error structure



- Real algorithms make errors that:
  - Have significant TF structure
  - Have both FP/FN errors simultaneously
- How do these factors affect intelligibility?
- Develop investigation framework to test the impact of structure in IBM estimation errors
- Idea: develop statistical model of estimation errors

Ising graphical model

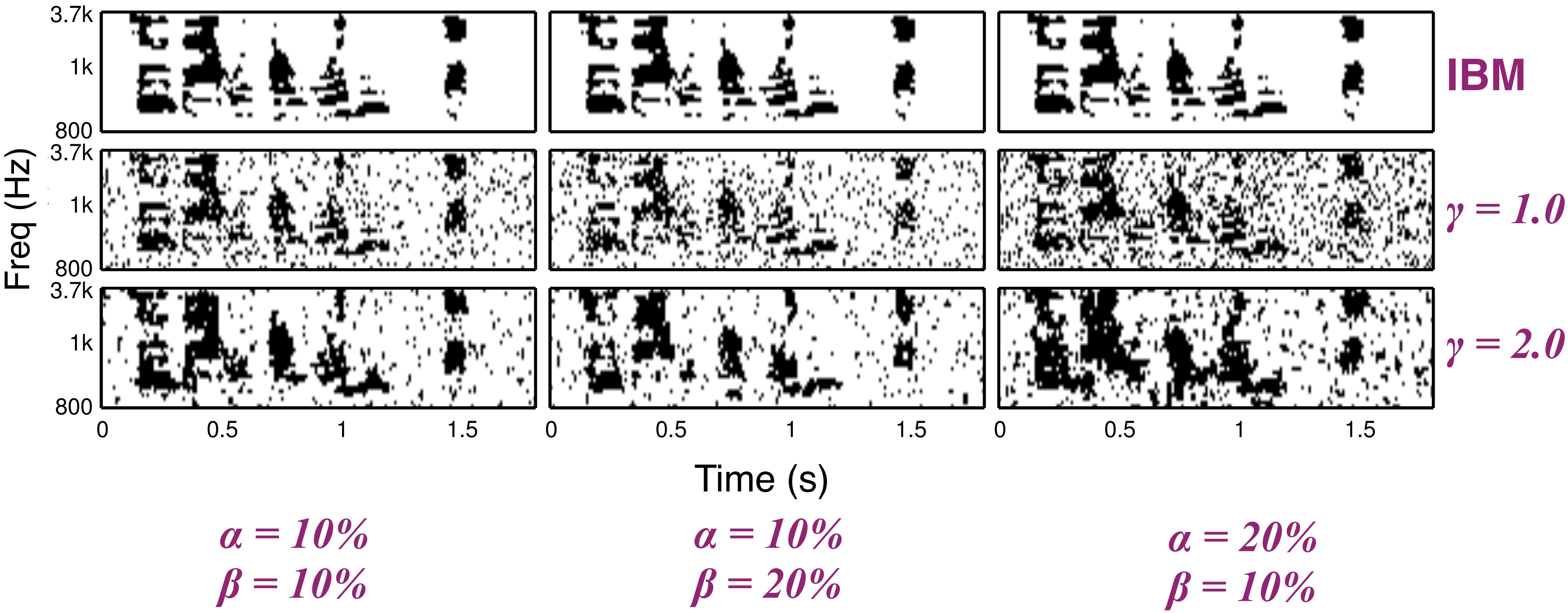
(Kressner & R., 2015)



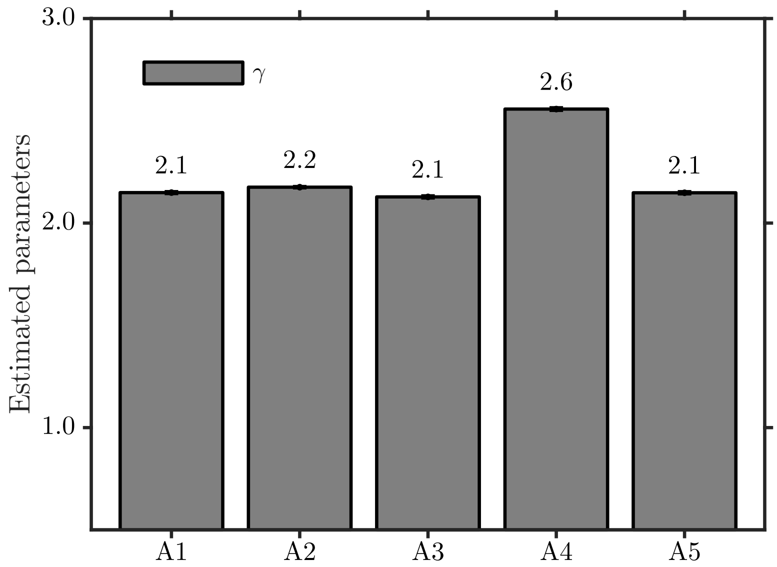
Training approach:
1. Generate speech mixtures
2. Estimate IBMs (e.g., GMM)
3. Estimate model parameters (MLE)

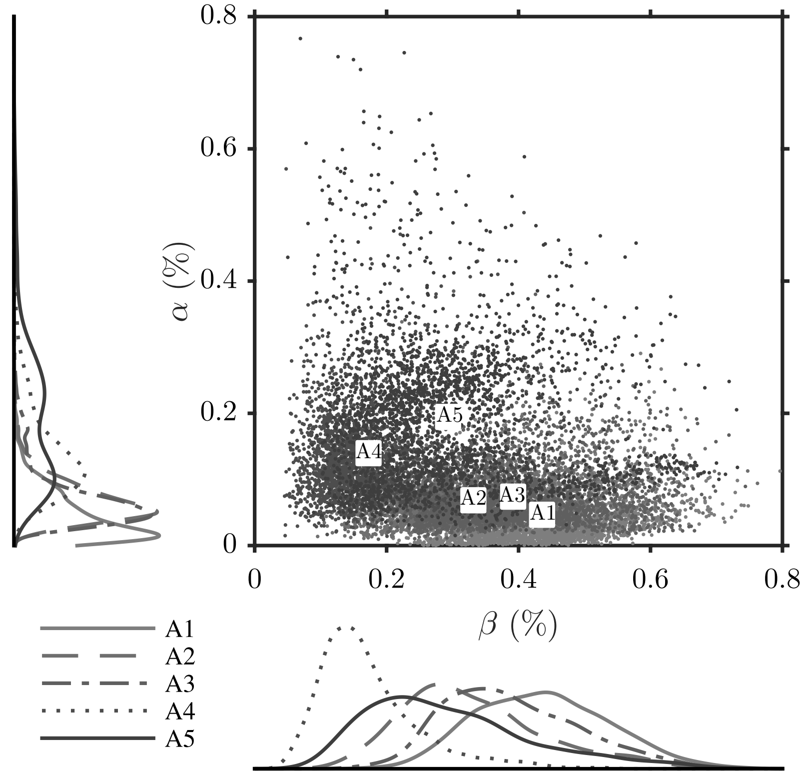
Testing approach:
1. Generate speech mixture
2. Calculate IBM
3. Draw a sample from *p(x|y)*
4. Test intelligibility with mask *x*

Example sampled masks



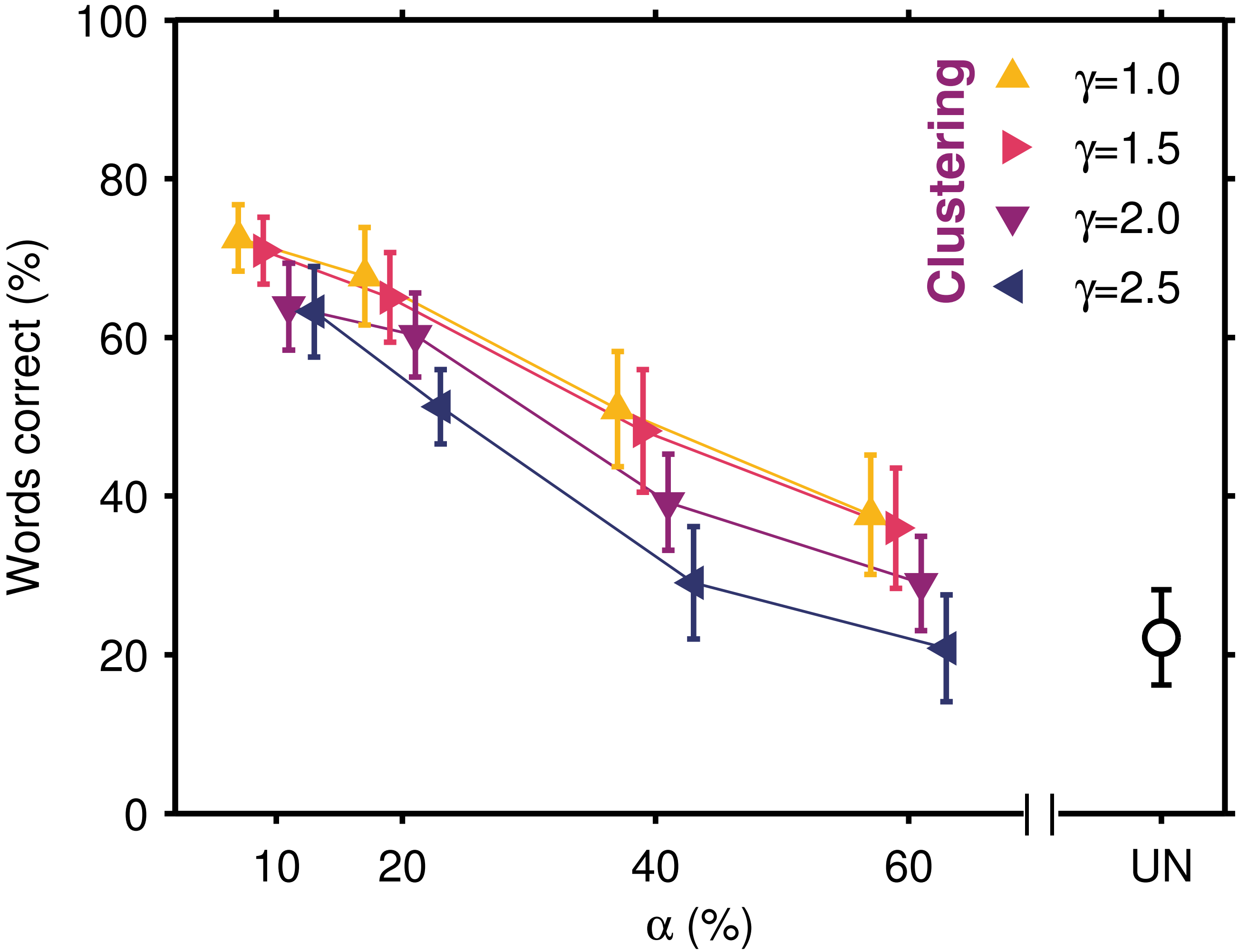
Experimental setup



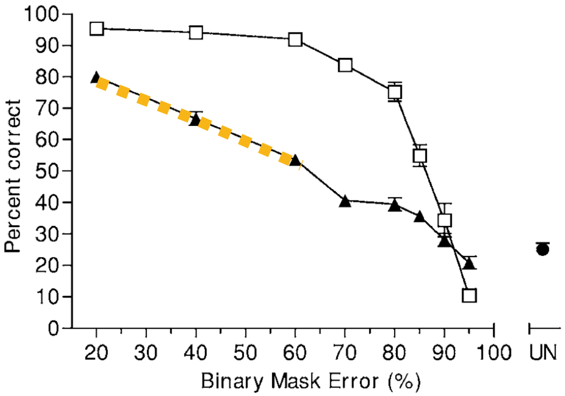


- Determine typical parameters
- Test word errors in 10 NH listeners for speech in babble (-5dB)
- Perform parametric exploration over:
  - FP and structure
  - FN and structure
  - FP, FN and structure

Clustering is detrimental



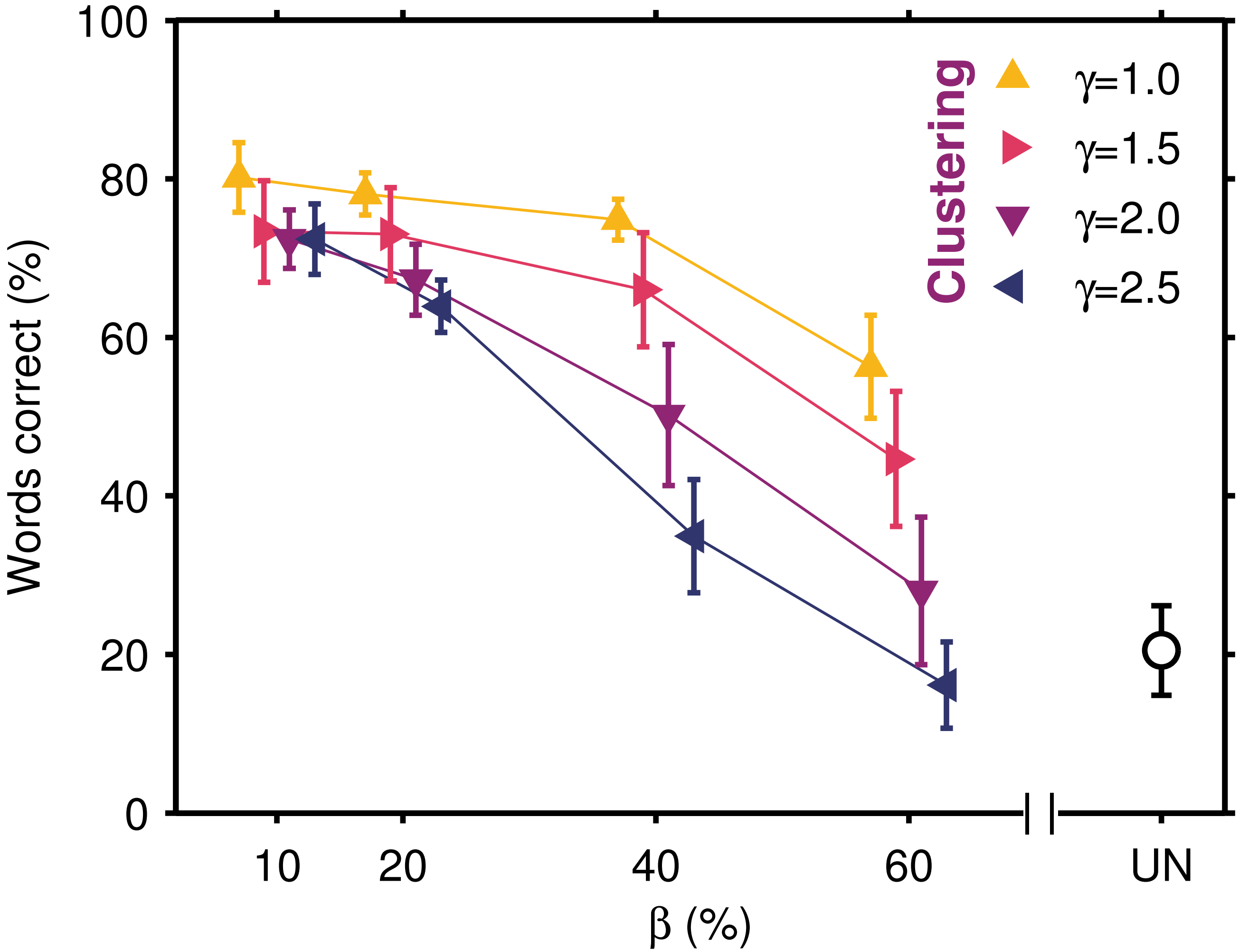
False positive error rate



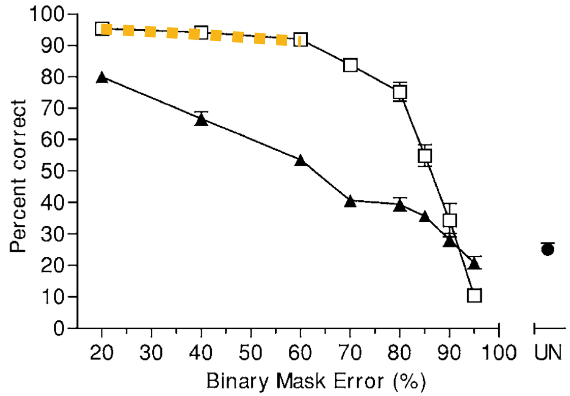
[Li and Loizou, 2008]

(Kressner & R., 2015)

Also, FN can be as detrimental as FP



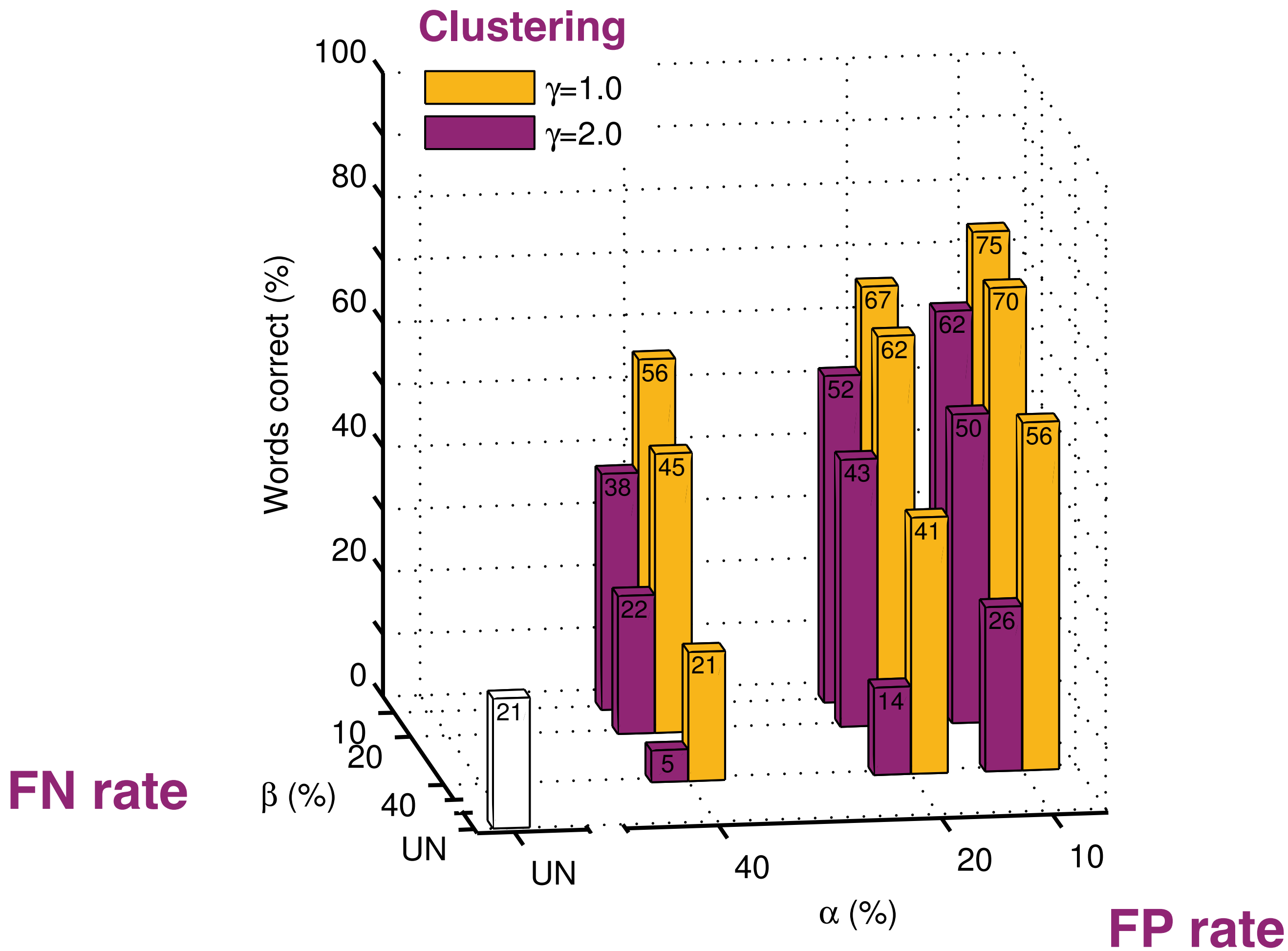
False negative error rate



[Li and Loizou, 2008]

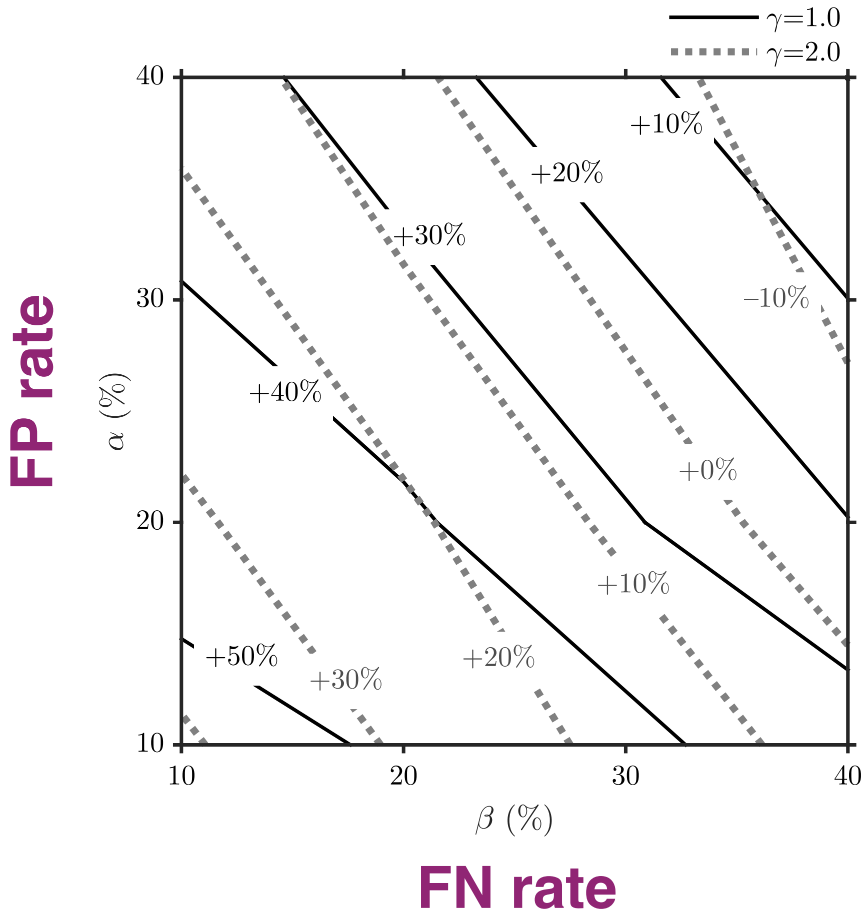
(Kressner & R., 2015)

Individual criteria insufficient



- Significant interactions: FN/structure and FP/FN/structure
- FM just as bad as FP even without structure (Kressner & R., 2015)

Changing criteria

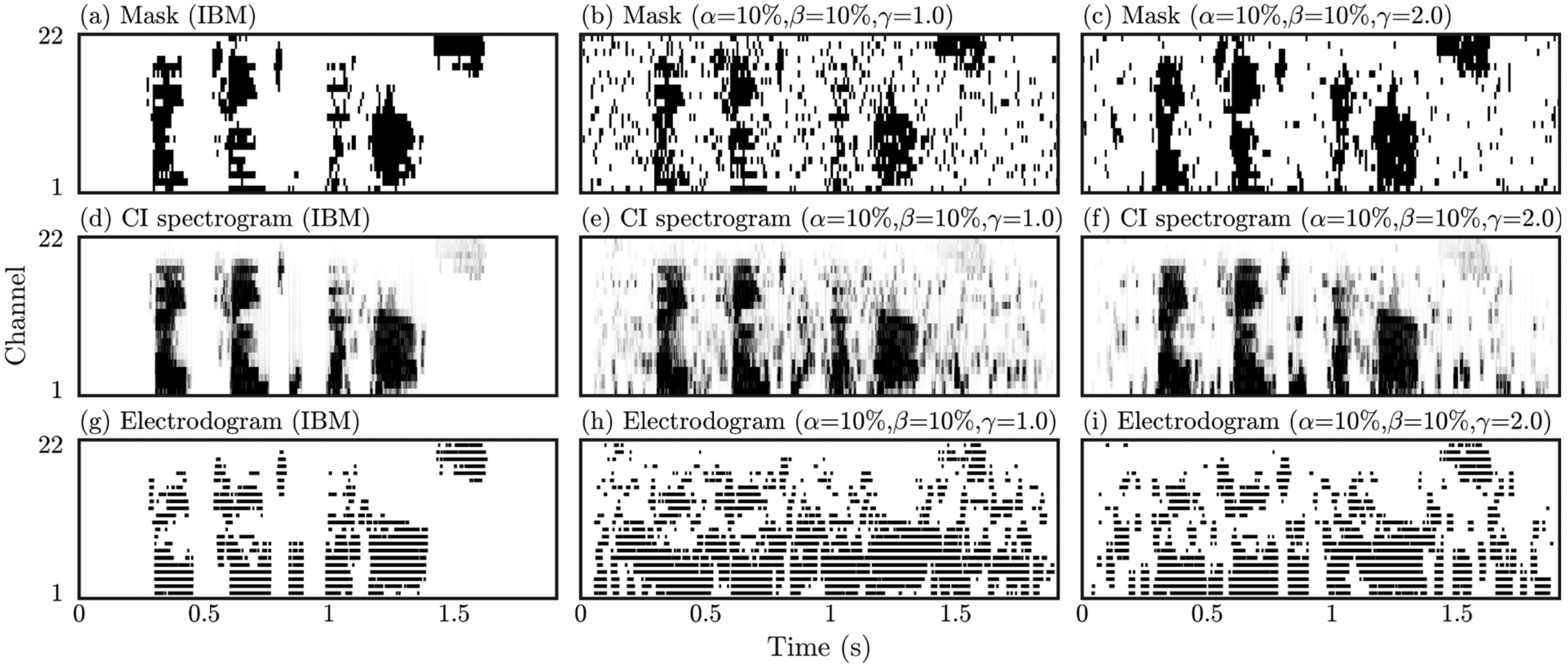


- Effect of clustering not captured by H-FA metric
- Effect of clustering qualitatively captured by STOI metric but with underprediction of error rates

(Kressner & R., 2015; Kressner, May & R., 2016)

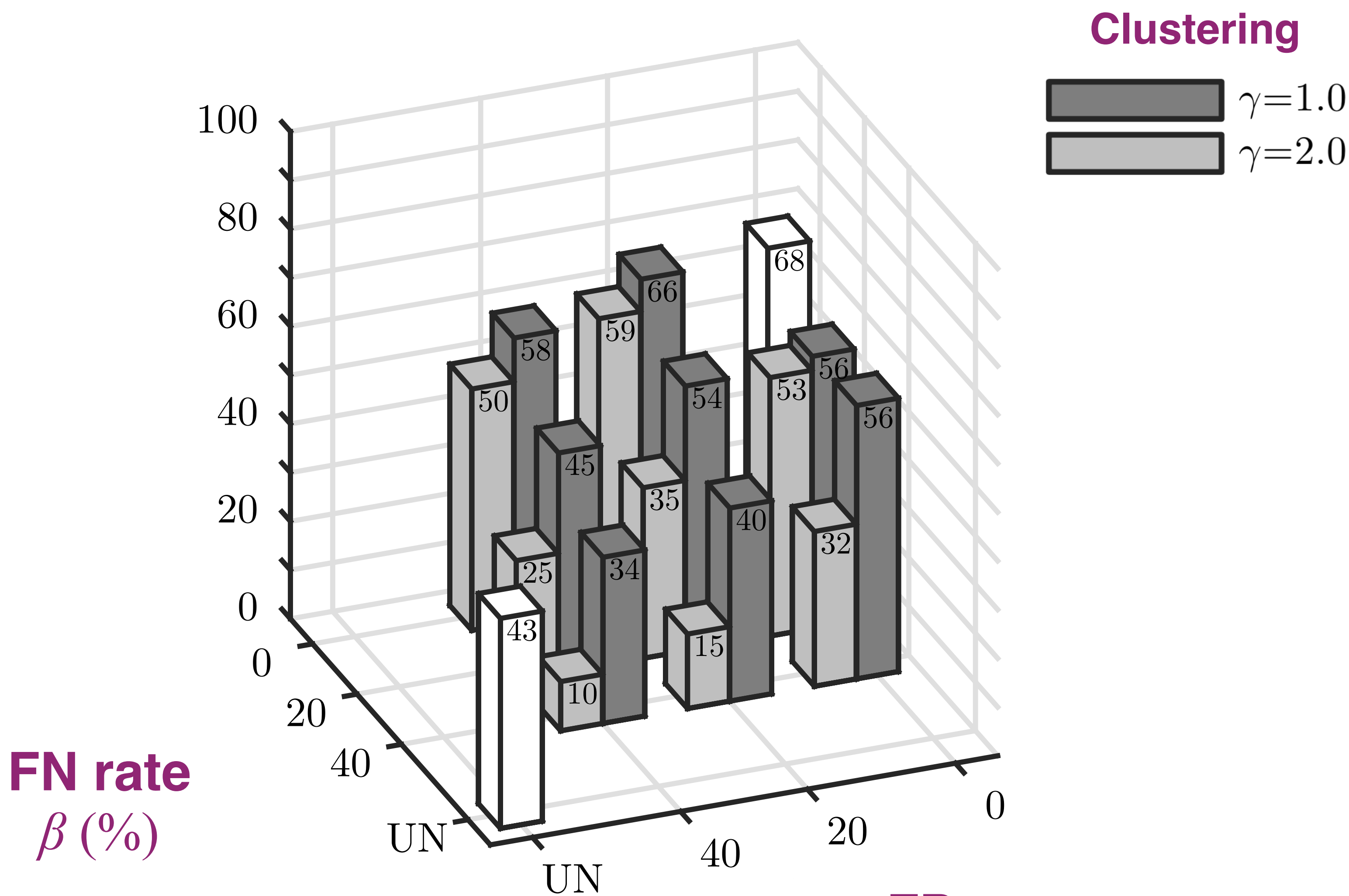
Cochlear implant intelligibility

- Test word errors in 8 CI wearers for speech in babble (delivered electrically)



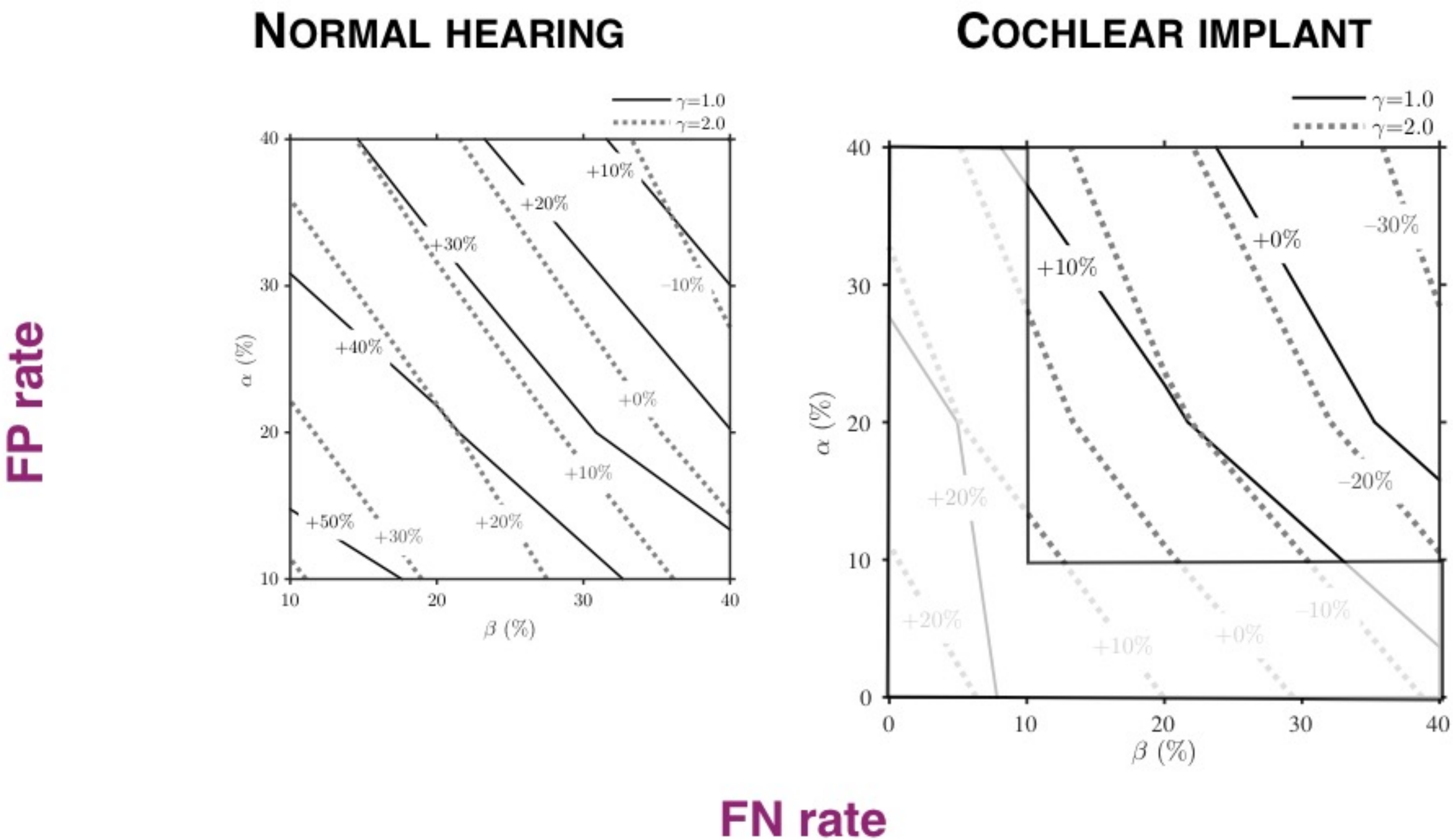
(Kressner, Westermann, Buchholz & R., 2015)

Consistent conclusions



(Kressner, Westermann, Buchholz & R., 2015)

More stringent criteria



(Kressner, Westermann, Buchholz & R., 2015)

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