Neuron Growth Output-Feedback Control by PDE Backstepping

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Abstract—Neurological injuries predominantly result in loss of functioning of neurons. These neurons may regain function after medical therapeutics, such as Chondroitinase ABC (ChABC), that promote axon elongation by manipulating the extracellular matrix, the network of extracellular macromolecules and minerals that control the tubulin protein concentration. We introduce an observer for the concentration of unmeasured tubulin along the axon, as well as in the growth cone, using the measurement of the axon length and the tubulin flux at the growth cone. We employ this observer in a boundary control law which actuates the tubulin concentration at the soma (nucleus), i.e., at the end of the axon distal from the measurement location. For this PDE system with a moving boundary, coupled with a two-state ODE system, we establish global exponential convergence of the observer and local exponential stabilization of the [axon, observer] system in the spatial $\mathcal{H}_1$-norm. The results require that the axon growth speed be bounded. For an open-loop observer, this is ensured by assumption (which requires that tubulin influx at the soma be limited), whereas for the output-feedback system the growth rate of the axon is ensured by assuming that the initial conditions of all the states, including the axon length, be sufficiently close to their setpoint values.

I. INTRODUCTION

Neuroscience is an interdisciplinary field studying how neurons perceive information and investigating nervous system-related damage [12], [23], [21]. Disorders and impairments, such as Parkinson’s disease, Alzheimer’s disease, and spinal cord injuries typically result from the loss of functionality of neurons, including the cessation of elongation [18], [7], [17]. Treatments such as ChABC can heal neurons and enable them to resume their activities [14], [2]. Essentially, this therapy manipulates the extracellular matrix (ECM) to regulate the activity of neurons as desired [11].

Neurons receive and transmit electrical signals containing perceptual information. This process begins when a signal enters the dendrites of a postsynaptic neuron. Then, the signal is transported through the axon. During transmission, the growth cone, located at the end of the axon, seeks the chemical cues to detect the neuron that will receive the signal [13]. After detecting the direction, tubulin dimers and monomers assemble to create microtubules which extend the axon with the assistance of ECM [1]. Hence, tubulin concentration dynamics in the axon are the primary regulator of axon elongation. These dynamics express the following behaviors: tubulin production in the soma, assembly and disassembly of microtubules in the axon, and the transportation process along the axon and in the growth cone [9]. Recent preclinical studies show that manipulation of ECM controls the axon growth, by which the tubulin concentration is controlled [4].

Researchers proposed different mathematical models to explain axon growth by considering the behavior of tubulin. One pioneering mathematical model describes the polymerization of tubulin [5]. In another model, the authors propose tubulin transportation as diffusion and include axon growth due to polymerization [26]. A PDE model of axon growth is presented in [20], and its stability properties are defined in [19]. Another axon growth model introduces a coupled PDE-ODE with a moving boundary and gives numerical results for tubulin concentration along the axon [10].

Besides computational purposes, the coupled PDE-ODE axon growth model has also begun to be studied from a control-theoretical perspective to stabilize axon growth [8]. Recent enhancements to the boundary control of PDEs have motivated researchers in different fields [16]. The contribution of [22] has introduced the method of successive approximation to obtain solutions to kernel PDEs by using Volterra type of transformation. These groundbreaking studies have extended the type of systems accompanying boundary control to the class of coupled PDE-ODE systems [24], [25]. While almost all of the studies dealt with a constant domain size in time, the authors of [15] developed a backstepping design for a parabolic PDE with a moving boundary, called the Stefan problem. In addition, recent research considers nonlinear PDE systems and proves the stability results in a local sense [6], [3]. While the results for local stabilization in nonlinear PDE systems have been achieved for hyperbolic PDEs, an output-feedback stabilization for the coupled nonlinear parabolic PDE-ODE with a moving boundary has not been studied.

This paper presents the output-feedback stabilization for the tubulin concentration model associated with axon growth dynamics. We obtain the linearized reference error system by considering the error variable from the steady-state solution of the system in the plant dynamics for a given desired axon length. We apply linearization to ODE state to deal with algebraic nonlinearity. By setting the measured output of the system as the axon length and the change of the tubulin concentration in the growth cone, we design an observer to estimate the plant state with an observer gain obtained by the kernel functions via the backstepping technique. These kernels are not analytically solvable, so we apply the method of successive approximation to guarantee the well-posedness of the solution. We rigorously prove the global stability for the observer error system and the local stability result.
for the closed-loop system with the output-feedback control
following the similar procedure to [8]. Numerical simulation
is performed to investigate the performance of the proposed observer
and output-feedback control designs, which illustrates
the desired performance in both the regulation of the
axon growth and the estimation of the tubulin concentration.

The paper is structured as follows. Section II introduces
the coupled PDE-ODE system with a moving boundary
modeling the tubulin concentration and the axon growth. Section
III presents the observer design via backstepping method, and
the stability analysis of the estimation error system. Section
IV proposes the observer-based output-feedback control
and the stability proof of closed-loop system. Section V provides
the simulation result for the closed-loop system using the
verified physical parameters. Section VI concludes the paper.

II. MODELING OF AXON GROWTH

This section presents the mathematical model of the axon
elaboration process governed by a coupled PDE-ODE with
a moving boundary. In this model, the concentration of tubulin
protein along the axon controls the growth of a newborn
axon. There are two underlying assumptions for modeling the
axonal growth given here: (i) the tubulin protein is entirely
responsible for the growth of an axon, (ii) and free tubulin
molecules are modeled as homogeneously continuous.

Let \( l(t) \) denote axon length, \( x \) denote the one-dimensional
coordinate along the axon, and \( c(x, t) \) denote the tubulin
concentration along this one-dimensional coordinate. The
subscripts \( c \) and \( s \) stand for growth cone and soma, respectively. That is, \( c_c(t) \) and \( c_s(t) \) represent the tubulin
concentration in the growth cone and soma, as shown in
Fig. 1. Free tubulin proteins move with the constant
velocity \( a \), and diffuse with the diffusivity constant \( D \),
the degradation along the axon occurs with the constant rate \( g \).
The constant \( l_c \) is the growth ratio of growth cone, \( r_g \)
and the chemical reaction rate of free tubulin monomers and dimers
to create microtubules. Thus, the tubulin dynamics associated with
the dynamics of the axon length are described as

\[
\begin{align*}
ct &= Dc_{xx}(x, t) - ac_x(x, t) - gc(x, t), \quad (1) \\
c_x(0, t) &= -q_s(t), \quad (2) \\
c(l(t), t) &= c_c(t), \quad (3) \\
l_c \dot{c}_c(t) &= (a - gc)(c_c(t) - Dc_x(l(t), t)) \\
&\quad - (r_g c_c(t) + r_g l_c(c_c(t) - c_s)) \quad (4)
\end{align*}
\]

\[
\begin{align*}
\dot{l}(t) &= r_g(c_c(t) - c_s), \quad (5)
\end{align*}
\]

where \( r_g \) is a lumped parameter introduced in [9], \( c_s \)
is an equilibrium concentration in the cone and \( q_s(t) \) is the
concentration flux of tubulin in the soma.

Let \( c_{eq}(x) \) be the tubulin concentration profile for a given
constant axon length \( l_\alpha \) the solution of which is given in
[10]. Let \( u(x, t), z_1(t), z_2(t), \) and \( U(t) \) be the reference
error states and input defined below:

\[
\begin{align*}
\hat{u}(x, t) &= c(x, t) - c_{eq}(x), \quad U(t) = -(q_s(t) - q^*_s) \quad (6) \\
z_1(t) &= c_c(t) - c_s, \quad z_2(t) = l(t) - l_\alpha \quad (7)
\end{align*}
\]

By subtracting the steady-state solution from (1)-(5), and
using (6)-(7), we obtain the reference error system as in [8].
The reference error system has algebraic nonlinearity in ODE
of the dynamics, so the linearization technique (defined in
[15]) is applied to deal with the nonlinearity. Then, we obtain the
following dynamics (see Section 12-2 in [15]):

\[
\begin{align*}
\hat{u}(x, t) &= D\hat{u}_{xx}(x, t) - a\hat{u}_x(x, t) - g\hat{u}(x, t), \quad (8) \\
u_x(0, t) &= U(t), \quad (9) \\
u(l(t), t) &= H^T X(t), \quad (10) \\
\dot{X}(t) &= AX(t) + Bu_x(l(t), t), \quad (11)
\end{align*}
\]

where \( X(t) = [z_1(t) \ z_2(t)]^T \) and
\[
A = \begin{bmatrix} \bar{a} & 0 \\ r_g & 0 \end{bmatrix}, \quad B = \begin{bmatrix} -\beta \\ 0 \end{bmatrix}, \quad H = \begin{bmatrix} \frac{1}{D} \\
\end{bmatrix}. \quad (12)
\]

Control Design Task: Develop an observer-based output-feedback control law for the input \( q_s(t) \) so that \( l(t) \) converges
to a desired (setpoint) axon length \( l_\alpha > 0 \), at least starting
from \( c(x, 0) \) sufficiently near \( c_{eq}(x) \) (in a suitable norm in
\( x \)) and \( l(0) \) sufficiently near \( l_\alpha \).

III. STATE ESTIMATION DESIGN

In this section, we state the assumptions on the axon length
and propose the first major theorem with providing its proof.

Assumption 1. The axon length \( l(t) \) maintains positive and
is upper bounded, i.e., there exists a positive constant \( \bar{l} \) such that the following inequality for all \( t \geq 0 \) holds:

\[
0 < l(t) \leq \bar{l}. \quad (13)
\]

Assumption 2. The time derivative of the axon length is also
bounded, i.e., there exists a positive constant \( \bar{v} \) such that the following inequality for all \( t \geq 0 \) holds:

\[

|\ddot{l}(t)| \leq \bar{v}. \quad (14)
\]

Before we state our major theorem, we define the \( H_1 \)-
norm as \( \|f(\cdot, t)\|_{H_1} = \sqrt{\int_0^l f^2(\cdot, t) + f_s^2(\cdot, t) \, dx} \) and
\[
\|f(\cdot, t)\|^2 := \int_0^l f(x, t)^2 \, dx.
\]

Theorem 1. Let Assumptions 1 and 2 hold. Consider the plant (8)-(11) and the available measurements

\[
y_1(t) = u_s(l(t), t), \quad y_2(t) = CX(t) \quad (15)
\]

where \( C = [0 \ 1] \). Also, consider the observer designed as

\[
\hat{u}_x(x, t) = D\hat{u}_{xx}(x, t) - a\hat{u}_x(x, t) - g\hat{u}(x, t) + p_s(x, l(t)) (u_x(l(t), t) - \hat{u}_s(l(t), t)), \quad (16)
\]

\[
\hat{u}_s(0, t) = U(t), \quad (17)
\]

\[
\hat{u}(l(t), t) = H^T X(t), \quad (18)
\]

\[
\dot{X}(t) = AX(t) + Bu_x(l(t), t) + LC(X(t) - \hat{X}(t)), \quad (19)
\]

Fig. 1: Schematic of neuron and state variables
where \( x \in [0, l(t)] \), \( L \) is chosen to make \((A - LC) \) Hurwitz, and the observer gain \( p_1(x, l(t)) = DP(x, l(t)) \) where \( P(x, l(t)) \) is the solution to the following PDE
\[
DP_{yy}(x, y) - DP_{xx}(x, y) + aP_y(x, y) = \lambda P(x, y), \quad (20)
\]
where \( \lambda > 0 \) is an arbitrary constant, and \( \gamma_1 \) is a constant satisfying \( \frac{D}{2} \leq \gamma_1 \). Then, the observer error system is exponentially stable in \( H_1 \)-norm, i.e., there exist positive constants \( M > 0 \) and \( \kappa > 0 \) such that the following norm estimate holds:
\[
\tilde{\Phi}(t) \leq M \tilde{\Phi}(0)e^{-\kappa t}, \quad (23)
\]
where \( \tilde{\Phi}(t) := ||u - \tilde{u}||_{H_1} + |X - \tilde{X}| \).

Theorem 1 is proved in the remainder of this section.

A. Observer design and backstepping transformation

1) Observer design and observer error system: Then, we define the observer error state as
\[
\tilde{u}(x, t) = u(x, t) - \tilde{u}(x, t), \quad \tilde{X}(t) = X(t) - \tilde{X}(t). \quad (24)
\]
Subtracting the observer system (16)-(19) from the plant (8)-(11), the observer error dynamics is obtained as
\[
\tilde{u}_t(x, t) = D\tilde{u}_{xx}(x, t) - a\tilde{u}_x(x, t) - g\tilde{u}(x, t) + p_1(x, l(t))\tilde{u}_x(l(t), t), \quad (25)
\]
\[
\tilde{u}_x(0, t) = 0, \quad (26)
\]
Taking the time and spatial derivatives of (29) together with the solution of (30)-(32), we obtain (20)-(22), and by choosing \( P(x, y) = \tilde{P}(x, y)e^{\gamma_1(l(t))} \), (20)-(22) become
\[
\tilde{P}_{yy}(x, y) - \tilde{P}_{xx}(x, y) = \frac{\lambda}{2D} \tilde{P}(x, y), \quad (35)
\]
\[
\tilde{P}(x, x) = e^{-\frac{\gamma_1}{2}x} \left( \frac{\lambda}{2D} x + \gamma_1 \right), \quad (36)
\]
\[
\tilde{P}_x(0, y) = \frac{a}{2D} \tilde{P}(0, y), \quad (37)
\]
which cannot be obtained. By applying the procedure in the previous section, we have the bound as \( |Q(x, y)| \leq Me^{2Mx} \).

B. Kernel PDE analysis by successive approximations

The method of successive approximations is applied to prove that (35)-(37) is well-posed. First, we apply the following change of spatial coordinate \( \bar{x} = y, \bar{y} = x \), and \( P^*(\bar{x}, \bar{y}) = P(x, y) \). Then, we have
\[
P_{xx}^*(\bar{x}, \bar{y}) - \frac{\lambda}{2D} P^*(\bar{x}, \bar{y}) = \frac{\lambda}{2D} P^*(\bar{x}, 0), \quad (38)
\]
\[
P_{xx}^*(\bar{x}, \bar{y}) = e^{-\frac{\gamma_1}{2}x} \left( \frac{\lambda}{2D} x + \gamma_1 \right), \quad (39)
\]
\[
P_y^*(\bar{x}, 0) = \frac{a}{2D} P^*(\bar{x}, 0). \quad (40)
\]

To convert this PDE to integral equation, we introduce \( \xi = \bar{x} + \bar{y}, \eta = \bar{x} - \bar{y} \), \( P^*(\bar{x}, \bar{y}) = G(\xi, \eta) \) where \( (\xi, \eta) \in T_1 \) defined as \( T_1 = \{\xi, \eta : 0 < \xi < 2l(t), 0 < \eta < \min(\xi, 2l(t) - \xi)\} \). The conditions (38)-(40) are rewritten with respect to \( G \) as
\[
G_{\xi\eta}(\xi, \eta) = \frac{\lambda}{8D} G(\xi, \eta), \quad (41)
\]
\[
G_\xi(\xi, 0) = e^{-\frac{a}{4D} \xi} \left( \frac{\lambda}{4D} \xi + \gamma_1 \right), \quad (42)
\]
\[
G_\xi(\xi, \xi) - G_\eta(\xi, \xi) = \frac{a}{2D} G(\xi, \xi). \quad (43)
\]

By applying the method of successive approximation, the solution to (41)-(43) is obtained. By following the procedure described in [22], we get \( G(\xi, \eta) \) is bounded and unique, so
\[
|P(x, y)| \leq Me^{2Mx}, \quad (44)
\]
where \( 0 < M < \bar{M} \) which guarantees the boundedness of the solution to (20)-(22).

C. Direct backstepping transformation

We use the following direct backstepping transformation
\[
\tilde{w}(x, t) = \tilde{u}(x, t) - \int_{x}^{l(t)} Q(x, y) \tilde{u}(y, t) dy. \quad (45)
\]

By applying (45) to the observer error system (25)-(28) and the target system (30)-(33), the conditions for the kernel function are obtained and to make sure the well-posedness of the solution to the kernel PDE, we write the conditions in the form of (38)-(40) which is well-posed, so the solution of \( Q(x, y) \) exists, which means direct transformation exists. As it is the case in the inverse transformation, the closed-form solution cannot be obtained. By applying the procedure in the previous section, we have the bound as \( |Q(x, y)| \leq Me^{2Mx} \).
D. Stability analysis of observer error system

We consider the following Lyapunov function
\[ \dot{V} = \dot{V}_{11} + \dot{V}_{12} + d_2 \dot{V}_2 + \frac{\gamma_1}{2} \tilde{w}^2(0, t)^2, \]
\[ \dot{V}_{11} = \frac{1}{2} d_1 ||\tilde{w}||^2, \quad \dot{V}_{12} = \frac{1}{2} ||\tilde{w}_x||^2, \quad \dot{V}_2 = \tilde{X}(t)^T P \tilde{X}(t), \]
where \( d_1, \ d_2 > 0 \) and \( P > 0 \) is a positive definite matrix satisfying the Lyapunov equation for some positive definite matrix \( Q \):
\[ (A - LC)^T P + P(A - LC) = -Q, \]
(48)

Then, we state the following lemma.

**Lemma 1.** Assume that (13) and (14) are satisfied for
\[ \tilde{w} = \min \left\{ \frac{D}{8t^2}, \frac{g + \lambda}{2\gamma_1} \right\}, \]
for all time \( t \geq 0 \). Then, we conclude that for sufficiently large enough \( d_1 > 0 \) and \( d_2 > 0 \), there exists a positive constant \( \alpha_1 = \min \left\{ d_1 \frac{D}{2}, d_1 (D + 2\lambda), (g + 2\lambda) \frac{\lambda_{\min}(Q)}{\lambda_{\max}(P)} \right\} \)
which satisfies the following norm estimates
\[ \dot{V} \leq -\alpha_1 \dot{V}. \]

**Proof.** Taking the time derivative of the Lyapunov functions along the target system (30)-(33), and applying Young’s, and Agmon’s inequalities, we get
\[ \dot{V} \leq -\frac{D}{2} ||\tilde{w}_x||^2 - d_1 \frac{D\gamma_1}{2} \tilde{w}(0, t)^2 - d_1 (g + \lambda)||\tilde{w}||^2 + \frac{\tilde{v} \epsilon_2}{2} ||\tilde{w}||^2 - \left( d_1 D + (g + \lambda) - \frac{2d_1}{D} - \frac{\epsilon_2}{2} \right) ||\tilde{w}_x||^2 - \gamma_1 \tilde{w}(0, t) \tilde{w}_x(0, t) + d_2 \tilde{v}_x \tilde{X}(t)^2 + \frac{\tilde{v}}{2} L_2 \tilde{v}^2 + \frac{d_1}{2}\frac{\tilde{v}}{2}\tilde{v}_x \tilde{X}(t)^2 + \left( \frac{d_1^2}{2\epsilon_2} + d_1 \frac{a}{2} + d_1 \frac{\tilde{v}}{2} + (g + \lambda) \right) \lambda_{\max}(HH^T) + \frac{1}{2\epsilon_2} \lambda_{\max}((H^T(A - LC))^2) ||\tilde{X}(t)||^2, \]
(51)

where \( \epsilon_i > 0 \) for \( i = 1, \ldots, 5 \) are arbitrarily small constants. We denote that \( F(x, \tilde{X}(t)) = F(x, \tilde{X}(t) + L_1)H^T \tilde{X}(t) - Q(x, \tilde{X}(t) + L_1)H^T \tilde{X}(t) \). Then, there exists positive constants \( L_1 > 0 \), for \( i = 1, 2, 3, 4 \), we have \( F(0, \tilde{X}(t))^2 \leq L_1 X^2 \), \( F(0, \tilde{X}(t))^2 \leq L_2 |\tilde{X}(t)|^2 \), \( \int_0^{l(t)} F_x(x, \tilde{X}(t))^2 dx \leq L_3 |\tilde{X}|^2 \), and \( \int_0^{l(t)} F_x(x, \tilde{X}(t))^2 dx \leq L_3 |\tilde{X}|^2 \). We also recall
\[ \lambda_{\min}(P)X^T X \leq \lambda_{\max}(P)X^T X, \]
(52)

where \( \lambda_{\min}(P) > 0 \) and \( \lambda_{\max}(P) > 0 \) are the smallest and the largest eigenvalues of \( P \). The constants \( d_1 \) and \( d_2 \) are
\[ d_1 \geq \frac{2a^2 + D\tilde{v}e_7}{D^2}, \]
\[ d_2 \geq \frac{2}{\lambda_{\min}(Q)} \left( \left( \frac{D}{2e_1} + d_1 \frac{a + \tilde{v}}{2} \right) \lambda_{\max}(H^TH) \right. \]
\[ + \left. \frac{(g + \lambda) \lambda_{\max}(H^TH) + \lambda_{\max}((H^T(A - LC))^2)}{2\epsilon_2} \right) + \left( \frac{d_1}{2} L_1 + \frac{1}{2\epsilon_4} L_2 + \frac{d_1}{2} L_3 + \frac{1}{2\epsilon_7} L_4 \right)^2 \right) \]
(54)

by recalling \( \gamma_1 \geq \frac{D}{\epsilon_7} \). Thus, one can show that (51) leads to
\[ \dot{V} \leq -d_1 \frac{\gamma_1}{2\lambda_{\min}(Q)} \tilde{w}(0, t)^2 - d_1 (D + 2\lambda) \tilde{V}_{12} - (g + 2\lambda) \tilde{V}_{11} - d_2 \lambda_{\max}(P) \tilde{V}_2 \]
\[ \leq -\alpha_1 \dot{V}. \]
(55)

Thus, Lemma 1 holds.

**Theorem 2.** Consider the closed-loop system (8)-(11) with the measurements (15), and the observer (16)-(19) under the output-feedback control law:
\[ U(t) = \frac{D\gamma_2 - \beta}{D} \tilde{u}(0, t) - \phi(\tilde{l}(t)^T - \gamma_2 \phi(\tilde{l}(t)^T \tilde{X}(t) - \frac{1}{D} \int_0^{l(t)} (\phi(y)^T - \gamma_2 \phi(y)^T) B\tilde{u}(y, t) dy \]
(56)

where \( \gamma_2 \geq \frac{D}{\epsilon_7} \) and \( \phi(x) \) is
\[ \phi(x)^T = \begin{bmatrix} H^T & K^T \end{bmatrix} e^{N_1 x} \begin{bmatrix} 0 \\ 1 \end{bmatrix}. \]
(57)

The matrices \( K = [k_1 \ k_2] \) and \( N_1 \in \mathbb{R}^{4 \times 4} \) is defined as
\[ N_1 = \begin{bmatrix} 0 & \frac{1}{D} (gI + A + \frac{a}{D} B^TH^T) \\ I & \frac{1}{D} (B^TH^T + aI) \end{bmatrix}, \]
(58)
where \( k_1 > \frac{\bar{a}}{L} \), and \( k_2 > 0 \). Then, there exist positive constants \( \bar{M} > 0 \), \( \kappa > 0 \) and \( \zeta > 0 \) such that if \( \Phi(0) < \bar{M} \) where \( \Phi(t) := ||u||_{H^1}^2 + ||\hat{u}||_{H^1}^2 + ||\hat{X}||^2 \), then the following norm estimate holds:

\[
\Phi(t) \leq \zeta \Phi(0) \exp(-\kappa t) .
\]

(59)

The closed-loop system is locally stable in \( H_1 \)-norm.

A. Backstepping transformation

The following direct and inverse transformations from \((\hat{u}, \hat{X})\) into \((\hat{w}, \hat{X})\) is implemented by using the gain kernels derived in [8]

\[
\hat{w}(x, t) = \hat{u}(x, t) - \int_x^{l(t)} k(x, y) \hat{u}(y, t) dy - \phi(x - l(t))^T \hat{X}(t),
\]

(60)

\[
\hat{u}(x, t) = \hat{w}(x, t) + \int_x^{l(t)} q(x, y) \hat{w}(y, t) dy + \phi(x - l(t))^T \hat{X}(t).
\]

(61)

Taking the time and spatial derivatives of the transformation above, the target \( \hat{w} \)-system is obtained as

\[
\hat{w}_t = D\hat{w}_{xx} - a\hat{w}_x - g\hat{w} + \hat{l}(t)E(x, \hat{X}(t)) + p_1(x, l(t))\tilde{u}_x(l(t), t),
\]

(62)

\[
\hat{w}_x(0, t) = \gamma_2 \hat{w}(0, t),
\]

(63)

\[
\hat{w}(l(t), t) = 0,
\]

(64)

\[
\hat{X}(t) = (A + BK)\hat{X}(t) + B\hat{w}_x(l(t), t) + B\hat{u}_x(l(t), t) + LC\hat{X}(t),
\]

(65)

where we denote \( E(x, \hat{X}(t)) = \phi(x - \hat{X}(t) - l) - k(x, \hat{X}(t) + l)^T \hat{X}(t) \). By evaluating the spatial derivative of (60) at \( x = 0 \), we derive the control law as in (56).

B. Stability analysis

Define the Lyapunov functions for the observer as

\[
\hat{V}_{11} = \frac{1}{2} d_3 ||\hat{w}||^2, \quad \hat{V}_{12} = \frac{1}{2} ||\hat{w}_x||^2, \quad \hat{V}_2 = \hat{X}(t)^T \hat{P} \hat{X}(t).
\]

(66)

Lyapunov function of closed-loop system is written as

\[
\hat{V}_{tot}(t) = c_1 \left( d_1 ||\hat{w}||^2 + ||\hat{w}_x||^2 \right) + c_2 \left( d_3 ||\hat{w}||^2 + ||\hat{w}_x||^2 \right) + c_3 \left( \hat{X}(t)^T \hat{P} \hat{X}(t) \right) + c_4 \left( \gamma_1 \hat{w}(0, t)^2 + \gamma_2 \hat{w}(0, t)^2 \right).
\]

(67)

where \( c_1 > 0 \) is chosen to sufficiently large. Then, we state the following lemma.

**Lemma 2.** Let Assumptions 1 and 2 hold with

\[
\bar{\psi} \leq \min \left\{ \frac{g}{3\bar{\gamma}_2}, \frac{D}{8\bar{\gamma}_2}, \frac{g + \lambda}{2\bar{\gamma}_1} \right\},
\]

(68)

for all time \( t \geq 0 \). Then, for sufficiently large enough \( d_3 > 0 \) and \( d_4 > 0 \), there exists a positive constant \( \alpha > 0 \) and \( \beta > 0 \) such that the following norm estimates holds

\[
\hat{V}_{tot} \leq -\alpha \hat{V}_{tot} + \beta \hat{V}_{tot}^{3/2}.
\]

(69)

**Proof.** By applying Young’s, Cauchy-Schwarz, Poincare’s, and Agmon’s inequalities, with the help of Assumption 1 and 2, and following the same strategy that is offered in the [8] for the Lyapunov analysis, one can derive (69) for

\[
\alpha = \min \left\{ \frac{1}{2}, d_3 \frac{D}{2}, \frac{g}{2}, \frac{\lambda}{\lambda_{\max}(P)} \right\},
\]

(70)

\[
\beta = \frac{r_g e_1^T}{\lambda_{\min}(P)} \left( \frac{1}{2} L_5 + \frac{1}{2} L_6 + \frac{1}{2} L_7 + \frac{1}{2} L_8 \right),
\]

(71)

where \( e_3 \leq \frac{\bar{a}}{\bar{\psi}} \) such that Lemma 2 holds.

To prove local stability, Lemma 2 from [8] guarantees the convergence to the origin. If the \( M \) holds for some \( M > 0 \), then \( |X| < r \). Lemma 3 from [8] proves that if \( (69) \), if \( V_{tot}(0) < M \), then \( V_{tot}(t) < M \) for all \( t > 0 \). In addition, \( \hat{l}(t) \) can be written as \( \hat{l}(t) = r_g e_1^T X(t) \), so we can bound \( \hat{l}(t) \) to handle in the normal equivalence as

\[
|\hat{l}(t)| \leq r_g e_1^T \left( \frac{\hat{V}_2}{\lambda_{\min}(P)} + \frac{\hat{V}_2}{\lambda_{\min}(P)} \right).
\]

(72)

This leads us \( |\hat{l}(t)|^2 \leq \delta^2 V_{tot}(t) \). Thus,

\[
V_{tot}(t) \leq V_{tot}(0) \exp\left(-\frac{\alpha}{2} t\right).
\]

(73)

The norm equivalence between the target and original systems is shown using the direct and inverse transformations. Taking square of (29), (45), (60), and (61) and applying Young’s and Cauchy-Schwarz inequalities, one can get the norm inequalities for the target system \( (\hat{w}, \hat{w}_x, \hat{w}, \hat{w}_x) \). Let \( \Psi = ||\hat{w}||_{H^1}^2 + ||\hat{X}\|^2 + ||\hat{u}||_{H^1}^2 \). Using the norm inequalities for \( \Psi \) and (67), one can obtain \( \bar{M} \Psi(t) \leq V_{tot}(t) \leq \bar{M} \Psi(t) \) holds. Therefore, we get

\[
\Psi(t) \leq \bar{M} \exp\left(-\frac{\alpha}{2} t\right) \Psi(0).
\]

(74)

Now, we apply the norm equivalence argument to the transformations between the target system and the original system by using (6) and (7). Let \( \Phi(t) = ||u||_{H^1}^2 + ||\hat{u}||_{H^1}^2 + ||\hat{X}||^2 \) so, one can obtain \( \bar{N} \Psi(t) \leq \Psi(t) \leq \bar{N} \Psi(t) \). Therefore, we get

\[
\Phi(t) \leq \frac{\bar{N}}{\bar{N}} \exp\left(-\frac{\alpha}{2} t\right) \Phi(0).
\]

(75)

Since the backstepping transformations are invertible, the local stability of \((\hat{u}, \hat{X}, \hat{w}, \hat{X})\) guarantees the local stability of \((u, X, \hat{u}, \hat{X})\), which completes the proof of Theorem 2.

V. NUMERICAL SIMULATION

Numerical simulation is performed for the plant (8)-(11), and observer (16)-(19) with a designed control law (56). We use the biological constants proposed in [10], as shown in Table I. The initial conditions for the plant are set as \( c_0(x) = 2c_\infty \) for tubulin concentration along the axon, and

| Parameter | Value | Parameter | Value |
|-----------|--------|-----------|--------|
| \( D \)   | \( 10 \times 10^{-9} m^2/s \) | \( r_g \) | 0.053 |
| \( a \)   | \( 1 \times 10^{-9} m^2/s \) | \( \gamma \) | 10^4 |
| \( g \)   | \( 5 \times 10^{-7} s^{-1} \) | \( l_c \) | 4 \mu m |
| \( r_g \) | \( 1.783 \times 10^{-5} m^3/(mols) \) | \( l_s \) | 12 \mu m |
| \( c_\infty \) | 0.0119 mols/m^3 | \( l_0 \) | 1 \mu m |
The axon length converges to the desired length.

The estimated tubulin concentration, $c_o(x,t) = \hat{u}(x,t) + c_{eq}(x)$, generated by the observer in (16)-(19) and shown in Fig. 2, converges all along the axon to the actual, unmeasured concentration $c(x,t)$ by about $t = 0.75$ min. Thereafter, both $c_o$ and $c$ converge together to the steady-state $c_{eq}(x)$ from $t = 0.75$ min till about $t = 2$ min. Note that $c_o$ converges to $c$ faster than $c$ converges to $c_{eq}$ and faster than $l$ converges to $l_0$.

Fig. 3: Closed-loop output-feedback response.

Fig. 3a shows that the axon length converges to the desired axon length $l_0$. Fig. 3b illustrates that the observer states converge to the actual tubulin concentration, by which the estimation of the tubulin concentration along the axon is achieved. The tubulin concentration along the axon converges to the steady-state solution, which demonstrates the effectiveness of the proposed output-feedback control law.

VI. CONCLUSIONS

This study proposes a novel output-feedback control for a coupled PDE-ODE dynamics with a moving boundary for neuron growth model by applying the PDE backstepping technique. We propose a PDE-observer and an output-feedback controller for axon elongation problem by designing an observer gain via backstepping, and show the stability analysis to estimate the unknown states in the plant dynamics. Finally, we verify our theoretical results in the simulation results using the biological parameters.

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