Neurongrowth control and estimation by PDE backstepping✩

Cenk Demir a,⁎, Shumon Koga b, Miroslav Krstic a

a Department of Mechanical and Aerospace Engineering, University of California, San Diego, USA
b Department of Electrical and Computer Engineering, University of California, San Diego, USA

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A B S T R A C T

Neurological disorders, such as spinal cord injuries, Parkinson’s disease and Alzheimer’s disease, limit the functionality of neurons. A recent medical therapy, Chondroitinase ABC (ChABC), aims to cure these conditions by restoring neuron functionality through axon growth for damaged neurons by manipulating the extracellular matrix (ECM), the network of macromolecules and minerals that surrounds neurons and controls their activity, thereby neurons produce tubulin proteins which elongate the axon. This process is modeled as a Partial Differential Equation (PDE), which represents the behavior of the tubulin concentration along the axon, with a moving boundary governed by Ordinary Differential Equations (ODE) consisting of the dynamics of the axon length and tubulin concentration in the growth cone. This paper proposes nonlinear design methods for a state feedback control law, an observer, and an output feedback control law for a one-dimensional model of axonal elongation. First, we introduce a novel backstepping method to obtain the target system and the associated state feedback control law. Using a similar backstepping method, we design a nonlinear observer and prove the local exponential stability of the observer-error system in the spatial $\mathcal{H}_1$-norm. The resulting output-feedback control law ensures the local exponential stability of the closed-loop system composed of the estimation error and the reference error states. The performance of the designed control and estimation methods is demonstrated in numerical simulation for neuron elongation by up to three orders of magnitude. Robustness to parameter changes up to 40% relative to the design/analysis model is demonstrated.

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1. Introduction

Background. Neuroscience is a leading multidisciplinary field that draws interest from medical science, engineering, biology, mathematics and so on (Anderson, 2005; Dayan & Abbott, 2005; Izhikevich, 2007; Kandel et al., 2000; Lael Kirati, Arabi, Tadjine, & Zayane, 2013; Trappenberg, 2009). Each of these disciplines plays a role in understanding how neurons function, how they are structured, and how to cure neuron-based diseases (Ribar & Sepulchre, 2021; Squire et al., 2012). Neurons are the main cells in the nervous system whose objective is to obtain perception by transmitting electrical signals. This transmission process starts with the entry of a signal to the neuron from its dendrite and ends with sending the signal to another neuron from its growth cone. When a neuron receives a signal, the growth cone seeks chemical cues in the extracellular matrix. These molecules create a path for the neuron to find the target neuron where the signal will be transmitted (Diehl, Henningsson, Heyden, & Perna, 2014). After detecting the path, the axon of the transmitter neuron elongates towards that direction, and electrical signals propagate along the axon. Such elongation and propagation occur because of a specific protein called “tubulin” that extends the axon towards the target neuron. Free tubulin monomers and dimers assemble and create microtubules which form the neuron’s cytoskeleton. However, due to neurological disorders such as Alzheimer’s disease (Maccioni, Muñoz, & Barbeito, 2001), Parkinson’s disease (Dauer & Przedborski, 2003) and spinal cord injuries (Liu et al., 1997), neurons start to degenerate, which causes axon elongation to stop or to shrink. Recently developed therapies such as ChABC have promising potential to cure these disorders, specifically spinal cord injuries (Bradbury & Carter, 2011; Karimi-Abdolrezaee, Eftekharpour, Wang, Schut, & Fehlings, 2010). ChABC therapy involves injecting bacterial enzymes into the area where the degenerated neurons are located, which digest the axon growth inhibitors (Frantz, Stewart, & Weaver, 2010; Lee, McKeon, & Bellamkonda, 2010; Lemons, Howland, & Anderson, 1999). After this therapy, axon growth sustains for a short distance, starting from approximately 70 µm and extending to 274.5 µm for Dorsal Root Ganglia neurons, as reported in Day et al. (2020). However, this study does not

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provide any results related to long-distance axon regeneration, a crucial factor for achieving functional recovery in spinal cord injury, where growth spans from micrometers to millimeters. This mechanism motivates our design of the control law in this paper to enhance axon elongation, aiming to achieve desired lengths in both millimeters and micrometers.

The behavior of tubulin proteins is crucial to understanding and controlling axon growth. There are many models that describe the behavior of tubulin proteins in neurons. Van Veen and Van Pelt (1994) developed a nonlinear ODE model that describes tubulin production, transportation, formation, and axon elongation. Garcia-Grajales, Jerusalem, and Goriely (2017) also offer a computational model that links axon growth and the mechanics of membrane, but it only uses microtubule assembly and disassembly processes to create a model, and does not include the production of tubulin or tubulin transportation. In another model, axon elongation is modeled as a coupled diffusion–reaction–advection Partial Differential Equation (PDE) with a boundary governed by Ordinary Differential Equation (ODE) (McLean, van Ooyen, & Graham, 2004) by considering tubulin production and transportation besides microtubule assembly and disassembly processes. Following this research, McLean and Graham (2006) analyze the stability of this coupled model.

Boundary control of PDE systems has been intensively studied over the last two decades (Krstic & Smyshlyaev, 2008). Specifically, the utilization of the method of successive approximation in Smyshlyaev and Krstic (2004) for backstepping transformation has enabled to obtain numerical and symbolic solutions for kernel PDEs. Following this initial contribution, backstepping-based boundary control for PDEs has been extended to the class of coupled PDE–ODE systems (Krstic, 2009; Susto & Krstic, 2010; Tang & Xie, 2011). Although most studies including the aforementioned ones considered a constant domain size in time, several prior work have focused on the boundary control of the Stefan problem, formulated as a parabolic PDE with a moving boundary governed by ODE, see Chen, Bentsman, and Thomas (2020), Dunbar, Petit, Rouchon, and Martin (2003), Ecklebe, Woittennek, Frank-Rotsch, Dropka, and Winkler (2021), Maiti and Corrion (2014), Petit (2010), Petrus, Bentsman, and Thomas (2012) and Izadi, Abdollahi, and Dubljevic (2015) for instance. Recent study (Koga, Diagne, & Krstic, 2018; Koga & Krstic, 2020) has designed a backstepping-based control strategy for the Stefan problem, where the authors have provided the global stability results for the nonlinear closed-loop systems by virtue of the maximum principle. Based on the backstepping design, an event-triggered control for the Stefan problem has been also developed in Rathnayake and Diagne (2022). On the other hand, the local stability results for nonlinear hyperbolic PDEs have been developed in several work (Buisson-Fenet, Koga, & Krstic, 2018; Coron, Vazquez, Krstic, & Bastin, 2013; Yu, Diagne, Zhang, & Krstic, 2020). However, without utilizing the maximum principle, even the local stability results had not been achieved for nonlinear parabolic PDEs with moving boundary besides our prior work (Demir, Koga, & Krstic, 2021).

In this paper, we consider the tubulin flux from soma to axon as the input, requiring specific state measurements for control law design. Practical implementation with such input is not straightforward, but is feasible through advanced methods such as fluorescence-based approaches and real-time live-cell imaging, as shown in Day et al. (2020) and Giacci et al. (2018).

Results. We ensure local regulation to the desired axon length, and to the corresponding tubulin equilibrium profile, by a state-feedback control law. We also provide a nonlinear observer and an observer-based output-feedback control law of the coupled PDE–ODE moving-boundary axon system.

First, a state-feedback control law under the measurement of tubulin concentration along the axon and axon length is constructed for a nonlinear plant by using a nonlinear backstepping transformation. With the proposed full-state feedback controller applied to the nonlinear plant dynamics, we show the local exponential stability of the closed-loop system composed of the axon length and tubulin concentration along the axon in $\mathcal{H}_1$-norm. Second, an exponentially stable nonlinear observer which successfully estimates the unmeasured tubulin concentration along the axon under an arbitrary control input, is constructed by using a novel nonlinear backstepping technique associated with the method of successive approximation. Finally, by using estimated states from the state estimator, and applying the designed feedback controller, the local exponential stability of the closed-loop system under the output feedback control scheme is proven. Specifically, the stability is obtained for the estimation error around zero, for the axon length around the desired set-point length, and for the tubulin concentration along the domain around the steady-state solution in $\mathcal{H}_1$-norm with explicitly given restrictions.

Contribution. With the recent discovery of axon regenerability as discussed in the background section, there is a significant potential for the application of control systems to regulate and guide this regeneration toward achieving desired outcomes. Consequently, this paper represents the pioneering research in the field of control systems related to axon regeneration, as it provides the design and analysis of control laws and observers for neuronal axon growth. This advancement is not only valuable for neuroscience. It also introduces methodological and theoretical advances in the control of the Stefan-type moving-boundary PDE–ODE systems. In our earlier work (Koga et al., 2018), where we developed control and state estimators for the classical Stefan model, the relation from heat flux at the phase interface to the position of the interface was of relative degree one. In our extension (Koga, Straub, Diagne, & Krstic, 2019), in which advection and reaction appear, as do in axon growth, the relative degree remained one. But in the axon growth, the relation arising at the growth cone, from protein flux to the axon end location, is of relative degree two. In addition, the ODE that represents the dynamics of tubulin concentration in the growth cone is nonlinear, whereas in the classical Stefan model, it is a simple integrator. The increase in the relative degree from one to two changes everything. First, the maximum principle for parabolic PDEs is no longer applicable, and global stability is not achievable. Second, not needing to meet the condition of the maximum principle, namely, that the inlet flux is above a certain value (analogous to the heat flux needing to be positive in the classical Stefan model of melting), comes as a blessing because there is no risk of model violation from the violation of the maximum principle. In physical terms, the model remains valid even if the axon is a little tubulin-starved relative to the equilibrium profile, since the tubulin equilibrium profile at the target length is strictly positive. So, local stability is not as catastrophic as in classical Stefan-type melting where, if stability is not global, island of solid may develop in the liquid domain Koga et al. (2018) and Koga et al. (2019). In the axon, slight undershooting of tubulin does not cause axon death.

While some of the contributions described above were previously presented only for the linearized system in our earlier works, such as Demir et al. (2021) and Demir, Koga, and Krstic (2022), our current contribution stands out as it both enhances and diverges significantly from our previous research in several key aspects:

- providing detailed stability analysis for a closed-loop system with coupled PDEs and nonlinear ODEs under state feedback control, without linearization,
Fig. 1. Schematic of neuron and state variables. Illustration created with BioRender (https://biorender.com).

- developing a novel nonlinear state observer and providing a comprehensive local stability analysis for both observer error and the output-feedback system,
- adding open-loop observer results, crucial for users focused on real-time tubulin estimation,
- illustrating theoretical findings via numerical simulations spanning short and long-range axon elongation across micrometer to millimeter scales, while also showcasing the robustness of the suggested output-feedback control strategy against parameter uncertainty (see Fig. 1).

Organization of the paper. The modeling of axon growth is presented in Section 2, and its full state-feedback controller with stability proof and simulations are constructed in Section 3. Section 4 provides a nonlinear observer design for axon growth by using the method of successive approximation, simulations, and stability proof of the proposed nonlinear observer. In Section 5, the observer-based output feedback control is introduced, simulations are performed and the stability proof of the closed-loop system is presented. Simulations to demonstrate the robustness of the proposed output-feedback control are given in Section 6. The paper ends with final remarks and future directions in Section 7.

Notation. Throughout the paper, norms on non-constant intervals are denoted as

\[
\|u(\cdot, t)\|_{L^2(0, l(t))} = \sqrt{\int_0^{l(t)} u(\cdot, t)^2 dx},
\]

\[
\|u(\cdot, t)\|_{H^1(0, l(t))} = \left( \int_0^{l(t)} u(\cdot, t)^2 + u'_x(\cdot, t)^2 dx \right)^{1/2}.
\]

2. Axon growth model: A moving-boundary PDE

Model of distributed tubulin concentration and axon length. Tubulin is a group of proteins responsible for the growth of axons. Two assumptions can be described to model this responsibility: Tubulins are modeled as a homogeneous continuum because free tubulin molecules are very small. Only tubulin is responsible for the growth of axon. With these assumptions, as proposed in Diehl, Henningsson, and Heyden (2016), Diehl et al. (2014), the axonal growth driven by a tubulin dynamics can be modeled as

\[
c_1(x, t) = DC_{\text{eq}}(x, t) - ac_1(x, t) - gc(x, t),
\]

\[
c_0(0, t) = q_1(t),
\]

\[
c(t, l) = c(t),
\]

\[
l(t) = c(t),
\]

\[
l(t) = \frac{d}{l_c}c(t) - l_c.
\]

where the tubulin concentration in the axon is \(c(x, t)\). Subscript \(s\) is used for the soma of the neuron, and subscript \(c\) is used for the cone of the neuron. The flux of concentration in the soma is represented as \(q_1(t)\) and the tubulin concentration in the cone is denoted as \(c(t)\). \(l(t)\) is the length of axon in \(x\)-coordinate. In (1), the constants \(g, D, a, \kappa\) represent tubulin degradation rate, tubulin diffusion constant, and tubulin velocity constant, respectively. The growth ratio is \(l(t) = \frac{V_c}{l_c}\) which depends on the cone cross-sectional area \(A\), and a volume of the growth cone \(V_c\). \(r_g\) is the reaction rate to create microtubules. \(r_g\) is the lumped parameter defined as \(r_g := \frac{\rho A}{r_s}\) where \(\rho\) is the density of assembled microtubules, and \(A\) is the effective area of created microtubules growth. \(c_{\text{eq}}\) is the equilibrium of the tubulin concentration in the cone. It causes the axon elongation to stop. We present the state feedback control problem next.

Control objective for the model. We pursue to drive the axon length to a given desired length \(l_s > 0\) by designing the state feedback control law of \(q_1(t)\). The associated steady-state solution \((c_{\text{eq}}(x), l_s)\) of the system (1)–(5) is then derived by considering an equilibrium of the tubulin concentration \(c_{\text{eq}}\). Thus, the control objective is formulated as

\[
\lim_{t \to \infty} l(t) = l_s,
\]

\[
\lim_{t \to \infty} c(x, t) = c_{\text{eq}}(x).
\]

Equilibrium profile of the model. We first obtain a steady-state solution of the concentration for a desired axon length \(l_s\). The steady-state solution of (1)–(5) is analytically solved as

\[
c_{\text{eq}}(x) = c_{\text{eq}}l_s e^{\lambda(x-l_s)} + c_{\text{eq}}l_s e^{-\lambda(x-l_s)},
\]

where

\[
\lambda_{\pm} = \frac{a \pm \sqrt{a^2 + 4Dg}}{2D}, \quad K_{\pm} = \frac{1}{2} \pm \frac{a - 2g}{2\sqrt{a^2 + 4Dg}}.
\]

The steady-state solution for the concentration flux in the soma, which is an input, is obtained as

\[
q_{s}^{*} = -c_{\text{eq}}(K_{+}l_{s}e^{\lambda_{+}(x-l_{s})} + K_{-}l_{s}e^{\lambda_{-}(x-l_{s})}).
\]

For readers who are interested, a comprehensive discussion of steady-state solutions for various parameters and their stability analysis can be found in Diehl et al. (2014).

Nonlinear error system. We introduce \(u(x, t), z_1(t), z_2(t)\), and \(U(t)\) as the reference error states and the reference error input, defined as

\[
u(x, t) := c(x, t) - c_{\text{eq}}(x),
\]

\[z_1(t) = c(t) - c_{\text{eq}}, \quad z_2(t) = l(t) - l_s,
\]

\[U(t) = -(q_1(t) - q_{s}^{*}).
\]

The reference error system is obtained by subtracting the steady-state solution (8) from the governing equations (1)–(5), resulting into

\[
u(x, t) = Du_{\text{eq}}(x, t) - au_{\text{eq}}(x,t) - gu(x, t),
\]

\[u_{\text{eq}}(0, t) = U(t),
\]

\[u(l(t), t) = c(t) - c_{\text{eq}}(l(t)),
\]

\[z_1(t) = a_1z_1(t) - \beta u_{\text{eq}}(l(t), t) - \kappa z_1(t)^2 + \beta_1 z_2(t),
\]

\[z_2(t) = r_g z_1(t),
\]

where the constants in (14)–(18) are

\[a_1 = \frac{\tilde{r}_g c_{\text{eq}}}{l_c} - g - \tilde{r}_g, \quad a_2 = c_{\text{eq}}(\lambda_{+}^2 K_{+} + \lambda_{-}^2 K_{-}),
\]

\[\beta = \frac{D}{l_c}, \quad \kappa = \frac{r_g}{l_c},
\]

(19)

(20)

(21)
and
\[ f_1(z_2(t)) = c_\infty \left( \frac{a-gl}{D} - K_+ \lambda_+ e^{l_z(t)} - K_- \lambda_- e^{-l_z(t)} \right) + \tilde{a}_2 z_2(t). \]

Let \( X \in \mathbb{R}^2 \) be an ODE state vector for the reference error states \( z_1(t) \) and \( z_2(t) \), defined by
\[ X(t) = [z_1(t) \ z_2(t)]^\top. \]

Rewriting the system (16)–(18) with respect to \( X(t) \), a nonlinear coupled PDE–ODE reference error system is given by
\[ u_i(x, t) = Du_i(x, t) - au_i(x, t) - gu_i(x, t), \]
\[ u_i(0, t) = U(t), \]
\[ u(l(t), t) = z_1(t) + \tilde{h}(z_2(t)), \]
\[ \dot{X}(t) = AX(t) + f(X(t)) + Bu_i(l(t), t), \]
where
\[ A = \begin{bmatrix} \tilde{a}_1 & \tilde{a}_2 \\ r_g & 0 \end{bmatrix}, \quad B = \begin{bmatrix} -\beta \\ 0 \end{bmatrix}. \]
\[ f(X(t)) = -K_+ z_2(t) + \tilde{h}(z_2(t)). \]
\[ \tilde{h}(z_2(t)) = c_\infty \left( 1 - K_+ e^{l_z(t)} - K_- e^{-l_z(t)} \right). \]

**Linearized error system.** Applying the linearization of \( X(t) \) around zero states to the nonlinear error system (23)–(26) leads to the following linearized reference error system:
\[ u_i(x, t) = Du_i(x, t) - au_i(x, t) - gu_i(x, t), \]
\[ u_i(0, t) = U(t), \]
\[ u(l(t), t) = H^T X(t), \]
\[ \dot{X}(t) = A_1 X(t) + Bu_i(l(t), t), \]
where the vector \( H \in \mathbb{R}^2 \) is defined as
\[ A_1 = \begin{bmatrix} \tilde{a}_1 & \tilde{a}_3 \\ r_g & 0 \end{bmatrix}, \quad H = \begin{bmatrix} 1 - \left( a - \frac{gl}{D} \right) \right. \]
\[ \tilde{a}_3 = \frac{a^2 - 2 \sigma_k w}{D}. \]

### 3. State-feedback control

#### 3.1. Backstepping

**Transformation into target system.** The state feedback control in this paper is designed by applying a backstepping transformation (Krstic & Smyslyhaev, 2008) to the linearized reference error system (30)–(33). The backstepping transformations and the associated gain kernel functions are given in the remainder of this section. Referring to Koga et al. (2018), we consider the following backstepping transformation
\[ w(x, t) = u(x, t) - \int_x^{l(t)} k(x, y) u(y, t) dy - \phi(x - l(t))^T X(t), \]
where \( k(x, y) \in \mathbb{R} \) and \( \phi(x - l(t)) \in \mathbb{R}^2 \) are the gain kernel functions to be determined. The desired target system for the linearized error system is proposed as
\[ u_i(x, t) = Du_i(x, t) - au_i(x, t) - gu(x, t) - \tilde{h}(l(t))F(x, X(t)), \]
\[ u_i(0, t) = \gamma u(0, t), \]
\[ u(l(t), t) = 0, \]
\[ \dot{X}(t) = (A_1 + BK^T) X(t) + Bu_i(l(t), t), \]
where \( K \in \mathbb{R}^2 \) is a feedback control gain vector chosen to make \( A_1 + BK^T \) Hurwitz. With the system matrices given in (27), by setting
\[ K = [k_1 \ k_2]^\top, \quad k_1 > \frac{\tilde{a}_1}{\beta}, \quad k_2 > \frac{\tilde{a}_3}{\beta}, \]
we obtain \( A_1 + BK^T \) Hurwitz. The redundant nonlinear term \( l(t)F(x, X(t)) \in \mathbb{R} \) in (36) is present due to the time-dependency of the moving boundary \( l(t) \) in the transformation (35), which is described by
\[ F(x, X(t)) = \left( \phi(x - l(t))^T - k(x, l(t))H^T \right) X(t). \]

**Gain kernel solutions.** By using the solution technique in Krstic (2009) and Tang and Xie (2011), taking the time and spatial derivatives of (35) together with the solution of (30)–(33), and substituting \( x = l(t) \) in both the transformation (35) and its spatial derivative, and by matching it with the target system (36)–(39), we have the following PDEs and an ODE for gain kernels.
\[ k_\alpha(x, y) - k_\beta(y, x) = \frac{a}{D} \left( k_\alpha(x, y) + k_\beta(y, x) \right), \]
\[ k_\alpha(x, y) + k_\alpha(x, x) = 0, \]
\[ k_\beta(y, l(t)) = -\frac{1}{D} \phi(x - l(t))B, \]
\[ D\phi''(x - l(t))^T - a \phi'(x - l(t))^T - \phi(x - l(t))^T (gl + A_1) - DK_\beta(y, l(t))H^T + ak(x, l(t))H^T = 0, \]
\[ \phi(0) = H, \]
\[ \phi'(0)^T = -\frac{1}{D} H^T BH^T + K^T. \]

The solution to (49)–(51) is given by (see Tang & Xie, 2011)
\[ \phi(x)^T = \left[ H^T \ K^T - \frac{1}{D} H^T BH^T \right] e^{lt} \begin{bmatrix} 1 \\ 0 \end{bmatrix}, \]
where the matrix \( N_1 \in \mathbb{R}^{4 \times 4} \) is defined as
\[ N_1 = \begin{bmatrix} 0 & \frac{1}{D} (gl + A_1 + \frac{a}{D} BH^T) \\ I & \frac{1}{D} (BH^T + al) \end{bmatrix}. \]

**Backstepping control law.** From the boundary condition (37) of the target system at \( x = 0 \) and the kernel solutions, we obtain the control law. Substituting \( x = 0 \) into the transformation (35) and its spatial derivative, and substituting (31), (37) and (48) into these equations, and setting the boundary condition (37), the control input is described as follows
\[ U(t) = \left( \frac{1}{D} H^T B + \gamma \right) u(0, t) - \frac{1}{D} \int_0^{l(t)} p(x)Bu(x, t)dx + p(l(t))X(t), \]
where \( p(x) = \phi'(-x)^T - \gamma \phi(x)^T. \) One can explicitly deduce the function \( p(x) \in \mathbb{R}^2 \) by using the kernel solution.
Fig. 2. The closed-loop response of the designed full-state feedback control system.

Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$D$</td>
<td>$10 \times 10^{-12}$ m$^2$/s</td>
<td>$r_h$</td>
<td>0.053</td>
</tr>
<tr>
<td>$a$</td>
<td>$1 \times 10^{-8}$ m/s</td>
<td>$\gamma$</td>
<td>$10^4$</td>
</tr>
<tr>
<td>$k$</td>
<td>$5 \times 10^{-7}$ s$^{-1}$</td>
<td>$l_i$</td>
<td>4 µm</td>
</tr>
<tr>
<td>$r_c$</td>
<td>$1.783 \times 10^{-5}$ m$^3$/(mol s)</td>
<td>$l_0$</td>
<td>12 µm</td>
</tr>
<tr>
<td>$c_\infty$</td>
<td>0.0119 mol/m$^3$</td>
<td>$l_\infty$</td>
<td>1 µm</td>
</tr>
</tbody>
</table>

3.2. Stability under full-state feedback

**Theorem 1.** Consider the closed-loop system consisting of the plant (23)–(26) with the control law (54). Suppose the control parameter $\gamma > 0$ is chosen to satisfy $\gamma \geq \frac{2}{D}$. Then, there exist $M > 0$, $c > 0$, and $\kappa > 0$, such that, if $Z(0) < M$ then the following norm estimate holds

$$Z(t) \leq cZ(0) \exp(-\kappa t),$$  \hspace{1cm} (55)

for all $t \geq 0$, in terms of the $H_1$-norm $$Z(t) = \|u(\cdot, t)\|_{H_1(0, l_i)} + X^T X,$$ \hspace{1cm} (56)

namely, the origin of the closed-loop systems is locally exponentially stable.

We prove this theorem in Section 3.4, as soon as we first illustrate it in a brief simulation section below.

3.3. Simulation: Axon elongation by up to three orders of magnitude

We perform simulations for the axon growth model by incorporating the biological parameters proposed by Diehl et al. (2014), which are shown in Table 1. The state-feedback controller remains unaffected by the desired length, denoted as $l_i$.

However, it is worth noting that the desired length is employed in the steady-state solution for the concentration flux in the soma, which serves as an input. In the simulation of the state-feedback control, as specified in (54), the initial conditions are set as $c_0(x) = 2c_\infty$ for tubulin concentration along the axon and $l_0 = 1$ µm for the axon length. The gain parameters of the closed-loop system are set as $k_1 = -0.1$, and $k_2 = 10^{13}$. When the state feedback control law is applied to the nonlinear dynamics in (1)–(2), the axon length, $l(t)$, successfully converges to the desired axon length, $l_i$ in Fig. 2(a). Moreover, Fig. 2(b) demonstrates that the tubulin concentration along the axon also converges to the equilibrium profile.

Simulations in Figs. 2(a) and 2(b) are informative to understand how the proposed control methods are effective in elongating the axon within one order of magnitude. However, axon lengths for inhibitory interneurons in the spinal cord are around 1 mm (Debanne, Campanac, Bialowas, Carlier, & Alcaraz, 2011). In Figs. 3(a) and 3(b), we apply our proposed state feedback controller to elongate the axon from the very small initial length, $l_0 = 1$ µm to three orders of magnitude of desired axon length, $l_s = 1$ mm for biological parameters in Table 1 and the equilibrium of the tubulin concentration in the cone, $c_\infty$. $c_\infty$ is chosen as $5.95 \times 10^{-3}$ mol/m$^3$. The state feedback control law is applied to the nonlinear dynamics in (1)–(2) by choosing the gains $k_1 = -5.3 \times 10^5$ and $k_2 = 1 \times 10^{13}$. The axon length, $l(t)$, successfully converges to the desired long-range axon length, $l_s$ in Fig. 3(a). Moreover, Fig. 3(b) demonstrates that the tubulin concentration along the axon also converges to equilibrium.
3.4. Stability proof under state-feedback control

**Nonlinear target system.** While the control design in the previous section is pursued on a linearized reference error system (30)–(33), we prove the local stability for the original nonlinear system (23)–(26) under the designed linear control law, which is linear in $u$ and $q$, but not in $l$. The nonlinear target system is obtained by applying the transformation (35) to the nonlinear system (23)–(26), arriving at

$$
\dot{u}(t) = Du_xu(x,t) - aw(x,t) - g w(x,t)
$$

$$(57)$$

$$\dot{u}(t) = \bar{h}(X(t))$$

$$(58)$$

$$X(t) = (A + BK)X(t) + f(X(t)) + Bu_x(x,t),$$

$$(59)$$

where

$$h^*(X(t)) = z_1(t) + \bar{h}(z_2(t)) - D^THX(t).$$

$$(60)$$

How to ensure local stability on a non-constant spatial interval. The stability property of the nonlinear target system (57)–(60) is equivalent to the closed-loop system consisting of the plant (23)–(26) with the control law (54) when the backstepping transformation (35) is invertible. We study the local stability of the target system by imposing the following two properties

$$0 < l(t) \leq \bar{l},$$

$$|\dot{l}(t)| \leq \bar{v},$$

$$(62)$$

$$(63)$$

for some $\bar{l} > l_0 > 0$ and $\bar{v} > 0$. We will derive the restricted initial state to satisfy these properties for all $t \geq 0$ later.

**Inverse transformation.** Through performing a similar procedure to the derivation of the direct transformation, one can obtain the inverse transformation as

$$u(x,t) = w(x,t) + \int_x^l q_1(x,y)w(y,t)dy + \psi(x - l(t))^\top X(t),$$

$$(64)$$

where the gain kernel functions $q_1(x,y) \in \mathbb{R}$ and $\psi(x - l(t)) \in \mathbb{R}^2$ satisfy

$$q_{xx}(x,y) - q_{yy}(x,y) = \frac{a}{D} \left(q_1(x,y) + q_3(x,y)\right),$$

$$(65)$$

$$q_2(x,y) + q_4(x,y) = 0,$$

$$(66)$$

$$q(x,l(t)) = -\frac{1}{D}\psi(x - l(t))^\top B,$$

$$(67)$$

$$D\psi''(x - l(t))^\top + a\psi'(x - l(t))^\top + (gl + A_1 + BK)^\top \psi(x - l(t))^\top = 0,$$

$$\psi(0) = H, \quad \psi'(0) = K.$$  

$$(68)$$

$$(69)$$

The same solution technique employed in the previous chapter, is equally applicable to (65)–(69). Therefore, we can explicitly obtain the solution for (65)–(69).

**Lyapunov analysis.** Hereafter, the $l_2$ norm is further shortened as $\|w\| := \|w(\cdot, t)\|_{l_2}$. Consider the following Lyapunov functionals

$$V_1 = \frac{1}{2}\|w\|^2, \quad V_2 = \frac{1}{2}\|u_x\|^2, \quad V_3 = X(t)^\top PX(t),$$

$$(70)$$

where $P > 0$ is a positive definite matrix satisfying the Lyapunov equation:

$$(A + BK)^\top P + P(A + BK) = -Q,$$

$$(71)$$

for some positive definite matrix $Q > 0$. We define the total Lyapunov function as

$$\dot{V} = d_1V_1 + V_2 + \frac{d_2}{2}w(0,t)^2 + d_3V_3,$$

$$(72)$$

where $d_1 > 0$ and $d_2 > 0$ are to be determined.

**Lemma 1.** Assume that properties (62)–(63) are satisfied with

$$\bar{v} = \min \left\{ \frac{\bar{g}}{\sqrt{2}}, \frac{\bar{d}}{\sqrt{2}} \right\}.$$  

$$(73)$$

for all $t \geq 0$. Then, for sufficiently large $d_1 > 0$ and small $d_2 > 0$, there exist positive constants $\beta_i > 0$ for $i \in \{1, 2, 3, 4\}$ such the following norm estimate holds for all $t \geq 0$:

$$\dot{V} \leq -\alpha V + \sum_{i=1}^4 \beta_i V_i^{1/2},$$

$$(74)$$

where $\alpha = \min \left\{ \frac{\bar{g}}{\sqrt{2}}, \frac{\bar{d}}{\sqrt{2}}, \frac{\lambda_{\min}(Q)}{2\max(P)}, \frac{d_2(\bar{d} + \bar{g})}{4} \right\}.$$

**Proof.** Taking the time derivative of the Lyapunov functions in (70) along the target system, one can obtain

$$\dot{V}_1 = -D\|w_x\|^2 - g\|w\|^2 - \left(\gamma D - \frac{a}{2}\right)w(0,t)^2$$

$$+ \int_0^{l(t)} F_x(X(t))w_x(x,t)dx + \frac{1}{2}\|l(t)w(l(t), t)^2$$

$$- \int_0^{l(t)} w_x(x,t)(\psi(x - l(t))^\top B + k(x, l(t))) h^*(X)dx$$

$$+ \int_0^{l(t)} w(x,t)\psi(x - l(t))^\top f(X(t))dx,$$

$$(75)$$

$$\dot{V}_2 = -D\|w_x\|^2 + a \int_0^{l(t)} u_x(x,t)w_x(x,t)dx$$

$$- \gamma g w(0,t)^2 - g\|w\|^2 - \gamma w(0,t)w_1(0,t)$$

$$- \int_0^{l(t)} F(l(t), X(t))u_x(l(t), t)$$

$$+ \int_0^{l(t)} F_1(X(t))w_1(x,t)dx$$

$$- \int_0^{l(t)} w_1(x,t)\dot{\psi}(x - l(t))^\top (f(X(t)) + \frac{a}{D}Bh^*(X))dx$$

$$- \int_0^{l(t)} w_1(x,t)\dot{\psi}(x - l(t))^\top Bh^*(X)dx,$$

$$(76)$$

$$\dot{V}_3 = -X(t)^\top QX(t) + \frac{d_2}{\bar{g}}(l(t), t)2B^TPX(t)$$

$$+ \kappa X(t)^\top (P_1 \epsilon_1^\top X(t)\epsilon_1^\top + e_1^\top X(t)\epsilon_1^\top P)X(t)$$

$$+ f_1(X(t))PX(t) + X(t)^\top P_1^x(X(t)).$$

$$(77)$$

Note that we selected $k_2$ such that

$$k_2 \geq \max\{\alpha_2, \frac{\bar{d}}{\bar{g}}\},$$

$$(78)$$

in order to demonstrate Hurwitz matrices of both $A + BK$ and $A_1 + BK$. Then, applying Agmon’s and Poincare’s inequalities, and Young’s inequality to (75)–(77) leads to

$$\dot{V}_2 \leq \frac{D}{2}\|w_x\|^2 - \frac{\gamma g}{2}w(0,t)^2 - (\gamma + \frac{a}{D})\|w_x\|^2$$

$$- \gamma w(0,t)w_1(0,t) + \int_0^{l(t)} \gamma F(0,X(t))w(0,t)$$

$$+ \int_0^{l(t)} F_1(X(t))w_1(x,t)dx + \frac{|l(t)|}{2}F(l(t), X(t))^2$$

+ $\gamma F_1(X(t))w_1(x,t)dx + \|l(t)|/2|F(l(t), X(t))|^2$.
Using the exponential inequality, the next step is to bound the nonlinear terms in \( (90) \) which is then the unit vector. Moreover, the following inequalities are given

\[
\int_0^l (\dot{\phi}(x - l(t))^T B - k(x, l(t))^T) \, dx \leq L_n,
\]

\[
\int_0^l (\phi(x - l(t))^T X - k(x, l(t))^T)^2 \, dx \leq L_n^2,
\]

\[
\int_0^l (\dot{\phi}(x - l(t))^T B - ak(x, l(t))^T)^2 \, dx \leq L_n^3.
\]

By using (87)–(89) and applying Cauchy–Schwarz inequality, and using (75), (79) and (80), recalling \( \gamma = \frac{2}{\lambda_{\min}} \), the time derivative of the total Lyapunov function (72) satisfies the following inequality

\[
\dot{V}_3 \leq -\alpha V + \beta_1 V^{3/2} + 2d_1^2 Dl_n h^*(X)^2 + d_1 \frac{1}{2} |r_x e_1^T X| h^*(X)^2 + 8d_1^2 Dl_n f(X(t)^2 + 8DL_{n2} f(X(t)^2 + 8DL_{n3} h^*(X)^2),
\]

where

\[
k_n = \max(c_\infty K_x \lambda_n^2, c_\infty K_x \lambda_n^2),
\]

\[
k_m = \max(c_\infty K_x \lambda_n^2, c_\infty K_x \lambda_n^2).
\]

Then, for sufficiently small norm of \( X \). Applying (93) and (94) to (90), we have the following inequality

\[
\dot{V} \leq -\alpha V + \beta_1 V^{3/2} + \beta_2 V^2 + \beta_3 V^{5/2} + \beta_4 V^3.
\]

Ensuring bounds on axon length and growth rate. In this subsection, we prove important lemmas to conclude with Theorem 1 ensuring the local stability of the closed-loop system. First, we give the following lemma.

**Lemma 2.** There exists a positive constant \( M_1 > 0 \) such that in the region \( \Omega_1 = \{(w, X) \in \mathcal{H}_1 \times \mathbb{R}^2 | V(t) < M_1 \} \) the conditions (62) and (63) are satisfied.

**Proof.** By using (22) and the plant equation (5), \( X(t) \) can be described as

\[
X(t) = \left[ \frac{\dot{l}(t)}{r_g(t)} \quad l(t) - l_i \right]^T.
\]

For any \( r > 0 \), if \( |X| < r \), the following two inequalities hold:

\[
\left| \frac{\dot{l}(t)}{r_g} \right| < r, \quad |l(t) - l_i| < r.
\]

The first inequality tells that if \( r < \frac{\dot{l}}{r_g} \), then the property of the system, (62), holds. Moreover, the second inequality can be written as \( r - r_i < \dot{l}(t) < \dot{l} + r_i \), and thus if both \( r < \dot{l} \) and \( r < \dot{l} - r_i \), then the condition (63) holds. Therefore, the constant, \( r \), is chosen as

\[
r = \min \left\{ \frac{\dot{l}}{r_g}, r_i, \dot{l} - r_i \right\}.
\]

Since we know \( |X|^2 \leq \frac{1}{\lambda_{\min}(P)} X^T PX \leq \frac{d_1}{\lambda_{\min}(P)} V \), we derive the setting \( M_1 = \frac{\lambda_{\min}(P)}{d_1} \). If \( V(t) < M_1 \) holds then \( |X| < r \) and thus the properties of the system, (62) and (63), are satisfied, by which we can conclude Lemma 2.

**Lemma 3.** There exists a positive constant \( M > 0 \) such that if \( V(0) < M \) then the conditions (62) and (63) are satisfied and the following norm estimate holds:

\[
V(t) \leq V(0) e^{\left( -\frac{\alpha}{2} t \right)}.
\]

**Proof.** For a positive constant \( M > 0 \), let \( \Omega := \{(w, X) \in \mathcal{H}_1 \times \mathbb{R}^2 | V(t) < M \} \). By Lemma 2, it is easily shown that if \( M \leq M_1 \) then \( \Omega \subset \Omega_1 \), and thus the conditions (62) and (63) are satisfied in the region \( \Omega \). Thus, by Lemma 1, the norm estimate (74) holds. Moreover, we set \( M \leq p^* \) where \( p^* \) is the root of the following polynomial with respect to \( V \) (except \( p^* = 0 \))

\[
-\frac{\alpha}{2} V + \beta_1 V^{3/2} + \beta_2 V^2 + \beta_3 V^{5/2} + \beta_4 V^3 \leq 0.
\]
Since $\alpha > 0$, $\beta_i > 0$ for $i = \{1, 2, 3, 4\}$ exist, the root of the polynomial always exists. Now, we can see that applying $V(t) \leq M$ to (74) leads to

$$\dot{V} \leq -\frac{\alpha}{2} V,$$

by which the norm estimate (104) is deduced. Since (104) is a monotonically decreasing function in time, by setting $M = min(M_1, p^*)$, the region $\Omega$ is shown to be an invariant set. Thus, if $V(0) < M$, then $V(t) < M$ for all $t \geq 0$, and one can conclude with Lemma 3.

Due to Lemma 3, and the equivalent norm estimate in the $H_1$-norm between the target system and the closed-loop system, one can obtain the local stability of the closed-loop system, which completes the proof of Theorem 1.

4. State estimation

4.1. Observer design and convergence

In the state feedback control law designed in the previous section, measurements of both the distributed tubulin concentration $c(x, t)$ along the domain and axon length $l(t)$ are required for the computation of the controller. The requirement of measuring the entire spatial concentration profile limits the practical applicability of the controller. To resolve the issue, we develop a nonlinear observer to reconstruct the entire concentration profile from the boundary measurements. The measured states are axon length $l(t)$ and the tubulin flux at the cone, $c_0(l(t), t)$.

Observer. We introduce the observer

$$\dot{\hat{c}}(x, t) = D\hat{c}_x(x, t) - a\hat{c}(x, t) - g\hat{c}(x, t)$$

$$+ p_1(x, l(t)) \left( c_0(l(t), t) - \hat{c}(l(t), t) \right),$$

$$\hat{c}_0(0, t) = U(t),$$

$$\hat{c}(l(t), t) = \hat{c}(c),$$

$$l\dot{\hat{c}}_x(t) = (a - gl_x)\hat{c}_x(t) - (r_x\hat{c}_x(t) + r_g\hat{c}_x(t) - c_\infty)$$

$$\quad - DC_0(l(t), t) + l_1(l(t) - \hat{l}(t)),$$

$$\dot{\hat{l}}(t) = r_g(\hat{c}_x(t) - c_\infty) + l_2(l(t) - \hat{l}(t)),$$

with the measurements

$$y_1(t) = c_0(l(t), t), \quad y_2(t) = C \begin{bmatrix} c_0(t) & \hat{l}(t) \end{bmatrix},$$

where $C = \begin{bmatrix} 0 & 1 \end{bmatrix}$, and, in the next theorem, state the convergence of the complete system shown in Fig. 4.

**Inverse backstepping transformation.** We return to proving Theorem 2 and define the observer error states as

$$\hat{c}(x, t) = c(x, t) - \hat{c}(x, t),$$

$$\hat{c}_0(t) = c_0(t) - \hat{c}(l(t), t),$$

Thus, we have

$$\hat{c}(x, t) = D\hat{c}_x(x, t) - a\hat{c}(x, t) - g\hat{c}(x, t)$$

$$- p_1(x, l(t)) \left( c_0(l(t), t) - \hat{c}(l(t), t) \right),$$

$$\hat{c}_0(0, t) = 0,$$

$$\hat{c}(l(t), t) = [1 0]\hat{X}(t),$$

$$\dot{\hat{X}}(t) = (\hat{A} - LC)\hat{X}(t) + \kappa\hat{e}_1\hat{X}(t)\hat{X}(t)^{\top}e_1$$

$$\quad - 2\kappa c_0(t)e_1\hat{X}(t),$$

where $\hat{X} = [\hat{c}_0(t) \hat{c}(l(t))]^\top$ and

$$\hat{A} = \begin{bmatrix} \hat{a}_1 & 0 \\ r_g & 0 \end{bmatrix}.$$

We consider the inverse backstepping transformation

$$\hat{c}(x, t) = \hat{w}(x, t) + \int_{0}^{l(t)} P(x, y)\hat{w}(y, t)dy,$$

where $P(x, y) \in \mathbb{R}$ is the gain kernel to be solved on the time-varying domain $\Omega(t) = [(x, y)|0 \leq y \leq x \leq l(t)]$. Let the target system be

$$\dot{\hat{w}}_x(x, t) = D\hat{w}_x(x, t) - a\hat{w}_x(x, t) - (g + \lambda)\hat{w}(x, t)$$

$$+ \hat{l}(t) \left( Q(x, l(t)) - P(x, l(t)) \right) \hat{w}(l(t), t),$$

$$\hat{w}(0, t) = \gamma_2\hat{w}(0, t),$$

$$\hat{w}(l(t), t) = [1 0]\hat{X}(t),$$

$$\dot{\hat{X}}(t) = (A - LC)\hat{X}(t) - f(\hat{X}(t)) - c_1(t)A_2\hat{X}(t),$$

where $Q(x, y) \in \mathbb{R}$ is also the gain kernel obtained from direct backstepping transformation and

$$A_2 = \begin{bmatrix} 2\frac{r_g}{\hat{a}_1} & 0 \\ 0 & 0 \end{bmatrix}.$$

Let the ODE observer gain $L$ be described as $L = \begin{bmatrix} l_1 & l_2 \end{bmatrix}^\top$, so one can show the conditions for the gains as

$$l_1 > \frac{\hat{a}_1l_2}{r_g}, \quad l_2 > \hat{a}_1.$$
which makes $A - LC$ Hurwitz. Taking the time and spatial derivatives of (121) together with the solution of (122)–(124) and the stability of $\tilde{X}(t)$, we obtain (134)–(136), and by choosing $P(x, y) = \tilde{P}(x, y)e^{\frac{\lambda}{2D}x+y}$, (134)–(136) become

$$\begin{align*}
\tilde{p}_y(x, y) - \tilde{p}_x(x, y) &= \frac{\lambda}{2D} \tilde{P}(x, y), \\
\tilde{P}(x, x) &= e^{\frac{\lambda}{2D}x + \gamma_1}, \\
\tilde{P}(0, y) &= -\frac{a}{2D} \tilde{P}(0, y),
\end{align*}
$$

which does not have an analytical solution. To guarantee the well-posedness of the solution, we need prove that $P(x, y)$ is bounded, so we apply the method of successive approximation to obtain a numerical solution, and to prove the boundedness of the solution. By using the method of successive approximation described in the Appendix, we obtain

$$|P(x, y)| \leq \gamma e^{2\gamma x},$$

which guarantees the boundedness of the solution to the gain kernel PDE in (134)–(136).

Observer convergence is stated next.

**Theorem 2.** Let the system properties (62) and (63) hold. Let $c_l(t)$ be bounded as

$$\zeta \leq c_l(t) \leq \bar{c},$$

where $\zeta > \zeta > 0$. Consider the plant (30)–(33) and the observer (107)–(111) with available measurements (112), let $L = [l_1 \ l_2]$ be chosen as

$$l_1 > \frac{\bar{a}_2}{\bar{r}_g}, \quad l_2 \geq \tilde{a} + \frac{2\bar{r}_g \bar{c}}{\bar{k}} + 4\bar{r}_g + \frac{1}{2},$$

and let the observer gain be $p_l(x, l(t)) = DP_l(x, l(t))$ where $P_l(x, l(t))$ is the solution to the following PDE

$$DP_l(x, y) = D a_l(x, y) + a_p(x, y) - a P_l(x, y) = \lambda P_l(x, y),$$

$$P_l(x, x) = \frac{\lambda}{2D}x + \gamma_1,$$

$$P_l(0, y) = 0,$$

where $\lambda > 0$ is an arbitrary constant, and $\gamma_1$ is a constant satisfying $\frac{\lambda}{2} \leq \gamma_1$. Then, the observer error system is locally exponentially stable in the $H_1$-norm, i.e., there exist $M, c_1 > 0$ and $\kappa > 0$ such that if $\tilde{\Phi}(0) < M$ then the following norm estimate holds:

$$\tilde{\Phi}(t) \leq c_2 \tilde{\Phi}(0)e^{-\kappa t},$$

where $\tilde{\Phi}(t) := \|c - \tilde{c}\|_{H_1(0,t)} + |X - \tilde{X}|$.

**Theorem 2** is proved immediately after the simulations in the next subsection.

4.2. Simulation: Estimation of unmeasured tubulin concentration profile in a 4x growth

We perform the simulation of the state estimation of the tubulin concentration by incorporating the biological parameters in Table 1. The observer gains for the decay rates of ODE states are set as $l_1 = 1$ and $l_2 = 12$. The parameter $\lambda$ for the decay rate of the PDE state is chosen as $0.05$ to obtain sufficiently fast convergence without causing a huge overshoot. In addition, the initial conditions for the observer are chosen $\tilde{c}(x, 0) = 0$. In Figs. 5(a) and 5(b), the open-loop control, $U(t) = b_1 \sin(\omega t) + b_2$, where $b_1 = 200$, $b_2 = -10$, and $\omega = 1.256$ rad/s, is applied to the plant and the estimator. Figs. 5(a) and 5(b) show that the observer governed by (107)–(111) converges to the unmeasured tubulin concentration generated by (1)–(5), within $t = 1$ min when the open-loop controller defined above is applied. In addition, the necessity of observer gain, $p_l(x, l(t))$, is demonstrated in Fig. 6. In this figure, when the axon grows for a long distance, the observer gain, $p_l(x, l(t))$, increases because more time is needed to see the effect of the soma on the growth cone, which explains why observer gain becomes higher and higher when the axon expands.

4.3. Stability analysis of observer error system

We use the following direct backstepping transformation

$$\hat{w}(x, t) = \tilde{c}(x, t) - \int_x^{t(x)} Q(x, y) \tilde{w}(y, t) dy.$$ 

By applying (138) to the observer error system (116)–(119) and the target system (122)–(124), the conditions for the kernel function are obtained as

$$DQ_l(x, y) = aQ_l(x, y) - DQ_l(x, y) - aQ_l(x, y) = \lambda Q(x, y),$$

$$Q(x, x) = \frac{\lambda}{2D}x + \gamma_1,$$

$$Q_l(0, y) = \gamma_1 Q_l(0, y).$$

We follow the same logic that we used for obtaining the solution of inverse backstepping transformation. First, we apply the following transformation $Q(x, y) = 2e^{\frac{\lambda}{2D}x+y}Q(x, y)$ to (139)–(141). Thus, the transformed kernel PDE is well-posed, so the solution of $Q(x, y)$ exists, which means direct transformation exists. Similar to the inverse transformation, the closed-form
solution of the direct kernel equation cannot be obtained. By applying the procedure in the Appendix, we have the bound as $|Q(x, y)| \leq T^e 2^X$.

We consider next the following Lyapunov function for the observer error target system
\[
\tilde{V} = \tilde{V}_{11} + \tilde{V}_{12} + d_2 \tilde{V}_2 + \frac{\gamma_1}{2} \tilde{w}(0, t)^2.
\]
where
\[
\tilde{V}_{11} = \frac{1}{2} d_1 \| \tilde{w} \|^2, \quad \tilde{V}_{12} = \frac{1}{2} \| \tilde{u}_x \|^2, \quad \tilde{V}_2 = d_2 \tilde{x}(t)^T P_1 \tilde{x}(t),
\]
and
\[
P_1 = \begin{bmatrix}
\tilde{a}(1 + \frac{2\bar{a}}{c}) + \frac{1}{2\bar{a}} & \frac{1}{2} \\
\frac{1}{2} & \tilde{a} + \frac{1}{2\bar{a}}
\end{bmatrix},
\]
where $\tilde{a} > 0$, and makes $P_1$ a positive definite matrix. In addition, we can denote that
\[
F(x, \tilde{x}(t)) = \left( P(x, \tilde{x}(t) + l_1) - Q(x, \tilde{x}(t) + l_1) \right) H^T \tilde{x}(t).
\]
Then, we state the following lemma.

**Lemma 4.** Assume that the system properties (62) and (63) are satisfied for $\tilde{v} = \frac{\bar{a}}{c}$, for all time $t \geq 0$. Then, we conclude that for sufficiently large gain parameter $\lambda > 0$, $d_1 > 0$, $d_2 > 0$, and $\tilde{a} > 0$, there exist a positive constant $\alpha_1 = \min \{ d_1^2, d_1 (D + 2\lambda), (g + 2\lambda), \frac{\tilde{a}}{2 \lambda} \}$ and $\beta_1 = d_2 \lambda \max(P_1)^2$ which satisfy the following norm estimate holds for all $t \geq 0$
\[
\dot{\tilde{V}} \leq -\alpha_1 \tilde{V} + \beta_1 \tilde{V}^{3/2}.
\]

**Proof.** Taking the time derivative of the Lyapunov functions along the target system (122)-(125), we have
\[
\dot{\tilde{V}}_{11} = d_1 D \tilde{w}(l(t), t) \tilde{w}(l(t), t) - d_1 \left( \frac{D \gamma_1}{2} \right) \tilde{w}(0, t)^2
\]
\[
- d_1 \tilde{l}(t) \int_0^{\tilde{t}(t)} \tilde{w}(x, t) F(x, \tilde{x}(t)) dx - \frac{d_1}{2} \tilde{w}(l(t), t)^2,
\]
\[
\dot{\tilde{V}}_{12} = H^T (A - L C) \tilde{x}(t) \tilde{w}(l(t), t) - d_1 \tilde{w}(l(t), t)^2,
\]
\[
\dot{\tilde{V}}_2 = H^T (A - L C) \tilde{x}(t) \tilde{w}(l(t), t) - \frac{1}{2} \tilde{l}(t) \tilde{w}(l(t), t)^2,
\]
where $\tilde{V}_1 \leq -d_1 \left( \frac{D \gamma_1}{2} \right) \tilde{w}(0, t)^2 - d_1 D \| \tilde{w}_x \|^2 - d_1 (g + \lambda) \| \tilde{w} \|^2
\]
\[
- \tilde{l}(t) \int_0^{\tilde{t}(t)} \tilde{w}_x(x, t) F(x, \tilde{x}(t)) dx,
\]
\[
\dot{\tilde{V}}_2 = d_2 \tilde{x}^T (A - L C)^T P_1 \tilde{x} + d_2 \tilde{x}^T \tilde{P}_1 \tilde{x} + d_2 f(\tilde{x}) P_1 \tilde{x} + \tilde{x}^T \tilde{P}_1 \tilde{x},
\]
where $d_1 > 0$ and $d_2 > 0$. Applying Young’s inequality, and by using (124)-(125) to the time derivative of $V_{11}$ in (148) leads to
\[
\dot{\tilde{V}}_{11} \leq -d_1 \left( \frac{D \gamma_1}{2} \right) \tilde{w}(0, t)^2 - d_1 D \| \tilde{w}_x \|^2 - d_1 (g + \lambda) \| \tilde{w} \|^2 + \frac{D \epsilon_1}{2} \tilde{w}_x(l(t), t)^2 - d_1 \tilde{l}(t) \int_0^{\tilde{t}(t)} \tilde{w}(x, t) F(x, \tilde{x}(t)) dx,
\]
\[
+ \left( \frac{d_1^2 D}{2e_4} + d_2 \epsilon_2 + \frac{d_2 (g + \lambda)}{2e_2} \right) \tilde{w}(l(t), t)^2,
\]
where $\epsilon_1 > 0$ is an arbitrarily small constant. Similarly, using Agmon’s inequalities and Young’s inequality into the time derivative of $V_{12}$ in (149) gives us
\[
\dot{\tilde{V}}_{12} \leq \gamma_1^2 \left( \frac{D \epsilon_1 + \epsilon_2 + \epsilon_3 (g + \lambda) + \tilde{v} + \tilde{v}_e}{2} \right) \tilde{w}(0, t)^2
\]
\[
- \left( \gamma_1 (g + \lambda) \right) \tilde{w}(0, t)^2 - \left( D - \frac{D}{4} \right) \| \tilde{w}_x \|^2 + \left( \frac{D}{2e_1} + d_1 \frac{a}{2} + \frac{\tilde{v}}{2e_1} \right) \tilde{w}(l(t), t)^2
\]
\[
+ \left( \frac{D}{2e_1} + d_1 \frac{a}{2} + \frac{\tilde{v}}{2e_1} \right) \tilde{w}(l(t), t)^2 + \frac{\| \tilde{l}(t) \|}{2e_4} \gamma_1 F(0, \tilde{x}(t))^2 + \frac{\| \tilde{l}(t) \|}{2e_5} \gamma_1 F(0, \tilde{x}(t))^2
\]
\[
+ \left( \frac{\| \tilde{l}(t) \|}{2e_1} \right) \int_0^{\tilde{t}(t)} \tilde{w}_x(x, t) F_i(x, \tilde{x}(t)) dx,
\]
where $\tilde{e}_1 > 0$ for $i = 1, \ldots, 5$ are arbitrarily small constants. By applying Young’s inequality, using Lyapunov equation, (93) and (94), the time derivative of $V_{12}$ in (150) is obtained as
\[
\dot{\tilde{V}}_2 \leq -d_2 \tilde{x}^T \tilde{c}_i(t) \tilde{c}_i(t) - d_2 \tilde{a} \tilde{x}_i(t)^2 + \frac{d_2 \lambda \max(P_1)}{2} \left( \tilde{x}^T \tilde{x} \right)^{3/2},
\]
by picking
\[
l_2 \geq \max \left\{ \frac{2\tilde{\alpha}}{\tilde{x}_c} + \frac{\tilde{a}^2 + 2r_5}{2\tilde{e}_c} \right. + \frac{2\tilde{r}_c}{\tilde{l}_c} + \frac{\tilde{a}^2 + 2r_5}{2\tilde{e}_c} \left. \right\},
\]
\[
\tilde{a} \leq \frac{3\tilde{r}_c l_2}{3\tilde{r}_c l_2 + 2\tilde{a} l_2}.
\]
Note that there exists $l_2$ and $\tilde{a}$ for any physical values of $\xi$ and $\tilde{e}$. Now, we can derive the observer gain $l_2$ as
\[
l_2 \geq \max \left\{ \frac{2\tilde{\alpha}}{\tilde{x}_c} + \frac{\tilde{a}^2 + 2r_5}{2\tilde{e}_c} \right. + \frac{2\tilde{r}_c}{\tilde{l}_c} + \frac{\tilde{a}^2 + 2r_5}{2\tilde{e}_c} \left. \right\}
\]
In addition, one can show that
\[
\tilde{\alpha} = \min \left\{ \frac{\tilde{r}_c \tilde{a}}{l_2}, 2\tilde{a} l_2 \right\}.
\]
which leads to
\[
\dot{V}_f \leq -d_2 \| \hat{x}^\top X \hat{x} + d_2 \kappa \lambda_{\text{max}}(P_1) \| \hat{x}^\top X \|^{3/2}.
\] (158)

Then, we use Young’s and Cauchy–Schwarz inequalities for $F$ terms. There exist positive constants $L_i > 0$, for $i = 1, 2, 3, 4$, which yield similar bounds as those in (82)–(85) for $F(\cdots)$ terms. With these inequalities and (151)–(153), the time derivative of (142) becomes
\[
\dot{V} \leq \frac{D}{2} \| \hat{w}_x \|^2 - \left( d_1 (g + \lambda) - \frac{\| \hat{e}_h \|}{2} \right) \| \hat{e}_w \|^2
\]
\[
- d_1 \frac{D_2}{2} \hat{w}_w (0, t)^2 - \left( d_1 D + (g + \lambda) - \frac{\| \hat{e}_\ell \|}{2} \right) \| \hat{w}_x \|^2
\]
\[
+ \frac{d_1 e_\ell}{2 \epsilon_1} + \frac{\| \hat{e}_\ell \|}{2 \epsilon_1} + \frac{d_1 \| \hat{e}_\sigma \|}{2 \epsilon_1} - \frac{d_1 \| \hat{e}_\kappa \|}{2 \epsilon_1} \| \hat{x}(t) \|^2
\]
\[
+ \frac{d_2 \kappa \lambda_{\text{max}}(P_1) \| X^\top X \|^{3/2}}{2 \epsilon_1} + \frac{\| \hat{e}_\lambda \|}{2 \epsilon_1} \| \hat{x}(t) \|^2.
\] (159)

By the positive definiteness of $P_1$, it holds that
\[
\lambda_{\text{min}}(P_1) \| X \| \leq \| \hat{X} \| \leq \lambda_{\text{max}}(P_1) \| \hat{X} \|,
\] (160)
where $\lambda_{\text{max}}(P_1) > 0$ and $\lambda_{\text{max}}(P_1) > 0$ are the smallest and the largest eigenvalues of $P_1$. Finally, by recalling $\gamma_1 \leq \frac{5}{2}$, and choosing constants $d_1$ and $d_2$ as
\[
d_1 \geq \frac{2a_1 + D \| \hat{e}_h \|}{D^2},
\] (161)
\[
d_2 \geq \frac{2 a_1}{a} \left( \frac{D}{2 \epsilon_1} + \frac{D_2}{2 \epsilon_1} + \frac{\| \hat{e}_\ell \|}{2 \epsilon_1} + \frac{\| \hat{e}_\sigma \|}{2 \epsilon_1} + \frac{d_1}{2 \epsilon_1} \left( \frac{1}{2 \epsilon_1} + \frac{L_2}{2 \epsilon_1} + \frac{\| \hat{e}_\kappa \|}{2 \epsilon_1} \right) \right).
\] (162)
one can show that (159) leads to
\[
\dot{V} \leq -d_1 \frac{D_2}{2} \hat{w}_w (0, t)^2 - d_1 (D + 2 \lambda) \hat{V}_{12} - (g + 2 \lambda) \hat{V}_{11}
\]
\[
- \frac{a_1}{2 \lambda_{\text{max}}(P_1)} \hat{V}_2 + d_2 \kappa \lambda_{\text{max}}(P_1) \hat{V}_2^{3/2}
\]
\[
\leq - \alpha_1 \hat{V} + \hat{p}_1 \hat{V}^{3/2}.
\] (163)
Thus, Lemma 4 holds. □

By using the same approach in Lemma 2, we set $\hat{M} = \min \left\{ \hat{M}_1, \hat{m}_1 \right\}$ where $\hat{M}_1 = \frac{\lambda_{\text{min}}(P_1)}{d_2}$ and $r$ is defined in (103). In addition, the inequality (163) ensures that $\hat{V}(t) < \hat{m}_1$ if $\hat{V}(0) < \hat{M}$ where $\hat{m}_1 = \frac{\alpha_1}{4 \hat{p}_1}$. Thus, it leads to
\[
\dot{\hat{V}} \leq - \alpha_1 \hat{V}.
\] (164)
Thus, if $\hat{V}(0) < \hat{M}$, then $\hat{V}(t) < \hat{M}$ for all $t \geq 0$. This allows us to conclude that the target $\hat{w}$-system (122)–(125) is locally exponentially stable in $\mathcal{H}_1$-norm, following a similar strategy utilized in state-feedback stability analysis.

Owing to backstepping transformation invertibility, the stability of $\hat{w}$-system renders the original $\hat{c}$-system (116)–(119) locally exponentially stable. This completes the proof of Theorem 2.

The estimation error flux in the cone is dominated by the length of the axon. It is bounded by $\mathcal{H}_1$-norm over the lengthy calculations of estimation error over the length of the axon and tubulin flux in the cone. Due to physically limited intuition, the axon does not grow rapidly. This underscores the importance of considering both axon length and tubulin flux within the cone to ensure the convergence of the estimator.

5. Observer-based control

5.1. Output-feedback design and stability

In this section, an output feedback control law is constructed using the estimated tubulin concentration by the proposed observer in Section 4 using the measurements (112). Let reference error state for the observer be
\[
\hat{u}(x, t) = \hat{c}(x, t) - c_{eq}(x).
\] (165)
By using (107)–(111), (11)–(13) and (165), we obtain the following nonlinear observer for the reference error system
\[
\hat{u}(x, t) = D\hat{u}_w(x, t) - a\hat{u}(x, t) - g\hat{u}(x, t)
\]
\[
+ \hat{p}_1(x, l(t))(u_u(l(t), t) - \hat{u}_u(l(t), t)),
\] (166)
\[
\hat{u}_u(x, t) = U(t),
\] (167)
\[
\hat{u}_u(l(t), t) = c_l\hat{x}(t) + h(z_l(t)).
\] (168)
\[
\hat{X}(t) = A\hat{X}(t) + B\hat{u}_u(l(t), t) + LC(X(t) - \hat{x}(t)) + f(\hat{x}(t)).
\] (169)

**Theorem 3.** Consider the closed-loop system (14)–(18) with the measurements (112), and the observer (166)–(169) under the output feedback control law:
\[
U(t) = \frac{D_2}{D} \hat{y}_w (0, t) + \hat{y}(l(t))\| y(t) \| - \gamma_2 \hat{y}(l(t))\| \hat{y}(t) \| \hat{x}(t)
\]
\[
- \frac{1}{D} \int_0^{l(t)} (\hat{y}(l(t))\| y(t) \| - \gamma_2 \hat{y}(l(t))\| \hat{y}(t) \|) B\hat{u}_u(l(t), t) dy,
\] (170)
where $\gamma_2 \geq \frac{a_1}{a}$ and $\| \hat{x}(t) \|$ is defined in (52). Then, there exist $\hat{M} > 0$, $\kappa > 0$ and $\zeta > 0$ such that if $\Gamma(0) < \hat{M}$ then the following norm estimate holds:
\[
\Gamma(t) \leq \zeta \Gamma(0) \exp(-\kappa t).
\] (171)
where $\Gamma(t) := \| \hat{u} \|_{\mathcal{H}_1((0, \infty))} + \| \hat{X} \|_{\mathcal{H}_1((0, \infty))} + \| \hat{X} \|_{\mathcal{H}_1((0, \infty))}^2$. Namely, the closed-loop system is locally stable in the sense of $\mathcal{H}_1$-norm.

This theorem is proven immediately after the next subsection with simulations of output feedback.

5.2. Simulation: Output-feedback control of axon growth

Under the closed-loop plant dynamics (1)–(5) with the output-feedback controller in (170) and the observer in (107)–(111), the axon length converges to the desired length, one order of magnitude higher than initial axon length, around by about $t = 3$ min as shown in Fig. 7(a). Also, Fig. 7(b) illustrates that the estimated tubulin concentration $\hat{c}(x, t)$ converges to the unmeasured actual tubulin concentration, $c(x, t)$. After the convergence, both estimated and true tubulin concentrations converge to the steady-state solution, $c_{eq}(x)$, which shows the effectiveness of our proposed output feedback control law.

5.3. Stability analysis

We return to proving Theorem 3. The following transformation from $(\hat{u}, \hat{X})$ into $(\hat{w}, \hat{X})$ is implemented by using (35) and (64). Taking the time and spatial derivatives of these transformations,
The axon length \( l(t) \) of the plant (1)-(5) converges to the desired length \( l_d \) by \( t = 3 \text{min} \).

(b) The estimated tubulin concentration, \( \hat{\gamma}(x, t) = \hat{u}(x, t) + c_{eq}(x) \), generated by the observer in (107)-(111), converges to the true tubulin concentration, \( \gamma(x, t) \), generated by nonlinear plant dynamics (1)-(5), and both converge to the steady-state solution, \( c_{eq}(x) \) by \( t = 2.5 \text{min} \). Note that the convergence of the estimator to the plant is achieved faster than the convergence of the plant to the desired equilibrium.

Fig. 7. Close-loop response of the plant and observer.

the target \( \hat{\gamma} \)-system is obtained as
\[
\hat{\gamma}(x, t) = \hat{u}(x, t) + c_{eq}(x)
\]
by evaluating the spatial derivative of (35) at \( x = 0 \), we derive the control law as in (170). Define the Lyapunov function for the closed-loop system as
\[
V_{tot}(t) = c_1 \hat{V}(t) + \frac{1}{2} \hat{\gamma}(x, t)^2 + \frac{1}{2} \hat{\gamma}(x, t)^2 + \frac{1}{2} \gamma(0, t)^2
\]
where \( c_1 > 0 \) is chosen to be sufficiently large, \( \hat{V}(t) \) is defined in (142)-(144). Then, the total Lyapunov function for the closed-loop output feedback system is also written as
\[
V_{tot}(t) = c_1 \left( d_1 \| \hat{\gamma}(x, t) \|^2 + \| \hat{\gamma}(x, t) \|^2 + \hat{\gamma}(0, t)^2 \right)
\]
we state the following lemma.

**Lemma 5.** Properties (62) and (63) hold with,
\[
\tilde{V} \leq \min \left\{ \frac{g}{\gamma^2}, \frac{D_1}{g \gamma^2} \right\}
\]
for all time \( t \geq 0 \). Then, for sufficiently large enough \( d_3 > 0 \) and small enough \( d_4 > 0 \), there exist positive constants \( \alpha > 0 \) and \( \beta > 0 \) such that the following norm estimate holds
\[
V_{tot} \leq -\alpha V_{tot} + \tilde{\beta}_1 V_{tot}^{3/2} + \tilde{\beta}_2 V_{tot}^2 + \tilde{\beta}_3 V_{tot}^{5/2} + \tilde{\beta}_4 V_{tot}^3.
\]
**Proof.** By applying Young’s, Cauchy–Schwarz, Poincare’s, and Agmon’s inequalities, with the help of the assumed condition (62) and (63), we obtain
\[
V_{tot} \leq -\alpha V_{tot} + \tilde{\beta}_1 V_{tot}^{3/2} + \tilde{\beta}_2 V_{tot}^2 + \tilde{\beta}_3 V_{tot}^{5/2} + \tilde{\beta}_4 V_{tot}^3,
\]
for
\[
\alpha = \min \left\{ \frac{1}{2} \alpha_1, \frac{d_1}{2} \frac{D_1}{g \gamma^2} \right\},
\]
\[
\tilde{\beta}_1 = \tilde{\beta} + \frac{r_s}{\lambda_{min}(P)} \left( \frac{L_{15} + L_{20} + L_{21} + L_{22}}{2} \right) \left( \frac{L_{15} + L_{20} + L_{21} + L_{22}}{2} \right) + \frac{2k_2}{\lambda_{max}(P)}
\]
\[
\tilde{\beta}_2 = \frac{8d_2^2 D L_{14} k_{21}^2}{2k_2 + \lambda_{min}(P)},
\]
\[
\tilde{\beta}_3 = \frac{d_4 r_s}{2k_2 + \lambda_{min}(P)},
\]
where \( L_i \) for \( i = 5, 6, 7, 8 \) are bounds of the nonlinear terms as in (82)-(85) such that Lemma 5 holds. □

To prove local stability, we need to show Lemma 2 to ensure convergence at all times. It satisfies that \( V_{tot}(t) < M_1 \) holds for some \( M > 0 \), then \( |X| < r \) where \( r \) is defined in (103). If \( V_{tot}(0) < M_1 \), then \( V_{tot}(t) < M_1 \) for all \( t > 0 \). In addition, \( \hat{t}(t) \) can be written as \( \hat{t}(t) = t e_{c1}^{-1} X(t) \), so we can bound \( \hat{t}(t) \) to handle in the norm equivalence as
\[
|\hat{t}(t)| \leq t e_{c1}^{-1} \left( \frac{\sqrt{V_2}}{\lambda_{min}(P)} + \sqrt{\frac{V_2}{\lambda_{max}(P)}} \right).
\]
The inequality above leads to \( |\hat{t}(t)|^2 \leq g^2 V_{tot}(t) \). Thus, it holds that
\[
V_{tot}(t) \leq V_{tot}(0) \exp \left( -\frac{\alpha}{2} \right).
\]
The norm equivalence between the target and original systems is shown using the direct and inverse transformations of both observer target and observer error target systems. First, let
\[
\Psi = \| \hat{\gamma}(x, t) \|^2 + |\hat{t}(t)|^2 + \| \gamma \|^2 + \| \gamma \|^2 + \| X \|^2.
\]
Using Agmon’s inequalities for \( \hat{w}(0, t) \) and \( \hat{w}(0, t) \) terms in \( V_{\text{tot}}(t) \), one can obtain positive constants \( M > 0 \) and \( M < 0 \) such that
\[
M \psi(t) \leq V_{\text{tot}}(t) \leq M \psi(t) \tag{189}
\]
holds. Therefore, applying (189) to (187), we get
\[
\psi(t) \leq \frac{M}{M} \exp \left( -\frac{\alpha t}{2} \right) \psi(0). \tag{190}
\]
Now, we apply the norm equivalence argument to the transformations between the target systems, (122)–(125) and (172)–(175) and observer error (116)–(119) and the reference error systems (166)–(169). Let \( \psi(t) \) be defined as
\[
\psi(t) = \| \hat{w}(0, t) \|^2 + |\hat{X}|^2 + \| \hat{v}(0, t) \|^2 + |\hat{X}|^2. \tag{191}
\]
Taking square of the transformations (121), (138), (35), and (64), and using Young’s and Cauchy–Schwarz inequalities, one can see that there exist positive constants \( N > 0, \) and \( N < 0 \) such that
\[
N \phi(t) \leq \psi(t) \leq N \phi(t) \tag{192}
\]
holds. Applying (192) to (190), we get
\[
\phi(t) \leq \frac{N}{N} \exp \left( -\frac{\alpha t}{2} \right) \phi(0). \tag{193}
\]
In the last step, we can apply norm equivalence argument between \( \phi(X, X) \)-system and \( \phi(u, X) \)-system. Let \( \Gamma(t) \) defined as
\[
\Gamma(t) = \| w \|_{H^1(0, t)}^2 + |X|^2 + \| \hat{u} \|_{H^1(0, t)}^2 + |\hat{X}|^2. \tag{194}
\]
Now, by taking square of (11) and (13), one can show that there exist positive constants \( K > 0 \) and \( K > 0 \) such that
\[
K \Gamma(t) \leq \Gamma(t) \leq K \Gamma(t) \tag{195}
\]
holds. Applying (195) to (193), we get
\[
\Gamma(t) \leq \frac{K}{K} \exp \left( -\frac{\alpha t}{2} \right) \Gamma(0). \tag{196}
\]
Namely, since the backstepping transformation for the target error system and for the observer system are invertible, the local stability of \( (\hat{w}, X, \hat{w}, X) \) guarantees the local stability of \( (u, X, \hat{u}, X) \), which completes the proof of Theorem 3.

6. Simulation: Robustness to large uncertainty in diffusion, advection, and reaction

In this section, we illustrate the robustness of the proposed output-feedback control under parameter uncertainty. Fig. 8 shows the simulation result under a mismatch between the parameters of the plant and those of the estimator. The plant parameters, \( D, a, \) and \( g \), are set to have \( +40\% \) errors in the upper figure, and to have \( -20\% \) errors in the lower figure. Both plots show that the performance of the proposed observer-based output feedback controller is robust to the parameter mismatch. Fig. 8(a) illustrates that the actual axon length converges successfully to the desired axon length. In addition, the convergence of the tubulin concentration is observed in Fig. 8(b) under the same parameter mismatch. In this figure, the estimated tubulin concentration converges to the actual tubulin concentration and both converge to the steady-state tubulin concentration. Note that the convergence of the estimated tubulin concentration to the actual tubulin concentration is achieved before either one converges to the steady-state concentration. The simulation study demonstrates a robust performance of the proposed output-feedback controller under parameter mismatches.

7. Conclusions

This paper proposes a novel state feedback controller, a state estimator, and an output-feedback controller for the coupled nonlinear PDE–ODE dynamics with a moving boundary modeling neuron growth. The backstepping technique is employed to design the controller and observer gains. The control law performs regulation of the axon length to a set point value, as well as local stabilization of tubulin to the corresponding equilibrium profile. A nonlinear observer estimates the tubulin from axon length and growth cone flux measurements. An output-feedback controller achieves the desired axon length, with a local stability guarantee. Finally, we verify the effectiveness of our proposed methods in simulation using the biological parameters in terms of performance in convergence speed, smoothness, and robustness.

In future research, we will consider an epoch of neurons instead of one neuron to promote the practical applicability of the controller to handle the neurological process on a macroscopic scale, such as brain modeling (Acharya, Ruf, & Nozari, 2022). Since current methods used to measure axon length and tubulin concentration are not able to take measurement samples for the continuous-time observer, designing a sampled-data observer with measurements obtained at a discrete time is an exciting direction to enhance the feasibility of the proposed method in practice.
Appendix

Method of successive approximation

Lemma 6. If property (62) hold for all time $t$. Then, for an arbitrary constant, $\lambda > 0$ and a constant $\frac{\lambda}{2D} \leq \gamma_1$, the gain kernel PDE,

$$DP_y(x,y) = DP_x(x,y) + aP(x,y) - aP(x,y) = \lambda P(x,y), \quad (A.1)$$

$$P(x,0) = 0, \quad (A.2)$$

has unique $C^2$ solutions which are bounded by

$$|P(x,y)| \leq \frac{\lambda}{2} \left(1 + \frac{i}{D} \left(e^{\frac{\lambda}{D} y} - 1\right)\right) e^{\frac{\lambda}{2D} \frac{y^2}{x^2} + \frac{1}{2} \left(e^{\frac{\lambda}{D} y} - 1\right) x}. \quad (A.4)$$

Proof. We follow the same calculation in Smyshlyaev and Krstic (2004), but we have a time-varying domain length, uniformly in time. If (62) holds for all time, then (A.1)–(A.3) has a unique solution in $C^2$ which is bounded by (A.4). □

References


Cenk Demir received a B.S. degree in Electrical and Electronics Engineering from Pamukkale University (Turkey) in 2013, and an M.S. degree in Electrical and Computer Engineering from the University of Delaware (USA) in 2018. He is currently a Ph.D. student at the Nonlinear and Adaptive Control Laboratory in Mechanical and Aerospace Engineering at the University of California, San Diego. He was an intern at ASML (USA), during the summers of 2022 and 2023. He received a scholarship award from the Republic of Turkey Ministry of Education for his M.S. and Ph.D. degrees. Additionally, he was honored with an Outstanding Teaching Assistant Award in Mechanical and Aerospace Engineering from UC San Diego in 2023.

His doctoral research focuses on distributed parameter systems, event-triggered control, delay compensation, adaptive control and their applications to biological systems and additive manufacturing.

Shumon Koga received the B.S. degree in Applied Physics from Keio University (Japan) in 2014, and the M.S. and Ph.D. degrees in Mechanical and Aerospace Engineering from the University of California, San Diego (USA) in 2016 and 2020, respectively. He is currently a Postdoctoral Researcher at Existential Robotics Laboratory in Electrical and Computer Engineering at the University of California, San Diego. He was an intern at NASA Jet Propulsion Laboratory (USA) and Mitsubishi Electric Research Laboratories (USA), during the fall of 2017 and the summer of 2018, respectively. He received the Robert E. Skelton Systems and Control Dissertation Award from UC San Diego Center for Control Systems and Dynamics in 2020, the O. Hugo Schuck Best Paper Award from American Automatic Control Council in 2019, and the Outstanding Graduate Student Award in Mechanical and Aerospace Engineering from UC San Diego in 2018, respectively.

His doctoral research interests included distributed parameter systems, optimization by extremum seeking, and their applications to additive manufacturing, battery management, thermal management in buildings, transportation systems, and global climate systems. He is currently focused on optimization and machine learning for robotics, in particular, Simultaneous Localization and Mapping (SLAM), path planning, and safety-critical systems.

Miroslav Krstic is Distinguished Professor of Mechanical and Aerospace Engineering, holds the Alspach endowed chair, and is the founding director of the Cymer Center for Control Systems and Dynamics at UC San Diego. He also serves as Senior Associate Vice Chancellor for Research at UCSD. As a graduate student, Krstic won the UC Santa Barbara best dissertation award and student best paper awards at CDC and ACC. Krstic has been elected Fellow of IEEE, IFAC, ASME, SIAM, AAAS, IET (UK), and AIAA (Assoc. Fellow) — and as a foreign member of the Serbian Academy of Sciences and Arts. He has received the Richard E. Bellman Control Heritage Award, Bode Lecture Prize, SIAM Reid Prize, Balakrishnan Award for Mathematics of Systems, ASME Oldenburger Medal, Nyquist Lecture Prize, Paynter Outstanding Investigator Award, Ragazzini Education Award, IFAC Nonlinear Control Systems Award, IFAC Distributed Parameter Systems Award, IFAC Adaptive and Learning Systems Award, Chestnut textbook prize, Control Systems Society Distinguished Member Award, the PECASE, NSF Career, and ONR Young Investigator awards, the Schuck (’96 and ’19) and Axelby paper prizes, and the first UCSD Research Award given to an engineer.

He serves as Editor-in-Chief of Systems & Control Letters and has been serving as Senior Editor in Automatica and IEEE Transactions on Automatic Control, as editor of two Springer book series, and has served as Vice President for Technical Activities of the IEEE Control Systems Society and as chair of the IEEE CSS Fellow Committee. Krstic has coauthored 18 books on adaptive, nonlinear, and stochastic control, extremum seeking, control of PDE systems including turbulent flows, and control of delay systems.