STUDY IN NOVEL PERIPHERAL NERVE INTERFACE and APPLICATION.

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ABSTRACT

Bi-directional exchange of information between the peripheral nervous system (PNS) and a computer interface can be achieved through the use of a peripheral nerve interface (PNI). Sophisticated PNI's can be used to augment a PNS compromised by injury or disease. In addition to supplementing the PNS, PNI's enable researchers to study the form and function of the PNS.

Deploying effective PNI's come with a set of challenges not unlike other neural engineering solutions; namely: low signal-to-noise ratio (SNR) from sensitivity limitations current equipment provide, functional resolution deficiencies and managing inadvertent stimulation as the whole field is still in its infancy, and the stability of the interface itself that tends to degrade over time from the body's inherent nature of attacking foreign objects.

There are many prominent figures in the field that are currently developing novel approaches and technologies to interface with the PNS. For example, imagine a system that can track internal biological markers that classify a disease state and automatically stimulate a peripheral nerve to provide non-pharmacological treatment of the medical condition; bringing the body and mind back to a 'normal' state, [6]. Imagine applying imaging techniques used in a different field of study in a novel way to increase the received SNR on electrodes, and consequentially the precision and accuracy of stimulation. Or, the ability to re-learn an 'every-day' function that has been affected by an injury or disease; for example, learning how to walk again after having a stroke that severs those neural pathways.

Of course there is no one-size-fits-all solution and there are many trade-offs between resolution, form, and longevity that vary greatly across applications. However, a successful implementation of a PNI should allow information to be both introduced to, and extracted from the PNS. In this paper, we will briefly introduce select techniques and their applications; and then explore how using the principles of engineering, one might use some easy-to-gather data to quickly derive a meaningful way to control the gait of a Parkinson's Disease (PD) patient.

INTRODUCTION

In the United States alone, it is estimated that 800,000 people will have upper limb loss in 2020. Current options for transradial and transhumeral amputees can restore lost functions; however, amputees are unable to control the prosthetic as desired because of the mechanical degrees-of-freedom. To eliminate some of these interface limitations, a reported 60% of patients are willing to experiment with implantable PNI's [1].

Invasive-ness, stability, and selectivity are among the primary trade-offs when considering a PNI for an appropriate application. There are invasive devices that provide high levels of selectivity by reducing the proximity between the electrodes and the target fiber; however, they tend to produce poor stability and accelerated fatigue failure. Nerve cuffs seem to be the least invasive option that offers high-stability, but they are also the least selective. Raspopovic, [4], has shown while possible to classify multiple concurrent signals, it has not been possible to differentiate more than two concurrent signals of

the same type. This impedes the proliferated use of nerve cuffs for prosthetic control. Figure below shows what a typical nerve cuff may look like and associated nerve.

Figure 1: nerve and nerve-cuff - https://www.microprobes.com/products/peripheral-electrodes/nerve-cuff

Because of the favorable properties of nerve cuffs mentioned above and their wide-spread use, it is essential to further the capabilities and selectivity of this type of PNI. Christie, [3], shows that even 11 years post-implant, the nerve cuff electrodes remain fully functional and reliably operational.

One novel idea is introduced in Hope, [2], where they attempt to address the shortcomings of nerve cuffs with techniques from the medical imaging field called Electrical Impedance Tomography, or EIT. We will discuss what EIT is and how, according to Hope, it can be used to enhance the degree to which nerve cuffs can be applied.

DISCUSSION

What is EIT? Electrical Impedance Tomography, invented by John Webster in 1978, is a type of non-invasive medical imaging in which the electrical properties of biological tissue are estimated and used to generate a tomographic image; this is done through surface electrode measurements. The variation in electrical conductivity of different tissues and the movement of fluids through the tissues are exploited through the stimulation of small alternating currents to better differentiate between normal and abnormal tissue. The figure below shows a tomographic image of a human thorax with streamlines and equipotential through z=0.35, [7].

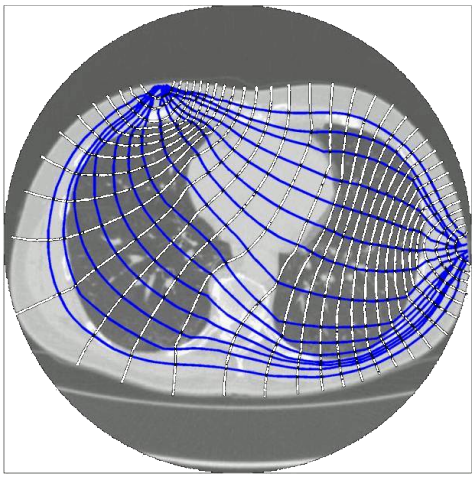

Figure 2: Andy Adler - http://eidors3d.sourceforge.net/tutorial/netgen/extrusion/thoraxmdl06a.jpg

In differential EIT, transient changes in the impedance distribution within the sample acts as the contrast agent. The change in impedance of neural tissue during activity in neural cells can be attributed to increased membrane conductivity during action potentials. Combining physiological

information on the mammalian brain to image cortical activity and nerve fiber impedance models, researchers have achieved spacial and temporal resolutions of .4mm and 3ms in rat brains. If replicated on a nerve cuff, this would provide sub-fascicle level selectivity, [2]. We see how powerful this technology can be if we are able to replicate it on a nerve cuff. Hope's results are encouraging and merit further investigation.

The following section was derived from raw data downloaded from, [8], PhysioNet. It contains information from Gait in Parkinson's Disease [https://doi.org/10.13026/C24H3N] which is made available under the ODC Attribution License.

This data is made available from three separate studies and contains measures of gait from 93 patients with idiopathic PD (mean age: 66.3 years; 63% men), and 73 healthy controls (mean age: 66.3 years; 55% men). The vertical ground reaction force is recorded of the subjects as they walk at their self-selected pace for approximately 2 minutes sampled at 100Hz. The placement of sensors (under each foot) is described by the table below; assuming that the origin (0,0) is center between the legs and the person is facing towards the positive Y axis:

Sensor	X	Y
L1	-500	-800
L2	-700	-400
L3	-300	-400
L4	-700	0
L5	-300	0
L6	-700	400
L7	-300	400
L8	-500	800
R1	500	-800
R2	700	-400
R3	300	-400
R4	700	0
R5	300	0
R6	700	400
R7	300	400
R8	500	800

This data can be used to create many useful statistics such as stride time, swing time, and stride-to-stride dynamics. However, our goal is to see if we can set up a method in which our nerve-cuffs can be used to help correct the gait in these PD patients. There is a total of 93 individual patient's and 73 individual controls; the general trend of each category can be easily seen to be the same, so we will for our purposes focus our efforts to a random patient and a random control. For this next section, we choose patient 35, and control 07; both from the *Silvi Frenkel-Toledo et al (Treadmill walking in PD; Mov Disorders, 2005)* study.

Note: figures below generated in Matlab; necessary code to re-create results included in Appendix.

Using the table above and the sensor collected data, we can calculate how the center of pressure changes as the individuals walk. The figure below shows exactly this:

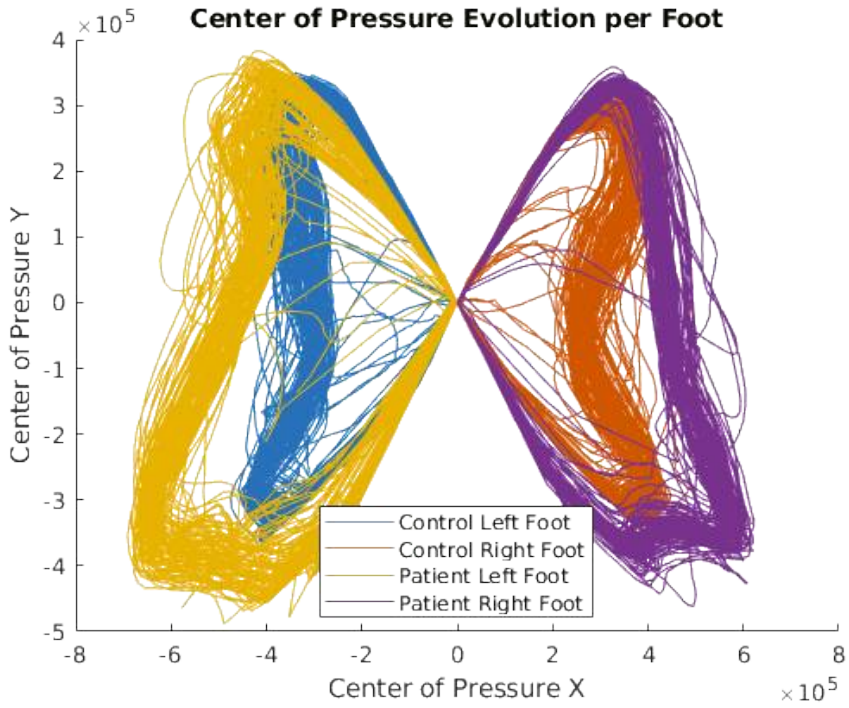

Figure 3: Center of Pressure Evolution – Matlab Code in Appendix

We can see clearly that the PD patient has much more variability in his/her stride. The question then becomes: how can we drive the PD patient's stride to the Control's stride. In order to answer this question, we will need to estimate the 'system' transfer function (TF). System in this case is a very rough first order approximation of the individuals; we are not presently interested in the disease or what neurological activity either individual experiences during their tests. We are only interested in whether or not we can make the motor mechanics of one persons walk, match the other. For the remainder of this section, we will only be concerned with the left foot. A similar calculation can be done for the other foot.

This is a very complicated undertaking as the systems are clearly non-linear; however, for a first order approximation, we can take some liberties in simplification. We will assume a stable TF that has the following form:

$$G(z) = \frac{z^{-1}\left(b_0+b_1z^{-1}+b_2z^{-2}\right)}{(1-p_1z^{-1})(1-p_2z^{-1})(1-p_3z^{-1})} = \frac{z^{-1}\left(b_0+b_1z^{-1}+b_2z^{-2}\right)}{1+a_1z^{-1}+a_2z^{-2}+a_3z^{-3}}$$

If we take the input to be just the linear progression of time since these individuals were told to walk and then timed, we can recursively estimate the poles and zeros of the TF above. Adding another pole or zero will simply drop out of our estimate as long as the system is stable, so the above assumption of the form can be used without much concern as it is just an estimate.

Expanding the TF, we get:

$$y(t) = b_0u(t-1) + b_1u(t-2) + b_2u(t-3) - a_1y(t-1) - a_2y(t-2) - a_3y(t-3)$$

And in matrix form, we can write this in terms of the regressors and parameters we want to estimate as:

$y(t) = \Phi^T \Theta$, where: $\Phi^T = \begin{bmatrix} u(t) & u(t-1) & u(t-2) & -y(t-1) & -y(t-2) & -y(t-3) \end{bmatrix}$,

and $\Theta = \begin{bmatrix} b_0 \\ b_1 \\ b_2 \\ a_1 \\ a_2 \\ a_3 \end{bmatrix}$.

Calculating this regressive equation yields the following results:

$$\Theta_{control} = \begin{bmatrix} 11.2813 \\ -23.9680 \\ 12.6865 \\ -2.1664 \\ 1.4362 \\ -0.2620 \end{bmatrix} \times 10^5, \text{ and } \Theta_{patient} = \begin{bmatrix} 41.5194 \\ -86.2546 \\ 44.7351 \\ -1.4469 \\ 0.1908 \\ 0.2686 \end{bmatrix} \times 10^5.$$

In order to determine if we can drive the patient system to the control system, we need to determine the controllability and observability of each system respectively. The controllability and observability matrices can be calculated as follows:

$O = \begin{bmatrix} C \\ CA \\ CA^2 \\ \vdots \\ CA^{n-1} \end{bmatrix}$, and $C = \begin{bmatrix} B & AB & A^2B & \cdots & A^{n-1}B \end{bmatrix}$. Where the matrices A,B and C can be generated from the estimated parameters above. Doing this, we get:

$$O_{control} = \begin{bmatrix} 1.0000 & 2.1664 & 3.2569 \\ 0.0000 & 1.0000 & 2.1664 \\ 0.0000 & 0.0000 & 1.0000 \\ 4.3327 & 1.8207 & 0.2620 \\ 1.0000 & 2.1664 & 0.0000 \\ 0.0000 & 1.0000 & 0.0000 \\ 11.2069 & -5.9607 & 1.1352 \\ 4.3327 & -1.4362 & 0.2620 \\ 1.0000 & 0.0000 & 0.0000 \end{bmatrix}, \text{ and } C_{patient} = \begin{bmatrix} 1.0000 & 1.4469 & 1.9028 \\ 0.0000 & 1.0000 & 1.4469 \\ 0.0000 & 0.0000 & 1.0000 \end{bmatrix}.$$

CONCLUSIONS

We see that $O_{control}$ has full column rank and $C_{patient}$ has full row rank; therefore, we have proven that our estimated PD patient system can be driven to our estimated Control system. The next step would be to determine the Grammians of each system so we can determine what that control force needs to be. Another method that could be more fruitful in illuminating any inherent patterns in the data is independent component analysis, or ICA. However our goal here was not to find what the force needs to be, just that there exists a force where we can drive one of our systems to the other. So what does

this mean in the context nerve-cuffs? From the above derivation, we have established that the force on each foot in the PD patient can be modified so that the PD patient's stride and swing match that of the Control. With the enhanced selectivity of Hope's nerve-cuffs, we can individually intercept the required neuromuscular pathways in a manner so that the resultant force on each foot matches. Hence, effectively canceling out the increased variability in the PD patients and facilitating social assimilation.

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APPENDIX

```
close all
clear all
clc

%Import patient and control data
C=importdata('SiCo07_01.txt');
P=importdata('SiPt35_01.txt');

%Define left and right foot sensors
t=C(:,1);
CL=C(:,2:9);
CR=C(:,10:17);
N=length(CL(:,2));
PL=P(:,2:9);
PR=P(:,10:17);

%Define sensor placement map
LX=[-500 -700 -300 -700 -300 -700 -300 -500]';
LY=[-800 -400 -400 0 0 400 400 800]';
RX=[500 700 300 700 300 700 300 500]';
RY=[-800 -400 -400 0 0 400 400 800]';


%Calculate center of Pressure
CPxL=CL*LX;
CPyL=CL*LY;
CPxR=CR*RX;
CPyR=CR*RY;

CP2xL=PL*LX;
CP2yL=PL*LY;
CP2xR=PR*RX;
CP2yR=PR*RY;


%Plot Center of Pressure
figure
hold on
plot(CPxL,CPyL)
plot(CPxR,CPyR)

plot(CP2xL,CP2yL)
plot(CP2xR,CP2yR)

xlabel('Center of Pressure X');
ylabel('Center of Pressure Y');
title('Center of Pressure Evolution per Foot');
legend('Control Left Foot','Control Right Foot','Patient Left Foot','Patient Right Foot');


%define input
w=randn(1,N);
w=t;

%initialize vectors
PHI=zeros(length(w)-3,6);
z=zeros(length(w)-3,1);
k=zeros(1,length(w)-3);


%Choose y for patient or control
%y=CPxL/10^5;     %CONTROL
y=CP2xL/10^5;     %PATIENT


%populate regressors
for i=4:length(w)
    PHI(i-3,:)=[w(i-1) w(i-2) w(i-3) -y(i-1) -y(i-2) -y(i-3)];

    z(i-3)=y(i);
```

```
    k(i-3)=t(i);
end

%calculate parameters
THETA=inv(PHI'*PHI)*PHI'*z


%create symbolic variable z
syms z;

%define p's and b's
b0=THETA(1);
b1=THETA(2);
b2=THETA(3);
a1=THETA(4);
a2=THETA(5);
a3=THETA(6);

%define z-transform of transfer function
G=z^-1*(b0+b1*z^-1+b2*z^-2) /   (1  +a1*z^-1  +a2*z^-2  +a3*z^-3);

%collect coefficients of the polynomials to define transfer function
[num,den]=numden(collect(G));
num=sym2poly(num);
den=sym2poly(den);

%define discrete-time system object with given tf and sampling time h
h=t(5)-t(4);
sys1=tf(num,den,h);

%Generate state-space model
[A,B,C,D]=tf2ss(num,den)

%Output controllability and observability matrices
C=[B, A*B, A^2*B]
O=[C; C*A; C*A^2]
```