Experimental Verification of Observations Relating to Parkinsonian Tremor

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Abstract—There have been recent efforts [1, 2] to understand the mechanism causing tremors at rest in patients suffering from Parkinson’s disease, from a control-systems perspective. From these efforts, it appears that one of the primary causes behind the tremors may be the increased sensorimotor loop delay in Parkinson’s patients. This increased sensorimotor loop delay when modeled as a delay in the motor control system, reveals several interesting observations that have been demonstrated through simulation studies. Furthermore, these observations have been used to propose some simplistic diagnostic tools for Parkinson’s disease. In this paper, we continue this exploration with the aid of two bench-top experiments (servo motor control and inverted pendulum control). We see if tremors similar to the ones seen in Parkinson’s disease can be recreated in these experiments and if the observations from the simulations studies can be validated. We then explore further how these observations can be used for the diagnosis of the disease.

I. INTRODUCTION

Parkinson’s disease (PD) is a degenerative disorder of the central nervous system [8] that is not yet fully understood, and is characterized by increased reaction times in voluntary movements [9]. Patients suffering from Parkinson’s disease often experience unintended oscillatory motion of body parts, especially in hands, termed as Parkinsonian tremor. These tremors are involuntary and are primarily observed when the patient is trying to keep still [3] and hence are termed as rest tremors.

Diagnosis of Parkinson’s disease is still a significant challenge since there are no test that will definitively identify the disease. Computer tomography (CT) and magnetic resonance imaging (MRI) brain scans appear normal with PD patients, but are sometimes used to rule out other disorders that could give rise to similar symptoms.

There have been a number of approaches to try and model the mechanism behind Parkinsonian tremor. For instance, one approach is to tune Van-der Pol’s oscillator equations to recreate an output that looks like the Parkinsonian tremors [10]. Although such an approach is simple, they lack any physical underpinnings nor does it provide a fundamental understanding of the mechanism causing the tremors. Alternatively, another approach is to develop statistical models and tests using experimental data [11]. Such approaches may be useful in certain scenarios, but may not be applicable over a wide range of cases and scenarios.

Recently, the mechanism behind these tremors have been examined from a control systems perspective [1, 2]. Here, we view the increased sensorimotor loop delay in PD as a key distinguishing feature and hypothesize that this increased delay causes Parkinsonian tremor. The view that the increased sensorimotor delay is a key aspect of PD is well-supported by the observation that the primary symptoms of PD are related to dysfunction of the sensorimotor circuit [12]. Furthermore, the increased reaction times (by as much as 0.1s) observed in PD patients as compared to the healthy individuals [9], [13], [14] also points to this. While there could be multiple delays in the forward and feedback loops in the sensorimotor loop originating from different components of the sensorimotor loop, and it is unclear which ones affect tremors, we show later that our analysis is valid irrespective of which component is contributing. Hence, the increased sensorimotor loop delay is modeled as a delay in the control system governing the motions of the body parts, and the rest tremors in Parkinson’s patients were hypothesized to be limit cycle oscillations set up due to a combination of the delay and inherent saturation in the system. Further, simple diagnostic tools were developed in [2] that take advantage of features of the limit cycle in the phase space (such as shape and size) to not only detect the presence of Parkinson’s disease but also diagnose the severity of the disease.

In this paper, we continue this exploration with the aid of two bench-top experiments (servo motor control and inverted pendulum control). We see if tremors similar to the ones seen in Parkinson’s disease can be recreated in these experiments and if the observations from the simulations studies in [2] can be validated using these experiments. We then explore further how these observations can be used for developing and improving diagnosis tools.

In the next section, we briefly summarize the findings in [2]. Then in section III, we validate these observations using the two experiments mentioned. In section IV, we explore how the sensorimotor loop delay (or the delay) can be modeled from the perspective of developing simplified models both for facilitating further analysis and exploring

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possible control strategies to control Parkinson’s tremors. In section V, we include some discussion on diagnosis of the disease using the ideas discussed in this paper, and then we close with some discussions and conclusions.

II. OBSERVATIONS FROM THE MODELING EFFORTS

In this section, we briefly summarize the model proposed in [1] and the qualitative observations and insights from the modeling effort [2] relevant to the features of the Parkinsonian tremor. In [1, 2] the motor control of the body parts (extremities) is treated as a closed-loop feedback control system. In this framework (shown in Figure 1), the uncontrolled dynamics of the body part can be represented as a dynamical model whose transfer function can be obtained from simple dynamical system analysis with some simplifying assumptions. The total motor response can be represented as a closed-loop feedback control system where the feedback path represents all the sensory feedback and the controller represent the neuro-system’s logic that determines the muscle actions. The sensorimotor loop delay is represented as a transport delay in the closed-loop system and any physiological saturation is represented as a saturation function in forward path.

Using simulations with the above model structure, qualitative observations have been made in [2] that both confirm several clinical observations and provide insights into the mechanism causing the Parkinsonian tremor and its characteristics. The key observations are listed below.

Observation 1: Simulation results suggest that the increased sensorimotor loop delay (larger delay) in Parkinson’s patients is one of the primary cause for Parkinsonian tremor. Observation 2: Simulation results suggest that the tremor induced by increased sensorimotor loop delay is independent of the initial condition and small external excitations. Observation 3: Simulation results also show that a patient trying to keep still (intended velocity=0) exhibits limit cycle oscillations referred to as rest tremor. Observation 4: In simulation, tremors often disappear when large-scale voluntary motion is attempted. Observation 5: Simulation results show that as sensorimotor loop delay increases, frequency of oscillation decreases, and therefore as the disease progresses a decrease in frequency is likely to be observed. Observation 6: Simulation results also show that increase in the sensorimotor loop delay, which results in a decrease in the frequency, in turn results in an increase in the amplitude of oscillation.

The reader should note that the observations 3, 4, 5 and 6 above are in line with clinical observations [1, 2, 6, 7].

In addition to the above observations, it is further observed in [2] that the Parkinsonian tremor exhibits limit-cycle characteristics. Furthermore, the area contained within the limit cycle (in phase space) is found to be directly correlated with the delay and saturation, whereas the aspect ratio of the limit cycle is found to have a direct relationship with delay.

In [2], a simple pendulum (representing the human hand) is used as a dynamical system and a PID controller is used to represent the controller. However, it is also noted in [2] that these choices are indicative and the qualitative observations would be valid for other similar systems.

Since it is claimed that in [2] that the observations are qualitative, we deliberately choose two different experiments and attempt to show that above observations arise primary from the structure (Figure 1) and are independent of the details of the dynamics of the body part.

III. EXPERIMENTAL VALIDATION

In this section, we attempt to validate our observations from the earlier modeling studies, using two table-top experiments. To verify the generality of the qualitative observations in [2], we intentionally choose two different experiments.

We consider two motion control experiments, an angular position control experiment for a servo motor and a rotary inverted pendulum balancing experiment. The former is a first-order, linear, stable system and the latter is a fourth-order, non-linear, unstable system. Thus, these two systems provide two very different platforms for validating the observations in [2]. Furthermore, the controller used in the servo position system is a Proportional-Derivative controller whereas a LQR controller is used in the rotary inverted pendulum system. With these motion-control experiments, we observe the effect of delay and saturation experimentally and see if the observation and the hypothesis from the previous section hold true. Both of these experiments are based on a QUBE Rotary Servo Experiment from QUANSER.

In both of the experiments, we first construct and verify a stable closed-loop control system with Proportional-Derivative and LQR controllers, respectively. In these stable closed-loop systems, we then study the effect of introducing a delay and saturation (as in Figure 1). We first describe results for the servo position control experiment.
A. Limit cycle

For lower delay (below 0.03 s), no oscillations are observed and the system converges to the desired reference value. When we introduce a larger delay, such as 0.05 s, and saturation limits of -10 to 10 units to servo position control system, we observe a closed trajectory in the phase space (angular velocity/ angular acceleration). Further, we observe that almost identical closed trajectories for different initial conditions with same delay and saturation level are obtained. Figure 2 shows phase space trajectories for experiment with different initial conditions. As observed in [2], the delay (increased sensorimotor loop delay) is seen to be a primary contributor to the tremor. The fact that oscillations are only observed beyond a certain threshold thus confirms observation 1. Further, the fact that identical closed-loop trajectories are obtained for different initial conditions with no inputs (zero intended velocity), further corroborates observations 2 and 3.

Next, to investigate the effect of the voluntary motion, we take a sinusoidal intended velocity of frequency 10 rad/s with amplitude 10 and 20 respectively. Figure 3 shows output velocity for two different values of amplitude. As seen from the Figure 3, it is observed that the trace of tremor is still present while the amplitude is low (10) whereas for higher value of amplitude, trace of tremor disappears confirming observation 4. It is not surprising in a nonlinear system to see amplitude-dependent response, and perhaps this is the explanation for the disappearance of tremors during voluntary motion. Next, we take saturation level as -10 to 10 units and various delays as shown in Figure 6. The values of the aspect ratio and the area of the limit cycle for a given delay are shown in table II. These results confirm the observation that the aspect ratio and the area of the limit cycle are both dependent on the delay. Further, as delay increases aspect ratio decreases and area of the limit cycle increases.

B. Features of the limit cycle

Pursuing further with the servo position control experimental setup, next, we consider the following two scenarios for further validating our observations.

1) Same delay and different saturation levels : Here, we take the delay as 0.05 s and different saturation levels as seen in the Figure 5. It can be seen from the plot that the area of the limit cycle increases with saturation levels, but the aspect ratio of the limit cycle is approximately same for different saturation levels. The values of the aspect ratio and area of the limit cycle for the given saturation is shown in table I. These results support the observation made on the features of the limit cycle obtained from the simulation results (as mentioned in the section II) that aspect ratio is independent of the saturation levels and area is dependent on the saturation levels. Further, it is also interesting to note that when no saturation limits are applied, the response obtained roughly corresponds to the response with saturations limits of ±15 units. This again indicates that the equipment has an inherent saturation and thus it is reasonable to assume that in a real patient, there is bound to be some physiological saturation.

2) Same saturation level and different delays : Here, we take a saturation level to be -10 to 10 units and various delays as shown in Figure 6. The values of the aspect ratio and the area of the limit cycle for a given delay are shown in table II. These results confirm the observation that the aspect ratio and the area of the limit cycle are both dependent on the delay. Further, as delay increases aspect ratio decreases and area of the limit cycle increases.
Fig. 5. Limit cycle obtained for different saturation levels.

TABLE I
VALUES OF ASPECT RATIO AND AREA OF THE LIMIT CYCLE FOR DELAY = 0.05 SEC AND VARIOUS SATURATION LEVELS

<table>
<thead>
<tr>
<th>Saturation Levels</th>
<th>Aspect Ratio</th>
<th>Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>-8 to 8</td>
<td>15.53</td>
<td>0.87x10^6</td>
</tr>
<tr>
<td>-10 to 10</td>
<td>15.63</td>
<td>1.32x10^6</td>
</tr>
<tr>
<td>-12 to 12</td>
<td>15.27</td>
<td>1.88x10^6</td>
</tr>
<tr>
<td>-15 to 15</td>
<td>15.15</td>
<td>2.80x10^6</td>
</tr>
</tbody>
</table>

TABLE II
VALUES OF ASPECT RATIO AND AREA OF THE LIMIT CYCLE FOR SATURATION LEVEL = -10 TO 10 AND VARIOUS DELAYS

<table>
<thead>
<tr>
<th>Delay (sec)</th>
<th>Aspect Ratio</th>
<th>Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.03</td>
<td>22.04</td>
<td>0.72x10^6</td>
</tr>
<tr>
<td>0.04</td>
<td>17.83</td>
<td>1.13x10^6</td>
</tr>
<tr>
<td>0.05</td>
<td>15.63</td>
<td>1.32x10^6</td>
</tr>
</tbody>
</table>

Fig. 6. Limit cycles obtained for different delays.

Next, we performed a similar set of experimental tests on rotary inverted pendulum system. The result of various experiments starting with different initial conditions are shown in Figure 7. Here again, similar limit-cycle-type behavior is observed. Next, the limit cycles obtained for different saturation levels with the same delay are shown in Figure 8. It can be seen from Figure 8 that for same delay and different saturation levels, limit cycle area increases but the aspect ratio remains the same. Further, limit cycles for different delays with the same saturation level shown in Figure 9 clearly indicate that both area and aspect ratio of limit cycle change as a function of the delay. Due to space limitations, we do not show all the results with the inverted pendulum setup, but trends similar to the one observed with the servo position control setup are seen.

IV. MODELING THE DELAY

In this section, we explore relatively simple ways to model the delay. These simplified models may make it convenient for further analysis or Parkinson’s disease and may also help us design controllers to mitigate the Parkinsonian tremor in future.

The open loop transfer function of the servo position control experiment with the Proportional-Derivative controller
and the delay is
\[ L(s) = e^{-T_d s} \frac{10.38s + 519}{s^2 + 7.89s} \] (1)

To facilitate analysis, we approximate the exponential function \( e^{-T_d s} \) as a rational function. Here, we use a pade approximation for this purpose [5].

Pade approximation of \( e^{-T_d s} \) involves the matching of the series expansion of \( e^{-T_d s} \) with the series expansion of a rational function whose numerator is a polynomial of degree \( p \) and whose denominator is a polynomial of degree \( q \). Taking \( p = 1 \) and \( q = 1 \), the approximation becomes
\[ e^{-T_d s} \approx \frac{b_0 T_d s + b_1}{a_0 T_d s + 1} \] (2)

For a 1st order pade approximation, we expand the \( e^{-T_d s} \) and right hand side of the equation (2) using McLaurin series and match as many of the initial terms as possible. The two series are
\[ e^{-T_d s} = 1 - T_d s + \frac{(T_d s)^2}{2!} - \frac{(T_d s)^3}{3!} + \frac{(T_d s)^4}{4!} - \ldots \]
and
\[ \frac{b_0 T_d s + b_1}{a_0 T_d s + 1} = b_1 + (b_0 - a_0 b_1) T_d s - a_0 (b_0 - a_0 b_1) (T_d s)^2 + \ldots \]

Matching the coefficients of the first four terms and solving them, we get
\[ e^{-T_d s} \approx \frac{1 - (T_d s/2)}{1 + (T_d s/2)} \] (3)

Similarly, a 2nd order pade approximation for \( e^{-T_d s} \) is given by,
\[ e^{-T_d s} \approx \frac{1 - (T_d s/2) + (T_d s)^2/12}{1 + (T_d s/2) + (T_d s)^2/12} \] (4)

Thus, the Pade approximation suggests that the delay can be viewed as approximately a non-minimum phase zero in the system.

Now, approximating the delay using a 1st order pade approximation, equation (1) becomes
\[ L(s) = \frac{1 - (T_d s/2) 10.38s + 519}{1 + (T_d s/2) s^2 + 7.89s} \] (5)

The characteristic equation for the closed loop then becomes (in the absence of saturation)
\[ 1 + L(s) = (2 + T_d s)(s^2 + 7.89s) + (2 - T_d)(10.38s + 519) \]

Viewing \( T_d \) as the variable parameters, and putting the characteristics equation in the root locus form, we get
\[ 1 + (T_d) s^3 + \frac{18.27}{2} s^2 - \frac{519}{2} s + 36.54 s + 1038 = 0 \] (6)

The root locus plot of the above equation (as \( T_d \) varies) is shown in Figure 10. From the root locus, it is obvious that as the delay \( T_d \) increases, the closed loop poles move towards the RHP. Furthermore, the value of the \( T_d \) beyond which the system becomes unstable is 0.04 s. From experimental tests, we find that the delay beyond which the system becomes unstable is 0.03 s. An alternative approach to estimate this threshold delay is to use Bode plots. Figure 11 shows the bode plot of the servo position control system (1). It can be seen from the Figure 11 that the delay margin for the servo position control system is 0.0388 s. Hence, a 1st order pade approximation appears to be a reasonable approximation when the delay in the system is very small. This estimate of the delay can be useful for analysis and control of Parkinsonian tremors. Thus, once we estimate the delay, we may be able to design controllers to control the tremors. Such a simple approximation may help construct models in the future for the purpose of designing controllers to minimize the tremors.
One idea explored in [2] is to use a simple pocket device consisting of an accelerometer or gyro sensor, microcontroller and a display, which can be used to record and analyze tremor data. Based on the discussion earlier about the presence of a limit cycle and the area and the aspect ratio of the limit cycle, the presence of the disease and the severity can be estimated. For instance, we have seen that the area of the limit cycle directly corresponds to the delay in the loop, which in turn corresponds to the severity of the disease. Therefore, a simple and preliminary diagnosis can be performed. These ideas can also be implemented in a smartphone application, which may significantly help diagnosis in remote areas of underdeveloped countries where a healthcare professional (traveling to these areas) could still carry a smartphone but accessibility to extensive facilities could be a challenge. Even if the specific details of the model and the controller are unknown (which is likely to be the case with a real patient), the same diagnostic test can be repeated for the same individual at different time instances to get an idea of the progress of the disease. The idea here is that for the same individual all other parameters are likely to remain constant and the differences between limit cycles at different time instances will purely be a function of the time delay/sensorimotor loop delay which indirectly is likely a measure of the severity of the disease.

VI. DISCUSSION

As discussed in section II, the delay and saturation are directly related to the area of the limit cycle. But we note that if the system parameters are constant (which is bound to be for a specific patient) but the controller gains change (which is again plausible for a human), then we may see an effect in the area of the limit cycle. With the servo motor control setup, Figure 12 shows an increase in the area of the limit cycle as the controller gains $K_p$ and $K_d$ are increased. Hence, in addition to the delay and saturation, in reality, there may be other factors that effect the area and aspect ratio of the limit cycle, and hence further development is needed before the above ideas can be turned into a successful diagnostic tool.

Finally, the next step would be to further validate these observations and ideas using data from Parkinson’s patients.

VII. CONCLUSIONS

By using two table top experiments and introducing a delay in the closed-loop, we were able to recreate and validate several observations relating to Parkinson’s disease (both from simulations studies and from clinical observations). We were able to reproduce limit-cycle oscillations representing rest tremors and explore the effect of the delay and link it with the severity of the disease. We then discussed ways to model the delay that can be used for early diagnosis. Finally, tests with real patients are needed to further validate these ideas.

REFERENCES