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

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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

- Delay embeddings for nonlinear dynamics (math)
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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:

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

- 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

**State Space**

\[ \mathbb{R}^N \]

\[ \mathcal{M} \]

\[ \phi_T(x(t)) = x(t + T) \]

**Delay coordinate map (DCM)**

\[ F(x(t_0 - T_s)) \]

\[ F(x(t_0)) \]
Reconstruction problems

- Widely used: time-series prediction, dimensionality estimation

- 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

![Diagram showing original state, measurement, and reconstruction](image.png)
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

\[ \| F(x_1) - F(x_2) \|_2 \propto \| x_1 - x_2 \|_2 \]
**Theorem (Eftekhar, Yap, Wakin, R., 2017):**

Under some regularity assumptions, if

\[ R(\mathcal{M}_{H,T,M}) > \dim(\mathcal{M}) \cdot \log \left( \frac{\frac{1}{\text{vol}(\mathcal{M})} \cdot \frac{\dim(\mathcal{M})}{\text{rch}(\mathcal{M})}}{M} \right) \]

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 \( x_1, x_2 \in \mathcal{M} \).

Stable rank: May scale like \( M \)?

Linear in dimension

Geometric regularity

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

- 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

(Carter & de Lecea, 2011)
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

Firing rate target \( \lambda_r \) → \( e \) → Controller \( u \) → Neural System \( y \)

LED input power

Spiking output

Estimated rate \( \hat{\lambda} \)

• 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

Closed-loop
- Firing Rate (spikes/s)
- Control Input (mW/mm²)

Open-loop
- Firing Rate (spikes/s)
- Control Input (mW/mm²)

Comparison between Closed-loop and Open-loop performance with a 1Hz modulation.
Disturbance Rejection

- **Closed-loop**
  - Firing Rate (spikes/s)
  - Control Input (mW/mm²)
  - 20 spikes/s
  - 1 mW/mm²

- **Open-loop**
  - Firing Rate (spikes/s)
  - Control Input (mW/mm²)
  - 20 spikes/s
  - 1 mW/mm²
Tracking Complex Desired Trajectories

Firing Rate (spikes/s)

Fano Factor
variance/mean

Time (s)

Closed-loop
Open-loop
Reference

20 spikes/s

1
Reduced Response Variability

Firing Rate (spikes/s)

Fano Factor

Time (s)

Closed-loop
Open-loop
Reference

20 spikes/s

Average Fano Factor

Closed loop
Open loop

cell 1
cell 2
cell 3
cell 4
cell 5

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Building algorithmic foundations
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

Estimated binary mask

<table>
<thead>
<tr>
<th>Classification Problem</th>
<th>ideal mask</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>estimated mask</td>
<td>1</td>
</tr>
<tr>
<td>0</td>
<td>false negative (FN)</td>
</tr>
<tr>
<td>true negative</td>
<td></td>
</tr>
</tbody>
</table>

True positive
False positive (FP)
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

False positive error rate

Structure
clustering over time and frequency

False negative error rate

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 $x$

(Kressner & R., 2015)
Example sampled masks

<table>
<thead>
<tr>
<th>Time (s)</th>
<th>Freq (Hz)</th>
<th>IBM</th>
<th>$\gamma = 1.0$</th>
<th>$\gamma = 2.0$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>800</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.5</td>
<td>1k</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3.7k</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.5</td>
<td>800</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>3.7k</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$\alpha = 10\%$  
$\beta = 10\%$  
$\alpha = 10\%$  
$\beta = 20\%$  
$\alpha = 20\%$  
$\beta = 10\%$
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

\[
\text{Words correct (\%)} = \begin{cases} 
\gamma = 1.0 \\
\gamma = 1.5 \\
\gamma = 2.0 \\
\gamma = 2.5 
\end{cases}
\]

False positive error rate

(Kressner & R., 2015)

[Li and Loizou, 2008]
Also, FN can be as detrimental as FP

Experiment 2 results

\[ \text{Words correct (\%)} \]

<table>
<thead>
<tr>
<th>( \beta ) (%)</th>
<th>10</th>
<th>20</th>
<th>40</th>
<th>60</th>
<th>UN</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \gamma = 1.0 )</td>
<td>( \gamma = 1.5 )</td>
<td>( \gamma = 2.0 )</td>
<td>( \gamma = 2.5 )</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

False negative error rate

(Kressner & R., 2015)

[Li and Loizou, 2008]
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)

![Image of spectrograms and electrodograms with masks and corresponding stimulation sequences.](image)
Consistent conclusions

FN rate \( \beta \) (%)

FP rate \( \alpha \) (%)

(Clustering)

\( \gamma = 1.0 \)
\( \gamma = 2.0 \)

(Kressner, Westermann, Buchholz & R., 2015)
More stringent criteria

(NORMAL HEARING)

(COCHLEAR IMPLANT)

(FP rate vs. FN rate)

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